Inter- and Intra-molecular Reactions of Allene-1,3-dicarboxylic Acid Esters with 2-Vinylfurans and 2-Vinylthiophenes. A Potential Route to a BC Ring Precursor of the Nagilactones

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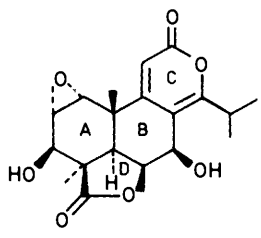
Intermolecular reaction of 4-(2-furyl)but-3-en-2-yl acetate (**10a**) with dimethyl allene-1,3-dicarboxylate leads to products derived from cycloaddition across the endocyclic furan diene or from substitution in the 5-position. 4-(5-Methyl-2-furyl)but-3-en-2-yl acetate (**10b**) gives only cycloaddition products whereas polymerisation occurs in the reactions of the allene ester with the corresponding 2-vinylthiophenes. In contrast, intramolecular reactions of both furans and thiophenes result in cycloaddition across the exocyclic diene system followed by rearrangement and dehydrogenation. The resultant tricyclic benzofurans and benzothiophenes, isolated in low yields, contain two of the rings of the nagilactone skeleton.

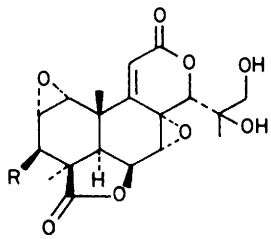
Nagilactone-C (**1**),[1] podolactone-A (**2**) and -B (**3**),[2] and ponalactone-A (**4**)[3] form a group of related norditerpenoids from Podocarpaceae which inhibit the expansion and mitosis of plant cells. Other members of this class show insecticidal activity[4] and antitumour properties,[5] and a simpler derivative (**5**) is an antifungal, but toxic, agent.[6] Structure–activity studies suggest that the pyrone or dihydropyrone ring C is necessary for biological activity whereas modulation of activity may be the result of changes of functionality in ring A.[5] Despite this diversity of cytological and physiological effects only two members of this group of compounds have been synthesized,[7] and it is only recently that attempts to develop a general synthesis of the basic skeleton have been recorded.[8]

We reasoned that an α,β-enone moiety, readily constructed by an aldol condensation, should provide the synthetic versatility required in ring A in any general approach to these natural products. We felt also that ring A should be made at a late stage since this would simplify the molecular framework of early intermediates to that of the linear tricycle (**6**). In a structure such as (**6**) the carbocyclic ring could be made convergently by a Diels–Alder reaction from an allene ester (**7**) and a diene lactone (**8**), with the possibility of carrying out the reaction intramolecularly. The advantage of this procedure would be that a δ-lactone rather than a γ-lactone ring C would result if the degree of orbital overlap indicated in molecular models were reproduced in the real molecule.

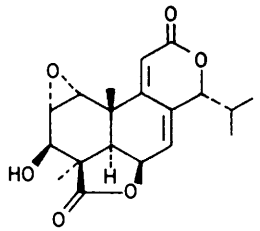
In our first study of this type of approach, we chose to replace the γ-lactone ring of compound (**8**) by a furan or thiophene, as in structure (**9**). The advantages accruing from the use of the heteroaromatic ring were reasoned to be that (*a*) the starting materials could be synthesized rapidly; (*b*) the 2-vinyl derivatives of furans and thiophenes are known to act as exocyclic dienes in Diels–Alder reactions;[9] and (*c*) the heteroaromatic ring could provide either the elements of the ring D lactone by oxidation or those of ring A by ring opening to a 1,4-diketone and subsequent aldol condensation.



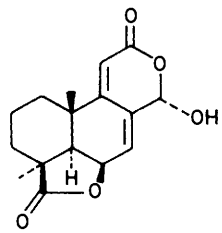
(**1**)



(**2**) R = H
(**3**) R = OH



(**4**)



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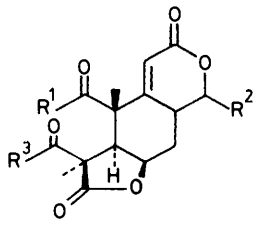
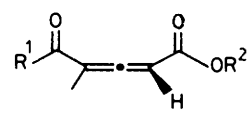
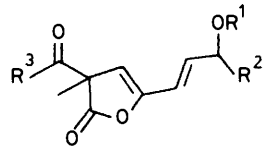


(**6**)



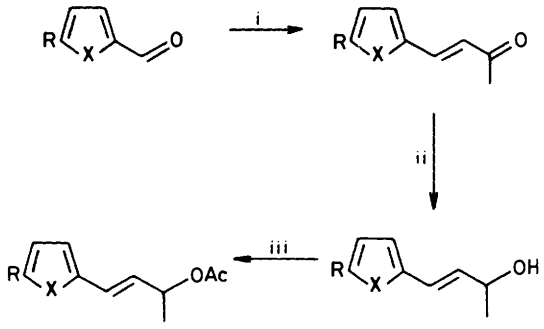
(**7**)



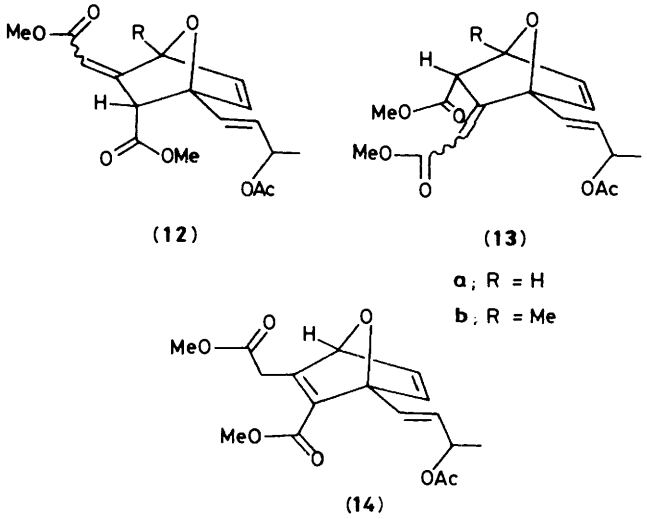
(**8**)

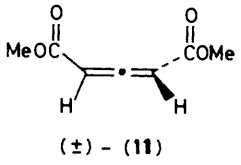
Results and Discussion

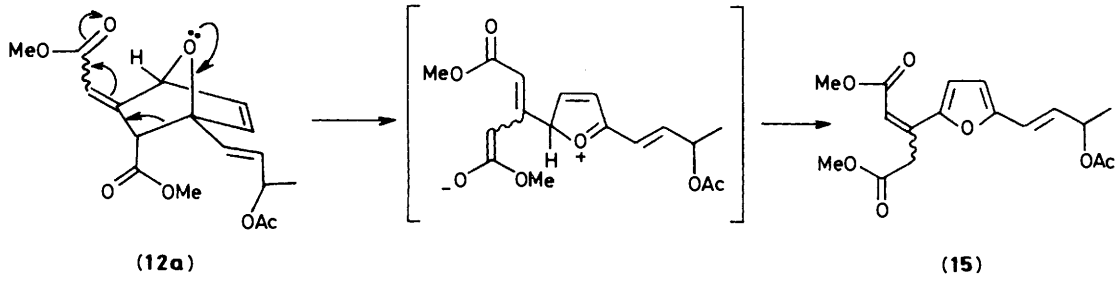
Intermolecular Reactions.—The requisite 2-vinyl heteroaromatics were readily prepared by aldol condensation of the corresponding 2-carbaldehydes with acetone, followed by sodium borohydride reduction using a slight modification of a procedure reported by Francke and Reith (Scheme 1).[10] For the



Scheme 1. *Reagents*: i, acetone, aq.NaOH; ii, $NaBH_4$ (4 equiv.), $Ba(OH)_2$; iii, Ac_2O, pyridine







Scheme 2.

intermolecular reactions the resultant alcohols (**9**) were converted into their corresponding acetate esters (**10**). The thiophenes (**10c**) and (**10d**) proved to be more stable and consequently easier to handle than their furan analogues (**10a**) and (**10b**) although all these compounds eliminated acetic acid to some extent on distillation, a fact which did not bode well for the thermal cycloaddition attempts.

