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OXIDATION OF THE TRITERPENIC HOPANE SKELETON BY PERACIDS

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Abstract. Triterpenoids of the hopane series are regioselectively oxidized with *m*-chloroperbenzoic acid at unactivated positions, yielding compounds hydroxylated either at C-17 or at C-21, or the corresponding 17(21)-epoxide.

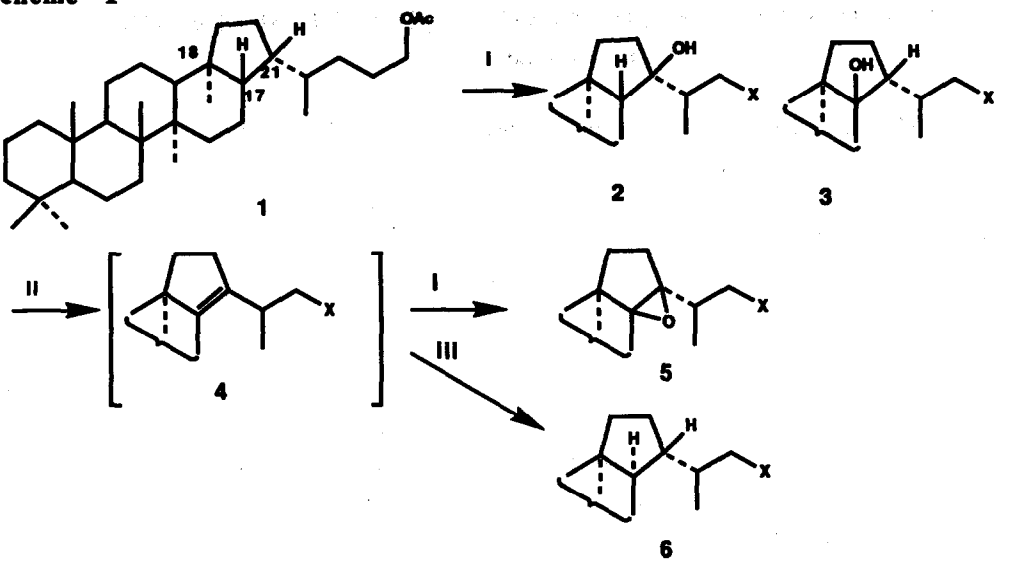
Among the molecular fossils of bacterial hopanoids,[1] many do not possess any longer the saturated C_{30} triterpenic skeleton of their precursors, like the aromatic and the 17(21) unsaturated or the *seco*- compounds encountered in sediments,[2] which result from still unknown oxidative processes. In the final hope of understanding better these transformations, we attempted the chemical oxidation of the easily available hopanoid **1**[3] with *m*-chloroperbenzoic acid (*m*CPBA) (Scheme 1), as peracids have already been reported to oxidize efficiently unactivated positions in polycyclic isoprenoids.[4]

When treated with *m*CPBA in $CHCl_3$ (5ml) as indicated in Table 1, hopanoid **1** (50mg) yielded after TLC separation on silicagel (cyclohexane/EtOAc, 8:2, v/v) compounds **2** (R_f=0.25), **3** (R_f=0.35) and **5** (R_f=0.55) next to unreacted starting material (R_f=0.60) (Scheme 1).

Table 1. Oxidation of hopanoid **1** by *m*CPBA.

Equivalents *m*CPBA	T ℃	Time h	% 1	2	3	5	Unknowns
10	25	24	50	12	8	4	26
5	25	120	35	10	20	6	29
5	60	8	5	/	/	15	80

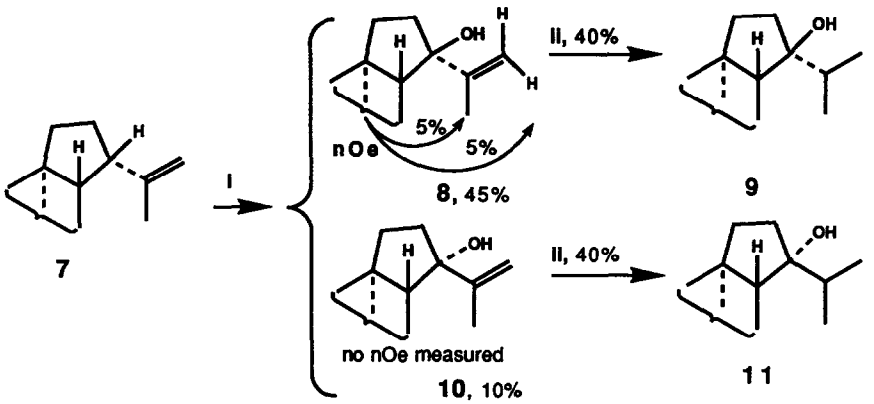
Scheme 1



Reagents: i, *m*CPBA, $CHCl_3$; ii, H^+; iii, see ref.11. X = CH_2CH_2OAc.

