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The attempted synthesis of 2*H*-1,4-benzoxazine, which is unreported in the literature, gives a mixture of polymeric aldolization products. The major product, isolated in crystalline form, is formulated as the cyclic trimer **5**.

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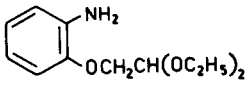
Although various substituted 1,4-benzoxazines (2), including some from natural sources (3), have been described in recent years, the synthesis of the parent compound **3** has not been reported in the literature.

A previous attempt (4) to obtain **3** by cyclization of the aminoaldehyde **2**, generated *in situ* by acid treatment of the acetal **1**, was unsuccessful. However, when the aminoacetal **1** was dissolved in anhydrous trifluoroacetic acid, formation of benzoxazine **3** was apparent after a few minutes. The ^{1}H nmr spectrum showed the expected signals for the heterocyclic ring in the immonium salt form. In this case, however, a further reaction quickly took place, and from the dark violet reaction mixture, the dimeric benzoxazine dye **4** was isolated (4).

We now report that the reaction of the acetal **1** with 0.5*M* hydrochloric acid at 60° in an atmosphere of very pure nitrogen mainly gives (35%) a polymeric aldolization product, formulated as the cyclic trimer **5** on the basis of its chemical and spectral properties. The product, m.p.



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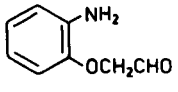

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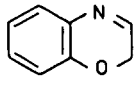

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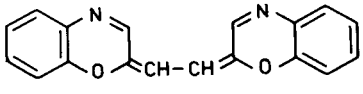

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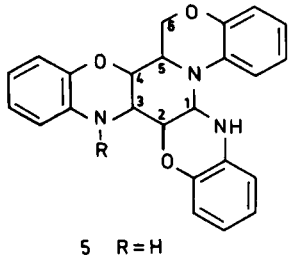
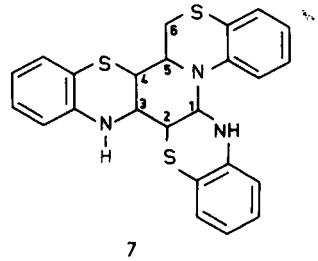


5 R=H
6 R=CH$_3$

145-147° (ethanol) exhibited λ max values in the uv spectrum at 218, 250 and 298 nm (log ε 4.58, 4.31 and 3.99, respectively) in methanol and a band at 3340 cm^{-1} in the ir spectrum. It showed M$^+$ at m/e 399 ($C_{24}H_{21}N_3O_3^+$) and diagnostic fragment ions at m/e 266 and 133 (base peak) formed by loss of one and two benzoxazine molecules, respectively. A distinguishing feature of the ^{1}H nmr spectrum, which was highly complex owing to the overlapping of signals, was a lowfield 1H doublet at δ 5.47, attributable to a methyne group linked to two nitrogen atoms. The ^{13}C nmr spectrum closely resembled that of the analogous benzothiazine trimer **7** (5) and exhibited, in addition to the aromatic carbon atoms, only six sp^3 hybridized carbon atoms, which is consistent with the cyclic structure **5** (see Table 1).



7

This assignment was further supported by the reaction of **5** with methyl iodide, which afforded the monomethyl derivate **6** as the main product. Compound **6** exhibited expected spectral features. The position of the methyl group was assigned on the basis of the downfield shift (*ca.* 6 ppm) of the C-3 signal in the ^{13}C nmr spectrum of the methyl derivate.

This study provides evidence that 1,4-benzoxazine is an elusive molecule which behaves somewhat similarly to the sulphur analogue 1,4-benzothiazine (7), and to other heterocyclic enamines in giving polymeric products. However, while **7** undergoes retroaldolization in trifluoroacetic acid readily to give the monomeric 1,4-benzothiazine (^{1}H nmr evidence), the benzoxazine analogue **5** is fairly stable toward acid-catalysed depolymerization. Unlike the trimer **7**, which is readily obtained on neutralization of the trifluoroacetic acid solution at room temperature, the formation of **5** requires heating at 60° for 1 hour.

