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Condensed Heterotricycles: 10,11-Ring-annealed Dibenz[*b*,*f*][1,4]oxazepines*†

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Reaction of iminochloride 7 with ethanolamine yields 11, which is transformed into the imidazodibenzoxazepine (12) by successive treatment with phosphorous oxychloride and alkali. Iminochlorides 7-10 are likewise converted into γ-hydroxypropylamines such as 13 and thence into pyrimidodibenzoxazepines (15-18). Iminochloride 9 and δ-hydroxybutylamine likewise afforded 30, which is transformed to the chlorobutyl derivative (31) and then cyclized to the diazepinodibenzoxazepine (32). The mercaptotriazolodibenzoxazepine (34) is obtained by fusion of the thione (33) with thiosemicarbazide. Hydrazinodibenzoxazepine (35) is obtained from the iminochloride 7, and then converted to the triazolodibenzoxazepines (38-44). The action of sodium azide on iminochlorides 7 and 9 leads to the formation of tetrazolodibenzoxazepines 45 and 46 respectively. 48 could not be cyclized to the pyrrolodibenzoxazepine (49). During the formation of iminochloride 9, an interesting benzoxazole (29) is obtained. In the reactions of 9 with amines, similar benzoxazoles 22, 24 and 27 are obtained as byproducts. Mechanisms for the formation of these benzoxazoles are suggested.

THE marked antidepressant properties of Sintamil (1)[2,3] and similar compounds and the potent neuroleptic activity of 2 and its analogues[4] prompted us to synthesize compounds of general structure 3. At the time we started this project, compounds having structural feature 3 were not known. In fact, there were only two reports of compounds (4)[5] and (5)[6] related to 3. Subsequently, a report has appeared on the pyrazinodibenzoxazepine (6)[7]. In this paper, we describe the synthesis of imidazo, pyrimido, triazolo and tetrazolodibenzoxazepines. Their biological properties are reported elsewhere[3].

The synthesis of the imidazodibenzoxazepine (12) started with the iminochloride 7 available from the corresponding lactam[1]. Treatment of 7 with ethanolamine gave 11, which upon successive reactions with phosphorus oxychloride and alkali afforded 12. An attempt to substitute the chlorine at position-11 in 7 by ethylenimine did not yield the desired product. This could conceivably be rearranged directly to 12.

The synthesis of the pyrimidodibenzoxazepine derivatives (15-18) proceeded similarly through the hydroxypropylamine derivatives of the type 13 obtained respectively from the corresponding iminochlorides. 17 was reduced to the amino compound 19.

In the reaction of iminochloride 9 with γ-hydroxypropylamine, apart from 13, a less basic orange-coloured compound was obtained as the minor product (~5-7%). It was isomeric with 13 and its spectral characteristics suggested it to have the structure 22. This was confirmed by its synthesis from 21 (obtained from 20) by treatment with γ-hydroxypropylamine. Similar byproducts from the reaction of 10 with γ-hydroxylpropylamine and of 9 with δ-hydroxybutylamine (see below) were assigned structures 23 and 24 respectively. A plausible mechanism for the formation of the byproduct 23 is shown. This observation has a remote parallel in the formation of 26 from lactam 25 by the action of phosphorus pentachloride[8]‡.

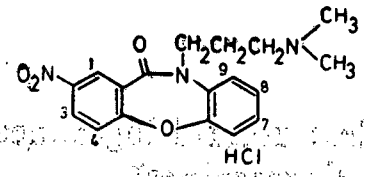
In a previous paper of this series[1], we had reported that the action of bases like pyrrolidine and N-methylpiperazine led to high yields of the expected products. A careful reinvestigation showed that with N-methylpiperazine, the normal product was formed exclusively, while with pyrrolidine, traces of 27 were isolable besides the expected product 28. The fact that the action of amines like γ-hydroxypropylamine on iminochlorides 9 and 10 leads to significantly more of the rearrangement products as compared to pyrrolidine and N-methylpiperazine must be attributed to a steric factor. Being less bulky, γ-hydroxypropylamine and δ-hydroxybutylamine are able to attack the fairly hindered position *para* to the nitro group more readily.

The elucidation of structures of the rearrangement products 22-24 and 27 gave us a clue to the structure of a byproduct in the preparation of the iminochloride 9. In large scale preparations of 9 from the corresponding lactam using phosphorus oxychloride and dimethylaniline, small quantities of an orange-coloured product, m.p. 218-20° were obtained. Its UV spectrum had maxima at 225, 253, 275, 310 and 387 nm. Its NMR spectrum showed a 6 proton singlet at δ 3 and a signal for 11 aromatic protons, among which the two protons *ortho* to the nitro group of the substituted nitrodiphenyl group were discernible. More significantly, we could also locate the two halves of an approximate A_2B_2 quartet at δ 6·7 and 7·7. These facts suggest that the byproduct may have structure 29. In connection with this structure assignment, it is to be noted that 4-amino-4'-nitrodiphenyl is orange-

*For a previous paper in this series, see K. Nagarajan *et al.*[1].

†CIBA contribution No. 349.

‡Brodrik *et al.* have reported the fission of 2-cyano- and 2-nitro-11-aryl dibenz[*b*,*f*][1,4]oxazepines by sodium ethoxide[9].



