Oxopyrazoline-spiro-oxirans. A New Class of Reactive Heterocycles

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Chemical and spectral properties of a series of 1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-ones, synthesized by the oxidation of 4-alkylidene- or 4-arylidene-1-aryl-2-pyrazolin-5-ones are reported.

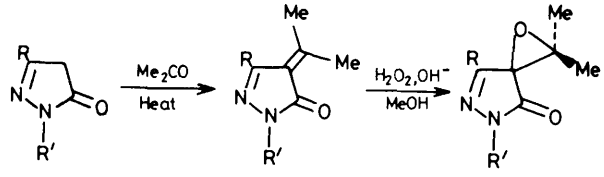
Experiments on the photochemical transformation of pyrazolidinones have led to the discovery of a novel heterocyclic ring system, the 1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-ones.[1] The synthesis and the chemistry of spiro-oxirans derived from oxygen, sulphur, and nitrogen heterocycles have been of interest for some time. The stereochemistry of the epoxidation of 2-arylmethylenecoumaran-3-ones (aurones),[2] 3-arylmethylene-flavones,[3] and of 2-arylmethylenebenzo[*b*]-thiophen-3(2*H*)-ones (thioaurones) [4] by various methods have been reported. Lactones of glycidic acids [5] and spiro-oxirans of 1-substituted-2-piperidones [6] and of pyrrolidine derivatives [7] have been used as intermediates in the syntheses of natural products. The labile antibiotic flavipucine is 6-methyl-2-(3-methyl-1-oxobutyl)-1-oxa-5-azaspiro[2.5]oct-6-ene-4,8-dione.[8] 1-Oxa-6-azaspiro[2.5]octane derivatives stabilized polymers [9] and colour in photographs [10] against light. Oxopyrroline-spiro-oxirans are reported to be products of the reaction of a pyrroline-2,3-dione with phenyl isocyanide [11] and of a porphyrin analogue with oxygen.[12]

An oxopyrazoline-spiro-oxiran, 2,2,7-trimethyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3a) is the major photoproduct when 5-methyl-2-phenyl-3-pyrazolidinone [13] is irradiated in acetone.[1] The observation that no pyrazolinone spiro-oxiran incorporating an aryl group on the oxiran ring can be isolated when the pyrazolidinone is irradiated in the presence of acetophenone suggested that such oxirans might be photolabile. This behaviour would be analogous to the photochemical instability of aryloxirans, which are known to undergo opening of the oxiran ring to give carbonyl ylides and to fragment to carbenes and carbonyl compounds.[14] Preliminary experiments have confirmed our expectation that oxopyrazoline-spiro-oxirans would have interesting photochemistry.[15] The synthesis and characterization of a series of these novel heterocyclic compounds, designed to probe the influence of structure on photochemical reactivity and on the nature of the reactive intermediates formed, is reported here.

Oxidation of the known 4-isopropylidenepyrazolinone (2a) [16] gave a spiro-oxiran (3a) identical with the photoproduct from the irradiation of 5-methyl-2-phenylpyrazolidin-3-one in acetone (Scheme 1). Analogous spiro-oxirans 2,2-dimethyl-5,7-diphenyl- (3b) and 2,2,7-trimethyl-5-*p*-methoxyphenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3c) were also prepared by similar reactions. Spectral and physical properties of the isopropylidenepyrazolinones (2) and of the oxirans (3) are reported in Tables 1 and 2.

Oxopyrazolin-spiro-oxirans (5) substituted with aryl groups on the oxiran ring (Table 2) are readily accessible from basic peroxide oxidation [17] of the corresponding 4-arylidenepyrazolinones (4) (Table 1) prepared by condensation of aldehydes with pyrazolinones (1) (Scheme 2).

The stereochemistry of arylidenepyrazolinones has been a subject of considerable study. Arylidenepyrazolinones (4a), (4b), (4e), and (4f), among others, have been assigned the *Z*-configuration by ^{1}H n.m.r. spectroscopy, and the proton data obtained for compounds (4) described in the present study (Table 1) are in good agreement with the data previously published.[18] Additional confirmation of the structure and stereochemistry of (4), however, is derived from analyses of the ^{13}C



(1) (2) (3)

