Thermal Rearrangement of Aryl(chloro)methylenetetrahydrofuran-2,4,5-triones: its Mechanism and the Chemistry of the Resulting Aroylchloromaleic Anhydrides

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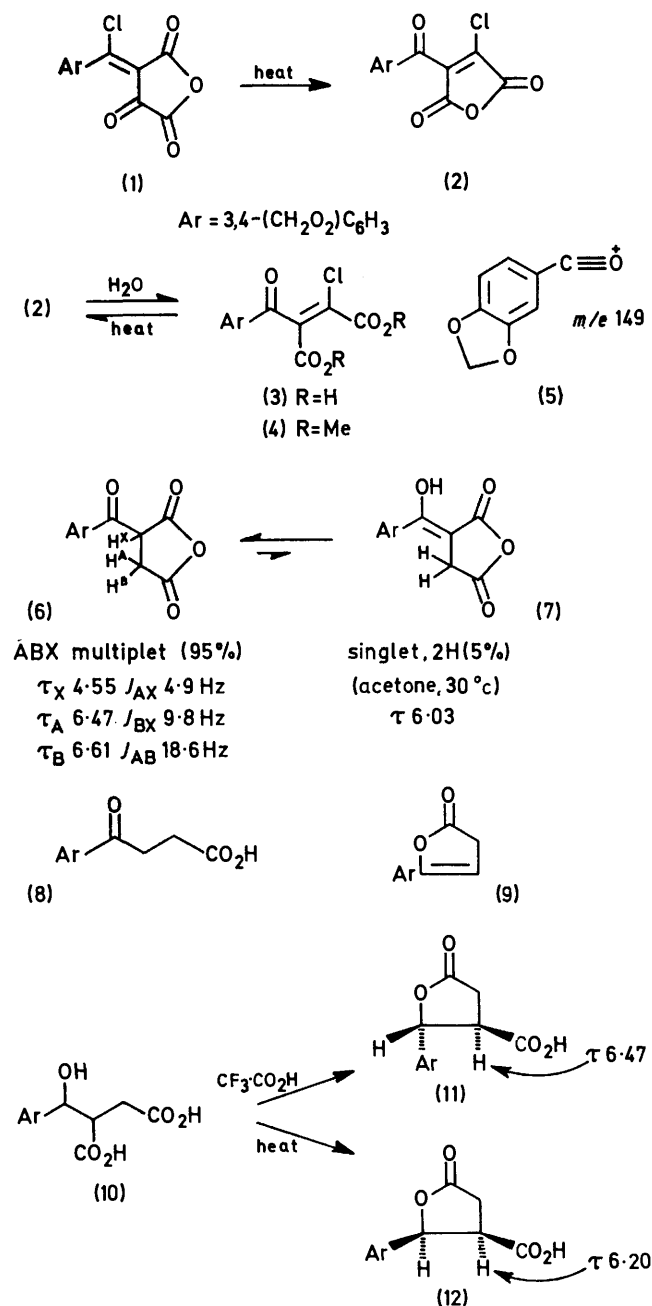
On heating above the m.p., aryl(chloro)methylenetetrahydrofuran-2,4,5-triones rearrange with double bond shift and carbonyl oxygen–chlorine interchange giving aroylchloromaleic anhydrides. ^{14}C Labelling studies and other work show the integrity of the carbon framework, and a mechanism involving formation of an oxet is proposed: this links mechanistically the formation and the rearrangement of the triones. Aspects of the chemistry of aroylchloromaleic anhydrides are reported.

ON heating above its m.p., the red trione (1) [1a] undergoes an unusual rearrangement [1b] involving interchange of a carbonyl oxygen and a chlorine atom, in conjunction with a double-bond shift. The product, orange-yellow chloro-(3,4-methylenedioxybenzoyl)maleic anhydride (2) retains the proton resonances of the methylenedioxyphenyl residue and has $\nu_{max.}$ (CHCl$_3$) 1 870, 1 780 (cyclic anhydride), and 1 660 cm^{-1} (unsaturated carbonyl). Treatment with water or aqueous sodium hydroxide converts it into the dicarboxylic acid (3) which gives a dimethyl ester (4) with diazomethane and reverts to (2) on heating. In accord with the structures given, both (2) and (4) undergo mass spectral fragmentation predominantly in one step to (5) (base peak), other ions [2] being formed from this. This behaviour contrasts with that for the trione (1).[1a]

Hydrogenation (Pd or Pt catalyst) of the anhydride (2) leads to saturation of the double bond together with dechlorination and gives the oxo-anhydride (6), hydrolysed to the known [3] 4-oxo-acid (8). In deuterioacetone solution (6) exists predominantly in the oxo-form in equilibrium with about 5% of the enol (7). The oxo–enol conversion is shown by addition of D$_2$O: rapid exchange causes disappearance of the quartet at τ 4.55 and collapse of the multiplet near τ 6.6. That the singlet at 6.03 genuinely belongs to a species in equilibrium with the oxo-form was demonstrated by transference of spin magnetisation by chemical exchange.[4a] Thus irradiation at the frequency of the AB multiplet of the ketone near τ 6.6 causes saturation of the singlet at τ 6.03 due to the enol methylene. On heating, the oxo-anhydride (6) loses carbon dioxide giving the β-unsaturated γ-lactone (9) ($\nu_{max.}$ 1 805 cm^{-1}).

