Stereocontrolled chiral synthesis of a *trans-anti-trans* tricycle by a transannular Diels–Alder reaction

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The racemic and chiral synthesis of *trans-cis-cis* macrocyclic triene **5** is described. Heating this compound at 262°C leads via a transannular Diels–Alder reaction to the tricyclic structure **6**, which can be further transformed into tricyclic compound **7**. This work constitutes a preliminary study for the synthesis of corticoids.

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On décrit la synthèse racémique et chirale du triène macrocyclique *trans-cis-cis* **5**. En chauffant à 262°C, ce composé subit une reaction de Diels–Alder transannulaire et conduit à l'adduit tricyclique **6** qui peut être transformé dans le composé **7**. Ce travail constitue une étude préliminaire en vue de la synthèse de corticostéroïdes.

Introduction

Recent interest in organic synthesis focused on macrocyclic compounds. Indeed many naturally occurring molecules containing medium and large rings have been isolated and progress in their synthesis led to the development of good methods of cyclization (1, 2). These investigations also revealed that *intermolecular* reactions of such macrocyclic structures might occur with high chemo, regio, and stereoselectivity (3, 4).

Very recently we pointed out the enormous synthetic potential residing in *intramolecular* reactions of macrocyclics, particularly transannular processes of such systems (5, 6). These transformations occur with high regio and stereoselectivity due to conformational restriction and proximity effects that become operative, increasing the rate of one reaction at the expense of others normally competing. Thus transannular processes on macrocarbocyclics are powerful tools for the synthesis of complex polycyclic skeletons (6*c*). For example, the Diels–Alder reaction of 14- or 13-membered macrocycles (**1** → **2** or **3** → **4**) (Scheme 1) should represent a good synthetic approach to polycyclic systems such as diterpenes, triterpenes, steroids, etc. Recent papers from our laboratory (7) and by Takahashi *et al.* (8) confirmed this prediction and showed the great potential of the transannular Diels–Alder reaction for the synthesis of natural products. We now wish to report our work on a new approach to the synthesis of corticosteroids.

Most of the natural corticosteroids have the *trans-anti-trans* (TAT) ring junction for the A, B, and C rings of the carbon skeleton. However, in recent communications, (7*e*, *d*) we demonstrated that the transannular Diels–Alder strategy is not appropriate for the direct construction of the TAT ring junction. On the contrary, the *trans-syn-cis* (TSC) ring junction is directly and easily accessible by the Diels–Alder reaction of a *trans-cis-cis* (TCC) macrocyclic triene (5). The hydroxyl or the keto group at position 11 in corticosteroids not only provides a route for a subsequent epimerization at C9, thereby delivering systems having TAT stereochemistry, but can also be exploited to induce chirality.

We report herein, as a preliminary study for the synthesis of corticoids, the racemic and chiral syntheses of macrocyclic compound **5** as well as its transformation into tricyclic compound **7** via compound **6** (Scheme 1).

Results and discussion

Racemic synthesis of macrocyclic triene 5

As previously described (7*f*), the synthesis of macrocyclic triene **5** was based on our original convergent approach (7*c*, *e*). Scheme 2 summarizes the preparation of the *Z* dienophile moiety. Thus alcohol **8** (9) was first benzylated, followed by removal of the benzylidene protecting group in acidic medium (85%). Diol **10** was then monosilylated (10) (51%) to afford alcohol **11**, which was oxidized (11) to aldehyde **12**. Without further purification, this crude aldehyde was used in a Wittig reaction with the ylide derived from the phosphonium salt **14**. The latter was prepared by condensing the THP derivative (12) of 2-bromoethanol **13** with ethyltriphenylphosphonium bromide (13*a*). The Wittig reaction provided a 55:45 mixture of *Z* and *E* olefins in a 63% yield from **11**. The geometry of these isomers was easily established by ^{13}C nmr spectroscopy. The C4-methyl in the *E* isomer, which is *cis*-disposed to the chain, displays a higher field chemical shift (17.1) than the corresponding *trans*-disposed methyl in the *Z* isomer (23.8). On the contrary the C5-methylene displays a higher field chemical shift (32.8) in the *Z* isomer than the corresponding C5-methylene in the *E* isomer (39.7). These findings are in complete agreement with assignments for *Z* and *E* olefins (13*b*). Furthermore, the stereochemistry of our olefin was firmly secured by a chemical proof (*vide infra*).

After chromatographic separation, the pure *Z* olefin **15***a* was desilylated (14) to give alcohol **16***a*, which was smoothly converted into the corresponding mesylate **17***a* (92%) followed by conversion into mesylate **20***a* facilitated its intramolecular cyclization to **21**, demonstrating ipso-facto the presence of the *Z* geometry. The same sequence of reactions was effected with the *E* isomer. The *E* compound **20***b* was, however, unable to cyclize in the same conditions used for the *Z* isomer **20***a*.

Dienophile **20***a* and the *trans-cis* diene **22** (7*c*) were coupled in dimethylformamide and tetrahydrofuran (1:1), producing triene **23** in 84% yield (Scheme 3). Subsequent alkylation with the anion of dimethyl malonate at 80°C gave

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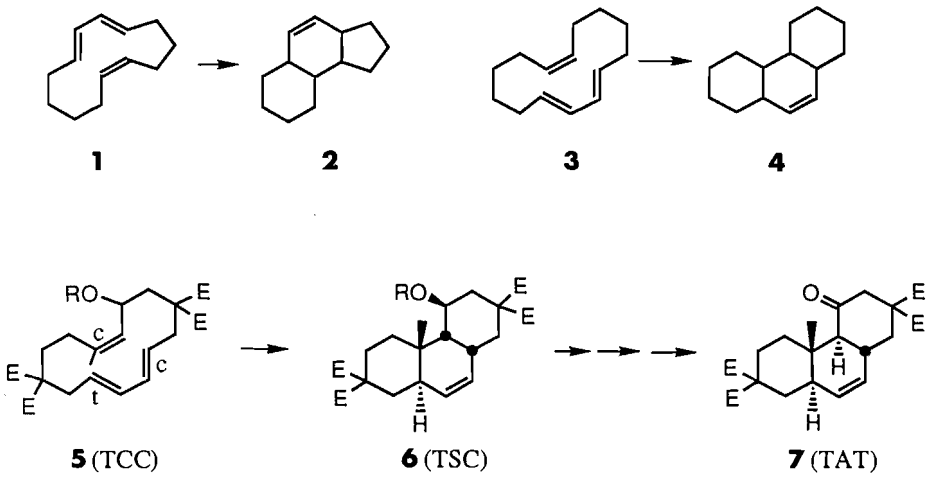
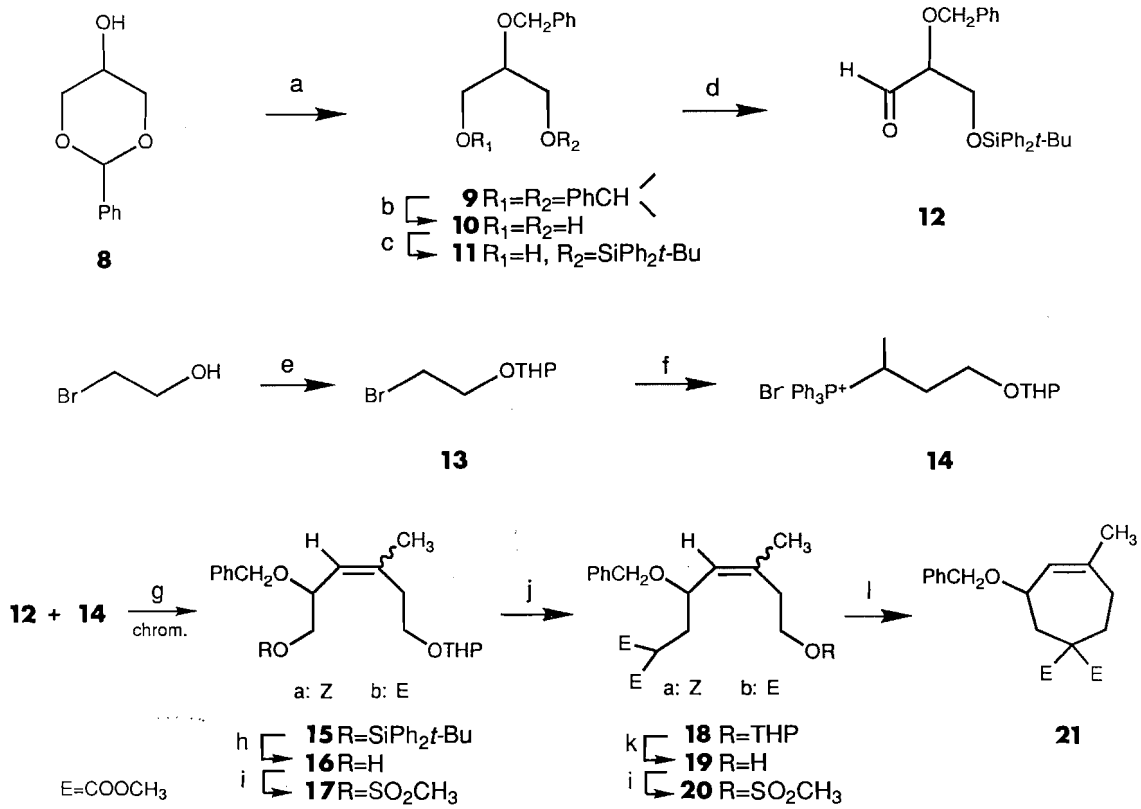


E = CO_2CH_3, R = $CH_2C_6H_5$ or $CH_2C_6H_4OCH_3$

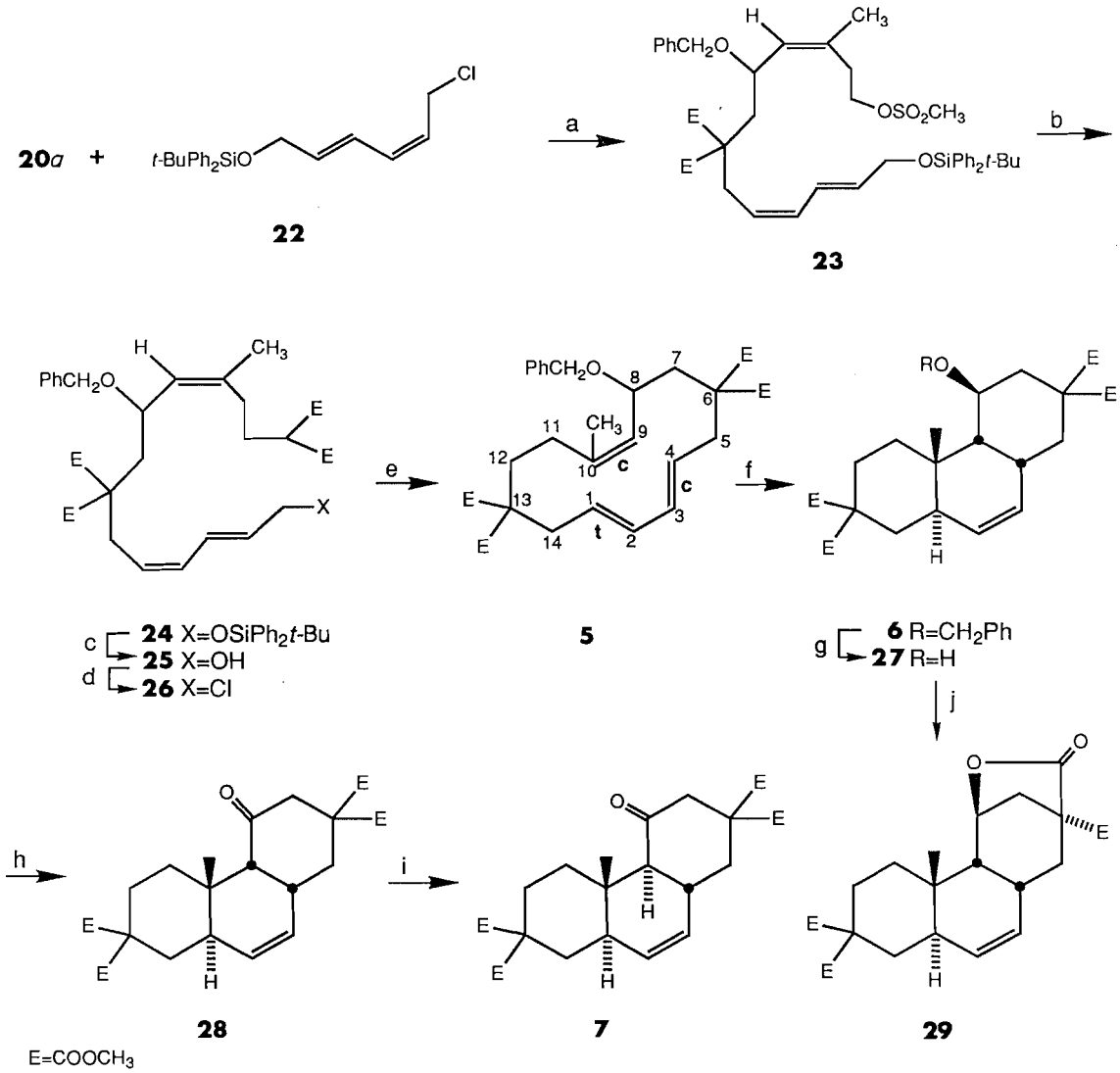
SCHEME 1



(a) $PhCH_2Br$, NaH, THF, 0°C to r.t. (b) HCl 10%, H_2O (85%) (c) *t*-$BuPh_2SiCl$, imidazole, THF, r.t. (51%) (d) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C to r.t. (e) DHP, PPTS, CH_2Cl_2, r.t. (82%) (f) (i) $Br^-Ph_3P^+CH_2CH_3$, HMDSK, toluene, THF, 0°C (ii) **13**, THF, 48 h, r.t. (81%) (g) (i) **14**, BuLi, hexane, THF, -78°C to 0°C (ii) **12**, THF, chromatography (*cis* = 36%, *trans* = 27% from alcohol **11**) (h) *n*-Bu_4NF, THF, 0°C to r.t. (93%) (i) CH_3SO_2Cl, Et_3N, CH_2Cl_2, 0°C (j) $CH_2(CO_2CH_3)_2$, NaH, THF/DMF 1:1, KI, 85°C (84%) (k) CH_3OH, PPTS, reflux (92%) (l) HMDSNa, THF/DMF 1:1, 80°C, 4.5 x 10^{-3} M (77%)

SCHEME 2

compound **24** (80%), which, after desilylation (14) (91%), led to alcohol **25**. The latter was then converted to the corresponding allylic chloride **26** by the procedure of Collington and Meyers (15). Finally, the crude chloride **26** was allowed to cyclize under high-dilution conditions (Cs_2CO_3, THF/DMF 1:1, 70°C, 10 h, 2.5 × 10^{-3} M, slow addition) to afford macrocyclic compound **5** (R = CH_2Ph) (75% from alcohol **25**).



(a) (i) **20a**, NaH, THF/DMF 1:1, 0°C to r.t. (ii) **22**, THF/DMF 1:1, r.t. (84%) (b) (i) $CH_2(CO_2CH_3)_2$, NaH, THF/DMF 1:1 (ii) **23**, THF/DMF, 80°C (80%) (c) *n*-Bu_4NF, THF, 0°C to r.t. (91%) (d) CH_3SO_2Cl, s-collidine, LiCl, DMF, r.t. (e) Cs_2CO_3, DMF/THF 1:1, 2.5 x 10^{-3} M, 75°C, slow addition (75% from alcohol **25**) (f) sealed tube, toluene, 270°C, 2.75 h (84%) (g) $SnCl_4$, CH_2Cl_2, r.t. (87%) (h) PCC, CH_2Cl_2, r.t. (87%) (i) Na_2CO_3, CH_3OH, 50°C, 9h (94%) (j) PTSA, C_6H_6, reflux (86%)

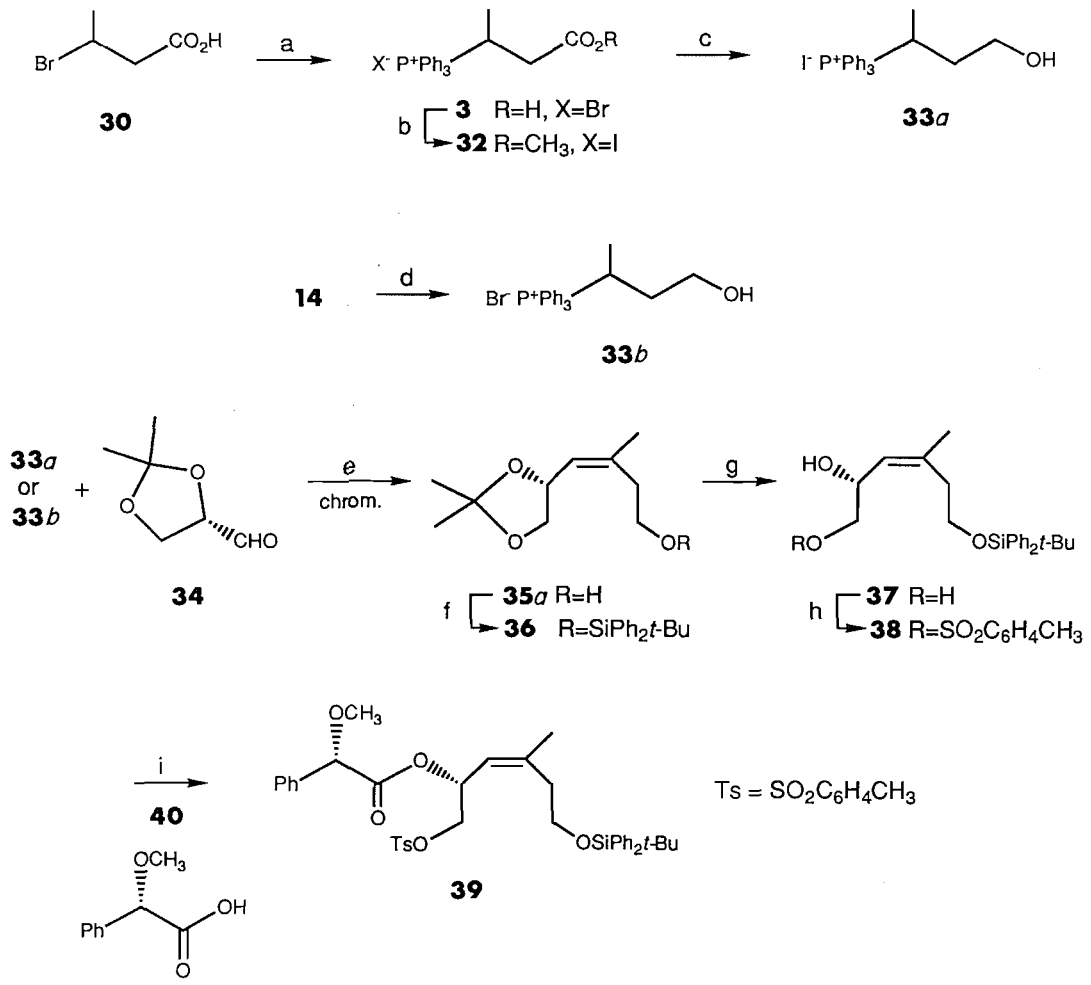
SCHEME 3

Chiral synthesis of macrocyclic triene 5

The chiral dienophile moiety was synthesized as indicated in Scheme 4. Thus 3-bromobutyric acid **30** was first treated with triphenylphosphine to give the corresponding phosphonium salt **31** (94%). Without further purification, the acid function of the phosphonium salt was esterified to its methyl ester **32** in 81% yield after crystallization. Reduction of ester **32** with diisobutylaluminum hydride produced alcohol **33***a* in 62% yield. The corresponding phosphonium bromide **33***b* was also prepared by methanolysis of the phosphonium salt **14** in the presence of pyridinium *p*-toluenesulfonate (83%).