a; R = Me, R' = Ph
b; R = Ph, R' = Ph
c; R = Me, R' = C_6H_4OMe-*p*

Scheme 1

Table 1. ^{1}H N.m.r. spectra of 4-alkylidene- or 4-arylidene-pyrazolinones

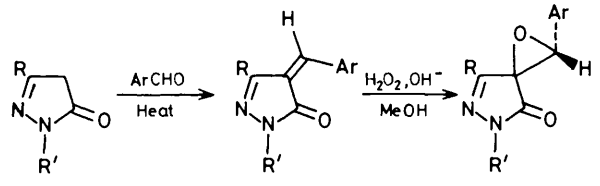
Compd.	δ ($CDCl_3$)
(2a) [a]	2.30 (s, 3 H), 2.35 (s, 3 H), 2.60 (s, 3 H), 7.2—7.9 (m, 5 H)
(2b) [b]	1.98 (s, 3 H), 2.68 (s, 3 H), 7.2—8.3 (m, 10 H)
(2c)	2.30 (s, 3 H), 2.33 (s, 3 H), 2.57 (s, 3 H), 3.77 (s, 3 H), 6.7—7.8 (m, 4 H)
(4a) [c]	2.15 (s, 3 H), 7.0—8.6 (m, 11 H)
(4b) [d]	6.2 (s, 1 H) and 8.1 (m, 15 H) [d]
(4c)	2.30 (s, 3 H), 3.78 (s, 3 H), 6.7—8.5 (m, 10 H)
(4d) [c]	(in CF_3CO_2H) 2.20 (s, 3 H), 7.0—8.2 (m, 10 H)
(4e) [e]	2.31 (s, 3 H), 7.27br (s, 1 H), 7.10—7.48 (m, 5 H), 7.95 (m, 2 H), 8.45 (m, 2 H)
(4f) [c]	2.29 (s, 3 H), 7.32br (s, 1 H), 7.01—7.56 (m, 5 H), 7.93 (m, 2 H), 8.45 (m, 2 H)
(4g) [f]	2.38 (s, 3 H), 7.52br (s, 1 H), 7.10—8.00 (m, 10 H), 8.58 (m, 1 H), 9.00 (m, 1 H)
(4h)	7.30—9.0 (m)
(4i) [g]	2.30 (s, 3 H), 3.88 (s, 3 H), 6.9—8.4 (m, 10 H)

[a] Ref. 17. [b] G. Desimoni, P. Righetti, G. Tacconi, and A. Vigliani, *Gazz. Chim. Ital.*, 1977, **107**, 91. [c] Ref. 18*a*. [d] Ref. 43. [e] V. P. Mamaev and M. A. Mikhaleva, *Chem. Heterocycl. Compd.*, 1967, **3**, 843. [f] B. P. Lugovkin, *J. Gen. Chem. USSR*, 1971, **41**, 2099.

Table 2. Physical data for oxopyrazoline-spiro-oxirans

Compd.	Method (Yield, %)	M.p. (°C), solvent *	δ ($CDCl_3$–$SiMe_4$)	Other spectral data M^+ and/or $\nu_{max.}/cm^{-1}$	Found (%) [Required (%)]
(3a)	A (76)	74.5—76, MeOH	1 65 (s, 3 H), 1.75 (s, 3 H), 2 15 (s, 3 H), 7.2—7.7 (m, 5 H)	*m/z* 230 ($CDCl_3$) 1 725	$C_{13}H_{14}N_2O_2$ C, 67.85; H, 6.05; N, 12.2 [C, 67 81; H, 6.13; N, 12.7]
(3b)	A (76)	117—118, EtOH	1.35 (s, 3 H), 1.80 (s, 3 H), 7.4—8.2 (m, 10 H)	$\nu_{max.}$ (KBr) 1 721	$C_{18}H_{16}N_2O_2$ C, 73.7; H, 5.55; N, 9.5 [C, 73.95; H, 5.52; N, 9.58]
(3c)	A (78)	116—117, hexane	1.66 (s, 3 H), 1.73 (s, 3 H), 2.14 (s, 3 H), 3.76 (s, 3 H), 6.7—7.7 (m, 4 H)	$\nu_{max.}$ (KBr) 1 716	$C_{14}H_{16}N_2O_3$ C, 64.35; H, 6.0; N, 10.5 [C, 64.60; H, 6.20; N, 10.76]
(5a)	B (47)	79.5—80, hexane	1.55 (s, 3 H), 4.70 (s, 1 H), 7.2—8.2 (m, 10)	$\nu_{max.}$ (KBr) 1 719	$C_{17}H_{14}N_2O_2$ C, 73.45; H, 5.15; N, 10.1 [C, 73.36; H, 5.07; N, 10.07]
(5b)	A (44)	167—178 (decomp.), MCH	4.80 (s, 1 H), 7.2—7.8 (m, 15 H)	*m/z* 340	$C_{22}H_{16}N_2O_2$ C, 77.7; H, 4.75; N, 8.25 [C, 77.63; H, 4.74; N, 8.23]
(5c)	A (18)	96—100, hexane–ether	1.50 (s, 3 H), 3.68 (s, 3 H), 4.73 (s, 1 H), 6.8—7.9 (m, 4 H), 7.4 (s, 5 H)	$\nu_{max.}$ (KBr) 1 712	$C_{18}H_{16}N_2O_3$ C, 70.25; H, 5.3; N, 9.15 [C, 70.11; H, 5.23; N, 9.09]
(5d)	A (52)	148—149.5, EtOAc	1.55 (s, 3 H), 4.80 (s, 1 H), 7.43 (s, 5 H), 8.18 (m, 4 H)	$\nu_{max.}$ (KBr) 1 726	$C_{17}H_{13}N_3O_4$ C, 63.1; H, 4.1; N, 12.95 [C, 63.15; H, 4.05; N, 13.00]
(5e)	A (78)	118—119, hexane	1.57 (s, 3 H), 4.74 (s, 1 H), 7.35 (m, 3 H), 7.42br (s, 4 H), 7.90 (m, 2 H)	$\nu_{max.}$ ($CHCl_3$) 1 712	$C_{17}H_{13}N_2O_2Cl$ C, 65.2; H, 4.1; N, 8.85 [C, 65.29; H, 4.19; N, 8.95]
(5f)	A (30)	151—153, toluene–hexane	1.56 (s, 3 H), 4.83 (s, 1 H), 7.10—7.6 (m, 5 H), 7.90 (m, 2 H), 8.20 (m, 2 H)	$\nu_{max.}$ (KBr) 1 720	$C_{17}H_{13}N_3O_4$ C, 63.15; H, 3.95; N, 12.9 [C, 63.15; H, 4.05; N, 13.00]
(5g)	A (63)	140—141 MCH	1.46 (s, 3 H), 4.88 (s, 1 H), 7.1—7.8 (m, 12 H)	*m/z* 328	$C_{21}H_{16}N_2O_2$ C, 76.85; H, 5.05; N, 8.5 [C, 76.81; H, 4.91; N, 8.53]
(5h)	A (54)	150—168 (decomp.) MCH	4.82 (s, 1 H), 6.7—7.9 (m, 17 H)	*m/z* 390	$C_{26}H_{18}N_2O_2$ C, 79.8; H, 4.7; N, 7.0 [C, 79.98; H, 4.65; N, 7.17]
(8)	A (56)	167—168 (decomp.) MCH–benzene (19 : 1)	2.50 (s, 6 H), 7.3—7.9 (m, 10 H)	*m/z* 360	$C_{20}H_{16}N_4O_3$ C, 66.85; H, 4.55; N, 15.6 [C, 66.66; H, 4.48; N, 15.55]