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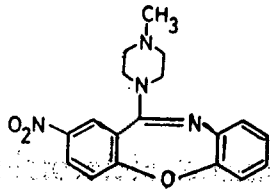

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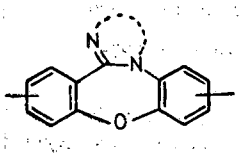

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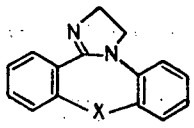
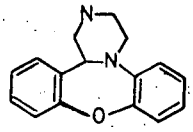


4 X = CH_2
5 X = NH



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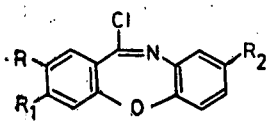
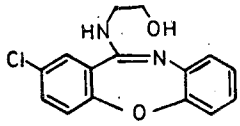


7 R = Cl $R_1 = R_2 = H$
8 $R = R_2 = H$; $R_1 = OCH_3$
9 $R = NO_2$; $R_1 = R_2 = H$
10 $R = NO_2$; $R_1 = H$; $R_2 = Cl$



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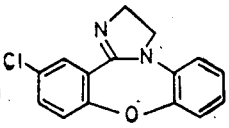

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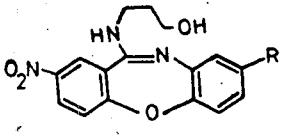
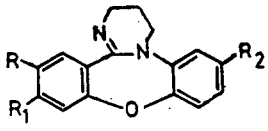
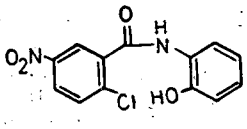


13 R = H
14 R = Cl



15 R = Cl; $R_1 = R_2 = H$
16 $R = R_2 = H$; $R_1 = OCH_3$
17 $R = NO_2$; $R_1 = R_2 = H$
18 $R = NO_2$; $R_1 = H$; $R_2 = Cl$
19 $R = NH_2$; $R_1 = R_2 = H$



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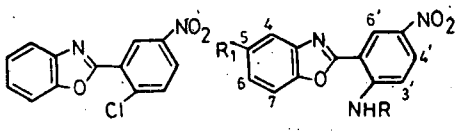
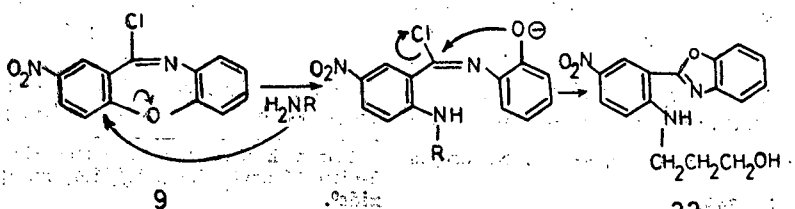


21

22 $R = (CH_2)_3OH$; $R_1 = H$
23 $R = (CH_2)_3OH$; $R_1 = Cl$
24 $R = (CH_2)_4OH$; $R_1 = H$



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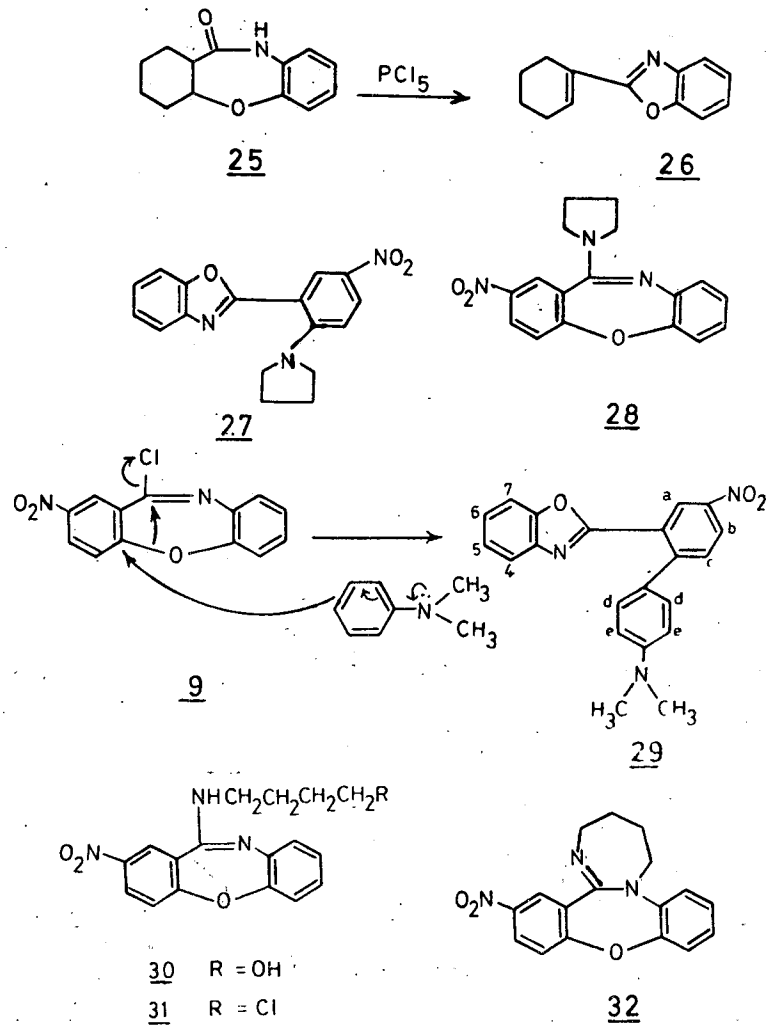


coloured and exhibits a maximum at 375 nm[10]. A mechanism for the formation of 29 from 9 has been suggested.

