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Condensed Heterotricycles*: Synthesis of Pyridine-annealed Dibenz[*b*,*f*][1,4]oxazepines†

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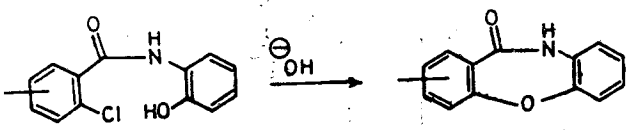
Cyclization of N-(2-chloro-5-nitrobenzoyl)-8-hydroxy-1,2,3,4-tetrahydroquinolines (7)-(9) using hot aqueous alkali affords pyridodibenzoxazepinones 10, 11 and 12 respectively. Heating the sodium salts of *o*-chlorobenzamides (16)-(19) in dimethylformamide affords similar pyridodibenzoxazepinones 20, 21, 22 and 23 respectively. Catalytic reduction of the nitrolactam 10 to the amine 33 followed by diazotization and deamination gives 20. Reaction of the nitrochlorobenzamides 7 and 9 with cyclic secondary bases leads to displacement of chlorine by amines, to give 14 and 15. Nitration of pyridodibenzoxazepinones 11 and 20 affords 31 and 32 respectively. The nitrolactams 12, 11, 22, 32 and 31 are reduced to the respective amines 34-38. Amine 34 is transformed to the chloracetyl (39) and to the morpholinoacetyl derivative (40) and to ethyl (41) and allyl (42) thioureas, while 37 is converted to the aminomethylene malonate 43. LAH reduction of 20 gives the pyridodibenzoxazepine 44. A second synthesis of the tetracyclic ring system is by the ring closure of the N-acetylphenoxytetrahydroquinoline 29 by phosphorus pentoxide. 30 is obtained and characterized as the iodide. The sultam 48 analogous to 10 is made from 47 in low yield.

In a previous paper, we reported on the following facile synthesis of the dibenz[*b*,*f*][1,4]oxazepine ring system[2].

Hot aq. alkali brought about the cyclization when the chlorine atom was activated by a *para*-nitro group. In the case of amides having a less activated chlorine, heating their sodium salts in DMF brought about ring-closure in moderate to high yields. This paper reports on an extension of this method to *o*-chlorobenzamides of 8-hydroxy-1,2,3,4-tetrahydroquinolines and its derivatives.



Catalytic reduction of 8-hydroxy-(1)- and 5-chloro-8-hydroxy-(2)-quinolines afforded the tetrahydro derivatives 4 and 5 respectively which were converted to the corresponding 2-chloro-5-nitrobenzamides 7 and 8 in high yields. Upon heating solutions of the amides in 1:1 equivalent of dil. aq. alkali, cyclization occurred to form the pyridobenzoxazepinones 10 and 11 in yields of 85 and 88% respectively. The reaction was extended to 8-hydroxy-1,2,3,4-tetrahydroquinaldine (6) whose 2-chloro-5-nitrobenzoyl derivative 9 underwent cyclization to afford 12 in 80% yield. When cyclic secondary bases were allowed to react with 7 and 9, displacement occurred largely to give 14 and 15, although a little of the tetracyclic lactams were also formed. The structures of the tetracyclic derivatives 10-12 were supported by elemental analyses and IR and NMR spectra. It may be noted that these are isomeric with the ring system present in alkaloids of the cularine type[3].

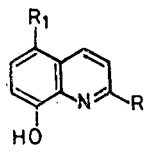
As was observed in the tricyclic series[2], *o*-chlorobenzoyl derivatives of 8-hydroxytetrahydroquinoline and tetrahydroquinaldine lacking a nitro group *para* to the chlorine atom could not be converted to tetracyclics by treatment with hot aq. alkali. However, heating their sodium salts in DMF induced cyclization. Thus the amides 16-19 could all be converted to 20-23 respectively. 20 was also obtained from 10 by catalytic reduction followed by deamination through diazotization. It could not be prepared from 25 (reduction product of 24) by treatment with nitrous acid. The NMR spectra of 21, 22, 23 and 36 presented interesting features which were revealing of the conformation of the methyl group and the tetrahydropyridine ring and are discussed elsewhere[4].

