Cyclisation Reactions of Azolylhydrazones Derived from Ethyl Cyanoacetate and Malononitrile. Formation of Azolo[5,1-*c*][1,2,4]triazines †[1,2]

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Ethyl 2-cyano-2-(1,2,4-triazol-5-ylhydrazono)acetate (2a) cyclised in aqueous ethanol to a mixture of ethyl 7-amino-1,2,4-triazolo[5,1-*c*][1,2,4]triazine-6-carboxylate (3a) and 4,7-dihydro-7-oxo-1,2,4-triazolo[5,1-*c*]-[1,2,4]triazine-6-carbonitrile (4a); in acetic acid the product was mainly the amino-ester (3a) whereas in pyridine or collidine, salts of the oxo-nitrile (4a) were formed exclusively. Similar solvent effects controlled the cyclisation of the cyano(pyrazol-5-ylhydrazono)acetate (2c), but the corresponding cyano(tetrazol-5-ylhydrazono)acetate (2d) gave only the amino-ester (3d) in acetic acid or pyridine. 2-(1,2,4-Triazol-5-ylhydrazono)malononitrile (17) cyclised unambiguously to 7-amino-1,2,4-triazolo[5,1-*c*][1,2,4]triazine-6-carbonitrile (18) in acetic acid or aqueous ethanol.

Drastic hydrolysis of the hydrazones (2a) and (17) and the triazolo[5,1-*c*][1,2,4]triazines (3a), (4a), and (18) with 6N-hydrochloric acid gave a hydrate of 1,2,4-triazolo[5,1-*c*][1,2,4]triazin-7(4*H*)-one (24). Selective hydrolysis of the same triazolotriazines afforded intermediates which were identical with known derivatives and which served to establish the [5,1-*c*] geometry of ring fusion. Mass spectral fragmentation of 7-aminoazolo[5,1-*c*]-[1,2,4]triazines confirms that the azole ring is more stable than the 1,2,4-triazine ring on electron impact.

DIAZOTISED 1*H*-aminoazoles (1) are versatile reagents[3] and couple with reactive methylene compounds to form hydrazones which may be cyclised to azolo[1,2,4]triazines. By this means indazolo[3,2-*c*]-,[4] pyrazolo-[5,1-*c*]-,[5,6] and 1,2,3-triazolo[5,1-*c*]-[1,2,4]triazines[7] have been prepared. More recently, 1,2,4-triazole-5-diazonium nitrate has been shown to couple with a range of reactive methylenic esters, ketones, and nitriles in the presence of sodium acetate to afford hydrazones of variable stability which were smoothly cyclised to 6,7-disubstituted 1,2,4-triazolo[5,1-*c*][1,2,4]triazines.[1]

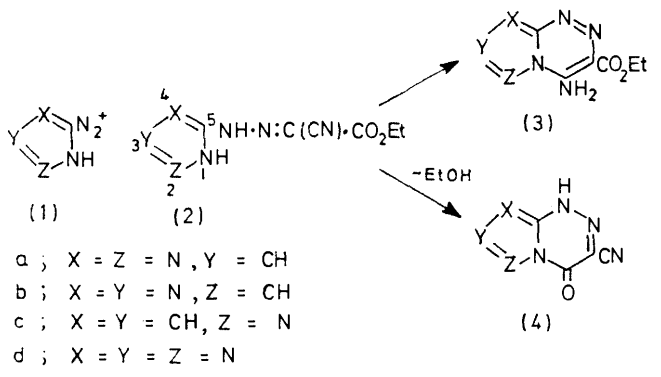
We now report further examples of these cyclisations: in particular we have scrutinised the reaction between diazotised 5-amino-1,2,4-triazole (1a) and ethyl cyanoacetate, since the hydrazone product (2a) can potentially cyclise with involvement of either the nitrile or the ester group (Scheme 1). Moreover, depending on whether N-1 or N-4 of the triazole ring is involved, cyclisation could lead to any of four possible products: the triazolo[5,1-*c*]triazines (3a) and (4a), and the isomeric triazolo[3,4-*c*]triazines (3b) and (4b). (However, only the [5,1-*c*] arrangement was encountered in previous studies.[1])

Reaction between 1,2,4-Triazole-5-diazonium Nitrate and Ethyl Cyanoacetate.—1,2,4-Triazole-5-diazonium

† This paper is designated Part IX of 'The Chemistry of Heterocyclic Compounds,' and Part XVII of 'Triazines and Related Products.' Previous papers in these series are (respectively) references 1 and 2.

[1] Part VIII, G. Tennant and R. J. S. Vevers, *J.C.S. Perkin I*, 1976, 421.
[2] Part XVI, E. J. Gray and M. F. G. Stevens, preceding paper.
[3] R. N. Butler, *Chem. Rev.*, 1975, **75**, 241.
[4] G. R. Bedford, F. C. Cooper, M. W. Partridge, and M. F. G. Stevens, *J. Chem. Soc.*, 1963, 5901; D. Fortuna, B. Stanovnik, and M. Tišler, *J. Org. Chem.*, 1974, **39**, 1833; R. Allmann, T. Debaerdemaeker, W. Grahn, and C. Reichardt, *Chem. Ber.*, 1974, **107**, 1555.
[5] M. W. Partridge and M. F. G. Stevens, *J. Chem. Soc.* (*C*), 1966, 1127.
[6] J. Slouka, V. Bekárek, and J. Kubatá, *Monatsh.*, 1974, **105**, 535; H. Reimlinger, A. Van Overstraeten, and H. G. Viehe, *Chem. Ber.*, 1961, **94**, 1036; H. Reimlinger and A. Van Overstraeten, *ibid.*, 1966, **99**, 3350.
[7] H. Mackie and G. Tennant, *Tetrahedron Letters*, 1972, 4719.

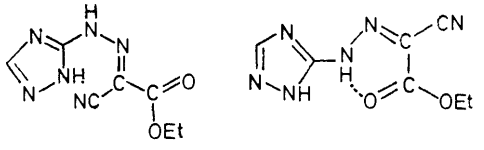
nitrate coupled as expected with ethyl cyanoacetate to afford a cream-coloured hydrazone (98%), which crystallised as a monohydrate from 70% aqueous ethanol. The hydrazone nature of the product was

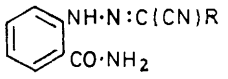


SCHEME 1

inferred from the u.v. spectrum ($\lambda_{max.}$ 371 nm), which is typical of other arylhydrazones[8] but differs qualitatively from the spectra of their arylazo-analogues.[9] Of the possible triazole NH tautomers we prefer that illustrated (2a) to the 4*H*-isomer (2b) or the 3-substituted 1*H*-isomer.[10]

No change in the u.v. spectrum of the hydrazone hydrate occurred on boiling in anhydrous acetone, and no cyclic products were detected (t.l.c.). However removal of the acetone furnished a yellow solid with an i.r. spectrum substantially modified in the N–H/O–H, C≡N, and C=O regions. Notably, the nitrile band at 2 225 decreased in intensity as a new peak at 2 204 cm^{-1} emerged; the carbonyl absorption at 1 720 also decayed,





(5) R = CN
(6) R = CO_2Et

being replaced by a band at 1 740 cm^{-1}. After 5 h in refluxing acetone, a mixture of the original hydrazone and a second component was present in the ratio *ca.* 1 : 1, and no further change in the ratio was apparent, even on prolonged boiling (25 h). The mixture containing both components reverted completely to the original hydrazone hydrate when recrystallised from 70% aqueous ethanol.

