Heterocyclic Syntheses. Part XXIII.[1] Synthesis and Reactions of 2,3-Dihydrobenzimidazoles

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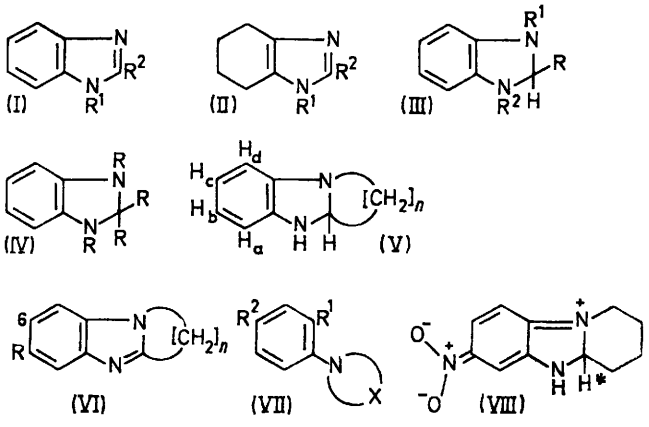
1,2-Dialkyl-2,3-dihydrobenzimidazoles have been produced by reduction of the aromatic parent compounds with lithium aluminium hydride and also directly by cyclization of the appropriate nitrenes generated from azides or from nitro-compounds by deoxygenation with trialkyl phosphites. The factors influencing the stability of the title compounds have been studied.

THE imidazole ring in benzimidazole (I; $R^1 = R^2 = H$) and its *N*-alkyl derivatives (I; R = alkyl) shows considerable stability towards reduction since hydrogenation over platinum catalysts affects only the benzene ring to produce the tetrahydrobenzimidazoles (II); analogously the naphthimidazoles give the corresponding tetrahydronaphthimidazoles.[2] With platinum oxide in acetic acid 1,3-diacetyl-2,3-dihydrobenzimidazole [3] (III; $R^1 = R^{2'} = Ac$) can be made from benzimidazole (I; $R^1 = R^2 = H$) which demonstrates that hydrogenation of the



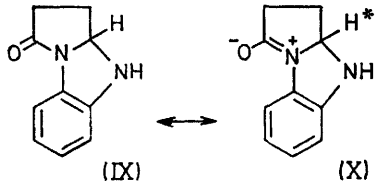
imidazole ring can occur but in the absence of a trapping agent the dihydro-compound reverts to the aromatic structure. Bohlmann [4] claimed to have prepared the 2,3-dihydrobenzimidazole (III; $R^1 = R^2 = H$) by reduction of benzimidazole (I; $R^1 = R^2 = H$) with lithium aluminium hydride. However, attempts by us to repeat this reaction failed and it is felt that the evidence for structure (III) which was based on the colour and analysis of its picrate is unsatisfactory. In fact it has been shown [5] that even fairly stable dihydrobenzimidazoles are dehydrogenated by picric acid.

