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A Stereoselective Intramolecular Cyclopropanation via a De Novo Class of Push-Pull Carbenes Derived from DMDO-Epoxidations of Chiral Ynamides

Hongyan Li, Jennifer E. Antoline, Jin-Haek Yang, Ziyad F. Al-Rashid^{*}, and Richard P. Hsung^{*}

Division of Pharmaceutical Sciences and Department of Chemistry, University of Wisconsin, Madison, WI 53705-2222

Abstract

This work describes the first examples of diastereoselective intramolecular cyclopropanations of a *de novo* class of push-pull carbenes derived from DMDO-epoxidations of chiral ynamides. This reaction sequence essentially constitutes a tandem epoxidation–cyclopropanation that effectively gives rise to a series of structurally unique amido-cyclopropanes. A plausible mechanistic model is proposed revealing insights into this novel cyclopropanation process.

Introduction

Epoxidations of alkynes have long been shown to give rise to oxocarbene formation via rearrangement of initial oxirene intermediates.¹ In the last three decades, a plethora of subsequent transformations of these oxocarbenes have been documented including Wolff rearrangement and further reaction of the resultant ketene, C-H insertion, hydrogen or alkyl migration, secondary oxidation, and formation of stable metalla-keto carbene complexes.² However, despite a diverse array of possible reactivities, efforts in exploring the vast synthetic potential through this simple π -bond oxidation has been rather underwhelming.¹ Our interest in chemistry of ynamides,^{3–5} a new class of electron rich and electronically biased alkynes, has provided us with a unique opportunity for the tuning and unleashing of such reactivity.

Specifically, as shown in Scheme 1, the postulated oxirenes **2** derived from epoxidation of ynamides **1**⁶ could rearrange to a *de novo* class of push-pull carbenes **3**, which possesses dual stabilization.⁷ While both intermediates **2** and **3** could undergo a second oxidation to afford keto-imides **6**⁸ with the former proceeding through bis-epoxides **5**, push-pull carbenes **3** represent a novel species that is intriguing both in reactivity and synthetic potential.⁹ Were such a carbene to arise, one may expect promiscuity with respect to the reactive partners it may choose [electron rich versus deficient] in transformations such as cyclopropanations.^{7b, 10} While we^{11,12} had communicated the possibility of succeeding in such cyclopropanation reaction manifold, we wish to report here details of these tandem ynamide-epoxidation–intramolecular cyclopropanation reactions via this novel class of chiral push-pull carbenes.

Results and Discussions

Chiral ynamides to be employed in this study could be readily constructed using the standard synthetic sequence illustrated in Scheme 2 for ynamide **11**. Ynamide **11** could be prepared through a copper(I)-catalyzed amide cross-coupling of acetylenic bromide **9** with amide **10** using conditions that were developed in our lab.^{13–15} Acetylenic bromides such as **9** could be accessed in a few steps using well established chemistry from respective alkynols such as **7**.

Epoxidation of ynamide **11** was accomplished employing 4.0 equiv of dimethyldioxirane¹⁶ [DMDO] [Scheme 3]. Although the optimized conditions called for the addition of DMDO solution through a syringe pump over 2–3 h, the oxidation process was highly selective for the ynamido-motif over the acrylic moiety, leading to the desired cyclopropanation product **12** in 63% yield as a 75:25 isomeric mixture. We were able to also demonstrate that the intramolecular cyclopropanation was equally effective when using ynamide **13** containing a simple olefin, and that the epoxidation remained selective for the ynamido-motif over the electron-rich olefin. The success in isolating cyclopropanation product **14** suggests that these novel push-pull oxocarbenes are electronically ambiphilic in nature.

Crystallographic data for 12-major

$C_{17}H_{17}NO_5$, $M = 315.32$, orthorhombic, $P2_12_12_1$, $a = 9.419(2)$, $b = 12.174(3)$, $c = 13.334(3)$ Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90^\circ$, $V = 1529.0(5)$ Å³, $T = 173(2)$ K, $Z = 4$, $\mu = 0.102$ mm⁻¹, 1562($R_{int} = 0.0271$), final R indices [$I > 2\sigma(I)$], $R_1 = 0.0300$, $wR_2 = 0.0699$, R indices (all data) $R_1 = 0.0332$, $wR_2 = 0.0718$.

Crystallographic data for 14-major

$C_{15}H_{15}NO_3$, $M = 257.28$, monoclinic, $P2_1$, $a = 8.293(2)$, $b = 6.0494(10)$, $c = 12.923(3)$ Å, $\alpha = 90$, $\beta = 98.616(17)$, $\gamma = 90^\circ$, $V = 641.0(2)$ Å³, $T = 173(2)$ K, $Z = 2$, $\mu = 0.093$ mm⁻¹, 1573($R_{int} = 0.0258$), final R indices [$I > 2\sigma(I)$], $R_1 = 0.0307$, $wR_2 = 0.0697$, R indices (all data) $R_1 = 0.0360$, $wR_2 = 0.0720$.

While the stereoselectivity is modest, the ynamide-epoxidation took place very effectively and is relatively faster than reported alkyne epoxidations.¹⁷ This reaction sequence constitutes a tandem ynamide-epoxidation-cyclopropanation, leading to a series of structurally unique if not unprecedented amido-cyclopropanes. The cyclopropanation process would most likely proceed through the push-pull oxocarbene derived via rearrangement of oxirene as proposed in Scheme 1, or alternatively, an electrophilic attack of the ynamide on the oxidant would give rise initially to an oxy-ketene-iminium ion intermediate **A** [see Figure].

Single crystal X-ray structures of **12-major** and **14-major** were attained to unambiguously assign the relative configuration of the major isomer [Scheme 3], thereby revealing the same sense of stereoselectivity for both cyclopropanation reactions [we note here that five X-ray determinations provided in this paper only established the relative stereochemistries]. Based on stereochemical assignments, a mechanistic model could be proposed as shown in Scheme 4.

Two possible conformational approaches could account for the stereochemical outcome of the intramolecular cyclopropanation: **15** and **16** or “*endo*” and “*exo*,” leading respectively to **12-** or **14-major** and **12-** or **14-minor**. Hartree-Fock 3-21G* calculations using SpartanTM program reveal that the oxocarbene motif itself would orient in a conformational manner where (a) the empty carbene p-orbital [red] is aligned with the nitrogen lone-pair [pink], allowing an n-to-p overlap; (b) the carbene lone pair [blue] is co-planar with the adjacent

carbonyl group for a perfect n-to- π^* delocalization; and lastly, (c) the carbene lone pair would prefer to point away from the oxazolidinone carbonyl to minimize electrostatic interactions. Such conformational preference further underscores the distinctiveness of these novel push-pull oxocarbenes.