A Wittig reaction with aldehyde **34** (16) in tetrahydrofuran led to a *Z* and *E* mixture (5:1) of olefins **35** in 60% yield. The respective geometries were assigned by ^{13}C nuclear magnetic resonance as described above. The optical purity of the separated *Z* olefin **35***a* was verified in the following manner. The hydroxyl functionality was protected as a silyl ether (10) leading to **36** (79%), which, after hydrolysis, provided diol **37** in 55% yield. Subsequent monotosylation of diol **37** to alcohol **38** (72%) allowed esterification with the chiral acid **40** and gave Mosher ester **39** (90%). This compound proved to be one single diastereomer by ^1H nmr spectroscopy. The same sequence of reactions was carried out with the *S* enantiomer of silyl ether **36**, already synthesized in our laboratory (7*g*). In this case, a different isomer of compound **39** (99%) was obtained, also homogenous by ^1H nmr spectroscopy.

The *Z* isomer of olefin **35**, purified by column chromatography, was benzoylated (89%) (Scheme 5) and then hydrolyzed to afford diol **42** (87%). After monotosylating diol **42**, the remaining free hydroxyl group was protected via treatment with *p*-methoxybenzyltrichloroacetimidate (17) (73%). Alkylation of benzyl ether **44** with dimethyl malon-



(a) PPh_3, toluene, reflux, 48 h (b) CH_3I, Na_2CO_3, NaI, acetone, reflux, 12 h (81%)
(c) DIBAL,CH_2Cl_2, -78°C, 2 h (62%) (d) *p*-PTS, CH_3OH, 50°C, 18 h (83%)
(e) (i) **33**, BuLi, hexane, THF, -78°C to 0°C; (ii) **34**, THF, chromatography (*cis*=50%, *trans*=10%) (f) *t*-$BuPh_2SiCl$, imidazole, DMF, 4 h (79%)
(g) PPTS, CH_3OH, r.t., 4 h (55%) (h) TsCl, NEt_3, DMAP, CH_2Cl_2, r.t., 3 h (60%)
(i) $Ph(OCH_3)CHCOOH$ (**40**), DCC, DMAP, CH_2Cl_2, r.t., 0.5 h (99%)

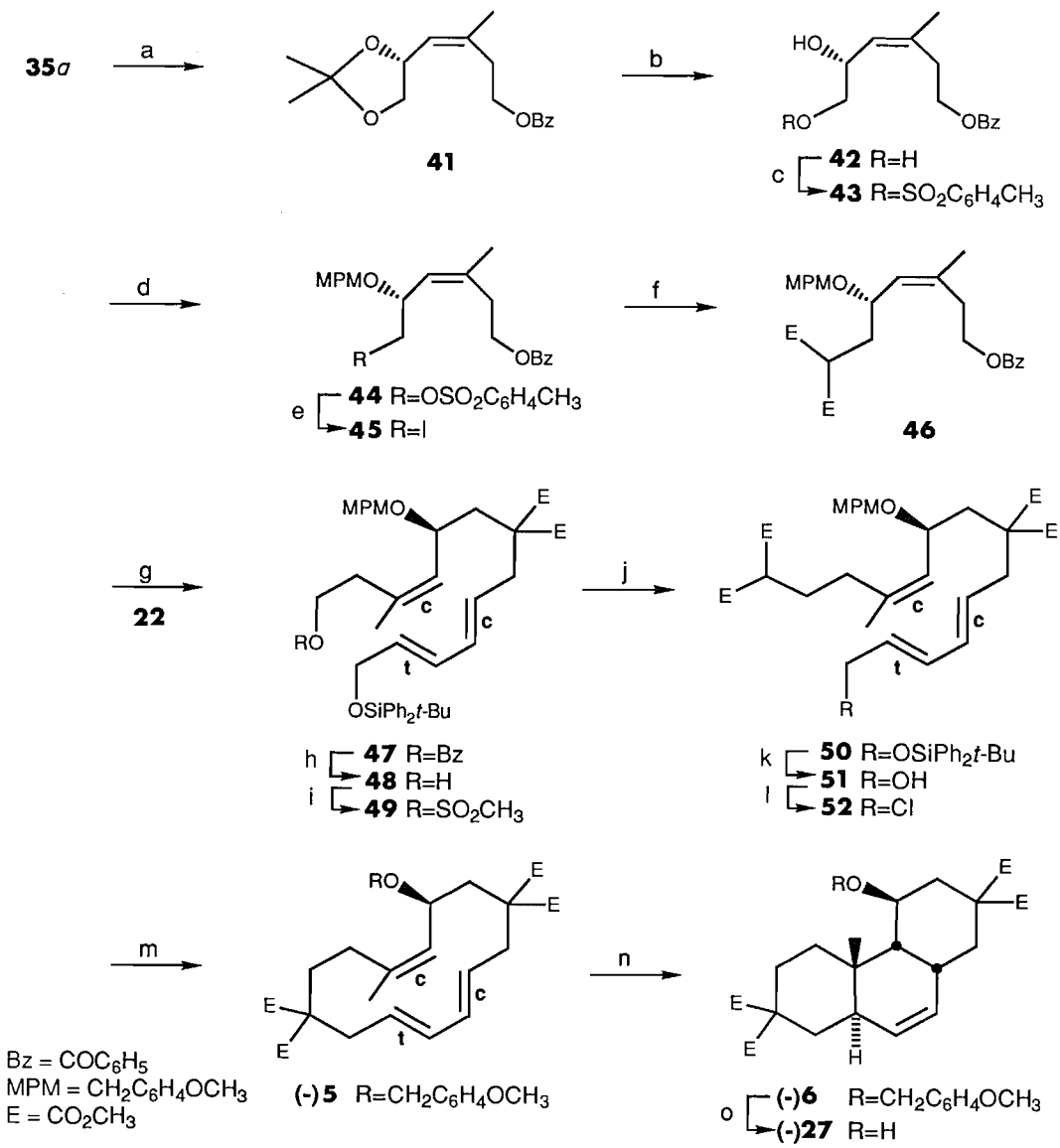
SCHEME 4

ate furnished compound **46** (72%). This adduct was then submitted to the coupling conditions previously described, yielding triene **47** in 87% yield. Alkylation with dimethyl malonate carried out on iodide **45** instead of tosylate **44** gave about the same yield (77%).

Hydrolysis of benzoate **47** in methanol afforded alcohol **48** (94%), which was transformed into mesylate **49** in 97% yield. The same strategy as described above was then applied to mesylate **49**. Thus condensation with the anion originating from dimethyl malonate (84%) followed by a treatment with fluoride ions gave alcohol **51** (94%) via compound **50**. Conversion of this alcohol into the corresponding allylic chloride **52** then allowed the cyclization leading to macrocyclic triene (−)**5** (R = $CH_2C_6H_4OCH_3$) obtained in 78% yield for the last two steps.

Transannular Diels–Alder reaction of macrocyclic trienes 5

When heated at 270°C for 2.75 h, racemic macrocyclic triene **5** (R = CH_2Ph) underwent transannular Diels–Alder reaction to give, in 84% yield, tricyclic compound **6** (R = CH_2Ph) and a mixture of two minor compounds, which were not separable by column chromatography (Scheme 3). The stereochemistry of the five asymmetric centers in the major compound can be predicted by an analysis of the possible transition states (see Scheme 6). Thus, the relative stereochemistry TSC at the ring junctions becomes apparent after examination of such transition states; only transition states 2 and 3 are structurally allowed. Approach 1 is not possible because it is sterically impossible to get the boat form of the central ring with a 1,2-diaxial disposition of ring C. Also, despite the equatorial disposition of the benzyl ether in approach 3 and the 1,3-diaxial interaction between one of the esters E and the benzyl ether in approach 2, the latter will be favored since the benzyl ether is sterically less encumbered and therefore energetically favored. Consequently, the major compound should be compound **6***a* with an equatorial benzyl ether after conformational change. This orientation was confirmed by nmr spectroscopy of the proton adjacent to the

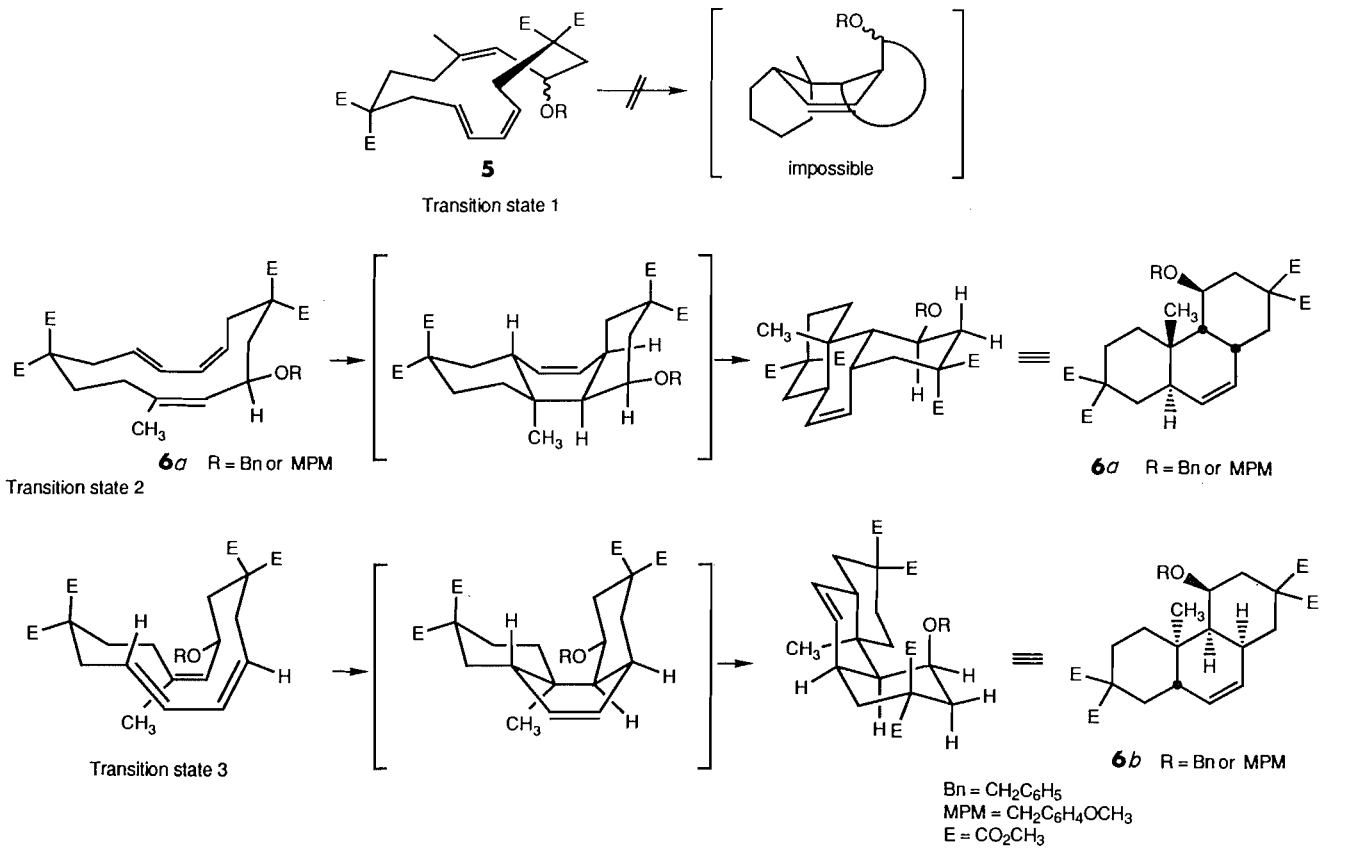


(a) BzCl, NEt_3, DMAP, CH_2Cl_2, r.t., 1.5 h (89%) **(b)** *p*-TSA, CH_3OH, r.t., 1.5 h (87%) (c) TsCl, NEt_3, DMAP, CH_2Cl_2, 0°C, 1.5 h (72%) **(d)** $Cl_3CC(NH)OCH_2C_6H_4OCH_3$, TfOH, Et_2O, 0°C, 3 h (73%) **(e)** NaI, nBu_4NI, acetone, 50°C, 70 h (99%) **(f)** $CH_2(CO_2CH_3)$, NaH, THF/DMF 1:1, KI, 85°C (77%) **(g)** (i) NaH, THF/DMF 1:1, 0°C to r.t.; (ii) **22**, THF/DMF 1:1, r.t. (87%) **(h)** K_2CO_3, CH_3OH, 65°C, 4 h (94%) **(i)** CH_3SO_2Cl, NEt_3,CH_2Cl_2, 0°C, 0.5 h (97%) **(j)** $CH_2(CO_2CH_3)_2$, NaH, THF/DMF 1:1, KI, 80°C (84%) **(k)** nBu_4NF, THF, 0°C to r.t. (94%) **(l)** CH_3SO_2Cl, NEt_3, *s*-collidine, LiCl, DMF, r.t. **(m)** Cs_2CO_3, DMF/THF 1:1, 2.5×10^{-3} M, 75°C, slow addition (78% from **51**) **(n)** sealed tube, toluene, 262°C, 3 h (82%) **(o)** DDQ, H_2O, CH_2Cl_2 (76%)

SCHEME 5

benzyl ether (3.76 ppm, doublet of doublets of doublets, 9.9, 9.9, and 4.4 Hz). Two larger coupling constants indicate an axial hydrogen and therefore an equatorial benzyl ether. It can also be predicted that one of the minor compounds should have an axial benzyl ether by virtue of the signal observed at 4.01 ppm (doublet of doublets of doublets, $J = 2.7$ Hz), which corresponds to the proton adjacent to the benzyl ether. Moreover, the TSC stereochemistry of the ring junctions could be established following an unequivocal chemical transformation in the chiral series (*vide infra*).

Diels–Alder reaction of the chiral macrocyclic triene was performed at 262°C in a sealed tube for 3 h (Scheme 5). As for the racemic compound, a major tricyclic compound was isolated in 84% yield along with a mixture of two minor compounds in 15% yield. The ^1H nmr spectrum of the major compound shows the same characteristic peaks observed in



SCHEME 6

the ^1H nmr spectrum of the major racemic tricyclic compound.

Synthesis of the trans-anti-trans *tricyclic compounds 7*

Removal of the benzyl protecting group in the racemic series was achieved with tin tetrachloride in dichloromethane (18) (87%) (Scheme 3) and with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone for the chiral series (76%) (Scheme 5). The resulting alcohol **27** was then oxidized by pyridinium chlorochromate to afford ketone **28** (Scheme 3) in 87% yield. The TSC relative stereochemistry of this ketone was confirmed by a single crystal X-ray diffraction analysis (19).

When these two reactions were performed on the two-compound mixture isolated from the chiral sequence, the same ketone **28** was obtained, thus proving the TSC stereochemistry and hence the structure ***6b*** proposed for one of the compounds in the mixture.[3] Finally, treatment with sodium carbonate in methanol at 65°C over 2.5 h converted ketone **28** into another ketone **7** (94%), which was spectroscopically and chemically different from the former (Scheme 3). This ketone **7** must obviously have the desired TAT stereochemistry obtained by isomerization at position C9. It must finally be noted that acidic treatment of alcohol **27** provided lactone **29** in 86% yield.

Conclusion

The formation of one major diastereomer in the Diels–Alder reaction points out the excellent control of stereochemistry at position C11. This has also been proven by the chiral synthesis of a tricyclic compound starting from an optically active precursor that had the appropriate absolute configuration for the C11 secondary benzyl ether. Moreover, the synthesis of lactone **29** allows a good differentiation of the two esters of a malonate. The carbonyl carbon of this lactone moiety could represent a precursor for the C18 hemiacetal function of aldosterone or other corticoids of this type.

Hence, this preliminary work demonstrates that a transannular Diels–Alder reaction on a suitable macrocycle followed by epimerization gives ready access to a tricyclic compound having a TAT stereochemistry. In addition, this method could be very promising for the synthesis of optically active corticosteroids. Work in this direction is currently underway in our laboratory.

Experimental

Infrared spectra were recorded on a Perkin–Elmer 681 spectrophotometer. The ^1H nmr and ^{13}C nmr spectra were taken on a Bruker WM-250 spectrometer. The following abbreviations are used in the text: s, singlet; d, doublet; t, triplet, q, quadruplet; m, multiplet. Mass spectra (ms) were recorded on a VG-Micromass ZAB-1F mass spectrometer. Melting points (mp) were measured on a Büchi apparatus and were not corrected. Thin-layer chromatography (tlc) was performed using silica gel 60 F-250. For flash chromatography Merck Kiesel gel (no. 9385) was used. Acetonitrile, amines, dimethylformamide (DMF), hexamethylphosphoramide (HMPA), and dichloromethane (CH_2Cl_2) were distilled from calcium hydride; methanol from magnesium and iodine; acetone and ethyl acetate from potassium carbonate; benzene, toluene, diethyl

[3]The second minor product in the mixture was not identified.

ether, and tetrahydrofuran (THF) from sodium and benzophenone ketyl. Unless otherwise specified, all reactions were carried out in a dry apparatus under argon or nitrogen.