The resistance of 2,3-dihydrobenzimidazoles to aromatization is expected to increase with progressive substitution of its hydrogens with, for instance, alkyl or acyl groups. Thus, the dihydro-compound (III; $R^1 = R^2 = H$) can be expected to be much less stable than its tetra-alkyl derivative (IV; R = alkyl) since (III) can readily lose a molecule of hydrogen while in the aromatization of (IV) carbon–carbon cleavage is involved. It was reasonable to assume that the di-alkylated dihydrobenzimidazoles (V) would be less unstable than the elusive parent structure (III; $R^1 = R^2 = H$). This was indeed confirmed because reduction of the imidazole [6] (VI; R = H, $n = 4$) with a large excess of lithium aluminium hydride in boiling ether for 8 days gave the dihydro-compound (V; $n = 4$) in quantitative yield. Its structure was deduced from its n.m.r. spectrum (in $CDCl_3$) which showed the aromatic protons at τ 3·4 (H_{b-d}) and at τ 3·67 (H_a) typical of an *o*-phenylenediamine. A broad band at τ 5·5 is assignable to the methine proton (N–CH–N) which at 100 MHz was resolved into a doublet (*J* 9 Hz) of doublets (*J* 3 Hz) showing coupling to each proton of the adjacent methylene group. A broad band at τ 6·3 (NH) was removed by deuteriation to reveal a broad 1H doublet (*J* 12 Hz) at τ 6·4 (N·CH_2) separated from its geminal partner at τ 7·3 because it is held in the plane of the benzene ring and is thus deshielded. The compound when exposed to air at room temperature reverted within 16 hr. to the parent compound (VI; R = H, $n = 4$) and even faster when kept at 100°. The rate of aromatization was easily followed from the disappearance of the NH-band at 3230 cm.$^{-1}$ in the i.r. spectrum. Even under nitrogen in the dark a 10% conversion occurred within 24 hr. Aromatization was immediate with oxidizing agents (MnO_2, H_2O_2) and also in carbon disulphide. The dihydrobenzimidazole (V; $n = 3$) was similarly obtained but its n.m.r. spectrum taken immediately after work up showed the product to be a mixture of the dihydro-compound (V; $n = 3$) (88%) and starting material. The reduction product yielded an *N*-acetyl derivative identical with an authentic specimen.[7] It is noteworthy that debenzylation of the *N*-benzyldihydro-compound (V; $n = 3$, NH=N·CH_2Ph) over palladium–charcoal with hydrogen yields only the aromatic compound (VI; R = H, $n = 3$) and not the expected 2,3-dihydrobenzimidazole (V; $n = 3$).[8] We have also reported [9] that the 1-alkyl-2-cyanobenzimidazole (I; $R^1 = [CH_2]_5Cl$, $R^2 = CN$)

[1] Part XXII, H. Suschitzky and M. E. Sutton, *J. Chem. Soc.* (*C*), 1968, 3058.
[2] H. Schubert and H. Fritsche, *J. prakt. Chem.*, 1958, **7**, 207; M. Hartmann and L. Pannizon, *Helv. Chim. Acta*, 1938, **21**, 1692.
[3] H. Bauer, *J. Org. Chem.*, 1961, **26**, 1649.
[4] F. Bohlmann, *Chem. Ber.*, 1952, **85**, 390.
[5] J. W. Clarke-Lewis, J. A. Edgar, J. S. Shannon, and M. J. Thompson, *Austral. J. Chem.*, 1964, **17**, 877.
[6] O. Meth-Cohn and H. Suschitzky, *J. Chem. Soc.*, 1963, 4666.
[7] O. Meth-Cohn, R. K. Smalley, and H. Suschitzky, *J. Chem. Soc.*, 1963, 1666.
[8] R. K. Grantham and O. Meth-Cohn, *J. Chem. Soc.* (*C*), 1969, 1444.
[9] R. Garner and H. Suschitzky, *J. Chem. Soc.* (*C*), 1967, 2536.

suffers fission of the imidazole ring when treated with lithium aluminium hydride to give *o*-phenylenediamine.

Next we investigated the possibility of making the dihydrobenzimidazoles (V) by cyclization of the appropriate *N*-2-azidophenyl derivative (VII; $R^1 = N_3$). Decomposition of these azides usually in hot nitrobenzene produces, however, the corresponding benzimidazoles (VI).[7] Saunders[10] suggested that dihydrobenzimidazoles were intermediates in this reaction but our previous attempts at isolating them failed. Trapping the unstable dihydro-compounds as an *N*-acyl derivative[7] (V; NH = NAc) was, however, successful. We considered that the use of a non-oxidizing solvent instead of nitrobenzene would prevent oxidation of the dihydro-intermediate. It was, in fact, found that decomposition of the *N*-2-azidophenylpiperidine (VII; $R^1 = N_3$, $R^2 =$ H, X = $[CH_2]_5$) in hot diglyme (diethyleneglycol dimethyl ether) gave the dihydrobenzimidazole (V; $n = 4$) identical with the compound obtained by lithium aluminium hydride reduction (*cf.* above). A corresponding result was obtained when the hetero-paraffinic component was morpholine (VII; $R^1 = N_3$, $R^2 =$ H, X = $[CH_2]_2$·O·$[CH_2]_2$). A 5-nitro-group in the azide ($R^1 = N_3$, $R^2 = NO_2$, X = $[CH_2]_5$) produced the dihydrobenzimidazole (XI; R = NO_2, X = $[CH_2]_3$) which was stable both in air and also when heated for 6 hr. at 80°. We attribute this stability to the appreciable contribution of the canonical structure (VIII) from which the starred hydrogen will not be easily lost as a hydride ion to form a molecule of hydrogen by combining with the NH-proton, a process essential to aromatization. An analogous case is that of the very stable dihydrobenzimidazole[8] (IX) in which hydride mobility is considerably