The “endo” and “exo” approaches are informally defined as the following. They are associated with the position of the vinyl strand [blue] with respect to the carbene lone pair. The “endo” approach is such that the vinyl strand points toward the lone pair, while “exo” being the vinyl strand pointing away the lone pair. Assumptions were made to ignore the possibility of olefin approaching from the sterically congested bottom face. Although TS-calculations were not conclusive [revealing a negligible ΔE value], based on aforementioned conformational preferences, simple molecular modelling suggests that the “endo” pathway seems to be better oriented conformationally than “exo” for a synchronous or concerted cyclopropanation transition state.

When pursuing other epoxidation-cyclopropanation examples, we appear to have reached the maximum in the diastereoselectivity as evident with cyclopropanation products **17–20**, although yields of for these tandem Epoxidation-cyclopropanations are quite high [Scheme 5]. While additional examples using ynamides **21** and **22** led to better diastereomeric ratios [Scheme 6], these reactions were not as effective giving either a lower yielding [see **23**] and/or a greater amount of keto-imide [see **24** and **26**].

Crystallographic data for 17-major [there are three independent molecules in the asymmetric unit all with the same relative C3-R, C4-R stereochemistry]

$C_{16}H_{17}NO_3$, $M = 271.31$, monoclinic, $P2_1$, $a = 11.821(3)$, $b = 5.9677(17)$, $c = 29.515(8)$ Å, $\alpha = 90$, $\beta = 94.257(4)$, $\gamma = 90^\circ$, $V = 2076.4(10)$ Å³, $T = 173(2)$ K, $Z = 6$, $\mu = 0.090$ mm⁻¹, 7331 ($R_{\text{int}} = 0.0474$), final R indices [$I > 2\sigma(I)$], $R_1 = 0.0432$, $wR_2 = 0.0940$, R indices (all data) $R_1 = 0.0682$, $wR_2 = 0.1056$.

Crystallographic data for 20-major

$C_{21}H_{19}NO_3$, $M = 333.37$, monoclinic, $P2_1$, $a = 10.959(2)$, $b = 6.0746(12)$, $c = 12.943(3)$ Å, $\alpha = 90$, $\beta = 102.432(3)$, $\gamma = 90^\circ$, $V = 841.4(3)$ Å³, $T = 100(2)$ K, $Z = 2$, $\mu = 0.009$ mm⁻¹, 1715 ($R_{\text{int}} = 0.0707$), final R indices [$I > 2\sigma(I)$], $R_1 = 0.0388$, $wR_2 = 0.0834$, R indices (all data) $R_1 = 0.0587$, $wR_2 = 0.0926$.

On the other hand, epoxidation-cyclopropanations using ynamides **27** and **28** were quite selective, leading to six-membered ring formation in cyclopropanation products **30** and **31** [Scheme 7]. In these reactions, although yields were lower, keto-imide formation was not a major concern. More importantly, stereochemical assignment of **30-major** through its single crystal X-ray structure is consistent with the proposed mechanistic model. From the molecular modeling, with an additional atom linkage [see **X** = CH₂ and NTs for ynamides **27** and **28**, respectively], the “endo” approach of the olefin during the cyclopropanation [see **33**] appears to be even better oriented conformationally than in the “exo” case [see **34**] for a synchronized transition state.

In addition, most revealingly, when using ynamide **29** [**X** = NTs, **R** = Me], the diastereomeric ratio of cyclopropane **32** dropped significantly relative to that of **31** [**X** = NTs, **R** = H]. This dramatic change suggests that the “endo” pathway as shown in **33** is being destabilized due to the enhanced steric interaction [**R** = Me vs. H].

Crystallographic data for 30-major

$C_{16}H_{17}NO_3$, $M = 271.31$, orthorhombic, $P2_12_12_1$, $a = 10.2183(9)$, $b = 10.4772(9)$, $c = 12.5802(11)$ Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90^\circ$, $V = 1346.8(2)$ Å³, $T = 123(2)$ K, $Z = 4$, $\mu = 0.093$ mm⁻¹, $1771(R_{\text{int}}=0.0298)$, final R indices [$I > 2\sigma(I)$], $R_1 = 0.0296$, $wR_2 = 0.0772$, R indices (all data) $R_1 = 0.0323$, $wR_2 = 0.0799$.

Conclusion

We have described here the first examples of diastereoselective intramolecular cyclopropanations of a *de novo* class of push-pull carbenes derived from DMDO-epoxidations of chiral ynamides. This reaction sequence essentially constitutes a tandem epoxidation-cyclopropanation that effectively gives rise to a series of structurally unique if not unprecedented amido-cyclopropanes. A plausible mechanistic model is also proposed here to reveal insights into this novel cyclopropanation process.

Experimental

General Information

All reactions were performed in flame-dried glassware under a nitrogen or argon atmosphere. Solvents were distilled prior to use. Reagents were used as purchased (Aldrich, Fluka), except where noted. Chromatographic separations were performed using Bodman 60 Å SiO₂. ¹H and ¹³C NMR spectra were obtained on Varian VI-400 and VI-500 spectrometers using CDCl₃ as solvent. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected or calibrated. Infrared spectra were collected on a Bruker Equinox 55/S FT-IR Spectrophotometer, and relative intensities are expressed qualitatively as s (strong), m (medium), and w (weak). TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 µm) and visualized using UV and a suitable chemical stain. Low-resolution mass spectra were obtained using an Agilent-1100-HPLC/MSD and can be either APCI or ESI, or were performed at University of Wisconsin Mass Spectrometry Laboratories. High-resolution mass spectral analyses were performed at University of Wisconsin Mass Spectrometry Laboratories. All spectral data obtained for new compounds are reported. X-Ray analyses were performed at the X-Ray facility in University of Minnesota.

General Procedures for Preparation of Ynamides via Cu(I)-Catalyzed Cross-Coupling

To a flame-dried 100-mL RB-flask were added a respective amide (2.07 g, 9.80 mmol), CuSO₄·5H₂O (368.0 mg, 1.47 mmol), 1,10-phenanthroline (529.0 mg, 2.94 mmol) and K₂CO₃ (3.38 g, 24.5 mmol), followed by anhyd toluene (15 mL) and the respective acetylenic bromide (3.20 g, 12.3 mmol). The flask was filled with Argon by three vacuum-flush cycles and the solution was heated in a 75 °C-oil bath overnight. When complete, the crude reaction mixture was cooled to rt, filtered through Celite™, and concentrated *in vacuo*. Purification of the crude residue using silica gel flash column chromatography (gradient eluent) gave the pure ynamide.

