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Transannular Diels-Alder Reaction Studies with an Activated Dienophile. An Enantioselective Synthesis of an A.B.C.[6.6.6.] *Trans-Syn-Cis* Tricycle.[1]

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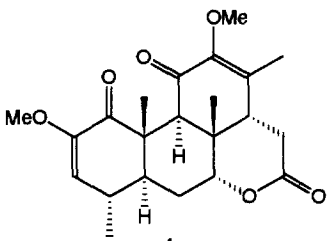
Abstract: *The synthesis and transannular Diels-Alder reaction of a chiral 14 membered trans-cis-cis (TCC) macrocyclic triene with an activated dienophile leading to an A.B.C.[6.6.6.] tricyclic compound are described. The outcome of the TADA reaction under thermal and catalyzed conditions is discussed.*

Introduction

Our laboratory has been developing in recent years, a strategy for the synthesis of polycyclic compounds via the transannular Diels-Alder reaction (TADA)[2]. In 1993, we reported[3] a transannular cycloaddition [4+2] of a TCC macrocyclic triene which afforded a tricyclic compound with an A.B.C. *trans-syn-cis* (TSC) ring junction stereochemistry. Our goal was to study the TADA reaction with an activated dienophile and to induce the relative diastereoselectivity and absolute stereochemistry with the help of two adjacent chiral centers on the macrocycle. If successful, this strategy could be used for the total synthesis of quassine **1** and bruceantine **2**[4,5] (Scheme 1), two members of the quassinoid family.



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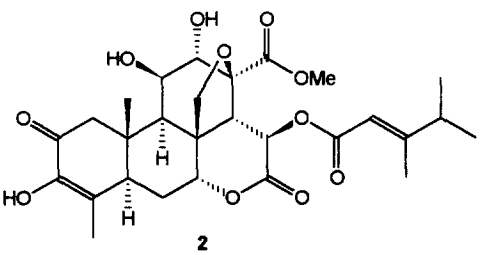

2

Scheme 1

Chemistry

The synthesis was started with pivaloate protection of commercial nerol followed by selective ozonolysis[6] to afford the aldehyde **3** (Scheme 2). Reduction of **3** followed by protection of the resulting alcohol **4** gave the silyloxyether **5**. Then an efficient deprotection/oxidation sequence[7] carried out on **5**

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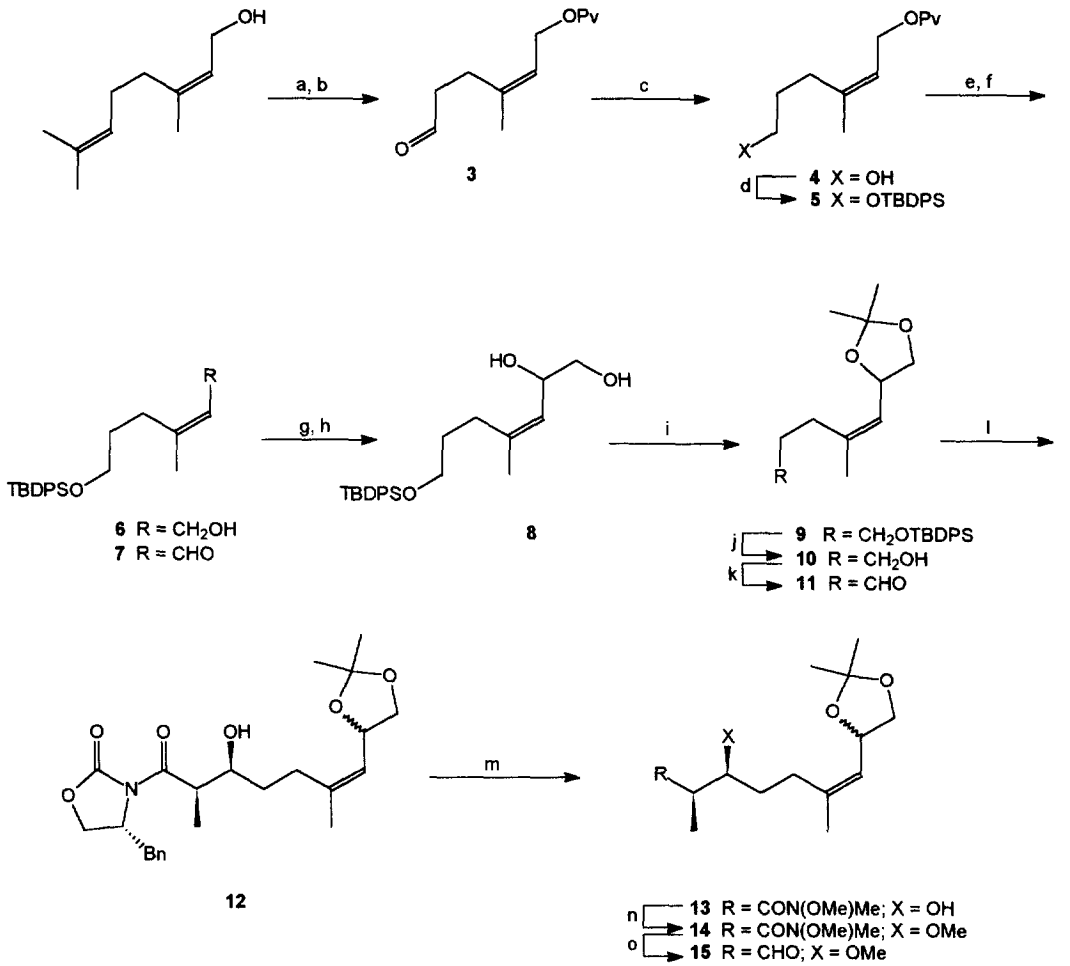
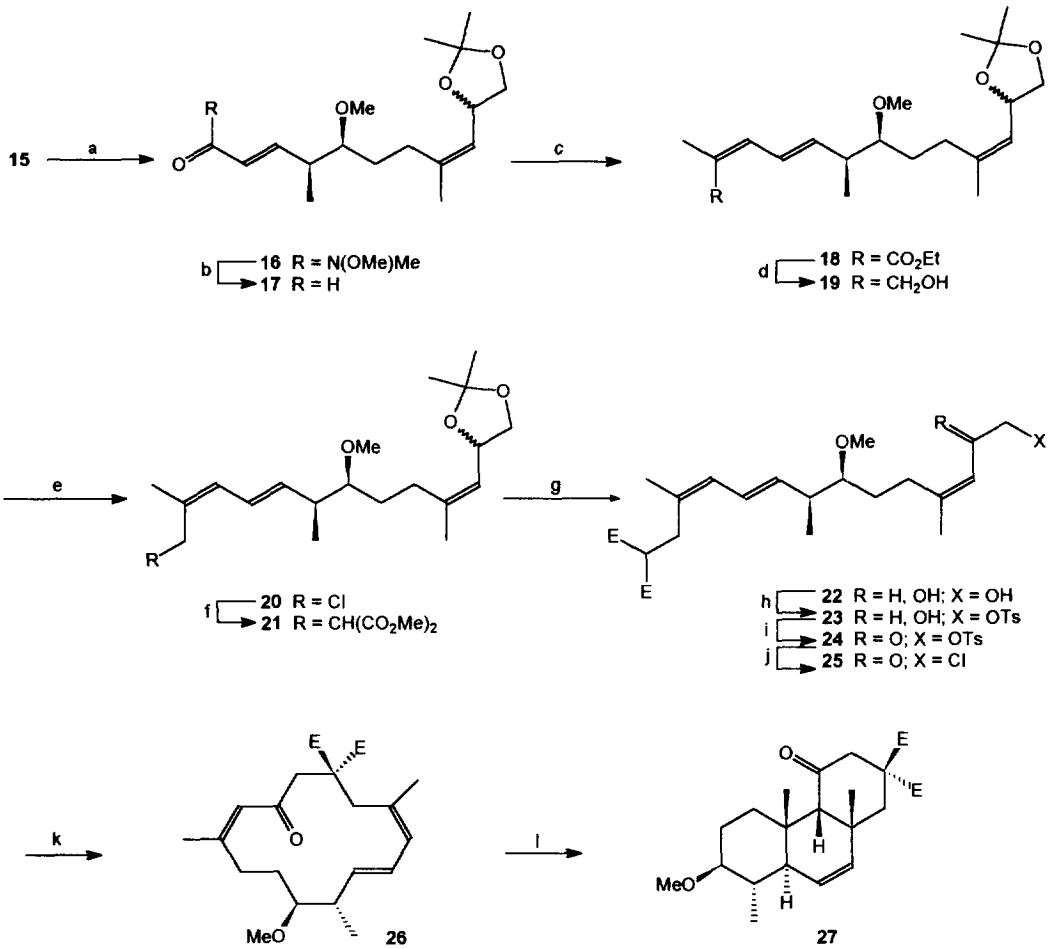
furnished the aldehyde **7** in good yield. The aldehyde **7** was treated with the Grignard's reagent $(CH_3)_2CHOSi(CH_3)_2CH_2MgCl$ to afford an unstable adduct which was oxidized immediately[8] to give the diol **8** in 74% yield. A subsequent protection of the formed diol **8** afforded acetonide **9**.



(a) PvCl, pyridine, CH_2Cl_2, 0°C; (b) O_3, CH_2Cl_2 -78°C then Zn(s), CH_3COOH, 55% for two steps; (c) $NaBH_4$, MeOH, 25°C, 58%; (d) TBDPSCl, imidazole, THF, 93%; (e) DIBAH, THF, -78°C; (f) $(COCl)_2$, DMSO, CH_2Cl_2, -78°C then Et_3N, 99% for two steps; (g) chloro(dimethyl)isopropoxymethylsilane, Mg, THF, -78°C; (h) H_2O_2, $NaHCO_3$, MeOH, reflux, 74% for two steps; (i) 2,2-dimethoxypropane, PTSA, acetone, 98%; (j) TBAF, THF, 99%; (k) see (f), 83%; (l) (R)-3-(1-oxopropyl)-4-benzyl-2-oxazolidinone, nBu_2BOTf, CH_2Cl_2, 0°C to -78°C, 66%, (m) $Al(Me)_3$, NH(OMe)Me HCl, CH_2Cl_2, 0°C, 87%; (n) MeI, NaH, THF/DMF, 0°C, 94%; (o) see (e), 99%.

