Total Synthesis of (−)-PA-48153C, a Novel Immunosuppressive 2-Pyranone Derivative

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Received June 1, 1995[⊗]

(−)-PA-48153C (**1**), an immunosuppressive agent, was synthesized by starting from (+)-methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2**) and (*S*)-(+)-methyl 3-hydroxy-2-methylpropionate (**3**). The key steps in this synthesis relied upon *trans*-diaxial ring opening of epoxy mesylate **11** in order to introduce the C-5β ethyl group, Wittig reaction of aldehyde **15** with a phosphorus ylide derived from phosphonium salt **28** to combine the cyclic segment **B** and the acyclic segment **C**, and regio- and stereoselective hydroboration of (*Z*)-olefin **29** in order to introduce the C-8α hydroxyl group. The absolute stereochemistry of PA-48153C was unambiguously determined to be the same as that of **1**.

Introduction

Immunosuppressive agents have been attracting much attention since the introduction of cyclosporin A (CsA)[1] and the more potent agent tacrolimus (FK506).[2] Both CsA and FK506 block T lymphocyte activation and are now important drugs for preventing organ rejection after transplant surgery. However, their clinical use is restricted by their significant nephrotoxicity[3] and antibody-mediated responses. The need for drugs possessing novel mechanisms of action or properties conducive to combination therapy led to the development of a variety of agents such as rapamycin,[4] mycophenolate mofetil,[5] 15-deoxyspergualin,[6] brequinar,[7] and purine nucleoside phosphorylase inhibitors.[8] These agents are also potentially useful for treatment of autoimmune diseases, such as rheumatoid arthritis, type I diabetes, psoriasis, and systemic lupus erythematosus.

In the course of our screening program for new immunosuppressive agents, PA-48153C (**1**),[9,10] a novel 2-pyranone derivative, was isolated from the fermentation product of *Streptomyces prunicolor* PA-48153. The structure of PA-48153C was established as **1** based on spectral data, and its relative stereochemistry was confirmed by X-ray crystallographic analysis.[11] PA-48153C showed a potent suppressive effect on the responses of both T and B lymphocytes to mitogens. However, significant cytotoxicity was observed in various tumor cells, and PA-48153C was found to be too toxic *in vivo* for therapeutic use.[12] As the first step toward the discovery of derivatives in which immunosuppressive activity might be dissociated from toxicity, we sought to develop a total synthesis of PA-48153C. In addition, we sought to establish absolute stereochemistry of this important natural product. Here, we report the first total synthesis of (−)-PA-48153C.

Results and Discussion

Since 5,6-dihydro-2*H*-pyran-2-ones (α,β-unsaturated δ-lactones) are widely distributed in both plants and microorganisms and possess a diverse range of biological activity,[13] a variety of synthetic approaches have been employed to prepare this system.[14] In considering various base-catalyzed reactions needed to manipulate the synthesis, we decided to construct a δ-lactone moiety from

[⊗] Abstract published in *Advance ACS Abstracts,* October 15, 1995.

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(3) Heering, P.; Schadewaldt, P.; Bach, D.; Grabensee, B. *Clin. Invest.* **1993**, *71*, 1010.

(4) Sehgal, S. N.; Molnar-Kimber, K.; Ocain, T. D.; Weichman, B. M. *Med. Res. Rev.* **1994**, *14*, 1.

(5) Allison, A. C.; Eugui, E. M. *Immunol. Rev.* **1993**, *136*, 5.

(6) Suzuki, S. *Ann. N.Y. Acad. Sci.* **1993**, *696*, 263.

(7) Makowka, L.; Sher, L. S.; Cramer, D. V. *Immunol. Rev.* **1993**, *136*, 51.

(8) Montgomery, J. A. *Med. Res. Rev.* **1993**, *13*, 209.

(9) (a) Yoshida, T.; Koizumi, K.; Kawamura, Y.; Matsumoto, K.; Itazaki, H. Japan Patent Kokai 5-310726, 1993. (b) *Idem.* European Patent 560389 A1, 1993.

(10) A recently reported plant-growth regulator, pironetin, isolated from *Streptomyces* sp. NK10958, seems to be identical with PA-48153C, see: (a) Kobayashi, S.; Tsuchiya, K.; Harada, T.; Nishide, M.; Kurokawa, T.; Nakagawa, T.; Shimada, N.; Kobayashi, K. *J. Antibiot.* **1994**, *47*, 697. (b) Kobayashi, S.; Tsuchiya, K.; Kurokawa, T.; Nakagawa, T.; Shimada, N.; Iitaka, Y. *Ibid.* **1994**, *47*, 703.

(11) Data of the X-ray crystallographic analysis of PA-48153C can be obtained from Mr. H. Nakai of these laboratories.

(12) A marine-derived 2-pyranone derivative, discodermolide, was reported to possess potent *in vivo* immunosuppressive properties, see: (a) Gunasekera, S. P.; Gunasekera, M.; Longley, R. E. *J. Org. Chem.* **1990**, *55*, 4912. Correction: *Ibid.* **1991**, *56*, 1346. (b) Longley, R. E.; Caddigan, D.; Harmody, D.; Gunasekera, M.; Gunasekera, S. P. *Transplantation* **1991**, *52*, 650. Correction: *Ibid.* **1993**, *55*, 236. (c) *Idem. Ibid.* **1991**, *52*, 656. For synthetic studies, see: (d) Nerenberg, J. B.; Hung, D. T.; Somers, P. K.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 12621. (e) Clark, D. L.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 5878. (f) Golec, J. M. C.; Gillespie, R. J. *Tetrahedron Lett.* **1993**, *34*, 8167. (g) Paterson, I.; Wren, S. P. *J. Chem. Soc., Chem. Commun.* **1993**, 1790. (h) Yang, G.; Myles, D. C. *Tetrahedron Lett.* **1994**, *35*, 2503.

(13) For recent papers, see: (a) Abe, K.; Yoshida, M.; Naoki, H.; Horinouchi, S.; Beppu, T. *J. Antibiot.* **1993**, *46*, 735. (b) Fu, X.; Sévenet, T.; Hamid, A.; Remy, F.; Païs, M. *Phytochemistry* **1993**, *33*, 1272. (c) Pereda-Miranda, R.; Hernández, L.; Villavicencio, M. J.; Novelo, M.; Ibarra, P.; Chai, H.; Pezzuto, J. M. *J. Nat. Prod.* **1993**, *56*, 583. (d) Aycard, J.-P.; Kini, F.; Kam, B.; Gaydou, E. M.; Faure, R. *Ibid.* **1993**, *56*, 1171. (e) Kohama, T.; Nakamura, T.; Kinoshita, T.; Kaneka, I.; Shiraishi, A. *J. Antibiot.* **1993**, *46*, 1512. (f) Tabuchi, H.; Ichihara, A. *J. Chem. Soc., Perkin Trans. 1* **1994**, 125. (g) Amemiya, M.; Someno, T.; Sawa, R.; Naganawa, H.; Ishizuka, M.; Takeuchi, T. *J. Antibiot.* **1994**, *47*, 541. (h) Sehlapelo, B. M.; Drewes, S. E.; Scott-Shaw, R. *Phytochemistry* **1994**, *37*, 847. (i) Matsuda, M.; Endo, Y.; Fushiya, S.; Endo, T.; Nozoe, S. *Heterocycles* **1994**, *38*, 1229. For a review on naturally occurring 6-substituted 5,6-dihydro-2*H*-pyran-2-ones, see: (j) Davies-Coleman, M. T.; Rivett, D. E. A. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Grisebach, H., Kirby, G. W., Tamm, Ch., Eds.; Springer-Verlag: New York, 1989; Vol. 55, pp 1–35.

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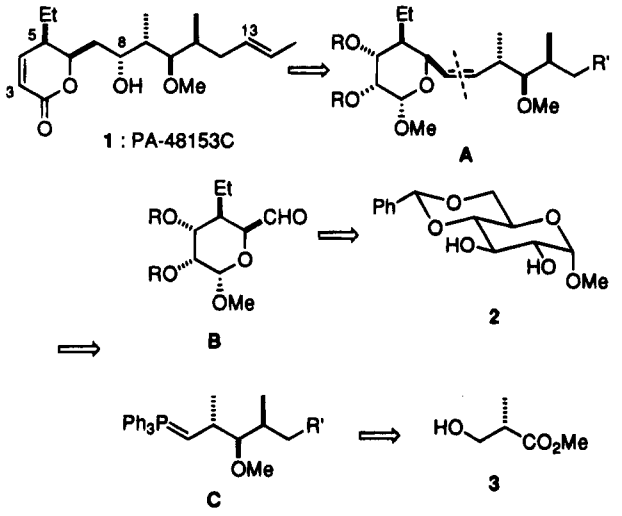
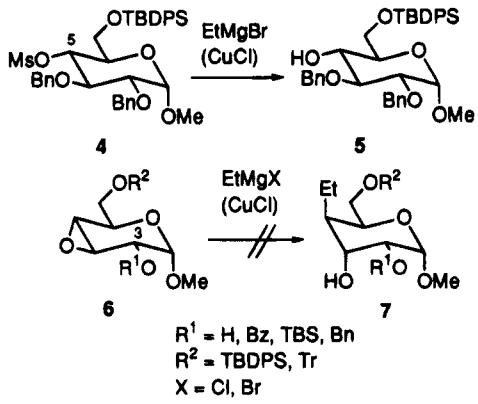
Scheme 1



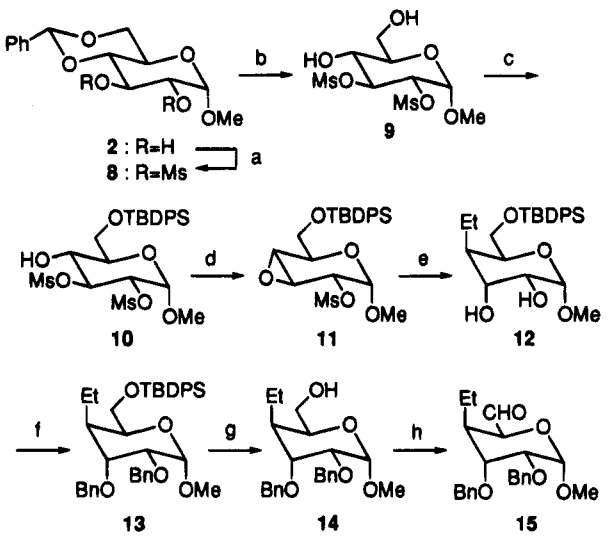
Scheme 2



a protected δ-lactol at the last step in the synthetic sequence. Additional consideration of structure **1** in which the sugar portion was clearly defined[15] guided the design of our retrosynthetic analysis shown in Scheme 1. The key intermediate **A** would be obtained by combining segment **B** and segment **C**, each of which would be prepared from commercially available optically active compounds, (+)-methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2**) and (*S*)-(+)-methyl 3-hydroxy-2-methylpropionate (**3**), respectively.