* MCH = methylcyclohexane.



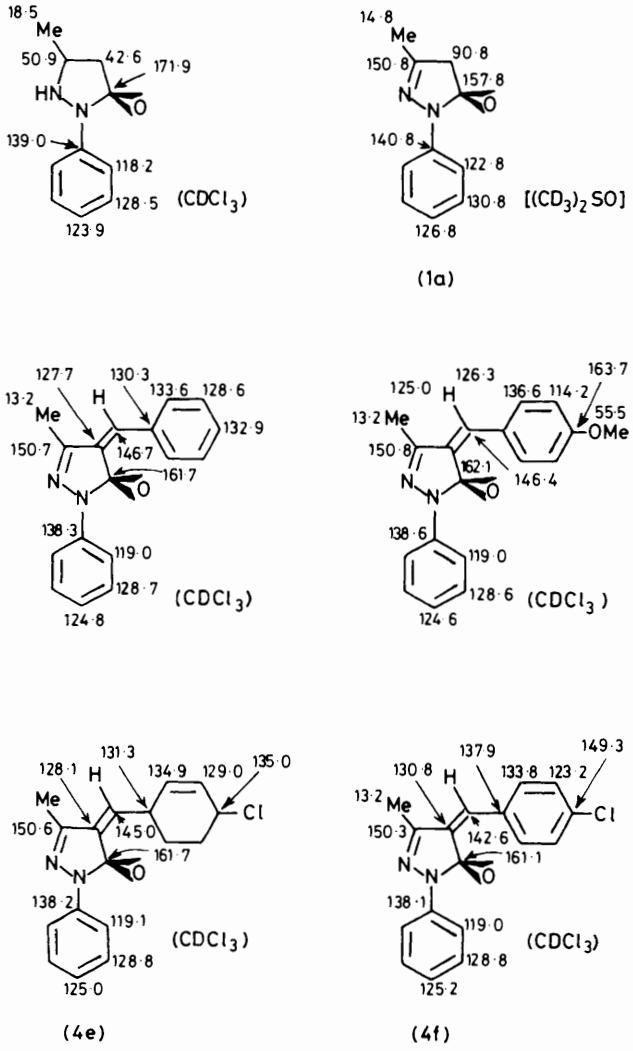
(1) (4) (5)

a; R = Me, R' = Ph, Ar = Ph
b; R = Ph, R' = Ph, Ar = Ph
c; R = Me, R' = C_6H_4OMe-*p* Ar = Ph
d; R = Me, R' = $C_6H_4NO_2$-*p* Ar = Ph
e; R = Me, R' = Ph Ar = C_6H_4Cl-*p*
f; R = Me, R' = Ph, Ar = $C_6H_4NO_2$-*p*
g; R = Me, R' = Ph, Ar = 2-naphthyl
h; R = Ph, R' = Ph, Ar = 2-naphthyl

Scheme 2

n.m.r. data summarized in Scheme 3 for the pyrazolinones (4a), (4e), (4f), and (4i; R = Me, R^1 = Ph, Ar = C_6H_4Me-*p*) and reference compounds 5-methyl-2-phenylpyrazolidin-3-one [19] and pyrazolinone (1a).[20] The assignments made are based on chemical-shift trends throughout the series as well as related to the reference compound shown at the top of Scheme 3. The assignments are confirmed by analysis of the off-resonance decoupled and/or undecoupled ^{13}C spectra for (4a), (4e), (4f), and (4i). In general, the chemical shifts for the pyrazolinone portion of each molecule, including the *N*-phenyl moiety, vary only slightly throughout the series, but *qualitatively* reflect the perturbation of electron density in the π system created by the *para*-substituent on the aryl ring of the arylidene group. The sp^2 carbon atom that is α to the carbonyl group of the pyrazolinone ring, and that may be viewed as the β-carbon atom of a substituted styrene, correlated well with σ^+ (see Figure).[21] Chemical shifts for the ring carbon atoms of the aryl ring in the arylidene system are assigned by process of elimination and substantiated by calculation using the additivity of the substituent chemical shifts.

