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Convergent Highly Stereoselective Preparation of the C12−C24 Fragment of Macrolactin A

Carlo Bonini,*,† Lucia Chiummiento,† Maddalena Pullez,† Guy Solladié,*,‡ and Françoise Colobert*,‡

Dipartimento di Chimica, Università degli Studi della Basilicata, via N. Sauro 85, 85100 Potenza, Italy, and Laboratoire de Stéréochimie associé au CNRS, Université Louis Pasteur, ECPM, 25 rue Becquerel, 67087 Strasbourg Cedex 2, France

bonini@unibas.it

Received March 18, 2004

The convergent synthesis of the C12−C24 fragment (lower part) of macrolactin A is described. The adapted strategy allowed building up the lower moiety by the assembly of three key intermediates via organometallic addition. One hydroxylic stereogenic center was introduced by the application of chiral sulfoxides methodology on fragment C19−C24. The preparation of the versatile 1,3-*anti* diol synthon C12−C16 was achieved via opening of chiral epoxide and subsequent oxidation to a hydroxy ketone. Finally, reductive elimination of the appropriate allylic dibenzoate with Na/Hg introduced directly the C16−C19 (*E*,*E*)-diene unit, in a highly efficient stereoselective fashion.

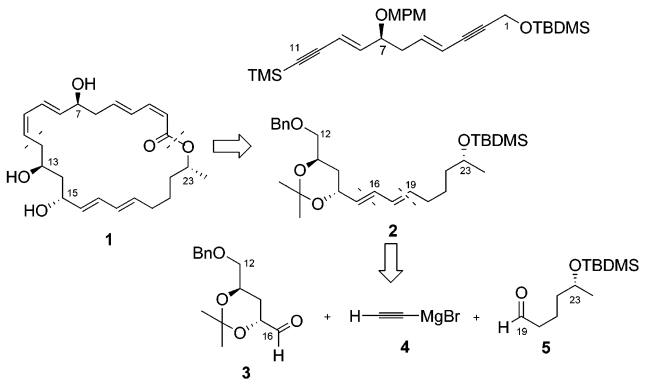
Introduction

Macrolactin A (**1**), a 24-membered polyene macrolide, was isolated in 1989 by Fenical and co-workers from a deep-sea bacterium of unclassified taxonomy along the coast of California[1] and belongs to the class of macrolactins whose other members were recently isolated.[2]

Macrolactin A displays strong cytotoxic activity in vitro on B16−F10 murine melanoma cell (IC_{50} = 3.5 μg/mL), as well as powerful antiviral activity against *Herpes simplex* types I and II and human HIV-1 virus replication.[1] The synthetically challenging structure combined with the unique biological activity attracted the attention of synthetic organic chemists. In 1992 Rychnovsky[3] established the relative and absolute stereochemistry of macrolactin A, and in 1996 Smith[4] published the first total synthesis. After 1998 two total syntheses appeared[5] with different partial syntheses and approaches.[6]

We report herein a highly stereoselective synthesis of the C12−C24 fragment of macrolactin A, using different original approaches for the introduction of the (*E*,*E*)-diene stereochemistry and of the stereogenic centers.

SCHEME 1



Results and Discussion

In many of the synthetic approaches the step-by-step addition of the synthons was applied to build up the stereogenic centers and the diene units (mainly by Stille-type coupling).[4−6] In our retrosynthetic analysis (Scheme 1), we proposed the disconnections at the lactone linkage

* To whom correspondence should be addressed. For C.B.: tel +39 0971 202254, fax + 39 0971 202223.
† Università degli Studi della Basilicata.
‡ Université Louis Pasteur.

(1) Gustafson, K.; Roman, M.; Fenical, W. *J. Am. Chem. Soc.* **1989**, *111*, 7519.
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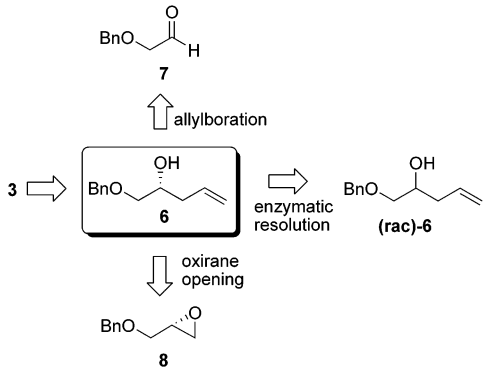
10.1021/jo049556l CCC: $27.50
Published on Web 06/25/2004

SCHEME 2



and the C11−C12 bond to generate the upper (C1−C11) and the lower (C12−C24, **2**) moieties. For the lower part **2** of the macrolide further disconnections would expect an organometallic convergent coupling between the two optically active aldehydes **3** and **5** and the Grignard reagent **4**. Key elements of the synthesis were (i) the use of a fully functionalized aldehyde **3**, containing a protected 1,3-*anti* diol and a primary protected hydroxyl group; (ii) the application of chiral sulfoxide chemistry for the synthesis of compound **5**; (iii) the coupling of advanced intermediates **3** and **5** by organometallic additions; and (iv) the stereocontrolled introduction of the (C16−C19) (*E*,*E*)-diene by a novel application of sodium amalgam reductive elimination of allylic dibenzoate.

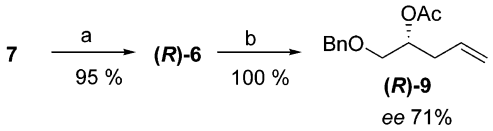
Synthesis of (C12−C16) Fragment 3. The aldehyde **3** has been already prepared by different approaches[7] requiring, however, long reaction sequences and overall fair yields. Our shorter synthetic strategy required as key intermediate the chiral homoallylic alcohol **6**. Different synthetic routes could be followed to this goal, as illustrated in the retrosynthetic Scheme 2: (i) the asymmetric allylboration of aldehyde **7**; (ii) the enzymatic resolution of rac-**6**; and (iii) the opening of the appropriate chiral glycidol **8**.

The Brown enantioselective allylboration reaction[8] performed in classical conditions on the commercially available benzyloxyacetaldehyde **7** with *B*-allyldiisopinocampheylborane was repeated several times (Scheme 3). Unfortunately, although (*R*)-**6** was obtained in good chemical yield, the HPLC analysis revealed only 71% ee, evaluated on the corresponding acetylated compound (*R*)-**9**.[9,10]

In the second approach (Scheme 4), (*rac*)-**6**, easily prepared by allylation of the benzyloxyacetaldehyde **7**, was subjected to biocatalytic resolution by transesterification in organic media or by hydrolysis of the corresponding acetate (*rac*)-**9**.

The enzymatic resolutions were performed, after initial screening, with *Pseudomonas* sp. lipase,[11] already successfully utilized for the desymmetrization and resolution of highly functionalized polyols.[12] Both hydrolysis and transesterification were successful in preparing highly enantiomerically enriched compounds. In particular the target alcohol (*R*)-**6** was obtained by hydrolysis of the acetate (*rac*)-**9** with 94% ee evaluated by HPLC. However, the low conversion (38%) for the hydrolysis prompted us to search for another approach.

