DISSERTATION

STUDIES ON THE STEREOCHEMISTRY OF GYMNOPILINS, THE POISONOUS PRINCIPLES OF *GYMNOPILUS SPECTABILIS*.

BY

HIROKO HARIGAYA

A THESIS SUBMITTED FOR THE DEGREE OF
DOCTOR OF SCIENCE
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Abbreviations

AIBN	2,2'-azobis(isobutyronitrile)
Ac_2O	acetic anhydride
BnCl	benzyl chloride
BOMCl	chloromethyl benzyl ether
Bu_3SnH	tributyltin hydride
BzCl	benzoyl chloride
BuLi	butyllithium
DIPT	diisopropyl tartrate
DMF	*N*,*N*-dimethylformamide
Et_3N	triethylamine
EtOAc	ethyl acetate
EtOH	ethanol
MeI	methyl iodide
MeOH	methanol
Me_2S	dimethyl sulfide
MOMCl	chloromethyl methyl ether
MS-4A	molecular sieves 4A
MTPA	(a)-methoxy-(a)-(trifluoromethyl)phenylacetic acid
NaOAc	sodium acetate
PhH	benzene
Ph_3P	triphenylphospine
PhSH	thiophenol
PvCl	pivaloyl chloride
$^{i}Pr_2NEt$	*N*,*N*-diisopropylethylamine
$^{i}PrOH$	2-propanol
Py	pyridine
TBAF	tetrabutylammonium fluoride

TBSCl	*tert*-butyldimethylchlorosilane
TBHP	*tert*-butylhydroperoxide
TFAA	trifluoromethylacetic anhydride
THF	tetrahydrofuran
$Ti(^iOPr)_4$	titanium tetraisopropoxide
TMEDA	*N,N,N′,N′*-tetramethylethylenediamine
TMSOTf	trimethylsilyl trifluoromethanesulfonate
TsCl	*p*-toluenesulfonyl chloride
TsOH	*p*-toluenesulfonic acid
$VO(acac)_2$	vanadium (III) acetylacetonate

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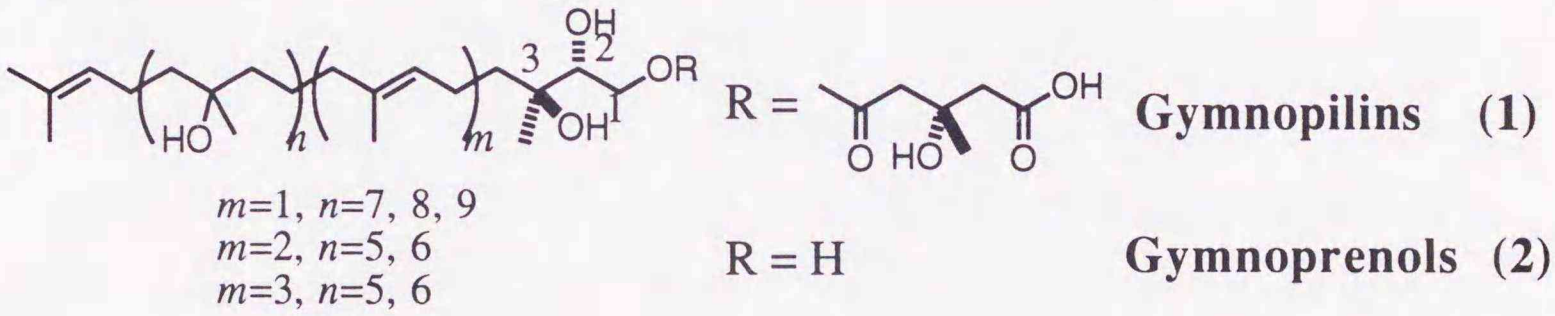
Introduction

Gymnopilins (**1**) were isolated as bitter principles from the poisonous mushroom *Gymnopilus spectabilis*, which was called Ohwaraitake (big laughter mushroom) in Japan, by Matsumoto and Nozoe's groups about 10 years ago.[1] Neuroexcitatory activity as well as cytotoxicity of **1** has been recently disclosed and focused in the fields of pharmacology and physiology.[2] Gymnopilins (**1**) are isoprenoid esters and hydrolyzed to oligoisoprenoid polyols named gymnoprenols (**2**) and 3-hydroxy-3-methylglutaric acid (HMGA).

Fig 1.



Gymnopilins (1)

R = H **Gymnoprenols (2)**

It naturally occurs as a mixture of many analogous compounds which are different each other in the number of isoprene and 2-isoprenol units. The gross structures of **1** were previously determined as shown in Fig 1 and the absolute configurations of the 1,2,3-triol part[2] and the HMGA moiety[3] were recently established as (2*R*,3*S*) and (3*S*) configurations, respectively, but the stereochemistry of the sequential 1,5-diol part remained still unknown. This thesis is mainly concerned with the presumption of the unclear stereochemistries of the 1,5-oligodiol moieties of gymnopilins (**1**) and gymnoprenols (**2**). It should be emphasized that discrimination among diastereoisomeric gymnoprenols (**2**) was deduced to be very difficult since all synthetic diastereoisomers with respect to the sequential 1,5-diol parts showed the same NMR spectra and the same

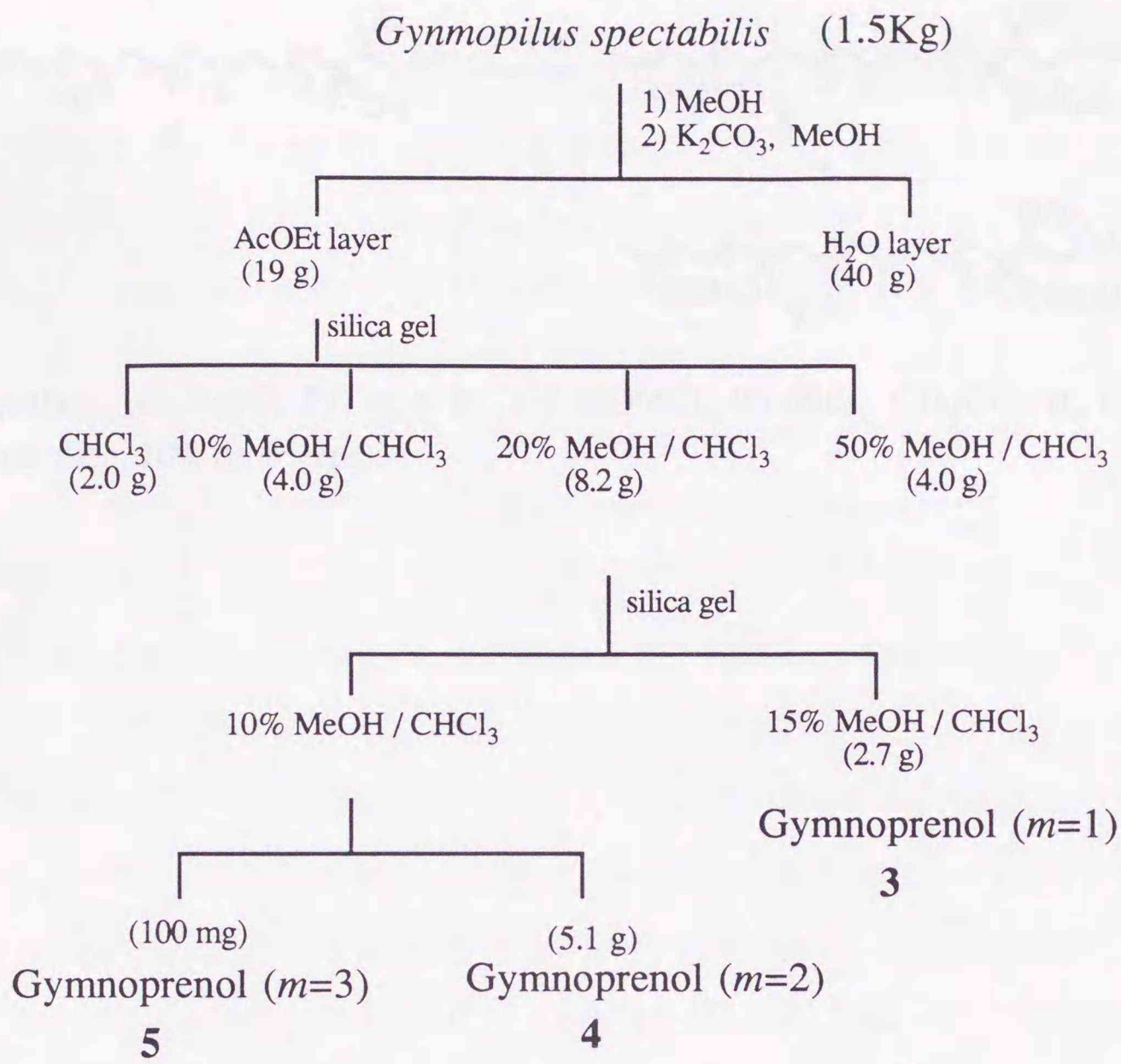
retention times in HPLC. A new method to amplify the stereochemical difference among gymnoprenol analogues had to be developed for this research. In this thesis, the author would like to describe extraction and purification of gymnoprenols, synthesis of some gymnoprenol analogues having various diastereoisomeric 1,5-polyol structures, and finally presumption of the stereochemistry of the natural products in comparison with these synthetic compounds by means of the newly developed method.

Chapter 1 Extraction and Isolation of Gymnoprenols (m=2, n=5 and 6)

Gymnopilins (**1**) and gymnoprenols (**2**) were previously isolated as a mixture of several analogues and their gross structures were determined by Matsumoto and Asakura in this laboratory.[1)]

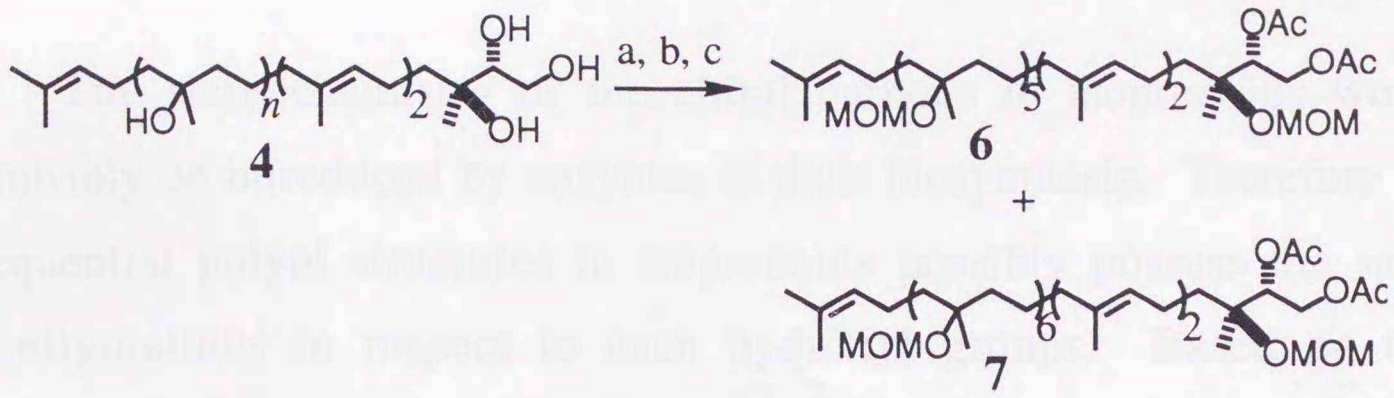
The mushroom collected in Aomori Prefecture (1.5 Kg) in 1986 was soaked in MeOH and treated with K_2CO_3. Most of gymnopilins were hydrolyzed into gymnoprenols by this treatment. The MeOH extracts were concentrated in vacuo and the residual mass was partitioned between EtOAc and water. The organic layer was concentrated and the residual mass (19 g) was purified by silica gel chromatography with MeOH-$CHCl_3$ as eluents. The $CHCl_3$ fraction contained a mixture of unsaturated fatty acid methyl esters. Gymnopilins and gymnoprenols were eluted in the fractions of 20% to 50% MeOH/$CHCl_3$. The fraction eluted with 20% MeOH/$CHCl_3$ amounted to 8.2 g which was further chromatographed on silica gel column using 10% to 15% MeOH/$CHCl_3$ as eluents and three fractions **3**, **4**, and **5** were obtained (100 mg, 5.1 g, and 2.7 g).

Scheme 1.



The fraction **4** (*m*=2) was a mixture of gymnoprenols (**2**) (*n*=5 and 6) whose primary and secondary hydroxyl groups were converted to acetates and the tertiary hydroxyl groups were protected by MOM groups (Scheme 2). The products thus obtained were separated by silica gel column chromatography using EtOAc-PhH as the solvents. The FD-MS spectra showed M^+1102 and 1234 for the faster moving compound **6** and the slower moving one **7**, respectively. Therefore, the former was gymnoprenol (**2**) (*m*=2, *n*=5; $C_{61}H_{114}O_{16}$=1102) and the latter was gymnoprenol (**2**) (*m*=2, *n*=6; $C_{68}H_{130}O_{18}$=1234). These compounds were used for the further structure presumption experiments.

Scheme 2.



Reagents: (a) Ac_2O, Py, rt, 6 h; (b) MOMCl, $^iPr_2NEt$, CH_2Cl_2, rt, 120 h; (c) separation, 20% (in 3 steps).

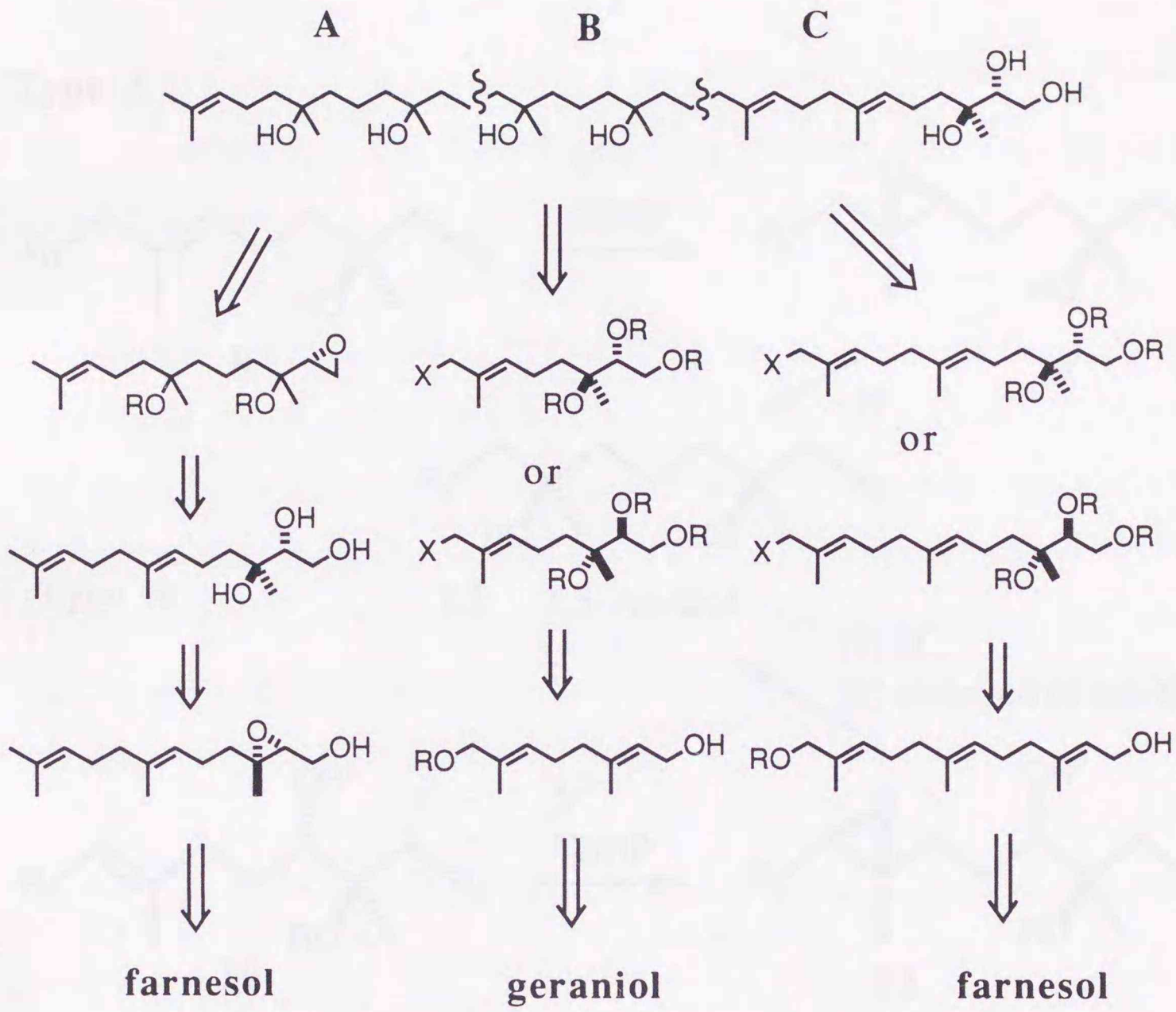
Chapter 2 Retrosynthesis of Gymnoprenol Analogues

The stereochemistry of the chiral carbons in isoprenoids would probably be introduced by enzymes in their biosynthesis. Therefore the sequential polyol structures in isoprenoids possibly possess the same configurations in respect to each hydroxyl groups. Based on this hypothesis, the author assumed that the sequential 1,5-diol structures in gymnoprenols (**2**) presumably have the same configurations and started this study from the synthesis of gymnoprenol analog having the 1,5-*syn*-diol structure.

Gymnoprenols (**2**) are linear oligoisoprenoids whose carbon chain must be constructed by the linkage of a few mono and/or sesquiterpenes such as geraniol and farnesol. For the introduction of 1,5-polyol system to the linear isoprenoid skeleton, vanadium catalysed oxidation of bishomoallylic alcohol seems to be a useful reaction. The substrate of this reaction will be furnished by the coupling reaction between an epoxide and an appropriate carbanion derived from a small terpene fragment. The author's retrosynthesis is depicted in Scheme 3.

The stereochemical aspects on the vanadium catalyzed epoxidation using TBHP of bishomoallylic alcohols were previously revealed on occasion of the syntheses of some marine triterpene polyethers achieved in our laboratory (Scheme 3).[4,5] There are two modes of oxidation depending on the position of a methyl group on the double bond of a substrate. A bishomoallylic alcohol (**8**) bearing a methyl group at the further end of the double bond selectively gives the *syn*-epoxide (**9**) (Type A) as shown in Scheme 4. On the contrary, a substrate (**10**) having a methyl group at the near end of the double bond selectively gives the *anti*-epoxide (**11**) (Type B).[6]

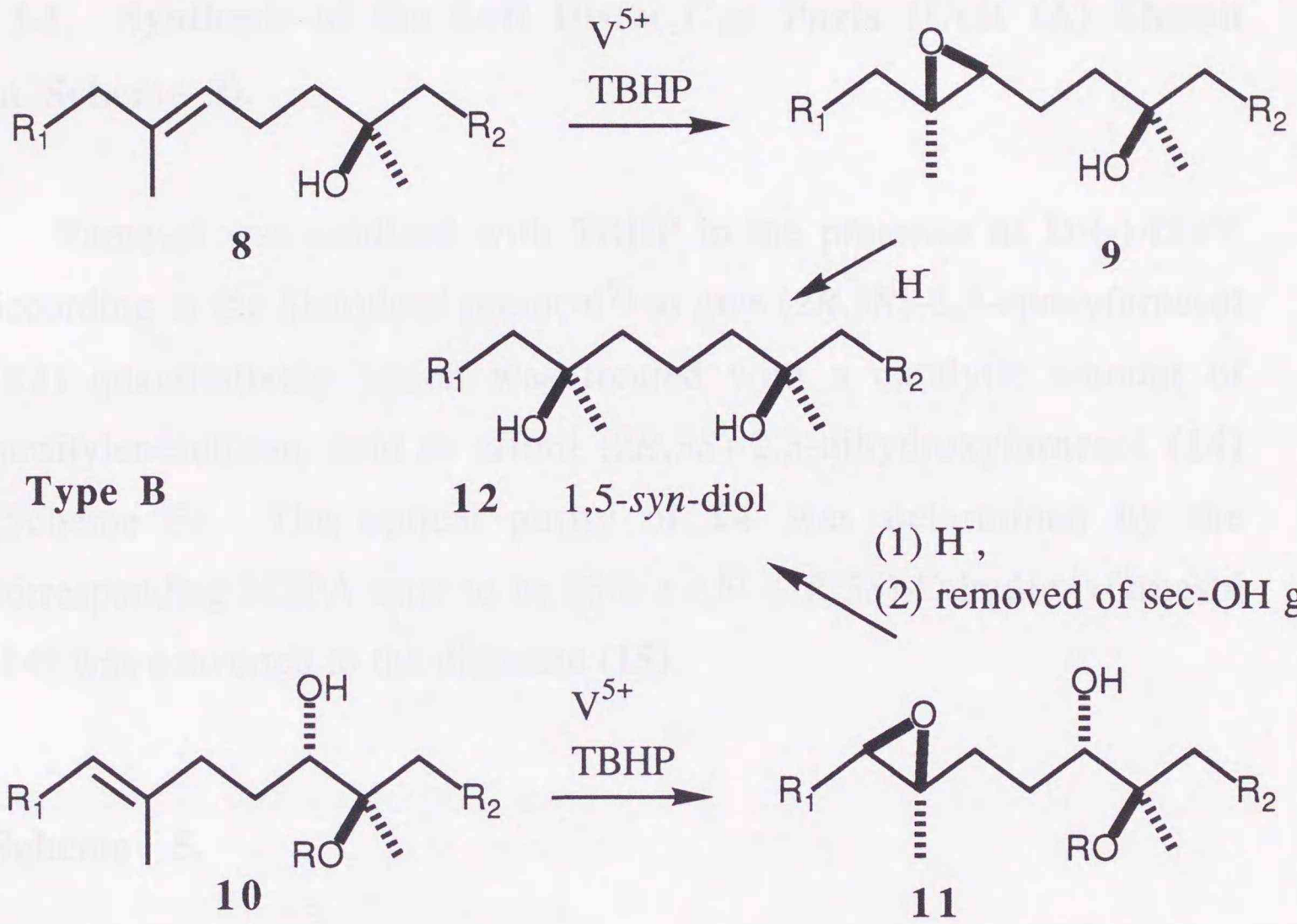
Scheme 3.



Both *syn*- and *anti*-epoxide (**9** and **11**) would be stereoselectively transformed into the same *syn*-diol (**12**) by proper treatments. The chiral epoxides of farnesol and geraniol with the known absolute configurations are easily prepared by the Sharpless asymmetric epoxidation.[7] The author decided to start the synthesis of these epoxides from geraniol and farnesol.

Scheme 4.

Type A



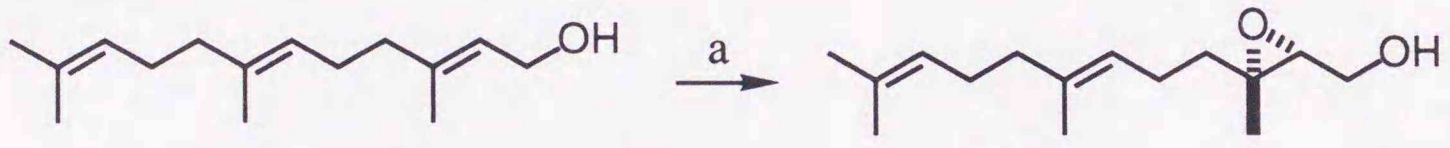
Type B

Chapter 3 Synthesis of Eight Diastereoisomeric Model Gymnoprenols (m=2, n=4)

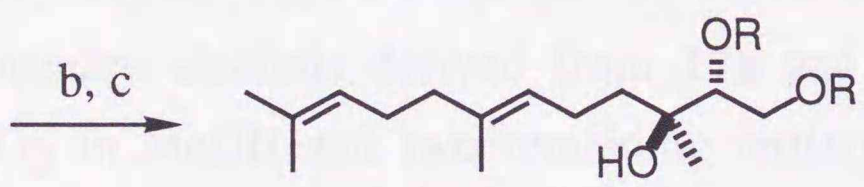
3-1. Synthesis of the Left Distal C_{15} Parts (Unit (A) Shown in Scheme 3).

Farnesol was oxidized with TBHP in the presence of D-(-)-DIPT according to the Sharpless' protocol[7] to give (2*R*,3*R*)-2,3-epoxyfarnesol (**13**) quantitatively which was treated with a catalytic amount of mesitylenesulfonic acid to afford (2*R*,3*S*)-2,3-dihydroxyfarnesol (**14**) (Scheme 5). The optical purity of **14** was determined by the corresponding MTPA ester to be 85% *e.e.*[8] (2*R*,3*S*)-Dihydroxyfarnesol (**14**) was converted to the diacetate (**15**).

Scheme 5.



farnesol **13**



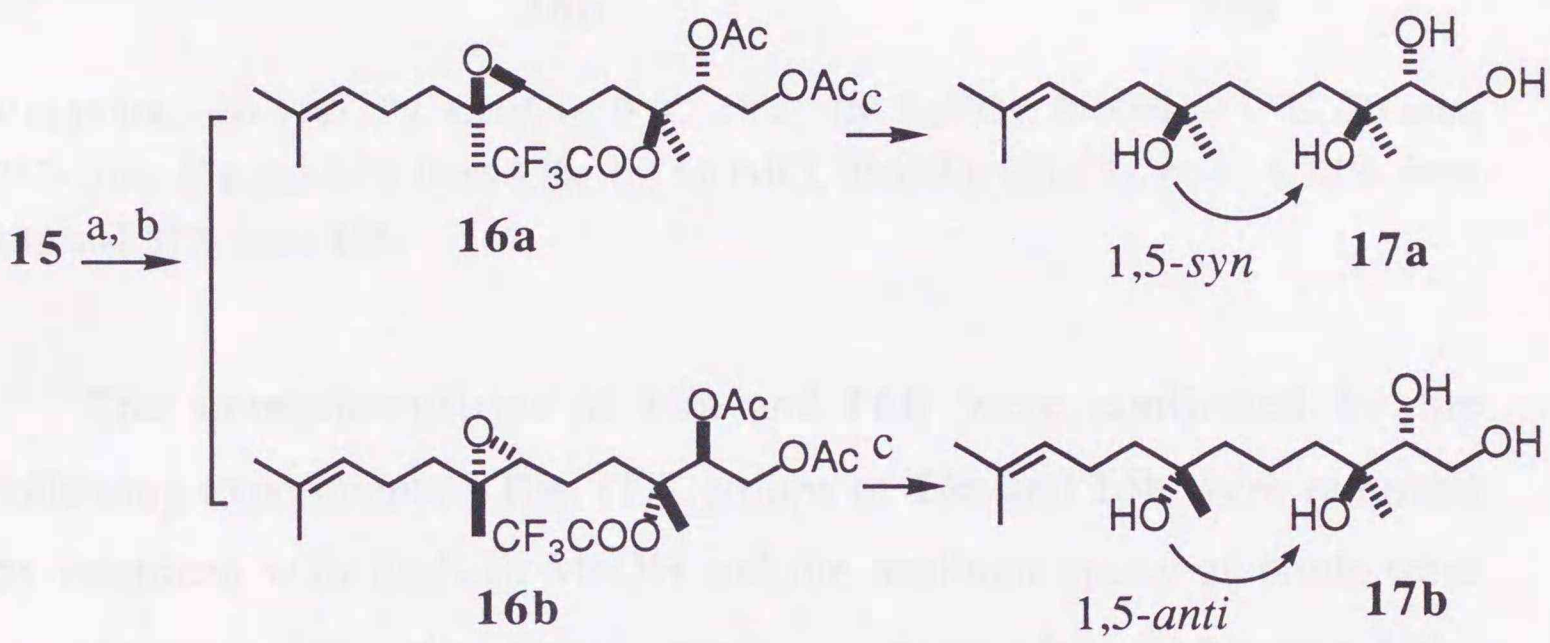
14; R= H
15; R= Ac

Reagents: (a) Ti(^{i}OPr)$_4$, D-(-)-DIPT, TBHP, MS-4A, CH_2Cl_2, -22 °C, 3 h, quant, 88% *e.e.*; (b) Mesitylenesulfonic acid, THF, H_2O, rt, 48 h, 81%, 85% *e.e.*; (c) Ac_2O, Py, CH_2Cl_2, rt, 15 h, 87%.

Epoxidation of the bishomoallylic alcohol **15** was carried out with TBHP and a catalytic amount of VO(acac)$_2$ (Scheme 6).[6] The two products were isolated as TFA esters and their separation was performed

by a Lobar column to give the *syn*-epoxide **16a** and the *anti*-epoxide **16b** in a ratio of 4.2 to 1. The epoxides were reduced with $LiAlH_4$ to the tetraols **17a** and **17b**, respectively.

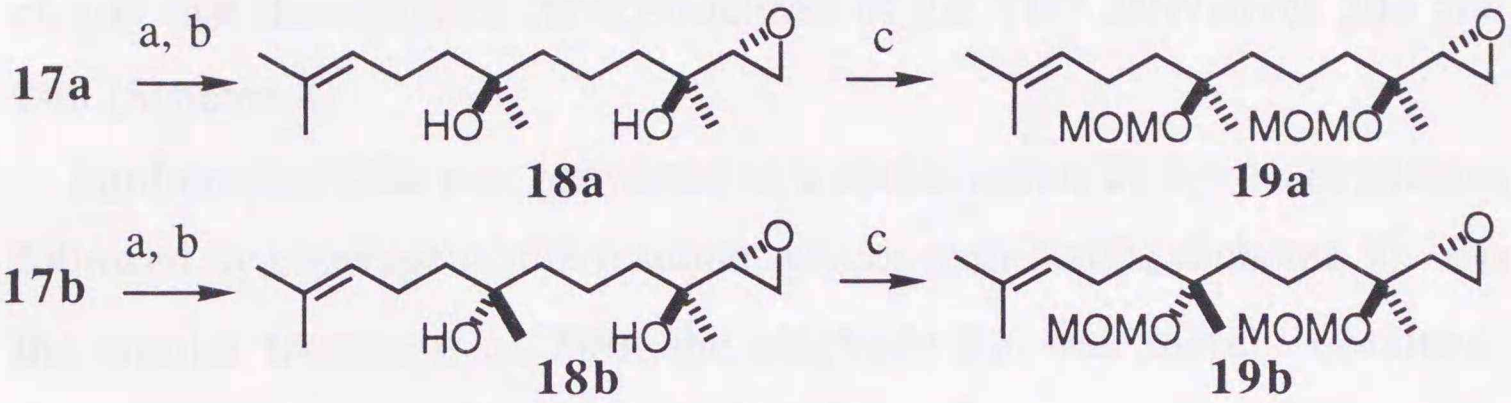
Scheme 6.



Reagents: (a) $VO(acac)_2$, TBHP, NaOAc, PhH, rt, 14 h; (b) TFAA, Py, CH_2Cl_2, -15 °C, 10 min, 54% (in 2 steps, the ratio of **16a/16b**=4.2:1); (c) $LiAlH_4$, THF, 0 °C, 1 h, 90% from **16a** and 100% from **16b**.

The distal epoxides were prepared from the corresponding tosylates of the primary alcohols derived from **17a** and **17b** by treatment with K_2CO_3 in MeOH and two remaining tertiary hydroxyl groups were protected by MOM groups to afford **19a** and **19b**, corresponding to the A fragments of gymnoprenol analogues (Scheme 7).

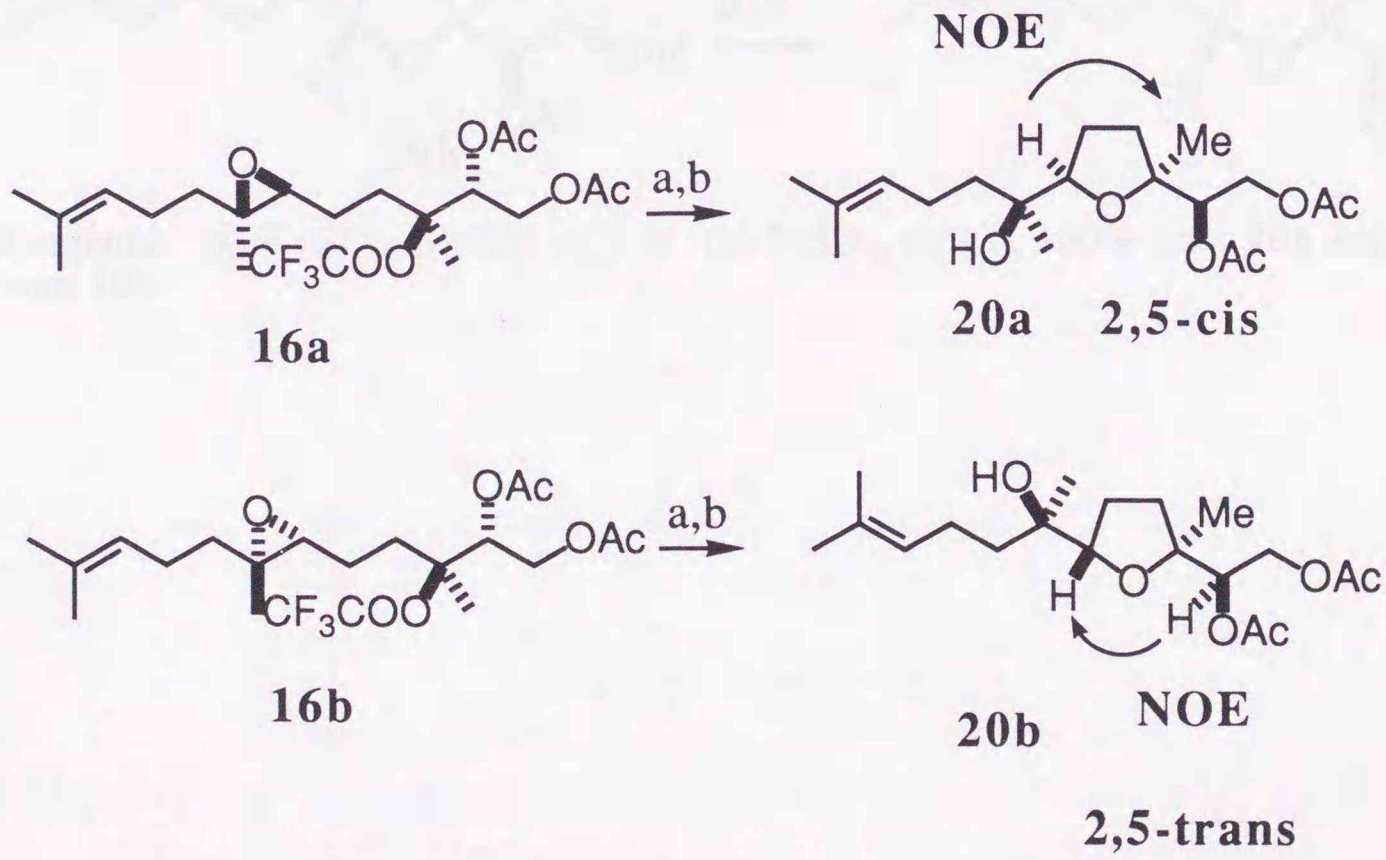
Scheme 7.



Reagents: (a) TsCl, Py, CH_2Cl_2, 0 °C, 18 h; (b) K_2CO_3, MeOH, -15 °C, 30 min, 78% from **17a** and 67% from **17b**; (c) MOMCl, $^iPr_2NEt$, CH_2Cl_2, rt, 40 h, 81% from **18a** and 87% from **18b**.

The stereochemistries of **16a** and **16b** were confirmed by the following experiments. The TFA groups of **16a** and **16b** were removed by treatment with Et_3N in MeOH and the resultant epoxy alcohols were transformed into the tetrahydrofuran derivatives **20a** and **20b**, respectively, by manipulation with TsOH in CH_2Cl_2 (Scheme 8).

Scheme 8.

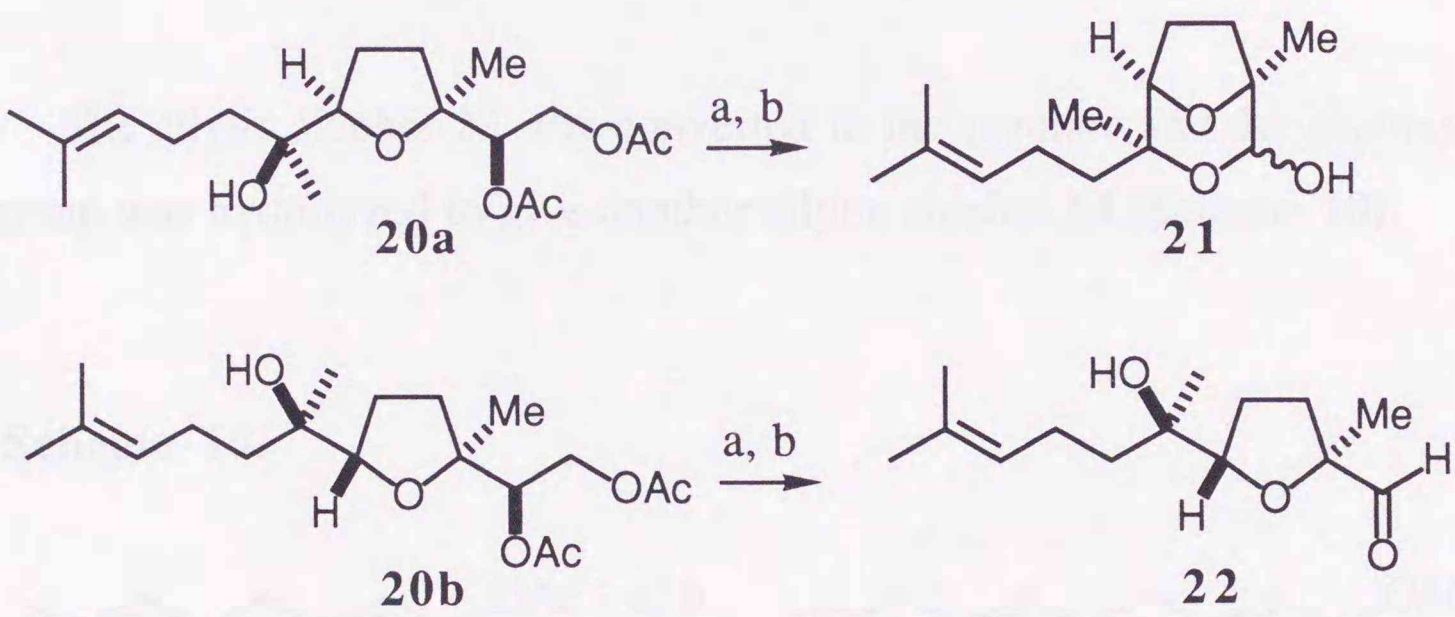


Reagents: (a) Et_3N, MeOH, rt, 1 h; (b) TsOH, CH_2Cl_2, rt, 1 h, 87% from **16a** and 97% from **16b**.

The NOE measurements among protons around the THF ring indicated clearly that the assigned stereostructures of the THF derivatives **20a** and **20b** (Scheme 8)

Furthermore, **20a** was converted to a cyclic acetal **21** by deacetylation followed by cleavage of the resultant glycol with $NaIO_4$ (Scheme 9). On the similar treatment of **20b**, the aldehyde **22** was merely obtained. Therefore, the epoxides **16a** and **16b** have the structures as shown in Scheme 6.

Scheme 9.



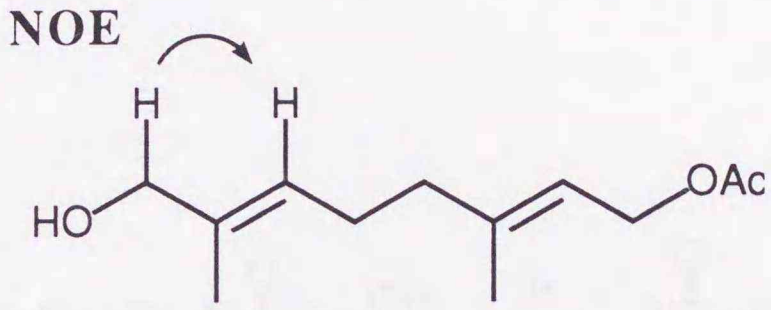
20a **21**

20b **22**

Reagents: (a) K_2CO_3, MeOH, rt, 1 h; (b) $NaIO_4$, rt, 1 h, 100% from **20a** and 90% from **20b**.

3-2. Synthesis of the Mesial and Head Parts (Corresponding to the Unit (B) and Unit (C) in Scheme 3)

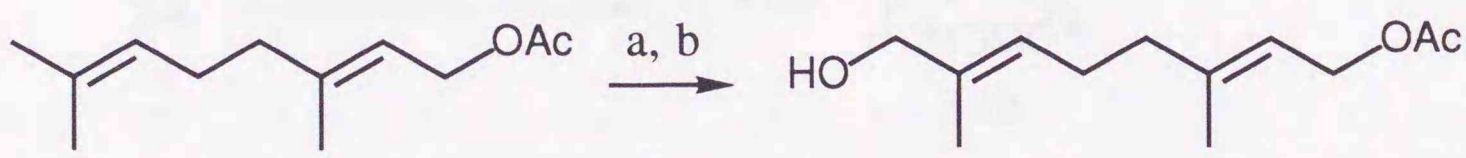
Regioselective oxidation of a distal methyl group of geranyl acetate was achieved by using SeO_2 following the Rappoport's procedure.[9] The structure of the product **23** was confirmed by its NOE experimemt.



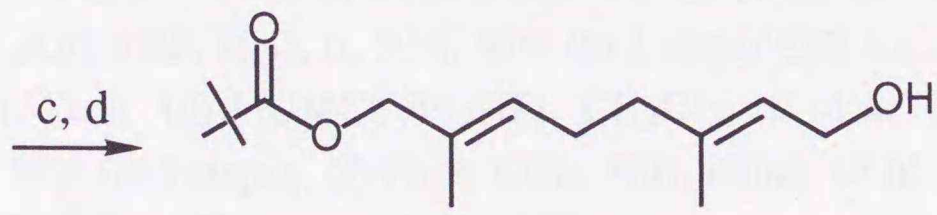
23

The allylic alcohol **23** was converted to the pivalate and the acetoxyl group was hydrolyzed to give another allylic alcohol **24** (Scheme 10).

Scheme 10.



geranyl acetate **23**

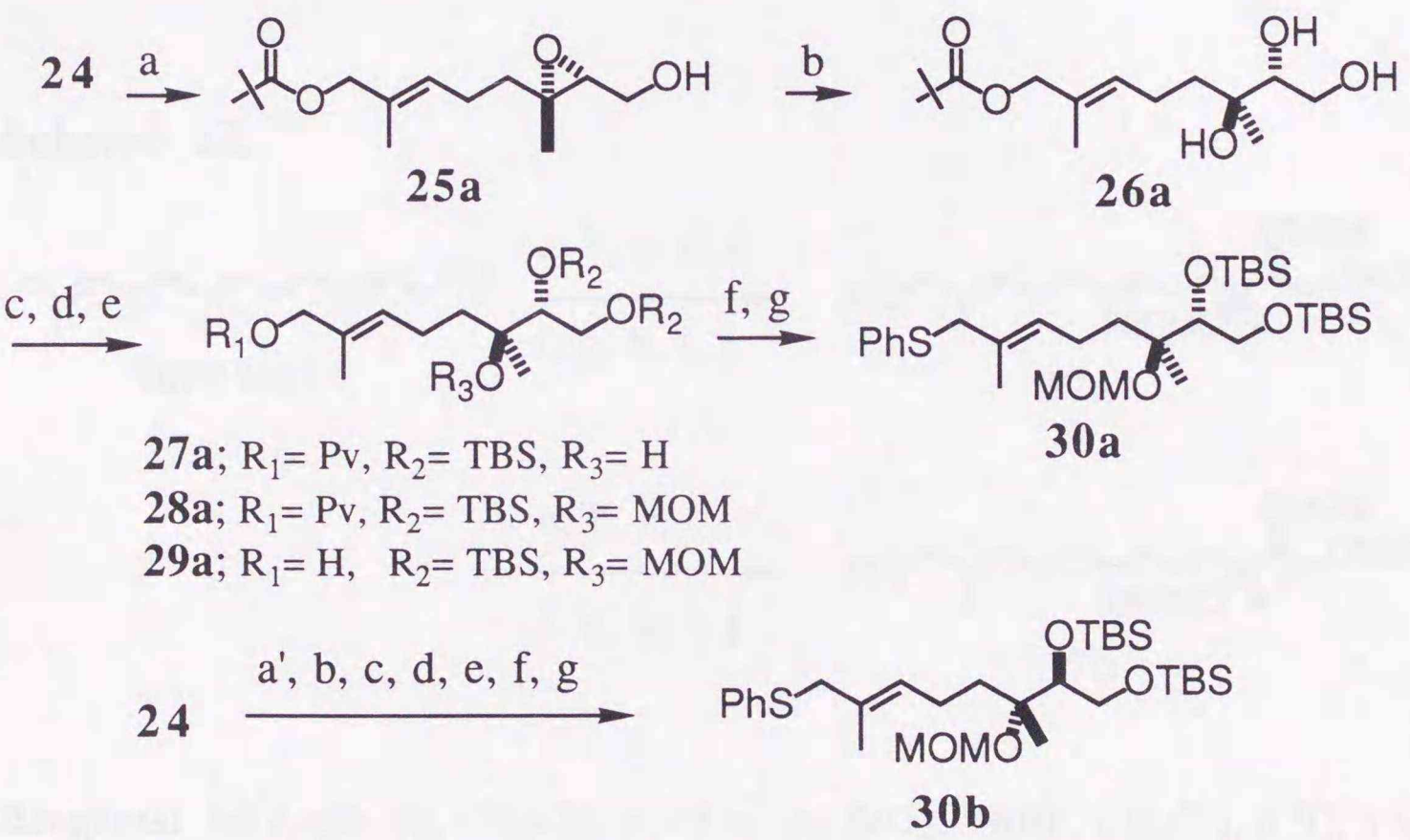


24

Reagents: (a) SeO_2, EtOH, reflux, 2 h; (b) $NaBH_4$, EtOH, ether, 0 °C, 1 h; (c) PvCl, Py, CH_2Cl_2, rt, 14 h; (d) NH_3, MeOH, rt, 120 h, 40% (in 4 steps).

The Sharpless asymmetric epoxidation[7] of **24** with TBHP and D-(-)-DIPT afforded the (2*R*,3*R*)-epoxy alcohol **25a** which was converted to the triol **26a** by the subsequent treatment with mesitylenesulfonic acid in THF/H_2O (Scheme 11). The optical purity of **26a** was determined to be 88% *e.e.* by the NMR analysis of the corresponding MTPA ester.[8]

Scheme 11.



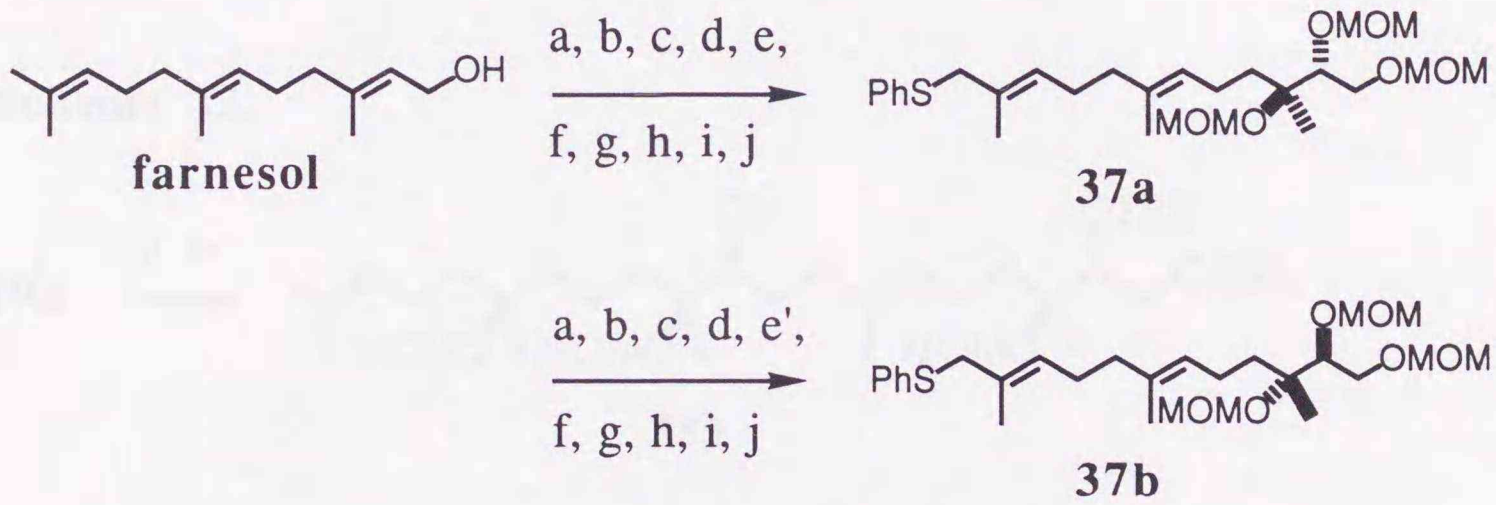
Reagents: (a) Ti(^{i}OPr)$_4$, D-(-)-DIPT, TBHP, MS-4A, CH_2Cl_2, -23 °C, 2 h; (a') Ti(^{i}OPr)$_4$, L-(+)-DIPT, TBHP, MS-4A, CH_2Cl_2, -23 °C, 2 h; (b) Mesitylene-sulfonic acid, THF, H_2O, rt, 50 h, 66% (in 2 steps) 85% *e.e.*; (c) TBSCl, imidazole, DMF, rt, 12 h; (d) MOMCl, ^{i}Pr$_2$NEt, CH_2Cl_2, rt, 14 h; (e) $LiAlH_4$, THF, 0 °C, 10 min, 59% (in 3 steps); (f) Ph_3P, CCl_4, PhH, reflux, 45 h; (g) NaSPh, DMF, 0 °C, 10 min, 76% from **29a**, and 34% from **24**.

The triol **26a** was transformed into the phenylthio ether **30a**. Thus the primary and secondary hydroxyl groups of **26a** were protected as

TBS ethers and the tertiary hydroxyl group was masked by a MOM group. The pivalate group of **28a** was removed by reduction with $LiAlH_4$ and the resultant allylic alcohol **29a** was converted to the sulfide **30a** through the following sequential treatment: 1) Ph_3P and CCl_4 in PhH; 2) NaSPh in DMF.[10] The thiophenyl group will serve to generate a carbanion on the allylic carbon so as to link this unit (B) to the unit (A).

The sulfide **30b**, antipode of **30a** was also synthesized by the similar sequential reactions starting from the Sharpless' oxidation of **24** with TBHP and L-(+)-DIPT (Scheme 11).[7]

Scheme 12.



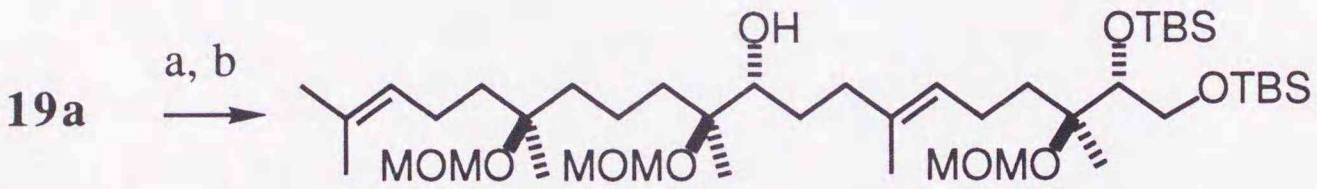
Reagents: (a) Ac_2O, Py, CH_2Cl_2, rt, 15 h; (b) SeO_2, TBHP, CH_2Cl_2, 0 °C, 5 h; (c) PvCl, Py, CH_2Cl_2, rt, 5 h; (d) NH_3, MeOH, rt, 40 h; (e) $Ti(^iOPr)_4$, D-(-)-DIPT, TBHP, MS-4A, CH_2Cl_2, -23 °C, 1 h; (e') $Ti(^iOPr)_4$, L-(+)-DIPT, TBHP, MS-4A, CH_2Cl_2, -23 °C, 1 h; (f) Mesitylenesulfonic acid, THF, H_2O, rt, 40 h; (g) MOMCl, $^iPr_2NEt$, CH_2Cl_2, rt, 40 h; (h) $LiAlH_4$, THF, 0 °C, 20 min; (i) Ph_3P, CCl_4, PhH, reflux, 15 h; (j) NaSPh, DMF, 0 °C, 10 min, 20% (**37a**) from **farnesol**, 16% (**37b**) from **farnesol**.