Another route attempted for the tetracyclic system involving a Bischler-Napieralski type ring-closure of 29 was only partially successful. 2-Aminodiphenyl ether was converted to 8-phenoxyquinoline (26) by Skraup reaction. Catalytic reduction to 28 was followed by acetylation to 29. The cyclization of 29 to 30 could not be brought about by $POCl_3$ even under forcing conditions, although the use of P_2O_5 gave a low yield of 30, characterized as the iodide. Treatment of 28 with phosgene followed by aluminium chloride could conceivably lead to 20, but this was not realized. An activating group *para* to the point of cyclization is known to favour the reaction. With this view in mind, we tried to synthesize the methoxy derivative 27; unfortunately, 2-amino-3′-methoxydiphenyl ether, under the conditions of the Skraup reaction, led only to tarry products, presumably due to demethylation and polymerization.

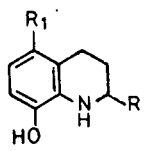
For purposes of biological screening, 11 and 20 were further nitrated to the nitro derivatives 31 and

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

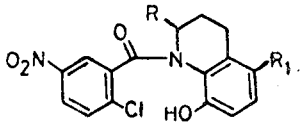
†CIBA contribution No. 347.



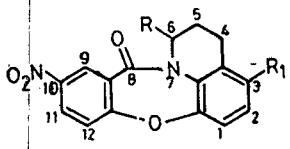
1 R = R_1 = H
2 R = H ; R_1 = Cl
3 R = CH_3; R_1 = H



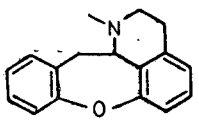
4 R = R_1 = H
5 R = H; R_1 = Cl
6 R = CH_3; R_1 = H



7 R = R_1 = H
8 R = H; R_1 = Cl
9 R = CH_3; R_1 = H



10 R = R_1 = H
11 R = H ; R_1 = Cl
12 R = CH_3; R_1 = H



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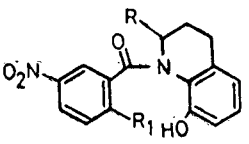
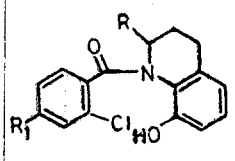
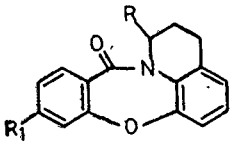


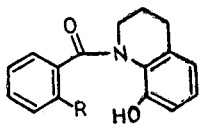
14 R = H; R_1 = N(CH)(CH)N-CH_3
15 R = CH_3; R_1 = N(CH)(CH)O



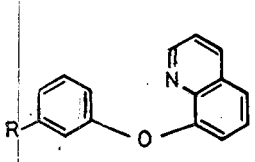
16 R = R_1 = H
17 R = CH_3; R_1 = H
18 R = CH_3; R_1 = NO_2
19 R = CH_3; R_1 = Cl



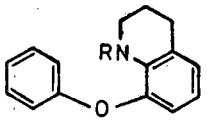
20 R = R_1 = H
21 R = CH_3; R_1 = H
22 R = CH_3; R_1 = NO_2
23 R = CH_3; R_1 = Cl



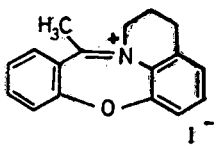
24 R = NO_2
25 R = NH_2



26 R = H
27 R = OCH_3



28 R = H
29 R = $COCH_3$



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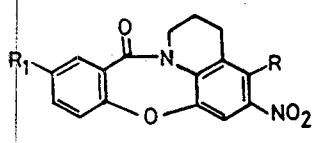
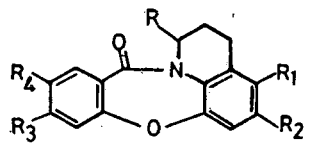


31 R = Cl ; R_1 = NO_2
32 R = R_1 = H



33 R = R_1 = R_2 = R_3 = H : R_4 = NH_2
34 R = CH_3; R_1 = R_2 = R_3 = H ; R_4 = NH_2
35 R = H; R_1 = Cl; R_2 = R_3 = H; R_4 = NH_2
36 R = CH_3; R_1 = R_2 = R_4 = H ; R_3 = NH_2
37 R = R_1 = R_3 = R_4 = H; R_2 = NH_2
38 R = R_3 = H; R_1 = Cl; R_2 = R_4 = NH_2
49 R = CH_3; R_1 = R_3 = R_4 = H ; R_2 = NH_2