Heating the 2-vinylfuran (**10a**) with dimethyl allene-1,3-dicarboxylate (**11**)[11] in tetrahydrofuran (THF) under reflux for one week produced a 54% yield of a mixture of isomeric 1:1 adducts after removal of unchanged acetate (16%) by column chromatography. The lack of a low-field α-furan proton [δ 7.22 in (**10a**)] signal in the 250 MHz ^1H n.m.r. spectrum of this mixture suggested that cycloaddition of the allene diester had occurred across the endocyclic diene system. The ^{13}C n.m.r. spectrum of the mixture established that there were three isomers present (approximate ratio 2:2:1). The minor isomer contained a $-CH_2CO-$ group as indicated by a triplet at 60 p.p.m. in the off-resonance decoupled ^{13}C n.m.r. spectrum and by an AB quartet at 4.05 p.p.m. in the 250 MHz ^1H n.m.r. spectrum. The remaining two isomers both showed only minor coupling (≤ 2 Hz) (allylic?) in the peaks due to the proton α to the methoxycarbonyl group (3.51 and 3.68 p.p.m.) and in the bridgehead proton peak (5.18 and 5.25 p.p.m.) which is consistent with their formulation as isomers of structure (**12a**) rather than of the regioisomeric structure (**13a**) in which coupling between these protons should be *ca.* 5 Hz. This assignment was made by comparison of our data with those reported for similar structures derived by the cycloaddition of ditrimethylsilyl allene-1,3-dicarboxylate to furfuryl alcohol and furfuryl benzyl ether,[12] and we made the assumption that the *endo*-stereochemistry of the non-conjugated methoxycarbonyl group proven in that study holds for compound (**12a**) as well. Of course the *exo*-isomers[13] of (**12a**) and (**13a**) should also exhibit a small coupling between the bridgehead and α-methoxycarbonyl protons and we cannot yet eliminate those entirely as possible formulations for the 1:1 adducts. Given that the assumption made above is correct, however, the minor component of the mixture is then most likely to be the positional isomer (**14**).

On raising the temperature of the reaction between compounds (**10a**) and (**11**) to that of boiling xylene a new 1:1 adduct was formed after 43 h in moderate yield (42%). The ^1H n.m.r. spectrum of this product appeared to be simply a superposition of those of compounds (**10a**) and (**11**) except that again the α-furan signal was absent, as was the allene methine singlet, the CO_2Me singlet was split into two and a new 2 H singlet had appeared. The chemical shift of this last signal (4.0 p.p.m.) clearly indicated that it derived from a glutaconic ester methylene by comparison with the spectra of other esters of this type in our possession, *e.g.* (**21**) and (**22a—d**) (4.11—4.15 p.p.m.) (3-unsubstituted esters 3.2—3.65 p.p.m.[14]) and all the spectral and microanalytical data were consistent with the structure (**15**) for the product. One possible pathway to compound (**15**) led

through the intermediate (**12a**) by the push–pull mechanism indicated in Scheme 2. However this mechanism was precluded by the production of an unknown, low-polarity material from the thermolysis of the mixture (**12a**) under conditions identical with those used for the formation of compound (**15**). No trace of (**15**) could be detected in the crude reaction product by t.l.c., or i.r. or ^{1}H n.m.r. spectroscopy. This experiment clearly also rules out the reversal of the initial Diels–Alder reaction at these higher temperatures. Other possible mechanisms for the formation of compound (**15**) include simple electrophilic substitution or [2 + 2] cycloaddition followed by cyclobutane ring opening (assisted by furan oxygen) but at this juncture we have no evidence for any mechanism.

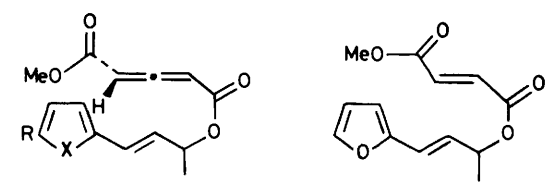
The reaction of the allene diester (**11**) with the 5-methyl-2-vinylfuran (**10b**), in which electrophilic-like attack at the α-position is blocked, results at lower temperature in cycloaddition across the furan ring as with compound (**10a**), albeit more sluggishly (benzene, reflux, 36% mixture of two major isomers after 160 h), whereas in xylene, under reflux, polymerisation occurred. From the close similarity of the 250 MHz ^{1}H and ^{13}C n.m.r. spectra of the mixture of the two cycloaddition products with those of compound (**12a**) the former were assigned the structures of the geometrical isomers (**12b**). The only significant difference between the off-resonance decoupled ^{13}C n.m.r. spectra of compounds (**12a**) and (**12b**) was a downfield shift of the two peaks at 82 and 83 p.p.m. in the former to 88—90 p.p.m. in the latter, consonant with the presence of a methyl group on the bridgehead carbon atoms of the two isomers (**12b**) which cause these signals.

In anticipation that the corresponding thiophenes might undergo addition across the exocyclic diene more readily than the furan,[15] the sulphur congeners (**10c**) and (**10d**) were heated with compound (**11**) under various conditions. Not surprisingly, no cycloaddition across the thiophene ring was observed at any of the temperatures tried [105 °C in toluene or xylene under reflux for (**10c**); THF, benzene, toluene, xylene, or decalin under reflux for (**10d**)] since such a process is rare.[16]

In none of these experiments was any product other than either starting material (**10c**) or (**10d**) or polymer isolated. No evidence for the presence of compounds derived by cycloaddition across the exocyclic diene could be found in the crude product mixtures.

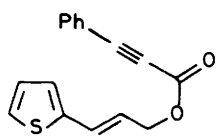
Intramolecular Reactions.—In the intramolecular reaction in esters of the type (**16**) it is highly unlikely that addition to the endocyclic diene will occur since this will result in a *trans*-oxacyclo-octene and attack at the 5-position in unsubstituted derivatives is impossible. Intermolecular versions of these two processes should be controllable by the use of high dilution. It was already known that cyclisation in the desired sense occurred in the close analogue (**17**) (toluene, sealed tube, 200 °C, 56%)[17] and in the thiophene (**18**) (acetic anhydride, reflux, 24%),[18] which lent support to our expectation of observing a similar cyclisation in the allene esters (**16**).

The mixed allene esters (**16**) were prepared by a modification of the literature method used to make the dimethyl ester (Scheme 3). Thus 3-chloroglutaconic anhydride (**20**)[19] was obtained in 31% overall yield as pale yellow crystals, m.p. 108—112 °C, from diethyl acetone-dicarboxylate by sequential treatment of the latter with phosphorus pentachloride (60—65 °C, 30 min) and 20% hydrochloric acid (reflux, 2.25 h), followed by digestion of the resultant, isolated diacid (**19**)[20] with acetic anhydride (0 °C, 24 h). The ^{1}H n.m.r. spectrum of the anhydride (**20**) showed two signals at δ 3.77 (2 H, d, *J* 2 Hz) and 6.38 (1 H, t, *J* 2 Hz) and the i.r. spectrum showed only typical anhydride bands at 1 750 and 1 805 cm^{-1}. That some of the hydroxypyrone tautomer of (**20**) was present in solutions in acetonitrile was indicated by a weak absorption in the u.v. spectrum at 346 nm (ε 2 300) in addition to the normal β-chloro-α,β-unsaturated carbonyl band at 228 nm (ε 12 600). Thus the equilibrium shown for compound (**20**) lies well on the anhydride side, a conclusion in accord with that reached for glutaconic anhydride itself.[21] The equilibrium may be driven towards the pyrone side by base, the addition of one equivalent of aqueous sodium hydroxide to a solution of compound (**20**) in acetonitrile resulting in an eight-fold increase in the absorbance of the band at 346 nm. Similarly treatment of compound (**20**) with sodium methoxide in methanol produced a deep-red solution from

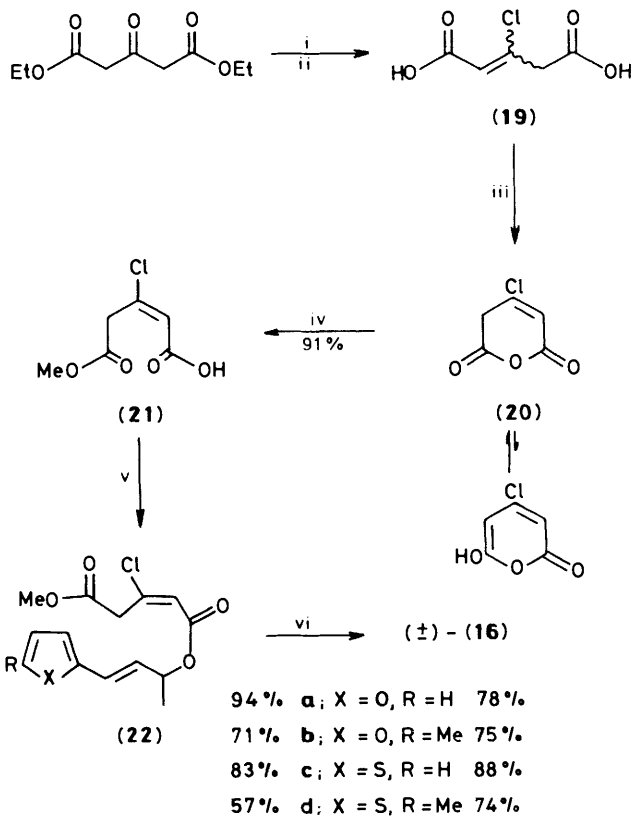


(±)-(**16**) **a**; X = O, R = H
b; X = O, R = Me
c; X = S, R = H
d; X = S, R = Me

(**17**)



(**18**)



Scheme 3. *Reagents*: i, PCl_5; ii, H_3O^+, reflux; iii, Ac_2O, 0 °C; iv, MeOH; v, (**9**), DCC, pyridine, CH_2Cl_2; vi, Et_3N, 4 °C

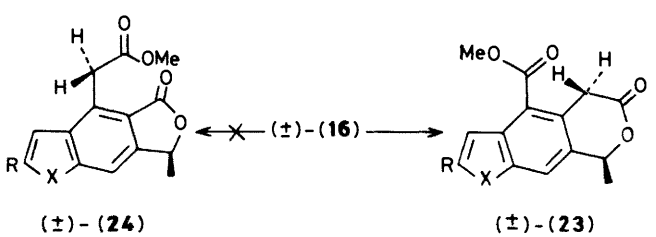
which the anhydride could be recovered (*ca.* 80%) after 5 min on acidification with trifluoroacetic acid.

