Ring Expansion of 3-Acetylcoumarin by Diazoethane: Lactones Derived from Oxepin, Oxocin, and Oxonin

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Diazoethane partly alkylates 3-acetylcoumarin giving 3-acetyl-4-ethylcoumarin, and partly expands the lactone ring giving, after addition of a second molecule of diazoethane, the benzoxepinopyrazoline (IX) as a racemate of assigned stereochemistry. This compound readily loses nitrogen and undergoes a second ring expansion to form the benzoxocin derivative (XII) as a single (racemic) stereoisomer. Treatment of (XII) with diazoethane induces immediate ring expansion giving the benzoxonin derivative (XIII), again as a single (racemic) stereoisomer. There is no further reaction with diazoalkanes, notwithstanding the presence of a highly activated double bond: the resistance is attributed to the internal compression that would result within a highly convoluted molecule if addition occurred.

The structures and conformations of the foregoing products and of some by-products have been established by spectroscopic methods. Additionally, the benzoxocin derivative (XII) has been shown to yield *meso*-dimethylsuccinic acid upon exhaustive ozonolysis, and a convenient method is described for the preparation of small amounts of dimethylmaleic anhydride by the reaction of diazomethane with methylmaleic anhydride.

A parallel is drawn between these reactions and certain of those found with quinone–diazoalkane adducts, and it is suggested that ring expansions are observed because the methyl group introduced with the diazoethane molecule forces the pyrazoline into the necessary conformation.

DURING our studies on the quinone (I) we examined the adducts (II; R = H, Me, or Et) formed by addition of the appropriate diazoalkanes and showed that in all cases thermolysis in benzene supplied nitrogen and an alkylated quinone (III; R = H, Me, or Et). The higher homologues also supplied substantial amounts of tropolones which had resulted from ring expansion to cycloheptane derivatives (IV; R = Me or Et) followed by enolisation.[1] Extension of this study to 3-acetylcoumarin (V; R = H) and diazoethane shows that the activated system is comparable to that in the quinone (I) and that similar reactions ensue. In this case, however, ring expansion provides a lactone (VI) in which the activated system has been regenerated and is not lost by enolisation, so that repeated ring expansion is possible. As there are few methods for synthesising complex lactones of intermediate ring sizes we have followed the process as far as a ring of nine members, where it stops abruptly.

As is known already,[2,3] diazomethane merely alkylates 3-acetylcoumarin giving (V; R = Me). Though the intermediate adduct (VII; R = H) is not observable, results from our own and other laboratories [2,4,5] establish that such a pyrazoline must be formed and must collapse spontaneously. Moreover, Danion-Bougot and Carrié have prepared the ester (VIII) corresponding to the lactone (VII; R = H) and shown it to be thermally unstable.[6] Thus the parallel with the quinone series is exact.

The parallel holds for the reaction with diazoethane also. Again the pyrazoline (VII; R = Me) escaped detection. One product was the alkylated coumarin (V; R = Et). The other must have been the seven-membered lactone (VI) but, since diazoethane was used in excess, only the adduct (IX) was actually isolated. Observations by Hamelin and Carrié [4b] in another series suggest that a second adduct, epimeric at position 3, might have been formed, but we did not notice it; however, formation of this epimer is sterically less favourable than formation of (IX), so that only small amounts would be expected, and these might well have been overlooked or lost by spontaneous decomposition giving some of the by-products noted.

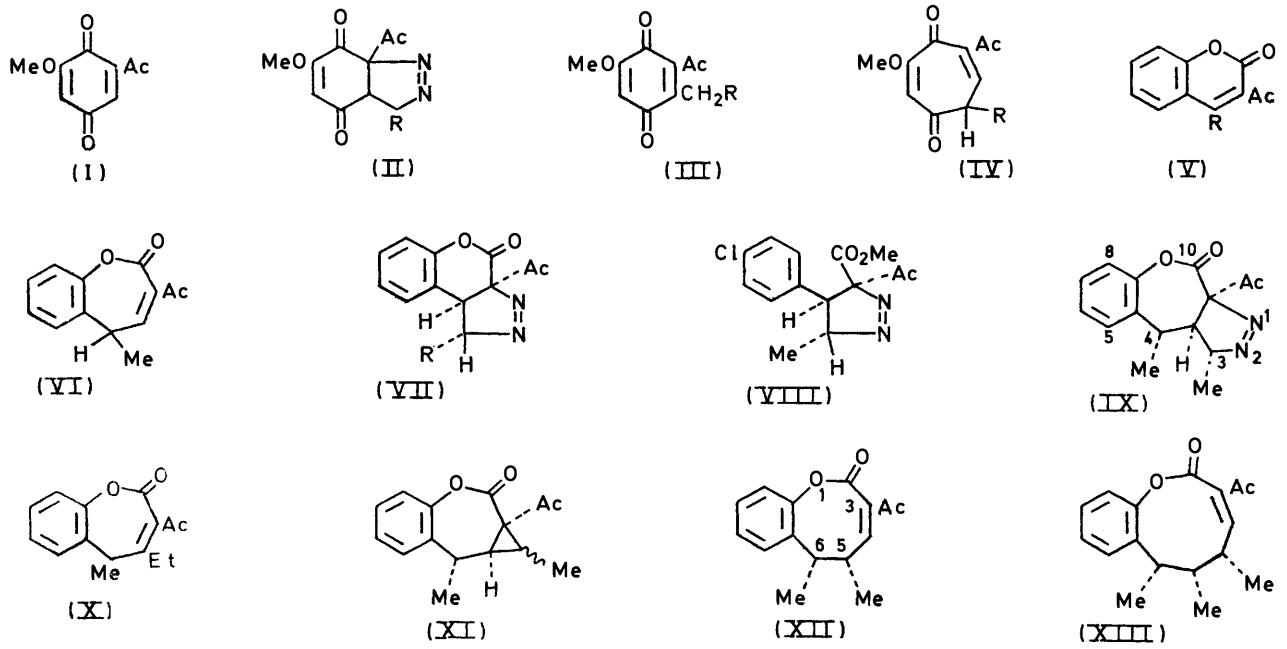
One by-product is the ethylated oxepin derivative (X). A second contains a cyclopropane ring (another parallel with the quinone series) and has structure (XI); it was difficult to separate from a contaminant that may have been a stereoisomer.