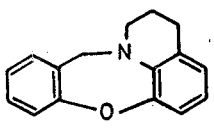


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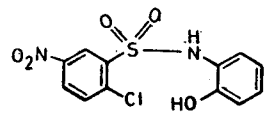
TABLE 1 — N-BENZOYL-8-HYDROXY-1,2,3,4-TETRAHYDROQUINOLINE DERIVATIVES*

Compound	m.p. °C	Crystallized from	Mol. formula	N (%)	
				Found	Calc.
7	151-52	Aq. MeOH	$C_{16}H_{13}ClN_2O_4$	8·41	8·42
8	174-75	C_6H_6-hexane	$C_{16}H_{12}Cl_2N_2O_4$	7·67	7·63
9	169-70	C_6H_6-hexane	$C_{17}H_{15}ClN_2O_4$	8·40	8·08
16	132-34	Aq. EtOH	$C_{16}H_{14}ClNO_2$	5·32	4·87
17	150-52	EtOH	$C_{17}H_{16}ClNO_2$	4·88	4·64
18	210-11	Aq. EtOH	$C_{17}H_{15}ClN_2O_4$	8·34	8·08
19	174-75	Aq. EtOH	$C_{17}H_{15}Cl_2NO_2$	4·37	4·17
24	158-59	EtOH	$C_{16}H_{14}N_2O_4$	9·01	9·39
25	165-66	MeOH	$C_{16}H_{16}N_2O_2$	10·08	10·44

*Satisfactory C, H analyses have been obtained in all the cases.



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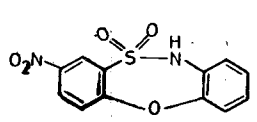

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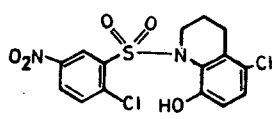

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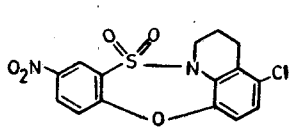

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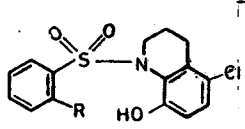

50 R = NO_2

51 R = NH_2

32 respectively. Amines 33-38 were prepared from the corresponding nitrotetracycles by catalytic reduction. Amine 34 was converted to the chloroacetyl derivative 39 and thence to the morpholino compound 40 and to ethyl (41) and allyl (42) thioureas, while 37 was transformed by reaction with diethyl ethoxymethylene malonate to the aminomethylene malonate (43)*. LAH reduction of 20 afforded 44 which was crystalline but could not be analysed satisfactorily. However, it gave an analytically pure picrate.

It has been reported[6] that the nitrochlorobenzene sulphonamide 45 cyclizes to 46 in hot pyridine. This could not be satisfactorily reproduced by us. However, we found that 45 could be cyclized to 46 in hot aq. alkali in 73% yield. Encouraged by this, we attempted the cyclization of the sulphonamide 47, obtained from 5 and 2-chloro-5-nitrobenzenesulphonyl chloride. Among several conditions tried, only NaOH in aq. dioxane gave the desired product 48, but only in a very low yield. As was observed with analogous earlier cases[2], diazotization of aminoamide 51 (from nitroamide 50) did not lead to cyclization to 48.

*The preparation of 43 was prompted by our finding of anti-influenzal activity for a number of aminomethylene malonates[5].

Experimental Procedure

M.ps. are uncorrected. IR (nujol), UV (95% ethanol) and mass spectra were run respectively on a Perkin-Elmer infracord spectrophotometer, Beckmann DK 2A spectrometer and a 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.

8-Hydroxy-1,2,3,4-tetrahydroquinoline (4)— A solution of 8-hydroxyquinoline (1) (22 g) in MeOH (200 ml) and acetic acid (18 ml) was shaken with hydrogen at atmospheric pressure and room temperature using platinum oxide as catalyst (0·6 g) until there was no more uptake of hydrogen. The mixture was filtered and the filtrate concentrated *in vacuo*. Addition of concentrated, aq. ammonia to the residue gave 4 (20 g), m.p. 116-18° (ref. 7).

