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Spirastrellolide Studies. Synthesis of the C(1)–C(25) Southern Hemispheres of Spirastrellolides A and B, Exploiting Anion Relay Chemistry

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Abstract

Construction of the C(1)–C(25) southern fragments of both spirastrellolide A and B are described. Highlights of the syntheses include effective use of the three component anion relay chemistry (ARC) tactic recently introduced by our laboratory, a stereoselective spirocyclization via concomitant Ferrier reaction to elaborate the **BC** spiroketal and use of two dithiane unions to install the **A** ring as well as C(22)–C(25) fragment. The synthesis proceeded with longest linear sequences of 33 and 32 steps respectively for spirastrellolide A and spirastrellolide B.

1. Introduction

Spirastrellolides A and B (**1** and **2**) comprise two architecturally unique polyketide natural products, isolated by Andersen and co-workers in 2003 and 2006 respectively from *Spirastrella coccinea*, a marine sponge endemic to the Caribbean (Scheme 1).¹ In 2004 extensive NMR studies permitted assignment of relative configurations of the three major segments of **1** [cf. C(3)–C(7), C(9)–C(24) and C(27)–C(38)].^{1b} The stereochemical relationship between the segments of both spirastrellolides A and B, except for the configuration at C(46), as well as the assignment of absolute configuration of the macrolide core followed in 2007 based on an X-ray analysis of a crystalline derivative obtained from a degradation product of spirastrellolide B (**2**).^{1c} Assignment of the final stereochemical issue, the C(46) stereogenic center was achieved in 2007 upon isolation of the cleaved side-chain fragment derived from a related congener (Spirastrellilide D).^{1d}

Spirastrellolide A (**1**) displays selective inhibition of protein phosphatase PP2A (IC₅₀ = 1 nM for PP2A and 50 nM for PP1), that in turn leads to premature cell entry into mitosis and thereby mitotic arrest.^{1a,b} Similar biological effects have been observed with Ser/Thr phosphatase inhibitors such as fostriecin, okadaic acid and calyculin A.^{1b,c} The biological properties of spirastrellolide B (**2**) have not been reported.

The architectural complexity and potential biomedical significance, in conjunction with the scarcity of natural materials have attracted the attention of the chemical community. To date,

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Supplementary Data

Spectroscopic and analytical data and selected experimental procedures associated with this article can be found in the online version.

one elegant total synthesis of spirastrellolide A methyl ester² by the Paterson group, as well as a number of synthetic studies have been reported.³ Herein we disclose a detailed account of our studies leading to construction of the C(1)–C(25) southern hemisphere of both spirastrellolides A and B.⁴

From the retrosynthetic perspective, disconnection of both A and B (**1** and **2**) at three strategic locations, the macrocyclic lactone, the C(25)–C(26) σ -bond, and the C(40)–C(41) trans π -bond (Scheme 1), suggests three potential advanced synthetic targets: side chain **3**, **DEF** bis-spiro ketal **4**, and **ABC** ring fragment **5**. Further disconnection of **5** reveals A-ring dithiane **6**, **BC** spiroketal **7** and known dithiane (–)-**8**. For construction of **7** we envisioned a 1,3-*anti* reduction of the C(13) ketone in diketone **9**, followed by acid-catalyzed spiroketalization. Construction of **9** in turn would call upon Type II Anion Relay Chemistry (ARC),⁵ an effective multicomponent union tactic recently introduced by our laboratory, that would employ commercially available epoxide (–)-**10**, bifunctional linchpin **11**, and dithiane **12**.

2. Results and Discussion

2.1 Construction of the C(10)–C(22) Spiroketal Fragments of Spirastrellolides A and B (**1** and **2**)

We began the synthesis by focusing on the C(10)–C(22) spirocyclic fragments of spirastrellolides A and B (Scheme 2). Construction of the requisite dithiane (+)-**12** entailed selective 1,2-diol protection of known triol (–)-**136** as an acetonide, the latter readily prepared in four steps from commercially available (–)-tri-*O*-acetyl- β -glucal, followed by methylation of the remaining hydroxy substituent.

