Synthetic Study on Gymnomitrol and Related Compounds. I. Preparation and Cyclopropane Ring Opening of 1,2,6-Trimethyltetraclclo[5.3.1.08,11.08,11]undecan-9-one

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1,2,6-Trimethyltetraclclo[5.3.1.02,6.08,11]undecan-9-one (4) was prepared from 1,5-dimethylbicyclo[3.3.0]octan-3-one (6) in fourteen steps. Its cyclopropane ring opening reaction was examined under various conditions. In all runs, 11-substituted 1,2,6-trimethyltricyclo[5.3.1.02,6]undecan-9-ones 20 were obtained as major products along with 7-substituted 1,2,8-trimethyltricyclo[6.3.0.02,6]undecan-4-ones 21 and two other products 22 and 23.

Keywords cyclopropane cleavage; tetracyclo[5.3.1.02,6.08,11]undecane; Claisen rearrangement; tricyclo[5.3.1.02,6]undecane; reductive alkylation

Gymnomitrol (1), one of the diquainone sesquiterpenoids, was isolated from the liverwort Gymnomitrion obtusum (Lindb) Pears in 1970 and its structure was assigned as 1, which possesses the unique tetracyclo[5.3.1.02,6]undecane framework, on the basis of chemical degradation and spectroscopic evidence.11 Because of the interesting structure, a number of chemists conducted synthetic studies and total synthesis of 1 have been achieved by several groups.21 In previous papers, we described the behavior of cyclopropane ring opening in the tetracyclo[3.3.0.02,8]octane compounds 2b and showed that acid-catalyzed nucelophilic substitution reactions of 2b gave mainly the bicyclo[3.2.1]octane derivatives 3b via a regioselective cleavage of the least reactive C(1)-C(2) bond (type B).33 On the other hand, compounds 2a afford the bicyclo[3.3.0]octanes 3a predominantly via the C(2)-C(8) bond cleavage (type A) in the same reactions. These results can be well interpreted in terms of steric hindrance of the gem-dimethyl groups at C(7) and stereoelectronic requirement, as discussed below. We planned a further application of the bicyclic cyclopropane ring cleavage of bicyclo[3.3.0]octanes to another ring system, i.e., the tetracyclo[5.3.1.02,6.08,11]undecane framework. 1,2,6-Trimethyltetraclclo[5.3.1.02,6.08,11]undecan-9-one (4) is a very attractive target for the following reasons. (a) The tetracycloundecane 4, which resembles the tricyclooctanone 2b in steric features around the cyclopropane ring, is expected to undergo the type B cyclopropane ring opening on acid-catalyzed nucleophilic substitution reactions. (b) Since the cyclopropane ring opening reaction proceeds via an $S_{N}2$-like mechanism, the relative configuration of the product should be as shown in 5, which has the same stereochemistry as that of gymnomitrol (1).

In this paper, we wish to describe the preparation of 1,2,6-Trimethyltetraclclo[5.3.1.02,6.08,11]undecan-9-one (4) and the features of its cyclopropane ring opening reactions.

