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Transannular Diels–Alder Studies of 14-Membered *cis–trans–trans* Macrocyclic Trienes Having Allylic Ether or Enone Dienophile

Rico Lavoie, Stéphane G. Ouellet, Carol Dallaire, Yves L. Dory, András Toró and Pierre Deslongchamps*

Laboratoire de synthèse organique, Département de chimie, Institut de pharmacologie de Sherbrooke, Université de Sherbrooke, Sherbrooke, Quebec, Canada J1K 2R1

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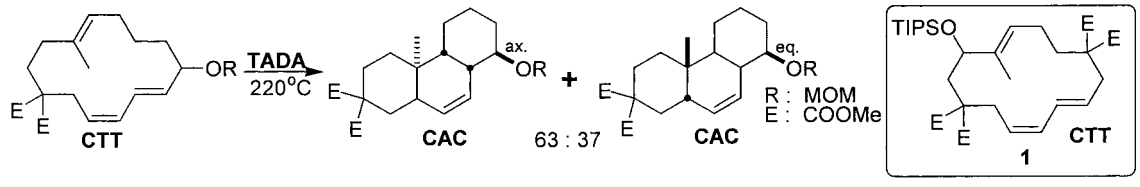
Abstract—Highly convergent, malonate alkylation based syntheses of the model macrocycles and their title investigations are reported. In the allylic ether dienophile case, a preference for tricycles with equatorial ether position was found at the transition state level. Ab initio calculations also show that the origin of this preference is not only steric but stereoelectronic as well. The enone dienophile case indicates that when the enone system is not totally twisted out of planarity by the macrocyclic environment, the Diels–Alder reaction follows the usual trend in terms of dienophile activation. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

Besides the fact that the transannular Diels–Alder (TADA) reaction is a powerful tool for the construction of polycyclic frameworks,[1] it can also contribute to our fundamental understanding of the Diels–Alder reaction itself. In this context, the TADA reaction of a *cis–trans–trans* (CTT) macrocyclic ether (Scheme 1) resulted in an unexpected distribution of tricycles where the major product had arisen from a sterically disfavored transition state (TS).[2] That time, we proposed that this outcome was induced via the allylic ether affecting the competing sterically favored TS with a rather strong negative stereoelectronic effect: the C–OMOM bond is antiperiplanar to the C–C bond to be formed, and its empty σ^* antibonding orbital is able to accept the electrons which would normally flow into the new C–C bond.

Investigation of a similar arrangement on the dienophile side can broaden our view on this phenomenon. Thus, we became interested in studying this effect on macrocycle **1**, too.

Moreover, allylic ether **1** might also allow us to prepare trienone **2** to investigate the TADA reaction from another aspect. Recently, we have experienced unusual thermic TADA reactions with certain TCC macrocycles: In an attempt to activate their dienophile by conjugating it to a ketone, the expected activation was not observed (Scheme 2).[3,4] We postulated that this effect was a result of the higher activation barrier required to twist the conjugated system out of planarity in order to reach the optimal *chair–boat–chair* macrocyclic conformation required for the TADA reaction. According to conformational considerations, the targeted macrocyclic trienone **2** could be optimal for the



Scheme 1.

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* Corresponding author. Tel.: +1-819-564-5300; fax: +1-819-820-6823; e-mail: pierre.deslongchamps@courrier.usherb.ca

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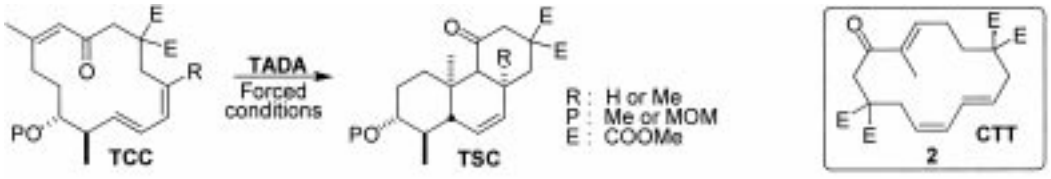


Scheme 2.

further investigations. Characteristically, under thermal conditions, these types of CTT macrocyclotrienic systems are known to generate *cis–anti–cis* (CAC) tricycles selectively to simplify the evaluation of the model studies.

Now, we report on the assembly of the required macrocyclic ether **1** and ketone **2** (Schemes 1 and 2) and their TADA studies from these different aspects.

Results and Discussion

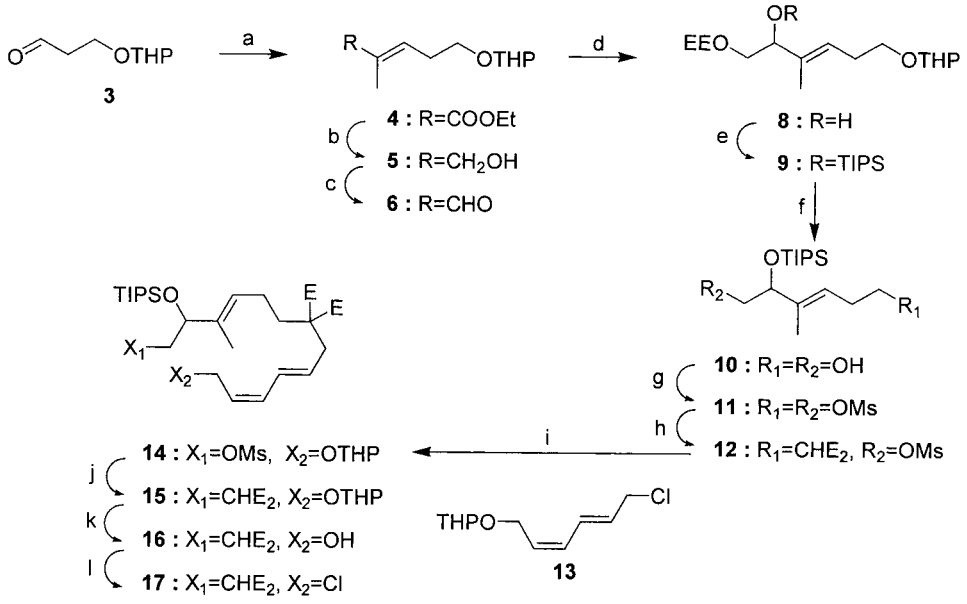
Synthesis and TADA studies of macrocycle 1

Synthesis of this macrocycle follows the highly convergent general strategy developed in our laboratory.[1] Accordingly, prefabricated, appropriately activated and protected diene and dienophile parts are assembled with two connectors into macrocycles. Thus, the synthetic plan is simplified to find the perfect accord between these parameters, particularly, coupling activation, convenient connectors and the correct order of the coupling steps.

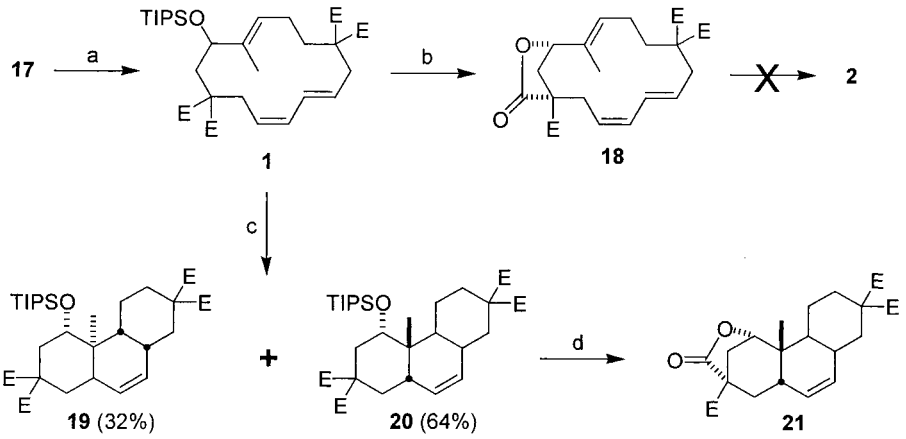
Construction of the trisubstituted *E*-dienophile began with the known aldehyde **3**, which was easily obtained from commercial 1,3-propanediol in two steps[5] (Scheme 3). Wittig–Horner–Emmons olefination of **3** with sodium triethyl phosphonopropionate[6] afforded ester **4** in 73% yield with an *E*/*Z* ratio of 4.7:1. The isomers were then easily separated by chromatography. A two-step routine sequence involving ester reduction of the major isomer of **4** to alcohol **5**, followed by Swern oxidation[7] led to α,β-unsaturated aldehyde **6** with 94% overall yield. Homologation of aldehyde **5** with the lithium salt of stannane **7**[8] afforded allylic alcohol **8** in 83% yield. Protection to silyl-ether **9** and a simultaneous hydrolytic deprotection of tetrahydro-pyranyl (THP) and ethoxyethyl (EE) ethers gave diol **10** with an overall yield of 82%.

At this stage, the choice of the connector was crucial for the success of the synthesis. Dimethyl malonate was considered suitable because it is symmetric, known to be thermally stable and its acidity allows for mild reaction conditions. Hence both alcohols in **10** were activated to the corresponding mesylate **11**. Interestingly, construction of the dienophile was concluded with the selective condensation on the less hindered side of dimesylate **11** with sodium dimethyl malonate to afford mesylated malonate **12** in an excellent yield of 92%.

Assembly of the acyclic triene for the desired macrocycle started with the alkylation of the potassium anion of dienophile **12** with the known chlorodiene **13**[9] to give the corresponding triene **14** in good yield. Attachment of the second



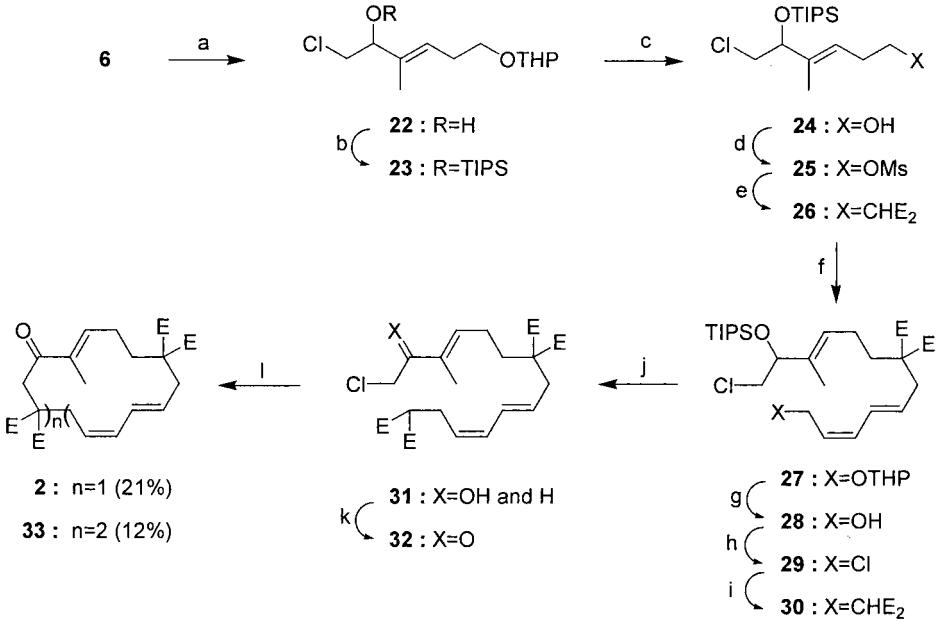
Scheme 3. (a) $(EtO)_2P(O)CH(CH_3)CO_2Et$, NaH, THF, 0°C to rt, 3 h, 78% (*E*/*Z* 4.7:1). (b) DIBALH, CH_2Cl_2, −78°C, 1 h, 99%. (c) DMSO, $(COCl)_2$, CH_2Cl_2, −78°C, 30 min then Et_3N, 94%. (d) Bu_3SnCH_2OEE (**7**), BuLi, THF, −78°C, 30 min, 83%. (e) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0°C, 1 h, 99%. (f) HCl 1N, THF, rt, 12 h, 82%. (g) MsCl, Et_3N, CH_2Cl_2, 0°C, 30 min, 95%. (h) $CH_2(CO_2Me)_2$, NaH, THF/DMF, 0°C then **11**, KI, 80°C, 2 h, 92%. (i) KHMDS, THF, 0°C, 30 min then **13,** DMF, rt, 16 h, 73%. (j) $CH_2(CO_2Me)_2$, KH, toluene, rt then **14**, 18-crown-6, KI reflux, 12 h, 80%. (k) PPTS, *i*-PrOH, 50°C, 10 h, 98%. (l) $(CCl_3)_2CO$, PPh_3, THF, −20°C, 96%.



