Triazines and Related Products. Part 24.[1] Synthesis of Pyrazol-4-ylidenehydrazinoimidazoles by Hydrazinolysis of Imidazo[5,1-*c*][1,2,4]-triazines † and 2-Arylazoimidazoles by Diazonium Coupling Reactions

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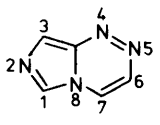
4-(Substituted)imidazo[5,1-*c*][1,2,4]triazine-8-carboxamides with ester, ketone, or cyano-groups in the 3-position undergo ring-opening with hydrazine and phenylhydrazine to yield substituted (pyrazol-4-ylidenehydrazino)imidazole-4-carboxamides. In some cases ring cleavage is initiated by attack of the hydrazine at C-4 of the imidazotriazine, and in others by nucleophilic attack at the 3-substituent. Examples of the same series of hydrazones can be prepared by coupling 5-diazoimidazole-4-carboxamide with activated pyrazoles. Diazotised arylamines couple with 5-aminoimidazole-4-carboxamide at C-2 to yield a series of intensely coloured 5-amino-2-arylazoimidazole-4-carboxamides, which can be cyclised to 8-arylazo-9*H*-purin-6(1*H*)-ones with ethyl formate in sodium ethoxide, and form mono- or di-acylamino-derivatives in formic acid or acetic anhydride. In no case was it found possible to prepare 2,5-diaminoimidazole-4-carboxamide by reductive cleavage of 5-amino-2-arylazoimidazole-4-carboxamides; only arylamines or unstable hydrazo-intermediates were identified. Reduction of 5-amino-2-(2-cyanophenylazo)imidazole-4-carboxamide with sodium dithionite or with hydrogen over a 10% palladium–charcoal catalyst afforded 5-amino-2-(3-aminoindazol-2-yl)imidazole-4-carboxamide.

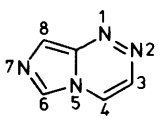
THE antitumour drug 5-(3,3-dimethyltriazen-1-yl)imidazole-4-carboxamide (1) (DTIC) can be photolysed in aqueous solution at pH 2—6 to yield initially 5-diazoimidazole-4-carboxamide (2) and thence the imidazolium olate (3) *via* an intermediate carbene species.[1,2] As the concentrations of intermediates (2) and (3) increase, coupling takes place and the maroon imidazoleazoimidazolium olate (4) is formed. A related violet compound, the aminoazoimidazole (6), is formed in high yield when 5-aminoimidazole-4-carboxamide (5) (AIC) is diazotised in the presence of an excess of amine (Scheme 1). We now report on our efforts to prepare analogues of these intensely coloured dyes.

When ethyl 4-amino-8-carbamoylimidazo[5,1-*c*]-[1,2,4]triazine-3-carboxylate (7) was refluxed in ethanolic hydrazine an orange compound ($\lambda_{max.}$ 425 nm) was formed. The product (65%) was not the simple hydrazide (9) ($\lambda_{max.}$ predicted *ca.* 380 nm) [3] but analysed as an isomer thereof ($C_7H_8N_8O_2$). On the basis of precedents established in the ring-opening of pyrazolotriazines [4] the orange product was assigned structure (12). Of the various tautomeric possibilities in this type of compound we prefer the hydrazonopyrazolinone arrangement [*cf.* the aminoazoimidazole (6) which absorbs at 490 nm]. An obvious pathway to this pyrazolinone would involve the sequence (7a) ⟶ (9) ⟶ (12) (Scheme 2), initiated by attack by hydrazine at the ester function. However, spectroscopic [3] and theoretical [5] considerations support

† In an earlier paper in this series (*J. Chem. Soc., Perkin Trans. 1*, 1981, 1424) incorrect numbering was used in naming the imidazo[5,1-*c*][1,2,4]triazines (shown in A). In this paper the correct, systematic numbering is applied (as in B).



A



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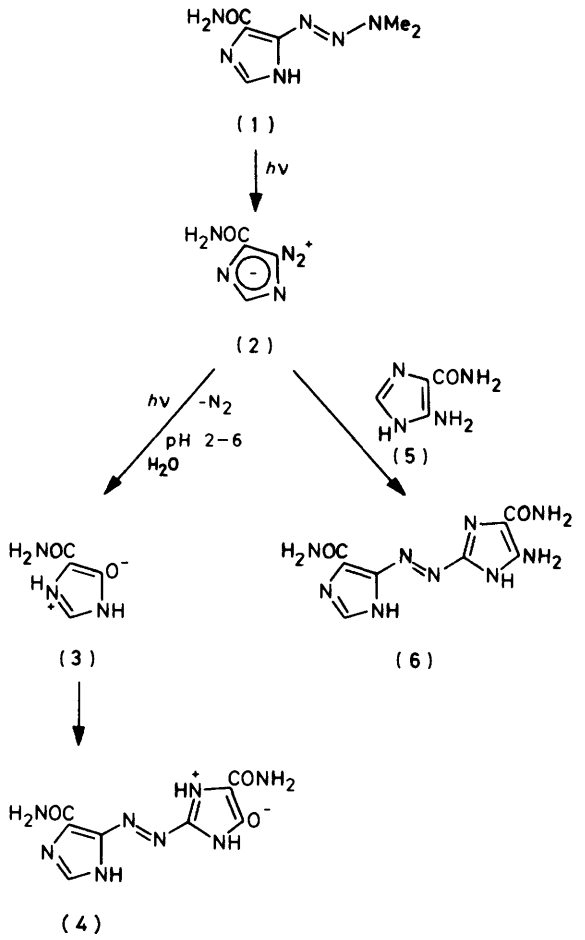
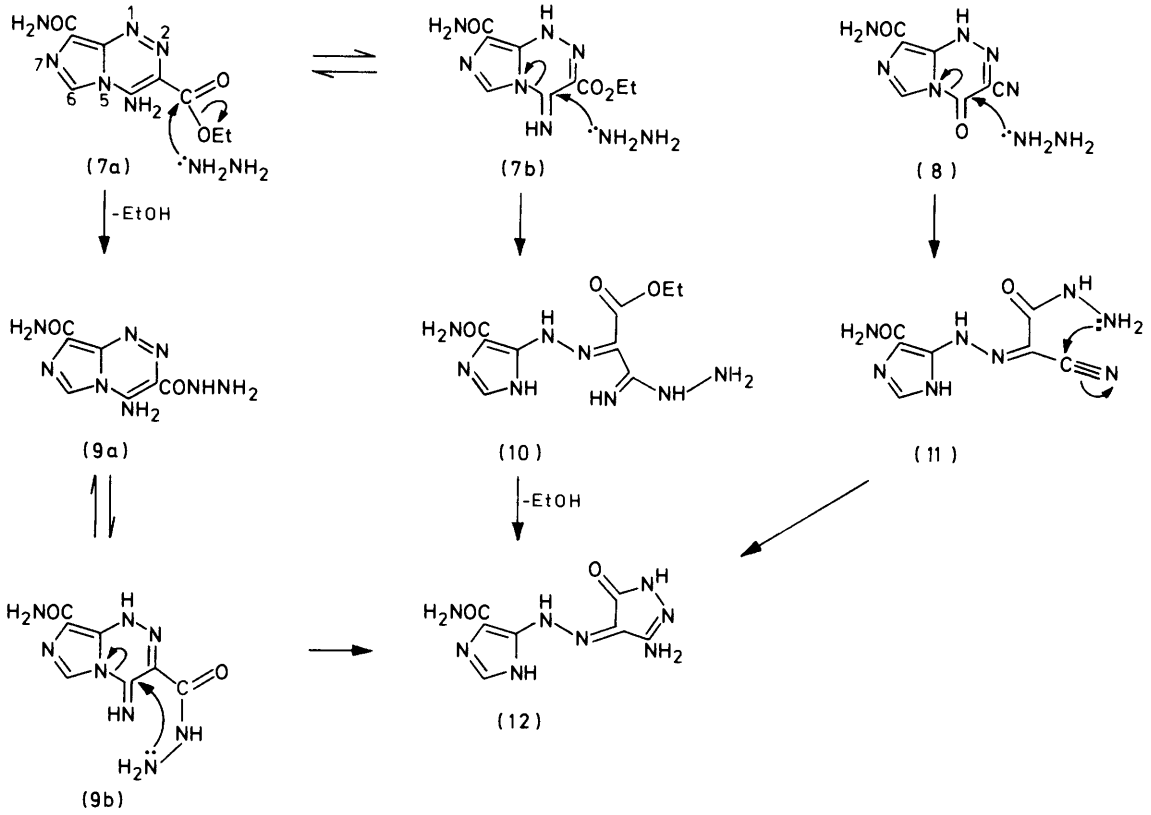