For the ARC tactic, construction of bifunctional linchpin **11** began with *C*-silylation of known dithiane (+)-**157** employing TESCl, followed by acidic hydrolysis of the acetonide to provide diol (–)-**17** (Scheme 3). Numerous methods were explored for the direct conversion of the diol to the epoxide. Surprisingly, the one pot Fraser-Reid protocol⁸ lead to predominant Brook rearrangement, while use of two step protocols relying on activation of the primary hydroxyl group resulted in extensive decomposition, presumably due to formation of sulfonium ion **20**.⁹ We therefore explored activation of the secondary hydroxyl instead of the primary.

Chemoselective acetylation of (–)-**17**, followed in turn by mesylation of the secondary hydroxyl and ring closure employing potassium carbonate furnished epoxide (–)-**18** in 64% overall yield. That (–)-**18** is epimeric at C(15) relative to the proposed retron (**11**) held little consequence since the C(15) hydroxyl would be eliminated later in the sequence to install the C(15)–C(16) olefin.

Unfortunately epoxide (–)-**18** did not display the expected reactivity with dithiane (+)-**12** required in the ARC coupling protocol. Even with extensive experimentation, varying the base, solvents and temperature, the yield of the coupled product (–)-**21** was modest at best (ca. 20–30%) (Scheme 4). The corresponding linchpin (–)-**11**, the C(15) diastereomer of (–)-**18**, prepared in analogous fashion, also proved unreactive. *In silico* conformational analysis employing MacroModel® suggested that the methyl substituent at C(14) causes the epoxide methylene to become buried within the dithiane ring.

Having experienced difficulties with both linchpins in implementing the initially proposed ARC tactic, we were forced to revise the synthetic plan. The simpler linchpin (–)-**25**, developed previously in our laboratory and shown to be a competent coupling partner in

Anion Relay Chemistry would be employed, making necessary a late stage introduction of the C(14) methyl group (Scheme 5).

Linchpin (–)-**25**, was readily prepared in a single step from epichlorohydrin and 2-TBS-1,3-dithiane.^{5a} With all partners in hand for the union, the revised three component ARC tactic was executed. Optimal conditions proved to be addition of linchpin (–)-**25** to the anion derived from (+)-**12**, generated by treatment with the Schlosser base (Scheme 6). The resultant intermediate, after Brook rearrangement was then alkylated with epoxide (–)-**10** to furnish the expected three component product (+)-**27** in 77% yield.

Pleasingly this reaction could be conveniently run on a 5 gram scale. It is important to note that under these conditions the Brook rearrangement occurs readily at –78 °C, with monoalkylation as the major pathway. Presumably the low temperature permits epoxide (–)-**25** to discriminate between **26** and the anion of (+)-**12**, thus avoiding formation of significant amounts of the alkylation product derived from **26** and (–)-**25**. Pleasingly removal of both dithiane groups with Hg(ClO₄)₂ **10** then proceeded without difficulty to furnish 1,4-bis-ketone (+)-**24** in 75% yield.

Selective *anti*-reduction of the β-hydroxy ketone in (+)-**24**, possessing the C(17) ketone, exploiting the Gribble-Evans protocol¹¹ was immediately followed by hydrolysis of the acetonide under acidic conditions. This reaction, as anticipated, proceeded with concomitant spiroketalization to furnish the desired spiroketal (+)-**28**, as well as spiroketal (+)-**29** and a small amount of hemiketal (+)-**30** (Scheme 7). The yields were 57, 24 and 3% respectively. Presumably spiroketal (+)-**29** arises via dehydration of an intermediate hemiketal, followed in turn by Ferrier reaction¹² of the resulting 1,2-glycal leading to spirocyclization (*vide infra*).

Initial studies to install the C(14) methyl group in a stereocontrolled fashion were performed on a slightly modified substrate, namely (+)-**31** possessing the C(20) *t*-butyldiphenylsilyl (BPS) ether instead of methyl ether (Scheme 8). This spiroketal was prepared in large quantity during our early studies on anion relay chemistry employing an analogous route to that used for preparation of (+)-**28** (see Supporting Information). Protection of the primary hydroxyl group as the BPS ether, followed in turn by benzylation of the remaining secondary hydroxyl, chemoselective removal of the TBS group, and Dess-Martin oxidation of the resulting hydroxyl furnished ketone (+)-**34**. Generation of the enolate with LHMDs at –78 °C, followed by treatment with MeI then led to a mixture of two methylation products (6:1 by NMR). Extensive NMR studies revealed that the desired regioisomer **35** was the minor product.