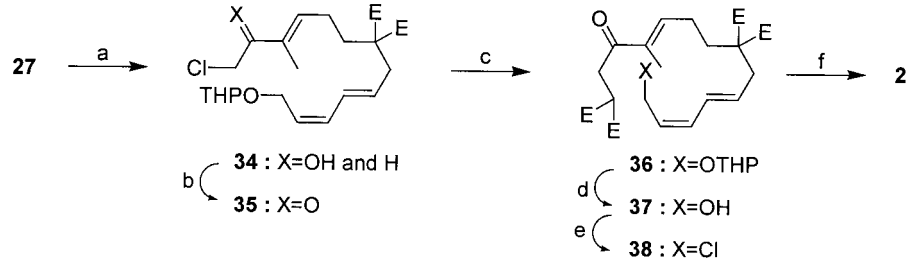
Scheme 4. (a) Cs_2CO_3, MeCN, 80°C, slow addition of **17** over 6 h, c_{final}: 1.7 mM, 71%. (b) TAS-F, THF, 50°C, 95%. (c) Toluene, 200°C, 2 h, 96% (**19**/**20** 1:2). (d) TAS-F, THF, rt, 12 h, 95%.

connector was achieved by nucleophilic displacement of the hindered mesylate with potassium dimethyl malonate to furnish bismalonate **15** in good yield. Deprotection to alcohol **16** and chlorination with a hexachloroacetone, triphenylphosphine (HCA/PPh_3) system afforded chloride **17** in an excellent yield. The macrocyclization (Scheme 4) was performed via slow addition of chloride **17** to a suspension of Cs_2CO_3 in acetonitrile under gentle reflux to obtain macrocyclic triene **1** in 71% yield. According to ^1H NMR analysis, the CTT stereochemistry was preserved throughout the reaction sequence. Interestingly, the silyl ether of **1** resisted any standard procedure of cleavage, but was finally deprotected with tris(dimethylamino)sulfur trimethylsilyldifluoride (TAS-F).[10] However, the free alcohol could not be isolated and only the clean transformation to lactone **18** was observed. Unfortunately, all attempts to open the lactone ring of **18** and oxidize the expected alcohol to yield the macrocyclic trienone **2** have failed.

When CTT macrocyclic ether **1** was heated for 2 h at 200°C, it underwent TADA reaction generating a pair of racemic CAC tricycles **19** and **20** (only one enantiomer is shown) in respective yields of 32 and 64%, an indication of moderate diastereoinduction (Scheme 4). The lowest temperature required for activation was found to be around 172°C, recovering 50% of the starting material after a 4 h reaction period. At 168°C, no tricycle could be detected. The stereochemical assignment was based on our previous studies[11] which showed that CTT macrocyclic trienes must yield tricycles having the CAC stereochemistry. Moreover, the CAC stereochemistry of tricycle **20** was firmly established by single crystal X-ray analysis[15] of lactone **21** obtained by



Scheme 5. (a) ICH_2Cl, BuLi, THF, −78°C, 30 min, 84%. (b) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0°C, 1 h. (c) PPTS, MeOH, 50°C, 1 h, 92% over 2 steps. (d) MsCl, Et_3N, CH_2Cl_2, 0°C, 1 h, 90%. (e) $CH_2(CO_2Me)_2$, NaH, THF/DMF, 0°C then **25**, KI, 80°C, 1 h, 94%. (f) KH, THF/DMF, 0°C then **13**, rt, 17 h, 51%. (g) Tos-OH, MeOH, rt, 1 h, 97%. (h) $(CCl_3)_2CO$, PPh_3, THF, −20°C, 1 h. (i) $CH_2(CO_2Me)_2$, KH, THF/DMF, rt, 30 min. (j) TBAF, THF, −20°C, 2 h, 86% over 3 steps. (k) Dess–Martin periodinane, CH_2Cl_2, 0°C to rt, 5 min, 96%. (l) Cs_2CO_3, CsI, MeCN, rt, 48 h.



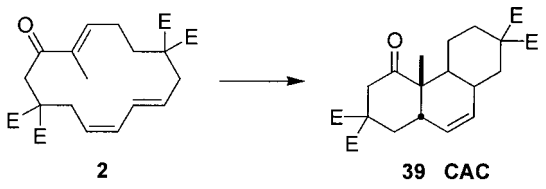
Scheme 6. (a) TBAF, THF, −20°C, 1 h, 83%. (b) Dess–Martin periodinane, CH_2Cl_2, 0°C to rt, 1 h, 98%. (c) NaH, $CH_2(CO_2Me)_2$, THF/DMF then **35**, 60°C, 3 h, 55%. (d) Tos-OH, MeOH, rt, 1 h, 94%. (e) $(CCl_3)_2CO$, PPh_3, THF, −20°C to rt, 1 h, 99%. (f) Cs_2CO_3, CsI, MeCN, 65°C, slow addition of **38** over 10 h, c_{final}: 1.7 mM, 54%.

deprotection and lactonization of the major alpha silyl ether **20**.

Synthesis and TADA studies of macrocycle 2

These results led us to adjust our synthetic plan in order to prevent the lactonization of the macrocycle. We have previously demonstrated that α-chloroketones are efficient electrophiles for malonate alkylations, as well as for macrocyclizations.[3,12] They can, therefore, offer a direct introduction of the required keto-group into the macrocycle, leaving only the exact order of the coupling steps to be found. The masked α-chloroketone functionality was introduced by in situ generated chloromethyl lithium,[13] homologating aldehyde **6** to yield alcohol **22**, which was protected as silylether **23** (Scheme 5). A three-step routine sequence through alcohol **24** and mesylate **25** afforded malonate **26** as the dienophile building block. It was alkylated with chlorodiene **13** and subsequently, the diene terminus of the formed acyclic triene **27** was arranged for the coupling to the second connector. Thus, deprotection to alcohol **28** and activation as chloride **29** afforded the substrate for the second malonate alkylation. Next, the other terminus of the formed malonate **30** was prepared for the macrocyclization by a deprotection to chlorohydrin **31**, followed by a Dess–Martin periodinane[14] oxidation to chloroketone **32**. During these transformations, all steps were accomplished in good to excellent yields. However, attempts to achieve high yield of macrocyclization, surprisingly, failed. In fact, only the condition described in Scheme 5 afforded macrocycle **2**, although in a disappointingly low 21% yield with 12% of dimeric macrocycle **33**. Changing reaction conditions such as differing base, solvent, reaction time and temperature did not improve the yield.

As a result of the poor macrocyclization step, we were prompted to try the reverse order of couplings for the macrocyclization (Scheme 6). As described above, triene **27** could be easily deprotected to chlorohydrin **34** and oxidized to chloroketone **35**. Nucleophilic displacement on **35** afforded malonate **36** in an acceptable yield of 55%. Finally, deprotection to alcohol **37**, and activation as allylic chloride **38**, prepared the other terminus for the macrocyclization in the usual manner. This step was performed under standard conditions to deliver macrocycle **2** in 54% yield without trace of the corresponding dimeric macrocycle **33**.



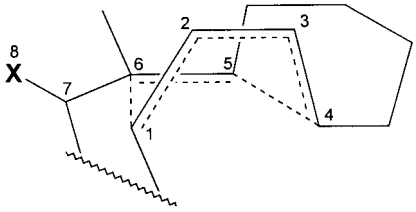
Scheme 7. For reaction conditions see text.

The thermal TADA reaction of macrocycle **2** was carried out in toluene at 150°C for 12 h in a sealed Pyrex tube to generate quantitatively CAC tricycle **39** (Scheme 7). No trace of TADA product was detected after refluxing macrocycle **2** in xylene (145°C) for 24 h. These experiments suggest the minimal activation temperature stands between 145 and 150°C. Having observed a moderate decrease in activation temperature with macrocyclic enone **2** over silylether **1** in the thermic TADA reaction, a larger activation effect could be anticipated with the use of a Lewis acid. Indeed, when macrocycle **2** was treated for 1 h with $SnCl_4$ (CH_2Cl_2) at 40°C, a clean conversion took place to give CAC tricycle **39** in 83% isolated yield. When $BF_3{\cdot}Et_2O$ (CH_2Cl_2) was used, the reaction was completed in 2 h at 23°C and tricycle **39** was isolated in 73% yield.

Rationalization

In order to gain deeper insight into the different conformations involved at the transition state, calculations[16] have been carried out at the 3.21G ab initio level of theory[17] (Table 1) and 3.21G* level[18] in the case of silicon containing structures. It is however necessary to remove the methyl ester groups during the calculations because they render the structures much too large to be easily handled even at this rather simple level of theory. Clearly, such changes are likely to affect the theoretical results, mostly because the conformation of the ring A (either chair or boat) is influenced a lot by the presence of the malonate groups on that ring. On the other hand the malonate groups on the ring C can be safely omitted because that ring remains identical in terms of substituents over all the series studied. The conformation for ring C was kept in the more likely chair conformation during our theoretical investigation. The calculations indicate that the *bbc* transition state would be favored over the *cbc* transition state by 1 kcal/mol in the simplest case (see column CH_2 in Table 1). The calculations were repeated at the same level of theory with the malonate group in ring A; it appeared that the geometry of the backbone is not affected either in the *bbc* or in the *cbc* transition structures, but the *bbc* transition state is now favored by

Table 1. Calculated transition state parameters (All energies are given with regards to the corresponding macrocycles, for which the energies are set to 0 kcal/mol. Values in brackets correspond to calculations, in which the A-ring methyl esters have been included). θ: dihedral angle; *a*: bond length 1–6; *b*: bond length 4–5



Transition state	C–X	CH_2	$CHOSiH_3$		C=O	C=O···BH_3	C=O···BF_3
			19	**20**	**39**	**39**	**39**
Chair–Boat–Chair	*a* (Å)	2.31	2.29	2.35	2.36	2.52	2.89
	b (Å)	2.22	2.24	2.20	2.15	2.06	1.98
	θ(1,6,7,8) (°)	–	65.1	173.1	102.6	98.5	96.2
	θ(5,6,7,8) (°)	–	177.8 (ax)	55.7 (eq)	145.0	156.2	172.5
	$\Delta H^{\ddagger}$ (kcal/mol)	50.20	50.76	50.28	46.52	37.48	31.67
	Ratio (%)	26	9	15	85	39	4
Boat–Boat–Chair	*a* (Å)	2.28	2.29	2.28	2.45	2.70	3.04
	b (Å)	2.22	2.21	2.21	2.06	1.93	1.87
	θ(1,6,7,8) (°)	–	152.9	93.7	111.1	106.2	104.3
	θ(5,6,7,8) (°)	–	90.7 (eq)	23.7 (ax)	0.0	0.2	3.3
	$\Delta H^{\ddagger}$ (kcal/mol)	49.20	49.78	49.15	47.99	37.21	29.83
	Ratio (%)	74	25	51	15	61	96
Composite	Ratio (%)	–	34	66	–	–	–
Experimental	Ratio (%)	–	33	67	–	–	–
	Temperature (°C)	Not optimized	≈180		≈150	≈40	

2.5 kcal/mol (corresponding to a ratio of 92:8 at 250°C). The calculations confirm that the malonate group in ring A determines the shape of that ring at the transition state, but it was still necessary to validate the ability of the 3.21G ab initio calculation to correctly model our CTT system.

The four transition states leading to **19** and **20** were modeled without malonates in rings A and C and by replacing the TIPS group by a SiH_3 (see column $CHOSiH_3$ in Table 1). The results are in excellent agreement with the experimental data and add much credibility to the following discussion. The calculations indicate that the major compound **20** (66%) would mostly arise from a *bbc* transition state with the silyloxy group in a pseudo-axial orientation, whereas the minor compound **19** (34%) would be mainly obtained via a *bbc* transition state again, but with the silyloxy group pseudo-equatorial (see Figs. 1 and 2). Both *cbc* transition states are disfavored and this trend should even be enhanced with malonates, so that the *cbc* transition states might not be of any significance to the final composition of Diels–Alder adducts. It is therefore worth noting that the theoretical ratio of *bbc* transition states (33:67) matches also exactly the **19**:**20** ratio experimentally observed. Therefore the *bbc* transition states are favored (see CH_2 and $CHOSiH_3$ data in Table 1) when ring A bears four sp3 centers (beside the two sp2 centers from the dienophile and diene). The calculations also show that the C_7–O_8 bond prefers to avoid being antiperiplanar to the forming $C_1\cdots C_6$ bond at the transition state as shown in the calculated dihedral angles (θ $C_1\cdots C_6$–C_7–O_8=93.7° for most stable *bbc* TS geometry and 152.9° for least stable *bbc* TS geometry). This result is surprising because the most stable TS geometry has an axial silyloxy group. However, the same effect has already been observed when an ether group was at the α position of a diene;[2] there too, the C–O bond from the alkoxy group preferred to avoid being antiperiplanar to the forming bond despite unfavorable steric effects.

By replacing the silyloxy group by a ketone, a sp2 center is now introduced in ring A. It then appears that the TS

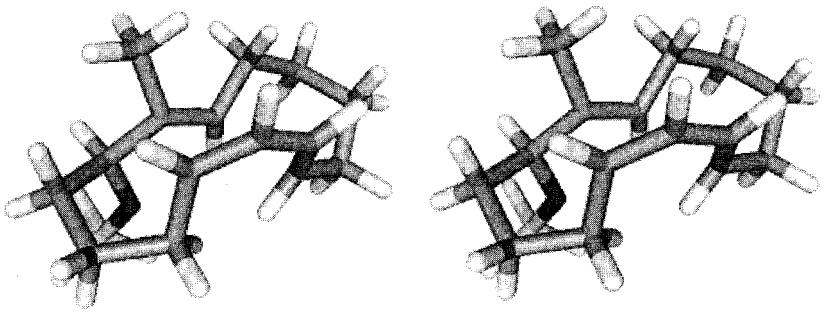


Figure 1. Stereoview of TS *bbc* leading to macrocycle **20**.

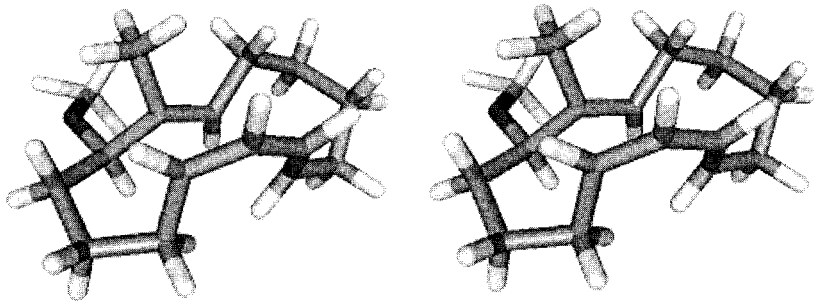


Figure 2. Stereoview of TS *bbc* leading to macrocycle **19**.

