Syntheses of Heterocyclic Compounds. Part XXII.[1] Routes to Naphthimidazoles and Imidazoquinolines

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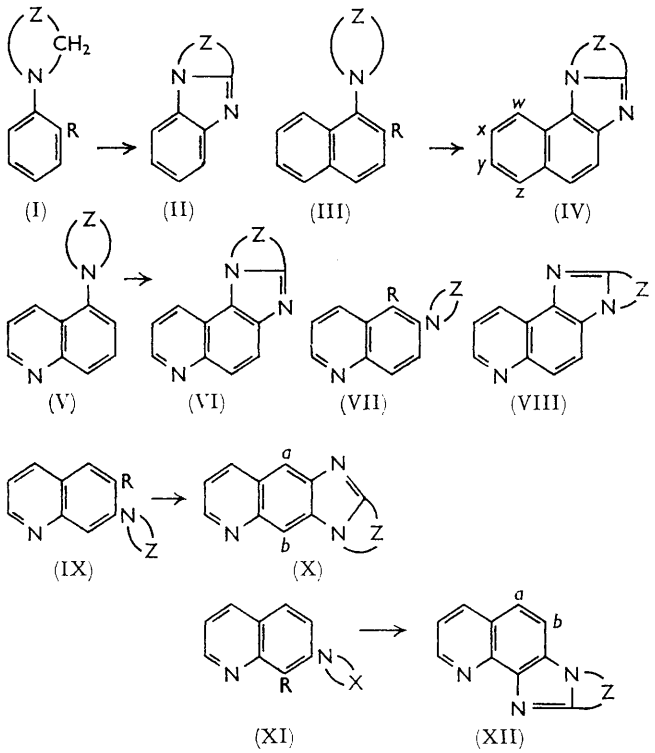
Various *N*-*o*-azidonaphthyl and -azidoquinolylheterocycles decomposed thermally in nitrobenzene and in some cases photolytically in benzene to give the title compounds. Similar cyclisations were effected by the action of triethyl phosphite on the corresponding nitro-compounds. Finally, oxidative ring-closure of some *o*-acylamido-analogues of the above naphthalenes and quinolines with performic acid is described. Yields of the various cyclisation methods reported in this and previous papers are compared.

We have recently described novel methods of cyclising t-amino-substituted *o*-nitro-benzenes, -naphthalenes, and -quinolines [*e.g.* (I)—(VI), R = NO_2] by thermolysis [2] or reduction [3] with titanous chloride to give the corresponding imidazoles often in high yield. Other routes to these new ring systems have now been studied.

Thermal decomposition of azides [*e.g.* (VII) ⟶ (VIII) R = N_3] to bring about ring-closure appeared feasible because of previous results in the benzene and pyridine series.[4,5] The required azides were prepared by treating an aqueous solution of the appropriate diazonium salt with sodium azide. Their pyrolysis was carried out in hot nitrobenzene and yields of the corresponding imidazoquinolines (VIII) were particularly high (*cf.* Table 1) except when the heterocyclic substituent was methylpiperazine (VII; Z = $[CH_2]_2$·NMe·$[CH_2]_2$); this appears to be a general experience.[4,6] The much lower yields of the imidazoquinolines (X) were mainly due to the instability of the intermediate diazonium compounds (IX; R = N_2) since we found that by using the more stable diazonium tetrafluoroborates (IX; R = $N_2^+BF_4^-$) the azide yields and with it those of the imidazoles were increased. Photolytic decomposition of azides in benzene also proved successful for preparing imidazoles {*e.g.* (I) ⟶ (II) R = N_3, Z = $[CH_2]_4$; (XIII) ⟶ (XIV) R = N_3, Z = $[CH_2]_4$}.

Attempted cyclisation of *N*-(2-azidobenzyl)hexahydroazepine (XV; R = N_3, Z = $[CH_2]_6$) by thermolysis in nitrobenzene gave only a small amount of the amino-compound (XV; R = NH_2, Z = $[CH_2]_6$).