Farnesol was also transformed into the sulfides **37a** and **37b**, which should serve as the unit (C) in order to synthesize gymnoprenol analogues (Scheme 12).

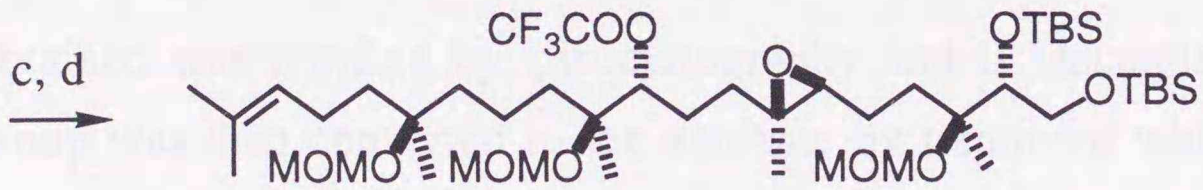
3-3. Extension of the Carbon Chain and Introduction of a New Asymmetric Center: Synthesis of the Eight Diastereoisomeric Model Compounds for Gymnoprenol (m=2, n=4)

The generation of the carbanion on the allylic carbon of **30a** was achieved on treatment with BuLi and TMEDA in THF. The coupling reaction of the epoxide **19a** with the resulting carbanion proceeded smoothly to give stereoselectively the sulfide alcohol whose phenylthio group was removed by Na/^{i}PrOH reduction and the bishomoallylic alcohol **38a** was obtained (Scheme 13).

Scheme 13.



38a



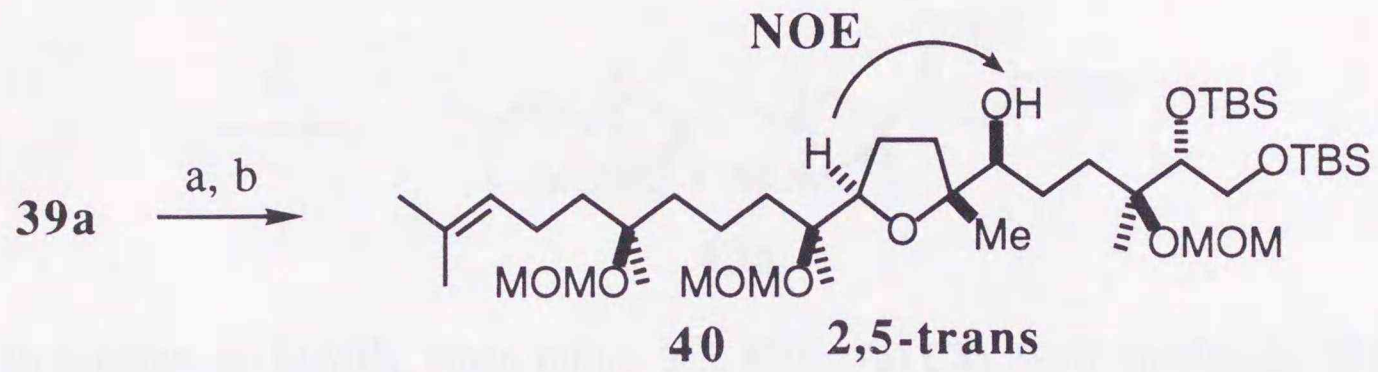
39a

Reagents: (a) **30a**, BuLi, TMEDA, THF, -30 °C, 30 min; (b) Na, ^{i}PrOH, THF, reflux, 4 h, 81% (in 2 steps); (c) $VO(acac)_2$, TBHP, NaOAc, PhH, 50 °C, 1 h; (d) TFAA, Py, CH_2Cl_2, -15 °C, 10 min, 58% (in 2 steps, the ratio of β-epoxide/ α-epoxide=4.8:1).

The newly formed secondary alcohol of **38a** participated in $VO(acac)_2$ catalyzed oxidation (type B mode)[6] and the *anti*-epoxide **39a** was formed

after treatment with TFAA in 58% yield. The ratio of β-epoxide/ α-epoxide was 4.8 to 1. The configuration of the β-epoxide in **39a** was confirmed by its conversion to the tetrahydrofuran derivative **40** whose stereochemistry was determined by its 2D-NOESY spectrum (The NOE was observed in the compound **40** as shown in Scheme 14).

Scheme 14.

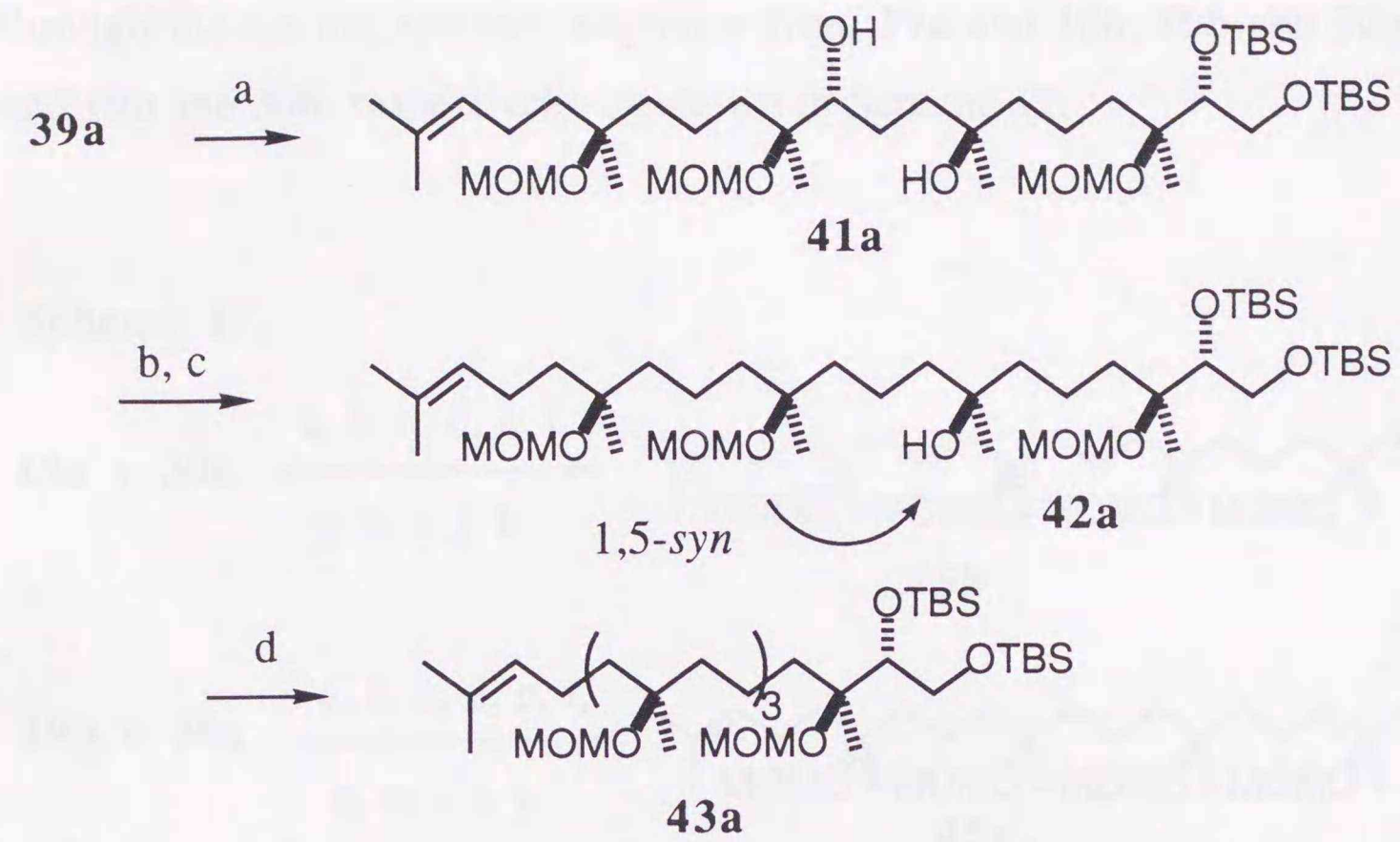


40 **2,5-trans**

Reagents: (a) Et_3N, MeOH, rt, 1 h; (b) TsOH, CH_2Cl_2, rt, 1 h, 89% (in 2 steps).

After separation of the major compound, the TFA group of **39a** was removed by reduction with $LiAlH_4$ in ether (Scheme 15). The diol **41a** obtained was purified by chromatography and its secondary hydroxyl group was then converted to the xanthate by treatment with CS_2, NaH, and imidazole in THF followed by MeI. Reduction of the xanthate with Bu_3SnH in PhH in the presence of AIBN as a radical initiator yielded **42a** with four sequential 1,5-glycol systems.

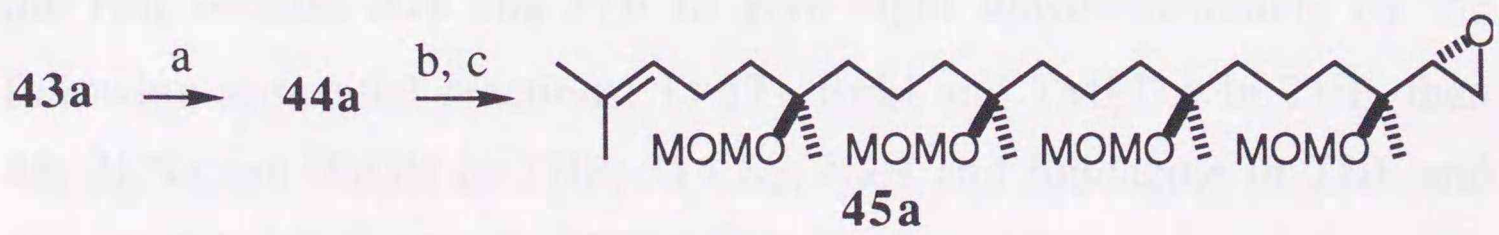
Scheme 15.



Reagents: (a) $LiAlH_4$, ether, reflux, 2 h, 80%; (b) CS_2, NaH, imidazole, THF then MeI, 0 °C, 1 h; (c) Bu_3SnH, AIBN, PhH, reflux, 45 min; (d) MOMCl, $^iPr_2NEt$, CH_2Cl_2, rt, 14 h, 82% (in 3 steps).

A free hydroxyl group in **42a** was masked by a MOM ether and two TBS groups in the resulting **43a** were removed with TBAF in THF to give a vicinal glycol **44a** (Scheme 16). Treatment of the resulting glycol with TsCl and pyridine in CH_2Cl_2 followed by K_2CO_3 in MeOH afforded the epoxide **45a** which correponds to the mesial part of a model gymnoprenol (n=4).

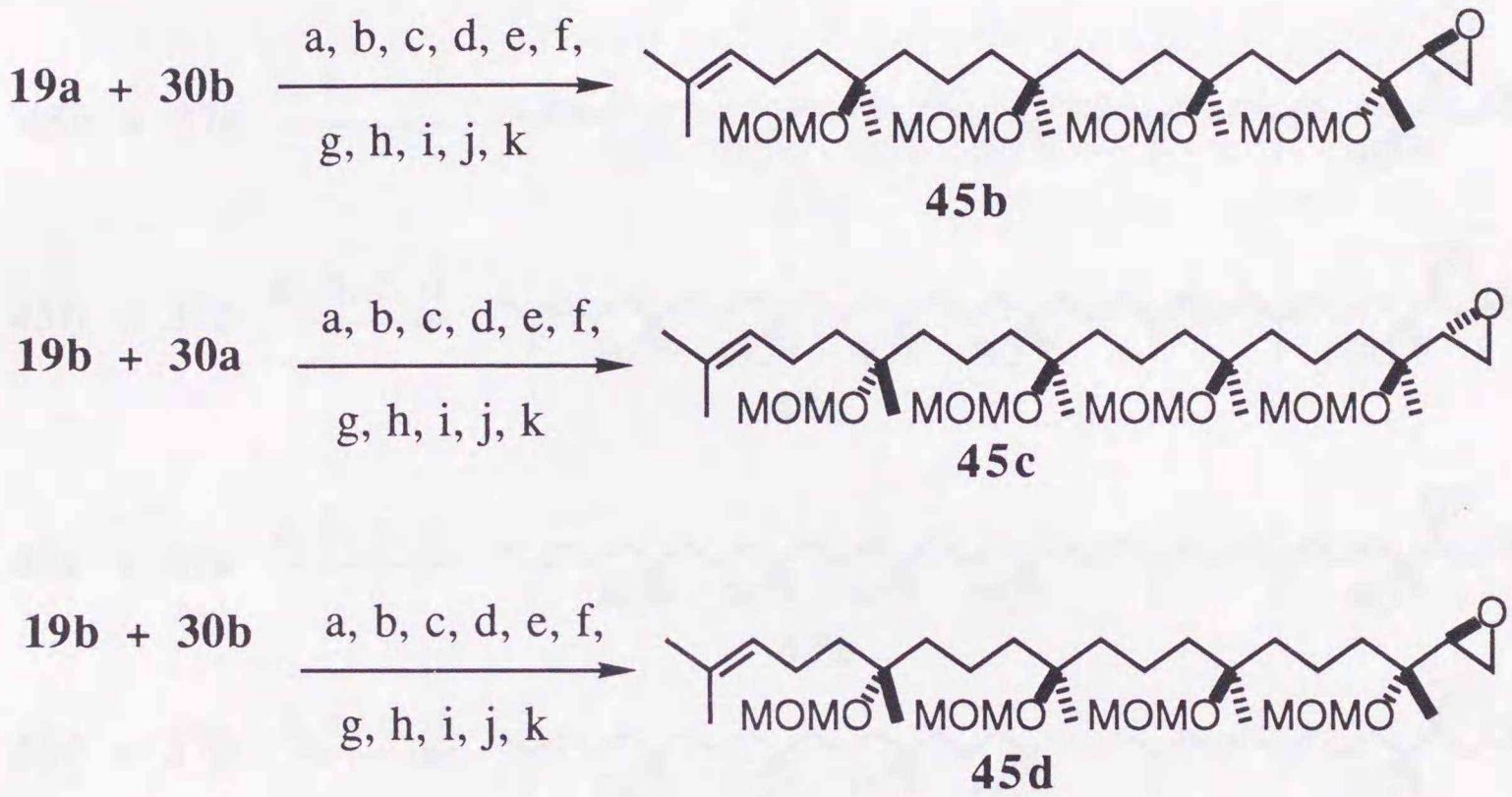
Scheme 16.



Reagents: (a) TBAF, THF, reflux, 1 h; (b) TsCl, Py, CH_2Cl_2, 0 °C, 40 h; (c) K_2CO_3, MeOH, rt, 1 h, 80% (in 3 steps).

Other three diastereoisomers of **45b**, **45c**, and **45d** were prepared through the similar reaction sequence from **19a** and **30b**, **19b** and **30a**, and **19b** and **30b**, respectively, as shown in Scheme 17.

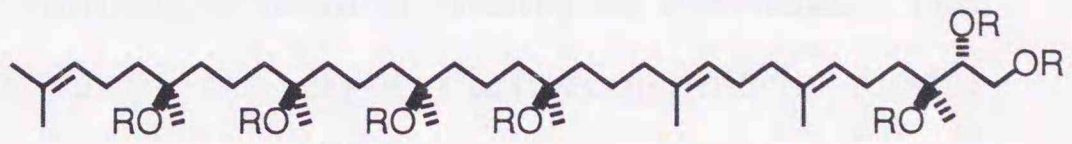
Scheme 17.



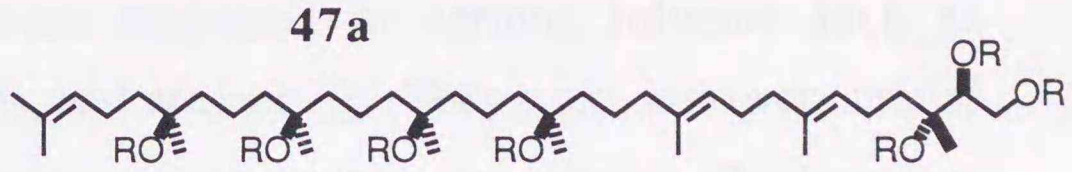
Reagents: (a) **30a**, BuLi, TMEDA, THF, -30 °C, 30 min; (b) Na, ^{i}PrOH, THF, reflux, 4 h; (c) $VO(acac)_2$, TBHP, NaOAc, PhH, 50 °C, 1 h; (d) TFAA, Py, CH_2Cl_2, -15 °C, 10 min; (e) $LiAlH_4$, ether, reflux, 2 h; (f) CS_2, NaH, imidazole, THF then MeI, 0 °C, 1 h; (g) Bu_3SnH, AIBN, PhH, reflux, 45 min; (h) MOMCl, $^{i}Pr_2NEt$, CH_2Cl_2, rt, 14 h; (i) TBAF, THF, reflux, 1 h; (j) TsCl, Py, CH_2Cl_2, 0 °C, 40 h; (k) K_2CO_3, MeOH, rt, 1 h, 9% from **19a** and **30b**, 9% from **19b** and **30a**, and 9% from **19b** and **30b**.

Each of the four diastereoisomeric epoxides **45a-d** was coupled with the two sulfides **37a** and **37b** to give eight diastereoisomers by the following sequential reactions: 1) **37**+ BuLi and TMEDA in THF, then **45**; 2) Na and ^{i}PrOH in THF; 3) CS_2, NaH and imidazole in THF and then MeI; 4) Bu_3SnH and AIBN in PhH (Scheme 18).

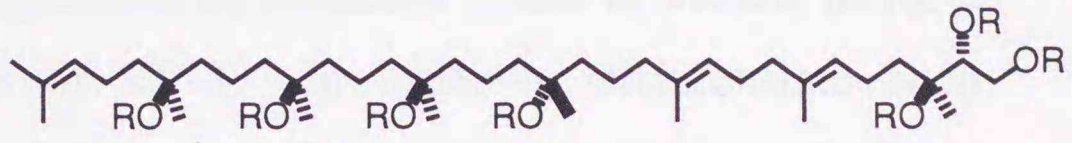
Scheme 18.

45a + 37a $\xrightarrow{\text{a, b, c, d}}$ 

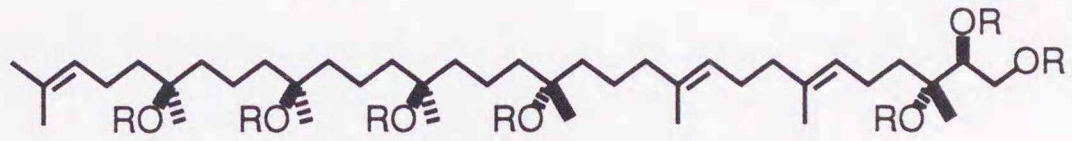
47a

45a + 37b $\xrightarrow{\text{a, b, c, d}}$ 

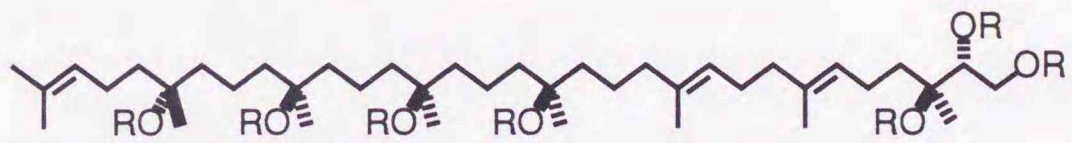
47b

45b + 37a $\xrightarrow{\text{a, b, c, d}}$ 

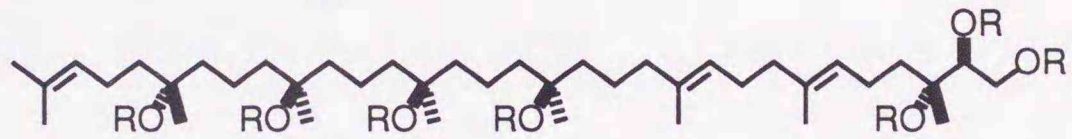
47c

45b + 37b $\xrightarrow{\text{a, b, c, d}}$ 

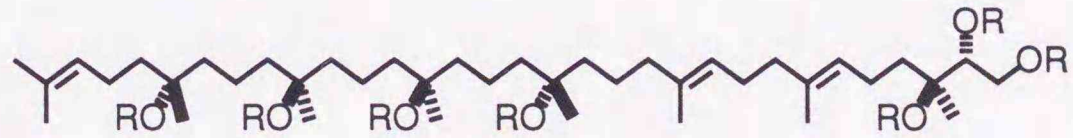
47d

45c + 37a $\xrightarrow{\text{a, b, c, d}}$ 

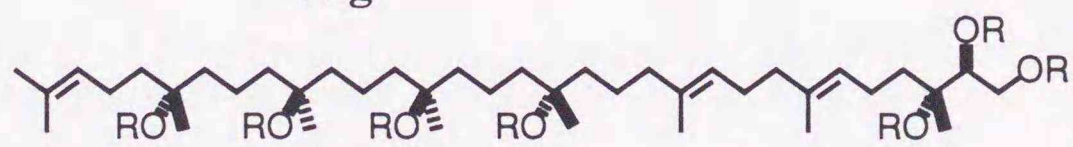
47e

45c + 37b $\xrightarrow{\text{a, b, c, d}}$ 

47f

45d + 37a $\xrightarrow{\text{a, b, c, d}}$ 

47g

45d + 37b $\xrightarrow{\text{a, b, c, d}}$ 

47h

R=MOM

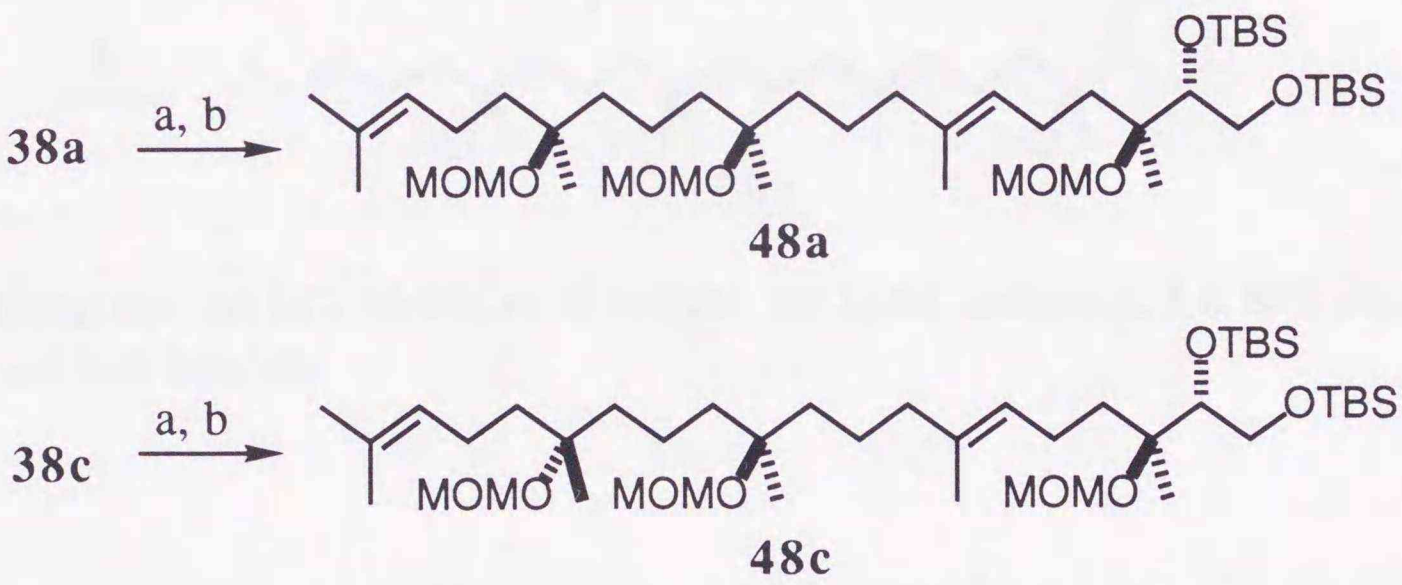
Reagents: (a) BuLi, TMEDA, THF, -30 °C, 30 min; (b) Na, ^{i}PrOH, THF, reflux, 30 min; (c) CS_2, NaH, imidazole, THF then MeI, 0 °C, 14 h; (d) Bu_3SnH, AIBN, PhH, reflux, 30 min, 43% from **45a** and **37a**, 39% from **45a** and **37b**, 52% from **45b** and **37a**, 43% from **45b** and **37b**, 34% from **45c** and **37a**, 41% from **45c** and **37b**, 41% from **45d** and **37a**, and 34% from **45d** and **37b**.

For the identification of the natural gymnoprenol with the synthetic compounds, reliable discrimination method should be essential. The ^{1}H- and ^{13}C-NMR spectra of the eight diastereoisomeric model compounds (**47a-h**) were measured in various solvents such as toluene-d_8, THF-d_4, Py-d_5, and acetone-d_6. They were, however, similar each other and no difference was observed among them. Furthermore, no difference was distinguished in retention times of HPLC using a column such as RP-18 or RP-8. In order to differentiate such configurationally slightly different compounds, another new method had to be developed.

Chapter 4 Discrimination of the Stereochemistry of the Sequential 1,5-Diol Systems. A New Method for the Introduction of MTP Groups to Tertiary Alcohols

Since discrimination of eight diastereoisomeric gymnoprenol analogues led to failure, the effects of various protective groups on tertiary alcohols were examined employing these diastereisomers. Two diastereoisomeric model gymnoprenols **48a** and **48c** (m=2, n=2) were synthesized by similar method (Scheme 19). Again there was no difference in their NMR spectra as well as HPLC retention times.

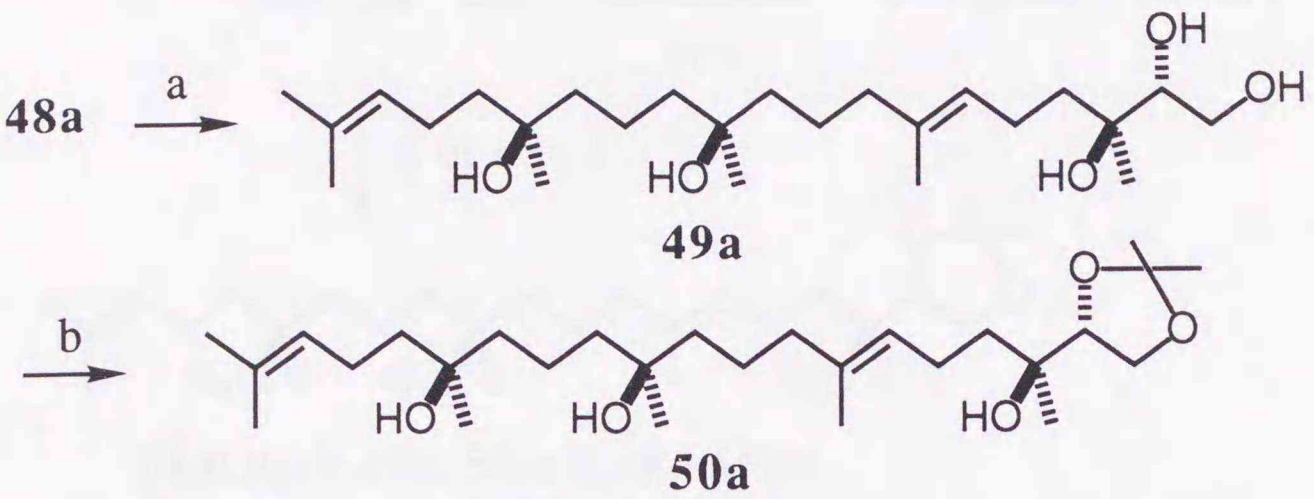
Scheme 19.



Reagents: (a) CS_2, NaH, imidazole, THF then MeI, 0 °C, 14 h; (b) Bu_3SnH, AIBN, PhH, reflux, 30 min, 92% from **38a** and 90% from **38c**.

All protective groups of **48a** and **48c** were removed and their primary and secondary hydroxyl groups were converted to the acetonides **50a** and **50c** (Scheme 20).

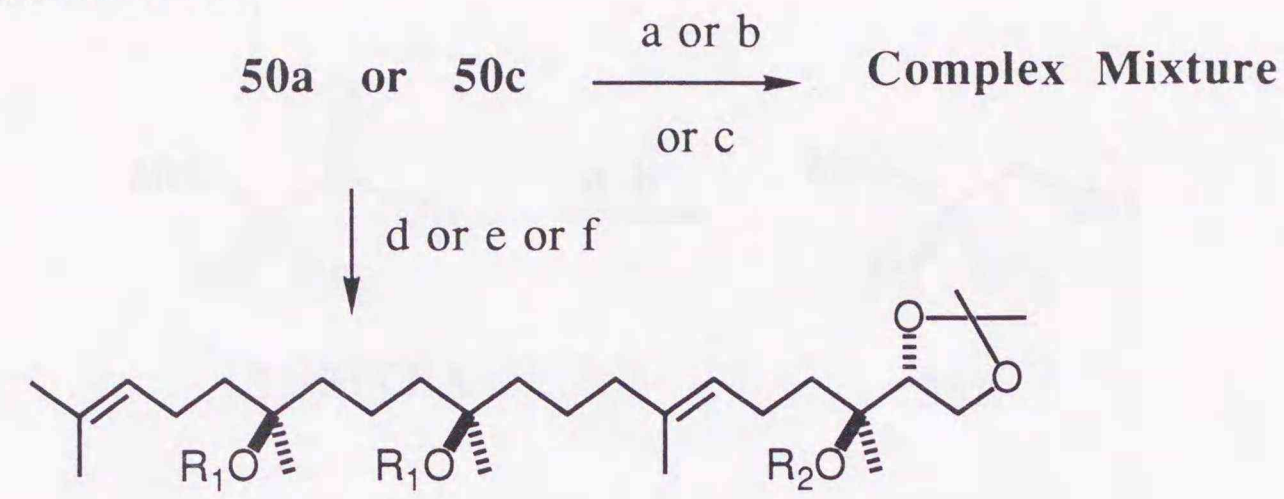
Scheme 20.



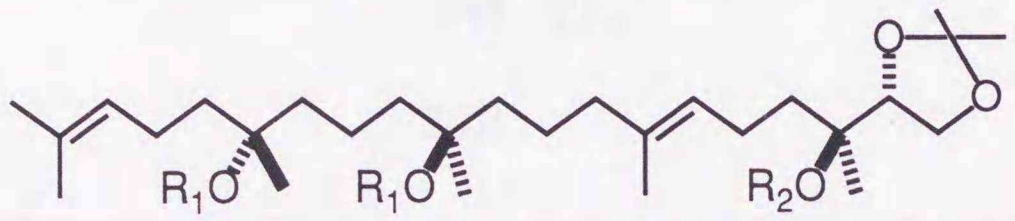
Reagents: (a) HCl, MeOH, rt, 30 h, 95%; (b) TsOH, acetone, rt, 1 h, 86% from **49a** and 76% from **48c**.

Acylation with Ac_2O, BzCl, or MTPACl[11] resulted in the formation of complex mixture. On the other hand, etherification with BnBr/NaH, MOMCl/$^{i}Pr_2NEt$, or BOMCl/$^{i}Pr_2NEt$ yielded the corresponding triethers, **51a**, **51c**, **52a**, **52c**, **53a**, and **53c**, and the diethers **54a** and **54c** in good yields (Scheme 21). Every pair of diastereoisomeric ethers, however, could not be differentiated by their NMR spectra and HPLC retention times.

Scheme 21.



51a; R_1=R_2=Bn, **52a**; R_1=R_2=MOM,
53a; R_1=R_2=BOM, **54a**; R_1=BOM, R_2=H

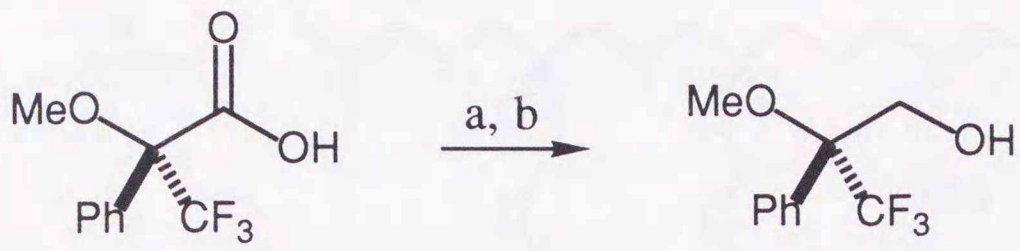


51c; R_1=R_2=Bn, **52c**; R_1=R_2=MOM,
53c; R_1=R_2=BOM, **54c**; R_1=BOM, R_2=H

Reagents: (a) Ac_2O, Py; (b) BzCl, Py; (c) MTPACl, Py; (d) BnBr, NaH, DMF, 0 °C, 30 min, 42% from **50a** and 44% from **50c**; (e) MOMCl, $^iPr_2NEt$, CH_2Cl_2, rt, 14 h, 77% from **50a** and 80% from **50c**; (f) BOMCl, $^iPr_2NEt$, CH_2Cl_2, rt, 14 h, 28% (**53a**) from **50a**, 28% (**54a**) from **50a**, 30% (**53c**) from **50c**, and 40% (**54c**) from **50c**.

In order to amplify the asymmetry of particular positions, introduction of chiral parts into diastereoisomeric fragments was designed. For this purpose, the MTPA ethers of the tertiary 1,5-glycol systems should be examined. Preparation of 2-methoxy-2-trifluoromethyl-2-phenylethoxy-methyl chloride (MTPEOMCl) was then attempted. (*R*)-MTPA was esterified with CH_2N_2 and the resulting ester was reduced to the alcohol (**55*R***) with $LiAlH_4$ (Scheme 22). (*R*)-MTP ethanol (**55*R***) was treated with paraformaldehyde and HCl gas to give the desired (*R*)-MTPEOMCl (**56*R***).[12)]

Scheme 22.



(*R*)-MTPA **55*R***

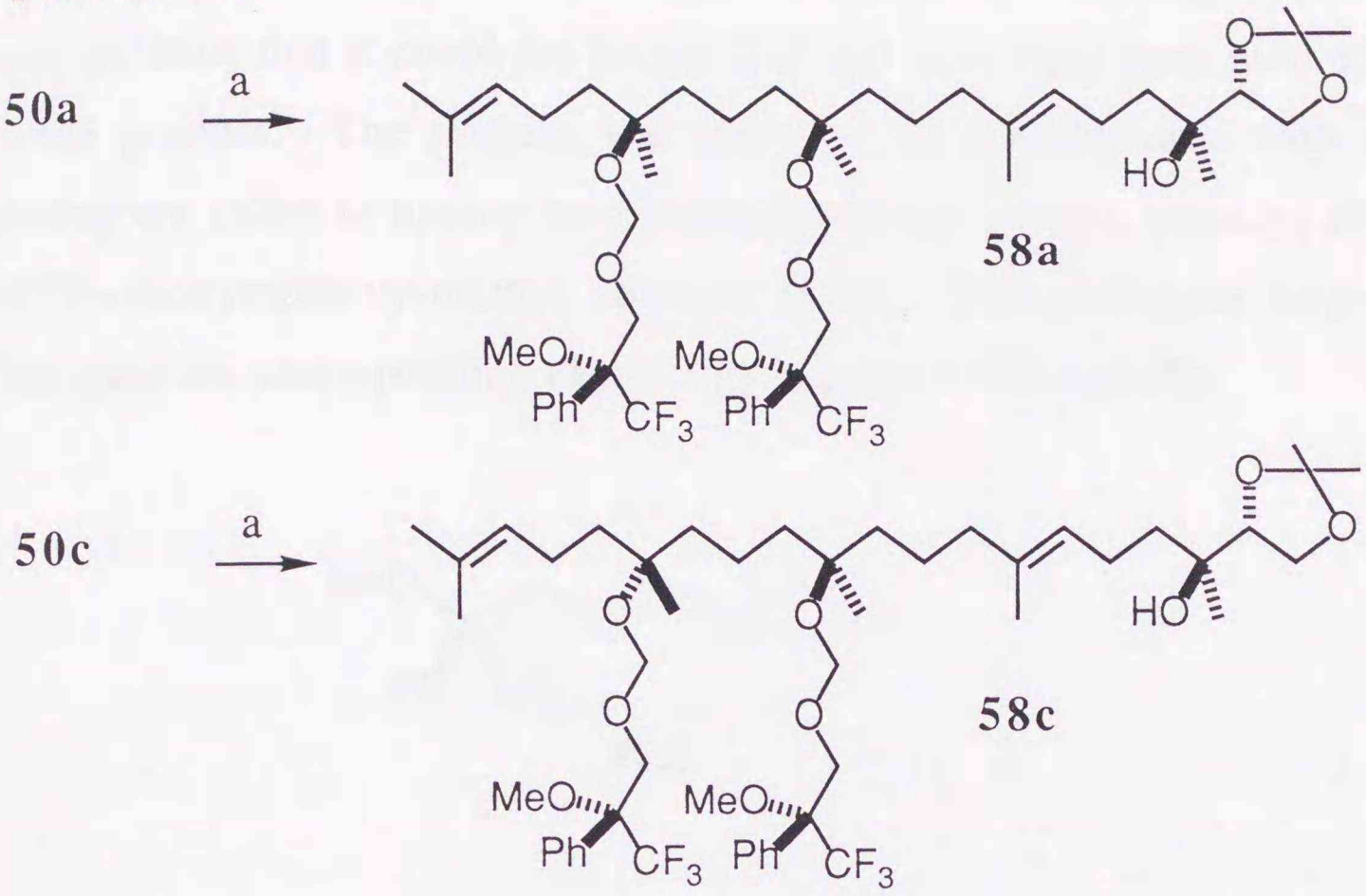
≡ **(*R*)-MTPEOMCl**

56*R*

Reagents: (a) CH_2N_2, ether, rt, 30 min, 100%; (b) $LiAlH_4$, THF, 0 °C, 1 h, 93%; (c) $(CH_2O)_X$, HCl(g), rt, 2 h.

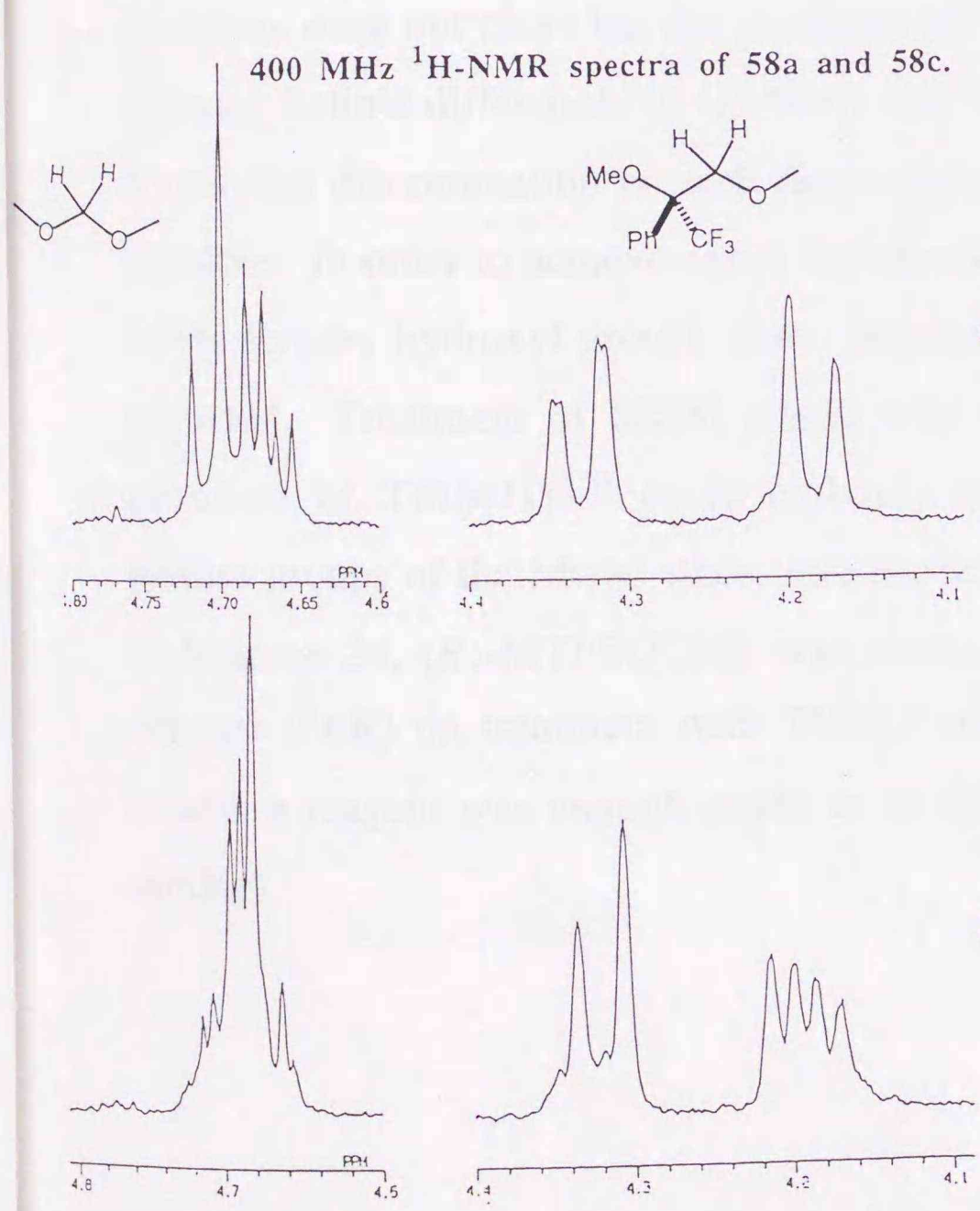
By means of the new reagent, the MTPEOM ethers of the various tertiary alcohols were prepared. Thus the triols **50a** and **50c** were treated with the new reagent **56*R*** in the presence of $^{i}Pr_2NEt$ in CH_2Cl_2 to give diethers **58a** and **58c** in which one of the tertiary alcohols at the head parts remaining unchanged (Scheme 23).

Scheme 23.

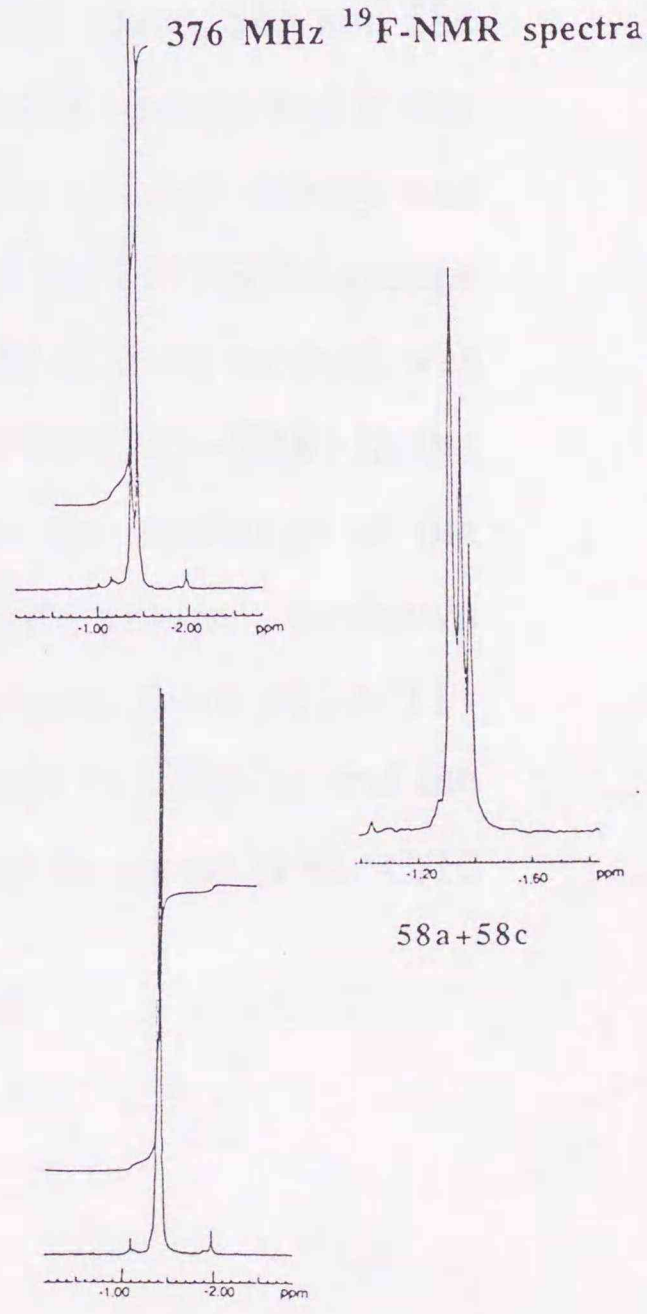


Reagents: (a) **56R**, $^{i}Pr_2NEt$, CH_2Cl_2, reflux, 40 h, 5% from **50a** and 5% from **50c**.

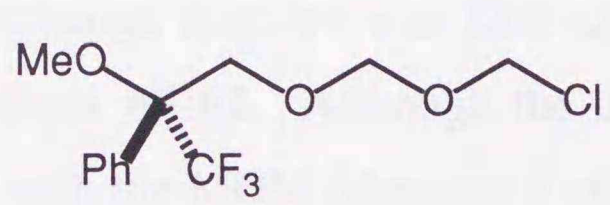
400 MHz ^{1}H-NMR spectra of 58a and 58c.



376 MHz ^{19}F-NMR spectra.



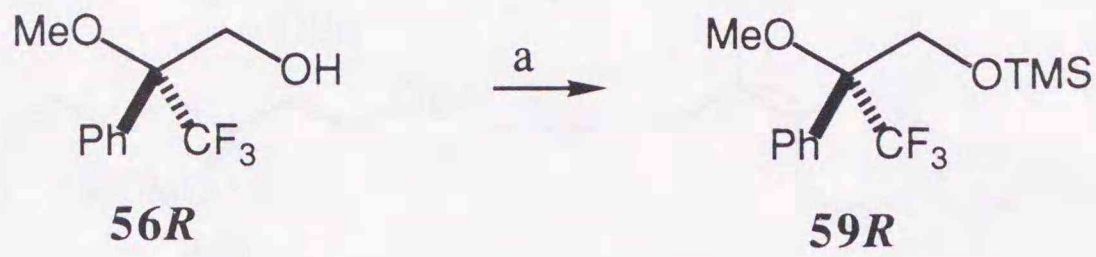
The yields of the MTPEOM ethers were poor since the reagent (**56*R***) was so labile that it could not be purified and must have been used as a crude product. The reagent was found to be contaminated with an analogous chloride having two methylenedioxy groups, namely, (*R*)-MTP-ethoxymethoxy-methyl chloride (**57*R***). This analogous reagent also gave the corresponding ethers with substrates **50a** and **50c**.



57R

The purifications of the MTPEOM ethers were also troublesome. The reactions were not clean but the produced MTPEOM ethers, **58a** and **58c** showed distinct differences in ^{1}H-NMR and ^{19}F-NMR spectra and it was found that discrimination of each diastereoisomeric 1,5-diol moiety was possible. In order to achieve easier introduction of the MTPEOM groups to the tertiary hydroxyl groups, some improvement of these method was required. Treatment of MOM ethers with MTPEOTMS (**59*R***) in the presence of TMSOTf[13] could probably realize the exchange of the methyl groups of the MOM ethers into the MTPEOM groups. As shown in Scheme 24, (*R*)-MTPEOTMS was easily prepared from (*R*)-MTP-ethanol (**56*R***) on treatment with TMSCl and Et_3N in CH_2Cl_2 and the resulting reagent was enough stable to be distilled in vacuo (130 °C/10 mmHg).

Scheme 24.



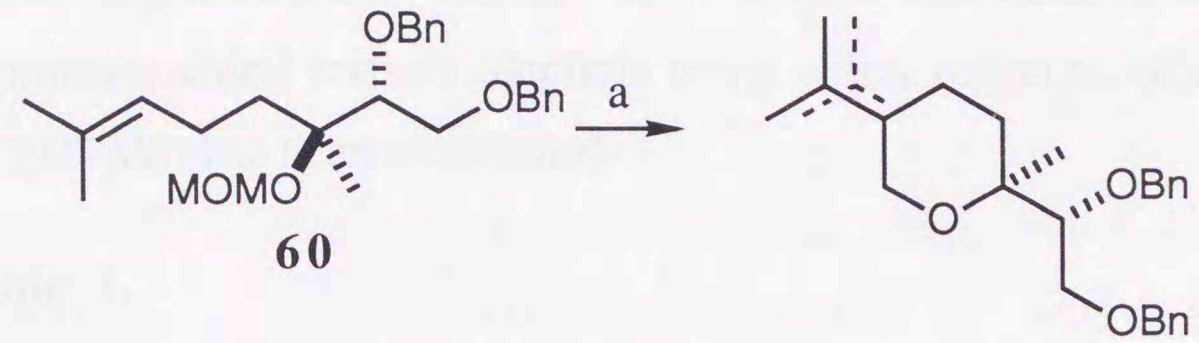
56*R* **59*R***

Reagents: (a) TMSCl, Et_3N, CH_2Cl_2, rt, 1 h, 82%.

The ether exchange reaction was first examined using the simpler tertiary MOM ethers **60-62**. Although the double bond of **60** reacted intramolecularly with the MOM ether and a cyclic ether was obtained, **61** and **62** having no double bond gave the desired MTPEOM ethers, **63*R*** and **64*R***, respectively, in good yields (Scheme 25). The MTPEOM derivative of **61**, namely **63*R***, showed the NMR signals due to the methylene protons of MTPE and benzyl protons at the same chemical shifts. Therefore, methyl ether instead of benzyl ether should be better as the protective group of the substrate. The reagent (*S*)-MTPEOTMS (**59*S***) was also prepared by the same procedure described for **59*R***.

The MOM ether **62** also reacted with (*S*)-MTPEOTMS (**59*S***) to give the (*S*)-MTPEOM ether (**64*S***) (Scheme 25), which was different from **64*R*** in the chemical shifts of its methylene protons adjacent to the MTPE chiral centers and of its dioxymethylene protons. The ^{19}F-NMR spectrum of **64*S*** indicated signals at clearly different chemical shift from that of **64*R***. Fortunately, the obtained diastereoisomeric pair **64*R*** and **64*S*** were enough stable to analyze by TLC and HPLC. Although ten times equivalent of MTPEOTMS were required in order to perform the reaction completely, this silyl ether could be recovered after the reaction.

Scheme 25.

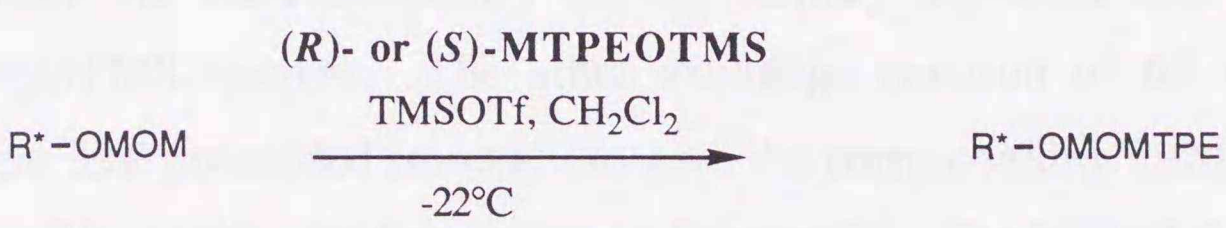


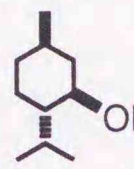
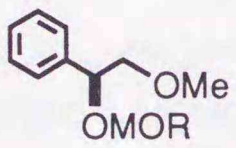
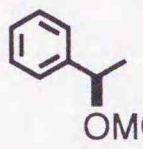
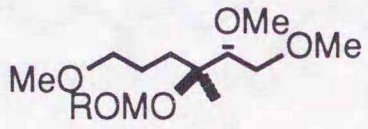
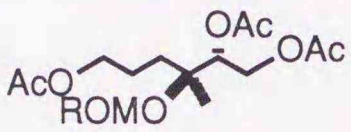
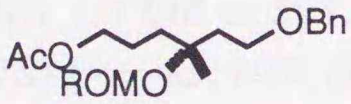
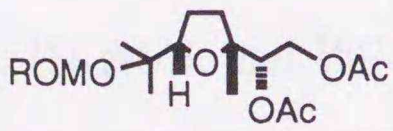
Reagents: (a) **59R**, TMSOTf, CH_2Cl_2, -22 °C, 5 min, 80% (**63*R***) from **61** and 79% (**64*R***) from **62**.

