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2-Alkenyl dioxolanylium cations, new reactive dienophiles in low temperature asymmetric Diels–Alder reactions

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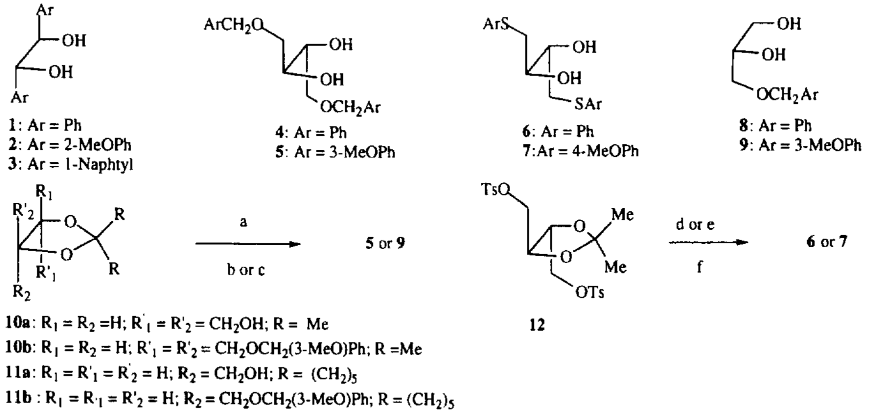
Abstract: Chiral orthoesters **14–22** were prepared by an exchange reaction with orthoester **13**. These compounds, after treatment with trimethylsilyltriflate or tin(IV) chloride, gave rise to vinyl dioxolanylium cations which proved to be very reactive dienophiles in various Diels–Alder reactions. © 1997, Elsevier Science Ltd. All rights reserved.

Some years ago, we reported efficient asymmetric Diels–Alder cycloadditions between camphor-derived oxazolinium intermediates and a wide variety of dienes[1]. The development of other types of cationic Diels–Alder reactions mediated by chiral cationic heterocycles seemed to be of interest with regard to the great reactivity of such species. In this respect, 2-alkenyl-1,3-dioxolane-2-ylium cations appeared to be promising candidates for such reactions. The use of 1,1-diethoxypropenylium cation generated from 3,3,3-triethoxypropene was first described by Gassman[2] and several other examples of Diels–Alder cycloadditions with vinyloxocarbenium as dienophiles have been recently reported[3–6]. Among the possible precursors of 1,3-dioxenium cations[7], 2-alkoxy-2-vinyl-1,3-dioxolanes appeared as easily accessible starting materials from chiral 1,2-diols. We report here the preparation of new chiral orthoesters and their use in asymmetric cationic Diels–Alder cycloadditions.

Nine enantiomerically pure 1,2-diols **1–9** were used in this study. Diols **1**, **2** and **3** were obtained using Sharpless asymmetric dihydroxylation[8,9,18,19] from the corresponding *E*-alkenes[10], whereas diols **4–9** were prepared according modification of known procedures[11,12] by the use of tartaric esters or 1,3-dioxolane **11a** as starting material (Scheme 1).



Scheme 1. a: NaH (1.6 eq.), $n\mathrm{Bu_4N^+I^-}$ (cat.), imidazole (cat.), 3-MeOPhCH$_2$Cl (1.23 eq.) THF, DMF, 2.5 h, 20°C. b: HCl (2N), THF, 2 days, 20°C. c: H_2SO_4 (2N), EtOH, 2 days, 100°C. d: NaH (4 eq.), PhSH (4 eq.), DMF, 3 h, 20°C. e: NaH (4 eq.), 4-MeOPhSH (4 eq.), DMF, 3 h, 20°C. f: HCl (2N), THF, 24 h, 70°C.

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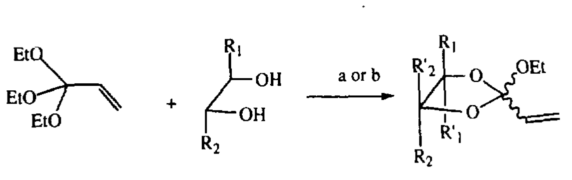
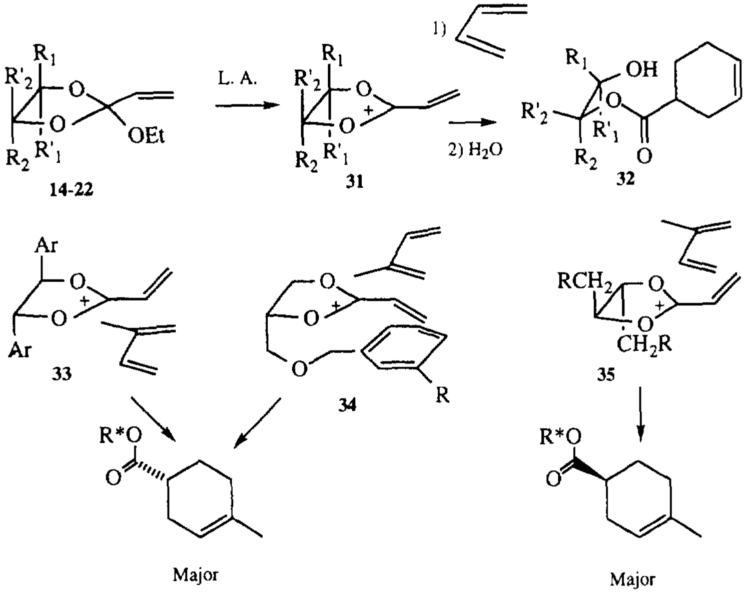


14: $R_1 = R_2 = Ph$; $R'_1 = R'_2 = H$
15: $R_1 = R_2 =$ 2-MeOPh ; $R'_1 = R'_2 = H$
16: $R_1 = R_2 =$ 1-Naphtyl ; $R'_1 = R'_2 = H$
17: $R_1 = R_2 = H$; $R'_1 = R'_2 = CH_2OBn$
18: $R_1 = R_2 = H$; $R'_1 = R'_2 = CH_2OCH_2(3\text{-}MeO)Ph$
19: $R_1 = R_2 = H$; $R'_1 = R'_2 = CH_2SPh$
20: $R_1 = R_2 = H$; $R'1 = R'2 = CH_2S(4\text{-}MeO)Ph$
21: $R_1 = R'_1 = R'_2 = H$; $R_2 = CH_2OBn$
22: $R_1 = R'_1 = R'_2 = H$; $R_2 = CH_2OCH_2(3\text{-}MeO)Ph$

Scheme 2. a: **13** (4 eq.), dioxane, 15 h, 80°C. b: **13** (20 eq.), $MgCl_2$ (0.25 eq.), CH_2Cl_2, 3 days, 20°C.



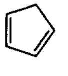
Scheme 3.

Chiral orthoesters were prepared following two procedures. In the first one, a mixture of diol and 3,3,3-triethoxypropene **13**[2] was heated in dioxane under a stream of argon in order to favor the formation of mixed orthoester by removing ethanol. However, better yields were generally obtained by mild exchange reaction catalyzed by magnesium dichloride[13] between diols **1–9** and 3,3,3-triethoxypropene **13** affording the corresponding orthoesters **14–22**. Because of their poor stability on silica gel or alumina, these compounds have been used in the following Diels–Alder reactions without any further purification (Scheme 2).

