Tetrahedron. Vol. 26, pp. 5959 to 5967 Pergamon Press 1970 Printed in Great Britain

1,3-DIPOLAR CYCLOADDITIONS—III*

ACTION OF DIAZOKETONES ON N-ARYLMALEIMIDES, WITH A SPECIAL NOTE ON THE PYROLYSIS OF THE RESULTING 5-KETO-PYRAZOLINES

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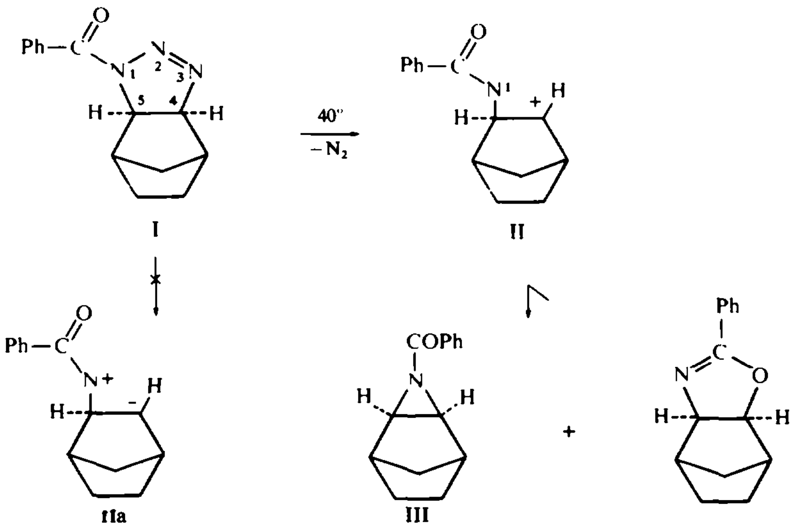
(*Recieved in the UK* 27 *February* 1970; *accepted for publication* 19 *August* 1970)

Abstract—3-Diazocamphor and 2-diazo-4'-nitropropiophenone react with N-arylmaleimides in the cold to yield the 5-keto-Δ^1-pyrazolines (V), while diazoacetophenone gives rise to the 5-keto-Δ^2-pyrazolines (VI). 3-Diazooxindole reacts, when heated with N-arylmaleimides, to give the corresponding cyclopropane derivatives (VII). Pyrolysis of (V) and (VI) yields only cyclopropane derivatives (VIII). The constitutions of the products have been investigated by means of IR, UV, NMR and mass spectra. The charge distribution on the possible ionic intermeidate in the thermal decomposition of pyrazolines is discussed and compared with that of triazolines.

INTRODUCTION

HUISGEN[1] found that the addition of benzazide to norbornene is followed, even at 40°, by loss of nitrogen from the 1-keto-Δ^2-triazoline (I), leading to the N-benzoylaziridine (III) and to an oxazoline structure (IV); the latter can only be formed via II where a negative charge is built up on the remaining nitrogen atom of the azido group (cf. Scheme A).



SCHEME A

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* This paper was presented in part at the Second International Congress of Heterocyclic Chemistry, Montpellier, France, 7–11 July 1969.

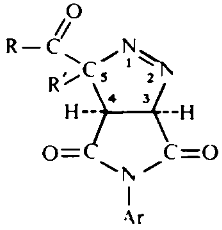
Part II—W. I. Awad and M. Sobhy, *Canad. J. Chem.* **47**, 1473 (1969)

Awad *et al.*[2] found that benzazide fails to react with N-arylmaleimides and instead it gives, together with the recovered maleimide, a compound of molecular formula $(PhNH)_2CO$.

We have investigated the pyrolysis of some 5-keto-Δ^1-pyrazolines (V) and 5-keto-Δ^2-pyrazolines (VI) (inter alia) which would be the carbon analogues of the keto-triazoline (I) and the results of this study are the subject of the present paper.

