Transannular Diels–Alder cyclization of a substituted 13-membered macrocyclic triene. An approach to the A.B.C.[6.6.5] rings of the *Veratrum* alkaloids

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The synthesis and Diels–Alder cyclization of a substituted macrocyclic 13-membered triene **45** is described. Tricyclic compound A.B.C.[6.6.5] **46** having ring junctions of *cis-anti-cis* (CAC) stereochemistry was used to investigate the possibility of introducing a hemiketal oxygen bridge between positions 9 and 4 of the *Veratrum* alkaloid skeleton.

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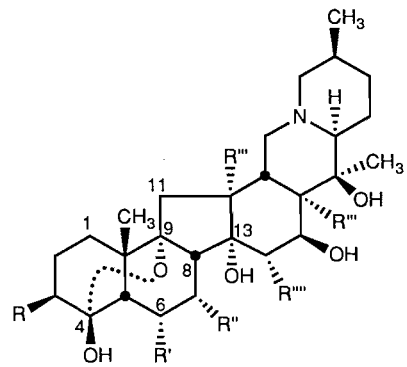
On décrit la synthèse et la cyclisation Diels–Alder d'un macrocycle substitué à 13 chaînons **45**. Le composé tricyclique A.B.C.[6.6.5] **46** de stéréochimie *cis-anti-cis* (CAC) en jonction de cycle a été utilisé pour étudier la possibilité d'introduire un pont d'oxygène hémicétalique entre les positions 9 et 4 des alkaloïdes *Veratrum*.

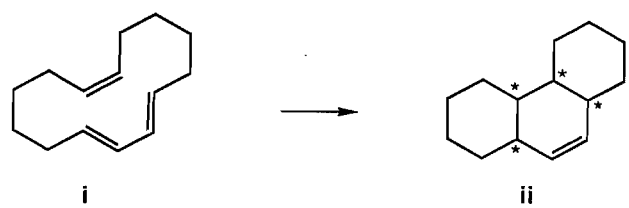
Veratrum alkaloids are an important category of natural compounds (1) obtained from the *Liliaceae* family, from *Veratrum album* in Europa and from *Veratrum viride* in North America. These alkaloids have been known since the early 1800's (2) for their sternutatory properties, but it was only in the late 1940's that their isolation and identification was undertaken systematically (3). At least 40 compounds from this family are now known and they all have the main hexacyclic skeleton presented in Fig. 1. There are four major types, differing in the hydroxylation pattern: germine (**1**) (4), veracevine (**2**) (5), protoverine (**3**) (4*a*, 6), and zygadenine (**4**) (7) and its 3-epimer cevine (**5**). These compounds are found in nature as esters of different carboxylic acids. The biological activity (8) of these steroidal alkaloids, particularly their ability to lower blood pressure (9), was studied in the 1950's.



1	Germine	R = β-OH, R' = R''' = H, R'' = R'''' = OH
2	Veracevine	R = β-OH, R' = R'' = R'''' = H, R''' = OH
3	Protoverine	R = β-OH, R' = R'' = R'''' = OH, R''' = H
4	Zygadenine	R = β-OH, R' = R'' = R''' = H, R'''' = OH
5	Cevine	R = α-OH, R' = R'' = R'''' = H, R''' = OH

FIG. 1. Ceveratrum major isometric alkamines.

In spite of the large pharmacological potential of these compounds, to our knowledge no group has attempted to devise a total synthesis of a *Veratrum* alkaloid. No doubt the presence of several asymmetric centers (17 in protoverine (**3**)) and an unusual presence of a tertiary hydroxyl group at position 9 (steroid numbering) could account for this situation. A synthetic strategy with a high degree of control on chemo-, regio-, and stereoselectivity has to be used in order to synthesize efficiently molecules of such complexity. Intramolecular processes (10–12) usually give excellent control on these factors. In recent years, our group has shown (13, 14) that the transannular Diels–Alder cyclization of macrocyclic trienes (see general formulation in Scheme 1, i → ii) is an efficient tool to synthesize functionalized 14-membered tricyclic A.B.C.[6.6.6] compounds with a high level of stereoselectivity.



SCHEME 1. Transannular Diels–Alder cyclization.

Moreover, this strategy was also been applied in a model study by Bérubé and Deslongchamp (15) from our group to synthesize a tricyclic homolog **8** (Scheme 2), namely an A.B.C.[6.6.5] skeleton, starting with a 13-membered macrocyclic *trans-trans-cis* (TTC) triene **7**, which was formed by the internal cyclization of an acyclic malonate chloride **6**. The use of an oxygen substituent on the dienophilic part of the macrocyclic triene showed the interesting possibility of introducing such a substituent at position 9 (steroid numbering) of the resulting tricyclic product. It was shown that the reaction of a *trans-trans-cis* (TTC) macrocyclic triene **7** leads to a mixture of tricyclic compounds **8** having *trans-syn-trans* (TST) and *cis-syn-cis* (CSC) geometries (2:1, respectively) at the ring junctions.

These preliminary results were used to devise a synthetic strategy leading to the A.B.C. rings of the *Veratrum* alkaloids. Indeed, in a recent model study (16) we showed (Scheme 3*a*) that the same strategy could be applied to the synthesis of an A.B.C.[6.6.5] tricyclic compound (see **11**) having the *cis-anti-cis* (CAC) geometry at the ring junctions. In this work and as shown in previous series (14*b*), it

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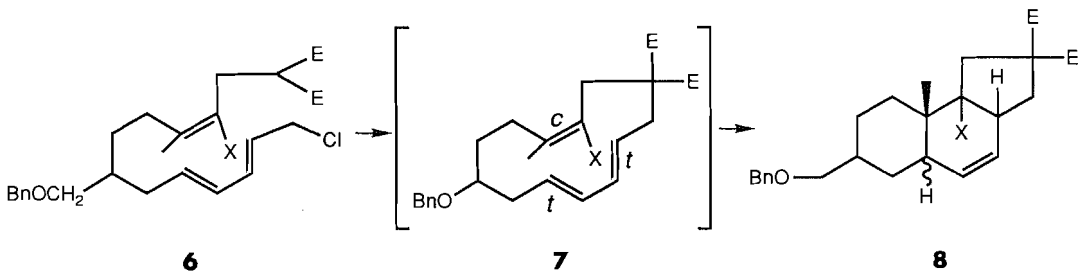
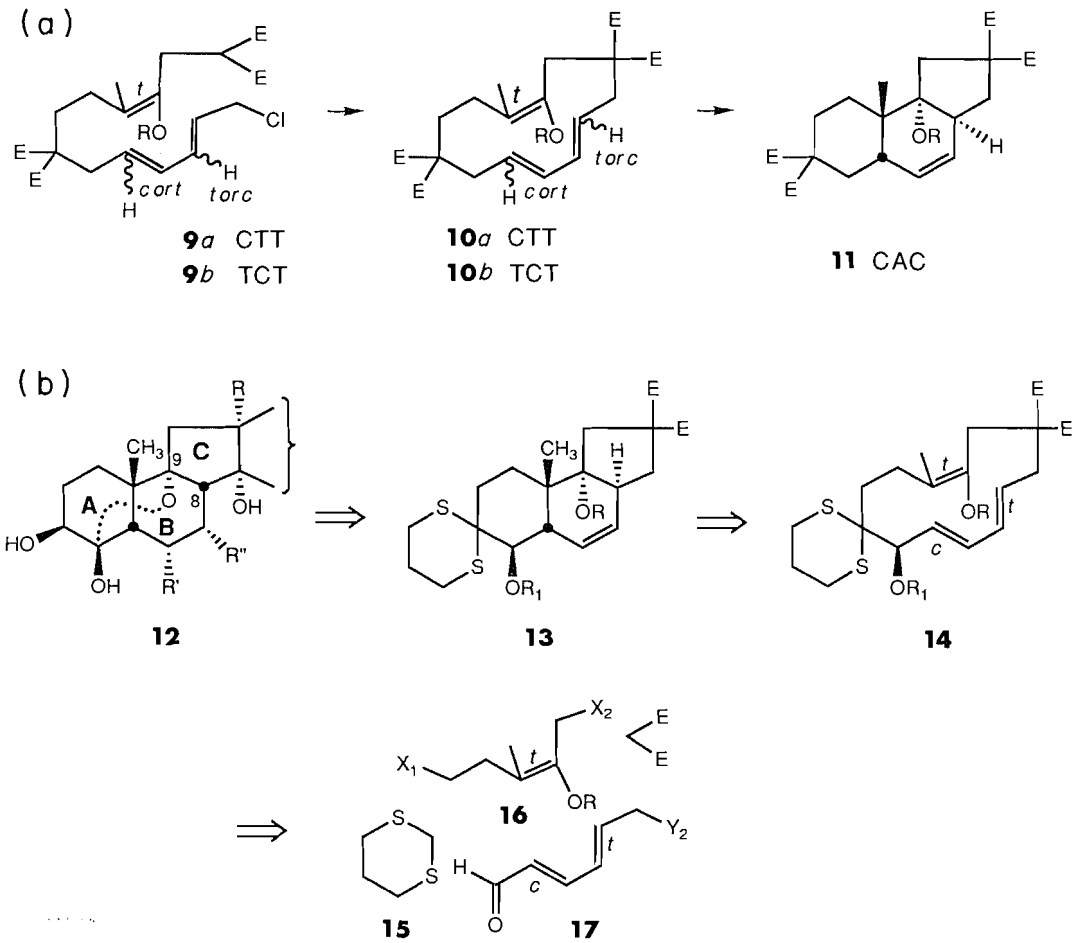


SCHEME 2. E = CO_2CH_3; X = OMOM; TST: *trans-syn-trans*; CSC: *cis-syn-cis*.

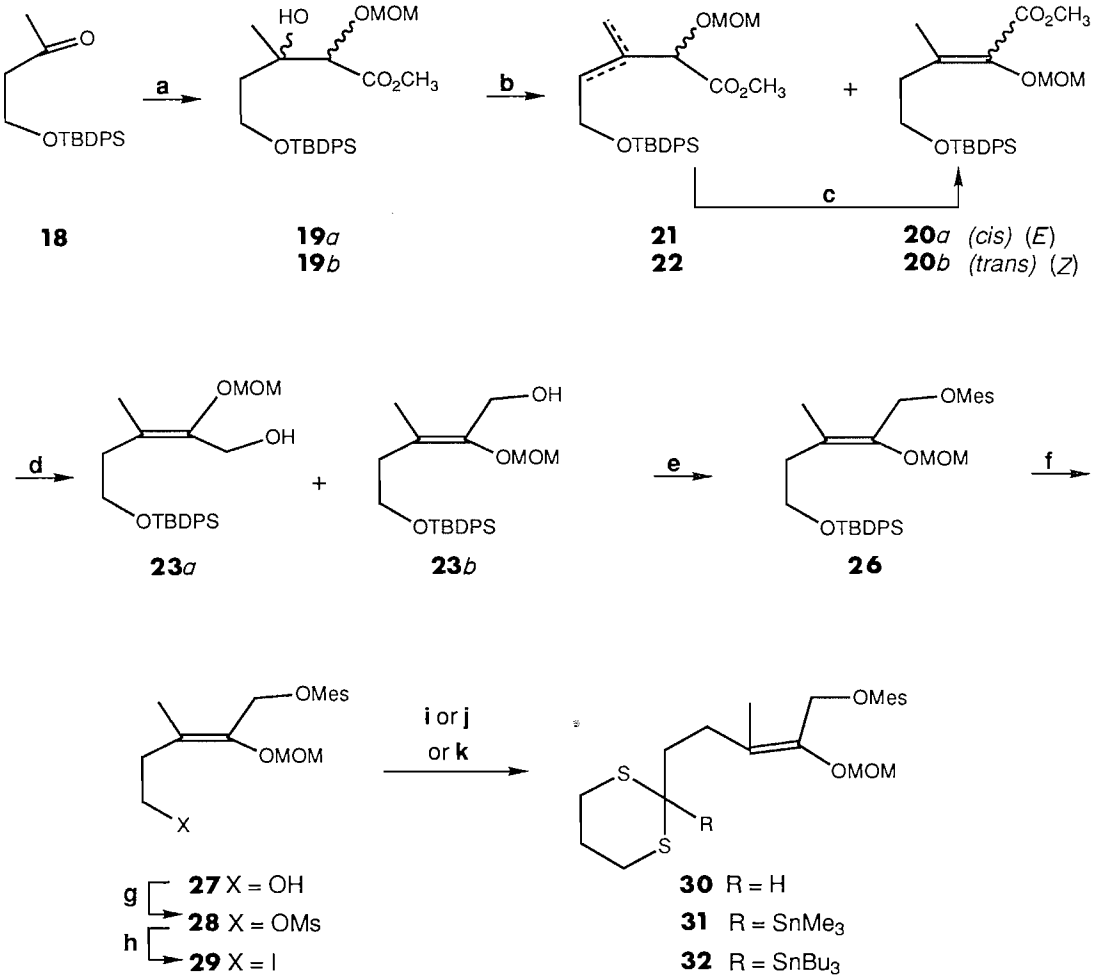


SCHEME 3

was found that both macrocyclic trienes **10***a* (CIT) and **10***b* (TCT) can give access to tricycle **11** (CAC).

The results of the first two model studies led us to devise a new route affording tricyclic intermediates that are more similar to the A.B.C.[6.6.5] portion of the general *Veratrum* skeleton. The retrosynthetic analysis shown in Scheme 3*b* indicates that the A.B.C. system (see **12**) might be formed from a tricyclic compound **13** itself obtained by a transannular Diels–Alder cyclization of macrocycle **14**. This macrocyclic triene might come from the assemblage of 1,3-dithiane (**15**), dienophile **16**, diene **17**, and dimethylmalonate in a highly convergent synthetic sequence. The use of 1,3-dithiane as a connector between dienophile **16** and diene **17** will insure the right oxidation level in the future ring A. The CT geometry in the diene **17** should give a CAC geometry in the final tricycle. The stereochemistry at position 8 will therefore have to be corrected with the help of functionalities left in ring C or B.

We will discuss now the synthesis of dienophile **16** and diene **17** as well as their assemblage to macrocycle **13**. We will then present the results of its Diels–Alder cyclization and we will report chemical transformations carried out on tricycle **13** to set the hemiketal bridge between positions 9 and 4.