SCHEME 1

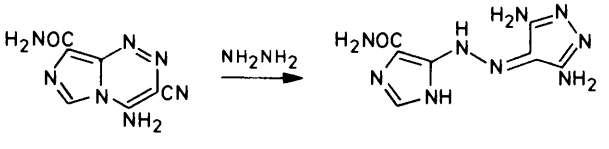
the proposal that the imino-form (7b) may be the preferred tautomer in this type of bicyclic 1,2,4-triazine and the pathway (7b) ⟶ (10) ⟶ (12), initiated by addi-



SCHEME 2

tion of hydrazine at the C-4 imino-group, is a more attractive alternative. The formation of the same hydrazonopyrazolinone (12) from the 3-cyanotriazinone (8) and hydrazine can be rationalised similarly by invoking addition of hydrazine at the lactam carbonyl to afford the hydrazide (11). This intermediate can then either cyclise directly to the observed product (12) or, alternatively, undergo ring-closure with the participation of the imidazole ring nitrogen, to generate the amino(imino)imidazotriazine carbohydrazide (9) and thence the final product (Scheme 2).

Conversion of the 4-amino-3-cyanoimidazotriazine (13) into the diaminopyrazole (14) was also probably initi-

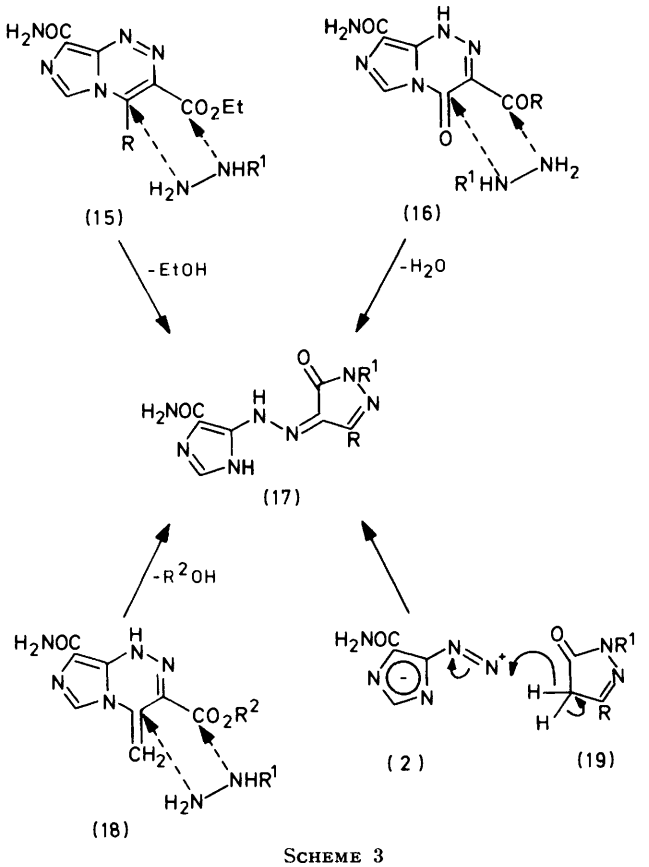


ated by attack of hydrazine at C-4 of the imino-tautomer of compound (13).

Both the 4-phenyltriazine (15; R = Ph) and the 3-benzoyltriazinone (16; R = Ph) reacted with hydrazine to yield the same orange hydrazonophenylpyrazolinone (17a). Likewise, the same starting materials afforded the hydrazonodiphenylpyrazolinone (17b) with phenylhydrazine. Although the exact timing of the covalent events in ring-opening cannot be deduced from these experiments, it is clear that the free amino-group of phenylhydrazine attacks the electron-deficient C-4 of the 4-phenyltriazine (15; R = Ph) in the one case, but the *exo*-cyclic benzoyl carbonyl in the triazinone (16; R = Ph) in the other (Scheme 3). This directional specificity was also observed in hydrazinolyses of the 3-acetyltriazinone (16; R = Me) and 4-methylenetriazines (18; R^2 = Me or Et). With unsubstituted hydrazine these three substrates all yielded the same hydrazonomethylpyrazolinone (17c); with phenylhydrazine they afforded the same hydrazonomethylphenylpyrazolinone (17d).

