STUDIES ON CONDENSED PYRAZOLES: SYNTHESIS OF NEW METHYL AND AMINO PYRAZOLO[1,5-*a*]PYRIMIDINES AND OF PYRAZOLO[5,1-*c*][1,2,4]TRIAZINES

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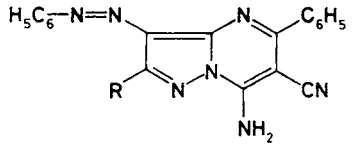
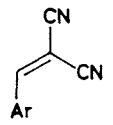
A variety of 3-arylazo 5-amino- and 7-aminopyrazolo-[1,5-*a*]pyrimidines were obtained via reacting *Ia*—*Id* with cinnamonitriles. The structure of products was confirmed via ^{1}H NMR. Both 5-amino- and 7-amino- 3-arylazo pyrazolo[1,5-*a*]pyrimidines reacted, with protons in acetic acid–sulphuric acid mixture to yield the corresponding 3-unsubstituted acetylaminopyrazolo-[1,5-*a*]pyrimidines. Diazotized *Ia* and *Ib* coupled with a variety of active methylene reagents to yield pyrazolo[5,1-*c*][1,2,4]triazines.

The chemistry of condensed pyrazoles has recently been reviewed[1-3]. The considerable biological activities of pyrazolopyrimidines[1] as adenosine cyclic monophosphate phosphodiesterase inhibitors[4], antischistosomal agents[5] and as antimetabolites[6] is perhaps beyond this interest. As a part of a biological chemistry project in these laboratories, samples of certain substituted alkyl- and amino- pyrazolo[1,5-*a*]pyrimidines and pyrazolo[5,1-*c*][1,2,4]triazines were required. Synthetic approaches to derivatives of both ring systems previously described by us[7-9] were tried. Thus, it has been found that *Ib* reacts with acrylonitrile to yield product which may be formulated as *II* or isomeric *III*. Structure *II* was established for product of cyanoethylation based on ^{1}H NMR which revealed two triplets at δ 3·2 and δ 4·35 for two CH_2 groups. If the reaction product was *III* one would expect the triplet at δ 4·35 to appear as multiplet as it would be coupled both with CH_2 and NH. Attempted cyclization of *II* into pyrazolo[1,5-*a*]pyrimidine derivative failed. Refluxing *II* in acetic acid resulted in formation of the acetylamino derivative *IV* also obtained on refluxing *Ib* in acetic acid. Dealkylation fo N-alkyl derivatives under similar conditions has been observed earlier[10,11].

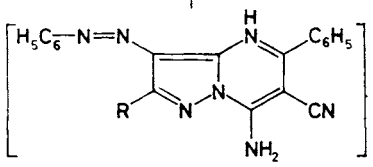
Synthesis of aminopyrazolo[1,5-*a*]pyrimidines via reaction of aminopyrazoles with cinnamonitriles was first reported from our laboratories[12]. It was assumed



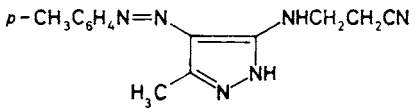
VIIa, R = NH_2
VIIb, R = OH



Va, Ar = C_6H_5
Vb, Ar = $C_6H_4OCH_3$-*p*

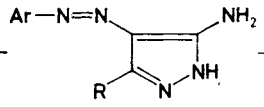


IX



III

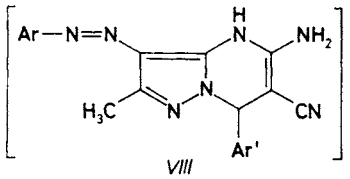
Ic, Id



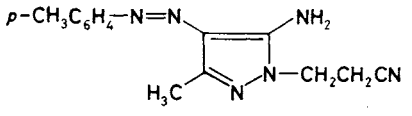
(Ib)

Ia, Ib

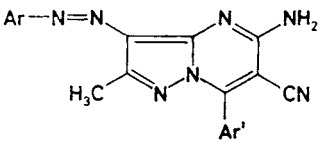
Ia, Ar = C_6H_5; R = CH_3
Ib, Ar = $C_6H_4CH_3$-*p*; R = CH_3
Ic, Ar = C_6H_5; R = NH_2
Id, Ar = C_6H_5; R = OH