*1-Bromo-2-[(2-tetrahydropyranyl)oxy]-ethane (**13**)*

To a stirred solution of 2-bromoethanol (74.93 g, 599.6 mmol) in dichloromethane (35 mL) were added, at 0°C, pyridinium *p*-toluenesulfonate (755 mg, 3.0 mmol) and dihydropyran (3.70 g, 44.0 mmol). The mixture was stirred for 1 h at room temperature. Potassium carbonate was then added and the mixture was filtered. After concentration, the residual oil was purified by column chromatography (5% to 10% of ethyl acetate in hexane) to yield bromide **13** (107.97 g, 86%); bp 70–75°C at 20 Torr (1 Torr = 133.3 Pa); ir ($CHCl_3$) ν: 3010, 2945, 2875, 2850, 1205, 1132, 1122, 1090, 1032 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 4.68 (1H, t, J = 3.3 Hz, -O-C*H*-O-), 4.02 (1H, dt, J = 11.2, 6.2 Hz, -CH_2OTHP), 3.94–3.85 (1H, m, -CH_2-O-CH-O-), 3.77 (1H, dt, J = 11.4, 6.3 Hz, -CH_2OTHP), 3.57–3.48 (3H, m, -CH_2-O-CH-O- and -CH_2Br), 1.88–1.50 (6H, m, -O-CH_2-(CH_2)$_3$-); ms m/e (70 eV): 207 (M^+ − H). Exact Mass (M^+) calcd: 207.0021; found: 207.0020.

*3-[(2-Tetrahydropyranyl)oxy]-1-methylpropyltriphenylphosphonium bromide (**14**)*

Potassium bis(trimethylsilyl)amide (122.4 mL, 0.5 M in toluene) was added to a suspension of ethyltriphenylphosphonium bromide (22.70 g, 61.2 mmol) in tetrahydrofuran (100 mL) at −78°C. The mixture was stirred at room temperature for 1 h and bromide **13** (19.18 g, 91.8 mmol) was then added at 0°C. The mixture was stirred at room temperature for 48 h. The white solid formed was filtered and dissolved in dichloromethane. After evaporation of dichloromethane, the solid was recrystallized from dichloromethane and hexane to yield the phosphonium salt **14** (24.74 g, 81%); mb 197–198°C; ir ($CHCl_3$) ν: 3010, 2940, 1440, 1240, 1115, 1080, 1035 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 8.03–7.66 (15H, m, 3 × -C_6H_5), 5.09–4.99 (1H, m, $Br^-P^+Ph_3$-C*H*(CH_3)-), 4.60–4.58 (1H, m, -O-C*H*-O-), 4.19–4.09 (1H, m, -O-CH-O-CH_2-), 3.91–3.80 (2H, m, -CH_2OTHP), 3.55–3.46 (1H, m, -O-CH-O-CH_2-), 2.35–2.17 (1H, m, -CH(CH_3)-CH_2-), 1.86–1.36 (7H, m, -CH(CH_3)-CH_2- and -O-CH_2-(CH_2)$_3$-), 1.44 (3H, dd, J = 19.8, 6.9 Hz, -CH(CH_3)-).

*2-Benzyloxy-1,3-propanediol (**10**)*

5-Hydroxy-2-phenyl-1,3-dioxane **8** (4.98 g, 27.7 mmol) (9) was added at 0°C to a stirred suspension of sodium hydride (1.23 g, 60% in oil, 30.7 mmol) in tetrahydrofuran (120 mL). The mixture was stirred at room temperature for 10 min. The temperature was reduced to 0°C and then benzyl bromide (3.62 mL, 30.4 mmol) was added. After stirring the solution at room temperature for 3 h, half of the tetrahydrofuran was evaporated followed by addition of water (36 mL) and 10% aqueous hydrochloric acid (84 mL). The mixture was heated to reflux for 1.5 h, then poured into a saturated solution of sodium carbonate and extracted with ethyl acetate. The organic layers were combined, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (50% to 100% of ethyl acetate in hexane) to afford diol **10** (4.30 g, 85%); ir ($CHCl_3$) ν: 3600, 3580, 3050, 2930, 2880, 1260, 1110, 1060 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.42–7.29 (5H, m, -CH_2-C_6H_5), 4.67 (2H, s, -C$H_2C_6H_5$), 3.84–3.69 (4H, m, -CH_2-CH(OBn)-CH_2-), 3.61 (1H, q, J = 4.6 Hz, -C*H*-(OCH_2-C_6H_5)), 2.05 (2H, s, -CH_2O*H*); ms m/e (70 eV): 182 (M^+), 151 (M^+ − CH_2OH). Exact Mass (M^+) calcd: 182.0943; found: 182.0945.

*3-Benzyloxy-3-[(*tert*-butyldiphenylsilyl)oxy]-propan-1-ol (**11**)*

Imidazole (344.0 mg, 5.05 mmol) and *tert*- butyldiphenylsilyl chloride (1.26 g, 4.57 mmol) were added at 0°C to a stirred solution of diol **10** (0.832 g, 4.57 mmol) in tetrahydrofuran (20 mL). The solution was stirred at room temperature for 3.5 h, after which tetrahydrofuran was evaporated. The residual oil was purified by column chromatography (25% to 100% of ethyl acetate in hexane) to afford alcohol **11** (1.06 g, 55%), doubly protected diol (0.874 g, 29%), and starting material **10** (0.137 g, 16%); ir ($CHCl_3$) ν: 3580, 3070, 3010, 2960, 2930, 2860, 1470, 1430, 1100 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.69–7.66 and 7.45–7.28 (15H, m, -$OCH_2C_6H_5$ and -OSi-(C_6H_5)$_2$*t*Bu), 4.64 (1H, d, J_{AB} = 11.7 Hz, -OCH_2Ph), 4.52 (1H, d, J_{AB} = 11.7 Hz, -OCH_2Ph), 3.84–3.71 (4H, m, -CH_2OH and -CH_2OSiPh$_2$*t*Bu), 3.67–3.60 (1H, m, -C*H*(OBn)-), 2.08 (1H, s, -CH_2O*H*), 1.06 (9H, s, -OSiPh$_2$C(CH_3)$_3$); ms m/e (70 eV): 285 (M^+ − *t*Bu − Ph − H). Exact Mass (M^+ − *t*Bu − Ph − H) calcd: 285.0947; found: 285.0955.

*2-Benzyloxy-3-[(*tert*-butyldiphenylsilyl)oxy]-propanal (**12**)*

Dimethyl sulfoxide (1.64 mL, 23.11 mmol) was added slowly at −78°C to a stirred solution of oxalyl chloride (1.01 mL, 11.56 mmol) in dichloromethane (28 mL). The solution was stirred for 10 mins and a solution of alcohol **11** (1.93 g, 4.60 mmol) in dichloromethane (14 mL) was added at −78°C. The mixture was stirred for 0.75 h and triethylamine (6.44 mL, 46.22 mmol) was then added at −78°C. The temperature of the mixture was raised to −10°C and the solution was stirred for 0.5 h. After addition of water, the mixture was extracted with dichloromethane and the organic layer was dried over magnesium sulfate and concentrated. The residual oil (1.81 g, 94% crude) was used for the next step without any purification; ir ($CHCl_3$) ν: 3070, 3010, 2930, 2860, 1738, 1730, 1430, 1115 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 9.76 (1H, d, J = 1.4 Hz, -C*H*O), 7.69–7.64 and 7.44–7.30 (15H, m, -OSi(C_6H_5)$_2$*t*Bu and -O-$CH_2C_6H_5$), 4.69 (1H, d, J_{AB} = 12.4 Hz, -OCH_2Ph), 4.65 (1H, d, J_{AB} = 12.4 Hz, -OCH_2Ph), 3.98–3.96 (2H, m, -CH_2OSiPh$_2$*t*Bu), 3.91 (1H, dd, J = 4.0 and 1.4 Hz, OHC-C*H*(OBn)-), 1.04 (9H, s, -OSiPh$_2$C(CH_3)$_3$); ms m/e (70 eV): 361 (M^+ − *t*Bu). Exact Mass (M^+ − *t*Bu) calcd: 361.1260; found: 361.1266.

*2-Benzyloxy-1-[(*tert*-butyldiphenylsilyl)oxy]-6-[(2-tetrahydropyranyl)oxy]-4-methylhex-3-ene (**15**)*

Butyllithium (185 μL, 1.6 M in hexane, 0.296 mmol) was added at −78°C to a stirred suspension of phosphonium bromide **14** (0.162 g, 0.325 mmol, dried under vacuum at 115–120°C for 12 h) in tetrahydrofuran (1.5 mL). The mixture was brought to 0°C and stirred until the solution became dark red (≈ 0.5 h). A solution of aldehyde **12** (0.100 g crude, 0.277 mmol) in tetrahydrofuran (1.5 mL) was then added at 0°C. After 10 min, the mixture was poured into a saturated solution of ammonium chloride and was extracted with ethyl ether. The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (5% ethyl acetate in hexane) to afford *Z* olefin **15***a* (45.2 mg, 43%) and *E* olefin **15***b* (33.8 mg, 32%); ir ($CHCl_3$) ν, *Z* and *E* isomers: 2950, 2855, 1112 cm^{-1}; ^1H nmr ($CDCl_3$) *Z* isomer, δ: 7.71–7.65 and 7.41–7.25 (15H, m, -$OCH_2C_6H_5$ and -OSi(C_6H_5)$_2$*t*Bu), 5.16 (1H, d, J = 10.0 Hz, -C*H*=C(CH_3)-), 4.62 (1H, d, J_{AB} = 12.0 Hz, -OCH_2Ph), 4.48 (1H, m, -O-C*H*-O-), 4.46 (1H, d, J_{AB} = 12.0 Hz, -OCH_2-Ph), 4.29 (1H, m, -C*H*(OBn)-), 3.85–3.68 (2H, m, -CH_2OTHP and -O-CH-O-CH_2-), 3.79 (1H, dd, J_{AB} = 10.5 Hz, J_{AX} = 6.8 Hz, -CH_2OSiPh$_2$*t*Bu), 3.60 (1H, dd, J_{AB} = 11.5 Hz, J_{BX} = 4.6 Hz, -CH_2OSiPh$_2$*t*Bu), 3.50–3.40 (1H, m, -O-CH-O-CH_2-), 3.39–3.28 (1H, m, -CH_2OTHP), 2.36–2.17 (2H, m, =C(CH_3)-CH_2-CH_2-), 1.78 (3H, s, -CH=C(CH_3)-), 1.76–1.42 (6H, m, -O-CH_2(CH_2)$_3$-), 1.05 (9H, s, -OSiPh$_2$C(CH_3)$_3$); ^{13}C nmr ($CDCl_3$) *Z* isomer, δ: 19.6, 23.8, 25.4, 26.9, 30.6, 32.8, 62.2, 65.7, 67.0, 70.2, 76.2, 98.8, 125.5, 127.2, 127.6, 128.2, 129.5, 133.8, 135.7, 138.2, 139.1; ^1H nmr ($CDCl_3$) *E* isomer, δ: 7.74–7.63 and 7.44–7.25 (15H, m, -O-CH_2-C_6H_5 and -OSi(C_6H_5)$_2$*t*Bu), 5.12 (1H, dm, J = 9.0 Hz, -C*H*=C(CH_3)-), 4.62 (1H, d, J_{AB} = 12.1 Hz, -OCH_2Ph), 4.60–4.56 (1H, m, -O-C*H*-O-), 4.43 (1H, d, J_{AB} = 12.1 Hz, -OCH_2Ph), 4.25–4.17 (1H, m, -C*H*(OBn)-), 3.85–3.76 (3H, m, -CH_2OSiPh$_2$-*t*Bu), 3.50–3.43 (2H, m, -CH_2OTHP and -O-CH-O-CH_2-), 2.30 (2H, t, J = 7.0 Hz, =C(CH_3)-CH_2-), 1.84–1.40 (6H, m, -O-CH_2-(CH_2)$_3$-), 1.54 (3H, d, J = 1.6 Hz, -CH=C(CH_3)-), 1.04 (9H, s, -OSiPh$_2$C(CH_3)$_3$); ^{13}C nmr ($CDCl_3$)

E isomer, δ: 17.1, 19.4, 25.4, 26.8, 30.7, 39.7, 62.1, 65.9, 66.8, 70.0, 76.1, 98.8, 124.7, 127.2, 127.6, 128.2, 129.5, 133.8, 135.7, 138.1, 139.1; ms *m/e* (70 eV): 501 (M^+ − *t*Bu). Exact Mass (M^+ − *t*Bu) calcd: 501.9711; found: 501.9711.

*(3Z)-2-Benzyloxy-6-[(2-tetrahydropyranyl)oxy]-4-methylhex-3-en-1-ol (**16**a)*

A solution of tetrabutylammonium fluoride in tetrahydrofuran (1M, 860 μL, 0.860 mmol) was added at 0°C to a stirred solution of silyl ether **15***a* (0.417 g, 0.748 mmol) in tetrahydrofuran (8.5 mL). The mixture was stirred at room temperature for 2 h and then poured into water and extracted with ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil obtained was purified by column chromatography (25% to 50% of ethyl acetate in hexane) to yield alcohol **16***a* (0.228 g, 95%); ir ($CHCl_3$) *ν*: 3580, 3470, 3010, 2945, 2875, 1452, 1212, 1120, 1060, 1030 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.36–7.26 (5H, m, -OCH$_2$C$_6$*H*$_5$), 5.22 (1H, d, *J* = 9.4 Hz, -C*H*=C(CH$_3$)-), 4.63 (d, 1H, J_{AB} = 11.6 Hz, -OC*H*$_2$Ph), 4.58–4.54 (1H, m, -O-C*H*-O-), 4.38 (1H, dd, J_{AB} = 11.6 Hz, J_{BX} = 0.9 Hz, -OC*H*$_2$Ph), 4.34–4.24 (1H, m, C*H*(OBn)-), 3.89–3.78 (2H, m, -C*H*$_2$OH and -O-CH-O-C*H*$_2$-), 3.68–3.39 (4H, m, -C*H*$_2$OTHP, -C*H*$_2$OH, and O-CH-O-C*H*$_2$-), 2.57–2.45 (1H, m, -CH$_2$O*H*), 2.34–2.23 (2H, m, =C(CH$_3$)-C*H*$_2$-CH$_2$OTHP), 1.83 (3H, dd, *J* = 1.3 Hz, -CH=C(C*H*$_3$)-), 1.82–1.49 (6H, m, -O-CH$_2$-(C*H*$_2$)$_3$-); ms *m/e* (70 eV): 280 (M^+ − CH$_2$OH). Exact Mass (M^+ − CH$_2$OH) calcd: 289.1804; found: 289.1801.

*(3E)-2-Benzyloxy-6-[(2'-tetrahydropyranyl)oxy]-4-methylhex-3-en-1-ol (**16**b)*

The preceding procedure was applied, using silyl ether **15***b* (99.2 mg, 0.178 mmol), tetrabutylammonium fluoride (1M in tetrahydrofuran, 215 μL, 0.215 mmol), and tetrahydrofuran (2.5 mL), and afforded alcohol **16***b* (50.0 mg, 88%); ^1H nmr ($CDCl_3$) δ: 7.35–7.28 (5H, m, -OCH$_2$C$_6$*H*$_5$), 5.16 (1H, dq, *J* = 9.2, 1.2 Hz, -C*H*=C(CH$_3$)-), 4.62 (1H, d, J_{AB} = 11.6 Hz, -OC*H*$_2$Ph), 4.59 (1H, t, *J* = 3.6 Hz, -O-C*H*-O-), 4.37 (1H, d, J_{AB} = 11.6 Hz, -OC*H*$_2$Ph), 4.31–4.22 (1H, m, -C*H*(OBn)-), 3.90–3.79 (2H, m, -C*H*$_2$OH and -O-CH-O-C*H*$_2$-), 3.64–3.44 (4H, m, -C*H*$_2$OTHP, -C*H*$_2$OH, and -O-CH-O-C*H*$_2$-), 2.36 (2H, t, *J* = 7.0 Hz, =C(CH$_3$)-C*H*$_2$-), 2.20–2.10 (1H, m, -CH$_2$O*H*), 1.83–1.46 (6H, m, -O-CH$_2$-(C*H*$_2$)$_3$-), 1.71 (3H, d, *J* = 1.2 Hz, -CH=C(C*H*$_3$)-).

*(3Z)-2-Benzyloxy-1-methanesulfonyloxy-6-[(2'-tetrahydropyranyl)oxy]-4-methylhex-3-ene (**17**a)*

Triethylamine (520 μL, 3.73 mmol) and methanesulfonyl chloride (160 μL, 2.07 mmol) were added at 0°C to a stirred solution of alcohol **16***a* (0.594 g, 1.86 mmol) in dichloromethane (11 mL). The mixture was stirred for 0.5 h and then poured into water and extracted with dichloromethane. The organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was used for the next reaction without any purification; ir ($CHCl_3$) *ν*: 3010, 3000, 2940, 2870, 1455, 1445, 1170 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.34–7.26 (5H, m, -OCH$_2$C$_6$*H*$_5$), 5.20 (1H, d, *J* = 9.1 Hz, -C*H*=C(CH$_3$)-), 4.62 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.54–4.44 (2H, m, -O-C*H*-O- and -C*H*(OBn)-), 4.40 (1H, dd, J_{AB} = 11.7 Hz, J_{BX} = 1.1 Hz, -OC*H*$_2$Ph), 4.25–4.17 (2H, m, -C*H*$_2$OSO$_2$CH$_3$), 3.88–3.76 (2H, m, -O-CH-O-C*H*$_2$ and -C*H*$_2$-OTHP), 3.66–3.35 (2H, m, -O-CH-O-C*H*$_2$- and -C*H*$_2$OTHP), 2.98 (3H, s, -SO$_2$C*H*$_3$), 2.49–2.22 (2H, m, =C(CH$_3$)-C*H*$_2$-), 1.83 (3H, d, *J* = 1.4 Hz, -CH=C(C*H*$_3$)-), 1.82–1.46 (6H, m, -O-CH$_2$-(C*H*$_2$)$_3$-), 1.82–1.46 (6H, m, -O-CH$_2$-(C*H*$_2$)$_3$-); ms *m/e* (70 eV): 313 (M^+ − OTHP). Exact Mass (M^+ − OTHP) calcd: 313.1110; found: 313.1106.