All the aforementioned hydrazonopyrazolinones may be considered (formally) as the products of coupling between 5-diazoimidazole-4-carboxamide (2) and the reactive methylene group of the pyrazolines. Indeed, the hydrazones (17a—d) could be prepared more efficiently than by the ring-fission route simply by coupling the preformed pyrazolinones (19a—d) with the diazoimidazole (2). These products had spectral characteristics (see Table 1) appropriate for hydrazono-tautomers.[4,6]

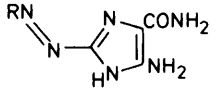
More intensely coloured dyes ($\lambda_{max.}$ 450—490 nm) were formed when AIC was employed as the π-excessive partner in coupling reactions with a series of arenediazonium salts in sodium acetate buffer. The products (20a—n) varied in colour from yellow to purple depending on their structures and on the solvent used for crystallisation. Thus dye (20e), formed by coupling diazotised *p*-anisidine



SCHEME 3

	R	R^1
a;	Ph	H
b;	Ph	Ph
c;	Me	H
d;	Me	Ph

with AIC, crystallised from aqueous ethanol as yellow needles, whereas the 2-cyanophenylazo-dye (20f) afforded purple crystals from aqueous acetone. However, both compounds gave very similar visible spectra in 95% ethanol solutions (see Table 1). The indicator nature of selected examples of the products (20) was illustrated by the colour changes and the bathochromic spectral shifts (Table 1) elicited by both alkali and acid. Notably, the

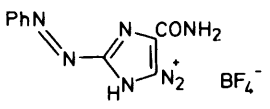


(20)

a; R = Ph
b; R = 4-BrC_6H_4
c; R = 4-ClC_6H_4
d; R = 4-MeC_6H_4
e; R = 4-MeO·C_6H_4
f; R = 2-CN·C_6H_4
g; R = 2-NO_2·C_6H_4
h; R = 3-NO_2·C_6H_4
i; R = 4-NO_2·C_6H_4
j; R = 4-AcC_6H_4
k; R = 4-H_2NSO_2·C_6H_4
l; R = 4-$AcNHSO_2$·C_6H_4
m; R = 4-[*N*-(pyrimidin-2-yl)sulphamoyl]phenyl
n; R = pyridin-3-yl

dyes formed intense violet cations in concentrated sulphuric acid; the violet colours reverted to red upon dilution of the acid with water. The dyes are formulated as *trans*-azo-geometrical isomers, but *cis*-isomers or hydrazono-tautomers are possible. Tautomer populations (and hence colour) in the solid state are, presumably, markedly influenced by the electronic nature of the substituent in the aryl fragment, and by solvation.

Even though the basic strength of the amino-group in AIC is weakened by attachment of the phenylazo-substituent at C-2, the parent dye (20a) afforded a stable diazonium tetrafluoroborate salt (21). Mono-formyl and -acetyl derivatives of selected dyes were assigned structures (22a—c) and (22d—f) respectively,



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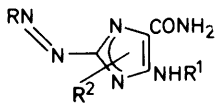
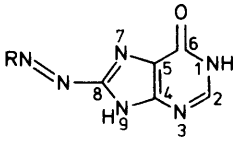


(22)

	R	R^1	R^2
a:	Ph	CHO	H
b:	4-BrC_6H_4	CHO	H
c:	3-NO_2·C_6H_4	CHO	H
d:	Ph	Ac	H
e:	4-ClC_6H_4	Ac	H
f:	3-NO_2·C_6H_4	Ac	H
g:	4-BrC_6H_4	Ac	Ac
h:	4-NO_2·C_6H_4	Ac	Ac

since the products no longer contained diazotisable amino-groups, and the protons of the 5-amino-group in the parent series (20), which characteristically absorb at δ 6.20—6.75 (see Table 1), were replaced by a downfield one-proton singlet at δ 8.25—10.45 in the acylamino-derivatives. The mono-formyl- (22a) and -acetyl-amines (22d) were readily hydrolysed to the parent amine (20a) in warm 2N-hydrochloric acid. Prolonged interaction of the dyes (20b) and (20i) with boiling acetic anhydride afforded impure diacetyl derivatives which were probably mixtures of isomeric ring-acetylated products (22g and h). Mono- or di-acylation of dyes (20) was marked by a pronounced hypsochromic shift in the long-wavelength absorption in the visible spectra of the products (see Table 1). The mono-acyl dyes did not give instantaneous violet colours with cold concentrated sulphuric acid; the colour only developed after a few seconds when the free amines were liberated upon hydrolysis. The diacyl dyes were not discoloured in sulphuric acid.

Sodium salts of 8-arylazo-9*H*-purin-6(1*H*)-ones(8-arylazohypoxanthines) (23a and b) were formed when the aminoimidazole-4-carboxamides (20a and c) were cyclised



(23)

a; R = Ph
b; R = 4 − ClC_6H_4

TABLE 1

Electronic absorption, i.r., and ^{1}H n.m.r. spectra of pyrazolylidenehydrazinoimidazoles, 2-arylazoimidazoles and 8-arylazo-9*H*-purin-6(1*H*)-ones

Compound	Electronic absorption spectra [a] Solvent	$\lambda_{max.}$/nm	I.r. spectra [b] $\nu_{max.}$/cm^{-1}	^{1}H N.m.r. spectra [c] Solvent	δ Values
(4) [d]	A	550	3 375br (bonded NH and OH), 1 640 (CO)		
(6) [d]	A	490	3 400br (bonded NH), 1 645 (CO)		
(6) [d] (CN for $CONH_2$)	B	512	3 320, 3 180 (NH), 2 210 (CN)		
(12)	B	252,[e] 425	3 340, 3 290, 3 160 (NH), 1 670 (CO)		
(14)	B	255,[e] 263,[e] 365,[e] 410	3 350, 3 260, 3 150 (NH), 1 680 (CO)		
(17a)	B	235, 275,[e] 415	3 450—3 300br (NH), 1 660 (CO)		
(17b)	B	255, 275,[e] 423	3 440, 3 280 3 160 (NH), 1 660 (CO)	F	7.4—8.1 (10 H, m, 2 × Ph), 8.8 (1 H, s, imidazole 2-H)
(17c)	B	247, 445	3.300 (NH), 1 670 (CO)	F	2.72 (3 H, s, CMe), 8.98 (1 H, s, imidazole 2-H)
(17d)	B	247, 404	3 440, 3 250, 3 130 (NH), 1 650 (CO)	F	2.57 (3 H, s, CMe), 7.55 (5 H, s, Ph), 8.9 (1 H, s, imidazole 2-H)
(20a)	B	454	3 400—3 150 (NH),	G	6.2 (2 H, br s, NH_2),
	C	485	1 680, 1 640 (CO)		7.0 (2 H, br s, $CONH_2$),
	D	462			7.55 (5 H, m, Ph)
	E	514			
(20b)	B	464	3 400—3 200 (NH), 1 680, 1 640 (CO)	G	6.4 (2 H, br s, NH_2), 7.1 (2 H, br s, $CONH_2$), 7.65 (4 H, s, Ar)
(20c)	B	466	3 450—3 200 (NH),	G	6.35 (2 H, br s, NH_2),
	C	498	1 680, 1 640 (CO)		7.05 (2 H, br s. $CONH_2$),
	D	480			7.60 (4 H, m, Ar)
	E	515			
(20d)	B	458	3 400—3 150 (NH),		
	C	495	1 670, 1 630 (CO)		
	D	468			
	E	500			
(20e)	B	462	3 400—3 200 (NH),		
	C	482	1 650, 1 610 (CO)		
	D	470			
	E	480			
(20f)	B	486	3 450—3 200 (NH), 2 250 (CN), 1 660, 1 595 (CO)		
(20g)	B	490	3 450—3 190 (NH), 1 690, 1 650 (CO)		
(20h)	B	474	3 450—3 150 (NH),	G	6.75 (2 H, br s, NH_2)
			1 665, 1 630 (CO),		7.35 (2 H, br s, $CONH_2$),
	C	492	1 530, 1 360 (NH_2)		8.0 (4 H, m, Ar)
	D	496			
	E	502			
(20i)	B	484	3 450—3 200 (NH), 1 700, 1 640 (CO)	G	7.30 (2 H, br s, $CONH_2$), 7.60—8.25 (6 H, br m, NH_2 and Ar)
(20j)	B	490	3 500—3 250 (NH), 1 650, 1 640 ($CONH_2$ and COMe)		
(20k)	B	470	3 400—3 200 (NH), 1 690, 1 640 (CO)		
(20l)	B	473	3 450—3 200 (NH), 1 710 (COMe), 1 660, 1 620 ($CONH_2$).		
(20m) [f]	B	470	3 450—3 050 (NH), 1 700, 1 650 (CO)	G	2.70 (3 H, s, Me), 2.90 (3 H, s, Me)
(20n)	B	464	3 450—3 150 (NH), 1 700, 1 650 (CO)		
(21)	B	366	3 500—3 250 (NH), 2 200 (N≡N), 1 695, 1 660 (CO)		
(22a)	B	398	3 350—3 300 (NH), 1 690 (CHO), 1 660, 1 620 ($CONH_2$)	G	7.5—8.0 (8 H, m, CHO, $CONH_2$, and Ar), 8.65 (1 H, br s, NH)
(22b)	B	410	3 450—3 300 (NH), 1 720 (CHO) 1 680, 1 635 ($CONH_2$)	G	7.5 (2 H, br s, $CONH_2$), 7.8 (5 H, s, CHO and Ar), 8.65 (1 H, br s, NH)