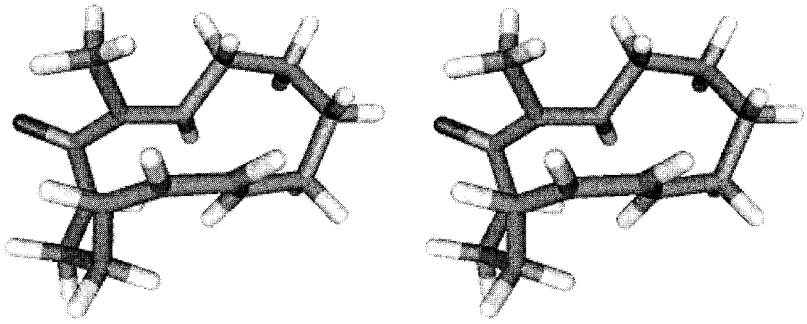
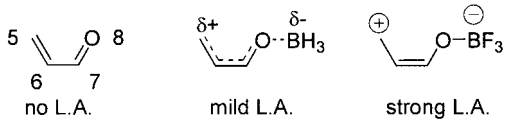


Figure 3. Stereoview of thermal TS *cbc* leading to macrocycle **39**.

geometry prefers to be in a *cbc* conformation although the C_5–C_6–C_7–O_8 dihedral angle θ is 35° (180−145°) away from the ideal 180° angle expected for optimal activation of the dienophile by the carbonyl. On the contrary, a dihedral angle of 0° allows perfect activation in the *bbc* TS (see Fig. 3). The bond distance *a* and *b* reflect this difference of activation because the *bbc* TS is more asymmetric (2.45 and 2.06 Å) than the *cbc* TS (2.36 and 2.15 Å). According to calculations, transforming the ether into a ketone activates the dienophile such that the activation energy is lowered by about 3 kcal/mol, resulting in a moderate decrease of TADA activation temperature (30°C).

Lewis acid catalysis of the enone has been modeled by adding BH_3 to replace mild Lewis acids like $SnCl_4$ as used in the present work, and BF_3 to mimic stronger Lewis acids. The effect of Lewis acid catalysis is threefold: (i) the activation energy is very much decreased (9 kcal/mol for BH_3 and 16 kcal/mol for BF_3), (ii) the transition state geometry becomes more and more asymmetric and (iii) the *bbc* TS geometry becomes increasingly favored as the strength of the Lewis acid grows up. The fall in activation energy was experimentally manifested by a decrease of about 110°C in the temperature of reaction. In order to understand the reasons for these three concomitant effects it is necessary to consider what happens on Lewis acid complexation of an enone (Scheme 8).



Scheme 8. Effects of Lewis acids on enones.

A Lewis acid tends to pull the electron density away from the dienophile which becomes more and more electron-deficient as the Lewis acid electron-withdrawing ability increases. In the process, the dienophile becomes increasingly activated (hence the catalysis effect observed), and at the same time the C_6–C_7 bond tends to take an olefinic character. Consequently, all parameters which fight that C_5–C_6–C_7–C_8 flattening process (dihedral angle close to 0 or 180°) will lead to less stable transition states. The *bbc* uncomplexed transition state which displays a dihedral angle of 0° is perfectly suitable for Lewis acid catalysis. On the other hand, the *cbc* transition state which is 35° away from flatness (without catalyst) must undergo unfavorable conformational changes whilst trying to reach the ideal flat arrangement. It can be expected that this strain effect will be more effective as the strength of the Lewis acid increases (see Figs. 4 and 5). In fact, the calculations show that only 4% of adduct would arise from a *cbc* TS on strong Lewis acid catalysis, presumably because of strong tension in that conformation.

Conclusion

We have demonstrated that a dienophile allylic ether prefers to avoid an antiperiplanar C–O bond geometry with respect to the nearest forming C–C bond. This is identical to the case where the ether is allylic to the diene system, in which case, it also prefers to avoid the antiperiplanar alignment even when unfavorable steric interactions occur.

As for the enone dienophile case, under thermal conditions, the results suggest that distorted enone systems still experience some activation (see *cbc* TS in column C═O of Table 1; decrease of the reaction temperature of 30°C).

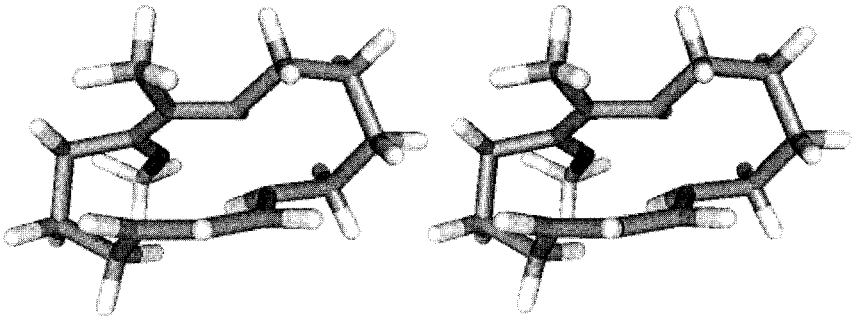


Figure 4. Stereoviews of BH_3 catalyzed TS *bbc* leading to macrocycle **39**.

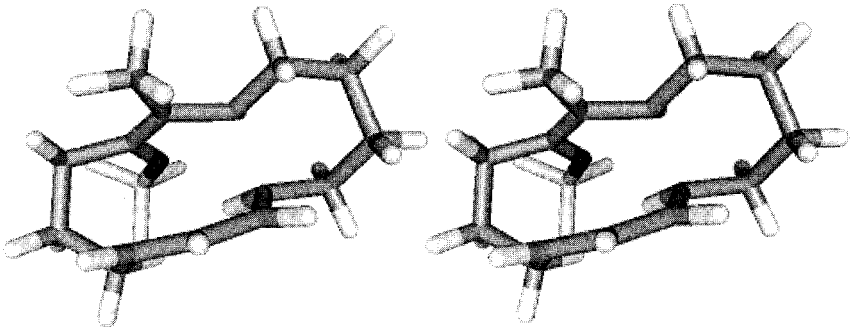


Figure 5. Stereoviews of BF_3 catalyzed TS *bbc* leading to macrocycle **39**.

On the other hand, Lewis catalysis is very sensitive to enone geometry so that enone systems that can easily adopt a flat geometry (see *bbc* TS in C═O···BX_3 columns of Table 1) without much tension benefit the most from catalysis (decrease of the reaction temperature of 110°C). Enone systems for which the flat geometry is strained (see *cbc* TS in C═O···BX_3 columns of Table 1) are less activated by Lewis acids and could even be deactivated in extreme cases of tension. Further experimental studies are currently underway to understand fully the meaning of these observations and to shed new light on the true nature of the Lewis acid catalyzed Diels–Alder reaction.

Experimental

For general experimental details, see our previous paper.[3]

(*E*) and (*Z*) Ethyl-2-methyl-5-tetrahydropyranyloxy-2-pentenoate (4E and 4Z). Triethyl phosphonopropionate (10.20 mL, 47.2 mmol) was added to an ice-cold THF (50 mL) suspension of sodium hydride (1.90 g, 47.2 mmol, 60% dispersion in oil) over 10 min. It was stirred for 30 min at 0°C then aldehyde **3** (5.74 g, 36.3 mmol) in THF (20 mL) was added. After allowing it to warm to 23°C over 3 h and quenching with NH_4Cl (sat.), it was extracted with a 1:1 mixture of ether/ethyl acetate. The organics were dried over $MgSO_4$ and concentrated. The olefin *E*/*Z* ratio was 4.7:1 by ^1H NMR. Chromatography (hexane/ethyl acetate, 4:1) afforded ester **4E** (6.37 g, 73%) first. IR (neat, ν, cm^{-1}): 2948, 2873, 1702, 1444, 1368, 1280, 1134. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.79 (1H, t, J=6.0 Hz, C(CH_3)═C*H*), 4.60 (1H, t, J=2.0 Hz, OC*H*O), 4.18 (2H, q, J=7.0 Hz, CH_3CH_2O), 3.90–3.80 (2H, m, $CH_aH_bOCHOCH_aH_b$(THP), 3.55–3.45 (2H, m, CH_aH_bOCH–OCH_aH_b(THP), 2.47 (2H, q, J=7.0 Hz C(CH_3)═$CHCH_2$), 1.85 (3H, s, C(CH_3)═CH), 1.85–1.45 (6H, m, $OCH_2(CH_2)_3$), 1.29 (3H, t, J=7.0 Hz, CH_3CH_2O); ^{13}C NMR (75 MHz, δ, $CDCl_3$): 168.0, 138.3, 129.5, 98.8, 65.8, 62.3, 60.4, 30.6, 29.4, 25.4, 19.5, 14.3, 12.5. MS (*m*/*e*): 242 (M^+); HR-MS: calcd for $C_{13}H_{22}O_4$: 242.1518; found: 242.1510. Second was **4Z** (0.47 g, 5%). IR (neat, ν, cm^{-1}): 3013, 2947, 2873, 1705, 1454, 1376, 1220, 1135, 1030. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.02 (1H, t, J=6.0 Hz, C(CH_3)═$CHCH_2$), 4.6 (1H, t, J=2.0 Hz, OC*H*O), 4.19 (2H, q, J=7.0 Hz, CH_3CH_2O), 3.90–3.75 (2H, m, CH_aH_bOCHO-CH_aH_b(THP), 3.55–3.40 (2H, m, CH_aH_bOCH–OCH_aH_b(THP), 2.75 (2H, q, J=7.0 Hz, C(CH_3)═$CHCH_2$), 1.91 (3H, s, C(CH_3)═CH), 1.90–1.45 (6H, m, OCH_2-$(CH_2)_3$), 1.30 (3H, t, J=7.0 Hz, CH_3CH_2O). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 167.9, 139.2, 128,6, 98.7, 66.7, 62.3, 60.1, 30.7, 30.2, 25.5, 20.6, 19.6, 14.2. MS (*m*/*e*): 212 $(M-CH_2O)^+$. HR-MS: calcd for $C_{12}H_{20}O_3$: 212.1412; found: 212.1410.

(*E*)-2-Methyl-5-tetrahydropyranyloxy-2-pentenol (5). Diisobutylaluminum hydride (DIBALH) (162.6 mL, 162.6 mmol, 1.0 M in CH_2Cl_2) was added over 15 min to a CH_2Cl_2 (500 mL) solution of ester **4E** (17.89 g, 73.93 mmol) at −78°C. The mixture was stirred for 1 h then the reaction was quenched with crushed $Na_2SO_4{\cdot}10H_2O$ (10 g). After 1 h stirring of the resulting slurry at 23°C, it was filtered, the solid was washed with ethyl acetate (2 L) and the filtrate was concentrated. Chromatography (hexane/ethyl acetate, 1:1) afforded alcohol **5** (14.68 g, 99%) as a colorless oil; IR (neat, ν, cm^{-1}): 3610, 3014, 2947, 2871, 1446, 1215, 1073, 1029. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.45 (1H, t, J=7.0 Hz,

C(CH_3)=C*H*), 4.59 (1H, t, *J*=2.0 Hz, OC*H*O), 4.01 (2H, s, CH_2OH), 3.80–3.90 (1H, m, OC*H*H(CH_2)$_3$), 3.80–3.70 (1H, dt, *J*=10.0 and 6.0 Hz, THPOC*H*H), 3.55–3.48 (1H, m, OCH*H*(CH_2)$_3$), 3.46–3.38 (1H, dt, *J*=10.0 and 6.0 Hz, THPOCH*H*), 2.35 (2H, q, *J*=7.0 Hz, THPOCH_2CH_2), 1.85–1.50 (9H, m, C(CH_3)=CH, OCH_2–(CH_2)$_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 136.7, 121.4, 98.6, 68.1, 66.7, 62.1, 30.5, 28.1, 25.2, 19.4, 13.5. MS (*m*/*e*): 200 (M^+); HR-MS: calcd for $C_{11}H_{20}O_3$: 200.1412; found: 200.1415.

(*E*)-2-Methyl-5-tetrahydropyranyloxy-2-pentenal (6). Dimethyl sulfoxide (DMSO) (2.57 mL, 35.95 mmol) in CH_2Cl_2 (10 mL) was slowly added to a CH_2Cl_2 (150 mL) solution of oxalyl chloride (1.60 mL, 17.98 mmol) at −78°C. After 15 min stirring, alcohol **5** (3.00 g, 14.98 mmol) in CH_2Cl_2 (50 mL) was added with canula. Upon stirring for 30 min, Et_3N (10.00 mL, 71.90 mmol) was added. It was allowed to warm to 23°C over 1 h, poured to water (100 mL) and extracted with CH_2Cl_2. The organics were dried over $MgSO_4$ and concentrated. Chromatography (hexane/ethyl acetate, 4:1) of the residue afforded aldehyde **6** (2.79 g, 94%) as a colorless oil; IR (neat, ν, cm^{-1}): 3015, 2948, 2873, 1682, 1214. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 9.41 (1H, s, C*H*O), 6.56 (1H, t, *J*=7.0 Hz, C(CH_3)=C*H*), 4.60 (1H, t, *J*=3.0 Hz, OC*H*O) 3.95–3.75 (2H, m, CH_a H_bOCHOC$H_a$$H_b$(THP)), 3.60–3.45 (2H, m, C$H_a$$H_b$OCH OC$H_a$$H_b$(THP)), 2.63 (2H, q, *J*=7.0 Hz THPOCH_2CH_2), 1.80–1.45 (9H, m, OCH_2(CH_2)$_3$, C(CH_3)=CH). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 195.2, 151.0, 140.6, 98.9, 65.5, 62.4, 30.6, 29.7, 25.4, 19.5, 9.3. MS (*m*/*e*): 198 (M^+), 168 ($M-CH_2O)^+$; HR-MS: calcd for $C_{11}H_{18}O_3$: 198.1256; found: 198.1254.