General Procedures for Intramolecular Cyclopropanations Through DMDO-Epoxidations of Ynamides

A respective ynamide (50.0 mg, 0.167 mmol) in acetone (12 mL) was stirred at rt. A solution of DMDO (6.0 mL, 0.11 M in acetone, 4.0 equiv) was added by syringe pump over 2 h (maintaining DMDO/acetone over dry ice). The reaction mixture was stirred for another 30 min before being filtered and concentrated *in vacuo*. The resulting mixture was purified by silica gel flash column chromatography (gradient elution: EtOAc in hexanes) to provide the desired amido cyclopropane as a pure product, or as an isomeric mixture. In most cases

of an isomeric mixture, when employing MPLC, the major isomer could be purified from the minor isomer with high *dr*, allowing unambiguous characterizations of the major isomer. Concise characterizations of the minor isomer are reported here whenever it could be sufficiently purified.

Ynamide 11— $R_f = 0.45$ [EtOAc]; $[\alpha]_D^{25} = -155$ (*c* 0.365, CH₂Cl₂); white solid: mp = 93–94 °C; ¹H NMR (400 MHz, CDCl₃) δ 2.27 (m, 2H), 2.36 (m, 2H), 3.73 (s, 3H), 4.23 (dd, 1H, *J* = 8.8, 7.2 Hz), 4.71 (dd, 1H, *J* = 8.8, 8.8 Hz), 5.00 (dd, 1H, *J* = 8.8, 7.2 Hz), 5.73 (ddd, 1H, *J* = 15.6, 1.6, 1.6 Hz), 6.80 (ddd, 1H, *J* = 15.6, 6.8, 6.8 Hz), 7.32–7.34 (m, 2H), and 7.39–7.47 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 17.6, 31.5, 51.7, 62.2, 70.3, 70.8, 71.3, 122.2, 127.0, 129.5, 129.6, 136.4, 146.9, 156.4, and 166.9; IR (film) cm⁻¹ 3030w, 2952w, 2918w, 2850w, 1759s, 1722m, 1408m, 1222m, 1069m, 949m, and 855w; mass spectrum (APCI): *m/e* (% relative intensity) 300 (100) (*M* + *H*)⁺, and 268 (95); HRMS (MALDI) *m/e* calcd for C₁₇H₁₇NO₄Na⁺ (*M* + Na⁺) 322.1055, found 322.1050.

Cyclopropane 12-Major— $R_f = 0.31$ [EtOAc]; $[\alpha]_D^{25} = -125$ (*c* 0.600, CH₂Cl₂); white solid: mp = 147–148 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.67 (dddd, 1H, *J* = 13.5, 9.5, 9.5, 5.0 Hz), 1.85 (ddd, 1H, *J* = 13.0, 8.0, 2.0 Hz), 2.03 (dd, 1H, *J* = 4.5, 4.0 Hz), 2.04 (ddd, 1H, *J* = 19.0, 9.5, 8.0 Hz), 2.10 (ddd, 1H, *J* = 19.0, 9.5, 2.0 Hz), 2.53 (d, 1H, *J* = 4.5 Hz), 3.76 (s, 3H), 4.20 (dd, 1H, *J* = 9.5, 8.5 Hz), 4.67 (dd, 1H, *J* = 9.0, 9.0 Hz), 4.91 (dd, 1H, *J* = 9.5, 9.0 Hz), 7.40–7.44 (m, 3H), and 7.45–7.48 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 21.0, 30.37, 30.40, 31.2, 52.5, 52.8, 61.1, 70.3, 128.5, 129.2, 129.7, 136.6, 158.4, 168.1, and 206.7; IR (film) cm⁻¹ 3063w, 2952w, 1759s, 1728s, 1402m, 1216m, 1092m, 1028m, and 933w; mass spectrum (APCI): *m/e* (% relative intensity) 316 (100) (*M* + *H*)⁺, and 284 (40); HRMS (MALDI) *m/e* calcd for C₁₇H₁₇NO₅Na⁺ (*M* + Na⁺) 338.1004, found 338.1001. **12-Minor**: pale yellow oil; $R_f = 0.22$ [EtOAc]; $[\alpha]_D^{25} = -65.8$ (*c* 0.480, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 1.39 (dddd, 1H, *J* = 13.0, 9.5, 9.5, 5.0 Hz), 1.81 (dd, 1H, *J* = 18.5, 9.5 Hz), 1.87 (dd, 1H, *J* = 13.0, 9.0 Hz), 1.96 (ddd, 1H, *J* = 18.5, 9.5, 9.0 Hz), 2.54 (d, 1H, *J* = 4.5 Hz), 2.60 (dd, 1H, *J* = 4.5, 4.5 Hz), 3.74 (s, 3H), 4.23 (dd, 1H, *J* = 9.5, 9.0 Hz), 4.64 (dd, 1H, *J* = 8.5, 8.5 Hz), 4.88 (dd, 1H, *J* = 9.5, 8.5 Hz), and 7.33–7.39 (m, 5H); ¹³C NMR (125 MHz, CDCl₃) δ 21.0, 30.5, 32.0, 32.9, 51.6, 52.9, 62.3, 70.8, 128.3, 129.4, 129.5, 136.4, 158.1, 169.3, and 206.0; IR (neat) cm⁻¹ 3062w, 2952w, 2907w, 1759s, 1742s, 1724s, 1439m, 1400m, 1243m, 1171m, 1089m, 1032m, and 902w; mass spectrum (APCI): *m/e* (% relative intensity) 316 (100) (*M* + *H*)⁺, and 284 (10); HRMS (MALDI) *m/e* calcd for C₁₇H₁₇NO₅Na⁺ (*M* + Na⁺) 338.1004, found 338.1005.

