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Stereoselective Approach to the Racemic Oxatetracyclic Core of Platensimycin

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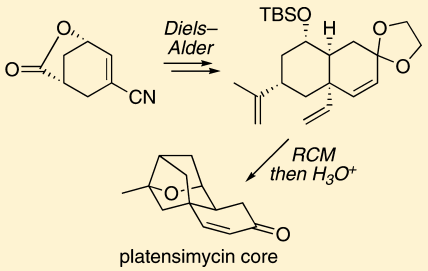
Supporting Information

ABSTRACT: A highly stereoselective synthesis of the racemic oxatetracyclic core of platensimycin has been accomplished from a known bicyclic epoxy lactone by an 11-step sequence that involves a Diels–Alder cyclcoaddition to construct its *cis*-decalenone structural motif with complete regio- and stereoselectivity and a ring-closing metathesis to establish its whole carbon framework.



Platensimycin (**1**), identified by Wang and co-workers from the fermentation broth of *Streptomyces platensis*, is a broad-spectrum antibiotic against Gram-positive bacteria that exerts its antibacterial effect by selectively inhibiting the β-ketoacy-(acyl-carrier-protein) synthase (FabF), one of the key enzymes in bacterial fatty acid biosynthesis, which has scarcely been targeted in drug discovery (Figure 1).[1] Owing to its unique

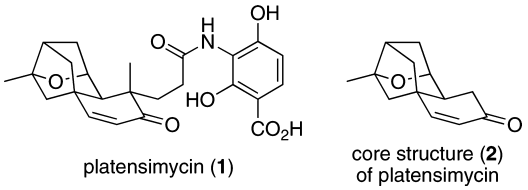
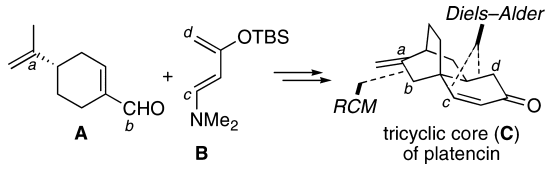


Figure 1. Platensimycin (**1**) and its tetracyclic core (**2**).

action mechanism, platensimycin exhibits no cross-resistance to key antibiotic-resistant strains including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-intermediate *S. aureus* (VISA), and vancomycin-resistant *Enterococcus faecium* (VREF). Moreover, it shows no observed toxicity in mice.[1a] These remarkable pharmacological profiles of platensimycin (**1**) as well as its intriguing molecular architecture featuring a unique oxatetracyclic core (**2**) connected, through a three-carbon amide linker, to a novel aromatic moiety immediately attracted the intense interest of the organic synthesis community. To date, various synthetic approaches to **1** and related natural and designed analogues have been reported since the first total synthesis of **1** via **2** by Nicolaou and co-workers.[2,3] In this Note, we describe a highly stereoselective route to the core structure **2** that exploits a Diels–Alder cycloaddition to construct a key carbobicyclic intermediate and a ring-closing metathesis to install an additional five-membered carbocyclic ring.

Our synthetic plan for **2** is based, in principle, on Tiefenbacher and Mulzer's approach to the tricyclic core (compound **C**, Scheme 1) of platencin,[4] another potent

Scheme 1. Synthesis of the Tricyclic Core (C) of Platencin by Tiefenbacher and Mulzer



antibiotic produced by *S. platensis*.[5] Their synthetic design involving the Diels–Alder reaction between commercially available (−)-perillaldehyde (**A**) and Rawal's diene **B** leading to a *cis*-decalenone intermediate and an RCM to construct a six-membered ring embedded in **C** enabled them to achieve an extremely succinct synthesis of **C**. With the successful precedent in mind, our target molecule **2** bearing an analogous but different carbon skeleton, and an additional oxygen functionality was traced retrosynthetically to protected carbobicyclic precursor **3**, in which two olefinic substituents and a protected hydroxy group are properly situated (Scheme 2). Ring-closing metathesis (RCM) between the vinyl and isopropenyl side chain at the C1 and C9 positions would afford a cyclopentene-containing carbotricyclic intermediate, and its acidic treatment would elicit deprotection at the C4 and C7 positions as well as concomitant intramolecular etherification to form **2**. Compound **3** could readily be prepared by standard functional group manipulation of **4**, the *cis*-decalenone ring system of which in turn could be constructed stereoselectively