The pyrazoline (IX) is unstable and rapidly decomposes in the presence of protic solvents or of silica giving a mixture of the oxepin (X), the cyclopropane (XI), and the oxocin derivative (XII) resulting from a new ring expansion. Much better yields of this oxocin derivative were obtained by thermolysis of the pyrazoline in benzene, and since the activated system is once again regenerated it was possible to continue the process. Diazoethane reacted rapidly with the oxocin derivative (XII) and again no pyrazoline was noted; the only product isolated was the desired oxonin derivative (XIII). Though this still contains the requisite activated system it does not react further with either diazomethane or diazoethane in excess even after relatively prolonged exposure and homologation could not be continued beyond this point.

In assigning structures and stereochemistry to the compounds discussed it is necessary to consider the conformation of the ester group. Studies on relatively simple esters and lactones show that the ester group takes up the *s-cis*-configuration unless constrained by the ring containing it to take up the *s-trans*-configuration;

[1] F. M. Dean, P. G. Jones, R. B. Morton, and P. Sidisunthorn, *J. Chem. Soc.*, 1964, 411.
[2] R. Clinging, F. M. Dean, and L. E. Houghton, *J. Chem. Soc.* (*C*), 1970, 897.
[3] H. Junek and W. Wilfinger, *Monatsh.*, 1970, **101**, 1123.
[4] J. Hamelin and R. Carrié, *Bull. Soc. chim. France*, (*a*) 1968, 3000; (*b*) 1972, 2054.
[5] H. Kisch, O. E. Polansky, and P. Schuster, *Tetrahedron Letters*, 1969, 805.
[6] R. Danion-Bougot and R. Carrié, *Bull. Soc. chim. France*, 1968, 2526.

in either case the ester group is planar.[7-11] Consequently, it is now usual to assume that the ester group is always planar. Into some of our compounds a planar ester function cannot reasonably be fitted, and we have to consider how much twisting is allowable. Polarisation and electron diffraction studies suggest that esters (lactones) do have some flexibility, with the planar arrangement at an energy minimum.[8,12,13] I.r. spectra



often signal the situation of a carbonyl group and some simple lactones have been examined;[14,15] but the method fails here because the carbonyl group is also affected by conjugation with adjacent ethylenic bonds, and the ether oxygen atom by conjugation with the benzene ring; and these effects are themselves subject to modification by twisting. In what follows we assume that the ester (lactone) function is *s-trans* and more or less planar with angles of twist of less than 30°. We have noted lactonic carbonyl frequencies varying between 1760 and 1708 cm^{-1} but refrain from attempting to explain them.

The i.r. spectrum of the pyrazoline (IX) indicates the presence of saturated lactonic and ketonic carbonyl groups and of an azo linkage. The n.m.r. spectrum (Table) confirms the presence of two secondary methyl groups, and the splitting patterns together with the results of decoupling experiments leave no doubt that the molecule contains the proton sequence depicted in diagram (XIV), where H_c is certainly adjacent to the azo link because of the low field at which it resonates. The shape of the molecule is determined largely by the *cis* fusion between the heterocyclic rings as demanded by the 1,3-dipolar cycloaddition and by the planar ester function so that the lactone ring adopts a boat conformation. Diagram (XV) shows this with the pyrazoline ring *exo*. Diagram (XVI) shows the pyrazoline ring *endo*; this arrangement is ruled out because it is relatively constricted and because it dictates for the torsion angle defined by H_a and H_b a value near 60°, whereas J_{ab} is 12 Hz, indicative of a torsion angle near to 180°. This angle is possible for the *exo*-conformation (XV) with the benzylic methyl group in the pseudoequatorial position it is allotted in the diagram. The pyrazoline methyl group can now be placed as shown in the same diagram because in the alternative site it comes within 2·6 Å of the other and the addition reaction would certainly avoid so close an approach, at any rate for the major product; where diazoethane additions are known to occur in both senses there is no comparable collision.[4b] The coupling constant J_{bc} is 8·5 Hz, but while this value agrees well with those for *trans*-protons in similar pyrazolines[4b,16] it is not reliably diagnostic by itself because the *cis*-coupling constants are near 7 Hz.

