Acid-catalysed Skeletal Rearrangement of an Epoxy Derivative of Terrecyclic Acid A. Formation of a 5-Oxatetracyclo[5.5.1.0^{4,13}.0^{10,13}]tridecane Derivative

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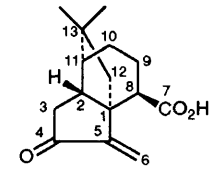
Treatment of the epoxide **3** which is derived from a sesquiterpene antitumour antibiotic, terrecyclic acid A **1**, with BF_3·OEt_2 in benzene, affords a skeletally rearranged ether **6** as the sole product; its structure was deduced from spectroscopic data including, 2D NMR data, to be [1*S*, 2*S*, 4*R*, 7*R*, 10*S*, 13*R*]-2-hydroxy-11,11-dimethyl-5-oxatetracyclo[5.5.1.0^{4,13}.0^{10,13}]tridecan-1-ylmethanol.

Terrecyclic acid A **1**, $C_{15}H_{20}O_3$, is produced by *Aspergillus terreus* Thom No. 14[1,2] and has the same novel carbon skeleton as that of quadrone **2**,[3] an antitumour substance from *A. terreus*. As the skeletal structures of **1** and **2** are not only highly strained but are also unique from the viewpoint of terpenoid biosynthesis, there have been many studies of their total synthesis[4] and biosynthesis.[5] In order to reduce the strain energy of **1** and to elucidate the biosynthetic relationships between **1** and other sesquiterpenes, we studied the acid-catalysed skeletal rearrangement of an epoxide **3** derived from **1**.

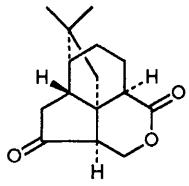
Hydroxy ester **4** was obtained by diisobutylaluminium hydride reduction of **1** followed by diazomethane treatment.[6] When diol **5**, obtained by lithium aluminium hydride reduction of **4**, was epoxidized with *m*-chloroperbenzoic acid, epoxide **3** was afforded stereospecifically. The configuration assigned to epoxide **3** was based on the presence of NOE cross peaks between one proton of C-6 methylene group and C-12 methylene protons and between the other proton of C-6 methylene group and a C-4 proton in a NOESYspectrum.

When the dihydroxylated epoxide **3** was treated with an excess of BF_3·OEt_2 in benzene at 0 °C for 0.5 h followed by quenching with aqueous sodium hydrogencarbonate solution, a diol **6** possessing an ether ring was obtained as the sole product. The high resolution mass spectrum (EI) of **6** showed that the molecular formula ($C_{15}H_{24}O_3$) had remained constant in the course of the rearrangement. The IR spectrum of **6** showed a band due to the presence of hydroxy group(s) at *ca.* 3400 cm^{-1}, but no signals assignable to a carbonyl group or an alkene were observed. Because the degree of unsaturation of **6** was four and any evidence of the presence of a double bond was not obtained, we deduced that the rearranged product **6** is tetracyclic. Acetylation of **6** afforded the corresponding diacetate **7**,† which indicated that two of the three oxygens of **6** were hydroxy and that the remaining oxygen might be a part of an ether.

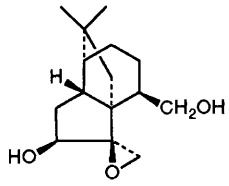
† Acetate **7** was also obtained by treatment of **3** with BF_3·OEt_2 in acetic anhydride.



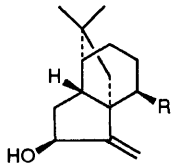
1



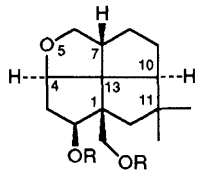
2



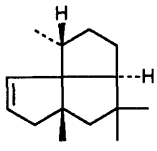
3



4; R = CO_2Me
5; R = CH_2OH



6; R = H
7; R = Ac

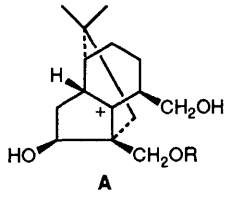


8

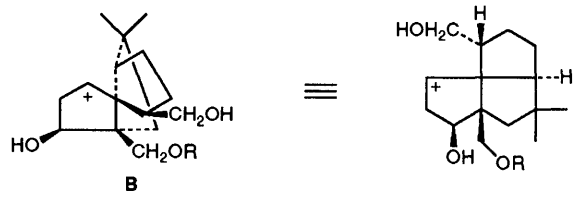
Interpretation of the extensive NMR data of compounds **6**‡ and **7** including ^1H–^1H COSY, ^{13}C–^1H COSY, HMBC and NOESY spectra afforded the structure of the rearranged product as **6**. The stereochemistry is compatible with the rearrangement pathway shown below, where **3**, possibly much more strained than **6**, might rearrange to **6** *via* **A** and **B**, two fairly strained cationic intermediates.

‡ ^1H NMR of **6** ($CDCl_3$, 500.1 MHz) δ 0.94 (3H, s, 11β-Me), 0.97 (3H, s, 11α-Me), 1.35 (1H, dd, *J* 13.8 and 1.1 Hz, 12α-H), 1.45 (1H, m, 8α-H), 1.52 (1H, m, 9β-H), 1.73 (1H, m, 9α-H), 1.89 (1H, dd, *J* 7.8 and 6.5 Hz, 10-H), 1.90 (1H, d, *J* 13.8 Hz, 12β-H), 1.99 (1H, m, 8β-H), 2.00 (1H, ddd, *J* 14.3, 4.0 and 3.8 Hz, 3β-H), 2.11 (1H, ddd, *J* 14.3, 5.5 and 4.7 Hz, 3α-H), 2.74 (1H, m, 7-H), 3.50 (1H, dd, *J* 9.0 and 4.5 Hz, 6α-H), 3.65 (1H, d, *J* 11.1 Hz, 1-CH_2), 3.84 (1H, dd, *J* 11.1 and 1.1 Hz, 1-CH_2), 4.00 (1H, dd, *J* 4.7 and 3.8 Hz, 4-H), 4.03 (1H, dd, *J* 5.5 and 4.0 Hz, 2-H), 4.10 (1H, dd, *J* 9.0 and 7.3 Hz, 6β-H).

^{13}C NMR of **6** ($CDCl_3$, 125.7 MHz) δ 25.6 (q, 11β-Me), 27.8 (t, C-9), 30.9 (q, 11α-Me), 33.9 (t, C-8), 36.4 (t, C-3), 40.6 (s, C-11), 45.9 (d, C-7), 51.2 (t, C-12), 57.9 (s, C-1), 61.5 (d, C-10), 66.8 (t, 1-CH_2), 74.9 (t, C-6), 77.1 (s, C-13), 81.7 (d, C-4), 91.4 (d, C-2).



A



B

It is interesting that the skeletally rearranged compounds **6** and **7** possess the same carbon skeleton and stereostructure as siliphinene **8**,[7] a natural sesquiterpene hydrocarbon isolated from *Silphium perfoliatum* (Compositae).

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