(**a**) $MOMOCHLiCO_2CH_3$, THF, -78°C, 97%; (**b**) pyridine, $SOCl_2$, -60 → -20°C, 85%;
(**c**) CH_3OK, CH_3OH, reflux, 71%; (**d**) DIBAL, CH_2Cl_2, -78°C;
(**e**) Mesitoic acid, DCC, DMAP, CH_2Cl_2, 25°C, 91%; (**f**) $n$$Bu_4NF$, THF (99%);
(**g**) MsCl, Et_3N, CH_2Cl_2, 0°C (quant.); (**h**) NaI, acetone, refl. (91%);
(**i**) $(CH_2)_3S_2CHLi$, -78°C, THF, 12%; (**j**) $(CH_2)_3S_2C((CH_3)_3Sn)Li$, THF, -78°C, 38%;
(**k**) $(CH_2)_3S_2C((C_4H_9)_3Sn)Li$, -78°C, THF, 87%

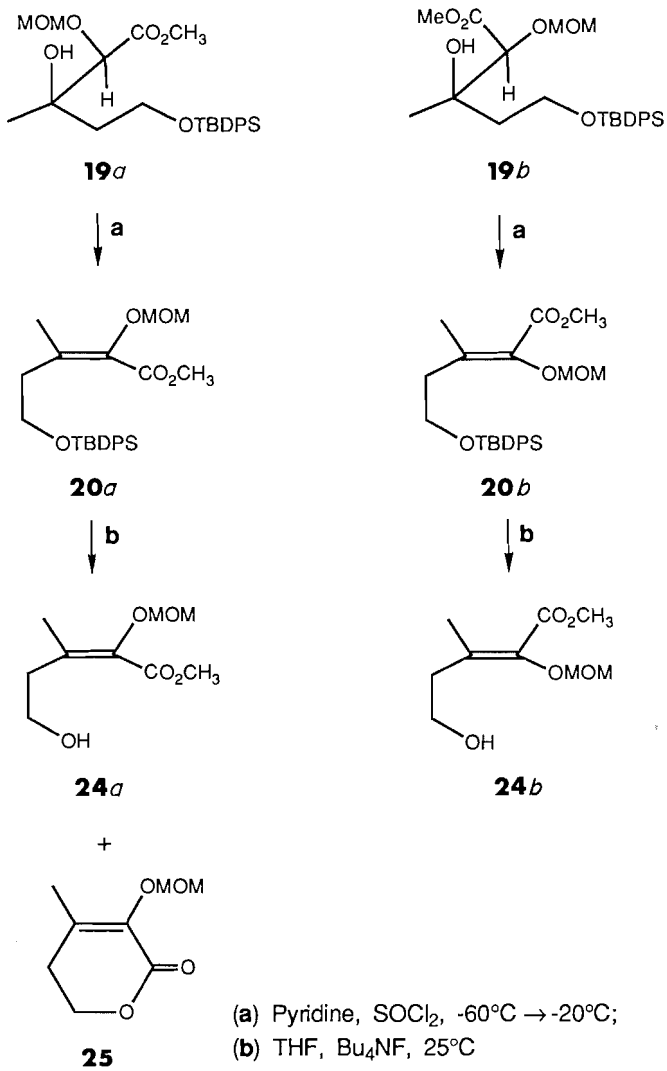
SCHEME 4

Dienophile 32

Following the methodology used previously (16), ketone **18** (Scheme 4) was alkylated in good yield with the lithium derivative of methyl methoxymethyloxyacetate (MOMO acetate) to afford a separable mixture of alcohols **19***a* and **19***b*. These, as a mixture, were dehydrated by thionyl chloride (17) in pyridine to α,β-unsaturated esters **20***a* and **20***b* (unseparable mixture) and unconjugated esters **21** and **22** in a ratio of (approximately) 1:1:2:2, respectively. Compounds **20***a* and **20***b* are the *cis* and *trans* isomers, respectively, and the double bond geometry was established by the following observations: a careful separation of diastereoisomers **19***a* and **19***b* provided an opportunity to obtain the pure α,β-unsaturated esters **20***a* and **20***b*, respectively, after dehydration (Scheme 5). These pure conjugated esters **20***a* and **20***b* were separately desilylated to the corresponding alcohols **24***a* and **24***b*. During this transformation, compound **24***a* was partly cyclized to lactone **25**, which was characterized. This cyclization proved that compound **24***a* was the *cis* (*E*) isomer. The two unconjugated esters **21** and **22** (Scheme 4) were converted to esters **20***a* and **20***b* by isomerization of the double bond with potassium methoxide in methanol.

The mixture of *E* and *Z* isomers **20** was reduced to easily separable alcohols **23***a* (*E* isomer) and **23***b* (*Z* isomer) with diisobutylaluminum hydride (DIBAL). Alcohol **23***b*, the *trans* isomer, was acylated with mesitoic acid (18) in the presence of dicyclohexylcarbodiimide (DCC) and *N*,*N*-dimethylaminopyridine (DMAP) to give mesitoate **26**, a hindered ester that is inert to butyllithium and to 1,3-dithiane anion used subsequently (*vide infra*). Desilylation of ether **26** with fluoride ion (19) and mesylation (20) of the resulting alcohol **27** led to mesylate **28**, which was transformed to iodide **29** by sodium iodide in refluxing acetone.

At this point, three 1,3-dithiane connectors were tested in the form of their anions: 1,3-dithiane, 2-trimethylstannyl-1,3-dithiane (21), and 2-tributylstannyl-1,3-dithiane (22). In our



SCHEME 5

hands, following a Seebach procedure (21, 22), the reaction of iodide **29** with 2-lithio-1,3-dithiane gave a low yield for adduct **30** (12%); with 2-lithio-2-trimethylstannyl-1,3-dithiane the yield for compound **31** was only 38%. Nevertheless, the use of 2-lithio-2-tributylstannyl-1,3-dithiane increased the yield to 87% for adduct **32**, the dienophilic synthon that has still to be alkylated with dienic synthon **36** to give the acyclic triene **44**.

Diene 36 and acyclic triene 44

Synthesis of diene **36** began with *cis-trans* diene **33** easily obtained from *cis*-but-2-ene-1,4-diol (14*a*, 16). Following previous work in our group, silylation of alcohol **33** (Scheme 6) with *tert*-butoxydiphenylsilyl chloride (23) led to diene **34** whose tetrahydropyranyl protecting group was then cleaved in *tert*-butanol in the presence of pyridinium *para*-toluenesulfonate (24) to obtain *cis-trans* allylic alcohol **35**. The use of *tert*-butanol instead of *i*-propanol (see ref. 16) eliminated an otherwise extensive exchange of the alkoxy group on the silyl ether moiety. Oxidation of alcohol **35** at low temperature (Swern conditions) (25) furnished aldehyde **36**.

The coupling reaction between dienophile **32** and aldehyde **36** was performed in good yield (86%) at low temperature (−93°C). We observed that the temperature of the reaction mixture has a critical influence on the yields. The *trans*-metallation of stannyl derivative **32** to the lithio derivative was first performed at −93°C by a fast addition of a precooled (−90°C) solution of butyllithium. A cooled (−90°C) solution of aldehyde **36** was then rapidly added to the mixture. Without these specific experimental conditions, several side reactions occurred, such as the formation of adduct **38** which comes from anionic attack on aldehyde **36** by the *para*-methyl group of the mesitoate moiety after its deprotonation by either butyllithium or internally by the 2-lithio-1,3-dithiane anion.

The alcohol function of **37** was silylated with *tert*-butyldimethylsilyl triflate and the resulting protected ester **39** was reduced to alcohol **40** with lithium aluminum hydride. Chloride **41**, obtained (26) from alcohol **40**, was converted to malonate **42** by substitution with methyl sodiomalonate. After selective cleavage of the terminal *tert*-butoxydiphenylsilyl ether of compound **42** with fluoride ion in methylene chloride (23), allylic alcohol **43** was converted to the desired acyclic triene, allylic chloride **44**.

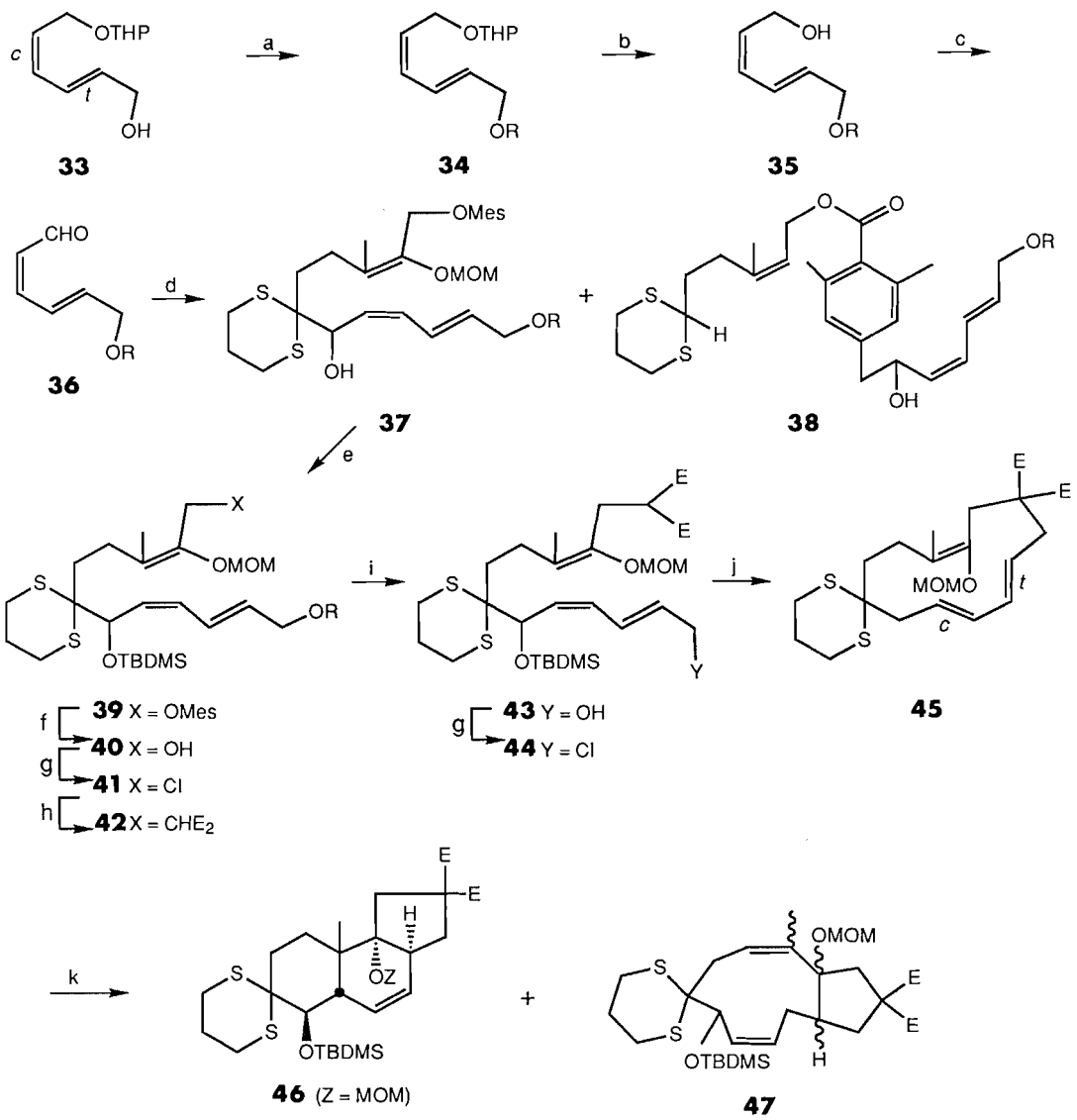
Macrocyclization and transannular Diels–Alder reaction

Slow addition of trienic malonate chloride **44** to a warm (78°C) solution of cesium carbonate and 18-crown-6 ether in acetonitrile led to the formation of macrocyclic triene **45** in 75% yield. Subsequent heating of this compound in toluene (220°C, 7 h) resulted in the smooth formation of a single tricycle **46** (76%) together with a secondary compound (16%) to which structure **47** has been assigned on the basis of its spectroscopic data. At a slightly higher temperature and a shorter reaction time (240°C, 1.5 h) the yield was somewhat lowered (**46** (69%) and **47** (15%)).

The assignment of stereochemistry for tricycle **46** was done on the basis of its nmr data, which show a very small coupling constant (1.8 Hz) between the allylic proton at position 5 (steroid numbering) and the proton at position 4 bearing the *O*-silyl group. This would be consistent with an equatorial–equatorial or an equatorial–axial coupling. The latter possibility has been discarded after the following considerations and analysis of molecular models.

Thus, on the basis of our previous results (14), macrocyclic triene CTT **45** should react to give only tricycle CAC. In the present instance (see Scheme 7), two stereoisomers **46***a* and **46***b*, which are different only in the relative configuration of the silyloxy group (as enantiomeric structures), are possible. Indeed, macrocyclic triene **45** can react through conformation **45**i or **45**ii to produce either tricycle **46***a* or **46***b* in their conformations **46***a*i and **46***b*i, respectively. The process **45**ii → **46***b*i must be disfavored due to the important steric hindrance from the silyloxy substituent, which has to take a pseudo-axial orientation. That steric interaction is absent in the process **45**i → **46***a*i in which the silyloxy substituent is in a pseudo-equatorial orientation. Thus, the favored process should lead to stereoisomer **46***a* in which both protons at positions 4 and 5 are equatorial (see the more stable conformation, **46***a*ii and **46***b*ii of **46***a* and **46***b*). This conclusion was later firmly secured by X-ray diffraction analysis of a crystalline derivative **62** (*vide infra*).

Compound **47** shows three olefinic protons (5.23, 5.45, and 5.60 ppm) and a methyl group attached to a double bond (1.45 ppm) in its nmr spectrum. By 2D nmr experiments it was possible to propose a bicyclic structure **47** for this compound, which could result from a transannular ene-type reaction (see **45**iii or **45**iv → **47**) (Scheme 8), examples of



(a) *t*-Butoxydiphenylsilylchloride (TBODPSCl), Et_3N, CH_2Cl_2, 99%; (b) *t*-BuOH, PPTS, 60°C, 51%; (c) DMSO, $(COCl)_2$, DIPEA, -78°C, 76%; (d) i): **32**, *n*-BuLi, -93°C, 15 s then **36**, THF, -90°C, 86%; (e) TBDMSTf, Et_3N, CH_2Cl_2, 0°C, 85%; (f) $LiAlH_4$, ether, 25°C, 82%; (g) MsCl, LiCl, collidine, DMF, 25°C (**41**, 90%; **44**, 82%); (h) E_2CHNa, THF:DMF (1:1), KI, 25°C, 81%; (i) Bu_4NF, CH_2Cl_2, 25°C, 88%; (j) Cs_2CO_3, 18-crown-6, CH_3CN, 78°C, 75%; (k) toluene, 220°C, 7 h, **46** (76%), **47** (16%).

