

Some Reactions with 3-Chloro-4-cyano-5,6-diphenyl Pyridazinone

S. A. SAID, M. M. HAMAD and A. M. EL-GENDY*

*Chemistry Department
Faculty of Science, Zagazig University
Zagazig, Egypt*

Treatment of 4-cyano-5,6-diphenyl 2(1H) pyridazinone with $\text{POCl}_3/\text{PCl}_5$ mixture gave 3-chloro-4-cyano-5,6-diphenyl pyridazine (I). The reactions of compound (I) with primary amines, hydrazine hydrate, 2-cyano-ethanoic acid hydrazide, thiourea, sodium methoxide, sodium azide, sodamide and/or active methylene compounds have been studied. Also the reactions of 3-amino-4,5-diphenyl-1H pyrazolo (3,4-c) pyridazine (III) with picric or salicylic acids, aromatic aldehydes, α -dicarbonyl compounds and/or 3-nitrophthalic anhydride have been investigated.

INTRODUCTION

In the present study 4-cyano-5,6-diphenyl 2(1H)-pyridazinone¹ reacted with $\text{POCl}_3/\text{PCl}_5$ mixture giving 3-chloro-4-cyano-5,6-diphenyl pyridazine²(I).

The well known reactivity of 3-halo substituents in the pyridazine nucleus prompted a study of the replacement of the chlorine atom with different types of nucleophiles. Thus, treatment of (I) with primary amines such as p-toluidine and/or benzylamine in boiling butanol gave 3-(p-tolylamino or benzylamino)-4-cyano-5,6-diphenyl pyridazine (IIa and b) respectively. The structure of (II) was confirmed by: (i) correct analytical data, (ii) IR spectra of compounds (IIa and b) showed absorption bands in the region (2220–2225 cm^{-1}) due to $\nu\text{C}\equiv\text{N}$, in the region (3340–3350 cm^{-1}) due to νNH and at 1610 cm^{-1} due to $\nu\text{C}=\text{N}$.

RESULTS AND DISCUSSION

As a part of our study on the reactivity of the chloro compound (I) towards different nucleophilic reagents, we found that fusion of compound (I) with hydrazine hydrate resulted in the formation of 3-amino-4,5-diphenyl-1H pyrazolo (3,4-c) pyridazine³(III).

The assigned structure for (III) was supported by its IR spectrum which revealed absorptions at 1600 cm^{-1} due to $\nu\text{C}=\text{N}$ and at 3350 cm^{-1} due to νNH . Reaction of compound (I) with 2-cyanoethanoic acid hydrazide in boiling butanol gave N-(4-cyano-5,6-diphenyl-3-pyridazinyl)- α -cyano ethanoic acid hydrazide (IV).

The structure of (IV) was established by IR spectrum which showed bands at 2210, 3250, 1650, cm^{-1} due to $\nu\text{C}\equiv\text{N}$, νNH and $\nu\text{C}=\text{O}$ respectively.

*Present address: Chemistry Department, Centre of Science and Mathematics, P.O. Box 1070, Taif, Saudi Arabia.

However, when (I) was submitted to the reaction with thiourea in boiling ethanol gave 3-mercapto derivative (V). The structure of (V) was confirmed by IR spectrum which exhibited absorptions characteristic of νSH , $\nu\text{C}\equiv\text{N}$ at 2550 and 2220 cm^{-1} respectively.

The reaction of compound (I) with sodium methoxide in methanol gave the corresponding 3-methoxy derivative (VI). The structure of (VI) was confirmed by IR spectrum which showed bands due to $\nu\text{C}\equiv\text{N}$, $\nu\text{C}=\text{N}$ and $\nu\text{C}-\text{O}-\text{C}$ (ether) at 2220, 1610 and 1050 cm^{-1} respectively.

On the other hand, when compound (I) was refluxed with sodium azide in dimethylformamide, 4-cyano-5,6-diphenyl tetrazolo (4,5-b) pyridazine (VII) was obtained. Compound (VII), like similar heterocyclic azides may exist as a true azide (VII) or as tetrazolopyrazole (VII).