EXPERIMENTAL

1-(*o*-Aminophenoxy)-2,2-diethoxyethane (1).

The acetal **1** was prepared, as previously described (4), by reduction of

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Table 1

^{13}C Nmr Data (δ in Ppm; Internal Standard: TMS) of Compounds **5**,**6** and **7** (sp^3 Region) (a)

Compound No.	C-1	C-2	C-3	C-4	C-5	C-6	C-7
5	59.1	73.3 (b)	49.4 (c)	73.4 (b)	49.8 (c)	66.0	
6	60.4	73.6	55.2	73.6	49.3	66.3	37.7
7	66.9	42.8	53.9	46.5	54.9	31.4	
Multiplicity (d)	d	d	d	d	d	t	q

(a) In deuteriochloroform (**5** and **6**) or in pentadeuteriopyridine (**7**) solution. (b,c) These assignments may be reversed. (d) Multiplicity in the off-resonance decoupled spectra.

the corresponding nitrocompound, which was obtained by condensation of sodium *o*-nitrophenoxide with bromoacetaldehyde diethyl acetal.

Benzoxazine Trimer **5**.

A.

A solution of 1-(*o*-aminophenoxy)-2,2-diethoxyethane (**1**) (1.3 g.) in 0.5*M* hydrochloric acid (160 ml.) was heated under a nitrogen atmosphere at 50-60° for 30 minutes. After cooling, the reaction mixture was extracted two times with chloroform and the combined extracts were washed with water and dried over sodium sulphate. Removal of the solvent under reduced pressure and fractionation of the oily residue (960 mg.) on a silica gel column (40 g.) in benzene, afforded the trimer **5** (270 mg., 35% yield) as a colourless powder (from ethanol), m.p. 145-147°; ir, uv, and nmr were previously discussed.

Anal. Calcd. for $C_{24}H_{21}O_3N_3$: C, 72.16; H, 5.30; N, 10.52; M, 399.1583. Found: C, 72.09; H, 5.61; N, 10.65; M^+, 399.1570.

B.

A solution of aminoacetal **1** (200 mg.) in anhydrous trifluoroacetic acid (1.5 ml.) was left at room temperature for 15 minutes. The reaction mixture was then neutralized with aqueous 2*N* sodium hydroxide (8 ml.) and excess of aqueous sodium bicarbonate and extracted with diethyl ether. Tlc examination (silicon dioxide, benzene and benzene-diethyl ether 9:1) revealed the formation of some slow-moving products but no trimer **5**. After removal of the solvent, the residue was dissolved in benzene and heated to reflux for *ca* 1 hour. Evaporation and fractionation of the reaction mixture by preparative tlc on silica gel in benzene gave 80 mg. (68% yield) of **5** as a colourless oil, which solidified on standing.

Methylation of **5**.

To a solution of **5** (100 mg.) in anhydrous dimethylsulfoxide (10 ml.), anhydrous potassium carbonate (90 mg.) and a large excess of methyl iodide (3 ml.) was added. The mixture was vigorously stirred for 7 hours at room temperature, diluted with water and extracted with chloroform. The organic layer was washed with water, dried and evaporated under reduced pressure. The brown oily residue (90 mg.), fractionated by preparative tlc on silica gel in benzene, gave **6** (52 mg., 50% yield), which crystallized from ethyl acetate as colourless prisms, m.p. 193-194; ir (chloroform): 3395 cm^{-1}; ^1H nmr (deuteriochloroform): 7.5-6.0 (12H, m, aromatic protons), 5.64 (1H, d, J = 4 cps, H-1), 3.15 (3H, s, CH_3), 5.0-3.0 (6H, very complex multiplet, remaining aliphatic protons); ^{13}C nmr: see table; ms: m/e 413 (M^+).

Anal. Calcd. for $C_{25}H_{23}N_3O_3$: C, 72.62; H, 5.61; N, 10.16. Found: C, 72.70; H, 5.48; N, 10.25.

Acknowledgement.

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