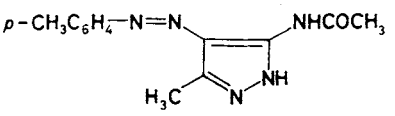


VIII



II





IV

VIa, Ar = Ar' = C_6H_5
VIb, Ar = $C_6H_4CH_3$-*p*; Ar' = C_6H_5
VIc, Ar = C_6H_5; Ar' = $C_6H_4OCH_3$-*p*
VId, Ar = $C_6H_4CH_3$-*p*; Ar' = $C_6H_4OCH_3$-*p*

SCHEME 1

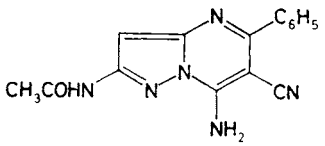
that ring nitrogen adds to the activated double bond system to yield the corresponding Michael adducts which then cyclizes yielding 5-amino-6,7-dihydropyrazolo[1,5-*a*]-pyrimidine derivative. Later Soto et al.[13] reported that the reaction of 3,5-diamino--4-benzylpyrazole with cinnamonitriles affords 2,7-diamino-4,5-dihydropyrazolo-[1,5-*a*]pyrimidines via attack of amino function on activated double bond and subsequent attack of the cyano function in the formed adduct by ring nitrogen atom. In order to decide whether ring nitrogen or exocyclic amino function is the first added nucleophile Hussein et al.[14] has prepared a series of 5-amino- and 7-amino-pyrazolo[1,5-*a*]pyrimidines. Comparing ^{1}H NMR data of these products it could be concluded that 5-aminopyrazolo[1,5-*a*]pyrimidines are the products of reaction of 3(5)-aminopyrazoles with cinnamonitriles as has been reported earlier[12]. However, this does not mean that the structures assumed by Soto et al.[13] for products of reaction of cinnamonitriles with 3,5-diamino-4-benzylpyrazole are in error. Amino functions are situated in such a way that they interfere with lone pair resonance of each other a situation that may lead to increased nucleophilicity of ring nitrogen. In order to check this the behaviour of *Ia*–*Id* toward arylidenemalononitrile *V* was investigated. While a methyl group in *Ia* and *Ib* would affect inductively and by hyperconjugation lone pair resonance of exocyclic amino function in *Ic* and the hydroxy function in *Id* would affect lone pair resonance by interference with its delocalization.

It has been found that *Ia* and *Ib* react with *Va* and *Vb* to yield products of addition and hydrogen elimination. These proved to be the 5-aminopyrazolo[1,5-*a*]pyrimidines *VIa*–*VIb* as their ^{1}H NMR spectra revealed amino protons at δ 4·0. If they were regioisomers *VII*, amino protons should have appeared at a lower field. The formation of *VIa* and *VIb* is assumed to proceed via initial addition of ring nitrogen to activated double bond in *V* followed by cyclization to yield the dihydropyrazolo-[1,5-*a*]pyrimidines *VIII* which aromatized readily via hydrogen elimination. Similar to *Ia* and *Ib*, compounds *Ic* and *Id* reacted with *Va* to yield products of addition and hydrogen elimination. These proved to be the 7-amino derivatives *VIIa* and *VIIb* from ^{1}H NMR evidence and are assumed to be formed via intermediacy of dihydro compound *IX*, which could, however, not be isolated.

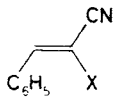
Compound *VIIa* was converted into the 3-unsubstituted pyrazolo[1,5-*a*]pyrimidine derivative *X* on reflux with acetic acid and sulphuric acid. This conversion is assumed to proceed via displacement of the azo function in *VIIa* by proton, followed by acetylation of the C-2 amino function. Exchange of arylazo function by proton in arylazopyrazoles under similar conditions has been previously reported[15].

Compound *Ic* also reacted with *XIa* to yield product of condensation via water and hydrogen elimination. This was formulated as *XIIa* and could be converted into *XIIIa* on reflux in acetic acid in presence of sulfuric acid. Similarly the acetyl-aminopyrazolo[1,5-*a*]pyrimidine *XIIIb* was obtained via refluxing *Ic* with *XIb* and

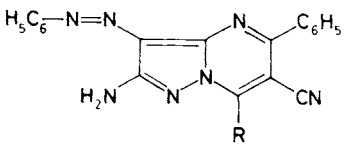
treatment of the so formed 7-hydroxypyrazolo[1,5-*a*]pyrimidine *XIIb* (or possible tautomers) with acetic acid in presence of sulphuric acid.



