The Dimroth Rearrangement. Part XII.[1] Transformation by Alkali of 4-Amino-3-benzyl-1,2,3-triazole and its 5-Substituted Derivatives into the Corresponding 4-Benzylamino Isomers. Retrogression of this Reaction in Neutral Solvents

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Contrary to expectations, 4-amino-3-benzyl-1,2,3-triazole (Ic), and its 5-carbamoyl and 5-carboxy-derivatives, are partly isomerized in hot, basic solutions to equilibrium mixtures rich in 4-benzylamino-1,2,3-triazole (IIc) and its 5-carbamoyl and 5-carboxy-derivatives respectively. These secondary amines, all stable at 25° and hitherto unknown, retrogress in hot *neutral* solvents to equilibrium mixtures rich in the primary amine starting material. It is shown how these two equilibria can be manipulated for preparative use.

New and improved preparations are described for (*a*) 4-amino-3-benzyl-1,2,3-triazole, by decarboxylation of the 5-carboxy-derivative; (*b*) this acid by alkaline hydrolysis of the corresponding amide; and (*c*) 4-amino-3-benzyl-5-cyano-1,2,3-triazole (Id), by the combined action of dimethylformamide and phosphoryl chloride on the related amide (the intermediate, 3-benzyl-5-cyano-4-dimethylaminomethyleneamino-1,2,3-triazole, was also isolated). The nitrile (Id) is dimerized by hot alkali to 6-amino-2-(4-amino-3-benzyl-1,2,3-triazol-5-yl)-9-benzyl-8-azapurine (IV).

Physical constants are reported including u.v. spectra and ionization constants.

4-AMINO-3-BENZYL-1,2,3-TRIAZOLE-5-CARBOXAMIDE * (Ia) is an important intermediate for 8-azapurines,[2] many of which are otherwise inaccessible. Triazoles with a different 5-substituent (or none) should also be

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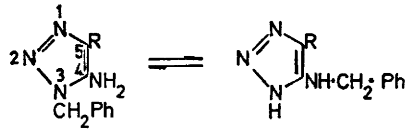
* The amino-group of aminotriazoles is consistently numbered 4, as in all other publications from this Department. The position of 'indicated hydrogen' (*e.g.* 3H) is identical with that of the alkyl-group in the 3-benzyl-derivatives, and is not known in the other examples.

[1] Part XI, D. J. Brown and B. T. England, *Austral. J. Chem.*, 1968, **21**, 2813; Part X, D. J. Brown and M. N. Paddon-Row, *J. Chem. Soc.* (*C*), 1967, 1928.

[2] (*a*) A. Albert, *J. Chem. Soc.* (*C*), 1968, 2076; (*b*) A. Albert and K. Tratt, *ibid.*, 344; (*c*) A. Albert, *ibid.*, 1969, 152.

useful but have been obtained only in poor yields.[3,4] In work on the improvement of these syntheses (see below) it was found that the benzyl-group in the series (Ia—c) has a tendency to migrate to the exocyclic amino-group.



(I) (II)

a; R = $CONH_2$
b; R = CO_2H
c; R = H
d; R = CN

In general, the novel secondary amines (IIa—c), were obtained by the action of hot bases on the primary amines (Ia—c). From such equilibrium mixtures, members of two pairs, (Ia) + (IIa) and (Ic) + (IIc), were separated by dissolution, in cold alkali, of the secondary amine which had an ionizable proton on N-3. The low solubility in water of the sodium salt of (Ib) allowed the separation of (Ib) from (IIb). The following criteria for separation were used: (i) Complete solubility in cold N-sodium hydroxide for all members of series (II). (ii) Absence of a red colour when the secondary amines (IIa, c), dissolved in ice-cold 2N-hydrochloric acid containing a little sodium nitrite, were added to alkaline 2-naphthol. (iii) Absence of a spot characteristic of the isomer when a paper chromatogram was developed in aqueous ammonium chloride. (iv) Absence of characteristic isomer peaks from i.r. and ^1H n.m.r. spectra [the latter proved useful in assaying mixtures of (Ib) and (IIb)]. Melting-points, completely reliable for indicating purity of the pair (Ic, IIc), were unsharp in the other examples.