A possible explanation for the spectral changes involves geometrical isomerisation of the hydrazone (2a). The original hydrazone hydrate might have structure (A) with the configuration stabilised by intermolecular hydrogen-bonding to water. In hot acetone an equilibrium may be established with geometrical isomer (B), which would be stabilised by intramolecular hydrogen bonding. Significantly, the model hydrazone (5),[8] which crystallises without the complicating water of crystallisation, shows two cyano-absorptions (at 2 236 and 2 210 cm^{-1}) in its i.r. spectrum. These values for the nitrile groups in two distinct geometrical environments correspond closely to the nitrile peaks encountered in the mixture of the two forms of the hydrazone (2a).

The hydrazone (6) also crystallised in two distinct forms. A deep yellow form (m.p. 185°), from aqueous ethanol or pyridine, contained no solvent; it crystallised from acetic acid as a pale yellow modification (m.p. 202—204°), analysis of which corresponded with a hemi-acetate. The high melting form reverted to the low melting form in pyridine. The mass spectra of the two samples were nearly identical, but significant differences in the i.r. and ^1H n.m.r. spectra were apparent (see Table 1). Similarly, two distinct forms of each of the hydrazones formed by coupling 4-chloro-[11] and 2-nitro-anilines[12] with ethyl cyanoacetate are reported, and the structures of these and other hydrazones have long been the subject of controversy.[13,14] Accordingly the structures assigned to forms (A) and (B) of the hydrazone (2a) should be considered as tentative at this stage, particularly in view of the carbonyl absorption (1 740 cm^{-1}) of the proposed intramolecularly bonded isomer the wavenumber of which is somewhat high for a hydrogen-bonded αβ-unsaturated ester.

Cyclisation of Ethyl 2-Cyano-2-(1,2,4-triazol-5-ylhydrazono)acetate.—The hydrazone hydrate (2a) was significantly more stable in boiling aqueous solution than related 1,2,4-triazol-5-ylhydrazones.[1] Forty percent of the starting material (18% after 45 min) was recovered after 10 min in boiling water, providing that the solution was rapidly cooled to 0 °C; t.l.c. showed the presence of the hydrazone and two triazolotriazines only. On a preparative scale it proved most convenient to heat the crude hydrazone in the aqueous ethanolic coupling medium containing an excess of sodium acetate for 1 h. The cyclised products, subsequently identified as ethyl 7-amino-1,2,4-triazolo[5,1-*c*][1,2,4]triazine-6-carboxylate (3a) and 4,7-dihydro-7-oxo-1,2,4-triazolo[5,1-*c*][1,2,4]-triazine-6-carbonitrile (4a), were isolated in the ratio *ca.* 2 : 1.

The course of cyclisation is strongly influenced by the nature of the solvent. In boiling acetic acid the hydrazone hydrate cyclises to the more basic product,

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[14] J. Buckingham, *Quart. Rev.*, 1969, **23**, 37.

TABLE 1

Spectroscopic characteristics of azolylhydrazones, other model hydrazones, and azolo[5,1-*c*][1,2,4]triazines

Compound	$\lambda_{max.}$/nm (log ε) [a]	$\nu_{max.}$/cm^{-1} [b,c]	τ Values [d]
Azolylhydrazones and model hydrazones			
(2a) [e]	371 (4.19)	3 525 (OH),[b] 3 340, 3 280, 3 160 (NH), 3 000—2 700br (bonded NH/OH), 2 225 (C≡N), 1 720 (C=O), 1 550 (C=N)	1.62 (1 H, s, H-3), 5.74 (2 H, q, *J ca.* 7 Hz, CH_2), 8.72 (3 H, t, *J ca.* 7 Hz, CH_3)
(2c) [f]	358 (4.15)	3 410,[b] 3 350, 3 160 (NH), 2 222 (C≡N), 1 702 (C=O)	2.30 (1 H, dd, H-3), 3.75 (1 H, dd, H-4), 5.70 (2 H, dq, CH_2), 8.71 (2 H, dt, CH_3)
(2d)	368 (3.99)	3 280 [b] (NH), 3 000—2 800 br (bonded NH), 2 235 (C≡N), 1 710 (C=O)	
(5) [g]	370	3 460,[b] 3 340 (NH), 2 236. 2 210 (C≡N), 1 669 (C=O)	
(6) [g,h]	362	3 495,[b] 3 382 (NH), 2 230 (C≡N), 1 705 (CO_2Et), 1 665 ($CONH_2$)	1.25 br (NH), 1.6—2.31 (4 H, m, ArH), 5.18 (2 H, q, *J ca.* 7 Hz, CH_2), 8.19 (3 H, t, *J ca.* 7 Hz, CH_3),
(6) [i]	362	3 430,[b] 3 385, 3 200 (NH), 2 225 (C≡N), 1 727 (CO_2Et), 1 693 (AcOH), 1 660 ($CONH_2$)	1.1br (NH), 1.5—2.23 (8 H, m, ArH) 5.17 (4 H, dq, CH_2), 6.0br (OH), 7.59 (3 H, s, $CH_3{\cdot}CO_2H$), 8.18 (6 H, dt, $CH_2{\cdot}CH_3$)
(17) [j]	374	3 500,[c] 3 100—2 700br (NH), 2 250 (C≡N), 1 690 (NH def.)	1.19 (1 H, s, H-3)
Azolo[5,1-*c*][1,2,4]triazines			
3(a)	215 (4.32), 229 (4.35), 282 (4.17), 325 (4.29)	3 355,[b] 3 280, 3 210, 3 140 (NH), 1 707 (C=O), 1 640 (NH def.)	1.23 (1 H, s, H-2), 5.55 (2 H, q, *J ca.* 7 Hz, CH_2), 8.62 (3 H, t, *J ca.* 7 Hz, CH_3)
(3c)	234 (4.14), 310 (4.05), 344 (3.92)	3 600,[b] 3 320 (NH), 1 685 (C=O), 1 655 (NH def.)	1.1br (2 H, NH_2), 1.61 (1 H, d, *J ca.* 3 Hz, H-2), 2.92 (1 H, d, *J ca.* 3 Hz, H-3), 5.54 (2 H, q, *J ca.* 7 Hz, CH_2), 8.61 (3 H, t, *J ca.* 7 Hz, CH_3)
(3d)	236 (4.28), 329 (4.28)	3 590,[b] 3 380, 3 290, 3 200 (NH), 1 721 (C=O), 1 640 (NH def.)	
(4a)	213 (4.35), 217sh (4.35), 253 (4.06), 257sh (4.05), 275 (3.95), 319 (4.41)	2 700br [c] (NH), 2 250 (C≡N), 1 700 (C=O)	1.45 (1 H, s, H-2)
(4a) [k]	223 (4.05), 244sh (3.58), 250 (3.74), 257 (3.86), 263 (3.89), 273sh (3.76), 332 (4.11)	3 140,[b] 3 080, 3 060 (arom. CH), 2 900—2 400br (NH), 2 235 (C≡N), 1 670 (C=O)	1.05 (2 H, d, pyridine H-2, H-6), 1.50 (1 H, m, pyridine H-4), 1.58 (1 H, s, H-2), 1.98 (2 H, t, pyridine H-3, H-5)
(4c)	269sh (3.84), 275 (3.86), 287sh (3.70), 295 (3.69), 345 (3.97)	3 100,[b] 2 700br (NH), 2 250 (C≡N), 1 698 (C=O)	1.0br (1 H, NH), 1.70 (1 H, d, H-2), 3.30 (1 H, d, H-3)
(10) [l,m]	*n*	3 400,[c] 3 250, 3 100—2 700br (NH/OH), 1 680 (C=O), 1 650 (NH def.)	1.28 (1 H, s, H-2), 0.47, 0.59, 1.48, 2.20 (4 H, s, 4 × NH)
(11)	223 (4.16), 280 (3.87), 332 (4.01)	3 300,[b] 3 130 (NH), 2 940, 2 920, 2 860 (alip. CH), 1 655 (C=O), 1 620 (NH def.)	1.29br (2 H, NH_2), 1.45 (1 H, s, H-2), 6.5br (4 H, $[CH_2]_2$), 8.53br (6 H, $[CH_2]_3$)
(12)	223 [o], 303	3 260 [b] (NH), 1 729, 1 702 (C=O)	1.23 (1 H, s, H-2), 5.75 (2 H, q, *J ca.* 7 Hz, CH_2), 7.80 (3 H, s, $COCH_3$), 8.79 (3 H, t, $CH_2{\cdot}CH_3$)
(13)	275 [o]	1 730,[b] 1 705 (C=O)	1.30 (1 H, s, H-2), 5.79 (2 H, q, CH_2), 7.60 (3 H, s, $COCH_3$), 8.83 (3 H, t, $CH_2{\cdot}CH_3$)
(16)	215 (4.22), 253 (3.98), 261sh (3.88), 320 (4.31)	2 300 [c] (C≡N), 1 720 (C=O)	1.39 (1 H, s, H-2), 5.89 (3 H, s, CH_3)
(18) [e]	210 (4.11), 228 (4.03), 279 (3.78), 284sh (3.77), 332 (3.90)	3 400,[c] 3 100—2 700br (NH/OH), 2 250 (C≡N), 1 670 (NH def.)	0.2br (2 H, NH_2), 1.20 (1 H, s, H-2)
(21) [m]	208 (4.06), 220sh (3.93), 261sh (3.64), 273 (3.68), 318 (4.00)	3 100 [c]—2 700br (NH), 1 740, 1 695 (C=O)	1.56 (1 H, s, H-2), 5.64 (2 H, q, *J ca.* 7 Hz, CH_2), 8.64 (3 H, t, *J ca.* 7 Hz, CH_3)
(22) [m]	*n*	3 350,[c] 3 200, 2 700br (NH), 1 740, 1 670 (C=O), 1 640 (NH def.)	1.59 (1 H, s, H-2), 2.15br (2 H, NH_2)
(24) [m]	213 (3.83), 241 (3.55), 246sh (3.53), 269sh (3.53), 298 (3.81)	3 200 [c]br, 2 700br (NH), 1 695 (C=O)	1.64 (1 H, s, H-2), 2.20 (1 H, s, H-6)
(24) [p]	240 (3.58), 296 (3.80)	3 220,[b] 3 000br(NH), 1 690 (C=O)	1.60 (1 H, s, H-2), 2.20 (1 H, s, H-6)
(24) [e]	290 (3.93)	1 710 [c] (C=O)	1.71 [q] (1 H, s, H-2), 2.54 [q] (1 H, s, H-6)

