The Imputed Formation of 1,2,3-Triazoles, Triazines, and Triazepines from Hydrazinobenzoquinolines and Nitrous Acid. A Correction

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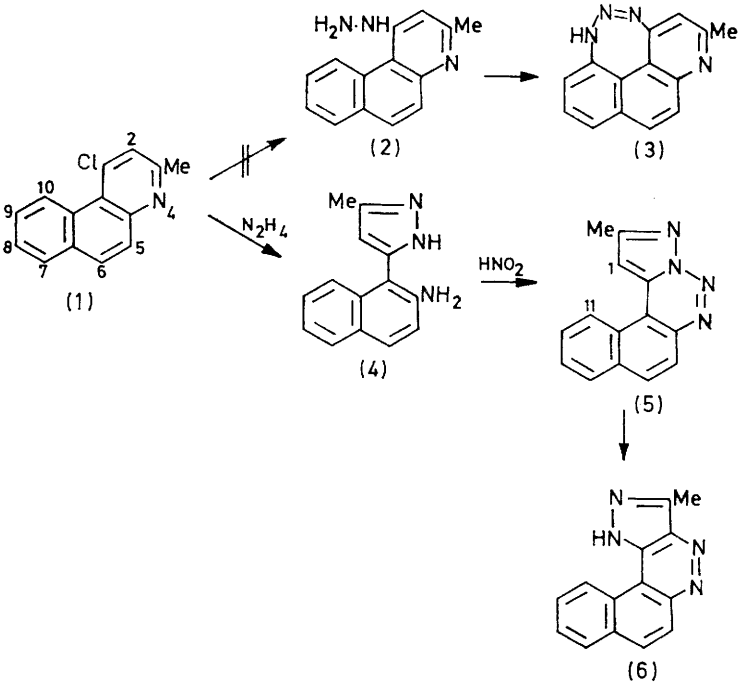
It has been claimed that the reactions of 1-chloro-3-methylbenzo[*f*]quinoline (1), 4-chloro-2-methylbenzo[*h*]-quinoline (7), 3-chloro-1-methylbenzo[*f*]quinoline (12), and 2-chloro-4-methylbenzo[*h*]quinoline (16) with hydrazine followed by nitrous acid give the 1,2,3-triazepine (3), the triazine (11), and the triazoles (15) and (19), respectively. These transformations are unprecedented. The products are now correctly identified as, respectively, the pyrazolotriazine (5), the azide (9), and the tetrazoles (14) and (18); the reactions involved are unexceptional. The first product isolated from the chloro-compound (1) and hydrazine is not the hydrazine (2) but the aminonaphthylpyrazole (4). The pyrazolotriazine (5) formed from this with nitrous acid rearranges thermally to the pyrazolopyridazine (6).

We recently described a synthesis of the first 1,2,3-triazepine, dibenzo[*d*,*f*][1,2,3]triazepine.[1] In view of the difficulty we experienced in obtaining this heterocyclic system, largely because of its instability, we were intrigued by a report by Tiagi and Joshi [2] of the formation of the 1,2,3-triazepine (3) by treatment of the hydrazine (2) with nitrous acid. Related cyclisations leading to the triazine (11) and the triazoles (15) and (19) from the isomeric hydrazines (8), (13), and (17), respectively, were also claimed.[2] This route to 1,2,3-triaza-heterocyclic systems, which is without precedent and reasonable mechanistic rationalisation, seemed worthy of reinvestigation. We now report that the structural assignments of the Indian workers are in error.