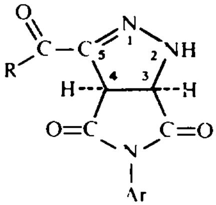
RESULTS AND DISCUSSION

When 3-diazocamphor and 2-diazo-4'-nitropropiophenone[3] are allowed to react with N-arylmaleimides the corresponding 5-keto-Δ^1-pyrazolines (V) are obtained. The interaction between diazoacetophenone[4] and N-arylmaleimides gives rise to the 5-keto-Δ^2-pyrazolines (VI) (νNH = 3250 cm^{-1}) (Table 1).



V

a; $R/R' = C_8H_{14}$; $Ar = C_6H_5$
$R/R' = C_8H_{14}$; $Ar = C_6H_4CH_3(p\text{-})$
c; $R/R' = C_8H_{14}$; $Ar = C_6H_4CH_3(o\text{-})$



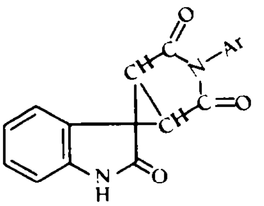
VI

a; $R = C_6H_5$; $Ar = C_6H_5$
b; $R = C_6H_5$; $Ar = C_6H_4CH_3(p\text{-})$
c; $R = C_6H_5$; $Ar = C_6H_4CH_3(o\text{-})$

$R/R' = C_8H_{14} =$

d; $R = C_6H_4NO_2(p\text{-})$; $R' = CH_3$; $Ar = C_6H_5$
e; $R = C_6H_4NO_2(p\text{-})$; $R' = CH_3$; $Ar = C_6H_4CH_3(p\text{-})$
f; $R = C_6H_4NO_2(p\text{-})$; $R' = CH_3$; $Ar = C_6H_4OCH_3(p\text{-})$

No reaction is observed when 3-diazooxindole[5] is allowed to react with N-arylmaleimides in the cold. However, upon refluxing in benzene solution, compounds of type VII are obtained in good yield probably via the corresponding unstable Δ^1-pyrazoline derivatives.



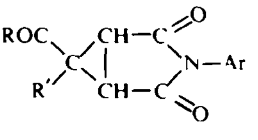
VII

a; $Ar = C_6H_5$
b; $Ar = C_6H_4CH_3(p\text{-})$
c; $Ar = C_6H_4CH_3(o\text{-})$

The structure of VIIa–c is established by a study of their IR, UV and NMR spectra. Thus, the IR spectra exhibit a band at 3200–3175 cm^{-1} due to the NH stretching vibration and three carbonyl stretching vibrations; a doublet in the region between 1786–1733 cm^{-1} attributed to the equivalent carbonyl groups of the succinimide ring[6] and a strong band at 1718 cm^{-1} from the lactam carbonyl absorption.[7] Furthermore, the IR spectra of VIIa–c show the characteristic cyclopropane deformation band in the 1020 cm^{-1} region[8] (Table 2). The strong K band in the UV spectra at λ_{max} 231–232 mμ (ε_{max} 28806–33900) close to that of isatin at λ_{max} 243 mμ (ε_{max} 24700) confirms the lactam structure occurring in 3,3-disubstituted oxindoles.[9] In the NMR spectrum* of VIIc, the integration results give a proton ratio of about 9:2:3. This would mean that the NH (1H) absorption is buried under the aromatic protons (8H). The methine resonance is a singlet at 3·78 ppm which supports the cyclopropane structure.