*(3E)-2-Benzyloxy-1-methanesulfoxy-6-[(2'-tetrahydropyranyl)oxy]-4-methylhex-3-ene (**17**b)*

The preceding procedure was applied, using alcohol **16***b* (42.1 mg, 0.132 mmol), methanesulfonyl chloride (11 μL, 0.142 mmol), and triethylamine (37 μL, 0.265 mmol), yielding mesylate **17***b* (53.2 mg, 100% crude); ^1H nmr ($CDCl_3$) δ: 7.34–7.28 (5H, m, -OCH$_2$C$_6$*H*$_5$), 5.16 (1H, d, *J* = 9.4 Hz, -C*H*=C(CH$_3$)-), 4.62 (1H, d, J_{AB} = 11.8 Hz, -OC*H*$_2$Ph), 4.62–4.58 (1H, m, -O-C*H*-O-), 4.48–4.37 (1H, m, -C*H*OBn-), 4.40 (1H, d, J_{AB} = 11.8 Hz, -OC*H*$_2$Ph), 4.26–4.13 (2H, m, -C*H*$_2$OSO$_2$CH$_3$), 3.91–3.81 (2H, m, -O-CH-O-CH$_2$- and -CH$_2$OTHP), 3.56–3.45 (2H, m, -O-CH-O-C*H*$_2$- and -C*H*$_2$OTHP), 2.99 (3H, s, -SO$_2$C*H*$_3$), 2.36 (2H, t, *J* = 6.9 Hz, =C(CH$_3$)-C*H*$_2$-), 1.88–1.47 (6H, m, -O-CH$_2$-(C*H*$_2$)$_3$-), 1.70 (3H, d, *J* = 1.3 Hz, -CH=C(C*H*$_3$)-).

*Methyl (5Z)-4-benzyloxy-8-[(2-tetrahydropyranyl)oxy]-2-methoxycarbonyl-6-methyloct-5-enoate (**18**a)*

Dimethyl malonate (1.12 mL, 9.84 mmol) was added at 0°C to a stirred suspension of sodium hydride (0.383 g, 60% in oil, 9.58 mmol) in tetrahydrofuran (5 mL) and dimethylformamide (5 mL). The mixture was stirred at room temperature for 0.5 h and a solution of mesylate **17***a* (0.739 g, 1.86 mmol) in tetrahydrofuran (2.5 mL) and dimethylformamide (2.5 mL) was then added followed by potassium iodide (0.462 g, 2.79 mmol). The mixture was heated at reflux (≈ 80°C) for 48 h, poured into a saturated solution of ammonium chloride, and extracted with a mixture of hexane and ether (2:1). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (20% ethyl acetate in hexane) to afford malonate **18***a* (0.717 g, 89%); ir ($CHCl_3$) *ν*: 3000, 2945, 2865, 1745, 1730, 1450, 1437, 1205 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.32–7.25 (5H, m, -OCH$_2$C$_6$*H*$_5$), 5.21 (1H, dq, *J* = 8.9, 1.2 Hz, -C*H*=C(CH$_3$)-), 4.57 (1H, t, *J* = 3.5 Hz, -O-C*H*-O-), 4.52 (1H, d, J_{AB} = 11.6 Hz, -OC*H*$_2$Ph), 4.25 (1H, d, J_{AB} = 11.6 Hz, -OC*H*$_2$Ph), 4.16 (1H, ddd, J_1 = J_2 = 8.9 Hz, J_3 = 4.5 Hz, -C*H*OBn-), 3.88–3.75 (2H, m, -O-CH-O-C*H*$_2$- and -C*H*$_2$OTHP), 3.66 and 3.65 (6H, 2s, -CH(CO$_2$C*H*$_3$)$_2$), 3.54–3.38 (3H, m, -C*H*(CO$_2$CH$_3$)$_2$, -O-CH-O-C*H*$_2$-, and -C*H*$_2$OTHP), 2.34 (2H, t, *J* = 7.2 Hz, =C(CH$_3$)-C*H*$_2$-), 2.24–2.09 (2H, m, -CH(OBn)-C*H*$_2$-), 1.80 (3H, br s, -CH=C(C*H*$_3$)-), 1.79–1.47 (6H, m, -O-CH$_2$-(C*H*$_2$)$_3$-); ms *m/e* (70 eV): 349 (M^+ − OTHP). Exact Mass (M^+ − OTHP) calcd: 349.1651; found: 349.1649.

*Methyl (5E)-4-benzyloxy-8-[(2-tetrahydropyranyl)oxy]-2-methoxycarbonyl-6-methyloct-5-enoate (**18**b)*

Sodium iodide (0.383 g, 2.55 mmol) was added to a solution of mesylate **17***b* (22.5 mg, 0.057 mmol) in acetone (3 mL). The mixture was heated at reflux for 3 h. After dilution with ethyl ether, the mixture was poured into a saturated solution of sodium thiosulfate and extracted with ethyl ether. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was quickly purified by column chromatography (10% to 25% ethyl acetate in hexane) to afford the corresponding iodide (11.8 mg, 49%), which was used immediately for the next reaction.

The preceding procedure was applied, using iodide (11.8 mg, 0.027 mmol) instead of mesylate, sodium hydride (6.4 mg, 60% in oil, 0.160 mmol), dimethyl malonate (19 μL, 0.165 mmol), tetrahydrofuran (0.2 mL), and dimethylformamide (0.2 mL), yielding malonate **18***b* (7.1 mg, 60%); ^1H nmr ($CDCl_3$) δ: 7.32–7.25 (5H, m, -OCH$_2$C$_6$*H*$_5$), 5.18 (1H, d, *J* = 8.9 Hz, -C*H*=C(CH$_3$)-), 4.62–4.58 (1H, m, -O-C*H*-O-), 4.52 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.25 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.10 (1H, ddd, J_1 = J_2 = 8.9 Hz, J_3 = 4.8 Hz, -C*H*OBn-), 3.89–3.79 (2H, m, -O-C*H*-O-CH$_2$- and -C*H*$_2$OTHP), 3.66 and 3.66 (6H, 2s, -CH(CO$_2$C*H*$_3$)$_2$), 3.64 (1H, dd, *J* = 8.2, 7.2 Hz, -C*H*(CO$_2$CH$_3$)$_2$), 3.54–3.44 (2H, m, -O-CH-O-C*H*$_2$- and -C*H*$_2$OTHP), 2.34 (2H, t, *J* = 6.9 Hz, =C(CH$_3$)-C*H*$_2$-), 2.24–2.00 (2H, m, -CH(OBn)-C*H*$_2$-), 1.90–1.50 (6H, m, -O-CH$_2$-(C*H*$_2$)$_3$-), 1.65 (3H, d, *J* = 1.3 Hz, -CH=C(C*H*$_3$)-).

*Methyl (5Z)-4-benzyloxy-8-hydroxy-2-methoxycarbonyl-5-methyloct-5-enoate (**19**a)*

Pyridinium *para*-toluenesulfonate (34.0 mg, 0.135 mmol) was added to a solution of ether **18***a* (74.6 mg, 0.172 mmol) in methanol (10 mL, 95%). The mixture was heated at reflux for 1.5 h, then the solvent was evaporated. The residual oil was purified by

column chromatography (25% to 50% ethyl acetate in hexane) to afford alcohol **19***a* (53.2 mg, 88%); ir (CH_2Cl_2) ν: 3600, 3490, 3060, 2950, 2880, 1750, 1730, 1437, 1215, 1157, 1055 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.33–7.26 (5H, m, -$OCH_2C_6H_5$), 5.27 (1H, d, J = 8.7 Hz, -C*H*=C(CH_3)-), 4.53 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.27 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.12 (1H, ddd, $J_1 = J_2$ = 8.8 Hz, J_3 = 5.0 Hz, -C*H*OBn-), 3.78–3.61 (3H, m, -C*H*(CO_2CH_3)$_2$ and -C*H*$_2$OH), 3.68 and 3.66 (6H, 2s, -CH-(CO_2CH_3)$_2$), 2.42–2.05 (4H, m, =C(CH_3)-C*H*$_2$- and -C*H*$_2$-CH(CO_2CH_3)$_2$), 1.78 (3H, d, J = 1.4 Hz, -CH=C(C*H*$_3$)-), 1.64 (1H, s, -CH_2O*H*); ms *m/e* (70 eV): 351 (MH^+). Exact Mass (MH^+) calcd: 351.1807; found: 351.1805.

*Methyl-(5E)-4-benzyloxy-8-hydroxy-2-methoxycarbonyl-6-methyloct-5-enoate (**19**b)*

The preceding procedure was applied, using ether **18***b* (7.4 mg, 0.017 mmol), pyridinium *para*-toluenesulfonate (4.0 mg, 0.016 mmol), and methanol (10 mL, 95%), yielding alcohol **19***b* (5.9 mg, 99%); ^1H nmr ($CDCl_3$) δ: 7.33–7.27 (5H, m, -OCH_2-C_6H_5), 5.20 (1H, dq, J = 8.9, 1.3 Hz, -C*H*=C(CH_3)-), 4.52 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.28 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.13 (1H, ddd, $J_1 = J_2$ = 8.8 Hz, J_3 = 4.8 Hz, -C*H*OBn-), 3.79–3.61 (3H, m, -C*H*(CO_2CH_3)$_2$ and -C*H*$_2$OH), 3.68 and 3.67 (6H, 2s, -CH(CO_2CH_3)$_2$), 2.30 (2H, t, J = 6.3 Hz, =C(CH_3)-C*H*$_2$-), 2.28–2.03 (2H, m, -C*H*$_2$-CH(CO_2CH_3)$_2$), 1.65 (3H, d, J = 1.3 Hz, -CH=C(C*H*$_3$)-), 1.58 (1H, s, -CH_2O*H*).

*Methyl (5Z)-4-benzyloxy-2-methoxycarbonyl-6-methyloct-5-enoate (**20**a)*

The same procedure as that used for **17***a* was applied: alcohol **19***a* (53.2 mg, 0.152 mmol), triethylamine (42 μL, 0.304 mmol), methanesulfonyl chloride (13 μL, 0.167 mmol), and dichloromethane (3 mL) yielding mesylate **20***a* (65.8 mg, 100% crude); ir ($CHCl_3$) ν: 3020, 2950, 1745, 1730, 1457, 1360, 1337, 1215, 1175 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.34–7.26 (5H, m, $OCH_2C_6H_5$), 5.32 (1H, d, J = 9.1 Hz, -C*H*=C(CH_3)-), 4.53 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.26 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.24 (2H, t, J = 6.9 Hz, -C*H*$_2$OMs), 4.08 (1H, ddd, $J_1 = J_2$ = 9.0 Hz, J_3 = 4.2 Hz, -C*H*(OBn)-), 3.68 (1H, dd, J = 6.2 Hz, -C*H*(CO_2CH_3)$_2$), 3.67 and 3.66 (6H, 2s, -CH(CO_2CH_3)$_2$), 3.01 (3H, s, -OSO_2CH_3), 2.58–2.48 and 2.22–2.00 (4H, 2m, =C(CH_3)-C*H*$_2$- and -C*H*$_2$-CH(CO_2CH_3)$_2$), 1.82 (3H, d, J = 1.4 Hz, -CH=C(CH_3)-).

*Methyl (5E)-4-benzyloxy-8-methanesulfonyloxy-2-methoxycarbonyl-6-methyloct-5-enoate (**20**b)*

The preceding procedure was applied, using alcohol **19***b* (10.3 mg, 0.029 mmol), triethylamine (8.2 μL, 0.059 mmol), methanesulfonyl chloride (2.5 μL, 0.032 mmol), and dichloromethane (0.5 mL), yielding mesylate **20***b* (10.1 mg, 80% crude); ^1H nmr ($CDCl_3$) δ: 7.33–7.27 (5H, m, -$OCH_2C_6H_5$), 5.23 (1H, dq, J = 8.8, 1.2 Hz, -C*H*=C(CH_3)-), 4.52 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.30 (2H, t, J = 6.7 Hz, -C*H*$_2$OMs), 4.27 (1H, d, J_{AB} = 11.7 Hz, -OC*H*$_2$Ph), 4.11 (1H, ddd, $J_1 = J_2$ = 8.8 Hz, J_3 = 4.7 Hz, -C*H*OBn-), 3.68 and 3.67 (6H, 2s, -CH(CO_2CH_3)$_2$), 3.64 (1H, dd, J = 8.2, 8.8 Hz, -C*H*(CO_2CH_3)$_2$), 3.00 (3H, s, -OSO_2CH_3), 2.48 (2H, t, J = 6.6 Hz, =C(CH_3)-C*H*$_2$-), 2.24–2.01 (2H, m, -C*H*$_2$-CH(CO_2CH_3)$_2$), 1.67 (3H, d, J = 1.2 Hz, -CH=C(C*H*$_3$)-).

*(4Z)-7-Benzyloxy-5,5-dimethoxycarbonyl-2-methylcyclohept-1-ene (**21**)*

Sodium bis(trimethylsilyl)amide (45 μL, 1 M in tetrahydrofuran, 0.045 mmol) was added at −78°C to a stirred solution of mesylate **20***a* (19.2 mg, 0.045 mmol) in tetrahydrofuran (5 mL) and dimethylformamide (5 mL). The temperature of the mixture was allowed to reach room temperature and then potassium iodide was added to the solution. The resulting mixture was stirred at 80°C for 4.5 h. After evaporation of the solvents under vacuum, the residual oil was purified by column chromatography (10% ethyl acetate in hexane) to yield cycloheptene **21** (11.5 mg, 77%); ir ($CHCl_3$) ν: 3020, 3010, 2950, 2855, 1728, 1455, 1435, 1245, 1215, 1090 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.35–7.24 (5H, m, -$OCH_2C_6H_5$), 5.54 (1H, m, -C*H*=C(CH_3)-), 4.59 (1H, d, J_{AB} = 12.0 Hz, -OC*H*$_2$Ph), 4.55 (1H, d, J_{AB} = 12.0 Hz, -OC*H*$_2$Ph), 4.16 (1H, d, J = 11.0 Hz, -C*H*OBn-), 3.71 and 3.69 (6H, 2s, -C(CO_2CH_3)$_2$-), 2.63 (1H, ddd, J_{AB} = 13.8 Hz, $J_{AX1} = J_{AX2}$ = 1.5 Hz, -CH(OBn)-C*H*$_2$-), 2.26 (1H, dd, J_{AB} = 13.8 Hz, J_{BX} = 10.4 Hz, -CH(OBn)-C*H*$_2$-), 2.18–2.13 (4H, m, =C(CH_3)-C*H*$_2$-C*H*$_2$-), 1.72 (3H, dd, $J_1 = J_2$ = 1.6 Hz, -CH=C(C*H*$_3$)-), ms *m/e* (70 eV): 332 (M^+), 241 (M^+ − CH_2Ph). Exact Mass (M^+) calcd: 332.1624; found: 332.1619.

*(3Z,9Z,11E)-5-Benzyloxy-13-[(tert-butyldiphenylsilyl)oxy]-1-methanesulfonyloxy-7,7-dimethoxycarbonyl-3-methyltrideca-3,9,11-triene (**23**)*

A solution of crude malonate **20***a* (65.8 mg, 0.154 mmol) in tetrahydrofuran (0.5 mL) and dimethylformamide (0.5 mL) was added at 0°C to a stirred suspension of sodium hydride (7.7 mg, 60% in oil, 0.193 mmol) in tetrahydrofuran (0.5 mL) and dimethylformamide (0.5 mL). After stirring for 0.5 h at room temperature the solution was cooled again to 0°C and then a solution of chloride **22** (7*e*) (86.4 mg, 0.232 mmol) in tetrahydrofuran (0.5 mL) and dimethylformamide (0.5 mL) was added at 0°C. The mixture was stirred for 10 h at room temperature and was then poured into a saturated solution of ammonium chloride and extracted with a mixture of hexane and ethyl ether (2:1). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% to 50% of ethyl acetate in hexane) to afford the triene **23** (99.4 mg, 86%); ir (CH_2Cl_2) ν: 3070, 3010, 2945, 2855, 1732, 1425, 1360, 1265, 1110 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.70–7.66, 7.46–7.34, and 7.28–7.16 (15H, 3m, -OSi(C_6H_5)$_2$*t*Bu, -O-CH_2-C_6H_5), 6.48 (1H, dd, J = 15.7, 11.1 Hz, -CH=CH-C*H*=CH-C*H*$_2$OSiPh$_2$*t*Bu), 6.11 (1H, dd, $J_1 = J_2$ = 11.1 Hz, -CH=C*H*-CH=CH-C*H*$_2$OSiPh$_2$*t*Bu), 5.80 (1H, dt, J = 15.7, 5.1 Hz, -CH=C*H*-C*H*$_2$OSiPh$_2$*t*Bu), 5.30 (1H, d, J = 9.4 Hz, -C*H*=C(CH_3)-), 5.25–5.14 (1H, m, -C*H*=CH-CH=CH-CH_2OSiPh$_2$-*t*Bu), 4.40 (1H, d, J_{AB} = 11.1 Hz, -OC*H*$_2$Ph), 4.27–4.12 (5H, m, -C*H*$_2$OSiPh$_2$*t*Bu, -C*H*$_2$$OSO_2CH_3$, -C*H*OBn-), 4.16 (1H, d, J_{AB} = 11.1 Hz, -OC*H*$_2$Ph), 3.56 and 3.53 (6H, 2s, -C(CO_2CH_3)$_2$-), 2.97 (3H, s, -OSO_2CH_3), 2.87 (2H, d, J = 7.9 Hz, -C(CO_2CH_3)$_2$-C*H*$_2$-CH=), 2.55–2.35 (2H, m, =C(CH_3)C*H*$_2$-), 2.23 (1H, dd, J_{AB} = 14.8 Hz, J_{AX} = 10.3 Hz, -C(CO_2CH_3)$_2$-C*H*$_2$-CHOBn-), 2.01 (1H, dd, J_{AB} = 14.8 Hz, J_{BX} = 2.6 Hz, -C(CO_2CH_3)$_2$-C*H*$_2$-CHOBn-), 1.79 (3H, d, J = 1.3 Hz, -CH=C(C*H*$_3$)-), 1.06 (9H, s, -OSi-Ph_2C(C*H*$_3$)$_3$); ms *m/e* (70 eV): 705 (M^+ − *t*Bu). Exact Mass (M^+ − *t*Bu) calcd: 705.2553; found: 705.2558.