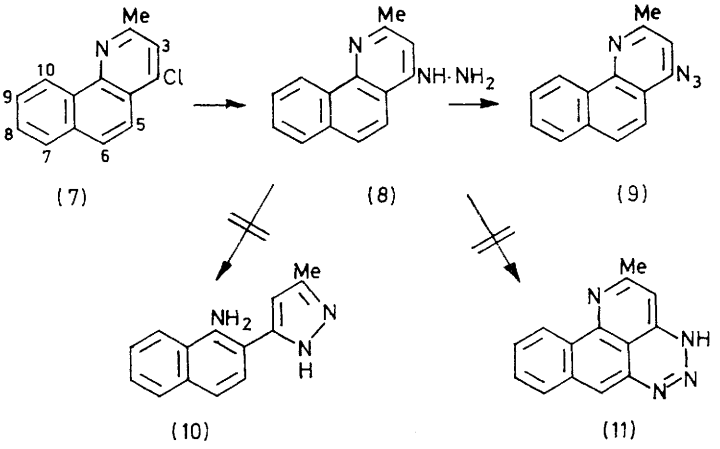
1-Chloro-3-methylbenzo[*f*]quinoline (1) was treated with hydrazine in refluxing glycerol as described by Tiagi and Joshi [2] to give a crystalline solid, m.p. 170—171 °C, which is presumably that claimed as the hydrazine (2) (reported [2] m.p. 161—162 °C). Treatment of this with nitrous acid gave a product A, $C_{14}H_{10}N_4$, m.p. 180—181 °C, corresponding to the triazepine (3) (reported [2] m.p. 180—181 °C). The high stability of this product, particularly towards acid, and our inability to detect an N–H function both spectroscopically by i.r. and n.m.r.† and chemically by alkylation and acylation led us to reject the triazepine structure (3). The product expected from treatment of the hydrazine (2) with nitrous acid is 1-azido-3-methylbenzo[*f*]quinoline. However this structure was ruled out for compound A by the absence of an azide i.r. absorption and also by synthesis of this azide by treatment of the chlorobenzoquinoline (1) with sodium azide in aqueous ethanol.

The problem of the structure of compound A is immediately resolved if the product from the chloro-compound (1) and hydrazine is the aminonaphthylpyrazole (4). This could arise from the hydrazine (2) by further reaction with hydrazine, and indeed analogous

† Tiagi and Joshi report an NH absorption at δ 8.35. In our spectrum this absorption showed fine structure and was not removed by addition of D_2O.

[1] S. F. Gait, M. E. Peek, C. W. Rees, and R. C. Storr, *J.C.S. Chem. Comm.*, 1972, 482; *J.C.S. Perkin I*, 1974, 1248.
[2] R. P. Tiagi and B. C. Joshi, *Bull. Chem. Soc. Japan*, 1972, **45**, 2507.

transformations have been observed previously with 4-chloroquinolines,[3] 4-chloro-1,8-naphthyridines,[4] and 4-chloroquinazolines [5] on treatment with hydrazine under comparable conditions. Spectral data support structure (4). Thus the chloro-compound (1) and the corresponding azide show low-field multiplets centred at δ 9.65 and 9.49 respectively for H-10. Such a low-field absorption is absent in the spectrum of the pyrazole (4) but would



be expected for the hydrazine (2); the pyrazole H-4 signal appears at δ 6.28. Careful attempts to convert the chloro-compound (1) into the hydrazine (2) with hydrazine under milder conditions failed.

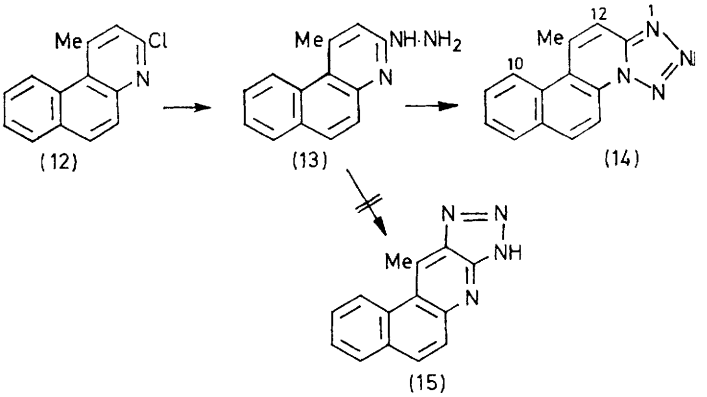
The reaction of the aminonaphthylpyrazole (4) with nitrous acid would be expected to give the triazine (5) (*cf.* ref. 3*a*), which is isomeric with the triazepine (3) and which better fits the available spectral and chemical properties of compound A. Predictably, the pyrazolotriazine (5) rearranges on heating to the more stable, isomeric pyrazolopyridazine (6). We therefore believe that the triazepine (3) reported by Tiagi and Joshi [2] is actually the triazine (5).

