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A biomimetic total synthesis of allomicrophyllone: protective Diels–Alder reaction as a stratagem

Goverdhan Mehta *, Tabrez Babu Khan

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India
School of Chemistry, University of Hyderabad, Hyderabad 500 046, India

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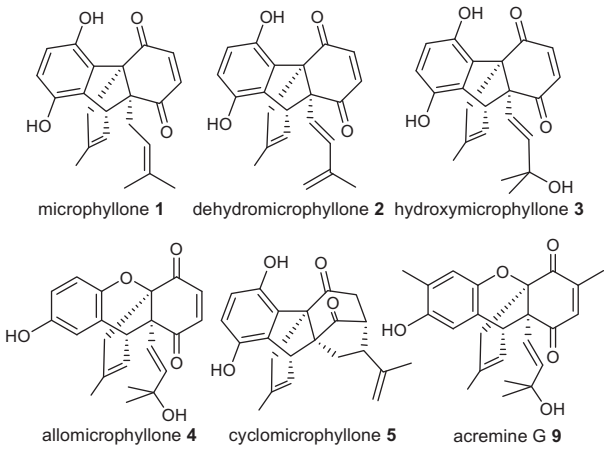
ABSTRACT

A biomimetic total synthesis of bioactive tetracyclic natural product allomicrophyllone has been achieved in which a protective Diels–Alder reaction employing a disposable sacrificial 1,3-diene directs the regioselectivity of the subsequent Diels–Alder reaction.

Ehretia microphylla Lamk. (syn. *Carmona retusa* Vahl. Masam) is an important medicinal plant in the Philippines and finds extensive use in traditional medical practices for the treatment of ailments ranging from coughs to dysentery.[1] From the aerial parts of the plant, isolation of triterpenes (ursolic acid and bauerenol), polyphenols (rosmarinic acid) and flavonoid glycosides (astragalin and nicotoflorin) has been reported.[2] A more recent[3] bioassay guided investigation of the aerial parts of the plants has led to the isolation of five closely related dimeric prenyl-benzoquinones namely microphyllone **1**,[2a] dehydromicrophyllone **2**, hydroxymicrophyllone **3**, allomicrophyllone **4** and cyclomicrophyllone **5**. Among these novel natural products, microphyllone **1** and allomicrophyllone **4** exhibited impressive inhibitory activity (IC_{50} 33 μM and IC_{50} 36 μM, respectively) on exocytosis of rat basophils caused by antigen-induced stimulation, indicating their role as antiallergic agents. During the structure elucidation of microphyllones **1–5**, Yamamura et al.[3] proposed an interesting Diels–Alder cycloaddition based scheme for their biosynthesis involving two representative monomeric units, the dienophilic benzoquinone **6** and the diene **7a** (Scheme 1). Broadly, an enzyme mediated C–C oxidative coupling in the putative Diels–Alder adduct **8** would lead to hydroxymicrophyllone **3** (path 'a'), while a C–O coupling in **8** would eventuate in allomicrophyllone **4** (path 'b') (Scheme 1). Quite surprisingly, synthetic endeavours towards any of the microphyllones **1–5** have not yet appeared in the literature despite their interesting biosynthetic origin and promising antiallergic[3] and hair growth stimulant and promoter[4] bioactivity.

Recently, we[5] and others[6] have reported the total synthesis of a natural product acremine G **9**,[7] having close structural resemblance to allomicrophyllone **4**, following a biogenetic-type Diels–Alder approach.[8] Seemingly straightforward adaptation of the successful biomimetic Diels–Alder strategy[5,6] in the context of acremine G **9** towards allomicrophyllone **4** met with regioselectivity hurdles which could be overcome through a tactical intervention involving a protective Diels–Alder reaction to facilitate the requisite biomimetic Diels–Alder reaction. In this Letter we disclose the successful application of the protective D–A tactic towards the first total synthesis of allomicrophyllone **4**.