In order to prepare cyclic segment **B** from glucopyranoside **2**, an axial ethyl group had to be introduced into the C-5 (based on the classical lactone numbering) position of the saccharide ring. However, due to the difficulty of the nucleophilic substitution reaction at this position, the Grignard reagent attacked the sulfur atom of mesylate **4** to provide alcohol **5**[16] in Scheme 2.[17] We also tried to introduce the ethyl group by *trans*-diaxial

Scheme 3[a]



[a] (a) MsCl, Py; (b) HCl; (c) TBDPS-Cl, imidazole (90% for a, b, c); (d) NaOMe (59%); (e) EtMgCl, CuCl (59%); (f) BnBr, NaH (81%); (g) Bu_4NF (97%); (h) DMSO, $(COCl)_2$ followed by Et_3N.

ring opening[18] of epoxide **6**,[19] but all attempts to obtain the ethyl compound **7** were unsuccessful.[20]

To overcome this problem, we decided to convert the protecting group for the C-3 alcohol of **6** to a mesyl group in order to increase the reactivity of the C-5 position.[21] Therefore, as shown in Scheme 3, dimesylate **10** was prepared from (+)-methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2**) according to a known procedure.[22] Treatment of dimesylate **10** with sodium methoxide in chloroform gave the required epoxide **11**, while using sodium hydride in *N,N*-dimethylformamide lowered the yield of the product.

Ring opening of **11** with ethylmagnesium chloride in ether–tetrahydrofuran in the presence of copper(I) chloride[23] led to the introduction of the expected axial ethyl group into the C-5 position (59%). The success of this reaction was ascribed to copper(I) chloride, without which no ethyl group introduction was observed. In addition, as in the case of **4**, excess Grignard reagent caused the subsequent demesylation to provide diol **12**. Protection of both hydroxyl groups of **12** as the benzyl ether, deprotection of the *tert*-butyldiphenylsilyl (TBDPS) group of **13** with tetra-*n*-butylammonium fluoride, and Swern oxidation of alcohol **14** furnished aldehyde **15** (segment B).

Scheme 4 shows the synthetic sequence for the preparation of the acyclic segment **C**. Among a number of reported methods for constructing a polypropionate-

(14) For recent synthetic work, see: (a) Tsubuki, M.; Kanai, K.; Honda, T. *Heterocycles* **1993**, *35*, 281. (b) Haase, B.; Schneider, M. P. *Tetrahedron Asymmetry* **1993**, *4*, 1017. (c) Pilli, R. A.; Murta, M. M. *J. Org. Chem.* **1993**, *58*, 338. (d) Tabuchi, H.; Hamamoto, T.; Miki, S.; Tejima, T.; Ichihara, A. *Ibid.* **1994**, *59*, 4749. (e) Masaki, Y.; Imaeda, T.; Kawai, M. *Chem. Pharm. Bull.* **1994**, *42*, 179. (f) Mori, Y.; Furukawa, H. *Ibid.* **1994**, *42*, 2161. (g) Noshita, T.; Sugiyama, T.; Kitazumi, Y.; Oritani, T. *Tetrahedron Lett.* **1994**, *35*, 8259. (h) Yang, Z.; Zhou, W. *Tetrahedron* **1994**, *51*, 1429. For a recent review, see: (i) Ogliaruso, M. A.; Wolfe, J. F. In *Synthesis of Lactones and Lactams*; Patai, S., Rappoport, Z., Eds.; John Wiley and Sons, Inc.: New York, 1993; pp 3–131, 271–396.

(15) Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159.

(16) Ito, Y.; Ogawa, T. *Carbohydr. Res.* **1990**, *202*, 165. Mesylate **4** was prepared from **5** (MsCl, Py).

(17) Sabol, M. A.; Andersen, K. K. *J. Am. Chem. Soc.* **1969**, *91*, 3603.

(18) *Trans*-diaxial opening is well documented, see: Challenger, S.; Procter, G. *Tetrahedron Lett.* **1986**, *27*, 391 and references cited therein.

(19) Prepared from methyl 2-*O*-benzoyl-3-*O*-(methanesulfonyl)-α-D-glucopyranoside[37] ((a) TBDPS-Cl or TrCl; (b) NaH, DME; (c) protection of the alcohol).

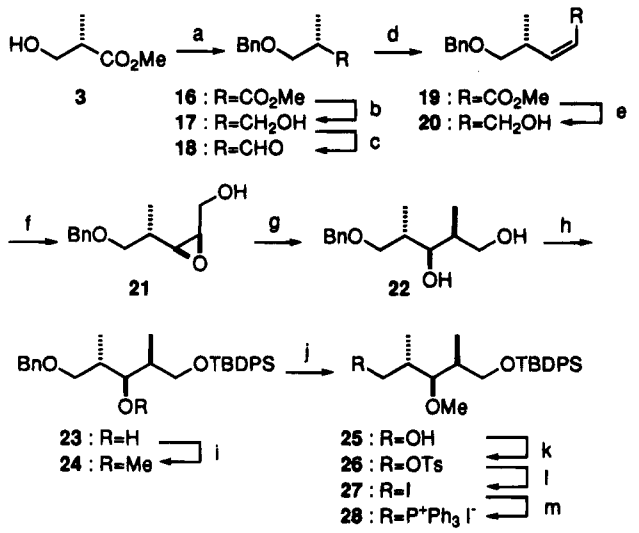
(20) Any C-5 ethyl group was not observed with or without copper(I) chloride.

(21) (a) Gao, L.-x.; Saitoh, H.; Feng, F.; Murai, A. *Chem. Lett.* **1991**, 1787. (b) Chong, J. M. *Tetrahedron Lett.* **1992**, *33*, 33.

(22) (a) Fraser-Reid, B.; Boctor, B. *Can. J. Chem.* **1969**, *47*, 393. (b) Morimoto, Y.; Mikami, A.; Shirahama, H. *J. Chem. Soc., Chem. Commun.* **1991**, 1376.

(23) (a) Corey, E. J.; Weigel, L. O.; Chamberlin, A. R.; Lipshutz, B. *J. Am. Chem. Soc.* **1980**, *102*, 1439. (b) Tatsuta, K.; Koguchi, Y.; Kase, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2525. For reviews on copper(I) catalyzed reactions, see: (c) Posner, G. H. *Org. React.* **1975**, *22*, 253. (d) Erdik, E. *Tetrahedron* **1984**, *40*, 641. (e) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Ibid.* **1984**, *40*, 5005.

Scheme 4[a]



[a] (a) $PhCH_2OC(=NH)CCl_3$, CF_3SO_3H (84%); (b) $LiAlH_4$ (94%); (c) DMSO, $(COCl)_2$ followed by Et_3N; (d) $(CF_3CH_2O)_2P(=O)CH_2CO_2Me$, $KN(TMS)_2$, 18-Crown-6 (82% for c, d); (e) DIBAL (95%); (f) MCPBA (93%); (g) $LiCuMe_2$ (67%); (h) TBDPS-Cl, imidazole; (i) MeI, NaH (91% for h, i); (j) H_2, $PdCl_2$ (86%); (k) TsCl, Et_3N, DMAP (99%); (l) NaI (95%); (m) Ph_3P (97%).

derived chain,[24] we adopted Nagaoka and Kishi's procedure,[25] which could be applied to various stereoisomers, to prepare the optically active diol **22** from (*S*)-(+)-methyl 3-hydroxy-2-methylpropionate (**3**). In order to avoid racemization of the asymmetric center, we employed acidic benzylation of **3**[26] and two-step conversion from ester **16** to aldehyde **18** (lithium aluminum hydride reduction of **16** and Swern oxidation of alcohol **17**) instead of direct reduction with diisobutylaluminum hydride. Next, bis(2,2,2-trifluoroethyl)[(methoxycarbonyl)methyl]-phosphonate[27] was employed for selective formation of *cis*-α,β-unsaturated ester **19**. A small amount of *trans*-**19** was also obtained, and the stereoselectivity was 9.7:1. With this *cis*-ester **19** available in high enantiomeric excess, the three consecutive asymmetric units were constructed according to the reported procedure.[28]

Selective protection of the primary hydroxyl group of **22** as a TBDPS ether, conversion of alcohol **23** to methyl ether **24**, and selective deprotection of the benzyl ether by catalytic hydrogenolysis using palladium(II) chloride provided alcohol **25**. Subsequent conversion of **25** to the corresponding tosylate **26**, treatment of **26** with sodium iodide in refluxing acetone, and displacement of iodide **27** with triphenylphosphine afforded the desired phosphonium salt **28** which could be the precursor of segment **C**.