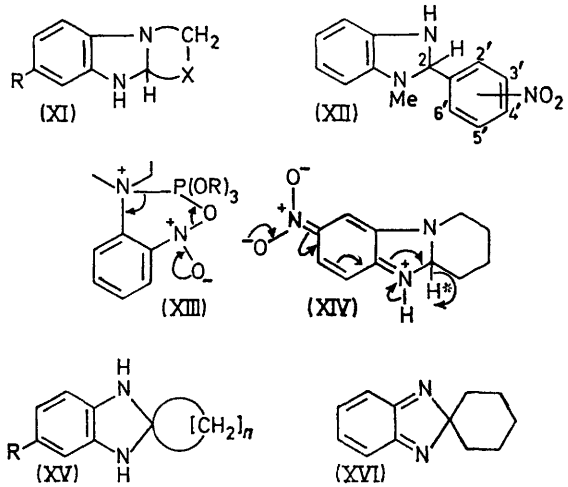


(IX) (X)

impaired in the contributing structure (X; H*). Similarly, the graded stability of the three nitrophenyl dihydrobenzimidazoles (XII; *o*-, *m*-, *p*-NO_2) is, according to Russian workers,[11] related to the electron availability at the 2-carbon atom in the imidazole ring. Hence resistance to aromatization is observed to be in the order 2′-NO_2 > 3′-NO_2 > 4′-NO_2.

Azides with other t-amino-substituents (VII; $R^1 =$ N_3, $R^2 = NO_2$, X = $[CH_2]_6$, $[CH_2]_2$·O·$[CH_2]_2$, and $[CH_2]_2$·NMe·$[CH_2]_2$) gave the corresponding equally stable dihydro-imidazoles (XI; R = NO_2, X = $[CH_2]_4$, CH_2·O·CH_2, and CH_2·NMe·CH_2), respectively. The dihydro-compound derived from the pyrrolidinoazide (VII; $R^1 = N_3$, $R^2 = NO_2$, X = $[CH_2]_4$) was a viscous, red uncrystallizable oil which was readily oxidized to the nitrobenzimidazole (VI; R = NO_2, $n = [CH_2]_3$); the i.r. spectrum of the former compound was consistent with the assigned structure.

Photolysis of the *N*-2-azidophenylpiperidine (VII, $R^1 = N_3$, $R^2 = NO_2$, X = $[CH_2]_5$) in benzene solution gave a quantitative yield of the dihydrobenzimidazole (XI; R = NO_2, X = $[CH_2]_3$).



(XI) (XII) (XIII) (XIV) (XV) (XVI)

We found that other negative groups in the 5-position of the azide (VII; $R^1 = N_3$, $R^2 = CF_3$, CN, or CO_2H) did not give stable dihydro-derivatives under the above reaction conditions (diglyme) as, in each case, the corresponding benzimidazole (VI; $R^1 = R^2$ in VII) was obtained. Also *N*-2-azido-5-nitrophenylpiperidine, an isomer of (VII; $R^1 = N_3$, $R^2 = NO_2$) but with the nitro-group *para* to the azide group, gave only the 2,3,4,5-tetrahydro-6-nitrobenzimidazole (VI; R = H, NO_2 at C-6). The dihydro-compound is unstable probably because its quinonoid contributor (XIV), unlike its analogue (VIII), is readily dehydrogened [*cf.* (XIV) at H*].

