Ring Transformations involving Chloroheterocycles. Part III.[1] Reaction of 4-Chloroquinazolines with Hydrazines

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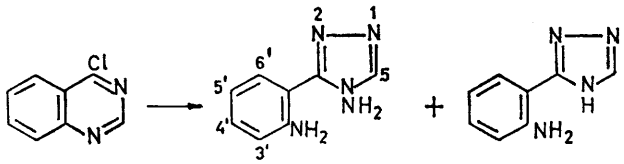
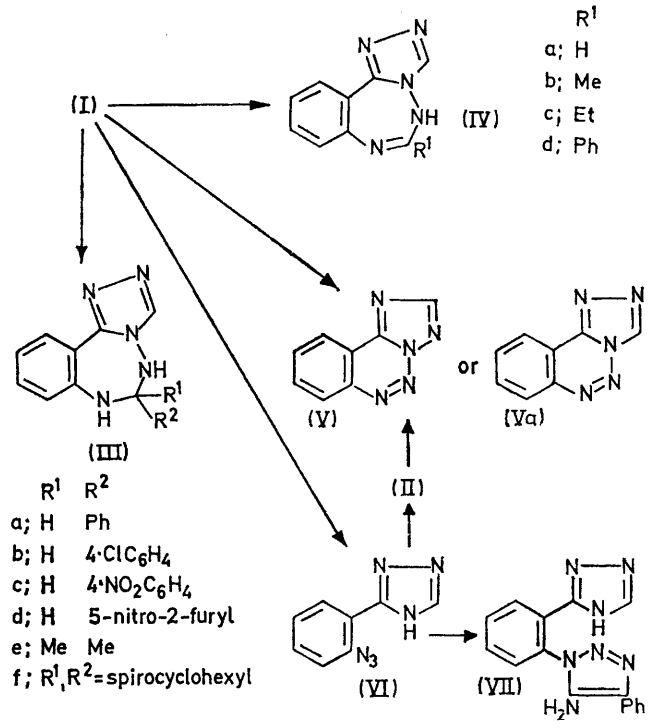
Treatment of 4-chloroquinazolines with hydrazine hydrate at 150 °C in a sealed tube gives 4-amino-3-(2-aminophenyl)-4*H*-1,2,4-triazoles. With 4-chloroquinazoline itself, a second product, 3-(2-aminophenyl)-4*H*-1,2,4-triazole, is also isolated. The novel 4-amino-4*H*-1,2,4-triazoles undergo ring closure with triethyl orthoesters to form 5*H*-1,2,4-triazolo[4,3-*d*][1,3,4]benzotriazepines, and with aldehydes and ketones to give 6,7-dihydro-5*H*-1,2,4-triazolo[4,3-*d*][1,3,4]benzotriazepines. 4-Amino-3-(2-aminophenyl)-4*H*-1,2,4-triazole has been shown to yield the 3-(2-azidophenyl)-4*H*-1,2,4-triazole with one equivalent of nitrous acid and 1,2,4-triazolo-[4,3-*c*][1,2,3]benzotriazine with two equivalents of nitrous acid. Treatment of 4-chloroquinazoline with substituted hydrazines yields 1,3-disubstituted 1*H*-1,2,4-triazoles. Mechanisms for these rearrangements are suggested.

4-Chloroquinolines and 5-chloro-1,8-naphthyridines rearrange with hydrazines to give pyrazoles.[1-3] In conjunction with the study of these reactions, 4-chloroquinazoline was treated with hydrazine hydrate at 150 °C in a sealed tube to give two products, the minor one containing four nitrogen atoms, $C_8H_8N_4$ (microanalysis; *m/e* 160) whose properties and reactions are consistent with the structure (II) (*cf.* ref. 4) and the major product containing five nitrogen atoms, $C_8H_9N_5$ (microanalysis; *m/e* 175). The n.m.r. spectrum of the major compound clearly showed the presence of four exchangeable NH protons at δ 7·2 (2H) and 7·1 p.p.m. (2H), a 4H multiple aromatic pattern, and a single proton at low field (δ 8·4 p.p.m.) which did not alter on deuteriation. The three protons at C-3′, -4′, -5′ in the products (I) and (II) were at δ 6·4—7·4 p.p.m. as is typical of aniline[5] (δ 6·5—7·1 p.p.m.) and not quinazoline[6]



(I) (II)

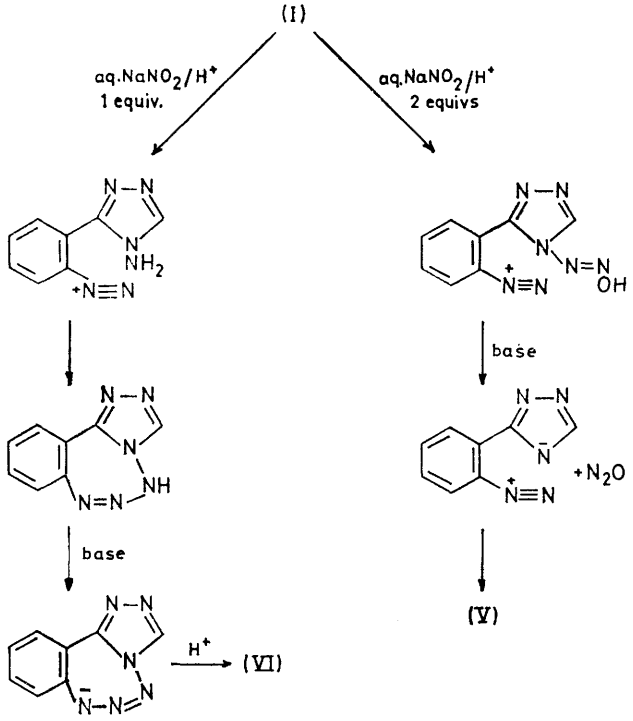
(δ 7·88—8·64 p.p.m.), strongly supporting ring-opened structures. The i.r. spectrum of the major product showed the presence of amino-groups with bands at 3400, 3300, 3250, and 3180 cm^{-1}. The major product was assigned the novel structure (I) and this was con-



