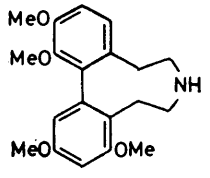
Diels–Alder Reactivity of Oxygenated Dienes and Furans. Synthesis of Oxygenated Biphenyls

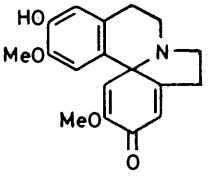
By **Edward McDonald,* Apichart Suksamrarn,** and **Robert D. Wylie,** University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW

2,3-Dimethoxybutadiene (4) (prepared by a new route from biacetyl) and 3,4-dimethoxyfuran (17) were heated with a series of styrenes to assess their potential for the synthesis of oxygenated biphenyls. Both dienes proved to be remarkably unreactive and only adducts (15) and (18) were obtained. Under comparable conditions 1-acetoxybutadiene (19) reacted in an efficient and regioselective manner with a variety of styrenes to give the trisubstituted cyclohexenes (21)—(25). 2,3-Dimethoxyfuran (28), generated *in situ*, reacted with phenylpropiolic ester in a non-regioselective manner to give a *ca.* 1 : 1 mixture of the highly functionalised biphenyls (42) and (43). The oxabicycloheptadiene (18) [from (4)] could not be aromatised but under varying acidic conditions it was hydrolysed to the oxabicycloheptenone (46) and gave the addition products (48) and (47) *via cis-exo*-addition.

OXIDATIVE phenol coupling [1] *in vivo* generates a wide variety of natural products having as a key structural feature an oxygenated biphenyl unit [*e.g.* (1)] or a 4-arylcyclohexa-2,5-dienone system [*e.g.* (2)]. Consequently there is a need for good routes for the synthesis of these units. Oxidative phenol coupling *in vitro* [2] has often



(1)



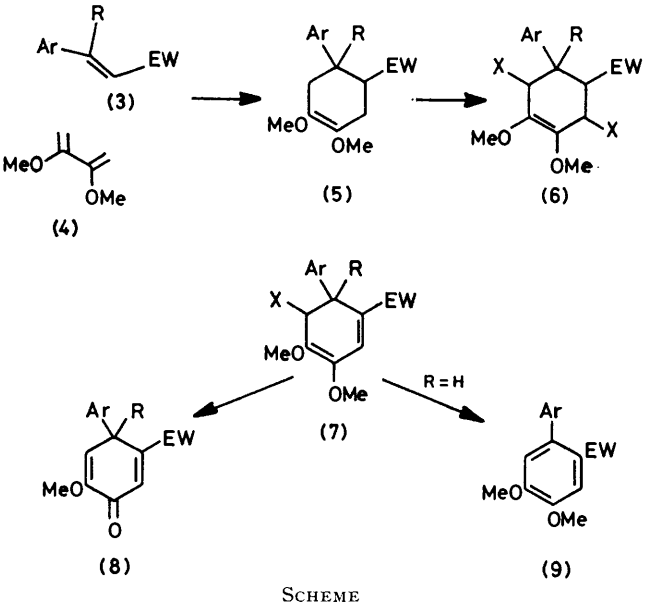
(2)

been used to this end, but yields were usually poor for this key step in the synthesis. New reagents have recently been introduced [3] for oxidative coupling of aromatic rings and we have drawn attention [4] to the design of the substrate for such reactions. With continuing progress oxidative coupling may soon be of general practical value: in the meantime we have investigated an alternative synthetic approach to biaryls and 4-arylcyclohexadienones and we now present our conclusions.

RESULTS AND DISCUSSION

The basis of the approach is summarised in the Scheme. A Diels–Alder reaction of a styrene (3) with 2,3-dimethoxybuta-1,3-diene (4) would generate (5) and transformation of (5) to the dienone (8) might be achieved by sequential allyllic bromination to (6), base-catalysed elimination, and silver-ion-assisted solvolysis of (7). When R = H, aromatisation of (7) should lead directly to the biphenyl (9). The viability of the whole scheme hinges on the initial Diels–Alder reaction and, prompted by the well known generalisation [5] that electron-rich dienes react well with electron-deficient dienophiles, we decided to study the reactions of diene (4) with a series of styrenes (3; R = H) having different electron-withdrawing groups (EW).

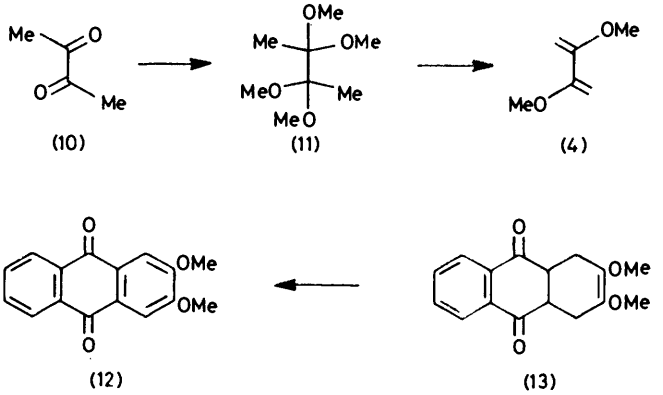
A synthesis of 2,3-dimethoxybutadiene (4) from buta-1,3-diene has been described [6] but the route appeared unsatisfactory and we therefore investigated a different approach. Reaction of biacetyl (10) with methanol–trimethyl orthoformate–sulphuric acid gave the bis-acetal (11). Distillation of crude (11) in the presence of ammonium dihydrogenphosphate and hydroquinone



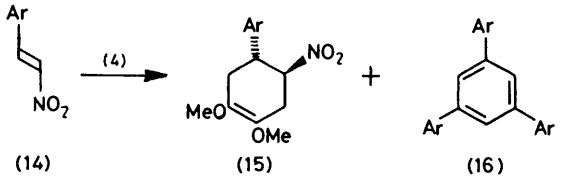
SCHEME

gave crude 2,3-dimethoxybutadiene (4) and the pure diene was obtained in 68% overall yield after redistillation.

The Diels–Alder reaction of diene (4) with naphthoquinone is reported [6] to give the *oxidised* adduct (12).

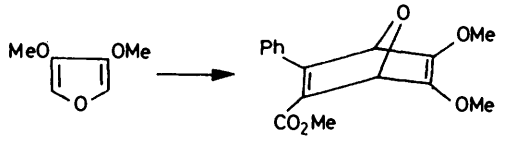


We repeated this reaction, and by careful work-up could isolate the initial adduct (13) which was converted to (12) by aeration of a solution in aqueous sodium hydroxide. Diels–Alder reactions of (4) were now attempted with a series of styrenes and with methyl phenylpropiolate.



(14) (15) (16)

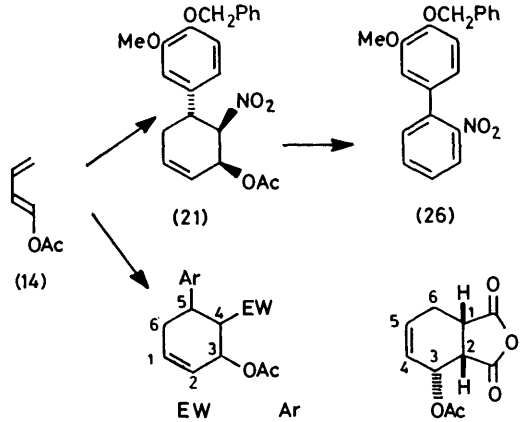
(Ar ≡ 3-benzyloxy-4-methoxyphenyl)



(17) (18)

The reactants in toluene were heated under reflux and the course of each reaction was followed by t.l.c. and by ^{1}H n.m.r. spectroscopy. The nitrostyrene (14) gave adduct (15) in 57% yield [and in addition a small amount of (16) formed by trimerisation of (14) and loss of nitrous acid] but no adduct was detected with any of the other dienophiles. Addition of BF_3 accelerated the polymerisation of diene (4) but did not catalyse the formation of the required adducts.