Pyrolysis of the pyrazoline derivatives

The pyrazoline derivatives (Va–f and VIa–c) give upon pyrolysis a single product to which the corresponding cyclopropane structure (VIII) is given. The thermal decomposition of the Δ^2-pyrazolines (VIa–c) probably proceeds by initial tautomerization to the corresponding less stable Δ^1-pyrazolines followed by expulsion of nitrogen.[10]



VIII

a; $R/R' = C_8H_{14}$; $Ar = C_6H_5$
b; $R/R' = C_8H_{14}$; $Ar = C_6H_4CH_3(p\text{-})$
c; $R/R' = C_8H_{14}$; $Ar = C_6H_4CH_3(o\text{-})$
d; $R = NO_2(p\text{-})C_6H_4$; $R' = CH_3$; $Ar = C_6H_5$
e; $R = NO_2(p\text{-})C_6H_4$; $R' = CH_3$; $Ar = C_6H_4CH_3(p\text{-})$
f; $R = NO_2(p\text{-})C_6H_4$; $R' = CH_3$; $Ar = C_6H_4OCH_3(p\text{-})$
g; $R = C_6H_5$; $R' = H$; $Ar = C_6H_5$
h; $R = C_6H_5$; $R' = R' = H$; $Ar = C_6H_4CH_3(p\text{-})$
i; $R = C_6H_5$; $R' = H$; $Ar = C_6H_4CH_3(o\text{-})$

The constitution of VIIIa–c is confirmed by their UV spectra which are very similar to that of cyclopropane-2,3-(N-phenyl)-dicarboximide:[11] λ_{max} 224–226 mμ (ε_{max} 5184–11000) and λ_{max} 223 mμ (ε_{max} 9700) respectively. The UV spectra of VIIIa–c show an additional weak R-band at λ_{max} 310 mμ (ε_{max} 100) which may be attributed to the electronic transition of the carbonyl group in the camphor moiety.

The assignment of cyclopropane structure to the compounds VIIId–f and VIIIg–i is substantiated by the results of NMR analyses.

The NMR spectrum of VIIIg is compatible with a cyclopropane structure. The methine protons represent an AB_2 spectrum which is close to AX_2 at 3·08 ppm [(2H)b] doublet and 3·58 ppm [(1H)a] triplet. So it can be analysed according to the first order: $J_{AB} = 3$ cps. This relatively low value of a *trans*-cyclopropane coupling, compared with that of *trans*-1,2,3-tribenzoyl-cyclopropane (IX)[12] ($J_{trans} \approx 6$ cps), may be due to the distortion of angles by the five-membered ring as revealed in the molecular model.

We thought that the introduction of a nitrophenyl ring into the diazoketone and the pyrolysis of the corresponding pyrazolines (Vd–f) would favour route b (cf. Scheme C). However, the NMR spectrum of VIIIf shows signals at 1·68 ppm [(3H)a]

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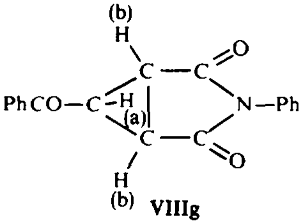
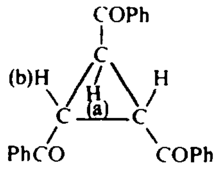
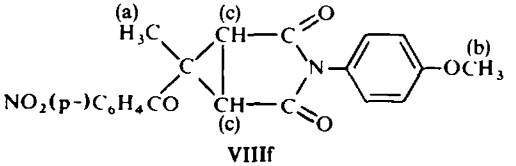
* This was run in dimethyl-d_6 sulfoxide solution



