Decomposition Products of Pyrazolines formed from 3-Alkylthioinden-1-ones and Diazomethane

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1-Pyrazolines are formed by the addition of diazomethane to 2-substituted 3-alkylthioinden-1-ones, and on pyrolysis they yield the corresponding 2-substituted 4-alkylthio-1-naphthols and 3-alkylthiomethylinden-1-ones. Diazomethane adds less readily to 3-methoxy-2-phenylinden-1-one and decomposition of the resulting pyrazoline yields only 4-methoxy-2-phenyl-1-naphthol which is partially converted into 2-phenyl-1,4-naphthoquinone during work-up.

METHYLATION of enolisable 1,3-dicarbonyl compounds with diazomethane gives mainly *O*-methyl ethers. If an excess of reagent is present the latter may react further to form pyrazolines, although relatively few such reactions have been reported.[1,2] Hantzsch and Czapp [3] found that 2-ethoxycarbonylindane-1,3-dione in the presence of a large excess of diazomethane gave 2-ethoxycarbonyl-4-methoxy-1-naphthol and suggested a methylation, addition, and ring expansion sequence for its formation. We now report the ready formation of pyrazolines from thioenol ethers of 2-phenylindane-1,3-dione and on the decomposition of the pyrazolines.

This work was initiated by the observation that 3-mercapto-2-phenylinden-1-one [4] on treatment with diazomethane yielded, in addition to the expected 3-methylthio-2-phenylinden-1-one (Ia), the 1-pyrazoline (IIa). Subsequently the latter was prepared in high yield by treating the thioether (Ia) with diazomethane. 3-Benzylthio-2-phenylinden-1-one (Ib) and 2-benzyl-3-benzylthioinden-1-one (Ic) were equally susceptible to the addition of diazomethane and yielded the pyrazolines (IIb) and (IIc) respectively. This behaviour is in contrast with that of 3-methoxy-2-phenylinden-1-one which required longer treatment with a large excess of diazomethane for complete conversion into the pyrazoline (IId).

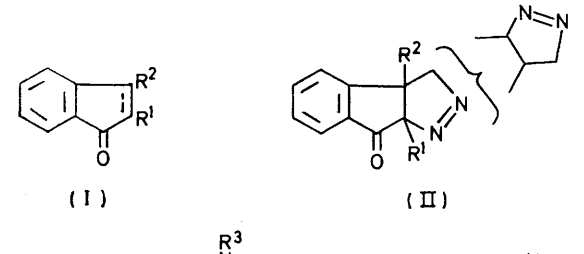
The 1-pyrazolines (IIa and d) were purified by crystallisation but on preparative t.l.c. they were converted into the corresponding 2-pyrazolines (IIIa and d). The 1-pyrazoline (IIb) was obtained only in crude form since all attempts to purify it resulted in formation of the 2-pyrazoline (IIIb). The benzylpyrazoline (IIc), on the other hand, did not tautomerise readily but could be converted into the 2-pyrazoline (IIIc) by treatment with acid. The 2-pyrazolines were characterised as their acetates (IVa—d).

While n.m.r. and i.r. data (Table 1) clearly identify the 1- and 2-pyrazoline structures they do not allow structures (II) and (III) to be distinguished from the isomers (indicated in brackets by partial structures) arising from methylene attack at C-2 rather than C-3 of the indenone. Eistert and Mennicke [5] have isolated 1-pyrazolines arising from both types of addition in the reaction of 2,3-diphenylinden-1-one with diazoethane but only one isomer from the reaction with diazomethane. In the present work one 1-pyrazoline only was obtained from each indenone. When 2-benzyl-3-benzylthioinden-1-one (Ic) was treated with a large excess of diazomethane the 1-pyrazoline (IIc) was accompanied by the rather unstable epoxide (V) which was identified by n.m.r. and i.r. spectroscopy.