The *cisoid* conformation of the diene (4) is undoubtedly destabilised by steric interference between the two methoxy groups and this might be a major source of the poor reactivity observed. Accordingly we next investigated the reactivity of the corresponding furan (17). 3,4-Dimethoxyfuran (17) has been described [7] but the detailed procedures for its preparation are inaccessible: our methods are reported in the Experimental section. Furan (17) reacted with methyl phenylpropiolate (in the presence of a trace of 2,6-di-t-butylphenol) to give the adduct (18) but none of the styrenes reacted. Some reactions of the adduct (18) are described later.

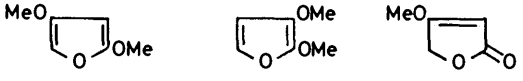


	EW	Ar
(22)	CN	Ph
(23)	COMe	Ph
(24)	CO_2Me	Ph
(25)	CO_2Me	p-$NO_2C_6H_4$

(20)

In sharp contrast to the diene (4) and furan (17) (*E*)-1-acetoxybuta-1,3-diene [8] (19) reacted with maleic anhydride and with every styrene tested to give the adducts (20)—(25) in good yield. Aromatisation of (21) (an oxidation) occurred in part during the Diels–Alder reaction, and could also be effected by heating pure (21) in pyridine, to give the biphenyl (26). It is quite clear from these results that *unsymmetrical* 1-acetoxybutadiene (19) is considerably more reactive than the *symmetrical* dienes (4) and (17) towards the *polarised* dienophiles of this study. The unsymmetrical dioxygenated furans (27) and (28) may therefore be sufficiently reactive to be of value for the synthesis of biphenyls oxygenated in the newly formed ring (such compounds are not available directly from 1-acetoxybutadiene): neither (27) nor (28) has previously been reported.

Although 2,4-dimethoxyfuran (27) appeared particularly attractive * we have so far been unable to prepare this compound. Reaction of the lithium derivative of methyl tetronate [9] (29) with methyl iodide



(27) (28) (29)

resulted in *C*-methylation only, and no sign of *O*-methylation was detected under a wide variety of conditions (see Experimental section), even when reactions were conducted in the presence of acetylenedicarboxylic ester in an effort to 'trap' the dimethoxyfuran (27) *in situ*. *O*-Acetylation and *O*-silylation were also attempted but from every experiment methyl tetronate (29) was recovered unchanged.

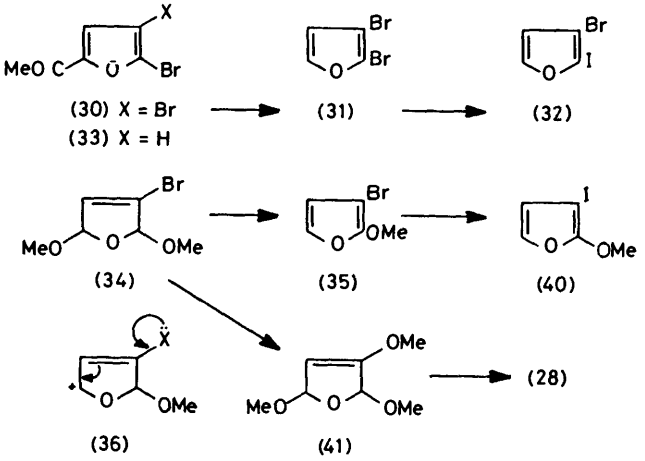
For the synthesis of 2,3-dimethoxyfuran (28) we first investigated nucleophilic substitution of halogenofurans. The dihalogenofurans (30),[10] (31),[10] and (32) (prepared as shown) were treated with methoxide ion in the presence of copper catalysts under a wide variety of conditions. No nucleophilic substitution was observed in any case even though the conditions chosen were successful in the benzenoid series [11] and on the monobromoester (33).[12] An alternative approach *via* a dihydrofuran was therefore developed.

Elimination of HBr from 3,4-dibromo-2,5-dimethoxytetrahydrofuran [13] gave the dihydrofuran (34). Aromatisation of (34) was achieved by acid-catalysed demethanolation at 250 °C and the unstable furan (35) was distilled directly from the reaction mixture in 28% yield. The formation of (35), $J_{4,5} = 2$ Hz, rather than the isomeric 4-bromo-2-methoxyfuran, is consistent with the intermediacy of the more stable linearly conjugated carbonium ion (36).

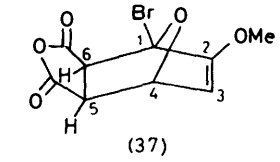
Reaction of freshly prepared 3-bromo-2-methoxyfuran

* The methoxy groups in (27) reinforce each other in polarising the molecule so that a strong and highly regiospecific interaction with styrenes (3) is predicted.

(35) with maleic anhydride gave the *exo*-adduct (37) ($J_{4,5} = 0$ Hz) in excellent yield, but the instability of the furan and the vigorous conditions required for its preparation led us to try trapping experiments using dienophile *in situ*. When the dihydrofuran (34) was heated with ethyl phenylpropiolate in toluene in the



presence of toluene-*p*-sulphonic acid, two isomeric biphenyls were isolated (*ca.* 1 : 1 ratio). The compound with higher R_F (t.l.c. on silica) gave i.r. spectra in which the broadness of the OH stretching frequency was independent of concentration; this behaviour expected



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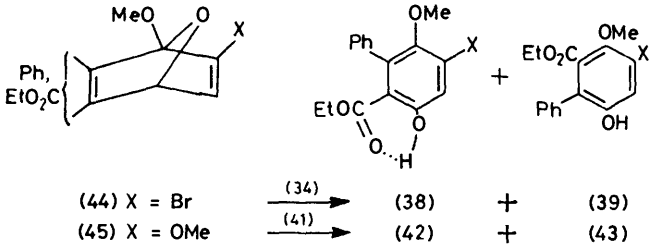
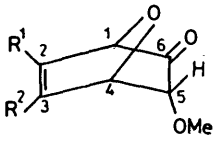


for (38) in which intramolecular hydrogen-bonding is possible. Conversely, the isomer with lower R_F and concentration-dependent i.r. spectra is assigned structure (39). Both assignments are fully supported by full analytical and spectral data and in particular the distinction between the isomers is confirmed by the appearance, only in the mass spectrum of (38), of a fragment at *m/e* 256 (loss of EtOH by a cyclic process).

2,3-Dimethoxyfuran (28) could not be prepared from (35), or from (40) by nucleophilic substitution, but copper-oxide-catalysed methanolysis of the vinyl bromide (34) gave the trimethoxydihydrofuran (41) in good yield. Demethanolation of (41) was attempted under a variety of acidic and strongly basic conditions, and although 2,3-dimethoxyfuran (28) could not be isolated, evidence for its formation (in xylene–toluene-*p*-sulphonic acid at reflux) was obtained by *in situ* trapping with ethyl phenylpropiolate. Two biphenyls (*ca.* 1 : 1 ratio) were isolated, and structures (42) and (43) were assigned on the same basis as for (38) and (39). All four adducts are clearly formed by aromatisation of the initial adducts (44) and (45) under the acidic reaction conditions.

