The Solvolytic Behaviour of *exo*- and *endo*-1,5-Dimethyl-9-oxobicyclo-[3,3,1]nonan-2-yl Toluene-*p*-sulphonates

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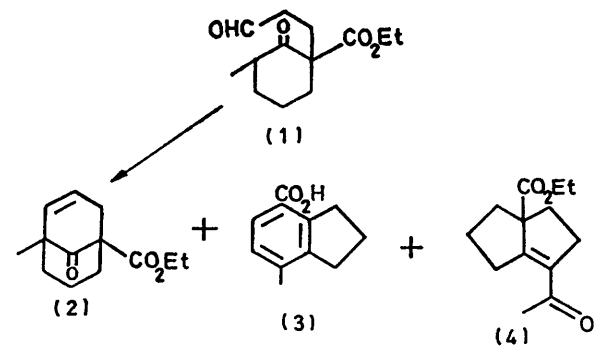
The buffered acetolysis of the *exo*-title compound gives mainly 1,5-dimethylbicyclo[3,3,1]non-2-en-9-one (9) (75%) and the corresponding *exo*- and *endo*-2-acetates (6 and 7; R = Ac) (13%) in the ratio of 1:12, whereas similar treatment of the *endo*-title compound gives 2,6-dimethylbicyclo[4,2,1]non-2-en-9-one (11) (51%), the corresponding tertiary acetates (12 and 13; R = Ac) (16%) accompanied by the enone (9) (8%), and the acetates (6 and 7; R = Ac) (25%) in a ratio of >24:1. These results are best explained in terms of ion-pair mechanisms. The fact that unbuffered acetolysis of both acetates (6 and 7; R = Ts) gives 1,4-dimethylindane (8) and 2-acetyl-5-methylbicyclo[3,3,0]oct-1-ene (10) in the same ratio (4:5) but in different yields (9 and 46%) suggests that (8) and (10) are both acid-catalysed rearrangement products of (11).

THE impetus for the work described in this paper arose from two unusual rearrangement products encountered [1] during the initial stages of the synthesis of clovene [2] when treatment of the ester (1) with sulphuric acid gave the indane-4-carboxylic acid (3) and bicyclo[3,3,0]octene ester [3] (4) in addition to the required keto-ester (2).

The keto-ester (2) can be converted into (3) by sulphuric acid treatment and the mechanism proposed [4] in Scheme 1 explains the isolation of this acid from the initial rearrangement mixture, which also yielded the esters (2) and (4).

Mild acidic treatment of the diketo-ester (1) gave a mixture of the epimeric ketols (5), which could be rearranged to the same mixture of products (2), (3), and (4), thus suggesting [1a] the somewhat unusual acyl shift



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[1] (*a*) D. B. Jhaveri, R. D. H. Murray, W. Parker, and R. A. Raphael, *Tetrahedron*, 1962, **18**, 55; (*b*) see S. Ranganathan, 'Fascinating Problems in Organic Reaction Mechanisms,' Holden–Day, 1967, p. 24.

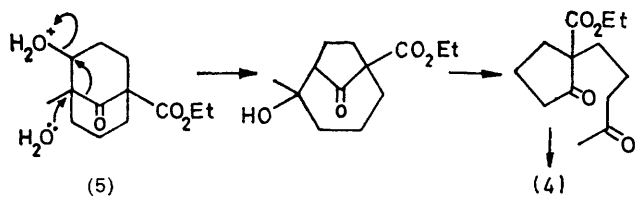
[2] P. Doyle, I. R. MacLean, R. D. H. Murray, W. Parker, and R. A. Raphael, *J. Chem. Soc.*, 1963, 239.

[3] W. F. Keir, *Tetrahedron*, 1966, **22**, 2581.

[4] Originally proposed by J. Martin, Ph.D. Thesis, University of Glasgow, 1964, (*cf.* the mechanism proposed in ref. 1*a*).

mechanism for the formation of (4) illustrated in Scheme 2.