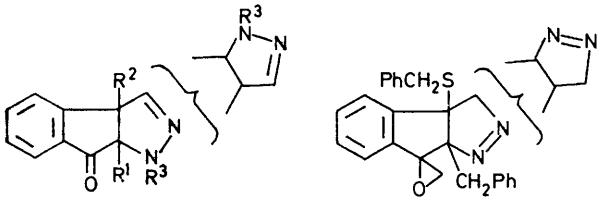
Each of the alkylthio-1-pyrazolines (IIa—c) on pyrolysis yielded two products, one colourless and one deep yellow. The colourless products were identified by spectroscopic data (Table 1) as 4-alkylthio-1-naphthols (VIa—c) and were characterised as their acetates (VIIa—c). The coloured products on the basis of their n.m.r.,

[1] D. Nasipuri and K. K. Biswas, *Tetrahedron Letters*, 1966, 2963.
[2] D. Nasipuri, A. K. Mitra, K. K. Biswas, and D. N. Roy, *Indian J. Chem.*, 1972, **10**, 897.
[3] A. Hantzsch and E. Czapp, *Ber.*, 1930, **63**, 566; *Cf.* F. Arndt, *ibid.*, p. 1180.
[4] K. Buggle, D. O'Sullivan, and N. D. Ryan, *Chem. and Ind.*, 1974, 164; *cf.* V. A. Usov, N. A. Korchevin, Ya. S. Tsetlin, and M. G. Voronkov, *Zhur. org. Khim.*, 1973, **9**, 2149.
[5] B. Eistert and W. Mennicke, *Chem. Ber.*, 1967, **100**, 3495.

i.r., and mass spectra were assigned the 3-alkylthiomethylinden-1-one structures (VIIIa—c). These compounds were slightly unstable and since it was difficult to purify them sufficiently for elemental analysis they were oxidised to the corresponding sulphoxides (IXa—c) which were then satisfactorily analysed. The n.m.r.

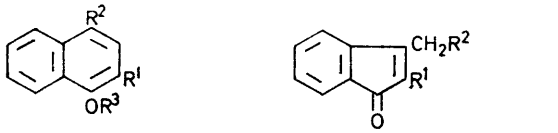


(I) (II)



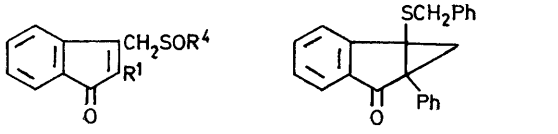
(III) R^3 = H
(IV) R^3 = Ac

(V)



(VI) R^3 = H
(VII) R^3 = Ac

(VIII)



(IX) (X)

	R^1	R^2	R^4
a	Ph	SMe	Me
b	Ph	SCH_2Ph	CH_2Ph
c	CH_2Ph	SCH_2Ph	CH_2Ph
d	Ph	OMe	
e	Ph	SPh	

spectra of the sulphoxides supported the assigned structures showing the deshielding effect ($\Delta\tau$ *ca.* 0·3 p.p.m.) of the sulphinyl group, relative to the thio-group, on the protons of each of the adjacent carbon atoms. Further support for these structures was obtained by isolating 3-methylsulphinylmethyl-2-phenylinden-1-one (IXa) in low yield from the reaction of lithium methylsulphinylmethanide with 3-phenylthio-2-phenylinden-1-one (Ie).

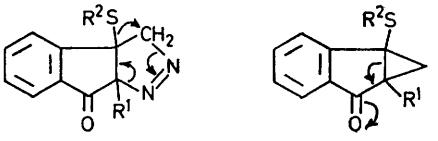
Pyrolysis of the 3-benzylthio-1-pyrazoline (IIb) gave, in addition to the naphthol (VIb) and the indenone (VIIIb), the cyclopropane (X) which was identified by its n.m.r. spectrum. Pyrolysis of this compound gave only the naphthol (VIb). Presumably the indenones (VIII) are formed by decomposition of the pyrazolines as shown in (A) whilst the naphthols (VI) arise *via* the cyclopropanes (B). Rearrangement *via* intermediate (A)