The stable dihydrobenzimidazoles (XI; R = NO_2) were also produced by deoxygenation of the dinitro-compounds (VII; $R^1 = R^2 = NO_2$) with boiling trimethyl phosphite which, it is claimed, generates nitrenes from nitro-compounds.[12] Such intermediates are very likely with our compounds, since the reagent gave the same products as the insertion reaction from azide pyrolysis. Triethyl phosphite was a less satisfactory reagent for the deoxygenation, probably owing to its higher b.p., since it yielded a complex mixture of the dihydro-compound, its parent benzimidazole, some amine (VII; R = NH_2, $R^2 = NO_2$), and tar. It is interesting that the trialkyl phosphite preferentially attacks the nitro-group *ortho* to the amino-substituent [*cf.* (VII; $R^1 = R^2 = NO_2$)]. This selective behaviour may be due to interaction between the reagent and the t-amino-group which may favour reduction of the *o*-nitro-group by geometry of the resulting intermediate [*e.g.* (XIII)]. Treatment of the nitro-compounds (VII; $R^1 = NO_2$, $R^2 = CF_3$, CN, or CO_2H) with trimethyl or triethyl phosphite gave only the corresponding benzimidazoles (VI;

[10] K. H. Saunders, *J. Chem. Soc.*, 1955, 3275.
[11] E. V. EL'tsov and Kh. L. Muravich-Aleksander, *J. Org. Chem. U.S.S.R.*, 1965, **1**, 1321.
[12] J. I. G. Cadogan, *Quart. Rev.*, 1968, **2**, 222.

$R^1 = R^2$ in VII) except in the case of the carboxylic acid (VII; $R^1 = NO_2$, $R^2 = CO_2H$) which yielded with triethyl phosphite the benzimidazole (VI; $R = CO_2Et$) due to traces of ethanol shown to be present in the reagent.

All dihydrobenzimidazoles of type (XI) were readily dehydrogenated by oxidizing agents such as hydrogen peroxide, manganese dioxide, nitrobenzene, lead tetra-acetate, tetrachloro-*p*-benzoquinone, dimethyl azodicarboxylate, and *N*-chloro-benzotriazole [13] as well as on an alumina or silica column to the corresponding benzimidazoles (VI) usually in quantitative yield. Since the dihydro-nitro-compounds (XI; $R = NO_2$) form scarlet solutions in a variety of solvents, a colour which is discharged upon dehydrogenation, the progress of the reaction can be followed visually or spectroscopically from the change of absorbance at the fixed wavelength of 409 mμ.

The reaction of aromatic *o*-diamines with cyclic ketones has also shown to be a route to dihydrobenzimidazoles.[14,15] For instance, when *o*-phenylenediamine and cyclohexanone were made to react in benzene the yellow spiro-compound (XV; $R = H$, $n = 5$) was reported to be formed but no physical evidence in support of this structure was given. We were able to confirm the preparation and also the structure of the product from spectral data. The compound (XV; $R = H$, $n = 5$) showed three resonances as singlets in the 60 MHz n.m.r. ($CDCl_3$) at τ 3·67 (4 aromatic protons), τ 4·44 (2 NH protons, lost on deuteriation) and at τ 8·45 (10 methylene protons).

The i.r. spectrum of (XV; $R = H$, $n = 5$) in Nujol showed a sharp band at 3340 $cm.^{-1}$ and a broader band at 3247 $cm.^{-1}$, the two having the typical appearance of a N–H vibration. This is confirmed by a grating spectrum in chloroform when only one band is found at 3384 $cm.^{-1}$. If a NH_2 group had been present, twin peaks would have been found in the solution spectrum. The compound (XV, $R = H$, $n = 5$) appears to break down in organic solvents since its i.r. spectrum in chloroform or carbon tetrachloride develops a band in the 1700 $cm.^{-1}$ region which behaves as a C=O vibration.