In contrast with (44) and (45) the related adduct (18) (see above) could not be aromatised to a biphenyl. Lacking a methoxy-group at the bridgehead, the oxygen bridge of (18) survived a wide range of conditions



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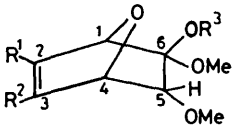

(47) R^3 = Me
(48) R^3 = Ac

isomer A: R^1 = CO_2Me, R^2 = Ph
isomer B: R^1 = Ph, R^2 = CO_2Me

designed to induce its removal. Thus the adduct (18) was recovered unchanged, or was transformed into an intractable complex mixture, after attempted reduction by Ph_3P,[14] Zn–AcOH, and Na–NH_3: treatment with sodium ethoxide or sodium hydride gave no aromatic product: and acidic reagents only affected the enediol ether system, as follows. Treatment of (18) with aqueous HCl gave a *ca.* 2 : 1 mixture of isomeric ketones (46), and the same products (in mixtures with a similar composition) were also obtained after dissolving (18) in trifluoroacetic acid, or in concentrated H_2SO_4 followed by quenching with ice. With methanolic HCl the isomeric acetals (47) were obtained while treatment with refluxing acetic acid gave a 3 : 1 mixture of the hemiacetal esters (48). Structures were assigned to the products (46)—(48) after careful assignments of their n.m.r. spectra assisted by deuteriation studies (Table). In all six compounds

^{1}H N.m.r. chemical shifts for adducts (46)—(48) (in all cases, isomer A is the major and isomer B the minor product)

Adduct	H-1	H-5-*exo* [a]	H-4 [a]	MeO-6-*endo*	MeO-5-*endo*	RO-6-*exo*	CO_2Me	Ph (3 H)	Ph (2 H)
(46A)	5.09	3.92 [b]	5.48		3.49		3.76	7.40	7.74
(46B)	5.03	3.94 [b]	5.61		3.60		3.74	7.40	7.68
(47A)	5.15 [c]	3.87	5.20 [c]	3.35	3.20	3.35 [a]	3.64	7.30	7.55
(47B)	5.04 [c]	3.81	5.34 [c]	2.90	3.47	3.32 [d]	3.64	7.30	7.55
(48A)	5.38	4.21 [b]	5.20	3.43	3.43	2.20	3.69	7.35	7.67
(48B)	5.55	4.02 [b]	5.38	3.07	3.49	2.15	3.70	7.35	7.67

[a] $J_{4,5}$ = 4.5 Hz for all the compounds. [b] Signal absent in product from CF_3CO_2D or CH_3CO_2D. [c] $J_{1,4}$ = 1 Hz. [d] Signal absent in product from CD_3OH.

$J_{4,5}$ is *ca.* 4.5 Hz proving [15] that H-5 is *exo* ($J_{4,5-endo}$ would be *ca.* 0 Hz, the dihedral angle being *ca.* 80°). The pairs are therefore not *endo-exo* stereoisomers, but regioisomers differing in their substituents at C-2 and C-3.

On mechanistic grounds, protonation at C-3 should be favoured by a phenyl group at C-5 (homoconjugation) so that the major product in each case should be isomer A. The spectral data are consistent with this assignment: in particular an unusually high-field OMe resonance seen in the spectra of the *minor* isomers of (48) and (47) can be assigned to a 6-*endo*-OMe shielded by a phenyl substituent at C-2;* and the downfield shift of H-5 in (48) supports the *exo*-OAc placing. Given these assignments, then the stereochemical course of the reactions leading to (48) and (47) is defined as *cis*-addition, with *exo*-protonation and *exo*-nucleophilic attack.

Conclusions.—With reactive dienophiles the doubly-oxygenated diene (4) and furans (17) and (28) gave, respectively, the adducts (15), (18), and a mixture of (42) and (43), but their potential for a general synthesis of oxygenated biphenyls is limited. With the symmetrical compounds (4) and (17) the problems are low reactivity and [for adducts from (17)] difficulty in removing the bridging oxygen atom, while the unsymmetrical furan (28) showed negligible regioselectivity. The 2,4-dioxygenated furans should suffer none of these disadvantages, but the compounds have so far remained elusive.

On the other hand, 1-acetoxybutadiene reacted in an efficient and regioselective manner with a variety of styrene derivatives to give a series of adducts which could be aromatised to biphenyls. The adducts are themselves of considerable synthetic potential.[16]

EXPERIMENTAL

2,3-*Dimethoxybuta*-1,3-*diene* (4).—A mixture of biacetyl (17.2 g, 0.2 mol), absolute methanol (25 ml, 1.25 mol), trimethyl orthoformate (63.6 g, 0.6 mol), and concentrated sulphuric acid (5 drops) was refluxed for 10 h. The excess of reagents were distilled off and the remaining liquid was vacuum-distilled. Ammonium dihydrogenphosphate (25 mg) and a few crystals of hydroquinone were added and the liquid was heated at *ca.* 100—110 °C. Methanol slowly distilled over, together with some remaining orthoformate. The temperature was raised and the colourless oily liquid collected between 129—135 °C (17.3 g or 76% of crude diene). Redistillation gave 2,3-dimethoxy-1,3-butadiene (15.5 g, 68%), b.p. 132—132.5 °C (lit.,[6] b.p. 134.5—135.5 °C) [*m/e*: 114 (M^+), 83; *m** = 62.18 (114→83); $\nu_{max.}$ 2 830, 1 627, 1 215, and 1 035 cm^{-1}; $\lambda_{max.}$ 231 nm; δ 3.57 (s, 2 × 3 H, MeO), 4.02 (d, *J* 1.5 Hz, 2 × 1 H, olefinic), and 4.57 (d, *J* 1.5 Hz, 2 × 1 H, olefinic)].

Diels–Alder Reactions of (4).—(*a*) *With naphthoquinone.* A mixture of 1,4-naphthoquinone (0.7 g, purified by sublimation) and 2,3-dimethoxy-1,3-butadiene (1.5 g) in benzene (1 ml) was refluxed for 30 h. After evaporation the residue was chromatographed (silica, CH_2Cl_2) to give 257 mg (21.3%) of the unstable adduct (13); *m/e* 272 (M^+); $\nu_{max.}$ 1 695 cm^{-1}; $\lambda_{max.}$ 252 and 295 (infl.) nm; $\lambda_{max.}$(alkali) 237, 245, and 281 nm (irreversible).

A solution of the adduct (13) (40 mg) in dichloromethane–methanol (0.2 ml) was stirred with aqueous sodium hydroxide (1N, 1.5 ml) at room temperature for 30 min. The yellow solid which separated was the anthraquinone (12) (32 mg, 81.0%), yellow crystals (from methanol), m.p. 235—236 °C (lit.,[6] m.p. 235—236 °C) (Found: C, 71.4; H, 4.6%. $C_{16}H_{12}O_4$ requires C, 71.63; H, 4.51%); *m/e* 268 (M^+, base-peak), 253, 238, 225, and 197; $\nu_{max.}$ 1 668 cm^{-1}; $\lambda_{max.}$ 237, 245, and 281 nm; δ 4.08 (s, 2 × 3 H, 2MeO), 7.70 (s, 2 H, Ar-H), 7.74 (m, 2 H, Ar-H), and 8.26 (m, 2 H, Ar-H)].

(*b*) *With nitrostyrene* (14) *to give* 4-(3-*benzyloxy*-4-*methoxy*)-*phenyl*-5-*nitro*-1,2-*dimethoxycyclohexene* (15). To a solution of the nitrostyrene (14) (1.9 g) in chloroform (1.5 ml) were added 2,3-dimethoxy-1,3-butadiene (1.6 g) and toluene (10 ml). The mixture was refluxed under nitrogen for 3 d. After evaporation the residue was chromatographed (silica, 40% CH_2Cl_2–pentane) to give 1.21 g (57.5%) of the adduct (15), m.p. 107—108 °C (from CH_2Cl_2–pentane) (Found: C, 66.15; H, 6.50; N, 3.40%. $C_{22}H_{25}O_6N$ requires C, 66.15; H, 6.31; N, 3.51%); *m/e* 399 (M^+) and 352; $\nu_{max.}$ 2 870, 1 600, 1 590, and 1 552 cm^{-1}; $\lambda_{max.}$ 225, 279 nm; δ 2.46 (m, 2 H, H_2-3), 2.84 (m, 2 H, H_2-6), 3.38 (m, 1 H, H-4), 3.62 and 3.65 (each s, 2 × 3 H, 2 × MeO), 3.84 (s, 3 H, aromatic MeO), 4.80 (m, 1 H, H-5), 5.12 (s, 2 H, PhCH_2O), 6.78 (m, 3 H, Ar-H), and 7.36 (m, 5 H, *Ph*CH_2O).