(*E*)-1-(1-Ethoxyethoxy)-3-methyl-6-tetrahydropyranyloxy-3-hexen-2-ol (8). To a solution of stannane **7** (20.96 g, 53.49 mmol) in THF (200 mL), *n*-butyllithium (31.0 mL, 49.66 mmol, 1.6 M in hexane) was added at −78°C. The mixture was stirred for 10 min then aldehyde **6** (7.56 g, 38.20 mmol) in THF (10 mL) was added. The mixture was stirred 30 min at −78°C then the reaction was quenched with NH_4Cl (sat.). It was extracted with ether, the extract was dried over $MgSO_4$, filtered and concentrated. Chromatography (hexane/ethyl acetate, 1:1) of the residue afforded compound **8** (9.61 g, 83%) and aldehyde **6** recovered (0.926 g, 4%). **8** IR (neat, ν, cm^{-1}): 3447, 2945, 2876, 1446, 1231, 1127. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 5.55 (1H, t, *J*=7.0 Hz, C(CH_3)=C*H*) 4.73 (1H, q, *J*=5.5 Hz, EtOC*H*(CH_3)O), 4.59 (1H, t, *J*=3.0 Hz, OC*H*O), 4.17 (1H, d broad, C*H*OH), 3.90–3.35 (8H, m, CH_3CH_2O, EEOCH_2, THPOCH_2, OCH_2(CH_2)$_3$), 2.35 (2H, q, *J*=7.0 Hz, THPOCH_2CH_2), 1.90–1.45 (9H, m, OCH_2(CH_2)$_3$, C(CH_3)=CH), 1.33 (3H, d, *J*=5.5 Hz, OCHCH_3), 1.21 (3H, dt, *J*=7.0 and 2.0 Hz, CH_3CH$_2$O); ^{13}C NMR (75 MHz, δ, $CDCl_3$): 135.5, 122.5, 99.5, 98.0, 75.1, 68.2, 66.2, 61.5, 60.5, 30.1, 27.8, 25.0, 19.3, 19.0, 14.7, 12.1; MS (*m*/*e*): 271 ($M-OCH_3)^+$; HR-MS: calcd for $C_{15}H_{27}O_4$: 271.1909; found: 271.1907.

(*E*)-1-(1-Ethoxyethoxy)-3-methyl-6-tetrahydropyranyloxy-2-(triisopropylsilyloxy)-3-hexene (9). 2,6-Lutidine (6.60 mL, 57.04 mmol) and triisopropylsilyl trifluoromethanesulfonate (TIPSOTf) (13.60 mL, 42.78 mmol) were added successively to a CH_2Cl_2 (200 mL) solution of alcohol **8** (8.61 g, 28.52 mmol) at 0°C. Upon stirring for 1 h at 0°C, the reaction was quenched with NH_4Cl (sat.) and extracted with CH_2Cl_2. The dried extract was concentrated. Chromatography (hexane/ethyl acetate, 9:1) afforded pure **9** (13.00 g, 99%) as a colorless oil. IR (neat, ν, cm^{-1}): 2945, 2867, 1463, 1383, 1129. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 5.44 (1H, t, *J*=7.0 Hz, C(CH_3)=C*H*) 4.67 (1H, dq, *J*=5.5 and 1.5 Hz, EtOC*H*(CH_3)O), 4.59 (1H, t, *J*=3.0 Hz, OC*H*O), 4.21 (1H, q, *J*=7.0 Hz, C*H*OTIPS), 3.90–3.30 (8H, m, CH_3CH_2O, EEOCH_2, THPOCH_2, OCH_2(CH_2)$_3$), 2.40–2.25 (2H, m, THPOCH_2–CH_2), 1.85–1.45 (9H, m, OCH_2(CH_2)$_3$, C(CH_3)=CH), 1.27 (3H, dd, *J*=5.5 and 1.5 Hz, OCHCH_3), 1.18 (3H, t, *J*=7.0 Hz, CH_3CH$_2$O), 1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 137.1, 122.9, 99.3, 99.0, 98.3, 77.0, 68.3, 67.9, 66.5, 61.6, 60.1, 59.9, 30.3, 28.0, 25.2, 19.3, 19.1, 17.6, 17.4, 14.9, 12.0, 11.4; MS (*m*/*e*): 476 (MNH_4^+); HR-MS: calcd for $C_{25}H_{54}NO_5Si$: 476.3771; found: 476.3768.

(*E*)-2-Triisopropylsilyloxy-3-methyl-3-hexene-1,6-diol (10). HCl (50 mL, 1.0 N) was added to a THF (200 mL) solution of **9** (5.1 g, 11.14 mmol) at 23°C. Following 12 h stirring, it was neutralized with $NaHCO_3$ (sat.) and extracted with ether. The dried extract was evaporated. Chromatography (hexane/ethyl acetate, 1:1) of the crude product afforded diol **10** (2.77 g, 82%) as a colorless oil. IR (neat, ν, cm^{-1}): 3615, 3425, 2947, 2869, 1464, 1388, 1094. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 5.47 (1H, t, *J*=7.0 Hz, C(CH_3)=C*H*), 4.22 (1H, t, *J*=5.5 Hz, C*H*OTIPS), 3.77 (2H, dt, *J*=6.5 and 2.0 Hz, CH_2CH_2OH), 3.53 (2H, d, *J*=5.5 Hz, HOCH_2CHOTIPS), 2.34 (2H, q, *J*=7.0 Hz, C(CH_3)=CHCH_2), 1.65 (3H, s, C(CH_3)=CH), 1.60 (2H, s, 2×O*H*), 1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$). ^{13}C NMR (75 MHz, d, $CDCl_3$): 137.5, 123.8, 78.1, 64.7, 61.7, 31.0, 17.9, 12.2, 11.7; MS (*m*/*e*): 271 ($M-OCH_3)^+$; HR-MS: calcd for $C_{15}H_{31}O_2Si$: 271.2093; found: 271.2090.

(*E*)-1,6-Bis(methanesulfonyloxy)-3-methyl-2-triisopropylsilyloxy-3-hexene (11). Et_3N (15.00 mL, 107 mmol) and methanesulfonyl chloride (MsCl) (4.20 mL, 53.6 mmol) was added successively to a stirred CH_2Cl_2 (100 mL) solution of **10** (2.90 g, 9.6 mmol) at 0°C. It was stirred for 30 min, quenched with NH_4Cl (sat.) and extracted with CH_2Cl_2. The dried extract was evaporated. Chromatography (hexane/ethyl acetate, 7:3) afforded **11** (4.15 g, 95%) as a yellow oil. IR (neat, ν, cm^{-1}): 3028, 2848, 2868, 1464, 1356, 1124. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 5.51 (1H, t, *J*=7.0 Hz, C=C*H*), 4.38 (1H, t, *J*=6.0 Hz, C*H*OTIPS), 4.21 (2H, t, *J*=7.0 Hz, MsOCH_2), 4.08 (2H, dd, *J*=6.0 and 2.0 Hz, MsOCH_2), 2.99 (6H, d, *J*=1.0 Hz, 2×CH_3SO_2), 2.51 (2H, q, *J*=7.0 Hz, C(CH_3)=CHCH_2), 1.67 (3H, s, C(CH_3)=CH), 1.04 (21H, m, Si(C*H*(CH_3)$_2$)$_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 137.1, 122.3, 75.1, 70.9, 68.5, 36.9, 27.3, 17.5, 11.8, 11.5. MS (*m*/*e*): 476 ($MNH_4)^+$; HR-MS: calcd for $C_{18}H_{42}NO_7SiS_2$: 476.2172; found: 476.2166.

(*E*)-Dimethyl-7-methanesulfonyloxy-5-methyl-6-triisopropylsilyloxy-4-heptenedicarboxylate (12). Dimethyl malonate (1.50 mL, 13.42 mmol) was added to an ice-cold THF/DMF (40 mL, 1:1) suspension of NaH (501 mg, 12.53 mmol, 60% dispersion in oil). It was stirred until the bubbling ceased then compound **11** (4.10 g, 8.95 mmol) in THF (10 mL) was added with canula. KI

(2.22 g, 13.42 mmol) was added and the mixture was heated for 2 h at 80°C. Upon cooling, it was neutralized with NH_4Cl (100 mL, sat.), extracted with a 1:1 mixture of hexane and ether. The dried extract was concentrated. Chromatography (hexane/ethyl acetate, 4:1) afforded compound **12** (4.05 g, 92%) as a colorless oil. IR (neat, ν, cm^{-1}): 3027, 2950, 2867, 1735, 1443, 1355, 1218. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.47 (1H, t, J=7.0 Hz, C(CH_3)=C*H*), 4.37 (1H, t, J=6.0 Hz, C*H*OTIPS), 4.08 (2H, dd, J=6.0 and 1.5 Hz, CH_2OMs), 3.74 (6H, s, 2×CO_2CH_3), 3.38 (1H, t, J=7.5 Hz, C*H*(CO_2CH_3)$_2$), 3.00 (3H, s, CH_3SO_3), 2.10 (2H, t, J=7.0 Hz, C(CH_3)=CHCH_2), 2.00–1.90 (2H, m, $CH_2CH_2CH(CO_2CH_3)_2$), 1.61 (3H, s, C(CH_3)=CH), 1.04 (21H, m, Si(C*H*(CH_3)$_2$)$_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 169.6, 135.2, 127.1, 75.6, 71.1, 52.4, 50.7, 37.3, 28.2, 25.0, 17.8, 12.2, 11.5. MS (*m*/*e*): 463 $(M-OCH_3)^+$, 451 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{21}H_{39}O_7SSi$: 463.2186; found: 463.2179.

(2*Z*,4*E*,10*E*)-7,7-Bis(methoxycarbonyl)-11-methyl-13-methanesulfonyloxy-1-tetrahydropyranyloxy-12-triisopropylsilyloxytrideca-2,4,10-triene (14). Potassium bis(trimethylsilyl) amide (KHMDS) (13.50 mL, 6.75 mmol, 0.5 M in MePh) was added dropwise to a THF (5 mL) solution of 12 (3.18 g, 6.43 mmol) at 0°C. After 30 min stirring, chloride **13**[9] (2.77 g, 12.86 mmol) in DMF (7 mL) was added, stirred for 16 h at 23°C, quenched with NH_4Cl (sat.) and extracted with an ether/hexane (1:1) mixture. The dried organics were evaporated. Chromatography (hexane/ethyl acetate, 4:1) afforded title compound 14 (3.16 g, 73%) as a yellow oil; IR (neat, ν, cm^{-1}): 3023, 2860, 1731, 1436, 1357. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.39 (1H, dd, J=15.0 and 12.0 Hz, OCH_2CH=CHC*H*=CH), 6.07 (1H, t, J=11.0 Hz, OCH_2CH=C*H*CH=CH), 5.60–5.45 (3H, m, OCH_2CH=CHCH=C*H*, C(CH_3)=C*H*), 4.63 (1H, t, J=3.0 Hz, OC*H*O), 4.37–4.30 (2H, m, C*H*OTIPS, THPOC*H*H), 4.16 (1H, dd, J=11.5 and 7.5 Hz, THPOCH*H*), 4.12–4.05 (2H, m, CH_2OMs), 3.90–3.80 and 3.55–3.45 (2×1H, 2m, OCH_2(CH_2)$_3$), 3.73 (6H, s, 2×CO_2CH_3), 2.99 (3H, m, CH_3SO_3), 2.72 (2H, d, J=7.5 Hz, CH=CHCH_2C(CO_2CH_3)$_2$), 1.95–1.80 (4H, m, =CHCH_2CH_2), 1.80–1.50 (9H, m, C(CH_3)=, OCH_2(CH_2)$_3$), 1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 170.8, 134.0, 130.3, 128.8, 127.2, 127.1, 126.3, 97.2, 75.4, 70.9, 62.2, 61.5, 57.1, 51.9, 36.8, 36.0, 31.7, 30.1, 25.0, 22.0, 19.0, 17.5, 11.8, 11.0. MS (*m*/*e*): 643 $(M-OCH_3)^+$; HR-MS: calcd for $C_{32}H_{55}O_9SiS$: 643.3336; found: 643.3329.