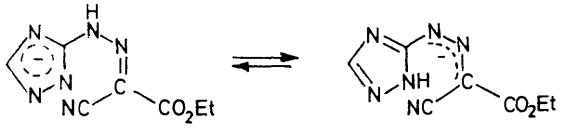
[a] Recorded on a Unicam SP 8000 spectrometer (in 95% ethanol). [b] Recorded on a Perkin–Elmer 157G spectrometer (KBr disc). [c] Recorded on a Unicam SP 200 spectrometer (Nujol suspension). [d] Recorded on a Varian HA-100 spectrometer (for solutions in [$^2H_6$]dimethyl sulphoxide). [e] Hydrate. [f] Crystallised from aqueous ethanol (ref. 5). [g] Ref. 8. [h] Crystallised from aqueous pyridine. [i] Hemiacetate solvate (from acetic acid). [j] Crude material. [k] Pyridinium salt. [l] Hemihydrate. [m] Ref. 1. [n] Insoluble in 95% ethanol. [o] Compound unstable in 95% ethanol. [p] Ref. 17. [q] After shaking with D_2O.

the amino-ester (3a), in 88—90% yield although traces of the oxo-nitrile were detected (t.l.c.). In the boiling bases pyridine and collidine the strongly acidic oxo-nitrile (4a) was formed exclusively as its pyridine and collidine salts. Acidification of the salts with N-hydrochloric acid furnished the pure oxo-nitrile hydrate, which crystallised as the unsolvated acid from ethanol—this was the most efficient route to this compound.

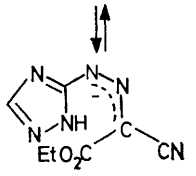
It was considered that the oxo-nitrile (4a) might originate from the amino-ester (3a) by a base-catalysed

ring-opening similar to that involved in the base-initiated ring-opening of 1,2,3-benzotriazin-4(3*H*)-imines.[15] The intermediacy of extensively delocalised hydrazone anions (7)—(9) would provide a logical mechanism for the isomerisation of the hydrazone, which could then cyclise irreversibly to the oxo-nitrile (4a). No evidence for this alternative route was found and the amino-ester was recovered from boiling pyridine, collidine, and triethylamine. These observations, coupled with its stability in boiling acetic acid and thermal stability in the solid state, and the corresponding unreactivity of the oxo-nitrile, point conclusively to the stable triazolo[5,1-*c*]triazine configuration (' a ' series) for these compounds rather than the triazolo-[3,4-*c*]triazine arrangement (' b ' series) [16] (Scheme 1).

Structure (3a) for the amino-ester is also supported by its spectroscopic features (Table 1), notably the chemical shift of H-2 (τ 1.23), which is well within the range expected for an N-1-fused triazole, but different from that anticipated for an N-4-fused skeletal isomer.[17] The ester was converted in alcoholic ammonia into an amide (10), identical with the product isolated from the cyclisation of the hydrazone formed by coupling 1,2,4-triazole-5-diazonium nitrate with cyanoacetamide,[1] and in boiling piperidine to the piperidino-amide (11). Both these compounds have the [5,1-*c*] skeleton as adjudged by the chemical shift of their triazole protons (Table 1). The amino-ester formed an unstable monoacetyl derivative (12) in boiling acetic anhydride which differed from the unstable monoacetyl derivative formed by treating the hydrazone hydrate (2a) with acetic anhydride. The absence of a C≡N absorption in the i.r. spectrum of this latter product confirms a cyclic structure. Support for

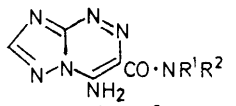


(7) (8)



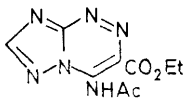
(9)

the 4-acetyl formulation (13) comes from the u.v. spectrum [$\lambda_{max.}$ 275 nm; *cf.* 303 nm for the derivative (12)], indicative of loss of the N=N chromophore.[5] As the hydrazone must undergo acetylation before cyclisation, a 1-acetyltriazolotriazine (14) is excluded. Attempts to exploit the reactivity of both amino- and ester groups in the triazolotriazine (3a) in a reaction with formamide failed to realise the expected pyrimido-triazolotriazine (15).