To execute the biomimetic Diels–Alder cycloaddition strategy towards allomicrophyllone **4**, synthesis of the two key monomeric units, the prenylated quinone **6** and prenylated diene **7a**, was undertaken along classical routes from readily available starting materials.

Gentisaldehyde **10**, obtained commercially, was routinely subjected to Wittig-Horner olefination to furnish the cinnamate ester **11**. Addition of excess methyllithium to **11** and periodate mediated oxidation of the quinol moiety in the resulting tertiary alcohol **12** led to the desired benzoquinone **6** (Scheme 2).

* Corresponding author. Tel.: +91 4023010785; fax: +91 4023012460.
E-mail addresses: gmsc@uohyd.ernet.in, gm@orgchem.iisc.ernet.in (G. Mehta).

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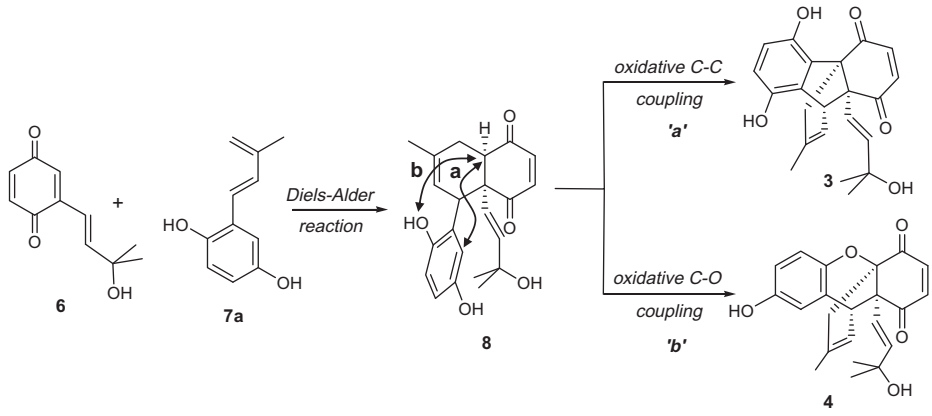
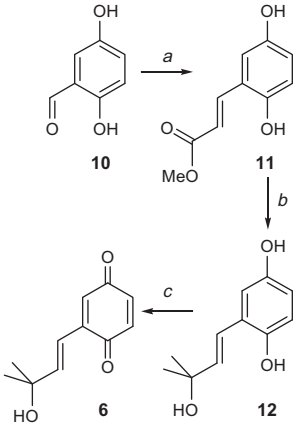
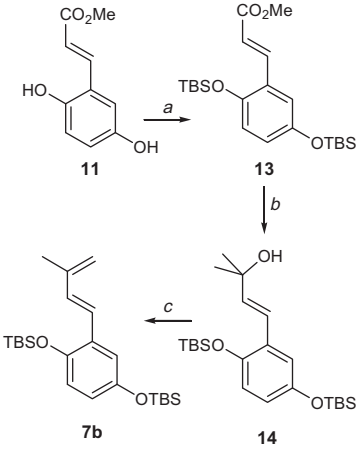


Scheme 1. Proposed biosynthetic pathways for **3** and **4**.



Scheme 2. Reagents and conditions: (a) $Ph_3P{=}CHCO_2Me$, C_6H_6, reflux, 2 h, 88%; (b) MeLi, THF, −30 °C, 1 h, 55% (based on the recovered starting material); (c) $NaIO_4$, MeOH/H_2O (2:1), 0 °C to rt, 1 h, 83%.

