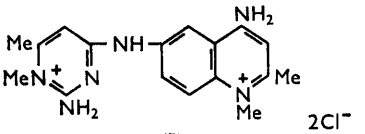
1044. *Bisquaternary Salts Related to Quinapyramine (Antrycide). Replacement of the Quinoline Nucleus by Other Heterocycles.*

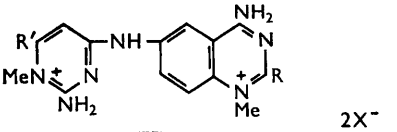
By S. S. Berg and E. W. Parnell.

Some analogues of quinapyramine [4-amino-6-(2-amino-4-methylpyrimid-6-ylamino)quinaldine 1,3′-bismethochloride] are described in which the quinaldine residue has been replaced by the bicyclic heterocyclic systems, quinazoline, phthalazine, indazole, benzothiazole, benzoxazole, benzisoxazole, and benzimidazole. Some of the compounds showed trypanocidal activity.

The trypanocidal activity of quinapyramine [1] (Antrycide) (I) led us to examine the effect on activity of replacing the quinaldine residue by quinazoline. The compounds (II; R′ = R″ = H or Me) obtained had similar activity to that of quinapyramine against *Trypanosoma congolense* and *T. rhodesiense*.* This suggested that the activity of these compounds might be a function of the pyrimidine portion and so some analogues of quinapyramine containing other bicyclic heterocyclic nuclei were prepared. Only those from phthalazine and benzoxazole showed significant activity, the former being comparable with quinapyramine.



(I)



(II)

Two general preparative routes were employed: (*a*) reaction of 2-amino-4-chloro-6-methylpyrimidine (III) with the appropriate heterocyclic diamine, with subsequent quaternisation; and (*b*) direct reaction of the methiodide of the pyrimidine (III) with the quaternary salt of the heterocyclic diamine.

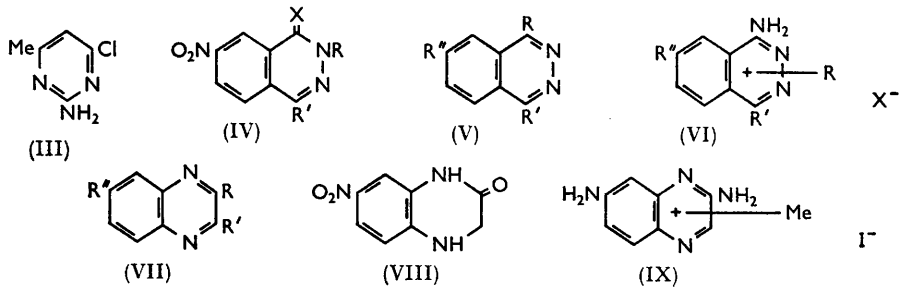
4,6-Diamino-2-methylquinazoline was prepared by reduction of 4-amino-2-methyl-6-nitroquinazoline [3] and was allowed to react with the chloro-compound (III). Treatment of the product with methyl toluene-*p*-sulphonate and subsequent conversion into the dichloride gave a product (II; R′ = R″ = Me, X = Cl) identical with that obtained from the methiodide of the pyrimidine (III) with 4,6-diamino-1,2-dimethylquinazolinium chloride [3] in hydrochloric acid.

Direct bromination of 6-nitrophthalide by recorded methods [4,5] was unsatisfactory for

* These compounds were claimed to be active in a patent [2] which appeared during the course of this work.

[1] Ainley, *J.*, 1953, 59.
[2] Curd and Young, Imperial Chemical Industries Limited, B.P. 696,692/1953.
[3] Berg, *J.*, 1961, 4041.
[4] Borsche, Diacont, and Hanau, *Ber.*, 1934, **67**, 676.
[5] Atkinson, Simpson, and Brown, *J.*, 1956, 1081.

large-scale preparations, but was better effected with 2,4-dibromo-5,5-dimethylhydantoin [6] in boiling chlorobenzene, and the product was converted directly into 1,2-dihydro-7-nitro-1-oxophthalazine (IV; R = R′ = H, X = O) by alkaline hydrolysis followed by treatment with hydrazine. The oxo-compound with phosphorus oxychloride–diethylaniline gave a better yield of the chloro-compound (V; R = Cl, R′ = H, R″ = NO_2) than was obtained by the method of Atkinson *et al.*[5] It was converted into the amine (V; R = NH_2, R′ = H, R″ = NO_2) by the published procedure.[5] In an alternative route, the phthalazone (IV; R = R′ = H, X = O) was treated with phosphorus pentasulphide in pyridine, affording the thiol (V; R = SH, R′ = H, R″ = NO_2), which with methyl sulphate in aqueous sodium hydroxide gave a mixture of *N*- and *S*-methyl derivatives. The *N*-methyl compound (IV; R = Me, R′ = H, X = S), which predominated, was separated by fractional crystallisation and was shown to be identical with an authentic specimen prepared from the phthalazone (IV; R = Me, R′ = H, X = O). When the methylation was effected with methyl iodide and sodium methoxide in anhydrous methanol, the *S*-methyl isomer (V; R = SMe, R′ = H, R″ = NO_2) predominated. Fusion of the S-methyl isomer with ammonium acetate gave the pure nitro-amine (V; R = NH_2, R′ = H, R″ = NO_2), but the crude mixture could also be used. This nitro-amine was also obtained by reaction of the thiol (V; R = SH, R′ = H, R″ = NO_2) with ammonium acetate and mercuric acetate. The nitro-amine was quaternised and the product was reduced to the methiodide (VI; R = Me, R′ = H, R″ = NH_2, X = I).



\+ — denotes attachment to one of the ring-N.

Reaction of 1,2-dihydro-4-methyl-7-nitro-1-oxophthalazine [7] (IV; R = H, R′ = Me, X = O) with phosphorus oxychloride gave the chloro-compound (V; R = Cl, R′ = Me, R″ = NO_2), which was converted *via* the 4-phenoxy-derivative into 4-amino-1-methyl-6-nitrophthalazine (V; R = NH_2, R′ = Me, R″ = NO_2). The methyl methosulphate was prepared, and was treated with ammonia to give a base which on trituration with ethereal hydrogen chloride gave the methochloride (VI; R = R′ = Me, R″ = NO_2, X = Cl). The corresponding ethiodide (VI; R = Et, R′ = Me, R″ = NO_2, X = I), prepared directly with ethyl iodide, was reduced to the amine (VI; R = Et, R′ = Me, R″ = NH_2, X = I). The parent base, 4,6-diamino-1-methylphthalazine (V; R = R″ = NH_2, R′ = Me), was obtained by reduction of the nitro-compound (V; R = NH_2, R′ = Me, R″ = NO_2).