With both optically active segments in hand, we examined various conditions of the Wittig reaction to obtain the key intermediate **A**. Although deprotonation of phosphonium salt **28** by potassium *tert*-butoxide or potassium bis(trimethylsilyl)amide was unsuccessful, *n*-butyllithium gave the phosphorus ylide, and the coupling reaction with aldehyde **15** proceeded smoothly to stereoselectively afford (*Z*)-olefin **29** as shown in Scheme 5.

Hydroboration of **29** in tetrahydrofuran under ultrasound followed by treatment with alkaline hydrogen peroxide was found to be regio- and stereoselective, giving the desired C-8α alcohol **30** (59%). Since other byproducts were rather messy, the alcohol **30** was the only compound which could be identified. We based the regiochemical assignment of the hydroxyl group on the ^1H NMR decoupling experiment,[29] and the stereochemistry was confirmed later in the synthesis by comparison with the natural product **1**. In this reaction, the preferred conformation of the pyranose ring of **29** is assumed to be as depicted in Scheme 6 on the grounds of NOESY.[30] In addition, this conformation around the C-9 stereocenter is probably favored because of the allylic strain effects.[31] Therefore, the regio- and stereoselectivity observed can be explained by the preferential attack of a borane complexed to the pyranose oxygen from the sterically less hindered face.

Next, the C-8 hydroxyl group of **30** was protected with the methoxymethyl (MOM) group in preparation for later operations in the synthesis. Since this C-8 alcohol was rather sterically hindered, a more bulky protecting group such as 2-methoxyethoxymethyl ether could not be used. Deprotection of the TBDPS group of **31** and Swern oxidation of alcohol **32** afforded aldehyde **33**. Horner–Emmons reaction of **33** using dimethyl (2-oxopropyl)-phosphonate gave *trans*-α,β-unsaturated ketone **34** in good yield, while the yield of the Wittig reaction using 1-(triphenylphosphoranylidene)-2-propanone was considerably low (26%). Conversion of **34** to the α,β-unsaturated *p*-tosylhydrazone **35** and reductive deoxygenation of carbonyl tosylhydrazone **35** with sodium borohydride in acetic acid[32] secured (*E*)-olefin **36** in which the double bond migrated stereoselectively to the desired position.

In order to apply the Tipson–Cohen reaction,[33] which is useful in the synthesis of unsaturated sugars, for introduction of the C-3 double bond, we converted **36** to dimesylate **38** through selective deprotection of both benzyl groups of **36** by sodium–liquid ammonia followed by mesylation of diol **37**. Elimination of vicinal sulfonyloxy groups from **38** using potassium iodide and zinc–copper couple in refluxing *N,N*-dimethylformamide pro-

(24) For recent work in this area, see: (a) Miyashita, M.; Yoshihara, K.; Kawamine, K.; Hoshino, M.; Irie, H. *Tetrahedron Lett.* **1993**, *34*, 6285. (b) Kigoshi, H.; Ojika, M.; Ishigaki, T.; Suenaga, K.; Mutou, T.; Sakakura, A.; Ogawa, T.; Yamada, K. *J. Am. Chem. Soc.* **1993**, *116*, 7443. (c) Nakata, T.; Komatsu, T.; Nagasawa, K. *Chem. Pharm. Bull.* **1994**, *42*, 2403. (d) Arimoto, H.; Nishiyama, S.; Yamamura, S. *Tetrahedron Lett.* **1994**, *35*, 9581. (e) Dominguez, E.; Carretero, J. C. *Tetrahedron* **1994**, *50*, 7557. (f) Hoffmann, R. W.; Dahmann, G.; Andersen, M. W. *Synthesis* **1994**, 629. (g) Paterson, I.; Bower, S.; McLeod, M. D. *Tetrahedron Lett.* **1995**, *36*, 175. For general reviews, see: (h) Mukaiyama, T. *Org. React.* **1982**, *28*, 203. (i) Heathcock, C. H. In *Asymmetric Syntheses*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, pp 111–212. (j) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1. (k) Hoffmann, R. W. *Ibid.* **1987**, *26*, 489.

(25) (a) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873. (b) Kishi, Y. *Pure Appl. Chem.* **1981**, *53*, 1163.

(26) (a) Iversen, T.; Bundle, D. R. *J. Chem. Soc., Chem. Commun.* **1981**, 1240. (b) Widmer, U. *Synthesis* **1987**, 568. (c) Paterson, I.; Lister, M. A. *Tetrahedron Lett.* **1988**, *29*, 585.

(27) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.

(28) Epoxidation of **20** and opening of the epoxide with lithium dimethylcuprate seemed to be highly selective as indicated.[25]

(29) Irradiation at C-6 H resulted in an alteration in the signal of C-7 H_2 to a doublet, while the signal pattern of C-8 H did not change. Irradiation at C-7 H_2 changed the signal patterns of both C-6 H and C-8 H.

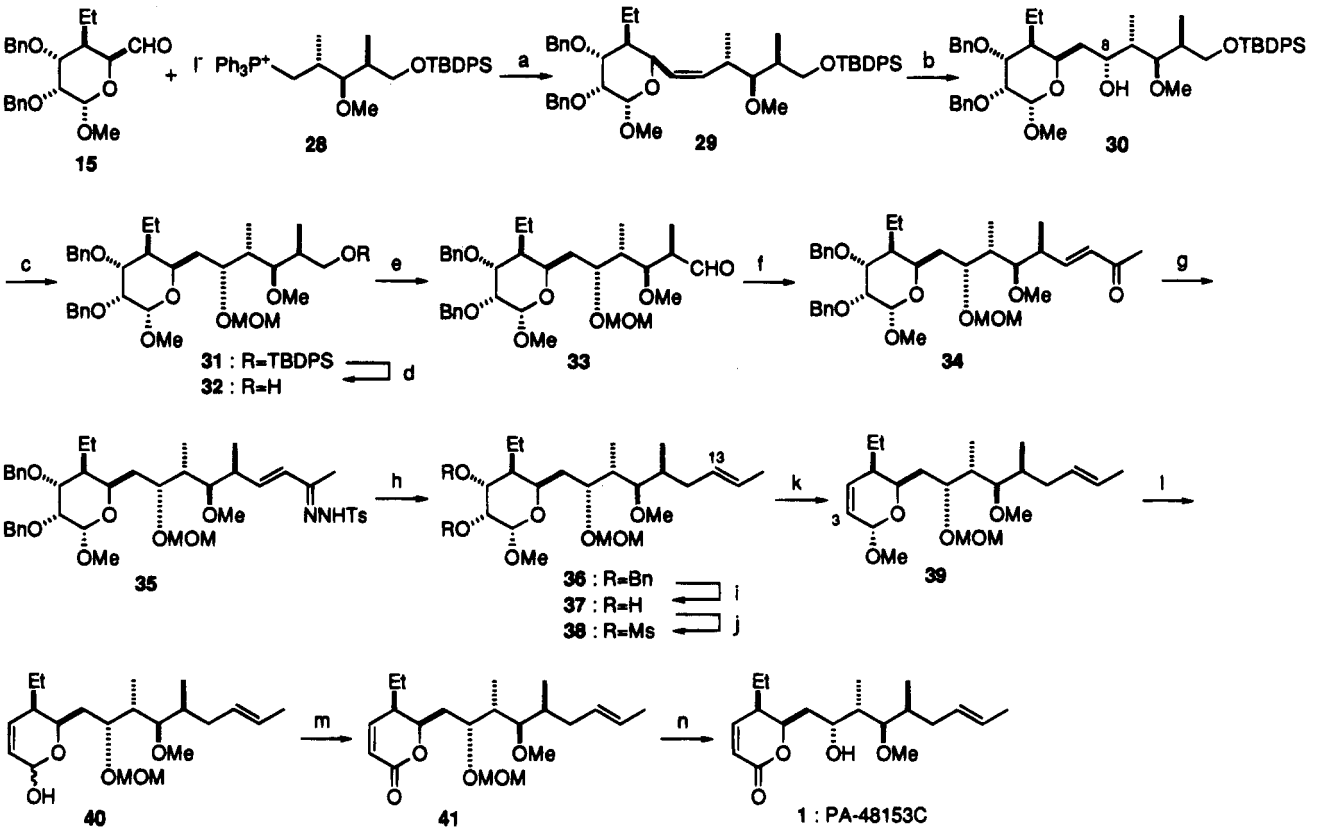
(30) There were correlations between C-2β H and C-4β H.

(31) (a) Schmid, G.; Fukuyama, T.; Akasaka, K.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 259. (b) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.

(32) (a) Hutchins, R. O.; Kacher, M.; Rua, L. *J. Org. Chem.* **1975**, *40*, 923. (b) Hutchins, R. O.; Natale, N. R. *Ibid.* **1978**, *43*, 2299.

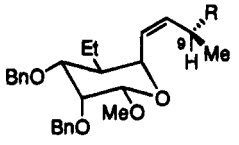
(33) (a) Tipson, R. S.; Cohen, A. *Carbohydr. Res.* **1965**, *1*, 338. (b) Fraser-Reid, B.; Boctor, B. *Can. J. Chem.* **1969**, *47*, 393. (c) Holder, N. L.; Fraser-Reid, B. *Ibid.* **1973**, *51*, 3357. For a general review, see: (d) Block, E. *Org. React.* **1984**, *30*, 457.

