Syntheses in the Pyrido- and Piperido-(1′ : 2′-1 : 2)*benziminazole Series.*

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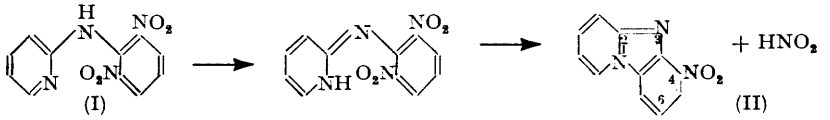
2-Chloro-1 : 3-dinitrobenzene condenses with 2-aminopyridine to form 2-(2 : 6-dinitroanilino)pyridine which at once begins to lose nitrous acid, thus producing 4-nitropyrido(1′ : 2′-1 : 2)benziminazole. 1-*o*-Azidophenylpiperidine is decomposed by heat to yield nitrogen and 2 : 3-dihydropiperido-(1′ : 2′-1 : 2)benziminazole, an unstable reducing agent, which at once gives up hydrogen, preferably to the reaction medium, to yield piperidobenziminazole identical with the reduction product of pyrido(1′ : 2′-1 : 2)-benziminazole. 1-*o*-Azidophenylpiperidine having substituents in the benzene ring, and analogous azides derived from hexahydroazepine, morpholine, and 1-ethoxycarbonylpiperazine undergo the above ring-closure, as does 4-azido-2-nitro-1 : 5-dipiperidinobenzene to form 5-nitro-6-piperidinopiperido-(1′ : 2′-1 : 2)benziminazole, which after reduction again undergoes the same ring-closure reaction to produce a pentacyclic base.

IN the preparation of 2-(2 : 6-dinitroanilino)pyridine (I) from 2-chloro-1 : 3-dinitrobenzene and 2-aminopyridine it was observed that after removal of the desired product from the crude reaction mass with boiling benzene there remained an almost equal weight of a yellow substance, m. p. *ca.* 265—270°. The latter proved to be a nitro-compound, reduced by iron–acetic acid to a diazotisable amine which coupled with Brenthol OP (2-hydroxy-3-naphtho-*o*-phenetidide) to a violet dye; and when it was observed that nitrous acid was evolved from the reaction solution it was realised that the substance must be 4-nitropyrido(1′ : 2′-1 : 2)benziminazole (II) produced from the tautomeric form of 2-(2 : 6-dinitroanilino)pyridine by Morgan and Stewart's reaction (*J.*, 1938, 1292) :

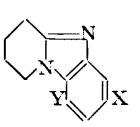


The above reaction was confirmed when it was found that 2-(2 : 6-dinitroanilino)-pyridine yields 4-nitropyrido(1′ : 2′-1 : 2)benziminazole and nitrous acid in boiling glycol monoethyl ether. This unequivocal synthesis shows that Stewart and Morgan's nitropyridobenziminazole is the 6-isomer (see below).

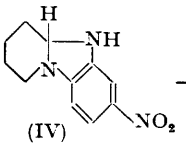
Reduction of 4-nitropyrido(1′ : 2′-1 : 2)benziminazole with hydrogen and platinum oxide in ethanol, as described by Morgan and Stewart (*loc. cit.*) for the 6-nitro-isomer, afforded a mixture of two amines, both diazotisable, one giving a blue and the other a bluish-red colour with Brenthol OP. It seemed likely that in the latter amine the pyridine ring was reduced. This result evoked the question as to whether it would prove possible to prepare the piperidobenziminazole by heating 1-*o*-azidophenylpiperidine, a reaction somewhat analogous to that by which Smith and Brown (*J. Amer. Chem. Soc.*, 1951, **73**, 2435) made carbazole from *o*-azidodiphenyl, thus providing an easier route to this series than *via* the very limited Morgan and Stewart reaction. Indeed, a compound provisionally assigned the constitution (III) was isolated by Spiegel and Kaufmann (*Ber.*, 1908, **41**, 682) among the substances produced from 1-(2 : 4-dinitrophenyl)piperidine by reduction with cold stannous chloride and by them supposed to be formed by interaction of the nitroso-group in 1-(4-nitro-2-nitrosophenyl)piperidine with the spatially close methylene group of the piperidine ring with elimination of water.

If this ionic reaction can take place it was reasonable to suppose that the free-nitrogen radical formed by decomposition of an azido-group in 1-(2-azido-4-nitrophenyl)piperidine would still more readily form a bond to give in the first instance a dihydrobenziminazole derivative. 1-(2-Amino-6-nitrophenyl)piperidine being to hand, it was diazotised, then converted into the azide, which was heated in dichlorobenzene. Nitrogen

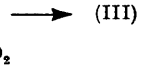
was given off beginning at about 130° and rapidly at 160—170° and there resulted a nitro-compound reducible to a diazotisable amine giving a bluish-red colour with Brenthol OP. A diazotisable amine or amines was present mixed with the nitro-compound. This result warranted the preparation of 1-(2 : 4-dinitrophenyl)piperidine, partial reduction and separation of the isomeric aminonitrophenylpiperidine by chromatography and differences in basicity. On diazotisation of the 2-amino-4-nitro-compound, conversion into the azide,



(III): X = NO_2, Y = H
(V): X = H, Y = NO_2
(VI): X = NHAc, Y = H



(IV)



(III)

and heating in dichlorobenzene there was isolated a nitro-compound, m. p. 219—220°, not altered on admixture with a sample of Spiegel and Kaufmann's base (III). Diazotisable amine was also present in the product. A probable source of the latter appeared to be reduction of some of the nitro-compound by the 2 : 3-dihydro-5-nitropiperidino(1′ : 2′-1 : 2)-benziminazole (IV) supposedly first formed from the free radical. Accordingly nitrobenzene was used as the heating medium and afterwards removed from the solutes by evaporation under a vacuum. Extraction of the distillate with dilute acid and titration with standard nitrite showed the presence of 85% of the theoretical weight of aniline, which was also isolated and converted into tribromoaniline. From the residual nitrobenzene Spiegel and Kaufmann's base (III) crystallised in 85% yield.

By analogy with the above, the product of the original experiment with 1-(2-amino-6-nitrophenyl)piperidine was 7-nitropiperido(1′ : 2′-1 : 2)benziminazole (V). Similarly 1-(2-amino-4-chlorophenyl)piperidine yielded the 5-chloro-compound.

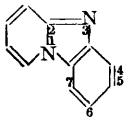
In all subsequent experiments the azide was not isolated but was taken up into nitrobenzene from the aqueous medium in which it was formed, then run slowly into more nitrobenzene at 170—180°, and the product was isolated when the evolution of nitrogen had ceased. The product invariably contained a little diazotisable amine, even when nitro-groups were absent from the molecule, but never in amount sufficient for isolation. The substances may be 1-*o*-aminophenyl-1 : 2 : 3 : 4-tetrahydropyridine and its analogues.

1-(4-Amino-2-nitrophenyl)piperidine was acetylated, and reduced to 1-(4-acetamido-2-aminophenyl)piperidine which produced 5-acetamidopiperidobenziminazole (VI) by the azide synthesis.

The four isomeric monoaminopiperidobenziminazoles have been prepared, their methods of preparation and relation of the two known monoaminopyrido(1′ : 2′-1 : 2)-benziminazoles being set out in the Table in which " M & S " indicate that a substance was first made, or a reaction carried out, by Morgan and Stewart (*loc. cit.*). Morgan and Stewart did not know whether their aminopyridobenziminazole, made from 4 : 6-dinitropyridobenziminazole by partial reduction, deamination, and reduction, was the 4- or 6-isomer. The present unequivocal synthesis of the 4-amino-isomer (II) shows that the Morgan and Stewart route produces the 6-amino-compound. Moreover the reduction of the latter to the 6-aminopiperidobenziminazole also prepared from (VI), proves that the azide synthesis does in fact produce the glyoxaline ring.

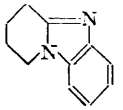
From hexahydroazepine (hexamethyleneimine) were prepared the 1-*o*-aminophenyl, 1-(2-amino-4-chlorophenyl), and 1-(2-amino-4-nitrophenyl) derivatives which were converted *via* the azides into the hexahydroazepino(1′ : 2′-1 : 2)benziminazole (VII) and its 5-chloro- (VIII) and 5-nitro-derivative (IX), the latter being reduced to the amine (X) whence acetylation, nitration, and deacetylation afforded the 5-amino-6-nitro-derivative (XI), deaminated to the 6-nitro-compound (XII) and reduced to the amine (XIII). The amino-group of the amine (X) condensed readily with (*a*) 2-amino-4-chloro-6-methyl-pyrimidine 1-methiodide, (*b*) twice with adipoyl chloride, and (*c*) formed a urea on treatment with carbonyl chloride. All these derivatives were capable of forming quaternary methiodides.

Pyrido(1′ : 2′-1 : 2)benziminazole, its piperido-analogue, and their monoamino-derivatives.