Scheme 2

Cleavage of the silylether gave the alcohol **10** in high yield. Swern oxidation of the alcohol **10** followed by Evans asymmetric aldolization[9] gave the adduct **12** in 66% yield. The chiral auxiliary was removed via transamidation, according to Weinreb's technique[10], yielding the amide **13**. The secondary alcohol **13** was protected as a methylether[11] and the amide **14** was reduced to furnish the chiral aldehyde **15** in high yield.

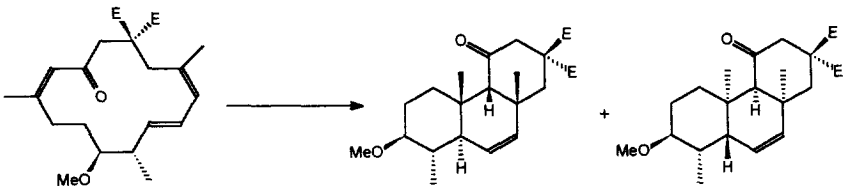


(a) $(MeO)_2P(O)CH_2CON(Me)OMe$, NaH, Et_2O, 0°C, 87%; (b) DIBAH, THF, -78°C, 85%; (c) $(CF_3CH_2O)_2P(O)CH(CH_3)CO_2Et$, KHMDS, 18-crown-6 ether, THF, -78°C, 93%; (d) DIBAH, CH_2Cl_2, -78°C, 100%; (e) hexachloroacetone, PPh_3, 2,6-lutidine, THF, -40°C; (f) dimethylmalonate, KH, KI, 18-crown-6 ether, toluene, 40°C, 82% for two steps; (g) AcOH, H_2O r.t., 99%; (h) TsCl, DMAP, Et_3N, CH_2Cl_2, -5°C, 74%; (i) Dess-Martin periodinane, CH_2Cl_2, r.t., 80%; (j) LiCl, DMF, r.t., 100%; (k) Cs_2CO_3, DMF, 45°C, 66%; (l) toluene, 220°C, 20 h, 90%.

Scheme 3

A stabilized Wittig[12] reaction followed by reduction afforded the *trans*-α,β unsatured aldehyde **17** (Scheme 3). A second olefination according to Still's method[13] followed by the reduction of the ester **18** gave the TCC triene **19**. Chlorination according to Schreiber's method[14] gave an unstable allylic chloride **20** which was immediately alkylated with the potassium salt of dimethylmalonate yielding acetonide **21** which under aqueous acidic conditions afforded the diol **22**. A three-step sequence of monotosylation, oxidation[15] and chlorination were then used to produce the chloroketone **25** in good yield. The macrocyclization was carried out in dry DMF with cesium carbonate at 40°C to furnish the 14-membered macrocyclic TCC triene **26** (Scheme 3) in 66% yield. The absolute configuration of **26** was confirmed by X-ray diffraction analysis (Figure 1). The results of thermal and catalyzed TADA reactions of TCC macrocycle **26** are given in Table 1. In the case of thermal TADA reaction, the cycloaddition gave only one tricycle **27** with a *trans-syn-cis* (TSC) stereochemistry as confirmed by X-ray diffraction analysis (Figure 2), while the other tricycle **28** was not observed. In the Lewis acid catalyzed TADA case, the Diels-Alder adduct was not observed, we could identify only the unreacted triene or degradation products.

Table 1. Results of TADA reaction for the TCC macrocyclictriene.



26 **27** **28**

Entry	Method[a)]	Temp., time	Yield[b)]	Products	Ratio[c)]
1	Thermal	272°C, 11 h	92%	**27**	>25:1
2	Thermal	220°C, 20 h	90%	**27**	>25:1
3	Thermal	190°C, 20 h	---	**27/26**	66:33
4	$SnCl_4$	60°C, 5 h	---	**26**	---
5	$SnCl_4$	110°C, 5 h	---	deg.	---
6	BF_3OEt_2	60°C, 5 h	---	**26**	---
7	BF_3OEt_2	110°C, 5h	---	deg.	---
8	Me_2AlCl	70°C, 5 h	---	**26**	---
9	Me_2AlCl	110°C, 5 h	---	deg.	---
10	$TiCl_4$	60°C, 5h	---	deg.	---

a) all reactions were performed in toluene.

b) isolated yield.

c) by N.M.R.^1H

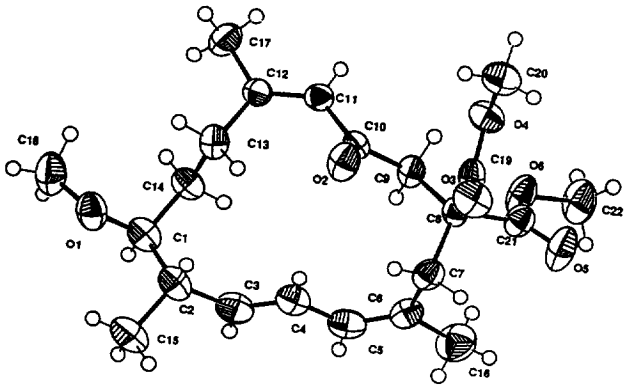


Figure 1

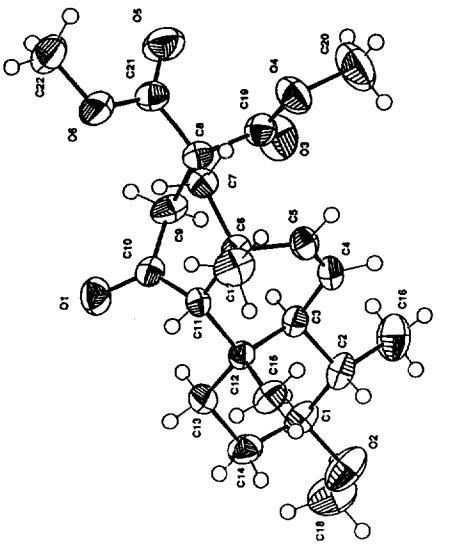
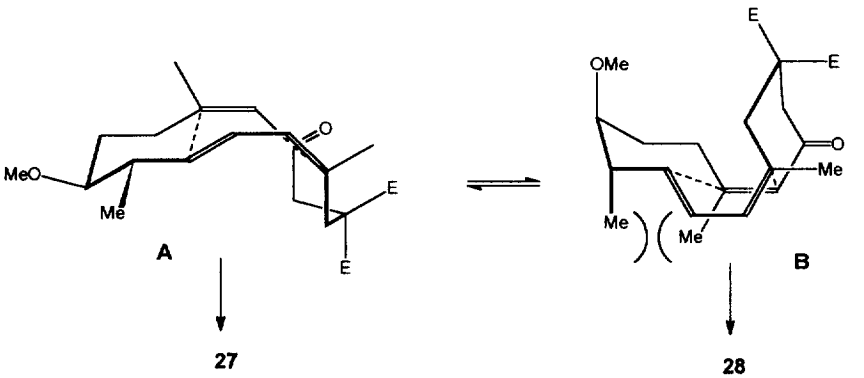


Figure 2

Results and Discussion

The high diastereoselectivity observed in the thermal TADA reaction can be explained by comparing the two possible transition states (Scheme 4) **A** and **B**. The transition state **B** is less favored than **A** as the methoxy and methyl substituents have to take an unfavored pseudo diaxial orientation resulting in severe steric interactions. This is not the case in transition state **A** where the two substituents are pseudoequatorial in a chair like transition state, the preferential formation of **27** over **28** is thus readily explained.



Scheme 4

At first glance, it is expected that Lewis acids should decreased the reaction temperature of the TADA reaction.[16] The results show that it is not the case here. However this apparently unusual behavior can be explained by the fact that molecular models show that to reach the transition state **A**, there must be a

considerable twisting of the enone system. In other words, this is an unusual case where the carbonyl group must first be deconjugated with the olefin in order to reach the chair-boat-chair geometry required for the Diels-Alder transition state.[17] Since Lewis acids increase the conjugation, they have a detrimental influence on the rate of reaction, contrary to what is normally observed. A similar result was also observed with another TCC macrocycle, harboring no methyl group on the diene.[18,19]

EXPERIMENTAL

All reactions were performed under nitrogen atmosphere with oven (150°C) or flame-dried glassware. All solvents were distilled prior to use; diethyl ether and tetrahydrofuran were dried by distilling over sodium benzophenone ketyl. Toluene, acetonitrile, dichloromethane and dimethylformamide were distilled over calcium hydride. Cesium carbonate and lithium chloride were flame-dried under reduced pressure before use. Analytical and preparative thin-layer chromatographies were carried out on precoated glass plates (0.25 mm) with 60 F-250 silica gel (Merck). Materials were detected by visualization under an ultraviolet lamp and/or by spraying with a solution of phosphomolybdic acid (10% in ethanol) followed by heating on a hot plate. Column chromatography was performed with 60 silica gel (230-400 mesh, Merck). Infrared spectra (IR) were taken on a Perkin-Elmer 1600 FT-IR spectrometer. The optical rotation ($[\alpha]_D$) measurements were obtained with a Perkin-Elmer 141 polarimeter. Proton and carbon nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AC-300 instrument. The following abbreviations were used: s, singulet; d, doublet; t, triplet; q, quartet; and m, multiplet. Chemical shifts are reported in δ values relative to chloroform (7.26 ppm) for ^1H NMR and (77.0 ppm) for ^{13}C NMR as internal standard. Where necessary COSY, NOESY and J-resolved were performed. Mass spectral (MS) assays were obtained on a VG Micromass ZAB-2F instrument. Melting points of crystalline materials were determined on a Büchi M-50 and on a Reichert appartatus and are uncorrected. Crystallographic analyses were performed on an Enraf-Nonius CAD-4 diffractometer.

(*Z*)-Methyl-1-(trimethylacetoxy)hex-2-en-6-al (3)

To a solution of nerol (50 g, 0.324 mol) in dichloromethane (250 mL) was added pyridine (51.26 g, 0.648 mol) and pivaloyl chloride (58.6 g, 0.486 mol) at 0°C. The mixture was stirred for 1.5 h at room temperature and the reaction was quenched with aqueous satured ammonium chloride (250 mL). The resulting mixture was extracted several times with dichloromethane and the combined organic phase was dried on magnesium sulfate, filtered and concentrated.

