REACTIONS OF 4-AROYL-3-CHLORO-6-PHENYLPYRIDAZINES WITH SOME NUCLEOPHILIC REAGENTS, SYNTHESIS OF SOME FUSED PYRIDAZINE DERIVATIVES

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As a part of our programme directed towards the synthesis of some fused pyridazine derivatives[1], we reported recently[2] a novel method for the synthesis of some 4-aroyl-6-phenylpyridazin-3(2*H*)-ones and 4-aroyl-3-chloro-6-phenylpyridazines as readily available starting materials for this purpose. In the present investigation the reaction of 4-aroyl-3-chloro-6-phenylpyridazines (*Ia – Ic*) with some nucleophiles is studied.

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses were carried out at the microanalytical unit, Cairo University. IR spectra (in KBr) were recorded on a Pye–Unicam SP 1200 spectrophotometer.

Reaction of *Ia – Ic* with Hydrazine Hydrate in Ethanol

A solution of 4-aroyl-3-chloro-6-phenylpyridazines *Ia – Ic* (0.5 g) in ethanol (20 ml) was treated with hydrazine hydrate (0.5 ml) and the reaction mixture was heated under reflux for 4 h. The solid formed after cooling was filtered off and crystallized from a suitable solvent to give the pyrazolinopyridazine derivatives *IIa – IIc*, as pale brown crystals (Table I).

Reaction of 4-Benzoyl-3-chloro-6-phenylpyridazine (*Ia*) with Hydrazine Hydrate in the Absence of Solvent

A mixture of *Ia* (0.5 g) and hydrazine hydrate (0.5 ml) was heated on a sand-bath at 140 °C for 1 h. The reaction mixture was boiled with water for 15 min and cooled. The solid formed was filtered off and crystallized from methanol to give the pyrazolinopyridazine derivative *IIa*. The product showed no depression when admixed with the corresponding product obtained in the previous experiment.

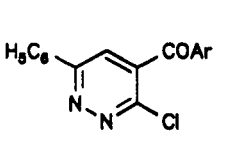
Reaction of 4-Benzoyl-6-phenylpyridazin-3(2*H*)-one Hydrazone (*III*) with Phosphorus Oxychloride

A mixture of the hydrazone *III* (1 g) and phosphorus oxychloride (5 ml) was heated on boiling water-bath for 1 h. The reaction mixture was treated with crushed ice (50 g) and made just alkaline by the addition of aqueous sodium hydroxide solution (10%). The resulting solid was filtered off and crystallized from

methanol to give *IIa*. It showed no depression when admixed with the product formed by the action of hydrazine hydrate on *Ia*.

Action of Hydroxylamine Hydrochloride on *Ia* and *Ib*

Hydroxylamine hydrochloride (0.12 g) dissolved in the least amount of water was added to a solution of 4-aroyl-3-chloro-6-phenylpyridazines *Ia*, *Ib* in pyridine (10 ml). The reaction mixture was heated under reflux for 7 h, cooled and poured over a mixture of water (50 ml) and concentrated hydrochloric acid (10 ml). The solid formed was filtered off and crystallized from a suitable solvent to give the isoxazolopyridazine derivatives *IVa*, *IVb* as colourless crystals (Table I).



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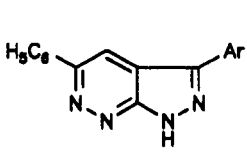

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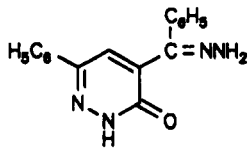

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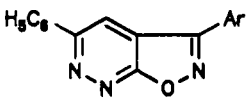

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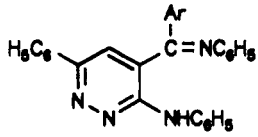

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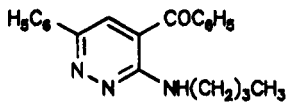

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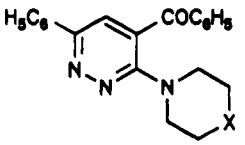

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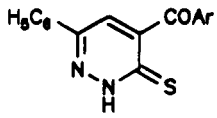
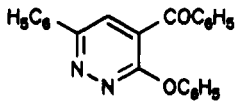


VIII



IX

In formulae *I*, *II*, *IV*, *V*, *VIII* : *a*, Ar = C_6H_5
b, Ar = *p*-$CH_3OC_6H_4$
c, Ar = *p*-ClC_6H_4

