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A Systematic Investigation of Quaternary Ammonium Ions as Asymmetric Phase Transfer Catalysts. Synthesis of Catalyst Libraries and Evaluation of Catalyst Activity

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Abstract

Despite over three decades of research into asymmetric phase transfer catalysis (APTC), a fundamental understanding of the factors that affect the rate and stereoselectivity of this important process are still obscure. This paper describes the initial stages of a long-term program aimed at elucidating the physical organic foundations of APTC employing a chemoinformatic analysis of the alkylation of a protected glycine imine with a libraries of enantiomerically enriched quaternary ammonium ions. The synthesis of the quaternary ammonium ions follows a diversity oriented approach wherein the tandem inter[4+2]/intra[3+2] cycloaddition of nitroalkenes serves as the key transformation. A two part synthetic strategy comprised of: (1) preparation of enantioenriched scaffolds and (2) development of parallel synthesis procedures is described. The strategy allows for the facile introduction of four variable groups in the vicinity of a stereogenic quaternary ammonium ion. The quaternary ammonium ions exhibited a wide range of activity and to a lesser degree enantioselectivity. Catalyst activity and selectivity are rationalized in a qualitative way based on the effective positive potential of the ammonium ion.

Introduction

Phase transfer catalysis (PTC) is an extremely useful method for performing nearly any type of reaction involving an ionic starting material or intermediate. A number of characteristics of PTC reactions make them especially attractive for industrial applications including, ease of scalability, their intrinsic “green nature”, and potential for extension to asymmetric variants (APTC).¹ One of the most useful aspects of APTC is the ability to catalyze a wide variety of reaction types, ranging from redox processes to many carbon-carbon bond forming reactions. However, despite over three decades of research into APTC, a fundamental understanding of the factors that affect catalyst activity and stereoselectivity are still obscure. The purpose of this report is to describe the initiation of a research program to elucidate the structural features that govern the activity and enantioselectivity of quaternary ammonium ion phase transfer catalysts. The research program consist of two separate components described in this and the accompanying paper.² In this report we describe the development of suitably flexible synthesis of chiral, non-racemic, quaternary ammonium ions by solution phase parallel synthesis as well as the collection of a large set of catalyst activity and selectivity data. In the accompanying report the data sets are analyzed by developing many quantitative structure-activity and selectivity-relationships (QSAR and

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Supporting Information Available: All of the kinetic runs for each catalyst, enantioselectivity determination and stirring rate experiments and copies of ¹H and ¹³C NMR spectra of all intermediates and selected catalysts. This material is available free of charge via the Internet at <http://pubs.acs.org>.

QSSR). An enolate alkylation reaction was chosen to initiate these studies for three reasons: (1) it is one of the oldest and most useful methods to form carbon-carbon bonds (2) many examples of PTC enolate alkylations are on record and (3) the methods to perform enolate alkylations in a catalytic enantioselective manner are very limited. APTC

The requirements for a catalytic, enantioselective enolate alkylation are the in-situ generation of an enolate, alkylation in the presence of a stereochemical controlling element and stereo-chemical stability of the product (Scheme 1). Although auxiliary-based methods for the diastereoselective alkylation of enolates truly revolutionized the practice of organic synthesis beginning in the 1970's,^{3,4} A general and selective processes for catalytic enantioselective alkylations remains elusive.⁵ In contrast to other carbon-carbon bond forming reactions of enolates (compare to e.g. aldol and Michael reactions), the rate of enolate alkylation is significantly less than addition to a π -system, thus the use of soft-enolization techniques which are crucial for catalytic π -addition reactions cannot be utilized for enolate alkylations.⁶ The use of more reactive enolates, and strong bases to generate them, introduces a host of compatibility issues thus preventing the implementation of similar stereocontrol elements under catalytic conditions.

Nevertheless, notable successes have been achieved that represent creative solutions to some of the challenges described above. For example, a lithio cycloalkanone enolate alkylation has been cleverly engineered using a triamine catalyst.^{7,8} Transition-metal-catalyzed allylations are the most intensely investigated class of asymmetric alkylation reactions, and have been extensively re-viewed.⁹ Ligand development has been critical in facilitating many α -aryl and α -alkenylations of carbonyl compounds under palladium catalysis, although they are typically limited to generation of quaternary centers to avoid product racemization.¹⁰ Two alternative strategies have recently been reported, the asymmetric alkylation of ketone-derived tributyltin enolates in the presence of chromium(salen) complexes,¹¹ and asymmetric dimethoxymethylation of N-acylthiazolidinethiones with an orthoester under catalysis by a nickel(BINAP) complex.¹² A single report of intramolecular alkylation of an enamine generated from a proline derivative is on record, but extension to intermolecular versions is unknown.¹³ Perhaps the most imaginative extension of enamine catalysis for alkylation-type reactions is the enantioselective α -allylation, α -enolation, α -vinylation and α -arylation of aldehydes via the intermediacy of chiral enaminium radicals.¹⁴

To date, PTC is the only catalytic process capable of reducing to practice the simplest of enolate alkylations, such as, methylation, ethylation and benzylation (*vide infra*).⁵ As a synthetic tool APTC is complementary to the recently developed transition metal coupling methods that are well suited for coupling with C-sp² electrophiles.¹⁵ The mode of operation of APTC is unique in that the base and electrophile are in separate phases, thereby allowing the generation of highly active chiral nucleophiles in the presence of an electrophile. The broad electrophile scope of APTC reactions developed thus far suggests that APTC will eventually be a general method for performing strong base chemistry catalytically, and enantioselectively.

The state of the art of APTC stands at an interesting crossroad. On the one hand, impressive advances have been achieved in the ability to execute catalytic reactions that involve reactive carbanions and tremendous potential still exists. On the other hand, without testable hypotheses about what structural features are dominant in conferring high activity and selectivity to phase transfer catalysts, researchers are constrained to make and test catalysts without guiding principles to aide in the process. Accordingly, rationalization of activity and selectivity of APTC is currently done *ad hoc*, with little understanding of the observed trends. This dilemma is not surprising. The rates and selectivities of APTC reactions are governed by interfacial transport, desolvation, and a host of non-bonded interactions which

are difficult to study. Still more challenging is the *a priori* design of asymmetric phase transfer catalysts. In fact, the most readily available and successful APTC's to date are the *cinchona* alkaloid derivatives. Unfortunately, these structures offer little opportunity for systematic modification.^{16,17}

If anything has been learned about asymmetric catalysis over the past 30 years it is that major advances in the state of the art are inexorably tied to the development of a solid, physical organic foundation upon which greater and greater improvements can be built.¹⁸ Therefore, we sought to establish a research strategy capable of elucidating the fundamental origins of the structure-activity and selectivity of asymmetric phase transfer catalysts. *To emphasize, the goals of this research were not simply to discover a new enantioselective catalyst, but rather, to investigate a new method for catalyst development.* The approach we have adopted is analogous to a drug design process consisting of iterations of synthesis, evaluation and modeling. Reported herein are the first iterations of synthesis (160 catalysts) followed by evaluation (activity and selectivity) and finally modeling (in the accompanying paper).²

Background

1. APTC Enolate Alkylations and Known Catalyst Motifs

Phase transfer catalysis has already proven to be a broadly applicable and general method to perform strong base chemistry catalytically.¹⁹ In a landmark publication, the Merck Process Group reported the enantioselective methylation of an indanone under PTC conditions employing an *N*-4-trifluoromethylbenzyl *cinchona* alkaloid derivative.²⁰ A second critical advance appeared in 1989 when O'Donnell demonstrated the selective alkylation of glycine imines under similar conditions (Scheme 2).²¹ O'Donnell's alkylation is an operationally simple method for α -amino acid synthesis and has since served as a benchmark for the development of new asymmetric phase transfer catalysts.²²

In the intervening 20 years, many variations of *cinchona* alkaloid catalysts have been reported. The first notable advances were from independent studies by Lygo²³ and Corey,²⁴ in which the incorporation of a 9-anthracenylmethyl moiety as the nitrogen substituent markedly improved the enantioselectivity (Chart 1). Analogously, Park and Jew developed a tri-fluorinated *N*-benzyl quaternary ammonium catalysts^{25a} and dimeric, meta-bridged cinchoninium catalysts.^{25b} In recent years, Maruoka and Ooi have introduced a large number of novel, non-*cinchona* alkaloid catalyst systems based on a binaphthyl scaffold which allows introduction of substituents in the 3,3' positions.²⁶ Similarly, employing an in situ generation and screening process, Lygo has discovered a useful locally C_2 (at the nitrogen) symmetric catalyst.^{23c} Shibasaki/Ohshima,²⁷ Sasai,²⁸ Arai/Nishida,²⁹ and others have independently developed two-centered (and higher) APTC's by incorporation of quaternary ammonium ions, about a C_n axis. In addition to extensive catalyst development, significant advances in other typically strong-base-promoted reactions have been recorded including double alkylation of glycine imines, ketone alkylations, Michael, aldol, Mannich, and Darzens reactions as well as epoxidations and aziridinations.^{19k,l,m,n}

2. Catalyst Activity

2.1. Mechanisms of Hydroxide-Initiated PTC—The broad utility of PTC has motivated numerous investigations from fields as far reaching as synthetic chemistry, chemical engineering, computational chemistry, physical chemistry and chemoinformatics. PTC reactions that use aqueous bases to generate carbanions are termed hydroxide-initiated PTC.³⁰ The mechanism of hydroxide-initiated PTC reactions is an intensely investigated subject that has been thoroughly reviewed from both a chemical³¹ and engineering³²

perspective. Pioneering studies by Makosza³³ and Starks³⁴ led to two distinct mechanistic descriptions, later termed the interfacial (Makosza) and extraction (Starks) mechanisms. The mechanisms differ in the mode in which the substrate-ammonium ion pair enters the organic phase (Figure 1). Numerous studies have provided experimental support for *both* the extraction^{35,36} and interfacial mechanisms.^{37,38,39} These studies have accumulated a number of phenomenological observables that are used as indicators to decipher which mechanism is dominant.^{31b} Reactions governed by the extraction mechanism show little dependence on stirring rate and first order kinetic behavior in substrate and catalyst. On the other hand, PTC reactions governed by the interfacial mechanism show a strong dependence on stirring rate, complex kinetic order in substrate, and fractional order in catalyst. The current understanding of hydroxide-initiated PTC reactions suggests a mechanistic continuum that is strongly dependent on substrate pKa and catalyst structure.^{31b} To summarize, the extraction mechanism is dominant at the two extremes of substrate acidity (pKa < 16 and pKa > 23) and the interfacial mechanism is dominant when the pKa of the substrate is between 16–23. The rationale is that reactions with highly acidic substrates are rate limited in extraction of the substrate enolate and non-acidic substrates are rate limited by the rate of hydroxide extraction. Thus, the interfacial mechanism is proposed to be most relevant for enolate alkylations.⁴⁰

2.2. Guidelines for the Design of Active Catalysts—The quaternary ammonium ion catalyst is obviously the most critical element of a PTC reaction, and as is the case for any catalytic reaction, the selection of the “optimal” catalyst is crucial.^{41,31b} The fact that there are two possible mechanisms, in combination with the possibility of many “off-cycle” pre-equilibria, all of which are a function of substrate and catalyst combination, has made identifying simple structure activity relationships difficult.^{31a} For reactions strictly following an extraction mechanism (e.g. S_N² displacements with N₃[−], CN[−], SCN[−], etc.) catalyst activity correlates well with lipophilicity.^{36,35,42} No such generalizable structure activity relationships exist for hydroxide-initiated PTC reactions.

For hydroxide-initiated PTC reactions small hydrophilic ammonium ions are often superior catalysts, which is a compounding source of confusion.^{43,44} For example, triethylbenzylammonium, a small hydrophilic quaternary ammonium ion is an efficient catalyst for a myriad of PTC enolate alkylations (e.g. nitriles, esters, ketones...etc.).⁴⁵ One approach has been to correlate a macroscopic observable such as interfacial surface tension to catalytic activity which unfortunately does not address the question of what catalyst attributes confer high activity.⁴⁶ In the most advanced SAR to date, the ammonium ion accessibility (or size) *and* solubility were varied simultaneously and the most active symmetrical catalyst for alkylations was tetraethylammonium bromide.⁴⁷ A useful quantitative correlation of structure to catalyst activity was subsequently derived, namely the structural parameter, *q* (Equation 1).⁴⁸ The *q* parameter is defined as the sum of the reciprocals of the number of carbons on each chain.⁴⁹ For hydroxide-initiated PTC reactions, such as the alkylation of enolates, *q* values between 1.5 and 2.0 are optimal. This analysis is useful for simple quaternary ammonium ions containing only alkyl chains (C_{1–4}) but extension to catalysts containing functional groups, changes in hybridization, rings, branch points, or stereogenic centers has not been reported.

$$q = \frac{1}{\#C_1} + \frac{1}{\#C_2} + \frac{1}{\#C_3} + \frac{1}{\#C_4}$$

Equation 1

where, C_n is the number of carbons in C_i :

3. Structural Considerations for Catalyst Enantioselectivity

The rationalization of enantioselectivity and reduction to design criteria is of preeminent importance to the study of catalytic processes.⁵⁰ The alkylation of O'Donnell's imine is by far the most studied enolate alkylation and two models have been proposed to rationalize the enantioselectivity observed with *cinchona* alkaloid derived catalyst (Figure 2).⁵¹ In a thorough computational study, O'Donnell and Lipkowitz analyzed the enolate molecular recognition event and origin of stereoselectivity of this important transformation.⁵² Computational results suggest selective binding of the catalyst to the *Si* face of the *Z*-enolate (Figure 2a). Subsequently, it has been proposed that catalysts bearing a 9-methylantracenyl group on nitrogen react through the *E*-enolate (Figure 2b).^{23,24}

The binding site of *cinchona* alkaloid derived catalysts has been probed by intermolecular nOe correlations between ammonium borohydrides and fluorides and indicates two "front-face" binding regions (Figure 3a).⁵³ These studies provide good support for strong hydrogen bonding interactions of the type $N^+CH\cdots O^-$ in solution which has also been identified in the solid state by X-ray crystallographic analysis of quaternary ammonium-enolate ion pairs.⁵⁴ High level calculations further corroborate that in solution, ammonium ion ester enolates tend to orient "face-on" to one of the faces of the ammonium (Figure 3b).^{51b} The combination of these analyses lends to a useful design mnemonic by inscribing the ammonium nitrogen in a tetrahedron (red) where the vertices are the four carbons bound to it. The face proximal to the oxygen is proposed to lead to more selective reaction of the substrate bound to it.

4. Objectives of this Study

Our initial survey of the literature revealed a few significant trends. Firstly, while a myriad of APTC methods have been developed for enolate π -addition reactions, the reports on analogous alkylation reactions remains limited, largely O'Donnell's glycine imine substrate.^{19m} It is not clear whether the lack of reports on new hydroxide-initiated PTC enolate alkylations is because known catalysts are insufficiently active, insufficiently selective, or both. What is clear, however, is that a more rational, systematic manner to develop quaternary ammonium ion catalysts is needed. Specifically, to elevate APTC to the state of rational design available to other catalytic enantioselective methods, two unique challenges need to be addressed. First, a method to estimate the activity of catalysts *a priori* is needed. This capacity would greatly alleviate the synthetic investment currently required to study APTC, and in so doing, facilitate discovery. Second, a clearer picture of structural features that confer high selectivity to asymmetric phase transfer catalysts is needed.

Each of these aspects is a daunting task because they require systematically varying the topology of a quaternary ammonium ion catalyst, which are difficult to synthesize in enantiopure form. Fortunately, the pharmaceutical drug discovery model provides close analogy for both of these challenges.⁵⁵ Thus, the first phase of these studies has been initiated in analogy to a phenotypic screening assay where catalyst activity will be evaluated as a function of molecular "pharmacodynamic" properties.⁵⁶ The intermolecular enantiotopic face discrimination event is analogous to molecular recognition of a substrate (or drug) by an enzyme, except that the synthetic effort is tantamount to building the enzyme binding pocket rather than the substrate.

We therefore set out to devise a research strategy that would provide a proof of principle as a catalyst development methodology. The key objectives were to develop *quantitative* analyses of both catalyst activity and enantioselectivity, in order to probe the underlying

hypothesis that a quantitative treatment of catalyst activity and selectivity as a function of catalyst structure would naturally lend to a more facile catalyst development process. To emphasize, the motivational factors for this study were *to probe the manner in which catalyst development is done, and not simply to develop a catalyst*. We therefore made two decisions before initiating this study. First the alkylation of O'Donnell's imine would serve as the benchmark reaction for catalyst screening, thereby foregoing a methodological development period. Second, an arbitrary, and modest, enantioselectivity threshold of ~80:20 was set as the point at which random catalyst screening would stop and a more systematic, QSAR guided, investigation would begin. After all, developing a QSAR model on a data set where catalyst selectivities exceed 99:1 is, in many ways, a moot point because the end-goal has already been reached. No limit for range of activity data was set initially, but the preliminary survey readily identified catalysts with activity differences up to four orders of magnitude which is well suited for a QSAR study. The design and synthesis of a suitably diverse libraries of quaternary ammonium ion catalysts and collection of activity and selectivity data for this initial data set is described below. A qualitative analysis of the observed trends follows which are reduced to quantifiable changes in the catalysts and interpreted mechanistically in the accompanying paper.² Ongoing studies (data not shown) indicate that these, quantitative models are readily utilized as a methodological tool for further catalyst optimization.

Results

1. Research Plan and Design

1.1. Scaffold Synthesis Method—Without testable hypothesis about what structural features will dominant in conferring high catalyst activity and selectivity, this endeavor was necessarily initiated as a discovery oriented program. The initial focus was set on (1) identifying a suitable scaffold (or scaffolds) that could be prepared in enantiopure fashion and would allow for substitution in multiple positions followed by (2) developing suitably flexible parallel synthesis procedures for the elaboration of the scaffold to a diverse library of quaternary ammonium ions. Concurrently the scaffold and most easily substituted positions were evaluated in the context of known quaternary ammonium design principles. The tandem [4+2]/[3+2] cycloaddition of nitroalkenes, a methodology extensively studied in these laboratories, was quickly identified as a reaction that embodies all of the requisite characteristics for scaffold preparation.⁵⁷

In the tandem cycloaddition of nitroalkenes, three key components, a nitroalkene, a dienophile and a dipolarophile combine to construct a new six-carbon unit forging four bonds, up to six contiguous stereogenic centers, and four rings. Lastly, the newly minted skeleton is transformed by hydrogenolysis, which proceeds by reductive N-O bond cleavage, followed by intramolecular reductive amination and lastly closure of the remaining ring to construct a pyrrolizidine ring system. Of the four possible permutations of inter- and intramolecularity, the tandem inter [4+2]/intra [3+2] family wherein the dipolarophile and nitroalkene are covalently tethered is the most powerful (Scheme 3).⁵⁸ Tethering the dipolarophile to either the α - or β -position of the dienophile results in bridged cycloadducts and generates primary amines after hydrogenolysis. Tethering the dipolarophile to the nitroalkene results in either a spiro-mode (1-position) or a fused-mode (2-position) cycloaddition and generates tertiary lactams after hydrogenolysis. Extensive investigation of this family has revealed many advantages including: (1) ease of preparation of the precursors, (2) flexibility in the electronic nature and configuration of the components, (3) high levels of absolute stereocontrol with chiral dienophiles, and (4) diversity of product structure.⁵⁹

1.2. Scaffold Selection—A key challenge to systematic investigation of APTC is the availability of catalyst scaffolds that allow for facile modification of sites proximal to the quaternary ammonium ion center.^{60,61} Both the spiro- and fused-mode cycloadditions create skeletons where the nitrogen is fixed in a central position of a rigid ring system thereby providing potential for the controlled installation of groups in the vicinity of the nitrogen. The fused mode, tandem inter [4+2]/intra [3+2] cycloaddition with a two-carbon tether was chosen for initial studies. In this mode the tandem cycloaddition/hydrogenolysis sequence generates a tricyclic cyclopentapyrrolizidin-2-one ring system bearing a hydroxy group at C(1) and a substituent at C(5) (Scheme 3). Prior to elaboration of a detailed parallel synthesis strategy, the local environment around the ammonium nitrogen was considered in the context of known design principles.

1.3. Scaffold Shape and Ammonium Ion Accessibility—By connecting the nitroalkene and the dipolarophile with a two-carbon tether, the ring fusions (C(7b)-N, C(7b)-C(5a), C(7b)-C(7a)) are dictated to all be cis, giving the scaffold a bowl shape (Figure 4). Library design efforts were initiated by inscribing the central ammonium nitrogen of the scaffold in a regular tetrahedron (red) to determine which faces will be accessible for Coulombic interactions. Clearly the concave face inscribed by C(2)-C(4)-C(7b) is shielded by the C(6)-C(7) methylenes rendering it sterically inaccessible. Initial molecular modeling⁶² indicated that a nitrogen substituent (R⁴) would occupy the face defined by C(2)-C(4)-C(9) to avoid steric interaction with a group at C(8). Therefore, the two most accessible faces of the ammonium ion tetrahedron appear to be the two situated on the convex face of the scaffold inscribed by C(2)-C(9)-C(7b) and C(4)-C(9)-C(7b) respectively.

1.4. Parallel Synthesis Design—The tandem inter [4+2]/intra [3+2] cycloaddition of nitroalkenes in the fused mode allows for the stereoselective introduction of groups at C(5) (R¹) and a hydroxy group at C(1) while preserving the relative configuration of the scaffold ring system (Scheme 4). The variable groups R¹, R², and R⁴ are situated on the convex face allowing for the evaluation of many different combinations of substituents. Because the C(5)-substituent (R¹) is the first point of diversification its variation was limited (either H or Me), thereby reducing the synthetic investment required for this initial survey. Moreover, the configuration of the C(1) center is dictated by the geometry of the dipolarophile thus introducing an additional element for diversification. After introduction of groups at C(1) and C(5) the scaffolds will be elaborated by means of parallel synthesis.

The forward synthetic analysis from the scaffold is outlined in Scheme 4. The hydroxyl group at C(1) was targeted for the next two points of diversification. Simple oxidation followed by addition of an organometallic reagent (R²-M) would allow for the introduction of groups directly in the vicinity of the C(2)-C(7b)-C(9) face. Also, alkylation of the resulting alcohol (or the original secondary alcohol) with simple alkyl halides (R³-X) would serve as a facile method for introducing groups on the concave face. Lastly, the nitrogen substituent (R⁴) is installed by a second alkylation to afford the final quaternary ammonium salts. This analysis served as a general framework from which the order of synthetic steps suitable for parallel synthesis was worked out experimentally.

1.5. Focused Libraries—To facilitate description of the libraries, the catalysts are divided into focused sets of increasing substitution (I–V). The R¹ substituent (H, Me) served to influence the position of the R⁴ substituent and to differentiate the accessibility of the two convex faces inscribed by C(3)-C(7b)-C(9) and C(2)-C(7b)-C(9). The R² substituent would play a complimentary role in terms of accessibility and interaction of the counterion. This group could be more extensively diversified because of its later stage of introduction in the synthesis. Because R³ is more distal to the nitrogen atom, the primary focus for this substituent was to serve as a lipophilicity modifier. The residue R⁴ was restricted primarily

to groups of varying π -surfaces. Additionally, because this group is introduced last, a larger degree of synthetic flexibility is available, thus facilitating a systematic investigation of the role of steric and electronic factors for these aryl rings. The proximity of this substituent to the positively charged nitrogen means that the character of this group should have a larger influence (through dipole and field effects) on the localized positive potential encompassing the nitrogen than any of the other groups. The overall degree of modification in the scaffold as outlined here should lead to sufficient variation in the catalyst structural properties for a QSAR analysis.

Chart 2). The simplest members of this group (Library **I**) bear no oxygen containing functionality and vary only in the nitrogen substituent (R^4). Oxygen functionality is introduced in Libraries **II** and **III** whereas additional steric and conformation influencing groups are introduced in Libraries **IV** and **V**. Quaternary ammonium ion library members will be referred to by Roman numeral (Libraries **I–V**) followed by a braced number set designating the order and number of groups introduced $\{X-X, X-X\}$. For example, in Scheme 6 the intermediate free amine $X\{R^1, R^2, R^3\}$ will be converted to library **V** $\{R^1, R^2, R^3, X-X\}$ through the action of reagents $\{X-X\}$.

The R^1 substituent (H, Me) served to influence the position of the R^4 substituent and to differentiate the accessibility of the two convex faces inscribed by C(3)-C(7b)-C(9) and C(2)-C(7b)-(C9). The R^2 substituent would play a complimentary role in terms of accessibility and interaction of the counterion. This group could be more extensively diversified because of its later stage of introduction in the synthesis. Because R^3 is more distal to the nitrogen atom, the primary focus for this substituent was to serve as a lipophilicity modifier. The residue R^4 was restricted primarily to groups of varying π -surfaces. Additionally, because this group is introduced last, a larger degree of synthetic flexibility is available, thus facilitating a systematic investigation of the role of steric and electronic factors for these aryl rings. The proximity of this substituent to the positively charged nitrogen means that the character of this group should have a larger influence (through dipole and field effects) on the localized positive potential encompassing the nitrogen than any of the other groups. The overall degree of modification in the scaffold as outlined here should lead to sufficient variation in the catalyst structural properties for a QSAR analysis.

2. Library Syntheses

2.1. Preparation of Tandem Cycloaddition Precursors—To accurately determine the rate and enantioselectivity for each catalyst (ca. 3 runs/catalyst), approximately 30 mg of each quaternary ammonium salt would be required, thus mandating the synthesis of gram quantities of the scaffolds for Libraries **I–V**. Thus, the first phase of this investigation was to develop robust, scalable routes to the cycloaddition precursors (nitroalkenes (*E,E*)-**1** and (*E,Z*)-**1** and chiral vinyl ethers **2** and **3**, above) in decagram quantities. Each of these cycloaddition precursors were readily prepared either directly following the known route or with small changes upon scale-up.⁶³ The preparation of the cycloaddition precursors **1**, **2**, and **3** is detailed in the Supporting Information.

2.2. Scaffold Preparation by Tandem Cycloaddition of Nitroalkenes—The centerpiece of the library synthesis was the use of the tandem cycloaddition of nitroalkenes to cast the polycyclic skeletons that will serve as parallel synthesis scaffolds. Known α -hydroxy lactam **4** was prepared in racemic form by tandem [4+2]/[3+2] cycloaddition of nitroalkene (*E,E*)-**1** with *n*-butyl vinyl ether via the intermediacy of nitronate **6** and nitroso acetal **7** (Scheme 5). Reductive hydrogenolysis afforded the tricyclic lactam ($\pm$)-**4a** in excellent overall yield (86% over three steps).

Likewise, enantiomerically enriched α -hydroxy lactams ($\pm$)-**4a** and **5** were readily prepared on scale in non-racemic form via the tandem cycloaddition with chiral vinyl and propenyl ethers **2** and **3** respectively (Scheme 6).⁶³ In this process, a standard set of reaction conditions was employed, namely exposure of a solution of nitroalkene and dienophile to $\text{TiCl}_2(\text{O}i\text{-Pr})_2$ at -78°C to afford the intermediate nitronate. Subsequent, thermal cycloaddition occurred over the course of 2–3 h upon standing at room temperature. The resulting nitroso acetals were immediately subjected to hydrogenolysis with Raney nickel in methanol to afford the lactams in 76% and 89% respectively (three steps) with high enantioselectivity (e.r. 96:4).⁶⁴ The epimeric α -hydroxy lactam ($\pm$)-**4b** (not previously described), was readily prepared in 63% yield following the standard protocol (e.r. 96:4). The elaboration of these scaffolds to the Libraries **I–V** respectively is detailed in the next section.

2.3. Preparation of Library I—The next phase of these studies involved the development of a suitably versatile parallel synthesis route to allow for the introduction of various substituents on the core scaffold. The simplest scaffold (Library **I**), containing only a single site of variation, was first targeted to address the introduction of groups in the key N-alkylation step.

To complete the synthesis of the C_s symmetric scaffold, reduction of the two oxygen functional groups was required. Removal of the hydroxyl group was accomplished by activation as a phenyl(thiono)carbonate **8** followed by Barton type deoxygenation under the action of $\text{Bu}_3\text{SnH}/\text{AIBN}$ to afford lactam **9** in good overall yield (64%, two steps) (Scheme 7).⁶⁵ Reduction of lactam **9** with borane•THF afforded the fully deoxygenated scaffold **16** for Library **I** as its borane adduct in 80% yield. With large quantities of borane adduct **10** in hand, N-quaternization conditions suitable for parallel synthesis could be investigated.

To facilitate the throughput of material, a method for the direct conversion of the amine borane adduct to the desired quaternary ammonium salts was sought that avoided the need for purification of intermediates. Heating amine-borane **10** in methanol in the presence of 1 M aq HCl led cleanly to the intermediate amine hydrochloride. The free base was liberated by partitioning the salt between 0.1 M aq NaOH and ether. Exposure of the free amine to a slight excess of benzylic and primary aliphatic bromides {**1–6**} in acetonitrile at room temperature led smoothly to the quaternary ammonium ions **I**{**1–6**} in 72–90%. The excess electrophile could easily be removed by either filtration through silica gel or trituration with ether analogous to the methods of Dehmloew⁶⁶ and Maruoka respectively.⁶⁷ Ultimately, it was decided that silica gel plug filtration followed by trituration with ether could be used as the general conditions for purification for other ammonium salts.

2.4. Preparation of Libraries II and III—The next level of complexity called for the synthesis of libraries of chiral, non-racemic ammonium salts to study their effectiveness as asymmetric phase transfer catalysts. The construction of Libraries **II** and **III** introduces a second parallel synthesis step, namely O-alkylation. These two libraries embodied three objectives aimed at investigating *both* enantioselectivity and rate: (1) to introduce groups with variable solubilizing abilities (rate) and (2) introduce variable π -surfaces and steric bulk (selectivity) and (3) investigate the effect of configuration at C(1) (selectivity).

The diastereomeric lactams ($\pm$)-**4a** and ($\pm$)-**4b** were reduced to the pyrrolizidines **11a** and **11b** with $\text{BH}_3\cdot\text{THF}$ (>10 equiv) in good to excellent yield (Scheme 8). These amines were also isolated as their borane adducts, thus protecting the amine from air oxidation⁶⁸ and subsequent alkylation in the next step. This sequence allowed for the preparation of multi-gram quantities of borane complexes **11a** and **11b** as crystalline solids which was a convenient stage for storage of material. Application of standard Williamson ether synthesis

conditions⁶⁹ (NaH, DMF) to borane complexes **11a** and **11b** allowed for facile elaboration to intermediates **II**{1–5} and **III**{1–5}. The introduction of simple hydrophobic groups (*n*-hexyl), hydrophilic groups (methoxyethoxymethyl, MEM) as well as aromatic carbocycles and heterocycles, in good yield under a standard set of reaction conditions. It is noteworthy that the inclusion of a MEM ether in these series required the use of either neutral or base-promoted deborylation conditions because of the acid lability of this group. Accordingly, aq. HCl was replaced with aq. Na₂CO₃ under otherwise identical reaction conditions. Elaboration of the intermediate borane adducts as described previously proceeded smoothly to afford quaternary ammonium salt libraries **II**{1–5,1–6} and **III**{1–5,1–6} in good yields over the three step process.

2.5. Preparation of Libraries IV and V

2.5.1. Introduction of R² Substituents: The presence of the hydroxyl group at C(1) allows for further diversification. This site was targeted for the introduction of different aliphatic and aromatic groups by organometallic addition to the corresponding C(1) ketone. Accordingly, Parikh von-Doering oxidation of **11a** furnished the desired ketone **13** in 98% yield (Scheme 9).⁷⁰ However, ketone **13** was not stable and was immediately carried on to the organometallic addition step. The increased acidity of the α -hydrogens, likely as a consequence of nitrogen complexation,⁷¹ required the use of softer, less Brønsted basic organocerium reagents.⁷² The resulting additions took place (40–98% yield) to form **15**{1–7} with complete β -diastereoselection as a consequence of the bowl shape of the core scaffold. Likewise, ketone **14** (an inseparable 12:1 mixture of C(5) diastereomers from cycloaddition with a propenyl ether) underwent the cerium-mediated addition to afford the tertiary alcohols **16**{1–7} in similar yields.

However, the inability to introduce bulky groups as well as poor reproducibility led to a modification of the synthetic route. Oxidation of alcohol **5** to α -keto lactam **17** afforded two important benefits over the initial route. First, the addition of Grignard reagents to this highly active dicarbonyl compound proceeded reproducibly and in excellent yields (95–97%) even with bulky nucleophiles. Second, the minor C(5) diastereomer could be removed by a single recrystallization. Reduction of the resulting lactams **18**{4,6,7} required elevated temperatures, presumably a consequence of the additional steric bulk proximal to the site of reduction. In this way, the corresponding amine-borane adducts **15** and **16** could be isolated in respectable yields (72–85%) without increasing the number of steps in the synthetic route.

2.5.2. Parallel Synthesis Toward Libraries IV and V: Extension of the developed parallel synthesis route to the more hindered tertiary alcohol at C(1) found in Libraries **IV** and **V** was straightforward (Scheme 10) and readily accomplished following the previously developed protocol. The R³ substituents in Libraries **IV** and **V** were limited to unfunctionalized aliphatic groups and electron rich (4-MeOC₆H₄) and electron deficient (3,5-(CF₃)₂C₆H₃) aromatic groups. Also, the 9-anthrylmethyl group at R⁴ was removed from this set,⁷³ but a larger number of groups of varying electronic makeup and size were introduced for R⁴ in Libraries **IV** and **V**.

2.6. Summary of Library Syntheses—A library of over 160 catalysts sharing the same core scaffold has been generated that incorporates the substituents below (Figure 5). Although this number represents only a small fraction of the complete matrix of ~1100 catalysts, the library represents a good approximation of the total structural space occupied by the complete matrix on the basis of preliminary data. The groups shown reflect the need to evaluate the roles of steric and electronic contributions, π -surface, lipophilicity, and polar surface area on the catalyst structure for a given phase transfer catalyzed reaction.

3. Collection of Kinetic Data

3.1. Refining a Kinetic Analysis—The base-promoted benzylation of glycine benzophenone imine *tert*-butyl ester **19** has become the benchmark reaction for investigation of new catalyst structures.^{19m} As such, a standard set of reaction conditions has been established, namely the use 50% aq. KOH solution and toluene.²² Given the intrinsic biphasic nature of PTC reactions, efficient mixing is essential to promote efficient transport and to minimize the errors associated with precipitation. For these reasons, a 4-mL (1 cm × 3.5 cm) cylindrical vial was chosen as the reaction vessel together with a 1.5 cm egg-shaped stir bar. This stir bar was large enough such that it traversed the interface and yet was small enough to ensure mixing as a consistent shearing motion.^{47,74,75} The scale of the reactions was dictated by the need to conduct multiple kinetic runs using 80–120 mg of starting ester **19** (thus dictating a minimally measurable amount of catalyst (4–8 mg)) and to maintain a reaction concentration of 0.33 M.

Under these conditions, orienting experiments utilizing 5 mol % of a catalyst at room temperature resulted in rapid reaction; most were complete within 1–3 min! Clearly this range of rates was not amenable to providing reproducible results. Decreasing the catalyst loading to 2.5 mol % and decreasing the temperature to 2–4 °C successfully slowed the reaction to a point where a range of rates could be observed.⁷⁶

Initial experiments with tetrabutylammonium bromide allowed for an examination of sampling methods to ensure reproducibility. Sampling from the bulk mixture gave inconsistent results and the sampling needle clogged frequently. A more reliable protocol involved stopping the agitation momentarily to allow the biphasic mixture to separate (~2 s), and sampling from the organic layer. Utilizing this protocol the reaction profile was reproducible; typically to within 1–2%, but always within 5% (see Supporting Information).

An important decision was an appropriate value to represent the rate data (e.g. k_p , k_{obs} , $t_{1/2}$, ...etc). Upon initial testing catalyst **1**, a significant induction period was observed over the course of the first 5% conversion. This type of behavior has previously been reported as a function of ammonium counterion and is indicative of an interfacial mechanism.^{40,77} The induction period was seen under the protocol wherein the base was added last. However, if the order of addition of reagents was changed such that the alkylating agent was added last, then the converse was observed and appearance of product was rapid at first, but quickly declined (a kinetic “burst”). Most importantly, regardless of the order of operations, the “time course” of the two reactions converges to a single rate. Given the significant variation at the onset of the reaction, it was decided to extract data that would be independent of the initial rate, namely $t_{1/2}$. Although this determination is labor intensive, since it would require monitoring each reaction to greater than 50% conversion, it has the added advantage of showing the entire reaction profile.

3.1 Stir Rate Dependence—The last critical decision to be made was a stirring rate that would sufficiently minimize errors from precipitation and still allow for the differences in catalyst activities to be observed. Hydroxide-initiated-PTC reactions can exhibit a rate dependence on stirring speed in excess of ~2000 rpm. At high enough stirring speeds there is little dependence which is consistent with the proposal that the influence of mixing is to increase the surface area to volume ratio (effectively concentration) of the biphasic,^{39a} and that phase transfer reagents can decrease the interfacial surface tension.^{46a}

To determine a suitable stirring speed for application to the standard protocol, the dependence of catalytic activity on stirring speed was determined for a variety of variably active quaternary ammonium ions. Reaction half-lives were determined following the experimental parameters noted above employing a range of stir rates (1038 – 2500 rpm).

The resulting observed half lives are plotted as a log/log in analogy to a dose-response graph (Figure 6).^{55,56} The top two curves represent catalysts with low catalytic activity while the two lower curves represent catalysts among the highest activity. Importantly, there is a sufficient range of stirring speeds, along which the activities of all of the catalysts surveyed are dependent (non-zero slope) on mixing rate. In choosing the stir rate with which all of the kinetic experiments were to be carried out, the important considerations were: (1) sufficient and consistent mixing, (2) operationally accessible, and (3) that the stir rate existed in a region where a reaction rate dependence was still observed. The stir rate of 1600 rpm fit within all three of these criteria (represented by the black vertical dotted line in Figure 6) and therefore, all of the remaining kinetic data were collected at this stir rate.

4. Summary of the Kinetic Data

4.1 Statistical Description—With a working analytical method in hand, a large subset of the ammonium salts was evaluated for their kinetic competence, represented as half-lives. The half-lives were determined by interpolation of the kinetic plot of percentage of product formation as a function of time. The reported half-life values represent averages over two runs with an average error of 4.5%.⁷⁸ Data from kinetic runs that resulted in errors exceeding 20% was discarded and repeated until an error of less than 20% was observed.

To date, half-lives for 102 of the 160 catalysts have been collected. The observed half-life data covers four orders of magnitude of activity that was deemed suitable for the initial investigation of the structural effects of catalyst on rate. The half-life data collected from these experiments ranged from 5 min to over 15 h and is summarized in logarithmic scale below (Figure 7). Of the 102 catalysts surveyed to date 52 of them exhibited half-lives of 20 min or less. Twenty-three catalysts make up the data between 20 min and 1 h, and the half-lives of the remaining 27 catalysts range from 1 h to 15 h.

4.2. Catalytic Activity of Library I—The half-life data for Library **I** is summarized in Table 1. These ammonium ions showed fairly poor catalytic activity exhibiting half-lives in the range of 5 to 12 h. The one exception was the catalyst containing an *n*-hexyl nitrogen substituent. In this case the half-life observed was only 13 min.

4.3. Catalytic Activity of Libraries II and III—The half-life data for Libraries **II** and **III** is summarized in Table 2. These ammonium salts are generally more active catalysts than those lacking an oxygen substituent and exhibited half-life range from 6 min to 5.7 h. Catalysts containing a non-hydrogen substituent at R³ are generally more active than the corresponding catalysts with hydrogen at R³. However, no clear dependence of the nature of the R³ substituent on catalyst activity was discernable. When R³ = H, the rate was markedly dependent on the configuration at C(1) (entries 5 vs. 6). However, when R³ ≠ H, the half-life was nearly independent on the C(1) configuration (entries 10 vs. 11, 12 vs. 13, 16 vs. 17, 21 vs. 22, and 23 vs. 24).

4.4. Catalytic Activity of Libraries IV and V—The half-life data for Libraries **IV** and **V** is summarized in Table 3. The activity of these catalysts appears to be largely dependent on the R² substituent within the series. Comparing catalysts with fixed R¹, R³, and R⁴, substituents, but with varying R² substituents, the following trend in rates holds: R² = *i*-Pr > Me > Ph. However, there are important exceptions. For example, catalysts containing R⁴ = 3,5-(CF₃)₂C₆H₃, R¹ = Me, R³ = benzyl, the following trend in half-life holds for R²: Me > *i*-Pr > *t*-Bu > Ph (entries 13, 26, 35, 39). Evidently, a compelling, but complex dependence of the bis(trifluoromethyl)phenyl group at R⁴ on the catalyst activity is observed. Moreover, ammonium salts containing R³ = *n*-hexyl are generally more active than catalysts with R³ ≠

n-hexyl with all other substituents held constant, which suggests a dependence on lipophilicity.

4.5. Other Quaternary Ammonium Ions—Varying the substituents on a common scaffold allowed for observation of a large range of rates. To determine how much of the “total possible” range of activity was being sampled tetramethylammonium bromide (TMAB, $q = 4.0$) was tested and exhibited a half-life of 1200 min (Table 4).⁷⁹ The similarly hydrophilic, but less accessible tetraethylammonium bromide ($q = 2.0$) exhibited a 20-fold rate increase over TMAB. The more lipophilic, but similarly accessible cation cetyltrimethyl (C_{19} total, $q = 3.06$) ammonium bromide was only three times faster than TMAB (entry 3). The rate increase from tetramethyl- to tetraethylammonium bromide was also seen in the use of tributylbenzylammonium bromide, which caused a further 20-fold rate increase. To directly address this dramatic effect of ammonium accessibility with catalysts more closely related to the common scaffold, one other small set of quaternary ammonium ions was constructed that replaces one of the pyrrolidine rings of the scaffold with an azetidine.⁸⁰ As expected, the ammonium ions containing an azetidine ring exhibited overall poor catalytic activity with half-lives ranging from 900 to 1000 min.

5. Enantioselectivity of the Catalysts

In addition to determining the substituent effects on rate, those structural features that most strongly affect enantioselectivity were of equal interest. Summarized below is the enantioselectivity data for all 143 chiral, non-racemic catalysts constructed to date. The enantiomeric ratio of benzylated product **20** was measured by purifying a sample by silica gel chromatography from a separate experiment at 2–4 °C with 2.5 mol % catalyst loading. The enantiomeric ratios were determined by CSP-HPLC by a known protocol.⁸¹

5.1. Enantioselectivity for Library II and III—The enantioselectivity data for the α -series (Library **II**, $R^1 = R^2 = H$) and the β -series (Library **III**, $R^2 = H$) is summarized in Table 5. For the α -series (Library **II**), little to no stereoinduction was observed, regardless of the combination of substituents (entry 1). In the β -series (Library **III**) catalysts with $R^3 = H$ produced low to moderate enrichment of the *S* enantiomer of **20** with $R^4 = 3,5-(CF_3)_2C_6H_3$ (entry 5, e.r. 57:43) exhibiting the largest selectivity. Relative to the α -series, catalysts with $R^3 =$ aliphatic consistently produced the *S* enantiomer in slightly greater enrichment (entries 8–13). Additionally, moderate enantioselectivity was observed in catalysts containing a 2-pyridyl group (where the point of attachment is the sp^2 carbon of the heteroaromatic ring) at R^3 (entries 20, 23, and 25) with the largest selectivity observed when $R^4 = 1$ -naphthyl. Similar results were observed in catalysts with $R^3 =$ benzyl within this series, apart from when $R^4 = Ph$ (entry 19) which resulted in decreased selectivity. Overall, the enantioselectivity data for the catalysts in Library **III** was greater than their diastereomeric counterparts Library **II**.

7.3. Enantioselectivity for Libraries IV and V—The enantioselectivities for catalysts with variable R^2 , R^3 , and R^4 groups while holding R^1 constant as a methyl group (excluding entry 1) are summarized in Table 6. See the Supporting Information for a fully tabularized list. Entries with the highest selectivities are highlighted. Introducing a methyl group at R^1 while maintaining a hydrogen and a benzyl group at R^2 and R^3 respectively did not lead to significant differences in the enantioselectivity apart from when the R^4 group was a 3,5-substituted aryl ring (entries 2–4). In this case, inversion of the C(1) configuration resulted in a comparable enantioselectivity (entries 5, 6).

The results for the catalysts with $R^2 = Me$ are similar to those catalysts with $R^2 = H$. Likewise, catalysts with a 3,5-substitution pattern on the aryl ring of R^4 consistently resulted

in the highest selectivities independent of the R^3 substituent (compare entry 7 to 8–12). Increasing the size of the R^2 substituent to isopropyl and *tert*-butyl resulted in a reversal in the selectivity (entries 13). As was the case with catalysts with $R^2 = \text{Me}$, the catalysts exhibiting a 3,5-substitution pattern on the aryl ring of R^4 with $R^2 = i\text{-Pr}$ and *t*-Bu produced the highest selectivities (entry 14). Catalysts containing $R^2 = \text{phenyl}$ are were variably selective for either the *S* or *R* enantiomer, apart from when R^4 was a 3,5-disubstituted aryl group (entries 15 and 16). However, the maximum enantioselectivity was observed when $R^4 = 3,5\text{-(CF}_3\text{)}_2\text{C}_6\text{H}_3$ (entries 19, 20, 22 and 25). This effect is independent of the oxygen substituent (R^3). Additionally, the substitution pattern of the trifluoromethyl groups on the aryl ring (R^4) proved to be important, as having groups at the 3- and 5- aryl position consistently resulted in greater enantioselectivity than having substituents at the 2- and 4- aryl positions or just the 4-aryl position (entry 23 and 24). Moreover, the presence of an alkyl group at R^1 (Me) is imperative as the analogous catalyst with $R^1 = \text{H}$ afforded significantly decreased enantioselectivity (entry 1). The installation of different groups at R^2 with π -surfaces while maintaining $R^3 = 3,5\text{-(CF}_3\text{)}_2\text{C}_6\text{H}_3$ produced similar results (entries 25 and 26). When $R^2 = i\text{-propyl}$ or *t*-butyl (entries 13 and 14) the enantioselectivity is significantly diminished in comparison to catalysts that contain an aromatic group in this position. Together these results attest to the importance of π -surface rather than steric bulk at R^2 for higher enantioselectivity.

Discussion

1. Analysis of Ammonium Ion Preparations

1.1 Synthetic Strategy—Since the discovery of asymmetric phase transfer catalysis with *cinchona* alkaloid derivatives, a significant level of effort has been devoted to the introduction of novel synthetic catalyst structures. Most of the synthetic endeavors fall into one of the following two synthetic strategies: (1) elaboration of a readily available source of chiral material by appending a non-stereogenic quaternary ammonium ion or (2) incorporation of a quaternary ammonium into a molecule in such a way that it lies on a symmetry axis. Although each of these approaches has seen some success, the synthetic strategy presented herein is significantly different and warrants discussion.

The approach presented here is unique in that the synthetic effort was focused on systematically varying the steric and electronic environment around a central stereogenic quaternary ammonium ion. To this end, the synthetic investment was divided into two different parts. The first part involved preparation of a nitrogen containing scaffold (a cyclopentapyrrolizidine) on a significant scale which was readily accomplished by application of the tandem inter [4+2]/intra [3+2] cycloaddition of nitroalkenes with only minor changes to the previously published routes. Notably, the tandem cycloaddition also served as a diversifying element in that it was in this step that the configuration at C(1) was set (Libraries **II** and **III**) and the R^1 group was introduced stereoselectively, which subsequently proved to be a critical catalyst structural feature.

The second synthetic component involved development of procedures amenable to parallel synthesis that introduced a variety of groups in the vicinity of the ammonium nitrogen. Ultimately, three operationally simple bond forming reactions were utilized to accomplish this goal that allowed for the catalysts to be prepared in a parallel fashion. The tandem cycloaddition naturally installs a hydroxyl group at C(1) which served as a functional handle for two parallel synthesis steps; a Grignard addition and an O-alkylation, leaving only N-quaternization as the final parallel synthesis step. Including the previously installed R^1 substituent a total of four variable groups were introduced. The diversity and number of groups utilized was greatest for the positions that could be incorporated in parallel (R^2 , 6; R^3 , 7; R^4 , 11) and the least for the group that required a recast skeleton (R^1 , 2). A good

appreciation for the shape of the catalyst(s) and disposition of the variable groups in relation to the ammonium nitrogen is necessary to facilitate a thorough analysis of the effect of each group (and combinations thereof) on catalytic activity and selectivity.

1.2. Catalyst Shape and Position of Groups—Library **I** is a logical starting point because the inherent symmetry simplifies the analysis. Below is a plot of the relative conformer energies as a function of a double dihedral driver about bonds C(5a)-C(6)-C(7)-C(7a) and C(7b)-N(3)-C(9)-C(10) for catalyst **I** (Figure 8).⁸² A full 360 degree rotation about the C(7b)-N(3)-C(9)-C(10) bond constitutes a full range of motion of the R⁴ substituent, in this case, a phenyl group. The R⁴ substituent can be found in two local sparsely populated minima corresponding to gauche conformations ($\pm 60^\circ$), which, in the case of Library **I**, are a pair of diastereomeric conformers. A single, highly-populated, global minimum is found when the R⁴ substituent is projected 180° away from the N(3)-C(9) bond. A small energetic barrier separates the global and local minima, but a “full range of motion” of the R⁴ substituent is prohibited because of steric interactions with the C(8)-methyl group. For the remainder of this discussion the R⁴ group will be projected in its global minimum of $\sim 180^\circ$.

Substitution of the ring system in any way removes the symmetry plane in the scaffold of Library **I**, therefore, all catalysts (except Library **I**), consist of at least six diastereomeric conformers. Because only one or two of these conformers are highly populated, in any projections or analysis from this point on the lowest energy conformer of the ring system will be depicted. The remaining three variable groups each reside in different faces of the central ammonium nitrogen (R¹ and R²). The R¹ and R² groups are placed directly on the right and left convex faces, and the R³ group resides in the concave face of the scaffold (see Figure 12).

2. Summary of Results

A brief summary of the rate and enantioselectivity data is necessary to facilitate the following discussion. The kinetic results are summarized in bar graph format in Figure 10. In general,

- Catalysts that bear an oxygen substituent at C(1) are more active than catalysts without.
- The configuration of the oxygen functional group does not influence the catalyst activity.
- Ethers are more active than the corresponding alcohols.
- Strong electron withdrawing groups (e.g. R⁴ = (3,5-CF₃)₂C₆H₃) on nitrogen decrease catalyst activity.
- Less dependence on the nitrogen substituent was observed when R² was aromatic (Ph, mesityl, 1-naphthyl).
- The catalytic activities of the unfunctionalized ring systems are not as high as tetraethylammonium but better than cetyltrimethyl ammonium in activity.

Given the large volume of data presented herein, a concise statistical summary provides a good indication of which data is the most interesting and worthy of detailed analysis. The relative contribution of the groups to the variation in the observed data is estimated by examining the standard deviation as a function of each group (R¹–R⁴).⁸³ That is, the larger deviation in the observed rate (or selectivity) as a function of group positional substitution, then the greater is the relationship of that substituent (R²–R⁴) to the observed effect (rate or selectivity, Figure 11). Therefore, the variation approximates the sensitivity of the rate and

selectivity to a structural change at the indicated substituent. Both catalyst activity and rate are influenced the most by the groups R^2 and R^4 , with the greatest dependence on R^4 . Also, in both cases, the R^3 group has the least influence. The R^1 group was not sufficiently varied for interpretation by this analysis.

3. Catalyst Activity

3.1 Effect of an Oxygen Substituent—The presence of an oxygen at C(1) is a natural consequence of the tandem cycloaddition utilized to construct the scaffolds. Indeed, a β -oxygen substituent is a common structural motif employed in many asymmetric quaternary ammonium phase transfer catalysts including the *cinchona* alkaloids.⁸⁴ Inclusion of an oxygen substituent β to the ammonium center strongly affects the catalytic activity (compare Libraries **I** and **II**), which has previously been reported for other catalyst systems.^{85,86} A more quantitative treatment of β -oxygen substitution is presented in the accompanying paper, but a qualitative analysis, as follows, is required to analyze the differences in catalyst activity in this data set.

Introduction of an oxygen atom two carbons removed from the ammonium center results in two related electronic effects: (1) it influences the direction of the dipole and (2) it modulates the magnitude of positive electrostatic potential interaction (δ^+). The electrostatic potential maps of the oxygenated and unoxygenated catalyst scaffolds are compared in Figure 12. In the C_s symmetric ammonium salts (Library **I**), the charge distribution is equally dispersed between the two convex faces. In contrast, inclusion of an alkoxy group two carbons removed from the ammonium nitrogen results in a considerable polarization of the positive potential toward the face to which it is attached (Library **II**, methoxy is included for simplicity). In Library **II** type ammonium ions the two convex faces are differentiated electronically, placing a greater positive potential on the left face. Similarly, the dipole vector in the Library **I** type ammonium ions bisects the R^4 substituent but is rotated $\sim 60^\circ$ clockwise in the Library **II** ammonium ions projecting the positive end toward the left convex face of the ammonium ion,

This analysis is consistent with a stronger electrostatic interaction with the left convex face than the right, which, in turn, is consistent with the experimentally observed fact that the R^2 substituent has a large effect on the observed rate and selectivity. Since both rate and selectivity are highly dependent on the R^2 group and little to no selectivity is observed when $R^1 = H$, our data seems most consistent with a selective “docking” of the enolate to the left convex face of the ammonium. That is, the oxygen serves to increase the positive potential on the left convex face and the R^1 group acts to sterically shield the right convex face of the ammonium ion.

3.2. Accessibility of the Ammonium Ion—The catalytic activity of PTC alkylation processes has been correlated with the accessibility of the ammonium nitrogen (in terms of q), where an optimum accessibility is found.⁴⁹ The observation of a maximum catalyst activity as a function of ammonium accessibility has two similar explanations. In the first, the accessibility of the ammonium nitrogen is related to the rate of exchange of anions, a kinetic phenomenon.⁴⁷ In the second, the accessibility of the ammonium nitrogen is related to the ability of the catalyst to decrease the interfacial tension and thereby facilitate enolate transfer, a thermodynamic phenomenon.^{46,87}

The data collected herein are largely consistent with these proposals, with the added complexity that the magnitude of the exposed positive potential (δ^+) should be considered as well. On the basis of the analysis above, the accessibility of the positive potential (δ^+ , left convex face) should be correlated with the steric bulk of the R^2 substituent. The sensitivity

of the catalytic activity to the R^2 substituent discussed above (Figure 11) advocates a strong dependence of the overall catalyst activity on the nitrogen accessibility (steric nature of R^2).

The dependence of the catalytic activity on the size of the R^2 substituent and electron withdrawing ability of the R^4 substituent is summarized tabularly in Table 7 (MR = molar refractivity).⁸⁸ The dependence is weak when the electronic character of R^4 is neutral or electron rich ($R^4 = C_6H_5$, 4-MeOC₆H₄), but strong when R^4 is strongly electron withdrawing (3,5-(CF₃)₂C₆H₃). In these catalysts an increase in the size of the R^2 substituent (Me to *i*-Pr to *t*-Bu, to Ph) leads to a significant rate enhancement, which is somewhat attenuated for larger aromatic groups (mesityl or naphthyl). This disparity may be rationalized by ammonium accessibility, such that catalysts with $R^2 = Ph$ have an optimum accessibility.

Rationalizing the effect of the R^2 substituent in terms of steric bulk makes intuitive sense because placing groups in this position modulates the relative accessibility of the positive potential at the two convex faces. However, other explanations are possible. For example, if the major structural perturbation of replacing a branched aliphatic group with an aromatic group is the introduction of a π -surface then the increase in catalyst activity could be caused by an affinity of catalyst for substrate (through π - π interactions). In this scenario, a shift in the equilibrium between catalyst⁺X⁻ (Br⁻ or HO⁻) and catalyst⁺enolate⁻ ion pair toward the enolate complex would be the origin of the net increase in observed catalyst activity.

Most consistent with the above analysis of charge polarization, the 3,5-(CF₃)₂C₆H₃ group must impart sufficient charge polarization to amplify the effect of the variable R^2 group. Interpretation of these observations in the context of a transfer rate limiting regime has led to the conclusion that an optimum ammonium accessibility, or charge exposure is likely. In other words, a greater charge exposure will increase the ammonium ions association with the anionic hydroxide surface. However, if the exposed δ^+ area or charge density is too great, then the catalyst will not dissociate away from the interface as readily.

3.3. Summary of Catalyst Activity Discussion—Three important elements can be inferred from the discussion of rate:

1. the observed increase in catalyst activity upon the inclusion of an oxygen substituent is attributed to the increase in the rate of ion pair formation and/or a decrease in interfacial tension
2. the observed decrease in catalyst activity upon the inclusion of the 3,5-(CF₃)₂C₆H₃ group at R^4 for small groups at R^2 (H, Me, *i*-Pr) is attributed to a diminished tendency of the ion-pair to transport from the interface to the organic phase for alkylation due to greater charge density at the ammonium center.
3. the observed increase in catalyst activity upon the inclusion of aryl groups at R^2 with $R^4 = 3,5-(CF_3)_2C_6H_3$ is attributed to an enhanced ability of the ion-pair to transport from the interface into the organic phase for alkylation because of an optimum surface exposure of the ammonium ion (kinetic) or a change in enolate binding equilibrium (thermodynamic).

4. Enantioselectivity

The intermolecular forces that have been proposed to contribute to enantioselectivity in APTC reactions include: (1) ROH $\cdots$ O-CR=CR₂ hydrogen bonding^{20a,c} (2) R₃N⁺-CHR-H $\cdots$ O-CR=CR₂ (α -CH hydrogen bonding)^{51b} (3) π - π interactions.^{20a,c} The most selective catalysts in this study do not contain OH hydrogen bond donating sites, therefore

intermolecular force (1) can be eliminated as a stereocontrolling element. The results here support the operation of interactions (2) and potentially (3).

The unique structural features of the catalyst scaffold include the intrinsic shielding of two of the four faces of the imaginary tetrahedron encompassing the nitrogen and the capacity to differentiate the two remaining exposed faces (c.f. Figure 12). The second feature arises from the modular nature of the cycloaddition-based construction which allows both exposed front faces to be differentiated electronically (β -oxygenation) and sterically (relative steric bulk of R^1 and R^2). Although those factors that control the topicity of the enolate reactivity are difficult to predict, the factors that dictate the relative binding strengths of the enolate to each of the tetrahedral faces are more easily controlled and predicted. Initially, these factors were the primary focus for the design and construction of the libraries.

The observed enantioselectivities are largely dependent on the substituents that influence the binding of the anion to the face of the hypothetical tetrahedron around the ammonium ion with the largest concentration of positive potential (R^2 and R^4 , Figure 12). The observation that the enantioselectivity is greatest for catalysts that bear strongly electron withdrawing groups on the nitrogen is consistent with the need for one or both of the following potential interactions: (1) α -CH-hydrogen bonding or (2) a tighter ion pair resulting from increased Coulombic interaction. Additionally, a π -surface is necessary at the R^2 substituent, presumably to engage in π -stacking interactions with the phenyl rings of the reacting enolate. Moreover, the presence of an alkyl group at R^1 is necessary to decrease the accessibility of the right hand face of the pyrrolizidine moiety because in its absence, the enantioselectivity is poor. This observation suggests that binding to the right hand face leads to lower selectivity because of the pseudo-enantiotopic local chirality. The aforementioned interactions seem to operate in concert as the absence of one of the interactions leads to significantly diminished enantioselectivities.

Conclusions

A synthetic strategy for the synthesis of diverse libraries of quaternary ammonium ions has been developed. The key feature of the synthetic strategy was to divide the preparative work into two distinct stages: (1) scaffold preparation and (2) diversity oriented parallel synthesis. In this way, a total of 160 structurally diverse quaternary ammonium ions were prepared that share a common scaffold constructed by a tandem inter[4+2]/intra[[3+2] cycloaddition of a nitroalkene. A method was developed for the collection of kinetic data of a biphasic reaction that is applicable over a wide range of catalyst activities (half-lives ranging from days to minutes). The range of data collected covers many orders of magnitude and therefore is well suited for analysis by the application of quantitative structure-activity relationships. Inclusion of an oxygen atom in the vicinity of the quaternary ammonium ion affects the catalytic activity. The catalyst enantioselectivity is strongly dependent on the substituent attached to the same carbon as the oxygen atom. These observations were rationalized in terms of a selective polarization of the positive potential on one of the faces of the tetrahedral ammonium over the other. The inclusion of a 3,5-substituted aromatic substituent on nitrogen proved crucial for catalyst enantioselectivity. With strongly electron withdrawing 3,5- tri-fluoromethyl groups, the previously observed dependencies on rate were amplified. The proposed dependencies of rate on the ammonium accessibility are consistent with the data reported herein with the added complexity that the magnitude of the "ammonium charge" or charge density should be considered as well. Quantitative models have been developed to describe both the reactivity and selectivity trends discussed herein and constitute the focus of the following paper.

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For General experimental details and literature preparations see the Supporting information.

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I. Preparative Studies: Tandem Cycloaddition Precursors and Scaffolds

A. Scale up of Alcohol (**Z**)-6

Preparation of Trimethyl(4,5,6,7-tetrahydrooxepin-2-yloxy)silane (S1**):** A jacketed 500-mL, three-necked, liquid addition flask fitted with a nitrogen inlet adaptor, and two rubber septa was fitted to a 1-L, two-necked, round-bottomed flask fitted with a magnetic stir bar, a rubber septum and an internal temperature probe (through rubber septum). To the addition flask was added diisopropylamine (36.5 mL, 209 mmol, 1.3 equiv) and THF (300 mL). The resulting solution was cooled to -78°C (bath temp) by addition of an acetone/ $\text{CO}_2(\text{s})$ bath to the jacket reservoir. Then, *n*-butyllithium (2.56 M in hexanes, 81.8 mL, 1.3 equiv) was added dropwise over 20 min. To the 1-L, two-necked, flask was added ϵ -caprolactone (18.4 g, 161 mmol), THF (150 mL) and trimethylsilyl chloride (26.5 mL, 209 mmol, 1.3 equiv) via syringe. The reaction vessel was brought to $< -80^{\circ}\text{C}$ by immersion in a hexanes/ N_2 bath. The freshly generated solution of LDA (above) was added dropwise at a rate that maintained an internal temperature $< -75^{\circ}\text{C}$ (ca. 1 h). The resulting turbid solution was allowed to warm to -25°C , and was then concentrated by rotary evaporation (15 mm Hg, 20 – 25°C). The resulting mixture was triturated with pentane (~ 100 mL) and filtered (Celite). The filtrate was again concentrated by rotary evaporation (15 mm Hg, 20 – 25°C). Purification by distillation (0.5 mm Hg, 43°C) afforded ketene acetal **S1** (24.8 g, 83%) as a clear colorless oil. The data collected was consistent with that previously reported.⁸⁹ Data for **S1**: bp: 58 – 60°C (2 – 3 mm Hg); $^1\text{H-NMR}$ (500 MHz, CDCl_3) 4.12 (t, $J = 5.9$, 1 H, HC(3)), 3.99 (dd, $J = 5.4$, 5.6, 2 H, $\text{H}_2\text{C}(7)$), 2.02 (dd, $J = 5.9$, 11.6, 2 H, $\text{H}_2\text{C}(4)$) 1.83 (ddd, $J = 5.7$, 10.7, 11.5, 2 H, $\text{H}_2\text{C}(6)$), 1.65–1.59 (m, 2 H, $\text{H}_2\text{C}(5)$), 0.22 (s, 9 H, $\text{H}_3\text{C}(5')$); $^{13}\text{C-NMR}$ (126 MHz, CDCl_3) 160.0 (C(2)), 83.1 (C(3)), 71.5 (C(7)), 31.3 (C(4)), 26.2 (C(6)), 23.3 (C(5)), 0.16 (C(5')) IR (neat, NaCl plate) 2931 (s), 2837 (m), 1682 (s), 1455 (m), 1355 (m); MS (ESI, Q-tof) 187 (21) [$\text{M}+1$], 171 (38), 147 (14), 132 (12), 129 (13), 117 (30), 75 (100), 69 (32), 55 (23), 54 (23); TLC R_f 0.77 (hexanes/ Et_2O , 4:1) [UV, KMnO_4].

Preparation of 6,7-dihydro-5H-oxepin-2-one (S2**):** To a 1.0-L, one-necked, round-bottomed flask fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet

adapter, fitted with a rubber septum, was added sequentially, palladium(0)bis(dibenzylidene)acetone (309 mg, 0.537 mmol, 0.01 equiv), allyl methyl carbonate (12.2 mL, 107 mmol, 2.0 equiv), and acetonitrile (268 mL). Silyl ketene acetal **S2** (1.0 g, 21.5 mmol) was then added via syringe. The resulting solution was placed in an oil bath pre-heated to 40 °C and allowed to stir. After being stirred for 30 min at 40 °C, the reaction mixture was removed from the oil bath and allowed to cool to room temperature. The solution was concentrated to approximately one-quarter of the total volume (~70 mL). This solution was passed through a plug of silica gel (20 mm × 5 cm) using hexanes/Et₂O (1:4, 3 × 50 mL). The filtrate was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) to afford 5.13 g (97%) of **S2** as a pale-yellow oil. This material is carried on to the next step without further purification. The data collected was consistent with that previously reported.⁹⁰ Data for **S2**: bp 70 °C (0.1 mm Hg); ¹H-NMR (500 MHz, CDCl₃) 6.41 (td, *J* = 4.4, 12.1, 1 H, HC(4)), 5.98 (d, *J* = 12.4, 1 H, HC(3)), 4.28 (m, 2 H, H₂C(7)), 2.50 (dd, *J* = 5.4, 10.2, 2 H, H₂C(5)), 2.12 (td, *J* = 6.6, 12.9, 2 H, H₂C(6)); ¹³C-NMR (126 MHz, CDCl₃) 169.2 (C(2)), 144.0 (C(4)), 121.9 (C(3)), 67.3 (C(7)), 30.1 (C(5)), 27.0 (C(6)); TLC *R*_f 0.20 (pentane/MTBE, 1:1) [KMnO₄].