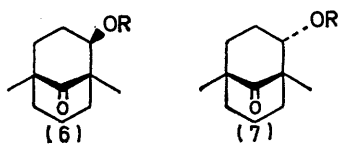
It was recognised that the epimeric forms of (5), with axial and equatorial hydroxy-groups, could provide a stereo-electronic control over the formation of (2) and (4) but unfortunately it proved impossible to separate them and since the 9-oxobicyclo[3,3,1]nonane 2-cation(s) apparently play a key role in these deep-seated rearrangements, we decided to study the behaviour of



(5) (4)

SCHEME 2

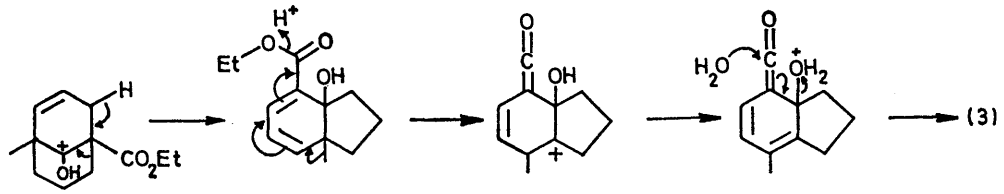
such species under milder and, as it transpired, more informative conditions; *viz.* acetolysis of the keto-tosylates [5a,b] (6 and 7; R = Ts).



(6) (7)

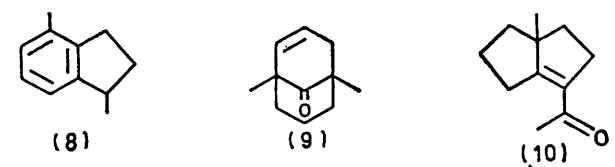
Initially the solvolysis of the tosylates (6 and 7; R = Ts) was carried out in acetic acid under reflux and the product distributions are shown in the Table. The dihydro-compound and comparison with an authentic sample synthesised from (4) by standard reactions.

The buffered (NaOAc) acetolysis of (6 and 7; R = Ts) was carried out in sealed ampoules at 80° for ten half-lives and the product distributions are shown in the Table.



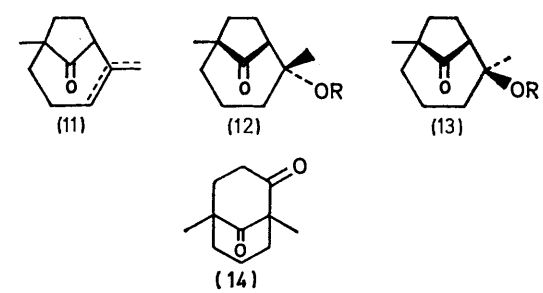
SCHEME 1

The structure of (11) followed from its spectral characteristics and the synthesis of an identical compound by



(8) (9) (10)

warming 1,5-dimethyl-*cis*-cyclo-oct-4-ene-1-carboxylic acid chloride in dichloroethane.[7] Separation of the



(11) (12) (13) (14)

mixture of the four keto-acetates proved fruitless on a preparative scale so the mixture was treated with lithium aluminium hydride and the products were oxidised with chromium trioxide in dimethylformamide [8]

Product distribution (%) from the unbuffered [a] and buffered acetolysis [b] of the tosylates (6 and 7; R = Ts)

Compound	(8)	(9)	(10)	(11)	(12; R = Ac) [c]	(13; R = Ac) [c]	(6; R = Ac)	(7; R = Ac)
(6; R = Ts) [a]	4	68	5				5	18
(7; R = Rs) [a]	20	19	26				23	12
(6; R = Ts) [b]		75		7	4	<1	1	12
(7; R = Ts) [b]		8		51	12	4	24	<1

[a] Anhydrous acetic acid, reflux, 5 h. [b] Sealed ampoules, buffered (NaOAc) acetic acid, 80°, ten half lives. [c] Relative configurational assignment between (12) and (13) has not yet been accomplished.

identities of the hydrocarbon [6] (8) and the bicyclic ketone [5a] (9) were confirmed by comparison with authentic samples and structural assignment to (10) was obtained by catalytic hydrogenation to the corresponding to give a mixture of (14) and (12 and 13; R = H). The mixture of the hydroxy-ketones (12 and 13; R = H) was then dehydrated to the ketone (11). This series of transformations showed that the carbon skeleton of (12 and 13; R = Ac) was identical to that of (11), but

[5] (*a*) J. Martin, W. Parker, and R. A. Raphael, *J. Chem. Soc.*, 1964, 289; (*b*) J. Martin, W. Parker, B. Shroot, and T. Stewart, *J. Chem. Soc.* (*C*), 1967, 101.

[6] B. B. Elsner and K. J. Parker, *J. Chem. Soc.*, 1957, 596.

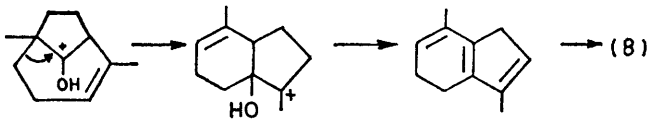
[7] W. F. Erman and M. C. Kretschmar, *J. Org. Chem.*, 1968, **33**, 1545.

