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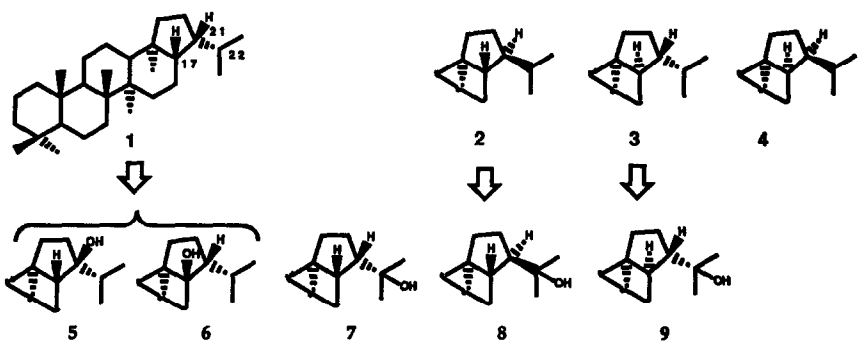
Dimethyldioxirane Oxidation of Isomeric Triterpenes of the Hopane Series.

Philippe Bisseret and Michel Rohmer*

Laboratoire de Chimie Microbienne, Unité de Recherche Associée au CNRS 135
Ecole Nationale Supérieure de Chimie de Mulhouse
3 rue A. Werner, 68093 Mulhouse, France.

Abstract: Dimethyldioxirane appeared as an efficient oxidant to convert easily and with good yields hopane 1 into hopan-21β-ol 5 and hopan-17β-ol 6, both useful precursors for the synthesis of geohopanoids, the other isomers moretane 2, 17α- hopane 3 and 17α-moretane 4 being much more resistant to oxidation.

Naturally occuring triterpenoids from the now well-known hopane series are found in living organisms (biohopanoids) mostly as derivatives from the 17β,21β skeleton 1 and in sediments (geohopanoids) as essentially derived from the thermodynamically more stable 17β,21α and 17α,21β frameworks 2 and 3, the fourth isomer of 17α,21α configuration 4 being yet only known as a synthetic compound. In order to understand better the diagenetically-induced transformations between the bio- and geohopanoids, we first examined the oxidation susceptibility of 1 using *m*-chloroperbenzoic acid (*m*-CPBA), which led to the obtention in modest yields of the tertiary alcohols 5 and 6, both valuable precursors for the synthesis of geohopanoids.[1] Considering the outstanding performance of dimethyldioxirane (DMDO),[2] recently enlightened by the regioselective oxyfunctionalization of saturated hydrocarbons,[3] we decided to revise this study with this oxidant and also to extend it to the three other isomers 2-4.



Experiments were carried out according to two procedures.[4] In the milder one (Procedure A), 2-4 were nearly entirely (>95%) recovered unchanged, whereas hopane 1 was recovered in 30% yield only being accompanied by the two tertiary alcohols 5 (30%) and 6 (20%). Using procedure B, hopane 1 disappeared (<5%) for the benefit of the two latter compounds (5, 50%; 6, 30%) and a complex mixture of minor less polar unidentified products (*ca.*15%). Both isomeric triterpenes, moretane 2 and 17α-hopane 3, began to react under these conditions and were recovered at about 70% next to their 22-hydroxy derivatives (respectively 8, 15% and 9, 10%), whereas an experiment performed on a small amount (0.3mg) of 4 did not reveal significant polar compounds leaving the starting material unchanged (tlc, gc).

