On the Diels-Alder reactions of pentadienyl maleates and citraconates[†]

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1. General Experimental Details

NMR spectra were recorded at 300K using a Bruker DPX/DRX 400 MHz or a Jeol JNM-GX270W spectrometer. Residual chloroform (δ 7.26), methanol (δ 3.31) and toluene (δ 2.09) were used as internal references for ¹H NMR spectra measured in these solvents. Residual chloroform (δ 77.1), and methanol (δ 49.0) were used as internal references for ¹³C NMR spectra. Assignment of proton signals was assisted by ¹H-¹H COSY, 1D-nOe and NOESY experiments when necessary; assignment of carbon signals was assisted by DEPT experiments. IR spectra were recorded on a Perkin-Elmer 1600 or Perkin-Elmer Paragon 1000 F.T.I.R. spectrometer as neat films on NaCl plates or as KBr pellets for solid products. Mass spectra were recorded by the Mass Spectrometer Facility of the Research School of Chemistry, Australian National University, Canberra. Electron Impact (EI) was carried out at 70 eV unless stated otherwise and Chemical Ionisation (CI) was accomplished at 40 eV and 70 eV with ammonia gas. Optical rotations were measured with an Optical Activity Limited AA-100 polarimeter. Microanalyses were performed at the Campbell Microanalytical Laboratory at the Department of Chemistry, University of Otago, New Zealand. Melting points were measured on a Reichert melting point stage and are uncorrected. HPLC was performed using a Waters 510EF chromatograph pump and Waters U6K injector monitored by an ISCO 226 UV spectrophotometer at $\lambda = 254$ nm and a Waters R403 refractive index detector. GC measurements were recorded on a Hewlett Packard 5890A gas chromatograph with a split/splitless capillary inlet and FID detector. GC data was processed using Hewlett Packard ChemStation software.

Reactions were conducted under a positive pressure of dry argon or nitrogen in flame-dried glassware. Solvents were dried and purified according to the methods of Perrin and Amarego.¹ Diethyl ether, toluene, THF and xylene were dried over sodium wire and distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Other commercial reagents were used as purchased. Analytical TLC was performed with Merck silica gel plates, precoated with silica gel 60 F254 (0.2 mm). Flash chromatography employed Merck Kiesegel 60 (230-400 mesh) silica gel. Hexane and ethyl acetate (distilled from laboratory grade solvents) were the principal eluents, although diethyl ether, dichloromethane, methanol and acetic acid (analytical grades) were also used when required.

2. Synthesis of Maleate Half Ester IMDA Precursors (Table 1, Structure 3)

Compounds **3a–h** were prepared from the eight dienols depicted in Fig. 3 by reaction with maleic anhydride, as illustrated in the Scheme associated with Table 1.

(2*E*)-Penta-2,4-dien-1-yl hydrogen maleate (3a):

Triethylamine (823 mg, 8.13 mmol), maleic anhydride (1.121 g, 11.4 mmol) and DMAP (62 mg, 0.51 mmol) were added to a stirred solution of (2*E*)-penta-2,4-dien-1-ol 1^2 (427 mg, 5.08 mmol) in dichloromethane (24 mL) at 0 °C. The mixture was stirred at this temperature for 10 min. The solution was allowed to warm to room temperature before being diluted with diethyl ether (100 mL). The mixture was washed with 2M HCl (50 mL), water (50 mL), saturated brine (50 mL), dried (NaSO₄) and concentrated *in vacuo*. The crude product was passed through a silica plug (hexanes/ethyl acetate/methanol/acetic acid 20:20:1:1) to give triene **3a** (775 mg, 4.26 mmol, 84%) as a clear yellow oil. $R_f = 0.37$ (hexanes/ethyl acetate/methanol/acetic acid 20:20:1:1). IR (neat): 3500–2600 (broad), 3046, 1730, 1714, 1644, 1633 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.40–6.28 (m, 4H), 5.78 (m, 1H), 5.33–5.24 (m, 1H), 5.18 (m, 1H), 4.76 (d, *J* = 6.5 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 167.0, 166.5, 136.2, 135.5, 133.1, 130.3, 125.3, 119.6, 66.4. EIMS *m/z* (%): 182 (M⁺, 10), 83 (100). HRMS: calcd for C₉H₁₀O₄ [M]⁺: 182.0579; found: 182.0581.

(2E,4E)-2,4-Hexadien-1-yl hydrogen maleate (3b)



Compound **3b** was prepared from commercially available (2*E*,4*E*)-2,4-hexadien-1-ol **7** in 88% isolated yield (880 mg scale) using the procedure described above for **3a**. Acid half-ester **3b** was obtained as a pale yellow oil. $R_f = 0.49$ (hexanes/ethyl acetate/acetic

acid/methanol 20:20:1:1). IR (neat): 3153, 3025, 2963, 2691, 1735, 1636 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 6.35 (d, J = 0.4 Hz, 2H), 6.34-6.21 (m, 1H), 6.10–5.98 (m, 1H), 5.86–5.21 (m, 2H), 4.71 (d, J = 6.8 Hz, 2H), 1.75 (d, J = 6.6 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 166.5, 166.3, 136.3, 133.0, 132.0, 130.0, 129.9, 121.7, 66.9, 18.1. EIMS m/z (%): 196 (M⁺, 7), 97 (100). HRMS: calcd for C₁₀H₁₂O₄ [M]⁺: 196.0736; found: 196.0738.

(2E,4E)-6-Methylhepta-2,4-dien-1-yl hydrogen maleate (3c)

Compound 3c was prepared from (E,E)-6-methylhepta-2,4-dienol 12³ in 96% isolated yield (1.0 g scale) using the procedure described above for 3a. Acid half-ester 3c was с́о₂н obtained as a clear yellow oil. $R_{f} = 0.45$ (hexanes/ethyl acetate/methanol/acetic acid 3c 20:20:1:1). IR (neat): 3600–2300 (broad), 2961, 1732, 1714, 1649, 1636 cm⁻¹. ¹H NMR (400 MHz, $CDCl_3$): δ 11.4 (broad s, 1H), 6.41–6.33 (m, 2H), 6.30 (dd, J = 15.2, 10.5 Hz, 1H), 6.00 (dd, J = 15.2, 10.2 Hz, 1H), 5.76 (dd, J = 15.3, 6.7 Hz, 1H), 5.65 (ddd, J = 15.3, 6.9, 6.9 Hz, 1H), 4.74 (d, J = 7.0 Hz, 2H), 2.34 (d sept, J = 6.7, 6.7 Hz, 1H), 0.99 (d, J = 6.7 Hz, 6H). ¹³C NMR (100 MHz, CDCl₂): δ 167.0, 166.0, 144.9, 137.1, 137.1, 134.5, 130.0, 125.8, 122.0, 67.3, 31.1, 22.1. EIMS m/z (%): 224 (M⁺, 5), 93 (100). HRMS: calcd for C₁₂H₁₆O₄ [M]⁺: 224.1049; found: 224.1047.

(2E,4E)-5-Benzovloxy-penta-2,4-dien-1-vl hvdrogen maleate (3d)



Triene **3d** was prepared from 1-(benzoyloxy)-5-hydroxy-1E,3E-pentadiene: 12^4 in 61% isolated yield (780 mg scale) using the procedure described above for 3a. The acid half-ester **3d** was obtained as a colourless oil. $R_f = 0.30$ (hexanes/ethyl acetate/methanol/acetic acid 20:20:1:1). IR (neat): 3079, 3027, 2952, 1732, 1714, 1664, 1645, 1632 cm^{-1} . ¹H NMR (270 MHz, CDCl₂): δ 10.42 (broad s, 1H), 8.10–8.07 (m, 2H), 7.69 (d, J = 12.1 Hz, 1H), 7.61 (tt, J = 7.3, 2.0 Hz, 1H), 7.50–7.45 (m, 2H), 7.04–6.33 (m, 3H), 6.22 (t, J = 11.5 Hz, 1H), 5.81 (dt, J = 14.8, 6.8 Hz, 1H), 4.79 (d, J = 6.8 Hz, 2H). ¹³C NMR (68 MHz, CDCl₃): δ 165.5, 164.7, 163.1, 139.7, 133.7, 129.9, 129.8, 129.8, 129.6, 129.6, 128.5, 125.7, 115.0, 65.0, 52.0. EIMS m/z (%): 302 (M^+ , 2), 105 (100). HRMS: calcd for $C_{16}H_{14}O_6$ [M]⁺: 302.0790; found: 302.0780.

(2E,4E)-5-Carbomethoxypenta-2,4-dien-1-yl hydrogen maleate (3e)



Triene **3e** was prepared from methyl (2E,4E)-6-hydroxy-2,4-hexadienoate **14⁵** in 92% isolated yield (60 mg scale) using the procedure described above for **3a**. The

acid half-ester **3e** was obtained as a colourless solid. $R_f = 0.29$ (hexanes/ethyl acetate/methanol/acetic acid 10:30:1:1). IR (neat): 3300-2700 (broad), 1716, 1650, 1621 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 10.40 (broad s, 1H), 7.28 (dd, J = 15.4, 11.0 Hz, 1H), 6.45 (dd, J = 15.4, 11.3 Hz, 1H), 6.40 (m, 2H), 6.16 (ddd, J = 15.2, 5.9, 5.9 Hz, 1H), 5.96 (d, J = 15.4 Hz, 1H), 4.84 (d, J = 15.4 Hz, 1Hz, 1H), = 6.1 Hz, 2H), 3.76 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 167.2, 166.7, 166.2, 143.0, 133.6, 133.2,

131.8, 129.9, 122.8, 65.5, 51.8. EIMS m/z (%): 240 (M⁺, 3), 99 (100). HRMS: calcd for C₁₁H₁₂O₆ [M]⁺: 240.0634; found: 240.0626.

Hydrogen (±)-(1S,2E)-1-methylpenta-2,4-dien-1-yl maleate (3f)



Triene **3f** was prepared from methyl hexa-3,5-dien-2-ol **15**⁸ in 58% isolated yield (300 mg scale) using the procedure described above for **3a**. The acid half-ester **3f** was obtained as a colourless oil. $R_f = 0.49$ (hexanes/ethyl acetate/methanol/acetic acid 20:20:1:1). IR (neat): 3400–2200 (broad), 1732, 1714 (C=O), 1633 (C=C) cm⁻¹. ¹H NMR (400 MHz, CDCl₃):

= 10.8 (1H, broad s), 6.42–6.23 (3H, m), 5.67 (1H, dd, J = 14.4, 7.1 Hz), 5.51 (1H, dq, J = 6.6, 0.5 Hz), 5.32–5.23 (1H, m), 5.16 (1H, m), 1.40 (3H, d, J = 6.6 Hz). ¹³C NMR (100 MHz, CDCl₃): = 166.4 (C), 166.2 (C), 135.7 (CH), 134.1 (CH), 133.7 (CH), 130.9 (CH), 130.5 (CH), 119.5 (CH), 73.4 (CH), 19.9 (CH). EIMS (70 eV) m/z (%): 196 ([M]⁺, 1), 178 ([M–H₂O]⁺, 3), 150 ([M–CH₂O₂]⁺, 25), 97 ([M–C₆H₉O]⁺, 35), 79 ([M–C₄H₅O₄]⁺, 100). HRMS: calcd for C₁₂H₁₆O₄ [M]⁺: 196.0736; found: 196.0736.

(2S,3S,4*E*,6*E*)-1,2-*O*-Isopropylidene-8-*tert*-butyldimethylsilyloxy-1,2-dihydroxyl-4,6-octadien-3-yl hydrogen (2*Z*)-2-butenedioate (3g)



Triene **3g** was prepared from (2R,3S,4E,6E)-1,2-*O*-isopropylidene-8-(tertbutyldimethylsilyloxy-6,6-octadiene-1,2,3-triol **16**⁶ in 88% isolated yield (758 mg scale) using the procedure described above for **3a**. The acid half-ester **3g** was obtained as an unstable pale yellow oil. $R_f = 0.49$. ¹H NMR /ppm 6.51–6.14 (4H, m, H5, H6, -RO₂CC*H*C*H*CO₂H), 5.90 (1H, dt, J = 14.8, 4.6 Hz, H7), 5.67–5.58

(1H, m, H4), 5.51 (1H, dd, J = 8.0, 4.1 Hz, H3), 4.31 (1H, td, J = 6.3, 4.1 Hz, H2), 4.24 (2H, dm, J = 4.6 Hz, 2 × H8), 4.09 (1H, dd, J = 8.5, 6.6 Hz, H1_a), 3.85 (1H, dd, J = 8.5, 6.1 Hz, H1_β), 1.41, 1.37 (6H, 2 × s, -C(CH₃)₂), 0.92 (9H, s, -SiC(CH₃)₃), 0.08 (6H, s, -Si(CH₃)₂-).

