Intramolecular Reactions of 1-Allylic 2,2-Dimethyl Ethylenetricarboxylates

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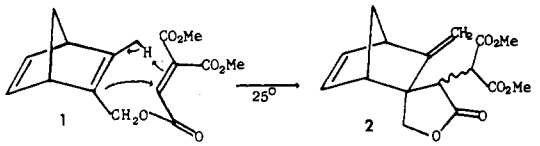
Abstract: 1-Allylic 2,2-dimethyl ethylenetricarboxylates undergo intramolecular cyclization reactions at 80–140 °C giving mixtures of ene adducts and dihydropyrans in which the α,β-unsaturated ester functions as diene in an inverse electron demand Diels–Alder reaction. The *trans*-crotyl triester **6** reacts at 135 °C giving a 1:1 mixture of the cis-substituted ene adduct **8** and the Diels–Alder adduct **7**. The *cis*-crotyl triester **12** gives the same ene adduct **8** and the Diels–Alder adduct **13**. The cinnamyl triester **14** undergoes a reversible Diels–Alder reaction at 80–120 °C with $\Delta H = -14.3$ kcal/mol and $\Delta S = -41$ eu. The ene adducts are of value as α-methylene lactone precursors while the pyrans will be of value in synthesis of iridoids and their analogues.

Introduction

Intramolecular ene reactions have recently been used as key steps in syntheses of prostaglandins, acorenone B, and chiral acetic acid.[1] We were interested in developing intramolecular ene reactions of unsaturated esters of allyl alcohols as a route to β-alkenyl α-methylene lactones such as alantolactone.[2] In this connection, we were interested in Kelly's observation that the norbornadienylmethyl ethylenetricarboxylate **1** underwent an intramolecular ene reaction at 25 °C to

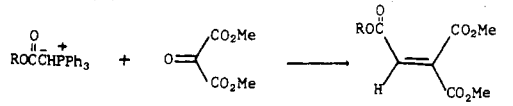


give **2**.[3] Since steric (strain relief) and electronic (tetrasubstituted electron-rich double bond) effects make this a particularly facile ene reaction it was of interest to determine whether this reaction could provide a general route to lactones.

Results and Discussion

Allylic dimethyl ethylenetricarboxylates were initially prepared by a modification of Kelly's procedure.[3] *tert*-Butyl glyoxylate[4] was condensed with dimethyl malonate giving *tert*-butyl dimethyl ethylenetricarboxylate (**5**) in 47% yield. Hydrolysis of **5** in trifluoroacetic acid, conversion to the mixed anhydride with trifluoroacetic anhydride, and reaction with the allyl alcohol in the presence of triethylamine gave the desired allylic dimethyl ethylenetricarboxylate in 20–55% yield.

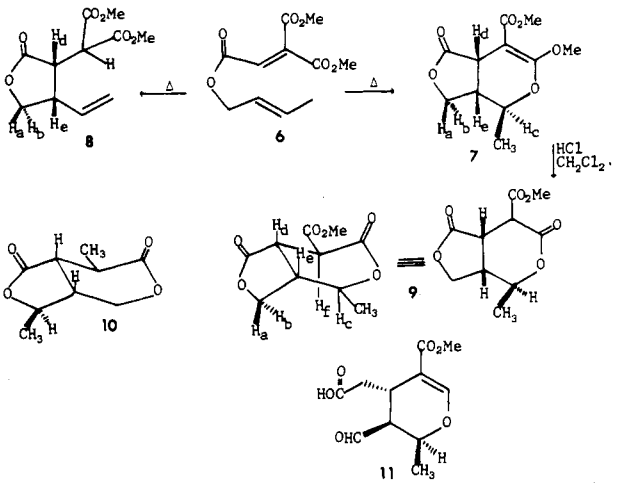
A more efficient preparation of the desired triesters is accomplished by a Wittig reaction of the appropriate alkoxycarbonylmethylenetriphenylphosphorane (**3**) with dimethyl oxomalonate (**4**).[5] The triester **5**, which is used in Kelly's



3 **4** **5**, R = t-butyl

procedure,[3] can be prepared in 79% yield in three steps from *tert*-butyl bromoacetate. By use of the allylic bromoacetate, the desired allylic dimethyl ethylenetricarboxylate can be prepared reproducibly, in large quantity, in 60–70% overall yield.

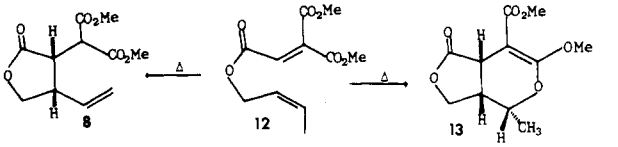
Our initial substrate, the *trans*-2-butenyl triester **6**, requires 200 h at 135 °C to react completely as determined by monitoring the NMR of the reaction mixture. The conditions required are more vigorous than those needed for cyclization of



1 since the alkene moiety of **6** is much less electron rich than that of **1**. Upon cooling the reaction mixture, **7** crystallizes in 22% yield. Chromatography of the mother liquor yields a single ene adduct **8** in 30% yield. The NMR of the crude reaction mixture indicates that **7** and **8** in a 1:1 ratio, are the only products formed. The pyranofuranone **7** arises via an intramolecular Diels–Alder reaction. The stereochemistry is determined by $J_{H_dH_e} = 7$ Hz, which is consistent with a cis ring fusion and too small for a trans ring fusion which would require trans diaxial hydrogens.[6] $J_{H_cH_e} = 11$ Hz indicates that the hydrogens are trans and that cis addition to the alkene has occurred. Treatment of **7** with dry hydrogen chloride in methylene chloride gives a quantitative yield of the lactone **9**. The three large vicinal coupling constants, $J_{H_cH_e} = 12$, $J_{H_dH_e} = 10$, $J_{H_dH_f} = 10$ Hz, indicate that the δ-lactone of **9** is in a boat form,[7] a conformation known to be stable for the structurally similar isoiridomyrmecin (**10**).[8]

The Diels–Alder adduct **7** bears a marked similarity to elenolic acid (**11**),[9] a secoiridoid with antiviral properties. Conversion of **7** to elenolic acid and its analogues is presently underway. Modified versions of this cycloaddition reaction should be of value in the synthesis of a variety of iridoids and the iridoid portion of indole alkaloids.

