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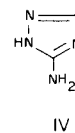
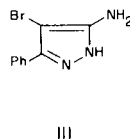
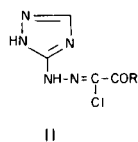
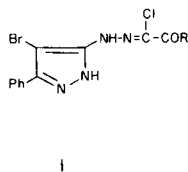
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The 4-bromo-3-phenylpyrazol-5-ylhydrazonyl chlorides (Ia,b) and 1,2,4-triazol-5-ylhydrazonyl chlorides (IIa,b) were prepared *via* coupling of diazotized 4-bromo-3-phenyl-5-aminopyrazole (III) and 5-amino-1,2,4-triazole (IV) with α -chloro derivatives of acetylacetone and of ethyl acetoacetate. Compounds Ia and IIa,b were utilised for the synthesis of several new heterocyclic derivatives.

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Diazotised 1*H*-aminoazoles are versatile reagents and their synthetic potentialities have received considerable recent attention (1-3). As a part of our program directed for the development of new procedures for the synthesis of fused heterocyclic azoles (4-8) we have previously reported (9) the synthesis of 3-phenylpyrazole-5-yl-hydrazonyl chloride from the reaction of diazotized 3-phenyl-5-aminopyrazole and α -chloroacetylacetone and ethyl α -chloroacetoacetate. We have been particularly interested to see if this procedure might be extended to include a more general method for the synthesis of, the otherwise not readily accessible (10), heterocyclic hydrazonyl halides. Moreover exploring the synthetic potentialities of this class of heterocyclic derivatives seemed to be of value. In the present paper we report the synthesis and chemical reactivity of hydrazonyl chloride derivatives Ia,b, IIa,b based on the coupling reaction of diazotised III, and IV with α -chloro derivatives of acetylacetone and of ethyl acetoacetate. Thus, it has been found that 5-amino-4-bromo-3-phenylpyrazole (III) reacts with nitrous acid to yield the corresponding diazonium chloride. The latter coupled with α -chloroacetylacetone and with ethyl α -chloroacetoacetate to yield the halohydrazides, Ia,b. In contrast to III attempted coupling of diazotised 5-amino-1,2,4-triazole (IV) in the presence of hydrochloric acid with α -chloroacetylacetone and ethyl α -chloroacetoacetate was unsuccessful. The diazotized aminotriazole under these conditions readily decomposed into the corresponding chloro



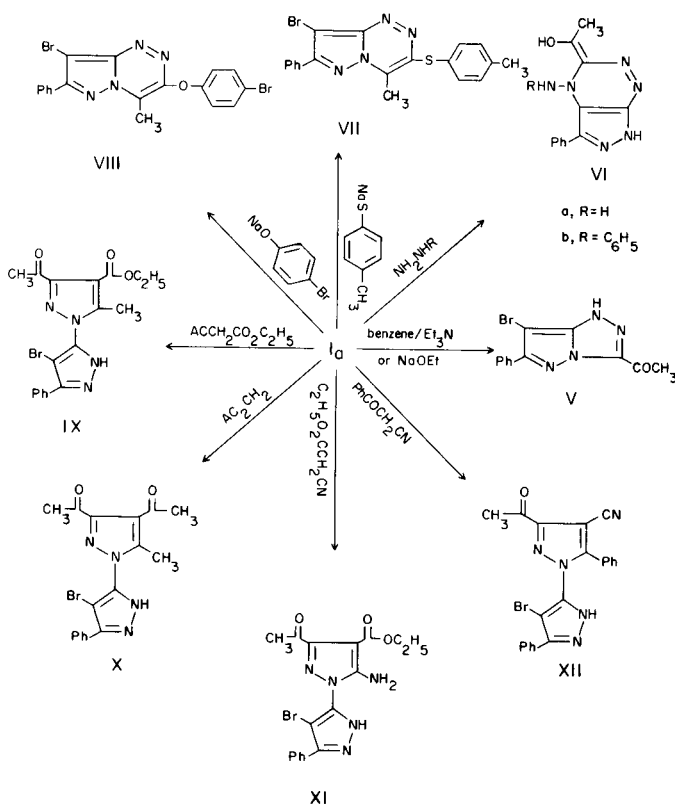
derivatives. However, when IV was diazotized in the presence of concentrated nitric acid under the experimental conditions previously described by Tennant, *et al.*, (2) the diazonium salt could be successfully coupled with α -chloroacetylacetone and ethyl α -chloroacetoacetate to yield the halohydrazide derivatives IIa,b.