(4*E*,10*E*,12*Z*)-Dimethyl-8,8-bis(methoxycarbonyl)-4-methyl-14-tetrahydropyranyloxy-3-triisopropylsilyloxytetradeca-4,10,12-trienedicarboxylate (15). Dimethyl malonate (0.85 mL, 7.43 mmol) was added to a stirred toluene (1 mL) suspension of KH (764 mg, 6.68 mmol, 35% dispersion in oil) at 23°C. After 30 min stirring, mesylate 14 (501 mg, 0.743 mmol) in toluene (5 mL), KI (3.32 g, 20.03 mmol) and 18-crown-6 (1.96 g, 6.68 mmol) was added. After refluxing for 12 h, the reaction mixture was quenched with NH_4Cl (sat.) and extracted with ether. The dried extract was evaporated. Chromatography (hexane/ethyl acetate, 4:1) afforded pure **15** (422 mg, 80%) as a colorless oil; IR (neat, ν, cm^{-1}): 3025, 2867, 1734, 1341, 1265. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.39 (1H, dd, J=15.0 and 12.0 Hz, OCH_2CH=CHC*H*=CH), 6.07 (1H, t, J=11.0 Hz, OCH_2CH=C*H*CH=CH), 5.60–5.45 (2H, m, OCH_2CH=CHCH=C*H*, 5.27 (1H, m, C(CH_3)=C*H*), 4.63 (1H, t, J=3.0 Hz, OC*H*O), 4.32 (1H, dd, J=11.5 and 6.0 Hz, THPOCH_a), 4.15 (2H, m, C*H*OTIPS, THPOCH_b), 3.95–3.85 and 3.55–3.45 (2×1H, 2m, OCH_aH_b(CH_2)$_3$), 3.72 and 3.71 (12H, 2s, 4×CO_2CH_3), 3.33 (1H, dd, J=8.0 and 2.0 Hz, C*H*(CO_2CH_3)$_2$), 2.71 (2H, d, J=7.5 Hz, CH=CHCH_2C(CO_2CH_3)$_2$), 2.20–2.05 (2H, m, CH_2CH(CO_2CH_3)$_2$), 1.90–1.80 (4H, m, (CH_3)=CHCH_2CH_2), 1.80–1.50 (9H, m, OCH_2(CH_2)$_3$, C(CH_3)=CH), 1.02 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.2, 169.8, 136.8, 130.6, 129.2, 128.9, 126.4, 125.5, 97.6, 75.6, 62.6, 62.0, 57.5, 52.2, 47.8, 36.3, 34.3, 32.1, 30.5, 25.3, 22.2, 19.3, 17.8, 12.1, 10.7; MS (*m*/*e*): 679 $(M-OCH_3)^+$, 667 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{36}H_{59}O_{10}Si$: 679.3877; found: 679.3878.

(4*E*,10*E*,12*Z*)-Dimethyl 8,8-bis(methoxycarbonyl)-14-hydroxy-4-methyl-3-triisopropylsilyloxytetradeca-4,10,12-trienedicarboxylate (16). Pyridinium *para*-toluenesulfonate (PPTS) (20 mg, 0.08 mmol) was added to an isopropanol (5 mL) solution of 15 (285 mg, 0.401 mmol). After heating the mixture for 10 h at 50°C, it was neutralized with NH_4Cl (sat.). Isopropanol was removed and the residue was extracted with ether. After evaporation of the dried extract, chromatography (hexane/ethyl acetate, 1:1) afforded compound **16** (248 mg, 98%) as a colorless oil. IR (neat, ν, cm^{-1}): 3609, 3538, 2867, 1732, 1440, 1269. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.38 (1H, dd, J=15.0 and 11.0 Hz, CH=CHC*H*=CHCH_2OH), 6.83 (1H, t, J=11.0 Hz, CH=C*H*–CH=CHCH_2OH), 5.60–5.45 (2H, m, C*H*=CHCH=C*H*CH_2OH), 5.27 (1H, m, C(CH_3)=C*H*), 4.28 (2H, dd, J=6.5 and 1.0 Hz, CH_2OH), 4.12 (1H, dd, J=7.5 and 2.0 Hz, C*H*OTIPS), 3.72 and 3.70 (12H, 2s, 4×CO_2CH_3), 3.33 (1H, dd, J=8.0 and 2.5 Hz, C*H*(CO_2CH_3)$_2$), 2.71 (2H, d, J=7.5 Hz, CH=CHCH_2C(CO_2CH_3)$_2$), 2.25–2.05 (2H, m, CH_2CHOTIPS), 1.90–1.80 (4H, m, C(CH_3)=CH–CH_2), 1.60 (1H, s broad, CH_2OH), 1.54 (3H, s, C(CH_3)=CH), 1.02 (21H, m, Si(C*H*(CH_3)$_2$)$_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.4, 169.9, 169.8, 136.8, 129.9, 129.4, 129.1, 128.8, 125.6, 75.7, 58.6, 57.5, 52.4, 47.9, 36.3, 34.4, 32.1, 22.2, 17.9, 12.2, 10.9. MS (*m*/*e*): 626 (M^+), 609 $(M-OH)^+$, 593 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{32}H_{53}O_9Si$: 609.3459; found: 609.3451.

(4*E*,10*E*,12*Z*)-Dimethyl-8,8-bis(methoxycarbonyl)-14-chloro-4-methyl-3-triisopropylsilyloxytetradeca-4,10,12-trienedicarboxylate (17). Triphenylphosphine (181 mg, 0.690 mmol) and hexachloroacetone (52 μL, 0.345 mmol) was added successively to a THF (3 mL) solution of alcohol **16** (216 mg, 0.345 mmol) at −20°C. After 10 min stirring at −20°C, it was poured to NH_4Cl (sat.) and extracted with ether. The dried extract was concentrated. Chromatography (hexane/ethyl acetate, 9:1) afforded **17** (215 mg, 96%) as a pale yellow oil; IR (neat, ν, cm^{-1}): 3026, 2951, 2866, 1732, 1440, 1269. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.39 (1H, dd, J=15.5 and 11.0 Hz, C*H*=CHCH_2Cl), 6.10 (1H, t, J=11.0 Hz, C*H*CH=CHCH_2Cl), 5.70–5.50 (2H, m, C*H*=CHCH=C*H*), 5.27 (1H, t, J=6.5 Hz, C(CH_3)=C*H*), 4.16 (2H, d, J=8.0 Hz, CH_2Cl), 4.15–4.05 (1H, m, C*H*OTIPS), 3.73 and 3.71 (12H, 2s, 4×CO_2CH_3), 3.33

(1H, dd, J=8.0 and 6.0 Hz, CH(CO_2CH_3)$_2$), 2.74 (2H, d, J=7.5 Hz, CH_2C(CO_2CH_3)$_2$) 2.25–2.05 (2H, m, CH_2CHO-TIPS), 1.95–1.80 (4H, m, C(CH_3)=CHCH_2CH_2), 1.54 (3H, s, C(CH_3)=CH), 1.02 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.3, 169.8, 137.0, 132.2, 131.4, 127.8, 125.5, 124.9, 75.7, 57.6, 52.4, 47.9, 39.2, 36.5, 34.4, 22.3, 22.3, 17.9, 12.2, 10.9. MS (*m/e*): 613 $(M-OCH_3)^+$, 609 $(M-Cl)^+$, 601 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{29}H_{46}O_9SiCl$: 601.2599; found: 601.2595.

(3*E*,5*Z*,11*E*)-Tetramethyl 11-methyl-10-[[tris(1-methylethyl)silyl]oxy]cyclotetradeca-3,5,11-triene-tetracarboxylate (1). A solution of allylic chloride **17** (75 mg, 0.116 mmol) in acetonitrile (3 mL)) was slowly added via a syringe pump to a vigorously stirred acetonitrile (41 mL) suspension of Cs_2CO_3 (75 mg, 0.116 mmol) over a period of 6 h at 80°C. After stirring for two additional hours and cooling, the mixture was filtered through a silica pad (3 cm) and concentrated. Chromatography (hexane/ethyl acetate, 4:1) of the residue afforded macrocycle **1** (50 mg, 71%) as a pale yellow oil. IR (neat, ν, cm^{-1}): 3026, 2867, 1731, 1441, 1219, 1064. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 6.21 (1H, dd, J=15.0 and 10.5 Hz, CH_2CH=CHCH=CH), 6.00 (1H, t, J=10.5 Hz, CH_2CH=CHCH=CH), 5.50–5.35 (2H, m, CH_2CH=CHCH=CH, C(CH_3)=CH), 5.06 (1H ddd, J=15.0, 10.0 and 4.0 Hz, CH_2CH=CHCH=CH), 4.11 (1H, dd, J=7.0 and 5.0 Hz CHOTIPS), 3.74 (3H, s, CO_2CH_3), 3.73 (6H, s, 2×CO_2CH_3), 3.70 (3H, s, CO_2CH_3), 2.90–2.58 (4H, m, CH_2CH=CHCH=CHCH_2), 2.30 (1H, dd, J=15.0 and 5.00 Hz, CHHCHOTIPS), 2.10–1.95 (5H, m, C(CH_3)=CHCH_2CH_2, CHHCHOTIPS), 1.58 (3H, s, C(CH_3)=CH), 1.00 (21H, m, Si(CH(CH_3)$_2$)$_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.8, 171.4, 171.0, 138.1, 131.1, 130.2, 127.6, 125.2, 75.4, 57.7, 55.2, 52.6, 52.5, 52.2, 38.6, 36.2, 30.7, 21.6, 18.1, 12.5, 12.2, 11.7. MS (*m/e*): 577 $(M-OCH_3)^+$, 565 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{29}H_{45}O_9Si$: 565.2833; found: 565.2828.

(3*Z*,5*E*,11*E*)-Trimethyl 12-methyl-15-oxo-14-oxabicyclo-[11,2,1]hexadeca-3,5,11-triene-1,8,8-tricarboxylate (18). Tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TAS-F) (9 mg, 0.03 mmol) was added to a THF (1 mL) solution of macrocycle **1** (20 mg, 0.032 mmol) at 23°C. After 1 h stirring, TAS-F (9 mg, 0.03 mmol) was added again and the stirring continued for 30 min at 23°C then for 1 h at 50°C. Upon cooling, the reaction mixture was quenched with NH_4Cl (sat.) and extracted with ether. The extract was dried over $MgSO_4$ and concentrated. Preparative thin layer chromatography (TLC) (20×20×0.05 cm^3, hexane/ethyl acetate 3:2) gave compound **18** (12.5 mg, 94%) as a colorless oil. IR (neat, ν, cm^{-1}): 3030, 2955, 1730, 1436, 1217. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 6.18–6.11 (2H, m, CH=CHCH=CH), 5.47–5.42 (2H, m, CH=CH–CH=CH), 5.20 (1H, t, J=2 Hz, CH=C(CH_3)), 5.04 (1H, d broad, J=9 Hz, CHC), 3.81 (3H, s, CO_2CH_3), 3.74 (6H, s, 2×CO_2CH_3), 3.00–2.59 (4H, m CH_2CH=CHCH=CHCH_2), 2.33 (1H, dd, J=14 and 2 Hz, CHHCO), 2.24–1.87 (5H, m, C(CH_3)CH_2CH_2, and CHHCO), 1.72 (3H, s, CH_3). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 174.2, 171.6, 171.4, 170.2, 133.2, 131.2, 131.1, 128.4, 128.0, 125.3, 79.6, 57.5, 53.8, 53.2, 52.7, 34.9, 33.4, 32.4, 30.9, 20.2, 14.4. MS *m/e*=422 (M^+).

4α,4aα,4bβ,8aβ,10aα- and 4α,4aβ,4bα,8aα,10aβ- Tetramethyl-1,3,4,4a,4b,5,6,8,8a,10a-decahydro-4a-methyl-4-[[tris(1-methylethyl)silyl]oxy]-2,2,7,7-phenanthrenetetracarboxylate (19) and (20). A solution of CTT macrocyclic triene **1** (21 mg, 34.5 μmol) and 2,6-lutidine (2 drops) in toluene (1.0 mL, previously degassed with five freeze–thaw cycles) was heated for 2 h in two vacuum sealed quartz tubes (washed with aqueous NH_4OH, water and acetone before drying) at 200°C in a temperature controlled oven. Upon cooling, the tubes were opened and the content was evaporated, purified by preparative TLC (hexane/ethyl acetate, 7:3) to afford two CAC tricycles: **19** (6.7 mg, 32%) and **20** (13.5 mg, 64%) as viscous oils. **19**: IR (neat, ν, cm^{-1}): 3024, 2952, 2867, 1730, 1458, 1250. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 5.30–5.15 (2H, AB, CH=CH), 4.25 (1H, dd, J=11.0 and 4.5 Hz, CHOTIPS), 3.70, 3.69, 3.66 and 3.65 (12H, 4s, 4×CO_2CH_3), 2.71 (1H, s br, C_1H), 2.55–2.39 (3H, m, C_3H), 2.27–2.15 (3H, m, $C_{8a}H$), 2.02 (1H, dd, J=14.0 and 6.0 Hz, C_1H), 1.92–1.88 (1H, m, $C_{4b}H$) 1.72 (1H, dd, J=12.5 and 1.5 Hz, C_3H) 1.55–1.40 (3H, m) 1.08 (21H, m, TIPS), 0.96 (3H, s, $C_{4a}CH_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 173.0, 172.2, 171.4, 130.2, 129.6, 67.2, 53.8, 52.9, 52.7, 52.5, 52.1, 52.0, 40.2, 38.7, 37.4, 34.9, 31.4, 31.2, 30.3, 29.6, 18.9, 18.3, 16.8, 13.2; MS (*m/e*): 565 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{29}H_{45}O_9Si$: 565.2833; found: 565.2822. 20: IR (neat, ν, cm^{-1}): 3024, 2952, 2867, 1730, 1458, 1250. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 5.65–5.60 (1H, m, CH=CH), 5.49 (1H, dd, J=10.0 and 3.0 Hz, CH=CH), 3.72 and 3.69 (12H, 2s, 4×CO_2CH_3), 3.56 (1H, dd, J=12.0 and 4.0 Hz, CHOTIPS), 2.50–2.45 and 2.40–2.00 and 2.00–1.50 (1H+6H+6H, 3m), 1.12 (3H, s, $C_{4a}CH_3$), 1.07 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 172.8, 171.9, 171.6, 130.5, 129.1, 78.4, 54.6, 53.8, 52.8, 52.5, 41.7, 40.4, 39.8, 34.4, 32.7, 32.1, 29.7, 28.6, 23.2, 21.5, 18.3, 13.7, 13.4, 12.8. MS (*m/e*): 565 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{29}H_{45}O_9Si$: 565.2833; found: 565.2822.