Preparation of 1,2,6-Trimethyltetraclclo[5.3.1.02,6.08,11]undecan-9-one (4) The starting material for the preparation of 4 is 1,5-dimethylbicyclo[3.3.0]octan-3-one (6), which was also used as the common synthetic intermediate for the synthesis of 1 by Coates et al.,20 and Paquette and Han.24 Treatment of 6 with lithium disopropylamide (LDA) followed by reaction with diphenyl disulfide gave 7 as a mixture of diastereoisomers in 64% yield. Due to easy enolization and steric hindrance of the C(1)-methyl group, reaction of the enolate anion generated from 7 with allyl bromide afforded the allyl vinyl ether 8 in 82% yield. Heating of the toluene solution of 8 in a sealed tube gave the Claisen rearrangement product 9 in 94% yield.20 This rearrangement occurred on the less hindered convex face via a chair form transition state affording a single product 9. Desulfurization of 9 under the Birch reaction conditions followed by trapping of the resulting lithium enolate with methyl iodide afforded 10 in 48% yield as a single compound, through approach of the nucleophile from the less hindered side.25,26,28 Though this compound 10 has already prepared as the synthetic intermediate for 1,26,28 we have developed an alternative and efficient route to 10. Ozonolysis of 10 followed by reductive work-up gave the aldehyde 11, which was subjected to chemoselective acetalization with 1.1 eq of ethylene glycol to afford 12 in 72% yield. The ketone 12 was reduced with lithium aluminium hydride (LiAlH4) to give 13 in nearly quantitative yield, and its mesylate 14 was converted into the olefin 15 in 86% yield. Deprotection of the acetal group in 15 and subsequent oxidation of the aldehyde 16 with chromic trioxide afforded the carboxylic acid 17 in 90% yield. The
carboxylic acid 17 was transformed into the diazoketone 19 via the acid chloride 18 in a usual manner.\(^{4,5}\) Upon treatment of 19 with copper(II) acetylacetonate (Cu(acac)_2) in boiling benzene, cyclopropanation smoothly took place and the expected product 4 was isolated in 64% yield.\(^{4,5}\)

Its structural assignment was supported by spectral considerations. Thus the mass spectrum (MS) and elemental analysis revealed that the product has the formula C_{14}H_{25}O, and its infrared (IR) spectrum showed a carbonyl band absorption at 1715 cm\(^{-1}\) due to the 5-membered ring ketone adjacent to the cyclopropane ring. The proton nuclear magnetic resonance (\(^1\)H-NMR) spectrum exhibited three singlet peaks at 1.02, 1.14, and 1.17 ppm due to the three methyl groups and no signal was observed below 2.70 ppm.

**Cyclopropane Ring Opening of 1,2,6-Trimethyltricyclo[5.3.1.0^{2,6}]jundecan-9-one (4)** There have been many reports concerning cyclopropane ring opening.\(^6\) In rigid cyclopropyl ketone systems, the C–C σ-bond which is well overlapped with the adjacent C=O π-orbital is known to be cleaved more easily than the other two C–C bonds.\(^5\) Thus, in the case of 2a, the C(2)–C(8) bond (the external bond) is cleaved more easily to afford the bicyclo[3.3.0]octanone 3a.\(^5\) On the other hand, we have found that, in the case of 2b, C(1)–C(2) bond (the internal bond) cleavage occurs exclusively or predominantly. This phenomenon is attributable to the steric hindrance of the gem-dimethyl groups at the C(7) position, because this opening proceeds via an S_2-like mechanism.\(^7\) In the case of 4, the C(6)-methyl group would prevent nucleophilic attack at the C(7) position. Therefore, it is expected that the nucleophilic attack would occur at the C(11) position and the C(8)–C(11) bond (the internal bond) would be cleaved to afford the tricyclo[5.3.1.0^{2,6}]jundecan skeleton 5. Furthermore, C(11) of 5 would have the same stereochemistry as that of 1.

Cleavage of the cyclopropane ring of 4 was examined under various conditions and the results are summarized in Table 1. As expected, moderate amounts of the tricyclo[5.3.1.0^{2,6}]octanones 20 were obtained along with 21, 22, and 23 in all runs. In particular, when methanol was used as a nucleophile, the C(8)–C(11) bond-cleaved product 20 (R = OMe) was selectively obtained without any 22 or 23 (see runs 4 and 5).

<table>
<thead>
<tr>
<th>Run</th>
<th>Reaction conditions</th>
<th>R</th>
<th>Yield (%)^a</th>
<th>20</th>
<th>21</th>
<th>22</th>
<th>23</th>
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<tbody>
<tr>
<td>1</td>
<td>1) HCO_2H, 90°C. 2) OH^-</td>
<td>OH</td>
<td>26 (29)#</td>
<td>12 (14)#</td>
<td>11 (12)#</td>
<td>4 (4)#</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1) HCO_2H, p-TsOH, 90°C. 2) OH^-</td>
<td>OH</td>
<td>29</td>
<td>13</td>
<td>13</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1) HCO_2H, conc. H_2SO_4, 90°C. 2) OH^-</td>
<td>OH</td>
<td>26</td>
<td>11</td>
<td>8</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MeOH, p-TsOH, reflux</td>
<td>OMe</td>
<td>65</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>MeOH, conc. H_2SO_4, reflux</td>
<td>OMe</td>
<td>90</td>
<td>10</td>
<td>0</td>
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<td></td>
</tr>
</tbody>
</table>