To enhance access to the desired C(14) isomer **35**, kinetic formation of the TMS enol ether was explored, anticipating that the adjacent ketal might provide the required chemoselective differentiation (Scheme 9). Unfortunately even the best conditions furnished a mixture of regioisomers (1.5:1) favoring the desired isomer. We could however hydrolyze the undesired isomer selectively to the open chain 1,3-diketone (+)-**39**.

Diketone (+)-**39** could then be recycled to ketone (+)-**37** by treatment with strong acid. Unfortunately all attempts to alkylate the anion derived from (+)-**38** lead to an intractable mixture of methylation products. We also explored cyclopropanation of (+)-**38** according to the method developed by Charette and co-workers,¹³ but again an inseparable mixture (3:1) of cyclopropane products resulted.

At this stage we turned to possible optimization of the Ferrier reaction observed earlier during the spirocyclization (Scheme 7). Treatment of the reduction product of (+)-**24** first with *p*-TsOH followed by aqueous HClO₄ pleasingly led to an increase in the yield of

Ferrier reaction product (+)-**29** (Scheme 10). Protection of the primary hydroxyl as a BPS ether and the secondary hydroxyl as a benzyl ether then provided olefin (+)-**40**. The overall yield of this sequence (**24**→**40**) was 45%.

Turning next to introduction of the C(14) equatorial methyl group, selective allylic oxidation at C(14) in (+)-**40** with selenium dioxide¹⁴ followed by nucleophilic substitution was now envisioned. The success of this scenario would critically depend upon the regio and stereoselective allylic oxidation to furnish the axial alcohol as the major product via an ene reaction mechanism. Given that the top face of the olefin is sterically more accessible, with the axial proton perfectly aligned with the π -system according to molecular model studies, such a reaction sequence appeared feasible. Indeed, treatment of olefin (+)-**40** with SeO_2 for 1.5 h at 120 °C in the presence of pyridine, employing a microwave reactor, provided alcohol (–)-**41** with 5:1 diastereoselectivity, along with some recovered starting material (Scheme 11). Longer reaction times or higher reaction temperatures resulted in better axial selectivity, albeit with a decrease in yield. From the perspective of material advancement the undesired equatorial diastereomer could be converted to the desired isomer exploiting Mitsunobu inversion.

Turning to the introduction of the C(14) methyl, substituent, Mitsunobu alkylation¹⁵ with bis(phenylsulfonyl)-methane proceeded smoothly, leading to *bis*-sulfone (+)-**42**, which was then fully reduced with LiDBB at –78 °C, employing *t*-BuOH as the proton source to furnish diol (+)-**43**.¹⁵ Final application of the Fraser-Reid protocol⁸ on (+)-**43** completed construction of (–)-**7**, the C(10)–C(22) fragment of spirastrellolide A (**1**).

2.2 Completion of the C(1)–C(25) Southern Hemisphere of Spirastrellolide A (**1**)

Construction of the requisite dithiane (–)-**6** comprising the C(1)–C(9) side chain began with known pyran (–)-**44**.¹⁶ Reduction of the methyl ester with LiAlH_4 , followed by protection of the resulting primary alcohol as the TBS ether led to (–)-**45**. Oxidative cleavage of the double bond to the corresponding aldehyde employing ozonolysis, followed by dithiane formation promoted by MgBr_2 then furnished dithiane (–)-**6**.

With dithiane (–)-**6** in hand, treatment with the Schlosser base at –78 °C followed by addition of epoxide (–)-**7** furnished coupled product (–)-**47** in excellent yield (Scheme 13). Noteworthy here, dithianes analogous to (–)-**6**, but possessing either a benzyl or *p*-methoxy benzyl protecting group instead of the TBS moiety are not competent nucleophiles, due to competitive deprotonation at the benzylic methylene group. Oxidative hydrolysis of the dithiane group in (–)-**47** employing $\text{Hg}(\text{ClO}_4)_2$,¹⁰ followed by reduction of the resulting β -hydroxy ketone according to the Gribble-Evans protocol¹¹ next furnished (–)-**48** in 71% yield in conjunction with 21% of the 1,3-*syn* diol (dr = 3.4:1). Chemoselective removal of the TBS group with camphor sulfonic acid, followed by protection of the primary alcohol as a pivalate ester then led to diol (–)-**49** as a crystalline solid. Both the connectivity and relative stereochemistry of (–)-**49** were established by single crystal X-ray analysis.⁴

To introduce the final C(23)–C(25) four-carbon side chain, we called upon the Honda precedent (Scheme 14),¹⁷ fully anticipating known dithiane (–)-**8** to deliver the desired 1,3-*syn* stereogenicity at C(22) as observed with dihydro cinnamaldehyde (Scheme 14).