The crude was dissolved in dichloromethane (1.25 L) and ozone was bubbled at -78°C. The reaction was monitored by TLC until the starting material had almost entirely disappeared. The reaction was quenched with acetic acid (350 mL) and zinc dust (190.65 g, 2.916 mol) and the slurry mixture was strirred for 2 h at room temperature. The solid was removed by filtration on celite pad and the filtrate was washed (3X) with aqueous satured sodium bicarbonate. The organic phase was dried over magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (20% ethyl acetate in hexane) to afford **3** as a colorless oil (37.9 g, 55%).

IR (neat): υ = 2970, 2725, 1726, 1155 cm^{-1} .

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.75 (1H, d, J = 1.5 Hz, CH_2CHO), 5.34 (1H, t, J = 7 Hz, $CH_2(CH_3)C=CHCH_2OPv$), 4.53 (2H, d, J = 7 Hz, CH_2OPv), 2.50 (4H, m, CH_2CH_2), 1.72 (3H, s, $CH_2(CH_3)C=CH$), 1.18 and 1.16 (9H, 2s, $O_2CC(CH_3)_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.4, 184.5, 178.4, 139.8, 120.8, 60.6, 42.1, 38.9, 27.1, 24.4, 23.0.

MS: m/e = 155 ($M^+ - C_4H_9$).

(*Z*)-3-Methyl-1-(trimethylacetate)hex-2-en-6-ol (4)

To a solution of aldehyde **3** (37.90 g, 0.179 mol) in methanol (300 mL) was added slowly $NaBH_4$ (8.10 g, 0.214 mol) at 0°C. The resulting mixture was strirred for 30 min and the reaction was quenched with aqueous satured ammonium chloride (300 mL). The mixture was extracted several times with diethyl ether. The organic phase was washed with brine and dried on magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (30% ethyl acetate in hexane) to give **4** as a colorless oil (22.28 g, 58%).

IR (neat): υ = 3382, 2966, 1726, 1155 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.32 (1H, t, J = 7 Hz, $CH_2(CH_3)C=CH$), 4.56 (2H, d, J = 7 Hz, CH_2OPv), 3.59 (2H, t, J = 6 Hz, $HOCH_2$), 2.18 (2H, t, J = 7 Hz, $CH_2(CH_3)C=CH$), 1.73 (3H, s, $CH_2(CH_3)C=CH$), 1.67 (2H, m, $HOCH_2CH_2$), 1.16 (9H, s, $O_2CC(CH_3)_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.7, 141.9, 119.9, 61.8, 61.0, 38.7, 30.5, 28.0, 27.1, 23.2.

MS: m/e = 215 (M^+- H).

HMRS: calcd. for $C_{12}H_{23}O_3$: 215.1647; found: 215.1646.

(*Z*)-6-(*tert*-Butyldiphenylsiloxy)-3-methyl-1-(trimethylacetoxy)hex-2-ene (5)

To a solution of alcohol **4** (10.05 g, 46.9 mmol) in THF (200 mL) was added *tert*-butylchlorodiphenylsilane (15.47 g, 56 mmol) and imidazole (5.47 g, 93.8 mmol) at room temperature. After stirring for 1 h, the reaction was quenched with aqueous satured ammonium chloride. The resulting mixture was extracted (3X) with diethyl ether and the combined phases were dired over magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (10% ethyl acetate in hexane) to furnish **5** as a colorless oil (20.36 g, 96%).

IR (neat): υ = 2961, 2858, 1726, 1111 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68 and 7.42 (10H, 2m, $Si(C_6H_5)_2$), 5.32 (1H, t, J = 7 Hz, $CH_2(CH_3)C=CH$), 4.56 (2H, d, J = 7 Hz, CH_2OPv), 3.67 (2H, t, J = 6 Hz, $TBDPSOCH_2$), 2.18 (2H, t, J = 7 Hz, $CH_2(CH_3)C=CH$), 1.73 (3H, s, $CH_2(CH_3)C=CH$), 1.67 (2H, m, $TBDPSOCH_2CH_2$), 1.19 (9H, s, $O_2C(CH_3)_3$), 1.07 (9H, s, $SiC(CH_3)_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.5, 141.9, 135.6, 135.4. 134.0, 129.6, 129.5, 127.6, 119.6, 63.8, 61.0, 38.7, 31.2, 28.4, 27.2, 26.9, 23.4, 19.2.

MS: m/e = 395 ($M^+ - C_4H_9$).

HMRS: calcd. for $C_{24}H_{31}O_3Si$: 395.2042; found: 395.2046.2046.

(*Z*)-6-(*tert*-Butyldiphenylsiloxy)-3-methylhex-2-en-1-ol (6)

To a solution of silyloxyether **5** (43.4 g, 95.8 mmol) in dichloromethane (400 mL) was added DIBAH (1.5 M in toluene, 192 mL, 288 mmol) at -78°C. After stirring for 1 h, the reaction was quenched with crushed Na_2SO_4 $10H_2O$ (300 g) and the slurry mixture was stirred for 1 h at room temperature. The aluminium salt was removed by filtration on fritted glass and the solid was washed several times with ethyl acetate. The filtrate was concentrated to afford **6** as a colorless oil (37.83 g, 100%).

IR (neat): υ = 3419, 2931, 2858, 1427, 1110 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.67 and 7.44 (10H, 2m, $Si(C_6H_5)_2$), 5.47 (1H, t, J = 7 Hz, $CH_2(CH_3)C=CH$), 4.11 (2H, d, J = 7 Hz, CH_2OH), 3.66 (2H, t, J = 6 Hz, $TBDPSOCH_2$), 2.19 (2H, t, J = 7 Hz, $CH_2(CH_3)C=CH$), 1.71 (3H, s, $CH_2(CH_3)C=CH$), 1.62 (2H, m, $TBDPSOCH_2CH_2$), 1.07 (9H, s, $SiC(CH_3)_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.7, 135.6, 133.8, 129.6, 127.7, 124.7, 63.2, 58.9, 30.8, 28.0, 26.9, 23.2.

MS: m/e = 311 (M^+ - C_4H_9).

HMRS: calcd. for $C_{19}H_{23}O_2Si$: 311.1467; found: 311.1464.

(*Z*)-7-(*tert*-Butyldiphenylsiloxy)-3-methylhex-2-en-1-al (7)

To a solution of oxalyl chloride (13.38 g, 105 mmol) in dichloromethane (250 mL) was added very slowly dimethyl sulfoxide (16.49 g, 211 mmol) at -78°C. The mixture was stirred for 30 min and a solution of alcohol **6** (35.31 g, 95.8 mmol) in dichloromethane (50 mL) was added by canula and rinse (10 mL). After stirring for 1 h, triethylamine (80 mL) was added to the reaction mixture, which was allowed to warm to room temperature during 1 h. The mixture was poured in water (250 mL) and extracted (3X) with dichloromethane. The organic phase was washed with brine, dried on magnesium sulfate, filtered and concentrated. The slurry residue was purified by flash chromatography (20% ethyl acetate in hexane) to give as a yellowish oil the aldehyde **7** (35.7 g, 99%).

IR (neat): υ = 2931, 2856, 1675, 1427, 1110 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.98 (1H, d, J = 8 Hz, CHO), 7.67 and 7.44 (10H, 2m, $Si(C_6H_5)_2$), 5.87 (1H, d, J = 8 Hz, $CH_2(CH_3)C=CH$), 3.70 (2H, t, J = 6 Hz, $TBDPSOCH_2$), 2.66 (2H, t, J = 7 Hz, $CH_2(CH_3)C=CH$), 1.95 (3H, s, $CH_2(CH_3)C=CH$), 1.75 (2H, m, $TBDPSOCH_2CH_2$), 1.06 (9H, s, $SiC(CH_3)_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.8, 164.2, 135.5, 134.8, 133.8, 129.7, 129.6, 127.7, 127.6, 62.9, 31.6, 29.1, 26.9, 26.5, 25.0, 19.2.

MS: m/e = 309 (M^+ - C_4H_9).

HMRS: calcd. for $C_{19}H_{21}O_2Si$: 311.1467; found: 311.1464.

(*Z*)-7-(*tert*-Butyldiphenylsiloxy)-2-hydroxy-4-methylhept-3-en-1-ol (8)

To a suspension of magnesium (4.17 g, 0.1715 at/g) in dry THF (150 mL) was added very slowly chloro(dimethyl)methylisopropoxysilane (24.46 g, 0.147 mol) at 0°C and a few drops of dibromoethane. When the reaction had started, the reflux was maintained for 1 h. The Grignard solution was cooled to room temperature and added slowly by canula to a solution of the aldehyde **7** (17.93 g, 48.9 mmol) in THF (200 mL) at -15°C. After stirring for 1 h at -15°C, the reaction was quenched with aqueous satured ammonium chloride at 0°C. The mixture was quickly extracted (3X) with chilled diethyl ether and the combined organic phases

were dried over magnesium sulfate, filtered and concentrated on vacuum rotary evaporator (ca. 20°C). After pumping off the residual solvent (50 torr) at 0°C, the yellowish crude adduct was dissolved in methanol (500 mL) and a solution of hydrogen peroxide 30% (44.3 mL, 0.440 mol) and sodium bicarbonate (4.11 g, 48.9 mmol) were added. The resulting mixture was refluxed for 3 h. The reaction mixture was cooled to room temperature and sodium thiosulfate pentahydrate (240 g, 0.978 mol) and brine were added to the mixture. The methanol was removed by means of a rotary evaporator and the aqueous residue was extracted several times with a mixture of ethyl acetate and diethyl ether (1:1). The organic phase was dried on magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (100% ethyl acetate) to afford as a colorless oil the diol **8** (14.38 g, 74%).