SCHEME 3[a]



[a] Reagents and conditions: (a) (+)-Ipc$_2$BOMe, allylMgBr, Et$_2$O, −78 °C to rt, 12 h; (b) Ac$_2$O, Pyr, DMAP, CH$_2$Cl$_2$, rt, 24 h.

In a third attempt we started with the commercially available[11] benzylglycidyl ether (*S*)-**8**, already bearing the stereogenic center at C13. Our first attempts at the regioselective opening of the epoxide ring with an appropriate vinyl organometallic reagent, following known procedures,[13] were found to be difficult to reproduce in large scale and highly dependent on different OH protecting groups. The oxirane ring opening with vinylmagnesium halide afforded generally a large amount of the corresponding halohydrin.

Therefore we undertook a systematic study[14] on a series of different glycidyl ethers, and good reproducible results have been achieved using various OH protecting groups. In particular, interesting results never before reported have been obtained in the opening of *tert*-butyldimethylsilyloxy derivatives to the corresponding silyl protected homoallylic alcohol.

By applying the developed protocol to our synthetic purpose, the regioselective opening of the oxirane ring on chiral compound **8** with vinylmagnesium bromide in THF at −20 °C in the presence of CuI (Scheme 5) afforded the alcohol **6** in 91% yield.[15]

Our initial strategy for the direct introduction of the two hydroxy groups at C15 and C16 was based on the application of the Sharpless AD[16] on the homoallylic alcohol **6** with the use of the appropriate AD mix-β reagent. However the reaction (Scheme 5) was not stereoselective (*syn*/*anti* 42:58 evaluated by ^{1}H NMR and ^{13}C NMR spectra of the corresponding acetonides).[17] The presence of a highly functionalized olefin such as **6**, with

(7) (a) Solladié, G.; Hutt, J. *Tetrahedron Lett.* **1987**, *28*, 797. For the synthesis of the precursor alcohol, see: (b) Brückner, R.; Weigand, W. *Synlett* **1996**, 225. (c) Solladié, G.; Colobert, F.; Denni, D. *Tetrahedron: Asymmetry* **1998**, *9*, 3081.

(8) Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1995**, *105*, 2092.

(9) Chiralcel column OJ.; eluent hexane/*i*-PrOH 99.5:0.5; flow rate 0.5 mL/min; t_R = 21.86; t_R = 28.49.

(10) After our use of (+)-Ipc$_2$BOMe we were recently aware that the use of DIP-Cl gives higher ee as reported in: Reddy, M. V. R.; Brown, H. C.; Ramachandran, P. V. *J. Organomet. Chem*. **2001**, *624*, 239.

(11) Purchased from Aldrich.

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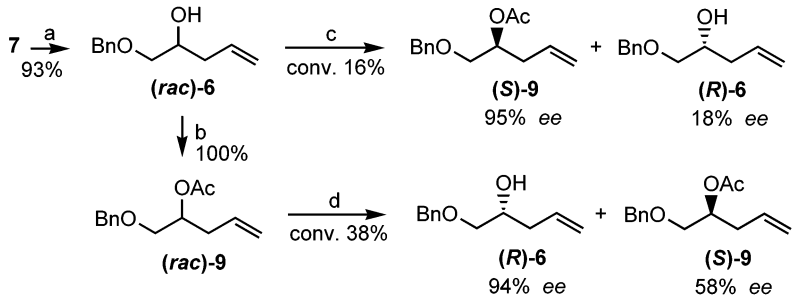
(14) Bonini, C.; Chiummiento, L.; Lopardo, M. T.; Pullez, M.; Colobert, F.; Solladié, G. *Tetrahedron Lett.* **2003**, *44*, 2695.

(15) Traces of the corresponding bromohydrin can be easily separated by column chromatography on the protected alcohol **6** as silyl ether (Scheme 6).

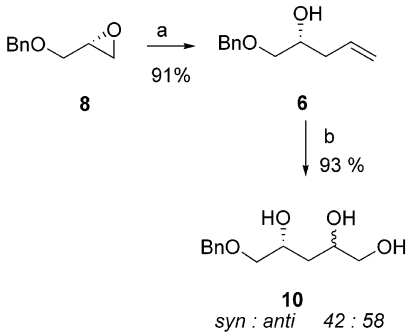
(16) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

SCHEME 4[a]



[a] Reagents and conditions: (a) allylMgBr, THF, 0 °C, 45 min; (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, 24 h; (c) PSL, vinyl acetate, Et_2O, rt, 21 h; (d) PSL, phosphate buffer 0.5 M, rt, 6 h.

SCHEME 5[a]



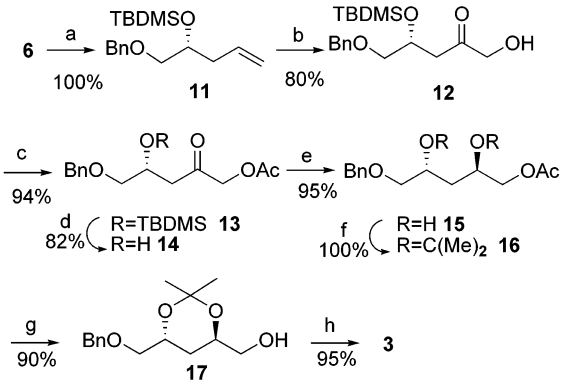
[a] Reagents and conditions: (a) vinylMgBr, CuI, THF, −20 °C, 1 h; (b) AD mix-β, *t*-BuOH/H_2O, 0 °C to rt, 10 h.

two proximate hydroxyl groups, could be responsible for the low chiral recognition of the asymmetric catalyst.

Failure of the Sharpless reaction led us to attempt the direct conversion of the alkene **6** into the α-hydroxyketone **12** (Scheme 6) via careful chemoselective oxidation, after previous protection of the secondary hydroxyl group as silyl ether **11**. We found the potassium permanganate oxidation in acidic medium[18] of **11** smoothly afforded the α-hydroxyketone **12** in 80% yield in only 2 h. This reaction is indeed a known[19] further example of oxidation of terminal alkene to an α-hydroxyketone in one step and represents, to our knowledge, a unique pattern of such reaction on an homoallylic alcohol.

After this crucial step, the subsequent protection of the primary hydroxyl group as acetate ester (94%) was followed by desilylation under acidic conditions (THF/AcOH/H_2O) to the β-hydroxyketone **14** in 82% yield.[20] With **14** in hand, we prepared the 1,3-*anti*-diol by diastereoselective reduction with $Me_4NBH(OAc)_3$,[21] obtaining the diol **15** with excellent yield (95%).