Compound Ia could be readily cyclised into the pyrazolo[1,5-*c*]-1,2,4-triazole derivatives V on treatment with benzene in the presence of triethylamine. This is similar to the reported ready cyclisation of 3-phenylpyrazol-5-yl-hydrazonyl chlorides into the corresponding pyrazolo[1,5-*c*]-1,2,4-triazoles (9). However, in contrast to the reported cyclisation of 3-phenylpyrazol-5-ylhydrazonyl chloride into pyrazolo[1,5-*c*]-*as*-triazines on treatment with hydrazine hydrate and with phenylhydrazine, compound Ia reacted with hydrazine hydrate and with phenylhydrazine to yield the pyrazolo[4,3-*c*]-*as*-triazines VIa,b, respectively.

Compound Ia reacted with *p*-thiocresol and with *p*-bromophenol in the presence of ethanolic sodium ethoxide to yield the pyrazolo[1,5-*c*]-*as*-triazines VII and VIII respectively. Similar to the aryl counter analogous (1), compound Ia reacted with active methylene reagents to yield 1-pyrazol-5-ylpyrazole derivatives. Thus Ia reacted with ethyl acetoacetate, acetylacetone, ethyl cyanoacetate and with benzoylacetone nitrile to yield the 1-pyrazol-5-ylpyrazole derivatives IX-XII. The structure of these derivatives was inferred from analytical and spectral data.

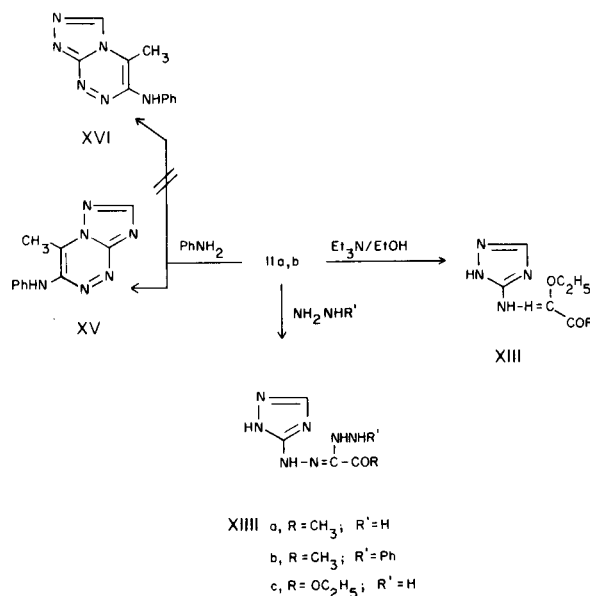
In contrast to the behaviour of Ia to the above reported

reagents, compound Ib did not condense with active methylene reagents. Under the experimental conditions, Ib underwent a self-condensation reaction. The nature of the products obtained will be the subject of a separate communication.



Compounds IIa,b did not cyclise into triazolotriazoles or triazolotriazines under conditions reported to effect cyclization of the pyrazol-5-yl counter analogs into fused pyrazole derivatives. Thus, with ethanolic triethylamine, in benzene solution, the ethanolate derivatives XIIIa,b were the only isolable products. Also with hydrazine hydrate and with phenylhydrazine, the hydrazine derivatives XIVa-c (or possible tautomers) were obtained.