Treatment of the *cis*-2-butenyl triester **12** for 200 h at 135 °C gives a 90:10 mixture of **8** and **13** as determined by NMR



spectroscopy. The unstable Diels–Alder adduct **13** cannot be

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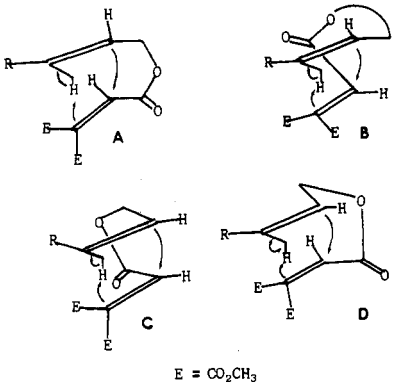
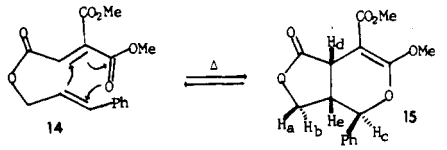


Figure 1. Transition states for the ene reactions of **6** (R = H, C and D), **12** (R = H, A and B), and **16** (R = CH_3, A, B, C, and D).

isolated but is clearly different from **7**, presumably with opposite stereochemistry at the methyl-bearing carbon. The ene adduct **8**, which is isolated in 43% yield, is identical with that obtained from **6**. The ^1H NMR spectrum does not allow an assignment of stereochemistry. However, formation of the trans substituted adduct from the cis alkene **12** (via transition state B, Figure 1) is sterically impossible, so **8** is assigned cis substitution.[1] The exclusive formation of the cis-substituted adduct from both of the analogous methyl *trans,cis*- and *trans,trans*-2,7-nonadienoates has been observed by Oppolzer.[1] Lactone **8** is stable at 135 °C for 72 h.

Lactone **8** is probably formed by a concerted ene reaction while pyranofuranones **7** and **13** are formed by a Diels–Alder reaction in which the α,β-unsaturated ester functions as the diene. The formation of a single stereoisomer with cis addition to the dienophile is consistent with a concerted reaction. To the best of our knowledge this is the first instance of an α,β-unsaturated ester functioning as a diene.[10] Two factors are responsible for this facile Diels–Alder reaction. The other ester groups facilitate an inverse electron demand Diels–Alder reaction and stabilize the resulting ketene acetal. Secondly, intramolecular Diels–Alder reactions are faster than their intermolecular analogues.[11] With the exception of quinone methides,[12] intramolecular Diels–Alder reactions of α,β-unsaturated carbonyl compounds have not been previously observed.

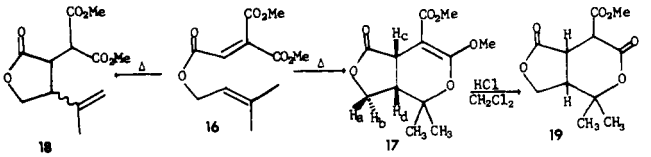
To establish that pyranofuranones **7** and **13** are not derived from ene adducts, the cinnamyl triester **14** was investigated. Heating **14** in benzene-d_6 at 85 °C led to a ~2:1 mixture of **14** and Diels–Alder adduct **15.** On raising the temperature to 115



°C the equilibrium shifts, giving a 8:1 mixture. Lowering the temperature to 80 °C reestablishes the 2:1 equilibrium. The structure of **15** is assigned on the basis of $J_{H_dH_e}$ = 7 Hz, which requires a cis ring fusion, and $J_{H_cH_e}$ = 11.5 Hz, which requires trans diaxial hydrogens. Examination of the equilibrium for the Diels–Alder reaction of the cinnamyl triester **14** at several temperatures between 80 and 130 °C gives $\Delta H = -14.3$ kcal/mol and $\Delta S = -41$ eu. This result is consistent with qualitative observations in similar Diels–Alder reactions.[13]

Since the Diels–Alder reaction is reversible and thermodynamically unfavored at higher temperatures while the ene reaction is probably irreversible, it is clear that the ratio of Diels–Alder adduct to ene adduct will be highly dependent on the reaction conditions. Low reaction temperatures will favor the Diels–Alder reaction, while higher temperatures should favor the ene adduct. This is observed with **16.**

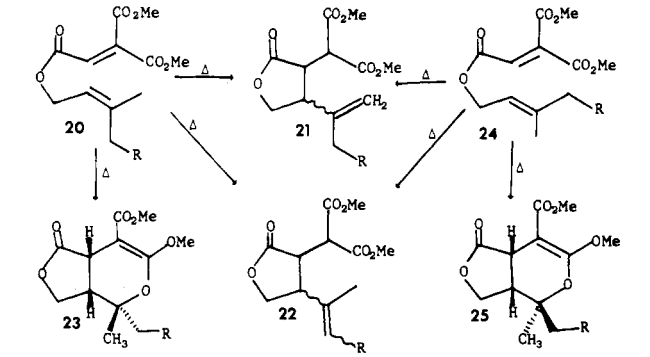
The 3-methyl-2-butenyl ester **16** is slightly more reactive than **6** and **12,** giving a 70:30 mixture of **18** and **17** in 112 h at



85 °C. Fractional crystallization from benzene-d_6 allows the isolation of **17,** which is assigned the cis stereochemistry from $J_{H_cH_d}$ = 8 Hz. Treatment of the **17:18** mixture with hydrogen chloride in methylene chloride converts **17** to **19** and leaves **18** unchanged. Heating **16** for 30 h at 120 °C, gives, after chromatography, a 95% yield of **18.** This result is consistent with a reversible Diels–Alder reaction.