SCHEME 6[a]



[a] Reagents and conditions: (a) TBDMSCl, imid., DMF, rt, 3 h; (b) $KMnO_4$, AcOH, acetone, H_2O, rt, 2 h; (c) Ac_2O, Pyr, CH_2Cl_2, rt, 24 h; (d) THF/AcOH/H_2O, rt to 50 °C, 48 h; (e) $Me_4NBH(OAc)_3$, AcOH, CH_3CN, −20 °C, 15 h; (f) $Me_2C(OMe)_2$, CSA, rt, 24 h; (g) NaOMe/MeOH, rt, 18 h; (h) Dess−Martin periodinane, CH_2Cl_2, rt, 3 h.

Protection of the diol **15** as acetonide **16** under usual conditions also made it possible to determine the relative stereochemistry and the diastereomeric ratio of the reduction via ^{13}C and ^1H NMR (de > 98%).[17a,b] The final steps for the synthesis of the C12−C16 fragment required the transformation of **16** to the aldehyde **3**. This was achieved by hydrolysis of the acetate ester **16** to give the alcohol **17** in 90% yield and subsequent oxidation to aldehyde **3** using the Dess−Martin periodinane procedure[22] (95% yield). The aldehyde **3** can be conveniently used in the further synthetic steps (see below) without purification in order to avoid any epimerization process. In summary, the key fragment **3** was obtained in nine steps starting from benzylglycidyl ether **8** with an overall yield of 46%, which greatly improves its preparation (in number of steps and overall yield) in comparison to the known early syntheses.[7]

Synthesis of (C19−C24) Fragment 5. The synthesis of fragment **5**[23] was performed using the well-known

(17) The relative stereochemistry of **10** was assigned by ^{13}C NMR chemical shift analysis of the derived acetonide. The ^{13}C NMR signals at $\delta = 24.6$ and 24.7 ppm and at $\delta = 100.7$ ppm are consistent with the presence of an *anti*-1,3-diol. The values at $\delta = 19.9$ and 30.8 ppm and at $\delta = 99.2$ ppm confirmed the presence of the *syn*-1,3-diol. The diastereomeric ratio was determined by ^1H NMR chemical shift analysis. The methyl groups of *anti*-acetonide have ^1H NMR chemical shifts of 1.29 ppm, and the methyl groups of *syn*-acetonide have ^1H NMR chemical shifts of 1.32 and 1.39 ppm. See: (a) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945. (b) Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511.

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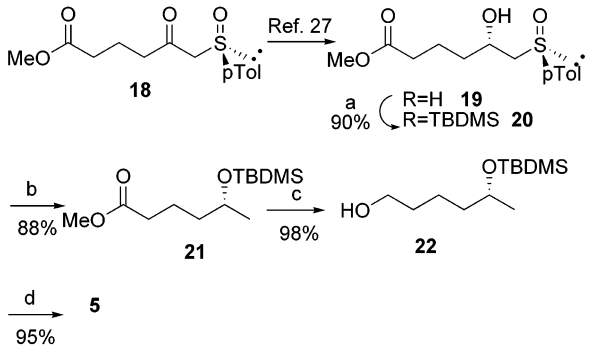
(20) Desilylation under usual conditions (using TBAF) was unsuccessful because of the strong basic conditions that affect the highly sensitive β-ketol system in **13**: Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(21) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560.

(22) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.

(23) For different approaches to the synthesis of **5**, see: Shiinan, I.; Fujisawa, H.; Ishii, T.; Fukuda, Y. *Heterocycles* **2000**, *52*, 1105 and references therein.

SCHEME 7[a]

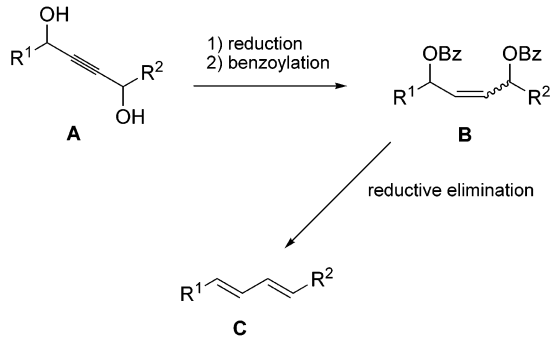


[a] Reagents and conditions: (a) TBDMSCl, imid., DMF, rt, 33 h; (b) Raney Ni, MeOH, rt, 16 h; (c) DIBAL, toluene, 0 °C, 2 h; (d) Dess−Martin periodinane, CH_2Cl_2, rt, 3 h.

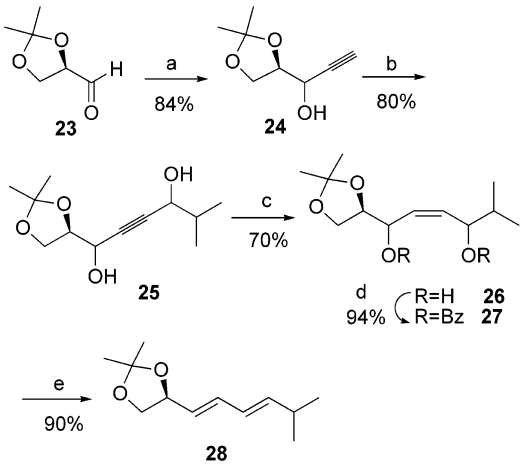
diastereoselective reduction of β-ketosulfoxides.[24] A partial achievement of this synthesis was already reported in late 2000.[25] The known β-ketosulfoxide **18** (prepared in one step from glutaric anhydride and (+)-(*R*)-methyl *p*-tolylsulfoxide)[26] was the starting chiral product (Scheme 7) for the introduction of the chiral hydroxyl group at C23. Reduction of β-ketosulfoxide **18** with DIBAL[27] afforded the β-hydroxysulfoxide [*S*,(S)*R*]-**19** (70%) with an excellent diastereoselectivity (de > 98%). The (*S*) absolute configuration of the hydroxylic carbon of **19** was assigned on the basis of the already published mechanism[24] and from the ^{1}H NMR spectra of the crude reduction mixture. Protection of the hydroxyl group with TBDMSCl and desulfurization with Raney nickel afforded the hydroxy ester **21**.[27] Reduction of the ester group with DIBAL (3 equiv) in toluene at 0 °C afforded the alcohol (*R*)-**22** in 98% yield,[28] with a sequence of five steps and 50% overall yield, which competes well with the reported synthesis of (*R*)-**22** by Marino,[5b] requiring seven steps from a commercially available product. Alcohol (*R*)-**22** was finally oxidized to the resulting aldehyde **5** in 95% yield using Dess−Martin periodinane protocol in CH_2Cl_2 at room temperature. In summary, aldehyde **5** was prepared in six steps from glutaric anhydride in 48% overall yield.