*Methyl (5Z,11Z,13E)-7-benzyloxy-15-[(tert-butyldiphenylsilyl)-oxy]-5-methyl-2,9,9-trimethoxycarbonylpentadeca-5,11,13-trienoate (**24**)*

Dimethyl malonate (100 μL, 0.875 mmol) was added at 0°C to a stirred suspension of sodium hydride (32.4 mg, 60% in oil, 0.810 mmol) in tetrahydrofuran (1 mL) and dimethylformamide (1 mL). The mixture was stirred at room temperature for 0.5 h and a solution of mesylate **23** (131.1 mg, 0.171 mmol) in tetrahydrofuran (1 mL) and dimethylformamide (1 mL) was added at 0°C. Potassium iodide (14 mg, 0.085 mmol) was then added and the mixture was heated at 85°C for 6 h, poured into a saturated solution of ammonium chloride, and extracted with a mixture of hexane and ethyl ether (2:1). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (10% of ethyl acetate in hexane) to yield malonate **24** (112.9 mg, 83%); ir ($CHCl_3$) ν: 3020, 3000, 2950, 2940, 1730, 1432, 1205, 1110, 1075 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.69–7.66, 7.46–7.35, and 7.28–7.09 (15H, m, -OSi(C_6H_5)$_2$*t*Bu and -$OCH_2C_6H_5$), 6.50 (1H, ddd, J = 15.0, 11.1, 1.0 Hz, -CH=CH-C*H*=CH-CH$_2$OSiPh$_2$*t*Bu), 6.09 (1H, dd, $J_1 = J_2$ = 11.1 Hz, -CH=C*H*-CH=CH-CH$_2$OSiPh$_2$*t*Bu), 5.79 (1H, dt, J = 15.0, 5.0 Hz, -CH=C*H*-CH_2SiPh$_2$*t*Bu), 5.30–5.18 (1H, m,

-C*H*=CH-CH=CH-CH_2OSiPh_2tBu), 5.16 (1H, dq, J = 9.0, 1.2 Hz, -C*H*=C(CH_3)-), 4.38 (1H, d, J_{AB} = 11.0 Hz, -OCH_2Ph), 4.24 (2H, dd, J = 5.0, 0.9 Hz, -CH_2OSiPh_2tBu), 4.15 (1H, d, J_{AB} = 11.0 Hz, -OCH_2Ph), 4.11–4.22 (1H, m, -C*H*OBn-), 3.72, 3.71, 3.56, and 3.50 (12H, 4s, 4 × -CO_2CH_3), 3.32 (1H, t, J = 6.9 Hz, -C*H*(CO_2CH_3)$_2$), 2.99–2.77 (2H, m, -C(CO_2CH_3)$_2$-CH_2-CH=), 2.33–2.21 and 2.17–1.92 (6H, 2m, -CH_2-CH(CO_2CH_3)$_2$, -CHO-Bn-CH_2-, and =C(CH_3)-CH_2-), 1.75 (3H, d, J = 1.2 Hz, -CH=C(CH_3)-), 1.06 (9H, s, -OSiPh_2C(CH_3)$_3$); ms *m/e* (70 eV): 741 (M^+ − *t*Bu). Exact Mass (M^+ − *t*Bu) calcd: 741.3095; found: 741.3087.

*Methyl (5Z,11Z,13*E*)-7-benzyloxy-15-hydroxy-5-methyl-2,9,9-trimethoxycarbonylpentadeca-5,11,13-trienoate (25)*

Tetrabutylammonium fluoride (170 μL, 1 M in tetrahydrofuran, 0.170 mmol) was added at 0°C to a stirred solution of silyl ether **24** (112.4 mg, 0.141 mmol) in tetrahydrofuran (3.5 mL). The mixture was stirred at room temperature for 1.75 h and then the solvent was evaporated. The residual oil was purified by column chromatography (25% to 50% ethyl acetate in hexane) to afford alcohol **25** (67.7 mg, 87%); ir ($CHCl_3$) ν: 3600, 3010, 2950, 1730, 1435, 1230, 1070 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.33–7.25 (5H, m, -O$CH_2C_6H_5$), 6.46 (1H, ddd, J = 15.2, 11.2, 1.2 Hz, -CH=CH-C*H*=CH-CH_2OH), 6.08 (1H, dd, J_1 = J_2 = 11.2 Hz, -CH=C*H*-CH=C*H*-CH_2OH), 5.85 (1H, dt, J = 15.2, 5.3 Hz, -CH=CH-CH_2OH), 5.28–5.18 (1H, m, -C*H*=CH-CH=CH-CH_2OH), 5.15 (1H, dq, J = 9.2, 1.3 Hz, -C*H*=C(CH_3)-), 4.40 (1H, d, J_{AB} = 11.1 Hz, -OCH_2Ph), 4.18 (2H, d, J = 5.3 Hz, -CH_2OH), 4.16 (1H, d, J = 11.1 Hz, -OCH_2Ph), 4.11 (1H, ddd, J_1 = J_2 = 9.7 Hz, J_3 = 2.7 Hz, -CHOBn-), 3.74, 3.73, 3.61 and 3.50 (12H, 4s, 4 × -CO_2CH_3), 3.32 (1H, t, J = 6.6 Hz, -CH(CO_2CH_3)$_2$), 2.89 (2H, d, J = 7.8 Hz, -C(CO_2CH_3)$_2$-CH_2-CH=), 2.35–2.22 and 2.06–1.92 (6H, 2m, -CH_2-CH(CO_2CH_3)$_2$, -CHOBn-CH_2, and =C(CH_3)-CH_2-), 1.75 (3H, d, J = 1.3 Hz, -CH=C(CH_3)-), 1.72 (1H, s, -CH_2OH); ms *m/e* (70 eV): 545 (M^+ − CH_3), 542 (M^+ − H_2O). Exact Mass (M^+ − CH_3) calcd: 545.2387; found: 545.2396.

*Methyl (5Z,11Z,13*E*)-7-benzyloxy-15-chloro-2,9,9-trimethoxycarbonyl-5-methylpentadeca-5,11,13-trienoate (26)*

s-Collidine (32 μL, 0.242 mmol) and methanesulfonyl chloride (19 μL, 0.242 mmol) were added at 0°C to a stirred solution of alcohol **25** (67.7 mg, 0.121 mmol) and lithium chloride (15.4 mg, 0.363 mmol) in dimethylformamide (1 mL). The mixture was stirred at 0°C for 2 h, was poured into water, and then extracted with a mixture of hexane and ethyl ether (2:1). The combined organic layers were washed with an aqueous solution of copper nitrate and with water, dried over magnesium sulfate, filtered, and concentrated. The crude chloride **26** (67.5 mg, 97%) residual oil was used immediately for the next reaction; ir ($CHCl_3$) ν: 2950, 2922, 2855, 1732, 1438, 1235, 1200, 1075 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.33–7.26 (5H, m, -O$CH_2C_6H_5$), 6.47 (1H, ddd, J = 14.9, 11.2, 1.0 Hz, -CH=CH-C*H*=CH-CH_2Cl), 6.07 (1H, dd, J_1 = J_2 = 11.2 Hz, -CH=C*H*-CH=CH-CH_2Cl), 5.80 (1H, dt, J = 14.9, 7.4 Hz, -CH=C*H*-CH_2Cl), 5.40–5.30 (1H, m, -C*H*=CH-CH=CH-CH_2Cl), 5.16 (1H, dq, J = 9.8, 1.2 Hz, -C*H*=C(CH_3)-), 4.41 (1H, d, J_{AB} = 11.1 Hz, -OCH_2Ph), 4.17 (1H, d, J_{AB} = 11.1 Hz, -OCH_2Ph), 4.19–4.06 (1H, m, -C*H*OBn-), 4.07 (2H, d, J = 7.4 Hz, -CH_2Cl), 3.74, 3.73, 3.61, and 3.53 (12H, 4s, 4x -CO_2CH_3), 3.31 (1H, t, J = 7.0 Hz, -C*H*(CO_2CH_3)$_2$), 2.99–2.78 (2H, m, -C(CO_2CH_3)$_2$-CH_2-CH=), 2.28, 2.07–1.92, and 1.84 (6H, dd, J = 14.8, 10.4 Hz, m and s, -CH_2-CH(CO_2CH_3)$_2$, -CHOBn-CH_2, and =C(CH_3)-CH_2-), 1.76 (3H, d, J = 1.2 Hz, -CH=C(CH_3)-).

*(1*E*,3Z,9Z)-8-Benzyloxy-10-methyl-6,6,13,13-tetramethoxycarbonylcyclotetradeca-1,3,9-triene (5)*

To a stirred suspension of cesium carbonate (190.2 mg, 0.584 mmol) in tetrahydrofuran (12 mL) and dimethylformamide (12 mL) at 75°C, was added during 10 hs a solution of chloride **26** (67.5 mg, crude, 0.117 mmol) in tetrahydrofuran (12 mL) and dimethylformamide (12 mL). The mixture was stirred for 10 more hours, then was cooled at room temperature, filtered, and evaporated under vacuum. The residual oil was purified by column chromatography (hexane/ethyl/acetate/dichloromethane, 7.5:0.5:2–7:1:2) yielding carbocycle **5** (48.5 mg, 74%); mp 161–162°C; uv (hexane) λ_{max}: 232, 266 nm; ir ($CHCl_3$) ν: 3010, 2950, 1760, 1437, 1205, 1215, 1175 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.40–7.31 (5H, m, -O$CH_2C_6H_5$), 6.08–5.94 (2H, m, -CH=C*H*-C*H*=CH-), 5.23–5.03 and 4.99–4.86 (2H, 2m, -C*H*=CH-CH=C*H*-), 5.02 (1H, d, J = 9.5 Hz, -C*H*=C(CH_3)), 4.44 (1H, d J_{AB} = 11.6 Hz, -OCH_2Ph), 4.05 (1H, d, J_{AB} = 11.6 Hz, -OCH_2Ph), 4.08–3.99 (1H, m, -C*H*OBn-), 3.77, 3.73, 3.71, and 3.49 (12H, 4s, 4x -CO_2CH_3), 2.98–2.74 (3H, m, -CH_2-CH=CH-CH=CH-CH_2-), 2.41 (1H, dd, J = 14.3, 11.9 Hz, -CH_2-CH=CH-), 2.33 (1H, dd, J = 14.6, 11.6 Hz, -CH(OBn)-CH_2-), 2.17–2.13 (2H m, -CH_2-C(CH_3)=), 1.74 (3H, d, J = 1.3 Hz, -CH=C(CH_3)-), 1.68 (1H, dd, J = 14.6, 2.6 Hz, -CHOBn-CH_2-), 1.42–1.23 (2H, m, -CH_2-CH_2-C(CH_3)=); ms *m/e* (70 eV): 542 (M^+). Exact Mass (M^+) calcd: 542.2516; found: 542.2517.

3β-Benzyloxy-1β-methyl-5,5,12,12-tetramethoxycarbonyl-trans-cisoid-cis-*tricyclo[8.4.0.0^{2,7}]tetradec-8-ene (6)*

A solution of macrocyclic triene **5** (R = CH_2Ph) (16.8 mg, 0.031 mmol) in toluene (0.2 mL) was heated in a sealed tube at 270°C for 2.75 h. The solvent was then evaporated and the residual oil was purified by column chromatography (10% to 25% ethyl acetate in hexane) to afford the tricyclic compound **6** (R = CH_2Ph) (14.2 mg, 85%) and a mixture of two other compounds (2.6 mg, 15%); mp 104–106°C; ir ($CHCl_3$) ν: 3020, 3030, 2955, 1730, 1435, 1455, 1220, 1250, 1265 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.38–7.25 (5H, m, -O$CH_2C_6H_5$), 5.27 (2H, s, H-C8 and H-C9), 4.61 (1H, d, J_{AB} = 10.8 Hz, -OCH_2Ph), 4.43 (1H, d, J_{AB} = 10.8 Hz, -OCH_2Ph), 3.76 (1H, ddd, J_1 = J_2 = 9.9 Hz, J_3 = 4.4 Hz, -C*H*OBn-), 3.70, 3.69, 3.69, and 3.65 (12H, 4s, 4x -CO_2CH_3), 2.93–2.73 and 2.46–1.27 (13H, m H-C2, H-C4, H-C6, H-C7, H-C10, H-C11, H-C13, H-C14), 0.92 (3H, s, -CH_3-C1); ms *m/e* (70 eV): 542 (M^+), 511 (M^+ − OCH_3). Exact Mass (M^+ − OCH_3) calcd: 511.2332; found: 511.2319.

3β-Hydroxy-1β-methyl-5,5,12,12-tetramethoxycarbonyl-trans-cisoid-cis-*tricyclo[8.4.0.0^{2,7}]tetradec-8-ene and (1S,3S)-3-hydroxy-1-methyl-5,5,12,12-tetramethoxycarbonyl*-trans-cisoid-cis-*tricyclo*[*8.4.0.0^{2,7}*]tetradec-8-ene (27)*

Tin tetrachloride (21 μL, 0.179 mmol) was added to a stirred solution of benzyl ether **6** (R = CH_2Ph) (5.4 mg, 0.010 mmol) in dichloromethane (1 mL). The mixture was stirred at room temperature for about 19 h,[4] poured into water, and extracted with dichloromethane. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (40% of ethyl acetate in hexane) to afford alcohol **27** (3.9 mg, 87%).

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone was added to a stirred solution of *para*-methoxybenzyl ether **6** (R = CH_2-$C_6H_4OCH_3$) (8.0 mg, 0.014 mmol) in dichloromethane (8 mL) and water (100 μL). The mixture was stirred at room temperature for 1.5 h, then was poured into water and extracted with dichloromethane. The residual oil was purified by column chromatography (25% to 50% ethyl acetate in hexane) to yield alcohol **27** (4.7 mg, 76%); $[\alpha]_D^{25}$ −88.5 (*c* 0.72, CH_2Cl_2); ir ($CHCl_3$) ν: 3600, 3020, 3010, 2950, 2920, 2850, 1727, 1455, 1450, 1435, 1255, 1245, 1205 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 5.26–5.20 (2H, m, H-C8 and H-C9), 4.03 (1H, ddd, J_1 = J_2 = 9.5 Hz, J_3 = 4.8 Hz, -C*H*OH-) 3.78, 3.70, 3.69, 3.67 (12H, 4s, 4x -CO_2CH_3), 2.88–2.83 and 2.49–1.47 (13H, m, H-C2, H-C4, H-C6, H-C7, H-C10, H-C11, H-C13, and H-C14), 0.92 (3H, s, -CH_3-C1); ms *m/e* (70 eV): 434 (M^+ − H_2O). Exact Mass (M^+ − H_2O) calcd: 434.1941; found: 434.1937.

[4]Variable reaction times. In some cases lactone **29** was also isolated.

1β-Methyl-5,5,12,12-tetramethoxycarbonyl-trans-cisoid-cis-*tricyclo[8.4.0.0^{2,7}]tetradec-8-en-3-one and (1S)-1-methyl-5,5,12,12-tetramethoxycarbonyl*-trans-cisoid-cis-*tricyclo[8.4.0.0^{2,7}]tetradec-8-en-3-one (28)*

Pyridinium chlorochromate (10.4 mg, 0.048 mmol) was added to a stirred solution of alcohol **27** (7.3 mg, 0.016 mmol) in dichloromethane (1 mL). The mixture was stirred for 1.5 h at room temperature, poured into water, and extracted with dichloromethane. The combined organic layers were washed with water, dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% to 40% ethyl acetate in hexane) to yield ketone **28** (6.3 mg, 87%); mp 150–151°C (racemix mixture); $[\alpha]_D^{25}$ −93.2 (*c* 0.63, CH_2Cl_2); ir ($CHCl_3$) ν: 3020, 2955, 1730, 1435, 1260, 1220 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 5.33–5.47 (2H, m, H-C8 and H-C9), 3.82, 3.74, 3.70, and 3.69 (12H, 4s, 4x -CO_2CH_3), 2.86 (1H, dd, J_{AB} = 14.7 Hz, J_W = 1.0 Hz, H-C4), 2.64 (1H, d, J_{AB} = 14.7 Hz, H-C4), 3.17–3.05 and 2.55–1.33 (11H, m, H-C2, H-C6, H-C7, H-C10, H-C11, H-C13, and H-C14), 0.90 (3H, s, -CH_3-C1); ms *m/e* (70 eV): 450 (M^+). Exact Mass (M^+) calcd: 450.1890; found: 450.1884.

1β-Methyl-5,5,12,12-tetramethoxycarbonyl-trans-transoid-trans-*tricyclo[8.4.0.0^{2,7}]tetradec-8-en-3-one and (1S)-methyl-5,5,12,12-tetramethoxycarbonyl*-trans-transoid-trans-*tricyclo[8.4.0.0^{2,7}]tetradec-8-en-3-one (7)*

Sodium carbonate (1.0 mg, 0.009 mmol) was added to a stirred solution of ketone **28** (3.1 mg, 0.007 mmol) in methanol (1 mL) and tetrahydrofuran (minimum amount necessary to solubilize ketone **28**). The mixture was heated at 65°C for 2.5 h, then poured into a saturated solution of ammonium chloride and extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% of ethyl acetate in hexane) to afford ketone **7** (2.9 mg, 94%); mp 114–115°C (racemix mixture); $[\alpha]_D^{25}$ +14.4 (*c* 0.30, CH_2Cl_2); ir ($CHCl_3$) ν: 2955, 2920, 2850, 1730, 1435, 1455, 1465, 1250, 1220 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 5.47 (1H, ddd, J_{AB} = 10.2 Hz, J_{BX1} = J_{BX2} = 2.2 Hz, H-C8 or H-C9), 5.37 (1H, dm, J_{AB} = 10.2 Hz, H-C8 or H-C9), 3.75, 3.74, 3.73, and 3.70 (12H, 4s, 4x -CO_2CH_3), 2.91 (1H, dd, J_{AB} = 14.0 Hz, J_W = 2.2 Hz, H-C4), 2.62 (1H, dd, J_{AB} = 14.0 Hz, J_W = 1.1 Hz, H-C4), 2.61–1.05 (11H, m, H-C2, H-C6, H-C7, H-C10, H-C11, H-C13, and H-C14), 0.95 (3H, s, -CH_3-C1); ms *m/e* (70 eV): 450 (M^+). Exact Mass (M^+) calcd: 450.1890, found: 450.1884.