To this end, the requisite aldehyde (+)-**50** was readily generated via a three step sequence involving protection of the free diol as the acetonide, removal of BPS group, and Dess-Martin oxidation (Scheme 15). Treatment of the latter with the lithium anion derived from (–)-**8**¹⁷ led to a mixture of adducts (6.5:1) in moderate yield. Surprisingly, the minor product proved to be the desired isomer, as established by the Kakisawa modification of the Mosher ester analysis of both diastereomers (see supporting material).¹⁸

Fortunately the desired diastomer could be obtained via a three step oxidation-reduction sequence (Scheme 16), involving reduction of the ketone derived from alcohol (+)-**51** with DIBAL-H to furnish exclusively the required stereogenicity at C(22), presumably via chelation control. This process could be carried out on the diastereomeric mixture derived from (+)-**50**.

Next, removal of the dithiane in (+)-**53** employing the Corey conditions (NCS, AgNO₃)¹⁹ furnished an α -hydroxy ketone, which was subjected to *anti*-reduction with Zn(BH₄)₂²⁰ employing 1,2-chelation control (Scheme 17). Acetonide protection of the resulting 1,2-diol completed the synthesis of the C(1)–C(25) southern hemisphere fragment of spirastrellolide A (**1**).

2.3 Completion of the C(1)–C(25) Southern Hemisphere of Spirastrellolide B (2)

Having achieved a workable, albeit not highly efficient synthesis of the C(1)–C(25) southern hemisphere of spirastrellolide A (**1**), we turned our attention to the corresponding southern hemisphere of spirastrellolide B (**2**), lacking a C(15)–C(16) olefin in ring B (**54**). Our synthetic plan was envisioned to diverge from the spirastrellolide A route (*vide supra*), not only by reducing the B ring olefin at the most opportune stage, but also by reordering installation of the right and left hand side chains (Scheme 18), thus avoiding excessive protecting group manipulations. In addition, we could explore the previously problematic introduction of the C(23)–C(26) fragment with correct stereogenicity of C(22) at an earlier stage in the synthetic sequence, as well as make overall improvements where appropriate.

The synthesis of **54** began with the previously prepared *bis*-sulfone (+)-**42**, which upon reduction with LiDBB proceeded chemoselectively to furnish alkene (+)-**57** (Scheme 19). Importantly, careful control of the amount of LiDBB permitted selective reduction of the *bis*-sulfone with only minor amounts of concomitant reduction of the benzyl ethers. Removal of the BPS protecting group, followed by Parikh-Doering oxidation²¹ then proceeded smoothly to afford aldehyde (+)-**59**. With ample quantities of (+)-**59** in hand, addition of the lithium anion derived from dithiane (–)-**8** gave alcohol (+)-**60** in modest yield, as a diastereomeric mixture (6.3:1) albeit again favoring the undesired β epimer at C(22). A small amount (ca. 10–15%) of aldehyde (+)-**59** could also be recovered.

Numerous other coupling protocols were explored including use of the Schlosser base, polar additives (HMPA or TMEDA), as well as chelation controlled conditions employing the cerium anion derived from (–)-**8**, the latter tactic employed with great success during our spongistatin total synthesis.²² However, in no case was a significant improvement in diastereoselectivity observed. Modifying the dithiane coupling partner by replacing the olefin moiety in (–)-**8** with a hydroxyl protected as a TBS ether²³ was also explored. In this case, almost exclusive formation of the undesired β epimer resulted (Scheme 20).

At this juncture, we turned to reduction of the C(15,16) olefin, the idea being that a possible conformational change of the spirocycle might lead to an increase of the desired α epimer upon dithiane addition. Olefin (+)-**57** was therefore selectively hydrogenated in the presence of two benzyl ethers employing the Adams catalyst to furnish (+)-**63** (Scheme 21). Selective removal of the BPS group, followed by Parikh-Doering oxidation provided access to spirocyclic aldehyde (+)-**65**, now lacking the C(15,16) olefin. Addition of the anion derived from (–)-**8** provided an improved yield (ca. 77%) of the coupling product (+)-**66**, however virtually no stereochemical preference was observed. Nonetheless, the increase in yield in conjunction with the 1:1 ratio constituted an improvement from the previously observed outcome vis-à-vis material advancement. Also of importance, the epimeric alcohols are separable by flash chromatography.