Final Coupling Assembly. We next turned out our attention to the critical, convergent coupling step of the two chiral aldehydes **3** and **5** with the acetylenic Grignard reagent **4** (Scheme 1) in order to introduce the (*E*,*E*)-diene moiety (C16−C19) of the lower part of macrolactin A. This kind of coupling could allow the synthesis of an alkyne diol of type **A** (Scheme 8), necessary to perform the stereocontrolled reductive elimination by Na/Hg of the corresponding alkene dibenzoate **B**, according to the well-known methodology to generate an all-*trans* diene as **C**.[29]

SCHEME 8



SCHEME 9[a]



[a] Reagents and conditions: (a) **4**, THF, 0 °C, 4 h; (b) *n*-BuLi, isobutyraldehyde, THF; −78 °C to rt, 16 h; (c) H_2, Pd/$BaSO_4$, Pyr/MeOH, rt, 2 h; (d) BzCl, Pyr/THF, rt, 6 h; (e) Na/Hg 6%, Na_2HPO_4, THF/MeOH, −20 °C, 4 h.

The crucial step of the reductive elimination was checked with a model compound bearing a similar sensitive α-hydroxyl group and protected as an acetonide. Therefore, as outlined in Scheme 9, the chosen model compound **25** was prepared starting from commercially available (*R*)-glyceraldehyde **23**. (*R*)-**23** was smoothly condensed with ethylnylmagnesium bromide **4** to give the propargylic alcohol **24** and then with isobutyraldehyde to obtain a mixture of diols **25**. Subsequent partial reduction to compound **26** and benzoylation afforded the key olefin **27**.

The reductive elimination was then achieved with the established procedure (Na/Hg 6%, Na_2HPO_4, THF/MeOH,

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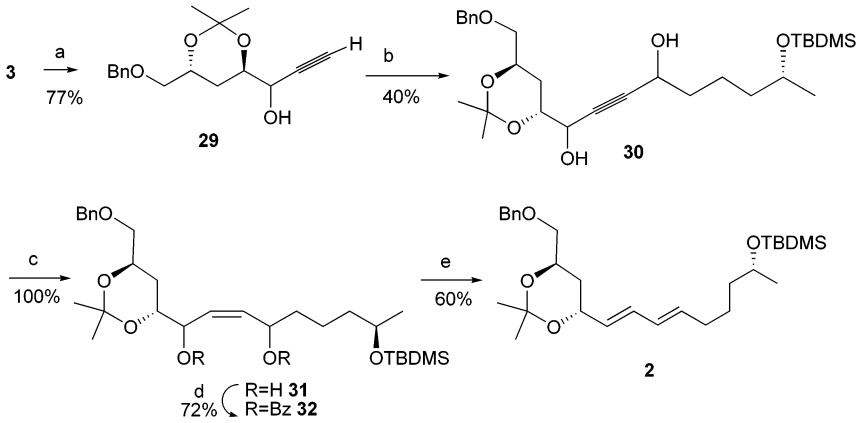
(28) *S*)-**22** was prepared for the synthesis of (+)-brefeldin A, using $LiAlH_4$ as reducing reagent, as reported: Solladié, G.; Lohse, O. *J. Org. Chem.* **1993**, *58*, 4555.

(29) (a) Solladié, G.; Stone, G. B.; Andrés, J.-M.; Urbano, A. *Tetrahedron Lett.* **1993**, *34*, 2835. For an overview of application of reductive elimination with Na/Hg to the synthesis of natural products, see: (b) Solladié, G.; Urbano, A.; Stone, G. B. *Tetrahedron Lett.* **1993**, *34*, 6489. (c) Solladié, G.; Urbano, A.; Stone, G. B. *Synlett* **1993**, 548. (d) Solladié, G.; Adamy, M.; Colobert, F. *J. Org. Chem.* **1996**, *61*, 4369. (e) Solladié, G.; Somny, F.; Colobert, F. *Tetrahedron*: *Asymmetry* **1997**, *8*, 801.

SCHEME 10[a]



[a] Reagents and conditions: (a) **4**, THF, 0 °C, 4 h; (b) *n*-BuLi, **5**, −78 °C, THF, rt, 16 h. (c) H_2, $Pd/BaSO_4$, Pyr/MeOH, rt, 2 h; (d) BzCl, Pyr/THF, rt, 19 h; (e) Na/Hg (6%), Na_2HPO_4, THF/MeOH, −20 °C, 5 h.

−20 °C), affording in an excellent 90% yield, after chromatography purification, the unique (*E*,*E*)-diene **28** without traces of other isomers.

In light of this successful result, we next turned out our attention to the final coupling of compounds **3** and **5** (Scheme 10). Aldehyde **3** was allowed to react with an excess of ethynylmagnesium bromide (**4**) in THF at 0 °C to give propargylic alcohol **29**, as an inseparable mixture of diastereomers (24/76 ratio determined by ^{1}H NMR).

Acetylenic alcohol **29** was then treated with 2.2 equiv of *n*-BuLi in THF at −78 °C to afford the corresponding lithium acetylide. Aldehyde **5** was added at −78 °C to give the diol **30**, as a mixture of diastereomers. Because of the moderate overall yield of this last reaction, we tried to improve it without remarkable results.[30]

Adduct **30** was therefore converted to (*Z*)-alkene **31** by partial stereoselective reduction with $Pd/BaSO_4$ in Pyr/MeOH under H_2 atmosphere. Activation of the free hydroxylic groups as dibenzoate esters with benzoyl chloride in Pyr/THF at room temperature afforded allylic dibenzoate (*Z*)-**32**.

Finally, the reductive elimination protocol on the dibenzoate **32** gave the diene **2** in 60% yield and >98% isomeric purity after column chromatography (no traces of other possible double bond isomers were observed). The (*E*) geometry for the C16−C17 (J = 15.2 Hz) and C18−C19 (J = 15.1 Hz) double bonds was established by ^{1}H NMR, showing it to be a single pure (*E*,*E*)-diene.

After this successful preparation of the lower part of macrolactin A, we are currently working on the preparation of the upper C1−C11 fragment and on their final couplings to complete macrolactin's skeleton. The results will be reported in due course.

Experimental Section

(+)-(2*R*)-1-Benzyloxy-pent-4-en-2-ol (6) (via Allylboration).[8a] To a solution of (+)-*B*-methoxydiisopinocampheylborane (1.57 g, 5.0 mL) in Et_2O at −78 °C was added dropwise over 20 min allylmagnesium bromide (1 M in Et_2O, 5.0 mL, 5.0 mmol). The resultant reaction mixture was stirred for 15 min at −78 °C and warmed to room temperature (1 h). The allylborane was cooled to −78 °C, and aldehyde **7** (0.5 g, 3.3 mmol) in Et_2O (1.5 mL) was added via cannula with stirring. The reaction mixture was stirred for 1 h at −78 °C and then allowed to warm to 25 °C. After 18 h the reaction mixture was quenced with 3 N NaOH (5.6 mL) and 30% H_2O_2 (2.3 mL), and the contents were refluxed for 1 h. The aqueous layer was extracted with Et_2O, and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Two purifications on silica gel (Et_2O/pentane 1:9 followed by $CHCl_3$/MeOH 99:1) provided the compound **6** as a colorless oil (0.6 g, 95%). Compound **6** shows the same spectroscopic data as reported in the literature.[13d]

(+)-(2*R*)-1-Benzyloxy-pent-4-en-2-ol (6) (via Enzymatic Hydrolysis). To a solution of allylmagnesium bromide (1 M in Et_2O, 5.0 mL, 5.0 mmol) in THF (5 mL) at 0 °C was quickly added a solution of aldehyde **7** (0.5 g, 3.3 mmol) in THF (2 mL). After 45 min at 0 °C a saturated aqueous solution of NH_4Cl was added (20 mL). The mixture was diluted with Et_2O (30 mL), and the aqueous phase was extracted with Et_2O. The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude residue was purified on silica gel (petroleum ether/EtOAc 85:15) to afford (*rac*)-**6** (0.59 g, 93%) as a colorless oil.