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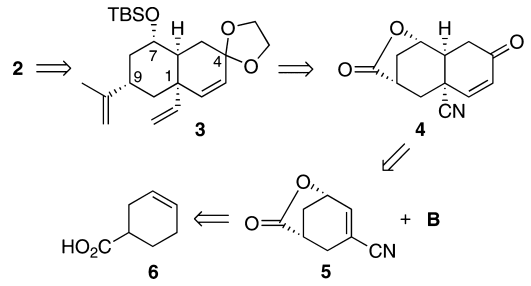
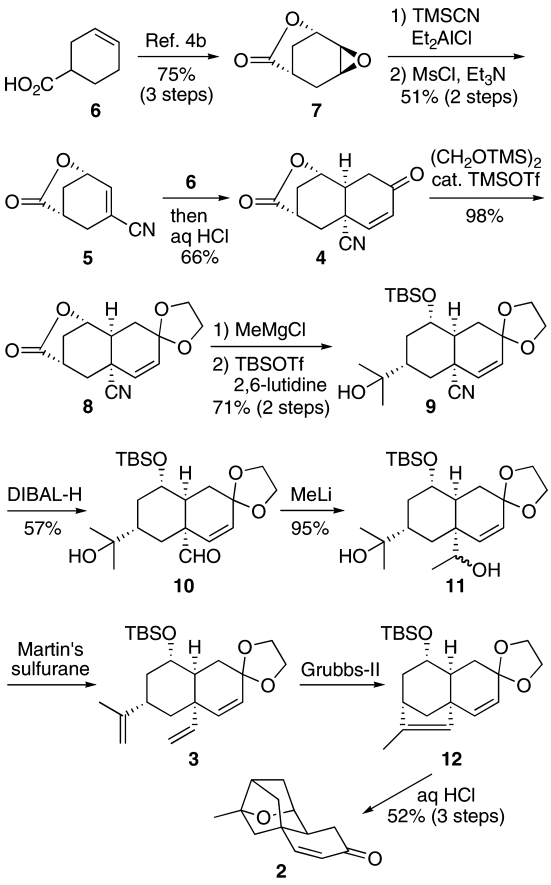
Scheme 2. Retrosynthetic Analysis of 2



via the Diels–Alder reaction of **5** with Rawal's diene **B** via preferential approach of **B** from the convex face of the bicyclic dienophile **5**. The cyano lactone **5** should readily be derived from 3-cyclohexene-1-carboxylic acid (**6**), which is known to be available in both racemic and enantiomerically pure forms; in the present synthesis, the racemate of **6** was employed as the starting material.

As shown in Scheme 3, our synthesis of **2** began with regioselective *trans*-diaxial ring opening of epoxide **7** with