TABLE 1

N.m.r. and i.r. data

Compound	τ Values (*J* in Hz)	$\nu_{max.}$/cm^{-1}
(Ic)	5·71 (2H, s), 6·23 (2H, s)	1693 (C=O)
(IIa)	4·98 (2H, q, *J* 19·3), 8·67 (3H, s)	1715 (C=O), 1587 (N=N)
(IIb)	5·03 (2H, q, *J* 19·0), 7·11 (2H, q, *J* 10·9)	1695 (C=O)
(IIc)	5·50 (2H, q, *J* 21·3), 6·44 (2H, q, J 14·6), 6·88 (2H, s)	1716 (C=O) 1588 (N=N)
(IId)	4·96 (2H, q, *J* 19·0), 7·4 (3H, s)	1715 (C=O)
(IIIa)	3·05 (1H, s), 3·25 (1H, s), 8·39 (3H, s)	3315 (NH), 1708 (C=O)
(IIIb)	2·90 (1H, s), 3·16 (1H, s), 6·68 (2H, s)	3285 (NH), 1703 (C=O)
(IIIc)	3·21 (1H, s), 3·62 (1H, s), 6·09 (2H, ABq) 6·73 (2H, q, *J* 13·56)	3322 (NH), 1722 (C=O)
(IIId)	2·87 (1H, s), 3·03 (1H, s), 7·01 (3H, s)	
(IVa)	2·93 (1H, s), 7·61 (3H, s), 8·68 (3H, s)	1725 (C=O), 1688 (C=O)
(IVb)	2·99 (1H, s), 7·09 (2H, q, *J* 11·3), 7·60 (3H, s)	1710 (C=O), 1680 (C=O)
(IVc)	3·11 (1H, s), 6·21 (2H, q, *J* 15·8), 6·69 (2H, s), 7·99 (3H, s)	1723 (C=O), 1699 (C=O)
(IVd)	2·83 (1H, s), 7·34 (3H, s), 7·61 (3H, s)	1721 (C=O), 1680 (C=O)
(V)	5·44 (2H, q, *J* 17·6), 6·27 (2H, q, *J* 3·8), 6·68 (2H, q, *J* 14·0), 6·82 (2H, s)	1585 (N=N)
(VIa)	4·08 (1H, s), 7·51 (3H, s)	3310 (OH)
(VIb)	4·03 (1H, s), 5·96 (2H, s)	3500 (OH)
(VIc)	4·87 (1H, s), 5·99 (2H, q, *J* 19·5), 6·03 (3H, s)	3500 (OH)
(VId)	3·23 (1H, s), 4·52 (1H, s), 6·00 (3H, s)	
(VIIa)	7·44 (3H, s), 7·81 (3H, s)	1755 (C=O)
(VIIb)	5·95 (2H, s), 7·92 (3H, s)	1725 (C=O)
(VIIc)	5·99 (2H, ABq), 5·94 (2H, s), 7·59 (3H, s)	1740 (C=O)
(VIId)	3·09 (1H, s), 6·00 (3H, s), 7·84 (3H, s)	1760 (C=O)
(VIIIa)	6·15 (2H, s), 7·95 (3H, s)	
(VIIIb)	6·24 (2H, s), 6·30 (2H, s)	
(VIIIc)	6·29 (2H, s), 6·43 (4H, s)	
(IXa)	5·80 (2H, ABq), 7·38 (3H, s)	1690 (C=O), 1045 (SO)
(IXb)	5·87 (2H, s), 5·98 (2H, ABq)	1698 (C=O), 1047 (SO)
(IXc)	5·99 (2H, s), 6·16 (2H, s), 6·32 (2H, s)	1704 (C=O), 1036 (SO)
(X)	6·45 (2H, ABq), 7·67 (2H, q, *J* 5·2)	1710 (C=O)

rules out the alternative bracketted structures for compounds (II) [and hence compounds (III)—(V)] which would be unlikely to form compounds (VIII) except through a cyclopropane intermediate.*



(A) (B)

A rearrangement somewhat similar to that shown in (A) involving bromine rather than the alkylthio-group has been suggested [6] to account for the products of the reaction between 3-bromo-4-phenylcyclobutene-1,2-dione and an excess of diazomethane. Phenyl migration has

* We are grateful to a referee for pointing this out.