The Diels–Alder cycloadditions were performed in anhydrous dichloromethane with dienes **23–30** in the presence of various Lewis acids generally at low temperature (Scheme 3). Results and reaction conditions are summarized in Table 1.

In nearly all cases, cycloadditions were achieved within a few minutes. This observation reflects the high reactivity of dioxolanylium intermediates and contrasts with cycloadditions previously described by Gassman[2] using orthoester **13** as starting material. This difference of reactivity could well be the result of distortion of the bond angles in 1,1-diethoxy propenylium cation whereas a near planar arrangement occurred in the corresponding dioxanylium cation **31**, increasing interaction with the vinylic side chain and consequently the rate of cycloadditions[14]. Moreover, a competitive experiment

Table 1. Percentage yield (diastereomeric ratio). a: TMSOTf (0.5 equiv.), −78°C, 15 min. b: $SnCl_4$ (1.5 equiv.), −78°C, 30 min. c: $SnCl_4$, 20°C, 12 h. d: $TiCl_4$, −78°C, 15 min



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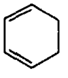

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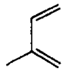

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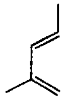

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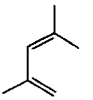

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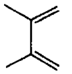

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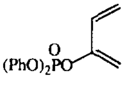

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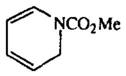

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Dienes Dienophiles	23	24	25	26	27	28	29	30
14	71^a (66:34)	74^a (66:34)	82^a (55:45)	67^a (55:45)	57^a (50:50)		20^c (50:50)	45^d (50:50)
15	64^b (69:31)	51^b (70:30)	65^b (63:37)	59^b (75:25)	42^b unpure	50^b (84:16)		
16			40^b (55:45)					
17			50^b (43:57)					
18			47^b (40:60)					
19			35^b (65:35)					
20			38^b (57:43)					
21	71^b (50:50)	71^b (50:50)	70^b (50:50)	55^b (50:50)	64^b (50:50)	54^b (50:50)		
22			65^b (50:50)					

performed between orthoesters **13** and **14** and 2-methylbutadiene **25** showed that adduct **14–25** was the only isolated product.

Trimethylsilyl triflate or tin(IV) chloride were generally the best activators with carbodienes. Yields were calculated for three steps, synthesis of orthoesters, cycloaddition and hydrolysis into esters. The modest yields observed with enolphosphate **29** and dihydropyridine **30** probably reflect the poor stability of these compounds in the presence of $SnCl_4$ or $TiCl_4$. In all cases *endo* adducts were obtained in more than 95% yield. The direction of the asymmetric induction was determined after reaction with an excess of MeMgBr for adducts **14–25** to **18–25** and comparison with (+)-terpineol and after reduction with $LiAlH_4$ for adducts **14–23** and **14–24** and comparison with the known alcohols[15,16]. The diastereoselectivities were measured by ^2H NMR in the presence of polybenzyl glutamate[17] for adducts **15–23** to **15–28** on the corresponding primary deuterated alcohols after reduction with $LiAlD_4$.

Cationic dienophiles derived from orthoesters **21** and **22** showed no diastereoselectivity. This feature could be due to the lack of electronic interaction between the dioxenium cation and the aromatic moiety and/or to poor control of the *s*-cis–*s*-trans equilibrium in cationic intermediate **34** in the transition state (Scheme 3). Moreover, analysis of the resulting esters adducts is complicated by the concomitant formation of primary and secondary esters. The problem of conformational equilibrium was overcome with orthoesters **14–16** and **17–20** which gave rise respectively to C-2 symmetric dioxenium cations **33** or **35** and a single ester after hydrolysis.

Two types of interaction have been examined in these cases. With orthoesters **14** and **16** purely steric interactions did not induce significant asymmetric induction. We tried to increase this sort of interaction, but the preparation of such diols became problematic. Thus, (*E*)-1,2-di(9-anthryl)ethylene was nearly insoluble and the Sharpless dihydroxylation failed with this compound. On the other hand, dihydroxylation of (*E*)-1,2-di[1-(2,4,6-trimethyl)phenyl]ethylene needed a stoichiometric amount of osmium tetroxide. The poor reactivity of this compound decreases the interest in the resulting diol as a chiral auxiliary.

Better results were observed with orthoester **15** as starting material. It is still not possible to attribute this better selectivity to steric or electronic factors. Possible electronic interactions betweeen lone pairs of oxygens of ethers and dioxolanylium cation could be postulated. For this reason, we also studied these cationic cycloadditions with orthoesters **17–20** as starting material. However, with 2-methyl butadiene no significant diastereoselectivity was observed. The anticipated interaction between lone pairs of oygens or sulfurs is probably overcome by the conformational mobility of the side chains.

In conclusion, we described an easy access to 2-alkenyl chiral orthoesters. These compounds in the presence of Lewis acids gave rise at low temperature to 2-vinyl dixolanylium cations, very reactive species in Diels–Alder cycloadditions. This feature warrants further studies to increase the diastereoselectivity of such cycloadditions with various analogues of orthoester **15**.

Experimental

General, see ref. 1c. NMR of mixtures are annoted (*M*) for the major diastereoisomer and (*m*) for the minor diastereoisomer if the corresponding protons are separated. In the case of equal mixtures, NMR are annoted (*A*) and (*B*) for differently attributed protons.

Preparation of **5**: To a solution of diol **10a** (219 mg, M=162 g/mol, 1.35 mmol) in THF (6.3 ml) and DMF (1.4 ml), was slowly added at 0°C sodium hydride 55% dispersed in mineral oil (191 mg, M=24 g/mol, 4.4 mmol, 1.6 eq.). After stirring at room temperature for 15 min, catalytic amounts of $nBu_4N^+I^-$ and imidazole were added successively, and finally 3-MeOPhCH_2Cl (485 µl, M=156.6 g/mol, 3.3 mmol, 1.23 eq.). After 3 h at room temperature, methanol (3 ml) was slowly added. The reaction mixture was evaporated to dryness and then purification by silica gel column chromatography (pentane then pentane 20/AcOEt 1, 15/1, 10/1, 5/1) gave **10b** (434 mg, M=402 g/mol, 1.08 mmol, 80%). To a solution of **10b** (488 mg, M=402 g/mol, 1.21 mmol) in THF (4.6 ml) was added HCl 2N (4.6 ml). After stirring at room temperature for 2 days, reaction mixture was diluted with dichloromethane (15 ml) and potassium carbonate (1.38 g) was slowly added. After filtration on cotton plug and evaporation to dryness, crude residue was extracted with dichloromethane (25 ml), dried on sodium sulfate. After filtration, evaporation to dryness afforded desired **5** (391 mg, M=362 g/mol, 1.08 mmol, quantitative). **5**: ^1H NMR: 7.25 (dd, $J_{\text{meta-ortho}}$=8.3, $J_{\text{meta-para}}$=8.3, 2H meta-OMe), 6.90–6.73 (m, aromatics), 4.57 (s, $2CH_2Ar$), 3.92 (m, C-2H+C-3H), 3.83 (s, 2OMe), 3.74 (dd, J=9.4, J=3, 2H, 2 CHaO), 3.64 (dd, J=9.4, J=4.2, 2H, 2CHbO). $[\alpha]^{23}{}_D=-4.7$ (c 7.2, $CHCl_3$). Anal. found: C 66.12% H 7.43%. Calcd. for $C_{20}H_{26}O_6$,C 66.28% H 7.23%.

