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PROPELLANES—XXVIII

ELECTROPHILIC REACTIONS OF PROPELLANES: EPOXIDATION OF OLEFINIC PROPELLANES[a]

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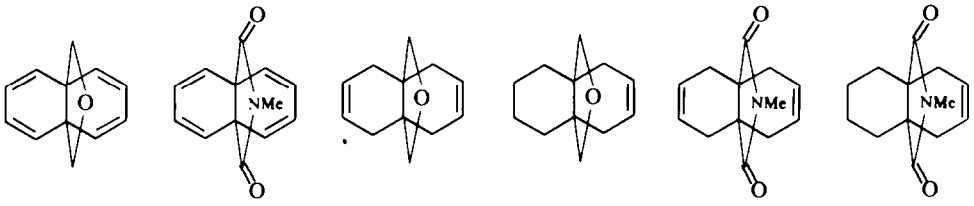
Abstract—Epoxidation of 12 - oxa[4.4.3]propella - 3,8 - diene and 12 - oxa[4.4.3]propell - 3 - ene is less selective than that of 11,13 - dioxo - 12 - methyl - 12 - aza[4.4.3]propella - 3,8 - diene and 11,13 - dioxo - 12 - methyl - 12 - aza[4.4.3]propell - 3 - ene. In the latter two substrates attack *syn*-to the imide ring is greater than that *anti*- to it.

After observing quite different course of attack of the tetraenic propellanes, **1** and **2**, by the same dienophile, 4 - phenyl - 1,2,4 - triazoline - 3,5 - dione, we presented a steric explanation for attack of **1** from "below" and invoked a secondary orbital interaction between the carbonyl orbitals of **2** and the lone pair orbitals of the dienophile as stabilizing the transition state for attack of **2** from "above".[1-3]

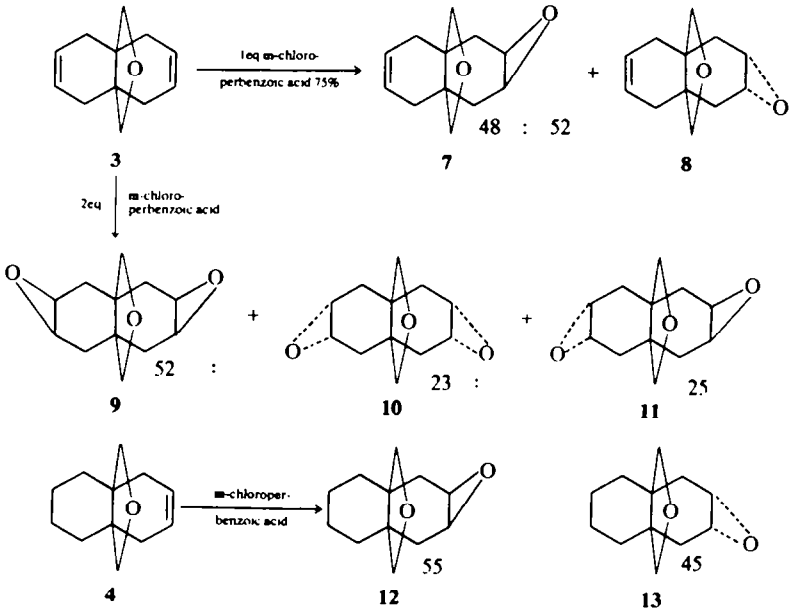


1 **2** **3** **4** **5** **6**

We then wished to study electrophilic attack of the olefinic propellanes **3–6** in general and to compare the relative behavior of the dienes **3** and **5** and the monoenes **4** and **6**. These reactions would presumably proceed by kinetic control. This paper describes epoxidation as an example of an electrophilic reaction. Forthcoming papers will present the results of addition of nitrenes and carbenoid reagents to the same substrates as further examples of electrophilic attack.[4]

The results with respect to the ethers **3** and **4** were disappointing in that the attack of each from above (leading to an epoxide *syn* with respect to the ether ring) occurred to practically the same extent as from below, leading to the *anti*-epoxide). Scheme 1 also shows that when **3** was treated with two equivalents of *m*-chloroperbenzoic acid a mixture of *bis*-epoxides was obtained. Separation by GLC showed that one of the two

[a]Part XXVII. C. Amith and D. Ginsburg, *Tetrahedron* **30**, 3415 (1974).