The MOM ethers (**A**, **B**, **C**, **D**, **E**, **F**, and **G**) were similarly converted to the corresponding (*R*)-MTPEOM ethers (**H*R***, **I*R***, **J*R***, **K*R***, **L*R*** **M*R***, and **N*R***) and (*S*)-MTPEOM ethers (**H*S***, **I*S***, **J*S***, **K*S***, **L*S***, **M*S***, and **N*S***), respectively, in good yields. The ^{19}F-NMR chemical shifts of these compounds were shown in Table 1. All compounds possessing

(*R*)-MTPEOM ethers indicated signals at different chemical shifts from those of (*S*)-MTPEOM ethers. Thus a new and reliable method to discriminate chiral tertiary alcohols using chiral reagents, (*R*)- and (*S*)-MTPEOTMS, has been established.

Table 1.

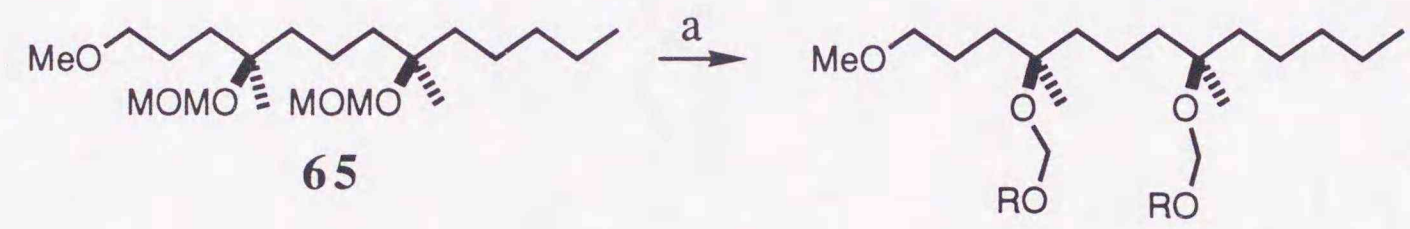


	MOM ethers (R=MOM)	MTPEOM ethers (R=MTPE)	^{19}F- NMR (ppm) Chemical shifts	yields (%)	Δδ (ppm)
A		**H*R***	-5.74	72	0.28
		H*S*	-5.46	70	
B		**I*R***	-7.13	68	0.40
		I*S*	-6.73	72	
C		**J*R***	-6.30	67	0.07
		J*S*	-6.23	67	
D		**K*R***	-6.18	79	0.16
		K*S*	-6.02	80	
E		**L*R***	-6.06	75	-0.41
		L*S*	-6.47	70	
F		**M*R***	-5.39	70	0.04
		M*S*	-5.35	70	
G		**N*R***	-6.42	86	0.10
		N*S*	-6.32	88	

Chapter 5 Presumption of the Stereochemistry of Natural Gymnoprenols

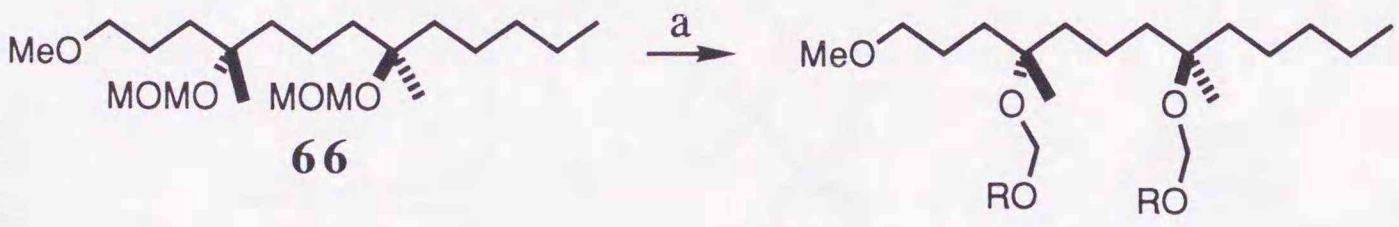
First, a model compound **65** having 1,5-*syn*-diol moiety and its isomer **66** with 1,5-*anti*-diol unit were prepared to examine the relationship between the stereochemistry of the tertiary 1,5-diols and that of MTPEOTMS reagent. The ether exchange reaction of **65** with the reagent **59*R*** proceeded smoothly to give the corresponding di-MTPEOM ether **67*R*** in 70% yield as shown in Scheme 26. The MTPEOM ethers, **67*S***, **68*R***, and **68*S*** were also prepared by the same reaction from **65** and **59*S***, **66** and **59*R***, and **66** and **59*S***, respectively, in good yields.

Scheme 26.



65

67*R*; R= (*R*)-MTPE
67*S*; R= (*S*)-MTPE



66

68*R*; R= (*R*)-MTPE
68*S*; R= (*S*)-MTPE

Reagents: (a) **59*R*** or **59*S***, TMSOTf, CH_2Cl_2, -22 °C, 5 min, 60% (**67*R***) from **65**, 60% (**67*S***) from **65**, 60% (**68*R***) from **66**, and 64% (**68*S***) from **66**.

The ^{1}H-NMR and ^{19}F-NMR spectra of these four compounds indicated different signal patterns and it was found that the distinction of the stereochemistry of the 1,5-glycol parts was possible by using this method.

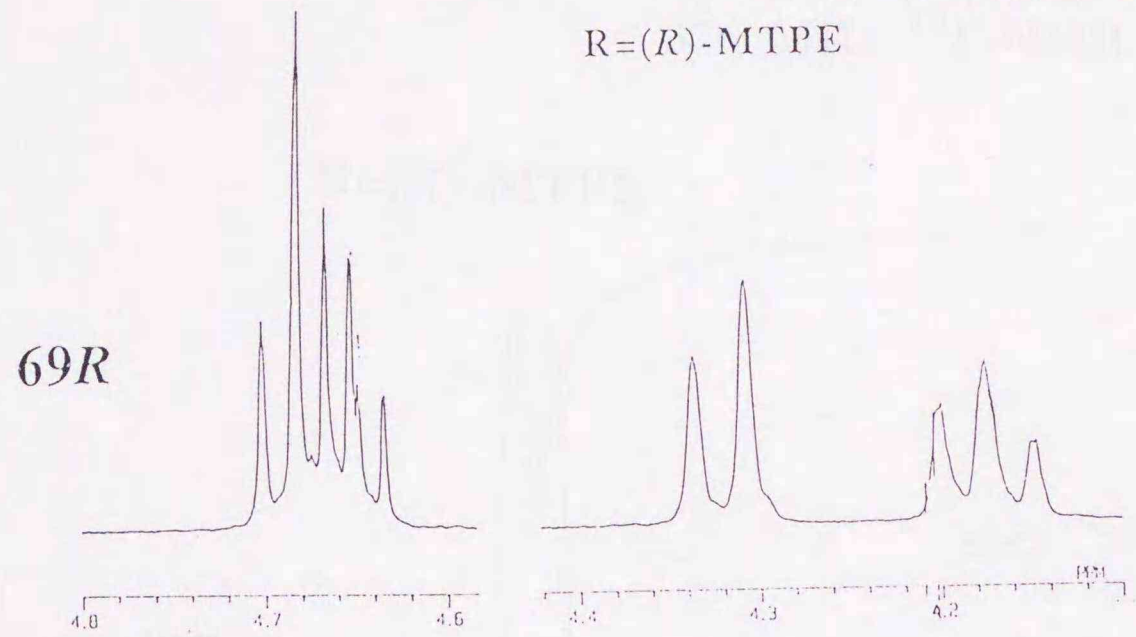
400 MHz ^{1}H-NMR spectra of 69*R*, 69*S*, 70*R*, and 70*S*.

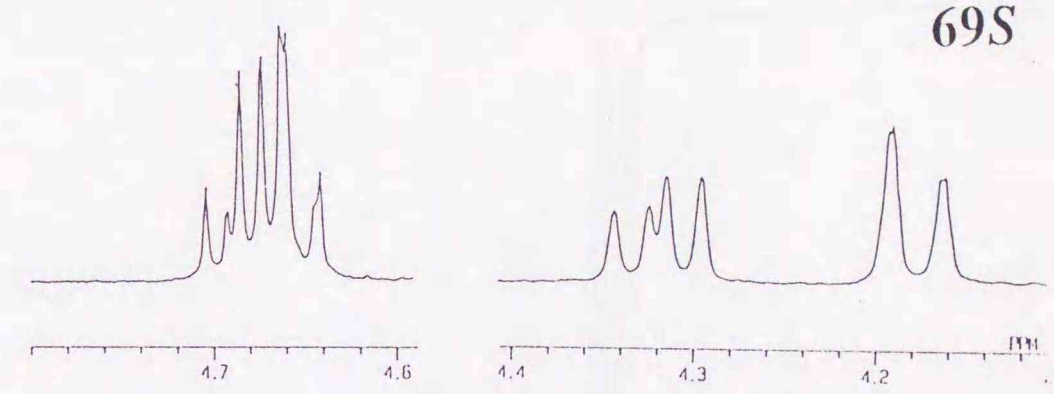
R=(*R*)-MTPE

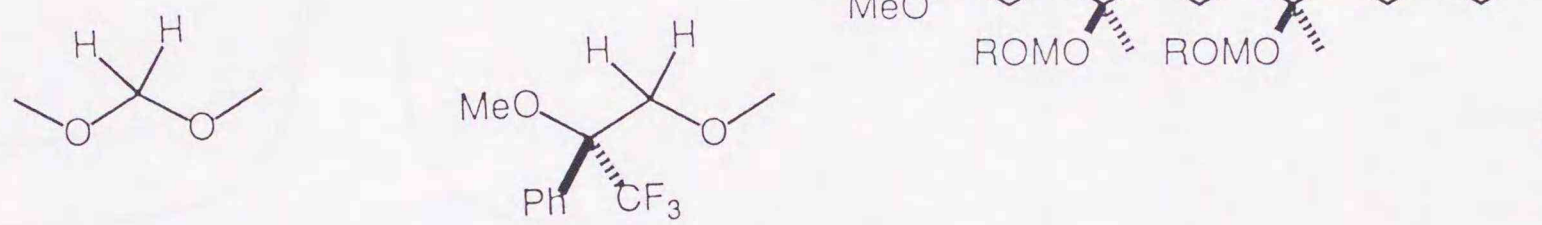
R=(*S*)-MTPE

69*R*

69*S*

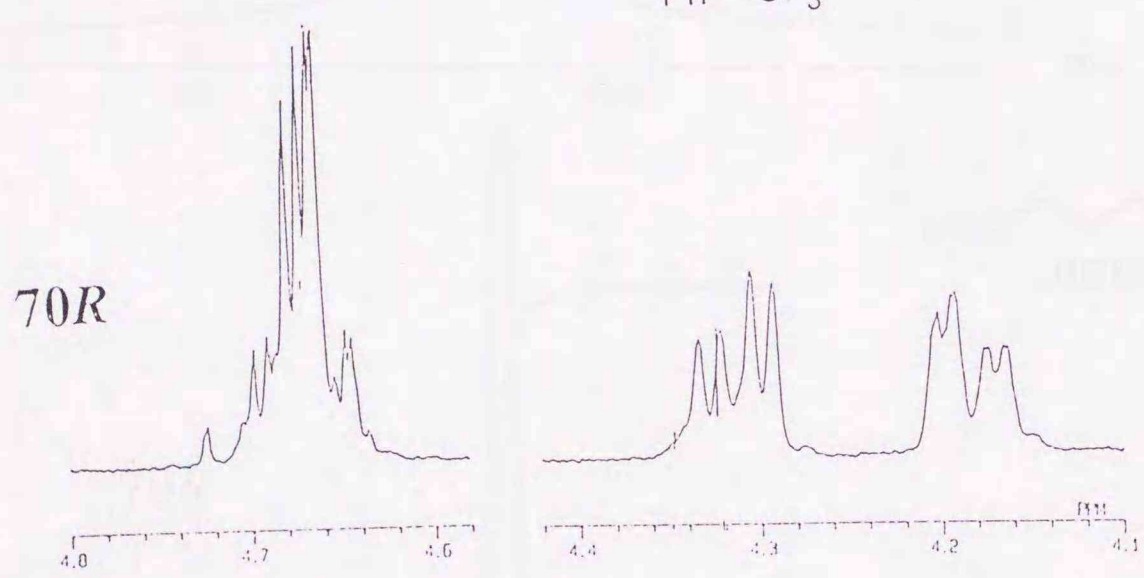


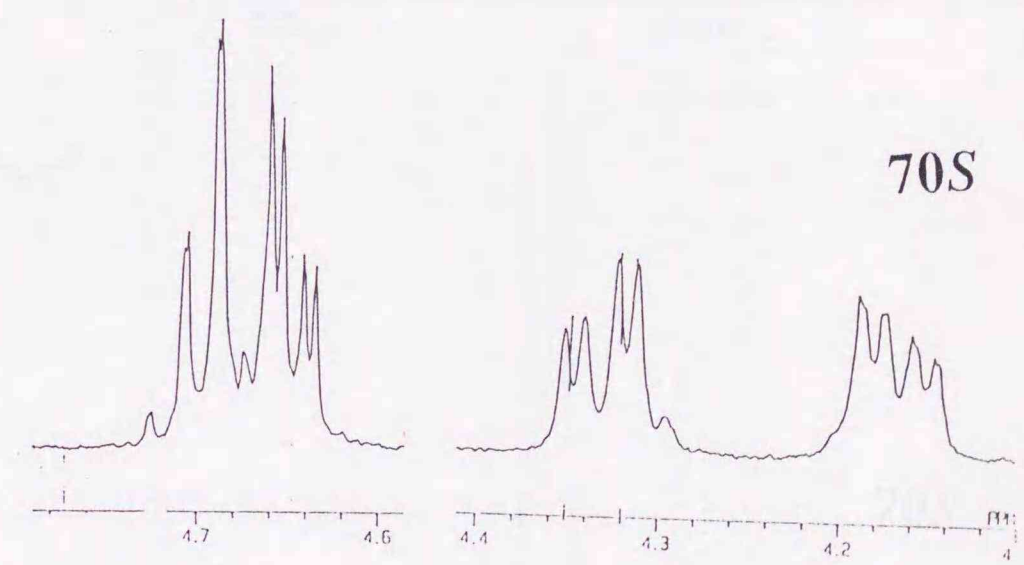


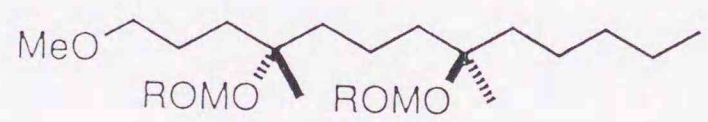


70*R*

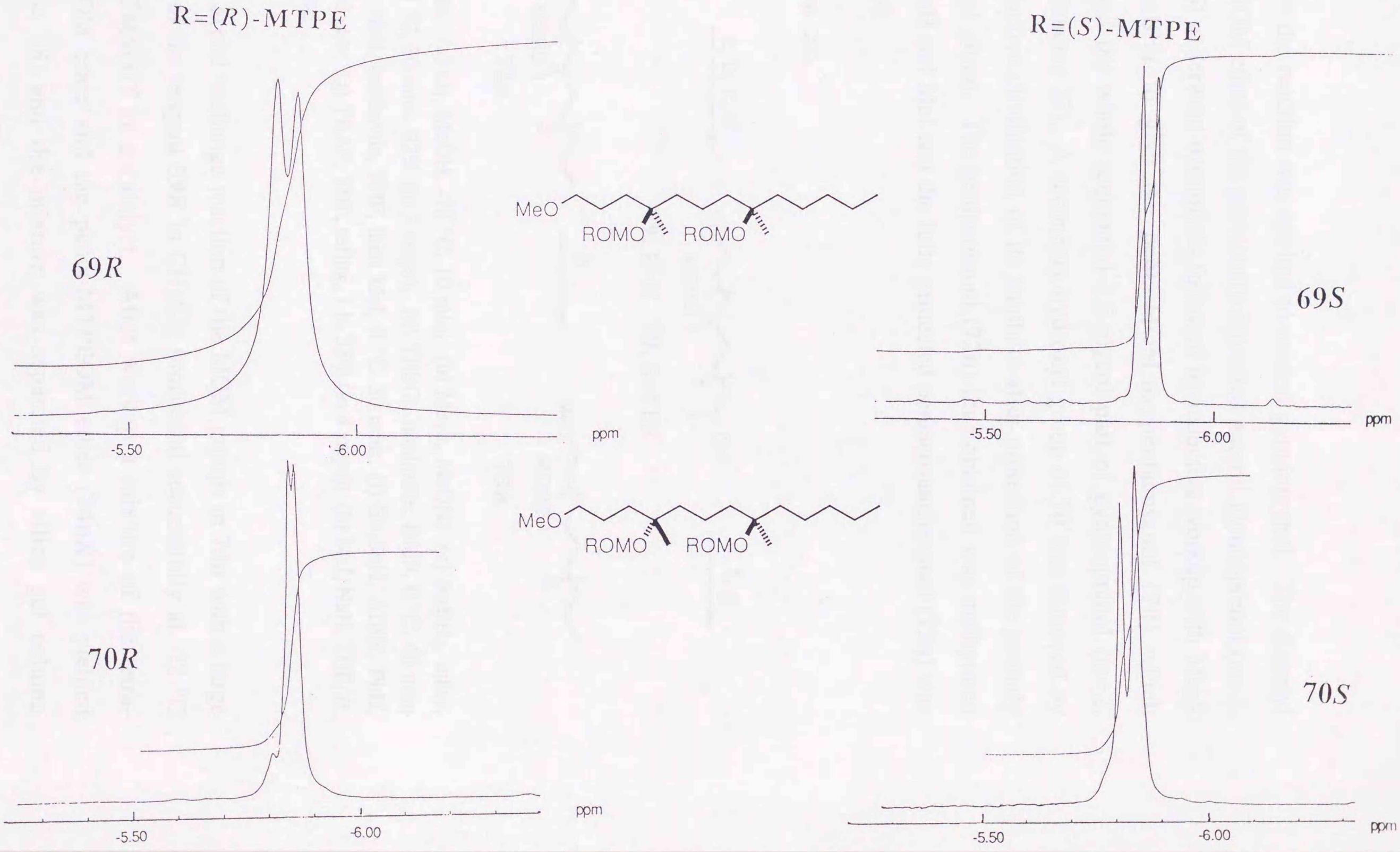
70*S*





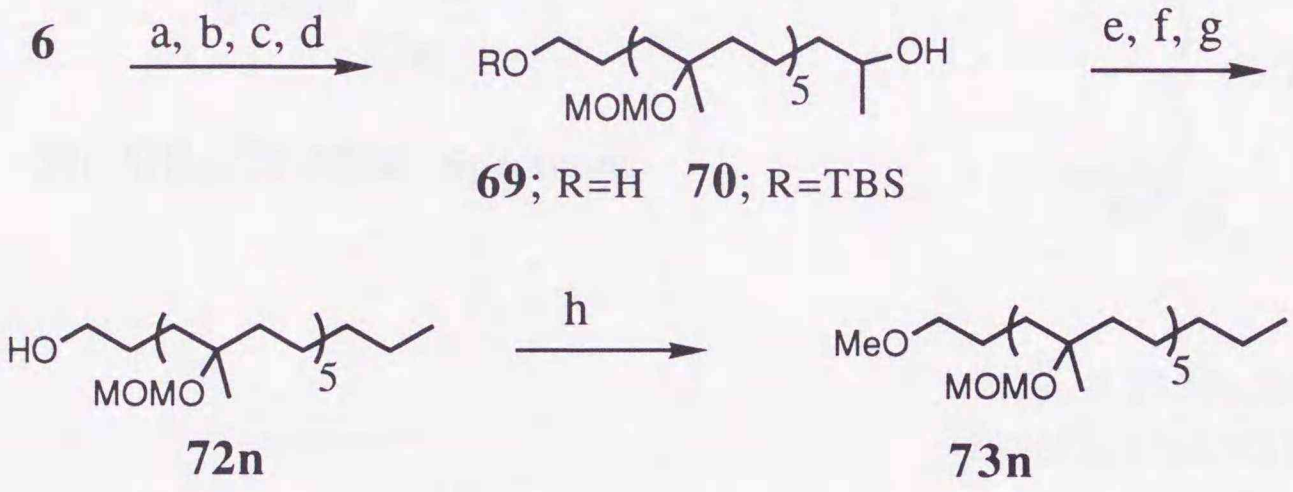


376 MHz ^{19}F-NMR spectra of 69*R*, 69*S*, 70*R*, and 70*S*.



Then the reaction was applied to natural gymnoprenol. The diacetyl hexa-MOM ether of the previously separated natural gymnoprenol (m=2, n=5) (**6**) underwent ozonolysis followed by reductive workup with Me_2S and $NaBH_4$ to give the penta-MOM-oxypentacosanol (**70**) which contained the whole sequential 1,5-glycol part of gymnoprenol (m=2, n=5) (Scheme 27). A secondary hydroxyl group of **70** was removed by the reductive elimination of its xanthate after protection of the primaly hydroxyl group. The pentacosanol (**72n**) thus obtained was methylated with NaH and MeI and the fully protected pentacosanehexanol (**73n**) was obtained.

Scheme 27.

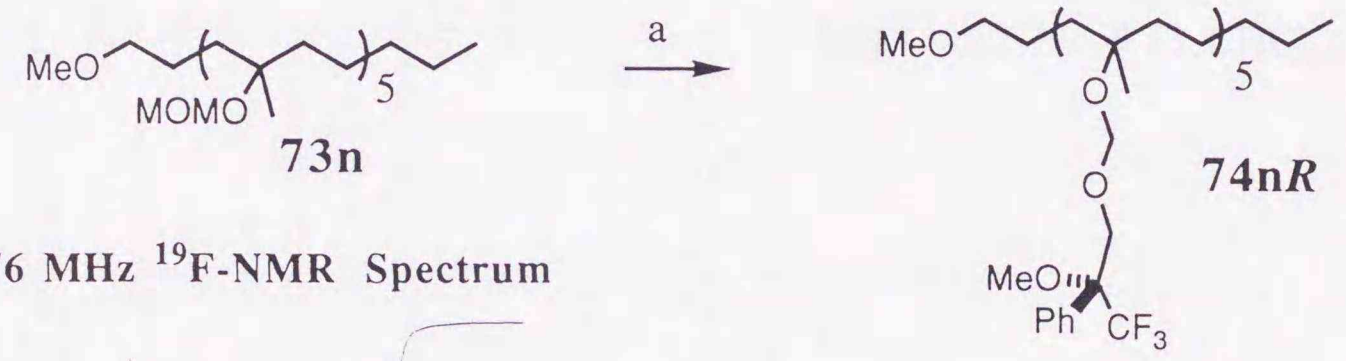


Reagents: (a) O_3, MeOH, -78 °C, 10 min; (b) Me_2S, MeOH; (c) $NaBH_4$, ether, EtOH, 0 °C, 30 mim, 92% (in 3 steps): (d) TBSCl, imidazole, DMF, 0 °C, 40 min; (e) CS_2, NaH, imidazole, THF, then MeI, 0 °C, 30 min; (f) Bu_3SnH, AIBN, PhH, reflux, 30 min; (g) TBAF, THF, reflux, 1 h, 35% (in 4 steps); (h) MeI, NaH, THF, rt, 40 h, 80%.

The acetal exchange reaction of the MOM groups in **73n** with a large excess of the reagent ***59R*** in CH_2Cl_2 proceeded successfully at -22 °C using TMSOTf as a catalyst. After workup a mixture of the tetra-MTPEOM ether and the penta-MTPEOM ether (***74nR***) was yielded (Scheme 28) and the mixture was separated by silica gel column

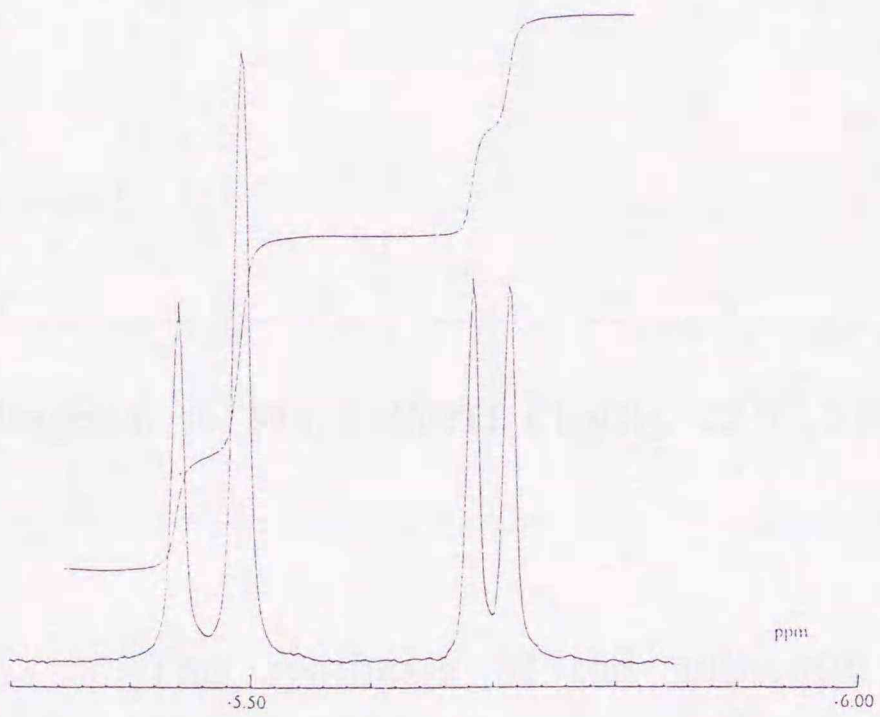
chromatography. The tetra-MTPEOM ether underwent again the acetal exchange reaction to give **74n*R***. The FD-MS spectrum of **74n*R*** showed peaks at m/z 1731 $(M+K)^+$ and 1715 $(M+Na)^+$ corresponding to the molecular formula $C_{86}H_{119}O_{16}F_{15}$. Its ^{19}F-NMR spectrum indicated five separated peaks and the ^1H-NMR spectrum showed equal signal intensities due to the dioxy methylene groups and the methylene groups adjacent to the MTP chiral centers. All spectral data supported the complete exchange of the five MOM groups into MTPEOM groups.

Scheme 28.



73n **74n*R***

376 MHz ^{19}F-NMR Spectrum



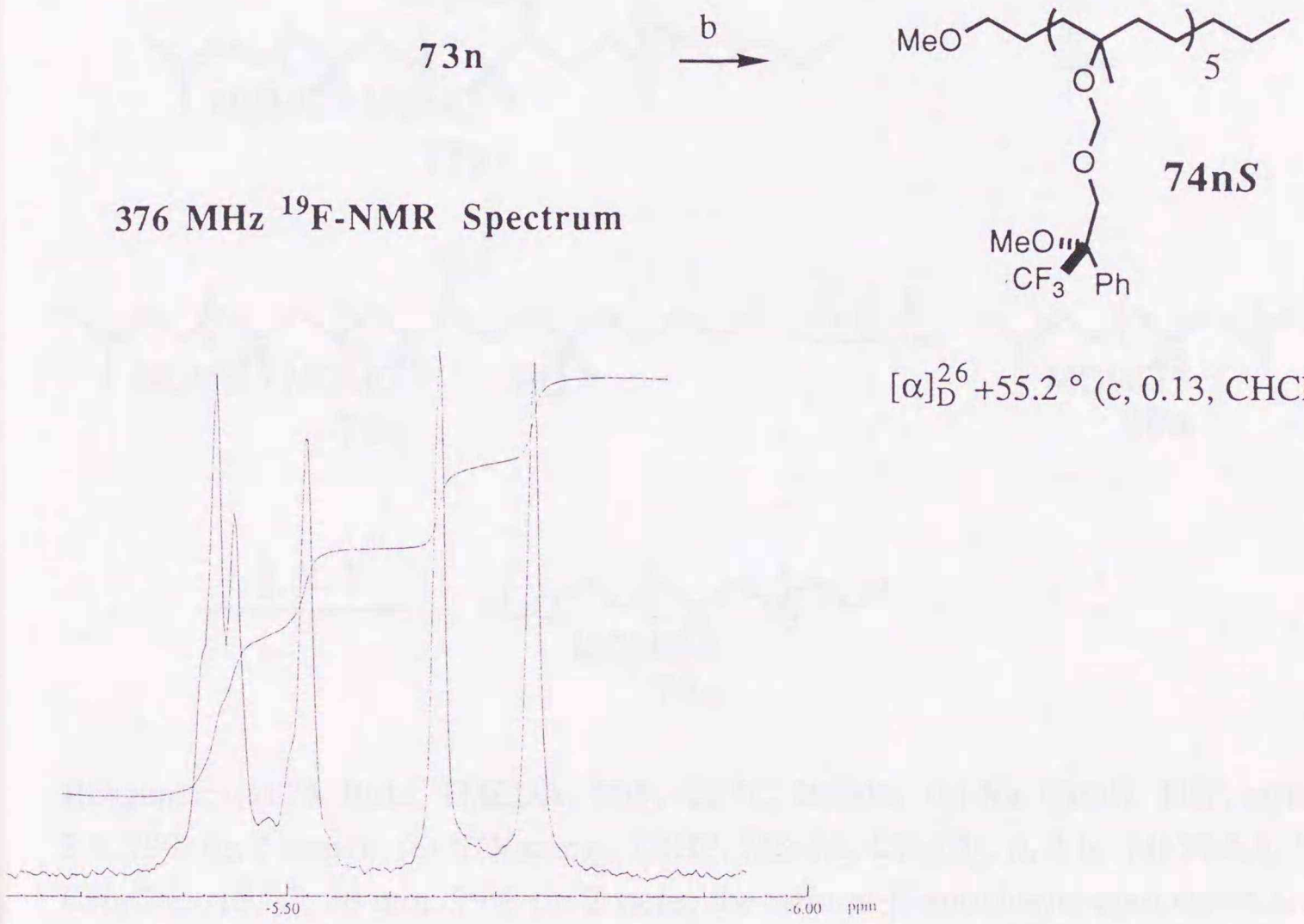
$[\alpha]_D^{26}$ +7.17 ° (c, 0.20, $CHCl_3$)
FD-MS, m/z 1715 $(M+Na)^+$
1731 $(M+K)^+$

Reagents: (a) **59*R***, TMSOTf, CH_2Cl_2, -22 °C, 5 min, 19%.

On the other hand, the MOM ether **73n** also reacted with (*S*)-MTPEOTMS (**59*S***) to give the corresponding (*S*)-MTPEOM ether (**74n*S***), which was different from **74n*R*** in the chemical shifts of its methylene protons adjacent to the MTPE chiral centers as well as its

dioxymethylene protons. The ^{19}F-NMR spectrum of **74n*S*** indicated the signals at clearly different chemical shifts from that of **74n*R*** (Scheme 29).

Scheme 29.

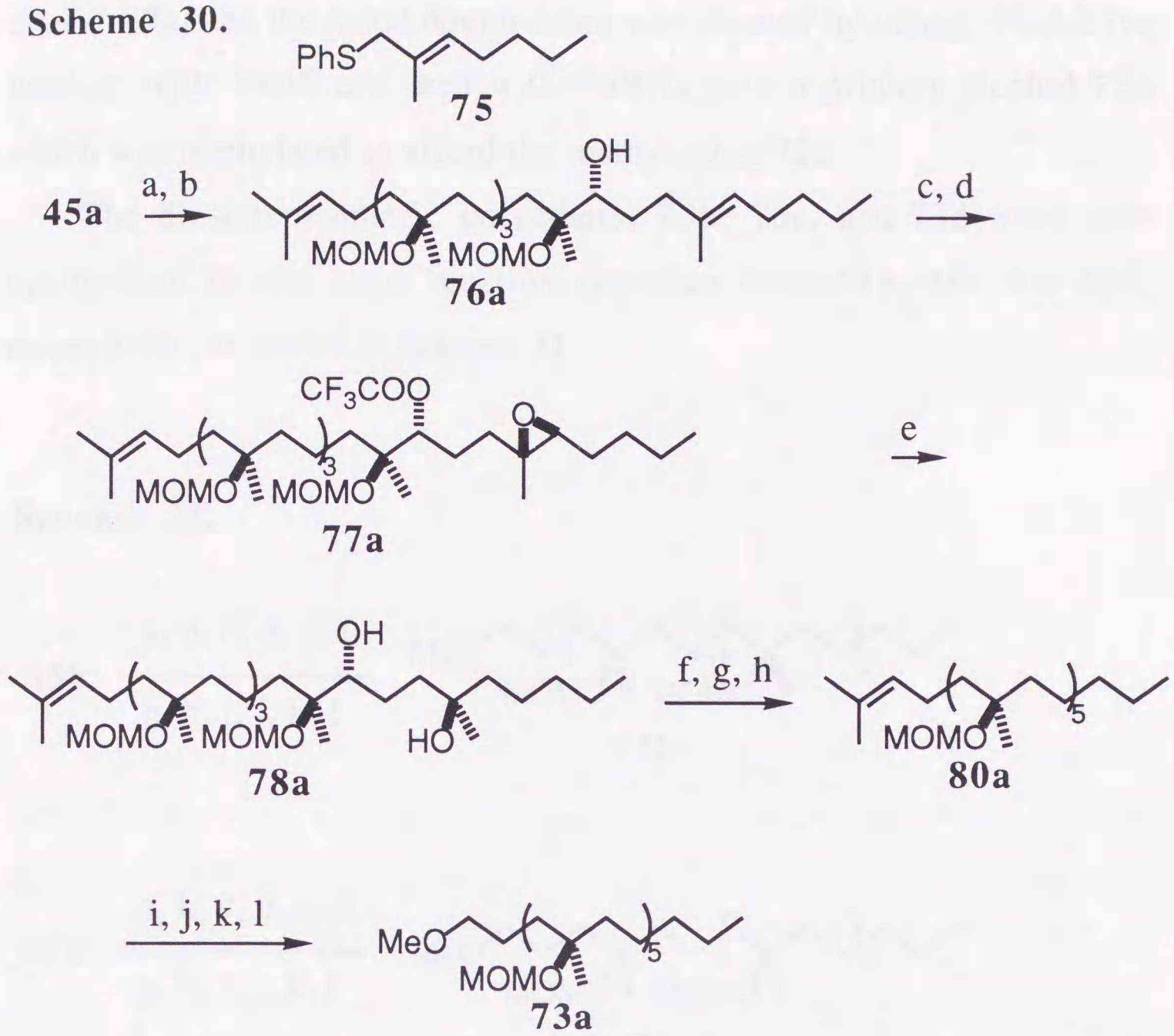


$[\alpha]_D^{26}$ +55.2 ° (c, 0.13, $CHCl_3$).

Reagents: (b) **59*S***, TMSOTf, CH_2Cl_2, -22 °C, 5 min, 19%.

The synthesis of the authentic samples bearing definite stereochemistry was carried out. The elongation of the previously synthesized polyol **45a** was achieved by the coupling reaction with the sulfide **75** using BuLi/TMEDA in THF and the phenylthio group was reductively removed by Na/^{i}PrOH in THF to give the bishomoallylic alcohol **76a** (Scheme 30).

Scheme 30.



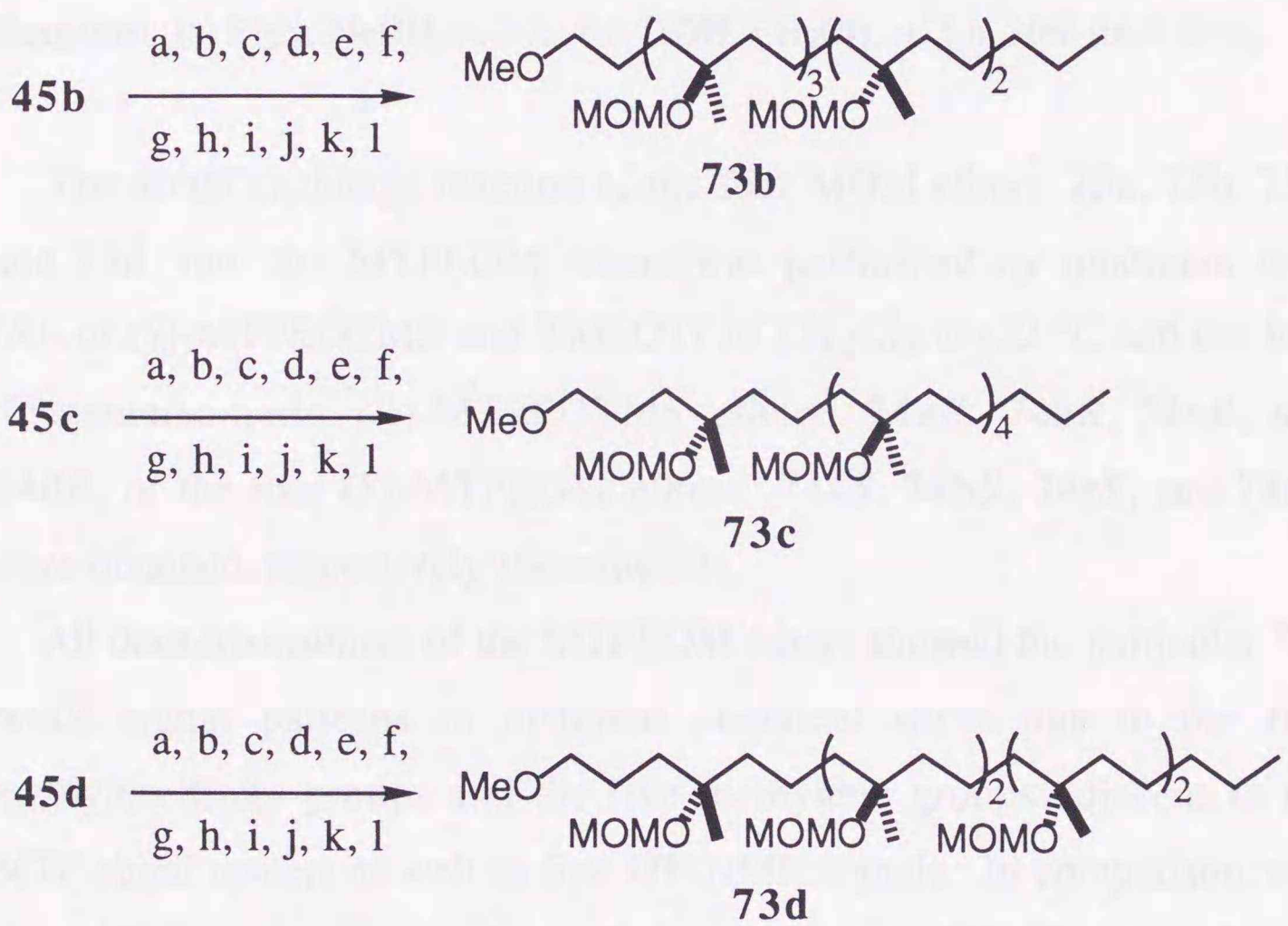
Reagents: (a) **75**, BuLi, TMEDA, THF, -22 °C, 30 min; (b) Na, ^{i}PrOH, THF, reflux, 3 h, 79% (in 2 steps); (c) $VO(acac)_2$, TBHP, MS-4A, CH_2Cl_2, rt, 4 h; (d) TFAA, Py, CH_2Cl_2, -15 °C, 30 min, 79% (in 2 steps, the ratio of β-epoxide/α-epoxide=4.5:1); (e) $LiAlH_4$, ether, reflux, 1 h, 70%; (f) CS_2, NaH, imidazole, THF then MeI, 0 °C, 1 h; (g) Bu_3SnH, AIBN, PhH, reflux, 1 h; (h) MOMCl, $^{i}Pr_2NEt$, CH_2Cl_2, rt, 14 h, 73% (in 3 steps); (i) MeI, NaH, THF, rt, 40 min, 34% (in 4 steps).

Then type B epoxidation of **76a** was performed as usual with $VO(acac)_2$, TBHP, and NaOAc in PhH and the subsequent esterification with TFAA and Py in CH_2Cl_2 furnished the epoxide **77a** stereoselectively. $LiAlH_4$ reduction of **77a** afforded the polyol with additional tertiary and secondary hydroxyl groups. Elimination of the secondary hydroxyl group was carried out by Bu_3SnH reduction of the corresponding xanthate. All hydroxyl groups were masked by MOM

ethers (**80a**) and the distal double bond was cleaved by ozone. Reductive workup with Me_2S and then with $NaBH_4$ gave a primary alcohol **72a** which was methylated to afford the methyl ether **73a**.

The diastereoisomeric polyethers, **73b**, **73c**, and **73d** were also synthesized by the same reaction sequence from **45b**, **45c**, and **45d**, respectively, as shown in Scheme 31.

Scheme 31.

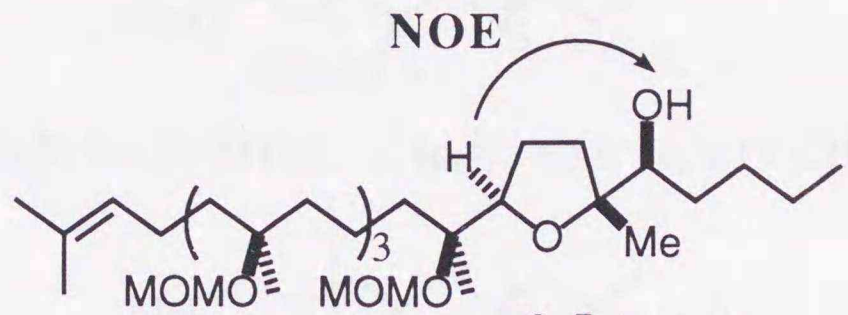


Reagents: (a) **75**, BuLi, TMEDA, THF, -22 °C, 30 min; (b) Na, ^{i}PrOH, THF, reflux, 3 h; (c) $VO(acac)_2$, TBHP, MS-4A, CH_2Cl_2, rt, 4 h; (d) TFAA, Py, CH_2Cl_2, -15 °C, 30 min; (e) $LiAlH_4$, ether, reflux, 1 h; (f) CS_2, NaH, imidazole, THF then MeI, 0 °C, 1 h; (g) Bu_3SnH, AIBN, PhH, reflux, 1 h; (h) MOMCl, $^{i}Pr_2NEt$, CH_2Cl_2, rt, 14 h; (i) MeI, NaH, THF, rt, 40 min, 13% from **45b**, 7% from **45c**, and 4% from **45d**.

The stereochemistry of the epoxide **77a** was verified by its conversion to a tetrahydrofuran derivative **81** by the successive treatment with

Et_3N/MeOH and $TsOH/CH_2Cl_2$ (Scheme 32) and observation of NOE experiment.

Scheme 32.



77a → (a, b) → **81a** → **2,5-trans**

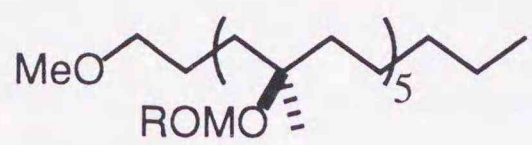
Reagents: (a) Et_3N, MeOH, rt, 1 h; (b) TsOH, CH_2Cl_2, rt, 1 h, 80% (in 2 steps).

The acetal exchange reaction of the four MOM ethers, **73a**, **73b**, **73c**, and **73d**, into the MTPEOM ethers was performed by treatment with (*R*)- or (*S*)-MTPEOTMS and TMSOTf in CH_2Cl_2 at -22 °C and the four diastereoisomeric (*R*)-MTPEOTMS ethers, **74a*R***, **74b*R***, **74c*R***, and **74d*R***, or the four (*S*)-MTPEOM ethers, **74a*S***, **74b*S***, **74c*S***, and **74d*S*** were obtained, respectively (Scheme 33).

All diastereoisomers of the MTPEOM ethers showed the particular ^{1}H-NMR signal patterns in different chemical shifts due to the five methylenedioxy groups and the five methylene groups adjacent to the MTP chiral centers as well as five ^{19}F-NMR signals. In comparison with these NMR spectra with those of the compound (**74n*R***) derived from natural gymnoprenol (*m*=2, *n*=5), only the data of **74a*S*** coincided perfectly with those of **74n*R***. In addition, the data of **74a*R*** also coincided with those of **74n*S***. The optical rotations of **74n*R***, **74a*S***, **74n*S***, and **74a*R*** were $[\alpha]_D^{26}$ +7.17° (c, 0.20, $CHCl_3$), $[\alpha]_D^{26}$ -9.58° (c, 0.13, $CHCl_3$), $[\alpha]_D^{26}$ +55.0° (c, 0.13, $CHCl_3$), and $[\alpha]_D^{26}$ -63.0° (c, 0.13, $CHCl_3$), respectively. Since **74n*R*** was possessing (*R*)-MTPEOM ethers and **74n*S*** was possessing (S)-MTPEOM ethers, **74n*R*** and **74n*S*** should

be the enantiomer of **74aS** and **74aR**, respectively.

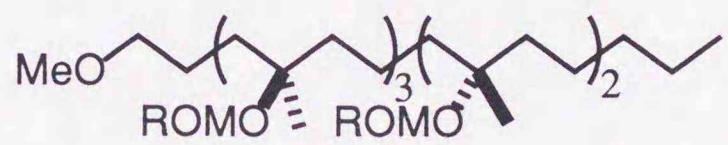
Scheme 33.

