The Chemistry of Compounds Derived by Microbial Oxidation of Benzene and Derivatives: Cycloadditions Involving 1,2-Isopropylidenedioxycyclohexadienes

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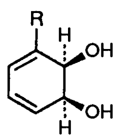
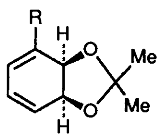
Various cycloadditions involving the cyclohexadiene derivatives **7–10** have been investigated. Diels–Alder reactions involving dimethyl acetylenedicarboxylate, nitrosobenzene and *N*-ethylmaleimide gave the adducts **11–14**, **16–17** and **18–23** respectively. Hydrolysis of the tricyclic compound **11** with pig liver esterase provided the optically active monoester **15**. Tropone, and three carbenes reacted with the diene **7** to give the polycyclic compounds **24** and **29**, **31** and **33** as expected. The structure of the adduct **24** was elucidated by X-ray crystallography. The ester **32** was converted into the lactone **36** by way of an oxa-Cope rearrangement of the aldehyde **34**. The dienes **7** and **8** reacted with diphenylketene in an unexpected fashion giving the enol ethers **27** and **28** as well as the expected [2 + 2] cycloaddition products **25** and **26**.

The conversion of benzene into cyclohexa-3,5-diene-1,2-*cis*-diol **1** by *Pseudomonas* spp was initially investigated in pioneering work by Gibson,[1] but it was the successful scale up of the biotransformation by Taylor and colleagues[2] that led to the material becoming commercially available for further elaboration. Through stereocontrolled oxidation reactions on the double bonds in the diene **1** syntheses of pinitol,[3] inositols[4] and conduritol-A[5] have been accomplished.

The biooxidation of simple benzene derivatives such as toluene and chlorobenzene can also be performed using *Pseudomonas*. A bonus is accrued in stereochemical terms in that the compounds obtained (*e.g.* **2** and **3**) are optically active. In those



1; R = H
2; R = Me
3; R = Cl
4; R = F
5; R = CF_3
6; R = 7-norborna-2, 5-dienyl



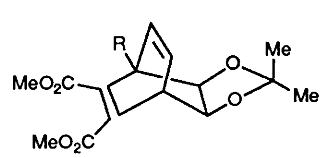
7; R = H
8; R = F
9; R = CF_3
10; R = 7-norbornadienyl

cases where the absolute configuration has been elucidated, the 1(*S*) form has been shown to be the major or sole enantiomer. Both compounds **2** and **3** have been used by Hudlicky as optically active starting materials for the preparation of enantiomerically pure prostaglandins[6] and sugar derivatives.[7] In addition, the work of Ribbons *et al.* has shown that polysubstituted benzene derivatives can be converted into cyclohexadienediols and the regioselectivity of the addition of dioxygen can be predicted with some accuracy.[8] Other researchers have reported that 2-methylnaphthalene[9] and some heterocyclic compounds[10] are also substrates for the dioxygenase enzymes.

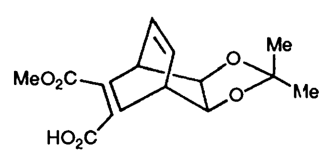
Results and Discussion

The controlled oxidation of benzene and derivatives has been a subject of interest at Sittingbourne Research Centre for some years and the diols **1–6** have been prepared in the Shell laboratories. We have recently been interested in taking the diols **1** and **4–6** obtained from *Pseudomonas* catalysed transformations, and subjecting the derived acetonides to various cycloadditions to give highly functionalised polycyclic products.[11] For example we have shown that the four dienes **7–10** react smoothly with dimethyl acetylenedicarboxylate to give adducts **11–14**. The addition of the alkyne takes place from the less hindered face. The product **11** can be 'de-symmeterized'[12,13] by hydrolysis using pig liver esterase. The half-ester that is obtained is optically active: the predominant isomer from such an hydrolysis would be expected to be the acid **15**,[14] but the absolute stereochemistry of the compound has not been confirmed. NMR studies on **15** involving chiral shift reagents have failed to reveal the presence of diastereoisomeric complexes. These experiments could be interpreted as indicating that the half-ester is enantiomerically pure but since racemic material is not available for use as a standard in these studies, this proposition must remain tentative.

Nitrosobenzene reacted with the acetal **7** to furnish the tricyclic compound **16**. Similarly addition of nitrosobenzene to the 7-substituted norbornadiene **10** gave the adduct **17**. The mode of the addition in the latter instance was confirmed by NOE experiments which demonstrated that the aromatic ring was adjacent to the proton –CH–N<.



11; R = H
12; R = F
13; R = CF_3
14; R = norbornadien-7-yl



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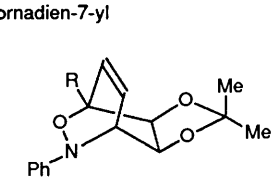


16; R = H
17; R = norbornadien-7-yl

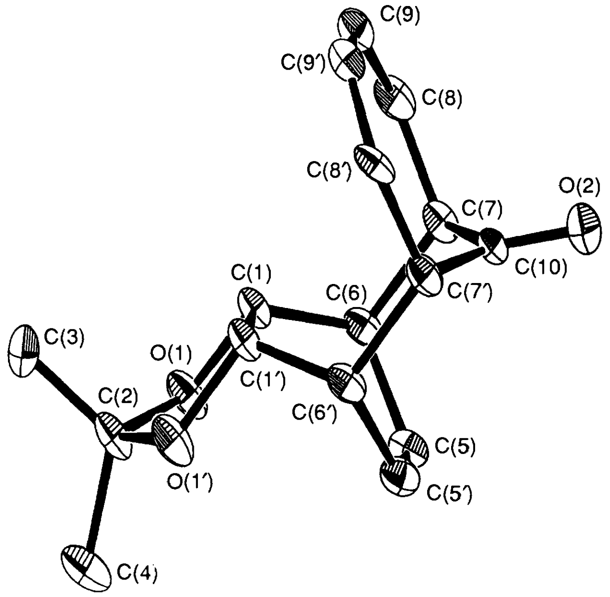
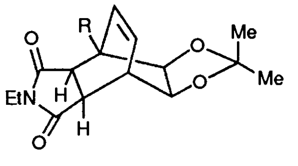
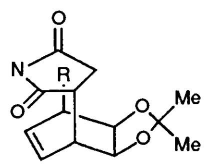


Fig. 1 Crystal structure of the ketone **24**

As expected,[15] *N*-ethylmaleimide adds to the diene **7** in a non-regioselective manner to give the adducts **18** and **21** in the ratio 2:3.[16] Similarly the trifluoromethyl compound **9** reacted with the amide to give two products **19** and **22** in the ratio 4:5, while the norbornadiene derivative **10** reacted with the same dienophile to furnish the adducts **20** and **23** (ratio 2:3).

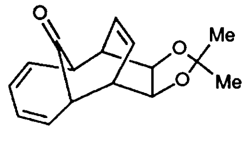


18; R = H
19; R = CF_3
20; R = norbornadien-7-yl



21; R = H
22; R = CF_3
23; R = norbornadien-7-yl

Tropone underwent a [6 + 4] cycloaddition with the diene **7** to afford only the adduct **24**: the structure of the product was confirmed by X-ray crystallography (Fig. 1). In contrast diphenylketene reacted in a non-specific manner with the diene **7** to give the expected [2 + 2] adduct **25** as the major product together with a lesser amount of the adduct **27** (note that reaction of diphenylketene and cyclohexa-1,3-diene yields only the [2 + 2]adduct.[16] More surprisingly, it was found that the fluoro compound **8** gave only a small amount of the cyclobutanone derivative **26**, affording the [4 + 2] adduct **28** as the major product. [4 + 2] Reactions involving the carbonyl group of ketenes as the dienophilic component are only rarely observed and are usually associated with a highly strained alkene or sterically encumbered diene.[17]



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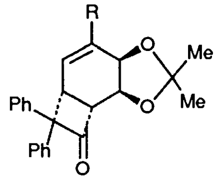
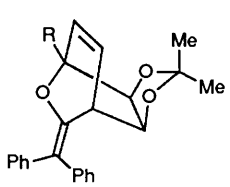
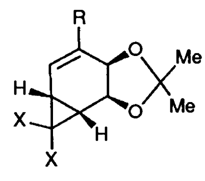


25; R = H
26; R = F

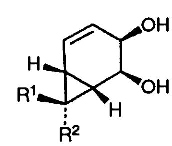


27; R = H
28; R = F

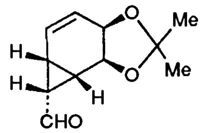
Dichlorocarbene reacted with the dienes **7** and **9** to give the tricyclic compounds **29** and **30** respectively. Similarly dibromocarbene added to the acetal **7** to furnish the cyclopropane derivative **31**. Ethoxycarbonylcarbene and the diene **7** produced a mixture of two adducts. Removal of the acetal moiety by acid treatment furnished the esters **32** and **33** in the ratio 5:6. The structure of the minor component **32** was determined by X-ray crystallography, while comparison of the NMR spectra of the compounds **32** and **33** led to the conclusion that the major component was the epimeric compound. Reprotection of the former compound followed by treatment with di-isobutylaluminium hydride gave the aldehyde **34** which existed in equilibrium with the enol **35** by way of an oxy-Cope rearrangement (ratio **34**:**35**, 9:1). Crystallisation of the mixture **34** and **35** gave solely the enol ether **35** (as shown by NMR spectroscopy) and this slowly reverted to the equilibrium mixture in solution. The bicyclic compound **35** is ripe for further elaboration. For example oxidation of the enol ether **35** with pyridinium chlorochromate afforded the lactone **36**.



29; R = H, X = Cl
30; R = CF_3, X = Cl
31; R = H, X = Br



32; R^1 = H, R^2 = CO_2Et
33; R^1 = CO_2Et, R^2 = H



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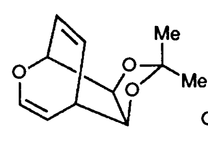

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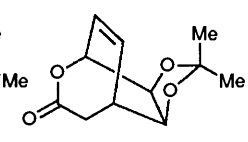

36

The reactivity of the dienes **7–10** has been explored and the regioselectivity of the reactions has been examined in a preliminary fashion. We are now pursuing syntheses of natural and unnatural sugars using selected cycloadducts as starting materials.

