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# FORMATION OF BENZO[a]PHENOXAZINE DERIVATIVES BY TRIETHYLPHOSPHITE-INDUCED DEOXYGENATION OF 1-(2-NITROPHENOXY) AND 2-(2-NITROPHENOXY)NAPHTHALENES*

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Summary: Reaction of 1-(2-nitrophenoxy)naphthalene or its β-isomer 7 with triethylphosphite produces benzo[a]phenoxazines 8 and 10, through the intermediate 6.

Although the use of triethylphosphite (TEP) for the construction of heterocycles by deoxygenation of aromatic nitrocompounds is wide-spread[1], the literature records only a limited number of studies on 2-nitrodiphenyl ethers and sulphides and none on 2-nitrophenyl naphthyl ethers. The elegant work of Cadogan and his coworkers has shown that unlike 2-nitrodiphenyl sulphides which do form phenothiazines albeit with rearrangement[2], 2-nitrodiphenyl ethers afford benzophosphoxazoles when reduced with TEP[3]. Likewise, pyrolysis of 2-azidodiphenyl sulphides leads to the formation of phenothiazines[4], whereas that of (2-azidophenyl) (2,6-dimethylphenyl) ether gives a benzoxazepine[3,5]. There is one instance of pyrolysis of 2-azidodiphenyl ether giving rise to traces of what was considered to be phenoxazine[6]. In an attempt to obtain naphthbenzoxazepine 12[7] we have studied the deoxygenation of 1-(2-nitrophenoxy)naphthalene 1 with TEP as well of the isomer 7. We obtained interesting results which we present in this note.

Heating of 1 (5 g) with TEP under reflux in nitrogen atmosphere for 10 hours and removal of excess TEP in vacuo gave a tarry residue. Chromatography over alumina in chloroform gave in the earlier fractions red crystals (100 mg)

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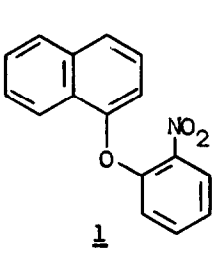
of 10. Subsequently benzophenoxazone 8 was obtained as orange crystals (250 mg), mp 190° (Found: C, 77.76; H, 3.85; N, 6.06; $M^+$ at m/z 247 . $C_{16}H_9NO_2$ requires C, 77.72; H, 3.67; N, 5.67: M, 247); $\nu_{C=O}$ 1640 $cm^{-1}$; $\lambda_{max}$ (MeOH) 237, 258, 360, 430 (log ε 4.15, 4.10, 4.19, 4.37); $^1H$ NMR ($CDCl_3$) : δ 8.66 (m, 1 H, C-1 H); 8.30 (m, 1 H, C-4 H); 7.1-7.9 (m, 6 H); 6.40 ppm (s, 1 H, C-6 H); $^{13}C$ NMR ($CDCl_3$) : δ 183.6 (C-5, d, J 4 Hz); 107.7 ppm (C-6; d, J 167 Hz), mixed mp undepressed with authentic sample prepared by the fusion of 2-methoxy-1,4-naphthoquinone with 2-aminophenol[8]. Initially we ruled out the intermediacy of benzo[a]phenoxazine 6 in the formation of 8 since the former is reported to oxidise spontaneously to blue coloured dyes and not to 8[9]. We were tempted to invoke the formation of the nitroso derivative 11 which by successive internal [4+2] cycloaddition, reorganisation of the cycloadduct to a dihydroderivative of 6 and subsequent oxidation can conceivably afford 6. However, the $^1H$ NMR spectrum of the crude TEP product prior to alumina chromatography showed the total absence of 8 (no signal at 6.4 ppm). Rapid chromatography on silica gel in chloroform resulted in the isolation of the known, unstable benzo[a]phenoxazine 6, mp 105-110° ($M^+$ at m/z 233). Exposure of a chloroform solution of 6 to air converted it gradually to 8 as the major product along with other coloured materials. Reaction of 2-(2-nitrophenoxy)naphthalene (7) with TEP also produced 6 in low yield. The formation of 6 in the reaction of 1 with TEP obviously involves a rearrangement and can be visualised to have occurred as shown.

The minor red product of reaction of 1 with TEP, tentatively formulated as 10 had the molecular formula $C_{32}H_{20}N_2O_2$ (Found: C, 83.36; H, 4.96; $M^+$ at m/z 464. Calculated C, 82.74; H, 4.34; M, 464). High resolution mass spectra confirmed the molecular formula. The UV spectrum had similarities to that of 8; $\lambda_{max}$ (MeOH) 430, 350, 290, 260 (log ε 4.10, 4.04; 4.19; 4.24). The $^1H$ NMR spectrum had the following signals : δ 8.53 (m, 1 H, C-1 H); 8.11 (m, 2 H, C-4 H + ?); 6.8-7.8 (m, 16 aromatic H) and 6.40 ppm (s, 1 H, C-6 H). The formation of 10 presumably involves insertion of species 2 into position 5 of 6 and further spontaneous oxidation of the resultant 9[10].