[6] W. Ried, W. Kuhn, and A. H. Schmidt, *Chem. Ber.*, 1974, **107**, 1147.

been observed in the decomposition of the adduct of diazoethane and 2,3-diphenylinden-1-one to 2-(α-methylbenzyl)-3-phenylinden-1-one.[7]

Pyrolysis of the methoxy-1-pyrazoline (IId) afforded only the naphthol (VId) which partially decomposed during t.l.c. to yield 2-phenyl-1,4-naphthoquinone.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded with a Perkin-Elmer R12 60 MHz spectrometer for solutions in [^{2}H]chloroform with tetramethylsilane as internal standard. I.r. spectra were obtained with a Perkin-Elmer I.R. 700 spectrometer for potassium bromide discs. N.m.r. and i.r. data are in Table 1. Preparative thin layer chromatography (p.l.c.) was carried out using Merck Kieselgel 60 PF254 + 366; light petroleum used as eluant had b.p. 40—60°. Analytical data for new compounds are given in Table 2.

Reaction of Diazomethane with the Indenones (Ia—d).—(*a*) A solution of the indenone (Ia) (729 mg) in ether (15 ml) was added to ethereal diazomethane (fourfold excess). After 3 h the orange colour had faded to pale yellow. The stoppered solution was kept overnight, concentrated, filtered, and the remaining ether removed on a rotary evaporator. The residual 3a,8a-*dihydro*-3a-*methylthio*-8a-*phenylindeno*[2,1-c]-*pyrazol*-8(3H)-*one* (IIa) crystallised from chloroform–methanol in needles (429 mg, 50%), m.p. 125° (decomp). The mother liquor was chromatographed and yielded the indenopyrazolone (IIIa) (304 mg, 36%), m.p. 142—145°.

(*b*) 3-Benzylthio-2-phenylindenone (Ib) (1·0 g) treated with ethereal diazomethane (fivefold excess) and kept for 24 h gave the crude indeno[2,1-*c*]pyrazol-8(3*H*)-one (IIb) (identified by n.m.r. spectroscopy) which after p.l.c. gave 3a-*benzylthio*-3a,8a-*dihydro*-8a-*phenylindeno*[2,1-c]*pyrazol*-8(1H)-*one* (IIIb) (1·128 g, 100%), m.p. 142·5—143·5°.

TABLE 2

Analytical data

Compound	Found (%) C	H	N	S	Formula	Required (%) C	H	N	S
(Ia)	76·0	5·1		12·5	$C_{16}H_{12}OS$	76·2	4·8		12·7
(Ic)	80·7	5·4		9·1	$C_{23}H_{18}OS$	80·7	5·3		9·3
(Ie)	79·9	4·4		10·0	$C_{21}H_{14}OS$	80·2	4·5		10·2
(IIa)	68·9	4·7	9·5	11·2	$C_{17}H_{14}N_2OS$	69·4	4·8	9·5	10·9
(IIc)	75·1	5·5	7·0	8·3	$C_{24}H_{20}N_2OS$	75·0	5·2	7·3	8·3
(IId)	73·8	5·4	10·4		$C_{17}H_{14}N_2O_2$	73·4	5·1	10·1	
(IIIa)	69·2	4·7	9·5		$C_{17}H_{14}N_2OS$	69·4	4·8	9·5	
(IIIb)	74·7	5·0	7·8	8·8	$C_{23}H_{18}N_2OS$	74·6	4·9	7·6	8·6
(IVa)	68·3	4·7	8·1	9·5	$C_{19}H_{16}N_2O_2S$	67·9	4·8	8·3	9·5
(IVb)	73·1	5·0	6·8	8·1	$C_{25}H_{20}N_2O_2S$	72·8	4·9	6·8	7·8
(IVc)	73·3	5·4	6·4	7·7	$C_{26}H_{22}N_2O_2S$	73·2	5·2	6·6	7·5
(IVd)	71·4	5·1	8·5		$C_{19}H_{16}N_2O_3$	71·2	5·0	8·8	
(VIa)	76·3	5·3		11·8	$C_{17}H_{14}OS$	76·7	5·3		12·0
(VIIa)	73·7	5·5		10·4	$C_{19}H_{16}O_2S$	74·0	5·2		10·4
(VIIb)	77·8	5·4		8·1	$C_{25}H_{20}O_2S$	78·1	5·2		8·3
(VIIc)	78·6	5·5		7·7	$C_{26}H_{22}O_2S$	78·4	5·6		8·0
(VIId)	78·3	5·5			$C_{19}H_{16}O_3$	78·1	5·5		
(VIIIa)	77·0	5·3		11·9	$C_{17}H_{14}OS$	76·7	5·3		12·0
(IXa)	72·4	5·1		11·1	$C_{17}H_{14}O_2S$	72·3	5·0		11·3
(IXb)	77·5	5·1		8·7	$C_{23}H_{18}O_2S$	77·1	5·1		8·9
(IXc)	77·6	5·4		8·8	$C_{24}H_{20}O_2S$	77·4	5·4		8·6