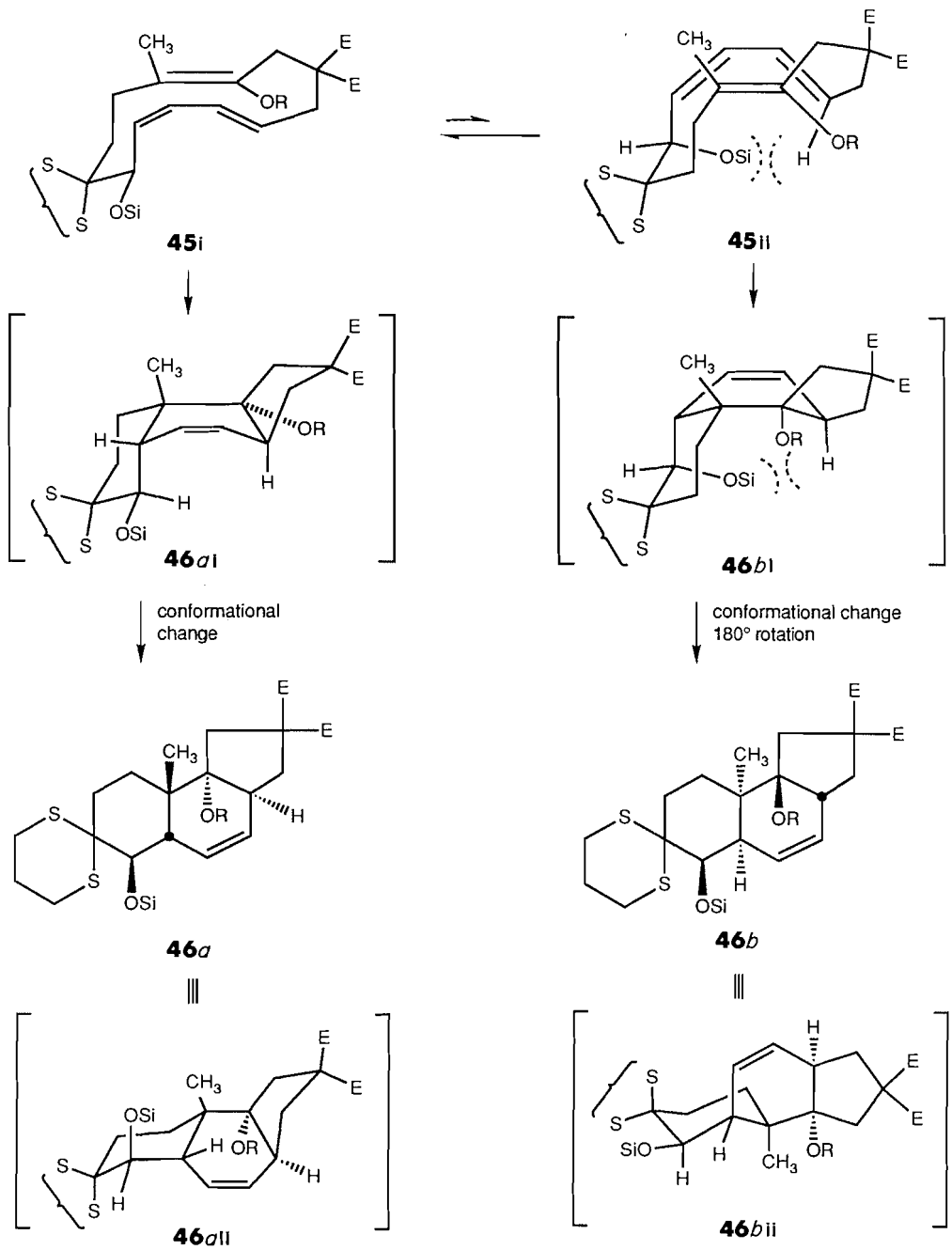
SCHEME 6. E = CO_2CH_3; R = TBODPS.

which were observed and reported previously (14*a*). The geometry of the newly formed double bond and the stereochemistry at the ring junction are still unknown. Molecular models show that this ene reaction may involve either proton H_A (**45**iii) or H_B (**45**iv), leading to different geometries for the trisubstituted olefin.

Towards the A.B.C. rings of Veratrum *alkaloids*

To test the validity of the present model series in an eventual sequence towards the A.B.C. rings of *Veratrum* alkaloids, we investigated the introduction of the oxygen bridge between positions 9 and 4.

The thioketal moiety of tricycle **46** (Scheme 9) was cleaved with mercuric chloride on calcium carbonate (27) in aqueous acetonitrile, and then the obtained ketone **54** was reduced with methanolic sodium borohydride to epimeric separable alcohols **55** and **56**, both useful for this preliminary investigation. The epimers were identified through their benzoate derivatives **57** and **58**, which showed that the proton at C_3 is axial in **57** (and therefore in **55**) (one coupling constant is 12.5 Hz) and equatorial in **58** (and therefore in **56**) (all the coupling constants are smaller than 3 Hz). Cleavage of the MOM protecting group of **57** and **58** in acid medium gave alcohols **59** and **60** selectively and in quantitative yield, leaving the *tert*-butyldimethylsilyl ether moiety unaffected. Subsequent treatment of silyl ether benzoate **59** with tetrabutylammonium fluoride led to hydroxybenzoate lactone **61** (19%) and diol lactone **62** (61%). The basicity of the reaction medium (presence of a catalytic amount of tetrabutyl ammonium hydroxide) was presumably sufficient to promote lactonization of the free 9-hydroxyl group with the adjacent methyl ester of the malonate moiety and to induce

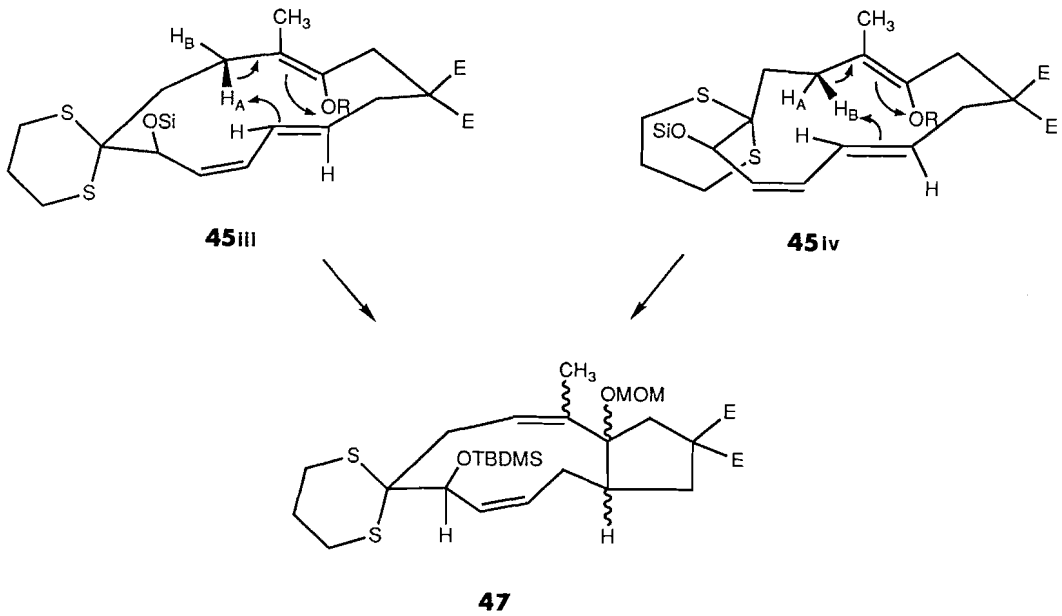


SCHEME 7. R = MOM; E = CO_2CH_3.

transesterification of the equatorial benzoate at position 3. X-ray diffraction analysis (see Fig. 2) of crystalline diol **62** (28) confirmed the α and axial orientation of the proton at C_3, as well as the predicted stereochemistry of all the asymmetric centers of the molecule, in particular the ones that had been formed during the transannular Diels–Alder reaction.

On the other hand, cleavage of silyl benzoate **58** with fluoride ion led to benzoate alcohol lactone **63** in good yield (81%). Even though compound **61** has its 9-hydroxyl inserted into a lactone bridge, and therefore not immediately available for a hemiketal bridging with position 4, we tested the oxidation of the axial β-hydroxyl at position 4 of that compound with PCC and obtained ketone **64** as the only product. We did not investigate any further reaction at this point, having learned that the oxidation of the 4-OH group should be performed before the MOM cleavage. On the other hand the presence of the lactone bridge gives the opportunity of differentiating the two ester moieties of the malonate connector, which is a lead for further studies.

In conclusion, we have shown that it is possible to synthesize in good yield a specifically functionalized tricyclic A.B.C.[6.6.5] skeleton, having a *cis-anti-cis* (CAC) stereochemistry at the ring junction, by a transannular Diels–Alder reaction of a macrocyclic triene. Very recently, Dory (29) from our group showed that the use of a sulfone connector (besides a malonate) and a *trans-trans* diene in a similar general strategy has given access to a CAT tricyclic skeleton. Applied to our problem, this modification should



SCHEME 8

lead to a CAT A.B.C.[6.6.5] skeleton having the desired stereochemistry at the position 8 ring junction. Further studies are in progress in order to use this method and complete the synthesis of the first three rings of the *Veratrum* alkaloid skeleton.

Experimental

All reactions were carried out under an argon or anhydrous nitrogen atmosphere. All solvents were dried before use. Chromatographic separations were made using Merck Kieselgel 60 (230–400 mesh ASTM). The infrared spectra (ir) were taken on a Perkin–Elmer 681 spectrophotometer or on a FT-IR Bomem MB-102. Proton nmr spectra were recorded on a Bruker WP-80 or Bruker WM-250 instrument. Carbon nmr spectra were recorded on a Bruker WM-250 instrument. Chemical shifts are reported in δ values relative to tetramethylsilane or chloroform. Abbreviations used are m: multiplet, s: singlet, d: doublet, t: triplet, dd: double doublets, etc. Mass spectral assays (ms *m/e*) and peak matching were obtained using a VG Micromass ZAB-1F spectrometer.

*Methyl 5-*tert*-butyldiphenylsilyloxy-3-hydroxy-2-methoxymethyloxy-3-methylpentanoate (**19**a and **19**b)*

To a cold (−78°C) solution of lithium diisopropyl amide (LDA), obtained from diisopropylamine (DIPA) (20.5 mL, 146 mmol) and BuLi (1.6 mL in hexane) (90 mL, 144 mmol) in tetrahydrofuran (500 mL) at −20°C, was added dropwise (3.5 h) a solution of methyl methoxymethyloxyacetate (19.43 g, 145 mmol) in tetrahydrofuran (150 mL). The mixture was stirred at −78°C for 15 min and a solution of ketone **18** (23.2 g, 71.17 mmol) in tetrahydrofuran (150 mL) was added dropwise (1 h). After an additional 60 min at −78°C and treatment with a saturated solution of ammonium chloride the mixture was extracted with methylene chloride; the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (19:1–7:3) as the eluent to afford alcohols **19***a* and **19***b* (31.9 g, 97.4%). These two diastereoisomers were separated on a small scale for their characterization.

Isomer **19**a (less polar): ir ($CHCl_3$): 3500, 1740 cm^{-1}; ^1H nmr ($CDCl_3$, δ ppm): 1.05 (9H, s, $-C(CH_3)_3$), 1.30 (3H, s, $-CH_3$), 1.90 (2H, m, $-CH_2-CH_2OTBDPS$), 3.33 (3H, s, $-OCH_3$), 3.77 (3H, s, $-CO_2CH_3$), 3.92 (2H, m, $-CH_2-OTBDPS$), 4.09 (1H, s, $-CH(CO_2CH_3)-$), 4.64 (2H, s, $-OCH_2O-$), 7.42 and 7.67 (10H, m, Ph_2).

Isomer **19**b (more polar): ir ($CHCl_3$): 3500, 1740 cm^{-1}; ^1H nmr ($CDCl_3$, δ ppm): 1.04 (9H, s, $-C(CH_3)_3$), 1.30 (3H, s, $-CH_3$), 1.80 (1H, dt, J = 6 and 15 Hz, $-CHH-CH_2OTBDPS$), 2.03 (1H, dt, J = 6 and 15 Hz, $-CHH-CH_2OTBDPS$), 3.38 (3H, s, $-OCH_3$), 3.75 (3H, s, $-CO_2CH_3$), 3.92 (2H, dd, J = 5.4 and 7 Hz, $-CH_2-OTBDPS$), 4.06 (1H, s, $-CH(CO_2CH_3)-$), 4.69 (2H, m, $-OCH_2O-$), 7.42 and 7.67 (10H, m, Ph_2).

*Methyl (2*E*) and (2*Z*)-5-*tert*-butyldiphenylsilyloxy-2-methoxymethyloxy-3-methylpent-2-enoate (**20**a and **20**b)*

Starting from alcohols **19***a* and **19***b* separately or a mixture of both:

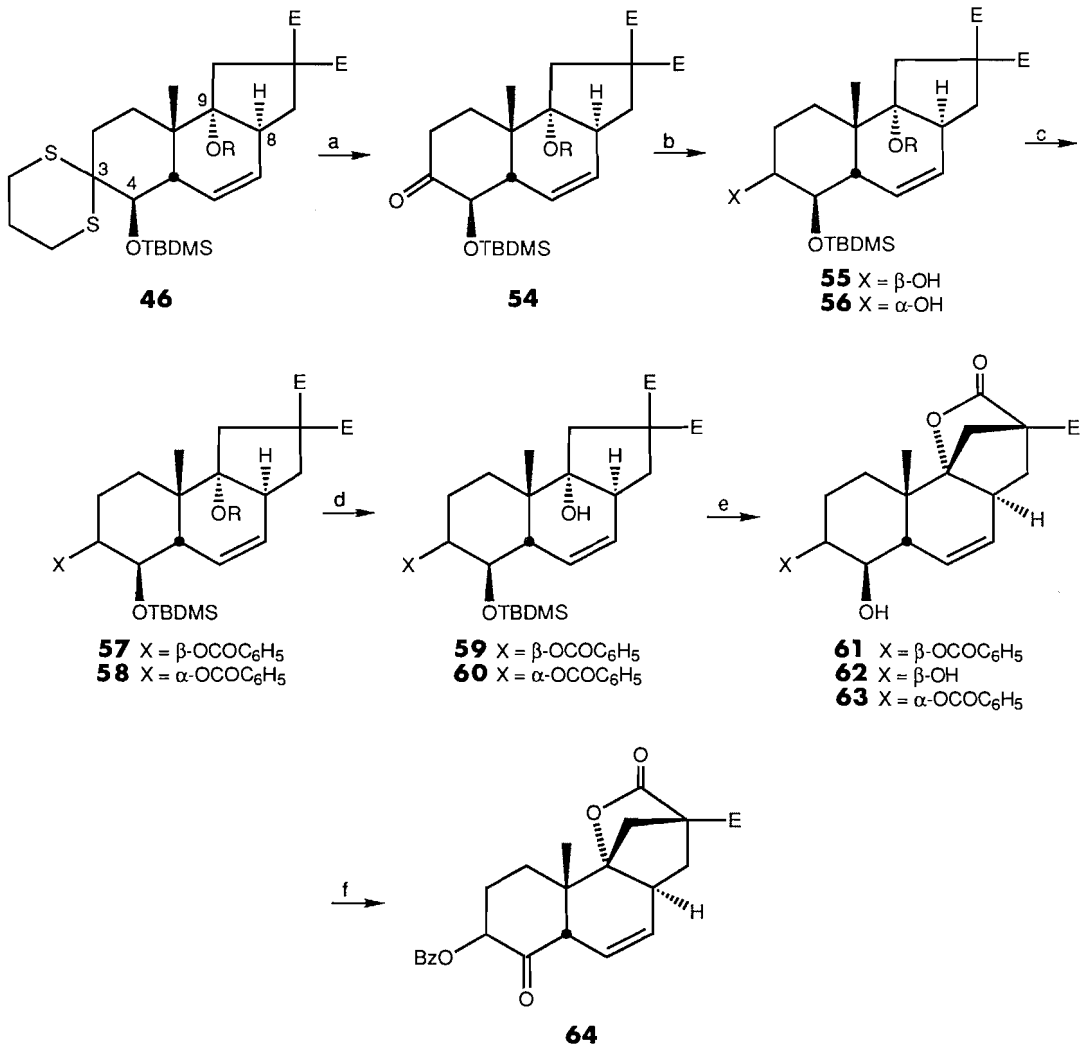
To a solution of mixed alcohols **19***a* and **19***b* (29.5 g, 64.1 mmol) in pyridine (400 mL), at −60°C, thionyl chloride (25 mL, 343 mmol) was added all at once. The mixture was stirred at −60°C 15 min, at −30°C for 30 min, and at −20°C for 100 min. A saturated solution of sodium bicarbonate was added and the mixture was extracted with methylene chloride. The organic layer was dried over magnesium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (19:1–7:3) as the eluent to afford a mixture of unseparable α,β-unsaturated esters **20***a* and **20***b* and the two separable isomers **21** and **22** (**20***a* and **20***b* (7.65 g, 27%); **21** and **22** (16.4 g, 58%)).