Experimental

Unless stated otherwise, all reagents were obtained from commercial suppliers and used without further purification. Benzene was dried over sodium wire. Light petroleum (b.p. 60–80 °C unless stated otherwise) and ethyl acetate were distilled from phosphorus pentoxide prior to use. Diethyl ether was distilled from sodium wire and benzophenone. Dichloromethane was distilled from calcium hydride. Brine refers to saturated aqueous sodium chloride.

Reactions were monitored by TLC on Merck Kieselgel 60 F_{254}, 0.25 mm plates. Preparative column chromatography was performed under low pressure using silica gel 60 H (0.04–0.063 mm/230–400 mesh) (Merck 9385). Solvent mixtures are expressed as volume:volume ratios.

250 MHz ^1H and 63 MHz ^{13}C NMR spectra were recorded on a Bruker AM250 spectrometer. Spectra were measured in deuteriochloroform unless stated otherwise and chemical shifts

are quoted in ppm downfield from tetramethylsilane. *J* values are given in Hz. IR spectra were recorded on a Perkin-Elmer 357 IR spectrophotometer as Nujol units unless stated otherwise. Mass spectra were obtained from the SERC Mass Spectrometry Centre, Swansea. Elemental analyses were conducted by Butterworth Laboratories Ltd., Teddington, UK.

Protection of cis-*Cyclohexa*-3,5-*diene*-1,2-*diol* **1**.—The diol **1** (1.12 g, 10 mmol) was dissolved in 2,2-dimethoxypropane (40 cm^3) and stirred in a flask cooled by an ice–salt bath. To the mixture was added a catalytic quantity of toluene-*p*-sulphonic acid monohydrate (0.2 g). After being stirred for 1 h the reaction mixture was quenched with triethylamine (0.5 cm^3). The solvent was evaporated under reduced pressure to give an oily residue which was diluted with diethyl ether (100 cm^3). The ethereal solution was washed with aqueous sodium hydroxide (1 mol dm^{-3}; 50 ml), which was subsequently back washed with diethyl ether (25 cm^3). The combined organic fractions were washed with distilled water (2 × 50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product (1.52 g) as a yellow oil. This oil was chromatographed eluting with ethyl acetate–light petroleum, (1:4) to give the acetal **7** as a colourless oil (1.09 g, 72%); δ_H 1.39 (3 H, d, *J* 1.0, CH_3), 1.41 (3 H, d, *J* 1.0, CH_3), 4.63 (2 H, m, 2 × OCH), 5.88 (2 H, m, 2 × OCHC*H*=CH) and 5.96 (2 H, m, 2 × HC=CHC*H*=CH); δ_C 24.7 (CH_3), 26.7 (CH_3), 70.3 (OCH), 104.6 (OCO), 123.6 (HC=CH*C*H=CH) and 125.3 (OCH*C*H=CH).

Protection of cis-3-*Fluorocyclohexa*-3,5-*diene*-1,2-*diol* **4**.—The diol **4** was recrystallized from diethyl ether–light petroleum (b.p. 40–60 °C) (1:9). The freshly recrystallised diol (0.593 g, 4.56 mmol) was dissolved in 2,2-dimethoxypropane (25 cm^3) and cooled to 0 °C in an ice-bath. A catalytic quantity of toluene-*p*-sulphonic acid monohydrate was added and the mixture was stirred for 2 h while its temperature was allowed to rise to ambient level. The reaction was then quenched by the addition of triethylamine (1 cm^3). The solvent was evaporated under reduced pressure to give an oily residue which was diluted with diethyl ether (25 cm^3) and washed with aqueous sodium hydroxide (1 mol dm^{-3}; 25 cm^3), brine (25 cm^3) and distilled water (2 × 25 cm^3). The organic phase was dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as an oil containing a few crystals. The crude product was subjected to column chromatography over silica gel, eluting with ethyl acetate–light petroleum (1:4). The first component eluted was the pure acetal **8** as a colourless oil (0.578 g, 3.4 mmol, 75%); δ_H 1.38 (3 H, d, *J* 0.5, CH_3), 1.41 (3 H, d, *J* 0.5, CH_3), 4.67 (1 H, dd, *J* 9.3 and 3.2, OCHCF), 4.82 (1 H, dddd, *J* 9.3, 3.7, 3.5 and 0.7, OCH), 5.54 (1 H, dd, *J* 11.4 and 6.3, FC=CH), 5.69 (1 H, dd, *J* 9.7 and 3.7, FC=CHCH=C*H*), 5.86 (1 H, dddd, *J* 9.7, 6.3, 5.2 and 0.7, FC=CHC*H*=CH). δ_C 24.7 (CH_3), 26.6 (CH_3), 70.5 (d, *J* 23.3, O*C*HCF), 73.8 (d, *J* 5.8, OCH), 101.6 (d, *J* 18.0, FC=*C*H), 106.7 (OCO), 121.9 (d, *J* 5.4, FC=CHCH=*C*H), 122.1 (d, *J* 6.6, FC=CH*C*H=CH) and 159.5 (d, *J* 270.4, CF).

Protection of cis-3-*Trifluoromethylcyclohexa*-3,5-*diene*-1,2-*diol* **5**.—The diol **5** (2.96 g, 16.4 mmol) was dissolved in AnalaR acetone and the solution cooled to 0 °C. Amberlyst-15 acid resin (0.3 g) was added and the mixture stirred for 2 h at 0 °C and overnight at ambient temperature. The resin was filtered off and the filtrate evaporated under reduced pressure to give the crude product as a viscous orange oil (3.38 g). This oil was subjected to column chromatography, eluting with ethyl acetate–light petroleum (1:4) to give the acetal **9** as a colourless oil (3.17 g, 88%). ν_{max}(neat)/cm^{-1} 3400br, 3000, 2925, 1610. δ_H 1.40 (3 H, s, CH_3), 1.42 (3 H, s, CH_3), 4.70 (1 H, dd, *J* 8.4 and 1.0, $OCHCCF_3$), 4.82 (1 H, dm, *J* 8.4, OCH), 6.05 (1 H, d, *J* 10, CF_3C=CHC*H*=CH), 6.08 (1 H, d, *J* 10, CF_3C=CHCH=C*H*) and 6.56 (1 H, cm, *J* 5 and 2, CF_3C=CH); δ_C 24.8 (CH_3), 26.4 (CH_3), 67.44 (q, *J* 0.7, O*C*HCCF$_3$), 71.7 (OCH), 106.2 (OCO), 120.5 (CF_3C=CH*C*H=CH), 123.6 (q, *J* 271.5, CF_3), 125.2 (q, *J* 30.8, *C*CF$_3$), 126.7 (q, *J* 6.0, CF_3C=CH) and 131.3 (q, *J* 1.3, CF_3C=CH=*C*H).

Protection of the Diol **6**.—The crude diol **6** was chromatographed over deactivated silica [eluent light petroleum–ethyl acetate (1:1, v/v)] to afford a white solid, m.p. 90–93 °C (ethyl acetate); ν_{max}($CHCl_3$)/cm^{-1} 3575, 3400–3200, 1400 and 1390; δ_H(C_5D_5N) 6.90–6.80 (2 H, m, 2 × C=CH), 6.68 (1 H, m, C=CH), 6.54 (1 H, m, C=CH), 6.04 (1 H, m, C=CH), 5.94 (1 H, m, C=CH), 5.56 (1 H, dt, C=CH), 4.64 (1 H, m, C*H*OH), 4.24 (1 H, d, *J* 6.5, C*H*OH), 3.79 (1 H, m, CH), 3.72 (1 H, m, CH) and 3.67 (1 H, s, CH). To a stirred solution of the dienediol **6** (0.24 g, 1.2 mmol) in 2,2-dimethoxypropane (15 cm^3) at room temperature under a nitrogen atmosphere was added a crystal of toluene-*p*-sulphonic acid. The resultant mixture was stirred at room temperature for 10 min. Dichloromethane (20 cm^3) was added to the mixture and the solution was washed with saturated aqueous sodium hydrogen carbonate (30 cm^3), 10% aqueous sodium hydroxide (30 cm^3) and brine (30 cm^3). The organic layer was dried and evaporated under reduced pressure to afford an oil, which was chromatographed over silica [eluent light petroleum–ethyl acetate (30:1, v/v)] to afford the *acetal* **10** (0.189 g, 65%); ν_{max}($CHCl_3$)/cm^{-1} 1255 and 1038; δ_H 6.89 (1 H, dddd, C=CH), 6.82 (1 H, dddd, C=CH), 6.65 (1 H, m, C=CH), 6.50 (1 H, m, C=CH), 5.95 (1 H, dd, *J* 5.8 and 9.6, CH), 5.75 (1 H, dd, *J* 3.8 and 9.6, CH), 5.50 (1 H, m, *J* 5.8, CH), 4.58 (1 H, dd, *J* 3.8 and 9, C*H*OH), 4.35 (1 H, d, *J* 9, C*H*OH), 3.74 (1 H, m, CH), 3.69 (1 H, m, CH), 3.36 (1 H, s, CH), 1.39 and 1.35 (6 H, 2 × s, 2 × CH_3); δ_C 144.9 (CH), 143.9 (CH), 141.3 (CH), 138.6 (CH), 136.8 (C), 124.4 (CH), 122.9 (CH), 120.4 (CH), 105.2 (C), 87.5 (CH), 73.6 (CH), 71.3 (CH), 52.6 (CH), 52.5 (CH), 26.9 (CH_3) and 25.2 (CH_3) (Found: M^+, 242.1307. $C_{16}H_{18}O_2$ requires *M*, 242.1307).