In the first run, the reaction mixture was chromatographed on alumina (grade III, 50% light petroleum–ether to pure ether) and a neutral compound, apart from the normal adduct, was isolated (7.5—8.00 mg from 200 mg of the starting nitrostyrene), m.p. 151—153 °C (from CH_2Cl_2–ether). It was characterised as the cyclic trimer (16); *m/e* 714 (M^+) and 91 (base-peak); $\nu_{max.}$ *ca.* 1 600 cm^{-1}; $\lambda_{max.}$ 269 and 294 nm; δ 3.94 (s, 3 × 3 H, 3 × MeO), 5.20 (s, 3 × 2 H, 3 × PhCH_2O), 7.05 (d, *J* 8 Hz, 3 × 1 H, H-6′), 7.35 (m, 3 × 7 H, H-2′, H-5′, and Ph), and 7.47 (s, 3 × 1 H, Ar-H).

Diethyl Diglycollate.—A mixture of diglycollic acid (60 g), absolute ethanol (250 ml), and concentrated sulphuric acid (10 drops) was refluxed for 4 h. The excess of ethanol was distilled off, the remaining liquid vacuum-distilled (oil pump), and diethyl diglycollate collected at 102—103 °C (0.8 mmHg) (lit.,[7a] b.p. 129—130 °C at 20 mmHg), yield 74.8 g (88%) [$\nu_{max.}$ 1 752 cm^{-1}; δ 1.30 (t, *J* 7 Hz, 2 × 3 H, Me), 4.23 (q, *J* 7 Hz, 2 × 2 H, CH_2CH_3), and 4.22 (s, 2 × 2 H, CH_2O)].

2,5-*Bisethoxycarbonyl*-3,4-*dihydroxyfuran.*—A cooled mixture of diethyl diglycollate (14.0 g, 0.1 mol) and diethyl oxalate (14.0 g, 0.1 mol) was added to dry sodium ethoxide (freshly prepared from 11.5 g of sodium metal). The mixture was stirred at room temperature for 2 h, then acidified (2N HCl) while cooling to give 14.8 g (61%) of 2,5-bisethoxycarbonyl-3,4-dihydroxyfuran, m.p. 191—192 °C (from methanol) (lit.,[7a] m.p. 186 °C) (Found: C, 49.40; H, 4.75. $C_{10}H_{12}O_7$ requires C, 49.18; H, 4.95%) [*m/e* 244 (M^+), 216, 198, and 170 (base-peak); $\nu_{max.}$ 3 460, 1 745, and 1 682 cm^{-1}; $\nu_{max.}$ (Nujol) 3 340, 1 685, and 1 655 cm^{-1}; $\lambda_{max.}$ 284 and 333 (infl.) nm; $\lambda_{max.}$ (alkaline) 222, 319, and 349 (infl.) nm; δ 1.41 (t, *J* 7 Hz, 2 × 3 H, Me), 4.45 (q, *J* 7 Hz, 2 × 2 H, CH_2), and 4.45 (br m, 2 × 1 H, OH)].

2,5-*Bisethoxycarbonyl*-3,4-*dimethoxyfuran.*—A mixture of the previously made dihydroxyfuran (4.88 g, 0.02 mol), dimethyl sulphate (K_2CO_3-dried, 7.6 g, 0.06 mol), and anhydrous potassium carbonate (7 g) in dry acetone (50 ml) was refluxed for 5.5 h, during which time more dimethyl sulphate (2 5 g, 0.02 mol) was added after intervals of 2 and 3 h. The hot solution was filtered and the filtrate evapor-

* The 6-*endo*-OMe must be pushed closer to C-2 than the 5-*endo*-OMe is to C-3, due to the additional oxy-function at C-6.

ated. Dilute aqueous ammonium hydroxide was added to the resulting residual, oily liquid, with vigorous stirring to give the colourless crystalline product, yield 4.6 g (84%), m.p. 88—89 °C (from hexane) (lit.,[7a] m.p. 89.5—90 °C) (Found: C, 53.45; H, 6.05. $C_{12}H_{16}O_4$ requires C, 52.99; H, 5.90); [*m/e* 272 (M^+, base-peak), 243, 277, and 199; *m** = 218.09 (272→243) and 174.45 (227→199); $\nu_{max.}$ 1 720 cm^{-1}; $\lambda_{max.}$ 275 nm; δ 1.40 (t, *J* 7 Hz, 2 × 3 H, Me), 4.03 (s, 2 × 3 H, MeO), and 4.40 (q, *J* 7 Hz, 2 × 2 H, CH_2O)].

3,4-*Dimethoxyfuran*-2,5-*dicarboxylic Acid*.—To a solution of 2,5-bisethoxycarbonyl-3,4-dimethoxyfuran (3.0 g) in dioxan (3 ml) was added 1N sodium hydroxide (60 ml) and the mixture refluxed for 5 h. The reaction mixture was filtered, cooled in an ice-bath, and acidified (1 N HCl) to give the white crystalline product, yield 2.2 g (92%), m.p. 255—257 °C (decomp.) (from methanol) [lit.,[7a] m.p. 243—245 °C (decomp.)]; [*m/e* 216 (M^+) (base-peak) and 170; $\nu_{max.}$(Nujol) 3 100—2 500 and 1 685 cm^{-1}; $\lambda_{max.}$ 272 nm; $\lambda_{max.}$ 268 nm; δ{$(CD_3)_2SO$} 3.95 (s, 2 × 3 H, MeO)].

3,4-*Dimethoxyfuran* (17).—3,4-Dimethoxyfuran-2,5-dicarboxylic acid (5.0 g) and a few pieces of boiling stone were placed in a Claisen flask equipped for distillation. Wood's metal was heated to 255—265 °C and the flask dipped into the molten metal so that three-quarters of it was submerged. The pale brown liquid (2.3 g, 79% crude product) which distilled over was redistilled and the colourless oil collected at 172—173 °C (1.8 g, 61% from the acid) (lit.,[7a] b.p. 172 °C) (Found: C, 56.0; H, 6.05%. $C_6H_8O_3$ requires C, 56.24; H, 6.29%); $\nu_{max.}$ 2 828, 1 630, 1 220, and 1 010 cm^{-1}; $\lambda_{max.}$ 226 nm; δ 3.73 (s, 2 × 3 H, MeO) and 6.90 (s, 2 × 1 H, olefinic).

For a small-scale (<1 g of the furandicarboxylic acid) preparation, the following procedure was preferable: the furandicarboxylic acid was placed in a pear-shaped flask which was equipped for reflux. The flask was dipped into the Wood's metal at 255—265 °C for 2 min. The reaction mixture was extracted with ether and washed with 5% aqueous sodium hydroxide and water, and dried. Upon evaporation of the solvent approximately the same yield of the crude dimethoxyfuran was obtained accompanied by more decomposition products.