Under reflux, neutral methanol smoothly opened the anhydride (**20**) to give only one of the four possible regio- and stereo-isomeric monomethyl esters, as a pale yellow solid, m.p. 58—60 °C. *X*-Ray crystallography established the structure of this ester as (*E*)-3-chloro-4-methoxycarbonylbut-2-enoic acid (**21**),[22] indicating that no change of configuration about the double bond had occurred on ring opening and that methanol had attacked the non-conjugated carbonyl group, a result analogous to that observed for the ring opening of glutaconic anhydride.[14]

Esterifications of the monoester (**21**) with the alcohols (**9**) (dicyclohexylcarbodi-imide, dichloromethane, pyridine) proceeded readily at room temperature but the resultant chlorodiesters (**22**) were highly susceptible to elimination of hydrogen chloride. Thus they could be partially purified by rapid chromatography on grade-5 alumina from which they were usually obtained contaminated with small quantities of non-polar material (yields quoted in Scheme 3 refer to these partially purified preparations). If grade-3 alumina was used the chlorodiesters (**22**) could be obtained free of non-polar material but then contained substantial amounts of the allene diesters (**16**). This ready elimination also precluded the use of 4-dimethylaminopyridine as an acylation catalyst[23] in the esterification step. Solutions of the chlorodiesters (**22**) in dry THF left overnight in the refrigerator (4 °C) in the presence of triethylamine gave the desired mixed allene diesters (**16**), which could be freed of coloured contaminants by passage through grade-3 alumina. I.r. bands at *ca.* 1970 cm^{-1} and sharp singlets for the vinyl protons at *ca.* 6 p.p.m. in the ^1H n.m.r. spectra evidenced the formation of the allene diesters (**16**). These allenes all polymerised on standing neat but they could be stored for long periods as 0.04M-solutions in toluene at −10 °C. Both types of ester (**22**) and (**16**) were decomposed to varying extents by silica gel.

Because of the extended reaction times necessary in the attempted Diels–Alder reactions on the furan analogues (**16a**) and (**16b**) it proved essential to silylate the glassware prior to reaction in order to minimise polymerisation. Even so, the allene ester (**16a**) in toluene under reflux produced a lot of polymer after 44 h and chromatography of the crude product on silica gel only allowed the isolation in poor yield (4%) of a waxy solid which obviously still contained some polymeric material by ^1H n.m.r. spectroscopy. However, a 0.4 p.p.m. downfield shift of the *C*-methyl doublet compared to its position in the spectrum of (**16a**) and the appearance of an extra 1 H singlet at 7.60 p.p.m. (7-H) together with two furan doublets (2.5 Hz) at 7.70 (α-proton) and 7.10 (β-proton) indicated that the major component of this solid was a benzofuran rather than the first-formed Diels–Alder adduct. This benzofuran was subsequently identified as (**23a**) by comparison of the spectral data with those of the analogues (**23b—d**).

Given the general instability of α-unsubstituted furans towards acids[13] (including glassware) it was expected that the 5-methyl congener (**16b**) would produce less polymer in the Diels–Alder reaction. This proved to be the case and a higher yield of a cyclised product (12%) was obtained after chromatography on silica gel and alumina as pale-yellow needles, m.p. 110—111 °C, although the rate of reaction was slower (toluene, reflux, 128 h). The ^1H n.m.r. spectrum of this solid (Figure) was exceedingly simple and again showed that the initial Diels–Alder adduct had rearranged and undergone dehydrogenation. The important features of the spectrum were the downfield shift of the *C*-methyl doublet from 1.38 p.p.m. in (**16b**) to 1.8 p.p.m., an extra aromatic proton singlet at 7.45 p.p.m. and, most significantly, the methylene group signal as an AB quartet (*J* 18.5 Hz) centred at 4.15 p.p.m. This signal showed that the cyclised product had the benzofuran-δ-lactone structure (**23b**) rather than the alternative γ-lactone (**24b**) in which the methylene is in a non-rigid position remote from the centre of chirality and should show as a singlet.[24] This assignment of ring size was confirmed by the i.r. absorption of the lactone carbonyl group at 1 740 cm^{-1} compared with 1 760 cm^{-1} for (**25**)[17] and by the mass spectrum of (**23b**) which showed a facile retro-Diels–Alder fragmentation of the lactone ring.[25] The ^1H n.m.r. spectra of other fractions from the column used to purify compound (**23b**) showed that probably as much again of this product was present mixed with co-eluting contaminants of indeterminate structure which were difficult to remove.



(±)-(**24**) (±)-(**23**)

In the thiophene series, the allene esters (**16c**) and (**16d**) gave the tricyclic δ-lactones (**23c**) and (**23d**) respectively with little improvement in the yields (6 and 10% respectively) but at dramatically faster rates (4 and 3.75 h respectively in toluene under reflux) compared with their furan counterparts. The reduced reaction times resulted in cleaner reactions and allowed a much easier separation of the benzothiophenes (**23c**) and (**23d**) by chromatography on silica gel and alumina as an off-white solid, m.p. 142—143 °C, and pale yellow needles, m.p. 98—99.5 °C, respectively. The thiophene series was also significantly different from the furan series in that the aromatic lactones (**23c**) and (**23d**) did not appear to form a reasonable proportion of the product until after treatment on the first silica gel column. As the losses of material (*ca.* 40—50%) did not correlate with the increase in relative amount of (**23c**) and (**23d**) in the product mixture after this purification step it appeared that a major part of the lactones (**23c**) and (**23d**) was being formed from a precursor on the column. An attempt was therefore made to convert the crude cycloaddition adducts directly into the aromatics by dehydrogenation with dichlorodicyanobenzoquinone, but only complex mixtures were obtained. In an alternative trapping experiment the crude reaction mixture from the allene ester (**16d**) was subjected to catalytic hydrogenation with palladium on charcoal. Only one equivalent of hydrogen was taken up and the reduced product still showed a tendency to decompose on silica-gel columns which suggested that it still contained compounds exhibiting some degree of unsaturation, possibly because the catalyst had been poisoned by the thiophene. These experiments were not investigated further.

The possibility that the actual dienophiles in these Diels–Alder reactions were the acetylenes (**26**) cannot be ruled out at this stage although the reduced activity of propiolic esters towards cycloadditions compared with the potency of allene-1,3-diesters in the same reactions would seem to militate against this.[26] However it is quite plausible that the acetylenes (**26**) and their isomers (**27**) were formed during the reactions as the disappearance of the allene methine proton signals from the ^1H n.m.r. spectra of the reaction mixtures was faster than the formation of product and it seems reasonable to assume that these acetylenes provided at least one exit from the desired cycloaddition pathway.

