SYNTHESIS OF 8,11-DIHYDRO-10-METHYL-8,11-DIPHENYLPYRAZOLO-[4′,3′ : 5,6]PYRANO[3,2-*e*][1,2,4]-TRIAZOLO[1,5-*c*]-PYRIMIDINE AND SOME DERIVATIVES

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We have found that *III* can be synthesized by reaction of *II* with hydrazine hydrate[1,2]. In continuation of this work and to our efforts to build unknown polynuclear heterocyclic compounds we attempted some reaction of *III* in order to get some novel heterocyclic derivatives. The reaction of *III* with different reagents is shown in Schemes 1, 2 and 3, as for the characterization of the heterocyclic compounds, see Table I.

EXPERIMENTAL

All melting point are uncorrected. IR spectra were recorded in KBr on a Perkin–Elmer 599 B spectrometer. ^{1}H NMR spectra were measured with a Varian XL-100 spectrometer. The mass spectra were obtained using an AEF MS-9 mass spectrometer operating at 70 eV. 6-Amino-5--cyano-3-methyl-1,4-diphenyl-1*H*,4*H*-pyrano[2,3-*c*]pyrazole (*I*) was prepared according to refs[3,4].

Ethyl N-(5-Cyano-1,4-dihydro-3-methyl-1,4-diphenylpyrano[2,3-*c*]-pyrazol-6-yl)methanimidate (*II*) (ref.[5])

A mixture of *I* (5 mmol), an equimolar amount of triethyl orthoformate and acetic anhydride (16 ml) was refluxed for 5 h. The solvent was removed under reduced pressure, the resulting solid product was crystallized from benzene/petroleum ether (1 : 1) as colourless needles. For $C_{23}H_{10}N_4O_2$ (384·4) calculated: 71·86% C, 5·2% H, 14·6% N; found: 71·50% C, 5·2% H, 14·8% N.

1,4-Dihydro-5-imino-3-methyl-1,4-diphenylpyrazolo[4′,3′ : 5,6]pyrano-[2,3-*d*]pyrimidin-6(5*H*)-amine (*III*) (ref.[5])

To a solution of *II* (3 mmol) in 20 ml of benzene, hydrazine hydrate (5 ml in 10 ml H_2O) was added and the reaction mixture was stirred for 45 min, then allowed to stand overnight. The precipitate formed was filtered off, dried and crystallized from benzene as colourless flakes. For $C_{21}H_{18}N_6O$ (370·4) calculated: 22·68% N; found: 22·97% N.

TABLE I

Physico-chemical data of prepared compounds

Product	Yield %	M.p. °C	IR ν, cm^{-1}	UV[a] λ_{max}, nm (log ε)	^{1}H NMR[b]
II	96	128	2 240 (CN)	255 (4·3)	1·4 t, 3 H (CH_3); 1·9 s, 3 H (CH_3); 4·38 q, 2 H (CH_2); 4·75 s, 1 H (pyran H); 7·25—7·65 m, 10 H (arom. H); 8·2 s, 1 H (CHOEt).
III[c]	41	208—209	3 380, 3 340 (NH_2); 3 100 (NH)	246 (4·2) 214 (4·2)	2·0 s, 3 H (CH_3); 5·0 s, 1 H (pyran H); 5·45 s, 1 H (NH); 7·2—7·9 m, 10 H (arom. H); 8·2 s, 1 H (pyrimidine H)·
Va[d]	82	267—268		272 (4·0)	2·0 s, 3 H (CH_3); 5·65 s, 1 H (pyran H); 7·2—7·95 m, 10 H (arom. H); 8·3 s, 1 H (triazole H); 9·2 s, 1 H (pyrimidine H).
Vb	76	265—266		255 (4·3)	2·0 s, 3 H (CH_3); 2·5 s, 3 H (CH_3); 5·55 s, 1 H (pyran H); 7·1—7·85 m, 10 H (arom. H); 8·9 s, 1 H (pyrimidine H).
VII[e]	98	262	1 735 (COO)	260 (4·5) 220 (4·4)	1·4 t, 3 H (CH_3); 2·0 s, 3 H (CH_3); 4·4 q, 2 H ($CH\alpha$); 5·7 s, 1 H (pyran H); 7·1—7·8 m, 10 H (arom. H); 9·1 s, 1 H (pyrimidine H).
VIII	34	173—175	1 715 (COO)		
IX	54	173—175	3 260 (NH)	270 (3·9) 238 (4·1) 214 (4·2)	2·0 s, 3 H (CH_3); 5·54 s, 1 H (pyran H); 6·6 s, 1 H (NH); 7·25—7·75 m, 10 H (arom. H); 8·7 s, 1 H (pyrimidine H).
X	72	336—338	3 260 (NH); 1 670 (amidic CO)	250 (3·5)	1·95 s, 3 H (CH_3); 5·5 s, 1 H (pyran H); 7·2—7·8 m, 15 H (arom. H).
XI	68	232—235	3 260 (NH)	326 (3·5) 264 (4·4)	