[8] G. Snatzke, *Chem. Ber.*, 1961, **94**, 729.

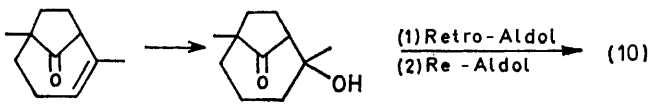
as yet the relative configurational assignment to the acetates (12 and 13; R = Ac) has not been accomplished.

Two salient points emerge from the unbuffered acetolysis results shown in Table 1; the markedly enhanced amount of rearranged products from the keto-tosylate (7; R = Ts) and the production of an aromatic hydrocarbon whose substitution pattern differs from that to be expected from the original investigation.[1a] The results from the buffered acetolysis (Table 1) are even more informative; the small amount of rearranged products from (6; R = Ts), the extent of rearrangement accompanying the solvolysis of (7; R = Ts), and the absence of aromatic products coupled with the appearance of the hitherto undetected [1a] bicyclo[4,2,1]nonane skeleton.

In relating the products from buffered and unbuffered acetolysis, it is notable that the keto-olefin(s) (11) are unaffected by heating with glacial acetic acid under reflux but are converted into a mixture of compounds (8)—(10) by treatment with toluene-*p*-sulphonic acid in benzene whereas the enone (9) is unaffected under both conditions. These results point to the ketone (11) as the key intermediate in the formation of (8) and (10), possibly by the pathways shown in Schemes 3 and 4.

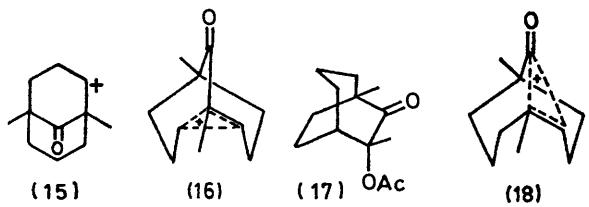


SCHEME 3

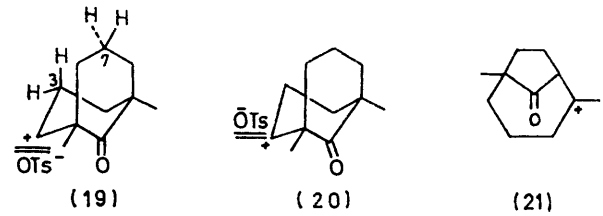


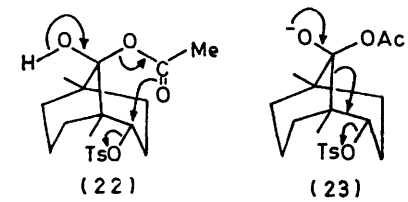
SCHEME 4

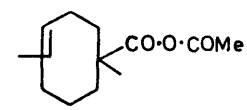
The striking difference in product distribution from the buffered acetolysis of (6 and 7; R = Ts) militates against the common intermediacy of the classical carbonium ion (15) and yet an explanation in terms of two distinct non-classical ions is also untenable on several counts. Such a species derived from (6; R = Ts) has the unlikely structure (16) and would demand the stereoselective production of (6; R = Ac) and the bicyclo[3,2,2]nonyl acetate (17). No trace of (17) has been found and the observed ratio (6; R = Ac) : (7; R = Ac) is 1 : 12.



Similarly, the sole intermediacy of the cation (18) for the solvolysis of (7; R = Ts) does not explain the observed ratio (6; R = Ac) : (7; R = Ac) being >24 : 1. However an explanation based on intimate ion pair–classical carbonium ion equilibria does seem to encompass all the observations. Ionisation of (6; R = Ts) to the ion-pair (19) followed either by counter-ion capture (from the *endo*-face of C-2) on loss of the stereoelectronically favoured *endo*-3-proton (note the associated relief of substantial C-3–C-7 methylene interaction) explains the overall product distribution particularly if there is an associated minor leakage from (19) to the classical cation (15). The corresponding ion-pair (20) formed from (7; R = Ts) could suffer solvent capture (leading to inverted acetate) or a stereoelectronically favoured acyl migration to give the tertiary cation (21) and hence the major solvolysis products. Here again an equilibrium between (15) and either (20) or (21) would account for the small amounts of (9) and (7; R = Ac) produced.