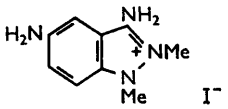
Attention was then turned from the phthalazines to the isomeric quinoxalines. Wolff *et al.*[8] condensed 4-nitro-1,2-phenylenediamine with butyl glyoxylate to give a mixture of isomeric quinoxalones. The corresponding chloro-compounds (VII; R = Cl, R′ = H, R″ = NO_2, or R = H, R′ = Cl, R″ = NO_2) were separated but structures were not assigned to the individual isomers. We find that partial reduction of 2,4-dinitrophenylglycine gives 1,2,3,4-tetrahydro-7-nitroquinoxal-2-one (VIII) which on conversion into the chloro-derivative with concomitant oxidation affords the compound (VII; R = Cl,

[6] Orazi and Meseri, *Anales Asoc. quím. argentina*, 1950, **38**, 307.
[7] Tirouflet, *Bull. Soc. Sci. Bretagne*, 1951, **26**, 7.
[8] Wolff, Pfister, Beutel, Wilson, Robinson, and Stevens, *J. Amer. Chem. Soc.*, 1949, **71**, 6.

R′ = H, R″ = NO_2). Since this work was completed, Cheeseman [9] has also prepared this chloro-compound by an unambiguous synthesis from 2-hydroxyquinazoline. The corresponding amine (VII; R = NH_2, R′ = H, R″ = NO_2) could not be quaternised or satisfactorily reduced. The known diamine [10] (VII; R = R″ = NH_2, R′ = H) was therefore converted into the diacetyl derivative and quaternised by fusion with methyl toluene-*p*-sulphonate. Hydrolysis of the corresponding iodide to the required diamine (IX) was accomplished only in very poor yield. The diamine (VII; R = R″ = NH_2, R′ = H) was therefore condensed with 2-amino-4-chloro-6-methylpyrimidine (III) but attempts to quaternise the resulting base failed.

Some compounds containing 5-membered heterocyclic rings were then synthesised. Reduction of 3-amino-1,2-dimethyl-5-nitroindazolium iodide [11] gave the corresponding diamine (X). The benzothiazole analogue (XI) and the corresponding ethiodide were obtained by quaternisation of 6-acetamido-2-aminobenzothiazole [12] followed by hydrolysis. 3-Amino-6-nitro-1,2-benzisoxazole (XII) was prepared by a modification of the method of Lindemann and Cissée [13] and was converted into the methiodide (through the methosulphate) and thence by reduction into 3,6-diamino-2-methyl-1,2-benzisoxazolium iodide (XIII).

2-Amino-5-nitrobenzoxazole (XIV; R = NH_2) was obtained by the reaction of 2-amino-4-nitrophenol with cyanogen bromide (cf. Pierron [14]). Fusion of 2-mercapto-5-nitrobenzoxazole (XIV; R = SH) with ammonium acetate and mercuric acetate gave a product whose analysis and chemical properties were consistent with its being the guanidine [XV; R = C(:NH)·NH_2], which on being heated lost ammonia to give compound (XIV;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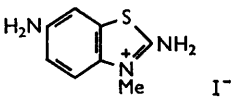
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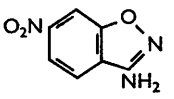
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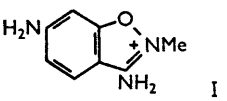
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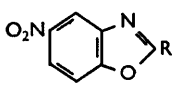
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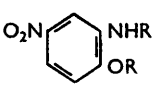
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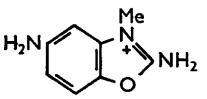
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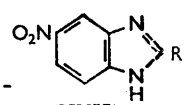
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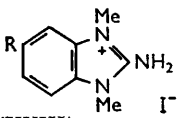

(XVIII)

R = NH_2). This aminobenzoxazole was soluble in dilute acid, but insoluble in 2N-aqueous sodium carbonate. Unexpectedly, it dissolved in 2N-aqueous sodium hydroxide, but was precipitated unchanged by acid. The possibility that this substance has the structure (XV; R = CN) was excluded by the absence of a band at 2200 $cm.^{-1}$ in the infrared spectrum (CN group), although it is possible that it passes into the phenol (XV; R = CN) in alkaline solution. Reduction of the methiodide of the nitrobenzoxazole (XIV; R = NH_2) afforded 2,5-diamino-3-methylbenzoxazolium iodide (XVI).

Kym and Ratner [15] have claimed the preparation of the amine (XVII; R = NH_2), m. p. 189—190°, by amination of the corresponding chloro-compound, which they obtained in poor yield from 5-nitrobenzimidazol-2-one. We were unable to repeat these preparations, but obtained the amine, m. p. 222—223° (decomp.), from 4-nitro 1,2-phenylenediamine and cyanogen bromide. On methylation it gave a mixture of two isomers; quaternisation of the mixture yielded 2-amino-1,3-dimethyl-5-nitrobenzimidazolium iodide (XVIII; R = NO_2) which was reduced to the diamine (XVIII; R = NH_2).

[9] Cheeseman, *J.*, 1961, 1246.
[10] Osdene and Timmis, *J.*, 1955, 2027.
[11] Parnell, *J.*, 1959, 2363.
[12] Kaufmann and Schultz, *Arch. Pharm.*, 1935, **273**, 31.
[13] Lindemann and Cissée, *Annalen*, 1929, **469**, 44.
[14] Pierron, *Ann. Chim. Phys.*, 1908, **15**, 191.
[15] Kym and Ratner, *Ber.*, 1912, **45**, 3258.

During this work an improved preparation of 2-amino-4-chloro-1-ethyl-6-methylpyrimidinium iodide [16] was developed.

Experimental

4,6-Diamino-2-methylquinazoline.—4-Amino-2-methyl-6-nitroquinazoline (48 g.) was suspended in methanol (800 ml.) and hydrogenated over Adams catalyst (4 g.) (uptake 16·15 l. in 2 hr.; 87·5%). After the catalyst had been filtered off, the green solution was evaporated *in vacuo*. A solution of the residue in 2N-acetic acid (350 ml.) was filtered through charcoal and basified (phenolphthalein) at 10—20° with 2N-sodium hydroxide. The yellow, crystalline *diamine* (36 g., 88%) was filtered off; a sample (1 g.), m. p. 240—245°, crystallised from water (25 ml.) as pale brown needles (0·7 g.), m. p. 244—246° (Found: C, 51·1; H, 6·8; N, 26·9; H_2O, 17·4. $C_9H_{10}N_4,2H_2O$ requires C, 51·45; H, 6·7; N, 26·65; H_2O, 17·1%).