Starting from isomers **21** and **22**:

To a solution of isomers **21** and **22** (16 g, 36.2 mmol) in anhydrous methanol (250 mL) was added potassium methoxide obtained from potassium (3 g, 77 mmol) dissolved in methanol (250 mL). The mixture was refluxed for 3 h, cooled, and poured into a saturated solution of ammonium chloride. The mixture was acidified to pH 6 with hydrochloric acid and extracted with methylene chloride. The organic layer was dried over sodium sulfate, evaporated, and the residue was purified by flash chromatography using hexane:ethyl acetate (19:1–7:3) as the eluent to afford pure α,β-unsatured esters **20***a* and **20***b* (11.3 g, 71%).

Isomer (E)-**20**a (obtained pure from pure **19***a*): ^1H nmr ($CDCl_3$, δ ppm): 1.03 (9H, s, $-C(CH_3)_3$), 1.90 (3H, s, $-CH_3$), 2.75 (2H, t, J = 7 Hz, $-CH_2-CH_2OTBDPS$), 3.50 (3H, s, $-OCH_3$), 3.71 (3H, s, $-CO_2CH_3$), 3.78 (2H, t, J = 7 Hz, $-CH_2-OTBDPS$), 4.80 (2H, s, $-OCH_2O-$), 7.41 and 7.67 (10H, m, Ph_2).

*Isomer (Z)-**20*** (obtained pure from pure **19***b*): ^1H nmr ($CDCl_3$, δ ppm): 1.04 (9H, s, $-C(CH_3)_3$), 1.98 (3H, s, $-CH_3$), 2.57 (2H, t, J = 7 Hz, $-CH_2-CH_2OTBDPS$), 3.44 (3H, s, $-OCH_3$), 3.77 (3H,



46 **54**

55 X = β-OH
56 X = α-OH

57 X = β-$OCOC_6H_5$
58 X = α-$OCOC_6H_5$

59 X = β-$OCOC_6H_5$
60 X = α-$OCOC_6H_5$

61 X = β-$OCOC_6H_5$
62 X = β-OH
63 X = α-$OCOC_6H_5$

64

(a) $HgCl_2$, $CaCO_3$, aq. CH_3CN, 25°C, 70%;
(b) $NaBH_4$, MeOH, 94%;
(c) C_6H_5COCl, Et_3N, DMAP, CH_2Cl_2, 25°C (**57**, 89%; **58**, 86%);
(d) HCl 6N, THF aq. 25°C, 98%;
(e) Bu_4NF, THF, 25°C (**61**, 19% and **62**, 61%; **63**, 81%);
(f) PCC, CH_2Cl_2, 25°C, 98%

SCHEME 9. E = CO_2CH_3; R = MOM.

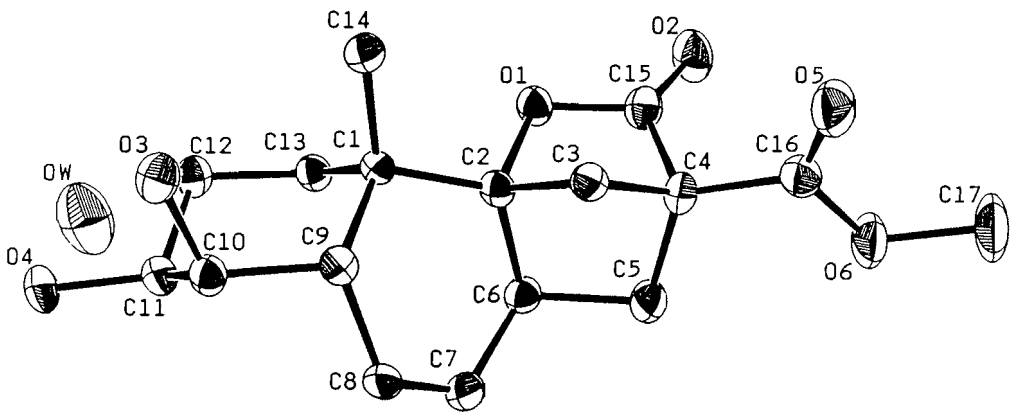


FIG. 2. Stereoview of crystalline **62**; 50% probability thermal ellipsoids are shown for the non-hydrogen atoms.

s, -CO_2CH_3), 3.78 (2H, t, J = 7 Hz, -CH_2-OTBDPS), 4.74 (2H, s, -OCH_2O-), 7.41 and 7.67 (10H, m, Ph_2).

Isomer ***21*** (less polar than **22**): ^{1}H nmr ($CDCl_3$, δ ppm): 1.04 (9H, s, -$C(CH_3)_3$), 2.37 (2H, q, J = 6.6 Hz, -CH_2-CH_2OTBDPS), 3.35 (3H, s, -OCH_3), 3.70 (3H, s, -CO_2CH_3), 3.79 (2H, dt, J = 6.8 Hz and 1.0 Hz, -CH_2-OTBDPS), 4.61 (1H, d J = 6.8 Hz, -OCHHO-), 4.66 (1H, d, J = 6.8 Hz, -OCHHO-), 4.62 (1H, s, -$CH(CO_2CH_3)$-), 5.13 (1H, s, CHH=), 5.26 (1H, s, CHH=), 7.40 and 7.66 (10H, m, Ph_2).

Isomer 22: ^{1}H nmr ($CDCl_3$, δ ppm): 1.04 (9H, s, -$C(CH_3)_3$), 1.46 (3H, d, J = 1.1 Hz, -CH_3), 3.38 (3H, s, -OCH_3), 3.74 (3H, s, -CO_2CH_3), 4.27 (2H, d, J = 6 Hz, -CH_2-OTBDPS), 4.56 (1H, s, -$CH(CO_2CH_3)$-), 4.65 (2H, s, -OCH_2O-), 5.82 (1H, t, J = 6 Hz, -CH=), 7.40 and 7.67 (10H, m, Ph_2).

*Methyl (2*E*)-5-hydroxy-2-methoxymethyloxy-3-methylpent-2-enoate (**24**a) and its conversion to 2-methoxymethyloxy-3-methylpent-2-en-5-olide (**25**)*

To a solution of pure **20***a* (22 mg, 0.05 mmol) in tetrahydrofuran (2 mL) was added at 0°C a solution of tetrabutylammonium fluoride (100 μL, 0.1 mmol). The mixture was stirred at room temperature for 2.5 h and the solvent was evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (4:1–3:2) as the eluent to afford pure lactone **25** (2 mg, 23%) and **24** (2.5 mg, 25%) (on silica gel, alcohol **24***a* partly forms lactone **25**). Lactone **25**: ir ($CHCl_3$, ν cm^{-1}): 1720, 1655; ^{1}H nmr ($CDCl_3$, δ ppm): 1.99 (3H, s, -CH_3), 2.50 (2H, t, J = 6.3 Hz, -CH_2CH_2-OCO-), 3.53 (3H, s, -OCH_3), 4.34 (2H, t, J = 6.2 Hz, -CH_2-CH_2-OCO-), 5.00 (2H, s, -OCH_2O-).

*Methyl (2*Z*)-5-hydroxy-2-methoxymethyloxy-3-methylpent-2-enoate (**24**b)*

To a solution of **20***b* (75 mg, 0.17 mmol) in tetrahydrofuran (6.0 mL), was added at 0°C a solution of tetrabutylammonium fluoride (340 μL, 0.34 mmol). The mixture was stirred at room temperature for 2 h and the solvent was evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (3:2) as the eluent to afford pure alcohol **24***b* (25 mg, 72%); ir ($CHCl_3$, ν cm^{-1}): 3600, 3460, 3030, 3010, 2950, 1720, 1640; ^{1}H nmr ($CDCl_3$, δ ppm): 2.09 (3H, s, -CH_3), 2.60 (2H, t, J = 6.3 Hz, -CH_2-CH_2OH), 3.53 (3H, s, -OCH_3), 3.79 (3H, s, -CO_2CH_3), 3.80 (2H, t, J = 6.3 Hz, -CH_2OH), 4.84 (2H, s, -OCH_2O-). Exact Mass calcd. for $C_9H_{16}O_5$: 172.0736 (M^+ − CH_3OH); found: 172.0734 ± 0.0005.

*(2*E*) and (2*Z*)-5-*tert*-Butyldiphenylsilyloxy-2-methoxymethyloxy-3-methylpent-2-en-1-ol (**23**a and **23**b)*

To a cold solution (−78°C) of esters **20** (8.55 g, 19.3 mmol) in methylene chloride (1 L) was added a solution of DIBAL (26 mL, 1.5 M, 39 mmol). The mixture was stirred vigourously for 2 h, then treated with decahydrated sodium sulfate (8 g). The mixture was warmed to room temperature, diluted with acetone (1 L), and stirred overnight. The mixture was dried over anhydrous sodium sulfate, filtered, and the residue on filter washed five times with acetone. Evaporation of the solvent left a residue, which was purified by flash chromatography using hexane:ethyl acetate (4:1–3:2) as the eluent to afford pure alcohols **23***a* (1.28 g, 16%) and **23***b* (6.60 g, 83%); ir (CH_2Cl_2, ν cm^{-1}): 3600, 3480, 3060, 2960, 2940, 2860, 1680. Exact Mass calcd. for $C_{24}H_{34}O_4Si$: 414.2226 (M^+); found: 414.2234 ± 0.0012.

*(*E*) Isomer **23**a* (less polar): ^{1}H nmr ($CDCl_3$, δ ppm): 1.04 (9H, s, -$C(CH_3)_3$), 1.64 (3H, s, -CH_3), 2.34 (2H, t, J = 6.5 Hz, -CH_2-CH_2OTBDPS), 2.93 (1H, t, J = 6 Hz, -OH), 3.50 (3H, s, -OCH_3), 3.66 (2H, t, J = 6.5 Hz, -CH_2OTBDPS), 4.12 (2H, d, J = 6 Hz, -CH_2OH), 4.87 (2H, s, -OCH_2O-), 7.41 and 7.66 (10H, m, Ph_2); ^{13}C nmr ($CDCl_3$, δ ppm): 15.4 (=C-CH_3), 19.0 (-$C(CH_3)_3$), 26.8 (-$C(CH_3)_3$), 35.8 (-CH_2-C=), 56.3 (OCH_3), 58.4 (CH_2-OTBDPS), 62.2 (CH_2-OH), 96.2 (OCH_2O), 119.7 (CH_3-C=C-), 127.7, 129.7, 133.5, 135.6 (C, aromatic), and 149.8 (C=C-OMOM).

*(Z) Isomer **23**b* (more polar): ^{1}H nmr ($CDCl_3$, δ ppm): 1.04 (9H, s, -$C(CH_3)_3$), 1.67 (3H, s, -CH_3), 2.39 (2H, t, J = 7 Hz, -CH_2-CH_2OTBDPS), 2.95 (1H, t, J = 6.4 Hz, -OH), 3.43 (3H, s, -OCH_3), 3.71 (2H, t, J = 7 Hz, -CH_2OTBDPS), 4.13 (2H, d, J = 6.4 Hz, -CH_2OH), 4.72 (2H, s, -OCH_2O-), 7.40 and 7.66 (10H, m, Ph_2); ^{13}C nmr ($CDCl_3$, δ ppm): 16.9 (=C-CH_3), 19.1 (-$C(CH_3)_3$), 26.8 (-$C(CH_3)_3$), 34.6 (-CH_2-C=), 56.2 (OCH_3), 58.5 (CH_2-OTBDPS), 62.3 (CH_2-OH), 96.7 (OCH_2O), 120.2 (CH_3-C=C-), 127.6, 129.6, 133.9, 135.6 (C, aromatic), and 148.9 (C=C-OMOM).

*(2Z)-5-*tert*-Butyldiphenylsilyloxy-2-methoxymethyloxy-3-methyl-1-(2,4,6-trimethylbenzoyloxy)pent-2-ene (**26**)*

To a solution of 2,4,6-trimethylbenzoic acid (mesitoic acid) (784 mg, 4.78 mmol), dicyclohexylcarbodiimide (1.39 g, 6.74 mmol), and 4-dimethylaminopyridine (400 mg, 3.28 mmol) in methylene chloride (8.8 mL) was added a solution of alcohol **23***b* (1.5 g, 3.62 mmol) in methylene chloride (3.7 mL). The mixture was stirred at room temperature for 7 days and a saturated solution of sodium bicarbonate was added. The mixture was extracted with methylene chloride, and the organic layer was dried over magnesium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (9:1–4:1) as the eluent to afford pure ester **26** (1.9 g, 94%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2960, 2940, 2860, 1720, 1610; ^{1}H nmr ($CDCl_3$, δ ppm): 1.03 (9H, s, -$C(CH_3)_3$), 1.75 (3H, s, -CH_3), 2.24 (6H, s, *ortho*-CH_3 of OMes), 2.27 (3H, s, *para*-CH_3 of OMes), 2.46 (2H, t, J = 7 Hz, -CH_2-CH_2OTBDPS), 3.37 (3H, s, -OCH_3), 3.72 (2H, t, J = 7 Hz, -CH_2-OTBDPS), 4.79 (2H, s, -OCH_2O-), 4.97 (2H, s, -CH_2-OMes), 6.82 (2H, s, CH aromatic), 7.38 and 7.66 (10H, m, Ph_2). Exact Mass calcd. for $C_{34}H_{44}O_5Si$: 503.2254 (M^+ − *tert*-butyl); found: 503.2250 ± 0.0015.

*(2Z)-2-Methoxymethyloxy-3-methyl-1-(2,4,6-trimethylbenzoyloxy)pent-2-en-5-ol (**27**)*

To a cold (0°C) solution of ester **26** (5.15 g, 9.2 mmol) in tetrahydrofuran (225 mL) was added a solution of tetrabutylammonium fluoride (18.4 mL, 18.4 mmol). The mixture was stirred at room temperature for 1.5 h and the solvent was evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (3:2) as the eluent to afford pure alcohol **27** (2.95 g, 99%); ir (CH_2Cl_2, ν cm^{-1}): 3620, 3500, 3060, 2990, 2960, 2930, 1720, 1610; ^{1}H nmr ($CDCl_3$, δ ppm): 1.84 (3H, s, -CH_3), 2.27 and 2.28 (9H, 2s, -CH_3 aromatic), 2.48 (2H, t, J = 6.4 Hz, -CH_2-CH_2OH), 3.46 (3H, s, -OCH_3), 3.73 (2H, t, J = 6.4 Hz, -CH_2-OH), 4.90 (2H, s, -OCH_2O-), 5.01 (2H, s, -CH_2-OMes), 6.84 (2H, s, CH aromatic). Exact Mass calcd. for $C_{18}H_{26}O_5$: 322.1780 (M^+); found: 322.1786 ± 0.0012.