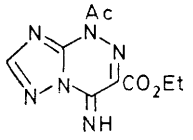


(10) $R^1 = R^2 = H$

(11) $R^1 = R^2 = [CH_2]_5$



(12)



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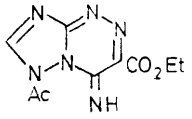

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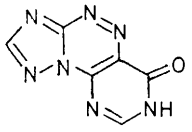

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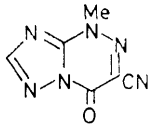


(16)

The pyridine and collidine salts of the oxo-nitrile (4a) can be crystallised unchanged from acetic acid; thus the pK_a of this triazolotriazine may be below that of acetic acid (4.76).[18,] * The C=O absorption (1 700 cm^{-1}) of the free oxo-nitrile (4a) is shifted to 1 670 and 1 680 cm^{-1} in the pyridine and collidine derivatives, respectively; this is consistent with salt formation rather than complex formation. The chemical shift of the triazole proton (τ 1.45) of the free oxo-nitrile confirms the [5,1-*c*] fusion, and the absorptions of the pyridine protons in its pyridinium salt closely correspond with those of pyridine picrate. Methylation of the oxo-nitrile (4a) with dimethyl sulphate afforded the 4-methyltriazinone (16), with spectroscopic characteristics in accord with those of other 4-methyltriazolotriazinones.[1]

Cyclisation of Ethyl 2-*Cyano*-2-(*pyrazol*-5-*ylhydrazono*)-*and* 2-*Cyano*-2-(*tetrazol*-5-*ylhydrazono*)-*acetates*.—In the light of the aforementioned observations it was appropriate to re-examine the cyclisation of the pyrazol-5-yl-hydrazone (2c) in various solvents; previously only one cyclic product (3c) had been isolated. A pure non-solvated hydrazone which crystallised from aqueous ethanol was readily obtained, as originally claimed.[5] In boiling benzene this hydrazone changed into a different form, although variations in the i.r. characteristics of the two forms were not as pronounced as in the triazole series; the second form reverted to the original in

* A referee has suggested that crystal lattice effects might make an acid weaker than acetic acid deposit crystals of its salt from acetic acid solution.

[15] M. S. S. Siddiqui and M. F. G. Stevens, *J.C.S. Perkin I*, 1974, 611.

[16] P. Guerret, R. Jacquier, and G. Maury, *J. Heterocyclic Chem.*, 1971, **8**, 643.

[17] J. Daunis, R. Jacquier, and P. Viallefont, *Bull. Soc. chim. France*, 1969, 2492.

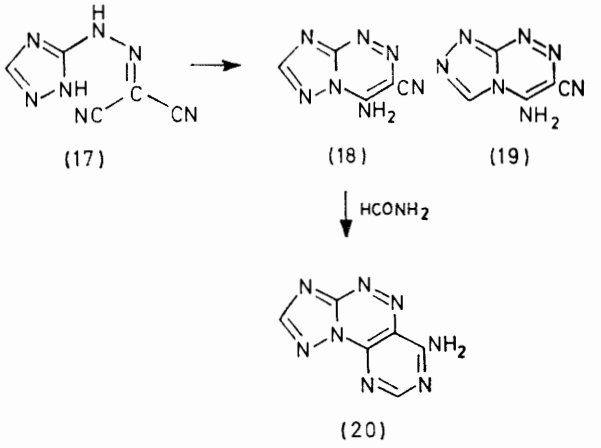
[18] A. Albert and E. P. Serjeant, ' Ionisation Constants of Acids and Bases,' Methuen, London, 1962.

aqueous ethanol. A ^{1}H n.m.r. spectrum of the original hydrazone in [$^2H_6$]dimethyl sulphoxide showed it to be a mixture of two closely similar isomers in that solvent. Evidently the geometrical isomers of this hydrazone are readily interconvertible. As originally reported,[5] the pyrazol-5-ylhydrazone (2c), from aqueous ethanol, cyclised (>95%) in boiling acetic acid to the amino-ester (3c), with an i.r. spectrum notable for a high frequency N–H stretching absorption at 3 600 cm^{-1}; the amino-ester was also slowly formed (95%) in the present work from the hydrazone (2c) in boiling ethanol. However, traces of the oxo-nitrile (4c) were detected, and this derivative was the sole product (as a pyridine salt) when pyridine was employed as the cyclising medium: the salt partially dissociated in boiling aqueous ethanol. The free acidic oxo-nitrile (4c) was liberated from the salt with N-hydrochloric acid, and the spectral characteristics of the oxo-nitrile and its salt agreed well with those of the corresponding triazole series (Table 1).

Efforts to diazotise 5-amino-1*H*-tetrazole in hydrochloric acid on a preparative scale were thwarted by the explosive nature of the diazonium salt.[19] On a small scale the salt was safely coupled with ethyl cyanoacetate to give a hydrazone (2d) with properties that varied depending on the pH of the coupling medium. When the pH was adjusted to 3 with sodium hydroxide a colourless hydrazone hydrate was isolated which crystallised from aqueous ethanol as the unsolvated hydrazone (2d). In sodium acetate buffer (pH 6) a yellow sodium salt of the hydrazone was obtained. Both the hydrazone and its salt cyclised in acetic acid to ethyl 7-aminotetrazolo[5,1-*c*][1,2,4]triazine-6-carboxylate (3d) in high yield. However, the free tetrazole hydrazone differed from its pyrazole and 1,2,4-triazole counterparts in also cyclising to the amino-ester (3d) in pyridine; the sodium salt was recovered from this solvent. We are unable to offer an explanation for this anomaly, and have abandoned our interest in this cyclisation.

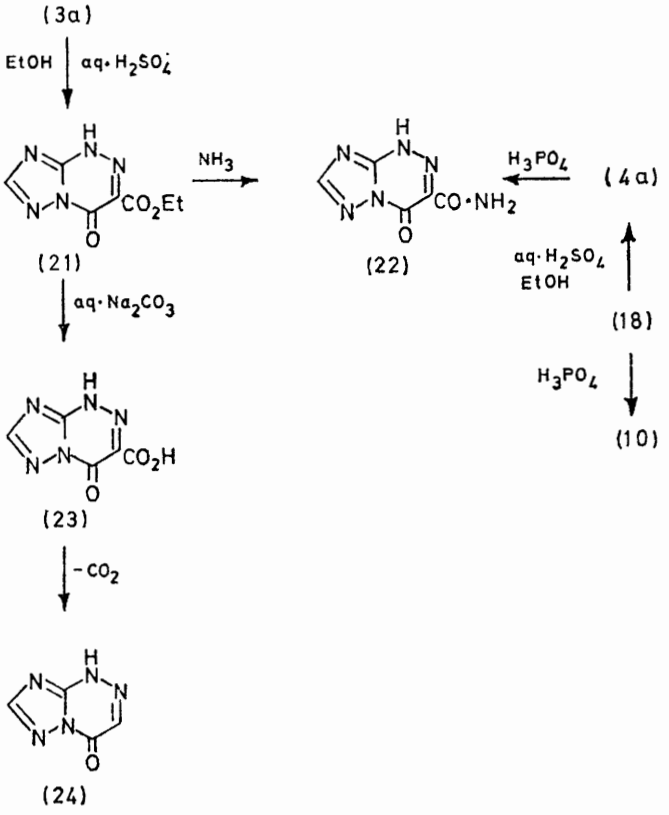
Preparation and Cyclisation of 2-(1,2,4-*Triazol*-5-*yl*-*hydrazono*)*malononitrile*.— 1,2,4-Triazole-5-diazonium nitrate coupled smoothly with malononitrile in sodium acetate buffer to afford the crude hydrazone (17), which cyclised on attempted crystallisation from aqueous ethanol to give the amino-nitrile (18). This cyclisation was also accomplished in acetic acid, or, most efficiently, simply by boiling the crude coupling mixture for 1 h. The amino-nitrile (hydrate) had spectroscopic properties (see Table 1) which unequivocally characterise it as a triazolo[5,1-*c*]triazine rather than the isomeric triazolo-[3,4-*c*]triazine (19). As expected it was also stable in boiling acetic acid or pyridine, but like many *o*-amino-nitriles [20] it cyclised to a fused amino-pyrimidine (20) in boiling formamide (Scheme 2).