The structure of (VII) was supported by IR spectrum which exhibited the absence of azide absorption band at 2160 cm^{-1} , but absorption bands at 1550 and 1660 cm^{-1} due to $\nu\text{N}=\text{N}$ are present. This favours the proposed structure (VII) for the tetrazolopyrazole derivative.

However, 3-amino-4-cyano-5,6-diphenyl pyridazine⁴(VIII) was easily obtained in a good yield when (I) was reacted with sodamide in boiling ethanol. Its IR spectrum showed $\nu\text{C}\equiv\text{N}$, νNH and $\nu\text{C}=\text{N}$ at 2225, 3380 and 1610 cm^{-1} respectively.

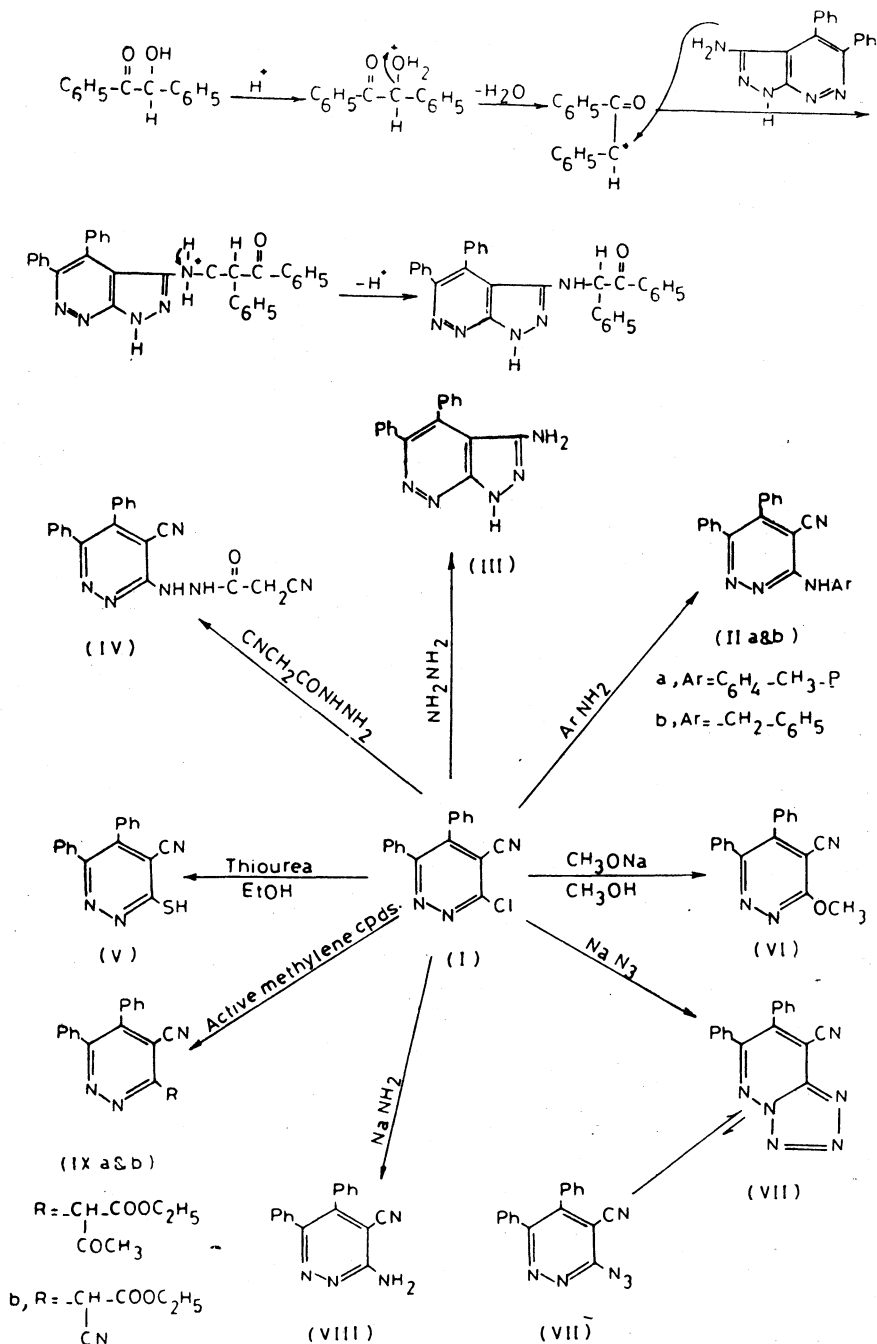
It has been found that⁵ compound (I) reacts with active methylene compounds such as ethylacetoacetate or ethylcyanoacetate in the presence of sodamide as a catalyst and dimethylformamide to give the corresponding 3-ethyl-(α -acetyl or α -cyano)-acetate-4-cyano-5,6-diphenyl pyridazine (IXa and b).