The u.v. spectrum of compound (XV; $R = H$, $n = 5$) was measured in 95% ethanol [λ 214 (ε 29,100), 258 (3720), 309 (4220) mμ] and 0·1N-hydrochloric acid [λ 229 (ε 6350), 283 (1485) mμ]. The peaks shift to lower wavelength in acid, typical of amines attached to aromatic rings. The spectrum in hydrochloric acid bears a fair similarity to the spectrum of *o*-phenylenediamine in aqueous solution.

Attempts to prepare various homologues of the spiro-compound (XV; $R = H$, $n = 5$) from cyclopentanone and cyclic ketones larger than cyclohexanone failed even with dehydrating agents (toluene-*p*-sulphonic acid or dicyclohexylcarbodi-imide) and prolonged reaction times when hydrocarbon solvents were used. In each case the starting materials were quantitatively recovered. 2,3-Dihydro-5-nitrobenzimidazole-2-spirocyclohexane (XV; $R = NO_2$, $n = 5$) was obtained from 4-nitro-*o*-phenylenediamine and cyclohexanone in toluene.

However, it was found that *o*-phenylenediamine could be made to react with cycloheptanone when sulpholane was used as solvent. Similarly, 4-nitro-*o*-phenylenediamine reacts with cycloheptanone in sulpholane to give 2,3-dihydro-5-nitrobenzimidazole-2-spirocycloheptane. The products were unstable and rapidly decomposed to intractable tars on contract with air. We also found that the yield of the spiro-compound (XV; $R = H$, $n = 5$) and rate of reaction were increased when *o*-phenylenediamine and cyclohexanone were made to react in sulpholane.

Acylation of compound (XV; $R = H$, $n = 5$) with *p*-nitrobenzoyl chloride in benzene or pyridine gave *NN'*-bis-*p*-nitrobenzoyl-*o*-phenylenediamine. With hot acetic anhydride *NN'*-diacetyl-*o*-phenylenediamine was obtained. The dihydro-compound was also broken down by warm mineral acid into *o*-phenylenediamine and cyclohexanone and by dry pyrolysis to *o*-phenylenediamine and an intractable tar.

Oxidation of compound (XV; $R = H$, $n = 5$) with manganese dioxide [16] gave the spiro-compound (XVI) which yielded a tetrabromo-compound with bromine in carbon tetrachloride and an adduct with dimethylacetylene dicarboxylate. When compound (XV; $R = H$, $n = 5$) was stirred in a solution of sodium methoxide, the same spiro-compound resulted.

EXPERIMENTAL

Preparation of t-Amino-nitrobenzenes (VII; $R^1 = NO_2$).—These were obtained by condensation of the appropriate 2-chloronitro-compound with the required secondary amines as described; [17] their m.p.'s were close to those reported in the literature.[18]

Preparation of t-Amino-anilines (VII; $R = NH_2$).—The 2,4-dinitrophenyl heterocycles (VII; $R^1 = R^2 = NO_2$) were reduced with sodium polysulphide,[10] and the other nitro-compounds either with iron and ammonium chloride or catalytically as described.[7] *3-Amino-4-piperidinobenzoic acid* which was obtained from its nitro-compound by treatment with an alkaline solution of ferrous sulphate [19] had m.p. 184° (Found: C, 65·5; H, 7·5. $C_{12}H_{16}N_2O_2$ requires C, 65·3; H, 7·3%). The *3-cyano-aniline* (VII; $R^1 = NH_2$, $R^2 = CN$, $X = [CH_2]_5$) had m.p. 56° (Found: C, 72·0; H,