Examination of the NMR spectrum of the allylic methyl of **18** indicates that **18** is ca. 1:1 mixture of stereoisomers. This appears to be the kinetic mixture since the ratio does not change during the course of the reaction. The ene reaction of **16** can proceed through the four possible transition states shown in Figure 1. The transition state B leading to trans-substituted **18** is highly strained. Therefore *trans*-**18** must be formed exclusively via transition state D (R = Me). However, **6** reacts to give **8** via transition state C (R = H) rather than D. Apparently replacement of a hydrogen with a methyl leads to unfavorable steric interactions in C which are not present in D.

The neryl triester **20** cyclizes in 6 h at 125 °C to a ca. 9:1 mixture of ene adducts **21** and **22** and pyran **23.** Chromatography gives a 3:2 mixture of **21** and **22** in 70% yield. The geranyl triester **24** behaves similarly, giving a 9:1 mixture of ene adducts **21** and **22** and pyran **25.** After chromatography a 2:3

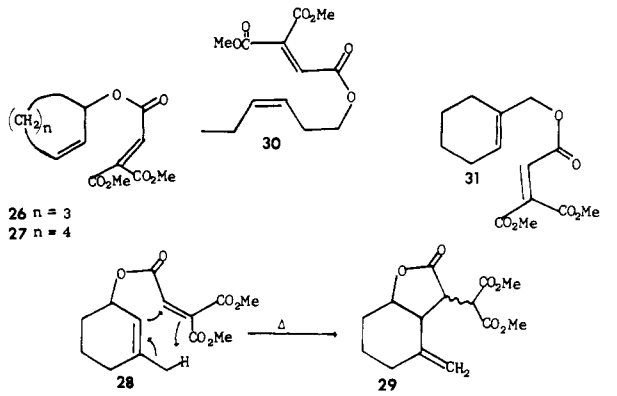


R = $CH_2CH{=}C(CH_3)_2$

mixture of **21** and **22** is obtained in 66% yield. Although the reversible formation and possible ring opening of the Diels–Alder adduct are complicating factors, the product ratio is consistent with a ca. 1.5:1 preference for secondary hydrogen over primary hydrogen abstraction and a ca. 1.5:1 preference for abstraction of hydrogen on the carbon trans to the ester.

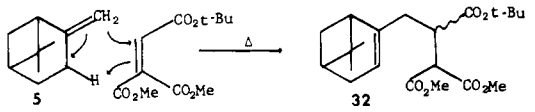
In order to test the applicability of this method to the synthesis of fused lactones, the cyclohexenyl and cycloheptenyl triesters **26** and **27** were investigated. In neither case can any ene adduct be detected. Slow decomposition of starting materials occurs at 200 °C. Apparently the steric constraints introduced by the ring prevent the reaction. The 3-methyl-2-cyclohexen-1-yl triester **28** reacts in 40 h at 110 °C in the presence of traces of pyridine to give exclusively the *exo*-methylene lactone **29** as a mixture of diastereomers. In the absence of pyridine isomerization of the exocyclic double bond occurs.

Attempted extension of this reaction to formation of δ-lac-



tones or spirolactones was unsuccessful. The *cis*-3-hexen-1-yl ester **30** undergoes slow decomposition at 220 °C. We[14] and others[1] have previously shown that formation of five-membered rings is much more facile than formation of six-membered rings in intramolecular ene reactions. The 1-cyclohexenylmethyl ester **31** undergoes slow decomposition at 195 °C.

For comparison purposes, the intermolecular ene reactions of **5** were investigated. Heating β-pinene and **5** for 40 h at 150



°C gives a 46% yield of **32** as a mixture of diastereomers. With 2-methyl-2-butene at 215 °C no ene adduct is formed and **5** decomposes. 2-Methyl-2-butene and trimethyl ethylenetricarboxylate[5] also give no ene adduct. Since β-pinene is an exceptionally reactive alkene the intramolecularity of the above reactions is an important feature in their success.

We are currently exploring the extension of this synthesis to the formation of cyclopentanones. The novel Diels–Alder reaction has a variety of applications to iridoid synthesis which are being explored. Attempted catalysis of these reactions with aluminum chloride leads to chlorine-containing lactones which will be reported on shortly.

Experimental Section

NMR spectra were determined on Varian A-60 or XL-100 or Perkin-Elmer R-32 spectrometers. The mass spectra were obtained with a AEI MS9 mass spectrometer. Infrared spectra were recorded on a Perkin-Elmer 283 spectrometer. All melting points (Pyrex capillary) and boiling points are uncorrected. Microanalyses were performed by Galbraith Laboratories. Benzene-d_6 (Aldrich) was stored over 3-A sieves under nitrogen.

***tert*-Butyl *tert*-Butoxyacetate.**[4] Treatment of 106.4 g (1.4 mol) of glycolic acid with 180 g (3.2 mol) of isobutylene and 1.6 mL of concentrated H_2SO_4 was carried out by the method of Carpino,[4] affording 138 g of crude product. Distillation gave 101 g (0.53 mol, 38% yield) of *tert*-butyl α-*tert*-butoxyacetate: bp 45–54 °C (0.1 mm); NMR ($CDCl_3$) δ 1.20 (9 H, s), 1.45 (9 H, s), and 3.9 ppm (2 H, s); IR (neat) 2976, 2948, 1756, 1728, 1473, 1391, 1367, 1306, 1250, 1226, and 845 cm^{-1}.

***tert*-Butyl α-Bromo-α-*tert*-butoxyacetate.**[4] Bromination of 57.8 g (0.308 mol) of *tert*-butyl α-*tert*-butoxyacetate with 54.8 g (0.307 mol) of *N*-bromosuccinimide and 0.01 g of benzoyl peroxide in 1 L of CCl_4 was accomplished by the method of Carpino.[4] The solution of the unstable α-bromo adduct was filtered and evaporated to give 94 g of crude product which was used directly without further purification. NMR of the crude product showed a signal at 6.23 ppm for the methine proton.