(2*E*,4*E*,6*S*,7*S*)-7,8-*O*-Isopropylidene-6-((*tert*-butyldimethylsilyl)oxy)-7,8-dihydroxy-2,4-octadien-1-yl hydrogen maleate (3h)



Triene **3h** was prepared from (2S,3S,4E,6E)-1,2-O-isopropylidene-3-((tert-

butyldimethylsilyl)oxy)-4,6-octadien-1,2,8-triol 17⁷ in 99% isolated yield (630 mg scale) using the

procedure described above for **3a**. The acid half-ester **3h** was obtained as as a pale yellow oil: $[\alpha]_D^{18} = -39.4^\circ$ (c = 0.62, dichloromethane); $R_f = 0.46$ (ethyl acetate:hexane:acetic acid (200:50:1)); (Found: M^+ , 426.2043, . $C_{21}H_{34}O_7Si$ requires *M*, 426.2074); IR (film): 3175, 2986, 2955, 2930, 2889, 2857, 1732, 1714, 1642, 1472, 1462, 1413, 1382, 1372 and 1256 cm⁻¹; _H (270 MHz, CDCl₃) 0.057 and 0.077 (6H, $2 \times s, -Si(CH_3)_2-$), 0.902 (9H, s, $-C(CH_3)_3$), 1.34 and 1.40 (6H, $2 \times s, -C(CH_3)_2-$), 3.79 (1H, dd, *J* 6.0, 8.6 Hz, C8-*H*), 3.95 (1H, dd, *J* 6.6, 8.6 Hz, C8-*H*), 4.05–4.16 (1H, m, C7-*H*), 4.32 (1H, t, *J* 5.6 Hz, C6-*H*), 4.80 (2H, d, *J* 7.0 Hz, C1-*H*), 5.71-5.86 (2H, m, C2-*H* and C5-*H*) 6.20–6.52 (2H, m, C3-*H* and C4-*H*) and 6.39 and 6.46 (2H, $2 \times d$, B and A of AB, J_{AB} 12.5 Hz, $-CH=CHCO_2H$); _C (68.1 MHz, CDCl₃) –4.73, –4.51, 18.3, 25.1, 25.9, 26.4, 65.1, 67.0, 72.9, 78.4, 109.4, 124.1, 129.0, 129.8, 134.4, 135.6, 136.1, 164.1 and 167.2; *m*/*z* (EI, 70 eV) 426 (0.1%), 227 (24), 210 (44), 101 (100), 75 (69) and 43 (27).

3. "Mix and Heat" Reactions Between Dienols and Maleic Anhydride (Table 1)

"Mix and Heat" Procedure for Dienol 1



Maleic anhydride (291 mg, 2.97 mmol) and BHT (66 mg, 0.30 mmol) were added to a stirred solution of 1^8 (249 mg, 2.97 mmol) in toluene (6 mL) at RT. The

reaction mixture was stirred at 110 °C for 2 h. The solution was cooled to -78 °C and an ethereal solution of diazomethane¹² was added drop wise until tlc confirmed that the reaction had proceeded to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was warmed to room temperature, concentrated *in vacuo*, a portion of the residue was dissolved in CDCl₃ and ¹H NMR analysis revealed an *exo:endo* adduct ratio of 3:97. The residue was chromatographed on silica (hexanes/ethyl acetate 7:3) to give cycloadduct **20a**⁹ (12.6 mg, 0.0642 mmol, 2%) followed by cycloadduct **19a**⁹ (315 mg, 1.61 mmol, 54%).



According to the general procedure detailed for dienol **1**, from (2E,4E)-2,4-hexadien-1-ol (103 mg, 1.05 mmol), maleic anhydride (103 mg, 1.05 mmol)

and BHT (44 mg, 0.20 mmol) in toluene (2 mL) at 110 °C for 70 min was obtained, after chromatography on silica (hexanes:ethyl acetate 5:1 then 2:1), 20b (7.9 mg, 0.038 mmol, 4%) and 19b (190 mg, 0.904 mmol, 86%). rel-Methyl (3aR,4S,5R,7aS)-5-methyl-3-oxo-1,3,3a,4,5,7ahexahydro-4-isobenzofurancarboxylate (20b): Colourless oil; $R_f = 0.23$ (hexane:ethyl acetate (5:1)); (Found: M⁺, 210.0891. C₁₁H₁₄O₄ requires M, 210.0892); IR (film): 3026, 2959, 2901, 1782, 1732, 1437, 1326, 1312 and 1216 cm⁻¹; $\delta_{\rm H}$ (270 MHz, CDCl₃) 1.18 (3H, d, J 7.3 Hz, C5-CH₃), 2.35 (1H, dd, J 3.6, 13.5 Hz, C3a-H), 2.87–2.99 (1H, m, C5-H), 2.96 (1H, d, J 3.6 Hz, C4-H), 3.11–3.27 (1H, m, C7a-H), 3.69 (3H, s, -CO₂CH₃), 3.87 (1H, dd, J 7.9, 11.4 Hz, C1-H), 4.51 (1H, dd, J 7.3, 7.9 Hz, C1-*H*), 5.65 (1H, dt, *J* 10.0, 3.3 Hz, C6-*H*) and 5.72 (1H, dt, *J* 10.0, 1.9 Hz, C7-*H*); $\delta_{\rm C}$ (68.1 MHz, CDCl₂) 22.0, 34.1, 36.4, 41.5, 42.7, 52.1, 70.6, 123.0, 134.5, 172.1 and 174.6; m/z (EI, 70 eV) 210 (0.5%), 179 (13), 105 (100), 91 (61) and 77 (20). rel-Methyl (3aS,4R,5R,7aS)-5-methyl-3-oxo-1,3,3a,4,5,7a-hexahydro-4-isobenzofurancarboxylate (19b): Colourless oil; $R_f = 0.13$ (hexane:ethyl acetate (2:1)); (Found: M^+ , 210.0893. C₁₁H₁₄O₄ requires M, 210.0892); IR (film): 3022, 2953, 2913, 1770, 1732 1435 and 1212 cm⁻¹; $\delta_{\rm H}$ (270 MHz, CDCl₃) 1.16 (3H, d, J 7.5 Hz, C5-CH₃), 2.62-2.77 (1H, m, C5-H), 3.09 (1H, t, J 5.3 Hz, C4-H), 3.14-3.26 (1H, m, C7a-H), 3.33 (1H, dd, J 5.3, 9.7 Hz, C3a-H), 3.75 (3H, s, -CO₂CH₃), 4.17 (1H, dd, J 4.4, 8.6 Hz, C1-H), 4.44 (1H, dd, J 7.8, 8.6 Hz, C1-*H*), 5.60 (1H, dt, *J* 10.1, 2.4 Hz, C7-*H*) and 5.82 (1H, ddd, *J* 2.4, 4.0, 10.1 Hz, C6-*H*); δ_{C} (68.1 MHz, CDCl₂) 17.8, 30.3, 35.3, 38.6, 42.1, 51.8, 71.4, 124.3, 133.9, 171.7 and 177.0; *m/z* (EI, 70 eV) 210 (19%), 178 (59), 150 (55), 105 (56) and 93 (100).

"Mix and Heat" Procedure for Dienol 12



According to the general procedure detailed for dienol 1, (E,E)-6-methylhepta-2,4-dienol 12³ (502 mg, 3.98 mmol), maleic anhydride (390 mg, 3.98 mmol) and BHT (88 mg, 0.40 mmol) in toluene (7.6 mL) was allowed to react at 110 °C for 100 min. After allowing the mixture to cool to RT, a portion was concentrated in vacuo, dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained acids 6c:5c:5c' (14:79:7) as a yellow oil. Following diazomethane treatment, the yellow oil contained methyl esters **20c**¹⁰:**19c**¹⁰:**19c**¹ (11:78:11) according to ¹H NMR analysis. This mixture was chromatographed on silica (hexanes/ethyl acetate 7:3) to give cycloadduct $20c^{10}$ (104 mg, 0.438 mmol, 11%), followed by cycloadduct $19c^{10}$ (659 mg, 2.76 mmol, 69%), and finally cycloadduct 19c' (75.6 mg, 0.317 mmol, 8%). Methyl (1S,5R,6Z,8S,9R)-8-iso-propyl-3-oxa-4-oxo-bicyclo[3.3.1]non-6ene-9-carboxylate (19c'): white crystalline solid after recrystallisation from hexanes/ethyl acetate 90:10. R_f = 0.26 (hexanes/ethyl acetate 70:30). mp 82–84 °C. IR (KBr): 3043, 2956 (C–H), 1731 $(C=O) \text{ cm}^{-1}$. ¹H NMR (400 MHz, CDCl₃): $\delta = 5.99 (1H, m)$, 5.80 (1H, ddd, J = 9.8, 5.8, 2.8 Hz), 4.23 (1H, dd, J = 11.4, 3.3 Hz), 4.06 (1H, ddd, J = 11.4, 1.3, 1.3 Hz), 3.72 (3H, s), 3.34-3.30 (1H, m), 2.78(1H, m), 2.10 (1H, m), 1.60 (1H, d sept, J = 9.6, 6.5 Hz), 1.12 (3H, d, J = 6.5 Hz), 0.96 (3H, d, J = 6.6 Hz)Hz). ¹³C NMR (100 MHz, CDCl₃): $\delta = 172.7$ (C), 169.2 (C), 131.1 (CH), 126.5, 69.3 (CH₂), 52.4 (CH₃), 48.5 (CH), 44.1 (CH), 39.8 (CH), 31.3 (CH), 29.1 (CH), 21.7 (CH₃), 20.6 (CH₃). EIMS (70 eV) m/z_{1} (%): 238 ([M]⁺, 25), 207 ([M-CH₂O]⁺, 10), 196 ([M-C₂H₆]⁺, 65), 180 ([M-C₂H₂O₂]⁺, 40), 138 ([M–C₅H₈O₂]⁺, 100). HRMS: calcd for C₁₃H₁₈O₄ [M]⁺: 238.1205; found: 238.1205. Anal. Calcd for C₁₃H₁₈O₄: C 65.53, H 7.61; found C 65.58, H 7.59.

"Mix and Heat" Procedure for Dienol 13



Maleic anhydride (152 mg, 1.55 mmol) and BHT (34 mg, 0.16 mmol) were

added to a stirred solution of 1-(benzoyloxy)-5-hydroxy-1*E*,3*E*-pentadiene 13^4 (316 mg, 1.55 mmol) in toluene (3 mL) at RT. The reaction mixture was stirred at 110 °C for 120 min. ¹H NMR analysis revealed a 1:99 mixture of *exo:endo* adducts. After diazomethane treatment, ¹H NMR analysis of the yellow oil revealed a 1:99 *exo:endo* mixture. The residue was chromatographed on silica (hexanes/ethyl acetate 1:1) to give cycloadduct **20d** (2.2 mg, 0.007 mmol, 0.5%), followed by cycloadduct **19d** (171

mg, 0.540 mmol, 35%). (±)-Methyl (3aS,6R,7S,7aR)-6-benzoyloxy-1-oxo-3,3a,6,7,7a-hexahydro-**7-isobenzofurancarboxylate** (20d): colourless oil. $R_f = 0.43$ (hexanes/ethyl acetate 1:1). IR (neat): 3060, 2987, 2954, 2916, 1781, 1739, 1714 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.01 (m, 2H), 7.58 (m, 1H), 7.44 (m, 2H), 6.21–6.16 (m, 1H), 6.02 (m, 1H), 6.00 (m, 1H), 4.58 (dd, J = 7.8, 7.8 Hz, 1H), 3.98 (dd, J = 11.5, 8.2 Hz, 1H), 3.76 (s, 3H), 3.57 (d, J = 3.2 Hz, 1H), 3.23 (m, 1H), 2.75 (dd, J = 13.8), 3.98 (dd, J = 11.5, 8.2 Hz, 1H), 3.76 (s, 3H), 3.57 (d, J = 3.2 Hz, 1H), 3.23 (m, 1H), 3.75 (dd, J = 13.8), 3.98 (dd, J = 13.8), 33.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 173.6, 169.3, 165.3, 133.5, 129.9, 129.7, 129.4, 128.5, 127.5, 70.1, 69.1, 52.7, 43.2, 41.3, 36.5. EIMS m/z (%): 316 (M⁺, 1%), 105 (100). Anal. calcd for C₁₇H₁₆O₆: C 64.55, H 5.10; found C 64.84, H 5.26. (±)-Methyl (3aS,6R,7R,7aS)-6-benzoyloxy-1oxo-3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylate (19d): white crystaline solid after recrystallisation from hexanes/ethyl acetate 70:30. $R_f = 0.13$ (hexanes/ethyl acetate 1:1). mp 174–175 °C. IR (KBr): 3060, 2987, 2954, 2916, 1781, 1739, 1714, 1601 cm⁻¹. ¹H NMR (270 MHz, $CDCl_{2}$: δ 8.09–8.07 (m, 2H), 7.53 (tt, J = 7.3, 1.5 Hz, 1H), 7.46–7.40 (m, 2H), 6.27 (ddd, J = 10.1, 10.15.3, 1.8 Hz, 1H), 5.94–5.90 (m, 2H), 4.46 (dd, J = 9.2, 7.3 Hz, 1H), 4.19 (dd, J = 9.2, 1.3 Hz, 1H), 3.74 (s, 3H), 3.68 (dd, J = 8.6, 5.1 Hz, 1H), 3.37–3.32 (m, 1H), 3.19 (t, J = 4.2 Hz, 1H). ¹³C NMR (68) MHz, CDCl₃): δ 174.7, 169.2, 166.0, 132.9, 131.1, 130.0, 129.6, 128.3, 127.0, 70.2, 63.5, 52.3, 41.4, 36.4, 36.2. EIMS *m/z* (%): 316 (M⁺, 1%), 105 (100). Anal. calcd for C₁₇H₁₆O₆: C 64.55, H 5.10; found C 64.79, H 5.15.