Scheme 3. Synthesis of Platensimycin Core 2



Nagata's reagent (Et_2AlCN) prepared in situ from TMSCN and Et_2AlCl;[6,7] **7** in turn was readily obtained from **6** in ca. 75% yield by a known three-step sequence.[6c,8] Exposure of the resulting β-hydroxy nitrile intermediate, which was rather unstable to silica gel column chromatography, to dehydration conditions (MsCl, Et_3N) delivered α,β-unsaturated nitrile **5** in 51% yield from **7**. The Diels–Alder reaction of **5** with Rawal's diene **B** followed by acidic treatment of the cycloaddition product gave **4** as a single isomer.[9] The stereochemistry of **4** was assigned by assuming that the diene **B** approached from the less hindered β-face of the dienophile **5** opposite the lactone bridge and confirmed by its eventual conversion into **2**. Protection of the ketone functionality of **4** as its ethylene acetal proceeded smoothly under Noyori's conditions,[10] furnishing **8** in excellent yield. The lactone **8** was treated with MeMgCl in THF/HMPA (4:1) to give a diol intermediate,[11] the secondary hydroxy group of which was then protected as its TBS ether **9**. The nitrile **9** was reduced with DIBAL-H to give aldehyde **10** in 57% yield. The modest yield of this conversion might be ascribable to the steric congestion around the cyano group, as well as to concomitant reductive C–O bond cleavage of the allylic acetal moiety.[12] The addition of MeLi to **10** afforded **11** as an inconsequential 1:1 mixture of diastereomers at the newly formed stereocenter. Subjection of the diol **11** to an excess amount of Martin's sulfurane brought about dehydration of both the secondary and tertiary hydroxy groups,[13] furnishing desired RCM precursor **3** without formation of any detectable amount of the corresponding tetrasubstituted (isopropylidene-type) olefin, as judged by its ^1H NMR analysis.[14] Despite the equatorial orientation of both the C1 and C9 olefinic substituents, which is unsuitable for ring closure, as well as considerable steric hindrance around the reaction sites, the RCM reaction of **3** could be achieved efficiently by slowly adding the second-generation Grubbs catalyst in two portions to **3** in toluene in the presence of 1,4-benzoquinone at an elevated temperature to afford tricyclic product **12**.[15] Finally, treatment of **12** with hydrochloric acid to remove the silyl and acetal protecting groups induced concurrent intramolecular etherification, providing the platensimycin core **2** in 52% overall yield from **11**, the ^1H and ^{13}C NMR spectra of which were identical to those of an authentic material.[2c]

In conclusion, a new synthesis of the platensimycin core **2** was achieved in 6.6% overall yield from the readily available epoxy lactone **7** by an 11-step sequence that features the regio- and stereoselective Diels–Alder reaction of the bicyclic unsaturated nitrile **5** with Rawal's diene **B** to form the *cis*-decalenone derivative **4** and the ring-closing metathesis of the sterically demanding intermediate **3** to install the five-membered carbocyclic ring embedded in **2**.

EXPERIMENTAL SECTION

General Information. IR spectra were recorded by an FT/IR spectrometer using an ATR (ZnSe) attachment. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, with TMS as an internal standard in $CDCl_3$. High-resolution MS data were obtained by operating in the EI or FAB mode. Column chromatography was performed using 70–230 mesh silica gel. Solvents for reactions were distilled prior to use: THF and DME from Na/benzophenone; CH_2Cl_2 and HMPA from CaH_2; toluene from $LiAlH_4$.

*rel-(1R,5R)-7-Oxo-6-oxabicyclo[3.2.1]oct-3-ene-3-carbonitrile (**5**).* Et_2AlCl (1.07 M in hexane, 38.5 mL, 41.2 mmol) and TMSCN (≥95%, 5.20 mL, ca. 39.5 mmol) were mixed under a nitrogen atmosphere at room temperature and stirred for 15 min. The solvent and TMSCl produced were then evaporated off in vacuo, and the reaction vessel was refilled with nitrogen. To the residue was added a solution of **7** (2.14 g, 15.3 mmol) in DME (50 mL) at 0 °C, with stirring, and the resulting mixture was gradually warmed to room temperature over 4 h. The reaction was quenched with saturated aq Rochelle's salt, and the mixture was extracted with EtOAc (× 3) and then with CH_2Cl_2 (× 1). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give a hydroxy nitrile (2.23 g) as an orange-colored oil, which was then taken up in CH_2Cl_2 (38 mL). To the solution were successively added Et_3N