1α,2β,3α,8α,11β-Trimethyl-2-methyl-14-oxo-15-oxatetracyclo[11.2.1.0^{2,11}.0^{3,8}]hexadec-9-ene-6,6,13-tricarboxylate (21). TAS-F (25.0 mg, 93.8 μmol) was added to a THF (2 mL) solution of tricycle **20** (5.7 mg, 9.9 μmol). After stirring for 12 h at 23°C, it was quenched with NH_4Cl (sat.) and extracted with ether. The dried extract was evaporated and purified by preparative TLC (hexane/ethyl acetate, 7:3) to afford lactone **21** (3.7 mg, 95%) as a crystalline product. Mp: 143–145°C (hexane/ether 9:1). IR (neat, ν, cm^{-1}): 2954, 2855, 1783,1734, 1440, 1251. ^{1}H NMR (300 MHz, δ, $CDCl_3$): 5.52 (1H, dt, J=10.5 and 1.0 Hz, $C_{10}H$), 5.36 (1H, dt, J=10.5 and 3.0 Hz, C_9H), 4.43 (1H, d, J=6.0 Hz, C_1H), 3.77, 3.69 and 3.67 (9H, 3s, 3×CO_2CH_3), 3.13 (1H, s br, C_8H), 2.70 (1H, dd, J=12.0 and 6.0 Hz, $C_{16}H$), 2.55–2.46 (2H, m, $C_{16}H$, C_7H), 2.46–2.35 (1H, m, $C_{11}H$), 2.20 (2H, d, J=5.0 Hz, $C_{12}H_2$), 2.13 (1H, dd, J=14.0 and 5.5 Hz, C_7H), 1.72–1.65 (1H, m, C_3H), 1.60–1.45 (4H, m, C_4H_2 and C_5H_2), 1.08 (3H, s, C_2CH_3). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 173.0, 169.9, 131.9, 130.6, 86.1, 52.8, 52.7, 52.2, 52.0, 51.4, 43.7, 37.9, 37.5, 35.8, 34.9, 33.0, 31.4, 31.1, 29.7, 22.2, 20.6; MS (*m/e*): 420 (M^+); HR-MS: calcd for $C_{22}H_{28}O_8$: 420.1784; found: 420.1793.

(*E*)-1-Chloro-3-methyl-6-tetrahydropyranyloxy-3-hexen-

2-ol (22). Chloroiodomethane (1.50 mL, 20.09 mmol) and *n*-butyllithium (12.2 mL, 17.00 mmol, 1.4 M hexane) was successively added to a THF (150 mL) solution of aldehyde **6** (3.06 g, 15.45 mmol) at −78°C. After 30 min stirring, it was quenched with NH_4Cl (sat.) and extracted with ether. The dried extract was concentrated. Chromatography (hexane/ethyl acetate, 7:3) afforded **22** (3.22 g, 84%) as a colorless oil. IR (neat, ν, cm^{-1}): 3424, 2944, 2870, 1441, 1352, 1200. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.57 (H, t, J=7.0 Hz, C=C*H*), 4.58 (1H, t, J=3.0 Hz, OC*H*O), 4.21 (1H, dt, J=8.0 and 4.0 Hz, C*H*OH), 3.90–3.80 (1H, m, OC*H*H$(CH_2)_3$), 3.73 (1H, dt, J=9.5 and 7.0 Hz, THPOC*H*H), 3.70–3.35 (4H, m, CH_2Cl, OCH*H*$(CH_2)_3$, THPOCH*H*), 2.39 (1H, d, J=4.0 Hz, O*H*), 2.35 (2H, q, J=7.0 Hz, C=CHCH_2), 1.90–1.45 (9H, m, C(CH_3)=C, $OCH_2(CH_2)_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 135.2, 124.8, 98.8, 76.6, 66.6, 62.3, 48.5, 30.6, 28.3, 25.4, 19.5, 12.2. MS (*m*/*e*): 266 $(M+NH_4)^+$, 249 $(M+H)^+$; HR-MS: calcd for $C_{12}H_{25}NO_3Cl$: 266.1523; found: 266.1532.

(*E*)-1-Chloro-3-methyl-6-tetrahydropyranyloxy-2-triisopropylsilyloxy-3-hexene (23). 2,6-Lutidine (13.30 mL, 113.9 mmol) and TIPSOTf (23.0 mL, 85.4 mmol) was successively added to a CH_2Cl_2 (300 mL) solution of **22** (14.17 g, 56.95 mmol) at 0°C. The mixture was stirred for 1 h, quenched with NH_4Cl (sat.) and extracted with ether. The extract was dried over $MgSO_4$ and concentrated. Chromatography (hexane/ethyl acetate, 4:1) afforded **23**, which was used in the next step without delay. IR (neat, ν, cm^{-1}): 2943, 2866, 1464, 1121. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.47 (1H, t, J=7.0 Hz, vinyl), 4.58 (1H, m, OC*H*O), 4.25 (1H, t, J=6.5 Hz, C*H*OTIPS), 3.90–3.80 (1H, m, OC*H*H$(CH_2)_3$), 3.80–3.70 (1H, m, THPOC*H*H), 3.50–3.35 (4H, m, CH_2Cl, THPOCH*H*, OCH*H*$(CH_2)_3$), 2.34 (2H, q, J=7.0 Hz, allyl), 1.85–1.45 (9H, m, C(CH_3)=CH, $OCH_2(CH_2)_3$), 1.04, (21H, m, Si(C*H*$(CH_3)_2)_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 135.9, 125.3, 98.7, 98.6, 78.6, 66.7, 66.6, 62.1, 62.1, 46.8, 30.6, 28.3, 25.5, 19.5, 19.4, 17.9, 17.7, 12.3, 10.9. MS (*m*/*e*): 361 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{18}H_{34}O_3SiCl$: 361.1966; found: 361.1974.

(*E*)-6-Chloro-4-methyl-5-triisopropylsilyloxy-3-hexenol (24). PPTS (1.4 g, 5.6 mmol) was added to a methanol (500 mL) solution of **23** (from the previous procedure). The reaction mixture was stirred for 1 h at 50°C. Upon cooling, it was neutralized with $NaHCO_3$ (300 mL, sat.). Methanol was evaporated and the residue was extracted with ether. The extract was dried over $MgSO_4$ and concentrated. Chromatography (hexane/ethyl acetate, 4:1) afforded alcohol **24** (16.61 g, 92% over two steps) as a colorless oil. IR (neat, ν, cm^{-1}): 3345, 2944, 2892, 2867, 1464, 1107, 1062. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.44 (1H, t, J=7.5 Hz, C(CH_3)=C*H*), 4.27 (1H, dd, J=7.5 and 6.0 Hz, C*H*OTIPS), 3.64 (2H, m, CH_2OH), 3.55–3.40 (2H, m, CH_2Cl), 2.34 (2H, m, C(CH_3)=CHCH_2), 1.64 (3H, s, C(CH_3)=CH), 1.58 (1H, s br, CH_2O*H*), 1.04 (21H, m, Si(C*H*$(CH_3)_2)_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 137.4, 124.8, 78.4, 61.9, 46.4, 31.1, 17.9, 12.2, 10.8. MS (*m*/*e*): 277 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{13}H_{26}O_2SiCl$: 277.1390; found: 277.1388.

(*E*)-6-Chloro-1-methanesulfonyloxy-4-methyl-5-triisopropylsilyloxy-3-hexene (25). Et_3N (36 mL, 257.8 mmol) and MsCl (6.00 mL, 77.3 mmol) were successively added to a CH_2Cl_2 (250 mL) solution of alcohol **24** (16.55 g, 51.6 mmol) at 0°C. After 1 h stirring, it was quenched with NH_4Cl (sat.) and extracted with CH_2Cl_2. The dried extract was evaporated. Chromatography (hexane/ethyl acetate, 4:1) afforded **25** (18.45, 90%) as a pale yellow oil. IR (neat, ν, cm^{-1}): 2944, 2867, 1464, 1357. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.44 (1H, t, J=7.0 Hz, C=C*H*), 4.24 (1H, t, J=6.0 Hz, C*H*OSi), 4.20 (2H, t, J=7.0 Hz, CH_2OMs), 3.45 (2H, m, CH_2Cl), 2.99 (3H, s, CH_3SO_3), 2.52 (2H, q, J=7.0 Hz, C=CHCH_2), 1.64 (3H, s, C(CH_3)=CH), 1.03 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 138.3, 122.2, 78.1, 68.6, 46.4, 37.4, 27.7, 17.9, 12.2, 11.0. MS (*m*/*e*): 355 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{14}H_{28}O_4SiSCl$: 355.1166; found: 355.1163.

(*E*)-Dimethyl-7-chloro-5-methyl-6-triisopropylsilyloxyhept-4-enedicarboxylate (26). Dimethyl malonate (13.2 mL, 115.3 mmol) was added dropwise to a THF/DMF (300 mL, 1:1) suspension of NaH (4.42 g, 110.6 mmol, 60% dispersion in oil) at 23°C. Once the evolution of hydrogen ceased, a solution of **25** (18.38 g, 46.1 mmol) in the same solvent mixture (120 mL) was added by canula. KI was added (11.48, 69.2 mmol) and the mixture was refluxed for 1 h. It was neutralized with NH_4Cl (300 mL, sat.), extracted with hexane/ether (3×300 mL, 1:1) and the dried extract was concentrated. Chromatography (hexane/ethyl acetate, 9:1) afforded **26** (18.89 g, 94%) as a colorless oil. IR (neat, ν, cm^{-1}): 2946, 2867, 1738, 1463, 1436, 1249. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.39 (1H, t, J=7.0 Hz, C=C*H*), 4.23 (1H, t, J=6.5 Hz, C*H*OSi), 3.73 (6H, s, 2×CO_2CH_3), 3.50–3.35 (3H, m, CH_2Cl, C*H*$(CO_2CH_3)_2$, 2.07 (2H, q, J=7.0 Hz, C=CHCH_2), 2.00–1.90 (2H, m, C=CHCH_2CH_2), 1.57 (3H, s, C(CH_3)=CH), 1.03 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 169.7, 135.9, 127.0, 78.5, 52.4, 50.8, 46.6, 28.3, 25.1, 17.9, 12.3, 10.6. MS (*m*/*e*): 391 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{18}H_{32}O_5SiCl$: 391.1707; found: 391.1702.

(2*Z*,4*E*,10*E*)-13-Chloro-7,7-bis(methoxycarbonyl)-11-methyl-1-tetrahydropyranyloxy-12-triisopropylsilyloxytrideca-2,4,10-triene (27). KH (1.02 g, 19.1 mmol, 35% dispersion in oil) was slowly added to a THF/DMF (30 mL, 1:1) solution of **26** (6.92 g, 15.9 mmol) at 0°C. After 30 min, solution of allylic chloride **13** (4.13 g, 191 mmol) in the same solvent mixture (40 mL) was added with canula. It was allowed to warm to 23°C, stirred for 17 h, quenched with NH_4Cl (50 mL, sat.) and extracted with ether. The dried organics were concentrated. Chromatography (toluene/ethyl acetate, 97:3) afforded **27** (4.98 g, 51%) as a colorless oil. IR (neat, ν, cm^{-1}): 2947, 2867, 1736, 1443, 1200. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.36 (1H, dd, J=15.0 and 11.0 Hz, OCH_2CH=CHC*H*=C), 6.05 (1H, t, J=11.0 Hz, OCH_2CH=C*H*), 5.55–5.47 (2H, m, C*H*=CHCH=C*H*), 5.38 (1H, t broad, J=7.0 Hz, C=C*H*), 4.60 (1H, t, J=3.0 Hz, OC*H*O), 4.32 (1H, dd, J=14.0 and 6.5 Hz, THPOC*H*H), 4.22–4.10 (2H, m, THPOCH*H*, C*H*OTIPS), 3.90–3.80 (1H, m, OC*H*H$(CH_2)_3$), 3.70 (6H, s, 2×CO_2CH_3), 3.55–3.35 (3H, m, CH_2Cl, OCH*H*$(CH_2)_3$), 2.70 (2H, d, J=7.5 Hz, CHCH_2C$(CO_2CH_3)_2$), 1.95–1.45 (10H, m, 5×CH_2), 1.01 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.4, 135.2,

130.8, 129.3, 129.0, 127.5, 126.5, 97.8, 78.6, 62.7, 62.1, 57.6, 52.3, 46.7, 36.4, 32.2, 30.6, 25.4, 22.4, 19.4 17.9, 12.3, 10.5. MS (*m/e*): 571 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{29}H_{48}O_7SiCl$: 571.2858; found: 571.2851.