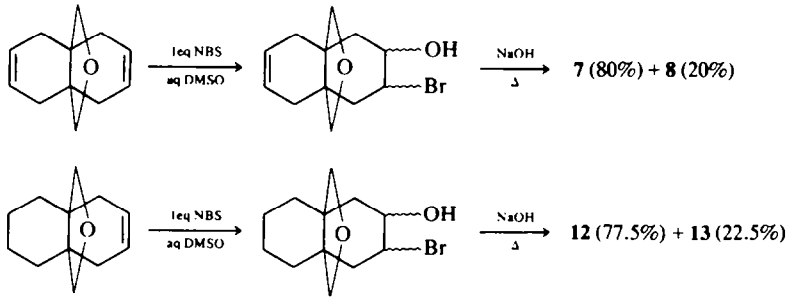
3 **7** **8** **9** **10** **11** **4** **12** **13**

Scheme 1.

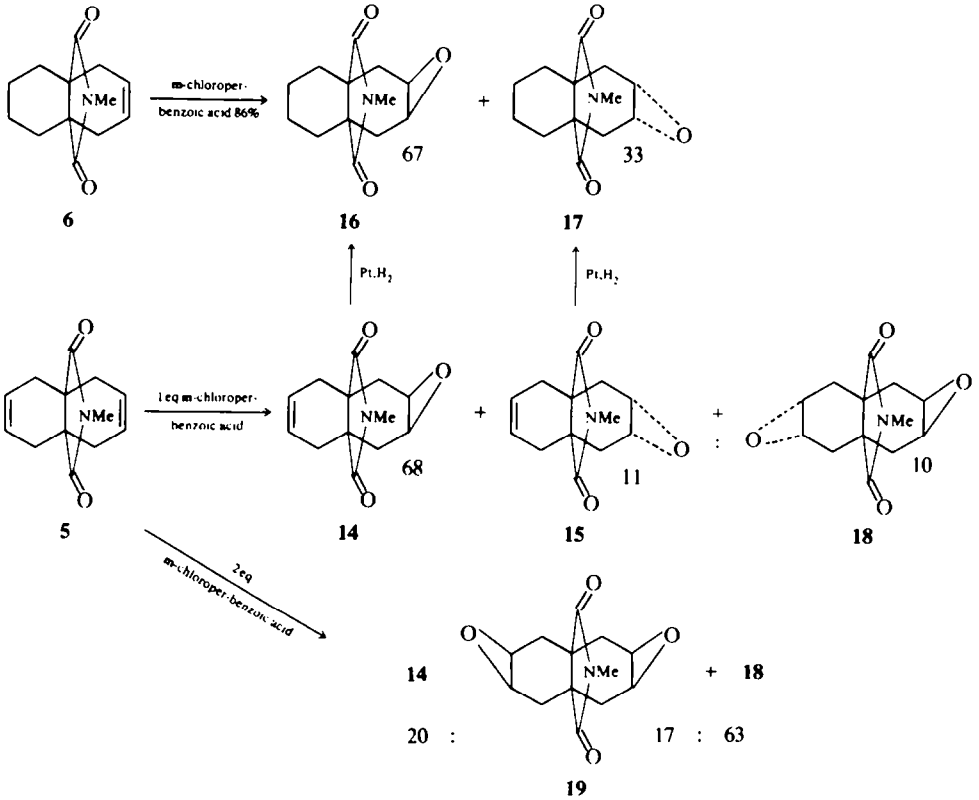
symmetrical *bis*-products formed as the major product in a ratio of 2:1 with respect to either the other symmetrical *bis*-epoxide or the unsymmetrical isomer.

