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NEW BENZOXAZINE AND BENZOTHIAZINE CYANINE DYES

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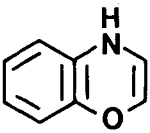
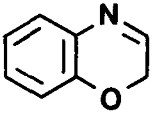
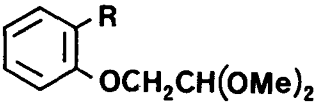
Whereas various substituted 1,4-benzoxazines have been described,[2] the parent compound, which theoretically may exist either in the enamine (1a) or the cyclic imine (1b) form, is still unknown. In an attempt to obtain (1) by an unambiguous and simple route, sodium o-nitrophenoxide was allowed to react with chloroacetaldehyde dimethyl acetal in anhydrous DMSO at 100° for 24 hr to give (2) (30%), $C_{10}H_{13}NO_5$, pale yellow needles, m.p. 36-37° (from EtOH), which on hydrogenation afforded the amino-acetal (3) as a colourless oil, $\nu_{max.}$ ($CC\ell_4$) 3430 and 3340 cm.$^{-1}$ Although the acetal (3) was easily hydrolysed, attempts to obtain the cyclisation product (1) using aqueous mineral acids under various conditions only resulted in the formation of intractable polymeric material.



(1a)



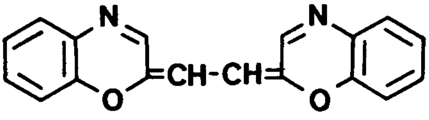
(1b)



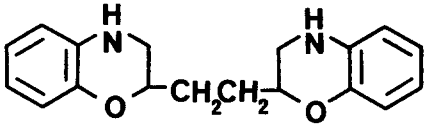
(2) R = NO_2
(3) R = NH_2

A different course of reaction was observed when (3) was dissolved in anhydrous TFA at room temperature. Examination of the reaction by NMR spectroscopy revealed that within a few minutes the acetal (3) underwent the expected transformation leading to the benzoxazine (1b), characterized by a 1H triplet at δ 8.67 (J 3.2Hz, H-3) and a 2H doublet at δ 5.50

(J 3.2Hz, H-2), and methanol (δ 3.60, s) which was rapidly converted into CF_3CO_2Me (δ 4.00, s). However, after an initial increase the signal of (1b) gradually disappeared. Subsequent removal of the solvent, and fractionation of the ethereal extract of the dark violet reaction mixture on a polyamide column in benzene led to the isolation of a new benzoxazine dye (20%), red plates, m.p. 252-254° (from EtOH), which proved to have structure (4).[3] This follows principally from the molecular formula, $C_{18}H_{12}N_2O_2$ (high resolution MS), and the characteristic pH-dependence of the visible spectrum (see Table 1) which shows a



(4)



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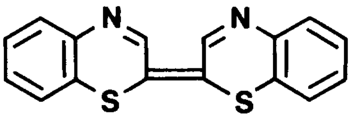
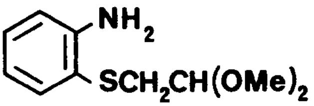


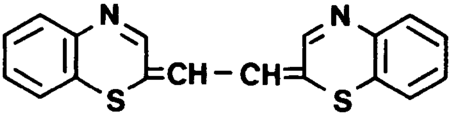
(6)

reversible bathochromic shift on acidification suggesting the presence of a cyanine-like chromophoric system, reminiscent of that characteristic of $\Delta^{2,2'}$-bi-(2H-1,4-benzothiazine) (6).[4] Further the NMR spectrum ($CDC\ell_3$) shows a complex multiplet at δ 7.03 accounting for 8 aromatic protons, and two sharp singlets at δ 7.80 and 6.06 (2H each) attributable to the two pairs of cyclic and exocyclic methine protons, respectively. Catalytic hydrogenation of (4) over Pd/C gave the corresponding octahydro derivative (5), $C_{18}H_{20}N_2O_2$, as a mixture of two stereoisomers (t.l.c.); $\lambda_{max.}$ (EtOH) 298, 247 and 217 nm, $\nu_{max.}$ ($CHC\ell_3$) 3370 cm.$^{-1}$, δ($CC\ell_4$) 6.53 (8H, m, ArH), 4.04 (2H, m, >CH), 3.24 (6H, m, $-CH_2N$ and NH, removed by D-exchange), and 1.82 (4H, m, exocyclic CH_2).

The formation of the benzoxazine dye (4) by TFA treatment of the amino-acetal (3) is intriguing and provides evidence for the marked reactivity of 2H-1,4-benzoxazine. Under similar conditions the amino-thioacetal (7) underwent the same transformation leading to the analogous benzothiazine dye (8) in better yield (30%); dark red prisms, m.p. 264-265° (from EtOAc), $C_{18}H_{12}N_2S_2$, (elemental analyses and MS), characterized by a 113 nm bathochromic shift on acidification, and NMR signals ($CDC\ell_3$) at δ 7.93 (2H, s, N=CH), 7.37 (8H, m, ArH), and 6.35 (2H, s, exocyclic =CH-).



(7)



(8)

Although expected, this reaction is of interest because it was previously found[4] that treatment of (7) with mineral acid in aqueous or methanolic solution produced mainly the $\Delta^{2,2'}$-bi-(2H-1,4-benzothiazine) (6) arising probably by oxidative coupling of the parent heterocyclic compound. However, the corresponding oxygen analogue was not obtained from (3) under these conditions. Thus (1) and its sulphur analogue behave differently and both remain elusive.

Table 1: UV spectra of the dyes (4), (8) and (6)

Compound	$\lambda_{max.}$ (MeOH)* nm (log ε)	$\lambda_{max.}$ (MeOH-H$^+$) (log ε)
(4)	204 (4.48)	204 (4.38)
	267 (4.44)	267 (4.36)
	465 (4.51)	350br (3.84)
		544 (4.49)
(8)	208 (4.62)	208 (4.60)
	283 (4.40)	285 (4.34)
	330br (4.08)	360br (3.94)
	507 (4.45)	620 (4.46)
(6)	267sh (4.47)	272 (4.45)
	274 (4.65)	292sh (4.13)
	454 (4.34)	366br (3.87)
	470sh (4.32)	562 (4.34)

* The data relative to (6) are in dioxan solution

References and Notes

1. The Italian authors are grateful to Consiglio Nazionale delle Ricerche, Roma, for partial financial support.

2. R.L. McKee, "The Chemistry of the Heterocyclic Compounds", Vol. 17 (ed. R.H. Wiley), pp. 377-441, Interscience, New York, 1962.

3. No attempt has been made to define the stereochemistry of (4). On standing in solution the isolated compound equilibrates with three additional dyes which appear to be (UV and MS evidence) the other possible geometrical isomers.

4. G. Prota, E. Ponsiglione and R. Ruggiero, Tetrahedron, **30** 2781 (1974).