Treatment of the chloro-anhydride (2) with aqueous sodium hydroxide followed by hydrogenation of the resulting diacid (3) over palladium yields the hydroxy-acid (10), accompanied by some of the γ-lactone (11) probably formed in the acidic work-up. The acid (10) affords the lactone (11), identical with an authentic

specimen,[5] when treated with trifluoroacetic acid. However thermal lactonisation of (10) gives a second, isomeric lactone (12) which is thermodynamically less stable and

(1)   (2)

Ar = 3,4-(CH$_2$O$_2$)C$_6$H$_3$

(3) R=H   (5)
(4) R=Me

(6)   (7)

ABX multiplet (95%)   singlet, 2H(5%)

τ_X 4·55 J_{AX} 4·9 Hz   (acetone,30 °c)
τ_A 6·47 J_{BX} 9·8 Hz τ 6·03
τ_B 6·61 J_{AB} 18·6 Hz

(8)   (9)

(10)   CF$_3$·CO$_2$H   (11) τ 6·47

heat

(12) τ 6·20

[1] (a) M. J. Begley, L. Crombie, R. G. Havard, and D. P. Reynolds, preceding paper; (b) L. Crombie and D. P. Reynolds, J.C.S. Chem. Comm., 1973, 265.

[2] B. Willhalm, A. F. Thomas, and F. Gautschi, Tetrahedron, 1964, 20, 1185.

[3] M. J. Bougault, Ann. Chim. Phys., 1908, 15, 491.

[4] (a) J. H. Noggle and R. E. Schirmer, ' The Nuclear Overhauser Effect,' Academic Press, London, 1971; (b) L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969.

[5] J. W. Cornforth, G. K. Hughes, and F. Lions, J. Proc. Roy. Soc. New South Wales, 1938, 72, 228.

is converted into (11) by treatment with acid: the mass spectra of the two lactones are similar. The structural assignments (11) and (12) may be made on the basis that there is less steric compression in the former: the

Although this stereoisomer may be the exclusive product from the hydrogenation, it is possible that an isomer mixture is produced and that the (RS,RS)-stereoisomer preferentially undergoes lactonisation to (11), as this
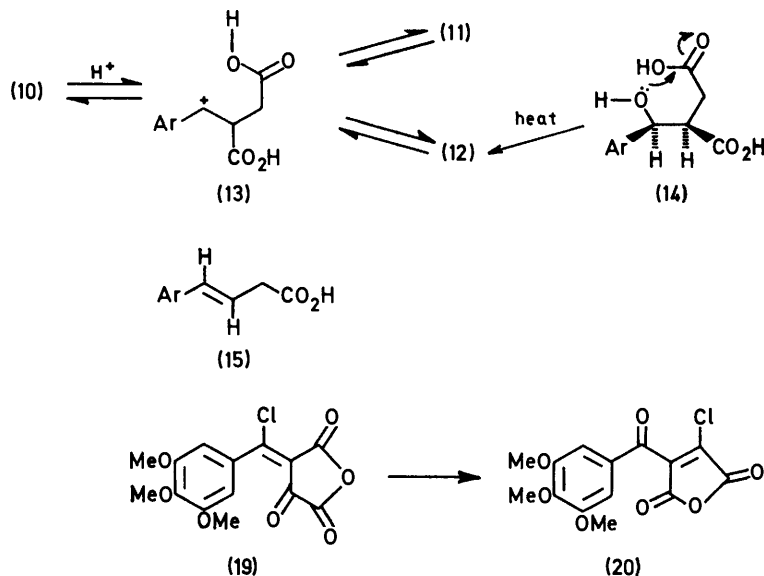
assignments are consistent with n.m.r. evidence as the 3-proton, cis-vicinal to the aryl group in (11) is shielded [4b] relative to its counterpart in (12). Ready acid-catalysed epimerisation of (12) must occur via a

accompanies (10). On heating the lactones (11) and (12) above their m.p.s both give the same trans-olefinic acid (15) (J 16.0 Hz for the olefinic protons) by decarboxylative elimination.
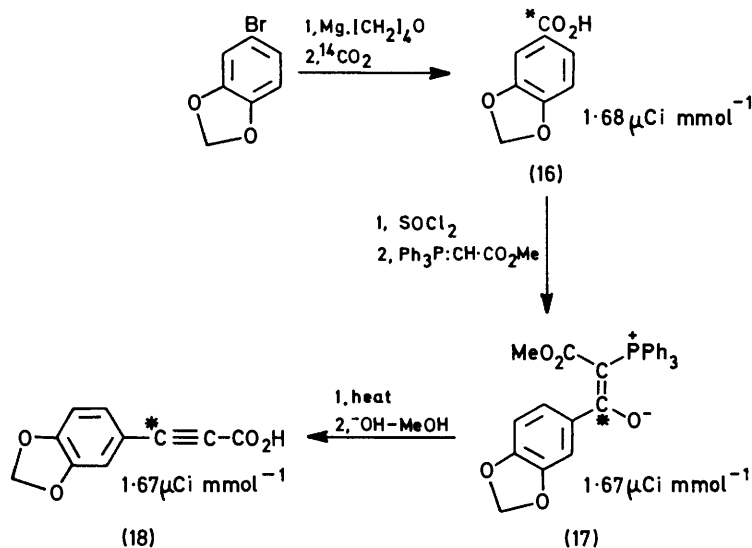
Scheme 1

stabilised 3,4-methylenedioxybenzyl carbocation (13), i.e. $A_{AL}1$ in Ingold's nomenclature.[6] · An eliminative mechanism is not operative, since deuterium was not incorporated when trifluoroacetic [²H]acid was employed. Thermal lactonisation, which gives the less stable isomer, must involve nucleophilic attack on the carboxy-group (14) and requires the hydroxy-acid (10) to have (SR,RS)-stereochemistry as indicated in (14).

