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1-METHYL-(D_3)-TRISHOMOCUBANE

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Summary: The acid catalysed rearrangement of 8-methyl-pentacyclo(5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$)undecan-8-*endo*-ol (8) to 3-methyl-(D_3)-trishomocuban-4-ol (9) provided the key step to the synthesis of the title compound (11).

The rearrangement of pentacyclo(5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$)undecan-8-*endo*-ol (1) to (D_3)-trishomocuban-4-ol (2) under strong acidic conditions was recently discussed.[1] In continuation of these studies we now wish to report a facile synthesis of 1-methyl-(D_3)-trishomocubane (11), based upon the smooth and stereoselective rearrangement of the tertiary alcohol 8 to 3-methyl-(D_3)-trishomocuban-4-ol (9). This synthetic route may find general application in the synthesis of 1-alkyl (or aryl)-D_3-trishomocubane and the more versatile 3-alkyl (or aryl)-(D_3)-trishomocuban-4-one such as 10.

The physical data of the newly described compounds appear in the Table 2.

The alcohol 8 was obtained by reduction of the monoketone 7[1,3] with CH_3MgI. Compound 8 could alternatively be prepared from the keto-ketal 4[4] in 85% yield. Reduction of 4 with CH_3MgI, followed by acid hydrolysis afforded the ketol 5. The absence of any carbonylic absorptions in the IR and NMR spectra indicated that 5 exists almost exclusively as the hemiacetal 6[5], which is only possible if the hydroxyl group of 5 has *endo*-configuration. The modified Huang-Minlon reduction of 5 afforded 8, the stereochemistry of which was confirmed by means of $Eu(fod)_3$-induced shifts of ^1H NMR signals.[6]

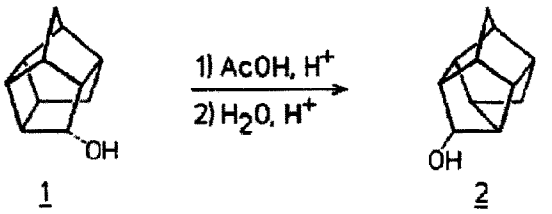
The rearrangement of 8 to 3-methyl-(D_3)-trishomocuban-4-ol (9) proceeded in good yield under relatively mild acidic conditions (reflux for 3 hours in a mixture of 10 ml 25% aqueous H_2SO_4 and 20 ml acetone). The proton-noise decoupled ^{13}C NMR spectrum of 9 exhibited twelve signals, indicating the formation of only one of the possible two diastereomers. The 3R,4R/3S,4S configuration assigned to 9 is based on extensive NMR studies.[7]

Oxidation of 9 with chromium trioxide in glacial acetic acid afforded 3-methyl-(D_3)-trishomocubanone (10), which upon reduction under modified Huang-Minlon conditions yielded the title compound (11).[8] The IR spectrum of 11 exhibited only two prominent absorption bands, whereas the proton-noise decoupled ^{13}C spectrum displayed the expected twelve signals of which two coincided.

Table. Physical properties of compounds 5b/6b, 8, 9, 10 and 11.

Compound	mp(°C)	IR(CCl_4, cm^{-1})	^{13}C NMR (δ from TMS in $CDCl_3$)
5b/6b	97-98[a]	3560(OH)	118.5(s), 89.3(s), 59.9(d), 57.8(d), 49.6(d), 47.9(d),
		3300(OH)	44.8(d), 44.1(d), 43.4(t), 42.0(d), 41.9(d), 19.0(q).
8	99-101[b]	3610(OH)	78.3(s), 50.9(d), 47.3(d), 44.7(d), 43.8(d), 43.3(d),
			41.4(d), 40.7(d), 36.4(d), 34.5(t), 29.6(t), 29.4(q).
9	113-114[a]	3600(OH)	80.3(d), 55.9(s), 51.7(d), 48.0(d), 47.1(d), 46.5(d),
			46.3(d), 45.5(d), 40.5(d), 33.4(t), 31.6(t), 14.6(q).
10	44-47[a]	1750(C=O)	218.1(C=O), 51.6(s), 49.8(d), 47.6(2xC,d), 46.9(d), 45.7(d),
			41.1(d), 40.8(d), 36.0(t), 33.8(t), 11.5(q).
11	59-62[a]	2960(s)	53.1(s), 52.0(d), 49.2(d), 47.8(2xC,d), 47.2(d), 46.6(d),
		2870(m)	43.7(d), 40.9(t), 33.9(t), 31.3(t), 18.1(q).

[a]After sublimation, [b]From ethyl acetate



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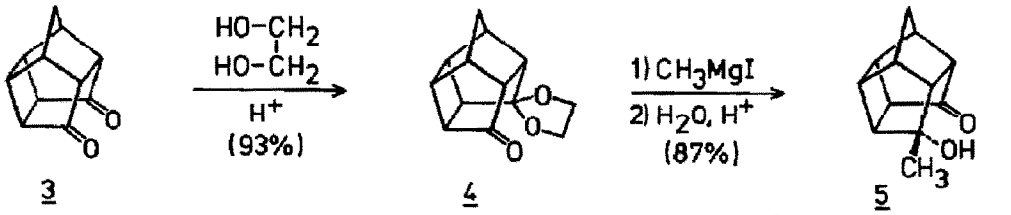

3 4 5 7 8 6 9 10 11

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References and Notes

1. T.G. Dekker and D.W. Oliver, S. Afr. J. Chem., 32, 45 (1979) and references cited therein.

2. Due to the complexity of the ^{1}H NMR spectra we prefer to characterise cage compounds by means of their ^{13}C NMR spectral data. All new compounds gave satisfactory microanalytical and/or high resolution mass data.

3. B.M. Lerman, F.Z. Galin, L.A. Umanskaya and G.A. Tolstikov, Zh. Org. Khim., 14, 2536 (1978).

4. P.E. Eaton, L. Cassar, R.A. Hudson and D.R. Huang, J. Org. Chem., 41, 1445 (1976).

5. Hemiacetal formation is quite common for cage ketols related to 5.[1]

6. Apart from the α-hydroxy proton signal (C-8-H) the largest lanthanide induced shift was observed for the *endo*-methylene proton of C-11.

7. To be published elsewhere.

8. Due to their volatility and high solubility in lipophilic solvents compounds 10 and 11 were obtained in low practical yields.

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