Likewise 5, m.p. 115-16° (aq. MeOH) (Found: C, 58·88; H, 5·67; N, 7·43. $C_9H_{10}ClNO$ requires C, 58·87; H, 5·49; N, 7·63%) and 6, m.p. 78-79° (ref. 8) were prepared.

N-(2-Chloro-5-nitrobenzoyl)-8-hydroxy-1,2,3,4-tetrahydroquinoline (7) — 2-Chloro-5-nitrobenzoyl chloride (24 g, 0·11 mole) in dry ether (100 ml) was added dropwise with stirring into a solution of 4 (16·5 g, 0·11 mole) in ether (100 ml) and sodium bicarbonate (18·5 g, 0·22 mole) in water (100 ml). The mixture was stirred for 2 hr and filtered. The precipitate was washed successively with water, dil. HCl and water. The etherial layer from the filtrate was separated, dried and evaporated to give some more product. The two crops were combined and crystallized from aq. methanol to give 7 (26·5 g), m.p. 151-52°; ν_{max} 1620 (C=O), 3200 cm^{-1} (OH). A number of amides were prepared by this procedure, and are listed in Table 1.

5-Chloro-2-acetoxybenzoyl chloride (4·3 g, 20 mmoles) and 5 (3·7 g, 20 mmoles) gave an amide (1·2 g), m.p. 225-30° (d), which was hydrolysed with NaOH (0·25 g) in water (5 ml) at room temperature. Acidification gave the 5-chlorosalicylamide of 5, m.p. 150-51° (aq. MeOH) (Found: C, 57·35; H, 4·03; N, 4·41. $C_{16}H_{13}Cl_2NO_3$ requires C, 56·82; H, 3·87; N, 4·14%); the salicylamide of 5 was similarly prepared, m.p. 138-41° (aq. MeOH) (Found: C, 63·39; H, 4·95; N, 4·56. $C_{16}H_{14}ClNO_3$ requires C, 63·28; H, 4·65; N, 4·61%).

TABLE 2 — PYRIDO[3,2,1][*d,e*]DIBENZ[*b,f*][1,4]OXAZEPINE DERIVATIVES*

Compound	m.p. °C	Crystallized from	Mol. formula	N (%) Found	N (%) Calc.
		USING PROCEDURE-A			
10	164-65	Acetone-MeOH	$C_{16}H_{12}N_2O_4$	9·31	9·46
11	167-69	MeOH	$C_{16}H_{11}ClN_2O_4$	8·14	8·47
12	120-21	CH_2Cl_2-MeOH	$C_{17}H_{14}N_2O_4$	9·06	9·03
		USING PROCEDURE-B			
20	168-70	Acetone-MeOH	$C_{16}H_{13}NO_2$	5·55	5·57
21	104-05	MeOH	$C_{17}H_{15}NO_2$	5·33	5·28
22	124-25	C_6H_6-MeOH	$C_{17}H_{14}N_2O_4$	9·40	9·03
23	186-87	$CHCl_3$-EtOH	$C_{17}H_{14}ClNO_2$	4·61	4·67
		USING PROCEDURE-C			
33	185-87	$CHCl_3$-MeOH	$C_{16}H_{14}N_2O_2$	10·16	10·52
34	158-62	Aq. MeOH	$C_{17}H_{16}N_2O_2$	10·28	9·99
35	169-71	MeOH	$C_{16}H_{13}ClN_2O_2$	9·70	9·32
35 (HCl)	284-86	MeOH-Et_2O	$C_{16}H_{14}Cl_2N_2O_2$	8·49	8·31
36	181-82	MeOH	$C_{17}H_{16}N_2O_2$	9·80	9·99
37	231-33	EtOH	$C_{16}H_{14}N_2O_2$	10·42	10·52
38	229-31	MeOH	$C_{16}H_{14}ClN_3O_2$	12·85	13·31
49	190-92	C_6H_6	$C_{17}H_{16}N_2O_2$	10·06	9·99

*Satisfactory C, H analyses have been obtained in all the cases.