***tert*-Butyl Glyoxylate (Hydrated).**[4] The crude *tert*-butyl *tert*-butoxybromoacetate (94 g) was stirred for 24 h at room temperature in 1 L of 1 M $NaHCO_3$. Continuous extraction with ether for 24 h followed by drying ($MgSO_4$) and evaporation of the ether yielded 40 g of crude aldehyde. The reaction was repeated with 60 g of bromide and gave 27 g of crude aldehyde. The products were combined and distilled, yielding 25 g of hydrated aldehyde (overall yield from *tert*-butyl α-*tert*-butoxyacetate, 35%): bp 44–45 °C (25 mm); NMR ($CDCl_3$) δ 1.50 (9 H, s), 4.4 (0.8 H, m), and 9.31 ppm (0.2 H, s); IR (neat) 3464, 2977, 2881, and 1752 cm^{-1}.

2-*tert*-Butyl 1,1-Dimethyl Ethylenetricarboxylate (5). As described by Kelly,[3] 4.74 g (0.037 mol) of hydrated *tert*-butyl glyoxylate, 4.29 g (0.33 mol) of dimethyl malonate, and 0.2 mL of piperidine in 150 mL of benzene were refluxed for 72 h with azeotropic removal of water. Evaporation of the reaction mixture to an oil (7.7 g) followed by column chromatography on 200 g of silica gel using 9:1 benzene–ether as eluant afforded 5.55 g of product contaminated with unreacted dimethyl malonate. Distillation yielded 4.1 g (47%) of pure triester **5**: bp 90–102 °C (0.12 mm); NMR ($CDCl_3$) δ 1.48 (9 H, s), 3.83 and 3.88 (6 H, 2 s), and 6.84 ppm (1 H, s); IR (neat) 2975, 2955, 2930, 1737, 1720, 1640, 1475, 1450, 1435, 1385, 1365, 1250, 1200, 1150, 1067, 990, 965, 920, 850, and 835 cm^{-1}.

Preparation of Allylic Dimethyl Ethylenetricarboxylates. General Procedure. A solution of ca. 2 mmol (0.5 g) of *tert*-butyl 2,2-dimethyl ethylenetricarboxylate (**5**) and 5 mL of trifluoroacetic acid (distilled and stored under N_2) was stirred. The excess trifluoroacetic acid was removed in vacuo after stirring for ca. 30 min. To the clear oil was added 0.5 mL of trifluoroacetic anhydride (distilled and stored under N_2). After 15 min an additional 0.5 mL of trifluoroacetic anhydride was added. The excess trifluoroacetic anhydride was removed after an additional 11 min of stirring. To the mixed anhydride, 5 mL of benzene (distilled from sodium–benzophenone) was added. The reaction mixture was cooled to −78 °C and a solution of 5 mL of benzene, 5 mL of triethylamine (distilled from KOH), and an excess (10–50%) of alcohol added. The reaction mixture was then allowed to warm up to ice-bath temperature and stirred for 1–2 h and at room temperature for 1 h. The reaction mixture (which was usually light red) was poured into 50 mL of ether and washed with 25 mL of 10% HCl and 50 mL of saturated salt solution. The organic layer was then dried over Na_2SO_4. After filtration and removal of solvent, the product was purified on 10 g of silica gel eluting with 50/50 ether–petroleum ether. The triester was then used immediately for the ene reaction.

1-(*trans*-2-Buten-1-yl) 2,2-dimethyl ethylenetricarboxylate (6) was prepared in 43% yield: NMR (benzene-d_6) δ 1.45 (3 H, d, J = 6 Hz), 3.32 and 3.63 (6 H, 2 s), 4.40 (2 H, d, J = 5 Hz), 5.45 (2 H, m), and 6.83 ppm (1 H, s); IR (neat) 3020, 2960, 1735, and 1650 cm^{-1}; *m/e* 242.080 (calcd for $C_{11}H_{14}O_6$, 242.079).

1-(3-Methyl-2-buten-1-yl) 2,2-dimethyl ethylenetricarboxylate (16) was prepared in 38% yield: NMR ($CDCl_3$) δ 1.72 and 1.77 (6 H, 2 s), 3.85 and 3.88 (6 H, 2 s), 4.73 (2 H, d, J = 7 Hz), 5.38 (1 H, t, J = 7 Hz), and 6.92 ppm (1 H, s); IR (neat) 1735 and 1671 cm^{-1}; *m/e* 256.094 (calcd for $C_{12}H_{16}O_6$, 256.094).

1-(*cis*-3-Hexen-1-yl) 2,2-dimethyl ethylenetricarboxylate (30) was prepared in 54% yield; NMR ($CDCl_3$) δ 0.98 (3 H, t, J = 8 Hz), 1.72–2.72 (4 H, m), 3.85 and 3.90 (6 H, 2 s), 4.22 (2 H, t, J = 7 Hz), 5.02–5.82 (2 H, m), and 6.92 ppm (1 H, s); IR (neat) 1742, 1735, and 1645 cm^{-1}.

1-(2-Cyclohepten-1-yl) 2,2-dimethyl ethylenetricarboxylate (27) was prepared in 48% yield: NMR (benzene-d_6) δ 1.1–2.1 (8 H, m), 3.30 (3 H, s), 3.63 (3 H, s), 5.3–6.4 (3 H, m), and 6.87 ppm (1 H, s).

1-(1-Cyclohexenylmethyl) 2,2-dimethyl ethylenetricarboxylate (31)[16] was prepared in 27% yield: NMR ($CDCl_3$) δ 1.6 (4 H, m), 1.9 (4 H, m), 3.85 (6 H, s), 4.00 (2 H, bd s), 5.67 (2 H, m), and 6.88 ppm (1 H, s).

1-Geranyl 2,2-dimethyl ethylenetricarboxylate (24) was prepared in 41% yield: NMR ($CDCl_3$) δ 1.62 and 1.68 (9 H, 2 s), 2.07 (4 H, m), 3.83 and 3.88 (6 H, 2 s), 4.71 (2 H, bd d, J = 7 Hz), 4.9–5.6 (2 H, m), and 6.92 (1 H, s); IR (neat) 1745, 1726, 1670, and 1650 cm^{-1}; *m/e* 324.156 (calcd for $C_{17}H_{24}O_6$, 324.157).