Preparation of (Z)-Methyl 6-Hydroxy-2-hexenoate ((Z)-S3): To a 100-mL, one-necked, round-bottomed flask fitted with a rubber septum, a large magnetic stir bar, and a nitrogen inlet adaptor, was added ester **S2** (4.5 g, 40.1 mmol) *via* syringe. Methanol (80 mL) was then added followed by potassium carbonate (554 mg, 4 mmol, 0.1 equiv). The suspension was stirred vigorously for 20 min, during which the solution gradually became opaque. The resulting suspension was poured into a 500-mL separatory funnel containing water (100 mL) and diluted with dichloro-methane (100 mL). The layers were separated and the aqueous was extracted with dichloromethane (5 × 50 mL). The combined organic extracts were dried (MgSO₄), filtered (cotton plug), and concentrated *via* rotary evaporation (15 mm Hg, 20–25 °C). The resulting clear oil was filtered through a small plug of silica gel (1.8 cm × 2 cm) with 25 mL EtOAc to remove any remaining base impurities. Concentration of the resulting solution yielded 5.19 g (89%) of geometrically pure (Z)-S3 as determined by ¹H-NMR analysis. The data collected was consistent with that previously reported.⁹¹ Data for (Z)-S3: ¹H-NMR (500 MHz, CDCl₃) 6.24 (td, *J* = 8.3, 11.5, 1 H, HC(4)), 5.87 (td, *J* = 1.4, 11.5, 1 H, HC(5)), 3.72 (s, 3 H, H₃C(7)), 3.61 (t, *J* = 5.9, 2 H, H₂C(1)), 2.74 (dt, *J* = 1.4, 8.2, 2 H, H₂C(C(3))), 1.73 (td, *J* = 8.3, 11.5, 1 H, H₂C(2)); ¹³C-NMR (126 MHz, CDCl₃) 167.5 (C(6)), 149.8 (C(4)), 120.2 (C(5)), 61.1 (C(1)), 51.3 (C(7)), 31.2 (C(2)), 25.1 (C(3)); IR (neat) 3423 (br), 2950 (m), 2870 (m), 2343 (w), 2361 (w), 1723 (s), 1645 (m), 1439 (s), 1408 (m), 1202 (s), 1173 (s); MS (ESI, Q-tof) 167(100), 145(35), 127(15); TLC *R*_f 0.22 (hexanes/EtOAc, 4:1) [UV, KmnO₄].

Preparation of Methyl (2*Z*,6*E*)-7-Nitro-2,6-octadienoate ((*E,Z*)-1): To a 500-mL, two-necked, round-bottomed flask fitted with a rubber septum and a nitrogen inlet adaptor was added alcohol (*Z*)-**S3** (3.0 g, 20.8 mmol) along with CH₂Cl₂ and DMSO (100 mL each). Triethylamine (17.4 mL, 125 mmol, 6.0 equiv) was added and the flask was immersed in a ice/NaCl(s) bath. Once the internal temperature reached −5 °C, SO₃•pyridine complex was added in a single portion (5.5 g, 31 mmol, 1.5 equiv). After two hours at < 0 °C an additional portion of SO₃•pyridine complex (5.5 g, 31 mmol, 1.5 equiv) was added. After another 2 h the reaction was quenched by pouring into a 500-mL separatory funnel containing 100 mL sat. aq. NH₄Cl. The organic phase was diluted with another 100 mL of CH₂Cl₂ and rinsed with NH₄Cl (3 × 50 mL) followed by CuSO₄ (1 × 50 mL), brine (100 mL) and H₂O (100 mL). The combined organic extracts were dried (MgSO₄), filtered over a silica gel plug (3 × 1 cm) and concentrated to afford 2.98 g (89%) of crude intermediate aldehyde as a light-yellow oil. The aldehyde was carried on directly to nitroalkene (*E,Z*)-1 without further purification as previously described. The data collected was consistent with that previously reported.⁹¹ Data for (*E,Z*)-1: ¹H-NMR: (500 MHz, CDCl₃) 7.10 (t, *J* = 7.8, 1 H, HC(3)), 6.19 (dd, *J* = 8.2, 10.9, 1 H, HC(6)), 5.85 (d, *J* = 11.4, 1 H, HC(7)), 3.70 (s, 3 H, H₃C(9)), 2.84 (dq, *J* = 1.6, 7.6, 2 H, H₂C(4)), 2.38 (m, 2 H, H₂C(5)), 2.16 (s, 3 H, H₃C(1)); ¹³C-NMR: (126 MHz, CDCl₃) 166.4 (C(8)), 147.1 (C(2)), 134.6 (C(6)), 121.1 (C(3)), 51.2 (C(7)), 27.3 (C(9, 1)), 12.5 (C(4,5)); IR: (neat) 3054 (w), 2987 (w), 2954 (w), 2254 (m), 1719 (s), 1650 (m), 1521 (s), 1440 (m); MS: (EI, 70eV) 197 (5), 182 (12), 168 (25), 150 (42), 149 (45), 93 (100), 91; TLC: *R*_f 0.57 (hexanes/EtOAc, 4:1) [UV, KMnO₄].

Preparation of Methyl (2*E*,6*E*)-7-Nitro-2,6-octadienoate ((*E,E*)-1): To a 1-L, three-necked, round-bottomed flask fitted with two rubber septa and a nitrogen inlet adaptor and an internal temperature probe (through a septum) was added alcohol (*E,E*)-**S3** (21 g, 147 mmol) along with CH₂Cl₂ and DMSO (147 mL each). Triethylamine (12 mL, 874 mmol, 6.0 equiv) was added and the flask was immersed in a ice/NaCl(s) bath. Once the internal temperature reached −5 °C, SO₃•pyridine complex was added in a single portion (29.4 g, 184 mmol, 1.25 equiv). After two hours at < 0 °C an additional portion of SO₃•pyridine complex (29.4 g, 184 mmol, 1.25 equiv) was added. After another 2 h the reaction was quenched by pouring into a 1-L separatory funnel containing 200 mL sat. aq. NH₄Cl. The organic phase was diluted with 150 mL of Et₂O and rinsed with NH₄Cl (3 × 100 mL) followed by CuSO₄ (2 × 100 mL), brine (100 mL) and sat. aq. NaHCO₃ (100 mL). The combined organic extracts were dried (MgSO₄), filtered over a silica gel plug (3 × 1 cm) and concentrated to afford the crude aldehyde as a light-yellow oil. The aldehyde was carried on directly to the nitroalkene without further purification as previously described to give 22.9 g (80%) of nitroalkene (*E,E*)-1 as a light-yellow oil. The data collected was consistent with that previously reported.⁹¹ Data for (*E,E*)-1: ¹H-NMR: (500 MHz, CDCl₃) 7.14 (t, *J* = 7.7, 1 H, HC(6)), 6.19 (td, *J* = 11.4, *J* = 7.6, 1 H, HC(3)), 5.85 (d, *J* = 11.9, 1 H, HC(2)), 3.70 (s, 3 H, H₃C(9)), 2.85 (m, 2 H), 2.38 (m, 2 H), 2.16 (s, 3 H, H₃C(8)); ¹³C-NMR: (126 MHz, CDCl₃) 166.5 (C(8)), 148.4 (C(2)), 146.2 (C(6)), 133.9 (C(3)), 122.5 (C(7)), 51.6 (C(9)), 26.5 (C(4)), 22.4 (C(5)), 12.6 (C(1)); IR: (neat) 2992 (w), 2953 (w), 2843 (w), 2255 (m), 1721 (s), 1662 (m), 1523 (s), 1438 (m), 1391 (m), 1334 (s), 1284 (m), 1213 (m), 1173 (m), 1042 (w), 971 (w), 906 (s); TLC: *R*_f 0.6 (hexanes/EtOAc, 4:1) [UV, KMnO₄].

Preparation of (1*R*,2*S*)-2-Phenylcyclohexyloxyethene (2): To a 250-mL, one-necked, round-bottomed flask, fitted with a drying tube containing calcium chloride with a reflux condenser attached open to air and a magnetic stir bar, was added sequentially, *n*-butyl vinyl ether (110 mL, 851 mmol, 30 equiv), alcohol (1*R*,2*S*)-2-phenylcyclohexanol⁹² (5.0 g, 28.4 mmol), followed by palladium(II) acetate-1,10-phenanthroline (115 mg, 0.284 mmol, 0.01 equiv). The flask was immersed in an oil bath and heated to 65 °C over 4 h. After stirring for 3 days, the reaction was allowed to cool to room temperature and concentrated to ½ of the total volume (~50 mL) by rotary evaporation (15 mm Hg, 20–25 °C). The resulting solution was filtered over a plug of silica gel (40 mm × 4 cm) and rinsed with hexanes/EtOAc/Et₃N (49:49:2, 3 × 30 mL) and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting pale-yellow oil was purified by silica gel column chromatography (4 cm × 10 cm, gradient elution, hexanes/EtOAc/Et₃N, 49:0:1, 48:1:1, 47:2:1, 44:5:1, 250 mL each) to afford 4.3 g (74%) of **2** as a colorless oil along with 1.2 g of recovered (1*R*,2*S*)-2-phenylcyclohexanol. The data collected was consistent with that previously reported.⁹¹ Data for **2**: bp: 85 °C (0.1 mm Hg); ¹H-NMR: (500 MHz, CDCl₃) 7.31–7.16 (m, 5 H), 6.05 (dd, *J* = 14.1, 6.5, 1 H, HC(1')), 4.11 (dd, *J* = 14.0, 1.1, 1 H, HC(2')), 3.84 (dt, *J* = 10.3, 4.5, 1 H, HC(1)), 3.77 (dd, *J* = 6.6, 1.1, 1 H, HC(2')), 2.65 (dt, *J* = 11.8, 3.5, 1 H, HC(2)), 2.25–2.20 (m, 1 H), 1.94–1.86 (m, 2 H), 1.78–1.74 (m, 1 H), 1.58–1.34 (m, 4 H); ¹³C-NMR: (126 MHz, CDCl₃) 151.1 (C(1')), 143.7 (C(7)), 128.2 (C(9)), 127.6 (C(8)), 126.2 (C(10)), 87.4 (C(2')), 81.8 (C(1)), 50.3 (C(2)), 34.1 (C(6)), 32.1 (C(3)), 25.9 (C(4)), 24.8 (C(5)); IR: (neat) 3031 (w), 2936 (s), 2859 (m), 1632 (s), 1559 (w), 1495 (w), 1449 (m), 1356 (w), 1183 (s), 1119 (m), 1076 (s), 818 (s); MS: (EI, 70 eV) 202 (100), 160 (3), 159 (28), 158 (11), 91 (100), 81 (17), 67 (8), 55 (6); TLC: *R*_f 0.90 (hexanes/Et₂O, 9:1) [*I*₂].

C. Scaffold Preparation by Tandem Cycloaddition of Nitroalkenes

1. Preparation of Scaffold for Library I:

Preparation of *rel*-(1*S*,3*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-7*b*-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one ((+/-)-4a): To a 50-mL, three-necked, round-bottom flask fitted with two rubber septa, a magnetic stir bar, a nitrogen inlet adaptor and an internal temperature probe, was added nitroalkene (*E,E*)-**1** (1.0 g, 5 mmol) followed by CH₂Cl₂ (20 mL). The internal temperature was brought to –60 °C by immersion in acetone/CO₂(s) bath. Then a Me₃Al was added (6.3 mL of a 2 M solution in toluene, 12.5 mmol, 2.5 equiv) via syringe followed by *n*-butyl vinyl ether (1.25 mL, 12.6 mmol, 2.5 equiv). The resulting bright yellow solution was allowed to stir at for 6 h, during which time the yellow color gradually faded. The reaction was quenched by the cautious addition of silica gel (ca. 2 g) via a long stem funnel until no bubbling was observed. The mixture was then poured into

a funnel containing more silica gel (~3 g, prewetted with EtOAc) and rinsed with ethyl acetate (200 mL). The resulting clear solution was dried (MgSO_4) to remove any adventitious water, filtered, and concentrated by rotary evaporation (15 mm Hg, 20–25 °C) to give a clear viscous oil. The intermediate nitronate was diluted with 50 mL of toluene and transferred to a 100-mL round-bottomed flask. The flask was fitted with a nitrogen inlet adaptor and NaHCO_3 was added (420 mg, 5 mmol, 1.0 equiv) along with a stir bar. The suspension was allowed to stir at room temperature for 7 h, then filtered and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting mixture of nitroso acetals was diluted in EtOAc/MeOH (9/1, 25 mL) and added to a test tube (6 cm $\times$ 14 cm) containing a spatula tip (~100 mg) of Raney Ni (previously washed with H_2O , MeOH, and EtOAc, 2 $\times$ 15 mL each) along with a magnetic stir bar. The tube was placed in a steel autoclave, which was then pressurized with H_2 (350 psi) and allowed to stir for 2 days. After 2 days the autoclave was *carefully* vented in a fume hood and the solution was filtered through a plug of Celite (5 cm $\times$ 5 cm) with EtOAc (200 mL). The resulting clear filtrate was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) and purified by silica gel column chromatography (2 cm $\times$ 6 cm, $\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 19:1, 10:1, 1:1, 100 mL each) to afford 778 mg (86%) of the racemic α -hydroxy lactam **4a** as a white powder. The data collected was consistent with that previously reported.⁹¹ Data for **4a**: mp: 108–115 °C; ^1H -NMR: (500 MHz, CDCl_3) 4.67 (d (br), J = 7.2, 1 H, HC(2)), 3.91 (ddd, J = 3.8, J = 8.5, J = 12.1, 1 H, HC(8)), 2.94 (ddd, J = 7.9, J = 8.1, J = 11.9, 1 H, HC(8)), 2.71–2.66 (m, 1 H, HO), 2.64 (dd, J = 7.5, J = 14.9, 1 H, HC(7a)), 2.28 (ddd, J = 4.9, J = 7.5, J = 12.5, 1 H, HC(5a)), 2.13 (ddd, J = 3.8, J = 8.0, J = 11.9, 1 H, HC(5)), 1.80 (m, 1 H, HC(5)), 1.72 (m, 2 H, HC(7), HC(5a)), 1.50 (m, 1 H, HC(7)), 1.33 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.27 (ddd, 1 H, J = 5.7, J = 10.6, 10.6, HC(6)); ^{13}C -NMR: (126 MHz, CDCl_3) 176.4 (C(2)), 75.5 (C(7b)), 72.8 (C(1)), 51.0 (C(7a)), 49.1 (C(5a)), 42.0 (C(4)), 31.4 (C(6)), 30.9 (C(7)), 24.8 (C(5)), 22.8 (C(8)); IR: (NaCl plate) 3283 (s, br), 2961 (s), 2860 (s), 1697 (s), 1677 (s), 1653 (s); MS: (ESI, Q-tof) 182 (13), 181 (99), 167 (11), 166 (100), 163 (10), 162 (15), 138 (56), 111 (17), 110 (16), 107 (26), 96 (27), 82 (33), 81 (26), 67 (21), 56 (29), 55 (37), 53 (18); TLC: R_f 0.20 (hexane/EtOAc, 4:1) [I_2 , KMnO_4].

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-oxo-

[(phenoxythiocarbonyl)oxy]-7*b*methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one ((+/-)-8**):** To a 50-mL, single-necked, round-bottomed flask fitted with a nitrogen inlet, a rubber septum, and a magnetic stir bar was added racemic α -hydroxy lactam **4a** (215 mg, 1.2 mmol) followed by dimethylaminopyridine (72 mg, 0.59 mmol, 0.5 equiv) and CH_2Cl_2 (17 mL). Lastly, pyridine (202 μL , 2.4 mmol, 2.0 equiv) was added followed by phenylchlorothionoformate (330 μL , 2.4 mmol, 2 equiv), both via syringe. The resulting light-yellow solution was stirred for 4 h at room temperature during which time it gradually became darker. The solution was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) and the residue was purified by silica gel column chromatography (2 cm $\times$ 10 cm, hexane/EtOAc, 4:1). Hot filtration followed by recrystallization hexanes/ CH_2Cl_2 (25:1, ~20 mL) afforded 294 mg (78%) of **8** as colorless rhomboids. Data for **8**: mp: 100–101 °C; ^1H -NMR: (500 MHz, CDCl_3) 7.42 (m, (second order), 2 H, HC(4')), 7.30 (dt (second order), J = 1.2, 7.2, 1 H, HC(5')), 7.14 (m, 2 H, HC(3')), 6.12 (dd, J = 1.0, 7.3, 1 H, HC(1)), 4.02 (ddd, J = 3.8, 8.6, 12.2, 1 H, HC(4)), 3.01 (m, 2 H, HC(4), HC(7a)), 2.34 (m, 1 H, HC(5a)), 2.18 (et, J = 3.8, 8.1, 8.1, 11.9, 1 H, HC(7)), 1.86 (ddd, J = 7.6, 7.6, 12.8, 1 H, HC(7 or 6)), 1.78 (m, 2 H, HC(5), HC(6)), 1.59 (et, J = 4.8, 8.2, 8.2, 13.0, 1 H, HC(5)), 1.39 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.37

(d, $J = 5.7$, 1 H, HC(6)); ^{13}C -NMR: (126 MHz, CDCl_3) 194.5 (C(1')), 169.8 (C(1)), 153.4 (C(2')), 129.5 (C(4')), 126.6 (C(5')), 121.8 (C(3')), 82.6 (C(2)), 75.6 (C(9)), 49.5 (C(3)), 48.7 (C(6)), 42.5 (C(8)), 31.4 (C(7)), 30.9 (C(4)), 25.7 (C(5)), 23.2, (C(10)); IR: (CH_2Cl_2 , film) 2966 (w), 2252(m), 1706 (s), 1490 (m), 1278 (s), 1208 (s); TLC: R_f 0.78 (hexanes/EtOAc, 1:1) [UV, KMnO_4]; HRMS: $\text{C}_{17}\text{H}_{19}\text{O}_3\text{NS}$ (317.10857); Calcd: 317.10857; Found: 317.10814. Analysis: $\text{C}_{17}\text{H}_{19}\text{O}_3\text{NS}$ (317.11); Calcd: C, 64.33; H, 6.03; N, 4.41%; Found: C, 64.44; H, 6.00; N, 4.50%.

Preparation of (3*S*,5*aS*,7*aR*,7*bR*)-Octahydro-7*b*-methyl-2*H*-cyclopenta[*gh*]-pyrrolizin-2-one ((+/-)-9**):** Thionocarbonate **8** (140 mg, 0.59 mmol) in benzene (40 mL) was added to a one-necked, round-bottomed flask *via* syringe which was fitted with a reflux condenser and a magnetic stir bar. Atop the reflux condenser was fitted a nitrogen inlet adaptor and a rubber septum. The round-bottomed flask was immersed in a preheated (100 °C) oil bath and allowed to come to reflux (~20 min). During this time, tributyltin hydride (1.08 mL, 0.77 mmol, 1.3 equiv) and AIBN (206 μL , 0.12 mmol, 0.2 equiv) were added to a separate, 25-mL, one-necked, conical flask along with 15 mL of benzene and a magnetic stir bar. Once the round-bottomed flask reached reflux, the tributyltin hydride AIBN solution was transferred dropwise *via* cannula over 3.5 h, maintaining a consistent gentle reflux. The resulting solution was allowed to reflux for an additional 2 h and then cooled to room temperature. Potassium fluoride (3.0 g, 51.6 mmol) was added to the resulting light-yellow solution and the resulting mixture was allowed to stir for an additional 3 h. The suspension was filtered (cotton plug) and the filtrate was concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The residue was purified by silica gel column chromatography (3 cm $\times$ 10 cm, hexane/EtOAc, 1:0, 9:1, 4:2, 7:3, 3:2 1:1, 50 mL each) with a plug of KF to afford 82.1 mg (83%) of lactam **9** as a colorless oil. Data for **9**: bp: 80 °C (0.1 mm Hg); ^1H -NMR: (500 MHz, CDCl_3) 3.88 (ddd, $J = 3.6$, 8.6, 12.0, 1 H, HC(4)), 2.94 (dd, $J = 8.0$, 16.6, 2 H, HC(1), HC(4)), 2.28 (dd, $J = 7.8$, 13.9, 1 H, HC(5*a*)), 2.15 (m, 3 H, HC(7*a*), HC(1), HC(7 or 6)), 1.94 (ddd, $J = 7.2$, 7.2, 20.6, 1 H, HC(5)), 1.76 (ddd, $J = 6.8$, 13.5, 13.6, 1 H, HC(7)), 1.62 (m, 2 H, HC(5), HC(7 or 6)), 1.42 (m, 1 H, HC(7 or 6)), 1.30 (s, 3 H, $\text{H}_3\text{C}(8)$); ^{13}C -NMR: (126 MHz, CDCl_3) 176.6 (C(2)), 79.1 (C(7*b*)), 48.5 (C(7*a*)), 44.1 (C(5*a*)), 42.2 (C(4)), 40.3 (C(1)), 33.3 (C(5)), 32.2 (C(6)), 31.3 (C(7)), 23.0 (C(8)); IR: (neat) 3019 (s), 2957 (m), 2865 (w), 2400 (m), 1676 (m), 1521 (m), 1400 (w), 1215 (s); MS: (ESI, Q-tof) 167 ($\text{M}^+ + 1$, 12), 166 (M^+ , 100); Mol. Formula: $\text{C}_{10}\text{H}_{15}\text{NO}$ (165.23); HRMS: $\text{C}_{10}\text{H}_{15}\text{NO}$: (165.1232); Calcd: 166.1232; Found: 166.1231; TLC: R_f 0.17 (hexanes/EtOAc, 1:1) [KMnO_4].

Preparation of (5*aS*,7*aR*)-Octahydro-7*b*-methyl-cyclopenta[*gh*]pyrrolizine•Borane (10**):** To a 100-mL, one-necked, round-bottomed flask fitted with a rubber septum, and a nitrogen inlet adaptor, was added lactam **15** (1.09 g, 6.6 mmol) and THF (60 mL). The flask was cooled to 0 °C in an ice bath and $\text{BH}_3 \cdot \text{THF}$ complex (3.0 equiv, 1.0 M solution, 7.0 mL) was added dropwise over 10 min (bubbling observed). The cooling bath was removed and the resulting clear solution was stirred for 8 h. The reaction was quenched by the addition of

30 mL of MeOH, and the reaction was concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting thick, glassy oil was purified by silica gel column chromatography (2 cm × 12 cm, hexanes/EtOAc, 10:1, 5:1, 3:1, 200 mL each) to afford 794 mg (80%) of borane complex **10** as a white wax. Data for **10**: ¹H-NMR: (500 MHz, CDCl₃) 3.27 (ddd, *J* = 7.0, 7.0, 11.9, 2 H, HC(2 and 4)), 3.14 (m, 2 H, HC(2 and 4)), 2.30 (m, 2 H, HC(5a), HC(7a)), 2.14 (ddd, *J* = 6.9, 6.9, 15.2, 2 H, HC(1), HC(5)), 1.86 (m, 2 H, CH₂), 1.56 (ddd, *J* = 9.8, 9.8, 10.3, 3 H, CH₂), 1.47 (s, 3 H, HC(8)), 1.26 (m, *J* = 6.6, 13.7, 2 H, CH₂), (0.8–2.5, br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 87.3 (C(7b)), 62.5 (C(2)), 52.2 (C(5a)), 31.9 (C(1)), 28.5 (C(8)), 24.9 (C(6)); IR: (NaCl plates, thin film) (m), 3020 (s) 2971 (w), 292 (w), 2400 (m), 2361 (m), 2326 (m), 1517 (m), 1475 (w), 1425 (w), 1361 (w), 1215 (s), 929 (m), 756 (s), 669 (s); MS: (ESI, Q-tof) 165 (M⁺, 10), 164 (83), 163 (19), 153 (13), 152 (100); Mol. Formula: C₁₀H₂₀BN; (165.08); HRMS: C₁₀H₁₉BN: (164.1611); Calcd: 164.1611; Found: 164.1611; TLC: *R_f* 0.54 (CH₂Cl₂/hexanes, 3:1) [I₂, CAM].

2. Preparation of the Scaffold for Library II:

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-7*b*-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (4a**):** To a 250-mL, three-necked, round-bottom flask fitted with two rubber septa, a magnetic stir bar, a nitrogen inlet adaptor and an internal temperature probe, was added nitroalkene (*E,E*)-**1** (3.68 g, 18.45 mmol) and chiral vinyl ether **2** (5.6 g, 28 mmol, 1.5 equiv) *via* syringe. The flask was then evacuated using high vacuum (~0.1 mm Hg) for 30 min and then was backfilled with N₂ and charged with CH₂Cl₂ (110 mL). The internal temperature was set to –85 °C (hexanes/N₂ bath). This yellow solution was stirred for 15 min, then freshly prepared TiCl₂(*Oi-Pr*)₂ solution⁹⁴ (1.2 M in CH₂Cl₂, 3.0 equiv) was added dropwise *via* syringe at a rate that the internal temperature did not rise above –70 °C (ca. 15 min). After addition of the Lewis acid, the cooling bath was replaced with an acetone/CO₂(s) bath and the resulting bright yellow solution was stirred for another 5 h maintaining an internal temperature ≤ –75 °C. Throughout the reaction the yellow color gradually faded and a white precipitate formed. After 5 h the reaction was quenched with triethylamine (6.1 equiv, 1.0 M in MeOH) *via* syringe maintaining an internal temperature of less than –40 °C. The cooling bath was then removed and the reaction mixture was allowed to warm to 0 °C (ca. 15 min). The resulting white suspension was then diluted with ethyl acetate (100 mL) and poured 1-L separatory funnel containing sat. aq. NH₄Cl (250 mL) and *tert*-butylmethyl ether (100 mL). The layers were separated and the organic phase was washed with sat. aq. NH₄Cl (2 × 50 mL), brine (1 × 100 mL) and sat. aq. NaHCO₃ (1 × 150 mL). The aqueous layers were combined and back extracted with *tert*-butylmethyl ether (3 × 100 mL). The combined organic layers were dried over NaHCO₃/MgSO₄ (1/1), filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting residue was filtered through a pad of silica gel (3 × 3 cm), eluting with ethyl acetate (100 mL) to remove any remaining amine impurities. The resulting clear solution was concentrated (15 mm Hg, 20–25 °C) to a pale-yellow residual oil in a 1-L one-necked, round-bottom flask. *Tert*-Butylmethyl ether (200 mL) was added followed by NaHCO₃ (1.5 g, 1.0 equiv) and a large magnetic stir bar. The flask was fitted with a nitrogen inlet adaptor, evacuated, backfilled with N₂ and allowed to stir at room temperature for 12 h. The suspension was stirred at room temperature for 12 h then filtered through Celite (3 × 3 cm) and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting mixture of nitroso acetals was diluted in EtOAc/MeOH (9/1, 25 mL) and added to a test tube (6 cm × 14 cm) containing a spatula tip (~200 mg) of Raney Ni

(previously washed with H₂O, MeOH, and EtOAc, 2 × 15 mL each) along with a magnetic stir bar. The tube was placed in a steel autoclave, which was then pressurized with H₂ (350 psi) and set on a stir-plate. After stirring for 2 days at room temperature the autoclave was *carefully* vented in a fume hood and the solution was through a plug of Celite (5 cm × 5 cm) with EtOAc (200 mL). The resulting clear solution was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) and purified by silica gel column chromatography (30 mm × 8 mm), CH₂Cl₂/EtOAc, 19:1, 10:1, 1:1, 200 mL each) to afford 2.76 g (76%, 3 steps) of α -hydroxy lactam **4a** as a white powder. The spectroscopic data are in accord with those previously reported.^{91,95} Data for **4a**: mp: 110–114 °C (hexanes/EtOAc); ¹H-NMR: (500 MHz, CDCl₃) 4.69 (d, *J* = 7.2, 1 H, HC(1)), 3.93 (ddd, *J* = 12.0, 8.5, 3.6, 1 H, HC(4)), 2.99–2.93 (m, 1 H, HC(4)), 2.70–2.64 (m, *J* = 7.4, 2 H, HOC(1), HC(7)), 2.33–2.27 (m, 1 H, HC(5a)), 2.18–2.12 (m, 1 H, HC(5)), 1.85–1.70 (m, 3 H, HC(6), H₂C(7)), 1.56–1.42 (m, 1 H, HC(5)), 1.35 (s, 3 H, H₃C(10)), 1.33–1.27 (m, 1 H, HC(6)); ¹³C-NMR: (126 MHz, CDCl₃) 176.6 (C(1)), 75.7 (C(9)), 72.9 (C(2)), 51.2 (C(3)), 49.3 (C(6)), 42.2 (C(8)), 31.6 (C(7)), 31.1 (C(5)), 24.9 (C(4)), 23.0 (C(10)); IR: (CDCl₃, film) 3390 (s), 2961 (s), 2860 (m), 1705 (s), 1325 (s); MS: (ESI, Qtof) 182 (100), 102 (14); Opt. Rot.: [α]_D²⁴ – 35.2, (c = 1.07, CH₂Cl₂): (known (99:1) = –36.9 (c = 1.00, CH₂Cl₂)^{91,95}; TLC: *R*_f 0.20 (hexane/EtOAc, 4:1) [I₂, KmnO₄].

Preparation of (1*S*,3*R*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-7*b*-

methyl-2*H*cyclopenta[*gh*]pyrrolizin•Borane (11a**):** To a 50-mL, two-necked, round-bottomed flask fitted with a rubber septum, a nitrogen inlet adaptor, a magnetic stir bar and an internal temperature probe (inserted through a rubber septum) was added lactam **4a** (181 mg, 1.0 mmol) and THF (1 mL). The flask was cooled to 0 °C in an ice bath, and BH₃•THF complex (5.0 equiv, 1.0 M solution, 5 mL) was added dropwise over 10 min (bubbling observed). The cooling bath was removed and the resulting clear solution was stirred for 2 h. The reaction was quenched by the addition of 20 mL of MeOH and the mixture was concentrated by rotary evaporation (15 mm Hg, 20–25 °C). This process was repeated three more times to afford the crude product as a white solid. Purification by silica gel column chromatography ((2 cm × 7 cm), hexanes/EtOAc, 95:5, 85:15, 3:1, 150 mL each) afforded ~185 mg of **11a**. Recrystallization from hexanes/MTBE (5:1) afforded 175 mg (96%) of the borane complex **11a** as white needles. Data for **11a**: mp: 164–165 °C (MTBE/hexanes); ¹H-NMR: (500 MHz, CDCl₃) 4.75 (dd, *J* = 8.1, 15.3, 1 H, HC(1)), 3.44 (dd, *J* = 6.5, 10.9, 1 H, HC(2)), 3.28 (ddd, *J* = 2.5, 6.7, 12.1, 1 H, HC(4)), 3.16 (dt, *J* = 6.6, 11.7, 1 H, HC(4)), 3.03 (m, 1 H, HC(2)), 2.39 (m, 2 H HC(5a), HC(7a)), 2.07–2.00 (m, 1 H, HC(7)), 1.99–1.90 (m, 1 H, HC(6)), 1.89–1.73 (m, 2 H, HC(6), HC(5)), 1.74–1.58 (m, 2 H, HC(7), HC(5)), 2.10–1.25 (s, broad, 3 H, H₃B), 1.48 (s, 3 H, H₃C(8)); ¹³C-NMR: (126 MHz, CDCl₃) 87.8 (C(7b)), 69.4 (C(1)), 66.0 (C(2)), 63.1 (C(4)), 55.1 (C(7a)), 53.1 (C(5a)), 32.1 (C(5)), 28.0 (C(7)), 26.4 (C(6)), 25.2 (C(8)); IR: (NaCl plate, film) 3018 (m), 2969 (m), 2872 (w), 2367 (m), 2363 (m), 2333 (m), 2276 (w), 1215 (s); MS: (ESI, Q-tof) 180 (42), 167 (21), 152 (100), 96 (59); Opt. rot.: [α]_D²⁴ – 1.74° (c = 1.0, CH₂Cl₂); TLC: *R*_f 0.33 (hexanes/EtOAc, 3:1) [I₂]. Analysis: C₁₀H₂₀BNO (181.08); Calcd: C, 66.33; H, 11.13; N, 7.73; Found: C, 66.05; H, 10.95; N, 7.52.

3. Preparation of Scaffold for Library III:

Preparation of (1R,3S,5aS,7aS,7bR)-Octahydro-1-hydroxy-7b-

methyl-2Hcyclopenta[gh]pyrrolizin-2-one (4b): To a 250-mL, three-necked, round-bottomed flask fitted with two rubber septa, a magnetic stir bar, a nitrogen inlet adaptor and an internal temperature probe, was added nitroalkene (*E,Z*)-**1** (2.0 g, 10.0 mmol) and chiral vinyl ether **2** (3.1 g, 15.1 mmol, 1.5 equiv) *via* syringe. The resulting yellow oil was then evacuated using high vacuum (~0.1 mm Hg) for 30 min. The flask was backfilled with N₂ and charged with CH₂Cl₂ (60 mL). The solution was cooled to -85 °C by immersion in a hexanes/N₂ bath. This cooled yellow solution was stirred for 15 min, then freshly prepared TiCl₂(O-*i*-Pr)₂ solution (1.2 M in CH₂Cl₂, 3.0 equiv) was added dropwise *via* syringe while maintaining an internal temperature < -70 °C (ca. 15 min). After addition of the Lewis acid, the cooling bath was replaced with an acetone/CO₂(s) bath and the resulting bright yellow solution was stirred for another 5 h while maintaining an internal temperature ≤ -72 °C. During the course of the reaction, the yellow color gradually faded and a white precipitate formed. After 5 h, the reaction was quenched with triethylamine (6.1 equiv, 1 M in MeOH) *via* syringe while maintaining an internal temperature < -40 °C. The cooling bath was then removed and the reaction mixture was allowed to warm to 0 °C (ca. 15 min). The resulting white suspension was then diluted with ethyl acetate (50 mL) and poured in a 500-mL separatory funnel containing a bi-phasic mixture of sat. aq. NH₄Cl and MTBE (100 mL each). The biphasic solution was separated and the organic extract was extracted with sat. aq. NH₄Cl solution (2 × 50 mL), H₂O (2 × 50 mL) and brine (2 × 50 mL). The combined aqueous layers were back extracted with MTBE (3 × 75 mL). The combined organic layers were dried over NaHCO₃/MgSO₄ (1/1), filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting residue was filtered through a pad of silica gel (3 × 3 cm), eluting with ethyl acetate (100 mL) to remove any remaining amine impurities. The resulting clear solution was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) to a pale-yellow residual oil in a 1-L one-necked, round-bottomed flask. Hexanes (200 mL) was added followed by NaHCO₃ (4.22 g, 50.0 mmol, 5.0 equiv) and a large a magnetic stir bar. The flask was fitted with a nitrogen inlet adaptor evacuated and backfilled with N₂ and immersed in a preheated 40 °C oil bath. The suspension was stirred at 40 °C (bath temperature) for 30 h then filtered through Celite (3 × 3 cm) and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting mixture of nitroso acetals was diluted in EtOAc/MeOH (9:1, 25 mL) and added to a test tube (6 cm × 14 cm) containing a spatula tip (~200 mg) of Raney Ni (previously washed with H₂O, MeOH, and EtOAc, 2 × 15 mL each) along with a magnetic stir bar. The tube was placed in a steel autoclave, which was then pressurized with H₂ (350 psi). After 2 days the autoclave was *carefully* vented in a fume hood and the solution was filtered through a plug of Celite (5 cm × 5 cm) with EtOAc (200 mL). The resulting clear filtrate was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) and purified by silica gel column chromatography (2 cm × 8 cm, CH₂Cl₂/EtOAc, 19:1, 10:1, 1:1, 100 mL each). Recrystallization from hot hexanes/EtOAc (10:1, ~50 mL) afforded 1.15 g (63%, 3 steps) of analytically pure α-hydroxy lactam **4b** as colorless needles. Data for **4b**: mp: 112–117 °C; ¹H-NMR: (500 MHz, CDCl₃) 4.68 (dd, *J* = 1.2, 7.3, 1 H, HC(1)), 3.90 (ddd, *J* = 3.7, 8.5, 12.0, 1 H, HC(4)), 3.05 (br, 1 H, HOC(1)), 2.93 (ddd, *J* = 1.2, 8.1, 12.0, 1 H, HC(4)), 2.63 (q, *J* = 7.3, 1 H, HC(7a)), 2.25 (m, 1 H, HC(5a)), 2.12 (m, 1 H, HC(5)), 1.79 (m, 1 H, HC(6)), 1.72 (m, 2 H, H₂C(7)), 1.49 (m, 1 H, HC(5)), 1.32 (s, 3 H, H₃C(8)), 1.27 (m, 1 H, HC(6)); ¹³C-NMR: (126 MHz, CDCl₃) 176.2 (C(1)), 75.8 (C(9)), 73.0 (C(2)), 51.2 (C(3)), 49.3 (C(6)), 42.2 (C(8)), 31.5 (C(4)), 31.1 (C(7)), 24.8 (C(8)), 23.0

(C(10)); IR: (KBr plate) 3302 (s, br), 2952 (s), 2864 (s), 1700 (s), 1653 (s); MS: (ESI, Q-tof) 181 (100), 166 (91), 38 (53), 107 (26), 82 (28), 55 (35); TLC: R_f 0.33 (EtOAc/CH₂Cl₂, 1:3) [I₂, KmnO₄]. Analysis: C₁₀H₁₅NO₂ (181.23); Calcd: C, 66.27; H, 8.34; N, 7.65; Found: C, 65.97; H, 8.32; N, 7.65; Opt. Rot: $[\alpha]_D^{24} +50.6$, (c = 1.03, CH₂Cl₂).

Preparation of (1R,3R,5aS,7aS,7bR)-Octahydro-1-[N-(3,5-Dinitrophenyl)carbamoyl]-7b-methyl-2H-cyclopenta[gh]pyrrolizin-2-one (S4): A 25 mL round-bottomed flask (A) was fitted with a reflux condenser, a nitrogen inlet adaptor, a rubber septum and a magnetic stir bar. The apparatus was opened and 3,5-dinitrobenzoyl azide (25 mg, 0.105 mmol, 1.2 equiv) was added as a solid. The apparatus was evacuated and backfilled with N₂ three times and toluene (5.0 mL) was added. The clear solution was immersed in a preheated (115 °C) oil bath and stirred at reflux for 30 min. In a separate, two-neck, 5 mL conical flask (B) fitted with a triangular magnetic stir bar, rubber septum and a nitrogen inlet adaptor the starting alcohol was added (17.2 mg, 0.087 mmol) followed by toluene (1.0 mL). The resulting solution (B) was transferred to flask (A) *via* cannula. The resulting light yellow solution was heated to reflux for 2 h and then allowed to cool to room temperature. The reaction mixture was concentrated *in vacuo*, and the crude product was purified by column chromatography (hexane/EtOAc (3/1, 1/1)) to afford 36 mg (75%) of enantioenriched (S4) as a white solid. The sample was compared to racemate as previously described.^{91,94,95} Data for (S4): ¹H-NMR: (500 MHz, CDCl₃) 9.65 (s, 1 H, HN), 8.71 (d, J = 2.0, 2 H), 8.67 (dd, J = 2.0, 2.0, 1 H), 5.03 (s, 1 H), 3.93 (ddd, 1 H, J = 3.9, 8.7, 12.6), 3.09 (m, 1 H), 2.40 (dd, J = 4.8, 9.0, 1 H), 2.28 (m, 2 H), 2.13 (m, 1 H), 1.87 (m, 2 H), 1.71 (m, 2 H), 1.43 (s, 3 H), 1.28 (m, 5 H), 0.85 (dd, J = 11.2, 13.1, 1 H); ¹³C-NMR: (126 MHz, *d*₇-DMF) 170.7 (C(2)), 152.9 (C(10)), 148.8 (C(11)), 141.8 (C(13)), 117.6 (C(14)), 111.8 (C(12)), 82.4 (C(7b)), 48.4 (C(1)), 50.1 (C(7a)), 48.1 (C(5a)), 41.9 (C(4)), 31.3 (C(6)), 30.9 (C(7)), 23.0 (C(9)); MS: (EI, 70 eV) 405(82), 390(100), 374(12), 187(24), 91(25), 75(40); TLC: R_f 0.32 (hexanes/EtOAc, 3:1) [I₂]; CSF-SFC: t_R = 11.27 min (96%) and 15.73 (4%) (Chiralpak AD, 125 bar, 40 °C, 15 % MeOH in CO₂, 3.0 mL/min, 220 nm).

Preparation of (1R,3R,5aS,7aS,7bR)-Octahydro-1-hydroxy-7b-methyl-2H-cyclopenta[gh]pyrrolizine-borane (11b): To a 100-mL, single-necked, round-bottomed flask fitted with a rubber septum, a magnetic stir bar, and a nitrogen inlet adaptor, was added lactam 4b (170 mg, 0.866 mmol) and THF (60 mL). The flask was cooled in an ice bath and BH₃·THF complex (30 equiv, 1.0 M solution, 9.0 mL) was added dropwise over 10 min (bubbling observed). The cooling bath was removed and the clear solution was stirred for 8 h. The reaction was quenched by the addition of 30 mL of MeOH and the mixture was concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting white solid was redissolved in 15 mL of MeOH (15 mL) and again concentrated by rotary evaporation (15 mm Hg, 20–25 °C). Purification by silica gel column chromatography ((2 cm × 7 cm), hexanes/EtOAc, 1:0, 10:1, 8:1, 5:1, 3:1, 100 mL each) afforded 130.2 mg

(77%) of borane complex **11b** as a white solid. Data for **11b**: mp: 88–91 °C; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 3.89, (br, 1 H, HC(1)), 3.54, (d, $J = 8.7$, 1 H, HO(C(1))), 3.33, (ddd, $J = 12.7$, 2.9, 1.3, 1 H, HC(2)), 3.30, (dd, $J = 12.6$, 5.22, 1 H, HC(4)), 3.19–3.10, (m, 2 H HC(7a), HC(5a)), 2.32–2.25, (m, 2 H, HC(2), HC(4)), 2.02–1.90, (m, 2 H, HC(6), HC(7)), 1.83–1.75, (m, 1 H, HC(6)), 1.55–1.45, (m, 3 H, HC(5), HC(6), HC(7)), 1.51, (s, 3 H $\text{H}_3\text{C}(8)$), 0.8–2.5, (br, 3 H, (H_3B)); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 87.5, (C(1)) 75.2, (C(7b)) 68.4, (C(2)) 64.1, (C(4)) 60.9, (C(7a)) 53.0, (C(5a)) 31.5, (C(5)) 30.7, (C(6)) 28.0, (C(7)) 25.2, (C(8)); IR: (NaCl plate, film) 3053 (m), 2986 (m), 2871 (w), 2386 (m), 2306 (m), 2253 (m), 1421 (w), 1382 (w), 1265 (s); MS: (ESI, Q-tof) 180 (100). Analysis: $\text{C}_{10}\text{H}_{20}\text{BNO}$ (181.08); Calcd: C, 66.33; H, 11.13; N, 7.73; Found: C, 66.32; H, 10.90; N, 7.66; TLC: R_f 0.33 (hexanes/EtOAc, 3:1) [I_2].

4. Preparation of Scaffold for Library IV:

Preparation of (3*R*,5*aS*,7*aS*,7*bR*)-Octahydro-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizin-1-one

•**Borane (13)**: To a 100-mL, three-necked, round-bottomed flask fitted with a nitrogen inlet adapter, a magnetic stir bar, and an internal temperature probe was added **11a** (500 mg, 2.76 mmol), CH_2Cl_2 (11.5 mL), and DMSO (2.3 mL). The resulting solution was cooled to -12°C in an ice/salt bath. To this solution was added diisopropylethylamine (2.41 mL, 13.8 mmol, 5.0 equiv) followed by a solution of $\text{SO}_3\cdot\text{pyridine}$ complex (1.32 g, 8.28 mmol, 3.0 equiv) in DMSO (4.6 mL) at rate such that the internal temperature remained $< -5^\circ\text{C}$ (~5 min). After stirring for an additional 20 min at -10°C , the cooling bath was removed and the solution was allowed to warm to room temperature (~10 min), then cooled to 0°C by re-immersion in the ice/salt bath. The solution was diluted with Et_2O (10 mL) and quenched with H_2O (10 mL). This mixture was poured into a 250-mL separatory funnel and the layers were separated. The aqueous extract was washed with Et_2O (2×25 mL). The organic extracts were washed with sat. aq. CuSO_4 solution (2×25 mL), sat. aq. NaHCO_3 solution (1×25 mL), brine (25 mL), the combined organic extracts dried over MgSO_4 , filtered through Celite (20 mm $\times$ 5 cm), and rinsed with TBME (3×10 mL). The filtrate was concentrated by rotary evaporation (15 mm Hg, 20 – 25°C) to afford 498 mg (99%) of **13** as a white solid without further purification. Data for **13**: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 3.89 (d, $J = 17.6$, 1 H, HC(2)), 3.55 (ddd, $J = 7.6$, 7.6, 12.2, 1 H, HC(4)), 3.48 (d, $J = 17.6$, 1 H, HC(2)), 3.16 (ddd, $J = 6.5$, 1 H, HC(4)), 2.63–2.57 (m, 2 H, HC(7a), HC(5a)), 2.40 ($J = 6.0$, 7.4, 9.4, 13.6, 1 H, HC(5)), 2.16–2.03 (m, 3 H, HC(7), HC(7)), 1.65 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.65–1.58 (m, 2 H, HC(5)), 1.48–1.41 (m, 1 H, HC(6)), 0.8–2.5 (br, 3 H, (H_3B))³; $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 212.1 (C(1)), 86.5 (C(7b)), 70.0 (C(2)), 64.9 (C(4)), 58.4 (C(7a)), 51.8 (C(5a)), 35.1 (C(6)), 32.3 (C(7)), 29.9 (C(5)), 24.4 (C(8)); IR: (NaCl plate, thin film) 2964 (s), 2865 (w), 2381 (s), 2333 (s), 2273 (s), 1755 (s), 1468 (m), 1419 (w), 1383 (m), 1195 (s), 1164 (s), 1071 (m), 913 (s), 732 (s); MS: (EI, 70eV) 179 (12), 178 (100), 165 (28), 150 (24), 137 (48), 121 (15), 108 (16), 95 (27); Mol. Formula: $\text{C}_{10}\text{H}_{18}\text{BNO}$ (179.07); HRMS: $\text{C}_{10}\text{H}_{17}\text{ONB}^+$: (178.1403); Calcd: 178.1403; Found: 178.1406; TLC: R_f 0.35 (hexanes/EtOAc, 3:2) [I_2 , CAM].

5. Preparation of Scaffold for Library V (via **20** and **21**):

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizin-2-one ((+)-5):

To a 100-mL, three-necked, round-bottomed flask fitted with two rubber septa, a magnetic stir bar, a nitrogen inlet adaptor and an internal temperature probe, was added nitroalkene (*E,E*)-**1** (1.0 g, 5.02 mmol) and chiral propenyl ether **3** (1.63 g, 7.53 mmol, 1.5 equiv) *via* syringe. The resulting yellow oil was then evacuated under high vacuum (~0.1 mm Hg) for 30 min. The flask was backfilled with N₂ and charged with CH₂Cl₂ (22 mL). The solution was cooled to -85 °C (internal temperature) using hexanes/N₂ bath. This yellow solution was stirred for 15 min, then freshly prepared TiCl₂(*Oi*-Pr)₂ solution (1.2 M in CH₂Cl₂, 12.6 mL, 15.1 mmol, 3.0 equiv) was added dropwise *via* syringe while maintaining an internal temperature ≤ -70 °C (ca. 15 min). After addition of the Lewis acid, the cooling bath was replaced with an acetone/CO₂(*s*) bath and the resulting bright yellow solution was stirred for another 5 h while maintaining an internal temperature ≤ -75 °C. During the course of the reaction, the yellow color gradually faded and a white precipitate formed. After 5 h the reaction was quenched with triethylamine (30.6 mL, 6.1 equiv, 1 M in MeOH) *via* syringe while maintaining an internal temperature of < -40 °C. The cooling bath was then removed and the reaction mixture was allowed to warm to 0 °C (ca. 15 min). The resulting white suspension was then diluted with ethyl acetate (50 mL) and poured onto a biphasic mixture of sat. aq. NH₄Cl and ethyl acetate (75 mL) in a 500-mL separatory funnel. The aqueous extract was washed with ethyl acetate (3 × 75 mL). The organic extracts were washed with sat. aq. NH₄Cl solution (2 × 50 mL), H₂O (2 × 50 mL) and brine (2 × 50 mL). The combined organic extracts were dried over NaHCO₃/MgSO₄ (1/1), filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting residue was filtered through a pad of silica gel (3 × 3 cm), eluting with ethyl acetate (100 mL) to remove any remaining amine impurities. The resulting clear solution was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) to a pale-yellow residual oil in a 1-L one-necked, round-bottomed flask. TBME (100 mL) was added followed by NaHCO₃ (5 g, 50.0 mmol, 10.0 equiv). The flask was equipped with a nitrogen inlet adaptor, a magnetic stir bar, and evacuated and backfilled with N₂ (3x). The suspension was stirred at room temperature for 12 h, then filtered through Celite (3 × 3 cm, cotton plug) and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting mixture of nitroso acetals was diluted in EtOAc/MeOH (9:1, 25 mL) and added to a test tube (6 cm × 14 cm) containing a spatula tip (~200 mg) of Raney Ni (previously washed with H₂O, MeOH, and EtOAc, 2 × 15 mL each) along with a magnetic stir bar. The tube was placed in a steel autoclave, which was then pressurized with H₂ (350 psi). After 2 days the autoclave was *carefully* vented in a fume hood and the solution was filtered through a plug of Celite (5 cm × 5 cm, cotton plug) with EtOAc (100 mL). The resulting clear solution was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) and purified by silica gel column chromatography (2 cm × 8 cm, hexanes/EtOAc, 9:1, 4:1, 7:3, 2:3, 1:4, 100 mL each) affording 870 mg (89%) of a mixture of epimeric α-hydroxy lactams **5** and **5S** as a white solid (11:1 by ¹H-NMR analysis). Data for **5**: ¹H-NMR: (500 MHz, CDCl₃) 4.63 (dd, *J* = 6.8, 1.5, 1 H, HC(4)), 4.05 (dd, *J* = 11.8, 7.4, 1 H, HC(4)), 2.73 (br, s, 1 H, OH), 2.59–2.46 (m, 2 H), 1.86–1.73 (m, 3 H), 1.67–1.55 (m, 1 H), 1.53–1.40 (m, 2 H), 1.34 (s, 3 H, H₃C(8)), 1.07 (d, *J* = 6.7, 3 H, H₃C(9)); ¹³C-NMR: (126 MHz, CDCl₃) 176.0 (C(2)), 75.4 (C(7*b*)), 72.4 (C(1)), 58.1 (C(5*a*)), 51.9 (C(7*a*)), 50.5 (C(4)), 42.1 (C(5)), 30.8 (C(6)), 25.2 (C(7)), 24.8 (C(9)), 17.5 (C(8)); IR: (NaCl plate, film) 3338 (br), 2959 (s), 2870 (s), 1685 (s), 1462 (m), 1412 (m), 1334 (m), 1269 (w), 1223 (s), 1142 (m), 1115 (w), 1097 (w), 1044 (w), 964 (w), 880 (w); MS: (ESI, Q-tof) 195.1 (67), 180.1 (100), 167.1 (12), 152.1 (56), 138.1 (14),

111 (43), 96.1 (15), 81.1 (24); TLC: R_f 0.20 (Hexanes/EtOAc, 1:1) [I_2]. Analysis: $C_{11}H_{17}NO_2$ (195.26); Calcd: C, 67.66; H, 8.78; N, 7.17; Found: C, 67.41; H, 9.05; N, 7.19.

Preparation of (1*R*,3*R*,5*R*,5*aS*,7*aS*,7*bR*)-Octahydro-1-[*N*-(3,5-Dinitrophenyl)-carbamoyl]-7*b*-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-2-one (S6**):** A 25 mL round-bottomed flask (A) was fitted with a reflux condenser, a nitrogen inlet adaptor, a rubber septum and a magnetic stir bar. The apparatus was opened and 3,5-dinitrobenzoyl azide (25 mg, 0.11 mmol, 1.1 equiv) was added as a solid. The apparatus was evacuated and backfilled with N_2 three times and toluene (4.8 mL) was added. The clear solution was immersed in a preheated (115 °C) oil bath and stirred at reflux for 30 min. In a separate, two-neck, 5 mL conical flask (B) fitted with a triangular magnetic stir bar, rubber septum and a nitrogen inlet adaptor the starting alcohol was added (18.9 mg, 0.096 mmol) followed by toluene (1.0 mL). The resulting solution (B) was transferred to flask (A) *via* cannula. The resulting light yellow solution was heated to reflux for 2 h and then allowed to cool to room temperature. The reaction mixture was concentrated *in vacuo*, and the crude product was purified by column chromatography (hexane/EtOAc (3/1, 1/1)) to afford 38 mg (98%) of enantioenriched **S6** as a white solid. The sample was compared to racemate as previously described.^{91,95} Data for **S6**: 1H -NMR: (500 MHz, $CDCl_3$) 9.90 (s, 1 H, NH), 8.61 (s, 1 H, HC(14)), 8.56 (s, 2 H, HC(12)), 5.89 (d, $J = 6.7$, 1 H, HC(1)), 4.12 (dd, $J = 7.4$, 11.9, 1 H, HC(4)), 2.71 (dd, $J = 9.5$, 14.1, 1 H), 2.69 (dd, $J = 10.7$, 23.5, 1 H), 1.96 (dd, $J = 7.0$, 7.0, 1 H), 1.93-1.81 (m, 2 H), 1.63-1.50 (m, 3 H), 1.46 (s, 3 H, $H_3C(9)$), 1.14 (d, $J = 6.7$, 3 H, $H_3C(15)$); ^{13}C -NMR: (126 MHz, $CDCl_3$) 220.6, 171.5, 152.6, 148.8, 141.2, 118.3, 118.2, 112.6, 75.9, 75.0, 58.3, 50.9, 42.7, 31.3, 26.3, 24.3, 17.7; TLC: R_f 0.34 (hexanes/EtOAc, 3:1) [I_2]; CSF-HPLC: t_R = 7.98 min (1%) and 9.88 (99%) (Chiralpak AD, 125 bar, 40 °C, 15 % MeOH in CO_2 , 3.0 mL/min, 220 nm).

Preparation of (3*R*,5*aS*,7*aS*,7*bR*)-Octahydro-5-methyl-7*b*-methyl-2*H*-cyclopenta[*gh*]pyrrolizin-1-one (14**):** To a 50-mL, three-necked, round-bottomed flask fitted with a nitrogen inlet adapter, a magnetic stir bar, and an internal temperature probe was added **12** (505 mg, 2.59 mmol), CH_2Cl_2 (10.8 mL), and DMSO (2.2 mL). The resulting solution was cooled to -12 °C in an ice/NaCl bath. To this solution was added diisopropylethylamine (2.25 mL, 12.9 mmol, 5.0 equiv) followed by the dropwise addition of a solution of $SO_3 \cdot$ pyridine complex (1.24 g, 7.76 mmol, 3 equiv) in DMSO (4.3 mL) while maintaining an internal temperature < -5 °C. After being stirred for 20 min at -10 °C, the cooling bath was removed and the mixture was allowed to warm to room temperature. This mixture was poured into a 250-mL separatory funnel and the layers were separated. The aqueous extract was washed with Et_2O (2 $\times$ 25 mL). The organic extracts were washed with sat. aq. $CuSO_4$ solution (2 $\times$ 25 mL), sat. aq. $NaHCO_3$ solution (1 $\times$ 25 mL), brine (25 mL), the combined organic extracts dried over $MgSO_4$, filtered through a Celite (20 mm $\times$ 5 cm, cotton plug), and rinsed with TBME (3 $\times$ 10 mL). The filtrate is concentrated *in vacuo* (15 mm Hg, 20–25 °C) to afford 498 mg (99%) of **14** as a white solid.

Data for **14**: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 3.98 (d, $J = 18.1$, 1 H, HC(2)), 3.49 (d, $J = 18.1$, 1 H, HC(2)), 3.39 (dd, $J = 6.4$, 12.8, 1 H, HC(4)), 3.23 (dd, $J = 12.4$, 12.4, 1 H, HC(4)), 2.59 (d, $J = 8.1$, 1 H, HC(7a)), 2.28-2.23 (m, 1 H, HC(7)), 2.15-2.07 (m, 2 H, HC(6), HC(5a)), 2.09-1.96 (m, 2 H, HC(7), HC(5)), 1.66 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.46-1.38 (m, 1 H, HC(6)), 1.10 (d, $J = 6.5$, 3 H, $\text{H}_3\text{C}(9)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^3$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 212.4 (C(1)), 87.3 (C(7b)), 72.0 (C(4)), 70.3 (C(2)), 60.9 (C(5a)), 57.9 (C(7a)), 38.1 (C(5)), 32.54 (C(7 or 6)), 32.45 (C(7 or 6)), 24.8 (C(8)), 17.5 (C(9)); IR: (NaCl plate, film) 2965 (s), 2964(s), 2963 (s), 2962 (m), 1757 (s), 1457 (w), 1383 (w), 1215 (s), 1163 (s), 745 (s); MS: (EI, 70 eV) 192 (100), 180 (50), 166 (32), 151 (71), 149 (67), 136 (32), 123 (19), 95 (44), 81 (100); Mol. Formula: $\text{C}_{11}\text{H}_{20}\text{BNO}$ (193.09); HRMS: $\text{C}_{11}\text{H}_{19}\text{BNO}^+$: (192.1560); Calcd: 192.1560; Found: 192.1560; TLC: R_f 0.45 ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$, 19:1) [I_2 , CAM].

Preparation of Scaffold for Library V via (α -Keto Lactam 17):

Preparation of (3R,5S,5aS,7aS,7bR)-Octahydro-5-methyl-7b-

methyl-2Hcyclopenta[gh]pyrrolizin-1,2-one (17): To a 50-mL, three-necked, round-bottomed flask fitted with a nitrogen inlet adapter, a magnetic stir bar, and an internal temperature probe was added **5** (491 mg, 2.51 mmol), CH_2Cl_2 (10.5 mL), and DMSO (2.1 mL). The resulting solution was cooled to -12°C in an ice/salt bath. To this solution was added diisopropylethylamine (2.2 mL, 12.6 mmol, 5.0 equiv) followed by the dropwise addition of a solution of $\text{SO}_3 \cdot \text{pyridine}$ complex (1.2 g, 7.54 mmol, 3.0 equiv) in DMSO (5.2 mL) while maintaining an internal temperature $< -5^\circ\text{C}$. After being stirred for 20 min at -10°C , the mixture was allowed to warm to room temperature. The mixture was then cooled to 0°C and diluted with CH_2Cl_2 (25 mL) and H_2O (25 mL). This mixture was poured into a 250-mL separatory funnel and the layers were separated. The aqueous extract was washed with CH_2Cl_2 (2×25 mL). The organic extracts were washed with sat. aq. CuSO_4 solution (2×25 mL), sat. aq. NaHCO_3 solution (1×25 mL), brine (25 mL), the combined organic extracts dried over MgSO_4 , filtered (cotton plug), and rinsed with TBME (3×10 mL). The resulting pale-yellow oil was purified by silica gel column chromatography ((10 mm $\times$ 10 cm column,) gradient elution, hexanes/ EtOAc , 3:1, 1:1, 1:3, 1:9, 100 mL each) followed by recrystallization (hexanes/TBME, 1:1, 25 mL) to afford 485 mg (82%) of **17** as white needles and as a single diastereomer. Data for **17**: mp: $83\text{--}84^\circ\text{C}$ (MTBE/Hexanes); $^1\text{H-NMR}$: (500 MHz, CDCl_3) 4.36 (ddd, $J = 1.2$, 7.7, 12.3, 1 H, HC(4)), 2.98 (dd, $J = 7.8$, 12.0, 1 H, HC(4)), 2.71 (dd, $J = 5.6$, 9.0, 1 H, HC(7a)), 2.13-2.04 (m, 1 H, HC(7)), 2.06-1.97 (m, 3 H, HC(6), HC(5a), HC(5)), 1.77-1.70 (m, 1 H, HC(7)), 1.45 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.40-1.32 (m, 1 H, HC(6)), 1.20 (d, $J = 5.9$, 3 H, $\text{H}_3\text{C}(9)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 203.6 (C(1)), 160.4 (C(2)), 74.4 (C(7b)), 57.0 (C(5a)), 55.8 (C(7a)), 51.9 (C(4)), 41.0 (C(5)), 32.8 (C(6)), 30.7 (C(7)), 25.1 (C(8)), 19.8 (C(9)); IR: (NaCl plate, film) 3496 (w), 3404 (w), 2961 (s), 2873 (s), 1760 (s), 1713 (s), 1462 (s), 1401 (s), 1332 (w), 1226 (s), 1180 (s), 1084 (m), 678 (w); MS: (EI, 70 eV) 193 (26), 165 (26), 150 (32), 122 (6), 107 (11), 93 (5), 81 (100); TLC: R_f 0.35 (hexanes/ EtOAc , 3:1) [I_2]. Analysis: $\text{C}_{11}\text{H}_{15}\text{N}$: (193.24); Calcd: C, 68.37; H, 7.82; N, 7.25; Found: C, 68.57; H, 8.02; N, 7.31.

Preparation of (1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizin•Borane (12**) and (1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizin•Borane (**S7**):** To a 25-mL, two-necked, round-bottomed flask equipped with a nitrogen adapter, a rubber septum and a magnetic stir bar was added sequentially **14** (63 mg, 0.326 mmol), THF (1.6 mL, 0.2 M), and BH₃•THF complex (1.6 mL, 1.0 M solution, 5.0 equiv) dropwise over 5 min during which gas evolution was observed. After being stirred for 2 h at room temperature, the reaction was quenched with methanol (5 mL) and the resulting solution was concentrated by rotary evaporation (15 mm Hg, 20–25°C) to afford crude **S7** as a mixture of diastereomers (5/9, ¹H-NMR). The crude mixture was purified by silica gel column chromatography (1.8 cm × 8 cm column, gradient elution, CH₂Cl₂/ether, 99:1, 49:1, 24:1, 47:3, 9:1, 25 mL each) to afford 22 mg (35%) of **S7** as a white solid. Data for **S7**: ¹H-NMR: (500 MHz, CDCl₃) 3.88 (dd, *J* = 4.4, 10.6, 1 H, HC(1)), 3.74 (d, *J* = 10.8, 1 H, OH), 3.56 (d, *J* = 12.7, 1 H, HC(2)), 3.37 (dd, *J* = 4.4, 12.7, 1 H, HC(2)), 3.24 (dd, *J* = 5.2, 12.7, 1 H, HC(4)), 2.85 (dd, *J* = 12.2, 12.2, 1 H, HC(4)), 2.39 (dd, *J* = 9.1, 9.1, 1 H, HC(7a)), 2.11–2.04 (m, 1 H, HC(7)), 1.91–1.84 (m, 2 H, HC(5a), HC(5)), 1.77–1.68 (m, 1 H, HC(6)), 1.66–1.63 (m, 1 H, HC(6)), 1.60 (s, 3 H, H₃C(8)), 1.41–1.32 (m, 1 H, HC(7)), 1.01 (d, *J* = 5.8, 3 H, H₃C(9)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 88.5 (C(7b)), 76.0 (C(1)), 71.1 (C(4)), 69.2 (C(2)), 62.1 (C(5a)), 61.4 (C(7a)), 34.8 (C(5)), 31.2 (C(7)), 29.6 (C(6)), 26.0 (C(8)), 16.5 (C(9)); IR: (CDCl₃) 3492 (s), 2964 (s), 2922 (s), 2869 (s), 2369 (s), 2318 (s), 2270 (s), 1454 (s), 1412 (m), 1381 (m), 1348 (m), 1250 (m), 1186 (s), 1160 (m), 1121 (m), 1048 (s), 1023 (m), 996 (m), 973 (m), 925 (m), 869 (m), 844 (w), 818 (w), 802 (w); MS: (EI, 70 eV) 194.2 (78), 181 (24), 166 (100), 150 (3), 138 (12), 124 (10), 110 (44), 96 (11), 84 (14); Mol. Formula: C₁₁H₂₂BNO (195.11); HRMS: C₁₁H₂₁BNO, (194.1716); Calcd: 194.1716; Found: 194.1720; TLC: *R*_f 0.61 (CH₂Cl₂/ether, 9:1) [I₂].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizin•Borane (12**):** To a 250-mL round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially **5** (931 mg, 4.77 mmol), THF (23.9 mL, 0.2 M), and BH₃•THF complex (23.9 mL, 1.0 M solution, 10.0 equiv) dropwise over 5 min during which gas evolution was observed. After being stirred for 4 h at room temperature, the reaction was quenched with methanol (40 mL) and the mixture was concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting colorless oil was purified by silica gel column chromatography (2 cm × 15 cm column, gradient elution, CH₂Cl₂/ether, 99:1, 49:1, 24:1, 47:3, 9:1, 100 mL each) to afford 875 mg (94%) of **12** as a white solid. Data for **12**: mp: 86.5–87.5 °C; ¹H-NMR: (500 MHz, CDCl₃) 4.81 (ddd, *J* = 7.2, 7.2, 10.5, 1 H, HC(1)), 3.46 (dd, *J* = 6.6, 10.3, 1 H, HC(2)), 3.17 (dd, *J* = 6.2, 12.5, 1 H, HC(4)), 3.02 (dd, *J* = 10.5, 10.5, 1 H, HC(2)), 2.82 (dd, *J* = 12.5, 12.5, 1 H, HC(4)), 2.34 (dd, *J* = 8.2, 17.0, 1 H, HC(7a)), 2.11–2.01 (m, 1 H, HC(5)), 1.94–1.85 (m, 2 H, HC(7), HC(5a)), 1.81–1.76 (m, 1 H, HC(6)), 1.76–1.67 (m, 2 H, HC(7), HC(6)), 1.56 (br, s, 1 H, OH), 1.50 (s, 3 H, H₃C(8)), 1.03 (d, *J* = 6.4, 3 H, H₃C(9)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 88.1 (C(7b)), 70.0 (C(4)), 68.8 (C(1)), 65.7 (C(2)), 62.0 (C(5a)), 55.1 (C(7a)), 34.6 (C(5)), 29.7 (C(7)), 26.4 (C(6)), 25.7 (C(8)), 16.4 (C(9)); IR: (CHCl₃ film) 3447 (br), 2962 (s), 2963 (s), 2964 (s), 2965 (m), 2378 (s), 2377 (s), 2375 (s), 1474 (m), 1457 (m), 1381 (w), 1214(s), 1166 (s), 1118 (m), 1088 (m), 141 (w), 1010 (w), 995 (w), 946 (w), 755 (s); MS: (EI, 70 eV) 194 ([M⁺-1], 8), 181 (16), 166 (100), 110 (60), 96 (12), 82 (8); TLC: *R*_f 0.36 (CH₂Cl₂/ether, 9:1) [I₂]. Analysis:

C₁₁H₂₂BNO, (195.1095); Calcd: C, 67.71; H, 11.37; N, 7.18; Found: C, 67.8%; H, 11.31; N, 7.06; Opt. Rot.: [α]_D²⁴ – 11.14° (c = 1.0, CHCl₃).