2-Amino-4-(4-amino-2-methylquinazol-6-ylamino)-6-methylpyrimidine.—4,6-Diamino-2-methylquinazoline (21 g.), 2-amino-4-chloro-6-methylpyrimidine (18 g.), water (250 ml.), and concentrated hydrochloric acid (7·5 ml.) were refluxed together for 1 hr. The solution was diluted with water (400 ml.), cooled in ice, and basified at 10—15° with 2N-sodium hydroxide. The precipitate was filtered off and crystallised as yellow needles (29 g., 80·5%), m. p. 343—344°, from aqueous methanol (Found: C, 59·4; H, 5·3; N, 34·75. $C_{14}H_{15}N_7$ requires C, 59·8; H, 5·35; N, 34·8%).

This base (5 g.) and methyl toluene-*p*-sulphonate (8·5 g.) were melted together and kept at 150° for 0·5 hr. After being cooled, the hygroscopic solid was powdered under acetone, and the solid was quickly filtered off and dried over silica gel. The product from eight similar fusions was dissolved in hot water (2 l.), and sodium chloride (600 g.) was added. The resulting yellow solid was filtered off and crystallised from 2N-acetic acid (1 l.) and concentrated hydrochloric acid, to give the *dimethochloride* (29 g., 46%), m. p. >360° (Found: C, 46·1; H, 5·85; Cl, 17·1; N, 23·75; H_2O, 8·9. $C_{16}H_{21}Cl_2N_7O_2,2H_2O$ requires C, 45·9; H, 6·0; Cl, 16·95; N, 23·4; H_2O, 8·6%).

3-Bromo-6-nitrophthalide.—6-Nitrophthalide (25·5 g.) (Borsche *et al.*[4]), 2,4-dibromo-5,5-dimethylhydantoin (21·2 g.), and chlorobenzene (210 ml.) were illuminated with a tungsten lamp and refluxed in a bath at 160—170°. Heating was continued until the evolution of hydrogen bromide ceased (6—8 hr.). After being cooled, the 5,5-dimethylhydantoin was filtered off and the filtrate evaporated *in vacuo*. The residual gums from four preparations were combined and distilled at *ca.* 0·3 mm. from a retort heated in an air-bath at 185—190°. The pale yellow distillate, containing some crystals of 5,5-dimethylhydantoin, was dissolved in dry benzene (450 ml.). Next day the solution was filtered, and evaporation *in vacuo* gave the product (100—112 g., 71—78·5%) which did not solidify. Borsche *et al.*[4] described it as a yellow glass, m. p. *ca.* 90°.

1,2-Dihydro-7-nitro-1-oxophthalazine.—3-Bromo-6-nitrophthalide (105·5 g.) in water (1055 ml.) was refluxed for 45 min. and sodium hydroxide (49 g.) in water (440 ml.) was added to the nearly clear solution, cooled to 60—70°. The red solution was filtered and mixed with hydrazine sulphate (54·5 g.) in water (3040 ml.) at 50—60°. The solution was treated with 2N-sodium hydroxide until just alkaline to litmus and then immediately adjusted to pH *ca.* 4 by addition of acetic acid. After being stirred at 60° for 15 min. the granular, yellow solid (41—53 g., 50—65%), m. p. 224—227°, was filtered off. Crystallisation from water or anisole gave the product as pale yellow needles, m. p. 237—239° (Atkinson *et al.*[5] give m. p. 232—233°) (Found: C, 50·55; H, 2·65; N, 22·2. Calc. for $C_8H_5N_3O_3$: C, 50·25; H, 2·6; N, 22·0%).

1-Mercapto-7-nitrophthalazine.—To a stirred suspension of 1,2-dihydro-7-nitro-1-oxophthalazine (20 g.) in anhydrous pyridine (100 ml.) was added phosphorus pentasulphide (24 g.). The mixture was stirred and heated at 100° for 1·5 hr. and the solution was then poured into water (1 l.). The sticky solid, which soon hardened, was filtered off, dissolved in 0·1N-sodium hydroxide (2 l.), and filtered through charcoal from sulphur. The filtrate was acidified with acetic acid, and the *product* (13·5—15·2 g., 62·5—70%), m. p. 222—225°, collected (Found: C, 46·95; H, 2·7; N, 19·95; S, 15·2. $C_8H_5N_3O_2S$ requires C, 46·4; H, 2·4; N, 20·3; S, 15·5%).

Methylation of 1-Mercapto-7-nitrophthalazine.—(*a*) A solution of N-sodium ethoxide (245 ml.) was added to a fine suspension of 1-mercapto-7-nitrophthalazine in dry ethanol (~ 1·1 l.), followed by methyl iodide (14·5 ml.), and the mixture was refluxed for 1 hr. The clear solution

was evaporated *in vacuo*, and the residue treated with water, filtered off, and washed with 0·1N-sodium hydroxide and finally water. This product (48 g., 82·5%), m. p. 142—146°, was a mixture of *S*- and *N*-methylated products which were not easily separated. However, in one experiment the S-*methyl isomer* predominated and was purified by crystallisation from benzene–light petroleum (b. p. 60—80°) and then from ethanol as felted yellow needles, m. p. 180—181° (Found: C, 48·25; H, 3·65; N, 19·3; S, 15·5. $C_9H_7N_3O_2S$ requires C, 48·9; H, 3·2; N, 19·0; S, 14·5%).

(*b*) 1-Mercapto-7-nitrophthalazine (1 g.) in water (20 ml.) containing sodium hydroxide (0·425 g.) was stirred with methyl sulphate (0·53 ml.) for 1 hr., and the yellow precipitate was filtered off, washed with 0·1N-sodium hydroxide and water, and dried. Crystallisation from benzene–light petroleum (b. p. 60—80°) gave the crude *product* (0·7 g.), m. p. 135—150° (decomp.). Several recrystallisations from benzene–light petroleum (b. p. 60—80°) gave the pure *N*-methyl isomer as orange prisms, m. p. 161—162° (decomp.), not depressed by authentic 1,2-dihydro-2-methyl-7-nitro-4-thiophthalazine. This product depressed the m. p. of the higher-melting isomer obtained in method (*a*).