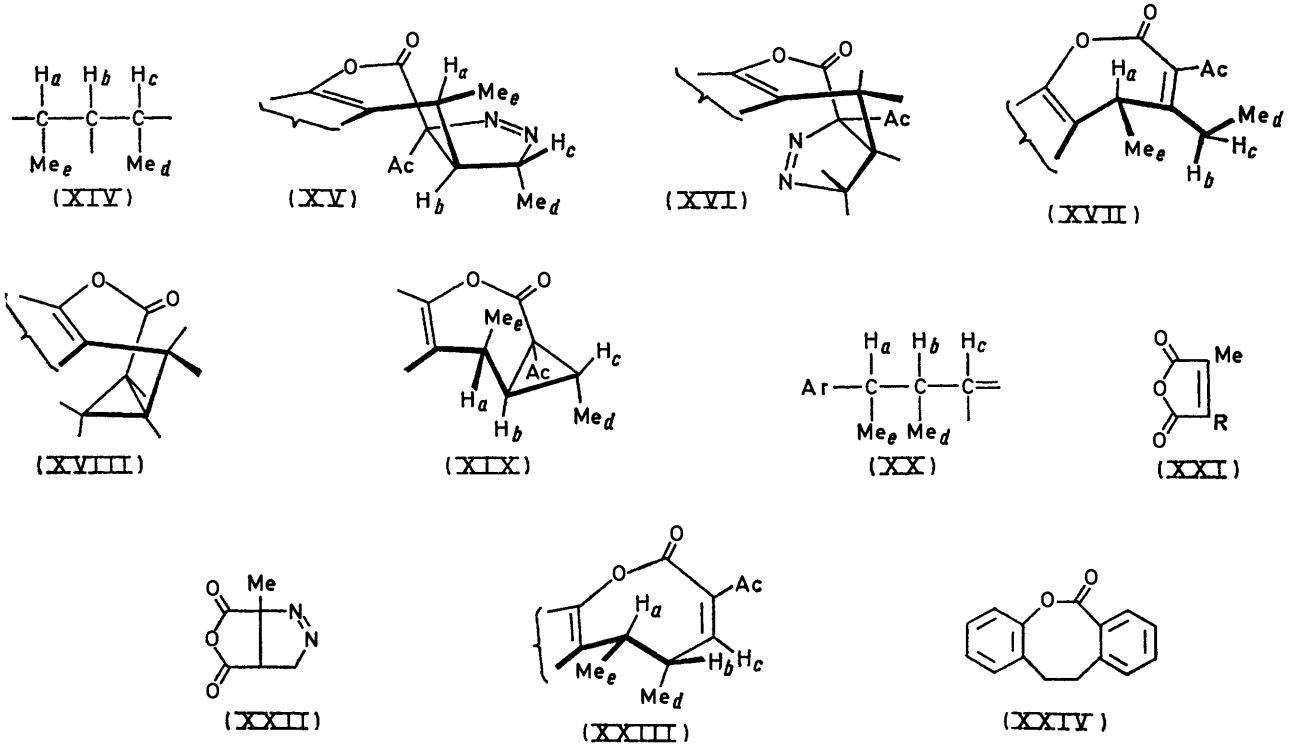
The ethylated lactone (X) has i.r. absorption characteristics very like those of the coumarin (V; R = Et), only one broad band at 1708 cm^{-1} being seen for the two carbonyl groups. The reasons have been discussed elsewhere;[2] briefly, the ethyl group causes the acetyl group to rotate out of conjugation with the ethylenic

[7] G. W. Wheland, ' Resonance in Organic Chemistry,' Wiley, New York, 1955, p. 235.
[8] J. M. O'Gorman, W. Shand, and V. Schomaker, *J. Amer. Chem. Soc.*, 1950, **72**, 4222.
[9] R. Huisgen and H. Ott, *Tetrahedron*, 1959, **6**, 253.
[10] S. Aleby, *Acta Chem. Scand.*, 1968, **22**, 811.
[11] A. M. Mathieson, *Tetrahedron Letters*, 1963, 81.
[12] R. J. W. Le Fèvre and A. Sundram, *J. Chem. Soc.*, 1962, 3904.
[13] B. Krishna, S. V. Mahadane, and B. Prakesh, *J. Chem. Soc.* (*B*), 1970, 954.
[14] K. K. Cheung, K. H. Overton, and C. A. Sim, *Chem. Comm.*, 1965, 634.
[15] R. C. Sheppard and S. Turner, *Chem. Comm.*, 1968, 77.
[16] D. E. McGreer and J. W. McKinley, *Canad. J. Chem.*, 1971, **49**, 105.

double bond so that the frequency rises. There must be a reciprocal effect on the ethyl group but the n.m.r. spectrum of the coumarin is normal and shows the usual methylenic quartet, so the effect is not large. In the ethylated lactone (X), on the other hand, the n.m.r. spectrum (Table) displays a complex multiplet which, though it could not be fully analysed, is consistent only with non-equivalence of the methylenic protons. Hence there must be some additional bar to rotation, and models show that it would be provided by a benzylic methyl group placed as shown in diagram (XVII) *i.e.* in the pseudoequatorial position on a boat-shaped lactone ring.