4-Chloro-2-methylbenzo[*h*]quinoline (7) on treatment with hydrazine gave the hydrazine (8), m.p. 172—173 °C, as reported.[2] In striking contrast with the chloro-compound (1), compound (7) could not be converted into the aminonaphthylpyrazole (10) even under vigorous conditions. This difference in reactivity between (2) and (8) possibly reflects the greater steric interaction across the 1- and 10-positions in (2). The expected low-field absorption of the proton on C-10 of the hydrazine (8) was observed at δ 9.27.

Treatment of the hydrazine (8) in hydrochloric acid with sodium nitrite, as described by Tiagi and Joshi, gave a yellow solution from which the azide (9), m.p. 145—146 °C, was precipitated on basification. This azide was identical with that prepared directly from the chloro-compound (7) with sodium azide. When the diazotisation was carried out in hydrochloric acid stronger that 2N, a pale yellow precipitate of the hydrochloride of the azide (9) was produced in amounts depending on the strength of the acid. Significantly this hydrochloride had m.p. 184—186 °C, close to that (189—190 °C) reported by Tiagi and Joshi for their product for which they assumed the triazine structure (11). Treatment of this hydrochloride with sodium carbonate liberated the free azide, which could be reconverted into the hydrochloride with hydrochloric acid. Thus we conclude that the triazine (11) claimed by Tiagi and Joshi is the azide (9) or its hydrochloride and that the sequence of transformations is entirely normal.

The trifluoromethyl analogue of chloro-compound (7) has also been converted into the corresponding azide *via* the hydrazine without complication.[6]

The 2-chlorobenzoquinoline derivatives (12) and (16) gave the corresponding hydrazines (13), m.p. 141—142 °C (*cf.*[2] 141—142 °C) and (17), m.p. 116—117 °C (*cf.*[2] 116—117 °C). In these cases further reaction with



hydrazine, such as occurred with compound (2), is not possible. The products from treatment of these hydrazines with nitrous acid are presumably the tetrazoles (14) and (18), respectively. Absence of the characteristic broad triazole N–H absorption in the i.r. spectra of both product rules out the proposed [2] triazole structures (15)

[3] (*a*) R. A. Bowie and B. Wright, *J.C.S. Perkin I*, 1972, 1109; (*b*) C. Alberti, *Gazzetta*, 1957, **87**, 772.

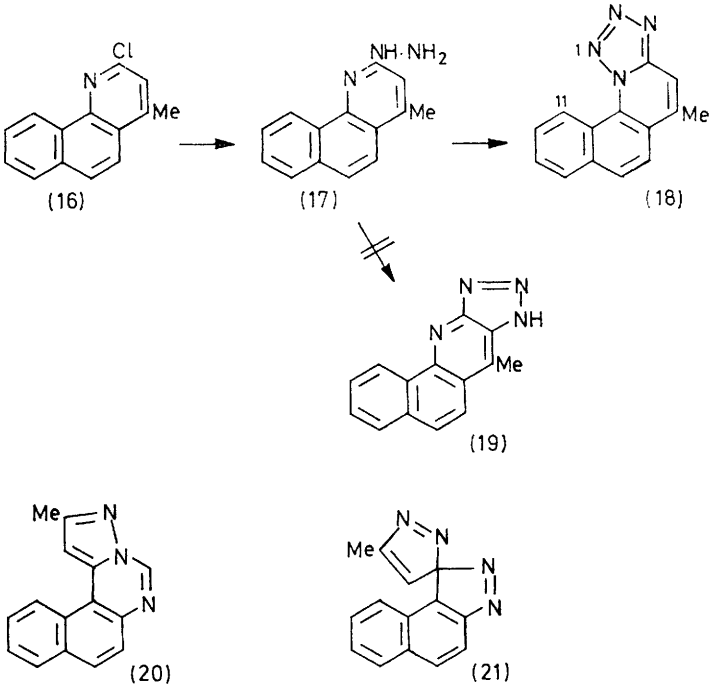
[4] R. A. Bowie, M. J. C. Mullan, and J. F. Unsworth, *J.C.S. Perkin I*, 1972, 1106.