Ynamide 13—yellow oil; $R_f = 0.37$ [33% EtOAc/hexanes]; $[\alpha]_D^{25} = -136$ (*c* 1.87, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 2.11 (m, 2H), 2.26 (dd, 2H, *J* = 7.2, 7.2 Hz), 4.22 (dd, 1H, *J* = 8.8, 7.2 Hz), 4.71 (dd, 1H, *J* = 8.8, 8.8 Hz), 4.89 (m, 2H), 5.00 (dd, 1H, *J* = 8.4, 7.2 Hz), 5.63 (dddd, 1H, *J* = 16.8, 10.4, 6.4, 6.4 Hz), 7.34 (m, 2H), and 7.40–7.47 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 18.4, 33.0, 62.3, 69.7, 70.8, 72.3, 115.8, 127.1, 129.4, 129.5, 136.6, 136.8, and 156.5; IR (neat) cm⁻¹ 3068w, 3035w, 2979w, 2918w, 2848w, 2267w, 1765s, 1641w, 1495w, 1477w, 1457w, 1404m, 1328w, 1186m, 1106m, 1081m, 1036m, and 1001m; mass spectrum (APCI): *m/e* (% relative intensity) 242 (100) (*M* + *H*)⁺, and 198 (10); HRMS (MALDI) *m/e* calcd for C₁₅H₁₅NO₂Na⁺ (*M* + Na⁺) 264.0995, found 264.0999.

Cyclopropane 14-Major— $R_f = 0.52$ [EtOAc]; $[\alpha]_D^{25} = -215$ (*c* 0.887, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 1.49 (dd, 1H, *J* = 5.5, 5.5 Hz), 1.53 (m, 1H), 1.77 (m, 3H), 2.05 (m, 2H), 4.19 (dd, 1H, *J* = 9.0, 9.0 Hz), 4.66 (dd, 1H, *J* = 9.0, 9.0 Hz), 4.92 (dd, 1H, *J* = 9.0, 9.0 Hz), 7.32–7.34 (m, 2H), and 7.38–7.41 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 19.8, 21.1, 27.5, 30.5, 47.7, 60.7, 69.8, 127.9, 129.3, 129.6, 137.8, 158.4, and 208.8; IR (film)

cm⁻¹ 3061w, 3036w, 3008w, 2947w, 2916w, 2882w, 1758s, 1726s, 1459m, 1413m, 1264m, 1216m, 1170m, 1080m, 1029m, 944w, and 923w; mass spectrum (APCI): m/e (% relative intensity) 258 (100) (M+1)⁺, and 214 (7); HRMS (MALDI) m/e calcd for C₁₅H₁₅NO₃Na⁺ (M+Na⁺) 280.0944, found 280.0946. **14-Minor**: *R_f* = 0.52 [EtOAc]; ¹H NMR (500 MHz, CDCl₃) δ 0.96 (m, 2H), 1.86 (ddd, 1H, *J* = 12.5, 7.5, 2.5 Hz), 2.05 (m, 2H), 2.23 (m, 1H), 2.36 (ddd, 1H, *J* = 8.0, 5.5, 5.5 Hz), 4.19 (dd, 1H, *J* = 9.0, 8.0 Hz), 4.71 (dd, 1H, *J* = 9.0, 9.0 Hz), 5.23 (dd, 1H, *J* = 8.5, 8.5 Hz), 7.31–7.33 (m, 2H), and 7.38–7.40 (m, 3H); mass spectrum (APCI): m/e (% relative intensity) 258 (100) (M + H)⁺, and 214 (5); HRMS (MALDI) m/e calcd for C₁₅H₁₅NO₃Na⁺ (M + Na⁺) 280.0944, found 280.0945.

Cyclopropane 17-Major—white waxy solid; *R_f* = 0.15 [50% EtOAc/hexanes]; [α]_D²⁵ = –78.9 (*c* 1.27, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 1.42 (dd, 1H, *J* = 5.5, 5.5 Hz), 1.63 (dd, 1H, *J* = 8.5, 6.0 Hz), 1.96 (m, 1H), 2.09–2.27 (m, 3H), 2.33 (ddd, 1H, *J* = 8.5, 5.0, 5.0 Hz), 2.90 (dd, 1H, *J* = 14.0, 9.5 Hz), 3.15 (dd, 1H, *J* = 14.0, 5.0 Hz), 4.01 (dddd, 1H, *J* = 9.5, 8.0, 6.0, 5.0 Hz), 4.05 (dd, 1H, *J* = 8.5, 6.0 Hz), 4.19 (dd, 1H, *J* = 8.0, 8.0 Hz), 7.16 (m, 2H), 7.25 (m, 1H), and 7.31 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 19.2, 21.0, 30.2, 30.9, 39.8, 47.2, 57.4, 67.5, 127.3, 129.1, 136.2, 157.8, and 209.1 (one carbon signal missing due to overlap at 129.1; IR (film) cm⁻¹ 3061w, 3029w, 3003w, 2947w, 2918w, 2883w, 1750s, 1727s, 1603w, 1497w, 1454w, 1422m, 1263m, 1226m, 1173m, 1077m, 1031m, 1021m, 988w, 947w, and 922w; mass spectrum (APCI): m/e (% relative intensity) 272 (100) (M + H)⁺; HRMS (MALDI) m/e calcd for C₁₆H₁₇NO₃Na⁺ (M + Na⁺) 294.1101, found 294.1104. **17-Minor**: yellow oil; *R_f* = 0.12 [50 % EtOAc/hexanes]; ¹H NMR (500 MHz, CDCl₃) δ 1.53 (dd, 1H, *J* = 5.5, 5.5 Hz), 1.62 (dd, 1H, *J* = 8.5, 5.5 Hz), 1.92 (m, 1H), 2.02 (m, 1H), 2.13 (m, 2H), 2.44 (ddd, 1H, *J* = 8.5, 5.0, 5.0 Hz), 2.65 (dd, 1H, *J* = 13.5, 9.0 Hz), 3.19 (dd, 1H, *J* = 13.5, 5.5 Hz), 3.97 (dd, 1H, *J* = 9.0, 7.5 Hz), 4.22 (dd, 1H, *J* = 8.5, 8.5 Hz), 4.45 (m, 1H), 7.15 (m, 2H), 7.26 (m, 1H), and 7.32 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 21.1, 21.8, 27.5, 31.3, 39.8, 46.9, 57.6, 67.9, 127.4, 129.07, 129.13, 135.8, 158.3, and 210.7; IR (neat) cm⁻¹ 3087w, 3060w, 3029w, 3004w, 2947w, 2918w, 1754s, 1727s, 1604w, 1513w, 1497w, 1478w, 1467w, 1425m, 1365w, 1289m, 1264m, 1228m, 1181m, 1161m, 1073m, 1027m, 943w, and 921w; mass spectrum (APCI): m/e (% relative intensity) 272 (100) (M + H)⁺; HRMS (MALDI) m/e calcd for C₁₆H₁₇NO₃Na⁺ (M + Na⁺) 294.1101, found 294.1105.