^a Isolated yield.  
^b Yield based on the consumed starting material 4.
stereochemistry of 20 and 21 were confirmed to be as shown in Table I on the basis of spectral considerations and the reaction mechanism. In the 1H-NMR spectrum of 20, the C(11) proton appeared as a singlet at 4.20 ppm, since the dihedral angle between the carbonyl proton and C(7) proton is close to 90°.11 On the other hand, IR spectrum of 22 showed a 5-membered ring ketone band at 1735 cm⁻¹ and its 1H-NMR spectrum exhibited a doublet (3H, J = 1 Hz) at 1.53 ppm due to the vinyl methyl group. The IR spectrum of 23 showed absorption bands at 1695 and 1625 cm⁻¹ due to an unsaturated 5-membered ring ketone moiety and its 1H-NMR spectrum exhibited a doublet (3H, J = 7.5 Hz) at 1.27 ppm due to the C(7) methyl protons. In the ultraviolet (UV) spectrum, the absorption maximum due to a 5-membered ring enone system was observed at 233 nm (ε = 11800).

A tentative reaction mechanism is depicted in Chart 3. The protonated compound 24 should be the common starting species of this reaction. Nucleophilic attack on the less hindered C(11) carbon of 24 affords the tricyclo[5.3.1.0²,8]octanone derivative 20 via 25 (path a), while nucleophilic attack on the hindered C(7) carbon affords the tricyclo[5.3.3.0²-10]undecane derivative 21 via 27 (path b). The cation 26, which could be formed by acid-catalyzed cyclopropane ring opening at the C(7)–C(8) bond, may also be an intermediate for 27 (path c). The formation of the olefinic derivatives 22 and 23 are clearly expressed as a result of the Wagner–Meerwein rearrangement of 26. Migration of the C(6) methyl group to the cationic center gives 28 (path d), which affords 22 and 23 via 29.

As described above, preparation of 1,2,6-trimethyltetraacyclo[5.3.1.0²,8]octan-9-one (4) and its cyclopropane ring opening reaction to the tricyclo[5.3.1.0²,6]-octanone derivative 20, having the basic skeleton of gymnornitol and the same stereochemistry of the C(11) substituent, were achieved. This methodology could serve as a novel and efficient route for the synthesis of gymnornitol (I).

**Experimental**

Melting points are uncorrected. IR spectra were recorded with a Hitachi 260-10 spectrometer. 1H-NMR spectra were measured with a Hitachi R-20 (90 MHz) or a JEOL FX-90Q (90 MHz) with tetramethylsilane as an internal standard. MS and high-resolution MS (High MS) were obtained with a Shimadzu QP-1000 or a JEOL JMS-D300 mass spectrometer. UV spectra were recorded with a Hitachi 124 spectrometer in 95% ethanol. For column chromatography, Silica gel 60 (E. Merck) was used. After drying over anhydrous sodium sulfate or lithium sulfate, all organic extracts were concentrated under reduced pressure.