An examination of the long-range ^{13}C–^1H coupling constants between the vinylic proton and the carbon atoms of the carbonyl and azomethine groups, respectively, of the pyrazolinone ring in (4a), (4e), (4f), and (4i) (Table 3) shows that the vinylic hydrogen atom is coupled to the carbon atom of the carbonyl group with the larger of the two coupling constants. This observation is consistent with a *trans*-orientation [22] of the hydrogen atom to the carbonyl group and provides additional confirmation of the *Z*-configuration of the exocyclic double bond in arylidene compounds (4). Isomerization



Scheme 3

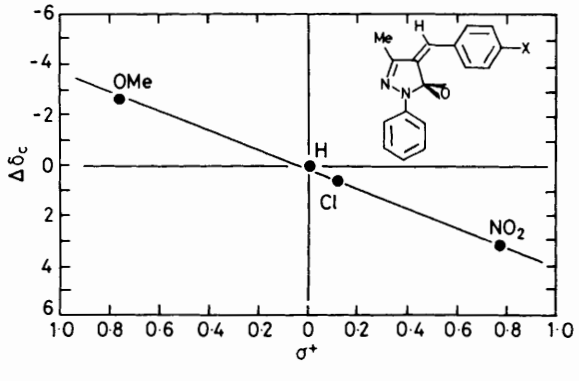


Figure. Plot of σ^+ against the difference in chemical shift of carbon 4 of the pyrazolinone ring for a series of *para*-substituted 4-arylidenepyrazolinones

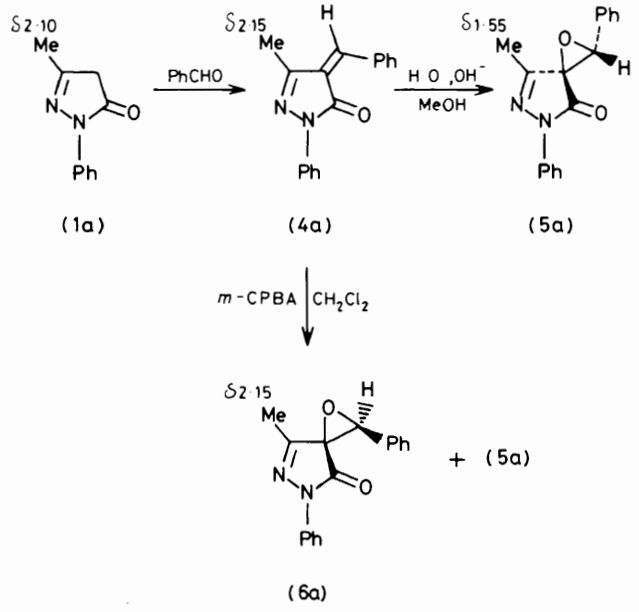
of arylidenepyrazolinones in solution has been detected by i.r. and u.v. spectroscopy.[23]

Arylidenepyrazolinone (4a) gives essentially a single oxiran when oxidized with basic hydrogen peroxide. When (4a) is allowed to stand with *m*-chloroperoxybenzoic acid, a mixture of two stereoisomeric oxirans is obtained, one of which is

Table 3. The long-range ^{13}C-^1H coupling constants for representative arylidenepyrazolinones [a]

Compound	$^3J_{C=O,H}$	$^3J_{C=N,H}$
(4a)	11.0	7.3
(4e)	11.6	7.7
(4f)	11.0	7.5
(4i)	11.0	7.4

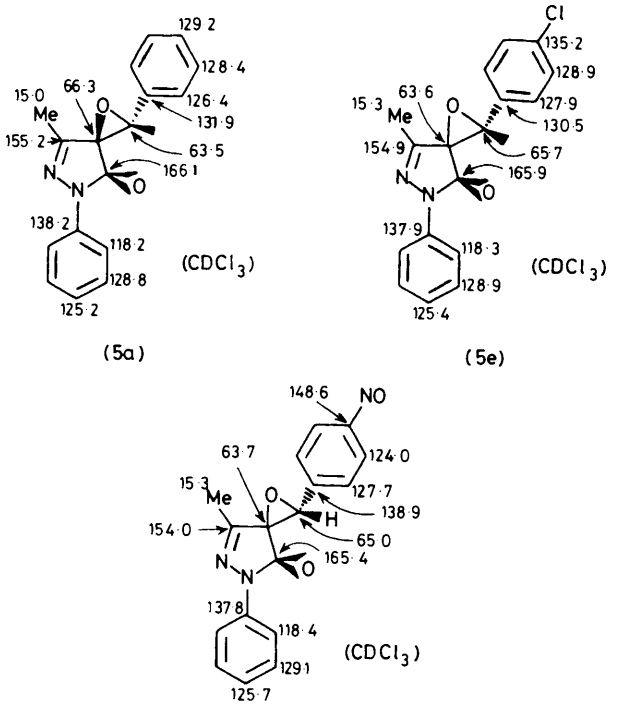
[a] Spectra obtained in $CDCl_3$ at 32 °C.