M. p. 178—179°

(M & S)



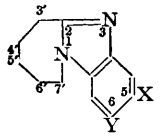
M. p. 101—102°
(106°, M & S)

Deamination of 6-amino- (M & S)

From *o*-azidophenylpiperidine

4-Amino-	M. p. 133—134° Reduction of 4-nitro-deriv. (II)	M. p. 177—177·5°
5-Amino-	Not known	M. p. 218—220° (*a*) Reduction of 5-nitro-deriv. (III) (*b*) Hydrolysis of acetyl deriv. (VI)
6-Amino-	M. p. 230—230·5° (220—230°, M & S) (*a*) Reduction of nitro-compound obtained by deaminating 4-amino-6-nitropyridobenziminazole (M & S) (*b*) Nitration of pyridobenziminazole and reduction	M. p. 198—200°
7-Amino-	Not known	M. p. 186—187° Reduction of 7-nitro-deriv. (V)

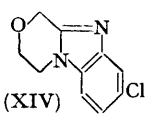
Similarly, 4-(2-amino-4-chlorophenyl)morpholine gave the morpholinobenziminazole (XIV), which owing to the weak directing effect of the chlorine atom yielded several nitro-compounds on nitration in sulphuric acid; from these one pure monoamine of undetermined orientation was isolated.



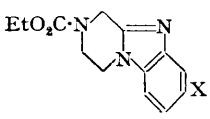
(VII) : X = H, Y = H.
(VIII) : X = Cl, Y = H.
(IX) : X = NO_2, Y = H.
(X) : X = NH_2, Y = H.

(XI) : X = NH_2, Y = NO_2.
(XII) : X = H, Y = NO_2.
(XIII) : X = H, Y = NH_2.

1-Ethoxycarbonylpiperazine was converted into its 4-*o*-aminophenyl and 4-(2-amino-4-chlorophenyl) derivatives from which were obtained the piperazinobenziminazole (XV) and its 5-chloro-derivative (XVI). The yields on ring closure were very poor.



(XIV)



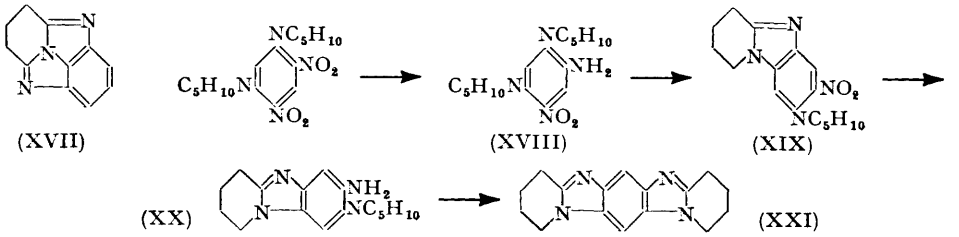
(XV) : X = H.
(XVI) : X = Cl.

Piperido- and the hydroazepino-benziminazole and their substitution products readily form quaternary ammonium compounds. They do not couple in dilute acid solution with diazonium salts, but 4- and 7-aminopiperido(1′ : 2′-1 : 2)benziminazole both couple to form aminoazo-compounds, as do their analogues and 4-aminopyrido-(1′ : 2′-1 : 2)benziminazole. A blue melt is formed with Michler's ketone in phosphorus oxychloride, giving a blue solution on dilution with water, but, unlike Crystal Violet, the coloured substance is destroyed by alkali. Piperidobenziminazole is partly dehydrogenated by palladium–charcoal in an inert gas at 300° in 15—20 minutes, but all is destroyed on longer heating. In experiments to find oxidising agents which would attack the polymethylene chain it was observed that both the piperido- and the hydroazepino-benziminazole, in an inert solvent, combine with one mol. of chlorine, bromine, or iodine. Part of this is given up as free halogen on treatment with aqueous acid and, in the case of chlorine, the benzene ring is then chlorinated.

It is probable that spatial relations are one of the factors which determine whether or not a bridge shall be formed by decomposition of the azido-compound. In general 1-*o*-azidophenylhexahydroazepine and its derivatives afford better yields than do the corresponding pipieridine derivatives, presumably because the distance from the *o*-position of the benzene ring to a methylene group is less in the former case. Steric effects may also account for the observation that, whilst 2-chloro-1 : 3-dinitrobenzene reacts easily with

piperidine, it reacts only slowly with hexahydroazepine, and each base reacts quite differently with 1 : 5-dichloro-2 : 4-dinitrobenzene (see below).

Decomposition of 7-azidopiperido(1′ : 2′-1 : 2)benziminazole gave a tar and no pure substance corresponding to the doubly ring-closed compound (XVII) could be isolated.



(XVII) (XVIII) (XIX)

(XX) (XXI)

A double ring-closure to form a fused pentacyclic system was brought about starting from 1 : 5-dinitro-2 : 4-dipiperidinobenzene by the annexed synthesis. The partial reduction [to (XVIII)] was easy but ring closure through the azide to the piperidobenziminazole (XIX) gave only a poor yield, as did further ring closure of the amine (XX) to the pentacyclic base (XXI). Further, 2-aminopyridine does not undergo the Morgan and Stewart reaction with 1 : 5-dichloro-2 : 4-dinitrobenzene in boiling glycol monoethyl ether but condenses twice to form 1 : 5-dinitro-2 : 4-di-(2-pyridylamino)benzene in good yield.

Experimental

Microanalyses by R. Rothwell.

Piperidobenziminazole and its derivatives.

Piperido(1′ : 2′-1 : 2)*benziminazole.*—1-*o*-Aminophenylpiperidine (Lellmann and Just, *Ber.*, 1891, **24**, 2103) (26·4 g., 0·15 mole), dissolved in hydrochloric acid (*d* 1·16; 45 c.c.) and water (200 c.c.), was diazotised at 5—10° with sodium nitrite (10·8 g.) in water (30 c.c.), excess of nitrous acid was destroyed, and the dark orange solution was run during 10 min. with stirring into 20% sodium acetate solution (300 c.c.) containing ice and sodium azide (9·0 g.); the mixture was set aside overnight. The oily azide was collected in nitrobenzene (100 c.c.) and added dropwise down the thermometer arm of a Claisen flask to nitrobenzene (300 c.c.) kept at 165—175°. Nitrogen was smoothly evolved, leaving an orange solution which was evaporated under a vacuum to small bulk (*ca.* 50 c.c.), and the hot liquid poured out to cool. The resulting crystals were collected, washed with cold light petroleum (b. p. 80—100°), and dissolved in hot dilute hydrochloric acid; the solution was boiled with charcoal, filtered, and cooled and the base (12·0 g., 46·5%) precipitated with sodium carbonate. The nitrobenzene filtrate was extracted with dilute hydrochloric acid and worked up as above, yielding more base (7·9 g., 30·5%) containing some diazotisable amine. The first fraction, crystallised three times from ethyl acetate and dried *in vacuo* at 100° for 2 hr., had m. p. 101—102° (Found: C, 76·7; H, 7·2; N, 16·2. Calc. for $C_{11}H_{12}N_2$: C, 76·7; H, 7·0; N, 16·3%); Morgan and Stewart (*loc. cit.*) give m. p. 106°.

The nitrobenzene removed under vacuum during the concentration was shaken twice with dilute hydrochloric acid; titration with 0·5N-sodium nitrite in presence of potassium bromide showed the presence of 0·042 mole (84%) of aniline. From another portion of the acid solution was obtained 2 : 4 : 6-tribromoaniline, m. p. and mixed m. p. 120°.

Piperido(1′ : 2′-1 : 2)benziminazole formed in ethyl acetate a *monopicrate*, m. p. 229—230° (from glycol monoethyl ether) (Found: C, 51·3; H, 4·4; N, 17·5. $C_{11}H_{12}N_2,C_6H_3O_7N_3$ requires C, 50·9; H, 3·7; N, 17·45%); at 100° with methyl iodide it formed a *methiodide*, m. p. 220—221° (from methanol–acetone) (Found: C, 45·8; H, 6·0; I, 40·3. $C_{12}H_{15}N_2I$ requires C, 45·8; H, 4·8; I, 40·4%); when boiled with iodine in chloroform it gave a brown precipitate of an iodine *addition product*, m. p. 150° (Found: I, 59·5. $C_{11}H_{12}N_2I_2$ requires I, 59·7%).

5-Chloropiperido(1′ : 2′-1 : 2)*benziminazole.*—1-(4-Chloro-2-nitrophenyl)piperidine (Lellmann and Geller, *Ber.*, 1888, **21**, 2283) (24·0 g., 0·1 mole) was reduced overnight in boiling ethanol (200 c.c.) with iron filings (30 g.) and hydrochloric acid (total 14·0 c.c., added during 12 hr.); the mixture, worked up in the usual way, afforded 1-(2-*amino*-4-*chlorophenyl*)*piperidine* (13·7 g., 0·065 mole), b. p. 188—192°/18—20 mm., m. p. 49·5—50° (from methanol) (Found: C, 62·3; H, 7·0; Cl, 17·2. $C_{11}H_{15}N_2Cl$ requires C, 62·8; H, 7·1; Cl, 16·9%). Dilute aqueous

hydrochloric acid produced the *hydrochloride*, m. p. 230—231°, colourless needles from water (Found : Cl^-, 14·2. $C_{11}H_{15}N_2Cl,HCl$ requires Cl^-, 14·3%); boiling acetic acid–acetic anhydride yielded the *acetyl* derivative, m. p. 95—96° (from methanol) (Found : C, 61·3; H, 6·0; N, 10·6. $C_{13}H_{17}ON_2Cl$ requires C, 61·8; H, 6·7; N, 11·1%); benzoyl chloride and aqueous sodium hydroxide afforded the *benzoyl* derivative, m. p. 105·0—105·5° (from ethyl methyl ketone) (Found : C, 69·1; H, 6·2; N, 8·6. $C_{18}H_{19}ON_2Cl$ requires C, 68·8; H, 6·0; N, 8·9%). The hydrochloride (37·0 g., 0·15 mole) was dissolved in hydrochloric acid (*d* 1·16; 30 c.c.) and hot water (200 c.c.) and cooled in ice, and the sludge of hydrochloride was diazotised at 5—8° with sodium nitrite (10·5 g.) in water (25 c.c.). After destruction of excess of nitrous acid the deep orange diazo-solution was run into one of sodium azide (12·6 g.) in 20% aqueous sodium acetate (300 c.c.), and the resultant pale yellow oily azide was treated as described above, yielding crude 5-*chloropiperido*(1′ : 2-1 : 2)*benziminazole* (25·4 g., 82%), m. p. 151—153°, containing a little diazotisable amine removed by crystallisation from ethylene dichloride; the final m. p. was 153—154° (Found : C, 63·8; H, 5·4; Cl, 17·0. $C_{11}H_{11}N_2Cl$ requires C, 63·9; H, 5·3; Cl, 17·2%). Alternatively the crude base was dissolved in rather more than one equiv. of hot 2N-hydrochloric acid and cooled, affording the *hydrochloride*, m. p. 295—296° (from water) (Found : Cl^-, 14·8. $C_{11}H_{11}N_2Cl$, HCl requires Cl, 14·6%).