Cyclopropane 18-Major—white powder; *R_f* = 0.50 [EtOAc]; [α]_D²⁵ = –5.93 (*c* 0.840, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 1.06 (dddd, 1H, *J* = 13.5, 9.5, 9.5, 5.0 Hz), 1.75 (dd, 1H, *J* = 13.0, 9.0 Hz), 1.86 (dd, 1H, *J* = 18.5, 9.5 Hz), 1.98 (ddd, 1H, *J* = 18.5, 9.0, 9.0 Hz), 2.48 (dd, 1H, *J* = 4.5, 4.5 Hz), 2.55 (d, 1H, *J* = 4.0 Hz), 2.89 (m, 2H), 3.68 (s, 3H), 4.08–4.17 (m, 2H), 4.46 (m, 1H), 7.17 (m, 2H), 7.25–7.28 (m, 1H), and 7.29–7.36 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 20.4, 30.6, 33.36, 33.43, 41.4, 52.8, 57.8, 68.7, 69.9, 127.5, 129.1, 129.3, 136.3, 158.5, 169.1, and 206.6; IR (film) cm⁻¹ 3062w, 3029w, 2952w, 2909w, 1754s, 1738s, 1726s, 1439m, 1283m, 1241m, 1199m, 1175m, 1093w, 1067w, and 1030w; mass spectrum (APCI): m/e (% relative intensity) 330 (100) (M + H)⁺, and 228 (10); HRMS (MALDI) m/e calcd for C₁₈H₁₉NO₅Na⁺ (M + Na⁺) 352.1155, found 352.1154.

Cyclopropane 19-Major—yellow oil; *R_f* = 0.25 [50% EtOAc/hexanes]; [α]_D²³ = 36.6 [*c* = 3.0, CH₂Cl₂]; ¹H NMR (500 MHz, CDCl₃) δ 0.88 (d, 3H, *J* = 7.0 Hz), 1.05 (d, 3H, *J* = 7.0 Hz), 2.07 (m, 1H), 2.11–2.29 (m, 3H), 2.32 (br, 1H), 2.55 (d, 1H, *J* = 4.7 Hz), 2.89 (brt, 1H, *J* = 4.7 Hz), 3.66 (br, 1H), 3.74 (s, 3H), 4.08 (dd, 1H, *J* = 7.0, 7.0 Hz), 4.25 (t, 1H, *J* = 9.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 14.6, 18.7, 21.2, 28.7, 30.7, 30.8, 52.9, 53.1, 61.2, 63.5, 159.0, 168.3, 207.0; IR (thin film) cm⁻¹ 2956w, 2926w, 2878w, 1754s, 1727s; mass spectrum (APCI): m/e (% relative intensity) 282 (100) (M + H)⁺; HRMS (MALDI) m/e calcd for C₁₄H₁₉NO₅Na⁺ (M + Na⁺) 304.1155, found 304.1157. **19-Minor**: *R_f* = 0.13 [50% EtOAc/hexanes]; ¹H NMR (400 MHz, CDCl₃) δ 0.91 (d, 3H, *J* = 7.0 Hz), 0.96 (d, 3H, *J* =

7.0 Hz), 1.71–1.77 (m, 1H), 2.15–2.26 (m, 4H), 2.67 (d, 1H, $J = 4.4$ Hz), 2.77–2.78 (m, 1H), 3.64–3.68 (m, 1H), 3.71 (s, 3H), 4.13 (dd, 1H, $J = 6.0, 8.4$ Hz), 4.31 (dd, 1H, $J = 8.4, 9.6$ Hz); mass spectrum (APCI): m/e (% relative intensity) 282.1 (100) ($M+H$)⁺.

Cyclopropane 20-Major—white powder; $R_f = 0.50$ [EtOAc]; $[\alpha]_D^{25} = +174$ (c 0.900, CH_2Cl_2); 1H NMR (400 MHz, $CDCl_3$) δ 1.53 (dd, 1H, $J = 5.6, 5.6$ Hz), 1.73–1.86 (m, 3H), 1.94 (dd, 1H, $J = 8.4, 6.0$ Hz), 2.09 (m, 2H), 5.13 (d, 1H, $J = 8.8$ Hz), 5.94 (d, 1H, $J = 8.8$ Hz), 6.85 (m, 2H), 6.95–6.98 (m, 2H), and 7.12 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 21.0, 27.5, 30.4, 48.4, 65.3, 79.7, 126.3, 128.1, 128.26, 128.30, 128.6, 134.9, 135.1, 158.4, and 209.0 (one carbon signal missing due to overlap (128.1)); IR (film) cm^{-1} 3091w, 3069w, 3038w, 2954w, 2937w, 2878w, 1741s, 1726s, 1500m, 1454m, 1420m, 1266m, 1235m, 1217m, 1201m, 1172m, 1106w, 1092w, 1078w, 1039w, 1023m, 998w, 969w, 949w, and 924m; mass spectrum (APCI): m/e (% relative intensity) 334 (100) ($M + H$)⁺, and 290 (95); HRMS (MALDI) m/e calcd for $C_{21}H_{19}NO_3Na^+$ ($M + Na^+$) 356.1257, found 356.1257.

20-Minor: $R_f = 0.47$ [EtOAc]; 1H NMR (500 MHz, $CDCl_3$) (two aliphatic proton signals missing, only resolved peaks presented due to ambiguity resulting from overlap) δ 1.02 (dd, 1H, $J = 5.5, 5.5$ Hz), 1.12 (dd, 1H, $J = 8.5, 6.0$ Hz), 2.15 (ddd, 1H, $J = 18.5, 9.0, 1.5$ Hz), 2.29 (dddd, 1H, $J = 12.5, 9.5, 9.5, 5.0$ Hz), 2.54 (ddd, 1H, $J = 8.5, 5.0, 5.0$ Hz), 5.35 (d, 1H, $J = 8.5$ Hz), 6.06 (d, 1H, $J = 8.5$ Hz), 6.83 (m, 2H), 6.96 (m, 2H), and 7.08 (m, 6H); mass spectrum (APCI): m/e (% relative intensity) 334 (100) ($M + H$)⁺, and 290 (95); HRMS (MALDI) m/e calcd for $C_{21}H_{19}NO_3Na^+$ ($M + Na^+$) 356.1257, found 356.1251.