1,2-*Dihydro*-2-*methyl*-7-*nitro*-1-*thiophthalazine*.—1,2-Dihydro-2-methyl-7-nitro-1-oxophthalazine (1·25 g.) (Atkinson *et al.*[5]), phosphorus pentasulphide (1·5 g.), and anhydrous pyridine (6·25 ml.) were stirred on the steam bath for 1·5 hr. The suspension was added to ice-water (100 ml.), and the yellow, granular solid was filtered off, washed with water, and dried. The crude product (2·3 g.) was extracted with benzene (50 ml.), and the extract concentrated to about 15 ml. After being cooled, unchanged material (0·9 g.), m. p. 177—179°, was filtered off, and evaporation of the filtrate gave the orange *thione* (0·3 g.), which crystallised from light petroleum as yellow prisms (0·2 g.), m. p. 160—162° (decomp.) (Found: C, 49·2; H, 3·45; S, 14·35. $C_9H_7N_3O_2S$ requires C, 48·9; H, 3·2; S, 14·5%).

1-*Chloro*-7-*nitrophthalazine*.—1,2-Dihydro-7-nitro-1-oxophthalazine (5 g.), diethylaniline (4·45 ml.), and redistilled phosphorus oxychloride (25 ml.) were heated on the steam bath for 20 min., a yellow-brown solution being formed. This was refluxed until a deep red colour started to appear (*ca.* 5 min.); the solution was then rapidly cooled and poured on ice (*ca.* 500 g.). The mixture was stirred with charcoal, then filtered and basified at $<10°$ with 50% w/w aqueous sodium hydroxide. The precipitate was collected and resuspended in iced water to remove phosphate. After being dried the product was triturated with light petroleum (b. p. 40—60°) and was obtained as a buff solid (2·9 g., 53%), m. p. 156—159° (decomp.) (Atkinson *et al.*[5] give m. p. 155—157°). Attempts to crystallise the product caused decomposition.

1-*Amino*-7-*nitrophthalazine*.—(*a*) Ammonium acetate (80 g.) and the mixture of methylation products of 1-mercapto-7-nitrophthalazine [8 g. prepared by method (*a*)] were melted at *ca.* 160° (internal temperature 130—135°) for 0·75 hr. The melt was cooled and poured into water (800 c.c.), and the suspension basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide. The solid was filtered off and dissolved at 60° in 2N-acetic acid (200 ml.); this solution was filtered and basified with 50% w/w aqueous sodium hydroxide; the orange precipitate formed yellow crystals (1·7 g.), m. p. 306—308° (decomp.), from dimethylformamide. Crystallisation from ethanol gave felted orange needles, m. p. 309—310° (decomp.) (Found: C, 50·2; H, 2·9; N, 29·8. Calc. for $C_8H_6N_4O_2$: C, 50·5; H, 3·15; N, 29·5%). [Atkinson *et al.*[5] give m. p. 303—304° (decomp.).]

(*b*) 1-Mercapto-7-nitrophthalazine (1 g.), mercuric acetate (1·6 g.), and ammonium acetate (10 g.) were melted and kept at 140° (internal temperature) for 0·5 hr. The melt was heated with 2N-acetic acid (20 ml.) at *ca.* 90° for 5 min., filtered from mercuric sulphide, and basified with concentrated aqueous ammonia. The precipitate crystallised from aqueous dimethylformamide as orange needles (0·35 g., 38%), m. p. 313—315° (decomp.), identical with an authentic specimen of the nitro-amine.

1-*Methylamino*-7-*nitrophthalazine*.—1-Mercapto-7-nitrophthalazine (1 g.), mercuric chloride (2·7 g.), and methylamine (10 ml.) were mixed and kept in a sealed tube at 25—30° for 24 hr. The excess of methylamine was then evaporated, the residue ground with water (100 ml.), and the suspension saturated with hydrogen sulphide. The black mixture was heated to 80°, then filtered and basified at 10—20° with concentrated aqueous ammonia. The yellow precipitate was filtered off, washed with water, and dissolved in hot 2N-hydrochloric acid (15 ml.). The hydrochloride which crystallised was filtered off, washed with acetone, and dissolved in warm water (15 ml.). The solution was treated with charcoal, then filtered and basified while

hot with concentrated aqueous ammonia, to give the *methylamino-compound* (0·4 g., 40%) that crystallised from aqueous dimethylformamide as pale yellow needles, m. p. 220—223° (decomp.) (Found: C, 52·7; H, 4·1; N, 27·1. $C_9H_8N_4O_2$ requires C, 52·95; H, 3·9; N, 27·45%).

1-*Amino*-7-*nitrophthalazine Methiodide*.—A suspension of 1-amino-7-nitrophthalazine (12·4 g.) in dry nitrobenzene (248 ml.) was heated with methyl sulphate (6·5 ml.) on the steam-bath for 3 hr. The mixture was cooled in ice and filtered, and the residue washed with ether. Crystallisation from methanol gave yellow needles (12·3 g.), m. p. 255—257° (decomp.), which were dissolved in boiling water (350 ml.); potassium iodide (150 g.) was added. The iodide separated as red needles (11·2 g., 52%), m. p. 268—270° (decomp.), identical with the product prepared by the method of Atkinson *et al.*[5]

1,7-*Diaminophthalazine Methiodide*.—1-Amino-7-nitrophthalazine methiodide (11·2 g.) was shaken in methanol (336 ml.) with Adams catalyst (1·12 g.) and hydrogen at atmospheric pressure with intermittent warming to *ca.* 40°. The reduction required *ca.* 7 hr. The solution was then boiled, filtered, and evaporated *in vacuo*. Crystallisation of the residue from aqueous potassium iodide gave the *methiodide* (7·8 g., 77%) as pale brown plates, m. p. 297—299° (decomp.) (Found: I, 39·9; N, 17·4; H_2O, 5·9. $C_9H_{11}IN_4,H_2O$ requires I, 39·6; N, 17·5; H_2O, 5·6%).

4-*Chloro*-1-*methyl*-6-*nitrophthalazine*.—1,2-Dihydro-4-methyl-7-nitro-1-oxophthalazine (10 g.) and redistilled phosphorus oxychloride (50 ml.) were refluxed for 0·25 hr., cooled in ice, and added to ice-water (750 ml.). The suspension was filtered (charcoal) and the filtrate basified to pH 10·0 with 50% w/w aqueous sodium hydroxide at 5—20°. The pink solid (8 g., 73·5%) which separated decomposed at 160—161°, after shrinking at 140°. Attempts to crystallise the product caused decomposition.