Scheme 5[a]



[a] (a) *n*-BuLi (61% from **14**); (b) B_2H_6, H_2O_2 (59%); (c) MOMCl, *i*-Pr_2NEt (100%); (d) Bu_4NF (99%); (e) DMSO, $(COCl)_2$ followed by Et_3N; (f) KO*t*-Bu, $(CH_3O)_2P(O)CH_2COCH_3$ (88% for e, f); (g) $TsNHNH_2$; (h) $NaBH_4$, HOAc (68% for g, h); (i) Na, NH_3 (76%); (j) MsCl, Py, DMAP (96%); (k) KI, Zn(Cu) (42%); (l) 75% aq. HOAc, 40°C; (m) Jones (68% for l, m); (n) 80% aq. HOAc, reflux (100%).

Scheme 6



29

R = CH(OMe)CH(Me)CH_2OTBDPS

ceeded successfully to afford olefin **39**. Efforts to convert diol **37** to olefin **39** from the corresponding 1-(dimethylamino)(methylene)acetal in a one-pot process[34] or efforts to effect samarium(II) iodide-promoted dideacetoxylation of the diacetoxy lactone[35] were unrewarding.

Selective hydrolysis of the protected δ-lactol in **39** with 75% aqueous acetic acid at 40 °C and oxidation of **40** using the Jones reagent in acetone gave δ-lactone **41**. We completed the total synthesis of PA-48153C (**1**) by deprotection of the MOM group of **41** using refluxing 80% aqueous acetic acid. The synthetic compound was identical in all respects, including biological activities and molecular rotation ($[\alpha]^{24}_D$ −142.9°), with the natural product from *Streptomyces prunicolor* PA-48153 ($[\alpha]^{27}_D$ −143.7°).[9] These results established the absolute stereochemistry of the natural product (−)-**1** as that depicted in the formula in Scheme 1 and Scheme 5.[36] With the completion of the total synthesis of PA-48153C (**1**), we next plan to prepare various derivatives using this synthetic route in an attempt to develop useful immunosuppressive agents.

Experimental Section

Melting points are uncorrected. ^1H NMR and ^{13}C NMR spectra were determined at 200 and 50.3 MHz, respectively. Liquid secondary ion mass spectra (LSIMS) and high resolution (HR)-LSIMS were determined using *m*-nitrobenzyl alcohol as a matrix. Unless otherwise stated, all reactions were carried out under a nitrogen atmosphere with anhydrous solvents that had been dried over type 4A molecular sieves. Drying of an organic phase over anhydrous sodium sulfate is simply indicated by the word "dried". Column chromatography using Merck silica gel 60 or a Merck Lobar column is referred to as "chromatography on silica gel".

Methyl 3,4-Anhydro-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-(methanesulfonyl)-α-D-allopyranoside (11). To a solution of 23.5 g (39.9 mmol) of **10**[22b] in 180 mL of 1:8 methanol–chloroform was added 6.47 g (120 mmol) of sodium methoxide at 0 °C. After this was stirred for 3 days at 25 °C, 12.9 g (240 mmol) of sodium methoxide was added at 0 °C. The mixture was stirred for 2 days at 25 °C and then poured into saturated ammonium chloride solution and extracted with chloroform. The organic layer was washed with water, dried, and concentrated. The crude product was chromatographed on silica gel using 1:2 ethyl acetate–hexane to afford 11.6 g (59%) of **11**, mp 96–97 °C. $[\alpha]^{24}_D$ +18.7° (*c* 1.03, $CHCl_3$). IR ($CHCl_3$) 3020, 2928, 1351, 1176, 959 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.07 (s, 9H), 3.16 (s, 3H), 3.38 (s, 3H), 3.48–3.53 (m, 1 H), 3.61 (d, *J* = 4.8

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Hz, 1H), 3.80−3.93 (2H, m), 4.00−4.13 (m, 1H), 4.86 (d, J = 5.0 Hz, 1H), 5.01 (dd, J = 2.4 and 5.0 Hz, 1H), 7.34−7.42 (m, 6H), 7.61−7.74 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 19.26, 26.80, 39.02, 49.47, 56.36, 56.88, 64.02, 67.68, 72.57, 96.20, 127.82, 129.95, 132.91, 132.96, 135.58. LSIMS m/z 951 $(2M - H)^+$, 491 $(M - H)^+$. Anal. Calcd for $C_{24}H_{32}O_7SSi$: C, 58.51; H, 6.55. Found: C, 58.59; H, 6.51.

Methyl 6-*O*-(*tert*-Butyldiphenylsilyl)-4-deoxy-4-*C*-ethyl-α-D-gulopyranoside (12). To 817 mg (8.25 mmol) of copper (I) chloride in 130 mL of ether was added 130 mL (260 mmol) of 2.0 M ethylmagnesium chloride in tetrahydrofuran at −30 °C. The mixture was stirred for 20 min, and 8.00 g (16.3 mmol) of **11** in 130 mL of ether was added dropwise over a 15-min period at −30 °C. After being stirred for 20 min, the mixture was allowed to warm to 0 °C and stirred for 40 min. The mixture was poured into saturated ammonium chloride solution and extracted with ethyl acetate. The organic solution was washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 1:1 ethyl acetate−hexane to afford 4.24 g (59%) of **12** as a colorless oil. $[\alpha]^{22}_D$ +54.4° (c 1.10, $CHCl_3$). IR ($CHCl_3$) 3564 and 3510 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 7.6 Hz, 3H), 1.05 (s, 9H), 1.11−1.51 (m, 2H), 1.80−1.92 (m, 1H), 3.42 (s, 3H), 3.58−3.72 (m, 1H), 3.63 (dd, J = 5.1 and 10.6 Hz, 1H), 3.78 (dd, J = 7.0 and 10.6 Hz, 1H), 3.90−4.00 (m, 1H), 4.02−4.16 (m, 1H), 4.74 (d, J = 3.4 Hz, 1H), 7.33−7.47 (m, 6H), 7.62−7.75 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 12.28, 17.72, 19.14, 26.76, 44.19, 55.59, 63.92, 65.26, 65.83, 71.07, 100.88, 127.67, 127.74, 129.70, 129.77, 133.35, 135.54, 135.62. LSIMS m/z 911 $(2M + Na)^+$, 467 $(M + Na)^+$. Anal. Calcd for $C_{25}H_{36}O_5Si$: C, 67.53; H, 8.16. Found: C, 67.33; H, 8.24.

Methyl 2,3-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-4-deoxy-4-*C*-ethyl-α-D-gulopyranoside (13). To 917 mg (38.2 mmol) of sodium hydride in 20 mL of *N,N*-dimethylformamide was added 2.58 g (5.80 mmol) **12** in 5 mL of *N,N*-dimethylformamide at −30 °C. To this mixture was added 5.0 mL (41.8 mmol) of benzyl bromide at −30 °C. The mixture was allowed to warm to 20 °C and stirred for 4 h, and then the reaction was quenched with methanol at −30 °C. The mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated. The residue was chromatographed on silica gel using 1:8 ethyl acetate−hexane to give 2.93 g (81%) of **13** as a colorless oil. $[\alpha]^{22}_D$ +16.7° (c 1.10, $CHCl_3$). IR ($CHCl_3$) 3006, 2926, 1111 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.65 (t, J = 7.6 Hz, 3H), 1.04 (s, 9H), 1.15−1.38 (m, 2H), 1.75−1.88 (m, 1H), 3.39−3.48 (m, 1H), 3.44 (s, 3H), 3.53 (dd, J = 5.9 and 10.3 Hz, 1H), 3.66−3.76 (m, 1H), 3.70 (dd, J = 7.5 and 10.3 Hz, 1H), 4.35−4.49 (m, 1H), 4.52 and 4.58 (ABq, J = 11.2 Hz, 2H), 4.69 (s, 2H), 4.70 (d, J = 3.4 Hz, 1H), 7.20−7.46 (m, 16H), 7.61−7.73 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 12.15, 17.55, 19.16, 26.75, 40.69, 55.65, 63.92, 66.65, 70.87, 71.56, 72.21, 73.09, 98.60, 127.40, 127.64, 127.85, 128.13, 128.16, 128.34, 129.61, 129.65, 133.40, 133.50, 135.60, 138.12, 138.83. LSIMS m/z 1271 $(2M + Na)^+$, 647 $(M + Na)^+$. HR-LSIMS m/z 647.3166 $(M + Na)^+$ (calcd for $C_{39}H_{48}NaO_5Si$ m/z 647.3166).

Methyl 2,3-Di-*O*-benzyl-4-deoxy-4-*C*-ethyl-α-D-gulopyranoside (14). A mixture of 2.91 g (4.66 mmol) of **13** and 14.4 mL (14.4 mmol) of 1.0 M tetra-*n*-butylammonium fluoride in tetrahydrofuran was stirred for 2.5 h at 25 °C. The mixture was diluted with ethyl acetate, washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 1:4 ethyl acetate−hexane to afford 1.75 g (97%) of **14** as a colorless oil. $[\alpha]^{22}_D$ +41.2° (c 1.08, $CHCl_3$). IR ($CHCl_3$) 3592 and 3486 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.73 (t, J = 7.6 Hz, 3H), 0.98−1.50 (m, 2H), 1.64−1.79 (m, 1H), 3.48 (s, 3H), 3.49−3.56 (m, 1H), 3.50 (dd, J = 4.0 and 11.8 Hz, 1H), 3.68 (dd, J = 7.4 and 11.8 Hz, 1H), 3.70−3.78 (m, 1H), 4.30−4.41 (m, 1H), 4.53 and 4.58 (ABq, J = 11.2 Hz, 2H), 4.65 and 4.75 (ABq, J = 12.6 Hz, 2H), 4.73 (d, J = 3.4 Hz, 1H), 7.21−7.45 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 12.39, 18.21, 41.49, 55.91, 63.36, 67.31, 71.07, 71.86, 72.35, 73.64, 98.71, 127.45, 127.78, 127.85, 128.02, 128.21, 128.39, 137.98, 138.79. LSIMS m/z 795 $(2M + Na)^+$, 409 $(M + Na)^+$. HR-LSIMS m/z 409.1995 $(M + Na)^+$ (calcd for $C_{23}H_{30}NaO_5$ m/z 409.1990).