Preparation of **6**: To freshly distilled DMF (2.5 ml) under argon were added sodium hydride 50% dispersed in mineral oil (408 mg, M=24 g/mol, 8.5 mmol, 4 eq.) and then dropwise thiophenol (870 µl, M=110 g/mol, 8.5 mmol, 4 eq.) at −10°C. After stirring for 20 min at −10°C, a solution of **12** (1 g, M=470 g/mol, 2.1 mmol) in DMF (2.5 ml) was added and reaction mixture was warmed up to room temperature. After stirring for 3 h, methanol (6 ml) was slowly added at 0°C. Reaction mixture was evaporated to dryness (with a vacuum pump to remove the excess of thiophenol). The resulting white residue was extracted with ethyl acetate (100 ml) and the organic phase was washed with brine (20 ml), dried on sodium sulfate, filtered and evaporated to dryness to give a yellow oil which was used for the next step without any further purification. To a solution of the crude compound in THF (45 ml) was added HCl 2N (25 ml) and reaction mixture was heated under reflux for 24 h. After cooling down to room temperature, sodium bicarbonate (4.56 g) was slowly added. The organic phase was washed with brine (60 ml). Aqueous phase was re-extracted with dichloromethane (2×200 ml) and with ethyl acetate (100 ml). Combined organic phases were evaporated under dryness and purified by silica gel column chromatography with heptane/AcOEt 2/1 to 1/10 to give desired diol **6** (456 mg, M=306 g/mol, 1.49 mmol, 71% on two steps). **6**: ^1H NMR: 7.37–7.14 (m, aromatics), 3.70 (m, C-2H+C-3H), 3.08 (2 overlapped dd, $2CH_2SPh$), 2.57 (d, 2OH). $[\alpha]^{20}{}_D=+29$ (c 0.4, $CHCl_3$). Anal. found: C 61.82% H 5.96%. Calcd. for $C_{16}H_{18}S_2O_2$+0.25 mol. H_2O: C 61.80% H 5.99%.

Preparation of **7**: To freshly distilled DMF (2.5 ml) under argon were successively added sodium hydride 50% dispersed in mineral oil (408 mg, M=24 g/mol, 8.5 mmol, 4 eq.) and then dropwise

4-methoxythiophenol (1 ml, M=140 g/mol, 8.5 mmol, 4 eq.) at −10°C. After stirring for 20 min at −10°C, a solution of **12** (1 g, M=470 g/mol, 2.1 mmol) in DMF (2.5 ml) was added and reaction mixture was warmed up to room temperature. After stirring for 3 h, methanol (6 ml) was slowly added at 0°C. Reaction mixture was evaporated to dryness (with a vacuum pump to remove the excess of 4-methoxythiophenol). The resulting residue was extracted with ethyl acetate (100 ml) and the organic phase was washed with brine (20 ml), dried on sodium sulfate, filtered and evaporated to dryness to give a yellow oil which was used for the next step without any further purification. To a solution of the crude compound in THF (45 ml) was added HCl 2N (25 ml) and reaction mixture was heated under reflux for 24 h. After cooling down to room temperature, sodium bicarbonate (4.56 g) was slowly added. The organic phase was washed with brine (60 ml). Aqueous phase was re-extracted with dichloromethane (2×200 ml) and with ethyl acetate (100 ml). Combined organic phases were evaporated under dryness and purified by silica gel column chromatography with heptane/AcOEt 2/1 to 1/10 to give desired diol **7** (646 mg, M=366 g/mol, 1.76 mmol, 84% on two steps). **7**: ^{1}H NMR (250 MHz): 7.35 (d, 4H ortho-SR), 6.80 (d, 4H ortho-MeO), 3.75 (s, 2MeO), 3.55 (m, C-2H+C-3H), 2.95 (2 overlapped dd, $2CH_2SPh$), 2.60 (d, 2OH). $[\alpha]^{20}_D$=+29.5 (c 0.25, $CHCl_3$). Anal found: C 58.93% H 6.13%. Calcd. for $C_{18}H_{22}S_2O_4$: C 58.99% H 6.05%.

Preparation of **9**: To a solution of **11a** (10 g, M=172 g/mol, 58.1 mmol) in THF (270 ml) and DMF (60 ml), was added sodium hydride 55% dispersed in mineral oil (4.1 g, M=24 g/mol, 94 mmol, 1.6 eq.). After stirring at room temperature for 20 min, were added successively $nBu_4N^+I^-$ and imidazole (catalytic amounts) and finally $3\text{-}MeOPhCH_2Cl$ (10.4 ml, M=156.6 g/mol, 71.5 mmol, 1.23 eq.). After 2 h at room temperature, methanol (60 ml) was slowly added. Reaction mixture was evaporated to dryness, then dichloromethane (400 ml) and water (100 ml) were added. Organic phase was dried on magnesium sulfate and after evaporation affording crude **11b**. After dissolution in ethanol (60 ml) **11b** was treated with sulfuric acid 2M (150 ml) and reaction mixture was heated up to 100°C for 2 days. After cooling down to room temperature, potassium carbonate (20 g) was slowly added. Solid precipitate was removed by filtration, followed by evaporation to dryness gave a residue which was dissolved in dichloromethane (500 ml). After washing with water (20 ml), organic phase was dried on solid potassium carbonate, filtered and evaporated to dryness. Desired **9** (9.8 g, M=212 g/mol, 80%) was obtained after distillation (140–145°C/0.2 mm Hg). **9**: ^{1}H NMR: 7.27 (dd, $J_{\text{meta-ortho}}$=8.3Hz, $J_{\text{meta-para}}$=8.3Hz, H meta-OMe), 6.94–6.79 (m, aromatics), 4.52 (s, CH_2Ar), 3.96–3.48 (m, C-$1H_2$+C-2H+C-$3H_2$), 3.81 (s, OMe), 3.20 (s, OH), 2.82 (s, OH). $[\alpha]^{23}_D$=−4.5 (c 18.0, $CHCl_3$). Anal. found: C 62.34% H 7.76%. Calcd. for $C_{10}H_{14}O_4$: C 62.25% H 7.60%.

General procedure for the preparation of orthoesters

Procedure A

To a solution of diol (1 mmol) in freshly distilled *p*-dioxane (2.1 ml) was added 3,3,3-triethoxypropene **13** (726 µl, M=174 g/mol, d 0.959, 4 mmol). Reaction mixture was heated at 80°C until tlc check showed disappearance of starting material (typically 15 h). After evaporation to dryness (with a vacuum pump to remove the excess of 3,3,3-triethoxypropene) orthoesters were used without any further purification.