According to the n.m.r. spectrum (Table) the cyclopropane derivative (XI) contains two secondary methyl groups along with three adjacent methine protons clearly distinguishable at 220 MHz and corresponding to the sequence (XIV). These facts immediately define the molecular skeleton which has a boat-shaped lactone ring with the cyclopropane ring disposed either *exo* or *endo*. The *endo*-arrangement (XVIII) has to be discarded since it forces a methyl group or a proton very close to the benzene ring; the methyl group would be within 2 Å if no distortion occurred, and while a proton would be accommodated more easily it would still be very strongly shielded in a way not consistent with the n.m.r. spectrum. The *exo*-arrangement shown in diagram (XIX) forms a much better basis for analysis. Beginning at the benzylic centre, the methine proton H_a must be placed in the plane of the benzene ring to account for its resonance at rather low field; correspondingly, the benzylic methyl group resonates at relatively high field and so occupies a place above the plane of the benzene ring where it will also be shielded by the cyclopropane ring.[17] The stereochemical analysis would be completed by a decision as to whether the two cyclopropane protons were *cis* or *trans*, but this is not easily accomplished because coupling constants in cyclopropanes are strongly influenced by electronegative substituents.[18-21] Though the splitting of 6·5 Hz is well within the usual range for *trans*-protons and rather lower than usual for *cis*-protons, preliminary attempts to extend rules for the dependence of coupling constants upon electronegativities [18] to fully analysed cyclopropanes of suitable types [19-21] show that the observed value could fit the *cis*- and the *trans*-situations equally well. Hence the placing of Me_d and H_c in (XIX) is tentative.

The oxocin derivative (XII) exhibits both lactonic and ketonic carbonyl bands in the i.r. spectrum; the n.m.r. spectrum (Table) establishes the methyl and methine proton sequence shown in diagram (XX). In the first place the stereochemistry is defined by exhaustive ozonolysis which provides *meso*-dimethylsuccinic acid, identical with an authentic specimen prepared [22] from dimethylmaleic anhydride. Since dimethylmaleic an-



[17] J. Tadanier and W. Cole, *J. Org. Chem.*, 1962, **27**, 4610.
[18] K. L. Williamson, C. A. Lanford, and C. R. Nicholson, *J. Amer. Chem. Soc.*, 1964, **86**, 762.
[19] H. Weitkamp and F. Korte, *Tetrahedron*, 1964, **20**, 2125.
[20] K. B. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.* 1963, **85**, 2788.
[21] T. Shono, T. Morikawa, A. Oka, and R. Oda, *Tetrahedron Letters*, 1964, 791.
[22] R. P. Linstead and M. Whalley, *J. Chem. Soc.*, 1954, 3722.

^{1}H N.m.r. spectra (solvent deuteriochloroform; internal standard tetramethylsilane)

Pyrazolone (IX) or (XV) at 100 MHz

				Decoupling experiment			
Origin	τ	Rel. int.	Mult.	Irradiation frequency (Hz)	Nucleus saturated	Surviving mult.	Coupling constant (Hz)
ArH	*ca.* 2·9	4	mm				
H_c	5·57	1	dq	2666·0	Me_d	d	J_{bc} 8·5
				2755·8	H_b	q	J_{cd} 7·0
H_a	6·95	1	dq				J_{ae} 6·5
				2646·8	Me_e	d	J_{ab} 12·0
H_b	*ca.* 7·45 *		m				
Me_d	8·36	3	d	2942·0	H_c	s	J_{cd} 7·0
Me_e	8·55	3	d	2802·0	H_a	s	J_{ae} 6·5
Me_f	7·52	3	s				

* Partly masked by acetyl protons Me_f. Obviously affected by irradiation of H_a and H_c though the changes could not be measured.

Benzoxepinone (X) or (XVII) at 100 MHz

Origin	τ	Rel. int.	Mult.	Coupling constant (Hz)
ArH	*ca.* 2·9	4	mm	
H_a	6·59	1	q	7·3
$H_b + H_c$	7·68	2	m	
Me_f	7·71	3	s	
Me_e	8·49	3	d	7·3
Me_d	8·82	3	m	7·5

Cyclopropa-oxepinone (XI) or (XIX) at 220 MHz

Origin	τ	Rel. int.	Mult.	Coupling constant (Hz)
ArH	*ca.* 2·9	4	mm	
H_a	6·66	1	dq	J_{ab} 7·5 J_{ad} 7·5
H_b	7·52	1	dd	J_{ab} 7·5 J_{bc} 6·5
Me_f	7·72	3	s	
H_c	7·91	1	dq	J_{ce} 6·0 J_{bc} 6·5
Me_e	8·75	3	d	J_{ce} 6·0
Me_d	8·85	3	d	J_{ad} 7·5

Benzoxocinone (XII) or (XXIII) at 100 MHz

				Decoupling experiment			
Origin	τ	Rel. int.	Mult.	Irradiation frequency (Hz)	Nucleus saturated	Surviving mult.	Coupling constant (Hz)
ArH	*ca.* 2·9	4	mm				
H_c	3·56	1	d				J_{bc} 2·0
H_a	6·38	1	dq	2640·0	Me	d	J_{ab} 5·0
H_b	7·04	1	m	2869·0	H_a	q *	J_{bd} 7·0
				3148·0	H_e	dq	J_{ab} 5·0 J_{bd} 7·0
Me_f	7·82	3	s				
Me_e	8·65	3	d	2869·0	H_a	s	J_{ae} 7·0
Me_d	8·91	3	d	2800·0	H_b	s	J_{bd} 7·0

* Broadened by interaction with H_c but further splitting not resolvable.