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(5.60 mL, 39.9 mmol) and MsCl (1.60 mL, 20.0 mmol) at 0 °C under a nitrogen atmosphere, and the mixture was gradually warmed to room temperature and stirred for 12 h. The mixture was quenched with saturated aq NH_4Cl and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 3:1) to give 1.15 g (51%) of **5** as a white solid: mp 45.0−45.5 °C; IR ν_{max} 3004 (w), 2222 (m), 1791 (s), 1121 (s), 963 (s), 885 (s); ^{1}H NMR δ 2.10 (d, J = 11.7 Hz, 1H), 2.59 (dt, J = 11.7, 5.3 Hz, 1H), 2.66 (dt, J = 18.8, 2.2 Hz, 1H), 2.73 (ddd, J = 18.8, 4.3, 2.3 Hz, 1H), 3.03−3.07 (m, 1H), 4.93 (td, J = 5.7, 0.8 Hz, 1H), 7.04 (dm, J = 5.7 Hz, 1H); ^{13}C NMR δ 30.3, 32.8, 36.5, 70.8, 115.4, 116.7, 143.6, 176.7; HRMS (EI) calcd for $C_8H_7O_2N$ (M^+) 149.0477, found 149.0473.

*rel-(1R,2R,7R,9R)-4,10-Dioxo-11-oxatricyclo[7.2.1.0^{2,7}]dodec-5-ene-7-carbonitrile (**4**).* To a stirred solution of **5** (174 mg, 1.17 mmol) in CH_2Cl_2 (4 mL) was added diene **B** (0.54 mL, 2.10 mmol) at 0 °C under a nitrogen atmosphere. The mixture was stirred at 40 °C for 20 min and then at room temperature for an additional 8 h. The mixture was diluted with THF (5 mL), and 1 M aq HCl (1.5 mL) was added at 0 °C. The mixture was gradually warmed to room temperature, stirred for 12 h, and quenched with saturated aq $NaHCO_3$. The mixture was extracted with EtOAc, and the extract was dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 1:3) to give 168 mg (66%) of **4** as a white solid: mp 92.0−92.3 °C; IR ν_{max} 2236 (w), 1777 (s), 1685 (s), 970 (s); ^{1}H NMR δ 1.95 (dd, J = 14.2, 2.3 Hz, 1H), 2.11 (d, J = 12.7 Hz, 1H), 2.33 (dd, J = 16.0, 14.9 Hz, 1H), 2.48 (dm, J = 12.7 Hz, 1H), 2.55 (dd, J = 16.0, 5.0 Hz, 1H), 2.58−2.64 (m, 1H), 2.83−2.87 (m, 1H), 3.20 (br dt, J = 14.9, 4.3 Hz, 1H), 4.85 (dd, J = 5.8, 3.9 Hz, 1H), 6.23 (d, J = 10.0 Hz, 1H), 6.67 (d, J = 10.0 Hz, 1H); ^{13}C NMR δ 31.1, 33.0, 34.8, 35.6, 36.4, 38.3, 78.7, 120.6, 129.2, 143.9, 174.5, 194.1; HRMS (FAB) calcd for $C_{12}H_{12}O_3N$ ([M + H]$^+$) 218.0817, found 218.0822.

*rel-(1R,2R,7R,9R)-4,4-Ethylenedioxy-10-oxo-11-oxatricyclo-[7.2.1.0^{2,7}]dodec-5-ene-7carbonitrile (**8**).* To a stirred solution of **4** (1.13 g, 5.19 mmol) in CH_2Cl_2 (40 mL) were successively added 1,2-bis(trimethylsiloxy)ethane (1.91 mL, 7.79 mmol) and TMSOTf (0.190 mL, 1.04 mmol) at −78 °C under a nitrogen atmosphere. The mixture was gradually warmed to 0 °C over 10 h and quenched with Et_3N. The resulting mixture was diluted with EtOAc, dried (Na_2SO_4), and concentrated in vacuo to give crude **8** as a solid. The solid was triturated with EtOAc and filtered to give 1.15 g (85%) of **8** as a white solid. The filtrate was concentrated in vacuo, and the residue was chromatographed over SiO_2 (hexane/EtOAc, 1:3) to give an additional amount (176 mg, 13%) of **8** as a white solid: mp 110.9−111.3 °C; IR ν_{max} 2228 (w), 1786 (vs), 1135 (s), 1062 (s), 977 (vs); ^{1}H NMR δ 1.68 (t, J = 13.5 Hz, 1H), 1.76−1.83 (m, 2H), 2.00 (d, J = 12.6 Hz, 1H), 2.36 (dm, J = 12.6 Hz, 1H), 2.44 (dm, J = 13.9 Hz, 1H), 2.71−2.75 (m, 1H), 3.05 (dt, J = 13.9, 3.7 Hz, 1H), 3.88−3.97 (m, 1H), 3.99−4.10 (m, 3H), 4.83 (dd, J = 5.7, 4.1 Hz, 1H), 5.73 (d, J = 10.0 Hz, 1H), 5.87 (dd, J = 10.0, 1.4 Hz, 1H); ^{13}C NMR δ 31.4, 32.9, 33.2, 34.0, 36.1, 37.2, 64.9, 65.1, 79.6, 103.7, 121.8, 129.4, 130.2, 175.2; HRMS (FAB) calcd for $C_{14}H_{16}O_4N$ ([M + H]$^+$) 262.1079, found 262.1082.

