

PREPARATION OF NAPHTHO[2,1-*e*]PYRAZOLO[5,1-*c*][1,2,4]TRIAZINE, DIPYRAZOLO[5,1-*c*:3',4'-*e*][1,2,4]TRIAZINES AND PYRAZOLO-[1,5-*c*][1,2,4]TRIAZINE DERIVATIVES

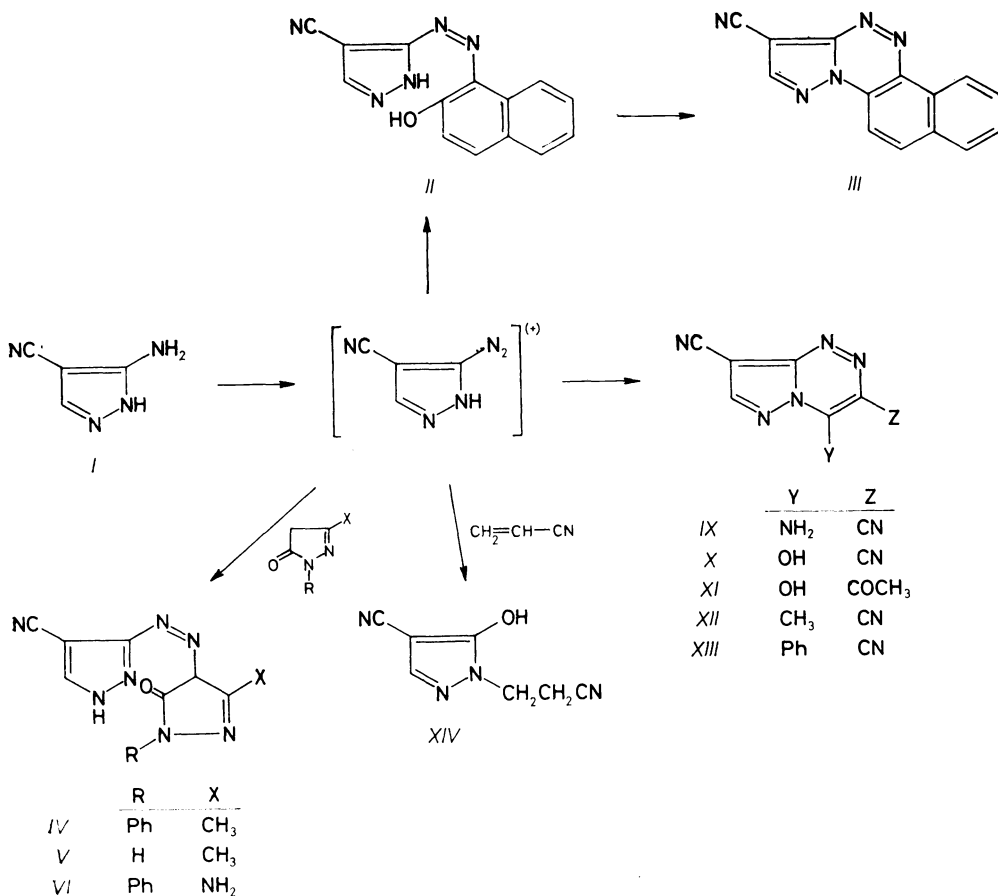
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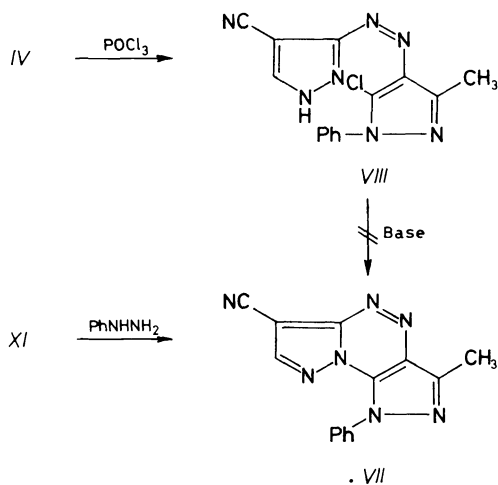
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Heterocyclic diazonium salts represent an interesting class of reactive substrates and their synthetic potentialities have received recent attention. As a part of our





SCHEME 1

program directed towards the synthesis of fused pyrazoles they are of interest as potential anti-inflammatory and antitumor agents^{1,2} (see Scheme 1).