VIIIg



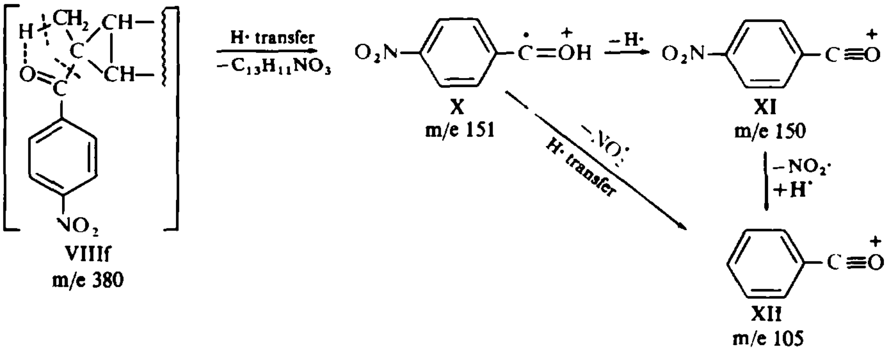
IX



VIIIf

singlet, 3·85 ppm [(3H)b] singlet and the methine resonance is also a singlet at 3·22 ppm [(2H)c]. All the other peaks in the spectrum arise from aromatic protons. This spectrum is in agreement with a cyclopropane structure. The alternative dihydrofuran structure (XV) would not show a single absorption for the methine resonance.

The mass spectrum* of VIIIf is also consistent with a cyclopropane structure. Its most characteristic features are the pronounced m/e 151, 150 and 105 peaks due to the production of the prominent ions X, XI and XII respectively (cf. Scheme B and Fig 1).



SCHEME B. Some fragmentation reactions of VIIIf

The alternative structure (XV) would not lead to such fragment ions.

The UV spectra of VIIId–i resemble that of cyclopropane-2,3-(N-phenyl)-dicarboximide with the expected bathochromic shift and hyperchromic effect (Table 2).

The IR spectra of VIIIa–i exhibit three carbonyl stretching frequencies (compare with VIIa–c) and the characteristic cyclopropane deformation band (Table 2).

These results lead to the conclusion, that in contrast to triazolines, the thermal decomposition of pyrazolines is consistent with an open chain zwitterionic intermediate (XIII) with a deficiency of electron charge developed on the remaining carbon atom of the diazo group (C_5) (a biradical mechanism is not excluded[13]).

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* The mass spectrum was carried ou in the Faculty of Science, University of Dijon, Dijon, France by courtesy of Dr. P. Fournari