5-*Nitropiperido*(1′ : 2′-1 : 2)*benziminazole* (III).—To 1-(2 : 4-dinitrophenyl)piperidine (Spiegel and Kaufmann, *loc. cit.*) (*ca.* 1 mole) dissolved in boiling ethanol (600 c.c.), was added during 3 hr. a solution of hydrated sodium sulphide (240 g.) and sulphur (32 g.) in water (300 c.c.), and the whole was boiled overnight. The ethanol was removed, the residue extracted with benzene (500 c.c.), and the solution washed with water; the benzene solution was then dried, filtered, and chromatographed on two columns, each 3 × 60 cm. and each containing active alumina (300 g.), giving a lower orange and an upper purple zone; the former was quickly eluted and consisted of 1-(2-amino-4-nitrophenyl)piperidine (*ca.* 47 g.) containing a little unchanged dinitro-compound. Further washing with benzene, until the eluate was straw-coloured, gave a mixture (*ca.* 81 g.) of the above with the isomeric purple 1-(4-amino-2-nitrophenyl)piperidine. The isomers were separated by grinding the solid with N-hydrochloric acid and filtering, the more basic 4-amino-2-nitro-compound dissolving. This process could not be applied to the crude product, a sharp separation not being possible until chromatography had removed gums. The orange isomer was dried, taken up in benzene, and filtered through a 4—5-cm. layer of active alumina, and the benzene removed, leaving crude base (52 g.). The total crude orange base (99 g., 41%) crystallised from benzene–light petroleum (b. p. 80—100°; 1 : 5), yielding pure 1-(2-amino-4-nitrophenyl)piperidine (54 g.), m. p. 96°. Spiegel and Utermann (*Ber.*, 1906, **39**, 2635) give m. p. 86°. The acid filtrate was basified, yielding 1-(4-amino-2-nitrophenyl)piperidine (18 g.) while the dried alumina from the columns extracted with chloroform yielded 11 g. (total 13%). Crystallisation from light petroleum (b. p. 80—100°) yielded the pure base, m. p. 116°. Spiegel and Utermann (*loc. cit.*) give m. p. 116°. In some preparations the orange fraction first obtained from the columns contained a considerable amount of 1-(2 : 4-dinitrophenyl)piperidine. This was separated by dissolving the whole in hydrochloric acid (*d* 1·16), diluting to *ca.* 3 vols., filtering off the precipitated dinitro-compound, and basifying the filtrate to recover 1-(2-amino-4-nitrophenyl)piperidine. For ring closure complete removal of the dinitro-compound was not necessary, as it was easily removed after diazotisation.

1-(2-Amino-4-nitrophenyl)piperidine (39 g.) was dissolved in hydrochloric acid (*d* 1·16; 35 c.c.) and hot water (250 c.c.), the solution was cooled to 5—7°, and the suspension of hydrochloride diazotised with sodium nitrite (12·5 g.) in water (25 c.c.); excess of nitrous acid was destroyed and the deep orange solution filtered from 1-(2 : 4-dinitrophenyl)piperidine (7·0 g.), then run during 10 min. with stirring into 20% aqueous sodium acetate (300 c.c.) containing sodium azide (12 g.). 1-(2-Azido-4-nitrophenyl)piperidine separated as yellow granules, rapidly becoming scarlet in direct sunlight. The azide was taken up in nitrobenzene and treated as described above. The crude crystalline 5-nitropiperidobenziminazole was washed with light petroleum (b. p. 80—100°), dissolved in boiling dilute hydrochloric acid (charcoal), filtered, and cooled to 10—15°, and the arylamine impurity was diazotised by excess of 2N-sodium nitrite (*ca.* 0·5 c.c.). The solution was poured into ice–aqueous sodium hydroxide containing a little 2-naphthol-3 : 6-disulphonic acid whereby the impurity was removed as water-soluble dye. The solid was collected, dried at 100°, and crystallised from chlorobenzene (200 c.c.), yielding the base (79·8% on amine used), m. p. 218·5—219·5° (very pale yellow leaflets) on further crystallisation from ethyl methyl ketone (Spiegel and Kaufmann, *loc. cit.*, give m. p. 219—220°) (Found : C, 60·8; H, 5·1; N, 19·6. Calc. for $C_{11}H_{11}O_2N_3$: C, 60·9; H, 5·1; N, 19·35%). Spiegel and Kaufmann's " Base A," made as described by them, did not depress this m. p.

5-Aminopiperido(1′ : 2′-1 : 2)*benziminazole*.—The above nitro-compound was reduced in methanol at 50—60° with hydrogen and Raney nickel in a Bergius autoclave; removal of the catalyst and solvent left the base in over 90% yield. The Béchamp method gave lower yields. Crystallised several times from methanol, the *amine*, m. p. 218—220°, was obtained as colourless needles (Found: C, 70·5; H, 7·4; N, 22·5. $C_{11}H_{13}N_3$ requires C, 70·6; H, 6·9; N, 22·5%). It was readily soluble in hot water and crystallised with water of crystallisation, the crystals melting at <100°, but the base was extracted from water with chloroform and was anhydrous on removal of the solvent. Boiled with acetic acid–acetic anhydride it yielded an *acetyl* derivative (VI), m. p. 219·5—220° (from chloroform, then ethyl acetate) (Found: C, 68·1; H, 6·7; N, 18·5. $C_{13}H_{15}ON_3$ requires C, 68·2; H, 6·55; N, 18·35%). The amine does not form an aminoazo-compound with diazotised *p*-chloroaniline in dilute acetic acid. The amine was also obtained by acetylating 1-(4-amino-2-nitrophenyl)piperidine (22·1 g., 0·1 mole) for 20 min. with boiling acetic acid (25 c.c.) and acetic anhydride (15 c.c.), the cooled solution poured into excess of ammonia which afforded scarlet 1-(*4-acetamido-2-nitrophenyl*)*piperidine*, m. p. 136—137° (from methanol) (Found: C, 59·8; H, 6·4; N, 16·1. $C_{13}H_{17}O_3N_3$ requires C, 59·5; H, 6·5; N, 16·0%). The latter was reduced at room temperature in methanol with Raney nickel and hydrogen, yielding 1-(*4-acetamido-2-aminophenyl*)*piperidine*, m. p. 132—133° (from ethyl acetate) (Found: C, 67·0; H, 8·1; N, 18·6. $C_{13}H_{19}ON_3$ requires C, 67·0; H, 8·15; N, 18·0%), which couples with diazotised *p*-chloroaniline in sodium acetate solution. The amine (3·5 g.) was diazotised in dilute hydrochloric acid, and the orange diazo-solution added dropwise to sodium azide (2·0 g.) in excess of aqueous 20% sodium acetate; the azido-compound was extracted into nitrobenzene and decomposed as described above; from the concentrated nitrobenzene crystallised 5-acetamidopiperidobenziminazole, m. p. 218—220° (from chlorobenzene), not depressed on admixture of the preceding sample.