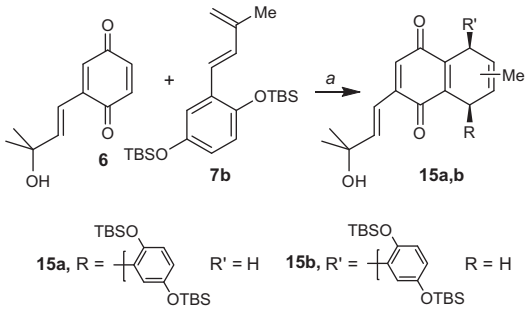


Scheme 3. Reagents and conditions: (a) TBSCl, imidazole, DMAP, DMF, 80 °C, 12 h, 90%; (b) MeLi, THF, −78 °C, 30 min, 90%; (c) MsCl, Et_3N, DMAP, CH_2Cl_2, 0 °C to rt, 1 h, 80%.

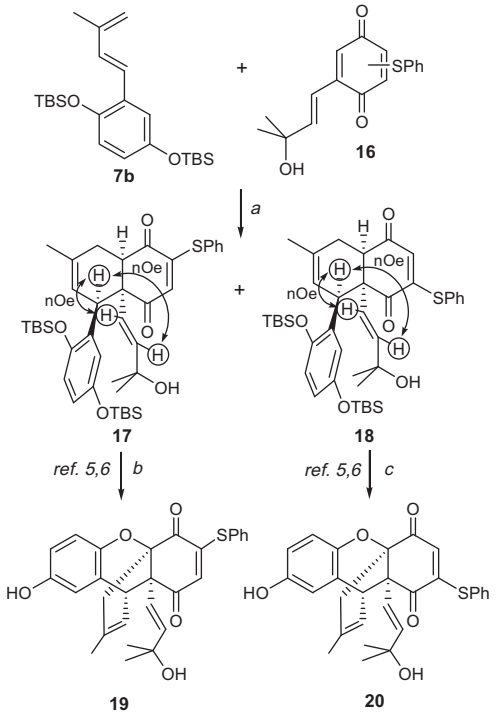
The cinnamate ester **11** also served as the precursor for the prenylated diene component **7a**. Protection of the phenolic hydroxyl groups in **11** as the TBS derivative **13** and addition of excess methyllithium led to the tertiary alcohol **12** (Scheme 3). Dehydration in **14** was smooth and furnished the required TBS protected diene **7b**.

With the prenylated benzoquinone **6** and the partner diene **7b** in hand, we explored the cycloaddition between them. In consonance with our recent observation,[5] the D–A reaction between **6** and **7b** was dramatically accelerated by the commonly used chromatographic silica gel (100–200 mesh) and the reaction was over in ~5 min under ambient conditions. However, the reaction turned out to be regioselective and deviant with only the unsubstituted benzoquinone double bond participating and undergoing concomitant oxidation to furnish quinones **15a**,**b** which were clearly unserviceable for further elaboration, Scheme 4. This necessitated devising a tactic that would subdue the reactivity of the unsubstituted quinone double bond and facilitate cycloaddition at the prenyl bearing double bond, thereby reversing the regioselectivity of the D–A reaction. Among the various options available, a disposable thiophenyl substitution on the unsubstituted double bond of **6** appeared to be a viable tactic as this moiety is known[10] to alter the regioselectivity of Diels–Alder reaction and could be dispensed with at an appropriate stage of the synthesis.

Thus, exposure of benzoquinone **6** to methanolic thiophenol furnished a mixture of regioisomeric thiophenyl substituted quinones **16** (Scheme 5). Reactions of thiophenylated quinones **16** with the diene **7b** in the presence of silica gel indeed reversed the quinone double bond regioselectivity and two [4+2]-adducts **17**[9] and **18**[9] (2:1 ratio) were obtained with complete stereoselectivity (Scheme 5). Regioisomeric nature and *endo*-stereochemistry of adducts **17** and **18** were deduced from 2D NMR data (HMBC, HMQC) and particularly on the basis of nOe between the benzylic methine proton and the olefinic proton on the neighbouring bridgehead prenyl group. The stereochemical outcome of the D–A reaction between **7b** and **16** leading exclusively to **17** and



Scheme 4. Reagents and conditions: (a) silica gel, rt, 5 min, 58% (based on the recovered **7b**).