We next studied oxidative cyclisation with performic acid a reagent which we had used successfully in the ring-closure of amines or their acyl derivatives to give benzimidazoles [*e.g.* (I; R = NH_2 or NHAc) ⟶ (II)].[7] The naphthalenes (XIII; R = NHCOPh or NHAc) gave good yields of the corresponding naphtho[1,2-*d*]imidazoles (XIV) when treated with hot performic acid except when the heterocyclic substituent was morpholino (XIII; R = ·NHCOPh, Z = $[CH_2]_2$·O·$[CH_2]$). No identifiable products were obtained which is surprising in view of the good yield of the analogous benzimidazole (II; Z = $[CH_2]_2$·O·CH_2) made under similar conditions.[7] Oxidation of the isomeric naphthalenes (III; R = NHAc, Z = $[CH_2]_{4-6}$), however, gave only low yields (*ca.* 5%, *cf.* Table 1) of the corresponding naphthoimidazoles (IV; Z = $[CH_2]_{3-5}$). This may be owing to the readiness with which β-acetamidonaphthalenes are oxidised to quinones even at low temperatures.[8] These



imidazoles are thus more efficiently prepared by thermal cyclisation [2] or by titanous chloride reduction [3] of the appropriate nitro-compound (III; R = NO_2).

In the quinoline series [(VII), (IX), and (XI) R = NHAc] the oxidative method again gave low yields (15—20%) of the imidazoquinolines [(VIII), (X), and (XII)] in contrast to the results obtained from the direct or reductive cyclisation of the nitro-compounds [2,3]

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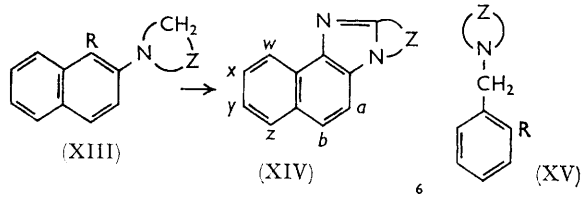
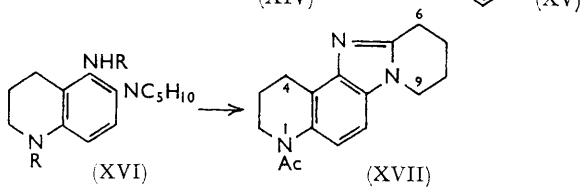
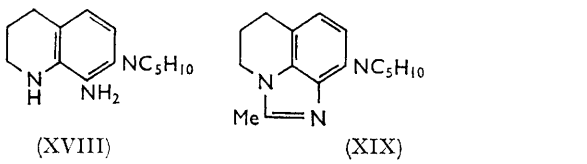
[3] H. Suschitzky and M. E. Sutton, *Tetrahedron*, 1968, **24**, 4581.
[4] K. H. Saunders, *J. Chem. Soc.*, 1955, 3275.
[5] O. Meth-Cohn, R. K. Smalley, and H. Suschitzky, *J. Chem. Soc.*, 1963, 1666.
[6] J. Schmutz and F. Kunzle, *Helv. Chim. Acta*, 1956, **39**, 1144; R. K. Smalley, *J. Chem. Soc.* (*C*), 1966, 80.
[7] O. Meth-Cohn and H. Suschitzky, *J. Chem. Soc.*, 1963, 466.
[8] S. F. D. Orr, P. Sims, and D. Manson, *J. Chem. Soc.*, 1956, 1337.

[(VII), (IX), and (XI), R = NO_2]. The reason is probably that the substituted quinolines are liable to be oxidised to water-soluble *N*-oxides or quinolinic acids under the reaction conditions,[9] which would account for the low recovery of products even after prolonged extraction. Although 1,2,3,4-tetrahydroquinoline and more particularly its acyl derivatives have been reported







to undergo ready cleavage of the reduced pyridine ring on oxidation to give anthranilic or benzoic acid derivatives [10] we were able to cyclise the tetrahydroquinoline (XVI; R = Ac) in high yield to the imidazoquinoline (XVII) with performic acid. Its structure was confirmed by its i.r. absorption at 1640 $cm.^{-1}$ (tertiary amide carbonyl) and its n.m.r. spectrum (in $CDCl_3$) [*cf.* (XVII)] which had chemical shifts at τ 2·87 (2H, aromatic), 5·93 (t, 9-CH_2), 6·15 (t, 2-CH_2), 6·90 (t, 4-CH_2), 7·79 (s, 1-MeCO), and at 7·7—8·1 (m, 3-, 7-, and 8-CH_2).