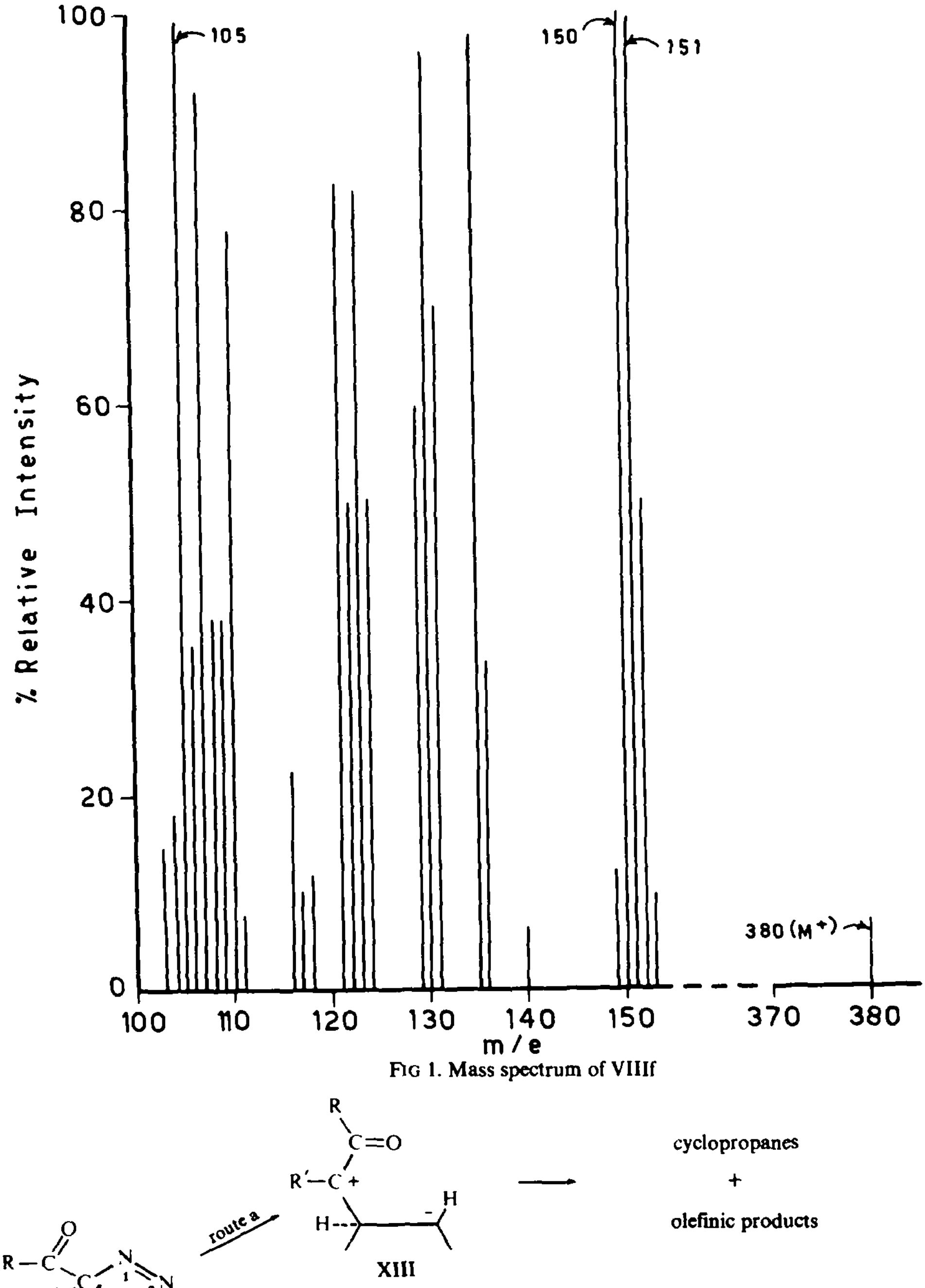
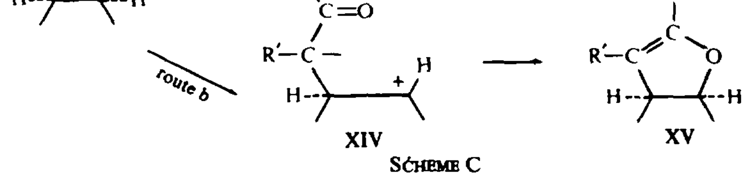


FIG 1. Mass spectrum of VIIIf

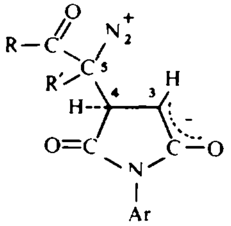


SCHEME C

XIV is thus exluded; for if it were ever formed, it would participate in a ring closure to oxygen leading to XV among other products.

This conclusion is compatible with the facts that pyrolysis of *cis*- and *trans*-3,5-dimethyl-3-acetyl-Δ^1-pyrazolines give among other products 2,3,5-trimethyl-4,5-dihydrofuran[14] and that when the 3 and 5 positions of the pyrazoline ring are occupied by acyl and carboxyl groups respectively, the main pyrolytic reaction may be the pyrone formation[15] since, in these examples, the carbonyl group is attached to the negatively charged carbon atom of the possible intermediate. But it contradicts the intermediacy of a pyrazolone[14] in the reaction of diazoketones with ketenes to yield unsaturated lactones, since such hypothesis necessitates route b (cf. Scheme C).

It should be noted that although delocalization is possible onto the carbonyl oxygen of the imide ring, yet such an oxygen atom is not available to participate in a ring closure reaction (XVI).



XVI

The persistence of the imide ring through the whole reaction prevents free rotation about the C_3—C_4 single bond (original olefinic double bond). The fact that no unsaturated products were isolated in the present investigation may be attributed to the bulky groups attached to the C_5 of the pyrazoline ring.[16]

From the present study and from the earlier results of other studies one can make a reasonable conclusion about the charge distribution on the possible ionic intermediate in the thermal decomposition of pyrazolines.