To a solution of alcohol (*rac*)-**6** (0.4 mg, 2.1 mmol) in CH_2Cl_2 (3 mL) were added triethylamine (0.2 mL, 2.5 mmol) and acetic anhydride (0.68 mL, 3.1 mmol) followed by a catalytic amount of DMAP. After 24 h at room temperature, the reaction mixture was treated with a saturated solution of NH_4Cl (10 mL). The aqueous layer was extracted with CH_2Cl_2. The organic layer was washed with brine before drying over Na_2SO_4. After concentration in vacuo pure compound (*rac*)-**9** was obtained as a colorless oil (0.49 g, 100%): R_f = 0.6 (petroleum ether/EtOAc 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.39 (m, 2H), 3.54 (m, 2H), 4.51 and 4.57 (AB system, J = 12 Hz, 2H), 5.10 (m, 2H), 5.78 (m, 2H), 7.32 (m, 5H)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 34.9, 70.5, 72.9, 73.5, 116.1, 127.5, 128.4, 135.0, 138.1, 169.3. EI-MS *m*/*z*: M^+, 234, (100), 91. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.80; H, 7.77. Analysis via HPLC using the following experimental conditions: Chiralcel OJ; eluent hexane/*i*-PrOH 99.5:0.5; flow rate 0.5 mL/min gave t_R = 21.86 and t_R = 28.49.

A 0.1 M solution of (*rac*)-**9** (2 g, 8.5 mmol) in 0.5 M phosphate buffer (pH = 7) was stirred vigorously at room temperature. *Pseudomonas* sp. lipase (PSL, 30 U/mg, 0.28 g) was added, and the reaction was monitored by TLC. After about 6 h the enzyme was filtered, and the filtrate was washed with EtOAc. After the separation of the phases the organic solvent was evaporated under reduced pressure. The crude

(30) Because of low conversion of compound **29**, it could be recovered unreacted. We tried to add first the aldehyde **5** to the ethynylmagnesiumbromide followed by the addition of either 2.2 equiv of *n*-Buli or EtMgBr and the aldehyde **3**, but it did not improve the yield of the resulting propargylic diol.

product was purified on a silica gel column (petroleum ether/EtOAc 9:1) to provide pure (+)-**(6)** (0.5 g, 31%), with the same spectroscopic data as reported in the previous preparation of **6**. The ee of 94% was determined via HPLC on the acetylated product using the following experimental conditions: Chiralcel OJ; eluent hexane/*i*-PrOH 99.5:0.5; flow rate 0.5 mL/min; t_R = 28.49.

(+)-(2*R*)-1-Benzyloxy-pent-4-en-2-ol (6) (via Oxirane Opening).[13] To a 0.15 M solution in THF of **8** (3.8 g, 23.2 mmol) and CuI (4.4 g, 23.2 mmol) at −20 °C was quickly added a solution 1 M in THF of vinylmagnesium bromide (92.8 mL, 92.8 mmol). After 20 min a saturated aqueous solution of NH_4Cl was added to the dark mixture reaction. The mixture was diluted with EtOAc and stirred until complete separation of the layers. The aqueous layer was extracted several times with EtOAc, and then the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated to afford **6** as a pure colorless oil without purification (4.1 g, 91%), with the same spectroscopical data as previously reported.

(−)-(2*R*)-1-Benzyloxy-2-(*tert*-butyldimethylsilyloxy)-pent-4-en (11). To a cooled (0 °C) solution of the alcohol **6** (4.1 g, 21.1 mmol) in DMF (50 mL) were added imidazole (4.3 g, 63.4 mmol) and TBDMSCl (47.7 g, 31.7 mmol). The mixture was stirred at room temperature for 3 h, hydrolyzed with H_2O (100 mL), and diluted with Et_2O (150 mL). The aqueous layer was extracted with Et_2O. The combined organic layers were washed with a saturated aqueous solution of NH_4Cl and with brine and dried over Na_2SO_4. The concentrate was purified by column chromatography (hexane/Et_2O 99:1) on silica gel to provide **11** (6.46 g, 100%) as a yellow oil. Compound **11** shows the same spectroscopic data reported in the literature.[13e,f]

(+)-(4*R*)-5-Benzyloxy-4-(*tert*-butyldimethylsilyloxy)-1-hydroxy-pentan-2-one (12). To a solution of acetone (170 mL), water (38 mL), and acetic acid (8 mL) was added the alkene **11** (6.5 g, 21.1 mmol). A solution of $KMnO_4$ (5.4 g, 34.3 mmol) in acetone (64 mL) and water (21 mL) was added dropwise, and the resulting mixture was stirred at room temperature for 2 h. EtOH was added until effervescence stopped. The crude was filtered over Celite and washed several times with hexane. The filtrate was concentrated, diluted with Et_2O, and washed with a saturated aqueous solution of $NaHCO_3$ until pH = 8. The organic layer was then washed with brine and dried over $MgSO_4$. The concentrate was purified by column chromatography on silica gel (hexane/EtOAc 85:25) to afford **12** as a colorless oil (5.7 g, 80%): R_f = 0.23 (hexane/EtOAc 8:2); $[\alpha]^{25}_D$ +19.4 (*c* 2, acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 2.56−2.72 (m, 2H), 3.14 (m, 1H), 3.36 and 3.48 (AB part of an ABX system, J_{AB} = 9.8 Hz, J_{AX} = 6.4 Hz, J_{BX} = 4.5 Hz, 2H), 4.24 (m, 2H), 4.35 (m, X part of an ABX system, 1H), 4.52 (s, 2H), 7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, 18.0, 25.7, 43.9, 68.3, 69.6, 73.4, 73.9, 127.6, 127.7, 128.4, 137.9, 208.5. EI-MS *m*/*z*: M^+, 338, (100), 91. Anal. Calcd for $C_{18}H_{30}O_4Si$: C, 63.87; H, 8.93. Found: C, 63.92; H, 8.89.