"Mix and Heat" Procedure for TBS-protected Methyl (2*E*,4*E*)-6-Hydroxy-2,4-hexadienoate (14)



Imidazole (96 mg, 0.68 mmol, 2.0 equiv), *tert*-butyldimethylsilyl chloride (76 mg, 0.51 mmol, 1.5 equiv), and DMAP (7.6 mg, 0.068 mmol, 0.2 equiv) were added to a solution of methyl (2*E*,4*E*)-6-hydroxy-2,4-hexadienoate (**14**)⁵ (48 mg, 0.34 mmol, 1.0 equiv) stirred in dichloromethane (1.5 mL) at RT under Ar. The reaction mixture was stirred for 75 min before being diluted into ethyl acetate (10 mL). The solution was washed with 2M HCl (2 × 10 mL), brine (2 × 10 mL), dried (Na₂SO₄) and concentrated *in vacuo* to give TBS-protected methyl (2*E*,4*E*)-6-hydroxy-2,4-hexadienoate. TBS-

Protected methyl (2*E*,4*E*)-6-hydroxy-2,4-hexadienoate, maleic anhydride (33 mg, 0.34 mmol, 1.0 equiv) and BHT (7.4 mg, 0.034 mmol, 0.1 equiv) were stirred in toluene (0.7 mL) at 110 °C for 11 h. The reaction mixture was cooled to RT before being concentrated *in vacuo*. The concentrated mixture was diluted in dichloromethane (0.5 mL) and stirred at 0 °C under Ar. Trifluoroacetic acid (385 mg, 3.38 mmol, 10.0 equiv) was added and the mixture was stirred at RT for 2 h. The mixture was concentrated *in vacuo* and diluted with diethyl ether (0.5 mL). The solution was cooled to -78 °C and an ethereal solution of diazomethane was added drop wise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo* and a portion of the residue was dissolved in CDCl₃ for ¹H NMR analysis. The residue contained *trans*-adduct **20e**¹⁰ : *cis*-adduct **19e**¹⁰ (≤1:99). The residues were subjected to chromatography on silica (hexanes/ethyl acetate 35:65) to give *cis*-adduct **19e**¹⁰ (46 mg, 0.18 mmol, 53%) as a colourless oil.

"Mix and Heat" Procedure for Hexa-3,5-dien-2-ol (15)



Maleic anhydride (156 mg, 1.59 mmol, 1.0 equiv) and BHT (35 mg, 0.16 mmol, 0.1 equiv) were added to a stirred solution of hexa-3,5-dien-2-ol **15**⁸ (156 mg, 1.59 mmol, 1.0 equiv) in toluene (3.2 mL) at RT. The reaction mixture was stirred at 110 °C for 2 h. After diazomethane treatment, ¹H NMR analysis of the crude product revealed four adducts **20f**-*lk*, **20f**-*ul*, **19f**-*lk*¹¹ and **19f**-*ul* in a 9:2:56:33 ratio. The residue was subjected to chromatography on silica (dichloromethane/diethyl ether 97:3) to give a mixture of the four adducts (236 mg, 1.13 mmol, 71%; **20f**-*lk*, **20f**-*ul*, **19f**-*lk*¹¹ and **19f**-*ul* = 10:1:57:32) eluting at $R_f = 0.24$. The product identities were determined by comparison of the GC and ¹H NMR spectra of the mixture to those of previously isolated and characterised compounds.

"Mix and Heat" Procedure for (2*R*,3*S*,4*E*,6*E*)-1,2-O-Iso-propylidene-8-tertbutyldimethylsilyloxy-6,6-octadiene-1,2,3-triol (16)



Dienol **16**⁶ (150 mg, 0.46 mmol) was dissolved in toluene (30 mL). Maleic anhydride (45 mg, 0.46 mmol) and BHT (10 mg, 0.05 mmol) were added and the reaction solution was heated to reflux for 30 h. The solvent

was removed in vacuo and the crude product was purified by column chromatography (1:1 Hex/EtOAc) to give two diastereoisomeric bis-lactones 19g-ul and 19g-lk, both endo adducts, in a 1:1 ratio (104 mg, 79%, $R_f = 0.53$, $R_f = 0.43$). (1S,3aR,3bS,6aS,8aR)-1-(4R)-2,2-dimethyl-1,3dioxolan-4-yl)-3,4-dioxo-1,3,3a,3b,4,6,6a,8a-octahydro-3,4-dioxobenzo[1,2-c:3,4-c']-difuran (**19g-***ul*): $R_f = 0.53$. Found: M⁺, 294.1102; $C_{15}H_{18}O_6$ requires 294.1103. $[\alpha]_D^{20^\circ} = -13.4^\circ$, (c = 0.65, acetone). IR (thin film): 2988, 2916, 1770, 1382, 1266, 1208, 1189, 1166, 1146, 1054, 1018 and 736 cm^{-1} . ¹H NMR /ppm 6.09 (1H, dt, J = 10.6, 1.8 Hz, H8), 5.97 (1H, ddd, J = 10.4, 3.8, 2.2 Hz, H7), 4.53 (1H, t, J = 8.6 Hz, H6_a), 4.36 (1H, dd, J = 9.0, 5.3 Hz, H1), 4.16–4.11 (2H, m, H4', H5'_a), 4.02-3.95 (1H, m, H5'), 3.84 (1H, dd, J = 10.3, 8.7 Hz, H6), 3.39 (1H, t, J = 6.8 Hz, H3a), 3.32-3.26(1H, m, H8a), 3.23-3.17 (1H, m, H6a), 2.99 (1H, dd, J = 9.5, 6.7 Hz, H3b), 1.44, 1.36 (6H, 2 × s, 1.14) $-C(CH_3)_2$). ¹³C NMR /ppm 176, 174 (C3, C4), 127, 124 (C7, C8), 110 ($-C(CH_3)_2$), 80.5, 73.2, 71.6, 67.9 (C1, C4', C5', C6), 38.8, 37.5, 35.7, 34.4 (C8a, C3a, C3b, C6a), 27.0, 25.11 (-C(CH₃)₂). m/z (EI, 70 eV) 294 (M⁺, 1%), 279 (M–CH₃⁺, 69), 219 (19), 101 (100), 91 (42), 73 (20), 55 (16) and 43 (47). (1S,3aS,4R,5R,7aS)-1-(4R)-2,2-Dimethyl-1,3-dioxolan-4-yl)-3,4-dioxo-1,3,3a,3b,4,6,6a,8aoctahydro-3,4-dioxo-benzo[1,2-c:3,4-c']-difuran (19g-lk) $R_f = 0.43$. Found: M⁺, 294.1109; $C_{15}H_{18}O_6$ requires 294.1103. $[\alpha]_D^{19^\circ} = +17.6^\circ$, (c = 0.94, CH₂Cl₂). IR (thin film): 2987, 2932, 1770, 1374, 1248, 1208, 1180, 1142, 1061, 1037, 1016 and 844 cm⁻¹. ¹H NMR /ppm 6.03 (1H, ddd, J =10.2, 3.3, 2.2 Hz, H8), 5.89 (1H, dt, J = 10.2, 2.2 Hz, H7), 4.49 (1H, dd, J = 8.8, 5.7 Hz, H6_a), 4.30 $(1H, td, J = 6.7, 4.8 Hz, H4'), 4.16 (1H, dd, J = 9.0, 6.6 Hz, H5'_{\alpha}), 4.13-4.09 (1H, m, H6), 3.95 (1H, t, t)$ *J* = 7.5 Hz, H1), 3.90 (1H, dd, *J* = 8.9, 4.7 Hz, H5'), 3.37–3.23 (3H, m, H3a, H3b, H6a), 3.16–3.07 $(1H, m, H8a), 1.39, 1.32 (6H, 2 \times s, -C(CH_3)_2)$. ¹³C NMR /ppm 175, 175 (C3, C4), 128, 127 (C7, C8), 110 (-C(CH₃)₂), 83.2, 77.2, 71.4, 67.4 (C1, C4', C5', C6), 38.0, 37.5, 36.7, 35.9 (C3a, C3b, C6a,

C8a), 26.8, 25.1 ($-C(CH_3)_2$). m/z (EI, 70 eV) 279 (M $-CH_3^+$, 100%), 219 (24), 101 (82), 91 (35)m 73 (19), 55 (24) and 43 (52).

"Mix and Heat" Procedure for 17



To a stirred solution of (2S,3S,4E,6E)-1,2-*O*-isopropylidene-3-((*tert*-butyldimethylsilyl)oxy)-4,6-octadien-1,2,8-triol **17**⁷ (100 mg, 0.304 mmol) in toluene (3.0 mL) at RT under argon was added maleic anhydride (30 mg, 0.30 mmol, 1 eq) and BHT (13 mg, 0.061 mmol, 0.2 eq). The solution was warmed to reflux and heating was continued for 67 h. The solution was cooled to -65 °C then an ethereal solution of diazomethane was added dropwise. On completion of the addition the solvent was evaporated to the give the crude product (127 mg) as a yellow oil. Chromatography of this material on silica (5 g) with hexane:ethyl acetate (3:1) then ethyl acetate gave the four adducts⁷ **20h**-*lk*, **20h**-*ul*, **19h**-*lk* and **19h**-*ul* in a 4:42:27:27 ratio (60.3mg, 0.137mmol, 45%).

4. IMDA Reactions of Pentadienyl Maleates 3 (Table 1)

IMDA reaction of triene 3a



Triene **3a** (308 mg, 1.69 mmol) and BHT (37.5 mg, 0.169 mmol) in toluene (169 mL) was stirred at 110 °C for 6 h. After allowing to cool to RT, the reaction mixture was concentrated *in vacuo*, a portion of the

residue dissolved in CDCl_3 and ¹H NMR analysis carried out. The residue contained **exo:endo** adducts (80:20) as a yellow oil. The residue was diluted in THF (10 mL) and cooled to -78 °C with stirring. An ethereal solution of diazomethane¹² was added dropwise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture

was concentrated *in vacuo*, a portion of the residues dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained **exo:endo** (78:22) as a yellow oil. The residue was chromatographed on silica (hexanes/ethyl acetate 7:3) to give cycloadduct **20a**⁹ (118 mg, 0.601 mmol, 37%) followed by cycloadduct **19a**⁹ (32.1 mg, 0.0.164 mmol, 10%).

IMDA reaction of triene 3b



To a stirred solution of triene **3b** (36.0 mg, 0.180 mmol) in toluene (36.6 mL) at RT under argon was added BHT (8.1 mg, 0.037 mmol). The solution was heated at 110 °C for 2h. The

solution was cooled to 0 °C before an ethereal solution of diazomethane¹² was added dropwise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N_2 gas through the solution. The mixture was concentrated *in vacuo* and the residues chromatographed on silica (hexanes:ethyl acetate 5:1 then 2:1) to give **20b** (21.8 mg, 0.104 mmol, 57%) and **19b** (9.8 mg, 0.046 mmol, 26%).