Pyrido[3,2,1-*de*]*dibenz*[*b,f*][1,4]*oxazepines*: *Cyclization of N-*(2-*chloro*-5-*nitrobenzoyl*)-8-*hydroxy*-1,2,3,4-*tetrahydroquinoline* (7) (*Procedure-A*) — A solution of 7 (3·3 g, 10 mmoles) in aq. NaOH (1*N*, 11 ml) was heated at 100° for 1 hr. The precipitate was collected and washed with water to give pyridodibenzoxazepinone (10) (2·5 g), m.p. 164-65° (acetone-MeOH); ν_{max} 1635 cm^{-1} (C=O); λ_{max} 227 (inflex), 270 nm (log ϵ 4·27, 4·10); NMR ($CDCl_3$): 2·07 (*qu*, J=6·5 Hz, C_5-H_2), 2·89 (*t*, J=6·5 Hz, C_4-H_2), 4·1 (*t*, J=6 Hz, C_6-H_2), 7·08 (*m*, C-1, C-2, C-3 protons), 7·35 (*d*, J=9 Hz, C_{12}-H), 8·32 (*d* of *d*, J=3, 9 Hz; C_{11}-H), 8·80 (*d*, J=3 Hz, C_9-H).

2-Chloro-5-nitrobenzamides could also be cyclized by heating under reflux in benzene with anhyd. potassium carbonate.

Cyclization of N-(2,4-*dichlorobenzoyl*)-8-*hydroxy*-1,2,3,4-*tetrahydroquinaldine* (19) (*Procedure-B*) — A solution of amide 19 (8·4 g, 25 mmoles) in dimethylformamide (100 ml) containing sodium hydride (50% suspension in mineral oil; 1·2 g, 25 mmoles) was refluxed for 1·5 hr; the solvent was removed *in vacuo*; water was added and the precipitate filtered and washed successively with water, dil. NaOH, water, dil. HCl and finally water to give the pyridodibenzoxazepinone (23) (6·3 g), m.p. 187° ($CHCl_3$-EtOH); ν_{max} 1610 cm^{-1} (C=O); NMR ($CDCl_3$): 1·25 (*d*, J=6·5 Hz, CH_3), 1·4-2·6 (*m*, C_5-H_2), 2·73 (*m*, C_4-H_2), 5·20 (*qu*, J=6·5 Hz, C_6-H), 6·9-7·4 (*m*, 5H, Ar-H), 7·83 ppm (*d*, J=9 Hz, C_9-H).

Cyclization could also be achieved in good yields using the sodium or potassium salt prepared by treatment of the phenolic amides with equivalent quantities of aq. alkali and evaporation.

The pyridodibenzoxazepinones obtained by procedures A and B are listed in Table 2.

Action of morpholine on amide 9 — Amide 9 (5·2 g, 15 mmoles) and morpholine (4·4 g, 50 mmoles) were heated on a steam-bath for 4 hr. Water was added to the mixture and the product filtered off to give the yellow morpholino amide 15 (5·6 g), m.p. 220-21° (CH_2Cl_2-benzene) (Found: C, 63·63; H, 5·92; N, 10·33. $C_{21}H_{23}N_3O_5$ requires C, 63·46; H, 5·83; N, 10·58%); ν_{max} 1610 cm^{-1} (C=O).

The action of N-methylpiperazine on amide 7 likewise gave the piperazino compound 14, m.p. 110° (acetone-ether) (Found: C, 63·06; H, 6·37; N, 13·84. $C_{21}H_{24}N_4O_4$ requires C, 63·62; H, 6·10; N, 14·13%) and the lactam 10, m.p. 165°.

2-*Nitropyridodibenzoxazepinone* (32) — Powdered lactam 20 (2 g) was added in small portions to conc. HNO_3 (20 ml) with stirring and cooling in an ice-bath. After being left at room temperature for 2½ hr, the solution was poured into ice-water. The crystalline precipitate was filtered and recrystallized from EtOH-benzene to give 32 (1·6 g), m.p. 169-70° (Found: C, 65·03; H, 4·31; N, 9·64. $C_{16}H_{12}N_2O_4$ requires C, 64·86;; H, 4·08; N, 9·46%); ν_{max} 1650 cm^{-1} (C=O); NMR ($CDCl_3$): 2·08 (*qu*, J=6·5 Hz, C_5-H_2); 2·93 (*t*, J=6·5 Hz, C_4-H_2), 4·12 (*t*, J=6 Hz, C_5-H_2), 7·10-7·75 (*m*, C-10, C-11, C-12 protons), 7·75-8·05 (C-1, C-3, C-12 protons).