4-*Amino*-1-*methyl*-6-*nitrophthalazine*.—4-Chloro-1-methyl-6-nitrophthalazine (15 g.), ammonium carbonate (60 g.), and phenol (120 g.) were heated on the steam-bath for 0·75 hr. The solution so obtained was cooled in ice, mixed with ice-water (600 ml.), and basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide at 0—10°. The brown precipitate was filtered off and washed with 2N-sodium hydroxide and water. The solid (19·5 g.), m. p. 215—220° (decomp.), was mainly 1-methyl-6-nitro-4-phenoxyphthalazine. It was added to ammonium acetate (90 g.) preheated to 180—185°. A clear red solution was obtained after 0·25 hr.; this was cooled in ice and treated with ice-water (600 ml.). The gummy mixture was basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide at 0—10°, and the yellow solid was filtered off and washed with water. The damp cake was dissolved in 2N-acetic acid (450 ml.), and the filtrate was basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide at 0—10°. The yellow *amine* (10·5 g., 73·5%), m. p. 274—275° (decomp.), was used without further purification. A sample crystallised from ethanol as yellow needles, m. p. 282° (decomp.) (Found: C, 52·7; H, 4·5; N, 27·0. $C_9H_8N_4O_2$ requires C, 52·95; H, 3·9; N, 27·45%).

The amine (1 g.) with methyl sulphate (0·62 g., 0·47 ml.) in nitrobenzene (10 ml.), gave the *methosulphate*, isolated as the *methochloride* (0·8 g., 64%) which crystallised from methanol–acetone as pink needles, m. p. 310—312° (decomp.) (Found: Cl, 14·2; N, 21·7. $C_{10}H_{11}ClN_4O_2$ requires Cl, 13·95; N, 22·0%).

The amine (15 g.), ethyl iodide (30 ml.), and 2-ethoxyethanol (150 ml.) were heated on the steam-bath for 5 hr., to give the *ethiodide* (11·2 g., 42%), orange needles, m. p. 283—285° (decomp.) (from water) (Found: I, 35·1; N, 15·6. $C_{11}H_{13}IN_4O_2$ requires I, 35·3; N, 15·5%).

4,6-*Diamino*-1-*methylphthalazine*.—4-Amino-1-methyl-6-nitrophthalazine (10 g.) in 3N-acetic acid (200 ml.) was hydrogenated at atmospheric pressure (Adams catalyst, 1 g.: uptake 89% in 4·5 hr.). The suspension was filtered and the filtrate basified (phenolphthalein) at 0—10° with 50% w/w aqueous sodium hydroxide. The *p roduct* (9 g.) crystallised from water (100 ml.) as brown needles (7 g., 82%), m. p. 274—275° (d ecomp.) (Found: C, 62·0; H, 5·9; N, 31·8. $C_9H_{10}N_4$ requires C, 62·05; H, 5·75; N, 32·2%).

4,6-*Diamino*-1-*methylphthalazine Ethiodide*.—4-Am ino-1-methyl-6-nitrophthalazine ethiodide (8 g.), suspended in ethanol (100 ml.), was similarly reduced (catalyst 0·8 g.; uptake 100% in 1 hr.). The suspension was warmed to effect solution and the catalyst was filtered off. When the filtrate was cooled in ice, the *ethiodide* (6 g., 82%) separated as brown prisms, m. p. 293—295° (decomp.) (Found: I, 38·2; N, 17·0. $C_{11}H_{15}IN_4$ requires I, 38·5; N, 17·0%).

2-*Amino*-4-(4-*amino*-1-*methylphthalazin*-6-*ylamino*)-6-*methylpyrimidine*.—4,6-Diami no-1-methylphthalazine (8 g.), 2-amino-4-chloro-6-methylpyrimidine (7 g.), and water (100 ml.)

containing concentrated hydrochloric acid (3 ml.) were refluxed for 1 hr. The hot solution was diluted with water (200 ml.), cooled to 5—10°, and basified (phenolphthalein) with 50% w/w aqueous sodium hydroxide. The pink solid which crystallised was filtered off and recrystallised from aqueous pyridine (500 ml. containing 100 ml. of pyridine). The *product* (11·3 g., 91%) separated as grey needles, m. p. 315—316° (decomp.) (softens at 181—184°) (Found: C, 55·85; H, 5·8; N, 32·6. $C_{14}H_{15}N_7,H_2O$ requires C, 56·1; H, 5·7; N, 32·75%).

This base (9 g.) was heated in nitrobenzene (150 ml.) with methyl sulphate (5·7 ml.) on the steam bath for 3 hr. After being cooled to 20°, the crude bismethosulphate was filtered off, washed with acetone, dissolved in water (300 ml.), treated with charcoal, and filtered. The filtrate was neutralised (litmus) with sodium hydrogen carbonate. Addition of sodium chloride caused the dimethochloride to crystallise. After being cooled in ice, the white solid was filtered off, washed with brine, and dissolved in warm 2N-acetic acid (300 ml.). Concentrated hydrochloric acid (30 ml.) was added to the filtered solution; the *dimethochloride* (8·5 g., 60·5%) separated as white needles, m. p. 322—324° (decomp.) (Found: Cl, 17·0; N, 24·25; H_2O, 6·3. $C_{16}H_{21}Cl_2N_7,1{\cdot}5H_2O$ requires Cl, 17·3; N, 23·95; H_2O, 6·6%).

2-Amino-4-chloro-6-methylpyrimidine Ethiodide.—2-Amino-4-chloro-6-methylpyrimidine (100 g.), ethyl sulphate (130 ml.), and dry nitrobenzene (200 ml.) were heated on the steam-bath for 16 hr. The cooled dark solution was mixed with ether (300 ml.) and extracted with water (3 × 100 ml.). After being washed with ether, the aqueous extract was neutralised with solid sodium hydrogen carbonate, a solid separating; this was starting material (30 g.). The filtrate was heated to *ca.* 60°, and sodium iodide (360 g.) added; cooling in ice caused the quaternary salt to separate as orange prisms (59 g.) containing some sodium iodide. This crystallised from 90% aqueous ethanol to give the product (25 g., 23·8% based on unrecovered starting material), m. p. 234—235° (decomp.) (Found: I, 42·3; N, 14·0; total halogen, 126·5 as AgX. Calc. for $C_7H_{11}ClIN$: I, 42·1; N, 13·7; total halogen as AgX, 125·0%). This product did not depress the m. p. of an authentic sample prepared by Stacey's method.[16]

3,5-Diamino-1,2-dimethylindazolium Iodide.—3-Amino-1,2-dimethyl-5-nitroindazolium iodide [11] (9·3 g.) was suspended in methanol (186 ml.) with Adams catalyst (0·93 g.) and hydrogenated at room temperature and pressure. Absorption of the theoretical quantity of hydrogen was complete in 0·3 hr. during which time the starting material dissolved and the product separated. The product was redissolved by warming the mixture to *ca.* 30° and the catalyst was filtered off. Treatment of the filtrate with ether (*ca.* 750 ml.) gave the *diamine* as buff crystals (7·3 g., 83%), m. p. 246—248° (decomp.) (from methanol) (Found: I, 41·2; N, 18·2. $C_9H_{13}IN_4$ requires I, 41·8; N, 18·4%).