Compound IIa reacted with aniline to yield the triazolo-[2,3-*c*]-*as*-triazine derivatives XVII. Attempts to isolate acyclic intermediate condensation products for this reaction were unsuccessful. Although two isomeric structures are possible for the cyclisation products (*c.f.*, structures XV and XVI), the triazolo[1,5-*c*]-*as*-triazine structure XV was considered most likely based on analogy to the well established behaviour of acyltriazole-5-yl hydrazones on cyclization under similar conditions (2).



EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Pye Unicam SP 1000 spectrophotometer. ¹H-N spectra were recorded on a Varian A-60 in DMSO using TMS as internal standard and chemical shifts are expressed as δ ppm.

4-Bromo-3-phenylpyrazol-5-yl Hydrazonyl Chloride (Ia,b).

A solution of diazotised III (prepared from 0.1 mole of III as has been previously described from 5-amino-3-phenylpyrazole (9) was added gradually to a cooled solution of α-chloroacetylacetone or ethyl

Table I

List of the 1-Pyrazol-5-ylpyrazole Derivatives

Compound	m.p. °	Yield %	Formula	Analysis, %		Ir cm ⁻¹
				Calcd./Found	C H	
IX	120	70	C ₁₈ H ₁₇ BrN ₄ O ₃	51.8	4.1	3100 (NH), 1710 (CO ₂ Et)
				52.0	3.9	
X (a)	144	70	C ₁₇ H ₁₅ BrN ₄ O ₂	52.9	3.9	3400-3100 (NH), 1700(CO)
				53.1	3.9	
XI (b)	150	75	C ₁₇ H ₁₅ BrN ₄ O ₂	48.4	4.0	3300 (NH ₂), 1745 (CO ₂ Et), 1700 (CO), 1620 (NH ₂)
				48.4	4.2	
XII	135	65	C ₂₁ H ₁₄ BrN ₅ O	58.3	3.4	3280 (NH), 2220 (CN) 1700 (CO)
				58.2	3.6	

(a) Calcd.: N, 14.4. Found: N, 14.5. Calcd.: Br, 20.6. Found: Br, 20.9. (b) Calcd.: N, 16.8. Found: N, 17.1.

α -chloroacetoacetate (0.1 mole) in ethanol (100 ml.) and sodium acetate (13 g.) with continual stirring. The temperature was kept at 0-5° during the addition. The solid product, so formed, was collected by filtration, washed with water, dried and crystallised from benzene-petroleum ether (60-80°). Compound Ia formed yellow crystals, yield 80%, m.p. 92°; ir: 1685 cm^{-1} (acetyl CO), and broad band at 3200-3400 cm^{-1} (NH).

Anal. Calcd. for $\text{C}_{12}\text{H}_{10}\text{BrClN}_2\text{O}$: C, 42.2; H, 2.9; N, 16.4; Br, 23.4. Found: C, 42.5; H, 3.1; N, 16.7; Br, 23.6.

Compound Ib formed yellow crystals, yield 70%, ir: 1740 cm^{-1} (ester CO) and broad band at 3150-3350 cm^{-1} (NH).

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{BrClN}_2\text{O}_2$: C, 42.0; H, 3.2; N, 15.1; Cl, 9.5. Found: C, 41.9; H, 3.2; N, 15.0; Cl, 9.5.

1,2,4-Triazol-5-ylhydrazonyl Chloride (IIa,b).

A solution of α -chloroacetylacetone or ethyl α -chloroacetoacetate (0.1 mole) in ethanol (100 ml.) was treated with a solution of anhydrous sodium acetate (3.5 g.) in the least amount of water, then with a solution of diazotized IV (prepared from 0.1 mole of IV and the appropriate quantities of nitric acid and sodium nitrite as has been described by Tennant, *et al.*) (2). The resulting solution was kept at 5° with stirring for 2 hours and the solid product, so formed was collected by filtration and crystallised from ethanol.

Compound IIa formed pale yellow crystals, yield 55%, m.p. 200°; ir: 1720 cm^{-1} (acetyl CO) and 3090-3200 cm^{-1} (chelated NH); $^1\text{H-nmr}$: 2.22 (s, 3H, CH_3), 8.25 (br, 1H, CH), 9.40 (s, 1H, NH) and 10.16 (br, 1H, NH).