Benzoxoninone (XIII) or (XXVII) at 100 MHz

				Decoupling experiment			
Origin	τ	Rel. int.	Mult.	Irradiation frequency (Hz)	Nucleus saturated	Surviving mult.	Coupling constant (Hz)
ArH	*ca.* 3·0	4	mm				
H_d	3·89	1	d *				J_{cd} 10·5
H_a	6·56	1	dq	2716·3	H_g	q	J_{ag} 7·5 J_{ab} 2·0
H_c	7·26	1	m	2716·3	H_b	dq	J_{cd} 10·5 J_{ce} 7·0
Me_h	8·08	3	s				
H_b	*ca.* 8·20	1	m	2881·1	H_a	dq	J_{bf} 7·0 J_{bc} 2·0
				2809·9	H_e	dq	J_{ab} 2·0 J_{bf} 7·0
Me_g	8·73	3	d	2881·1	H_a	s	J_{ag} 7·5
Me_e	8·86	3	d	2809·9	H_c	s	J_{ce} 7·0
Me_f	9·22	3	d	2716·3	H_b	s	J_{bf} 7·0

* This nucleus could not be saturated because of its large value of J_{cd}.

TABLE (*Continued*)

Benzoxoninone (XXXI) at 100 MHz

Origin	τ	Rel. int.	Mult.	Coupling constant (Hz)
ArH	*ca.* 3·0	4	mm	
H_e	3·51	1	t	$J_{ce,de}$ 9·0
H_a	6·55	1	dq	J_{ab} 2·0, J_{ag} 7·0
$H_c + H_d$	*ca.* 7·5	2	mm	
H_b	7·9	1	m	
Me_h	8·04	3	s	
Me_f	8·71	3	d	J_{bf} 7·0
Me_g	9·07	3	d	J_{ag} 7·0

hydride is not conveniently obtainable by the published method [23] we made it from methylmaleic anhydride (XXI; R = H) on the grounds that this should behave towards diazomethane as quinones do. Accordingly, with diazomethane, it gave the pyrazoline (XXII), pyrolysis of which supplied dimethylmaleic anhydride (XXI; R = Me) in good yields provided that dilute solutions were used to avoid polymerisation. It follows that the methyl groups in (XII) are *cis*.

Two conformations can be written for the oxocin ring in (XII); one is chair- or step-shaped, rigid, and attainable only by twisting the ester function so that it is non-planar, the carbonyl group being conjugated with neither the ether oxygen atom nor the ethylenic double bond. As it offers no compensatory advantages and is in any case very difficult to fit to the n.m.r. spectrum it has to be rejected. The other conformation is boat-shaped and leads to structure (XXIII) for the compound. The coupling constant J_{bc} between the vinylic and the next methine proton is 2 Hz which, as Garbisch [24] has shown, in systems of this type corresponds to a torsion angle close to 90° since there is a π-contribution to be added to the usual Karplus value. The other dihedral coupling constant, J_{ab}, is about 5 Hz, suggesting a torsion angle near 40° between the protons concerned which allows the methyl groups to be comfortably staggered. Nevertheless, the methyl groups have been accommodated by twisting the ester function which, if planar, forces them into precise eclipse. As the ester need be twisted through not more than 20°, however, loss of conjugation is probably not serious and the i.r. band at 1740 cm^{-1} appears to confirm a normal situation comparable to the boat conformation adopted by compound [25] (XXIV).

The structure (XIII) for the oxonin derivative is established by the i.r. spectrum, which confirms the presence of lactonic and conjugated ketonic carbonyl groups, and by the n.m.r. spectrum (Table), which, with decoupling experiments, defines unequivocally the proton sequence shown in diagram (XXV). The stereochemical analysis begins with the ester function now in a ring just large enough to accommodate a somewhat twisted *s-cis* unit but the result is a constricted system containing torsion angles not compatible with the n.m.r. spectrum and must be rejected. With an *s-trans* ester function there are two conformational possibilities differing in the disposition of the central ethylidene group. In arrangement (XXVI) this group folds in towards the ester function giving a bowl-shaped molecule; in the other it is turned outwards giving a boat-chair conformation. The dihedral splittings can be rationalised only in terms of this latter conformation and establish for the methyl substituents the positions shown in diagram (XXVII). Starting at the vinylic proton H_d (Table), a splitting of 10·5 is observed consistent with a torsion angle approaching 170° as found in structure (XXVII) where H_c is nearly coplanar with the vinylic proton and *s-trans* to it. This locates one methyl group. Next, J_{bc} is small (*ca.* 2 Hz) indicating a torsion angle near to 90°. These splittings are particularly important because they are easily accommodated in structure (XXVII) but not in any structure based upon conformation (XXVI) no matter how the methyl groups are placed. The third torsion angle is also near to 90° since J_{ab} is again small, but this is possible in either conformation and does not distinguish between them. This analysis, which shows all three methyl groups to be *cis*, independently accords the *cis* relation to the two secondary methyl groups brought in from the parent oxocin derivative (XXIII).

The mass spectrum of the oxonin derivative exhibits a feature unique in this series. The chief fragmentation of the molecular ion is into two particles with *m/e* 121 and 151 and can be accommodated by a fission into two parts as indicated by the wavy line in (XXVIII), which, however, would give fragments with *m/e* 120 and 152. Evidently one proton can be transferred, and models show that the transfer of H_c indicated by the dotted line is stereochemically reasonable. It would also result in the relatively stable fragment ions (XXIX) and (XXX).