The diazepine analogue of 17 was synthesized as follows. Treatment of the iminochloride 9 with δ-hydroxybutylamine gave 30 as the major and 24 as the minor products. The action of phosphorus oxychloride on 30 led to the formation of chloro-derivative (31), which was not cyclized by aq. NaOH. However, heating 31 above its m.p. afforded, in a moderate yield, 32, different from 28 which had been prepared directly from 9 by the action of pyrrolidine.

Triazolodibenzoxazepines were prepared through 11-hydrazinoderivatives. Reaction of dibenzoxazepinethione (33)[1] with thiosemicarbazide led directly to 34. The intermediate thiosemicarbazone must have lost the elements of ammonia to form the mercapto derivative, rather than lose hydrogen sulphide to form an aminotriazole. The reaction of iminochloride 7 with hydrazine led to a mixture of the hydrazine 35 and traces of the bimolecular azine mentioned earlier[1]. 35 was converted to 38 by refluxing with triethyl orthoformate and to 39 through the trifluoroacetyl derivative (36) by refluxing with trifluoracetic anhydride. The chloracetyl derivative 37 was cyclized to the chloromethyltriazole (40) which was further transformed to 41-43 by reaction with appropriate bases. Reaction of 35 with cyanogen bromide led to the aminotriazole (44) in moderate yields.

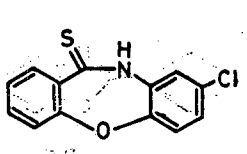
The tetrazolodibenzoxazepines (45) and (46) were synthesized by the reaction of iminochlorides 7 and 9 respectively with sodium azide. The isomeric azide structures (47) were ruled out for these products since their IR spectra had no characteristic azide band around 2150 cm^{-1}.

An attempted cyclization of 48 to a pyrrolodibenzoxazepine (49) was unsuccessful.

Experimental Procedure

M.ps. are uncorrected. IR (nujol), UV (95% EtOH) and mass spectra were run respectively on Perkin-Elmer infracord spectrophotometer, Beckman DK 2A spectrometer and Varian Mat CH7 mass spectrometer. NMR spectra were run on a Varian A60 spectrometer. Chemical shifts are quoted in ppm downfield from TMS as the internal standard.

Action of $POCl_3$ and dimethylaniline on 2-nitrodibenz[b,f][1,4]oxazepin-11(10H)-one — A mixture of the benzoxazepinone[11] (10 g, 40 mmoles), $POCl_3$ (80 ml) and dimethylaniline (3 ml) was refluxed overnight. Excess $POCl_3$ was removed *in vacuo*, using toluene to expel the last traces. Ice and water were added to the solid residue which was then extracted with methylene chloride. The extract was filtered from the insoluble recovered lactam, and the filtrate washed with water, dried and evaporated. The residue was triturated with a little methylene chloride-hexane mixture and filtered to give iminochloride 9 (8 g), m.p. 182-84°. The filtrate was



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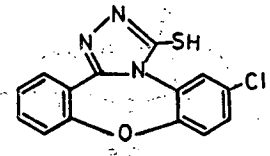

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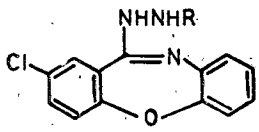
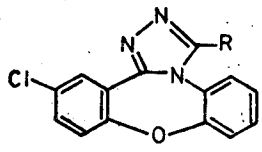


35 : R=H

36 : R=CF_3CO

37 : R=$ClCH_2CO$



38 : R=H

39 : R=CF_3

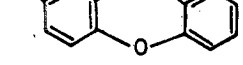
40 : R=CH_2Cl

41 : R=CH_2NEt_2

42 : R=CH_2N O

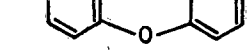
43 : R=CH_2N N-CH_3

44 : R=NH_2



45 : R=Cl

46 : R=NO_2



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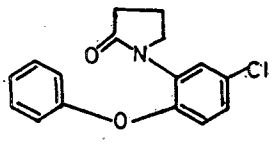

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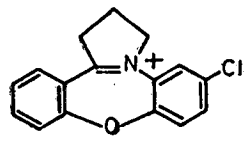

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evaporated and the residue (0·5 g) chromatographed on a column of silica gel (20 g) in a mixture of benzene and chloroform (1:3). Using the same solvent mixture for elution, 20 ml fractions were collected. Fractions 1-5 gave some more iminochloride 9 (0·1 g), m.p. 188-91°. Fractions 6-20 gave orange crystals (0·15 g), which recrystallized from EtOH to give the benzoxazole 29 (0·1 g), m.p. 218-20° (Found: C, 70·62; H, 5·15; N, 11·81. $C_{21}H_{17}N_3O_3$ requires C, 70·18; H, 4·77; N, 11·69%); λ_{max} 225 (inflex), 253, 275 (shoulder), 310 (shoulder), 387 nm (log ϵ 4·34, 4·34, 4·26, 4·06, 4·28); MS: *m/e* 359 (M^+), 342, 329, 313, 312, 297, 269, 241; NMR ($CDCl_3$): 3·00 (*s*, Ar-NMe_2), 6·70 (*d*, J=9 Hz, $2H_e$), 7·0-7·5 (H_c and H at C-4, C-5, C-6 and C-7), 7·70 (*d*, J=9 Hz, $2H_d$), 8·18 (*d*, J=3 Hz, H_a) and 8·28 (*d* of *d*, J=9, 3 Hz, H_b).