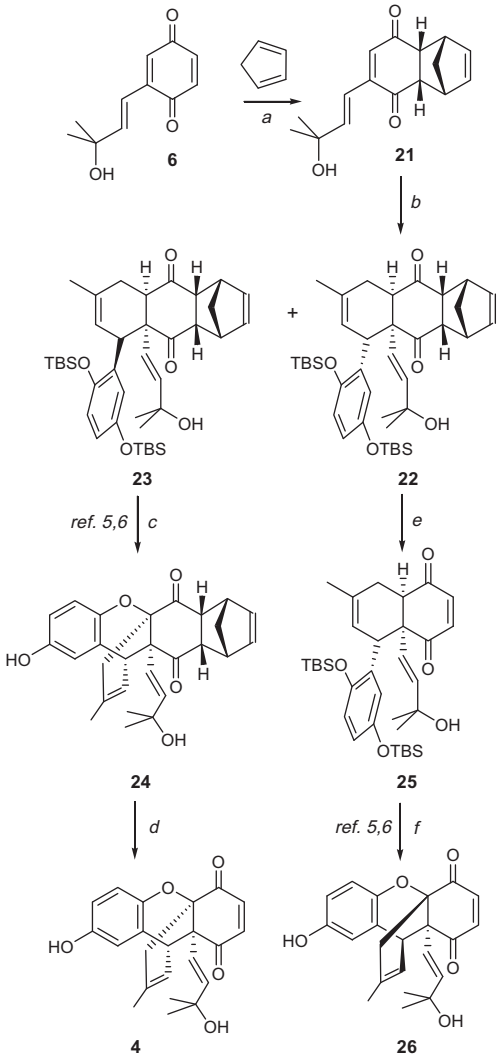


Scheme 5. Reagents and conditions: (a) silica gel, rt, 5–6 h, 60% (overall, based on the recovered **7b**, **17** = 41% and **18** = 19%); (b) anhydrous KF, 30% HBr in glacial AcOH, DMF, O_2, rt, 36 h, 60%; (c) anhydrous KF, 30% HBr in glacial AcOH, DMF, O_2, rt, 36 h, 54%.

18 appears to be substantially influenced by the presence of the remote thiophenyl group on the quinone moiety. Such regio- and stereochemical effects have been previously observed and well documented in the D–A reactions of dienes with related sulfinyl-1,4-benzoquinones.[11,12]

The stage was now set to orchestrate the one-pot radical mediated intramolecular oxidative coupling reaction, recently discovered by Stratakis and co-workers[6] and extended by us,[5] in **17** and **18**, involving successive desilylation, epimerization and cyclization. Both, **17** and **18** on exposure to in situ generated HF under oxygen blanket led to thiophenylated allomicrophyllone derivatives **19**[9] and **20**,[9] respectively (Scheme 5). Structure of **19** was secured by X-ray structure determination[13] and confirmed the presence of the allomicrophyllone framework. Reductive desulphurisation in **19** and **20** was expected to deliver the natural product allomicrophyllone **5**. However, various protocols to reductively remove thiophenyl group in **19**/**20** proved unsuccessful and we were forced to change track.

At this stage, we considered the possibility of a protective D–A reaction to precede the desired D–A reaction to block the more reactive unsubstituted double bond of the benzoquinone **6** employing cyclopentadiene (CP) as the sacrificial diene. Indeed, D–A reaction of **6** with CP was smooth and furnished a single *endo*-adduct **21**[9] in a regio- and stereoselective manner. Silica-gel mediated D–A reaction between **21** and the diene **7b** led to two [4+2]-adducts *exo*-**22**[9] and *endo*-**23**[9] in a ratio of 3:1, respectively (Scheme 6). Clearly, the altered stereoelectronic environment in the *endo*-adduct **21** profoundly impacted the stereoselectivity of the D–A reaction with **7b** and the *exo*-adduct **22** was formed as the major product.[12] In the context of the target allomicrophyllone **4**, it was the *endo*-adduct **23** that was serviceable and further one-pot cyclization with in situ generated HF as described by Stratakis and co-workers[6] led to the hexacyclic **24** embodying the allomicrophyllone moiety (Scheme 6). Retro-[4+2] reaction on **24** under static thermal activation disengaged the sacrificial cyclopentadiene