73a —a→ 

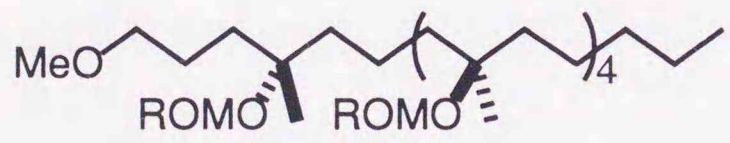
74a*R*; R=(*R*)-MTPE $[\alpha]_D^{26}$ -63.0° (c, 0.13, $CHCl_3$)

73a —b→ 

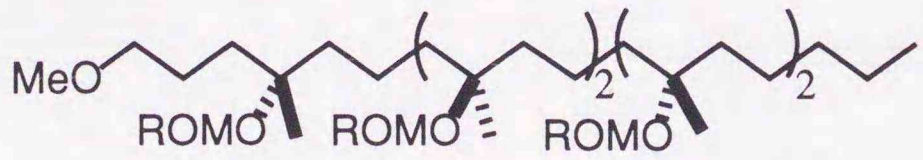
74a*S*; R=(*S*)-MTPE $[\alpha]_D^{26}$ -9.60° (c, 0.13, $CHCl_3$)

73b —a or b→ 

74b*R*; R=(*R*)-MTPE $[\alpha]_D^{25}$ -66.0° (c, 0.10, $CHCl_3$)
74b*S*; R=(*S*)-MTPE $[\alpha]_D^{25}$ -15.0° (c, 0.13, $CHCl_3$)

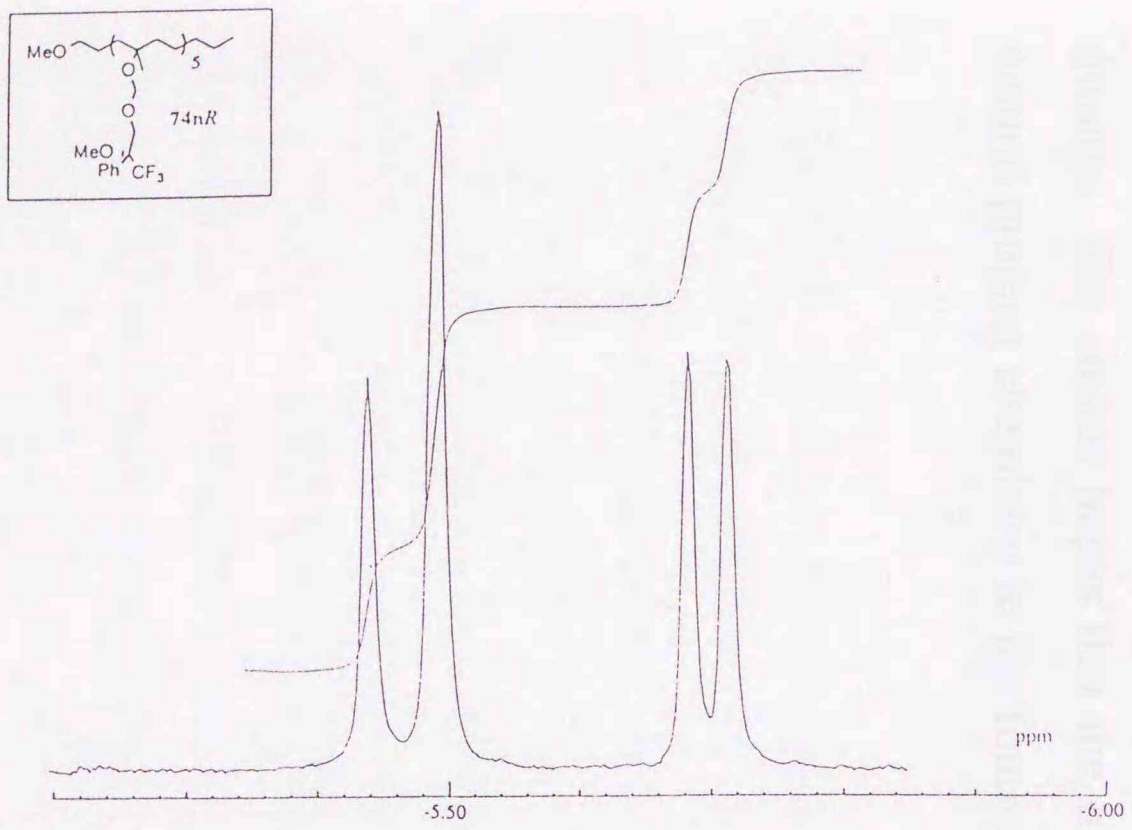
73c —a or b→ 

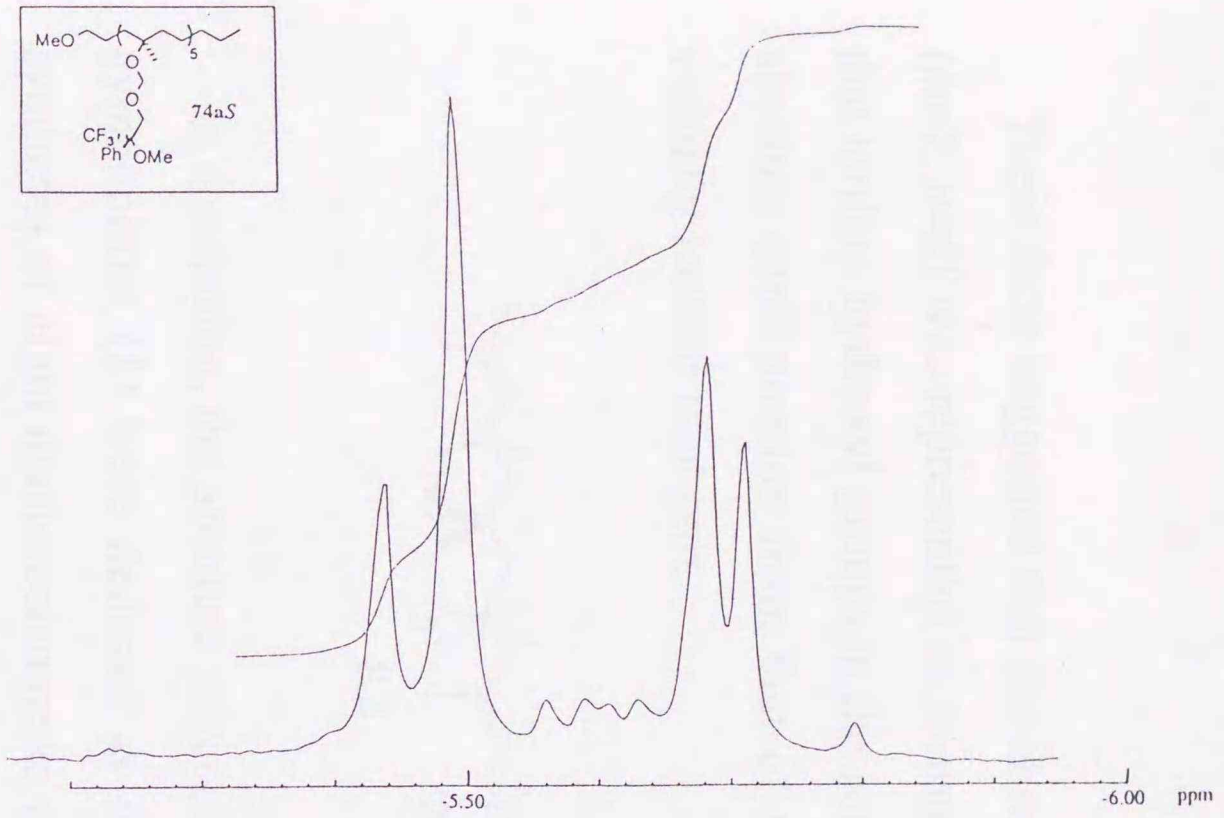
74c*R*; R=(*R*)-MTPE $[\alpha]_D^{24}$ -18.0° (c, 0.13, $CHCl_3$)
74c*S*; R=(*S*)-MTPE $[\alpha]_D^{24}$ -32.0° (c, 0.13, $CHCl_3$)

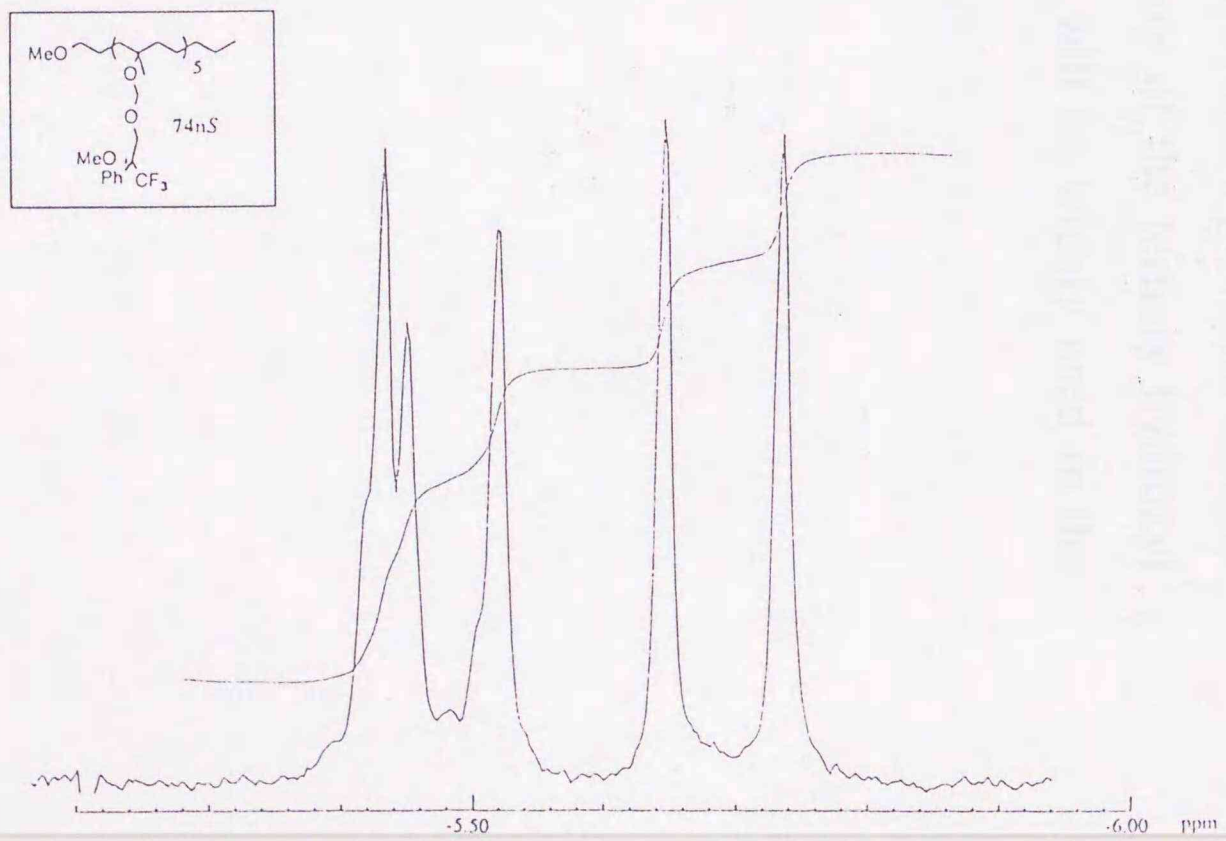
73d —a or b→ 

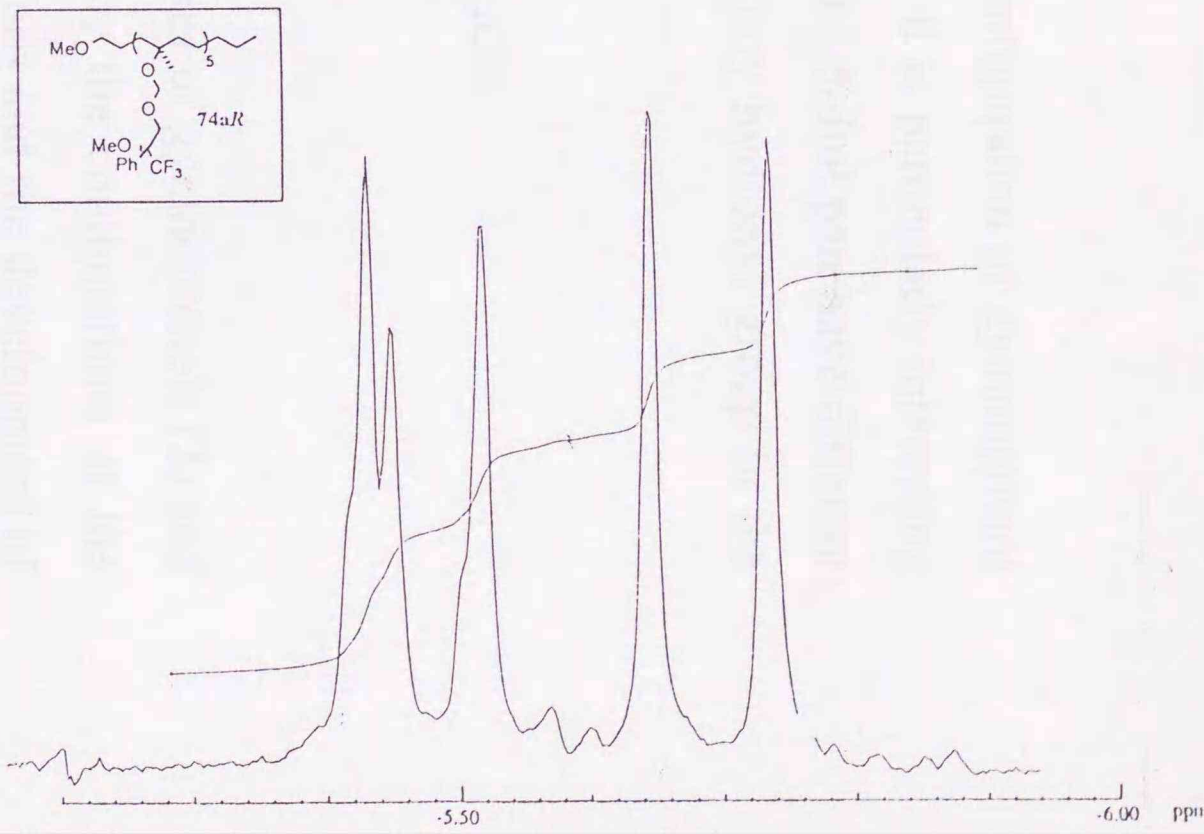
74d*R*; R=(*R*)-MTPE $[\alpha]_D^{25}$ -20.0° (c, 0.10, $CHCl_3$)
74d*S*; R=(*S*)-MTPE $[\alpha]_D^{25}$ -68.0° (c, 0.10, $CHCl_3$)

Reagents: (a) **59*R***, TMSOTf, CH_2Cl_2, -22 °C, 5 min, 18% (**74a*R***) from **73a**, 22% (**74b*R***) from **73b**, 18% (**74c*R***) from **73c**, and 22% (**74d*R***) from **73d**; (b) **59*S***, TMSOTf, CH_2Cl_2, -22 °C, 5 min, 18% (**74a*S***) from **73a**, 30% (**74b*S***) from **73b**, 18% (**74c*S***) from **73c**, and 22% (**74d*S***) from **73d**.

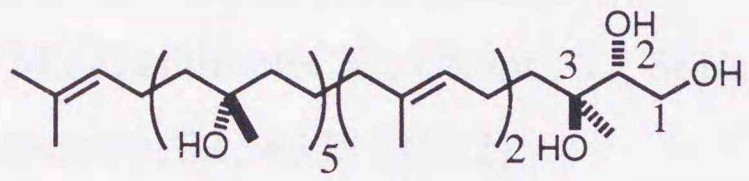

MeO
O
5
O
74n*R*
MeO
Ph
CF3
ppm
-5.50
-6.00


MeO
O
5
O
74a*S*
CF3
Ph
OMe
-5.50
-6.00
ppm


MeO
O
5
O
74n*S*
MeO
Ph
CF3
-5.50
-6.00
ppm


MeO
O
5
O
74a*R*
MeO
Ph
CF3
-5.50
-6.00
ppm

These facts suggested that the absolute configuration of gymnoprenol (m=2, n=5) was represented as formula **82**. It is particularly interesting that tertiary hydroxyl groups in the sequential 1,5-diol part have different absolute configuration from that of the tertiary hydroxyl group in the vicinally located triol part.



82

In conclusion, the absolute stereochemistries of gymnoprenols (**2**) and gymnopilins (**1**) were deduced as shown by the combinations of the syntheses of eight diastereoisomeric compounds and the development of the new chiral reagents, (*R*)-MTPEOTMS **59*R*** and (*S*)-MTPEOTMS **59*S***. The method developed in this thesis provides a powerful tool for discrimination of the absolute stereochemistry of the tertiary hydroxyl groups. The author hopes that the method will be widely used in the natural product chemistry in the future.[14)]

References and Notes

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Experimental Section

General.

Melting points are uncorrected. Optical rotations were measured on a JASCO DIP-360 digital polarimeter. IR spectra were recorded on a JASCO IR-S spectrometer on NaCl cell. ^{1}H-NMR spectra were recorded on a Hitachi R-90H (90 MHz), a R-250H (250 MHz), a JEOL Model JMN-FX-400 (400 MHz) and a Bruker RLX (400 MHz) spectrometers. Chemical shifts of ^{1}H- and ^{13}C-NMR spectra are expressed in δ values relative to the internal standard tetramethylsilane and those of ^{19}F-NMR spectra are expressed in δ values relative to the external standard freon-113. Splitting patterns are designed as "s, d, t, q, and br", these symbols indicate "singlet, doublet, triplet, quartet, and broad", respectively. Low and high resolution mass spectra were obtained on a JEOL Model JMX-DX 300, a JMS-DX303, and a 01SD-2 spectrometers. Unless otherwise noted, non-aqueous reactions were carried out under an argon atmosphere. Ether and tetrahydrofuran (THF) were distilled from sodium metal/benzophenone ketyl. Benzene (PhH), dichloromethane (CH_2Cl_2), diisopropylethylamine ($^{i}Pr_2NEt$), *N*,*N*-dimethylformamide (DMF), hexane, pyridine, *N*,*N*,*N*',*N*'-tetramethylethylenediamine (TMEDA), and triethylamine (Et_3N) were distilled from CaH. Methanol (MeOH) was distilled from $Mg(OMe)_2$. Molecular sieves 4A (MS-4A) were finely powdered and activated at 180 °C for 10 h in vacuo. All other commercial reagents were used without special purification. Analytical and preparative thin layer chromatographies were carried out by precoated silica gel plates (Macherey-Nagel DC-Fertigplatten SIL G-25 UV_{254}). Merck Kieselgel 60 Art 7734 was used for column chromatography. Medium pressure column chromatography was performed employing Lobar Grobe B

(310-25) and Li Chroprep Si 60 (40-63 mm) (Merck) equipped with FMI LAB POMP MODEL RP SY. Analytical and preparative HPLC were carried out with a JASCO UVIDEC-100V UV spectrometer and an ALTEX 156 refractive index detector.

Extraction and Isolation of Gymnoprenols.

The mushroom collected in Aomori Prefecture (1.50 kg) in 1986 was soaked in MeOH (1.50 l) and treated with K_2CO_3. The MeOH extracts were concentrated in vacuo and the residual mass was dissolved in H_2O (1.00 l) and extracted four times with EtOAc (1.00 l). The EtOAc extracts were purified roughly by silica gel column chromatography to yield 2.00 g, 4.00 g, 8.20 g, and 4.00 g of $CHCl_3$, 10% MeOH/$CHCl_3$, 20% MeOH/$CHCl_3$ or 50% MeOH/$CHCl_3$ fractions, respectively. The further elution of 20% MeOH/$CHCl_3$ gave rise to 100 mg (gymnoprenols, m=3), 5.10 g (gymnoprenols, m=2), and 2.70 g (gymnoprenols, m=1) of gymnoprenols.

(2*R*,3*S*,6*E*,10*E*,34*E*)-1,2-Diacetoxy-3,15,19,23,27,31-hexakis-(methoxymethoxy)-3,7,11,15,19,23,27,31,35-nonamethyl-hexatriaconta-6,10,34-triene (6).

A mixture of gymnoprenols **4** (m=2, n=5 and 6) (2.50 g, 3.13 mmol), Ac_2O (50 ml), and Py (50 ml) in CH_2Cl_2 (100 ml) was stirred at room temp for 6 h. The reaction was quenched by satd $NaHCO_3$ soln and the product was extracted with EtOAc. The organic layers were washed with satd citric acid soln and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification of the residual oil by silica gel column chromatography (MeOH/$CHCl_3$=1:4) gave a mixture of the gymnoprenol diacetates (2.68 g, quant).

MOMCl (2.00 ml, 26 mmol) was added to a soln of the obtained diacetate (2.68 g, 3.13 mmol) and $^iPr_2NEt$ (12 ml) in CH_2Cl_2 (60 ml) cooled at 0 °C. After stirring at room temp for 120 h, the reaction mixture was poured into satd citric acid soln and extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by

silica gel column chromatography (EtOAc/PhH=1:1.5-1:1) to yield the hexa-MOM ether **6** (*n*=5) (665 mg, 19%), the hepta-MOM ether **7** (*n*=6) (957 mg, 32%), the penta-MOM ether (*n*=5) (595 mg, 18%), and the hexa-MOM ether (*n*=6) (846 mg, 23%). The penta-MOM ether (*n*=5) and the hexa-MOM ether (*n*=6) were reacted again and yielded the hexa-MOM ether **6** (552 mg, 16%) and the hepta-MOM ether **7** (803 mg, 21%), respectively.

6: $[\alpha]_D^{22}$ +0.62° (c, 0.95, $CHCl_3$); IR (neat), 2920, 1745, 1460, 1450, 1370, 1240, 1220, 1140, 1090, 1030, and 915 cm^{-1}; ^1H-NMR (400 MHz, C_6D_6), 1.23, 1.26, 1.27, 1.28, 1.29, 1.30, 1.67, 1.70, 1.71, and 1.74 (each 3H, s, 10 x Me), 1.50-1.80 (34H, m, C_4-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, C_{28}-H_2, C_{29}-H_2, C_{30}-H_2, and C_{32}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{33}-H_2), 3.23, 3.34, 3.36, 3.36, 3.37, and 3.37 (each 3H, s, 6 x MeO), 4.27 (1H, dd, J = 11.7 and 8.8 Hz, C_1-H), 4.58 and 4.73 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.75 (1H, dd, J = 11.7 and 2.3 Hz, C_1-H), 4.73, 4.74, 4.74, 4.76, and 4.76 (each 2H, s, 5 x OCH_2O), 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{34}-H), and 5.85 (1H, dd, J = 8.8 and 2.3 Hz, C_2-H); FD-MS, *m/z* 1103 (MH^+, 5.8), 1102 (M^+, 3.2), and 1040 (M^+-$MeOCH_2OH$, 2.7).

(2*R*,3*R*)-2,3-Epoxyfarnesol (13).

To a suspension of D-(-)-DIPT (2.06 g, 8.80 mmol), $Ti(^iOPr)_4$ (2.02 ml, 6.80 mmol) and MS-4A (30.0 g) in CH_2Cl_2 (500 ml) cooled at -15 °C was added a soln of farnesol (30.0 g, 135 mmol) in CH_2Cl_2 (100 ml). After cooling to -23 °C, TBHP (50.0 ml, 200 mmol, 4.0 M in CH_2Cl_2) was added over 1 h. The reaction mixture was stirred at -23 °C for 3 h, poured into satd tartaric acid soln, stirred at room temp for 30 min, and filtered through a plug of Celite. Filtrate was concentrated

in vacuo and the residue was purified by silica gel column chromatography (EtOAc/PhH=1:4) to give nearly pure **13** (32.1 g, 100%, 88% *e.e.*) as a colorless oil: $[\alpha]_D^{22}$ +5.82° (c, 2.10, $CHCl_3$); IR (neat), 3400, 2960, 2920, 2840, 1450, 1440, 1390, 1260, 1220, 1110, 1040, and 870 cm^{-1}; ^1H-NMR (90 MHz, $CDCl_3$), 1.30, 1.60, 1.60, and 1.68 (each 3H, s, 4 x Me), 1.80-2.30 (8H, m, C_4-H_2, C_5-H_2, C_8-H_2, and C_9-H_2), 2.95 (1H, t, J = 4.9 Hz, C_2-H), 3.76 (2H, d, J = 4.9 Hz, C_1-H_2), and 5.10 (2H, bt, J = 5.9 Hz, C_6-H and C_{10}-H); EI-MS, m/z 238 (M^+, 0.12) and 220 (M^+-H_2O, 0.49); HR-EI-MS, m/z Calcd for $C_{15}H_{26}O_2$ (M^+): 238.1934. Found: 238.1953.

(2*R*,3*S*,6*E*)-3,7,11-Trimethyldodeca-6,10-diene-1,2,3-triol (14).

A soln of epoxyfarnesol (**13**) (32.1 g, 135 mmol) and mesitylenesulfonic acid (2.00 g, 10 mmol) in THF/H_2O (800/200 ml) was stirred at room temp for 48 h. The reaction mixture was neutralized with Et_3N and the solvent was removed in vacuo. The residue was purified by silica gel column chromatography (acetone/$CHCl_3$=1:4-1:1) to afford **14** (27.9 g, 81%, 85% *e.e.*) as a colorless oil: $[\alpha]_D^{22}$ +4.96° (c, 2.20, $CHCl_3$); IR (neat), 3400, 2960, 2920, 2840, 1450, 1440, 1380, 1190, 1110, 1090, 1030, 930, 890, 840, and 810 cm^{-1}; ^1H-NMR (90 MHz, $CDCl_3$), 1.25, 1.61, 1.61, and 1.67 (each 3H, s, 4 x Me), 1.80-2.40 (8H, m, C_4-H_2, C_5-H_2, C_8-H_2, and C_9-H_2), 3.75 (1H, t, J = 4.6 Hz, C_2-H), 3.78 (2H, d, J = 4.6 Hz, C_1-H_2), 5.08 (1H, bt, J = 5.6 Hz, C_6-H), and 5.13 (1H, bt, J = 5.6 Hz, C_{10}-H); EI-MS, m/z 256 (M^+, 0.06) and 238 (M^+-H_2O, 1.2); HR-EI-MS, m/z Calcd for $C_{15}H_{26}O_2$ (M^+): 238.1934. Found: 238.1952.

(2*S*,3*S*,6*E*)-1,2-Bisacetoxy-3,7,11-trimethyldodeca-6,10-diene-3-ol (15).

Ac_2O (40 ml) was added to a soln of the triol **14** (27.9 g, 109 mmol) in Py (50 ml) and CH_2Cl_2 (300 ml) at room temp. The soln was stirred at room temp for 15 h. The mixture was poured into a mixture of ice and satd $NaHCO_3$ soln and extracted with ether. The combined organic extracts were washed with 0.5 M HCl soln and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:4) yielded **15** (32.2 g, 87%) as a colorless oil: $[\alpha]_D^{24}$ +8.81° (c, 3.55, $CHCl_3$); IR (neat), 3460, 2960, 2920, 2860, 1750, 1730, 1450, 1380, 1250, 1220, 1130, 1060, 1040, 990, 950, 880, and 850 cm^{-1}; ^{1}H-NMR (90MHz, $CDCl_3$), 1.21, 1.61, 1.61, and 1.67 (each 3H, s, 4 x Me), 2.11 and 2.20 (each 3H, s, 2 x CH_3CO), 1.80-2.40 (8H, m, C_4-H_2, C_5-H_2, C_8-H_2, and C_9-H_2), 4.12 (1H, dd, J = 12.1 and 8.4 Hz, C_1-H), 4.68 (1H, dd, J = 12.1 and 2.9 Hz, C_1-H), 5.08 (1H, dd, J = 8.4 and 2.9 Hz, C_2-H), and 5.10 (2H, m, C_6-H and C_{10}-H); EI-MS, *m/z* 340 (M^+, 0.03) and 322 (M^+-H_2O, 2.0); HR-EI-MS, *m/z* Calcd for $C_{19}H_{32}O$ (M^+): 340.2251. Found: 340.2255.

(2*S*,3*S*,6*S*,7*S*)-1,2-Bisacetoxy-6,7-epoxy-3-trifluoroacetyloxy-3,7,11-trimethyldodeca-10-ene (16a) and (6*R*,7*R*)-isomer (16b).

$VO(acac)_2$ (233 mg, 0.88 mmol) was added to a mixture of the bishomoallylic alcohol **15** (15.0 g, 44 mmol), TBHP (20.0 ml, 86 mmol, 4.3 M in CH_2Cl_2), and MS-4A (45.0 g) in CH_2Cl_2 (300 ml) at room temp and the mixture was stirred at room temp for 14 h. The reaction was quenched with Et_3N and the mixture was filtered. The solvent was removed in vacuo, the residue was dissolved in satd $Na_2S_2O_3$/satd $NaHCO_3$ (2:1) soln and the product was extracted with ether. The

combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

To a mixture of the crude product, Py (20 ml), and CH_2Cl_2 (150 ml) cooled at -15 °C was added TFAA (9.30 ml, 66 mmol) dropwise over 30 min. After stirring for 10 min, H_2O was added and the product was extracted with ether. The combined extracts were washed with satd $CuSO_4$ soln, H_2O, brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:5) to yield a mixture of **16a** and **16b** and further purified by Lobar column chromatography (ether/hexane=1:1) to give **16a** (8.52 g, 43%) and its (6*R*,7*R*)-isomer (**16b**) (1.99 g, 11%).

The (6*S*,7*S*)-isomer **17a**: $[\alpha]_D^{22}$ +10.1° (c, 4.85, $CHCl_3$); IR (neat), 2960, 2920, 2840, 1790, 1755, 1450, 1370, 1220, 1160, 1125, 1070, 1050, 885, 780, and 750 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 1.24, 1.24, 1.60, and 1.67 (each 3H, s, 4 x Me), 2.05 and 2.11 (each 3H, s, 2 x CH_3CO), 1.30-1.80 (6H, m, C_4-H_2, C_5-H_2, and C_8-H_2), 1.80-2.40 (2H, m, C_9-H_2), 2.67 (1H, t, J = 6.4, C_6-H), 4.11 (1H, dd, J = 12.0 and 7.9 Hz, C_1-H), 4.43 (1H, dd, J = 12.0 and 3.1 Hz, C_1-H), 5.06 (1H, tt, J = 1.2 and 7.3 Hz, C_{10}-H), and 5.53 (1H, dd, J = 7.9 and 3.1 Hz, C_2-H); EI-MS, *m/z* 452 (M^+, 0.06); HR-EI-MS, *m/z* Calcd for $C_{21}H_{31}O_7F_3$ (M^+): 452.2022. Found: 452.2008.

The (6*R*,7*R*)-isomer **17b**: $[\alpha]_D^{22}$ +18.9° (c, 4.05, $CHCl_3$); IR (neat), 2960, 2920, 2840, 1790, 1755, 1450, 1370, 1240, 1160, 1130, 1070, 1050, 880, 780, and 740 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 1.25, 1.25, 1.61, and 1.68 (each 3H, s, 4 x Me), 2.05 and 2.11 (each 3H, s, 2 x CH_3CO), 1.30-1.80 (6H, m, C_4-H_2, C_5-H_2, and C_8-H_2), 1.80-2.40 (2H, m, C_9-H_2), 2.69 (1H, dd, J = 5.5 and 7.3 Hz, C_6-H), 4.10 (1H, dd, J = 12.2 and 7.9 Hz, C_1-H), 4.41 (1H, dd, J = 12.2 and 3.1 Hz, C_1-H), 5.07 (1H, t, J = 1.2 and 7.3 Hz, C_{10}-H), 5.06 (1H, dd, J = 7.9 and 3.1 Hz,

C_2-H); EI-MS, *m/z* 452 (M^+, 0.03); HR-EI-MS, *m/z* Calcd for $C_{21}H_{31}O_7F_3$ (M^+): 452.2022. Found: 452.2024.

(2*R*,3*S*,7*R*)-3,7,11-Trimethyldodeca-10-ene-1,2,3,7-tetraol (17a).

To a suspension of $LiAlH_4$ (4.77 g, 130 mmol) in THF (500 ml) cooled at 0 °C was added a soln of the epoxide **16a** (14.2 g, 31 mmol) in THF (100 ml). After heating at reflux temp for 1 h, the mixture was cooled to 0 °C and the excess hydrides were decomposed with EtOAc. The reaction mixture was partitioned between EtOAc and 2 M HCl soln. The combined EtOAc extracts were washed with H_2O, brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by silica gel column chromatography (acetone/$CHCl_3$=1:1-1:4) to afford **17a** (7.72 g, 90%) as a colorless oil: $[\alpha]_D^{20}$ +2.10° (c, 2.00, $CHCl_3$); IR (neat), 3320, 2960, 2900, 1455, 1375, 1340, 1300, 1260, 1180, 1150, 1090, 1030, 930, 920, 880, 840, and 810 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 1.13, 1.18, 1.62, and 1.68 (each 3H, s, 4 x Me), 1.30-1.80 (8H, m, C_4-H_2, C_5-H_2, C_6-H_2, and C_8-H_2), 1.80-2.40 (2H, m, C_9-H_2), 2.57 (2H, m, OH), 3.54 (1H, bt, *J* = 4.6 Hz, C_2-H), 3.60-3.80 (2H, m, C_1-H_2), and 5.12 (1H, t, *J* = 6.6 Hz, C_{10}-H); EI-MS, *m/z* 274 (M^+, 0.03), 256 (M^+-H_2O, 0.31), 238 (M^+-$2H_2O$, 1.7), and 220 (M^+-$3H_2O$, 1.1); HR-EI-MS, *m/z* Calcd for $C_{15}H_{30}O_4$ (M^+): 274.2145. Found: 274.2128.

(2*R*,3*S*,7*S*)-1,2-Epoxy-3,7,11-trimethyldodeca-10-ene-3,7-diol (18a).

TsCl (7.40 g, 39 mmol) was added to a soln of the tetraol **17a** (7.10 g, 26 mmol) and Py (15 ml) in CH_2Cl_2 (150 ml) cooled at 0 °C and the mixture was stirred at 0 °C for 18 h. The reaction mixture was poured into H_2O and extracted with ether. The organic layers were washed with

satd citric acid soln, brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

K_2CO_3 (8.50 g, 61 mmol) was added to a soln of crude product in MeOH (150 ml) cooled at -15 °C. After stirring for 30 min, the mixture was poured into satd citric acid soln and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (acetone/$CHCl_3$=1:9-1:4) furnished **18a** (5.10 g, 78%) as a colorless oil: $[\alpha]_D^{25}$ +11.0° (c, 2.55, $CHCl_3$); IR (neat), 3400, 2490, 2900, 1460, 1375, 1260, 1180, 1140, 1080, 1030, 980, 920, 875, 840, 920, 875, 840, 820, 780, 740, and 720 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 1.18, 1.31, 1.68, and 1.69 (each 3H, s, 4 x Me), 1.30-1.80 (8H, m, C_4-H_2, C_5-H_2, C_6-H_2, and C_8-H_2), 1.80-2.40 (2H, m, C_9-H_2), 2.60-3.00 (3H, m, C_2-H and C_1-H_2), and 5.13 (1H, bt, J = 6.8 Hz, C_{10}-H); EI-MS, m/z 256 (M^+, 0.08), 238 (M^+-H_2O, 0.40), and 220 (M^+-$2H_2O$, 1.1); HR-EI-MS, m/z Calcd for $C_{15}H_{26}O$ (M^+-H_2O): 238.1934. Found: 238.1925.

(2*R*,3*S*,7*S*)-1,2-Epoxy-3,7-bis(methoxymethoxy)-3,7,11-trimethyldodeca-10-ene (19a).

MOMCl (3.80 ml, 50 mmol) was added to a soln of **18a** (5.10 g, 20 mmol) and ^{i}Pr$_2$NEt (21 ml) in CH_2Cl_2 (150 ml) cooled at 0 °C. After stirring at room temp for 40 h, the reaction was quenched with satd citric acid soln and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:9-1:4) to give **19a** (5.53 g, 81%): $[\alpha]_D^{21}$ -2.25° (c, 2.50, $CHCl_3$); IR (neat), 2960, 2920, 1460, 1405, 1380, 1310, 1265, 1205, 1150, 1090, 1040, 920, 870, and 830 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$),

1.20, 1.20, 1.61, and 1.68 (each 3H, s, 4 x Me), 1.30-1.80 (8H, m, C_4-H_2, C_5-H_2, C_6-H_2, and C_8-H_2), 1.80-2.40 (2H, m, C_9-H_2), 2.71 (1H, dd, J = 5.0 and 4.0 Hz, C_1-H), 2.76 (1H, dd, J = 5.0 amd 3.1 Hz, C_1-H), 2.97 (1H, dd, J = 4.0 and 3.1 Hz, C_2-H), 3.37 and 3.37 (each 3H, s, 2 x MeO), 4.68 and 4.78 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.69 (2H, s, OCH_2O), and 5.10 (1H, tt, J = 1.4 and 6.1 Hz, C_{10}-H); FI-MS, m/z 344 (M^+, 33); HR-FI-MS, m/z Calcd for $C_{19}H_{36}O_5$ (M^+): 344.2572. Found: 344.2579.

(2*R*,3*S*,7*R*)-2,3-Epoxy-3,7-bis(methoxymethoxy)-3,7,11-trimethyldodeca-10-ene (19b).

The (7*R*)-isomer (**19b**) (1.44 g, 56%, in 4 steps) was synthesized similarly starting from **16b** (3.57 g, 7.90 mmol): $[\alpha]_D^{25}$ -3.68° (c, 3.90, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$), 1.20, 1.20, 1.61, and 1.68 (each 3H, s, 4 x Me), 1.30-1.80 (8H, m, C_4-H_2, C_5-H_2, C_6-H_2, and C_8-H_2), 1.80-2.40 (2H, m, C_9-H_2), 2.71 (1H, dd, J = 5.0 and 4.0 Hz, C_1-H), 2.76 (1H, dd, J = 5.0 and 3.1 Hz, C_1-H), 2.97 (1H, dd, J = 4.0 and 3.1 Hz, C_2-H), 3.37 and 3.37 (each 3H, s, 2 x MeO), 4.68 and 4.78 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.69 (2H, s, OCH_2O), and 5.10 (1H, tt, J = 1.4 and 6.1 Hz, C_{10}-H).

(2*E*,6*E*)-3,7-Dimethyl-8-pivaloyloxyocta-2,6-diene-1-ol (24).

A mixture of geranyl acetate (100 g, 510 mmol) and SeO_2 (80.0 g, 720 mmol) in EtOH (1.60 l) was heated at 85 °C for 2 h. Then the reaction mixture was cooled to 0 °C and filtered through a plug of Celite. After concentrated in vacuo, the residue was diluted with EtOH (800 ml) and ether (200 ml) and the soln was cooled to 0 °C. To the soln was added $NaBH_4$ (20.0 g, 528 mmol). After stirring for 1 h, 2 M HCl soln (200 ml) was added dropwise over 1 h, and the mixture was filtered through a plug of Celite. The filtrate was concentrated, the product was

poured into 2 M HCl soln, and extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by distillation under reduced pressure (130 °C/2 mmHg), affording **23** (60.0 g, 55%, 2 steps) as a colorless oil.

PvCl (50 ml, 406 mmol) was added to a soln of the allylic alcohol **23** (60.0 g, 283 mmol) and Py (40 ml) in CH_2Cl_2 (300 ml) cooled at 0 °C. The mixture was stirred at room temp for 14 h, poured into 0.2 M HCl soln (700 ml), and extracted with CH_2Cl_2. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

The residual oil was dissolved in MeOH (2.00 l) and ammonia gas was passed into the soln for 2 h. After stirring at room temp for 120 h, the soln was concentrated in vacuo. The crude product was purified by silica gel column chromatography (EtOAc/PhH=1:4) to yield pure **24** (52.1 g, 72%, 2 steps) as a colorless oil: IR (neat), 3300, 2940, 2840, 1725, 1710, 1480, 1450, 1400, 1360, 1280, 1225, 1150, 1030, 1000, 960, 850, and 775 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 1.21 (9H, s, Me_3CCO), 1.64, and 1.67 (each 3H, s, 2 x Me), 1.90-2.10 (4H, m, C_4-H_2 and C_5-H_2), 4.14 (2H, d, J = 6.6 Hz, C_8-H_2), 4.44 (2H, s, C_1-H_2), and 5.42 (2H, t, J = 5.9 Hz, C_3-H and C_7-H); EI-MS, m/z 254 (M^+, 0.06) and 152 (M^+-$OCOCMe_3$, 2.8); HR-EI-MS, m/z Calcd for $C_{14}H_{23}O_2$ (M^+-MeO): 223.1699. Found: 223.1699.

(2*R*,3*S*,6E)-3,7-Dimethyl-8-pivaloyloxyocta-6-ene-1,2,3-triol (26a).

To a suspension of D-(-)-DIPT (8.30 g, 35 mmol), Ti(^{i}OPr)$_4$ (8.78 ml, 30 mmol) and MS-4A (100 g) in CH_2Cl_2 cooled at -15 °C was added a soln of **24** (30.0 g, 118 mmol) in CH_2Cl_2 (100 ml). After cooling to -23 °C, TBHP (41 ml, 180 mmol, 4.3 M in CH_2Cl_2) was added dropwise

over 1 h. The reaction mixture was stirred at -23 °C for 1 h, poured into satd tartaric acid soln, stirred for 30 min at room temp, and filtered through a plug of Celite. Filtrate was concentrated in vacuo and the residue was purified by silica gel column chromatography (EtOAc/PhH=1:4) to give **25a** as a colorless oil: $[\alpha]_D^{24}$ -0.62° (c, 2.50, $CHCl_3$); IR (neat), 3400, 2960, 2920, 2880, 1730, 1485, 1460, 1400, 1390, 1370, 1285, 1155, 1035, 960, 940, 870, and 780 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 1.21 (9H, s, Me_3CCO), 1.30 and 1.64 (each 3H, s, 2 x Me), 1.80-2.20 (4H, m, C_4-H_2 and C_5-H_2), 2.94 (1H, t, J = 5.4 Hz, C_2-H), 3.74 (2H, bd, J = 5.4 Hz, C_1-H_2), 4.45 (2H, s, C_8-H_2), and 5.42 (1H, bt, J = 6.2 Hz, C_6-H); EI-MS, m/z 253 (M^+-OH, 0.08), and 169 (M^+-$OCOCMe_3$, 1.6); HR-EI-MS, m/z Calcd for $C_{15}H_{25}O_3$ (M^+-OH): 253.1805. Found: 253.1805.

A mixture of the epoxyalcohol **25a** and mesitylenesulfonic acid (2.00 g, 10 mmol) in THF/H_2O (800/200 ml) was stirred at room temp for 50 h. The reaction mixture was neutralized with Et_3N and the solvent was removed in vacuo. The residue was purified by silica gel column chromatography (acetone/$CHCl_3$=1:4-1:1) to afford **26a** (22.5 g, 66%, 86% *e.e.*, 2 steps) as a colorless oil: $[\alpha]_D^{26}$ +5.48° (c, 2.35, $CHCl_3$); IR (neat), 3400, 2960, 2920, 2860, 1730, 1480, 1460, 1400, 1370, 1285, 1230, 1160, 1080, 1030, l940, 860, and 720 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 1.21 (9H, s, Me_3CCO), 1.24 and 1.65 (each 3H, s, 2 x Me), 1.60-2.00 (2H, m, C_4-H_2), 2.00-2.40 (2H, m, C_5-H_2), 2.50-3.00 (2H, m, C_1-H_2), 3.48 (1H, t, J = 4.8 Hz, C_2-H), 4.44 (2H, s, C_8-H_2), and 5.44 (1H, t, J = 6.8 Hz, C_6-H); EI-MS, m/z 186 (M^+-Me_3CCOOH, 3.5); HR-EI-MS, m/z Calcd for $C_{10}H_{18}O_3$ (M^+-Me_3CCOOH): 186.1256. Found: 186.1241.

(2*S*,3*S*,6*E*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3-methoxy-methoxy-3,7-dimethyl-8-pivaloyloxyocta-6-ene (28a).

TBSCl (31.0 g, 206 mmol) was added to a soln of the triol **26a** (22.5 g, 78 mmol) and imidazole (32.0 g, 470 mmol) in DMF (50 ml) and stirring was continued at room temp for 12 h. The reaction mixture was diluted with H_2O and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/hexane=1:9) gave **27a** (34.2 g, 85%): $[\alpha]_D^{21}$ +8.36° (c, 2.85, $CHCl_3$); IR (neat), 3530, 2930, 2860, 1740, 1470, 1400, 1365, 1280, 1260, 1160, 1100, 1060, 1010, 965, 940, 880, 840, 810, 780, and 670 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 0.10 (12H, s, 2 x Me_2Si), 0.90 and 0.92 (9H, s, 2 x ^{t}BuSi), 1.17 and 1.66 (each 3H, s, 2 x Me), 1.21 (9H, s, Me_3CCO), 1.60-2.00 (2H, m, C_4-H_2), 2.00-2.40 (2H, m, C_5-H_2), 3.40-3.80 (3H, m, C_1-H_2 and C_2-H), 4.44 (2H, s, C_8-H_2), and 5.34 (1H, t, J = 7.0 Hz, C_9-H); EI-MS, *m/z* 517 (MH^+, 0.08), 499 (M^+-OH, 0.14), and 415 (M^+-$OCOCMe_3$, 1.7); HR-EI-MS, *m/z* Calcd for $C_{27}H_{57}O_5Si_2$ (MH^+): 517.3746. Found: 517.3783.

MOMCl (15 ml, 200 mmol) was added to a soln of the di-silyl ether **27a** (34.2 g, 66 mmol), ^{i}Pr$_2$NEt (70 ml), and DMAP (800 mg, 6.56 mmol) in CH_2Cl_2 cooled at 0 °C and the mixture was stirred at room temp for 14 h. Then the reaction mixture was poured into satd citric acid soln and the product was extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by silica gel column chromatography (ether/hexane=1:9) to yield **28a** (27.0 g, 73%): $[\alpha]_D^{23}$ +12.9° (c, 0.55, $CHCl_3$); IR (neat), 2960, 2940, 2880, 1740, 1470, 1400, 1370, 1290, 1260, 1150, 1130, 1080, 1040, 1010, 970, 940, 925, 840, 820, 790, and 750 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 0.06, 0.06, 0.08, and 0.12 (each 3H, s, 2 x Me_2Si), 0.88 and 0.90 (9H, s, 2 x ^{t}BuSi), 1.15 and 1.62 (each 3H, s, 2 x Me), 1.20 (9H, m, Me_3CCO), 1.60-2.00

(2H, m, C_4-H_2), 2.00-2.40 (2H, m, C_5-H_2), 3.36 (3H, s, MeO), 3.57 (1H, t, J = 8.8 Hz, C_2-H), 4.00 (2H, d, J = 8.8 Hz, C_1-H_2), 4.43 (2H, s, C_8-H_2), 4.66 and 4.76 (each 1H, d, J = 7.1 Hz, 2 x OCH_2O), and 5.40 (1H, t, J = 7.0 Hz, C_6-H); EI-MS, *m/z* 560 (M^+, 0.11); HR-EI-MS, *m/z* Calcd for $C_{29}H_{60}O_6Si_2$ (M^+): 560.3930. Found: 560.3936.

(2*S*,3*S*,6*E*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3-methoxymethoxy-3,7-dimethylocta-6-ene-8-ol (29a).

To a suspension of $LiAlH_4$ (1.70 g, 43 mmol) in THF (300 ml) was added a soln of **28a** (24.0 g, 43 mmol) in THF (100 ml) cooled at 0 °C over 30 min. The reaction mixture was stirred at 0 °C for 20 min and the excess hydrides were decomposed with EtOAc After filtering through a plug of Celite, the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:9-1:4) yielded **29a** (19.9 g, 97%): $[\alpha]_D^{23}$ +14.2° (c, 2.50, $CHCl_3$); IR (neat), 2960, 2920, 2860, 1475, 1465, 1390, 1380, 1360, 1255, 1130, 1080, 1030, 960, 920, 840, 820, 785, and 750 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 0.06, 0.06, 0.08, and 0.12 (each 3H, s, 2 x Me_2Si), 0.88 and 0.91 (9H, s, 2 x ^{t}BuSi), 1.15 and 1.67 (each 3H, s, 2 x Me), 1.60-2.00 (2H, m, C_4-H_2), 2.00-2.40 (2H, m, C_5-H_2), 3.00 (2H, m, C_8-H_2), 3.36 (3H, s, MeO), 3.50 (1H, dd, J = 9.0 and 7.0 Hz, C_2-H), 3.90-4.10 (2H, m, C_1-H_2), 4.65 and 4.76 (each 1H, d, J = 7.0 Hz, OCH_2O), and 5.35 (1H, t, J = 6.0 Hz, C_6-H); EI-MS, *m/z* 476 (M^+, 0.10); HR-EI-MS, *m/z* Calcd for $C_{22}H_{52}O_5Si_2$ (M^+): 476.3355. Found 476.3394.

(2*S*,3*S*,6*E*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3,7-dimethyl-3-methoxymethoxy-8-phenylthio-6-octene (30a).

A soln of the alcohol **29a** (19.9 g, 42 mmol), Ph_3P (16.4 g, 63 mmol) and CCl_4 (100 ml) in PhH (400 ml) was heated at reflux temp for 45 h.

After cooling to 0 °C, hexane (500 ml) was added and the mixture was filtered and concentrated in vacuo.

To a soln of the crude product in DMF (200 ml) cooled at 0 °C was added a soln of NaSPh, generated from PhSH (6.40 ml, 62 mmol) and NaH (1.20 g, 50 mmol) in DMF (100 ml) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min, poured into H_2O, and extracted with ether. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:9) afforded **30a** (17.9 g, 76%, 2 steps): $[\alpha]_D^{24}$ +13.8° (c, 2.55, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1470, 1460, 1440, 1390, 1380, 1360, 1250, 1130, 1070, 1030, 1005, 960, 940, 920, 840, 815, 780, and 740 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$), 0.06, 0.06, 0.06, and 0.12 (each 3H, s, 2 x Me_2Si), 0.87, and 0.91 (each 9H, s, 2 x ^{t}BuSi), 1.10, and 1.74 (each 3H, s, 2 x Me), 1.60-2.00 (2H, m, C_4-H_2), 2.00-2.40 (2H, m, C_5-H_2), 3.34 (3H, s, MeO), 3.40-3.60 (3H, m, C_2-H and C_1-H_2), 3.96 (2H, d, J = 8.8 Hz, C_8-H_2), 4.62 and 4.76 (each 1H, d, J = 7.3 Hz, OCH_2O), 5.16 (1H, t, J = 6.0 Hz, C_6-H), and 7.20-7.40 (5H, m, Ph); FI-MS, *m/z* 568 (M^+, 100); HR-FI-MS, *m/z* Calcd for $C_{30}H_{56}O_4SSi_2$ (M^+): 568.3428. Found 568.3429.

(2*R*,3*R*,6*E*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3,7-dimethyl-3-methoxymethoxy-8-phenylthio-6-octene (30b).

The (2*R*,3*R*)-isomer was synthesized from **24** (20.0 g, 79 mmol) by the same reaction sequence and 15.0 g of **30b** (34%, 7 steps) was obtained: $[\alpha]_D^{24}$ -13.8° (c, 2.90, $CHCl_3$).

(2*E*,6*E*,10*E*)-1-Acetoxy-3,7,11-trimethyl-2,6,10-dodecatriene (31).

A soln of farnesol (10.0 g, 45 mmol), Ac_2O (50 ml) and Py (50 ml) in

CH_2Cl_2 (100 ml) was stirred at room temp for 15 h. The reaction was quenched with satd $NaHCO_3$ soln cooled at 0 °C and the mixture was extracted with ether. The organic layers were washed with 0.5 M HCl soln and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:9) gave **31** (12.0 g, 100%) as a colorless oil: IR (neat), 2940, 2920, 2840, 1750, 1450, 1390, 1360, 1280, 1230, 1110, 1025, and 960 cm^{-1}; ^1H-NMR (250 MHz, $CDCl_3$), 1.59, 1.59, 1.67, and 1.69 (each 3H, s, 4 x Me), 2.04 (3H, s, CH_3CO), 1.80-2.20 (8H, m, C_4-H_2, C_5-H_2, C_8-H_2, and C_9-H_2), 4.58 (2H, d, J = 7.3 Hz, C_1-H_2), 5.20-5.40 (2H, m, C_6-H and C_{10}-H), and 5.33 (1H, t, J = 7.3 Hz, C_2-H); EI-MS, *m/z* 264 (M^+, 1.5) and 204 (M^+-AcOH, 2.7); HR-EI-MS, *m/z* Calcd for $C_{17}H_{28}O_2$ (M^+): 264.2089. Found: 264.2103.

(2*E*,6*E*,10*E*)-3,7,11-Trimethyl-12-pivaloyloxydodeca-2,6,10-triene-1-ol (32).

A mixture of SeO_2 (562 mg, 5.02 mmol), the acetate **31** (6.36 g, 24 mmol) and TBHP (7.54 ml, 79 mmol) in CH_2Cl_2 (200 ml) was stirred at 0 °C for 5 h. Then the reaction was quenched with satd $Na_2S_2O_3$ soln and the product was extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:4) to give the corresponding allylic alcohol (2.96 g, 42%) and the recovered acetate **31** (2.16 g, 34%): IR (neat), 3400, 2920, 2840, 1740, 1720, 1680, 1445, 1385, 1230, 1020, and 850 cm^{-1}; ^1H-NMR (250 MHz, $CDCl_3$), 1.59, 1.65, and 1.69 (each 3H, s, 3 x Me), 2.04 (3H, s, CH_3CO), 1.80-2.20 (8H, m, C_4-H_2, C_5-H_2, C_8-H_2, and C_9-H_2), 3.98 (2H, s, C_{12}-H_2), 4.58 (2H, d, J = 7.3 Hz, C_1-H_2), 5.10 (1H, bt, J = 6.4 Hz, C_6-H), and 5.30-5.50 (2H, m, C_2-H and C_{10}-H); EI-MS, *m/z* 280 (M^+, 0.23),

262 (M^+-H_2O, 0.18), 220 (M^+-AcOH, 1.1), and 202 (M^+-H_2O-AcOH, 1.4); HR-EI-MS, Calcd for $C_{17}H_{28}O_3$ (M^+): 280.2038. Found: 280.2055.

PvCl (3.80 ml, 31 mmol) was added to a soln of the allylic alcohol (2.84 g, 10 mmol) and Py (8.00 ml) in CH_2Cl_2 (30 ml) cooled at 0 °C. The reaction mixture was stirred at room temp for 5 h. The reaction mixture was poured into satd citric acid soln and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was dissolved in MeOH (50 ml) and ammonia gas was passed into the soln at room temp for 1 h. After stirring for 50 h, the soln was concentrated in vacuo. The crude product was purified by silica gel column chromatography (EtOAc/PhH=1:4) to yield **32** (2.96 g, 90%): IR (neat), 3400, 2960, 2900, 2840, 1730, 1670, 1485, 1465, 1460, 1400, 1390, 1370, 1285, 1230, 1155, 1105, 1030, 1005, 955, 940, 850, 775, and 745 cm^{-1}; ^1H-NMR (250 MHz, $CDCl_3$), 1.18, 1.21, and 1.21 (each 3H, s, Me_3CCO), 1.61, 1.64, and 1.68 (each 3H, s, 3 x Me), 1.80-2.20 (8H, m, C_4-H_2, C_5-H_2, C_8-H_2, and C_9-H_2), 4.16 (2H, d, J = 7.3 Hz, C_1-H_2), 4.44 (2H, s, C_{12}-H_2), 5.12 (1H, bt, J = 6.3 Hz, C_6-H), and 5.30-5.50 (2H, m, C_2-H and C_{10}-H); EI-MS, *m/z* 322 (M^+, 0.03), and 304 (M^+-H_2O, 0.14); HR-EI-MS, *m/z* Calcd for $C_{20}H_{34}O_3$ (M^+): 322.2508. Found: 322.2510.

(2*R*,3*R*,6*E*,10*E*)-2,3-Epoxy-3,7,11-trimethyl-12-pivaloyloxy-dodeca-6,10-diene-1-ol (33a).

A soln of the allylic alcohol **32** (2.50 g, 7.75 mmol) in CH_2Cl_2 (10 ml) was added to a suspension of (D)-(-)-DIPT (544 mg, 2.33 mmol), Ti(^{i}OPr)$_4$ (0.57 ml, 1.94 mmol) and MS-4A (10.0 g) in CH_2Cl_2 (40 ml) cooled at -15 °C. After cooling to -23 °C, TBHP (2.40 ml, 12 mmol, 4.8 M in CH_2Cl_2) was added dropwise over 1 h. The reaction mixture was stirred at -23 °C for 1 h and the reaction was quenched with satd

tartaric acid soln. After stirring at room temp for 30 min, the mixture was filtered through a plug of Celite. The mixture was concentrated in vacuo. The residual oil was purified by silica gel column chromatography (EtOAc/PhH=1:4) to yield **33a** (2.62 g, 100%, 88% *e.e.*): $[\alpha]_D^{22}$ +4.19° (c, 1.90, $CHCl_3$); IR (neat), 3400, 2980, 2960, 2920, 2880, 1730, 1485, 1460, 1400, 1390, 1370, 1285, 1230, 1160, 1110, 1035, 960, 940, 870, and 780 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 1.18, 1.21, and 1.21 (each 3H, s, Me_3CCO), 1.30, 1.61, and 1.63 (each 3H, s, 3 x Me), 1.60-2.00 (2H, m, C_4-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_9-H_2), 2.98 (1H, dd, J = 6.7 and 4.6 Hz, C_2-H), 3.69 (1H, dd, J = 6.7 and 12.2 Hz, C_1-H), 3.84 (1H, dd, J = 4.6 and 12.2 Hz, C_1-H), 4.42 (2H, s, C_{12}-H_2), 5.12 (1H, bt, J = 7.3 Hz, C_6-H), and 5.42 (1H, bt, J = 5.9 Hz, C_{10}-H); EI-MS, *m/z* 338 (M^+, 0.12), 320 (M^+-H_2O, 0.04), 307 (M^+-CH_2OH, 0.18) and 236 (M^+-Me_3CCOOH, 1.1); HR-EI-MS, *m/z* Calcd for $C_{20}H_{34}O_4$ (M^+): 338.2457. Found: 338.2480.

(2*E*,6*E*,10*S*,11*R*)-2,6,10-Trimethyl-1-pivaloyloxydodeca-2,6-diene-10,11,12-triol (34a).