[5] R. A. Bowie and D. A. Thomason, *J.C.S. Perkin I*, 1972, 1842.

[6] A. S. Dey and M. M. Joullié, *J. Heterocyclic Chem.*, 1965, **2**, 120.

and (19). In our hands the product from (13) had the same m.p., 214—215 °C, as that reported,[2] but that from (17) had m.p. 190—193 °C whereas Tiagi and Joshi report 160—161 °C. The tetrazole (18) shows a very low-field absorption centred at δ 10.37 for the C-11 proton consistent with its 'helicene-like' structure.* As expected, the isomer (14) does not show this low field absorption; the H-10 signal appears at δ 8.75.

Although we have not investigated the reactions of the hydrazines (8), (13), and (17) and the aminonaphthylpyrazole (4) with formic acid we suggest that the structures assigned [2] to the products of these reactions



are also in error. The hydrazine (8) presumably gave the formohydrazide; indeed the reported analysis (Found: N, 16.8. $C_{15}H_{13}N_3O$ requires 16.7%) fits this much better than the proposed product of cyclisation onto carbon. The 2-hydrazinoquinoline derivatives (13) and (17) presumably gave the fused 1,2,4-triazoles resulting from cyclisation of the formohydrazides onto nitrogen rather than carbon,[7] and the aminonaphthopyrazole (4) presumably gave the pyrazolopyrimidine (20). This last cyclisation has been effected in closely related systems with triethyl orthoformate.[4]

The isomerisation of the pyrazolotriazine (5) to the pyrazolopyridazine (6) described above is worthy of comment since thermal rearrangements of fused 1,2,3-triazines of this general type do not appear to have been reported before, though the somewhat related thermal rearrangement of 3-aryl-3,4-dihydro-4-imino-1,2,3-benzotriazines to 4-anilino-1,2,3-benzotriazines has been described by Stevens.[8] The acid-catalysed counterpart of a rearrangement closely related to the conversion of (5) into (6) has been reported and is reasonably considered to proceed through the open diazonium ion.[9] Our thermal rearrangement, in glycerol, may involve a similar diazonium ion or a dipolar species, and either would lead unambiguously to the product (6). However we cannot, at present, rule out a mechanism involving two successive 1,2-shifts (*i.e.* two [1,5] sigmatropic rearrangements) *via* the spiro-compound (21); this mechanism could give three possible isomers, including (6), but the structure (6) of the only product isolated is confirmed by its spectroscopic properties. It shows a characteristically broad pyrazole NH stretching absorption, and a downfield shift of the H-10 signal (δ 9.55) resulting from the helicene-like interaction with the pyrazole ring; the methyl absorption shows no such comparable shift.

EXPERIMENTAL

I.r. spectra are recorded for Nujol mulls.

Reactions of Chlorobenzoquinolines with Hydrazine Hydrate.—(i) *1-Chloro-3-methylbenzo*[f]*quinoline* (1).[10] The chloro-compound (500 mg, 2.2 mmol) and hydrazine hydrate (80%; 0.5 ml, 12.5 mmol) were heated under reflux in glycerol (25 ml) for 12 h. The resulting solution was cooled and poured into ice–water, and the precipitate was collected and recrystallised from methanol to give 5-(2-

* The 12-proton in naphtho[2,1-*h*]quinoline absorbs at δ 11.2 (R. H. Martin, E. V. Douckt, and F. Geerts-Evrard, *Tetrahedron*, 1964, **20**, 1495).

[7] W. Marckwald and E. Meyer, *Ber.*, 1900, **33**, 1885; W. Marckwald and M. Chain, *ibid.*, p. 1895.

[8] H. N. E. Stevens and M. F. G. Stevens, *J. Chem. Soc.* (*C*), 1970, 765.

[9] E. Koenigs and M. von Loesch, *J. prakt. Chem.*, 1935, **143**, 59; M. S. Gibson, *Chem. and Ind.*, 1962, 698.