[1] Part II, R. A. Bowie and B. Wright, *J.C.S. Perkin I*, 1972, 1109.
[2] C. Alberti, *Gazzetta*, 1957, **87**, 772.
[3] R. A. Bowie, M. J. C. Mullan, and J. F. Unsworth, *J.C.S. Perkin I*, 1972, 1106.
[4] K. T. Potts and E. G. Brugel, *J. Org. Chem.*, 1970, **35**, 3448.
[5] H. Spiesecke and W. G. Schneider, *J. Chem. Phys.*, 1961, **35**, 731; F. Langenbucher, E. D. Schmid, and R. Mecke, *ibid.*, 1963, **39**, 1901.
[6] W. L. F. Armarego and R. E. Willette, *J. Chem. Soc.*, 1965, 1258; A. R. Katritzky, R. E. Reavill, and F. J. Swinbourne, *J. Chem. Soc.* (*B*), 1966, 351.

firmed by the reaction of (I) with benzaldehyde to give 6,7-dihydro-6-phenyl-5*H*-1,2,4-triazolo[4,3-*d*][1,3,4]-benzotriazepine (IIIa; $R^1 = H$, $R^2 = Ph$). The n.m.r. spectrum of (IIIa; Table 4) showed the resonance for R^1 as a doublet of doublets which on deuteriation became a singlet. Similarly, reaction of (I) with triethyl orthoformate gave 5*H*-1,2,4-triazolo[4,3-*d*][1,3,4]benzotriazepine (IVa; $R^1 = H$), the n.m.r. spectrum of which (Table 6) showed the resonance for R^1 as a doublet which became a singlet on deuteriation. Treatment of (I) with other aldehydes and triethylorthoesters gave further novel compounds (IIIb—f) and (IVb—d) which are the first reported examples of the 5*H*-1,2,4-triazolo[4,3-*d*]-[1,3,4]benzotriazepine ring system.

4-Amino-3-(2-aminophenyl)-4*H*-1,2,4-triazole (I) on reaction with two equivalents of nitrous acid, gave 1,2,4-triazolo[1,5-*c*][1,2,3]benzotriazine [4,7] (V) in good yield. A possible mechanism (Scheme 1) for the formation of (V) involves the loss of nitrous acid.[8] The same product was also obtained from the reaction of nitrous acid with 3-(2-aminophenyl)-4*H*-1,2,4-triazole (II). The available data do not exclude representation of this product (V) as 1,2,4-triazolo[4,3-*c*][1,2,3]benzotriazine [4,7] (Va). However, reaction of equimolar amounts of

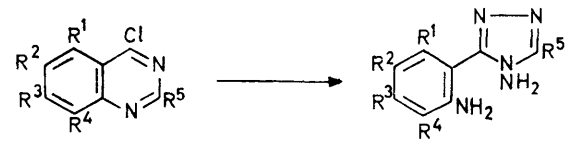


SCHEME 1

compound (I) and nitrous acid gave 3-(2-azidophenyl)-4*H*-1,2,4-triazole (VI) in 70% yield (Scheme 1). The i.r. spectrum of (VI) clearly showed azide bands at 2130 and 2090 cm^{-1}.

Treatment of 3-(2-azidophenyl)-4*H*-1,2,4-triazole (VI) with phenylacetonitrile under basic conditions gave the novel product 5-amino-4-phenyl-1-[2-(4*H*-1,2,4-triazol-3-yl)phenyl]-1*H*-1,2,3-triazole (VII), and reduction of (VI) with sodium borohydride in isopropanol yielded 3-(2-aminophenyl)-4*H*-1,2,4-triazole (II).

The formation of 4-amino-3-(2-aminophenyl)-4*H*-1,2,4-triazole (I) was also shown to take place by treatment of 4-hydrazinoquinazoline with hydrazine hydrate, suggesting that the hydrazino-derivative could be an intermediate in the formation of (I) and (II), and of 4-mercaptoquinazoline with hydrazine hydrate; both reactions being carried out in a sealed tube.



(VIII) (IX)

	R^1	R^2	R^3	R^4	R^5
a;	H	H	H	H	Me
b;	H	H	H	H	Et
c;	H	H	H	H	Pr^n
d;	H	H	H	H	Pr^i
e;	H	H	H	H	CH_2Ph
f;	H	H	H	H	Ph

	R^1	R^2	R^3	R^4	R^5
g;	H	Cl	H	H	H
h;	H	Me	H	H	H
i;	H	H	Cl	H	H
j;	H	Cl	H	Cl	H
k;	H	H	Cl	H	Me
m;	Cl	H	H	H	H

Other novel 4-amino-4*H*-1,2,4-triazoles (IXa—m) have been prepared by reaction of the corresponding 4-chloroquinazoline (VIII) and hydrazine hydrate in a sealed tube (Table 7).

Treatment of 4-chloro-2-n-propylquinazoline with hydrazine hydrate at 150 °C for 18 h in a sealed tube gave a mixture of 1,2-bis-(2-n-propylquinazolin-4-yl)-hydrazine (Xa) and the expected product (IXc). However, further heating of the mixture at 200 °C for 5 h yielded only (IXc). Similarly with 2-benzyl-4-chloroquinazoline, a mixture of 1,2-bis-(2-benzylquinazolin-4-yl)hydrazine (Xb) and the triazole (IXe) was obtained at 150 °C.

4-Hydrazino-2-phenylquinazoline [9] (XI) was obtained from the reaction of 4-chloro-2-phenylquinazoline and hydrazine hydrate at 150 °C in a sealed tube. However, reaction of 4-hydrazino-2-phenylquinazoline with hydrazine hydrate at 200 °C in a sealed tube gave the expected 4-amino-3-(2-aminophenyl)-5-phenyl-4*H*-1,2,4-triazole (IXf).