1-Neryl 2,2-dimethyl ethylenetricarboxylate (20) was prepared in 46% yield: NMR ($CDCl_3$) δ 1.62, 1.68, and 1.77 (9 H, 3 s), 2.12 (4 H, m), 3.83 and 3.87 (6 H, 2 s), 4.67 (2 H, bd d, J = 7 Hz), 4.80–5.55 (2 H, m), and 6.87 ppm (1 H, s); IR (neat) 1735, 1728 and 1650 cm^{-1}; *m/e* 324.155 (calcd for $C_{17}H_{24}O_6$, 324.157).

1-(2-Cyclohexen-1-yl) 2,2-dimethyl ethylenetricarboxylate (26) was prepared in 26% yield: NMR ($CDCl_3$) δ 1.0–2.3 (6 H, m), 3.83 and 3.87 (6 H, 2 s), 5.38 (1 H, m), 5.5–6.2 (2 H, m), and 6.93 ppm (1 H, s); IR (neat) 1740, 1722, and 1647 cm^{-1}; *m/e* 268.096 (calcd for $C_{13}H_{16}O_6$, 268.095).

1-(3-Methyl-2-cyclohexen-1-yl) 2,2-dimethyl ethylenetricarboxylate (28) was prepared in 20% yield: NMR ($CDCl_3$) δ 1.5–2.15 (9 H, m), 3.83 and 3.88 (6 H, 2 s), 5.05–5.65 (2 H, m), and 6.92 ppm (1 H, s); IR (neat) 1745, 1723, 1673, and 1644 cm^{-1}; *m/e* 282.111 (calcd for $C_{14}H_{18}O_6$, 282.110).

Allylic Bromoacetates. The procedure for 3-methyl-2-butenyl bromoacetate is typical. A solution of 5 mL (57 mmol) of bromoacetyl bromide in 15 mL of ethyl ether (distilled from sodium-benzophenone) was cooled to −78 °C. A solution of 2.37 g (27.6 mmol) of 3-methyl-2-buten-1-ol and 3.9 mL (28 mmol) of triethylamine (distilled from CaH_2) in 15 mL of dry ethyl ether was slowly added to the bromoacetyl bromide solution. After the addition was complete, the reaction mixture was stirred for 1 h at −78 °C and then allowed to slowly warm to room temperature. The reaction mixture was poured into 75 mL of 10% HCl and 100 mL of ether. The organic phase was separated and washed with 10% $NaHCO_3$ and then brine. The ether was dried with $MgSO_4$. Filtration and removal of the solvent gave the crude bromoacetate in quantitative yield. The product was distilled (64–65 °C, 0.8 Torr) to yield 4.92 g (86%) of pure bromoacetate.

Alkoxycarbonylmethyltriphenylphosphonium Bromide. A General Procedure. To 11 mmol (2.89 g) of triphenylphosphine dissolved in a benzene–hexane mixture (the triphenylphosphine was dissolved in 30–50 mL of benzene and hexane was added till the solution became cloudy) was added 10 mmol of allyl or propargyl bromoacetate. The reaction mixture was stirred overnight. Filtration of the salt gave material (90–100% yield) sufficiently pure to use in the subsequent reaction. The spectral data of the individual compounds are given below.

***tert*-Butyl:** NMR ($CDCl_3$) δ 1.23 (9 H, s), 5.18 (2 H, d, J_{PH} = 14 Hz), and 7.67 ppm (15 H, m); mp 186–186.5 °C. Anal. ($C_{24}H_{26}BrO_2P$) C, H.

***trans*-2-Butenyl:** NMR ($CDCl_3$) δ 1.58 (3 H, bd d, J = 6 Hz), 4.30 (2 H, bd d, J = 6 Hz), 5.30 (2 H, d, J_{PCH} = 14 Hz), 5.0–5.5 (2 H, m), and 7.6 ppm (15 H, m). Anal. ($C_{24}H_{24}BrO_2P$) C, H.

***cis*-2-Butenyl:** NMR ($CDCl_3$) δ 1.56 (3 H, bd d, J = 7 Hz), 4.52 (2 H, bd d, J = 7 Hz), 5.1–5.8 (2 H, m), 5.46 (2 H, d, J_{PCH} = 14 Hz), and 7.8 ppm (15 H, m).

Cinnamyl: NMR ($CDCl_3$) δ 4.60 (2 H, bd d, J = 6 Hz), 5.45 (2 H, d, J_{PCH} = 14 Hz), 5.88 (1 H, d of t, J = 16, 6.2 Hz), 6.51 (1 H, bd d, J = 16 Hz), 7.23 (5 H, s), and 7.5–8.0 ppm (15 H, m).

Dimethyl oxomalonate was prepared by the procedure of Gilman and Johnson.[15] Nitrogen tetroxide (30–40 g) was condensed into a flask containing phosphorus pentoxide and stirred for 1 h. The dried N_2O_4 was then distilled into a flask, cooled with an ice–water bath, containing 30 g (0.22 mol) of distilled dimethyl malonate. The solution was stirred at 5 °C for 5–6 h and at room temperature for 3 days. The excess nitrogen tetroxide was removed by gentle heating. Phosphorus pentoxide and carbon tetrachloride were added and the mixture was heated. The carbon tetrachloride solution was decanted from the P_2O_5 into another flask containing fresh P_2O_5. The original P_2O_5 was washed with additional carbon tetrachloride and the washings were placed with the fresh P_2O_5. This was refluxed for 1–2 h and stirred overnight. The solution was decanted and the P_2O_5 again washed. The CCl_4 was distilled off and the product distilled at 95–97 °C (20 Torr) (lit. bp 195 °C[5]) to yield 29 g (87%) of dimethyl oxomalonate.