1β-Methyl-5,12,12-trimethoxycarbonyl-trans-cisoid-cis-*tricyclo[8.4.0.0^{2,7}]tetradec-8-ene-5,3β-carbolactone (29)*

para-Toluenesulfonic acid (1.0 mg, 0.005 mmol) was added to a stirred solution of alcohol **27** (1.0 mg, 0.002 mmol) in benzene (0.5 mL). The mixture was heated at 65°C for 1.5 h, poured into a solution of sodium bicarbonate (5%), and extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% of ethyl acetate in hexane) to yield lactone **29** (0.8 mg, 86%); ir ($CHCl_3$) ν: 3015, 2950, 2920, 1780, 1730, 1450, 1435, 1255, 1220 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 5.58 (1H, ddd, J_{AB} = 9.8 Hz, J_{BX1} = J_{BX2} = 2.3 Hz, H-C8 or H-C9), 5.35 (1H, dm, J_{AB} = 9.8 Hz, H-C9 or H-C8), 4.82 (1H, d, *J* = 4.3 Hz, H-C3), 3.78, 3.77, 3.72 (9H, 3s, 3x -CO_2CH_3), 2.81–1.28 (13H, m, H-C2, H-C4, H-C6, H-C7, H-C10, H-C11, H-C13, and H-C14), 0.94 (3H, s, -CH_3-C1); ms *m/e* (70 eV): 420 (M^+). Exact Mass (M^+) calcd: 420.1784; found: 420.1781.

2-Carboxy-1-methylethyltriphenylphosphonium bromide (31)

A stirred mixture of triphenylphosphine (28.88 g, 0.110 mmol) and 3-bromobutanoic acid **30** (18.39 g, 0.110 mmol) in toluene (250 mL) was heated at reflux for 24 h. The solid was filtered and washed with toluene to afford phosphonium salt **31** (44.48 g, 94% crude); ir ($CHCl_3$) ν: 3500–2400, 3030, 3010, 2955, 1730, 1440, 1215 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 8.30 (1H, s, -COO*H*), 7.86–7.69 (15H, m, aromatic protons), 4.61–4.40 (1H, m, $Br^-P^+Ph_3$-$CH(CH_3)$-), 3.18–2.87 (2H, m, -CH_2-CO_2H), 1.41 (3H, dd, *J* = 18.8, 6.9 Hz, $Br^-P^+Ph_3CH(CH_3)$-).

2-Methoxycarbonyl-1-methyltriphenylphosphonium iodide (32)

Sodium iodide (22.54 g, 0.150 mmol), sodium carbonate (10.62 g, 0.100 mmol), and iodomethane (12.5 mL, 0.2 mol) were added to a stirred solution of phosphonium bromide **31** (43.00 g, 0.100 mol) in acetone (1 L). The mixture was heated at reflux for 12 h. The solvent was then evaporated and the residue was dissolved in dichloromethane. After filtration and evaporation of the solvent, the residue was purified by recrystallization from dichloromethane and hexane to afford phosphonium salt **32** (39.85 g, 81%); mp 163–165°C; ir ($CHCl_3$) ν: 3010, 2935, 1735, 1588, 1485, 1455, 1440, 1230, 1215, 1105 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.93–7.71 (15H, m, aromatic protons), 4.90–4.73 (1H, m, $I^-P^+Ph_3$-$CH(CH_3)$-) 3.71 (3H, s, -CO_2CH_3), 2.92 (1H, ddd, J_1 = J_2 = 15.6 Hz, J_3 = 2.9 Hz, -$CH_2CO_2CH_3$), 2.40 (1H, m, -$CH_2CO_2CH_3$), 1.50 (3H, dd, *J* = 18.6, 7.0 Hz, $I^-P^+Ph_3$-$CH(CH_3)$-).

3-Hydroxy-1-methylpropyltriphenylphosphonium iodide (33a)

Diisobutylaluminium hydride (5.0 mL, 7.52 mmol) was added at −78°C to a stirred solution of ester **32** (1.229 g, 2.51 mmol) in dichloromethane (20 mL). The mixture was stirred at −78°C for 2 h. Decahydrated sodium sulfate (775 mg, 2.41 mmol) was then added at −78°C and the mixture was allowed to warm up slowly to room temperature. After stirring for 12 h, anhydrous sodium sulfate was added and the salts were filtered and washed with acetone. The filtrate was concentrated and the residual solid was recrystallized from hexane and dichloromethane to yield phosphonium salt **33** (0.717 g, 62%); mp 219–221°C, ir ($CHCl_3$) ν: 3350, 3020, 2950, 1440, 1215, 1112 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.95–7.86 and 7.78–7.65 (15H, m, aromatic protons), 5.12–4.96 (1H, m, $I^-P^+Ph_3$-$CH(CH_3)$-), 4.48 (1H, dd, *J* = 7.7, 6.6 Hz, -CH_2OH), 4.04–3.92 and 3.80–3.71 (2H, 2m, -CH_2OH), 2.28–2.13 (1H, m, -CH_2-CH_2OH), 1.40 (3H, dd, *J* = 19.5, 6.8 Hz, $I^-P^+Ph_3$-$CH(CH_3)$-), 1.03–1.12 (-CH_2-CH_2OH).

3-Hydroxy-1-methylpropyltriphenylphosphonium bromide (33b)

Pyridinium *para*-toluenesulfonate (861 mg, 3.43 mmol) was added to a stirred solution of phosphonium bromide **14** (17.10 g, 34.27 mmol) in methanol (250 mL). The solution was heated at 50°C for 18 h and then sodium bicarbonate (0.864 g, 10.29 mmol) was added. The mixture was filtered and the filtrate was evaporated. The residual solid was dissolved in dichloromethane and the mixture was again filtered. After evaporation of the filtrate, the residual solid was recrystallized from dichloromethane and hexane to yield phosphonium salt **33***b* (11.81 g, 83%).[5]

(2R)-1,2-O-Isopropylidene-4-methylhex-3-en-1,2,6-triol (35)

Butyllithium (30.2 mL, 1.6 M in hexane, 48.3 mmol) was added at −78°C to a stirred suspension of phosphonium bromide **33** (10.06 g, 24.2 mmol, dried under vacuum at 115–120°C for 48 h) in tetrahydrofuran (62 mL). The temperature was allowed to reach 0°C and the solution was stirred until it became dark red (≈0.5 h). A solution of aldehyde **34** (5.43 g, 41.8 mmol) in tetrahydrofuran (62 mL) was then added at 0°C. After 10 min, the mixture was poured into a saturated solution of ammonium chloride and extracted with dichloromethane and with ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% ethyl acetate in hexane) to afford *Z* olefin **35***a*[6] (2.23 g, 50%)[7] and *E* olefin **35***b*[6] (0.443 g, 10%)[7]; $[\alpha]_D^{25}$, *E* isomer −12.2 (*c* 4.20, $CHCl_3$); ir ($CHCl_3$) ν, *Z* isomer: 3610, 3480, 3005, 2980, 2930, 2870, 1445, 1370, 1380, 1215, 1155, 1050 cm^{-1}; ir ($CHCl_3$) ν, *E* isomer: 3610, 3480, 3005, 2985, 2935, 2870, 1450, 1320, 1330, 1235, 1228, 1155, 1150 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ, *Z* isomer: 5.39 (1H, d, *J* = 8.5 Hz, -C*H*=C(CH_3)-), 4.78 (1H,

[5]Spectral data are identical with those obtained for **33***a*.

[6]Volatile compounds.

[7]Yield calculated from phophonium salt **33**.

ddd, $J_1 = J_2 = 8.2$ Hz, $J_3 = 5.9$ Hz, -OCH$_2$-C*H*-O-), 4.06 (1H, dd, $J_{AB} = 8.0$ Hz, $J_{AX} = 5.9$ Hz, -OC*H*$_2$-CH-O-), 3.69 (2H, t, $J = 6.2$ Hz, -C*H*$_2$OH), 3.56 (1H, dd, $J_{AB} = 8.0$ Hz, $J_{BX} = 8.0$ Hz, -OC*H*$_2$-CH-O-), 2.52–2.30 (2H, m, -C*H*$_2$-CH$_2$OH), 1.79 (3H, d, $J = 1.4$ Hz, -CH=C(C*H*$_3$)-), 1.41 and 1.38 (6H, 2s, -O-C(C*H*$_3$)$_2$-O-), 1.96 (1H, s, -CH$_2$O*H*); ^{13}C nmr ($CDCl_3$) δ, *Z* isomer: 23.6, 25.8, 26.6, 35.5, 60.0, 69.4, 72.3, 108.8, 124.9, 139.3; ^{1}H nmr ($CDCl_3$) δ, *E* isomer: 5.28 (1H, dq, $J = 8.6$, 1.3 Hz, -C*H*=C(CH$_3$)-), 4.80 (1H, ddd, $J_1 = J_2 = 8.3$ Hz, $J_3 = 5.9$ Hz, -OCH$_2$-C*H*-O-), 4.06 (1H, dd, $J_{AB} = 8.1$ Hz, $J_{AX} = 5.9$ Hz, -OC*H*$_2$-CH-O-), 3.70 (2H, t, $J = 6.4$ Hz, -C*H*$_2$OH), 3.50 (1H, dd, $J_{AB} = 8.1$ Hz, $J_{BX} = 8.1$ Hz, -OC*H*$_2$-CH-O-), 2.29 (2H, td, $J = 6.4$, 1.1 Hz, -C*H*$_2$-CH$_2$OH), 1.74 (3H, d, $J = 1.4$ Hz, -CH=C(C*H*$_3$)-), 1.41 and 1.38 (6H, 2s, -O-C(C*H*$_3$)$_2$-O-); ^{13}C nmr ($CDCl_3$) δ, *E* isomer: 16.6, 25.9, 26.9, 42.5, 60.2, 69.4, 72.7, 108.9, 124.6, 138.4; ms *m/e* (70 eV): 186 (M^+), 171 ($M^+ - CH_3$). Exact Mass (M^+) calcd: 186.1256; found: 186.1254.

*(2R)-(3Z)-6-Benzoyloxy-1,2-O-isopropylidene-4-methylhex-3-ene-1,2-diol (**41**)*

Triethylamine (225 μL, 1.62 mmol), benzoyl chloride (150 μL, 1.30 mmol), and dimethylaminopyridine (26 mg, 0.22 mmol) were added at 0°C to a stirred solution of alcohol **35***a* (0.201 g, 1.08 mmol) in dichloromethane (11 mL). The mixture was stirred at 0°C for 1.5 h, then poured into a saturated solution of ammonium chloride and extracted with dichloromethane. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (40% ethyl acetate in hexane) to yield benzoate **41** (0.280 g, 89%); $[\alpha]_D^{25}$ −0.9 (*c* 1.30, $CHCl_3$), ir ($CHCl_3$) *ν*: 3020, 2990, 2940, 1718, 1455, 1280, 1250, 1220, 1115, 1058 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 8.05–8.01, 7.59–7.53, and 7.46–7.40 (5H, 3m, -OCOC$_6$*H*$_5$), 5.34 (1H, d, $J = 8.9$ Hz, -C*H*=C(CH$_3$)-), 4.82 (1H, ddd, $J_1 = J_2 = 8.1$ Hz, $J_3 = 6.0$ Hz, -OCH$_2$-C*H*-O-), 4.39 (2H, td, $J = 6.6$, 1.2 Hz, -C*H*$_2$OBz), 3.96 (1H, dd, $J_{AB} = 8.1$ Hz, $J_{AX} = 6.0$ Hz, -OC*H*$_2$-CH-O-), 3.46 (1H, dd, $J_{AB} = 8.1$ Hz, $J_{BX} = 8.1$ Hz, -OC*H*$_2$-CH-O-), 2.72–2.47 (2H, m, -C*H*$_2$OBz), 1.86 (3H, d, $J = 1.5$ Hz, -CH=C(C*H*$_3$)-), 1.40 and 1.36 (6H, 2s, -O-C(C*H*$_3$)$_2$-O-); ms *m/e* (70 eV): 290 (M^+), 275 ($M^+ - CH_3$). Exact Mass (M^+) calcd: 290.1518; found: 290.1524.

*(2R)-(3Z)-6-Benzoyloxy-4-methylhex-3-en-1,2-diol (**42**)*

para-Toluenesulfonic acid monohydrate (55 mg, 0.29 mmol) was added at 0°C to a stirred solution of acetonide **41** (0.280 g, 0.96 mmol) in methanol (23 mL). The mixture was stirred at room temperature for 1.5 h, then poured into a saturated solution of sodium chloride and extracted with dichloromethane. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (80% of ethyl acetate in hexane then pure ethyl acetate) to afford diol **42** (0.212 g, 87%); mp 47–48°C; $[\alpha]_D^{25}$ −8.9 (*c* 1.06, $CHCl_3$); ir ($CHCl_3$) *ν*: 3600, 3010, 2965, 2935, 1718, 1450, 1275, 1215, 1118 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 8.05–8.01, 7.60–7.54, 7.48–7.42 (5H, 3m, -OCOC$_6$*H*$_5$), 5.34 (1H, d, $J = 9.5$ Hz, -C*H*=C(CH$_3$)-), 4.57–4.47 (1H, m, -C*H*OH-), 4.42 (2H, t, $J = 6.8$ Hz, -C*H*$_2$OCOPh), 3.62–3.42 (2H, m, -C*H*$_2$OH), 2.61 (2H, t, $J = 6.8$ Hz, -C*H*$_2$CH$_2$OBz), 2.07 (1H, d, $J = 3.1$ Hz, -CHO*H*-), 1.94 (1H, t, $J = 5.7$ Hz, -CH$_2$O*H*), 1.84 (3H, d, $J = 1.1$ Hz, -CH=C(C*H*$_3$)-); ms *m/e* (70 eV): 219 ($M^+ - CH_2OH$).

*(2R)-(3Z)-6-Benzoyloxy-1-[(para-toluenesulfonyl)oxy]-4-methylhex-3-en-2-ol (**43**)*

Triethylamine (110 μL, 0.79 mmol), *para*-toluenesulfonyl chloride (0.179 g, 0.94 mmol), and dimethylaminopyridine (70 mg, 0.58 mmol) were added at 0°C to a stirred solution of diol **42** (0.180 g, 0.72 mmol) in dichloromethane (18 mL). The mixture was stirred at 0°C for 1.5 h, then poured into a saturated solution of ammonium chloride and extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% to 50% ethyl acetate in hexane, then pure ethyl acetate) to give tosylate **43** (0.210 g, 72%) and diol **42** (25.3 mg, 14%); $[\alpha]_D^{25}$ −33.8 (*c* 1.71, $CHCl_3$); ir ($CHCl_3$) *ν*: 3590, 3020, 2950, 1717, 1600, 1452, 1365, 1275, 1220, 1190, 1175, 1120, 1100 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 8.02–7.98, 7.79–7.76, 7.61–7.54, 7.47–7.41, and 7.34–7.31 (9H, 5m, -OCOC$_6$*H*$_5$, -CH$_2$OSO$_2$-C$_6$*H*$_4$CH$_3$), 5.23 (1H, d, $J = 9.0$ Hz, -C*H*=C(CH$_3$)-), 4.72–4.62 (1H, m, -C*H*OH-), 4.37 (2H, t, $J = 6.8$ Hz, -C*H*$_2$OCOPh), 4.01–3.86 (2H, m, -C*H*$_2$OTs), 2.53 (2H, td, $J = 6.8$, 2.2 Hz, -C*H*$_2$CH$_2$OCOPh), 2.43 (3H, s, -OSO$_2$C$_6$H$_4$C*H*$_3$), 2.11 (1H, d, $J = 3.6$ Hz, -CHO*H*-), 1.80 (3H, d, $J = 1.4$ Hz, -CH=C(C*H*$_3$)-).

*(2R)-(3Z)-6-Benzoyloxy-2-[(para-methoxybenzyl)oxy]-1-[(para-toluenesulfonyl)oxy]-4-methylhex-3-ene (**44**)*

A solution of trichloro-*para*-methoxybenzylacetimidate (0.569 g, 2.01 mmol) in ethyl ether (1 mL) was added to a solution of alcohol **43** (0.204 g, 0.50 mmol) in ethyl ether (20 mL). The mixture was cooled to 0°C and trifluoromethanesulfonic acid (40 μL, solution 1 μL in 1 mL of ethyl ether, 0.0005 mmol) was added. The mixture was stirred at 0°C for 3 h, then poured into a saturated solution of sodium carbonate and extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% of ethyl acetate in hexane and 2% acetone in toluene) to afford ether **44** (0.214 g, 73%); $[\alpha]_D^{25}$ −8.5 (*c* 1.30, $CHCl_3$); ir ($CHCl_3$) *ν*: 3020, 2930, 1718, 1612, 1600, 1515, 1450, 1360, 1275, 1250, 1212, 1178 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 8.02–7.99, 7.76–7.73, 7.59–7.53, 7.46–7.40, 7.28–7.25, 7.14–7.11, and 6.84–6.80 (13H, 7m, -OCOC$_6$*H*$_5$, -OSO$_2$C$_6$*H*$_4$CH$_3$, -OCH$_2$C$_6$*H*$_4$OCH$_3$), 5.14 (1H, d, $J = 9.1$ Hz, -C*H*=C(CH$_3$)-), 4.42 (1H, d, $J_{AB} = 11.3$ Hz, -OC*H*$_2$C$_6$H$_4$OCH$_3$), 4.38–4.30 (1H, m, -C*H*(OMPM)-), 4.32 (2H, t, $J = 7.0$ Hz, -C*H*$_2$OCOPh), 4.24 (1H, d, $J_{AB} = 11.3$ Hz, -OC*H*$_2$C$_6$H$_4$OCH$_3$), 4.03–3.92 (2H, m, -C*H*$_2$OTs), 3.78 (3H, s, -OCH$_2$C$_6$H$_4$OC*H*$_3$), 2.46 (2H, t, $J = 7.0$ Hz, -C*H*$_2$-CH$_2$OBz), 2.40 (3H, s, -OSO$_2$C$_6$H$_4$C*H*$_3$), 1.83 (3H, d, $J = 1.2$ Hz, -CH=C(C*H*$_3$)-).