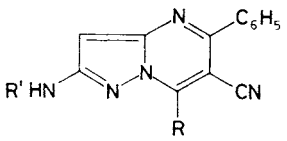
X



XI a, X = COC_6H_5
XI b, X = $COOC_2H_5$

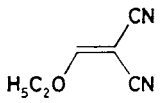


XII a, R = C_6H_5
XII b, R = OH

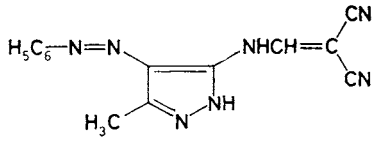


XIII a, R = C_6H_5; R' = H
XIII b, R = OH ; R' = $COCH_3$

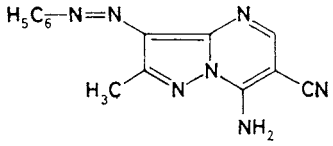
In contrast to behaviour of *I* toward acrylonitrile and *V* compound *Ia* reacted with ethoxymethylenemalononitriles (*XIV*) to yield the acylamine crotonate *XV*. Compound *XV* is assumed to be formed via addition of the exocyclic amino function in *Ia* to the α,β-unsaturated linkage in *XIV* and ethanol elimination. Cyclization of *XV* in acetic acid gave *XVI*. We believe that although the ring nitrogen is the most nucleophilic center in *Ia* it is also the most hindered one. Reactive intermediates leading to addition of this moiety at the double bond in *XIV* will be, in contrast to those involved in formation of *II* or *VIa* from acrylonitrile or *IV*, sterically unfavored. Thus, exclusive attack by less nucleophilic exocyclic amino function occurs.



XIV

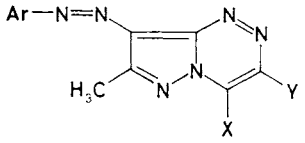


XV



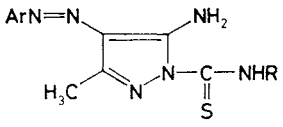
XVI

Diazotisation of aminopyrazoles has been reported to yield corresponding diazonium salts that are converted into pyrazolo[5,1-*c*][1,2,4]triazines via reaction with active methylene reagents or via reacting the diazobetaines with both electron poor and electron rich olefins[16,17]. In order to prepare arylpyrazolo[5,1-*c*][1,2,4]triazines, compounds *Ia* and *Ib* were diazotised[17] and the resulting diazonium salts were coupled with active methylene reagents. Thus, with ethyl cyanoacetate the pyrazolo-[5,1-*c*][1,2,4]triazines *XVIIa* and *XVIIb* were obtained. Similarly, coupling of *Ia* and *Ib* with malononitrile afforded *XVIIc* and *XVIId*. Coupling of *Ia* with ethyl acetoacetate yielded directly the cyclic triazine *XVIIe* formed either via coupling and water elimination or via addition of a diazobetaine to the double bond in the ethyl acetoacetate enolate and water elimination from the formed cycloadduct.

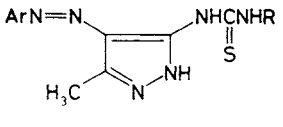


XVII a, Ar = C_6H_5; X = NH_2; Y = $COOC_2H_5$
XVII b, Ar = $C_6H_4CH_3$-*p*; X = NH_2; Y = $COOC_2H_5$
XVII c, Ar = C_6H_5; X = NH_2; Y = CN
XVII d, Ar = $C_6H_4CH_3$-*p*; X = NH_2; Y = CN
XVII e, Ar = C_6H_5; X = OH; Y = $COOC_2H_5$

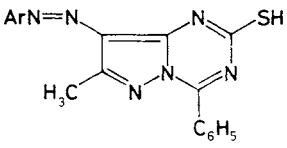
The reaction of benzoyl isothiocyanate with aminoazoles has been extensively utilized[18-20] for synthesis of heterocyclic thioureas which could be efficently cyclized into the corresponding condensed mercapto-1,3,5-triazines. In the present work we have investigated the behaviour of *Ia* and *Ib* toward ethoxycarbonylisothiocyanate and benzoylisothiocyanate with the aim of preparing arylazopyrazolo-[1,5-*a*][1,3,5]triazines. Although the required proucts could not be prepared, a variety of N-thiocarbonylpyrazoles and of pyrazolyl thioureas could be synthesized.