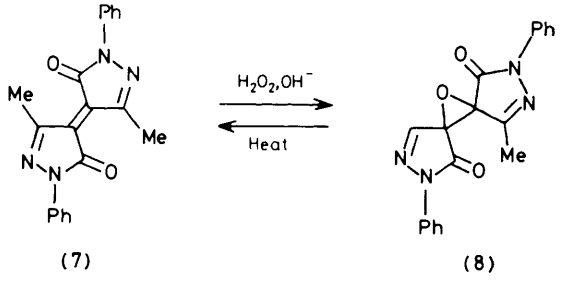
Scheme 4

identical with the product from the peroxide oxidation. The oxiran (5a) has been assigned the stereochemistry shown in Scheme 4 on the basis of the upfield shift of the singlet for the methyl group of this compound (δ 1.55) created by the shielding anisotropy of the *syn* phenyl ring, relative to the signal for the methyl group in pyrazolinone (1a) (δ 2.10), arylidenepyrazolinone (4a) (δ 2.15) and in the isomeric oxiran (6a) from the peroxy-acid oxidation (δ 2.15), where the phenyl ring is *anti* to the methyl group. An *X*-ray crystallographic structure determination of oxiran (5e) has confirmed this stereochemical assignment.[24] Thus basic peroxide oxidation of the enone system in (4a) proceeds as predicted with a rotation of the phenyl group on the β-carbon atom away from the carbonyl group to minimize adverse steric interactions and to allow orbitals of the carbonyl group to overlap with those of the carbanionic centre at carbon-4 during the closure of the oxiran ring.[25,2a] The two stereoisomeric oxirans formed in the relatively slow reaction with peroxy-acid arise from the stereospecific oxidation [26] of enones of differing configuration present in solution.[23]

^1H N.m.r., as well as other spectroscopic, data for the oxirans (5) are given in Table 2. Further confirmation of structure for the spiro-oxirans (5a), (5e), and (5f) is derived from analysis of their ^{13}C n.m.r. spectra. These data are summarized in Scheme 5. As with the spectra of the arylidenepyrazolinones, assignment of the signals for the carbon atoms was performed in a self-consistent manner. The oxiran carbons, especially, are readily assigned on the basis of chemical shift and relative intensities of the two signals in the proton



Scheme 5

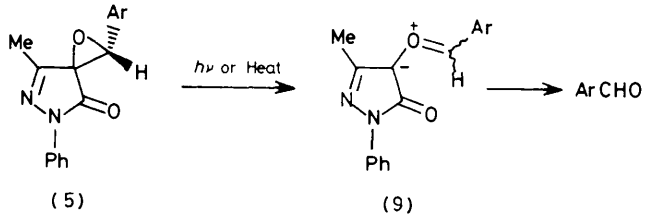


Scheme 6

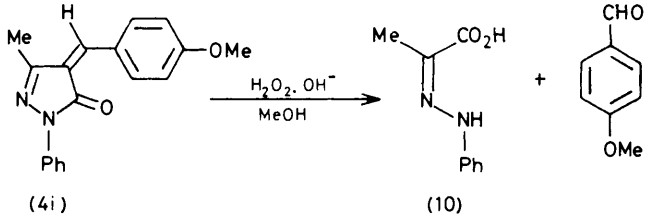
noise-decoupled spectra and confirmed by the results of resonance single-frequency-off-resonance decoupling.

In addition to the spiro-oxirans described above, the pale yellow symmetrical spiro-oxiran (8) has been synthesized from the intensely blue 3,3′-dimethyl-1,1-diphenyl-4,4′-bi-2-pyrazoline-5,5′-dione (7), also known as Pyrazole Blue [13,27] (Scheme 6). Pyrazole Blue oxide (8) reverts on melting to Pyrazole Blue, a deoxygenation reaction that has been induced photochemically [14] as well as thermally [28-30] in other oxirans. For example, *trans*-2,3-diphenyloxiran, upon irradiation in a matrix of 3-methylpentane at −196 °C is partially converted into (*E*)-1,2-diphenylethene.[14] Matrix viscosity experiments provided evidence that the alkene arises from a loss of oxygen from the oxiran and is not the product of the combination of two phenylmethylene fragments, also formed upon photolysis.[14]

Thermal deoxygenation reactions of possible biological significance have been observed for oxirans such as arene oxides, intermediates in the metabolism of polycyclic aromatic hydrocarbons, that have been implicated in mutagenesis and carginogenesis.[28] Arene oxides undergo deoxygenation reactions at room temperature in the presence of nitrogen and



Scheme 7



Scheme 8

sulphur compounds.[29] Deoxygenation also occurs upon heating 9,10-epoxy-9,10-dihydrophenanthrene to 200 °C.[30]

Pyrazole Blue oxide (8) decomposes on prolonged heating (6 h) in refluxing toluene or xylene, but Pyrazole Blue, the expected deoxygenation product, cannot be detected in the resulting mixture. By contrast, deoxygenation occurs within minutes when (*E*)-1,2-diphenylethene is added to a solution of (8) in toluene under reflux. As far as can be determined by t.l.c., *trans*-2,3-diphenyloxiran is not formed during the course of this reaction, which is currently being investigated in more detail.