*(2Z)-5-Mesyloxy-2-methoxymethyloxy-3-methyl-1-(2,4,6-trimethylbenzoyloxy)pent-2-ene (**28**)*

To a cold (0°C) solution of alcohol **27** (2.49 g, 7.73 mmol) and triethylamine (4.3 mL, 30.9 mmol) in methylene chloride (100 mL) was added mesyl chloride (950 μL, 12.3 mmol). The mixture was stirred at 0°C for 30 min and a saturated solution of sodium bicarbonate was added. The mixture was extracted with methylene chloride, and the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography with hexane:ethyl acetate (3:2) as the eluent to afford pure mesylate **28** (3.09 g, 98%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2990, 2960, 2930, 1725, 1360; ^{1}H nmr ($CDCl_3$, δ ppm): 1.86 (3H, s, -CH_3), 2.27 (9H, s, -CH_3 aromatic), 2.64 (2H, t, J = 7 Hz, -CH_2-CH_2OMs), 2.97 (3H, s, -SO_2-CH_3), 3.44 (3H, s, -OCH_3), 4.29 (2H, t, J = 7 Hz, -CH_2-OMs), 4.91 (2H, s, -OCH_2O-), 5.01 (2H, s, -CH_2-OMes), 6.84 (2H, s, CH aromatic). Exact Mass calcd. for $C_{19}H_{28}O_7S$: 400.1556 (M^+); found: 400.1563 ± 0.0014.

*(2Z)-5-Iodo-2-methoxymethyloxy-3-methyl-1-(2,4,6-trimethylbenzoyloxy)pent-2-ene (**29**)*

To a solution of mesylate **28** (2.25 g, 5.63 mmol) in acetone (340 mL) was added sodium iodide (38 g, 253 mmol). The mix-

ture was heated at 56°C for 5.5 h and then acetone was evaporated. The residue was dissolved in ether (500 mL) and filtered. The solvent was evaporated and the residue was purified by flash chromatography using hexane:ethyl acetate (7:3) as the eluent to afford pure iodide **29** (2.2 g, 91%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2990, 1725, 1610; ^1H nmr ($CDCl_3$, δ ppm): 1.83 (3H, s, $-CH_3$), 2.28 (9H, s, $-CH_3$ aromatic), 2.77 (2H, t, J = 7.5 Hz, $-CH_2-CH_2I$), 3.18 (2H, t, J = 7.5 Hz, $-CH_2I$), 3.46 (3H, s, $-OCH_3$), 4.91 (2H, s, $-OCH_2O-$), 4.99 (2H, s, $-CH_2-$OMes, 6.84 (2H, s, CH aromatic). Exact Mass calcd. for $C_{18}H_{25}O_4I$: 432.0799 (M^+); found: 432.0817 ± 0.0013.

*(2Z)-2-Methoxymethyloxy-3-methyl-6,6-(propylenedithio)-1-(2,4,6-trimethylbenzoyloxy)hex-2-ene (**30**)*

A solution of butyllithium (1.6 M in hexane) (285 μL, 0.46 mmol) was added to a cold (−30°C) solution of 1,3-dithiane (55.7 mg, 0.46 mmol) in tetrahydrofuran (0.6 mL). The mixture was stirred between −35°C and −25°C for 100 min. Then it was cooled to −78°C and a solution of iodide **29** (150 mg, 0.347 mmol) in tetrahydrofuran (0.6 mL) was added. The mixture was stirred at −78°C for 3 h and at −45°C for 1 h. Water was then added and the mixture was extracted with methylene chloride. The organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (9:1–3:2) as the eluent to afford pure **30** (17 mg, 12%) and iodide **29** (100 mg, 66%). ^1H nmr ($CDCl_3$, δ ppm): 1.79 (3H, s, $-CH_3$), 1.86 (2H, m, $-SCH_2CH_2CH_2S-$), 1.89 and 2.13 (2H, m, $-CH_2-CHS_2$), 2.27 (9H, s, $-CH_3$ aromatic), 2.38 (2H, m, $=C(CH_3)-CH_2CH_2-$), 2.85 (4H, m, $-SCH_2CH_2CH_2S-$), 3.46 (3H, s, $-OCH_3$), 4.02 (1H, t, J = 7 Hz, -S-CH-S-), 4.88 (2H, s, $-OCH_2O-$), 4.99 (2H, s, $-CH_2-$OMes), 6.83 (2H, s, CH aromatic).

*(2Z)-2-Methoxymethyloxy-3-methyl-6,6-(propylenedithio)-6-trimethylstannyl-1-(2,4,6-trimethylbenzoyloxy)hex-2-ene (**31**)*

To a cold (−78°C) solution of 2-trimethylstannyl-1,3-dithiane (864 mg, 3.06 mmol) in tetrahydrofuran (4.3 mL), was added a solution of LDA obtained at 0°C from DIPA (421 μL, 3.01 mmol) and BuLi (1.6 M in hexane) (1.9 mL, 3.04 mmol) in tetrahydrofuran (4.3 mL). The mixture was stirred at −30°C for 3 h and at −78°C for 30 min. Then a solution of iodide **29** (632 mg, 1.46 mmol) in tetrahydrofuran (3 mL) was added. The mixture was stirred at this temperature for an additional 1.5 h, treated with water, and warmed to room temperature. The mixture was extracted with methylene chloride; the organic layer was dried over sodium sulfate, evaporated, and the residue was purified by flash chromatography using hexane:ethyl acetate (19:1–7:3) as the eluent to afford pure **31** (325 mg, 38%) and **30** (111 mg, 18%); ^1H nmr ($CDCl_3$, δ ppm): 0.28 (9H, t, $J_{Sn(119)-H}$ = 27.2 Hz, $J_{Sn(117)-H}$ = 26.1 Hz, $-Sn-(CH_3)_3$), 1.85 (3H, s, $-CH_3$), 2.05 (2H, m, $-SCH_2CH_2CH_2S-$), 2.27 and 2.30 (9H, s, CH_3 aromatic), 2.31 (4H, m, $=C(CH_3)-CH_2-CH_2-$), 2.40 (2H, m, -SCHH-CH_2-CHH-S-), 3.15 (2H, m, -SCHH-CH_2-CHH-S-), 3.45 (3H, s, $-OCH_3$), 4.90 (2H, s, $-OCH_2O-$), 5.02 (2H, s, $-CH_2-$OMes), 6.85 (2H, s, CH aromatic).

*(2Z)-2-Methoxymethyloxy-3-methyl-6,6-(propylenedithio)-6-tributylstannyl-1-(2,4,6-trimethylbenzoyloxy)hex-2-ene (**32**)*

To a solution of 2-tributylstannyl-1,3-dithiane (2 g, 4.9 mmol) in tetrahydrofuran (7 mL) at −78°C, was added a solution of LDA obtained at 0°C from DIPA (690 μL, 4.9 mmol) and BuLi (1.6 M in hexane) (2.9 mL, 4.6 mmol) in tetrahydrofuran (7 mL). The mixture was stirred at −30°C for 3 h and at −78°C for 30 min. Then a solution of iodide **29** (967 mg, 2.24 mmol) maintained in tetrahydrofuran (6 mL) at −30°C was added. The mixture was stirred at this temperature for an additional 75 min and water was added. The solution was warmed to room temperature. The mixture was extracted with methylene chloride and the organic layer was dried with sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (19:1–9:1) as the eluent to afford pure **32** (1.383 g, 87%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2960, 2920, 2860, 1720, 1610; ^1H nmr ($CDCl_3$, δ ppm): 0.90 (9H, t, J = 7.2 Hz, $-(CH_2)_3-CH_3$), 1.08 (6H, m, $-Sn-CH_2-$), 1.34 (6H, m, J = 7 Hz, $-CH_2-CH_2-CH_3$), 1.55 (6H, m, $-Sn-CH_2-CH_2-$), 1.86 (3H, s, $-CH_3$), 2.05 (2H, m, $-SCH_2CH_2CH_2S-$), 2.21 and 2.33 (4H, m, $=C(CH_3)-CH_2-CH_2-$), 2.27 and 2.30 (9H, s, $-CH_3$ aromatic), 2.43 (2H, m, -SCHH-CH_2-CHH-S-), 3.15 (2H, m, SCHH-CH_2-CHH-S-), 3.45 (3H, s, $-OCH_3$), 4.90 (2H, s, $-OCH_2O-$), 5.03 (2H, s, $-CH_2-$OMes), 6.84 (2H, s, CH aromatic). Exact Mass calcd. for $C_{34}H_{58}O_4S_2Sn$: 657.2094 (M^+ − *tert*-butyl); found: 657.2105 ± 0.0018.

*(2Z,4E)-6-*tert*-Butoxydiphenylsilyloxy-1-tetrahydropyranyloxyhexa-2,4-diene (**34**)*

To a solution of alcohol **33** (2.32 g, 11.7 mmol) and triethylamine (2.5 mL, 17.8 mmol) in methylene chloride (50 mL) was added *tert*-butoxydiphenylsilyl chloride (3.2 mL, 12.2 mmol) at 0°C. The mixture was stirred at room temperature for 40 min and a saturated solution of ammonium chloride was added. The mixture was extracted with hexane:ether (4:1); the organic layer was dried with sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ether (4:1) as the eluent to afford pure **34** (5.25 g, 99%); ir (CH_2Cl_2, ν cm^{-1}): 3050, 2980, 2940, 2860, 1430; ^1H nmr ($CDCl_3$, δ ppm): 1.31 (9H, s, $-OC-(CH_3)_3$), 1.47–1.86 (6H, m, $-OCH_2-(CH_2)_3-$), 3.49 and 3.87 (2H, m, $-OCH_2-(CH_2)_3-$), 4.20 (1H, dd, J = 7.5 and 12.5 Hz, THPO-CHH-CH=CH-), 4.35 (1H, dd, J = 7.5 and 12.5 Hz, THPO-CHH-CH=CH-), 4.34 (2H, d, J = 4.6 Hz, $-CH_2-$OTBODPS), 4.65 (1H, t, J = 3.5 Hz, -O-CH(O-)-), 5.57 (1H, dt, J = 7 and 10.9 Hz, THPO-CH_2-CH=CH-), 5.83 (1H, dt, J = 5.2 and 15 Hz, -CH=CH-CH_2OTBODPS), 6.16 (1H, dd, J = 11.1 and 11.1 Hz, THPO-CH_2-CH=CH-), 6.60 (1H, dd, J = 11.5 and 15 Hz, CH=CH-CH_2OTBODPS), 7.37 and 7.67 (10H, m, Ph_2). Exact Mass calcd. for $C_{27}H_{36}O_4Si$: 395.1679 (M^+ − *tert*-butyl); found: 395.1674 ± 0.0011.

*(2Z,4E)-6-*tert*-Butoxydiphenylsilyloxyhexa-2,4-dien-1-ol (**35**)*

To a solution of **34** (16.7 g, 36.9 mmol) in *tert*-butanol (270 mL) was added pyridinium *para*-toluenesulfonate (1.68 g, 6.7 mmol). The mixture was heated to 60°C for 10 h and then a saturated solution of sodium bicarbonate was added. The mixture was extracted with hexane:ether (4:1), and the organic layer was dried with sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (9:1–3:2) as the eluent to afford pure alcohol **35** (6.89 g, 51%) and starting **34** (6.2 g, 37%); ir (CH_2Cl_2, ν cm^{-1}): 3600, 3060, 2980, 2940, 2880; ^1H nmr ($CDCl_3$, δ ppm): 1.31 (9H, s, $-OC(CH_3)_3$), 4.30 (2H, dd, J = 5.7 and 5.7 Hz, $-CH_2OH$), 4.35 (2H, d, J = 5.2 Hz, $-CH_2-$OTBODPS), 5.59 (1H, ddd, J = 7.5, 7.5, and 10.9 Hz, HO-CH_2-CH=CH-), 5.84 (1H, ddd, J = 5, 5, and 15 Hz, -CH=CH-CH_2OTBODPS), 6.10 (1H, dd, J = 11.5 and 11.5 Hz, HO-CH_2-CH=CH-), 6.54 (1H, dd, J = 12 and 15 Hz, -CH=CH-CH_2OTBODPS), 7.37 and 7.67 (10H, m, Ph_2). Exact Mass calcd. for $C_{22}H_{28}O_3Si$: 311.1103 (M^+ − *tert*-butyl); found: 311.1082 ± 0.0009.

*(2Z,4E)-6-*tert*-Butoxydiphenylsilyloxyhexa-2,4-dien-1-al (**36**)*

To a solution of oxalyl chloride (1.7 mL, 19.5 mmol) in methylene chloride (52 mL) at −78°C was added dimethyl sulfoxide (2.8 mL, 39.5 mmol). The mixture was stirred at −78°C for 10 min and a solution of alcohol **35** (5.5 g, 15.0 mmol) in methylene chloride (42 mL) was added. The mixture was stirred for 50 min at −78°C, and diisopropylethylamine (DIPEA) (10.5 mL, 60.4 mmol) was added. The mixture was stirred for 15 min at −78°C and for 25 min at 0°C, water was added, and the mixture was extracted with methylene chloride. The organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (9:1) as the eluent to afford pure aldehyde **36** (4.15 g, 76%); ^1H nmr ($CDCl_3$, δ ppm): 1.31 (9H, s, $-OC(CH_3)_3$), 4.45 (2H, d, J = 4 Hz, $-CH_2-$OTBODPS), 5.84 (1H, dd, J = 8 and 11 Hz, HCO-CH=CH-), 6.21 (1H, dt, J = 5 and 15 Hz, -CH=CH-CH_2OTBODPS), 6.98 (1H, dd, J = 11.5 and

11.5 Hz, HCO-CH=CH-), 7.38 and 7.66 (11H, m, Ph_2 and -CH=CH-CH_2OTBODPS), 10.17 (1H, d, J = 8 Hz, HCO-).

*(2Z,8Z,10*E*)-12-*tert*-Butoxydiphenylsilyloxy-7-hydroxy-2-methoxymethyloxy-3-methyl-6,6-(propylenedithio)-1-(2,4,6-trimethylbenzoyloxy)dodeca-2,8,10-triene (**37**)*

To a cold (−93°C) solution of **32** (485 mg, 0.68 mmol) in tetrahydrofuran (7.6 mL) was added rapidly a cold (−90°C) solution of BuLi (1.6 M in hexane) (850 μL, 1.36 mmol) and, 15 s later, a cold (−93°C) solution of aldehyde **36** (790 mg, 2.16 mmol) in tetrahydrofuran (11 mL) was added. The mixture was stirred at −93°C for 35 min and a saturated solution of ammonium chloride was added. The mixture was warmed to room temperature and extracted with methylene chloride. The organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (9:1–4:1) as the eluent to afford pure alcohol **37** (462 mg, 86%), and a small amount of **38** (15 mg, 3%).