Nitrenes can be generated by deoxygenation of nitro-compounds with tervalent organophosphorus compounds such as boiling triethyl phosphite.[11] By this method we were able to bring about reductive ring-closure of some of our *ortho*-substituted nitro-compounds. Thus treatment of the nitro-derivatives [(I; Z = $[CH_2]_4$), (V; Z = $[CH_2]_2{\cdot}O{\cdot}[CH_2]_2$), (XI; Z = $[CH_2]_5$) and (XIII; Z = $[CH_2]_5$), R = NO_2 in every case] with an excess of boiling triethyl phosphite for 40 hr. gave reasonable yields (*cf.* Table 1) of the corresponding imidazoles [(II), (VI), (XII), and (XIV)]. Attempted ring-closure of the hexahydroazepine (XV; R = NO_2, Z = $[CH_2]_7$) was again unsuccessful. Apparently interposition of a methylene group between the ring and the heterocycle is geometrically unfavourable to nitrene insertion into the α-methylene group to give a six-membered ring. The preference of nitrenes to form five-membered rings is well documented.[12]

The nitronaphthalene derivatives required for the syntheses were made by the condensation of a 1-halogeno-2-nitro- or 2-halogeno-1-nitro-naphthalene with the appropriate heterocycle in boiling ethanol as described.[3] Amines were derived by reduction in the usual way.

The various nitroquinolyl heterocycles were made by methods analogous to the naphthalenes.[3] In the catalytic reduction of the 5-nitroquinoline (VII; R = NO_2, Z = $[CH_2]_5$) and the 8-nitroquinoline (XI; R = NO_2, Z = $[CH_2]_5$) not only the nitro-group but also the pyridine ring was reduced to give the corresponding amino-tetrahydroquinolines [(XVI; R = H) and (XVIII)] in quantitative yield. Acylation of the amino-compounds was performed by conventional methods. In the case of the aminotetrahydroquinoline (XVIII) acetylation with a mixture of acetic acid and acetic anhydride produced the corresponding benzimidazole (XIX) in quantitative yield.

EXPERIMENTAL

Preparation of Amino-compounds.—The nitroquinolines [(V), (VII), (IX), and (XI), R = NO_2] and nitronaphthalenes [(III) and (XIII), R = NO_2] obtained by a previously described route [3] were reduced in batches (20—30 g.) with stannous chloride as follows. The nitro-compound (1 mol.) dissolved in the minimum quantity of 6N-hydrochloric acid was added slowly to a hot solution (*ca.* 80°) of stannous chloride dihydrate (6 mol.) dissolved in 6N-hydrochloric acid (30% w/v). After complete addition the heating was continued for 1 hr.; after being cooled the reaction mixture was slowly stirred into an excess of aqueous sodium hydroxide (40%). The amine was either filtered off or extracted with chloroform; 80% yields were generally obtained. Reduction was also carried out with Raney nickel and hydrogen on solutions of the nitro-compound in benzene. This method proved more convenient in the case of the nitro-naphthalenes. Results are given in the Tables 2 and 3.

Reduction of the 5-nitro-6-piperidino- and the 8-nitro-7-piperidino-quinoline with Raney nickel and hydrogen gave, unexpectedly, a quantitative yield of *5-amino-1,2,3,4-tetrahydro-6-piperidinoquinoline*, m.p. 71° (Found: C, 73·0; H, 9·0; N, 18·5. $C_{14}H_{21}N_3$ requires C, 72·7; H, 9·2; N, 18·2%) and *8-amino-1,2,3,4-tetrahydro-7-piperidinoquinoline*, m.p. 74—75° (Found: C, 73·0; H, 9·1; N, 18·4. $C_{14}H_{21}N_3$ requires C, 72·7; H, 9·2; N, 18·2%) respectively.

Acylation of the N-(2-*Aminoquinolyl*)- *and* N-(2-*Aminonaphthyl*)-*Heterocycles.*—The amines were acetylated with a refluxing mixture of acetic anhydride and acetic acid for 15 min. Benzoylation was carried out with benzoyl chloride and pyridine for 15 min. on a steam-bath. Crystallisation was usually from aqueous ethanol or ethyl acetate. Results are given in the Tables 2 and 3.

Acetylation of the 8-aminotetrahydroquinoline (XVIII) gave a quantitative yield of the *tetrahydropyridinobenzimidazole* (XIX), m.p. 157—158° [from light petroleum (b.p. 60—80°)] (Found: C, 75·2; H, 8·3; N, 16·4.