TABLE 1 (*continued*)

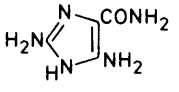
Compound	Electronic absorption spectra [a] solvent	$\lambda_{max.}$/nm	I.r spectra [b] $\nu_{max.}$/cm^{-1}	^{1}H N.m.r. spectra [c] Solvent	δ Values
(22c)	B	438	3 400—3 100 (NH), 1 700 (CHO), 1 670, 1 595 ($CONH_2$)	G	7.55 (2 H, br s, $CONH_2$), 8.25 (6 H, m, NH, CNO and Ar).
(22d)	B	395	3 350—3 200 (NH), 1 700 (COMe), 1 680, 1 650 ($CONH_2$)	G	2.25 (3 H, s, Me), 7.45 (2 H, br s, $CONH_2$), 7.75 (5 H, m, Ph), 10.4 (1 H, br s, NH)
(22e)	B	410	3 400—3 200 (NH), 1 710 (COMe), 1 690, 1 660 ($CONH_2$)	G	2.25 (3 H, s, Me), 7.45 (2 H, br s, $CONH_2$), 7.75 (4 H, m, Ar), 10.35 (1 H, br s, NH)
(22f)	B	408	3 450—3 250 (NH), 1 700 (COMe), 1 660, 1 595 ($CONH_2$)	G	2.25 (3 H, s, Me), 7.5 (2 H, br s, $CONH_2$), 8.2 (4 H, m, Ar), 10.45 (1 H, br s, NH)
(22g)	B	400	3 500—3 300 (NH), 1 750, 1 695 (2 × COMe), 1 660, 1 580 ($CONH_2$)	G	1.9 (1.5 H, s, Me), 2.25 (3 H, s, Me), 2.35 (1.5 H, s, Me), 7.8 (4 H, s, Ar), 10.0 (1 H, br s, NH)
(22h)	B	429	3 500—3 250 (NH), 1 710, 1 695 (2 × COMe), 1 660, 1 600 ($CONH_2$), 1 530, 1 350 (NO_2)	G	2.25 (3 H, s, Me), 2.26 (1.5 H, s, Me), 2.4 (1.5 H, s, Me), 7.5 (2 H, br s, $CONH_2$), 8.2 (4 H, m, Ar), 10.1 (1 H, br s, NH)
(23a)	B	377	3 200br (NH), 1 690 (CO)		
(23b)	B	386	3 500—3 100 (NH), 1 680 (CO)		

A DMF; B 95% ethanol; C 95% ethanol containing 6N-hydrochloric acid; D 95% ethanol containing concentrated aqueous ammonia; E 95% ethanol containing concentrated sulphuric acid; F trifluoroacetic acid; G [$^2H_6$]dimethyl sulphoxide.

[a] Recorded on a Unicam SP 8000 spectrometer. [b] Recorded on a Unicam SP 200 spectrometer (KBr disc). [c] Recorded on a Varian EM 360A spectrometer with $SiMe_4$ as internal standard. [d] Ref. 1. [e] Inflexion. [f] DMF of crystallisation.

with ethyl formate in sodium ethoxide solution. The formylamine (22a) also cyclised in poor yield to the hypoxanthine (23a) in aqueous alkaline conditions, but more efficiently in sodium ethoxide solution. In agreement with other work [7,8] no coupling was observed between hypoxanthine itself and diazotised aniline or 4-chloroaniline under a range of conditions.

Our efforts to corroborate the claim [9] that 2,5-diaminoimidazole-4-carboxamide (24) can be prepared by reduction of the azo-compound (20b) were not successful (Table 2). Reduction of a series of dyes (20) with tin(II) chloride in hydrochloric acid led to the isolation or detection (t.l.c.) of the arylamine fragment only. Acidic reduction mixtures, which presumably contained the elusive diamine (24), rapidly darkened upon basification



(24)

and the diamine could not be recovered, either as a salt or as the base. The characteristic azo-colours of the dyes (20a—f) were rapidly discharged in the presence of sodium dithionite, but, again, no diamine (24) could be identified amongst the products. Hydrogenation of the dyes (20a—c) over a palladium catalyst at atmospheric presure, or in the presence of hydrazine–Raney nickel in ethanol, afforded unstable hydrazo-derivatives which rapidly re-oxidised to the starting materials in air. Similarly, the 2-cyanophenylazo-dye (20f) yielded the unstable hydrazo-derivative (25) upon catalytic hydrogenation in methanol over palladium; in air the azo-dye was reformed. However, at elevated temperature under hydrogen the intermediate hydrazo-derivative underwent an intramolecular amine-nitrile addition [10,11] to afford the 3-aminoindazole (26) which was isolated as a hydrochloride salt (Scheme 4).