1-*tert*-Butyl 2,2-Dimethyl Ethylenetricarboxylate (5). A General Procedure via the Ylide Method.[5] To a solution of 4.00 g (8.75 mmol) of phosphonium salt **3** and 10 drops of phenolphthalein dissolved in 80 mL of water and enough ethanol to dissolve the salt was added 10% NaOH to a phenolphthalein end point. The ylide was extracted into 100 mL of CH_2Cl_2. The organic layer was filtered through K_2CO_3 and the solvent removed. To the ylide (oil) was added 1.27 g (8.71 mmol) of dimethyl oxomalonate dissolved in 50 mL of benzene. After stirring for 1 h the solvent was removed in vacuo and 250 mL of petroleum ether (distilled) was added. The reaction mixture was cooled overnight (freezer). The triphenylphosphine oxide was filtered and washed with petroleum ether. Removal of the petroleum ether yielded 1.93 g (89%) of fairly pure material. This was purified further by column chromatography (10 g of silica gel, eluting with 75/25 petroleum ether–ether), yielding 1.71 g of pure **5**. The triester **5** prepared in this manner was identical by IR and NMR with authentic material.[3]

1-(*trans*-Butenyl) 2,2-dimethyl ethylenetricarboxylate (6) was prepared from 2.25 g (4.95 mmol) of phosphonium salt and 0.81 g (5.0 mmol) of dimethyl oxomalonate. Purification on 10 g of silica gel, eluting with 1:1 petroleum ether–ether, gave a 73% yield of product which was identical with that prepared from *tert*-butyl dimethyl ethylenetricarboxylate.

1-(*cis*-Butenyl) 2,2-dimethyl ethylenetricarboxylate (12) was prepared in 60% yield: IR (neat) 1740, 1725, 1650, 1435, 1260 (bd), 1070 cm^{-1}; NMR (CCl_4) δ 1.71 (3 H, bd d, J = 6 Hz), 3.78 (3 H, s), 3.80 (3 H, s), 4.70 (2 H, bd d, J = 6 Hz), 5.3–5.9 (2 H, m), and 6.78 ppm (1 H, s); *m/e* 242.077 (calcd for $C_{11}H_{14}O_6$, 242.079).

1-Cinnamyl 2,2-dimethyl ethylenetricarboxylate (14) was prepared in 65% yield and purified on silica gel, eluting with 1:1 petroleum ether–ether: IR (neat) 1740 (bd), 1620, 1435, 1260, 1170 cm^{-1}; NMR (CCl_4) δ 3.75 (6 H, s), 4.75 (2 H, bd d, J = 6 Hz), 6.15 (1 H, d of t, J = 16, 6 Hz), 6.63 (1 H, bd d, J = 16 Hz), 6.80 (1 H, s), and 7.2 ppm (5 H, m).

Ene Reaction of *trans*-2-Buten-1-yl Ester (6). Into an NMR tube, rinsed with triethylamine and dried, was added a solution of 0.167 g of butenyl triester **6** in 2.5 mL of benzene-d_6. The reaction mixture was heated (sealed tube) for 210 h at 135 °C. The NMR of the mixture in benzene-d_6 indicated that a 1:1 mixture of **7** and **8** was formed. The methyl of **7** absorbs at δ 0.91 (J = 6 Hz). Upon cooling, **7** crystallized out of solution and filtration yielded 37 mg (22%) of **7** (mp 169–175 °C). Recrystallization from benzene–hexane gave an analytically pure sample (mp 180–181 °C) of **7**. The filtrate was evaporated in vacuo and purified on 9 g of silica gel to yield 60 mg (30%) of pure lactone **8** (mp 119–120 °C). The spectral data for **8** follow: IR ($CHCl_3$) 1780, 1745 cm^{-1}; NMR ($CDCl_3$) δ 3.0–3.7 (3 H, m, H_c, H_d, and H_e) 3.76 (3 H, s), 3.83 (3 H, s), 4.20 (1 H, d of d, J = 9.3, 1 Hz, H_b), 4.46 (1 H, d of d, J = 9.3, 5 Hz, H_a), 5.16 (1 H, d, of d of d, J = 16, 2, 0.5 Hz), 5.20 (1 H, d of d, J = 9, 2 Hz), and 5.73 ppm (1 H, d of d of d, J = 16, 10.5, 9 Hz). Anal. ($C_{11}H_{14}O_6$) C, H. The spectral data for **7** follow: IR ($CHCl_3$) 1785, 1710, and 1620 cm^{-1}; NMR ($CDCl_3$) δ 1.49 (3 H, d, J = 6.2 Hz), 2.34 (1 H, d of d of d of d, J = 1.5, 5.5, 7, and 11 Hz, H_e), 3.75 (3 H, s), 3.83 (1 H, d, J = 7 Hz, H_d), 3.87 (3 H, s), 3.92 (1 H, d of q, J = 11, 6.2 Hz, H_c), 4.10 (1 H, d of d, J = 1.5, 10.1 Hz, H_b), and 4.44 ppm (1 H, d of d, J = 5.5, 10.1 Hz, H_a). Anal. ($C_{11}H_{14}O_6$) C, H.

Reaction of Pyranofuranone 7 with Hydrogen Chloride. Dry hydrogen chloride (by bubbling through H_2SO_4 prior to reaction) was bubbled for several minutes into a methylene chloride (distilled from CaH_2) solution containing 52.4 mg (0.216 mmol) of **7**. After an additional 0.5 h of stirring the reaction mixture was poured into a saturated salt solution and extracted with 50 mL of methylene chloride. The solvent was removed after drying over Na_2SO_4 to yield 52 mg (theory 49 mg) of crystalline **9**. Recrystallization from chloroform–hexane gave an analytical sample (mp 163–165 °C): IR ($CHCl_3$) 1785, 1760, 1745 cm^{-1}; NMR (acetone-d_6) δ 1.43 (3 H, d, J = 6.5 Hz), 2.7–3.1 (1 H, m, H_e), 3.72 (1 H, d of d, J = 10, 10 Hz, H_d), 3.80 (3 H, s), 3.98 (1 H, d, J = 10 Hz, H_f), 4.29 (1 H, d, of d, J = 10, 3 Hz, H_b) 4.64 (1 H, d of d, J = 10, 8 Hz, H_a), 4.72 (1 H, d of q, J = 12, 6.5 Hz, H_c). Anal. ($C_{10}H_{12}O_6$) C, H.