Compounds **2**, **3** and **5** all appeared as ring C, D or E tertiary-functionalized hopanoids from their greater polarity than **1**, the absence of new ^{1}H-NMR signals between 2.5 and 5.0 ppm[5] and the characteristic hopanoid ring C fragmentation at m/z=191 in their MS.[6] Compounds **2** and **3** were structurally closely related with almost superposable IR and MS spectra. They both possess an hydroxylic group, as suggested the weak IR absorption in CCl_4 solution at 3620 cm^{-1}. Its localisation at C-21 and C-17 in the case respectively of **2** and **3** was made possible by comparison of their ^{13}C-NMR spectrum (100MHz, DEPT) with that of hopanoid **1**. In agreement with the reported retention of configuration of *m*CPBA attacks at unactivated tertiary C-H bonds,[4] we assigned the 21β–OH and 17β-OH configurations to **2** and **3**. This could be supported for compound **2** by ^{1}H-NMR, as its spectrum was similar to that of synthetic 21β-hydroxyhopane **9** but very different from that of 21α-epimer **11**. These two compounds (Scheme 2) were obtained by SeO_2 allylic oxidation of hop-22(29)-ene **7**, TLC separation of the two unsaturated tertiary alcohols **8** and **10**, and Wilkinson hydrogenation.[7] In the SeO_2 oxidation, the privileged formation of the 21β-OH epimer, supported by the n.O.e., follows a stereochemical outcome as rationalized in the preparation of a kainic acid derivative.[8]

Scheme 2



Reagents and conditions: i, SeO_2, EtOH : THF (1:1, v/v), 12h, 18°C;
ii, $Rh(PPh_3)_3Cl$, $PhCH_3$: EtOH (2:1, v/v), 3h, 60°C.

Hopanoids **2** and **3** appeared sensitive toward acidic medium: they were converted into the $\Delta^{17(21)}$ olefin **4** merely on standing in $CHCl_3$ solution, putting thus light on the structure of **5**[5] as a 17(21) epoxide (Scheme 1). The structure of **5** was supported in MS by the ions at m/z 512 (M^+) and m/z 383 (M^+-side-chain) and more conclusively in 200MHz ^{1}H-NMR as its spectrum appeared very similar to that of 17(21)-epoxyhopane.[9] From the two possible isomers, only one was obtained. The β stereochemistry resulting from the preferential approach of the peracid opposite to the 18α methyl group is the most probable, as reported previously for the epoxidation of hop-17(21)-ene.[10] Considering the structure of compounds **2**, **3**, and **5**, the action of *m*CPBA appears very valuable in the expedient preparation of several classes of hopanoids encountered in petroleums and sediments. Indeed, a $\Delta^{17(21)}$ unsaturated carboxylic C_{32} hopanoid has been reported in a Paris basin petroleum,[2b] and recently the series of C_{32} to C_{35} unsaturated hydrocarbons has been identified by GC-MS from Moroccan phosphate sediments and shales.[2c] Both **4** and **5** would also serve as good starting materials for the preparation of *seco*-hopanoids[2d] and more interestingly the first compound could be hydrogenated, using the acidic conditions reported by Tsuda *et al.*[11] for hop-17(21)-ene hydrogenation, with a yield up to 80%, into the saturated hopanoid **6** possessing the 17α(H),21β(H) skeleton of characteristic ^{1}H-NMR methyl group signals,[12] widely encountered in sediments.[2e]

This first study on the chemical oxidation of the saturated biohopanoid skeleton proved fruitful not only because it gives a facile access to some geohopanoids but also because it puts forward the oxidative sensitivity of the two diagenetically fragile C-17 and C-21/H bonds. Indeed the 17β(H),21β(H)-hopane skeleton of the biohopanoids is thermodynamically less stable than the 17β(H),21α(H) and 17α(H),21β(H)-frameworks of geohopanoids found in mature sediments.[13] The yields in characterized products remain nevertheless modest so that it could take benefit from further essays in less acidic medium and/or in the presence of catalysts as recently described in the hydroxylation of low molecular weight saturated hydrocarbons catalyzed by manganese porphyrins.[14]

Acknowledgments

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5 All new compounds have spectral data (^{1}H-NMR, ^{13}C-NMR, IR, MS) entirely consistent with the assigned structures. *Selected data*; **2**: m.p. 185-186°C; ^{1}H-NMR (200MHz, $CDCl_3$) δ 0.718(3H, s), 0.797 (3H, s), 0.822 (3H, s), 0.851 (3H, s), 0.939 (3H,s), 0.962 (3H,s), 1.011 (3H, d, J = 6.3Hz), 2.055 (3H, s), 4.06 (2H, broad t, J = 6 Hz). **3**: m.p. 195-196°C; ^{1}H-NMR (200MHz, $CDCl_3$) δ 0.784 (3H, s), 0.799 (3H, s), 0.823 (3H, s), 0.853 (3H, s), 0.978 (3H, s), 1.01 (3H, d, J = 6.5 Hz), 1.030 (3H, s), 2.053 (3H, s), 4.04 (2H, dd, J = 2 and 6.5 Hz). **4**: m.p. 140-140.5°C; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.798 (3H, s), 0.832 (3H, s), 0.858 (6H, s), 0.939 (3H,s), 0.999 (3H, d, J = 6.8 Hz), 1.055 (3H, s), 2.050 (3H, s), 2.1 (2H, m), 2.25 (1H, dt, J = 4.14 Hz), 4.01 (2H, t, J = 7 Hz). **5**: m.p. 204-205°C; ^{1}H-NMR (200MHz, $CDCl_3$) δ 0.800 (3H, s), 0.829 (3H, s), 0.853 (6H, s), 1.034 (3H, s), 1.063 (6H, s), 1.083 (3H, d, J = 6.5 Hz), 2.061 (3H, s), 4.04 (2H, t, J = 6.5 Hz).
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