[10] A. Albert, D. J. Brown, and H. Duewell, *J. Chem. Soc.*, 1948, 1284; A. K. Mallams and S. S. Israelstam, *J. Org. Chem.*, 1964, **29**, 3548.

amino-1-*naphthyl*)-3-*methylpyrazole* (4) (240 mg, 70%), m.p. 170—171 °C (lit.,[2] m.p. 161—162 °C for the product from this reaction) (Found: C, 75.6; H, 5.7; N, 19.0. $C_{14}H_{13}N_3$ requires C, 75.3; H, 5.8; N, 18.8%); $\nu_{max.}$ 3 400, 3 370, 3 230br, 1 620, 1 582, 1 252, 1 023, 961, 933, 818, 801, and 794 cm^{-1}; δ ($CDCl_3$) 2.33 (3 H, s, CH_3), 3.75—4.20 (3 H, NH, removed by D_2O), 6.28 (1 H, s, pyrazole H-4), and 6.93—8.00 (6 H, m, aromatic); *m/e* 223 (M^+).

The same product was obtained in lower yield by using a 1.5 : 1 molar ratio of hydrazine to chloro-compound as described by Tiagi and Joshi.[2] No reaction occurred in ethanol at room temperature over 24 h and in refluxing ethanol a complex mixture was obtained from which a small amount of the pyrazole (4) was the only isolable product.

(ii) 4-*Chloro*-2-*methylbenzo*[h]*quinoline* (7).[10] Treatment of this chloro-compound with hydrazine under the conditions described above gave 4-hydrazino-2-methylbenzo[*h*]-quinoline (8) (65%), which was purified by sublimation under reduced pressure and recrystallisation from petrol–benzene–ethanol to give needles, m.p. 174—175 °C (lit.,[2] 170—171 °C); *m/e* 223 (M^+); $\nu_{max.}$ 3 320, 3 120, 1 598, 1 570, 1 290, 819, 799, 764, and 718 cm^{-1}; δ ($CDCl_3$) 2.68 (3 H, s, CH_3), 3.56 (2 H, NH, removed by D_2O), 5.90—6.35 (1 H, NH, removed by D_2O), 6.77 (1 H, s, H-3), 7.19—7.84 (5 H, m, aromatic), and 9.27 (1 H, m, H-10). A similar yield was obtained from the reaction in refluxing ethanol (3 h). Prolonged heating of the chloro-compound (7) and hydrazine in glycerol or in ethanol in a sealed tube gave only the hydrazine (8) and no indication of the formation of the pyrazole (10).

(iii) 3-*Chloro*-1-*methylbenzo*[f]*quinoline* (12).[11] By the standard procedure this chloro-compound gave 3-hydrazino-1-methylbenzo[*f*]quinoline (13) (60%), needles from ether–petroleum, m.p. 141—142 °C (lit.,[2] 141—142 °C); *m/e* 223 (M^+); $\nu_{max.}$ 3 280br, 1 610, 1 509, 871, 833, 823, and 754 cm^{-1}; δ ($CDCl_3$) 3.12 (3 H, s, CH_3), 4.05 (2 H, NH, removed by D_2O), 6.10 (1 H, NH, removed by D_2O), 6.89 (1 H, s, H-2), 7.34—8.10 (5 H, m, aromatic), and 8.80 (1 H, m, H-10).

(iv) 2-*Chloro*-4-*methylbenzo*[h]*quinoline* (16).[11] This chloro-compound gave 2-hydrazino-4-methylbenzo[*h*]-quinoline (17) (60%), crystals from ether–petroleum, m.p. 116—117 °C (lit.,[2] 116—117 °C); *m/e* 223 (M^+); $\nu_{max.}$ 3 350br, 1 630, 1 605, 1 520, 1 227, 859, 821, 800, 752, and 725 cm^{-1}; δ ($CDCl_3$) 2.49 (3 H, s, CH_3), 3.95 (2 H, NH, removed by D_2O), 6.02 (1 H, NH, removed by D_2O), 6.57 (1 H, s, H-3), 7.40—7.97 (5 H, m, aromatic), and 9.18 (1 H, m, C-10).