6-Acetamido-2-amino-3-methylbenzothiazolium Iodide.—6-Acetamido-2-aminobenzothiazole [12] (30 g.) in boiling methanol (450 ml.) was refluxed overnight with methyl iodide (30 ml.). A solid which separated was filtered off [22·3 g., 44·5%; m. p. 310—314° (decomp.)]. Treatment of the mother liquor with an equal volume of ether gave a further crop (6·7 g., 12·5%), m. p. 303—307° (decomp.). The quaternary salt crystallised from water as buff blades, m. p. 311—313° (decomp.) (Found: I, 36·1; N, 12·3; S, 9·3. $C_{10}H_{12}IN_3OS$ requires I, 36·4; N, 12·1; S, 9·2%). The *ethiodide* was prepared similarly as white needles (from ethanol–ether), m. p. 230—234° (decomp.) (Found: I, 35·8; N, 11·6. $C_{11}H_{14}IN_3OS$ requires I, 35·0; N, 11·6%).

2,6-Diamino-3-methylbenzothiazolium Iodide.—The foregoing acetyl compound (29 g.) in N-hydrochloric acid (290 ml.) was refluxed for 1 hr. The cooled solution was neutralised with solid sodium hydrogen carbonate, then warmed to 90°, and sodium iodide (58 g.) was added. After being cooled, the *product* (23 g., 90%) was filtered off; it crystallised from water as pale yellow needles, m. p. 271—273° (decomp.) (Found: I, 41·6; N, 13·9; S, 10·7. $C_8H_{10}IN_3S$ requires I, 41·3; N, 13·7; S, 10·4%). The *ethiodide* was similarly prepared as white prisms (from ethanol–ether), m. p. 235—236° (decomp.) (Found: I, 39·4; N, 13·8. $C_9H_{12}IN_3S$ requires I, 39·6; N, 13·1%).

6-Nitro-1,2-benzisoxazole-3-carboxhydrazide.—3-Methoxycarbonyl-6-nitrobenzisoxazole (48 g.) was heated in hot ethanol (1160 ml.) with hydrazine hydrate (13·4 ml.) for 0·5 hr., then cooled in ice, and the product (36 g., 75%) which separated was filtered off; it had m. p. 174—177° (Lindemann and Cissée [13] give m. p. 170°).

The hydrazide (25 g.) was ground in a mortar with concentrated hydrochloric acid (75 ml.) and washed with water (75 ml.) on to ice (75 g.). Sodium nitrite (12·5 g.) in water (63·5 ml.)

[16] Stacey, Imperial Chemical Industries Limited, B.P. 674,259/1952.

was added all at once, and the whole was shaken for 5—10 min. The hydrazide was converted into a bulky solid which was filtered off, washed with water, and dried *in vacuo* to give the azide (24·5 g., 94%), decomp. *ca.* 90°.

3-*Benzyloxycarbonylamino*-6-*nitro*-1,2-*benzisoxazole*.—The azide (15 g.), anhydrous toluene (150 ml.), and benzyl alcohol (7·5 ml.) were mixed together and heated carefully. An exothermic reaction occurred with evolution of nitrogen, and after the reaction had subsided the solution was refluxed for a further 0·3 hr. After being cooled, the *product* (15 g., 74·5%), m. p. 189—191° (sinters at 175°), was filtered off; it crystallised from ethanol as plates, m. p. 191—192·5° (Found: C, 57·3; H, 3·9; N, 13·3. $C_{15}H_{11}N_3O_5$ requires C, 57·5; H, 3·5; N, 13·4%).

3-*Amino*-6-*nitro*-1,2-*benzisoxazole*.—The above urethane (20 g.), suspended in acetic acid (60 ml.), was heated on the steam-bath whilst hydrogen bromide was passed in for 3 hr. The dark solution was poured into water (1 l.); the yellow precipitate of amine (10 g., 87%) melted at 220—224° (Lindemann and Cissée [13] give m. p. 234°). Crystallisation from methanol raised the m. p. to 234°.

The amine (17 g.) in dry nitrobenzene (170 ml.) was heated with methyl sulphate (9·9 ml.) on the steam-bath for 1·5 hr., cooled, and poured into ether (800 ml.). The solid was collected and dissolved in warm water (170 ml.); the solution was clarified with charcoal, and sodium iodide (65 g.) was added to the filtrate; the 3-*amino*-2-*methyl*-6-*nitro*-1,2-*benzisoxazolium iodide* (9·0 g., 50%) which separated crystallised from ethanol as pale yellow needles, m. p. 211—212° (decomp.) (Found: I, 39·8; N, 12·7. $C_8H_8IN_3O_3$ requires I, 39·6; N, 13·0%).

3,6-*Diamino*-2-*methyl*-1,2-*benzisoxazolium Iodide*.—3-Amino-2-methyl-6-nitro-1,2-benzisoxazolium iodide (16·4 g.) was hydrogenated in methanol (328 ml.) with Adams catalyst (1·64 g.) at room temperature and pressure. After removal of the catalyst the solution was poured into ether (1·3 l.). The *product* was precipitated as a cream solid (11·6 g., 78%), m. p. 239—241° (decomp.), which crystallised from aqueous sodium iodide as cream needles, m. p. 244° (decomp.) (Found: I, 42·4; N, 13·9. $C_8H_{10}IN_3O,0{\cdot}5H_2O$ requires I, 42·2; N, 13·95%).

2-*Amino*-5-*nitrobenzoxazole*.—2-Amino-4-nitrophenol (76·5 g.) was dissolved in ethanol (190 ml.) and diluted with water (190 ml.). To this supersaturated solution was added cyanogen bromide (54·5 g.), and the mixture was mechanically shaken overnight. The fine yellow solid was filtered off and stirred with hot water; the mixture was filtered and the solid (66·5 g.) had m. p. 290—295° (decomp.). Crystallisation from dimethylformamide (270 ml.) gave the *product* as minute yellow needles (51·5 g., 64%), m. p. 304° (decomp.) (Found: C, 47·3; H, 3·2; N, 23·0. $C_7H_5N_3O_3$ requires C, 47·0; H, 2·8; N, 23·4%). It was soluble in 2N-hydrochloric acid and 2N-sodium hydroxide, insoluble in 2N-acetic acid and 2N-sodium carbonate.