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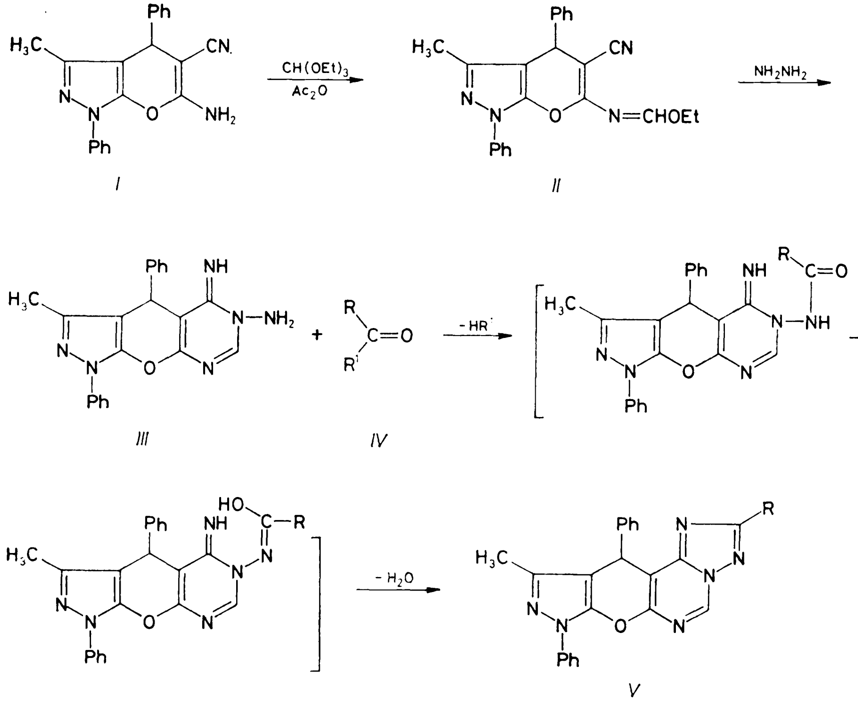
[a] Solvents: DMF for *Va*, *Vb*; MeOH for *II*, *III*, *VII*, *IX*, *X*, *XI*. [b] Solvents: $CDCl_3$ for *II*, *III*, *Va*, *Vb*, *VII*; CD_3SOCD_3 for *IX*, *X*. [c] M^+ 370; [d] M^+ 380; [e] M^+ 452.

8,11-Dihydro-10-methyl-8,11-diphenylpyrazolo[4',3' : 5,6]pyrano-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (*Va*)

Compound *III* (1 mmol) was refluxed in excess of formic acid (*IVa*) or ethyl formate (*IVb*) (10 ml) or with an equimolar amount of ethyl formate/DMF (6 ml) for 10 h, or with an equimolar amount of triethyl orthoformate in DMF (4 ml) for 30 min. After cooling the precipitate formed was collected and crystallized from benzene. For $C_{22}H_{16}N_6O$ (380·4) calculated: 69·46% C, 4·24% H, 21·32% N; found: 69·54% C, 4·48% H, 21·26% N.