*rel-(4′aS,6′S,8′S,8′aS)-8′-(tert-Butyldimethylsilyloxy)-6′-(1-hydroxy-1-methylethyl)1′,5′,6′,7′,8′,8′a-hexahydrospiro[1,3-dioxolane-2,2′(4′aH)-naphthalene]-4′a-carbonitrile (**9**).* To a stirred solution of **8** (318 mg, 1.22 mmol) in THF/HMPA (4:1, 10 mL) was added MeMgCl (3.0 M in THF, 1.80 mL, 5.48 mmol) at 0 °C under a nitrogen atmosphere. After 6 h of stirring, the mixture was quenched with saturated aq NH_4Cl and extracted with EtOAc. The extract was dried (Na_2SO_4) and concentrated in vacuo. The residue was roughly chromatographed over SiO_2 to give a diol intermediate as an oil, which was taken up in CH_2Cl_2 (13 mL). To the solution were successively added 2,6-lutidine (0.210 mL, 1.83 mmol) and TBSOTf (0.340 mL, 1.46 mmol) at −78 °C under a nitrogen atmosphere. After 2 h of stirring at the same temperature, the mixture was quenched with wet Et_3N (2 mL) and diluted with EtOAc. The mixture was dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 3:1) to give 352 mg (71%) of **9** as a pale yellow solid: mp 160.4−160.8 °C; IR ν_{max} 2234 (w), 1250 (m), 1118 (s), 1012 (s), 839 (s); ^{1}H NMR δ 0.068 (s, 3H), 0.078 (s, 3H), 0.88 (s, 9H), 1.00−1.10 (m, 1H), 1.18 (s, 3H), 1.20 (s, 3H), 1.32 (br tt, J = 12.7, 2.4 Hz, 1H), 1.69 (t, J = 12.7 Hz, 1H), 1.95−2.03 (m, 2H), 2.18 (dm, J = 13.0 Hz, 1H), 2.31 (dd, J = 14.7, 4.1 Hz, 1H), 2.46 (dm, J = 14.7 Hz, 1H), 3.87−4.04 (m, 5H), 5.53 (dd, J = 9.8, 1.7 Hz, 1H), 5.81 (br dd, J = 9.8, 1.4 Hz, 1H); ^{13}C NMR δ −4.7, −3.8, 18.0, 25.9 (3C), 26.7, 27.4, 32.4, 36.7, 37.2, 42.1, 45.5, 64.1, 64.9, 68.1, 71.7, 103.1, 121.9, 129.0, 132.5; HRMS (FAB) calcd for $C_{22}H_{38}O_4NSi$ ([M + H]$^+$) 408.2570, found 408.2570.