Before examining mechanisms for the rearrangement (1) ——► (2) it was considered desirable to establish unequivocally that the α-carbon atom bearing chlorine in (1) becomes the α-carbon atom bearing carbonyl oxygen in (2). To this end, 3,4-methylenedioxyphenyl[3-¹⁴C]-propiolic acid (18) was prepared by using the Wittig

[6] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Cornell University Press, 2nd edn., 1969.

approach to acetylene synthesis (Scheme 1).[7] 3,4-Methylenedioxyphenylmagnesium bromide [8] was carboxylated with $^{14}CO_2$ and the resulting 3,4-methylenedioxy[1-^{14}C]benzoic acid (16) was converted into the acid chloride and treated with methoxycarbonylmethylenetriphenylphosphorane. Pyrolysis of the betaine (17) and hydrolysis then gave [3-^{14}C]-(18).

Treatment of 3,4-methylenedioxyphenyl[3-^{14}C]propiolic acid with oxalyl chloride yielded [α-^{14}C]-(1) which was pyrolytically converted into [^{14}C]-(2). The positioning of the label at the α-position was demonstrated by degradation to [^{14}C]benzoic acid and extraction of the label as $^{14}CO_2$ from the carboxy-group (Scheme 2).

SCHEME 2
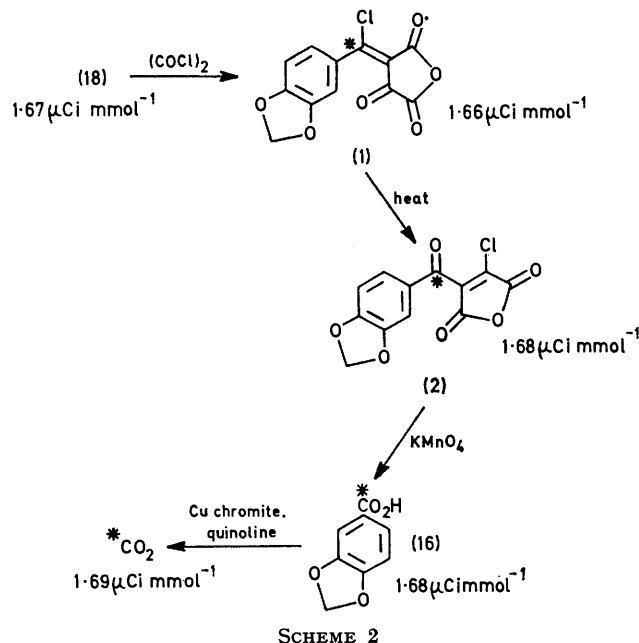
Since all the radioactivity is carried by the latter, the integrity of the carbon atom attached to the aromatic ring is maintained in the rearrangement.

In the case being studied (1) (with Ar = 3,4-$CH_2O_2C_6H_3$) it was also observed that migration of the rearranging system from C-1 of the aromatic ring to C-6 would pass unnoticed. That such a rearrangement does not occur was shown by pyrolytically converting the trimethoxy-analogue (19) into (20). The product contained equivalent aromatic protons (2 H singlet, τ 2.55) as required by structure (20).

With these possible rearrangements of the carbon framework disposed of, the only reasonable inference is chlorine–oxygen interchange, and any plausible mechanism appears to require formation of an oxet [(22) or (26)]. The addition of carbonyl compounds to alk-1-ynyl ethers and sulphides, alk-1-ynylamines, and phenylacetylenes, when catalysed by boron trifluoride, is reported to give αβ-unsaturated esters.[9,10] With

very electrophilic carbon atoms the catalyst can sometimes be omitted and in the uncatalysed addition of
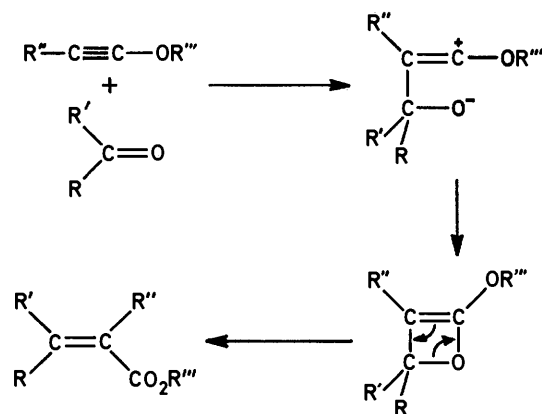
SCHEME 3

hexafluoroacetone to ethoxyacetylene an oxet intermediate has been isolated.[11] In the case of hexachloroacetone the oxet was too unstable to be isolated but it could be detected by n.m.r.[12] A mechanism as in Scheme 3 has been proposed.

Cyclisations of arylpropiolyl chloro-oxalyl anhydrides are envisaged in Scheme 4 as giving initially a zwitterion

SCHEME 4

(21). At lower temperatures this yields the red trione (1), but if the chlorine transfer is reversible then, at

[7] G. Markl, *Chem. Ber.*, 1961, **94**, 3005; S. T. D. Gough and S. Trippett, *J. Chem. Soc.*, 1962, 2333.