In formula *IV*: *a*, R = H ; R' = OH *b*, R = H ; R' = OC_2H_5 *c*, R = CH_3 ; R' = OH

In formula *V* : *a*, R = H *b*, R = CH_3

SCHEME 1

8,11-Dihydro-2,10-dimethyl-8,11-diphenylpyrazolo[4',3' : 5,6]pyrano-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin (*Vb*)

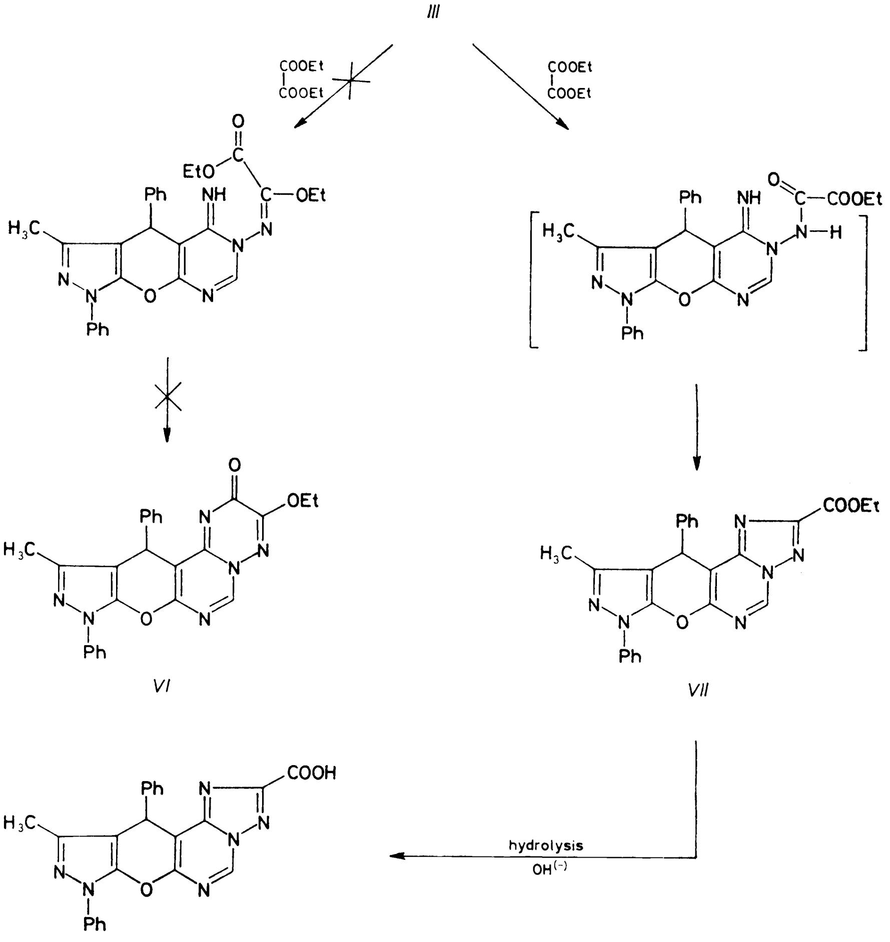
A mixture of *III* (1 mmol) and excess of glacial acetic acid (*IVc*) (10 ml) was refluxed for 10 h. After cooling and dilution with water, the solid product was separated. It was collected, dried and crystallized from benzene. For $C_{23}H_{18}N_6O$ (394·4) calculated: 70·05% C, 5·11% H; found: 69·16% C, 5·29% H.

Ethyl-8,11-dihydro-10-methyl-8,11-diphenylpyrazolo-[4',3' : 5,6]-pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-carboxylate (*VII*)

A mixture of *III* (1 mmol) and diethyl oxalate (1 mmol) in absolute ethanol (100 ml) was refluxed for 5 h. The precipitate formed after cooling was collected and crystallized from ethanol. For $C_{25}H_{20}N_6O_3$ (452·5) calculated: 66·36% C, 4·46% H, 18·57% N; found: 65·7% C, 4·28% H, 18·71% N.

Ethyl-8,11-dihydro-10-methyl-8,11-diphenylpyrazolo[4',3' : 5,6]pyrano-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-carboxylic acid (*VIII*)

The ester *VII* (1 mmol) was refluxed with 20 ml of 2M-NaOH for 5 h. The mixture was cooled,