Anal. Calcd. for $\text{C}_8\text{H}_6\text{ClN}_4\text{O}$: C, 32.0; H, 3.2; N, 37.3; Cl, 18.9. Found: C, 32.1; H, 3.0; N, 37.4; Cl, 18.7.

Compound IIb, pale yellow crystals, yield 50%, m.p. 203°; ir: 1700 cm^{-1} (ester CO) and broad band at 3400 cm^{-1} (NH); $^1\text{H-nmr}$: 1.48 (t, 3H, CH_3), 4.33 (q, 2H, CH_2), 8.33 (s, 1H, CH) and 11.25 (br, 2H, NH).

Anal. Calcd. for $\text{C}_8\text{H}_8\text{ClN}_4\text{O}_2$: C, 33.1; H, 3.8; N, 32.2; Cl, 16.3. Found: C, 33.3; H, 3.6; N, 32.4; Cl, 16.1.

3-Acetyl-6-phenyl-7-bromopyrazolo[1,5-c]-1,2,4-triazole (V).

Method A.

A suspension of Ia (2.0 g.) in benzene (50 ml.) was treated with ethanolic solution of triethylamine (100 ml.). The reaction mixture was refluxed for 2 hours and then evaporated under vacuum. The remaining product was triturated with petroleum ether (60-80°) and the resulting solid product was collected by filtration and crystallised from benzene-petroleum ether mixture. Compound V formed yellow crystals, m.p. 69°, yield 75%; ir: 2800-3200 cm^{-1} (NH), 1680 cm^{-1} (CO) and 1620 cm^{-1} (N=C).

Anal. Calcd. for $\text{C}_{12}\text{H}_9\text{BrN}_4\text{O}$: C, 47.2; H, 3.0; Br, 26.2. Found: C, 47.4; H, 3.3; Br, 26.3.

Method B.

To an ethanolic solution of sodium ethoxide (prepared from 0.11 g. of sodium metal and 25 ml. of ethanol), 0.005 mole of Ia was added. The reaction mixture was refluxed for 2 hours, left overnight at room temperature, and then evaporated *in vacuo*. The residue obtained was triturated with water and the resulting solid product was collected by filtration, dried, and identified (m.p. and mixed m.p.) as V, yield 70%.

6-Amino-7- α -hydroxyethylene-5-phenylpyrazolo[4,3-c]-as-triazine (VIa).

A solution of Ia (0.005 mole) in ethanol (50 ml.) was treated with hydrazine hydrate (0.01 mole, 99%). The reaction mixture was refluxed for 3 hours and then evaporated under vacuum. The remaining product was triturated with water, collected by filtration and crystallised from ethanol. Compound VIa formed yellowish-brown crystals, yield 70%; ir: 1620 cm^{-1} (NH_2) and 3000-3420 cm^{-1} (NH).

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_6\text{O}$: C, 56.2; H, 4.7; N, 32.8. Found: C, 56.1; H, 4.6; N, 32.5.

6-Anilino-7- α -hydroxyethylene-5-phenylpyrazolo[4,3-c]-as-triazine (VIb).

Compound Ia was treated with phenylhydrazine using the experimental procedure described above for its reaction with hydrazine hydrate. The reaction product was crystallised from ethanol. Compound VIb formed yellow crystals, m.p. 210°, yield 65%.

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{N}_6\text{O}$: C, 65.0; H, 4.8; N, 25.3. Found: C, 65.1; H, 4.8; N, 25.2.

8-Bromo-4-methyl-7-phenyl-3-(*p*-methylthiophenyl)pyrazolo[1,5-c]-as-triazine (VII).

A solution of *p*-thiocresol (0.005 mole) in ethanolic sodium ethoxide (prepared from 0.11 g. of sodium metal and 25 ml. of ethanol) was treated with Ia (0.005 mole). The reaction mixture was left overnight at room temperature. The solid product, so formed, was filtered off, washed several times with water and dried. Compound VII formed brown crystals from ethanol, yield 70%, m.p. 127°.