The secondary amines, stable as solids at 20° for at least 3 months, retrogressed to the primary amines when heated in a neutral solvent.

4-Amino-3-benzyl-1,2,3-triazole-5-carboxylic acid (Ib) came to an approximately 1·4 : 1 equilibrium with the isomer (IIb) when boiled with 1N-potassium hydroxide. The amide (Ia) with 2·5N-potassium hydroxide gave a similar mixture of the acids (Ib) and (IIb) when heated for a longer period. Because the amide is readily prepared from benzyl azide and cyanoacetamide,[3] this is the best method for preparing the acid (Ib) especially as the isomer (IIb) was converted into the acid (Ib) when boiled briefly with ethanol. Hitherto the acid (Ib) could be obtained (20%) only by condensation[3] of benzyl azide with cyanoacetic acid.

4-Benzylamine-1,2,3-triazole-5-carboxylic acid (IIb) has two acidic groups, one at $\mathrm{p}K_a$ 4 (CO_2H), and the other near $\mathrm{p}K_a$ 9 (3-NH); but the 3-benzyl isomer (Ib) has only one acidic group, as expected, namely at $\mathrm{p}K_a$ 4 (CO_2H). The ^1H n.m.r. of the latter in deuteriodimethyl sulphoxide, showed τ 2·70 (5H, C_6H_5), 3·43 (2H, NH_2, exchangeable H), and 4·54 (2H, CH_2). The peak at 3·4 was sharp because of bonding between amino- and carboxy-groups; but the band of the corresponding secondary amine in the 4-benzylamino-isomer (IIb) was too much broadened (by coupling to CH_2) to be resolved. The rest of the n.m.r. spectrum of this isomer (IIb) showed τ 2·67 (5H), 3·6br (1H, 3-NH, exchangeable H), and 5·55 (2H, CH_2).

With n-butanol instead of water in the above reaction, some 4-benzylamino-1,2,3-triazole-5-carboxamide (IIa) [formed by isomerization of the starting material (Ia)] escaped hydrolysis. The weakly acidic properties of the amide (IIa) (see Table) enabled it to be precipitated at a higher pH than the two stronger acids (Ib) and (IIb) formed at the same time. The amide (Ia) was unchanged when heated just above its melting point, or when boiled with pyridine, cyclohexylamine, or 2N-ethanolic sodium ethoxide.

Retrogression of amide (IIa) to the isomer (Ia) in boiling ethanol occurred more slowly than for the corresponding acid (IIb); the latter reaction was presumably catalysed[5] by hydrogen ions from the carboxy-group. Retrogression of the amide (IIa) was, however, practically complete in boiling pentanol (*ca.* 140°).

4-Amino-3-benzyl-5-cyano-1,2,3-triazole (Id) has previously been prepared only in poor yields, either from condensation[3] of benzyl azide and malononitrile (17%) or from[4] ethyl chloroformate and the amide (Ia) (31%). A new almost quantitative synthesis has been achieved by the combined action of phosphoryl chloride and dimethylformamide on the amide (Ia). This approach was suggested by the protective effect[6] on amino-groups of the 'amido-dichlorides' (here, $Me_2N{\cdot}CHCl_2$) which readily[7] convert amides into nitriles. The amidine intermediate (III), a weak base, was hydrolysed to the required amino-nitrile (Id) by dilute acid. The known destructive effects[8,9] of an inorganic acid chloride on an unprotected *o*-amino-compound were thus avoided.

The nitrile (Id), unchanged both when heated just above its melting point or when boiled in pyridine, was converted into a dimer when gently heated with alkali; no isomer (IId) could be detected. That this dimer was 6-amino-2-(4-amino-3-benzyl-1,2,3-triazol-5-yl)-9-benzyl-8-azapurine (IV) followed from elemental analysis and the physical properties. ^1H N.m.r., in deuteriodimethyl sulphoxide gave bands at τ 1·75 (2H) and 3·12 (2H), both of which disappeared when D_2O was added; the former band arose from NH_2 in the azapurine ring (*cf.* a 6-amino-8-azapurine *); the latter band

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* Found for 6-amino-9-benzyl-8-azapurine in same solvent: 1·61 (3H, contracted to 1H when D_2O was added, NH_2 + $C_{(2)}H$), 2·63 (5H, C_6H_5); 4·19 (2H, CH_2).