Two alternative schemes [9] must be considered for the solvolytic behaviour of (7; R = Ts). Addition of acetic acid to the carbonyl group of (7; R = Ts) and subsequent participation (22) by the acetate carbonyl group during ionisation of the tosyloxy-group would lead to the inverted acetate (6; R = Ac) but this does not explain the formation of the bicyclo[4,2,1]nonyl compounds and would require the concomitant operation of another reaction pathway. A variant of this suggestion involves the addition of acetate anion to the carbonyl group of (7; R = Ts) followed by fragmentation to the cyclo-octenyl mixed anhydride (23) ⟶ (24), which in turn recyclises to (21) *via* an intramolecular displacement of the acetate anion by the trisubstituted

[9] Similar arguments have been put forward by Gassman and his co-workers in analysing the solvolytic behaviour of 7-oxygenated norbornyl tosylates (P. G. Gassman and J. L. Marshall, *J. Amer. Chem. Soc.*, 1966, **88**, 2822; P. G. Gassman and J. C. MacMillan, *ibid.*, 1969, **91**, 5527, and references cited therein).

double bond. By analogy,[10] however, this process would be expected to give mainly (7; R = Ac). The product balance from solvolysis of (7; R = Ts) is virtually complete hence if this pathway is operative the mixed anhydride (24) must be extremely reactive in buffered acetic acid. Accordingly, an attempt was made to prepare (24) by treatment of the sodium salt of 1,5-dimethyl-*cis*-cyclo-oct-4-ene-1-carboxylic acid with acetyl chloride but the product consisted mainly of the keto-olefin(s) (11) accompanied by a small inseparable amount of the desired anhydride.

Hence, until solvolytic behaviour of the mixed anhydride can be rigorously established, the ion-pair mechanisms for the buffered acetolysis of both (6 and 7; R = Ts) seem the most likely.

EXPERIMENTAL

M.p.s were determined on a Kofler block and are corrected. B.p.s are uncorrected. The chromatographic adsorbents used were either Woelm Grade I alumina (neutral) or silica gel; thin-layer chromatoplates were prepared from Merck's 'Kieselgel G.' Light petroleum refers to the fraction b.p. 40—60°. All organic extracts were dried with anhydrous magnesium sulphate.

Analytical gas–liquid chromatograms were run on the Perkin-Elmer models F11 and Fraktometer 451. U.v. spectra were determined on a Unicam SP 800 and routine i.r. spectra on Unicam SP 200 and Perkin-Elmer 157 machines. ^{1}H N.m.r. spectra were measured on a Perkin-Elmer R10 60 MHz spectrometer with carbon tetrachloride as solvent, unless otherwise stated, with tetramethylsilane as internal reference.

exo- *and* endo-1,5-*Dimethyl*-9-*oxobicyclo*[3,3,1]*nonan*-2-*yl Acetates* (6 and 7; R = Ac).—A solution of the requisite alcohol [5a,b] in acetic anhydride was treated with dry pyridine and set aside at room temperature for 12 h. Normal isolation procedure gave the exo-*acetate* (6; R = Ac) as needles, m.p. 52—53°, τ 4·91 (1H, $W_{\frac{1}{2}}$ 7 Hz) (Found: C, 69·55; H, 9·2. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%). The corresponding endo-*acetate* (6; R = Ac) was an oil, τ 5·31 (1H, t J_{obs} 9 Hz, $W_{\frac{1}{2}}$ 20 Hz) (Found: C, 69·35; H, 8·8%).

Acetolysis of the Tosylate (7; R = Ts).—A solution of the tosylate (7; R = Ts) (1 g) in anhydrous acetic acid [11] (20 ml) was heated under reflux for 5 h. Normal work-up gave a red oil, which was adsorbed on Grade I alumina (20 g) from light petroleum. Elution with the same solvent gave 1,4-dimethylindane (8) (0·093 g) identical in all respects with an authentic sample.[7] Further elution gave 1,5-*dimethylbicyclo*[3,3,1]*non*-2-*en*-9-*one* (9) (0·086 g) [5a,b] and subsequent elution with ether–light petroleum (1 : 9) gave a three-component mixture which was treated with ethanolic semicarbazide acetate.(*) Treatment of the resultant semicarbazone (0·173 g) with dilute mineral acid and ether extraction gave 2-*acetyl*-5-*methylbicyclo*[3,3,0]*oct*-1-*ene* (10), b.p. 54—55° at 0·7 mmHg, n_D^{21} 1·5070, $\nu_{max.}$ (film) 1670 cm^{-1}, $\lambda_{max.}$ (EtOH) 252 nm (ε 10,000); semicarbazone, m.p. 209—211° (decomp.); 2,4-dinitrophenylhydrazone, m.p. 172—174°. This compound corresponded in all respects with a conjugated ketone of unproven structure previously isolated [5a] from boric acid treatment of an epimeric mixture of (6 and 7; R = H). Ether extraction of the semicarbazone (*) mixture gave the acetates (6 and 7; R = Ac) (0·157 g) in the ratio of 1 : 1·9 [g.l.c. (5% Q.F.1)].