Methyl 5,6-*Dimethoxy*-2-*phenyl*-7-*oxabicyclo*[2.2.1]*hepta*-2,5-*diene*-3-*carboxylate* (18).—A mixture of methyl phenylpropiolate (1.6 g), 3,4-dimethoxyfuran (1.48 g), and a few crystals of 2,6-di-t-butyl-*p*-cresol in toluene (2 ml) was refluxed under nitrogen for 44 h. The solvent was evaporated and the residue chromatographed (alumina, grade III, 10% dichloromethane–hexane) to give the recovered propiolate ester (680 mg), and the adduct (18) as a yellow semi-solid (1.48 g, 51.4 or 70.7% based on recovered starting material); *m/e* 288 (M^+), 299, 213, and 171; $\nu_{max.}$ 2 840, 1 710, 1 694, and 1 612 cm^{-1}; $\lambda_{max.}$ 284 nm; δ 3.72 (s, 2 × 3 H, 2 × MeO), 3.76 (s, 3 H, MeO), 5.08 (d, *J* 2.5 Hz, 1 H, allylic), 5.30 (d, *J* 2.5 Hz, 1 H, allylic), 7.30 (m, 3 H, aromatic), and 7.65 (m, 2 H, aromatic).

Methyl 5-*Methoxy*-6-*oxo*-3(2)-*phenyl*-7-*oxabicyclo*[2.2.1]-*hept*-2-*ene*-2(3)-*carboxylate* (46A *and* B).—The foregoing adduct (18) (70 mg) was dissolved in cold trifluoroacetic acid (1.5 ml). After stirring for 5 min the solvent was evaporated off and the residue partitioned between ether and water. The ether extract was evaporated and the residue chromatographed (p.l.c., SiO_2, 1.5% MeOH–$CHCl_3$) to give a *ca.* 4 : 1 mixture of isomeric keto-acids (46A and B); $\nu_{max.}$ 1 720 and 1 770 cm^{-1}; $\lambda_{max.}$ 285 nm; see the Table for n.m.r. data; *m/e* 274 (M^+), 246 ([M − CO]$^+$), 245, 215, 214, 202 {[$Ph(C_4H_2O)CO_2Me$]$^+$}, and 171 (202 − OMe); *m** 220.9 (274→246), 186.2 (246→214), and 144.7 (202→171). With CF_3CO_2D, the [3-^{2}H] adduct was obtained; *m/e* 275 (M^+) 247, 216, 215, 202, and 171; see the Table for n.m.r. data.

The same products were also obtained as follows. (*a*) *With aqueous* HCl. Adduct (18) (35 mg) in acetone (0.5 ml) and water (0.3 ml) was treated with 2—3 drops 1N HCl at 40—45 °C for 15 min to give a 2 : 1 mixture of (46A and B) (30 mg). (*b*) *With concentrated* H_2SO_4. Adduct (18) (55 mg) was dissolved in ice-cold concentrated H_2SO_4 (1 ml), and ice–water added after 10 min. Work-up gave a 2 : 1 mixture of (46A and B) (40 mg).

Methyl 5,6,6-endo-*trimethoxy*-3(2)-*phenyl*-7-*oxabicyclo*-[2.2.1]*hept*-2-*ene*-2(3)-*carboxylate* (47A *and* B). The bicyclic adduct (18) (80 mg) was dissolved in saturated methanolic HCl (2 ml) and the solution was warmed at 50—55 °C for 2 min and then evaporated to dryness. The residue was dissolved in ether–CH_2Cl_2 (10 : 1), washed (H_2O), dried, and evaporated to give a 2 : 1 mixture of the isomeric acetals (47A and B) (75 mg); $\nu_{max.}$ 1 710 cm^{-1}; $\lambda_{max.}$ 284 nm; see the Table for n.m.r. data; *m/e* 320 (M^+), 289 [M^+ − OMe]$^+$, 229, 214, and 171. The reaction was repeated using CD_3OH to give the [6-*exo*-CD_3O]acetals (see Table).

Methyl 6-exo-*Acetoxy*-5-endo,6-endo-*dimethoxy*-3(2)-*phenyl*-7-*oxabicyclo*[2.2.1]*hept*-2-*ene*-2(3)-*carboxylate* (48A *and* B).—The bicyclic adduct (18) (50 mg) was dissolved in glacial acetic acid. After 30 min the solvent was evaporated off and the residue chromatographed (p.l.c.; SiO_2; 2% MeOH–$CHCl_3$) to give a 3 : 1 mixture of the isomers (48A and B); $\nu_{max.}$ 1 700 and 1 740 cm^{-1}, $\lambda_{max.}$ 286 nm; see the Table for n.m.r. spectra.

(E)-1-*Acetoxybuta*-1,3-*diene* [8] (19).—Crotonaldehyde (105 g) was added slowly during 1 h to refluxing isopropenyl acetate (250 g) containing toluene-*p*-sulphonic acid (2.0 g) and copper(II) acetate (0.5 g). Heating was continued for a further 30 min and then the flask was set up for distillation and the bath temperature at 110—130 °C. After 2—2.5 h, when most of the acetone and unreacted isopropenyl acetate had been collected, the reaction mixture was vacuum-distilled to give acetoxybutadiene (138 g; 82%), b.p. 44—45 °C at 1.02 mmHg. Analysis of the ^{1}H n.m.r. spectrum revealed that acetoxybutadiene prepared in this way * is essentially the pure (*E*), isomer and this material was used for all the Diels–Alder reactions described below; *m/e* 112 (M^+) and 70 (base-peak); $\nu_{max.}$ 1 660 and 1 755 cm^{-1}; $\lambda_{max.}$ 233 nm; δ 2.12 (3 H, s, MeCO), 5.09 (1 H, dd, *J* 10 and 2 Hz, H-4*E*), 5.20 (1 H, dd, *J* 16.5 and 2 Hz, H-4*Z*), 6.01 (1 H, dd, *J* 12 and 10.5 Hz, H-2), 6.35 (1 H, ddd, *J* 16.5, 10.5, and 10 Hz, H-3), and 7.41 (1 H, d, *J* 12 Hz, H-1).

Diels–Alder Reactions of (E)-1-*Acetoxybuta*-1,3-*diene* (19). —(*a*) *With maleic anhydride*. Acetoxybutadiene (19) (2.5 g) was added to a solution of maleic anhydride (900 mg) in benzene (1 ml), and the solution (which became hot) was set aside at room temperature for 1 h. Evaporation and trituration with pentane gave the crystalline adduct (20) (1.93 g, 100%), m.p. 56—57.5 °C (from ether–hexane) (lit.,[18] m.p. 56—57.5 °C); $\nu_{max.}$ 1 740, 1 780, and 1 860 cm^{-1}; δ 2.03 (3 H, s, MeCO), 2.60 (2 H, m, H-6-α and -β), 3.41 (1 H, ddd, *J* 10, 8, and 4 Hz, H-1), 3.57 (1 H, dd, *J* 10 and 5 Hz, H-2), 5.42 (1 H, m, H-3), and 6.10 (2 H, m, H-4 and H-5). Decoupling experiments revealed: $J_{1.2}$ = 10 Hz; $J_{2.3}$ = 5 Hz; $J_{1.6\alpha}$ = 8 Hz; $J_{1.6\alpha}$ = 4 Hz; $J_{6\alpha.6\beta}$ = 17 Hz; δ 2.44 (H-6α), 2.78

* Reaction of crotonaldehyde with acetic anhydride–sodium acetate [17] gave acetoxybutadiene as an *E*–*Z* mixture (60% yield).

(H-6β). The adduct (200 mg) was converted into phthalic anhydride (38 mg, 27%), m.p. 128—129 °C (lit.,[19] m.p. 130—131 °C), by heating under reflux in pyridine for 40 h.