With structure (XXVII) the oxonin derivative possesses an ethylenic system that is both highly activated and exposed to attack by diazoalkanes, yet no reaction occurs. Models suggest that as the ethylenic carbon atoms accept a diazoalkane and rehybridise, the attached acetyl group and proton have to be turned inwards into a space where there is already a methyl substituent (Me_f). The resulting congestion could be expected to expel the diazoalkane again provided that the energy barrier to the reverse cycloaddition is not high. Reversibility at 260° has been noted by Crawford and Mishra [26] but we [2] have detected reversibility at temperatures as low as *ca.* 50°,

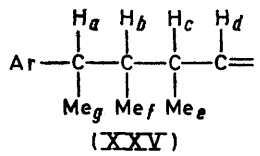
R. Anschütz, *Annalen*, 1928, **461**, 163.
E. W. Garbisch, *J. Amer. Chem. Soc.*, 1964, **86**, 5561.

[25] W. Baker, W. D. Ollis, and T. S. Zealley, *J. Chem. Soc.*, 1952, 1447; R. Crossley, A. P. Downing, M. Nogradia, A. Braga de Oliveira, W. D. Ollis, and I. O. Sutherland, *J.C.S. Perkin I*, 1973, 205.
[26] R. J. Crawford and A. Mishra, *J. Amer. Chem. Soc.*, 1966, **88**, 3963.

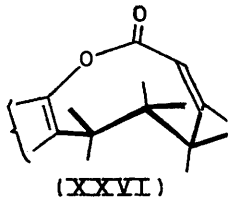
so we believe that this provides an adequate explanation of the apparent inertness of the system.

Diazomethane reacted with the eight-membered lactone (XII) to give a mixture from which only a small amount of one product was obtained pure. This resembled the nine-membered lactone closely and is allocated structure (XXXI) mainly on the basis of the n.m.r. spectrum (Table).

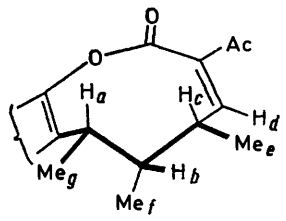
Groups led by McGreer [16,27] and by Carrié [4,6] consider that pyrazolines undergo thermal collapse in a fashion largely determined by the conformation of the ring system, and our results accord with their views. For example, the pyrazoline (VII; R = H) can take up conformation (XXXII; R = H) and concerted loss of



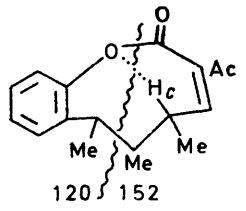
(XXV)



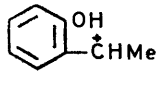
(XXVI)



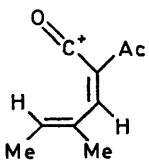
(XXVII)



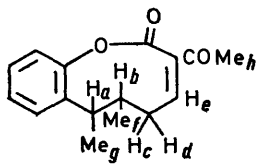
(XXVIII)



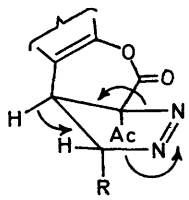
(XXIX)



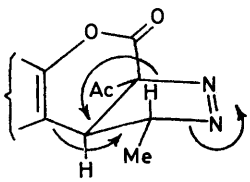
(XXX)



(XXXI)



(XXXII)



(XXXIII)

nitrogen would then be accompanied by hydrogen migration giving the coumarin (V; R = Me). Similarly, the pyrazoline (VII; R = Me) can take up conformation (XXXII; R = Me) and the coumarin (V; R = Et) would result. But the arrangement now contains the equivalent of a 1,3-diaxial interaction, and if this is removed by inverting the pyrazoline conformation then the situation is as shown in diagram (XXXIII), where nitrogen loss would be accompanied by aryl migration. This accounts well for the fact that diazomethane converts 3-acetylcoumarin into 3-acetyl-4-methylcoumarin, whereas diazoethane gives a mixture of a coumarin and ring-expanded products. It also accounts for the ability of diazoethane (but not diazomethane) to produce higher ring homologues; for the retention of stereochemistry at the ethylidene groups; and for the parallels noted with adducts in the quinone series. It further provides an explanation for the fact that aryl, aralkyl, and acyl migrations all occur, and that all three types are similarly successful in competition with hydrogen migration. We reserve comment on cyclopropane formation, which is evidently much more complex.[16,27,28]

[27] D. E. McGreer, N. W. K. Chiu, M. G. Vinje, and K. C. Wong, *Canad. J. Chem.*, 1965, **34**, 1407.

EXPERIMENTAL

^{1}H N.m.r. spectra were determined upon solutions in deuteriochloroform with tetramethylsilane as internal standard; analyses are first-order only. I.r. spectra were usually obtained by using potassium bromide discs. U.v. spectra were determined upon 10^{-3}—10^{-4}M-solutions in ethanol. Molecular weights were derived by mass spectrometry.

Action of Diazoethane on 3-Acetylcoumarin.—A solution of diazoethane (*ca.* 7·2 g) in ether (400 ml) was mixed with a solution of 3-acetylcoumarin (4·9 g) also in ether (300 ml) kept at 0°. After 35 min, volatile materials were removed by evaporation under reduced pressure from a bath at 0° leaving a pale yellow oil that solidified when kept for some hours under light petroleum (b.p. 60—80°). The product decomposed readily when warmed or when brought into contact with silica, but it could be purified by rapid crystallisation from light petroleum (b.p. 60—80°) and then gave (3R*,3aR*,4S*,10aR*)-10a-*acetyl*-3,3a,4,10a-*tetrahydro*-3,4-*dimethyl*[1]*benzoxepino*[3,4-c]*pyrazol*-10-*one* (IX) as needles (1·33 g), m.p. 114—115° (some samples had m.p. 119—120°) (decomp.), $\lambda_{max.}$ ($CHCl_3$) 266 and 274 nm (log ε 3·06 and 3·02), $\nu_{max.}$ 1757 (lactone CO), 1717 (acetyl CO), and 1556 cm^{-1} (azo) (Found: C, 66·1; H, 6·1; N, 10·5. $C_{15}H_{16}N_2O_3$ requires C, 66·2; H, 5·9; N, 10·3%).