The structure of (IXa and b) was confirmed by IR spectra which revealed absorptions characteristic of $\nu\text{C}=\text{O}$ (ketone), $\nu\text{C}=\text{O}$ (ester) and $\nu\text{C}\equiv\text{N}$ at 1680, 1740 and 2220 cm^{-1} respectively for (IXa), $\nu\text{C}=\text{O}$ (ester) and $\nu\text{C}\equiv\text{N}$ at 1735 and 2225 cm^{-1} respectively for (IXb).

As a point of interest, in this investigation the reaction of compound (III) with picric acid in boiling acetone or with salicylic acid in acetic acid gave the corresponding pyrazole picrate derivative (X) and pyrazolo salicylate derivative (XI) respectively.

The structures of compounds (X) and (XI) were supported by IR spectra which showed absorption bands at 1530, 1320 cm^{-1} due to νNO_2 and at 1610 cm^{-1} due to $\nu\text{C}=\text{N}$ for (X) and at 1620 cm^{-1} due to $\nu\text{C}=\text{N}$, at 1710 cm^{-1} due to $\nu\text{C}=\text{O}$ and at 3220 cm^{-1} due to νOH for (XI).

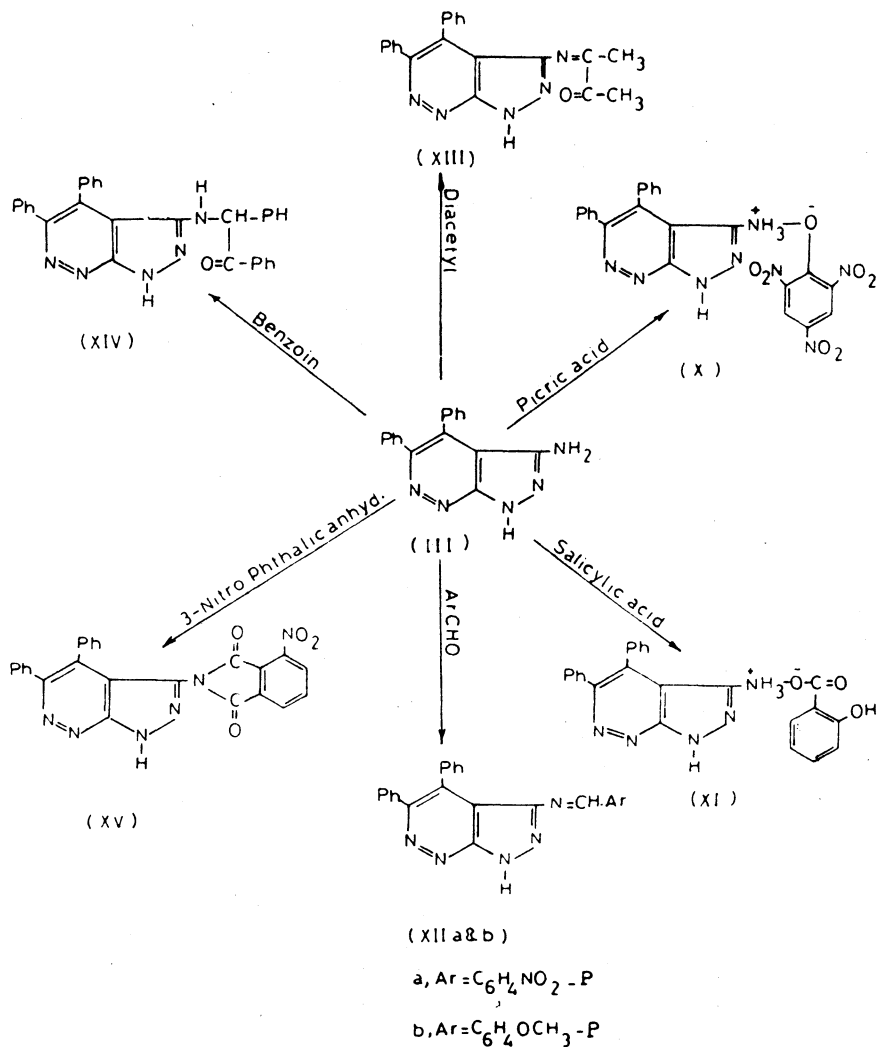
The amino group at position 3 in the pyrazole ring of (III) exhibits the normal characteristic of this group. Thus, compound (III) condensed with aromatic aldehydes such as p-nitrobenzaldehyde or p-methoxybenzaldehyde giving the corresponding 3-(p-nitrobenzylidene amino or p-methoxybenzylidene amino)-4,5-diphenyl-1H pyrazolo (3,4-c)pyridazine (XIIa and b) respectively. The IR spectrum of (XIIa) showed $\nu\text{C}=\text{N}$ at