(2*Z*,4*E*,10*E*)-13-Chloro-7,7-bis(methoxycarbonyl)-11-methyl-12-triisopropylsilyloxytrideca-2,4,10-trienol (28). *para*-Toluenesulfonic acid monohydrate (Tos-OH) (362 mg, 19 mmol) was added to a solution of **27** (5.89 g, 9.5 mmol) in methanol (300 mL). After 1 h stirring and neutralization with $NaHCO_3$ (sat.), methanol was evaporated. The aqueous phase was extracted with ether and the dried organics were concentrated. Chromatography (hexane/ethyl acetate, 7:3) afforded **28** (4.88 g, 97%) as a colorless oil. IR (neat, ν, cm^{-1}): 3412, 2866, 1735, 1441, 1243. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.31 (1H, dd, *J*=15.0 and 11.0 Hz, $HOCH_2CH{=}CHCH$), 5.97 (1H, t, *J*=11.0 Hz, $HOCH_2{-}CH{=}CH$), 5.55–5.45 (2H, m, $CH{=}CHCH{=}CH$), 5.35 (1H, t broad, *J*=7.0 Hz, $C{=}CH$), 4.21 (2H, d, *J*=7.0 Hz, CH_2OH), 4.17 (1H, t, *J*=6.5 Hz, CHOTIPS), 3.67 (6H, s, $2\times CO_2CH_3$), 3.45–3.30 (2H, m, CH_2Cl), 2.66 (2H, d, *J*=7.5 Hz, $CHCH_2{-}C(CO_2CH_3)_2$), 2.07 (1H, s broad, OH), 1.90–1.80 (4H, m, $C{=}CHCH_2CH_2$), 1.52 (3H, s, $C(CH_3){=}CH$), 0.98 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 170.3, 135.1, 129.8, 129.3, 129.1, 128.7, 127.3, 78.4, 58.4, 57.6, 52.3, 46.6, 36.3, 32.1, 22.3, 17.8, 12.2, 10.4. MS (*m/e*): 499 $(M-OCH_3)^+$, 487 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{24}H_{40}O_6SiCl$: 487.2282; found: 487.2271.

(3*Z*,5*E*,11*Z*)-Dimethyl-8,8-bis(methoxycarbonyl)-14-chloro-12-methyl-13-triisopropylsilyloxytetradeca-3,5,11-trienedicarboxylate (30). Triphenylphosphine (891 μg, 3.4 mmol) and hexachloroacetone (385 μL, 2.55 mmol) was added successively to a THF (25 mL) solution of alcohol **28** (900 mg, 1.70 mmol) at −20°C. The mixture was stirred for 1 h, quenched with NH_4Cl (25 mL, sat.) and extracted with ether (3×50 mL). The dried extract was concentrated. Chromatography (hexane/ethyl acetate, 7:3) afforded chloride **29** as a pale yellow oil. Due to its instability, this product was immediately used for the next step without being characterized: Dimethyl malonate (580 mL, 5.1 mmol) was added dropwise over 5 min to a THF/DMF (10 mL, 1:1) suspension of KH (226 mg, 4.25 mmol, 35% dispersion in oil). After 30 min, a THF (10 mL) solution of allylic chloride **29** was added with canula. It was stirred for 30 min, neutralized with NH_4Cl (35 mL, sat.), extracted with ether and CH_2Cl_2. The dried organics were concentrated. Chromatography (hexane/ethyl acetate, 4:1) afforded compound **30**, used in the next step without delay. IR (neat, ν, cm^{-1}): 2951, 2867, 1739, 1440, 1388, 1230. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.32 (1H, dd, *J*=15.0 and 11.0 Hz, $CHCH_2CH{=}CHCH$), 5.95 (1H, t, *J*=11.0 Hz, $CHCH_2CH{=}CH$), 5.48 (1H, dt, *J*=15.0 and 7.5 Hz, $CHCH_2CH{=}CHCH{=}CH$), 5.36 (1H, t broad, *J*=6.5 Hz, $C{=}CH$), 5.23 (1H, dd, *J*=15.5 and 7.5 Hz, $CHCH_2CH{=}CH{-}CH{=}CH$), 4.17 (1H, t, *J*=6.5 Hz, CHOTIPS), 3.67 (12H, 2s, $4\times CO_2CH_3$), 3.45–3.30 (3H, m, $CH(CO_2CH_3)_2$, CH_2Cl), 2.69 (4H, t broad, *J*=7.5 Hz, $2\times CH_2CH{=}CH$), 1.90–1.80 (4H, m, $C{=}CHCH_2CH_2$), 1.52 (3H, s, $C(CH_3){=}CH$), 0.99 (21H, m, TIPS). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.3, 169.0, 135.1, 130.7, 128.8, 128.7, 127.4, 125.3, 78.5, 57.6, 52.4, 52.3, 51.3, 46.7, 36.3, 32.1, 27.0, 22.3, 17.8, 12.1, 10.5. MS (*m/e*): 601 $(M-C_3H_7)^+$; HR-MS: calcd for $C_{29}H_{46}O_9SiCl$: 601.2599; found: 601.2594.

(3*Z*,5*E*,11*Z*)-Dimethyl-8,8-bis(methoxycarbonyl)-14-chloro-13-hydroxy-12-methyltetradeca-3,5,11-trienedicarboxylate (31). Tetrabutylammonium fluoride (TBAF) (4.55 mL, 4.55 mmol, 1.0 M in THF) was added to a THF (25 mL) solution of **30** (from the previous procedure) at −20°C. After stirring for 2 h, it was neutralized with NH_4Cl (35 mL, sat.) and extracted with ether. The dried extract was concentrated and chromatographed (hexane/ethyl-acetate, 7:3) to afford **31** (715 mg, 86% over 3 steps) as a colorless oil. IR (neat, ν, cm^{-1}): 3525, 3006, 2852, 1734, 1439, 1272. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.34 (1H, dd, *J*=15.0 and 11.0 Hz, $CH{=}CHCH_2C$, 5.97 (1H, t, *J*=11.0 Hz, $CHCH_2CH{=}CH$), 5.52–5.40 (2H, m, $CH{-}CHCH_2C$, $C{=}CH$), 5.24 (1H, dt, *J*=11.0 and 7.5 Hz, $CHCH_2CH{=}CH$), 4.14 (1H, m, CHOH), 3.69 (12H, s, $4\times CO_2CH_3$), 3.60–3.45 (2H, m, CH_2Cl), 3.37 (1H, t, *J*=7.5 Hz, $CH(CO_2CH_3)_2$), 2.71 (4H, t broad, *J*=7.5 Hz, $2\times CH_2CH{=}CH$), 2.45 (1H, d, *J*=3.5 Hz, OH), 2.00–1.80 (4H, m, CH_2CH_2), 1.58 (3H, s, $C(CH_3){=}CH$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.3, 169.1, 134.3, 130.7, 128.8, 126.9, 125.4, 76.5, 57.5, 52.5, 52.3, 51.4, 48.4, 36.2, 32.0, 27.0, 22.3, 11.9. MS (*m/e*): 471 $(M-OH)^+$, 457 $(M-OCH_3)^+$; HR-MS: calcd for $C_{22}H_{30}O_8Cl$: 457.1629; found: 457.1622.

(3*Z*,5*E*,11*Z*)-Dimethyl-8,8-bis(methoxycarbonyl)-14-chloro-12-methyl-13-oxo-tetradeca-3,5,11-trienedicarboxylate (32). Dess–Martin periodinane (400 mg, 0.944 mmol) was added to a CH_2Cl_2 (5 mL) solution of **31** (384 mg, 0.786 mmol) at 0°C. After 5 min stirring at 23°C, it was neutralized with $NaHCO_3$ (sat.), diluted with CH_2Cl_2 (50 mL) and $Na_2S_2O_3{\cdot}5H_2O$ (1 g) was added. After an additional hour of stirring, it was extracted with CH_2Cl_2. The dried organics were concentrated and chromatographed (hexane/ethyl acetate, 7:3) to afford chloroketone **32** (368 mg, 96%) as a colorless oil; IR (neat, ν, cm^{-1}): 2955, 1735, 1690, 1440, 1271, 1235, 1203. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.55 (1H, t, *J*=7.0 Hz, $C{=}CH$), 6.33 (1H, dd, *J*=15.0 and 11.0 Hz, $CH{=}CHCH_2C$), 5.94 (1H, t, *J*=11.0 Hz, $CHCH_2CH{=}CH$), 5.43 (1H, dt, *J*=15.0 and 7.5 Hz, $CH{=}CHCH_2C$), 5.23 (1H, dt, *J*=11.0 and 7.5 Hz, $CHCH_2CH{=}CH$), 4.38 (2H, s, CH_2Cl), 3.66 (12H, 2s, $4\times CO_2CH_3$), 3.34 (1H, t, *J*=7.5 Hz, $CH(CO_2CH_3)_2$), 2.70 (4H, m, $2\times CH_2CH{=}CH$), 2.20–2.10 (2H, m, $C{=}CHCH_2$), 1.95–1.90 (2H, m, $C{=}CHCH_2CH_2$), 1.73 (3H, s, $C(CH_3){=}CH$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 192.1, 171.0, 169.0, 142.7, 135.6, 130.5, 129.1, 128.2, 125.8, 57.2, 52.4, 51.2, 45.0, 36.4, 31.2, 27.0, 24.0, 11.3; MS (*m/e*): 455 $(M-OCH_3)^+$, 450 $(M-HCl)^+$; HR-MS: calcd for $C_{22}H_{28}O_8Cl$: 455.1473; found: 455.1466.

(3*E*,5*Z*,11*E*)-Tetramethyl-11-methyl-10-oxo-3,5,11-cyclotetradecatriene-1,1,8,8-tetracarboxylate (2) and (3*E*,5*Z*,11*E*,17*E*,19*Z*,25*E*)-octamethyl-11,25-dimethyl-10,24-dioxo-3,5,11,17,19,25-cyclooctacosahexaene-1,1,8,8,15,15,22,22-octacarboxylate (33). An acetonitrile (1 mL) solution of chloroketone **32** (50 mg, 0.102 mmol) was added to a vigorously stirred acetonitrile (60 mL) suspension of Cs_2CO_3 (334 mg, 1.02 mmol) and CsI (295 mg, 1.02 mmol). The mixture was stirred in the dark for 48 h at 23°C, filtered through a silica pad (3 cm) and

concentrated. Chromatography (hexane/ethyl acetate, 4:3) afforded both title compounds. Macrocycle **2**: 10 mg, (21%) as a white solid: mp 143–145°C (hexane/ether, 9:1). IR (neat, ν, cm^{-1}): 2954, 2853, 1732, 1663, 1436, 1289, 1172. ^1H NMR (300 MHz, δ, C_6D_6, 350 K): 6.23 (1H, t, J=7.5 Hz, C=C*H*), 6.02 (1H, t, J=11.0 Hz, CH_2CH=C*H*), 5.76 (1H, dd, J=15.0 and 11.0 Hz, C*H*=$CHCH_2$), 5.30 (1H, dt, J=15.0 and 7.0 Hz, CH=C*H*CH_2), 5.16 (1H, dt, J=11.0 and 9.0 Hz, CH_2CH=CH), 3.49 and 3.36 (12H, 2s, 4×CO_2CH_3), 3.48 (2H, s, $ClCH_2C$=O), 3.00 and 2.70 (2×2H, 2d, J=7.0 and 9.0 Hz, CH=$CHCH_2$), 2.15–2.05 (2H, m, C=$CHCH_2$), 2.00–1.90 (2H, m, C=$CHCH_2CH_2$), 1.74 (3H, s, $C(CH_3)$=CH). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 198.7, 171.3, 170.6, 146.1, 135.0, 132.9, 131.5, 127.8, 124.4, 58.3, 55.2, 52.7, 38.2, 34.9, 30.0, 29.7, 24.3, 11.2; MS (*m*/*e*): 450 $(M)^+$; HR-MS: calcd for $C_{23}H_{30}O_9$: 450.1890; found: 450.1884. Dimer 33: 6 mg, (13%) colorless oil: IR (neat, ν, cm^{-1}): 2955, 1732, 1669, 1436, 1201. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.58 (2H, t, J=7.0 Hz, 2×C=C*H*), 6.20–6.00 (4H, m, 2×CH_2CH=C*H*C*H*=$CHCH_2$), 5.45 (2H, dt, J=15.0 and 7.0 Hz, 2×CH_2CH=CHCH=C*H*CH_2), 5.18 (2H, dt, J=10.0 and 9.0 Hz, 2×CH_2 C*H*=CHCH=$CHCH_2$), 3.73 and 3.71 (24H, 2s, 8×CO_2CH_3), 3.28 (4H, s, 2×CH_2C=O), 2.85 (4H, d, J=9.0 Hz, 2×CH_2CH=CHCH=$CHCH_2$), 2.65 (4H, d, J=7.0 Hz, 2×CH_2CH=CHCH=C*H*CH_2), 2.15–2.05 (4H, m, 2×$C(CH_3)$=C*H*CH_2), 2.00–1.90 (4H, m, 2×$C(CH_3)$=$CHCH_2CH_2$), 1.70 (6H, s, 2×$C(CH_3)$=CH). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 198.0, 170.9, 141.5, 137.3, 132.1, 129.1, 128.3, 125.1, 57.5, 55.1, 52.9, 52.7, 40.4, 36.1, 31.2, 30.9, 24.1, 11.5. MS (*m*/*e*): 900 (M^+); HR-MS: calcd for $C_{46}H_{60}O_{18}$: 900.3779; found: 900.3770.