(*b*) *With a nitrostyrene.* A solution of acetoxybutadiene (4.5 g) and 4-benzyloxy-3-methoxynitrostyrene [20] (2.85 g) in toluene (7 ml)–chloroform (1 ml) was refluxed under N_2 for 3 d. After evaporation the residue was chromatographed on a silica column. Elution with dichloromethane–hexane (3 : 2) gave the aromatised adduct, 4-*benzyloxy*-3-*methoxy*-2′-*nitrobiphenyl* (26) (380 mg, 11%) as yellow crystals, m.p. 102—103 °C (from dichloromethane–pentane) (Found: C, 71.85; H, 5.15; N, 4.1. $C_{20}H_{17}NO_4$ requires C, 71.63; H, 5.11; N, 4.18%); *m/e* 355 (M^+), 244 ($[M - C_7H_7]^+$), and 91 ($[C_7H_7]^+$, base-peak); $\nu_{max.}$ 1 360, 1 570, and 1 605 cm^{-1}; $\lambda_{max.}$ 242 and 284 (sh) nm; δ 3.82 (3 H, s, OMe); 5.13 (2 H, s, OCH_2Ph), 6.75 (1 H, dd, *J* 8 and 1.5 Hz, H-6), 6.80 (1 H, H-2), 6.90 (1 H, d, *J* 8 Hz, H-5), 7.38 (8 H, m, Ph + H-4′, 5′,6′), and 7.73 (1 H, dd, *J* 8 and 1.5 Hz, H-3′). Further elution with solvent of increasing polarity gave the *adduct* (21) (1.62 g, 41%), m.p. 150—151 °C (from ether–pentane) (Found: C, 66.6; H, 5.7; N, 3.4. $C_{22}H_{23}NO_6$ requires C, 66.49; H, 5.83; N, 3.52%); $\nu_{max.}$ 1 370, 1 550, and 1 740 cm^{-1}; $\lambda_{max.}$ 228 and 279 nm; δ 2.06 (3 H, s, MeCO), 2.45 (2 H, m, H-6), 3.67 (1 H, m, H-1), 3.86 (3 H, s, OMe), 5.00 (1 H, m, H-2), 5.08 (2 H, s, OCH_2Ph), 5.85 (1 H, m, H-3), 6.08 (2 H, m, H-4 and H-5), 6.78 (3 H, m, Ar-H), and 7.35 (5 H, m, Ph); *m/e* 397 (M^+), 337 ($[M - HOAc]^+$), and 91 ($[C_7H_7]^+$, base-peak). The biphenyl (26) was also prepared by heating under reflux a solution of adduct (21) (45 mg) in pyridine (1.5 ml) for 50 h (yield 37%).

(*c*) *With cinnamonitrile.* A solution of acetoxybutadiene (2.36 g) and cinnamonitrile (1.29 g; 40% *cis*, 60% *trans*) in toluene (3 ml) was refluxed for 3 d. After evaporation the residue was chromatographed on a silica column, eluting with 60—80% dichloromethane–hexane to give first unreacted cinnamonitrile (440 mg), then a mixture of cis- *and* trans-3-*acetoxy*-4-*cyano*-5-*phenylcyclohex*-1-*ene* (22) (0.89 g; 37%), m.p. 148—155 °C (Found: C, 74.9; H, 6.35; N, 5.85. $C_{15}H_{14}NO_2$ requires C, 74.66; H, 6.27; N, 5.81%); *m/e* 241 (M^+) and 181 ($[M - HOAc]^+$); *m** 135.9 (241→181); $\nu_{max.}$ 1 730 and 2 242 cm^{-1}; $\lambda_{max.}$ 262 nm; δ 1.81 and 2.13 (each 3 H, s, MeCO *cis* and *trans*), 2.60 (2 H, m, H-6), 3.23 (2 H, m, H-4 and H-5), 5.34 and 5.48 (each 1 H, m, H-3 *cis* and *trans*), 5.96 (2 H, m, H-1 and H-2), and 7.26 (5 H, m, Ph).

(*d*) *With benzylideneacetone.* A solution of acetoxybutadiene (5.9 g), benzylideneacetone (2.92 g), and 2,6-di-t-butyl-4-methylphenol (5 mg) in toluene (4 ml) was heated under reflux (N_2) for 2.5 d. After evaporation, the residue was chromatographed on a silica column eluting with 40—90% dichloromethane–hexane to give unreacted benzylideneacetone (0.63 g) and adduct (23) (3.76 g; 73%), 3-*acetoxy*-4-*acetyl*-5-*phenylcyclohex*-1-*ene* (23), m.p. 73—74 °C (from ether–hexane) (Found: C, 74.65; H, 6.75. $C_{16}H_{18}O_3$ requires C, 74.39; H, 7.02%); *m/e* 258 (M^+), 198 ($[M - HOAc]^+$), 155 ($[M - HOAc - Ac]^+$, base-peak); $\nu_{max.}$ 1 715—1 740 cm^{-1}; $\lambda_{max.}$ 221 and 258 nm; δ 1.97 and 2.00 (each 3 H, s, 2 × MeCO), 2.38 (2 H, m, H-6), 3.30 (2 H, m, H-4 and H-5), 5.66 (1 H, m, H-3), 5.98 (2 H, m, H-1 and H-2), and 7.18 (5 H, m, Ph).

(*e*) *With methyl cinnamate.* A solution of acetoxybutadiene (2.0 g), methyl *trans*-cinnamate (1.62 g), and 2,6-di-t-butyl-4-methylphenol (5 mg) in toluene (3 ml) was refluxed (N_2) for 2 d. After evaporation the residue was chromatographed on a silica column, eluting with 60—80% dichloromethane–hexane to give unreacted methyl cinnamate (302 mg) and *methyl* 3-*acetoxy*-5-*phenylcyclohex*-1-*ene*-4-*carboxylate* (24) (1.57 g; 71%), m.p. 128—129 °C (from dichloromethane–pentane) (Found: C, 69.7; H, 6.3. $C_{16}H_{18}O_4$ requires C, 70.05; H, 6.61%); *m/e* 274 (M^+), 214 ($[M - HOAc]^+$), and 155; $\nu_{max.}$ 1 735 cm^{-1}; $\lambda_{max.}$ 262 nm; δ 2.02 (3 H, s, MeCO), 2.32 (2 H, m, H-6), 3.24 (2 H, m, H-4 and H-5), 3.40 (3 H, s, OMe), 5.66 (1 H, m, H-3), 5.89 (2 H, m, H-1 and H-2), and 7.20 (5 H, m, Ph).

(*f*) *With methyl* p-*nitrocinnamate.* A solution of acetoxybutadiene (2.6 g) and methyl *trans*-*p*-nitrocinnamate (1.04 g) in toluene (4 ml) was refluxed for 28 h. After evaporation the residue was chromatographed on a silica column, eluting with 60—100% dichloromethane–hexane to give in different fractions two isomers of adduct (25) (1.38 g; 87%): *methyl* 3-*acetoxy*-5-p-*nitrophenylcyclohex*-1-*ene*-4-*carboxylate* (25); *isomer A*, m.p. 191—193 °C (from dichloromethane–hexane (Found: C, 60.2; H, 5.4; N, 4.35. $C_{15}H_{15}NO_6$ requires C, 60.18; H, 5.37; N, 4.39%); $\nu_{max.}$ 1 600, 1 610, and 1 735—1 740 cm^{-1}; $\lambda_{max.}$ 270 nm; δ 1.83 (3 H, s, MeCO), 2.54 (2 H, m, H-6), 3.40 (2 H, m, H-4 and H-5), 3.45 (3 H, s, OMe), 5.33 (1 H, m, H-3), 6.01 (2 H, m, H-1 and H-2), 7.40 (2 H, d, *J* 8 Hz, H-2′ and H-6′), and 8.12 (2 H, d, *J* 8 Hz, H-3′ and H-5′); *m/e* 319 (M^+) and 277 (base-peak, $[M - CH_2{=}C{=}O]^+$).

The slower-running (25), *isomer B*, had m.p. 130—132 °C (from dichloromethane–pentane); $\nu_{max.}$ 1 597, 1 605, and 1 735—1 740 cm^{-1}; $\lambda_{max.}$ 270 nm; δ 2.03 (3 H, s, MeCO), 2.33 (2 H, m, H-6); 3.29 (2 H, m, H-4 and H-5), 3.45 (3 H, s, OMe), 5.69 (1 H, m, H-3), 6.01 (2 H, m, H-1 and H-2), 7.37 (2 H, d, *J* 8 Hz, H-2′ and H-6′), and 8.13 (2 H, d, *J* 8 Hz, H-3′ and H-5′).