Ynamide 21—yellow oil; $R_f = 0.26$ [33% EtOAc/hexanes]; $[\alpha]_D^{25} = -140$ (c 0.30, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 2.21–2.29 (m, 4H), 3.70 (s, 3H), 4.16 (dd, 1H, $J = 9.0, 5.5$ Hz), 4.40 (d, 1H, $J = 7.0$ Hz), 4.46 (dd, 1H, $J = 8.5, 8.5$ Hz), 4.79 (ddd, 1H, $J = 8.5, 7.0, 5.5$ Hz), 5.84 (ddd, 1H, $J = 15.5, 1.5, 1.5$ Hz), 6.89 (ddd, 1H, $J = 15.5, 7.0, 7.0$ Hz), 7.18–7.20 (m, 2H), 7.24–7.27 (m, 4H), and 7.30–7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 31.4, 51.7, 53.8, 60.0, 66.7, 70.7, 72.3, 122.2, 127.6, 127.9, 128.6, 128.7, 129.0, 129.3, 138.9, 139.9, 147.2, 156.4, and 167.0; IR (neat) cm^{-1} 3063w, 3031w, 2983w, 2952w, 2910w, 2272w, 1772s, 1722s, 1660m, 1415m, 1282m, 1201s, 1160m, 1121m, and 1035m; mass spectrum (APCI): m/e (% relative intensity) 390 (100) ($M + H$)⁺, 358 (20), and 254 (10); HRMS (MALDI) m/e calcd for $C_{24}H_{23}NO_4Na^+$ ($M + Na^+$) 412.1519, found 412.1503.

Ynamide 22—yellow oil; $R_f = 0.35$ [50% EtOAc/hexanes]; $[\alpha]_D^{23} = 15.3$ [$c = 4.0$, CH_2Cl_2]; 1H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, 3H, $J = 6.8$ Hz), 2.41–2.49 (m, 2H), 2.49–2.54 (m, 2H), 3.72 (s, 3H), 4.30 (dq, 1H, $J = 6.8, 13.6$ Hz), 5.69 (d, 1H, $J = 8.0$ Hz), 5.89 (dt, 1H, $J = 1.7, 15.6$ Hz), 6.97 (dt, 1H, $J = 6.4, 15.2$ Hz), 7.25 (m, 1H), 7.34–7.44 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 17.8, 31.7, 51.8, 58.3, 70.5, 70.7, 79.8, 122.4, 126.2, 129.0, 129.2, 134.2, 147.1, 156.2, 167.0; IR (thin film) cm^{-1} 3034w, 2951w, 1750s, 1497m; mass spectrum (APCI): m/e (% relative intensity) 314 (100) ($M + H$)⁺; HRMS (MALDI) m/e calcd for $C_{18}H_{19}NO_4Na$ ($M + Na$)⁺ 336.1206, found 336.1204.

Cyclopropane 23-Major—pale yellow oil; $R_f = 0.15$ [50% EtOAc/hexanes]; $[\alpha]_D^{25} = +4.19$ (c 0.535, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 0.46 (dddd, 1H, $J = 13.5, 10.0, 10.0, 5.0$ Hz), 1.50 (m, 2H), 1.80 (ddd, 1H, $J = 18.5, 9.0, 9.0$ Hz), 2.42 (dd, 1H, $J = 4.5, 4.5$ Hz), 2.45 (d, 1H, $J = 4.5$ Hz), 3.68 (s, 3H), 3.96 (dd, 1H, $J = 9.0, 5.5$ Hz), 4.12 (d, 1H, $J = 10.5$ Hz), 4.37 (dd, 1H, $J = 9.0, 9.0$ Hz), 4.66 (ddd, 1H, $J = 10.5, 9.0, 5.5$ Hz), 7.18–7.23 (m, 4H), 7.27–7.31 (m, 4H), and 7.33–7.36 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.1, 30.4, 34.3, 34.7, 52.8, 53.7, 57.7, 59.9, 67.8, 127.5, 127.6, 127.7, 128.8, 129.3, 129.5, 141.3, 141.5, 159.0, 169.5, and 206.5; IR (neat) cm^{-1} 3060w, 3029w, 2952w, 2911w, 1757s, 1741s, 1722s, 1494w, 1438m, 1407m, 1383m, 1281m, 1237s, 1199m, 1175s, 1096m, 1068m, and

1031m; mass spectrum (APCI): m/e (% relative intensity) 406 (100) ($M + H$)⁺; HRMS (MALDI) m/e calcd for $C_{24}H_{23}NO_5Na^+$ ($M + Na^+$) 428.1468, found 428.1484.

Keto-Imide 24—pale yellow oil; $R_f = 0.48$ [50% EtOAc/hexanes]; $[\alpha]_D^{25} = -71.9$ (c 0.795, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 2.52 (m, 2H), 2.62 (ddd, 1H, $J = 18.0, 8.0, 6.0$ Hz), 2.69 (ddd, 1H, $J = 18.0, 8.0, 7.0$ Hz), 3.74 (s, 3H), 4.53 (dd, 1H, $J = 9.5, 3.0$ Hz), 4.59 (dd, 1H, $J = 9.5, 8.0$ Hz), 4.76 (d, 1H, $J = 6.5$ Hz), 5.25 (ddd, 1H, $J = 8.0, 6.5, 3.0$ Hz), 5.86 (ddd, 1H, $J = 15.5, 1.5, 1.5$ Hz), 6.93 (ddd, 1H, $J = 15.5, 6.5, 6.5$ Hz), 7.14 (d, 2H, $J = 7.5$ Hz), 7.21 (m, 2H), 7.28 (m, 1H), and 7.32–7.40 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.9, 37.5, 51.2, 51.7, 55.6, 67.5, 122.3, 127.7, 128.5, 128.6, 129.1, 129.40, 129.41, 137.5, 139.0, 146.5, 153.7, 166.6, 166.9, and 195.6; IR (neat) cm^{-1} 3061w, 3029w, 2982w, 2951w, 2903w, 1786s, 1720s, 1658m, 1496w, 1450w, 1436w, 1393m, 1342m, 1275m, 1204s, 1128m, 1072m, and 1031m; mass spectrum (APCI): m/e (% relative intensity) 422 (55) ($M + H$)⁺, 390 (50), and 254 (100); HRMS (MALDI) m/e calcd for $C_{24}H_{23}NO_6Na^+$ ($M + Na^+$) 444.1323, found 444.4323.

