

AN UNUSUAL STEREOSPECIFIC EPOXIDATION WITH "PER-AMBERLYST 15"^(R)

Charles W. Jefford,* Gérald Bernardinelli,

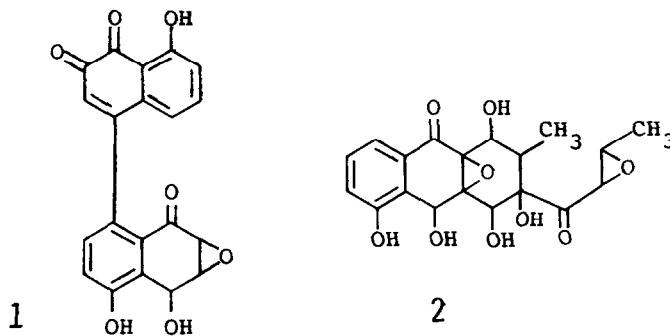
Jean-Claude Rossier, Shigeo Kohmoto and John Boukouvalas

Department of Organic Chemistry and Laboratory of Crystallography,

University of Geneva, 1211 Geneva 4, Switzerland

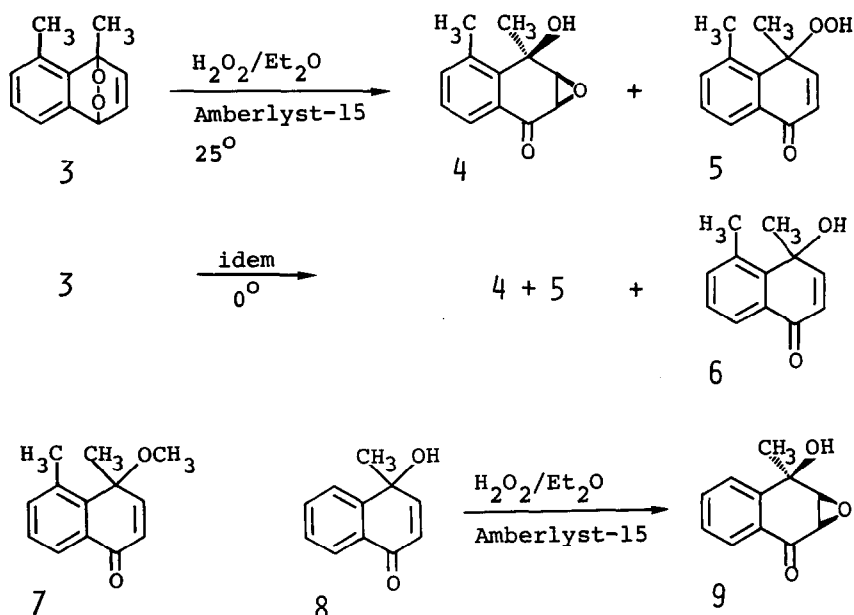
Summary, 4-Methyl-4-naphthoquinol and its 5-methyl derivative on treatment with per-Amberlyst 15 are converted to the corresponding cis-2,3-epoxides in high yields. The latter structure was determined by X-ray crystallography.

Several natural products possess the 2,3-epoxy-4-quinol structure [1-3]. Mycochryson (1), a metabolite of an unnamed, inoperculate discomycete and cervicarcin (2) an antitumor agent produced by *Streptomyces ogaensis* are typical examples [2,3]. Nonetheless, little has been reported on the preparation of 2,3-epoxy-4-quinols [4], and as far as we are aware, syntheses of the related 2,3-epoxy-4-naphthoquinols have yet to be attempted.



In connection with work [5-7] on the chemistry of peroxide intermediates, we thought that 2,3-epoxy-4-naphthoquinols might be accessible by the addition of hydrogen peroxide to 1,4-dihydronaphthalene-1,4-endoperoxides. Consequently, we undertook the perhydrolysis of 1,8-dimethyl-1,4-dihydronaphthalene-1,4-peroxide (3) [8]. Treatment of 3 (2 mmol) with an ether solution of hydrogen peroxide (1.5 N, 10 ml) and Amberlyst-15 (0.5 g) at room temperature for 7 h gave a single epoxide 4 in 42% yield [9] together with the expected hydroperoxide 5 (36% yield) [10]. Separation of the isomers 4 and 5 was achieved by repeated preparative TLC over silica gel using 3% MeOH in CH₂Cl₂ as eluant (R_f = 0.41 and 0.34 respectively). The cis-hydroxy epoxide structure of 4 was determined by X-ray analysis on a single crystal (Fig.) [11].

Repetition of the perhydrolysis at a lower temperature (0°), gave a similar amount (39%) of hydroperoxide 5. However, epoxide 4 was sharply diminished in quantity ($\sim 4\%$), while 4,5-dimethyl-4-naphthoquinol (6) appeared in its stead (35%). It may be deduced that the quinol 6 is the precursor to the epoxide 4. This deduction proved to be correct since the treatment of 6 with per-Amberlyst-15 gave epoxide 4 in 92% yield. Under these conditions the hydroperoxide 5 remained unchanged as did 4-methoxy-4,5-dimethylnaphthoquinone (7) [6].