EXPERIMENTAL

Melting points are uncorrected. ¹H NMR spectra were recorded on a Hitachi Perkin-Elmer Va 60 spectrometer in (CD₃)₂SO with TMS as an internal standard and chemical shifts are expressed as δ (in ppm). IR spectra were obtained with a Perkin-Elmer 257 spectrometer (KBr). Analytical data were obtained from the Micro analytical centre, Cairo University.

1-(4-Cyano-5-pyrazolylazo)-2-naphthol *II*

A solution of 3-amino-4-cyanopyrazole *I* (1.08 g, 0.01 mol) in hydrochloric acid (3 ml, 50%) was cooled to 0°C and treated with sodium nitrite solution (0.7 g dissolved in the least amount of water). The solution was stirred for 30 min, then added to a solution of 2-naphthol (1.4 g, 0.01 mol) in ethanol (40 ml) containing sodium acetate (5.0 g). The solid product formed on standing was collected, washed several times with hot water, dried and crystallized from ethanol to give *II* (yield 85%) with m.p. 250°C. For C₁₄H₉N₅O (263.3) calculated: 63.87% C, 3.45% H; found: 63.60% C, 3.50% H. IR spectrum (cm⁻¹): 3 400 br (OH), 2 220 (CN), 1 610 (C=N).

Cyclization of II. A solution of *II* (2.63 g, 0.01 mol) in acetic anhydride (20 ml) was refluxed for 2 h. The solvent was then evaporated under reduced pressure and the solid residue was crystallized from acetic acid to give naphthol[2,1-*e*]pyrazolo[5,1-*c*][1,2,4]triazine-1-carbonitrile *III* (yield 85%) with m.p. 300°C. For C₁₄H₇N₅ (245.2) calculated: 68.56% C, 2.88% H; found: 68.30% C, 3.20% H. IR spectrum (cm⁻¹): 2 220 (CN), 1 620 (C=N). ¹H NMR: 9.0–8.0 m, 6 H (naphthalene; 9.1 s, 1 H (H-2)).

3-[(1-Phenyl-3-methyl-5-oxo-4,5-dihydro)-4-pyrazolylazo]-
-1*H*-pyrazole-4-carbonitrile *IV*

A solution of diazotized *I* (prepared following the above procedure from *I*, 1.08 g, 0.01 mol) was poured gradually onto a solution of 1-phenyl-3-methyl-5-pyrazolone (1.7 g, 0.01 mol) in pyridine (50 ml). The reaction mixture was stirred at room temperature for 1 h. The solid product so formed was crystallized from ethanol to give *IV* (yield 87%) with m.p. 242°C. For $C_{14}H_{11}N_7O$ (293.3) calculated: 57.33% C, 3.78% H; found: 57.10% C, 3.90% H. IR spectrum (cm^{-1}): 2 215 (CN), 1 660 (C=O), 1 610 (C=N). 1H NMR: 9.1 s, 1 H (NH); 8.4 s, 1 H (H-3); 7.2 m, 5 H (phenyl); 2.3 s, 3 H (CH₃).

3-[(3-Methyl-5-oxo-1*H*-4,5-dihydro)-4-pyrazolylazo]-1*H*-pyrazole-4-carbonitrile *V*

It was prepared following the above procedure from diazotized *I* (0.01 mol), 3-methyl-5-pyrazolone (0.01 mol) and pyridine (50 ml). The product *V* was crystallized from ethanol (yield 72%), m.p. 260°C. For $C_8H_7N_7O$ (213.2) calculated: 45.06% C, 3.31% H; found: 45.24% C, 3.4% H. IR spectrum (cm^{-1}): 2 215 (CN), 1 660 (C=O), 1 610 (C=N).

3-[(3-Amino-1-phenyl-5-oxo-4,5-dihydro)-4-pyrazolylazo]-
-1*H*-pyrazole-4-carbonitrile *VI*

It was prepared following the above procedure from diazotized *I* (0.01 mol), 1-phenyl-3-amino-5-pyrazolone (0.01 mol) and pyridine (50 ml). The product *VI* crystallized from methanol (yield 85%), m.p. 255°C. For $C_{13}H_{10}N_8O$ (294.3) calculated: 53.05% C, 3.42% H; found: 53.10% C, 3.27% H. IR spectrum (cm^{-1}): 3 450—3 350 (NH₂), 2 220 (CN), 1 680 (C=O).