Ene Reaction of *cis*-2-Buten-1-yl 2,2-Dimethyl Ethylenetricarboxylate (12). A solution of 202 mg (0.834 mmol) of *cis*-butenyl triester and 4 μL of pyridine in 1 mL of benzene-d_6 was heated at 137 ± 2 °C for 200 h. A 9:1 mixture of **8** and **13** was present as determined by the absorption of the methyl group of **13** at 0.75 δ (J = 6 Hz) in benzene-d_6. The isomeric **7** absorbs at δ 0.91. The solvent was removed and the product purified on 10 g of silica gel (eluting with 1:1 petroleum ether–ether) to give 87 mg (43%) of pure lactone (**8**). Lactone **8** derived from the *cis*-butenyl triester was identical with that derived from the *trans*-butenyl triester by chromatographic and spectral comparison. The unstable **13** was not isolated.

Diels–Alder Reaction of Cinnamyl 2,2-Dimethyl Ethylenetricarboxylate (14). A solution of 164 mg (0.54 mmol) of cinnamyl triester (**14**) and 4 μL of pyridine in 0.8 mL of benzene-d_6 was heated to 85 °C for 144 h. Crystallization of **15** occurred upon cooling. Filtration of the product yielded 63 mg (38%) of **15**. A portion was recrystallized from benzene for analysis: mp 163.5–164.5 °C; IR ($CHCl_3$) 1785, 1710, 1680, 1620 cm^{-1}; NMR ($CDCl_3$) δ 2.72 (1 H, d of d of d, J = 11.5, 7.0, 5.2 Hz, H_e), 3.80 (3 H, s), 3.82 (3 H, s), 3.96 (1 H, d, J = 7 Hz, H_d), 3.97 (1 H, bd d, J = 10 Hz, H_b), 4.29 (1 H, d of d, J = 10, 5.2 Hz, H_a) 4.70 (1 H, d, J = 11.5 Hz, H_c), 7.5 (5 H, m). Anal. ($C_{16}H_{16}O_6$) C, H.

A solution of 0.176 g of **14** and 3 μL of pyridine in 1.0 mL of benzene-d_6 was degassed and sealed in an NMR tube. The solution was allowed to reach equilibrium at various temperatures as determined by examination of the NMR spectrum. The temperatures, ratio of **15**/**14**, and time to reach equilibrium are 90 °C, 0.47, 72 h; 102 °C, 0.26, 48 h; 113 °C, 0.14, 24 h; 122 °C, 0.099, 24 h. This gives ΔH = −14.3 ± 1 kcal/mol and ΔS = −41 ± 1 eu.

Ene Reaction of 3-Methyl-2-buten-1-yl Ester 16. Triester **16** (71 mg, 0.28 mmol) was heated for 30 h at 120 °C. Chromatography of the crude product on 3 g of silica gel using 9:1 benzene–ether as eluant

gave 69 mg (97%) of **18** as a ca. 1:1 mixture of diastereomers: NMR ($CDCl_3$) δ 1.70, 1.76 (3 H, 2 bd s), 3.1-4.1 (9 H, m), 4.4-4.6 (2 H, m), and 4.80 and 4.93 (2 H, 2 s); IR (neat) 1775, 1753, 1737, 1645, and 910 cm^{-1}.

In the manner described 98 mg (0.38 mmol) of prenyl triester **16** was heated for 112 h at 85 °C. A 70:30 mixture of **18** and **17** was present as determined by examination of the NMR spectrum in benzene-d_6. The allylic methyls of **18** were compared to the methyl singlets of **17** at δ 0.86 and 0.91. Cooling the reaction mixture caused 8 mg (8%) of pyranofuranone **17** to crystallize. Recrystallization from benzene-hexane give pure **17,** mp 141-142 °C. The filtrate was concentrated and dissolved in 2 mL of methylene chloride. Treatment of this solution with dry HCl as described previously yielded (after chromatography on 10 g of silica gel eluting with ether) 60 mg (61%) of ene adduct **18** and 7 mg (8%) of bislactone **19.** The spectral data for pyranofuranone **17** follow: IR (CH_2Cl_2) 1785, 1710, 1680, 1615 cm^{-1}; NMR ($CDCl_3$) δ 1.28 (3 H, s), 1.47 (3 H, s), 2.64 (1 H, d of d of d, J = 8, 6.7, 4 Hz, H_d), 3.78 (3 H, s), 3.82 (3 H, s), 3.82 (1 H, d, J = 8 Hz, H_c), 4.08 (1 H, d of d, J = 10, 4 Hz, H_b), and 4.42 ppm (1 H, d of d, J = 10. 6.7 Hz, H_a). Anal. ($C_{12}H_{16}O_6$) C, H. The spectral data for bislactone **19** follow: IR ($CHCl_3$) 1785, 1750, 1740 cm^{-1}; NMR ($CDCl_3$) δ 1.38 (3 H, s), 1.51 (3 H, s), 2.7-3.1 (1 H, m), 3.76 (2 H, bd s), 3.91 (3 H, s), 4.21 (1 H, d of d, J = 11, 2 Hz), and 4.54 ppm (1 H, d of d, J = 11, 7 Hz).