With 4,5-dichloroquinazoline [10] and hydrazine hydrate only a 10% yield of (IXm) was obtained. The major product (50%) was 3-(2-amino-6-chlorophenyl)-4*H*-1,2,4-triazole (XII). This was the only case where we obtained a greater yield of the deaminotriazole product.

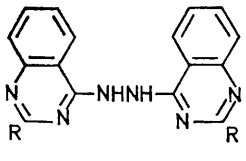
[7] R. A. Bowie, L. M. Fisher, and D. A. Thomason, unreported work.

[8] K. T. Potts, *Chem. Rev.*, 1961, **61**, 87; P. G. Gassman and K. Shudo, *J. Amer. Chem. Soc.*, 1971, **93**, 5899.

[9] M. Claesen and H. Vanderhaeghe, *Bull. Soc. chim. belges*, 1959, **68**, 220.

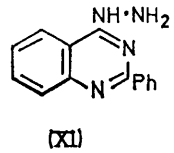
[10] H. C. Scarborough, B. C. Lawes, J. L. Minielli, and J. L. Compton, *J. Org. Chem.*, 1962, **27**, 957.

In the preparation of compounds (IXa—k) trace amounts of the corresponding deaminotriazole products were sometimes seen as judged by t.l.c. only.



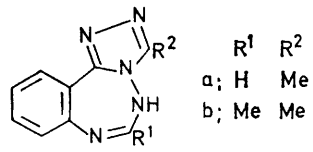
(X)

R
a; Pr^n
b; CH_2Ph



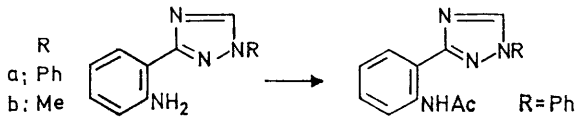
(XI)

(XII)



(XIII)

	R^1	R^2
a;	H	Me
b;	Me	Me



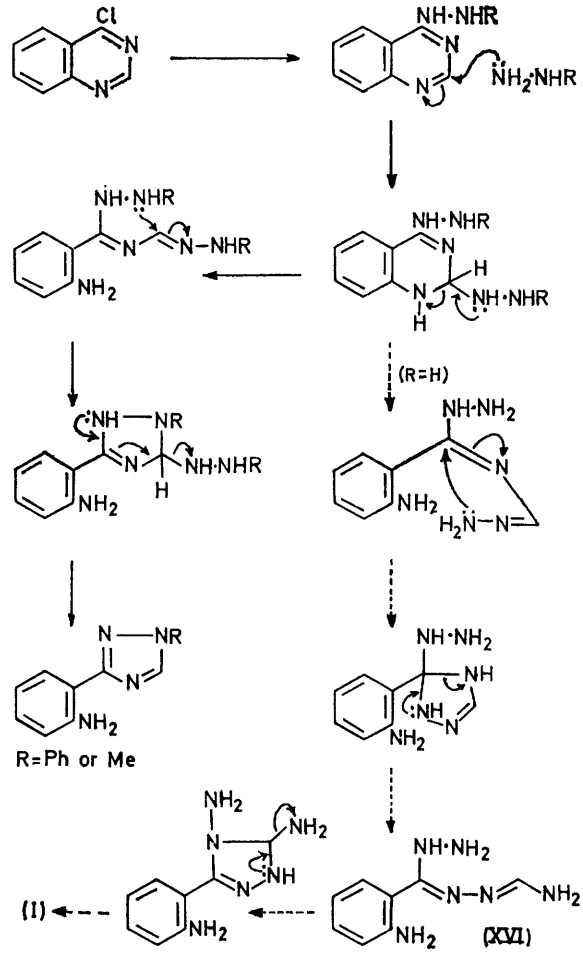
(XIV) (XV)

4-Amino-3-(2-aminophenyl)-5-methyl-4*H*-1,2,4-triazole (IXa) was obtained from 4-chloro-2-methylquinazoline and hydrazine hydrate in reasonable yield (40%). Treatment of (IXa) with triethyl orthoformate and triethyl orthoacetate gave further examples (XIIIa, b) of the novel 5*H*-1,2,4-triazolo[4,3-*d*][1,3,4]-benzotriazepine ring system.

4-Chloroquinazoline and phenylhydrazine in boiling anisole yielded 3-(2-aminophenyl)-1-phenyl-1*H*-1,2,4-triazole (XIVa). The structure of the product was established by n.m.r. studies since the proton in the triazole ring shifted downfield by δ 1·5 p.p.m. in Hexametapol compared to deuteriochloroform as solvent (*cf.* pyrazoles [1]). An attempted Pschorr reaction on (XIVa) was unsuccessful which gave further support for the structure suggested. Compound (XIVa) and acetic anhydride were heated together to give (XV), the n.m.r. spectrum of which showed the proton *ortho* to the acetamido-group at lower field (δ 8·45 p.p.m.) than in the corresponding amino-compound [(XIVa); δ 6·78 p.p.m.], thus confirming the postulated ring-opened structure for (XIVa).

The reaction of 4-chloroquinazoline and methylhydrazine in boiling toluene or in a sealed glass tube likewise gave the 1,3-disubstituted 1*H*-1,2,4-triazole [(XIVb); downfield shift (δ 0·65 p.p.m.) of triazole proton in Hexametapol compared to deuteriochloroform as solvent].

A two-step mechanism for the rearrangement of 4-chloroquinazoline with substituted hydrazines to give 1,3-disubstituted 1*H*-1,2,4-triazoles is suggested (Scheme 2; unbroken arrows). We have shown that reaction of 4-hydrazinoquinazolinium hydrochloride and phenylhydrazine in boiling ethanol for 72 h gave 3-(2-aminophenyl)-4*H*-1,2,4-triazole (II) proving that the hydrazino-group at C-4 of the quinazoline dictates the final product and that the hydrazino-group at C-2 is only needed to



SCHEME 2

ring-open the heterocyclic portion of the quinazoline structure.