TABLE 2

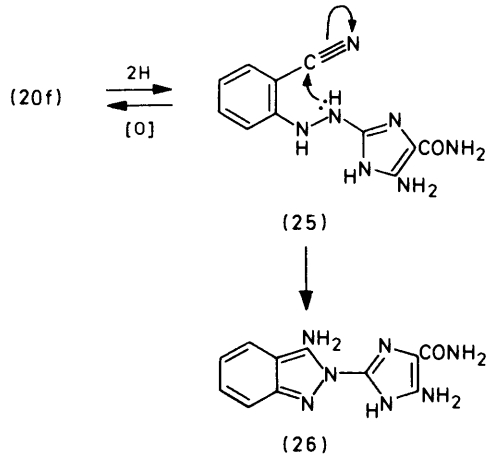
Reduction of 5-amino-2-arylazoimidazole-4-carboxamides

Starting material	Reduction conditions	Product(s) identified [a]
(20a)	A, B, C	Aniline
	D	Crude hydrazo-compound
(20b)	A	[b]
	C	4-Bromoaniline
	D, E	Crude hydrazo-compound
	F	[b]
(20c)	B	4-Chloroaniline
(20f)	A	Anthranilonitrile
	B	(26)
	E	[b]
(22d)	G	Acetanilide
(22e)	A	4-Chloroaniline

A Tin(II) chloride in hydrochloric acid; B sodium dithionite in aqueous ethanol; C Raney nickel–hydrazine in 95% ethanol at 45 °C; D Raney nickel–hydrazine in 95% ethanol at 20 °C; E catalytic hydrogenation in methanol over 10% palladium on charcoal; F catalytic hydrogenation in methanol–hydrochloric acid over 10% palladium on charcoal; G catalytic hydrogenation in acetic acid–acetic anhydride over 10% palladium on charcoal.

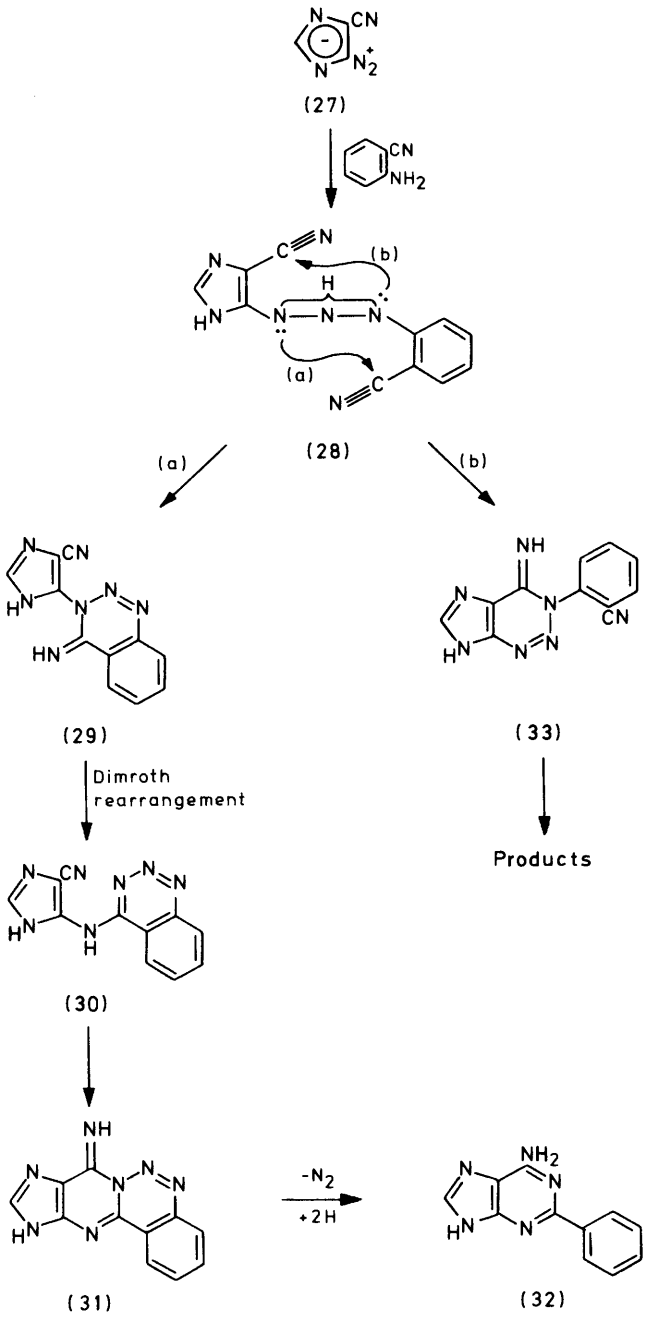
[a] Products compared (i.r. and t.l.c.) with authentic materials. [b] See Experimental section.

Although diazotisation of 5-aminoimidazole-4-carbonitrile under normal procedures (*i.e.* with an excess of amine) affords the azoimidazole (6; CN for $CONH_2$),[1] the diazonitrile (27) couples with anthranilonitrile at pH 6.5—7 to yield the yellow triazine (28). In earlier papers



SCHEME 4

in this series [11,12] we have shown that 1,3-bis(2-cyanophenyl)triazenes undergo a succession of amino-nitrile cyclisations, rearrangement, and decomposition reactions in a ' one-pot ' process to generate 4-amino-2-arylquinazolines. In the case of the triazine (28) two modes of cyclisation are possible [Scheme 5; routes (a) and (b)] depending upon which nitrile function suffers initial nucleophilic attack. In fact, when triazene (28) was boiled in 90% aqueous ethanol, the product (75%) proved to be identical with an authentic specimen of 2-phenyladenine (32). A logical pathway to this product [Scheme 5; route (a)] involves the sequence (28) ⟶ (29) ⟶ (30) ⟶ (31) ⟶ (32). No evidence for the alternative pathway [Route (b)] was adduced. This would involve nucleophilic attack at the cyano-group of the π-excessive imidazole ring to form the intermediate (33); this is mechanistically less likely than reaction at the arylcyano-group.



SCHEME 5

EXPERIMENTAL

5-(3-Amino-4,5-dihydro-5-oxopyrazol-4-ylidenehydrazino)-imidazole-4-carboxamide (12).—(a) A solution of ethyl 4-amino-8-carbamoylimidazo[5,1-*c*][1,2,4]triazine-3-carboxylate (7) [3] (0.5 g) in ethanol (15 ml) was boiled with hydrazine hydrate (1.0 ml) for 0.5 h. On cooling, the *aminopyrazoline* (12) (65%) was deposited, which formed orange crystals, m.p. 280 °C (decomp.) [from *N*,*N*-dimethylformamide (DMF)–ethanol] (Found: C, 35.3; H, 3.5%; M^+, 236.077 01. $C_7H_8N_8O_2$ requires C, 35.6; H, 3.4%; *M*, 236.076 36).