The products shown in Scheme 1 were all oils. Although for the symmetrical *bis*-adducts a singlet was observed for the four CH_2O protons and an AB quartet, as expected was observed for the corresponding protons in the unsymmetrical *bis*-adduct, compound **7** also showed an AB quartet but **8**, by coincidence, a singlet. It might be argued that indeed, if one of these were destined to exhibit a quartet, it is more reasonable with respect to the magnetic environment of the CH_2O protons, that **7** should indeed be the one to more magnetically unsymmetrical than **8**. But we believe that this argument does not carry enough weight to be used as configurational proof. In point of fact, it is not all that important to assign configuration when the two isomeric mono-epoxides from **3** and **4** are formed unselectively. Since all of the compounds in Scheme 1 were oils, this adds further difficulty. Their configurations rest on one assumption only. It is assumed that bromine being larger than OH, the steric hindrance exhibited by the CH_2O hydrogens would be greater towards the former and the bromohydrin more likely to form from **3** and **4**, respectively, would have bromine *anti*- to the ether ring. The mixture of bromohydrins was heated with base affording a mixture of epoxides separable by GLC and then correlated to those formed by direct epoxidation. Scheme 2 summarizes the respective results. Clearly the selectivity is much greater (3:1) when a large bromonium ion is the attacking reagent as compared to the smaller HO^+ (1:1).

We shall not attempt a scholarly explanation (which can



Scheme 2.

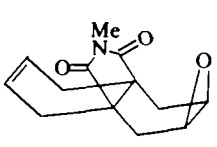


Scheme 3.

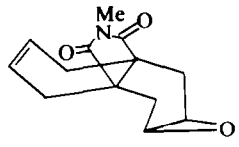
always be made by hindsight) for the surprising ratio of **9**:**10**:**11**. It may have to do with the preferred conformations of **3** and **4** and of their respective monoepoxides. We are concurrently using lanthanide shift reagents to study conformations of such propellanes[5] and possibly this may be of eventual help in understanding the ratio of *bis*-epoxides.

But we prefer to turn to the epoxidation of **5** and **6** in order to observe whether it is possible to invoke secondary orbital effects to explain selectivity of attack from above. Our problem was simpler technically in that we were now dealing with solids. Indeed, it is for this reason that we have a frame of reference for certainty in configurational assignment. Scheme 3 summarizes the results.

The results of epoxidation of **5** show that attack occurs from above more than six times as much as from below. In the case of **6**, the selectivity is less, only 2:1 in the same direction. The monoepoxides from **6** were reduced quantitatively to afford, respectively, those obtained from **5**, as shown in the scheme. The unsymmetrical *bis*-epoxide **18** was obtained as a by-product on monoepoxidation of **5** and then only in 9% yield. Epoxidation of **5** with 2 moles of *m*-chloroperbenzoic acid affords only the unsymmetrical *bis*-epoxide **18** and only one symmetrical *bis*-epoxide which therefore must have the *syn–syn*-configuration **19**. Epoxidation of the preformed **14** also gives only the *syn–anti* compound **18** and the *syn–syn*-isomer **19** in a ratio of 3:1. The *anti*-epoxide **15** affords only the unsymmetrical **18**. Thus, all along the line, attack from above is preferred to that from below. All of these facts could equally be interpreted in the reverse manner as so far we have only established relative configurations of all of these compounds. However, the X-ray structure of **14** was established and was shown not only to have the *syn*-configuration but also the conformation **14a** rather than **14b**.[6] It is not immediately apparent why this should be so as a simplistic prediction based mainly on

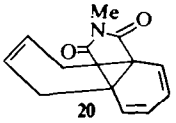


14a



14b

electrostatic considerations might have preferred **14b**. Perhaps it has to do with the packing mode in the crystal. Perhaps it is connected with the relative stability in solution of the conformations **5a** for **5** and **3a** for **3**.[5] The structure of **5** in the crystalline state indeed corresponds to **5a** and it was found also that the trienic compound **20** is isomorphous with **5a** and therefore presumably exists in the analogous conformation; although, of course, the cyclohexadiene ring would be closer to planarity.[7]



20

Clearly were the conformation of **5** in solution only **5a** one might expect much more attack from below, for geometric reasons. However, it is clear that inversion may readily occur and evidently the carbonyl orbitals are indeed capable of assisting in the approach of the epoxidizing agent from above.