However, a similar two-step reaction mechanism to explain the formation of 4-amino-3-(2-aminophenyl)-4*H*-1,2,4-triazole (I) from the reaction of 4-chloroquinazoline and hydrazine hydrate is not so straightforward as it involves the breaking of a C=N bond and elimination of ammonia (Scheme 2; broken arrows). The mechanism from intermediate (XVI) onwards requires that the hydrazino-group should react *via* the NH and not the NH_2 group to yield the *N*-aminotriazole since no chemical or physical evidence was obtained for the presence of dihydrotetrazines (which are known [8,11] to rearrange to *N*-aminotriazoles). In support of this suggestion, it has been reported [12] that methylhydrazine and phenylhydrazine are respectively further alkylated

[11] F. Dallacker, *Monatsh.*, 1960, **91**, 294.
[12] R. L. Hinman, *J. Org. Chem.*, 1958, **23**, 1587.

on the already substituted nitrogen atom due to its greater nucleophilicity.

EXPERIMENTAL

N.m.r. spectra were determined on a Varian A60 or a Varian HA100 instrument with tetramethylsilane as internal reference. I.r. spectra are for Nujol mulls and were recorded on a Perkin-Elmer model 157 spectrophotometer. Mass spectra were measured using a Hitachi RMU-6E or an AEI MS9 spectrometer.

Synthesis of Unreported 4-Chloroquinazolines. General Procedure.[10]—A quinazolin-4-one (0·06 mol), dimethylaniline (0·12 mol), and phosphoryl chloride (0·06 mol) in dry benzene (120 ml) were stirred under reflux for 2·25 h. The mixture was then cooled and the insoluble matter was removed by filtration. The mother liquor was diluted with benzene (150 ml) and the solution was washed with water (200 ml), and then with 20% aqueous sodium hydroxide (3 × 200 ml). The solution was again washed with water, dried ($MgSO_4$), and finally concentrated to give the required product (Table 1).

TABLE 1

Analytical data for chloroquinazolines

Compounds (VIII)	M.p. (°C)	Formula	Calc. (%) C	H	Cl	N	Found (%) C	H	Cl	N	Solvent of crystallisation	Yield (%)
(b)	55—57	$C_{10}H_9ClN_2$	62·35	4·7	18·4	14·55	62·0	4·6	18·2	14·5	*	65
(c)	b.p. 100—105°/0·3 mmHg	$C_{11}H_{11}ClN_2$	63·9	5·35	17·15	13·55	63·7	5·6	17·0	13·5		85
(d)	68—70	$C_{11}H_{11}ClN_2$	63·9	5·35	17·15	13·55	63·6	5·2	17·0	13·6	*	85
(k)	94—96	$C_9H_6Cl_2N_2$	50·75	2·8	33·3	13·15	50·9	3·0	33·1	13·4	*	60

* Light petroleum (b.p. 60—80°).

TABLE 2

N.m.r. data (δ/p.p.m.; $CDCl_3$) for chloroquinazolines

Compds. (VIII)	R^1	R^5	Aromatic complex
(b)	8·2 (H, m)	3·15 (2H, q, $ArCH_2$)	7·5—8·0 (3H)
(c)	8·2 (H, m)	3·1 (2H, t, $ArCH_2$)	7·45—8·0 (3H)
(d)	8·15 (H, m)	3·25 (H, m, ArCH)	7·35—7·95 (3H)
(k)	8·1 (H, m)	2·8 (3H, s, CH_3)	7·5—8·0 (2H)

s = Singlet; b = broad; m = multiplet; t = triplet; q = quartet.

4-Amino-3-(2-aminophenyl)-4H-1,2,4-triazole (I).—*Method A.* 4-Chloroquinazoline[13] (8·0 g) and 100% hydrazine hydrate (25 ml) were heated in a sealed glass tube at 120—150 °C for 6 h. After cooling, the *solid* was filtered, washed with water, and crystallised from ethanol (yield 66%), m.p. 153—155° (Found: C, 54·7; H, 5·1; N, 40·0%; M^+, 175. $C_8H_9N_5$ requires C, 54·85; H, 5·2; N, 40·0%; *M*, 175). $\lambda_{max.}$ (MeOH) 202 (log ε 4·26), 213 (4·26), and 300 nm (3·36); δ [$(CD_3)_2SO$] 8·4 (1H, s, 5-H), 7·9 (1H, m, 6-H), 6·45—7·4 (3H, m, ArH), 7·2 (2H, s, NH_2), and 2·9 p.p.m. (2H, s, NH_2); $\nu_{max.}$ 3400, 3300, 3250, and 3180 (NH_2) cm^{-1}. Evaporation of the hydrazine hydrate mother liquors gave an oily residue which solidified on trituration with aqueous ethanol. The resulting solid was crystallised from methanol (yield 22%) to give 3-(2-aminophenyl)-4*H*-1,2,4-triazole (II), m.p. 147—148° (lit.,[4] 144—145°) δ [$(CD_3)_2SO$] 8·4 (H, s, 5-H), 7·9 (H, m, 6′-H), 6·5—7·35 (3H, m, ArH), 6·5—6·75br (2H, NH_2), and 10·5br p.p.m. (H, NH), *m/e* 160 (M^+, 100%); $\lambda_{max.}$ (MeOH) 217 (log ε 4·43), 245 (3·90), and 314 nm (3·50), $\nu_{max.}$ 3460, 3350 (NH_2), and 3200—2700 (NH) cm^{-1}.

Method B. Reaction of 4-hydrazinoquinazoline hydrochloride[9] (2·0 g) with either 100% hydrazine hydrate (10 ml) or phenylhydrazine (8 ml) under the above conditions gave compound (I) in 30—40% yields.

Method C. Reaction of 4-mercaptoquinazoline[14] (4·0 g) and 100% hydrazine hydrate (15 ml) under the above conditions gave compound (I), after crystallisation from ethyl acetate, in 30% yield.