2-*Guanidino*-4-*nitrophenol*.—2-Mercapto-5-nitrobenzoxazole [17] (2 g.), mercuric acetate (3·3 g.), and ammonium acetate (10 g.) were melted at 160° (internal temperature 150°) for 0·5 hr. The cooled melt was mixed with 2N-acetic acid (20 ml.), warmed to 60°, and then filtered. Basification with concentrated aqueous ammonia gave the *product* as yellow needles (0·9 g.), m. p. 300° (decomp.) (changes form at 270°). After being purified by precipitation from acetic acid the compound had m. p. 303—304° (decomp.) (Found: C, 43·1; H, 4·3; N, 28·0. $C_7H_8N_4O_3$ requires C, 43·8; H, 4·1; N, 28·5%).

2-*Amino*-5-*nitrobenzoxazole from* 2-*Guanidino*-4-*nitrophenol*.—2-Guanidino-4-nitrophenol (1 g.) was heated at 280° for 0·5 hr., ammonia being evolved. The cooled solid was triturated with 2N-acetic acid and filtered off. After precipitation from 2N-hydrochloric acid with sodium hydrogen carbonate, the product (0·4 g.) had m. p. 304° (decomp.) undepressed on admixture with the material described above.

2-*Amino*-3-*methyl*-5-*nitrobenzoxazolium Iodide*.—To 2-amino-5-nitrobenzoxazole (18 g.) with methyl sulphate (10·4 ml.) in dry nitrobenzene (180 ml.) at 150° (0·5 hr.) gave, after normal treatment an *iodide* (15·3 g., 47%), yellow prisms, decomp. 205—210° (Found: I, 39·85; N, 13·1. $C_8H_8IN_3O_3$ requires I, 39·6; N, 12·8%).

2,5-*Diamino*-3-*methylbenzoxazolium Iodide*.—The foregoing salt (5 g.) was hydrogenated in methanol (150 ml.) as above. The gummy product was dissolved in water for further use.

2-*Amino*-5-*nitrobenzimidazole*.—To 4-nitro-1,2-phenylenediamine (40·5 g.) in dioxan (648 ml.) and water (162 ml.) was added cyanogen bromide (28·4 g.), and the mixture was shaken overnight and then evaporated *in vacuo*. The residual solid was treated with 1·2N-sodium hydroxide

[17] Deck and Dains, *J. Amer. Chem. Soc.*, 1933, **55**, 4986.

(500 ml.) at 60°. The mixture was filtered (charcoal) and kept at 60° whilst ammonium chloride (17 g.) in water (100 ml.) was added. After being cooled, the *product* (34 g., 72%), m. p. 220—223° (decomp.), crystallised as yellow needles. It recrystallised from water as a hemihydrate, m. p. 222—223° (decomp.) (Found: C, 45·0; H, 3·85; N, 30·0; H_2O, 5·0. Calc. for $C_7H_6N_4O_2,0{\cdot}5H_2O$: C, 44·9; H, 3·7; N, 30·0; H_2O, 4·8%) [Kym and Ratner [15] give m. p. 189—190°].

Methylation of 2-Amino-5-nitrobenzimidazole.—The base (27 g.) with methyl sulphate (21·6 ml.) in 2N-sodium hydroxide (227 ml.) gave a mixture (22·3 g., 76·5%), m. p. 257—307° (decomp.), of two *N*-methylbenzimidazoles that was used without separation to give a single quaternary salt (see below).

2-Amino-1,3-dimethyl-5-nitrobenzimidazolium Iodide.—To the foregoing mixture (22·3 g.) in anhydrous nitrobenzene (223 ml.) at 150° was added methyl sulphate (12·3 ml.). After 0·25 hr. the mixture was cooled, and acetone (670 ml.) was added. The resultant crystals were filtered off, washed with acetone, and dissolved in warm water (117 ml.). Sodium iodide (30 g.) was added. The *di-iodide* (26·0 g., 67%) which separated was filtered off; it crystallised from water as yellow prisms, m. p. 304—305° (decomp.) (Found: I, 38·1; N, 16·6. $C_9H_{11}I_2N_4O_2$ requires I, 38·0; N, 16·8%).

2,5-Diamino-1,3-dimethylbenzimidazolium Iodide.—2-Amino-1,3-dimethyl-5-nitrobenzimidazolium iodide (28·4 g.) was hydrogenated in methanol (568 ml.) as usual, to give a *diamine iodide* (87%) as colourless needles, m. p. 274—275° (decomp.) (from ethanol) (Found: I, 41·8; N, 18·3. $C_9H_{13}IN_4$ requires I, 41·8; N, 18·4%).

1,2,3,4-Tetrahydro-7-nitro-2-oxoquinoxaline.—To *N*-(2,4-dinitrophenyl)glycine [18] (10 g.) in methanol (200 ml.) was added sodium hydrogen carbonate (8·4 g.) dissolved in the minimum amount of water, and to the stirred suspension were added during 30 min. sodium sulphide nonahydrate (26 g.) and sodium hydrogen carbonate (8·4 g.) in water (60 ml.). An exothermic reaction occurred and the temperature rose to *ca.* 45°. After being stirred at room temperature for 4 hr. the mixture was cooled in ice and the precipitated sodium salts were filtered off and dissolved in warm water (700 ml.). After being filtered, the solution was acidified with acetic acid. The *product* (4·4 g., 55%) crystallised. It recrystallised from nitrobenzene as red plates with a bluish reflex, m. p. 262—264° (decomp.) (Found: C, 50·3; H, 3·75; N, 21·3. $C_8H_7N_3O_3$ requires C, 49·8; H, 3·6; N, 21·7%).

2-Chloro-7-nitroquinoxaline.—1,2,3,4-Tetrahydro-7-nitro-2-oxoquinoxaline (1·0 g.), phosphorus pentachloride (0·85 g.) and phosphorus oxychloride (6·5 ml.) were heated on the steam-bath for 1 hr. The cooled mixture was poured on ice; the dark brown solid which separated was filtered off and extracted with light petroleum (b. p. 60—80°) to give the product (0·2 g.), m. p. 190—193°, which crystallised from ethanol as slender cream needles, m. p. 193—194° identical with the compound, m. p. 191—193°, prepared by the method of Wolff *et al.*[8] (Found: C, 45·6; H, 2·2; Cl, 17·3. Calc. for $C_8H_4Cl_2N_3O_2$: C, 45·8; H, 1·9; Cl, 17·0%) (Cheeseman [9] gives m. p. 188—190°).