Methyl 2,3-Di-*O*-benzyl-6-dehydro-4-deoxy-4-*C*-ethyl-α-D-gulopyranoside (15). To a solution of 0.66 mL (9.29 mmol) of dimethyl sulfoxide in 15 mL of dichloromethane was added 0.64 mL (7.05 mmol) of oxalyl chloride at −78 °C. After this was stirred for 10 min, a solution of 1.28 g (3.31 mmol) of **14** in 5 mL of dichloromethane was added. The solution was allowed to warm to −40 °C, and then 1.8 mL (12.9 mmol) of triethylamine was added. The mixture was allowed to warm to 0 °C, diluted with water, and extracted with dichloromethane. The organic phase was washed with water, dried, and evaporated to afford 1.27 g of **15**, which was used for the Wittig reaction without further purification. IR ($CHCl_3$) 1734 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.73 (t, J = 7.6 Hz, 3H), 1.03−1.49 (m, 2H), 2.12−2.28 (m, 1H), 3.47 (s, 3H), 3.50−3.56 (m, 1H), 3.74−3.79 (m, 1H), 4.52 and 4.58 (ABq, J = 12.6 Hz, 2H), 4.70 and 4.79 (ABq, J = 12.6 Hz, 2H), 4.76 (d, J = 2.8 Hz, 1H), 4.82 (d, J = 3.8 Hz, 1H), 7.22−7.44 (m, 10H), 9.63 (s, 1H).

(2*R*,3*S*,4*R*)-1-(Benzyloxy)-5-[(*tert*-butyldiphenylsilyl)-oxy]-2,4-dimethyl-3-pentanol (23). To a solution of 5.65 g (23.7 mmol) of **22**[25a] in 100 mL of *N,N*-dimethylformamide were added 3.06 g (44.9 mmol) of imidazole and 6.7 mL (25.9 mmol) of *tert*-butyldiphenylsilyl chloride. The mixture was stirred for 14 h at 25 °C, diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1:10 ethyl acetate−hexane to afford 11.3 g of **23**, which was used for the next reaction without further purification. IR ($CHCl_3$) 3476 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.85 (d, J = 6.8 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H), 1.07 (s, 9H), 1.70−2.01 (m, 2H), 3.57 (d, J = 5.8 Hz, 2H), 3.62−3.79 (m, 3H), 4.52 (s, 2H), 7.21−7.44 (m, 10H), 7.61−7.77 (m, 5H). LSIMS m/z 953 $(2M + H)^+$, 477 $(M + H)^+$, 419 $(M - C_4H_9)^+$.

(2*R*,3*S*,4*R*)-1-(Benzyloxy)-5-[(*tert*-butyldiphenylsilyl)-oxy]-3-methoxy-2,4-dimethylpentane (24). To a solution of the above product **23** in 180 mL of *N,N*-dimethylformamide was added 5.9 mL (94.7 mmol) of iodomethane. The mixture was cooled to 0 °C, and 2.05 g (85.5 mmol) of sodium hydride was added. The mixture was stirred for 30 min at 0 °C and for 1 h at 25 °C, and then the reaction was quenched with methanol at 0 °C. The mixture was diluted with water and extracted with ethyl acetate. The organic solution was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1:20 ethyl acetate−hexane to give 10.6 g (91%, two steps) of **24** as a colorless oil. $[\alpha]^{22}_D$ −2.10° (c 1.11, $CHCl_3$). IR ($CHCl_3$) 2926, 1110 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.76 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.07 (s, 9H), 1.80−1.99 (m, 2H), 3.38 (s, 3H), 3.41 (dd, J = 2.7 and 8.2 Hz, 1H), 3.43−3.71 (m, 4H), 4.51 (s, 2H), 7.22−7.44 (m, 10H), 7.62−7.71 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 9.79, 14.88, 19.29, 26.90, 36.78, 37.59, 60.90, 66.41, 72.83, 72.94, 81.81, 127.29, 127.34, 127.61, 128.26, 129.56, 133.89, 133.94, 135.49, 135.57, 138.88. LSIMS m/z 513 $(M + Na)^+$, 491 $(M + H)^+$. Anal. Calcd for $C_{31}H_{42}O_3Si$: C, 75.87; H, 8.63. Found: C, 76.01; H, 8.62.

(2*S*,3*S*,4*R*)-5-[(*tert*-Butyldiphenylsilyl)oxy]-3-methoxy-2,4-dimethyl-1-pentanol (25). A solution of 2.31 g (4.71 mmol) of **24** in 83 mL of methanol was hydrogenated using 137 mg (0.774 mmol) of palladium(II) chloride for 20 min. The mixture was filtered through Celite, and the filtrate was concentrated. The crude product was chromatographed on silica gel using 1:1 ether−hexane to afford 1.62 g (86%) of **25** as a colorless oil. $[\alpha]^{22}_D$ +5.27° (c 1.15, $CHCl_3$). IR ($CHCl_3$) 3470 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.82 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 1.07 (s, 9H), 1.74−1.97 (m, 2H), 3.38 (dd, J = 2.7 and 8.2 Hz, 1H), 3.47 (s, 3H), 3.49−3.73 (m, 4H), 7.32−7.46 (m, 6H), 7.58−7.71 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 10.37, 14.83, 19.25, 26.88, 37.67, 38.44, 61.19, 66.28, 67.15, 86.55, 127.66, 129.65, 133.68, 135.55. LSIMS m/z 401 $(M + H)^+$. Anal. Calcd for $C_{24}H_{36}O_3Si$: C, 71.95; H, 9.06. Found: C, 71.97; H, 9.11.

(2*R*,3*R*,4*R*)-5-[(*tert*-Butyldiphenylsilyl)oxy]-3-methoxy-2,4-dimethylpentyl *p*-Toluenesulfonate (26). To a solution of 9.54 g (23.8 mmol) of **25** in 200 mL of dichloromethane were added 6.79 g (35.5 mmol) of *p*-toluenesulfonyl chloride, 5.0 mL (35.9 mmol) of triethylamine, and 4.34 g (35.6 mmol) of 4-(dimethylamino)pyridine. The mixture was stirred for 2.5

h at 25 °C and then diluted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 1:5 ether–hexane to afford 13.1 g (99%) of **26** as a colorless oil. IR ($CHCl_3$) 2926, 1359, and 1175 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.69 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 1.05 (s, 9H), 1.64–2.00 (m, 2H), 2.44 (s, 3H), 3.28 (s, 3H), 3.30 (dd, J = 2.4 and 9.4 Hz, 1H), 3.51 (dd, J = 6.2 and 9.8 Hz, 1H), 3.59 (dd, J = 8.4 and 9.8 Hz, 1H), 4.10 (d, J = 4.2 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.35–7.46 (m, 6H), 7.59–7.70 (m, 4H), 7.80 (d, J = 8.4 Hz, 2H). LSIMS m/z 555 $(M + H)^+$, 497 $(M - C_4H_9)^+$. HR-LSIMS m/z 555.2594 $(M + H)^+$ (Calcd for $C_{31}H_{43}O_5SSi$ m/z 555.2598).

(2*R*,3*R*,4*R*)-5-[(*tert*-Butyldiphenylsilyl)oxy]-3-methoxy-2,4-dimethylpentyl Iodide (27). To a solution of 13.1 g (23.6 mmol) of **26** in 180 mL of acetone was added 7.36 g (47.2 mmol) of sodium iodide. The mixture was refluxed 15 h and then filtered through Celite, and the filtrate was diluted with ethyl acetate. The organic layer was washed with saturated sodium sulfite solution and brine and then dried and concentrated. The crude product was chromatographed on silica gel using 1:19 ethyl acetate–hexane to afford 11.4 g (95%) of **27** as colorless oil. IR ($CHCl_3$) 2954, 2924, 1109 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.73 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H), 1.08 (s, 9H), 1.37–1.56 (m, 1H), 1.74–1.90 (m, 1H), 3.36 (dd, J = 2.4 and 9.4 Hz, 1H), 3.39–3.53 (m, 2H), 3.53 (s, 3H), 3.53 (dd, J = 6.0 and 10.2 Hz, 1H), 3.63 (dd, J = 9.0 Hz and 10.2 Hz, 1H), 7.33–7.48 (m, 6H), 7.62–7.72 (m, 4H). HR-LSIMS m/z 533.1352 $(M + Na)^+$ (calcd for $C_{24}H_{35}INaO_2Si$ m/z 533.1349).

(2*R*,3*R*,4*R*)-[5-[(*tert*-Butyldiphenylsilyl)oxy]-3-methoxy-2,4-dimethylpentyl]triphenylphosphonium Iodide (28). To a solution of 11.4 g (22.3 mmol) of **27** in 50 mL of acetonitrile was added 6.10 g (23.3 mmol) of triphenylphosphine. The mixture was refluxed for 45 h and then concentrated, and the residue was washed with ether three times to remove excess triphenylphosphine. The resulting residue was dried under vacuum to give 16.8 g (97%) of **28** as a white foam. $[\alpha]^{22}_D$ +18.2° (*c* 1.05, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.62 (d, J = 6.8 Hz, 3H,), 0.78 (d, J = 6.8 Hz, 3H), 1.05 (s, 9H), 1.77–2.15 (m, 2H), 3.35–3.93 (m, 5H), 3.43 (s, 3H), 7.30–7.44 (m, 6H), 7.57–7.96 (m, 19H). HR-LSIMS m/z 645.3310 $(M - I)^+$ (calcd for $C_{42}H_{50}O_2PSi$ m/z 645.3315).

