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PROPELLANES—XXIX

ELECTROPHILIC REACTIONS OF 11,13-DIOXO-12-METHYL-12-AZA[4.4.3]PROPELLA-3,8-DIENE: ATTACK BY NITRENES[a]

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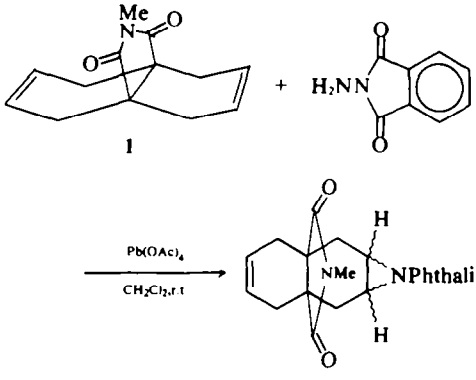
Abstract—Several substituted nitrenes prepared from different precursors were studied as electrophilic reagents towards several propellane dienes. The configurational selectivity is not as high as in other electrophilic reactions.

The methylimide **1** of known X-ray structure in the crystalline state[1] and of known relative conformational stability[2] (as shown) has been used as a substrate for electrophilic attack by cationoid reagents (in epoxidation)[a] and by a carbenoid reagent.[3] We now report its reaction with several nitrenes.[4]

The substrate **1** was subjected to reaction with the nitrene formed from N-aminophthalimide by lead tetraacetate. Much of the starting material was recovered unchanged after 5 hr at room temp. but the mixture of phthalimido-aziridines **2** and **3** obtained is again reminiscent of the already known behavior of **1**. These products were formed in a ratio of 3:1 (by NMR) and perhaps here too attack from above, *syn*- to the imide ring is preferred. However, this has not been unequivocally proved.



2 (3 parts) + **3** (1 part)
H: dotted bond H: solid bond
22%
+ **1** (recovered), 71%

Each of the aziridines was treated with excess hydrazine and the resulting amino-aziridine was treated with lead tetraacetate to obtain the amino-nitrene in the hope that this may *intra*molecularly attack the remaining double bond in this intermediate to give the cage-like product shown in Scheme 1. The realization of this hope did not appear likely from a study of Dreiding models, simulating the aziridine rings. Indeed each of the isomeric amino-nitrenes decomposed with nitrogen evolution, affording, within minutes in each case, the starting material **1**.

The nitrene from **3** has the correct configuration to undergo the above intramolecular reaction. The fact that **1** is obtained more or less at the same rate from the two configurationally different nitrenes supports the fact that the cage compound (which, in principle may lose nitrogen as well) did not form at all. Another procedure reacting the amino aziridine with mercuric acetate in aqueous tetrahydrofuran at room temp, followed by treatment with sodium borohydride in aqueous NaOH also expelled nitrogen and afforded **1**.

Preparation of a nitrene from ethyl N-*p*-nitrobenzenesulfonoxyurethan shown in Scheme 2 led to a higher yield of products, in somewhat lower selectivity but here too **1** was recovered to the extent of 50%.

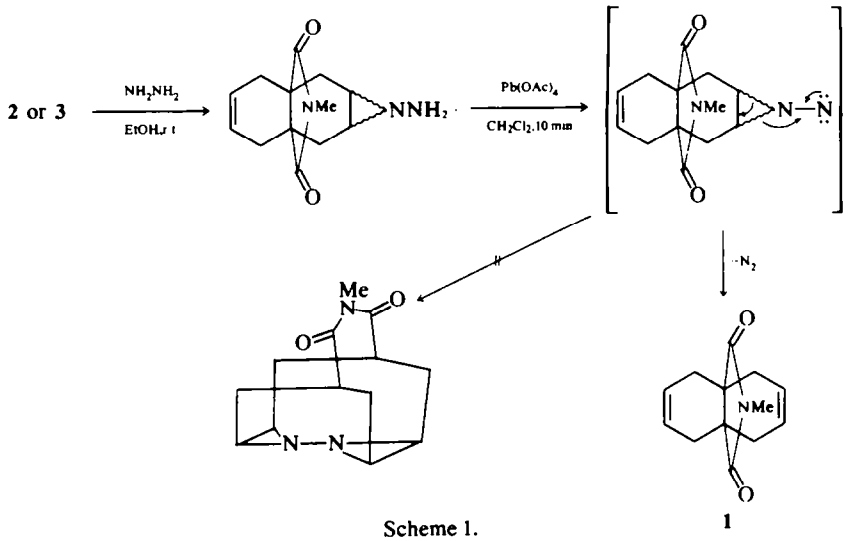
Since we obtained much lower selectivity in epoxidation of the dienic ether **6** as compared to **1**[a] we studied the reaction of phthalimidonitrene with **6** as here we expected solids due to the phthalimido residue rather than oils.[a] Here too, much of the starting material was recovered unchanged. We believe on the basis of the multiplicity of the CH_2O protons in the products that the configurations are as shown (Scheme 3) but this is not proven. The low selectivity affords small motivation indeed to invest work in such unequivocal proof.

