Synthesis and Reactions of Some 4-(3-oxo-1,3-diaryl-propyl)-1-phenyl-3,5-pyrazolidinediones

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Summary: Pyrazolidinedione derivatives (II) are prepared through the hitherto unknown nucleophilic addition of 1-phenyl-3,5-pyrazolidinedione to chalcones (I). Reactions of II with phenylhydrazine, hydrazine hydrate, hydroxylamine hydrochloride and aromatic amines afford the corresponding phenylhydrazones, diazepene derivatives, oximes and arylidene derivatives. Behaviour of II towards polyphosphoric acid, Grignard reagents, phosphorus pentasulphide and acetylating agent has also been investigated.

Substituted pyrazolidinediones have received considerable attention in recent years and their application as dyes for plastics, paper and varnishes [1] have been reported. Pyrazolidinedione derivatives exhibiting analgesic [2] antipyretic [3], antirheumatic [4] and antiphlogistic [5] activities have also been reported. This prompted us to synthesize new pyrazolidinedione derivatives through the hitherto unknown nucleophilic addition of 1-phenyl-3,5-pyrazolidinedione to chalcones and study the behaviour of the adducts towards different reagents.

The syntheses of various compounds are outlined in Scheme 1. The reaction of benzal (Ia), 4'-methoxybenzal (Ib) and 4'-chlorobenzal (Ic)-acetophenone with 1-phenyl-3,5-pyrazolidinedione in presence of sodium ethoxide gave 4-(3-oxo-1,3-diaryl propyl)-1-phenyl-3,5-pyrazolidinediones (IIa-c). The structures of the adducts (IIa-c) were derived from their spectral data. Their IR showed two bands for pyrazolidinedione carbonyl groups and for ketonic groups at 1740 and 1680 cm^{-1} (broad) and a band for νNH at 3440-3430 cm^{-1}. The mass spectrum of IIa exhibited peaks at m/z 384 (3.3%), 264 (30.4%) 208 (72.8%); 176 (33.1%), 105 (66.8%), 77 (100%) and 51 (33.1%).

It was reported [6] that the heterocyclic ring in 1,2-diphenyl-3,5-pyrazolidinedione can be opened by the action of phenylhydrazine. In the present investigation, it was found that the reaction of IIa-c with phenylhydrazine in boiling ethanol afforded the corresponding phenylhydrazone derivatives (IIIa-c). No trace for the heterocyclic ring opening product was isolated. The structures of the products IIIa-c were rigidly confirmed on the basis of their IR spectra which showed νC=O (doublet) at 1740-1730 cm^{-1}, 1690-1680 cm^{-1}, νC=N at 1610-1600 cm^{-1} and NH 3460-3430 cm^{-1}. The mass spectrum of IIIa was characterised by the absence of the parent ion but showed the cations of benzal-acetophenone phenylhydrazone (m/z 298; 49.3%) and 1-phenyl-3,5-pyrazolidinedione (m/z 176; 23.6%).

On the other hand, condensation of IIa-c with hydrazine hydrate in boiling ethanol afforded the corresponding diazepine derivatives (IVa-c). The structures of IVa-c were estab-

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lished on the basis of their elemental analyses and their IR spectra which showed bands at 1675, 1670 cm^{-1}, 1645-1635 cm^{-1} and 3310-3300 cm^{-1} for νC=O, νC=N and νNH and the absence of the band at 1740 cm^{-1}.

Condensation of IIa and IIc with hydroxylamine hydrochloride gave the corresponding oximes Va and Vb. The infrared spectra showed νC=O (doublet) at 1735-1730, 1685 cm^{-1}, νC=N at 1600 cm^{-1} and νNH at 3260-3160 cm^{-1}.

As a point of interest, the adducts IIa and IIc were condensed with aromatic aldehydes, namely, p-chlorobenzaldehyde and anisaldehyde when the corresponding 4-(2-aroyl-3-aryl-1-phenyl-2-propenyl)-1-phenyl-3,5-pyrazolidinediones (VIa-c). The infrared spectra of VIa-c showed bands at 1740-1730 cm^{-1}, 1680-1675 cm^{-1} and 3480-3440 cm^{-1} for νC=O, νC=C and νNH.