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[14] H. A. Staab and F. Vögtle, *Chem. Ber.*, 1965, **98**, 2681.
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[16] O. Meth-Cohn and H. Suschitzky, *Chem. and Ind.*, 1969, 443.
[17] D. P. Ainsworth and H. Suschitzky, *J. Chem. Soc.*, 1966, 111.
[18] E. Lellmann and W. Geller, *Chem. Ber.*, 1888, **21**, 2281; M. D. Nair and R. Adams, *J. Amer. Chem. Soc.*, 1961, **83**, 3518; H. Markwald and E. Chain, G.P. 119,785/1901; S. I. Burnistrov and S. M. Antonento, *Ukrain. khim. Zhur.*, 1961, **27**, 73; N. Tuttle, *J. Amer. Chem. Soc.*, 1923, **45**, 1906; L. P. Albro, R. Baltzyl and A. P. Phillips, *J. Org. Chem.*, 1949, **14**, 771; R. H. Harradence and F. Lions, *J. Proc. Roy. Soc. New South Wales*, 1937, **70**, 406; B. G. Le Fèvre and E. B. Turner, *J. Chem. Soc.*, 1927, 1113; J. F. Bunnett, T. Kato, and N. S. Nudelman, *J. Org. Chem.*, 1969, **34**, 785.
[19] W. A. Jacobs and M. Heidelberger, *J. Amer. Chem. Soc.*, 1917, **39**, 1435.

7·6. $C_{12}H_{15}N_3$ requires C, 71·6; H, 7·5%) and the *3-trifluoromethylaniline hydrochloride* (VII; $R^1 = NH_2$, $R^1 = CF_3$, X = $[CH_2]_5$) had m.p. 193° (Found: C, 51·6; H, 6·1; $C_{12}H_{15}F_3N_2$,HCl requires C, 51·4; H, 5·75%).

Preparation of Azides.—Conversion of the above anilines into azides was carried out by diazotization followed by addition of sodium azide as described.[7] The products were checked by i.r. spectroscopy (a band at *ca.* 2100 cm.$^{-1}$ due to N_3) and used without purification.

Decomposition of Azides.—The azide (2 g.) dissolved in diglyme (10 ml.) was added slowly to boiling diglyme (50 ml.) and the mixture was maintained under reflux for a further 10 min. The solvent was removed under reduced pressure and trituration of the residue with light petroleum gave the dihydrobenzimidazoles in the case of the nitro-azides (VII; $R^1 = N_3$, $R^2 = NO_2$) which were recrystallized from ethyl acetate–light petroleum (see Table); other azides

1 2-Dihydrobenzimidazoles (XI) formed on pyrolysis of azides in diglyme in *ca.* 75% yield

Imidazole (XI)			Found (%)			Reqd. (%)	
R	X	M.p.	C	H	Formula	C	H
(1) H	$[CH_2]_3$	119°			*a*		
(2) H	$[CH_2]_2$				*a*		
(3) H	$(CH_2{\cdot}O{\cdot}CH_2)$	125			*a*		
(4) NO_2	$[CH_2]_2$	*b*					
(5) NO_2	$[CH_2]_3$	129	60·5	5·8	$C_{11}H_{13}N_3O_2$	60·3	6·0
(6) NO_2	$[CH_2]_4$	119	62·2	5·7	$C_{12}H_{15}N_3O_2$	61·8	6·5
(7) NO_2	$(CH_2{\cdot}O{\cdot}CH_2)$	155	53·9	5·3	$C_{10}H_{11}N_3O_3$	54·3	5·0
(8) NO_2	$(CH_2{\cdot}NMe{\cdot}CH_2)$	175	56·1	6·1	$C_{11}H_{14}N_4O_2$	56·4	6·0

[a] Too unstable for analysis *cf.* text. [b] Red, unstable oil.

gave the corresponding benzimidazoles (VI). The *trifluoromethyl-derivative* (VI; $R = CF_3$, $n = 4$)had m.p. 134—135° (Found: C, 59·7; H, 5·1. $C_{12}H_{11}F_3N_2$ requires C, 60·0; H, 4·6%); the *cyano-compound* (VI; R = CN, $n = 4$) had m.p. 175° (Found: C, 73·1; H, 6·0. $C_{12}H_{11}N_3$ requires C, 73·1; H, 5·6%) and the *carboxylic acid* (VI; $R = CO_2H$, $n = 4$) had m.p. 298° (from diglyme) and was identical with an authentic sample.[20]

Photolysis of *N*-2-azido-4-nitrophenylpiperidine (0·5 g.) in benzene (800 ml.) for 18 hr. with a medium-pressure mercury lamp (Hanovia-125 w) gave the 2,3-dihydro-5-nitrobenzimidazole (0·3 g.) (XI; $R = NO_2$; X = $[CH_2]_3$), m.p. 129° identical with an authentic sample.