(3*E*,9*E*,11*Z*)-1-Chloro-7,7-bis(methoxycarbonyl)-3-methyl-13-tetrahydropyranyloxytrideca-3,9,11-trien-2-ol (34). TBAF (13.0 mL, 13.0 mmol, 1.0 M in THF) was added to a solution of **27** (1.6 g, 2.60 mmol) in THF (10 mL), at −20°C. Upon stirring for 1 h at −20°C, it was neutralized with NH_4Cl (sat.) and extracted with ether. The dried extract was concentrated and chromatographed (hexane/ethyl acetate, 7:3) to afford alcohol **34** (994 mg, 83%) as a colorless oil; IR (neat, ν, cm^{-1}): 3448, 2870, 1732, 1440, 1341, 1268. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.36 (1H, dd, J=15.0 and 11.0 Hz, C*H*=$CHCH_2C$), 6.05 (1H, t, J=11.0 Hz, OCH_2CH=C*H*), 5.55–5.45 (3H, m, C*H*=CHCH=C*H*, C=C*H*), 4.61 (1H, t, J=3.0 Hz, OC*H*O), 4.30 (1H, dd, J=13.0 and 6.5 Hz, THPOC*H*H), 4.15–4.10 (2H, m, C*H*OH, THPOCH*H*), 3.90–3.80 (1H, m, OC*H*$H(CH_2)_3$), 3.70 (6H, s, 2×CO_2CH_3), 3.60–3.45 (3H, m, CH_2Cl, OCH*H*$(CH_2)_3$), 2.69 (2H, d, J=7.5 Hz, CH=$CHCH_2$), 2.47 (1H, t, J=3.0 Hz, O*H*), 2.00–1.50 (13H, m, $C(CH_3)$=$CHCH_2CH_2$, $OCH_2(CH_2)_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 171.4, 134.3, 130.8, 129.2, 127.0, 126.6, 97.8, 76.5, 62.7, 62.2, 57.5, 52.4, 48.5, 36.3, 32.1, 30.5, 25.4, 22.4, 19.3, 12.0. MS (*m*/*e*): 476 $(M+NH_4)^+$. HR-MS: calcd for $C_{23}H_{39}NO_7Cl$: 476.2415; found: 476.2409.

(3*E*,9*E*,11*Z*)-1-Chloro-7,7-bis(methoxycarbonyl)-3-methyl-13-tetrahydropyranyloxytrideca-3,9,11-trien-2-one (35). Dess–Martin periodinane (2.72 g, 6.41 mmol) was added to a solution of alcohol **34** (980 mg, 2.13 mmol) in CH_2Cl_2 (50 mL) at 0°C. Upon stirring for 1 h at 23°C, it was neutralized with $NaHCO_3$ (sat.) and $Na_2S_2O_3$ (2 g) was added. It was stirred for an additional hour then extracted with CH_2Cl_2. The dried extract was concentrated and chromatographed (hexane/ethyl acetate, 7:3) to afford chloroketone **35** (948 mg, 98%) as a colorless oil. IR (neat, ν, cm^{-1}): 2951, 2870, 1733, 1690, 1439, 1267, 1201. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.53 (1H, t, J=7.0 Hz, C=C*H*), 6.36 (1H, dd, J=15.0 and 11.0 Hz, C*H*=$CHCH_2C$), 6.03 (1H, t, J=11.0 Hz, OCH_2CH=C*H*), 5.50–5.40 (2H, m, C*H*=CHCH=C*H*), 4.57 (1H, t, J=3.0 Hz, OC*H*O), 4.38 (2H, s, CH_2Cl), 4.29 (1H, dd, J=13.0 and 7.0 Hz, THPOC*H*H), 4.11 (1H, dd, J=13.0 and 7.0 Hz, THPOCH*H*), 3.85–3.75 (1H, m, OC*H*$H(CH_2)_3$), 3.69 (6H, s, 2×CO_2CH_3), 3.67–3.40 (1H, m, OCH*H*$(CH_2)_3$), 2.70 (2H, d, J=7.5 Hz, CH=$CHCH_2$), 2.20–2.10 (2H, m, C=$CHCH_2$), 2.00–1.90 (2H, m, C=$CHCH_2CH_2$), 1.85–1.45 (9H, m, $C(CH_3)$=CH, $OCH_2(CH_2)_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 192.1, 171.0, 142.6, 133.9, 130.5, 129.3, 128.7, 126.8, 97.8, 67.0, 62.6, 62.1, 57.3, 52.5, 44.9, 36.6, 31.3, 30.5, 25.3, 24.0, 19.3, 11.4. MS (*m*/*e*): 474 $(M+NH_4)^+$, 355 $(M-OTHP)^+$. HR-MS: calcd for $C_{23}H_{37}NO_7Cl$: 474.2258; found: 474.2254.

(4*E*,10*E*,12*Z*)-Dimethyl-8,8-bis(methoxycarbonyl)-4-methyl-3-oxo-14-tetrahydropyranyloxytetradeca-4,10,12-trienedicarboxylate (36). Dimethyl malonate (0.435 mL, 3.82 mmol) was added dropwise to a THF/DMF (100 mL, 1:1) suspension of NaH (226 mg, 4.25 mmol, 60% dispersion in oil). Once the evolution of hydrogen gas ceased, a solution of chloroketone **35** (810 mg, 1.91 mmol) in THF (2 mL) was added with canula. It was heated to 60°C, stirred for 3 h, quenched with NH_4Cl (sat.) and extracted with ether. The extract was dried over $MgSO_4$ and evaporated. Chromatography (hexane/ethyl acetate, 4:1) of the crude product afforded **36** (575 mg, 55%) as a colorless oil. IR (neat, ν, cm^{-1}): 2953, 1735, 1671, 1437, 1443, 1269, 1201. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.62 (1H, t, J=7.0 Hz, $C(CH_3)$=C*H*), 6.39 (1H, dd, J=15.0 and 11.0 Hz, $THPOCH_2CH$=CHC*H*=CH), 6.06 (1H, t, J=11.0 Hz, $THPOCH_2CH$=C*H*CH=CH), 5.55–5.45 (2H, m, $THPOCH_2CH$=CHCH=C*H*), 4.60 (1H, t, J=3.0 Hz, OC*H*O), 4.32 (1H, dd, J=13.0 and 7.0 Hz, THPOC*H*H), 4.14 (1H, dd, J=13.0 and 7.0 Hz, THPOCH*H*), 3.90 (1H, t, J=7.0 Hz, $CH(CO_2CH_3)_2$), 3.85–3.80 (1H, m, OC*H*H $(CH_2)_3$), 3.73 and 3.71 (12H, 2s, 4×CO_2CH_3), 3.50–3.45 (1H, m, OCH*H*$(CH_2)_3$), 3.28 (2H, d, J=7.0 Hz, CH_2CH–$(CO_2CH_3)_2$), 3.28 (2H, d, J=7.5 Hz, CH=$CHCH_2C$ $(CO_2CH_3)_2$), 2.20–2.10 (2H, m, $C(CH_3)$=CH–CH_2), 2.00–1.90 (2H, m, $C(CH_3)$=$CHCH_2CH_2$), 1.85–1.45 (9H, m, $C(CH_3)$=CH, $OCH_2(CH_2)_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 197.4, 171.1, 169.5, 141.7, 137.1, 130.7, 129.3, 128.8, 97.8, 67.1, 62.6, 62.2, 57.4, 52.7, 52.5, 46.8, 36.7, 31.5, 30.5, 25.4, 23.9, 19.4, 11.1. MS (*m*/*e*): 552 (M^+). HR-MS: calcd for $C_{28}H_{40}O_{11}$: 552.2570; found: 552.2882.

(4*E*,10*E*,12*Z*)-Dimethyl-8,8-bis(methoxycarbonyl)-14-hydroxy-4-methyl-3-oxotetradeca-4,10,12-trienedicarboxylate (37). Tos-OH (17 mg, 10 mol%) was added to a methanol (300 mL) solution of **36** (485 mg, 0.878 mmol). Upon stirring for 1 h, it was quenched with $NaHCO_3$ (5 mL, sat.). Methanol was evaporated and the residue was extracted with ether. The dried extract was evaporated and chromatographed (hexane/ethyl acetate, 1:1) to afford **37**

(385 mg, 94%) as a colorless oil. IR (neat, ν, cm^{-1}): 3542, 3005, 2955, 1732, 1668, 1436, 1272, 1100. ^1H NMR (300 MHz, δ, $CDCl_3$): 6.62 (1H, t, J=7.0 Hz, C=C*H*), 6.37 (1H, dd, J=15.0 and 11.0 Hz, $HOCH_2CH$=CHC*H*), 6.01 (1H, t, J=11.0 Hz, $HOCH_2CH$=C*H*), 5.60–5.45 (2H, m, C*H*=CH–CH=C*H*), 4.26 (2H, d, J=7.0 Hz, CH_2OH), 3.90 (1H, t, J=7.0 Hz, $CH(CO_2CH_3)_2$), 3.73 and 3.71 (12H, 2s, 4×CO_2CH_3), 3.28 (2H, d, J=7.0 Hz, $CH_2CH(CO_2CH_3)_2$), 2.72 (2H, d, J=7.5 Hz, $CH_2C(CO_2CH_3)_2$), 2.20–2.10 (2H, m, C=CHCH_2), 2.00–1.90 (2H, m, C=CHCH_2CH_2), 1.72 (3H, s, C(CH_3)=CH). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 197.5, 171.1, 169.5, 141.7, 137.1, 129.9, 129.3, 129.1, 129.0, 63.1, 58.6, 57.4, 52.7, 52.6, 46.8, 36.7, 36.5, 31.4, 23.9, 11.1. MS (*m/e*): 468 (M^+); HR-MS: calcd for $C_{23}H_{32}O_{10}$: 468.1995; found: 468.2001.

(3*E*,5*Z*,11*E*)-Tetramethyl-11-methyl-10-oxo-3,5,11-cyclotetradecatriene-1,1,8,8-tetracarboxylate (2). Triphenylphosphine (196 mg, 0.747 mmol) and hexachloroacetone (65 μL, 0.411 mmol) was added successively to a THF (10 mL) solution of alcohol **37** (175 mg, 0.374 mmol) at −20°C. Upon stirring for 1 h, the reaction mixture was allowed to warm to 23°C for another additional hour of stirring. It was quenched with NH_4Cl (sat.) and extracted with ether. The dried extract was concentrated and chromatographed (hexane/ethyl acetate, 7:3) to afford sensitive allylic chloride **38** (180 mg, 99%) as a colorless oil, which was used immediately in the next step without being characterized: An acetonitrile (4 mL) solution of chloride **38** (136 mg, 0.279 mmol) was added slowly via syringe pump over 10 h to a vigorously stirred acetonitrile (160 mL) suspension of Cs_2CO_3 (909 mg, 2.79 mmol) and CsI (404 mg, 1.40 mmol) at 65°C. After an additional 7 h stirring at 65°C, the cooled reaction mixture was filtered through a silica pad (3 cm) and evaporated. (*Note*: small quantity of chloride **38** solution remaining at the tip of the syringe was shown homogenous by TLC analysis, indicating its stability during the reaction period.) Chromatography (hexane/ethyl acetate, 7:3) afforded macrocycle **2** (68 mg, 54%), which was identical with that obtained by the former macrocyclization of compound **32**.

4aβ,4bα,8aα,10aβ-Tetramethyl-4a-methyl-4-oxo-1,3,4,4a,4b,5,6,8,8a,10a-decahydrophenanthrene-2,2,7,7-tetracarboxylate (39). A solution of macrocycle **2** (28 mg, 62 μmol) in dry toluene (0.5 mL, previously degased with five freeze–thaw cycles) was heated in a vacuum sealed Pyrex tube (washed sequentially with aqueous NH_4OH, water and acetone before drying) for 3 h at 170°C in a temperature controlled oven. Upon cooling, the tubes were opened and the content was evaporated. Preparative TLC (hexane/ethyl acetate, 3:2) afforded tricycle **39** (26 mg, 93%) as a white solid. Mp: 148–150°C (hexane/ether, 9:1). IR (neat, ν, cm^{-1}): 2953, 2853, 1784, 1433, 1248, 1203, 1124, 1081. ^1H NMR (300 MHz, δ, $CDCl_3$): 5.32–5.22 (2H, AB, J_{AB}=10.5 Hz, C*H*=C*H*), 3.71, 3.67, 3.65 and 3.60 (12H, 4s, 4×CO_2CH_3), 2.96 (1H, dd, J=15.0 and 2.0 Hz, C_3H), 2.65–2.35 (7H, m, C_1H_2, C_3H, C_8H_2, $C_{8a}H$, $C_{10a}H$), 2.20–2.13 (2H, m, C_6H_2), 1.60–1.40 (3H, m, $C_{4b}H$, C_5H_2), 1.17 (3H, s, $C_{4a}CH_3$). ^{13}C NMR (75 MHz, δ, $CDCl_3$): 210.0, 172.8, 171.5, 171.1, 170.8, 131.1, 129.1, 54.8, 53.1, 52.7, 52.4, 52.1, 49.6, 41.7, 38.7, 37.9, 34.5, 31.0, 30.7, 23.8, 18.2. MS (*m/e*): 450 (M^+); HR-MS: calcd for $C_{23}H_{30}O_9$: 450.1890; found: 450.1884.

4aβ,4bα,8aα,10aβ-Tetramethyl-4a-methyl-4-oxo-1,3,4,4a,4b,5,6,8,8a,10a-decahydrophenanthrene-2,2,7,7-tetracarboxylate (39). $SnCl_4$ (60 μL, 60 μmol, 1 M in CH_2Cl_2) was added to a CH_2Cl_2 (1 mL) solution of macrocycle **2** (6 mg, 13 μmol) at 23°C. It was stirred for 30 min at 23°C then for 1 h at 40°C. A blue coloration was observed. Water was added and the mixture was extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and concentrated. Preparative TLC (hexane/ethyl acetate 3:2) of the residue afforded tricycle **39** as a white solid (5 mg 83%), which was identical to that obtained in the previous procedure.

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