Cyclisation of the adduct IIa with freshly prepared polyphosphoric acid furnished 1,4-dihydro-2,4,6-triphenyl-pyrano 2,3-c pyrazol-3(2H)-one (VII). The infrared spectrum of VII showed bands at 1670 cm^{-1}, 1640 cm^{-1} and 3320 cm^{-1} for νC=O, νC=C and νNH.

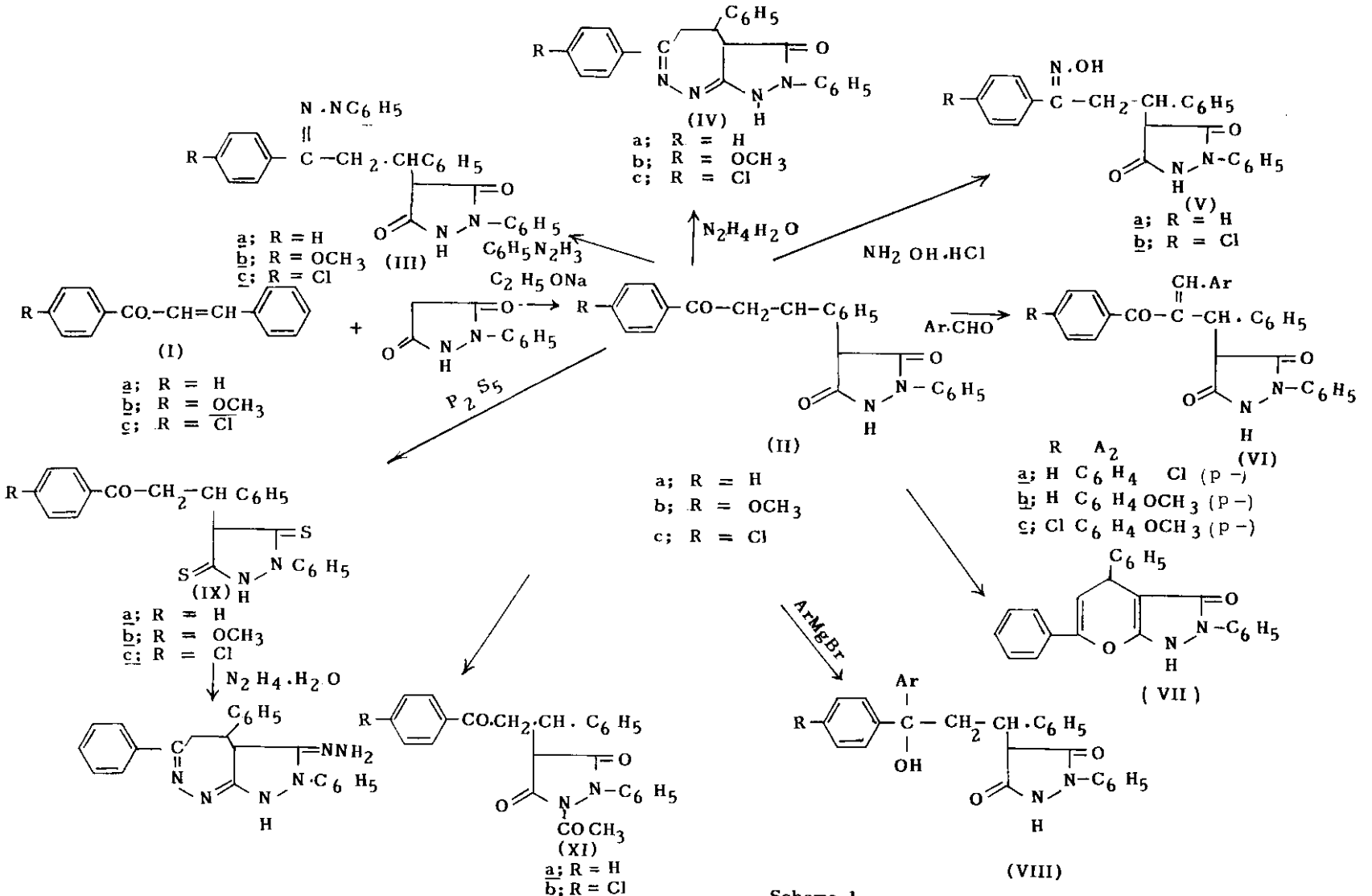
It was stated [7] previously that phenylmagnesium bromide adds to the exocyclic bond of 4-arylidene-1-phenyl-3,5-pyrazolidinedione. In the present investigation, it was found that when IIb and IIc were treated with phenylmagnesium bromide and/or with p-methoxyphenylmagnesium bromide, it resulted in the formation of VIIIa-c, respectively, whose structures were confirmed from its infrared doublet of νC=O of pyrazolidinedione at 1745-1740 cm^{-1} and 1690 cm^{-1}, νNH and OH centered at 3440 cm^{-1}.