3,6-Diacetamidoquinoxaline Methiodide.—3,6-Diacetamidoquinoxaline [10] (6·0 g.) and methyl toluene-*p*-sulphonate (5·0 g.) were fused at 160° for 0·5 hr. Treating a solution of the product in hot water (180 ml.) with sodium iodide (40 g.) and crystallising the precipitate (6·6 g.) from aqueous sodium iodide or methanol gave the pure *methiodide*, m. p. 233—236° (decomp.) raised to 301—303° (decomp.) after drying at 100°/15 mm. (Found: I, 30·7; N, 13·5. $C_{13}H_{15}IN_4O_2,2H_2O$ requires I, 30·2; N, 13·25%).

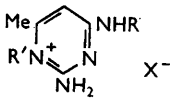
3,6-Diaminoquinoxaline Methiodide.—3,6-Diacetamidoquinoxaline methiodide (0·5 g.) and N-hydrochloric acid (5 ml.) were refluxed for 1 hr. The solution was filtered and neutralized with solid sodium hydrogen carbonate, and potassium iodide was added. The resultant brown solid (0·15 g.) was filtered off and washed with acetone. Crystallisation from aqueous sodium iodide gave the *diamine methiodide* as bronze plates, m. p. 233—235° (decomp.) (Found: C, 34·0; H, 3·9; I, 39·9. $C_9H_{11}IN_4,H_2O$ requires C, 33·8; H, 3·75; I, 39·7%).

2-Amino-4-(3-aminoquinoxalin-6-ylamino)-6-methylpyrimidine.—3,6-Diaminoquinoxaline [10] (3·4 g.) and 2-amino-4-chloro-6-methylpyrimidine (3·4 g.) in 2N-hydrochloric acid (102 ml.) were refluxed for 1 hr. After addition of water, the solution was basified with 50% w/w aqueous sodium hydroxide, to give the *product* (5·0 g., 90%), which crystallised from aqueous ethanol as buff needles, m. p. 288—290° (decomp.) (Found: C, 51·1; H, 5·5; N, 33·3; H_2O, 11·9. $C_{13}H_{13}N_7,2H_2O$ requires C, 51·5; H, 6·3; N, 32·3; H_2O, 11·9%).

[18] Abderhalden and Blumberg, *Z. physiol. Chem.*, 1910, **65**, 319.

Condensation of the Chloropyrimidine Quaternary Salt with the Heterocyclic Diamine Quaternary Salts. General Method.—The chloropyrimidine quaternary iodide (0·1 mol.), and the diamine quaternary salt (0·1 mol.) in 2N-hydrochloric acid (50 ml.) and water (350 ml.) were refluxed

Bisquaternary salts.



No.	R and salt *	R′	X	Yield (%)	Cryst. from	M. p. (decomp.)
1	4-Amino-2-methylquinazol-6-yl, A † ...	Me	Cl	70	2N-AcOH–HCl	⩽360°
2	4-Aminophthalazin-6-yl, B	Me	I	100		281—283
3	,, ,, A	,,	Cl	87	2N-AcOH–HCl	327
4	4-Amino-1-methylphthalazin-6-yl, D ...	Et	I	47·5	EtOH–Et_2O	305
5	3-Amino-1-methylindazol-6-yl, B	Me	I	91	H_2O	261—263
6	,, ,, ,, A	,,	Cl	73	H_2O	271—272
7	2-Aminobenzothiazol-6-yl, A	Me	Cl	79	H_2O	295—298
8	,, ,, D	Et	I	76·5	H_2O	308—309
9	,, ,, C	,,	Cl	64	EtOH–Et_2O	273—275
10	3-Amino-1,2-benzisoxazol-6-yl, B	Me	I	56	H_2O	235—245
11	,, ,, ,, A	,,	Cl	47	MeOH–$COMe_2$	260
12	2-Aminobenzoxazol-6-yl, B	Me	I	60	Aq. NaI	309—310
13	2-Amino-1-methylbenzimidazol-6-yl, B	Me	I	100	H_2O	332—334
14	,, ,, ,, A	,,	Cl	88	2N-HCl	315—320

* A = methochloride, B = methiodide, C = ethochloride, D = ethiodide.

† The *dichloride* was obtained directly from the reaction solution by neutralisation with sodium hydrogen carbonate, followed by addition of brine.

No.	Found (%) C	H	N	Hal	H_2O	Formula	Required (%) C	H	N	Hal	H_2O
1	46·1	5·85	23·75	17·1	8·9	$C_{16}H_{21}Cl_2N_7,2H_2O$	45·9	6·0	23·4	16·95	8·6
2			—						—		
3	—	—	24·6	17·9	4·9	$C_{15}H_{19}Cl_2N_7,H_2O$	—	—	24·8	17·9	4·5
4	—	—	15·5	40·4	5·5	$C_{18}H_{25}I_2N_7,2H_2O$	—	—	15·6	40·4	5·7
5	—	—	16·0	42·9	6·0	$C_{15}H_{21}I_2N_7,2H_2O$	—	—	16·6	43·0	6·1
6	44·0	6·4	23·1	18·0	—	$C_{15}H_{21}Cl_2N_7,2H_2O$	44·3	6·2	24·1	17·5	—
7	—	—	20·7	17·1	7·35	$C_{14}H_{18}Cl_2N_6S,2H_2O$	—	—	20·5	17·4	7·3
8	—	—	13·3	40·4	10·2	$C_{16}H_{22}I_2N_6S,3·5H_2O$	—	—	13·3	40·8	10·1
9	—	—	18·6	16·0	10·6	$C_{16}H_{22}Cl_2N_6S,2·5H_2O$	—	—	18·4	15·9	10·1
10	—	—	14·2	43·0	8·7	$C_{14}H_{18}I_2N_6O,3H_2O$	—	—	14·2	42·8	9·1
11	—	—	24·1	20·4	—	$C_{14}H_{18}Cl_2N_6O$	—	—	23·6	19·9	—
12	—	—	15·6	47·3	—	$C_{14}H_{18}I_2N_6O$	—	—	15·6	47·1	—
13	—	—	16·6	43·0	6·1	$C_{15}H_{21}I_2N_7,2H_2O$	—	—	16·6	43·2	6·1
14	—	—	23·35	17·4	8·95	$C_{15}H_{21}Cl_2N_7,2H_2O$	—	—	24·15	17·55	8·95

for 1 hr. The di-iodide, which crystallised on cooling, was converted into the corresponding dichloride by metathesis with silver chloride. The *products* are given in the Table. In some cases equally satisfactory results were obtained if the hydrochloric acid was omitted.

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Chemical Research Division B, Messrs. May and Baker Limited,
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