Synthesis of 6,7-Dihydro-5H-1,2,4-triazolo[4,3-d][1,3,4]-benzotriazepines (IIIa—f; *Table* 3).—To the *N*-aminotriazole (I) (0·02 mol) in ethanol (50 ml) was added the aldehyde or ketone (0·02 mol). The solution was then heated under reflux for 18 h. Evaporation of the solvent gave a residue which crystallised from aqueous ethanol.

Synthesis of 1,2,4-Triazolo[4,3-d][1,3,4]benzotriazepines (IVa—d; XIIIa, b).—The *N*-aminotriazole (0·02 mol) and triethyl orthoester (0·04 mol) were heated under reflux in ethanol (20 ml) for 0·5—4·0 h (the triethyl orthoester could also be used as solvent). On cooling, the precipitate was filtered off and washed thoroughly with ethyl acetate or ethanol. Evaporation of the mother liquors gave further quantities of the required product (see Table 5).

1,2,4-Triazolo[4,3-c][1,2,3]benzotriazine (V).—(A) 4-Amino-3-(2-aminophenyl)-4*H*-1,2,4-triazole (1·75 g, 0·01 mol) was dissolved in 2N-hydrochloric acid (20 ml). Sodium nitrite (0·14 g, 0·02 mol) in water (5 ml) was added dropwise to the stirred solution at 0—5 °C. Stirring was continued for 1 h at 0—5 °C and then the solution was allowed to warm to room temperature overnight. The solution was neutralised with 2N-sodium hydroxide and the precipitate was filtered off, washed with water and crystallised (80%) from light petroleum (b.p. 100—120°), m.p. 134—136° (lit.,[4] 135—136°).

(B) Diazotisation of 3-(2-aminophenyl)-4*H*-1,2,4-triazole (0·01 mol) with sodium nitrite (0·01 mol) in dilute hydrochloric acid gave triazolo[4,3-*c*][1,2,3[benzotriazine (80%).[4]

3-(2-Azidophenyl)-4H-1,2,4-triazole (VI).—Diazotisation of 4-amino-3-*o*-aminophenyl-4*H*-1,2,4-triazole (5·25 g, 0·03 mol) with sodium nitrite (2·0 g, 0·03 mol) in dilute hydrochloric acid as described in the previous reaction (A) gave the *azidophenyltriazole* (70%), m.p. 152—154° (Found: C, 51·6; H, 3·3; N, 45·3%; M^+, 186. $C_8H_6N_6$ requires C, 51·6; H, 3·25; N, 45·15%; *M*, 186), δ ($CDCl_3$) 8·35 (H, m, 6′-H), 8·05 (H, s, 5-H), 7·15—7·6 (3H, m, aromatic), and 7·25br p.p.m. (H, NH), $\nu_{max.}$ 3100—2600 (NH) and 2130 and 2090 (N_3) cm^{-1}.

[13] W. L. F. Armarego, *J. Appl. Chem.*, 1961, **11**, 70.
[14] D. Libermann and A. Rouaix, *Bull. Soc. chim. France*, 1959, 1793.

Sodium Borohydride Reduction of 3-(2-*Azidophenyl*)-4H-1,2,4-*triazole*.—Sodium borohydride (0·2 g) was added to the azidophenyltriazole (0·5 g) in isopropanol (10 ml) and the mixture heated under reflux for 6 h. The solvent was evaporated off and the residue extracted with ethyl acetate and the extracts were washed with water and dried over $MgSO_4$. Evaporation of the ethyl acetate gave 3-(2-aminophenyl)-4*H*-1,2,4-triazole (II) (70%), m.p. 146—148°.

8·4 (H, s, 5-H triazole), 7·0—8·25 (9H, m, aromatic), and 7·0—7·9br p.p.m. (H, NH), $\nu_{max.}$ 3350, 3250 (NH_2), and 3200—2700 (NH) cm^{-1}.

Synthesis of Substituted N-*Aminotriazoles* (IX).—The substituted 4-chloroquinazoline (3·0 g) and 100% hydrazine hydrate (10 ml) were heated in a sealed glass tube at 140—200° for 6—24 h. On cooling crystallisation sometimes occurred. Evaporation of the hydrazine hydrate and crystallisation of the residue from ethyl acetate or ethanol gave the *N*-aminotriazoles as crystalline solids (Table 7).

In some of the reactions the corresponding 1,2,4-triazole was detected by t.l.c. but was not isolated.

Heating the 4-chloroquinazolines and hydrazine hydrate at 200 °C in sealed tubes usually resulted in the shattering of the glass tubes due to the presence of hydrogen chloride. However, no explosions occurred when the corresponding 4-hydrazino-derivatives and hydrazine hydrate were used, even after 24 h at 200 °C.

1,2-*Bis*-(2-*n*-*propylquinazolin*-4-*yl*)*hydrazine* (Xa).—The addition of 100% hydrazine hydrate (10 ml) to 4-chloro-2-n-

TABLE 3

Analytical data for 6,7-dihydro-5*H*-1,2,4-triazolo[4,3-*d*][1,3,4]benzotriazepines

Compounds (III)	M.p. (°C)	Formula	Calc. (%) C	H	Cl	N	Found (%) C	H	Cl	N	Solvent of crystallisation	Yield (%)	$\nu_{max.}$/cm^{-1} NH region
(a)	176—178	$C_{15}H_{13}N_5$	68·4	5·0		26·6	68·2	5·1		26·4	EtOH–H_2O	80	3250, 3150
(b)	204	$C_{15}H_{12}ClN_5$	60·5	4·05	11·95	23·5	60·3	4·0	12·1	23·2	Pr^nOH	90	3250, 3180
(c)	227—229	$C_{15}H_{12}N_6O_2$	58·45	3·9		27·25	58·5	3·9		27·05	AcOH	90	3250, 3180
(d)	215—216	$C_{13}H_{10}N_6O_3$	52·35	3·4		28·2	52·6	3·5		27·9	AcOH–H_2O	80	3250, 3150
(e)	170—172	$C_{11}H_{13}N_5$	61·4	6·1		32·55	61·6	6·3		32·6	EtOAc	80	3250, 3150
(f)	210—212	$C_{14}H_{17}N_5$	65·85	6·7		27·45	66·0	6·9		27·8	MeOH–H_2O	90	3300, 3250