Another type of thermal instability is observed for some of the spiro-oxirans (5), which fragment during isolation to lose an aryl aldehyde. For example, the odour of benzaldehyde is discernible during the work-up of the spiro-oxiran (5a), and benzaldehyde is detected by ^{1}H n.m.r. spectroscopy in the mixture obtained when (5a) is refluxed in toluene for 11 h (peak at δ 9.9, enhanced by the addition of benzaldehyde). A carbonyl ylide, such as (9), known to form upon thermal [31] as well as photochemical [14,15] opening of oxiran rings is postulated to be the intermediate in the formation of the aldehyde (Scheme 7). The likelihood that such an intermediate is involved is supported by our inability to isolate an oxiran when 4-*p*-methoxybenzylidenepyrazolinone (4i) [32] is oxidized with basic hydrogen peroxide. This reaction gives instead *p*-methoxybenzaldehyde and the phenylhydrazone of pyruvic acid (10) [33] (Scheme 8). Facile cleavage of the carbon–carbon bond of the oxiran would be expected in this case because of the stabilization of the resulting dipolar ion by the *p*-methoxy-group. Our earlier photochemical work [15] has shown that the carbonyl ylide (9) reacts with nucleophilic solvents such as water (or methanol) to give aldehydes (or acetals) and 3-methyl-1-phenyl-4,5-dihydroxypyrazole.[34] We have shown that 3-methyl-1-phenyl-4,5-dihydroxypyrazole is converted into the phenylhydrazone of pyruvic acid (10) under the conditions used to oxidize 4-*p*-methoxybenzylidenepyrazolinone (4i). The conversion most likely proceeds by oxidation of the dihydroxypyrazole to 3-methyl-1-phenyl-2-pyrazoline-4,5-dione,[35,34c] which is known to undergo ring opening in alkali to give the 3-phenylhydrazone of 2,3-dioxobutanoic acid,[7a] a compound that would be expected to be oxidatively decarboxylated in basic hydrogen peroxide [36] to (10).

The oxidation of pyrazolinone (1a) in basic peroxide also is

reported to give (10).[37] *p*-Methoxybenzylidenepyrazolinone (4i) does not fragment to give (1a) to a significant extent under the conditions employed in the oxidation reaction excluding the possibility that *p*-methoxybenzaldehyde and (10) are obtained as a result of a retro-aldol reaction of (4i).

Of the pyrazolinone-spiro-oxirans that have been tested, (3a), (3b), (3c), (5a), (5c), and (5f), all except (3b) react as oxidising agents toward a solution of potassium iodide in acetic acid as evidenced by a positive starch–iodine test. The oxiran with a *p*-nitrophenyl group on the oxiran ring, (5f), as well as (3c), are the most reactive, giving the test at room temperature, while the others require heating. The reaction product in the case of the oxiran (3c) was found by t.l.c. and by isolation of the alkene to be the isopropylidenepyrazolinone (2c). Similar deoxygenations of oxirans to alkenes using sodium iodide in acetic acid to prepare an iodohydrin, which is then reduced with stannous chloride in hydrochloric acid, have been reported.[38] To our knowledge, however, oxirans have not been reported to oxidize iodide ion in acetic acid, especially at room temperature, though this behaviour is well known for oxaziridines.[39] The reaction presumably proceeds by the formation of an iodohydrin as an intermediate followed by an elimination promoted by iodide ion.[40]

The experimental work reported here, as well as the photochemistry described in our preliminary communication,[15] have established oxopyrazoline-spiro-oxirans as a class of heterocycles that have thermal as well as photochemical lability. Our failure to isolate an oxopyrazoline-spiro-oxiran containing a *p*-methoxyphenyl group on the oxiran ring is particularly interesting in light of the preparation of a number of *p*-methoxyphenylspiro-oxirans of other heterocyclic systems such as the aurones [2a] and flavones.[3a] We continue to explore the chemical and photochemical consequences of the interaction of the pyrazolinone ring with a spiro-oxiran system.

Experimental

General.—^{1}H N.m.r. spectra were obtained on a Varian A-60 and T-60, Hitachi Perkin-Elmer R-20B spectrometer, or JEOL FX-90Q or FX-100 spectrometer, which was also used for ^{13}C n.m.r. spectra. I.r. spectra were recorded on a Perkin-Elmer 237 or 337 grating spectrophotometer. Mass spectral studies were conducted using a Hitachi Perkin-Elmer RME-6E spectrometer or an MS-902 high-resolution instrument.

M.p.s were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Solutions were concentrated on a Büchi rotating evaporator under vacuum. Eastman chromagram sheets (silica gel) were used for t.l.c. and silica gel 60 (PF 254, E. Merck) was employed for thick-layer separations. Woelm neutral alumina, grade II, packed in benzene, was used for column chromatography. Microanalyses for C, H, and N were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee, or Spang Microanalytical Laboratory, Eagle Harbor, Michigan. Spectral data for the compounds prepared in this work, as well as melting points, yields, and analytical data for the new spiro-oxirans, are recorded in Tables 1, 2, and 3.

General Procedure for the Preparation of Oxopyrazoline-spiro-oxirans.—The 4-arylidene (or alkylidene) pyrazolinone (*ca.* 2—4 mmol) was suspended in methanol (25 ml). A solution of hydrogen peroxide (30%, 7–10 ml) was added to the stirred suspension, followed by a solution of sodium hydroxide (10%, *ca.* 0.5 ml).[17]

Method A. As soon as the coloured suspension of the original pyrazolinone was converted into a white precipitate, the mixture was filtered. The crude spiro-oxiran was washed with methanol (*ca.* 5 ml), dried, and recrystallized.