Acetolysis of the Tosylate (6; R = Ts).—Treatment of the tosylate (6; R = Ts) under identical conditions to those described before gave the indane (8) (4%), the bicyclononenone (9) (68%), the bicyclo-octene (10) (5%), and the acetates (6; R = Ac) (5%) and (7; R = Ac) (18%).

Ethyl 4-[1-(*Dioxolan*-2-*yl*)*ethyl*]*bicyclo*[3,3,0]*oct*-4-*ene*-1-*carboxylate*.—A mixture of the acetyl-ester (4) (7·62 g), ethylene glycol (10 ml), ethyl orthoformate (20 ml), and naphthalenesulphonic acid (0·5 g) was heated slowly in an oil-bath to 150° and over a 3 h period the ethanol and ethyl formate produced were removed by distillation. Normal isolation procedures then gave the pure *ethylene acetal* of the *ester* (4) (7·3 g), b.p. 135° at 0·6 mmHg, n_D^{22} 1·4755 (Found: C, 66·9; H, 8·8. $C_{15}H_{24}O_4$ requires C, 67·15; H, 9·0%).

2-*Acetyl*-5-*hydroxymethylbicyclo*[3,3,0]*octane*.—A solution of the foregoing acetal-ester (6·79 g) in ether (50 ml) was treated with lithium aluminium hydride (0·50 g). Work-up after treatment with mineral acid gave the *hydroxy-ketone* (3·07 g), b.p. 102° at 0·15 mmHg, n_D^{20} 1·4940 (Found: C, 72·5; H, 10·1. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·95%); the 2,4-*dinitrophenylhydrazone*, prisms, had m.p. 85—87° (from ethyl acetate) (Found: C, 65·05; H, 6·4; N, 15·45. $C_{17}H_{22}N_4O_5$ requires C, 65·35; H, 6·1; N, 15·45%); the *toluene*-p-*sulphonate*, prisms, had m.p. 79—80° (from ethyl acetate) (Found: C, 64·4; H, 7·2. $C_{18}H_{24}O_4S$ requires C, 64·25; H, 7·2%).

2-*Acetyl*-5-*methylbicyclo*[3,3,0]*octane*.—The above tosylate (1·20 g) in ether was treated with lithium aluminium hydride (0·5 g) and the mixture heated under reflux for 4 h. The crude product was treated with Jones reagent and normal work-up gave the *ketone* (0·51 g), b.p. 121—123° at 23 mmHg, n_D^{20} 1·4859 (Found: C, 79·2; H, 10·9. $C_{11}H_{18}O$ requires C, 79·45; H, 10·9%); the 2,4-*dinitrophenylhydrazone*, prisms, had m.p. 109—111° (from ethyl acetate–methanol) (Found: C, 59·15; H, 6·35; N, 16·2. $C_{17}H_{22}N_4O_4$ requires C, 58·95; H, 6·4; N, 16·2%). Catalytic hydrogenation of the enone (10) gave a product identical in all respects with this ketone.

Buffered Acetolysis of the Tosylates (6 and 7; R = Ts).—On a preparative scale the following procedure was adopted: a solution of (7; R = Ts) (1 g) and freshly fused sodium acetate (0·49 g) in anhydrous acetic acid (40 ml) was heated at 100° for 7 h. Normal work-up gave a yellow oil (0·55 g), which was adsorbed on Grade I neutral alumina (22 g) from light petroleum. Elution with the same solvent gave the enone (9) (0·01 g). Elution with ether–light petroleum (1 : 200) gave 2,6-*dimethylbicyclo*[4,2,1]*non*-2-*en*-9-*one* and 1-*methyl*-5-*methylenebicyclo*[4,2,1]*nonan*-9-*one* [both (11)] (0·23 g) in the ratio of 2·7 : 1, b.p. 91° at 12 mmHg, $\nu_{max.}$ (CCl_4) 1738, 899, and 816 cm^{-1}, τ 4·50br (m), 5·27 (narrow m), 8·21 (s), 8·97 and 9·02 (s) (Found: C, 80·4; H, 9·65. $C_{11}H_{16}O$ requires C, 80·45; H, 9·8%). Further elution with ether–light petroleum (1 : 9) gave a mixture (0·242 g) of the four keto-acetates (6), (7), (12), and (13) (R = Ac) which was reduced with lithium aluminium hydride; the resultant crude product (0·35 g) was dissolved in dry dimethylformamide and treated with chromium trioxide [8] (1·4 g) and concentrated sulphuric acid (two drops).