Procedure B

To a solution of 3,3,3-triethoxypropene **13** (3.5 ml, M=174 g/mol, d 0.959, 19.5 mmol) in dichloromethane (2.2 ml) under argon was added magnesium chloride (24 mg, M=95 g/mol, 250 µmol). After stirring for 15 min at room temperature a solution of diol (1 mmol) in dichloromethane (2.2 ml) was added. Reaction mixture was typically stirred at room temperature for 3 days (until tlc check showed disappearance of starting material). After evaporation to dryness (with a vacuum pump to remove the excess of 3,3,3-triethoxypropene), orthoesters were used without any further purification.

Orthoesters **16**, **18** to **20** were contaminated with unidentified by-products and gave no clean NMR, but could nevertheless be used for Diels–Alder reactions.

14: ^{1}H NMR (C_6D_6, 250 MHz): 7.60–7.13 (m, aromatics), 6.52 (dd, $J_{trans}=17.2$, $J_{cis}=10.6$, $C\mathit{H}=CH_2$), 6.11 (dd, $J_{tgem}=1.3$, $CH=C\mathit{H}_2$ cis to the orthoester function), 5.46 (dd, $CH=C\mathit{H}_2$ trans to the orthoester function), 5.36 (d, C-4H), 5.17 (d, C-5H), 4.12 (m, OCH_2), 1.50 (t, Me). ^{13}C NMR (C_6D_6, 62.96 MHz): 136.5 ($\mathit{C}H=CH_2$), 134.7 ($CH=\mathit{C}H_2$), 127.9, 127.7, 127.3, 126.9, 126.5, 126.4 (aromatics), 115.9 (C-2), 85.9, 85.3 (C-4+C-5), 57.5 ($O\mathit{C}H_2CH_3$), 14.9 ($OCH_2\mathit{C}H_3$).

15: ^{1}H NMR (C_6D_6, 250 MHz): 8.08 (dd, $J_{meta}=1.8$, $J_{ortho}=7.5$, H ortho-MeO), 7.82 (dd, $J_{meta}=1.8$, $J_{ortho}=7.5$, H ortho-MeO), 7.12–6.85 (m, aromatics), 6.28 (dd, $J_{trans}=17.2$, $J_{cis}=10.4$, $C\mathit{H}=CH_2$), 5.88 (d, J=8.7, C-4H), 5.87 (dd, $J_{gem}=1.9$, $CH=C\mathit{H}_2$ cis to the orthoester function), 5.72 (d, J=8,7, C-5H), 5.16 (dd, $CH=C\mathit{H}_2$ trans to the orthoester function), 3.93 (m, $OC\mathit{H}_2CH_3$), 2.93 (s, OMe), 2.88 (s, OMe), 1.20 (t, Me). ^{13}C NMR (C_6D_6, 62.96 MHz): 157.8 ($\mathit{C}H=CH_2$), 135.8 ($CH=\mathit{C}H_2$), 129.0–127.0 (aromatics meta-OMe), 120.8 (aromatics para-OMe), 116.1 (C-2), 110.1 (aromatics ortho-OMe), 80.1, 79.2 (C-4+C-5), 58.0 ($O\mathit{C}H_2CH_3$), 15.6 ($OCH_2\mathit{C}H_3$).

17: ^{1}H NMR (C_6D_6, 250 MHz): 7.31–7.02 (m, aromatics), 6.10 (dd, $J_{trans}=17.4$, $J_{cis}=10.4$, $C\mathit{H}=CH_2$), 5.72 (dd, $J_{gem}=2.3$, $CH=C\mathit{H}_2$ cis to the orthoester function), 5.06 (dd, $CH=C\mathit{H}_2$ trans to the orthoester function), 4.47–3.33 (m, 2 $C\mathit{H}_2OBn$+C-4H+C-5H+$OC\mathit{H}_2$), 4.28 (2 overlapped d, 2$C\mathit{H}_2Ph$), 1.10 (t, 2Me).

21: ^{1}H NMR (C_6D_6, 250 MHz), diastereomeric ratio 52:48: 7.25–7.03 (m, aromatics), 6.07 (dd, $J_{trans}=16.7$, $J_{cis}=10.8$, $C\mathit{H}=CH_2$ (*M*)), 6.03 (dd, $J_{trans}=16.7$, $J_{cis}=10.8$, $C\mathit{H}=CH_2$ (*m*)), 5.68 (dd, $J_{gem}=1.9$Hz, $CH=C\mathit{H}_2$ cis to the orthoester function (*M*)), 5.61 (dd, $J_{gem}=1.9$Hz, $CH=C\mathit{H}_2$ cis to the orthoester function (*m*)), 5.05 (dd, $CH=C\mathit{H}_2$ trans to the orthoester function (*M*)), 5.04 (dd, $CH=C\mathit{H}_2$ trans to the orthoester function (*m*)), 4.33 (m, C-4H), 4.25 (2 overlapped d, $C\mathit{H}_2Ph$), 4.00–3.13 (m, C-5H_2+OCH_2+$OC\mathit{H}_2CH_3$), 1.13 (t, 2Me).

22: ^{1}H NMR (C_6D_6, 250 MHz), diastereomeric ratio 52:48: 7.13–6.68 (m, aromatics), 6.06 (dd, $J_{trans}=17.7$, $J_{cis}=11.2$, $C\mathit{H}=CH_2$ (*M*)), 6.03 (dd, $J_{trans}=17.7$, $J_{cis}=11.2$, $C\mathit{H}=CH_2$ (*m*)), 5.69 (dd, $J_{gem}=2.0$, $CH=C\mathit{H}_2$ cis to the orthoester function (*M*)), 5.62 (dd, $J_{gem}=2.0$, $CH=C\mathit{H}_2$ cis to the orthoester function (*m*)), 5.05 (dd, $CH=C\mathit{H}_2$ trans to the orthoester function (*M*)), 5.04 (dd, $CH=C\mathit{H}_2$ trans to the orthoester function (*m*)), 4.33 (m, H4), 4.28 (2 overlapped d, $C\mathit{H}_2Ph$), 4.02–3.15 (m, C-5H_2+OCH_2+$OC\mathit{H}_2CH_3$), 3.34 (s, OMe), 1.12 (t, 2Me).

General procedure for the low temperature Diels–Alder reactions

To a solution of orthoester (1 mmol, unpurified from the diol, see procedure A or B) and diene (4 mmol) in anhydrous dichloromethane (8 ml) at −78°C under argon, was added dropwise tin(IV) chloride 1M in solution in dichloromethane (1.3 ml, 1.3 eq./orthoester). After stirring for 15–30 min, reaction mixture was diluted with dichloromethane (20 ml) and after addition of saturated sodium bicarbonate (3.6 ml), was allowed to warm up to room temperature. Organic phase was dried on sodium sulfate, filtered and evaporated to dryness. Desired cycloadducts were obtained by silica gel column chromatography with heptane, heptane/AcOEt 8/1 to 1/2.