In a similar manner, 4-methyl-4-naphthoquinol 8 [12] was converted to a single epoxide 9 in 90% yield. Its structure was assigned by analogy with that of 4 [13]. Amberlyst-15 pre-treated with hydrogen peroxide in ether was equally effective as an epoxidizing agent, converting 6 and 8 to 4 and 9 respectively at room temperature over 16 h. However, larger amounts of Amberlyst-15 were needed to attain high yields. The conventional peracids, such as *m*-chloro and *p*-nitroperbenzoic acid, reacted with 6 and 8, but much less effectively. Moreover, the reactions were not as clean and a pair of epoxides was obtained in each case in yields of about 30%.

The present behavior of per-Amberlyst-15 is unusual. Normally, peracids and hydrogen peroxide are unable to epoxidize enones except when bases or transition metal complexes are present [14]. The high reactivity together with the stereospecificity observed requires the presence of a hydroxy group, as methoxy and hydroperoxy substituents are ineffective (cf. 5 and 7). A pre-association between the quinol and a persulfonic acid residue of the resin seems likely, thereby creating a transition state energetically and entropically favorable for regio-selective oxygen atom transfer [15].

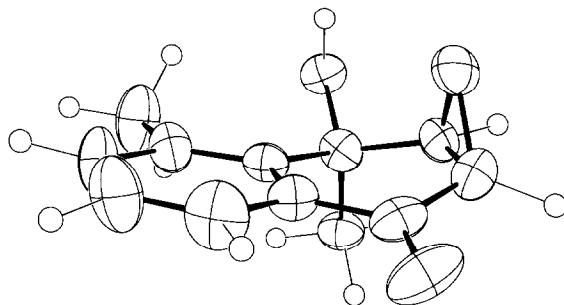


Fig. Perspective drawing of the structure of epoxide 4

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- [9] Compound 4: m.p. 153-4°; $^1\text{H NMR } \delta$ (CDCl_3) 1.62 (3H, s), 2.60 (1H, bs), 2.65 (3H, s), 3.77 (2H, s), 7.29 (1H, t, $J = 7$ Hz), 7.43 (1H, d, $J = 7$ Hz), 7.73 (1H, d, $J = 7$ Hz); IR (CH_2Cl_2) 3645, 3550, 1685 cm^{-1} ; MS m/e 204 (M^+), 189, 186, 173, 161, 158, 86, 84; Anal. found: C 70.39, H 6.10; calcd for $\text{C}_{12}\text{H}_{12}\text{O}_3$: C 70.56, H 5.93%.
- [10] Compound 5: m.p. 106-8°; $^1\text{H NMR } \delta$ (CDCl_3) 1.76 (3H, s), 2.70 (3H, s), 6.43 (1H, d, $J = 12$ Hz), 7.08 (1H, d, $J = 12$ Hz), 7.37 (1H, t, $J = 7$ Hz), 7.44 (1H, d, $J = 7$ Hz), 8.04 (1H, d, $J = 7$ Hz), 8.25 (1H, bs); IR (neat) 3305, 1662 cm^{-1} ; MS m/e 204 (M^+), 188, 173, 145, 115; Anal. found: C 70.29, H 6.21; calcd for $\text{C}_{12}\text{H}_{12}\text{O}_3$: C 70.56, H 5.93%.
- [11] Crystal data: $\text{C}_{12}\text{H}_{12}\text{O}_3$, $M = 204.2$, monoclinic, space group $\text{P}2_1/\text{c}$, $a = 8.350(1)$, $b = 8.459(1)$, $c = 14.689(3)$ Å, $\beta = 96.019(7)^\circ$, $U = 1031.8$ Å³, $Z = 4$, $D_c = 1.315$ g cm^{-3} . Data were collected on an automatic four-circle Philips PW 1100 diffractometer equipped with a graphite monochromator using $\text{Mo-K}\alpha$ radiation. Lorentz and polarization corrections were applied. 1427 independent reflexions were recorded ($\omega - 2\theta$ scan) of which 654 had $|F_o| > 3\sigma(F_o)$ and $|F_o| > 6.0$. The carbon and oxygen atoms were refined anisotropically, while the hydrogen atoms, except that of the OH group, were calculated. The H of the OH group was located from a difference electron density map. The structure was refined to $R = 0.051$ ($R_w = 0.038$, with $\omega = (F_o/32)^2$ for $|F_o| \leq 32$ and $\omega = (32/F_o)^2$ for $|F_o| > 32$). Observed and calculated structure factors may be obtained on request from G.B. Crystallographic data has been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.
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- [13] Compound 9: m.p. 144-6°; $^1\text{H NMR } \delta$ (CDCl_3) 1.55 (3H, s), 2.50 (1H, bs), 3.78 (1H, d, $J = 4$ Hz), 3.83 (1H, d, $J = 4$ Hz), 7.42 (1H, t, $J = 7$ Hz), 7.68 (1H, t, $J = 7$ Hz), 7.76 (1H, d, $J = 7$ Hz), 7.87 (1H, d, $J = 7$ Hz); IR (CCl_4) 3590, 3420, 1696 cm^{-1} ; MS m/e 190 (M^+), 175, 161, 147, 129, 115, 105, 91, 77, 69, 65, 51; Anal. found: C 69.20, H 5.61; calcd for $\text{C}_{11}\text{H}_{10}\text{O}_3$: C 69.45, H 5.31%.
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