A soln of the epoxyalcohol **33a** (2.62 g, 7.75 mmol) and mesitylenesulfonic acid (100 mg, 0.42 mmol) in THF/H_2O (50/12 ml) was stirred at room temp for 40 h. The mixture was neutralized with Et_3N and the solvent was removed in vacuo. The residual oil was purified by silica gel column chromatography (acetone/$CHCl_3$=1:4-1:1) to afford **34a** (2.46 g, 89%): $[\alpha]_D^{20}$ +3.70° (c, 2.50, $CHCl_3$); IR (neat), 3400, 2960, 2900, 1720, 1480, 1460, 1400, 1370, 1230, 1160, 1090, 1030, 955, 940, 880, 850, and 775 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 1.16, 1.20, and 1.20 (each 3H, s, Me_3CCO), 1.24, 1.61, and 1.61 (each 3H, s, 3 x Me), 1.40-1.80 (2H, m, C_4-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_9-H_2), 3.48 (1H, t, J = 4.9 Hz, C_2-H), 3.78 (2H, d, J = 4.9 Hz, C_1-H_2), 4.43 (2H,

s, C_{12}-H_2), 5.13 (1H, bt, J = 6.7 Hz, C_6-H), and 5.40 (1H, bt, J = 6.7 Hz, C_9-H); EI-MS, m/z 357 (MH^+, 0.08), 356 (M^+, 0.04), and 303 (M^+-$3H_2O$, 0.31); HR-EI-MS, m/z Calcd for $C_{20}H_{36}O_5$ (M^+): 356.2563. Found: 356.2537.

(2*R*,3*S*,6*E*,10*E*)-1,2,3-Tris(methoymethoy)-3,7,11-trimethyl-12-pivaloyloxydodeca-6,10-diene (35a).

MOMCl (3.20 ml, 42 mmol) was added to a soln of the triol **34a** (2.46 g, 6.90 mmol) and $^iPr_2NEt$ (10 ml) in CH_2Cl_2 (25 ml) cooled at 0 °C and the reaction mixture was stirred at room temp for 40 h. The reaction was quenched with satd citric acid soln and the mixture was extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:5) gave **35a** (2.65 g, 79%): $[\alpha]_D^{22}$ -15.0° (c, 2.35, $CHCl_3$); IR (neat), 3000, 2940, 2820, 1735, 1485, 1470, 1460, 1400, 1380, 1285, 1215, 1150, 1110, 1050, 1030, 920, and 860 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 1.18, 1.21, and 1.21 (each 3H, s, Me_3CCO), 1.25, 1.62, and 1.64 (each 3H, s, 3 x Me), 1.40-1.80 (2H, m, C_9-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_9-H_2), 3.36, 3.34, and 3.39 (each 3H, s, 3 x MeO), 3.62 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 3.72 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 3.90 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.42 (2H, s, C_{12}-H_2), 4.63 (2H, s, OCH_2O), 4.67 and 4.29 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.68 and 4.91 (each 1H, d, J = 6.7 Hz, OCH_2O), 5.10 (1H, t, J = 6.1 Hz, C_6-H), and 5.41 (1H, t, J = 6.1 Hz, C_{10}-H); EI-MS, m/z 457 (MH^+-MeOH, 0.03); HR-EI-MS, m/z Calcd for $C_{25}H_{45}O_7$ (MH^+-MeOH): 457.3165. Found: 457.3158.

(2*R*,3*S*,6*E*,10*E*)-1,2,3-Tris(methoxymethoxy)-3,7,11-trimethyldodeca-6,10-diene-12-ol (36a).

The pivalate **35a** (2.65 g, 5.44 mmol) in THF (10 ml) was added dropwise to a suspension of $LiAlH_4$ (207 mg, 5.45 mmol) in THF (30.0 ml) cooled at 0 °C over 30 min. The reaction mixture was stirred at 0 °C for 20 min and the excess hydrides were decomposed with EtOAc After filtration through a plug of Celite, the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:9-1:4) gave **36a** (1.93 g, 88%): $[\alpha]_D^{22}$ -18.9° (c, 2.10, $CHCl_3$); IR (neat), 3400, 2960, 2920, 1450, 1400, 1380, 1350, 1320, 1210, 1110, 1030, 920, 860, and 740 cm^{-1}; ^1H-NMR (250 MHz, $CDCl_3$), 1.24, 1.60, and 1.65 (each 3H, s, 3 x Me), 1.40-1.80 (2H, m, C_4-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_9-H_2), 3.36, 3.37, and 3.40 (each 3H, s, 3 x MeO), 3.62 (1H, dd, J = 6.7 and 10.4 Hz, C_1-H), 3.72 (1H, dd, J = 6.7 and 1.8 Hz, C_2-H), 3.90 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 3.97 (2H, s, C_{12}-H_2), 4.63 (2H, s, OCH_2O), 4.67 and 4.79 (each 1H, d, J = 6.8 Hz, OCH_2O), 4.68 and 4.95 (each 1H, d, J = 6.8 Hz, OCH_2O), 5.10 (1H, t, J = 6.7 Hz, C_6-H), and 5.38 (1H, t, J = 6.7 Hz, C_{10}-H); EI-MS, *m/z* 341 (MH^+-2MeOH, 0.08); HR-EI-MS, *m/z* Calcd for $C_{19}H_{33}O_5$ (M^+-2MeOH): 341.2328. Found: 341.2328.

(2*R*,3*S*,6*E*,10*E*)-12-Phenylthio-1,2,3-tris(methoxymethoxy)-3,7,11-trimethyldodeca-6,10-diene (37a).

A soln of the alcohol **36a** (1.93 g, 4.77 mmol), Ph_3P (1.88 g, 7.16 mmol) and CCl_4 (40 ml) in PhH (60 ml) was heated at reflux temp for 15 h. After cooling to 0 °C, hexane (100 ml) was added and the reaction mixture was filtered and concentrated in vacuo.

To a solution of the crude product in DMF (40 ml) cooled at 0 °C was added a soln of NaSPh, generated from PhSH (0.73 ml, 7.16 mmol) and NaH (149 mg, 6.20 mmol) in DMF (10 ml) cooled at 0 °C. After stirring at 0 °C for 10 min, H_2O was added and the product was extracted with

ether. The organic soln was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:9) to yield **37a** (2.01 g, 85%): $[\alpha]_D^{22}$ -15.9° (c, 2.65, $CHCl_3$); IR (neat), 2920, 2880, 1585, 1490, 1440, 1380, 1320, 1310, 1210, 1150, 1110, 1030, 920, 870, 750, and 690 cm^{-1}; ^1H-NMR (250 MHz, $CDCl_3$), 1.23, 1.56, and 1.72 (each 3H, s, 3 x Me), 1.40-1.80 (2H, m, C_4-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_9-H_2), 3.35, 3.36, and 3.39 (each 3H, s, 3 x MeO), 3.47 (2H, s, C_{12}-H_2), 3.62 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 3.71 (1H, dd, J = 7.3 and 1.2 Hz, C_2-H), 3.90 (1H, dd, J = 10.4 and 1.2 Hz, C_1-H), 4.66 and 4.78 (each 1H, d, J = 6.7 Hz, OCH_2O), 4.68 and 4.90 (each 1H, d, J = 6.7 Hz, OCH_2O), 5.03 (1H, t, J = 6.7 Hz, C_6-H), and 5.20 (1H, t, J = 6.7 Hz, C_9-H); FI-MS, *m/z* 568 (M^+, 100); HR-FI-MS, *m/z* Calcd for $C_{30}H_{56}O_4SSi_2$ (M^+): 568.3428. Found: 568.3429.

(2*R*,3*S*,6*E*,10*E*)-12-Phenylthio-1,2,3-tris(methoxymethoxy)-3,7,11-trimethyldodeca-6,10-diene (37b).

The (2*R*,3*S*)-isomer was synthesized from the allylic alcohol **32** (1.50 g, 4.65 mmol) by the same reaction sequence to yield **37b** (966 mg, 42%, 6 steps): $[\alpha]_D^{23}$+15.8° (c, 3.10, $CHCl_3$).

1-Phenylthio-2-methyl-2-heptene (75).

The sulfide **75** (6.61 g, 77%, 2 steps) was prepared by the substitution reaction of the corresponding chloride starting from 2-methyl-2-heptene-1-ol (5.00 g, 39 mmol) as the same reaction mentioned before : IR (neat), 3020, 2940, 2920, 2840, 1585, 1575, 1480, 1465, 1455, 1440, 1380, 1220, 1090, 1065, 1025, 740, and 680 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 0.85 (3H, t, J = 6.7 Hz, C_7-H_3), 1.00-1.60 (4H, m, C_5-H_2 and C_6-H_2), 1.80-2.00 (2H, m, C_4-H_2), 3.37 (2H, s, C_1-H_2), and 7.00-8.00 (5H, m,

Ph); EI-MS, *m/z* 220 (M^+, 14); HR-EI-MS, *m/z* Calcd for $C_{14}H_{20}S$ 220.1297 (M^+): 220.1286. Found: 220.1297.

(*2S*,*3S*,*6E*,*10R*,*11S*,*15S*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3,11,15-tris-(methoxymethoxy)-3,7,11,15,19-pentamethylicosa-6,18-diene-10-ol (38a).

BuLi (13 ml, 20 mmol, 1.5 M in hexane) was added to a soln of the sulfide **30a** (7.45 g, 13 mmol), the epoxide **19a** (4.53 g, 13 mmol) and TMEDA (20 ml) in THF (110 ml) cooled at -30° C. After stirring at -30 °C for 30 min, the reaction mixture was poured into H_2O and the product was extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH= 1:20-1:10) yielded a coupling product.

Na metal (5.90 g) was added to a soln of the coupling product and ^{i}PrOH (150 ml) in THF (200 ml) at reflux temp. After heating for 4 h, the mixture was concentrated in vacuo, poured into satd citric acid soln, and extracted with ether. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (EtOAc/PhH=1:20-1:10) to afford **38a** (7.74 g, 74%, 2 steps): $[\alpha]_D^{24}$ +18.1° (c, 1.85, $CHCl_3$); IR (neat), 3480, 2960, 2920, 2840, 1470, 1460, 1380, 1360, 1350, 1310, 1250, 1210, 1145, 1130, 1090, 1070, 1030, 960, 920, 840, 820, 785, and 750 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.14, 0.14, 0.26, and 0.31 (each 3H, s, 2 x Me_2Si), 1.00 and 1.01 (each 9H, s, 2 x ^{t}BuSi), 1.15, 1.20, 1.23, 1.62, 1.70, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (12H, m, C_4-H_2, C_9-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.00 (1H, d, J = 4.9 Hz, OH), 3.13, 3.25, and 3.29 (each 3H, s, 3 x MeO), 3.57 (1H, ddd,

J = 1.2, 1.8, and 4.9 Hz, C_{10}-H), 3.67 (1H, dd, J = 6.7 and 10.4 Hz, C_1-H), 3.87 (1H, dd, J = 6.7 and 1.2 Hz, C_2-H), 4.23 (1H, dd, J = 10.4 and 1.2 Hz, C_1-H), 4.51 and 4.59 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.60-4.80 (4H, s, OCH_2O), 5.25 (1H, t, J = 7.3 Hz, C_{18}-H), and 5.43 (1H, t, J = 7.3 Hz, C_7-H); FI-MS, *m/z* 805 (MH^+, 57), 804 (M^+, 34), 774 (MH^+-MeO, 40), 743 (MH^+-2MeO, 36), and 711 (MH^+-2MeO-MeOH, 18); HR-FI-MS, *m/z* Calcd for $C_{43}H_{89}O_9Si_2$ (MH^+): 805.6045. Found: 805.6080.

(2*S*,3*S*,7*S*,10*R*,11*S*,15*S*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3,11,15-tris(methoxymethoxy)-3,7,11,15,19-pentamethylicosa-18-ene-7,10-diol (41a).

$VO(acac)_2$ (90 mg, 0.34 mmol) was added to a mixture of the bishomoallylic alcohol **38a** (3.00 g, 3.73 mmol), TBHP (6.00 ml, 26 mmol, in CH_2Cl_2) and NaOAc (900 mg, 11 mmol) in PhH (90 ml) heated at 50 °C and heating was continued for 1 h. The reaction mixture was poured into satd $Na_2S_2O_3$/$NaHCO_3$ (200/100 ml) soln and the product was extracted with ether. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

A soln of the crude product and Py (10 ml) in CH_2Cl_2 (30 ml) was cooled at -15 °C, into which TFAA (1.20 ml, 8.50 mmol) was added dropwise over 15 min. After stirring at -15 °C for 10 min, H_2O was added and the mixture was extracted with ether. The crude extracts were washed with satd $CuSO_4$ soln , H_2O and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (ether/hexane=1:1) to yield the mixture of **39a** and **39b** and further purified by Lobar column chromatography (ether/hexane=1:1) to give the *anti*-epoxide **39a** (1.37 g, 40%) and the *syn*-epoxide **39b** (284 mg, 8%).

39a: $[\alpha]_D^{22}$ +2.99° (c, 2.50, $CHCl_3$); IR (neat), 2960, 2920, 2850, 1790,

1470, 1380, 1360, 1340, 1250, 1220, 1150, 1090, 1070, 1030, 960, 920, 840, 780, and 730 cm^{-1}; ^1H-NMR (250 MHz, $CDCl_3$), 0.06, 0.05, 0.08, and 0.12 (each 3H, s, 2 x Me_2Si), 0.88 and 0.90 (9H, s, 2 x ^tBuSi), 1.15, 1.19, 1.24, 1.25, 1.61, and 1.68 (each 3H, s, 6 x Me), 1.40-2.20 (16H, m, C_4-H_2, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 2.68 (1H, t, J = 6.1 Hz, C_6-H), 3.36 (1H, dd, J = 6.7 and 10.4 Hz, C_1-H), 3.87 (1H, dd, J = 6.7 and 1.2 Hz, C_2-H), 4.23 (1H, dd, J = 10.4 and 1.2 Hz, C_1-H), 4.51 and 4.59 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.60-4.80 (4H, m, OCH_2O), 5.25 (1H, t, J = 7.3 Hz, C_{18}-H), and 5.43 (1H, t, J = 7.3 Hz, C_7-H); FI-MS, m/z 917 (MH^+, 24), 885 (MH^+-MeOH, 20), and 855 (MH^+-$MeOCH_2OH$, 26); HR-FAB-MS, m/z Calcd for $C_{41}H_{76}O_7F_3Si_2$ (M^+-$MeOCH_2OH$-$MeOCH_2$): 793.5082. Found: 793.5037.

To a suspension of $LiAlH_4$ (580 mg, 15 mmol) in ether (100 ml) cooled at 0 °C was added a soln of the epoxide **39a** (1.37 g, 1.50 mmol) in ether (30 ml). After heating at reflux temp for 2 h, the reaction mixture was cooled to 0 °C and the excess hydrides were decomposed with EtOAc. After filteration through a plug of Celite, the mixture was concentrated in vacuo. The residual oil was purified by silica gel column chromatography (EtOAc/PhH=1:4-1:1.5) to give the *anti*-diol **41a** (1.11 g, 89%): $[\alpha]_D^{20}$ +13.0° (c, 2.85, $CHCl_3$); IR (neat), 2960, 2920, 2860, 1475, 1465, 1380, 1360, 1260, 1150, 1130, 1090, 1080, 1040, 970, 920, 840, 820, 790, and 750 cm^{-1}; ^1H-NMR (250 MHz, $CDCl_3$), 0.06, 0.06, 0.09, 0.12 (each 3H, s, 2 x Me_2Si), 0.88 and 0.91 (9H, s, 2 x ^tBuSi), 1.13, 1.17, 1.20, 1.20, 1.61, and 1.68 (each 3H, s, 6 x Me), 1.40-2.20 (18H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 3.36, 3.37, and 3.40 (each 3H, s, 3 x MeO), 3.48 (1H, dd, J = 6.7 and 10.4 Hz, C_1-H), 3.59 (1H, dd, J = 6.7 and 1.8 Hz, C_2-H), 3.98 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.60-4.80

(6H, m, 3 x OCH_2O), and 5.10 (1H, t, C_3-H); FI-MS, *m/z* 823 (MH^+, 100), and 822 (M^+, 75); HR-FI-MS, *m/z* Calcd for $C_{43}H_{90}O_{10}Si_2$ (M^+): 822.6073. Found: 822.6103.

(2*S*,3*S*,7*S*,11*S*,15*S*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3,11,15-tris(methoxymethoxy)-3,7,11,15,19-pentamethylicosa-18-ene-7-ol (42a).

To a suspension of NaH (80 mg, 3.33 mmol) and imidazole (8 mg, 0.12 mmol) in THF (10 ml) cooled at 0 °C was added a soln of the diol **36a** (1.03 g, 1.12 mmol) in THF (5.0 ml). After stirring at 0 °C for 30 min, CS_2 (0.40 ml, 6.65 mmol) was added and stirring was continued for 30 min. MeI (0.42 ml, 6.75 mmol) was added and the mixture was stirred for another 1 h. The reaction mixture was poured into satd citric acid soln and the product was extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

Bu_3SnH (0.40 ml, 1.47 mmol) was added to a mixture of the crude product and AIBN (18 mg, 0.11 mmol) in PhH (100 ml) at reflux temp. After heating for 45 min, the mixture was concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:5-3:10) gave **42a** (865 mg, 86%): $[\alpha]_D^{19}$ +9.08° (c, 2.00, $CHCl_3$); IR (neat), 3500, 2980, 2920, 2880, 1480, 1470, 1385, 1370, 1260, 1150, 1140, 1100, 1080, 1040, 970, 930, 845, 820, 790, and 750 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.03, 0.04, 0.06, and 0.10 (each 3H, s, 2 x Me_2Si), 0.85 and 0.88 (9H, s, 2 x ^{t}BuSi), 1.11, 1.14, 1.16, 1.17, 1.58, and 1.66 (each 3H, s, 6 x Me), 1.40-2.20 (20H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 3.34, 3.34, and 3.35 (each 3H, s, 3 x MeO), 3.47 (1H, dd, J = 6.7 and 10.4 Hz, C_1-H), 3.57 (1H, dd, J = 6.7 and 1.2 Hz, C_2-H), 3.96 (1H, dd, J = 10.4

and 1.2 Hz, C_1-H), 4.64 and 4.72 (each 1H, d, OCH_2O), 4.65 and 4.66 (each 1H, d, OCH_2O), 4.71 (2H, s, OCH_2O), and 5.08 (1H, t, J = 7.0 Hz, C_{18}-H); FI-MS, *m/z* 807 (MH^+, 43), and 806 (M^+, 17); HR-FI-MS, *m/z* Calcd for $C_{43}H_{91}O_9Si_2$ (MH^+): 807.6226. Found: 807.6235.

(2*S*,3*S*,7*S*,11*S*,15*S*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3,7,11,15-tetrakis(methoxymethoxy)-3,7,11,15,19-pentamethylicosa-18-ene (43a).

MOMCl (0.21 ml, 2.76 mmol) was added to a soln of the alcohol **42a** (865 mg, 1.07 mmol) and $^iPr_2NEt$ (1.00 ml) in CH_2Cl_2 (10 ml) cooled at 0 °C and the reaction mixture was stirred at room temp for 14 h. The reaction was quenched with satd citric acid soln and the product was extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by silica gel column chromatography (EtOAc/PhH=1:5) to yield **43a** (862 mg, 95%): $[\alpha]_D^{20}$ +8.07° (c, 2.35, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1475, 1465, 1380, 1365, 1310, 1255, 1210, 1150, 1130, 1090, 1080, 1060, 965, 920, 840, 820, 785, and 750 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.11, 0.11, 0.29, and 0.35 (each 3H, s, 2 x Me_2Si), 0.99 and 1.05 (9H, s, 2 x ^{t}BuSi), 1.08, 1.23, 1.23, 1.24, 1.61, and 1.69 (each 3H, s, 6 x Me), 1.40-2.20 (20H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 3.28, 3.28, 3.28, and 3.30 (each 3H, s, 4 x MeO), 3.68 (1H, dd, J = 6.7 and 10.4 Hz, C_1-H), 3.89 (1H, dd, J = 6.7 and 1.8 Hz, C_2-H), 4.23 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.71, 4.68 and 4.70 (each 2H, s, 3 x OCH_2O), 4.60-4.80 (1H, m, OCH_2O), and 5.25 (1H, t, J = 7.3 Hz, C_{18}-H); FI-MS, *m/z* 851 (MH^+, 15) and 757 (M^+-3MeO, 13); HR-FAB-MS, *m/z* Calcd for $C_{39}H_{80}O_{10}Si$ (MH^+-Si(Me)$_2$^{t}Bu): 736.5521. Found: 736.5513.

(2*R*,3*S*,7*S*,11*S*,15*S*)-1,2-Epoxy-3,7,11,15-tetrakis-(methoxy-methoxy)-3,7,11,15,19-pentamethylicosa-18-ene (45a).

TBAF (7.10 ml, 7.05 mmol) was added to a soln of the di-silyl ether **43a** (2.00 g, 2.35 mmol) in THF (70 ml) at reflux temp and heating was continued for 1 h. After cooling to room temp, the soln was concentrated in vacuo. Purification by silica gel column chromatography (acetone/$CHCl_3$=1:2-1:1) gave **45a** (1.50 g, 100%) as a colorless oil: $[\alpha]_D^{22}$ +3.88° (c, 2.00, $CHCl_3$); IR (neat), 3420, 3000, 2900, 1470, 1410, 1385, 1350, 1310, 1270, 1215, 1150, 1100, 1040, 920, 870, and 740 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 1.170, 1.25, 1.25, 1.26, 1.66, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (20H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 3.12, 3.33, 3.34, and 3.34 (each 3H, s, 4 x MeO), 3.60-4.00 (3H, m, C_1-H_2 and C_2-H), 4.54, 4.71, 4.72, and 4.73 (each 2H, s, 4 x OCH_2O), and 5.29 (1H, t, J = 7.3 Hz, C_{18}-H); FAB-MS, *m/z* 604 (M^+-H_2O, 5.91).

TsCl (672 mg, 3.52 mmol) was added to a soln of the diol **45a** (1.50 g, 2.35 mmol) and Py (5.00 ml) in CH_2Cl_2 (60 ml) cooled at 0 °C. After stirring at 0 °C for 40 h, the reaction mixture was poured into satd citric acid soln and extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

K_2CO_3 (3.00 g, 22 mmol) was added to a soln of the product in MeOH (80 ml) at room temp. After stirring at room temp for 1h, the reaction mixture was poured into satd citric acid soln and extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by silica gel column chromatography (EtOAc/PhH=1:4-1:2) to give **45a** (1.00 g, 71%, 3 steps) as a colorless oil: $[\alpha]_D^{22}$ -0.77° (c, 2.75, $CHCl_3$); IR (neat), 2960, 2920, 2800, 1470, 1460, 1410, 1380, 1310, 1270, 1210, 1150, 1100, 1040, 920, and 830 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 1.17,

1.25, 1.26, 1.26, 1.66, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (20H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 2.39 (1H, t, J = 4.9 Hz, C_1-H), 2.56 (1H, dd, J = 4.9 and 2.5 Hz, C_2-H), 2.87 (1H, t, J = 4.9 and 2.5 Hz, C_1-H), 3.26, 3.33, 3.34, and 3.34 (each 3H, s, 4 x MeO), 4.65 and 4.79 (each 1H, d, OCH_2O), 4.70-4.80 (6H, m, 3 x OCH_2O), and 5.29 (1H, t, J = 7.3 Hz, C_{18}-H); EI-MS, m/z 510 (M^+-$MeOCH_2OH$-MeOH, 0.34), and 480 (M^+-2$MeOCH_2OH$, 0.65); FI-MS, m/z 605 (MH^+, 66), and 604 (M^+, 22); HR-EI-MS, m/z Calcd for $C_{30}H_{54}O_6$ (M^+-$MeOCH_2OH$-MeOH): 510.3920. Found: 510.3923.

(2*S*,3*R*,7*S*,11*S*,15*S*)-1,2-Epoxy-3,7,11,15-tetrakis(methoxymethoxy)-3,7,11,15,19-pentamethylicosa-18-ene (45b).

The (2*S*,3*R*)-isomer was prepared by the same reaction sequence from the sulfide **30b** (3.37 g, 5.92 mmol) and the epoxide **19a** (1.70 g, 4.93 mmol) to afford **45b** (266 mg, 9%, 11 steps): $[\alpha]_D^{22}$ +2.47° (c, 2.50, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.17, 1.25, 1.26, 1.26, 1.66, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (20H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 2.38 (1H, dd, J = 4.9 and 3.7 Hz, C_1-H), 2.56 (1H, dd, J = 4.9 and 4.1 Hz, C_1-H), 2.88 (1H, dd, J = 4.1 and 3.7 Hz, C_2-H), 3.26, 3.33, 3.35, and 3.35 (each 3H, s, 4 x MeO), 4.65 and 4.74 (1H, d, J = 7.3 Hz, OCH_2O), 4.73 (6H, s, 3 x OCH_2O), and 5.29 (1H, t, J = 7.3 Hz, C_{18}-H).

(2*R*,3*S*,7*S*,11*S*,15*R*)-1,2-Epoxy-3,7,11,15-tetrakis(methoxymethoxy)-3,7,11,15,19-pentamethylicosa-18-ene (45c).

The (15*R*)-isomer was synthesized by the same reaction sequence from the sulfide **30a** (216 mg, 0.38 mmol) and the epoxide **19b** (109 mg,

0.32 mmol) to give **45c** (18 mg, 9%, 11 steps): $[\alpha]_D^{24}$ -1.74° (c, 2.35, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.17, 1.25, 1.26, 1.26, 1.66, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (20H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 2.39 (1H, t, J = 4.9 Hz, C_1-H), 2.56 (1H, dd, J = 4.9 and 2.5 Hz, C_1-H), 2.87 (1H, t, J = 2.5 Hz, C_2-H), 3.26, 3.33, 3.34, and 3.34 (each 3H, s, 4 x MeO), 4.65 and 4.79 (each 1H, d, OCH_2O), 4.70-4.80 (6H, m, 3 x OCH_2O), and 5.29 (1H, t, J = 7.3 Hz, C_{18}-H).

(2*S*,3*R*,7*S*,11*S*,15*R*)-1,2-Epoxy-3,7,11,15-tetrakis(methoxymethoxy)-3,7,11,15,19-pentamethylicosa-18-ene (45d).

By the same reaction sequence, the (2*S*,3*R*,15*R*)-isomer (**45d**) (18 mg, 9%, 11 steps) was prepared from the sulfide **30b** (216 mg, 0.38 mmol) and the epoxide **19b** (109 mg, 0.32 mmol): $[\alpha]_D^{25}$ +0.97° (c, 1.55, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.170, 1.26, 1.26, 1.26, 1.66, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (20H, m, C_4-H_2, C_5-H_2, C_6-H_2, C_8-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (2H, m, C_{17}-H_2), 2.38 (1H, dd, J = 4.9 and 1.2 Hz, C_1-H), 2.55 (1H, dd, J = 4.9 and 1.8 Hz, C_1-H), 2.87 (1H, dd, J = 1.2 and 1.8 Hz, C_2-H), 3.27, 3.33, 3.35, and 3.35 (each 3H, s, 4 x MeO), 4.65 and 4.79 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.70-4.80 (6H, m, 3 x OCH_2O), and 5.29 (1H, t, J = 7.3 Hz, C_{18}-H).

(2*R*,3*S*,6*E*,10*E*,14*R*,15*S*,19*S*,23*S*,27*S*)-1,2,3,15,19,23,27-Heptakis(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyldotriaconta-6,10,30-triene-14-ol (46a).

BuLi (0.16 ml, 0.24 mmol, 1.5 M in Hexane) was added to a soln of the sulfide **37a** (76 mg, 0.15 mmol), the epoxide **45a** (52 mg, 0.09 mmol), and TMEDA (1.00 ml) in THF (5.00 ml) cooled at -30 °C.

After stirring at -30 °C for 30 min, the reaction was quenched with H_2O and the product was extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:4) gave a coupling product.

Na metal (1.20 g, 8.70 mmol) was added to a soln of the obtained coupling product and ^{i}PrOH (8.00 ml) in THF (8.00 ml) heated at reflux temp. After heating for 30 min, the reaction mixture was poured into satd citric acid soln and extracted with ether. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:9-1:4) to give **46a** (64 mg, 74%): $[\alpha]_D^{22}$ -4.40° (c, 1.30, $CHCl_3$); IR (neat), 3400, 2920, 2760, 1470, 1450, 1400, 1380, 1300, 1260, 1240, 1210, 1150, 1090, 1030, and 920 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 1.13, 1.26, 1.27, 1.28, 135, 1.58, 1.58, 1.66, and 1.73 (each 3H, s, 9 x Me), 1.20-2.00 (24H, m, C_4-H, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.19, 3.22, 3.28, 3.32, 3.34, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.60 (1H, m, C_{14}-H), 3.18 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 4.01 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.14 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.50-5.20 (14H, m, 7 x OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H); FD-MS, m/z 1015 ($(M+Na)^+$, 3.2), and 975 (M^+-OH, 1.1).

(2*R*,3*S*,6*E*,10*E*,15*R*,19*R*,23*S*,27*S*)-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47a).

To a suspension of NaH (5 mg, 0.21 mmol) and imidazole (1 mg, 0.02 mmol) in THF (3.00 ml) was added a soln of the alcohol **46a**

(64 mg, 0.06 mmol) in THF (1.00 ml) cooled at 0 °C. After stirring at 0 °C for 30 min, CS_2 (0.05 ml, 0.83 mmol) was added and stirring was continued for 30 min. MeI (0.05 ml, 0.83 mmol) was added and the the mixture was stirred for another 14 h. The reaction mixture was poured into satd citric acid soln and extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

Bu_3SnH (0.03 ml, 0.11 mmol) was added to a mixture of the crude product and AIBN (2 mg, 0.01 mmol) in PhH (3.00 ml) at reflux temp. After heating at reflux temp for 30 min, the reaction mixture was cooled to room temp and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:5-1:3) afforded **47a** (36 mg, 58%): $[\alpha]_D^{24}$ -8.36° (c, 1.80, $CHCl_3$); IR (neat), 2920, 1470, 1450, 1400, 1380, 1310, 1260, 1210, 1150, 1090, 1030, and 920 cm^{-1}; ^1H-NMR (400 MHz, C_6D_6), 1.25, 1.26, 1.27, 1.28, 1.35, 1.66, 1.69, 1.72, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2) 3.22, 3.28, 3.32, 3.33, 3.35, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.81 (1H, dd, J = 7.3 and 10.3 Hz, C_1-H), 4.00 (1H, dd, J = 7.3 and 2.0 Hz, C_2-H), 4.13 (1H, dd, J = 10.3 and 2.0 Hz, C_1-H), 4.55 and 4.56 (each 1H, d, J = 6.4 Hz, OCH_2O), 4.61 and 4.79 (each 1H, d, J = 6.8 Hz, OCH_2O), 4.73, 4.74, 4.74, and 4.74 (each 2H, s, 4 x OCH_2O), 4.75 and 5.11 (each 1H, d, J = 6.8 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H); ^{13}C-NMR (100 MHz, C_6D_6), 16.0, 16.1, 17.6, 18.4, 20.1, 22.0, 22.5, 23.0, 24.0, 24.1, 25.8, 27.2, 37.2, 39.4, 39.7, 40.3, 40.4, 40.6, 54.9, 55.2, 55.4, 55.9, 69.8, 78.0, 78.1, 78.1, 79.3, 80.3, 91.0, 91.3, 96.8, 97.5, 124.9, 125.1, 125.4, 127.9, 128.5, 130.9, 134.9, and 135.1; FD-MS, *m/z* 999 ($(M+Na)^+$, 13) and 882 (M^+-$MeOCH_2OH$, 3.1).

(2*S*,3*R*,6*E*,10*E*,15*R*,19*R*,23*S*,27*S*)-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47b).

The (2*S*,3*R*)-isomer was prepared by the same reaction sequence from the sulfide **37b** (203 mg, 0.41 mmol) and the epoxide **45a** (190 mg, 0.31 mmol) to afford **47b** (120 mg, 39%, 4 steps): $[\alpha]_D^{21}$+ 8.56° (c, 2.00, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 1.25, 1.26, 1.27, 1.28, 1.34, 1.66, 1.69, 1.72, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.22, 3.27, 3.32, 3.33, 3.35, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.80 (1H, dd, J = 7.3 and 10.7 Hz, C_1-H), 4.00 (1H, dd, J = 7.3 and 2.0 Hz, C_2-H), 4.13 (1H, dd, J = 10.7 and 2.0 Hz, C_1-H), 4.53 and 4.56 (each 1H, d, J = 6.3 Hz, OCH_2O), 4.66 and 4.78 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.72, 4.73, 4.73, and 4.74 (each 2H, s, 4 x OCH_2O), 4.74 and 5.10 (each 1H, d, J = 6.3 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H); ^{13}C-NMR (100 MHz, C_6D_6), 16.0, 16.1, 17.7, 18.4, 20.1, 22.0, 22.5, 23.0, 24.1, 24.10, 25.8, 27.2, 37.20, 39.4, 39.7, 40.3, 40.4, 40.6, 54.9, 55.2, 55.4, 55.9, 69.8, 78.0, 78.1, 78.1, 79.3, 80.2, 91.0, 91.3, 96.8, 97.5, 124.9, 125.1, 125.4, 127.9, 128.5, 130.9, 135.0, and 135.2.

(2*R*,3*S*,6*E*,10*E*,15*S*,19*R*,23*S*,27*S*)-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47c).

The (15*S*)-isomer was synthesized by the same reaction sequence from the sulfide **37a** (129 mg, 0.24 mmol) and the epoxide **45b** (120 mg, 0.20 mmol) to give **47c** (100 mg, 52%, 4 steps): $[\alpha]_D^{22}$ -8.23° (c, 1.55,

$CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.25, 1.26, 1.27, 1.28, 1.34, 1.66, 1.69, 1.72, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.22, 3.27, 3.32, 3.33, 3.35, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.80 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 4.00 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.13 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.53 and 4.56 (each 1H, d, J = 6.7 Hz, OCH_2O), 4.66 and 4.79 (each 1H, d, J = 6.7 Hz, OCH_2O), 4.73, 4.73, 4.73, and 4.74 (each 2H, s, 4 x OCH_2O), 4.74 and 5.11 (each 1H, d, J = 6.7 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H); ^{13}C-NMR (100 MHz, C_6D_6), 16.0, 16.1, 17.7, 18.4, 20.1, 22.0, 22.5, 23.0, 24.1, 24.1, 25.8, 27.2, 37.2, 39.4, 39.7, 40.3, 40.4, 40.6, 54.9, 55.2, 55.4, 55.9, 69.8, 78.0, 78.1, 78.1, 79.3, 80.2, 91.0, 91.3, 96.8, 97.5, 124.9, 125.1, 125.4, 127.9, 128.5, 130.9, 134.9, and 135.1.

(2*S*,3*R*,6*E*,10*E*,15*S*,19*R*,23*S*,27*S*)-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47d).

By the same reaction sequence, the (2*S*,3*R*,15*S*)-isomer (**47d**) (83 mg, 43%, 4 steps) was prepared from the sulfide **33b** (120 mg, 0.24 mmol) and the epoxide **39b** (120 mg, 0.20 mmol): $[\alpha]_D^{23}$ +8.55° (c, 1.75, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.25, 1.26, 1.27, 1.28, 1.34, 1.66, 1.69, 1.72, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.22, 3.27, 3.32, 3.33, 3.35, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.80 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 4.00 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.13 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.53

and 4.56 (each 1H, d, J = 6.7 Hz, OCH_2O), 4.66 and 4.78 (each 1H, d, J = 6.7 Hz, OCH_2O), 4.72, 4.73, 4.73, and 4.74 (each 2H, s, 4 x OCH_2O), 4.74 and 5.11 (each 1H, d, J = 6.7 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H); ^{13}C-NMR (100 MH, C_6D_6), 16.0, 16.1, 17.7, 18.4, 20.1, 22.0, 22.5, 23.0, 24.1, 24.1, 25.8, 27.2, 37.2, 39.4, 39.7, 40.3, 40.4, 40.6, 54.9, 55.2, 55.4, 55.9, 69.8, 78.0, 78.1, 78.1, 79.3, 80.2, 91.0, 91.3, 96.8, 97.5, 124.9, 125.1, 125.4, 127.9, 128.5, 130.9, 135.0, and 135.1.

(2*R*,3*S*,6*E*,10*E*,15*R*,19*R*,23*S*,27*R*-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47e).

The (27*R*)-isomer (**47e**) (5 mg, 34%, 4 steps) was synthesized from the sulfide **37a** (10 mg, 0.020 mmol) and the epoxide **45c** (9 mg, 0.015 mmol): $[\alpha]_D^{24}$ -8.10° (c, 0.33, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.26, 1.27, 1.28, 1.29, 1.35, 1.66, 1.70, 1.73, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.22, 3.28, 3.32, 3.34, 3.35, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.81 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 4.01 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.14 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.53 and 4.56 (each 1H, d, J = 6.7 Hz, OCH_2O), 4.67 and 4.79 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.73, 4.74, 4.74, and 4.75 (each 2H, s, 4 x OCH_2O), 4.75 and 5.12 (each 1H, d, J = 6.7 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

(2*S*,3*R*,6*E*,10*E*,15*R*,19*R*,23*S*,27*S*)-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47f).

The (2*S*,3*R*,27*R*)-isomer was prepared similaly from the sulfide **37b** (10 mg, 0.020 mmol) and the epoxide **45c** (9 mg, 0.015 mmol) to afford **47f** (6 mg, 41%, 4 steps): $[\alpha]_D^{24}$ +8.20° (c, 0.33, $CHCl_3$); ^{1}H-NMR (250MHz, C_6D_6), 1.25, 1.26, 1.28, 1.28, 1.35, 1.66, 1.70, 1.72, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.22, 3.27, 3.32, 3.33, 3.35, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.81 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 4.01 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.14 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.53 and 4.56 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.66 and 4.79 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.73, 4.74, 4.74, and 4.75 (each 2H, s, 4 x OCH_2O), 4.74 and 5.12 (each 1H, d, J = 7.3 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

(2*R*,3*S*,6*E*,10*E*,15*S*,19*R*,23*S*,27*R*)-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47g).

The (15*S*,27*R*)-isomer was synthesized by the same reaction sequence from the sulfide **33a** (10 mg, 0.020 mmol) and the epoxide **39d** (9 mg, 0.015 mmol) to yield **47g** (6 mg, 41%, 4 steps): $[\alpha]_D^{24}$ -8.50° (c, 0.30, CHCl3); ^{1}H-NMR (250 MHz, C6D6), 1.25, 1.26, 1.27, 1.28, 1.34, 1.66, 1.69, 1.72, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, and C_{26}-H_2, C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.22, 3.27, 3.32, 3.33, 3.35, 3.35, and 3.36

(each 3H, s, 7 x MeO), 3.81 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 4.00 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.13 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.53 and 4.56 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.66 and 4.79 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.73, 4.73, 4.73, and 4.74 (each 2H, s, 4 x OCH_2O), 4.74 and 5.12 (each 1H, d, J = 7.3 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

(2*S*,3*R*,6*E*,10*E*,15*S*,19*R*,23*S*,27*R*)-1,2,3,15,19,23,27-Heptakis-(methoxymethoxy)-3,7,11,15,19,23,27,31-octamethyl-dotriaconta-6,10,30-triene (47h).

The (2*S*,3*R*,15*S*,27*R*)-isomer was prepared from the sulfide **37b** (10 mg, 0.020 mmol) and the epoxide **45d** (9 mg, 0.015 mmol) to afford **47h** (5 mg, 34% 4 steps): $[\alpha]_D^{23}$ +8.30° (c, 0.33, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.25, 1.27, 1.27, 1.28, 1.35, 1.66, 1.70, 1.72, and 1.73 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.22, 3.28, 3.32, 3.34, 3.35, 3.35, and 3.36 (each 3H, s, 7 x MeO), 3.81 (1H, dd, J = 7.3 and 10.4 Hz, C_1-H), 4.01 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.13 (1H, dd, J = 10.4 and 1.8 Hz, C_1-H), 4.53 and 4.56 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.66 and 4.79 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.73, 4.73, 4.73, and 4.74 (each 2H, s, 4 x OCH_2O), 4.75 and 5.12 (each 1H, d, J = 7.3 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

^{1}H-NMR (400 MHz, C_5D_5N) of **47a** and **47c**

47a: 1.28, 1.28, 1.30, 1.30, 1.36, 1.67, 1.68, 1.68, and 1.70 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2),

2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.35, 3.37, 3.40, 3.41, 3.41, 3.42, and 3.43 (each 3H, s, 7 x MeO), 3.84 (1H, dd, J = 7.3 and 10.3 Hz, C_1-H), 4.02 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.16 (1H, dd, J = 10.3 and 1.8 Hz, C_1-H), 4.70 and 4.72 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.80 and 4.85 (each 1H, d, J = 6.3 Hz, OCH_2O), 4.82, 4.82, 4.83, and 4.83 (each 2H, s, 4 x OCH_2O), 4.82 and 5.14 (each 1H, d, J = 6.4 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

47c: 1.28, 1.28, 1.30, 1.30, 1.36, 1.68, 1.68, 1.68, and 1.70 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.34, 3.37, 3.40, 3.41, 3.41, 3.42, and 3.43 (each 3H, s, 7 x MeO), 3.84 (1H, dd, J = 7.3 and 10.7 Hz, C_1-H), 4.02 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.16 (1H, dd, J = 10.7 and 1.8 Hz, C_1-H), 4.70 and 4.72 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.80 and 4.85 (each 1H, d, J = 6.4 Hz, OCH_2O), 4.82, 4.82, 4.83, and 4.83 (each 2H, s, 4 x OCH_2O), 4.82 and 5.14 (each 1H, d, J = 6.4 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

^{1}H-NMR of **47a** and **47c** (400 MHz, C_7D_8)

47a: 1.20, 1.21, 1.22, 1.23, 1.28, 1.62, 1.65, 1.68, and 1.69 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.19, 3.24, 3.28, 3.29, 3.30, 3.30, and 3.31 (each 3H, s, 7 x MeO), 3.71 (1H, dd, J = 7.3 and 10.3 Hz, C_1-H), 3.89 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.03 (1H, dd, J = 10.3 and 1.8 Hz, C_1-H), 4.48 and 4.50 (each 1H, d, J = 6.4 Hz, OCH_2O), 4.60 and 4.71 (each 1H, d, J = 7.3 Hz, OCH_2O),

4.65, 4.65, 4.66, and 4.66 (each 2H, s, 4 x OCH_2O), 4.64 and 5.02 (each 1H, d, J = 6.4 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

47c: 1.20, 1.21, 1.22, 1.23, 1.28, 1.62, 1.65, 1.69, and 1.69 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.19, 3.24, 3.28, 3.29, 3.30, 3.30, and 3.31 (each 3H, s, 7 x MeO), 3.71 (1H, dd, J = 7.3 and 10.3 Hz, C_1-H), 3.89 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 4.03 (1H, dd, J = 10.3 and 1.8 Hz, C_1-H), 4.48 and 4.50 (each 1H, d, J = 6.6 Hz, OCH_2O), 4.60 and 4.71 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.65, 4.66, 4.66, and 4.66 (each 2H, s, 4 x OCH_2O), 4.64 and 5.02 (each 1H, d, J = 6.6 Hz, OCH_2O), and 5.20-5.40 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

^{1}H-NMR of **47a** and **47c** (400 MHz, acetone-d6)

47a: 1.18, 1.18, 1.19, 1.19, 1.22, 1.61, 1.61, 1.64, and 1.66 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.31, 3.31, 3.31, 3.31, 3.31, 3.33, and 3.36 (each 3H, s, 7 x MeO), 3.59 (1H, dd, J = 7.3 and 10.3 Hz, C_1-H), 3.73 (1H, dd, J = 7.3 and 1.8 Hz, C_2-H), 3.92 (1H, dd, J = 10.3 and 1.8 Hz, C_1-H), 4.59 and 4.61 (each 1H, d, J = 6.8 Hz, OCH_2O), 4.65, 4.66, 4.66, and 4.66 (each 2H, s, 4 x OCH_2O), 4.67 and 4.91 (each 1H, d, J = 6.8 Hz, OCH_2O), 4.69 and 4.78 (each 1H, d, J = 6.4 Hz, OCH_2O), and 5.10-5.20 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

47c: 1.17, 1.18, 1.19, 1.19, 1.22, 1.61, 1.61, 1.64, and 1.66 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H, and C_{28}-H_2),

2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.30, 3.31, 3.31, 3.31, 3.31, 3.33, and 3.36 (each 3H, s, 7 x MeO), 3.59 (1H, dd, J = 7.3 and 10.3 Hz, C_1-H), 3.73 (1H, dd, J = 7.3 and 2.0 Hz, C_2-H), 3.92 (1H, dd, J = 10.3 and 2.0 Hz, C_1-H), 4.59 and 4.61 (each 1H, d, J = 6.8 Hz, OCH_2O), 4.65, 4.66, 4.66, and 4.66 (each 2H, s, 4 x OCH_2O), 4.67 and 4.91 (each 1H, d, J = 6.4 Hz, OCH_2O), 4.69 and 4.78 (each 1H, d, J = 6.8 Hz, OCH_2O), and 5.10-5.20 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

^{1}H-NMR of **47a** and **47c** (400 MHz, THF-d4)

47a: 1.17, 1.18, 1.18, 1.19, 1.22, 1.62, 1.63, 1.65, and 1.68 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.30, 3.30, 3.31, 3.31, 3.31, 3.33, and 3.35 (each 3H, s, 7 x MeO), 3.60 (1H, dd, J = 7.3 and 10.5 Hz, C_1-H), 3.73 (1H, dd, J = 7.3 and 2.0 Hz, C_2-H), 3.92 (1H, dd, J = 10.5 and 2.0 Hz, C_1-H), 4.57 and 4.59 (each 1H, d, J = 6.4 Hz, OCH_2O), 4.64, 4.64, 4.64, and 4.65 (each 2H, s, 4 x OCH_2O), 4.65 and 4.91 (each 1H, d, J = 6.4 Hz, OCH_2O), 4.67 and 4.76 (each 1H, d, J = 7.3 Hz, OCH_2O), and 5.10-5.20 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

47c: 1.17, 1.18, 1.18, 1.19, 1.22, 1.62, 1.63, 1.65, and 1.68 (each 3H, s, 9 x Me), 1.50-2.00 (26H, m, C_4-H_2, C_{13}-H_2, C_{16}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, C_{22}-H_2, C_{24}-H_2, C_{25}-H_2, C_{26}-H_2, and C_{28}-H_2), 2.00-2.40 (10H, m, C_5-H_2, C_8-H_2, C_9-H_2, C_{12}-H_2, and C_{29}-H_2), 3.31, 3.31, 3.31, 3.31, 3.31, 3.33, and 3.35 (each 3H, s, 7 x MeO), 3.60 (1H, dd, J = 7.3 and 10.3 Hz, C_1-H), 3.73 (1H, dd, J = 7.3 and 2.0 Hz, C_2-H), 3.92 (1H, dd, J = 10.3 and 2.0 Hz, C_1-H), 4.57, 4.59 (each 1H, d, J = 6.8 Hz, OCH_2O), 4.64, 4.64, 4.64, and 4.65 (each 2H, s, 4 x OCH_2O), 4.65 and 4.91 (each 1H, d, J = 6.8 Hz, OCH_2O), 4.67 and 4.76 (each 1H, d, J = 7.3 Hz, OCH_2O), and 5.10-5.20 (3H, m, C_6-H, C_{10}-H, and C_{30}-H).

(2*S*,3*S*,6*E*,11*S*,15*S*)-1,2-Bis(*tert*-butyldimethylsilyloxy)-3,11,15-tris(methoxymethoxy)-3,7,11,15,19-pentamethyl-eicosa-6,18-diene (48a).

To a suspension of NaH (250 mg, 10 mmol) and imidazole (10 mg, 0.15 mmol) in THF (90 ml) was added a soln of the alcohol **38a** (2.77 g, 3.45 mmol) in THF (10 ml) cooled at 0 °C. After stirring at 0 °C for 30 min, CS_2 (1.30 ml, 22 mmol) was added and stirring was continued for 30 min. MeI (1.30 ml, 22 mmol) was added and the mixture was stirred for another 14 h. The reaction mixture was poured into satd citric acid soln and the product was extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

Bu_3SnH (2.50 ml, 9.29 mmol) was added to a mixture of the crude product and AIBN (30 mg, 0.18 mmol) in PhH (100 ml) at reflux temp. After heating at reflux temp for 30 min, the reaction mixture was cooled to room temp and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:5-1:3) afforded **48a** (2.50 g, 92%): $[\alpha]_D^{24}$ +7.13° (c, 1.60, $CHCl_3$); IR (neat), 2960, 2920, 2840, 1470, 1410, 1380, 1465, 1310, 1255, 1210, 1145, 1130, 1090, 970, 925, 840, 820, 785, and 750 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.17, 0.17, 0.30, and 0.36 (each 3H, s, 2 x Me_2Si), 1.04 and 1.08 (each 9H, s, 2 x ^{t}BuSi), 1.24, 1.24, 1.27, 1.66, 1.66, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.30, 3.33, and 3.33 (each 3H, s, 3 x MeO), 3.71 (1H, dd, J = 6.7 and 10.4 Hz, C_1-H), 3.90 (1H, d, J = 6.7 Hz, C_2-H), 4.26 (1H, d, J = 10.4 Hz, C_1-H), 4.72, 4.72, and 4.72 (each 2H, s, 3 x OCH_2O), 5.29 (1H, t, J = 6.7 Hz, C_{18}-H), and 5.37 (1H, t, J = 7.3 Hz, C_6-H).

(2*S*,3*S*,6*E*,11*S*,15*S*)-3,7,11,15,19-Pentamethylicosa-6,18-diene-1,2,3,11,15-pentaol (49a).

One drop of 12 M HCl was added to a soln of the di-MOM ether **48a** (600 mg, 0.76 mmol) in MeOH (20 ml) and the mixture was stirred at room temp for 30 h. The reaction mixture was neutralized with Et_3N and concentrated in vacuo. The residual oil was purified by silica gel chromatography (EtOAc/PhH=1:5-1:3) to afford **49a** (309 mg, 95%): $[\alpha]_D^{20}$ +8.88° (c, 0.35, $CHCl_3$); IR (neat), 3400, 2960, 2920, 1470, 1460, 1380, 1180, 1090, 1025, 930, 880, 850, and 760 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 1.16, 1.18, 1.23, 1.62, 1.62, and 1.69 (each 3H, s, 6 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.48 (1H, bt, J = 5.0 Hz, C_2-H), 3.76 (2H, bd, J = 5.0 Hz, C_1-H_2), 5.12 (1H, t, J = 6.7 Hz, C_{18}-H), and 5.15 (1H, t, J = 7.3 Hz, C_6-H); FAB-MS, *m/z* 429 (M^+, 9.3), 375 (MH^+-$3H_2O$, 22), and 339 (MH^+-$5H_2O$, 6.3); HR-FAB-MS, *m/z* Calcd for $C_{25}H_{49}O_5$ (M^+): 429.3580. Found: 429.3566.

(2*S*,3*S*,6*E*,11*S*,15*S*)-1,2-Isopropyridenedioxy-3,7,11,15,19-pentamethylicosa-6,18-diene-3,11,15-triol (50a).

A catalytic amount of TsOH (5 mg, 0.03 mmol) was added to a soln of the pentaol **49a** (309 mg, 0.72 mmol) in acetone (10 ml) and the mixture was stirred at room temp for 1 h. The soln was neutralized with Et_3N and concentrated in vacuo. The product was purified by silica gel chromatography (EtOAc/PhH=1:5-1:3) to afford **36a** (290 mg, 86%): $[\alpha]_D^{23}$ +3.01° (c, 0.95, $CHCl_3$); IR (neat), 3400, 2960, 2920, 1470, 1460, 1380, 1270, 1210 1070, 920, and 860 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 1.17, 1.18, 1.24, 1.61, 1.62, and 1.69 (each 3H, s, 6 x Me), 1.37 and 1.42 (each 3H, s, Me_2C), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2,

C_{13}-H_2 C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.94 (1H, t, J = 6.1 Hz, C_2-H), 3.93 (2H, d, J = 6.1 Hz, C_1-H_2), and 5.13 (2H, t, J = 6.4 Hz, C_6-H and C_{18}-H); FAB-MS, m/z 469 (MH^+, 2.8), 452 (MH^+-OH, 1.7), and 415 (MH^+-$3H_2O$, 6.9); HR-FAB-MS, m/z Calcd for $C_{28}H_{53}O_5$ (M^+): 469.3893. Found: 469.3874.