Anal. Calcd. for $\text{C}_{19}\text{H}_{15}\text{BrN}_4\text{S}$: C, 55.5; H, 3.7; Br, 19.5; S, 7.4. Found: C, 55.8; H, 3.8; Br, 19.6; S, 7.7.

8-Bromo-3-(*p*-bromophenyl)-4-methyl-7-phenylpyrazolo[1,5-c]-as-triazine (VIII).

Compound Ia was treated with *p*-bromophenol under the experimental conditions described above for its reaction with *p*-thiocresol. The reaction product was crystallised from benzene-petroleum ether (60-80°) mixture. Compound VIII, brown crystals, m.p. 152°, yield 60%.

Anal. Calcd. for $\text{C}_{18}\text{H}_{12}\text{Br}_2\text{N}_4\text{O}$: C, 46.9; H, 2.4; N, 12.2; Br, 34.7. Found: C, 46.8; H, 2.6; N, 12.0; Br, 34.6.

Reaction of I with Active Methylene Reagents.

To an ethanolic solution of sodium ethoxide (prepared from 0.11 g. of sodium metal in 25 ml. of ethanol) was added 0.005 mole of Ia then a solution of 0.005 mole of the active methylene reagent in 10 ml. of ethanol. The reaction mixture was then stirred overnight at room temperature, then poured into ice cold water (50 ml.) and acidified with concentrated hydrochloric acid. The reaction product, so formed, was collected by filtration and crystallised from benzene-petroleum ether (60-80°). The pyrazolo-5-ylpyrazole derivatives IX-XII are listed in table I.

Reaction of IIa,b with:

a Ethanol-triethylamine Mixture.

A solution of IIa (2.0 g.) in ethanol (20 ml.) was treated with triethylamine (5 ml.). The reaction mixture was refluxed for five hours and then evaporated. The remaining product was triturated with petroleum ether (80-100°). The resulting solid was collected by filtration and crystallised from ethanol. Compound XIII formed yellow crystals, yield 44%, m.p. 219; ir: 1700 cm^{-1} (CO) and a broad band at 3100-3250 cm^{-1} (NH).

Anal. Calcd. for $\text{C}_8\text{H}_8\text{N}_4\text{O}$: C, 42.3; H, 5.8; N, 33.2. Found: C, 42.1; H, 5.6; N, 33.4.

b Hydrazines.

A solution of each of IIa,b (0.1 mole) in ethanol (100 ml.) was treated with the appropriate hydrazine (0.1 mole). The reaction mixture was refluxed for one hour then evaporated *in vacuo*. The remaining product was triturated with water, collected by filtration and crystallised from ethanol.

Compound XIV formed colourless crystals, yield 50%, m.p. 252°. *Anal.* Calcd. for $\text{C}_5\text{H}_9\text{N}_7\text{O}$: C, 32.8; H, 4.9; N, 53.6. Found: C, 32.7; H, 4.8; N, 53.4.

Compound XIVb formed pale yellow crystals, yield 52%, m.p. 216°. *Anal.* Calcd. for $\text{C}_{11}\text{H}_{13}\text{N}_7\text{O}$: C, 51.7; H, 5.0; N, 38.3. Found: C, 51.8; H, 5.0; N, 38.0.

Compound XIVc formed colourless crystals, m.p. 240°, yield 45%. Found: C, 32.9; H, 5.0; N, 46.2.

Anal. Calcd. for $C_6H_{11}N_2O_2$: C, 33.0; H, 5.2; N, 46.0.

c With Aniline.

A mixture of IIa (2.0 g.) and aniline (1.0 ml.) was heated at 100° (bath-temperature) for six hours. The reaction mixture was then triturated with ethanol and the solid product, so formed, was collected by filtration. Compound XV formed yellow crystals from ethanol, m.p. 208°, yield 50%.

Anal. Calcd. for C, 58.4; H, 4.4; N, 37.2. Found: C, 58.3; H, 4.5; N, 37.0.

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