Reductive Cyclizations.—The nitro-compound (VII; R = NO_2) (2·0 g.) was boiled in trimethyl phosphite (80 ml.) under nitrogen for 8—10 hr. The solvent was evaporated off and the residue was shaken up with a mixture of chloroform and water. Evaporation of the chloroform layer gave the dihydrobenzimidazole. The 2,3-dihydrobenzimidazoles [Table, nos. (4)—(8)] were obtained in 50—60% yield and other benzimidazoles (VI; $R = CF_3$ or CN, $n = 4$) in *ca.* 65% yield.

With triethyl phosphite following the same procedure mixtures of the dihydro- (XI; $R = NO_2$) and parent benzimidazole (VI; $R = NO_2$) were obtained. From the nitrocarboxylic acid (VII; $R^1 = NO_2$, $R^2 = CO_2H$) the *ethyl ester* (VI; $R = CO_2Et$, $n = 4$) and some tar were obtained. The former had m.p. 125° (Found: C, 68·7; H, 6·6. $C_{14}H_{16}N_2O_2$ requires C, 68·8; H, 6·6%).

Reduction of Benzimidazoles with Lithium Aluminium Hydride.—To a suspension of lithium aluminium hydride (0·5 g.) in boiling ether (300 ml.) was added to the tetrahydropyrido[1,2-*a*]benzimidazole (VI; R = H, $n = 4$); the apparatus was then flushed through with nitrogen. The reaction mixture was maintained under reflux for 8 days and then water was added dropwise to hydrolyse the reducing agent. Air was excluded by passing nitrogen through the reaction mixture continuously. Excess of water was taken up by magnesium sulphate and solids were filtered off. Removal of the ether from the filtrate *in vacuo* gave hexahydropyrido[1,2-*a*]benzimidazole (100%) as a white solid the structure of which was established by n.m.r. spectroscopy (*cf.* text). When the reaction was carried out in the cold no reaction occurred.

When the reduced compound was dissolved in carbon disulphide the solution turned yellow and the parent benzimidazole (VI; R = H, $n = 4$) separated. When the mixture was heated to 100° dehydrogenation was complete after 2 hr. as judged from the disappearance of bands at 3230 and 734 cm.$^{-1}$ and appearance of bands at 758, 1010, 1160, 1330, and 1440 cm.$^{-1}$ in the i.r. spectrum. At room temperature exposure to air caused dehydrogenation within 16 hr.

The pyrrolo[1,2-*a*]benzimidazole (VI; R = H, $n = 3$) when treated with lithium aluminium hydride as above gave the reduced benzimidazole (V; $n = 3$) (88%) and starting material. It suffered dehydrogenation under the same conditions as described above and on treatment with acetic anhydride and acetic acid gave 4-acetyl-2,3,3*a*,4-tetrahydropyrrolo[1,2-*a*]benzimidazole, m.p. 86° (lit.,[7] m.p. 85—86°).

Reduction of benzimidazole (2·0 g.) with lithium aluminium hydride under similar conditions for 1, 2, and 8 days gave only starting material.

Dehydrogenation of the Dihydrobenzimidazoles.—Dehydrogenation was effected by the oxidizing agents listed in the Discussion to give the corresponding benzimidazoles which were identical with authentic samples (i.r. and mixed m.p.).