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[11] P. J. Bunyan and J. I. G. Cadogan, *J. Chem. Soc.*, 1963, 42; J. I. G. Cadogan, M. Cameron-Wood, R. K. Mackie, and R. J. G. Searle, *ibid.*, 1965, 4831, and subsequent papers; R. J. Sundberg, *J. Amer. Chem. Soc.*, 1966, **88**, 3781.
[12] R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, 1964, **64**, 149.

Table 1

Yields of imidazoquinolines (VIII), (X), and (XII) and of naphthimidazoles (IV) and (XIV) by azide decomposition (Method A) or by cyclisation of the appropriate acetylated amines with performic acid (Method P) or of the nitro-compounds with $(EtO)_3P$ (Method E), with titanous chloride [3] (Method T) or by heating [2] (H)

		Yield (%) of method						Found (%)				Required (%)		
Quinoline	Z	A	P	E	T	H	M.p.	C	H	N	Formula	C	H	N
(VIII)	$[CH_2]_3$ §	86	18	50	Quant.	88 §	184° §							
	$[CH_2]_4$	88	20	77	Quant.		125 §							
	$[CH_2]_5$	93	25	62			152	76·2	6·4	17·4	$C_{15}H_{15}N_3$	76·0	6·4	17·7
	$CH_2{\cdot}O{\cdot}[CH_2]_2$	90					152	69·1	5·1	18·7	$C_{13}H_{11}N_3O$	69·3	4·9	18·7
	$CH_2{\cdot}NMe{\cdot}[CH_2]_2$	42					176	70·2	5·8	23·1	$C_{14}H_{14}N_4$	70·5	5·9	23·5
(X)	$[CH_2]_3$	20 (90) *	15		Quant.	0 ‡	210 §							
	$[CH_2]_4$	25			Quant.	0 ‡	250 §							
	$[CH_2]_5$	30 (75) *			Quant.	0 ‡	228 §							
(XII)	$[CH_2]_3$	46	15	—	28		238 §							
	$[CH_2]_4$	50		23	20	72 ‡	232 §							
	$[CH_2]_5$	52			35		257 §							
	$CH_2{\cdot}O{\cdot}[CH_2]_2$	60					243	69·1	5·1	18·4	$C_{13}H_{11}N_3O$	69·3	4·9	18·7
(VI)	$[CH_2]_3$	11	5	—	Quant.	80	213 §							
	$[CH_2]_4$			60	82		190 §							
	$[CH_2]_5$				Quant.		161 §							
Naphthalene														
(IV)	$[CH_2]_3$		5 †		Quant.	77	147 §							
	$[CH_2]_4$	30	5 †		74	66	128 §							
	$[CH_2]_5$		8 †		Quant.		155 §							
(XIV)	$[CH_2]_3$		72 (82) †		Quant.	30	160 §							
	$[CH_2]_4$	25	85 (92) †		72		162 §							
	$[CH_2]_5$		84	62			115	81·1	7·0	11·6	$C_{16}H_{16}N_2$	81·3	6·8	11·9
	$CH_2{\cdot}O{\cdot}[CH_2]_2$		0			32	147	75·1	5·7	12·2	$C_{14}H_{12}N_2O$	75·0	5·4	12·5

* The azides were made by the diazonium tetrafluoroborate method. † The benzoylated amine was used. ‡ Ref. 2. § Ref. 3.

Table 2

N-(2-Aminoquinolyl) heterocycles obtained by reduction of the corresponding nitro-compounds with stannous chloride or hydrogen and Raney nickel in *ca.* 80% yield and some of their *N*-acetyl derivatives