IR (neat): υ = 3386, 3070, 2931, 2858, 1427, 1111 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.67 and 7.44 (10H, 2m, $Si(C_6\underline{H}_5)_2$), 5.21 (1H, d, J = 8 Hz, $CH_2(CH_3)C=C\underline{H}$), 4.47 (1H, dt, J = 8 Hz and 4 Hz, $C\underline{H}(OH)CH_2OH$), 3.67 (2H, t, J = 6 Hz, $TBDPSOC\underline{H}_2$), 3.48 (2H, m, $C\underline{H}_2OH$), 2.20 (2H, m, $C\underline{H}_2(CH_3)C=CH$), 1.70 (3H, s, $CH_2(C\underline{H}_3)C=CH$), 1.61 (2H, m, $TBDPSOCH_2C\underline{H}_2$), 1.07 (9H, s, $SiC(C\underline{H}_3)_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.1, 135.5, 133.7, 129.7, 127.7, 124.4, 68.6, 66.5, 63.1, 30.7, 28.5, 26.9, 23.2, 19.2.

MS: m/e = 367 (M^+ - OCH_3).

HMRS: calcd. for $C_{23}H_{31}O_2Si$: 367.2093; found: 367.2088.

(*Z*)-1-(*tert*-Butyldiphenylsiloxy)-6,7-(isopropylidenedioxy)-4-methylhept-4-ene (9)

To a solution of diol **8** (14.38 g, 36 mmol) in acetone (350 mL) was added 2,2-dimethoxypropane (18.75 g, 180 mmol) and PTSA (0.34 g, 1.8 mmol) at 0°C. After stirring for 1 h, the reaction was quenched with aqueous satured sodium bicarbonate. The mixture was extracted with diethyl ether and the combined organic phases were dried over magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (35% ethyl acetate in hexane) to give **9** as a colorless oil (15.49 g, 98%).

IR (neat): υ = 3070, 2932, 2858, 1472, 1111, 1058 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.67 and 7.41 (10H, 2m, $Si(C_6\underline{H}_5)_2$), 5.17 (1H, dd, J = 8 Hz and 1 Hz, $CH_2(CH_3)C=C\underline{H}$), 4.80 (1H, dt, J = 8 Hz and 6 Hz, $C\underline{H}$-acetonide), 3.97 (1H, dd, J = 8 Hz and 6 Hz, $C\underline{H}_2$-acetonide), 3.65 (2H, t, J = 6 Hz, $TBDPSOC\underline{H}_2$), 3.45 (1H, t, J = 8 Hz, $C\underline{H}_2$-acetonide), 2.30 and 2.11 (2H, 2m, $C\underline{H}_2(CH_3)C=CH$), 1.70 (3H, d, J = 1 Hz, $CH_2(C\underline{H}_3)C=CH$), 1.61 (2H, m, $TBDPSOCH_2C\underline{H}_2$), 1.38 and 1.36 (6H, 2s, $C(C\underline{H}_3)_2$), 1.07 (9H, s, $SiC(C\underline{H}_3)_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.5, 133.8, 129.6, 127.6, 122.8, 108.7, 69.5, 63.3, 31.4, 28.6, 26.8, 26.0, 23.5, 19.2.

MS: m/e = 381 (M^+ - C_4H_9).

HMRS: calcd. for $C_{23}H_{29}O_3Si$: 381.1886; found: 381.1882.

(*Z*)-6,7-(Isopropylidenedioxy)-4-methylhept-4-en-1-ol (10)

To a solution of silylether **9** (15.89 g, 36 mmol) in THF (350 mL) was added TBAF (1.0 M in THF, 54 mL, 54 mmol). After stirring for 1 h, the solvent was evaporated under reduce pressured and the residual slurry

was purified by flash chromatography (50% ethyl acetate in hexane) to afford as a colorless oil the alcohol **10** (7.20 g, 99%).

IR (neat): υ = 3430, 2984, 2937, 2871, 1669, 1375, 1056 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.23 (1H, dd, J = 8 Hz and 1 Hz, $CH_2(CH_3)C=CH$), 4.79 (1H, dt, J = 8 Hz and 6 Hz, CH-acetonide), 4.05 (1H, dd, J = 8 Hz and 6 Hz, CH_2-acetonide), 3.55 (3H, m, CH_2OH and CH_2-acetonide), 2.59 (1H, m broad, OH), 2.37 (1H, dt, J = 13 Hz and 8 Hz, $CH_2(CH_3)C=CH$), 2.10 (1H, q, J = 7 Hz, $CH_2(CH_3)C=CH$), 1.72 (3H, d, J = 1 Hz, $CH_2(CH_3)C=CH$), 1.67 (2H, m, $HOCH_2CH_2$), 1.38 and 1.36 (6H, 2s, $C(CH_3)_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.8, 134.8, 123.1, 108.8, 72.3, 69.6, 60.8, 30.2, 26.7, 25.9, 23.1.

MS: m/e = 200 (M^+).

HMRS: calcd. for $C_{11}H_{20}O_3$: 200.1412; found: 200.1423.

(*Z*)-6,7-(Isopropylidenedioxy)-4-methylhept-4-en-1-al (11)

The same procedure applied to prepare the aldehyde **7** was used with the following quantities: alcohol **10** (7.20 g, 36 mmol), oxalyl chloride (5.03 g, 40 mmol), DMSO (6.19 g, 79.2 mmol) and triethylamine (21.86 g, 216 mmol) in dichloromethane (120 mL). The reaction afforded as a colorless oil the aldehyde **11** (5.94 g, 83%).

IR (neat): υ = 2984, 2935, 2726, 1724, 1376, 1057 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.76 (1H, s, CHO), 5.22 (1H, dd, J = 8 Hz and 1 Hz, $CH_2(CH_3)C=CH$), 4.77 (1H, dt, J = 8 Hz and 6 Hz, CH-acetonide), 4.05 (1H, dd, J = 8 Hz and 6 Hz, CH_2-acetonide), 3.47 (1H, t, J = 8 Hz, CH_2-acetonide), 2.44 (4H, m, CH_2CH_2CHO), 1.72 (3H, d, J = 1 Hz, $CH_2(CH_3)C=CH$), 1.38 and 1.36 (6H, 2s, $C(CH_3)_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.0, 139.8, 123.9, 108.7, 72.1, 69.3, 42.1, 26.6, 25.7, 24.3, 23.0.

MS: m/e = 198 (M^+).

HMRS: calcd. for $C_{11}H_{18}O_3$: 198.1256; found: 198.1254.

(*Z*)-[3(2*R*,3*S*,8*S*)4*R*]-3[3-Hydroxy-8,9-(isopropylidenedioxy)-2,6-dimethyl-6-nonenoyl]-4-benzyl-2-oxazolidinone and (*Z*)-[3(2*R*,3*S*,8*R*)4*R*]-3[3-hydroxy-8,9-(isopropylidenedioxy)-2,6-dimethyl-6-nonenoyl]-4-benzyl-2-oxazolidinone (12)

To a solution of (R)-3-(1-oxopropyl)-4-benzyl-2oxazolidinone (6.29 g, 27 mmol) in dichloromethane (200 mL) was added very slowly *n*-dibutylborontriflate (8.03 mL, 31.6 mmol) at 0°C. After stirring for 10 min at 0°C, triethylamine (3.55g, 35.1 mmol) was added very slowly. The mixture was cooled to -78°C and a solution of the aldehyde **11** (5.94 g, 30 mmol) in dichloromethane (100 mL) was added slowly by canula. After stirring for 3 h at -78°C, the reaction was quenched with a solution of methanol and pH 7 phosphate buffer (3:1, 90 mL). The mixture was warmed up to 0°C and a mixture of methanol and hydrogen peroxide 30% (2:1, 120 mL) was added slowly. After stirring for 1 h, the cloudy mixture was extracted several times with dichloromethane. The combined organic layers were washed with 5% aqueous sodium bicarbonate, brine, dried on magnesium sulfate and concentrated. The crude product was purified by flash chromatography (50% ethyl acetate in hexane) yielding as a viscous colorless oil a mixture of two diastereoisomers **12** (5.95 g, 66%).

IR (neat): υ = 3504, 2983, 1780, 1695, 1454, 1381, 1212, 1054 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 7.30 (5H, m, C_6H_5), 5.23 and 5.21 (1H, 2d, J = 8 Hz, $CH_2(CH_3)C=CH$), 4.77 (1H, dt, J = 8 Hz and 6 Hz, CH-acetonide), 4.67 (1H, m, BnCHN), 4.20 (2H, m, $BnCHCH_2O$), 4.05 (1H, m, CH_2-acetonide), 3.86 (1H, m, CHOH), 3.73 (CH_3)CHCO), 3.51 and 3.47 (1H, 2t, J = 8 Hz, CH_2-acetonide), 3.23 (1H, dd, J = 13 Hz and 3 Hz, CH_2Ph), 3.05 (1H, m, CHOH), 2.77 (1H, dd, J = 13 Hz and 9 Hz, CH_2Ph), 2.44-2.15 (2H, m, $CH_2(CH_3)C=CH$), 1.72 (3H, d, J = 1 Hz, $CH_2(CH_3)C=CH$), 1.65 (2H, m, $CH_2CH_2(CH_3)C=CH$), 1.38 (6H, m, $C(CH_3)_2$), 1.26 and 1.24 (3H, 2d, J = 7 Hz, $CHCH_3$).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3, 176.8, 153.0, 142.6, 141.7, 135.0, 134.9, 129.4, 128.9, 128.4, 127.4, 123.4, 123.3, 108.7, 72.5, 72.3, 70.4, 69.7, 69.5, 66.1, 66.0, 55.0, 42.6, 42.3, 42.1, 37.7, 35.8, 31.9, 31.8, 31.7, 28.6, 28.3, 26.8, 25.9, 23.4, 23.1, 11.2, 10.7.
MS: m/e = 431 (M^+).
HMRS: calcd. for $C_{24}H_{33}O_6N$: 431.2308; found: 431.2310.
$[\alpha]_D^{25}$ = -42° (c = 1.05 in dichloromethane).