Compound 37: ir (CH_2Cl_2, ν cm^{-1}): 3050, 2980, 1720; ^{1}H nmr ($CDCl_3$, δ ppm): 1.30 (9H, s, -OC$(CH_3)_3$), 1.77 (3H, s, -CH_3), 1.78 (3H, m, -$SCH_2CH_2CH_2S$- and =C(CH_3)-CH_2-CHH-), 2.01 (1H, ddd, J = 5, 11.7, and 14.5 Hz, =C(CH_3)-CH_2-CHH-), 2.27 (9H, s, -CH_3 aromatic), 2.38 (1H, ddd, J = 4.9, 12.2, and 12.2 Hz, =C(CH_3)-CHH-CH_2-), 2.48 (1H, ddd, J = 5.3, 12.4, and 12.4 Hz, =C(CH_3)-CHH-CH_2-), 2.60 (2H, m, -SCHH-CH_2-CHH-S-), 2.76 (1H, d, J = 2.2 Hz, -CH-OH), 2.92 (2H, m, -SCHH-CH_2-CHH-S-), 3.45 (3H, s, -OCH_3), 4.38 (2H, d, J = 4.1 Hz, -CH_2-OTBODPS), 4.85 (1H, d, J = 6.6 Hz, -OCHHO-), 4.88 (1H, d, J = 6.6 Hz, -OCHHO-), 4.92 (1H, d, J = 10 Hz, -CH-OH), 4.97 (2H, s, -CH_2-OMes), 5.56 (1H, dd, J = 10 and 10.5 Hz, -CH(OH)-CH=CH-), 5.90 (1H, dt, J = 5 and 15 Hz, -CH=CH-CH_2OTBODPS), 6.31 (1H, dd, J = 11.3 and 11.3 Hz, -CH(OH)-CH=CH-), 6.78 (1H, dd, J = 12.5 and 15 Hz, -CH=CH-CH_2OTBODPS), 6.83 (2H, s, CH aromatic), 7.35 and 7.66 (10H, m, Ph_2). Exact Mass calcd. for $C_{44}H_{58}O_7S_2Si$: 790.3393 (M^+); found: 790.3387 ± 0.0023.

Compound 38: ^{1}H nmr ($CDCl_3$, δ ppm): 1.31 (9H, s, -OC$(CH_3)_3$), 1.80 (3H, s, -CH_3), 1.85 (2H, m, -$SCH_2CH_2CH_2S$-), 1.90 (1H, m, =C(CH_3)-CH_2-CHH-), 2.10 (1H, m, =C(CH_3)-CH_2-CHH), 2.27 (6H, s, -CH_3 aromatic), 2.40 (2H, m, =C(CH_3)-CH_2-), 2.75 (2H, m, Ar-CH_2-CH(OH)-), 2.84 (4H, m, -SCH_2-CH_2-CH_2-S-), 3.46 (3H, s, -OCH_3), 4.02 (1H, t, J = 7 Hz, -CH-S_2), 4.35 (2H, d, J = 5 Hz, -CH_2-OTBODPS), 4.78 (1H, m, -CH(OH)-), 4.88 (2H, s, -OCH_2O-), 5.00 (2H, s, -CH_2-OMes), 5.44 (1H, dd, J = 10 and 10.5 Hz, -CH(OH)-CH=CH-), 5.85 (1H, dt, J = 5 and 15 Hz, -CH=CH-CH_2OTBODPS), 6.07 (1H, dd, J = 11 and 11 Hz, -CH(OH)-CH=CH-), 6.60 (1H, dd, J = 12 and 15 Hz, -CH=CH-CH_2OTBODPS), 6.88 (2H, s, CH aromatic), 7.36 and 7.66 (10H, m, Ph_2).

*(2Z,8Z,10*E*)-12-*tert*-Butoxydiphenylsilyloxy-7-tert-butyldimethylsilyloxy-2-methoxymethyloxy-3-methyl-6,6-(propylenedithio)-1-(2,4,6-trimethylbenzoyloxy)dodeca-2,8,10-triene (**39**)*

To a solution of alcohol **37** (1.115 g, 1.41 mmol) and triethylamine (980 μL, 7.04 mmol) in methylene chloride (26 mL) was added at 0°C, *tert*-butyldimethylsilyl triflate (500 μL, 2.2 mmol). The mixture was stirred at 0°C for 80 min and a saturated solution of sodium bicarbonate was added. The mixture was extracted with methylene chloride, and the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography with hexane:ethyl acetate (9:1) as the eluent to afford pure **39** (1.09 g, 85%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 3050, 2980, 2960, 2930, 2860, 1720, 1610; ^{1}H nmr ($CDCl_3$, δ ppm): 0.02 and 0.10 (6H, 2s, -OSi$(CH_3)_2$C$(CH_3)_3$), 0.89 (9H, s, -OSi$(CH_3)_2$C$(CH_3)_3$), 1.30 (9H, s, -OC$(CH_3)_3$), 1.80 (3H, s, -CH_3), 1.82–2.12 (4H, m, -$SCH_2CH_2CH_2S$- and =C(CH_3)-CH_2-CH_2-), 2.28 (9H, s, -CH_3 aromatic), 2.47 (2H, m, =C(CH_3)-CH_2-), 2.76 (4H, m, -SCH_2-CH_2-CH_2-S-), 3.43 (3H, s, -OCH_3), 4.37 (2H, d, J = 4.3 Hz, -CH_2-OTBODPS), 4.84 (1H, d, J = 6.6 Hz, -OCHHO-), 4.88 (1H, d, J = 6.6 Hz, -OCHHO-), 4.88 (1H, d, J = 10 Hz, -CH(OTBDMS)-), 4.99 (2H, s, -CH_2-OMes), 5.55 (1H, dd, J = 10.4 and 10.5 Hz, -CH(OTBDMS)-CH=CH-), 5.88 (1H, dt, J = 4.4 and 14.9 Hz, -CH=CH-CH_2OTBODPS), 6.19 (1H, dd, J = 11.3 and 11.3 Hz, -CH(OTBDMS)-CH=CH-), 6.77 (1H, dd, J = 12.4 and 14.8 Hz, -CH=CH-CH_2OTBODPS), 6.83 (2H, s, CH aromatic), 7.35 and 7.67 (10H, m, Ph_2). Exact Mass calcd. for $C_{50}H_{72}O_7S_2Si_2$: 904.4258 (M^+); found: 904.4232 ± 0.0026.

*(2Z,8Z,10*E*)-12-*tert*-Butoxydiphenylsilyloxy-7-tert-butyldimethylsilyloxy-2-methoxymethyloxy-3-methyl-6,6-(propylenedithio)dodeca-2,8,10-trien-1-ol (**40**)*

To a solution of mesitoate **39** (2.16 g, 2.39 mmol) in ether (80 mL) was added, at 0°C, lithium aluminum hydride (136 mg, 3.6 mmol). The mixture was stirred at 0°C for 30 min and at room temperature for 90 min. A saturated solution of ammonium chloride and ice were added and the mixture was extracted with methylene chloride. The organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (9:1–3:2) as the eluent to afford pure alcohol **40** (1.478 g, 82%); ir (CH_2Cl_2, ν cm^{-1}): 3500, 3060, 2980, 2960, 2940, 2860; ^{1}H nmr ($CDCl_3$, δ ppm): 0.03 and 0.11 (6H, 2s, -OSi$(CH_3)_2$C$(CH_3)_3$), 0.90 (9H, s, -OSi$(CH_3)_2$C$(CH_3)_3$), 1.31 (9H, s, -OC$(CH_3)_3$), 1.73 (3H, s, -CH_3), 1.75–2.12 (4H, m, -$SCH_2CH_2CH_2S$- and =C(CH_3)-CH_2-CH_2-), 2.40 (2H, m, =C(CH_3)-CH_2-), 2.77 (4H, m, -SCH_2-CH_2-CH_2-S-), 3.02 (1H, t, J = 6.3 Hz, -OH), 3.48 (3H, s, -OCH_3), 4.14 (2H, d, J = 6.3 Hz, -CH_2-OH), 4.38 (2H, d, J = 4.3 Hz, -CH_2-OTBODPS), 4.80 (2H, s, -OCH_2O-), 4.88 (1H, d, J = 10 Hz, -CH(OTBDMS)-), 5.55 (1H, dd, J = 10.3 and 10.4 Hz, -CH(OTBDMS)-CH=CH-), 5.88 (1H, dt, J = 4.5 and 14.9 Hz, -CH=CH-CH_2OTBODPS), 6.20 (1H, dd, J = 11.3 and 11.3 Hz, -CH(OTBDMS)-CH=CH-), 6.77 (1H, dd, J = 12.3 and 14.2 Hz, -CH=CH-CH_2OTBODPS), 7.36 and 7.67 (10H, m, Ph_2). Exact Mass calcd. for $C_{40}H_{62}O_6S_2Si_2$: 758.3526 (M^+); found: 758.3508 ± 0.0022.

*(2Z,8Z,10*E*)-12-*tert*-Butoxydiphenylsilyloxy-7-tert-butyldimethylsilyloxy-1-chloro-2-methoxymethyloxy-3-methyl-6,6-(propylenedithio)dodeca-2,8,10-triene (**41**)*

To a cold (0°C) solution of alcohol **40** (1.47 g, 1.94 mmol), lithium chloride (742 mg, 17.5 mmol), and collidine (1.25 mL, 9.46 mmol) in dimethylformamide (10 mL) was added mesyl chloride (475 μL, 6.14 mmol). The mixture was stirred at 0°C for 15 min, then at room temperature for 1 h, and a saturated solution of ammonium chloride was then added together with a saturated solution of sodium bicarbonate. The mixture was extracted with hexane:ether (1:1) and the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (4:1) as the eluent to afford pure chloride **41** (1.357 g, 90%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2980, 2960, 2940, 2860, 1660; ^{1}H nmr ($CDCl_3$, δ ppm): 0.02 and 0.10 (6H, 2s, -OSi$(CH_3)_2$C$(CH_3)_3$), 0.89 (9H, s, -OSi$(CH_3)_2$C$(CH_3)_3$), 1.30 (9H, s, -OC$(CH_3)_3$), 1.74 (3H, s, -CH_3), 1.70–2.13 (4H, m, -$SCH_2CH_2CH_2S$- and =C(CH_3)-CH_2-CH_2-), 2.44 (2H, m, =C(CH_3)-CH_2), 2.77 (4H, m, -SCH_2-CH_2-CH_2-S-), 3.47 (3H, s, -OCH_3), 4.27 (2H, s, -CH_2Cl), 4.37 (2H, d, J = 4.4 Hz, -CH_2-OTBODPS), 4.88 (2H, s, -OCH_2O-), 4.87 (1H, d, J = 10 Hz, -CH(OTBDMS)-), 5.55 (1H, dd, J = 10.5 and 10.5 Hz, -CH(OTBDMS)-CH=CH-), 5.88 (1H, dt, J = 4.5 and 14.8 Hz, -CH=CH-CH_2OTBODPS), 6.20 (1H, dd, J = 11.3 and 11.3 Hz, -CH(OTBDMS)-CH=CH-), 6.77 (1H, dd, J = 12.5 and 14.5 Hz, -CH=CH-CH_2OTBODPS), 7.37 and 7.67 (10H, m, Ph_2); ms *m/e*: 740 (M^+ − HCl).

*(3Z,9Z,11*E*)-13-*tert*-Butoxydiphenylsilyloxy-8-tert-butyldimethylsilyloxy-1,1-bis-methoxycarbonyl-3-methoxymethyloxy-4-methyl-7,7-(propylenedithio)trideca-3,9,11-triene (**42**)*

Dimethyl malonate (200 μL, 1.75 mmol) was added at 0°C to a suspension of NaH (60% in oil) (64 mg, 1.6 mmol) in tetrahydro-

furan:dimethylformamide (1:1) (4 mL). The mixture was stirred at room temperature for 15 min and a solution of chloride **41** (201 mg, 0.259 mmol) in tetrahydrofuran:dimethylformamide (1:1) (2 mL) was added at 0°C together with a small quantity (5 mg) of potassium iodide. The mixture was stirred at room temperature for 3 h and a saturated solution of ammonium chloride was added to the solution. The mixture was extracted with hexane:ether (1:1), and the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (4:1) as the eluent to afford pure **42** (183 mg, 81%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2980, 2960, 2935, 1735; ^1H nmr ($CDCl_3$, δ ppm): 0.01 and 0.09 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.89 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.30 (9H, s, $-OC(CH_3)_3$), 1.64 (3H, s, $-CH_3$), 1.75–2.00 (4H, m, $-SCH_2CH_2CH_2S-$ and $=C(CH_3)-CH_2-CH_2-$), 2.36 (2H, m, $=C(CH_3)-CH_2-$), 2.76 (4H, m, $-SCH_2-CH_2-CH_2-S-$), 2.85 (2H, d, J = 7.6 Hz, $-CH_2-CH(CO_2CH_3)_2$), 3.44 (3H, s, $-OCH_3$), 3.71 (6H, s, $(CO_2CH_3)_2$), 3.71 (1H, t, J = 7.6 Hz, $CH(CO_2CH_3)_2$), 4.37 (2H, d, J = 4.2 Hz, $-CH_2$-OTBODPS), 4.74 (2H, s, $-OCH_2O-$), 4.86 (1H, d, J = 10 Hz, -CH(OTBDMS)-), 5.54 (1H, dd, J = 10.5 and 10.5 Hz, -CH(OTBDMS)-CH=CH-), 5.87 (1H, dt, J = 4.2 and 14.6 Hz, $-CH=CH-CH_2$OTBODPS), 6.19 (1H, dd, J = 11.4 and 11.4 Hz, -CH(OTBDMS)-CH=CH-), 6.76 (1H, dd, J = 12 and 14.9 Hz, $-CH=CH-CH_2$OTBODPS), 7.36 and 7.67 (10H, m, Ph_2). Exact Mass calcd. for $C_{45}H_{68}O_9S_2Si_2$: 872.3843 (M^+); found: 872.3827 ± 0.0026.

*(3Z,9Z,11E)-8-*tert*-Butyldimethylsilyloxy-1,1-bis-methoxycarbonyl-3-methoxymethyloxy-4-methyl-7,7-(propylenedithio)trideca-3,9,11-trien-13-ol (**43**)*

A solution of tetrabutylammonium fluoride (1.0 M in THF, 2.4 mL, 2.4 mmol) was added at 0°C to a solution of **42** (865 mg, 0.99 mmol) in methylene chloride (17 mL). The mixture was stirred at 0°C for 15 min and at room temperature for 3.5 h, then diluted with water. The mixture was extracted with ether and the organic layer was dried over sodium sulfate. Then the solution was filtered on a silica gel pad and the solvent was evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (3:2) as the eluent to afford pure alcohol **43** (539 mg, 88%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2990, 2960, 2860, 1735; ^1H nmr ($CDCl_3$, δ ppm): 0.01 and 0.10 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.89 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.64 (3H, s, $-CH_3$), 1.91 (4H, m, $-SCH_2CH_2CH_2S-$ and $=C(CH_3)-CH_2-CH_2-$), 2.38 (2H, m, $=C(CH_3)-CH_2-$), 2.84 (4H, m, $-SCH_2-CH_2-CH_2-S-$), 2.85 (2H, d, J = 7.9 Hz, $-CH_2-CH(CO_2CH_3)_2$), 3.47 (3H, s, $-OCH_3$), 3.71 and 3.72 (6H, 2s, $(CO_2CH_3)_2$), 3.71 (1H, t, J = 7.6 Hz, $-CH(CO_2CH_3)_2$), 4.24 (2H, s large, $-CH_2-OH$), 4.77 (2H, s, $-OCH_2O-$), 4.79 (1H, d, J = 10 Hz, -CH(OTBDMS)-), 5.60 (1H, dd, J = 10.5 and 10.5 Hz, -CH(OTBDMS)-CH=CH-), 5.92 (1H, dt, J = 5 and 15 Hz, $-CH=CH-CH_2OH$), 6.17 (1H, dd, J = 11.2 and 11.2 Hz, -CH(OTBDMS)-CH=CH-), 6.59 (1H, dd, J = 12 and 15 Hz, $-CH=CH-CH_2OH$). Exact Mass calcd. for $C_{29}H_{50}O_8S_2Si$: 618.2716 (M^+); found: 618.2710 ± 0.0018.