Similarly, nitration of 11 (1 g) using conc. HNO_3 (10 ml) and H_2SO_4 (10 ml) at 0° gave the dinitrolactam 31 (0·8 g), m.p. 195-97° (acetone), (Found: C, 51·16; H, 2·68; N, 11·18. $C_{16}H_{10}ClN_3O_6$ requires C, 51·46; H, 2·94; N, 11·10%), while nitration of 21 afforded the TLC pure 2-nitro derivative which appeared to be a hydrate, m.p. 55-80°.

Aminodibenzoxazepinone (33) — Nitrolactam (10, 14·8 g) in methanol (500 ml) was shaken with

hydrogen at atmospheric pressure and room temperature in the presence of Adam's catalyst (0·15 g) till H_2 uptake ceased. The mixture was filtered and the filtrate evaporated to give amine 33 (11·3 g), m.p. 185-87° ($CHCl_3$-MeOH); ν_{max} 1625 (C=O); 3280 and 3360 cm^{-1} (NH), forming a HCl salt, m.p. 282-83° (ethanol) (Found: C, 63·25; H, 5·20; N, 9·02. $C_{16}H_{15}ClN_2O_2$ requires C, 63·48; H, 4·99; N, 9·26%).

M.ps. and analytical data of amino derivatives 33-38 and 49 obtained by reduction (procedure-C) are listed in Table 2.

Chloracetyl derivative 39 — Amine 34 (2·8 g), chloracetyl chloride (1·1 g) and triethylamine (1·5 g) in chloroform (25 ml) were heated under reflux for 10 hr. The solution was washed with 2*N* HCl and dried. Removal of chloroform and crystallization of the residue from MeOH gave 39 (3·0 g), m.p. 206-8° (Found: C, 63·94; H, 5·23; N, 7·97. $C_{19}H_{17}ClN_2O_3$ requires C, 63·96; H, 4·80; N, 7·85%); ν_{max} 1630 and 1680 (C=O), 3410 cm^{-1} (NH).

Morpholinoacetamide 40 — The foregoing chloracetyl derivative (0·7 g) and morpholine (0·5 g) were heated together at 100° for 4 hr. Water was added; a gum separated and this was taken up in EtOH and treated with HCl gas to give 40 HCl, m.p. 258-61° (d) (EtOH) (Found: C, 60·30; H, 6·11; N. 8·88. $C_{23}H_{26}ClN_3O_4.H_2O$ requires C, 59·74; H, 6·06; N, 9·09%); ν_{max} 1635 and 1690 cm^{-1} (C=O).

Ethyl thiourea 41 — Amine 34 (3·5 g, 12·5 mmoles), ethyl isothiocyanate (1·1 g, 12·5 mmoles) and EtOH (10 drops) were heated at 70° for 2 hr. The product was triturated with ether, filtered and crystallized from $CHCl_3$-EtOH to give thiourea 41 (4·2 g), m.p. 212-15° (Found: C, 65·42; H, 5·93; N, 11·68. $C_{20}H_{21}N_3O_2S$ requires C, 65·38; H, 5·76; N, 11·44%); ν_{max} 1610 (C=O); 3290 and 3370 cm^{-1} (NH).

The allylthiourea 42 of 34 was likewise prepared and crystallized from acetone-EtOH, m.p. 192-94° (Found: C, 66·52; H, 5·64; N, 10·76. $C_{21}H_{21}N_3O_2S$ requires C, 66·48; H, 5·58; N, 11·08%); ν_{max} 1625 (C=O); 3330 and 3170 cm^{-1} (NH).