							Acetyl derivatives					
	M.p. or	Found (%)			Reqd. (%)		Found (%)				Reqd. (%)	
Quinoline	b.p./mm.	C	H	Formula	C	H	M.p.	C	H	Formula	C	H
5-Amino-6-pyrrolidino-	123°	73·0	6·9	$C_{13}H_{15}N_3$	73·2	7·1	234°	70·2	6·8	$C_{15}H_{17}N_3O$	70·6	6·7
5-Amino-6-piperidino-	166	74·3	7·1	$C_{14}H_{17}N_3$	74·0	7·5	172	71·7	7·2	$C_{16}H_{19}N_3O$	71·4	7·1
5-Amino-6-perhydroazepino-	124	74·6	7·8	$C_{15}H_{19}N_3$	74·7	7·9	138	72·1	7·6	$C_{17}H_{21}N_3O$	72·0	7·5
5-Amino-6-morpholino-	166	67·9	6·6	$C_{13}H_{15}N_3O$	68·1	6·6						
5-Amino-6-*N'*-methylpiperazino-	178	69·1	7·3	$C_{14}H_{18}N_4$	69·4	7·5						
6-Amino-7-pyrrolidino-	93	73·1	7·1	$C_{13}H_{15}N_3$	73·2	7·1	250	70·8	7·0	$C_{15}H_{17}N_3O$	70·6	6·7
6-Amino-7-piperidino-	130	74·0	7·7	$C_{14}H_{17}N_3$	74·0	7·5	146	71·0	6·9	$C_{16}H_{19}N_3O$	71·4	7·1
6-Amino-7-perhydroazepino-	165/2	74·6	8·0	$C_{15}H_{19}N_3$	74·7	7·9						
6-Amino-7-morpholino-	174	67·9	6·6	$C_{13}H_{15}N_3O$	68·1	6·6						
8-Amino-7-pyrrolidino-	77	72·9	6·8	$C_{13}H_{15}N_3$	73·2	7·1						
8-Amino-7-piperidino-	65	73·8	7·6	$C_{14}H_{17}N_3$	74·0	7·5						
8-Amino-7-morpholino-	147	68·3	6·6	$C_{13}H_{15}N_3O$	68·1	6·6						

Table 3

N-(2-Aminonaphthyl)heterocycles obtained by reduction of the corresponding nitrocompounds with stannous chloride or hydrogen and Raney nickel in *ca.* 80% yield and their *N*-benzoyl derivatives

							Benzoyl derivatives					
	M.p. or	Found (%)			Reqd. (%)		Found (%)				Reqd. (%)	
Naphthalene	b.p./mm.	C	H	Formula	C	H	M.p.	C	H	Formula	C	H
1-Amino-2-pyrrolidino [a]	66°	79·2	7·6	$C_{14}H_{16}N_2$	79·2	7·6	206°	79·4	6·2	$C_{21}H_{20}N_2O$	79·7	6·4
1-Amino-2-piperidino-	116	79·2	8·2	$C_{15}H_{18}N_2$	79·6	8·0	147	80·2	6·7	$C_{22}H_{22}N_2O$	80·0	6·7
1-Amino-2-perhydroazepino- [b]	58	79·5	8·5	$C_{16}H_{20}N_2$	79·9	8·4	154	80·2	7·1	$C_{23}H_{24}N_2O$	80·2	7·0
1-Amino-2-morpholino-	97	73·6	7·0	$C_{14}H_{16}N_2O$	73·6	7·1	203	75·6	6·2	$C_{21}H_{20}N_2O_2$	75·9	6·1
2-Amino-1-pyrrolidino-	95	78·8	7·7	$C_{14}H_{16}N_2$	79·2	7·6	103	80·1	6·6	$C_{21}H_{20}N_2O$	79·7	6·4
2-Amino-1-piperidino-	65	79·7	8·0	$C_{15}H_{18}N_2$	79·6	8·0	124	79·7	6·7	$C_{22}H_{22}N_2O$	80·0	6·7
2-Amino-1-perhydroazepino-	177/0·4	79·9	8·3	$C_{16}H_{20}N_2$	79·9	8·4	103	80·3	7·0	$C_{23}H_{24}N_2O$	80·2	7·0

[a] The *acetyl derivative* had m.p. 218° (Found: C, 75·1; H, 6·9. $C_{16}H_{18}N_2O$ requires C, 75·6; H, 7·1%). [b] The acetyl derivative had m.p. 153° (Found: C, 76·6; H, 7·8. $C_{18}H_{22}N_2O$ requires C, 76·6; H, 7·9%).

$C_{16}H_{21}N_3$ requires C, 75·3; H, 8·3; N, 16·5%) and of the 5-aminotetrahydroquinoline (XVI; R = H) the *diacetyl derivative* (XVI; R = Ac), m.p. 136° [from light petroleum (b.p. 80—100°)] (Found: C, 68·7; H, 8·0; N, 13·1. $C_{18}H_{25}N_3O_2$ requires C, 68·6; H, 8·0; N, 13·3%).