Additional evidence for the structure of the amino-nitrile (18) and the other triazolotriazines described in this paper was provided by their partial and complete hydrolysis.



SCHEME 2

Hydrolytic Transformations of 1,2,4-*Triazolo*[5,1-c]-[1,2,4]*triazines*.—Hydrolysis of the amino-ester (3a) with aqueous ethanolic sulphuric acid yielded the oxo-ester (21), which has been previously isolated from the



SCHEME 3

cyclisation of diethyl 2-(1,2,4-triazol-5-ylhydrazono)-malonate.[1] This oxo-ester has been shown to undergo alkaline hydrolysis to the oxo-acid (23) and further

[19] J. F. Riordan and B. L. Vallee, *Methods Enzymol.*, 1972, **25**, (Part B), pp. 525—526.

[20] E. C. Taylor and A. McKillop, ' The Chemistry of Cyclic Enaminonitriles and *o*-Aminonitriles,' Interscience, New York, 1970, p. 270.

decarboxylation to the known triazolotriazinone (24),[1] prepared unequivocally by cyclisation, with formic acid, of 4-amino-2,3-dihydro-3-imino-1,2,4-triazin-5(4*H*)-one[17] —this reaction sequence further confirms the triazolo-[5,1-*c*]triazine geometry of amino-ester (3a). The oxo-nitrile (4a) in its turn was hydrolysed in polyphosphoric acid to the amide (22), identical with that previously formed[1] by ammonolysis of the oxo-ester (21). The amino-nitrile (18) yielded the amino-amide (10) in polyphosphoric acid and the oxo-nitrile (4a) in aqueous ethanolic sulphuric acid.

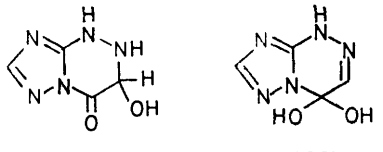
When the hydrazones (2a) and (17) and the triazolo-triazines (3a), (4a), and (18) were boiled for prolonged periods in 6N-hydrochloric acid the product (55—60%) in each case was a hydrate of the triazinone (24).

It seems likely that hydrolysis of the hydrazone (2a) proceeds *via* the sequence (2a) ⟶ (3a) ⟶ (21) ⟶ (23) ⟶ (24) and of the hydrazone (17) *via* the sequence (17) ⟶ (18) ⟶ (4a) ⟶ (22) ⟶ (23) ⟶ (24) (Scheme 3). The corresponding pyrazol-5-yl-hydrazone (2c) and the pyrazolotriazine amino-ester (3c) are both hydrolysed in 6N-hydrochloric acid to form pyrazolo[5,1-*c*][1,2,4]triazin-7(4*H*)-one in a related process.[5]

The hydrate of the triazolotriazinone (24) was formed independently from the pure triazinone in N-hydrochloric acid and shown to revert to the unsolvated form in boiling acetic acid. Although the mass spectrum of the hydrate showed a molecular ion (*m/e* 137) corresponding to the triazinone (24) it appears not to be a simple solvate because of the substantial differences in the spectroscopic properties (Table 1) of the hydrate and parent triazolotriazinone.

On the reasonable assumption that covalent hydration would involve the π-deficient triazine ring of (24),[21] two adducts (25) and (26) are possible. Structure (25) is supported by the i.r. spectrum of the hydrate (C=O at 1 710 cm^{-1}), but is contraindicated by the ^1H n.m.r. spectrum; H-6 in the hydrate (25) would be expected to absorb considerably upfield of the observed signal at τ 2.54. This value is reasonable for H-6 in the *gem*-diol (26), yet the i.r. spectrum militates against this structure assignment.

Although 6,7-diphenyl-1,2,4-triazolo[5,1-*c*][1,2,4]tri-azine[2] is known to undergo acid-promoted nucleophilic addition at C-7 [as in the diol (26)] the structure of the hydrate of the triazolotriazinone (24) must remain open.

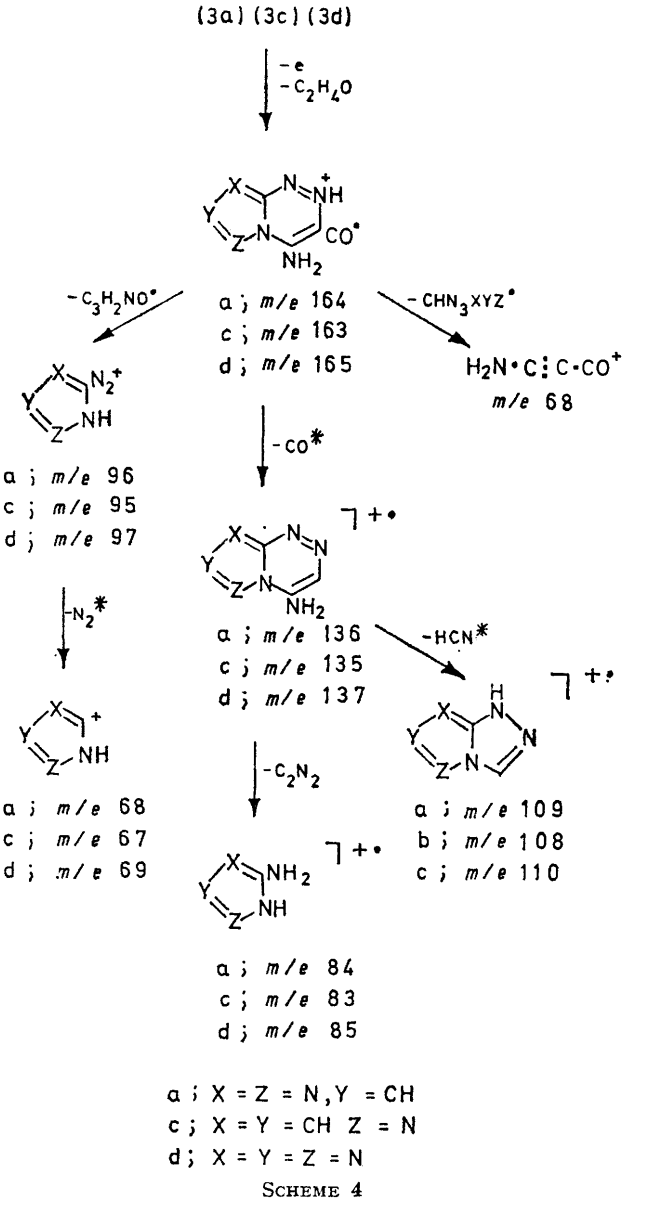


(25) (26)

Indeed, the whole problem of adduct formation in monocyclic 1,2,4-triazines[22] and bicyclic 1,2,4-triazines is worthy of further study.

[21] A. Albert, 'Heterocyclic Chemistry,' The Athlone Press, London, 2nd edn., 1968, p. 125.

Mass Spectra of 7-Aminoazolo[5,1-c][1,2,4]*triazines.*— The mass spectra of the 1,2,4-triazolotriazine amino-ester (3a) and the corresponding tetrazolotriazine



SCHEME 4

derivative (3d) closely parallel the spectrum of the pyrazolotriazine amino-ester (3c).[23] The major fragmentation pathways of these compounds, together with possible structures for the important ions, are recorded in Scheme 4 (metastable-supported transitions are denoted by an asterisk). Although a minor N_2 loss from the tetrazole ring in the tetrazolotriazine amino-ester (3d) was observed, the available data (Table 2) confirm that of the two rings in the bicyclic systems the azole ring is the more stable to electron impact. The

[22] W. W. Paudler and T.-K. Chen, *J. Heterocyclic Chem.*, 1970, **7**, 767.