The residual light petroleum solutions were combined and concentrated leaving an oil which crystallised from ether–light petroleum (b.p. 40—60°) (1 : 1) giving 3-*acetyl*-4-*ethylcoumarin* (V; R = Et) as long needles (2·3 g), m.p. 75—76°, $\lambda_{max.}$ 280 and 317 nm (log ε 4·04 and 3·76), $\nu_{max.}$ 1705 (coumarin and acetyl CO) and 1604 cm^{-1} (aromatic), τ 8·70 (3H, t, *J* 7·5 Hz, CH_2·CH_3), 7·44 (3H, s, CO·CH_3), 7·20 (2H, q, *J* 7·5 Hz, CH_2·CH_3), and 2·33 and 2·59 (4H, mm, ArH) (Found: C, 72·5; H, 5·6. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%).

The mother liquors from this coumarin were left to evaporate yielding an oil that did not crystallise. It was dissolved in benzene–light petroleum (b.p. 60—80°) and passed down a long silica column which cracked badly at first because of the evolution of nitrogen from the pyrazoline

[28] J. P. Deleux, G. Leroy, and J. Weiler, *Tetrahedron*, 1973, **29**, 1135.

still present. Elution was conducted with benzene (2 l) and supplied fractions containing two products that were separated by rechromatography on thick-layer silica plates (Kieselgel GF 254) with acetone–light petroleum (b.p. 40—60°) as eluant; elution of the bands with methanol gave the products as oils, one of which crystallised when kept and appeared to consist of a mixture (0·2 g) of stereoisomers corresponding to structure (XI). Repeated crystallisation of this mixture from light petroleum (b.p. 40—60°) eventually furnished (1R*,1aR*,8R*,8aR*)-1a-*acetyl*-1,1a,8,8a-*tetrahydro*-1,8-*dimethylcyclopropa*[c][1]*benzoxepin*-2-*one* (XI) as prisms (0·07 g), m.p. 96—97°, $\lambda_{max.}$ 255, 265, and 273 nm (log ε 3·28, 3·18, and 2·98), $\nu_{max.}$ 1746 (lactone CO), 1701 (acetyl CO), and 1608 cm^{-1} (aromatic) (Found: C, 73·7; H, 6·5. $C_{15}H_{16}O_3$ requires C, 73·7; H, 6·6%). The other oil (0·11 g) from thick-layer chromatography did not crystallise though it behaved chromatographically and otherwise as a single substance; we consider it to be 3-acetyl-4-ethyl-5-methyl-1-benzoxepin-2(5*H*)-one (X), $\lambda_{max.}$ 224 and 290 nm (log ε 4·18 and 3·47), $\nu_{max.}$ (film) 1708 (lactone and acetyl CO) and 1608 cm^{-1} (aromatic) (Found: *M*, 244. Calc. for $C_{15}H_{16}O_3$: *M*, 244).

Continued elution of the silica column with benzene–chloroform gave 3-acetyl-4-ethylcoumarin (0·07 g) and a trace of the oxocin (XII) obtained in quantity as in the next experiment.

(5R*,6R*)-3-*Acetyl*-5,6-*dihydro*-5,6-*dimethyl*-1-*benzoxocin*-2-*one* (XII).—(i) The oxepinopyrazolone (IX) (1·0 g) dissolved in cold ethanol (20 ml) and readily liberated nitrogen at about 60°. After 15 min effervescence ceased and the ethanol was removed under reduced pressure leaving an oil that was chromatographed on silica from benzene–light petroleum (b.p. 40—60°) (4 : 1). The first fractions contained two compounds which were separated by thick-layer chromatography on Kieselgel GF 254 from acetone–light petroleum (1 : 5), thus giving the cyclopropane derivative (XI) (0·06 g) and the oxepinone (X) (0·04 g) as oils identified chromatographically and spectroscopically with samples obtained as in the preceding experiment. Later fractions from the column were obtained by elution with benzene and supplied the *oxocinone*, which separated from light petroleum (b.p. 60—80°) as long needles (0·35 g), m.p. 120·5—121·5°, $\lambda_{max.}$ 245, 255, and 271 nm (log ε 3·40, 3·10, and 2·86), $\nu_{max.}$ 1740 (lactone CO), 1667 (acetyl CO), and 1624 and 1605 cm^{-1} (aromatic and olefinic) (Found: C, 73·5; H, 6·6%; *M*, 244. $C_{15}H_{16}O_3$ requires C, 73·7; H, 6·6%; *M*, 244). The 2,4-*dinitrophenylhydrazone* formed orange prisms, m.p. 209—211°, $\lambda_{max.}$ 260, 279, and 372 nm (log ε 4·03, 3·87, and 4·40), $\nu_{max.}$ 3325 (NH), 1742 (lactone CO), and 1623 and 1603 cm^{-1} (aromatic and olefinic) (Found: C, 59·2; H, 4·7; N, 13·2. $C_{21}H_{20}N_4O_6$ requires C, 59·2; H, 4·7; N, 13·2%).