As a furan ring in any tricyclic product would be more advantageous than a thiophene from the point of view of conversion into a lactone[27] or into the carbocyclic ring A of the

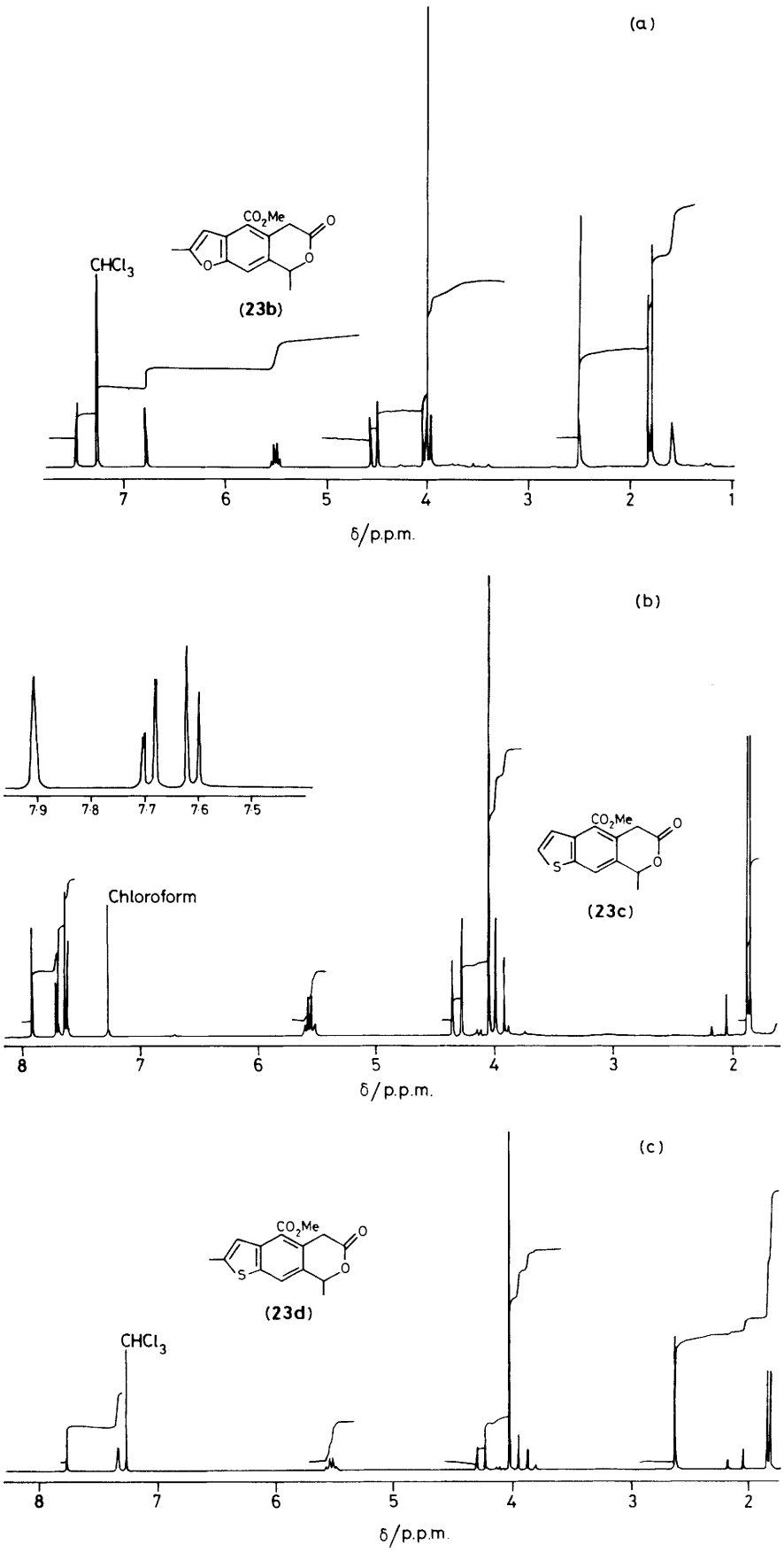
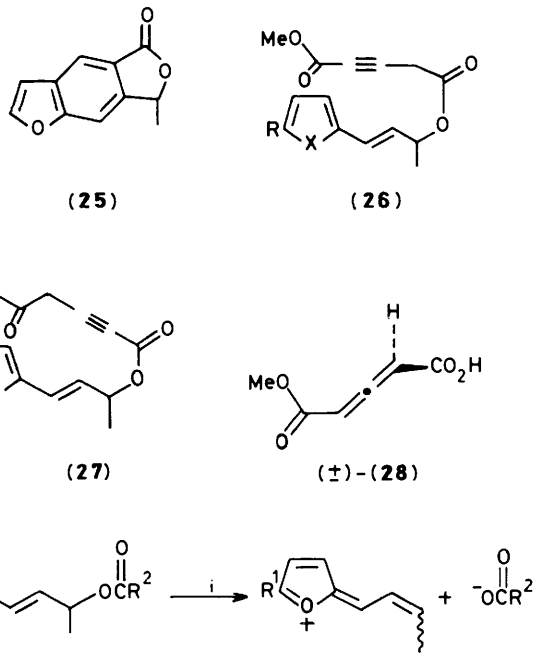


Figure. ^{1}H N.m.r. spectra for compounds (**23b—d**)



Scheme 4. *Reagents*: i, Lewis acids

natural products we felt that it would be desirable to increase the rate and the yield in the cyclisation of the furan congeners (**16a**) (**16b**). In an attempt to do this, compounds (**16a**) and (**16b**) were treated with a range of Lewis acids of varying strength. The production of an orange or red colour on mixing the allene esters (**16a**) and (**16b**) with the Lewis acid [$Al(OPr^i)_3$ or Cp_2TiCl_2] signified no reaction whereas an immediate blue colour (with $ZnCl_2$, ZnI_2, $MgBr_2$, or Et_2AlCl) was indicative of decomposition with formation of polymer. In a control experiment the 2-vinylfuran acetate (**10a**) containing no allene moiety also produced a blue colour and polymer on treatment with magnesium bromide–ether. This fact, together with the isolation of a small quantity of the allene monoacid (**28**) from the interaction of compound (**16a**) and zinc iodide–ether, suggested that the major pathway mediated by Lewis acids was the allylic cleavage of the C–O bond (Scheme 4). It is also conceivable that similar cleavage occurs in the thermal reactions as the thermal elimination of acetic acid from the esters (**10**) is quite facile, although we have never observed any products consistent with that mode of decomposition from the intramolecular reactions.

Conclusions

The isolation of the tricyclic benzofurans and benzothiophenes (**23**) in the intramolecular reactions despite the obviously low reactivity of the 2-vinyl heteroaromatics as exocyclic dienes indicates the possibility of a general route to nagilactone precursors involving the construction of ring B by a Diels–Alder reaction. The simultaneous closure of ring C requires the intramolecular process to be more efficient than at present in order for it to compete effectively with alternative degradation or polymerisation pathways. In turn, this requirement probably relies on the use of a diene which is electronically more active than a 2-vinyl heteroaromatic compound and on a dienophile which does not, or cannot, undergo isomerisation to give a less active species.

Alternatively, an intermolecular process may be considered for the formation of ring B. In this case ring C is annelated in a subsequent step, but again the use of simple 2-vinyl heteroaromatic compounds is contra-indicated.

Experimental

M.p.s are uncorrected and were determined using a Gallenkamp apparatus. Dry ether and dry THF were obtained by distillation from potassium diphenylketyl under argon. Dry dichloromethane was distilled from phosphorus pentaoxide. Benzene, toluene, and xylene used in the Diels–Alder reactions were dried by and stored over sodium wire. Pyridine and triethylamine were dried by distillation from barium oxide and storage over potassium hydroxide. Light petroleum (b.p. 60–80 °C) used for column chromatography was distilled. Merck silica-gel, No. 9385, and BDH neutral alumina were used for gravity column chromatography. Ether refers to diethyl ether.

I.r. spectra were recorded for samples either neat (liquids) or as solutions (solids) in chloroform or dichloromethane using a Perkin-Elmer 298 spectrometer. ^1H N.m.r. spectra* were recorded on a Varian EM360A (60 MHz) or on a Bruker WM250 (250 MHz) spectrometer for solutions in $CDCl_3$ using Me_4Si as internal standard unless otherwise indicated. The multiplicity of signals is expressed by the following symbols: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dt = double triplet, br = broad. U.v. spectra were recorded on a Unicam SP1800 spectrometer. ^{13}C N.m.r. spectra were recorded on a Bruker WM250 (62.9 MHz) spectrometer. Mass spectra were recorded on an A.E.I. MS9 or a VG Micromass 7070 instrument.

Pre-silylated glassware used in the Diels–Alder reactions in the furan series was prepared as follows: the vessel was flame-dried and allowed to cool under argon; it was then washed once with dry triethylamine, twice with a solution (2% w/v) of dichlorodimethylsilane in chloroform, once more with dry triethylamine and finally once with dry THF; flushing with argon until solvent had evaporated completed the sequence.