(+)-(4*R*)-1-Acetyloxy-5-benzyloxy-4-(*tert*-butyldimethylsilyloxy)-pentan-2-one (13). To a solution of **12** (3.9 g, 11.5 mmol) in CH_2Cl_2 (50 mL) at room temperature were added pyridine (1.6 mL, 17.3 mmol), acetic anhydride (1.3 mL, 17.3 mmol), and a catalytic amount of DMAP. After 24 h the mixture was cooled at 0 °C, and a 10% aqueous solution of HCl was added until pH = 1. The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ and then with brine and dried over Na_2SO_4. The concentrate was purified by chromatography on silica gel (petroleum ether/EtOAc 9:1) to afford **13** as a pale yellow oil (4.1 g, 94%): R_f = 0.40 (petroleum ether/EtOAc 9:1); $[\alpha]^{25}_D$ +13.3 (*c* 1, acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.14 (s, 3H), −0.12 (s, 3H), 0.94 (s, 9H), 2.24 (s, 3H), 2.68 and 2.76 (AB part of an ABX system, J_{AB} = 15.3 Hz, J_{AX} = 6.5 Hz, J_{BX} = 5.2 Hz, 2H), 3.45 and 3.55 (AB part of an ABX system, J_{AB} = 9.8 Hz, J_{AX} = 7 Hz, J_{BX} = 6 Hz, 2H), 4.43 (m, X part of two ABX systems, 1H), 4.59 (s, 2H), 4.69 and 4.81 (AB system, J = 17 Hz, 2H), 7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, 18.0, 20.5, 25.8, 44.2, 68.0, 69.0, 73.3, 73.8, 127.7, 128.4, 138.0, 170.1, 202.1. EI-MS *m*/*z*: M^+ − 15, 368, (100), 91. Anal. Calcd for $C_{20}H_{32}O_5Si$: C, 63.12; H, 8.48. Found: C, 63.18; H, 8.52.

(+)-(4*R*)-1-Acetyloxy-5-benzyloxy-4-hydroxy-pentan-2-one (14). In a solution (343.8 mL) of acetic acid, THF, and water (ratio 3/1/1, respectively) was dissolved the ketone **13** (4.3 g, 11.2 mmol), and the mixtures was stirred at room temperature for 18 h. The acetic acid was removed under reduced pressure (40 mmHg), and the resulting mixture was diluted with EtOAc, washed with a saturated aqueous solution of $NaHCO_3$ and then with brine, and dried over Na_2SO_4. The solvent was removed in vacuo, and the mixture was purified on silica gel (hexane/EtOAc 6:4) to provide **14** as a yellow oil (2.4 g, 82%): R_f = 0.48 (hexane/EtOAc 6:4); $[\alpha]^{25}_D$ +22.2 (*c* 1, acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3H), 2.61 and 2.69 (AB part of an ABX system, J_{AB} = 18 Hz, J_{AX} = 9 Hz, J_{BX} = 4.5 Hz, 2H), 2.79 (bs, 1H), 3.46 and 3.54 (AB part of an ABX system, J_{AB} = 9.4 Hz, J_{AX} = 6 Hz, J_{BX} = 4.3 Hz, 2H), 4.29 (m, X part of two ABX systems, 1H), 4.56 (s, 2H), 4.69 (s, 2H), 7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 42.4, 60.7, 68.5, 73.1, 73.4, 127.7, 127.9, 128.4, 137.7, 170.2, 203.3. EI-MS *m*/*z*: M^+ − 59, 207; (100), 91. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.10; H, 6.84.

(+)-(2*R*,4*R*)-5-Acetyloxy-1-benzyloxy-2,4-pentan-diol (15). A solution of $(Me)_4NHB(OAc)_3$ (15.4 g, 58.6 mmol) in CH_3CN (40 mL) and acetic acid (20 mL) was stirred at room temperature for 30 min and after was cooled to −20 °C. A solution of **14** (1.9 g, 7.3 mmol) in CH_3CN (16 mL) was cannulated therein and stirred at this temperature for 15 h. A saturated solution of Rochelle salts was added (100 mL), and the mixture was diluted with CH_2Cl_2 (150 mL). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ and with brine and then dried over Na_2SO_4. The filtrate was concentrated under reduced pressure and purified by column chromatography of silica gel (petroleum ether/EtOAc 1:1) to afford the pure **15** as a yellow oil (1.9 g, 95%): R_f = 0.19 (petroleum ether/EtOAc 1:1); $[\alpha]^{25}_D$ +11 (*c* 1 acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.59−1.65 (m, 2H), 2.10 (s, 3H), 2.65 (bs, 1H), 2.78 (bs, 1H), 3.42 and 2.54 (AB part of an ABX system, J_{AB} = 9.2 Hz, J_{AX} = 7.6 Hz, J_{BX} = 2 Hz, 2H), 3.99−4.19 (m, 4H), 4.57 (s, 2H), 7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 35.9, 67.2, 67.7, 68.8, 73.6, 74.5, 128.0, 128.2, 128.8, 138.0, 171.5. EI-MS *m*/*z*: M^+, 268; (100), 91. Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.64; H, 7.49.

(+)-Acetic Acid [(4*R*,6*R*)]-6-Benzyloxymethyl-2,2-dimethyl-[1,3]dioxan-4-yl Methyl Ester (16). To the diol **15** (0.50 g, 1.9 mmol) were added 2,2-dimethoxypropane (20 mL) and a catalytic amount of camphorsulfonic acid (0.04 g, 0.19 mmol) at room temperature. After 24 h the solvent was removed in vacuo, and the crude was diluted with Et_2O. A saturated aqueous solution of $NaHCO_3$ was added, and the organic layer was washed with brine and then dried over Na_2SO_4. The filtrate was concentrated under reduced pressure and purified by silica gel chromatography (hexane/EtOAc 9:1) to afford **16** as a yellow oil (0.57 g, 100%): R_f = 0.52 (hexane/EtOAc 9:1); $[\alpha]^{25}_D$ +15 (*c* 0.66, acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 3H), 1.42 (s, 3H), 1.56−1.69 (m, 2H), 2.10 (s, 3H), 3.47 and 3.55 (AB part of a ABX system, J_{AB} = 10.3 Hz, J_{AX} = 6.2 Hz, J_{BX} = 4.3 Hz, 2H), 3.99−4.16 (m, 4H), 4.58 and 4.64 (AB system, J = 12.2 Hz, 2H), 7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 24.7, 24.8, 30.6, 65.0, 66.1, 66.3, 72.5, 73.4, 100.7, 127.6, 127.7, 128.4, 138.2, 171.0. EI-MS *m*/*z*: M^+ − Me, 293, (100), 91. Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.27; H, 7.89.