Cyclopropane 25-Major— $R_f = 0.25$ [50% EtOAc/hexanes]; $[\alpha]_D^{25} = 7.60$ [c 2.0, CH_2Cl_2]; 1H NMR (500 MHz, $CDCl_3$) δ 0.86 (d, 3H, $J = 6.5$ Hz), 2.93 (m, 2H), 2.26 (m, 2H), 2.37 (br, 1H), 2.55 (d, 1H, $J = 4.7$ Hz), 2.92 (brt, 1H, $J = 4.0$ Hz), 4.04 (br, 1H), 5.56 (d, 1H, $J = 8.5$ Hz), 7.27–7.31 (m, 2H), 7.32–7.42 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.9, 21.1, 30.4, 30.9, 52.5, 53.0, 56.1, 79.9, 127.0, 128.7, 135.1, 158.0, 168.2, 206.8; IR (thin film) cm^{-1} 3038w, 2925w, 2854w, 1758s, 1733s; mass spectrum (APCI): m/e (% relative intensity) 330 (100) ($M + H$)⁺; HRMS (MALDI) m/e calcd for $C_{18}H_{19}NO_5Na$ ($M + Na$)⁺ 352.1161, found 352.1160.

Keto-Imide 26— $R_f = 0.10$ [50% EtOAc/hexane]; $[\alpha]_D^{25} = 6.00$ [c 1.80, CH_2Cl_2]; 1H NMR (400 MHz, $CDCl_3$) δ 1.00 (d, 3H, $J = 6.8$ Hz), 2.66 (dq, 2H, $J = 1.1, 6.5$ Hz), 2.93 (t, 2H, $J = 7.6$ Hz), 3.74 (s, 3H), 4.72 (p, 1H, $J = 6.8$ Hz), 5.85 (d, 1H, $J = 7.6$ Hz), 5.92 (dt, 1H, $J = 1.4, 15.6$ Hz), 7.00 (dt, 1H, $J = 6.8, 13.6$ Hz), 7.28–7.48 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 17.8, 25.1, 37.4, 51.8, 54.2, 81.5, 122.4, 126.0, 128.8, 129.1, 129.5, 132.7, 153.4, 167.0, 195.7; IR (thin film) cm^{-1} 3388bs, 2957s, 1695s, 1443s, 1250s; mass spectrum (APCI): m/e (% relative intensity) 346 (100) ($M + H$)⁺; HRMS (MALDI) m/e calcd for $C_{18}H_{19}NO_6Na$ ($M + Na$)⁺ 368.1110, found 368.1105.

Ynamide 27—yellow oil; $R_f = 0.35$ [50 % EtOAc/hexanes]; $[\alpha]_D^{25} = -123$ (c 1.31, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 1.44 (m, 2H), 1.91 (dddd, 2H, $J = 8.5, 7.0, 7.0, 1.5, 1.5$ Hz), 2.17 (m, 2H), 4.22 (dd, 1H, $J = 9.0, 7.0$ Hz), 4.71 (dd, 1H, $J = 9.0, 9.0$ Hz), 4.87 (dddd, 1H, $J = 17.0, 2.0, 1.5, 1.5$ Hz), 4.89 (dddd, 1H, $J = 10.5, 2.0, 1.0, 1.0$ Hz), 5.00 (dd, 1H, $J = 9.0, 7.0$ Hz), 5.65 (dddd, 1H, $J = 17.0, 10.5, 6.5, 6.5$ Hz), 7.33–7.35 (m, 2H), and 7.39–7.46 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 27.8, 32.5, 62.3, 69.5, 70.8, 72.6, 115.2, 127.0, 129.4, 129.5, 136.5, 137.9, and 156.5; IR (neat) cm^{-1} 3068w, 3035w, 2930w, 2861w, 1765s, 1405m, 1186m, 1107m, 1001m, and 914w; mass spectrum (APCI): m/e (% relative intensity) 256 (100) ($M + H$)⁺, and 164 (15); HRMS (MALDI) m/e calcd for $C_{16}H_{17}NO_2Na$ ($M + Na$)⁺ 278.1157, found 278.1155.

Ynamide 28—pale yellow oil; $R_f = 0.31$ [100 % EtOAc/hexanes]; $[\alpha]_D^{25} = -119$ (c 1.03, CH_2Cl_2); 1H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 3.24 (br dd, 1H, $J = 14.2, 7.2$ Hz), 3.59 (dddd, 1H, $J = 14.2, 6.0, 1.2, 1.2, 1.2$ Hz), 4.00 (d, 1H, $J = 18.4$ Hz), 4.15 (dd, 1H, $J = 8.8, 7.2$ Hz), 4.23 (dd, 1H, $J = 18.4, 0.8$ Hz), 4.66 (dd, 1H, $J = 8.8, 8.8$ Hz), 4.80 (m, 1H), 4.82 (dddd, 1H, $J = 16.8, 1.2, 1.2, 1.2$ Hz), 5.03 (dddd, 1H, $J = 10.0, 1.2, 1.2, 1.2$ Hz), 5.53 (dddd, 1H, $J = 17.2, 10.0, 7.2, 6.0$ Hz), 7.10–7.12 (m, 2H), 7.32 (d, 2H, $J = 8.0$ Hz), 7.36–7.40 (m, 3H), and 7.70 (d, 2H, $J = 8.4$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 36.3, 48.9,

61.9, 66.2, 70.9, 74.6, 120.1, 126.9, 128.1, 129.5, 129.75, 129.84, 131.9, 136.0, 136.2, 143.6, and 155.5; IR (neat) cm^{-1} 3067w, 3035w, 2985w, 2914w, 1776s, 1405m, 1342m, 1159s, 1105m, 1091m, 993w, and 893w; mass spectrum (APCI): m/e (% relative intensity) 411 (100) ($M + H$)⁺, and 232 (20); HRMS (MALDI) m/e calcd for $C_{22}H_{22}N_2O_4SNa$ ($M + Na$)⁺ 433.1198, found 433.1194.