4-(2-Furyl)but-3-en-2-one,[28] 4-(5-methyl-2-furyl)but-3-en-2-one,[29] 4-(2-thienyl)but-3-en-2-one,[30] and 4(5-methyl-2-thienyl)-but-3-en-2-one[31] were prepared according to the method recorded in the literature for the first-named compound.[28]

Preparation of the Allylic Alcohols (**9**). *General Procedure.*—To an ice-cooled, stirred suspension of sodium borohydride (28 mmol, 4 equiv.) in THF–water (9:1; 20 ml) containing barium hydroxide (50 mg) was added dropwise during 15 min a solution of the (2-heteroaryl)but-3-en-2-one (28 mmol) in THF–water (9:1; 15 ml). The mixture was then stirred at room temperature for 21 h. Dilute (10% v/v) aqueous sulphuric acid was added until the mixture was at pH 6, followed by dilute (5% w/v) aqueous sodium carbonate to bring the mixture back to pH 8. Most of the THF was removed by rotary evaporation and the resultant liquid was extracted with ether (3 × 40 ml). The ethereal extracts were combined, washed successively with aqueous sodium hydrogen carbonate (1 × 100 ml), water (1 × 100 ml), and brine (3 × 100 ml), and dried (Na_2SO_4). Rotary evaporation after filtration gave a yellow oil that was chromatographed on alumina (grade 4, 70 g) using ethyl acetate–benzene (1:10) as eluant to give: 4-(2-furyl)but-3-en-2-ol (**9a**)[10] as a pale yellow oil (92%), 4-(*5-methyl-2-furyl*)*but-3-en-2-ol* (**9b**) as a very pale yellow oil (99%) (Found: C, 71.2; H, 7.9. $C_9H_{12}O_2$ requires C, 71.05; H, 7.95%), $\nu_{max.}$ 3 345 cm^{-1}, δ 1.32 (3 H, d, *J* 6 Hz, 2-Me), 1.92 (1 H, br s, exchanged with D_2O), 2.28 (3 H, s, 5′-Me), 4.37 (1 H, dq, *J* 3 Hz, *J′* 6 Hz, 2-H), and 6.03 (4 H, m, vinyl + furan-H); *m/z* 152 (M^+, 79%), 147 (23), 145 (10), 109 (54), and 95 (100); 4-(2-thienyl)but-3-en-2-ol (**9c**)[32] as a pale

* Primed numbers in the n.m.r. assignments refer to the heteroaromatic substituent throughout the Experimental section.

yellow oil (86%); 4-(5-*methyl*-2-*thienyl*)*but*-3-*en*-2-*ol* (**9d**) as a very pale yellow oil (85%), $\nu_{max.}$ 3 400 cm^{-1}, δ 1.32 (3 H, d, *J* 6 Hz, 2-Me), 1.95 (1 H, br s, exchanged with D_2O), 2.43 (3 H, s, 5′-Me), 4.33 (1 H, quintet, *J* 6 Hz, 2-H), 5.85 (1 H, right arm of ABq, each peak split into doublets, *J* 6 Hz, *J′* 16 Hz, 3-H), and 6.52 (3 H, m, 4-H + 3′-H + 4′-H), *m/z* 168 (M^+, 42%), 151 (25), 150 (30), 135 (25), 125 (50), and 111 (100).

Preparation of the Allylic Acetates (**10**). *General Procedure.*—To an ice-cooled, stirred mixture of acetic anhydride (30 mmol) and dry pyridine (30 mmol) in dry toluene (20 ml) was added dropwise during 1 min a solution of the but-3-en-2-ol (15 mmol) in dry toluene (2 ml). The solution was kept at 4 °C in the refrigerator for 36 h, the solvents were removed by rotary evaporation and the residual orange-red oil was either distilled (furans) or chromatographed on silica gel (thiophenes) using benzene as eluant to give: 4-(2-*furyl*)*but*-3-*en*-2-*yl acetate* (**10a**) as a very pale yellow oil (80%), b.p. 74—75 °C/0.35 mmHg (Found: C, 66.8; H, 7.1. $C_{10}H_{12}O_3$ requires C, 66.65; H, 6.70%); $\nu_{max.}$ 1 725 cm^{-1}; δ_H 1.33 (3 H, d, *J* 6 Hz, 2-Me), 2.03 (3 H, s, OAc), 5.37 (1 H, dq, *J* 2 Hz, *J′* 6 Hz, 2-H), 6.20 (4 H, m, 3-H + 4-H + 3′-H + 4′-H), and 7.22 (1 H, d, *J* 2 Hz, 5′-H); δ_C 20.1 (q), 21.1 (q), 70.4 (d), 108.5 (d), 111.1 (d), 119.6 (d), 127.3 (d), 142.0 (d), 151.9 (s), and 170.0 (s); 4-(5-*methyl*-2-*furyl*)*but*-3-*en*-2-*yl acetate* (**10b**) as a pale yellow oil (80%), b.p. 90—95 °C/0.4 mmHg (some decomp.); $\nu_{max.}$ 1 740 cm^{-1} (Found: C, 68.3; H, 7.5. $C_{11}H_{14}O_3$ requires C, 68.0; H, 7.25%); δ 1.35 (3 H, d, *J* 6 Hz, 2-Me), 2.05 (3 H, s, OAc), 2.30 (3 H, s, 5′-Me), 5.35 (1 H, quintet, *J* 6 Hz, 2-H), and 5.7—6.3 (4 H, m, 3-H + 4-H + 3′-H + 4′-H); *m/z* 194 (M^+, 18%), 151 (20), 135 (28), 134 (24), 91 (22), and 43 (100); 4-(2-*thienyl*)*but*-3-*en*-2-*yl acetate* (**10c**) as a very pale yellow oil (75%) (Found: C, 61.2; H, 6.35. $C_{10}H_{12}O_2S$ requires C, 61.2; H, 6.15%); $\nu_{max.}$ 1 735 cm^{-1}; δ 1.30 (3 H, d, *J* 6 Hz, 2-Me), 2.0 (3 H, s, OAc), 5.35 (1 H, quintet, *J* 6 Hz, 2-H), 5.85 (1 H, dd, *J* 6 Hz, *J′* 15 Hz, 3-H), 6.60 (1 H, d, *J* 15 Hz, 4-H), and 6.75—7.10 (3 H, m, 3′-H + 4′-H + 5′-H); *m/z* 196 (M^+, 25%), 153 (22), 137 (32), 136 (32), 135 (60), 97 (25), and 43 (100); 4-(5-*methyl*-2-*thienyl*)*but*-3-*en*-2-*yl acetate* (**10d**) as a very pale yellow oil (60%) (Found: C, 62.6; H, 6.85. $C_{11}H_{14}O_2S$ requires C, 62.8; H, 6.7%), $\nu_{max.}$ 1 740 cm^{-1}; δ 1.33 (3 H, d, *J* 6 Hz, 2-Me), 2.03 (3 H, s, OAc), 2.42 (3 H, s, 5′-Me), 5.35 (1 H, quintet, *J* 6 Hz, 2-OH), 5.78 (1 H, one half of an ABq, *J* 6 Hz, *J′* 16 Hz, 3-H), and 6.58 (3 H, m, 4-H + 3′-H + 4′-H); *m/z* 210 (M^+, 36%), 168 (38), 151 (69), 150 (52), 149 (60), 137 (71), 135 (76), and 134 (100).

Cycloaddition of Dimethyl Allene-1,3-*dicarboxylate to* 4-(2-*Furyl*)*but*-3-*en*-2-*yl Acetate.*—A solution of dimethyl allene-1,3-dicarboxylate (0.54 g, 3.5 mmol) and the acetate (**10a**) (0.62 g, 3.5 mmol) in dry THF (30 ml) was heated at a bath temperature of 70 °C for 160 h. After cooling and rotary evaporation the residue from the reaction was chromatographed on silica gel (80 g) using first ethyl acetate–light petroleum (1:12) to elute the starting acetate then ethyl acetate–dichloromethane (1:4) to elute the adducts as an orange-yellow oil (0.61 g, 54%), $\nu_{max.}$ 1 745, 1 720, and 1 680 cm^{-1}; δ_H (250 MHz) 1.26 [3 × d, CH_3CH(OAc), three isomers], 2.00 (3 × s, OAc, three isomers), 3.51 (br s, $CH(CO_2Me)_2$, one isomer), 3.60 (3 × s, CO_2Me, three isomers), 3.68 (m, *J* ≤ 2 Hz, $CH(CO_2Me)_2$, one isomer), 4.05 (ABq, *J* 12 Hz, $CH_2(CO_2Me)_2$), 5.18 [d, *J* 2 Hz, CH(OR), one isomer], 5.25 [br s, CH(OR), one isomer], 5.36 [sextuplet, CH(OAc), two isomers], and 5.9—6.5 (complex m, vinylic protons, three isomers); δ_C 20 [2 × q, CH_3CH(OAc)], 21 [q, CH_3CH(OAc)], 51.2 (3 × q, OAc), 54 (2 × d, $CH(CO_2Me)_2$), 60 (t, $CH_2(CO_2Me)_2$), 69 [d, CH(OR)], 82 [d, CH(OR)], 83 [d, CH(OR)], 89.5 [s, C(OR)], 90.5 [s, C(OR)], 113 (2 × d, vinylic), 124 (d, vinylic), 125 (d, vinylic), 132—136 (number of vinylic carbons, multiplicity uncertain), 139 (d, vinylic), and 154.4, 155.1, 165.9, 166, 169, 169.3, 169.6 (all s, CO).