(b) Interaction of 3-cyano-1,4-dihydro-4-oxoimidazo-[5,1-*c*][1,2,4]triazine-8-carboxamide (8) [3] (0.5 g) with hydrazine hydrate in boiling ethanol (as above) furnished the same (i.r.) aminopyrazolinone (68%).

5-(3,5-Diamino-4H-pyrazol-4-ylidenehydrazino)imidazole-4-carboxamide (14).—Interaction of 4-amino-3-cyanoimidazo[5,1-*c*][1,2,4]triazine-8-carboxamide (13) [3] (0.5 g) and hydrazine hydrate (1 ml) in boiling ethanol (15 ml) as above afforded the orange *diaminopyrazole* (14) (60%), m.p. 335—345 °C (decomp.) (from DMF–ethanol) (Found: C, 35.9; H, 4.0; N, 52.9%; M^+, 235.093 00. $C_7H_9N_9O$ requires C, 35.7; H, 3.8; N, 53.6%; *M*, 235.092 51).

5-(4,5-Dihydro-5-oxo-3-phenylpyrazol-4-ylidenehydrazino)-imidazole-4-carboxamide (17a).—(a) Ethyl 8-carbamoyl-4-phenylimidazo[5,1-*c*][1,2,4]triazine-3-carboxylate (15; R = Ph) [3] (0.5 g) and hydrazine hydrate (1 ml) were boiled in ethanol (15 ml) for 3 h. The precipitated *phenylpyrazolinone* (17a) (65%) gave orange crystals, m.p. 280—282 °C (decomp.) (from DMF–ethanol) [Found: C, 51.8; H, 4.9;

N, 30.4%; M^+, 297.0972. $C_{13}H_{11}N_7O_2\cdot(CH_3)_2NCHO$ requires C, 51.9; H, 4.6; N, 30.3%; M, 297.0974].

(b) The same (i.r.) phenylpyrazolinone (60%) was formed when 3-benzoyl-1,4-dihydro-4-oxoimidazo[5,1-*c*][1,2,4]triazine-8-carboxamide (16; R = Ph) [3] was treated with hydrazine hydrate in ethanol as above.

3.8; N, 41.7%; M^+, 235.081 76. $C_8H_9N_7O_2$ requires C, 40.85; H, 3.8; N, 41.7%; M, 235.081 68).

(b) The same (i.r.) methylpyrazolinone (95%) was formed when 5-diazoimidazole-4-carboxamide was stirred with 3-methylpyrazolin-5(4*H*)-one (19c) (1 mol equiv.) in ethanol in the dark (3 h) at 25 °C.

TABLE 3

Synthesis and microanalytical data of 5-amino-2-arylazoimidazole-4-carboxamides

Compound	Reaction conditions	M.p. (°) † (with decomp.)	Yield (%)	Formula	% Found (required) C	H	N
(20b) *	A	282	58 [a]	$C_{10}H_8BrN_6O$	38.6 (38.8)	3.0 (2.9)	27.6 (27.2)
(20c)	A	283	75 [a]	$C_{10}H_9ClN_6O$	45.3 (45.4)	3.4 (3.4)	32.0 (31.8)
(20d)	A	261	61 [a]	$C_{11}H_{12}N_6O\cdot0.5H_2O$	52.1 (52.1)	5.3 (5.1)	33.7 (33.2)
(20e)	A	248	63 [b]	$C_{11}H_{12}N_6O_2$	51.0 (50.8)	4.9 (4.6)	
(20f)	B	254	57 [c]	$C_{11}H_9N_7O\cdot H_2O$	48.3 (48.3)	3.9 (4.0)	35.3 (35.8)
(20g)	C	310	50 [d]	$C_{10}H_9N_7O_3$	43.6 (43.6)	3.2 (3.3)	36.0 (35.6)
(20h)	C	278	83 [d]	$C_{10}H_9N_7O_3$	44.0 (43.6)	3.2 (3.3)	35.8 (35.6)
(20i)	C	>300	94 [d]	$C_{10}H_9N_7O_3$	44.0 (43.6)	3.2 (3.3)	35.6 (35.6)
(20j)	A	244	66 [d]	$C_{12}H_{12}N_6O_2$	52.7 (52.9)	4.3 (4.4)	30.9 (30.9)
(20k)	A	259	57 [e]	$C_{10}H_{11}N_7O_3S$	38.4 (38.8)	3.6 (3.6)	31.4 (31.7)
(20l)	A	218	71 [d]	$C_{12}H_{13}N_7O_4S\cdot H_2O$	39.5 (39.0)	4.0 (4.1)	26.7 (26.6)
(20m)	A	288	52 [d]	$C_{14}H_{13}N_9O_3S\cdot Me_2NCHO$	44.6 (44.3)	4.25 (4.3)	29.8 (30.4)
(20n)	A	271	71 [c]	$C_9H_9N_7O\cdot H_2O$	43.4 (43.4)	4.3 (4.4)	39.3 (39.3)

A arylamine diazotised in 2N-hydrochloric acid; B arylamine diazotised in 8N-hydrochloric acid; C arylamine diazotised in 5N-hydrochloric acid.

Recrystallisation solvents: [a] aqueous methanol; [b] aqueous ethanol; [c] aqueous acetone; [d] DMF; [e] dimethyl sulphoxide.

* Ref. 9. † Temperature at which decomposition started.

(c) Interaction of 5-diazoimidazole-4-carboxamide (2) [13] (0.68 g) and 3-phenylpyrazolin-5(4*H*)-one (19a) (0.8 g), stirred in ethanol at 25 °C in the dark (3 h), yielded the same (i.r.) phenylpyrazolinone (75%).

5-(4,5-*Dihydro*-5-*oxo*-1,3-*diphenylpyrazol*-4-*ylidenehydrazino*)*imidazole*-4-*carboxamide* (17b).—(a) Interaction of the 4-phenyltriazine (15; R = Ph) [3] or the 3-benzoyltriazinone (16; R = Ph) (0.5 g) and phenylhydrazine (1.5 ml) in boiling ethanol (15 ml) for 6 h gave the deep red *diphenylpyrazolinone* (17b) (60 and 65%, respectively). The product crystallized from DMF–ethanol as red needles, m.p. 345—350 °C (decomp.) (Found: C, 61.4; H, 4.0; N, 25.95%; M^+, 373. $C_{19}H_{15}N_7O_2$ requires C, 61.1; H, 4.0; N, 26.3%; M, 373).

(b) Coupling between 5-diazoimidazole-4-carboxamide and 1,3-diphenylpyrazolin-5(4*H*]-one (19b) (1 mol equiv.) in ethanol in the dark at 25 °C for 3 h yielded the same (i.r.) diphenylpyrazolinone (95%).