Aminomethylene malonate 43 — 2-Aminopyridodibenzoxazepinone (37, 4·7 g) and diethyl ethoxymethylenemalonate (5 g) were heated at 150° for ½ hr to give 43 (6·2 g), m.p. 135-36° (EtOH) (Found: C, 66·32; H, 5·69; N, 6·53. $C_{24}H_{24}N_2O_6$ requires C, 66·04; H, 5·54; N, 6·42%); ν_{max} 1625 (C=C), 1660, 1675 and 1710 cm^{-1} (C=O).

Deamination of 33 *to dibenzoxazepinone* 20 — A suspension of amine 33 (2·66 g, 10 mmole) in conc. HCl (5 ml), conc. H_2SO_4 (1 ml) and water (25 ml) was cooled to 0° and treated under stirring with sodium nitrite (0·8 g, 11 mmoles) in water (3 ml). After 1 hr at 0°, the mixture was poured into hypophosphorus acid (32%, 20 ml) and stirred at 0° for 1 hr. After being left at room temperature for 20 hr, the mixture was filtered and the precipitate washed with dil. NaOH and water. Crystallization from acetone-methanol gave 20 (1·8 g), m.p. 168-70°, m.m.p. with a sample prepared by procedure-B remained undepressed (Found: C, 76·05; H, 4·97; N, 5·55. $C_{16}H_{13}NO_2$ requires C, 76·47; H, 5·22; N, 5·57%); ν_{max} 1630 cm^{-1} (C=O); λ_{max} 265 nm (log ϵ 3·81); NMR ($CDCl_3$): 2·02 (*qu*, J=6·5 Hz, C_5-H_2), 2·82 (*t*, J=6·5 Hz, C_4-H_2); 4·08 (*t*, J=6 Hz, C_6-H_2), 6·83-7·67 (*m*, 6H, Ar-*H*), 7·92 (*m*, C_9-*H*).

LAH reduction of lactam 20 — Lactam 20 (2·5 g) in dioxane (100 ml) was added dropwise to a suspension of LAH (0·9 g) in ether (90 ml) at room temperature with stirring. The mixture was set aside overnight and treated with water to decompose the excess hydride and complex. The organic layer was removed and concentrated *in vacuo*. The residue was taken up in ether and the solution extracted with dil. HCl. The acid extract was basified and 44 thus produced was extracted into ether. Evaporation of the dried ether extract left 44 as an oil (1·2 g) which crystallized on standing, m.p. 85-88°, picrate, m.p. 138-39° (acetone-hexane) (Found: C, 57·01; H, 3·53; N, 12·16. $C_{22}H_{18}N_4O_8$ requires C, 56·65;; H, 3·89; N, 12·01%).

8-*Phenoxy*-1,2,3,4-*tetrahydroquinoline* (28) — 8-Phenoxyquinoline (26, 5·9 g) was converted to the HCl salt and hydrogenated at atmospheric pressure and room temperature, using Adam's catalyst to give 28 HCl (4·5 g), m.p. 200-3°; free base 28, m.p. 78-79° (ref. 9).

Acetylation of 28 (1·7 g) using acetic anhydride (5 ml) and triethylamine (2 ml) at 100° for 1 hr gave 29 (1·8 g), m.p. 78-80° (aq. EtOH) (Found: C, 76·44; H, 6·21; N, 5·54. $C_{17}H_{17}NO_2$ requires C, 76·38; H, 6·41; N, 5·54%); ν_{max} 1660 cm^{-1} (C=O).

Reaction of 28 (4·5 g) with phenylisocyanate (2·4 g) in refluxing benzene (25 ml) for 14 hr gave the phenylurea (5·2 g), m.p. 143-44° (Found: C, 76·88; H, 5·93; N, 8·28. $C_{22}H_{20}N_2O_2$ requires C, 76·72; H, 5·85; N, 8·13%); ν_{max} 1645 (C=O), 3340 cm^{-1} (NH).

Pyridodibenzoxazepine (30) — A solution of acetyl derivative 29 (2·5 g) in xylene (100 ml) was heated with P_2O_5 (35 g) under reflux for 16 hr. Xylene was decanted off. The residual sludge was dissolved in water and the solution treated with excess KI. The resultant salt was fractionally crystallized from ethanol-ether to give 30 (0·2 g), m.p. 203-5° (d) (Found: C, 53·75; H, 4·60; N, 4·15. $C_{17}H_{16}INO$ requires C, 54·12; H, 4·28; N, 4·15%); λ_{max} 246, 305 nm (log ϵ 4·23, 3·80).