Cycloaddition of Dimethyl Allene-1,3-*dicarboxylate to* 4-(5-*Methyl*-2-*furyl*)*but*-3-*en*-2-*yl Acetate.*—A solution of dimethyl allene-1,3-dicarboxylate (0.28 g, 1.79 mmol), the acetate (**10b**) (0.29 g, 1.49 mmol), and a few crystals of hydroquinone in benzene (6 ml) was heated at reflux for 160 h. After rotary evaporation of the cooled reaction mixture, the resultant red oil was chromatographed on silica gel (50 g) using ethyl acetate–light petroleum (1:6) to elute the starting material, then ethyl acetate–light petroleum (1:1) to give a mixture of adducts as a yellow oil (188.6 mg, 36%), $\nu_{max.}$ 1 745, 1 720, and 1 680 cm^{-1}; δ_H (250 MHz) 1.30—1.38 [2 × d, CH_3CH(OAc), two isomers], 1.70 [s, CH_3C(OR), one isomer], 1.77 [s, CH_3C(OR), one isomer], 2.06 (2 × s, OAc, two isomers), 3.69 (2 × s, CO_2Me, two isomers), 5.45 [sextuplet, CH(OAc), two isomers], and 5.9—6.4 (m, vinylic, two isomers); δ_C 15.1 [q, CH_3C(OR)], 15.4 [q, CH_3C(OR)], 20.2 [q, CH_3CH(OAc)], 21.1 [q, CH_3CH(OAc)], 51.3 (q, OAc), 51.8 (q, OAc), 56.3 (d, $CH(CO_2Me)_2$), 56.4 (d, CH·CO_2Me), 87.8 [s, C(Me)OR], 88.5 [s, C(Me)OR], 89.0 [s, C(OR)], 89.4 [s, C(OR)], 111.8 (d, vinylic), 112.2 (d, vinylic), 124.4 (d, vinylic), 125.9 (d, vinylic), 132—140 (number of vinylic carbons, multiplicity uncertain), and 158.6, 159.4, 166.5, 169.6, 169.8, 170.4 (all s, CO).

Substitution Reaction between Dimethyl Allene-1,3-*dicarboxylate and* 4-(2-*Furyl*)*but*-3-*en*-2-*yl Acetate.*—A solution of dimethyl allene-1,3-dicarboxylate (0.54 g, 3.5 mmol) and the acetate (**10a**) (0.62 g, 3.5 mmol) in dry xylene (30 ml) was heated at a bath temperature of 130—140 °C for 42 h. The reaction mixture was cooled, evaporated under a high vacuum and the resultant red oil was chromatographed on neutral alumina (grade 3, 80 g) using ethyl acetate–dichloromethane (1:20) as eluant to give in the early fractions a yellow-orange oil (0.49 g, 42%) (Found: C, 60.5; H, 6.3. $C_{17}H_{20}O_7$ requires C, 60.7; H, 6.00%), $\nu_{max.}$ 1 740, 1 710 cm^{-1}; δ 1.38 [3 H, d *J* 6 Hz, $MeCH$(OAc)], 2.07 (3 H, s, OAc), 3.67 (3 H, s, CO_2Me), 3.73 (3 H, s, CO_2Me), 4.00 (2 H, s, $CH_2(CO_2Me)_2$), 5.43 [1 H quintet, *J* 6 Hz, CH(OAc)], 6.23 (3 H, m), and 6.53 (2 H, m).

3-*Chloroglutaconic Anhydride* (**20**).—To well-stirred diethyl acetonedicarboxylate (60.01 g, 0.297 mol) was added in portions phosphorus pentachloride (68.55 g, 0.329 mol) during 30 min during which time the mixture turned red and warmed to 60 °C. After the addition the mixture was heated at 60—65 °C for 30 min, then cooled in an ice-bath and carefully poured onto ice (100 g). The reaction flask was rinsed with dichloromethane–water (1:1; 300 ml) and this suspension was also added to the ice. The resultant two-phase mixture was separated into layers and the aqueous layer was extracted with dichloromethane (3 × 100 ml). The organic layer and extracts were combined and rotary evaporated to give a red oil (48.95 g). This oil was suspended in hydrochloric acid (20%; 250 ml) and the mixture was boiled for 2.5 h. The solution was evaporated to dryness, first on the rotary evaporator and then under high vacuum, and the resultant crude, orange chloro diacid (**19**) was dried over phosphorus pentaoxide *in vacuo* overnight to give an orange-brown solid (32.92 g, 67.5%), m.p. 110—115 °C (lit.,[19] 129 °C). The crude diacid (5 g, 30.4 mmol) was added to redistilled acetic anhydride (25 ml, 0.244 mol) cooled in an ice-bath. The mixture was stirred and warmed slightly to effect dissolution and then stored at −10 °C for 2 h. The acetic anhydride was removed on a CO_2-rotary evaporator and the red solid residue was extracted into portions of hot cyclohexane. On cooling, the yellow cyclohexane extracts deposited the anhydride (**20**) as yellow needles (2.05 g, 46%, 31% overall), m.p. 108—112 °C (lit.,[19] 113—114 °C) (Found: C, 40.7; H, 2.1; Cl, 23.75. Calc. for $C_5H_3ClO_3$: C, 41.0; H, 2.05; Cl, 24.2%), $\nu_{max.}$ 1 805, 1 750, and 1 640 cm^{-1}; δ 3.77 (2 H, d, *J* 2 Hz, 4-H), 6.38 (1 H, d, *J* 2 Hz, 2-H); *m/z* 146 (M^+, 3%), 102 ($M^+ - CO_2$, 68%), 67 ($M^+ - CO_2$ –

Cl, 100%); $\lambda_{max.}$(MeCN) 288 (ε 12 600 dm^3 mol^{-1} cm^{-1}), 346 nm (2 300).

3-Chloro-4-methoxycarbonylbut-2-enoic Acid (**21**).—3-Chloroglutaconic anhydride (**20**) (2.24 g, 15.27 mmol) was dissolved in absolute methanol (30 ml) and the pale yellow solution was stirred under reflux for 3 h. Rotary evaporation of the cooled reaction solution yielded a yellow oil which crystallised after evacuation under high vacuum to give a yellow solid (2.47 g, 91%), m.p. 54—56 °C. This material was satisfactory for most purposes but an analytical sample could be obtained by recrystallisation from light petroleum (b.p. 40—60 °C) as very pale yellow *crystals* (2.14 g, 79%), m.p. 58—60 °C (Found: C, 40.1; H, 3.9; Cl, 19.35. $C_6H_7ClO_4$ requires C, 40.35; H, 3.95; Cl, 19.85%); $\nu_{max.}$ 3 480—2 580, 1 720, 1 700, and 1 635 cm^{-1}; δ_H 3.82 (3 H, s, CO_2Me), 4.13 (2 H, s, 4-H), 6.30 (1 H, s, 3-H), and 10.70 (1 H, br s, CO_2H); δ_C 41.6 (t), 52.4 (q), 121.4 (d), 149.6 (s), 168.1 (s), and 168.8 (s); *m/z* 178 (M^+, 9%), 147 (M^+ − OMe, 56), 146 (M^+ − HOMe, 57), 118 (18), 99 (M^+ − CO_2 − Cl, 24), and 59 (100).