The m.ps of the various substituted aziridines indicates that these are surely not compounds in which inversion about nitrogen is slow.[5] It is probable that the large groups choose to conform to a conformation in which they are as far as possible from exerting electrostatic or non-bonding interactions with other portions of the molecule. But this can be said definitively only if an X-ray study were conducted. We have had the kind cooperation of colleagues where such results were essential to us but we do not think we can justify such studies with the abovementioned compounds, our personal curiosity notwithstanding. We may, in further work employ the observed differences in mass spectral fragmentations with respect to the abundance of respective ions (see Experimental) in order to prove whether our configurational assignments are indeed correct. This would, of course, require deuteration and this may best be done when more stereoselective nitrene reactions have been found in other propellane substrates.

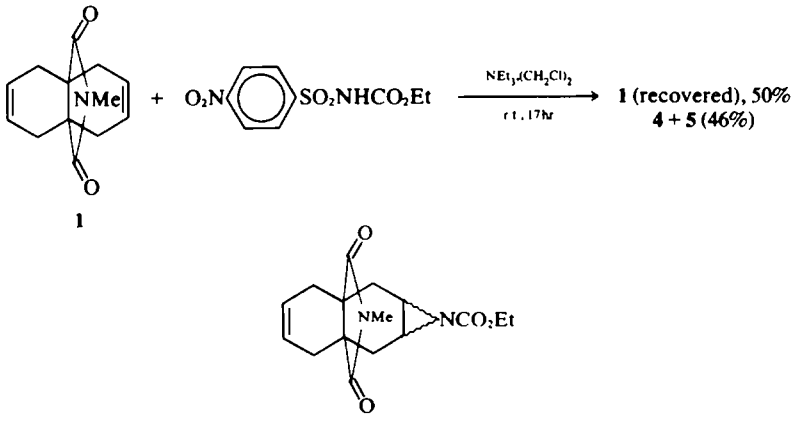
EXPERIMENTAL

IR spectra were measured on a Perkin Elmer model 257 grating spectrophotometer. NMR spectra were measured on a Varian T-60 spectrometer. Mass spectra were measured on an Atlas CH4 instrument using the heated inlet system at 200°, maintaining the

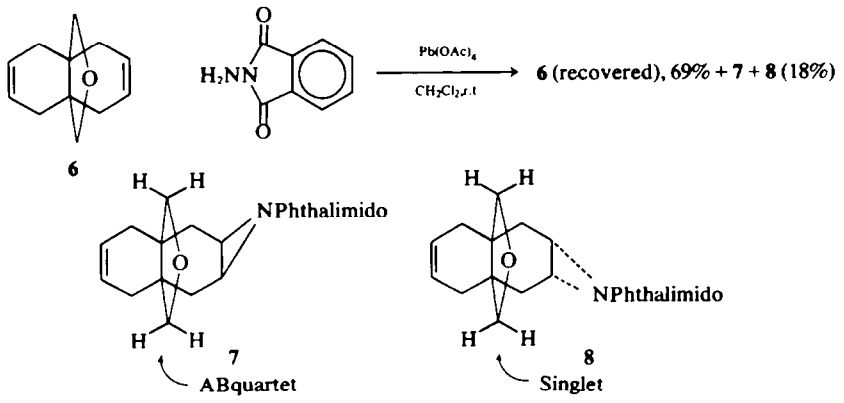
[a]Part XXVIII. W. J. W. Mayer, I. Oren and D. Ginsburg, *Tetrahedron* in press.



Scheme 1.



Scheme 2.



Scheme 3.

ionization current at 20 μA and the electron energy at 70 eV. Some were measured on a Varian 711 spectrometer using the heated inlet system at 200°. The electron energy was maintained at 100 eV. Only the major fragments are listed. All m.ps are uncorrected.