**1R,5S,RS,1S,5R,5S,10S,10R**-1,5-Dimethyl-2-phenylthioctacyclo[3.3.3.0³-7,0]octan-3-one (7)

Under a nitrogen atmosphere, hexamethylphosphoramide (HMPA; 1.55 g, 8.65 mmol) was added dropwise to a solution of LDA, generated from disopropylamine (740 mg, 7.33 mmol) and n-butyllithium (1.28 M in hexane, 5.8 ml, 7.40 mmol) in tetrahydrofuran (THF, 7 ml) at −78 °C, and the mixture was stirred for 1 h at the same temperature. A solution of 6 (748 mg, 4.92 mmol) in THF (5 ml) and a solution of diphenylsulfide (1.60 g, 7.33 mmol) in THF (10 ml) were successively added dropwise to the mixture at −78 °C. The whole was stirred for 1 h at the same temperature and then for an additional 12 h, during which time the reaction mixture was gradually warmed to room temperature. After addition of saturated NH₄Cl solution, the mixture was extracted with ether (25 ml × 3). The combined extracts were successively washed with 10% HCl solution, water, saturated NaHCO₃ solution, and brine, then dried, and evaporated. The residue was chromatographed on silica gel with benzene–hexane (3:2) to give 7 (824 mg, 64%) as a pale yellow oil. IR (CCl₄, cm⁻¹): 3060, 1740, 1590. 1H-NMR (CDCl₃) δ: 1.01, 1.05, 1.12 (total 6H, each s, 1-Me, 5-Me), 0.8–2.0 (6H, m), 2.0–2.3 (2H, m, 4-H), 3.29, 3.35 (total 1H, each s, 2-H), 7.0–7.5 (5H, m, aromatic H). MS m/z (%): 260 (M⁺, 43), 95 (100). High MS Caled for C₂₂H₂₅NO: 306.1234. Found: 306.1244.

**1R,5S,RS,1R,5R,5S,10S,10R**-1,5-Dimethyl-2-phenylthio-3-(2-propenyl) bicyclo[3.3.0]octan-3-one (6)

Under a nitrogen atmosphere, HMPA (309 mg, 1.72 mmol) was added dropwise to a solution of LDA, prepared from disopropylamine (178 mg, 1.76 mmol) and n-butyllithium (1.6 M in hexane, 1.1 ml, 1.80 mmol) in THF (3 ml) at −78 °C, and the whole was stirred for 15 min at the same temperature. A solution of 7 (380 mg, 1.46 mmol) in THF (2 ml) was added dropwise to the mixture at −78 °C. The whole was stirred for 10 min at the same temperature and then for 20 min at 0 °C. Allyl bromide (212 mg, 1.75 mmol) was added dropwise to the mixture at 0 °C. The whole was stirred for 1 h at 0 °C and 20 h at room temperature. After addition of saturated NH₄Cl solution, the mixture was extracted with ether (10 ml × 3). The combined extracts were washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–acetone (10:1) to give 8 (360 mg, 82%) as a pale yellow oil. IR (CHCl₃, cm⁻¹): 3060, 1630, 1585. 1H-NMR (CDCl₃) δ: 0.99, 1.07 (each 3H, each s, 1-Me, 5-Me), 1.2–2.0 (6H, m), 2.48 (2H, s, 4-H), 4.35–4.6 (2H, m, OCH₂C=C) 5.0–5.4 (2H, m, –CH₂=CH₂), 5.6–6.1 (1H, m, –CH=CH₂), 6.9–7.4 (5H, m, aromatic H). MS m/z (%): 300 (M⁺, 35), 259 (32), 217 (100). High MS Caled for C₂₂H₂₅NO: 306.1545. Found: 300.1539.

**1R,5S,RS,1S,5R,5S,10S,10R**-1,5-Dimethyl-2-phenylthio-2-(2-propenyl)bicyclo[3.3.0] octan-3-one (9)

A solution of 8 (222 mg, 0.740 mmol) in toluene (10 ml) was heated in a sealed tube at 180 °C for 20 h. After the solution had cooled, the solvent was evaporated off. The residue was chromatographed on silica gel with hexane–AcOEt (10:1) to give 9 (209 mg, 94%) as a pale yellow oil. IR (CHCl₃, cm⁻¹): 3070, 1720, 1640, 1580, 920. 1H-NMR (CDCl₃) δ: 0.96, 1.04 (each 3H, each s, 1-Me, 5-Me), 1.2–2.6 (8H, m), 2.00, 2.90 (2H, AB-q, J = 18 Hz, 4-H), 4.8–5.2 (2H, m, –CH=CH₂), 5.8–6.4 (1H, m, –CH=CH₂), 7.0–7.5 (5H, m, aromatic H). MS m/z (%): 300 (M⁺, 25), 259 (27), 191 (25), 95 (100). High MS Caled for C₂₂H₂₅NO: 306.1545. Found: 300.1531.