Addition of Dimethyl Acetylenedicarboxylate to cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7** *in Aqueous Medium*.—The acetal **7** (0.15 g, 1 mmol) was suspended in distilled water (2 cm^3) along with dimethyl acetylenedicarboxylate (0.12 cm^3, 0.14 g, 1 mmol). The mixture was stirred overnight and then extracted with ethyl acetate (2 × 5 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product (0.28 g) as a white crystalline solid. The crude product was subjected to column chromatography using, as eluent, ethyl acetate in light petroleum (1:3). This afforded the pure *adduct* **11** as a white crystalline solid (0.22 g, 76%) m.p. 90 °C; δ_H 1.26 (3 H, s, CH_3), 1.34 (3 H, s, CH_3), 3.79 (6 H, s, 2 × OCH_3), 4.23 (2 H, m, 2 × CH), 4.38 (2 H, m, 2 × OCH) and 6.39 (2 H, m, 2 × C=CH); δ_C 25.5 (CH_3), 25.7 (CH_3), 44.4 (CH), 52.3 (OCH_3), 113.7 (OCO), 131.3 (C=*C*H), 141.3 (C=C), 165.8 (C=O); ν_{max}/cm^{-1} 1717 and 1715 (C=O stretch); *m*/*z* (CI) 312 [$(M + NH_4)^+$, 10%], 295 [$(M + H)^+$, 100%], 195 (73), 100 (40), 85 (22) [Found: $(M + H)^+$ 295.1182; C, 61.2; H, 6.3%. $C_{15}H_{18}O_6$ requires (M + H) 295.1181; C, 61.2; H, 6.2%].

Addition of Dimethyl Acetylenedicarboxylate to cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7** *in benzene*.—The acetal **7** (1.52 g, 10 mmol) and dimethyl acetylenedicarboxylate (1.22 cm^3, 1.42 g, 10 mmol) were dissolved in dry benzene (20 cm^3). The mixture was refluxed for 24 h under an atmosphere of nitrogen and then evaporated under reduced pressure to give the crude product (2.95 g) as a pale yellow crystalline solid. This was subjected to column chromatography to afford the adduct **11** (2.50 g, 85%) m.p. 90 °C.

Addition of Dimethyl Acetylenedicarboxylate to cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* 7 *in Ethanediol.*—Dimethyl acetylenedicarboxylate (0.6 cm^3, 0.71 g, 5 mmol) and the acetal **7** (0.760 g, 5 mmol) were suspended in ethanediol (20 cm^3). The mixture was stirred for 41 h after which it was diluted with distilled water (40 cm^3) and extracted with ethyl acetate (3 × 40 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a solid (2.140 g). Column chromatography of the latter afforded the adduct **11** (1.170 g, 75%) as a white crystalline solid.

Addition of Dimethyl Acetylenedicarboxylate to cis-1,2-*Isopropylidenedioxy*-3-*fluorocyclohexa*-3,5-*diene* **8** *in Aqueous Medium.*—Dimethyl acetylenedicarboxylate (0.14 g, 0.12 cm^3, 1 mmol) and the acetal **8** were suspended in distilled water (2 cm^3). The mixture was stirred at ambient temperature for 6 d after which it was extracted with ethyl acetate (2 × 5 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a viscous oil (0.377 g). This was subjected to column chromatography, eluting with ethyl acetate–light petroleum (1:4). The first component eluted was the desired adduct as a viscous oil. The oil was dissolved in diethyl ether and then an equal volume of light petroleum (b.p. 40–60 °C) was added. The solvent was evaporated under reduced pressure to give the pure *product* **12** as a white crystalline solid (0.279 g, 90%), m.p. 79 °C; δ_H 1.22 (3 H, s, CH_3), 1.29 (3 H, s, CH_3), 3.68 (3 H, s, OCH_3), 3.78 (3 H, s, OCH_3), 4.30 (1 H, m, CH), 4.35 (1 H, m, OCH), 4.49 (1 H, m, FCCHO), 6.29 (FCCH=C*H*) and 6.40 (1 H, m, FCC*H*=CH); δ_C 25.55 (CH_3) 25.60(CH_3), 41.9 (d, *J* 1.9, CH), 52.5 (OCH_3), 52.6 (OCH_3), 78.0 (d, *J* 5.6, OCH), 79.8 (d, *J* 18.7, FC*C*HO), 100.1 (d, *J* 201.8, CF), 115.1 (OCO), 130.2 (d, *J* 9.8, FCCH=*C*H), 131.1 (d, *J* 27.2, FC*C*H=CH), 131.75 (d, *J* 5.2, FCC=*C*CO_2CH_3), 147.4 (d, *J* 25.6, FC*C*=CCO_2CH_3), 162.6 (d, *J* 2.8, FCCCO_2CH_3) and 164.1 (d, *J* 1.6, FCC=CCO_2CH_3); *m/z* (EI) 313 [(M + H)$^+$, 7%], 297 (11), 253 (2), 235 (6), 223 (12), 213 (5), 191 (7), 181 (74), 163 (4), 151 (7), 136 (3), 123 (4), 100 (100) and 60 (5) [Found: (M + H)$^+$ 313.1087. $C_{15}H_{17}FO_6$ requires (M + H) 313.1089] (Found: C, 57.7; H, 5.6; F, 6.1. $C_{15}H_{17}FO_6$ requires C, 57.7; H, 5.5; F, 6.1%).

Addition of Dimethyl Acetylenedicarboxylate to cis-1,2-*Isopropylidenedioxy*-3-*fluorocyclohexa*-3,5-*diene* **8** *in Ethanediol.*—Dimethyl acetylenedicarboxylate (0.14 g, 0.12 cm^3, 1 mmol) and the acetal **8** (0.17 g, 1 mmol) were suspended in ethanediol (2 cm^3). The mixture was stirred at ambient temperature for 6 d, and then diluted with distilled water (20 cm^3) and extracted with diethyl ether (4 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a viscous oil (0.457 g). Purification as described above gave the adduct **12** as a white crystalline solid (0.306 g, 98%).

Addition of Dimethyl Acetylenedicarboxylate to cis-1,2-*Isopropylidenedioxy*-3-*trifluoromethylcyclohexa*-3,5-*diene* **9** *in Benzene.*—The acetal **9** (0.11 g, 0.5 mmol) and dimethyl acetylenedicarboxylate (0.5 cm^3) were dissolved in dry benzene (3.0 cm^3) and the mixture was refluxed for 75 h under an atmosphere of nitrogen. The benzene was evaporated under reduced pressure to give a yellow oil, which was subjected to column chromatography over silica gel eluting with ethyl acetate–light petroleum (1:4). This afforded the pure adduct **13** as a white crystalline solid (0.15 g, 83%) m.p. 95 °C; δ_H 1.28 (3 H, s, CH_3), 1.35 (3 H, s, CH_3), 3.77 (3 H, s, OCH_3), 3.82 (3 H, s, OCH_3), 4.44 (1 H, m, OCH), 4.47 (1 H, m, CH), 4.62 (1 H, dm, *J* 7. OCH), 6.37 (1 H, dm, *J* 7.6, C=CH) and 6.56 (1 H, ddm, *J* 7.6 and 7.5, C=CH); δ_C 25.4 (CH_3), 25.7 (CH_3), 42.3 (O=CCCH), 52.6 (OCH_3), 52.7 (OCH_3), 78.6 (2 × OCH), 115.1 (OCO), 125.4 (q, *J* 281, CF_3), 127.0 (q, *J* 3.2, C=*C*H), 133.7 (C=*C*H), 137.1 (2 × C=*C*C=O), 162.8 (C=O) and 165.5 (C=O); *m/z* (CI) 380 [(M + NH_4)$^+$, 100%], 280 (16), 101 (5), 100 (6), 52 (9) [Found: (M + NH_4)$^+$ 380.1327. $C_{16}H_{17}F_3O_6$ requires (M + NH_4) 380.1321].

Addition of Dimethyl Acetylenedicarboxylate to the Tetrene **10**.—To a stirred solution of the acetal **10** (0.06 g, 0.25 mmol) in dry benzene (3 cm^3) at room temperature under a nitrogen atmosphere was added dimethyl acetylenedicarboxylate (0.035 g, 30 cm^3, 0.25 mmol). The resultant mixture was refluxed for 54 h after which it was evaporated under reduced pressure to afford a yellow oil, which was chromatographed over silica [eluent light petroleum–ethyl acetate (10:1 and 6:1 v/v)] to afford the *adduct* **14** (0.062 g, 65%); ν_{max}($CHCl_3$)/cm^{-1} 1725; δ_H 6.99 (2 H, t, 2 × C=CH), 6.76 (1 H, d, C=CH), 6.61 (2 H, t, 2 × C=CH), 6.23 (1 H, t, C=CH), 4.26 (2 H, m, C*H*OH), 4.18 (2 H, d, C*H*OH), 3.89 (1 H, m, CH), 3.82 (3 H, s, CO_2CH_3), 3.71 (3 H, s, CO_2CH_3), 3.66 (1 H, m, C*H*), 3.02 (1 H, s, CH), 1.30 and 1.23 (6 H, 2s, 2 × CH_3); δ_C 168.2 (C), 163.6 (C), 152.0 (C), 147.4 (CH), 146.6 (CH), 140.7 (CH), 139.9 (CH), 135.6 (CH), 133.1 (CH), 130.2 (CH), 113.0 (C), 86.4 (CH), 82.0 (CH), 79.4 (CH), 55.2 (C), 53.0 (CH), 52.8 (CH), 52.2 (CH_3), 52.2 (CH_3), 41.5 (CH), 25.8 (CH_3) and 25.7 (CH_3) (Found: M$^+$, 384.1575. $C_{22}H_{24}O_6$ requires *M*, 384.1573).

Enantioselective Hydrolysis of the Diester **11** *by Porcine Liver Esterase.*—To the diester **11** (0.10 g, 0.34 mmol) in buffer solution (100 × 10^{-3} mol dm^{-3} potassium phosphate, pH 8; 10 ml) and acetone (5 cm^3) was added the enzyme (150 units, 115 mm^3 porcine liver esterase, Biocatalysts Ltd.). The reaction was stirred overnight at ambient temperature. The reaction mixture was acidified (pH 3) by the addition of dilute hydrochloric acid (2 mol dm^{-3}) and extracted with ethyl acetate (6 × 10 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the product **15** as a white crystalline solid (0.092 g, 97%), m.p. 154 °C, $[\alpha]_D^{25}$ −34° [*c* 5.7 (CH_2Cl_2)]; δ_H 1.25 (3 H, s, CH_3), 1.33 (3 H, s, CH_3), 3.88 (3 H, s, OCH_3), 4.34 (2 H, m, 2 × OCH), 4.39 (1 H, m, CH), 4.61 (1 H, m, CH), 6.30–6.43 (2 H, br m, 2 × HC=C*H*) and 10.90 (1 H, br s, CO_2H); δ_C 25.5 (CH_3), 25.7 (CH_3), 45.0 (CH), 45.4 (CH), 53.5 (OCH_3), 77.9 (OCH), 78.0 (OCH), 113.8 (OCO), 130.6 (HC=*C*H), 131.7 (HC=*C*H), 141.8 (C=*C*) 145.0 (C=*C*), 165.4 (C=O) and 167.4 (C=O); *m/z* (CI) 298 [(M + NH_4)$^+$, 59%], 281 [M + H)$^+$, 87%], 198 (56), 181 (100), 101 (22), 100 (13) and 85 (6) [Found: (M + H)$^+$ 281.1025. $C_{14}H_{16}O_6$ requires (M + H) 281.1025].