Undaunted, we also explored varying the structure of the nucleophilic partner employed in the dithiane union process with both trityl and BPS protected congeners (–)-**67** and (–)-**68** (Scheme 22). However, in both cases, the larger substituents β to the dithiane anion led to an increase in the ratio of the undesired β epimer.

To correct the undesired stereogenicity at C(22) in (+)-**66**, an oxidation-reduction sequence, identical to that employed in our first generation approach, was put into play (Scheme 23) to produce (+)-**71** with the desired stereochemistry at C(22). Oxidative removal of dithiane moiety, again employing the Corey protocol¹⁹ furnished α -hydroxy ketone (+)-**72**, which was subjected to chelation controlled 1,2-reduction²⁰ of the C(23) carbonyl followed by protection of the resulting 1,2-diol as an acetonide to provide (+)-**73**. Removal of both benzyl groups, followed by use of the Fraser-Reid tactic⁸ then provided epoxide (+)-**74** ready for union with the C(1)–C(10) **A**-ring dithiane-(–)-**6**.

Towards this end, treatment of epoxide (+)-**74** with the anion derived from dithiane (–)-**6** proceeded smoothly to furnish alcohol (+)-**75** in 86% yield (Scheme 24), which upon removal of dithiane moiety employing MeI/CaCO₃, followed by 1,3-*anti* reduction led to diol (+)-**76**. Completion of the synthesis of the C(1)–C(25) southern hemisphere of spirastrellolide B (+)-**54** was then achieved by protection of 1,3-diol as an acetonide and removal of the TBS ether.

3. Summary

Effective syntheses of the C(1)–C(25) southern hemispheres of both spirastrellolide A (**1**) and B (**2**) have been achieved. In the case of spirastrellolide A (**1**), the synthesis required 33 steps and proceeded in 0.20% overall yield, whereas the second generation approach to spirastrellolide B (**2**) required 32 steps and proceeded in 0.60% overall yield. Both syntheses feature four dithiane unions, including a highly effective three component anion relay (ARC) tactic to access the linear precursor of the **BC** spiroketal. Further studies toward the total syntheses of spirastrellolides A and B continue in our laboratory.

4. Experimental

Acetonide (+)-**5**. To a solution of ketone (+)-**53A** (0.0019 g, 2.9 mmol) in Et₂O (0.7 mL) at 0 °C was added a solution of Zn(BH₄)₂ in Et₂O (0.07 mL, 0.15M, 0.011 mmol). The resulting solution was stirred for 40 min at 0 °C, and a saturated NaHCO₃ aqueous solution (2 mL) was then added. The mixture was extracted with Et₂O (3 mL $\times$ 3), and the combined organic layers were washed with brine (2 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. Without further purification, the resulting diol was dissolved in acetone/2,2-dimethoxypropane (0.7/0.1 mL). To the resulting solution at room temperature was added TsOH (1 mg, 5 mmol). After 30 min at room temperature, triethylamine (0.6 mL) was added, and the resulting mixture was concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate/hexanes (1:4) as eluent, provided 0.0013 g (64%) of (+)-**5** as a colorless oil: $[\alpha]_D^{20} = +9.1$ ($c = 0.15$, C₆H₆); IR (neat) 3078, 2934, 2872, 1730, 1458, 1377, 1221, 1158, 1103 cm^{–1}; ¹H NMR (500 MHz, C₆D₆) δ 6.17 (ddd, $J = 17.3, 10.4, 6.7$ Hz, 1H), 5.56 (dd, $J = 10.0, 2.6$ Hz, 1H), 5.44 (dd, $J = 10.0, 1.9$ Hz, 1H), 5.11 (app dt, $J = 17.3, 1.5$ Hz, 1H), 5.08 (app dt, $J = 10.5, 1.4$ Hz, 1H), 4.63 (d, $J = 6.5$ Hz, 1H), 4.39–4.26 (m, 4H), 3.95 (dd, $J = 10.0, 6.1$ Hz, 1H), 3.93 (d, $J = 9.3$ Hz, 1H), 3.80 (app td, $J = 9.5, 2.7$ Hz, 1H), 3.61–3.56 (m, 1H), 3.53 (ddd, $J = 11.0, 9.4, 5.2$ Hz, 1H), 3.31–3.25 (m, 1H), 3.19 (s, 3H), 3.16–3.11 (m, 1H), 2.20 (ddd, $J = 14.3, 4.5, 2.8$ Hz, 1H), 2.02 (ddd, $J = 13.0, 9.7, 6.3$ Hz, 1H), 1.95–1.82 (m, 4H), 1.79–1.72 (m, 3H), 1.70–1.65 (m, 3H), 1.64 (s, 3H), 1.56 (s, 3H), 1.55 (s, 3H), 1.47 (app td, $J = 13.5, 4.1$ Hz, 1H), 1.40 (s, 3H), 1.36–1.22 (m, 4H), 1.20 (d, $J = 6.7$ Hz, 3H), 1.17 (s, 9H), 1.10–1.02 (m, 2H), 0.76 (d, $J = 7.1$ Hz, 3H); ¹³C NMR (125 MHz, C₆D₆) δ 177.6, 142.3, 133.5, 129.1, 113.5, 108.5, 100.2, 93.5, 81.6, 75.8, 74.6, 74.5, 74.1,