SCHEME 2

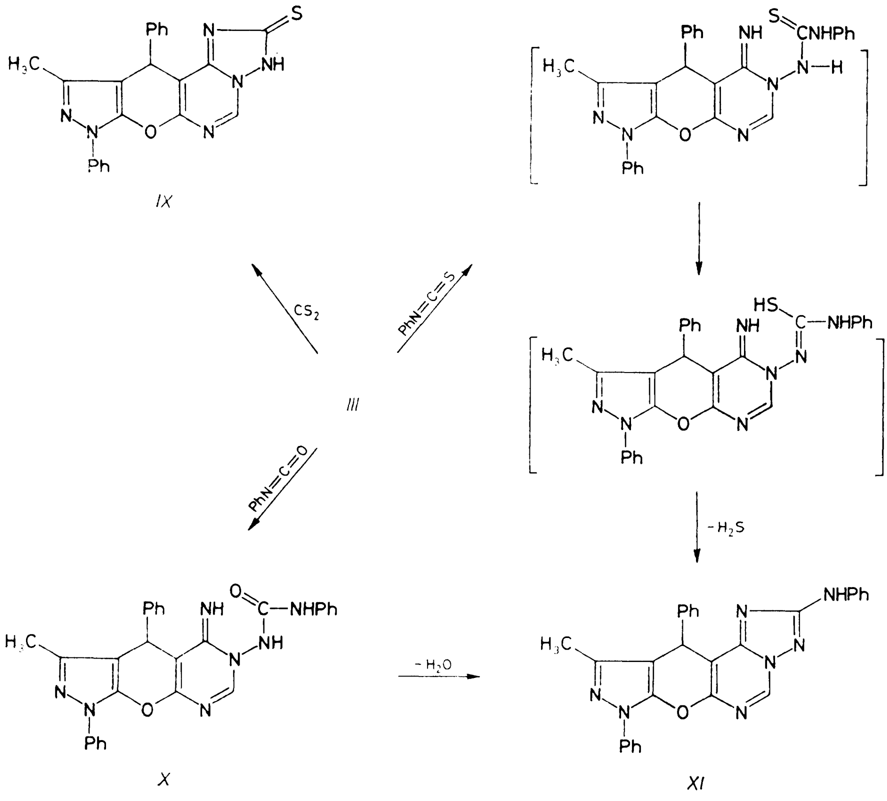
neutralized with diluted HCl, filtered and crystallized from benzene. For $C_{23}H_{16}N_6O_3$ (324·5) calculated: 64·1% C, 3·8% H, 19·8% N; found: 64·82% C, 4·21% H, 19·75% N.

8,11-Dihydro-10-methyl-8,11-diphenylpyrazolo[4′,3′ : 5,6]pyrano-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2(3*H*)-thione (*IX*)

To a solution of *III* (1 mmol) in 100 ml absolute ethanol excess of carbon disulphide (5 ml) was added. The reaction mixture was heated on a water bath for 4 h. The precipitate formed after cooling was collected and crystallized from benzene/ethanol mixture (4 : 1). For $C_{22}H_{15}N_6OS$ (411·5) calculated: 7·79% S; found: 7·28% S.

1,4-Dihydro-5-imino-3-methyl-1,4-diphenylpyrazolo[4′,3′ : 5,6]pyrano-[2,3-*d*]pyrimidine-6(5*H*)-phenyl urea (*X*)

Phenyl isocyanate (1 mmol) was added to a solution of *III* (1 mmol) in 100 ml ethanol. The reaction mixture was refluxed for 12 h. After cooling the precipitate formed was collected and crystallized from benzene. For $C_{28}H_{23}N_7O_2$ (489·5) calculated: 20·03% N; found: 20·28% N.



Scheme 3

8,11-Dihydro-10-methyl-N-8,11-triphenylpyrazolo[4',3' : 5,6]pyrano-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-amine (*XI*)

A mixture of *III* (1 mmol) and phenyl isothiocyanate (1 mmol) in ethanol (100 ml) was refluxed for 20 h. The product precipitated after cooling was collected and crystallized from ethanol. For $C_{28}H_{21}N_7O$ (471·5) calculated: 71·32% C, 4·49% H; found: 71·91% C, 4·48% H.

Preparation of *XI* from *X*

About 3 ml of concentrated hydrochloric acid was added to a solution of *X* (1 mmol) in 100 ml of ethanol, the mixture was refluxed for 5 h. After cooling and dilution with water a solid product separated. It was collected and crystallized from benzene, yield 32%, m.p. 230—235°C, m.m.p. with authentic sample 230—232°C. IR spectrum (cm^{-1}): 3 260 (NH). For $C_{28}H_{21}N_7O$ (471·5) calculated: 71·32% C, 4·49% H; found: 71·55% C, 4·28% H.

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