(2*S*,3*R*,4*R*,5*R*,6*R*,3′*S*,4′*R*,5′*R*)-(1′*Z*)-1′-[3,4-Bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-6′-[(*tert*-butyldiphenylsilyl)oxy]-4′-methoxy-3′,5′-dimethyl-1′-hexene (29). To a solution of 2.82 g (3.65 mmol) of **28** in 8 mL of tetrahydrofuran was added 2.2 mL (3.52 mmol) of 1.6 M *n*-butyllithium in hexane at −78 °C. The solution was allowed to warm to −40 °C, and the resulting orange solution was cooled to −78 °C. A solution of 1.27 g of the above-mentioned aldehyde **15** in 5 mL of tetrahydrofuran was added dropwise. The mixture was allowed to warm to 20 °C, stirred for 3 h, and poured into saturated ammonium chloride solution. The mixture was extracted with ethyl acetate, and the organic solution was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1:8 ethyl acetate–hexane to afford 1.53 g (61% from **14**) of **29** as a colorless oil. $[\alpha]^{24}_D$ +38.9° (*c* 1.04, $CHCl_3$). IR ($CHCl_3$) 3002, 2956, 2926, 1110, 1086, 702 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.72 (t, J = 7.6 Hz, 3H), 0.75 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 7.6 Hz, 3H), 1.06 (s, 9H), 1.40–1.75 (m, 2H), 1.78–1.95 (m, 1H), 1.95–2.07 (m, 1H), 2.65–2.87 (m, 1H), 3.21 (dd, J = 2.4 and 9.4 Hz, 1H), 3.32 (s, 3H), 3.36–3.72 (m, 4H), 3.43 (s, 3H), 4.48–4.78 (m, 5H), 5.03–5.12 (m, 1H), 5.35–5.57 (m, 2H), 7.20–7.46 (m, 16H), 7.60–7.71(m, 4H). ^{13}C NMR ($CDCl_3$) δ 9.79, 12.12, 17.89, 18.09, 19.29, 26.90, 35.86, 37.81, 55.97, 60.57, 70.61, 71.75, 77.21, 84.07, 98.97, 127.29, 127.61, 127.86, 127.94, 128.02, 128.10, 128.15, 128.26, 129.58, 133.87, 135.57, 138.25, 138.68. LSIMS m/z 789 $(M + K)^+$, 773 $(M + Na)^+$. Anal. Calcd for $C_{47}H_{62}O_6Si$: C, 75.16; H, 8.32. Found: C, 74.85; H, 8.32.

(2*S*,3*R*,4*R*,5*R*,6*R*,2′*R*,3′*S*,4′*R*,5′*R*)-1′-[3,4-Bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-6′-[(*tert*-butyldiphenylsilyl)oxy]-4′-methoxy-3′,5′-dimethyl-2′-hexanol (30). To a solution of 174 mg (0.232 mmol) of **29** in 3.0 mL of tetrahydrofuran was added 2.3 mL (2.3 mmol) of 1.0 M borane–tetrahydrofuran complex in tetrahydrofuran at 0 °C. The solution was treated with ultrasound for 30 min while being kept in a 15–20 °C water bath. The residue was quenched with 0.7 mL of ethanol at −20 °C, and then 1.0 mL of 3 N sodium hydroxide solution and 1.0 mL of 30% hydrogen peroxide solution were added sequentially. The mixture was stirred for 30 min at 40 °C, and then the residue was quenched with saturated sodium sulfite solution at 0 °C. The whole mixture was extracted with ethyl acetate, and the product solution was washed with brine, dried, and concentrated. The residue was chromatographed on silica gel using 1:4 ethyl acetate–hexane to afford 105 mg (59%) of **30** as a colorless oil. $[\alpha]^{22}_D$ +24.2° (*c* 1.08, $CHCl_3$). IR ($CHCl_3$) 3470 (OH) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.75 (t, J = 7.4 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H), 1.05 (s, 9H), 1.33–1.78 (m, 6H), 1.80–1.98 (m, 1H), 3.38–3.50 (m, 2H), 3.43 (s, 6H), 3.53 (dd, J = 5.9 and 10.2 Hz, 1H), 3.62 (dd, J = 7.6 and 10.2 Hz, 1H), 3.69–3.75 (m, 1H), 4.05 (br t, J = 5.3 Hz, 1H), 4.44–4.57 (m, 1H), 4.48 and 4.57 (ABq, J = 12.7 Hz, 2H), 4.62 (d, J = 4.2 Hz, 1H), 4.67 (s, 2H), 7.20–7.48 (m, 16H), 7.59–7.70 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 11.32, 11.75, 12.47, 17.87, 19.29, 26.88, 38.46, 40.25, 43.42, 55.78, 61.23, 66.56, 68.56, 70.88, 71.45, 72.13, 73.48, 77.22, 85.45, 98.66, 127.31, 127.64, 127.85, 128.07, 128.13, 128.31, 129.64, 133.68, 135.57, 138.19, 138.98. LSIMS m/z 791 $(M + Na)^+$, 737 $(M - OCH_3)^+$. HR-LSIMS m/z 791.4317 $(M + Na)^+$ (calcd for $C_{47}H_{64}O_7NaSi$ m/z 791.4316).

(2*S*,3*R*,4*R*,5*R*,6*R*,2′*R*,3′*R*,4′*R*,5′*R*)-6′-[3,4-Bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-1′-[(*tert*-butyldiphenylsilyl)oxy]-3′-methoxy-5′-[(methoxymethyl)-oxy]-2′,4′-dimethylhexane (31). To a solution of 1.17 g (1.52 mmol) of **30** in 15 mL of dichloromethane were added 2.0 mL (11.5 mmol) of *N*,*N*-diisopropylethylamine and 0.75 mL (9.87 mmol) of chlolomethyl methyl ether. The mixture was stirred for 5 h at 25 °C and then 2.5 h at 40 °C. The mixture was diluted with water and extracted with ethyl acetate. The organic solution was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1:3 ethyl acetate–hexane to give 1.24 g (100%) of **31** as a colorless oil. $[\alpha]^{23}_D$ +21.8° (*c* 1.00, $CHCl_3$). IR ($CHCl_3$) 3064, 3004, 2956, 2926, 1110, 1086, 1037, 703 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.69 (d, J = 6.8 Hz, 3H), 0.77 (d, J = 6.8 Hz, 3H), 0.78 (t, J = 6.3 Hz, 3H), 1.06 (s, 9H), 3.22–3.73 (m, 5H), 3.37 (s, 3H), 3.47 (s, 3H), 3.48 (s, 3H), 3.97 (br t, J = 6.2 Hz, 1H), 4.37 (dt, J = 2.2 and 6.7 Hz, 1H), 4.51 and 4.58 (ABq, J = 12.4 Hz, 2H), 4.62 (d, J = 5.6 Hz, 1H), 4.64 (s, 2H), 4.71 and 4.75 (ABq, J = 9.6 Hz, 2H), 7.22–7.45 (m, 16H), 7.61–7.72 (m, 4H). LSIMS m/z 1648 $(2M + Na)^+$, 835 $(M + Na)^+$. Anal. Calcd for $C_{49}H_{68}O_8Si$: C, 72.38; H, 8.43. Found: C, 72.50; H, 8.57.

(2*S*,3*R*,4*R*,5*R*,6*R*,2′*S*,3′*R*,4′*R*,5′*R*)-6′-[3,4-Bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-3′-methoxy-5′-[(methoxymethyl)oxy]-2′,4′-dimethyl-1′-hexanol (32). The procedure described for the preparation of **14** was repeated using 1.10 g (1.35 mmol) of **31** and 4.0 mL (4.0 mmol) of 1.0 M tetra-*n*-butylammonium fluoride in tetrahydrofuran to afford, after chromatography on silica gel using 1:1 ethyl acetate–hexane, 766 mg (99%) of **32** as a colorless oil. $[\alpha]^{22}_D$ +27.5° (*c* 1.00, $CHCl_3$). IR ($CHCl_3$) 3622 and 3478 (OH) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.76 (t, J = 7.4 Hz, 3H), 0.83 (d, J = 7.0 Hz, 6H), 3.32–3.45 (m, 2H), 3.38 (s, 3H), 3.47 (s, 3H), 3.49 (s, 3H), 3.57-3.73 (m, 3H), 3.95 (br t, J = 6.2 Hz, 1H), 4.38 (dt, J = 2.2 and 6.7 Hz, 1H), 4.51 and 4.59 (ABq, J = 12.6 Hz, 2H), 4.63 (d, J = 6.0 Hz, 1H), 4.65 (s, 2H), 4.71 and 4.74 (ABq, J = 13.1 Hz, 2H), 7.24–7.45 (m, 10H). LSIMS m/z 1171 $(2M + Na)^+$, 597 $(M + Na)^+$. Anal. Calcd for $C_{33}H_{50}O_8$: C, 68.96; H, 8.77. Found C, 68.73; H, 8.78.