14–23: Yield 71% (66:34) Major diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz) Major diastereoisomer: 7.37–7.08 (m, aromatics), 6.15 (dd, J=5.7, J=3.0, C-5H), 5.79 (d, J=6.5, $PhC\mathit{H}OCO$), 5.62 (dd, J=3.0, C-6H), 4.95 (dd, J=3.2, $PhC\mathit{H}OH$), 3.22 (m, C-1H), 3.02 (ddd, J=3.9, J=9.2, J=7.8, C-2H), 2.90 (m, C-4H), 2.45 (d, OH), 1.86 (ddd, J=3.6, C-3Ha), 1.42 (ddd, J=2.0, J=2.0, J=8.2, C-7Ha), 1.37 (ddd, J=12.9, J=2.8, C-3Hb), 1.25 (ddd, J=3.5, C-J=3.5, 7Hb). ^{13}C NMR ($CDCl_3$, 62.96 MHz): 172.8 (C=O), 137.8 (C-5), 132.2 (C-6), 128.2–126.9 (aromatics), 79.7, 77.1 ($Ph\mathit{C}HOCO$, $Ph\mathit{C}HOH$), 49.7 (C-7), 46.1 (C-2), 43.4 (C-5), 42.5 (C-4), 29.1 (C-3). Minor diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): 7.37–7.08 (m, aromatics), 6.10 (dd, J=5.7, J=3.0, C-5H), 5.77 (d, J=6.5, $PhC\mathit{H}OCO$), 5.61 (dd, J=3.0, C-6H), 4.93 (dd, J=3.2, $PhC\mathit{H}OH$), 3.28 (m, C-1H), 3.07 (ddd, J=3.9, J=9.2, J=7.8, C-2H), 2.90 (m, C-4H), 2.58 (d, OH), 1.92 (ddd, J=3.6, C-3Ha), 1.42 (ddd, J=2.0, J=2.0, J=8.2, C-7Ha), 1.37 (ddd, J=12.9, J=2.8, C-3Hb), 1.25 (ddd, J=3.5, J=3.5, C-7Hb). ^{13}C NMR ($CDCl_3$, 62.96 MHz): 178.6 (C=O), 137.8 (C-5), 132.2 (C-6), 128.1–126.9 (aromatics), 79.7, 77.1 ($Ph\mathit{C}HOCO$, $Ph\mathit{C}HOH$), 49.7 (C-7), 46.1 (C-2), 43.4 (C-5), 42.7 (C-4), 29.1 (C-3).

14–24: Yield 74% (66:34): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.25–7.01 (m, aromatics), 6.24 (2 overlapped dd, J=6.8, J=6.8, C-5H), 5.98 (2 overlapped dd, J=6.5, C-6H), 5.81 (d, J=7.0, PhC*H*OCO(*M*)), 5.73 (d, J=7.6, PhC*H*OCO(*m*)), 5.07 (broad s, OH(*M*)), 5.03 (broad s, OH(*m*)), 4.90 (2 overlapped dd, PhC*H*OH), 2.92 (m, C-1H), 2.68 (2ddd, C-2H), 2.56 (m, C-4H), 1.82–0.87 (m, C-3H$_2$+C-7H$_2$+C-8H$_2$)

14–25: Yield 82% (55:45): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.27–7.05 (m, aromatics), 5.88 (d, J=6.9, PhC*H*OCO(*m*)), 5.86 (d, J=7.4, PhC*H*OCO(*M*)), 5.38 (m, C-3H), 4.94 (2 overlapped dd, J=2.8, PhC*H*OH), 2.60 (m, C-1H), 2.53 (d, OH(M)), 2.49 (d, OH(*m*)), 2.23 (m, C-2H$_2$), 1.97 (m, C-5H$_2$), 1.73 (m, C-6H$_2$), 1.58 (s, Me).

14–26: Yield 67% (55:45): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.27–7.06 (m, aromatics), 5.86 (2 overlapped d, J=6.6(*m*), J=7.4(*M*), PhC*H*OCO), 5.36 (m, C-3H), 4.96 (2 overlapped dd, PhC*H*OH), 2.72 (m, C-1H), 2.59 (d, J=3.1, OH(*M*)), 2.49 (d, J=3.6, OH(*m*)), 1.94 (m, C-2H+C-5H$_2$), 1.73 (m, C-6H$_2$), 1.57 (s, C-4Me), 0.76 (d, J=6.8, C-2Me(*m*)), 0.64 (d, J=6.9, C-2Me(*M*)).

14–27: Yield 57% (50:50): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.35–7.13 (m, aromatics), 5.97 (d, J=7, PhC*H*OCO(*A*)), 5.90 (d, J=7, PhC*H*OCO(*B*)), 5.12 (m, C-3H), 4.99 (2 overlapped dd, PhC*H*OH), 2.65 (d, J=3, OH(*B*)), 2.55 (d, J=3, OH(*A*)), 2.47 (m, C-1H), 1.96 (m, C-5H$_2$), 1.83 (m, C-6H$_2$), 1.58 (s, C-4Me), 0.95 (s, 2 C-2Me(*A*)), 0.86 (s, 2 C-2Me(*B*)).

14–29: Yield 20% (50:50): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.43–7.07 (m, aromatics), 5.90 (2 overlapped dd, PhC*H*OCO), 4.98 (2 overlapped dd, J=7, J=7, PhC*H*OH), 4.65 (m, C-3H), 2.62 (m, C-1H), 2.59 (2 overlapped dd, OH), 2.37 (m, C-2H$_2$), 2.08 (m, C-5H$_2$), 1.78 (m, C-6H$_2$).

14–30: Yield 45% (50:50): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.39–7.00 (m, aromatics), 6.38 (2 overlapped dd, C-7H), 6.10 (2 overlapped dd, C-8H), 5.83 (m, PhC*H*OCO), 5.18 (m, C-1H), 4.95 (m, PhC*H*OH), 3.75 (s, OMe(*A*)), 3.71 (s, OMe(*B*)), 3.26 (m, C-3H$_2$), 2.93 (m, C-6H), 2.83 (m, C-4H), 1.83 (m, C-5H$_2$).

15–23: Yield 64% (69:31): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.39–6.46 (m, aromatics), 6.08 (2 overlapped dd, J=5.4, J=2.7, C-5H), 5.67 (m, ArC*H*OCO), 5.52 (2 overlapped dd, J=3, C-6H), 5.15 (dd, J=J=6, ArC*H*OH(*M*)), 5.10 (dd, J=J=6.4, ArC*H*OH(*m*)), 3.83 (s, OMe(*M*)), 3.79 (s, OMe (*m*)), 3.64 (s, OMe (*M*)), 3.55 (s, OMe (*m*)), 3.19 (m, C-1H), 2.99 (2ddd, C-2H), 2.93 (d, OH), 2.87 (m, C-4H), 1.83 (ddd, C-3Ha), 1.41 (m, C-7Ha), 1.27 (m, C-3Hb+C-7Hb).