[3] J. R. E. Hoover and A. R. Day, *J. Amer. Chem. Soc.*, 1956, **78**, 5832.

[4] A. Dornow and J. Helberg, *Chem. Ber.*, 1960, **93**, 2001.

[5] B. R. Brown, D. L. Hammick, and S. G. Heritage, *J. Chem. Soc.*, 1953, 3820.

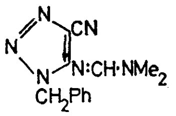
[6] H. Bredereck, R. Gompper, K. Klemm, and H. Rempfer, *Chem. Ber.*, 1959, **92**, 837.

[7] H. Eilingsfeld, M. Seefelder, and H. Weidinger, *Angew. Chem. Internat. Edn.*, 1960, **72**, 48.

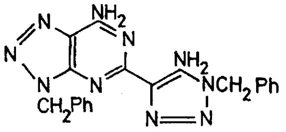
[8] E. Uhlfelder, *Ber.*, 1903, **36**, 1824.

[9] L. McMaster and F. F. Ahmann, *J. Amer. Chem. Soc.*, 1928, **50**, 145.

from NH_2 in the triazole ring (*cf.* 4·39 for 4-amino-3-benzyl-1,2,3-triazole). The other bands in the spectrum were at 2·7, a nearly fused doublet (10H, $2C_6H_5$), and 4·21 + 4·52 (2H each; $2CH_2$). No $C{\vdots}N$ band near 2220 cm.$^{-1}$ was present in the i.r. spectrum. 2-Amino-3-cyanopyridine was similarly dimerized[10] to 4-amino-2-(2-aminopyrid-3-yl)-1,3,8-triazanaphthalene.



(III)



(IV)

4-Amino-3-benzyl-1,2,3-triazole (Ic), previously made by decarboxylation of the acid (Ib) in boiling dimethylaniline, was better prepared (75%) by boiling this acid with anhydrous pyridine (10 min.); 20% of the isomer (IIc) was obtained as a by-product. When compounds (Ib) or (Ic) were boiled for longer periods (3—30 hr.) the ratio of primary to secondary amine changed from 3·8 : 1 (as above) to 1·1 : 1. Formation of secondary amine from the amine (Ic) was slight below 115°, even in boiling 2·5N-potassium hydroxide. Boiling cyclohexylamine (pK_a 10·8; b.p. 135°) gave the largest yield of secondary amine (ratio 0·3 : 1).

Ionization constants and u.v. spectra

Substance	Species[a]	Ionization in water (20°)				Spectroscopy in water[c]		
		pK_a	Spread ±	Conc. (M)	A.w.l.[b] mμ	$\lambda_{max.}$ (mμ)	log ε	pH
1,2,3-Triazole								
4-Benzylamino-5-carbamoyl	0[d]					233, 272	3·93, 3·80	5·0
	—	7·55	0·05	10^{-4}	300	*229*, 276	*3·78*, 3·80	10·0
4-Amino-3-benzyl-5-carbamoyl	0[d]					230, 261[e]	3·89, 3·93	(50% ethanol)
4-Benzylamino-5-carboxy	0[d]					233, 272	4·00, 3·87	2·0
	—	4·00	0·05	10^{-4}	275	*230*, 266	*3·88*, 3·71	6·6
	2—	9·28	0·03	10^{-4}	260	*227*, 263	*4·11*, 4·12	12·0
4-Amino-3-benzyl-5-carboxy	0[d]					229, 261	3·86, 3·93	2·0
	—[f]	4·03	0·02	10^{-4}	272	225, 254	3·89, 3·87	7·9
4-Amino-3-benzyl-5-cyano-	0[d]					*216*, 228, 251	*3·96*, 3·95, 3·82	E[g]
3-Benzyl-5-cyano-4-dimethylaminomethyleneamino	0					*215*, *257*, 285	*4.27*, *3·98*, 4·14	E[g]
4-Benzylamino	0					253	3·63	M[g]
	—	9·66	0·05	10^{-4}	265			
4-Amino-3-benzyl	0					241	3·73	7·0
	+	1·78	0·04	10^{-4}	260	262[h]	3·66	—0·3