Decomposition of Azides.—The required amine (2 g.) was diazotised with sodium nitrite and hydrochloric acid or alternatively a solution of the amine in tetrafluoroboric acid was treated with sodium nitrite at 0° to −10°. The resulting diazonium chloride or tetrafluoroborate solution was slowly run into a stirred aqueous solution of sodium azide (slight excess) and sodium acetate (100 g.) at 0°. As nitrogen was liberated the azide separated out as an oil or as a solid. The mixture was extracted with chloroform and the extract was dried ($MgSO_4$) and yielded the azide after evaporation of the solvent. A solution of the azide in nitrobenzene (50 ml.) was added dropwise to nitrobenzene (150 ml.) kept at 170—180°. Decomposition of the azide was complete within 30 min. The solvent was removed under reduced pressure and the residue solidified on being washed with light petroleum (b.p. 40—60°). Purification of the crude imidazo-compound was performed by chromatography on alumina with benzene usually followed by sublimation *in vacuo*. Yields of imidazoles are set out in Table 1.

The *N*-(2-azidobenzyl)perhydroazepine yielded much tar on decomposition and a small amount of *N*-(2-aminobenzyl)perhydroazepine.[13]

Photolysis of azides was performed in benzene solution under nitrogen in a Hanovia Photochemical Reactor with a medium-pressure arc tube. *N*-(2-Azidophenyl)piperidine gave the tetrahydropyridobenzimidazole [4] (II; Z = $[CH_2]_4$) (75%), m.p. 99°, and 2-aminophenyl piperidine (I; R = NH_2, Z = $[CH_2]_4$) (5%). *N*-2-(1-Azidonaphthyl)piperidine (XIII; R = N_3, Z = $[CH_2]_5$) gave the naphthimidazole [3] (XIV; Z = $[CH_2]_4$), m.p. 128 (33%).

Oxidative Cyclisations.—A solution of the required *N*-acetylaminonaphthyl- or *N*-acetylamino-quinolyl heterocycle (2 g.) in formic acid (98%, 12 ml.) was treated with hydrogen peroxide (100 vol.; 6 ml.) and the mixture was warmed on a steam-bath until the vigorous reaction subsided (*ca.* 20 min.). Neutralization of the mixture with aqueous sodium carbonate (saturated) followed by extraction with chloroform yielded the various imidazoles in yields indicated in Table 1.

Cyclisation of the tetrahydroquinoline (XVI; R = Ac)

TABLE 4

Chemical shifts (τ values) and coupling constants of protons in the naphthimidazoles (IV) and (XIV)

Structure		Aromatics							Methylenes §					
Type	Z	H_w	H_x	H_y	H_z	H_a	H_b	J H_a/H_b (c./sec.)	α	β	γ	δ	ε	>—CH_2O—
(IV)	$[CH_2]_3$ †	2·15	(2·11		2·69)	2·48	2·21	9·0	5·90 [b]	7·12 [c]	7·50 [b]			
(IV)	$[CH_2]_4$ †	(1·98			2·79)	2·48	2·22	9·0	5·83 [b]	(8·19 [d])		7·03 [b]		
(IV)	$[CH_2]_5$ †	1·78			2·70)	2·41	2·18	9·0	5·46 [b,e]	(8·18 [e])			6·92 [b,e]	
(XIV)	$[CH_2]_3$ *	1·54	(2·21		2·57)	2·73	2·46	9·0	6·01 [b]	7·39 [c]	7·03 [b]			
(XIV)	$[CH_2]_4$ *	1·51	(2·17		2·65)	2·75	2·49	9·0	6·01 [b]	(8·02 [d])		6·96 [b]		
(XIV)	$[CH_2]_5$ *	1·59	(2·27		2·71)	2·83	2·54	9·0	6·0 [b,e]	(*ca.* 8·2 [e])			7·0 [b,e]	
(XIV)	$CH_2O{\cdot}[CH_2]_2$ †	(2·00			2·59)	2·76	2·39	9·0	(6·03 [a])					4·99 [a]

* In CS_2 solution (HA100). † In $CDCl_3$ solution (A60). § Labelled α, β, γ *etc.* from *N*.
[a] Singlet. [b] Triplet. [c] Quintet. [d] Multiplet. [e] Broad.