15–24: Yield 51% (70:30): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.43–6.64 (m, aromatics), 6.53 (d, J=J=5.7, ArC*H*OCO(*M*)), 6.48 (d, J=6.6, J=6.6, ArC*H*OCO(*m*)), 6.25 (2 overlapped dd, J=7.2, J=7.2, C-5H), 6.03 (dd, J=6.5, C-6H(*m*)), 5.94 (dd, J=7.2, C-6H(*M*)), 5.13 (d, J=7.4, ArC*H*OH(*m*)), 5.10 (d, J=7.4, ArC*H*OH(*M*)), 3.83 (s, OMe(*M*)), 3.78 (s, OMe (*m*)), 3.60 (s, OMe (*M*)), 3.56 (s, OMe (*m*)), 3.13 (d, OH(*m*)), 2.98 (d, OH(*M*)), 2.94 (m, C-1H), 2.69 (m, C-2H), 2.56 (m, C-4H), 1.68 (m, C-3H$_2$), 1.46 (m, C-7Ha), 1.27 (C-7Hb+C-8H$_2$).

15–25: Yield 65% (63:37): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.37–6.52 (m, aromatics), 7.08 (2 overlapped d, J=6.9, ArC*H*OCO(*M*+*m*)), 5.34 (m, C-3H), 5.08 (2 overlapped dd, J=7.2, J=7.5, ArC*H*OH(*M*+*m*)), 3.81 (s, OMe), 3.56 (s, OMe), 3.06 (d, OH(*m*)), 3.05 (d, OH(*M*)), 2.53 (m, C-1H), 2.17 (m, C-2H$_2$), 1.94 (m, C-5H$_2$), 1.68 (m, C-6H$_2$), 1.63 (s, Me).

15–26: Yield 59% (75:25): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.43–6.64 (m, aromatics), 6.58 (d, J=6.8, ArC*H*OCO(*M*)), 6.56 (d, J=6.8, ArC*H*OCO(*m*)), 5.35 (m, C-3H), 5.12 (2 overlapped dd, J=7.7, ArCHOH(*M*+*m*)), 3.82 (s, OMe), 3.58 (s, OMe), 3.17 (2 overlapped d, OH(*M*+*m*)), 2.67 (m, C-1H), 1.94 (m, C-2H$_2$+C-5H$_2$), 1.75 (m, C-6H$_2$), 1.64 (s, C-4Me), 0.83 (d, J=6.6, C-2Me(*m*)), 0.65 (d, J=6.6, C-2Me(*M*)).

15–28: Yield 50% (84:16): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.41–6.67 (m, aromatics), 6.58 (2 overlapped d, J=6.2, ArC*H*OCO(*M*+*m*)), 5.13 (2 overlapped dd, J=7.6, ArC*H*OH(*M*+*m*)), 3.84 (s, OMe), 3.61 (s, OMe), 3.08 (2 overlapped d, OH(*M*+*m*)), 2.58 (m, C-1H), 2.13 (m, C-2H$_2$), 1.97 (m, C-5H$_2$), 1.63 (m, C-6H$_2$+C-3Me+C-4Me).

16–25: Yield 40% (55:45): ^{1}H NMR (CDCl$_3$, 250 MHz): 8.08–7.22 (m, aromatics), 6.91 (2 overlapped d, J=7, ArC*H*OCO(*M*+*m*)), 5.89 (2 overlapped dd, J=1, ArC*H*OH(*M*+*m*)), 5.35 (m, C-3H), 2.67 (m, C-1H), 2.22 (m, C-2H$_2$), 1.97 (m, C-5H$_2$), 1.73 (m, C-6H$_2$), 1.63 (s, C-4Me).

17–25: Yield 50% (43:57): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.37–7.24 (m, aromatics), 5.36 (m, C-3H), 5.17 (m, C*H*OCO), 4.57 (d, J=11.9, C*Ha*Ph), 4.51 (s, C*H*$_2$Ph), 4.48 (d, J=11.9, C*Hb*Ph), 4.11 (m, C*H*OH), 3.74 (dd, J=10.6Hz, J=4.6Hz, COOCHC*Ha*OBn), 3.65 (dd, J=4.6Hz, COOCHC*Hb*OBn), 3.49 (m, C*H*$_2$OBn), 2.71 (d, J=4.9, OH(*m*)), 2.69 (d, J=4.9, OH(*M*)), 2.54 (m, C-1H), 2.20 (m, C-2H$_2$), 1.97 (m, C-5H$_2$), 1.74 (m, C-6H$_2$), 1.65 (s, Me).

18–25: Yield 47% (40:60): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.25 (2dd, J=7, J=7, aromatic C-5H), 6.92–6.75 (m, aromatics), 5.33 (m, C-3H), 5.17 (m, C*H*OCO), 4.48 (s, 2OC*H*$_2$Ar), 4.11 (m, C*H*OH), 3.79 (s, 2OMe), 3.68 (m, COOCHC*Ha*OBn), 3.65 (dd, J=4.6, COOCHC*Hb*OBn), 3.50 (m, C*H*$_2$OBn), 2.69 (d, J=5, OH(*m*)), 2.67 (d, J=5, OH(*M*)), 2.53 (m, C-1H), 2.19 (m, C-2H$_2$), 1.95 (m, C-5H$_2$), 1.71 (m, C-6H$_2$), 1.61 (s, Me).

19–25: Yield 35% (65:35): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.48–7.24 (m, aromatics), 5.34 (m, C-3H), 5.05 (m, C*H*OCO), 3.99 (m, C*H*OH), 3.20 (m, COOCHC*H*$_2$SPh), 2.93 (m, CH$_2$SPh), 2.65 (m, C-1H), 2.33 (m, C-2H$_2$), 1.97 (m, C-5H2), 1.88 (m, C-6H$_2$), 1.62 (s, Me).

20–25: Yield 38% (57:43): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.31 (dd, J=8.6, aromatics, C-2H, C-6H), 6.81 (dd, J=8.6, J=3.6, aromatics, C-3H, C-5H), 5.33 (m, C-3H), 4.95 (m, C*H*OCO), 4.12 (m, C*H*OH), 3.79 (s, 2OMe), 3.12 (2 overlapped dd, J=13.4, J=7.0, COOCHC*Ha*SAr), 3.03 (2 overlapped dd, J=6.7, COOCHC*Hb*SAr), 2.86 (2 overlapped dd, J=13.4, J=7.9, C*Ha*SAr), 2.73 (2 overlapped dd, J=8.3, C*Hb*SAr), 2.47 (m, C-1H), 2.17 (m, C-2H2), 1.96 (m, C-5H2), 1.70 (m, C-6H2), 1.63 (s, Me).

21–23a (primary ester): Yield 71% (50:50): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.52–7.25 (m, aromatics), 6.18 (dd, J=5.6, J=3.0, C-5H), 5.92 (dd, J=3, C-6H), 4.57 (s, OC*H*$_2$Ph), 4.14 (m, C*H*$_2$OCO), 4.04 (m, C*H*OH), 3.55 (dd, J=4.4, J=10.5, C*Ha*O), 3.48 (dd, J=5.7, C*Hb*O), 3.21 (m, C-1H), 2.98 (ddd, J=3.8, J=9.5, J=8.6, C-2H), 2.93 (m, C-4H), 2.58 (d, J=4.8, OH), 1.92 (ddd, J=12.4, J=3.8, C-3Ha), 1.43 (m, C-7Ha+C-3Hb), 1.28 (m, C-7Hb). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 174.8 (C=O), 137.8 (C-5), 137.6 (C hypso), 132.2 (C-6), 128.4, 127.8, 127.7 (aromatics), 73.4, 70.8, 68.9, 65.2 (*C*H$_2$OCO, *C*HOH, *C*H$_2$O, O*C*H$_2$Ph), 49.6 (C-2), 45.7 (C-7), 43.2 (C-1), 42.5 (C-4), 29.2 (C-3).