[23] M. H. Palmer, P. N. Preston, and M. F. G. Stevens, *Org. Mass Spectrometry*, 1971, **5**, 1085.

TABLE 2

Mass spectra of azolylhydrazones and azolo[5,1-*c*][1,2,4]triazines measured at 70 eV (A.E.I.–G.E.C. MS902 spectrometer; source temperature in the range 100—150 °C) (relative intensities in parentheses)

Compd.	
(2a)	208 (M^+, 9), 164 (27), 162 (27), 136 (100), 135 (46), 109 (18), 96 (18), 84 (36), 68 (27), 54 (27), 53 (36), 52(27), 45 (73).
(2d)	209 (M^+, 15), 181 (9), 165 (36), 137 (13), 69 (8), 68 (19), 54 (10), 53 (7).
(3a)	208 (M^+, 18), 164 (33), 136 (100), 109 (15), 96 (23), 84 (23), 68 (30), 54 (23), 53 (39).
(3c) [a]	207 (M^+, 100), 163 (100), 135 (100), 108 (48), 95 (70), 83 (100), 68 (38), 67 (31), 54 (28), 53 (86), 52 (86).
(3d)	209 (M^+, 22), 181 (22), 165 (86), 137 (30), 110 (3), 97 (4), 81 (13), 69 (38), 68 (85), 54 (50), 53 (36).
(10)	179 (M^+, 40), 165 (13), 151 (65), 135 (13), 124 (43), 109 (13), 96 (20), 95 (20), 84 (100), 68 (35).
(11)	247 (M^+, 7), 164 (3), 136 (6), 109 (6), 96 (15), 84 (100), 68 (15).
(12)	250 (M^+, 12), 235 (40), 208 (38), 164 (77), 136 (100), 135 (18), 109 (17), 96 (24), 84 (34), 68 (24), 54 (15), 53 (22), 43 (20).
(13)	250 (M^+, 9), 208 (70), 164 (54), 136 (100), 135 (23), 109 (12), 96 (23), 84 (26), 68 (18), 54 (9), 53 (12), 43 (62).
(18)	161 (M^+, 100), 134 (18), 109 (3), 96 (76), 68 (20), 53 (33).

[a] Ref. 23.

triazolotriazine piperidide (11) shows a similar fragmentation, but the related amino-amide (10) and amino-nitrile (18) deviate substantially from this pathway: the spectrum of the amino-amide (10) however shows major ions at *m/e* 109, 96, 84, and 68, in common with the amino-ester; the amino-nitrile (18) shows only two ions of significance: the molecular ion (*m/e* 161) and the triazol-5-yldiazonium ion (*m/e* 96).

The spectra of the two acetyl derivatives (12) and (13) were substantially similar to that of the parent amino-ester (Table 2) after an initial keten loss, and the spectrum of the hydrazone (2a) showed evidence of a thermally induced cyclisation to both the amino-ester (3a) and the oxo-nitrile (4a).

EXPERIMENTAL

T.l.c. separations were accomplished on silica gel (0.25 mm) with benzene–acetone (6 : 4) as developing solvent.

Ethyl 2-Cyano-2-(1,2,4-triazol-5-ylhydrazono)acetate (2a).—A stirred solution of 5-amino-1,2,4-triazole (8.4 g, 0.1 mol) in concentrated nitric acid (s.g. 1.42; 10 ml) and water (25 ml) was treated at 0 °C with sodium nitrite (7.6 g, 0.11 mol) in water (10 ml) over 30 min. The pale yellow diazonium solution was stirred for a further 1 h at 0—5 °C, neutralised with sodium acetate trihydrate (25 g), and treated with ethyl cyanoacetate (11.3 g, 0.1 mol), run in dropwise (10 min). The suspension was diluted with more water (50 ml) to ensure adequate mixing and stirred for a further 2 h at 0—5 °C. The yellow solid was collected, washed with the minimum of ice–water, and dried. The crude product (20.6 g, 98%) crystallised from 70% aqueous ethanol to afford the *(hydrazono)cyanoacetate hydrate* as cream-coloured needles, m.p. 177—178° (Found: C, 36.9; H, 4.8; N, 37.1. $C_7H_8N_6O_2,H_2O$ requires C, 37.2; H, 4.4; N, 37.2%).

Solutions of the product (2a) (2 g) in water (100 ml) were boiled for 10 or 45 min and kept at 0 °C. After 7 days unchanged hydrazone (0.8 and 0.35 g, respectively) was recovered. T.l.c. of the mother liquors showed the presence of ethyl 7-amino-1,2,4-triazolo[5,1-*c*][1,2,4]triazine-6-carboxylate (3a) and 4,7-dihydro-7-oxo-1,2,4-triazolo[5,1-*c*]-[1,2,4]triazine-6-carbonitrile (4a).

Ethyl 2-(2-Carbamoylphenylhydrazono)-2-cyanoacetate (6).—This (hydrazono)cyanoacetate was prepared by coupling diazotised anthranilamide with ethyl cyanoacetate in the presence of an excess of sodium acetate trihydrate.[8] The (hydrazono)cyanoacetate (2.0 g) was boiled in acetic acid (10 ml) for 1 h. A yellow mass of needles (1.7 g) of the *hemiacetate solvate* was deposited on cooling; m.p. 202—203° (sinters 185°) (Found: C, 53.4; H, 5.1; N, 19.2. $C_{12}H_{12}N_4O_3,CH_3CO_2H$ requires C, 53.8; H, 4.8; N, 19.3%). The hemiacetate solvate reverted to the unsolvated hydrazone when crystallised from aqueous pyridine [identical (i.r.) with an authentic sample [8]].

Ethyl 7-Amino-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-carboxylate* (3a).—(i) A solution of 1,2,4-triazole-5-diazonium nitrate (0.03 mol) in aqueous nitric acid (prepared as above) was added dropwise with stirring at 0—10 °C to a mixture of ethyl cyanoacetate (0.03 mol) and anhydrous sodium acetate (3.2 g) in water (8.0 ml) and ethanol (20.0 ml). The mixture was stirred at room temperature for 1 h, heated under reflux for 1 h, and then filtered to remove a small amount of insoluble material. Evaporation furnished a solid which was boiled in water (50 ml) for 5 min and cooled. The *triazolotriazine* (1.2 g) was deposited, and crystallised from ethanol–acetic acid as plates, m.p. 210° (Found: C, 40.0; H, 4.0; N, 40.2. $C_7H_8N_6O_2$ requires C, 40.4; H, 3.9; N, 40.4%). More (0.7 g) of the amino-ester was recovered by extraction of the aqueous mother liquor with chloroform.

(ii) The pure hydrazone hydrate (2a) (0.31 g) in ethanol (5.0 ml) and water (2.0 ml) was heated under reflux with anhydrous sodium acetate (0.12 g) for 1 h. The mixture was evaporated and triturated with water to yield the amino-ester (0.14 g), identical (mixed m.p. and i.r. spectrum) with an authentic specimen. The aqueous mother liquor was evaporated and the residual solid extracted with boiling methanol to afford a gummy solid which was heated under reflux with chloroform. The chloroform-soluble fraction afforded more of the amino-ester (0.04 g).

(iii) The hydrazone hydrate (2a) (0.42 g) was boiled in acetic acid (10.0 ml) for 2 h and the solution evaporated. The residue, triturated with ether–methanol, afforded the same amino-ester (88%).

The amino-ester (3a) was unchanged after being heated at 220 °C for 1 h, or from boiling acetic acid, pyridine, collidine, or triethylamine (4 h). In boiling formamide (2 h) the amino-ester gave an intractable black solid.