XVIII, R = COC_6H_5
XXI, R = $COOC_2H_5$



XIX, R = COC_6H_5
XXII, R = H



XX

In formulae *XVIII*-*XXII*: *a*, Ar = C_6H_5 *b*, Ar = $C_6H_4CH_3$-*p*

Thus, *Ia* and *Ib* reacted with benzoyl isothiocyanate to yield 1 : 1 adducts. These are assigned structure *XVIII* based on ^{1}H NMR spectra which revealed presence of an amino function. Compounds *XVIIIa* and *XVIIIb* were efficiently isomerized to *XIXa* and *XIXb* on reflux in ethanol with catalytic amount of sodium ethoxide. However attempted cyclization of the latter into pyrazolo[1,5-*a*][1,3,5]triazines *XX* failed under a variety of conditions. Similarly *Ia* and *Ib* reacted with ethoxycarbonyl isothiocyanate to yield the N-thiocarbonyl derivatives *XXIa* and *XXIb*. These were converted into the thioureas *XXIIa* and *XXIIb* on reflux in ethanol with sodium ethoxide.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded (KBr disc) on a Pye Unicam SP-1000 spectrometer. ^{1}H NMR spectra were recorded on a Varian A-90 MHz in hexadeuteriodimethylsulfoxide using tetramethylsilane as internal standard and chemical shifts are expressed as δ (ppm). Compounds *Ia*, *Ic* and *Id* were prepared by previously reported procedures[21,22].

5-Amino-3-methyl-4-(*p*-tolylazo)pyrazole (*Ib*)

A solution of 2-*p*-tolylhydrazone-3-oxocrotononitrile[21] (2·0 g, 0·01 mol) in ethanol (50 ml) was treated with hydrazine hydrate (0·6 ml, 0·01 mol). The reaction mixture was refluxed for 1 h then poured onto water. The solid product was collected by filtration. Compound *Ib* formed brown crystals, yield 1·6 g (70%); m.p. 178°C (ethanol). IR spectrum (cm^{-1}): 3 430—3 350 (NH_2, NH); 1 630 (NH, N=N). For $C_{11}H_{13}N_5$ (215·1) calculated: 61·4% C, 6·1% H, 32·5% N; found: 61·4% C, 6·4% H, 32·4% N.

5-Amino-1-(2-cyanoethyl)-3-methyl-4-(*p*-tolylazo)pyrazole (*II*)

A solution of *Ib* (2·0 g, 0·01 mol) in pyridine (20 ml) was treated with acrylonitrile (0·6 g, 0·01 mol). The reaction mixture was refluxed for 3 h then poured onto water. The solid product was collected by filtration and crystallised from ethanol. Compound *II* formed yellow crystals, m.p. 190°C (ethanol), yield 1·7 g (65%). IR spectrum (cm^{-1}): 3 350—3 320 (NH); 2 215 (CN); 1 630 (NH, N=N). ^{1}H NMR spectrum: 2·7 s, 3 H (CH_3); 2·8 s, 3 H (CH_3); 3·08 s, 2 H (NH_2); 3·2 t, 2 H (CH_2); 4·35 t, 3 H (CH_2); 7·5—8·16 m, 4 H (aryl protons). For $C_{14}H_{16}N_6$ (268·3) calculated: 62·6% C, 6·0% H, 31·3% N; found: 62·6% C, 6·0% H, 31·2% N.

5-Acetylamino-3-methyl-4-(*p*-tolylazo)pyrazole (*IV*)

a) A solution of *II* (2·3 g, 0·01 mol) in acetic acid (15 ml) was refluxed for 3 h then evaporated in vacuo. The remnant was triturated with water and the resulting solid was collected by filtration. Compound *IV* formed yellow crystals, m.p. 125°C (ethanol), yield 18·0 g (70%). IR spectrum (cm^{-1}): 3 340—3 325 (NH); 1 700 (CO), 1 620 (NH). ^{1}H NMR spectrum: 2·2 s, 3 H ($COCH_3$); 2·6 s, 3 H (CH_3); 2·7 s, 3 H (CH_3); 7·16—7·7 m, 6 H (aryl and NH protons). For $C_{13}H_{15}N_5O$ (257·3) calculated: 60·7% C, 5·9% H, 27·2% N; found: 60·5% C, 5·8% H, 27·2% N.

b) A solution of *Ib* (2·0 g, 0·01 mol) in acetic acid (15 ml) was refluxed for 3 h then evaporated under vacuo. The remaining solid was treated as described above and the product was identified (m.p. and mixed m.p.) as *IV*.