Ynamide 29—yellow oil; R_f = 0.70 [50 % EtOAc/hexane]; $[\alpha]_D^{25}$ = -113.8 [c 1.28, CH_2Cl_2]; 1H NMR (400 MHz, $CDCl_3$) δ 1.75 (s, 3H), 2.42 (s, 3H), 3.10 (d, 1H, J = 14.0 Hz), 3.46 (d, 1H, J = 13.6 Hz), 3.92 (d, 1H, J = 18.4 Hz), 4.12 (dd, 1H, J = 7.2, 9.2 Hz), 4.21 (dd, 1H, J = 0.8, 18.4 Hz), 4.43 (s, 1H), 4.66 (dd, 1H, J = 8.8, 8.8 Hz), 4.75–4.79 (m, 2H), 7.05–7.07 (m, 2H), 7.32–7.38 (m, 5H), 7.70–7.72 (d, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 21.8, 36.0, 52.2, 61.9, 66.1, 71.0, 74.8, 115.7, 126.9, 128.2, 129.5, 129.7, , 129.8, 136.0, 136.2, 139.0, 143.6, 155.5; IR (Thin film) cm^{-1} 3548m, 3066brs, 2980s, 2914s, 2360m, 2262s, 1775s, 1158s; mass spectrum (APCI): m/e (% relative intensity) 425.1 (100) ($M + H$)⁺, 262.1 (40); HRMS (MALDI) m/e calcd for $C_{23}H_{24}N_2O_4SNa$ ($M + Na$)⁺ 447.1355, found 447.1360.

Cyclopropane 30-Major— R_f = 0.19 [100 % EtOAc/hexanes]; $[\alpha]_D^{25}$ = -195 (c 0.770, CH_2Cl_2); white solid; mp = 138–140 °C; 1H NMR (400 MHz, $CDCl_3$) δ 1.25 (m, 1H), 1.37 (dddd, 1H, J = 13.2, 8.0, 8.0, 3.6 Hz), 1.58 (m, 2H), 1.66 (m, 1H), 1.74 (m, 2H), 2.11 (ddd, 1H, J = 18.4, 8.8, 8.8 Hz), 2.36 (ddd, 1H, J = 18.8, 5.2, 5.2 Hz), 4.19 (dd, 1H, J = 8.8, 8.8 Hz), 4.65 (dd, 1H, J = 8.8, 8.8 Hz), 4.87 (dd, 1H, J = 8.8, 8.8 Hz), 7.30–7.34 (m, 2H), and 7.37–7.42 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.1, 18.8, 21.8, 26.4, 36.3, 46.3, 60.8, 69.5, 128.2, 129.3, 129.5, 138.0, 159.3, and 204.4; IR (film) cm^{-1} 3033w, 2918w, 2863w, 1759s, 1687m, 1402m, 1217m, 1038m, 915w, and 878w; mass spectrum (APCI): m/e (% relative intensity) 272 (100) ($M + H$)⁺; HRMS (MALDI) m/e calcd for $C_{16}H_{17}NO_3Na$ ($M + Na$)⁺ 294.1106, found 294.1104.

Cyclopropane 31-Major—pale yellow oil; R_f = 0.19 [EtOAc]; $[\alpha]_D^{25}$ = -116 (c 0.720, CH_2Cl_2); 1H NMR (500 MHz, $CDCl_3$) δ 1.51 (br m, 1H), 1.75 (dd, 1H, J = 8.5, 6.5 Hz), 2.18 (ddd, 1H, J = 6.5, 6.5, 1.0 Hz), 2.45 (t, 3H, J = 0.5 Hz), 2.52 (br d, 1H, J = 12.0 Hz), 3.02 (d, 1H, J = 18.5 Hz), 3.89 (ddd, 1H, J = 12.5, 2.0, 1.0 Hz), 4.10 (dd, 1H, J = 18.5, 1.5 Hz), 4.21 (dd, 1H, J = 8.5, 8.5 Hz), 4.63 (dd, 1H, J = 9.0, 9.0 Hz), 4.75 (dd, 1H, J = 9.0, 9.0 Hz), 7.30–7.32 (m, 2H), 7.33 (dq, 2H, J = 8.5, 0.5 Hz), 7.36–7.38 (m, 3H), and 7.57 (d, 2H, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.5, 21.8, 25.8, 43.1, 45.2, 53.1, 60.4, 69.9, 127.7, 128.1, 129.4, 129.8, 130.3, 133.0, 137.3, 144.7, 158.5, and 197.2; IR (neat) cm^{-1} 3063w, 3035w, 2986w, 2912w, 2855w, 1756s, 1707m, 1597w, 1403m, 1348m, 1163s, 1037m, and 937m; mass spectrum (APCI): m/e (% relative intensity) 427 (100) ($M + H$)⁺; HRMS (MALDI) m/e calcd for $C_{22}H_{22}N_2O_5SNa$ ($M + Na$)⁺ 449.1147, found 449.1140.

Cyclopropane 32-Major—yellow oil; R_f = 0.50 [5% MeOH/ CH_2Cl_2]; $[\alpha]_D^{25}$ = $+29.7$ [c 0.32, CH_2Cl_2]; 1H NMR (500 MHz, $CDCl_3$) δ 1.13 (d, 1H, J = 6.5 Hz), 1.30 (s, 3H), 2.16 (d, 1H, J = 6.5 Hz), 2.45 (s, 3H), 2.77 (d, 1H, J = 12.0 Hz), 2.97 (d, 1H, J = 18.0 Hz), 3.96 (d, 1H, J = 12.0 Hz), 4.0 (d, 1H, J = 18.0 Hz), 4.33 (dd, 1H, J = 6.0, 6.0 Hz), 4.66 (m, 2H), 7.33–7.39 (m, 5H), 7.49–7.50 (m, 2H), 7.57 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 21.8, 22.1, 31.8, 48.7, 48.9, 53.4, 61.5, 71.2, 127.7, 128.3, 129.2, 129.6, 130.3, 132.1, 136.8, 144.9, 157.6, 195.1; IR (Thin film) cm^{-1} 3064brs, 2981s, 2924s, 2852s, 2360s, 2341s, 1752s, 1709s, 1164s; mass spectrum (APCI): m/e (% relative intensity) 441.1 (100) ($M + H$)⁺, 285.1 (54), 255.1 (23); HRMS (MALDI) m/e calcd for $C_{23}H_{24}N_2O_5SNa$ ($M + Na$)⁺ 463.1304, found 463.1300.

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Figure.
A Proposed Mechanistic Model

Scheme 1.*De Novo* Carbenes from Epoxidations of Ynamides.

Scheme 2.
Synthesis of Ynamide **11**.

Scheme 3.
Epoxidation and Cyclopropanation of Ynamides **11** and **13**.

Scheme 4.
A Proposed Mechanistic Model.

Scheme 5.
Ynamide-Epoxidation-Cyclopropanation Examples.

Scheme 6.
Attempts of Improving the Diastereoselectivity.

Scheme 7.
Epoxidation–Cyclopropanations of Ynamides **27–29**.