The ene reaction of neryl ester (20) was carried out in a manner similar to the ene reaction of the geranyl triester. A solution of 0.222 g of neryl triester **20,** 9 μL of pyridine, and 1 mL of benzene-d_6 yielded 0.23 g of crude product. The NMR shows ca. 10% of **23** as determined by the methyl absorption at δ 0.92 in benzene-d_6. Purification (8 g of silica gel eluting with 1:1 ether-petroleum ether) gave 0.155 g (70%) of a 3:2 mixture of **21:22:** IR (neat) 1780, 1755, 1745 cm^{-1}; NMR (benzene-d_6) δ 1.32 (0.4 × 3 H, s, CH_3 of **22**), 1.50 and 1.60 (6 H, 2 bd s, $CH{=}C(CH_3)_2$), 1.6-2.2 (0.6 × 4 H, m, CH_2 of **21**), 2.48 (0.4 × 2 H, bd t, J = 6.5 Hz, CH_2 of **22**) 3.0-4.1 (5 H, m), 3.34, 3.36, 3.38, 3.57 (6 H, 4 s), 4.74 (0.6 × 2 H, bd s, $=CH_2$ of **21**), 5.06 (1.4 H, m, =CH); mass spectrum *m/e* 324 (M^+), 292, 261, 193. The NMR was examined in benzene since this led to better separation of the resonances due to **21** and **22.** Anal. ($C_{17}H_{24}O_6$) C, H.

Ene Reaction of Geranyl Ester (24). A solution of 0.309 g of geranyl triester **24,** 8 μL of pyridine, and 1 mL of benzene-d_6 was placed in an NMR tube and sealed. The reaction mixture was heated at 125 °C for 6 h, at which time no more starting material could be seen by NMR. The NMR showed ca. 10% of **25** as determined by the methyl absorption of δ 0.90 in benzene-d_6. Removal of the solvent gave 0.33 g of crude product. A 2:3 mixture of **21** and **22** (205 mg, 66%) was obtained by chromatography on 8 g of silica gel eluting with 1:1 ether-petroleum ether: IR (neat) 1780, 1755, 1745 cm^{-1}; NMR (benzene-d_6) δ 1.31 (0.6 × 3 H, bd s, CH_3 of **22**), 1.50 and 1.60 (6 H, 2 s, $C{=}C(CH_3)_2$), 1.7-2.1 (0.4 × 4 H, m, CH_2 of **21**), 2.3-2.8 (0.60 × 2 H, m, CH_2 of **22**), 3.0-4.0 (5 H, m), 3.33, 3.36, 3.39, and 3.57 (6 H, 4 s), 4.74 (0.4 × 2 H, bd, s, $=CH_2$ of **21**), 5.06 (1.6 × 1 H, m, C=CH); mass spectrum *m/e* 324 (M^+) 292, 261, 193. The NMR was examined in benzene since this led to better separation of resonances due to **21** and **22.**

Ene Reaction of 3-Methyl-2-cyclohexen-1-yl Triester (28). A solution of 67 mg of 3-methyl-2-cyclohexenyl triester **28,** 2 μL of pyridine, and 0.5 mL of benzene-d_6 was heated at 95-110 °C (sealed tube) for 40 h. The NMR spectrum showed a small amount of Diels-Alder adduct as determined by the absorption at δ 0.83 in benzene-d_6. Purification of the crude product on 10 g of silica gel, eluting with 1:1 ether-petroleum ether, gave 30 mg (45%) of pure **29** which appeared to be a mixture of isomers since four methyl peaks were observed in the NMR: IR (neat) 1775, 1755, 1740 cm^{-1}; NMR ($CDCl_3$) δ 1.1-2.4 (7 H, m), 3.2-3.9 (3 H, m), 3.74, 3.75 (sh on 3.76), 3.76, 3.83 (6 H, 4 s), 4.6-5.0 ppm (3 H, m); *m/e* 282.119 (calcd for $C_{14}H_{18}O_6$, 282.110).

Attempted Ene Reaction of *cis*-3-Hexenyl Ester 30. In a heavy-walled, resealable tube washed with 10 μL of pyridine was placed 111 mg of *cis*-3-hexenyl triester dissolved in 10 mL of toluene. After heating for 60 h at 220 °C, thin layer chromatography showed no starting material but several new spots.

Attempted Ene Reaction of 2-Cyclohexenyl Ester 26. In a heavy-walled resealable tube were heated 146 mg of triester, 10 μL of pyridine, and 10 mL of toluene. After heating for 36 h at 220 °C, the starting material was gone (as indicated by TLC). Removal of the solvent in vacuo gave a brown oil whose NMR had no vinyl protons.

Attempted Ene Reaction of 2-Cyclohepten-1-yl Ester 27. A solution of 0.134 g of **27** and 0.5 mL of benzene-d_6 was heated in a sealed NMR tube (washed with pyridine and dried) for 64 h at 135 °C. Thin layer chromatography showed 12 spots (50/50 ether-petroleum ether) from R_f 0.0 to 0.8.

Attempted Ene Reaction of 1-Cyclohexenyl Methyl Ester 31. A solution of 163 mg of triester and 0.5 mL of benzene-d_6 was heated in a sealed NMR tube (washed with pyridine and dried) at 120 °C for 48 h and 175 °C for 96 h. Thin layer chromatography showed several spots.

Ene Reaction of *tert*-Butyl 2,2-Dimethyl Ethylenetricarboxylate (5) with β-Pinene. A solution of 90 mg (0.66 mmol) of β-pinene and 0.154 g (0.63 mmol) of **5** in 1.5 mL of benzene-d_6 was heated to 150 °C for 40 h. The solvent was removed and the product purified on 9 g of silica gel eluting with 9:1 petroleum ether-ether to yield 0.110 g (46%) of pure ene adduct: IR (neat) 2980, 2960, 2920, 1755, 1740, 1255, 1150 cm^{-1}; NMR (CCl_4) δ 0.80 and 0.83 (0.5 + 0.5 × 3 H, 2 s), 1.12 (1 H, bd d, J = 8 Hz), 1.25 (3 H, s), 1.33 (9 H, s), 1.7-2.5 (7 H, m), 2.6-3.2 (1 H, m), 3.48 (0.5 H, J = 9 Hz) and 3.66 (0.5 H, J = 8 Hz), 3.63 (6 H, s), 5.1 (1 H, m). Anal. ($C_{21}H_{32}O_6$) C, H.

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