Preparation of 2,3-Dihydrobenzimidazole-2-spirocycloalkanes.—The compound (XV; R = H, $n = 5$) was prepared as reported [14] and gave yellow needles, m.p. 138° (from ethanol) [lit., m.p. 130° (from chloroform)]. When a mixture of *o*-phenylenediamine, cyclohexanone, and sulpholan was heated on a water-bath for 1·5 hr. and then poured into water, 2,3-dihydrobenzimidazole-2-spirocyclohexane (XV; R = H, $n = 5$) was obtained in 96% yield. We also prepared the compound (XV; R = H, $n = 5$) from *o*-phenylenediamine and the sodium bisulphite compound of cyclohexanone in refluxing ethanol.[21]

2,3-Dihydro-5-nitrobenzimidazole-2-spirocyclohexane (XV; $R = NO_2$, $n = 5$) was obtained in 75% yield from 4-nitro-*o*-phenylenediamine and cyclohexanone in refluxing toluene. It formed dark-red needles, m.p. 163—164° when recrystallized from ethyl acetate–light petroleum (b.p. 60—80°) (Found: C, 61·7; H, 6·4; N, 17·8%. $C_{12}H_{15}N_3O_2$ requires C, 61·8; H, 6·5; N, 18·0%); ν (Nujol) 3380 and 3160 cm.$^{-1}$; τ $(CD_3)_2SO$ 2·47 (6-H, *ortho*-split, *J* 8·5 Hz, *meta*-split, *J* 2 Hz), 3·08 (4-H, *meta*-split, *J* 2 Hz), 3·77 (7-H, *ortho*-split, *J* 9 Hz). The imine protons (NH) appeared as two singlets at τ 2·25 and 3·43 which were lost on deuteriation; the methylene protons appeared as a broad singlet at τ 8·38.

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An equimolar mixture of *o*-phenylenediamine and cycloheptanone in sulpholan was heated on a water-bath for 3 hr. and then poured into water. Evaporation of an ether extract gave an oil from which 2,3-dihydrobenzimidazole-2-spirocycloheptane (XV; R = H, $n = 6$) was isolated (23%) by chromatography with benzene on alumina. Its n.m.r. spectrum in CCl_4 showed shifts at τ 3·22 (ArH), 6·29 (NH, lost on deuteriation), and τ 8·52 (paraffinic H). Its i.r. spectrum (neat film) had an absorption at 3450 $cm.^{-1}$ due to NH. The product readily decomposed in air into an intractable tar. In a similar manner 2,3-dihydro-5-nitrobenzimidazole-2-spirocycloheptane (XV; R = NO_2, $n = 6$) was prepared from 4-nitro-*o*-phenylenediamine and cycloheptanone in sulpholane. The product was an unstable red oil; its n.m.r. spectrum in $CDCl_3$ showed shifts at τ 2·38 (6-H), 2·83 (4-H), 3·70 (7-H), 4·08 and 5·02 (NH lost on deuteriation), and 8·1 (methylene protons).

Attempted Acylation of (XV; R = H, n = 5).—The title compound when treated with *p*-nitrobenzoyl chloride or acetic anhydride suffered ring-opening as described.

Action of Heat on (XV; R = H, n = 5).—The dihydro-compound (100 mg.) when heated at 120°/80 mm. in a vacuum sublimation apparatus gave white needles (20 mg.) which were shown by i.r. and mixed m.p. to be *o*-phenylenediamine. The residue was an intractable tar.

Oxidation of (XV; R = H, $n = 5$).—A suspension of the compound (1 g.) and activated manganese dioxide (5 g.) in benzene (50 ml.) was stirred at room temperature for 70 hr. Evaporation of the solution after removal of the manganese dioxide gave the spiro-compound (XVI) as prisms, m.p. 65—65·5° [from light petroleum (b.p. 60—80°)] (Found: C, 77·5; H, 7·5; N, 15·0. $C_{12}H_{14}N_2$ requires C, 77·4; H, 7·6; N, 15·0%); M^+ 186.

When a solution of (XV; R = H, $n = 5$) in N-methanolic sodium methoxide was stirred for 2 days at room temperature the same spiro-compound (XVI) was formed.

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