6. Preparation of Scaffold for Library VI:

Preparation of rel (2S,2aR,5aS)-6-[6a-methylperhydrocyclopenta[b]pyrrole]-methanol

(**S8**): To a 500-mL, three-necked, round-bottomed flask fitted with a nitrogen inlet adaptor, a magnetic stir bar, a rubber septum and an internal temperature probe was added *n*-butyl vinyl ether (1.4 mL, 10.5 mmol, 2.5 equiv), CH₂Cl₂ (100 mL), and trimethylaluminum (10.5 mL, 10.5 mmol, 2.5 equiv, 1.0 M). The resulting clear solution was allowed to stir for 10 min. as the vessel was cooled to –77 °C by submersion in an *i*-PrOH/CO₂(s) bath. Nitroalkene (590 mg, 4.2 mmol) was dissolved in CH₂Cl₂ (100 mL) and was transferred to the trimethylaluminum solution by cannulation while maintaining an internal temperature < –70 °C (ca. 45 min). The resulting orange solution was allowed to stir for an additional 3 h during which time the color gradually faded. The mixture was quenched by the slow, cautious addition of silica gel *via* a long stem addition funnel until no bubbling was observed (~2 g). The mixture filtered through more silica gel (~1 g, prewetted with EtOAc) and rinsed with ethyl acetate (80 mL). The resulting clear filtrate was dried (MgSO₄), filtered, and concentrated by rotary evaporation (15 mm Hg, 20–25 °C) to yield 3.8 g (98%) of the intermediate nitronates as a clear oil.

The clear oil was transferred to a 250-mL, single-necked, round-bottomed flask with benzene (150 mL). The flask was fitted with a reflux condenser, a nitrogen inlet adaptor and a magnetic stir bar and immersed in a preheated (85 °C) oil bath. After 12 h, the starting material was consumed (TLC), and the light-yellow solution was allowed to cool to room temperature. The solvent was removed by rotary evaporation (15 mm Hg, 20–25 °C) to give the intermediate nitrosoacetals as a viscous, light-yellow oil. The crude nitroso acetals were dissolved in methanol in methanol (20 mL) and transferred to a test tube (3 × 14 cm) containing Raney nickel (~50 mg, previously washed with H₂O, MeOH, and EtOAc, 2 × 10 mL each) and a magnetic stir bar. The test tube was placed in a steel autoclave which was then pressured with H₂ (300 psi) and placed on a stir plate. The reaction was stirred under H₂ for 28 h, and was then filtered through a pad of Celite, washing with 150 mL methanol. The filtrate was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) and purified by silica gel column chromatography (2 cm × 5 cm, gradient elution: CH₂Cl₂/MeOH/NH₄OH, 20:1:0.01, 10:2:0.01, 150 mL each) to afford 456 mg (70%, 3 steps) of amino alcohol **S8** as a white solid. Data for **S8**: mp: 154–160 °C; ¹H-NMR: (500 MHz, CDCl₃) 3.95 (dd, *J* = 11.3, 2.0, 1.0, 1 H, HC(1)), 3.67 (dd, *J* = 11.5, 3.9, 1 H, HC(4)), 2.96 (p, *J* = 5.60, 1 H, HC(4)), 2.84–2.79 (m, 1 H, HC(4)), 2.21 (tt, 1 H), 1.96–1.80 (m, 2 H, HC(5), HC(6)), 1.79–1.71 (m, 1 H, HC(5)), 1.62–1.51 3 H, HC(6), H₂C(7)) 1.45–1.40 (m, 1 H, HC(5a)), 1.29, (s, 3 H, H₃C(8)); ¹³C NMR: (126 MHz, CDCl₃) 72.4 (C(2a)), 62.1 (C(1)), 50.7 (C(5a)), 50.4(C(2)), 47.8 (C(4)), 34.8 (C(5)), 30.7 (C(6)), 27.9 (C(7)), 27.6 (C(8)); IR: (NaCl plate) 329 (s, br), 2949 (s), 2858 (s), 1692 (m), 1682 (m), 1633.6 (m), 1455 (m); MS: (EI, 70eV) 155 (8), 97 (10), 96(100), 83 (19), 82(32), 42 (9), 36 (20); GC: (Method 1) *t*_R 5.96 min; TLC: *R*_f: 0.26 (CH₂Cl₂/CH₃OH/NH₄OH, 20:3:0.1) [I₂, KmnO₄].

Preparation of (rel)-(1*S*,3*aS*,5*aR*,5*bR*)-1-boranyl-5*b*-methyl-cyclopenta[*ef*]-azoniabicyclo[3.2.0]heptane (S9): To a 100-mL, three-necked, round-bottomed flask fitted with a nitrogen inlet adaptor, two rubber septa, an internal temperature probe, and a magnetic stir bar was added amino alcohol **S8** (420 mg, 2.71 mmol) as a solution in THF (25 mL). To this solution was added triphenylphosphine (0.711 g, 2.71 mmol, 1.0 equiv). The resulting slightly cloudy solution was allowed room temperature until all of the phosphine was dissolved (15 min) and was then brought to -1°C by use of a salt/ice bath. Diisopropylazodicarboxylate (DIAD, 0.53 mL, 2.71 mmol, 1.0 equiv) was then added dropwise over 5 min maintaining an internal temperature of $\leq 3^{\circ}\text{C}$. During the addition of the first three fifths of DIAD, the orange color quickly dissipated, but persisted during the addition of the last two fifths. The reaction was allowed to stir for an additional 25 min during which time it gradually turned from orange to a very light-yellow. At this point the reaction was judged to be complete (TLC) and was quenched by the addition of $\text{BH}_3\cdot\text{THF}$ solution (1.0 M THF, 13.6 mL, 13.6 mmol) over 10 min maintaining an internal temperature of $\leq 5^{\circ}\text{C}$. The reaction was allowed to stir for an additional 30 min and the remaining borane was quenched by *carefully* pouring the mixture into a 250-mL separatory funnel containing H_2O (50 mL), which bubbled vigorously. The milky white mixture was extracted with dichloromethane ($3 \times 50\text{ mL}$). The combined organic were dried (MgSO_4), filtered (cotton plug) and concentrated by rotary evaporation (15 mm Hg, $20\text{--}25^{\circ}\text{C}$). Purification of **S9** by silica gel chromatography (3 cm $\times$ 16 cm, gradient elution, hexanes/EtOAc, 93:7, 90:10, 85:15) afforded 329 mg of **S9** as a white solid which was then sublimed (70°C , cold water, 0.2 mm Hg) to afford 324.0 mg (79%) of analytically pure **S9** as a white, waxy solid. Data for **S9**: mp: $154\text{--}156^{\circ}\text{C}$; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 3.90 (t, $J = 10.25$, 1 H, HC(1)), 3.19–3.14 (m, 1 H, HC(7)), 3.06–3.02 (m, 1 H, HC(7)), 2.93 (dd, $J = 6.1$, 1 H, HC(1)), 2.50–2.46 (m, 2 H, HC(2), HC(5)), 2.10–1.60 (m, 9 H, HC(1)), 1.50 (s, 3 H, HC(9)), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^3$); $^{13}\text{C NMR}$: (126 MHz, CDCl_3) 87.0 (C(8)), 64.3 (C(1)), 63.9 (C(7)), 51.7 (C(2)), 36.9 (C(5)), 31.3 (C(3)), 31.1 (C(6)), 29.4 (C(4)), 19.9 (C(9)); IR: (KBr plate) 2962 (s), 2968 (s), 2358 (s), 2260 (s), 1772 (w), 1734 (w), 1716 (w), 1699 (w), 1683 (w), 1652 (w), 1635 (w), 1558 (m), 1521 (m), 1540 (m), 1474 (m), 1456 (s), 1376 (s), 1167 (s); MS: (EI, 70 ev) 137 (2), 149 (22), 150 (100), 151 (53), 152 (5). Analysis: $\text{C}_9\text{H}_{18}\text{BN}$: (151.06); Calcd: C, 71.56; H, 12.08; N, 9.27%; Found: C, 71.37; H, 12.08; N, 9.22%; TLC: R_f 0.31 (hexane/EtOAc, 4:1) [CAM].

III. Parallel Syntheses: Library Intermediates and Quaternary Ammonium Bromides

A. Variable Group R²: Organometal Ketone Additions

1. Cerium-Mediated Additions to Keto Amine 13:

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (15{2}): To a 25-mL, two-necked, round-

bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (559 mg, 1.50 mmol, 1.5 equiv). The flask was immersed in a preheated oil bath (140 °C) under vacuum (< 0.1 mm Hg) for 2 h. The flask was backfilled with nitrogen, allowed to cool to room temperature, and then immersed in an ice bath. To the solid was added THF (4.0 mL), via syringe, and the resulting milky, heterogenous mixture was allowed to stir vigorously at room temperature for 2 h. The mixture was then sonicated and stirred intermittently for 15 min intervals over a 2 h time period. The flask was then immersed in an ice bath and methylmagnesium bromide (2.7 M, 556 μL , 1.5 mmol, 1.5 equiv) was added via syringe. The ice bath was removed and the solution was stirred at room temperature for 1.5 h. The flask was immersed in an ice bath and ketone **13** (179 mg, 1.0 mmol) was added as a solution in THF (1.0 mL) via syringe. After stirring for 30 min while immersed in an ice bath, the reaction was quenched with sat. aq. NH_4Cl solution (5.0 mL). The biphasic mixture was poured into a 125-mL separatory funnel containing sat. aq. NH_4Cl solution (20 mL) and Et_2O (20 mL). The layers were separated and the aqueous extract was washed with Et_2O (2×25 mL). The organic extracts were washed with sat. aq. NaHCO_3 (1×25 mL), brine (1×25 mL), and the combined organic extracts were dried over MgSO_4 , filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting pale-yellow oil was purified by silica gel column chromatography (2 cm $\times$ 8 cm, gradient elution, $\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 1:0, 99:1, 49:1, 19:1, 50 mL each) to afford **15{2}** (134 mg, 68%) as a white solid. Data for **15{2}**: ^1H -NMR: (500 MHz, CDCl_3) 3.88 (ddd, $J = 6.3, 10.6, 10.3$, 1 H, HC(4)), 3.37 (d, $J = 13.4$, 1 H, HC(2)), 3.33 (d, $J = 13.6$, 1 H, HC(2)), 3.31–3.27 (m, 1 H, HC(4)), 2.35–2.34 (m, 1 H, HC(5a), HC(5)), 2.16–2.13 (m, 1 H, HC(7a)), 1.96–1.89 (m, 2 H, HC(7), HC(6)), 1.80–1.68 (m, 2 H, HC(7), HC(6)), 1.54–1.49 (m, 1 H, HC(5)), 1.50 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.41 (s, 3 H, $\text{H}_3\text{C}(9)$), 0.8–2.5 (br, 3 H, (H_3B)⁹³); ^{13}C -NMR: (126 MHz, CDCl_3) 89.2 (C(7b)), 78.1 (C(1)), 74.7 (C(2)), 63.7 (C(7a)), 63.6 (C(4)), 52.2 (C(5a)), 34.6 (C(6)), 30.5 (C(8 or 9)), 29.6 (C(5)), 27.3 (C(7)), 25.8 (C(8 or 9)); IR: (thin film) 3503 (s), 2383 (s), 2329 (s), 2277 (s), 1301 (m), 1258 (m), 1178 (m), 1124 (w), 1070 (m), 1018 (w), 953 (w), 850 (w); MS: (EI, 70eV) 194.2 (93), 181 (34), 166 (50), 138 (6), 110 (57), 96 (100), 81 (18); Mol. Formula: $\text{C}_{11}\text{H}_{22}\text{BNO}$ (195.18); HRMS: $\text{C}_{11}\text{H}_{21}\text{BNO}^+$ (194.1716); Calcd: 194.1716; Found: 194.1714; TLC: R_f 0.25 ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 19:1) [I_2 , CAM].

Preparation of (1S,3S,5aS,7aS,7bR)-Octahydro-1-hydroxy-1-isopropyl-7b-

methyl-2Hcyclopenta[gh]pyrrolizine•Borane (15{3}): To a 25-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (559 mg, 1.50 mmol, 1.5 equiv). The flask was immersed in a preheated oil bath (140 °C) and stirred under vacuum (< 0.1 mm Hg) for 2 h. The flask was backfilled with nitrogen, allowed to cool to room temperature, and then immersed in an ice bath. To the solid was added THF (4.0 mL), and the resulting milky, heterogenous mixture was allowed to stir vigorously at room temperature for 2 h. The mixture was then sonicated and stirred intermittently for 15 min intervals over a 2 h time period. The flask was then immersed in an ice bath and isopropylmagnesium chloride (1.9 M, 811 μL , 1.5 mmol, 1.5 equiv) was added via syringe. The ice bath was removed and the solution was stirred at room temperature for 1.5 h. The flask was immersed in an ice bath and ketone **13** (179 mg, 1.0 mmol) was added as a solution in THF (1.0 mL) via syringe. After stirring for 30 min while immersed in an ice bath, the reaction was quenched with sat. aq. NH_4Cl solution (5.0 mL). The biphasic mixture was poured into a 125-mL separatory funnel containing sat. aq.

NH₄Cl solution (20 mL) and Et₂O (20 mL). The layers were separated and the aqueous extract was washed with Et₂O (2 × 25 mL). The organic extracts were washed with sat. aq. NaHCO₃ (1 × 25 mL), brine (1 × 25 mL), and the combined organic extracts were dried over MgSO₄, filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting pale-yellow oil was purified by silica gel column chromatography (1.8 cm × 8 cm, gradient elution, CH₂Cl₂/EtOAc, 1:0, 99:1, 49:1, 19:1, 50 mL each) to afford **15{3}** (89 mg, 40%) as a white solid. Data for **15{3}**: ¹H-NMR: (500 MHz, CDCl₃) 3.98 (ddd, *J* = 6.6, 11.1, 11.5, 1 H, HC(4)), 3.39 (d, *J* = 13.8, 1 H, HC(2)), 3.35 (d, *J* = 9.0, 1 H, HC(2)), 3.34–3.31 (m, 1 H, HC(4)), 2.46–2.43 (m, 2 H, HC(5a), HC(5)), 2.20–2.17 (m, 1 H, HC(7a)), 2.00–1.90 (m, 2 H, HC(7), HC(6)), 1.80 (m, 1 H, HC(6)), 1.74–1.67 (m, 1 H, HC(7)), 1.67–1.60 (m, 1 H, HC(9)), 1.53–1.49 (m, 1 H, HC(5)), 1.48 (s, 3 H, H₃C(8)), 1.40 (br, s, 1 H, OH), 0.91 (d, *J* = 2.4, 3 H, H₃C(10)), 0.90 (d, *J* = 2.5, 3 H, H₃C(10')), 0.8–2.5 (br, 3 H, (H₃B)³); ¹³C-NMR: (126 MHz, CDCl₃) 89.0 (C(7b)), 82.4 (C(1)), 74.2 (C(2)), 63.2 (C(4)), 62.5 (C(7a)), 51.4 (C(5a)), 39.7 (C(9)), 35.5 (C(6)), 30.0 (C(5)), 27.9 (C(7)), 25.5 (C(8)), 16.9 (C(10)), 16.7 (C(10')); IR: (thin film) 3433 (s), 2411 (m), 2319 (s), 2270 (s), 1309 (w), 1280 (s), 1162 (m), 1070 (w), 988 (m), 975 (w), 849 (w), 703 (w); MS: (ESI, Q-tof) 222 (89), 209 (50), 194 (34), 178 (18), 166 (16), 124 (21), 110 (65), 96 (100), 81 (20); Mol. Formula: C₁₃H₂₆BNO (223.16); HRMS: C₁₃H₂₅BNO (222.2029); Calcd: 222.2029; Found: 222.2030; TLC: *R*_f 0.40 (hexanes/EtOAc, 4:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-phenyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (15{5}**):**

To a 25-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added CeCl₃•7H₂O (559 mg, 1.50 mmol, 1.5 equiv). The flask was immersed in a preheated oil bath (140 °C) and stirred under vacuum (< 0.1 mm Hg) for 2 h. The flask was backfilled with N₂, allowed to cool to room temperature, and then immersed in an ice bath. To the solid was added THF (4.0 mL), and the resulting milky, heterogenous mixture was allowed to stir vigorously at room temperature for 2 h. The mixture was then sonicated and stirred intermittently for 15-min intervals over a 2 h time period. The flask was then immersed in an ice bath and phenylmagnesium bromide (3.0 M, 500 μL, 1.5 mmol, 1.5 equiv). The ice bath was removed and the solution was stirred at room temperature for 1.5 h. The flask was immersed in an ice bath and ketone **13** (179 mg, 1.0 mmol) was added as a solution in THF (1.0 mL) via syringe. After stirring for 30 min while immersed in an ice bath, the reaction was quenched with sat. aq. NH₄Cl solution (5.0 mL). The biphasic mixture was poured into a 125-mL separatory funnel containing sat. aq. NH₄Cl solution (20 mL) and Et₂O (20 mL). The layers were separated and the aqueous extract was washed with Et₂O (2 × 25 mL). The organic extracts were washed with sat. aq. NaHCO₃ (1 × 25 mL), brine (1 × 25 mL), and the combined organic extracts were dried over MgSO₄, filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting pale-yellow oil was purified by silica gel column chromatography (1.8 cm × 8 cm, gradient elution, CH₂Cl₂/EtOAc, 1:0, 99:1, 49:1, 19:1, 50 mL each) to afford **15{5}** (131 mg, 51%) as a white solid. Data for **15{5}**: ¹H-NMR: (500 MHz, CDCl₃) 7.42–7.36 (m, 4 H, HC(10), HC(11)), 7.33–7.28 (m, 1 H, HC(12)), 4.28–4.20 (m, 1 H, HC(4)), 3.81 (d, *J* = 13.9, 1 H, HC(2)), 3.68 (d, *J* = 13.9, 1 H, HC(2)), 3.45–3.40 (m, 1 H, HC(4)), 2.75 (dd, *J* = 3.0, 8.3, 1 H, HC(7a)), 2.45–2.36 (m, 2 H, HC(5a), HC(5)), 2.12–2.02 (m, 2 H, HC(7), HC(6)), 1.94–1.78 (m, 3 H, HC(7), HC(6), OH), 1.63–1.58 (m, 1 H, HC(5)), 1.58 (s, 3 H, H₃C(8)), 0.8–2.5 (br, 3 H,

(H₃B)⁹³; ¹³C-NMR: (126 MHz, CDCl₃) 145.1 (C(9)), 129.0 (C(10 or 11)), 128.0 (C(10 or 11)), 124.9 (C(12)), 89.2 (C(7b)), 82.1 (C(1)), 74.9 (C(2)), 64.3 (C(7a)), 63.3 (C(4)), 52.2 (C(5a)), 35.2 (C(6)), 29.7 (C(5)), 27.3 (C(7)), 25.9 (C(8)); IR: (thin film) 3433 (s), 2411 (m), 2319 (s), 2270 (s), 1309 (w), 1280 (s), 1162 (m), 1070 (w), 988 (m), 975 (w), 849 (w), 703 (w); MS: (EI, 70 eV) 254.2 (62), 243.2 ([M⁺], 66), 228 (20), 210 (10), 178 (8), 158 (48), 149 (15), 138 (11), 123 (46), 110 (100); Mol. Formula: C₁₆H₂₄BNO; 257.18; HRMS: C₁₆H₂₁NO: (243.1623); Calcd: 243.16232; Found: 243.16251; TLC: *R*_f 0.20 (CH₂Cl₂/EtOAc, 19:1) [I₂, CAM].

Cerium Mediated Additions to 20. Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-methyl-5-methyl-7*b*-methyl-2Hcyclopenta[*gh*]pyrrolizine•Borane (16{2}): To a 100-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added CeCl₃•7H₂O (2.30 g, 8.70 mmol, 1.5 equiv). The flask was immersed in a preheated oil bath (140 °C) and stirred under vacuum (~0.1 mm Hg). After 2 h the flask was backfilled with nitrogen, allowed to cool to room temperature, and then immersed in an ice bath. To the solid was added THF (25 mL), and the resulting milky, heterogenous mixture was allowed to stir vigorously at room temperature for 2 h. The mixture was then sonicated and stirred intermittently for 15 min intervals over a 2 h time period. The flask was then immersed in an ice bath and methylmagnesium bromide (3.0 M, 3.0 mL, 1.50 mmol, 1.5 equiv). The ice bath was removed and the solution was stirred at room temperature for 1.5 h. The flask was immersed in an ice bath and ketone **14** (1.12 g, 5.80 mmol) was added as a solution in THF (4.0 mL). After being stirred for 30 min while immersed in an ice bath, the reaction was quenched with sat. aq. NH₄Cl solution (20 mL). The biphasic mixture was poured into a 250-mL separatory funnel containing sat. aq. NH₄Cl solution (30 mL) and Et₂O (40 mL). The layers were separated and the aqueous extract was washed with Et₂O (2 × 50 mL). The organic extracts were washed with sat. aq. NaHCO₃ (1 × 50 mL), brine (1 × 50 mL), and the combined organic extracts were dried over MgSO₄, filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25°C). The resulting paleyellow oil was purified by silica gel column chromatography (2 cm × 12 cm, gradient elution, CH₂Cl₂/ether, 1:0, 99:1, 49:1, 24:1, 9:1, 4:1, 100 mL each) to afford **16{2}** (1.1 g, 87%) as a white solid. Data for **16{2}**: mp: 84–85°C (MTBE:Hexanes); ¹H-NMR: (500 MHz, CDCl₃) 3.43 (d, *J* = 12.0, 1 H, HC(2)), 3.28 (dd, *J* = 6.8, 12.6, 1 H, HC(4)), 3.25 (d, *J* = 12.3, 1 H, HC(2)), 2.97 (dd, *J* = 12.2, 12.2, 1 H, HC(4)), 2.13 (et, *J* = 4.8, 8.1, 9.6, 12.7, 1 H, HC(5)), 2.06 (ddd, *J* = 8.2, 8.2, 7.8, 1 H, HC(7a)), 2.02–1.96 (m, 1 H, HC(7)), 1.85 (dd, *J* = 7.0, 7.0, 1 H, HC(5a)), 1.83–1.70 (m, 3 H, HC(7), HC(6), HC(6)), 1.61 (s, 3 H, H₃C(9)), 1.52 (s, 3 H, H₃C(8)), 1.38 (d, *J* = 4.7, 1 H, OH), 0.99 (d, *J* = 6.5, 3 H, H₃C(10)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 88.9 (C(7b)), 75.5 (C(1)), 74.9 (C(2)), 73.4 (C(4)), 61.9 (C(7a)), 61.8 (C(5a)), 34.0 (C(5)), 31.0 (C(9)), 29.7 (C(6)), 27.1 (C(7)), 26.0 (C(8)), 16.5 (C(10)); IR: (CHCl₃) 3969 (br), 2962 (s), 2870 (s), 2380 (s), 2331 (s), 2276 (s), 1459 (s), 1381 (s), 1340 (m), 1180 (s), 1134 (s), 1064 (s), 1049 (w), 1019 (w), 960 (s), 871 (w), 826 (m); MS: (EI, 70 eV) 208 (4), 195 (16), 180 (48), 124 (28), 110 (100), 96 (16), 81 (8); Mol. Formula: C₁₂H₂₄BNO (209.14); HRMS: C₁₂H₂₃BNO: (208.1873); Calcd: 208.1873; Found: 208.1875; TLC: *R*_f 0.33 (CH₂Cl₂/Et₂O, 19:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-isopropyl-5-methyl-7*b*methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (16{3}): To a 100-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (2.90 g, 7.77 mmol, 1.5 equiv). The flask was immersed in a preheated oil bath (140 °C) and stirred under vacuum (~0.1 mm Hg). After 2 h the flask was backfilled with nitrogen, allowed to cool to room temperature, and then immersed in an ice bath. To the solid was added THF (22 mL), and the resulting milky, heterogenous mixture was allowed to stir vigorously at room temperature for 2 h. The mixture was then sonicated and stirred intermittently for 15 min intervals over a 2 h time period. The flask was then immersed in an ice bath and isopropyl magnesium chloride (1.8 M, 4.3 mL, 1.50 mmol, 1.5 equiv) was added via syringe. The ice bath was removed and the solution was stirred at room temperature for 1.5 h. The flask was immersed in an ice bath and ketone **14** (1.0 g, 5.18 mmol) was added as a solution in THF (4.0 mL). After stirring for 30 min while immersed in an ice bath, the reaction was quenched with sat. aq. NH_4Cl solution (20 mL). The biphasic mixture was poured into a 250-mL separatory funnel containing sat. aq. NH_4Cl solution (30 mL) and Et_2O (40 mL). The layers were separated and the aqueous extract was washed with Et_2O (2×50 mL). The organic extracts were washed with sat. aq. NaHCO_3 (1×50 mL), brine (1×50 mL), and the combined organic extracts were dried over MgSO_4 , filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting pale-yellow oil was purified by silica gel column chromatography (2 cm $\times$ 10 cm, gradient elution, $\text{CH}_2\text{Cl}_2/\text{ether}$, 1:0, 99:1, 49:1, 24:1, 47:3, 9:1, 17:3, 100 mL each) to afford **16{3}** (931 mg, 79%) as a pale yellow oil. Data for **16{3}**: ^1H -NMR: (500 MHz, CDCl_3) 3.60 (d, $J = 13.5$, 1 H, HC(2)), 3.51 (dd, $J = 7.9$, 12.2, 1 H, HC(4)), 3.31 (d, $J = 13.5$, 1 H, HC(2)), 3.16 (dd, $J = 10.7$, 12.1, 1 H, HC(4)), 2.42–2.32 (m, 1 H, HC(5)), 2.18 (dd, $J = 7.0$, 9.1, 1 H, HC(7a)), 2.09–1.98 (m, 1 H, HC(7)), 1.89–1.83 (m, 3 H, HC(6), HC(6), HC(5a)), 1.82–1.69 (m, 2 H, HC(7), HC(9)), 1.49 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.37 (br, s, 1 H, OH), 0.99 (d, $J = 6.6$, 3 H, $\text{H}_3\text{C}(12)$), 0.91 (d, $J = 6.8$, 3 H, $\text{H}_3\text{C}(10)$), 0.87 (d, $J = 6.9$, 3 H, $\text{H}_3\text{C}(11)$), 0.8–2.5 (br, 3 H, (H_3B)⁹³); ^{13}C -NMR: (126 MHz, CDCl_3) 89.4 (C(7b)), 80.2 (C(1)), 77.1 (C(2)), 74.1 (C(4)), 60.9 (C(7a)), 60.0 (C(5a)), 38.3 (C(9)), 34.5 (C(5)), 31.3 (C(6)), 25.4 (C(7)), 25.3 (C(8)), 17.6 (C(12)), 17.0 (C(10)), 16.8 (C(11)); IR: (CHCl_3) 3507 (br), 2964 (s), 2866 (m), 2380 (s), 2326 (s), 2268 (s), 1465 (m), 1171 (m), 1000 (w); MS: (EI, 70 eV) 236 (18), 234 (24), 223 (23), 208 (30), 192 (7), 180 (15), 124 (36), 110 (100), 96 (12), 81 (10); Mol. Formula: $\text{C}_{14}\text{H}_{28}\text{BNO}$ (237.19); HRMS: $\text{C}_{14}\text{H}_{27}\text{BNO}$: (236.2186); Calcd: 236.2186; Found: 236.2183; TLC: R_f 0.40 ($\text{CH}_2\text{Cl}_2/\text{ether}$, 19:1) [I_2 , CAM].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-phenyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (16{5}): To a 50-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (1.74 g, 4.66 mmol, 1.5 equiv). The flask was immersed in a preheated oil bath (140 °C) and stirred under vacuum (~0.1 mm Hg). After 2 h the flask was

backfilled with nitrogen, allowed to cool to room temperature, and then immersed in an ice bath. To the solid was added THF (14 mL), and the resulting milky, heterogenous mixture was allowed to stir vigorously at room temperature for 2 h. The mixture was then sonicated and stirred intermittently for 15 min intervals over a 2 h time period. The flask was then immersed in an ice bath and phenylmagnesium bromide (2.9 M, 1.6 mL, 1.50 mmol, 1.5 equiv) was added via syringe. The ice bath was removed and the solution was stirred at room temperature for 1.5 h. The flask was immersed in an ice bath and ketone **14** (600 mg, 3.11 mmol) was added as a solution in THF (2.0 mL) via syringe. After stirring for 30 min while immersed in an ice bath, the reaction was quenched with sat. aq. NH_4Cl solution (15 mL). The biphasic mixture was poured into a 250-mL separatory funnel containing sat. aq. NH_4Cl solution (30 mL) and Et_2O (40 mL). The layers were separated and the aqueous extract was washed with Et_2O (2×50 mL). The organic extracts were washed with sat. aq. NaHCO_3 (1×50 mL), brine (1×50 mL), and the combined organic extracts were dried over MgSO_4 , filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25°C). The resulting pale-yellow oil was purified by silica gel column chromatography (1.8 cm $\times$ 10 cm, gradient elution, hexanes/TBME, 9:1, 4:1, 7:3, 1:1, 1:4, 50 mL each) to afford **16{5}** (828 mg, 98%) as a white solid. Data for **16{5}**: mp: 81.5–82 °C (MTBE:Hexanes); ^1H -NMR: (500 MHz, CDCl_3) 7.37 (d, $J = 4.3$, 1 H, HC(10)), 7.31 (m, 1 H, HC(12)), 4.10 (d, $J = 13.7$, 1 H, HC(2)), 3.70 (d, $J = 13.6$, 1 H, HC(2)), 3.68 (dd, $J = 8.3$, 12.0, 1 H, HC(4)), 3.29 (dd, $J = 10.8$, 12.1, 1 H, HC(4)), 2.75 (dd, $J = 6.1$, 9.3, 1 H, HC(7a)), 2.64–2.55 (m, 1 H, HC(5)), 2.34–2.37 (m, 1 H, HC(5a)), 1.99–1.93 (m, 3 H, $\text{H}_2\text{C}(7)$, HC(6)), 1.93–1.83 (m, 1 H, HC(6)), 1.80 (br, s, 1 H, OH), 1.55 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.02 (d, $J = 6.6$, 3 H, $\text{H}_3\text{C}(13)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); ^{13}C -NMR: (126 MHz, CDCl_3) 146.0 (C(9)), 128.9 (C(11)), 128.0 (C(12)), 125.1 (C(10)), 89.6 (C(7b)), 79.3 (C(1)), 78.8 (C(2)), 74.5 (C(4)), 62.6 (C(5a)), 59.8 (C(7a)), 34.7 (C(5)), 31.5 (C(7)), 25.1 (C(8)), 24.1 (C(6)), 17.7 (C(13)); IR: (CHCl_3 film) 3475 (br), 2960 (s), 2871 (s), 2377 (s), 2327 (s), 2271 (s), 1494 (w), 1447 (m), 1266 (w), 1172 (s), 1131 (m), 1067 (w), 1004 (m), 954 (w), 876 (w), 700 (s); MS: (EI, 70 eV) 268.2 (24), 257.2 (23), 242.1 (11), 224.1 (3), 192.1 (4), 178.1 (4), 158 (14), 137.1 (11), 124.1 (26), 110.1 (100); Mol. Formula: $\text{C}_{17}\text{H}_{26}\text{BNO}$ (271.21); HRMS: $\text{C}_{17}\text{H}_{23}\text{NO}$: (257.1780); Calcd: 257.1780; Found: 257.1775; TLC: R_f 0.58 (hexanes/TBME, 1:1) [I_2 , CAM].

3. Grignard Additions to Keto Amide 17:

Preparation of (1R,3S,5S,5aS,7aS,7bR)-Octahydro-1-hydroxy-1-(tert-butyl)-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizin-2-one (18{4}): To a 25-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added **17** (100 mg, 0.518 mmol) followed by THF (5.0 mL). The flask was immersed in an acetone/ $\text{CO}_2(\text{s})$ and stirred for 20 min. Then, $t\text{-BuLi}$ (1.6 M, 648 μL , 2.0 equiv) was added dropwise over 5 min via syringe. After being stirred for 10 min, the acetone/ $\text{CO}_2(\text{s})$ bath was replaced with an ice bath and the reaction was stirred for 1 hr. The reaction was quenched by the dropwise addition of sat. aq. NH_4Cl solution (15 mL) and further diluted with Et_2O (10 mL). The biphasic mixture was poured into a 125-mL separatory funnel containing sat. aq. NH_4Cl solution (10 mL) and Et_2O (30 mL). The layers were separated and the aqueous extract was washed with Et_2O (2×25 mL). The organic extracts were washed with H_2O (1×25 mL), brine (1×25 mL), and the combined organic extracts were dried over Na_2SO_4 , filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25°C). The resulting pale-yellow oil was purified by silica gel

column chromatography (1.8 cm $\times$ 6cm, gradient elution, hexanes/TBME, 17:3, 5:1, 3:1, 3:1, 3:2, 25 mL each) to afford **18{4}** (43 mg, 33%) as a white solid. Data for **18{4}**: ^1H -NMR: (500 MHz, CDCl_3) 4.30 (dd, $J = 8.6, 12.2$, 1 H, HC(4)), 2.63 (dd, $J = 7.3, 12.2$, 1 H, HC(4)), 2.55 (s, 1 H, HC(OH)), 2.38 (d, $J = 8.0$, 1 H, HC(7a)), 2.07 (dd, $J = 5.3, 12.7$, 1 H, HC(7)), 1.99 (dd, $J = 7.3, 15.3$, 1 H, HC(5)), 1.86 (ddd, $J = 6.4, 6.4, 12.8$, 1 H, HC(6)), 1.78 (ddd, $J = 2.1, 7.4, 9.8$, 1 H, HC(5a)), 1.64–1.56 (m, 1 H, HC(7)), 1.40 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.11 (d, $J = 7.1$, 3 H, $\text{H}_3\text{C}(11)$), 1.09–1.02 (m, 1 H, HC(6)), 0.97 (s, 9 H, $\text{H}_3\text{C}(10)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); ^{13}C -NMR: (126 MHz, CDCl_3) 179.3 (C(2)), 83.2 (C(1 or 7b)), 76.6 (C(1 or 7b)), 59.3 (C(5a)), 51.4 (C(4)), 49.6 (C(7a)), 37.8 (C(5)), 37.3 (C(10)), 33.9 (C(6)), 29.8 (C(7)), 25.0 (C(11)), 23.9 (C(8)), 21.3 (C(9)); IR: (CDCl_3 , film) 3404 (br), 2958 (s), 2865 (s), 2248 (w), 1678 (s), 1464 (m), 1395 (m), 1365 (m), 1340 (m), 1230 (w), 1181 (w), 1147 (w), 1115 (w), 1087 (w), 1057 (w), 1015 (w), 994 (w), 910 (w), 766 (w); MS: (EI, 70 eV) 251.2 (1), 236.2 (1.8), 218 (1.9), 195.1 (100), 166.1 (2.7), 152.1 (3.1), 140.1 (2.8), 110.1 (8.7); Mol. Formula: $\text{C}_{15}\text{H}_{25}\text{NO}_2$ (251.36); HRMS: $\text{C}_{15}\text{H}_{25}\text{NO}_2$, (251.1885); Calcd: 251.1885; Found: 251.1883; TLC: R_f 0.25 (hexanes/TBME, 3:1) [I_2].

Preparation of (1S,3S,5S,5aS,7aS,7bR)-Octahydro-1-hydroxy-1-(2,4,6-trimethylphenyl)-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (18{6}): To a 25-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added **17** (100 mg, 0.517 mmol) followed by THF (2.7 mL). The flask was immersed in an ice bath and mesitylmagnesium bromide (0.39 M, 2.0 mL, 1.5 equiv) was added dropwise via syringe. After being stirred for 10 min, the cooling bath was removed and the solution was stirred at room temperature for 20 min. The reaction flask was immersed in an ice bath and the reaction was quenched with sat. aq. NH_4Cl solution (15 mL). The biphasic mixture was poured into a 125-mL separatory funnel containing sat. aq. NH_4Cl solution (10 mL) and Et_2O (30 mL). The layers were separated and the aqueous extract was washed with Et_2O (2×25 mL). The organic extracts were washed with H_2O (1×25 mL), brine (1×25 mL), and the combined organic extracts were dried over MgSO_4 , filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25°C). The resulting pale-yellow oil was purified by silica gel column chromatography (1.8 cm $\times$ 8 cm, gradient elution, hexanes/ EtOAc , 9:1, 4:1, 7:3, 1:1, 25 mL each) to afford **18{6}** (157 mg, 97%) as a white solid. Data for **18{6}**: mp: 101–102 °C (hexanes: EtOAc); ^1H -NMR: (500 MHz, CDCl_3) 6.92 (s, 1 H, HC(11)), 6.68 (s, 1 H, HC(11)), 4.17 (dd, $J = 7.3, 11.7$, 1 H, HC(4)), 3.47 (s, 1 H, OH), 2.65 (dd, $J = 7.6, 10.1$, 1 H, HC(4)), 2.64 (dd, $J = 10.4, 11.6$, 1 H, HC(5)), 2.48 (s, 3 H, $\text{H}_3\text{C}(8, 13, \text{or } 14)$), 2.41 (s, 3 H, $\text{H}_3\text{C}(8, 13, \text{or } 14)$), 2.22 (s, 3 H, $\text{H}_3\text{C}(8, 13, \text{or } 14)$), 1.98–1.92 (m, 1 H, HC(7)), 1.84–1.79 (m, 1 H, HC(7a)), 1.78–1.66 (m, 3 H, HC(7), HC(6), HC(5a)), 1.55–1.48 (m, 1 H, HC(6)), 1.09 (d, $J = 6.7$, 3 H, $\text{H}_3\text{C}(15)$), 1.08 (s, 3 H, $\text{H}_3\text{C}(8, 13, \text{or } 14)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); ^{13}C -NMR: (126 MHz, CDCl_3) 179.1 (C(2)), 139.4 (C(9)), 138.3 (C(10 or 12)), 136.6 (C(10 or 12)), 133.9 (C(10 or 12)), 131.9 (C(11)), 130.8 (C(11)), 82.3 (C(1)), 75.3 (C(7b)), 60.2 (C(5)), 58.9 (C(7a)), 50.9 (C(4)), 41.7 (C(5a)), 29.9 (C(6)), 27.1 (C(7)), 23.8 (C(8, 13 or 14)), 22.3 (C(8, 13, or 14)), 21.2 (C(8, 13, or 14)), 20.7 (C(8, 13, or 14)), 17.7 (C(15)); IR: (NaCl plate, film) 3404 (br), 3000 (s), 2959 (s), 2922 (s), 2870 (s), 1693 (s), 1610 (m), 1560 (w), 1460 (s), 1407 (s), 1379 (m), 1351 (m), 1280 (w), 1232 (m), 1120 (m), 1072 (m), 1035 (m), 978 (w), 851 (m); MS: (EI, 70 eV) 313 (10), 295 (84), 285 (4), 280 (6), 270 (3), 252 (5), 147 (100), 138 (10), 124 (21), 119 (29),

110 (90); Mol. Formula: $C_{20}H_{27}NO_2$ (313.43); HRMS: $C_{20}H_{27}NO_2$: (313.2042); Calcd: 313.2042; Found: 313.2045; TLC: R_f 0.32 (hexanes/EtOAc, 3:1) [I_2 , CAM].

Preparation of (1*R*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-[1]naphthyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizin-2-one (18{7}): To a 25-mL, two-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added **17** (100 mg, 0.517 mmol) followed by THF (2.7 mL). The flask was immersed in an ice bath and 1-naphthylmagnesium bromide (0.4 M, 2.0 mL, 1.5 equiv) was added dropwise via syringe. After being stirred for 10 min, the cooling bath was removed and the reaction was stirred at room temperature for 20 min. The biphasic mixture was poured into a 125-mL separatory funnel containing sat. aq. NH_4Cl solution (10 mL) and Et_2O (30 mL). The layers were separated and the aqueous extract was washed with Et_2O (2 $\times$ 25 mL). The organic extracts were washed with H_2O (1 $\times$ 25 mL), brine (1 $\times$ 25 mL), and the combined organic extracts were dried over $MgSO_4$, filtered (cotton plug), and concentrated by rotary evaporation (15 mm Hg, 20–25°C). The resulting pale-yellow oil was purified by silica gel column chromatography (1.8 cm $\times$ 8 cm, gradient elution, hexanes/ $EtOAc$, 9:1, 4:1, 7:3, 1:1, 25 mL each) to afford **18{7}** (157 mg, 95%) as a white solid. Data for **18{7}**: mp: 150–151 °C (hexanes/ $EtOAc$); 1H -NMR: (500 MHz, $CDCl_3$) 8.43 (d, J = 8.4, 1 H, HC(11)), 7.87 (d, J = 7.9, 1 H, HC(14)), 7.78 (d, J = 7.9, 1 H, HC(16)), 7.56–7.48 (m, 2 H, HC(12), HC(13)), 7.34–7.28 (m, 2 H, HC(17), HC(18)), 4.27 (dd, J = 6.8, 11.5, 1 H, HC(4)), 3.44 (br, s, 1 H, OH), 2.96 (dd, J = 7.6, 10.1, 1 H, HC(7*a*)), 2.69 (dd, J = 10.0, 11.5, 1 H, HC(4)), 2.21–2.14 (m, 1 H, HC(7)), 2.00–1.92 (m, 1 H, HC(7)), 1.83–1.73 (m, 3 H, HC(6), HC(5*a*), HC(5)), 1.60–1.55 (m, 1 H, HC(6)), 1.11 (d, J = 6.4, 3 H, H_3C (19)), 0.87 (s, 3 H, H_3C (8)), 0.8–2.5 (br, 3 H, (H_3B)⁹³); ^{13}C -NMR: (126 MHz, $CDCl_3$) 177.2 (C(2)), 138.9 (C(9)), 135.0 (C(15)), 131.1 (C(10)), 129.3 (C(16)), 129.1 (C(14)), 126.6 (C(11)), 126.0 (C(12 or 13)), 125.7 (C(12 or 13)), 124.7 (C(17 or 18)), 124.7 (C(17 or 18)), 84.1 (C(1 or 7*b*)), 75.9 (C(1 or 7*b*)), 58.9 (C(5*a*)), 57.9 (C(7*a*)), 51.2 (C(4)), 41.9 (C(5)), 30.0 (C(6)), 27.0 (C(7)), 24.4 (C(8)), 17.7 (C(19)); IR: (NaCl plate, film) 3386 (s), 3050 (w), 3007 (m), 2959 (s), 2871 (s), 1693 (s), 1596 (w), 1509 (m), 1461 (s), 1411 (s), 1352 (m), 1376 (m), 1330 (m), 1280 (m), 1230 (s), 1213 (m), 1174 (w), 1131 (s), 1074 (s), 1030 (w), 967 (w), 915 (w), 862 (w), 802 (s); MS: (EI, 70 eV) 321 (19), 293 (6), 183 (9), 165 (13), 155 (68), 127 (46), 110 (100); Mol. Formula: $C_{21}H_{23}NO_2$ (321.41); HRMS: $C_{21}H_{23}NO_2$: (321.1729); Calcd: 321.1729; Found: 321.1732; TLC: R_f 0.28 (hexanes/ $EtOAc$, 3:1) [I_2 , CAM].

Preparation of (1*R*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-(*tert*-butyl)-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (16{4}): To a 25-mL, single-necked, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum, a reflux condenser, and a magnetic stir bar was added sequentially **18{4}** (29 mg, 0.115 mmol), THF (200 μ L), and $BH_3 \cdot THF$ complex (3.3 mL, 1.0 M solution, 20 equiv). The reaction flask was immersed in an oil bath and heated to reflux (70 °C). After being stirred for 12 h at reflux, the solution was allowed to reach room temperature, then quenched by dropwise addition of methanol (10 mL) and then concentrated by rotary evaporation (15 mm Hg, 20–25°C). The

resulting colorless oil was purified by silica gel column chromatography (1.8 cm $\times$ 8 cm column, gradient elution, hexanes/TBME, 19:1, 9:1, 3:1, 3:2, 25 mL each) to afford 27 mg (93%) of **16{4}** as a white solid. Data for **16{4}**: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 3.80 (d, $J = 13.9$, 1 H, HC(2)), 3.63 (dd, $J = 8.5$, 12.0, 1 H, HC(4)), 3.23 (d, $J = 13.8$, 1 H, HC(2)), 3.23–3.18 (m, 1 H, HC(4)), 2.48–2.40 (m, 1 H, HC(7a)), 2.41 (dd, $J = 6.8$, 9.2, 1 H, HC(5)), 2.09–1.99 (m, 1 H, HC(7)), 1.91–1.84 (m, 3 H, $\text{H}_2\text{C}(6)$, HC(5a)), 1.72–1.63 (m, 1 H, HC(7)), 1.62 (br, s, 1 H, HO), 1.46 (s, 3 H, $\text{H}_3\text{C}(8)$), 0.99 (d, $J = 6.6$, 3 H, $\text{H}_3\text{C}(9)$), 0.92 (s, 3 H, $\text{H}_3\text{C}(11)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 89.7 (C(1 or 7b)), 83.0 (C(1 or 7b)), 75.7 (C(2)), 74.6 (C(4)), 59.6 (C(5a)), 56.5 (C(7a)), 37.5 (C(10)), 35.0 (C(5)), 32.1 (C(6)), 25.5 (C(10)), 25.4 (C(7)), 24.7 (C(8)), 18.1 (C(11)); IR: (CDCl_3 film) 3503 (s), 2961 (s), 2872 (s), 2376 (s), 2327 (s), 2271 (s), 1465 (m), 1400 (w), 1378 (m), 1335 (w), 1267 (w), 1174 (m), 1140 (m), 1091 (w), 1057 (w), 1002 (w), 980 (w), 958 (w), 940 (w), 910 (s), 882 (w), 841 (w), 733 (s), 649 (w); MS: (ESI, Q-tof) 422.2 (10), 344.2 (25), 318.2 (40), 308.2 (100); Mol. Formula: $\text{C}_{15}\text{H}_{30}\text{BNO}$ (251.22); HRMS: $\text{C}_{15}\text{H}_{27}\text{NO}$: (237.2093); Calcd: 237.2093; Found: 237.2091; TLC: R_f 0.27 (hexanes/TBME, 3:1) [I_2 , CAM].

Preparation of (1R,3S,5S,5aS,7aS,7bR)-Octahydro-1-hydroxy-1-mesityl-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (16{6}): To a 25-mL round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum, a reflux condenser, and a magnetic stir bar was added sequentially **18{6}** (50 mg, 0.160 mmol), THF (200 μL), and $\text{BH}_3\cdot\text{THF}$ complex (3.2 mL, 1.0 M solution, 20 equiv). The reaction flask was immersed in an oil bath and heated to reflux (70 $^\circ\text{C}$). After being stirred for 12 h at reflux, the solution was allowed to reach room temperature and was quenched with methanol (5 mL) and concentrated by rotary evaporation (15 mm Hg, 20–25 $^\circ\text{C}$). The resulting colorless oil was purified by silica gel column chromatography (1.8 cm $\times$ 8 cm column, gradient elution, hexanes/TBME, 19:1, 9:1, 4:1, 3:1, 25 mL each) to afford 36 mg (72%) of **16{6}** as a white solid. Data for **16{6}**: mp: 131–132 $^\circ\text{C}$ (MTBE/hexanes); $^1\text{H-NMR}$: (500 MHz, CDCl_3) 6.81 (s, 2 H, HC(11)), 4.09 (d, $J = 14.1$, 1 H, HC(9)), 4.02 (d, $J = 14.1$, 1 H, HC(9)), 3.72 (dd, $J = 8.2$, 12.1, 1 H, HC(4)), 3.29 (dd, $J = 9.9$, 12.0, 1 H, HC(4)), 3.10 (dd, $J = 6.0$, 8.5, 1 H, HC(7a)), 2.62–2.52 (m, 1 H, HC(5)), 2.52 (s, 6 H, $\text{H}_3\text{C}(13)$, $\text{H}_3\text{C}(13)$), 2.40–2.31 (m, 1 H, HC(7)), 2.22 (s, 3 H, $\text{H}_3\text{C}(14)$), 2.06–1.98 (m, 1 H, HC(7)), 1.99–1.93 (m, 3 H, $\text{H}_2\text{C}(6)$, HC(5a)), 1.51 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.04 (d, $J = 6.7$, 3 H, $\text{H}_3\text{C}(14)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 139.1 (C(12)), 136.9 (C(9)), 136.4 (C(10)), 132.5 (C(11)), 88.4 (C(7b)), 82.4 (C(1)), 79.9 (C(2)), 75.1 (C(4)), 62.5 (C(7a)), 60.6 (C(5a)), 35.4 (C(5)), 31.8 (C(6)), 27.0 (C(7)), 25.6 (C(8)), 25.1 (C(13 or 14)), 20.4 (C(13 or 14)), 18.2 (C(15)); IR: (thin film) 3508 (s), 2383 (s), 2319 (s), 2274 (s), 1606 (m), 1378 (s), 1309 (w), 1287 (w), 1187 (s), 1128 (w), 1071 (m), 1034 (m), 943 (m), 860 (w), 734 (w); MS: (ESI, Q-tof) 314.2 (12), 300.2 (30), 296.2 (100), 268.2 (25); Mol. Formula: $\text{C}_{20}\text{H}_{32}\text{BNO}$ (313.29); HRMS: $\text{C}_{20}\text{H}_{30}\text{NO}$: (300.2327); Calcd: 300.2327; Found: 300.2332; TLC: R_f 0.33 (hexanes/TBME, 9:1) [I_2 , CAM].

Preparation of (1*R*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-hydroxy-1-[1]naphthyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (16{7}): To a 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum, a reflux condenser, and a magnetic stir bar was added sequentially **18{7}** (50 mg, 0.156 mmol), THF (200 μ L), and $\text{BH}_3\cdot\text{THF}$ complex (3.1 mL, 1.0 M solution, 20 equiv). The reaction flask was immersed in an oil bath and heated to reflux (70 $^\circ\text{C}$). After being stirred for 12 h at reflux, the solution was allowed to reach room temperature, then quenched with methanol (5 mL) and then concentrated by rotary evaporation (15 mm Hg, 20–25 $^\circ\text{C}$). The resulting colorless oil was purified by silica gel column chromatography (1.8 cm $\times$ 8 cm column, gradient elution, hexanes/TBME, 19:1, 9:1, 3:1, 3:2, 25 mL each) to afford 42 mg (85%) of **16{7}** as a white solid. Data for **16{7}**: mp: 151–153 $^\circ\text{C}$ (MTBE:Hexanes); $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.44 (d, $J = 8.5$, 1 H, HC(11)), 7.87 (d, $J = 7.9$, 1 H, HC(14)), 7.81 (d, $J = 8.2$, 1 H, HC(16)), 7.67 (d, $J = 7.3$, 1 H, HC(18)), 7.55–7.47 (m, 2 H, HC(12), HC(17)), 7.40 (dd, $J = 7.8$, 7.8, 1 H, HC(13)), 4.23 (d, $J = 13.4$, 1 H, HC(2)), 4.04 (d, $J = 13.5$, 1 H, HC(2)), 3.66 (dd, $J = 7.5$, 12.2, 1 H, HC(4)), 3.25–3.19 (m, 2 H, HC(7a), HC(4)), 2.60–2.50 (m, 1 H, HC(5)), 2.40–2.32 (m, 1 H, HC(7)), 2.22 (br, s, 1 H, OH), 2.10–2.01 (m, 1 H, HC(7)), 2.00–1.93 (m, 3 H, $\text{H}_2\text{C}(6)$, HC(5a)), 1.54 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.05 (d, $J = 6.5$, 3 H, $\text{H}_3\text{C}(19)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 139.2 (C(9)), 135.3 (C(15)), 131.2 (C(10)), 130.0 (C(16)), 129.6 (C(14)), 126.4 (C(11)), 126.3 (C(12 or 17)), 125.9 (C(12 or 17)), 124.8 (C(13)), 124.2 (C(18)), 88.1 (C(7b)), 80.9 (C(1)), 76.5 (C(2)), 74.6 (C(4)), 61.3 (C(5a)), 60.4 (C(7a)), 34.8 (C(5)), 31.0 (C(6)), 26.8 (C(7)), 25.7 (C(8)), 17.5 (C(19)); IR: (thin film) 3475 (m), 2383 (s), 2332 (s), 2269 (s), 1596 (w), 1444 (w), 1309 (w), 1202 (w), 1163 (m), 1134 (m), 1067 (w), 1040 (w), 1000 (w), 933 (w), 872 (w), 808 (m), 782 (s); MS: (ESI, Q-tof) 422.2 (10), 344.2 (25), 318.2 (40), 308.2 (100); Mol. Formula: $\text{C}_{21}\text{H}_{28}\text{BNO}$ (321.26); HRMS: $\text{C}_{21}\text{H}_{26}\text{NO}$, (308.2014); Calcd: 308.2014; Found: 308.2011; TLC: R_f 0.39 (hexanes/TBME, 3:1) [I_2 , CAM].

B. Variable Group R^3 : Williamson Ether Synthesis—

1. General Procedure (I) for the Preparation of Library Intermediates: To a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol X (X mg, 0.X mmol) and DMF (2.74 mL, ~ 0.35 M). The flask was then immersed in an ice/ NaCl bath for 15 min. Sodium hydride (xx mg, 0.xx mmol, 1.2 equiv) was weighed into a vial in a glove box then transferred to the flask in one portion (bubbling was observed). The resulting solution was allowed to stir for 15 min then alkyl bromide (X μL , 0.X mmol, 1.2 equiv) was added via syringe in a single portion. The resulting cloudy mixture was stirred for 2 h, then quenched by pouring onto ice water (20 mL). This mixture was transferred to a 125-mL separatory funnel where an additional 20 mL of water was added and the aqueous phase was extracted with dichloromethane (3×20 mL). The organic extracts were washed with water (2×20 mL), and brine (2×20 mL), then the combined organic extracts were dried (MgSO_4). The flocculant suspension was filtered through a small pad of Celite (1 cm $\times$ 2 cm) and concentrated by rotary evaporation (15 mm Hg, 20–25 $^\circ\text{C}$) to afford a thick oil. Purification by silica gel chromatography (1.8 cm $\times$ 8 cm column, gradient elution, hexanes/ EtOAc , 1:9, 1:3, 1:1) afforded X mg (XX%) of ether X{x}.

2. Preparation of Amino•Borane Intermediates II{2–5}

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-benzyloxy-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine •Borane (II{2}): Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11a** (54.3 mg, 0.30 mmol), dimethylformamide (3.0 mL, ~0.1 M), then sodium hydride (9.1 mg, 0.36 mmol, 1.2 equiv) at 0 °C. After 15 min, benzyl bromide (42.8 μ L, 0.36 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 h then quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 65.1 mg (78%) of benzyl ether **II{2}** as a clear, viscous oil. Data for **II{2}**: ^1H -NMR: (500 MHz, CDCl_3) 7.41–7.23 (m, 5 H, HC(11), HC(12), HC(13)), 4.52–4.45 (m, 3 H, $\text{H}_2\text{C}(9)$, HC(1)), 3.48 (dd, $J = 6.3, 10.9$, 1 H, HC(2)), 3.30–3.25 (m, 1 H, HC(4)), 3.20–3.15 (m, 1 H, HC(4)), 3.14–3.01 (m, 1 H, HC(4)), 2.46 (dd, $J = 7.8, 15.8$, 1 H, HC(7*a*)), 2.40 (dd, $J = 6.5, 15.1$, 1 H, HC(5*a*)), 2.36–2.34 (m, 1 H, HC(7*a*)), 2.19–2.17 (m, 1 H, HC(7)), 2.07–1.99 (m, 1 H, HC(6)), 1.88–1.75 (m, 2 H, HC(6), HC(5)), 1.69 (m, 1 H, HC(7), HC(5)), 1.50 (s, 3 H, $\text{H}_3\text{C}(8)$), 0.8–2.5 (br, 3 H, (H_3B))⁹³; ^{13}C -NMR: (126 MHz, CDCl_3) 137.9 (C(10)), 128.5 (C(12)), 127.8 (C(13)), 127.5 (C(11)), 87.7 (C(7*b*)), 76.6 (C(1)), 72.2 (C(9)), 64.3 (C(2)), 63.1 (C(4)), 53.6 (C(7*a*)), 53.1 (C(5*a*)), 32.1 (C(5)), 28.0 (C(6)), 26.6 (C(7)), 25.3 (C(8)); IR: (CDCl_3 , film) 3014 (m), 2698 (m), 2929 (m), 2858 (m), 2362 (m), 2326 (m), 2276 (m), 241 (w), 1480 (m), 1453 (m), 1380 (w), 115 (s); MS: (EI, 70eV) 270 (15), 242 (22), 166 (100), 151 (33), 91 (70); Mol. Formula: $\text{C}_{17}\text{H}_{26}\text{BNO}$ (271.21); HRMS: $\text{C}_{17}\text{H}_{25}\text{NOB}$: (270.2029); Calcd: 270.2029; Found: 270.2029; TLC: R_f 0.39 (EtOAc/Hexanes, 1:3) [I_2 , CAM].

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (II{3}): Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11a** (54.3 mg, 0.30 mmol), dimethylformamide (3.0 mL, ~0.1 M), then sodium hydride (9.1 mg, 0.36 mmol, 1.2 equiv) at 0 °C. After 15 min, 1-bromohexane (51 μ L, 0.36 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 h then more sodium hydride was added (4.5 mg, 0.18 mmol, 0.6 equiv) followed by more 1-bromohexane (25 μ L, 0.18 mmol, 0.6 equiv). After another 2 h the process was repeated a third time, sequentially adding NaH (2.3 mg, 0.09 mmol, 0.3 equiv), then 1-bromohexane (12 μ L, 0.09 mmol, 0.3 equiv). After another 2 h the reaction was quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 58 mg (73%) of *n*-hexyl ether **II{3}** as a clear, viscous oil. Data for **II{3}**: ^1H -NMR: (500 MHz, CDCl_3) 4.30 (dd, $J = 7.8, 15.4$, 1 H, C(1)), 3.44 (dd, $J = 6.4, 10.9$, 1 H, HC(2)), 3.39 (dt, $J = 2.3, 6.6$, 2 H, HC(9)), 3.26 (ddd, $J = 2.7, 6.7, 11.9$, 1 H, HC(4)), 3.15 (dt, $J = 6.6, 11.7$, 1 H, HC(4)), 3.03 (dd, $J = 8.9, 11.5$, 1 H, HC(2)), 2.45–2.35 (m, 1 H, HC(6 or 7)), 2.05–1.98 (m, 1 H, HC(7*a*)), 1.97–1.89 (m, 1 H,

HC(5a)), 1.85–1.76 (m, 1 H, HC(6 or 7)), 1.56–1.50 (m, 4 H, (CH₂)₂), 1.48 (s, 3 H, H₃C(8)), 1.34–1.25 (m, 8 H, (CH₂)₄), 0.88 (t, $J = 6.9$, 3 H, H₃C(14)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 87.6 (C(7b)), 76.6 (C(1)), 70.2 (C(2)), 64.2 (C(7a)), 63.1 (C(4)), 53.6 (C(9)), 53.1 (C(5a)), 32.0 (C(6)), 31.6 (C(10)), 29.8 (C(11)), 27.9 (C(5)), 26.4 (C(7)), 25.8 (C(12 or 13)), 25.3 (C(8)), 22.5 (C(12 or 13)), 13.9 (C(14)); IR: (NaCl plate, film) 2935 (m), 2933 (m), 2858 (m), 2379 (m), 2340 (m), 2283 (m), 1163 (m); MS: (ESI, Q-tof) 264 (25), 251 (15), 236 (100), 180 (21), 166 (64), 150 (22), 110 (25), 96 (69), 84 (29), 55 (19); Mol. Formula: C₁₆H₃₂BNO (265.24); HRMS: C₁₆H₃₁BNO: (264.2499); Calcd: 264.2499; Found: 264.2499; TLC: R_f 0.62 (hexanes/EtOAc, 3:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(methoxyethoxymethoxy)-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (II{4}): Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11a** (54.3 mg, 0.30 mmol), dimethylformamide (3.0 mL, ~0.1 M), then sodium hydride (9.1 mg, 0.36 mmol, 1.2 equiv) at 0 °C. After 15 min, freshly distilled methoxyethoxymethyl chloride was added (57 μ L, 0.50 mmol, 1.7 equiv) via syringe. The solution was stirred for 2 h then quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 70.3 mg (87%) of ether **II{4}** as a clear, viscous oil. Data for **II{4}**: ¹H-NMR: (500 MHz, CDCl₃) 4.70 (m, 2 H, H₂C(9)), 4.57 (dd, $J = 8.1$, $J = 15.5$, 1 H, HC(1)), 3.68 (ddt, $J = 5.1$, 10.9, 16.2, 2 H, H₂C(10)), 3.55 (ddd, $J = 1.5$, 3.9, 5.4, 2 H, HC(11)), 3.50 (dd, $J = 6.5$, 11.1, 1 H, HC(2)), 3.40 (s, 3 H, HC(12)), 3.26 (ddd, $J = 2.7$, 6.8, $J = 12.3$, 1 H, HC(4)), 3.16 (m, 1 H, HC(4)), 3.08 (m, 1 H, HC(2)), 2.44 (dd, $J = 8.1$, 16.1, 2 H, HC(7a), HC(5a)), 2.39 (m, 2 H, HC(7), HC(6)), 2.03 (m, 1 H, HC(6)), 1.93 (m, 1 H, HC(5)), 1.81 (m, 1 H, HC(7)), 1.75 (m, 1 H, HC(5)), 1.66 (m, 3 H, HC(8)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 95.3 (C(9)), 87.4 (C(7b)), 74.9 (C(1)), 71.7 (C(10)), 67.4 (C(11)), 64.5 (C(2)), 63.1 (C(4)), 59.1 (C(12)), 53.9 (C(7a)), 53.1 (C(5a)), 31.9 (C(5)), 28.0 (C(7)), 26.9 (C(6)), 25.1 (C(8)); IR: (CDCl₃, film) 3019 (m), 2399 (w), 1734 (w), 1700 (w), 1653 (m), 1215 (s), 758 (s), 669 (m); MS: (ESI, Q-tof) 268 (41), 240 (65), 224 (47), 196 (67), 166 (96), 150 (64), 149 (88), 96 (93), 89 (87), 59 (100); Mol. Formula: C₁₄H₂₈BNO₃ (269.10); HRMS: C₁₄H₂₇BNO₃: (268.2084); Calcd: 268.2084; Found: 268.2084; TLC: R_f 0.18 (hexanes/TBME, 9:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (II{5}): Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11a** (54 mg, 0.3 mmol), dimethylformamide (3.0 mL, ~0.1 M), then sodium hydride (9.1 mg, 0.36 mmol, 1.2 equiv) at 0 °C. After 15 min, 2-fluoropyridine (26 μ L, 0.36 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 h then quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I

afforded 73 mg (95%) of ether **II{5}** as a clear, viscous oil. Data for **II{5}**: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.14 (dd, $J = 1.7, 5.0$, 1 H, HC(13)), 7.56 (m, 1 H, HC(11)), 6.88 (dd, $J = 5.2, 6.4$, 1 H, HC(12)), 6.70 (d, $J = 8.3$, 1 H, HC(10)), 5.69 (dd, $J = 7.8, 14.9$, 1 H, HC(1)), 3.73 (dd, $J = 6.8, 11.7$, 1 H, HC(2)), 3.41 (ddd, $J = 4.5, 6.8, 11.6$, 1 H, HC(4)), 3.29 (m, 2 H, HC(2), HC(4)), 2.81 (q, $J = 7.7$, 1 H, HC(5a)), 2.44 (m, 1 H, HC(7a)), 2.16 (et, $J = 4.5, 6.9, 8.9, 13.4$, 1 H, HC(6)), 1.89 (m, 3 H, HC(7), HC(6), HC(5)), 1.70 (ddt, $J = 5.4, 8.8, 10.5$, 2 H, HC(7), HC(5)), 1.56 (s, 3 H, HC(8)), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^{93}$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 162.6 (C(9)), 147.0 (C(13)), 138.7 (C(11)), 117.1 (C(12)), 110.8 (C(10)), 88.0 (C(7b)), 72.9 (C(1)), 65.0 (C(2)), 63.4 (C(4)), 54.0 (C(7a)), 52.8 (C(5a)), 33.1 (C(5)), 28.5 (C(6)), 27.3 (C(7)), 25.1 (C(8)); IR: (CDCl_3 , film) 3149 (w), 2971 (w), 2382 (w), 2253 (s), 1793 (w), 1470 (m), 1433 (w), 1382 (m), 1096 (m); MS: (EI, 70eV) 257 (21), 149 (100), 134 (39), 120 (15), 108 (17), 96 (19), 78 (13), 55 (18); Mol. Formula: $\text{C}_{15}\text{H}_{23}\text{BN}_2\text{O}$ (258.17); HRMS: $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}$ (245.1654); Calcd: 245.1654; Found: 245.1649; TLC: R_f 0.20 (hexane/TBMS, 93/7) [I_2 , CAM].

3. Preparation of Amino•Borane Intermediates **III{2–5}**

*Preparation of (1R,3S,5aS,7aS,7bR) Octahydro-1-benzyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (**III{2}**)*

Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11b** (25 mg, 0.14 mmol), dimethylformamide (1.5 mL, ~0.1 M), then sodium hydride (4 mg, 0.17 mmol, 1.2 equiv) at 0 °C. After 15 min, benzyl bromide (20 μL , 0.17 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 h then quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 35 mg (95%) of benzyl ether **III{2}** as a clear, viscous oil. Data for **III{2}**: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.33 (m, 5 H, HC(11), HC(12), HC(13)), 4.50 (dd, 2 H, $J = 3.4, 11.7$, $\text{H}_2\text{C}(9)$), 3.88 (ddd, 1 H, $J = 5.9, 5.9, 8.3$, HC(1)), 3.46 (dd, 1 H, $J = 6.1, 12.8$, HC(2)), 3.40 (m, 1 H, HC(4)), 3.35 (dd, 1 H, $J = 8.5, 12.7$, HC(2)), 2.99 (ddd, 1 H, $J = 6.6, 10.3, 10.3$, HC(4)), 2.37–2.27 (m, 2 H, HC(7a), HC(6)), 1.98–1.676 (m, 3 H, HC(7), HC(6)), HC(5)), 1.56 (s, 3 H, $\text{H}_3\text{C}(8)$), 1.55–1.40 (m, 3 H, HC(7), HC(6), HC(5)), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^3$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 137.6 (C(10)), 128.5 (C(12)), 127.9 (C(13)), 127.6 (C(11)), 86.8 (C(7b)), 80.0 (C(1)), 72.0 (C(9)), 66.6 (C(2)), 64.2 (C(4)), 58.9 (C(7a)), 51.3 (C(5a)), 33.2 (C(5)), 31.0 (C(7)), 29.1 (C(6)), 24.8 (C(8)); IR: (CDCl_3 , film) 3019 (s), 2971 (m), 2858 (w), 2400 (m), 2361 (w), 269 (w), 1602 (w), 1524 (m), 1475 (w), 1421 (m), 1215 (s), 928 (m), 756 (s), 669 (s); MS: (ESI, Q-tof); Mol. Formula: $\text{C}_{17}\text{H}_{26}\text{BNO}$ (271.21); HRMS: $\text{C}_{17}\text{H}_{24}\text{NO}$ (258.1858); Calcd: 258.1858; Found: 258.1864; TLC: R_f 0.45 (hexanes/EtOAc).