TABLE 4

N.m.r. data [δ/p.p.m.; $(CD_3)_2SO$] for dihydro-1,2,4-triazolobenzotriazepines [a]

Compounds (III)	3-H	11-H	Aromatic complex	R^2	R^1	NH
(a)	8·4	8·15 (m)	← 6·7—7·75 (8H) →		5·45 (H, d of d)	7·1—7·75 (2H)
(b)	8·35	8·1 (m)	← 6·6—7·75 (7H) →		5·5 (H, d of d)	7·05—7·75 (2H)
(c)	8·3	8·05 (m)	← 6·65—8·2 (7H) →		5·65 (H, d of d)	7·75 (H, d), 7·35 (H, d)
(d)	8·45	8·1 (m)	← 6·55—7·9 (5H) →		5·85 (H, d of d)	7·85 (H, d), 7·5 (H, d)
(e)	8·35	8·0 (m)	6·5—7·2 (3H)	← 1·25 (6H, $2CH_3$) →		6·5—7·2 (2H)
(f)	8·5	8·1 (m)	6·4—7·45 (3H)	← 1·55 (10H, $5CH_2$) →		7·0 (H), 6·5 (H)

[a] Signals were sharp singlets unless otherwise designated. d = Doublet; d of d = doublet of doublets.

TABLE 5

Analytical data for 5*H*-1,2,4-triazolo[4,3-*d*][1,3,4]benzotriazepines

Compound	M.p. (°C)	Formula	Calc. (%) C	H	N	*M*	Found (%) C	H	N	M^+	Solvent of crystallisation	Yield (%)
(IVa)	176—178	$C_9H_7N_5$	58·4	3·8	37·8	185	58·1	4·0	37·4	185		80
(IVb)	339—341	$C_{10}H_9N_5$	60·3	4·55	35·15	199	60·1	4·8	34·9	199		80
(IVc)	284—285	$C_{11}H_{11}N_5$	61·95	5·2	32·85	213	61·8	5·2	32·9	213		80
(IVd)	261—262	$C_{15}H_{11}N_5$	68·95	4·25	26·8	261	68·6	4·5	26·5	261	Cellosolve	50
(XIIIa)	313—316	$C_{10}H_9N_5$	60·3	4·55	35·15	199	60·6	4·9	34·9	199		50
(XIIIb)	315—317	$C_{11}H_{11}N_5$	61·95	5·2	32·85	213	61·8	5·3	33·0	213	EtOH	60

TABLE 6

N.m.r. data (δ/p.p.m.) for triazolobenzotriazepines [a]

Compound	3-H	R^2	11-H	R^1	Aromatic complex	NH	Solvent
(IVa)	8·25		7·9 (m)	6·5 (H, d)	6·6—7·4 (3H)	9·2 (d)	$(CD_3)_2SO$
(IVb)	8·7		7·85 (m)	2·1 (3H, CH_3)	6·7—7·45 (3H)	7·6 (b)	$CDCl_3$
(IVc)	8·3		7·85 (m)	2·25 (2H, q, CH_2)	6·8—7·35 (3H)	8·65	$(CD_3)_2SO$
(IVd)	8·5		7·85 (m)	← 6·9—8·0 (8H) →		9·15	$(CD_3)_2SO$
(XIIIa)		2·5 (3H, CH_3)	7·8 (m)	6·8 (H, d)	6·8—7·6 (3H)	9·75 (d)	$(CD_3)_2SO$–CF_3CO_2H
(XIIIb)		2·4 (3H, CH_3)	7·75 (m)	2·0 (3H, CH_3)	6·8—7·5 (3H)	9·15 (b)	$(CD_3)_2SO$–CF_3CO_2H

[a] Signals were sharp singlets unless otherwise designated.

5-*Amino*-4-*phenyl*-1-[2-(4H-1,2,4-*triazol*-3-*yl*)*phenyl*]-1H-1,2,3-*triazole* (VII).—A solution of 3-(2-azidophenyl)-4*H*-1,2,4-triazole (0·9 g, 0·005 mol) and phenylacetonitrile (0·6 g, 0·005 mol) in methanol (20 ml) was heated under reflux with a solution of sodium metal (0·4 g) in methanol (20 ml) for 3 h. The salt, recovered from the evaporated mixture, was washed with methanol, suspended in water, acidified with dilute sulphuric acid, and the precipitate was collected and crystallised from ethanol to give the *triazolophenyltriazole* (VII; 0·3 g), m.p. 215° (Found: C, 63·0; H, 4·4; N, 32·3%; M^+, 303. $C_{16}H_{13}N_7$ requires C, 63·35; H, 4·3; N, 32·35%; *M*, 303), δ [$(CD_3)_2SO$] 5·3br (2H, NH_2),

propylquinazoline (3·0 g) caused immediate precipitation of a yellow *solid* (90%) which crystallised from benzene, m.p. 248—250° (Found: C, 71·30; H, 6·50; N, 22·50%; M^+, 372. $C_{22}H_{24}N_6$ requires C, 70·95; H, 6·50; N, 22·55%; *M*, 372), δ ($CDCl_3$) 8·2 (2H, m, 5-H aromatic), 6·65—7·65 (6H, m, aromatic), 2·65 (4H, m, CH_2), and 10·0—10·5br p.p.m. (2H, NH), $\nu_{max.}$ 3200 (NH) cm^{-1}.