[a] Neutral species (0), anion (—), dianion (2—), cation (+). [b] Analytical wavelength for spectrometric determination. performed as in A. Albert and E. P. Sergeant, ' Ionization Constants of Acids and Bases,' Methuen, London, 1962. [c] Inflections in italics. [d] The basic pK_a lies below 0 (spectral evidence). [e] From J. R. E. Hoover and A. R. Day, *J. Amer. Chem. Soc.*, 1956, **78**, 5832. [f] There is no other pK_a between 0 and 14. [g] In ethanol (E) or methanol (M). [h] Ref. *e* gives 254 mμ (log ε 3·58) in solution of undefined acidity.

In retrogression, the secondary amine (IIc) gave a primary : secondary amine ratio of 0·27 : 1 when boiled in pyridine (10 min.); when boiled with pyridine or n-butanol for longer periods (3 hr.) the same ratios (1·1 : 1 and 3 : 1 respectively) were obtained as with the primary amine (Ic).

Finally 4-benzylamino-1,2,3-triazole-5-carboxylic acid (IIb), when decarboxylated in boiling pyridine, gave a primary : secondary amine ratio of 3·2 : 1 after being boiled for 10 min., but a ratio 1·1 : 1 after 4 hr. These figures indicate that pyridine shifts the equilibrium in favour of the isomeric acid (Ib) before decarboxylation can occur, and that the usual equilibrium of (Ic) $\rightleftharpoons$ (IIc) in pyridine is reached only when the mixture is boiled for a longer period.

Ionization and ultraviolet spectra are recorded in the Table. The acidic pK_a value of 4-benzylamino-1,2,3-triazole-5-carboxamide (7·55) is similar to that[2a] of 4-amino-1,2,3-triazole-5-carboxamide (7·79); this is additional support for structure (IIa). 4-Benzylamino-1,2,3-triazole, lacking the electron-attracting group in the 5-position, is a much weaker acid. The pK_a values of the carboxylic acids in the Table were discussed above; those of the primary amine should be compared with the very similar values (4·27 and 9·43) of 4-amino-1,2,3-triazole-5-carboxylic acid.[2a] With an electron-attracting group in the 5-position, basic strength virtually disappears, but rises to pK_a 1·78 in 4-amino-3-benzyl-1,2,3-triazole (*cf.* 2·27 for 4-amino-3-methyl-1,2,3-triazole[11]).

The single-peak u.v. spectrum of 4-amino-3-benzyl-1,2,3-triazole resembles that of 4-amino-3-methyl-1,2,3-triazole[11] ($\lambda_{max.}$ 238 mμ, log ε 3·73); the cations of these two compounds also have spectra which agree in position and intensity. The insertion of electron-attracting groups into the 5-position (see Table) shifts the maximum to longer wavelengths and intensifies it. Compared to the primary amines, each secondary amine has a maximum which is both displaced to a longer wavelength and less intense.

DISCUSSION

These Dimroth-type rearrangements were unexpected, especially so since it was recently shown[2c] that the amide (Ia) was unchanged when heated in an excess of 3N-ethanolic ammonia for 4 hr. at 180°. A recent

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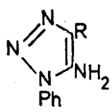
[10] E. C. Taylor, A. J. Crovetti, and R. J. Knopf, *J. Amer. Chem. Soc.*, 1958, **80**, 427.

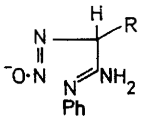
[11] A. Albert, *J. Chem. Soc.* (*C*), 1969, 2379.

review[12] of Dimroth rearrangements indicated that almost all examples from the 1,2,3-triazole series have had a large rigid group (usually phenyl), or a strongly electron-attracting substituent, in the 3-position. The sole example with a benzyl-group in this position (4-amino-3-benzyl-5-phenyl-1,2,3-triazole) produced only 8% of the 4-benzylamino-isomer at equilibrium in boiling pyridine, and it was concluded[13] that a 3-benzyl group was unfavourable to Dimroth rearrangements.