*Preparation of (1R,3S,5aS,7aS,7bR) Octahydro-1-hexyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (**III{3}**)*

Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11b** (40 mg, 0.20 mmol), dimethylformamide (2 mL,

~0.1 M), then sodium hydride (15 mg, 0.6 mmol, 3.0 equiv) at 0 °C. After 15 min, 1-bromohexane (84 μ L, 0.6 mmol, 3.0 equiv) was added via syringe. The solution was stirred for 2 h then quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 40 mg (84%) of *n*-hexyl ether **III{3}** as a clear, viscous oil. Data for **III{3}**: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 3.76 (td, $J = 6.0, 8.9$, 1 H, HC(1)), 3.47 (dd, $J = 6.1, 12.7$, 1 H, HC(2)), 3.43-3.34 (m, 3 H, HC(4), $\text{H}_2\text{C}(9)$), 3.23 (dd, $J = 8.9, 12.7$, 1 H, HC(4)), 3.01 (m, 1 H, HC(2)), 2.36-2.27 (m, 2 H, HC(6), HC(7)), 2.23 (dd, $J = 6.0, 11.8$, 1 H, HC(7a)), 2.01-1.86 (m, 2 H, HC(5a), HC(5)), 1.77-1.71 (m, 2 H, (CH_2)), 1.54 (s, 3 H, HC(8)), 1.28 (m, 9 H, (CH_2)), 0.88 (t, 3 H, $J = 7.0$, HC(14)), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^3$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 86.7 (C(7b)), 80.4 (C(1)), 70.4 (C(2)), 66.8 (C(7a)), 64.1 (C(4)), 58.9 (C(9)), 51.2 (C(5a)), 33.2 (C(6)), 31.6 (C(10)), 31.1 (C(11)), 29.8 (C(5)), 29.1 (C(7)), 25.7 (C(12 or 13)), 24.8 (C(8)), 22.5 (C(12 or 13)), 14.0 (C(14)); IR: (CDCl_3 , film) 2964 (m), 2950 (s), 2930 (s), 2858 (m), 2361 (s), 2341 (s), 262 (m), 1654 (w), 1631 (w), 1475 (w), 1457 (w), 1378 (w), 1365 (w), 163 (w), 1126 (w), 1092 (w); MS: (ESI, Q-tof) 264 (83), 252 (100), 179 (12); Mol. Formula: $\text{C}_{16}\text{H}_{32}\text{BNO}$ 265.24; HRMS: $\text{C}_{16}\text{H}_{31}\text{BNO}$ (264.2499); Calcd: 264.2499; Found: 264.2487; TLC: R_f 0.67 (hexanes/EtOAc, 3:1) [I_2].

Preparation of (1R,3S,5aS,7aS,7bR) Octahydro-1-(methoxyethoxymethoxy)-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (III{4}): Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11b** (200 mg, 1.1 mmol), dimethylformamide (3.6 mL, ~0.3 M), then sodium hydride (32 mg, 1.32 mmol, 1.2 equiv) at 0 °C. After 15 min, methoxyethoxymethyl chloride (151 μ L, 1.32 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 h then quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 127 mg (43%) of methoxyethoxymethyl ether **III{4}** as a clear, viscous oil. Data for **III{4}**: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 4.81 (m, 2 H, HC(9), HC(1)), 4.73 (ddd, $J = 7.1, 7.1, 7.1$, 1 H, HC(9)), 3.98 (m, 1 H, HC(2)), 3.71 (m, 2 H, $\text{H}_2\text{C}(10)$), 3.56 (dd, $J = 3.7, 5.6$, 1 H, $\text{H}_2\text{C}(11)$), 3.39 (s, 3 H, HC(12)), 3.03 (m, 2 H, HC(7a), HC(5a)), 2.96 (m, 1 H, HC(4)), 2.70 (ddd, 1 H, $J = 6.2, 11.1, 11.0$, HC(2)), 2.12 (m, 2 H, HC(4), HC(5)), 1.83 (m, 3 H, HC(5), HC(6), HC(7)), 1.51 (m, 1 H, HC(6)), 1.40 (m, 1 H, HC(7)), 1.31 (s, 3 H, HC(8)); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 94.3 (C(11)), 92.1 (C(11)), 90.7 (C(11)), 82.5 (C(9)), 82.0 (C(9)), 71.7 (C(2)), 67.4 (C(12)), 66.8 (C(13)), 59.0 (C(1)), 57.7 (C(14)), 56.6 (C(8)), 53.5 (C(3)), 51.5 (C(6)), 31.4 (C(7)), 30.6 (C(5)), 30.4 (C(4)), 27.6 (C(10)); IR: (NaCl plate, film) 2932 (s), 2879 (m), 2366 (s), 2331 (s), 2276 (m), 1653 (w), 1478 (m), 1452 (m), 1379 (m), 1162 (s), 1121 (s), 1097 (s), 1051 (s), 989 (m), 934 (w), 849 (m), 796 (w), 668 (w); MS: (ESI, Q-tof) 256 (100), 257 (16); Mol. Formula: $\text{C}_{14}\text{H}_{25}\text{NO}_3$ 255.18; HRMS: $\text{C}_{14}\text{H}_{26}\text{NO}_3$ (256.1913); Calcd: 256.1913; Found: 256.1903; TLC: R_f 0.35 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9/1) [I_2].

Preparation of (1*R*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-7*b*-

methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (III{5}): Following General Procedure I, a two-necked, 25-mL, round-bottomed flask equipped with a nitrogen inlet adapter, a rubber septum and a magnetic stir bar was added sequentially alcohol **11b** (25 mg, 0.14 mmol), dimethylformamide (1.5 mL, ~0.1 M), then sodium hydride (4 mg, 0.17 mmol, 1.2 equiv) at 0 °C. After 15 min, 2-fluoropyridine (7.4 μ L, 0.17 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 h then quenched onto ice water (20 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 33 mg (93%) of 2-pyridyl ether **III{5}** as a clear, viscous oil. Data for **III{5}**: ¹H-NMR: (500 MHz, CDCl₃) 8.09 (ddd, *J* = 0.6, 1.9, 5.0, 1 H, HC(13)), 7.56 (ddd, *J* = 2.0, 7.1, 8.4, 1 H, HC(11)), 6.86 (ddd, *J* = 0.8, 5.1, 7.0, 1 H, HC(12)), 6.74 (d, *J* = 8.3, 1 H, HC(10)), 5.27 (ddd, *J* = 5.9, 7.5, 7.3, 1 H, HC(1)), 3.80 (dd, *J* = 6.2, 13.0, 1 H, C(2)), 3.47 (ddd, *J* = 4.2, 7.3, 11.4, 1 H, HC(4)), 3.38 (dd, *J* = 7.7, 12.9, 1 H, HC(2)), 3.22 (ddd, *J* = 6.7, 3.7, 10.7, 1 H, HC(4)), 2.49 (dd, *J* = 5.3, 12.6, 1 H, HC(7*a*)), 2.40–2.29 (m, 1 H, HC(5*a*), HC(5 or 6)), 2.04–1.85 (m, 1 H, HC(5 or 6), HC(7))), 1.69–1.51 (m, 3 H, HC(6), HC(7), HC(5)), 1.61 (s, 3 H, H₃C(8)), 0.8–2.5 (br, 3 H, (H₃B)³); ¹³C-NMR: (126 MHz, CDCl₃) 162.8 (C(9)), 146.6 (C(13)), 138.7 (C(11)), 117.1 (C(12)), 111.5 (C(10)), 86.6 (C(7*b*)), 75.9 (C(1)), 66.9 (C(2)), 64.6 (C(4)), 58.3 (C(7*a*)), 51.6 (C(5*a*)), 33.1 (C(5)), 30.9 (C(6)), 29.2 (C(7)), 24.8 (C(8)); IR: (NaCl plate, film) 2953 (s), 2864 (m), 2374 (m), 2330 (m), 2277 (m), 1598 (s), 1570 (s), 1470 (s), 1433 (s), 1371 (m), 1307 (m), 1272 (s), 1252 (m), 1163 (m), 142 (w), 1097 (w), 1049 (w), 1014 (w); MS: (ESI, Q-tof) 257 (8), 255 (16), 246 (25), 245 (100), 162 (12), 150 (31); Mol. Formula: C₁₅H₂₃BN₂O (258.17); HRMS: C₁₅H₂₄BN₂O 257.1825; Calcd: 257.1825; Found: 257.1815; TLC: *R_f* 0.55 (hexanes/EtOAc, 3:1) [I₂].

4. Preparation of Amino•Borane Intermediates IV{2–5, 2–3}

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-7*b*-

methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (IV{2,2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **15{2}** (49 mg, 0.250 mmol), dimethylformamide (2.5 mL, ~0.1 M), then sodium hydride (9.0 mg, 0.375 mmol, 1.2 equiv) at 0 °C. After 15 min, benzyl bromide (60 μ L, 0.500 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 64 mg (89%) of benzyl ether **IV{2,2}** as a clear, viscous oil. Data for **IV{2,2}**: ¹H-NMR: (500 MHz, CDCl₃) 7.37–7.26 (m, 5 H, HC(12), HC(13), HC(14)), 4.40 (s, 2 H, H₂C(10)), 3.64 (dd, *J* = 6.7, 10.3, 1 H, HC(4)), 3.56 (d, *J* = 13.5, 1 H, HC(2)), 3.25 (dd, *J* = 4.5, 11.0, 1 H, HC(4)), 3.24 (d, *J* = 13.4, 1 H, HC(2)), 2.39–2.33 (m, 1 H, HC(5*a*)), 2.29–2.22 (m, 2 H, HC(7*a*), HC(5)), 2.22–2.13 (m, 1 H, HC(7)), 1.86–1.78 (m, 1 H, HC(6)), 1.77–1.69 (m, 2 H, HC(7), HC(6)), 1.49 (s, 3 H, H₃C(8 or 9)), 1.47 (s, 3 H, H₃C(8 or 9)), 1.47–1.43 (m, 1 H, HC(5)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 139.0 (C(11)), 129.0 (C(12, 13, or 14)), 128.0 (C(12, 13, or 14)), 127.0 (C(12, 13, or 14)), 88.7 (C(7*b*)), 81.8 (C(1)), 70.8 (C(2)), 65.3 (C(10)), 64.4 (C(7*a*)), 64.0 (C(4)), 52.1 (C(5*a*)), 34.3 (C(6)), 29.5 (C(5)), 27.3 (C(7)), 25.6 (C(8 or 9)), 25.5 (C(8 or 9)); IR: (NaCl plate, film) 2966 (s), 2858 (m), 2375 (s), 2326 (s), 2279 (s), 1454 (m), 1382 (m), 1172 (s), 1087 (m), 1028 (m), 933 (w), 905 (w), 855 (w), 754 (s) (696 (m); MS: (EI, 70 eV) 284 (5), 271 (1), 256

(2), 180 (100), 165 (28), 149 (3), 138 (2), 122 (4), 109 (8); Mol. Formula: C₁₈H₂₈BNO (285.23); HRMS: C₁₈H₂₇BNO, (284.2186); Calcd: 284.2186; Found: 284.2184; TLC: *R_f* 0.23 (hexanes/TBME, 9:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-7*b*-

methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (IV{2,3}): To a one-necked, round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar is added sequentially **15{2}** (49 mg, 0.250 mmol), dimethylformamide (2.5 mL, 0.1 M) and sodium hydride (6 mg, 0.250 mmol). After being stirred for 15 min, 1-bromohexane (41 μ L, 0.250 mmol) was added. After being stirred for 2 h, NaH (6 mg, 0.250 mmol) was added. After being stirred for 15 min, 1-bromohexane (41 μ L, 0.250 mmol) was added. After being stirred for 2 h, NaH (6 mg, 0.250 mmol) was added. After being stirred for 15 min, 1-bromohexane (41 μ L, 0.250 mmol) was added. After 2 h, the reaction was quenched with water (10 mL) at 0 °C. Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 47 mg (69%) of hexyl ether **IV{2,3}** as a clear, viscous oil. Data for **IV{2,3}**: ¹H-NMR: (500 MHz, CDCl₃) 3.64 (ddd, *J* = 6.5, 10.2, 10.0, 1 H, HC(4)), 3.48 (d, *J* = 13.4, 1 H, HC(2)), 3.29 (ddd, *J* = 1.6, 6.6, 6.6, 2 H, H₂C(10)), 3.28 (m, 1 H, HC(4)), 3.14 (d, *J* = 13.4, 1 H, HC(2)), 2.33 (m, 1 H, HC(5a)), 2.25 (m, 1 H, HC(5)), 2.15 (dd, *J* = 6.3, 8.1, 1 H, HC(7a)), 2.07 (ddd, *J* = 6.2, 6.2, 13.1, 1 H, HC(7)), 1.85 (dddd, *J* = 7.3, 7.3, 7.2, 12.6, 1 H, HC(6)), 1.77–1.71 (m, 1 H, HC(6)), 1.71–1.64 (m, 1 H, HC(6)), 1.54–1.49 (m, 3 H, HC(5), H₂C(11)) 1.49 (s, 3 H, H₃C(8)), 1.35 (s, 3 H, H₃C(9)), 1.35–1.25 (m, 6 H, H₂C(12), H₂C(13), H₂C(14)), 0.88 (dd, *J* = 6.9, 6.9, 3 H, H₃(15)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 88.6 (C(7b)), 81.1 (C(1)), 70.3 (C(2)), 64.6 (C(7a)), 63.7 (C(4)), 62.9 (C(10)), 52.1 (C(5a)), 34.5 (C(6)), 31.8 (C(13)), 30.3 (C(11)), 29.6 (C(5)), 27.0 (C(7)), 26.1 (C(12 or 14)), 25.7 (C(8)), 25.1 (C(9)), 22.7 (C(12 or 14)), 14.2 (C(15)); IR: (NaCl plate, film) 2931 (s), 2865 (s), 2376 (s), 2326 (s), 2279 (s), 1456 (s), 1378 (s), 1301 (m), 1172 (s), 1086 (s), 1021 (m), 965 (w), 924 (w), 851 (w), 756 (s); MS: (EI, 70 eV) 278 (13), 265 (6), 250 (16), 194 (10), 180 (100), 165 (38), 150 (6), 138 (10), 123 (13), 110 (41); Mol. Formula: C₁₇H₃₄BNO (279.27); HRMS: C₁₇H₃₃BNO, (278.2655); Calcd: 278.2655; Found: 278.2656; TLC: *R_f* 0.35 (hexanes/TBME, 9:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-7*b*-

methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (IV{3,2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **15{3}** (30 mg, 0.134 mmol), dimethylformamide (1.3 mL, ~0.1 M), then sodium hydride (4.8 mg, 0.202 mmol, 1.5 equiv) at 0 °C. After 15 min, benzyl bromide (24 μ L, 0.202 mmol, 1.5 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 39 mg (92%) of benzyl ether **IV{3,2}** as a clear, viscous oil. Data for **IV{3,2}**: ¹H-

NMR: (500 MHz, CDCl₃) 7.37–7.33 (m, 4 H, HC(13), HC(14)), 7.31–7.27 (m, 1 H, HC(15)), 4.49 (d, $J = 11.3$, 1 H, HC(11)), 4.42 (d, $J = 11.3$, 1 H, HC(11)), 3.84–3.77 (m, 1 H, HC(4)), 3.63 (d, $J = 14.5$, 1 H, HC(2)), 3.39 (d, $J = 14.5$, 1 H, HC(1)), 3.29 (dd, $J = 8.5$, 8.5, 1 H, HC(4)), 2.41–2.32 (m, 3 H, HC(7a), HC(5a), HC(5)), 2.27–2.20 (m, 1 H, HC(6)), 2.22–2.16 (m, 1 H, HC(9)), 1.96–1.88 (m, 1 H, HC(7)), 1.78–1.66 (m, 2 H, HC(7), HC(6)), 1.49 (s, 3 H, H₃C(8)), 1.44–1.40 (m, 1 H, HC(5)), 1.00 (d, $J = 6.8$, 3 H, H₃C(10)), 0.96 (d, $J = 6.8$, 3 H, H₃C(10')), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 138.5 (C(12)), 128.7 (C(13)), 127.6 (C(15)), 127.1 (C(14)), 88.6 (C(1)), 87.5 (C(7b)), 65.1 (C(11)), 64.1 (C(2)), 63.1 (C(4)), 58.4 (C(7a)), 51.5 (C(5a)), 35.9 (C(7)), 30.6 (C(9)), 30.4 (C(5)), 28.3 (C(6)), 25.1 (C(8)), 18.4 (C(10)), 17.6 (C(11)); IR: (CHCl₃) 3071 (w), 3028 (w), 2964 (s), 2379 (s), 2326 (s), 2278 (s), 2234 (w), 1957 (w), 1876 (w), 1812 (w), 1727 (w), 1599 (w), 1496 (m), 1468 (m), 1454 (s), 1379 (s), 1330 (w), 1264 (m), 1168 (s), 1085 (s), 1063 (s), 1028 (m), 970 (w), 912 (s), 850 (w), 794 (w), 734 (s), 697 (s); MS: (EI, 70 eV) 312 (41), 299 (4), 268 (6), 256 (8), 220 (5), 208 (100), 193 (27), 164 (8), 149 (16), 126 (24); Mol. Formula: C₂₀H₃₂BNO (313.29); HRMS: C₂₀H₃₁BNO, (312.2499); Calcd: 312.2499; Found: 312.2497; TLC: R_f 0.25 (hexanes/TBME, 4:1) [I₂, CAM].

Preparation of (1R,3S,5aS,7aS,7bR) Octahydro-1-benzyl-1-phenyl-7b-

methyl-2Hcyclopenta[gh]pyrrolizine•Borane (IV{5,2}):

Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **15**{5,2} (60 mg, 0.233 mmol), dimethylformamide (2.3 mL, ~0.1 M), then sodium hydride (8.4 mg, 0.350 mmol, 1.5 equiv) at 0 °C. After 15 min, benzyl bromide (42 μL, 0.350 mmol, 1.5 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL).

Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 80 mg (98%) of benzyl ether **IV**{5,2} as a clear, viscous oil. Data for **IV**{5,2}: ¹H-NMR: (500 MHz, CDCl₃) 7.41–7.36 (m, 4 H), 7.34–7.30 (m, 3 H), 7.30–7.23 (m, 3 H), 4.32 (d, $J = 11.5$, 1 H, HC(2)), 4.01 (ddd, $J = 14.3$, 14.3, 14.2, 2 H, HC(13)), 3.98 (d, $J = 11.9$, 1 H, HC(2)), 4.00–3.95 (m, 1 H, HC(4)), 3.46–3.42 (m, 1 H, HC(4)), 2.68 (dd, $J = 3.9$, 8.3, 1 H, HC(7a)), 2.58–2.53 (m, 1 H, HC(7)), 2.44–2.46 (m, 2 H, HC(5a), HC(5)), 2.05–2.01 (m, 1 H, HC(6)), 1.94–1.83 (m, 2 H, HC(7), HC(6)), 1.57 (dd, 7.9, 10.5, 1 H, HC(5)), 1.51 (s, 3 H, H₃C(8)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 142.2 (C(9)), 138.1 (C(14)), 128.9, 128.5, 128.1, 127.5, 127.0, 126.0, 88.6 (C(7b)), 85.9 (C(1)), 66.1 (C(2)), 65.6 (C(13)), 65.4 (C(4)), 62.7 (C(7a)), 52.0 (C(5a)), 35.5 (C(6)), 29.9 (C(5)), 27.2 (C(7)), 25.7 (C(8)); IR: (CHCl₃) 3064 (w), 3031 (w), 2965 (s), 2869 (m), 2376 (s), 2332 (s), 2277 (s), 2243 (m), 1497 (m), 1448 (m), 1379 (w), 1177 (s), 1132 (w), 1088 (m), 1059 (s), 1027 (w), 911 (s), 849 (w), 732 (s), 699 (s); MS: (EI, 70 eV) 333.2 (1), 332.2 (1), 318.2 (1), 242.1 (100), 227.1 (9), 105 (32); Mol. Formula: C₂₃H₃₀BNO (347.30); HRMS: C₂₃H₂₇NO, (333.2093); Calcd: 333.20927; Found: 333.20927; TLC: R_f 0.28 (hexanes/TBME, 9:1) [I₂, CAM].

5. Preparation of Amino•Borane Intermediates V{2–7, 2–7}

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-benzyloxy-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (V{1,2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **12** (30 mg, 0.154 mmol), dimethylformamide (1.5 mL, ~0.1 M), then sodium hydride (5.5 mg, 0.231 mmol, 1.2 equiv) at 0 °C. After 15 min, benzyl bromide (27 μ L, 0.231 mmol, 1.2 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 40 mg (91%) of benzyl ether V{1,2} as a clear, viscous oil. Data for V{1,2}: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.33 (m, 5 H, HC(11), HC(12), HC(13)), 4.53 (ddd, $J = 6.6, 6.6, 10.7$, 1 H, HC(1)), 4.51 (d, $J = 11.7$, 1 H, HC(1)), 4.45 (d, $J = 11.4$, 1 H, HC(9)), 3.51 (dd, $J = 6.5, 10.4$, 1 H, HC(2)), 3.16 (dd, $J = 6.1, 12.5$, 1 H, HC(4)), 3.06 (dd, $J = 10.6, 10.6$, 1 H, HC(2)), 2.82 (dd, $J = 12.5, 12.5$, 1 H, HC(4)), 2.42 (dd, $J = 8.0, 17.0$, 1 H, HC(7a)), 2.09–2.00 (m, 1 H, HC(5)), 2.00–1.92 (m, 1 H, HC(7)), 1.89–1.85 (m, 1 H, HC(5a)), 1.82–1.76 (m, 1 H, HC(7)), 1.75–1.70 (m, 2 H, $\text{H}_2\text{C}(6)$), 1.51 (s, 1 H, $\text{H}_3\text{C}(8)$), 1.02 (d, $J = 6.4$, 3 H, $\text{H}_3\text{C}(14)$), 0.8–2.5 (br, 3 H, $(\text{H}_3\text{B})^3$); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 138.1 (C(10)), 128.6 (C(13)), 128.0 (C(12)), 127.8 (C(11)), 88.1 (C(7b)), 76.0 (C(1)), 72.0 (C(9)), 70.0 (C(4)), 64.3 (C(2)), 62.0 (C(5a)), 53.3 (C(7a)), 34.6 (C(5)), 29.6 (C(6)), 26.7 (C(7)), 25.9 (C(8)), 16.4 (C(16)); IR: (NaCl plate, film) 3064 (w), 3021 (w), 2960 (s), 2922 (s), 2872 (s), 2379 (s), 2326 (s), 2276 (s), 2234 (w), 1654 (w), 1497 (w), 1472 (m), 1456 (s), 1380 (m), 1364 (s), 1326 (w), 1305 (w), 1234 (w), 1186 (s), 1167 (s), 1142 (s), 1124 (s), 1054 (m), 1018 (w), 991 (m), 956 (w), 913 (s), 844 (w), 810 (w), 698 (s); MS: (EI, eV) 284 (18), 256 (19), 228 (5), 180 (100), 165 (31), 110 (30), 91 (71), 84 (13); Mol. Formula: $\text{C}_{18}\text{H}_{28}\text{BNO}$ (285.23); HRMS: $\text{C}_{18}\text{H}_{27}\text{BNO}$, (284.2186); Calcd: 284.21858; Found: 284.21909; TLC: R_f 0.25 (hexanes/TBME, 9:1) [I_2 , CAM].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*)-Octahydro-1-benzyloxy-1-methyl-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (V{2,2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16{2}** (42 mg, 0.200 mmol), dimethylformamide (2.0 mL, ~0.1 M), then sodium hydride (7.2 mg, 0.300 mmol, 1.5 equiv) at 0 °C. After 15 min, benzyl bromide (48 μ L, 0.4 mmol, 2.0 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 58 mg (97%) of benzyl ether V{2,2} as a clear, viscous oil. Data for V{2,2}: $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.36–7.27 (m, 5 H, HC(12), HC(13), HC(14)), 4.43 (d, $J = 11.1$, 1 H, HC(10)), 4.35 (d, $J = 11.1$, 1 H, HC(10)), 3.50 (d, $J = 11.6$, 1 H, HC(2)), 3.35 (d, $J = 11.6$, 1 H, HC(2)), 3.23 (dd, $J = 6.3, 12.5$, 1 H, HC(4)), 2.96 (dd, $J = 12.4, 12.4$, 1 H,

HC(4)), 2.21–2.12 (m, 2 H, HC(7a), HC(7)), 2.10–2.01 (m, 1 H, HC(5)), 1.88–1.83 (m, 2 H, HC(5a), HC(7)), 1.78–1.74 (m, 1 H, HC(6)), 1.75 (s, 3 H, H₃C(9)), 1.71–1.64 (m, 1 H, HC(6)), 1.57 (s, 3 H, H₃C(8)), 0.99 (d, $J = 6.4$, 3 H, H₃C(15)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 138.7 (C(11)), 128.5 (C(13)), 127.6 (C(12)), 127.2 (C(14)), 88.7 (C(7b)), 79.9 (C(1)), 73.5 (C(4)), 73.3 (C(2)), 65.8 (C(10)), 62.1 (C(5a)), 61.3 (C(7a)), 33.5 (C(5)), 29.0 (C(6)), 27.3 (C(7)), 26.3 (C(8)), 25.9 (C(9)), 16.0 (C(15)); IR: (CHCl₃) 2961 (s), 2398 (s), 2282 (s), 1497 (w), 1457 (s), 1384 (m), 1152 (s), 1063 (m), 1028 (m), 956 (w), 697 (m); MS: (EI, 70 eV) 298 (4), 270 (4), 194 (100), 179 (20), 110 (28), 91 (28); Mol. Formula: C₁₉H₃₀BNO (299.26); HRMS: C₁₉H₂₉BNO, (298.2342); Calcd: 298.2342; Found: 298.2341; TLC: R_f 0.30 (hexanes/TBME, 9:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-methyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (V{2,7}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16{2}** (42 mg, 0.200 mmol), dimethylformamide (2.0 mL, ~0.1 M), then sodium hydride (7.2 mg, 0.300 mmol, 1.5 equiv) at 0 °C. After 15 min, 4-methoxybenzyl bromide (32 μ L, 0.220 mmol, 1.1 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 58 mg (86%) of 4-methoxybenzyl ether **V{2,7}** as a clear, viscous oil. Data for **V{2,7}**: ¹H-NMR: (500 MHz, CDCl₃) 7.23 (d, $J = 8.6$, 2 H, HC(13)), 6.87 (d, $J = 8.7$, 2 H, HC(12)), 4.35 (d, $J = 10.6$, 1 H, HC(10)), 4.26 (d, $J = 10.6$, 1 H, HC(10)), 3.80 (s, 1 H, H₃C(13)), 3.48 (d, $J = 11.6$, 1 H, HC(2)), 3.32 (d, $J = 11.6$, 1 H, HC(2)), 3.21 (dd, $J = 6.3$, 12.4, 1 H, HC(4)), 2.95 (dd, $J = 12.4$, 12.4, 1 H, HC(4)), 2.19–2.10 (m, 2 H, HC(7a), HC(7)), 2.08–2.00 (m, 1 H, HC(5)), 1.90–1.82 (m, 2 H, HC(7), HC(5a)), 1.77–1.74 (m, 1 H, HC(6)), 1.74 (s, 3 H, H₃C(9)), 1.70–1.62 (m, 1 H, HC(6)), 1.56 (s, 3 H, H₃C(8)), 0.98 (d, $J = 6.4$, 3 H, H₃C(16)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 159.2 (C(14)), 130.7 (C(11)), 128.9 (C(13)), 113.9 (C(12)), 88.7 (C(7b)), 79.8 (C(1)), 73.5 (C(4)), 73.3 (C(2)), 65.5 (C(10)), 62.1 (C(5a)), 61.2 (C(7a)), 55.4 (C(15)), 33.4 (C(5)), 29.0 (C(6)), 27.3 (C(7)), 26.3 (C(8)), 25.9 (C(9)), 16.0 (C(16)); IR: (NaCl plate, film) 2958 (s), 2929 (s), 2835 (s), 2396 (s), 2330 (s), 2282 (s), 1612 (s), 1586 (w), 1514 (s), 1457 (s), 1384 (s), 1349 (w), 1337 (w), 1302 (m), 1249 (s), 1166 (s), 1152 (s), 1108 (w), 1092 (m), 1064 (s), 1036 (s), 956 (m), 910 (w), 873 (w), 823(s); MS: (EI, 70 eV) 328 (8), 194 (100), 179 (49), 164 (3), 151 (3), 121 (52), 110 (34); Mol. Formula: C₂₀H₃₂BNO₂ (329.28); HRMS: C₂₀H₃₁BNO₂, (328.2448); Calcd: 328.2448; Found: 328.2448; TLC: R_f 0.28 (hexanes/TBME, 9:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (V{2,3}): To a one-necked, round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar is added

sequentially **16** {2} (40 mg, 0.191 mmol), dimethylformamide (1.9 mL, 0.1 M) and sodium hydride (5 mg, 0.191 mmol). After being stirred for 15 min, 1-iodohexane (28 μ L, 0.191 mmol) was added. After being stirred for 2 h, NaH (5 mg, 0.191 mmol), was added. After being stirred for 15 min, 1-iodohexane (28 μ L, 0.191 mmol) was added. After being stirred for 2 h, NaH (5 mg, 0.191 mmol) was added. After being stirred for 15 min, 1-iodohexane (28 μ L, 0.191 mmol) was added. After 2 h, the reaction was quenched with water (10 mL) at 0 °C. Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 31 mg (55%) of hexyl ether **V**{2,3} as a clear, viscous oil. Data for **V**{2,3}: ¹H-NMR: (500 MHz, CDCl₃) 3.40 (d, *J* = 11.7, 1 H, HC(2)), 3.25 (m, 4 H, HC(10), HC(2), HC(4)), 2.95 (dd, *J* = 12.4, 12.4, 1 H, HC(4)), 2.11–2.02 (m, 3 H, HC(7a), HC(7), HC(5)), 1.81 (dd, *J* = 6.4, 9.8, 1 H, HC(5a)), 1.73 (m, 2 H, HC(7), HC(6)), 1.69–1.62 (m, 1 H, HC(6)), 1.59 (s, 1 H, H₃C(9)), 1.52 (s, 3 H, H₃C(8)), 1.52–1.46 (m, 2 H, HC(11)), 1.33–1.22 (m, 6 H, HC(12), HC(13), HC(14)), 0.98 (d, *J* = 6.4, 3 H, H₃C(16)), 0.88 (dd, *J* = 6.9, 6.9, 3 H, H₃C(15)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 88.65 (C(9)), 79.08 (C(2)), 73.55 (C(1 or 12)), 73.36 (C(1 or 12)), 63.69 (C(8)), 62.05 (C(3)), 61.47 (C(6)), 33.56 (C(7)), 31.85 (C(14, 15 or 16), 30.37 (C(13)), 29.11 (C(5)), 26.89 (C(4)), 26.24 (C(10)), 26.05 (C(14, 15, or 16)), 25.63 (C(11)), 22.74 (C(14, 15, or 16)), 16.12 (C(18)), 14.19 (C(17)); IR: (CDCl₃, film) 2957 (s), 2931 (s), 2872 (s), 2396 (s), 2284 (s), 2241 (w), 1730 (w), 1459 (s), 1381 (m), 1348 (w), 1184 (s), 1168 (s), 1149 (s), 1064 (m), 913 (s); MS: (ESI, 70 eV) 292 (51), 279 (7), 264 (20), 250 (5), 222 (3), 208 (13), 194 (100), 184 (30), 179 (41), 164 (8), 137 (6), 124 (22), 110 (67); Mol. Formula: C₁₈H₃₆BNO (293.30); HRMS: C₁₈H₃₅BNO, (292.2812); Calcd: 292.28118; Found: 292.28154; TLC: *R*_f 0.35 (hexanes/TBME, 9:1) [I₂, CAM].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyl-1-isopropyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (V**{3,2}):** Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16**{3} (59 mg, 0.250 mmol), dimethylformamide (2.5 mL, ~0.1 M), then sodium hydride (9.0 mg, 0.375 mmol, 2.0 equiv) at 0 °C. After 15 min, benzyl bromide (60 μ L, 0.500 mmol, 2.0 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 80 mg (98%) of benzyl ether **V**{3,2} as a clear, viscous oil. Data for **V**{3,2}: ¹H-NMR: (500 MHz, CDCl₃) 7.37–7.28 (m, 5 H, HC(13), HC(14), HC(15)), 4.51 (d, *J* = 11.1, 1 H, HC(11)), 4.38 (d, *J* = 11.1, 1 H, HC(11)), 3.63 (d, *J* = 14.3, 1 H, HC(2)), 3.60 (d, *J* = 14.3, 1 H, HC(2)), 3.36 (dd, *J* = 8.3, 12.1, 1 H, HC(4)), 3.14 (dd, *J* = 10.3, 12.1, 1 H, HC(4)), 2.45–2.38 (m, 1 H, HC(7)), 2.37 (dd, *J* = 7.7, 16.4, 1 H, HC(7a)), 2.29–2.21 (m, 1 H, HC(5)), 2.21–2.13 (m, 1 H, HC(9)), 1.84–1.77 (m, 3 H, H₂C(6), HC(5a)), 1.67–1.61 (m, 1 H, HC(7)), 1.48 (s, 3 H, H₃C(8)), 0.99 (d, *J* = 6.8, 1 H, H₃C(10)), 0.93 (d, *J* = 6.8, 3 H, H₃C(10')), 0.84 (d, *J* = 6.7, 3 H, H₃C(16)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 138.3 (C(12)), 128.6 (C(13) or C(15)), 127.6 (C(14)), 127.3 (C(13) or C(15)), 88.8 (C(7b) or C(1)), 85.1 (C(7b) or C(1)), 74.0 (C(4)), 69.4 (C(2)), 64.8 (C(11)), 59.6 (C(5a)), 57.1 (C(7a)), 34.7 (C(5)), 31.6 (C(6)), 30.3 (C(9)), 24.8 (C(7)), 24.7 (C(8)), 18.2 (C(10)), 17.7 (C(10')), 17.6 (C(16)); IR: (CDCl₃, film) 2962 (s), 2922 (s), 2870 (s), 2374 (s), 2327 (s), 2272 (s), 1497 (w), 1454 (s), 1379 (m), 1170 (s), 1147 (m), 1131 (m), 1057 (m), 1027 (m), 868 (w), 697 (m); MS: (EI, 70 eV) 326 (6), 234 (6), 270 (11), 222 (s), 207 (21);

Mol. Formula: C₂₁H₃₄BNO (327.31); HRMS: C₂₁H₃₃BNO, (326.2655); Calcd: 326.2655; Found: 326.2652; TLC: *R_f* 0.24 (hexanes/TBME, 9:1) [I₂].

Preparation of (1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-isopropyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (V{3,3}): To a one-necked, round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar is added sequentially **16{3}** (59 mg, 0.250 mmol), dimethylformamide (2.5 mL, 0.1 M) and sodium hydride (6 mg, 0.250 mmol). After being stirred for 15 min, 1-bromohexane (35 μ L, 0.250 mmol) was added. After being stirred for 2 h, NaH (6 mg, 0.250 mmol), was added. After being stirred for 15 min, 1-bromohexane (35 μ L, 0.250 mmol) was added. After being stirred for 2 h, NaH (6 mg, 0.250 mmol) was added. After being stirred for 15 min, 1-bromohexane (35 μ L, 0.250 mmol) was added. After 2 h, the reaction was quenched with water (10 mL) at 0 °C. Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 37 mg (44%) of hexyl ether **V{3,3}** as a clear, viscous oil. Data for **V{3,3}**: ¹H-NMR: (500 MHz, CDCl₃) 3.51 (d, *J* = 14.2, 1 H, HC(2)), 3.45 (d, *J* = 14.2, 1 H, HC(2)), 3.40-3.26 (m, 3 H, HC(4), H₂C(14), 3.18 (dd, *J* = 10.5, 12.0, 1 H, HC(4)), 2.42-2.32 (m, 2 H, HC(7), HC(5)), 2.27 (dd, *J* = 7.0, 9.3, 1 H, HC(7*a*)), 2.01 (hept, *J* = 6.8, 1 H, HC(9)), 1.87-1.77 (m, 3 H, H₂C(6), HC(5*a*)), 1.60-1.51 (m, 3 H, HC(7), H₂C(13)), 1.45 (s, 3 H, H₃C(8)), 1.38-1.32 (m, 2 H, H₂C(14)), 1.36-1.25 (m, 4 H, H₂C(15), H₂C(16)), 0.96 (d, *J* = 6.7, 3 H, H₃C(10)), 0.91 (d, *J* = 6.8, 3 H, H₃C(10)), 0.89 (dd, *J* = 6.9, 6.9, 3 H, H₃C(11)), 0.82 (d, *J* = 6.8, 3 H, H₃C(17)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 88.7 (C(1) or C(7*b*)), 84.1 (C(1) or C(7*b*)), 74.2 (C(4)), 69.3 (C(2)), 62.1 (C(12)), 59.6 (C(5*a*)), 57.0 (C(7*a*)), 34.7 (C(5)), 31.9 (C(15)), 31.6 (C(6)), 30.2 (C(13)), 29.9 (C(9)), 26.2 (C(14)), 24.6 (C(8)), 24.4 (C(7)), 22.7 (C(16)), 18.2 (C(10) or C(11)), 17.6 (C(10) or C(11) or C(17)), 17.6 (C(10) or C(11) or C(17)), 14.2 (C(16)); IR: (CDCl₃, film) 2957 (s), 2230 (s), 2870 (s), 2376 (s), 2327 (s), 2273 (s), 1457 (s), 1378 (s), 1270 (w), 1170 (s), 1147 (m), 1084 (s); MS: (EI, 70 eV) 320 (25), 318 (50), 307 (7), 292 (6), 278 (9), 276 (10), 264 (49), 236 (9), 222 (100), 207 (47), 192 (19), 180 (17), 164 (13), 137 (7), 124 (30), 110 (77); Mol. Formula: C₂₀H₄₀BNO (321.35); HRMS: C₂₀H₃₉BNO, (320.3125); Calcd: 320.3125; Found: 320.3125; TLC: *R_f* 0.34 (hexanes/TBME, 9:1) [I₂].

Preparation of (1*R*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (V{5,2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16{5}** (68 mg, 0.250 mmol), dimethylformamide (2.5 mL, ~0.1 M), then sodium hydride (9.0 mg, 0.375 mmol, 2.0 equiv) at 0 °C. After 15 min, benzyl bromide (60 μ L, 0.500 mmol, 2.0 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 80 mg (89%) of benzyl ether **V{5,2}** as a clear, viscous oil. Data for **V{5,2}**: ¹H-

NMR: (500 MHz, CDCl_3) 7.39 (m, 4 H), 7.33 (m, 3 H), 7.28 (d, $J = 7.1$, 1 H), 7.21 (d, $J = 6.8$, 2 H), 4.17 (d, $J = 11.3$, 1 H, HC(13)), 4.14 (d, $J = 13.8$, 1 H, HC(2)), 3.97 (d, $J = 11.1$, 1 H, HC(13)), 3.96 (d, $J = 13.5$, 1 H, HC(2)), 3.46 (dd, $J = 7.9$, 12.3, 1 H, HC(4)), 3.21 (dd, $J = 11.2$, 12.2, 1 H, HC(4)), 2.79 (dd, $J = 8.0$, 8.0, 1 H, HC(7a)), 2.73–2.63 (m, 1 H, HC(7)), 2.52–2.42 (m, 1 H, HC(5)), 1.97–1.88 (m, 4 H, HC(7), $\text{H}_2\text{C}(6)$, HC(5a)), 1.52 (s, 3 H, $\text{H}_3\text{C}(8)$), 0.96 (d, $J = 6.6$, 3 H, $\text{H}_3\text{C}(18)$), 0.8–2.5 (br, 3 H, (H_3B)⁹³); ^{13}C -NMR: (126 MHz, CDCl_3) 141.8 (C(9) or C(14)), 138.0 (C(9) or C(14)), (128.7, 128.5, 128.1, 127.6, 127.4, 126.4) (C(10), C(11), C(12), C(15), C(16), C(17)), 88.8 (C(1) or C(7b)), 83.4 (C(1) or C(7b)), 73.6 (C(4)), 70.6 (C(2)), 66.3 (C(13)), 62.2 (C(7a)), 60.3 (C(5a)), 34.4 (C(5)), 30.9 (C(6)), 25.0 (C(8)), 24.2 (C(7)), 17.3 (C(18)); IR: (NaCl plate, film) 2960 (s), 2329 (s), 1497 (m), 1172 (s), 1136 (w), 1058 (s), 931 (w), 700 (s); MS: (EI, 70 eV) 358.2 (3), 256.1 (100), 241.1 (11), 105 (35); Mol. Formula: $\text{C}_{24}\text{H}_{32}\text{BNO}$ (361.33); HRMS: $\text{C}_{24}\text{H}_{29}\text{BNO}$, (358.2342); Calcd: 358.2342; Found: 358.2336; TLC: R_f 0.25 (hexanes/TBME, 9:1) [I_2].

Preparation of (1R,3S,5S,5aS,7aS,7bR) Octahydro-1-(4-methoxy-benzyloxy)-1-phenyl-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (V{5,7}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16{5}** (68 mg, 0.250 mmol), dimethylformamide (2.5 mL, ~0.1 M), then sodium hydride (9.0 mg, 0.375 mmol, 2.0 equiv) at 0 °C. After 15 min, 4-methoxybenzyl bromide (40 μL , 0.275 mmol, 1.1 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 89 mg (91%) of 4-methoxybenzyl ether **V{5,7}** as a clear, viscous oil. Data for **V{5,7}**: ^1H -NMR: (500 MHz, CDCl_3) 7.39 (m, 4 H, HC(10), HC(11)), 7.33 (m, 1 H, HC(12)), 7.11 (d, $J = 8.7$, 2 H, HC(15)), 6.84 (d, $J = 8.7$, 2 H, HC(16)), 4.12 (d, $J = 13.4$, 1 H, HC(13)), 4.09 (d, $J = 10.7$, 1 H, HC(2)), 3.94 (d, $J = 13.4$, 1 H, HC(13)), 3.89 (d, $J = 10.6$, 1 H, HC(2)), 3.79 (s, 3 H, $\text{H}_3\text{C}(18)$), 3.45 (dd, $J = 7.9$, 12.3, 1 H, HC(4)), 3.20 (dd, $J = 11.2$, 12.1, 1 H, HC(4)), 2.77 (dd, $J = 7.9$, 7.9, 1 H, HC(7a)), 2.70–2.61 (m, 1 H, HC(7)), 2.50–2.40 (m, 1 H, HC(5)), 1.96–1.83 (m, 4 H, HC(7), $\text{H}_2\text{C}(6)$, HC(5a)), 1.51 (s, 3 H, $\text{H}_3\text{C}(8)$), 0.96 (d, $J = 6.6$, 3 H, $\text{H}_3\text{C}(19)$); ^{13}C -NMR: (126 MHz, CDCl_3) 159.2 (C(19)), 141.9 (C(11)), 130.1 (C(16)), 129.0 (C(17)), 128.7 (C(12) or C(11)), 128.1 (C(12)), 126.5 (C(10) or C(11)), 113.9 (C(16)), 88.8 (C(1) or C(7b)), 83.2 (C(1) or C(7b)), 73.6 (C(4)), 70.6 (C(13)), 66.0 (C(2)), 62.0 (C(7a)), 60.3 (C(5a)), 55.4 (C(18)), 34.4 (C(5)), 30.8 (C(6)), 25.0 (C(8)), 24.1 (C(7)), 17.3 (C(19)), 0.8–2.5 (br, 3 H, (H_3B)⁹³); IR: (CDCl_3 , film) 2957 (s), 2922 (s), 2869 (s), 2369 (s), 2329 (s), 2274 (s), 1613 (s), 1585 (w), 1514 (s), 1457 (s), 1379 (m), 1301 (m), 1249 (s), 1173 (s), 1136 (m), 1116 (w), 1033 (s), 823 (m), 756 (s), 700 (s); MS: (EI, 70 eV) 388.2 (1), 256.2 (100), 241.2 (17), 105 (38); Mol. Formula: $\text{C}_{25}\text{H}_{34}\text{BNO}_2$ (391.35); HRMS: $\text{C}_{25}\text{H}_{31}\text{BNO}_2$, (388.2448); Calcd: 388.2448; Found: 388.2444; TLC: R_f 0.22 (hexanes/TBME, 9:1) [I_2].

Preparation of (1*R*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-phenyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (V{5,3}): To a one-necked, round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar is added sequentially **16{5}** (64 mg, 0.236 mmol), dimethylformamide (2.4 mL, 0.1 M) and sodium hydride (6 mg, 0.250 mmol). After being stirred for 15 min, 1-bromohexane (33 μ L, 0.236 mmol) was added. After being stirred for 2 h, NaH (6 mg, 0.250 mmol), was added. After being stirred for 15 min, 1-bromohexane (33 μ L, 0.236 mmol) was added. After being stirred for 2 h, NaH (6 mg, 0.250 mmol) was added. After being stirred for 15 min, 1-bromohexane (33 μ L, 0.236 mmol) was added. After 2 h, the reaction was quenched with water (10 mL) at 0 °C. Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 63 mg (75%) of hexyl ether **V{5,3}** as a clear, viscous oil. Data for **V{5,3}**: ¹H-NMR: (500 MHz, CDCl₃) 7.33 (dd, *J* = 7.3, 7.3, 2 H, HC(10)), 7.29–7.24 (m, 3 H, HC(11), HC(12)), 4.03 (d, *J* = 13.6, 1 H, HC(2)), 3.85 (d, *J* = 13.6, 1 H, HC(2)), 3.45 (dd, *J* = 8.1, 12.2, 1 H, HC(4)), 3.24 (dd, *J* = 11.1, 12.0, 1 H, HC(4)), 3.13 (ddd, *J* = 6.4, 6.4, 8.9, 1 H, HC(13)), 2.82 (ddd, *J* = 6.5, 6.5, 8.9, 1 H, HC(13)), 2.70–2.61 (m, 2 H, HC(7*a*), HC(7)), 2.59–2.50 (m, 1 H, HC(5)), 1.90 (m, 4 H, HC(7), H₂C(6), HC(5*a*)), 1.47 (s, 3 H, H₃C(8)), 1.47–1.41 (m, 2 H, H₂C(14)), 1.32–1.20 (m, 4 H, H₂C(15), H₂C(16)), 1.23–1.15 (m, 2 H, H₂C(17)), 1.00 (d, *J* = 6.6, 3 H, H₃C(19)), 0.86 (t, *J* = 7.2, 3 H, H₃C(18)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 142.3 (C(9)), 128.5 (C(10)), 127.8 (C(11)), 126.3 (C(12)), 88.8 (C(7*b*) or C(1)), 82.4 (C(7*b*) or C(1)), 73.8 (C(4)), 70.2 (C(2)), 63.8 (C(13)), 63.2 (C(7*a*)), 56.0 (C(5*a*)), 34.5 (C(5)), 31.7 (C(7*b*)), 31.1 (C(6)), 29.9 (C(14)), 26.1 (C(16)), 24.9 (C(8)), 23.4 (C(7)), 22.7 (C(15)), 17.4 (C(18)), 14.1 (C(19)); IR: (NaCl plate, film) 2950 (s), 2929 (s), 2869 (s), 2377 (s), 2329 (s), 2274 (s), 1457 (s), 1337 (m), 1379 (m), 1173 (s), 1137 (m), 1092 (m), 1064 (m), 924 (w), 868 (w), 751 (w), 700 (s); MS: (EI, 70 eV) 352.2 (3), 341.2 (6), 326.2 (4), 270.1 (4), 256.1 (100), 241.1 (29), 110.1 (24); Mol. Formula: C₂₃H₃₈BNO (355.36); HRMS: C₂₃H₃₅NO (341.2719); Calcd: 341.2719; Found: 341.2722; TLC: *R*_f 0.35 (hexanes/TBME, 9:1) [I₂].

Preparation of (1*R*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(3,5-bis(trifluoromethyl)benzyloxy)-1-phenyl-5-methyl-7*b*-methyl-2*H*cyclopenta[*gh*]pyrrolizine•Borane (V{5,6}):

To a two-necked, 25-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16{5}** (105 mg, 0.287 mmol), THF (2.0 mL, 0.1 M), then potassium hydride (19 mg, 0.474 mmol, 1.22 equiv). The flask was immersed in an ice/NaCl cooling bath. To the resulting mixture was added 3,5-bis(trifluoromethyl)benzyl bromide dropwise, via syringe, as a solution in THF (2.0 mL). The bath was removed and the reaction was allowed to reach room temperature. After being stirred for 2 h at room temperature, the flask was immersed in an ice bath and the reaction was quenched with sat. aq. ammonium chloride (5.0 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 146 mg (76%) of 3,5-bis(trifluoromethyl)benzyl ether **V{5,6}** as a clear, viscous oil. Data for **V{5,6}**: ¹H-NMR: (500 MHz, CDCl₃) 7.75 (s, 1 H, HC(17)), 7.60 (s, 2 H, HC(15)), 7.39–7.38 (m, 4 H, HC(10), HC(11)), 7.36–7.31 (m, 1 H, HC(12)), 4.24 (d, *J* = 12.4, 1 H, HC(13)), 4.16 (d, *J* = 13.2, 1 H, HC(2)), 4.07 (d, *J* = 12.4, 1 H, HC(13)), 3.93 (d, *J* = 13.2, 1 H, HC(2)), 3.42 (dd, *J* = 7.7, *J* = 12.4, 1 H, HC(4)), 3.21 (dd, *J* = 11.8, *J* = 11.8, 1 H, HC(4)), 2.91 (dd, *J* = 8.4, *J* = 8.4, 1 H, HC(7*a*)), 2.64–2.55 (m, 1 H, HC(7)), 2.45–2.35 (m, 1

H, HC(5)), 2.03–2.87 (m, 4 H, HC(7), H₂C(6), HC(5a)), 1.53 (s, 3 H, H₃C(8)), 1.00 (d, $J = 6.5$, 3 H, H₃C(20)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 140.9 (C(9 or 14)), 140.8 (C(9 or 14)), 130.2 (q, $J = 33.2$, C(19)), 127.1 (C(10)), 127.1 (C(11)), 127.1 (C(12)), 126.7 (C(15)), 121.5 (hept, $J = 3.8$, C(17)), 88.9 (C(7b)), 84.1 (C(1)), 73.4 (C(4)), 71.2 (C(2)), 65.1 (C(13)), 60.6 (C(7a or 5a)), 60.6 (C(7a or 5a)), 34.5 (C(5)), 30.7 (C(6)), 25.1 (C(7)), 25.0 (C(8)), 17.0 (C(20)); IR: (CDCl₃, film) 3063 (w), 2962 (s), 2931 (s), 2874 (s), 2376 (s), 2331 (s), 2277 (s), 2243 (s), 1808 (w), 1624 (m), 1497 (m), 1461 (s), 1448 (s), 1366 (s), 1279 (s), 1174 (s), 1134 (s), 1091 (s), 1016 (m), 994 (m), 957 (w), 911 (s), 844 (s), 812 (w), 704 (s); MS: (ESI, Q-tof) 494.2 (75), 484.2 (100); Mol. Formula: C₂₆H₃₀BF₆NO (497.32); HRMS: C₂₆H₂₈NOF₆, (484.2075); Calcd: 484.2075; Found: 484.2064; TLC: R_f 0.38 (hexanes/TBME, 9:1) [I₂].

Preparation of (1R,3S,5S,5aS,7aS,7bR) Octahydro-1-benzyloxy-1-(2,4,6-trimethylphenyl)-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane (V{6,2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16{6}** (31 mg, 0.099 mmol), dimethylformamide (1.0 mL, ~0.1 M), then sodium hydride (3.6 mg, 0.148 mmol, 1.5 equiv) at 0 °C. After 15 min, benzyl bromide (18 μ L, 0.148 mmol, 1.5 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 39 mg (98%) of benzyl ether **V{6,2}** as a clear, viscous oil. Data for **V{6,2}**: ¹H-NMR: (500 MHz, CDCl₃) 7.32 (dd, $J = 7.2$, 7.2, 1 H, HC(19)), 7.29–7.25 (m, 1 H, HC(20)), 7.23 (d, $J = 7.2$, 1 H, HC(18)), 6.86 (s, 2 H, HC(11)) 4.28 (d, $J = 11.1$, 1 H, HC(16)), 4.25 (d, $J = 14.1$, 1 H, HC(2)), 4.17 (d, $J = 11.0$, 1 H, HC(16)), 4.07 (d, $J = 13.8$, 1 H, HC(2)), 3.94 (dd, $J = 9.3$, 11.6, 1 H, HC(4)), 3.25 (dd, $J = 6.9$, 11.8, 1 H, HC(4)), 2.99 (dd, $J = 9.1$, 9.1, 1 H, HC(7a)), 2.54 (s, 3 H, H₃C(13)) 2.52 (s, 3 H, H₃C(14)), 2.25 (s, 3 H, H₃C(15)), 2.26–2.19 (m, 1 H, HC(5)), 2.15–2.09 (m, 1 H, HC(7)), 2.01–1.98 (m, 1 H, HC(5a)), 1.90–1.84 (m, 2 H, H₂C(6)), 1.41 (s, 3 H, H₃C(8)), 1.13 (d, $J = 6.9$, 3 H, H₃C(21)), 0.8–2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 138.4, 138.0, 137.0, 137.0, 132.3, 132.1, 128.5, 127.6, 127.3, 87.5 (C(1 or 7b)), 87.4 (C(1 or 7b)), 74.6 (C(4)), 71.8 (C(2)), 66.9 (C(16)), 64.4 (C(7a)), 59.5 (C(5a)), 36.2 (C(5)), 33.0 (C(6)), 28.5 (C(15)), 25.6 (C(8)), 25.0 (C(13 or 14)), 24.6 (C(13 or 14)), 20.5 (C(7)), 19.9 (C(21)); IR: (CDCl₃, film) 3028 (w), 2950 (s), 2930 (s), 2865 (s), 2376 (s), 2330 (s), 2277 (m), 2241 (m), 1610(m), 1454 (s), 1379 (m), 1348 (w), 1277 (w), 1173 (s), 1086 (s), 1063 (s), 1028 (s), 993 (w), 911 (s), 872 (w); MS: (EI, 70 eV) 400.3 (1), 389.2 (2), 298.2 (100), 281.2 (4), 147.1 (47), 124.1 (26); Mol. Formula: C₂₇H₃₈BNO (403.41); HRMS: C₂₇H₃₅NO, 389.2719; Calcd: 389.2719; Found: 389.2719; TLC: R_f 0.25 (hexanes/TBME, 9:1) [I₂].

Preparation of (1R,3S,5S,5aS,7aS,7bR) Octahydro-1-benzyloxy-1-(1-naphthyl)-5-methyl-7b-methyl-2Hcyclopenta[gh]pyrrolizine•Borane V{7,2}: Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet

adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16**{7} (38 mg, 0.118 mmol), dimethyl-formamide (1.2 mL, ~0.1 M), then sodium hydride (4.3 mg, 0.177 mmol, 1.5 equiv) at 0 °C. After 15 min, benzyl bromide (21 μ L, 0.177 mmol, 1.5 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 45 mg (93%) of benzyl ether **V**{7,2} as a clear, viscous oil. Data for **V**{7,2}: ¹H-NMR: (500 MHz, CDCl₃) 8.58 (d, *J* = 8.0, 0.6 H), 8.53-8.50 (m, 1 H), 7.95-7.85 (m, 4 H), 7.54-7.48 (m, 4 H), 7.31-7.25 (m, 4 H), 7.16-7.13 (m, 3 H), 4.71 (d, *J* = 13.5, 0.6 H), 4.47 (d, *J* = 11.4, 1 H), 4.21 (d, *J* = 11.1, 0.6 H), 4.05-3.98 (m, 1.6 H), 3.91-3.84 (m, 1.6 H), 3.78 (d, *J* = 10.5, 1 H), 3.73 (dd, *J* = 8.2, 11.8, 0.6 H), 3.60 (dd, *J* = 9.3, 9.3, 1 H), 3.30 (dd, *J* = 11.2, 11.2, 0.6 H), 3.25 (dd, *J* = 6.2, 12.5, 1 H), 3.04-2.95 (m, 0.6 H), 2.89 (dd, *J* = 12.5, 12.5, 1 H), 2.79 (dd, *J* = 8.7, 8.7, 0.6 H), 2.59-2.50 (m, 1 H), 2.45-2.37 (m, 0.6 H), 2.26-2.11 (m, 3 H), 2.03-1.80 (m, 5H), 1.72 (s, 3 H), 1.35 (s, 1.8 H), 1.09 (d, *J* = 6.5, 1.8 H), 1.06 (d, *J* = 6.3, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 138.13, 138.08, 136.6, 136.0, 135.1, 134.8, 131.4, 130.3, 129.8, 129.6, 129.2, 128.4, 128.0, 127.7, 127.6, 126.4, 126.3, 126.2, 126.0, 125.9, 125.8, 125.78, 126.76, 125.7, 124.6, 124.3, 88.8, 86.9, 85.3, 85.0, 73.5, 72.8, 72.4, 70.6, 67.2, 66.8, 64.1, 63.4, 60.3, 54.8, 34.5, 33.7, 31.1, 28.7, 28.6, 27.7, 25.0, 25.3, 17.8, 16.1; IR: (CDCl₃, film) 3050 (w), 2959 (s), 2929 (s), 2870 (m), 2397 (s), 2326 (s), 2279 (m), 2242 (m), 1602 (w), 1509 (w), 1498 (w), 1455 (s), 1380 (s), 1336 (w), 1287 (w), 1241 (w), 1173 (s), 1142 (m), 1113 (m), 1059 (s), 1026 (m), 959 (w), 911 (s), 865 (w), 804 (s), 780 (s), 733 (s), 699 (s), 648 (m); MS: (EI, 70 eV) 426.2 (9), 408.2 (5), 398.2 (64), 382.2 (8), 306.1 (100), 290.1 (94), 270.1 (8), 155.0 (11); Mol. Formula: C₂₈H₃₄BNO (411.3867); HRMS: C₂₈H₃₅BNO, (412.2812); Calcd: 412.2812; Found: 412.2640; TLC: R_f 0.40 (hexanes/TBME, 4:1) [I₂, CAM].

Preparation of (1R,3S,5S,5aS,7aS,7bR)-Octahydro-1-benzyl-5-methyl-7b-

methyl-2Hcyclopenta[gh]pyrrolizine•Borane (β -V{2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **S6** (22 mg, 0.113 mmol), dimethylformamide (1.1 mL, ~0.1 M), then sodium hydride (4 mg, 0.17 mmol, 1.5 equiv) at 0 °C. After 15 min, benzyl bromide (20 μ L, 0.17 mmol, 1.5 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 28 mg (88%) of benzyl ether β -V{2} as a clear, viscous oil. Data for β -V{2}: ¹H-NMR: (500 MHz, CDCl₃) 7.35 (m, 4 H, HC(11), HC(12)), 7.28 (m, 1 H, HC(13)), 4.63 (d, *J* = 11.7, 1 H, HC(9)), 4.38 (d, *J* = 11.7, 1 H, HC(9)), 3.79-3.75 (m, 2 H, HC(2), HC(1)), 3.26-3.21 (m, 2 H, HC(2), HC(4)), 3.04 (dd, *J* = 12.2, 12.2, 1 H, HC(4)), 2.40 (dd, *J* = 7.9, 7.9, 1 H, HC(7a)), 2.07-2.01 (m, 1 H, HC(7)), 1.86-1.81 (m, 2 H, HC(5a), HC(5)), 1.81-1.73 (m, 1 H, HC(6)), 1.71-1.66 (m, 1 H, HC(6)), 1.60 (s, 3 H, H₃C(8)), 1.60-1.52 (m, 1 H, HC(7)), 1.00 (d, *J* = 5.9, 3 H, H₃C(14)), 0.8-2.5 (br, 3 H, (H₃B)⁹³); ¹³C-NMR: (126 MHz, CDCl₃) 138.1 (C(10)), 128.5 (C(12)), 127.8 (C(13)), 127.7 (C(11)), 88.0 (C(7b)), 81.8 (C(1)), 73.0 (C(4)), 70.8 (C(9)), 67.7 (C(2)), 60.9 (C(5a)), 58.2 (C(7a)), 35.4 (C(5)), 30.6 (C(7)), 29.7 (C(6)), 25.0 (C(8)), 16.6 (C(14)); IR: (CDCl₃, film) 2956 (s), 2915 (s), 2872 (s), 2383 (s), 2328 (s), 2262 (s), 1496 (w), 1455 (s), 1379 (m), 1316 (w), 1273 (w), 1234 (w), 1177 (s), 1106 (m), 1067 (m), 1014 (w), 913 (m), 862 (w), 798 (w); MS: (ESI, Q-tof) 284.2 (70), 272.2 (100), 192.2 (35), 141 (12); Mol. Formula: C₁₈H₂₈BNO 285.23; HRMS:

$C_{18}H_{26}NO$, (272.2014); Calcd: 272.2014; Found: 272.2008; TLC: R_f 0.24 (hexanes/TBME, 9:1) [I_2].

Preparation of (1*R*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-(*tert*-butyl)-5-methyl-7*b*-methyl-2Hcyclopenta[*gh*]pyrrolizine•Borane (V{4,2}): Following General Procedure I, to a two-necked, 10-mL round-bottomed flask equipped with a nitrogen inlet adapter, rubber septum and a magnetic stir bar was added sequentially alcohol **16{4}** (25 mg, 0.100 mmol), tetrahydrofuran (1.0 mL, ~0.1 M), then potassium hydride (6 mg, 0.149 mmol, 1.5 equiv) at 0 °C. After 15 min, benzyl bromide (26 μ L, 0.149 mmol, 1.5 equiv) was added via syringe. The solution was stirred for 2 hr then quenched onto ice water (10 mL). Extraction and purification by silica gel column chromatography as described in General Procedure I afforded 33 mg (97%) of benzyl ether **V{4,2}** as a clear, viscous oil. Data for **V{4,2}**: 1H -NMR: (500 MHz, $CDCl_3$) 7.38–7.33 (m, 4 H, HC(13), HC(14)), 7.30–7.27 (m, 1 H, HC(15)), 4.83 (d, J = 11.2, 1 H, HC(2)), 4.56 (d, J = 11.2, 1 H, HC(2)), 3.81 (d, J = 15.2, 1 H, HC(11)), 3.77 (d, J = 15.1, 1 H, HC(11)), 3.32 (dd, J = 8.0, 12.4, 1 H, HC(4)), 3.15 (dd, J = 11.2, 12.0, 1 H, HC(4)), 2.59 (dd, J = 6.9, 9.6, 1 H, HC(7*a*)), 2.57–2.48 (m, 1 H, HC(7)), 2.09–2.01 (m, 1 H, HC(5)), 1.80–1.72 (m, 3 H, H_2C (6), HC(5*a*)), 1.65–1.59 (m, 1 H, HC(7)), 1.48 (s, 3 H, H_3C (8)), 1.00 (s, 9 H, H_3C (10)), 0.72 (d, J = 6.6, 3 H, H_3C (16)), 0.8–2.5 (br, 3 H, (H_3B) 93); ^{13}C -NMR: (126 MHz, $CDCl_3$) 138.5 (C(12)), 128.6 (C(14)), 127.6 (C(15)), 127.2 (C(13)), 88.7 (C(1 or 7*b*)), 86.8 (C(1 or 7*b*)), 74.0 (C(4)), 68.6 (C(2)), 68.5 (C(11)), 59.7 (C(5*a*)), 59.5 (C(7*a*)), 39.2 (C(9)), 34.3 (C(5)), 31.4 (C(6)), 27.6 (C(10)), 24.6 (C(7)), 24.4 (C(8)), 16.9 (C(16)); IR: ($CDCl_3$, film) 2960 (s), 2871 (s), 2382 (s), 2328 (s), 2274 (s), 1728 (w), 1604 (w), 1497 (w), 1455 (s), 1401 (w), 1378 (m), 1318 (w), 1285 (w), 1235 (w), 1175 (s), 1133 (m), 1092 (s), 1061 (m), 1028 (m), 1007 (w), 977 (w), 955 (w), 926 (m), 913 (m), 869 (w), 735 (s), 698 (s); MS: (EI, 70 eV) 338.2 (13), 270.1 (12), 236.2 (100), 221.2 (3.9), 204.1 (3), 178.1 (10), 164.1 (3), 138.1 (3), 124.1 (4), 110.1 (10.2); Mol. Formula: $C_{22}H_{36}BNO$ (341.34); HRMS: $C_{22}H_{33}NO^+$, (327.2562); Calcd: 327.2562; Found: 327.2556; TLC: R_f 0.28 (hexanes/TBME, 9:1) [I_2].

A. Variable Group R^4 : Deborylation and *N*-Quaternization—

1. Parallel Synthesis Step II–III: General Procedure II: A solution of borane adduct **X** (XX mg, XX mmol) in CH_3OH (0.03 M) was transferred to a 250-mL, round-bottomed, flask fitted with a reflux condenser, a magnetic stir-bar, and a nitrogen inlet adapter with a rubber septum. Lastly, 1.0 M aq. HCl solution (x.x mL, 5.0 equiv) was added via syringe. The resulting clear solution was immersed in an oil bath (preheated, 60 °C) and stirred for 12 h. The mixture was allowed to cool to room temperature and was concentrated by rotary evaporation (15 mm Hg, 20–25 °C) whereupon a 0.1 M aq. NaOH solution (xx.x mL, 6.0 equiv) was added. The resulting solution was tested to assure basicity by pH paper (typically pH ~11–14). The basic solution was extracted with Et_2O (3 $\times$ 100 mL) and the combined extracts were dried (K_2CO_3). The resulting flocculant suspension was filtered (cotton plug),

and concentrated by rotary evaporation (15 mm Hg, 20–25 °C) to furnish the crude intermediate amine as a pale-yellow oil. The amine was dissolved in acetonitrile (0.2 M) and distributed among five 20-mL test tubes fitted in a Büchi SynCore reactor (Figure X) which were then evacuated and backfilled with N₂. An alkyl bromide (x.x mL, x.x mmol, 1.2 equiv) was added to each test tube *via* syringe (the solid bromides were added as solids) and the reactor was set to agitate at 200 rpm. After 12 h, the individual reaction mixtures were concentrated by rotary evaporation (15 mm Hg, 20–25 °C). Each salt was purified by silica gel plug filtration (1.8 cm × 5 cm, CH₂Cl₂/EtOAc, 1:1 (50 mL), then CH₂Cl₂/methanol 49:1, 24:1, 9:1 (50 mL each) afforded the product ammonium salts as a clear, sticky residues. The residues were triturated with Et₂O (~10 mL) in a 20-mL scintillation vial to free flowing solids which were then concentrated by rotary evaporation (15 mm Hg, 20–25 °C). The resulting solids were dried under vacuum (0.1 mm Hg, 20–25 °C) for 12 h to afford the final quaternary ammonium bromides X/x/ as free flowing powers.