IMDA reaction of triene 3c



Triene **3c** (234 mg, 1.04 mmol) and BHT (23.0 mg, 0.104 mmol) in toluene (210 mL) was stirred at 110 °C for 3 h. After allowing to cool to RT, the reaction mixture

was concentrated *in vacuo*, a portion of the residue dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained **exo:endo** adducts (79:21) as a yellow oil. The residue was diluted in diethyl ether (5 mL) and cooled to -78 °C with stirring. An ethereal solution of diazomethane¹² was added dropwise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo*, a portion of the residues dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained **exo:endo** (85:15) as a yellow oil. The residues were chromatographed on silica (hexanes/ethyl acetate 7:3) to give cycloadduct **20c**¹⁰ (92.5 mg, 0.388 mmol, 42%) followed by cycloadduct **19c**¹⁰ (16.7 mg, 0.0701 mmol, 8%).

IMDA reaction of triene 3d



A solution of triene 3d (92.3 mg, 0.305 mmol, 1.0 equiv) and BHT (6.8 mg, 0.031 mmol, 0.1 equiv) in toluene

(31 mL) was stirred at 90 °C for 3.5 h. The reaction mixture was concentrated in vacuo, a portion of the residue dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained *trans*-adduct **6d** : cis-adduct 5d (43:57). The reaction mixture was concentrated in vacuo and the residues chromatographed on silica (hexanes/ethyl acetate/methanol/acetic acid 20:20:1:1) to give a mixture containing *trans*-adduct **6d** (28.9 mg) eluting at $R_f = 0.28$, followed by *cis*-adduct **5d** (29.0 mg, 0.096 mmol, 31%) eluting at $R_f = 0.17$. The mixture eluting at $R_f = 0.28$, containing *trans*-adduct 6d, was purified by HPLC [Alltech Altima C₁₈ column, eluting with methanol/water/acetic acid 56:44:0.5, 11.25 mL min⁻¹] to give *trans*-adduct **6d** at $t_{R} = 26.5 \text{ min} (17 \text{ mg}, 0.056 \text{ mmol}, 18\%). (±)-(3aS,6R,7S,7aR)-$ 6-Benzoyloxy-1-oxo-3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylic acid (6d): colourless oil. $R_f = 0.28$ (hexanes/ethyl acetate/methanol/acetic acid 20:20:1:1). IR (neat): 3600–2500 (OH), 1788, 1722, 1714 (C=O), 1601, 1584 (aryl C=C) cm⁻¹. ¹H NMR (400 MHz, CD₃OD): δ = 8.04 (2H, dd, J = 8.4, 1.4 Hz), 7.62 (1H, m), 7.48 (2H, m), 6.27 (1H, m), 6.00 (1H, m), 5.98 (1H, m), 4.60 (1H, dd, J = 7.6, 7.6 Hz), 4.04 (1H, dd, J = 11.4, 8.0 Hz), 3.50 (1H, d, J = 3.3 Hz), 3.29–3.20 (1H, m), 2.92 (1H, dd, dd, dd) = 1.04 Hz J = 13.7, 3.3 Hz). ¹³C NMR (100 MHz, CD₃OD): $\delta = 176.8$ (C), 172.1 (C), 166.9 (C), 134.5 (CH), 131.7 (CH), 131.1 (C), 130.7 (CH), 129.6 (CH), 127.9 (CH), 71.7 (CH₂), 71.0 (CH), 44.6 (CH), 42.3 (CH), 38.0 (CH). EIMS (70 eV) *m*/*z* (%): 302 ([M]⁺, 1), 284 ([M–H₂O]⁺, 1), 256 ([M–CH₂O₂]⁺, 2), 105 ($[M-C_0H_0O_5]^+$, 100), 77 ($[M-C_{10}H_0O_6]^+$, 60). HRMS: calcd for $C_{16}H_{14}O_6$ [M]⁺: 302.0790; found: 302.0795. For confirmation of stereochemistry, a portion of trans-adduct 6d was treated with diazomethane to give trans-adduct 20d. (±)-(3aS,6R,7R,7aS)-6-Benzoyloxy-1-oxo-3,3a,6,7,7ahexahydro-7-isobenzofurancarboxylic acid (5d): white colourless crystals after recrystallisation from cyclohexane/ethyl acetate 80:20. $R_f = 0.17$ (hexanes/ethyl acetate/methanol/acetic acid 20:20:1:1). mp 185–187 °C (lit. 186–188 °C recrystallised from cyclohexane).¹³ ¹H NMR (400 MHz, CD₃OD): δ = 8.03 (2H, d, J = 7.0 Hz), 7.55 (1H, m), 7.42 (2H, m), 6.18 (1H, ddd, J = 9.8, 5.3, 1.8 Hz), 5.99 (1H, dd, J = 10.2, 2.9 Hz), 5.83 (1H, m), 4.48 (1H, dd, J = 9.2, 7.0 Hz), 4.18 (1H, d, J = 9.4 Hz), 3.73 (1H, dd, J = 8.4, 4.7 Hz), 3.41-3.36 (1H, m), 3.34 (1H, m). ¹³C NMR (100 MHz, CD₃OD): $\delta = 178.2$ (C), 172.7 (C), 167.7 (C), 134.1 (CH), 133.5 (CH), 131.3 (C), 131.1 (CH), 129.4 (CH), 127.3 (CH), 71.2 (CH₂), 65.7 (CH), 42.2 (CH), 38.0 (CH), 37.7 (CH). EIMS (70 eV) m/z (%): 302 ([M]⁺, 10), 257 ([M–CHO₂]⁺, 5), 197 ([M–C₇H₅0]⁺, 10), 136 ([M–C₈H₆O₄]⁺, 20), 122 ([M–C₉H₈O₄]⁺, 30), 105 ([M–C₉H₉O₅]⁺, 100), 77 ([M–C₁₀H₉O₆]⁺, 70). HRMS: calcd for C₁₆H₁₄O₆ [M]⁺: 302.0790; found: 302.0786. For confirmation of stereochemistry, a portion of *cis*-adduct **5d** was treated with diazomethane to give *cis*-adduct **19d**.

IMDA reaction of triene 3e



Triene **3e** (38.9 mg, 0.162 mmol) and BHT (3.6 mg, 0.016 mmol) in toluene (16 mL) was stirred at 110 °C for 9.5 h.

After allowing to cool to RT, the reaction mixture was concentrated *in vacuo*, a portion of the residue dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained **exo:endo** adducts (74:26) as a yellow oil. The residue was then stirred in diethyl ether (2 mL) at -78 °C. An ethereal solution of diazomethane¹² was added dropwise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo*, a portion of the residues dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained **exo:endo** adducts (75:25) as a yellow oil. The residue was then applied to column chromatography on silica (hexanes/ethyl acetate 50:50) to give *trans*-adduct **20e**¹⁰ (11.5 mg, 0.0452 mmol, 28%) followed by *cis*-adduct **19e**¹⁰ (5.1 mg, 0.0201 mmol, 12%).

IMDA reaction of half-ester 3f



A solution of triene **3f** (292.1 mg, 1.489 mmol, 1.0 equiv) and BHT (32.8 mg, 0.149 mmol, 0.1 equiv) in toluene (15 mL) was stirred at 110 °C for 3 h. The reaction mixture was concentrated *in*

vacuo, diluted in dichloromethane (1 mL) and cooled to -78 °C with stirring. An ethereal solution of diazomethane was added dropwise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The reaction mixture was concentrated *in vacuo*, a portion of the residue dissolved in CDCl₃ and ¹H NMR analysis carried out. The residue contained *trans,lk*-IMDA adduct **35**, *trans,ul*-IMDA adduct **36**, *cis,lk*-IMDA adduct **37**¹¹ and *cis,ul*-IMDA adduct **38** (61:18:10:11, respectively). The residue was subjected to chromatography on silica (dichloromethane/diethyl ether 97:3) to give a mixture of *trans,lk*-IMDA adduct **35**, *trans,ul*-IMDA adduct **38** (145 mg, 0.690 mmol, 46%, *trans,lk*-IMDA adduct **35**, *trans,ul*-IMDA adduct **36**, *cis,lk*-IMDA adduct **35**, *trans,ul*-IMDA adduct **37**¹¹ and *cis,ul*-IMDA adduct **38** (68:17:9:6)), eluting at R_f = 0.24. The isolated mixture was not separated by chromatography. The product ratios were determined by comparison of the GC and ¹H NMR of the mixture to the previously isolated and characterised compounds.

IMDA reaction of triene 3g



(2S,3S,4*E*,6*E*)-1,2-*O*-isopropylidene-8-*tert*-butyldimethylsilyloxy-1,2-dihydroxyl-4,6-octadien-3-yl hydrogen (2*Z*)-2-butenedioate **3g** (49 mg, 0.15 mmol) was heated in toluene at reflux, in the presence of BHT (2.5 mg, 0.02 mmol), under Ar, overnight. The toluene was removed *in vacuo* and the residue was diluted with Et_2O . The crude cycloadducts were treated with an ethereal solution of diazomethane (*ca.* 0.5 M) until a yellow colour persisted. The solvent was removed *in vacuo* and the mixture subjected to column chromatography, using Hex/Et₂O (1:1), to give the compounds *trans*-adduct **20g**⁶ and *cis*-adduct **19g**⁶ (**20g:19g** in a ratio of 86:14, 66%).

IMDA reaction of triene 3h



To a stirred solution of (2E,4E,6S,7S)-7,8-*O*-isopropylidene-6-((*tert*-butyldimethylsilyl)oxy)-7,8dihydroxy-2,4-octadien-1-yl hydrogen maleate (**3h**) (137mg, 0.322mmol) in toluene (64.4mL) at RT under argon was added BHT (14.2mg, 0.0646mmol, 0.2eq). The solution was warmed to reflux and heating was continued for 17h. The solution was cooled to 0°C, then an ethereal solution of diazomethane was added. On completion of the addition the solvent was evaporated to give the crude product (148.1mg) as a yellow oil. Chromatography of this material on silica (5g) with hexane:ethyl acetate (4:1) gave the **adducts (41** and **42**)⁷ (86.3mg, 0.196mmol, 62%, **41:42** (89:11)).

5. Synthesis of Sorbyl Citraconate Esters 9 and 10 (Scheme 2)

Method A is regioselective for isomer 9.



To a stirred solution of (2E,4E)-2,4-hexadien-1-ol (7) (2.00 g, 20.4 mmol) in dichloromethane (100 mL) at 0 °C under argon was added triethylamine (3.00 mL, 21.5 mmol, 1.05 eq), citraconic anhydride (2.74 mL, 30.6 mmol) and N,N-dimethylaminopyridine (0.124 g, 1.01 mmol). On completion of the addition the solution was warmed to RT and

stirring was continued for 30 min. An extra amount of triethylamine (1.56 mL, 11.2 mmol), citraconic anhydride (1.60 mL, 14.3 mmol) and N,N-dimethylaminopyridine (0.124 g, 0.510 mmol) was added and stirring was continued for 3 h. The reaction mixture was partitioned against 10% aqueous hydrochloric acid (50 mL), water (50 mL) and brine (50 mL) then dried, filtered and evaporated to give the crude product (6.021 g) as a yellow oil. The crude product was adsorbed onto silica (9 g) then loaded onto a silica column (90 g) and eluted with hexanes:ethyl acetate (2:1), ethyl acetate, ethyl acetate:acetic acid (165:1) then ethyl acetate:acetic acid:methanol (38:1:1) to give **9** (3.70 g, 17.5 mmol,

86%) and **10** (602 mg, 2.86 mmol, 14%). **1**-((2*E*,4*E*)-2,4-hexadien-1-yl) **4**'-hydrogen (2'Z)-2'methyl-2'-butenedioate (9). Wax. $R_f = 0.18$ (hexanes/ethyl acetate/acetic acid/methanol 260:130:1:1). IR (neat): 3432, 3025, 2959, 2915, 1731, 1698, 1650 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 11.0 (br s, 1H), 6.26 (dd, *J* = 15.2, 10.3 Hz, 1H), 6.10–5.97 (m, 1H), 5.85 (q, *J* = 1.8 Hz, 1H), 5.74 (dq, *J* = 14.9, 6.8 Hz, 1H), 5.62 (dt, *J* = 15.2, 7.0 Hz, 1H), 4.69 (d, *J* = 7.0 Hz, 2H), 2.07 (d, *J* = 1.8 Hz, 3H), 1.74 (3d, *J* = 6.8 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 169.4, 168.3, 147.6, 135.5, 131.4, 130.2, 122.5, 120.2, 66.2, 20.8, 18.1. CI/NH₃ (40 eV) *m/z* (%): 210 (M⁺, 7), 39 (100). HRMS: calcd for C₁₁H₁₄O₄ [M]⁺: 210.0892; found: 210.0892. **1**-((2*E*,4*E*)-2,4-hexadien-1-yl) 4'-hydrogen (2'Z)-3'-methyl-2'-butenedioate (10) Wax. $R_f = 0.05$ (hexanes/ethyl acetate/acetic acid/methanol 260:130:1:1). IR (neat): 3412, 3026, 2936, 1713, 1650 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 6.29 (dd, *J* = 14.9, 10.3 Hz, 1H), 6.16 (q, *J* = 1.5 Hz, 1H), 6.13–5.99 (m, 1H), 5.87–5.56 (m, 2H), 4.70 (d, *J* = 7.0 Hz, 2H), 2.14 (d, *J* = 1.5 Hz, 3H), 1.78 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 168.6, 166.6, 146.5, 136.1, 132.0, 130.1, 122.9, 122.1, 66.6, 22.2, 18.2. EIMS *m/z* (%): 210 (M⁺, 2), 39 (100). HRMS: calcd for C₁₁H₁₄O₄ [M]⁺: 210.0892; found: 210.0892.