Treatment of 2-chlorodibenz[*b,f*][1,4]oxazepin-11-(10H)-one (15 g) with $POCl_3$ (120 ml) and dimethylaniline (4·5 ml) gave iminochloride 7 (10·5 g), m.p. 132-34° (ref. 12).

Likewise 2-nitro-8-chlorodibenz[*b,f*][1,4]oxazepin-11(10H)-one (12 g) gave iminochloride 10 (8·5 g) (Et_2O) (Found: C, 50·61; H, 2·35; N, 9·28. $C_{13}H_6Cl_2N_2O_3$ requires C, 50·51; H, 1·96; N, 9·28%); ν_{max} 1620 cm^{-1} (C=N).

3-*Methoxydibenz*[*b,f*][1,4]*oxazepin*-11(10*H*)-*one* — A solution of 2-amino-3′-methoxydiphenyl ether (24 g) in dry toluene (50 ml) was added dropwise with stirring to an ice-cold solution of $COCl_2$ in toluene (20% w/v, 200 ml). After 1 hr at 0°, the mixture was refluxed overnight. Toluene was removed *in vacuo* and the residue distilled to give 2-isocyanato-3′-methoxydiphenyl ether (23·4 g), b.p. 158-62°/2 mm.

The above isocyanate (22·5 g, 0·1 mole) in *o*-dichlorobenzene (50 ml) was added dropwise with stirring into a suspension of anhyd. $AlCl_3$ (1·5 g, 0·11 mole) in the same solvent (30 ml) at 100°. After the addition was over, the mixture was heated with stirring at 150° for 1 hr, cooled and treated with ice-cold dil. HCl. The precipitate was filtered, washed with hexane and crystallized first from ethanol and then from DMF to give the methoxy lactam (7 g), m.p. 191° (softening above 180°) (Found: C, 69·93; H, 4·98; N, 6·16. $C_{14}H_{11}NO_3$ requires C, 69·70; H, 4·59; N, 5·80%).

3-*Methoxy*-11-*chlorodibenz*[*b,f*][1,4]*oxazepine* (8) — The above lactam (6·5 g) was treated with $POCl_3$ (50 ml) and dimethylaniline (2 ml) as usual to give the iminochloride 8 (5·7 g), m.p. 125-27° (Et_2O-hexane) (Found: C, 65·10; H, 4·16; N, 5·79. $C_{14}H_{10}ClNO_2$ requires C, 64·75; H, 4·32; N, 5·39%); ν_{max} 1620 cm^{-1} (C=N).

Reaction of aminoalcohols with 11-*chlorodibenz*[*b,f*]-[1,4]*oxazepines:* 2-*Nitro*-11(3-*hydroxy*-1-*propyl*)*amino-dibenz*[*b,f*][1,4]*oxazepine* (13) *and* 2-[2-(3-*hydroxy*-1-*propyl*)*amino*-5-*nitrophenyl*]*benzoxazole* (22) — Iminochlo-

ride 9 (12·3 g, 45 mmoles), 3-amino-1-propanol (6·8 g, 90 mmoles) and ethanol (100 ml) were refluxed for 16 hr. The ethanol was evaporated and water added to the residue. The precipitate was filtered, ground with 1*N* HCl and again filtered to remove neutral product (A). The acid extract was neutralized with ammonia and the basic product removed by filtration and crystallized from ethanol to give 13 (8·2 g), m.p. 188-90° (Found: C, 61·36; H, 5·13; N, 13·62. $C_{16}H_{15}N_3O_4$ requires C, 61·33; H, 4·83; N, 13·41%); ν_{max} 3260 cm^{-1} (NH, OH); λ_{max}, 253, 275, 310 nm (inflex) (log ϵ 4·26, 4·16, 3·80); NMR ($CDCl_3$): 1·90 (*qu*, 2H, C-C*H*$_2$-C), 3·25-3·90 (*m*, 4H, N-C*H*$_2$, OC*H*$_2$), 4·65 (*bs*, 1H, O*H*), 6·70-7·77 (*m*, 5 Ar-*H* and N*H*), 8·30 (*d* of *d*, *J*=9, 3 Hz, C_3—H), 8·40 (*d*, *J*=3 Hz, C_1—*H*).