Reaction of **1** *with phthalimidonitrene.* To a soln of 1[6] (1.52 g) in CH_2Cl_2 (filtered through Alox; 45 ml) was added in one portion N-aminophthalimide[7] (5.2 g, 4.6 eq). To this suspension was added with stirring during 5 hr at room temp a soln of lead tetraacetate (BDH, 14 g; 4.6 eq) in CH_2Cl_2 (Alox filtered; 40 ml), under N_2. Lead diacetate which precipitated was removed by filtration. The filtrate was shaken with cold (0°) 1% NaOH aq. until the aq phase remained alkaline. The organic layer was dried ($MgSO_4$) and the solvent removed in a vacuum. The crude yellow solid residue

(2.38 g) was chromatographed on a column containing aluminium oxide (Merck Alox, deact 6% H_2O; 48 g) at 0°.[8] Hexane (85)–ethyl acetate (15) (300 ml) eluted **1** (1.08 g, 71%, m.p. 157–158°). Hexane (60)–EtOAc (40) (900 ml) eluted **2** and **3** (590 mg; 22%) in a ratio of 3:1 (judged by intensity of two N–C$\underline{H}_3$ singlets at τ 7.02 and 7.05, respectively). Pure **2** (221 mg) was formed by 3 crystallizations, m.p. 230–232° (CH_2Cl_2–hexane). The combined mother liquors were chromatographed again on a column containing silica (15 g, grade II—deactivated with 10% water) at 0°.[8] Elution with hexane–ether afforded more of **2** (100 mg; m.p. 225–227°) and pure **3** (129 mg), m.p. 240–244° (benzene–hexane).

Isomer **2**. M.p. 230–232°. (Found: C, 66.64; H, 4.96; N, 11.19; M.W. 377. $C_{21}H_{19}N_3O_4$ requires: C, 66.83; H, 5.07; N, 11.14%, M.W. 377.39). NMR ($CDCl_3$): τ 2.20 (s, 4 arom H); 4.07 (t, J = 3 Hz, 2 vinylic H); 7.02 (s, NC$\underline{H}_3$); 7.16 (bs, 2C$\underline{H}$NC$\underline{H}$) 7.20–8.50 (complex m, 8H). IR ($CHCl_3$): 1760, 1705, 1690, 1370, 1320, 1140 cm^{-1}. M.S. (*m/e*): 377 (M^+, 13), 230(15), 162(100), 130(64), 104(37), 78(12).

Isomer **3**. M.p. 240–244°. (Found: C, 66.69; H, 5.06; N, 11.08%, M.W. 377). NMR ($CDCl_3$): τ 2.25 (s, 4 arom H); 4.05 (5 line system, J = 2 Hz, 2 vinylic H); 6.70–8.40 (complex m, 10H) + 7.05 (s, NC$\underline{H}_3$). IR ($CHCl_3$): 1760, 1710, 1680, 1370, 1320, 1145 cm^{-1}. M.S. (*m/e*): 377(M^+, 8), 230(20), 162(10), 130(8), 104(15), 78(100).

Reaction of **1** *with nitrene from substituted urethan.* To a soln of **1** (0.87 g) and ethyl N-*p*-nitrobenzenesulfonoxyurethan[9] (3.5 g; 3 eq) in 1,2-dichloroethane (Fluka puriss, filtered through Alox; 30 ml) was added during 2.5 hr at room temp. with magnetic stirring a soln of triethylamine (1.33 g; 3.3 eq) in 1,2-dichloroethane (15 ml). The clear yellow soln was stirred for 17 additional hr. Ether (100 ml) was added and the whole was extracted with cold (0°) 1% NaOH aq until the aq phase remained alkaline. The organic layer was dried ($MgSO_4$) and the solvent removed in a vacuum. The crude product (2.0 g) was chromatographed on a column of neutral alumina (as above; 45 g) at 0°.[8] Hexane (90)–EtOAc (10) (200 ml) eluted **1** (433 mg, 50%, m.p. 155–157°). Hexane (70)–EtOAc (30) (300 ml) eluted **4** + **5** (554 mg; 46%) in a ratio of 3:2 (judged by intensities of N–C$\underline{H}_3$ singlets at τ 7.10 and 7.20 respectively). Crystallization from ether–hexane gave one pure isomer, **5** (140 mg), m.p. 147–148°. Recrystallization gave the analytical sample (108 mg), m.p. 147–148° (benzene–hexane). The combined mother liquors were again chromatographed on a column of silica (as above, 23 g) at 0°.[8] Hexane–ether (1:1) eluted an oil (276 mg) which solidified on standing. It afforded **4** (160 mg), m.p. 102–108° (ether–hexane). Two recrystallizations afforded the analytical sample (62 mg), m.p. 110–111° (benzene–hexane).