6-Aminopiperido(1′ : 2′-1 : 2)*benziminazole*.—5-Acetamidopiperidobenziminazole (5·75 g.) was dissolved in sulphuric acid (*d* 1·84; 30 c.c.) at −10° to −5° with stirring (*ca.* 2 hr.); then at −10° during 15 min. nitric acid (*d* 1·48; 1·1 c.c.) mixed with sulphuric acid (*d* 1·84; 5 c.c.) was added and the temperature was allowed to rise to 0° in 1 hr. The whole was poured on ice, brought to pH 4—5 with aqueous sodium hydroxide (*d* 1·36) with internal ice cooling, then to pH 7—8° with a slurry of sodium carbonate. The yellow precipitate consisted of *5-acetamido-6-nitropiperido*(1′ : 2′-1 : 2)*benziminazole* (5·7 g.), m. p. 199—200° (from ethyl methyl ketone) (Found: C, 56·8; H, 5·9; N, 20·5. $C_{13}H_{14}O_3N_4$ requires C, 57·0; H, 5·1; N, 20·4%). The acetyl group was removed by boiling 2N-hydrochloric acid in 15 min., and the solution was further boiled with charcoal and filtered; on cooling there separated 5-amino-compound hydrochloride, orange leaflets, m. p. 304° (decomp.) with previous sintering. Aqueous sodium carbonate produced the scarlet *base*, m. p. 266—267° (from glycol monoethyl ether) (Found: C, 57·1; H, 5·5; N, 24·2. $C_{11}H_{12}O_2N_4$ requires C, 56·9; H, 5·2; N, 24·1%). The nitro-amine (2·45 g.) was dissolved in hydrochloric acid (*d* 1·16; 4 c.c.) and water (6 c.c.) and diazotised at 3—5° with sodium nitrite (0·75 g.) in water (2·5 c.c.); excess of nitrous acid was removed from the filtered solution which was poured into dilute hypophosphorous acid. Nitrogen was rapidly evolved and the temperature rose to 39°; after 30 min. the solution was boiled with carbon, filtered, and basified, yielding *6-nitropiperido*(1′ : 2′-1 : 2)*benziminazole* (1·95 g., 85%), m. p. 217—219° (from methanol) (Found: C, 60·8; H, 5·2; N, 19·70. $C_{11}H_{11}O_2N_3$ requires C, 60·8; H, 5·1; N, 19·35%). The nitro-group was reduced with hydrogen and Raney nickel in methanol at 60°/5 atm.; removal of catalyst and solvent left colourless crystals of *6-aminopiperido*(1′ : 2′-1 : 2)*benziminazole*, m. p. 198—200° (from ethyl acetate with a little methanol) (Found: C, 70·6; H, 6·9; N, 23·1. $C_{11}H_{13}N_3$ requires C, 70·6; H, 6·9; N, 22·5%). The m. p. was not depressed on admixture with the amine obtained by reduction of 6-aminopyridino(1′ : 2′-1 : 2)benziminazole (see below).

7-Aminopiperido(1′ : 2′-1 : 2)*benziminazole*.—1-(2 : 6-Dinitrophenyl)piperidine (Borsche and Rantscheff, *Annalen*, 1911, **379**, 166) was partly reduced in ethanol with aqueous sodium disulphide as described above for 1-(2 : 4-dinitrophenyl)piperidine. Chromatography of the product in benzene removed dark impurities, the yellow eluate was evaporated to dryness, converted into the hydrochloride with ethanol–hydrochloric acid, and diluted with acetone, and the precipitated 1-(*2-amino-6-nitrophenyl*)*piperidine hydrochloride* (80%), m. p. 220—221° (decomp.), was collected and air-dried (Found: Cl^-, 13·6. $C_{11}H_{15}O_2N_3$,HCl requires Cl^-, 13·8%). The hydrochloride (25·7 g., 0·1 mole) was diazotised in dilute hydrochloric acid and converted into the azide, a dark oil, which was decomposed as described above, but no crystals separated when the nitrobenzene was evaporated to small volume. The nitrobenzene was removed in steam from the acidified (hydrochloric) solution, from which a base (13·3 g.) was

precipitated by pouring the filtered solution into aqueous sodium hydroxide. Adding the base to hot 2N-hydrochloric acid and cooling produced the hydrochloride from which a diazotisable base was removed by washing with acetone. The hydrochloride was again basified, yielding the ***nitrobenziminazole*** (V), m. p. 107—108°, pale yellow needles [from light petroleum (b. p. 80—100°)] (Found: C, 60·7; H, 5·0; N, 19·3. $C_{11}H_{11}O_2N_3$ requires C, 60·8; H, 5·07; N, 19·4%). The crude hydrochloride (9·0 g.), m. p. 258—260° (decomp.), was boiled for 3½ hr. with iron filings (15 g.), acetic acid (15 c.c.), 20% aqueous sodium acetate (15 c.c.), and water (95 c.c.). The black mass was made alkaline, filtered hot, and washed with hot water. Needles (2 g.) separated from the cooled filtrate from which chloroform extracted more base (1·2 g.), whilst 3·3 g. were recovered from the dried iron oxides. The whole was converted into the *7-acetamide*, m. p. 236—237° (from ethanol) (Found: C, 68·2; H, 6·5; N, 18·2. $C_{13}H_{15}ON_3$ requires C, 68·0; H, 6·6; N, 18·4%). Hydrolysis with boiling 2N-hydrochloric acid and basification produced the ***amine***, m. p. 186—187° (from benzene) (Found: C, 70·4; H, 7·1; N, 22·4. $C_{11}H_{13}N_3$ requires C, 70·6; H, 6·9; N, 22·5%).

Pyrido(1′ : 2′-1 : 2)benziminazole and its derivatives.

Pyrido(1′ : 2′-1 : 2)benziminazole.—Piperido(1′ : 2′-1 : 2)benziminazole (2·0 g.) was carried downwards, during 20 min., in a slow stream of nitrogen or carbon dioxide through palladised charcoal supported on asbestos in a jacketed tube 1 × 35 cm., heated at 306°. The sublimate was extracted with boiling light petroleum (b. p. 60—80°), which removed unchanged piperidobenziminazole, leaving pyrido(1′ : 2′-1 : 2)benziminazole, m. p. 178—179°, pale yellow prisms (from chlorobenzene). Morgan and Stewart (*loc. cit.*) give m. p. 178—179°. With methyl iodide at 100° for 16 hr. it afforded the *methiodide*, m. p. 246—247° (from water) (Found: C, 46·3; H, 3·4; I, 41·6. $C_{12}H_{11}N_2I$ requires C, 46·5; H, 3·55; I, 41·0%).

4-Nitropyrido(1′ : 2′-1 : 2)benziminazole (II).—2-Chloro-1 : 3-dinitrobenzene (58 g., 0·287 mole) (cf. Gunstone and Tucker, *J. Appl. Chem.*, 1952, **2**, 206), 2-aminopyridine (35 g., 0·371 mole), and calcium carbonate (5·0 g.) were boiled under reflux in glycol monoethyl ether (225 c.c.) for 24 hr. Nitrogen oxides were evolved. The mixture was steam-distilled from dilute aqueous hydrochloric acid until chlorodinitrobenzene was removed, and the filtered solution was basified with sodium carbonate. The crude air-dried product (39 g.) was extracted three times with boiling benzene, leaving a yellow insoluble substance (14·3 g.). Chromatography of the benzene solution provided orange *2-(2 : 6-dinitroanilino)pyridine* (I) (14·2 g.), m. p. 117—119° (from methanol) (Found: C, 50·7; H, 3·15. $C_{11}H_8O_4N_4$ requires C, 50·9; H, 3·1%). In ethanol it affords the white *hydrochloride*, sinters at 220—223°, decomp. *ca.* 225°, hydrolysed by water to the free base (Found: Cl^-, 12. $C_{11}H_8O_4N_4$,HCl requires Cl, 11·95%). With methyl iodide at 100° for 7 hr. it afforded the ***methiodide***, m. p. 207—208° (decomp.) (crystallised from water; then extracted with ethyl acetate) (Found: C, 36·3; H, 2·6; I, 30·5. $C_{12}H_{11}O_4N_4I$ requires C, 36·0; H, 2·6; I, 31·6%). The above substance insoluble in benzene was extracted with boiling glycol monoethyl ether, and the solution was filtered and cooled yielding *4-nitropyrido(1′ : 2′-1 : 2)-benziminazole* (II) (6·1 g.), m. p. 272°. Evaporation of the solvent to small volume gave a second crop (1·0 g.) (Found: C, 61·9; H, 3·3; N, 19·85. $C_{11}H_7O_2N_3$ requires C, 62·0; H, 3·3; N, 19·75%). The same compound (0·8 g.) was produced by boiling 2-(2 : 6-dinitroanilino)-pyridine (3·0 g.) in glycol monoethyl ether for 16 hr.; nitrous acid was detected in the vapour throughout the period.

4-Aminopyrido(1′ : 2′-1 : 2)benziminazole.—The above nitro-compound (7·1 g.) was reduced by boiling for 3 hr. with iron filings (10·0 g.), water (125 c.c.), and glacial acetic acid (20 c.c.); the mixture was brought to pH 9—10 with aqueous sodium hydroxide, then filtered hot, and the iron oxides were washed with hot water. The filtrate deposited cream-coloured needles (1·7 g.); chloroform extracted more base (4·0 g.) from the dried iron oxides. The ***amine*** crystallised from benzene in pale yellow needles, m. p. 133—134° (Found: C, 72·0; H, 4·7; N, 23·1. $C_{11}H_9N_3$ requires C, 72·2; H, 4·9; N, 22·9%). With boiling acetic acid–acetic anhydride it gave the acetyl derivative hydrate, m. p. 106—108° (decomp.) (dried in the air), rising to 142—144° on drying at 100° *in vacuo*. Crystallised from acetic anhydride it yielded needles of the *acetyl derivative acetate*, m. p. 147—149° (Found: C, 63·1; H, 5·3; N, 14·5; $C_{15}H_{15}O_3N_3$ requires C, 63·2; H, 5·3; N, 14·7%).

To the amine dissolved in dilute hydrochloric acid was added diazotised *p*-chloroaniline, then aqueous sodium acetate; a scarlet aminoazo-compound was at once precipitated, and crystallised from ethyl methyl ketone as a crimson powder, m. p. 265°. This in turn afforded a yellow diazo-solution, giving a violet pigment with Brenthol OP.