7-Amino-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-carboxamide* (10).—(i) A solution of the amino-ester (3a) (0.62 g) in absolute ethanol (100 ml) was saturated at 0 °C with dry ammonia gas and left at room temperature for 70 h. The mixture was filtered to remove insoluble solid and evaporated to afford the amino-amide, as its hemihydrate (0.49 g), m.p. >220° (decomp.) (from water), identical (i.r.) with an authentic sample.[1]

(ii) The aminocyanotriazolotriazine (18) (0.64 g) was stirred in polyphosphoric acid (5.0 ml) at 80 °C for 3 h. The diluted and neutralised (sodium hydrogen carbonate) mixture gave the same amino-amide hemihydrate (0.56 g).

7-Amino-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-NN-pentamethyleneamide* (11).—The amino-ester (3a) (1.0 g) was refluxed in piperidine (8 ml) for 30 min and the solution

evaporated. The *piperidide* (84%) crystallised from acetone with m.p. 234—235° (Found: C, 48.3; H, 5.8; N, 39.4. $C_{10}H_{13}N_7O$ requires C, 48.6; H, 5.7; N, 39.7%).

Ethyl 7-Acetamido-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-carboxylate* (12).—The amino-ester (3a) (1.0 g) was boiled in acetic anhydride (5.0 ml) for 2.5 h. Trituration of the cooled solution with ice–water furnished the *acetamidotriazolotriazine* (1.0 g), m.p. 188—189° (from ethyl acetate) (Found: C, 42.8; H, 4.3; N, 33.6. $C_9H_{10}N_6O_3$ requires C, 43.2; H, 4.0; N, 33.6%).

Ethyl 4-Acetyl-4,7-dihydro-7-imino-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-carboxylate* (13).—The hydrazone hydrate (2a) (1.0 g) was boiled in acetic anhydride (5.0 ml) for 0.5 h. The *triazolotriazine* (86%), deposited when the mixture was shaken with ice–water, had m.p. 178—179° (from ethyl acetate) (Found: C, 42.9; H, 4.4; N, 33.5. $C_9H_{10}N_6O_3$ requires C, 43.2; H, 4.0; N, 33.6%).

4,7-Dihydro-7-oxo[1,2,4]*triazolo*[5,1-c][1,2,4]*triazine-6-carbonitrile* (4a).—(i) A solution of 1,2,4-triazole-5-diazonium nitrate (0.03 mol) was coupled with ethyl cyanoacetate in aqueous ethanol in the presence of an excess of sodium acetate and the crude hydrazone was cyclised *in situ* under reflux (1 h). Following removal of the amino ester (3a) as described earlier the aqueous mother liquor was concentrated to 25 ml and warmed to redissolve some solid which separated, and the warm solution was acidified with 2N-hydrochloric acid. The precipitated oxo-nitrile hydrate (0.98 g), m.p. 235—245° (decomp.), $\nu_{max.}$ 3 550, 3 400—3 100br, and 2 700br (NH and OH), 2 250 (CN), and 1 700 cm^{-1} (CO), was crystallised from ethanol to afford the anhydrous *oxo-nitrile* (0.66 g), sublimes 240° (decomp.) (Found: C, 37.2; H, 1.4; N, 51.9%; M^+, 162. $C_5H_2N_6O$ requires C, 37.0; H, 1.2; N, 51.9%; *M*, 162), which was stable in boiling acetic acid (2 h).

(ii) The pure hydrazone hydrate (2a) (0.31 g) was boiled in aqueous ethanol containing sodium acetate in the manner previously described. Following removal of the amino-ester (3a) the chloroform-insoluble residue was acidified with 2N-hydrochloric acid. Crystallisation of the precipitated oxo-nitrile hydrate from ethanol afforded the anhydrous oxo-nitrile (0.05 g), identical (i.r. spectrum) with the sample prepared before.

(iii) The amino-nitrile (18) (0.65 g) was boiled in aqueous 2M-sulphuric acid (7.5 ml) and ethanol (20.0 ml) for 1 h. The mixture was concentrated and the solid collected and combined with a second crop obtained by extracting the aqueous mother liquor with chloroform, to afford the same oxo-nitrile (0.32 g), sublimes 240° (decomp.) (from ethanol), identical (mixed m.p. and i.r. spectrum) with the above samples.

(iv) The hydrazone hydrate (2a) (1.0 g) was boiled in pyridine (5 ml) for 30 min. The cooled solution deposited the *oxo-nitrile pyridinium salt* (0.9 g), which crystallised from acetone as white needles, m.p. 208—210° (sinters 185°) (Found: C, 49.4; H, 3.0; N, 40.95. $C_5H_2N_6O,C_5H_5N$ requires C, 49.8; H, 2.9; N, 40.7%). The same pyridinium salt (80%) was obtained when the oxo-nitrile (4a) was boiled in pyridine (5 min). The pyridinium salt was recovered unchanged from boiling acetic acid (2 h).

When the salt was acidified with 2N-hydrochloric acid a precipitate of the oxo-nitrile hydrate, identical (i.r.) with the aforementioned sample, was deposited.

(v) The hydrazone hydrate (2a) in boiling collidine similarly afforded the *oxo-nitrile collidinium salt* (85%), m.p. 203—205° (from acetone) (Found: C, 55.0; H, 4.6. $C_5H_2N_6O,C_8H_{11}N$ requires C, 54.6; H, 4.7%). Acidification of the salt with 2N-hydrochloric acid yielded the oxo-nitrile hydrate, identical (i.r.) to previous samples.

4,7-Dihydro-4-methyl-7-oxo-1,2,4-triazolo]5,1-c][1,2,4]*triazine-6-carbonitrile* (16).—The nitrile (4a) (0.24 g) in anhydrous acetone (50.0 ml) was heated under reflux with dimethyl sulphate (0.9 ml) and anhydrous potassium carbonate (1.6 g) for 4 h. The filtered mixture was evaporated and the resultant red oil was treated with ether and water to yield a solid product, more of which was obtained by extracting the aqueous phase with chloroform (total 0.16 g). The *methyltriazolotriazinone* formed prisms, m.p. 169° (from ethanol) (Found: C, 40.7; H, 2.3; N, 47.7%; M^+, 176. $C_6H_4N_6O$ requires C, 40.9; H, 2.3; N, 47.7%; *M*, 176).

Ethyl 7-Aminopyrazolo[5,1-c][1,2,4]*triazine-6-carboxylate* (3c).—A solution of ethyl 2-cyano-2-(pyrazol-5-yl-hydrazono)acetate (2c) (from aqueous ethanol) [5] (1.0 g) was boiled in ethanol (50 ml) for 48 h. The concentrated solution afforded the amino-ester (0.95 g), m.p. 154—155° (lit.,[5] m.p. 154—155°). T.l.c. of the mother liquor showed the presence of starting hydrazone and the oxo-nitrile (4c).

4,7-Dihydro-7-oxopyrazolo[5,1-c][1,2,4]*triazine-6-carbonitrile* (4c).—Ethyl 2-cyano-2-(pyrazol-5-ylhydrazono)-acetate (2c) (from aqueous ethanol) [5] (1.0 g) was boiled in pyridine (5.0 ml) for 15 min. The pyridinium salt [1.0 g; m.p. >300° (decomp.)] which crystallised from the cooled solution did not give reliable microanalytical figures. It partially dissociated in boiling ethanol (reduction in intensity of the pyridine proton signals in the ^1H n.m.r. spectrum). Acidification of the crude pyridinium salt with N-hydrochloric acid afforded the *oxo-nitrile*, m.p. >250° (decomp.) (from ethanol) (Found: C, 44.5; H, 2.0%; M^+, 161. $C_6H_3N_5O$ requires C, 44.7; H, 1.9%; *M*, 161).