*(2R)-(3Z)-6-Benzoyloxy-1-iodo-2-[(para-methoxybenzyl)oxy]-4-methylhex-3-ene (**45**)*

Sodium iodide (183 mg, 1.221 mmol) and tetrabutylammonium iodide (680 mg, 1.854 mmol) were added to a stirred solution of tosylate **44** (32.0 mg, 0.061 mmol) in acetone (5 mL) and the mixture stirred for 70 h at 50°C. The solvent was then evaporated and the residual solid was purified by column chromatography (25% of ethyl acetate in hexane) to yield iodide **45** (28.9 mg, 99%); $[\alpha]_D^{25}$ +10.1 (*c* 1.34, $CHCl_3$); ir ($CHCl_3$) *ν*: 3010, 1718, 1515, 1278, 1215 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 8.03–8.00, 7.59–7.52, 7.46–7.40, 7.27–7.22, and 6.87–6.83 (9H, 5m, -OCOC$_6$*H*$_5$ and -OCH$_2$C$_6$*H*$_4$OCH$_3$), 5.25 (1H, d, $J = 9.0$ Hz, -C*H*=C(CH$_3$)-), 4.49 (1H, d, $J_{AB} = 11.3$ Hz, -OC*H*$_2$C$_6$H$_4$OCH$_3$), 4.40 (2H, dt, $J_1 = J_2 = 6.9$ Hz, -C*H*$_2$OCOPh), 4.34 (1H, d, $J_{AB} = 11.3$ Hz, -OC*H*$_2$C$_6$H$_4$OCH$_3$), 4.22–4.14 (1H, m, -C*H*(OMPM)-), 3.78 (3H, s, -OCH$_2$C$_6$H$_4$OC*H*$_3$), 3.24–3.09 (2H, m, -CH$_2$I), 2.53 (2H, td, $J = 6.9$, 3.8 Hz, -C*H*$_2$-CH$_2$OBz), 1.89 (3H, d, $J = 1.4$ Hz, -CH=C(C*H*$_3$)-); ms *m/e* (70 eV): 480 (M^+), 449 ($M^+ - OCH_3$), 342 ($M^+ - I$). Exact Mass (M^+) calcd: 480.0799; found: 480.0788.

*Methyl (4S)-(5Z)-8-benzoyloxy-4-[(para-methoxybenzyl)oxy]-2-methoxycarbonyl-6-methyloct-5-enoate (**46**)*

The same procedure as used for **18***a* was applied using the following quantities: sodium hydride (0.133 g, 50% in oil, 2.76 mmol), dimethyl malonate (335 μL, 2.93 mmol), tosylate **44** (0.270 g, 0.51 mmol), potassium iodide (111 mg, 0.67 mmol), tetrahydrofuran (15 mL), dimethylformamide (15 mL), and afforded malonate **46** (0.179 g, 72%) and unreacted tosylate (28.3 mg, 10%).

Similarly, the above procedure was applied using iodide **45** and the following quantities: sodium hydride (16 mg, 60% in oil, 0.400 mmol), dimethyl malonate (48 μL, 0.42 mmol), iodide (28.9 mg, 0.060 mmol), tetrahydrofuran (1.5 mL), dimethylformamide (1.5 mL). Malonate **46** (22.3 mg, 77%) and unreacted iodide (3.3 mg, 11%) were obtained; $[\alpha]_D^{25}$ −16.8 (*c* 1.20, $CHCl_3$);

ir ($CHCl_3$) ν: 3020, 2958, 2858, 1730, 1715, 1610, 1512, 1450, 1440, 1272, 1248, 1215 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 8.04–8.00, 7.57–7.51, 7.44–7.38, 7.18–7.15, and 6.85–6.81 (9H, 5m, -OCO-C_6H_5, -$OCH_2C_6H_4OCH_3$), 5.27 (1H, dq, J = 9.0, 1.2 Hz, -CH=$C(CH_3)$-), 4.41 (1H, d, J_{AB} = 11.3 Hz, -$OCH_2C_6H_4OCH_3$), 4.39 (2H, td, J = 6.9, 2.0 Hz, -CH_2OBz), 4.15 (1H, d, J_{AB} = 11.3 Hz, -$OCH_2C_6H_4OCH_3$), 4.20–4.11 (1H, m, -CH(OMPM)-), 3.77 (3H, s, -$OCH_2C_6H_4OCH_3$), 3.67 and 3.64 (6H, 2s, -CO_2CH_3), 3.62 (1H, t, J = 6.2 Hz, -$CH(CO_2CH_3)_2$), 2.52 (2H, t J = 6.9 Hz, -CH_2-CH_2OBz), 2.22–2.00 (2H, m, -CH_2-$CH(CO_2CH_3)_2$), 1.87 (3H, d, J = 1.2 Hz, -CH=$C(CH_3)$-); ms m/e (70 eV): 484 (M^+), 469 (M^+-CH_3), 453 (M^+-OCH_3). Exact Mass (M^+) calcd: 484.2097; found: 484.2082.

*(5S)-(3Z,9Z,11E)-1-Benzoyloxy-13-[(*tert-*butyldiphenylsilyl)oxy]-5-[(*para-*methoxybenzyl)oxy]-7,7-dimethoxycarbonyl-3-methyltrideca-3,9,11-triene (**47**)*

The procedure employed for **23** was applied using the following quantities: malonate **46** (0.295 g, 0.61 mmol), sodium hydride (35 mg, 50% in oil, 0.73 mmol), chloride **22** (*7e*) (0.207 g, 0.73 mmol), tetrahydrofuran (2 × 3.5 mL), dimethylformamide (2 × 3.5 mL), and afforded triene **47** (0.432 g, 87%); $[\alpha]_D^{25}$ +23.4 (*c* 1.15, $CHCl_3$); ir ($CHCl_3$) ν: 3025, 2955, 2940, 2860, 1735, 1518, 1440, 1280, 1250, 1205, 1115 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 8.03–7.99 (2H, m, -$OCOC_6H_5$), 7.69–7.63 (4H, m, -$OSi(C_6H_5)_2tBu$), 7.55–7.48 (1H, m, -$OCOC_6H_5$), 7.42–7.33 (8H, m, -$OSi(C_6H_5)_2tBu$ and -$OCOC_6H_5$), 7.18–7.12 and 6.83–6.77 (4H, 2m, -OC_6H_4-OCH_3), 6.53 (1H, ddd, J = 15.0, 11.0, 0.9 Hz, -CH=CH-CH=CH_2OSiPh_2tBu), 6.04 (1H, dd, J_1 = J_2 = 11.1 Hz, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 5.75 (1H, dt, J = 15.0, 5.0 Hz, -CH=CH-CH=CH_2OSiPh_2tBu), 5.27 (1H, dq, J = 8.0, 1.1 Hz, -CH=$C(CH_3)$-), 5.25–5.16 (1H, m, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 4.38–4.04 (7H, m, -CH(OMPM)-, -CH_2OSiPh_2tBu, -$OCH_2C_6H_4OCH_3$, and -CH_2OBz), 3.75 (3H, s, -$OCH_2C_6H_4OCH_3$), 3.57 and 3.48 (6H, 2s, 2 × -CO_2CH_3), 2.89 (2H, d, J = 7.6 Hz, -$C(CO_2CH_3)_2$-CH_2-CH=CH-), 2.52 (2H, t, J = 6.9 Hz, -CH_2-CH_2OBz), 2.29 (1H, dd, J_{AB} = 14.8 Hz, J_{AX} = 10.4 Hz, -CH(OMPM)-CH_2-), 2.03 (1H, dd, J_{AB} = 14.8 Hz, J_{BX} = 2.6 Hz, -CH(OMPM)-CH_2-), 1.85 (3H, d, J = 1.1 Hz, -CH=$C(CH_3)$-), 1.05 (9H, s, -$OSiPh_2C(CH_3)_3$); ms m/e (70 eV): 818 (M^+), 761 (M^+-tBu). Exact Mass (M^+-tBu) calcd: 761.3146; found: 761.3140.

*(5S)-(3Z,9Z,11E)-13-[(*tert-*Butyldiphenylsilyl)oxy]-5-[(*para-*methoxybenzyl)oxy]-7,7-dimethoxycarbonyl-3-methyltrideca-3,9,11-trien-1-ol (**48**)*

Potassium carbonate (73 mg, 0.53 mmol) was added to a stirred solution of benzoate **47** (0.432 g, 0.53 mmol) in methanol (35 mL), the stirring being continued at 65°C for 4 h. After dilution in dichloromethane, the solution was poured into a saturated solution of ammonium chloride and extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (25% to 50% of ethyl acetate in hexane) to afford alcohol **48** (0.352 g, 94%); $[\alpha]_D^{25}$ +33.0 (*c* 1.84, $CHCl_3$); ir ($CHCl_3$) ν: 3600, 3020, 2960, 2935, 2860, 1730, 1518, 1440, 1430, 1250, 1220, 1115 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.70–7.66 and 7.42–7.35 (10H, 2m, -$OSi(C_6H_5)_2tBu$), 7.24–7.19 and 6.84–6.79 (4H, 2m, -$OCH_2C_6H_4$-OCH_3), 6.51 (1H, dd, J = 15.1, 11.1 Hz, -CH=CH-CH_2OSiPh_2tBu), 6.10 (1H, dd, J_1 = J_2 = 11.1 Hz, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 5.80 (1H, dt, J = 15.1, 5.2 Hz, -CH=CH-CH_2OSiPh_2tBu), 5.17 (2H, m, -CH=C-(CH_3)-, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 4.35 (1H, d, J_{AB} = 10.7 Hz, -$OCH_2C_6H_4OCH_3$), 4.24–4.14 (3H, m, -CH(OMPM)-, -CH_2OSiPh_2tBu), 4.10 (1H, d, J_{AB} = 10.7 Hz, -$OCH_2C_6H_4OCH_3$), 3.75 (3H, s, -$OCH_2C_6H_4OCH_3$), 3.69–3.60 (2H, m, -CH_2OH), 3.58 and 3.52 (6H, 2s, 2 × -CO_2CH_3), 2.97–2.78 (2H, m, -$C(CO_2CH_3)_2$-CH_2-CH=CH-), 1.99–1.48 (4H, m, -CH(OMPM)-CH_2- and =$C(CH_3)$-CH_2), 1.78 (3H, d, J = 1.2 Hz, -CH=$C(CH_3)$-), 1.07 (9H, s, -$OSiPh_2C(CH_3)_3$); ms m/e (70 eV): 657 (M^+-tBu).

*(5S)-(3Z,9Z,11E)-13-[(*tert-*Butyldiphenylsilyl)oxy]-1-methanesulfonyloxy-5-[(*para-*methoxybenzyl)oxy]-7,7-dimethoxycarbonyl-3-methyltrideca-3,9,11-triene (**49**)*

The procedure described for **17***a* was applied using the following quantities: alcohol **48** (0.352 g, 0.49 mmol), methanesulfonyl chloride (46 μL, 0.59 mmol), triethylamine (103 μL, 0.74 mmol), dichloromethane (10 mL), and yielded mesylate **49** (0.379 g, 97%); $[\alpha]_D^{25}$ +25.4 (*c* 1.12, $CHCl_3$); ir ($CHCl_3$) ν: 3015, 2955, 2930, 2860, 1730, 1612, 1515, 1428, 1438, 1250, 1205, 1175 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.70–7.64 and 7.43–7.34 (10H, m, -$OSi(C_6H_5)_2tBu$), 7.22–7.17 and 6.85–6.80 (4H, m, -$OCH_2C_6H_4OCH_3$), 6.53 (1H, dd, J = 15.0, 11.4 Hz, -CH=CH-CH_2OSiPh_2tBu), 6.11 (1H, dd, J_1 = J_2 = 11.4 Hz, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 5.80 (1H, dt, J = 15.0, 5.0 Hz, -CH=CH-CH_2-$OSiPh_2tBu$), 5.30 (1H, d, J = 8.6 Hz, -CH=$C(CH_3)$-), 5.26–5.17 (1H, m, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 4.33 (1H, d, J_{AB} = 10.7 Hz, -$OCH_2C_6H_4OCH_3$), 4.26–4.15 (5H, m, -CH_2OMs, -CH_2OSiPh_2tBu, and -CH(OMPM)-), 4.10 (1H, d, J_{AB} = 10.7 Hz, -$OCH_2C_6H_4OCH_3$), 3.76 (3H, s, -$OCH_2C_6H_4OCH_3$), 3.56 and 3.52 (6H, 2s, 2 × -CO_2CH_3), 2.97 (3H, s, -OSO_2CH_3), 2.87 (2H, d, J = 8.3 Hz, -$C(CO_2CH_3)_2$-CH_2-CH=CH-), 2.60–2.37 (2H, m, =$C(CH_3)$-CH_2-), 2.22 (1H, dd, J_{AB} = 14.8 Hz, J_{AX} = 10.2 Hz, -CH(OMPM)-CH_2-), 2.00 (1H, dd, J_{AB} = 14.8 Hz, J_{BX} = 2.7 Hz, -CH(OMPM)-CH_2-), 1.80 (3H, d, J = 1.2 Hz, -CH=$C(CH_3)$-), 1.06 (9H, s, -$OSiPh_2C(CH_3)_3$); ms m/e (70 eV): 735 (M^+-tBu).

*Methyl (7S)-(5Z,11Z,13E)-15-[(*tert-*butyldiphenylsilyl)oxy]-7-[(*para-*methoxybenzyl)oxy]-5-methyl-2,9,9-trimethoxycarbonylpentadeca-5,11,13-trienoate (**50**)*

The procedure described for **24** was applied: mesylate **49** (0.378 g, 0.48 mmol), dimethyl malonate (305 μL, 2.67 mmol), sodium hydride (121 mg, 50% in oil, 2.53 mmol), potassium iodide (40 mg, 0.24 mmol), tetrahydrofuran (7.5 mL), dimethylformamide (7.5 mL) afforded malonate **50** (0.330 g, 84%); $[\alpha]_D^{25}$+14.4 (*c* 1.02, $CHCl_3$); ir ($CHCl_3$) ν: 3010, 2950, 2860, 1732, 1512, 1435, 1220, 1200, 1110 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.70–7.64 and 7.43–7.34 (10H, m, -$OSi(C_6H_5)_2tBu$), 7.25–7.18 and 6.87–6.80 (4H, 2m, -$OCH_2C_6H_4OCH_3$), 6.54 (1H, dd, J = 15.0, 11.0 Hz, -CH=CH-CH_2OSiPh_2tBu), 6.09 (1H, dd, J_1 = J_2 = 11.0 Hz, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 5.79 (1H, dt, J = 15.0, 5.0 Hz, -CH=CH-CH_2OSiPh_2tBu), 5.30–5.19 (1H, m, -CH=CH-CH=CH-CH_2OSiPh_2tBu), 5.16 (1H, d, J = 8.9 Hz, -CH=$C(CH_3)$-), 4.31 (1H, d, J_{AB} = 10.6 Hz, -$OCH_2C_6H_4OCH_3$), 4.25 (2H, d, J = 4.7 Hz, -CH_2OSiPh_2tBu), 4.19–4.08 (1H, m, -CH(OMPM)-), 4.08 (1H, d, J_{AB} = 10.6 Hz, -$OCH_2C_6H_4OCH_3$), 3.76 (3H, s, -$OCH_2C_6H_4OCH_3$), 3.72, 3.71, 3.56, and 3.48 (12H, 4s, 4 × -CO_2CH_3), 3.33 (1H, t, J = 6.8 Hz, -$CH(CO_2CH_3)_2$), 2.99–2.77 (2H, m, -$C(CO_2CH_3)_2$-CH_2-CH=CH-), 2.25 (1H, dd, J = 14.8, 10.3 Hz, -CH(OMPM)-CH_2-), 2.00–1.91 (5H, m, -CH-(OMPM)-CH_2-, =$C(CH_3)$-CH_2-CH_2-), 1.76 (3H, d, J = 1.1 Hz, -CH=$C(CH_3)$-), 1.06 (9H, s, -$OSiPh_2C(CH_3)_3$); ms m/e (70 eV): 828 (M^+), 785 (M^+-CH_3OH + H), 771 (M^+-tBu). Exact Mass (M^+-tBu): 771.3200; found: 771.3192.

*Methyl (7S)-(5Z,11Z,13E)-15-hydroxy-7-[(*para-*methoxybenzyl)oxy]-5-methyl-2,9,9-trimethoxycarbonylpentadeca-5,11,13-trienoate (**51**)*

The procedure used for **25** was applied: silyl ether **50** (0.133 g, 0.161 mmol), tetrabutylammonium fluoride (175 μL, 1 M in tetrahydrofuran, 0.175 mmol, 1.1 equiv.), tetrahydrofuran (4 mL) gave alcohol **51** (89.6 mg, 94%); $[\alpha]_D^{25}$ +12.4 (*c* 1.01, $CHCl_3$); ir ($CHCl_3$) ν: 3600, 3050, 2955, 2880, 1730, 1512, 1435, 1440, 1250, 1200, 1177, 1075 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.27–7.20 and 6.89–6.84 (4H, 2m, -$OCH_2C_6H_4OCH_3$), 6.45 (1H, dd, J = 15.2, 11.5 Hz, -CH=CH-CH_2OH), 6.08 (1H, dd, J_1 = J_2 = 11.5 Hz, -CH=CH-CH=CH-CH_2OH), 5.85 (1H, dt, J = 15.2, 5.0 Hz, -CH=CH-CH_2OH), 5.24–5.17 (1H, m, -CH=CH-CH=CH-CH_2OH), 5.15 (1H, d, J = 9.1 Hz, -CH=$C(CH_3)$-), 4.33 (1H, d, J_{AB} = 10.7 Hz, -$OCH_2C_6H_4OCH_3$), 4.18 (2H, d, J = 6.0 Hz,

-CH_2OH), 4.14–4.04 -(1H, m, -CH(OMPM)-), 3.91 (1H, d, J_{AB} = 10.7 Hz, -OCH_2C$_6$H$_4$OCH$_3$), 3.80 (3H, s, -OCH$_2$-C$_6$H$_4$OCH_3), 3.74, 3.73, 3.62, and 3.51 (12H, 4s, 4 × -CO$_2$CH$_3$), 3.31 (1H, t, J = 6.4 Hz, -CH(CO$_2$CH$_3$)$_2$), 2.88 (2H, d, J = 6.8 Hz, -C(CO$_2$CH$_3$)$_2$-CH_2-), 2.29 (1H, dd, J = 14.8 Hz, 10.4 Hz, -CH(OMPM)-CH_2-) 2.03, 1.92 (5H, m, -CH(OMPM)-CH_2-, =C(CH$_3$)-CH_2-CH_2-), 1.75 (3H, d, J = 1.3 Hz, -CH=C(CH_3)-); ms m/e (70 eV): 591 (MH$^+$), 572 (M$^+$−H$_2$O), 558 (M$^+$−CH$_3$OH).