Reduction to 4-aminopiperidobenziminazole. In working up the product of reduction of 4-nitropyrido(1′ : 2′-1 : 2)benziminazole with hydrogen and platinum oxide in ethanol there was obtained a fraction, m. p. 170—172°, of lower solubility in methanol which, because it produced a bluish-red pigment on diazotisation and coupling with Brenthol OP, was considered to be probably the above amine. Recrystallised from ethyl acetate it had m. p. 176—177°. 4-Aminopyrido(1′ : 2′-1 : 2)benziminazole (0·8 g.) was therefore reduced in methanol (25 c.c.) with platinum oxide (0·1 g.) at 95°/60 atm. for 3 hr. Removal of catalyst and methanol left a colourless compound, m. p. 176—177° (from ethyl acetate), not depressed with the above amine which must therefore be *4-aminopiperido*(1′ : 2′-1 : 2)*benziminazole*. The samples were mixed and again crystallised; the m. p. was 177—177·5° (Found: C, 70·4; H, 7·4; N, 22·0. $C_{11}H_{13}N_3$ requires C, 70·6; H, 6·9; N, 22·5%).

Nitration. Pyrido(1′ : 2′-1 : 2)benziminazole (2·3 g.) was dissolved with cooling in sulphuric acid (*d* 1·84; 8·0 c.c.), then nitrated during 20 min. with nitric acid (*d* 1·48; 0·6 c.c.) mixed with sulphuric acid (*d* 1·84; 3·0 c.c.), at 10—15°. The whole was stirred for 1 hr., warmed to 40—50° for 15 min., poured into ice-water, and neutralised with ammonia, and the solid collected and dried (3·0 g.; m. p. 260—270°); crystallised from chlorobenzene, then methanol, it formed yellow needles (1·7 g.), m. p. 271—272° (Found: C, 61·8; H, 3·3; N, 19·50. Calc. for $C_{11}H_{17}O_2N_3$: C, 61·9; H, 3·3; N, 19·7%). Morgan and Stewart's 4(6)-nitropyrido(1′ : 2′-1 : 2)benziminazole, prepared as described by them (*loc. cit.*), had m. p. 268—269° (from chlorobenzene, then methanol) (Morgan and Stewart give m. p. 260—262°), not depressed on admixture with the above nitro-compound but depressed with the 4-nitro-isomer. Both samples were reduced with iron filings–acetic acid, and the amines were extracted from the iron oxides with boiling chlorobenzene, as a yellow powder, m. p. and mixed m. p. 230—230·5° (after two crystallisations from ethyl methyl ketone) (Morgan and Stewart give m. p. 229—230°) (Found: C, 72·0; H, 5·0; N, 23·0. Calc. for $C_{11}H_9N_3$: C, 72·2; H, 4·9; N, 22·9%). There can be no doubt that the yellow colour of this amine, commented on by Morgan and Stewart, is inherent and due to its high unsaturation, as is also the case with the 4-isomer. Further the diazo-derivatives of both amines give violet shades on coupling with Brenthol OP and other " red-forming " 2-hydroxynaphthalene-3-carboxyamides. The above amine (0·75 g.) was reduced in methanol (25 c.c.) at 90—100°/50 atm. with platinum oxide and hydrogen for 1 hr.; evaporation of the filtered solution left colourless granules of 6-aminopiperidobenziminazole, m. p. and mixed m. p. 195—197°.

2′ : 3′ : 4′ : 5′ : 6′ : 7′-Hexahydroazepino(1′ : 2′-1 : 2)*benziminazole and its derivatives.*

2′ : 3′ : 4′ : 5′ : 6′ : 7′-Hexahydroazepino(1′ : 2′-1 : 2)*benziminazole* (VII).—*o*-Chloronitrobenzene (79 g., 0·5 mole) was dissolved in hot butanol (100 c.c.) and to the solution was added hexahydroazepine (hexamethyleneimine) (70 c.c.), then sodium carbonate (3 g.) dissolved in water (15 c.c.), followed by solid sodium carbonate (23·5 g.); the whole was boiled with stirring for 24 hr. The cold solution was filtered, the solids were washed with butanol, and the butanol was removed by heating the filtrate under a vacuum, leaving a yellow oil (97 g., 0·44 mole as 1-*o*-nitrophenyl derivative), $n_D^{22\cdot3}$ 1·601. The oil was reduced with iron filings (150 g.) in boiling ethanol (300 c.c.), hydrochloric acid (*d* 1·16; 15 c.c.) being added in portions; after 18 hr. the solution was made alkaline and filtered, and the iron oxides were washed with hot ethanol which was removed from the filtrate leaving an oil, which was washed with aqueous sodium carbonate and distilled. This yielded 1-o-*aminophenylhexahydroazepine* (64 g., 0·336 mole), b. p. 160°/10 mm., $n_D^{23\cdot5}$ 1·564. The base yielded a *monohydrochloride*, m. p. 165—166° (Found: Cl^-, 15·6. $C_{12}H_{18}N_2$,HCl requires Cl^-, 15·65%). The amine (47·5 g., 0·25 mole) was diazotised, converted into the azido-derivative, an oil, which was decomposed in nitrobenzene as described above, and from the concentrated nitrobenzene solution the crude base crystallised (34 g.); more (6 g.) was recovered by extracting the nitrobenzene filtrate with dilute acid. Crystallisation from ethyl methyl ketone, then benzene, yielded the *hexahydroazepinobenziminazole*, m. p. 125—126° (Found: C, 77·6; H, 7·3; N, 15·3. $C_{12}H_{14}N_2$ requires C, 77·4; H, 7·5; N, 15·05%). It formed a *methiodide*, m. p. 232—234° (from water) (Found: C, 48·7; H, 5·4; N, 8·6. $C_{13}H_{17}N_2I$ requires C, 47·6; H, 5·2; N, 8·5%).

5-Chlorohexahydroazepino(1′ : 2′-1 : 2)*benziminazole* (VIII).—To 1 : 4-dichloro-2-nitrobenzene (192 g., 1·0 mol.), dissolved in boiling ethanol (300 c.c.), was added dropwise hexahydroazepine (230 c.c.), and the whole was boiled overnight. The ethanol was removed. The residue solidified when washed with dilute hydrochloric acid. It was crystallised from ethanol, yielding the 1-(*4-chloro-2-nitrophenyl*) *derivative*, m. p. 56° (Found: C, 56·7; H, 6·2; N, 10·5. $C_{12}H_{15}O_2N_2Cl$ requires C, 56·6; H, 5·9; N, 11·0%). Reduction with iron–ethanol as described

above afforded the 1-(4-chloro-2-aminophenyl) derivative, b. p. 198—200°/20 mm., n_D^{23} 1·5800, giving a *hydrochloride*, m. p. 200—202° [Found : Cl^-, 13·7%; *M* (titration with $NaNO_2$), 259. $C_{12}H_{17}N_2Cl,HCl$ requires Cl^-, 13·6%; *M*, 261]. This was converted by the steps described above into the *5-chlorobenziminazole derivative* (72% crude), m. p. 107—109° (from ethyl acetate) (Found : C, 65·3; H, 5·8; Cl, 16·0. $C_{12}H_{13}N_2Cl$ requires C, 65·5; H, 5·9; Cl, 16·1%) [*hydrochloride*, sinters at 255°, m. p. 259—261° (Found : Cl^-, 13·2, 13·3. $C_{12}H_{13}N_2Cl,HCl,0·5H_2O$ requires Cl^-, 13·3%); *methiodide*, m. p. 273—274° (Found : C, 43·2; H, 4·6; I, 34·0. $C_{13}H_{16}N_2ClI$ requires C, 43·0; H, 4·4; I, 35·0%)].

Passing a slow stream of chlorine into a solution of the base (2·2 g.) in chloroform (15 c.c.) at 0° gave a precipitate (2·4 g.), m. p. 314° (decomp.), of a *dichloride* (Found : C, 50·7; H, 4·4; Cl, 36·4. $C_{12}H_{13}N_2Cl_3$ requires C, 49·4; H, 4·5; Cl, 36·5%). A few grains placed on starch–iodide paper moistened with sodium carbonate left a blue mark; chlorine was evolved on treatment with warm dilute hydrochloric acid. The compound reacted with boiling water and a base was precipitated on addition of sodium carbonate to the cool solution. Apparently self-chlorination occurred in the aromatic ring producing the 5 : x-*dichlorobenziminazole*, m. p. 176—177° (thrice crystallised from ethyl acetate) (Found : C, 57·2; H, 5·1; Cl, 27·4. $C_{12}H_{12}N_2Cl_2$ requires C, 56·5; H, 4·7; Cl, 27·8%). No chlorine was removed from the last compound by boiling aqueous sodium hydroxide or alcoholic potassium hydroxide. Sundry piperidino- and hexahydroazepino-benziminazoles were similarly treated with chlorine or bromine and invariably a precipitate containing loosely-held halogen was formed, but no systematic study of the substances was made. The residue (1·3 g.) left on removal of the chloroform had not the above properties but was not unchanged starting material and it had an odour not unlike that of chloral; it was not further examined.