Scheme 6. Reagents and conditions: (a) MeOH, 0 °C, 30 min, 95%; (b) **7b**, silica gel, rt, 72 h, 67% (overall, based on the recovered **7b**, **22** = 51% and **23** = 16%); (c) anhydrous KF, 30% HBr in glacial AcOH, DMF, O_2, rt, 72 h, 58%; (d) diphenylether, sealed tube, 200 °C, 6 h, 50%; (e) diphenylether, sealed tube, 175 °C, 1 h, 50%; (f) anhydrous KF, 30% HBr in glacial AcOH, DMF, O_2, rt, 72 h, 25%.

moiety to deliver allomicrophyllone **4**[9] which was found to be spectroscopically (^{1}H & ^{13}C NMR) identical with the natural product.

Since the *exo*-adduct **22** was readily available, we elaborated it into an epimer of allomicrophyllone. It turned out that the *exo*-adduct **22** was amenable to retro-[4+2] reaction at this stage to deliver **25** in moderate yield. Exposure of **25** to in situ generated HF led to one-pot successive desilylation, epimerization and cyclization to furnish *epi*-allomicrophyllone **26**[9] (Scheme 6).

In short, we have accomplished a total synthesis of the dimeric natural product allomicrophyllone following a biomimetic Diels–Alder reaction between rapidly assembled monomeric diene and dienophilic units. The desired D–A reaction was preceded by a protective Diels–Alder reaction with a disposable sacrificial cyclopentadiene to ensure the requisite regioselectivity.

Acknowledgements

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described here and the X-ray data collection were carried out at IISc, Bangalore and we thank Mr. Saikat Sen for solving the crystal structure.

Supplementary data

Supplementary data associated with (cystallographic details for compound **19**) this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.10.063.