In his classical studies[14] of the rearrangement of 3-phenyl-4-amino-1,2,3-triazole (Va) and its 5-ethoxycarbonyl derivative (Vb) to the corresponding secondary amines (*e.g.* 4-anilino-1,2,3-triazole), Dimroth made a distinction between equilibria achieved by heat alone and those accomplished by hot bases. For these 3-phenyl-derivatives, both equilibria strongly favour the secondary amines, which are almost quantitatively produced in the presence of bases. For this purpose, pyridine was as effective as ethanolic sodium ethoxide. Only moderate retrogression could be attained by heat in a neutral solvent (*e.g.* ethanol at 150°), which gave an equilibrium mixture containing 23% of the primary amine (Vb); the same percentage remained when the amine (Vb) was similarly heated, proof that equilibrium had been reached. The action of bases in promoting conversion into secondary amines was traced[14] to stabilization of the open-chain intermediates, which were diazotate anions of type (VI). [Rotation of the carbon atom in the amidino-group of (VI) effects transition from the primary to the secondary amine.]



(V)



(VI)

a; R = H
b; R = CO_2Et

The present work shows that a 3-benzyl group favours a Dimroth-type rearrangement more than expected. However, compared with Dimroth's 3-phenyl series, the heat-mediated equilibria lie more in the direction of the primary amines. This makes possible a preparatively worthwhile retrogression, hitherto unknown in Dimroth reactions. Moreover, the base-mediated equilibria in the 3-benzyl series usually require a stronger base than pyridine or even ammonia [the need for a strong base is most evident if the 5-position is occupied by a —M group which could disturb conjugation in the intermediate (VI)]. There were also strong indications in the 3-benzyl series that not only must a critical strength of alkali be reached, but a critical temperature also. The critical temperature required for retrogression was a factor in the 3-phenyl series also.[14] Dimroth also showed that solubility, but not dielectric constant, influenced the degree of retrogression attained. In the present work, retrogression (at equilibrium) was less complete with an unsubstituted 5-position as with 5-amido- and carboxy-substituents (and apparently $-CO_2^-$).

The main implication for preparative chemistry of the present work is that in the synthesis and manipulation of 3-aralkyl- (and possibly 3-alkyl)-1,2,3-triazoles, it is important to check that the product is not (even partly) soluble in alkali.

EXPERIMENTAL

M.p.s are uncorrected. Reactions with potassium hydroxide were carried out in polypropene vessels. Yields refer to material sufficiently pure to give only one spot in chromatography on two Whatman No. 1 papers, one (A) developed with 3% aqueous ammonium chloride, and one (B) with butan-1-ol–5N-acetic acid, (7 : 3); the papers were viewed in 254 nm. light. Specimens were applied to these papers in aqueous pyridine.

U.v. spectra were determined on an Optica manual instrument. The i.r. spectra were obtained on a Unicam SP 200 instrument in Nujol (also in hexachlorobutadiene when relevant areas were blocked by Nujol). N.m.r. spectra were determined on a Perkin-Elmer model R10 instrument, operating at 33·5° and 60 Mc/sec.; tetramethylsilane was the internal standard.

4-*Benzylamino*-1,2,3-*triazole*-5-*carboxylic Acid* (IIb).—(*a*) 4-Amino-3-benzyl-1,2,3-triazole-5-carboxylic acid (Ib) (0·44 g., 0·002 mole), prepared as below, and 1N-aqueous potassium hydroxide (5 ml.) were heated under reflux for 6 hr. (the mixture remained clear throughout). This solution was then added to a boiling solution of sodium chloride (5 g.) in water (15 ml.). The suspension was set aside at 4° overnight. The sodium salt of the starting material was filtered off, dissolved in boiling water (15 ml.), and acidified (to pH 2) to give 55% of the starting material (Ib), m.p. 170° (decomp.) (see below). The filtrate from the salt, acidified with 5N-sulphuric acid (to pH 2) deposited 4-*benzylamino*-1,2,3-*triazole*-5-*carboxylic* acid (IIb) (40%). After recrystallization from 30 parts of methanol (2 crops), this melted at 154° (effervescing) if placed in bath at 144°. It was soluble in *ca.* 9000 parts of water at 25° [Found (for material dried at 25° and 0·01 mm.): C, 55·0; H, 4·85; N, 25·9. $C_{10}H_{10}N_4O_2$ requires C, 55·0; H, 4·6; N, 25·7%]; R_F 0·70 bright violet (solvent A). It was found that the above sodium chloride treatment caused no retrogression of the acid (IIb). When the reaction mixture was heated for 5 days instead of 6 hr., the yield of the acid (IIb) was 45%. A practical test for the absence of acid (Ib) from acid (IIb) was found: a 10% solution of the latter in 1N-sodium hydroxide should remain clear overnight, after being seeded with a trace of the isomer (Ib).