Hexahydro-5-nitroazepino(1′ : 2′-1 : 2)benziminazole (IX).—To 1-chloro-2 : 4-dinitrobenzene (202 g., 1·0 mol.) in boiling ethanol (300 c.c.) was added dropwise hexahydroazepine (230 c.c.), and the whole was boiled overnight, then cooled, and the orange cake was collected and washed with water. Crystallisation from methanol, then light petroleum (b. p. 80—100°), yielded the 2 : 4-*dinitrophenyl derivative*, m. p. 108—109°, yellow leaflets (Found : C, 54·3; H, 5·9; N, 15·8. $C_{12}H_{15}O_4N_3$ requires C, 54·3; H, 5·7; N, 15·8%). To the damp cake (91—92% yield) dissolved in boiling ethanol (0·8—1·0 l.) was added during 3 hr. a solution of sodium disulphide prepared from hydrated sodium sulphide (240 g.) and sulphur (32 g.) in water (500 c.c.), and the whole was boiled overnight and the ethanol removed. The residue was taken up in benzene (700 c.c.), washed with cold water until the washings were pale yellow, and filtered, and the benzene was removed. To the residue was added hydrochloric acid (*d* 1·16), and the resultant solid hydrochlorides were collected and washed with a little hydrochloric acid. Basification of the filtrate produced 1-(4-*amino*-2-*nitrophenyl*)*hexahydroazepine*, m. p. 76—77°, dark purple needles [from light petroleum (b. p. 80—100°)] (Found : C, 61·2; H, 7·5; N, 17·5. $C_{12}H_{17}O_2N_3$ requires C, 61·2; H, 7·2; N, 17·9%). The filter cake was washed in water (1 l.) which leached out a little more of the above compound; then it was dissolved in boiling methanol (1 l.), basified with methanolic potassium hydroxide, treated with charcoal, filtered, and cooled, whereupon 1-(2-*amino*-4-*nitrophenyl*)*hexahydroazepine* crystallised. It was collected, dried, dissolved in benzene, and filtered through active alumina (6 × 2·5 cm.) which retained a black substance; the base (94·0 g., 0·4 mol.) crystallised in large orange prisms. A sample (21·4 g.) was distilled in a short-path still at 172·8—173·5°/0·15 mm. and the first fraction (8·1 g.) proved to be the pure base, m. p. 67—68·5° (Found : C, 61·2; H, 7·5; N, 17·7. $C_{12}H_{17}O_2N_3$ requires C, 61·2; H, 7·2; N, 17·85%). As described for the piperidine analogue the above base was converted *via* the azido-derivative into *hexahydro-5-nitroazepino*(1′ : 2′-1 : 2)*benziminazole*, m. p. 174—175° (from chlorobenzene) (Found : C, 62·3; H, 5·7; N, 18·0. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·63; N, 18·1%), reduced with hydrogen and Raney nickel in methanol at 50—55°/30 atm. to the *amine* (X), m. p. 180·5—181°, obtained free from a pink impurity after five crystallisations from methanol (Found : C, 71·8; H, 7·3; N, 21·0. $C_{12}H_{15}N_3$ requires C, 71·7; H, 7·5; N, 20·9%). Boiled with acetic acid–acetic anhydride the amine afforded the *acetyl* derivative, m. p. 254—255° (from glycol monoethyl ether) (Found : C, 68·9; H, 7·1; N, 17·1. $C_{14}H_{17}ON_3$ requires C, 69·1; H, 7·0; N, 17·3%). The amine (6 g.), dissolved in methanol (15 c.c.) and poured into water (150 c.c.), afforded a clear solution which, when shaken with excess of ethyl chloroformate with portionwise addition of aqueous sodium hydroxide to pH 10, afforded the *ethoxycarbonyl derivative* (8·1 g.), m. p. 238—240° (from methanol) (Found : C, 66·1; H, 6·6; N, 15·3. $C_{15}H_{19}O_2N_3$ requires C, 66·0; H, 6·98; N, 15·35%), which with methyl iodide at 100° (17 hr.) yielded 5-*ethoxycarbonylaminohexahydro*-1-*methylazepino*(1′ : 2′-1 : 2)*benziminazolinium iodide*, m. p. 270—272° (decomp.) (Found : C, 46·2; H, 5·3.

$C_{16}H_{22}O_2N_3I$ requires C, 46·3; H, 5·3%). The amine was condensed with 2-hydroxy-3-naphthoic acid in boiling toluene with phosphorus trichloride and worked up by steam-distillation from aqueous sodium hydroxide and precipitation with sodium hydrogen carbonate, providing *hexahydro-5-(2-hydroxy-3-naphthamido)azepino*(1′ : 2′-1 : 2)*benziminazole*, m. p. 310—311° (from ethylene glycol) (Found : C, 74·0; H, 5·8; N, 11·6. $C_{23}H_{21}O_2N_3$ requires C, 74·5; H, 5·6; N, 11·3%). To the amine (4·0 g.) dissolved in hot water (100 c.c.) with 2N-hydrochloric acid (10 c.c.) was added 2-amino-4-chloro-6-methylpyrimidine 1-methiodide, (5·7 g.) dissolved in boiling water (100 c.c.), followed by aqueous sodium acetate added dropwise to remove hydrochloric acid as liberated; after 7 min. the solution was filtered and treated with sodium iodide to precipitate 2-*amino*-4-[*hexahydroazepino*(1′ : 2′-1 : 2)*benziminazol*-5-*ylamino*]-1 : 6-*dimethylpyrimidinium* 1-*iodide*, m. p. *ca.* 220° (rapid heating) (from methanol) (Found : C, 47·3; H, 5·1; N, 18·7. $C_{18}H_{23}N_6I$ requires C, 48·0; H, 5·1; N, 18·6%). This compound with methyl iodide at 100° (17 hr.) afforded the *trimethyl compound di-iodide*, m. p. 335° (from water) (Found : C, 37·5; H, 4·3. $C_{19}H_{26}N_6I,H_2O$ requires C, 37·4; H, 4·6%). To the amine (8·0 g.) in boiling benzene was added adipoyl chloride (3·0 c.c.) in benzene and the resultant thick mass was further diluted with benzene. After cooling, the solid was collected, basified, and boiled with methanol, yielding *NN′*-di(hexahydroazepinobenziminazol-5-yl)adipamide, m. p. 345° (decomp.) (from glycol), quaternised as above to the 1 : 1′-*dimethyl compound* 1 : 1′-*di-iodide*, m. p. 345° (decomp.) (from water) (Found : C, 49·0; H, 5·4; $C_{32}H_{42}O_3N_6I_2$ requires C, 48·2; H, 5·3%). Passing carbonyl chloride into a solution of the base in warm water produced a thick precipitate which was collected, dissolved in boiling water, and poured into aqueous ammonia, yielding the urea, m. p. 335°, as colourless leaflets (from glycol), quaternised by heating with methyl toluene-*p*-sulphonate at 120°, rising to 160° during 2 hr., cooling, washing with ether, dissolution in boiling water, and addition of sodium iodide to *di*(*hexahydro*-1-*methylazepinobenziminazol*-5-*yl*)-*urea di-iodide*, m. p. 316—318° (decomp.) (from water) (Found : C, 45·0; H, 4·7; I, 34·6. $C_{27}H_{34}ON_6I_2$ requires C, 45·5; H, 4·8; I, 35·7%).

Hexahydro-5-*hydroxyazepino*(1′ : 2′-1 : 2)*benziminazole*.—The orange diazonium salt derived from the 5-amino-compound is very stable to heat. The amine (8·0 g.) was diazotised in phosphoric acid (20 c.c.) and water (40 c.c.), and the diazo-solution was added dropwise during 40 min. to phosphoric acid (60 c.c.) stirred and heated in a graphite bath at 130—140°; after 75 min. the diazo-reaction had become weak and the cooled solution was poured into water (*ca.* 400 c.c.). The pH was brought to 7—7·5 with 33% aqueous sodium hydroxide (120 c.c.) which precipitated most of the product as brown flakes. These were collected and dissolved in boiling water (150 c.c.) with 2N-hydrochloric acid (20 c.c.), and the solution was dropped into excess of boiling 2N-sodium carbonate, yielding at first a dark gum which was discarded, then cream-coloured granules. The latter were dissolved in dilute sodium hydroxide solution, and from the filtered solution sodium hydrogen carbonate precipitated the *phenol* (1·6 g.), m. p. 295—296° (from methanol) (Found : C, 71·2; H, 7·2. $C_{12}H_{14}ON_2$ requires C, 71·3; H, 6·9%).

6-*Aminohexahydroazepino*(1′ : 2′-1 : 2)*benziminazole* (XIII).—5-Acetamidohexahydroazepinobenziminazole (13·2 g.) was dissolved during 2 hr. with stirring in cold sulphuric acid (*d* 1·84; 100 c.c.) at −10° to −5° and nitrated at that temperature with nitric acid (*d* 1·4; 2·4 c.c.) in sulphuric acid (*d* 1·84; 10 c.c.) added during 15 min.; after a further 15 min. the whole was poured on ice. A sample poured on ice and aqueous sodium hydroxide yielded yellow 5-*acetamidohexahydro*-6-*nitroazepino*(1′ : 2′-1 : 2)*benziminazole*, m. p. 190—191° (from ethyl methyl ketone, then chlorobenzene) (Found : C, 58·8; H, 5·9; N, 19·0. $C_{14}H_{16}O_3N_4$ requires C, 58·4; H, 5·6; N, 19·4%). The remainder was hydrolysed by boiling the acid solution for 5 min., cooling, and pouring on ice and aqueous sodium hydroxide (sufficient to bring the pH to 7—8), the scarlet 5-*amino*-6-*nitro-base* (XI) being precipitated; it had m. p. 295—296° (decomp.) (from glycol monoethyl ether, then sublimed at 185°/0·003 mm.) (Found : C, 58·3; H, 5·7. $C_{12}H_{14}O_2N_4$ requires C, 58·5; H, 5·7%). The nitro-amine (4·9 g.) was deaminated by diazotisation and treatment with hypophosphorous acid, yielding *hexahydro*-6-*nitroazepino*(1′ : 2′-1 : 2)-*benziminazole* (XII) (2·1 g.), m. p. 196—197° (after sublimation at <170°/0·003 mm., then chromatography on alumina from benzene and development with benzene–chloroform and finally crystallisation from ethyl acetate) (Found : C, 62·3; H, 5·7; N, 18·3. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·63; N, 18·1%). Reduction of this compound (1·0 g.) by hydrogen with Raney nickel in methanol at 50°/50 atm. yielded the *amine* (XIII) (0·86 g.), m. p. 198—199° (from benzene) (Found : C, 71·9; H, 7·6; N, 21·0. $C_{12}H_{15}N_3$ requires C, 71·7; H, 7·5; N, 20·9%).