**1R,5S,RS,1S,5R,5S,10S,10R**-1,2,5-Trimethyl-2-(2-propenyl)bicyclo[3.3.0]octan-3-one (10)

A solution of 9 (33 mg, 0.11 mmol) in THF (1 ml) was added to a solution of lithium (5.0 mg, 0.72 mmol) in liquid ammonia (10 ml) at −78 °C. The mixture was stirred for 5 min, then HMPA (0.5 ml, 2.9 mmol) and methyl iodide (0.10 ml, 1.6 mmol) were successively added at −78 °C. The ammonia was evaporated off. After addition of water, the mixture was extracted with ether (10 ml × 3). The combined extracts were washed with brine, dried, and evaporated. The residue was chromatographed on...
silica gel with hexane–AcOEt (20:1) to afford 10 (11 mg, 48% as a pale yellow oil.\(^{33}\) IR (CCl\(_4\)) cm\(^{-1}\): 3070, 1735, 1640, 995, 915. \(^{1}H\)-NMR (CDCl\(_3\)) \(\delta\): 0.95, 0.99, 1.16 (each 3H, each s, 1-Me, 2-Me, 5-Me), 0.9–1.9 (6H, m), 2.12 (2H, t, \(J=5.5\) Hz, 2-Me), 7.05–7.10 (4H, m, \(-C\text{H}-\)). MS m/z (%): 206 (M\(^{+}\), 5.6), 95 (100). High MS Caled for C\(_{19}\)H\(_{20}\)O\(_{2}\): 206.1688. Found: 206.1661.

(1R,2S,3R,5S)-(±)-1-(3-Dioxolan-2-yl)-1,2,3,5-tetrahydroxy-cyclohexane (3.30 g, 3.00 mmol) was added dropwise to a solution of TFA (4 mL, 53 mmol) in dichloromethane (10 mL) and methanol (15 mL) for 4 h at \(-78^\circ\text{C}\). After removal of the excess ozone by flushing the reaction mixture with dry \(\text{N}_2\), dimethyl sulfoxide (1.2 mL) was added and the whole mixture was stirred for 6 h at room temperature. Evaporation of the solvents gave crude \(1\) as a colorless oil. IR (CCl\(_4\)) cm\(^{-1}\): 3240, 1740, 1725. \(^{1}H\)-NMR (CDCl\(_3\)) \(\delta\): 0.40, 1.18, 1.23 (each 3H, each s, 1-Me, 2-Me, 5-Me), 1.5–1.9 (6H, m), 2.12 (2H, t, \(J=5.5\) Hz, 2-Me), 6.90–7.10 (4H, m, \(-C\text{H}-\)). MS m/z (%): 220 (M\(^{+}\), 78.7), 216 (M\(^{+}\)-H, 8.6). High MS Caled for C\(_{19}\)H\(_{20}\)O\(_{3}\): 220.1726. Found: 220.1734.

(1R,2S,3R,5S)-(±)-1-(3-Dioxolan-2-yl)-1,2,3,5-tetrahydroxy-cyclohexane (3.30 g, 3.00 mmol) was added dropwise to a solution of \(1\) (263 mg, 1.04 mmol) in ether (10 mL) at 0 \(^{\circ}\text{C}\) and the whole was stirred for 30 min at 0 \(^{\circ}\text{C}\). After addition of saturated potassium sodium tartrate solution, the precipitate was filtered off. The filtrate was dried, and evaporated to give 12 (258 mg, 97%) as a colorless oil. IR (CCl\(_4\)) cm\(^{-1}\): 3550, 3520. \(^{1}H\)-NMR (CDCl\(_3\)) \(\delta\): 0.79, 0.82, 0.84, 1.00, 1.02 (each 3H, each s, 1-Me, 2-Me, 5-Me), 0.44, 1.93 (each 2H, ABq, \(J=15.5\) Hz, 2-Me), 6.65 (2H, CH\(_2\)-OCH\(_3\)), 5.75 (2H, CH\(_2\)-Cl), 4.11 (3H, br, OH), 3.6–4.1 (5H, m, OCH\(_3\)-CO\(_2\)), 3.4–3.8 (2H, m, \(-C\text{H}-\)). MS m/z (%): 254 (M\(^{+}\), 0.4), 236 (2.5), 221 (1.7), 73 (100). High MS Caled for C\(_{19}\)H\(_{20}\)O\(_{3}\): 254.1882. Found: 254.1893.