Method B is the procedure reported by White and Sheldon, which gives a 1:1 mixture of 9 and 10.¹⁴



To a stirred solution of (2E,4E)-2,4-hexadien-1-ol (7) (1.96 g, 20.0 mmol) in benzene (4 mL) at RT under argon was added pyridine (1.60 mL, 48.3 mmol) and citraconic anhydride (1.80 mL, 20.0 mmol). On completion of the addition the solution was warmed to 50 °C and stirring was continued for 8 h. The solvent was evaporated then dichloromethane (50 mL) was

added and this was partitioned against 10% aqueous hydrochloric acid (2×50 mL), water (50 mL) and brine (50 mL) then dried, filtered and evaporated to give the crude product (3.87 g) as a yellow oil. Half of the crude product (1.91 g) was columned in two portions on silica (50 g) with hexanes:ethyl acetate:acetic acid:methanol (260:130:1:1) to give the title compounds (**9** and **10**) (1.847 g, 8.79 mmol, 44% (corresponding to an overall yield of 89%), **9:10** (50:50)).

(1*S*,2*S*,5*R*,6*R*)-2-(*tert*-Butyldimethylsilyl)oxymethyl-5,6-dimethyl-1,2,5,6-tetrahydrophthalic anhydride (25) and (1*S*,2*S*,5*R*,6*R*)-2-(*tert*-butyldimethylsilyl)oxymethyl-1,5-dimethyl-1,2,5,6tetrahydrophthalic anhydride (26)



To a stirred solution of (2E,4E)-1-((*tert*-butyldimethylsilyl)oxy)-2,4-hexadiene **24**¹⁵ (0.429 g, 2.02 mmol) in toluene (4.0 mL) was added citraconic anhydride (181 μ L, 2.02 mmol) and BHT (89.0 mg, 0.40 mmol) at RT under argon. The solution was heated at 110 °C for 36 h. The solution was concentrated *in vacuo* and then applied to chromatography on silica with hexanes, hexanes:diethyl ether (20:1 then 10:1), hexanes:ethyl acetate

(20:1 then 10:1) then ethyl acetate to give recovered starting material (24) (86.4 mg, 0.406 mmol, 20%) followed by 25 (0.369 g, 1.10 mmol, 71%, (80% conversion)) and 26 (0.116 g, 0.358 mmol, 22% (at 80% conversion)). (1S,2S,5R,6R)-2-(tert-Butyldimethylsilyl)oxymethyl-5,6-dimethyl-1,2,5,6tetrahydrophthalic anhydride (25): White crystalline solid after recrystallisation from *tert*-butyl methyl ether. mp 79–80 °C. $R_{e} = 0.50$ (hexanes/ethyl acetate 10:1). IR (KBr): 3039, 2982, 2956, 2933, 2881, 2857, 1839, 1777 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.85 (dt, J = 9.2, 3.1 Hz, 1H), 5.74 (dt, J= 9.2, 2.9 Hz, 1H), 4.17 (dd, J = 9.9, 9.0 Hz, 1H), 3.99 (dd, J = 9.9, 7.3 Hz, 1H), 3.14 (d, J = 4.8 Hz, 1H), 2.56–2.42 (m, 1H), 2.19–2.05 (m, 1H), 1.48 (s, 3H), 1.29 (d, J = 7.5 Hz, 3H), 0.907 (s, 9H), 0.102 (s, 6H). ¹³C NMR (68 MHz, CDCl₃): δ 174.0, 170.7, 134.4, 131.0, 62.2, 50.6, 49.9, 38.7, 38.2, 25.9, 22.1, 18.3, 15.4, -5.25, -5.27. EIMS (40 eV) m/z (%): 309 (M⁺, 6), 267 (100). HRMS: calcd for $C_{16}H_{25}O_{4}Si$ $[M - CH_3]^+$: 309.1522; found: 309.1532. (1S,2S,5R,6R)-2-(tert-Butyldimethylsilyl)oxymethyl-1,5-dimethyl-1,2,5,6-tetrahydrophthalic anhydride (26): Colourless oil. R_f = 0.36 (hexanes/ethyl acetate 10:1). IR (neat): 2955, 2950, 2883, 2857, 1850, 1780 cm^{-1} . ¹H NMR (270 MHz, CDCl₃): δ 5.92–5.81 (m, 2H), 3.98 (dd, J = 10.1, 4.6 Hz, 1H), 3.77 (dd, J = 10.1, 4.6 \text{Hz}, 1\text{Hz})), 3.77 (dd, J = 10.1, 4.6 \text{Hz}, 10.1, 4.6 \text{Hz})), 3.77 (dd, J = 10.1, 4.6 \text{Hz}, 10.1, 4 10.1, 7.3 Hz, 1H), 2.86 (d, J = 5.3 Hz, 1H), 2.51–2.38 (m, 1H), 2.17–2.08 (m, 1H), 1.52 (s, 3H), 1.49 (d, J = 7.3 Hz, 3H), 0.885 (s, 9H), 0.071 (s, 6H).¹³C NMR (68 MHz, CDCl₃): δ 174.4, 170.5, 135.4, 130.4, 61.8, 55.4, 48.7, 45.5, 29.7, 25.9, 23.0, 18.3, 16.9, -5.42. EIMS (40 eV) m/z (%): 309 (M⁺, 4), 267 (100). HRMS: calcd for C₁₆H₂₅O₄Si [M–CH₃]⁺: 309.1522; found: 309.1511.

(3aS,6R,7R,7aS)-6,7-Dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-

isobenzofurancarboxylic acid (11)

To a stirred solution of (\pm) -(1S,2S,5R,6R)-2-(tertbutyldimethylsilyl)oxymethyl-5,6-dimethyl-1,2,5,6-tetrahydrophthalic

anhydride (**25**) (218 mg, 0.672 mmol) in dichloromethane (2.5 mL) at 0 °C under argon was added trifluoroacetic acid (514 μ L, 6.72 mmol). On completion of the addition the solution was warmed to RT and stirring was continued for 2 h. Evaporation of the solvent gave the crude product (168 mg) as a yellow oil. Chromatography of this material on silica (hexanes:ethyl



acetate:methanol:acetic acid 50:10:0.3:0.3, 60:30:0.45:0.45 then 50:50:0.5:0.5) gave the title compound (**11**) (132 mg, 0.628 mmol, 94%) as a white crystalline solid after recystallisation from *tert*-butyl methyl ether. mp 171–174 °C [lit.¹⁴ 168–170 °C]. $R_f = 0.25$ (hexanes/ethyl acetate/methanol/acetic acid 60:30:0.45:0.45). IR (KBr): 3393, 3018, 2979, 2935, 2891, 1766, 1758, 1707, 1694 cm⁻¹. ¹H NMR (270 MHz, CDCl₃/CD₃OD): δ 5.72 (ddd, J = 10.1, 4.2, 2.4 Hz, 1H), 5.48 (dt, J = 10.1, 2.3 Hz, 1H), 4.36 (dd, J = 8.6, 7.7 Hz, 1H), 4.10 (dd, J = 8.6, 4.2 Hz, 1H), 3.20–3.07 (m, 1H), 2.97 (d, J = 9.4 Hz, 1H), 2.37–2.23 (m, 1H), 1.44 (s, 3H), 1.15 (d, J = 7.3 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃/CD₃OD): δ 179.2, 176.6, 134.1, 123.1, 71.0, 45.6, 44.3, 37.6, 35.2, 26.4, 17.4. EIMS (40 eV) *m/z* (%): 210 (M⁺, 20), 107 (100). HRMS: calcd for C₁₁H₁₄O₄ [M]⁺: 210.0892; found: 210.0896.

(±)-(3aS,6R,7R,7aS)-6,7a-Dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7isobenzofurancarboxylic acid (22)

To a stirred solution of (\pm) -(1S,2S,5R,6R)-2-(tert-butyldimethylsilyl)oxymethyl-1,5-dimethyl-1,2,5,6-tetrahydrophthalic anhydride (**26**) (21.6 mg, 0.0666 mmol) in dichloromethane (2.5 mL) at 0 °C under argon was added trifluoroacetic acid (51.0 μ L, 0.666 mmol). On completion of the addition the solution was warmed to RT and stirring was continued for 2 h. Evaporation of the solvent gave the crude product (16.7 mg) as a yellow oil. Chromatography of this material on silica (3 g) with



hexanes:ethyl acetate:methanol:acetic acid (50:10:0.3:0.3, 60:30:0.45:0.45 then 50:50:0.5:0.5) gave the

title compound (**22**) (10.6 mg, 0.0504 mmol, 76%) as a crystalline solid. mp 112–114 °C (from *tert*butyl methyl ether). $R_f = 0.54$ (hexanes/ethyl acetate/methanol/acetic acid 60:30:0.45:0.45). IR (KBr): 3361, 3024, 2972, 2884, 1764, 1707 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.88–5.74 (m, 1H), 5.59 (dt, J = 10.1, 2.4 Hz, 1H), 4.56 (dd, J = 8.8, 7.9 Hz, 1H), 4.20 (dd, J = 8.8, 4.6 Hz, 1H), 2.98 (d, J = 6.2 Hz, 1H), 2.84–2.70 (m, 2H), 1.50 (s, 3H), 1.16 (d, J = 7.5 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 183.5, 173.6, 133.0, 123.9, 71.7, 51.7, 43.0, 42.6, 30.4, 24.2, 17.5. EIMS (40 eV) m/z (%): 210 (M⁺, 14), 107 (100). HRMS: calcd for C₁₁H₁₄O₄ [M]⁺: 210.0892; found: 210.0892.

Carboxylic acids **11** and **22** were converted into the corresponding methyl esters (**11-methyl ester** and **22-methyl ester**, respectively) to facilitate identification.

(±)-Methyl (3aS,6R,7R,7aS)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7isobenzofurancarboxylate (11-methyl ester)

To a stirred solution of (±)-(3aS,6R,7R,7aS)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7ahexahydro-7-isobenzofurancarboxylic acid (**11**) (57.0 mg, 0.271 mmol) in diethyl ether (10 mL) at -65 °C and cooled to -78 °C. An ethereal solution of diazomethane¹² was added dropwise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo* and the residues chromatographed on silica (hexanes:ethyl



acetate 10:1, 5:1 then 2:1) to give the title compound (**11-methyl ester**) (57.8 mg, 0.258 mmol, 95%) as a colourless oil. $R_f = 0.13$ (hexanes/ethyl acetate 5:1). IR (neat): 2977, 2951, 2913, 2828, 1777, 1769, 1738, 1731 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.72 (ddd, J = 10.1, 4.2, 2.4 Hz, 1H), 5.51 (dt, J =10.1, 2.2 Hz, 1H), 4.38 (dd, J = 8.6, 7.7 Hz, 1H), 4.10 (dd, J = 8.6, 4.4 Hz, 1H), 3.71 (s, 3H), 3.22–3.09 (m, 1H), 3.00 (d, J = 9.4 Hz, 1H), 2.41–2.27 (m, 1H), 1.44 (s, 3H), 1.14 (d, J = 7.5 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 176.3, 174.4, 133.7, 123.1, 70.7, 51.7, 45.5, 44.4, 37.6, 35.0, 25.8, 17.2. EIMS *m/z* (%): 224 (M⁺, 36), 80 (100). HRMS: calcd for C_{1.2}H_{1.6}O₄ [M]⁺: 224.1049; found: 224.1050.