Hexahydro-1-(2-*amino*-6-*nitrophenyl*)*azepine*.—To 2-chloro-1 : 3-dinitrobenzene (50 g.) in boiling ethanol (250 c.c.) was added dropwise hexahydroazepine (57·0 c.c.), and the whole was

boiled for 6 hr., then cooled. The separated solid (16 g.) was collected and washed with water; evaporation to small bulk produced a further 8·0 g. Removal of the solvent left a neutral oil which could not be crystallised either before or after chromatography in benzene on alumina. The mixed solids, when crystallised from light petroleum (b. p. 80—100°) and then from methanol, yielded the 2 : 6-*dinitrophenyl derivative*, m. p. 73—74° (Found : C, 54·2; H, 6·0; N, 15·2. $C_{12}H_{15}O_4N_3$ requires C, 54·3; H, 5·7; N, 15·8%). This (20 g.) was reduced in boiling ethanol (200 c.c.) with sodium disulphide [from sodium sulphide nonahydrate (18·2 g.) and sulphur (2·42 g.)] added during 3 hr., and the whole boiled for 20 hr. That part of the product soluble in benzene was chromatographed on alumina, giving a yellow bottom band, an orange main band, and a narrow dark band at the top. The orange band afforded red needles which melted at room temperature but when set aside and scratched afforded an orange form of the 2-*amino*-6-*nitrophenyl derivative*, m. p. 56—57° [from light petroleum (b. p. 80—100°)] (Found : C, 61·2; H, 7·4; N, 17·7. $C_{12}H_{17}O_2N_3$ requires C, 61·2; H, 7·2; N, 17·9%).

Other benziminazoles.

5-*Chloromorpholino*(4′ : 3′-1 : 2)*benziminazole* (XIV).—4-(4-Chloro-2-nitrophenyl)morpholine (Harradence and Lions, *J. Proc. Roy. Soc. N.S.W.*, 1937, **70**, 406) was reduced with neutral iron filings in ethanol to 4-(2-*amino*-4-*chlorophenyl*)*morpholine* (81%), m. p. 135—137° (from methanol) (Found : C, 56·8; H, 6·1; N, 13·0. $C_{10}H_{13}ON_2Cl$ requires C, 56·6; H, 6·1; N, 13·2%). Diazotisation produced a clear brown-yellow solution which on interaction with sodium azide afforded a grey granular azido-compound, m. p. 80—81° (decomp.; slow heating). The azide was decomposed in nitrobenzene and after concentration the crystalline material was collected and converted into 5-*chloromorpholino*(4′ : 3′-1 : 2)*benziminazole hydrochloride*, m. p. 228—230° (from methanol) (Found : Cl^-, 14·3. $C_{10}H_9ON_2Cl$,HCl requires Cl^-, 14·5%), from which was obtained the free *base* (XIV), m. p. 200—200·5° (from ethyl acetate) (Found: C, 57·2; H, 4·2; N, 13·1. $C_{10}H_9ON_2Cl$ requires C, 57·6; H, 4·3; N, 13·4%). At 100° the base formed a *methiodide*, m. p. 242—244° (decomp.) (from water, then washed with acetone) (Found : I, 35·9. $C_{11}H_{12}ON_2ClI$ requires I, 36·2%). As the yield of crude base was only 50% the nitrobenzene was removed from the filtrate by steam-distillation from dilute hydrochloric acid, from which after cooling and filtering sodium carbonate liberated a mixture of bases, m. p. <100°. Chromatography on alumina from benzene afforded the base (XIV) in the first eluate, after which the m. p. fell and by again chromatographing the later eluates there was obtained a *base*, m. p. 100—100·5° (Found : C, 54·7; H, 4·5; Cl, 18·7%). It afforded a picrate, m. p. 230—232°, was not diazotisable and occurred in every preparation of (XIV) but it was not further investigated.

Nitration. The base (XIV) (9·0 g.) was dissolved in sulphuric acid (*d* 1·84; 50 c.c.) and nitrated at 10—15° during 10 min. with nitric acid (*d* 1·48; 1·85 c.c.) mixed with sulphuric acid (*d* 1·84; 6·0 c.c.); after ½ hr. the solution was warmed to 40°, then poured on ice and brought to pH 10—11 with aqueous sodium hydroxide and the insoluble material was collected from the cooled solution. By fractional crystallisation from chlorobenzene were obtained colourless needles (7·2 g.) of a *nitro-compound*, m. p. 219—220° (Found : C, 47·0; H, 3·1; N, 16·1. $C_{10}H_8O_3N_3Cl$ requires C, 47·3; H, 3·1; N, 16·6%). The latter was reduced with Raney nickel and hydrogen at 60—65°/100 atm. in methanol; crystals separated from the cold methanol and were removed from the nickel with hot methanol, producing x-*amino*-5-*chloromorpholino*-(4′ : 3′-1 : 2)*benziminazole*, m. p. 262—263°, as colourless needles (Found : C, 53·8; H, 5·3; N, 19·2. $C_{10}H_{10}ON_3Cl$ requires C, 53·8; H, 4·5; N, 18·8%). The base does not form an aminoazo-compound with diazotised *p*-chloroaniline in dilute acetic acid. The original nitro-compound must have been a eutectic mixture of three isomers since by evaporating the methanol filtrates there were obtained two crude bases, one, m. p. 218—235°, soluble in hot chlorobenzene, the other, m. p. 218—240°, insoluble in chlorobenzene. Both these bases afforded aminoazo-compounds with diazotised *p*-chloroaniline.

Partial Reduction of 4-(2 : 4-*Dinitrophenyl*)*morpholine.*—4-(2 : 4-Dinitrophenyl)morpholine (Harradence and Lions, *loc. cit.*) was reduced with sodium disulphide as described above for the piperidine analogue, and the product was chromatographed on alumina from benzene, giving an upper red and lower yellow fraction. Neither of these yielded pure compounds and better separation resulted by utilisation of their difference in basicity or the solubility of their hydrochlorides. Treatment of either fraction with aqueous hydrochloric acid (*d* 1·16) yielded a sparingly soluble hydrochloride of the yellow isomer, freed by basification, as was the red isomer from the filtrate. Each fraction was then further purified by dissolution in 0·5N-hydrochloric acid to which aqueous sodium acetate was added to pH 2—3, whereupon the yellow base

separated; at pH 4—5 a mixture separated and at pH 6—7 the red base. Alternatively, the mixture was dissolved in aqueous acetic acid and hydrochloric acid added to pH 3—4: the yellow base crystallised, leaving nearly pure red base in solution. The yellow base, since its diazo-derivative afforded a red pigment with Brunthol OP, was probably 4-(2-*amino*-4-*nitrophenyl*)*morpholine*; it had m. p. 153—153·5° (from methanol) (Found: C, 53·7; H, 6·2; N, 18·4. $C_{10}H_{13}O_3N_3$ requires C, 53·8; H, 5·85; N, 18·85%). The red base was probably 4-(4-*amino*-2-*nitrophenyl*)*morpholine* and had m. p. 133—135° (from ethyl acetate) (Found: C, 54·1; H, 5·4; N, 19·1%); its diazo-derivative afforded a purple pigment with Brenthol OP, typical of a *NN*-dialkyl *p*-diamine.

4′-N-*Ethoxycarbonylpiperazino*(1′ : 2′-1 : 2)*benziminazole* (XV).—1-Ethoxycarbonylpiperazine (18 g.) was boiled in ethanol (20 c.c.) with *o*-chloronitrobenzene (9·0 g.) for 48 hr., the ethanol was removed, and the residual oil poured into water and extracted with benzene. Removal of the benzene left a mobile orange oil, n_D^{20} 1·553. Chromatography of a sample from benzene over alumina gave a single fast-moving orange band, and evaporation of the eluate left an orange oil, n_D^{20} 1·557. The oil (13·3 g.) was reduced with neutral iron in ethanol, giving an oil which crystallised. The crystals were taken up in chloroform, the solution filtered, and the solvent removed, leaving crude amine (10·9 g.) which was crystallised from light petroleum affording 1-2-*aminophenyl*-4-*ethoxycarbonylpiperazine*, m. p. 109·5—110° (Found: C, 62·5; H, 7·9; N, 16·8. $C_{13}H_{19}O_3N_3$ requires C, 62·6; H, 7·6; N, 16·9%). The amine (5·0 g.) was dissolved in warm water (44 c.c.) and hydrochloric acid (*d* 1·16; 6·0 c.c.); on cooling, the hydrochloride separated [m. p. 240° (decomp.)] and was diazotised to a deep yellow-brown solution which on interaction with sodium azide produced a brown oil. The latter was taken up in nitrobenzene, and decomposed at 170—180°, and the solution concentrated *in vacuo*. Aniline was found in the distillate. As no solid separated from the residue it was extracted with dilute hydrochloric acid; addition of aqueous sodium acetate gave a black precipitate which was removed, and from the filtrate aqueous ammonia liberated a base which was extracted into benzene and chromatographed on alumina, giving, from the bottom up, a small yellow band, a long pale yellow zone, a small pale orange, and a small black band. The benzene eluate of the pale yellow zone yielded a yellow oil (0·25 g.), giving a solid, m. p. 124—125°, from ethyl acetate. Drying and extraction of the yellow zone with methanol also gave an oil (0·55 g.), giving a solid, m. p. 124—125°, from ethyl acetate. Addition of picric acid to the filtrates gave a picrate, m. p. 216—218° (decomp.); this was collected and decomposed with dilute aqueous sodium hydroxide, and the base taken into benzene which was then removed; the residue, crystallised from ethyl acetate, had m. p. 126—127°. Mixed m. p.s having shown all samples to be identical they were mixed and crystallised from ethyl acetate, yielding 4′-*ethoxycarbonylpiperazino*(1′ : 2′-1 : 2)-*benziminazole* (XV) (0·3 g.), m. p. 126—127° (Found: C, 63·4; H, 6·6; N, 16·8. $C_{13}H_{15}O_2N_3$ requires C, 63·8; H, 6·1; N, 17·1%).