2. Preparation of Quaternary Ammonium Bromides I{1–6}: Following General Procedure II, amino borane **10** (785 mg, 4.8 mmol) was added to a 250-mL, round-bottomed flask as a solution in 150 mL of MeOH (~0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 M aq. HCl solution (24 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 114 µL, 0.96 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 212 mg, 0.96 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 212 mg, 0.96 mmol, 1.2 equiv), 9-bromomethylantracene (tube 4, 260 mg, 0.96 mmol, 1.2 equiv), 3,5-(bistrifluoromethyl)benzyl bromide (tube 5, 176 µL, 0.96 mmol, 1.2 equiv), 1-bromohexane (tube 6, 140 µL, 0.96 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(5*a*S,7*a*R)-3-Benzyl-octahydrocyclopenta[gh]pyrrolizinium Bromide (I{1}): Data for I{1}: Yield: 223 mg (84%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.74 (m, 2 H), 7.42 (m, 3 H), 4.82 (s, 2 H), 4.36 (m, 2 H), 3.13 (m, 2 H), 2.80 (t, $J = 8.5$, 2 H), 2.50 (qd, $J = 7.2$, 14.6, 2 H), 2.05-1.96 (m, 2 H), 2.01 (s, 3 H), 1.79 (dt, $J = 6.3$, 13.0, 2 H), 1.70 (m, 2 H); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 134.6, 132.4, 132.1, 131.2, 99.7, 62.2, 61.5, 53.4, 33.1, 29.3, 23.6; MS: (ESI, Q-tof) 242 (100); Mol. Formula: $\text{C}_{17}\text{H}_{24}\text{BrN}$ (322.28); HRMS: $\text{C}_{17}\text{H}_{24}\text{N}$: (242.1909); Calcd: 242.1909; Found: 242.1906; TLC: R_f 0.21 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(5*a*S,7*a*R)-3-(1-Naphthylmethyl)-octahydrocyclopenta[gh]-pyrrolizinium Bromide (I{2}): Data for I{2}: Yield: 267 mg (90%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.34 (d, $J = 7.2$, 1 H), 8.11 (d, $J = 8.6$, 1 H), 7.91 (dd, $J = 3.8$, 8.1, 2 H), 7.64 (t, $J = 7.7$, 1 H), 7.53 (dd, $J = 7.4$, 17.9, 2 H), 5.29 (s, 2 H), 4.38 (m, 2 H), 3.08 (m, 2 H), 2.91 (m, 2 H), 2.58 (dt, $J = 7.3$, 14.6, 2 H), 2.22 (s, 3 H), 2.03 (m, 2 H), 1.77 (dt, $J = 6.3$, 12.6, 2 H), 1.69 (td, $J = 7.9$, 11.4, 2 H); MS: (ESI, Q-tof) 293 (24), 292 (100); Mol. Formula: $\text{C}_{21}\text{H}_{26}\text{BrN}$ (372.34); HRMS: $\text{C}_{21}\text{H}_{26}\text{N}$: (292.2065); Calcd: 292.2065; Found: 292.2056; TLC: R_f 0.27 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(5*a*S,7*a*R)-3-(2-Naphthylmethyl)octahydrocyclopenta[gh]-pyrrolizinium Bromide (I{3}): Data for **I{3}**: Yield: 243 mg (82%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.19 (s, 1 H), 7.87 (m, 1 H), 7.75 (td, $J = 5.4, 11.5, 3$ H), 7.49 (m, 2 H), 5.05 (s, 2 H), 4.39 (td, $J = 6.5, 12.7, 2$ H), 3.09 (m, 2 H), 2.82 (s, 2 H), 2.58 (dt, $J = 7.1, 14.6, 2$ H), 2.08 (s, 3 H), 2.00 (m, 2 H), 1.76 (dt, $J = 6.0, 12.6, 2$ H), 1.68 (m, 2 H); MS: (ESI, Q-tof) 293 (22), 292 (100); Mol. Formula: $\text{C}_{21}\text{H}_{26}\text{BrN}$ (372.34); HRMS: $\text{C}_{21}\text{H}_{26}\text{N}^+$: (292.2065); Calcd: 292.2065; Found: 292.2055; TLC: R_f 0.26 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(5*a*S,7*a*R)-3-(9-Anthrylmethyl)-Octahydro-cyclopenta[gh]pyrrolizinium Bromide (I{4}): Data for **I{4}**: Yield: 265 mg (77%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.68 (d, 2 H, $J = 9.0$), 8.47 (s, 1 H), 7.96 (d, 2 H, $J = 7.7$), 7.68 (m, 2 H), 7.48 (t, 2 H, $J = 7.1$), 5.72 (s, 2 H), 4.00 (m, 2 H), 3.01 (s, 2 H), 2.75 (m, 2 H), 2.64 (dt, 2 H, $J = 7.3, J = 14.6$), 2.40 (s, 3 H), 1.99 (m, 2 H), 1.66 (m, 6H); MS: (ESI, Q-tof) 343.2 (27),

342 (98), 192 (13), 191 (100); Mol. Formula: $C_{25}H_{28}BrN$ (422.40); HRMS: $C_{25}H_{28}N^+$: (342.222); Calcd: 342.2222; Found: 342.2216; TLC: R_f 0.31 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of Preparation of *rel*-(5a*S*,7a*R*)-3-(3,5-Bis(trifluoromethyl)benzyl)-octahydrocyclopenta[*gh*]pyrrolizinium Bromide (I{5}): Data for **I{5}**: Yield: 120 mg (86%), free-flowing white powder⁹⁶; ¹H-NMR: (500 MHz, $CDCl_3$) 8.40 (s, 2 H), 7.94 (s, 1 H), 5.31 (s, 2 H), 4.27 (ddd, J = 6.7, 12.3, 18.3, 2 H), 3.11 (ddd, J = 6.4, 12.0, 12.0, 2 H), 2.81 (s (broad), 1 H), 2.61 (ddd, J = 6.7, 13.9, 14.1, 2 H), 2.07 (s, 3 H, $H_3C(10)$), 2.02 (dd, J = 7.6, 12.8, 2 H), 1.83 (dd, J = 6.3, 13.3, 2 H), 1.71 (dd, J = 8.5, 16.7, 2 H); MS: (ESI, Q-tof) 379 (23), 378 (100); Mol. Formula: $C_{19}H_{22}BrF_6N$ (458.28); HRMS: $C_{19}H_{22}F_6N^+$: (378.1656); Calcd: 378.1656; Found: 378.1659; TLC: R_f 0.30 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(5*aS*,7*a**R*)-3-Hexyloctahydrocyclopenta[*gh*]pyrrolizinium Bromide (II{6}):** Data for II{6}: Yield: 180 mg (72%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 3.95 (td, $J = 7.1$, $J = 12.4$, 2 H), 3.83 (m, 2 H), 3.38 (m, 2 H), 2.63 (m, 2 H), 2.33 (qd, $J = 7.2$, $J = 14.8$, 2 H), 1.96 (m, 4 H), 1.81 (m, 4 H), 1.73 (s, 3 H), 1.44 (m, 2 H), 1.33 (m, 4 H), 0.89 (t, $J = 7.0$, 3 H); MS: (ESI, Q-tof) 237 (26), 236 (100); Mol. Formula: $\text{C}_{16}\text{H}_{30}\text{BrN}$ (316.32); HRMS: $\text{C}_{16}\text{H}_{30}\text{N}^+$: (236.2378); Calcd: 236.2378; Found: 236.2370; TLC: R_f 0.35 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

3. Preparation of Quaternary Ammonium Bromides II{1–5, I–6}: Following General Procedure II, amino borane **11a** (488.9 mg, 2.7 mmol) was added to a 250-mL, round-bottomed flask as a solution in 150 mL of MeOH (~0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 M aq. HCl solution (24 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 108 μL , 0.9 mmol, 2.0 equiv), 1-bromomethylnaphthalene (tube 2, 199 mg, 0.9 mmol, 2.0 equiv), 2-bromomethylnaphthalene (tube 3, 199 mg, 0.9 mmol, 2.0 equiv), 9-bromomethylantracene (tube 4, 244 mg, 0.9 mmol, 2.0 equiv), 3,5-(bistrifluoromethyl)benzyl bromide (tube 5, 93 μL , 0.9 mmol, 2.0 equiv), 1-bromohexane (tube 6, 130 μL , 0.9 mmol, 2.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*a**S*,7*b**R*) Octahydro-1-hydroxy-3-benzyl-7b-methylcyclopenta[*gh*]pyrrolizinium Bromide (II{1, I}):** Data for II{1, I}: Yield: 109 mg (72%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CD_3OD) 7.54 (m, 1 H), 4.72 (dd, $J = 6.0$, 13.6, 1 H), 4.47 (q, $J = 12.8$, 2 H), 3.85 (dd, $J = 5.9$, 12.7, 1 H), 3.74 (m, 2 H), 3.22 (dd, $J = 5.9$, 12.7, 1 H), 2.72 (ddd, $J = 6.4$, 11.2, 13.1, 1 H), 2.43 (dt, $J = 7.4$, 14.9, 1 H), 2.16 (m, 1 H), 2.05 (m, 1 H), 1.88 (m, 4 H), 1.77 (s, 3 H, Me); MS: (ESI, Q-tof) 259 (27), 258 (100), 221 (40), 187 (49); Mol. Formula: $\text{C}_{17}\text{H}_{24}\text{BrNO}$ (338.28); HRMS: $\text{C}_{17}\text{H}_{24}\text{NO}^+$: (258.1858); Calcd: 258.1858; Found: 258.1862; TLC: R_f 0.08 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-(1-naphthylmethyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{1,2}): Data for II{1,2}: Yield: 103 mg (59%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CD_3OD) 8.30 (d, $J = 8.6$, 1 H), 8.11 (d, $J = 8.3$, 1 H), 8.04 (d, $J = 7.8$, 1 H), 7.86 (s, 1 H), 7.73 (s, 1 H), 7.63 (dd, $J = 8.6$, $J = 8.0$, 2 H), 5.00 (s, 1 H), 4.86 (m, 1 H), 3.81 (dd, $J = 5.9$, 12.7, 1 H), 3.73 (t, 1 H, $J = 6.8$), 3.18 (s, 1 H), 2.81 (m, 2 H), 2.52 (dt, $J = 6.8$, 14.8, 1 H), 2.10 (m, 2 H), 1.92 (s, 3 H), 1.87 (m, 3 H); MS: (ESI, Q-tof) 309 (2), 308 (100), 221(32), 187 (47); Mol. Formula: $\text{C}_{21}\text{H}_{26}\text{BrNO}$ (388.34); HRMS: $\text{C}_{21}\text{H}_{26}\text{NO}$: (308.2014); Calcd: 308.2014; Found: 308.2026; TLC: R_f 0.10 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-(2-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (II{1,3}): Data for II{1,3}: Yield: 96 mg (56%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.12 (s, 1 H), 8.04 (s, 1 H), 8.02 (s, 1 H), 7.97 (m, 2 H), 7.62 (m, 3 H), 4.78 (s, 1 H), 4.64 (s, 1 H), 3.95 (s, 1 H), 3.81 (m, 2 H), 3.26 (dd, $J = 6.1$, 12.7, 1 H), 2.76 (ddd, $J = 6.7$, 10.9, 13.1, 2 H), 2.48 (s, 1 H), 2.12 (s, 1 H), 1.90 (m, 3 H), 1.82 (s, 3 H); MS: (ESI, Q-tof) 309 (26), 308 (100), 221 (32), 187 (63); Mol. Formula: $\text{C}_{21}\text{H}_{26}\text{BrNO}$ (388.34); HRMS: $\text{C}_{21}\text{H}_{26}\text{NO}$: (308.2014); Calcd: 308.2014; Found: 308.2017; TLC: R_f 0.09 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxyl-3-(9-anthrylmethyl)-cyclopenta[*gh*]pyrrolizinium Bromide (II{1,4}): Data for II{1,4}: Yield: 107 mg (54%), free-flowing yellow powder; $^1\text{H-NMR}$: (500 MHz, CD_3OD) 7.41 (s, 1 H), 7.13 (d, $J = 9.0$, 2 H), 6.80 (dd, $J = 4.3$, 8.4, 2 H), 6.34 (m, 2 H), 6.21 (dd, $J = 6.8$, 14.7, 2 H), 2.35 (m, 2 H), 1.87 (m, 1 H), 1.46 (m, 2 H), 1.39 (dd, $J = 6.9$, 12.8, 1 H), 1.07 (ddd, $J = 7.1$, 14.6, 14.5, 1 H), 0.72 (s, 3 H), 0.65 (m, 2 H), 0.40 (m, 3 H); MS: (ESI, Q-tof) 360 (8), 359 (30), 358 (100), 192 (19), 191 (99); Mol. Formula: $\text{C}_{25}\text{H}_{28}\text{BrNO}$ (438.40); HRMS: $\text{C}_{25}\text{H}_{28}\text{NO}$: (358.2171); Calcd: 358.2171; Found: 358.2184; TLC: R_f 0.12 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aR*,7*bR*) Octahydro-1-hydroxyl-3-(3,5-bistrifluoromethylbenzyl)-cyclopenta[*gh*]pyrrolizinium Bromide (II{1,5}): Data for II{1,5}: Yield: 125 mg (59%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CD_3OD) 8.25 (s, 2 H), 8.24 (s, 1 H), 4.76 (dd, $J = 5.8, 13.5$, 1 H), 4.68 (q, $J = 13.0, 2$ H), 3.84 (m, 1 H), 3.73 (td, $J = 6.8, 13.3$, 1 H), 2.77 (m, 1 H), 2.49 (dt, $J = 7.0, 14.4$, 1 H), 2.18 (m, 1 H), 2.09 (td, $J = 5.7, 12.8$, 1 H), 1.93 (m, 1 H), 1.80 (s, 3 H); MS: (ESI, Q-tof) 340 (17), 339 (83), 25 (31), 219 (68), 212 (100); Mol. Formula: $\text{C}_{19}\text{H}_{22}\text{BrF}_6\text{NO}$ (474.28); HRMS: $\text{C}_{19}\text{H}_{22}\text{F}_6\text{NO}^+$: (394.1606); Calcd: 394.1606; Found: 394.1606; TLC: R_f 0.13 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aR*,7*bR*) Octahydro-1-hydroxyl-3-hexyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{1,6}): Data for II{1,6}: Yield: 89 mg (59%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 4.55 (q, $J = 5.9$, 1 H), 4.02 (dt, $J = 12.1, 6.78$, 1 H), 3.70 (dd, $J = 5.9, 12.6$, 1 H), 3.58 (td, $J = 7.1, 12.1$, 1 H), 3.53 (dd, $J = 5.7, 12.7$, 1 H), 3.21 (m, 1 H), 2.60 (m, 2 H), 2.27 (tdd, 1 H, $J = 6.8, 8.6, 14.0$), 2.14 (ddd, $J = 5.8, 10.4, 19.7$, 1 H), 1.90 (m, 6 H), 1.59 (s, 3 H), 1.40 (m, 6 H), 0.94 (t, $J = 7.0$, 3 H); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 98.0, 68.4, 67.3, 61.4, 58.4, 56.1, 51.1, 33.5, 31.3, 28.6, 26.5, 26.3, 25.5, 23.5, 22.4, 13.9; MS: (ESI, Q-tof) 253 (20), 252 (100), 221 (24), 187 (71); Mol. Formula: $\text{C}_{16}\text{H}_{30}\text{BrNO}$ (332.32); HRMS: $\text{C}_{16}\text{H}_{30}\text{NO}^+$: (252.2327); Calcd: 252.2327; Found: 252.2332; TLC: R_f 0.19 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides II{2,1–6}: Following General Procedure II, amino borane **II{2}** (888 mg, 3.3 mmol) was added to a 250-mL, round-bottomed flask as a solution in 150 mL of MeOH (~0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 M aq. HCl solution (24 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 78 μ L, 0.66 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 145 mg, 0.66 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 145 mg, 0.66 mmol, 1.2 equiv), 9-bromomethylantracene (tube 4, 178 mg, 0.66 mmol, 1.2 equiv), 3,5-(bistrifluoromethyl)benzyl bromide (tube 5, 120 μ L, 0.66 mmol, 1.2 equiv), 1-bromohexane (tube 6, 92 μ L, 0.66 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-Benzyl-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{2,1}): Data for **II{2,1}**: Yield: 205 mg (88%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.68 (m, 2 H), 7.43 (m, 3 H), 7.32 (m, 3 H), 7.25 (d, $J = 6.3$, 2 H), 5.01 (d, $J = 12.5$, 1 H), 4.93 (dd, $J = 5.7$, 12.9, 1 H), 4.63 (dd, $J = 7.2$, 9.8, 1 H), 4.50 (m, 3 H), 4.02 (m, 1 H), 3.61 (ddd, $J = 6.4$, 9.3, 12.1, 1 H), 3.17 (dd, $J = 3.9$, 12.7, 1 H), 3.05 (dd, $J = 6.9$, 14.2, 1 H), 2.76 (m, 1 H), 2.45 (dt, $J = 8.6$, 15.2, 1 H), 2.17 (s, 3 H), 2.10 (m, 5 H), 1.84 (m, 1 H); MS: (ESI) 348 (100); Mol. Formula: $\text{C}_{24}\text{H}_{30}\text{BrNO}$ (428.41); HRMS: $\text{C}_{24}\text{H}_{30}\text{NO}^+$: (348.2327); Calcd: 348.2327; Found: 348.2322; TLC: R_f 0.23 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(1-naphthylmethyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{2,2}): Data for **II{2,2}**: Yield: 253 mg (97%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.23 (d, $J = 7.1$, 1 H), 8.20 (d, $J = 8.5$, 1 H), 7.83 (d, $J = 8.2$, 1 H), 7.79 (d, $J = 8.1$, 1 H), 7.59 (t, $J = 7.7$, 1 H), 7.49 (t, $J = 7.5$, 1 H), 7.36 (t, $J = 7.6$, 1 H), 7.30-7.27 (m, 4 H, $J = 1.8, 5.7$), 7.17 (dd, $J = 1.7, 7.5$, 1 H), 5.33 (d, $J = 13.1$, 1 H) 5.23 (d, $J = 13.0$, 1 H), 4.85 (dd, $J = 5.4, 12.5$, 1 H), 4.70 (m, 1 H), 4.45 (d, $J = 11.6$, 1 H), 4.39 (d, $J = 11.6$, 1 H), 3.90 (td, $J = 5.9, 11.7$, 1 H), 3.54 (ddd, $J = 6.5, 9.5, 11.9$, 1 H), 3.13 (m, 2 H), 2.90 (s, 1 H), 2.63 (dt, $J = 8.6, 15.5$, 1 H), 2.26 (s, 3 H), 2.07 (m, 2 H), 1.88-1.72 (m, 3 H); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 136.9, 133.6, 133.6, 133.0, 130.8, 129.1, 128.5, 128.0, 127.6, 127.5, 126.0, 125.3, 125.2, 123.1, 98.9, 72.8, 63.6, 60.3, 56.4, 54.9, 50.7, 33.4, 28.7, 26.2, 23.9; MS: ESI 398 (100); Mol. Formula: $\text{C}_{28}\text{H}_{32}\text{BrNO}$, (478.46); HRMS: $\text{C}_{28}\text{H}_{32}\text{NO}^+$, (398.2484); Calcd: 398.2484; Found: 398.2480; TLC: R_f 0.32 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 1:9) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(2-naphthylmethyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{2,3}): Data for **II{2,3}**: Yield: 261 mg (100%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.16 (s, 1 H), 7.90-7.87 (m, 1 H), 7.72 (m, 3 H), 7.50 (m, 2 H), 7.30-7.21 (m, 3 H) 7.22-7.20 (m, 2 H), 5.22 (d, $J = 12.5$, 1 H), 4.96 (dd, $J = 5.8, 12.8$, 1 H), 4.79 (dd, $J = 12.6, 24.6$, 1 H), 4.68 (s(broad), 1 H), 4.45 (s, 2 H), 4.05-4.01 (m, 1 H), 3.63-3.57 (m, 1 H), 3.19 (dd, $J = 3.8, 12.7$, 1 H), 3.06 (t, $J = 6.7$, 1 H), 2.80 (s(broad), 1 H), 2.54 (m(broad), 1 H), 2.12 (s, 3 H), 2.04 (m, 1 H); Mol.

Formula: $C_{28}H_{32}BrNO$ (478.46); HRMS: $C_{28}H_{32}NO^+$, (398.2484); Calcd: 398.2484; Found: 398.2475; TLC: R_f 0.28 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*)Octahydro-1-benzyloxy-3-(9-anthrylmethyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{2,4}): Data for **II{2,4}**: Yield: 186 mg (64%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.88 (d, $J = 9.1$, 1 H), 8.51 (d, $J = 9.5$, 2 H), 8.00 (d, $J = 8.3$, 2 H), 7.75 (m, 1 H), 7.66 (m, 1 H), 7.50 (m, 2 H), 7.24-7.21 (m, 3 H), 7.12-7.10 (m, 2 H), 5.77 (d, $J = 14.1$, 1 H), 5.61 (d, $J = 14.1$, 1 H), 4.85 (dd, $J = 5.4$, 13.2, 1 H), 4.52 (dd, $J = 4.7$, 11.9, 1 H), 4.42 (d, $J = 11.6$, 1 H), 4.31 (d, $J = 11.5$, 1 H), 3.81 (td, $J = 6.3$, 12.5, 1 H), 3.35 (dd, $J = 7.8$, 14.5, 1 H), 3.30-3.24 (m, 1 H), 3.02 (m, 1 H), 2.74 (dd, $J = 4.7$, 12.6, 1 H), 2.61 (dt, $J = 8.3$, 15.4, 2 H), 2.46 (s, 1 H), 2.05 (m, 2 H), 1.90-1.61 (m, 4 H), 1.33-1.25 (m, 2 H); MS: (ESI, Q-tof) 449 (49), 448 (100), 354 (37), 191 (54); Mol. Formula: $C_{32}H_{34}BrNO$ (528.52); HRMS: $C_{32}H_{34}NO^+$, (448.2640); Calcd: 448.2640; Found: 448.2628; TLC: R_f 0.35 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*)Octahydro-1-benzyloxy-3-(3,5-trifluoromethylbenzyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (II{2,5}): Data for **II{2,5}**: Yield: 20 mg (64%), free-flowing white powder⁹⁶; 1H -NMR: (500 MHz, $CDCl_3$) 8.34 (s, 2 H), 7.95 (s, 1 H), 7.31 (m, 3 H), 7.24 (m, 2 H), 5.56 (d, $J = 12.7$, 1 H), 4.99 (dd, $J = 5.7$, 12.6, 1 H), 4.90 (d, $J = 12.7$, 1 H), 4.64-4.61 (m(so), 1 H), 4.52 (d, $J = 11.6$, 1 H), 4.48 (d, $J = 11.6$, 1 H), 3.83-3.78 (m(so), 1 H), 3.71-3.65 (m(so), 1 H), 3.10 (dd, $J = 3.2$, 12.7, 1 H), 3.02 (dd, $J = 7.5$, 12.8, 1 H), 2.81-2.75 (m(br), 1 H), 2.56 (td, $J = 8.1$, 15.1, 1 H), 2.18-2.05 (m, 2 H), 2.09 (s, 3 H), 1.91-1.82 (m, 3 H); MS: (ESI, Q-tof) 485 (33), 484 (100), 399 (14), 398 (49); Mol. Formula: $C_{26}H_{28}BrF_6NO$ (564.40); HRMS: $C_{26}H_{28}F_6NO^+$, (484.2075); Calcd: 484.2075; Found: 484.2063; TLC: R_f 0.21 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bS*)Octahydro-1-benzyloxy-3-hexyl-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{2,6}): Data for II{2,6}: Yield: 99 mg (43%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.33 (m, 5 H), 4.59 (dd, 1 H, *J* = 6.1, 17.1), 4.54 (s, 1 H), 4.45 (dd, 1 H, *J* = 6.9, 13.4), 3.84 (td, 1 H, *J* = 6.1, 12.3), 3.62 (m, 1 H), 3.30 (td, 1 H, *J* = 6.0, 17.9), 3.04 (m, 1 H), 2.60 (dd, 1 H, *J* = 7.4, 15.0), 2.52 (dd, 1 H, *J* = 6.3, 12.6), 2.32 (td, 1 H, *J* = 6.8, 20.5), 2.03 (dt, 1 H, *J* = 6.0, 13.3), 1.87 (m, 5 H), 1.74 (s, 3 H), 1.33 (dd, 2 H, *J* = 5.0, 9.3), 0.89 (t, 3 H, *J* = 7.0); MS: (ESI, Q-tof) 343 (32), 342 (100), 259 (21), 258 (92); Mol. Formula: C₂₃H₃₆BrNO (422.44); HRMS: C₂₃H₃₆NO⁺, (342.2797); Calcd: 342.2797; Found: 342.2797; TLC: *R_f* 0.38 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of Quaternary Ammonium Bromides: II{3,1-6}: Following General Procedure II, amino borane II{3} (441.6 mg, 1.68 mmol) was added to a 250-mL, round-bottomed flask as a solution in 150 mL of MeOH (~0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 M aq. HCl solution (24 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 40 uL, 0.33 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 73 mg, 0.33 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 73 mg, 0.33 mmol, 1.2 equiv), 9-bromomethylantracene (tube 4, 90 mg, 0.33 mmol, 1.2 equiv), 3,5-(bistrifluoromethyl)benzyl bromide (tube 5, 61 uL, 0.33 mmol, 1.2 equiv), 1-bromohexane (tube 6, 78 uL, 0.56 mmol, 2.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-benzylcyclopenta-[*gh*]pyrrolizinium Bromide (II{3,1}): Data for II{3,1}: Yield: 96 mg (83%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.73 (dd, *J* = 2.2, 7.1, 2 H), 7.45 (d, *J* = 4.7, 3 H), 5.05 (d, *J* = 12.5, 2 H), 4.42 (m, 2 H), 3.97 (m, 1 H), 3.66 (dd, *J* = 5.6, 7.4, 1 H), 3.37 (m, 2 H), 3.18 (d, *J* = 12.8, 1 H), 3.06 (s, 1 H), 2.73 (s, 1 H), 2.49–2.40 (m, 1 H), 2.05 (s, 1 H), 1.81 (m, 3 H), 1.48 (s, 1 H), 1.26 (m, 6H), 0.85 (t, *J* = 6.9, 3 H); MS: (ESI, Q-tof) 342.2 (100), 343.3(28), 336.3(10); Mol. Formula: C₂₃H₃₆BrNO (422.44); HRMS: C₂₃H₃₆NO: (342.2797); Calcd: 342.2797; Found: 342.2786; TLC: *R*_f 0.32 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-[1]naphthylmethylcyclopenta[*gh*]pyrrolizinium Bromide (II{3,2}): Data for II{3,2}: Yield: 109 mg (84%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.31 (d, *J* = 7.2, 1 H), 8.20 (d, *J* = 8.6, 1 H), 7.88 (t, *J* = 7.8, 2 H), 7.65 (t, *J* = 7.3, 1 H), 7.54 (t, *J* = 7.5, 1 H), 7.46 (t, *J* = 7.3, 1 H), 5.35 (d, *J* = 13.1, 1 H), 5.18 (d, *J* = 13.1, 1 H), 4.99 (dd, *J* = 5.4, 12.7, 1 H), 4.50 (m, 1 H), 3.88 (m, 1 H), 3.61 (dt, *J* = 6.3, 11.3, 1 H), 3.35 (t, *J* = 6.5, 2 H), 3.14 (m, 2 H), 2.88 (m, 1 H), 2.65 (m, 1 H), 2.26 (s, 3 H), 2.06 (ddd, *J* = 6.5, 13.0, 19.3, 2 H), 1.80 (m, 3 H), 1.44 (p, *J* = 6.6, 2 H), 1.23 (m, 6 H), 0.84 (t, *J* = 6.9, 3 H); MS: (ESI, Q-tof) 394 (8), 393 (40), 392 (100); Mol. Formula: C₂₇H₃₈BrNO (472.50); HRMS: C₂₇H₃₈NO: (392.2953); Calcd: 392.2953; Found: 392.2957; TLC: *R*_f 0.35 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-[2]naphthylmethylcyclopenta[*gh*]pyrrolizinium Bromide (II{3,3}): Data for II{3,3}: Yield: 98 mg (75%),

free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.18 (s, 1 H), 7.89 (dd, $J = 4.0$, 5.3, 1 H), 7.75 (d, $J = 10.2$, 3 H), 7.51 (td, $J = 3.1$, 5.2, 2 H), 5.22 (d, $J = 12.5$, 1 H), 5.03 (dd, $J = 5.6$, 12.7, 1 H), 4.70 (d, $J = 12.5$, 1 H), 4.44 (m, 1 H), 3.98 (m, 1 H), 3.63 (dt, $J = 6.1$, 11.1, 1 H), 3.33 (m, 2 H), 3.19 (dd, $J = 3.0$, 12.8, 1 H), 3.05 (dd, $J = 7.6$, 12.7, 1 H), 2.77 (dd, $J = 7.5$, 11.1, 1 H), 2.56 (m, 1 H), 2.10 (s, 3 H), 2.05 (dd, $J = 5.0$, 11.0, 2 H), 1.81 (m, 3 H), 1.44 (m, 2 H), 1.22 (m, 8 H), 0.82 (t, $J = 6.8$, 3 H); MS: (ESI, Q-tof) 394 (6), 393 (34), 392 (100), 324 (10), 309 (4), 252 (19), 196 (8); Mol. Formula: $\text{C}_{27}\text{H}_{38}\text{BrNO}$ (472.50); HRMS: $\text{C}_{27}\text{H}_{38}\text{NO}$: (392.2953); Calcd: 392.2953; Found: 392.2936; TLC: R_f 0.37 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-[9]anthrylmethylcyclopenta[gh]pyrrolizinium Bromide (II{3,4}): Data for **II{3,4}**: Yield: 133 mg (92%), free-flowing yellow powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.65 (d, $J = 7.8$, 1 H), 8.43 (t, $J = 7.4$, 1 H), 8.21 (dd, $J = 1.3$, 7.7, 1 H), 8.16 (dd, $J = 1.3$, 7.7, 1 H), 7.78 (m, 2 H), 7.59 (m, 2 H), 4.53 (dd, $J = 5.6$, 13.2, 1 H), 4.26 (d, $J = 13.8$, 2 H), 4.19 (m, 1 H), 3.43 (d, $J = 6.25$, 7 H), 3.01 (m, 2 H), 2.61 (m, 1 H), 2.34 (dd, $J = 7.2$, 13.8, 1 H), 1.88 (m, 6 H), 1.65 (s, 3 H), 1.27 (m, 13 H), 0.93 (t, $J = 6.9$, 3 H); MS: (ESI, Q-tof) 442 (83), 336 (100), 252 (75); Mol. Formula: $\text{C}_{31}\text{H}_{40}\text{BrNO}$ (522.56); HRMS: $\text{C}_{31}\text{H}_{40}\text{NO}$: (442.3110); Calcd: 442.3110; Found: 442.3098; TLC: R_f 0.35 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-(3,5-bistrifluoromethylbenzyl)cyclopenta[gh]pyrrolizinium Bromide (II{3,5}): Data for **II{3,5}**: Yield: 137 mg (88%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.38 (s, 2 H), 7.94 (s, 1 H), 5.58 (d, $J = 12.6$, 1 H), 4.98 (m, 2 H), 4.42 (dd, $J = 5.4$, 7.1, 1 H), 3.78 (m, 1 H), 3.67 (m, 1 H), 3.38 (dtd, $J = 6.6$, 9.1, 15.8, 2 H), 3.12 (d, $J = 12.5$, 1 H), 2.99 (s, 1 H),

2.76 (s, 1 H), 2.60 (m, 1 H), 2.07 (s, 5 H), 1.83 (m, 3 H), 1.49 (m, 2 H), 1.25 (m, 7 H), 0.85 (t, $J = 6.9$, 3 H); ^{13}C -NMR: (126 MHz, CDCl_3) 133.3, 133.0, 132.3(q), 123.9, 122.7 (q), 99.7, 71.3, 64.5, 60.4, 58.2, 55.2, 50.5, 33.5, 31.4, 29.4, 28.5, 25.9, 25.6, 23.3, 22.4, 13.8; MS: (ESI, Q-tof) 479 (29), 478 (100); Mol. Formula: $\text{C}_{25}\text{H}_{34}\text{BrF}_6\text{NO}$ (558.44); HRMS: $\text{C}_{25}\text{H}_{34}\text{F}_6\text{NO}$: (478.2545); Calcd: 478.2545; Found: 478.2539; TLC: R_f 0.32 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-hexyl-cyclopenta[*gh*] pyrrolizinium Bromide (II{3,6}): Data for **II{3,6}**: Yield: 104 mg (91%), free-flowing white powder; ^1H -NMR: (500 MHz, CDCl_3) 4.62 (dd, $J = 5.6$, 12.8, 1 H), 4.30 (m, 1 H), 3.98 (ddd, $J = 6.7$, 9.3, 11.8, 1 H), 3.81 (ddd, $J = 5.2$, 6.7, 11.9, 1 H), 3.66 (dt, $J = 4.6$, 12.2, 1 H), 3.55 (dd, $J = 3.3$, 12.9, 1 H), 3.50 (td, $J = 6.4$, 9.1, 1 H), 3.40 (td, $J = 6.6$, 9.1, 1 H), 3.22 (dt, $J = 4.3$, 12.3, 1 H), 2.99 (dd, $J = 7.8$, 12.9, 1 H), 2.61 (m, 1 H), 2.27 (td, $J = 8.1$, 15.5, 1 H), 2.06 (m, 2 H), 1.84 (s, 3 H), 1.76 (m, 4 H), 1.54 (m, 3 H), 1.30 (m, 12 H), 0.89 (dt, 6 H, $J = 3.1$, 6.9); MS: (ESI, Q-tof) 337 (30), 336 (100); Mol. Formula: $\text{C}_{22}\text{H}_{42}\text{BrNO}$ (416.48); HRMS: $\text{C}_{22}\text{H}_{42}\text{NO}$: (336.3266); Calcd: 336.3266; Found: 336.3269; TLC: R_f 0.42 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

4. Preparation of Quaternary Ammonium Bromides II{4,1-6}: Following General Procedure II, amino borane **II{4}** (432 mg, 1.68 mmol) was added to a 250-mL, round-bottomed flask as a solution in 150 mL of MeOH (~0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 M aq. HCl solution (24 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 40.8 uL, 0.34 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 75 mg, 0.34 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 75 mg, 0.34 mmol, 1.2 equiv), 9-bromomethylantracene (tube 4, 92 mg, 0.34 mmol, 1.2 equiv), 3,5-(bistrifluoromethyl)benzyl bromide (tube 5, 62 uL, 0.34 mmol, 1.2 equiv), 1-bromohexane (tube 6, 80 uL, 0.56 mmol, 2.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-methoxyethoxymethoxy-3-benzyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{4,1}): Data for **II{4,1}**: Yield: 91 mg (76%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.75 (m, 2 H), 7.43 (dd, $J = 1.8$, 5.1, 3 H), 4.85 (d, $J = 12.4$, 1 H), 4.75 (m, 2 H), 4.70 (s, 2 H), 4.26 (ddd, $J = 6.6$, 12.2, 1 H), 3.63-3.56 (m, 2 H), 3.50 (dd, $J = 6.8$, 6.2, 12.7, 1 H), 3.45 (t, $J = 4.6$, 2 H), 3.24 (s, 3 H), 3.19 (dd, $J = 5.0$, 12.5, 1 H), 2.96 (dd, $J = 7.8$, 14.1, 1 H), 2.85-2.80 (m, 1 H), 2.48 (ddd, $J = 7.6$, $J = 14.6$, 14.7, 1 H), 2.04 (s, 3 H), 2.04-1.96 (m, 2 H) 1.87-1.73 (m, 3 H); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 133.0, 130.1, 129.6, 129.1, 97.7, 96.0, 74.9, 71.5, 67.7, 63.2, 60.4, 60.2, 58.9, 54.6, 51.0, 33.0, 28.0, 26.4, 23.4; MS: (ESI, Q-tof) 347 (28), 346 (100), 192 (13), 174 (37), 133 (18); Mol. Formula: $\text{C}_{21}\text{H}_{32}\text{BrNO}_3$ (426.39); HRMS: $\text{C}_{21}\text{H}_{32}\text{NO}_3$, (346.2382); Calcd: 346.2382; Found: 346.2372; TLC: R_f 0.26 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-methoxyethoxymethoxy-3-(1-naphthylmethyl)cyclopenta[*gh*]pyrrolizinium Bromide (II{4,2}): Data for **II{4,2}**: Yield: 110 mg (82%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.32 (d, $J = 7.1$, 1 H), 8.18 (d, $J = 8.6$, 1 H), 7.88 (d, $J = 8.2$, 2 H), 7.64 (dd, $J = 7.2$, 7.2, 1 H), 7.53 (dd, $J = 7.5$, 7.5, 2 H) 7.48 (dd, $J = 7.7$, 7.7, 2 H) 5.32 (d, $J = 13.1$, 1 H) 5.23 (d, $J = 13.1$, 1 H) 4.82 (dd, $J = 5.9$, 13.7, 1 H), 4.68-4.63 (m, 3 H) 4.31 (ddd, $J = 6.6$, 12.3, 12.36, 1 H), 3.53 (m, 2 H), 3.49-3.43 (m, 1 H), 3.37 (dd, $J = 4.1$, 8.8, 2 H), 3.16 (s, 3 H), 3.14 (dd, $J = 5.9$, 12.8, 1 H), 3.05 (t, $J = 7.8$, 14.2, 1 H), 2.99-2.95 (m, 1 H), 2.62-2.55 (m, 1 H), 2.25 (s, 3 H), 2.05-1.95 (m, 2 H), 1.90-1.71 (m, 3 H); MS: (ESI, Q-tof) 397 (32), 396 178 (100), 179 (18);

Mol. Formula: C₂₅H₃₄NO₃Br (476.45); HRMS: C₂₅H₃₄NO₃, (396.2539) Calcd: 396.2539; Found: 396.2535; TLC: *R_f* 0.26 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-methoxyethoxymethoxy-3-(2-naphthylmethyl)cyclopenta[*gh*]pyrrolizinium Bromide (II{4,3}): Data for **II{4,3}**: Yield: 126 mg (94%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.20 (s, 1 H), 7.91-7.89 (m, 1 H), 7.79 (s (broad), 2 H), 7.78-7.76 (m, 1 H), 7.52-7.50 (m, 2 H), 5.05 (d, *J* = 12.5, 1 H), 4.96 (d, *J* = 12.5, 1 H), 4.85 (dd, *J* = 5.9, 12.7, 1 H), 4.74 (dd, *J* = 5.5, 13.3, 1 H), 4.69 (q, *J* = 6.8, 2 H), 4.31 (ddd, *J* = 6.3, 12.0, 12.7, 1 H), 3.56 (dd, *J* = 4.1, 8.4, 2 H), 3.53-3.48 (m, 1 H), 3.38 (dd, *J* = 4.5, 4.6, 2 H), 3.20 (dd, *J* = 5.1, 12.7, 1 H), 3.09 (s, 3 H), 3.01 (dd, *J* = 7.9, 14.1, 1 H), 2.89-2.84 (m, 1 H), 2.55 (ddd, *J* = 7.6, 14.3, 14.6, 1 H), 2.12 (s, 3 H), 2.05-1.98 (m, 2 H), 1.87-1.74 (m, 3 H); MS: (ESI, Q-tof) 397 (35), 396 (100), 179 (12); Mol. Formula: C₂₅H₃₄NO₃Br (476.45); HRMS: C₂₅H₃₄NO₃, (396.2539); Calcd: 396.2539; Found: 396.2532; TLC: *R_f* 0.30 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-methoxyethoxymethyl-3-(9-anthrylmethyl)cyclopenta[*gh*]pyrrolizinium Bromide (II{4,4}): Data for **II{4,4}**: Yield: 134 mg (90%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.73 (d, *J* = 9.0, 2 H), 8.53 (s, 1 H), 8.44 (m, 1 H), 8.00 (dd, *J* = 3.8, 8.2, 2 H), 7.74 (m, 2 H), 7.50 (q, 3 H), 5.71 (q, *J* = 14.3, 2 H), 4.94 (td, *J* = 6.2, 14.1, 1 H), 4.74 (dd, *J* = 7.0, 16.1, 1 H), 4.57 (dd, *J* = 6.7, 18.6, 2 H), 4.23 (dd, *J* = 5.9, 12.8, 1 H), 4.11 (m, 1 H), 3.87 (td, *J* = 6.0, 12.1, 1 H), 3.67 (m, 1 H), 3.54 (t, *J* = 4.5, 1 H), 3.44 (m, 2 H), 3.39 (s, 1 H), 3.28 (m, 2 H), 3.16 (m, 1 H), 3.09 (s, 1 H), 2.76 (dd, *J* = 6.5, 12.8, 1 H), 2.54 (m, 1 H), 2.44 (s, 3 H), 2.34 (m, 1 H), 1.90 (m, 5 H), 1.74 (s, 3 H); MS: (ESI, Q-tof) 447 (40), 446 (100), 256 (40), 191 (46); Mol. Formula: C₂₉H₃₆BrNO₃ (526.50); HRMS: C₂₉H₃₆NO₃, (446.2695); Calcd: 446.2695; Found: 446.2686; TLC: *R_f* 0.34 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-methoxyethoxymethyl-3-(3,5-trifluoromethylbenzyl)cyclopenta[*gh*]pyrrolizinium Bromide (II{4,5}): Data for II{4,5}: Yield: 120 mg (76%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.42 (s, 2 H), 7.94 (s, 1 H), 5.32 (s, 2 H), 4.77 (dd, $J = 5.8, 13.7$, 1 H), 4.73 (d, $J = 6.8$, 1 H), 4.70 (d, $J = 6.8$, 1 H), 4.65 (dd, $J = 5.8, 12.6$, 1 H), 4.22 (td, $J = 6.9, 12.2$, 1 H), 3.63-3.54 (m, 2 H), 3.47 (dd, $J = 5.8, 12.4$, 1 H), 3.48-3.39 (m, 2 H), 3.17 (dd, $J = 5.7, 12.7$, 1 H), 3.14 (s, 3 H), 2.94 (dd, $J = 7.8, 14.3$, 1 H), 2.84 (ddd, $J = 6.0, 12.4, 13.4$, 1 H), 2.56 (ddd, $J = 7.1, 14.7, 15.1$, 1 H), 2.08 (s, 3 H), 2.06-1.97 (m, 2 H), 1.88-1.73 (m, 3 H); MS: (ESI, Q-tof) 483 (30), 482 (100), 174 (25), 133 (28); Mol. Formula: $\text{C}_{23}\text{H}_{30}\text{BrF}_6\text{NO}_3$ (562.38); HRMS: $\text{C}_{23}\text{H}_{30}\text{F}_6\text{NO}_3^+$ (482.2130); Calcd: 482.2130; Found: 482.2119; TLC: R_f 0.27 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-methoxyethoxymethoxy-3-hexylcyclopenta[*gh*]pyrrolizinium Bromide (II{4,6}): Data for II{4,6}: Yield: 92 mg (77%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 4.77 (d, $J = 7.0$, 2 H), 4.73 (d, $J = 7.0$, 2 H), 4.52 (dd, $J = 5.3, 12.9$, 1 H), 4.45 (dd, $J = 5.8, 12.8$, 1 H), 3.95 (t, $J = 6.2$, 1 H), 3.77-3.67 (m, 2 H), 3.58-3.47 (m, 3 H), 3.42-3.56 (m, 1 H), 3.37 (s, 3 H), 2.93 (dd, $J = 7.6, 13.9$, 1 H), 2.69 (ddd, $J = 7.1, 12.6, 12.8$, 1 H), 2.32 (ddd, $J = 7.1, 13.9, 14.1$, 1 H), 2.09-1.85 (m, 3 H), 1.83 (s, 3 H), 1.81-1.74 (m, 4 H), 1.50-1.39 (m, (broad), 1 H), 1.35-1.32 (m, 3 H), 0.89 (t, $J = 7.0$, 3 H); MS: (ESI, Q-tof) 341 (31), 340 (100), 133 (24); Mol. Formula: $\text{C}_{20}\text{H}_{38}\text{BrNO}_3$ (420.42); HRMS: $\text{C}_{20}\text{H}_{38}\text{NO}_3^+$ (340.2852); Calcd: 340.2852; Found: 340.2845; TLC: R_f 0.36 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides II{5,1-6}: Following General Procedure II, amino borane II{5} (960 mg, 3.72 mmol) was added to a 250-mL, round-bottomed flask as a solution in 150 mL of MeOH (~0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 M aq. HCl solution (24 mL, 5.0

equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 100 μ L, 0.75 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 166 mg, 0.75 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 166 mg, 0.75 mmol, 1.2 equiv), 9-bromomethylantracene (tube 4, 203 mg, 0.75 mmol, 1.2 equiv), 3,5-(bistrifluoromethyl)benzyl bromide (tube 5, 62 μ L, 0.34 mmol, 1.2 equiv),⁹⁶ 1-bromohexane (tube 6, 110 μ L, 0.75 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyl)-3-benzyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{5,1}): Data for **II{5,1}**: Yield: 240 mg (92%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.15 (d, *J* = 4.7, 1 H), 7.85 (dd, *J* = 2.9, 6.6, 1 H), 7.62–7.58 (m, 1 H), 7.47–7.43 (m(br), 3 H), 6.95 (t, *J* = 6.0, 1 H), 6.71 (d, *J* = 8.3, 1 H), 5.87 (dd, *J* = 6.3, 14.3, 1 H), 5.05 (d, *J* = 12.4, 1 H), 4.95 (dd, *J* = 6.2, 12.9, 1 H), 4.79 (d, *J* = 12.4, 1 H), 4.58–4.52 (m, (so), 1 H), 3.44 (dt, *J* = 7.2, 12.5, 1 H), 3.24 (dd, *J* = 6.3, 12.9, 1 H), 3.14 (q, *J* = 7.7, 1 H), 2.98 (m, (broad), 1 H), 2.63–2.55 (m, 1 H), 2.15 (s, 3 H, H₃C(10)), 2.08–1.99 (m, (broad), 2 H), 1.90–1.78 (m, (broad), 3 H); MS: (ESI, Q-tof) 336.2 (30), 335.2 (100), 264 (23), 263 (99), 185.0 (56); Mol. Formula: C₂₂H₂₇BrN₂O (415.37); HRMS: C₂₂H₂₇N₂O⁺, (335.2123); Calcd: 335.2123; Found: 335.2121; TLC: *R*_f 0.24 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-3-(1-naphthylmethyl)-cyclopenta[*gh*]pyrrolizinium Bromide (II{5,2}): Data for II{5,2}: Yield: 274 mg (94%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.42 (d, 1 H, *J* = 7.1), 8.26 (d, 1 H, *J* = 8.6), 8.09 (dd, 1 H, *J* = 1.3, 4.9), 7.90 (t, 1 H, *J* = 7.6), 7.65 (t, 1 H, *J* = 7.5), 7.57-7.51 (m, 3 H), 6.92 (dd, 1 H, *J* = 5.4, 6.7), 6.62 (d, 1 H, *J* = 8.4), 6.04 (dd, 1 H, *J* = 6.1, 14.1), 5.44 (d, 1 H, *J* = 13.0), 5.30 (d, 1 H, *J* = 13.1), 4.98 (dd, 1 H, *J* = 6.2, 13.0), 4.50 (m, (broad), 1 H), 3.26 (dd, 2 H, *J* = 5.9, 13.0), 3.11 (m, (broad), 1 H), 2.72-2.64 (m, 1 H), 2.35 (s, 3 H, (H₃C(C10))), 2.10-1.99 (m, 2 H), 1.90-1.77 (m, 3 H); MS: (ESI, Q-tof) 386 (35), 385 (100), 264 (22), 263 (90), 185.0 (47); Mol. Formula: C₂₆H₂₉BrN₂O, 465.43; HRMS: C₂₆H₂₉N₂O⁺, (385.2280); Calcd: 385.2280; Found: 385.2276; TLC: *R*_f 0.30 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyl)-3-[2]naphthylmethyl-cyclopenta[*gh*]pyrrolizinium Bromide (II{5,3}): Data for II{5,3}: Yield: 251 mg (87%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.29 (s, 1 H), 8.18 (d, *J* = 4.3, 1 H), 7.91 (d, *J* = 7.5, 2 H), 7.80 (m, 2 H), 7.58 (t, *J* = 7.7, 1 H), 7.52 (d, *J* = 4.2, 2 H), 6.94 (t, *J* = 6.1, 1 H), 6.69 (d, *J* = 8.2, 1 H), 5.91 (dd, *J* = 6.3, 14.2, 1 H), 5.25 (d, *J* = 12.5, 1 H), 5.01 (dd, *J* = 6.1, 12.8, 1 H), 4.96 (d, *J* = 12.5, 1 H), 4.63 (s, 1 H), 3.44 (dt, *J* = 6.3, 12.0, 1 H), 3.22 (dd, *J* = 6.3, 12.8, 1 H), 3.16 (q, *J* = 7.9, 1 H), 3.03 (s (broad), 1 H), 2.69-2.59 (m, 1 H), 2.22 (s, 3 H), 2.10-2.00 (m, 2 H), 1.92-1.77 (m, 3 H); ¹³C-NMR (126 MHz, CDCl₃) 161.7, 146.9, 139.1, 133.5, 133.3, 132.7, 129.1, 128.8, 128.4, 127.5, 127.3, 126.7, 126.6,

118.0, 110.7, 98.0, 71.5, 62.4, 60.6, 60.5, 54.3, 51.0, 33.0, 28.3, 26.9, 23.6; MS: (ESI, Q-tof) 386.2 (34), 385.2 (100), 263.1 (50), 185 (31) 133 (29); Mol. Formula: $C_{26}H_{29}BrN_2O$ (465.43); HRMS: $C_{26}H_{29}N_2O^+$, (385.2280); Calcd: 385.2280; Found: 385.2276; TLC: R_f 0.27 (CH_2Cl_2 /MeOH, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyl)-3-[9]anthrylmethylcyclopenta[gh]pyrrolizinium Bromide (II{5,4}): Data for **II{5,4}**: Yield: 250 mg (78%), free-flowing pale-yellow powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.88 (d, $J = 9.0$, 1 H), 8.72 (d, $J = 9.0$, 1 H), 8.55 (s, 1 H), 8.01 (m, 3 H), 7.77 (t, $J = 7.5$, 1 H), 7.71 (t, $J = 7.7$, 1 H), 7.54-7.49 (m, 3 H), 6.87 (dd, $J = 5.1$, 7.1, 1 H), 6.55 (d, $J = 8.3$, 1 H), 6.05 (dd, $J = 6.2$, 14.5, 1 H), 5.99 (d, $J = 14.2$, 1 H), 5.74 (d, $J = 14.2$, 1 H), 4.51 (dd, $J = 6.4$, 3.1, 1 H), 4.29 (dt, $J = 7.3$, 2.2, 1 H), 3.41 (dd, $J = 7.8$, 15.3, 1 H), 3.31 (m, (broad), 1 H), 3.24 (dt, $J = 7.0$, 12.2, 1 H), 2.93 (dd, $J = 6.0$, 13.1, 1 H), 2.78 (dt, $J = 7.1$, 14.4, 1 H), 2.54 (s, 3 H), 2.09-1.90 (m, 3 H), 1.82-1.66 (m, 3 H); MS: (ESI, Q-tof) 436 (41), 435.2 (100), 236 (41), 191 (70); Mol. Formula: $C_{30}H_{31}BrN_2O$ (515.48); HRMS: $C_{30}H_{31}N_2O^+$, (435.2436); Calcd: 435.2436; Found: 435.2434; TLC: R_f 0.31 (CH_2Cl_2 /MeOH, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyl)-3-(3,5-trifluoromethylbenzyl)cyclopenta[gh]pyrrolizinium Bromide (II{5,5}): Data for **II{5,5}**: Yield: 45 mg (63%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.57 (s, 2 H), 8.18 (d, $J = 4.5$, 1 H), 7.99 (s, 1 H), 7.63 (m, 1 H), 6.99 (dd, $J = 5.4$, 6.8, 1 H), 6.74 (d, $J = 8.2$, 1 H), 5.84 (dd, $J = 7.9$, 14.3, 1 H), 5.77 (d, $J = 12.7$, 1 H), 4.94-4.83 (m, (broad), 2 H), 4.74 (dd, $J = 6.0$, 12.6, 1 H), 3.30 (m, 1 H), 3.12-3.03 (m, (second order), 3 H), 2.64-2.56 (m, 1 H), 2.23 (s, 3 H), 2.16-1.98 (m, 3 H), 1.90-1.81 (m, 2 H); MS: (ESI, Q-tof)

472.2 $[M^+ + 1]$ (31), 471.2 $[M^+ + 1]$ (100); Mol. Formula: $C_{24}H_{25}BrF_6N_2O$ (551.36); HRMS: $C_{24}H_{25}F_6N_2O^+$: (471.1871); Calcd: 471.1871; Found: 471.1862; TLC: R_f 0.21 (CH_2Cl_2 /MeOH, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyl)-3-hexylcyclopenta[gh]pyrrolizinium Bromide (II{5,6}): Data for II{5,6}: Yield: 70 mg (27%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.16 (ddd, $J = 0.8, 2.0, 5.1$, 1 H), 7.85 (dd, $J = 3.0, 6.5$, 2 H), 7.60 (ddd, $J = 2.0, 7.2, 8.3$, 1 H), 7.45 (m, 3 H), 6.95 (ddd, $J = 0.9, 5.1, 7.1$, 1 H), 6.70 (d, $J = 8.3$, 1 H), 5.87 (dd, $J = 6.3, 14.3$, 1 H), 5.05 (d, $J = 12.4$, 1 H), 4.96 (dd, $J = 6.2, 12.9$, 1 H), 4.77 (d, $J = 12.4$, 1 H), 4.61 (dt, $J = 7.1, 12.1$, 1 H), 3.44 (ddd, $J = 6.5, 6.3, 12.2$, 1 H), 3.23 (dd, $J = 6.4, 12.9$, 1 H), 3.14 (q, $J = 7.7$, 1 H), 3.02-2.97 (m, 1 H), 2.58 (dt, $J = 6.9, 14.6$, 1 H), 2.16 (s, 3 H), 2.08-2.00 (m, 2 H), 1.91-1.78 (m, 3 H), 1.33-1.20 (m, (second order), 1 H), 0.88 (t, $J = 7.1$, 3 H); MS: (ESI, Q-tof) 329 (100); Mol. Formula: $C_{21}H_{33}BrN_2O$ (409.40); HRMS: $C_{21}H_{33}N_2O^+$: (329.2593); Calcd: 329.2593; Found: 329.2580 TLC: R_f 0.38 (CH_2Cl_2 /MeOH, 9:1) [I_2].

4. Preparation of Quaternary Ammonium Bromides III{1-5,1-6}: Following General Procedure II, amino borane **11b** (50 mg, 0.28 mmol) was added to a 50-mL round-bottomed flask as a solution in 9.5 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (1.5, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 39 mg, 0.33 mmol, 1.1 equiv), 1-bromomethylnaphthalene (tube 2, 67 mg, 0.3 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 73 mg, 0.33 mmol, 1.1 equiv), 9-bromomethylantracene (tube 4, 49 mg, 0.18 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 5, 63.7 μ L, 0.18 mmol, 1.2 equiv), 1-bromohexane (tube 6, 36 μ L, 0.25 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

III{1,1}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-benzyl-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (III{1,1}): Data for **III{1,1}**: Yield: 64 mg (69%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.61 (m, 2 H), 7.52 (m, 3 H), 4.98 (d, $J = 12.2$, 1 H), 4.56 (d, $J = 12.2$, 1 H), 4.25 (d, $J = 3.1$, 1 H), 3.84 (dd, $J = 1.6$, 13.7, 1 H), 3.74 (m, 2 H), 3.38 (dd, $J = 6.4$, 11.5, 1 H), 2.71 (dd, $J = 8.5$, 17.1, 1 H), 2.59 (t, $J = 8.8$, 1 H), 2.24 (m, 1 H), 2.13 (m, 1 H), 1.90 (m, 2 H), 1.85 (s, 3 H), 1.78 (ddd, $J = 4.7$, 12.9, 16.9, 2 H), 1.62 (ddd, $J = 4.8$, 9.4, 12.1, 1 H); MS: (ESI, Q-tof) 259 (21), 258 (100), 166 (13); Mol. Formula: $\text{C}_{17}\text{H}_{24}\text{BrNO}$ (338.28); HRMS: $\text{C}_{17}\text{H}_{24}\text{NO}^+$: (258.1858); Calcd: 258.1858; Found: 258.1855; TLC: R_f 0.09 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

III{1,2}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-(1-naphthyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (III{1,2}): Data for **III{1,2}**: Yield: 88 mg (82%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.72 (d, $J = 8.6$, 1 H), 8.09 (d, $J = 8.3$, 1 H), 8.00 (d, $J = 8.0$, 1 H), 7.94 (d, $J = 7.2$, 1 H), 7.67 (ddd, $J = 1.3$, 6.8, 8.5, 1 H), 7.61 (td, $J = 7.2$, 10.3, 2 H), 5.57 (d, $J = 12.9$, 1 H), 5.01 (d, $J = 12.9$, 1 H), 4.30 (s, 1 H),

3.98 (d, $J = 13.6$, 1 H), 3.92 (dd, $J = 6.2$, 12.1, 1 H), 3.20 (dd, $J = 6.0$, 11.6, 1 H), 2.77 (dd, $J = 8.7$, 16.5, 1 H), 2.66 (t, $J = 9.1$, 1 H), 2.23 (m, 1 H), 2.14 (td, $J = 6.8$, 13.6, 1 H), 2.00 (s, 3 H), 1.93 (m, 1 H), 1.69 (m, 3 H); MS: (ESI, Q-tof) 310 (4), 309 (32), 308 (100); Mol. Formula: $C_{21}H_{26}BrNO$ (388.34); HRMS: $C_{21}H_{26}NO^+$: (308.2014); Calcd: 308.2014; Found: 308.2033; TLC: R_f 0.10 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

III{1,3}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-(2-naphthyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (III{1,3}): Data for **III{1,3}**: Yield: 98 mg (84%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.37 (s, 1 H), 8.07 (d, $J = 7.3$, 1 H), 7.88 (d, $J = 8.4$, 1 H), 7.83 (d, $J = 7.2$, 1 H), 7.67 (dd, $J = 1.6$, 8.4, 1 H), 7.52 (m, 3 H), 5.99 (d, $J = 3.3$, 1 H), 5.31 (d, $J = 12.1$, 1 H), 4.61 (d, $J = 12.0$, 1 H), 4.54 (s, 1 H), 4.30 (d, $J = 13.3$, 1 H), 3.83 (ddd, $J = 6.2$, 12.3, 12.4, 1 H), 3.30 (dd, $J = 6.3$, 11.6, 1 H), 3.15 (d, $J = 11.7$, 1 H), 2.89 (dd, $J = 9.1$, 9.1, 1 H), 2.74 (dd, $J = 8.9$, 16.3, 1 H), 2.28 (dd, $J = 6.7$, 13.9, 1 H), 2.16 (m, 1 H), 1.93 (s, 3 H), 1.76 (m, 5 H); MS: (ESI, Q-tof) 310 (5), 309 (23), 308 (100); Mol. Formula: $C_{21}H_{26}BrNO$ (388.34); HRMS: $C_{21}H_{26}NO^+$: (308.2014); Calcd: 308.2014; Found: 308.2024; TLC: R_f 0.10 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

III{1,4}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-(9-anthracenylmethyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (III{1,4}): Data for **III{1,4}**: Yield: 33 mg (51%), free-flowing yellow powder; 1H -NMR: (500 MHz, $CDCl_3$) 9.10 (d, $J = 9.1$, 1 H), 8.62 (s, 1 H), 8.22 (s, 1 H), 8.07 (dd, $J = 8.4$, 27.8, 2 H), 7.86 (m, 1

H), 7.68 (m, 1 H), 7.55 (td, $J = 8.0, 11.4$, 2 H), 6.38 (d, $J = 13.9$, 1 H), 5.62 (d, $J = 14.0$, 1 H), 4.62 (s, 1 H), 4.43 (d, $J = 13.2$, 1 H), 3.67 (dt, $J = 6.2, 12.3$, 1 H), 3.34 (t, $J = 9.3$, 1 H), 2.94 (dd, $J = 3.0, 13.1$, 1 H), 2.76 (dd, $J = 8.8, 16.1$, 1 H), 2.47 (dd, $J = 5.7, 12.1$, 1 H), 2.26 (s, 3 H), 2.08 (dd, $J = 7.3, 14.0$, 1 H), 1.90 (tt, $J = 6.9, 13.5$, 1 H), 1.74 (dd, $J = 6.4, 13.4$, 1 H), 1.51 (m, 5 H); ^{13}C -NMR: (126 MHz, CDCl_3) 134.4, 134.3, 133.2, 131.0, 130.8, 128.9, 126.5, 126.3, 125.0, 121.9, 100.4, 75.5, 64.3, 63.3, 62.3, 56.0, 53.6, 30.9, 29.8, 28.0, 24.8; MS: (ESI, Q-tof) 359 (11), 358 (36), 306 (27), 305 (83), 191 (43), 168 (10); Mol. Formula: $\text{C}_{25}\text{H}_{28}\text{BrNO}$ (438.40); HRMS: $\text{C}_{25}\text{H}_{28}\text{NO}^+$: (358.2171); Calcd: 358.2171; Found: 358.2156; TLC: R_f 0.13 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-(3,5-bistrifluoromethylbenzyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{1,5}): Data for III{1,5}: ^1H -NMR: (500 MHz, CDCl_3) 8.24 (s, 2 H), 8.21 (s, 1 H), 5.20 (d, 1 H, $J = 12.6$), 4.75 (d, 1 H, $J = 12.7$), 4.29 (dd, 1 H, $J = 2.2, 8.8$), 3.85 (ddd, 1 H, $J = 6.4, 12.3, 12.2$), 3.63 (dd, 1 H, $J = 1.8, 13.9$), 3.44 (m, 3 H), 2.74 (dd, 1 H, $J = 9.2, 17.0$), 2.62 (dd, 1 H, $J = 8.7, 8.7$), 2.29 (m, 1 H), 2.15 (m, 1 H), 1.96 (m, 2 H), 1.88 (s, 3 H), 1.75 (m, 3 H); MS: (ESI, Q-tof) 394 (100); Mol. Formula: $\text{C}_{19}\text{H}_{22}\text{BrF}_6\text{NO}$ (474.2785); HRMS: $\text{C}_{19}\text{H}_{22}\text{F}_6\text{NO}^+$: (394.1606); Calcd: 394.1606; Found: 394.1595; TLC: R_f 0.16 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hydroxy-3-hexyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{1,6}): Data for III{1,6}: Yield: 54 mg (79%), free-flowing white powder; ^1H -NMR: (500 MHz, CDCl_3) 5.66 (d, $J = 8.9$, 1 H), 5.41 (d, $J =$

9.1, 1 H), 4.28 (s, 1 H), 4.22 (s, 1 H), 4.15 (d, $J = 13.1$, 1 H), 3.91 (dd, $J = 6.6$, 11.6, 1 H), 3.75 (m, 6 H), 3.55 (d, $J = 12.9$, 2 H), 2.71 (dd, $J = 8.4$, 16.6, 1 H), 2.58 (m, 2 H), 2.47 (t, $J = 9.4$, 1 H), 2.15 (m, 5 H), 1.81 (m, 10 H), 1.74 (s, 3 H), 1.62 (m, 3 H), 1.40 (m, 10 H), 0.94 (t, $J = 6.5$, 3 H); MS: (ESI, Q-tof) 252 (100); Mol. Formula: $C_{16}H_{30}BrNO$ (332.32); HRMS: $C_{16}H_{30}NO^+$: (252.2327); Calcd: 252.2327; Found: 252.2327; TLC: R_f 0.13 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides III{2,1–6}: Following General Procedure II, amino borane **X** (324 mg, 1.2 mmol) was added to a 100-mL round-bottomed flask as a solution in 42 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (6.0, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 30 μ L, 0.24 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 82 mg, 0.37 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 66 mg, 0.3 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide⁹⁶ (tube 4, 31 mg, 0.104 mmol, 1.2 equiv), 9-bromomethylantracene (tube 5, 60 mg, 0.24 mmol, 1.2 equiv), 1-bromohexane (tube 6, 31 μ L, 0.24 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-benzyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (III{2,1}): Data for **III{2,1}**: Yield: 61 mg (71%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.64 (dd, 2 H, $J = 1.6$, 7.6) 7.41 (m, 8), 5.14 (d, 1 H, $J = 12.0$), 4.87 (ddd, 1 H, $J = 6.4$, 12.4, 12.8), 4.72 (d, 3 H, $J = 11.7$) 4.65 (d, 1 H, $J = 12.0$), 4.61 (d, 1 H, $J = 11.7$) 4.08 (d, 1 H, $J = 3.0$), 4.01 (dd, 2 H, $J = 1.8$, 14.0), 3.48 (dd, 1 H, $J = 2.3$, 13.9), 3.29 (dd, 1 H, $J = 6.4$, 11.5), 3.06 (dd, 1 H, $J = 8.6$, 14.9), 2.71 (dd, 1 H, $J = 9.0$, 9.0), 2.39 (ddd, 1 H, $J = 6.7$, 6.7, 13.7), 2.15–2.10 (m, 1 H), 2.04 (s, 3 H), 1.89–1.80 (m, 3 H), 1.75–1.67 (m, 1 H); ^{13}C -NMR: (126 MHz, $CDCl_3$) 136.6, 133.1, 130.3, 129.6, 129.2, 128.8, 128.4, 127.6, 97.8, 81.8, 71.8, 63.3, 63.2, 61.4, 56.5, 52.1, 30.1, 29.4, 27.2, 24.2; MS: (ESI, Q-tof) 348 (100), 349 (31); Mol. Formula: $C_{24}H_{30}BrNO$ (428.40); HRMS: $C_{24}H_{30}NO^+$: (348.2327); Calcd: 348.2327; Found: 348.2312; TLC: R_f 0.25 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(1-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{2,2}): Data for **III{2,2}**: Yield: 117 mg (81%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.51 (d, $J = 8.6$, 1 H), 8.26 (d, $J = 7.2$, 1 H), 7.95 (d, $J = 8.3$, 1 H), 7.88 (d, $J = 8.2$, 1 H), 7.64 (dd, $J = 1.7$, 7.7, 1 H), 7.55 (dd, $J = 7.3$, 8.1, 1 H), 7.49 (m, 1 H), 7.46 (d, $J = 4.4$, 3 H), 7.44-7.34 (m, 3 H), 5.39 (d, $J = 12.8$, 1 H), 5.32 (d, $J = 12.6$, 1 H), 5.10 (m, 1 H), 4.87 (d, $J = 11.5$, 1 H), 4.60 (d, $J = 10.9$, 1 H), 4.12 (d, $J = 4.4$, 1 H), 4.03 (dd, $J = 2.0$, 13.4, 1 H), 3.42 (dd, $J = 3.6$, 13.5, 1 H), 3.31-3.21 (m, 1 H), 3.17 (dd, $J = 6.5$, 11.3, 1 H), 2.82 (dd, $J = 9.8$, 9.8, 1 H), 2.41-2.35 (m, 1 H), 2.23 (s, 3 H), 2.17-2.09 (m, 1 H), 1.91-1.61 (m, 2 H); MS: (ESI, Q-tof) 399 (), 398 (100), 258 (40); Mol. Formula: $\text{C}_{28}\text{H}_{32}\text{BrNO}$ (478.46); HRMS: $\text{C}_{28}\text{H}_{32}\text{NO}^+$: (398.2484); Calcd: 398.2484; Found: 398.2476; TLC: R_f 0.2 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(2-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{2,3}): Data for **III{2,3}**: Yield: 93 mg (79%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.11 (s, 1 H), 7.88 (dd, $J = 8.0$, 16.5, 3 H), 7.74 (dd, $J = 1.7$, 8.4, 1 H), 7.59-7.54 (m, 2 H), 7.38 (ddd, $J = 11.2$, 18.2, 27.0, 6 H), 5.33 (d, $J = 11.8$, 1 H), 5.02 (ddd, $J = 6.3$, 12.3, 12.3, 1 H), 4.83-4.77 (m, 3 H), 4.65 (d, $J = 11.7$, 1 H), 4.45 (d, $J = 11.7$, 1 H), 4.13-4.00 (m, 3 H), 3.74 (dddd, $J = 6.2$, 6.2, 12.2, 12.2, 1 H), 3.40-3.33 (m, 2 H), 3.18-3.10 (m, 2 H), 2.98 (ddd, $J = 3.6$, 6.9, 12.6, 1 H), 2.75 (dd, $J = 9.3$, 9.3, 1 H), 2.5-2.51 (m, 1 H), 2.48-2.42 (m, 1 H), 2.36-2.29 (m, 1 H), 2.17-2.11 (m, 1 H), 2.10 (s, 3 H), 2.06-2.01 (m, 1 H), 1.91-1.83 (m, 2 H), 1.78-1.63 (m, 3 H); MS: (ESI, Q-tof) 399 (39), 398 (100), 258 (49); Mol. Formula: $\text{C}_{28}\text{H}_{32}\text{BrNO}$ (478.46);