(2*S*,3*S*,6*E*,11*S*,15*R*)-1,2-Isopropyridenedioxy-3,7,11,15,19-pentamethylicosa-6,18-diene-3,11,15-triol (50c).

The (15*R*)-isomer was prepared by the same reaction sequence from **49c** (907 mg, 1.13 mmol) to give **50c** (360 mg, 68%): $[\alpha]_D^{23}$ +3.55° (c, 0.95, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 1.17, 1.18, 1.24, 1.61, 1.62, and 1.69 (each 3H, s, 6 x Me), 1.37, and 1.42 (each 3H, s, Me_2C), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.94 (1H, t, J = 6.1 Hz, C_2-H), 3.93 (2H, d, J = 6.1 Hz, C_1-H_2), and 5.13 (2H, t, J = 6.4 Hz, C_6-H and C_{18}-H).

(2*S*,3*S*,6*E*,11*S*,15*S*)-3,11,15-Trisbezyloxy-1,2-isopropyridene-dioxy-3,7,11,15,19-pentamethylicosa-6,18-diene (51a).

BnBr (0.08 ml, 0.67 mmol) was added to a mixture of the triol **50a** (30 mg, 0.06 mmol) and NaH (23 mg, 0.96 mmol) in DMF (1.50 ml) cooled at 0 °C and stirring was continued for 30 min. After stirring at room temp for 40 h, the mixture was poured into H_2O and extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (ether/hexane=1:4) to afford **51a** (20 mg, 42%): ^{1}H-NMR (400 MHz, C_6D_6), 1.19, 1.19, 1.25, 1.32, 1.48, 1.63, 1.66, and 1.73 (each 3H, s, 8 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2,

and C_{17}-H_2), 3.93 (1H, dd, J = 8.3 and 7.1 Hz, C_1-H), 4.09 (1H, dd, J = 8.3 and 6.5 Hz, C_1-H), 4.20 (1H, dd, J = 7.1 and 6.5 Hz, C_2-H), 4.37 and 4.37 (each 2H, s, 2 x $PhCH_2$), 4.41 and 4.49 (each 1H, d, J = 11.7 Hz, $PhCH_2$), 5.28 (1H, t, J = 7.1 Hz, C_{18}-H), and 5.35 (1H, t, J = 7.1 Hz, C_6-H).

(2*S*,3*S*,6*E*,11*S*,15*R*)-3,11,15-Trisbezyloxy-1,2-isopropyridene-dioxy-3,7,11,15,19-pentamethylicosa-6,18-diene (51c).

The (15*R*)-isomer was prepared by the same reaction sequence from **50c** (30 mg, 0.06 mmol) to give **51c** (21 mg, 44%): ^{1}H-NMR (400 MHz, C_6D_6), 1.19, 1.19, 1.25, 1.32, 1.48, 1.63, 1.66, and 1.73 (each 3H, s, 6 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.93 (1H, dd, J = 8.3 and 7.3 Hz, C_1-H), 4.09 (1H, dd, J = 8.3 and 6.4 Hz, C_1-H), 4.20 (1H, dd, J = 7.3 and 6.4 Hz, C_2-H), 4.36 and 4.37 (each 2H, s, 2 x $PhCH_2$), 4.41 and 4.49 (each 1H, d, J = 11.7 Hz, $PhCH_2$), 5.28 (1H, t, J = 7.1 Hz, C_{18}-H), and 5.35 (1H, t, J = 7.1 Hz, C_6-H).

(2*S*,3*S*,6*E*,11*S*,15*S*)-1,2-Isopropyridenedioxy-3,11,15-trismethoxy-methoxy-3,7,11,15,19-pentamethylicosa-6,18-diene (52a).

MOMCl (0.03 ml, 0.40 mmol) was added to a soln of the triol **50a** (20 mg, 0.04 mmol) and ^{i}Pr$_2$NEt (0.20 ml) in CH_2Cl_2 (1.00 ml) cooled at 0 °C. After stirring at room temp for 14 h, the reaction was quenched with satd citric acid soln and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:4) to give **52a** (20 mg, 77%): ^{1}H-NMR (400 MHz, C_6D_6), 1.24, 1.24, 1.33, 1.33, 1.46, 1.66, 1.71, and 1.73 (each

3H, s, 8 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.22, 3.33, and 3.33 (each 3H, s, 3 x MeO), 3.98 (1H, dd, J = 8.3 and 6.9 Hz, C_1-H), 4.08 (1H, dd, J = 8.3 and 6.9 Hz, C_1-H), 4.16 (1H, t, J = 6.9 Hz, C_2-H), 4.72 and 4.72 (each 2H, s, 2 x OCH_2O), 4.62 and 4.81 (each 1H, d, J = 7.3 Hz, OCH_2O), 5.29 (1H, t, J = 6.7 Hz, C_{18}-H), and 5.34 (1H, t, J = 7.3 Hz, C_6-H).

(2*S*,3*S*,6*E*,11*S*,15*R*)-1,2-Isopropyridenedioxy-3,11,15-trismethoxy-methoxy-3,7,11,15,19-pentamethylicosa-6,18-diene (52c).

The (15*R*)-isomer was prepared by the same reaction sequence from **50c** (30 mg, 0.06 mmol) to give **52c** (31 mg, 80%): ^{1}H-NMR (400 MHz, C_6D_6), 1.24, 1.24, 1.33, 1.33, 1.46, 1.66, 1.71, and 1.73 (each 3H, s, 8 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.22, 3.33, and 3.33 (each 3H, s, 3 x MeO), 3.98 (1H, dd, J = 8.3 and 6.9 Hz, C_1-H), 4.08 (1H, dd, J = 8.3 and 6.9 Hz, C_1-H), 4.16 (1H, t, J = 6.9 Hz, C_2-H), 4.72 and 4.72 (each 2H, s, 2 x OCH_2O), 4.62 and 4.81 (each 1H, d, J = 7.3 Hz, OCH_2O), 5.29 (1H, t, J = 6.7 Hz, C_{18}-H), and 5.34 (1H, t, J = 7.3 Hz, C_6-H).

(2*S*,3*S*,6*E*,11*S*,15*S*)-3,11,15-Trisbezyloxymethoxy-1,2-isopropyridenedioxy-3,7,11,15,19-pentamethylicosa-6,18-diene (53a) and (2*S*,3*S*,6*E*,11*S*,15*S*)-11,15-dibezyloxymethoxy-1,2-isopropyridenedioxy-3,7,11,15,19-pentamethylicosa-6,18-diene-3-ol (54a).

BOMCl (0.04 ml, 0.29 mmol) was added to a soln of the triol **50a** (20 mg, 0.04 mmol) and ^{i}Pr$_2$NEt (0.20 ml) in CH_2Cl_2 (5.00 ml) cooled at

0 °C. After stirring at room temp for 14 h, the reaction was quenched with satd citric acid soln and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to yield the tri-BOM ether **53a** (10 mg, 28%) and the di-BOM ether **54a** (12 mg, 40%).

53a : ^{1}H-NMR (400 MHz, C_6D_6), 1.26, 1.26, 1.32, 1.36, 1.46, 1.63, 1.66, and 1.73 (each 3H, s, 8 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.98 (1H, dd, J = 8.3 and 6.9 Hz, C_1-H), 4.09 (1H, d, J = 8.3 Hz, C_1-H), 4.20 (1H, d, J = 6.9 Hz, C_2-H), 4.69 and 4.69 (2H, s, 2 x $PhCH_2$), 4.55 and 4.63 (each 1H, d, J = 11.7 Hz, $PhCH_2$), 4.83 and 4.83 (each 2H, s, 2 x OCH_2O), 4.78 and 4.93 (each 1H, d, J = 7.3 Hz, OCH_2O), 5.28 (1H, t, J = 7.1 Hz, C_{18}-H), and 5.35 (1H, t, J = 7.1 Hz, C_6-H).

54a: ^{1}H-NMR (400 MHz, C_6D_6), 1.23, 1.26, 1.26, 1.33, 1.38, 1.64, 1.66, 1.73 (each 3H, s, 8 x Me.), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.83 (2H, d, J = 10.3 Hz, C_1-H_2), 3.96 (1H, t, J = 10.3 Hz, C_2-H), 4.69 and 4.69 (each 2H, s, 2 x $PhCH_2$), 4.83 and 4.83 (each 2H, s, 2 x OCH_2O), and 5.28 (2H, t, J = 7.1 Hz, C_{18}-H, and C_6-H).

(2*S*,3*S*,6*E*,11*S*,15*R*)-3,11,15-Trisbezyloxymethoxy-1,2-isopropyridenedioxy-3,7,11,15,19-pentamethylicosa-6,18-diene (53c) and (2*S*,3*S*,6*E*,11*S*,15*R*)-11,15-dibezyloxymethoxy-1,2-isopropyridenedioxy-3,7,11,15,19-pentamethylicosa-6,18-diene-3-ol (54c).

The (15*R*)-isomers (**53c** and **54c**) were prepared by the same reaction

sequence from **50c** (20 mg, 0.04 mmol), respectively, to give the tri-BOM ether **53c** (11 mg, 30%) and the di-BOM ether **54c** (12 mg, 40%).

53c: ^{1}H-MNR (400 MHz, C_6D_6), 1.26, 1.26, 1.32, 1.36, 1.46, 1.63, 1.66, and 1.74 (each 3H, s, 8 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.98 (1H, dd, J = 8.3 and 6.9 Hz, C_1-H), 4.09 (1H, d, J = 8.3 Hz, C_1-H), 4.20 (1H, d, J = 6.9 Hz, C_2-H), 4.69 and 4.69 (each 2H, s, 2 x $PhCH_2$), 4.55 and 4.63 (each 1H, d, J = 11.7 Hz, $PhCH_2$), 4.83 and 4.83 (each 2H, s, 2 x OCH_2O), 4.78 and 4.93 (each 1H, d, J = 7.3 Hz, OCH_2O), 5.28 (1H, t, J = 7.1 Hz, C_{18}-H), and 5.35 (1H, t, J = 7.1 Hz, C_6-H).

54c: ^{1}H-NMR (400 MHz, C_6D_6), 1.23, 1.26, 1.26, 1.33, 1.38, 1.64, 1.66, and 1.73 (each 3H, s, 8 x Me), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.83 (2H, d, J = 10.5 Hz, C_1-H_2), 3.96 (1H, t, J = 10.5 Hz, C_2-H), 4.69 and 4.69 (2H, s, 2 x $PhCH_2$), 4.83 and 4.83 (2H, s, 2 x OCH_2O), and 5.28 (2H, t, J = 7.1 Hz, C_{18}-H, and C_6-H).

(*R*)-Methoxytrifluoromethyl-phenylethanol (56*R*).

CH_2N_2 was added to a soln of (*R*)-MTPA (1.82 g, 7.77 mmol) in ether (60 ml) at room temp. After the color of the soln changed yellow, the soln was concentrated in vacuo. Purification by silica gel column chromatography (ether/hexane=1:4) gave (*R*)-MTPA methyl ester (1.93 g, 100%): $[\alpha]_D^{25}$ +70.5° (c, 3.25, $CHCl_3$); IR (neat), 2960, 2840, 1760, 1500, 1455, 1440, 1275, 1170, 1120, 1110, 1080, 1040, 1030, 1000, 910, 810, 770, 740, 720, and 700 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 3.56 (3H, d, J = 1.2 Hz, COMe), 3.91 (3H, s, COOMe),and 7.00-8.00 (5H, m, Ph); EI-MS, *m/z* 248 (M^+, 5.5), 218 (MH^+-OMe, 2.5), 201 (M^+-COOMe, 1.4), and 189 (C-COOMe, 100); HR-EI-MS, *m/z* Calcd for

$C_{11}H_{11}O_3F_3$ (M^+): 248.0660. Found: 248.0675.

To a suspension of $LiAlH_4$ (579 mg, 15 mmol) in THF (40 ml) was added a soln of (*R*)-MTPA methyl ester (1.93 g, 7.61 mmol) in THF (10 ml) cooled at 0 °C. After stirring at 0 °C for 1 h, the excess hydrides were decomposed with EtOAc. The crude soln was filtered through a plug of Celite and the filtrete was concentrated in vacuo. Purification by silica gel column chromatography (ether/hexane=1:1) afforded ***55R*** (1.56 g, 93%): $[\alpha]_D^{25}$ -21.2° (c, 3.40, $CHCl_3$); IR (neat), 3460, 2960, 2860, 1500, 1470, 1455, 1300, 1280, 1270, 1150, 1130, 1080, 1060, 1030, 1000, 950, 940, 920, 860, and 770 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 2.10 (1H, dd, J = 5.5 and 7.9 Hz, OH), 3.43 (3H, s, COMe), 3.98 (1H, dd, J = 5.5 and 12.8 Hz, C_2-H), 4.19 (1H, dd, J = 7.9 and 12.8 Hz, C_2-H), and 7.00-8.00 (5H, m, Ph); EI-MS, *m/z* 220 (M^+, 2.4), and 189 (M^+-CH_2OH, 66); HR-EI-MS, *m/z* Calcd for $C_{10}H_{11}O_2F_3$ (M^+): 220.0711. Found: 220.0704.

(*R*)-Methoxytrifluoromethyl-phenylethoxymethylchloride (56*R*).

Dry HCl gas was passed into a mixture of (*R*)-MTP ethanol (***55R***) (1.00 g, 4.55 mmol) and paraformaldehyde (150 mg, 5.00 mmol) for 2 h. The mixture was diluted with hexane (50 ml) and dried over Mg_2SO_4. After being concentrated in vacuo, the crude MTPEOMCl (***56R***) was obtained: ^{1}H-NMR (250 MHz, C_6D_6), 3.12 (3H, s, MeO), 4.01 (2H, s, C^*CH_2O), 4.80 and 4.89 (each 1H, d, J = 7.3 Hz, OCH_2O), 7.00-8.00 (5H, m, Ph): FI-MS, *m/z* 268 (M^+, 100); HR-FI-MS, *m/z* Calcd for $C_{11}H_{12}O_2ClF_3$ (M^+): 268.0789, Found: 268.0462.

(2*S*,3*S*,6*E*,11*S*,15*S*)-1,2-Isopropyridenedioxy-11,15-bis[(*R*)-methoxy-trifluoromethylphenylethoxy]methoxy-3,7,11,15,19-pentamethylicosa-6,18-diene-3-ol (58a).

The reagent **56*R*** (120 mg, 0.42 mmol) was added to a soln of the triol **50a** (50 mg, 0.11 mmol) and $^{i}Pr_2NEt$ (0.50 ml) in CH_2Cl_2 (3.00 ml) heated at reflux temp. After heating at reflux temp for 40 h, the reaction was quenched with satd citric acid soln and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4 filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to yield the di-MTPEOM ether **58a** (5 mg, 5%): ^{1}H-NMR (400 MHz, C_6D_6), 1.17, 1.17, 1.23, 1.34, 1.39, 1.65, 1.68, and 1.74 (each 3H, s, 8 x Me.), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.29 and 3.29 (each 3H, s, 2 x MeO), 3.30 (2H, m, C_1-H_2), 3.97 (1H, t, J = 10.3 Hz, C_2-H), 4.19 and 4.33 (2H, d, J = 10.2 Hz, C*CH_2O), 4.33 and 4.33 (2H, d, J = 11.2 Hz, C*CH_2O), 4.66 and 4.71 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.68 and 4.70 (each 1H, d, J = 7.3 Hz, OCH_2O), 5.20-5.30 (2H, m, C_6-H and C_{18}-H), and 7.00-8.00 (10H, m, 2 x Ph); FD-MS, m/z 934 (M^+, 62).

(2*S*,3*S*,6*E*,11*S*,15*R*)-1,2-Isopropyridenedioxy-11,15-bis[(*R*)-methoxy-trifluoromethylphenylethoxy]methoxy-3,7,11,15,19-pentamethylicosa-6,18-diene-3-ol (58c).

By the same reaction sequence, **58c** (5 mg, 5%) was obtained from **50c** (50 mg, 0.11 mmol) and **56*R*** (120 mg, 0.42 mmol): ^{1}H-NMR (400 MHz, C_6D_6), 1.17, 1.17, 1.23, 1.34, 1.39, 1.65, 1.68, and 1.73 (each 3H, s, 8 x Me.), 1.40-2.20 (14H, m, C_4-H_2, C_9-H_2, C_{10}-H_2, C_{12}-H_2, C_{13}-H_2, C_{14}-H_2, and C_{16}-H_2), 2.00-2.40 (6H, m, C_5-H_2, C_8-H_2, and C_{17}-H_2), 3.29 and 3.29 (each 3H, s, 2 x MeO), 3.30 (2H, m, C_1-H_2), 3.97 (1H, t, J = 10.3 Hz, C_2-H), 4.18 and 4.32 (2H, d, J = 11.7 Hz, C*CH_2O), 4.20 and 4.32 (each 1H, d, J = 11.7 Hz, C*CH_2O), 4.67 and 4.71 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.67 and 4.71 (each 1H, d, J = 7.3 Hz,

OCH_2O), 5.20-5.30 (2H, m, C_6-H and C_{18}-H) and 7.00-8.00 (10H, m, 2 x Ph).

4,8,12,16,20-Pentakis(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosa-1,24-diol (69).

Ozone gas was bubbled into a soln of the MOM ether **6** (658 mg, 0.57 mmol) in MeOH (20 ml) cooled at -78 °C for 10 min. The reaction was quenched with two drops of Me_2S. O_2 gas was passed for 30 min and the soln was concentrated in vacuo.

$NaBH_4$ (300 mg, 7.90 mmol) was added to a soln of the crude product in ether/EtOH (10/10 ml) cooled at 0 °C. The reaction mixture was stirred at 0 °C for 30 min, poured into satd citric acid soln, and the product was extracted with ether. The organic soln was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (acetone/$CHCl_3$=1:1) gave **69** (415 mg, 92%): $[\alpha]_D^{22}$ +0.01° (c, 3.25, $CHCl_3$); IR (neat), 3400, 2960, 1470, 1380, 1300, 1250, 1210, 1145, 1090, 1035, and 920 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 1.18, 1.18, 1.18, 1.18, and 1.18 (each 3H, s, 5 x Me), 1.20 (3H, d, J = 6.1 Hz, C_{25}-H_3), 1.50-1.80 (34H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, and C_{23}-H_2), 3.36, 3.36, 3.36, 3.36, and 3.36 (each 3H, s, 5 x MeO), 3.40 (1H, m, C-OH), 3.64 (2H, bt, J = 1.7 Hz, C_1-H_2), 3.81 (1H, bt, J = 6.1 Hz, C_{24}-H), and 4.67, 4.67, 4.67, 4.67, and 4.69 (each 2H, s, 5 x OCH_2O); FI-MS, m/z 755 (MH^+, 100).

4,8,12,16,20-Pentakis(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosane-1-ol (72n).

TBSCl (31 mg, 0.21 mmol) was added to a soln of the diol **69**

(130 mg, 0.17 mmol) and imidazole (35 mg, 0.51 mmol) in DMF (5.00 ml) cooled at 0 °C and the soln was stirred at 0 °C for 40 min. The reaction mixture was poured into H_2O and the product was extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography gave **70** (97 mg, 65%): ^{1}H-NMR (250 MHz, $CDCl_3$), 0.14 (6H, s, Me_2Si), 0.89 (9H, s, ^{t}BuSi), 1.18, 1.18, 1.18, 1.18, and 1.18 (each 3H, s, 5 x Me), 1.20 (3H, bd, J = 6.0 Hz, C_{25}-H_3), 1.50-1.80 (34H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, and C_{23}-H_2), 3.36, 3.36, 3.36, 3.36, and 3.36 (each 3H, s, 5 x MeO), 3.40 (1H, m, CH-OH), 3.81 (1H, bt, J = 6.0 Hz, C_{24}-H), 4.67 (2H, bt, J = 2.0 Hz, C_1-H_2), and 4.69, 4.69, 4.69, 4.69, and 4.69 (each 2H, s,5 x OCH_2O).

CS_2 (0.10 ml, 1.67 mmol) was added to a mixture of the alcohol **70** (97 mg, 0.11 mmol), NaH (20 mg, 0.83 mmol) and imidazole (1 mg, 0.02 mmol) in THF (10 ml) cooled at 0 °C. After stirring for 30 min at 0 °C, MeI (0.10 ml, 1.67 mmol) was added and the mixture was stirred at room temp for 10 h. The reaction was quenched with H_2O and the product was extracted with ether. The organic soln was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

Bu_3SnH (0.07 ml, 0.26 mmol) was added to a mixture of the crude product and AIBN (2 mg, 0.01 mmol) in PhH (10 ml) at reflux temp and heating was continued for 30 min. Then the soln was cooled to room temp and the mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:4-1:1.5) to afford **71** (57 mg, 60%): $[\alpha]_D^{30}$ -1.72° (c, 2.00, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 0.14 (6H, s, Me_2Si), 0.96 (3H, t, J = 6.4 Hz, C_{25}-H_3), 1.05 (9H, s, ^{t}BuSi), 1.25, 1.26, 1.29, 1.29, and 1.30 (each 3H, s, 5 x Me), 1.40-1.80 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-

H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.34, 3.35, 3.37, 3.37, and 3.37 (each 3H, s, 5 x MeO), 3.63 (2H, t, J = 4.9 Hz, C_1-H_2), and 4.73, 4.73, 4.75, 4.75, and 4.75 (each 2H, s, 5 x OCH_2O).

TBAF (0.10 ml, 0.10 mmol) was added to a soln of the silyl ether **71** (57 mg, 0.07 mmol) in THF (5.00 ml) at reflux temp. After heating at reflux temp for 1 h, the soln was cooled to room temp, and concentrated in vacuo. The residual oil was purified by silica gel column chromatography (acetone/$CHCl_3$=1:4) to give **72n** (44 mg, 90%) as a colorless oil: $[\alpha]_D^{25}$ +0.44° (c, 1.20, $CHCl_3$); IR (neat), 3400, 2960, 1470, 1460, 1385, 1320, 1270, 1210, 1150, 1090, 1040, and 920 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.4 Hz, C_{27}-H_3), 1.20, 1.25, 1.27, 1.28, and 1.28 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.30, 3.34, 3.35, 3.36, and 3.36 (3H, s, 5 x MeO), 3.49 (2H, m, C_1-H_2), 4.77, 4.73, 4.73, 4.74, and 4.74 (2H, s, 5 x OCH_2O); FD-MS, m/z 762 $((MH+Na)^+$, 100).

1-Methoxy-4,8,12,16,20-pentakis(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosane (73n).

MeI (0.04 ml, 0.64 mol) was added to a mixture of the alcohol **72n** (44 mg, 0.06 mmol) and NaH (10 mg, 0.42 mmol) in THF (3.00 ml) cooled at 0 °C and stirring was continued for 30 min. After stirring at room temp for 40 h, the mixture was poured into H_2O and extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=2:3) to afford **73n** (36 mg, 80%): $[\alpha]_D^{23}$ +0.98° (c, 0.70, $CHCl_3$); IR (neat), 3000, 1470, 1385,

1310, 1250, 1210, 1150, 1090, 1040, and 920 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.7 Hz, C_{25}-H_3), 1.23, 1.25, 1.26, 1.28, and 1.28 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, C_1-OMe), 3.28 (2H, bt, J = 4.9 Hz, C_1-H_2), 3.32, 3.35, 3.36, 3.36, and 3.36 (each 3H, s, 5 x MeO), 4.71, 4.73, 4.73, 4.75, and 4.75 (2H, s, 5 x OCH_2O); FD-MS, m/z 775 ($(M+Na)^+$, 17).

(5E,9*R*,10*S*,14*S*,18*S*,22*S*)-10,14,18,22-Tetrakis(methoxymethoxy)-6,10,14,18,22,26-hexamethylheptacosa-5,25-diene-9-ol (76a).

BuLi (5.00 ml, 3.33 mmol, 1.5 M in hexane) was added to a soln of the sulfide **75** (547 mg, 2.48 mmol), the epoxide **45a** (750 mg, 1.24 mmol), and TMEDA (2.30 ml) in THF (30 ml) cooled at -22 °C. After stirring at -22 °C for 30 min, the reaction mixture was poured into H_2O and the product was extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

Na metal (2.50 g, 109 mmol) was added to a soln of the coupling product and ^{i}PrOH (30 ml) in THF (30 ml) heated at reflux temp. After heating at reflux temp for 3 h, the mixture was poured into satd citric acid soln and extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:4-1:2) yielded **76a** (703 mg, 79%): $[\alpha]_D^{25}$ +7.59° (c, 1.50, $CHCl_3$); IR (neat), 3480, 2920, 1470, 1450, 1380, 1300, 1260, 1200, 1140, 1090, 1030, and 915 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 0.94 (3H, t, J = 4.5 Hz, C_1-H_3), 1.21, 1.26, 1.27, 1.27, 1.66, 1.72, and 1.73 (each 3H, s,7 x Me), 1.30-2.00 (26H, m, C_2-H_2, C_3-H_2, C_8-H_2, C_{11}-H_2, C_{12}-H_2, C_{13}-H_2, C_{15}-H_2,

C_{16}-H_2, C_{17}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, and C_{23}-H_2), 2.00-2.40 (6H, m, C_4-H_2, C_7-H_2, and C_{24}-H_2), 3.18, 3.34, 3.35, and 3.35 (each 3H, s, 4 x MeO), 4.58 and 4.64 (2H, d, J = 7.3 Hz, OCH_2O), 4.73, 4.73, and 4.73 (each 2H, s, 3 x OCH_2O), and 5.30-5.40 (2H, m, C_3-H and C_{25}-H); EI-MS, *m/z* 591 (M^+-$MeOCH_2OH$-MeO, 0.2), 561 (M^+-2$MeOCH_2OH$-MeO, 0.5), and 530 (M^+-4$MeOCH_2OH$, 1.9); FI-MS, *m/z* 717 (MH^+, 100), 716 (MH^+, 15), and 685 (M^+-MeO, 52).

(5*S*,6*R*,9*R*,10*S*,14*S*,18*S*,22*S*)-5,6-Epoxy-9-trifluoroacetyloxy-10,14,18,22-tetrakis(methoxymethoxy)-6,10,14,18,22,26-hexamethylheptacosa-25-ene (77a).

$VO(acac)_2$ (13 mg, 0.05 mmol) was added to a mixture of the bishomoallylic alcohol **76a** (680 mg, 0.95 mmol), TBHP (0.80 ml, 4.3 M in CH_2Cl_2, 3.44 mmol), and MS-4A (1.80 g) in CH_2Cl_2 (35 ml) at room temp. After stirring at room temp for 4 h, Et_3N was added and the mixture was filtered, and the eluent was concentrated in vacuo. The crude product was poured into satd $Na_2S_3O_3$/$NaHCO_3$ (2:1) soln and extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

TFAA (0.27 ml, 1.90 mmol) was added dropwise to a soln of the crude product and Py (3.00 ml) in CH_2Cl_2 (30 ml) cooled at -15 °C and the reaction mixture was stirred at -15 °C for 30 min. The mixture was poured into H_2O and extracted with ether. The organic soln was washed with satd $CuSO_4$ soln, H_2O and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by Lobar column chromatography (ether/hexane=1:1) to give **77a** (467 mg, 79%): $[\alpha]_D^{27}$ -5.16° (c, 2.20, $CHCl_3$); IR (neat), 2960, 2900, 1790, 1470, 1460, 1385, 1220, 1170, 1150, 1095, 1040, 970, 920, 870, 780, and 730 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.94 (3H, t, J = 4.5 Hz, C_1-H_3), 1.09, 1.15,

1.25, 1.25, 1.27, 1.66, and 1.73 (each 3H, s, 7 x Me), 1.30-2.00 (28H, m, C_2-H_2, C_3-H_2, C_4-H_2, C_7-H_2, C_8-H_2, C_{11}-H_2, C_{12}-H_2, C_{13}-H_2, C_{15}-H_2, C_{16}-H_2, C_{17}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, and C_{23}-H_2), 2.00-2.40 (2H, m, C_{24}-H_2), 2.56 (1H, t, J = 6.7 Hz, C_4-H), 3.25, 3.33, 3.35, and 3.35 (each 3H, s, 4 x MeO), 4.51 and 4.64 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.72, 4.73, and 4.73 (each 2H, s, 3 x OCH_2O), 5.29 (1H, t, J = 7.3 Hz, C_{25}-H), and 5.20-5.40 (1H, m, C_9-H); FI-MS, *m/z* 829 (MH^+, 69), 828 (M^+, 19), 797 (M^+-MeO, 46), 785 (M^+-C_3H_7, 100), and 731 (32.4, M^+-CF_3CO); HR-FI-MS, *m/z* Calcd for $C_{43}H_{80}O_{11}F_3$ (MH^+): 829.5674. Found: 829.5605.

(6*R*,9*R*,10*S*,14*S*,18*S*,22*S*)-10,14,18,22-Tetrakis(methoxymethoxy)-6,10,14,18,22,26-hexamethylheptacosa-25-ene-6,9-diol (78a).

To a suspension of $LiAlH_4$ (79 mg, 2.08 mmol) in ether (20 ml) was added a soln of the epoxide **77a** (430 mg, 0.52 mmol) in ether (5.00 ml) cooled at 0 °C. After heating at reflux temp for 1 h, the mixture was cooled to 0 °C and the excess hydrides were decomposed with EtOAc. The crude soln was filtered through a plug of Celite and the residue was concentrated vacuo. Purification by silica gel column chromatography (EtOAc/PhH=1:2-1:1) gave **78a** (268 mg, 70%): $[\alpha]_D^{26}$ +7.06° (c, 1.80, $CHCl_3$); IR (neat), 3400, 2960, 2920, 1470, 1460, 1380, 1300, 1265, 1210, 1150, 1090, 1040, and 920 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.7 Hz, C_{27}-H_3), 1.19, 1.25, 1.25, 1.27, 1.28, 1.66, and 1.74 (each 3H, s, 7 x Me), 1.30-2.00 (30H, m, C_2-H_2, C_3-H_2, C_4-H_2, C_5-H_2, C_7-H_2, C_8-H_2, C_{11}-H_2, C_{12}-H_2, C_{13}-H_2, C_{15}-H_2, C_{16}-H_2, C_{17}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, and C_{23}-H_2), 2.00-2.40 (2H, m, C_{24}-H_2), 3.19, 3.34, 3.35, and 3.36 (each 3H, s, 4 x MeO), 3.50-3.70 (1H, m, C_9-H), 4.58 and 4.65 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.73, 4.74, and 4.74

(each 2H, s, 3 x OCH_2O), and 5.29 (1H, t, J = 7.6 Hz, C_{25}-H); FI-MS, m/z 735 (MH^+, 100), 734 (M^+, 26), and 673 (M^+-$MeOCH_2OH$, 23); HR-FI-MS, m/z Calcd for $C_{41}H_{83}O_{10}$ (MH^+): 735.6001. Found: 735.5959.

(6*R*,10*R*14*S*,18*S*,22*S*)-10,14,18,22-Tetrakis(methoxymethoxy)-6,10,14,18,22,26-hexamethylheptacosa-25-ene-6-ol (79a).

A soln of the diol **78a** (245 mg, 0.33 mmol) in THF (5.00 ml) was added to a suspension of NaH (24 mg, 1.00 mmol) and imidazole (2 mg, 0.03 mmol) in THF (10 ml) cooled at 0 °C. After stirring at 0 °C for 30 min, CS_2 (0.10 ml, 1.67 mmol) was added and stirring was continued for 30 min. MeI (0.10 ml, 1.67 mmol) was added and the mixture was stirred at 0 °C for another 1 h. The reaction mixture was poured into satd citric acid soln and the product was extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

Bu_3SnH (0.18 ml, 0.67 mmol) was added to a mixture of the crude product and AIBN (3 mg, 0.02 mmol) in PhH (20 ml) at reflux temp. After heating at reflux temp for 1 h, the mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=1:4-1:2) to give **79a** (223 mg, 93%): $[\alpha]_D^{27}$ + 0.57° (c, 1.40, $CHCl_3$); IR (neat), 3500, 2960, 1470, 1455, 1380, 1300, 1250, 1145, 1090, 1035, and 915 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.7 Hz, C_1-H_3), 1.24, 1.25, 1.27, 1.27, 1.29, 1.66, and 1.73 (each 3H, s, 7 x Me), 1.30-2.00 (30H, m, C_2-H_2, C_3-H_2, C_4-H_2, C_5-H_2, C_7-H_2, C_8-H_2, C_{11}-H_2, C_{12}-H_2, C_{13}-H_2, C_{15}-H_2, C_{16}-H_2, C_{17}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, and C_{23}-H_2), 2.00-2.40 (2H, m, C_{24}-H_2), 3.34, 3.35, 3.35, and 3.36 (each 3H, s, 4 x MeO), 4.73, 4.74, 4.74, and 4.74 (each 2H, s, 4 x OCH_2O), and 5.29 (1H, t, J = 7.6 Hz, C_{25}-H); FI-MS, m/z 719 (MH^+,

18), 675 (MH^+-$MeOCH_2$, 11), and 613 (M^+-$MeOCH_2O$-$MeOCH_2$, 19); FAB-MS, *m/z* 719 (MH^+, 15), 717 (M^+-H, 11), 700 (M^+-H_2O, 21), and 639 (M^+-$MeOCH_2OH$-OH, 12); HR-FAB-MS, *m/z* Calcd for $C_{41}H_{81}O_9$ (M^+-H): 717.5881. Found: 717.5856.

(6*R*,10*R*,14*S*,18*S*,22*S*)-6,10,14,18,22-Pentakis(methoxymethoxy)-6,10,14,18,22,26-hexamethylheptacosa-25-ene (80a).

MOMCl (0.11 mg, 1.46 mmol) was added to a soln of the alcohol **79a** (210 mg, 0.29 mmol) and $^iPr_2NEt$ (1.00 ml) in CH_2Cl_2 (10 ml) cooled at 0 °C and the reaction mixture was stirred at room temp for 14 h. The reaction mixture was poured into satd citric acid soln and the product was extracted with ether. The extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude oil was purified by silica gel column chromatography (EtOAc/PhH=1:4-1:2) to yield **80a** (174 mg, 78%): $[\alpha]_D^{25}$ +0.53° (c, 1.45, $CHCl_3$); IR (neat), 2960, 1470, 1455, 1380, 1300, 1250, 1145, 1090, 1035, 915 cm^{-1}; ^1H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, *J* = 6.7 Hz, C_1-H_3), 1.25, 1.25, 1.27, 1.28, 1.28, 1.66, and 1.73 (each 3H, s, 7 x Me), 1.30-2.00 (30H, m, C_2-H_2, C_3-H_2, C_4-H_2, C_5-H_2, C_7-H_2, C_8-H_2, C_{11}-H_2, C_{12}-H_2, C_{13}-H_2, C_{15}-H_2, C_{16}-H_2, C_{17}-H_2, C_{19}-H_2, C_{20}-H_2, C_{21}-H_2, and C_{23}-H_2), 2.00-2.40 (2H, m, C_{24}-H_2), 3.33, 3.34, 3.36, 3.36, and 3.36 (each 3H, s, 4 x MeO), 4.73, 4.73, 4.74, 4.74, and 4.74 (each 2H, s, 5 x OCH_2O), and 5.29 (1H, t, *J* = 6.7 Hz, C_{25}-H); FI-MS, *m/z* 763 (M^+, 29), 719 (MH^+-$MeOCH_2$, 65), and 702 (M^+-$MeOCH_2O$, 16); HR-FAB-MS, *m/z* Calcd for $C_{41}H_{80}O_8$ (M^+-$MeOCH_2OH$): 700.2213. Found: 700.5890.

(4*R*,8*R*,12*R*,16*R*,20*R*)-4,8,12,16,20-Pentakis(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosanol (72a).

Ozone gas was passeed into a soln of **80a** (160 mg, 0.21 mmol) in

MeOH (15 ml) cooled at -78 °C for 5 min. The reaction was quenched with two drops of Me_2S and O_2 gas was bubbled into the soln for 30 min. The solvent was evaporated in vacuo.

$NaBH_4$ (100 mg, 2.80 mmol) was added to a soln of the crude product in ether/EtOH (5.00/5.00 ml) cooled at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and poured into satd citric acid soln. The product was extracted with ether and the organic soln was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/PhH=2:3-1:1) gave **72a** (143 mg, 92%): $[\alpha]_D^{25}$ -0.54° (c, 1.45, $CHCl_3$); IR (neat), 3400, 2960, 1470, 1460, 1385, 1320, 1270, 1210, 1150, 1090, 1040, 920 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.4 Hz, C_{25}-H_3), 1.20, 1.25, 1.27, 1.28, and 1.28 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.30, 3.34, 3.35, 3.36, and 3.36 (each 3H, s, 5 x MeO), 3.49 (2H, m, C_1-H_2), and 4.77, 4.73, 4.73, 4.74, and 4.74 (each 2H, s, 5 x OCH_2O); FD-MS, *m/z* 762 ((MH+ Na)$^+$, 100); FAB-MS, *m/z* 690 (MH^+-MeOH-OH, 4.3), 659 (M^+-$MeOCH_2OH$-OH, 7.3), 553 (MH^+-3$MeOCH_2OH$, 5.7), 490 (M^+-4$MeOCH_2OH$, 24), and 429 (M^+-5$MeOCH_2OH$, 100); HR-FAB-MS, *m/z* Calcd for $C_{39}H_{78}O_9$ (MH^+-MeOH-OH): 690.5646. Found: 690.5619.

(4*R*,8*R*,12*R*,16*R*,20*R*)-1-Methoxy-4,8,12,16,20-pentakis-(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosane (73a).

MeI (0.10 ml, 1.61 mol) was added to a mixture of the alcohol **72a** (135 mg, 0.18 mmol) and NaH (20 mg, 0.83 mmol) in THF (6.00 ml) cooled at 0 °C and the mixture was stirred for 30 min. After stirring at room temp for 40 h, the mixture was poured into H_2O and extracted with

ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/PhH=2:3) to afford **73a** (51 mg, 37%): $[\alpha]_D^{23}$ -1.02° (c, 0.50, $CHCl_3$); IR (neat), 3000, 1470, 1385, 1310, 1250, 1210, 1150, 1090, 1040, and 920 cm^{-1}; ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.7 Hz, C_{25}-H_3), 1.23, 1.25, 1.26, 1.28, and 1.28 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, C_1OMe), 3.28 (2H bt, J = 4.9 Hz, C_1-H_2), 3.32, 3.35, 3.36, 3.36, and 3.36 (each 3H, s, 5 x MeO), and 4.71, 4.73, 4.73, 4.75, and 4.75 (2H, s, 5 x OCH_2O); FD-MS, *m/z* 775 ($(M+Na)^+$, 16); FAB-MS, *m/z* 687 (M^+-MeOH-$MeOH_2$, 2.4), 647 (M^+-$MeOCH_2OH$-$MeOCH_2$, 2.5), and 411 (MH^+-5$MeOCH_2O$-MeO, 14); HR-FAB-MS, *m/z* Calcd for $C_{39}H_{75}O_9$ (M^+-MeOH-$MeOH_2$): 687.5411. Found: 687.5401.

(4*R*,8*R*,12*R*,16*S*,20*S*)-1-Methoxy-4,8,12,16,20-pentakis-(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosane (73b).

The (16*S*,20*S*)-isomer was prepared similarly from the epoxide **45b** (150 mg, 0.25 mmol) to give **73b** (25 mg, 13%, 12 steps): $[\alpha]_D^{24}$ -1.30° (c, 0.30, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.7 Hz, C_{25}-H_3), 1.23, 1.25, 1.26, 1.29, and 1.29 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, C_1OMe), 3.28 (2H bt, J = 4.9 Hz, C_1-H_2), 3.32, 3.35, 3.36, 3.36, and 3.36 (each 3H, s, 5 x MeO), and 4.71, 4.73, 4.73, 4.75, and 4.75 (2H, s, 5 x OCH_2O).

(4*S*,8*R*,12*R*,16*R*,20*R*)-1-Methoxy-4,8,12,16,20-pentakis-(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosane (73c).

From the epoxide **45c** (149 mg, 0.25 mmol), the (4*S*)-isomer **73c** (13 mg, 7%, 12 steps) was synthesized similarly: $[\alpha]_D^{23}$ +0.41° (c, 0.65, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.7 Hz, C_{25}-H_3), 1.23, 1.25, 1.27, 1.29, and 1.29 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, C_1OMe), 3.28 (2H bt, J = 4.9 Hz, C_1-H_2), 3.32, 3.35, 3.36, 3.36, and 3.36 (each 3H, s, 5 x MeO), and 4.71, 4.73, 4.73, 4.75, and 4.75 (2H, s, 5 x OCH_2O).

(4*S*,8*R*,12*R*,16*S*,20*S*)-1-Methoxy-4,8,12,16,20-pentakis-(methoxymethoxy)-4,8,12,16,20-pentamethylpentacosane (73d).

The (4*S*,16*S*,20*S*)-isomer (**73d**) (6 mg, 4%, 12 steps) was obtained from the epoxide **39d** (110 mg, 0.18 mmol) by the same reaction sequence: $[\alpha]_D^{21}$ -5.23° (c, 0.40, $CHCl_3$); ^{1}H-NMR (250 MHz, C_6D_6), 0.96 (3H, t, J = 6.4 Hz, C_{25}-H_3), 1.23, 1.25, 1.26, 1.29, and 1.29 (each 3H, s, 5 x Me), 1.3-2.0 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, C_1OMe), 3.30 (2H bt, J = 4.9 Hz, C_1-H_2), 3.32, 3.36, 3.36, 3.36, and 3.36 (each 3H, s, 5 x MeO), 4.71, 4.73, 4.73, 4.75, and 4.75 (2H, s, 5 x OCH_2O).

(*R*)-Methoxy-1-trifluoromethyl-1-phenyl-2-trimethylsilyloxy-ethane (59*R*).

TMSCl (1.06 ml, 8.24 mmol) was added to a soln of (*R*)-MTP ethanol (**56*R***) (1.53 g, 6.95 mmol) and Et_3N (2.90 ml, 21 mmol) in THF (30 ml) at room temp. After stirring at room temp for 1 h, the reaction mixture

was poured into H_2O and the product was extracted with ether. The organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual oil was purified by distillation under reduced pressure (130 °C/10 mmHg) to afford the pure **59*R*** (1.66 g, 82%): $[\alpha]_D^{26}$-2.68° (c, 3.40, $CHCl_3$); IR (neat), 2960, 1265, 1250, 1160, 1120, 1070, 1040, 980, 960, 880, 850, 765, and 700 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 0.09 (9H, s, Me_3Si), 3.41 (3H, s, COMe), 4.03 and 4.16 (each 1H, d, J = 11.7 Hz, C_2-H_2), and 7.00-8.00 (5H, m, Ph); FI-MS, *m/z* 292 (M^+, 75) and 103 ($PhCCH_2$, 100); HR-EI-MS, *m/z* Calcd for $C_{13}H_{19}O_2F_3Si$ (M^+): 292.1111. Found: 292.1092.

(*S*)-Methoxy-1-trifluoromethyl-1-phenyl-2-trimethylsilyloxy-ethane (59*S*).

The (*S*)-isomer was prepared from (*S*)-MTPA (1.00 g, 4.27 mmol) by the same reaction sequence to yield **59*S*** (912 mg, 73%, 3 steps): $[\alpha]_D^{25}$ +2.79° (c, 3.10, $CHCl_3$).

(1*R*,2*R*,5*R*)-2-Isopropyl-1-methoxymethoxy-5-methyl-cyclohexane (Menthol MOM ether) (A).

Etherification of menthol (500 mg, 3.17 mmol) with MOMCl (0.48 ml, 6.34 mmol) and ^{i}Pr_2NEt (2.00 ml) in CH_2Cl_2 (10 ml) yielded the corresponding MOM ether **A** (630 mg, 99%): $[\alpha]_D^{21}$ +85.1° (c, 3.80, $CHCl_3$); IR (neat), 3000, 2960, 2920, 1475, 1470, 1460, 1390, 1375, 1215, 1180, 1165, 1145, 1110, 1090, 1045, 1035, 980, 960, and 920 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 0.78 (3H, d, J = 6.7 Hz, Me), 0.91 (6H, d, J = 6.1 Hz, Me_2C), 1.00-2.50 (8H, m, C_2-H, C_3-H_2, C_4-H_2, C_5-H, and C_6-H_2), 3.32 (1H, dd, J = 3.7 and 9.8 Hz, C_1-H), 3.39 (3H, s, MeO), and 4.59 and 4.78 (2H, d, J = 6.7 Hz, OCH_2O) ; EI-MS, *m/z* 200 (M^+, 0.7) and 169 (M^+-MeO, 0.8); HR-EI-MS, *m/z* Calcd for $C_{12}H_{24}O_2$ (M^+):

200.1776. Found: 200.1772.

1-Phenyl-2-methoxy-1-methoxymethoxyethane (B).

Manderic acid (400 mg, 2.63 mmol) was converted to the MOM ether **B** (424 mg, 82%, in 4 steps) by the following reaction sequence: 1) CH_2N_2 in ether (20 ml); 2) MOMCl (0.50 ml, 6.58 mmol) and $^iPr_2NEt$ (2.00 ml) in CH_2Cl_2 (10 ml); 3) $LiAlH_4$ (165 mg, 4.34 mmol) in THF (10 ml); 4) MeI (0.68 ml, 11 mmol) and NaH (260 mg, 11 mmol) in THF (10 ml): $[\alpha]_D^{21}$ -177° (c, 3.15, $CHCl_3$); IR (neat), 3040, 3020, 2960, 2920, 2800, 1500, 1455, 1200, 1150, 1130, 1100, 1090, 1070, 1040, 1025, 980, 940, 920, 870, 770, and 700 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 3.38 (3H, s, MeO), 3.40 (3H, s, MeOMO), 3.51 (1H, dd, J = 10.4 and 3.7 Hz, C_2-H), 3.66 (1H, dd, J = 10.4 and 7.9 Hz, C_2-H), 4.60 and 4.66 (2H, d, J = 7.3 Hz, OCH_2O), 4.83 (1H, dd, J = 3.7 and 7.9 Hz, C_1-H) and 7.20-7.80 (5H, m, Ph); EI-MS, *m/z* 196 (M^+, 0.3), 151 (M^+-$MeOCH_2$, 27), and 135 (M^+-$MeOCH_2O$, 7.9); HR-EI-MS, *m/z* Calcd for $C_{11}H_{16}O_3$ (M^+): 196.1099. Found: 196.1112.

1-Phenyl-1-methoxymethoxyethane (C).

Etherification of 1-phenyl-ethanol (500 mg, 4.09 mmol) with MOMCl (1.00 ml, 13 mmol) and $^iPr_2NEt$ (2.00 ml) in CH_2Cl_2 (10 ml) yielded the corresponding MOM ether **C** (664 mg, 98%): $[\alpha]_D^{27}$ -0.15° (c, 3.70, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1500, 1455, 1375, 1360, 1300, 1285, 1220, 1155, 1100, 1075, 1035, 1025, 1005, 990, 920, 765, and 700 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 1.48 (3H, d, J = 4.9 Hz, C_1-H_3), 3.37 (3H, s, MeO), 4.55 and 4.58 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.75 (1H, q, J = 7.3 Hz, C_1-H); EI-MS, *m/z* 166 (M^+, 0.4); HR-EI-MS, *m/z* Calcd for $C_{10}H_{14}O_2$ (M^+): 166.0994. Found: 166.0991.

(3*S*)-1,2,6-Trismethoxy-3-methoxymethoxy-3-methylhexane (D).

(3*S*)-1,2-Diacetoxy-6-hydroxy-3-methoxymethoxy-3-methylhexane (60 mg, 0.21 mmol) was converted to the MOM ether **D** (46 mg, 86%, in 2 steps) by the following reaction sequence: 1) $LiAlH_4$ (16 mg, 0.42 mmol) in THF (4.00 ml); 2) MeI (0.03 ml, 0.48 mmol) and NaH (25 mg, 1.10 mmol) in THF (2.0 ml): $[\alpha]_D^{30}$ -1.06° (c, 0.80, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$), 1.26 (3H, s, Me), 1.40-2.00 (4H, m, C_4-H_2 and C_5-H_2), 3.28 (1H, bt, J = 6.4 Hz, C_6-H), 3.50 (1H, dd, J = 6.8 and 1.5 Hz, C_2-H), 3.55 (1H, dd, J = 6.8 and 9.8 Hz, C_1-H), 3.87 (1H, dd, J = 1.5 and 9.8 Hz, C_1-H), and 4.66 and 4.74 (2H, d, J = 7.3 Hz).

(3*S*)-1,2,6-Triacetoxy-3-methoxymethoxy-3-methylhexane (E).

The epoxyalcohol **10** (100 mg, 0.29 mmol) was converted to the MOM ether **E** (50 mg, 52%, in 5 steps) by the following reaction sequence: 1) MOMCl (0.05 ml, 0.66 mmol) and ^{i}Pr$_2$NEt (0.50ml) in CH_2Cl_2 (5.00 ml); 2) ozone gas was passed in MeOH (10 ml) for 5 min; 3) two drops of Me_2S; 4) $NaBH_4$ (100 mg, 2.80 mmol) in ether/EtOH (5.00/5.00 ml); 5) Ac_2O (1.00 ml) in Py (1.00 ml) and CH_2Cl_2 (3.00 ml): $[\alpha]_D^{22}$ +0.44° (c, 0.70, $CHCl_3$); ^{1}H-NMR(250 MHz, C_6D_6) 1.11 (3H, s, Me), 1.71, 1.74, and 1.76 (each 3H, s, 3 x CH_3CO), 1.20-2.00 (4H, m, C_4-H_2 and C_5-H_2), 3.18 (3H, s, MeO), 3.97 (2H, t, J = 5.5 Hz, C_6-H_2), 4.19 (1H, dd, J = 11.4 and 8.6 Hz, C_1-H), 4.47 and 4.64 (2H, d, J = 7.3 Hz, OCH_2O), 4.66 (1H, dd, J = 11.4 and 1.8 Hz, C_1-H), and 5.45 (1H, dd, J = 8.6 and 1.8 Hz, C_2-H); FAB-MS, m/z 335 (MH^+, 0.3) and 334 (M^+, 0.04); HR-FAB-MS, m/z Calcd for $C_{15}H_{26}O_8$ (M^+): 334.1635. Found: 334.1601.

(3*R*)-6-Acetoxy-1-bezyloxy-3-methoxymethoxy-3-methyl-hexane (F).

Epoxyfarnesol (**13**) (100 mg, 0.42 mmol) was converted to the MOM ether **F** (60 mg, 43%, in 7 steps) by the following reaction sequence: 1) BnCl (0.25 ml, 2.10 mol) and NaH (53 mg, 2.20 mmol) in DMF (3.00 ml); 2) $LiAlH_4$ (22 mg, 0.58 mmol) in THF (8.00 ml); 3) MOMCl (0.05 ml, 0.66 mmol) and $^iPr_2NEt$ (1.00 ml) in CH_2Cl_2 (5.00 ml); 4) ozone gas was passed in MeOH (15 ml) for 5 min; 5) two drops of Me_2S; 6) $NaBH_4$ (50 mg, 1.40 mmol) in ether/EtOH (5.00/5.00 ml); 7) Ac_2O (1.00 ml) in Py (1.00 ml) and CH_2Cl_2 (2.00 ml): $[\alpha]_D^{22}$-1.60° (c, 0.7, $CHCl_3$); ^{1}H-NMR(250 MHz, C_6D_6) 1.10 (3H, s, Me), 1.74 (3H, s, CH_3CO), 1.20-2.00 (6H, m, C_2-H_2, C_4-H_2, and C_5-H_2), 3.18 (3H, s, MeO), 3.96 (2H, t, J = 5.5 Hz, C_1-H_2), 4.19 (1H, dd, J = 11.4 and 8.6 Hz, C_2-H), 4.50 and 4.52 (2H, d, J = 7.3 Hz, OCH_2O), and 4.40 (2H, t, J = 7.1 Hz, C_1-H_2); FAB-MS, *m/z* 323 (M^+-H, 0.2); HR-FAB-MS, *m/z* Calcd for $C_{18}H_{27}O_5$ (M^+-H): 323.1856. Found: 323.1832.