The neutral part (4 g) was crystallized from methanol to give 2-nitrodibenz[*b,f*][1,4]oxazepin-11(10H)-one (1·5 g) arising by hydrolysis of 9. The methanol mother liquor gave a second crop of crystals (1 g), which was purified by recrystallizations from Et_2O and MeOH to give benzoxazole 22, m.p. 170-72°, m.m.p. with authentic sample (see below) remained undepressed (Found: C, 61·33; H, 4·83; N, 13·41%); ν_{max} 3520 (OH), 3260 cm^{-1} (NH); λ_{max} 217, 267 (inflex), 278, 287, 295, 373 nm (log ϵ 4·29, 4·11, 4·17, 4·19, 4·15, 4·36); NMR ($CDCl_3$+DMSO-d_6+D_2O): 2·0 (*qu*, 2H, *J*=7 Hz, —C—C*H*$_2$—C), 3·50 (*t*, 2H, *J*=7 Hz, N—C*H*$_2$—), 3·80 (*t*, 2H, *J*=7 Hz, OC*H*$_2$—); 6·70 (*d*, *J*=9 Hz, C_3—*H*), 7·0-7·85 (*m*, 4H, Ar—*H*), 8·03 (*d* of *d*, *J*=9, 3 Hz, $C_{4'}$—*H*), 8·73 (*d*, *J*=3 Hz, $C_{6'}$—*H*).

22 formed an O-acetyl derivative, m.p. 129-31° (EtOH) (Found: C, 60·55; H, 5·01; N, 12·09. $C_{18}H_{17}N_3O_5$ requires C, 60·84; H, 4·82; N, 11·83%); ν_{max} 1730 cm^{-1} (C=O); NMR ($CDCl_3$): 2·10 (*s*, 3H, C*H*$_3$), 2·13 (*qu*, 2H, *J*=6 Hz, C—C*H*$_2$—C), 3·47 (*q*, 2H, *J*=6 Hz, N—C*H*$_2$), 4·28 (*t*, 2H, OC*H*$_2$), 6·62 (*d*, *J*=9 Hz, $C_{3'}$—*H*), 7·15-7·85 (*m*, 4H, Ar—*H*), 8·10 (*d* of *d*, *J*=9, 3 Hz, $C_{4'}$—*H*), 8·82 (*d*, *J*=3 Hz, $C_{6'}$—*H*), 9·15 (*t*, *J*=6 Hz, N*H*).

Likewise iminochloride 10 and 3-amino-1-propanol gave the hydroxypropylaminodibenzoxazepine (14) (50%), m.p. 142-44° (Et_2O) (Found: C, 55·58; H, 4·25; N, 12·13. $C_{16}H_{14}ClN_3O_4$ requires C, 55·26; H, 4·06; N, 12·08%); ν_{max} 3250b cm^{-1} (OH, NH); and the benzoxazole 23 (~3%), m.p. 260° (softening above 190°) (Found: C, 55·41; H, 4·16; N, 11·96. $C_{16}H_{14}ClN_3O_4$ requires C, 55·26; H, 4·06; N, 12·08%); ν_{max} 3520 (OH), 3250 cm^{-1} (NH); λ_{max} 238 (inflex), 265, 273, 285 (inflex), 295, 304, 375 nm (log ϵ 4·15, 4·19, 4·17, 4·08, 4·10, 4·01, 4·32).

Similarly iminochloride 9 was heated with 4-amino-1-butanol to give 30 (82%), m.p. 117-19° (benzene) (Found: C, 62·82; H, 5·47; N, 12·89. $C_{17}H_{17}N_3O_4$ requires C, 62·37; H, 5·24; N, 12·84%); ν_{max} 3300 and 3220 cm^{-1} (OH, NH); λ_{max} 254, 275, 320 nm (inflex) (log ϵ 4·25, 4·15, 3·70), and the benzoxazole 24 (~1%), m.p. 146-48° (Et_2O-MeOH) (Found: C, 62·29; H, 5·31; N, 12·89. $C_{17}H_{17}N_3O_4$ requires C, 62·37; H, 5·24; N, 12·84%); ν_{max} 3510 (OH), 3250 cm^{-1} (NH); λ_{max} 217, 266 (inflex), 277, 287, 295, 375 nm (log ϵ 4·34, 4·15, 4·20, 4·22, 4·17, 4·38).

Iminochloride 7 and ethanolamine gave 2-chloro-11-(2-hydroxyethyl)aminodibenz[*b,f*][1,4]oxazepine (11) as an oil (90%), while 7 and 3-amino-1-propanol gave the corresponding hydroxypropylamino derivative (85%), m.p. 157-59° (aq. EtOH) (Found: C, 63·11; H, 5·23; N, 9·58. $C_{16}H_{15}ClN_2O_2$ requires C, 63·47; H, 4·99; N, 9·25%); ν_{max} 3200b cm^{-1} (OH, NH), and 8 and 3-aminopropanol gave 3-methoxy-11-(3-hydroxy-1-propyl)aminodibenzoxazepine-(85%), m.p. 122-24° (EtOH) (Found: C, 68·58; H, 6·34; N, 9·68. $C_{17}H_{18}N_2O_3$ requires C, 68·44; H, 6·08; N, 9·39%).