5-*Chloro*-4′-*ethoxycarbonylpiperazino*(1′ : 2′-1 : 2)*benziminazole* (XVI).—1-Ethoxycarbonylpiperazine (12·1 g.), 1 : 4-dichloro-2-nitrobenzene (7·35 g.), and ethanol (25 c.c.) were heated on the steam-bath for 20 hr., the ethanol was removed, and the orange gum treated with water and extracted with benzene which on evaporation left an orange oil. This was reduced directly with iron in aqueous acetic acid. The cold mixture was filtered and the iron oxides were dried; both filtrate and oxides were extracted with chloroform, which on evaporation and crystallisation of the residues from light petroleum (b. p. 80—100°), then from ethyl acetate, yielded colourless granules of 1-(2-*amino*-4-*chlorophenyl*)-4-*ethoxycarbonylpiperazine*, m. p. 119—120° (Found: C, 55·2; H, 6·6; N, 14·8. $C_{13}H_{18}O_2N_3Cl$ requires C, 55·0; H, 6·35; N, 14·8%). Diazotisation (7·8 g.) and reaction with sodium azide produced a pinkish solid azido-derivative which was collected, dissolved in nitrobenzene, and decomposed. The basic products were extracted with dilute hydrochloric acid, recovered by basification, taken up into ethyl acetate, and converted into the picrate (4·8 g.). This was decomposed with dilute aqueous sodium hydroxide. Then benzene-extraction yielded crude base (2·2 g.), m. p. 109—119°. On chromatography from benzene on alumina the first eluate afforded the *base* (XVI), m. p. 129—131° (from ethyl acetate) (Found: C, 56·3; H, 5·2; N, 14·8. $C_{13}H_{14}O_2N_3Cl$ requires C, 55·9; H, 5·0; N, 15·0%).

1-*Amino*-5-*nitro*-2 : 4-*dipiperidinobenzene* (XVIII).—To a solution of piperidine (40 c.c.) in boiling ethanol (150 c.c.) was added with stirring during 30 min. 2 : 4-dichloro-1 : 5-dinitrobenzene (11·85 g.), and the whole was boiled for 1 hr. and cooled; the yellow crystals were collected, washed with water, and dried (91%; m. p. 116—117°). The compound contained no chlorine. A sample, crystallised from glacial acetic acid, yielded 1 : 5-dinitro-2 : 4-dipiperidinobenzene, m. p. 117—118° (Found: C, 57·7; H, 5·6; N, 16·9. Calc. for $C_{16}H_{22}O_4N_4$: C, 57·5; H, 6·6; N, 16·8%) (Le Fèvre and Turner, *J.*, 1927, 1118, give m. p. 130—131°). The latter

(87 g.) was reduced in boiling ethanol with sodium disulphide [from sodium sulphide nonahydrate (62·5 g.) and sulphur (8·35 g.)] added during 20 min., and the whole was boiled overnight; the ethanol was removed, and water was added to the residue which was then extracted with benzene and washed with cold water until the washings were pale yellow. The benzene solution was filtered, dried (Na_2SO_4), and taken to dryness; the residue crystallised, was collected, washed with ethanol at 3—5°, and air-dried (43 g.). The solid was dissolved in 2N-hydrochloric acid (300 c.c.) and filtered from unchanged dinitro-compound (3·7 g.), and the filtrate was poured slowly into boiling dilute aqueous sodium hydroxide; an oil was precipitated which crystallised in deep crimson granules and there was collected from the hot solution the *base* (XVIII) (37·0 g.), m. p. 129—130° not altered by crystallisation from ethyl acetate (Found: C, 63·4; H, 8·3; N, 18·6. $C_{16}H_{24}O_2N_4$ requires C, 63·2; H, 7·9; N, 18·6. $C_{16}H_{24}O_2N_4$ requires C, 63·2; H, 7·9; N, 18·4%).

5-Amino-6-piperidinopiperido(1′ : 2′-1 : 2)benziminazole (XIX).—Diazotisation of the above base (21·2 g.) afforded the deep orange-brown diazo-solution which, added to sodium azide in aqueous sodium acetate, gave a tarry azide. A crystalline form was obtained by adding sodium acetate to the diazo-solution, followed by sodium azide. Either form dissolved in nitrobenzene and, when heated to 120—130°, evolved not only nitrogen but also nitrogen oxides; heating was continued to 170—180°, the nitrobenzene was reduced to small volume *in vacuo*, and the residue was extracted with diluted hydrochloric acid, boiled to remove nitrobenzene, and basified with sodium carbonate. The dry crude product was extracted with boiling light petroleum (b. p. 80—100°) (*ca.* 250 c.c.), from which crystallised an orange substance (*ca.* 1·0 g.), m. p. 100—110°. The insoluble portion was dissolved in benzene and chromatographed on alumina, yielding a large orange fraction which on evaporation provided a sticky orange base (8·5 g.) converted by ethanolic hydrochloric acid into a hydrochloride (7·1 g.), decomp. 240° (after washing with cold acetone). The hydrochloride on basification yielded an orange-red mass (5·1 g.) consisting of orange and red crystals which proved to be two forms of *5-nitro-6-piperidinopiperido(1′ : 2′-1 : 2)benziminazole* (XIX), scarlet needles, m. p. 137—140°, resolidifying to an orange form, m. p. 155—156° (Found: C, 63·9; H, 7·8; N, 19·0. $C_{16}H_{20}O_2N_4$ requires C, 64·0; H, 6·66; N, 18·66%). Slow evaporation *in vacuo* at room temperature of the substance in ethyl methyl ketone solution yielded the red needles; quick crystallisation from a concentrated solution in the ketone gave both forms; a less concentrated solution gave the red needles first (removed from the warm solution), then orange plates from the filtrate evaporated *in vacuo*. Reduction in methanol with Raney nickel and hydrogen at 50—55°/50 atm. yielded the *amine* (XX), which had m. p. 189—191° after sublimation *in vacuo*, chromatography on alumina from benzene, development with benzene–chloroform, and crystallisation from ethyl acetate (Found: C, 71·1; H, 8·0; N, 21·1. $C_{16}H_{22}N_4$ requires C, 71·1; H, 8·2; N, 20·7%).

Di[piperido(1′ : 2′-1 : 2)glyoxalino](4′ : 5′-1 : 2)(5″ : 4″-4 : 5)benzene (XXI).—The above amine (1·7 g.) in dilute hydrochloric acid was diazotised, yielding a reddish-orange solution which, added with stirring to sodium azide in aqueous sodium acetate, produced the azido-derivative as pale pink granules. These were heated in nitrobenzene and worked up as described above. Basification of the hydrochloric acid solution produced a dark sticky mass from which the liquid was decanted. From this liquid were slowly deposited purple leaflets which, twice crystallised from ethyl methyl ketone, yielded pinkish needles of a strong base, m. p. 284—287°. After 2 more days the liquid deposited a further crop (0·3 g.) from which at 245°/0·003 mm. was obtained a colourless sublimate of the *base* (XXI), m. p. 279—280° (Found: C, 72·0; H, 7·0; N, 21·3. $C_{16}H_{18}N_4$ requires C, 72·2; H, 6·8; N, 21·0%). The residue from the sublimation was a fluffy purple mass, m. p. >300° after sintering.

2 : 4-Dinitro-1 : 5-di-(2-pyridylamino)benzene.—2 : 4-Dichloro-1 : 5-dinitrobenzene (9·6 g.) and 2-aminopyridine (16·0 g.) were boiled in glycol monoethyl ether (60 c.c.) for 24 hr. No nitrous oxide was evolved. Solid began to separate during boiling and, on cooling, the mass set solid. The solid was collected, washed with more solvent, then water, and dried, yielding the *base* (10·3 g.), m. p. 236—238° (from chlorobenzene) (Found: C, 54·3; H, 3·9; N, 23·4. $C_{16}H_{12}O_4N_6$ requires C, 54·6; H, 3·4; N, 23·8%).

Attempts to condense 2 : 4-dichloro-1 : 5-dinitrobenzene with hexahydroazepine under the conditions used for piperidine led to a compound which did not give correct analyses for the expected product and afforded no nitro-amine on reduction with sodium disulphide.

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