2-*Methylnaphtho*[1,2-e]*pyrazolo*[1,5-c][1,2,3]*triazine* (5).—Sodium nitrite (240 mg, 3.5 mmol) in water was added slowly to a solution of the pyrazole (4) (450 mg, 2 mmol) in 2N-hydrochloric acid (20 ml) below 2 °C. The resulting solid was filtered off, washed with water, dried, and recrystallised from ethanol to give 2-*methylnaphtho*[1,2-e]*pyrazolo*[1,5-c]-[1,2,3]*triazine* (5) (275 mg, 61%) as yellow needles, m.p. 180—181 °C [lit.,[2] m.p. 180—181° for the 'triazepine' (3)] (Found: C, 71.8; H, 4.2; N, 23.8. $C_{14}H_{10}N_4$ requires C, 71.8; H, 4.3; N, 23.9%); *m/e* 234 (M^+) and 206 ($M^+ - N_2$); $\nu_{max.}$ 3 155 (C–H), 1 586, 1 280, 824, 779, 751, and 712 cm^{-1}; δ ($CDCl_3$) 2.65 (3 H, s, CH_3), 7.08 (1 H, s, H-1), 7.63—8.25 (5 H, m, aromatic), and 8.54 (1 H, m, H-11). The n.m.r. spectrum was unchanged by addition of D_2O.

3-*Methylbenzo*[f]*pyrazolo*[4,5-c]*cinnoline* (6).—The naphthopyrazolotriazine (5) (100 mg) was heated in glycerol at 200 °C for 3 min, and the resulting solution was poured into water to give a colourless solid. This was filtered off and recrystallised from ethanol–pyridine to give 3-*methylbenzo*[f]*pyrazolo*[4,5-c]*cinnoline* (6) (52%), m.p. 253—256 °C (Found: C, 71.6; H, 4.3; N, 24.05. $C_{14}H_{10}N_4$ requires C, 71.8; H, 4.3; N, 23.9%); *m/e* 234 (M^+) and 206 ($M^+ - N_2$); $\nu_{max.}$ 3 150br (NH), 1 614, 1 200, 1 146, 1 098, 985, 831, and 737 cm^{-1}; δ [$(CD_3)_2SO$] 2.71 (3 H, s, CH_3), 7.52—7.88 (3 H, m, aromatic), 7.88—8.34 (2 H, ABq H-6 and -7), and 9.55 (1 H, m, H-11).

1-*Azido*-3-*methylbenzo*[f]*quinoline*.—The chloro-compound (1) (600 mg) and sodium azide (600 mg) were heated under reflux in aqueous ethanol (80%; 25 ml), for 30 min. On cooling a yellow solid separated and this was filtered off and recrystallised from ethanol to give 1-*azido*-3-*methylbenzo*[f]*quinoline* (450 mg, 75%), as yellow needles, m.p. 143—144 °C (Found: C, 72.0; H, 4.3; N, 23.6. $C_{14}H_{10}N_4$ requires C, 71.8; H, 4.3; N, 23.9%); *m/e* 234 (M^+) and 206 ($M^+ - N_2$); $\nu_{max.}$ 2 115 (N_3), 1 565, 1 530, 1 341, 1 270, 1 236, 842, and 758 cm^{-1}; δ ($CDCl_3$) 2.65 (3 H, s, CH_3), 7.07 (1 H, s, H-2), 7.48—8.07 (5 H, m, aromatic), and 9.53 (1 H, m, H-10).

4-*Azido*-2-*methylbenzo*[h]*quinoline* (9).—(i) The chloro-compound (7) (2.5 g) and sodium azide (3.0 g) were heated under reflux in aqueous ethanol for 24 h. After cooling the resulting solid was filtered off and recrystallised from ethanol to give 4-*azido*-2-*methylbenzo*-[h]*quinoline* (9) (1.4 g, 55%), as pale yellow needles, m.p. 145—146 °C (Found: C, 71.7; H, 4.4; N, 23.6. $C_{14}H_{10}N_4$ requires C, 71.8; H, 4.3; N, 23.9%); *m/e* 234 (M^+) and 206 ($M^+ - N_2$); $\nu_{max.}$ 2 130 (N_3) 1 595, 1 349, 1 270, 976, 823, 800, 758, and 718 cm^{-1}; δ ($CDCl_3$) 2.75 (3 H, s, CH_3), 7.04 (1 H, s, H-3), 7.56—7.90 (5 H, m, aromatic), and 9.25 (1 H, m, H-10).