*rel-(4′aS,6′S,8′S,8′aS)-8′-(tert-Butyldimethylsilyloxy)-6′-(1-hydroxy-1-methylethyl)1′,5′,6′,7′,8′,8′a-hexahydrospiro[1,3-dioxolane-2,2′(4′aH)-naphthalene]-4′acarbaldehyde (**10**).* To a stirred solution of **9** (39.4 mg, 96.8 μmol) in CH_2Cl_2/THF (1:1, 1 mL) was added DIBAL-H (1.02 M in hexane, 0.300 mL, 306 μmol) at 0 °C under a nitrogen atmosphere. After 30 min of stirring, the mixture was warmed to room temperature and stirred for an additional 30 min. The mixture was quenched with saturated aq Rochelle's salt and stirred for 5 min. The mixture was diluted with EtOAc, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 2:1) to give 22.5 mg (57%) of **10** as a white solid: mp 94.7−95.2 °C; IR ν_{max} 2709 (w), 1727 (s), 1095 (s), 836 (s), 776 (s); ^{1}H NMR δ 0.085 (s, 3H), 0.090 (s, 3H), 0.89 (s, 9H), 0.96−1.07 (m, 1H), 1.17 (s, 3H), 1.19 (s, 3H), 1.24−1.32 (m, 1H), 1.36−1.46 (m, 1H), 1.78 (dm, J = 12.5 Hz, 1H), 1.85 (dd, J = 14.5, 4.3 Hz, 1H), 1.91−1.98 (m, 1H), 2.01 (dm, J = 11.9 Hz, 1H), 2.35 (br d, J = 14.5 Hz, 1H), 3.85−4.08 (m, 5H), 5.57 (d, J = 10.2 Hz, 1H), 5.87 (d, J = 10.2 Hz, 1H); ^{13}C NMR δ −4.7, −3.8, 18.0, 25.9 (3C), 26.6, 27.4, 31.7, 32.6, 36.8, 41.8, 42.2, 52.3, 64.0, 64.8, 69.4, 71.9, 103.7, 131.3, 132.4, 200.6; HRMS (FAB) calcd for $C_{22}H_{38}O_5SiNa$ ([M + Na]$^+$) 433.2385, found 433.2388.

*rel-(4′aS,6′S,8′S,8′aS)-2-{8′-(tert-Butyldimethylsilyloxy)-4′a-(1-hydroxyethyl)4′a,5′,6′,7′,8′,8′a-hexahydrospiro[1,3-dioxolane-2,2′(1′H)-naphathalen]-6-yl}-2-propanol (**11**).* To a stirred solution of **10** (41.7 mg, 102 μmol) in THF (1.2 mL) was added MeLi (1.14 M in ether, 0.450 mL, 513 μmol) at 0 °C under a nitrogen atmosphere. The mixture was gradually warmed to room temperature and stirred for 5 h. The mixture was quenched with saturated aq NH_4Cl, diluted with EtOAc, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 2:3) to give 41.1 mg (95%) of **11** as a colorless oil: IR ν_{max} 3446 (m), 1255 (s), 1097 (vs), 1062 (vs), 835 (s); ^{1}H NMR δ 0.070 (s, 3H), 0.074 (s, 3H), 0.89 (s, 9H), 0.92−1.01 (m, 1H), 1.16−1.20 (m, 9H), 1.25−1.32 (m, 4H), 1.50−1.62 (m, 1H), 1.78−1.88 (m, 1H), 1.94−2.02 (m, 1H), 2.08 (dd, J = 14.7, 4.5 Hz, 0.5 × 1H), 2.17 (dd, J = 14.7, 4.5 Hz, 0.5 × 1H), 2.32 (br t, J = 14.7 Hz, 1H), 3.84−4.04 (m, 6H), 5.48 (dd, J = 10.2, 1.7 Hz, 0.5 × 1H), 5.64 (dd, J = 10.2, 1.3 Hz, 0.5 × 1H), 5.67 (dd, J = 10.2, 1.2 Hz, 0.5 × 1H), 5.77 (dd, J = 10.2, 1.7 Hz, 0.5 × 1H); ^{13}C NMR δ −4.70/−4.67, −3.8/−3.7, 18.0/18.1, 25.98/25.99 (3C), 26.6/26.9, 27.0/27.4, 29.8/30.1, 30.5/31.2, 37.0, 42.3, 42.47/42.51, 43.3/43.6, 44.3, 64.0, 64.6/64.7, 70.5/70.6, 71.2, 72.3/72.4, 104.2, 128.7/129.2, 137.8/139.2; HRMS (FAB) calcd for $C_{23}H_{43}O_5Si$ ([M + H]$^+$) 427.2879, found 427.2883.