Scheme-1. Reactions of Compounds (I)

1600 cm^{-1} and νNO_2 at 1330 and 1510 cm^{-1} , which support the structure.

Also, it has been found that³ compound (III) condenses with diacetyl or benzoin to give the inil derivative (XIII) and 3-(α -benzylamino)-4,5-diphenyl-1H pyrazolo (3,4-c) pyridazine (XIV) respectively.



Scheme-2. Reactions of Compound (III)

The structure of compounds (XIII) and (XIV) was confirmed by IR spectra which exhibited absorption bands at 1680 and 1600 due to $\nu\text{C} = \text{O}$ and $\nu\text{C} = \text{N}$ respectively for (XIII) and at 1690, 1600 and 3200 cm^{-1} due to $\nu\text{C} = \text{O}$, $\nu\text{C} = \text{N}$ and νNH respectively for (XIV). It is believed that the formation of (XIV) proceed according to Scheme 1.

Ultimately, we found that compound (III) reacts with 3-nitrophthalic anhydride to give 3-(3-nitrophthalimido)-4,5-diphenyl 1H pyrazolo (3,4-c) pyridazine (XV). The IR spectrum of (XV) revealed absorption bands at 1790, 1730 cm^{-1} due to $\nu\text{C} = \text{O}$ (anhydride), at 1530, 1350 cm^{-1} due to νNO_2 and at 1600 cm^{-1} due to $\nu\text{C} = \text{N}$.

EXPERIMENTAL

All melting points reported are uncorrected. Infrared spectra (KBr) were recorded on a Pye-Unicam spectrophotometer (in cm^{-1}).

Action of $\text{POCl}_3/\text{PCl}_5$ on 4-cyano-5,6-diphenyl 2(1H) pyridazinone: formation of (I)

A suspension of 4-cyano-5,6-diphenyl 2(1H) pyridazinone (0.01 mole), POCl_3 (0.05 mole) and PCl_5 (0.05 mole) were heated on a waterbath for 2 hrs., poured slowly onto crushed ice. The resultant solid filtered off and crystallized from a proper solvent to give (I) (cf. Table 1).

Action of amines on (I): formation of (IIa and b)

A solution of (I) (0.01) mole and an amine (0.01 mole) in butanol (10 ml) was refluxed for 6 hrs. and cooled to give (II) which was crystallized from a suitable solvent (cf. Table 1).

Reaction of (I) with hydrazine: formation of (III)

A mixture of (II) (1 g) and hydrazine hydrate (5 ml) was fused for 1 hr. The solid obtained was treated with ethanol and recrystallized from ethanol to give (III) (cf. Table 1).