A solution of the azide (9) in ether was saturated with hydrogen chloride to give a yellow precipitate of 4-azido-2-methylbenzo[*h*]quinoline hydrochloride, m.p. 184—186°; $\nu_{max.}$ 2 190, 2 140 (N_3) 1 645, 1 625, 1 587, 1 300, 1 247, 1 038, 868, 830, and 762 cm^{-1}.

(ii) Sodium nitrite (240 mg, 3.5 mmol) in water was added to a solution of 4-hydrazino-2-methylbenzo[*h*]quinoline (8) (200 mg, 0.9 mmol) in 2N-hydrochloric acid (20 ml) below 2 °C. The yellow solution was basified to pH 10 with sodium carbonate solution and the resulting precipitate collected, washed with water, and recrystallised from ethanol to give the azide (9) (132 mg, 65%), m.p. 145—146 °C, identical with that obtained by procedure (i).

Treatment of the hydrazine (8) with sodium nitrite in 40% hydrochloric acid gave a yellow precipitate (without addition of sodium carbonate), m.p. 184—186 °C, identical with the hydrochloride of 4-azido-2-methylbenzo[*h*]quinoline (9). (Tiagi and Joshi [2] report m.p. 189—190 °C for the product from the diazotisation of 4-hydrazino-2-methylbenzo[*h*]quinoline.) The hydrochloride was converted into the free azide, m.p. 145—146 °C, by addition of sodium carbonate to its aqueous solution.

11-*Methylbenzo*[f]*tetrazolo*[5,1-a]*quinoline* (14).—Sodium nitrite (240 mg, 3.5 mmol) in water was added below 2 °C to a solution of 3-hydrazino-1-methylbenzo[*f*]quinoline (13) (200 mg, 0.9 mmol) in 2N-hydrochloric acid (20 ml). After 30 min, the resulting yellow precipitate was filtered off. The filtrate was basified with sodium carbonate and extracted with methylene chloride. Material from the extracts was combined with the precipitate and crystallised

[11] C. E. Kaslow and N. B. Sommer, *J. Amer. Chem. Soc.*, 1946, **68**, 644.

from benzene–ethanol to give 11-*methylbenzo*[f]*tetrazolo*-[5,1-a]*quinoline* (14) (110 mg, 53%) as yellow crystals, m.p. 214—215 °C [lit.,[2] m.p. 214—215 °C for the product from this reaction assigned the triazole structure (15)] (Found: C, 71.5; H, 4.2; N, 24.2. $C_{14}H_{10}N_4$ requires C, 71.8; H, 4.3; N, 23.9%); *m/e* 234 (M^+) and 206 ($M^+ - N_2$); $\nu_{max.}$ (KBr) 1 627, 1 450, 1 110, 828, and 749 cm^{-1}; δ ($CDCl_3$) 3.10 (3 H, s, CH_3), 7.42—8.05 (6 H, m, aromatic), and 8.75 (1 H, m, H-6).

5-*Methylbenzo*[h]*tetrazolo*[5,1-a]*quinoline* (18).—2-Hydrazino-4-methylbenzo[*h*]quinoline was treated with sodium nitrite as described above for the hydrazine (13) to give 5-*methylbenzo*[h]*tetrazolo*[5,1-a]*quinoline* (18) (55%), m.p. 199—200 °C (lit.,[2] 160—161 °C for the product from this reaction) (Found: C, 71.5; H, 4.2; N, 24.2. $C_{14}H_{10}N_4$ requires C, 71.8; H, 4.3; N, 23.9%); *m/e* 234 (M^+) and 206 ($M^+ - N_2$); $\nu_{max.}$ (KBr) 3 060, 2 930, 1 640, 1 609, 1 460, 1 091, 1 108, 871, 851, 817, and 760 cm^{-1}; δ ($CDCl_3$) 2.70 (3 H, s, CH_3), 7.58—7.96 (6 H, m, aromatic), and 10.37 (1 H, d, H-11).

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