Addition of Nitrosobenzene to cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7**.—The acetal **7** (0.152 g, 1 mmol) and nitrosobenzene (0.107 g, 1 mmol) were dissolved in dry benzene (5 cm^3) and the mixture was stirred at ambient temperature for 24 h. The colour of the solution turned from blue to pale blue–green. The mixture was evaporated under reduced pressure to give the crude product as a solid which was recrystallised from light petroleum (b.p. 40–60 °C) to give the pure adduct **16** as white fibrous crystals (0.166 g, 64%) m.p. 173 °C; δ_H 1.34 (6 H, s, 2 × CH_3), 4.64 (1 H, m, CH), 4.72 (2 H, m, 2 × CH), 4.88 (1 H, m, CH), 6.08 (1 H, m, C=CH), 6.47 (1 H, m, C=CH), 7.00 (3 H, 3 × Aryl H) and 7.23 (2 H, m, 2 × Aryl H); δ_C 25.5 (CH_3), 25.7 (CH_3), 59.9 (CH), 69.7 (CH), 73.7 (CH), 73.8 (CH), 110.6 (OCO), 117.7 (C=*C*H), 122.6 (C=*C*H), 128.5 (Aryl CH), 128.7 (Aryl CH), 129.5 (Aryl CH) and 151.0 (Aryl C); *m/z* (EI) 259 (M$^+$, 57%), 172 (36), 130 (100), 113 (22), 107 (32), 104 (28), 100 (24), 95 (58), 85 (23) and 77 (69) (Found: M$^+$ 259.1218. $C_{15}H_{17}NO_3$ requires *M*, 259.1208).

Addition of Nitrosobenzene to the Polyene **10**.—To a stirred solution of the acetal **10** (0.085 g, 0.35 mmol) in water (2 cm^3) at room temperature under a nitrogen atmosphere was added nitrosobenzene (0.035 g, 0.35 mmol). The resultant mixture was stirred at room temperature for 15 h after which it was extracted with diethyl ether (20 cm^3), the extract was dried ($MgSO_4$) and evaporated under reduced pressure to afford a yellow oil, which was chromatographed over silica [eluent light petroleum–ethyl acetate (19:1 and 9:1, v/v)] to afford the *adduct* **17** (0.08 g, 66%), $\nu_{max}(CHCl_3)/cm^{-1}$ 1498, 1250, 1035 and 710; δ_H 7.23 (2 H, m, Ar-H), 7.15 (2 H, m, 2 × C=CH), 6.95 (3 H, m, Ar-H), 6.72 (2 H, m, 2 × C=CH), 6.37 (1 H, td, C=CH), 5.98 (1 H, dddd, C=CH), 4.70–4.58 (2 H, m, CH and C*H*OH), 4.36 (1 H, dd, C*H*OH), 3.88 (2 H, m, 2 × CH), 3.06 (1 H, s, CH) and 1.30 (6 H, 2s, 2 × CH_3) (Found: M^+ 349.1678. $C_{22}H_{23}NO_3$ requires M, 349.1678).

Addition of N-*Ethylmaleimide to* cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7** *in Benzene solution.*—*N*-Ethylmaleimide (0.125 g, 1 mmol) was dissolved in sodium-dried benzene (5 cm^3) along with the acetal **7** (0.15 g, 1 mmol) and the mixture was stirred at ambient temperature for 48 h. The mixture was then evaporated under reduced pressure to give the crude product as a solid (0.267 g). This was subjected to column chromatography eluting with ethyl acetate–light petroleum (1:2). The first component eluted was the endo/syn *adduct* **21** (0.10 g, 37%) m.p. 125 °C; δ_H 1.06 (3 H, t, CH_2CH_3), 1.34 (3 H, s, CH_3), 1.48 (3 H, s, CH_3), 3.27 (2 H, m, 2 × O=CCH), 3.40 (2 H, m, 2 × CH), 3.46 (2 H, q, NCH_2), 4.13 (2 H, m, 2 × OCH and 6.10 (2 H, m, 2 × C=CH); δ_C 12.9 (CH_2CH_3), 24.2 (CH_3), 26.3 (CH_3), 33.5 (NCH_2), 36.8 (CH), 37.6 (CH), 74.0 (OCH), 112.5 (OCO), 131.4 (HC=CH) and 179.1 (NC=O). ν_{max}/cm^{-1} 1710s (C=O stretch); *m/z* (EI) 262 [$(M - CH_3)^+$, 5.6%], 220 (10.0), 219 (10.7), 191 (9.2), 176 (5.9), 174 (6.8), 162 (3.7), 147 (9.9), 146 (14.6), 121 (8.6), 120 (26.2), 118 (11.7), 103 (10.7), 100 (44.0), 93 (8.6), 92 (75.5), 91 (100), 85 (17.1), 79 (6.5), 78 (15.0), 77 (17.3), 70 (5.4), 65 (17.6), 59 (9.3), 56 (6.9), 55 (6.4), 52.4 (5.4), 50.9 (9.0), 44.5 (9.5), 43 (82.9), 41 (16.3) and 39 (18.4) [Found: $(M + H)^+$ 278.1395; $C_{15}H_{19}NO_4$ requires (M + H) 278.1392].

The second component eluted was the endo/anti *adduct* **18** (0.16 g, 59%) m.p. 203–206 °C; δ_H 1.06 (3 H, t, CH_2CH_3), 1.27 (3 H, s, CH_3), 1.31 (3 H, s, CH_3), 2.70 (2 H, m, 2 × O=CCH), 3.40 (2 H, m, 2 × CH), 3.45 (2 H, q, NCH_2), 4.26 (2 H, s, 2 × OCH) and 6.01 (2 H, m, 2 × C=CH); δ_C 12.9 (CH_2CH_3), 24.9 (CH_3), 25.3 (CH_3), 33.8 (NCH_2), 36.8 (CH), 37.6 (CH), 74.0 (OCH), 112.5 (OCO), 131.4 (HC=CH) and 179.1 (NC=O); ν_{max}/cm^{-1} 1705s (C=O stretch); *m/z* (EI) 262 [$(M - CH_3)^+$, 11.8%], 219 (15.0), 191 (11.2), 190 (10.4), 176 (8.4), 174 (7.8), 147 (10.2), 146 (16.1), 121 (7.9), 120 (28.3), 118 (11.8), 103 (8.1), 100 (45.1), 93 (9.2), 92 (80.3), 91 (100), 85 (20.3), 79 (6.7), 78 (18.2), 77 (19.1), 70 (5.3), 65 (16.6), 59 (6.9), 56 (6.5), 55 (6.2), 52 (5.6), 51 (9.5), 44 (11.9), 43 (84.5), 41 (16.6) and 39 (18.7) [Found: $(M + H)^+$ 278.1393; $C_{15}H_{19}O_4N$ requires (M + H) 278.1392].

Addition of N-*Ethylmaleimide to* cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7** *in Aqueous Medium.*—*N*-Ethylmaleimide (0.125 g, 1 mmol) and the acetal **7** (0.15 g, 1 mmol) were suspended in distilled water (5 cm^3) and stirred for 10 min at ambient temperature; a thick precipitate formed. The mixture was stirred for 4 d after which it was extracted with ethyl acetate (2 × 5 cm^3). The combined organic fractions were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product (0.24 g) as a white solid. This was subjected to column chromatography eluting with ethyl acetate–light petroleum (1:2). The first component eluted was the *endo/syn* adduct **21** (0.040 g, 14%). The second component eluted was the *endo/anti* adduct **18** (0.180 g, 65%).

Addition of N-*Ethylmaleimide to* cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7** *in Ethanediol.*—*N*-Ethylmaleimide (0.125 g, 1 mmol) and acetal **7** (0.152 g, 1 mmol) were suspended in ethanediol (5 cm^3) and stirred for 10 min at ambient temperature; a white precipitate formed. The mixture was stirred for 41 h, diluted with distilled water (40 cm^3) and extracted with ethyl acetate (2 × 40 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a solid (0.443 g). Column chromatography of this furnished the *endo/syn* adduct **21** (0.026 g, 9%) and the *endo/anti* adduct **18** (0.177 g, 64%).

Addition of N-*Ethylmaleimide to* cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7** *in Chloroform Solution.*—*N*-Ethylmaleimide (0.125 g, 1 mmol) and the acetal **7** (0.152 g, 1 mmol) were dissolved in AnalaR chloroform (5 cm^3) and the mixture was stirred at ambient temperature for 3 d. It was then evaporated under reduced pressure to give the crude product as a solid (0.290 g). Column chromatography of this gave the *endo/syn* adduct **21** (0.137 g, 49%) and the *endo/anti* adduct **18** (0.136 g, 49%).

Addition of N-*Ethylmaleimide to* cis-1,2-*Isopropylidene*-3-*trifluoromethylcyclohexa*-3,5-*diene* **9**.—*N*-Ethylmaleimide (0.12 g, 1 mmol) and the acetal **9** (0.22 g, 1 mmol) were dissolved in dry benzene and the resultant mixture was heated at reflux under nitrogen for 72 h. Removal of benzene under reduced pressure gave the crude product (0.40 g) as a white solid. This was subjected to column chromatography eluting with ethyl acetate–light petroleum (1:3).