Attempted Preparation of 2,4-*Dioxygenated-furans.*—Methylation of methyl tetronate [9] (29) was attempted using the following conditions: (*a*) $MeOSO_2F$–K_2CO_3–$CDCl_3$, reflux, 24 h: (*b*) $[Me_3O][BF_4]$–NPr^i_2Et–CH_2Cl_2, reflux, 24 h: (*c*) $HC(OMe)_3$–concentrated H_2SO_4–MeOH, reflux, 24 h: and (*d*) $Li[NPr^i_2]$–THF–MeI. The following silylation procedures were also tried: (*a*) $Li[NPr^i_2]$–THF–Me_3SiCl, 0 °C to reflux: (*b*) Me_3SiCl–Et_3N–$ZnCl_2$–benzene, 40 °C, 24 h:[21] and (*c*) Me_3SiCl–Et_3N, 40 °C, 6 h, then distillation.[22] No furan was detected in any of these reactions, nor were adducts formed when the reactions were repeated in the presence of acetylenedicarboxylic acid ester.

3-*Bromo*-2-*iodofuran* (32).—A 1.53M solution of butyllithium in hexane (2 ml) was added to a pre-cooled (−78 °C) solution of 2,3-dibromofuran [10] (31) (0.58 g) in dry ether (10 ml). The bath temperature was allowed to reach −30 °C before adding a solution of iodine (0.76 g) in ether (10 ml). When the bath temperature had reached 0 °C, the reaction mixture was poured into water (20 ml) and the ether extract was washed with aqueous $Na_2S_2O_3$, water, and saturated brine, and dried over Na_2SO_4. The ether was removed by distillation at atmospheric pressure to give crude 3-bromo-2-iodofuran (0.65 g; 94%), shown to be free of starting material by g.l.c. analysis. Attempted purification of this unstable compound resulted in decomposition, and microanalysis of the small sample proved unsatisfactory, but the structure is confirmed by the following data; *m/e* 274, 272 (M^+, ^{81}Br, ^{79}Br); $\nu_{max.}$ 1 550 cm^{-1}; $\lambda_{max.}$ 277 and 262 nm; δ 6.45 and 7.55 (each 1 H, d, *J* 2 Hz; H-4 and H-5 respectively).

3-*Bromo*-2,5-*dimethoxy*-2,5-*dihydrofuran* (34).—Bromine (37.1 g) was added dropwise to a stirred solution of 2,5-dimethoxy-2,5-dihydrofuran [13] (92 g) in carbon tetrachloride (3 l) and the reaction mixture was stirred at 25 °C for 20 h.

Evaporation of the solvent afforded 3,4-dibromo-2,5-dimethoxytetrahydrofuran (217 g) as a mixture of isomers; which was immediately added to a solution of sodium methoxide (from 26 g sodium) in dry methanol (500 ml). The resulting solution was refluxed for 3 h, then poured into water (600 ml). Ether extraction gave a crude product (116 g) which was vacuum-distilled to give *3-bromo-2,5-dimethoxy-2,5-dihydrofuran* (34) (112 g; 74%), a colourless liquid, b.p. 88—91 °C at 14 mmHg (Found: C, 34.4; H, 4.4; Br, 38.1. $C_6H_9BrO_3$ requires C, 34.4; H, 4.3; Br, 38.2%); *m/e* 209, 207 ($[M - H]^+$), 179, and 177 ($[M - OMe]^+$) (pairs of ions, ^{81}Br and ^{79}Br); $\nu_{max.}$ 1 630 cm^{-1}; $\lambda_{max.}$ 218 nm; $\delta(CCl_4)$ 3.32, 3.36, and 3.38 (each 3 H, s, 3 × OMe), and 5.42, 5.65, and 6.12 (each 1 H, m, H-2, H-5, and H-4 respectively).

3-Bromo-2-methoxyfuran (35).—The foregoing dihydrofuran (30 g) was added dropwise to a hot (250 °C) mixture of di-n-butyl phthalate (30 ml) and concentrated H_2SO_4 (0.1 ml) in a 3-necked flask fitted with a pressure-equalised dropping funnel, thermometer, and distillation head. The distillate (b.p. 89—120 °C) was collected in a flask containing solid K_2CO_3 (1 g) cooled by a solid CO_2–acetone bath. Vacuum-distillation of the crude distillate gave pure 3-bromo-2-methoxyfuran (b.p. 41—44 °C at 15 mmHg) [1.9 g; 7.5, or 12.9% based on recovered starting material (12.6 g; b.p. 89—91 °C at 15 mmHg]. The freshly prepared furan had *m/e* 178, 176 (M^+) and 147, 145 ($[M - OMe]^+$) (^{81}Br and ^{79}Br); $\nu_{max.}$ 1 560 cm^{-1}; $\lambda_{max.}$ 222 and 273 nm; δ 3.94 (3 H, s, OMe), and 6.24 and 6.83 (each 1 H, d, *J* 2 Hz; H-5 and H-4 respectively). Storage led to complete decomposition, even after 15 h at 0 °C under N_2, and no microanalysis could be performed.

3-Iodo-2-methoxyfuran (40).—A 1.5M solution of butyllithium in hexane (3 ml) was added to a solution of the foregoing freshly-prepared bromofuran (0.7 g) in dry ether (5 ml) at −78 °C (N_2). When the bath temperature had reached −30 °C a solution of iodine (1.14 g) in ether (4 ml) was added, and at 20 °C the reaction mixture was poured into water. The ether extract was washed with aqueous $Na_2S_2O_5$, water, and saturated brine, and dried (Na_2SO_4) before evaporating at 0 °C (rotary) to give the title iodofuran (40) as a red oil (0.81 g), homogeneous by t.l.c.; *m/e* 224 (M^+) and 209 ($[M - Me]^+$); δ 3.92 (3 H, s, OMe), and 6.31 and 6.95 (each 1 H, d, *J* 2 Hz; H-5 and H-4 respectively).

2,3,5-Trimethoxy-2,5-dihydrofuran (41).—Copper(II) oxide (14.4 g) was added to a solution of sodium methoxide (from 49.4 g sodium) in dry methanol (690 ml). Bromomethoxydihydrofuran (34) (28.7 g) was added to the suspension which was then refluxed (N_2 atmosphere) for 20 h. After cooling, the reaction mixture was filtered, evaporated, and the residue partitioned between ether and water. Evaporation of the ether extract gave the crude product which was vacuum-distilled to give cis- and trans-*2,3,5-trimethoxy-2,5-dihydrofuran* (41) (18.7 g; 85%), b.p. 118—119 °C at 30 mmHg (Found: C, 52.5; H, 7.7. $C_7H_{12}O_4$ requires C, 52.5; H, 7.5%); *m/e* 159 ($[M - H]^+$) and 129 ($[M - OMe]^+$); $\nu_{max.}$ 1 670 cm^{-1}; $\lambda_{max.}$ 211 and 250 nm; δ (both isomers) 3.40, 3.42, and 3.73 (each 3 H, s, 3 × OMe), and 4.84 (1 H, m, H-4); δ (*cis*-isomer, 44%) 5.6 (1 H, d, $J_{2,5}$ 3.5 Hz, H-2) and 5.82 (1 H, dd, *J* 3.5 and 1.5 Hz, H-5); δ (*trans*-isomer, 56%) 5.32 (1 H, s, H-2) and 5.56 (1 H, d, $J_{4,5}$ 1.5 Hz).