(*Z*)-(2*R*,3*S*,8*S*)-3-Hydroxy-8,9-(isopropylidenedioxy)-N-methoxy-N,2,6-trimethylnon-6-en-1-amide and (*Z*)-(2*R*,3*S*,8*S*)-3-hydroxy-8,9-(isopropylidenedioxy)-N-methoxy-N,2,6-trimethylnon-6-en-1-amide (13)

To a suspension of N,O-dimethylhydroxylamine hydrochloride (2.69 g, 27.6 mmol) in dry dichloromethane (50 mL) at 0°C was added slowly trimethylaluminium (2.0 M in toluene, 13.8 mL, 27.6 mmol). The mixture was warmed to room temperature and was stirred for 30 min. The resulting mixture was cooled to -10°C and a solution of alcohol **12** (5.95 g, 13.8 mmol) in dichloromethane (20 mL) was added by canula plus rinse (5 mL). The reaction mixture was stirred overnight. The yellowish solution was added dropwise added by canula into a mixture of 1 M tartaric acid and hexane (1:1, 70 mL) and the mixture was stirred for 1 h. The mixture was extracted with dichloromethane (3X). The organic phase was washed with brine, dried over magnesium sulfate, filtered and concentrated. The crude was purified by flash chromatography (50% ethyl acetate in hexane) to give a mixture of two diastereoisomers **13** as a colorless oil (3.77 g, 87%).
IR (neat): υ = 3458, 2981, 2938, 2875, 1645, 1457, 1378, 1217, 1056 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 5.22 (1H, m, $CH_2(CH_3)C=CH$), 4.82 (1H, m, CH-acetonide), 4.03 (1H, m, CH_2-acetonide), 3.77 (1H, m, CHOH), 3.68 (3H, s, $NOCH_3$), 3.47 and 3.45 (1H, t, J = 8 Hz, CH_2-acetonide), 3.18 (3H, s, NCH_3), 2.82 (1H, m, $CHCH_3$), 2.27 (2H, m, $CH_2(CH_3)C=CH$), 1.73 (3H, s, $CH_2(CH_3)C=CH$), 1.61 (2H, m, $CH_2CH_2(CH_3)C$), 1.40 and 1.38 (6H, 2s, $C(CH_3)_2$), 1.17 and 1.15 (3H, 2d, J = 7 Hz, $CHCH_3$).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.7, 141.9, 123.3, 123.0, 108.7, 72.4, 70.6, 70.5, 69.6, 61.5, 39.5, 39.1, 32.3, 31.9, 28.6, 28.5, 26.8, 25.9, 23.5, 23.3, 11.4, 10.4.
MS: m/e = 300 (M^+ - CH_3).
HMRS: m/e = calcd. for $C_{15}H_{26}O_5N$: 300.1811; found: 300.1807.
$[\alpha]_D^{25}$ = -3° (c = 1.04 in dichloromethane).

(*Z*)-(2*R*,3*S*,8*S*)-8,9-(Isopropylidenedioxy)-N,3-dimethoxy-N,2,6-trimethylnon-6-en-1-amide and (*Z*)-(2*R*,3*S*,8*R*)-8,9-(isopropylidenedioxy)-N,3-dimethoxy-N,2,6-trimethylnon-6-en-1-amide (14)

To a solution of amide **13** (3.77 g, 12.0 mmol) in THF (60 mL) and DMF (24 mL) at 0°C were added iodomethane (17.03 g, 120 mmol) and NaH (60% in oil, 1.20 g, 29.9 mmol) under a flow of nitrogen. After stirring for 23 h at 0°C, the reaction was quenched with pH 7 phosphate buffer (130 mL) and was extracted with diethyl ether (3X). The combined organic phases were washed with brine, dried over magnesium sulfate, filtered and concentrated. The yellowish crude product was purified by flash chromatography (50% ethyl acetate in hexane) yielding a colorless oil as a mixture of two diastereoisomers **14** (3.70 g, 94%).

IR (neat): υ = 2980, 2936, 2875, 1661, 1458, 1377, 1057 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.15 (1H, d, J = 9 Hz, $CH_2(CH_3)C=CH$), 4.76 (1H, dt, J = 8.5 Hz and 6 Hz, CH-acetonide), 4.01 (1H, m, CH_2-acetonide), 3.68 (3H, s, $NOCH_3$), 3.46 and 3.44 (1H, t, J = 8 Hz, CH_2-acetonide), 3.40 and 3.38 (3H, 2s, $CHOCH_3$), 3.25 (1H, m, $CHOCH_3$), 3.17 (3H, s, NCH_3), 3.07 (1H, m, $CH(CH_3)$), 2.17 (2H, m, $CH_2(CH_3)C=CH$), 1.71 (3H, s, $CH_2(CH_3)C=CH$), 1.55 (2H, m, $CH_2CH_2(CH_3)C$), 1.40 and 1.37 (6H, 2s, $C(CH_3)_2$), 1.20 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.4, 122.6, 108.7, 82.5, 72.5, 69.5, 61.5, 58.4, 58.0, 39.2, 30.9, 27.8, 27.6, 26.8, 26.0, 23.5, 23.3, 14.5.

MS: m/e = 329 (M^+).

HMRS: calcd. for $C_{17}H_{31}O_5N$: 329.2202; found: 329.2201.

$[\alpha]_D^{25}$ = +3° (c = 0.95 in dichloromethane).

(*Z*)-(2*R*,3*S*,8*S*)-8,9-(Isopropylidenedioxy)-3-methoxy-2,6-dimethylnon-6-en-1-al and (*Z*)-(2*R*,3*S*,8*R*)-8,9-(isopropylidenedioxy)-3-methoxy-2,6-dimethylnon-6-en-1-al (15)

To a solution of the amide **14** (3.70 g, 11.2 mmol) in THF (160 mL) at -78°C was added DIBAH (1.5 M in toluene, 22.5 mL, 33.7 mmol) slowly. After stirring for 1 h, the mixture was added by canula into a mixture of 1M aqueous tartaric acid and hexane (1:1, 160 mL) and the resulting mixture was stirred for 1 h at room temperature. The mixture was extracted with diethyl ether (3X) and the combined organic phases were washed with brine, dried over magnesium sulfate, filtered and concentrated. The crude was purified by flash chromatography (30% ethyl acetate in hexane) to give as a colorless oil the aldehyde **15** which was a mixture of two diastereoisomers (2.89 g, 96%).

IR (neat): υ = 2982, 2936, 2872, 1725, 1456, 1375, 1058 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.66 (1H, d, J = 4 Hz, CHO), 5.11 (1H, d, J = 9 Hz, $CH_2(CH_3)C=CH$), 4.66 (1H, m, CH-acetonide), 3.91 (1H, m, CH_2-acetonide), 3.41 (2H, m, CH_2-acetonide and $CHOCH_3$), 3.24 and 3.21 (3H, 2s, $CHOCH_3$), 2.48 (1H, m, $CHCH_3$), 2.08 (2H, m, $CH_2(CH_3)C=CH$), 1.64 and 1.63 (3H, 2s, $CH_2(CH_3)C=CH$), 1.48 (2H, m, $CH_2CH_2(CH_3)C$), 1.28 and 1.25 (6H, 2s, $C(CH_3)_2$), 0.98 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.6, 140.4, 140.0, 123.3, 123.0, 108.4, 80.1, 79.8, 72.2, 72.0, 69.2, 57.4, 57.2, 48.7, 29.9, 29.6, 28.1, 26.5, 25.7, 23.2, 23.1, 7.9, 7.7.

MS: m/e = 270 (M^+).

HMRS: calcd. for $C_{15}H_{26}O_4$: 270.1831; found: 270.1826.

$[\alpha]_D^{25}$ = -38° (c = 0.69 in dichloromethane).

(2*E*,8*Z*)-(4*S*,5*S*,10*S*)-10,11-(Isopropylidenedioxy)-N,5-dimethoxy-N,4,8-trimethylundeca-2,8-dien-1-amide and (2*E*,8*Z*)-(4*S*,5*S*,10*R*)-10,11-(isopropylidenedioxy)-N,5-dimethoxy-N,4,8-trimethylundeca-2,8-dien-1-amide (16)

To a suspension of sodium hydride (60% in oil, 0.512 g, 12.8 mmol) in diethyl ether (200 mL) at 0°C was added slowly the requirest phosphonate amide (3.33 g, 13.9 mmol) and the mixture was stirred for 30 min. A solution of aldehyde **15** (2.88 g, 10.7 mmol) in diethyl ether (20 mL) was added to the reaction mixture. After stirring for 45 min at room temperature, the reaction was quenched with aqueous satured ammonium chloride and extracted several times with diethyl ether. The organic layer was dried on magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (50% ethyl acetate in hexane) yielding **16** (two diastereoisomers) as a viscous oil (3.29 g, 87%).

IR (neat): υ = 2982, 2936, 2872, 1725, 1456, 1375, 1058 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.83 (1H, dd, J = 15 Hz and 8 Hz, $\underline{H}C=CHCON(OCH_3)CH_3$)), 6.30 (1H, d, J = 15 Hz, $CH=C\underline{H}CON$), 5.08 (1H, d, J = 9 Hz, $CH_2(CH_3)C=C\underline{H}$), 4.66 (1H, m, $C\underline{H}$-acetonide), 3.91 (1H, t, J = 8 Hz, CH_2-acetonide), 3.61 (3H, s, $NOCH_3$), 3.37 (1H, q, J = 8 Hz, CH_2-acetonide), 3.28 and 3.26 (3H, 2s, $CHOCH_3$), 3.14 (3H, s, NCH_3), 2.98 (1H, m, $C\underline{H}OCH_3$), 2.54 (1H, m, $CHCH_3$), 2.08 (2H, m, $CH_2(CH_3)C=CH$), 1.63 (3H, s, $CH_2(CH_3)C=CH$), 1.48 (2H, m, $CH_2CH_2(CH_3)C$), 1.30 and 1.27 (6H, 2s, $C(CH_3)_2$), 0.99 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8, 149.1, 142.3, 142.0, 123.0, 122.8, 118.6, 108.7, 83.7, 72.6, 72.4, 69.5, 61.6, 57.6, 57.4, 39.5, 39.3, 32.3, 29.6, 28.0, 27.9, 26.8, 26.0, 23.5, 23.4, 15.3.

MS: m/e = 355 (M^+).

HMRS: calcd. for $C_{19}H_{33}O_5N$: 355.2359; found: 355.2356.

$[\alpha]_D^{25}$ = -26° (c = 0.43 in dichloromethane).