In this investigation, a series of compounds have been prepared for the purpose of studying the reaction in the heterocyclic ring in compounds IIa-c. Reactions of IIa-c with phosphorus pentasulphide in boiling xylene gave 1,3-diaryl-3-(1-phenyl-3,5-dithioxo-4-pyrazolidinyl)-1-propanone (IXa-c), the structure of IX was supported from: i) correct elemental analyses, ii) infrared spectra exhibited characteristic absorption bands for ν(N-C=S) at 1480-1470 cm^{-1}, νC=S at 1380-1350 cm^{-1} νNH at 3460-3440 cm^{-1} and νC=O at 1670 cm^{-1}, iii) chemically via the reaction of IXa with hydrazine hydrate to give X, a reaction in which condensation and cyclisation takes place, the infrared spectra of X exhibited characteristic absorption bands for νC=N at 1620 cm^{-1}, νNH at 3340 cm^{-1} and were devoid of νC=S.

It is known [8] that acetylation of pyrazolines gives the N-acetyl derivatives corresponding to replacement of the amino hydrogen. In the present investigation, acetylation has been applied to compounds II with the same result. Thus, treatment of IIa and IIc with acetyl chloride in pyridine afforded the corresponding N-acetyl derivatives XIa and XIb, respectively the infrared spectra of XI showed bands at 1740 cm^{-1} and 1685-1680 cm^{-1} characteristic of νC=O and were devoid of νNH.

Experimental

All melting points are uncorrected. IR spectra were recorded, for KBr discs, on a Unicam SP 1200 spectrophotometer and Mass spectra on an AEI-MS 902 mass spectrometer at 70eV electron energy, 6 KV accelerating


(I)
a; R = H
b; R = OCH3
c; R = Cl
(II)
a; R = H
b; R = OCH3
c; R = Cl
(III)
a; R = H
b; R = OCH3
c; R = Cl
(IV)
a; R = H
b; R = OCH3
c; R = Cl
(V)
a; R = H
b; R = Cl
(VI)
a; H C6H4 Cl (p-)
b; H C6H4 OCH3 (p-)
c; Cl C6H4 OCH3 (p-)
(VII)
(VIII)
(IX)
a; R = H
b; R = OCH3
c; R = Cl
(XI)
a; R = H
b; R = Cl
C2H5ONa
N2H4H2O
NH2 OH.HCl
Ar.CHO
P2S5
N2H4.H2O
ArMgBr

Scheme 1

voltage and an ion source temperature at 130°C using a direct insertion probe.

Addition of 1-phenyl-3,5-pyrazolidinedione to chalcones: Formation of IIa-c.

A mixture of each of the chalcones Ia-c (0.01 mole), 1-phenyl-3,5-pyrazolidinedione (0.01 mole), sodium ethoxide (0.01 mole) and ethanol (50 ml) was heated under reflux for 20 hours. The solid separated on cooling, dilution with water and acidification with hydrochloric acid; it was filtered and crystallized from a suitable solvent to give IIa-c respectively.

Reaction of IIa-c with hydrazines: Formation of IIIa-c and IVa-c.