EXPERIMENTAL

M.ps are uncorrected. IR spectra were measured on a Perkin Elmer model 237 spectrometer; NMR spectra on a Varian T-60 instrument and mass spectra on an Atlas CH4 spectrometer maintaining the ionization current at 20 μA and the electron energy at 70 eV. Molecular ions were determined by peak matching on a Varian 711 spectrometer, electron energy 100 eV. Solvents were removed in a rotatory evaporator at 25–30 torr. Preparative TLC was conducted on plates of basic alumina (20 × 20 cm, 40 g, type E) alumina PF 254 + 366 made by E. Merck.

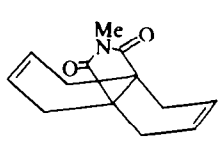
Direct epoxidation of **3**

(a) To a cold soln of **3**[8] (881 mg) in CH_2Cl_2 (10 ml) cooled in an ice bath was added dropwise during 10 min an ice-cold soln of *m*-chloroperbenzoic acid (85%; 1.1 g) in CH_2Cl_2 (20 ml). The mixture was stirred magnetically at room temp for 48 hr. 10% Na_2SO_3 was added until starch-iodide paper showed no color. The aqueous phase was extracted with CH_2Cl_2 (200 ml) and the organic layer was washed with 5% $NaHCO_3$aq (30 ml), water (30 ml) and sat NaClaq (30 ml). It was then dried ($MgSO_4$) and the solvent removed. The product mixture (920 mg) formed a transparent slightly yellow viscous oil. GLC showed after injection of CH_2Cl_2 soln that 25% was unreacted **3** (ret. time 2.5 min) and the monoepoxides **8** and **7** formed in 75% yield in a ratio of 52:48 (ret. time 13.8; 17 min) on 3% XE60 on Gaschrom Q (100–120 mesh, 1 = 2m, diam. 1/4 in) at 140° at He flow rate of 64.5 ml/min. (M^+, high resol. peak matching, 192.11471; $C_{12}H_{16}O_2$ requires: M.W. 192.115028).

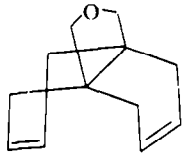
Isomer **7**. NMR ($CDCl_3$): τ 4.40 (bs, 2 vinylic H); 6.30 (ABq, J = 8 Hz, $4CH_2O$); 6.78 (m, 2H, α-epoxide); 7.98 (m, 8H, allylic and β-epoxide). IR ($CHCl_3$): 3000(m), 1030(s), 992(m), 920(s) cm^{-1}.

Isomer **8**. NMR ($CDCl_3$): τ 4.40 (t, 2 vinylic H); 6.34 (s, $4CH_2O$); 6.80 (m, 2H, α-epoxide); 7.94, 8.05 (dd, 4 allylic, 4β-epoxide). IR ($CHCl_3$): 3000(m), 1030(s), 992(m), 920(s) cm^{-1}.

(b) *bis-Epoxidation.* To the same soln of **3** was added similarly *m*-CPBA (85%; 2.2 g) in CH_2Cl_2 (30 ml) and stirring maintained for 48 hr. Workup as above afforded a colorless resin (1 g; 96%). GLC as above at 160° and He flow rate of 40 ml/min separated four compounds in the following order of ret. time: monoepoxides (2%; 5.9 min), **11** (25%; 16.7 min), **10** (23%; 21.4 min), **9** (52%; 30.6 min). (Found: C, 69.28; H 7.90; M^+, high resol. peak matching,



5a



3a

208.1095–208.1099. $C_{12}H_{16}O_3$ requires: C, 69.21; H, 7.74%. M.W. 208.109943).

Isomer **9**. NMR ($CDCl_3$): τ 6.34 (s, $4CH_2O$); 6.80 (m, 4H, α-epoxide); 8.05 (q, J = 16 Hz, 8H, β-epoxide). IR ($CHCl_3$): 3000(m), 1015(s), 980(m), 915(m) cm^{-1}.

Isomer **10**. NMR ($CDCl_3$): τ 6.45 (s, $4CH_2O$); 6.82 (m, 4H, α-epoxide); 8.00 (q, J = 15 Hz, 8H, β-epoxide). IR ($CHCl_3$): 3000(m), 1040(m), 1010(s), 998(m), 920(m) cm^{-1}.