(±)-(3aS,6R,7R,7aS)-6,7a-Dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-

isobenzofurancarboxylate (22-methyl ester)

To a stirred solution of (\pm) -(3aS,6R,7R,7aS)-6,7a-dimethyl-1-oxo-1,3,3a,6,7,7ahexahydro-7-isobenzofurancarboxylic acid (**22**) (23.2 mg, 0.110 mmol) in diethyl ether (10 mL) at - $65 \,^{\circ}$ C was added dropwise an ethereal solution of diazomethane¹² until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo* and the residues chromatographed on silica (hexanes:ethyl acetate 10:1, 5:1)



then 2:1) gave the title compound (**22-methyl ester**) (23.5 mg, 0.105 mmol, 95%) as a colourless oil. $R_f = 0.10$ (hexanes/ethyl acetate 5:1). IR (neat): 3025, 2971, 1878, 1768, 1731 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.70 (dt, J = 9.9, 3.1 Hz, 1H), 5.57 (dt, J = 9.9, 2.0 Hz, 1H), 4.56 (dd, J = 9.9, 7.9 Hz, 1H), 4.17 (dd, J = 9.9, 8.1 Hz, 1H), 3.63 (s, 3H), 2.81 (d, J = 5.7 Hz, 1H), 2.85–2.73 (m, 1H), 2.72–2.59 (m, 1H), 1.41 (s, 3H), 1.14 (d, J = 7.5 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 180.5, 172.3, 129.9, 123.9, 69.9, 51.6, 50.3, 43.0, 41.2, 28.2, 26.5, 18.5. EIMS *m/z* (%): 224 (M⁺, 26), 107 (100). HRMS: calcd for C₁₂H₁₆O₄ [M]⁺: 224.1049; found: 224.1049.

7. Preparation of Sorbyl Citraconate *Exo* Adducts 15 and 27 (Scheme 5)

1-((2E,4E)-2,4-Hexadien-1-yl) 4'-methoxymethyl (2'Z)-3'-methyl-2'-butenedioate (27)



To a stirred solution of 1-((2*E*,4*E*)-2,4-hexadien-1-yl) 4'-hydrogen (2'*Z*)-3'methyl-2'-butenedioate (**9**) (57.4 mg, 0.273 mmol) in dichloromethane (1 mL) at RT under argon was added triethylamine (189 μ L, 1.37 mmol) and chloromethyl methyl ether (51.9 μ L, 0.683 mmol). Stirring was continued for 10 min then the reaction mixture was diluted with dichloromethane (10 mL) and partitioned against sat. aq. NaHCO₃ (10 mL), water (10 mL), 2 M HCl (10 mL), water (10 mL) and brine (10 mL) then dried, filtered and evaporated to give the crude product (61.9 mg) as a yellow oil. Chromatography of this material on silica

(hexanes:ethyl acetate 10:1, 5:1 then 2:1) gave the title compound (27) (40.8 mg, 0.160 mmol, 59%) as a colourless oil. $R_f = 0.43$ (hexanes/ethyl acetate 5:1). IR (neat): 3000, 2956, 2852, 1724, 1654 cm⁻¹.

¹H NMR (270 MHz, CDCl₃): δ 6.24 (1H, dd, *J* 10.3, 14.9 Hz, C3-*H*), 6.10–5.97 (m, 1H), 5.88 (q, *J* = 1.8 Hz, 1H), 5.75 (dq, *J* = 14.9, 6.8 Hz, 1H), 5.61 (dt, *J* = 14.9, 6.8 Hz, 1H), 5.36 (s, 2H), 4.62 (d, *J* = 6.8 Hz, 2H), 3.51 (s, 3H), 2.08 (d, *J* = 1.8 Hz, 3H), 1.76 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 168.2, 164.4, 144.9, 135.1, 131.3, 130.2, 123.0, 120.8, 91.6, 65.3, 57.9, 20.5, 18.2. EIMS (40 eV) *m*/*z* (%): 254 (M⁺, 1), 45 (100). HRMS: calcd for C_{1.3}H₁₈O₅ [M]⁺: 254.1154; found: 254.1160.

(±)-Methoxymethyl (3aS,6R,7R,7aS)-6,7-dimethyl-1-oxo-

1,3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylate (29) and (\pm) methoxymethyl (3aS,6S,7S,7aR)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7ahexahydro-7-isobenzofurancarboxylate (30)

To a stirred solution of 1-((2E,4E)-2,4-hexadien-1-yl) 4'-methoxymethyl (2'Z)-3'-methyl-2'-butenedioate (**27**) (35.4 mg, 0.139 mmol) in toluene (28.0 mL) at RT under argon was added BHT (6.1 mg, 0.014 mmol). The solution was heated at 110 °C for 19 h. Evaporation of the solvent gave the crude product as a yellow oil. Chromatography of this material



on silica (hexanes:ethyl acetate 10:1, 5:1 then 2:1) gave **30** (29.9 mg, 0.118 mmol, 84%) and **29** (4.1 mg, 0.016 mmol, 12%). **Methoxymethyl (3aS,6S,7S,7aR)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylate (30):** White needles after recrystallisation from *tert*-butyl methyl ether. mp 89.4–90.5 °C. $R_r = 0.44$ (hexanes/ethyl acetate 5:1). IR (KBr): 3023, 2974, 2909, 2837, 1774, 1742 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.75–5.65 (m, 2H), 5.26 (s, 3H), 4.43 (dd, J = 7.9, 6.8 Hz, 1H), 3.80 (dd, J = 11.4, 7.9 Hz, 1H), 3.45 (s, 2H), 3.16–2.96 (m, 2H), 2.17 (d, J = 13.6 Hz, 1H), 1.58 (s, 3H), 1.04 (d, J = 7.5 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 174.4, 173.9, 136.1, 121.9, 90.8, 69.6, 57.8, 46.4, 44.6, 38.7, 37.8, 19.6, 16.9. EIMS *m*/*z* (%): 236 (M–H₂O⁺, 0.2), 45 (100). HRMS: calcd for C₁₃H₁₆O₄ [M–H₂O]⁺: 236.1049; found: 236.1053. **Methoxymethyl (3aS,6R,7R,7aS)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylate (29):** Colourless oil. $R_r = 0.34$ (hexane/ethyl acetate 5:1). IR (neat): 2975, 2916, 2850, 1770, 1773, 1738, 1732 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.79 (ddd, J = 10.1, 4.2, 2.4 Hz, 1H), 5.55 (dt, J = 10.1, 2.2 Hz, 1H), 5.34 (d, J = 6.2 Hz, 1H), 5.31 (d, J = 6.2 Hz, 1H), 4.41 (dd, J = 8.8, 7.5 Hz, 1H), 4.16 (dd, J = 8.8, 4.0 Hz, 1H), 3.50 (s, 3H), 3.25–3.13 (m, 1H), 3.08 (1d, J = 9.2 Hz, 1H), 2.47–2.34 (m, 1H), 1.51 (s, 3H), 1.21 (d, J = 7.5 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 176.3, 173.7, 134.0,

123.2, 91.1, 70.8, 58.0, 44.7, 44.4, 37.6, 35.1, 26.1, 17.3. EIMS (80 eV) *m/z* (%): 254 (M⁺, 1), 45 (100). HRMS: calcd for C₁₃H₁₈O₅ [M]⁺: 254.1154; found: 254.1148.

(±)-(3a*S*,6*R*,7*S*,7a*R*)-6,7-Dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7isobenzofurancarboxylic acid (21)

To a stirred solution of (±)-methoxymethyl (3aS,6S,7S,7aR)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylate (**30**) (17.5 mg, 0.0688 mmol) in dichloromethane (3.0 mL) at RT under argon was added trifluoroacetic acid (54.1 μ L, 0.688 mmol). Stirring was continued for 18 h then the solvent was evaporated to give the crude product (20.0 mg) as a yellow oil. Chromatography of this material on silica with hexanes:ethyl acetate (2:1) then hexanes:ethyl acetate:methanol:acetic acid (60:30:0.45:0.45) gave the title compound (**21**) (13.9 mg, 0.0661 mmol, 96%) as a



white crystalline solid after recrystallisation from *tert*-butyl methyl ether. mp 138–140 °C. $R_f = 0.32$ (hexanes/ethyl acetate/methanol/acetic acid 60:30:0.45:0.45). IR (KBr): 3398, 2980, 2965, 2918, 1790, 1692 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.75–5.65 (m, 2H), 4.45 (dd, J = 7.9, 7.0 Hz, 1H), 3.81 (dd, J = 11.4, 7.9 Hz, 1H), 3.30–3.14 (m, 1H), 3.04–2.91 (m, 1H), 2.14 (d, J = 13.4 Hz, 1H), 1.59 (s, 3H), 1.05 (d, J = 7.3 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 181.3, 174.0, 135.9, 122.2, 69.7, 45.9, 44.6, 38.4, 37.9, 20.0, 17.0. EIMS (40 eV) *m/z* (%): 193 (M–OH⁺, 0.5), 121 (100). HRMS: calcd for C₁₁H₁₃O₃ [M–OH]⁺: 193.0865; found: 193.0865.

(±)-Methyl (3a*S*,6*R*,7*S*,7a*R*)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7isobenzofurancarboxylate (21-methyl ester)

To a stirred solution of (\pm)-(3a*S*,6*R*,7*S*,7a*R*)-6,7-dimethyl-1-oxo-1,3,3a,6,7,7ahexahydro-7-isobenzofurancarboxylic acid (**21**) (9.2 mg, 0.044 mmol) in diethyl ether (5 mL) at -65 °C dropwise was added an ethereal solution of diazomethane¹² until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo* and the residues chromatographed on silica (hexanes:ethyl acetate 5:1 then



2:1) to give (**45**) (6.2 mg, 0.028 mmol, 64%) as a crystalline solid after recrystallisation from *tert*-butyl methyl ether. mp 108–109 °C (lit.¹⁴ 94–96 °C). $R_f = 0.55$ (hexanes/ethyl acetate 2:1). IR (KBr): 3025,

2995, 2916, 2849, 1786, 1730 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.75–5.62 (m, 2H), 4.43 (dd, *J* = 7.9, 7.3 Hz, 1H), 3.79 (dd, *J* = 11.4, 7.9 Hz, 1H), 3.71 (s, 3H), 3.11–2.95 (m, 2H), 2.13 (d, *J* = 13.6 Hz, 1H), 1.54 (s, 3H), 1.03 (d, *J* = 7.5 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 175.4, 173.9, 136.1, 122.0, 69.6, 52.3, 46.1, 44.9, 38.7, 38.0, 19.8, 16.9. EIMS *m*/*z* (%): 224 (M⁺, 2), 119 (100). HRMS: calcd for C₁₂H₁₆O₄ [M]⁺: 224.1049; found: 224.1058.

1-((2E,4E)-2,4-Hexadien-1-yl) 4'-methoxymethyl (2'Z)-2'-methyl-2'-butenedioate (28)



To a stirred solution of 1-((2E,4E)-2,4-hexadien-1-yl) 4'-hydrogen (2'Z)-2'methyl-2'-butenedioate (**10**) (34.8 mg, 0.167 mmol) in dichloromethane (1mL) at RT under argon was added triethylamine (57.4 μ L, 0.414 mmol) and chloromethyl methyl ether (15.1 μ L, 0.199 mmol). Stirring was continued for 5 min then the reaction mixture was diluted with dichloromethane (10 mL) and partitioned against sat. aq. NaHCO₃ (10 mL), water (10 mL), 2M HCl (10 mL), water (10 mL) and brine (10 mL) then dried, and concentrated *in vacuo*. Chromatography of this material on silica (hexanes:ethyl acetate 10:1 then 5:1) gave (**28**) (36.6 mg, 0.144

mmol, 86%) as a colourless oil. $R_f = 0.43$ (hexanes/ethyl acetate 5:1). IR (neat): 3001, 2957, 2852, 1734, 1654 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 6.28 (dd, J = 15.2, 10.3 Hz, 1H), 6.12–5.99 (m, 1H), 5.87 (q, J = 1.5 Hz, 1H), 5.77 (dq, J = 14.9, 6.8 Hz, 1H), 5.66 (dt, J = 15.2, 6.8 Hz, 1H), 5.26 (s, 2H), 3.72 (d, J = 6.8 Hz, 2H), 3.44 (s, 3H), 2.07 (d, J = 1.5 Hz, 3H), 1.76 (d, J = 6.8 Hz, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 168.3, 164.0, 146.2, 135.4, 131.4, 130.2, 122.9, 120.3, 90.8, 66.0, 57.7, 20.6, 18.2. EIMS (40 eV) m/z (%): 254 (M⁺, 1), 45 (100). HRMS: calcd for C₁₃H₁₈O₅ [M]⁺: 254.1154; found: 254.1159.