In formulae *VII* : *a*, X = CH_2
b, X = O

TABLE I
Analytical data of newly synthesized compounds

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated / Found					IR, cm^{-1}
			% C	% H	% Cl	% N	% S	
IIa	225 – 226[a] 52	$C_{17}H_{12}N_4$ (272.3)	75.00 74.80	4.41 4.50		20.58 20.30		3 000 – 3 260 (NH)
IIb	230 – 232[b] 55	$C_{18}H_{14}N_4O$ (302.3)	71.52 71.70	4.63 4.80		18.54 18.30		3 000 – 3 260 (NH)
IIc	269 – 270[c] 58	$C_{17}H_{11}ClN_4$ (306.8)	66.55 66.70	3.58 3.90	11.58 11.60	18.27 17.80		3 000 – 3 260 (NH)
IVa	129 – 130[b] 62	$C_{17}H_{11}N_3O$ (273.3)	74.72 75.00	4.02 4.20		15.38 15.50		
IVb	154 – 155[d] 67	$C_{18}H_{13}N_3O_2$ (303.3)	71.28 70.80	4.29 4.70		13.86 14.00		
Va	200 –202[e] 60	$C_{29}H_{22}N_4$ (426.5)	81.69 82.40	5.16 4.70				3 400 (NH)
Vb	218 – 220[e] 62	$C_{30}H_{24}N_4O$ (456.5)	78.94 79.10	5.26 4.80		12.88 12.10		3 400 (NH)
VI	152 – 153[b] 61	$C_{21}H_{21}N_3O$ (331.4)	76.13 76.50	6.34 6.50		12.68 12.50		3 360 (NH); 1 625 (CO)
VIIa	103 – 105[f] 64	$C_{22}H_{21}N_3O$ (343.4)	76.96 77.00	6.12 5.80		12.24 12.60		1 650 (CO)
VIIb	122 – 124[d] 60	$C_{21}H_{19}N_3O_2$ (345.4)	73.04 73.30	5.50 5.80		12.17 12.50		1 660 (CO)
VIIIa	248 – 250[c] 61	$C_{17}H_{12}N_2OS$ (292.4)	69.86 70.00	4.10 4.50		9.58 10.00	10.95 11.00	3 020 – 2 820 (NH–CS); 1 130 (C=S); 1 655 (CO)
VIIIc	257 – 258[g] 67	$C_{17}H_{11}ClN_2OS$ (326.8)	62.48 62.30	3.36 3.70	9.80 9.40	8.57 8.30	10.87 11.00	3 030 – 2 820 (NH–CS); 1 135 (C=S); 1 660 (CO)
IX	115 – 117[d] 65	$C_{23}H_{16}N_2O_2$ (352.4)	78.40 78.10	4.54 4.80		7.95 8.00		1 660 (CO)

Crystallized from: [a] methanol; [b] ethanol; [c] benzene–ethanol mixture; [d] benzene–light petroleum; [e] methanol–benzene mixture; [f] light petroleum; [g] butanol.

Reaction of Aniline with 4-Aroyl-3-chloro-6-phenylpyridazines *Ia*, *Ib*

A mixture of *Ia* or *Ib* (0.01 mol) and aniline (0.02 mol) was heated on a sand-bath at 140 °C for 1 h. The resulting melt was boiled with water for 10 min, cooled and the solid formed was filtered off and crystallized from methanol–benzene mixture to give the Schiff bases *Va* and *Vb*, respectively (Table I).

Reaction of 4-Benzoyl-3-chloro-6-phenylpyridazine (*Ia*) with Butylamine or Secondary Amines

To a solution of *Ia* (0.01 mol) in ethanol (20 ml), butylamine, piperidine or morpholine (0.01 mol), respectively, was added and the reaction mixture was heated under reflux for 7 h. The solid formed after cooling was filtered off and crystallized from ethanol to give *VI*, *VIIa* or *VIIb*, respectively, as yellow crystals (Table I).

Reaction of *Ia*, *Ic* with Thiourea

Thiourea (0.5 g) dissolved in the least amount of water was added to a solution of 4-aroyl-3-chloro-6-phenylpyridazines *Ia*, *Ic* (1 g) in ethanol (20 ml). The reaction mixture was heated under reflux for 10 h, and left to cool. The yellow solids obtained were filtered off and crystallized from a suitable solvent to give *VIIIa* or *VIIIc*, respectively, as yellow crystals (Table I).

Reaction of *Ia* with Phenol

A mixture of *Ia* (0.01 mol), anhydrous sodium carbonate (0.5 g) and phenol (0.01 mol) was heated on a sand-bath at 140 °C for 1 h, cooled and then treated with water. The solid obtained was filtered off and crystallized from benzene–light petroleum mixture to give the ether *IX*, as colourless crystals (Table I).

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2. Ismail M. F., Sayed F. S., Emara S. A., Shindy A. A.: Z. Naturforsch., B *46*, 1720 (1991).