Action of 2-cyano ethanoic acid hydrazide on (I): formation of (IV)

A solution of (I) (0.01 mole) and 2-cyano ethanoic acid hydrazide (0.01 mole) in butanol (5 ml) was refluxed for 3 hrs. and cooled to give (IV) which was crystallized from a suitable solvent (cf. Table 1).

Action of thiourea on (I): formation of (V)

A solution of (I) (0.1 mole) in ethanol (20 ml) and thiourea (0.01 mole) was boiled under reflux for 2 hrs. and cooled to give (V) which was crystallized from a proper solvent (cf. Table 1).

Action of $\text{CH}_3\text{ONa}/\text{CH}_3\text{OH}$ on (I): formation of (VI)

A solution of (I) (0.01 mole) in CH_3OH (20 ml) and a CH_3ONa (0.01 mole) was refluxed for 3 hrs., the reaction mixture poured in water (100 ml) and the solid obtained was crystallized from a suitable solvent to give (VI) (cf. Table 1).

Action of sodium azide on (I): formation of (VII)

A mixture of (I) (0.01 mole) and sodium azide (0.05 mole) in acetic acid (50 ml) was refluxed for 5 hrs. The product obtained after concentration was crystallized from a proper solvent to give (VII) (cf. Table 1).

Reaction of (I) with sodamide: formation of (VIII)

A solution of (I) (0.01 mole) in ethanol (20 ml) and sodamide (0.01 mole) was boiled under reflux for 2 hrs. and cooled to give (VIII) which was crystallized from a suitable solvent (cf. Table 1).

Reaction of (I) with active methylene compounds: formation of (IXa and b)

To a solution of (I) (0.01 mole) in DMF (20 ml), ethyl acetoacetate or ethyl cyanoacetate (0.01 mole) and sodamide (0.04 mole) were added. The mixture was refluxed for 2 hrs., poured in H₂O (100 ml) and the solution was acidified with dilute hydrochloric acid. The solid obtained was crystallized from a proper solvent to give (IXa and b) (cf. Table 1).

Action of picric acid on (III): formation of (X)

A solution of (III) (0.01 mole) in acetone was treated by a solution of picric acid (0.01 mole) in acetone, and the mixture was heated on a water bath for $\frac{1}{4}$ hr. The solid which separated was crystallized from acetone to give (X) as bright red crystals (cf. Table 1).

Reaction of (III) with salicylic acid: formation of (XI)

A mixture of (IV) (0.01 mole) and salicylic acid (0.01 mole) in acetic acid (20 ml) was refluxed for 3 hrs. The reaction mixture was diluted with water and the solid obtained was crystallized from dil. acetic acid to give (XI) (cf. Table 1).

Reaction of (III) with aromatic aldehydes: formation of (XIIa and b)

To a solution of (III) (0.01 mole) in ethanol (20 ml), p-nitrobenzaldehyde or anisaldehyde (0.01 mole) was added, and the reaction mixture was refluxed for $\frac{1}{4}$ hr. The solid obtained after cooling was crystallized from a proper solvent to give (XIIa and b) (cf. Table 1).

Action of diacetyl on (III): formation of inil drivative (XIII)

A mixture of (III) (0.01 mole) and diacetyl (0.01 mole) in ethanol (30 ml) was refluxed for 2 hrs. The solid separated was crystallized from ethanol to give (XII) (cf. Table 1).

Reaction of (III) with benzoin: formation of (XIV)

A mixture of (III) (0.01 mol) and benzoin (0.01 mole) in acetic acid (10 ml) was refluxed for 3 hrs. The solid obtained after cooling was crystallized from the proper solvent to give (XIV) (cf. Table 1).