(1R,2S,3R,5S)-(±)-1-(3-Dioxolan-2-yl)-1,2,3,5-tetrahydroxy-cyclohexane (3.30 g, 3.00 mmol) was added dropwise to a solution of 12 (263 mg, 1.04 mmol) in ether (10 mL) at 0 \(^{\circ}\text{C}\) and the whole was stirred for 30 min at 0 \(^{\circ}\text{C}\). After addition of saturated potassium sodium tartrate solution, the precipitate was filtered off. The filtrate was dried, and evaporated to give 13 (258 mg, 97%) as a colorless oil. IR (CCl\(_4\)) cm\(^{-1}\): 3550, 3520. \(^{1}H\)-NMR (CDCl\(_3\)) \(\delta\): 0.79, 0.82, 0.84, 1.00, 1.02 (each 3H, each s, 1-Me, 2-Me, 5-Me), 0.44, 1.93 (each 2H, ABq, \(J=15.5\) Hz, 2-Me), 6.65 (2H, CH\(_2\)-OCH\(_3\)), 5.75 (2H, CH\(_2\)-Cl), 4.11 (3H, br, OH), 3.6–4.1 (5H, m, OCH\(_3\)-CO\(_2\)), 3.4–3.8 (2H, m, \(-C\text{H}-\)). MS m/z (%): 254 (M\(^{+}\), 0.4), 236 (2.5), 221 (1.7), 73 (100). High MS Caled for C\(_{19}\)H\(_{20}\)O\(_{3}\): 254.1882. Found: 254.1893.

The Reaction of 4 with Formic Acid (Run 1) A solution of 4 (250 mg, 1.23 mmol) in 98–100% formic acid (5 mL) was heated at 120 \(^{\circ}\text{C}\). After removal of the formic acid, methanol (3 mL) was added to the residue and the mixture was basified with 5% NaOH solution. The whole was stirred for 30 min at room temperature. After removal of the solvents, the mixture was extracted with CHCl\(_3\) (10 mL x 3). The combined extracts were washed with brine, dried, and evaporated. The residual was chromatographed on silica gel with hexane–AcOEt (4:1) to give 20 (R = OH) (71 mg, 26%), 21 (27 mg, 11%), 22 (27 mg, 11%), 23 (10 mg, 4%), and recovered 4 (25 mg, 10%).

(1R,2S,3R,5S,7R,8S,11R,SR)-1-Hydroxy-1,2,6-trimethylcyclohexane (5.3.3.33) judecan-9-one (4) Oxalyl chloride (1.04 g, 18.9 mmol) was added dropwise to a solution of 17 (855 mg, 4.11 mmol) in benzene (5 mL) at 0 \(^{\circ}\text{C}\) and the whole was stirred for 1 h at 0 \(^{\circ}\text{C}\). Removal of the volatile (CHCl\(_3\)), the crude acid chloride 18. The solution of 18 in benzene (5 mL) was added dropwise to a solution of an excess of diazomethane in ether at 0 \(^{\circ}\text{C}\) and the whole was stirred for an additional 30 min at 0 \(^{\circ}\text{C}\). Removal of the solvents and excess diazomethane afforded the crude diazoketone 19. The solution of 19 in benzene (20 mL) was added dropwise to a refluxing solution of Cu(aac)\(_2\) (108 mg, 0.41 mmol) in benzene (50 mL) and the whole was refluxed for 4 h. After evaporation of the solvent, the residue was diluted with ether and the dilute solution was passed through a pad of Florisil. The filtrate was concentrated to leave the crude product, which was chromatographed on silica gel with hexane–AcOEt (4:1) to give 20 (R = OH) (71 mg, 26%), 21 (27 mg, 11%), 22 (27 mg, 11%), 23 (10 mg, 4%), and recovered 4 (25 mg, 10%).