(*b*) 4-Amino-3-benzyl-1,2,3-triazole-3-carboxamide (Ia) (10 g.), prepared as below, and 2·5N-aqueous potassium hydroxide (45 ml.) were heated under reflux as above until clear (*ca.* 100 hr.). Water (65 ml.) was added and the cooled solution was filtered to remove starting material. The filtrate was acidified (to pH 2) and the precipitate of acids, purified through the sodium salts as above, gave

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[12] D. J. Brown, in 'Mechanisms of Molecular Migrations,' ed. B. S. Thyagarajan, Interscience-Wiley, New York, 1968, vol. 1, p. 209.

[13] E. Lieber, T. S. Chao, and C. N. Ramachandra Row, *J. Org. Chem.*, 1957, **22**, 654; E. Lieber, C. N. Ramachandra Row, and T. S. Chao, *J. Amer. Chem. Soc.*, 1957, **79**, 5962.

[14] O. Dimroth, (*a*) *Annalen*, 1909, **364**, 183; (*b*) 1910, **377**, 127.

4-benzylamino-1,2,3-triazole-5-carboxylic acid (IIb) (35%), m.p. 154°, and 4-amino-3-benzyl-1,2,3-triazole-5-carboxylic acid (Ib) (55%).

4-*Amino*-3-*benzyl*-1,2,3-*triazole*-5-*carboxamide* (Ia).—This was prepared in 80% yield from cyanoacetamide, as in the literature;[3] it was either recrystallized from 175 parts of of ethanol or boiled with 5 parts of ethanol, cooled, and filtered (filtrate rejected). The product had m.p. 233—235° (lit.,[3] 233—235°); R_F 0·0 bright violet (Solvent A).

4-*Amino*-3-*benzyl*-1,2,3-*triazole*-5-*carboxylic Acid* (Ib).—(*a*) This compound was made by hydrolysis of the amide (Ia), as described above, and had m.p. 173° (decomp.) (from 270 parts of ethanol). The m.p. varied greatly with the heating conditions, but was repeatable when the specimen was inserted at 163° and heated at 3°/min. [Found (for material dried at 110° in air): C, 55·0; H, 4·6; N, 25·8%]; R_F 0·80 dull violet (solvent A). Its R_F value and i.r. and n.m.r. spectra were identical with those of a specimen prepared as in the literature.[3]

(*b*) *Made by retrogression.* 4-benzylamino-1,2,3-triazole-5-carboxylic acid (IIb) (0·44 g.) and ethanol (18 ml.) were heated under reflux for 1 hr. Refrigeration at −15° effected deposition of 70% of the acid (Ib), m.p. 172° (eff.). The filtrate was taken to dryness at 30°, and the residue was heated under reflux with chloroform (10 ml.) for 10 min.; the solution was filtered and the filtrate was taken to dryness. The residue was ground under 1N-sodium hydroxide (0·5 ml.) to remove 4-benzylamino-1,2,3-triazole (see below). The insoluble material was 4-amino-3-benzyl-1,2,3-triazole (Ic) (14%), m.p. 128° (from water) and identical with authentic material described below. The chloroform-insoluble substance was unchanged starting material (13%), m.p. 154°. The acid (Ib), when similarly heated with ethanol, was recovered unchanged.