Methoxymethyl (3aS,6R,7R,7aS)-6,7a-dimethyl-1-oxo-1,3,3a,6,7,7ahexahydro-7-isobenzofurancarboxylate (31) and (±)methoxymethyl (3aS,6R,7S,7aR)-6,7a-dimethyl-1-oxo-1,3,3a,6,7,7ahexahydro-7-isobenzofurancarboxylate (32)

To a stirred solution of 1-((2E,4E)-2,4-hexadien-1-yl) 4'-methoxymethyl (2'Z)-2'-methyl-2'-butenedioate (**28**) (34.9 mg, 0.137 mmol) in toluene (28.0 mL) at RT under argon was added BHT (6.0 mg, 0.027 mmol). The



solution was heated at 110 °C for 22 h. Evaporation of the solvent gave the crude product as a yellow oil. Chromatography of this material on silica (hexanes:ethyl acetate 5:1 then 2:1) gave compounds (**32** and **31**) (34.5 mg, 0.136 mmol, 99%, **32:31** (93:7). (Adduct **31** was unable to be isolated and characterised. The structure of this compound is speculative and based on limited proton NMR analysis of mixtures only.) **Methoxymethyl** (**3a***S*,*6R*,*7S*,*7aR*)-*6*,*7a*-**dimethyl**-1-**oxo**-1,*3*,*3a*,*6*,*7*,*7a*-**hexahydro**-7-**isobenzofurancarboxylate** (**32**): Colourless oil. $R_r = 0.18$ (hexanes/ethyl acetate 5:1). IR (neat): 2969, 2935, 2878, 1778, 1731 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.81 (dt, *J* = 9.7, 2.9 Hz, 1H), 5.67 (ddd, *J* = 9.7, 3.1, 2.4 Hz, 1H), 5.35 (d, *J* = 6.0 Hz, 1H), 5.17 (d, *J* = 6.0 Hz, 1H), 4.54–4.46 (m, 1H), 4.10 (dd, *J* = 12.1, 8.3 Hz, 1H), 3.63–3.51 (m, 1H), 3.48 (s, 3H), 2.62–2.49 (m, 1H), 2.48 (d, *J* = 3.3 Hz, 1H), 1.32 (d, *J* = 7.5 Hz, 3H), 1.07 (s, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 177.9, 173.1, 133.9, 122.3, 90.7, 68.6, 57.8, 51.2, 43.9, 39.2, 34.5, 23.1, 17.2. EIMS *m/z* (%): 224 (M⁺, 2), 45 (100). HRMS: calcd for C₁₃H₁₈O₅ [M]⁺: 254.1154; found: 254.1141.

Methoxymethyl (3a*S*,6*R*,7*S*,7a*R*)-6,7a-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylic acid (23)

To a stirred solution of (±)-methoxymethyl (3aS,6R,7S,7aR)-6,7a-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylate (**32**) (29.3 mg, 0.115 mmol) in dichloromethane (5.0 mL) at RT under argon was added trifluoroacetic acid (90.6 μ L, 1.15 mmol). Stirring was continued for 6 h then the solvent was evaporated to give the crude product as a yellow oil. Chromatography of this material on silica with hexanes:ethyl acetate (10:1, 5:1 then 2:1:) then hexanes:ethyl acetate:methanol:acetic acid (50:50:0.5:0.5) gave the title compound (**23**) (21.4 mg, 0.102 mmol, 89%) as a



crystalline solid after recrystallisation from *tert*-butyl methyl ether. mp 157–160 °C. $R_f = 0.19$ (hexanes/ethyl acetate 2:1). IR (KBr) 2975, 2937, 2913, 2880, 1773, 1767, 1704, 1698 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.80 (dt, J = 9.9, 3.1 Hz, 1H), 5.68 (ddd, J = 9.9, 3.1, 2.4 Hz, 1H), 4.09 (dd, J = 11.9, 8.3 Hz, 1H), 4.54–4.47 (m, 1H), 3.59–3.46 (m, 1H), 2.70–2.55 (m, 1H), 2.48 (d, J = 3.1 Hz, 1H), 1.33 (d, J = 7.7 Hz, 3H), 1.06 (s, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 178.9, 178.2, 134.1, 122.1, 68.7, 50.8, 43.7, 39.0, 34.6, 23.3, 17.1. EIMS m/z (%): 211 (M+H⁺, 1), 121 (100). HRMS: calcd for C₁₁H₁₅O₄ [M+H]⁺: 211.0970; found: 211.0978.

Methoxymethyl (3aS,6R,7S,7aR)-6,7a-dimethyl-1-oxo-1,3,3a,6,7,7a-

hexahydro-7-isobenzofurancarboxylate (23-methyl ester)

To a stirred solution of (±)-methoxymethyl (3aS,6R,7S,7aR)-6,7a-dimethyl-1-oxo-1,3,3a,6,7,7a-hexahydro-7-isobenzofurancarboxylic acid (**23**) (8.9 mg, 0.042 mmol) in diethyl ether (5 mL) at -65 °C dropwise was added an ethereal solution of diazomethane¹² until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo* and the residues chromatographed on silica (hexanes:ethyl acetate 5:1 then 2:1) to give compound (**23-methyl ester**) (9.4 mg,



0.042 mmol, 100%) as a colourless oil. $R_f = 0.15$ (hexanes/ethyl acetate 5:1). IR (film): 3030, 2967, 2919, 2876, 2849, 1779, 1731 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 5.80 (dt, J = 9.7, 2.9 Hz, 1H), 5.67 (dt, J = 9.7, 2.9 Hz, 1H), 4.54–4.46 (m, 1H), 4.09 (dd, J = 12.1, 8.3 Hz, 1H), 3.71 (s, 3H), 3.65–3.52 (m, 1H), 2.59–2.47 (m, 1H), 1.29 (d, J = 7.5 Hz, 3H), 1.25 (d, J = 3.3 Hz, 1H), 1.06 (s, 3H). ¹³C NMR (68 MHz, CDCl₃): δ 178.0, 174.0, 134.1, 122.2, 68.5, 52.0, 51.2, 44.0, 39.3, 34.5, 23.0, 17.3. EIMS *m/z* (%): 224 (M⁺, 4), 121 (100). HRMS: calcd for C₁₂H₁₆O₄ [M]⁺: 224.1049; found: 224.1046.

8. Thermolyses of Sorbyl Citraconate Half Esters (Scheme 6)

Thermolysis of a 1:1 mixture of 9 and 10 in xylene under the conditions of White and Sheldon



A stirred solution of 1-((2E,4E)-2,4-hexadien-1-yl) 4'-hydrogen (2'Z)-3'-methyl-2'-butenedioate (**9**) and 1-((2E,4E)-2,4-hexadien-1-yl) 4'-hydrogen (2'Z)-2'-methyl-2'-butenedioate (**10**) (**9**:**10** (50:50)) (96.3 mg, 0.458 mmol) in xylene (3.98 mL) was warmed to reflux under argon and heating was continued for 15h.¹⁴ The solvent was evaporated, the residue was redissolved in CDCl₃ and proton NMR analysis

was carried out. The crude material contained compounds **11**, **21**, **22** and **23** (**11**:**21**:**22**:**23** (51:16:27:6)) (mass balance = 90.6 mg, 94%) as a yellow oil. To a stirred solution of the crude material in dichloromethane (8.3 mL) at RT under argon was added trifluoroacetic acid (155 μ L, 1.97 mmol). Stirring was continued for 24 h and then the solvent and trifluoroacetic acid were evaporated. The residue was redissolved in CDCl₃ and proton NMR analysis was carried out. The crude material contained compounds **11**, **21**, **22** and **23** (**11**:**21**:**22**:**23** (50:14:28:8)) (mass balance = 83.0 mg, 89%) as a yellow oil.



Thermolysis of 10 in xylene under the conditions of White and Sheldon

A stirred solution of 1-((2*E*,4*E*)-2,4-hexadien-1-yl) 4'-hydrogen (2'Z)-2'-methyl-2'-butenedioate (**10**) (16.7 mg, 0.0794 mmol) in xylene (0.69 mL) was warmed to reflux under argon and heating was continued for 15 h.¹⁴ The solvent was evaporated, the residue was redissolved in CDCl₃ and proton NMR analysis was carried out. The crude material contained compounds **11**, **21**, **22** and **23** (**11**:**21**:**22**:**23** (55:7:28:10)) as a yellow oil. To a stirred solution of the crude material in dichloromethane (1.7 mL) at RT under argon was added trifluoroacetic acid (31 µL, 0.39 mmol). Stirring was continued for 24 h and then the solvent and trifluoroacetic acid were evaporated. The residue was redissolved in CDCl₃ and proton NMR analysis was carried out. The crude material contained compounds 40c, 39c, 40d and 39d (**11**:**21**:**22**:**23** (53:11:29:7)) (mass balance = 15.2 mg, 91%) as a yellow oil.

Thermolysis of 9 in xylene under the conditions of White and Sheldon



A stirred solution 1-((2*E*,4*E*)-2,4-hexadien-1-yl) 4'-hydrogen (2'*Z*)-3'-methyl-2'-butenedioate (**9**) (69.6 mg, 0.331 mmol) in xylene (2.90 mL) was warmed to reflux under argon and heating was continued for 15 h.¹⁴ The solvent was evaporated, the residue was redissolved in CDCl₃ and proton NMR analysis was carried out. The crude material contained compounds **11**, **21**, **22** and **23** (**11**:21:22:23 (54:11:24:11)) as a yellow oil. To a stirred solution of the crude material in dichloromethane (7.0 mL) at RT under argon was added trifluoroacetic acid (129 μ L, 1.64 mmol). Stirring was continued for 24 h and then the solvent and trifluoroacetic acid were evaporated. The residue was redissolved in CDCl₃ and proton NMR analysis was carried out. The crude material contained compounds **11**, **21**, **22** and **23** (**11**:21:22:23 (11:21:22:23 (52:12:29:7)) (mass balance = 62.5 mg, 90%) as a yellow oil.



Mix and heat reaction between sorbyl alcohol (7) and citraconic anhydride (8)

A stirred solution (2*E*,4*E*)-2,4-hexadien-1-ol (**7**) (50.7 mg, 0.517 mmol) and citraconic anhydride (**8**) (46.3 μ L, 517 mmol) in xylene (4.50 mL) was warmed to reflux under argon and heating was continued for 15 h.¹⁴ The solvent was evaporated, the residue was redissolved in CDCl₃ and proton NMR analysis was carried out. The crude material contained compounds **11**, **21**, **22** and **23** (**11**:**21**:**22**:**23** (57:7:30:6)) as a yellow oil. To a stirred solution of the crude material in dichloromethane (10.9 mL) at RT under argon was added trifluoroacetic acid (202 μ L, 2.57 mmol). Stirring was continued for 24 h and then the solvent and trifluoroacetic acid were evaporated. The residue was redissolved in CDCl₃ and proton NMR analysis was carried out. The crude material contained compounds **11**, **21**, **22** and **23** (**11**:**21**:**22**:**23** (58:7:29:7)) (mass balance = 108.7 mg, 95%) as a yellow oil.

IMDA reaction of triene 10 in DMSO



Triene **10** (83.5 mg, 0.397 mmol) in DMSO (40 mL, 10 mM) was stirred at 120 °C for 16 h. After allowing to cool, the reaction mixture was concentrated *in vacuo*. The residue was diluted in THF (4 mL) and cooled to -78 °C with stirring. An ethereal solution of diazomethane was added dropwise until tlc confirmed the reaction had gone to completion. Excess diazomethane was removed by bubbling N₂ gas through the solution. The mixture was concentrated *in vacuo*, and the residues were chromatographed on silica (hexanes/ethyl acetate, 90:10 to 70:30) to give a mixture of cycloadducts **22-methyl ester** and **23-methyl ester** (51.5 mg, 58%; **22-methyl ester** : **23 methyl ester** = 8:92).

9. NMR Stacked Plots

Time course proton NMR thermolysis experiment on 10



To 1-((2*E*,4*E*)-2,4-hexadien-1-yl) 4'-hydrogen (2'*Z*)-2'-methyl-2'-butenedioate (**10**) (20.2 mg, 0.0961 mmol) was added d_8 -toluene (835 µL) under argon at RT. The resulting solution was transferred to an NMR tube and this was heated to 110 °C. At specific time intervals (0 min, 15 min, 30 min, 45 min, 60 min, 90 min, 2 h, 4 h, 8 h, 16 h, 24 h, 48 h, 70 h, 93 h and 140 h), the NMR tube was cooled rapidly by immersion in ice water and a proton NMR spectrum was recorded. Stack plots of these spectra are illustrated in the following Figure.