Reaction of 5-Aminopyrazoles *I* with Cinnamonitriles *V* and *XI*

A solution of each *I* (0·01 mol) in pyridine (20 ml) was treated with the appropriate *V* and *XI* (0·01 mol). The reaction mixture was refluxed for 3 h then evaporated in vacuo. The remaining solid was triturated with water (20 ml) and acidified with conc. hydrochloric acid (30 ml). The product was collected by filtration and crystallised from the appropriate solvent.

5-Amino-6-cyano-2-methyl-7-phenyl-3-phenylazopyrazolo[1,5-*a*]*pyrimidine-6-carbonitrile* (VIa), brown crystals (ethanol–dioxane), m.p. 200°C, yield 1·8 g (50%). IR spectrum (cm^{-1}): 3 450, 3 320, 3 240, 3 170 (NH_2, NH); 2 125 (CN); 1 640 (NH_2). ^1H NMR spectrum: 7·15 s, 2 H (NH_2); 7·45—8·15 m, 10 H (C_6H_5), 8·55 s, 2 H (NH_2). For $C_{20}H_{15}N_7$ (353·4) calculated: 68·0% C, 4·2% H, 27·8% N; found: 68·3% C, 4·0% H, 27·9% N.

5-Amino-2-methyl-7-phenyl-3-p-tolylazopyrazolo[1,5-*a*]*pyrimidine-6-carbonitrile* (VIb), brown crystals (ethanol), m.p. 220°C, yield 1·89 (50%). IR spectrum (cm^{-1}): 3 450, 3 300 (NH_2); 2 220 (CN); 1 640 (NH_2). For $C_{21}H_{17}N_7$ (367·4) calculated: 68·7% C, 4·6% H, 26·7% N; found: 68·9% C, 4·7% H, 26·5% N.

5-Amino-2-methyl-7-(p-methoxyphenyl)-3-phenylazopyrazolo[1,5-*a*]*pyrimidine-6-carbonitrile* (VIc), brown crystals (ethanol–dioxane), yield 2·3 g (60%), m.p. 270°C. IR spectrum (cm^{-1}): 3 460, 3 360 (NH_2); 2 225 (CN); 1 640 (NH, N=N). For $C_{21}H_{17}N_7O$ (383·4) calculated: 65·8% C, 4·4% H, 25·6% N; found: 65·9% C, 4·5% H, 25·8% N.

5-Amino-2-methyl-7-(p-methoxyphenyl)-3-(p-tolylazo)pyrazolo[1,5-*a*]-*pyrimidine-6-carbonitrile* (VId), brown crystals, m.p. 262°C, yield 2·4 g (60%). IR spectrum (cm^{-1}): 3 450, 3 320 (NH_2); 2 215 (CN); 1 640 (NH_2). For $C_{22}H_{19}N_7O$ (397·4) calculated: 66·5% C, 4·8% H, 24·7% N; found: 66·7% C, 4·9% H 24·5% N.

2,7-*Diamino-5-phenyl-3-phenylazopyrazolo*[1,5-*a*]*pyrimidine-6-carbonitrile* (VIIa), yellow crystals (ethanol), yield 2·3 g (65%), m.p. 282°C. IR spectrum (cm^{-1}): 3 460, 3 320 (NH_2); 2 225 (CN); 1 620 (NH, N=N). For $C_{19}H_{14}N_8$ (354·4) calculated: 64·4% C, 3·9% H, 31·6% N; found: 64·2% C, 3·9% H, 31·5% N.

7-Amino-2-hydroxy-5-phenyl-3-phenylazopyrazolo[1,5-*a*]*pyrimidine-6-carbonitrile* (VIIb), brown crystals (ethanol), yield 2·0 g (55%), m.p. >300°C. IR spectrum (cm^{-1}): 3 450—3 220 (NH, CH); 2 225 (CN); 1 680 (CO); 1 630 (NH_2). For $C_{19}H_{13}N_7O$ (355·4) calculated: 64·1% C, 3·7% H, 27·6% N; found: 64·0% C, 3·5% H, 27·2% N.

2-*Amino-5,7-diphenyl-3-phenylazopyrazolo*[1,5-*a*]*pyrimidine-6-carbonitrile* (XIIa), yellow crystals (ethanol), yield 2·5 g (60%), m.p. 210°C. IR spectrum (cm^{-1}): 3 370, 3 320 (NH_2); 2 210 (CN). For $C_{25}H_{17}N_7$ (415·4) calculated: 72·3% C 4·1% H, 23·6% N; found: 72·5% C, 4·0% H, 23·3% N.