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9. All new compounds reported here are racemic and characterized on the basis of spectroscopic data (IR, ^{1}H, ^{13}C NMR and mass). Spectral data for some of the key compounds follows: *Compound* **17** IR (neat) $\bar{\nu}_{max}$ = 3447, 2929, 2857, 1690, 1660, 1567, 1488, 1251, 1207, 920 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.40–7.31 (m, 3H), 7.19 (d, J = 7 Hz, 2H), 6.55 (dd, J = 3, 8 Hz, 1H), 6.52 (d, J = 8 Hz, 1H), 6.44 (d, J = 3 Hz, 1H), 5.82 (d, J = 16 Hz, 1H), 5.68 (d, J = 16 Hz, 1H), 5.36 (br s, 1H), 5.32 (s, 1H), 4.11 (br s, 1H), 3.00 (d, J = 7 Hz, 1H), 2.94 (d, J = 18 Hz, 1H), 2.01 (dd, J = 7, 18 Hz, 1H), 1.82 (s, 3H), 1.31 (s, 3H), 1.28 (s, 3H), 0.99 (s, 9H), 0.97 (s, 9H), 0.23 (s, 3H), 0.21 (s, 3H), 0.14 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.25, 194.38, 155.50, 149.79, 146.75, 138.37, 135.55 (2C), 133.02, 131.81, 129.91, 129.75 (2C), 129.41, 128.96, 127.87, 123.02, 122.16, 119.30, 118.83, 70.81, 56.70, 49.62, 40.45, 29.80, 29.68, 29.65, 26.10 (3C), 25.75 (3C), 23.35, 18.30, 18.19, −4.04, −4.20, −4.36, −4.43 ppm; HRMS (ES) m/z calcd for $C_{40}H_{56}O_5SSi_2Na$ (M+Na)$^+$: 727.3285; found: 727.3268; *Compound* **18** IR (thin film) $\bar{\nu}_{max}$ = 3482, 2956, 2928, 2857, 2360, 1669, 1487, 1250, 1208, 921, 839 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42–7.33 (m, 3H), 7.21 (d, J = 7 Hz, 2H), 6.62 (s, 2H), 6.51 (s, 1H), 5.89 (d, J = 16 Hz, 1H), 5.67 (d, J = 16 Hz, 1H), 5.42 (s, 1H), 5.39 (br s, 1H), 4.18 (br s, 1H), 2.92 (dd, J = 3, 7 Hz, 1H), 2.76 (d, J = 18 Hz, 1H), 1.98 (dd, J = 7, 18 Hz, 1H), 1.78 (s, 3H), 1.37 (s, 3H), 1.32 (s, 3H), 1.03 (s, 9H), 0.96 (s, 9H), 0.26 (s, 3H), 0.16 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.47, 193.94, 158.09, 149.46, 147.46, 139.00, 135.59 (2C), 133.09, 131.22, 130.01, 129.91 (2C), 128.56, 128.19, 127.91, 123.27, 122.06, 119.54, 119.16, 70.80, 57.39, 50.04, 40.70, 29.70 (2C), 29.61, 26.09 (3C), 25.72 (3C), 23.24, 18.40, 18.14, −3.89, −4.29, −4.40, −4.44 ppm; HRMS (ES) m/z calcd for $C_{40}H_{56}O_5SSi_2Na$ (M+Na)$^+$: 727.3285; found: 727.3282; *Compound* **19** mp 237–238 °C IR (thin film) $\bar{\nu}_{max}$ = 3392, 2924, 1700, 1670, 1557, 1456, 1216, 1194 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48–7.43 (m, 5H), 6.67 (d, J = 9 Hz, 1H), 6.54–6.51 (m, 2H), 5.75 (d, J = 16 Hz, 1H), 5.72 (s, 1H), 5.65 (d, J = 16 Hz, 1H), 5.62 (br s, 1H), 4.70 (br s, –OH), 3.75 (d, J = 6 Hz, 1H), 2.75 (d, J = 19 Hz, 1H), 2.55 (d, J = 19 Hz, 1H), 1.70 (br s, 3H), 1.22 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 192.38, 190.37, 157.37, 149.93, 144.84, 142.90, 135.41 (2C), 131.45, 130.52, 130.32 (2C), 127.89, 127.55, 126.94, 122.30, 121.74, 117.39, 114.74, 114.14, 81.08, 70.86, 54.31, 38.94, 36.22, 