3-*Methylthio*-2-*phenylinden*-1-*one* (Ia).—3-Mercapto-2-phenylinden-1-one (261 mg) was added to a solution of diazomethane (threefold excess) in ether. After 2 h the solvent was removed. P.l.c. of the residue with ether–light petroleum (85 : 15) as eluant yielded the S-*methyl thioether* (Ia) (239 mg, 87%) as a red oil and 3a,8a-*dihydro*-3a-*methylthio*-8a-*phenylindeno*[2,1-c]*pyrazol*-8(1H)-*one* (IIIa) (46 mg, 13%), m.p. 142—145 °C.

2-*Benzyl*-3-*benzylthioinden*-1-*one* (Ic).—A solution of toluene-α-thiol (0·788 g) in benzene (50 ml) was added over 6 h to a stirred solution of 2-benzylindane-1,3-dione (1·5 g) and boron trifluoride–ether complex (20 ml) in benzene (150 ml) maintained at 55—56°. The mixture was refluxed for 8 h, cooled, and washed with water and then with aqueous sodium hydroxide (5%) until the washings were colourless. The benzene extracts were washed with a saturated solution of sodium chloride, dried (Na_2SO_4), and evaporated. P.l.c. of the residue with ether–light petroleum (1 : 2) afforded the *indenone* (Ic) (0·786 g, 36%), m.p. 97—98° (ether–light petroleum).

2-*Phenyl*-3-*phenylthioinden*-1-*one* (Ie).—2-Phenylindane-1,3-dione (4·0 g) when treated with benzenethiol as described in the previous experiment, yielded the *indenone* (Ie) (2·47 g, 62%), m.p. 100—101°.

(*c*) 2-Benzyl-3-benzylthioinden-1-one (Ic) (478 mg) with ethereal diazomethane (ninefold excess) gave after 72 h 8a-*benzyl*-3a-*benzylthio*-3a,8a-*dihydroindeno*[2,1-c]*pyrazol*-8(3H)-*one* (IIc) (426 mg, 79%), m.p. 127° (decomp.) and the epoxide (V) (52 mg; 9%) as an oil.

(*d*) 3-Methoxy-2-phenylinden-1-one (Id) (309 mg) with ethereal diazomethane (ninefold excess) gave after 72 h 3a,8a-*dihydro*-3a-*methoxy*-8a-*phenylindeno*[2,1-c]*pyrazol*-8(1H)-*one* (IIId) (141 mg, 38·9%), 2-phenyl-1,4-naphthoquinone (14 mg, 4·6%), m.p. 110° (lit.,[8] 109—110°), and unchanged 3-methoxy-2-phenylinden-1-one (Id) (142 mg, 45·7%).

The experiment was repeated with 3-methoxy-2-phenylinden-1-one (242 mg) and diazomethane (fortyfold excess). The initial orange colour of the solution slowly faded over 3 days. After 1 week the solution afforded the *isomeric indeno*[2,1-c]*pyrazol*-8(3H)-*one* (IId) (182 mg, 64%), m.p. 130° (decomp.) and the indenopyrazol-8(1*H*)-one (IIId) (52 mg, 18%) as an oil.

Acetylation of the Indenopyrazolones (IIIa—d).—Acetyl bromide (an excess) was added dropwise at room tempera-

[7] B. Eistert, H. Fink, T. Schulz, and J. Riedinger, *Annalen*, 1971, **750**, 1.