5-(4,5-*Dihydro*-3-*methyl*-5-*oxopyrazol*-4-*ylidenehydrazino*)-*imidazole*-4-*carboxamide* (17c).—(a) Interaction of the 4-methylenetriazines (18; R^2 = Me or Et) [3] (0.5 g), or the 3-acetyltriazinone (16; R = Me) [3] (0.5 g) and hydrazine hydrate (1.0 ml) in boiling ethanol (15 ml) for 3 h yielded the crude *methylpyrazolinone* (17c) (70, 68, and 65%, respectively) which crystallised from DMF–ethanol as orange needles, m.p. 260—265 °C (decomp.) (Found: C, 40.5; H,

5-(4,5-*Dihydro*-3-*methyl*-5-*oxo*-1-*phenylpyrazol*-4-*ylidenehydrazino*)*imidazole*-4-*carboxamide* (17d).—(a) This *methylphenylpyrazolinone* (65, 70, and 72%, respectively) was formed when the 4-methylenetriazines (18; R^2 = Me or Et) [3] or the 3-acetyltriazinone (16; R = Me) [3] (0.5 g) were boiled with phenylhydrazine (1 ml) in ethanol (15 ml) for 3 h. The products were identical (i.r.) and crystallised from DMF–ethanol as deep red crystals, m.p. 320 °C (decomp.) (Found: C, 54.3; H, 4.2; N, 31.5%; M^+, 311.113 06. $C_{14}H_{13}N_7O_2$ requires C, 54.0; H, 4.2; N, 31.5%; M, 311.112 93).

(b) 5-Diazoimidazole-4-carboxamide coupled with 3-methyl-1-phenylpyrazolin-5(4*H*)-one (19d) (1 mol equiv.) in ethanol at 25 °C in the dark (3 h). The red product (96%) was identical (i.r.) with the foregoing samples.

5-*Amino*-2-*phenylazoimidazole*-4-*carboxamide* (20a).—Aniline (3.72 g) was diazotised in stirred ice-cold 2N-hydrochloric acid (80 ml), by the dropwise addition of sodium nitrite (2.76 g) in water (10 ml), and then added in portions at 0 °C to a solution of 5-aminoimidazole-4-carboxamide hydrochloride (6.48 g) in water (200 ml) containing an excess of sodium acetate trihydrate (to pH 6.5). The precipitated product was collected, washed with water and crystallised from aqueous methanol to furnish the *phenylazoimidazole hydrate* (93%) as orange plates, m.p. 175 °C (decomp.) (Found: C, 48.8; H, 4.6; N, 34.4. $C_{10}H_{10}N_6O\cdot H_2O$ requires C, 48.4; H, 4.8; N, 33.9%).

Experimental details for the syntheses of other arylazoimidazoles and analytical data are recorded in Table 3.

4-Carbamoyl-2-phenylazoimidazole-5-diazonium Tetrafluoroborate (21).—The deep purple solution formed when the phenylazoimidazole (20a) (0.23 g) was dissolved in 10% aqueous tetrafluoroboric acid (5 ml) at 0 °C became orange upon the dropwise addition of sodium nitrite (0.69 g) in water (2 ml). The precipitated orange *diazonium tetrafluoroborate* (21) (65%), m.p. 147 °C (decomp.) was purified by the addition of diethyl ether to the solution in 1-methylpyrrolidin-2-one. Satisfactory microanalytical figures for this compound were not obtained.

Reduction of 5-Amino-2-arylazoimidazole-4-carboxamides.—(a) *With tin*(II) *chloride.* The azo-dye (20b) (5.0 g) was partially dissolved in ethanol (50 ml) and stirred with a solution of tin(II) chloride dihydrate (6.0 g) in 10N-hydrochloric acid (30 ml). The red colour was discharged immediately and a yellow solid precipitated. The collected product was treated with an excess of hydrogen sulphide in water and precipitated tin residues were filtered off. The concentrated filtrate afforded an unidentified white solid (0.2 g), which crystallised from water as white needles, m.p. 12.5; N, 29.7. $C_{11}H_7ClN_6O\cdot0.5H_2O$ requires C, 46.6; H, 2.8; Cl, 12.5; N, 29.6%).

TABLE 4

Synthesis and microanalytical data of acyl derivatives of 5-amino-2-arylazoimidazole-4-carboxamides (22)

Compound	Reaction conditions (reflux time/h)	Yield (%)	M.p. (°C) † (with decomp.)	Formula	% Found (required) C	H	N
(22b)	A (1)	73 [a]	250	$C_{11}H_9BrN_6O_2$	39.2 (39.2)	2.5 (2.7)	24.9 (24.9)
(22c)	A (2)	90 [a]	258	$C_{11}H_9N_7O_4\cdot H_2O$	41.5 (41.1)	3.4 (3.4)	30.0 (30.5)
(22d) *	B (2)	59 [b]	258	$C_{12}H_{12}N_6O_2$	52.6 (52.9)	4.2 (4.4)	31.0 (30.9)
(22e)	B (2.5)	69 [c]	260	$C_{12}H_{11}ClN_6O_2$	47.3 (47.0)	3.7 (3.6)	28.0 (28.0)
(22f)	B (2)	69 [b]	232	$C_{12}H_{11}N_7O_4$	45.3 (45.4)	3.6 (3.5)	30.8 (30.9)
(22g)	B (24)	35 [a]	247	$C_{14}H_{13}BrN_6O_3$	42.5 (42.8)	3.3 (3.3)	20.9 (21.4)
(22h)	B (24)	43 [b]	288	$C_{14}H_{13}N_7O_5$	46.3 (46.8)	3.7 (3.6)	27.2 (27.3)

A 98—100% Formic acid; B acetic acid–acetic anhydride (1 : 1).

Recrystallisation solvents: [a] acetic acid; [b] aqueous acetone; [c] ethanol.

* Hydrolysed to starting amine (20a) in 2N-hydrochloric acid at 95 °C. † Temperature at which decomposition started.

5-Formylamino-2-phenylazoimidazole-4-carboxamide (22a).—The azo-compound (20a) (1.0 g) was refluxed in 98—100% formic acid for 1 h. The *formylaminoimidazole* (22a) (54%), deposited when the cooled solution was stirred with water (20 ml), crystallised from acetic acid as yellow needles, m.p. 269 °C (decomp.) (Found: C, 51.4; H, 3.8; N, 32.8. $C_{11}H_{10}N_6O_2$ requires C, 51.2; H, 3.9; N, 32.6%). Hydrolysis of the formylaminoimidazole in 2N-hydrochloric acid (95%) for 1 h, followed by neutralisation to pH 6.5, afforded the starting amine (20a) in 95% yield.

Details of the synthesis, physical characteristics, and microanalytical data of other acyl derivatives of 5-amino-2-arylazoimidazole-4-carboxamides are recorded in Table 4.