29.69, 29.65, 22.53 ppm; HRMS (ES) m/z calcd for $C_{28}H_{26}O_5SNa$ (M+Na)$^+$: 497.1399; found: 497.1999; *Compound* **20** IR (thin film) $\bar{\nu}_{max}$ = 3445, 1669, 1558, 1473, 1204, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48–7.41 (m, 5H), 6.64 (d, J = 9 Hz, 1H), 6.60 (d, J = 3 Hz, 1H), 6.55 (dd, J = 3, 9 Hz, 1H), 5.97 (s, 1H), 5.81 (d, J = 16 Hz, 1H), 5.66 (d, J = 16 Hz, 1H), 5.65 (d, J = 6 Hz, 1H), 4.48 (br s, –OH), 3.84 (d, J = 6 Hz, 1H), 2.68 (d, J = 19 Hz, 1H), 2.51 (d, J = 19 Hz, 1H), 1.70 (br s, 3H), 1.25 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 192.31, 190.17, 156.58, 149.70, 145.02, 143.43, 135.50 (2C), 131.86, 130.51, 130.32 (2C), 130.03, 127.81, 127.40, 122.52, 121.93, 117.31, 114.80, 114.13, 80.41, 70.92, 55.16, 39.20, 36.51, 29.68 (2C), 22.46 ppm; HRMS (ES) m/z calcd for $C_{28}H_{26}O_5SNa$ (M+Na)$^+$: 497.1399; found: 497.1377; *Compound* **21** IR (thin film) $\bar{\nu}_{max}$ = 3421, 2973, 1654, 1273, 1130, 976 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.64 (d, J = 16 Hz, 1H), 6.59 (s, 1H), 6.52 (d, J = 16 Hz, 1H), 6.06 (br s, 2H), 3.54 (br s, 2H), 3.28 (dd, J = 4, 9 Hz, 1H), 3.23 (dd, J = 4, 9 Hz, 1H), 1.67 (br s, –OH), 1.55 (d, J = 9 Hz, 1H), 1.44 (d, J = 9 Hz, 1H), 1.38 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 199.60, 198.73, 147.50, 147.27, 135.53, 135.09, 135.08, 118.58, 71.32, 49.08, 48.92, 48.88, 48.84, 48.56, 29.48 (2C) ppm; HRMS (ES) m/z calcd for $C_{16}H_{18}O_3Na$ (M+Na)$^+$: 281.1154; found: 281.1161; *Compound* **22** IR (thin film) $\bar{\nu}_{max}$ = 3500, 2930, 1703, 1486, 1248, 1200, 913, 839, 780 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.57 (d, J = 8 Hz, 1H), 6.52 (dd, J = 3, 8 Hz, 1H), 6.35 (d, J = 3 Hz, 1H), 5.91 (dd, J = 3, 6 Hz, 1H), 5.83 (dd, J = 3, 6 Hz, 1H), 5.39 (d, J = 5 Hz, 1H), 4.95 (s, 2H), 4.64 (d, J = 5 Hz, 1H), 3.47 (br s, 1H), 3.38 (br s,1H), 3.33 (dd, J = 4, 10 Hz, 1H), 3.28 (dd, J = 4, 10 Hz, 1H), 3.03 (dd, J = 8, 10 Hz, 1H), 2.50 (dd, J = 10, 18 Hz, 1H), 2.41 (dd, J = 8, 18 Hz, 1H), 1.78 (s, 3H), 1.45 (d, J = 9 Hz, 1H), 1.31 (d, J = 9 Hz, 1H), 1.06 (s, 9H), 1.04 (s, 3H), 0.95 (s, 9H), 0.84 (s, 3H), 0.21 (s, 3H), 0.20 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 210.67, 210.35, 149.64, 147.87, 140.06, 136.95, 136.05, 132.34, 130.89, 125.78, 123.65, 121.90, 120.11, 118.71, 70.30, 56.82, 51.55, 50.08, 48.57, 48.24, 46.86, 44.67, 38.85, 30.19, 29.20, 28.44, 25.93 (3C), 25.76 (3C), 23.13, 18.29, 18.28, −3.96, −4.38, −4.40, −4.61 ppm; HRMS (ES) m/z calcd for $C_{39}H_{58}Si_2O_5Na$ (M+Na)$^+$: 685.3721; found: 685.3722; *Compound* **23** IR (thin film) $\bar{\nu}_{max}$ = 3460, 2929, 1698, 1487, 1249, 915, 839, 780 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.58 (s, 2H), 6.54 (s, 1H), 6.17 (dd, J = 3, 6 Hz, 1H), 5.96 (dd, J = 3, 6 Hz, 1H), 5.64 (d, J = 16 Hz, 1H), 5.57 (d, J = 16 Hz, 1H), 5.24 (br s, 1H), 4.0 (br s, 1H), 3.33 (br s, 1H), 3.06 (br s,1H), 2.76 (d, J = 18 Hz, 1H), 2.34 (dd, J = 4, 10 Hz, 1H), 2.15 (d, J = 6 Hz, 1H), 2.04 (dd, J = 4, 10 Hz, 1H), 1.77 (s, 3H), 1.66–1.50 (m, 3H), 1.33 (s, 3H), 1.28 (s, 3H), 1.00 (s, 9H), 0.98 (s, 9H), 0.22 (s, 3H), 0.21 (s, 3H), 0.20 (s, 3H), 0.12 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.67, 209.24, 149.07, 148.31, 138.14, 137.00, 134.55, 133.88, 130.20, 129.48, 124.32, 121.39, 119.45, 118.66, 70.92, 57.07, 52.34, 51.15, 49.59, 49.35, 48.17, 47.67, 38.78, 30.04, 29.68, 26.07 (3C), 25.75 (3C), 24.57, 23.64, 18.31, 18.26, −3.98, −4.28, −4.39, −4.41 ppm; HRMS (ES) m/z calcd for $C_{39}H_{58}Si_2O_5Na$ (M+Na)$^+$: 685.3721; found: 685.3721; allomicrophyllone (**4**) IR (thin film) $\bar{\nu}_{max}$ = 3420, 2928, 1684, 1522, 1205, 1017 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.84 (d, J = 10 Hz, 1H), 6.61 (d, J = 8 Hz, 1H), 6.57 (d, J = 3 Hz, 1H), 6.52 (dd, J = 3, 8 Hz, 1H), 6.50 (d, J = 10 Hz, 1H), 5.76 (d, J = 16 Hz, 1H), 5.67 (d, J = 16 Hz, 1H), 5.64 (d, J = 6 Hz, 1H), 4.61 (br s, –OH), 3.77 (d, J = 6 Hz, 1H), 2.73 (d, J = 19 Hz, 1H), 2.50 (d, J = 19 Hz, 1H), 1.69 (s, 3H), 1.22 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.64, 192.97, 149.82, 144.91, 143.20, 139.18, 138.44, 131.65, 127.55, 122.40, 121.88, 117.45, 114.75, 114.22, 80.57, 70.85, 54.70, 38.96, 36.07, 29.68, 29.66, 22.51 ppm; HRMS (ES) m/z calcd for $C_{22}H_{22}O_5Na$ (M+Na)$^+$: 389.1365; found: 389.1361; *epi*-allomicrophyllone (**26**) IR (thin film) $\bar{\nu}_{max}$ = 3373, 2970, 1691, 1608, 1493, 1205, 895 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.99 (d, J = 8 Hz, 1H), 6.88 (d, J = 10 Hz, 1H), 6.64 (d, J = 10 Hz, 1H), 6.61 (dd, J = 3, 8 Hz, 1H), 6.42 (d, J = 3 Hz, 1H), 6.29 (d, J = 16 Hz, 1H), 5.64 (d, J = 16 Hz, 1H), 5.18 (br s, 1H), 4.44 (br s, –OH), 3.77 (br s, 1H), 2.83 (d, J = 16 Hz, 1H), 2.58 (d, J = 16 Hz, 1H), 1.74 (br s, 3H), 1.32 (s, 3H), 1.30 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 197.14, 195.33, 150.30, 146.16, 143.30, 140.48, 140.35, 137.60, 125.41, 124.07, 121.82, 119.66, 114.22, 113.14, 85.73, 71.01, 63.69, 49.20, 38.22, 30.03, 29.76, 16.33 ppm; HRMS (ES) m/z calcd for $C_{22}H_{22}O_5Na$ (M+Na)$^+$: 389.1365; found: 389.1369.
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12. For a discussion on the stereoelectronic control of Diels–Alder reaction, see: (a) Mehta, G.; Uma, R. *Acc. Chem. Res.* **2000**, *33*, 278–286; (b) Brocksom, T. J.; Nakamura, J.; Ferreira, M. L.; Brocksom, U. *J. Braz. Chem. Soc.* **2001**, *12*, 597–622.
13. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, CCDC-793648. An ORTEP diagram of compound **19** with 30% ellipsoidal probability is shown below.