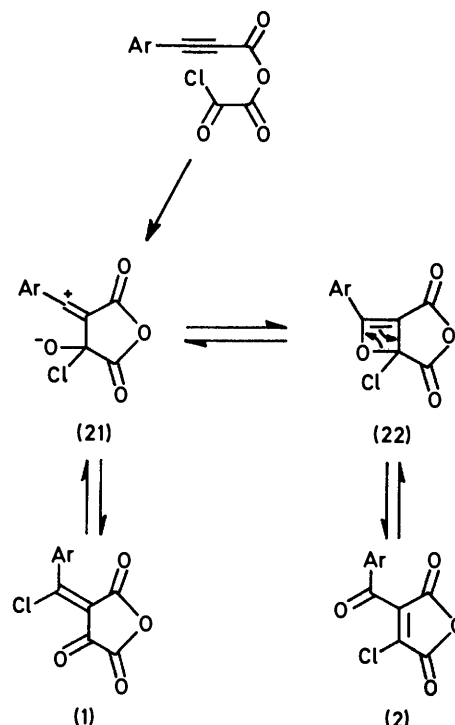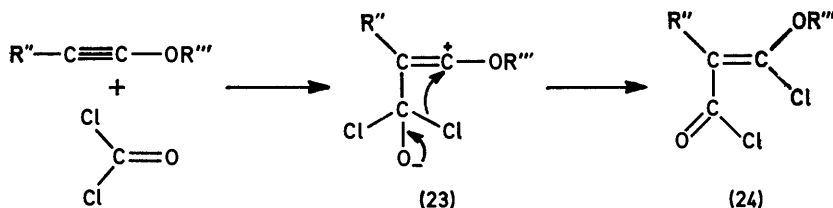[8] C. Feugas, *Bull. Soc. chim. France*, 1964, 1892.

[9] H. Vieregge, H. M. Schmidt, J. Renema, H. J. T. Bos, and J. F. Arens, *Rec. Trav. chim.*, 1966, **85**, 929.

[10] H. G. Viehe, 'Chemistry of Acetylenes,' Dekker, New York, 1969.

[11] W. J. Middleton, *J. Org. Chem.*, 1965, **30**, 1307.

[12] G. van den Bosch, H. J. T. Bos, and J. F. Arens, *Rec. Trav. chim.*, 1966, **85**, 567; 1970, **89**, 133.

higher temperatures and under conditions of thermo-dynamic control, ring closure could give the oxet (22), and electrocyclic ring opening permits the formation of the anhydride (2). A reaction which resembles the lower temperature phase of this reaction is the addition of carbonyl chloride to alkynyl ethers (Scheme 5) in which formation of a zwitterion (23) is postulated: the
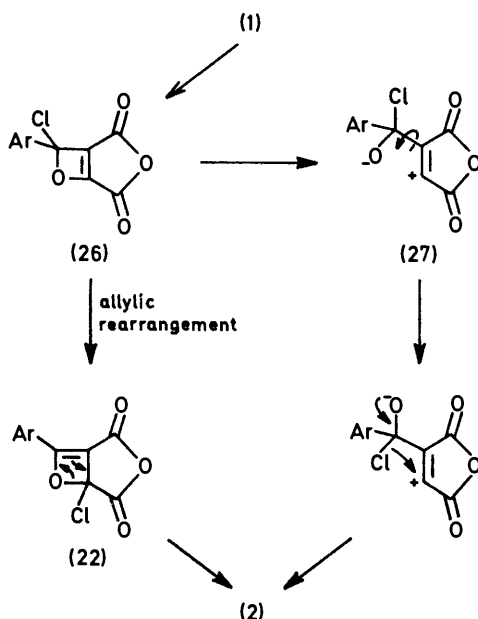
involve an ion pair (25) which could itself be interposed between (21) and (1).

Two other pathways (Scheme 7) were considered, but appear less attractive. Thus in the zwitterionic inter-mediate (27), charge is confined on an sp^2 orbital and no delocalisation is possible: this species, and the tran-sition state leading to it, are expected to be of higher

SCHEME 5

latter then transfers a chloride anion in preference to forming an oxet.[12] In the case cited, cis-addition
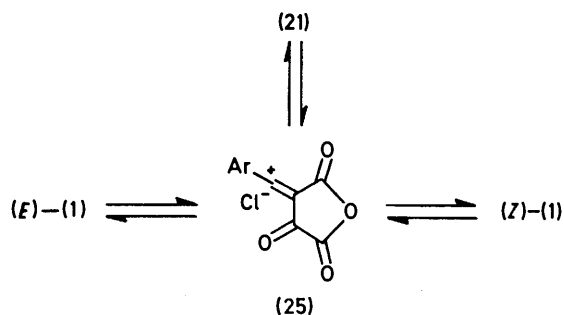
SCHEME 6

SCHEME 7

occurs to give exclusively the Z-isomer (24), and this was isomerised to a ZE-mixture on distillation. For the trione (1), in which the crystals are approximately 83% Z, 17% E, the isomerisation mechanism may

energy than in the case of (21) where the p orbital is unoccupied and charge stabilisation by the aromatic ring with its electron-donating substituents is possible. Allylic rearrangement, (26) ⟶ (22), also seems less likely, since this must proceed via an ion pair or a radical pair, and the energy required for this process is not compensated for by release of the high strain energy of the oxet ring.