(ii) The oxepinopyrazolone (IX) (0·62 g) was heated in boiling benzene (freshly dried by distillation; 12 ml) for 3·5 h. Removal of the solvent left a yellow oil which partly crystallised when kept with a little ether. Crystallisation of the solid from light petroleum gave the oxocinone (0·28 g), m.p. and mixed m.p. 121°. The material left in the mother liquors was chromatographed on silica as in (i) and benzene eluted a further amount (0·08 g) of the oxocinone.

(3aR*,6aS*)-3a,6a-*Dihydro*-6a-*methyl*-3H-*furo*[3,4-c]*pyrazole*-4,6-*dione* (XXII).—Citraconic anhydride (4·45 g) was added to diazomethane (*ca.* 5 g) in ether (250 ml) at 0°. During 1 h the product separated as needles (7·0 g) sufficiently pure for further use. For analytical purposes this product was further purified by precipitating it from a solution in acetone by the addition of light petroleum (b.p. 40—60°), which supplied the *furopyrazoledione* as a powder, m.p. 131—132°, $\nu_{max.}$ 1850 and 1795 (cyclic anhydride) and 1565 cm^{-1} (azo) (Found: C, 46·7; H, 3·6; N, 18·5%; *M*, 154. $C_6H_6N_2O_3$ requires C, 46·8; H, 3·9; N, 18·2%; *M*, 154).

Dimethylmaleic Anhydride.—The furopyrazoledione (XXII) (0·50 g) was heated in refluxing toluene (freshly dried by distillation; 50 ml) for 1 h, then the cooled and filtered solution was rapidly washed first with a little aqueous sodium hydrogen carbonate and then with water. Removal of the solvent *in vacuo* left an oil which solidified. The solid was washed with a little ether and purified by sublimation at 90—100° and 30 mmHg, giving the anhydride as needles, m.p. 95° (lit.,[23] 95—96°). The compound gave an n.m.r. spectrum consisting of a singlet at τ 7·96, and it was further identified by conversion into the corresponding imide, m.p. 118—119·5° (lit.,[29] 119—120°).

Ozonolysis of the Oxocinone (XII).—Ozonised oxygen was passed into a solution of the oxocinone (0·40 g) in dichloromethane (25 ml) at 0° for 2·5 h, then ozone was swept out by a stream of oxygen passed for 15 min. The solvent was removed by evaporation at 0° under reduced pressure, water (25 ml) was added to the residue, and the mixture was warmed for 25 min. The yellow oil that separated from the solution upon cooling was collected into ether and found by t.l.c. to consist mainly of dimethylsuccinic acid.

One contaminant appeared to be an α-ketonic acid which was removed by dissolving the oil in dilute aqueous potassium hydroxide and oxidising it with aqueous hydrogen peroxide (30%; 1 ml) at 25° for 25 min and then at 50° for 15 min. The resulting solution was washed with ether and acidified, and the product was collected into ether from which it was recovered as an oil which slowly crystallised, giving *meso*-dimethylsuccinic acid as needles (0·133 g), m.p. 179°, identical (mixed m.p. and i.r. data) with an authentic specimen prepared from dimethylmaleic anhydride.[22]

(5R*,6S*,7S*)-3-*Acetyl*-6,7-*dihydro*-5,6,7-*trimethyl*-1-*benzoxonin*-2(5H)-*one* (XIII).—The oxocinone (XII) (0·60 g) in ether (60 ml) was treated at 0° with diazoethane (*ca.* 1 g) in ether (150 ml). After 30 min the volatile materials were removed by evaporation at 0° under reduced pressure and the residual oil (0·69 g) was kept under light petroleum until it crystallised. Recrystallised from light petroleum (b.p. 60—80°), the solid supplied the *oxoninone* as needles (0·43 g), m.p. 152—153° (a less stable modification, m.p. 132—133°, was sometimes encountered), $\lambda_{max.}$ 245 and 255 nm (log ε 3·29 and 3·22), $\nu_{max.}$ 1760 (lactone CO), 1668 (acetyl CO), and 1638 cm^{-1} (aromatic and olefinic), $\nu_{max.}$ ($CHCl_3$) 1764 (lactone CO) and 1670 cm^{-1} (acetyl CO) (Found: C, 75·0; H, 7·3%; M^+, 272·141235. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·4%; *M*, 272·141133).

This oxoninone was recovered almost quantitatively from further treatment with diazoethane or with diazomethane during 1 h at 0°.

(6R*,7R*)-3-*Acetyl*-6,7-*dihydro*-6,7-*dimethyl*-1-*benzoxonin*-2(5H)-*one* (XXXI).—The oxocinone (XII) (0·11 g) in ether (15 ml) was treated at 0° with diazomethane (*ca.* 0·5 g) in ether (60 ml) for 30 min, and the product was obtained by spontaneous evaporation of the solvent *etc.*, also at 0°. The resulting oil was chromatographed on silica from benzene–light petroleum (b.p. 40—60°) (4 : 1) giving two main frac-

[29] M. E. Baguley, H. France, R. P. Linstead, and M. Whalley, *J. Chem. Soc.*, 1955, 3521.

tions of similar character. The preponderant one failed to crystallise and could not be purified further. The minor fraction crystallised giving the *oxoninone*, which separated from light petroleum (b.p. 60—80°) as prisms (0·017 g), m.p. 110—113°, $\nu_{max.}$ 1750 (lactone CO) and 1670 cm^{-1} (acetyl CO) (Found: C, 74·2; H, 6·8. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%).

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