8-Phenylazo-9H-purin-6(1H)-one (23a).—Ethyl formate (2 ml) was added to a solution of 5-amino-2-phenylazoimidazole-4-carboxamide (20a) (1.0 g) in ethanolic sodium ethoxide [prepared from sodium (1.0 g) in ethanol (25 ml)]. The mixture was refluxed (3 h), cooled, and the precipitated sodio-derivative acidified with 2N-hydrochloric acid to liberate the *phenylazo-9H-purinone hemihydrate* (67%), which crystallised from acetic acid with m.p. >300 °C (decomp.) (Found: C, 52.4; H, 3.3; N, 33.4. $C_{11}H_8N_6O\cdot0.5H_2O$ requires C, 53.0; H, 3.6; N, 33.7%). The same (i.r.) compound was formed (55%) when 5-formylamino-2-phenylazoimidazole-4-carboxamide (22a) was boiled in ethanolic sodium ethoxide and the product isolated as above.

Interaction of 5-amino-2-(4-chlorophenylazo)imidazole-4-carboxamide (20c) and ethyl formate in sodium ethoxide solution, as above, afforded *8-(4-chlorophenylazo)-9H-purin-6(1H)-one hemihydrate* (23b) (75%), m.p. >300 °C (decomp.) (from acetic acid) (Found: C, 46.6; H, 2.6; Cl, 233 °C (decomp.); $\lambda_{max.}$ (EtOH) 263 nm; *m/z* 267 ($M^+ + 2$, 46%), 265 (M^+, 46), and 250 (100). Basification of the filtrate with concentrated aqueous ammonia gave a solution which darkened rapidly. An ether extract afforded 4-bromoaniline (2.4 g), identical (i.r.) with an authentic sample.

(b) *With sodium dithionite.* The azo-dyes were dissolved in 50% aqueous ethanol and sufficient dithionite added to effect discharge of the red colour of the solution. The mixtures were heated on a steam-bath for 0.5 h. Solvent was then removed by vacuum-evaporation and ethanol extracts of the organic residue were examined by t.l.c.

(c) *With hydrogen over 10% palladium on charcoal.* The azo-dye (20b) (2.2 g) was partially dissolved in methanol (40 ml) and hydrogenated at atmospheric pressure over 10% palladium on charcoal (1 g). After 5 h, 180 ml of hydrogen had been absorbed (theoretical uptake for complete reduction of the azo-linkage = 320 ml). The cream coloured precipitate of crude *5-amino-2-(4-bromophenylhydrazino)-imidazole-4-carboxamide* rapidly re-oxidised to the starting azo-compound (20b) on exposure to air. The crude hydrazine was returned to the hydrogenation flask and acidified with 10N-hydrochloric acid (1 ml). Re-hydrogenation at atmospheric pressure resulted in the expected uptake of hydrogen in 3 h. The methanolic solution was filtered and the insoluble organic material dissolved in water. The filtered aqueous solution was evaporated to dryness to leave an unidentified white solid (0.8 g), m.p. >300 °C (with decomp.); $\lambda_{max.}$ (EtOH) 280 nm; $\nu_{max.}$ (KBr) 3 400—3 100 (bonded NH), 1 700, 1 680, and 1 640 cm^{-1} (CO); *m/z* 192 (66%), 177 (83), 136 (100), 135 (87), and 124 (42). 4-

Bromoaniline was detected (t.l.c.) when the filtrate was basified with concentrated aqueous ammonia.

(d) *With hydrazine–Raney nickel.* Solutions of azo-compounds (1 g) in 95% ethanol (50 ml) containing Raney nickel (1 g) were treated in portions at 20 °C with hydrazine hydrate (10 ml). In some cases precipitates of unstable hydrazo-compounds were deposited; these precipitates rapidly re-oxidised to the starting azo-compounds in air. When the reductions were conducted at 45 °C, dark solutions were formed from which the appropriate arylamines were the only products isolated.

Details of the products obtained under different reduction conditions are listed in Table 2.

5-Amino-2-(3-amino-2H-indazol-2-yl)imidazole-4-carboxamide (26).—5-Amino-2-(2-cyanophenylazo)imidazole-4-carboxamide (20f) (2.5 g) was partially dissolved in methanol (100 ml) and hydrogenated at atmospheric pressure over 10% palladium on charcoal (1 g). After 14 h only half the volume of hydrogen had been absorbed (200 ml). The cream precipitate of crude 5-amino-2-(2-cyanophenylhydrazino)imidazole-4-carboxamide (25) (2.1 g) rapidly re-oxidised to the starting azo-compound on exposure to air. Continued hydrogenation of this product at 35 °C (48 h) and atmospheric pressure resulted in the uptake of a further volume of hydrogen (200 ml). The filtered solution was evaporated to dryness and the residue triturated with 2N-hydrochloric acid. The *indazolylimidazole hydrochloride* thus formed (48%) had m.p. 214—216 °C (decomp.) (Found: C, 41.3; H, 4.5; N, 31.2; H_2O, 7.1. $C_{11}H_{11}N_7O{\cdot}HCl{\cdot}1.25H_2O$ requires C, 41.8; H, 4.5; N, 31.0; H_2O, 7.1%); $\lambda_{max.}$ (EtOH) 273 and 328 nm; $\nu_{max.}$ (KBr) 3 450—3 150 (bonded NH), 1 660 and 1 630 cm^{-1} (CO); *m/z* 257 (M^+, 22%), 240 (19), 214 (24), 213 (19), 145 (48), 133 (73), 118 (100), 91 (51), 77 (19), 64 (22), and 43 (95).

1-(4-Cyanoimidazol-5-yl)-3-(2-cyanophenyl)triazene (28) (*with C. P. Turnbull*).—5-Amino-4-cyanoimidazole (0.4 g) [14] in 2N-hydrochloric acid (4 ml) was diazotised at 0 °C by the dropwise addition of sodium nitrite (0.26 g) in water (4 ml). The excess of nitrous acid was destroyed by urea, and the diazonium solution was stirred with anthranilonitrile (0.4 g) in water (15 ml) at 0 °C for 2 h. The precipitated *triazene* (80%) crystallised from acetone, m.p. 187 °C (decomp.) (Found: C, 55.3; H, 3.1; N, 41.2. $C_{11}H_7N_7$ requires C, 55.7; H, 2.95; N, 41.1%); $\nu_{max.}$ (KBr) 3 200 (NH) and 2 223 cm^{-1} (CN).

The triazene (0.5 g) was boiled in 90% aqueous ethanol (10 ml) for 1 h and the solvent was evaporated. The residue, crystallised from water, afforded 2-phenyladenine (75%), m.p. 325 °C (lit.,[15] m.p. 321 °C); $\lambda_{max.}$ (water) 237 and 268 nm; the i.r. spectrum was identical with that of an authentic sample.[15]

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