EXPERIMENTAL

Chloro-(3,4-methylenedioxybenzoyl)maleic Anhydride (2).— The red trione (1) is rearranged by heating above its m.p. Some charring occurs and it is convenient to use a sublim-ation apparatus. For larger batches the following method was used. 3,4-Methylenedioxyphenylpropiolic acid (8.5 g) in benzene (50 cm³) was refluxed with oxalyl chloride (8 cm³) for 2 h. The solvent was then evaporated off, and the crude product transferred to a sublimation apparatus. After heating (180 °C) at 0.1 mmHg the solid melted and boiled vigorously. The rearranged product distilled onto the cold finger, and crystallisation from anhydrous benzene–hexane gave the *anhydride* (2) (9.35 g, 73%) as orange-yellow needles, m.p. 143—145° (Found: C, 51.5; H, 1.95; Cl, 12.55%; M^+, 279.9773. $C_{12}H_5ClO_6$ requires C, 51.3; H, 1.8; Cl, 12.65%; M, 279.9774), $\nu_{max.}$ (CHCl₃) 1 873m and 1 795s (cyclic anhydride), 1 660 (aryl, αβ-unsaturated ketone), and 1 620 cm⁻¹, $\lambda_{max.}$ (CHCl₃) 257 (ε 7 140) and 297 nm (7 630), τ [(CD₃)₂CO] 2.22 (1 H, dd, $J_{5,6}$ 8, $J_{2,6}$ 2 Hz, H-6), 2.46 (1 H, d, J 2 Hz, H-2), 2.95 (1 H, d, J 8 Hz, H-5), and 3.78 (2 H, s, CH₂O₂), m/e 282 (28%), 280 (84), and 149 (100).

Hydrolysis of the Anhydride (2).—(a) The anhydride (1.0 g) was dissolved in cold aqueous sodium hydroxide (10%; 4 cm³). The solution was cooled in ice, acidified with hydrochloric acid, and extracted with ethyl acetate. The dried (MgSO₄) extracts were evaporated; crystallis-ation from benzene–hexane–ethyl acetate gave crystals of *chloro-(3,4-methylenedioxybenzoyl)maleic acid* (3) (798 mg, mg, 75%), m.p. 143—145° (decomp.) (Found: C, 48.6; H, 2.6; Cl, 12.4. $C_{12}H_7ClO_7$ requires C, 48.3; H, 2.35; Cl, 11.9%), $\nu_{max.}$ (mull) 1 725 and 1 708 (carboxy), 1 663 (aryl, αβ-unsaturated ketone), and 1 632 cm⁻¹, $\lambda_{max.}$ (EtOH) 234 (ε 17 600), 280 (6 780), and 322 nm (9 270), τ [(CD₃)₂CO] 2.42 (1 H, dd, $J_{5,6}$ 8, $J_{2,6}$ 2 Hz, H-6), 2.62 (1 H, d, $J_{2,6}$ 2 Hz, H-2), 2.99 (1 H, d, $J_{5,6}$ 8 Hz, H-5), 3.85 (2 H, s, CH₂O₂), and 2.5br (2 H, CO₂H, exchanged on shaking with D₂O).

(b) A suspension of the anhydride (2) (213 mg) in water (10 cm³) was heated on a steam-bath for 10 min (if heating is prolonged, further reaction occurs). Work-up yielded the acid (3) (154 mg, 68%), m.p. 142—144° (decomp.). Sublimation of the acid (3) (12 mg) at 156 °C and 0.1 mmHg gave back the anhydride (2) (7.5 mg), m.p. 142—145° (from benzene–hexane).

Treatment of the diacid (3) with ethereal diazomethane gave the dimethyl ester (4), a viscous oil (molecular distillation) (Found: C, 51.65; H, 3.6; Cl, 10.55%; M^+, 326. $C_{14}H_{11}ClO_7$ requires C, 51.5; H, 3.4; Cl, 10.9%; M, 326), $\nu_{max.}$ (CHCl₃) 1 730 (ester), 1 665 (aryl, αβ-unsaturated ketone), and 1 620 cm⁻¹, $\lambda_{max.}$ (EtOH) 234 (ε 17 600), 282 (6 750), and 325 nm (9 200), τ [(CD₃)₂CO] 2.40 (1 H, dd, $J_{5,6}$ 8, $J_{2,6}$ 2 Hz, H-6), 2.60 (1 H, d, $J_{2,6}$ 2 Hz, H-2), 2.97 (1 H, d, $J_{5,6}$ 8 Hz, H-5), (2 H, s, CH₂O₂), 6.09 (3 H, s, CO₂Me), and 6.23 (3 H, s, CO₂Me), m/e 328 (5%), 326 (14), and 149 (100).

Hydrogenation of the Anhydride (2) *in Ethyl Acetate.*— The anhydride (2.38 g) in anhydrous ethyl acetate (40 cm³) was hydrogenated at atmospheric temperature and pressure over 10% palladium–charcoal (uptake 1.9 mol. equiv.). The filtered solution was evaporated, and the residue crystallised from anhydrous benzene–acetone–hexane as short needles of 3,4-*methylenedioxybenzoylsuccinic anhydride* (6) (1.80 g, 85%), m.p. 145—146° (decomp.) (Found: C, 58.4; H, 3.3%; M^+, 248. $C_{12}H_8O_7$ requires C, 58.1; H, 3.25%; M, 248), $\nu_{max.}$ (CHCl₃) 1 880m and 1 790s (cyclic anhydride), 1 677 (aryl ketone), and 1 608 cm⁻¹, $\lambda_{max.}$ (CHCl₃) 239 (ε 13 300), 285 (5 530), and 327 nm (10 200), τ [(CD₃)₂CO] 2.17 (1 H, dd, $J_{5,6}$ 8, $J_{2,6}$ 2 Hz, H-6), 2.47 (1 H, d, $J_{2,6}$ 2 Hz, H-2), 2.97 (1 H, d, $J_{5,6}$ 8 Hz, H-5), 3.81 (2 H, s, CH₂O₂), 4.55 (1 H, dd, X part of ABX multiplet, disappears on addition of D₂O), ca. 6.55 (2 H, m, AB part of ABX multiplet, analysis [13] gives τ_A 6.47, τ_B 6.61; J_{AX} 4.9, J_{BX} 9.8, J_{AB} 18.6 Hz), and 6.03 (s, methylene of enol), m/e 248 (11%), 204 (10), 149 (100), 121 (24), 65 (23), and 63 (24).