(+)-[(4*R*,6*R*)-6-Benzyloxymethyl-2,2-dimethyl-[1,3]dioxan-4-yl] Methanol (17). To a solution of the acetonide **16** (0.57 g, 1.9 mmol) in dry methanol (20 mL), at room temperature, was quickly added a catalytic amount of metallic sodium. The mixture was stirred for 18 h, and then the solvent was removed under reduced pressure. The crude mixture was diluted with EtOAc (20 mL) and washed with brine. The

organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The mixture was purified by chromatography on silica gel (hexane/EtOAc 6:4) to provide **17** as a colorless oil (0.45 g, 90%). Compound **17** shows the same spectroscopic data reported in the literature.[7b,c]

(+)-(4*R*,6R)-6-Benzyloxymethyl-2,2-dimethyl-[1,3]dioxane-carbaldehyde (3). Into a solution of Dess−Martin periodinane (0.48 g, 1.13 mmol) in dry CH_2Cl_2 (3.5 mL), at room temperature, was cannulated a solution of the alcohol **17** (0.20 g, 0.75 mmol) in dry CH_2Cl_2 (7 mL). After 3 h the pale pink mixture was transferred into an Erlenmeyer flask containing a saturated aqueous solution of $NaHCO_3$ (20 mL) and a small amount of $Na_2S_2O_5$. The separated organic layer was washed with brine, dried over Na_2SO_4, and filtered, and the solvent was removed in vacuo. The crude mixture of the aldehyde **3** (0.19 g, 95%), a yellow oil, was utilized in the next step without previous purification. Compound **3** shows the same spectroscopic data reported in the literature.[7a]

(+)-Methyl [5*S*,(S)*R*]-5-(*tert*-Butyldimethylsilyloxy)-6-(*p*-tolylsulfinyl)hexanoate (20). The reaction and the spectroscopic data were already reported;[27a] $[\alpha]^{25}_D$ +149 (*c* 1, $CHCl_3$).

(−)-Methyl (5*S*)-5-(*tert*-Butyldimethylsilyloxy)hexanoate (21). The reaction and the spectroscopic data were already reported.[27]

(−)-(5*R*)-5-(*tert*-Butyldimethylsilyloxy)-hexan-1-ol (22). To a 0 °C cooled solution of the ester **21** (0.50 g, 1.9 mmol) in dry toluene (10 mL) was added dropwise a solution of DIBAL (1.5 M in toluene, 3.8 mL, 5.8 mmol). The mixture was stirred for 2 h. At the same temperature a saturated aqueous solution of sodium and potassium tartrate (20 mL) was added and left until complete dissolution. Then EtOAc was added, and the mixture was stirred until complete separation of the layers. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo. The crude colorless oil **22** (0.44 g, 98%) was not purified. R_f = 0.38 (hexane/Et_2O 1:1); $[\alpha]^{25}_D$ −10.3 (*c* 1.6, $CHCl_3$). The spectroscopic data were reported for (*ent*)-**22**.[29]

(−)-(5*R*)-5-(*tert*-Butyldimethylsilyloxy)-hexanal (5). The oxidation of the alcohol **22** (0.20 g, 0.86 mmol) was performed with the Dess−Martin periodinane according to the conditions followed for the oxidation of the alcohol **17**. The crude was purified by column chromatography on silica gel (hexane/Et_2O 1:1) to afford compound **5** (0.19 g, 95%) as a white oil. Compound **5** shows the same spectroscopic data as reported in the literature.[23]

(4*R*,6*R*)-1-(6-Benzyloxymethyl-2,2-dimethyl-[1,3]dioxan-4-yl)-prop-2-yne-1-ol (29). To a 0 °C cooled solution of ethynylmagnesium bromide **4** (0.5 M in THF, 2.3 mL, 1.13 mmol) in dry THF (0.25 mL) was added dropwise by syringe a solution of the aldehyde **3** (0.20 g, 0.76 mmol) in dry THF (1.5 mL). The mixture was stirred at this temperature for 4 h, and then a saturated aqueous solution of NH_4Cl (10 mL) was added. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine and dried over Na_2SO_4. The filtrate was then concentrated under reduced pressure and purified on silica gel by column chromatography (hexane/EtOAc 7:3) to give the alcohols **29** (0.17 g, 77%), a mixture 24:76 of diastereomers, as a colorless oil: R_f = 0.50 (hexane/EtOAc 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42 (s, 6H), 1.64−2.07 (m, 2H), 2.39 (bd, 1H), 2.45 (d, J = 2.2 Hz, 1H), 2.52 (bd, 1H), 3.44−3.57 (m, 2H), 3.87−4.48 (m, 3H), 4.57 and 4.63 (AB system, J = 12.2 Hz, 2H), 7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 24.8, 24.9, 25.0, 28.6, 30.4, 64.4, 65.3, 66.3, 66.6, 68.8, 70.0, 72.3, 72.4, 73.3, 73.4, 74.1, 74.2, 80.9, 81.0, 100.9, 101.1, 127.6, 127.7, 128.3, 128.4, 130.1, 138.2. EI-MS *m*/*z*: M^+ − Me, 275, (100), 91. Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.38; H, 7.59.

(4*R*,6*R*,8*R*)-1-(6-Benzyloxymethyl-2,2-dimethyl-[1,3]-dioxan-4-yl)-8-(*tert*-butyldimethylsilyloxy)-non-2-yne-1,4-diol (30). To a stirring and −78 °C cooled solution of the alkynol **29** (0.20 g, 0.7 mmol) in THF (3 mL) was added dropwise a solution of *n*-BuLi (1.6 M in hexane, 0.9 mL, 1.5 mmol). After 45 min, at the same temperature, a solution of the aldehyde **5** (0.19 g, 0.8 mmol) in THF (4 mL) was slowly added. The temperature was allowed to warm to room temperature, and the mixture was stirred for 20 h. The reaction mixture was then diluted with Et_2O (20 mL) and washed with a saturated aqueous solution of NH_4Cl (25 mL). The aqueous layer was extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was then purified on silica gel by column chromatography (Et_2O/hexane 6:4) to give the diols **30** (0.14 g, 40%) (a mixture of diastereomers) as a colorless oil: R_f = 0.21 (Et_2O/hexane 7:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.053 (s, 6H), 0.89 (s, 9H), 1.12 (d, J = 6 Hz, 3H), 1.41 (s, 6H), 1.44−2.38 (m, 8H), 2.55 (m, 2H), 3.45 and 3.53 (AB part of an ABX system, J_{AB} = 10.4 Hz, J_{AX} = 6.4 Hz, J_{BX} = 4.3 Hz, 2H), 3.60−4.50 (m, 5H), 4.56 and 4.62 (AB system, J = 12.2 Hz, 2H), 7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7, −4.4, 18.1, 21.3, 21.4, 23.7, 24.7, 24.8, 25.0, 25.9, 28.5, 30.5, 37.6, 38.8, 39.2, 62.3, 62.4, 64.5, 65.4, 66.3, 66.7, 68.4, 68.9, 70.1, 72.5, 73.3, 81.8, 87.2, 87.3, 100.9, 101.1, 127.6, 127.7, 128.4, 138.2. Anal. Calcd for $C_{29}H_{48}O_6Si$: C, 66.88; H, 9.29. Found: C, 66.91; H, 9.24.