[10] A. C. Cope, D. L. Nealy, P. Schneiner, and G. Wood, *J. Amer. Chem. Soc.*, 1965, **87**, 3130.

[11] S. Winstein, C. Hanson, and E. Grunwald, *J. Amer. Chem. Soc.*, 1948, **70**, 812.

Normal work-up followed by chromatography on silica gel separated 1,5-dimethylbicyclo[3,3,1]nonane-2,9-dione (14) from the epimeric ketols (12) and (13) (R = H) (0·14 g).

For accurate product analyses, the following procedure was adopted. The first-order rate constants for buffered (NaOAc) acetolysis of (6 and 7; R = Ts) ($k_1 = 6{\cdot}61 \times 10^{-5}$ s^{-1} and $1{\cdot}39 \times 10^{-4}$ s^{-1}, respectively, at 80·0° ± 0·1°) were determined.[12] The requisite tosylate (37 mg), with sodium acetate (25 mg) and anhydrous acetic acid was then heated in a sealed glass ampoule for ten half-lives. The product distribution was then determined by g.l.c. on a 6 ft 5% Q.F.1, 1/4 in column, temperature programmed from 100 to 175° at 3° min^{-1}.

1,5-Dimethylbicyclo[4,2,1]*nonan-9-one*.—A solution of the epimeric mixture (11) in ethyl acetate was hydrogenated over 10% palladium–charcoal. The resultant ketone, $\nu_{max.}$ (CCl_4) 1733 cm^{-1}, showed no olefinic absorption bands. The corresponding *2,4-dinitrophenylhydrazone*, needles, had m.p. 141—142° (from ethanol) (Found: C, 59·15; H, 6·2; N, 16·5. $C_{17}H_{22}N_4O_4$ requires C, 58·95; H, 6·4; N, 16·5%).

Dehydration of the 5-Hydroxy-1,5-dimethylbicyclo[4,2,1]*nonan-9-ones* (12 and 13; R = H).—The mixture of ketols (12 and 13; R = H) was dissolved in pyridine and treated with phosphoryl chloride. Normal work-up gave the keto-olefin(s) (11).

2,6-Dimethylbicyclo[4,2,1]*non-2-en-9-one and 1-Methyl-5-methylenebicyclo*[4,2,1]*nonan-9-one* (11).—The keto-tosylate (7; R = Ts) (0·168 g) was heated under reflux with aqueous sodium hydroxide [5a] (1N; 1·5 ml) and water (2 ml) for 30 min. After removal of the water, the dry residue was suspended in benzene (2 ml), treated with oxalyl chloride (1 ml) and set aside at room temperature for 4 h. Removal of the solvent gave a brown solid which was then heated in dichloroethane [7] for 10 min. Normal work-up then gave a sample of the isomers (11) (15 mg) identical to that obtained from buffered acetolysis of (7; R = Ts).

Rearrangement of the Keto-olefins (11).—The keto-olefin(s) (11) were unaffected by heating under reflux with anhydrous acetic acid for 12 h. However, treatment with toluene-*p*-sulphonic acid in benzene under reflux for 4 h effected a complete rearrangement of (11) into a mixture of (8), (9), and (10).

Attempted Preparation of Acetic 1,5-Dimethylcyclo-oct-4-ene-1-carboxylic Anhydride (24).—(*a*) The keto-tosylate (7; R = Ts) was unaffected by treatment with sodium acetate in benzene–dioxan under reflux for 72 h.

(*b*) The dry sodium salt of 1,5-dimethylcyclo-oct-4-ene-1-carboxylic acid [5a] was heated under reflux with acetyl chloride in benzene for 1 h. Normal work-up produced a mixture consisting mainly of (11) with a small inseparable amount of the desired mixed anhydride.

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[12] C. G. Swain and C. R. Morgan, *J. Org. Chem.*, 1964, **29**, 2097.