*(3Z,9Z,11E)-8-*tert*-Butyldimethylsilyloxy-13-chloro-1,1-bis-methoxycarbonyl-3-methoxymethyloxy-4-methyl-7,7-(propylenedithio)trideca-3,9,11-triene (**44**)*

Mesyl chloride (230 μL, 2.97 mmol) was added to a cold (0°C) solution of alcohol **43** (540 mg, 0.874 mmol), lithium chloride (634 mg, 14.9 mmol), and collidine (660 μL, 5.0 mmol) in dimethylformamide (6 mL). The mixture was stirred at 0°C for 15 min and at room temperature for 4 h and then a saturated solution of ammonium chloride was added. The mixture was extracted with hexane:ether (1:1), and the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (7:3) as the eluent to afford pure chloride **44** (484 mg, 87%); ^1H nmr ($CDCl_3$, δ ppm): 0.00 and 0.10 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.88 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.64 (3H, s, $-CH_3$), 1.95 (4H, m, $-SCH_2CH_2CH_2S-$ and $=C(CH_3)-CH_2-CH_2-$), 2.35 (2H, m, $=C(CH_3)-CH_2-$), 2.81 (6H, m, $-SCH_2-CH_2-CH_2-S-$ and $-CH_2-CH(CO_2CH_3)_2$), 3.47 (3H, s, $-OCH_3$), 3.72 (6H, s, $(CO_2CH_3)_2$), 3.73 (1H, t, J = 7 Hz, $-CH(CO_2CH_3)_2$), 4.15 (2H, d, J = 7 Hz, $-CH_2-Cl$), 4.77 (2H, s, $-OCH_2O-$), 4.76 (1H, d, J = 10 Hz, -CH(OTBDMS)-), 5.65 (1H, dd, J = 10.3 and 10.3 Hz, -CH(OTBDMS)-CH=CH-), 5.88 (1H, dt, J = 7.5 and 15 Hz, $-CH=CH-CH_2Cl$), 6.16 (1H, dd, J = 11.2 and 11.2 Hz, -CH(OTBDMS)-CH=CH-), 6.63 (1H, dd, J = 11.3 and 14.8 Hz, $-CH=CH-CH_2Cl$).

*(3Z,9Z,11E)-8-*tert*-Butyldimethylsilyloxy-1,1-bis-methoxycarbonyl-3-methoxymethyloxy-4-methyl-7,7-(propylenedithio)cyclotrideca-3,9,11-triene (**45**)*

To a warm (78°C) solution of cesium carbonate (1.025 g, 3.14 mmol) and 18-crown-6 (870 mg, 3.29 mmol) in acetonitrile (350 mL) was added dropwise a solution of chloride **44** (390 mg, 0.613 mmol) in acetonitrile (26 mL). The addition was done at a rate of 12 mL in 2 h, 6.5 mL in 2.5 h, and 7.5 mL in 3.5 h. The mixture was heated at 78°C for an additional 8 h, then cooled, filtered, and the solvents were evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (9:1–4:1) as the eluent to afford pure macrocycle **45** (276 mg, 75%); ir (CH_2Cl_2, ν cm^{-1}): 3060, 2990, 2960, 2930, 1735; ^1H nmr ($CDCl_3$, δ ppm): 0.08 and 0.15 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.94 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.36 (1H, dd, J = 9.6 and 13.5 Hz, $=C(CH_3)-CH_2-CHH-$), 1.58 (3H, s, $-CH_3$), 1.80–2.21 (4H, m, $-SCH_2CH_2CH_2S-$ and $=C(CH_3)-CHH-CHH-$), 2.49 (1H, d, J = 15 Hz, =C(OMOM)-CHH-), 2.59–2.83 (4H, m, -SCHH-CH_2-CHH-S-, $=C(CH_3)-CHH-$ and $-CH=CH-CHH-$), 3.19–3.35 (4H, m, -SCHH-CH_2-CHH-S-, =C(OMOM)-CHH- and $-CH=CH-CHH-$), 3.52 (3H, s, $-OCH_3$), 3.72 and 3.73 (6H, 2s, $(CO_2CH_3)_2$), 4.67 (1H, d, J = 6.2 Hz, -OCHHO-), 4.82 (1H, d, J = 6.2 Hz, -OCHHO-), 4.94 (1H, d, J = 9.3 Hz, -CH(OTBDMS)-), 5.45 (1H, ddd, J = 5, 11, and 15 Hz, $-CH=CH-CH_2-$), 5.59 (1H, dd, J = 10.5 and 10.5 Hz, -CH(OTBDMS)-CH=CH-), 6.00 (1H, dd, J = 11 and 11 Hz, -CH(OTBDMS)-CH=CH-), 6.55 (1H, dd, J = 10.8 and 15 Hz, $-CH=CH-CH_2-$); ^1H nmr (C_6D_6, δ ppm): 0.21 and 0.29 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 1.07 (9H, s, $-OSi(CH:i3)_2C(CH_3)_3$), 1.60 (3H, s, $-CH_3$), 1.67 (3H, m, $-SCH_2CH_2CH_2S-$ and $=C(CH_3)-CH_2-CHH-$), 2.05 (1H, m, $=C(CH_3)-CH_2-CHH-$), 2.40 (3H, m, -SCHH-CH_2-CHH-S- and $=C(CH_3)-CHH-$), 2.74 (1H, d, J = 15.3 Hz, =C(OMOM)-CHH-), 2.94–3.18 (4H, m, -SCHH-CH_2-CHH-S-, $=C(CH_3)-CHH-$, and $-CH=CH-CHH-$), 3.27 and 3.30 (6H, 2s, $(CO_2CH_3)_2$), 3.38 (3H, s, $-OCH_3$), 3.53 (1H, d, J = 15.3 Hz, =C(OMOM)-CHH-), 3.59 (1H, dd, J = 11.2 and 13.6 Hz, $-CH=CH-CHH-$), 4.59 (1H, d, J = 6.1 Hz, -OCHHO-), 4.72 (1H, d, J = 6.1 Hz, -OCHHO-), 5.23 (1H, d, J = 8.4 Hz, -CH(OTBDMS)-), 5.60 (1H, ddd, J = 5, 11, and 15 Hz, $-CH=CH-CH_2-$), 5.94 (2H, dd, J = 11 Hz, -CH(OTBDMS)-CH=CH-), 6.89 (1H, dd, J = 10 and 14.9 Hz, $-CH=CH-CH_2-$); ^{13}C nmr ($CDCl_3$, δ ppm): −4.4 ($-Si(CH_3)_2-$), 15.5 ($C=C-CH_3$), 18.4 ($-C(CH_3)_3$), 24.1, 25.1, 27.1, 27.6, 32.8, 34.4, 35.3 ($7 \times CH_2$), 26.1 ($-C(CH_3)_3$), 52.5, 52.7 ($-CO_2CH_3$), 55.4, 57.1 ($-C(S_2)-$ and $-C(CO_2CH_3)_2-$), 57.0 ($-OCH_3$), 76.7 (-CH(OTBDMS)-), 97.7 ($-OCH_2O-$), 124.9 ($-C=C-CH_3$), 129.6, 130.0, 130.1, 131.1 ($-CH=CH-CH=CH-$), 142.6 (=C-OMOM). Exact Mass calcd. for $C_{29}H_{48}O_7S_2Si$: 600.2611 (M^+); found: 600.2599 ± 0.0017.

*rel(1S,2R,6S,9S,10R)-10-*tert*-Butyldimethylsilyloxy-4,4-bis-methoxycarbonyl-2-methoxymethyloxy-1-methyl-11,11-(propylenedithio)tricyclo[7.4.0.$0^{2,6}$]tridec-7-ene (**46**)*

Macrocycle **45** (48 mg) was dissolved in toluene (1.2 mL) and heated, in a sealed quartz tube at 240°C for 1.5 h. The solvent was evaporated and the residue was purified by flash chromatography using hexane:ethyl acetate (4:1) as the eluent to afford pure tricycle **46** (33 mg, 69%) and bicycle **47** (7 mg, 15%).

The same reaction was done with macrocycle **45** (45 mg) in toluene (0.9 mL) at 220°C for 7 h to give tricycle **46** (34 mg, 76%) and bicycle **47** (7 mg, 16%).

*Tricyclic compound **46**:* ir (CH_2Cl_2, ν cm^{-1}): 3050, 2980, 2960, 2930, 1735; ^1H nmr ($CDCl_3$, δ ppm): 0.13 and 0.19 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.94 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.25 (3H,

s, $-CH_3$), 1.45–3.0 (16H, m, $-S(CH_2)_3S-$, $-C(CH_3)-CH_2-CH_2-$, $-CH_2-C(CO_2CH_3)_2-CH_2-$, and -CH-CH=CH-CH-), 3.33 (3H, s, $-OCH_3$), 3.67 and 3.70 (6H, 2s, $(CO_2CH_3)_2$), 3.99 (1H, d, J = 1.8 Hz, -CH(OTBDMS)-), 4.70 (1H, d, J = 7.4 Hz, -OCHHO-), 4.76 (1H, d, J = 7.4 Hz, -OCHHO-), 5.18 (1H, d, J = 10 Hz, -CH=CH-), 5.41 (1H, d, J = 10 Hz, -CH=CH-). Exact Mass calcd. for $C_{29}H_{48}O_7S_2Si$: 600.2611 (M^+); found: 600.2605 ± 0.0017.

Bicyclic compound ***47***: ir (CH_2Cl_2, ν cm^{-1}): 3060, 2990, 2960, 2930, 2860, 1735; ^1H nmr ($CDCl_3$, δ ppm): 0.01 and 0.11 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.90 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.45 (3H, s, $-CH_3$), 1.61 (1H, d, J = 15 Hz, -CH(OTBDMS)-CH=CH-CHH-), 1.84–2.07, 2.48–3.09, and 3.26 (11H, m, $-S(CH_2)_3S-$ and $-CH_2-C(CO_2CH_3)_2-CH_2-CH-$), 2.30 (1H, dd, J = 10.5 and 15.5 Hz, $-C(CH_3)$=CH-CHH-), 2.55 (1H, dd, J = 12.5 and 15 Hz, -CH(OTBDMS)-CH=CH-CHH-), 2.86 (1H, d, J = 15 Hz, $-C(CH_3)$=CH-CHH-), 3.34 (3H, s, $-OCH_3$), 3.72 and 3.74 (6H, 2s, $(CO_2CH_3)_2$), 4.63 (1H, d, J = 7 Hz, -OCHHO-), 4.66 (1H, d, J = 7 Hz, -OCHHO-), 4.68 (1H, d, J = 10 Hz, -CH(OTBDMS)-), 5.23 (1H, ddd, J = 5, 12.5, and 12.5 Hz, -CH(OTBDMS)-CH=CH-CH_2-), 5.45 (1H, dd, J = 10 and 12 Hz, -CH(OTBDMS)-CH=CH-), 5.60 (1H, d, J = 10 Hz, $-C(CH_3)$=CH-CH_2-). Exact Mass calcd. for $C_{29}H_{48}O_7S_2Si$: 600.2611 (M^+); found: 600.2605 ± 0.0017.

*rel(1S,2R,6S,9S,10R)-10-*tert*-Butyldimethylsilyloxy-4,4-bis-methoxycarbonyl-2-methoxymethyloxy-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-en-11-one (**54**)*

Mercuric chloride (103 mg, 0.38 mmol) was added to a mixture of **46** (57 mg, 0.095 mmol) and calcium carbonate (43 mg, 0.43 mmol) in acetonitrile:water (4:1) (8 mL). The mixture was stirred at room temperature for 21 h and water was added. The mixture was extracted with hexane:ether (1:1); the organic layer was washed with water, dried over sodium sulfate, and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (4:1) as the eluent to afford pure ketone **54** (34 mg, 70%); ^1H nmr ($CDCl_3$, δ ppm): 0.02 and 0.07 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.88 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.40 (3H, s, $-CH_3$), 1.68–2.13 (3H, m, $-CH_2-CH_2CO-$ and -CH-CH=), 2.20 (1H, d, J = 13.6 Hz, -C(OMOM)-CHH- or $-C(CO_2CH_3)_2-CHH-$), 2.55 (1H, d, J = 15.8 Hz, -C(OMOM)-CHH-or $-C(CO_2CH_3)_2-CHH-$), 2.58 (1H, s, -CH-CH=), 2.75 (1H, d, J = 15.6 Hz, -C(OMOM)-CHH- or $-C(CO_2CH_3)_2-CHH-$), 2.83 (1H, d, J = 13.3 Hz, -C(OMOM)-CHH- or $-C(CO_2CH_3)_2-CHH-$), 2.80 (2H, m, $-CH_2-CH_2-CO-$), 3.32 (3H, s, $-OCH_3$), 3.68 and 3.70 (6H, 2s, $(CO_2CH_3)_2$), 3.80 (1H, m, -CH(OTBDMS)-), 4.66 (1H, d, J = 7.6 Hz, -OCHHO-), 4.78 (1H, d, J = 7.6 Hz, -OCHHO-), 5.25 and 5.36 (2H, m, -CH=CH-).

*rel(1S,2R,6S,9S,10R,11R) and rel(1S,2R,6S,9S,10R,11S)-10-*tert*-Butyldimethylsilyloxy-4,4-bis-methoxycarbonyl-2-methoxymethyloxy-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-en-11-ol (**56** and **55** respectively)*

To a cold (0°C) solution of ketone **54** (34 mg, 67 μmol) in methanol (10 mL) was added sodium borohydride (70 mg). The mixture was stirred at room temperature for 1 h and a saturated solution of ammonium chloride was added. The mixture was extracted with methylene chloride, and the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (3:1) as the eluent to afford pure alcohols **55** (16 mg, 47%) and **56** (16 mg, 47%).

Compound ***55*** (less polar): ^1H nmr ($CDCl_3$, δ ppm): 0.13 and 0.15 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.94 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.22 (3H, s, $-CH_3$). 1.46–1.80 (4H, m, $-CH_2-CH_2-$CH(OH)-), 2.22 (1H, d, J = 13.5 Hz, $-C(CO_2CH_3)_2-CHH-$), 2.41 (1H, s, -CH-CH=), 2.49 (1H, d, J = 15.6 Hz, -C(OMOM)-CHH-), 2.70 (1H, d, J = 15.6 Hz, -C(OMOM)-CHH-), 2.77 (1H, m, -CH-CH=), 2.89 (1H, dd, J = 7.5 and 13.5 Hz, $-C(CO_2CH_3)_2-$CHH-), 3.33 (3H, s, $-OCH_3$), 3.68 and 3.71 (6H, 2s, $(CO_2CH_3)_2$), 3.66 (1H, m, -CH(OH)-), 3.90 (1H, dd, J = 3 and 3 Hz, -CH(OTBDMS)-), 4.68 (1H, d, J = 7.5 Hz, -OCHHO-), 4.76 (1H, d, J = 7.5 Hz, -OCHHO-), 5.20 (1H, d, J = 10 Hz, -CH=CH-), 5.33 (1H, d, J = 10 Hz, -CH=CH-).