21–23b (secondary ester): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.42–7.25 (m, aromatics), 6.18 (dd, J=5.6, J=3.0, C-5H), 5.95 (dd, J=3.4, C-6H), 4.99 (m, C*H*OCO), 4.57 (s, OC*H*$_2$Ph), 3.79 (m, C*H*$_2$OH), 3.66 (m, C*H*$_2$OBn), 3.24 (m, C-1H), 3.02 (ddd, C-2H), 2.92 (m, C-4H), 2.23 (dd, J=7.7, OH), 1.93 (m, C-3Ha), 1.46 (m, C-7Ha+C-3Hb), 1.29 (m, C-7Hb). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 174.5 (C=O), 137.8 (C-5), 137.7 (C hypso), 132.2 (C-6), 128.4, 127.8, 127.6 (aromatics), 73.4, 73.0, 69.1, 62.7 (*C*H$_2$OH, *C*HOCO, *C*H$_2$OBn, *C*H$_2$Ph), 49.6 (C-2), 45.8 (C-7), 43.3 (C-1), 42.5 (C-4), 29.2 (C-3).

21–24a (primary ester): Yield 71% (50:50): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.43–7.25 (m, aromatics), 6.32 (dd, J=7.9, J=1, C-5H), 6.12 (dd, J<1Hz, C-6H), 4.57 (s, OC*H*$_2$Ph), 4.14 (m, C*H*$_2$OCO), 4.03 (m, C*H*OH), 3.56 (dd, J=3.9, J=9.4, C*Ha*OBn), 3.48 (dd, J=5.8, C*Hb*OBn), 2.92 (m, C-1H), 2.67 (ddd, J=2.2, J=9.4, J=8.9, C-2H), 2.57 (m, C-4H), 1.82–1.20 (m, J=12.9, J=2.7, C-3H$_2$+C-7H$_2$+C-8H$_2$) ^{13}C NMR (CDCl$_3$, 62.96 MHz): 176.0 (C=O), 137.7 (C-5), 135.3 (C hypso), 131.2 (C-6), 128.4, 127.7 (aromatics), 73.5, 70.8, 69.0, 65.3 (*C*H$_2$OCO, *C*HOH, *C*H$_2$OBn, O*C*H$_2$Ph), 42.7 (C-2), 32.5, 29.7, 29.3, 25.3, 24.3 (C-7, C-8, C-4, C1, C-3).

21–24b (secondary ester): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.38–7.25 (m, aromatics), 6.32 (overlapped dd, J=7.8, J<1, C-5H), 6.16 (overlapped dd, J<1, C-6H), 5.01 (m, C*H*OCO), 4.57 (2 overlapped d, OC*H*$_2$Ph), 3.79 (m, C*H*$_2$OH), 3.65 (m, C*H*$_2$OBn), 2.95 (m, C-1H), 2.69 (ddd, J=1.1, J=7.6, J=4.5, C-2H), 2.61 (m, C-4H), 1.83–1.20 (C-3H$_2$+C-7H$_2$+C-8H$_2$). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 177.5 (C=O), 137.7 (C-5), 135.3 (C hypso), 131.2 (C-2), 128.4, 127.8, 127.6 (aromatics), 73.4, 73.0, 69.0, 62.7 (*C*H$_2$OCO, *C*HOH, *C*H$_2$OBn, O*C*H$_2$Ph), 42.8 (C-2), 32.5, 29.8, 29.3, 25.2, 24.3 (C-7, C-8, C-4, C-1, C-3).

21–25a (primary ester): Yield 70% (50:50): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.42–7.23 (m, aromatics), 5.34 (m, C-3H), 4.54 (s, OC*H*$_2$Ph), 4.39 (dd, J=10.9, J=4.9Hz, C*Ha*OCO), 4.33 (dd, J=5.4, C*Hb*OCO), 4.02 (m, C*H*OH), 3.54 (dd, J=9.9, J=4.4, C*Ha*OBn), 3.47 (dd, J=6.4, C*Hb*OBn), 2.63 (broad s, OH), 2.53 (m, C-1H), 2.23 (m, C-2H$_2$), 2.00 (m, C-5H$_2$), 1.73 (m, C-6H$_2$), 1.67 (s, Me). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 176.0 (C=O), 138 (C-4), 133.5 (C hypso), 128.0, 127.5, 119.0 (C-3+aromatics), 73, 71, 69, 66, 65 (*C*H$_2$OCO, *C*HOH, *C*H$_2$OBn, O*C*H$_2$Ph), 39 (C4-1, 29, 27.5, 25 (C-5, C-2, C-6), 23 (Me).

21–25b (secondary ester): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.40–7.25 (m, aromatics), 5.37 (m, C-3H), 5.06 (m, C*H*OCO), 4.56 (2 overlapped d, OC*H*$_2$Ph), 3.82 (m, C*H*$_2$OH), 3.69 (dd, J=10.3, J=4.9, C*Ha*OBn), 3.64 (dd, J=4.9, C*Hb*OBn), 2.56 (m, C-1H), 2.25 (m, C-2H$_2$), 2.01 (m, C-5H$_2$), 1.74 (m, C-6H$_2$), 1.67 (s, Me). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 176 (C=O), 138 (C-4), 133 (C hypso), 128, 127, 119 (C-3+aromatics), 73, 72.5, 68, 62.5 (*C*H$_2$OH, *C*HOCO, *C*H$_2$OBn, O*C*H$_2$Ph), 39 (C4), 29, 27.5, 25 (C-5, C-2, C-6), 23 (Me).

21–26a (primary ester): Yield 55% (50:50): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.38–7.22 (m, aromatics), 5.31 (m, C-3H), 4.54 (s, OC*H*$_2$Ph), 4.19 (dd, J=11.5, J=4.9, C*Ha*OCO), 4.11 (d, C*Hb*OCO), 4.02 (m, C*H*OH), 3.54 (dd, J=9.8, J=4.1, C*Ha*OBn), 3.47 (dd, J=5.7, C*Hb*OBn), 2.62 (m, C-1H), 2.54 (broad s, OH), 1.94 (m, C-5H$_2$), 1.78 (m, C-6H$_2$), 1.70 (m, C-2H), 1.63 (s, C-4Me), 0.84 (d, J=6.4,C-2Me). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 175.1 (C=O), 137.6 (C-4), 133.1 (C hypso), 128.4, 127.8, 127.7, 125.8 (C-3+aromatics), 73.4, 70.8, 68.9, 65.1 (*C*H$_2$OCO, *C*HOH, *C*H$_2$OBn, O*C*H$_2$Ph), 43.3 (C-1), 31.1, 29.5, 23.4 (C-5, C-2, C-6), 16.6 (C-4*Me*), 14.2 (C-2*Me*).