Preparation of the Chloro Diesters (**22**).* *General Procedure.*—To a stirred solution of the but-3-en-2-ol (**9**) (5.61 mmol), the acid (**21**) (1.05 g, 5.9 mmol), and dry pyridine (0.5 ml, 6.18 mmol) in dry dichloromethane (20 ml) was added dropwise during 5 min a solution of *N,N'*-dicyclohexylcarbodi-imide (1.23 g, 5.97 mmol) in dry dichloromethane (3 ml). During the addition the colour of the solution deepened to an orange-brown and a precipitate appeared. The mixture was stirred at room temperature for 23 h. The solid was filtered off and washed with dry ether (3 × 10 ml). The filtrate and washings were combined and treated with glacial acetic acid–methanol (1:1, 3 ml) to destroy any remaining di-imide. The mixture was then rotary evaporated and the residue was azeotroped first with toluene (2 × 15 ml) to remove acetic acid, then with methanol (2 × 10 ml) to remove toluene. The resultant red oil (1.5—2.0 g) was chromatographed on neutral alumina (grade 5) using ethyl acetate–dichloromethane (1:10) as eluant to give: 4-(2-*furyl*)*but*-3-*en*-2-*yl* 3-*chloro*-4-*methoxycarbonylbut*-2-*enoate* (**22a**) as a yellow oil (94%) (Found: M^+, 298.0608. $C_{14}H_{15}{}^{35}ClO_5$ requires M^+, 298.0607, $\nu_{max.}$ 1 740, 1 720, 1 665, and 1 640 cm^{-1}; δ_H (250 MHz) (two geometrical isomers, *ca.* 1:1) 1.40 (2 × 3 H, 2 × d, *J* 6 Hz, 1-H), 3.72 (2 × 3H, 2 × s, CO_2Me), 4.11 (2 × 2 H, 2 × s, 4″-H), 5.52 (2 × 1 H, sextuplet, 2-H), 6.06—6.56 (2 × 5 H, m, 3-H + 4-H + 2″-H + 3′-H + 4′-H), and 7.35 (2 × 1 H, br s, 5′-H); δ_C 20 (2 × q), 42 (2 × t), 53 (2 × q, OMe), 71 (2 × d), 109.5, 111, 120, 122, 127.5, 143 (all 2 × d), 148, 152 (both 2 × s), and 164, 168 (both 2 × s, CO); *m/z* 298 (M^+, 13%), 161 [$MeO_2CCH_2C(Cl)$=$CHCO^+$, 100], 138 [C_4H_3OCH=$CHCH(Me)OH^+$, 22], 137 (43), 121 [C_4H_3OCH=$CHCH(Me)^+$, 78%]; 4-(5-*methyl*-2-*furyl*)*but*-3-*en*-2-*yl* 3-*chloro*-4-*methoxycarbonylbut*-2-*enoate* (**22b**) as a yellow oil (71%), $\nu_{max.}$ 1 735, 1 720, 1 665, and 1 640 cm^{-1}; δ_H (250 MHz) (two geometrical isomers, *ca.* 3:1) 1.40 (2 × 3 H, 2 × d, *J* 7 Hz, 1-H), 2.28 (2 × 3 H, 2 × s, 5′-Me), 3.70 (2 × 3 H, 2 × s, CO_2Me), 4.15 (2 × 2 H, 2 × m, 4″-H), 5.5 (2 × 1 H, quintet, 2-H), and 5.9—6.5 (m, 3-H + 4-H + 3′-H + 4′-H + 2″-H); δ_C (values given for major isomer) 13.5 (5′-Me), 20.3, 41.5, 52.3 (OMe), 71.6 107.5, 110.2, 120.5, 122.4, 125.1, 146.7, 150.4, 152.4, and 163.3, 168.2 (CO); *m/z* 312 (M^+, 9%), 161 [$MeO_2CCH_2C(Cl)$=$CH{\cdot}CO^+$, 53], 151 [MeC_4H_2OCH=$CHCH(Me)OH^+$, 57], and 135 (100); 4-(2-*thienyl*)*but*-3-*en*-2-*yl* 3-*chloro*-4-*methoxycarbonylbut*-2-*enoate* (**22c**) as an orange oil (83%); $\nu_{max.}$ 1 735, 1 720, and 1 645 cm^{-1}; δ_H (250 MHz) (two geometrical isomers, *ca* 3:1) 1.36 (3 H, d, *J* 7 Hz, 1-H, minor isomer), 1.41 (3 H, d, *J* 7 Hz, 1-H, major isomer), 3.71 (3 H, s, CO_2Me, minor isomer), 3.73 (3 H, s, CO_2Me, major isomer), 4.11 (2 × 2 H, quintet, 4″-H), 5.51 (2 × 1 H, sextuplet, 2-H), 6.00 (2 × 1 H, 2 × dd, *J* 7 Hz, *J'* 16 Hz, 3-H), 6.28 (2 × 1 H, 2 × s, 2″-H), 6.74 (2 × 1 H, 2 × d, *J* 16 Hz, 4-H), 6.98 (2 × 2 H, m, 3′-H + 4′-H), and 7.18 (2 × 1 H, 2 × d, *J* 5 Hz, 5′-H); δ_C (values given for major isomer) 20.2, 41.5, 52.3 (OMe), 71.3, 122.3, 124.7, 125.2, 126.4, 127.4, 127.7, 141.2, 146.9, and 164.5, 170.1 (CO); *m/z* 314 (M^+, 99%), 161 (64), 153 (38), 137 [C_4H_3SCH=$CHCH(Me)^+$, 100], and 97 (58); 4-(5-*methyl*-2-*thienyl*)*but*-3-*en*-2-*yl* 3-*chloro*-4-*methoxycarbonylbut*-2-*enoate* (**22d**) as an orange oil (57%), $\nu_{max.}$ 1 750, 1 720, and 1 645 cm^{-1}, δ_H (250 MHz) (two geometrical isomers, *ca.* 2:1) 1.39 (2 × 3 H, 2 × d, *J* 9 Hz, 1-H), 2.43 (2 × 3 H, 2 × s, 5′-Me), 3.70 (2 × 3 H, 2 × s, CO_2Me), 4.14 (2 × 2 H, 2 × m, 4″-H), 5.50 (2 × 1 H, quintet, 2-H), 5.92 (2 × 1 H, 2 × dd, *J* 8 Hz, *J'* 18 Hz, 3-H), 6.31 (2 × 1 H, 2 × s, 2″-H), 6.68 (2 × 1 H, 2 × d, *J* 4 Hz, 3′-H or 4′-H), 6.75 (2 × 1 H, 2 × d, *J* 18 Hz, 4-H), and 6.86 (2 × 1 H, 2 × d, *J* Hz, 3′-H or 4′-H); *m/z* 328 (M^+, 16%), 168 [MeC_4H_2SCH=$CH{\cdot}CH(OH)Me^+$, 28], 167 (31), 161 (14), 151 (MeC_4H_2SCH=$CHCHMe^+$, 80), and 111 (100).

Preparation of the Allene Diesters (**16**).† *General Procedure.*—To a stirred, ice-cooled solution of the chloro diester (**22**) (2.8 mmol) in dry THF (10 ml) was added dropwise dry triethylamine (3.36 mmol) during 3 min. The resultant solution was stored at 4 °C for 24 h during which time a precipitate had appeared. The solid was filtered off and washed with dry ether (3 × 10 ml). The combined filtrate and washings were washed with 0.2M-hydrochloric acid (4 × 40 ml), water (1 × 40 ml), brine (3 × 40 ml), and dried (Na_2SO_4). Rotary evaporation after filtration generally left yellow to orange oils which were usually sufficiently pure by ^1H n.m.r. spectroscopy for use in the Diels–Alder reactions. Analytical samples were prepared by chromatography on grade 3 alumina using ethyl acetate–light petroleum (1:15) as eluant, and obtained as yellow to orange oils: 4-(2-*furyl*)*but*-3-*en*-2-*yl* 4-*methoxycarbonylbuta*-2,3-*dienoate* (**16a**) as an unstable oil (78%), $\nu_{max.}$ 1 970, 1 720, and 1 650 cm^{-1}, δ 1.42 (3 H, d, *J* 6 Hz, 1-H), 3.75 (3 H, s, CO_2Me), 5.52 (1 H, dq, *J* 2 Hz, *J'* 6 Hz, 2-H), 6.00 (2 H, s, 2″-H + 4″-H), 6.25 (4 H, m, 3-H + 4-H + 3′-H + 4′-H), and 7.27 (1 H, d, *J* 2 Hz, 5′-H); *m/z* 262 (M^+, 18%), 203 (M^+ − CO_2Me, 24), 137 (82), 125 (MeO_2CCH=C=$CHCO^+$, 47), 121 (100), and 91 (94); 4-(5-*methyl*-2-*furyl*)*but*-3-*en*-2-*yl* 4-*methoxycarbonylbuta*-2,3-*dienoate* (**16b**) as an orange oil (75%) (Found: C, 65.4; H, 6.4. $C_{15}H_{16}O_5$ requires C, 65.20; H, 5.85%), $\nu_{max.}$ 1 970, 1 720, and 1 665 cm^{-1}; δ 1.38 (3 H, d, *J* 6 Hz, 1-H), 2.28 (3 H, s, 5′-Me), 3.73 (3 H, s, CO_2Me), 5.43 (1 H, m, 2-H), and 6.00—6.30 (6 H, m, 3-H + 4-H + 3′-H + 4′-H + 2″-H + 4″-H); 4-(2-*thienyl*)*but*-3-*en*-2-*yl* 4-*methoxycarbonylbuta*-2,3-*dienoate* (**16c**) as a yellow-orange oil (88%) (Found: C, 60.6; H, 5.6. $C_{14}H_{14}O_4S$ requires C, 60.4; H, 5.05%); $\nu_{max.}$ 1 970, 1 730 cm^{-1}; δ_H (250 MHz) (two diastereoisomers, *ca.* 1:1) 1.41 (2 × 3 H, 2 × d, *J* 9 Hz, 1-H), 3.75 (2 × 3 H, 2 × s, CO_2Me), 5.54 (2 × 1 H, quintet, 2-H), 6.09 (2 × 1 H, 2 × dd, *J* 9 Hz, *J'* 16 Hz, 3-H), 6.28 (2 × 2 H, 2 × s, 2″-H + 4″-H), 6.86 (2 × 1 H, 2 × d, *J* 16 Hz, 4-H), 7.01 (2 × 1 H, m, 3′-H or 4′-H), 7.10 (2 × 1 H, m, 3′-H or 4′-H), and 7.37 (2 × 1 H, 2 × d, *J* 6 Hz, 5′-H); δ_C shows an allenic central carbon signal at δ 219.5; *m/z* 278 (M^+, 10%), 219 (M^+ − CO_2Me, 39), 154 (33), 138 (C_4H_3SCH=$CHCHMe^+$, 78), and 97 (100); 4-(5-*methyl*-2-*thienyl*)*but*-3-*en*-2-*yl* 4-*methoxycarbonylbuta*-2,3-*dienoate* (**16d**) as a deep orange oil (74%) (Found: C, 61.7; H, 5.75. $C_{15}H_{16}O_4S$ requires C, 61.6; H, 5.5%);

* In the n.m.r. assignments of compounds (**22**), the double-primed numbers refer to the butenoate chain.