HRMS: $C_{28}H_{32}NO^+$: (398.2484); Calcd: 398.2484; Found: 398.2473; TLC: R_f 0.27 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(9-anthracenylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{2,4}): Data for **III{2,4}**: Yield: 32 mg (29%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 9.10 (d, $J = 9.1$, 1 H), 8.62 (s, 1 H), 8.21 (d, $J = 8.9$, 1 H), 8.10 (d, $J = 8.4$, 2 H), 8.04 (d, $J = 8.5$, 2 H), 7.86 (m, 1 H), 7.68 (dd, $J = 7.2$, 7.2, 1 H), 7.55 (dd, $J = 8.0$, 18.3, 2 H), 6.38 (d, $J = 13.9$, 1 H), 5.62 (d, $J = 14.0$, 1 H), 4.62 (s, 1 H), 4.43 (d, $J = 13.2$, 1 H), 3.67 (ddd, $J = 6.2$, 12.3, 12.3, 1 H), 3.34 (dd, $J = 9.3$, 9.3, 1 H), 2.94 (dd, $J = 3.0$, 13.1, 1 H), 2.76 (dd, $J = 8.8$, 16.1, 1 H), 2.47 (dd, $J = 5.7$, 12.1, 1 H), 2.30-2.27 (m, 1 H), 2.26 (s, 3 H), 2.08 (dd, $J = 7.0$, 13.4, 1 H), 1.90 (dddd, $J = 6.9$, 6.9, 13.5, 13.5, 1 H), 1.74 (dd, $J = 6.4$, 13.4, 1 H), 1.58-1.44 (m, 3 H); MS: (ESI, Q-tof) 449 (41), 448 (100), 256 (20), 191 (60); Mol. Formula: $C_{32}H_{34}BrNO$ (528.52); HRMS: $C_{32}H_{34}NO^+$: (448.2640); Calcd: 448.2640; Found: 448.2633; TLC: R_f 0.31 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-hexyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{2,6}): Data for **III{2,6}**: Yield: 64mg (76%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.36 (ddd, $J = 4.4$, 8.5, 12.6, 2 H), 7.27 (s, 1 H), 4.58 (s, 1 H), 4.49 (d, $J = 11.7$, 2 H), 4.22 (m, 2 H), 4.12 (m, 1 H), 3.99 (d, $J = 14.3$, 1 H), 3.54 (m, 2 H), 3.29 (m, 1 H), 2.71 (dd, $J = 9.4$, 13.6, 1 H), 2.57 (dd, $J = 7.5$, 7.5, 1 H), 2.22 (m, 2 H), 2.09 (dd, $J = 6.0$, 16.5, 1 H), 1.81 (m, 4 H), 1.70 (s, 3 H), 1.26 (s, 1 H), 0.87 (dd, $J = 5.1$, 5.1, 3 H); MS: (ESI, Q-tof); Mol. Formula: $C_{23}H_{36}BrNO$ (422.44); HRMS: $C_{23}H_{36}NO^+$: (342.2791); Calcd: 342.2797; Found: 342.2782; TLC: R_f 0.31 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides **III{3,1–6}**: Following General Procedure II, amino borane **III**{3} (560 mg, 2.22 mmol) was added to a 100-mL round-bottomed flask as a solution in 50 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (12.0, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 53 μ L, 0.44 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 69 mg, 0.37 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 66 mg, 0.3 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 44 μ L, 0.24 mmol, 1.2 equiv), 9-bromomethylantracene (tube 5, 65 mg, 0.24 mmol, 1.2 equiv), 1-bromohexane (tube 6, 62 μ L, 0.44 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

III{3,1}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-benzyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III**{3,1})**: Data for **III**{3,1}: Yield: 145 mg (93%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.69 (dd, $J = 1.9, 7.0, 2$ H), 7.45 (m, 3 H), 5.16 (d, $J = 11.9, 1$ H), 4.90 (m, 1 H), 4.62 (d, $J = 11.9, 1$ H), 3.94 (dd, $J = 8.3, 22.7, 1$ H), 3.62 (td, $J = 6.7, 8.8, 1$ H), 3.47 (td, $J = 6.3, 8.9, 1$ H), 3.39 (d, $J = 13.9, 1$ H), 3.25 (dd, $J = 6.5, 11.5, 1$ H), 3.07 (dd, $J = 8.6, 15.4, 1$ H), 2.64 (t, $J = 9.2, 1$ H), 2.40 (m, 1 H), 2.13 (m, 1 H), 2.03 (s, 3 H), 1.82 (m, 3 H), 1.67 (m, 3 H), 1.34 (m, 7 H), 0.91 (t, $J = 7.1, 3$ H); MS: (ESI, Q-tof) 393 (12), 343 (28), 342 (100), 336 (8); Mol. Formula: $\text{C}_{23}\text{H}_{36}\text{BrNO}$ (422.44); HRMS: $\text{C}_{23}\text{H}_{36}\text{NO}^+$: (342.2797); Calcd: 342.2797; Found: 342.2782; TLC: R_f 0.28 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-(1-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{3,2}): Data for **III{3,2}**: Yield: 117 mg (81%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.70 (d, *J* = 8.5, 1 H), 8.30 (d, *J* = 7.2, 1 H), 7.98 (d, *J* = 8.2, 1 H), 7.92 (d, *J* = 7.6, 1 H), 7.58 (ddd, *J* = 6.2, 13.2, 24.1, 3 H), 5.40 (d, *J* = 12.6, 1 H), 5.32 (d, *J* = 12.6, 1 H), 5.07 (dt, *J* = 6.2, 12.7, 1 H), 4.04 (dd, *J* = 1.8, 13.9, 1 H), 3.96 (d, *J* = 3.3, 1 H), 3.76 (td, *J* = 6.8, 8.8, 1 H), 3.51 (m, 1 H), 3.35 (ddd, *J* = 4.2, 12.9, 24.2, 3 H), 3.23 (m, 2 H), 3.14 (dd, *J* = 6.2, 11.5, 1 H), 2.72 (t, *J* = 9.5, 1 H), 2.39 (m, 1 H), 2.20 (s, 3 H), 2.10 (td, *J* = 7.4, 17.8, 2 H), 1.78 (ddd, *J* = 15.8, 24.6, 37.5, 5 H), 1.56 (s, 1 H), 1.29 (m, 7 H), 0.92 (t, *J* = 7.1, 3 H); MS: (ESI, Q-tof) 394 (8), 393 (34), 392 (100), 336 (13); Mol. Formula: C₂₇H₃₈BrNO (472.50); HRMS: C₂₇H₃₈NO⁺: (392.2953); Calcd: 392.2953; Found: 392.2951; TLC: *R*_f 0.31 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-(2-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{3,3}): Data for **III{3,3}**: Yield: 93 mg (79%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.17 (s, 1 H), 7.91 (d, *J* = 8.6, 2 H), 7.88 (d, (broad), *J* = 7.3, 1 H), 7.78 (dd, 1 H, *J* = 1.6, 8.4), 7.59-7.54 (m, 2 H), 5.37 (d, *J* = 11.9, 1 H), 5.09 (dt, *J* = 6.3, 12.4, 12.4, 1 H), 4.78 (d, *J* = 11.9, 1 H), 4.04 (dd, *J* = 1.7, 13.8, 1 H), 3.94 (d, *J* = 2.8, 1 H), 3.67 (ddd, *J* = 6.6, 8.9, 9.1, 1 H), 3.52 (ddd, *J* = 6.3, 8.9, 12.7, 1 H), 3.34 (dd, *J* = 2.1, 14.0, 1 H), 3.28 (dd, *J* = 6.5, 11.4, 1 H), 3.12 (dd, *J* = 9.2, 16.1, 1 H), 2.67 (t, *J* = 9.2, 1 H), 2.42 (ddd, *J* = 7.2, 13.8, 13.8, 1 H), 2.14 (dd, *J* = 6.7, 13.4, 1 H), 2.09 (s, 3 H), 1.91-1.61 (m, 7 H), 1.52-1.46 (m, 2 H), 1.40-1.37 (m, 6 H), 0.93 (t, *J* =

7.1, 3 H); MS: (ESI, Q-tof) 393 (31), 392 (100); Mol. Formula: $C_{27}H_{38}BrNO$ (472.50); HRMS: $C_{27}H_{38}NO^+$: (392.2953); Calcd: 392.2953; Found: 392.2950; TLC: R_f 0.30 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-(9-anthracenylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{3,4}): Data for **III{3,4}**: Yield: 76 mg (73%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.85 (d, $J = 8.5$, 1 H), 8.66 (m, 1 H), 8.08 (d, $J = 8.2$, 2 H), 7.81 (t, $J = 6.9$, 1 H), 7.55 (m, 3 H), 5.87 (d, $J = 13.7$, 1 H), 5.71 (d, $J = 13.7$, 1 H), 4.22 (d, $J = 14.1$, 1 H), 4.13 (d, $J = 3.3$, 1 H), 4.07 (dt, $J = 6.3$, 12.3, 1 H), 3.84 (m, 1 H), 3.80 (td, $J = 6.8$, 8.9, 2 H), 3.59 (td, $J = 6.4$, 9.0, 1 H), 3.14 (m, 1 H), 2.76 (t, $J = 9.3$, 1 H), 2.62 (dd, $J = 5.9$, 11.7, 1 H), 2.23 (s, 1 H), 2.06 (m, 4 H), 1.83 (m, 5 H), 1.42 (m, 6 H), 0.92 (t, $J = 7.1$, 3 H); MS: (ESI, Q-tof) 442 (100); Mol. Formula: $C_{31}H_{40}BrNO$ (522.56); HRMS: $C_{31}H_{40}NO^+$: (442.3110); Calcd: 442.3110; Found: 442.3110; TLC: R_f 0.35 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-(3,5-bistrifluoromethylbenzyl)-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (III{3,5}): Data for **III{3,5}**: Yield: 97 mg (87%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.30 (s, 2 H), 7.98 (s, 1 H), 5.87 (d, $J = 12.2$, 1 H), 5.27 (ddd, $J = 6.3$, 12.1, 12.3, 1 H), 4.73 (d, $J = 12.2$, 1 H), 3.96 (d, $J = 3.2$, 1 H), 3.68 (m, 2 H), 3.46 (m, 2 H), 3.24 (dd, $J = 6.6$, 11.1, 1 H), 3.06 (dd, $J = 8.7$, 15.8, 1 H), 2.69 (dd, $J = 9.1$, 9.1, 1 H), 2.45 (m, 1 H), 2.16 (m, 1 H), 2.11 (s, 3 H), 1.86 (m, 4 H), 1.67 (m, 3 H), 1.42 (dd, $J = 7.3$, 14.8, 2 H), 1.33 (m, 4 H), 0.90 (t, 3 H, $J = 7.1$); MS: (ESI, Q-tof) 479 (26), 478 (100); Mol. Formula: $C_{25}H_{34}BrF_6NO$ (558.44); HRMS: $C_{25}H_{34}F_6NO^+$: (478.2545); Calcd: 478.2545; Found: 478.2541; TLC: R_f 0.29 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-hexyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{3,6}): Data for **III{3,6}**: Yield: 115 mg (94%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 4.16 (td, *J* = 5.0, 9.7, 1 H), 3.92 (d, *J* = 12.2, 2 H), 3.45 (m, 6 H), 2.72 (dt, *J* = 5.9, 9.7, 1 H), 2.50 (t, *J* = 7.7, 1 H), 2.29 (td, *J* = 7.4, 14.9, 1 H), 2.08 (m, 2 H), 1.81 (m, 6 H), 1.70 (s, 3 H), 1.52 (m, 7 H), 1.28 (ddd, *J* = 5.9, 11.0, 25.6, 13 H), 0.89 (t, *J* = 5.7, 6 H); MS: (ESI, Q-tof) 337 (28), 336 (100); Mol. Formula: C₂₂H₄₂BrNO (416.48); HRMS: C₂₂H₄₂NO⁺: (336.3266); Calcd: 336.3266; Found: 336.3256; TLC: *R*_f 0.42 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-3-hexyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{4,1}): Data for **III{4,1}**: ¹H-NMR: (500 MHz, CDCl₃) 7.70 (m, 2 H) 5.24 (d, 1 H, *J* = 12.2) 7.45 (m, 3H) 5.15 (d, 1 H, *J* = 9.7) 4.96 (dd, 1 H, *J* = 6.3, 11.7) 4.88 (m, 2 H) 4.58 (dd, 1 H, *J* = 5.6, 13.1) 4.30 (dd, 1 H, *J* = 4.0, 8.0) 3.77 (m, 2 H) 3.58 (ddd, 2 H, *J* = 2.9, 6.1, 8.4) 3.38 (m, 3 H) 3.24 (ddd, 1 H, *J* = 7.1, 12.8, 12.5) 3.07 (m, 1 H) 2.67 (m, 1 H) 2.39 (m, 1 H) 2.15 (m, 1 H) 2.04 (d, 3 H, *J* = 15.5) 1.77 (m, 5 H) 4.00 (s, 1 H); MS: (ESI, Q-tof) 346 (100); Mol. Formula: C₂₁H₃₂BrNO₃ (426.39); HRMS: C₂₁H₃₂NO₃: (346.2382); Calcd: 346.2382; Found: 346.2372; TLC: *R*_f 0.26 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of Quaternary Ammonium Bromides III{5,1-6}: Following General Procedure II, amino borane **III{5}** (252 mg, 96 mmol) was added to a 100-mL round-bottomed flask as a solution in 33 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (4.8, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary

evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 22 μ L, 0.18 mmol, 1.1 equiv), 1-bromomethylnaphthalene (tube 2, 44 mg, 0.2 mmol, 1.1 equiv), 2-bromomethylnaphthalene (tube 3, 58 mg, 0.26 mmol, 1.1 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (44 μ L, 0.24 mmol, 1.2 equiv), 9-bromomethylantracene (tube 5, 65 mg, 0.24 mmol, 1.2 equiv), 1-bromohexane (tube 6, 34 μ L, 0.24 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-3-benzyl-7b-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{5,1}**):** Data for **III{5,1}**: Yield: 50 mg (73%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.19 (d, *J* = 3.7, 1 H), 7.77-7.74 (m, 1 H), 7.48 (d, *J* = 7.3, 2 H), 7.41 (dd, *J* = 7.3, 7.3, 1 H), 7.34 (dd, *J* = 7.1, 7.1, 2 H), 7.06 (dd, *J* = 5.1, 6.9, 1 H), 6.94 (d, *J* = 8.2, 1 H), 5.47 (s, 1 H), 5.43 (d, *J* = 12.2, 1 H), 5.18 (s, 1 H), 4.55 (d, *J* = 11.5, 1 H), 4.25 (d, *J* = 14.0, 1 H), 3.38 (d, *J* = 13.9, 1 H), 3.22 (d, *J* = 30.4, 2 H), 2.78 (dd, *J* = 8.8, 8.8, 1 H), 2.50 (s, 1 H), 2.30 (ddd, *J* = 7.1, 7.1, 13.9, 1 H), 2.14 (s, 3 H), 1.95-1.70 (m, 4 H); MS: (ESI, Q-tof) 336 (28), 335 (100); Mol. Formula: C₂₂H₂₇BrN₂O (415.37); HRMS: C₂₂H₂₇N₂O⁺: (335.2123); Calcd: 335.2123; Found: 335.2114; TLC: *R*_f 0.23 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-3-(1-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{5,2}): Data for III{5,2}: Yield: 69 mg (74%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.50 (d, *J* = 8.7, 1 H), 8.24 (d, *J* = 7.2, 1 H), 8.16 (dd, *J* = 1.5, 4.8, 1 H), 7.92 (d, *J* = 8.2, 1 H), 7.86 (d, *J* = 8.1, 1 H), 7.79 (ddd, *J* = 2.0, 8.4, 8.4, 1 H), 7.50-7.47 (m, 1 H), 7.43 (dd, *J* = 7.5, 7.5, 1 H), 7.28-7.24 (m, 1 H), 7.05 (dd, *J* = 8.1, 14.2, 2 H), 5.58 (dd, *J* = 8.2, 15.4, 2 H), 5.29 (d, *J* = 12.7, 1 H), 5.17 (ddd, *J* = 6.2, 12.2, 12.3, 1 H), 4.17 (s, 1 H), 3.61 (s, 1 H), 3.51 (dd, *J* = 3.7, 14.6, 1 H), 3.26 (d, *J* = 3.5, 1 H), 3.15 (dd, *J* = 6.1, 11.3, 1 H), 2.78 (dd, *J* = 7.8, 7.8, 1 H), 2.40 (ddd, *J* = 7.5, 14.0, 13.4, 1 H), 2.32-2.24 (m, 1 H), 2.22 (s, 3 H), 1.96-1.71 (m, 5 H), 1.34 (dd, *J* = 2.0, 5.5, 1 H), 1.23 (ddd, *J* = 1.6, 7.1, 7.1, 1 H); MS: (ESI, Q-tof) 385 (100); Mol. Formula: C₂₆H₂₉BrN₂O (465.43); HRMS: C₂₆H₂₉N₂O⁺: (385.2280); Calcd: 385.2280; Found: 385.2275; TLC: *R*_f 0.26 (CH₂Cl₂/MeOH, 9:1) [I₂].

III{5,2}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-3-(2-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{5,3}): Data for III{5,3}: Yield: 103 mg (91%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.22 (dd, *J* = 1.5, 4.8, 1 H), 7.83 (m, 3 H), 7.69 (dd, *J* = 1.5, 8.5, 1 H), 7.61 (s, 1 H), 7.52 (m, 3 H), 7.16 (dd, *J* = 5.1, 7.1, 1 H), 7.05 (d, *J* = 8.0, 1 H), 5.64 (d, *J* = 12.0, 1 H), 5.46 (s, 1 H), 5.36 (ddd, *J* = 6.4, 12.3, 12.2, 1 H), 4.66 (d, *J* = 12.1, 1 H), 4.35 (dd, *J* = 1.7, 14.4, 1 H), 3.32 (dd, *J* = 2.7, 14.2, 1 H), 3.24 (ddd, *J* = 7.2, 7.2, 14.4, 2 H), 2.83 (dd, *J* = 9.0, 9.0, 1 H), 2.54-2.48 (m, 1 H), 2.31 (ddd, *J* = 7.6, 7.6, 14.9, 1 H), 2.22 (s, 3 H), 1.96-1.66 (m, 4 H); MS: (ESI, Q-tof) 385 (100); Mol. Formula: C₂₆H₂₉BrN₂O (465.43); HRMS: C₂₆H₂₉N₂O⁺: (385.2280); Calcd: 385.2280; Found: 385.2276; TLC: *R*_f 0.21 (CH₂Cl₂/MeOH, 9:1) [I₂].

III{5,3}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-3-(9-anthracenylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{5,4}): Data for III{5,4}: Yield: 68 mg (66%), free-flowing yellow powder; ¹H-NMR: (500 MHz, CDCl₃) Rotamer S: Data for Major is below 8.99 (d, *J* = 9.3, 1 H), 8.66 (s, 1 H), 8.61 (d, *J* = 9.0, 1 H), 8.22 (d, *J* = 4.0, 1 H), 8.09 (d, *J* = 8.6, 2 H), 7.92 (m, 1 H), 7.84 (m, 1 H), 7.62 (m, 1 H), 7.44 (dd, *J* = 7.1, 7.1, 1 H), 7.15 (m, 2 H), 6.01 (d, *J* = 13.8, 1 H), 5.96 (d, *J* = 13.8, 1 H), 5.68 (d, *J* = 3.2, 1 H), 4.39 (m, 2 H), 3.62 (dd, *J* = 4.2, 14.5, 1 H), 3.40 (m, 1 H), 2.91 (dd, *J*

= 8.2, 8.2, 1 H), 2.72 (dd, $J = 6.0, 12.1$, 1 H), 2.40 (m, 2 H), 1.93 (m, 2 H), 1.89 (s, 3 H), 1.83 (m, 1 H); MS: (ESI, Q-tof) 436 (32), 435 (100); Mol. Formula: $C_{30}H_{31}BrN_2O$ (515.48); HRMS: $C_{30}H_{31}N_2O^+$: (435.2436); Calcd: 435.2436; Found: 435.2426; TLC: R_f 0.23 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

III{5,5}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-3-(3,5-bis(trifluoromethyl)benzyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{5,5}): Data for **III{5,5}**: Yield: 97 mg (88%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.18 (d, $J = 4.9$, 1 H), 7.98 (s, 2 H), 7.90 (s, 1 H), 7.79 (dd, $J = 6.8, 6.8$, 1 H), 7.11 (dd, $J = 4.4, 6.9$, 1 H), 6.96 (d, $J = 8.2$, 1 H), 6.11 (d, $J = 12.3$, 1 H), 5.52-5.43 (m, 2 H), 4.56 (d, $J = 12.3$, 1 H), 4.08 (dd, $J = 6.7, 12.6$, 1 H), 3.5-3.42 (m, 1 H), 3.17 (dd, $J = 6.6, 10.7$, 2 H), 2.85 (dd, $J = 8.6, 8.6$, 1 H), 2.51 (s, 1 H), 2.32 (dd, $J = 5.5, 11.8$, 1 H), 2.25 (s, 3 H), 1.98-1.77 (m, 4 H); MS: (ESI, Q-tof) 471 (100), 472 (30); Mol. Formula: $C_{24}H_{25}BrF_6N_2O$ (551.36); HRMS: $C_{24}H_{25}F_6N_2O^+$: (471.1871); Calcd: 471.1871; Found: 471.1865; TLC: R_f 0.20 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

III{5,6}

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-(2-pyridyloxy)-3-hexyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (III{5,6}): Data for **III{5,6}**: Yield: 44 mg (54%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.14 (ddd, $J = 0.6, 1.9, 5.0$, 1 H), 7.65 (ddd, $J = 2.0, 7.2, 8.3$, 1 H), 6.98 (ddd, $J = 0.8, 5.0, 7.1$, 1 H), 6.73 (d, $J = 8.3$, 1 H), 5.44 (d, $J = 3.0$, 1 H), 4.17-3.99 (m, 4 H), 3.71 (ddd, $J = 4.9, 11.7, 11.5$, 1 H), 3.48 (dt, $J = 3.9, 12.2$, 1 H), 2.93-2.88 (m, 1 H), 2.67 (t, $J = 8.0$, 1 H), 2.42 (ddd, $J = 7.3, 14.4, 14.4$, 1 H), 2.28-2.20 (m, 1 H), 2.10-2.01 (m, 1 H), 1.95-1.85 (m, 4 H), 1.84 (s, 3 H), 1.49 - 1.43 (m, 1 H), 1.26-1.17 (m, 5 H), 0.83 (t, $J = 6.9$, 3 H); MS: (ESI, Qtof) 329 (100), 330 (29); Mol. Formula: $C_{21}H_{33}BrN_2O$ (409.40); HRMS: $C_{21}H_{33}N_2O^+$: (329.2593); Calcd: 329.2593; Found: 329.2580; TLC: R_f 0.33 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

5. Preparation of Quaternary Ammonium Bromides IV{2–7,1–7,1–11}

Preparation of Quaternary Ammonium Bromides IV{2,2, R^4 }: Following General Procedure II, amino borane V{2,2} (210 mg, 0.74 mmol) was added to a 250-mL, round-bottomed flask as a solution in 150 mL of MeOH (~0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 M aq. HCl solution (24 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 23 mg, 0.30 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 80 mg, 0.3 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 80 mg, 0.3 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-benzyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (IV{2,2,1}): Data for IV{2,2,1}: Yield: 63 mg (57%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.78–7.75 (m, 2 H), 7.48–7.42 (m, 3 H), 7.31–7.24 (m, 3 H), 7.18 (d, $J = 7.1$, 2 H), 5.38 (d, $J = 12.4$, 1 H), 5.34 (d, $J = 13.0$, 1 H), 4.45 (d, $J = 11.4$, 1 H), 4.26–4.21 (m, 2 H), 3.86–3.78 (m, 1 H), 3.72 (dd, $J = 6.8, 12.2$, 1 H), 3.44 (d, $J = 13.1$, 1 H), 2.83–2.79 (m, 1 H), 2.68 (dd, $J = 6.4, 13.5$, 1 H), 2.49–2.40 (m, 1 H), 2.27–2.20 (m, 1 H), 2.12 (s, 3 H), 2.12–2.04 (m, 1 H), 1.91–1.80 (m, 1 H), 1.80–1.75 (m, 1 H), 1.75 (s, 3 H); MS: (ESI, Q-tof) 362.2 (100); Mol. Formula: $\text{C}_{25}\text{H}_{32}\text{BrNO}$, (442.43); HRMS: $\text{C}_{25}\text{H}_{32}\text{NO}^+$: (362.2484); Calcd: 362.2484; Found: 362.2479; TLC: R_f 0.22 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-(1-naphthylmethyl)-7*b*-methylcyclopenta[gh]pyrrolizinium Bromide (IV{2,2,2}): Data for **IV{2,2,2}**: Yield: 71 mg (58%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.44–8.35 (m, 1 H), 8.17–8.10 (m, 1 H), 7.88–7.74 (m, 2 H), 7.59 (t, $J = 7.2$, 1 H), 7.53–7.47 (m, 1 H), 7.34 (s, 1 H), 7.25–7.16 (m, 3 H), 7.12–7.07 (m, 2 H), 5.60–5.42 (m, 2 H), 5.17–4.97 (m, 1 H), 4.41 (d, $J = 11.4$, 1 H), 4.13 (d, $J = 11.6$, 1 H), 3.83–3.73 (m, 1 H), 3.51–3.44 (m, 1 H), 3.36–3.28 (m, 1 H), 2.93–3.67 (m, 3 H), 2.33 (s, 3 H), 2.26–2.18 (m, 1 H), 2.11 (s, 1 H), 1.91–1.71 (m, 3 H), 1.75 (s, 3 H); MS: (ESI, Q-tof) 412.3 (100); Mol. Formula: $\text{C}_{29}\text{H}_{34}\text{BrNO}$ (492.49); HRMS: $\text{C}_{29}\text{H}_{34}\text{NO}^+$: (412.2640); Calcd: 412.2640; Found: 412.2636; TLC: R_f 0.25 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-(2-naphthylmethyl)-7*b*-methylcyclopenta[gh]pyrrolizinium Bromide (IV{2,2,3}): Data for **IV{2,2,3}**: Yield: 64 mg (53%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.21 (s, 1 H), 7.94–7.88 (m, 1 H), 7.83–7.74 (m, 3 H), 7.56–7.48 (m, 2 H), 7.28–7.17 (m, 3 H), 7.13 (d, $J = 7.4$, 2 H), 5.56–5.34 (m, 2 H), 4.45–4.40 (m, 1 H), 4.42 (d, $J = 11.0$, 1 H), 4.17 (d, $J = 11.4$, 1 H), 3.85–3.70 (m, 2 H), 3.47 (d, $J = 13.0$, 1 H), 2.88–2.69 (m, 2 H), 2.64–2.50 (m, 1 H), 2.28–2.17 (m, 1 H), 2.19 (s, 3 H), 2.12–2.04 (m, 1 H), 1.91–1.73 (m, 3 H), 1.75 (s, 3 H); MS: (ESI, Q-tof) 412.3 (100); Mol. Formula: $\text{C}_{29}\text{H}_{34}\text{BrNO}$ (492.49); HRMS: $\text{C}_{29}\text{H}_{34}\text{NO}^+$: (412.2640); Calcd: 412.2640; Found: 412.2631; TLC: R_f 0.25 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides IV{2,3,1–3}: Following General Procedure II, amino borane **IV{2,3}** (103 mg, 0.37 mmol) was added to a 50-mL round-

bottomed flask as a solution in 12 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (3.68 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 82 mg, 0.478 mmol, 4.0 equiv), 1-bromomethylnaphthalene (tube 2, 79 mg, 0.358 mmol, 3.0 equiv), 2-bromomethylnaphthalene (tube 3, 79 mg, 0.358 mmol, 3.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-benzyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{2,3,1}): Data for IV{2,3,1}: Yield: 41 mg (51%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.79-7.73 (m, 2 H), 7.48-7.42 (m, 3 H), 5.35 (d, *J* = 12.3, 1 H), 5.17 (d, *J* = 13.0, 1 H), 4.27-4.18 (m, 1 H), 3.84 (ddd, *J* = 6.0, 12.1, 12.1, 1 H), 3.79-3.73 (m, 1 H), 3.32 (d, *J* = 12.9, 2 H), 3.30 (dd, *J* = 6.9, 15.2, 1 H), 3.11 (dd, *J* = 6.4, 15.1, 1 H), 2.76-2.70 (m, 1 H), 2.66 (dd, *J* = 7.2, 14.7, 1 H), 2.53-2.42 (m, 1 H), 2.19-2.00 (m, 2 H), 2.09 (s, 3 H), 1.86-1.72 (m, 3 H), 1.60 (s, 3 H), 1.47-1.38 (m, 2 H), 1.30-1.15 (m, 6H), 0.84 (t, *J* = 6.9, 3 H); MS: (ESI, Q-tof) 356.3 (100); Mol. Formula: C₂₄H₃₈BrNO (436.47); HRMS: C₂₄H₃₈NO⁺: (356.2953); Calcd: 356.2953; Found: 356.2951; TLC: *R*_f 0.32 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-(1-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{2,3,2}): Data for IV{2,3,2}: Yield: 45 mg (51%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.42-8.36 (m, 1 H), 8.16-8.10 (m, 1 H), 7.85 (d, *J* = 7.7, 1 H), 7.82-7.76 (m, 1 H), 7.61 (dd, *J* = 7.6, 7.6, 1 H), 7.51 (dd, *J* = 7.5, 7.5, 1 H), 7.41-7.33 (m, 1 H), 5.53 (d, *J* = 12.5, 1 H), 5.31 (d, *J* = 12.9, 1 H), 5.06 (d, *J* = 12.6, 1 H), 3.84-3.75 (m, 1 H), 3.35 (d, *J* = 12.9, 2 H), 3.25 (dd, *J* = 7.1, 15.2, 1 H), 2.99 (dd, *J* = 6.3, 15.0, 1 H), 2.84-2.69 (m, 3 H), 2.30 (s, 3 H), 2.15-2.05 (m, 2 H), 1.83-1.74 (m, 3 H), 1.60 (s, 3 H), 1.38-1.25 (m, 2 H), 1.22-1.09 (m, 6H), 0.79 (t, *J* = 7.0, 3 H); MS: (ESI, Q-tof) 406.3 (100); Mol. Formula: C₂₈H₄₀BrNO (486.53); HRMS: C₂₈H₄₀NO⁺: (406.3110); Calcd: 406.3110; Found: 406.3099; TLC: *R*_f 0.35 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-(2-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{2,3,3}): Data for IV{2,3,3}: Yield: 51 mg (57%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.21 (s, 1 H), 7.94-7.89 (m, 1 H), 7.83-7.74 (m, 3 H), 7.56-7.48 (m, 2 H), 5.53-5.46 (m, 1 H), 5.27-5.17 (m, 1 H), 4.55-4.39 (m, 1 H), 3.87-3.73 (m, 2 H), 3.35 (d, *J* = 12.9, 1 H), 3.26 (dd, *J* = 7.2, 13.6, 1 H), 3.04 (dd, 1 H, *J* = 6.9, 13.3), 2.78-2.67 (m, 2 H), 2.65-2.54 (m, 1 H), 2.18-2.02 (m, 2 H), 2.16 (s, 3 H), 1.88-1.72 (m, 3 H), 1.60 (s, 3 H), 1.45-1.29 (m, 2 H), 1.24-1.11 (m, 6H), 0.80 (t, *J* = 6.8, 3 H); MS: (ESI, Q-tof) 406.3 (100); Mol. Formula: C₂₈H₄₀BrNO (486.53); HRMS: C₂₈H₄₀NO⁺: (406.3110); Calcd: 406.3110; Found: 406.3109; TLC: *R*_f 0.35 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of Quaternary Ammonium Bromides IV{3,2,R⁴}: Following General Procedure II, amino borane IV{3,2} (533 mg, 1.68 mmol) was added to a 50-mL round-bottomed flask as a solution in 56 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (8.4 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among four test tubes that were subsequently charged with benzyl bromide (tube 1, 87 mg, 0.509 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 116 mg, 0.509 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 116 mg, 0.509 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 156 mg, 0.509 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-3-benzyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{3,2,1}): Data for **IV{3,2,1}**: Yield: 235 mg (99%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.82-7.77 (dd, *J* = 2.2, 7.2, 2 H), 7.44-7.37 (s, 3 H), 7.30-7.21 (m, 3 H), 7.19-7.15 (m, 2 H), 5.50 (d, *J* = 12.5, 1 H), 4.77 (d, *J* = 13.4, 1 H), 4.62-4.53 (m, 1 H), 4.46 (d, *J* = 11.3, 1 H), 4.21 (d, *J* = 11.3, 1 H), 3.91-3.82 (m, 1 H), 3.72 (d, *J* = 13.5, 1 H), 3.49 (dd, *J* = 7.2, 12.3, 1 H), 2.83-2.76 (m, 1 H), 2.73 (dd, *J* = 8.2, 8.2, 1 H), 2.67-2.56 (m, 1 H), 2.42-2.32 (m, 1 H), 2.31-2.21 (m, 1 H), 2.09-1.99 (m, 1 H), 1.96 (s, 3 H), 1.86-1.76 (m, 2 H), 1.69-1.59 (m, 1 H), 1.28 (d, *J* = 6.8, 3 H), 1.05 (d, *J* = 6.8, 3 H); MS: (ESI, Q-tof) 390.3 (100); Mol. Formula: C₂₇H₃₆BrNO (470.48); HRMS: C₂₇H₃₆NO⁺: (390.2797); Calcd: 390.2797; Found: 390.2789; TLC: *R_f* 0.21 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-3-(1-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{3,2,2}): Data for **IV{3,2,2}**: Yield: 194 mg (74%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.35 (s, 1 H), 8.24 (s, 1 H), 7.66 (s, 1 H), 7.53 (dd, *J* = 7.9, 7.9, 1 H), 7.45-7.40 (m, 2 H), 7.18-7.13 (m, 3 H), 7.02 (d, *J* = 5.9, 2 H), 6.99-6.89 (m, 1 H), 5.62-5.49 (m, 2 H), 4.82 (d, *J* = 13.8, 1 H), 4.37 (d, *J* = 11.2, 1 H), 4.00 (d, *J* = 11.3, 1 H), 3.76-3.67 (m, 1 H), 3.54 (d, *J* = 13.9, 1 H), 3.26-3.16 (m, 1 H), 3.03-2.94 (m, 2 H), 2.78 (dd, *J* = 7.3, 7.3, 1 H), 2.39-2.16 (m, 2 H), 2.30 (s, 3 H), 2.11-2.02 (m, 1 H), 1.85-1.75 (m, 2 H), 1.63-1.55 (m, 1 H), 1.35 (d, *J* = 6.8, 3 H), 1.04 (d, *J* = 6.8, 3 H); MS: (ESI, Q-tof) 440.3 (100); Mol. Formula: C₃₁H₃₈BrNO

(520.54); HRMS: $C_{31}H_{38}NO^+$: (440.2953); Calcd: 440.2953; Found: 440.2960; TLC: R_f 0.25 (CH_2Cl_2 /MeOH, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-3-(2-naphthylmethyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{3,2,3}): Data for IV{3,2,3}: Yield: 195 mg (75%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.22 (s, 1 H), 7.86-7.81 (m, 1 H), 7.74 (d, $J = 8.3$, 1 H), 7.64-7.55 (m, 2 H), 7.45-7.42 (m, 2 H), 7.20-7.14 (m, 3 H), 7.11-7.08 (m, 2 H), 5.62 (d, $J = 12.8$, 1 H), 4.92-4.82 (m, 1 H), 4.83 (d, $J = 13.4$, 1 H), 4.41 (d, $J = 11.3$, 1 H), 4.11 (d, $J = 11.2$, 1 H), 3.87-3.78 (m, 1 H), 3.69 (d, $J = 13.4$, 1 H), 3.49-3.41 (m, 1 H), 2.95-2.89 (m, 1 H), 2.82-2.71 (m, 2 H), 2.37 (hept, $J = 6.9$, 1 H), 2.29-2.21 (m, 1 H), 2.10-2.02 (m, 1 H), 2.07 (s, 3 H), 1.86-1.75 (m, 2 H), 1.68-1.60 (m, 1 H), 1.33 (d, $J = 6.8$, 3 H), 1.03 (d, $J = 6.7$, 3 H); MS: (ESI, Q-tof) 440.3 (100); Mol. Formula: $C_{31}H_{38}BrNO$ (520.54); HRMS: $C_{31}H_{38}NO^+$: (440.2953); Calcd: 440.2953; Found: 440.2960; TLC: R_f 0.25 (CH_2Cl_2 /MeOH, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-3-(3,5-trifluoromethyl benzyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{3,2,5}): Data for IV{3,2,5}: Yield: 199 mg (66%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.32 (s, 2 H), 7.83 (s, 1 H), 7.25-7.19 (m, 3 H), 7.15-7.10 (m, 2 H), 5.88 (d, $J = 12.7$, 1 H), 5.17-5.09 (m, 1 H), 4.88 (d, $J = 13.2$, 1 H), 4.47 (d, $J = 11.5$, 1 H), 4.16 (d, $J = 11.5$, 1 H), 3.94-3.85 (m, 1 H), 3.47 (d, $J = 13.1$, 1 H), 3.02-2.93 (m, 2 H), 2.80-2.70 (m, 2 H), 2.38 (hept, $J = 6.7$, 1 H), 2.31-2.22 (m, 1 H), 2.12-1.99 (m, 1 H), 2.04 (s, 3 H), 1.91-1.77 (m, 2 H), 1.74-1.65 (m, 1 H), 1.31 (d, $J = 6.7$, 3 H), 1.02 (d, $J = 6.7$, 3 H); MS: (ESI, Q-tof) 526.3 (100); Mol. Formula: $C_{29}H_{34}BrF_6NO$ (606.48); HRMS: $C_{29}H_{34}NOF_6^+$: (526.2545); Calcd: 526.2545; Found: 526.2549; TLC: R_f 0.30 (CH_2Cl_2 /MeOH, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(3,5-trifluoromethylbenzyl)-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (IV{5,2,5}):

Following General Procedure II, benzyl ether IV{5,2} (69 mg, 0.268 mmol) was added to a 50-mL round-bottomed flask as a solution in 8.9 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (1.3 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine (30 mg, 0.09 mmol) was dissolved in acetonitrile along with 3,5-bis(trifluoromethyl)benzyl bromide (33 mg, 0.108 mmol, 2.0 equiv) and was allowed to react for 12 h. Purification of described in General Procedure II afforded 44 mg (75%) of the quaternary ammonium ion IV{5,2,5} as a free flowing white power. Data for IV{5,2,5}: Yield: 44 mg (75%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.12 (s, 1 H), 7.93 (s, 1 H), 7.76 (d, *J* = 7.5, 1 H), 7.64 (dd, *J* = 7.6, 7.6, 1 H), 7.55 (dd, *J* = 7.3, 7.3, 1 H), 7.30–7.24 (m, 1 H), 7.12 (dd, *J* = 2.1, 7.5, 1 H), 5.59 (d, *J* = 12.5, 1 H), 4.80 (s, 1 H), 4.59 (d, *J* = 13.0, 1 H), 4.37 (d, *J* = 11.6, 1 H), 4.07 (d, *J* = 11.0, 1 H), 3.91 (d, *J* = 11.0, 1 H), 3.62 (d, *J* = 13.1, 1 H), 3.44–3.39 (m, 1 H), 3.32 (dd, *J* = 8.1, 8.1, 1 H), 3.15–3.08 (m, 1 H), 2.61–2.45 (m, 1 H), 2.26 (s, 3 H), 2.16–2.03 (m, 1 H), 2.01–1.95 (m, 1 H), 1.87 (ddd, *J* = 7.8, 14.5, 14.3, 1 H); ¹³C-NMR: (126 MHz, CDCl₃) 139.1, 136.7, 133.4, 132.53 (q, *J* = 34.3), 132.5, 130.0, 129.8, 128.7, 128.2, 127.4, 126.7, 124.2, 122.8 (q *J* = 273), 99.6, 84.5, 66.8, 64.5, 61.4, 59.3, 58.9, 52.0, 32.1, 28.1, 26.7, 24.0; MS: (ESI, Q-tof) 560.2 (100); Mol. Formula: C₃₂H₃₂BrF₆NO (640.50); HRMS: C₃₂H₃₂F₆NO⁺: (560.2388); Calcd: 560.2388; Found: 560.2388; TLC: *R*_f 0.32 (CH₂Cl₂/MeOH, 9:1) [I₂].

6. Preparation of Quaternary Ammonium Bromides V{1–7,1–7,1–11}

Preparation of Quaternary Ammonium Bromides V{1,2,R⁴}: Following General Procedure II, amino borane V{1,2} (533 mg, 1.68 mmol) was added to a 100-mL round-bottomed flask as a solution in 37 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (5.5 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among seven test tubes that were subsequently charged with benzyl bromide (tube 1, 40 mg, 0.235 mmol, 1.5 equiv), 1-bromomethylnaphthalene (tube 2, 42 mg, 0.188 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 42 mg, 0.188 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 58 mg, 0.188 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 54 mg, 0.188 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 38 mg, 0.188 mmol, 1.2 equiv), 1-bromohexane (tube 7, 129 mg, 0.785 mmol, 5.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

V{1,2,1}

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-benzyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{1,2,1}): Data for V{1,2,1}: Yield: 63 mg (90%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.64 (d, $J = 6.7$, 2 H), 7.43-7.31 (m, 8H), 5.14 (d, $J = 12.3$, 1 H), 4.99-4.93 (dd, $J = 6.9$, 17.2, 1 H), 4.65 (d, $J = 12.3$, 1 H), 4.63 (d, $J = 11.7$, 1 H), 4.57 (d, $J = 11.7$, 1 H), 4.37 (dd, $J = 11.9$, 11.9, 1 H), 3.87 (dd, $J = 6.2$, 12.5, 1 H), 3.10 (dd, $J = 6.1$, 11.5, 1 H), 2.88-2.82 (m, 2 H), 2.45-2.40 (s, 1 H), 2.15-2.06 (m, 1 H), 2.06-1.95 (m, 1 H), 2.04 (s, 3 H), 1.93-1.78 (m, 3 H), 1.20 (d, $J = 6.4$, 3 H); MS: (ESI, Q-tof) 362.2 (100); Mol. Formula: $\text{C}_{25}\text{H}_{32}\text{BrNO}$ (442.43); HRMS: $\text{C}_{25}\text{H}_{32}\text{NO}^+$: (362.2484); Calcd: 362.2484; Found: 362.2484; TLC: R_f 0.20 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(1-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{1,2,2}):

Data for V{1,2,2}: Yield: 77 mg (99%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.25-8.16 (m, 2 H), 7.85-7.73 (m, 2 H), 7.53-7.47 (m, 1 H), 7.49 (dd, *J* = 7.6, 14.6, 1 H), 7.40-7.26 (m, 7H), 5.54 (d, *J* = 13.0, 1 H), 5.25 (d, *J* = 13.0, 1 H), 5.17-5.08 (m, 1 H), 4.72 (dd, *J* = 11.9, 11.9, 1 H), 4.64 (d, *J* = 11.8, 1 H), 4.49 (d, *J* = 11.8, 1 H), 3.56 (dd, *J* = 6.1, 12.4, 1 H), 3.06 (dd, *J* = 5.9, 11.3, 1 H), 2.91 (dd, *J* = 8.4, 16.9, 1 H), 2.74 (t, *J* = 11.8, 11.8, 1 H), 2.59-2.53 (m, 1 H), 2.31 (s, 3 H), 2.04-1.75 (m, 5 H), 1.59 (s, 3 H), 1.21 (d, *J* = 6.3, 3 H) MS: (ESI, Q-tof) 412.3 (100); Mol. Formula: C₂₉H₃₄BrNO (492.49); HRMS: C₂₉H₃₄NO⁺: (412.2640); Calcd: 412.2640; Found: 412.2633; TLC: *R*_f 0.23 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{1,2,3}):

Data for V{1,2,3}: Yield: 65 mg (84%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.15 (s, 1 H), 7.91-7.82 (m, 1 H), 7.73-7.62 (m, 3 H), 7.52-7.44 (m, 2 H), 7.39-7.28 (m, 5 H), 5.33 (d, *J* = 12.3, 1 H), 5.10 (dd, *J* = 6.9, 17.2, 1 H), 4.93 (d, *J* = 12.4, 1 H), 4.65 (d, *J* = 14.1, 1 H), 4.62 (d, *J* = 14.1, 1 H), 4.42 (dd, *J* = 11.9, 11.9, 1 H), 3.94 (dd, *J* = 6.2, 12.4, 1 H), 3.11 (dd, *J* = 6.0, 11.4, 1 H), 2.89 (dd, *J* = 8.5, 16.9, 1 H), 2.83 (dd, *J* = 11.4, 11.4, 1 H), 2.47-2.41 (m, 1 H), 2.15-1.94 (m, 2 H), 2.13 (s, 3 H), 1.92-1.74 (m, 3 H), 1.20 (d,

$J = 6.4$, 3 H); MS: (ESI, Q-tof) 412.3 (100); Mol. Formula: $C_{29}H_{34}BrNO$ (492.49); HRMS: $C_{29}H_{34}NO^+$: (412.2640); Calcd: 412.2640; Found: 412.2625; TLC: R_f 0.24 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(3,5-trifluoromethylbenzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{1,2,5}): Data for V{1,2,5}: Yield: 84 mg (98%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.40 (s, 2 H), 7.90 (s, 1 H), 7.38-7.27 (m, 5 H), 5.58 (d, $J = 12.4$, 1 H), 5.32-5.24 (m, 1 H), 5.13-5.04 (m, 1 H), 4.61 (d, $J = 11.6$, 1 H), 4.58 (d, $J = 11.6$, 1 H), 4.44 (dd, $J = 11.6$, 11.6, 1 H), 3.83 (dd, $J = 6.1$, 12.5, 1 H), 3.06-3.00 (m, 1 H), 2.95-2.84 (m, 2 H), 2.42-2.36 (m, 1 H), 2.26-2.15 (m, 1 H), 2.00-1.97 (m, 1 H), 2.09 (s, 3 H), 1.89-1.79 (m, 3 H), 1.19 (d, $J = 6.2$, 3 H); MS: (ESI, Q-tof) 498.2 (100); Mol. Formula: $C_{27}H_{30}BrF_6NO$ (578.43); HRMS: $C_{27}H_{30}F_6NO^+$: (498.2232); Calcd: 498.2232; Found: 498.2222; TLC: R_f 0.28 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-hexyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{1,2,6}): Data for V{1,2,6}: Yield: 65 mg (95%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.40-7.30 (m, 5 H), 4.63 (dd, $J = 7.9$, 14.6, 1 H), 4.60 (d, $J = 11.5$, 1 H), 4.57 (d, $J = 11.5$, 1 H), 4.11 (dd, $J = 6.2$, 12.5, 1 H), 3.71-3.58 (m, 3 H), 3.49 (ddd, $J = 4.4$, 4.4, 12.2, 1 H), 3.31 (dd, $J = 8.9$, 12.5, 1 H), 2.84-2.78 (m, 1 H), 2.37-2.20 (m, 2 H), 2.17 (s, 2 H), 2.13-2.02 (m, 1 H), 1.92-1.81 (m, 3 H), 1.84 (s, 3 H), 1.80-1.64 (m, 2 H), 1.51-1.40 (m, 2 H), 1.36-1.27 (m, 4 H), 1.16 (d, $J = 6.3$, 3 H), 0.89 (t, $J = 7.1$, 3 H); MS: (ESI, Q-tof) 356.3 (100); Mol. Formula: $C_{24}H_{38}BrNO$ (436.47); HRMS: $C_{24}H_{38}NO^+$: (356.2953); Calcd: 356.2953; Found: 356.2947; TLC: R_f 0.25 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{1,2,7}): Data for V{1,2,7}: Yield: 84 mg (96%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.52–7.48 (m, 3 H), 7.40–7.28 (m, 5 H), 5.08 (d, $J = 12.4$, 1 H), 4.83 (dd, $J = 6.9$, 16.8, 1 H), 4.62 (d, $J = 11.9$, 1 H), 4.54 (d, $J = 11.9$, 1 H), 4.52 (d, $J = 11.9$, 1 H), 4.42 (dd, $J = 11.7$, 11.7, 1 H), 4.17 (dd, $J = 6.2$, 12.5, 1 H), 3.19 (dd, $J = 6.2$, 11.6, 1 H), 3.00 (dd, $J = 11.2$, 11.2, 1 H), 2.90 (dd, $J = 8.2$, 16.4, 1 H), 2.50–2.45 (m, 1 H), 2.22–2.12 (m, 1 H), 2.12–1.99 (m, 1 H), 2.10 (s, 3 H), 1.95–1.80 (m, 3 H), 1.34 (s, 18H), 1.24 (d, $J = 6.5$, 3 H); MS: (ESI, Q-tof) 474.4 (100); Mol. Formula: $\text{C}_{33}\text{H}_{48}\text{BrNO}$ (554.64); HRMS: $\text{C}_{33}\text{H}_{48}\text{NO}^+$: (474.3736); Calcd: 474.3736; Found: 474.3723; TLC: R_f 0.32 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{1,2,8}): Data for V{1,2,8}: Yield: 77 mg (99%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.56 (d, $J = 8.6$, 2 H), 7.40–7.31 (m, 5 H), 6.85 (d, $J = 8.4$, 2 H), 5.07 (d, $J = 12.4$, 1 H), 5.00–4.90 (m, 1 H), 4.65–4.52 (m, 3 H), 4.31 (dd, $J = 11.9$, 1 H), 3.90–3.82 (m, 1 H), 3.80 (s, 3 H), 3.07 (dd, $J = 6.5$, 11.2, 1 H), 2.83 (dd, $J = 8.03$, 15.8, 2 H), 2.44–2.38 (m, 1 H), 2.14–2.05 (m, 1 H), 2.05–1.93 (m, 1 H), 2.03 (s, 3 H), 1.91–1.76 (m, 3 H), 1.20 (d, $J = 6.4$, 3 H); MS: (ESI, Q-tof) 392.3 (100); Mol. Formula: $\text{C}_{26}\text{H}_{34}\text{BrNO}_2$ (472.46); HRMS: $\text{C}_{26}\text{H}_{34}\text{NO}_2^+$: (392.2590); Calcd: 392.2590; Found: 392.2578; TLC: R_f 0.18 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides $V\{2,2,R^4\}$: Following General Procedure II, amino borane $V\{2,2\}$ (397 mg, 1.33 mmol) was added to a 100-mL round-bottomed flask as a solution in 44 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (6.6 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among seven test tubes that were subsequently charged with benzyl bromide (tube 1, 48 mg, 0.279 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 50 mg, 0.279 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 50 mg, 0.279 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 70 mg, 0.279 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 64 mg, 0.279 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 70 mg, 0.279 mmol, 1.2 equiv), 1-bromohexane (tube 7, 70 mg, 0.279 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-benzyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide ($V\{2,2,1\}$): Data for $V\{2,2,1\}$: Yield: 79 mg (74%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.80–7.77 (m, 2 H), 7.51–7.43 (m, 3 H), 7.38–7.29 (m, 3 H), 7.24 (d, $J = 6.7$, 2 H), 5.20 (d, $J = 12.2$, 1 H), 4.86 (d, $J = 12.2$, 1 H), 4.51 (d, $J = 13.5$, 1 H), 4.49 (d, $J = 11.1$, 11.1, 1 H), 4.41 (d, $J = 11.0$, 1 H), 4.37 (d, $J = 11.0$, 1 H), 3.24 (d, $J = 13.3$, 1 H), 3.18 (dd, $J = 6.7$, 11.7, 1 H), 2.71 (dd, $J = 8.4$, 8.4, 1 H), 2.59–2.52 (m, 1 H), 2.39–2.19 (m, 2 H), 2.16 (s, 3 H), 1.96 (m, 1 H), 1.89 (m, 2 H), 1.84 (s, 3 H), 1.20 (d, $J = 6.6$, 3 H); MS: (ESI, Q-tof) 376.3 (100); Mol. Formula: $\text{C}_{26}\text{H}_{34}\text{BrNO}$ (456.46); HRMS: $\text{C}_{26}\text{H}_{34}\text{NO}^+$: (376.2640); Calcd: 376.2640; Found: 376.2638; TLC: R_f 0.22 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2] [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-(1-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,2,2}):

Data for V{2,2,2}: Yield: 91 mg (77%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.42 (d, *J* = 8.6, 1 H), 8.30 (d, *J* = 7.1, 1 H), 7.92–7.87 (m, 2 H), 7.66 (dd, *J* = 7.6, 7.6, 1 H), 7.52 (m, 2 H), 7.30–7.21 (m, 3 H), 7.18–7.12 (m, 2 H), 5.53 (d, *J* = 12.9, 1 H), 5.43 (d, *J* = 12.9, 1 H), 4.61 (d, *J* = 13.2, 1 H), 4.44 (dd, *J* = 11.7, 11.7, 1 H), 4.38 (d, *J* = 11.1, 1 H), 4.29 (d, *J* = 11.1, 1 H), 3.24 (d, *J* = 13.3, 1 H), 2.98 (dd, *J* = 6.8, 11.6, 1 H), 2.78 (dd, *J* = 8.3, 8.3, 1 H), 2.62 (d, *J* = 9.5, 1 H), 2.36–2.20 (m, 2 H), 2.31 (s, 3 H), 1.98–1.83 (m, 3 H), 1.92 (s, 3 H), 1.10 (d, *J* = 6.5, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 137.4, 134.2, 134.0, 132.7, 131.4, 129.2, 128.5, 127.9, 127.6, 127.2, 126.1, 125.4, 125.3, 124.2, 100.3, 79.7, 72.0, 70.0, 65.9, 61.4, 60.3, 59.1, 34.2, 29.2, 25.1, 24.7, 24.7, 15.5; MS: (ESI, Q-tof) 426.3 (100); Mol. Formula: C₃₀H₃₆BrNO (506.52); HRMS: C₃₀H₃₆NO⁺: (426.2797); Calcd: 426.2797; Found: 426.2801; TLC: *R*_f 0.24 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,2,3}):

Data for V{2,2,3}: Yield: 96 mg (81%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.27 (s, 1 H), 7.95 (d, *J* = 8.3, 1 H), 7.86–7.82 (m, 3 H), 7.57–7.52 (m, 2 H), 7.31–7.22 (m, 3 H), 7.21–7.18 (m, 2 H), 5.32 (d, *J* = 12.2, 1 H), 5.07 (d, *J* = 12.3, 1 H), 4.60 (d, *J* = 13.2, 1 H), 4.54 (dd, *J* = 11.4, 1 H), 4.40 (d, *J* = 11.0, 1 H), 4.34 (d, *J* = 11.0, 1 H), 3.23 (d, *J* = 13.2, 1 H), 3.19 (dd, *J* = 7.2, 12.0, 1 H), 2.73 (dd, *J* = 8.3, 8.3, 1 H), 2.59–2.52 (m, 1 H),

2.36–2.27 (m, 1 H), 2.27–2.15 (m, 1 H), 2.2 (s, 3 H), 1.98–1.90 (m, 1 H), 1.90–1.85 (m, 2 H), 1.87 (s, 3 H), 1.19 (d, $J = 6.5$, 3 H); MS: (ESI, Q-tof) 426.3 (100); Mol. Formula: $C_{30}H_{36}BrNO$ (506.52); HRMS: $C_{30}H_{36}NO^+$: (426.2797); Calcd: 426.2797; Found: 426.2806; TLC: R_f 0.25 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{2,2,5}):

Data for **V{2,2,5}**: Yield: 98 mg (71%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.40 (s, 2 H), 7.98 (s, 1 H), 7.34–7.27 (m, 3 H), 7.23–7.18 (m, 2 H), 5.43 (d, $J = 12.5$, 1 H), 5.37 (d, $J = 12.5$, 1 H), 4.55 (d, $J = 13.1$, 1 H), 4.44 (d, $J = 11.1$, 1 H), 4.38 (d, $J = 11.1$, 1 H), 4.36 (dd, $J = 10.6$, 10.6, 1 H), 3.24 (d, $J = 13.1$, 1 H), 3.11 (dd, $J = 6.1$, 11.3, 1 H), 2.76 (dd, $J = 8.0$, 8.0, 1 H), 2.51–2.41 (m, 2 H), 2.32–2.23 (m, 1 H), 2.16 (s, 3 H), 1.99–1.87 (m, 3 H), 1.82 (s, 3 H), 1.16 (d, $J = 6.2$, 3 H); MS: (ESI, Q-tof) 512.2 (100); Mol. Formula: $C_{28}H_{32}BrF_6NO$ (592.45); HRMS: $C_{28}H_{32}NOF_6^+$: (512.2388); Calcd: 512.2388; Found: 512.2395; TLC: R_f 0.30 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-methyl-3-hexyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{2,2,6}):

Data for **V{2,2,6}**: Yield: 30 mg (28%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.33 (m, 5 H), 4.47 (d, $J = 11.1$, 1 H), 4.37 (d, $J = 11.0$, 1 H), 3.41 (dd, $J = 6.9$, 6.9, 2 H), 3.01 (d, $J = 8.9$, 1 H), 2.92 (d, $J = 8.9$, 1 H), 2.82 (dd, $J = 6.0$, 12.2, 1 H), 2.49 (dd, $J = 11.8$, 11.8, 1 H),

2.07–2.00 (m, 2 H), 1.94–1.81 (m, 5 H), 1.72–1.63 (m, 3 H), 1.46–1.40 (m, 3 H), 1.36–1.34 (m, 8H), 0.97 (d, $J = 6.5$, 3 H), 0.90 (t, $J = 7.0$, 3 H); MS: (ESI, Q-tof) 370.3 (100); Mol. Formula: $C_{25}H_{40}BrNO$ (450.50); HRMS: $C_{25}H_{40}NO^+$: (370.3110); Calcd: 370.3110; Found: 370.3109; TLC: R_f 0.40 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyl-3-(3,5-*tert*-butyl-benzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,2,7}): Data for V{2,2,7}: Yield: 109 mg (82%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.57 (d, $J = 1.7$, 2 H), 7.50 (s, 1 H), 7.34–7.27 (m, 3 H), 7.24–7.22 (m, 2 H), 5.22 (d, $J = 12.3$, 1 H), 4.74 (d, $J = 12.3$, 1 H), 4.58 (dd, $J = 11.2$, 11.2, 1 H), 4.47 (d, $J = 13.2$, 1 H), 4.41 (s, 2 H), 3.22 (d, $J = 11.9$, 1 H), 3.21 (d, $J = 12.8$, 1 H), 2.65 (dd, $J = 8.6$, 8.6, 1 H), 2.61–2.56 (m, 1 H), 2.32–2.18 (m, 2 H), 2.16 (s, 3 H), 2.00–1.92 (m, 1 H), 1.90–1.86 (m, 2 H), 1.84 (s, 3 H), 1.35 (s, 18H), 1.23 (d, $J = 6.6$, 3 H); MS: (ESI, Q-tof) 488.4 (100); Mol. Formula: $C_{34}H_{50}BrNO$ (568.67); HRMS: $C_{34}H_{50}NO^+$: (488.3892); Calcd: 488.3892; Found: 488.3893; TLC: R_f 0.33 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyl-3-(4-methoxy-benzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,2,8}): Data for V{2,2,8}: Yield: 88 mg (77%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.71 (d, $J = 8.7$, 2 H), 7.34–7.28 (m, 3 H), 7.22 (d, $J = 6.7$, 2 H), 6.94 (d, $J = 8.4$, 2

H), 5.11 (d, $J = 12.3$, 1 H), 4.78 (d, $J = 12.4$, 1 H), 4.48–4.40 (m, 2 H), 4.41 (d, $J = 11.0$, 1 H), 4.37 (d, $J = 11.0$, 1 H), 3.82 (s, 3 H), 3.20 (d, $J = 13.3$, 1 H), 3.14 (dd, $J = 6.7$, 11.7, 1 H), 2.67 (dd, $J = 8.4$, 8.4, 1 H), 2.55–2.48 (m, 1 H), 2.33–2.17 (m, 2 H), 2.11 (s, 3 H), 1.97–1.89 (m, 1 H), 1.88–1.83 (m, 2 H), 1.81 (s, 3 H), 1.17 (d, $J = 6.5$, 3 H); MS: (ESI, Q-tof) 406.3 (100); Mol. Formula: $C_{27}H_{36}BrNO_2$ (486.48); HRMS: $C_{27}H_{36}NO_2^+$: (406.2746); Calcd: 406.2746; Found: 406.2748; TLC: R_f 0.20 (CH_2Cl_2 /MeOH, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides $V\{2,3,R^4\}$: Following General Procedure II, amino borane $V\{2,3\}$ (397 mg, 1.35 mmol) was added to a 100-mL round-bottomed flask as a solution in 45 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (6.8 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among seven test tubes that were subsequently charged with benzyl bromide (tube 1, 38 mg, 0.220 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 48 mg, 0.220 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 48 mg, 0.220 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 67 mg, 0.220 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 62 mg, 0.220 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 44 mg, 0.220 mmol, 1.2 equiv), 1-bromohexane (tube 7, 90 mg, 0.549 mmol, 3.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-benzyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide ($V\{2,3,1\}$): Data for $V\{2,3,1\}$:

Yield: 76 mg (92%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.80–7.76 (m, 2 H), 7.47–7.42 (m, 3 H), 5.17 (d, $J = 12.2$, 1 H), 4.80 (d, $J = 12.2$, 1 H), 4.49 (dd, $J = 11.3$, 11.3, 1 H), 4.40 (d, $J = 13.2$, 1 H), 3.26 (t, $J = 6.6$, 2 H), 3.18 (dd, $J = 6.6$, 11.6, 1 H), 3.13 (d, $J = 13.2$, 1 H), 2.58 (t, $J = 8.1$, 8.1, 1 H), 2.55–2.51 (m, 1 H), 2.40–2.30 (m, 1 H),

2.21–2.08 (m, 1 H), 2.11 (s, 3 H), 1.90–1.81 (m, 3 H), 1.68 (s, 3 H), 1.49–1.42 (m, 2 H), 1.32–1.19 (m, 6H), 0.86 (t, $J = 6.9$, 3 H); MS: (ESI, Q-tof) 370.3 (100); Mol. Formula: $C_{25}H_{40}BrNO$ (450.50); HRMS: $C_{25}H_{40}NO^+$: (370.3110); Calcd: 370.3110; Found: 370.3101; TLC: R_f 0.28 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-(1-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,3,2}):

Data for **V{2,3,2}**: Yield: 90 mg (98%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.37 (d, $J = 8.6$, 1 H), 8.34 (d, $J = 6.4$, 1 H), 7.93 (dd, $J = 8.2$, 14.1, 1 H), 7.67 (dd, $J = 7.7$, 7.7, 1 H), 7.55 (dd, $J = 6.4$, 14.3, 2 H), 5.51 (d, $J = 12.9$, 1 H), 5.40 (d, $J = 12.9$, 1 H), 4.58 (d, $J = 13.2$, 1 H), 4.45 (dd, $J = 11.6$, 11.6, 1 H), 3.30–3.21 (m, 1 H), 3.20–3.14 (m, 2 H), 3.02 (dd, $J = 6.8$, 11.7, 1 H), 2.70 (dd, $J = 8.1$, 8.1, 1 H), 2.64–2.58 (m, 1 H), 2.42–2.30 (m, 1 H), 2.27 (s, 3 H), 2.25–2.12 (m, 1 H), 1.93–1.79 (m, 3 H), 1.76 (s, 3 H), 1.44–1.34 (m, 2 H), 1.27–1.12 (m, 9H), 0.83 (t, $J = 6.8$, 3 H); MS: (ESI, Q-tof) 420.3 (100); Mol. Formula: $C_{29}H_{42}BrNO$ (500.55); HRMS: $C_{29}H_{42}NO^+$: (420.3266); Calcd: 420.3266; Found: 420.3265; TLC: R_f 0.30 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,3,3}): Data for V{2,3,3}: Yield: 82 mg (90%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.26 (s, 1 H), 7.96 (d, *J* = 7.3, 1 H), 7.91–7.83 (m, 3 H), 7.59–7.52 (m, 2 H), 5.29 (d, *J* = 12.3, 1 H), 5.02 (d, *J* = 12.3, 1 H), 4.55 (dd, *J* = 11.5, 11.5, 1 H), 4.52 (d, *J* = 13.3, 1 H), 3.29–3.18 (m, 3 H), 3.15 (d, *J* = 13.2, 1 H), 2.66–2.60 (m, 1 H), 2.56–2.53 (m, 1 H), 2.42–2.33 (m, 1 H), 2.21–2.12 (m, 1 H), 2.17 (s, 3 H), 1.91–1.82 (m, 3 H), 1.72 (s, 3 H), 1.48–1.40 (m, 2 H), 1.30–1.17 (m, 9H), 0.84 (t, *J* = 6.9, 3 H); MS: (ESI, Q-tof) 420.3 (100); Mol. Formula: C₂₉H₄₂BrNO (500.55); HRMS: C₂₉H₄₂NO⁺: (420.3266); Calcd: 420.3266; Found: 420.3271; TLC: *R*_f 0.31 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,3,5}): Data for V{2,3,5}: Yield: 101 mg (95%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.26 (s, 1 H), 7.96 (d, *J* = 7.3, 1 H), 7.91–7.83 (m, 3 H), 7.59–7.52 (m, 2 H), 5.29 (d, *J* = 12.3, 1 H), 5.02 (d, *J* = 12.3, 1 H), 4.55 (dd, *J* = 11.5, 11.5, 1 H), 4.52 (d, *J* = 13.3, 1 H), 3.29–3.18 (m, 3 H), 3.15 (d, *J* = 13.2, 1 H), 2.66–2.60 (m, 1 H), 2.56–2.53 (m, 1 H), 2.42–2.33 (m, 1 H), 2.21–2.12 (m, 1 H), 2.17 (s, 3 H), 1.91–1.82 (m, 3 H), 1.72 (s, 3 H), 1.48–1.40 (m, 2 H), 1.30–1.17 (m, 9H), 0.84 (t, *J* = 6.9, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 133.4, 133.3, 132.4 (q, *J* = 34), 124.2, 122.9 (q, *J* = 273), 100.4, 79.0, 72.2, 71.1, 63.5, 61.94, 61.87, 58.8, 34.9, 31.66, 30.1, 29.68, 26.0, 23.9, 23.7, 23.5, 22.6, 15.6, 14.1; MS: (ESI, Q-tof) 506.3 (100); Mol. Formula: C₂₇H₃₈BrF₆NO (586.49); HRMS: C₂₇H₃₈NOF₆⁺: (506.2858); Calcd: 506.2858; Found: 506.2859; TLC: *R*_f 0.39 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-hexyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,3,6}): Data for V{2,3,6}: Yield: 36 mg (44%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 4.31 (d, *J* = 13.1, 1 H), 3.80 (ddd, *J* = 5.7, 11.4, 11.4, 1 H), 3.73–3.61 (m, 4 H), 3.55 (ddd, *J* = 5.0, 11.7, 11.7, 1 H), 3.36 (t, *J* = 6.7, 2 H), 2.65–2.50 (m, 2 H), 2.33–2.15 (m, 2 H), 1.96–1.74 (m, 5 H), 1.88 (s, 3 H), 1.62–1.41 (m, 5 H), 1.52 (s, 3 H), 1.38–1.24 (m, 7H), 1.13 (d, *J* = 6.7, 3 H), 0.91–0.87 (m, 6H); MS: (ESI, Q-tof) 364.4 (100); Mol. Formula: C₂₄H₄₆BrNO