(±)-*2,3-Dibromo-1,1,4,4-tetramethoxybutane*.—A solution of bromine (1.6 g) in dry methanol (10 ml) was added to a vigorously stirred solution of 2,5-dimethoxy-2,5-dihydrofuran (1.3 g) in dry methanol (10 ml) at 0 °C. The reaction mixture was stirred at 20 °C for 48 h before adding 10% aqueous NaOH (20 ml). Ether extraction followed by evaporation gave a residue which was triturated with methanol–water to give crystalline (±)-*2,3-dibromo-1,1,4,4-tetramethoxybutane* (0.8 g after recrystallisation from methanol), m.p. 95—96 °C (Found: C, 28.6; H, 4.85; Br, 47.25. $C_8H_{16}Br_2O_4$ requires C, 28.6; H, 4.75; Br, 47.5%); *m/e* 305 ($[M - OMe]^+$), 273 ($[M - OMe - MeOH]^+$), and 75 (base-peak, $[MeO{=}CHOMe]^+$); δ 3.46 (6 H, s, 2 × OMe), 3.50 (6 H, s, 2 × OMe), 4.36 [2 H, dd, *J* 3 and 1.5 Hz, 2 × C*H*$(OMe)_2$], and 4.70 (2 H, dd, 2 × CHBr).

The foregoing reaction was carried out as an attempt to prepare 3-bromo-2,4,5-trimethoxytetrahydrofuran. The unwanted methanolysis was clearly acid-catalysed and so the reaction was repeated in the presence of epichlorohydrin [23] (0.93 g) but with no change. In the presence of potassium carbonate no reaction was observed.

1-Bromo-2-methoxy-7-oxabicyclo[2.2.1]*hept-2-ene-5,6-dicarboxylic* exo-*Anhydride* (37).—Maleic anhydride (98 mg) was added to a solution of freshly prepared 3-bromo-2-methoxyfuran (35) (177 mg) in benzene (1 ml). The mixture was warmed gently to dissolve the anhydride and an exothermic reaction was observed. After standing at 20 °C for 15 h, the reaction mixture was cooled to 0°C and filtered to give the title *adduct* (37) (248 mg; 97%), m.p. 138—142 °C (Found: C, 39.55; H, 2.8; Br, 29.2. $C_9H_7BrO_5$ requires C, 39.3; H, 2.5; Br, 29.0%); *m/e* 276, 274 (M^+) and 248, 246 ($[M - CO]^+$) (^{81}Br and ^{79}Br); $\nu_{max.}$ (Nujol), 1 585, 1 795, and 1 865 cm^{-1}; $\lambda_{max.}$ 218, 250, and 295 nm; δ 3.23 and 3.43 (2 H, AB quartet, *J* 6 Hz, H-5 and H-6), 3.63 (3 H, s, OMe), and 5.24 and 6.27 (each 1 H, d, *J* 2 Hz, H-4 and H-3 respectively). The *endo*-stereochemistry is assigned on the basis of the lack of coupling between H-4 and H-5.

Diels–Alder Reactions of Ethyl Phenylpropiolate.—(*a*) *With 3-bromo-2-methoxyfuran* (35). The bromomethoxyfuran (35) was generated *in situ* by heating the dihydrofuran (34) (0.36 g) in toluene (10 ml) at reflux with toluene-*p*-sulphonic acid (5 mg) in the presence of ethyl phenylpropiolate (0.42 g) (N_2 atmosphere). After 3 d the cooled solution was extracted with aqueous Na_2CO_3: the alkaline extract was acidified and extracted with chloroform to give a crude phenolic product mixture. P.l.c. [SiO_2, 1 : 1 ether–light petroleum (b.p. 40—60 °C)] gave at R_F = 0.5 *ethyl 5-bromo-3-hydroxy-6-methoxybiphenyl-2-carboxylate* (38) (30 mg; 4.3%) [Found: *m/e* 352.0123, 350,0140. $C_{16}H_{15}BrO_4$ requires *m/e* 352.0134 (^{81}Br) and 350.0153 (^{79}Br)]; $\nu_{max.}$ 1 580, 1 600, 1 710, and 3 200—3 600 cm^{-1}; $\lambda_{max.}$ 210, 220, and 295 nm; δ 0.8 (3 H, t, CH_3CH_2O), 4.02 (2 H, q, CH_3CH_2O), 3.42 (3 H, s, OMe), and 7.38 (m, 7 H, Ph, Ar-H, and OH); *m/e* 352, 350 (M^+); 306, 304 ($[M - EtOH]^+$); 291, 289 ($[M - EtOH - Me]^+$); and 263, 261 ($[M - EtOH - Me - CO]^+$): and at R_F = 0.2, *ethyl 6-hydroxy-3,4-dimethoxybiphenyl-2-carboxylate* (39) (40 mg; 6%) (Found: M^+, 352.0101, 350.0128. $C_{16}H_{15}BrO_4$ requires M^+ 352.0134, 350,0153); $\nu_{max.}$ 1 580, 1 710, and 3 300—3 500 cm^{-1}; $\lambda_{max.}$ 210, 217, 231, and 298 nm; δ 0.94 (3 H, t, CH_3CH_2O), 3.90 (2 H, q, CH_3CH_2O), 3.84 (3 H, s, OMe), 5.08 (1 H, s, exchanged with D_2O, OH), and 7.35 (6 H, m, Ar-H); *m/e* 352, 350 (M^+), 307, 305 ($[M - OEt]^+$), 291, 289; 277, 275; 263, and 261.

(*b*) *With 2,3-dimethoxyfuran* (28). The furan was generated *in situ* by adding a solution of 2,3,5-trimethoxy-2,5-dihydrofuran (41) (0.32 g) in dry xylene (5 ml) in ten portions during 72 h to a refluxing solution of ethyl phenylpropiolate (0.36 g) and toluene-*p*-sulphonic acid (25 mg) in

dry xylene (10 ml). After cooling, the solution was washed with water and brine, dried, and evaporated to give a residue which was partitioned between ether and 5% aqueous sodium hydroxide. The alkaline extract was acidified and extracted with ether to give the crude phenolic products (0.28 g). Column chromatography [SiO_2, light petroleum (b.p. 40—60 °C)–ether] then gave *ethyl 3-hydroxy-5,6-dimethoxybiphenyl-2-carboxylate* (140 mg; 23%), m.p. 84—86 °C (from hexane) (Found: C, 67.20; H, 6.1. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); $\nu_{max.}$ 1 500, 1 573, 1 597, and 3 060—3 300 cm^{-1}; $\lambda_{max.}$ 223, 260, and 314 nm; δ 0.68 (3 H, t, CH_3CH_2O), 3.89 (2 H, q, CH_3CH_2O), 3.41 (3 H, s, 6-OMe), 3.92 (3 H, s, 5-OMe), 6.55 (1 H, s, H-4), 7.3 (6 H, m, Ph and OH); *m/e* 302 (M^+), 257 ($[M - OEt]^+$), 256 ($[M - HOEt]^+$), 241 ($[M - EtOH - Me]^+$), and 213 ($[M - EtOH - Me - CO]^+$). Further elution gave the non-crystalline *ethyl 6-hydroxy-3,4-dimethoxybiphenyl-2-carboxylate* (110 mg; 18%) (Found: C, 67.85; H, 6.3. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); $\nu_{max.}$ 1 593, 1 610, 1 715, 3 450, and 3 400—3 500 cm^{-1}; $\lambda_{max.}$ 215, 247, and 298 nm; δ 0.96 (3 H, t, CH_3CH_2O), 4.24 (2 H, q, CH_3CH_2O), 3.87 and 3.90 (each 3 H, s, OMe), 5.0 (1 H, exchangeable, OH), 6.65 (1 H, s, H-5), and 7.4 (5 H, m, Ph); *m/e* 302 (M^+) 257 ($[M - OEt]^+$), 241, and 213.

We thank the S.R.C. for financial support.

[8/1609 *Received*, 8*th September*, 1978]

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