Identification of alcohols 5 and 6 was straightforward (^{1}H-, ^{13}C-nmr), as the former itself and the 30-acetoxyethyl homologue of the latter were already synthesized in our laboratory.[1] ^{1}H-Nmr analyses of the C-17 and C-21 isomers of the well-known diplopterol 7 have already been published,[5] enabling us to identify the two other oxidation products as 22-hydroxy-21α-hopane 8 and 22-hydroxy-17α-hopane 9. Confirmation of these latter structures came from the gc-ms analyses of the corresponding *O*-trimethylsilyl (TMS) -ethers, which exhibited ms spectra similar to that obtained with the TMS-ether from diplopterol 7, and from gc with an order of elution characteristic for the corresponding hydrocarbons 1-3. If the identity of 9 could be further supported by its melting point [mp(MeOH)=169-171°C] in accordance to the literature,[5b] we found for its isomer 8 a value [mp(MeOH or hexane)=208-209°C] *ca.* 20°C lower to the published ones[5a,6], encouraging us to look for an independent proof to support unambiguously both structures. This was made possible by a direct C-17 and C-21 isomerization experiment run on diplopterol 7 in liquid sulphur[7], which enabled characterization (gc-ms of the TMS-ethers, ^{1}H-nmr), although as minor compounds, of the same tertiary alcohols as above.

On hopane 1, DMDO appeared to attack, as reported so far on other saturated hydrocarbons,[3] with retention of configuration, leading regioselectively to the hydroxy-derivatives 5 and 6 as sole major (80%) products much more efficiently than *m*-CPBA and, in particular, without formation of any 17,21-epoxide.[1] As illustrated for the first time with an oxidant of choice reported representative of some monooxygenase enzymes,[3a] geohopane frameworks 2 and 3 appeared in comparison much more inert and were attacked significantly only at the 22 position, whereas from hopane 1, the 22-hydroxy derivative 7 was not detected. On a synthetic view-point this opens the possibility, starting from 2, to prepare 8 itself recently isolated from a fern[5a] or its more highly hydroxylated derivatives found in some angiosperms.[8]

Extension of this work to other triterpenic hydrocarbons would be worthwhile.

Acknowledgement: Miss M. Seemann is thanked for the preparation of the DMDO solution according to reference 3b.

References and Notes

1. P. Bisseret, D. Armspach, S. Neunlist, and M. Rohmer, *Tetrahedron Lett.*, 1990, 45, 6523 and references cited therein.
2. (a) For a review see: R. W. Murray, *Chem. Rev.*, 1989, 89, 1187; (b) Preparation of the DMDO solutions according to: W. Adam, J. Bialas, and L. Hadjiarapoglou, *Chem. Ber.*, 1991, 124, 2377.
3. (a) R. W. Murray, R. Jeyaraman, and L. Mohan, *J. Am. Chem. Soc.*, 1986, 108, 2470; (b) R. Mello, M. Fiorentino, C. Fusco, and R. Curci, *J. Am. Chem. Soc.*, 1989, 111, 6749.
4. **Procedure A.** To the saturated solution of a hopane isomer (1-4) in CH_2Cl_2 is added a 0.07M DMDO acetonic solution in large excess (*ca.* 15 eq.). After 12h at room temperature and evaporation to dryness, the mixture of hopanoids is directly analyzed by tlc using Cy:EtOAc (98:2, v/v) as eluent yielding the tertiary alcohols 5 (R_f=0.1) and 6 (R_f=0.2). **Procedure B.** As above but the hydrocarbon is submitted three times successively to the action of DMDO 3h at room temperature and a last time 12h at room temperature, bringing the medium to dryness between each addition of oxidant.
5. (a) N. Tanaka, T. Noguchi, K. Kawashima, K. Kurihara, T. Matsudo, T. Murakami, Y. Saiki, and C.-M. Chen, *Yakugaku Zasshi*, 1987, 107, 586; (b) R. E. Corbett, and C. K. Heng, *J. Chem. Soc.* (C), 1971, 1886.
6. Y. Tsuda, K. Isobe, S. Fukushima, H. Ageta, and K. Iwata, *Tetrahedron Lett.*, 1967, 23.
7. The experiment was run on diplopterol 7 at 200°C during 90min in an excess of molten sulphur as indicated in: P. Bisseret, and M. Rohmer, *Tetrahedron Lett.*, 1990, 31, 7445. Both isomers of diplopterol 8 and 9 were thus isolated by tlc as a 1:3 mixture in less than 5% yield, next to a residue (*ca.* 10%) of slightly less polar starting diplopterol and a complex mixture of unidentified compounds.
8. P. Chakrabarti, *Tetrahedron*, 1969, 25, 3301.

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