† In the n.m.r. assignments of compounds (**16**), the double-primed numbers refer to the butadienoate chain.

$\nu_{max.}$ 1 970, 1 725 cm^{-1}; δ 1.35 (3 H, d, *J* 8 Hz, 1-H), 2.38 (3 H, s, 5′-Me), 3.62 (3 H, s, CO_2Me), 5.40 (1 H, quintet, 2-H), 5.80 (1 H, dd, *J* 7 Hz, *J′* 15 Hz, 3-H), 6.10 (2 H, s, 2″-H + 4″-H), and 6.50—6.85 (3 H, m, 4-H + 3′-H + 4′-H); *m/z* 292 (M^+, 26%), 233 (50), 152 (84), and 111 (100).

Diels–Alder Reactions.—(*a*) 6-(1-*Hydroxyethyl*)-4-*methoxycarbonylbenzofuran*-5-*ylacetic acid lactone* (**23a**). A solution of the allene (**16a**) (700 mg, 2.67 mmol) and a few crystals of hydroquinone in dry toluene (20 ml) under nitrogen was heated to reflux in pre-silylated glassware for 44 h. The reaction mixture was cooled and filtered to remove polymeric material (239 mg, m.p. > 260 °C). The filtrate was rotary evaporated and the residual dark brown oil was chromatographed on grade 5 alumina (45 g) using ethyl acetate–benzene (1:2) as eluant. The product was obtained as an orange oil (70 mg) which showed peaks in the ^1H n.m.r. spectrum corresponding to the *benzofuran* (**23a**) (yield calculated from the integration = 28 mg, 4%) at δ 1.82 (3 H, d, *J* 6 Hz, 1′-Me), 3.98 (3 H, s, CO_2Me), 4.27 (2 H, ABq, *J* 18 Hz, CH_2CO), 5.45 (1 H, q, *J* 6 Hz, 1′-H), 7.10 (1 H, d, *J* 2.5 Hz, 3-H), 7.60 (1 H, s, 7-H), 7.70 (1 H, d, *J* 2.5 Hz, 2-H) plus peaks at δ 1.50 (2 × d, *J* 6 Hz), 3.50—3.75 (m), 6.0—6.3 (m), and 7.28 (m). The mass spectrum showed an ion at *m/z* 260 which would correspond to M^+ for (**23a**) and the i.r. spectrum showed bands at 1 750, 1 730, and 1 645 cm^{-1}. The u.v. spectrum contained bands at 268 and 294 (shoulder) consistent with a benzofuran structure.[9]

(*b*) 6-(1-*Hydroxyethyl*)-2-*methyl*-4-*methoxycarbonylbenzofuran*-5-*ylacetic acid lactone* (**23b**). A solution of the allene (**16b**) (115 mg, 0.416 mmol) in dry toluene (8.5 ml) in pre-silylated glassware was heated to reflux under argon in the presence of hydroquinone (10 mg) for 128 h. The orange-brown solution was allowed to cool and filtered from the hydroquinone which precipitated out. The filtrate was rotary evaporated to yield a brown oil which was chromatographed on grade 5 alumina (10 g) using ethyl acetate–benzene (1:2) as eluant. The product eluted with another compound as a yellow oil (44 mg) in the early fractions. This oil was subjected to a second column of alumina (grade 4, 10 g) using ethyl acetate–toluene (1:7) as eluant. Fractions containing the product were concentrated to a yellow solid which was recrystallised (ethyl acetate–cyclohexane) to give the *benzofuran* (**23b**) as pale yellow needles (14 mg, 12%), m.p. 110—111 °C (Found: C, 65.45; H, 5.15. $C_{15}H_{14}O_5$ requires C, 65.70; H, 5.15%); $\nu_{max.}$ 1 740, 1 720 cm^{-1}; $\lambda_{max.}$(EtOH) 226 (ε 39 900 $dm^3\ mol^{-1}\ cm^{-1}$), 268 (12 100), and 310 (9 100); δ 1.80 (3 H, d, *J* 6 Hz, 1′-Me), 2.43 (3 H, s, 2-Me), 3.95 (3 H, s, CO_2Me), 4.15 (2 H, ABq, *J* 19 Hz, CH_2CO), 5.38 (1 H, q, *J* 6 Hz, 1′-H), 6.67 (1 H, s, 3-H), and 7.45 (1 H, s, 7-H); *m/z* 274 (M^+, 84%), 259 (25), 243 (19), 231 ($MH^+ - CO_2$, 100), 203 (20), 199 (20), and 115 (18).

(*c*) 6-(1-*Hydroxyethyl*)-4-*methoxycarbonylbenzothiophen*-5-*ylacetic acid lactone* (**23c**). A solution of the allene (**16c**) (466.2 mg, 1.68 mmol) and hydroquinone (30 mg) in dry toluene (7.5 ml) was heated to reflux for 4 h. The reaction mixture was cooled and rotary evaporated to give an orange-brown viscous oil. This oil was triturated with either–light petroleum (1:1) and the triturate was decanted and rotary evaporated to give an orange oil, which was chromatographed on grade 5 alumina (20 g) using ethyl acetate–benzene (1:20) as eluant. Early fractions were combined to give a yellow-orange oil (165.3 mg) which was rechromatographed on silica gel (15 g) using ethyl acetate–benzene (1:7) as eluant. Fractions containing the product were concentrated to a yellow oil (99.7 mg) which solidified on standing. This solid was recrystallised (ether–cyclohexane) to give the *benzothiophene* (**23c**) as cream crystals (28 mg, 6%), m.p. 142—143 °C (Found: M^+, 276.0458. $C_{14}H_{12}O_4S$ requires M^+, 276.0456); $\nu_{max.}$ 1 740, 1 725 cm^{-1}; δ_H (250 MHz) 1.87 (3 H, d, *J* 7 Hz, 1′-Me), 4.06 (3 H, s, CO_2Me), 4.18 (2 H, ABq, *J* 19 Hz, CH_2CO), 5.57 (1 H, q, *J* 7 Hz, 1′-H), 7.61 (1 H, d, *J* 6 Hz, 2-H), 7.69 (1 H, dd, *J* 0.8 Hz, *J′* 6 Hz, 3-H), and 7.92 (1 H, br s, 7-H); *m/z* 276 (M^+, 100%), 261 (M^+ − Me, 23), 245 (M^+ − OMe, 20), 233 ($MH^+ - CO_2$, 90), and 216 (10).

(*d*) 6-(1-*Hydroxyethyl*)-2-*methyl*-4-*methoxycarbonylbenzothiophen*-5-*ylacetic acid lactone* (**23d**). A solution of the allene (**16d**) (609.4 mg, 2.08 mmol) and hydroquinone (50 mg) in dry toluene (12 ml) was heated to reflux for 3.75 h. After cooling, the reaction mixture was rotary evaporated and the resultant orange oil was triturated with ether–light petroleum (1:1). The triturate was decanted from polymeric material and concentrated to an orange oil (547.1 mg) which was chromatographed on silica gel (60 g) using ethyl acetate–benzene (1:7) as eluant. The early fractions were concentrated to a yellow oil (239.7 mg) which was rechromatographed on grade 4 alumina (25 g) using ethyl acetate–benzene (1:20) as eluant. Fractions containing the product were concentrated to a pale yellow solid which was recrystallised (ethyl acetate–cyclohexane) to give the *benzothiophene* (**23d**) as pale yellow needles (60 mg, 10%), m.p. 98—99.5 °C (Found: C, 61.8; H, 4.9. $C_{15}H_{14}O_4S$ requires C, 62.05; H, 4.85%); $\nu_{max.}$ 1 740, 1 725 cm^{-1}; δ_H (250 MHz) 1.84 (3 H, d, *J* 7 Hz, 1′-Me), 2.62 (3 H, s, 2-Me), 4.03 (3 H, s, CO_2Me), 4.09 (2 H, ABq, *J* 19 Hz, CH_2CO), 5.53 (1 H, q, *J* 7 Hz, 1′-H), 7.33 (1 H, s, 3-H), and 7.77 (1 H, s, 7-H); *m/z* 290 (M^+, 100%), 275 (27), 259 (17), 247 ($MH^+ - CO_2$, 99), and 231 (8).

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