The Reaction of 4 with Formic Acid (Run 1) A solution of 4 (250 mg, 1.23 mmol) in 98–100% formic acid (5 mL) was heated at 120 \(^{\circ}\text{C}\). After removal of the formic acid, methanol (3 mL) was added to the residue and the mixture was basified with 5% NaOH solution. The whole was stirred for 30 min at room temperature. After removal of the solvents, the mixture was extracted with CHCl\(_3\) (10 mL x 3). The combined extracts were washed with brine, dried, and evaporated. The residual was chromatographed on silica gel with hexane–AcOEt (4:1) to give 20 (R = OH) (71 mg, 26%), 21 (27 mg, 11%), 22 (27 mg, 11%), 23 (10 mg, 4%), and recovered 4 (25 mg, 10%).
of the product on silica gel afforded 20 (R = OH) (9.5 mg, 26%), 21 (R = OMe) (4.1 mg, 11%), 22 (2.8 mg, 8%), and 23 (7.1 mg, 21%).

The Reaction of 4 with Methanol and ρ-TsOH (Run 4) A mixture of 4 (20 mg, 0.098 mmol), ρ-TsOH (trace), and methanol (10 ml) was refluxed for 4 h. After removal of the methanol, water was added to the residue and the mixture was extracted with AcOEt (10 ml × 3). The combined extracts were washed with saturated NaHCO₃ solution and brine, then dried, and evaporated. The residue was chromatographed on silica gel with hexane-ether (10:1) to give 20 (R = OMe) (15 mg, 65%) and 21 (R = OMe) (5.3 mg, 23%).

\[(RS,2RS,6RS,7SR,11RS)-11-Methoxy-1,2,6-trimethyltricyclo[5.3.1.0²⁵]jundecan-9-one (20, R = OMe); Colorless crystals. mp 31–32°C. IR (CHCl₃) cm⁻¹: 1705. \^H-NMR (CDCl₃) δ: 0.96, 1.03, 1.12 (each 3H, each s, 1-Me, 2-Me, 6-Me), 0.7–3.0 (11H, m), 3.34 (3H, s, OCH₃), 3.64 (1H, s, 11-H). MS m/z (%): 236 (M⁺, 19), 221 (9), 96 (100). Anal. Calcd for C₁₃H₂₄O₂: C, 76.22; H, 10.24. Found: C, 76.09; H, 10.12.

\[(RS,2RS,6SR,7RS,8RS)-7-Methoxy-1,2,8-trimethyltricyclo[6.3.0.0²⁵]jundecan-4-one (21, R = OMe); A colorless oil. IR (CHCl₃) cm⁻¹: 1730. \^H-NMR (CDCl₃) δ: 0.90, 0.98, 1.16 (each 3H, each s, 1-Me, 2-Me, 8-Me), 0.8–2.8 (11H, m), 3.17 (1H, d, J = 8.5 Hz, 7-H), 3.40 (3H, s, OCH₃). MS m/z (%): 236 (M⁺, 9.5), 221 (12), 149 (100). High MS Calcd for C₁₃H₂₄O₂: 236.1777. Found: 236.1789.

The Reaction of 4 with Methanol and Concentrated Sulfuric Acid (Run 5) A mixture of 4 (22 mg, 0.11 mmol), concentrated H₂SO₄ (trace), and methanol (10 ml) was refluxed for 30 h. The usual work-up as described above afforded an oil. Column chromatography of the product on silica gel afforded 20 (R = OMe) (23 mg, 90%) and 21 (R = OMe) (2.7 mg, 10%).

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References