The anhydride (2) (480 mg) in anhydrous ethyl acetate (20 cm³), hydrogenated over Adams catalyst (48 mg) (uptake 2.0 mol. equiv.), gave 3,4-methylenedioxybenzoylsuccinic anhydride (6) (260 mg, 61%).

Hydrolysis of the Succinic Anhydride (6).—A solution of the anhydride (167 mg) in aqueous sodium hydroxide (10%; 2 cm³) was kept for 16 h, acidified with hydrochloric acid, and extracted with ethyl acetate. The dried (MgSO₄) extracts were evaporated. N.m.r. data [(CD₃)₂CO] suggested the presence of a mixture (ca. 1 : 3) of 3,4-methylene-dioxybenzoylsuccinic acid and 4-oxo-4-(3,4-methylenedioxy-phenyl)butyric acid (8) {τ 2.27 (1 H, dd, $J_{5,6}$ 8, $J_{2',6}$ 2 Hz, H-6'), 2.53 (1 H, d, $J_{2',6'}$ 2 Hz, H-2'), 3.04 (1 H, d, J 8 Hz, H-5'), 3.88 (2 H, s, CH₂O₂), and ca. 6.7 and 7.3 (4 H, [AB]₂ multiplet, vicinal CH₂)}. Sublimation, at 155 °C and 0.01 mmHg, completed decarboxylation and gave the oxobutyric acid (8) (99 mg), m.p. 136—137° (lit.,[3] 136°) (Found: C, 59.15; H, 4.5%; M^+, 222. Calc. for $C_{11}H_{10}O_5$: C, 59.45; H, 4.55%; M, 222), $\nu_{max.}$ (mull) 1 707 (carboxy) and 1 667 cm⁻¹ (aryl ketone), $\lambda_{max.}$ (EtOH) 229 (ε 18 000), 273 (7 010), and 308 nm (7 740).

Thermolysis of the Succinic Anhydride (6).—Sublimation, at 155 °C and 0.1 mmHg, of the anhydride (6) (389 mg) gave, on crystallisation of the sublimate from acetone, 5-(3,4-*methylenedioxyphenyl*)*furan*-2(3H)-*one* (9) (209 mg) as thin blades, m.p. 156—158° (Found: C, 64.95; H, 4.1%; M^+, 204. $C_{11}H_8O_4$ requires C, 64.7; H, 3.95%; M, 204), $\nu_{max.}$ (CHCl₃) 1 805 (βγ-unsaturated γ-lactone) and 1 650

cm⁻¹, $\lambda_{max.}$ (EtOH) 213 (ε 25 200), 272 (9 906), 285 (6 870), and 289infl cm⁻¹ (6 190), τ (CDCl₃) 2.90 (1 H, dd, $J_{5',5'}$ 8, $J_{2',6'}$ 8, $J_{2',6}$ 2 Hz, H-6'), 3.00 (1 H, d, $J_{2',6'}$ 2 Hz, H-2'), 3.22 (1 H, d, $J_{5',6'}$ 8 Hz, H-5'), 4.06 (2 H, s, CH₂O₂), 4.44 (1 H, t, J 3 Hz, H-4), and 6.67 (2 H, d, J 3 Hz, 3-H₂).

Hydrogenation of the Chloro-anhydride (2) *in Aqueous Base.*—The chloro-anhydride (2) (597 mg) in aqueous sodium hydroxide (0.5N; 10 cm³) was hydrogenated over 10% palladium–charcoal (50 mg) (uptake 2.8 mol. equiv.). The filtered solution was acidified with hydrochloric acid and extracted with ethyl acetate. The dried (MgSO₄) extracts were evaporated and p.l.c. on silica [benzene–dioxan–acetic acid (200 : 25 : 4)] gave, as the low R_F band, (α-*hydroxy-3,4-methylenedioxybenzyl*)*succinic acid* (10) which after crystallisation from benzene–ethyl acetate–hexane melted at 124—126° and, as heating was continued, re-solidified, and melted again at 156—159° (Found: C, 54.0; H, 4.65. $C_{12}H_{12}O_7$ requires C, 53.75; H, 4.5%), $\nu_{max.}$ (mull) 1 719 (carboxy carbonyl) and 1 610 cm⁻¹, $\lambda_{max.}$ (EtOH) 204 (ε 25 500), 236 (3 320), and 287 nm (2 970), τ [(CD₃)₂CO] 3.0br (3 H, OH and CO₂H, exchanged on addition of D₂O), ca. 3.1 (3 H, m, aromatic), 4.03 (2 H, s, CH₂O₂), 5.06 (1 H, d, $J_{2,3}$ 7 Hz, α-H), 6.79 (1 H, q, CH·CO₂H), and 7.55 (2 H, m, CH_2·CO₂H). The high R_F band proved to be trans-2-(3,4-methylenedioxyphenyl)-5-oxotetrahydrofuran-3-carboxylic acid (11) (76 mg), which formed blades (from ethyl acetate–hexane), m.p. 164—165° (decomp.) (lit.,[5] 164—165°), identical (mixed m.p. and i.r. spectrum) with an authentic specimen [5] (Found: C, 57.3; H, 4.05%; M^+, 250. Calc. for $C_{12}H_{10}O_6$: C, 57.6; H, 4.05%; M, 250), $\nu_{max.}$ (mull) 1 745 (γ-lactone) and 1 723 cm⁻¹ (acid carbonyl), $\lambda_{max.}$ (EtOH) 203 (32 000), 238 (3 500), and 287 nm (2 900), τ[(CD₃)₂CO)] 3.0—3.2 (3 H, m, aromatic), 3.99 (2 H, s, CH₂·O₂), 4.40 (1 H, d, $J_{2,3}$ 8 Hz, H-2), 6.47 (1 H, m, H-3), and 7.05 (2 H, m, 4-H₂).