(2*E*,8*Z*)-(4*S*,5*S*,10*S*)-10,11-(Isopropylidenedioxy)-5-methoxy-4,8-dimethylundeca-2,8-dien-1-al and (2*E*,8*Z*)-(4*S*,5*S*,10*R*)-10,11-(isopropylidenedioxy)-5-methoxy-4,8-dimethylundeca-2,8-dien-1-al (17)

The same procedure as the one used to synthesize the aldehyde **15** was used with the following quantities: amide **16** (3.29 g, 9.26 mmol) and DIBAH (1.5 M in toluene, 18.5 mL, 27.8 mmol) in THF (150 mL). The aldehyde **17** was obtained as a colorless oil which was as a mixture of two diastereoisomers (2.33 g, 85%).

IR (neat): υ = 2980, 2934, 2873, 1691, 1058 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.50 (1H, d, J = 8 Hz, $C\underline{H}O$), 6.86 (1H, dd, J = 16 Hz and 6 Hz, $\underline{H}C=CHCHO$), 6.10 (1H, dd, J = 16 Hz and J = 8 Hz, $HC=C\underline{H}CHO$), 5.18 (1H, d, J = 9 Hz, $CH_2(CH_3)C=C\underline{H}$), 4.74 (1H, m, $C\underline{H}$-acetonide), 4.00 (1H, dd, J = 8 Hz and 6 Hz, CH_2-acetonide), 3.46 (1H, q, J = 8 Hz, CH_2-acetonide), 3.38 and 3.36 (3H, 2s, $CHOCH_3$), 3.12 (1H, m, $C\underline{H}OCH_3$), 2.81 (1H, m, $C\underline{H}CH_3$), 2.17 (2H, m, $CH_2(CH_3)C=CH$), 1.71 and 1.70 (3H, 2s, $CH_2(CH_3)C=CH$), 1.48 (2H, m, $CH_2CH_2(CH_3)C$), 1.38 and 1.35 (6H, 2s, $C(CH_3)_2$), 1.08 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.9, 159.9, 159.8, 142.0, 141.5, 132.6, 123.3, 123.1, 108.7, 83.4, 72.5, 72.4, 69.5, 57.5, 57.4, 38.6, 38.5, 32.3, 29.1, 28.2, 26.7, 26.0, 23.5, 23.4, 14.3, 14.2.

MS: m/e = 296 (M^+).

HMRS: calcd. for $C_{17}H_{28}O_4$: 296.1987; found: 296.1985.
$[\alpha]_D^{25}$ = -51° (c = 1.19 in dichloromethane).

Ethyl (2*Z*,4*E*,10*Z*)-(6*S*,7*S*,12*S*)-12,13-(isopropylidenedioxy)-7-methoxy-2,6,10-trimethyltrideca-2,4,10-trienoate and ethyl (2*Z*,4*E*,10*Z*)-(6*S*,7*S*,12*R*)-12,13-(isopropylidenedioxy)-7-methoxy-2,6,10-trimethyltrideca-2,4,10-trienoate (18)

To a solution of bis(trifluoroethyl)-2-phosphonoproprionate (2.68 g, 7.73 mmol) and 18-crown-6 ether (10.2 g, 38.6 mmol) in THF (100 mL) at -78°C was added KHMDS (0.5 M in toluene, 15.5 mL, 7.73 mmol) slowly. After stirring for 20 min, a solution of the aldehyde **17** (2.29 g, 7.73 mmol) in THF (50 mL) was added by canula and the reaction mixture was stirred for 1 h at -78°C and 1 h at room temperature. The reaction was quenched with aqueous satured ammonium chloride and extracted several times with diethyl ether. The combined organic phases were dried over magnesium sulfate, filtered and concentrated. The crude was purified by flash chromatography (20% ethyl acetate in hexane) to afford a colorless oil **18** which was a mixture of two diastereoisomers (2.73 g, 93%).
IR (neat): υ = 2980, 1706, 1638, 1219, 1107 cm^{-1}.
^1H NMR (300 MHz, $CDCl_3$): δ = 7.13 (1H, dd, J = 15 Hz and 11 Hz, $CHCH=C(CH_3)$), 6.36 (1H, d, J = 11 Hz, $HC=C(CH_3)$), 5.82 (1H, dd, J = 15 Hz and 8 Hz, $HC=CHCH=C(CH_3)$), 5.14 (1H, d, J = 9 Hz, $CH_2(CH_3)C=CH$), 4.74 (1H, m, CH-acetonide), 4.17 (2H, q, J = 7 Hz, OCH_2CH_3), 3.97 (1H, dd, J = 8 Hz and 6 Hz, CH_2-acetonide), 3.46 (1H, q, J = 8 Hz, CH_2-acetonide), 3.34 and 3.31 (3H, 2s, $CHOCH_3$), 3.00 (1H, m, $CHOCH_3$), 2.56 (1H, m, $CHCH_3$), 2.15 (2H, m, $CH_2(CH_3)C=CH$), 1.90 (3H, s, $HC=C(CH_3)$), 1.68 (3H, s, $CH_2(CH_3)C=CH$), 1.48 (2H, m, $CH_2CH_2(CH_3)C$), 1.37 and 1.33 (6H, 2s, $C(CH_3)_3$), 1.27 (3H, t, J = 7 Hz, OCH_2CH_3), 1.01 (3H, d, J = 7 Hz, $CHCH_3$).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.5, 142.7, 142.4, 142.0, 140.5, 127.5, 124.6, 122.9, 122.8, 108.6, 84.2, 72.6, 72.5, 69.5, 60.0, 57.3, 57.0, 39.2, 39.0, 29.3, 28.0, 26.7, 25.9, 23.5, 23.4, 20.6, 15.7, 14.2.
MS: m/e = 365 (M^+ - CH_3).
HMRS: calcd. for $C_{21}H_{33}O_5$: 365.2328; found: 365.2335.
$[\alpha]_D^{25}$ = -21° (c = 0.42 in dichloromethane).

(2*Z*,4*E*,10*Z*)-(6*S*,7*S*,12*S*)-12,13-(Isopropylidenedioxy)-7-methoxy-2,6,10-trimethyltrideca-2,4,10-trien-1-ol and (2*Z*,4*E*,10*Z*)-(6*S*,7*S*,12*R*)-12,13-(isopropylidenedioxy)-7-methoxy-2,6,10-trimethyloxytrideca-2,4,10-trien-1-ol (19)

To a solution of ester **18** (2.72 g, 7.1 mmol) in dichloromethane (150 mL) at -78°C was added DIBAH (1.5 M in toluene, 14.3 mL, 21.4 mmol) slowly. After stirring for 1 h the reaction was quenched with acetone (5 mL) and crushed sodium sulfate decahydrate (22 g, 71 mmol), then the resulting slurry was stirred for 1 h at room temperature. The jelly was filtered and the residue was washed with ethyl acetate (5 x 100 mL). The filtrate was concentrated under reduce pressure and the crude was purified by flash chromatography (50% ethyl acetate in hexane) yielding as a viscous oil the alcohol **19** (a mixture of two diastereoisomers) (2.40 g, 100%).
IR (neat): υ = 3451, 2933, 1455, 1377, 1057 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.33 (1H, dd, J = 15 Hz and 11 Hz, CHCH=C(CH_3)), 5.89 (1H, d, J = 11 Hz, HC=C(CH_3)), 5.56 (1H, dd, J = 15 Hz and 8 Hz, HC=CHCH=CH(CH_3)), 5.14 (1H, d, J = 9 Hz, CH_2(CH_3)C=CH), 4.71 (1H, m, CH-acetonide), 4.33-4.08 (2H, m, CH_2OH), 3.97 (1H, m, CH_2-acetonide), 3.45 (1H, q, J = 8 Hz, CH_2-acetonide), 3.35 and 3.34 (3H, 2s, CHOCH_3), 2.98 (1H, m, CHOCH_3), 2.45 (1H, m, CHCH_3), 2.15 (2H, m, CH_2(CH_3)C=CH), 1.84 (3H, s, HC=C(CH_3)), 1.72 (3H, s, CH_2(CH_3)C=CH), 1.70 to 1.48 (2H, m, CH_2CH_2(CH_3)C), 1.39 and 1.37 (6H, 2s, C(CH_3)$_2$), 1.01 (3H, d, J = 7 Hz, CHCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.5, 142.4, 136.0, 135.9, 135.7, 135.4, 127.8, 127.6, 125.0, 122.5, 122.4, 108.8, 84.3, 84.2, 72.8, 69.4, 69.3, 61.6, 61.5, 57.3, 57.1, 39.8, 39.6, 29.3, 29.1, 27.7, 27.3, 26.7, 26.1, 23.6, 23.5, 21.4, 16.7, 16.6.

MS: m/e = 365 (M^+ - CH_3OH).

HMRS: calcd. for $C_{19}H_{30}O_3$: 306.2195; found: 306.2200.

$[\alpha]_D^{25}$ = -20° (c = 1.0 in dichloromethane).

(3*Z*,9*E*,11*Z*)-(2*S*,7*S*,8*S*)-13-Chloro-1,2-(isopropylidenedioxy)-8-methoxy-4,8,12-trimethyltrideca-3,9,11-triene and (3*Z*,9*E*,11*Z*)-(2*R*,7*S*,8*S*)-13-chloro-1,2-(isopropylidenedioxy)-8-methoxy-4,8,12-trimethyltrideca-3,9,11-triene (20)

To a solution of the alcohol **19** (516 mg, 1.5 mmol) in THF (15 mL) at -40°C (acetonitrile and dry ice bath) were added in the following order 2,6-lutidine (320 mg, 3 mmol), hexachloroacetone (317 mg, 1.2 mmol) and triphenylphosphine (433 mg, 1.65 mmol). The solution was stirred for 10 min and the solvent was evaporated under reduced pressure. The white residue was purified quickly by flash chromatography (50% ethyl acetate in hexane) to afford a yellowish oil (unstable product). The product was used immediately in the next reaction.

IR (neat): υ = 2981, 2933, 2872, 1455, 1374, 1058 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.26 (1H, dd, J = 15 Hz and 11 Hz, CHCH=C(CH_3)), 5.95 (1H, d, J = 11 Hz, HC=C(CH_3)), 5.66 (1H, dd, J = 15 Hz and 8 Hz, HC=CHCH=C(CH_3)), 5.17 (1H, d, J = 9 Hz, CH_2(CH_3)C=CH), 4.77 (1H, m, CH-acetonide), 4.18 (2H, m, CH_2Cl), 4.01 (1H, dd, J = 8 Hz and 6 Hz, CH_2-acetonide), 3.46 (1H, q, J = 8 Hz, CH_2-acetonide), 3.37 and 3.35 (3H, 2s, CHOCH_3), 2.99 (1H, m, CHOCH_3), 2.52 (1H, m, CHCH_3), 2.18 (2H, m, CH_2(CH_3)C=CH), 1.88 (3H, s, HC=C(CH_3)), 1.73 (3H, s, CH_2(CH_3)C=CH), 1.57 (2H, m, CH_2CH_2(CH_3)C), 1.41 and 1.38 (6H, 2s, C(CH_3)$_2$), 1.03 (3H, d, J = 7 Hz, CHCH_3).

Methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*,14*S*)-14,15-(isopropylidenedioxy)-9-methoxy-2-methoxycarbonyl-4,8,12-trimethylpentadeca-4,6,12-trienoate and methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*,14*R*)-14,15-(isopropylidenedioxy)-9-methoxy-2-methoxycarbonyl-4,8,12-trimethylpentadeca-4,6,12-trienoate (21)

To a suspension of potassium hydride previously washed with hexane (75% in oil, 264 mg, 4.95 mmol) in toluene (10 mL) at 0°C were added dimethylmalonate (693.6 mg, 5.25 mmol) and 18-crown-6 ether (1.98 g, 7.5 mmol). After completion of the hydrogen evolution, the clear solution was heated to 50°C and a solution of the allylic chloride **20** (542 mg, 1.5 mmol) in toluene (5 mL) and potassium iodide were added. The black solution was stirred for 5 h; then quenched with aqueous satured ammonium chloride and extracted with diethyl

ether (3X). The organic layer was washed with brine, dried on magnesium sulfate, filtered and concentrated. The crude product was purified by flash chromatography (30% ethyl acetate in hexane) to give **21** as a colorless oil (mixture of two diastereoisomers) (556.6 g, 82% in two steps).

IR (neat): υ = 2955, 2872, 1739, 1473, 1378, 1239, 1155, 1057 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.24 (1H, dd, J = 15 Hz and 11 Hz, $CHCH=C(CH_3)$), 5.85 (1H, d, J = 11 Hz, $HC=C(CH_3)$), 5.53 (1H, dd, J = 15 Hz and 8 Hz, $HC=CHCH=C(CH_3)$), 5.15 (1H, d, J = 9 Hz, $CH_2(CH_3)C=CH$), 4.77 (1H, m, CH-acetonide), 3.99 (1H, m, CH_2-acetonide), 3.69 and 3.68 (6H, 2s, CO_2CH_3), 3.53 (1H, t, J = 8 Hz, $CH(CO_2CH_3)_2$), 3.45 (1H, q, J = 8 Hz, CH_2-acetonide), 3.34 and 3.32 (3H, 2s, $CHOCH_3$), 2.95 (1H, m, $CHOCH_3$), 2.77 (2H, m, $CH_2CH(CO_2CH_3)_2$), 2.48 (1H, m, $CHCH_3$), 2.13 (2H, m, $CH_2(CH_3)C=CH$), 1.72 (3H, s, $HC=C(CH_3)$), 1.70 (3H, s, $CH_2(CH_3)C=CH$), 1.50 (2H, m, $CH_2CH_2(CH_3)C$), 1.39 and 1.36 (6H, 2s, $C(CH_3)_2$), 1.00 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 142.5, 142.2, 135.3, 131.4, 128.7, 125.7, 122.8, 122.7, 108.6, 84.4, 72.6, 72.5, 69.5, 57.3, 57.1, 52.5, 50.1, 39.2, 39.1, 31.4, 29.4, 28.2, 28.1, 26.8, 26.0, 23.5, 23.4, 23.0, 16.1.

MS: m/e = 452 (M^+).

HMRS: m/e = calcd. for $C_{25}H_{40}O_7$: 452.2774; found: 452.2766.

$[\alpha]_D^{25}$ = -19° (c = 1.08 in dichloromethane).

Methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*,14*S*)-14,15-dihydroxy-9-methoxy-2-methoxycarbonyl-4,8,12-trimethylpentadeca-4,6,12-trienoate and methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*,14*R*)-14,15-dihydroxy-9-methoxy-2-methoxycarbonyl-4,8,12-trimethylpentadeca-4,6,12-trienoate (22)

A solution of the acetonide **21** (540 mg, 1.14 mmol) in acetic acid and water (4:1, 75 mL) was stirred for 2 h. The solution was neutralized by addition of sodium bicarbonate until a pH of 8 was reached and the resulting mixture was extracted several times with dichloromethane. The combined organic phases were dried over magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (100% ethyl acetate) yielding **22** as a very viscous oil which was a mixture of two diastereoisomers (466 mg, 99%).

IR (neat): υ = 3419, 2955, 1737, 1436, 1079 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.24 (1H, dd, J = 15 Hz and 11 Hz, $CHCH=C(CH_3)$), 5.86 (1H, d, J = 11 Hz, $HC=C(CH_3)$), 5.49 and 5.47 (1H, 2dd, J = 15 Hz and 8 Hz, $HC=CHCH=C(CH_3)$), 5.20 and 5.15 (1H, 2d, J = 9 Hz, $CH_2(CH_3)C=CH$), 4.46 (1H, m, CHOH) 3.70 (6H, 2s, CO_2CH_3), 3.53 (3H, m, $CH(CO_2CH_3)_2$ and CH_2OH), 3.34 and 3.31 (3H, 2s, $CHOCH_3$), 3.01 (1H, m, $CHOCH_3$), 2.78 and 2.76 (2H, 2d, J = 8 Hz, $CH_2CH(CO_2CH_3)_2$), 2.48 (1H, m, $CHCH_3$), 2.23 and 2.07 (2H, 2m, $CH_2(CH_3)C=CH$), 1.74 (3H, s, $HC=C(CH_3)$), 1.71 and 1.69 (3H, 2s, $CH_2(CH_3)C=CH$), 1.55 (2H, m, $CH_2CH_2(CH_3)C$), 1.01 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 141.6, 140.9, 135.4, 135.3, 131.6, 131.5, 128.7, 128.6, 126.0, 125.8, 124.7, 124.0, 84.6, 83.1, 68.7, 68.4, 66.6, 57.0, 55.1, 52.5, 50.1, 39.3, 31.5, 29.0, 28.2, 27.8, 23.7, 23.0, 16.7, 16.3.

MS: m/e = 430 ($M^+ + NH_4$).

HMRS: calcd. for $C_{22}H_{40}O_7N$: 430.2805; found: 430.2801.

$[\alpha]_D^{25}$ = -19° (c = 1.08 in dichloromethane).

Methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*,14*S*)-14-hydroxy-9-methoxy-2-methoxycarbonyl-4,8,12-trimethyl-15-[(*para*-toluenesulfonyl)oxy]pentadeca-4,6,12-trienoate and methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*,14*R*)-14-hydroxy-9-methoxy-2-methoxycarbonyle-4,8,12-trimethyl-15-[(*para*-toluenesulfonyl)oxy]pentadeca-4,6,12-trienoate (23)

To a solution of the diol **22** (385 mg, 0.933 mmol) in dichloromethane (18 mL) at -5°C were added triethylamine (1.9 mmol), dimethylaminopyridine (91 mg, 0.746 mmol) and tosylchloride (267 mg, 1.40 mmol). After stirring for 1 h, the mixture was poured into aqueous satured ammonium chloride and extracted several times with dichloromethane. The combined organic phases were dried over magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (50% ethyl acetate in hexane) to afford an unstable product **23** which was quickly used in the next reaction (391 mg, 74%).

IR (neat): υ = 3399, 2926, 2856, 1736, 1609, 1438, 1366, 1175 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.77 (2H, d, J = 8 Hz, $CH_3(C_6H_4)SO_2$), 7.33 (2H, d, J = 8 Hz, $CH_3(C_6H_4)SO_2$), 6.24 (1H, dd, J = 15 Hz and 11 Hz, $CHCH{=}C(CH_3)$), 5.84 (1H, d, J = 11 Hz, $HC{=}C(CH_3)$), 5.50 and 5.46 (1H, 2dd, J = 15 Hz and 8 Hz, $HC{=}CHCH{=}C(CH_3)$), 5.08 and 5.05 (1H, 2d, J = 9 Hz, $CH_2(CH_3)C{=}CH$), 4.57 (1H, m, CHOH), 3.91 (2H, m, CH_2OTs), 3.69 (6H, s, CO_2CH_3), 3.54 (1H, t, J = 8 Hz, $CH(CO_2CH_3)_2$), 3.29 and 3.28 (3H, 2s, $CHOCH_3$), 2.95 (1H, m, $CHOCH_3$), 2.76 and 2.73 (2H, 2d, J = 8 Hz, $CH_2CH(CO_2CH_3)_2$), 2.46 (1H, m, $CHCH_3$), 2.43 (3H, s, $CH_3(C_6H_4)SO_2$), 2.25 and 2.07 (2H, 2m, $CH_2(CH_3)C{=}CH$), 1.73 (3H, s, $HC{=}C(CH_3)$), 1.66 and 1.64 (3H, s, $CH_2(CH_3)C{=}CH$), 1.47 (2H, m, $CH_2CH_2(CH_3)C$), 0.98 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 142.7, 141.9, 135.3, 135.1, 132.6, 131.6, 131.5, 129.7, 128.6, 128.5, 127.9, 126.0, 125.8, 124.7, 122.7, 122.0, 84.5, 83.2, 73.3, 73.2, 66.0, 65.7, 56.9, 55.4, 52.5, 50.1, 39.3, 31.4, 28.8, 28.1, 27.8, 23.3, 23.1, 22.9, 21.5, 16.6, 16.2.

$[\alpha]_D^{25}$ = -9.4° (c = 1.00 in dichloromethane).

Methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*)-9-methoxy-2-methoxycarbonyl-4,8,12-trimethyl-14-oxo-15-[(*para*-toluenesulfonyl)oxy]pentadeca-4,6,12-trienoate (24)

To a solution of the alcohol **23** (82 mg, 0.145 mmol) in dichloromethane (1.5 mL) was added Dess-Martin periodinane (123 mg, 0.290 mmol). After stirring for 1 h the reaction was quenched with aqueous saturated sodium bicarbonate and sodium thiosulfate (10 eq.) and the resulting mixture was stirred for 30 min. The mixture was extracted with dichloromethane (3X) and the combined organic layers were dried over magnesium sulfate, filtered and concentrated. The crude product was purified by flash chromatography (20% ethyl acetate in hexane) to give **24** as a yellowish oil (65.3 mg, 80 %).