*rel-(1R,3R,4R,5aR,9aR)-4,5,9,9a-Tetrahydro-3-methyl-3H-1,4:3,5a-dimethano-2benzoxepin-8(1H)-one (**2**).* To a stirred solution of **11** (58.3 mg, 137 μmol) in toluene (9.1 mL) was added a solution of Martin's sulfurane (249 mg, 370 μmol) in toluene (3 mL) at room temperature under a nitrogen atmosphere. After 3 h, an additional solution of Martin's sulfurane (88.6 mg, 132 μmol) in toluene (3 mL) was added, and the resulting mixture was stirred for 1 h before being quenched with saturated aq $NaHCO_3$. The mixture was extracted with EtOAc, and the extract was successively washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 10:1) to give **3** (ca. 60 mg) containing small amounts of impurities: ^{1}H NMR δ 0.08 (s, 3H), 0.09 (s, 3H), 0.89 (s, 9H), 1.15−1.25 (m, 1H), 1.33 (t, J = 13.0 Hz, 1H), 1.47−1.53 (m, 1H), 1.57 (dt, J = 13.0, 2.5 Hz, 1H), 1.71 (s, 3H), 1.91−1.97 (m, 2H), 2.02 (dd, J = 14.1, 4.2 Hz, 1H), 2.23 (dm, J = 14.1 Hz, 1H), 3.85−4.09 (m, 5H), 4.67−4.71 (m, 2H), 5.00 (dd, J = 17.2, 1.3 Hz, 1H), 5.03 (dd, J = 10.4, 1.3 Hz, 1H), 5.52 (dd, J = 10.1, 1.7 Hz, 1H), 5.67 (dd, J = 17.2, 10.4 Hz, 1H), 5.73 (dd, J = 10.1, 1.5

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Hz, 1H). Compound **3** just obtained and 1,4-benzoquinone (8.6 mg, 75.9 mmol) were dissolved in toluene (4 mL) under a nitrogen atmosphere. To the solution was added a solution of the second-generation Grubbs catalyst (17.4 mg, 20.4 μmol) in toluene (1 mL) at 90 °C over a period of 1 h. After 18 h of stirring at the same temperature, an additional amount of the catalyst (18.6 mg, 21.9 μmol) in toluene (1 mL) was added over 1 h, and the mixture was stirred for a further 23 h. After cooling, the mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 30:1) to give **12** (32.3 mg), which was taken up in THF (4 mL). To the solution was added aq HCl (2 M, 2 mL) at 0 °C, and the mixture was stirred at room temperature for 25 h. To the solution was added additional aq HCl (2M, 1 mL), and the mixture was stirred for further 28 h before being quenched with saturated aq $NaHCO_3$. The mixture was extracted with EtOAc, and the extract was successively washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 3:2) to give 14.6 mg (52%) of **2** as a colorless oil: IR ν_{max} 3020 (vw), 1678 (vs), 1138 (w), 1038 (w), 994 (w), 821 (w); ^{1}H NMR δ 1.44 (s, 3H), 1.66 (d, J = 11.4 Hz, 1H), 1.72−1.79 (m, 2H), 1.89 (d, J = 11.5 Hz, 1H), 1.92−1.98 (m, 2H), 2.27−2.44 (m, 4H), 4.16 (br t, J = 3.4 Hz, 1H), 5.94 (d, J = 10.0 Hz, 1H), 6.62 (d, J = 10.0 Hz, 1H); ^{13}C NMR δ 23.1, 37.4, 37.9, 42.2, 42.7, 44.1, 46.2, 51.7, 79.0, 87.0, 128.9, 155.2, 199.1; HRMS (EI) calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1149.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

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Notes

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