(2*S*,3*R*,4*R*,5*R*,6*R*,2′*R*,3′*R*,4′*R*,5′*R*)-6′-[3,4-Bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-3′-methoxy-5′-[(methoxymethyl)oxy]-2′,4′-dimethyl-1′-hexanal (33). To a solution of 0.20 mL (2.82 mmol) of dimethyl sulfoxide in 7.0 mL of dichloromethane was added 0.19 mL (2.17 mmol) of oxalyl chloride at −78 °C. After being stirred for 10 min, a solution of 526 mg (0.915 mmol) of **32** in 5.0 mL of dichloromethane was added. The solution was stirred for 30 min at −78 °C, and then 0.64 mL (4.60 mmol) of triethylamine was

added. The mixture was allowed to warm to 0 °C for 20 min, diluted with water, and extracted with 4:1 benzene−ether. The organic phase was washed with water, dried, and evaporated to afford 496 mg of **33** as a colorless oil, which was used immediately for the next reaction without further purification. IR ($CHCl_3$) 1720 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.76 (t, J = 7.4 Hz, 3H), 0.85 (d, J = 7.0 Hz, 3H), 1.06 (d, J = 7.0 Hz, 3H), 2.39−2.55 (m, 1H), 3.24 (s, 3H), 3.39 (s, 3H), 3.42−3.50 (m, 1H), 3.48 (s, 3H), 3.62−3.73 (m, 1H), 3.78 (dd, J = 1.6 and 9.8 Hz, 1H), 4.04 (br t, J = 5.9 Hz, 1H), 4.37 (dt, J = 2.2 and 6.7 Hz, 1H), 4.51 and 4.59 (ABq, J = 12.4 Hz, 2H), 4.62 (d, J = 3.8 Hz, 1H), 4.65 (s, 2H), 4.69 and 4.72 (ABq, J = 14.2 Hz, 2H), 7.20−7.42 (m, 10H), 9.89 (s, 1H).

(2*S*,34*R*,5*R*,6*R*,5′*S*,6′*R*,7′*R*,8′*R*)-(3′*E*)-9′-[3,4-Bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-6′-methoxy-8′-[(methoxymethyl)oxy]-5′,7′-dimethyl-3′-nonen-2′-one (34). To a solution of 0.96 mL (6.59 mmol) of dimethyl (2-oxopropyl)phosphonate in 7.0 mL of tetrahydrofuran was added 674 mg (6.02 mmol) of potassium *tert*-butoxide at 0 °C. After this was stirred for 1.5 h at 25 °C, a solution of the above product **33** in 2.0 mL of tetrahydrofuran was added at 0 °C. The mixture was warmed to 55 °C, stirred for 1 h, and poured into saturated ammonium chloride solution. The mixture was extracted with ethyl acetate, and the organic solution was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1:3 ethyl acetate−hexane to afford 493 mg (88%, two steps) of **34** as a colorless oil. $[\alpha]^{22}_D$ + 24.1° (*c* 1.07, $CHCl_3$). IR ($CHCl_3$) 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.76 (t, J = 7.4 Hz, 3H), 0.85 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.0 Hz, 3H), 2.27 (s, 3H), 2.50−2.69 (m, 1H), 3.23 (dd, J = 1.6 and 9.8 Hz, 1H), 3.36 (s, 3H), 3.37 (s, 3H), 3.42−3.52 (m, 1H), 3.49 (s, 3H), 3.63−3.75 (m, 1H), 3.97 (br t, J = 6.2 Hz, 1H), 4.37 (dt, J = 2.4 and 6.7 Hz, 1H), 4.51 and 4.59 (AB q, J = 12.4 Hz, 2H), 4.62 (d, J = 4.0 Hz, 1H), 4.65 (s, 2H), 4.68 and 4.71 (AB q, J = 12.0 Hz, 2H), 6.11 (dd, J = 1.2 and 16.0 Hz, 1H), 6.98 (dd, J = 6.6 and 16.0 Hz, 1H), 7.21−7.43 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 11.09, 11.39, 12.20, 17.67, 27.18, 38.54, 40.81, 42.65, 55.57, 56.48, 60.30, 71.08, 71.29, 72.02, 77.24, 85.28, 97.14, 99.01, 127.39, 127.69, 127.88, 128.04, 128.16, 128.23, 128.34, 128.42, 128.46, 128.51, 129.70, 138.19, 138.79, 152.71, 198.68. LSIMS m/z 635 $(M + Na)^+$. HR-LSIMS m/z 635.3558 $(M + Na)^+$ (calcd for $C_{36}H_{52}O_8Na$ m/z 635.3557).

(2*S*,3*R*,4*R*,5*R*,6*R*,5′*S*,6′*R*,7′*R*,8′*R*)-(2′*E*)-9′-[3,4-Bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-6′-methoxy-8′-[(methoxymethyl)oxy]-5′,7′-dimethyl-2′-nonene (36). To a solution of 479 mg (0.781 mg) of **34** in 5.0 mL of methanol was added 216 mg (1.16 mmol) of *p*-toluenesulfonohydrazide. The mixture was stirred for 2 h at 25 °C and concentrated to afford (2*S*,3*R*,4*R*,5*R*,6*R*,5′*S*,6′*R*,7′*R*,8′*R*)-(2′*E*)-9′-[3,4-bis(benzyloxy)-5-ethyl-tetrahydro-2-methoxy-2*H*-pyran-6-yl]-6′-methoxy-8′-[(methoxymethyl)oxy]-5′,7′-dimethyl-3′-nonen-2′-one *p*-toluenesulfonylhydrazone (**35**) which was used immediately for the next reaction without purification.

A solution of sodium borohydride−acetic acid was prepared by dissolving 142 mg (3.76 mmol) of sodium borohydride in 5.0 mL of glacial acetic acid with ice-bath cooling while keeping the temperature between 15 and 20 °C. This solution was added to the above product, and the mixture was stirred for 2 h at 25 °C and then extracted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine and then dried and concentrated. The residue was chromatographed on silica gel using 1:4 ethyl acetate−hexane to give 319 mg (68%, two steps) of **36** as a colorless oil. $[\alpha]^{23}_D$ +28.8° (*c* 1.28, $CHCl_3$). IR ($CHCl_3$) 3002, 2958, 2928, 1453, 1139, 1094, 1036 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.75 (t, J = 7.4 Hz, 3H), 0.80 (d, J = 6.8 Hz, 6H), 1.66 (d, J = 5.0 Hz, 3H), 1.90−2.25 (m, 2H), 3.14 (dd, J = 1.6 and 9.8 Hz, 1H), 3.38 (s, 3H), 3.42−3.53 (m, 1H), 3.48 (s, 3H), 3.49 (s, 3H), 3.61−3.73 (m, 1H), 3.95 (br t, J = 6.3 Hz, 1H), 4.36 (dt, J = 2.3 and 6.9 Hz, 1H), 4.51 and 4.59 (ABq, J = 12.4 Hz, 2H), 4.62 (d, J = 4.8 Hz, 1H), 4.64 (s, 2H), 4.71 and 4.74 (ABq, J = 16.5 Hz, 2H), 5.33−5.57 (m, 2H), 7.23−7.43 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 10.10, 12.15, 12.47, 17.67, 18.02, 35.80, 38.51, 40.93, 42.22, 42.27, 55.46, 56.44, 60.70, 71.00, 71.10, 71.99, 73.19, 76.60, 77.21, 84.52, 97.05, 98.93, 126.20, 127.35, 127.64, 127.86, 128.07, 128.13, 128.29, 130.53, 138.22, 138.76. LSIMS m/z 1219 $(2M + Na)^+$, 621 $(M + Na)^+$. HR-LSIMS m/z 621.3763 $(M + Na)^+$ (calcd for $C_{36}H_{54}O_7Na$ m/z 621.3764).

(2*S*,3*R*,4*R*,5*R*,6*R*,2′*R*,3′*R*,4′*R*,5′*S*)-(7′*E*)-5-Ethyl-tetrahydro-2-methoxy-6-[4′-methoxy-2′-[(methoxymethyl)oxy]-3′,5′-dimethyl-7′-nonenyl]-2*H*-pyran-3,4-diol (37). To 10 mL of anhydrous liquid ammonia was added 201 mg (8.74 mmol) of sodium. To this blue solution was added a solution of 280 mg (0.467 mmol) of **36** in 3.0 mL of tetrahydrofuran at −78 °C, and then the mixture was stirred for 15 min at the same temperature. The reaction was quenched with ammonium chloride, and then the mixture was allowed to warm to 25 °C under a nitrogen stream. The mixture was diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1:1 ethyl acetate−hexane to afford 150 mg (76%) of **37** as a colorless oil. $[\alpha]^{22}_D$ +60.8° (*c* 1.00, $CHCl_3$). IR ($CHCl_3$) 3566 and 3510 (OH) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.81 (d, J = 7.0 Hz, 3H), 0.83 (d, J = 7.0 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H), 1.67 (d, J = 4.2 Hz, 3H), 1.91−2.24 (m, 2H), 3.12 (dd, J = 1.6 and 9.8 Hz, 1H), 3.39 (s, 3H), 3.47 (s, 3H), 3.48 (s, 3H), 3.57−3.72 (m, 1H), 3.88−4.00 (m, 2H), 4.17−4.27 (m, 1H), 4.70 (d, J = 6.0 Hz, 1H), 4.72 (s, 2H), 5.34−5.55 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 10.18, 12.48, 12.58, 17.75, 18.02, 35.80, 36.14, 38.52, 41.36, 46.80, 55.49, 56.44, 60.65, 63.14, 65.10, 71.19, 77.82, 84.72, 97.13, 101.28, 126.26, 130.45. LSIMS m/z 859 $(2M + Na)^+$, 441 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{42}O_7$: C, 63.13; H, 10.11. Found: C, 63.12; H, 9.92.