Rearrangement (*and Hydrolysis*) *of* 4-*Amino*-3-*benzyl*-1,2,3-*triazole*-5-*carboxamide* (Ia).—The amide (0·66 g., 0·003 mole), potassium hydroxide (85% pellets; 0·4 g., 2 equiv.), and n-butanol (6 ml.) were heated under reflux for 4 hr. The solvent was removed at 80° in a rotary evaporator; water (3 ml.) was added to the residue and the distillation was repeated. The flask contents, adjusted to 6 ml. and set aside at 25°, was filtered to remove starting material (15%) (m.p. 232—234°) and the filtrate was acidified (to pH 2) with 5N-sulphuric acid. The precipitate, a mixture of three triazole acids, was filtered off (whenever this precipitation was omitted, the following separation failed through supersaturation). The precipitate, dissolved in 1N-potassium hydroxide (3 ml.), was added to a boiling solution of sodium chloride (1·5 g.) in water (4·5 ml.); the suspension was refrigerated overnight. The insoluble sodium salt was filtered off, dissolved in boiling water (2 ml.), and acidified (to pH 2). This precipitated 4-amino-3-benzyl-1,2,3-triazole-5-carboxylic acid (Ib) (31%), m.p. 171° (eff.). The filtrate from the sodium salt, acidified with phosphoric acid (to pH 6), deposited 4-*benzylamino*-1,2,3-*triazole*-5-*carboxamide* (IIa). After repetition of this precipitation from alkali and rapid recrystallization from 240 parts of boiling water, the yield was 30%. It softened and resolidified when introduced into bath at 200°, and had m.p. 232—234° (retrogression to starting material) [Found (for material dried at 25° and 0·01 mm.): C, 55·3; H, 5·3; N, 32·0. $C_{10}H_{11}N_5O$ requires C, 55·3; H, 5·1; N, 32·2%]; R_F 0·60, dull slate streak (Solvent A); $\nu_{max.}$ 3360m, 3190m, 1655s (C–O stretch), 1625m, 1595m, 1265m, 1245m, 980m, and 700m cm.$^{-1}$; compared with 4-amino-3-benzyl-1,2,3-triazole-5-carboxamide (Ia): $\nu_{max.}$ 3390s, 3280s broad, 1650s (C–O stretch), 1625s, 1580s, 1560s, 1520m, 1240m, and 740s cm.$^{-1}$. The above filtrate (pH 6), further acidified with 5N-sulphuric acid (to pH 2) deposited 4-benzylamino-1,2,3-triazole-5-carboxylic acid (IIb) (14%), m.p. 152° (eff.).

Retrogression of the Amide (IIa).—The amide (1 g.) and n-pentanol (40 ml.) were heated under reflux for 4 hr. The residue that remained after the solvent had been removed under reduced pressure was stirred with N-sodium hydroxide (8 ml.) at 20°. Filtration gave 90% of 4-amino-3-benzyl-1,2,3-triazole-5-carboxamide (Ia), m.p. 233—235° (lit.,[3] 233—235°); the i.r. spectrum was as given above for the amide (Ia).

4-*Amino*-3-*benzyl*-5-*cyano*-1,2,3-*triazole* (Id).—To a suspension of the amide (Ia) (1·1 g., 0·005 mole) in dimethylformamide (5 ml.), stirred at 0°, was added phosphoryl chloride (0·85 ml., 0·01 mole). The solution was stirred for 5 min. at 0°, 10 min. at 25°, and finally 15 min. at 80° ± 1° (bath temperature). It was cooled to 25°, mixed with N-hydrochloric acid (5 ml.) and heated under reflux for 5 min.; refrigeration gave 90% of 4-amino-3-benzyl-5-cyano-1,2,3-triazole, m.p. 182° (from 14 parts of ethanol) (lit.[3] 179—180°; 184° [4]); the m.p. was not raised above 182° when the product was sublimed, boiled with chloroform (rejected), or stirred at 20° with 0·1N-sodium hydroxide [Found (for material dried at 60° and 0·01 mm.): C, 60·25; H, 4·7; N, 35·3. Calc. for $C_{10}H_9N_5$: C, 60·3; H, 4·6; N, 35·2%]; $\nu_{max.}$ 3370 + 3200s, 2220m (C≡N stretch), 1655s, 1600s, 1325m, 1230m, 720m, and 680m cm.$^{-1}$. When the reaction was completed at 70° (instead of 80°), the yield was only 60%; reaction at 100° gave a very impure product.