IR (neat): υ = 2955, 1739, 1615, 1367, 1179, 1010 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.80 (2H, d, J = 8 Hz, $CH_3(C_6H_4)SO_2$), 7.33 (2H, d, J = 8 Hz, $CH_3(C_6H_4)SO_2$), 6.22 (1H, dd, J = 15 Hz and 11 Hz, $CHCH{=}C(CH_3)$), 6.12 (1H, s, $CH_2(CH_3)C{=}CH$), 5.86 (1H, d, J = 11 Hz, $HC{=}C(CH_3)$), 5.53 (1H, dd, J = 15 Hz and 8 Hz, $HC{=}CHCH{=}C(CH_3)$), 4.46 (2H, s, CH_2OTs), 3.69 (6H, s, CO_2CH_3), 3.54 (1H, t, J = 8 Hz, $CH(CO_2CH_3)_2$), 3.34 (3H, s, $CHOCH_3$), 3.05 (1H, m, $CHOCH_3$), 2.76 (4H, m, $CH_2(CH_3)C{=}CH$ and $CH_2CH(CO_2CH_3)_2$), 2.46 (1H, m, $CHCH_3$), 2.44 (3H, s,

$CH_3(C_6H_4)SO_2$), 1.89 (3H, s, $CH_2(CH_3)C=CH$), 1.72 (3H, s, $HC=C(CH_3)$), 1.50 (2H, m, $CH_2CH_2(CH_3)C$), 1.01 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.6, 169.3, 165.5, 145.2, 135.5, 134.8, 132.4, 131.3, 129.8, 128.7, 128.0, 125.6, 118.3, 84.9, 84.2, 72.2, 57.3, 52.4, 50.1, 39.4, 37.5, 31.3, 30.9, 29.1, 28.6, 25.8, 22.9, 21.5, 15.8.

MS: m/e = 582 ($M^+ + NH_4$).

HMRS: calcd. for $C_{29}H_{44}O_9NS$: 582.2737; found: 582.2745.

$[\alpha]_D^{25}$ = -8° (c = 0.80 in dichloromethane).

Methyl (4*Z*,6*E*,12*Z*)-(8*S*,9*S*)-15-chloro-9-methoxy-2-methoxycarbonyl-4,8,12-trimethyl-14-oxopentadeca-4,6,12-trienoate (25)

To a solution of the tosylate **24** (236 mg, 0.419 mmol) in DMF (4 mL) was added lithium chloride (178 mg, 4.2 mmol). After stirring for 15 min the reaction was quenched with water and extracted with diethyl ether and hexane (3X, 1:1). The combined organic phases were washed with brine, dried on magnesium sulfate, filtered and concentrated. The crude product was purified over a silica gel plug (50% ethyl acetate in hexane) yielding **25** as a colorless oil (100%).

IR (neat): υ = 2931, 1740, 1615, 1441, 1199, 1101 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.23 (1H, dd, J = 15 Hz and 11 Hz, $CHCH=C(CH_3)$), 6.18 (1H, s, $CH_2(CH_3)C=CH$), 5.85 (1H, d, J = 11 Hz, $HC=C(CH_3)$), 5.55 (1H, dd, J = 15 Hz and 8 Hz, $HC=CHCH=C(CH_3)$), 4.04 (2H, s, CH_2Cl), 3.67 (6H, s, $CO2CH_3$), 3.53 (1H, t, J = 8 Hz, $CH(CO_2CH_3)_2$), 3.35 (3H, s, $CHOCH_3$), 3.04 (1H, m, $CHOCH_3$), 2.76 (3H, m, $CH_2(CH_3)C=CH$ and $CH_2CH(CO_2CH_3)_2$), 2.46 (2H, m, $CH_2(CH_3)C=CH$ and $CHCH_3$), 1.91 (3H, s, $CH_2(CH_3)C=CH$), 1.72 (3H, s, $HC=C(CH_3)$), 1.58 (2H, m, $CH_2CH_2(CH_3)C$), 1.01 (3H, d, J = 7 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.7, 169.3, 164.6, 135.6, 131.3, 128.7, 125.6, 119.6, 85.0, 57.4, 52.4, 50.1, 49.2, 39.6, 37.4, 31.4, 30.7, 29.6, 29.2, 25.8, 23.0, 15.9.

MS: m/e = 428 (M^+).

HMRS: calcd. for $C_{22}H_{33}O_6Cl$: 428.1965; found: 428.1953.

$[\alpha]_D^{25}$ = +9.8° (c = 1.00 in dichloromethane).

(4*Z*,10*E*,12*Z*)-(8*S*,9*S*)-8-Methoxy-1,1-bis(methoxycarbonyl)-5,9,13-trimethyl-8-methoxycyclotetradeca-4,10,12-trien-3-one (26)

To a suspension of cesium carbonate (4.92 g, 13.3 mmol) in DMF (328 mL) at 45°C was added a solution of the chloroketone **25** (1.43 g, 3.33 mmol) in DMF (5 mL) with a syringe pump over 3 h. After the addition was completed, the yellow solution was stirred for another 4 h. The solvent was evaporated under reduced pressure then the residue was dissolved in ethyl acetate and filtered through a pad of silica gel. The filtrate was concentrated and purified by flash chromatography (10% ethyl acetate in toluene) yielding **26** as a white solid (0.856 g , 66%). A sample of macrocycle **26** was crystallized in dichloromethane and hexane to afford a single clear crystal (mp 135-137°C) which were analyzed by X-ray diffraction.

IR (neat): υ = 2953, 1737, 1688, 1625, 1451, 1182 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.18 (1H, dd, J = 15 Hz and 11 Hz, CHCH=C(CH_3)), 5.94 (1H, s, $CH_2(CH_3)C$=CH), 5.86 (1H, d, J = 11 Hz, HC=C(CH_3)), 5.13 (1H, dd, J = 15 Hz and 8 Hz, HC=CHCH=C(CH_3)), 3.72 and 3.69 (6H, 2s, $(CO_2CH_3)_2$), 3.71 and 3.68 (1H, d, J = 14 Hz, C(O)CH_2), 3.41 (1H, d, J = 19 Hz, CH=C(CH_3)CH_2), 3.28 (3H, s, CHOCH_3), 3.20 (1H, m, $CH_2(CH_3)C$=CH), 2.94 (1H, m, CHOCH_3), 2.80 (1H, d, J = 19 Hz, CH=C(CH_3)CH_2), 2.77 (1H, d, J = 14 Hz, C(O)CH_2), 2.33 (1H, m, $CHCH_3$), 2.05 (1H, m, $CH_2CH_2(CH_3)C$), 1.79 (3H, s, $CH_2(CH_3)C$=CH), 1.74 (1H, m, $CH_2(CH_3)C$=CH), 1.53 (3H, s, HC=C(CH_3)), 1.09 (1H, m, $CH_2CH_2(CH_3)C$), 1.02 (3H, d, J = 6 Hz, $CHCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.4, 172.1, 170.8, 156.2, 134.6, 132.2, 130.7, 127.2, 124.9, 84.0, 57.2, 53.7, 52.9, 44.4, 41.5, 35.2, 29.7, 28.6, 24.0, 23.5, 23.3, 18.4.

MS: m/e = 392 (M^+).

HMRS: calcd. for $C_{22}H_{32}O_6$: 392.2199; found: 392.2202.

$[\alpha]_D^{25}$ = -10° (c = 1.00 in dichloromethane).

(11*S*,12*S*)-12-Methoxy-5,5-dimethoxycarbonyl-1,7,11-trimethyl-*trans-cisoid-cis*-tricyclo[8.4.0.0^{2,7}]tetradec-7-en-3-one (27)

A solution of the TCC macrocyclic triene **26** (254.4 mg, 0.648 mmol) in toluene (9 mL, previously degazed, freeze-thaw cycle five times) was heated in a vacuum sealed pyrex tube (washed with aqueous ammonium hydroxide, water and acetone before using) for 20 h at 220°C. The tube was cooled then opened, the solution was transferred and concentrated. The residue was purified by flash chromatography (30% ethyl acetate in hexane) to afford the tricycle TSC **27** as a crystalline product (229 mg, 90%). A sample was crystallized in ether and hexane to give colorless crystals (mp 97-98.5°C) which were submitted to X-ray diffraction analysis.

IR (neat): υ = 2951, 2823, 1739, 1688, 1438, 1376, 1252, 1091 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.71 (1H, dd, J = 10 Hz and 2 Hz, H*7*), 5.36 (1H, ddd, J = 10 Hz, 3 Hz and 1 Hz, H*8*), 3.74 (3H, s, CO_2CH_3), 3.70 (3H, s, CO_2CH_3), 3.35 (3H, s, OCH_3), 3.18 (1H, d, J = 15 Hz, H*4*α), 2.66 (1H, dd, J = 15 Hz and 2 Hz, H*4*β), 2.63 (1H, m, H*12*α), 2.39 (1H, d, J = 15 Hz, H6β), 2.09 (1H, s, H*2*), 2.02 (1H, m, H*13*β), 1.97 (1H, d, J = 15 Hz, H6α), 1.61 (1H, ddd, J = 11 Hz, 5 Hz and 2 Hz, H*10*α), 1.58-1.48 (3H, m, H*11*β, H*13*α and H*14*), 1.22 (3H, s, CH_3*7*), 1.17 (1H, m, H*14*), 1.06 (3H, d, J = 6 Hz, CH_3*11*), 1.02 (3H, s, CH_3*1*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.8, 171.5, 171.1, 133.2, 127.5, 85.0, 62.8, 56.7, 53.2, 52.9, 44.0, 43.5, 41.4, 37.7, 36.6, 36.2, 34.1, 31.2, 29.6, 25.2, 21.7, 15.2.

MS: m/e = 392 (M^+).

HMRS: calcd. for $C_{22}H_{32}O_6$: 392.2199; found: 392.2202.

$[\alpha]_D^{25}$ = -2.2° (c = 1.00 in dichloromethane).

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