Isomer **4**. M.p. 110–111°. (Found: C, 63.35; H, 6.59; N, 9.11, M.W. 304. $C_{16}H_{20}N_2O_4$ requires: C, 63.14; H, 6.62; N, 9.21%, M.W. 304.34). NMR ($CDCl_3$): τ 4.12 (t, J = 3 Hz, 2 vinylic H); 5.92 (q, J = 7 Hz, 2 OC$\underline{H}_2$CH$_3$); 7.10 (s, NC$\underline{H}_3$); 7.20–7.90 (m, 7H); 8.00–8.60 (m, 3H), 8.74 (t, J = 7 Hz, 3OCH$_2$C$\underline{H}_3$). IR ($CHCl_3$): 1765, 1690, 1430, 1380, 1370, 1280 cm^{-1}. M.S. (*m/e*): 304 (M^+, 17), 181 (20), 153 (55), 91 (28), 78 (100), 77 (43), 56 (38).

Isomer **5**. M.p. 147–148° (Found: C, 62.98; H, 6.56; N, 9.04%; M.W. 304). NMR ($CDCl_3$): τ 4.09 (5-line system, J = 2 Hz, 2 vinylic H); 5.92 (q, J = 7 Hz, 2OC$\underline{H}_2$CH$_3$); 7.00–7.60 (m, 4H) + 7.17 (s, NC$\underline{H}_3$); 7.67 (m, 2H); 8.00–8.60 (m, 4H); 8.75 (t, J = 7 Hz, 3OCH$_2$C$\underline{H}_3$). IR ($CHCl_3$): 1765, 1685, 1430, 1385, 1365, 1100 cm^{-1}. M.S. (*m/e*): 304 (M^+, 12), 181 (32), 153 (100), 91 (40), 77 (25), 69 (75), 68 (65), 56 (29).

Reaction of **6** *with phthalimidonitrene.* To a soln of **6**[10] (1.23 g) in CH_2Cl_2 (Alox filtered; 50 ml) was added in one portion N-aminophthalimide[7] (5.2 g; 4.6 eq). To this suspension was added with stirring during 5 hr a soln of lead tetraacetate (14 g; 4.6 eq) in CH_2Cl_2 (Alox filtered; 40 ml) under dry (P_2O_5) N_2 at room temp. Workup as for corresponding reaction of **1** gave crude product (2.0 g) which was chromatographed on a column of neutral alumina (as above) at 0°.[8] Hexane (90)–EtOAc (10) (150 ml) eluted **6** (0.87 g; 69%) as a yellowish oil. Hexane (80)–EtOAc (20) (500 ml) eluted a mixture of **7** + **8** (416 mg; 18%) in a ratio of 42:58 (judging by integral of C$\underline{H}_2$O protons in the mixture). Crystallization twice gave one pure isomer **8** (110 mg), m.p. 206–208° (EtOAc–hexane). The combined mother liquors were again chromatographed on a column of silica (grade II; 21 g) at 0°.[8] Elution with hexane (70)–(ether (30) (300 ml) gave **7** (105 mg). The analytical sample (49 mg) had m.p. 167–168° (EtOAc–hexane). More of the latter eluant (300 ml) gave more **8** (74 mg). The analytical sample (43 mg) had m.p. 208–209° (EtOAc–hexane).

Isomer **7**. M.p. 167–168°. (Found: C, 71.38; H, 6.04; N, 8.31; M.W. 336. $C_{20}H_{20}N_2O_3$ requires: C, 71.41; H, 5.99; N, 8.33%; M.W. 336.38). NMR ($CDCl_3$): τ 2.20 (bs, 4 arom H); 4.32 (t, J = 2 Hz, 2 vinylic H); 6.18, 6.35 (ABq, J = 8 Hz, 4C$\underline{H}_2$O); 7.17 (t, J = 2.5 Hz, 2C$\underline{H}$N); 7.20–8.50 (complex m, 8H). IR ($CHCl_3$): 1765, 1710, 1375, 1150, 995 cm^{-1}. M.S. (*m/e*): 336 (M^+, 23), 188 (62), 175 (93), 163 (15), 129 (82), 121 (82), 104 (47), 92 (42), 91 (100).

Isomer **8**. M.p. 208–209°. (Found: C, 71.37; H, 6.00; N, 8.27%; M.W. 336). NMR ($CDCl_3$): τ 2.20 (bs, 4 arom H); 4.38 (bs, 2 vinylic H); 6.32 (s, 4C$\underline{H}_2$O); 7.50–8.50 + 7.85 (m + bs, 8H). IR ($CHCl_3$): 1760, 1708, 1375, 1150, 995, 900 cm^{-1}. M.S. (*m/e*): 336 (M^+, 46), 188 (32), 175 (47), 163 (100), 129 (99), 121 (32), 104 (80), 92 (99).

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[4] We thank Prof. J. I. G. Cadogan for the benefit of his experience, freely offered in discussions before this work was undertaken.

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