Method B. Spiro-oxiran (5a), which is soluble in the reaction mixture described under Method A, was isolated by dilution of the methanol solution with water, and extracted twice with ether. The ether layer was dried over magnesium sulphate, filtered, and the solvent removed under reduced pressure. The residue was purified by recrystallization from hexane.

Preparation of 4-*Isopropylidene*-1-p-*methoxyphenyl*-3-*methyl*-2-*pyrazolin*-5-*one* (2c).—1-*p*-Methoxyphenyl-3-methyl-2-pyrazolin-5-one (1c) was prepared [41] from *p*-methoxyphenylhydrazine hydrochloride [42] and diketen (Aldrich, 50% in acetone, isolated by vacuum distillation); δ ($CDCl_3$) 2.15 (s, 3 H), 3.32 (s, 2 H), 3.78 (s, 3 H), and 6.8—7.7 (m, 4 H). When warmed with acetone, (1c) gave the isopropylidenepyrazolinone (2c) as yellow needles, m.p. 170—171 °C (hexane) (Found: C, 68.85; H, 6.5; N, 11.35. Calc. for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47).

m-*Chloroperoxybenzoic Acid Oxidation of the Benzylidene-pyrazolinone* (4a).—A solution of 4-benzylidene-3-methyl-1-phenyl-2-pyrazolin-5-one (4a) (3.93 g, 0.016 mol) and *m*-chloroperoxybenzoic acid (3.22 g, Aldrich, 85%, 0.016 mol) in dichloromethane (90 ml) was allowed to stand for a week at room temperature. The solution was decanted from crystals of *m*-chlorobenzoic acid and worked up by washing sequentially with solutions of sodium thiosulphate and sodium hydrogencarbonate, and with water. The organic layer was dried over magnesium sulphate. The oil obtained after removal of the solvent was separated by chromatography into two stereoisomeric spiro-oxirans assigned structure (6a) (135 mg, eluted with benzene), δ ($CDCl_3$) 2.15 (s, 3 H), 4.50 (s, 1 H), and 7.2—8.0 (m, 10 H) and (5a) (759 mg, eluted with benzene–ether, 95 : 5), along with intermediate fractions containing both compounds (350 mg).

The major steroisomer (5a), however, is more conveniently prepared by oxidation of the benzylidenepyrazolinone (4a) by Method B.

Preparation of 1-p-*Methoxyphenyl*-4-*benzylidene*-3-*methyl*-2-*pyrazolin*-5-*one* (4c).—A mixture of the pyrazolinone (1c) [41] (0.82 g, 3.9 mmol) and benzaldehyde (0.53 g, 5.0 mmol) was heated to 130 °C for 30 min using two boiling sticks to assist in the evolution of water. Dilution with an equal volume of methanol of the red syrup that resulted gave 1-p-*methoxyphenyl*-4-*benzylidene*-3-*methyl*-2-*pyrazolin*-5-*one* as red crystals (0.54 g, 47%), m.p. 86—87.5 °C (ethanol, drop of acetic acid) (Found: C, 74.0; H, 5.5; N, 9.55. Calc. for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58%).

Preparation of 1,3-*Diphenyl*-4-(2-*naphthylidene*)-2-*pyrazolin*-5-*one* (4h).—The pyrazolinone (1b) [43] (3.50 g, 0.015 mol) was heated to 160 °C with 2-naphthaldehyde (2.50 g, 0.016 mol, Aldrich) for 1 h. The naphthylidenepyrazolinone (4h) (3.32 g, 59%) was obtained as dark-red crystals, m.p. 136—137 °C (ethanol–acetone, 19 : 1), *m/z* 374 (M^+) (Found: C, 83.25; H, 4.9; N, 7.5. Calc. for $C_{28}H_{18}N_2O$: C, 83.40; H, 4.85; N, 7.48%).

Pyrolysis of Pyrazole Blue Oxide (8).—Pyrazole Blue oxide (8) (0.30 g, 0.83 mmol) was heated in a test tube in an oil-bath at 175 °C for 0.2 h. The dark brown mass that resulted was triturated with methanol (3 ml) and Pyrazole Blue (7) was collected on a filter (0.19 g, 66%), m.p. 241—242 °C (lit.,[27] m.p. 230 °C), *m/z* 344 (M^+).

Thermal Decomposition of Pyrazole Blue Oxide (8) *in Toluene or Xylene.*—Pyrazole Blue oxide (8) (0.30 g, 0.83 mmol) was dissolved in toluene or xylene (4 ml). The solutions were

heated under reflux for 6 h, and the resulting dark-brown solutions analyzed by t.l.c. (benzene) for the presence of Pyrazole Blue (7), which was not detected. All attempts to isolate other components by chromatography failed.

In contrast, when (*E*)-1,2-diphenylethene (0.30 g, 1.66 mmol) was added to a solution of Pyrazole Blue oxide (0.30 g, 0.83 mmol) in toluene (4 ml), the solution turned a deep blue within minutes after reflux was initiated. After 2 h at reflux temperature, the dark-blue mixture was cooled, and the precipitate collected on a filter, washed with toluene, and dried *in vacuo* for 6 h to give Pyrazole Blue (7) (0.13 g, 45%), m.p. 241—242 °C (lit.,[27] m.p. 230 °C), *m/z* 344 (M^+).

trans-2,3-Diphenyloxiran was not detected in the filtrate by t.l.c. (benzene) analysis. Preparative layer chromatography (benzene) of the residue isolated after the evaporation of the solvent provided (*E*)-1,2-diphenylethene (0.21 g, 70% recovery).