TABLE 5

Chemical shift (τ values) and coupling constants of protons in the imidazo[4,5-*g*]- (X), imidazo[4,5-*h*]- (XII), imidazo[5,4-*f*]- (VI), and imidazo[4,5-*f*]- (VIII) quinolines in deuteriochloroform

Structure		Aromatics *						Methylenes †					
Type	Z	Py–2H	Ph–3H	Py–4H	Bz–Ha	Bz–Hb	J H_a/H_b (c./sec.)	α	β	γ	δ	ε	>—CH_2O—
(X)	$[CH_2]_3$	1·14	2·73	1·74	2·14	1·95	*ca.* Zero	5·95 [b]	(6·8 ⟷ 7·5 [d])				
(X)	$[CH_2]_4$	1·13	2·72	1·71	2·10	1·94	*ca.* Zero	5·88 [b]	(⟵ 7·93 [d] ⟶)		6·87 [b]		
(X)	$[CH_2]_5$	1·18	2·78	1·76	2·12	1·97	*ca.* Zero	5·80	(⟵ 8·1 ⟶)			6·89	
(XII)	$[CH_2]_3$	1·06	2·72	1·89	2·55	2·65	8·0	5·98 [b]	7·40 [c]	6·99 [b]			
(XII)	$[CH_2]_4$	1·09	2·76	1·91	2·58	2·69	9·0	6·02 [b]	(⟵ 8·05 [d] ⟶)		6·82 [b]		
(XII)	$[CH_2]_5$	1·06	2·76	1·88	2·50	2·62	9·0	5·86	⟵ (*ca.* 8·2 ⟶)			6·84	
(XII)	$CH_2O{\cdot}[CH_2]_2$	1·08	2·75	1·91	2·57	2·73	9·0	(⟵ 5·98 [a] ⟶)					5·03
(VI)	$[CH_2]_3$	1·27	2·82	2·08	2·04	2·11	9·5	5·90 [b]	(6·9 ⟶ 7·6 [d])				
(VI)	$[CH_2]_4$	1·33	2·90	1·97	2·08	2·13	8·5	5·88 [b]	(7·8 ⟶ 8·3 [d])		7·0 [b]		
(VI)	$[CH_2]_5$	1·27	2·76	1·59	2·08	2·15	9·0	5·54 [b]	(8·0 ⟷ 8·4)			6·94	
(VI)	$CH_2O{\cdot}[CH_2]_2$	1·22	2·74	1·71	2·06	2·11	9·5	5·55 [b]	5·84 [b]				5·01 [a]
(VIII)	$[CH_2]_3$	1·25	2·65	1·19	2·56	2·25	9·0	6·08 [b]	7·46 [c]	7·04 [b]			
(VIII)	$[CH_2]_4$	1·17	2·52	1·05	2·40	2·10	9·0	5·88 [b]	(⟵ 7·93 [d] ⟶)		6·85 [b]		
(VIII)	$[CH_2]_5$	1·19	2·58	1·12	2·49	2·15	9·0	5·94	(*ca.* 8·2 ⟶)			6·92	
(VIII)	$CH_2O{\cdot}[CH_2]_2$	1·17	2·48	1·05	2·32	2·02	9·0	(⟵ 5·75 [a] ⟶)					4·87 [a]
(VIII)	$CH_2NMe{\cdot}CH_2$ §	1·17	2·51	1·05	2·40	2·08	9·0	5·86 [b]	7·10 [b]				

* J 2/3 = 4·0—4·5 c./sec.; J 2/4 = 1·5—2·0 c./sec.; J 3/4 = 8·0—8·5 c./sec. † Labelled α, β, γ *etc.* from *N*. § NMe at τ 7·49. >—CH_2N at τ 6·10.
[a] Singlet. [b] Triplet. [c] Quintet. [d] Multiplet.

[13] O. Meth-Cohn, H. Suschitzky, and M. E. Sutton, *J. Chem. Soc.* (*C*), 1968, 1722.

(1 g.) by the above method yielded 1-*acetyl*-1,2,3,4,6,7,8,9-*octahydropyrido*[2,1-*b*]*imidazo*[4,5-*f*]*quinoline* (XVII) (0·75 g., 88%), m.p. 152—153° (vacuum sublimation) (Found: C, 71·4; H, 7·3; N, 15·5. $C_{16}H_{19}N_3O$ requires C, 71·4; H, 7·1; N, 15·6%).

Cyclisation with Triethyl Phosphite.—The required nitro-compound (2 g.) was heated in triethyl phosphite (80 ml.) at 140° under nitrogen for 40 hr. After removal of the solvent under reduced pressure the residue was chromatographed (alumina and chloroform) and the resulting product was further purified by vacuum sublimation. Results are given in Table 1.

Details of n.m.r. spectra of the various imidazoles measured on a Varian HA 60 instrument are noted in Tables 4 and 5.

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