4-Amino-3-(2-aminophenyl)-5-n-propyl-4H-1,2,4-triazole (IXc).—The mixture obtained from the addition of 100% hydrazine hydrate (15 ml) to 4-chloro-2-n-propylquinazoline (3·0 g) was heated in a sealed tube at 150 °C for 18 h and the precipitated solid was shown to contain (Xa) and the expected product (IXc). Further heating for 5 h at 200 °C gave the required product (IXc) only (Table 7)

4-Amino-3-(2-aminophenyl)-5-phenyl-4H-1,2,4-triazole (IXf).—4-Chloro-2-phenylquinazoline (3·0 g) and 100% hydrazine hydrate (10 ml) were heated in a sealed glass tube at 150 °C for 8 h to give 4-hydrazino-2-phenylquinazoline [9] (XI) (90%), m.p. 217—218° (lit.,[9] 216—217°). A mixture of 4-hydrazino-2-phenylquinazoline (2·7 g) and 100% hydrazine hydrate (10 ml) was heated in a sealed tube for 15 h at 200 °C. On cooling, the pale yellow solid was filtered off and shown to be (IXf) (Table 7).

1,2-Bis-(2-benzylquinazolin-4-yl)hydrazine (Xb).—To 2-benzyl-4-chloroquinazoline (3·0 g) in warm ethanol (15 ml) was slowly added 100% hydrazine hydrate (3 ml). An exothermic reaction occurred and on cooling the yellow precipitate was filtered and crystallised from n-butanol (yield 70%), m.p. 289—291° (Found: C, 77·1; H, 5·4; N, 17·7%; M^+, 468. $C_{30}H_{24}N_6$ requires C, 76·9; H, 5·15; N, 17·95%; *M*, 468), δ [$(CD_3)_2SO$] 8·15 (2H, m, 5-H aromatic), 7·15—7·65 (16H, m, aromatic), and 4·05 p.p.m. (4H, s, $2CH_2$), $\nu_{max.}$ 3300 (NH) cm^{-1}.

4-Amino-3-(2-aminophenyl)-5-benzyl-4H-1,2,4-triazole (IXe).—*Method A.* Reaction of 1,2-bis-(2-benzylquinazolin-4-yl)hydrazine (Xb) (2·0 g) and 100% hydrazine hydrate (8 ml) in a sealed tube at 200 °C for 5 h gave the required product (IXe) (Table 7).

Method B. 2-Benzyl-4-chloroquinazoline and 100% hydrazine hydrate in a sealed glass tube at 150 °C for 5 h gave a mixture of (Xb) and (IXe).

Reaction of 4,5-Dichloroquinazoline and Hydrazine Hydrate.

TABLE 7

Analytical data for 4-amino-4*H*-1,2,4-triazoles

Compounds (IX)	M.p. (°C)	Formula	Calc. (%) C	H	Cl	N	Found (%) C	H	Cl	N	Solvent of crystallisation	Yield (%)	$\nu_{max.}$/cm^{-1} NH_2 region
(a)	155—157	$C_9H_{11}N_5$	57·1	5·85		37·0	57·0	5·8		37·4	EtOAc	40	3450, 3350, 3300, 3200:
(b)	129—131	$C_{10}H_{13}N_5$	59·1	6·45		34·45	59·0	6·3		34·7	EtOH	60	3450, 3300, 3100
(c)	93—95	$C_{11}H_{15}N_5$	60·8	6·95		32·25	60·4	6·9		32·4	EtOAc–L.P.*	60	3400, 3300, 3250, 3150
(d)	129—131	$C_{11}H_{15}N_5$	60·8	6·95		32·25	60·8	6·7		32·5	EtOAc	30	3450, 3350, 3250, 3150:
(e)	162—164	$C_{15}H_{15}N_5$	67·9	5·7		26·4	68·1	5·7		26·7	EtOAc	50	3350, 3300, 3150
(f)	181—183	$C_{14}H_{13}N_5$	66·9	5·2		27·85	67·2	5·3		27·7	EtOAc–L.P.	50	3450, 3350, 3250, 3150
(g)	155—157	$C_8H_8ClN_5$	45·8	3·8	16·9	33·4	46·2	4·0	16·8	33·1	EtOAc–L.P.	50	3400, 3250, 3150
(h)	79—81	$C_9H_{11}N_5,0·5H_2O$	54·55	6·05		35·35	54·5	6·1		35·4	EtOAc–L.P.	30	3450, 3350, 3300, 3200:
(i)	178—180	$C_8H_8ClN_5$	45·8	3·8	16·9	33·4	46·4	4·1	17·2	33·1	EtOH	20	3400, 3350, 3300, 3150
(j)	166—168	$C_8H_7Cl_2N_5$	39·35	2·85	29·05	28·7	39·4	2·9		28·8	EtOAc–L.P.	30	3400, 3300, 3100
(k)	226—228	$C_9H_{10}ClN_5$	48·3	4·45	15·85	31·3	48·3	4·7	15·8	31·0	EtOH	50	3450, 3400 3300 3150:
(m)	179—182	$C_8H_8ClN_5$	45·8	3·8	16·9	33·4	46·2	3·9		33·6	EtOAc	10	3400, 3350, 3200, 3150:

* L.P. = Light petroleum (b.p. 60—80°).

TABLE 8

N.m.r. data (δ/p.p.m.) for 4-amino-4*H*-1,2,4-triazoles [a]