To a solution of the adduct (IIa-c) (0.01 mole) in ethanol (20 ml), phenylhydrazine or hydrazine hydrate (0.01 mole) was added and the reaction mixture refluxed for 10 hours. The solid that separated on cooling was crystallized from a suitable solvent to give IIIa-c and IVa-c, respectively.

Reaction of IIa and IIc with hydroxylamine hydrochloride: Formation of Va and Vb.

Hydroxylamine hydrochloride (0.01 mole) and sodium acetate (0.01 mole) dissolved in least amount of water was added to a solution of IIa or IIc (0.01 mole) in ethanol (20 ml). The reaction mixture was refluxed for 10 hours, concentrated, cooled, the solid product was separated out, filtered off, recrystallized from a suitable solvent to give Va and Vb, respectively.

Reaction of IIa and IIc with aldehydes: Formation of VIa-c.

A solution of II (0.01 mole), p-chlorobenzaldehyde or anisaldehyde (0.01 mole), piperidine (few drops) in ethanol (30 ml) was refluxed for 5 hours. The solid which separated after cooling was crystallized from a suitable solvent to give VIa-c respectively.

Action of polyphosphoric acid on the adduct IIa: Formation of VII.

Compound IIa (1.5 g) after dissolving in polyphosphoric acid prepared from phosphorus pentoxide (15 g) and orthophosphoric acid (10 ml) was heated in an oil bath maintained at 220° with occasional shaking (2 hours). The contents were poured over crushed ice (300 g) during stirring, extracted with ether, and the ethereal solution first washed with aqueous sodium hydroxide (5%) and then with water. The ethereal solution was dried (anhydrous $MgSO_4$), and then evaporated to give a solid which was crystallized from a suitable solvent to give VII.

Action of Grignard reagents on IIb and IIc: Formation of VIIa-c.

The solution of phenylmagnesium bromide or p-methoxyphenylmagnesium bromide prepared from 0.03 moles of bromobenzene or p-bromoanisole and 0.03 moles of Mg was added to a solution of IIb or IIc (0.01 mole) in dry ether. The solution obtained was refluxed for 4 hours in a boiling water bath and left overnight. The reaction mixture was then hydrolysed with saturated solution of ammonium chloride and extracted with ether. The ethereal solution was dried and evaporated. The residue thus obtained was washed several times with light petrol (40-60°) and recrystallized from a suitable solvent to give VIIIa-c respectively.

Action of phosphorus pentasulfide on IIa-c: Formation of IXa-c.

A mixture of IX (0.01 mole) and phosphorus pentasulfide (0.01 mole) in dry xylene (30 ml) was refluxed for 6 hours. The reaction mixture was