73.4, 72.1, 66.3, 62.9, 61.6, 56.1, 43.6, 42.0, 41.2, 38.7, 37.2, 36.2, 35.1, 34.4, 32.3, 32.0, 27.3, 27.0, 26.5, 26.3, 25.6, 24.0, 23.4, 17.3, 17.2; HRMS (ESI, M+Na) m/z 729.4539 (calcd for $C_{40}H_{66}O_{10}Na$: 729.4554).

Alcohol (+)-**54**. TBAF in THF (0.1 mL, 1.0M, 0.10 mmol) was added to a solution of (+)-**76A** (0.006 g, 0.0081 mmol) in THF (0.4 mL) at 0 °C. After stirring for 1 h aqueous saturated NH_4Cl was added and the resulting mixture was extracted with EtOAc (3×). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate/hexanes (1:9→3:7) as eluent, gave 0.005 g (98%) of (+)-**54** as white foam: $[\alpha]_D^{23} = +26.0$ ($c = 0.133$, $CHCl_3$); IR (neat) 3450, 2933, 1639, 1457, 1377, 1250, 1220, 1092 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 5.94 (ddd, $J = 17.4, 10.4, 7.0$, 1H), 5.15 – 5.05 (m, 2H), 4.36 (dd, $J = 6.0, 0.8$, 1H), 4.19–4.12 (m, 1H), 4.04 – 3.97 (m, 1H), 3.93 (dd, $J = 10.3, 6.0$, 1H), 3.82–3.76 (m, 2H), 3.59 (dd, $J = 9.3, 0.9$, 1H), 3.58–3.52 (m, 2H), 3.47 (td, $J = 10.3, 2.1$, 1H), 3.41 (ddd, $J = 11.3, 9.4, 5.0$, 1H), 3.31 (s, 3H), 3.03 – 2.95 (m, 1H), 2.73 (t, $J = 5.4$, 1H), 2.02–1.92 (m, 2H), 1.85 – 1.65 (m, 7H), 1.64 – 1.50 (m, 7H), 1.49 – 1.16 (m, 7H), 1.44 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.32 (s, 3H), 1.07 (d, $J = 6.8$, 3H), 0.88 (d, $J = 6.6$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.1, 113.9, 108.2, 100.5, 95.2, 81.5, 78.6, 76.1, 74.6, 74.4, 72.1, 71.4, 63.2, 62.9, 61.7, 56.0, 42.7, 42.2, 40.3, 38.4, 37.0, 36.3, 35.7, 34.7, 32.0, 31.8, 27.5, 26.7, 26.4, 25.8, 25.1, 23.7, 22.8, 18.4, 17.2; HRMS (ES, M+Na) m/z 647.4110 (calcd for $C_{35}H_{60}O_9Na$: 647.4135).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Scheme 1.

Scheme 2.

Scheme 3.

Scheme 4.

Scheme 5.

Scheme 6.

Scheme 8.

Scheme 9.

Scheme 11.

Scheme 12.

Scheme 13.

Scheme 14.

Scheme 15.

Scheme 16.

Scheme 17.

Scheme 18.

Scheme 19.

Scheme 20.

Scheme 22.

Scheme 23.

Scheme 24.