Time course proton NMR thermolysis experiment on 9



To 1-((2*E*,4*E*)-2,4-hexadien-1-yl) 4'-hydrogen (2'*Z*)-3'-methyl-2'-butenedioate (**9**) (18.8 mg, 0.0894 mmol) was added d_8 -toluene (777 µL) under argon at RT. The resulting solution was transferred to an NMR tube and this was heated to 110 °C. At specific time intervals (0 min, 15 min, 30 min, 45 min, 60 min, 90 min, 2 h, 4 h, 8 h, 16 h, 24 h, 48 h, 70 h, 93 h and 140 h), the reaction mixture was quenched in ice water and a proton NMR spectrum was recorded. Stack plots of these spectra are illustrated in the following Figure.



Example "Mix and Heat" NMR Experiment

Reaction between maleic anhydride and dienol 13 under conditions of Becher et al.¹³



NMR experiments were performed in order to provide evidence on mechanism of the reaction between maleic anhydride and a pentadienol (Scheme 1). It was hoped that the presence of either proposed intermediate **3** or proposed intermediate **4**

would be observed. Equimolar quantities of the dienol and maleic anhydride were dissolved in deuterated chloroform and the solution was placed in an NMR tube. The tube was heated to 55°C for 8.5 hours, with ¹H NMR spectra recorded at regular intervals. Only the starting materials and bicyclic lactone acid are observable by NMR, as illustrated in the following stack plot.



10. Pentadienyl Maleate IMDA Transition Structures (Figure 1 and Figure 2)

	endo-TS	exo-TS
	HF=-649.81764	HF=-649.81799
	ZPVE = 0.17827	ZPVE = 0.17815
	23	23
	C 1 36826502 0 99343039 0 59769348	C -1 02224814 -0 60511445 0 14020649
	C 0 65390430 2 11760896 0 17942606	C -1.04145542 1 53519676 1 57865690
	C = 0.70404048 + 2.21222000 + 0.40446422	C = 0.22010604 + 2.22644641 + 0.71248272
	C = 0.70494940 2.31233909 0.49440422 C = 1.42260246 1.40969079 1.22959102	C = 0.35010004 2.35044041 0.71246272 C = 0.02471758 1 07046228 0 17022622
	C = 1.45500240 1.40808078 1.25858102	C = 0.92471738 = 1.97040538 = 0.17953055
	C -0.99531720 -0.01454918 -0.10000155	C 1.48935500 0.75034488 0.49555215
	C 0.3934/1/0 -0.64152150 -0.26149026	C 0.2/165/53 -0.61936111 -0.3819/08/
	C 1.10328824 -0.39227071 -1.56306835	C 2.72262567 0.14113476 -0.12628878
	O 0.66114828 -0.63397426 -2.66123959	C 1.26288811 -1.71576556 -0.07404911
T T	O 2.35380278 0.13426973 -1.42120253	O 2.56191608 -1.29740322 -0.09890247
	C 2.66188979 0.61649386 -0.08731646	C -2.09622022 -0.02520839 -0.666663277
	C -1.64607332 -1.44539801 0.85812000	O -1.94866161 0.60426416 -1.70515289
	O -1.09193171 -1.96286969 1.81780447	O 0.99170169 -2.86959830 0.15101036
l H a l A l	O -2.98209443 -1.58483553 0.63931490	O -3.33334861 -0.27080283 -0.14627007
3-s-cis-syn	H 1.19463994 0.59679969 1.59452364	H -1.29503380 -1.22453711 0.98747388
	H 1.07488904 2.72640414 -0.62076214	H -0.56750278 0.79973304 2.21725324
	H -1.23551036 3.10161161 -0.03496528	H -2.07306215 1.76858609 1.82465927
	H -0 96342720 0 75004776 1 95918760	H -0 83411841 3 18898833 0 26267757
	H -2 51168875 1 51041253 1 32594064	H 1 30742273 2 53609047 -0 66867863
	H -1 60391918 -0 24091140 -0 97520296	H 1 31148753 0 36201709 1 50295358
	$H = 0.0353280 - 1.33462812 \pm 0.40832166$	H 0.36462507 -0.22620101 -1.30402763
	H 3 10846626 0 16627032 0 45057207	H = 3.63404162 + 0.220221111 + 1.57472705 H = 3.63404162 + 0.34202043 + 0.44474182
	H = 3.35040020 + 0.10027752 + 0.3557257 H = 3.33504004 + 1.46488880 + 0.23018561	H = 2.86802104 0.47328704 = 1.16007162
	$H = 2.22468552 = 2.15704071 \pm 2.5020117$	$H = 2.07602054 \ 0.12200702 \ 0.76420017$
	п-3.32406333-2.13/949/11.3303011/	n -3.97093034 0.12209793 -0.70429917
	IIE = 640.91524	IIE = 640.91549
	HF = -049.81534	HF = -049.81348
	ZPVE = 0.17823	ZPVE = 0.1/812
	22	22
	23	23
i j jo	C 1.06408283 1.2608/9/0 0.682/351/	C -0./5266885 -0.90896183 0.26838/88
0 0	C 0.35062797 2.19718088 -0.06685352	C -1.26546015 1.07132834 1.78406752
	C -1.05687053 2.23209193 -0.09138473	C -0.95929684 2.09103429 0.90786179
I Ĥ	C -1.83608911 1.34429341 0.62133057	C 0.26975328 2.17024646 0.21918712
2 o trono ovn	C -0.88948840 -0.75071157 -0.28366357	C 1.22936085 1.17354323 0.37986856
3-5- <i>11 ans-</i> 5yn	C 0.48186747 -0.61339421 -0.07099142	C 0.37935646 -0.48927160 -0.43409333
	C 1.44519131 -0.45030219 -1.21475554	C 2.48726282 1.01948623 -0.42886689

Cartesian coordinates and energies of B3LYP/6-31+G(d) optimized TS geometries.

	O 1.29436888 -0.89671708 -2.32709201	C 1.70360851 -1.21017157 -0.32944508
	O 2.57101920 0.25408516 -0.89991110	O 2.78679185 -0.39518900 -0.49155920
	C 2.51147454 0.96875666 0.36179065	C -2.10860450 -0.81414086 -0.27787301
	C -1.74989576 -1.53518939 0.60947852	O -3.09271767 -1.37155939 0.17952432
	O -2.86230793 -1.94746827 0.33418313	O 1.84740899 -2.39418810 -0.14927592
	O -1.18465340 -1.77094761 1.83716373	O -2.18926149 -0.03758289 -1.40443003
	H 0.70591227 0.99062898 1.67235166	H -0.65557515 -1.59002232 1.10709411
	H 0.87881248 2.73702769 -0.85277893	H -0.50509519 0.52414905 2.32802776
	H -1.53103144 2.84489583 -0.85576346	H -2.28047618 0.94036560 2.14713328
	H -1.48307288 0.88647513 1.53797871	H -1.76149739 2.74721999 0.57662382
	H -2.90714084 1.28723234 0.44935126	H 0.34463441 2.85725431 -0.62252296
	Н -1.30837669 -0.57254713 -1.26679897	H 1.31389645 0.72952993 1.37095704
	H 0.90069991 -1.12531895 0.79404329	H 0.20674709 -0.06471982 -1.42175820
	H 2.98552681 0.35960220 1.13914937	H 3.36155453 1.48090034 0.04067571
	H 3.11142056 1.87003659 0.20703120	H 2.37878741 1.41627205 -1.44559246
	H -1.82556591 -2.31128163 2.33456918	H -3.12061891 -0.07135026 -1.68927876
	HF=-649.80908	HF=-649.80882
	ZPVE = 0.17793	ZPVE = 0.17773
	23	23
1	C 1.18366947 1.19285283 0.61615075	C -0.62859091 -0.91662398 0.45442097
	C 0.25110987 2.18550050 0.30631791	C -1.05547188 1.25134421 1.82168607
	C -1.10051411 2.10320969 0.69291035	C -1.00693866 2.11971319 0.75331842
	C -1.60859575 1.03363601 1.39984477	C 0.07286621 2.16647043 -0.15430161
	C -0.86563998 -0.79074580 -0.15320018	C 1.14356953 1.28360352 -0.01826970
	C 0.49513428 -0.53691592 -0.30684196	C 0.36669911 -0.52082554 -0.44070445
	C 1.07123268 -0.08186403 -1.61899603	C 2.27704928 1.10543375 -0.99167398
	O 0.61644821 -0.33742055 -2.70950056	C 1.74941086 -1.12666033 -0.43883385
	O 2.20429902 0.66468937 -1.49651900	O 2.71406066 -0.27151428 -0.88381175
	C 2.48795270 1.11398172 -0.14475109	C -2.02940392 -0.86731365 0.00399307
	C -1.29473608 -1.79663169 0.83833431	O -2.40037804 -0.31068460 -1.01192597
0 0	O -0.61668191 -2.16127576 1.77944480	O 2.02566483 -2.25404119 -0.10839940
2-c-oic-anti	O -2.54583618 -2.31730603 0.67344488	O -2.95195906 -1.49664733 0.79468982
3-5-CIS-allu	H 1.14169436 0.71536300 1.59155844	H -0.36149580 -1.47983054 1.34489413
	H 0.50912464 2.91232667 -0.46401152	H -0.16508931 0.84123984 2.28321563
	H -1 79392253 2 81759080 0 25272051	H -1 97461178 1 13577906 2 38915866
	H -0.98812540.0.41879618.2.04043432	H -1 91458814 2 65136322 0 47770116
	H -2 68016427 0 93779252 1 55507713	H = 0.06590633 2.70545091 = 1.08991080
	H -1 55198176 -0 48190225 -0 93607754	H 1 42964875 1 02015254 0 99943331
	H 1 15974513 -1 15716455 0 29539526	H 0.00485595 -0.26498654 -1.43720243
	H 3 19040835 0 41571161 0 32249439	H 3 15561774 1 70976456 -0 74681860
	H 2 98012031 2 08310514 -0 26388868	H 1 97597154 1 31441710 -2 02514313
	H -2 95041046 -1 98925524 -0 14727626	H -2 51864745 -1 94110066 1 54244078
	11 2.95011010 1.9692521 0.11727620	11 2.51001715 1.51110000 1.51211070
	HF = -649.80054	HF = -649.80250
	ZPVE = 0.17764	ZPVE = 0.17756
	23	23
	C 1.29195017 1.15007926 0.58752382	C -0.95331987 -0.61136691 -0.40416317
	C 0.40253366 2.1/94858/ 0.2/8/1110	C -1./5082068 1.3924/669 0.86365992
	C -0.94659854 2.15311323 0.67734440	C -0.74486467 2.28879240 0.55589630
	C -1.49102333 1.10669919 1.39635544	C 0.62601216 2.00233808 0.73816897
	C -0.93391867 -0.70578368 -0.11732354	C 1.0168/036 0.75809446 1.22509044
	C 0.44288829 -0.58481040 -0.30543666	C 0.43235653 -0.58147373 -0.23853636
	C 1.02047904 -0.15902119 -1.62973140	C 2.41377738 0.20638547 1.26309724
	0.51757025 -0.36831382 -2.70701063	C 1.18099618 -1.66989138 0.49775482
	0 2.21338348 0.49643666 -1.53801518	0 2.31169241 -1.23115241 1.12597421
	C 2.56156245 0.96692846 -0.20938667	C -1.66061627 -0.14988173 -1.62107054
	C -1.60450/36 -1.68314112 0.77530857	U -2./3650869 -0.590/5256 -1.96196846
	O -2.79580794 -1.89796221 0.73632859	O 0.86607636 -2.83237757 0.53963663
3-s-trans-anti	0-0.84529801-2.34733522 1.70346785	U -1.04788812 0.79559341 -2.39968333
	H 1.24425040 0.68950455 1.57076415	H -1.53/90598 -1.3044/3/5 0.19239149
	H 0.67894995 2.87840131 -0.51059495	H -1.64172281 0.64265951 1.63795012
	H -1.62035908 2.87378873 0.21789052	H -2.77071192 1.58149258 0.54180628
	H -0.89242770 0.51636593 2.08097394	H -1.00249863 3.17170217 -0.02678578
	H -2.56529092 1.02772488 1.53354591	H 1.36071856 2.65434335 0.26632427
	Н -1.59532495 -0.31809404 -0.88350115	H 0.36737311 0.29827377 1.96848202
	H 1.122/4490 -1.23343474 0.25071133	H 1.03890513 -0.14606576 -1.03374448
	Н 3.23784291 0.24302968 0.25876867	H 2.91569510 0.37045442 2.22183157
	H 3.10825110 1.89986336 -0.37347745	H 3.04426976 0.60804419 0.46044902
	H 0.10238695 -2.18105065 1.57656359	H -0.28344476 1.18024246 -1.93976269

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