N-(2-*Chloro*-5-*nitrobenzenesulphonyl*)-*o*-*aminophenol* (45) — To a solution of *o*-aminophenol (11 g, 0·1 mole) in pyridine (50 ml) cooled to 10°, was added 2-chloro-5-nitrobenzenesulphonyl chloride (25·6 g, 0·1 mole) in small portions. The mixture was stirred at room temperature for 20 hr and then poured into aq. HCl (4*N*, 600 ml), when a solid separated, which crystallized from aq. AcOH to give 45 (31 g), m.p. 130-34°; the melting point changed to 149-51° upon crystallization from $CHCl_3$ (Found: C, 43·77; H, 2·68; N, 9·10. $C_{12}H_9ClN_2O_5S$ requires C, 43·85; H, 2·76; M, 9·52%).

Sultam 46 — Sulphonamide 45 (32·9 g, 0·1 mole) and NaOH (8 g, 0·2 mole) in water (800 ml) was heated with stirring at 70° for 24 hr. The solution was cooled, decanted from gummy material and acidified with conc. HCl. The separated product was filtered and recrystallized from aq. EtOH to give 46 (21·5 g), m.p. 152-53°; lit.[5], m.p. 156-58°, (Found: C, 49·47; H, 2·81; N, 10·05; S, 11·34. $C_{12}H_8N_2O_5S$ requires C, 49·32; H, 2·76; N, 9·59; S, 10·95%). A different crystalline form of 46, m.p. 135-36°, was also once obtained from the same solvent (Found: C, 49·29; H, 2·56; N, 9·77%).

N-(2-*Chloro*-5-*nitrobenzenesulphonyl*)-5-*chloro*-8-*hydroxy*-1,2,3,4-*tetrahydroquinoline* (47) — Reaction of 2-chloro-5-nitrobenzenesulphonyl chloride (9 g, 35 mmoles) in ether (100 ml) with 5-chloro-8-hydroxy-1,2,3,4-tetrahydroquinoline (5) (6·5 g, 35 mmoles) in ether (30 ml) and water (25 ml) containing sodium bicarbonate (6 g) as usual gave the crude

product (6·6 g), which upon purification by filtration through a column of silica gel (50 g) in chloroform gave pure 47 (2·5 g), m.p. 140-41° (Found: C, 45·02; H, 3·04; N, 6·75. $C_{15}H_{12}Cl_2N_2O_5S$ requires C, 44·70; H, 3·02; N, 6·95%).

Sultam 48 — A solution of sulphonamide 47 (0·4 g) in dioxane (5 ml) containing NaOH (40 mg) in water (5 ml) was heated at 100° for 4 hr, and then evaporated to dryness. Water was added and the gummy product crystallized from acetone-MeOH to give 48, m.p. 188-90°; MS: *m/e* 368 (M^+, ^{37}Cl), 366 (M^+, ^{35}Cl), 304, 302, 274, 272, 258, 256.

N-(2-Nitrobenzenesulphonyl)-5-chloro-8-hydroxy-1,2,3,4-tetrahydroquinoline (50) — Reaction of the sulphonyl chloride (3·7 g, 20 mmoles) with 5-chloro-8-hydroxy-1,2,3,4-tetrahydroquinoline 5 (4·5 g, 20 mmoles) in the presence of triethylamine (2 g) in refluxing benzene (50 ml) for 1 hr gave 50 (3·9 g), m.p. 105-11° (MeOH) (Found: C, 49·11; H, 3·95; N, 7·45. $C_{15}H_{13}ClN_2O_5S$ requires C, 48·86; H, 3·56; N, 7·45%).

N-(2-Aminobenzenesulphonyl)-5-chloro-8-hydroxy-1,2,3,4-tetrahydroquinoline (51) — It was obtained by catalytic reduction of 50 at atmospheric pressure and room temperature using platinum oxide as catalyst, m.p. 113-15° (EtOH) (Found: C, 53·38; H, 4·79; N, 8·07. $C_{15}H_{15}ClN_2O_3S$ requires C, 53·20; H, 4·46; N, 8·27%).

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