EXPERIMENTAL

All m.ps are uncorrected. Analyses were carried out by Medizinisch-Chemisches Institut, und Pregl-Laboratorium der universität, Graz, Austria and by Ain Shams University Microanalytical Unit, Abbassia, Cairo. IR spectra were measured on a Perkin–Elmer Infracord Model 137 spectrophotometer using the KBr wafer technique. UV spectra were measured on a Unicam SP 700 double-beam recording spectrophotometer using EtOH solns. NMR spectra* were run in $CDCl_3$ soln in a Varian A-60 spectrometer.

Preparation of 3-*diazocamphor*. α-Camphorquinone-3-hydrazone (7 g), anhydrous Na_2SO_4 (2·5 g), red HgO (15 g) and 100 ml of sodium-dried Et_2O were shaken for 30 min. The reaction was catalysed by the addition of 0·1 ml of a cold saturated soln of alcoholic KOH. The soln was filtered and the residue washed several times with anhydrous ether. 3-Diazocamphor in Et_2O soln was used for the addition reactions.

Action of 3-*diazocamphor on* N-*arylmaleimides*. A soln of the maleimide (1·7 g) in dry Et_2O was treated with an Et_2O soln of 3-diazocamphor prepared as above. The reaction mixture was allowed to stand overnight in an ice chest. A colourless ppt was formed which was filtered off, washed with Et_2O and recrystallized from benzene–hexane as colourless crystals (Table 1).

Action of 2-*diazo*-4′-*nitropropiophenone and diazoacetophenone on N-arylmaleimides*. A soln of the maleimide (1·7 g) in dry benzene was treated with a benzene soln of the corresponding diazoketone (2-diazo-4′-nitropropiophenone 4 g in 20 ml dry benzene; diazoacetophenone 3 g in 20 ml dry benzene). The reaction mixture was allowed to stand overnight at room temp. A colourless solid was formed which was filtered off, washed with benzene, and recrystallized from EtOH as colourless crystals (Table 1).

* The NMR spectra were carried out at the Organisch-Chemisches Institut der Universität, Heidelberg by courtesy of Dr. A. Mannschreck

TABLE 1. Δ^1- AND Δ^2-PYRAZOLINE DERIVATIVES

Compound	Yield %	Melting point	Formula	Analysis						Infrared
				Required			Found			ν NH (cm^{-1})
				C	H	N	C	H	N	
Va	60	205° (decomp)	$C_{20}H_{21}N_3O_3$	68·37	5·98	11·96	68·50	6·16	12·03	—
Vb	50	180° (decomp)	$C_{21}H_{23}N_3O_3$	69·04	6·30	11·50	68·89	6·44	11·51	—
Vc	70	197° (decomp)	$C_{21}H_{23}N_3O_3$	69·04	6·30	11·50	69·11	6·39	11·39	—
Vd	66	148° (decomp)	$C_{19}H_{14}N_4O_5$	60·31	3·70	14·81	60·34	4·01	14·82	—
Ve	65	153° (decomp)	$C_{20}H_{16}N_4O_5$	61·22	4·08	14·28	61·30	4·18	14·11	—
Vf	60	160° (decomp)	$C_{20}H_{16}N_4O_6$	58·82	3·92	13·72	58·81	4·29	13·67	—
VIa	70	199° (decomp)	$C_{18}H_{13}N_3O_3$	67·71	4·07	13·16	67·73	4·00	12·81	3250
VIb	65	196° (decomp)	$C_{19}H_{15}N_3O_3$	68·46	4·50	12·61	68·24	4·44	12·90	3250
VIc	70	173° (decomp)	$C_{19}H_{15}N_3O_3$	68·46	4·50	12·61	68·35	4·56	12·49	3250