Ethyl 2-Cyano-2-(1H-tetrazol-5-ylhydrazono)acetate (2d).—5-Amino-1*H*-tetrazole (2.0 g) in 0.5N-hydrochloric acid (200 ml) at 0 °C was diazotised with sodium nitrite (1.4 g) in water (10 ml). (WARNING: A violent detonation of the diazonium salt occurred when this reaction was repeated on twice the scale.) The diazonium solution was gently stirred at 0 °C for 30 min, adjusted to pH 3 with powdered sodium hydroxide (4.0 g), and treated dropwise (10 min) with ethyl cyanoacetate (2.6 g). The precipitate was stirred at 0 °C (1 h), collected, and crystallised from aqueous ethanol to yield the *(hydrazono)cyanoacetate hydrate* (85%), m.p. 175—176° (decomp.) (Found: C, 31.4; H, 4.2; N, 43.5%; M^+, 209. $C_6H_7N_7O_2,H_2O$ requires C, 31.7; H, 4.0; N, 43.2%; *M*, 209) Further crystallisation from ethanol furnished the unsolvated *(hydrazono)cyanoacetate*, m.p. 160—162° (decomp.) (Found: C, 34.3; H, 3.2; N, 46.7. $C_6H_7N_7O_2$ requires C, 34.4; H, 3.3; N, 46.9%).

When the coupling medium was adjusted to pH 6 with an excess of sodium acetate trihydrate, the product was the yellow *sodium salt* (76%) of the (hydrazono)cyanoacetate hydrate, m.p. 134° (decomp.) (from aqueous ethanol) (Found: C, 29.2; H, 3.3; N, 39.4. $C_6H_6NaN_7O_2,H_2O$ requires C, 28.9; H, 3.2; N, 39.4%).

Ethyl 7-Aminotetrazolo[5,1-c][1,2,4]*triazine-6-carboxylate* (3d).—A solution of ethyl 2-cyano-2-(1*H*-tetrazol-5-yl-hydrazono)acetate (2d) (1.0 g) in acetic acid (20 ml) was boiled (3 h) and evaporated. The residue, crystallised from ethanol, afforded the *tetrazolotriazine* (0.9 g), m.p. 128—130° (Found: C, 34.2; H, 3.4; N, 47.2. $C_6H_7N_7O_2$ requires C, 34.4; H, 3.3; N, 46.9%). The same tetrazolotriazine (70%) was obtained when the sodium salt of the hydrazone (2d) was boiled in acetic acid.

When the cyano(tetrazolylhydrazono)acetate (2d) (0.1 g) was boiled in pyridine (5 ml) for 30 min, the aminotetrazolotriazine (3d) was obtained (t.l.c.) as the major product, together with minor amounts of unidentified materials.

7-Amino-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-carbonitrile* (18).—(i) 5-Amino-1,2,4-triazole (1.3 g) was diazotised in aqueous nitric acid in the manner previously described. The pale yellow diazonium solution was added dropwise with stirring at 0—10 °C to a solution of malononitrile (1.0 g) and anhydrous sodium acetate (1.6 g) in water (4.0 ml) and ethanol (10.0 ml). The mixture was stirred at room temperature (2 h) and the crude 2-(1,2,4-triazol-5-ylhydrazono)malononitrile (17) (1.9 g) was collected; m.p. >190° (decomp.), $\nu_{max.}$ 3 480 and 3 100—2 700br (NH), 2 240 (CN), and 1 690 cm^{-1} (NH def.), τ [$(CD_3)_2SO$] 1.19 (1 H, s, H-3), $\lambda_{max.}$ 374 nm. The crude hydrazone (1.0 g) was heated under reflux in acetic acid (10 ml) for 2 h and evaporated. The residue, triturated with water, afforded the *amino-nitrile hydrate* (0.9 g), m.p. >300° (decomp.) (from ethanol–acetic acid) (Found: C, 33.5; H, 2.6; N, 55.0. $C_5H_3N_7,H_2O$ requires C, 33.5; H, 2.8; N, 54.8%).

(ii) Diazotised 5-amino-1,2,4-triazole (0.03 mol) was coupled with malononitrile as above. The buffered mixture was stirred at room temperature (1 h), heated under reflux (1 h), and cooled. The solid which separated (2.3 g) was identical (i.r.) with the amino-nitrile hydrate.

The triazolotriazine hydrate was recovered unchanged from boiling acetic acid or pyridine (4 h).

6-Aminopyrimido[4,5-c][1,2,4]*triazolo*[5,1-c][1,2,4]*triazine* (20).—The amino-nitrile hydrate (18) (1.0 g) was boiled in formamide (10.0 ml) for 1 h and the mixture diluted with water. The dried solid was purified by sublimation (300 °C at 5 mmHg) to yield the *aminopyrimidotriazolotriazine* (0.5 g), m.p. >350° (Found: C, 38.1; H, 2.4; N, 59.4%; M^+, 188. $C_6H_4N_8$ requires C, 38.3; H, 2.1; N, 59.6%; *M*, 188).

Ethyl 4,7-Dihydro-7-oxo-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-carboxylate* (21).—The amino-ester (3a) (0.83 g) in ethanol (20.0 ml) was boiled with aqueous 2M-sulphuric acid (7.5 ml) for 1 h. The concentrated mixture afforded the triazinone (0.35 g), m.p. 204° (from ethanol), identical (mixed m.p and i.r. spectrum) with an authentic sample (lit.,[1] m.p. 204°).

4,7-Dihydro-7-oxo-1,2,4-triazolo[5,1-c][1,2,4]*triazine-6-carboxamide* (22).—The oxo-nitrile (4a) (0.65 g) was stirred in polyphosphoric acid (5.0 ml) at 80 °C for 3 h. The cooled mixture, diluted with water, and neutralised (solid sodium hydrogen carbonate), yielded the triazolotriazinone (0.7 g), m.p. >300° (from dimethylformamide), identical (i.r. spectrum) with an authentic sample (lit.,[1] m.p. >300°).

1,2,4-Triazolo[5,1-c][1,2,4]*triazin-7*(4H)*-one* (24).—(i) Ethyl 2-cyano-2-(1,2,4-triazol-5-ylhydrazono)acetate (2a) (1.0 g) was boiled in 6N-hydrochloric acid (2 h), and the solution was evaporated to dryness. The residue, crystallised from aqueous ethanol, yielded a *hydrate* of the triazinone (55%), m.p. 199—200° (Found: C, 31.0; H, 3.2, N, 44.8. $C_4H_3N_5O,H_2O$ requires C, 31.0; H, 3.2; N, 45.2%). When the triazinone hydrate (0.5 g) was boiled in acetic acid (5 ml) it afforded the unsolvated triazolotriazinone (0.4 g), identical (m.p. and mixed m.p. and i.r. spectrum) with a sample prepared by heating 4-amino-2,3-dihydro-3-imino-1,2,4-triazin-5(4*H*)-one in formic acid.[17]

When the unsolvated triazolotriazinone (24) [17] (0.3 g) was boiled in N-hydrochloric acid (20 ml) for 4 h, the triazolotriazinone hydrate (60%) was formed, identical (u.v., and i.r.) with the aforementioned sample.

(ii) The same triazolotriazinone hydrate (55, 55, 58, and 60% yields, respectively) was obtained when the crude hydrazone (17) and the triazolotriazines (3a), (4a), and (18) were boiled in 6N-hydrochloric acid (2 h).

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