The Amidine Intermediate (III).—A similar batch, cooled from 80° to 25°, was added to crushed ice (*ca.* 50 g.) and neutralized with 2N-ammonia (*ca.* 12 ml.). The precipitate of 3-*benzyl*-5-*cyano*-4-*dimethylaminomethyleneamino*-1,2,3-*triazole* (80%) had m.p. 118° [from 5 parts of benzene–light petroleum, b.p. 60—80° (1 : 1)] very soluble in chloroform, only feebly soluble in boiling water [Found (for material dried at 60° and 0·01 mm.): C, 61·5; H, 5·65; N, 33·4. $C_{13}H_{14}N_6$ requires C, 61·4; H, 5·55; N, 33·1%]; $\nu_{max.}$ 2200m (C≡N stretch), 1635s, broad (C=N stretch), 1555s, 1490m, 1425s, 1405m, 1325m, 1120m, 735m, and 695m cm.$^{-1}$; τ([$^2H_6$]DMSO) 1·68 (1H, ⁚CH), 2·66 (5H, C_6H_5), 4·59 (2H, CH_2) 6·79 + 6·87 (d, 2CH_3, splitting due to partial double-bond character of C–NMe_2; no change after addition of D_2O). The compound was quantitatively converted into the nitrile (Id) when boiled in 1N-hydrochloric acid for 5 min.

Dimer (IV) *of the Nitrile* (Id).—4-Amino-3-benzyl-5-cyano-1,2,3-triazole (0·6 g.), 85% potassium hydroxide pellets (0·4 g., 2 equiv.), and ethanol (9 ml.) were heated under reflux for 1 hr.; the amide (Ia) (55%) was filtered off, m.p. 230—232°. The filtrate, taken to dryness at 40° and diluted with water (3 ml.), deposited 6-*amino*-2-(4-*amino*-3-*benzyl*-1,2,3-*triazole*-5-*yl*)-9-*benzyl*-8-*azapurine* (IV) (40%), m.p. 259° from constant-boiling aqueous pyridine [Found (for material dried at 110° and 0·01 mm.): C, 60·3; H, 4·85; N, 35·0. $C_{20}H_{18}N_{10}$ requires C, 60·3; H, 4·6; N, 35·2%]; $\nu_{max.}$ 3460br, 3310, 3110br, 1650, 1615, 1590, 1545, 1340, 1210, and 680 (all m) cm.$^{-1}$.

4-*Amino*-3-*benzyl*-1,2,3-*triazole* (Ic).—The carboxylic acid

(Ib) (2·2 g.) and anhydrous pyridine (10 ml.) were heated under reflux for 10 min. after which the mixture was cooled. Water (7 ml.) was added to the mixture and solvents were removed on a rotary evaporator at 50°. The residue was dried ($CaCl_2$), powdered, and stirred with N-sodium hydroxide (15 ml.). The insoluble material was pure 4-amino-3-benzyl-1,2,3-triazole, m.p. 129° (from 12 parts of boiling water) [Found (for material dried at 60° and 0·01 mm.): C, 62·2; H, 6·0; N, 31·9. Calc. for $C_9H_{10}N_4$: C, 62·05; H, 5·8; N, 32·15%]; τ([$^2H_6$]DMSO), 2·66 (5H, Ph), 3·12 (1H, 5-H), 4·39 sharp (2H, NH_2, exchangeable), 4·60 (2H, CH_2).

4-*Benzylamino*-1,2,3-*triazole* (IIc).—4-Amino-3-benzyl-1,2,3-triazole (Ic) (0·3 g.) and freshly distilled cyclohexylamine (2 ml.) were heated under reflux for 3 hr.; all remained in solution. The solvent was removed at 75° under reduced pressure and the residue was stirred with 1N-sodium hydroxide (2·5 ml.); starting material (23%), was filtered off, m.p. 127°. The filtrate, acidified (to pH 5) with acetic acid, gave 70% of 4-*benzylamino*-1,2,3-*triazole*, m.p. 110° (from 30 parts of boiling water; recovery 95%). It had a strong odour of geranium leaf [Found (for material dried at 24° and 0·01 mm.): C, 62·2; H, 5·8; N, 32·5. $C_9H_{10}N_4$ requires C, 62·05; H, 5·8; N, 32·15%]; τ([$^2H_6$]DMSO), 2·65 (6H, Ph + 4-NH; became 5H when D_2O was added), 2·95 (1H, 5-H), 3·95 (1H, N-3, exchangeable with D_2O), 5·65 (d, 2H, CH_2 coupled to NH, exchangeable).

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