3-[(5-Chloro-1-phenyl-3-methyl)-4-pyrazolylazo]-1*H*-pyrazole-4-carbonitrile *VIII*

A mixture of *IV* (2.93 g, 0.01 mol), PCl_5 (1.5 g) and $POCl_3$ (8 ml) was heated on water bath for 10 h. The reaction mixture was poured into crushed ice (300 g), the solid product obtained was filtered off, washed several times with water, dried and crystallized from acetic acid to give *VIII* (yield 45%), not melting below 303°C. For $C_{14}H_{10}ClN_7$ (311.7) calculated: 53.93% C, 3.23% H; found: 54.00% C, 3.50% H. IR spectrum (cm^{-1}): 3 200 (CN), 1 605 (C=N).

Reaction of Diazotized *I* with Active Hydrogen Reagents

A solution of diazotized *I* was poured gradually onto a solution of the appropriate active hydrogen reagent (0.1 mol) in 200 ml ethanol containing 10 g sodium acetate, dissolved in 20 ml H₂O, with continual stirring. The reaction mixture was then stirred at room temperature for 2 h and the solid product so formed was refluxed in AcOH for 2 h, and allowed to cool. The solid obtained was crystallized from suitable solvent to give (*IX*—*XIII*) (cf. Table I).

1-Phenyl-3-methyldipyrazolo[5,1-*c* : 3',4'-*e*][1,2,4]-triazine-6-carbonitrile *VII*

A solution of *XI* (2.03 g, 0.01 mol) in acetic acid (25 ml) and hydrochloric acid (6.3 ml) was refluxed with phenylhydrazine for 20 h. After cooling the reaction mixture was poured into cold water, the oily residue was crystallized from acetic acid to give *VII* (yield 43%), not melting below 300°C. For $C_{14}H_9N_7$ (275.3) calculated: 61.08% C, 3.29% H; found: 61.30% C, 3.40% H. IR spectrum (cm^{-1}): 2 215 (CN), 1 615 (C=N). 1H NMR: 8.1 s, 1 H (H-2); 7.0—7.5 m, 5 H (Ph); 2.1 s, 3 H (CH₃).

TABLE I
Properties and spectral data for compounds IX — XIII

Com- pound	Y	Z	Reaction time, h	Yield %	M.p. °C	IR spectrum cm ⁻¹	¹ H NMR spectrum	Formula (M.w.)	Calculated/Found	
									% C	% H
IX	NH ₂	CN	3	60	>300 ^a	3 250, 2 200— 2 185, 1 630	8·8 s, 1 H (H-2), 3·8 br, 2 H (NH ₂)	C ₇ H ₃ N ₇ (185·2)	45·40 45·41	1·63 1·62
X	OH	CN	3	63	265 ^b	3 300, 2 200— 2 190, 1 700, 1 610		C ₇ H ₂ N ₆ O (186·1)	45·16 45·30	1·08 2·00
XI	OH	COCH ₃	4	70	240 ^b	3 400 br, 2 205, 1 700, 1 610	8·5 s, 1 H (H-2), 2·3 s, 1 H (H-b), 2·2 s, 3 H (CH ₃)	C ₈ H ₅ N ₅ O ₂ (203·2)	47·29 47·50	2·48 2·60
XII	CH ₃	CN	4	65	>300 ^a	2 200, 1670		C ₉ H ₇ N ₅ O (201·2)	53·72 53·90	3·50 3·82
XIII	Ph	CN	3	50	260 ^a	2 220—2 180, 1 620		C ₁₃ H ₆ N ₆ (246·2)	63·41 63·50	2·45 2·70

Crystallized from: ^a ethanol, ^b acetic acid.

1-(2-Cyanoethyl)-5-hydroxypyrazole-4-carbonitrile *XIV*

A solution of diazoized *I* was poured gradually onto a solution of acrylonitrile (0.01 mol) in ethanol (30 ml) containing few drops of triethylamine. The reaction mixture was stirred at room temperature for 3 h and the solid product so formed was crystallized from dioxan to give *XIV* (yield 35%), m.p. 210°C. For $C_7H_6N_4O$ (162.1) calculated: 51.85% C, 3.73% H; found: 51.70% C, 3.90% H. IR spectrum (cm^{-1}): 3 250 br (OH), 2 250–2 220 ($2 \times$ CN).

REFERENCES

1. Archer S., Yarinsky A.: *Prog. Drug. Res.* 16, 11 (1972).
2. Jaffe J. J., Meymarian E., Doremus H. M.: *Nature (London)* 230, 408 (1971).