Compounds (IX)	R^1	R^2	R^3	R^4	R^5	NH	Solvent
(a)	7·9 (H, m)	←	6·5—7·3 (3H, m)	→	2·35 (3H, CH_3)	6·1 (2H), 5·95 (2H)	$(CD_3)_2SO$
(b)	7·8 (H, m)	←	6·45—7·2 (3H, m)	→	2·7 (2H, q, $ArCH_2$)	6·0 (2H), 5·85 (2H)	$(CD_3)_2SO$
(c)	7·55 (H, m)	←	6·6—7·45 (3H, m)	→	2·8 (2H, t, $ArCH_2$)	5·0 (2H), 4·6br (2H)	$CDCl_3$
(d)	7·45 (H, m)	←	6·7—7·35 (3H, m)	→	3·25 (H, m, CH)	4·8 (2H), 3·9—4·7 (2H)	$CDCl_3$
(e)	7·85 (H, m)	←	6·5—7·3 (3H, m)	→	4·2 (2H, CH_2)	6·1 (2H, b), 5·95 (2H)	$(CD_3)_2SO$
(f)	7·75 (H, m)	←	6·55—8·2 (8H, m)	→		6·1 (2H, b), 5·95 (2H)	$(CD_3)_2SO$
(g)	8·1 (H)		← 6·5—7·25 (2H, m) →		8·5 (H)	6·45 (2H), 6·3 (2H)	$(CD_3)_2SO$
(h)	7·6 (H)	2·2 (3H, CH_3)	← 6·6—7·0 (2H, m) →		8·4 (H)	6·2 (2H), 5·8 (2H)	$(CD_3)_2SO$
(i)	8·0 (H, d)	←	6·55—6·95 (2H, m)	→	8·45 (H)	6·55 (2H, b), 6·3 (2H)	$(CD_3)_2SO$
(j)	8·15 (H, d)		7·45 (H, d)		8·55 (H)	6·6 (2H), 6·4 (2H)	$(CD_3)_2SO$
(k)	8·0 (H, d)	←	6·5—6·95 (2H, m)	→	2·4 (3H, CH_3)	6·5 (2H, b), 5·95 (2H)	$(CD_3)_2SO$
(m)		←	6·6—7·25 (3H, m)	→	8·5 (H)	5·8 (2H), 5·15 (2H)	$(CD_3)_2SO$

[a] Signals were sharp singlets unless otherwise stated.

—100% Hydrazine hydrate (8 ml) was added cautiously to 4,5-dichloroquinazoline (2·5 g) and heated at 150 °C for 5 h in a sealed glass tube. A yellow solid was obtained which crystallised from ethanol–light petroleum (b.p. 40—60°) to give 3-(2-*amino*-6-*chlorophenyl*)-4H-1,2,4-*triazole* (XII) (50%), m.p. 209—211° (Found: C, 49·2; H, 3·6; Cl, 18·3; N, 28·5%; M^+, 194. $C_8H_7N_4Cl$ requires C, 49·35; H, 3·6; Cl, 18·25; N, 28·8%; *M*, 194), δ [$(CD_3)_2SO$] 8·4 (H, s, 5-H), 6·7—7·25 (3H, m, aromatic), and 5·6br p.p.m. (2H, NH_2), NH not observed. $\nu_{max.}$ 3400, 3340 (NH_2), and 3200—2700 (NH) cm^{-1}.

The mother liquors were evaporated and the residues crystallised from ethyl acetate to give 4-amino-3-(2-amino-6-chlorophenyl)-4*H*-1,2,4-triazole (IXm) (Table 7).

3-(2-*Aminophenyl*)-1-*phenyl*-1H-1,2,4-*triazole* (XIVa).—4-Chloroquinazoline (0·03 mol), phenylhydrazine (0·09 mol), and anisole (10 ml) were heated on an oil-bath to 56 °C to give a vigorous reaction and the internal temperature rose to 136 °C. When the temperature began to fall the mixture was heated under reflux for a further 3 h. On cooling, a saturated sodium carbonate solution was added until the reaction mixture was basic. The excess of phenylhydrazine was removed by steam distillation and the residual oil was triturated with ice-cold ethanol to give a *solid* which was crystallised from light petroleum (b.p. 100—120°) (yield 25%), m.p. 90—92° (Found: C, 71·0; H, 5·1; N, 23·8%; M^+, 236. $C_{14}H_{12}N_4$ requires C, 71·15; H, 5·1; N, 23·7%; *M*, 236), δ ($CDCl_3$) 8·55 (H, s, 5-H), 8·2 (H, m, 6′-H), 6·7—7·75 (8H, m, aromatic), and 5·6 p.p.m. (2H, s, NH_2); $\nu_{max.}$ 3430 and 3300 (NH_2) cm^{-1}.

When compound (XIVa) was heated under reflux with acetic anhydride, 3-(2-*acetamidophenyl*)-1-*phenyl*-1H-1,2,4-*triazole* (XV) was obtained in 90% yield, m.p. 124—126° (Found: C, 69·0; H, 5·0; N, 20·3%; M^+, 278. $C_{16}H_{14}N_4O$ requires C, 69·05; H, 5·05; N, 20·15%; *M*, 278), δ ($CDCl_3$) 8·75 (H, m, 6′-H), 8·7 (H, s, 5-H), 7·0—8·45 (8H, m, aromatic), 11·35 (H, s, NH), and 7·75 p.p.m. (3H, s, CH_3), $\nu_{max.}$ 3450 (NH) and 1675 (C=O) cm^{-1}.

3-(2-*Aminophenyl*)-1-*methyl*-1H-1,2,4-*triazole* (XIVb).—*Method A*. 4-Chloroquinazoline (0·03 mol) and excess of methylhydrazine (8 ml) were heated in a sealed tube at 120—150° for 6 h. After allowing the mixture to cool overnight, the crystalline *solid* was filtered off and crystallised from ethanol (yield 30%), m.p. 148—150° (Found: C, 61·8; H, 5·8; N, 32·4%; M^+, 174. $C_9H_{10}N_4$ requires C, 62·05; H, 5·8; N, 32·15%; *M*, 174), δ ($CDCl_3$) 8·05 (H, m, 6′-H), 8·0 (H, s, 5-H), 6·65—7·15 (3H, m, aromatic), 5·45br (2H, NH_2), and 3·85 p.p.m. (3H, s, CH_3), $\nu_{max.}$ 3430 and 3300 (NH_2) cm^{-1}.

Method B. Methylhydrazine (0·09 mol) was added carefully to a suspension of 4-chloroquinazoline (0·03 mol) in toluene (10 ml). A vigorous reaction occurred and the internal temperature rose to 70°. The temperature soon subsided and the mixture was heated under reflux for 3 h. After cooling, the solid was filtered off and crystallised from ethanol to give 3-(2-aminophenyl)-1-methyl-1*H*-1,2,4-triazole (XIVb) (20%).

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