Lactonisation of the Hydroxy-diacid (10).—(a) *Thermal.* The hydroxy-diacid (216 mg) was heated in an oil-bath at 130 °C for 10 min. Crystallisation from ethyl acetate–hexane gave cis-2-(3,4-*methylenedioxyphenyl*)-5-*oxotetra-hydrofuran*-3-*carboxylic acid* (12) (102 mg), m.p. 160—163° (decomp.) (Found: C, 57.65; H, 4.05%; M^+, 250. $C_{12}H_{10}O_6$ requires C, 57.6; H, 4.05%; M, 250), $\nu_{max.}$ (mull) 1 730 cm⁻¹ (acid and lactone carbonyls), $\lambda_{max.}$ (EtOH) 202 (ε 30 300), 238 (3 670), and 287 nm (3 110), τ [(CD₃)₂CO] 3.15 (3 H, s, aromatic), 4.01 (2 H, s, CH₂O₂), 4.20 (1 H, d, $J_{2,3}$ 8 Hz, H-2), 6.20 (1 H, q, H-3), and 7.11 (2 H, d, 4-H₂).

(b) *Acid-catalysed.* The hydroxy-diacid (10) (71 mg) was dissolved in trifluoroacetic acid (1 ml). After 5 min the solution was evaporated to give a quantitative yield of trans-2-(3,4-methylenedioxyphenyl)-5-oxotetrahydrofuran-3-carboxylic acid (11), m.p. 156—159°, i.r. spectrum identical with that of an authentic sample. Repetition with trifluoroacetic [²H]acid gave a sample having no deuterium incorporated (n.m.r.).

Epimerisation of the cis-*Lactone* (12).—The cis-lactone (12) was dissolved in trifluoroacetic acid. After 5 min the solution was evaporated and the residue crystallised from ethyl acetate–hexane to afford the trans-isomer (11), m.p. 164—165° (i.r. and n.m.r. comparison). Repetition with trifluoroacetic [²H]acid left the n.m.r. spectrum unchanged.

Decarboxylation of the Lactone Acids (11) *and* (12).—The trans-isomer (11) (70 mg) was heated at 180 °C for 30 min. The residue was dissolved in aqueous sodium hydroxide

[13] E. D. Becker, 'High Resolution NMR,' Academic Press, New York, 1969.

(10%); the solution was washed with chloroform, acidified, and extracted with chloroform. Evaporation of the dried ($MgSO_4$) extracts gave *trans*-4-(3,4-methylenedioxyphenyl)-but-3-enoic acid (15) (52 mg), which crystallised from aqueous ethanol as plates, m.p. 115—116° (lit.,[5] 117—118°), τ ($CDCl_3$) 3.1—3.3 (3 H, m, aromatic), 3.58 (1 H, d, with broadening due to unresolved allylic coupling, $J_{3,4}$ 16 Hz, H-4), 3.93 (1 H, dt, $J_{3,4}$ 16, $J_{2,3}$ 6.5 Hz, H-3), 4.08 (2 H, s, CH_2O_2), and 6.75 (2 H, d, with broadening due to unresolved allylic coupling, $J_{2,3}$ 6.5 Hz, 2-H_2).

The same procedure with the *cis*-lactone (12) also gave the acid (15) (82%), identical (n.m.r. spectrum) with that above.

Rearrangement of (α-Chloro-3,4,5-trimethoxybenzylidene)-tetrahydrofuran-2,4,5-trione (19).—The trione (19) (1.0 g) was heated in a sublimation apparatus at 180 °C and 0.1 mmHg and the product distilled onto the cold finger. The i.r. spectrum of the crude product showed contamination with starting material (band at 1 720 cm⁻¹), and the material was resublimed at 180 °C to complete the conversion. Crystallisation from anhydrous benzene–hexane yielded *chloro-(3,4,5-trimethoxybenzoyl)maleic anhydride* (20) (523 mg) as orange prisms, m.p. 104—105° [Found: C, 51.6; H, 3.6; Cl, 10.55%; M (vapour phase osmometry), 330.5. $C_{14}H_{11}ClO_7$ requires C, 51.45; H, 3.6; Cl, 10.85%; M, 326.5], $v_{max.}$ ($CHCl_3$) 1 870m and 1 785s (cyclic anhydride), 1 660 (aryl, αβ-unsaturated ketone), and 1 621 cm⁻¹, $\lambda_{max.}$ ($CHCl_3$) 258 (ε 4 880) and 306 nm (6 640), τ [(CD_3)$_2$CO] 2.55 (2 H, s, H-2 and -6) and 6.10 (9 H, s, OMe), *m/e* 328 (33%), 326 (100), and 195 (100).

[14]C Labelling Study of the Rearrangement of the Trione (1). —Radiochemical counting techniques. A Nuclear Enterprises NE 8130 automatic scintillation counter was used. Samples (1—2 mg) of soluble compounds were accurately weighed (Cahn electrobalance) and solutions in dioxan (10 cm³) were prepared. A sample (2 cm³) was introduced into a 20 cm³ vial and mixed with dioxan-based scintillator (NE250) (10 cm³), and the activity was recorded. Counting efficiency was measured by addition of a ^{14}C-labelled internal standard (10 μl; 3.86 × 10⁵ disint. min⁻¹ cm⁻³). Background radiation was recorded (blank containing scintillator solution only) and averaged 23 counts min⁻¹. Barium carbonate was suspended in a gel composed of toluene-based scintillator (NE233) and the gelling agent (Carb-O-Sil).