Thermal Fragmentation of the Spiro-oxiran (3a).—The spiro-oxiran (3a) (290 mg) was refluxed in moist toluene (20 ml) under nitrogen for 11 h. Drying of the solution and removal of the solvent gave an oil, δ ($CDCl_3$) 9.9; peak enhanced by the addition of benzaldehyde to the sample.

Oxidation of the 4-p-*Methoxybenzylideneoxopyrazoline* (4i).—4-*p*-Methoxybenzylidenepyrazolinone (4i) (1.0 g, 0.0034 mol), prepared from (1a) and *p*-anisaldehyde,[32] was suspended in methanol (20 ml) treated with hydrogen peroxide (30%; 2 ml) and sodium hydroxide (6M; 6 drops). A clear, yellow solution resulted. Dilution with water (50 ml) gave an oil which was extracted into ether. Removal of ether after washing with saturated sodium chloride solution and drying over magnesium sulphate resulted in an oil (770 mg) of which *ca.* 60% was *p*-methoxybenzaldehyde by n.m.r. δ ($CDCl_3$) 3.80 (s), 6.8—8.0 (m), and 9.8 (s).

Acidification with concentrated hydrochloric acid of the aqueous layer from the extraction gave a yellow precipitate (140 mg), which was identified as the phenylhydrazone of pyruvic acid (10), yellow crystals, m.p. 178—179 °C (decomp). (ethanol)] m.p. of an authentic sample [33] 182 °C (decomp.) (ethanol)]. δ [$(CD_3)_2SO$] 2.0 (s, 3 H), 6.6—7.4 (m, 6 H), and 9.7 (s, 1 H); [$(CD_3)_2SO$ with added D_2O] δ 2.0 (s, 3 H) and 6.6—7.4 (m, 5 H). Microanalysis correct for $C_9H_{10}N_2O_2$.

Because of reports in the literature [37] that the pyrazolinone (1a) is oxidized by basic hydrogen peroxide to the phenylhydrazone (10), 4-*p*-methoxybenzylidenepyrazolinone (4i) (1.0 g, 0.0034 mol) in methanol (20 ml) was subjected to the basic conditions (6M-NaOH, 4 drops, pH 9—10) present during the oxidation reaction above to ensure that it did not undergo a retro-aldol reaction to give the pyrazolinone (1a) and *p*-methoxybenzaldehyde. No significant decomposition of (4i) was observed.

Pyruvic Acid Phenylhydrazone (10) *from the Oxidation of* 3-*Methyl*-1-*phenyl*-4,5-*dihydroxypyrazole*.—3-Methyl-1-phenyl-2-pyrazoline-4,5-dione [34c,35] (104 mg) was dissolved in methanol (15 ml) to give a deep purple solution. The colour was discharged to a pale yellow by the addition of a few mg of sodium borohydride under a stream of nitrogen, and the solution acidified instantly to pH 6 with 50% aqueous acetic acid. Upon reduction of the volume of the solution under reduced pressure and cooling, white crystals of 3-methyl-1-phenyl-4,5-dihydroxypyrazole (38 mg), m.p. 188—195 °C (decomp.) (lit.,[34] m.p. 190 °C) were obtained.

A suspension of the dihydroxypyrazole in methanol (5 ml) was treated with sodium hydroxide (1M; 3 drops) and hydrogen peroxide (30%; 5 drops), and acidified with concentrated hydrochloric acid. Dilution of the solution to twice its volume with water, cooling, and scratching gave yellow crystals, m.p. 184—185 °C (decomp.), m.p. of authentic sample of (10) [33] taken simultaneously 188—190 °C (decomp.).

Reaction of Spiro-oxirans with Potassium Iodide in Acetic Acid.—The spiro-oxiran being tested (2 mg) was dissolved in glacial acetic acid (10 drops). Potassium iodide (12 drops; 5% aqueous solution) and starch indicator (2 drops) were then added. The spiro-oxirans (3c) and (5f) gave an immediate colour at room temperature. Those that did not react immediately at room temperature were heated after the addition of more acetic acid (15 drops) to restore homogeneity to the solution. The oxirans that responded on heating were, in order of reactivity, (3a), (5c), and (5a). The oxiran (3b) did not react even after 20 min of heating to boiling.

The reaction was carried out on a larger scale with the oxiran (3c). When (3c) (0.25 g, 1 mmol) in acetic acid (10 ml) was treated with potassium iodide (0.33 g, 2 mmol, in 1 ml of water), the colour of iodine was immediately visible. When a small sample was diluted with water, extracted with chloroform, and inspected by t.l.c. (ether), the presence of both the oxiran (3c) and the isopropylidene compound (2c) was clearly visible. Excess of potassium iodide (2.50 mg) was added to the flask, and it was allowed to stand overnight. Filtration of the reaction mixture gave (2c) (125 mg, 53% recovery, m.p. 172—173 °C).

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