(2*R*,5*S*)-Tetrahydro-2-[(1*S*)-1,2-diacetoxyethyl]-5-[1-methyl-1-methoxymethoxyethyl]-2-methylfuran (G).

Etherification of (2*R*,5*S*)-tetrahydro-2-[(1*S*)-1,2-diacetoxyethyl]-5-[1-methyl-1-hydroxy]-2-methylfuran (150 mg, 0.52 mmol) with MOMCl (0.10 ml, 1.32 mmol) and $^iPr_2NEt$ (0.8 ml) in CH_2Cl_2 (5.0 ml) yielded the corresponding MOM ether **G** (173 mg, 100%): IR (neat), 2960, 2920, 2880, 1750, 1470, 1450, 1370, 1240, 1220, 1145, 1090, 1060, 1040, 990, 970, 920, 880, and 850 cm^{-1}; ^{1}H-NMR (250 MHz,), 1.20, 1.22, and 1.22 (each 3H, s, 3 x Me), 1.61 (2H, bt, J = 9.2 Hz, C_3-H_2), 1.80-2.00 (2H, m, C_4-H_2), 2.02 and 2.08 (each 3H, s, 2 x CH_3CO), 3.36 (3H, s, MeO), 3.88 (1H, t, J = 7.0 Hz, C_5-H), 4.16 (1H, dd, J = 12.2 and 8.5 Hz, $C_{2'}$-H), 4.47 (1H, dd, J = 12.2 and 1.8 Hz, $C_{2'}$-H), 4.69 and 4.79

(each 1H, d, J = 7.3 Hz, OCH_2O), and 5.18 (1H, dd, J = 8.5 and 1.8 Hz, $C_{1'}$-H); EI-MS, m/z 317 (M^+-Me, 0.4) and 271 (M^+-$MeOCH_2O$, 0.6) ; FD-MS, m/z 333 (MH^+, 1.4) ; HR-EI-MS, m/z Calcd for $C_{15}H_{25}O_7$ (M^+-Me): 317.1600. Found: 317.1616.

(4*R*,8*R*)-1-Methoxy-4,8-bis(methoxymethoxy)-4,8-dimethyl-tridecane (69a) and (4*R*,8*S*)-1-Methoxy-4,8-bis(methoxy-methoxy)-4,8-dimethyltridecane (69c).

The MOM ethers (**69a** and **69c**) were similarly synthesized according to the procedure for natural gymnoprenol derivatives. **48a** (320 mg, 0.41 mmol) gave di-methoxymethyl ethers **69a** (46 mg, 31%, 7 steps) and **48c** (162 mg, 0.21 mmol) afforded **69c** (20 mg, 27%, 7 steps).

69a: IR (neat), 3000, 1470, 1385, 1310, 1250, 1210, 1150, 1090, 1040, and 920 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 0.96 (3H, t, J = 6.7 Hz, C_{13}-H_3), 1.22 and 1.22 (each 3H, s, 3 x Me), 1.30-2.00 (18H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, and C_{12}-H_2), 3.18 (3H, s, MeO), 3.31 and 3.33 (each 3H, s, 2 x MeOMO), 3.28 (2H, bt, J = 7.9 Hz, C_1-H_2), and 4.70 and 4.72 (2H, s, OCH_2O); FI-MS, m/z 363 (MH^+, 4.1), 331 (M^+-MeO, 14.3).

69c : 1H-NMR (250 MHz, C_6D_6), 0.95 (3H, t, J = 7.0 Hz, C_{13}-H_3), 1.21 and 1.21 (each 3H, s, 3 x Me), 1.30-2.00 (18H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, and C_{12}-H_2), 3.18 (3H, s, MeO), 3.27 (2H, bt, J = 7.9 Hz, C_1-H_2), 3.31 and 3.33 (each 3H, s, MeOMO), and 4.70 and 4.71 (2H, s, OCH_2O).

(1*R*,2*R*,5*R*)-2-Isopropyl-1-[(*R*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-5-methylcyclohexane (Menthol MTPEOM ether) (H*R*).

One drop of TMSOTf was added to a soln of the MOM ether **A** (5 mg,

0.025 mmol) and (*R*)-MTPEOTMS reagent **59*R*** (73 mg, 0.25 mmol) cooled at -22 °C. After stirring at -22 °C for 5 min, the reaction was quenched by two drops of Py. The reaction mixture was poured into satd $NaHCO_3$ soln and extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (ether/hexane=1:9) gave **H*R*** (7 mg, 72%): $[\alpha]_D^{21}$ +43.5° (c, 0.40, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1450, 1170, 1120, 1080, 1050, 1030, 770, 720, and 710 cm^{-1}; ^{1}H-NMR (250 MHz, $CDCl_3$), 0.85 (3H, d, J = 7.3 Hz, Me), 0.87 (3H, d, J = 6.8 Hz, MeC), 0.97 (3H, d, J = 6.8 Hz, MeC), 1.00-2.50 (8H, m, C_2-H, C_3-H_2, C_4-H_2, C_5-H, and C_6-H_2), 3.24 (1H, dd, J = 4.2 and 10.4 Hz, C_1-H), 3.28 (3H, s, MeO), 4.12 and 4.18 (each 1H, d, J = 11.7 Hz, C*CH_2O), 4.56 and 4.71 (each 1H, d, J = 6.8 Hz, OCH_2O) and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.74 (3F, s); FAB-MS, *m/z* 196 (MH^+, 0.7); HR-FAB-MS, *m/z* Calcd for $C_{21}H_{32}O_3F_3$ (MH^+): 389.2304. Found: 389.2332.

(1*R*,2*R*,5*R*)-2-Isopropyl-1-[(*S*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-5-methylcyclohexane (Menthol MTPEOM ethers) (H*S*).

The (*S*)-MTPE compound **H*S*** was prepared similarly by the same method in 70% yield: $[\alpha]_D^{24}$ +16.2° (c, 0.27, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$), 0.83 (3H, d, J = 6.8 Hz, Me), 0.88 (3H, d, J = 6.8 Hz, MeC), 0.97 (3H, d, J = 6.8 Hz, MeC), 1.00-2.50 (8H, m, C_2-H, C_3-H_2, C_4-H_2, C_5-H, and C_6-H_2), 3.26 (1H, dd, J = 4.2 and 10.4 Hz, C_1-H), 3.29 (3H, s, MeO), 4.11 and 4.30 (each 1H, d, J = 11.7 Hz, C*CH_2O), 4.58 and 4.80 (each 1H, d, J = 6.8 Hz, OCH_2O) and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.46 (3F, s).

1-Phenyl-2-methoxy-1-[(*R*)-methoxy-trifluoromethylphenyl-ethoxy]methoxyethane (I*R*).

The (*R*)-MTPE compound **I*R*** was prepared similarly by the same method in 68% yield: $[\alpha]_D^{22}$-66.1° (c, 0.20, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1450, 1260, 1170, 1100, 1035, 1020, 920, 870, 800, 770, 720, and 710 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 3.11 (3H, s, MeO), 3.26 (3H, s, MeOC*), 3.32 (1H, dd, J = 10.3 and 3.9 Hz, C_2-H), 3.54 (1H, dd, J = 10.3 and 8.3 Hz, C_2-H), 4.05 and 4.61 (each 1H, d, J = 11.2 Hz, C*CH_2O), 4.56 and 4.60 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.85 (1H, dd, J = 3.9 and 8.3 Hz, C_1-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -7.13 (3F, s); FD-MS, *m/z* 384 (M^+, 2.8).

1-Phenyl-2-methoxy-1-[(*S*)-methoxy-trifluoromethylphenyl-ethoxy]methoxyethane (I*S*).

The (*S*)-MTPE compound **I*S*** was prepared similarly by the same method in 72% yield: $[\alpha]_D^{24}$-85.8° (c, 0.20, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 3.12 (3H, s, MeO), 3.25 (3H, s, MeOC*), 3.32 (1H, dd, J = 10.3 and 3.5 Hz, C_2-H), 3.57 (1H, dd, J = 10.3 and 8.3 Hz, C_2-H), 4.01 and 4.55 (each 1H, d, J = 11.2 Hz, C*CH_2O), 4.59 and 4.63 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.85 (1H, dd, J = 3.5 and 8.3 Hz, C_1-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.77 (3F, s).

1-Phenyl-1-[(*R*)-methoxy-trifluoromethylphenylethoxy]-methoxyethane (J*R*).

The (*R*)-MTPE compound **J*R*** was prepared similarly by the same method in 67% yield: $[\alpha]_D^{21}$ +68.3° (c, 0.27, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1450, 1110, 1110, 1070, 1030, 1020, 1000, 930, 920, 760, 710, and 700 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 1.41 (3H, d, J = 6.4 Hz, Me), 3.21 (3H, s, MeOC*), 3.90 (1H, dd, J = 1.5 and 11.2 Hz, C*CHO),

4.37 (1H, d, J = 11.2 Hz, C*CHO), 4.44 and 4.52 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.66 (1H, q, J = 6.4 Hz, C_1-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.30 (3F, s); EI-MS, m/z 196 (M^+, 0.1); HR-EI-MS, m/z Calcd for $C_{19}H_{21}O_3F_3$ (M^+): 354.1143. Found: 354.1458.

1-Phenyl-1-[(*S*)-methoxy-trifluoromethylphenylethoxy]-methoxyethane (J*S*).

The (*R*)-MTPE compound **JS** was prepared similarly by the same method in 67% yield: ^{1}H-NMR (400 MHz, C_6D_6), 1.41 (3H, d, J = 6.5 Hz, Me), 3.21 (3H, s, MeOC*), 4.00 (2H, d, J = 11.2 Hz, C*CHO), 4.26 (1H, dd, J = 1.5 and 11.2 Hz, C*CHO), 4.44 and 4.49 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.61 (1H, q, J = 6.5 Hz, C_1-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.23 (3F, s).

(3*S*)-1,2,6-Trismethoxy-3-[(*R*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-3-methylhexane (K*R*).

The (*R*)-MTPE compound **K*R*** was prepared similarly by the same method in 79% yield: $[\alpha]_D^{24}$ +25.1° (c, 0.27, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1460, 1390, 1175, 1120, 1025, 770, 720, and 710 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 1.20 (3H, s, Me), 1.40-2.00 (4H, m, C_4-H_2 and C_5-H_2), 3.16, 3.17, and 3.47 (each 3H, s, 3 x MeO), 3.23 (2H, ddd, J = 2.9, 6.8, and 12.7 Hz, C_6-H), 3.27 (3H, s, MeOC*), 3.43 (1H, dd, J = 6.8 and 2.0 Hz, C_2-H), 3.51 (1H, dd, J = 6.8 and 9.8 Hz, C_1-H), 3.84 (1H, dd, J = 2.0 and 9.8 Hz, C_1-H), 4.17 (1H, dd, J = 0.9 and 11.7 Hz, C*CHO), 4.27 (1H, d, J = 11.7 Hz, C*CHO), 4.66 and 4.74 (each 1H, d, J = 7.3 Hz, OCH_2O), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), 6.18 (3F, s); FD-MS, m/z 437 (M^+, 3.4).

(3*S*)-1,2,6-Trismethoxy-3-[(*S*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-3-methylhexane (K*S*).

The (*S*)-MTPE compound **K*S*** was prepared similarly by the same method in 80% yield: $[\alpha]_D^{24}$ -25.1° (c, 0.27, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 1.20 (3H, s, Me), 1.40-2.00 (4H, m, C_4-H_2 and C_5-H_2), 3.16, 3.17, and 3.46 (each 3H, s, 3 x MeO), 3.23 (2H, ddd, J = 2.9, 7.3, and 13.2 Hz, C_6-H), 3.28 (3H, s, MeOC*), 3.40 (1H, dd, J = 6.8 and 2.0 Hz, C_2-H), 3.51 (1H, dd, J = 6.8 and 10.4 Hz, C_1-H), 3.82 (1H, dd, J = 2.0 and 10.4 Hz, C_1-H), 4.15 (1H, dd, J = 1.2 and 11.2 Hz, C*CHO), 4.28 (1H, d, J = 11.2 Hz, C*CHO), 4.64 and 4.77 (each 1H, d, J = 7.3 Hz, OCH_2O), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.02 (3F, s)

(3*S*)-1,2,6-Triacetoxy-3-[(*R*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-3-methylhexane (L*R*).

The (*R*)-MTPE compound **L*R*** was prepared similarly by the same method in 79% yield: $[\alpha]_D^{26}$ -3.50° (c, 0.2, $CHCl_3$); IR (neat), 2920, 1740, 1450, 1370, 1240, 1170, 1030, and 720 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 1.11 (3H, s, Me), 1.40-2.00 (4H, m, C_4-H_2 and C_5-H_2), 1.72, 1.74, and 1.76 (each 3H, s, 3 x CH_3CO), 3.21 (3H, s, MeOC*), 3.77 and 3.77 (each 1H, dt, J = 12.2 and 2.0, C_6-H), 4.15 (1H, dd, J = 11.7 and 8.7 Hz, C_1-H), 4.15 and 4.35 (each 1H, d, J = 11.7 Hz, C*CH_2O), 4.72 and 4.82 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.70 (1H, dd, J = 11.7 and 1.8 Hz, C_1-H), 5.48 (1H, dd, J = 8.7 and 1.8 Hz, C_2-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.06 (3F, s); FAB-MS, *m/z* 196 (M^+, 0.4); HR-FAB-MS, *m/z* Calcd for $C_{24}H_{33}O_9F_3$ (M^+): 522.2077. Found: 522.2047.

(3*S*)-1,2,6-Triacetoxy-3-[(*S*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-3-methylhexane (L*S*).

The (*S*)-MTPE compound **L*S*** was prepared similarly by the same method in 70% yield: $[\alpha]_D^{26}$ +5.93° (c, 0.27, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 1.08 (3H, s, Me), 1.40-2.00 (4H, m, C_4-H_2, C_5-H_2), 1.72, 1.74, and 1.76 (each 3H, s, 3 x CH_3CO), 3.20 (3H, s, MeOC*), 3.76 and 3.76 (each 1H, dt, J = 11.1 and 2.0 Hz, C_6-H), 4.14 (1H, dd, J = 11.7 and 8.7 Hz, C_1-H), 4.23 and 4.34 (each 1H, d, J = 11.7 Hz, C*CH_2O), 4.72 and 4.78 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.69 (1H, dd, J = 11.7 and 1.8 Hz, C_1-H), 5.48 (1H, dd, J = 8.7 and 1.8 Hz, C_2-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.47 (3F, s)

(3*R*)-6-Acetoxy-1-bezyloxy-3-[(*R*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-3-methylhexane (M*R*).

The (*R*)-MTPE compound **M*R*** was prepared similarly by the same method in 70% yield: $[\alpha]_D^{25}$ +5.19° (c, 0.27, $CHCl_3$); IR (neat), 2960, 2920, 1750, 1740, 1720, 1460, 1320, 1280, 1250, 1175, 1120, 1030, 770, and 720 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 0.99 (3H, s, Me), 1.40-2.00 (6H, m, C_2-H_2, C_4-H_2, and C_5-H_2), 1.73 (3H, s, 3 x CH_3CO), 3.24 (3H, s, MeOC*), 3.96 (2H, t, J = 6.4 Hz, C_1-H_2), 4.05 and 4.20 (each 1H, d, J = 11.2 Hz, C*CH_2O), 4.40 (1H, d, J = 7.1 Hz, C_6-H_2), 4.50 and 4.53 (each 1H, d, J = 7.3 Hz, OCH_2O), and 7.00-8.20 (10H, m, 2 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.39 (3F, s); FAB-MS, m/z 512 (M^+, 0.1); HR-FAB-MS, m/z Calcd for $C_{27}H_{34}O_6F_3$ (M^+-H): 511.2308. Found: 511.2286.

(3*R*)-6-Acetoxy-1-bezyloxy-3-[(*S*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-3-methylhexane (M*S*).

The (*S*)-MTPE compound **M*S*** was prepared similarly by the same

method in 70% yield: $[\alpha]_D^{25}$ -9.88° (c, 0.27, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.99 (3H, s, Me), 1.40-2.00 (6H, m, C_2-H_2, C_4-H_2, and C_5-H_2), 1.73 (3H, s, 3 x CH_3CO), 3.24 (3H, s, MeOC*), 3.96 (2H, t, J = 6.4 Hz, C_1-H_2), 4.05 and 4.20 (2H, d, J = 11.7 Hz, C*CH_2O), 4.40 (1H, d, J = 7.1 Hz, C_6-H_2), 4.50 and 4.52 (2H, d, J = 7.8 Hz, OCH_2O), and 7.00-8.20 (10H, m, 2 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.35 (3F, s).

(2*R*,5*S*)-Tetrahydro-2-[(1*S*)-1,2-diacetoxyethyl]-5-[1-methyl-1-[(*R*)-methoxy-trifluoromethylphenylethoxy]methoxyethyl]-2-methylfuran (N*R*).

The (*R*)-MTPE compound **N*R*** was prepared similarly by the same method in 86% yield: $[\alpha]_D^{25}$ +20.0° (c, 0.47, $CHCl_3$); IR (neat), 2960, 2920, 2880, 1745, 1370, 1240, 1220, 1160, 1040, 1000, 930, 770, and 710 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 1.08, 1.15, and 1.19 (each 3H, s, 3 x Me), 1.30-2.00 (4H, m, C_4-H_2 and C_5-H_2), 1.73 and 1.78 (each 3H, s, 2 x CH_3CO), 3.28 (3H, s, MeOC*), 3.68 (1H, t, J = 7.3 Hz, C_5-H), 4.15 (1H, dd, J = 1.5 and 11.7 Hz, C*CHO), 4.30 (1H, dd, J = 8.7 and 11.7 Hz, C_2,-H), 4.44 (1H, d, J = 11.7 Hz, C*CHO), 4.74 and 4.81 (2H, d, J = 7.3 Hz, OCH_2O), 4.74 (1H, dd, J = 2.5 and 11.7 Hz, C_2'-H), 5.50 (1H, dd, J = 2.5 and 8.7 Hz, C_1'-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.42 (3F, s); FAB-MS, *m/z* 505 (M^+-H, 0.1); HR-FAB-MS, *m/z* Calcd for $C_{24}H_{32}O_8F_3$ (M^+-H): 505.2050. Found: 505.2059.

(2*R*,5*S*)-Tetrahydro-2-[(1*S*)-1,2-diacetoxyethyl]-5-[1-methyl-1-[(*S*)-methoxy-trifluoromethylphenylethoxy]methoxyethyl]-2-methylfuran (N*S*).

The (*S*)-MTPE compound **N*S*** was prepared similarly by the same method in 88% yield: $[\alpha]_D^{26}$ +16.3° (c, 0.53, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 1.06, 1.14, and 1.18 (each 3H, s, 3 x Me), 1.30-2.00 (4H, m,

C_4-H_2 and C_5-H_2), 1.74, and 1.78 (each 3H, s, 2 x CH_3CO), 3.29 (3H, s, MeOC*), 3.68 (1H, t, J = 7.3 Hz, C_5-H), 4.25 (1H, dd, J = 1.4 and 11.7 Hz, C*CHO), 4.29 (1H, dd, J = 8.8 and 11.2 Hz, $C_{2'}$-H), 4.34 (1H, d, J = 11.7 Hz, C*CHO), 4.76 (2H, s, OCH_2O), 4.73 (1H, dd, J = 2.4 and 11.2 Hz, $C_{2'}$-H), 5.49 (1H, dd, J = 2.4 and 8.8 Hz, $C_{1'}$-H), and 7.00-8.20 (5H, m, Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.32 (3F, s).

(4*R*,8*R*)-1-Methoxy-4,8-bis[(*R*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-4,8-dimethyltridecane (69*R*).

The (*R*)-MTPE compound **69*R*** was prepared similarly by the same method in 60% yield: $[\alpha]_D^{25}$ +7.61° (c, 0.60, $CHCl_3$); IR (neat), 2960, 2880, 1480, 1460, 1390, 1250, 1070, 1120, 1080, 1040, 1000, 970, 840, 770, 720, and 710 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 0.96 (3H, t, J = 7.1 Hz, C_{13}-H_3), 1.15 and 1.15 (each 3H, s, 2 x Me), 1.40-2.00 (18H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, and C_{12}-H_2), 3.18 (3H, s, MeO), 3.24 (2H, t, J = 5.1 Hz, C_1-H_2), 3.28 and 3.29 (each 3H, s, MeOC*), 4.16 (1H, dd, J = 1.0 and 11.7 Hz, C*CHO), 4.19 (1H, dd, J = 1.0 and 11.7 Hz, C*CHO), 4.32 (2H, d, J = 11.7 Hz, C*CH_2O), 4.64 and 4.69 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.66 and 4.69 (each 1H, d, J = 7.3 Hz, OCH_2O), and 7.00-7.70 (10H, m, 2 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.09 and -6.12 (each 3F, s); FD-MS, *m/z* 777 ((M+K)$^+$, 42) and 762 ((M+Na)$^+$, 72).

(4*R*,8*R*)-1-Methoxy-4,8-bis[(*S*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-4,8-dimethyltridecane (69*S*).

The (*S*)-MTPE compound **69*S*** was prepared similarly by the same method in 60% yield: $[\alpha]_D^{25}$ -37.6° (c, 0.22, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.96 (3H, t, J = 7.3 Hz, C_{13}-H_3), 1.14 and 1.15 (each 3H, s, 2 x Me), 1.40-2.00 (18H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2,

C_{10}-H_2, C_{11}-H_2, and C_{12}-H_2), 3.18 (3H, s, MeO), 3.25 (2H, t, J = 5.1 Hz, C_1-H_2), 3.29 and 3.30 (each 3H, s, MeOC*), 4.18 (2H, dd, J = 1.0 and 11.2 Hz, C*CH_2O), 4.32 (1H, d, J = 11.2 Hz, C*CHO), 4.33 (1H, d, J = 11.2 Hz, C*CHO), 4.65 and 4.67 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.67 and 4.70 (2H, d, J = 7.3 Hz, OCH_2O), and 7.00-7.70 (10H, m, 2 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.07 and -6.11 (each 3F, s).

(4*S*,8*R*)-1-Methoxy-4,8-bis[(*R*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-4,8-dimethyltridecane (70*R*).

The (*R*)-MTPE compound **70*R*** was prepared similarly by the same method in 60% yield: $[\alpha]_D^{25}$ +14.3° (c, 0.40, $CHCl_3$); IR(neat), 2960, 2880, 1460, 1380, 1270, 1170, 1120, 1040, 1000, 770, and 720 cm^{-1}; ^{1}H-NMR (400 MHz, C_6D_6), 0.96 (3H, t, J = 7.1 Hz, C_{13}-H_3), 1.14 and 1.15 (each 3H, s, 2 x Me), 1.40-2.00 (18H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, and C_{12}-H_2), 3.18 (3H, s, MeO), 3.25 (2H, t, J = 5.1 Hz, C_1-H_2), 3.29 and 3.30 (each 3H, s, MeOC*), 4.18 (1H, dd, J = 1.0 and 11.2 Hz, C*CHO), 4.19 (1H, dd, J = 1.0 and 11.2 Hz, C*CHO), 4.31 (1H, d, J = 11.2 Hz, C*CHO), 4.32 (1H, d, J = 11.2 Hz, C*CHO), 4.65 and 4.68 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.66 and 4.69 (each 1H, d, J = 7.3 Hz, OCH_2O), and 7.00-7.70 (10H, m, 2 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.10 and -6.11 (each 3F, s); FAB-MS, *m/z* 505 (M^+, 0.1); HR-FAB-MS, *m/z* Calcd for $C_{38}H_{56}O_7F_6$ (M^+): 738.3931. Found: 738.3945.

(4*S*,8*R*)-1-Methoxy-4,8-bis[(*S*)-methoxy-trifluoromethyl-phenylethoxy]methoxy-4,8-dimethyltridecane (70*S*).

The (*S*)-MTPE compound **70*S*** was prepared similarly by the same method in 64% yield: $[\alpha]_D^{25}$ -22.5° (c, 0.40, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.96 (3H, t, J = 7.3 Hz, C_{13}-H_3), 1.15 and 1.15 (each 3H, s,

2 x Me), 1.40-2.00 (18H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, and C_{12}-H_2), 3.18 (3H, s, MeO), 3.24 (2H, t, J = 5.4 Hz, C_1-H_2), 3.29 and 3.30 (each 3H, s, MeOC*), 4.16 (1H, dd, J = 1.0 and 11.7 Hz, C*CHO), 4.18 (1H, dd, J = 1.0 and 11.7 Hz, C*CHO), 4.33 (1H, d, J = 11.7 Hz, C*CHO), 4.34 (1H, d, J = 11.7 Hz, C*CHO), 4.64 and 4.70 (each 1H, d, J = 7.3 Hz, OCH_2O), 4.65 and 4.70 (each 1H, d, J = 7.3 Hz, OCH_2O), and 7.00-7.70 (10H, m, 2 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -6.07 and -6.11 (each 3F, s).

1-Methoxy-4,8,12,16,20-pentakis[(*R*)-methoxy-trifluoro-methylphenylethoxy]methoxy-4,8,12,16,20-pentamethyl-pentacosane (74n*R*).

The (*R*)-MTPEOM ether **74n*R*** (4 mg, 19%) was prepared by the same method starting from the MOM ether **73n** (10 mg, 0.013 mmol) and **59*R*** (192 mg, 0.66 mmol): $[\alpha]_D^{26}$ +7.20° (c, 0.20, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.16, 1.19, 1.21, 1.23, and 1.25 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 6.8 Hz, C_1-H_2), 3.29, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.43, -5.48, -5.48, -5.68, and -5.71 (each 3F, s): FD-MS, m/z 1731 ($(M+K)^+$, 2.2), 1715 ($(M+Na)^+$, 11).

1-Methoxy-4,8,12,16,20-pentakis[(*S*)-methoxy-trifluoro-methylphenylethoxy]methoxy-4,8,12,16,20-pentamethyl-pentacosane (74n*S*).

The (*S*)-MTPEOM ether **74n*S*** (2 mg, 18%) was prepared by the

same method starting from the MOM ether **73a** (5 mg, 0.007 mmol) and **59*R*** (96 mg, 0.33 mmol): $[\alpha]_D^{26}$ -55.0° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.96 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.17, 1.18, 1.21, 1.23, and 1.24 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 6.8 Hz, C_1-H_2), 3.30, 3.30, 3.32, 3.32, and 3.32 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.42, -5.44, -5.51, -5.64, and -5.73 (each 3F, s).

(4*R*,8*R*,12*R*,16*R*,20*R*)-1-Methoxy-4,8,12,16,20-pentakis[(*R*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74a*R*).

The (*R*)-MTPEOM ether **74a*R*** (2 mg, 18%) was prepared by the same method starting from the MOM ether **73a** (5 mg, 0.007 mmol) and **59*R*** (96 mg, 0.33 mmol): $[\alpha]_D^{26}$ -63.0° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.17, 1.19, 1.21, 1.23, and 1.25 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 6.8 Hz, C_1-H_2), 3.29, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.42, -5.44, -5.51, -5.64, and -5.73 (each 3F, s).

(4*R*,8*R*,12*R*,16*R*,20*R*)-1-Methoxy-4,8,12,16,20-pentakis[(*S*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74a*S*).

The (*S*)-MTPEOM ether **74a*S*** (2 mg, 18%) was prepared by the same method starting from the MOM ether **73a** (5 mg, 0.007 mmol) and **59*S*** (96 mg, 0.33 mmol): $[\alpha]_D^{26}$-9.60° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.16, 1.19, 1.21, 1.23, and 1.24 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 6.8 Hz, C_1-H_2), 3.30, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.43, -5.48, -5.48, -5.68, and -5.71 (each 3F, s).

(4*R*,8*R*,12*R*,16*S*,20*S*)-1-Methoxy-4,8,12,16,20-pentakis[(*R*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74b*R*).

The (*R*)-MTPEOM ether **74b*R*** (1.5 mg, 22%) was prepared by the same method starting from the MOM ether **73b** (3 mg, 0.004 mmol) and **59*R*** (58 mg, 0.20 mmol): $[\alpha]_D^{25}$ -66.0° (c, 0.10, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.17, 1.19, 1.21, 1.23, and 1.25 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 6.8 Hz, C_1-H_2), 3.30, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.39, -5.44, -5.53, -5.69, and -5.75 (each 3F, s).

(4*R*,8*R*,12*R*,16*S*,20*S*)-1-Methoxy-4,8,12,16,20-pentakis[(*S*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74b*S*).

The MOM ether **73b** (3 mg, 0.004 mmol) was converted to the (*S*)-MTPEOM ether **74b*S*** (2 mg, 30%) by the same method: $[\alpha]_D^{25}$ -15.0° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.16, 1.19, 1.21, 1.23, and 1.24 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 7.3 Hz, C_1-H_2), 3.29, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.48, -5.48, -5.48, -5.64, and -5.71 (each 3F, s).

(4*S*,8*R*,12*R*,16*R*,20*R*)-1-Methoxy-4,8,12,16,20-pentakis[(*R*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74c*R*).

The (*R*)-MTPEOM ether **74c*R*** (2 mg, 18%) was prepared by the same method starting from the MOM ether **73c** (5 mg, 0.007 mmol) and **59*R*** (96 mg, 0.33 mmol): $[\alpha]_D^{24}$ -18.0° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.160, 1.19, 1.21, 1.23, and 1.25 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 5.8 Hz, C_1-H_2), 3.28, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.42, -5.44, -5.54, -5.64, and -5.72 (each

3F, s).

(4*S*,8*R*,12*R*,16*R*,20*R*)-1-Methoxy-4,8,12,16,20-pentakis[(*S*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74c*S*).

The MOM ether **73c** (5 mg, 0.007 mmol) was converted to the (*S*)-MTPEOM ether **74c*S*** (2 mg, 18%) by the same method: $[\alpha]_D^{24}$-32.0° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.17, 1.19, 1.21, 1.23, and 1.24 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 7.3 Hz, C_1-H_2), 3.29, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.43, -5.45, -5.48, -5.68, and -5.72 (each 3F, s).

(4*S*,8*R*,12*R*,16*S*,20*S*)-1-Methoxy-4,8,12,16,20-pentakis[(*R*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74d*R*).

The (*R*)-MTPEOM ether **74d*R*** (1.5 mg, 22%) was prepared by the same method starting from the MOM ether **73d** (3 mg, 0.004 mmol) and **59*R*** (58 mg, 0.20 mmol): $[\alpha]_D^{25}$ -20.0° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, J = 7.1 Hz, C_{25}-H_3), 1.16, 1.19, 1.21, 1.23, and 1.25 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2, C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, J = 6.0 Hz, C_1-H_2), 3.29, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O),

4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.39, -5.44, -5.55, -5.69, and -5.73 (each 3F, s).

(4*S*,8*R*,12*R*,16*S*,20*S*)-1-Methoxy-4,8,12,16,20-pentakis[(*S*)-methoxy-trifluoromethylphenylethoxy]methoxy-4,8,12,16,20-pentamethylpentacosane (74d*S*).

The MOM ether **73d** (3 mg, 0.004 mmol) was converted to the (*S*)-MTPEOM ether **74d*S*** (1.5 mg, 22%) by the same method: $[\alpha]_D^{25}$ -68.0° (c, 0.13, $CHCl_3$); ^{1}H-NMR (400 MHz, C_6D_6), 0.97 (3H, t, *J* = 7.1 Hz, C_{25}-H_3), 1.17, 1.19, 1.21, 1.23, and 1.24 (each 3H, s, 5 x Me), 1.30-2.00 (36H, m, C_2-H_2, C_3-H_2, C_5-H_2, C_6-H_2, C_7-H_2, C_9-H_2, C_{10}-H_2, C_{11}-H_2, C_{13}-H_2, C_{14}-H_2, C_{15}-H_2, C_{17}-H_2, C_{18}-H_2, C_{19}-H_2, C_{21}-H_2, C_{22}-H_2 C_{23}-H_2, and C_{24}-H_2), 3.19 (3H, s, MeO), 3.26 (2H, t, *J* = 6.0 Hz, C_1-H_2), 3.29, 3.30, 3.31, 3.31, and 3.31 (each 3H, s, 5 x MeOC*), 4.10-4.40 (10H, m, 5 x C*CH_2O), 4.60-4.80 (10H, m, 5 x OCH_2O), and 7.00-7.70 (30H, m, 5 x Ph); ^{19}F-NMR (376 MHz, C_6D_6), -5.44, -5.45, -5.47, -5.64, and -5.71 (each 3F, s).

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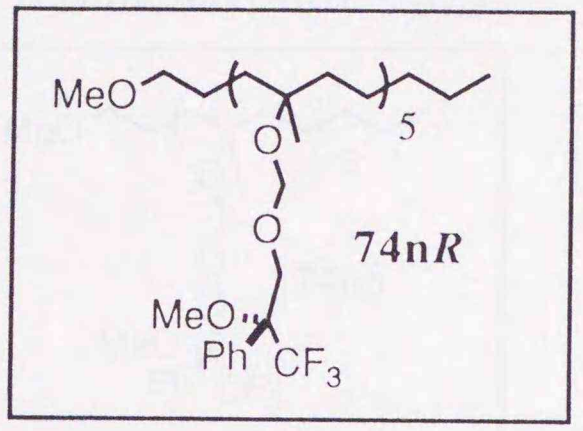
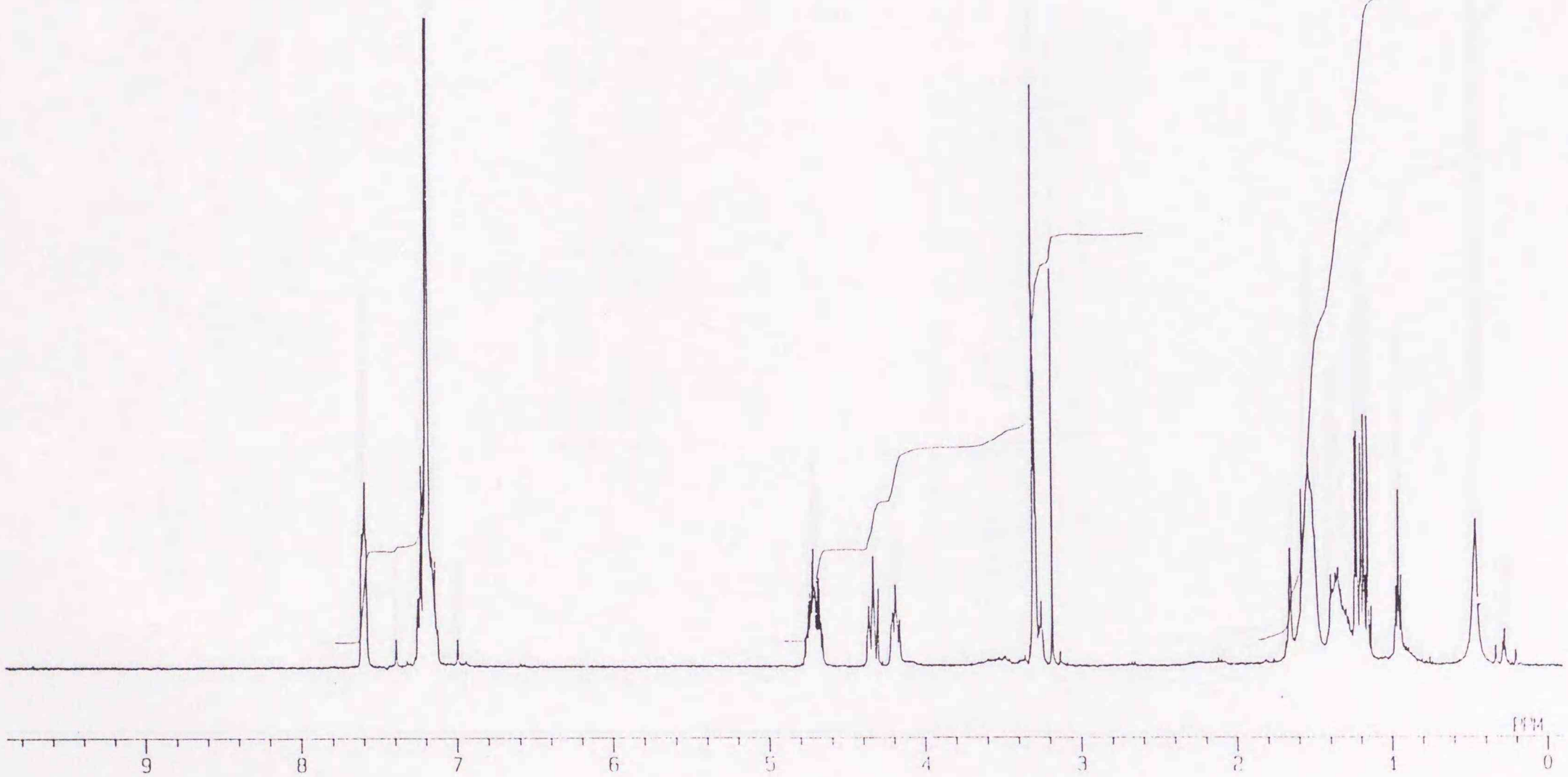
Thanks are given to my parents and all of my friends around me.

^{1}H-NMR (400 MHz, C_6D_6)





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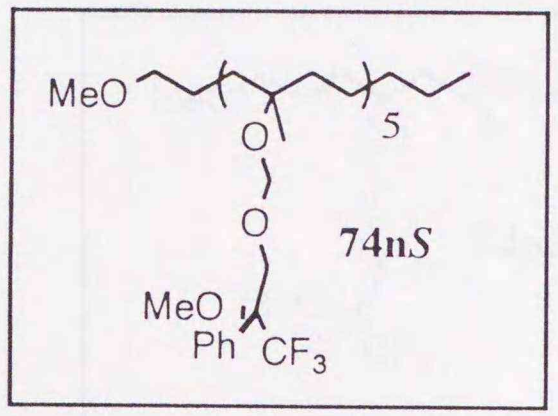

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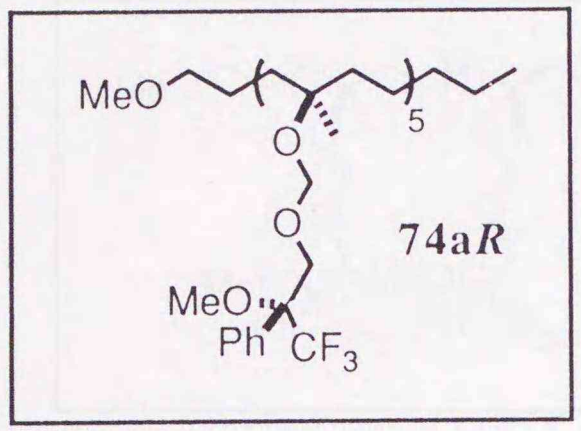
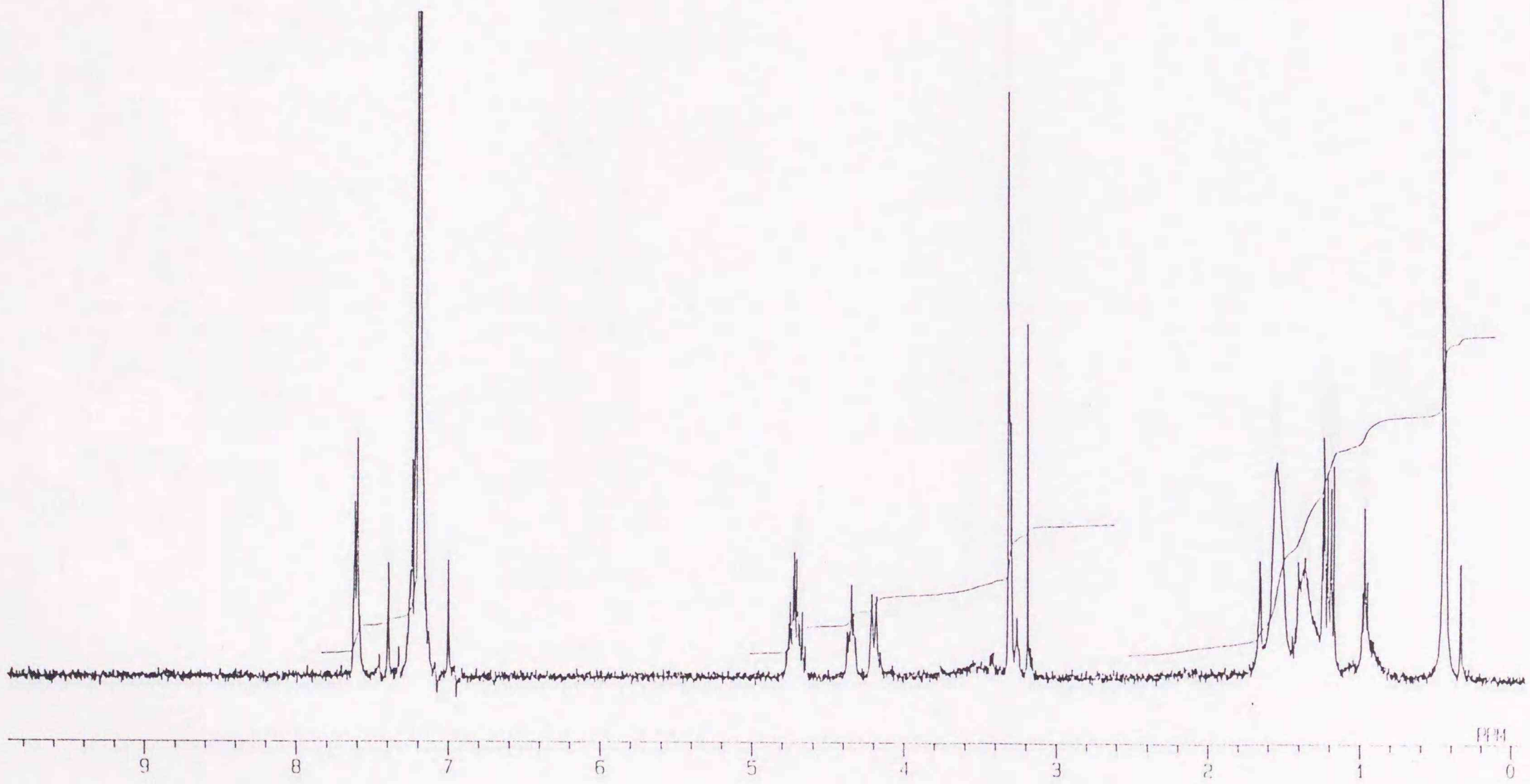


74a*R*



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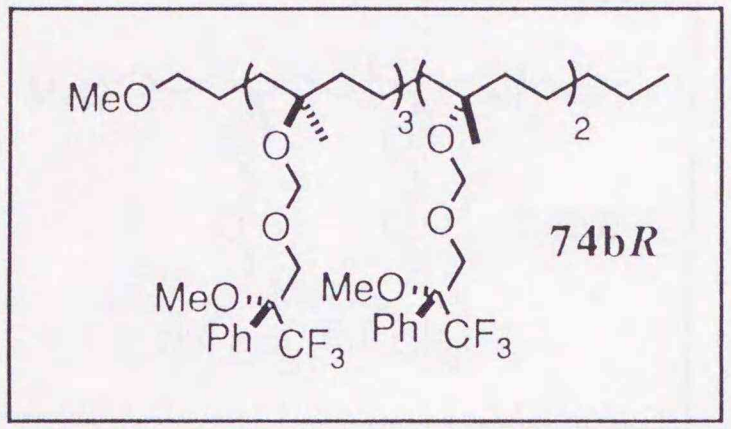
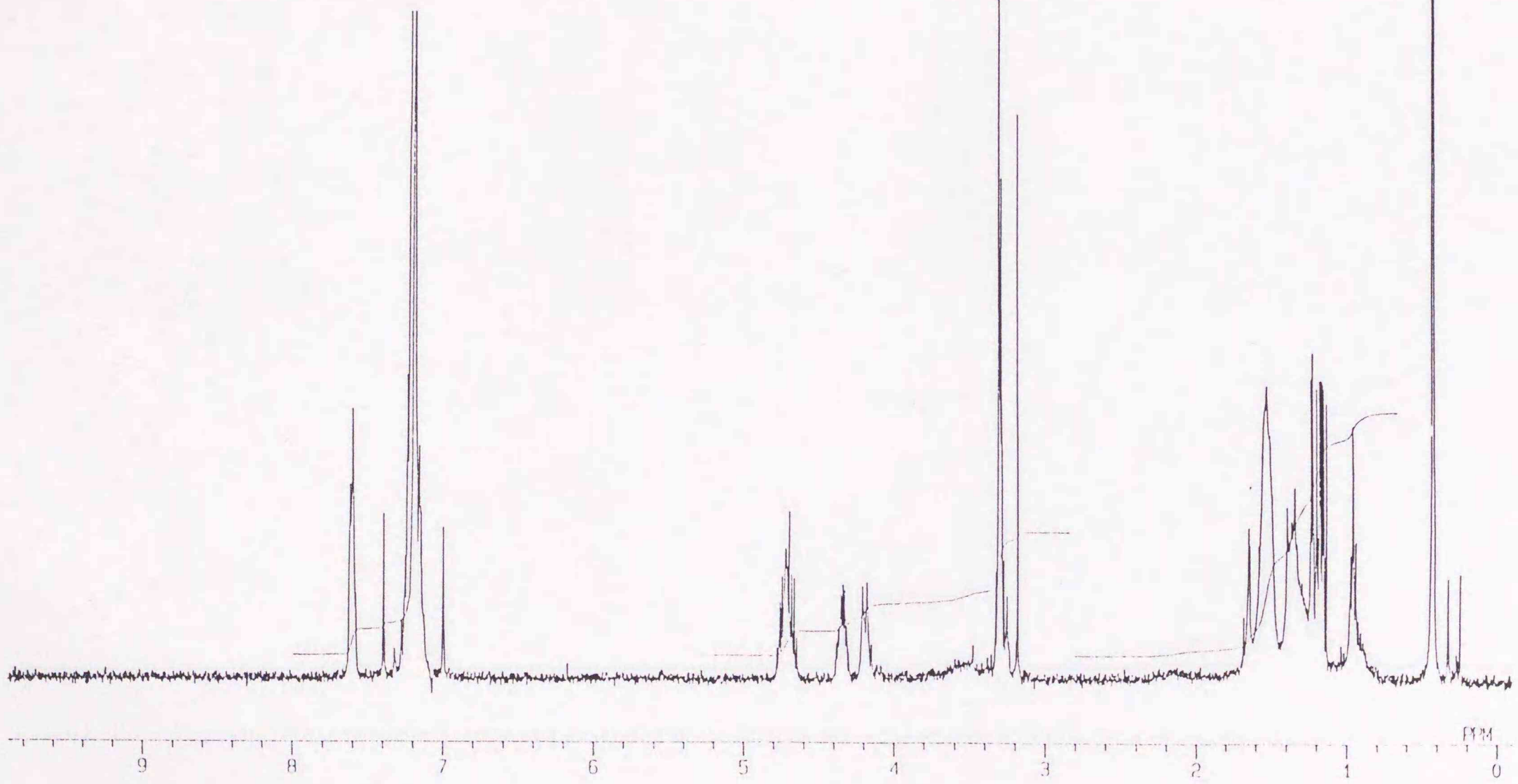


74b*R*



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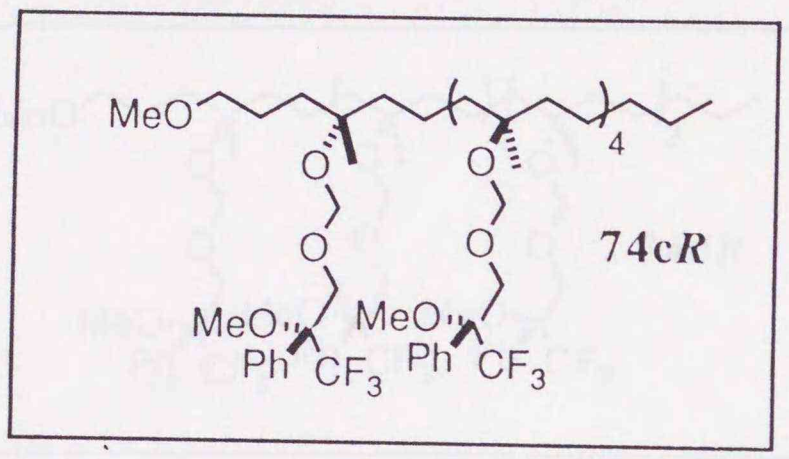
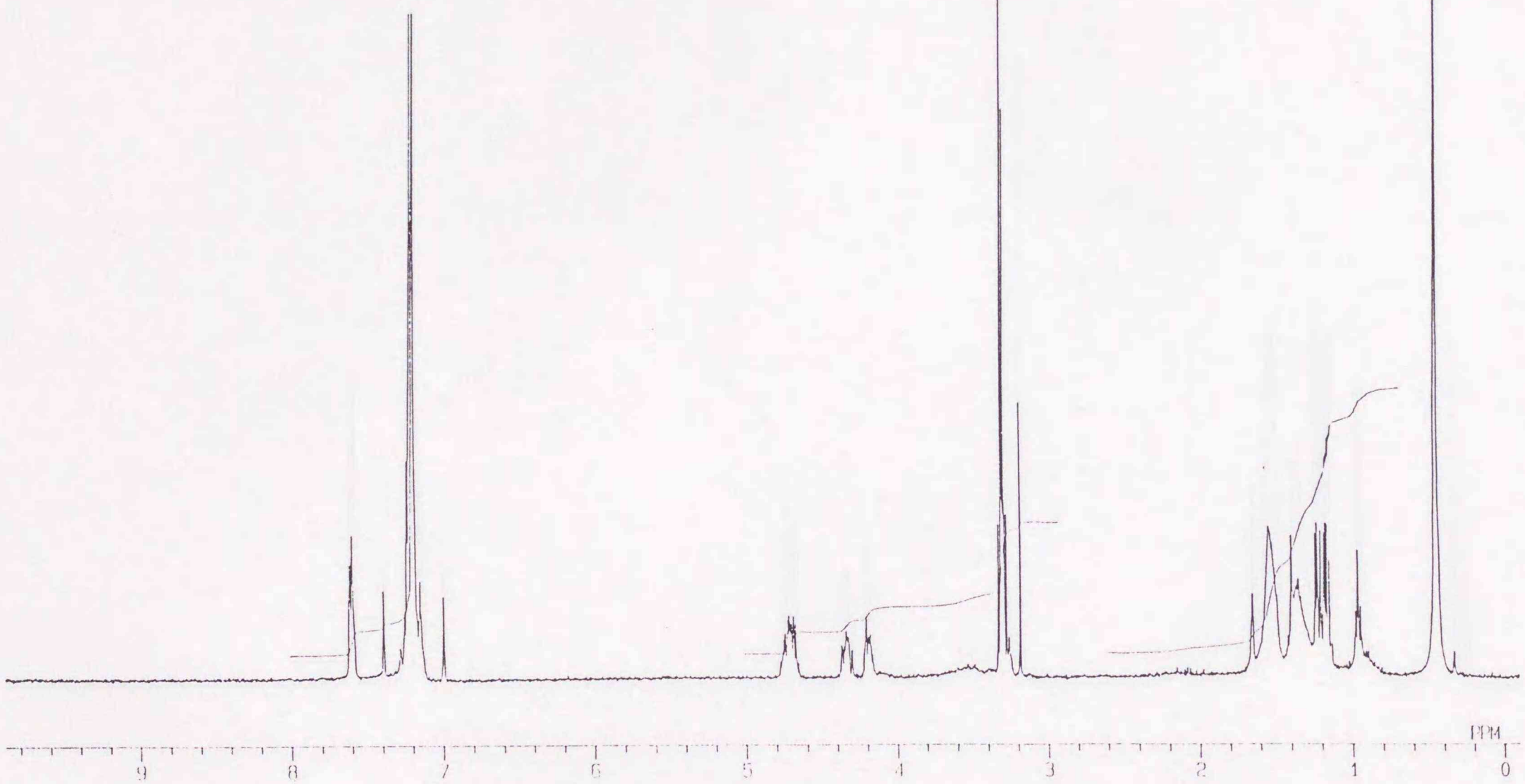