Isomer **11**. NMR ($CDCl_3$): τ 6.40 (ABq, J = 8 Hz, $4CH_2O$); 6.82 (m, 4H, α-epoxide); 8.05 (m, 8H, β-epoxide). IR ($CHCl_3$): 3000(m), 1050(s), 1020(s), 995(m), 920(m) cm^{-1}.

Direct epoxidation of **4**

To a soln of **4**[9] (232 mg) in CH_2Cl_2 (5 ml) cooled in an ice bath was added dropwise during 10 min an ice-cold soln of *m*-CPBA (885% 855 mg) in CH_2Cl_2 (35 ml). The large excess is required to effect complete reaction. Stirring was maintained for 1 week. After workup as above the product mixture was obtained as a slightly yellow oil (255 mg). GLC as above at 130° and He flow rate of 16.6 ml/min afforded **12** and **13** in a ratio of 55:45 (ret. time 16.5, 25.7 min). (Found: C, 74.02; H, 9.48 M^+, high resol. peak matching,

194.1299 - 194.1313. $C_{12}H_{18}O_2$ requires: C, 74.19; H, 9.34%. M.W. 194.130678).

Isomer **12**. NMR ($CDCl_3$): τ 6.38 (ABq, J = 8 Hz, 4CH_2O); 6.80 (m, 2H, α-epoxide); 8.10 (m, 4H, β-epoxide); 8.54 (m, 8 CH_2).

Isomer **13**. NMR ($CDCl_3$): τ, 6.28 (s, 4CH_2O); 6.77 (m, 2H, α-epoxide); 8.05 (m, 4H, β-epoxide); 8.50 (m, 8 CH_2).

Epoxidation of **3** via *bromohydrins*

N-bromosuccinimide (151 mg) was added in one portion to a soln of **3** (115 mg) in dry DMSO (3.25 ml) to which had been added water (0.05 ml). The mixture was stirred under N_2 at room temp for 1 hr. Water (20 ml) was added. The aqueous phase was extracted several times with ether (160 ml) and the extract dried ($MgSO_4$). Removal of solvent afforded a transparent viscous oil (180 mg). (GLC showed the presence of two compounds (ret. time 22.6, 20.3 min. 1% XE60 on Gaschrom Q, He flow 4 ml/min, 140°) but these were not separated preparatively.) The oil was treated with aqueous (1.5 ml) NaOH (21 mg) and the whole was stirred for 1 hr at room temp. Water was added (20 ml) and the whole was extracted with CH_2Cl_2 (160 ml). The organic layer was washed with sat NaCl aq, dried($MgSO_4$) and the solvent was removed, affording the mixture of epoxides as a transparent viscous oil (85 mg). GLC showed that it contained 29% of **3**. Of the remaining 71% the ratio of **7**:**8** was 4:1. These products were identical with those described above.

Epoxidation of **4** via *bromohydrins*

NBS (231 mg) was added as above to **4** (116 mg) in DMSO (3.25 ml)-H_2O (0.05 ml). After the same workup the bromohydrin mixture (2 products by GLC, ret. time 24.1, 21.6 min) was obtained as a transparent viscous oil (182 mg). After its treatment with base as above the epoxide mixture was obtained (71 mg). GLC showed the ratio of **12**:**13** to be 77.5:22.5. These products were identical with those described above.

Epoxidation of **6**

To a soln of **6**[6] (200 mg) in CH_2Cl_2 (1 ml) cooled in an ice-salt bath was added dropwise a soln of *m*-CPBA (85%; 220 mg) in CH_2Cl_2 (3 ml). The mixture was stirred at room temp for 20 hr. More CH_2Cl_2 (20 ml) was added and the precipitated *m*-chlorobenzoic acid was removed by filtration. After workup as above removal of solvent afforded the product mixture (203 mg). In prep TLC using EtOAc-hexane (1:1), 100 mg of mixture afforded **16** (41 mg) and **17** (23 mg; total yield 61%) but GLC showed presence of **6** (14%), **16** (41 mg) and **17** (23 mg; total yield 61%) but GLC showed presence of **6** (14%), **16** (58%), **17** (28%).