The first component eluted was the endo/syn *adduct* **22** (0.13 g, 38%), m.p. 119–123 °C; δ_H 1.06 (3 H, t, CH_2CH_3), 1.35 (3 H, s, CH_3), 1.50 (3 H, s, CH_3), 3.41 (1 H, dd, *J* 8.2 and 3.1, O=CCH), 3.42–3.52 (3 H, m, NCH_2, CH), 3.54 (1 H, d, *J* 8.2, CF_3CCHC=O), 4.23 (1 H, dd, *J* 8.1 and 3.5, OCH), 4.29 (1 H, d, *J* 8.1, CF_3CCHO), 6.08 (1 H, d, *J* 8.5, CF_3CCH=CH) and 6.26 (1 H, t, *J* 8.5 and 6.6 CF_3CCH=C*H*); δ_C 12.9 (CH_3CH_2), 24.2 (CH_3), 26.2 (CH_3), 33.9 (CH_2), 36.7 (CH), 38.0 (CF_3CCHC=O), 38.1 ($CF_3CCHCHC$=O), 50.63 (q, *J* 27.6, CCF_3), 74.2 (CF_3-CCHCHO), 74.7 (q, *J* 3.0, CF_3C CHO), 125.9 (q, *J* 281.4, CF_3), 127.5 (q, *J* 3.3, CF_3CCH=CH), 132.8 (CF_3CCH=CH), 174.6 (C=O) and 177.4 (C=O); ν_{max}/cm^{-1} 1705s (C=O stretch); *m/z* (CI) 363 [$(M + NH_4)^+$, 100%], 362 (0.2), 349 (0.2), 347 (0.4), 346 (2.2), 345 (0.3), 331 (0.3), 330 (1.9), 307 (0.2), 305 (0.4), 304 (0.6), 100 (1.5) and 52 (1.4) [Found: $(M + NH_4)^+$ 363.1528; $C_{16}H_{18}F_3NO_4$ requires $(M + NH_4)$ 363.1531].

Later fractions contained the endo/anti *adduct* **19** (0.17 g, 50%), m.p. 169 °C; δ_H 1.08 (3 H, t, CH_2CH_3), 1.29 (3 H, s, CH_3), 1.33 (3 H, s, CH_3), 2.88 (2 H, m, 2 × O=CCH), 3.48 (2 H, q, NCH_2), 3.57 (1 H, m, CH), 4.39 (2 H, m, 2 × OCH), 6.08 (1 H, d, *J* 8.7, CF_3CCH=CH) and 6.22 (1 H, dd, *J* 8.7 and 6.4, CF_3CCH=C*H*); δ_C 12.8 (CH_3CH_2), 24.7 (CH_3), 25.3 (CH_3), 34.1 (CH_2), 36.0 (CH), 40.8 (CF_3CCHC=O), 41.2 (CF_3-CCHCHC=O), 50.4 (q, *J* 27.7, CCF_3), 77.4 ($CF_3CCHCHO$), 77.7 (CF_3CCHO), 110.8 (OCO), 124.8 (q, *J* 3.5, CF_3CCH=CH), 125.8 (q, *J* 282.3, CF_3), 131.0 (CF_3CCH=CH), 172.5 (C=O) and 175.2 (C=O); ν_{max}/cm^{-1} 1700s (C=O stretch); *m/z* (CI) 363 [$(M + NH_4)^+$, 100%], 361 (0.5), 349 (0.1), 348 (0.2), 347 (0.9), 346 (4.6), 345 (0.2), 344 (0.2), 343 (0.1), 335 (0.1), 332 (0.1), 307 (0.1), 305 (0.2), 304 (0.2), 304 (0.3), 302 (0.1), 100 (1.9), 58 (1.4) and 52 (1.9) [Found: $(M + NH_4)^+$ 363.1528; $C_{16}H_{18}F_3NO_4$ requires $(M + NH_4)$ 363.1531].

Addition of N-*Ethylmaleimide to the Acetal* **10**.—To a stirred solution of the acetal **10** (0.077 g, 0.32 mmol) in water (2 cm^3) at room temperature under a nitrogen atmosphere was added *N*-ethylmaleimide (0.04 g, 0.32 mmol). The mixture was stirred at room temperature for 15 h. An additional amount of *N*-ethylmaleimide (35 mg, 0.28 mmol) was added and the reaction mixture was stirred for 2 h at room temperature. The reaction mixture was extracted with diethyl ether (20 cm^3) and the extract dried and evaporated under reduced pressure to afford a pale brown oil, which was chromatographed over silica [eluent light petroleum–ethyl acetate (10:1, 5:1 and 2:1, v/v)] to afford in the first fractions the *adduct* **23** (42%) as a colourless oil; ν_{max}($CHCl_3$)/cm^{-1} 1694, 1403, 1352 and 908; δ_H 6.95 (2 H, m, C=CH), 6.59 (2 H, m, C=CH), 5.96 (2 H, m, C=CH), 4.10 (1 H, dd, CH), 3.82 (1 H, dd, CH), 3.78 (1 H, br s, CH), 3.65 (1 H, br s, CH), 3.44 (2 H, q, NCH_2), 3.40 (1 H, s, CH), 3.30 (1 H, m, CH), 3.22 (1 H, dd, CH), 3.06 (1 H, d, CH), 1.40 (6 H, 2s, 2 × CH_3) and 1.05 (3 H, t, CH_3) [Found: (M^+ + 1) 368.1862 $C_{22}H_{25}NO_4$ requires (M + 1) 368.1862].

The more polar compound was the *adduct* **20** (0.03 g, 27%); ν_{max}($CHCl_3$)/cm^{-1} 1694 and 908; δ_H 7.06 (1 H, m, C=CH), 6.96 (1 H, m, C=CH), 6.63 (1 H, m, C=CH), 6.50 (1 H, m, C=CH), 5.89 (1 H, m, *J* 1, 6.1 and 8.4, C=CH), 5.77 (1 H, d, *J* 8.4, C=CH), 4.34 (1 H, dd, *J* 7.2, CHO), 4.14 (1 H, dddd, *J* 3.1 and 7.2, CHO), 3.91 (1 H, m, CH), 3.70 (1 H, m, CH), 3.43 (2 H, q, NCH_2), 3.30 (1 H, ddddd, *J* 2.8, 3.1 and 6.1, CH), 3.11 (1 H, s, CH), 2.65 (1 H, dd, CH), 2.53 (1 H, d, CH), 1.25 (6 H, 2s, 2 × CH_3) and 1.05 (3 H, t, CH_3) (Found: M^+, 367.1784. $C_{22}H_{25}NO_4$ requires *M*, 367.1784).

Addition of Tropone to cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7**.—The acetal **7** (0.15 g, 1 mmol) and tropone (0.32 g, 3 mmol) were dissolved in dry benzene (5 cm^3) and the mixture was refluxed for 4 d. The product was filtered off and washed with light petroleum (b.p. 40–60 °C) to give a white crystalline solid (0.11 g). The filtrate was concentrated under reduced pressure and subjected to column chromatography eluting with ethyl acetate–light petroleum (1:3). This afforded the pure *product* **24** (0.05 g) and gave the following combined yield of product (0.16 g, 62%), m.p. 205–220 °C (decomp.); δ_H 1.26 (3 H, s, CH_3), 1.33 (3 H, s, CH_3), 2.99 (2 H, m, 2 × CH), 3.59 (2 H, m, 2 × O=C–CH), 4.69 (2 H, s, 2 × OCH), 5.61 (2 H, m, 2 × C=CC=CH), 6.05 (2 H, m, 2 × C=CCH=C) and 6.17 (2 H, m, 2 × C=CH); δ_C 24.7 (CH_3), 25.7 (CH_3), 35.4 (2 × CH), 57.3 (2 × O=C*C*H), 77.2 (2 × OCH), 107.8 (OCO), 125.2 (2 × C=CC=*C*), 125.8 (2 × C=*C*C=C), 131.9 (2 × C=C) and 206.2 (C=O); ν_{max}cm^{-1} 1708 (C=O stretch); *m/z* (EI) 258 (M^+, 8.1%), 243 (21.8), 200 (8.9), 199 (5.2), 183 (9.0), 172 (10.6), 129 (9.4), 128 (12.6), 115 (8.8), 108 (8.3), 107 (100), 106 (6.3), 95 (39.9), 94 (36.5), 91 (11.8), 78 (25.2) and 77 (16.9) (Found: M^+, 258.1248. $C_{16}H_{18}O_3$ requires *M*, 258.1256).

Addition of Diphenylketene to cis-1,2-*Isopropylidenedioxycyclohexa*-3,5-*diene* **7**.—The diene **7** (0.15 g, 1 mmol) and diphenylketene (0.29 g, 1.5 mmol) were heated under reflux in dry THF (tetrahydrofuran) for 20 h under an atmosphere of nitrogen. Water (20 cm^3) followed by saturated aqueous sodium hydrogen carbonate were added to give pH 8. The mixture was extracted with diethyl ether (3 × 20 cm^3). The combined organic phases were dried ($MgSO_4$), filtered and evaporated under reduced pressure. The residue was subjected to column chromatography eluting with ethyl acetate–light petroleum (1:15) to give the enol ether **27** (0.092 g, 27%), m.p. 153 °C; ν_{max}/cm^{-1} 1277; δ_H 1.33 (3 H, s, CH_3), 1.34 (3 H, s, CH_3), 3.92 (1 H, ddd, *J* 6.0, 4.0 and 2.0, PhC=CC*H*), 4.45 (1 H, dd, *J* 7.0 and 4.0, PhC=CCHC*H*O), 4.61 (1 H, dd, *J* 7.0 and 4.1, PhC=CCHCHOC*H*O), 5.11 (1 H, ddd, *J* 4.5, 4.1 and 2.0, PhC=COC*H*), 6.39 (2 H, m, 2 × HC=C*H*) and 7.20–7.60 (10 H, m, 10 × Aryl H). δ_C 25.51 (CH_3), 25.56 (CH_3), 40.62 (PhC=C*C*H), 71.69 (OCH), 73.91 (OCH), 76.00 (OCH), 110.74 (OCO), 114.70 (Ph*C*=CO), 125.80 (Aryl CH), 127.70 (Aryl CH), 128.42 (Aryl CH), 129.01 (PhC=CCHCH=*C*H), 129.47 (Aryl CH), 130.84 (Aryl CH), 131.48 (PhC=CCH*C*H=CH), 139.55 (Aryl C), 140.95 (Aryl C) and 144.92 (PhC=*C*O); *m/z* (EI) 346 (M^+, 46%), 276 (7), 259 (3), 246 (63), 217 (5), 194 (100), 165 (95), 152 (4), 139 (5), 115 (5), 105 (2), 95 (24), 85 (2), 77 (7), 66 (6) and 51 (2) (Found: C, 79.8; H, 6.6%; M^+, 346.1569. $C_{23}H_{22}O_3$ requires C, 79.7; H, 6.4%; *M*, 346.1569).