2-*Amino-7-hydroxy-5-phenyl-3-phenylazopyrazolo*[1,5-*a*]*pyrimidine-6-carbonitrile* (XIIb), yellow crystals (ethanol, yield 2·1 g (60%), m.p. 195°C. IR spectrum (cm^{-1}): 3 480, 3 350 (NH_2, CH); 2 215 (CN). For $C_{19}H_{13}N_7O$ (355·4) calculated: 64·2% C, 3·7% H, 27·6% N; found: 64·3% C, 3·5% H, 27·3% N.

Pyrazolo[1,5-*a*]pyrimidines *X* and *XIII*

A solution of *VIa* (or *XIIa*, *XIIb*) (2·0 g) in acetic acid (15 ml) was treated with sulphuric acid (1·5 ml). The reaction mixture was refluxed for 3 h then evaporated in vacuo. The remnant was triturated with water and neutralised by ammonia. The solid product was collected by filtration and crystallised.

2-Acetylamino-7-amino-5-phenylpyrazolo[1,5-*a*]*pyrimidine-6-carbonitrile* (X), pale yellow crystals (ethanol), yield 1·9 g (65%) m.p. 275°C. IR spectrum (cm^{-1}): 3 320 (NH); 2 220 (CN); 1 640 (CO). For $C_{15}H_{12}N_6O$ (292·3) calculated: 61·7% C, 4·1% H, 28·8% N; found: 61·6% C, 4·3% H, 28·5% N.

2-Amino-5,7-diphenylpyrazolo[1,5-*a*]*pyrimidine-6-carbonitrile* (XIIIa), brown crystals (ethanol), yield 1·8 g, (58%), m.p. 250°C. IR spectrum (cm^{-1}): 3 350 (NH); 2 220 (CN); 1 630 (CO). For $C_{21}H_{15}N_5O$ (311·4) calculated: 73·3% C 4·2% H, 22·5% N; found: 73·4% C, 4·0% H, 22·4% N.

2-Acetylamino-7-hydroxy-5-phenylpyrazolo[1,5-*a*]*pyrimidine-6-carbonitrile* (XIIIb), orange crystals (acetic acid–water), yield 1·9 g, (65%), m.p. 260°C. IR spectrum (cm^{-1}): 3 480—3 340 (OH, NH); 2 230 (CN); 1 650 (CO). For $C_{15}H_{11}N_5O_2$ (293·3) calculated: 61·4% C, 6·1% H, 23·9% N; found: 61·3% C, 6·0% H, 23·9% N.

3-Methyl-4-phenylazopyrazol-5-yl Aminomethylenemalonitrile (*XV*)

A solution of *Ia* (2·0 g; 0·01 mol) in ethanol (20 ml) was treated with triethylamine and *XIV* (1·1 g, 0·01 mol). The reaction mixture was refluxed and the solid product collected by filtration was crystallised from dioxane; yellow crystals, m.p. >300, yield 1·7 g, (75%). IR spectrum (cm^{-1}): 3 400—3 350 (NH); 2 215 (CN), 1 630 (NH). ^1H NMR spectrum: 2·6 s, 3 H (CH_3); 7·4—7·8 m, 5 H (C_6H_5); 8·4 s, 1 H (NH); 9·1 s, 1 H (NH). For $C_{14}H_{11}N_7$ (227·3) calculated: 60·6% C, 4·8% H, 43·1% N; found: 61·0% C, 5·0% H, 43·0% N.

7-Amino-2-methyl-3-phenylazopyrazolo[1,5-*a*]pyrimidine-6-carbonitrile (*XVI*)

A solution of *XV* (2·3 g, 0·01 mol) in acetic acid (36 ml) was refluxed for 3 h and then poured onto water. The solid product, collected by filtration, formed yellow crystals (acetic acid), yield 1·2 g (50%); m.p. 220°C. IR spectrum (cm^{-1}) 3 420, 3 370 (NH_2), 2 210 (CN), 1 620 (NH). For $C_{14}H_{11}N_7$ (227·3) calculated: 60·6% C, 48% H, 43·1% N; found: 60·3% C, 4·6% H, 43·1% N.

Arylazopyrazolo[5,1-*c*]-1,2,4-triazines *XVII*

A solution of *Ia* (or *Ib*) (0·01 mol) in acetic acid (50 ml) was treated with hydrochloric acid (3·0 ml) followed by a solution of sodium nitrite (0·7 g) in water (c. 2 ml). The reaction mixture was stirred for 10 min then poured onto a solution of the appropriate active methylene reagent (*Va* or *Vb*, *XIa*, *XIb*) (0·01 mol) dissolved in ethanol (50 ml) containing sodium acetate (3·0 g).