(444.53); HRMS: $C_{24}H_{46}NO^+$ (364.3579); Calcd: 364.3579; Found: 364.357; TLC: R_f 0.42 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (V{2,3,7}): Data for V{2,3,7}: Yield: 101 mg (99%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.55 (d, $J = 1.7$, 2 H), 7.49 (s, 1 H), 5.21 (d, $J = 12.3$, 1 H), 4.68 (d, $J = 12.3$, 1 H), 4.59 (dd, $J = 11.3$, 11.3, 1 H), 4.33 (d, $J = 13.1$, 1 H), 3.27 (t, $J = 6.7$, 2 H), 3.22 (dd, $J = 6.5$, 11.6, 1 H), 3.10 (d, $J = 13.2$, 1 H), 2.60–2.55 (m, 1 H), 2.53 (dd, $J = 8.6$, 1 H), 2.31–2.22 (m, 1 H), 2.17–2.08 (m, 1 H), 2.12 (s, 3 H), 1.90–1.80 (m, 3 H), 1.70 (s, 3 H), 1.52–1.44 (m, 2 H), 1.35 (s, 18H), 1.31–1.20 (m, 6H), 1.26 (d, $J = 6.5$, 3 H), 0.86 (t, $J = 6.9$, 3 H); MS: (ESI, Q-tof) 482.4 (100); Mol. Formula: $C_{33}H_{56}BrNO$ (562.71); HRMS: $C_{33}H_{56}NO^+$ (482.4362); Calcd: 482.4362; Found: 482.4358; TLC: R_f 0.41 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-methyl-3-(4-methoxybenzyl)-5-methyl-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (V{2,3,8}): Data for V{2,3,8}: Yield: 85 mg (98%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.70 (d, $J = 8.7$, 2 H), 6.94 (d, $J = 8.7$, 2 H), 5.09 (d, $J = 12.4$, 1 H), 4.73 (d, $J = 12.4$, 1 H), 4.44 (dd, $J = 11.4$, 11.4, 1 H), 4.36 (d, $J = 13.2$, 1 H), 3.82 (s, 3 H), 3.26 (t, $J = 6.6$, 2 H), 3.16 (dd, $J = 6.6$, 11.7, 1 H), 3.11 (d, $J = 13.2$, 1 H), 2.56 (dd, $J = 8.1$, 8.1, 1 H), 2.54–2.49 (m, 1 H), 2.38–2.29 (m, 1 H), 2.19–2.09 (m, 1 H), 2.08 (s, 3 H), 1.88–1.81 (m, 3 H), 1.66 (s, 3 H), 1.51–1.40 (m, 2 H), 1.33–1.19 (m, 9H), 0.86 (t, $J = 6.9$, 3 H); MS: (ESI, Q-tof) 400.3 (100); Mol. Formula: $C_{26}H_{42}BrNO_2$ (480.52); HRMS: $C_{26}H_{42}NO_2^+$ (400.3216); Calcd: 400.3216; Found: 400.3212; TLC: R_f 0.23 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides $V\{2,7,R^4\}$: Following General Procedure II, amino borane $V\{2,7\}$ (163 mg, 0.495 mmol) was added to a 50-mL round-bottomed flask as a solution in 17 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (2.5 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among five test tubes that were subsequently charged with benzyl bromide (tube 1, 14 mg, 0.08 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 17 mg, 0.08 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 17 mg, 0.08 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 25 mg, 0.08 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 23 mg, 0.08 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxy-benzyloxy)-1-methyl-3-benzyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide ($V\{2,7,1\}$):

Data for $V\{2,7,1\}$: Yield: 25 mg (76%) free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.79–7.76 (m, 2 H), 7.47–7.44 (m, 3 H), 7.14 (d, $J = 8.6$, 2 H), 6.84 (d, $J = 8.6$, 2 H), 5.19 (d, $J = 12.3$, 1 H), 4.79 (d, $J = 12.2$, 1 H), 4.49 (dd, $J = 11.5$, 11.5, 1 H), 4.34 (d, $J = 10.6$, 1 H), 4.31 (d, $J = 10.6$, 1 H), 3.78 (s, 3 H), 3.18 (d, $J = 13.4$, 1 H), 3.15 (dd, $J = 7.5$, 12.4, 1 H), 2.66 (dd, $J = 8.5$, 8.5, 1 H), 2.56–2.52 (m, 1 H), 2.32–2.18 (m, 2 H), 2.14 (s, 3 H), 1.98–1.91 (m, 1 H), 1.88–1.84 (m, 2 H), 1.82 (s, 3 H), 1.19 (d, $J = 6.5$, 3 H); MS: (ESI, Q-tof) 406.3 (100); Mol. Formula: $\text{C}_{27}\text{H}_{36}\text{BrNO}_2$ (486.48); HRMS: $\text{C}_{27}\text{H}_{36}\text{NO}_2^+$: (406.2746); Calcd: 406.2746; Found: 406.2749; TLC: R_f 0.21 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxy-benzyloxy)-1-methyl-3-(1-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,7,2}): Data for V{2,7,2}: Yield: 30 mg (85%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.39 (d, *J* = 8.6, 1 H), 8.32 (d, *J* = 6.5, 1 H), 7.97–7.86 (m, 2 H), 7.67 (dd, *J* = 7.1, 7.1, 2 H), 7.57–7.51 (m, 2 H), 7.08 (d, *J* = 8.7, 2 H), 6.77 (d, *J* = 8.8, 2 H), 5.54 (d, *J* = 12.9, 1 H), 5.39 (d, *J* = 12.9, 1 H), 4.56 (d, *J* = 13.3, 1 H), 4.46 (dd, *J* = 11.7, 11.7, 1 H), 4.31 (d, *J* = 10.6, 1 H), 4.23 (d, *J* = 10.6, 1 H), 3.75 (s, 3 H), 3.20 (d, *J* = 13.3, 1 H), 2.97 (dd, *J* = 6.8, 11.7, 1 H), 2.76 (dd, *J* = 8.5, 8.5, 1 H), 2.65–2.60 (m, 1 H), 2.32–2.19 (m, 2 H), 2.30 (s, 3 H), 1.98–1.84 (m, 3 H), 1.91 (s, 3 H), 1.11 (d, *J* = 6.5, 3 H); MS: (ESI, Q-tof) 456.3; Mol. Formula: C₃₁H₃₈BrNO₂ (536.54); HRMS: C₃₁H₃₈NO₂⁺: (456.2903); Calcd: 456.2903; Found: 456.2906; TLC: *R*_f 0.25 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxy-benzyloxy)-1-methyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,7,3}): Data for V{2,7,3}: Yield: 30 mg (85%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.26 (s, 1 H), 7.96 (d, *J* = 8.4, 1 H), 7.91–7.80 (m, 3 H), 7.60–7.51 (m, 2 H), 7.12 (d, *J* = 8.6, 2 H), 6.80 (d, *J* = 8.6, 2 H), 5.32 (d, *J* = 12.3, 1 H), 5.03 (d, *J* = 12.3, 1 H), 4.60–4.50 (m, 2 H), 4.33 (d, *J* = 10.6, 1 H), 4.29 (d, *J* = 10.6, 1 H), 3.74 (s, 3 H), 3.21–3.13 (m, 2 H), 2.71 (dd, *J* = 8.4, 8.4, 1 H), 2.58–2.53 (m, 1 H), 2.36–2.15 (m, 2 H), 2.19 (s, 3 H), 1.98–1.90 (m, 1 H), 1.90–1.83 (m, 2 H), 1.86 (s, 3 H), 1.20 (d, *J* = 6.5, 3 H); MS: (ESI, Q-tof) 456.3 (100); Mol. Formula: C₃₁H₃₈BrNO₂ (536.54); HRMS: (C₃₁H₃₈NO₂⁺: (456.2903); Calcd: 456.2903; Found: 456.2900; TLC: *R*_f 0.24 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-methyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,7,5}): Data for **V{2,7,5}**: Yield: 33 mg (80%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.40 (s, 2 H), 7.97 (s, 1 H), 7.13 (d, $J = 8.6$, 2 H), 6.82 (d, $J = 8.6$, 2 H), 5.37 (d, $J = 12.5$, 1 H), 5.37 (d, $J = 12.5$, 1 H), 4.37 (d, $J = 10.9$, 1 H), 4.37 (dd, $J = 7.2$, 10.9, 1 H), 4.31 (d, $J = 10.7$, 1 H), 3.77 (s, 3 H), 3.21 (d, $J = 13.1$, 1 H), 3.09 (dd, $J = 6.2$, 11.3, 1 H), 2.74 (dd, $J = 8.0$, 8.0, 1 H), 2.53–2.38 (m, 2 H), 2.30–2.21 (m, 1 H), 2.15 (s, 3 H), 1.98–1.85 (m, 3 H), 1.81 (s, 3 H), 1.15 (d, $J = 6.2$, 3 H); MS: (ESI, Q-tof) 542.3 (100); Mol. Formula: $\text{C}_{29}\text{H}_{34}\text{BrF}_6\text{NO}_2$ (622.48); HRMS: $\text{C}_{29}\text{H}_{34}\text{F}_6\text{NO}_2^+$: (542.2494); Calcd: 542.2494; Found: 542.2488; TLC: R_f 0.28 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-methyl-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{2,7,7}): Data for **V{2,7,7}**: Yield: 33 mg (82%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.57 (d, $J = 1.7$, 2 H), 7.50 (dd, $J = 1.7$, 1.7, 1 H), 7.16 (d, $J = 8.7$, 2 H), 6.85 (d, $J = 8.8$, 2 H), 5.22 (d, $J = 12.3$, 1 H), 4.71 (d, $J = 12.3$, 1 H), 4.59 (dd, $J = 11.3$, 1 H), 4.43 (d, $J = 13.2$, 1 H), 4.33 (s, 2 H), 3.79 (s, 3 H), 3.25–3.08 (m, 2 H), 2.63 (dd, $J = 8.7$, 8.7, 1 H), 2.61–2.56 (m, 1 H), 2.30–2.12 (m, 2 H), 2.16 (s, 3 H), 2.00–1.92 (m, 1 H), 1.90–1.84 (m, 2 H), 1.83 (s, 3 H), 1.35 (s, 18H), 1.23 (d, $J = 6.6$, 3 H); MS: (ESI, Q-tof) 518.4 (100); Mol. Formula: $\text{C}_{35}\text{H}_{52}\text{BrNO}$ (598.70); HRMS: $\text{C}_{35}\text{H}_{52}\text{NO}_2^+$: (518.3998); Calcd: 518.3998; Found: 518.3997; TLC: R_f 0.31 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides $\text{V}\{3,2,\text{R}^4\}$: Following General Procedure II, amino borane $\text{V}\{3,2\}$ (456 mg, 1.39 mmol) was added to a 100-mL round-bottomed flask as a solution in 50 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (7.0 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among seven test tubes that were subsequently charged with benzyl bromide (tube 1, 40 mg, 0.230 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 51 mg, 0.230 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 51 mg, 0.230 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 71 mg, 0.230 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 65 mg, 0.230 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 66 mg, 0.230 mmol, 1.2 equiv), 1-bromohexane (tube 7, 95 mg, 0.573 mmol, 3.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-3-benzyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide ($\text{V}\{3,2,1\}$): Data for $\text{V}\{3,2,1\}$: Yield: 91 mg (98%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.90–7.85 (m, 2 H), 7.45 (d, $J = 5.3$, 3 H), 7.32–7.25 (m, 3 H), 7.20–7.16 (m, 2 H), 5.35 (d, $J = 12.1$, 1 H), 4.83 (d, $J = 12.0$, 1 H), 4.77 (d, $J = 13.7$, 1 H), 4.53 (d, $J = 11.0$, 1 H), 4.18 (d, $J = 11.0$, 1 H), 3.83 (dd, $J = 9.6, 12.2$, 1 H), 3.70 (d, $J = 13.7$, 1 H), 3.19 (dd, $J = 9.9, 9.9$, 1 H), 2.77 (dd, $J = 8.0, 8.0$, 1 H), 2.53–2.33 (m, 4 H), 2.00 (s, 3 H), 1.96–1.86 (m, 2 H), 1.81–1.74 (m, 1 H), 1.23 (d, $J = 6.8$, 3 H), 1.01 (d, $J = 6.5$, 6 H); MS: (ESI, Q-tof) 404.3 (100); Mol. Formula: $\text{C}_{28}\text{H}_{38}\text{BrNO}$ (484.51); HRMS: $\text{C}_{28}\text{H}_{38}\text{NO}^+$: (404.2953); Calcd: 404.2953; Found: 404.2955; TLC: R_f 0.23 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of rel-(1S,3R,5S,5aS,7aS,7bR) Octahydro-1-benzyloxy-1-isopropyl-3-(1-naphthylmethyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{3,2,2}):

Data for **V{3,2,2}**: Yield: 95 mg (93%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.37–8.30 (m, 2 H), 7.83 (d, $J = 7.9$, 1 H), 7.79 (d, $J = 7.7$, 1 H), 7.60 (t, $J = 7.6$, 1 H), 7.49 (t, $J = 7.4$, 1 H), 7.45–7.36 (m, 1 H), 7.24–7.18 (m, 3 H), 7.11–7.06 (m, 2 H), 5.73 (d, $J = 12.8$, 1 H), 5.61 (d, $J = 12.7$, 1 H), 4.90 (d, $J = 13.6$, 1 H), 4.45 (d, $J = 10.9$, 1 H), 4.01 (d, $J = 10.9$, 1 H), 3.90 (dd, $J = 11.4$, 11.4, 1 H), 3.66 (d, $J = 13.6$, 1 H), 2.89 (dd, $J = 8.5$, 11.9, 1 H), 2.81 (dd, $J = 6.6$, 9.7, 1 H), 2.60–2.55 (m, 1 H), 2.54–2.43 (m, 2 H), 2.35–2.26 (m, 1 H), 2.19 (s, 3 H), 2.02–1.85 (m, 2 H), 1.80–1.70 (m, 1 H), 1.24 (d, $J = 6.8$, 3 H), 0.94 (d, $J = 6.8$, 3 H), 0.88 (d, $J = 6.5$, 3 H); MS: (ESI, Q-tof) 454.3 (100); Mol. Formula: $\text{C}_{32}\text{H}_{40}\text{BrNO}$ (534.57); HRMS: $\text{C}_{32}\text{H}_{40}\text{NO}^+$: (454.3110); Calcd: 454.3110; Found: 454.3105; TLC: R_f 0.25 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of rel-(1S,3R,5S,5aS,7aS,7bR) Octahydro-1-benzyloxy-1-isopropyl-3-(2-naphthylmethyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{3,2,3}):

Data for **V{3,2,3}**: Yield: 94 mg (92%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.35 (s, 1 H), 7.97–7.92 (m, 1 H), 7.90 (dd, $J = 1.7$, 8.5, 1 H), 7.81–7.77 (m, 2 H), 7.55–7.48 (m, 2 H), 7.24–7.19 (m, 3 H), 7.14–7.10 (m, 2 H), 5.49 (d, $J = 12.1$, 1 H), 5.07 (d, $J = 12.1$, 1 H), 4.82 (d, $J = 13.7$, 1 H), 4.48 (d, $J = 11.0$, 1 H), 4.10 (d, $J = 10.9$, 1 H), 3.91 (dd, $J = 9.7$, 12.1, 1 H), 3.71 (d, $J = 13.6$, 1 H), 3.18 (dd, $J = 7.1$, 12.3, 1 H), 2.78 (dd, $J = 6.9$, 9.5, 1 H), 2.54–2.33 (m, 4 H), 2.05 (s, 3 H), 1.97–1.87 (m, 2 H), 1.81–1.72 (d, $J = 4.0$, 1 H), 1.26 (d, $J = 6.8$, 3 H), 1.04 (d, $J = 6.2$, 3 H), 1.00 (d, $J = 6.8$, 3 H); MS: (ESI, Q-tof) 454.3 (100); Mol. Formula: $\text{C}_{32}\text{H}_{40}\text{BrNO}$ (534.57); HRMS: $\text{C}_{32}\text{H}_{40}\text{NO}^+$: (454.3110); Calcd: 454.3110; Found: 454.3104; TLC: R_f 0.27 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{3,2,5}): Data for V{3,2,5}: Yield: 110 mg (93%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.48 (s, 2 H), 7.96 (s, 1 H), 7.31–7.23 (m, 2 H), 7.20–7.12 (m, 2 H), 5.84 (d, *J* = 12.3, 1 H), 5.25–5.18 (m, 1 H), 4.88 (d, *J* = 13.3, 1 H), 4.56 (d, *J* = 11.2, 1 H), 4.18 (d, *J* = 11.2, 1 H), 3.61 (t, *J* = 11.9, 2 H), 3.57 (dd, *J* = 11.9, 11.9, 1 H), 3.15–3.09 (m, 1 H), 2.77 (dd, *J* = 8.3, 8.3, 1 H), 2.60–2.49 (m, 1 H), 2.49–2.32 (m, 3 H), 2.03 (s, 3 H), 1.96–1.89 (m, 2 H), 1.82–1.74 (m, 1 H), 1.25 (d, *J* = 6.7, 3 H), 1.04 (d, *J* = 6.6, 3 H), 0.99 (d, *J* = 6.8, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 136.9, 133.38, 133.36, 133.2, 132.2 (q, *J* = 33.7), 128.8, 128.2, 127.4, 123.9, 123.0 (q, *J* = 273), 99.0, 84.2, 71.6, 68.9, 65.6, 63.0, 57.5, 57.1, 35.0, 31.9, 31.8, 31.0, 23.5, 22.9, 18.7, 18.6, 18.0, 16.3; MS: (ESI, Q-tof) 540.3 (100); Mol. Formula: C₃₀H₃₆BrF₆NO (620.51); HRMS: C₃₀H₃₆F₆NO⁺: (540.2701); Calcd: 540.2701; Found: 540.2692; TLC: *R*_f 0.31 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-isopropyl-3-hexyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{3,2,6}): Data for V{3,2,6}: Yield: 66 mg (73%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.44 (d, *J* = 7.1, 2 H), 7.36 (t, *J* = 7.3, 2 H), 7.31 (t, *J* = 7.3, 1 H), 4.64 (dt, *J* = 10.8, 20.1, 2 H), 4.16 (d, *J* = 14.0, 1 H), 3.97 (ddd, *J* = 5.0, 12.0, 12.0, 1 H), 3.88 (dd, *J* = 8.4, 12.3, 1 H), 3.25–3.16 (m, 2 H), 2.60 (dd, *J* = 6.7, 9.6, 1 H), 2.57–2.56 (m, 2 H), 2.39–2.31 (m, 1 H), 2.13–2.00 (m, 2 H), 1.94–1.84 (m, 2 H), 1.77–1.66 (m, 2 H), 1.66 (s, 3 H), 1.57–1.51 (m, 1 H), 1.43–1.30 (m, 5 H), 1.11 (d, *J* = 6.7, 3 H), 0.96 (d, *J* = 6.8, 3 H), 0.89 (t, *J* = 6.9, 3 H), 0.83 (d, *J* = 6.6, 3 H); MS: (ESI, Q-tof) 398.3 (100); Mol. Formula: C₂₇H₄₄BrNO (478.55); HRMS: C₂₇H₄₄NO⁺: (398.3423); Calcd: 398.3423; Found: 398.3417; TLC: *R*_f 0.39 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyl-1-isopropyl-3-(3,5-tert-butylbenzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{3,2,7}):

Data for **V{3,2,7}**: Yield: 115 mg (99%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.67 (d, $J = 1.7$, 2 H), 7.51 (s, 1 H), 7.32–7.24 (m, 3 H), 7.21–7.17 (m, 2 H), 5.41 (d, $J = 12.2$, 1 H), 4.92 (d, $J = 13.7$, 1 H), 4.59 (d, $J = 12.2$, 1 H), 4.54 (d, $J = 11.1$, 1 H), 4.24 (d, $J = 11.1$, 1 H), 3.78 (dd, $J = 8.2$, 12.4, 1 H), 3.68 (d, $J = 13.7$, 1 H), 3.37 (dd, $J = 8.1$, 12.6, 1 H), 2.79 (dd, $J = 8.2$, 8.2, 1 H), 2.47–2.31 (m, 4 H), 2.04 (s, 3 H), 2.00–1.88 (m, 2 H), 1.87–1.79 (m, 1 H), 1.37 (s, 18H), 1.22 (d, $J = 6.8$, 3 H), 1.07 (t, $J = 6.7$, 6 H); MS: (ESI, Q-tof) 516.4 (100); Mol. Formula: $\text{C}_{36}\text{H}_{54}\text{BrNO}$ (596.72); HRMS: $\text{C}_{36}\text{H}_{54}\text{NO}^+$: (516.4205); Calcd: 516.4205; Found: 516.4190; TLC: R_f 0.35 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyl-1-isopropyl-3-(4-methoxybenzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{3,2,8}):

Data for **V{3,2,8}**: Yield: 93 mg (94%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.80 (d, $J = 8.7$, 2 H), 7.34–7.25 (m, 3 H), 7.21–7.17 (m, 2 H), 6.96 (d, $J = 8.6$, 2 H), 5.27 (d, $J = 12.3$, 1 H), 4.72 (d, $J = 13.6$, 2 H), 4.53 (d, $J = 10.9$, 1 H), 4.19 (d, $J = 10.9$, 1 H), 3.84 (s, 3 H), 3.80 (dd, $J = 9.5$, 12.3, 1 H), 3.69 (d, $J = 13.7$, 1 H), 3.22 (dd, $J = 7.9$, 12.1, 1 H), 2.76 (dd, $J = 7.0$, 9.2, 1 H), 2.53–2.41 (m, 2 H), 2.41–2.34 (m, 2 H), 1.98 (s, 3 H), 1.95–1.87 (m, 2 H), 1.82–1.73 (m, 1 H), 1.23 (d, $J = 6.8$, 3 H), 1.02 (d, $J = 6.9$, 3 H), 1.01 (d, $J = 6.7$, 3 H); MS: (ESI, Q-tof) 434.3 (100); Mol. Formula: $\text{C}_{29}\text{H}_{40}\text{BrNO}_2$ (514.54); HRMS: $\text{C}_{29}\text{H}_{40}\text{NO}_2^+$: (434.3059); Calcd: 434.3059; Found: 434.3055; TLC: R_f 0.20 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides V{3,3, R^4 }: Following General Procedure II, amino borane **V{3,3}** (245 mg, 0.762 mmol) was added to a 100-mL round-bottomed flask as a solution in 23 mL of MeOH (0.03 M). The flask was fitted with a reflux

condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (3.5 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among seven test tubes that were subsequently charged with benzyl bromide (tube 1, 20 mg, 0.115 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 25 mg, 0.115 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 25 mg, 0.115 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 35 mg, 0.115 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 32 mg, 0.115 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 23 mg, 0.115 mmol, 1.2 equiv), 1-bromohexane (tube 7, 48 mg, 0.288 mmol, 3.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of rel-(1S,3R,5S,5aS,7aS,7bR) Octahydro-1-hexyloxy-1-isopropyl-3-benzyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{3,3,1}): Data for **V{3,3,1}**:

Yield: 46 mg (99%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.90–7.82 (m, 2 H), 7.47–7.41 (m, 3 H), 5.17 (d, *J* = 12.1, 1 H), 5.00–4.94 (m, 1 H), 4.54 (d, *J* = 13.6, 1 H), 4.00 (dd, *J* = 11.1, 11.1, 1 H), m, 2 H), 2.56–2.46 (m, 1 H), 2.44–2.34 (m, 1 H), 2.24–2.16 (m, 1 H), 2.00–1.91 (m, 2 H), 1.96 (s, 3 H), 1.77–1.67 (m, 1 H), 1.64–1.56 (m, 3 H), 1.48–1.40 (m, 2 H), 1.34–1.17 (m, 3 H), 1.20 (d, *J* = 6.6, 3 H), 1.14 (d, *J* = 6.8, 3 H), 0.90 (d, *J* = 6.8, 3 H), 0.85 (dd, *J* = 6.0, 7.0, 3 H); MS: (ESI, Q-tof) 398 (100); Mol. Formula: C₂₇H₄₄BrNO (478.55); HRMS: C₂₇H₄₄NO⁺: (398.3423); Calcd: 398.3423; Found: 398.3416; TLC: *R_f* 0.25 (CH₂Cl₂/MeOH, 9:1) [I₂].

V{3,3,2}

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-isopropyl-3-(1-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,3,2}):

Data for V{3,3,2}: Yield: 50 mg (99%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.37 (d, *J* = 7.2, 1 H), 8.27 (d, *J* = 8.5, 1 H), 7.87 (t, *J* = 8.5, 2 H), 7.62 (t, *J* = 7.7, 1 H), 7.54–7.44 (m, 2 H), 5.67 (d, *J* = 12.9, 1 H), 5.63 (d, *J* = 12.9, 1 H), 4.72 (d, *J* = 13.6, 1 H), 4.09 (dd, *J* = 11.5, 11.5, 1 H), 3.50 (d, *J* = 13.5, 1 H), 3.26 (dd, *J* = 6.9, 15.4, 1 H), 3.02 (dd, *J* = 8.1, 12.0, 1 H), 2.94 (dd, *J* = 6.1, 14.9, 1 H), 2.74 (dd, *J* = 6.5, 9.7, 1 H), 2.72–2.60 (m, 2 H), 2.45 (m, 2 H), 2.48–2.39 (m, 1 H), 2.18–2.08 (m, 1 H), 2.15 (s, 3 H), 2.00–1.94 (m, 2 H), 1.75–1.65 (m, 1 H), 1.44–1.30 (m, 2 H), 1.27–1.14 (m, 6H), 1.16 (d, *J* = 6.7, 3 H), 1.10 (d, *J* = 6.4, 3 H), 0.84 (d, *J* = 6.8, 3 H), 0.81 (t, *J* = 6.9, 3 H); MS: (ESI, Q-tof) 448.3 (100); Mol. Formula: C₃₁H₄₆BrNO (528.61); HRMS: C₃₁H₄₆NO⁺: (448.3579); Calcd: 448.3579; Found: 448.3573; TLC: *R_f* 0.28 (CH₂Cl₂/MeOH, 9:1) [I₂].

V{3,3,3}

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-isopropyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,3,3}):

Data for V{3,3,3}: Yield: 46 mg (91%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.34 (s, 1 H), 7.95–7.92 (m, 1 H), 7.90 (dd, *J* = 1.7, 8.5, 1 H), 7.80–7.75 (m, 2 H), 7.55–7.48 (m, 2 H), 5.36 (d, *J* = 12.1, 1 H), 5.20 (d, *J* = 12.0, 1 H), 4.62 (d, *J* = 13.5, 1 H), 4.11–4.06 (dd, *J* = 10.8, 10.8, 1 H), 3.55 (d, *J* = 13.5, 1 H), 3.30 (dd, *J* = 6.9, 15.4, 1 H),

3.20 (dd, $J = 8.0, 12.0$, 1 H), 3.00 (dd, $J = 6.3, 14.8$, 1 H), 2.72–2.61 (m, 1 H), 2.70 (dd, $J = 7.0, 9.7$, 1 H), 2.60–2.56 (m, 1 H), 2.44–2.33 (m, 1 H), 2.25–2.15 (m, 1 H), 2.02 (s, 3 H), 1.97–1.91 (m, 2 H), 1.76–1.66 (m, 1 H), 1.44–1.32 (m, 2 H), 1.27–1.14 (m, 6H), 1.22 (d, $J = 6.7$, 3 H), 1.18 (d, $J = 6.7$, 3 H), 0.89 (d, $J = 6.8$, 3 H), 0.81 (t, $J = 7.0$, 3 H); MS: (ESI, Q-tof) 448.4 (100); Mol. Formula: $C_{31}H_{46}BrNO$ (528.61); HRMS: $C_{31}H_{46}NO^+$: (448.3579); Calcd: 448.3579; Found: 448.3577; TLC: R_f 0.29 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-isopropyl-3-(3,5-trifluoromethyl-benzyl)-5-methyl-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (V{3,3,5}): Data for V{3,3,5}: Yield: 59 mg (99%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 8.49 (s, 2 H), 7.94 (s, 1 H), 5.70 (d, $J = 12.2$, 1 H), 5.37 (d, $J = 12.3$, 1 H), 4.70 (d, $J = 13.2$, 1 H), 3.83 (dd, $J = 11.0, 11.0$, 1 H), 3.44 (d, $J = 13.1$, 1 H), 3.36 (dd, $J = 6.9, 15.3$, 1 H), 3.26 (dd, $J = 7.9, 11.9$, 1 H), 3.08 (dd, $J = 6.3, 14.7$, 1 H), 2.75–2.66 (m, 2 H), 2.58–2.53 (m, 1 H), 2.45–2.34 (m, 1 H), 2.23–2.16 (m, 1 H), 2.01 (s, 3 H), 1.98–1.92 (m, 2 H), 1.76–1.68 (m, 1 H), 1.51–1.38 (m, 2 H), 1.36–1.18 (m, 6 H), 1.21 (s, 3 H, $J = 6.1$), 1.16 (d, $J = 6.8$, 3 H), 0.88 (d, $J = 6.8$, 3 H), 0.85 (t, $J = 6.9$, 3 H); MS: (ESI, Q-tof) 534.3 (100); Mol. Formula: $C_{29}H_{42}BrF_6NO$ (614.54); HRMS: $C_{29}H_{42}F_6NO^+$: (534.3171); Calcd: 534.3171; Found: 534.3167; TLC: R_f 0.32 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*S*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-isopropyl-3-hexyl-5-methyl-7*b*-methyl-cyclopenta[*gh*]pyrrolizinium Bromide (V{3,3,6}): Data for V{3,3,6}: Yield: 43 mg (98%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 4.25 (d, $J = 13.8$, 1 H), 4.07 (d, $J = 13.8$, 1 H), 4.00–3.82 (m, 2 H), 3.56–3.33 (m, 6H), 2.81–2.70 (m, 1 H), 2.55 (dd, $J = 6.6, 9.6$, 1 H), 2.49–2.40 (m, 1 H), 2.21–2.12 (m, 3 H), 2.04–1.84 (m, 4 H), 1.81–1.64 (m, 2 H), 1.69 (s, 3 H), 1.64–1.48 (m, 4 H), 1.48–1.20 (m, 6H), 1.09 (d, $J = 6.7$, 3 H), 1.05 (d, $J = 6.7$, 3 H), 0.91–0.87 (m, 6H), 0.85 (d, $J = 6.8$, 3 H); MS: (ESI, Q-tof) 392.4 (100); Mol. Formula: $C_{26}H_{50}BrNO$ (472.58); HRMS: $C_{26}H_{50}NO^+$: (392.3892); Calcd: 392.3892; Found: 392.3882; TLC: R_f 0.40 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-isopropyl-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,3,7}): Data for V{3,3,7}: Yield: 56 mg (99%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.65 (d, *J* = 1.5, 2 H), 7.49 (s, 1 H), 5.25 (d, *J* = 12.2, 1 H), 4.71 (t, *J* = 12.8, 2 H), 3.96 (dd, *J* = 8.8, 12.3, 1 H), 3.54 (d, *J* = 13.6, 1 H), 3.42 (dd, *J* = 8.1, 12.3, 1 H), 3.39–3.33 (m, 1 H), 3.15 (dd, *J* = 6.0, 14.5, 1 H), 2.70 (dd, *J* = 7.0, 9.0, 1 H), 2.60–2.50 (m, 1 H), 2.47–2.40 (m, 1 H), 2.40–2.32 (m, 1 H), 2.29–2.20 (m, 1 H), 2.01 (s, 3 H), 1.99–1.92 (m, 2 H), 1.81–1.73 (m, 1 H), 1.49–1.42 (m, 2 H), 1.38–1.20 (m, 6H), 1.36 (s, 18H), 1.22 (d, *J* = 6.8, 3 H), 1.14 (d, *J* = 6.8, 3 H), 0.97 (d, *J* = 6.8, 3 H), 0.85 (t, *J* = 6.8, 3 H); MS: (ESI, Q-tof) 510.5 (100); Mol. Formula: C₃₅H₆₀BrNO (590.76); HRMS: C₃₅H₆₀NO⁺: (510.4675); Calcd: 510.4675; Found: 510.4674; TLC: *R*_f 0.35 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-isopropyl-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,3,8}): Data for V{3,3,8}: Yield: 48 mg (98%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.78 (d, *J* = 8.7, 2 H), 6.93 (d, *J* = 8.6, 2 H), 5.10 (d, *J* = 12.0, 1 H), 4.92–4.86 (m, 1 H), 4.48 (d, *J* = 13.6, 1 H), 3.95 (dd, *J* = 10.4, 10.4, 1 H), 3.82 (s, 3 H), 3.52 (d, *J* = 13.6, 1 H), 3.34 (dd, *J* = 6.8, 15.3, 1 H), 3.26–3.20 (m, 1 H), 3.09 (dd, *J* = 6.2, 14.7, 1 H), 2.72–2.57 (m, 2 H), 2.51–2.46 (m, 1 H), 2.45–2.33 (m, 1 H), 2.24–2.13 (m, 1 H), 1.97–1.91 (m, 2 H), 1.95 (s, 3 H), 1.75–1.67 (m, 1 H), 1.48–1.41 (m, 2 H), 1.33–1.18 (m, 6H), 1.19 (d, *J* = 6.0, 3 H), 1.14 (d, *J* = 6.8, 3 H), 0.90 (d, *J* = 6.8, 3 H), 0.85 (t, *J* = 6.9, 3 H); MS: (ESI, Q-tof) 428.4 (100); Mol. Formula: C₂₈H₄₆BrNO₂ (508.57); HRMS: C₂₈H₄₆NO₂⁺: (428.3529); Calcd: 428.3529; Found: 428.3529; TLC: *R*_f 0.21 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of Quaternary Ammonium Bromides V{3,7,R⁴}: Following General Procedure II, amino borane V{3,7} (502 mg, 1.40 mmol) was added to a 100-mL round-bottomed flask as a solution in 50 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (7.0 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 20 mg, 0.116 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 26 mg, 0.116 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 26 mg, 0.116 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 35 mg, 0.116 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 33 mg, 0.116 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 23 mg, 0.116 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxy-benzyloxy)-1-isopropyl-3-benzyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,7,1}): Data for V{3,7,1}: Yield: 38 mg (75%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.90–7.82 (m, 2 H), 7.49–7.42 (m, 3 H), 7.08 (d, *J* = 8.6, 2 H), 6.80 (d, *J* = 8.6, 2 H), 5.31 (d, *J* = 12.1, 1 H), 4.83 (d, *J* = 12.1, 1 H), 4.72 (d, *J* = 13.7, 1 H), 4.45 (d, *J* = 10.6, 1 H), 4.11 (d, *J* = 10.6, 1 H), 3.83 (dd, *J* = 9.62, 12.0, 1 H), 3.77 (s, 3 H), 3.69 (d, *J* = 13.6, 1 H), 3.19 (dd, *J* = 7.9, 12.2, 1 H), 2.74 (dd, *J* = 6.86, 9.45, 1 H), 2.54–2.30 (m, 4 H), 1.98 (s, 3 H), 1.96–1.84 (m, 2 H), 1.79–1.70 (m, 1 H), 1.22 (d, *J* = 6.8, 3 H), 1.01 (t, *J* = 7.1, 6 H); MS: (ESI, Q-tof) 434.3 (100); Mol. Formula: C₂₉H₄₀BrNO₂ (514.54); HRMS: C₂₉H₄₀NO₂⁺: (434.3059); Calcd: 434.3059; Found: 434.3058; TLC: *R*_f 0.22 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxy-benzyloxy)-1-isopropyl-3-(1-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,7,2}): Data for V{3,7,2}: Yield: 42 mg (77%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.38 (d, *J* = 7.2, 1 H), 8.26 (d, *J* = 8.6, 1 H), 7.88 (t, *J* = 7.34, 2 H), 7.62 (t, *J* = 7.2, 1 H), 7.56–7.46 (m, 2 H), 7.00 (d, *J* = 8.6, 2 H), 6.74 (d, *J* = 8.6, 2 H), 5.73 (d, *J* = 12.8, 1 H), 5.58 (d, *J* = 12.8, 1 H), 4.87 (d, *J* = 13.7, 1 H), 4.38 (d, *J* = 10.6, 1 H), 3.96 (d, *J* = 10.9, 1 H), 3.96–3.92 (m, 1 H), 3.73 (s, 3 H), 3.67 (d, *J* = 13.6, 1 H), 2.93 (dd, *J* = 7.5, 12.2, 1 H), 2.80 (dd, *J* = 6.5, 9.8, 1 H), 2.57–2.40 (m, 3 H), 2.35–2.26 (m, 1 H), 2.16 (s, 3 H), 2.00–1.87 (m, 2 H), 1.79–1.68 (m, 1 H), 1.23 (d, *J* = 6.8, 3 H), 0.94 (d, *J* = 6.8, 3 H), 0.90 (d, *J* = 6.0, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 159.4, 133.9, 133.4, 132.8, 130.8, 129.3, 129.0, 128.9, 127.5, 126.0, 125.50, 125.48, 124.2, 114.1, 95.5, 83.9, 72.4, 69.1, 64.7, 61.7, 57.3, 57.1, 55.4, 34.7, 31.1, 31.0, 23.8, 23.1, 18.9, 18.0, 16.6; MS: (ESI, Q-tof) 484.3 (100); Mol. Formula: C₃₃H₄₂BrNO₂ (564.60); HRMS: C₃₃H₄₂NO₂⁺: (484.3216); Calcd: 484.3216; Found: 484.3215; TLC: *R*_f 0.25 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-isopropyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,7,3}): Data for V{3,7,3}: Yield: 38 mg (69%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.35 (s, 1 H), 7.96 (d, *J* = 8.3, 1 H), 7.91 (dd, *J* = 1.7, 8.3, 1 H), 7.85–7.81 (m, 2 H), 7.56–7.45 (m, 2 H), 7.03 (d, *J* = 8.6, 2 H), 6.73 (d, *J* = 8.7, 2 H), 5.47 (d, *J* = 12.1, 1 H), 5.07 (d, *J* = 12.2, 1 H), 4.79 (d, *J* = 13.7, 1 H), 4.41 (d, *J* = 10.6, 1 H), 4.04 (d, *J* = 10.6, 1 H), 3.90 (dd, *J* = 9.2, 12.1, 1 H), 3.71 (s, 3 H), 3.16 (dd, *J* = 7.1, 12.6, 1 H), 2.76 (dd, *J* = 6.9, 9.4, 1 H), 2.52–2.33 (m, 5 H), 2.04 (s, 3 H), 1.96–1.85 (m, 2 H), 1.78–1.69 (m, 1 H), 1.25 (d, *J* = 6.8, 3 H), 1.05 (d, *J* = 6.1, 3 H), 0.99 (d, *J* = 6.8, 3 H); MS: (ESI, Q-tof) 484.3 (100); Mol. Formula: C₃₃H₄₂BrNO₂ (564.60); HRMS: C₃₃H₄₂NO₂⁺: (484.3216); Calcd: 484.3216; Found: 484.3221; TLC: *R*_f 0.26 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxy-benzyloxy)-1-isopropyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,7,5}**):** Data for **V{3,7,5}**: Yield: 52 mg (82%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.48 (s, 2 H), 7.96 (s, 1 H), 7.07 (d, $J = 8.6$, 2 H), 6.79 (d, $J = 8.6$, 2 H), 5.81 (d, $J = 12.4$, 1 H), 5.27–5.20 (m, 1 H), 4.84 (d, $J = 13.2$, 1 H), 4.48 (d, $J = 10.8$, 1 H), 4.12 (d, $J = 10.8$, 1 H), 3.76 (s, 3 H), 3.62 (dd, $J = 9.5$, 11.9, 1 H), 3.57 (d, $J = 13.4$, 1 H), 3.14 (dd, $J = 7.51$, 11.0, 1 H), 2.75 (dd, $J = 8.3$, 8.3, 1 H), 2.60–2.48 (m, 1 H), 2.48–2.31 (m, 3 H), 2.02 (s, 3 H), 1.95–1.87 (m, 2 H), 1.80–1.71 (m, 1 H), 1.23 (d, $J = 6.7$, 3 H), 1.05 (d, $J = 6.7$, 3 H), 0.99 (d, $J = 6.8$, 3 H); MS: (ESI, Q-tof) 570.3 (100); Mol. Formula: $\text{C}_{31}\text{H}_{38}\text{BrF}_6\text{NO}_2$ (650.53); HRMS: $\text{C}_{31}\text{H}_{38}\text{F}_6\text{NO}_2^+$ (570.2807); Calcd: 570.2807; Found: 570.2805; TLC: R_f 0.31 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxy-benzyloxy)-1-isopropyl-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,7,7}**):** Data for **V{3,7,7}**: Yield: 47 mg (78%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.67 (d, $J = 1.7$, 2 H), 7.51 (s, 1 H), 7.11 (d, $J = 8.6$, 2 H), 6.82 (d, $J = 8.7$, 2 H), 5.37 (d, $J = 12.2$, 1 H), 4.87 (d, $J = 13.7$, 1 H), 4.61 (d, $J = 12.2$, 1 H), 4.46 (d, $J = 10.6$, 1 H), 4.17 (d, $J = 10.6$, 1 H), 3.80 (dd, $J = 8.21$, 12.5, 1 H), 3.78 (s, 3 H), 3.68 (d, $J = 13.7$, 1 H), 3.40 (dd, $J = 8.0$, 12.5, 1 H), 2.77 (dd, $J = 7.54$, 8.9, 1 H), 2.45–2.31 (m, 4 H), 2.03 (s, 3 H), 1.99–1.86 (m, 2 H), 1.85–1.76 (m, 1 H), 1.37 (s, 18H), 1.21 (d, $J = 6.8$, 3 H), 1.07 (d, $J = 6.8$, 6 H); MS: (ESI, Q-tof) 546.4 (100); Mol. Formula: $\text{C}_{37}\text{H}_{56}\text{BrNO}_2$ (626.75); HRMS: $\text{C}_{37}\text{H}_{56}\text{NO}_2^+$ (546.4311); Calcd: 546.4311; Found: 546.4317; TLC: R_f 0.33 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*S*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-isopropyl-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{3,7,8}): Data for V{3,7,8}: Yield: 35 mg (66%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.79 (d, $J = 8.7$, 2 H), 7.10 (d, $J = 8.6$, 2 H), 6.95 (d, $J = 8.6$, 2 H), 6.81 (d, $J = 8.7$, 2 H), 5.23 (d, $J = 12.2$, 1 H), 4.75 (d, $J = 12.4$, 1 H), 4.66 (d, $J = 13.7$, 1 H), 4.45 (d, $J = 10.6$, 1 H), 4.12 (d, $J = 10.6$, 1 H), 3.84 (s, 3 H), 3.83–3.73 (m, 1 H), 3.77 (s, 3 H), 3.67 (d, $J = 13.7$, 1 H), 3.20 (dd, $J = 8.1$, 12.2, 1 H), 2.73 (dd, $J = 6.8$, 9.5, 1 H), 2.52–2.28 (m, 4 H), 1.96 (s, 3 H), 1.94–1.85 (m, 2 H), 1.75 (s, 1 H), 1.21 (d, $J = 6.7$, 3 H), 1.04–0.99 (m, 6H); MS: (ESI, Q-tof) 464.3 (100); Mol. Formula: $\text{C}_{30}\text{H}_{42}\text{BrNO}_3$ (544.56); HRMS: $\text{C}_{30}\text{H}_{42}\text{NO}_3^+$: (464.3165); Calcd: 464.3165; Found: 464.3170; TLC: R_f 0.19 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides V{4,2,R⁴}: Following General Procedure II, amino borane V{4,2} (102 mg, 0.300 mmol) was added to a 25-mL round-bottomed flask as a solution in 0 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (1.5, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among one test tube that were subsequently charged with 3,5-bis(trifluoromethyl)benzyl bromide (tube 1, 281 mg, 0.915 mmol, 5.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-*tert*-butyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{4,2,5}): Data for V{4,2,5}: Yield: 108 mg (93%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.53 (s, 2 H), 7.97 (s, 1 H), 7.31 (m, 3 H), 7.22-7.19 (m, 2 H), 5.71 (d, $J = 12.3$, 1 H), 5.60 (d, $J = 12.3$, 1 H), 4.80 (d, $J = 10.8$, 1 H), 4.67 (d, $J = 13.8$, 1 H), 4.24 (d, $J = 10.8$, 1 H), 3.84 (dd, $J = 11.2$, 1 H), 3.74 (d, $J = 13.7$, 1 H), 3.12 (dd, 1 H, $J = 7.9$, 11.9, 1 H), 2.97 (dd, $J = 6.8$, 9.5, 1 H), 2.54-2.47 (m, 2 H), 2.36-2.26 (m, 1 H), 2.00 (s, 3 H), 1.92-1.83 (m, 2 H), 1.79-1.72 (m, 1 H), 1.17 (s, 9 H), 0.88 (d, $J = 6.7$, 3 H); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 136.8, 133.4, 133.2, 132.3 (q, $J = 33.7$), 128.8, 128.3, 127.3, 124.0, 122.9 (q, $J = 273$), 98.8, 85.8, 72.0, 68.8, 67.5, 63.6, 58.4, 57.2, 39.4, 34.8, 30.8, 28.0, 23.5, 23.1, 15.7; MS: (ESI, Q-tof) 554.2 (100); Mol. Formula: $\text{C}_{31}\text{H}_{38}\text{BrF}_6\text{NO}$ (634.53); HRMS: $\text{C}_{31}\text{H}_{38}\text{F}_6\text{NO}^+$: 554.2858; Calcd: 554.2858; Found: 554.2866; TLC: R_f 0.30 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides V{5,2,R⁴}: Following General Procedure II, amino borane V{5,2} (597 mg, 1.65 mmol) was added to a 100-mL round-bottomed flask as a solution in 50 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (7.5, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among eight test tubes that were subsequently charged with benzyl bromide (tube 1, 44 mg, 0.259 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 58 mg, 0.259 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 58 mg, 0.259 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 80 mg, 0.259 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 80 mg, 0.259 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 52 mg, 0.259 mmol, 1.2 equiv), 4-trifluoromethylbenzyl bromide (tube 7, 20 mg, 0.085 mmol, 1.2 equiv), 4-cyanobenzyl bromide (tube 8, 17 mg, 0.085 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-benzyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{5,2,1}): Data for V{5,2,1}: Yield: 107 mg (95%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.77 (d, *J* = 8.2, 2 H), 7.67 (t, *J* = 7.5, 2 H), 7.57 (t, *J* = 7.3, 2 H), 7.42 (d, *J* = 7.8, 2 H), 7.40–7.31 (m, 3 H), 7.31–7.24 (m, 2 H), 7.12 (d, *J* = 6.8, 2 H), 5.25 (d, *J* = 12.0, 1 H), 5.03 (dd, *J* = 11.9, 11.9, 1 H), 4.30 (d, *J* = 13.1, 1 H), 3.99 (d, *J* = 10.6, 1 H), 3.82 (d, *J* = 10.7, 1 H), 3.53 (d, *J* = 13.0, 1 H), 3.45 (dd, *J* = 9.3, 9.3, 1 H), 3.36 (d, *J* = 12.1, 1 H), 2.98 (dd, *J* = 6.0, 11.4, 1 H), 2.85 (dd, *J* = 5.72, 9.75, 1 H), 2.49–2.39 (m, 1 H), 2.29 (s, 3 H), 2.27–2.15 (m, 2 H), 1.98–1.91 (m, 2 H), 1.30 (d, *J* = 6.3, 3 H); MS: (ESI, Q-tof) 438.3 (100); Mol. Formula: C₃₁H₃₆BrNO (518.53); HRMS: C₃₁H₃₆NO⁺: (438.2797); Calcd: 438.2797; Found: 438.2784; TLC: *R_f* 0.21 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(1-naphthylmethyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{5,2,2}): Data for V{5,2,2}: Yield: 113 mg (92%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.91 (dd, *J* = 8.4, 14.2, 2 H), 7.85 (t, *J* = 8.3, 2 H), 7.74 (d, *J* = 7.7, 2 H), 7.67 (t, *J* = 7.7, 2 H), 7.58 (d, *J* = 7.4, 1 H), 7.57–7.53 (m, 2 H), 7.51 (d, *J* = 7.2, 1 H), 7.47 (dd, *J* = 5.7, 13.6, 2 H), 7.32–7.23 (m, 1 H), 7.10 (dd, *J* = 2.0, 7.4, 2 H), 5.55 (d, *J* = 12.8, 1 H), 4.74 (d, *J* = 11.9, 1 H), 4.69 (d, *J* = 13.9, 1 H), 4.53 (d, *J* = 12.8, 1 H), 3.98 (d, *J* = 11.0, 1 H), 3.91 (d, *J* = 11.0, 1 H), 3.62 (d, *J* = 13.3, 1 H), 3.39 (dd, *J* = 9.1, 9.1, 1 H), 3.04 (d, *J* = 10.4, 1 H),

2.90 (dd, $J = 6.4, 11.5$, 1 H), 2.55 (dd, $J = 11.2, 21.0$, 1 H), 2.46 (s, 3 H), 2.37–2.27 (m, 1 H), 2.16 (d, $J = 9.0$, 1 H), 2.02–1.95 (m, 2 H), 1.22 (d, $J = 6.4$, 3 H); MS: (ESI, Q-tof) 488.3 (100); Mol. Formula: $C_{35}H_{38}BrNO$ (568.59); HRMS: $C_{35}H_{38}NO^+$: (488.2953); Calcd: 488.2953; Found: 488.2956; TLC: R_f 0.24 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,2,3}):

Data for **V{5,2,3}**: Yield: 110 mg (90%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.86–7.79 (m, 5 H), 7.75 (t, $J = 7.7$, 2 H), 7.68–7.60 (m, 3 H), 7.57–7.50 (m, 2 H), 7.31–7.25 (m, 3 H), 7.12 (dd, $J = 1.9, 7.5$, 2 H), 5.48 (d, $J = 12.1$, 1 H), 5.18 (dd, $J = 11.9, 11.9$, 1 H), 4.35 (d, $J = 13.0$, 1 H), 4.00 (d, $J = 10.7$, 1 H), 3.84 (d, $J = 10.7$, 1 H), 3.53 (dd, $J = 12.4, 12.4$, 2 H), 3.47 (dd, $J = 9.2, 9.2$, 1 H), 3.06 (dd, $J = 6.0, 11.3$, 1 H), 2.89 (dt, $J = 2.75, 5.63$, 10.2, 1 H), 2.51–2.40 (m, 1 H), 2.35 (s, 3 H), 2.29–2.15 (m, 2 H), 1.99–1.93 (m, 2 H), 1.32 (d, $J = 6.4$, 3 H); MS: (ESI, Q-tof) 488.3 (100); Mol. Formula: $C_{35}H_{38}BrNO$ (568.59); HRMS: $C_{35}H_{38}NO^+$: (488.2953); Calcd: 488.2953; Found: 488.2943; TLC: R_f 0.25 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,2,5}):

Data for **V{5,2,5}**: Yield: 1 mg (85%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.93 (s, 2 H), 7.91 (s, 1 H), 7.76 (d, $J = 7.42$, 2 H), 7.72 (t, $J = 7.7$, 2 H), 7.63 (t, $J = 7.2$, 1 H), 7.33–7.27 (m, 3 H), 7.13 (dd, $J = 2.1, 7.3$, 2 H), 5.96 (d, $J = 12.3$, 1 H), 5.34 (dd, $J = 11.7, 11.7$, 1 H), 4.01 (d, $J = 10.6$, 1 H), 3.98 (d, $J = 13.1$, 1 H), 3.84 (d, $J = 10.6$, 1 H), 3.58 (d, $J = 13.2$, 1 H), 3.49 (dd, $J = 9.4, 9.4$, 1 H), 3.39 (d, $J = 12.4$, 1 H), 3.00 (dd, $J = 6.1, 11.0$, 1 H), 2.82 (dd, $J = 5.8, 10.2$, 1 H), 2.51–2.40 (m, 1 H), 2.35 (s, 3 H), 2.31–2.18 (m, 2 H), 2.04–1.92 (m, 2 H), 1.32 (d, $J = 6.3$, 3 H); ^{13}C -NMR: (126 MHz, $CDCl_3$) 139.0, 136.6, 133.2, 132.5 (q, $J = 34$); 132.0, 130.7, 130.3, 128.6, 128.2, 127.7, 127.4, 124.3, 125.8 (q, $J = 273$), 100.8, 83.4, 68.8, 67.7, 67.1, 60.8, 59.5, 53.1, 34.2, 28.0, 27.3, 24.2, 14.8; MS: (ESI, Q-tof) 574.3 (100); Mol. Formula: $C_{33}H_{34}BrF_6NO$ (654.52); HRMS: $C_{33}H_{34}NOF_6^+$: (574.2545); Calcd: 574.2545; Found: 574.2541; TLC: R_f 0.28 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,2,7}): Data for V{5,2,7}: Yield: 113 mg (83%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.78 (d, $J = 7.4$, 2 H), 7.68 (t, $J = 7.7$, 2 H), 7.58 (t, $J = 7.4$, 1 H), 7.40 (s, 1 H), 7.33–7.28 (m, 5 H), 7.18–7.13 (m, 2 H), 5.17 (d, $J = 11.8$, 1 H), 5.10 (dd, $J = 11.9$, 11.9, 1 H), 4.35 (d, $J = 13.1$, 1 H), 4.01 (d, $J = 10.6$, 1 H), 3.80 (d, $J = 10.6$, 1 H), 3.54 (d, $J = 13.1$, 1 H), 3.49 (dd, $J = 9.4$, 9.4, 1 H), 3.25 (d, $J = 12.0$, 1 H), 2.92 (dd, $J = 5.9$, 11.4, 1 H), 2.90–2.85 (m, 1 H), 2.49–2.39 (m, 1 H), 2.30 (s, 3 H), 2.25–2.15 (m, 2 H), 1.98–1.92 (m, 2 H), 1.31 (s, 18H), 1.30 (d, $J = 6.5$, 3 H); MS: (ESI, Q-tof) 550.4 (100); Mol. Formula: $\text{C}_{39}\text{H}_{52}\text{BrNO}$ (630.74); HRMS: $\text{C}_{39}\text{H}_{52}\text{NO}^+$: (550.4049); Calcd: 550.4049; Found: 550.4048; TLC: R_f 0.31 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,2,8}): Data for V{5,2,8}: Yield: 105 mg (89%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.76 (d, $J = 7.5$, 2 H), 7.67 (t, $J = 7.7$, 2 H), 7.57 (t, $J = 7.4$, 1 H), 7.36 (d, $J = 8.7$, 2 H), 7.32–7.23 (m, 3 H), 7.16–7.10 (m, 2 H), 6.84 (d, $J = 8.7$, 2 H), 5.17 (d, $J = 12.1$, 1 H), 4.98 (t, $J = 11.9$, 1 H), 4.28 (d, $J = 13.0$, 1 H), 3.99 (d, $J = 10.7$, 1 H), 3.82 (d, $J = 10.6$, 1 H), 3.78 (s, 3 H), 3.52 (d, $J = 13.1$, 1 H), 3.44 (dd, $J = 9.3$, 9.3, 1 H), 3.31 (d, $J = 12.2$, 1 H), 2.96 (dd, $J = 6.0$, 11.4, 1 H), 2.84 (dd, $J = 5.71$, 10.1, 1 H), 2.50–2.38 (m, 1 H), 2.26 (s, 3 H), 2.25–2.15 (m, 2 H), 1.98–1.89 (m, 2 H), 1.29 (d, $J = 6.4$, 1 H); MS: (ESI, Q-tof) 468.3 (100); Mol. Formula: $\text{C}_{32}\text{H}_{38}\text{BrNO}_2$ (548.55); HRMS: $\text{C}_{32}\text{H}_{38}\text{NO}_2^+$: (468.2903); Calcd: 468.2903; Found: 468.2901; TLC: R_f 0.20 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(4-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,2,9}): Data for V{5,2,9}: Yield: 35 mg (89%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.77 (m, 2 H), 7.69 (dd, *J* = 7.8, 7.8, 2 H), 7.64-7.57 (m, 5 H) 7.30 (m, 3 H), 7.13 (m, 2 H), 5.50 (d, *J* = 12.1, 1 H), 5.12 (dd, *J* = 11.8, 11.8, 1 H), 4.21 (d, *J* = 13.1, 1 H), 4.01 (d, *J* = 10.7, 1 H), 3.84 (d, *J* = 10.7, 1 H), 3.57 (d, *J* = 13.1, 1 H), 3.45 (dd, *J* = 9.3, 9.3, 1 H), 3.44 (d, *J* = 12.2, 1 H), 2.97 (dd, *J* = 6.1, 11.3, 1 H), 2.82 (dd, *J* = 5.9, 10.1, 1 H), 2.46 (m, 1 H), 2.31 (s, 3 H), 2.25 (m, 2 H), 1.96 (m, 2 H), 1.30 (d, *J* = 6.4, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 139.1, 136.8, 133.7, 133.4, 132.6, 132.3, 130.5, 130.2, 128.7, 128.3, 127.7, 127.5, 126.10, 126.07, 122.7, 100.1, 83.4, 69.6, 67.8, 67.1, 60.8, 60.5, 54.3, 34.3, 28.4, 26.9, 24.3, 15.0; MS: (ESI, Q-tof) 506.3 (100); Mol. Formula: C₃₂H₃₅BrF₃NO (586.53); HRMS: C₃₂H₃₅F₃NO⁺: (506.2671); Calcd: 506.2671; Found: 506.2670; TLC: *R_f* 0.25 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-phenyl-3-(4-cyanobenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,2,10}): Data for V{5,2,10}: Yield: 35 mg (95%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.77 (d, *J* = 7.4, 2 H), 7.71-7.63 (m, 6H), 7.60 (dd, *J* = 7.3, 7.3, 1 H), 7.31-7.26 (m, 3 H), 7.13-7.10 (m, 2 H), 5.54 (d, *J* = 12.0, 1 H), 5.13 (dd, *J* = 11.8, 11.8, 1 H), 4.16 (d, *J* = 13.2, 1 H), 4.01 (d, *J* = 10.6, 1 H), 3.83 (d, *J* = 10.6, 1 H), 3.58 (d, *J* = 13.1, 1 H), 3.48-3.40 (m, 2 H), 2.94 (dd, *J* = 6.1, 11.2, 1 H), 2.80 (dd, *J* = 5.8, 10.0, 1 H), 2.50-2.40 (m, 1 H), 2.30 (s, 3 H), 2.30-2.17 (m, 2 H), 2.00-1.92 (m, 2 H), 1.29 (d, *J* = 6.3, 1 H); MS: (ESI, Q-tof)

463.3 (100); Mol. Formula: $C_{32}H_{35}BrN_2O$ (543.54); HRMS: $C_{32}H_{35}N_2O^+$: (463.2749); Calcd: 463.2749; Found: 463.2742; TLC: R_f 0.19 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides $V\{5,3,R^4\}$: Following General Procedure II, amino borane $V\{5,3\}$ (403 mg, 1.13 mmol) was added to a 100-mL round-bottomed flask as a solution in 43 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (6.9, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among six test tubes that were subsequently charged with benzyl bromide (tube 1, 37 mg, 0.215 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 48 mg, 0.215 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 48 mg, 0.215 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 66 mg, 0.215 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 61 mg, 0.215 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, (43 mg, 0.215 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-phenyl-3-benzyl-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide ($V\{5,3,1\}$): Data for $V\{5,3,1\}$: Yield: 82 mg (89%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.65 (t, J = 8.1, 2 H), 7.62 (d, J = 8.07, 2 H), 7.53 (t, J = 7.2, 1 H), 7.41 (d, J = 6.61, 2 H), 7.39–7.31 (m, 3 H), 5.22 (d, J = 12.0, 1 H), 5.02 (dd, J = 11.9, 11.9, 1 H), 4.21 (d, J = 13.0, 1 H), 3.44 (d, J = 13.2, 1 H), 3.34 (d, J = 12.0, 1 H), 3.31 (dd, J = 9.28, 9.28, 1 H), 2.98 (dd, J = 6.1, 11.4, 1 H), 2.90 (ddd, J = 6.4, 8.8, 8.8, 1 H), 2.83 (dd, J = 6.0, 10.1, 1 H), 2.74 (ddd, J = 6.7, 8.8, 8.8, 1 H), 2.40–2.30 (m, 1 H), 2.28–2.19 (m, 1 H), 2.25 (s, 3 H), 2.12–2.03 (m, 1 H), 1.98–1.84 (m, 2 H), 1.41–1.34 (m, 2 H), 1.31 (d, J = 6.4, 3 H), 1.27–1.10 (m, 6H), 0.84 (t, J = 7.2, 3 H); MS: (ESI, Q-tof) 432.3 (100); Mol. Formula: $C_{30}H_{42}BrNO$ (512.56); HRMS: $C_{30}H_{42}NO^+$: (432.3266); Calcd: 432.3266; Found: 432.3263; TLC: R_f 0.25 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-phenyl-3-(1-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,3,2}):

Data for **V{5,3,2}**: Yield: 94 mg (93%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.93–7.87 (m, 3 H), 7.85 (d, *J* = 8.1, 1 H), 7.62–7.59 (m, 4 H), 7.58–7.44 (m, 4 H), 5.54 (d, *J* = 12.8, 1 H), 4.71 (dd, *J* = 11.8, 11.8, 1 H), 4.63 (d, *J* = 13.3, 1 H), 4.57 (d, *J* = 12.8, 1 H), 3.54 (d, *J* = 13.2, 1 H), 3.26 (dd, *J* = 8.9, 8.9, 1 H), 3.01 (dd, *J* = 5.5, 10.1, 1 H), 2.93 (dd, *J* = 6.5, 11.5, 1 H), 2.87–2.87 (m, 2 H), 2.56–2.46 (m, 1 H), 2.43–2.33 (m, 1 H), 2.09–2.01 (m, 1 H), 2.01–1.91 (m, 2 H), 1.36 (dd, *J* = 6.9, 14.0, 2 H), 1.26 (d, *J* = 6.4, 2 H), 1.24–1.07 (m, 8H), 0.82 (t, *J* = 7.2, 3 H); MS: (ESI, Q-tof) 482.3 (100); Mol. Formula: C₃₄H₄₄BrNO (562.62); HRMS: C₃₄H₄₄NO⁺: (482.3423); Calcd: 482.3423; Found: 482.3428; TLC: *R_f* 0.28 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-phenyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,3,3}):

Data for **V{5,3,3}**: Yield: 103 mg (99%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.85–7.79 (m, 3 H), 7.73–7.66 (m, 4 H), 7.65–7.57 (m, 3 H), 7.56–7.50 (m, 2 H), 5.44 (d, *J* = 12.1, 1 H), 5.14 (dd, *J* = 11.9, 11.9, 1 H), 4.27 (d, *J* = 13.0, 1 H), 3.53 (d, *J* = 12.1, 1 H), 3.43 (d, *J* = 13.0, 1 H), 3.34 (dd, *J* = 9.3, 9.3, 1 H), 3.06 (dd, *J* = 6.1, 11.3, 1 H), 2.91 (ddd, *J* = 6.38, 8.90, 8.90, 1 H), 2.87 (dd, *J* = 5.8, 10.2, 1 H), 2.75 (dd, *J* = 6.7, 15.5, 1