TABLE 2. CYCLOPROPANE DERIVATIVES

Compound	Yield %	Melting point	Formula	Analysis						Ultraviolet		Infrared		
				required			Found			λ_{max} (mμ)	ε_{max}	νNH (cm^{-1})	νCO (cm^{-1})	Cyclopropyl deformation (cm^{-1})
				C	H	N	C	H	N					
VIIa	73	261° (decomp)	$C_{18}H_{12}N_2O_3$	71·05	3·94	9·21	71·18	4·02	9·25	231	30365	3175	1786, 1733 1718	1020
VIIb	60	270° (decomp)	$C_{19}H_{14}N_2O_3$	71·70	4·40	8·81	71·71	4·42	9·08	232	33900	3200	1786, 1727 1712	1026
VIIc	65	262° (decomp)	$C_{19}H_{14}N_2O_3$	71·70	4·40	8·81	71·62	4·49	8·90	231	28806	3175	1786, 1727 1712	1018
VIIIa	65	138°	$C_{20}H_{21}NO_3$	74·30	6·50	4·33	74·06	6·57	4·35	225 310	8503 100	—	1786, 1742 1718	1010
VIIIb	60	158°	$C_{21}H_{23}NO_3$	74·75	6·87	4·15	74·49	7·08	4·18	226 310	11000 100	—	1786, 1742 1715	1010
VIIIc	75	237°	$C_{21}H_{23}NO_3$	74·75	6·87	4·15	74·87	7·13	4·15	224 310	5184 100	—	1786, 1742 1718	1010
VIIId	70	207–209°	$C_{19}H_{14}N_2O_5$	65·14	4·00	8·00	65·13	4·29	8·07	259	22910	—	1792, 1730 1695	1036
VIIIe	70	195–197°	$C_{20}H_{16}N_2O_5$	65·93	4·36	7·69	65·99	4·76	7·67	260	23680	—	1789, 1724 1695	1040
VIIIf	75	193–195°	$C_{20}H_{16}N_2O_6$	63·15	4·21	7·36	63·45	4·51	7·42	260	23895	—	1792, 1728 1695	1036
VIIIg	66	181–182°	$C_{18}H_{13}NO_3$	74·22	4·50	4·81	74·01	4·83	4·82	250	22000	—	1786, 1718 1684	1042
VIIIh	60	186–188°	$C_{19}H_{15}NO_3$	74·75	4·91	4·59	74·44	5·05	4·52	252	30700	—	1789, 1721 1686	1036
VIIIi	76	197–198°	$C_{19}H_{15}NO_3$	74·75	4·91	4·59	74·72	5·11	4·62	250	18109	—	1786, 1718 1686	1040

Action of 3-diazooxindole on N-arylmaleimides. A soln of the maleimide (1·7 g) in dry benzene was added to the diazoketone (1·6 g) soln in the same solvent. The mixture was refluxed for 10 min. A colourless solid deposited which was filtered off, washed with benzene and recrystallized from EtOH as fine colourless crystals (Table 2).

Thermal decomposition of the pyrazoline derivatives. (*a*) Δ^1-pyrazolines (Va–c). Pyrazolines (Va–c) were heated just above the m.p. (oil bath) for 3h. The cold residue was then extracted several times with cyclohexane and the product was recrystallized from the same solvent as colourless crystals (VIIIa–c) (Table 2).

(*b*) Δ^1-pyrazolines (Vd–f). Pyrazolines (Vd–f) were similarly treated. Extraction was carried out with light petroleum (b.p. 100–120°) and the product was recrystallized from benzene–hexane as pale yellow crystals (VIIId–f) (Table 2).

(*c*) Δ^2-pyrazolines (VIa–c). Pyrazolines (VIa–c) were similarly treated. Extraction was carried out with light petroleum (b.p. 60–80°) and the product was recrystallized from benzene–hexane as fine colourless crystals (VIIIg–i) (Table 2).

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