*Methyl (7*S*)-(5*Z*,11*Z*,13*E*)-15-chloro-7-[(para-methoxybenzyl)oxy]-5-methyl-2,9,9-trimethoxycarbonylpentadeca-5,11,13-trienoate (**52**)*

The procedure used for **26** was applied: alcohol **51** (87.2 mg, 0.148 mmol), *s*-collidine (43 μL, 0.325 mmol), methanesulfonyl chloride (23 μL, 0.296 mmol), dimethylformamide (2.5 mL), lithium chloride (19 mg, 0.443 mmol) yielded chloride **52** (89.4 mg, 99% crude); ir ($CHCl_3$) ν: 3010, 2950, 2930, 2850, 1730, 1512, 1435, 1212, 1205 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.25–7.20 and 6.89–6.84 (4H, 2m, -OCH$_2$C$_6$$H_4OCH_3$), 6.45 (1H, dd, J = 15.0, 11.2 Hz, -CH=CH-CH$_2$Cl), 6.06 (1H, dd, J_1 = J_2 = 11.2 Hz, -CH=CH-CH=CH-CH$_2$Cl), 5.79 (1H, dt, J = 15.0, 7.4 Hz, -CH=CH-CH$_2$Cl), 5.39–5.28 (1H, m, -CH=CH-CH=CH-CH$_2$Cl), 5.37 (1H, dq, J = 8.8, 1.2 Hz, -CH=C(CH$_3$)-), 4.34 (1H, d, J_{AB} = 10.8 Hz, -OCH_2C$_6$H$_4$OCH$_3$), 4.09 (1H, d, J_{AB} = 10.8 Hz, -OCH_2C$_6$H$_4$OCH$_3$), 4.07 (2H, d, J = 7.4 Hz, -CH_2Cl), 4.13–4.03 (1H, m, -CH(OMPM)-), 3.80 (3H, s, -OCH$_2$-C$_6$H$_4$OCH_3), 3.74, 3.73, 3.61, and 3.54 (12H, 4s, 4 × -CO$_2$CH_3), 3.31 (1H, t, J = 6.9 Hz, -CH(CO$_2$CH$_3$)$_2$), 3.01–2.75 (2H, m, -(CO$_2$CH$_3$)$_2$-CH_2-CH=CH), 2.27 (1H, dd, J = 14.9, 10.5 Hz, -CH(OMPM)-CH_2), 2.06–1.92 (5H, m, -CH(OMPM)-CH_2-, =C(CH$_3$)-CH_2-CH_2-), 1.76 (3H, d, J = 1.2 Hz, -CH=C(CH_3)-); ms m/e (70 eV): 608 (M$^+$), 573 (M$^+$−Cl).

*(3*S*)-(4*Z*,10*E*,12*Z*)-3-[(para-Methoxybenzyl)oxy]-5-methyl-1,1,8,8-tetramethoxycarbonylcyclotetradeca-4,10,12-triene ((−)**5**)*

The procedure used for racemic **5** (R=Bn) was applied: chloride **52** (87.4 mg, 0.144 mmol crude), cesium carbonate (258 mg, 0.731 mmol), tetrahydrofuran (30 mL), dimethylformamide (30 mL) led to cyclic triene **5** (R=CH$_2$C$_6$H$_4$OCH$_3$) (66.1 mg, 78% for 2 steps); mp 184–186°C;[α]$_D^{25}$ −54.5 (*c* 1.01, $CHCl_3$); ir ($CHCl_3$) ν: 3010, 2950, 1730, 1512, 1435, 1205 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.31–7.27 and 6.93–6.90 (4H, 2m, -OCH$_2$C$_6$$H_4OCH_3$), 6.08–5.97 (2H, m, -CH=CH-CH=CH-), 5.34–5.19 and 4.99–4.86 (2H, 2m, -CH=CH-CH=CH-), 5.01 (1H, d, J = 9.6 Hz, -CH=C(CH$_3$)-), 4.38 (1H, d, J_{AB} = 11.4 Hz, -OCH_2C$_6$H$_4$OCH$_3$), 4.06–3.97 (1H, m, -CH(OMPM)-), 3.83 (3H, s, -OCH$_2$C$_6$H$_4$OCH_3), 3.77, 3.73, 3.70, and 3.50 (12H, 4s, 4 × -CO$_2$CH_3), 2.96–2.72 (3H, m, -CH_2-CH=CH-CH=CH-CH_2-), 2.44 (1H, dd, J = 14.3, 12.0 Hz, -CH_2-CH=CH-), 2.30 (1H, dd, J = 14.8, 11.4 Hz, -CH(OMPM)-CH_2-), 2.17–2.13 (2H, m, =C(CH$_3$)-CH_2-), 1.74 (3H, d, J = 0.8 Hz, -CH=C(CH_3)-), 1.66 (1H, dd, J = 14.8, 2.6 Hz, -CH(OMPM)-CH_2-), 1.42–1.23 (2H, m, =C(CH$_3$)-CH$_2$-CH_2); ms m/e (70 eV): 572 (M$^+$). Exact Mass (M$^+$) calcd: 572.2621; found: 572.2627.

*(3*S*,1*S*)-3-[para-Methoxybenzyl)oxy]-1-methyl-5,5,12,12-tetramethoxycarbonyl*-trans-cisoid-cis-*tricyclo[8.4.0^{2,7}]tetradec-8-ene ((-)**6**)*

A solution of macrocyclic triene **5** (R = CH$_2$C$_6$H$_4$OCH$_3$) (8.8 mg, 0.015 mmol) in toluene (0.5 mL) was heated in a sealed tube at 262°C for 3 h. The solvent was evaporated and the residual oil was purified by column chromatography (10% to 25% of ethyl acetate in hexane) to afford tricyclic compound **6** (R = CH$_2$C$_6$H$_4$OCH$_3$) (7.2 mg, 82%) and a mixture of two compounds (1.5 mg, 17%); [α]$_D^{25}$ −49.3 (*c* 0.98, $CHCl_3$); ir (CH_2Cl_2) ν: 3060, 2990, 2960, 1730, 1615, 1515, 1440, 1270, 1250 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.32–7.28 and 6.89–6.84 (4H, 2m, -OCH$_2$C$_6$$H_4OCH_3$), 5.27 (2H, s, -$CH$=$CH$-), 4.53 (1H, d, J_{AB} = 10.2 Hz, -OCH_2C$_6$H$_4$OCH$_3$), 4.36 (1H, d, J_{AB} = 10.2 Hz, -OCH_2C$_6$H$_4$OCH$_3$), 3.83–3.63 (1H, m, -CH(OMPM)-), 3.79 (3H, s, -OCH$_2$C$_6$H$_4$OCH_3), 3.71, 3.71, 3.70, 3.69 (12H, 4s, 4x -CO$_2$CH_3), 2.95–1.21 (13H, m, H-C2, H-C4, H-C6, H-C7, H-C10, H-C11, H-C13, and H-C14), 0.91 (3H, s, -CH_3-C1); ms m/e (70 eV): 572 (M$^+$), 554 (M$^+$ − H$_2$O). Exact Mass (M$^+$) calcd: 572.2621; found: 572.2630.

*(2*R*)-(3*Z*)-6-[(tert-Butyldiphenylsilyl)-oxy]-1,2-*O*-isopropylidene-4-methylhex-3-ene-1,2-diol (**36**)*

Imidazole (23 mg, 0.336 mmol) and *tert*-butyldiphenylsilyl chloride (73 μL, 0.284 mmol) were added to a stirred solution of alcohol **35***a* (48.1 mg, 0.259 mmol) in dimethylformamide (1.5 mL). The mixture was stirred at room temperature for 4 hs, then poured into a saturated solution of ammonium chloride and extracted with ethyl ether. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (5% to 50% ethyl acetate in hexane) to yield silyl ether **36** (86.1 mg, 79%); [α]$_D^{25}$ (*R*): +3.6 (*c* 1.22, $CHCl_3$); (*S*): −4.5 (*c* 1.49 ($CHCl_3$); ir ($CHCl_3$) ν: 3020, 2930, 2860, 1430, 1215, 1110, 1055 cm^{-1}; ^{1}H nmr ($CDCl_3$)δ: 7.68–7.64 and 7.44–7.35 (10H, 2m, -OSi(C$_6$$H_5$)$_2$*t*Bu), 5.22 (1H, d, J = 8.8 Hz, -CH=C(CH$_3$)-), 4.63 (1H, ddd, J_1 = J_2 = 8.6 Hz, J_3 = 6.0 Hz, -OCH$_2$-CH-O-), 3.84 (1H, dd, J_{AB} = 8.0 Hz, J_{AX} = 6.0 Hz, -OCH_2-CH-O-), 3.74–3.56 (2H, m, -CH_2-OSiPh$_2$*t*Bu), 3.40 (1H, dd, app t, J_{AB} = J_{BX} = 8.0 Hz, -OCH_2-CH-O-), 2.58–2.18 (2H, m, -CH_2-CH$_2$OSiPh$_2$*t*Bu), 1.69 (3H, d, J = 1.4 Hz, -CH=C(CH_3)-), 1.39 and 1.36 (6H, 2s, -O-C(CH_3)$_2$-O-), 1.04 (9H, s, -OSiPh$_2$C(CH_3)$_3$); ms m/e (70 eV): 424 (M$^+$), 409 (M$^+$ − CH$_3$), 367 (M$^+$ − *t*Bu).

*(2*R*)-(3*Z*)-6-[(tert-Butyldiphenylsilyl)oxy]-4-methylhex-3-en-1,2-diol (**37**)*

Pyridinium *para*-toluenesulfonate (10.2 mg, 0.041 mmol) was added at 0°C to a stirred solution of acetonide **36** (86.1 mg, 0.203 mmol) in methanol (2 mL). The mixture was stirred for 4 h at room temperature (until the appearance of triol by TLC). The mixture was poured into a saturated solution of sodium chloride and extracted with dichloromethane. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated. The residual oil was purified by column chromatography (50% ethyl acetate in hexane) to yield diol **37** (42.8 mg, 55%) and starting material **36** (40.1 mg, 45%). The starting material was then recycled twice to afford diol **37** (67.5 mg, 87% total); [α]$_D^{25}$ (*R*): −10.2 (*c* 1.54, $CHCl_3$); (S): +10.8 (*c* 1.59, $CHCl_3$); ir ($CHCl_3$) ν: 3580, 3450, 3015, 2960, 2930, 2860, 1430, 1215, 1110 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.69–7.64 and 7.45–7.36 (10H, 2m, -OSi(C$_6$$H_5$)$_2$*t*Bu), 5.40 (1H, d, J = 7.8 Hz, -CH=C(CH$_3$)-), 4.35 (1H, ddd, J_1 = J_2 = 7.6 Hz, J_3 = 3.8 Hz, -CHOH-), 3.71–3.44 (4H, m, -CH_2OH and -CH_2OSiPh$_2$*t*Bu), 2.61–2.19 (2H, m, -CH_2-CH$_2$OSiPh$_2$*t*Bu), 1.68 (3H, d, J = 1.3 Hz, -CH=C(CH_3)-), 1.05 (9H, s, -OSiPh$_2$C(CH_3)$_3$); ms m/e (70 eV): 353 (M$^+$ − OCH$_3$). Exact Mass (M$^+$ − OCH$_3$) calcd: 353.1937; found: 353.1935.

*(2*R*)-(3*Z*)-6-[(tert-Butyldiphenylsilyl)oxy]-1-[(para-toluenesulfonyl)-oxy]4-methylhex-3-en2-ol (**38**)*

The procedure used for **43** was applied: diol **37** (31.3 mg, 0.082 mmol), *para*-toluenesulfonyl chloride (17.0 mg, 0.090 mmol), triethylamine (12.5 μL, 0.090 mmol), dimethylaminopyridine (10.0 mg, 0.082 mmol), and dichloromethane (1 mL) yielded tosylate **38** (25.9 mg, 60%) and starting material **37** (8.5 mg, 27%). The starting material was then recycled to afford tosylate **38** (33.2 mg, 76% total); [α]$_D^{25}$ (*R*): − 24.3 (*c* 1.42, $CHCl_3$); (*S*): +25.6 (*c* 1.37, $CHCl_3$); ir ($CHCl_3$) ν: 3450, 3020, 2950, 2930, 2860, 1430, 1362, 1230, 1190, 1175, 1110 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.80–7.76, 7.66–7.61, 7.47–7.30 (14H, 3m, -OSi(C$_6$$H_5$)$_2$*t*Bu and -OSO$_2$-C$_6$$H_4CH_3$), 5.26 (1H, dq, J = 8.0, 1.2 Hz, -CH=C(CH$_3$)-), 4.49–4.41 (1H, m, -CHOH-), 3.97–3.85 and 3.67–3.59 (4H, 2m, -CH_2OSiPh$_2$*t*Bu and -CH_2OTs), 2.49–2.31 and 2.24–2.14 (2H, 2m, -CH_2-CH$_2$OSiPh$_2$*t*Bu), 2.43 (3H, s, -OSO$_2$C$_6$H$_4$CH_3), 2.09–1.96 (1H, s, -CHOH-), 1.64 (3H, d, J = 1.3 Hz, -CH=C(CH_3), 1.02 (9H, s, -OSiPh$_2$C(CH_3)$_3$.

*(2R)-(3Z)-6-[(*tert*-Butyldiphenylsilyl)oxy]-2-[(2S)-2-methoxy-2-phenylacetoxy]-1[(*para*-toluenesulfonyl)-oxy]4-methylhex-3-ene (39)*

(2*S*)-2-Phenyl-2-methoxyacetic acid (**40**) (20) (11.3 mg, 0.068 mmol), dicyclohexylcarbodiimide (14.1 mg, 0.068 mmol), and dimethylaminopyridine (4.0 mg, 0.034 mmol) were added at 0°C to a stirred solution of (*R*) alcohol **38** (18.5 mg, 0.034 mmol) in dichloromethane (1 mL). The mixture was stirred for 0.75 h at 0°C and then filtered on Celite. After evaporation of the solvent, the residual solid was purified by column chromatography (25% ethyl acetate in hexane) to afford ester **39** (24.3 mg, 99%); $[\alpha]_D^{25}$ +48.2 (*c* 1.17, $CHCl_3$); ir ($CHCl_3$) ν: 3020, 2930, 2855, 1748, 1430, 1365, 1172, 1110 cm^{-1}; ^1H nmr ($CHCl_3$) δ: 7.70–7.59 and 7.42–7.25 (19H, -OSi(C_6H_5)$_2t$Bu, -$OSO_2C_6H_4CH_3$, and -OCOCH(OCH_3)C_6H_5), 5.56–5.48 (1H, m, -C*H*(OCOCH(OCH_3)Ph)-), 4.90 (1H, d, *J* = 9.2 Hz, -C*H*=C(CH_3)-), 4.66 (1H, s, -OCOC*H*(OCH_3)Ph), 3.94–3.92 and 3.65–3.44 (4H, 2m, -CH_2-$OSO_2C_6H_4CH_3$ and -CH_2OSiPh_2tBu), 3.37 (3H, s, -OCOCH-(OCH_3)Ph), 2.47–2.35 and 2.06–1.96 (2H, 2m, -CH_2-CH_2-OSiPh_2tBu), 2.40 (2H, s, -$OSO_2C_6H_4CH_3$), 1.55 (3H, d, *J* = 1.3 Hz, -CH=C(C*H*$_3$)-), 0.99 (9H, s, -OSiPh_2C(CH_3)$_3$).

*(2S)-(3Z)-6-[(*tert*-Butyldiphenylsilyl)oxy]-2-[(2S)-2-methoxy-2-phenylacetoxy]-1-[(*para*-toluenesulfonyl)oxy]-4-methylhex-3-ene (39)*

The previous procedure was applied: (2*S*)-2-phenyl-2-methoxyacetic acid (**40**) (20) (9.0 mg, 0.055 mmol), dicyclohexylcarbodiimide (11.0 mg, 0.055 mmol), (*S*) alcohol **38** (14.7 mg, 0.027 mmol), dimethylaminopyridine (3.3 mg, 0.027 mmol), and dichloromethane (1 mL) yielded ester **39** (16.8 mg, 90%); $[\alpha]_D^{25}$ +0.9 (*c* 1.13, $CHCl_3$); ^1H nmr ($CDCl_3$) δ: 7.64–7.59, 7.54–7.51, 7.43–7.31, and 7.23–7.19 (19H, 4m, -OSi(C_6H_5)$_2t$Bu, -OSO_2-$C_6H_4CH_3$, and -OCOCH(OCH_3)C_6H_5), 5.48–5.39 (1H, m, -C*H*-(OCOCH(OCH_3)Ph),-), 5.07 (1H, d, *J* = 9.4 Hz, -C*H*=C(CH_3)-), 4.69 (1H, s, -OCOC*H*(OCH_3)Ph), 3.81 (2H, d, *J* = 5.2 Hz, -CH_2O-$SO_2C_6H_4CH_3$), 3.69–3.49 (2H, m, -CH_2OSi-Ph_2tBu), 3.36 (3H, s, -OCOCH(OC*H*$_3$)Ph), 3.56–3.45 (1H, m, -C*H*$_2$-CH_2OSiPh_2tBu), 2.39 (3H, s, -$OSO_2C_6H_4CH_3$), 2.17–2.06 (1H, m, -C*H*$_2$-CH_2OSi-Ph_2tBu), 1.64 (3H, d, *J* = 1.4 Hz, -CH=C(C*H*$_3$)-), 1.00 (9H, s, -OSiPh_2C(CH_3)$_3$).

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