H), 2.44–2.19 (m, 2 H), 2.30 (s, 3 H), 2.13–2.05 (m, 1 H), 1.97–1.87 (m, 2 H), 1.40–1.34 (m, 2 H), 1.33 (d, $J = 6.4$, 3 H), 1.28–1.09 (m, 7H), 0.83 (t, $J = 7.2$, 3 H); MS: (ESI, Q-tof) 482.3 (100); Mol. Formula: $C_{34}H_{44}BrNO$ (562.62); HRMS: $C_{34}H_{44}NO^+$: (482.3423); Calcd: 482.3423; Found: 482.3423; TLC: R_f 0.29 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-phenyl-3-(3,5-trifluoromethyl-benzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,3,5}): Data for V{5,3,5}: Yield: 104mg (90%), free-flowing white powder; 1H -NMR: (500 MHz, $CDCl_3$) 7.90 (s, 2 H), 7.69–7.63 (m, 4 H), 7.61–7.56 (m, 1 H), 5.92 (d, $J = 12.3$, 1 H), 5.32 (dd, $J = 11.6$, 11.6, 1 H), 3.88 (d, $J = 13.1$, 1 H), 3.49 (d, $J = 13.1$, 1 H), 3.39–3.32 (m, 2 H), 3.00 (dd, $J = 6.0$, 11.0, 1 H), 2.91 (dd, $J = 6.5$, 15.2, 1 H), 2.79 (dd, $J = 6.19$, 10.1, 1 H), 2.75 (dd, $J = 6.67$, 15.4, 1 H), 2.43–2.20 (m, 2 H), 2.30 (s, 3 H), 2.15–2.09 (m, 1 H), 2.00–1.89 (m, 2 H), 1.42–1.35 (m, 2 H), 1.33 (d, $J = 6.3$, 3 H), 1.28–1.12 (m, 6H), 0.84 (t, $J = 7.2$, 3 H); ^{13}C -NMR: (126 MHz, $CDCl_3$) 139.4, 133.3, 132.5 (q, $J = 34.2$), 132.1, 130.4, 130.1, 127.3, 124.3, 125.8 (q, $J = 273$), 100.8, 82.8, 68.9, 67.8, 64.8, 60.9, 59.5, 53.2, 34.2, 31.6, 29.6, 28.0, 27.2, 25.7, 24.3, 22.6, 14.8, 14.1; MS: (ESI, Q-tof) 568.3 (100); Mol. Formula: $C_{32}H_{40}BrF_6NO$ (648.56); HRMS: $C_{32}H_{40}NOF_6^+$: (568.3014); Calcd: 568.3014; Found: 568.3007; TLC: R_f 0.39 ($CH_2Cl_2/MeOH$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-phenyl-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,3,7}): Data for V{5,3,7}: Yield: 105 mg (93%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.67 (d, *J* = 7.3, 2 H), 7.62 (t, *J* = 7.7, 2 H), 7.52 (t, *J* = 7.2, 1 H), 7.40 (s, 1 H), 7.30 (s, 2 H), 5.16 (d, *J* = 11.9, 1 H), 5.08 (dd, *J* = 11.9, 11.9, 1 H), 4.26 (d, *J* = 12.9, 1 H), 3.44 (d, *J* = 12.9, 1 H), 3.34 (dd, *J* = 9.3, 9.3, 1 H), 3.22 (d, *J* = 12.0, 1 H), 2.95–2.87 (m, 2 H), 2.84 (dd, *J* = 5.8, 9.9, 1 H), 2.73 (dd, *J* = 6.8, 15.5, 1 H), 2.39–2.29 (m, 1 H), 2.26 (s, 3 H), 2.23–2.15 (m, 1 H), 2.12–2.05 (m, 1 H), 1.96–1.86 (m, 2 H), 1.42–1.35 (m, 2 H), 1.35–1.11 (m, 27H), 0.84 (t, *J* = 7.2, 3 H); MS: (ESI, Q-tof) 544.5 (100); Mol. Formula: C₃₈H₅₈BrNO (624.78); HRMS: C₃₈H₅₈NO⁺: (544.4518); Calcd: 544.4518; Found: 544.4509; TLC: *R*_f 0.41 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-hexyloxy-1-phenyl-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,3,8}): Data for V{5,3,8}: Yield: 87 mg (90%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.67–7.59 (m, 4 H), 7.52 (t, *J* = 7.1, 1 H), 7.35 (d, *J* = 8.7, 2 H), 6.84 (d, *J* = 8.8, 2 H), 5.13 (d, *J* = 12.2, 1 H), 4.94 (dd, *J* = 11.9, 11.9, 1 H), 4.19 (d, *J* = 12.8, 1 H), 3.78 (s, 4 H), 3.42 (d, *J* = 13.2, 1 H), 3.33–3.26 (m, 2 H), 2.96 (dd, *J* = 6.0, 11.4, 1 H), 2.90 (ddd, *J* = 6.3, 8.7, 8.7, 1 H), 2.81 (dd, *J* = 6.0, 10.2, 1 H), 2.73 (dd, *J* = 6.7, 15.4, 1 H), 2.42–2.29 (m, 1 H), 2.28–2.16 (m, 1 H), 2.22 (s, 3 H), 2.10–2.03 (m, 1 H), 1.98–1.85 (m, 2 H), 1.40–1.34 (m, 2 H), 1.30 (d, *J* = 6.4, 3 H), 1.27–1.10 (m, 6H), 0.84 (t, *J* = 7.2, 3 H); MS: (ESI, Q-tof) 462.3 (100); Mol. Formula: C₃₁H₄₄BrNO₂ (542.59); HRMS: C₃₁H₄₄NO₂⁺: (462.3372); Calcd: 462.3372; Found: 462.3372; TLC: *R*_f 0.25 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of Quaternary Ammonium Bromides V{5,6,R⁴}: Following General Procedure II, amino borane V{5,6} (80 mg, 0.161 mmol) was added to a 100-mL round-bottomed flask as a solution in 5.4 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (0.8, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among three test tubes that were subsequently charged with benzyl bromide (tube 1, 8 mg, 0.048 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 2, 15 mg, 0.048 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 3, 10 mg, 0.048 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of rel-(1R,3R,5S,5aS,7aS,7bR) Octahydro-1-(3,5-trifluoromethylbenzyloxy)-1-phenyl-3-benzyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{5,6,1}): Data for V{5,6,1}: Yield: 21 mg (79%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.79–7.75 (m, 2 H), 7.75 (s, 1 H), 7.69 (t, $J = 7.8$, 2 H), 7.60 (t, $J = 7.3$, 1 H), 7.54 (s, 2 H), 7.44–7.33 (m, 5 H), 5.31 (d, $J = 12.1$, 1 H), 5.13 (dd, $J = 11.9$, 11.9, 1 H), 4.34 (d, $J = 13.0$, 1 H), 4.16 (d, $J = 12.0$, 1 H), 3.95 (d, $J = 12.0$, 1 H), 3.59 (d, $J = 13.1$, 1 H), 3.49 (dd, $J = 9.4$, 9.4, 1 H), 3.30 (d, $J = 12.1$, 1 H), 3.04 (dd, $J = 6.0$, 11.4, 1 H), 2.90 (dd, $J = 5.9$, 10.3, 1 H), 2.45–2.20 (m, 2 H), 2.31 (s, 3 H), 2.20–2.10 (m, 1 H), 2.02–1.92 (m, 2 H), 1.33 (d, $J = 6.4$, 3 H); $^{13}\text{C-NMR}$: (126 MHz, CDCl_3) 139.5, 138.2, 133.1, 131.9 (q, $J = 33.5$), 130.9, 130.5, 130.2, 129.3, 129.1, 127.6, 127.1, 123.2 (q, $J = 273$), 121.9, 99.5, 83.9, 69.3, 67.0, 65.4, 61.5, 60.7, 52.8, 34.0, 28.1, 27.5, 24.2, 14.7; MS: (ESI, Q-tof) 574.3 (100); Mol. Formula: $\text{C}_{33}\text{H}_{34}\text{BrF}_6\text{NO}$ (654.52); HRMS: $\text{C}_{33}\text{H}_{34}\text{NOF}_6^+$: (574.2545); Calcd: 574.2545; Found: 574.2549; TLC: R_f 0.28 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of rel-(1R,3R,5S,5aS,7aS,7bR) Octahydro-1-(3,5-trifluoromethylbenzyloxy)-1-phenyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{5,6,5}): Data for V{5,6,5}: Yield: 21 mg (66%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.93 (s, 1 H), 7.89 (s, 2 H), 7.79 (s, 1 H), 7.76–7.70 (m, 3 H), 7.70–7.63 (m, 2 H), 7.55 (s, 2 H), 6.00 (d, $J = 12.3$, 1 H), 5.41 (dd, $J = 11.7$, 11.7, 1 H), 4.16 (d, $J = 11.9$, 1 H), 4.02 (d, $J = 13.0$, 1 H), 3.96 (d, $J = 12.0$, 1 H), 3.65 (d, $J = 13.1$, 1 H), 3.52 (dd, $J = 9.3$, 9.3, 1 H), 3.34 (d, $J = 12.4$, 1 H), 3.09 (dd, $J = 11.0$, 6.0, 1 H), 2.86 (dd, $J = 5.8$, 10.1, 1 H), 2.45–2.26 (m, 2 H), 2.36 (s, 3 H), 2.24–2.15 (m, 1 H), 2.07–1.93 (m, 2 H), 1.35 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 710.2 (100); Mol. Formula: $\text{C}_{35}\text{H}_{32}\text{BrF}_{12}\text{NO}$ (790.52); HRMS: $\text{C}_{35}\text{H}_{32}\text{NOF}_{12}^+$: (710.2292); Calcd: 710.2292; Found: 710.2285; TLC: R_f 0.35 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(3,5-trifluoromethylbenzyloxy)-1-phenyl-3-(4-methoxybenzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{5,6,8}): Data for **V{5,6,8}**: Yield: 22 mg (82%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.80–7.72 (m, 3 H), 7.76 (t, $J = 7.8$, 2 H), 7.59 (t, $J = 7.3$, 1 H), 7.54 (s, 2 H), 7.35 (d, $J = 8.7$, 2 H), 6.86 (d, $J = 8.8$, 2 H), 5.22 (d, $J = 12.1$, 1 H), 5.06 (dd, $J = 12.0$, 12.0, 1 H), 4.33 (d, $J = 13.1$, 1 H), 4.16 (d, $J = 12.0$, 1 H), 3.95 (d, $J = 12.0$, 1 H), 3.79 (s, 3 H), 3.56 (d, $J = 13.1$, 1 H), 3.48 (dd, $J = 9.3$, 9.3, 1 H), 3.25 (d, $J = 12.2$, 1 H), 3.02 (dd, $J = 6.0$, 11.5, 1 H), 2.88 (dd, $J = 5.6$, 10.3, 1 H), 2.43–2.31 (m, 1 H), 2.31–2.18 (m, 2 H), 2.28 (s, 3 H), 2.18–2.10 (s, 1 H), 2.01–1.91 (m, 2 H), 1.32 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 604.3 (100); Mol. Formula: $\text{C}_{34}\text{H}_{36}\text{BrF}_6\text{NO}_2$ (684.55); HRMS: $\text{C}_{34}\text{H}_{36}\text{NO}_2\text{F}_6^+$: (604.2650); Calcd: 604.2650; Found: 604.2649; TLC: R_f 0.29 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides V{5,7,R⁴}: Following General Procedure II, amino borane **V{5,7}** (606 mg, 1.55 mmol) was added to a 100-mL round-bottomed flask as a solution in 47 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (7.0, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among five test tubes that were subsequently charged with benzyl bromide (tube 1, 34 mg, 0.199 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 45 mg, 0.199 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 45 mg, 0.199 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 62 mg, 0.199 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 57 mg, 0.199 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-phenyl-3-benzyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{5,7,1}):

Data for **V{5,7,1}**: Yield: 89 mg (98%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.77 (d, *J* = 7.3, 2 H), 7.68 (t, *J* = 7.7, 2 H), 7.57 (t, *J* = 7.3, 1 H), 7.45–7.40 (m, 2 H), 7.39–7.31 (m, 3 H), 7.04 (d, *J* = 8.7, 2 H), 6.81 (d, *J* = 8.7, 2 H), 5.24 (d, *J* = 12.2, 1 H), 5.02 (dd, *J* = 11.9, 11.9, 1 H), 4.27 (d, *J* = 13.2, 1 H), 3.92 (d, *J* = 10.2, 1 H), 3.77 (s, 3 H), 3.70 (d, *J* = 10.2, 1 H), 3.50 (d, *J* = 13.1, 1 H), 3.44 (dd, *J* = 9.0, 9.0, 1 H), 3.35 (d, *J* = 12.1, 1 H), 2.96 (dd, *J* = 6.1, 11.5, 1 H), 2.85 (dd, *J* = 5.5, 9.9, 1 H), 2.49–2.39 (m, 1 H), 2.29 (s, 3 H), 2.25–2.11 (m, 2 H), 1.99–1.89 (m, 2 H), 1.29 (t, *J* = 7.1, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 159.5, 139.2, 133.0, 130.3, 129.9, 129.3, 129.2, 129.1, 128.9, 127.5, 114.0, 99.3, 83.2, 69.2, 67.3, 66.6, 61.5, 60.6, 55.4, 53.5, 34.0, 28.1, 27.2, 24.1, 14.8; MS: (ESI, Q-tof) 468.3 (100); Mol. Formula: C₃₂H₃₈BrNO₂ (548.55); HRMS: C₃₂H₃₈NO₂⁺: (468.2903); Calcd: 468.2903; Found: 468.2899; TLC: *R*_f 0.21 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-phenyl-3-(1-naphthylmethyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{5,7,2}):

Data for **V{5,7,2}**: Yield: 95 mg (95%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.94 (d, *J* = 8.7, 1 H), 7.89 (d, *J* = 8.3, 1 H), 7.86–7.82 (m, 2 H), 7.74 (d, *J* = 7.4, 2 H), 7.67 (t, *J* = 7.7, 2 H), 7.59–7.54 (m, 2 H), 7.52–7.43 (m, 2 H), 7.02 (d, *J* = 8.7, 2 H), 6.78 (d, *J* = 8.7, 2 H), 5.54 (d, *J* = 12.8, 1 H), 4.73–4.64 (m, 2 H), 4.52 (d, *J* = 12.8, 1 H), 3.91 (d, *J* = 10.9, 1 H), 3.83 (d, *J* = 10.9, 1 H), 3.75 (s, 3 H), 3.59 (d, *J* = 13.3, 1 H), 3.38 (dd, *J* = 9.1, 9.1, 1 H), 3.02 (d, *J* = 10.9, 1 H), 2.87 (dd, *J* = 6.2, 11.6, 1 H), 2.61–2.50 (m, 1 H), 2.45 (s, 3 H), 2.35–2.26 (m, 1 H), 2.20–2.11 (m, 1 H), 1.98 (d, *J* = 10.1, 3 H), 1.22 (d, *J* = 6.4, 3 H); MS: (ESI, Q-tof) 518.3 (100); Mol. Formula: C₃₆H₄₀BrNO₂ (598.61); HRMS: C₃₆H₄₀NO₂⁺: (518.3059); Calcd: 518.3059; Found: 518.3065; TLC: *R*_f 0.25 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-phenyl-3-(2-naphthylmethyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,7,3}): Data for **V{5,7,3}**: Yield: 92 mg (92%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.86–7.78 (m, 5 H), 7.75 (t, $J = 7.7$, 3 H), 7.69–7.57 (m, 3 H), 7.56–7.48 (m, 2 H), 7.03 (d, $J = 8.7$, 2 H), 6.80 (d, $J = 8.7$, 2 H), 5.46 (d, $J = 11.9$, 1 H), 5.15 (dd, $J = 11.9$, 11.9, 1 H), 4.33 (d, $J = 12.8$, 1 H), 3.93 (d, $J = 10.2$, 1 H), 3.77 (d, $J = 10.3$, 1 H), 3.76 (s, 3 H), 3.54 (d, $J = 12.1$, 1 H), 3.51–3.43 (m, 2 H), 3.03 (dd, $J = 6.0$, 11.3, 1 H), 2.91–2.86 (m, 1 H), 2.51–2.40 (m, 1 H), 2.34 (s, 3 H), 2.27–2.17 (m, 2 H), 1.99–1.93 (m, 2 H), 1.31 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 518.3 (100); Mol. Formula: $\text{C}_{36}\text{H}_{40}\text{BrNO}_2$ (598.61); HRMS: $\text{C}_{36}\text{H}_{40}\text{NO}_2^+$: (518.3059); Calcd: 518.3059; Found: 518.3071; TLC: R_f 0.26 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-phenyl-3-(3,5-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,7,5}): Data for **V{5,7,5}**: Yield: 97 mg (85%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.92 (s, 2 H), 7.91 (s, 1 H), 7.81–7.68 (m, 4 H), 7.63 (t, $J = 7.1$, 1 H), 7.04 (d, $J = 8.7$, 2 H), 6.82 (d, $J = 8.7$, 2 H), 5.94 (d, $J = 12.3$, 1 H), 5.32 (dd, $J = 11.6$, 11.6, 1 H), 3.94 (d, $J = 10.3$, 2 H), 3.78 (s, 3 H), 3.55 (d, $J = 13.0$, 1 H), 3.48 (dd, $J = 9.4$, 9.4, 1 H), 3.36 (d, $J = 11.4$, 1 H), 2.98 (dd, $J = 5.7$, 10.5, 1 H), 2.84–2.78 (m, 1 H), 2.52–2.38 (s, 1 H), 2.34 (s, 3 H), 2.25 (s, 2 H), 2.03–1.93 (m, 2 H), 1.31 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 604.3 (100); Mol. Formula: $\text{C}_{34}\text{H}_{36}\text{BrF}_6\text{NO}_2$ (684.55); HRMS: $\text{C}_{34}\text{H}_{36}\text{NO}_2\text{F}_6^+$: (604.2650); Calcd: 604.2650; Found: 604.2635; TLC: R_f 0.29 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-(4-methoxybenzyloxy)-1-phenyl-3-(3,5-tert-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{5,7,7}): Data for V{5,7,7}: Yield: 103 mg (94%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.78 (d, *J* = 7.5, 2 H), 7.68 (t, 2 H, *J* = 7.7), 7.57 (t, *J* = 7.4, 1 H), 7.40 (t, *J* = 1.6, 1 H), 7.33 (d, *J* = 1.4, 2 H), 7.07 (d, *J* = 8.6, 2 H), 6.83 (d, *J* = 8.7, 2 H), 5.17 (d, *J* = 11.7, 1 H), 5.09 (dd, *J* = 12.0, 12.0, 1 H), 4.33 (d, *J* = 13.0, 1 H), 3.95 (d, *J* = 10.2, 1 H), 3.78 (s, 3 H), 3.73 (d, *J* = 10.2, 1 H), 3.51 (d, *J* = 13.6, 1 H), 3.48 (dd, *J* = 9.4, 9.4, 1 H), 3.24 (d, *J* = 12.0, 1 H), 2.92–2.84 (m, 2 H), 2.51–2.38 (m, 1 H), 2.30 (s, 3 H), 2.27–2.12 (m, 2 H), 1.98–1.92 (d, *J* = 6.4, 2 H), 1.31 (s, 18H), 1.29 (d, *J* = 6.3, 3 H); MS: (ESI, Q-tof) 580.4 (100); Mol. Formula: C₄₀H₅₄BrNO₂ (660.77); HRMS: (C₄₀H₅₄NO₂⁺: (580.4155); Calcd: 580.4155; Found: 580.4160; TLC: *R*_f 0.31 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of Quaternary Ammonium Bromides V{6,2,R⁴}: Following General Procedure II, amino borane V{6,2} (110 mg, 0.273 mmol) was added to a 100-mL round-bottomed flask as a solution in 9.1 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (1.4, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among three test tubes that were subsequently charged with benzyl bromide (tube 1, 13 mg, 0.073 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 2, 94 mg, 0.915 mmol, 5.0 equiv), 4-methoxybenzyl bromide (tube 3, 15 mg, 0.073 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyl-1-(2,4,6-trimethylphenyl)-3-benzyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{6,2,1}): Data for V{6,2,1}: Yield: 25 mg (74%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.57-7.43 (m, 2 H), 7.44-7.38 (m, 3 H), 7.32-7.27 (m, 3 H), 7.20-7.14 (m, 3 H), 6.98 (s, 1 H), 5.25 (d, *J* = 12.0, 1 H), 4.94 (dd, *J* = 11.6, 11.6, 1 H), 4.38 (d, *J* = 13.2, 1 H), 4.22 (d, *J* = 10.3, 1 H), 4.13-4.07 (m, 2 H), 3.58 (d, *J* = 13.2, 1 H), 3.37 (d, *J* = 12.0, 1 H), 3.11 (dd, *J* = 6.3, 11.4, 1 H), 2.83 (dd, *J* = 5.9, 9.3, 1 H), 2.74 (s, 3 H), 2.52 (s, 3 H), 2.51-2.42 (m, 1 H), 2.34 (s, 3 H), 2.26-2.17 (m, 2 H), 2.16 (s, 3 H), 1.94-1.83 (m, 2 H), 1.30 (d, *J* = 6.4, 3 H); MS: (ESI, Q-tof) 480.3 (100); Mol. Formula: C₃₄H₄₂BrNO (560.61); HRMS: C₃₄H₄₂NO⁺: (480.3266); Calcd: 480.3266; Found: 480.3260; TLC: *R_f* 0.26 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyl-1-(2,4,6-trimethylphenyl)-3-(3,5-bis(trifluoromethyl)benzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (V{6,2,5}): Data for V{6,2,5}: Yield: 22 mg (65%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.11 (s, 2 H), 7.94 (s, 1 H), 7.34-7.29 (m, 3 H), 7.20-7.16 (m, 3 H), 7.02 (s, 1 H), 5.82 (d, *J* = 12.2, 1 H), 5.22 (dd, *J* = 11.5, 11.5, 1 H), 4.25 (d, *J* = 10.3, 1 H), 4.25-4.15 (m, 2 H), 4.13 (d, *J* = 10.2, 1 H), 3.57 (d, *J* = 13.1, 1 H), 3.30 (d, *J* = 12.3, 1 H), 3.07 (dd, *J* = 6.2, 11.0, 1 H), 2.81-2.75 (m, 1 H), 2.76 (s, 3 H), 2.45 (s, 3 H), 2.52-2.42 (m, 1 H), 2.35 (s, 3 H), 2.24 (s, 3 H), 2.28-2.20 (m, 2 H), 1.90-1.84 (m, 2 H), 1.31 (d, *J* = 6.4, 3 H); MS: (ESI, Q-tof) 616.3 (100); Mol. Formula: C₃₆H₄₀BrF₆NO (696.60); HRMS: C₃₆H₄₀F₆NO⁺: (616.3014); Calcd: 616.3014; Found: 616.3024; TLC: *R_f* 0.30 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-(2,4,6-methylphenyl)-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{6,2,8}): Data for **V{6,2,8}**: Yield: 28 mg (78%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 7.47 (d, *J* = 8.7, 2 H), 7.33-7.27 (m, 3 H), 7.19-7.16 (m, 2 H), 7.13 (s, 1 H), 6.97 (s, 1 H), 6.90 (d, *J* = 8.7, 2 H), 5.16 (d, *J* = 12.2, 1 H), 4.90 (dd, *J* = 11.6, 11.6, 1 H), 4.37 (d, *J* = 12.9, 1 H), 4.22 (d, *J* = 10.3, 1 H), 4.11 (dd, *J* = 9.3, 9.3, 1 H), 4.09 (d, *J* = 11.3, 1 H), 3.81 (s, 3 H), 3.55 (d, *J* = 13.2, 1 H), 3.31 (d, *J* = 12.2, 1 H), 3.08 (dd, *J* = 6.4, 11.5, 1 H), 2.81 (dd, *J* = 6.0, 9.4, 1 H), 2.73 (s, 3 H), 2.51 (s, 3 H), 2.50-2.42 (m, 1 H), 2.34 (s, 3 H), 2.24-2.16 (m, 2 H), 2.14 (s, 3H), 1.93-1.81 (m, 2 H), 1.29 (d, *J* = 6.4, 3 H); MS: (ESI, Q-tof) 510.3 (100); Mol. Formula: C₃₅H₄₄BrNO₂ (590.63); HRMS: C₃₅H₄₄NO₂⁺: (510.3372); Calcd: 510.3372; Found: 510.3382; TLC: *R*_f 0.25 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of Quaternary Ammonium Bromides V{7,2,R⁴}: Following General Procedure II, amino borane **V{7,2}** (258 mg, 0.627 mmol) was added to a 50-mL round-bottomed flask as a solution in 21 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (3.1, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among five test tubes that were subsequently charged with benzyl bromide (tube 1, 25 mg, 0.149 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 2, 46 mg, 0.149 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 3, 30 mg, 0.149 mmol, 1.2 equiv), 4-cyanobenzyl bromide, (tube 4, 29 mg, 0.149 mmol, 1.2 equiv), 4-trifluoromethylbenzyl bromide, (tube 5, 36 mg, 0.149 mmol, 1.2 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-(1-naphthyl)-3-benzyl-5-methyl-7*b*-methylcyclopenta[gh]pyrrolizinium Bromide (V{7,2,1}): Data for V{7,2,1}: Yield: 70 mg (97%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.52 (d, *J* = 8.7, 1 H), 8.13-8.08 (m, 2 H), 8.03 (d, *J* = 7.2, 1 H), 7.74 (dd, *J* = 7.4, 7.4, 1 H), 7.68-7.64 (m, 2 H), 7.29-7.26 (m, 3 H), 7.16 (dd, *J* = 7.5, 7.5, 1 H), 7.11-7.08 (m, 2 H), 6.92 (dd, *J* = 7.8, 7.8, 2 H), 6.37 (d, *J* = 7.4, 1 H), 5.17 (d, *J* = 12.0, 1 H), 5.08 (dd, *J* = 12.0, 12.0, 1 H), 4.65 (d, *J* = 13.0, 1 H), 4.12 (d, *J* = 10.4, 1 H), 3.90 (d, *J* = 10.4, 1 H), 3.83 (dd, *J* = 9.5, 9.5, 1 H), 3.55 (d, *J* = 13.1, 1 H), 2.94 (dd, *J* = 5.9, 11.4, 1 H), 2.90-2.86 (m, 1 H), 2.76 (d, *J* = 12.0, 1 H), 2.59-2.50 (m, 1 H), 2.35 (s, 3 H), 2.30-2.17 (m, 2 H), 1.99-1.95 (m, 2 H), 1.31 (d, *J* = 6.3, 3 H); MS: (ESI, Q-tof) 488.3 (100); Mol. Formula: C₃₅H₃₈BrNO (568.59); HRMS: C₃₅H₃₈NO⁺: (488.2953); Calcd: 488.2953; Found: 488.2958; TLC: *R*_f 0.27 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-(1-naphthyl)-3-(3,5-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[gh]pyrrolizinium Bromide (V{7,2,5}): Data for V{7,2,5}: Yield: 40 mg (45%), free-flowing white powder; ¹H-NMR: (500 MHz, CDCl₃) 8.50 (d, *J* = 8.7, 1 H), 8.04-8.02 (m, 2 H), 8.04 (d, *J* = 7.3, 1 H), 7.77-7.73 (m, 2 H), 7.71-7.63 (m, 2 H), 7.32 (s, 2 H), 7.29-7.27 (m, 3 H), 7.11-7.06 (m, 2 H), 5.66 (d, *J* = 12.1, 1 H), 5.28 (dd, *J* = 11.8, 11.8, 1 H), 4.57 (d, *J* = 12.8, 1 H), 4.09 (d, *J* = 10.3, 1 H), 3.87 (dd, *J* = 9.5, 9.5, 1 H), 3.82 (d, *J* = 10.3, 1 H), 3.70 (d, *J* = 13.1, 1 H), 2.94 (d, *J* = 12.2, 1 H), 2.90-2.82 (m, 2 H), 2.62-2.53 (m, 1 H), 2.46 (s, 3 H), 2.33-2.20 (m, 2 H), 2.03-1.96 (m, 2 H), 1.32 (d, *J* = 6.3, 3 H); ¹³C-NMR: (126 MHz, CDCl₃) 136.5, 135.3, 133.1, 132.8, 132.5, 132.4 (q, *J* = 34.0), 131.5, 130.4, 130.0, 128.9, 128.6, 128.3, 128.1, 127.9, 126.3, 124.9, 124.2, 124.1, 122.4 (q, *J* = 274), 99.0, 84.6, 68.4, 67.5, 65.6, 61.4, 59.8, 53.8, 34.0, 28.4, 27.6, 25.0, 14.7; MS: (ESI, Q-tof) 624.3 (100); Mol. Formula: C₃₇H₃₆BrF₆NO (704.5823); HRMS: C₃₇H₃₆F₆NO⁺: (624.2701); Calcd: 624.2701; Found: 624.2696; TLC: *R*_f 0.35 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-(1-naphthyl)-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{7,2,8}): Data for V{7,2,8}: Yield: 62 mg (82%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.52 (d, $J = 8.7$, 1 H), 8.12-8.07 (m, 2 H), 8.02 (d, $J = 7.4$, 1 H), 7.74 (dd, $J = 7.5$, 7.5, 1 H), 7.67-7.63 (m, 2 H), 7.30-7.26 (m, 3 H), 7.12-7.09 (m, 2 H), 6.43 (d, $J = 8.7$, 2 H), 6.29 (d, $J = 7.5$, 1 H), 5.08 (d, $J = 12.1$, 1 H), 5.00 (dd, $J = 12.0$, 12.0, 1 H), 4.64 (d, $J = 13.1$, 1 H), 4.12 (d, $J = 10.3$, 1 H), 3.89 (d, $J = 10.3$, 1 H), 3.82 (dd, $J = 9.4$, 9.4, 1 H), 3.67 (s, 3 H), 3.53 (d, $J = 13.2$, 1 H), 2.91 (dd, $J = 5.9$, 11.4, 1 H), 2.90-2.84 (m, 2 H), 2.70 (d, $J = 12.1$, 1 H), 2.60-2.50 (m, 1 H), 2.32 (s, 3 H), 2.30-2.15 (m, 2 H), 1.98-1.94 (m, 2 H), 1.30 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 518.3 (100); Mol. Formula: $\text{C}_{36}\text{H}_{40}\text{BrNO}_2$ (598.61); HRMS: $\text{C}_{36}\text{H}_{40}\text{NO}_2^+$: (518.3059); Calcd: 518.3059; Found: 518.3065; TLC: R_f 0.28 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-(1-naphthyl)-3-(4-trifluoromethylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{7,2,9}): Data for V{7,2,9}: Yield: 59 mg (74%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.52 (d, $J = 8.7$, 1 H), 8.15-8.10 (m, 2 H), 8.04 (d, $J = 7.4$, 1 H), 7.79 (dd, $J = 7.5$, 7.5, 1 H), 7.71-7.66 (m, 2 H), 7.30-7.25 (m, 3 H), 7.18 (d, $J = 8.2$, 2 H), 7.12-7.09 (m, 2 H), 6.55 (d, $J = 7.7$, 2 H), 5.39 (d, $J = 12.0$, 1 H), 5.18 (dd, $J = 11.9$, 11.9, 1 H), 4.55 (d, $J = 13.1$, 1 H), 4.14 (d, $J = 10.3$, 1 H), 3.92 (d, $J = 10.3$, 1 H), 3.84 (dd, $J = 9.3$, $J = 9.3$, 1 H), 3.59 (d, $J = 13.1$, 1 H), 2.90 (dd, $J = 5.9$, 11.2, 1 H), 2.87-2.83 (m, 1 H), 2.75 (d, $J = 12.0$, 1 H), 2.60-2.50 (m, 1 H), 2.36 (s, 3 H), 2.32-2.19 (m, 2 H), 2.01-1.95 (m, 2 H), 1.30 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 556.3; Mol. Formula: $\text{C}_{36}\text{H}_{37}\text{BrF}_3\text{NO}$ (636.58); HRMS: $\text{C}_{36}\text{H}_{37}\text{F}_3\text{NO}^+$: (556.2827); Calcd: 556.2827; Found: 586.2837; TLC: R_f 0.30 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-1-(1-naphthyl)-3-(4-cyanobenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (V{7,2,10}): Data for V{7,2,10}: Yield: 57 mg (76%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.50 (d, $J = 8.6$, 1 H), 8.16-8.11 (m, 2 H), 8.04 (d, $J = 7.3$, 1 H), 7.79 (dd, $J = 7.6$, 7.6, 1 H), 7.71-7.66 (m, 2 H), 7.31-7.25 (m, 3 H), 7.22 (d, $J = 8.5$, 2 H), 7.11-7.08 (m, 2 H), 6.54 (d, $J = 7.9$, 2 H), 5.47 (d, $J = 12.4$, 1 H), 5.22 (dd, $J = 11.7$, 11.7, 1 H), 4.48 (d, $J = 13.1$, 1 H), 4.14 (d, $J = 10.3$, 1 H), 3.92 (d, $J = 10.3$, 1 H), 3.84 (dd, $J = 9.5$, 9.5, 1 H), 3.59 (d, $J = 13.1$, 1 H), 2.89 (dd, $J = 5.9$, 11.3, 1 H), 2.85-2.81 (m, 1 H), 2.73 (d, $J = 11.9$, 1 H), 2.59-2.51 (m, 1 H), 2.35 (s, 3 H), 2.33-2.19 (m, 2 H), 2.02-1.96 (m, 2 H), 1.30 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 513.3 (100); Mol. Formula: $\text{C}_{36}\text{H}_{37}\text{BrN}_2\text{O}$ (593.60); HRMS: $\text{C}_{36}\text{H}_{37}\text{N}_2\text{O}^+$: (513.2906); Calcd: 513.2906; Found: 513.2899; TLC: R_f 0.26 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides $\beta\text{-V}\{1,2,R^4\}$: Following General Procedure II, amino borane $\beta\text{-V}\{2\}$ (164 mg, 0.589 mmol) was added to a 100-mL round-bottomed flask as a solution in 19 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (2.9, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among seven test tubes that were subsequently charged with 1-bromomethylnaphthalene (tube 1, 22 mg, 0.104 mmol, 1.2 equiv), 2-bromomethylnaphthalene (tube 3, 22 mg, 0.104 mmol, 1.2 equiv), 3,5-bis(trifluoromethyl)benzyl bromide (tube 4, 31 mg, 0.104 mmol, 1.2 equiv), 3,5-bis(*t*-butyl)benzyl bromide (tube 5, 29 mg, 0.104 mmol, 1.2 equiv), 4-methoxybenzyl bromide (tube 6, 31 mg, 0.104 mmol, 1.2 equiv), 1-bromohexane (tube 7, 68 mg, 0.435 mmol, 5.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

$\beta\text{-V}\{1,2,2\}$

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(1-naphthylmethyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide ($\beta\text{-V}\{1,2,2\}$):

Data for $\beta\text{-V}\{1,2,2\}$: Yield: 42 mg (98%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.48 (d, $J = 8.6$, 1 H), 8.30 (d, $J = 7.2$, 1 H), 7.94 (d, $J = 8.2$, 1 H), 7.87 (d, $J = 8.2$, 1 H), 7.56 (dd, $J = 7.3$, 7.3, 1 H), 7.50–7.45 (m, 5 H), 7.43–7.37 (m, 1 H), 7.32 (dd, $J = 7.8$, 7.8, 1 H), 4.87 (d, $J = 12.6$, 1 H), 4.59 (d, $J = 12.6$, 1 H), 4.75 (dd, $J = 11.9$, 11.9, 1 H), 4.92–4.52 (m, 3 H), 4.12 (d, $J = 3.4$, 1 H), 4.03 (d, $J = 14.1$, 1 H), 3.52 (d, $J = 11.3$, 1 H), 3.18 (dd, $J = 5.8$, 11.3, 1 H), 2.82 (dd, $J = 9.5$, 9.5, 1 H), 2.69 (dd, $J = 5.9$, 10.3, 1 H), 2.24 (s, 3 H), 2.19–2.10 (m, 2 H), 1.90–1.77 (m, 2 H), 1.73–1.63 (m, 1 H), 1.25 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 412.3 (100); Mol. Formula: $\text{C}_{29}\text{H}_{34}\text{BrNO}$ (492.49); HRMS: $\text{C}_{29}\text{H}_{34}\text{NO}^+$: (412.2640); Calcd: 412.2640; Found: 412.2632; TLC: R_f 0.25 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

$\beta\text{-V}\{1,2,3\}$

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(2-naphthylmethyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide ($\beta\text{-V}\{1,2,3\}$):

Data for $\beta\text{-V}\{1,2,3\}$: Yield: 39 mg (91%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.09 (s, 1 H), 7.90–7.84 (m, 3 H), 7.73 (dd, $J = 1.7$, 8.4, 1 H), 7.59–7.51 (m, 2 H), 7.48–7.34 (m, 5 H), 5.39 (d, $J = 11.9$, 1 H), 4.79 (d, $J = 11.8$, 1 H), 4.77 (d, $J = 11.7$, 1 H), 4.71 (dd, $J = 11.9$, 11.9, 1 H), 4.64 (d, $J = 11.7$, 1 H), 4.14–4.08 (m, 2 H), 3.53 (d, $J = 11.1$, 1 H), 3.32 (dd, $J = 6.0$, 11.3, 1 H), 2.74 (dd, $J = 9.2$, 9.2, 1 H), 2.59 (dd, $J = 5.9$, 9.9, 1 H), 2.24–2.07 (m, 2 H), 2.10 (s, 3 H), 1.89–1.77 (m, 2 H), 1.73–1.61 (m, 1 H), 1.26 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 412.3 (100); Mol. Formula: $\text{C}_{29}\text{H}_{34}\text{BrNO}$ (492.49); HRMS: $\text{C}_{29}\text{H}_{34}\text{NO}^+$: (412.2640); Calcd: 412.2640; Found: 412.2639; TLC: R_f 0.26 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(3,5-bis(trifluoromethyl)benzyl)-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide (β -V{1,2,5}): Data for β -V{1,2,5}: Yield: 45mg (89%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 8.20 (s, 2 H), 7.94 (s, 1 H), 7.46–7.31 (m, 5 H), 5.84 (d, $J = 12.1$, 1 H), 4.96 (dd, $J = 11.7$, 11.7, 1 H), 4.75 (d, $J = 11.3$, 1 H), 4.69 (d, $J = 12.1$, 1 H), 4.54 (d, $J = 11.3$, 1 H), 4.13 (s, 1 H), 3.68 (dd, $J = 14.1$, 24.4, 2 H), 3.23 (dd, $J = 6.0$, 11.0, 1 H), 2.76 (dd, $J = 9.5$, 9.5, 1 H), 2.57–2.48 (m, 1 H), 2.31–2.22 (m, 1 H), 2.19–2.09 (m, 1 H), 2.11 (s, 3 H), 1.91–1.78 (m, 2 H), 1.75–1.65 (m, 1 H), 1.24 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 498.2 (100); Mol. Formula: $\text{C}_{27}\text{H}_{30}\text{BrF}_6\text{NO}$ (578.43); HRMS: $\text{C}_{27}\text{H}_{30}\text{F}_6\text{NO}^+$: (498.2232); Calcd: 498.2232; Found: 498.2214; TLC: R_f 0.29 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-hexyl-5-methyl-7b-methylcyclopenta[gh]pyrrolizinium Bromide β -V{1,2,6}: Data for β -V{1,2,6} Yield: 33 mg (87%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.38–7.31 (m, 3 H), 7.27–7.24 (m, 2 H), 4.56 (d, $J = 11.7$, 1 H), 4.48 (d, $J = 11.7$, 1 H), 4.39 (d, $J = 13.3$, 1 H), 4.25 (dd, $J = 6.1$, 11.1, 1 H), 4.12 (s, 1 H), 4.03 (d, $J = 12.7$, 1 H), 3.57–3.50 (m, 1 H), 3.31–3.22 (m, 1 H), 3.05 (dd, $J = 11.9$, 11.9, 1 H), 2.59–2.48 (m, 2 H), 2.17–2.05 (m, 2 H), 1.91–1.70 (m, 5 H), 1.68 (s, 3 H), 1.38 (s, 1 H), 1.32–1.20 (m, 5 H), 1.15 (d, $J = 6.3$, 3 H), 0.86 (t, $J = 6.8$, 3 H); MS: (ESI, Q-tof) 356.3 (100); Mol. Formula: $\text{C}_{24}\text{H}_{38}\text{BrNO}$ (436.47); HRMS: $\text{C}_{24}\text{H}_{38}\text{NO}^+$: (356.2953); Calcd: 356.2953; Found: 356.2944; TLC: R_f 0.37 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9/1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(3,5-*tert*-butylbenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (β -V{1,2,7}): Data for β -V{1,2,7}: Yield: 42 mg (87%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.50–7.48 (m, 1 H), 7.41–7.31 (m, 5 H), 7.29 (d, $J = 1.7$, 2 H), 4.71 (d, $J = 11.3$, 1 H), 4.58 (d, $J = 11.3$, 1 H), 4.68 (s, 2 H), 4.23 (s, 1 H), 4.18 (d, $J = 14.1$, 1 H), 4.04 (d, $J = 14.1$, 1 H), 3.82 (dd, $J = 11.8$, 11.8, 1 H), 3.44 (dd, $J = 5.9$, 11.1, 1 H), 2.73 (dd, $J = 9.6$, 9.6, 1 H), 2.70–2.61 (m, 1 H), 2.35 (dd, $J = 6.5$, 10.1, 1 H), 2.16–2.08 (m, 2 H), 1.96–1.90 (m, 1 H), 1.93 (s, 3 H), 1.84–1.75 (m, 1 H), 1.29 (s, 18H), 1.20 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 474.4 (100); Mol. Formula: $\text{C}_{33}\text{H}_{48}\text{BrNO}$ (554.64); HRMS: $\text{C}_{33}\text{H}_{48}\text{NO}^+$: (474.3736); Calcd: 474.3736; Found: 474.3723; TLC: R_f 0.30 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of *rel*-(1*R*,3*R*,5*S*,5*aS*,7*aS*,7*bR*) Octahydro-1-benzyloxy-3-(4-methoxybenzyl)-5-methyl-7*b*-methylcyclopenta[*gh*]pyrrolizinium Bromide (β -V{1,2,8}): Data for β -V{1,2,8}: Yield: 39 mg (92%), free-flowing white powder; $^1\text{H-NMR}$: (500 MHz, CDCl_3) 7.54 (d, $J = 8.7$, 2 H), 7.44–7.32 (m, 5 H), 6.93 (d, $J = 8.7$, 2 H), 5.07 (d, $J = 12.0$, 1 H), 4.70 (d, $J = 11.7$, 1 H), 4.59 (d, $J = 11.7$, 1 H), 4.58 (d, $J = 12.1$, 1 H), 4.41 (dd, $J = 11.9$, 11.9, 1 H), 4.09 (d, $J = 3.0$, 1 H), 4.02 (d, $J = 14.0$, 1 H), 3.82 (s, 3 H), 3.60 (d, $J = 11.7$, 1 H), 3.25 (dd, $J = 6.0$, 11.3, 1 H), 2.68 (dd, $J = 9.1$, 9.1, 1 H), 2.50 (dd, $J = 5.8$, 10.0, 1 H), 2.27–2.19 (m, 1 H), 2.16–2.07 (m, 1 H), 2.01 (s, 3 H), 1.88–1.65 (m, 3 H), 1.22 (d, $J = 6.3$, 3 H); MS: (ESI, Q-tof) 392.3 (100); Mol. Formula: $\text{C}_{26}\text{H}_{34}\text{BrNO}_2$ (472.46); HRMS: $\text{C}_{26}\text{H}_{34}\text{NO}_2^+$: (392.2590); Calcd: 392.2590; Found: 392.2582; TLC: R_f 0.19 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1) [I_2].

Preparation of Quaternary Ammonium Bromides VI{1-3}: Following General Procedure II, amino borane **S9** (453 mg, 3.0 mmol) was added to a 100-mL round-bottomed flask as a solution in 100 mL of MeOH (0.03 M). The flask was fitted with a reflux condenser, a magnetic stir bar, and a nitrogen inlet adapter. Lastly, 1.0 N aq. HCl solution (15 mL, 5.0 equiv) was added via syringe. The resulting solution was heated and then concentrated by rotary evaporation (15 mm Hg, 20–25 °C) as described General Procedure II. The resulting free amine was dissolved in acetonitrile and was distributed among three test tubes that were subsequently charged with benzyl bromide (tube 1, 142 μL , 1.2 mmol, 1.2 equiv), 1-bromomethylnaphthalene (tube 2, 308 mg, 1.4 mmol, 1.2 equiv), 9-bromomethylantracene (tube 4, 179.5mg, 0.662 mmol, 1.0 equiv). After being agitated for 12 h, the reaction mixtures were worked up and the products isolated and purified as described in General Procedure II.

VI{1}

Preparation of (rel)-(1S,3aS,5aR,5bR)-1-Benzyl-5b-methylcyclopenta[ef]-azoniabicyclo[3.2.0]heptane Bromide (VI{1}): Data for VI{1}: Yield: 33 mg (87%), free-flowing white powder; mp: 222–223°C (CH₃CN/Et₂O, decomposition); ¹H-NMR: (500 MHz, CDCl₃) 7.78 (d, *J* = 8.2, 2 H, HC(12)), 7.323–7.244 (m, 1 H, HC(13), 1 H, HC(14)), 5.31 (d, *J* = 12.1 1 H, HC(10)), 5.09 (t, *J* = 12.0 1 H, HC(1)), 4.72 (d, *J* = 12.1, 1 H, HC(10)), 4.18 (dt, *J* = 12.1, 4.77, 1 H, HC(7)), 3.31–3.29 (m, 1 H, HC(2)), 3.07 (dd, *J* = 6.3, 12.0 1 H, HC(1)), 3.00 (dd, 1 H, HC(6)), 3.08–2.86 (m, 2 H, HC(5), HC(7)), 2.40 (p, *J* = 7.05, 1 H, HC(3)), 2.03–1.94 (m, 2 H, HC(3), HC(4)), 1.923 (s, 3 H, H₃C(9)), 1.90–1.72 (m, 2 H, HC(4), HC(6)); MS: (ESI, Q-tof) 230 (2), 229 (17), 228 (100) 134 (5), 91 (9); TLC: *R_f* 0.12 (CH₂Cl₂/MeOH, 9:1) [I₂]; Mol. Formula: C₁₆H₂₂BrN (308.26). Analysis: C₁₆H₂₂N⁺ (228.17); Calcd: C, 62.34; H, 7.19; N, 25.90 %; Found: C, 62.01; H, 6.79; N, 26.01 %.

Preparation of (rel)-(1*S*,3*aS*,5*aR*,5*bR*)-1-(1-Naphthylmethyl)-5*b*-methylcyclopenta[ef]-azoniabicyclo[3.2.0]heptane Bromide VI{2}: Data for **VI{2}**: Yield: 217 mg (52%), free-flowing white powder; mp: 182–183°C (CH₃CN/Et₂O, decomposition); ¹H-NMR: (500 MHz, CDCl₃) 8.47 (d, *J* = 8.8, 1 H, HC(19)), 8.13 (d, *J* = 7.1, 1 H, HC(13)), 7.80 (d, *J* = 8.1, 1 H, HC(12)), 7.61 (t *J* = 7.7, 1 H, HC(14)), 7.48 (t *J* = 7.4, 1 H, HC(18)), 7.38 (t *J* = 7.7, 1 H, HC(17)), 5.70 (d, *J* = 13.2, 1 H, HC(10)), 5.31 (d, *J* = 13.2, 1 H, HC(10)), 5.18 (t *J* = 11.1, 1 H, HC(1)), 4.21 (dt *J* = 11.84, 7.08, 1 H, HC(7)), 3.421–3.364 (m, 1 H, HC(2)), 3.07 (dd, *J* = 11.8, 5.29, 1 H, HC(1)), 3.03–2.97 (m, 1 H, HC(5)), 2.90 (dd, 11.71, 6.6 1 H, HC(7)), 2.41 (p, 7.3 1 H, HC(6)), 2.1 196 s, 3 H, HC(9)), 2.18–2.0 (m, 1 H, HC(6)), 1.8–1.95 (m, 5 H, HC(3, 6)), HC(4)), HC(6)); ¹³C-NMR: (126 MHz, CDCl₃) 133.8, 132.2, 132.1, 130.8, 129.0, 127.6, 126.2, 125.3, 124.9, 123.8, 96.9, 62.8, 62.3, 55.5, 50.5, 35.5, 30.5, 29.6, 28.1, 19.5; MS: (ESI, Q-tof) 279 (10), 278 (100); Mol. Formula: C₂₀H₂₄BrN 358.31; HRMS: C₂₀H₂₄N⁺, (278.1909); Calcd: (278.1909); Found: 278.1904; TLC: *R*_f 0.15 (CH₂Cl₂/MeOH, 9:1) [I₂].

Preparation of (rel)-(1*S*,3*aS*,5*aR*,5*bR*)-1-(2-Naphthylmethyl)-5*b*-methyl-cyclopenta[*ef*]-azoniabicyclo[3.2.0]heptane Bromide VI{3}: Data for VI{3}: ¹H-NMR: (500 M, CHCl₃) 8.30 (s, 1 H), 7.77 (m, 4 H), 7.46 (m, 2 H), 5.56 (d, 1 H, *J* = 12.2), 5.19 (t, 1 H, *J* = 10.9), 4.97 (d, 1 H, *J* = 12.2), 4.22 (dt, 1 H, *J* = 7.6, *J* = 11.9), 3.38 (td, 1 H, *J* = 4.7, *J* = 13.3), 3.03 (m, 2 H), 2.94 (dd, 1 H, *J* = 8.0, *J* = 13.1), 2.46 (td, 1 H, *J* = 7.5, *J* = 14.8), 2.12 (m, 1 H), 2.05 (s, 3 H), 1.84 (m, 4 H); MS: (ESI, Q-tof) 279.2 (32), 278.2 (100), 149.0(8); Mol. Formula: C₂₀H₂₄NBr 358.32; HRMS: (C₂₀H₂₄N⁺, 278.1909); Calcd: 278.1909; Found: 278.1917; TLC: R_f 0.17 (CH₂Cl₂/MeOH, 9/1) [I₂].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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80. For the details of the synthesis see the Supplemental Information.

81. Regis-*R*, *R*-Welk-O 1, 1 mL/min, 95% hexanes, 5% *i*-PrOH.
82. Calculated using an MMFF double dihedral driver in Spartan '08 V1.1.1 followed by PM3 single point energies.
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Figure 1.
Two mechanisms of nucleophile transfer in hydroxide-initiated PTC Reactions

Figure 2.
Models to rationalize the enantioselectivity of *cinchona* derived PTC catalysts.

Figure 3.
Two potentially generalizable levels of analysis for ammonium ion enolate binding.

Figure 4.
The steric environment the pyrrolizidine scaffold.

Figure 5.
Substituents included in the catalyst library.

Figure 6.
Effect of stir rate on reaction half-life with catalysts of varying structure and activity.

Figure 7.
Histogram of $t_{1/2}$ data in logarithmic form.

Figure 8.
Conformer Energy as a function N-C(9) rotation and C(6)-C(7) bond rotation.

Figure 9.
Representation of the convex faces of the ammonium scaffold.

Figure 10.
Structural Clustering of Kinetic Data

Figure 11.

Variation in rate and selectivity as a function of positional group substitution.

Figure 12.

Electrostatic potential surfaces (M06-2X/6-31G(d)) of scaffolds for Library **I** (no oxygen) and Library **II** (with oxygen). The difference in the maximum positive potential on the left and right faces for the **I** is 1.2 kcal/mol and for **II** is 4.7 kcal/mol (relative energies are 0 kcal/mol and 3.5 kcal/mol).

Scheme 1.

Scheme 2.

Scheme 3.

Scheme 4.

Scheme 5.

Scheme 6.

Scheme 7.

Scheme 8.

Scheme 9.

Scheme 10.

Scheme 11.

Chart 1.

Chart 2.

Table 1

Half-life Data for Library I.

entry	Library #	R ⁴	<i>t</i> _{1/2} , min
1	I{1}	C ₆ H ₅	940
2	I{2}	1-naphthyl	730
3	I{3}	2-naphthyl	na
4	I{4}	9-anthryl	324
5	I{5}	3,5-(CF ₃) ₂ C ₆ H ₃	na
6	I{6}	<i>n</i> -hexyl	12.8

Table 2

Half-life data for Library **II** and **III**.

entry	Library #	R ³	R ⁴	C(1)- configuration	t _{1/2} , min
1	II {1,1}	H	C ₆ H ₅	α	181
2	II {1,2}	H	1-naphthyl	α	179
3	II {1,4}	H	9-anthryl	α	298
4	II {1,5}	H	3,5-(CF ₃) ₂ C ₆ H ₃	α	346
5	II {1,3}	H	2-naphthyl	α	245
6	III {1,3}	H	2-naphthyl	β	72
7	II {2,1}	C ₆ H ₅	C ₆ H ₅	α	10
8	II {2,2}	C ₆ H ₅	1-naphthyl	α	18
9	II {2,3}	C ₆ H ₅	2-naphthyl	α	12.1
10	II {3,1}	<i>n</i> -hexyl	C ₆ H ₅	α	11.7
11	III {3,1}	<i>n</i> -hexyl	C ₆ H ₅	β	14.8
12	II {3,2}	<i>n</i> -hexyl	1-naphthyl	α	6.6
13	III {3,2}	<i>n</i> -hexyl	1-naphthyl	β	9.5
14	III {3,3}	<i>n</i> -hexyl	2-naphthyl	β	13.5
15	II {3,5}	<i>n</i> -hexyl	3,5-(CF ₃) ₂ C ₆ H ₃	α	12.7
16	II {3,6}	<i>n</i> -hexyl	<i>n</i> -hexyl	α	4.6
17	III {3,6}	<i>n</i> -hexyl	<i>n</i> -hexyl	β	5.5
18	II {4,1}	MEM	C ₆ H ₅	α	17.5
19	II {4,2}	MEM	1-naphthyl	α	12.3
20	II {4,3}	MEM	2-naphthyl	α	22.8
21	II {5,1}	2-pyridyl	C ₆ H ₅	α	17.1
22	III {5,1}	2-pyridyl	C ₆ H ₅	β	11.1

entry	Library #	R ³	R ⁴	C(1)- configuration	t _{1/2} , min
23	III{5,2}	2-pyridyl	1-naphthyl	α	6.6
24	III{5,2}	2-pyridyl	1-naphthyl	β	11
25	III{5,3}	2-pyridyl	2-naphthyl	α	12.7
26	III{5,4}	2-pyridyl	9-anthryl	α	21.1
27	III{5,5}	2-pyridyl	3,5-(CF ₃) ₂ C ₆ H ₃	α	31.8

Table 3

Half-life Data for Library IV and V.

entry	Library #	R ¹	R ²	R ³	R ⁴	C(1)- configuration	t _{1/2} , min
1	IV{2,2,1}	H	Me	C ₆ H ₅	C ₆ H ₅	α	93.5
2	IV{2,2,2}	H	Me	C ₆ H ₅	1-naphthyl	α	51.1
3	IV{3,2,1}	H	<i>i</i> -Pr	C ₆ H ₅	C ₆ H ₅	α	19.5
4	IV{3,2,5}	H	<i>i</i> -Pr	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	26.1
5	IV{5,2,5}	H	C ₆ H ₅	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	16.3
6	V{1,2,1}	Me	H	C ₆ H ₅	C ₆ H ₅	α	32.5
7	V{1,2,8}	Me	H	C ₆ H ₅	4-(MeO)C ₆ H ₄	α	51.8
8	V{1,2,8}	Me	H	C ₆ H ₅	4-(MeO)C ₆ H ₄	β	53.9
9	V{1,2,7}	Me	H	C ₆ H ₅	3,5-(<i>t</i> -Bu) ₂ C ₆ H ₃	β	9.78
10	V{1,2,6}	Me	H	C ₆ H ₅	<i>n</i> -hexyl	α	24.7
11	V{2,2,1}	Me	Me	C ₆ H ₅	C ₆ H ₅	α	20.7
12	V{2,2,3}	Me	Me	C ₆ H ₅	2-naphthyl	α	23.0
13	V{2,2,5}	Me	Me	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	899.7
14	V{2,2,8}	Me	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	α	19.9
15	V{2,2,7}	Me	Me	C ₆ H ₅	3,5-(<i>t</i> -Bu) ₂ C ₆ H ₃	α	15.1
16	V{2,2,6}	Me	Me	C ₆ H ₅	<i>n</i> -hexyl	α	28.1
17	V{2,3,1}	Me	Me	<i>n</i> -hexyl	C ₆ H ₅	α	23.0

entry	Library #	R ¹	R ²	R ³	R ⁴	C(1)- configuration	t _{1/2} , min
18	V{2,3,2}	Me	Me	<i>n</i> -hexyl	1-naphthyl	α	75.8
19	V{2,3,3}	Me	Me	<i>n</i> -hexyl	2-naphthyl	α	30.7
20	V{2,3,5}	Me	Me	<i>n</i> -hexyl	3,5-(CF ₃) ₂ C ₆ H ₃	α	236.0
21	V{2,3,8}	Me	Me	<i>n</i> -hexyl	4-(MeO)C ₆ H ₄	α	26.5
22	V{2,3,7}	Me	Me	<i>n</i> -hexyl	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	28.9
23	V{2,3,6}	Me	Me	<i>n</i> -hexyl	<i>n</i> -hexyl	α	21.1
24	V{2,7,1}	Me	Me	4-(MeO)C ₆ H ₄	C ₆ H ₅	α	17.9
25	V{3,2,1}	Me	<i>i</i> -Pr	C ₆ H ₅	C ₆ H ₅	α	132.1
26	V{3,2,5}	Me	<i>i</i> -Pr	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	122.1
27	V{3,2,7}	Me	<i>i</i> -Pr	C ₆ H ₅	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	28.6
28	V{3,3,1}	Me	<i>i</i> -Pr	<i>n</i> -hexyl	C ₆ H ₅	α	41.8
29	V{3,3,3}	Me	<i>i</i> -Pr	<i>n</i> -hexyl	2-naphthyl	α	20.3
30	V{3,3,5}	Me	<i>i</i> -Pr	<i>n</i> -hexyl	3,5-(CF ₃) ₂ C ₆ H ₃	α	62.4
31	V{3,3,8}	Me	<i>i</i> -Pr	<i>n</i> -hexyl	4-(MeO)C ₆ H ₄	α	42.7
32	V{3,2,6}	Me	<i>i</i> -Pr	C ₆ H ₅	<i>n</i> -hexyl	α	86.0
33	V{3,7,5}	Me	<i>i</i> -Pr	4-(MeO)C ₆ H ₄	3,5-(CF ₃) ₂ C ₆ H ₃	α	60.9
34	V{3,7,8}	Me	<i>i</i> -Pr	4-(MeO)C ₆ H ₄	4-(MeO)C ₆ H ₄	α	249.4
35	V{4,2,5}	Me	<i>i</i> -Bu	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	95.8
36	V{5,2,1}	Me	C ₆ H ₅	C ₆ H ₅	C ₆ H ₅	α	10.6

entry	Library #	R ¹	R ²	R ³	R ⁴	C(1)- configuration	t _{1/2} , min
37	V{5,2,2}	Me	C ₆ H ₅	C ₆ H ₅	1-naphthyl	α	12.2
38	V{5,2,3}	Me	C ₆ H ₅	C ₆ H ₅	2-naphthyl	α	10.3
39	V{5,2,5}	Me	C ₆ H ₅	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	9.5
40	V{5,2,8}	Me	C ₆ H ₅	C ₆ H ₅	4-(MeO)C ₆ H ₄	α	17.5
41	V{5,2,9}	Me	C ₆ H ₅	C ₆ H ₅	(4-CF ₃)C ₆ H ₄	α	16.0
42	V{5,2,10}	Me	C ₆ H ₅	C ₆ H ₅	(4-CN)C ₆ H ₄	α	14.4
43	V{5,3,1}	Me	C ₆ H ₅	n-hexyl	C ₆ H ₅	α	9.5
44	V{5,3,2}	Me	C ₆ H ₅	n-hexyl	1-naphthyl	α	18.7
45	V{5,3,3}	Me	C ₆ H ₅	n-hexyl	2-naphthyl	α	13.1
46	V{5,3,5}	Me	C ₆ H ₅	n-hexyl	3,5-(CF ₃) ₂ C ₆ H ₃	α	4.9
47	V{5,3,8}	Me	C ₆ H ₅	n-hexyl	4-(MeO)C ₆ H ₄	α	9.9
48	V{5,3,7}	Me	C ₆ H ₅	n-hexyl	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	8.5
49	V{5,6,1}	Me	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	C ₆ H ₅	α	7.9
50	V{5,6,5}	Me	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	3,5-(CF ₃) ₂ C ₆ H ₃	α	7.0
51	V{5,6,8}	Me	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	4-(MeO)C ₆ H ₄	α	6.9
52	V{5,7,1}	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	C ₆ H ₅	α	19.9
53	V{5,7,2}	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	1-naphthyl	α	19.2
54	V{5,7,3}	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	2-naphthyl	α	12.0
55	V{5,7,5}	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	3,5-(CF ₃) ₂ C ₆ H ₃	α	18.6

entry	Library #	R ¹	R ²	R ³	R ⁴	C(1)- configuration	t _{1/2} , min
56	V{5,7,7}	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	14.6
57	V{7,2,1}	Me	1-naphthyl	C ₆ H ₅	C ₆ H ₅	α	13.7
58	V{7,2,5}	Me	1-naphthyl	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	28.7
59	V{7,2,8}	Me	1-naphthyl	C ₆ H ₅	4-(MeO)C ₆ H ₄	α	11.3
60	V{7,2,9}	Me	1-naphthyl	C ₆ H ₅	(4-CF ₃)C ₆ H ₄	α	11.8
61	V{7,2,10}	Me	1-naphthyl	C ₆ H ₅	(4-CN)C ₆ H ₄	α	48.6
62	V{6,2,1}	Me	2,4,6-(CH ₃) ₂ C ₆ H ₂	C ₆ H ₅	C ₆ H ₅	α	12.2
63	V{6,2,8}	Me	2,4,6-(CH ₃) ₂ C ₆ H ₂	C ₆ H ₅	4-(MeO)C ₆ H ₄	α	11.8

Table 4

Half-life Data for other Quaternary Ammonium Ions.

entry	Library #	catalyst	R ⁴	t _{1/2} , min
1	-	Me ₄ N	-	12,000
2	-	Et ₄ N	-	480
3	-	Me ₃ NC ₁₆ H ₃₃	-	2800
4	-	<i>n</i> -Bu ₃ NBn	-	21
5	VI{1}	-	C ₆ H ₅	890
6	VI{2}	-	1-naphthyl	1000
7	VI{3}	-	2-naphthyl	1090

Table 5

Enantioselectivity of Library **II** and **III**.^a

entry	Library #	R ³	R ⁴	er, <i>S</i> : <i>R</i>
1	II {1-5,1-6}	-	-	50:50 ±3
2	III {1,2}	H	1-naphthyl	48:52
3	III {1,3}	H	2-naphthyl	55:45
4	III {1,4}	H	9-anthryl	50:50
5	III {1,5}	H	3,5-(CF ₃) ₂ C ₆ H ₃	57:43
6	III {1,6}	H	<i>n</i> -hexyl	52:48
7	III {1,1}	H	C ₆ H ₅	55:45
8	III {3,2}	<i>n</i> -hexyl	1-naphthyl	48:52
9	III {3,3}	<i>n</i> -hexyl	2-naphthyl	55:45
10	III {3,4}	<i>n</i> -hexyl	9-anthryl	47:53
11	III {3,5}	<i>n</i> -hexyl	3,5-(CF ₃) ₂ C ₆ H ₃	52:48
12	III {3,6}	<i>n</i> -hexyl	<i>n</i> -hexyl	53:47
13	III {3,1}	<i>n</i> -hexyl	C ₆ H ₅	54:46
14	III {2,2}	C ₆ H ₅	1-naphthyl	64:36
15	III {2,3}	C ₆ H ₅	2-naphthyl	48:52
16	III {2,4}	C ₆ H ₅	9-anthryl	44:56
17	III {2,5}	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	57:43
18	III {2,6}	C ₆ H ₅	<i>n</i> -hexyl	58:42
19	III {2,1}	C ₆ H ₅	C ₆ H ₅	53:47
20	III {5,2}	2-pyridyl	1-naphthyl	64:36
21	III {5,3}	2-pyridyl	2-naphthyl	48:52
22	III {5,4}	2-pyridyl	9-anthryl	54:46
23	III {5,5}	2-pyridyl	3,5-(CF ₃) ₂ C ₆ H ₃	58:42
24	III {5,6}	2-pyridyl	<i>n</i> -hexyl	57:43
25	III {5,1}	2-pyridyl	C ₆ H ₅	60:40

^aThis is a representative summary. For a full tabular listing see the Supporting Information.

Table 6

Enantioselectivity of Libraries IV and V.^a

entry	Library #	R ¹	R ²	R ³	R ⁴	C(1)-config.	er, S:R
1	IV{1,2,5}	H	Ph	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	56:44
2	V{1,2,X}	Me	H	C ₆ H ₅	<i>l</i> -3,6 or 8	α	50:50±4
3	V{1,2,5}	Me	H	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	56:44
4	V{1,2,7}	Me	H	C ₆ H ₅	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	60:40
5	V{1,2,2}	Me	H	C ₆ H ₅	<i>l</i> -3 or 6-8	β	50:50±5
6	V{1,2,5}	Me	H	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	β	63:37
7	V{2,X,X}	Me	Me	2,3,7	<i>l</i> -6,8	α	50:50±4
8	V{2,3,7}	Me	Me	<i>n</i> -hexyl	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	58:42
9	V{2,2,5}	Me	Me	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	57:43
10	V{2,2,7}	Me	Me	C ₆ H ₅	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	57:43
11	V{2,7,5}	Me	Me	4-(MeO)C ₆ H ₄	3,5-(CF ₃) ₂ C ₆ H ₃	α	59:41
12	V{2,7,7}	Me	Me	4-(MeO)C ₆ H ₄	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	57:43
13	V{3,X,X}	Me	<i>i</i> -Pr	2,3,7	<i>l</i> -8	α	41:59±5
14	V{4,2,5}	Me	<i>i</i> -Bu	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	37:63
15	V{5,X,X}	Me	C ₆ H ₅	2,3	<i>l</i> -2,3,8	α	50:50±6
16	V{5,3,5}	Me	C ₆ H ₅	<i>n</i> -hexyl	3,5-(CF ₃) ₂ C ₆ H ₃	α	79:21
17	V{5,3,7}	Me	C ₆ H ₅	C ₆ H ₅	3,5-(<i>i</i> -Bu) ₂ C ₆ H ₃	α	61:39

entry	Library #	R ¹	R ²	R ³	R ⁴	C(1)-config.	er, S: <i>R</i>
18	V{5,2,X}	Me	C ₆ H ₅	C ₆ H ₅	2,3	α	50:50 $\pm$ 5
19	V{5,2,5}	Me	C ₆ H ₅	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	81:19
20	V{5,6,5}	Me	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	3,5-(CF ₃) ₂ C ₆ H ₃	α	81:19
21	V{5,X,X}	Me	C ₆ H ₅	6,7	1,2,3,8	α	50:50 $\pm$ 5
22	V{5,7,5}	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	3,5-(CF ₃) ₂ C ₆ H ₃	α	81:19
23	V{5,7,7}	Me	C ₆ H ₅	4-(MeO)C ₆ H ₄	3,5-(<i>t</i> -Bu) ₂ C ₆ H ₃	α	63:37
24	V{X,2,X}	Me	5,7	C ₆ H ₅	1,8,9,10,11	α	50:50 $\pm$ 6
25	V{7,2,5}	Me	1-naphthyl	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	81:19
26	V{6,2,5}	Me	mesityl	C ₆ H ₅	3,5-(CF ₃) ₂ C ₆ H ₃	α	76:24

^aThis is a representative summary. For a full tabular listing see the Supporting Information.

Table 7

Half-lives (min) of Selected Catalysts with $R^1 = \text{Me}$, $R^3 = \text{Ph}$ and Variable R^2 and R^4 .

R^2	MR^a	R^4		
		C_6H_5	$3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3$	$4\text{-(MeO)C}_6\text{H}_4$
Me	6.88	21	900	18
<i>i</i> -Pr	16.08	132	122	174
<i>t</i> -Bu	20.85	-	96	-
phenyl	25.28	11	10	18
mesityl	42.97	12	62	12
1-naphthyl	42.45	14	29	11

^aMR = molar refractivity of the R^2 substituent calculated by Chemdraw.