Table-1: Physical data of various compounds

Compd.	M.P°	Yield %	Mol. Formula	Found %				Required %			
				C	H	N	S	C	H	N	S
IIa	213(a)	40	$C_{24}H_{20}N_2O_3$	74.7	5.3	7.5....		75.00	5.21	7.29....	
IIb	198(a)	45	$C_{25}H_{22}N_2O_4$	72.7	5.5	6.4		72.46	5.31	6.76	
IIc	188(b)	43	$C_{24}H_{19}ClN_2O_3$	69.1	4.5	6.8		68.82	4.54	6.69	
IIIa	184(b)	60	$C_{30}H_{26}N_4O_2$	76.1	5.6	11.5		75.95	5.49	11.81	
IIIb	164(b)	58	$C_{31}H_{28}N_4O_3$	73.7	5.7	10.8		73.81	5.56	11.11	
IIIc	153(b)	62	$C_{30}H_{25}ClN_4O_2$	70.6	5.2	10.8		70.80	4.92	11.01	
IVa	192(a)	60	$C_{24}H_{20}N_4O$	75.9	5.6	14.6		75.79	5.26	14.74	
IVb	195(a)	62	$C_{25}H_{22}N_4O_2$	73.6	5.4	13.5		73.17	5.37	13.66	
IVc	162(a)	64	$C_{24}H_{19}ClN_4O$	72.3	5.3	10.7		72.18	5.26	10.53	
Vb	205(c)	68	$C_{24}H_{20}ClN_3O_3$	66.5	4.8	9.9		66.44	4.61	9.69	
VIa	236(a)	58	$C_{31}H_{23}ClN_2O_3$	73.4	4.6	5.4		73.45	4.54	5.53	
VIb	224(a)	50	$C_{32}H_{26}N_2O_4$	76.6	5.1	5.4		76.69	5.18	5.58	
VIc	232(a)	53	$C_{32}H_{25}ClN_2O_4$	71.8	4.7	4.9		71.58	4.66	5.22	
VII	140(d)	30	$C_{24}H_{18}N_2O_2$	78.8	5.1	7.4		78.69	4.92	7.65	
VIIIa	214(b)	42	$C_{31}H_{28}N_2O_4$	75.6	5.8	5.9		75.61	5.69	5.69	
VIIIb	244(b)	33	$C_{30}H_{25}ClN_2O_3$	72.3	5.2	5.6		72.51	5.04	5.64	
VIIIc	220(a)	36	$C_{31}H_{27}ClN_2O_4$	70.8	4.9	5.4		70.66	5.13	5.32	
IXa	66(a)	58	$C_{24}H_{20}N_2OS_2$	69.5	4.6	6.9	15.4	69.23	4.81	6.73	15.38
IXb	103(a)	52	$C_{25}H_{22}N_2O_2S_2$	67.5	5.1	6.3	14.4	67.26	4.93	6.28	14.35
IXc	195(a)	56	$C_{24}H_{19}ClN_2OS_2$	64.1	4.3	6.4	14.4	63.93	4.22	6.22	14.21
X	195(e)	51	$C_{24}H_{22}N_6$	73.3	5.7	21.4		73.10	5.58	21.32	
XIa	205(a)	60	$C_{26}H_{22}N_2O_4$	73.3	5.3	6.4		73.24	5.16	6.57	
XIb	200(b)	63	$C_{26}H_{21}ClN_2O_4$	67.8	4.7	5.8		67.75	4.56	6.08	

The compounds recrystallized from (a) ethanol, (b) benzene, (c) toluene, (d) light petrol (100-120°), (e) light petrol (40-65°).

filtered off while hot. The xylene layer was concentrated, cooled, the solid product was separated, filtered off and then crystallized from a suitable solvent to give IXa-c respectively.

Reaction of IXa with hydrazine hydrate: Formation of X.

To a solution of IXa (0.01 mole) 73 ethanol (20 ml), hydrazine hydrate (0.03 mole) was added and the reaction mixture refluxed for 10 hours. The solid that separated on cooling was crystallized from a suitable solvent to give X.

Acetylation of IIa and IIc: Formation of XIa and XIb.

A solution of IIa or IIc (1 g) in dry pyridine (10 ml) was treated with acetyl chloride (5 ml) and left overnight at room temperature. The mixture was poured on crushed ice and the product filtered off, washed with water and recrystallized from a suitable solvent to give XIa and XIb, respectively.

References

1. Porter, S.W.Otto and W. Wehrb, *Belg., Apr. 30, 616, 190 (1962); C.A., **58**,1466 (1963).*
2. J. Mayer and O. Nemecek, *Czech., Jan.15, 106, 252 (1963); C.A., **60**, 8039 (1964).*
3. S. Tawab, A. Mustafa and M. Kira, *Nature, **186**, 165 (1960).*
4. J.R.A.G. Geigy, *Brit., Mar 20, 921, 467; Swiss, Apl Aug. 34 (1959) 8 pp; C.A., **58**,10062 (1963).*
5. J. Mayer, J. Otvrtnik and O. Nemecek, *Czech., Mar 15, 103, 65; C.A., **60**, 8038 (1964)*
6. A. Mustafa, M. Kira and S. Nakhla, *J.Org.Chem., **26**, 3389 (1961).*
7. A. Mustafa, M. Kira and M. El-Essawi, *J.Org.Chem., **25**,34 (1960)*
8. G.H. Sayed, *Indian J.Chem., **19B**, 364 (1980).*