Isomer **16**. M.p. 120–122° (EtOAc-hexane). (Found: C, 66.39; H, 6.90; N, 6.02; M.W. 235. $C_{13}H_{17}NO_3$ requires C, 66.36; H, 7.28; N, 5.95%, M.W. 235.27). NMR ($CDCl_3$): τ 6.82 (t, 2H, α-epoxide); 7.02 (s, NCH_3); 7.70, 8.03 (ABX, J_{AB} = 16 Hz, 4H, β-epoxide); 8.10–8.67 (m, 8 CH_2). IR (KBr): 2980, 2940, 2850, 1770, 1690 cm^{-1}.

Isomer **17**. M.p. 128–130°C (EtOAc-hexane). (Found: C, 66.45; H, 6.92; N, 6.00, M.W. 235). NMR ($CDCl_3$): τ 6.90 (t, 2H, α-epoxide); 6.98 (s, NCH_3); 7.30, 8.13 (ABX, J_{AB} = 15 Hz, 4H, β-epoxide); 8.47 (m, 8 CH_2).

Epoxidation of **5**

(a) A soln of **5**[9] (109 mg) in CH_2Cl_2 (1 ml) was heated with *m*-CPBA (85%; 100 mg) in CH_2Cl_2 (6 ml) and worked up exactly as for **6**. The product (103 mg) was separated by TLC. GLC showed the presence of **5** (11%) **14** (68%), **15** (11%) and the *bis*-adduct **18** (10%).

Isomer **14**. M.p. 199–200° (EtOAc-hexane). (Found: C, 66.89; H, 6.45; N, 6.10; M.W. 233. $C_{13}H_{15}NO_3$ requires: C, 66.93; H, 6.48; N, 6.01% M.W. 233.26). NMR ($CDCl_3$): τ 4.09 (t, 2 vinylic H); 6.87 (t, 2H, α-epoxide); 7.05 (s, NCH_3); 7.14, 8.09 (ABX, J_{AB} = 15 Hz, 4H, β-epoxide); 7.50, 8.10 (ABX, J_{AB} = 15 Hz, 4 allylic H). IR (KBr): 3020–2840, 1760, 1685 cm^{-1}.

(b) *bis-Epoxidation.* Conducted as above; **3** (54 mg) and *m*-CPBA (110 mg) gave after 48 hr at room temp a product mixture (55 mg) separated by TLC. GLC showed the presence of **14** (20%), **18** (63%) and **19** (17%).

Isomer **18**. M.p. 175–177° (EtOAc-hexane). (Found: C, 62.38; H, 6.13; N, 5.66; M.W. 249. $C_{13}H_{15}NO_4$ requires: C, 62.64; H, 6.07; N, 5.62%, M.W. 249.26). NMR ($CDCl_3$): τ 6.77 (t, 2H, α-epoxide); 6.90 (t, 2H, α-epoxide); 7.00 (s, NCH_3); 7.32, 7.73 (ABX, J_{AB} = 15 Hz, 4H, β-epoxide); 7.97 (m, 4H, β-epoxide). IR (KBr): 3020, 2920, 2840, 1765, 1690 cm^{-1}.

Isomer **19**. M.p. 244–246° (EtOAc-hexane). (Found: C, 62.37; H, 6.08; N, 5.51; M.W. 249). NMR ($CDCl_3$): τ 6.92 (t, 4H, α-epoxide); 7.00 (s, NCH_3); 7.33, 8.13 (ABX, J_{AB} = 15 Hz, 8H, β-epoxide).

Reduction of **14**. A soln of **14** (7 mg) in EtOAc (5 ml) was reduced at 1 atm H_2 pressure at room temp in presence of PtO_2. After 12 hr subjection to these conditions **16** was obtained (6 mg) identical by m.p., m.m.p. and spectroscopically with **16** described above.

Reduction of **15**. Analogous reduction of **15** (10 mg) afforded **17** (10 mg) identical in all respects to **17** described above.

Epoxidation of **14**. As above, gave recovered **14** (11%) and a mixture of **18** (74%) and **19** (26%) as determined by GLC.

Epoxidation of **15**. As above, afforded **18** exclusively.

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