Ethyl 7-amino-2-methyl-3-phenylazopyrazolo[5,1-*c*]-1,2,4-*triazine-6-carboxylate* (XVIIa), orange crystals (ethanol), yield 1·9 g, (60%), m.p. 260°C. IR spectrum (cm^{-1}): 3 285, 3 230 (NH_2); 1 960 (CO); 1 630 (N=N, NH). For $C_{15}H_{15}N_7O_2$ (325·5) calculated: 66·3% C, 4·5% H, 30·1% N; found: 55·5% C, 4·2% H, 30·0% N.

Ethyl 7-amino-2-methyl-3-(p-tolylazo)pyrazolo[5,1-*c*]-1,2,4-*triazine-6-carboxylate* (XVIIb), brown crystals (ethanol), yield 1·7 g (50%), m.p. 230°C. IR spectrum (cm^{-1}): 3 220, 3 160, 3 100 (NH_2, NH); 2 940 (CH_3); 2 220 (CN); 1 720 (CO), 1 600 (NH, N=N). For $C_{16}H_{17}N_7O_2$ (339·4) calculated: 56·6% C, 5·0% H, 28·9% N; found: 56·5% C, 5·2% H, 28·5% N.

7-Amino-2-methyl-3-phenylazopyrazolo[5,1-*c*]-1,2,4-*triazine-6-carbonitrile* (XVIIc), yellow crystals (dioxane), yield 1·7 g, (60%), m.p. 250°C. IR spectrum (cm^{-1}): 3 290, 3 340 (NH_2); 2 220 (CN); 1 650 (NH, N=N). For $C_{13}H_{10}N_8$ (278·3) calculated: 56·1% C, 3·6% H, 40·2% N; found: 56·3% C, 3·5% H, 40·1% N.

7-*Amino*-2-*methyl*-3-(*p-tolylazo*)*pyrazolo*[5,1-*c*]-1,2,4-*triazine*-6-*carbonitrile* (XVIId), brown crystals (dioxane), 1·5 g, (60%), m.p. 210°C. IR spectrum (cm^{-1}): 3 340, 3 310 (NH_2); 2 940 (CH_3); 2 225 (CN), 1 560 (N=N, NH, N=N). For $C_{14}H_{12}N_8$ (292·3) calculated: 57·5% C, 4·1% H, 38·4% N; found: 57·4% C, 4·3% H, 38·2% N.

Ethyl 2,7-*dimethyl*-3-*phenylazopyrazolo*[5,1-*c*]-1,2,4-*triazine*-6-*carboxylate* (XVII), brown crystals (acetic acid), yield 1·9 g, (50%), m.p. 210°C. IR spectrum (cm^{-1}): 2 950, 2 910 (2-CH_3); 1 730 (CO); 1 570 (NH, N=N). For $C_{16}H_{16}N_6O_2$ (324·3) calculated: 59·3% C, 5·0% H, 25·9% N; found: 59·3% C, 4·5% H, 25·7% N.

5-Amino-4-arylazo-3-methyl-1-thiocarbamoylpyrazole Derivatives *XVIII* and *XXI*

To a solution of either benzoyl isothiocyanate (0·01 mol) or ethoxycarbonyl isothiocyanate (0·01 mol) in dry acetone (50 ml), were added 0·01 mol of *Ia* or *Ib*. The reaction mixture was refluxed 2 h, the solvent was evaporated in vacuo. The residue was triturated with ethanol and crystallized.

5-*Amino*-3-*methyl*-1-(N-*benzoylthiocarbamoyl*)-4-*phenylazopyrazole* (XVIIIa), yellow crystals (ethanol), yield 1·8 g (50%); m.p. 210°C. IR spectrum (cm^{-1}): 3 400, 3 200, 3 170 (NH_2, NH); 1 670 (CO). For $C_{18}H_{16}N_6OS$ (364·4) calculated: 59·3% C, 4·3% H, 23·1% N, 8·8% S; found: 59·4% C, 4·2% H, 22·9% N, 8·5% S.

5-*Amino*-3-*methyl*-1-(N-*benzoylthiocarbamoyl*)-4-(*p-tolylazo*)*pyrazole* (XVIIIb), yellow crystals (ethanol), yield 1·4 g, (40%); m.p. 230°C. IR spectrum (cm^{-1}): 3 440, 3 360—3 330 (NH_2, NH), 1 705—1 650 (CO, NH). For $C_{19}H_{18}N_6OS$ (378·4) calculated: 60·3% C, 4·8% H, 22·2% N, 8·5% S; found: 60·3% C, 4·7% H, 22·4% N, 8·4% S.