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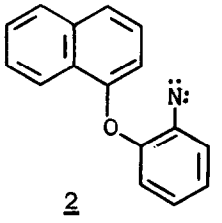


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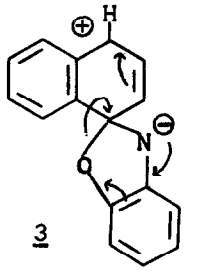


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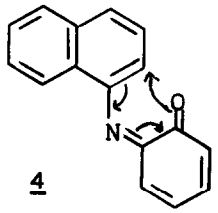


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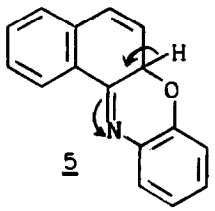


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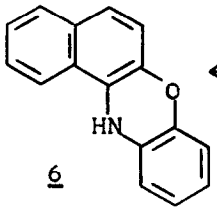


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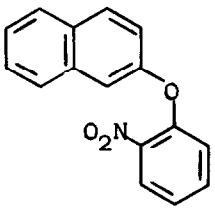


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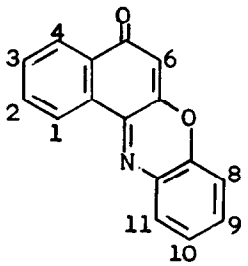


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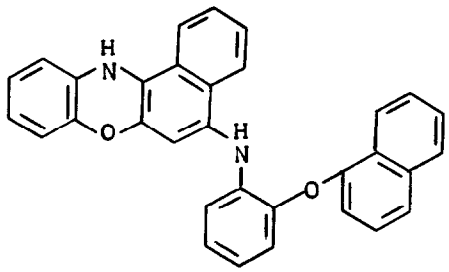


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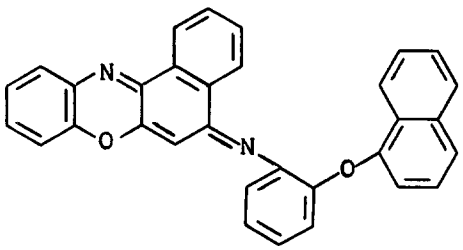


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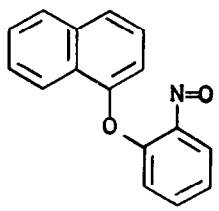


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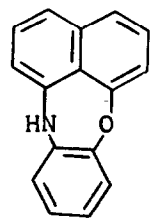


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References

1. P. A. S. Smith in "Nitrenes", W. Lwowski, Ed. Interscience Publishers, New York, 114 (1970).

2. J. I. G. Cadogan, S. Kulik, C. Thomson and M. J. Todd, J. Chem. Soc., 2437 (1970).

3. J. I. G. Cadogan, D. S. B. Grace, P. K. K. Lim and B. S. Tait, J. Chem. Soc. Chem. Commun. 520 (1972).

4. J. I. G. Cadogan and S. Kulik, J. Chem. Soc. C 2621 (1971).

5. J. I. G. Cadogan and P. K. K. Lim, Chem. Commun. 1431 (1971).

6. P. A. S. Smith, B. B. Brown, R. K. Putney and R. F. Feinisch, J. Am. Chem. Soc., 75, 6335 (1953).

7. K. Nagarajan, J. David, Y. S. Kulkarni, S. B. Hendi, S. J. Shenoy and P. Upadhyaya, European J. Med. Chem. in press (1984).

8. A. Butenandt, E. Biekert and W. Schafer, Liebigs Annalen Der Chemie 632, 134 (1960).

9. H. Goldstein and Z. Ludwig-Semelitch, Helv. Chim. Acta 2, 655 (1919).

10. Alternatively a referee has made the reasonable suggestion that during the reaction, 1 could be partly reduced to the amine which could then condense with 8 to afford 10 directly. This does not appear to be the case, since reaction between 8 and 1-(2-aminophenoxy)naphthalene in refluxing benzene in the presence of triethylamine for 12 hr led to recovery of starting materials. In boiling xylene, using p-toluene-sulphonic acid catalyst, 8 was recovered in 65% yield. Additionally a yellow product very tentatively considered to be the 6-(2-methylbenzyl) derivative of 8 was formed in about 10% yield, mp 187-190° (Found: C, 81.43; H, 5.06; N, 3.80; $M^+$ at m/z 351. $C_{24}H_{17}NO_2$ requires C, 82.03; H, 4.89; N, 3.99; M, 351); $^1H$ NMR ($CDCl_3$) : δ 8.70 (m, 1 H, C-1 H); 8.33 (m, 1 H, C-4 H); 6.90-7.90 (m, 10 H); 4.10 (s, 2 H, $CH_2$); 2.27 ppm (s, 3 H, $CH_3$). The characteristic singlet due to the proton at C-6 in 8 was lacking in the spectrum of the product. Presumably, the reaction involves addition of the methyl group to the quinone-imine system in 8, followed by oxidation of the resultant naphthyl amine.

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