Later fractions contained the *ketone* **25** (0.112 g, 32%), m.p. 152 °C; ν_{max}/cm^{-1} 1770; δ_H 1.36 (3 H, s, CH_3), 1.40 (3 H, s, CH_3), 3.95 (1 H, dm, *J* 8.9, PhCC*H*), 4.12 (1 H, dd, *J* 8.9 and 2.3, O=CCH), 4.53 (1 H, dm, *J* 6.0, HC=CHC*H*O), 4.68 (1 H, dd, *J* 6.0 and 2.3, O=CCHC*H*O), 5.51 (1 H, dd, *J* 10.7 and 3.5, PhCCHC*H*=CH), 5.65 (1 H, dm, *J* 10.7, PhCHCH=C*H*) and 7.20–7.60 (10 H, m, 10 × Aryl H; δ_C 26.36 (CH_3), 28.00 (CH_3), 32.85 (PhC*C*H), 54.57 (O=CC*H*), 69.26 (O=CCH*C*HO), 69.55 (HC=CH*C*HO), 78.54 (Ph*C*Ph), 109.15 (OCO), 126.19 (PhCCH*C*H=CH), 126.88 (Aryl CH), 127.05 (Aryl CH), 127.48 (Aryl CH), 127.55 (Aryl CH), 128.20 (Aryl CH), 128.63 (PhCCHCH=*C*H), 129.04 (Aryl CH), 139.15 (Aryl C), 139.99 (Aryl C) and 206.00 (C=O); *m/z* (EI) 346 (M^+, 10%), 288 (5), 276 (49), 261 (6), 246 (22), 233 (6), 220 (26), 194 (97), 185 (7), 165 (100), 152 (5), 139 (5), 127 (4), 115 (7), 105 (2), 95 (21), 77 (6), 66 (3) and 51 (2) (Found: C, 79.6; H, 6.5%; M^+ 346.1569. $C_{23}H_{22}O_3$ requires C, 79.7; H, 6.4%; *M*, 346.1569).

Addition of Diphenylketene to cis-3-*Fluoro*-1,2-*isopropylidenecyclohexa*-3,5-*diene* **8**.—The diene **8** (0.17 g, 1.0 mmol) and diphenylketene (0.29 g, 0.3 cm^3, 1.5 mmol) were dissolved in dry THF (5 cm^3) and the mixture stirred at room temp. for 24 h. Water (20 cm^3) followed by saturated aqueous sodium hydrogen carbonate were added to give pH 8. The solution was extracted with diethyl ether (3 × 20 cm^3) and the combined organic fractions were washed with brine (60 cm^3) and water (60 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product. This was subjected to column chromatography over silica gel eluting with ethyl acetate–light petroleum (1:20) to give the *enol ether* **28** (0.279 g, 74%), m.p. 154 °C; δ_H 1.34 (3 H, s, CH_3), 1.38 (3 H, s, CH_3), 3.82 (1 H, m, FCC=CCH), 4.50–4.63 (2 H, br m, 2 × OCH, 6.30–6.47 (2 H, br m, 2 × C=CH) and 7.15–7.50 (10 H, br m, 10 × Aryl H); δ_C 25.478 (CH_3), 25.526 (CH_3), 40.664 (d, *J* 2.05, FCC=C*C*H), 75.580 (d, *J* 7.44, OCH), 78.613 (d, *J* 22.58, FC*C*HO), 111.923 (OCO), 112.946 (d, *J* 229.71, OCF), 116.251 (Ph*C*=CO), 126.326 (Aryl CH), 127.113 (Aryl CH), 127.811 (Aryl CH), 128.578 (Aryl CH), 128.801 (d, *J* 28.04, FC*C*=CH), 129.458 (Aryl CH), 130.688 (Aryl CH), 131.412 (d, *J* 11.40, FCCH=*C*H), 138.403 (Aryl C), 140.007 (Aryl C) and 141.490 (d, *J* 5.93, PhC=*C*O); *m/z* (EI) 364 (M^+, 15%), 264 (12), 215 (4), 194 (76), 182 (3), 165 (100), 139 (2), 113 (15), 77 (11) and 51 (7) (Found: M^+, 364.1475. $C_{23}H_{21}FO_3$ requires *M*, 364.1475).

Later fractions contained the *ketone* **26** (0.033 g, 9%), m.p. 125 °C; δ_H 1.38 (3 H, s, CH_3), 1.46 (3 H, s, CH_3), 4.11 (2 H, m, 2 × CH), 4.64 (1 H, d, *J* 6.4, FCCHO), 4.83 (1 H, tm, *J* 6.4, 5.6 and 1.9, CHO), 5.05 (1 H, dm, *J* 16.5, 2.4 and 2.4, FC=CH) and 7.15–7.55 (10 H, br m, 10 × Aryl H). δ_C 25.879 (CH_3), 27.717 (CH_3), 33.869 (d, *J* 7.69, PhC*C*H), 54.699 (d, *J* 2.25, O=C*C*H), 68.468 (d, *J* 23.52, FC*C*HO), 71.642 (d, *J* 6.97, CHO), 78.79 (d, *J* 3, Ph*C*Ph), 104.046 (d, *J* 18.69, FC=*C*H), 110.268 (OCO), 126.962 (Aryl CH), 127.169 (Aryl CH), 127.272 (Aryl CH), 127.742 (Aryl CH), 128.438 (Aryl CH), 129.148 (Aryl CH), 138.775 (Aryl C), 139.584 (Aryl C), 156.793 (d, *J* 260.07, CF) and 204.659 (C=O); *m/z* (EI) 364 (M^+, 57%), 294 (4), 275 (3), 264 (18), 235 (6), 220 (32), 194 (100), 165 (92), 183 (2), 165 (92), 155 (2), 139 (5), 113 (12), 91 (2), 84 (4) and 63 (2) (Found: M^+ 364.1475. $C_{23}H_{21}FO_3$ requires *M*, 364.1475).

7,7-*Dichloro*-2,3-*isopropylidenedioxybicyclo*[4.1.0]*hept*-4-*ene* **29**.—A mixture of the diene **7** (0.61 g, 4.0 mmol), 50% aqueous sodium hydroxide (11 cm^3) and a catalytic amount of triethylbenzylammonium chloride (TEBAC), was stirred vigorously at room temp. Chloroform (9 cm^3) was added dropwise over a period of 1 h to the emulsion which was then stirred for a further 6 h. After this it was diluted with water (40

cm^3) and chloroform (40 cm^3). The aqueous layer was separated and extracted with chloroform (3 × 20 cm^3). The organic fractions were combined, dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude product as an oil (1.11 g). This was purified by flash chromatography eluting with ethyl acetate–petroleum (b.p. 40–60 °C) (1:6) to yield the pure *product* **29** as a creamy coloured crystalline solid (0.92 g, 97%), m.p. 43.5–45.5 °C, R_F 0.45 (ethyl acetate–light petroleum 1:6); δ_H 1.37 and 1.39 (2 × 3 H, 2s, 2 × acetal methyl), 2.29 (2 H, m, 1-H and 6-H), 4.35 (1 H, m, *J* 6.9, 2.5 and 1.7, 3-H), 4.64 (1 H, m, *J* 6.9, and 1.0, 2-H), 5.76 (1 H, m, *J* 10.2 and 2.5, 4-H) and 5.96 (1 H, cm, *J* 10.2, 4.0, 2.2 and 1.7, 5-H); δ_C 25.9 (CH_3, acetal), 27.4 (C-6), 27.7 (CH_3, acetal), 28.7 (C-1), 63.2 (C-7), 67.9 (C-2), 70.4 (C-3), 109.4 (isopropylidene), 120.8 (C-5) and 128.4 (C-4); *m/z* (CI) 194 [(M + H)$^+$, 15%], 194 (14), 177 (30), 159 (65), 141 (100), 113 (8), 107 (6), 94 (9) and 76 (62) [Found: (M + H)$^+$ 235.0293; $C_{10}H_{12}Cl_2O_2$ requires (M + H) 235.0292].

7,7-*Dichloro*-2,3-*isopropylidenedioxy*-4-*trifluoromethylbicyclo*[4.1.0]*hept*-4-*ene* **30**.—A mixture of the diene **9** (0.66 g, 3.0 mmol), 50% aqueous sodium hydroxide (9 cm^3) and a catalytic amount of TEBAC (10–15 mg) was stirred vigorously at room temp. Dry chloroform (7.5 cm^3) was added dropwise to the emulsion over a period of 1 h after which stirring was continued for a further 8 h. Further aqueous sodium hydroxide (12 cm^3) was added, followed again by slow dropwise addition of chloroform (9 cm^3). Stirring was continued for 12 h after which the mixture was diluted successively with water (30 cm^3) and chloroform (30 cm^3). It was then filtered through a Celite pad. The pad was washed with chloroform (15 cm^3). The two layers were separated and the aqueous phase extracted with chloroform (2 × 20 cm^3). The organic fractions were combined, dried ($MgSO_4$), filtered and evaporated under reduced pressure to yield the crude product as a dark brown oil (1.23 g). This was purified by flash chromatography eluting with ethyl acetate–light petroleum (b.p. 40–60 °C) (1:10) to yield the pure *product* as a fragrant oil (0.88 g, 97%) R_F 0.55 (ethyl acetate–light petroleum 1:6); δ_H 1.41 (6 H, s, 2 × acetal methyl), 2.43 (2 H, m, 1-H and 6-H), 4.53 (1 H, d, *J* 6.7, 3-H), 4.73 (1 H, dd, *J* 6.7 and 1.2, 2-H) and 6.60 (1 H, m, *J* 5.0 and 1.3, 5-H); δ_C 25.8 (CH_3, acetal), 27.1 (C-6), 27.3 (CH_3, acetal), 29.6 (C-1), 62.5 (*J* 2.5, C-7), 68.3 (C-3), 68.9 (C-2), 110.7 (isopropylidene), 122.9 (CF_3), 126.2 (*J* 5.9, C-5) and 129.0 (*J* 29.5, C-4); *m/z* (CI) 303 [(M + H)$^+$, 15%], 289 (2), 287 (6), 244 (5), 227 (100), 209 (74), 193 (3), 175 (35), 161 (14), 145 (6), 76 (58) and 43 (13) [Found: (M + H)$^+$ 303.0166; $C_{11}H_{11}Cl_2F_3O_2$ requires (M + H) 303.0167].