Action of pyrrolidine on iminochloride 9 — Iminochloride 9 (1·4 g) and pyrrolidine (0·8 g) were heated together under reflux in ethanol (20 ml) for 16 hr. Ethanol was evaporated and water added to the residue which was then extracted with ether. The ether-extractable material was separated by means of 1*N* HCl into basic and neutral parts. The base (1·2 g) crystallized from MeOH to give the pyrrolidinodibenzoxazepine (28)[1] (0·9 g), m.p. 151-53°; MS: *m/e* 309 (M^+), 292, 280, 272, 254, 240, 234, 194.

The neutral part (~50 mg) was identical with the pyrrolidinophenylbenzoxazole 27 (see below).

2-(2-Chloro-5-nitrophenyl)benzoxazole (21) — N-(2-Chloro-5-nitrobenzoyl)-2-aminophenol (20)[11] (3 g) and PPA (30 g) were heated together at 100° for 6 hr. The mixture was cooled and treated with ice-chips. The precipitated solid was filtered and recrystallized from ethanol to give 21 (0·5 g), m.p. 173-75° (Found: C, 56·45; H, 2·85; N, 10·48. $C_{13}H_7ClN_2O_3$ requires C, 56·84; H, 2·57; N, 10·20%).

Action of amines on 2-(2-chloro-5-nitrophenyl)benzoxazole (21): *2-[2-(3-Hydroxy-1-propyl)amino-5-nitrophenyl]benzoxazole* (22) — Benzoxazole 21 (0·4 g), 3-aminopropanol (0·3 g) and ethanol (10 ml) were heated under reflux for 16 hr and the solution diluted with water to give 22 (0·15 g), m.p. 172-74° (MeOH) (Found: C, 61·31; H, 5·13; N, 13·34. $C_{16}H_{15}N_3O_4$ requires C, 61·33; H, 4·83; N, 13·41%); found to be identical with the byproduct from the reaction of 9 with 3-amino-1-propanol.

2-[2-(N-Pyrrolidino)-5-nitrophenyl]benzoxazole (27) — Benzoxazole 21 (0·55 g) and pyrrolidine (0·3 g) underwent reaction to give 27 (0·3 g), m.p. 127-29° (EtOH) (Found: C, 66·08; H, 5·15; N, 13·52. $C_{17}H_{15}N_3O_3$ requires C, 66·01; H, 4·89; N, 13·59%); λ_{max} 283, 380 nm (log ϵ 4·01, 4·28).

2-[2-(N-Methyl-1-piperazinyl)-5-nitrophenyl]benzoxazole — Benzoxazole 21 (0·55 g) and N-methylpiperazine (0·4 g) gave the product (0·4 g), m.p. 158-60° (EtOH) (Found: C, 64·03; H, 5·55; N, 16·38. $C_{18}H_{18}N_4O_3$ requires C, 63·83; H, 5·36; N, 16·38%); λ_{max} 292, 365 nm (log ϵ 4·22, 4·15).

Imidazodibenzoxazepine 12 — 2-Chloro-11-(2-hydroxyethylamino) dibenz[*b,f*][1,4]oxazepine (11) (6·5 g), $POCl_3$ (25 ml) and toluene (25 ml) were heated under reflux for 1 hr. Toluene and the excess $POCl_3$ were removed *in vacuo* and ice-chips added to the residue. The solution was basified with aq. NaOH and extracted with chloroform. The chloroform extract was evaporated and the residue treated with ethanolic HCl to give 12 HCl, which crystallized from EtOH-ether (yield 4·7 g), m.p. 291-93° (Found: C, 56·94; H, 4·48; N, 8·63. $C_{15}H_{12}Cl_2N_2O$ requires C, 56·98; H, 4·14; N, 8·86%).

Pyrimidodibenzoxazepine 15-18 — 2-Chloro-11-(3-hydroxy-1-propyl)aminodibenzoxazepine (7·5 g) was treated with $POCl_3$ (30 ml) as before to give the HCl salt of pyrimidodibenzoxazepine 15 (5·8 g), m.p. 296-98° (EtOH-ether) (Found: C, 56·24; H, 5·05; N, 8·94. $C_{16}H_{14}Cl_2N_2O.H_2O$ requires C, 56·82; H, 4·47; N, 8·28%); NMR of free base ($CDCl_3$): 1·97 (*qu*, 2H, *J*=6 Hz, —C—C*H*$_2$—C), 3·67 (broad *t*, 4H,

J=6 Hz, 2N-CH_2), 6·87-7·40 (*m*, 6H, Ar-*H*), 7·77 (*d*, J=2 Hz, C_1—*H*).

Likewise were obtained from the respective propanolamines, the hydrochlorides of 16, 17, and 18. Pyrimidodibenzoxazepine hydrochloride (16 HCl) (80%), m.p. 180-82° (EtOH) (Found: C, 62·03; H, 5·92; N, 8·13. $C_{17}H_{17}ClN_2O_2.\frac{1}{2}H_2O$ requires C, 62·71; H, 5·56; N, 8·61%); pyrimidodibenzoxazepine-17 hydrochloride (80%), m.p. >300° (EtOH) (Found: C, 57·70; H, 4·24; N, 12·92. $C_{16}H_{14}ClN_3O_3$ requires C, 57·93; H, 4·25; N, 12·67%); λ_{max} 226, 270 nm (log ϵ 4·45, 4·12); and pyrimidodibenzoxazepine-18 hydrochloride (70%), m.p. >300° (EtOH-ether) (Found: C, 50·43; H, 4·30; N, 11·05. $C_{16}H_{13}Cl_2N_3O_3.H_2O$ requires C, 50·01; H, 3·94; N, 10·94%).