[8] Th. Zincke and A. Breuer, *Annalen*, 1884, **226**, 23

ture to the indenopyrazolone and the mixture stirred overnight. Water (a few drops) was added and the mixture was taken up in chloroform. The chloroform extracts were washed with water, dried, evaporated, and the residue separated by t.l.c. ($CHCl_3$) to give the 1-*acetyl derivatives*: (IVa) (95%), m.p. 195—196° (from methanol–chloroform); (IVb) (95%), m.p. 145° [from chloroform–ether–light petroleum (b.p. 40—60°)]; (IVc) (100%), m.p. 157—158° (from methanol–chloroform); and (IVd) (45%) m.p. 205—206° (from methanol).

Pyrolysis of the Indenopyrazolones (IIa—d).—The indenopyrazolones were heated at 125° for 1 h. The dark brown residue was taken up in chloroform and separated by t.l.c. The pyrazolone (IIa) (392 mg) gave *4-methylthio-2-phenyl-1-naphthol* (VIa) (251 mg, 71%), m.p. 72—73° (from benzene–light petroleum) and *3-methylthiomethyl-2-phenylinden-1-one* (VIIIa) (55 mg, 16%), m.p. 105—106° (from methanol), *m/e* 266 (94%), 219 (100), and 189 (65). The pyrazolone (IIb) (232 mg) afforded the *4-benzylthio-2-phenyl-1-naphthol* (VIb) as an oil (81 mg, 38%), 3-benzylthiomethyl-2-phenylinden-1-one (VIIIb) as an oil (25 mg, 11%), *m/e* 342 (47%), 251 (76·5), 222 (100), and 91 (88), and 1a-benzylthio-1a,6a-dihydro-6a-phenylcycloprop[*a*]inden-6(1*H*)-one (X) as an oil (65 mg, 30%).

The pyrazolone (IIc) (220 mg) gave 2-benzyl-4-benzylthio-1-naphthol (VIc) as an oil (56 mg, 27%) and 2-benzyl-(3-benzylthiomethylinden-1-one (VIIIc) as an oil (93 mg, 46%). The pyrazolone (IId) (153 mg) yielded the 4-methoxy-2-phenyl-1-naphthol (VIc) as an oil (87 mg, 63%), 2-phenyl-1,4-naphthoquinone (17 mg, 13%), m.p. 110°, and the indenopyrazolone (IIId) (30 mg, 20%).

Acetylation of the 1-Naphthols (VIa—d).—The naphthols were acetylated with acetyl bromide: the *acetate* (VIa) had m.p. 99—100°; (VIb), m.p. 108—109·5°; (VIc), m.p. 86—86·5°; and (VId), m.p. 97—98°.

Oxidation of the Alkylthiomethylinden-1-ones (VIIIa—c).—Hydrogen peroxide (2 drops; 30%) was added to a stirred solution of the indenone (100 mg) in acetic acid and stirring was continued until the starting indenone had reacted completely (t.l.c.). The reaction mixture was dissolved in chloroform and the solution was washed with water (5 × 50 ml), dried, concentrated, and chromatographed with chloroform as eluant. The major band contained the *sulphoxide* which was crystallised from chloroform–ether: (IXa) (71%), m.p. 151—152°; (IXb) (100%), m.p. 150—151°; and (IXc) (99%), m.p. 154—155°.

Reaction of 2-Phenyl-3-phenylthioinden-1-one with Lithium Methylsulphinylmethanide.—n-Butyl-lithium (5 ml; 15% in hexane) was added to dimethyl sulphoxide under nitrogen and the mixture was stirred for 0·5 h. 2-Phenyl-3-phenylthioindenone (0·559 g) was added and the solution was stirred overnight. The mixture was taken up in chloroform and acidified with dilute hydrochloric acid. The organic layer was washed successively with water, aqueous sodium carbonate, water, and a saturated solution of sodium chloride, and dried (Na_2SO_4). The solution was concentrated *in vacuo* and chromatographed. Separation of a yellow band near the base line gave 3-methylsulphinylmethyl-2-phenylindenone (IXa) (30 mg), m.p. 152—152·5°, identical (i.r. spectrum and mixed m.p.) with the sample obtained above.

We thank Professor E. M. Philbin for her interest in the work, and the Minister for Education, Republic of Ireland, and Kerry County Council for provision of grants (to D. O'S.).

[4/2024 *Received*, 1*st October*, 1974]