7,7-*Dibromo*-2,3-*isopropylidenedioxybicyclo*[4.1.0]*hept*-4-*ene* **31**.—A mixture of the diene **7** (0.56 g, 3.67 mmol), 50% aqueous sodium hydroxide (2 cm^3), dichloromethane (1 cm^3), freshly distilled bromoform (1.77 g, 7 mmol) and tributylamine (0.15 cm^3) was stirred vigorously at 35–45 °C for 3 h. Addition of some more bromoform (1.83 g, 7.2 mmol), 50% aqueous sodium hydroxide (1 cm^3) and tributylamine (0.1 cm^3) was followed by stirring at 45 °C for a further 4 h. The solution was diluted with water (5 cm^3) and dichloromethane (5 cm^3). The organic layer was then separated and the aqueous layer extracted with dichloromethane (3 × 5 cm^3). The organic fractions were combined, washed with water (5 cm^3), dil. hydrochloric acid (5 cm^3) and brine (5 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure to yield the crude product as a brown oil. This was purified by flash chromatography using as eluent dichloromethane–light petroleum (b.p. 40–60 °C) (1:2) to yield the *adduct* **31** as creamy coloured crystals (0.8 g, 67%), m.p. 80.7–82.7 °C, R_F 0.29 (dichloromethane–light petroleum 1:2); δ_H 1.35 and 1.37 (2 × 3 H, 2 × s, 2 × acetal methyl), 2.35 (2 H, cm, 1-H and 6-H), 4.36 (1 H, cm, *J* 7.0, 2.9 and 1.5, 3-H), 4.58 (1 H, dd, *J* 7.0 and 1.0, 2-H), 5.79 (1 H, dd, *J* 10.2 and 2.9, 4-H) and 5.98 (1 H, cm, *J* 10.2 and 1.5, 5-H), δ_C 25.8 (CH_3, acetal), 27.6 (CH_3, acetal), 28.2 (C-6), 30.0 (C-1), 32.8 (C-7), 69.3 (C-2), 70.3 (C-3), 109.4 (acetal), 123.2 (C-5) and 128.4 (C-4); *m/z* (CI) 325 [(M + H)$^+$, 10%], 284 (11), 266 (28), 249 (43), 204 (5), 185 (100), 169 (2), 157 (9), 122 (2), 106 (17), 94 (11), 76 (30) and 43 (8) [Found: (M + H)$^+$ 324.9262; $C_{10}H_{12}Br_2O_2$ requires (M + H) 324.9262].

2,3-*Dihydroxy*-7-endo-*ethoxycarbonylbicyclo*[4.1.0]*hept*-4-*ene* **32** *and* 2,3-*Dihydroxy*-7-exo-*ethoxycarbonylbicyclo*[4.1.0]-*hept*-4-*ene* **33**.—The diene **7** (2 g, 13.1 mmol) was dissolved in dry ether (6.5 cm^3) and stirred with rhodium(II) acetate dimer (58 mg, 0.13 mmol) at room temp. under an atmosphere of nitrogen. To this mixture over a period of 24 h was added ethyl diazoacetate (1.48 g, 1.36 cm^3, 13 mmol) dissolved in dry ether (4 cm^3) in such a manner that for the second half of the addition, the rate of addition was one half of that initially employed. Stirring was continued for 12 h before addition of a further equivalent of ethyl diazoacetate (1.48 g, 13 mmol) in a similar fashion. After the mixture had been stirred for a further 6 h, the catalyst was removed by centrifugation. The solution was evaporated under reduced pressure and the remaining crude oil was purified by flash chromatography eluting with ethyl acetate–light petroleum (b.p. 40–60 °C) (1:30) to furnish a mixture of *exo*/*endo* adducts (2.18 g, 70%), R_F 0.35 (ethyl acetate–light petroleum 1:4) which could not be separated.

The mixture of adducts (1.19 g, 5 mmol) was dissolved in 80% aqueous acetic acid (75–100 cm^3) and stirred at 70 °C for 8–10 h. The aqueous acid was removed under reduced pressure at 35 °C leaving the crude product as an oil behind. This was purified by flash chromatography eluting with ethyl acetate–light petroleum (b.p. 40–60 °C) (2:1). The first component eluted was the exo-*adduct* **33** as a colourless oil (0.46 g, 47%) R_F 0.33 (ethyl acetate–light petroleum 2:1); δ_H 29.24 (3 H, t, *J* 7.2, CH_3, ethyl), 1.67 (1 H, dd, *J* 4.9 and 3.6, 7-H), 1.96 (1 H, cm, *J* 8.5, 5.6 and 3.6, 6-H), 2.12 (1 H, m, *J* 8.1, 4.9 and 2.9, 1-H), 3.91 (1 H, m, *J* 4.9, 2.6 and 1.4, 3-H), 4.11 (2 H, q, *J* 7.5, CH_2, ethyl), 4.27 (1 H, m, *J* 4.9, 2.9 and 1.4, 2-H), 5.42 (1 H, dd, *J* 10.2, 1.4 and 1.4, 4-H) and 6.08 (1 H, m, *J* 10.2, 5.2 and 2.6, 5-H); δ_C 14.0 (CH_3, ethyl), 19.7 (C-6), 25.1 (C-1), 27.6 (C-7), 60.8 (CH_2, ethyl), 63.9 (C-2), 65.3 (C-3), 126.7 (C-4), 127.5 (C-5) and 171.0 (carbonyl); ν_{max}/cm^{-1} 1723 (s) C=O stretch; *m/z* (CI) 216 [(M + NH_4)$^+$, 100%] [Found: (M + NH_4)$^+$ 216.1236; $C_{10}H_{14}O_4$ requires (M + NH_4) 216.1235].

The second component eluted was the endo *adduct* **32** as a white crystalline solid (0.39 g, 39%), m.p. 87.5–89.5 °C, R_F 0.24 (ethyl acetate–light petroleum 2:1); δ_H 1.23 (3 H, t, *J* 7.2, CH_3, ethyl), 1.71 (1 H, m, *J* 8.5, 8.5 and 3.2, 1-H), 1.94 (1 H, m, *J* 9.0, 8.5 and 3.7, 6-H), 2.08 (1 H, dd, *J* 9.0 and 8.5, 7-H), 4.08 (2 H, q, *J* 7.5, CH_2, ethyl), 4.12 (1 H, dd, *J* 4.6 and 3.8, 3-H), 4.32 (1 H, dd, *J* 4.6 and 3.2, 2-H), 5.88 (1 H, dd, *J* 10.1 and 3.8, 4-H) and 5.96 (1 H, dd, *J* 10.1 and 3.7, 5-H); δ_C 14.1 (CH_3, ethyl), 17.2 (C-1), 21.9 (C-6), 26.4 (C-7), 60.3 (CH_2, ethyl), 63.8 (C-2), 64.7 (C-3), 125.5 (C-5), 130.0 (C-4) and 171.2 (carbonyl); $\nu_{max}(CHCl_3)/cm^{-1}$ 1725(s), C=O stretch; *m/z* (CI) 216 [(M + NH_4)$^+$, 40%], 198 (8), 181 (100), 135 (3), 124 (10) and 107 (3) [Found: (M + NH_4)$^+$ 216.1236. $C_{10}H_{14}O_4$ requires (M + NH_4), 216.1235].

Acetalisation of the Adduct **32**.—The adduct **32** (0.39 g, 2 mmol) was dissolved in 2,2-dimethoxypropane (50 cm^3) at 0 °C. A catalytic amount of toluene-*p*-sulphonic acid was added and the solution was stirred for 2–3 h. Upon completion of the reaction, the solution was quenched with triethylamine (1.0 cm^3) to precipitate ammonium hydrochloride as a white solid. The solution was filtered and evaporated under reduced pressure to yield the crude product. This was purified by flash chromatography eluting with ethyl acetate–light petroleum (b.p. 40–60 °C) (1:3) to give the protected *adduct* 7-

ethoxycarbonyl-2,3-isopropylidenedioxybicyclo[4.1.0]hept-4-ene as a colourless oil (0.47 g, 98%), R_F 0.47 (ethyl acetate–light petroleum 1:3); δ_H 1.14 (3 H, t, *J* 7.0, CH_3, ethyl), 1.29 (3 H, s, acetal methyl), 1.35 (3 H, s, acetal methyl), 1.68 (1 H, m, *J* 8.0, 8.0 and 0.5, 1-H), 1.91 (2 H, cm, 6-H and 7-H), 3.98 (2 H, q, *J* 7.0, CH_2, ethyl), 4.46 (1 H, dd, *J* 7.3 and 1.8, 3-H), 4.74 (1 H, dd, *J* 7.3 and 0.5, 2-H) and 5.69 (2 H, 4-H and 5-H); δ_C 14.1 (CH_3, ethyl), 17.1 (C-1), 17.2 (C-6), 24.1 (C-7), 25.1 (CH_3, acetal), 27.4 (CH_3, acetal), 60.2 (CH_2, ethyl), 69.3 (C-2), 70.2 (C-3), 108.6 (o, acetal), 120.9 (C-5), 127.4 (C-4) and 169.3 (carbonyl); $\nu_{max}(CHCl_3)/cm^{-1}$ 1725 (C=O stretch); *m/z* (CI) 239 [(M + H)$^+$ 20%], 198 (33), 181 (100) and 107 (2) [Found: (M + H)$^+$ 239.1283. $C_{13}H_{18}O_4$ requires (*M* + H) 239.1283].

6,7-*Isopropylidenedioxy*-2-*oxabicyclo*[3.2.2]*nona*-3,8-*diene* **35**.—A solution of diisobutylaluminium hydride in dichloromethane (1.5 mol dm^{-3}, 0.65 cm, 1 mmol) was added to a stirred solution of the *endo* adduct acetal (0.14 g, 0.61 mmol) in dichloromethane (10 cm^3) at −90 to −100 °C under nitrogen. The reaction mixture was stirred for 10 min before it was quenched by slow addition of methanol (15 cm^3), the temperature being kept as low as possible. The solution was then allowed to warm up to room temp. slowly over 12 h. The aluminium residues were filtered off and the remaining solution evaporated under reduced pressure to yield a crude oil. This was purified by flash chromatography eluting with ethyl acetate–light petroleum (b.p. 40–60 °C) (1:6). The first component eluted was starting material (0.01 g, 7%).