(2*Z*,4*R*,6*R*,8*R*)-1-(6-Benzyloxymethyl-2,2-dimethyl-[1,3]-dioxan-4-yl)-8-(*tert*-butyldimethylsilyloxy)-non-2-ene-1,4-diol (31). To a solution of alkyndiol **30** (0.06 g, 0.11 mmol) in Pyr/MeOH 2/1 (2.7 mL) was added Pd/$BaSO_4$ (20 wt %, 0.012 g), and then the mixture was put under a hydrogen atmosphere. After 2 h the mixture was diluted with Et_2O and filtered over Celite, and the solvents were removed in vacuo. The crude residue was diluted with Et_2O and washed with brine. The organic layer was dried over $MgSO_4$ and filtered. Concentration under reduced pressure afforded **31** (0.06 g, 100%), a mixture of diastereomers, as a yellow oil that was used in the next step without further purification: R_f = 0.21 (Et_2O/hexane 7:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.89 (s, 9H), 1.12 (d, J = 6.0 Hz, 3H), 1.30−1.49 (m, 10H), 1.59 (m, 2H), 1.68−1.93 (m, 2H), 3.39−3.66 (m, 2H), 3.72−4.25 (m, 3H), 4.30−4.66 (m, 4H), 5.40−5.72 (m, 2H), 7.30 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ-4.6, −4.4, 18.2, 21.7, 23.7, 23.8, 24.7, 24.9, 25.0, 25.9, 28.1, 31.3, 37.0, 38.2, 66.3, 66.5, 67.3, 67.5, 67.8, 68.5, 68.9, 69.1, 69.5, 69.8, 70.4, 72.4, 73.5, 100.7, 100.9, 127.6, 127.7, 128.4, 128.5, 128.8, 130.9, 136.6, 137.5, 137.6, 138.2. Anal. Calcd for $C_{29}H_{50}O_6Si$: C, 66.63; H, 9.64. Found: C, 66.69; H, 9.63.

(2*Z*,4*R*,6*R*,8*R*)-Benzoic Acid 4-Benzoyloxy-1-(6-benzyloxymethyl-2,2-dimethyl-[1,3]-dioxan-4-yl)-8-(*tert*-butyldimethylsilyloxy)-non-2-enyl Ester (32). To a solution of the alkendiol **31** (0.06 g, 0.11 mmol) in pyridine (1.12 mL) at room temperature was added a solution of benzoyl chloride (0.03 mL, 0.28 mmol) in THF (0.4 mL). After 19 h the mixture was diluted with Et_2O and put into an Erlenmeyer flask, cooled to 0 °C, and washed with a 10% aqueous solution of HCl (5 mL). The solution of HCl was added until pH = 1. The mixture was then washed with a saturated aqueous solution of $NaHCO_3$ and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude was purified on silica gel by chromatography (hexane/Et_2O 85:15) to afford **32** (0.06 g, 72%), a mixture of diastereomers, as a colorless oil: R_f = 0.16 (hexane/Et_2O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.05 (m, 6H), 0.86 (m, 9H), 1.07 (m, 3H), 1.36 (s, 3H), 1.40 (s, 3H), 1.42−1.95 (m, 8H), 3.35−3.55 (m, 2H), 3.73 (m, 1H), 4.01−4.23 (m, 2H), 4.63−4.75 (m, 2H), 5.60−5.84 (m, 2H), 5.99 (m, 2H), 7.30 (m, 5H), 7.38−7.72 (m, 5H), 8.00−8.19 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.8, −4.4, 18.1, 21.5, 23.7, 23.8, 24.6, 24.7, 24.9, 25.9, 30.1, 30.3, 35.0, 39.5, 65.1, 66.1, 66.2, 67.9, 68.3, 68.4, 71.2, 71.5, 71.8, 72.2, 72.6, 73.3, 73.4, 100.8, 127.6−133.7, 138.2, 165.3, 165.6, 171.2. Anal. Calcd for $C_{43}H_{58}O_8Si$: C, 70.65; H, 8.00. Found: C, 70.67; H, 8.07.

(+)-[1*R*,4*R*,6*R*,5*E*,7*E*]-[8-(6-Benzyloxymethyl-2,2-dimethyl-[1,3]-dioxan-4-yl)-1-methyl-octa-5,7-dienyloxy]-*tert*-butyldimethylsilane (2). To a solution of **32** (0.04 g, 0.05 mmol) in THF/MeOH 3/1 (3.5 mL) at room temperature was quickly added sodium hydrogenphosphate (Na_2HPO_4, 0.05 g, 0.38 mmol). After 5 min the mixture was cooled at −20 °C, and Na/Hg 6% (0.21 g, 0.55 mmol) was added and stirred for an additional 5 h. The mixture was diluted with Et_2O and filtered over silica gel. The residue was dried over $MgSO_4$ and concentrated under reduced pressure. The crude was then purified on silica gel by column chromatography (hexane/Et_2O 85:15) to give **2** (0.008 g, 60%) as a colorless oil: R_f = 0.32 (hexane/Et_2O 85:15); $[\alpha]^{25}_D$ +25 (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.89 (s, 9H), 1.12 (d, J = 6.2 Hz, 3H), 1.37−1.51 (m, 4H), 1.42 (s, 6H), 1.75 (t, J = 8 Hz, 2H), 2.07 (m, 2H), 3.48 and 3.52 (AB part of an ABX system, J_{AB} = 10.3 Hz, J_{AX} = 6.2 Hz, J_{BX} = 4.3 Hz, 2H), 3.78 (qt, $J \approx$ 6 Hz, 1H), 4.10 (tdd, X part of an ABX system, 1H), 4.40 (tdd, $J_{4'-5A'} \approx J_{4'-5B'} \approx J_{4'-8} \approx$ 7 Hz, 1H), 4.56 and 4.62 (AB system, J = 12.2 Hz, 2H), 5.58 (dd, J_{7-8} = 15.2 Hz, $J_{4'-8}$ = 6.3 Hz, 1H), 5.70 (dt, J_{5-6} = 15 Hz, J_{4-5} = 7 Hz, 1H), 6.01 (dd, J_{5-6} = 15 Hz, J_{6-7} = 10.5 Hz, 1H), 6.18 (dd, J_{7-8} = 15.2 Hz, J_{6-7} = 10.4 Hz, 1H), 7.3 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.3, −4.0; 18.5, 24.3, 25.3, 25.8, 25.9, 26.3, 33.0, 34.6, 39.6, 66.5, 67.8, 68.8, 73.1, 73.7, 100.8, 128.0, 128.1, 128.8, 130.0, 131.0, 131.8, 136.0, 138.7. Anal. Calcd for $C_{29}H_{48}O_4Si$: C, 71.26; H, 9.90. Found: C, 71.30; H, 9.83.

Acknowledgment. Thanks are due the University of Basilicata and the MIUR (FIRB-Progettazione, preparazione e valutazione biologica e farmacologica di nuove molecole organiche quali potenziali farmaci innovativi grant) for financial support.

Supporting Information Available: General procedures for the preparation of compounds **24**−**28**; ^{1}H NMR data for compounds **24**−**28** and ^{13}C data for compound **28**; copies of ^{1}H, ^{13}C, and COSY NMR spectra for compound **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO049556L