Azepinodibenzoxazepine (32) — Butanolamine 30 (8·0 g) was treated with $POCl_3$ as usual. The product in this case was the chloro compound 31 (3·6 g), m.p. 134-36° (EtOH) (Found: C, 59·24; H, 4·95; N, 12·31. $C_{17}H_{16}ClN_3O_3$ requires C, 59·05; H, 4·66; N, 12·15%); λ_{max} 254, 275 nm (inflex) (log ϵ 4·26, 4·17).

The chloro compound 31 (4 g) was heated at 140-50° for 3 hr. The residue was triturated with ethanol, filtered and treated with ethanolic HCl. The product crystallized from ethanol to give the HCl salt of azepine 32 (2 g), m.p. 170° (d) (Found: C, 56·10; H, 5·28; N, 11·52. $C_{17}H_{16}ClN_3O_3.H_2O$ requires C, 56·13; H, 4·99; N, 11·55%). The free base 32 had m.p. 171-72° (EtOH) (Found: C, 65·90; H, 5·12; N, 13·88. $C_{17}H_{15}N_3O_3$ requires C, 66·01; H, 4·89; N, 13·59%); λ_{max} 210, 262, 320 nm (sh) (log ϵ 4·50, 4·31, 3·81); NMR ($CDCl_3$): 1·92 [*m*, 4H, —C—(CH_2)$_2$—C], 3·53 (*m*, 4H, 2-NCH_2), 6·7-7·6 (*m*, 6H, Ar-*H*), 8·00-8·35 (*m*, 2H, C_1-*H* and C_3-*H*).

Aminopyrimidodibenzoxazepine (19) — Nitropyrimidodibenzoxazepine (17) hydrochloride (4·4 g) was hydrogenated in methanol (150 ml) at atmospheric pressure and room temperature, using platinum oxide as catalyst (0·2 g) until 3 moles of hydrogen were taken up, to give a product (3·1 g) which crystallized from ethanol to give the HCl salt of 19 (2·5 g), m.p. >300° (Found: C, 57·93; H, 6·13; N, 12·51. $C_{16}H_{16}ClN_3O.1\frac{1}{2}H_2O$ requires C, 58·65; H, 5·77; N, 12·77%).

Triazolodibenzoxazepines 34, 38-44: *Mercaptotriazolodibenzoxazepine* (34) — Thione (3)[1] (2·6 g, 10 mmoles) was fused with thiosemicarbazide (1 g, 11 mmoles) at 130° for 18 hr. The product was cooled, triturated with water and filtered. After washing with ethanol, it recrystallized from acetone-MeOH to give 34 (0·9 g), m.p. 292-94° (Found: C, 55·84; H, 3·00; N, 13·61. $C_{14}H_8ClN_3OS$ requires C, 55·71; H, 2·66; N, 13·93%); MS: *m/e* 303 (M^+, ^{37}Cl), 301 (M^+, ^{35}Cl).

2-*Chloro*-11-*hydrazinodibenzoxazepine* (35) — Iminochloride 7 (4 g) and hydrazine hydrate (85%, 15 ml) were left in ethanol (150 ml) for 2 days at room temperature. The solution was concentrated *in vacuo*, treated with water and extracted with benzene. The benzene layer was shaken with dil. HCl. The acid extract was made alkaline and re-extracted with ether. The etherial layer was dried and evaporated to give hydrazine 35 (2·4 g), m.p. 109-11° (Et_2O-hexane), MS: *m/e* 261 (M^+, ^{37}Cl), 259 (M^+, ^{35}Cl), 232, 230, 193.

Triazolodibenzoxazepine 38 — Hydrazine 35 (3 g) and triethyl orthoformate (10 ml) were heated under reflux for 6 hr. Ether was added and the product filtered and recrystallized from ethanol to give 38 (2·5 g), m.p. 212-14° (Found: C, 62·37; H, 3·07; N, 15·83. $C_{14}H_8ClN_3O$ requires C, 62·35; H, 2·99; N, 15·58%).

The toluene sulphonate salt had m.p. 100-102°, (EtOH-ether) (Found: C, 55·04; H, 4·15; N, 9·23. $C_{21}H_{16}ClN_3O_4S.H_2O$ requires C, 54·85; H, 3·95; N, 9·14%).

Triazolodibenzoxazepine 39 — Hydrazine 35 (4 g) and trifluoracetic anhydride (15 ml) were mixed when a vigorous reaction occurred. The clear solution soon deposited crystals of the trifluoracetyl derivative 36, m.p. 195-98° (Found: C, 51·20; H, 2·79; N, 11·53. $C_{15}H_9ClF_3N_3O_2$ requires C, 50·65; H, 2·55; N, 11·81%); ν_{max} 1690 cm^{-1} (C=O).