Compound ***56*** (more polar): ^1H nmr ($CDCl_3$, δ ppm): 0.07 and 0.08 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.89 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.23 (3H, s, $-CH_3$), 1.45–1.70 (3H, m, $-CH_2-$CHH-CH(OH)-), 2.02 (1H, m, $-CH_2-$CHH-CH(OH)-), 2.22 (1H, d, J = 13 Hz, $-C(CO_2CH_3)_2-CHH-$), 2.25 (1H, s, -CH-CH=), 2.51 (1H, d, J = 15.5 Hz, -C(OMOM)-CHH-), 2.66 (1H, d, J = 15.5 Hz, -C(OMOM)-CHH-), 2.89 (1H, d, J = 13 Hz, $-C(CO_2CH_3)_2-CHH-$), 2.90 (1H, m, -CH-CH=), 3.34 (3H, s, $-OCH_3$), 3.69 and 3.71 (7H, 2s, $(CO_2CH_3)_2$ and -CH(OH)-), 3.89 (1H, dd, J = 2.3 and 2.3 Hz, -CH(OTBDMS)-), 4.70 (1H, d, J = 7.4 Hz, -OCHHO-), 4.77 (1H, d, J = 7.5 Hz, -OCHHO-), 5.34 (1H, d, J = 10 Hz, -CH=CH-), 5.45 (1H, d, J = 10 Hz, -CH=CH-).

*rel(1S,2R,6S,9S,10R,11S)-11-Benzoyloxy-10-*tert*-butyldimethylsilyloxy-4,4-bis-methoxycarbonyl-2-methoxymethyloxy-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-ene (**57**)*

Procedure A

To a solution of alcohol **55** (16 mg, 31.3 μmol) and triethylamine (150 μL, 1.08 mmol) in methylene chloride (5 mL) were added at 0°C benzoyl chloride (40 μL, 0.34 mmol) and a few milligrams of DMAP. The mixture was stirred at room temperature for 24 h and a saturated solution of sodium bicarbonate was added. The mixture was extracted with methylene chloride, and the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (4:1) as the eluent to afford pure **57** (17 mg, 89%); ^1H nmr ($CDCl_3$, δ ppm): −0.07 and 0.04 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.91 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.32 (3H, s, $-CH_3$), 1.56–1.75 (3H, m, $-CH_2-$CHH-CH(OBz)-), 2.15 (1H, ddd, J = 3, 12, and 12 Hz, $-CH_2-CHH_{ax}-$CH(OBz)-), 2.25 (1H, d, J = 13.4 Hz, $-C(CO_2CH_3)_2-$CHH-), 2.43 (1H, s, -CH-CH=), 2.50 (1H, d, J = 15.5 Hz, -C(OMOM)-CHH-), 2.72 (1H, d, J = 15.5 Hz, -C(OMOM)-CHH-), 2.82 (1H, m, -CH-CH=), 2.91 (1H, dd, J = 7.5 and 13.5 Hz, $-C(CO_2CH_3)_2-CHH-$), 3.35 (3H, s, $-OCH_3$), 3.69 and 3.72 (6H, 2s, $(CO_2CH_3)_2$), 4.19 (1H, dd, J = 2.5 Hz and 2.5 Hz, -CH(OTBDMS)-), 4.71 (1H, d, J = 7.4 Hz, -OCHHO-), 4.79 (1H, d, J = 7.4 Hz, -OCHHO-), 4.90 (1H, ddd, J = 3, 5, and 12.5 Hz, $-CH_{ax}$(OBz)-), 5.38 (2H, s, -CH=CH-), 7.42 (2H, m, *meta*-H of OBz), 7.55 (1H, m, *para*-H of OBz), 8.04 (2H, m, *ortho*-H of OBz).

*rel(1S,2R,6S,9S,10R,11R)-11-Benzoyloxy-10-*tert*-butyldimethylsilyloxy-4,4-bis-methoxycarbonyl-2-methoxymethyloxy-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-ene (**58**)*

Using procedure A described above, compound **56** (16 mg, 31.3 μmol) afforded, after flash chromatography, compound **58** (16.5 mg, 86%); ir (CH_2Cl_2, ν cm^{-1}): 3050, 2980, 1730; ^1H nmr ($CDCl_3$, δ ppm): 0.12 and 0.16 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.92 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.29 (3H, s, $-CH_3$), 1.48–1.92 (3H, m, $-CH_2-$CHH-CH(OBz)-), 2.12 (1H, m, $-CH_2-CHH_{eq}-$CH(OBz)-), 2.28 (1H, d, J = 13.3 Hz, $-C(CO_2CH_3)_2-CHH-$), 2.31 (1H, m, -CH-CH=), 2.53 (1H, d, J = 15.6 Hz, -C(OMOM)-CHH-), 2.72 (1H, d, J = 15.6 Hz, -C(OMOM)-CHH-), 2.92 (1H, d, J = 13 Hz, $-C(CO_2CH_3)_2-CHH-$), 2.93 (1H, m, -CH-CH=), 3.36 (3H, s, $-OCH_3$), 3.66 and 3.72 (6H, 2s, $(CO_2CH_3)_2$), 4.00 (1H, s, -CH(OTBDMS)-), 4.74 (1H, d, J = 7.4 Hz, -OCHHO-), 4.80 (1H, d, J = 7.5 Hz, -OCHHO-), 4.99 (1H, d, J = 2.6 Hz, $-CH_{eq}$(OBz)-), 5.20 (1H, d, J = 10 Hz, -CH=CH-), 5.28 (1H, d, J = 10 Hz, -CH=CH-), 7.42 (2H, dd, J = 7.5 and 7.5 Hz, *meta*-H of OBz), 7.55 (1H, m, *para*-H of OBz), 7.99 (2H, m, *ortho*-H of OBz). Exact Mass calcd. for $C_{33}H_{48}O_9Si$: 585.2883 (M^+ − OMe); found: 585.2876 ± 0.0017.

*rel(1S,2R,6S,9S,10R,11S)-11-Benzoyloxy-10-*tert*-butyldimethylsilyloxy-4,4-bis-methoxycarbonyl-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-en-2-ol (**59**)*

Procedure B

To a solution of **57** (17 mg, 0.028 mmol) in tetrahydrofuran:water (4:1) (5.5 mL) was added a solution of 6 M hydro.chloric acid (15 drops). The mixture was stirred at room temperature for 15 h and a saturated solution of sodium bicarbon-

ate was added. The mixture was extracted with methylene chloride; the organic layer was dried over sodium sulfate and evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (7:3) as the eluent to afford pure alcohol **59** (16 mg, quantitative); ^{1}H nmr ($CDCl_3$, δ ppm): -0.08 and 0.03 (6H, 2s, $-OSi(CH_3)_2$-$C(CH_3)_3$), 0.91 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.32 (3H, s, $-CH_3$), 1.55–1.80 (3H, m, $-CH_2$-CHH-CH(OBz)-), 2.1–2.35 (2H, m, $-CH_2$-CHH-CH(OBz)- and -CH-CH=), 2.13 (1H, s, -C(OH)-CHH-), 2.31 (1H, s, -C(OH)-CHH-), 2.39 (1H, d, J = 14.3 Hz, $-C(CO_2CH_3)_2$-CHH-), 2.64 (1H, m, -CH-CH=), 2.76 (1H, dd, J = 7.5 and 14.3 Hz, $-C(CO_2CH_3)_2$-CHH-), 3.72 and 3.76 (6H, 2s, $(CO_2CH_3)_2$), 4.19 (1H, dd, J = 2 and 2 Hz, -CH(OTBDMS)-), 4.91 (1H, ddd, J = 3, 3, and 12 Hz, -CH(OBz)-), 5.41 (1H, d, J = 10 Hz, -CH=CH-), 5.49 (1H, d, J = 10 Hz, -CH=CH-), 7.42 (2H, m, *meta*-H of OBz), 7.55 (1H, m, *para*-H of OBz), 8.04 (2H, m, *ortho*-H of OBz).

*rel(1S,2R,6S,9S,10R,11R)-11-Benzoyloxy-10-tert-butyldimethylsilyloxy-4,4-bis-methoxycarbonyl-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-en-2-ol (**60**)*

Using procedure B, compound **58** (16 mg, 0.026 mmol) afforded, after flash chromatography, compound **60** (14.5 mg, 98%); ir (CH_2Cl_2, ν cm^{-1}): 3600, 3050, 2960, 2930, 2860, 1720; ^{1}H nmr ($CDCl_3$, δ ppm): 0.11 and 0.17 (6H, 2s, $-OSi(CH_3)_2C(CH_3)_3$), 0.93 (9H, s, $-OSi(CH_3)_2C(CH_3)_3$), 1.30 (3H, s, $-CH_3$), 1.53–1.90 (3H, m, $-CH_2$-CHH-CH(OBz)-), 2.07–2.17 (1H, m, $-CH_2$-CHH-CH(OBz)-), 2.15 (1H, s, -C(OH)-CHH-), 2.23 (1H, s, -CH-CH=), 2.34 (1H, s, -C(OH)-CHH-), 2.38–2.47 (1H, m, $-C(CO_2CH_3)_2$-CHH-), 2.74 (1H, s, -CH-CH=), 2.75 (1H, m, $-C(CO_2CH_3)_2$-CHH-), 3.71 and 3.76 (6H, 2s, $(CO_2CH_3)_2$), 4.00 (1H, m, -CH(OTBDMS)-), 5.01 (1H, d, J = 3 Hz, -CH(OBz)-), 5.25 (1H, dm, J = 10 Hz, -CH=CH-), 5.37 (1H, dm, J = 10 Hz, -CH=CH-), 7.42 (2H, m, *meta*-H of OBz), 7.55 (1H, m, *para*-H of OBz), 8.00 (2H, m, *ortho*-H of OBz). Exact Mass calcd. for $C_{31}H_{44}O_8Si$: 555.2778 (M^+ − OH); found: 555.2760 ± 0.0016.

*rel(1S,2R,4R,6S,9S,10R,11S)-11-Benzoyloxy-4-methoxycarbonyl-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-en-10-ol-4,2-carbolactone (**61**)*

Procedure C

To a solution of **59** (16 mg, 0.028 mmol) in tetrahydrofuran (10 mL) was added a solution of tetrabutylammonium fluoride (56 μL, 0.056 mmol). The mixture was stirred at room temperature for 90 min and the solvent was evaporated. The residue was purified by flash chromatography using hexane:ethyl acetate (3:2) as the eluent to afford pure **61** (2.5 mg, 19%) and **62** (6 mg, 61%).

*Compound **61*** (less polar): ir (CH_2Cl_2, ν cm^{-1}): 3600, 3050, 2980, 1780, 1735, 1715; ^{1}H nmr ($CDCl_3$, δ ppm): 1.42 (3H, s, $-CH_3$), 150–2.22 and 2.35–2.55 (9H, m, 4 × $-CH_2$- and -CH-CH=), 2.80 (1H, m, -CH-CH=), 3.82 (3H, s, CO_2CH_3), 4.23 (1H, dd, J = 2 and 2 Hz, -CH(OH)-), 5.02 (1H, ddd, J = 2.5, 3.5, and 12 Hz, -CH(OBz)-), 5.42 (1H, ddd, J = 2, 2, and 10 Hz, -CH=CH-), 5.73 (1H, ddd, J = 2.5, 2.5 ,and 10 Hz, -CH=CH-), 7.47 (2H, m, *meta*-H of OBz), 7.60 (1H, m, *para*-H of OBz), 8.04 (2H, m, *ortho*-H of OBz). Exact Mass calcd. for $C_{24}H_{26}O_7$: 426.1678 (M^+); found: 426.1675 ± 0.0013.

*Compound **62*** (more polar): ir (CH_2Cl_2, ν cm^{-1}): 3600, 3050, 2980, 1785, 1735; ^{1}H nmr (CD_2Cl_2, δ ppm): 1.32 (3H, s, $-CH_3$), 1.53–2.00 and 2.28–2.46 (9H, m, 4 × $-CH_2$- and -CH-CH=), 2.73 (1H, m, -CH-CH=), 3.60 (1H, ddd, J = 2.5, 3.5, and 12 Hz, -CH(OH)-CH_2-), 3.77 (3H, s, CO_2CH_3), 3.95 (1H, dd, J = 2.8 and 2.8 Hz, $-CH_2$-CH(OH)-CH(OH)-), 5.33 (1H, ddd, J = 2.2, 2.2, and 10.1 Hz, -CH=CH-), 5.64 (1H, ddd, J = 2.7, 2.7, and 10.2 Hz, -CH=CH-). Exact Mass calcd. for $C_{17}H_{22}O_6$: 322.1416 (M^+); found: 322.1413 ± 0.0009.

*rel(1S,2R,4R,6S,9S,10R,11R)-11-Benzoyloxy-4-methoxycarbonyl-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-en-10-ol-4,2-carbolactone (**63**)*

Using procedure C, compound **60** (7.5 mg, 0.013 mmol) afforded, after flash chromatography, compound **63** (4.5 mg, 81%); ir (CH_2Cl_2, ν cm^{-1}): 3600, 3050, 2980, 1785, 1735, 1710: ^{1}H nmr ($CDCl_3$, δ ppm): 1.42 (3H, s, $-CH_3$), 1.54–2.62 (9H, m, 4 × $-CH_2$- and -CH-CH=), 2.94 (1H, m, -CH-CH=), 3.82 (3H, s, CO_2CH_3), 4.17 (1H, s, -CH(OH)-), 5.17 (1H, d, J = 2.8 Hz, -CH(OBz)-), 5.33 (1H, ddd, J = 2.2, 2.2, and 10.1 Hz, -CH=CH-), 5.60 (1H, ddd, J = 2.7, 2.7, and 10.1 Hz, -CH=CH-), 7.44 (2H, m, *meta*-H of OBz), 7.58 (1H, m, *para*-H of OBz), 7.99 (2H, m, *ortho*-H of OBz). Exact Mass calcd. for $C_{24}H_{26}O_7$: 426.1678 (M^+); found: 426.1688 ± 0.0013.

*rel(1S,2R,4R,6S,9S,11S)-11-Benzoyloxy-4-methoxycarbonyl-1-methyltricyclo[7.4.0.0^{2,6}]tridec-7-en-10-one-4,2-carbolactone (**64**)*

To a solution of **61** (1 mg, 2.2 μmol) in methylene chloride (1 mL) was added pyridinium chlorochromate (5 mg, 23.2 μmol). The mixture was stirred at room temperature for 3 h and was filtered on Florisil using ethyl acetate as a solvent. The solvent was evaporated and the residue was purified by flash chromatography using hexane:ethyl acetate (3:2) as the eluent to afford pure ketone **64** as the only product; ir (CH_2Cl_2, ν cm^{-1}): 3030, 2960, 2930, 2860, 1790, 1740; ^{1}H nmr ($CDCl_3$, δ ppm): 1.30 (3H, s, $-CH_3$), 1.50–2.55 (8H, m, 4 × $-CH_2$-), 3.00 (2H, m, -CH-CH=CH-CH-), 3.83 (3H, s, CO_2CH_3), 5.52 (1H, dd, J = 7.5 and 7.5 Hz, -CH(OBz)-), 5.58 (1H, dm, J = 10 Hz, -CH=CH-), 5.92 (1H, ddd, J = 2.5, 2.5, and 10 Hz, -CH=CH-), 7.5 (3H, m, *meta*-H and *para*-H of OBz), 8.09 (2H, m, *ortho*-H of OBz). Exact Mass calcd. for $C_{24}H_{24}O_7$: 424.1514 (M^+); found: 424.1514 ± 0.0012.

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