21–26b (secondary ester): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.33–7.20 (m, aromatics), 5.33 (m, C-3H), 5.05 (m, C*H*OCO), 4.53 (2 overlapped d, OC*H*$_2$Ph), 3.81 (m, C*H*$_2$OH), 3.68 (dd, J=9.9, J=4.9, C*Ha*OBn), 3.62 (dd, J=4.9, C*Hb*OBn), 2.61 (m, C-1H+OH), 1.94 (m, C-5H$_2$), 1.78 (m, C-2H+C-6H$_2$), 1.63 (s, C-4Me), 0.84 (d, J=7.4, C-2Me). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 178 (C=O), 137.6 (C-4), 133.1 (C hypso), 128.4, 127.8, 127.6, 119 (C-3+aromatics), 73.4, 72.8, 69.1, 62.8 (*C*H$_2$OH, *C*HOCO, *C*H$_2$OBn, O*C*H$_2$Ph), 43.3 (C-1), 31.1, 29.5, 23.4 (C-5, C-2, C-6), 19.5 (C-4*Me*), 16.5 (C-2*Me*).

21–27a (primary ester): Yield 64% (50:50): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.37–7.20 (m, aromatics), 5.04 (m, C-3H), 4.53 (s, OC*H*$_2$Ph), 4.21 (dd, J=11.5, J=4.1, C*Ha*OCO), 4.12 (dd, J=6.2, C*Hb*OCO), 4.03 (m, C*H*OH), 3.55 (dd, J=9.0, J=4.1, C*Ha*OBn), 3.48 (dd, J=7.4, C*Hb*OBn), 2.64 (m, C-1H), 1.90 (m, C-5H$_2$), 1.81 (m, C-6H$_2$), 1.62 (s, C-4Me), 1.08 (s, C-2Me cis to CO), 0.88 (s, C-2Me trans to CO).^{13}C NMR (CDCl$_3$, 62.96 MHz): 175.0 (C=O), 137.6 (C-4), 133.5 (C hypso), 131.7, 131.0, 128.4, 127.8, 127.7, 127.6 (C-3+aromatics), 73.4, 70.9, 68.9, 65.0 (*C*H$_2$OCO, *C*HOH, *C*H$_2$OBn, O*C*H$_2$Ph), 50.0 (C-1), 34.3 (C-2), 30.1, 29.1, (C-5, C-6), 24.6, 23.3, 22.4 (3Me).

21–27b (secondary ester): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.38–7.22 (m, aromatics), 5.05 (m, C-3H+C*H*OCO), 4.53 (s, OC*H*$_2$Ph), 3.81 (m, C*H*$_2$OH), 3.66 (dd, C*H*$_2$OBn), 2.35 (m, C-1H), 2.24 (broad s, OH), 1.88 (m, C-5H$_2$), 1.78 (m, C-6H$_2$), 1.62 (s, C-4Me), 1.11 (s, C-2Me cis to CO), 0.90 (s, C-2Me trans to CO). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 174.8 (C=O), 137.6 (C-4), 131.8 (C hypso), 131.1, 128.4, 127.8, 127.7 (C-3H+aromatics), 73.4, 72.8, 69.2, 66.4 (C*H*$_2$OH, C*H*OCO, C*H*$_2$OBn, OC*H*$_2$Ph), 50.0 (C-1), 34.4 (C-2), 30.1, 29.1 (C-5, C-6), 24.6, 23.4, 22.4 (Me).

21–28a (primary ester): Yield 54% (50:50): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.37–7.27 (m, aromatics), 4.54 (s, OC*H*$_2$Ph), 4.15 (overlapped dd, CH$_2$OCO), 4.03 (m, C*H*OH), 3.54 (dd, J=9.4, J=4.5, C*Ha*OBn), 3.46 (dd, J=5.8, C*Hb*OBn), 2.59 (broad s, OH), 2.53 (m, C-1H), 2.22–1.84 (m, C-6H$_2$+C-5H$_2$+C-2H$_2$), 1.58 (2s, 2Me). ^{13}C NMR (CDCl$_3$, 62.96 MHz): 176.0 (C=O), 137.6 (C-4), 128.4, 127.8, 127.7, 123.7, 119.0 (C-3+aromatics), 70.8, 68.9, 65.2, 60.5 (*C*H$_2$OCO, *C*HOH, *C*H$_2$OBn, O*C*H$_2$Ph), 40.1 (C4-1, 33.6, 30.8, 25.8 (C-5, C-2, C-6), 18.9, 18.8 (2Me).

21–28b (secondary ester): ^{1}H NMR (CDCl$_3$, 250 MHz): 7.39–7.24 (m, aromatics), 5.06 (m, C*H*OCO), 4.56 (2 overlapped d, OC*H*$_2$Ph), 3.82 (m, C*H*$_2$OH), 3.69 (dd, J=10.7, J=4.9, C*Ha*OBn), 3.64 (dd, J=4.9, C*Hb*OBn), 2.58 (m, C-1H), 2.26-1.85 (m, C-5H$_2$+C-6H$_2$+C-2H$_2$), 1.62 (2s, 2Me).^{13}C NMR (CDCl$_3$, 62.96 MHz): 175.8 (C=O), 137.6 (C-4), 128.4, 127.8, 127.7, 127.6, 123.7 (C-3+aromatics), 73.3, 72.8, 68.9, 62.5 (*C*H$_2$OH, *C*HOCO, *C*H$_2$OBn, O*C*H$_2$Ph), 40.1 (C4-1, 33.5, 30.8, 25.8 (C-5, C-2, C-6), 18.9, 18.8 (2Me).

22–25a (primary ester): Yield 65% (50:50): ^{1}H NMR (CDCl$_3$, 200 MHz): 7.27 (dd, J=7.1, J=7.1, aromatic, C-5H), 6.87 (m, aromatics), 5.36 (m, C-3H), 4.55 (s, OCH_2Ar), 4.20 (2 overlapped dd, CH_2OCO), 4.06 (m, *CH*OH), 3.82 (MeO), 3.56 (dd, J=9.6, J=4.4, *CHa*OAr), 3.48 (dd, J=5.9, *CHb*OAr), 2.54 (m, C-1H), 2.22 (m, C-$2H_2$), 1.99 (m, C-$5H_2$), 1.74 (m, C-$6H_2$), 1.67 (s, Me).

22–25b (secondary ester): ^1H NMR ($CDCl_3$, 200 MHz): 7.27 (dd, J=7.1, J=7.1, aromatic, C-5H), 6.87 (m, aromatics), 5.37 (m, C-3H), 5.07 (m, *CH*OCO), 4.55 (s, OCH_2Ar), 3.85 (m, CH_2OH), 3.67 (2 overlapped dd, CH_2OAr), 2.55 (m, C-1H), 2.23 (m, C-$2H_2$), 2.00 (m, C-$5H_2$), 1.75 (m, C-$6H_2$), 1.66 (s, Me).

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