The second component was the *enol ether* **35** as a white crystalline solid (0.055 g, 47%), m.p. 53.5–54.5 °C, R_F 0.51 (ethyl acetate–light petroleum 1:6); δ_H 1.32 (3 H, s, acetal methyl), 1.35 (3 H, s, acetal methyl), 2.52 (1 H, dd, *J* 8.6 and 7.9, 5-H), 4.30 (1 H, dd, *J* 6.2 and 1.3, 1-H), 4.66 (1 H, dd, *J* 8.6 and 7.1, 4-H), 4.75 (2 H, m, 6-H and 7-H), 5.84 (1 H, m, *J* 8.9 and 6.2, 8-H), 5.88 (1 H, d, *J* 7.1, 3-H) and 6.53 (1 H, m, *J* 8.9, 7.9 and 1.3, 9-H); δ_C 24.7 (CH_3, acetal), 25.8 (CH_3, acetal), 32.4 (C-5), 70.3 (C-1), 77.2 (C-6), 78.8 (C-7), 101.2 (C-4), 108.5 (acetal), 120.9 (C-8), 139.5 (C-9) and 145.5 (C-3); $\nu_{max}(CHCl_3)/cm^{-1}$ 972, 851 (vinyl ether); *m/z* (EI) 194 [(M$^+$) 15%], 179 (17), 136 (73), 119 (22), 107 (100), 100 (4), 91 (30), 85 (6), 79 (45), 68 (22), 59 (4), 51 (7) and 43 (28) (Found: M$^+$, 194.0943. $C_{11}H_{14}O_3$ requires *M*, 194.0942). With time, a solution of **35** in $CDCl_3$ gave ^1H NMR signals corresponding to the aldehyde **34**; δ_H 1.36 (3 H, s, acetal methyl), 1.45 (3 H, s, acetyl methyl), 2.05 (1 H, m, 7-H), 2.13 (1 H, m, 6-H), 2.24 (1 H, m, 1-H), 4.42 (1 H, m, 3-H), 4.74 (1 H, 2-H), 5.73 (1 H, d, 4-H), 5.79 (1 H, d, 5-H) and 9.28 (1 H, d, 8-H).

The third component was the corresponding primary *alcohol* (0.018 g, 15%), R_F 0.05 (ethyl acetate–light petroleum 1:6) as a colourless oil; ν_{max}/cm^{-1} 3410 (OH); δ_H 1.36 (3 H, s, acetal methyl), 1.42 (3 H, s, acetal methyl), 1.50 (1 H, cm, *J* 8.4 and 6.5, 7-H), 1.66 (2 H, m, 1-H and 6-H), 3.46 (2 H, m, *J* 11.5, 8.4 and 6.5, 8-H and 9-H), 4.16 (1 H, m, *J* 6.7, 2.5 and 2.0, 3-H), 4.62 (1 H, m, *J* 6.7, 2-H), 5.57 (1 H, dd, *J* 10.4 and 2.5, 4-H) and 5.95 (1 H, m, *J* 10.4, 4.9 and 2.0, 5-H); δ_C 13.6 (C-1), 15.1 (C-6), 23.7 (C-7), 26.0 (CH_3, acetal), 27.9 (CH_3, acetal), 58.5 (C-8), 69.8 (C-2), 70.9 (C-3), 108.8 (acetal), 124.4 (C-5) and 125.5 (C-4); *m/z* (CI) 197 [(M + H)$^+$, 10%], 181 (3), 156 (100), 138 (80), 121 (52), 108 (20), 101 (22), 91 (28), 81 (2), 76 (10) and 60 (3) [Found: (M + H)$^+$ 197.1178. $C_{11}H_{17}O_3$ requires (M + H) 197.1177].

6,7-*Isopropylidenedioxy*-2-*oxabicyclo*[3.2.2]*non*-8-*en*-3-*one* **36**.—The enol ether **35** (0.04 g, 0.2 mmol) was dissolved in dichloromethane (1–2 cm^3) and pyridinium chlorochromate (0.09 g, 0.42 mmol) was added. The mixture was stirred at room temp. for 12 h after which it was evaporated under reduced pressure and the residue redissolved as far as possible in ether (10 cm^3). A black gum was filtered off and triturated with ether (10 cm^3). The combined ether fractions were evaporated under reduced pressure and purified by flash chromatography eluting with ether to give **36** as a white crystalline *solid* (0.02 g, 45%), m.p. 71–72 °C, R_F 0.06 (ethyl acetate–light petroleum 1:6); δ_H 1.32 (3 H, s, acetal methyl), 1.35 (3 H, s, acetal methyl), 2.86 (3 H, m, 2 × 4-H and 5-H), 5.60 (1 H, m, 1-H), 4.75 (2 H, m, 6-H and 7-H), 6.34 (1 H, m, 8-H) and 6.50 (1 H, m, 9(H); δ_C 24.6 (CH_3, acetal), 25.6 (CH_3, acetal), 33.2 (C-5), 37.3 (C-4), 70.2 (C-1), 76.6 (C-6), 77.2 (C-7), 109.6 (acetal), 128.4 (C-4), 137.9 (C-9) and 169.8 (carbonyl); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (C=O stretch); *m/z* (CI) 228 [(M + NH_4)$^+$, 97%], 211 (28), 194 (7), 170 (10), 152 (11), 135 (2), 124 (10), 107 (4), 100 (10), 81 (4) and 39 (2) [Found: (M + NH_4)$^+$ 228.1235. $C_{11}H_{18}NO_4$ requires (M + NH_4) 228.1235].

X-Ray Structure Determination of Ketone **24**.—*Crystal data.* $C_{16}H_{18}O_3$, M = 258.3, monoclinic, a = 6.746(2), b = 9.484(3), c = 10.713(2) Å, β = 98.75(2)°, U = 643.4 Å^3, space group $P2_1/m$, Z = 2, D_c = 1.33 g cm^{-3}, μ(Mo − Kα) = 0.52 cm^{-1}, $F(000)$ = 276. Data were measured at room temperature on a Hilger and Watts Y290 four-circle diffractometer in the range $2 \le \theta \le 24°$. A crystal of approximate dimensions 0.25 × 0.25 × 0.3 mm was used for data collection. 1178 Reflections were collected of which 651 were unique with $I \ge 3\sigma(I)$. Data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by Direct methods and refined using the SHELX suite of programs.

The asymmetric unit was seen to contain only half of the molecule, the second half being generated by reflection through

Table 1 Fractional atomic coordinates for the ketone **24**

Atom	*x*	*y*	*z*
O(1)	0.2642(9)	0.1313(4)	0.0371(4)
O(2)	−0.1126(12)	0.2500	−0.5001(6)
C(1)	0.2661(11)	0.1671(6)	−0.1005(5)
C(2)	0.3399(18)	0.2500	0.1157(8)
C(3)	0.5623(20)	0.2500	0.1413(10)
C(4)	0.2348(22)	0.2500	0.2414(10)
C(5)	−0.1077(12)	0.1783(7)	−0.1503(6)
C(6)	0.0800(12)	0.1050(6)	−0.1807(5)
C(7)	0.0838(12)	0.1117(6)	−0.3370(5)
C(8)	0.2811(13)	0.0805(7)	−0.3761(6)
C(9)	0.4217(13)	0.1715(7)	−0.4055(6)
C(10)	−0.0004(16)	0.2500	−0.3977(8)

Table 2 Bond lengths (Å)

Bond	Length (Å)	Bond	Length (Å)
O(1)–C(1)	1.442(6)	O(1)–C(2)	1.429(7)
O(2)–C(10)	1.190(11)	C(1)–C(6)	1.508(10)
C(1)–C(1′)	1.571(11)	C(2)–C(3)	1.484(16)
C(2)–C(4)	1.555(13)	C(5)–C(6)	1.518(10)
C(5)–C(5′)	1.360(13)	C(6)–C(7)	1.595(7)
C(7)–C(8)	1.477(10)	C(7)–C(10)	1.522(8)
C(8)–C(9)	1.350(10)	C(9)–C(9′)	1.489(14)

Table 3 Bond angles (°)

Bond	Angle (°)	Bond	Angle (°)
C(2)–O(1)–C(1)	107.5(5)	O(1)–C(2)–O(1′)	104.0(7)
C(6)–C(1)–O(1)	107.5(5)	C(3)–C(2)–O(1)	111.3(6)
C(4)–C(2)–O(1)	106.9(7)	C(4)–C(2)–C(3)	115.6(8)
C(5)–C(6)–C(1)	111.3(5)	C(7)–C(6)–C(1)	112.6(5)
C(7)–C(6)–C(5)	109.1(6)	C(8)–C(7)–C(6)	114.4(6)
C(10)–C(7)–C(6)	112.1(5)	C(10)–C(7)–C(8)	111.1(6)
C(7)–C(10)–C(7′)	119.0(8)	C(9)–C(8)–C(7)	128.7(6)
C(7)–C(10)–O(2)	120.2(4)		

a mirror plane containing the C(2), C(3), C(4), C(10) and O(2) atoms, which was implicit in the space group symmetry.

In the final least squares cycles all the atoms were allowed to vibrate anisotropically. Hydrogen atoms were included at calculated positions on sp^3 carbons which were not located on special positions [C(1), C(6) and C(7)]. All remaining hydrogen positions were visible in the final difference Fourier, but were not refined due to insufficient data.

Final residuals after 10 cycles of full-matrix least squares refinement were $R = 0.0871$ for unit weights. The total number of parameters varied was 94. Max. final shift/esd was 0.004, the average being 0.001. The max. and min. residual densities were 0.20 and -0.17 e $Å^{-3}$ respectively. Final fractional atomic coordinates and bond distances and angles are given in Tables 1, 2 and 3 respectively. Tables of anisotropic temperature factors, hydrogen atom positions and both interatomic and intramolecular distances are available as supplementary data from the CCDC.* The molecule is shown in Fig. 1 along with the labelling scheme used.

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* For full details of Cambridge Crystallographic Data Centre deposition scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1991, Issue 1.

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