5-*Amino*-3-*methyl*-1-(N-*ethoxycarbonylthiocarbamoyl*)-4-*phenylazopyrazole* (XXIa), yellowish-brown crystals (ethanol), yield 2·3 g (70%), m.p. 230°C. IR spectrum (cm^{-1}): 3 300—3 180 (NH_2, NH); 2 985, 2 960 (CH_3); 1 670 (CO). For $C_{19}H_{16}N_6O_2S$ (332·3) calculated: 50·5% C, 4·9% H, 25·3% N; 9·6% S; found: 50·4% C, 4·5% H, 25·1% N, 9·8% S.

5-*Amino*-3-*methyl*-1-(N-*ethoxycarbonylthiocarbamoyl*)-4-(*p-tolylazo*)*pyrazole* (XXIb), yellow crystals (ethanol), yield 1·3 g, (40%), m.p. 200°C. IR spectrum (cm^{-1}): 3 300, 3 250 (NH_2, NH); 2 980, 2 950 (CH_3); 1 725 (CO). ^1H NMR spectrum: 0·28 s, 3 H (CH_3); 0·67 s, 3 H (CH_3); 1·2—1·45 t, 3 H (CH_3); 2·35—2·55 m, 3 H (3 NH); 4·2 q, 2 H (CH_2); 7·2—7·8 m, 4 H (C_6H_4). For $C_{15}H_{18}N_6O_2S$ (346·3) calculated: 52·0% C, 5·2% H, 24·3% N, 9·2% S; found: 52·2% C, 5·3% H, 24·5% N, 9·3% S.

4-Arylazo-3-methylpyrazole-5-thiourea derivatives *XIX* and *XXII*

Compound *XVIIIa* (or *XVIIIb*, *XXIa*, *XXIb*) (0·01 mol) was heated under reflux in ethanol in presence of catalytic amount of sodium ethoxide for 3 h. The reaction mixture was treated with hydrochloric acid. The solid product was collected by filtration and crystallized from the proper solvent.

3-*Methyl*-5-(N-*benzoylthiocarbamoylamino*)-4-*phenylazopyrazole* (XIXa), yellow crystals, yield 1·4 g (40%), m.p. 280°C. IR spectrum (cm^{-1}): 3 390—3 250 (NH); 1 680 (CO). For $C_{18}H_{16}N_6OS$ (364·4) calculated: 59·3% C, 4·4% H, 23·0% N, 8·8% S; found: 59·3% C, 4·4% H, 23·2% N, 8·7% S.

3-*Methyl*-5-(N-*benzoylthiocarbamoylamino*)-4-(*p-tolylazo*)*pyrazole* (XIXb), yellow crystals, yield 1·8 g (50%), m.p. 300°C. IR spectrum (cm^{-1}): 3 400—3 350 (NH); 1 640 (NH). For $C_{19}H_{18}$·N_6OS (378·4) calculated: 60·3% C, 4·8% H, 22·2% N, 8·5% S; found: 60·2% C, 4·6% H, 22·3% N, 8·6% S.

3-*Methyl*-4-*phenylazopyrazol*-5-*ylthiourea* (XXIIa), brown crystals (methanol), yield 1·6 g (50%), m.p. 165°C. IR spectrum (cm^{-1}): 3 400—3 300 (NH, NH_2); 1 630 (NH). For $C_{11}H_{12}N_6S$ (360·3) calculated: 50·8% C, 4·7% H, 32·3% N, 12·2% S; found: 50·7% C, 4·9% H, 32·5% N, 12·4% S.

3-*Methyl*-4-(*p*-*tolylazo*)*pyrazol*-5-*ylthiourea* (XXIIb), brown crystals (ethanol), yield 1·3 g (40%), m.p. 155°C. IR spectrum (cm^{-1}): 3 450—3 320 (NH, NH_2); 1 620 (NH). ^1H NMR spectrum: 2·3—2·9 m, 10 H (2 CH_3, 2 H, NH_2); 7·2—7·8 m, 4 H (C_6H_4). For $C_{12}H_{14}N_6S$ (274·3) calculated: 52·6% C, 5·2% H, 30·7% N, 11·7% S; found: 52·5% C, 5·4% H, 30·3% N, 11·3% S.

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