(2*S*,3*R*,4*R*,5*R*,6*R*,5′*S*,6′*R*,7′*R*,8′*R*)-(2′*E*)-9′-[5-Ethyl-tetrahydro-3,4-bis(methanesulfonyloxy)-2-methoxy-2*H*-pyran-6-yl]-6′-methoxy-8′-[(methoxymethyl)oxy]-5′,7′-dimethyl-2′-nonene (38). To a solution of 84 mg (0.201 mmol) of **37** in 1.0 mL of pyridine were added 0.08 mL (1.04 mmol) of methanesulfonyl chloride and 83 mg (0.678 mmol) of 4-(dimethylamino)pyridine at 0 °C. The mixture was stirred for 30 min at the same temperature and then diluted with water and extracted with dichloromethane. The organic layer was washed with 1 M hydrochloric acid solution, water, 5% sodium bicarbonate solution, and water and then dried and concentrated. The crude product was chromatographed on silica gel using 1:3 ethyl acetate−hexane to afford 110 mg (96%) of **38** as a colorless oil. $[\alpha]^{22}_D$ +43.0° (*c* 1.00, $CHCl_3$). IR ($CHCl_3$) 1353 and 1176 (SO_2) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.80 (d, J = 7.0 Hz, 3H), 0.82 (d, J = 7.0 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H), 1.67 (d, J = 3.0 Hz, 3H), 1.91−2.20 (m, 2H), 3.07−3.18 (m, 1H), 3.14 (s, 6H), 3.40 (s, 3H), 3.47 (s, 3H), 3.50 (s, 3H), 3.97 (br t, J = 6.0 Hz, 1H), 4.35−4.47 (m, 1H), 4.72 (s, 2H), 4.74 (d, J = 5.2 Hz, 1H), 4.77−4.85 (m, 1H), 4.92−5.02 (m, 1H), 5.31−5.58 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 10.34, 11.64, 12.54, 18.02, 18.11, 18.17, 35.76, 38.48, 38.75, 38.97, 41.65, 55.53, 55.57, 56.65, 60.63, 76.11, 76.62, 77.21, 84.60, 96.76, 97.32, 126.34, 130.35. LSIMS m/z 1171 $(2M + Na)^+$, 597 $(M + Na)^+$. HR-LSIMS m/z 597.2382 $(M + Na)^+$ (calcd for $C_{24}H_{46}O_{11}NaS_2$ m/z 597.2377).

(2*S*,5*R*,6*R*,2′*R*,3′*R*,4′*R*,5′*S*)-(7′*E*)-5-Ethyl-5,6-dihydro-2-methoxy-6-[4′-methoxy-2′-[(methoxymethyl)oxy]-3′,5′-dimethyl-7′-nonenyl]-2*H*-pyran (39). To a solution of 173 mg (0.301 mmol) of **38** in 5 mL of *N,N*-dimethylformamide were added 1.0 g (6.02 mmol) of potassium iodide and 400 mg of zinc−copper couple (91%−5%, purchased from Kanto Chemical Co., Inc.). After this was refluxed for 4 h, 153 mg (0.922 mmol) of potassium iodide and 63 mg (1.01 mmol) of zinc−copper couple were added. The mixture was refluxed for 1.5 h, filtered through Celite, diluted with water, and extracted with ethyl acetate. The organic solution was washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 3:17 ethyl acetate−hexane to afford 49 mg (42%) of **39** as a colorless oil. $[\alpha]^{24}_D$ −53.8° (*c* 1.01, $CHCl_3$). IR ($CHCl_3$) 2960, 2928, 2878, 1095, 1046, 965 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.82 (d, J = 7.0 Hz, 3H), 0.83 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H), 1.67 (d, J = 3.8 Hz, 3H), 1.90−2.27 (m, 2H), 3.20 (dd, J = 1.5 and 9.7 Hz, 1H), 3.39 (s, 3H), 3.46 (s, 3H), 3.51 (s, 3H), 3.96−4.12 (m, 2H), 4.73 and 4.77 (ABq, J = 14.3 Hz, 2H), 4.80 (dd, J = 1.0 and 2.6 Hz, 1H), 5.38−5.50 (m, 2H), 5.72 (ddd, J = 0.8, 2.6, and 10.0 Hz, 1H), 6.16 (ddd, J = 1.0, 5.9, and 10.0 Hz, 1H). ^{13}C NMR

($CDCl_3$) δ 10.23, 11.47, 12.53, 18.04, 20.79, 35.78, 37.33, 38.45, 38.50, 41.54, 55.45, 55.48, 60.72, 67.41, 76.74, 84.39, 96.26, 97.51, 124.89, 126.22, 130.56, 134.27. LSIMS m/z 407 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{40}O_5$: C, 68.71; H, 10.48. Found: C, 68.47; H, 10.33.

(5*R*,6*R*,2′*R*,3′*R*,4′*R*,5′*S*)-(7′*E*)-5-Ethyl-5,6-dihydro-6-[4′-methoxy-2′-[(methoxymethyl)oxy]-3′,5′-dimethyl-7′-nonenyl]-2*H*-pyran-2-one (41). A solution of 36.7 mg (0.095 mmol) of **39** in 1.2 mL of 75% aqueous acetic acid was stirred for 30 min at 40 °C. The solvent was evaporated under reduced pressure to afford (2*R* and 2*S*,5*R*,6*R*,2′*R*,3′*R*,4′*R*,5′*S*)-(7′*E*)-5-ethyl-5,6-dihydro-6-[4′-methoxy-2′-[(methoxymethyl)-oxy]-3′,5′-dimethyl-7′-nonenyl]-2*H*-pyran-2-ol (**40**) as a colorless oil, which was used in the next reaction without purification. IR ($CHCl_3$) 3580 and 3390 (OH) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.84 (d, J = 7.6 Hz, 3H), 0.85 (d, J = 6.4 Hz, 3H), 0.95 (t, J = 7.5 Hz, 3H), 1.68 (d, J = 4.4 Hz, 3H), 3.14 (dd, J = 2.0 and 9.4 Hz, 1H), 3.40 (s, 3H), 3.51 (s, 3H), 3.93–4.20 (m, 2H), 4.75 and 4.78 (ABq, J = 14.1 Hz, 2H), 5.26–5.36 and 6.23–6.30 (each m, 1H), 5.34–5.60 (m, 2H), 5.80 (dd, J = 2.6 and 10.3 Hz, 1H), 6.17 (dd, J = 6.0, and 10.3 Hz, 1H).

To a solution of crude **40** in 1.0 mL of acetone was added Jones reagent dropwise until the brown color persisted. After being stirred for 1 h at 25 °C, the reaction was quenched with 2-propanol. The mixture was diluted with saturated sodium bicarbonate solution and extracted with ethyl acetate. The organic solution was washed with brine, dried, and concentrated. The crude product was chromatographed using 1:3 ethyl acetate–hexane to afford 23.8 mg (68%, two steps) of **41** as a colorless oil. $[\alpha]^{24}_D$ −108.9° (*c* 2.09, $CHCl_3$). IR ($CHCl_3$) 1715 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.83 (d, J = 7.0 Hz, 3H), 0.83 (d, J = 7.0 Hz, 3H), 0.97 (t, J = 7.6 Hz, 3H), 1.67 (d, J = 4.2 Hz, 3H), 3.15 (dd, J = 2.0 and 9.4 Hz, 1H), 3.37 (s, 3H), 3.49 (s, 3H), 4.04 (br t, J = 6.2 Hz, 1H), 4.59 (ddd, J = 3.6, 4.9, and 8.3 Hz, 1H), 4.70 and 4.73 (ABq, J = 12.4 Hz, 2H), 5.32–5.54 (m, 2H), 6.03 (d, J = 10.0 Hz, 1H), 7.01 (dd, J = 6.1, and 10.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 10.44, 10.99, 12.67, 18.03, 20.73, 35.64, 35.83, 38.48, 40.90, 55.57, 60.79, 75.87, 77.51, 84.61, 97.73, 120.82, 126.34, 130.35, 150.56, 164.44. LSIMS m/z 759 $(2M + Na)^+$, 391 $(M + Na)^+$. Anal. Calcd for $C_{21}H_{36}O_5$: C, 68.45; H, 9.85. Found: C, 68.20; H, 9.80.

(5*R*,6*R*,2′*R*,3′*S*,4′*R*,5′*S*)-(7′*E*)-5-Ethyl-5,6-dihydro-6-(2′-hydroxy-4′-methoxy-3′,5′-dimethyl-7′-nonenyl)-2*H*-pyran-2-one (PA-48153C) (1). A solution of 20.9 mg (0.0568 mmol) of **41** in 1.0 mL of 80% aqueous acetic acid was refluxed for 3 h. The solvent was evaporated under reduced pressure. The crude product was chromatographed on silica gel using 2:3 ethyl acetate–hexane to afford 18.4 mg (100%) of **1** that was identical in all respects, including molecular rotation ($[\alpha]^{24}_D$ −142.9° (*c* 0.50, $CHCl_3$)), with the natural product from *S. prunicolor* PA-48153 (mp 78–79 °C. ($[\alpha]^{27}_D$ −143.7° (*c* 0.50, $CHCl_3$)). IR (KBr) 3505 (OH), 1728 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.96 (d, J = 6.4 Hz, 3H), 0.97 (d, J = 7.4 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 1.67 (d, J = 4.6 Hz, 3H), 2.09 (m, 1H), 2.29 (m, 1H), 2.99 (dd, J = 4.6 and 6.2 Hz, 1H), 3.45 (d, J = 2.6 Hz, 1H), 3.47 (s, 3H), 4.19 (m, 1H), 4.74 (ddd, J = 4.0, 4.0, and 8.0 Hz, 1H), 5.25–5.54 (m, 2H), 6.03 (dd, J = 0.7 and 9.7 Hz, 1H), 7.01 (dd, J = 5.8 and 9.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 11.47, 12.65, 15.69, 18.45, 21.23, 36.56, 37.15, 37.70, 39.35, 39.53, 62.06, 67.81, 78.11, 91.53, 121.24, 127.38, 129.18, 151.21, 165.22. LSIMS m/z 671 $(2M + Na)^+$, 347 $(M + Na)^+$, 235 $(M + H)^+$. Anal. Calcd for $C_{19}H_{32}O_4$: C, 70.33; H, 9.94. Found: C, 70.08; H, 9.86).[9]

Acknowledgment. We wish to thank Dr. S. Uyeo for his encouragement and valuable advice throughout this work, and Dr. I. Horibe for his helpful discussions.

JO951000Y