The trifluoracetyl derivative (2 g) was heated with trifluoracetic anhydride (7 ml) under reflux for 4 hr, and the solution concentrated. Water and ammonia were added and the precipitate filtered. This was triturated with ether and hexane and then crystallized from the same solvent mixture to give 39 (0·8 g), m.p. 124-26° (Found: C, 53·65; H, 2·44; N, 12·03. $C_{15}H_7ClF_3N_3O$ requires C, 53·35; H, 2·09; N, 12·44%).

Chloromethyltriazolodibenzoxazepine (40) — Chloracetyl chloride (4·56 g, 40 mmoles) in dry ether (30 ml) was added to a stirred mixture of hydrazine 35 (10·4 g, 40 mmoles) in ether (100 ml) and sodium bicarbonate (6·8 g, 80 mmoles) in water (50 ml) and cooled in an ice-bath. The mixture was stirred for 2 hr, set aside overnight and filtered to give the chloracetamide 37 (11·9 g), m.p. 185-86° (d) (acetone) (Found: C, 53·24; H, 3·45; N, 12·79. $C_{15}H_{11}Cl_2N_3O_2$ requires C, 53·59; H, 3·29; N, 12·50%); ν_{max} 1695 (C=O), 3400 cm^{-1} (NH).

The above amide (11·9 g) and PPA (200 g) were heated together at 130-40° with stirring for 4 hr. The mixture was cooled, decomposed with ice and ammonia and extracted with ether to give the chloromethyldibenzoxazepine (40) (8·7 g), m.p. 170-72° (Et_2O) (Found: C, 56·89; H, 2·70; N, 13·00. $C_{15}H_9Cl_2N_3O$ requires C, 56·62; H, 2·85; N, 13·20%).

Aminomethyltriazolodibenzoxazepines 41-43 — Chloromethyl derivative 40 (3·5 g, 11 mmoles) and N-methylpiperazine (2·2 g, 22 mmoles) were heated together at 100° for 2 hr. Water was added and the precipitate extracted into ether. The basic product 43 was recovered by acid extraction (yield, 4 g), m.p. 154-57°. The HCl salt of 43 crystallized from ethanol (3·5 g), m.p. 277° (d) (Found: C, 52·79; H, 5·24; N, 15·60. $C_{20}H_{22}Cl_3N_5O$ requires C, 52·82; H, 4·88; N, 15·40%).

Similarly, treatment of 40 (2·5 g) with morpholine gave the morpholinomethyl compound 42 (2·3 g), m.p. 223-24° (MeOH) (Found: C, 62·20; H, 4·92; N, 14·87. $C_{19}H_{17}ClN_4O_2$ requires C, 61·87; H, 4·65; N, 15·19%), and with diethylamine yielded the diethylaminotriazole 41 (2·3 g), m.p. 137-39° (Et_2O-hexane) (Found: C, 64·58; H, 5·68; N, 15·84. $C_{19}H_{19}ClN_4O$ requires C, 64·31; H, 5·39; N, 15·79%).

Aminotriazolodibenzoxazepine 44 — Hydrazine 35 (2·6 g) and cyanogen bromide (1 g) were heated together in ethanol (50 ml) under reflux for 8 hr. After removal of ethanol, water and ammonia were added to give a precipitate (2·6 g) which was purified by two crystallizations from ethanol to give 44 (0·7 g), m.p. >300° (Found: C, 58·99; H, 3·47; N, 19·95. $C_{14}H_9ClN_4O$ requires C, 59·06; H, 3·19; N, 19·68%); ν_{max}: 3100 and 3250 cm^{-1} (NH).

Tetrazolodibenzoxazepines (45) *and* (46) — Iminochloride 7 (2·65 g, 10 mmoles) and sodium azide (0·65 g, 10 mmoles) were heated in acetone (70 ml) and water (3 ml) under reflux for 16 hr. Removal of acetone, addition of water and crystallization of the precipitate from acetone-EtOH gave the tetrazole 45 (1·8 g), m.p. 213-15° (Found: C, 57·84; H, 2·84; N, 20·93. $C_{13}H_7ClN_4O$ requires C, 57·68; H, 2·61; N, 20·70%).

Similar treatment of 9 (5·5 g, 20 mmoles) with sodium azide (1·3 g) gave crude 46 (4·8 g). Crystallization from ethanol gave 1·9 g of pure 46, m.p. 223-25° (Found: C, 55·59; H, 2·68; N, 24·39. $C_{13}H_7N_5O_3$ requires C, 55·52; H, 2·51; N, 24·90%).

Pyrrolidone 48 — 2-Amino-4-chlorodiphenyl ether (11 g, 50 mmoles) treated with γ-bromobutyryl chloride (9·3 g, 50 mmoles) in ether (200 ml) and sodium bicarbonate (4·2 g) in water (50 ml) gave the γ-bromobutyramide (17·2 g), m.p. 87-90° (Et_2O-hexane) (Found: C, 51·80; H, 4·35; N, 3·51. $C_{16}H_{15}BrClNO_2$ requires C, 52·13; H, 4·10; N, 3·80%), A mixture of the amide (3·69 g) and sodium hydride (50% suspension in mineral oil, 0·5 g) in dioxane (50 ml) was refluxed for 4 hr. Another lot of sodium hydride (0·5 g) was added and the refluxing continued for 2 hr. The mixture was filtered and the filtrate evaporated to give pyrrolidone 48 (2·6 g) as an oil.

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