TABLE I
PHYSICAL DATA OF VARIOUS COMPOUNDS PREPARED

Compound	M.pt. °C	Solvent for crystn* Yield (%)	Mol. formula (M. Wt.)	Analysis (%)		
				Calcd.	Found	
I	125	E 85	C ₁₇ H ₁₉ N ₃ Cl (291.7)	C	69.9	70.2
				H	3.45	3.7
IIa	210	M 60	C ₂₄ H ₁₈ N ₄ (362.4)	C	79.5	79.1
				H	5.0	5.1
IIb	215	Bu 65	C ₂₄ H ₁₈ N ₄ (362.4)	C	79.5	79.2
				H	5.0	4.9
III	220	E 50	C ₁₇ H ₁₃ N ₅ (287.3)	C	71.07	71.2
				H	4.56	4.5
				N	24.36	24.3
IV	175	Bu 70	C ₂₀ H ₁₄ N ₆ O (354.3)	C	67.8	68.0
				H	3.9	3.8
V	235	E 40	C ₁₇ H ₁₁ N ₃ S (289.3)	C	70.57	71.0
				H	3.8	4.0
VI	214	B 75	C ₁₈ H ₁₃ N ₃ O (287.3)	C	75.2	75.6
				H	4.5	4.2
VII	160	A 65	C ₁₇ H ₁₉ N ₆ (298.3)	C	68.45	68.1
				H	3.37	3.4
VIII	185	E 80	C ₁₇ H ₁₂ N ₄ (272.3)	C	74.98	74.8
				H	4.44	4.9
IXa	98	E 72	C ₂₃ H ₁₉ N ₃ O ₃ (385.4)	C	71.6	71.2
				H	4.96	5.1
IXb	135	M 70	C ₂₃ H ₁₆ N ₄ O ₂ (368.4)	C	71.72	71.5
				H	4.3	4.1
X	253	Ac 75	C ₂₃ H ₁₆ N ₃ O ₇ (516.4)	C	53.4	53.1
				H	3.12	3.5
XI	210	A 65	C ₂₄ H ₁₉ N ₃ O ₃ (425.5)	C	67.75	67.5
				H	4.5	4.2
XIIa	248	A 75	C ₂₄ H ₁₆ N ₆ O ₂ (420.4)	C	68.55	68.2
				H	3.8	4.0
XIIb	142	E 70	C ₂₅ H ₁₉ N ₃ O (405.4)	C	74.06	74.16
				H	4.72	5.0
XIII	160	Bu 65	C ₂₁ H ₁₇ N ₃ O (355.4)	C	70.9	70.2
				H	4.82	5.1
XIV	127	E 60	C ₃₁ H ₂₃ N ₃ O (481.6)	C	77.3	77.5
				H	4.81	4.5
XV	137	E 75	C ₂₅ H ₁₄ N ₆ O ₄ (462.4)	C	64.9	65.1
				H	3.05	3.2

*E = Ethanol; M = Methanol; Bu = Butanol; A = Acetic Acid; Ac = Acetone and B = Benzene.

Fusion of (III) with 3-nitrophthalic anhydride: formation of (XV)

To 2.8 g of (III) (0.01 mole), 3-nitrophthalic anhydride (0.01 mole) was added, and the mixture was fused in an oil bath for 2 hrs. The reaction mixture was treated with ethyl alcohol, and the solid obtained was crystallized from a proper solvent to give (XV) (cf. Table 1).

REFERENCES

1. Schmidt and Druey, *Helv. Chim. Acta*, **37**, 134 (1954).
2. M. A. El-Hashah, M. Y. El-Kady and M. M. Mohamed, *Indian J. Chem.*, **18B**, 136 (1979).
3. Neelima, Balkrishen Bhat and Amiya Prasad Bhaduri, *J. Heterocyclic Chem.*, **23**, 925 (1986).
4. Julian Pomorski, H. J. Den Hertog, *Rocz. Chem.*, **47**, 341 (1973), *Chem. Abstr.*, **79**, 66220 j (1973).
5. Edward W. Badger and Waite H. Moos, *J. Heterocyclic Chem.*, **23**, 1515 (1986).

[Received: 7 March 1988; Accepted: 1 June 1989].

AJC-60

**SYMPOSIUM
ON
PHOTOPHYSIOLOGY AND PHOTOMEDICINE
DELHI.**

February, 14-18, 1990.

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