3,4-Methylenedioxyphenyl[1-^{14}C]benzoic Acid.—Piperonal was decarbonylated with palladium–charcoal[14] to give 1,2-methylenedioxybenzene which, on treatment with *N*-bromosuccinimide, yielded 1-bromo-3,4-methylenedioxybenzene.[15]

To stirred magnesium turnings (2.4 g, 0.1 mol) in anhydrous tetrahydrofuran (40 cm³), under dry nitrogen, a few drops of ethylene dibromide were added, to initiate the reaction. 1-Bromo-3,4-methylenedioxybenzene (20.1 g, 0.1 mol) was added to maintain the temperature between 45 and 55 °C, and the mixture was then stirred for 1 h. [^{14}C]Carbon dioxide {from concentrated sulphuric acid (5 cm³) and aqueous sodium [^{14}C]carbonate (*ca.* 0.25 cm³; 0.25 mCi)} was passed into the Grignard reagent in nitrogen. Carbon dioxide (cylinder) was then passed in. After 2 h, solid carbon dioxide was added; the mixture was kept overnight, then poured into hydrochloric acid (100 cm³)

and ice (300 g). The product was extracted into ethyl acetate and washed with aqueous sodium hydroxide (10%). The basic extracts were acidified and the precipitate crystallised from ethanol to give 3,4-methylenedioxy-[1-^{14}C]benzoic acid (16), further crystallised to constant activity (1.68 μCi mmol⁻¹).

3,4-Methylenedioxyphenyl[3-^{14}C]propiolic   Acid.—3,4-Methylenedioxy[1-^{14}C]benzoic acid (12.2 g; 1.68 μCi mmol⁻¹) was refluxed with thionyl chloride (25 cm³) for 9 h. The excess of thionyl chloride was evaporated off, and the residue dissolved in benzene. The solution was added to stirred methoxycarbonylmethylenetriphenylphosphorane[16] (49.0 g) in benzene (750 cm³). Next day the precipitate was collected and washed with water to remove the phosphonium salt. The water-insoluble residue was combined with the benzene filtrate and the mixture was evaporated. The residue crystallised from aqueous ethanol to give the *betaine* (17) (31.3 g, 89%), prisms, m.p. 197—198°, specific activity 1.67 μCi mmol⁻¹. Analytical and spectroscopic data were determined for an inactive sample prepared by the same procedure (Found: C, 72.05; H, 5.0. $C_{29}H_{20}O_5P$ requires C, 72.25; H, 4.8%), τ ($CDCl_3$; 60 MHz) 1.9—2.7 (2 H, m, aromatic H-2 and -6), 3.22 (1 H, d, *J* 8 Hz, H-5), 4.11 (2 H, s, CH_2O_2), and 6.83 (3 H, s, MeO_2C).

By Markl's procedure,[7] the labelled betaine (17) (31.1 g; 1.67 μCl mmol⁻¹) was pyrolysed at 0.1 mmHg with a small flame. The yellow distillate, which solidified on cooling, was dissolved in methanol and aqueous 50% sodium hydroxide (50 cm³) was added. Next day the solution was evaporated, the residue treated with water, the insoluble triphenylphosphine oxide filtered off, and the filtrate cooled and acidified. Crystallisation from ethyl acetate afforded needles of 3,4-methylenedioxyphenyl[3-^{14}C]propiolic acid (18) (7.7 g, 63%), specific activity 1.67 μCi mmol⁻¹.

Preparation and Rearrangement of the Labelled Aryl(chloro)-methylene Trione (1).—A suspension of 3,4-methylene-dioxyphenyl[3-^{14}C]propiolic acid (4.4 g; 1.67 μCi mmol⁻¹) in benzene (25 cm³) was refluxed for 2 h with oxalyl chloride (10 g). After evaporation a portion of the crude product (*ca.* 450 mg) was removed and crystallised from benzene to give red plates of the trione (1) (377 mg), specific activity 1.66 μCi mmol⁻¹. The solution for counting was decolourised by addition of water (0.1 cm³).

The remainder of the product was rearranged, without further purification, by heating in a sublimation apparatus at 175 °C and 0.2 mmHg. Crystallisation from benzene–hexane gave the anhydride (2) (2.1 g), specific activity 1.68 μCi mmol⁻¹ [decolourised by water (0.1 cm³)].

Degradation of the Labelled Chloromaleic Anhydride (2).—Potassium permanganate (1.3 g) in water (40 cm³) was added over 30 min to stirred, refluxing, labelled chloromaleic anhydride (561 mg; 1.68 μCi mmol⁻¹) in water (20 cm³). Aqueous 10% sodium hydroxide was added and the manganese dioxide was filtered off and washed. The filtrate was acidified with hydrochloric acid and extracted with ethyl acetate. The dried ($MgSO_4$) extracts were evaporated and the residue (295 mg) purified by p.l.c. on silica [benzene–dioxan–acetic acid (100 : 20 : 4) as eluant], followed by sublimation (170 °C and 0.1 mmHg), and finally crystallisation from ethanol to constant activity, to give 3,4-methylenedioxy[1-^{14}C]benzoic acid (85 mg), specific activity 1.68 μCi mmol⁻¹.

Labelled methylenedioxybenzoic acid (54 mg; 1.68 μCi

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