74c*R*



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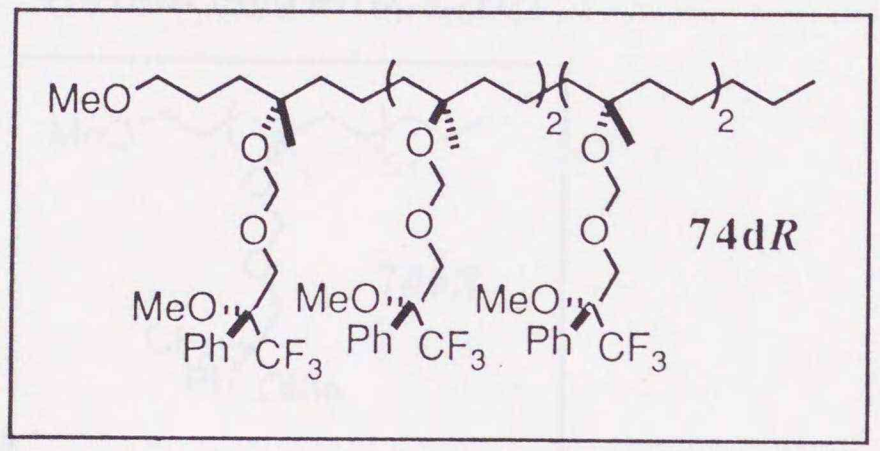
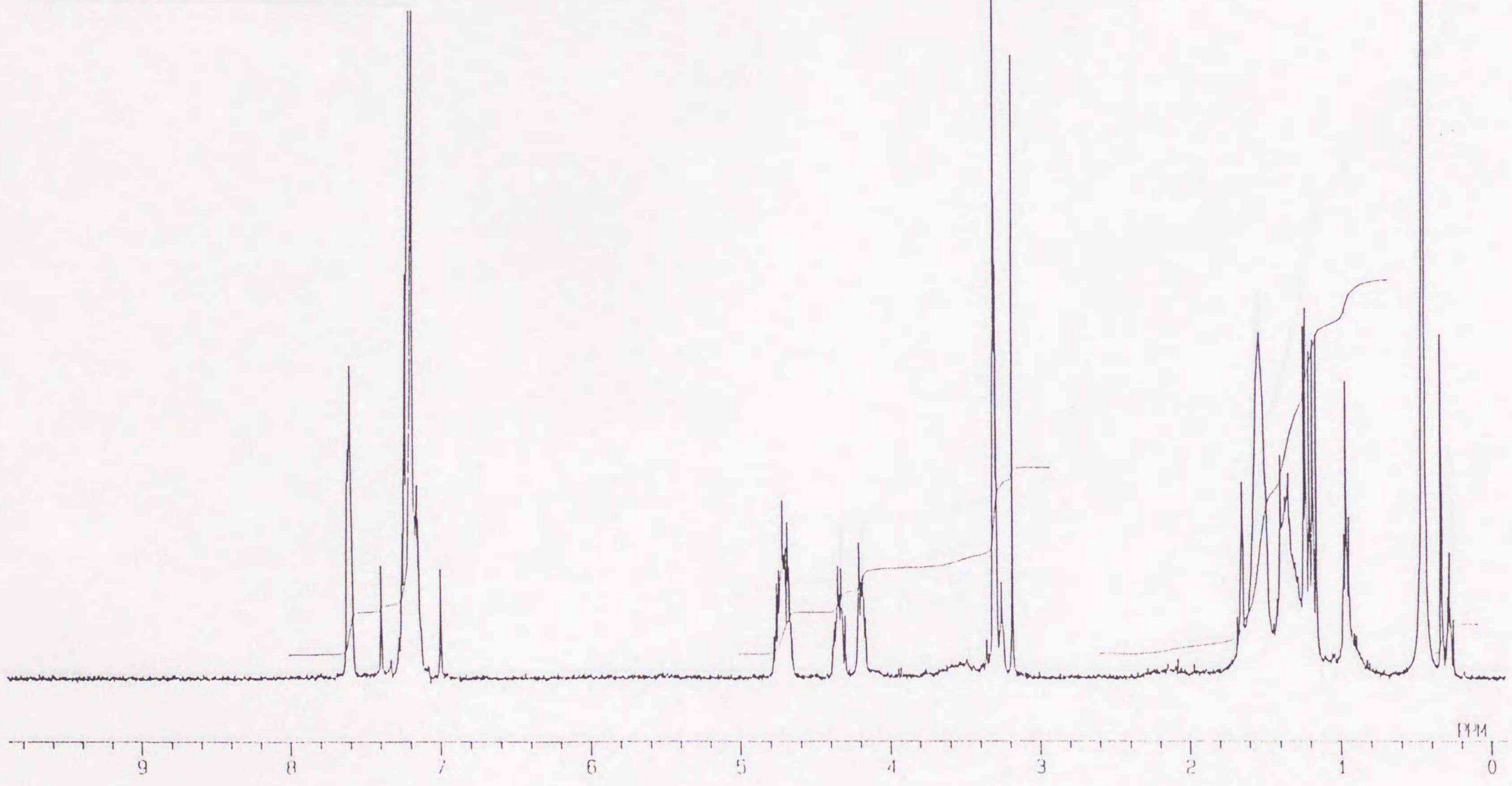


74d*R*



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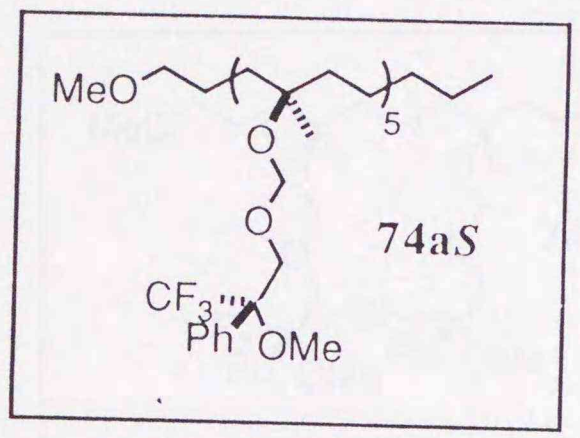
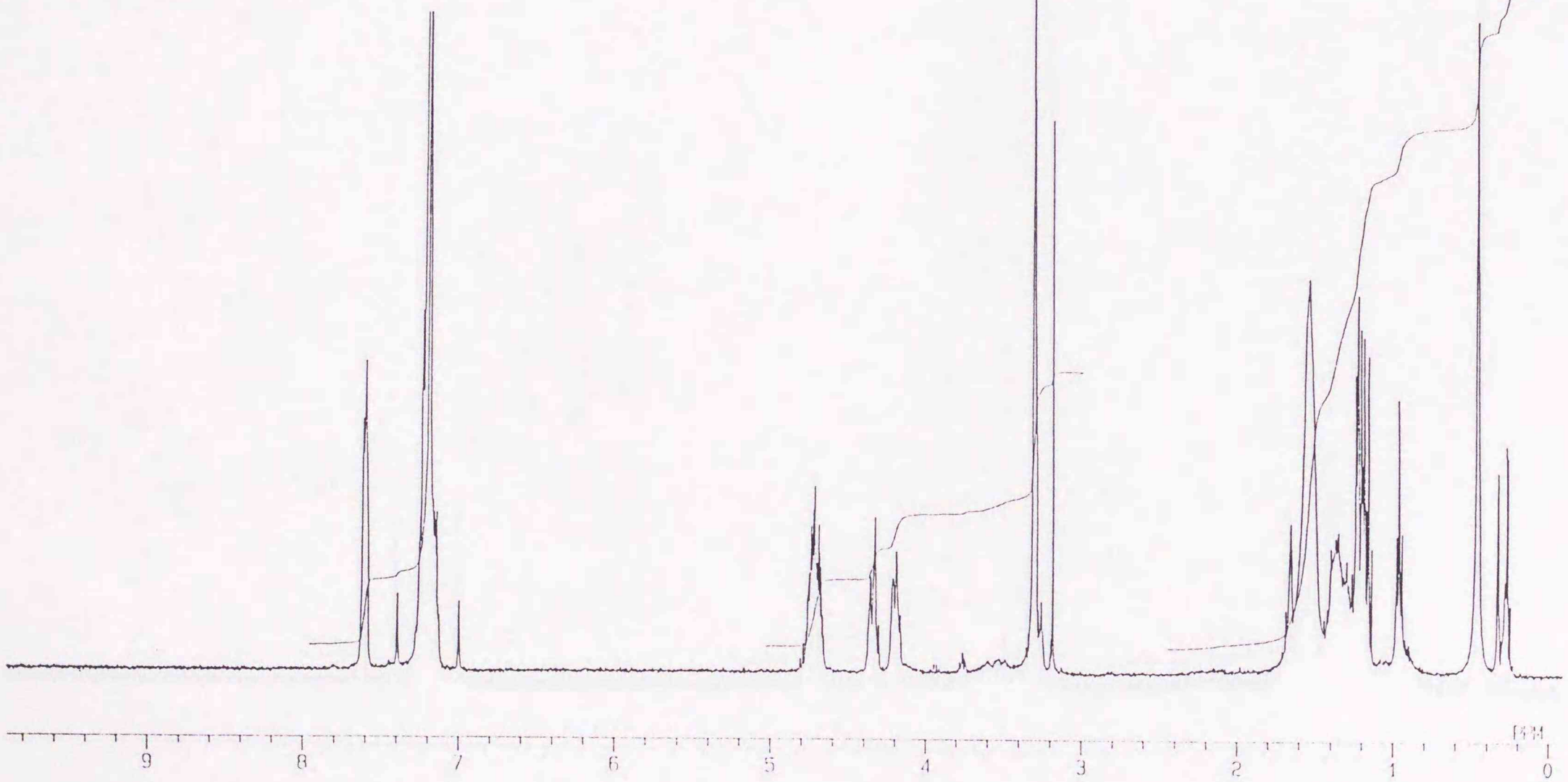


74a*S*



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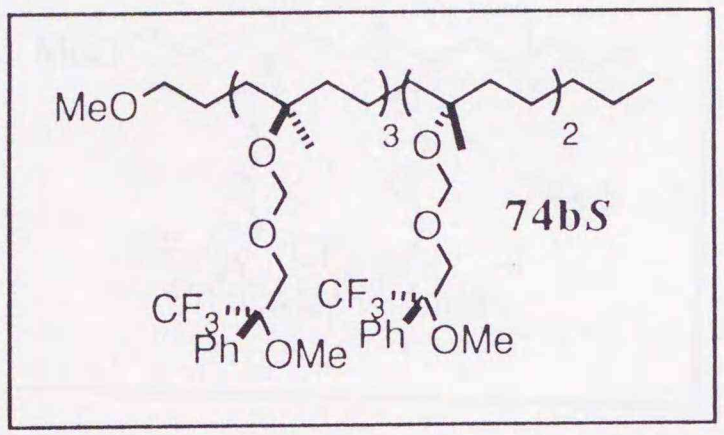

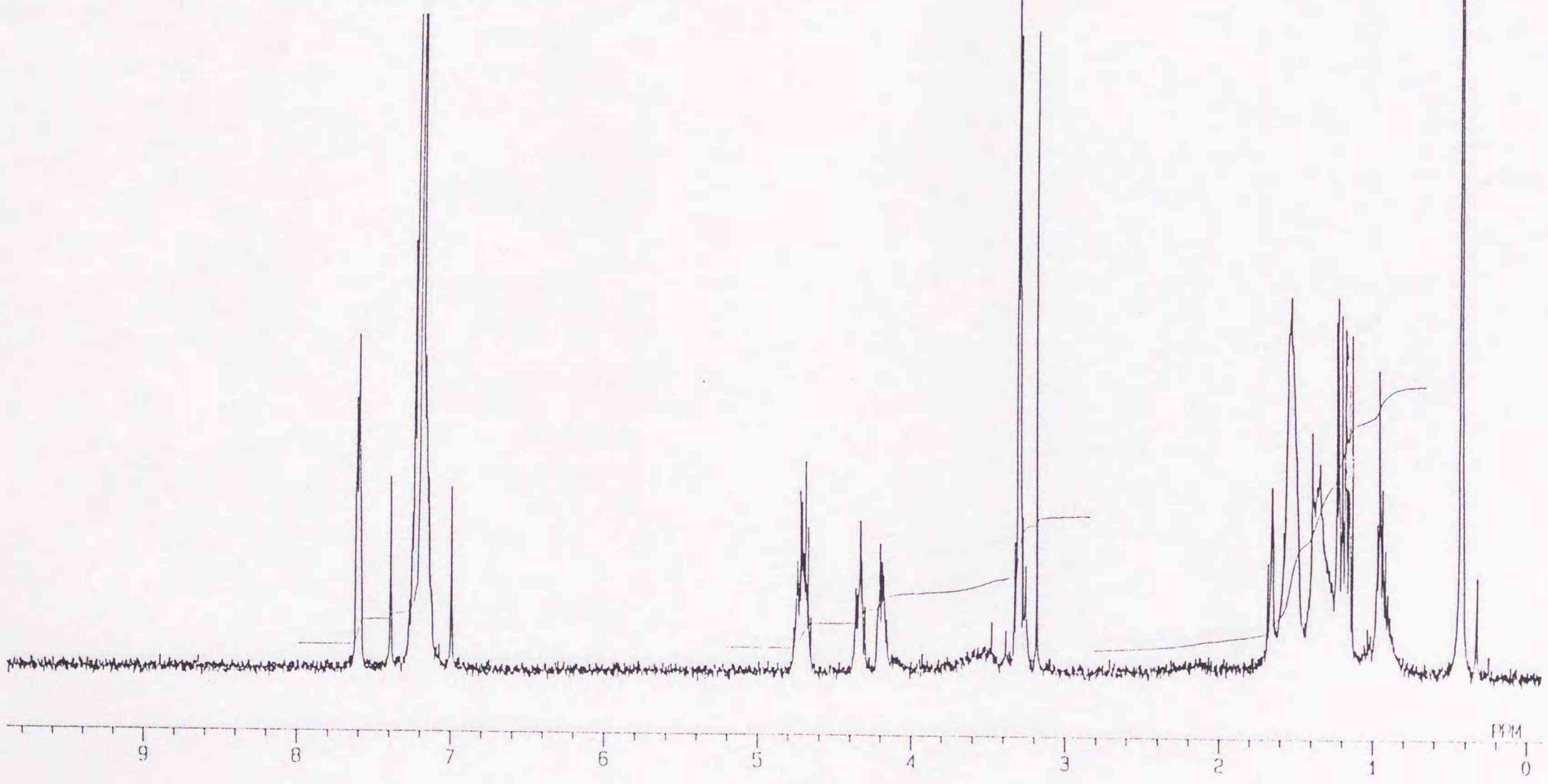

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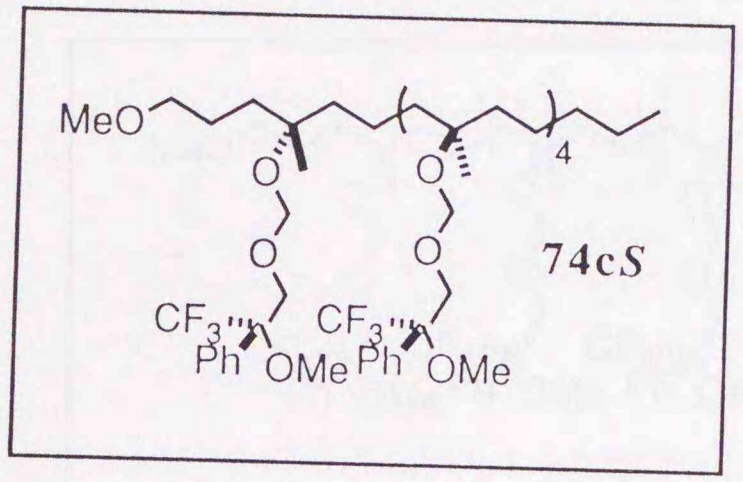

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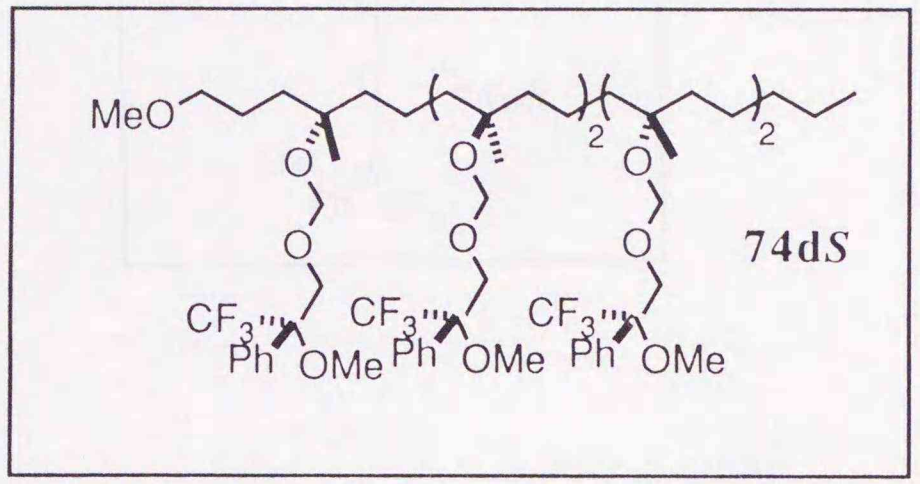
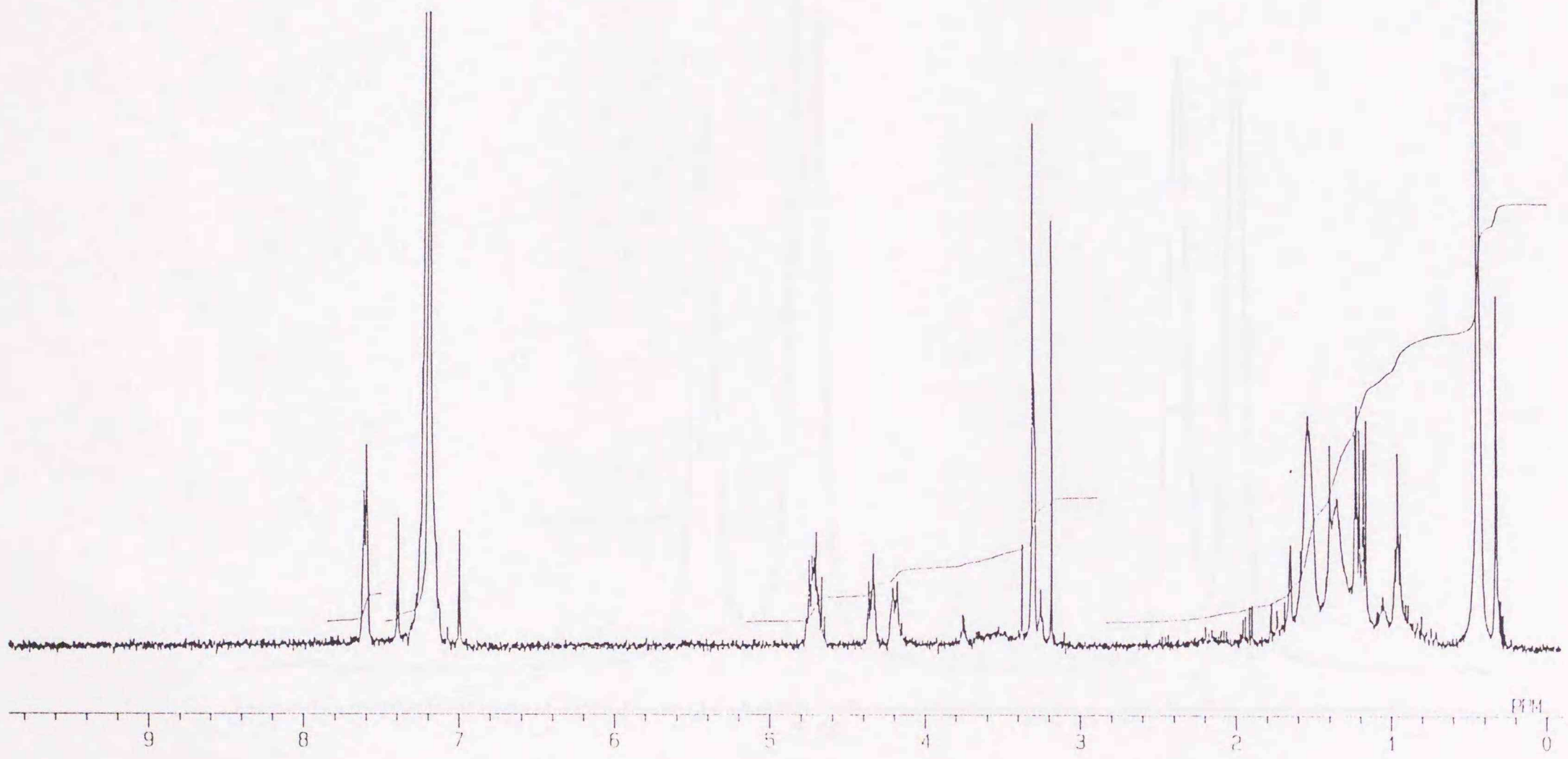
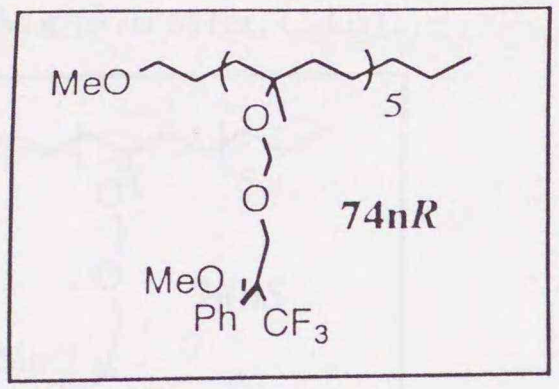


74dS

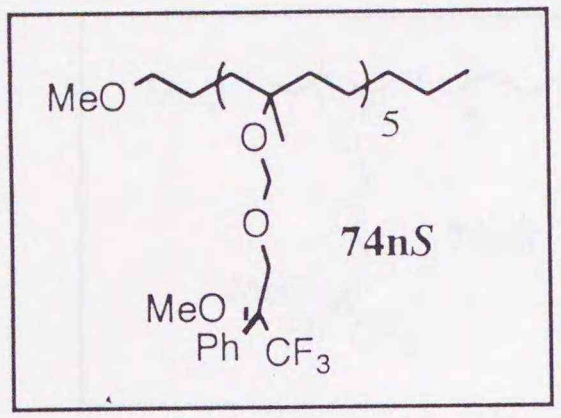


^{19}F-NMR (376 MHz, C_6D_6)

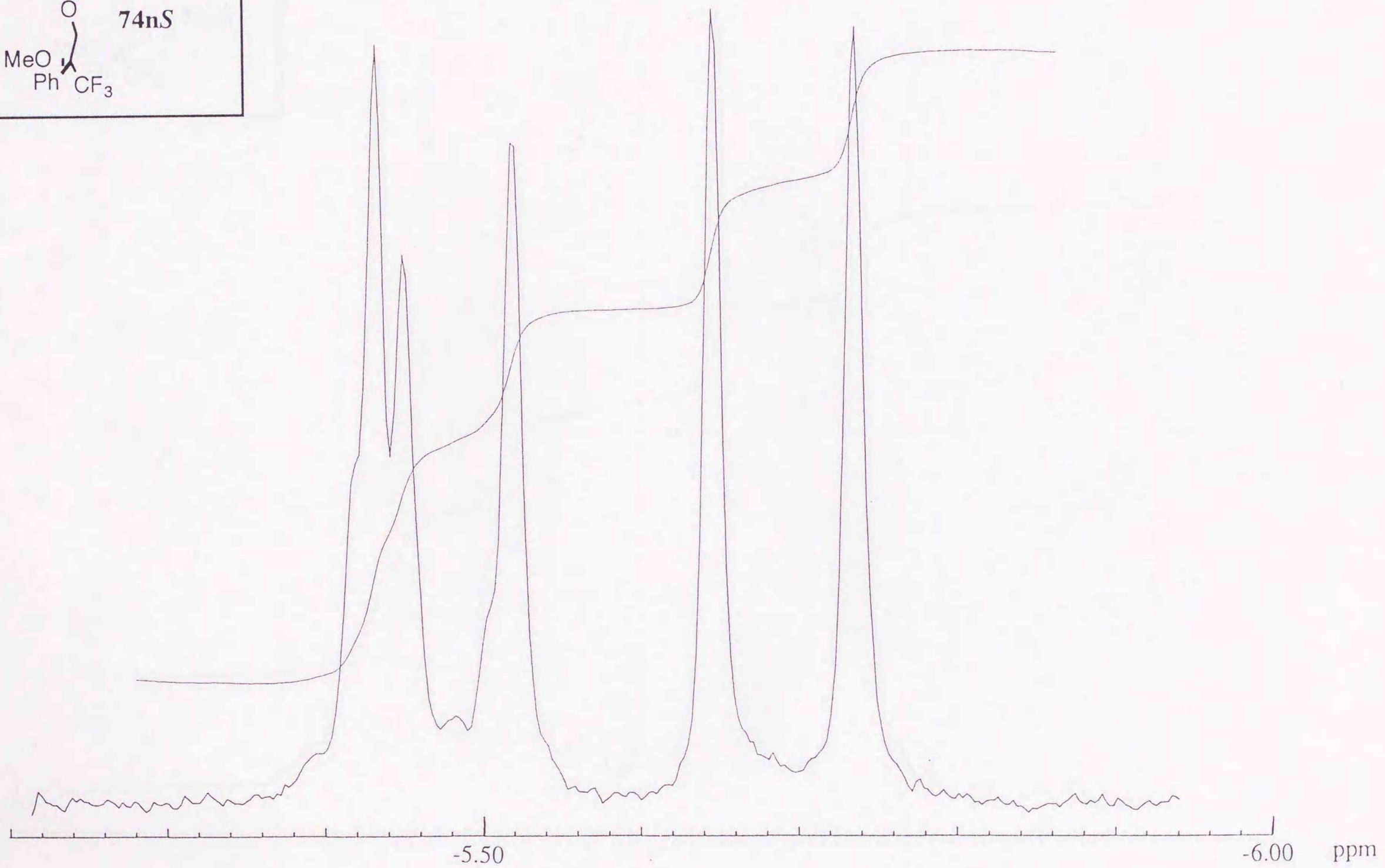


74n*R*

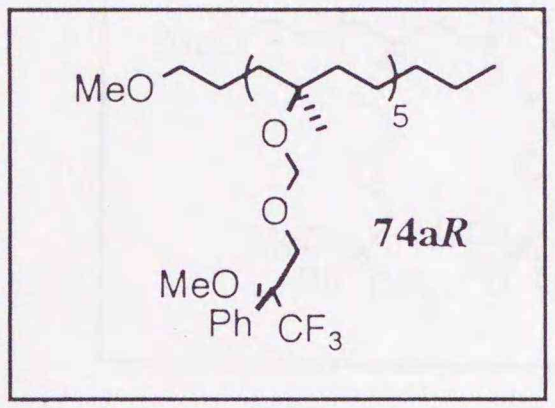
^{19}F-NMR (376 MHz, C_6D_6)



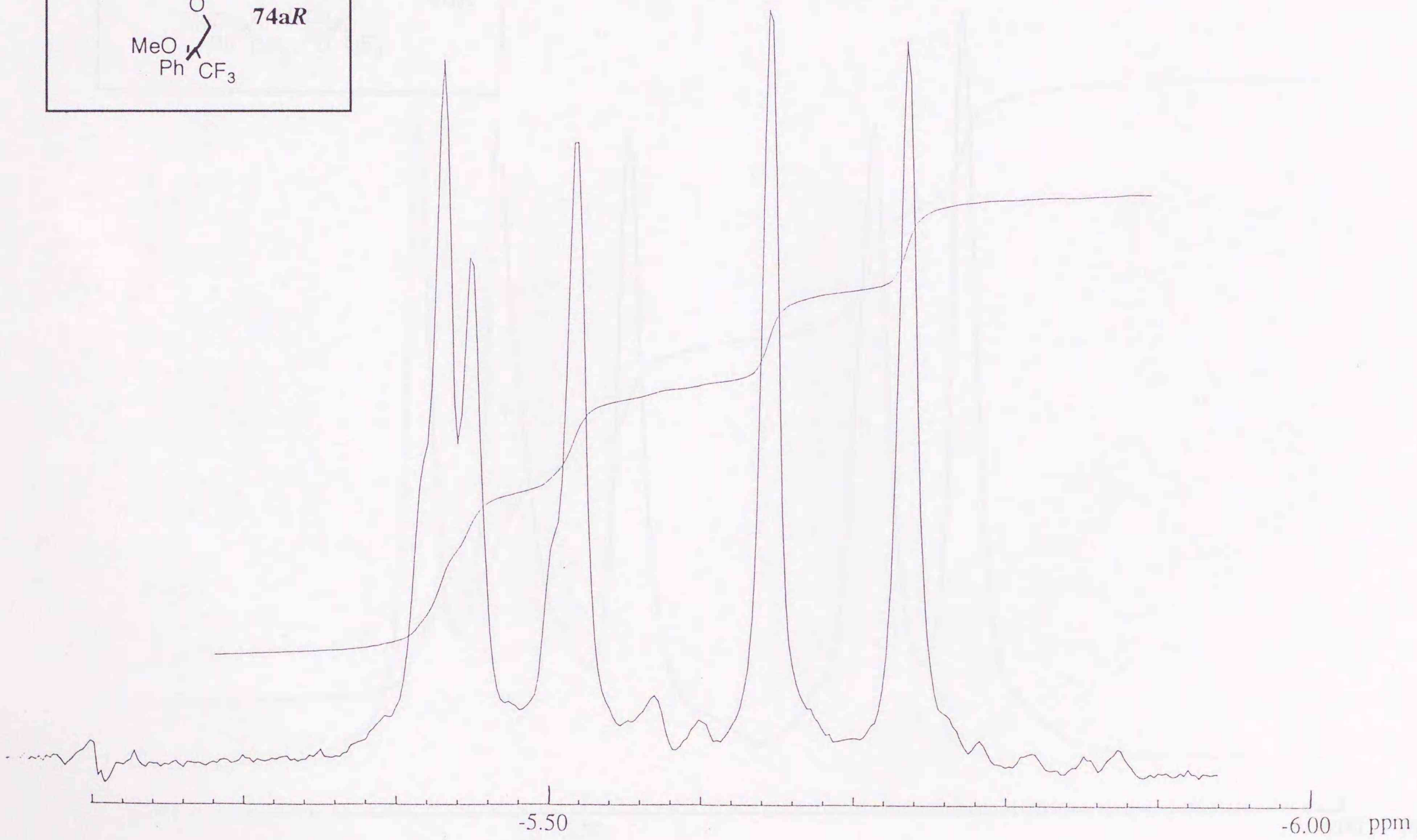
74n*S*



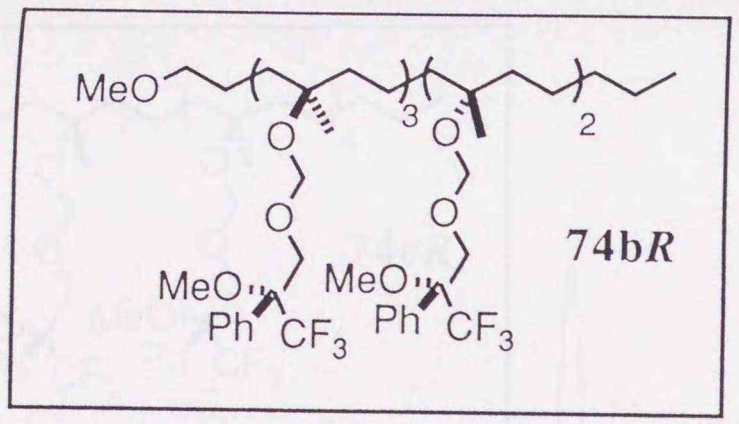
^{19}F-NMR (376 MHz, C_6D_6)



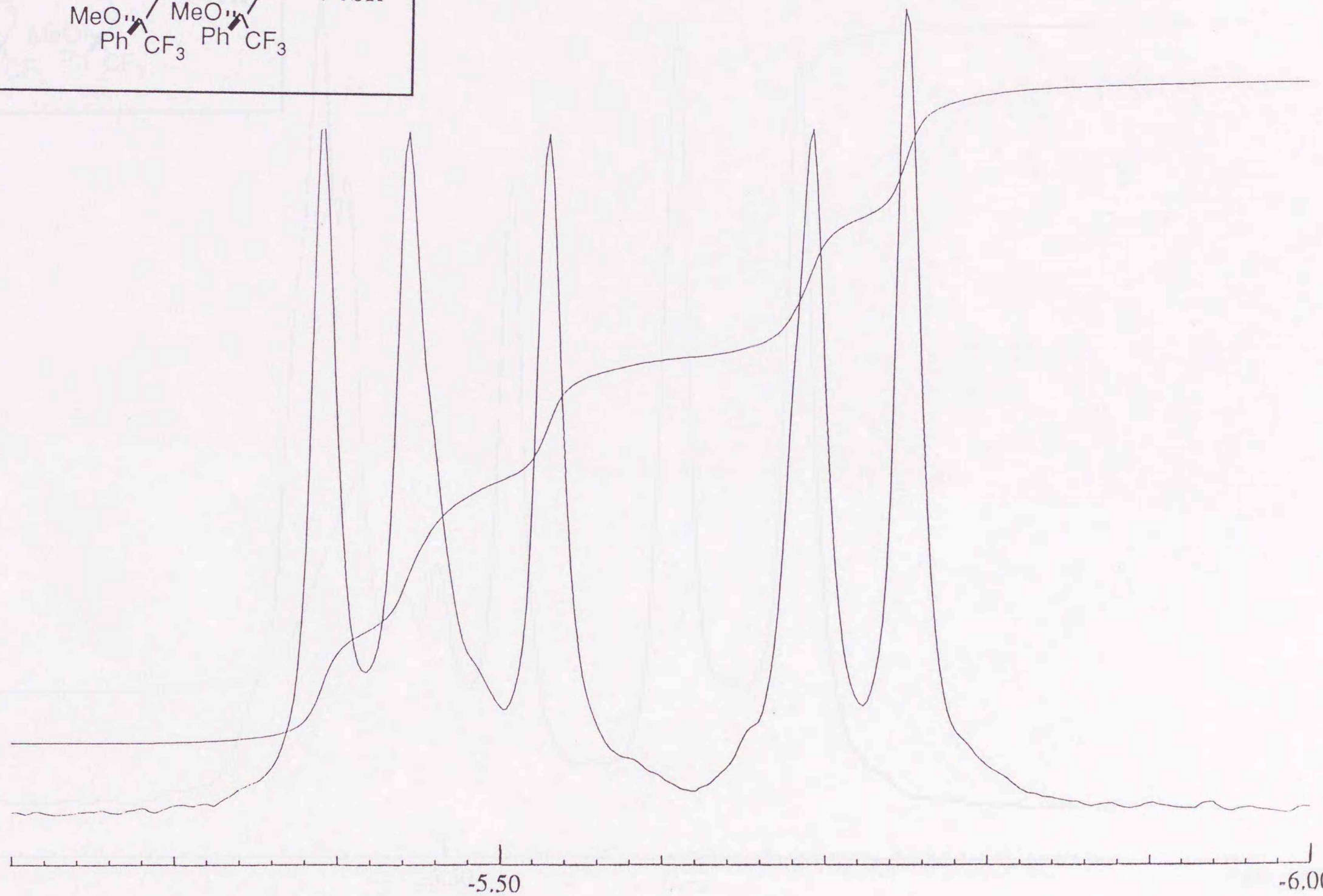
74a*R*



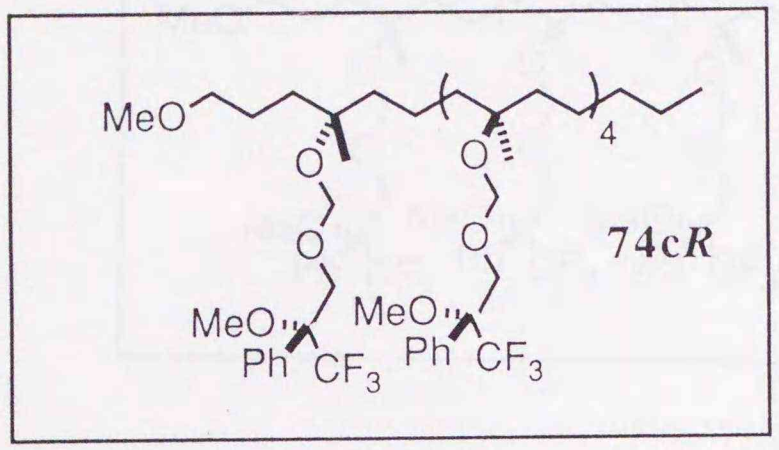
^{19}F-NMR (376 MHz, C_6D_6)

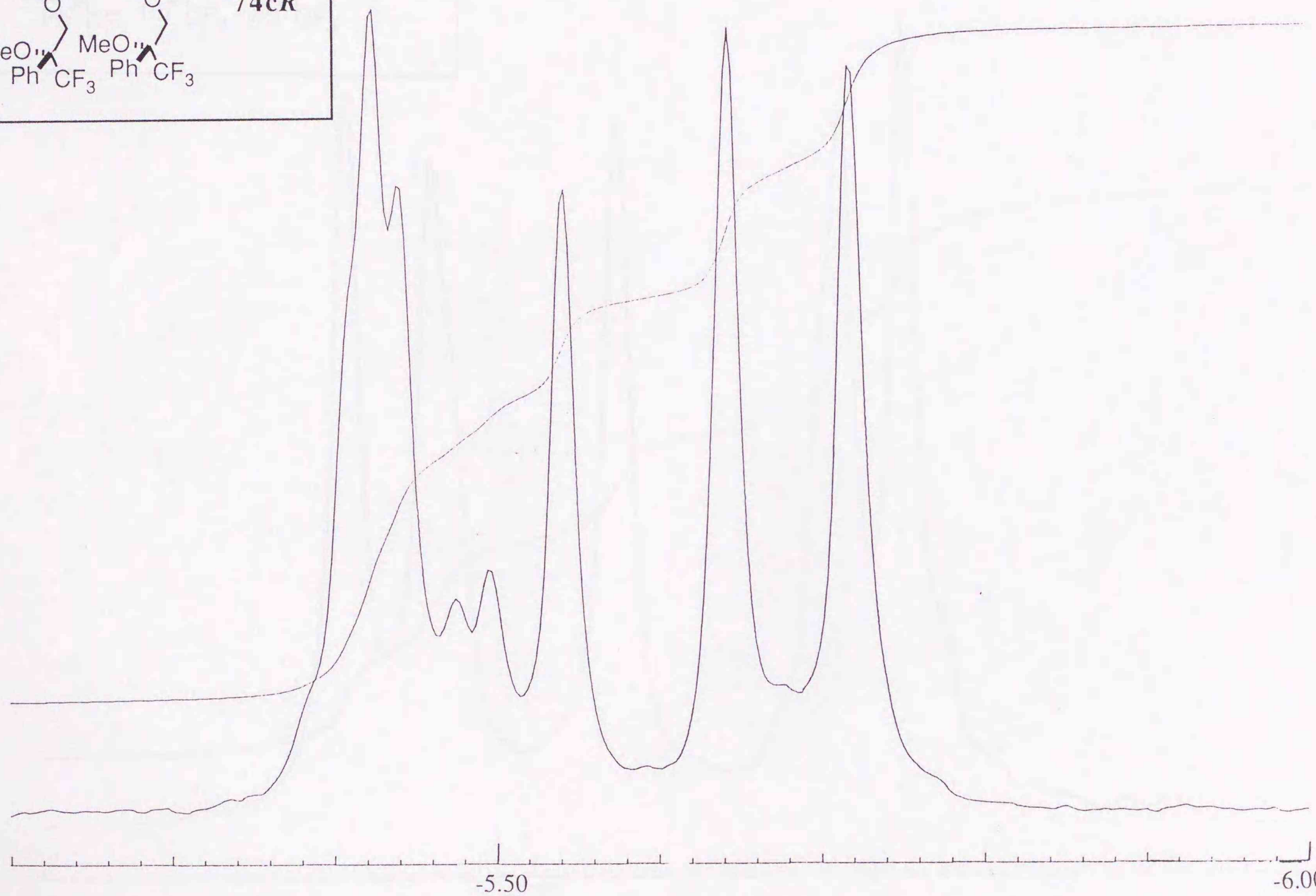


74b*R*

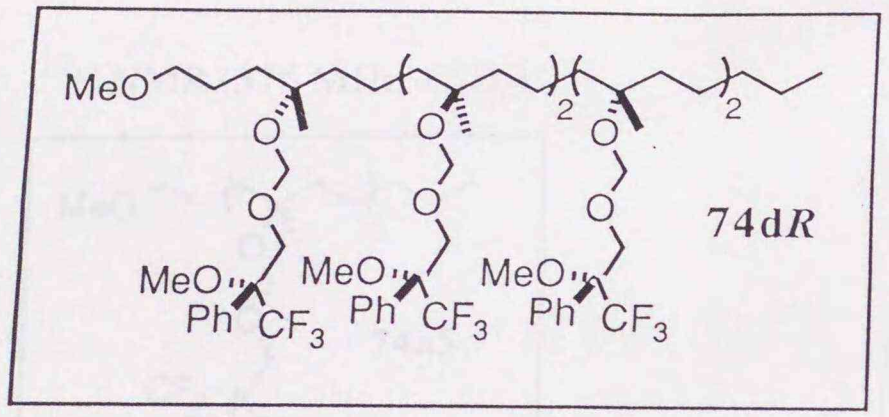


^{19}F-NMR (376 MHz, C_6D_6)

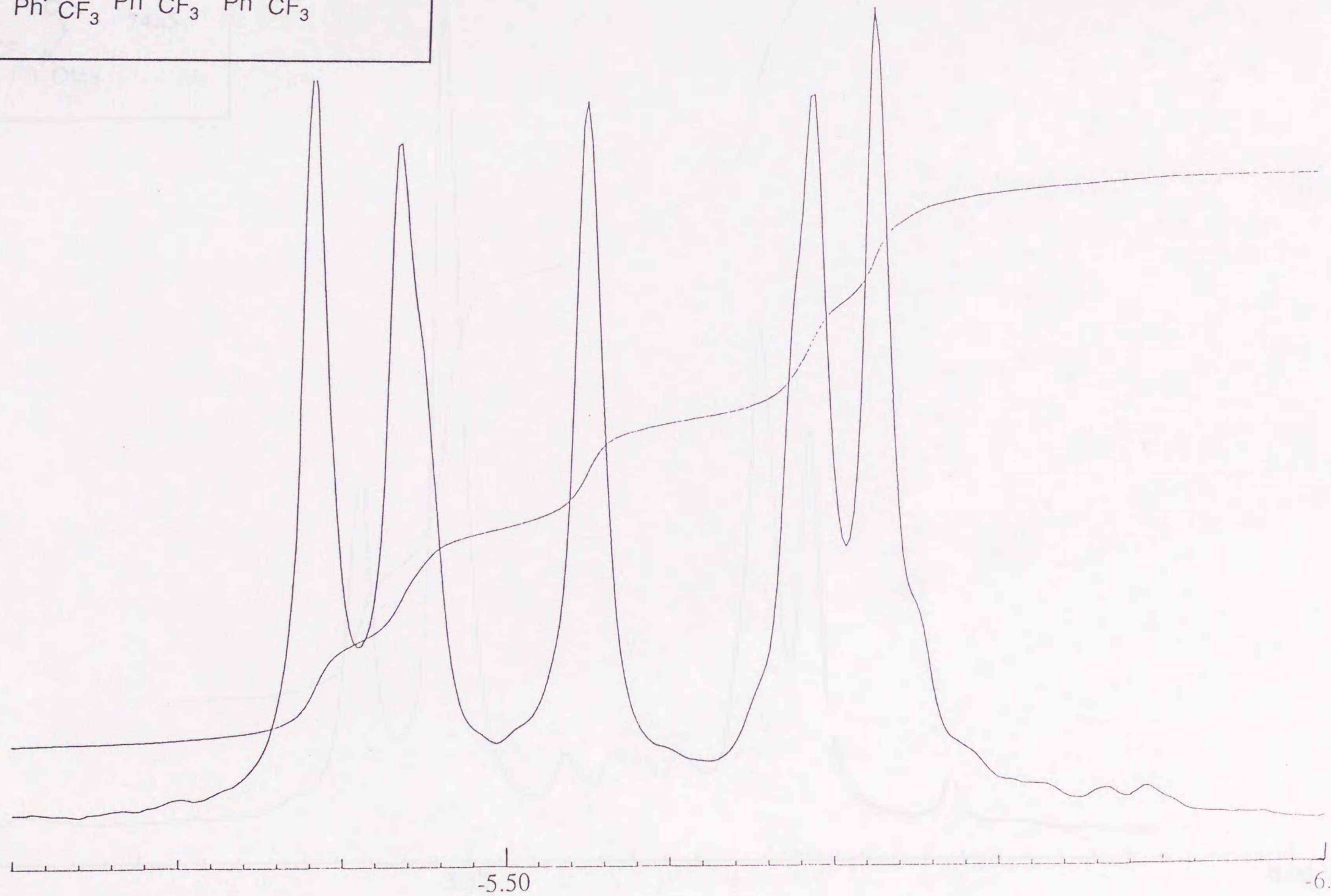




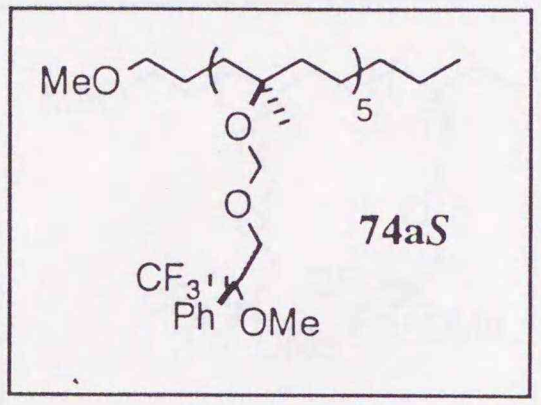
^{19}F-NMR (376 MHz, C_6D_6)



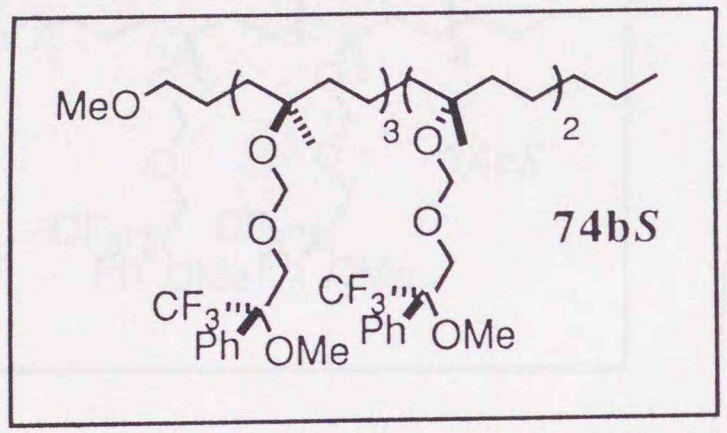
74d*R*

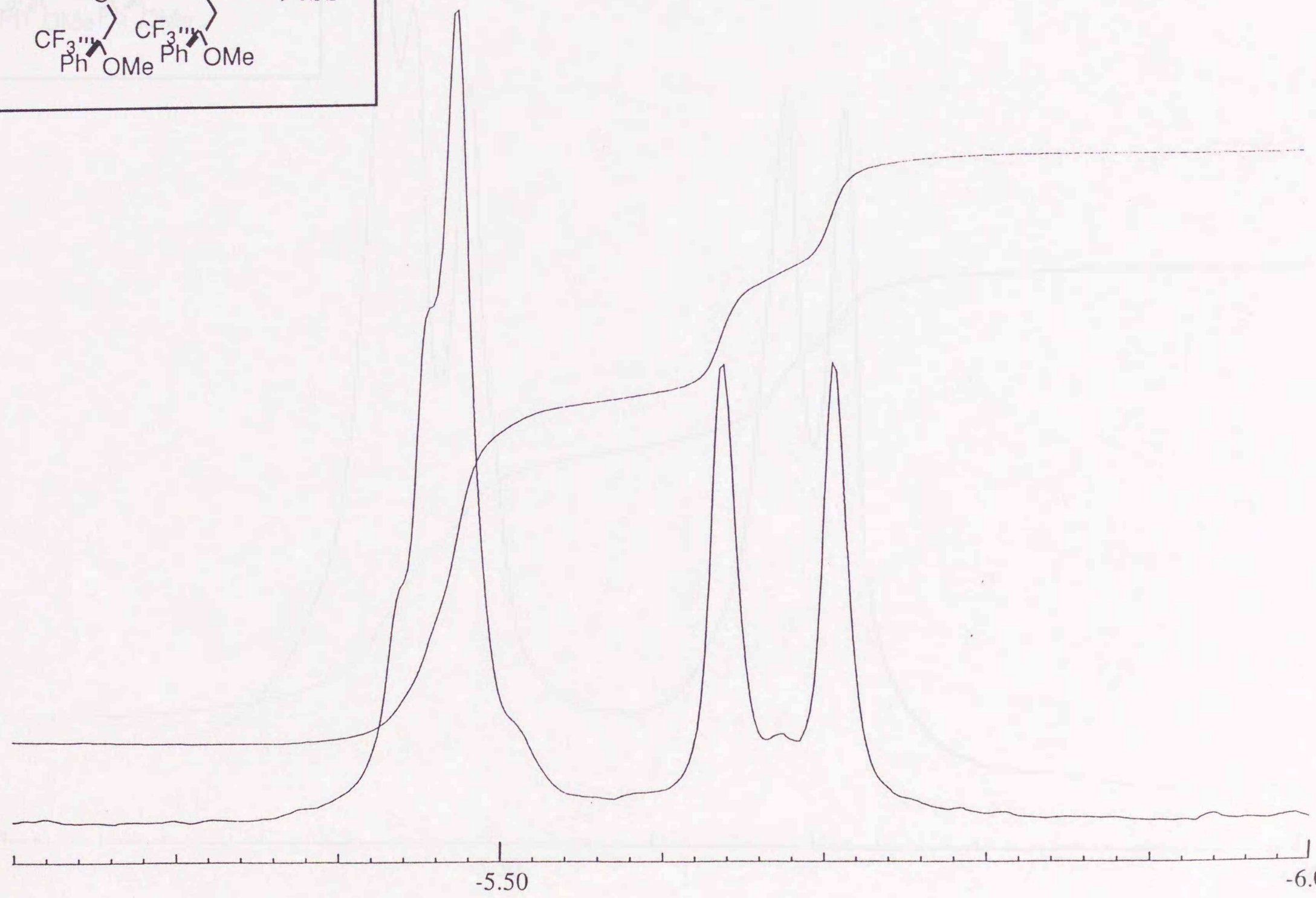


^{19}F-NMR (376 MHz, C_6D_6)



^{19}F-NMR (376 MHz, C_6D_6)





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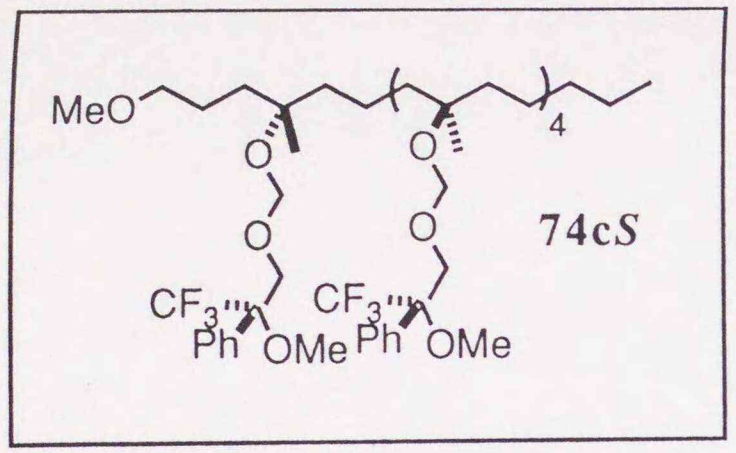

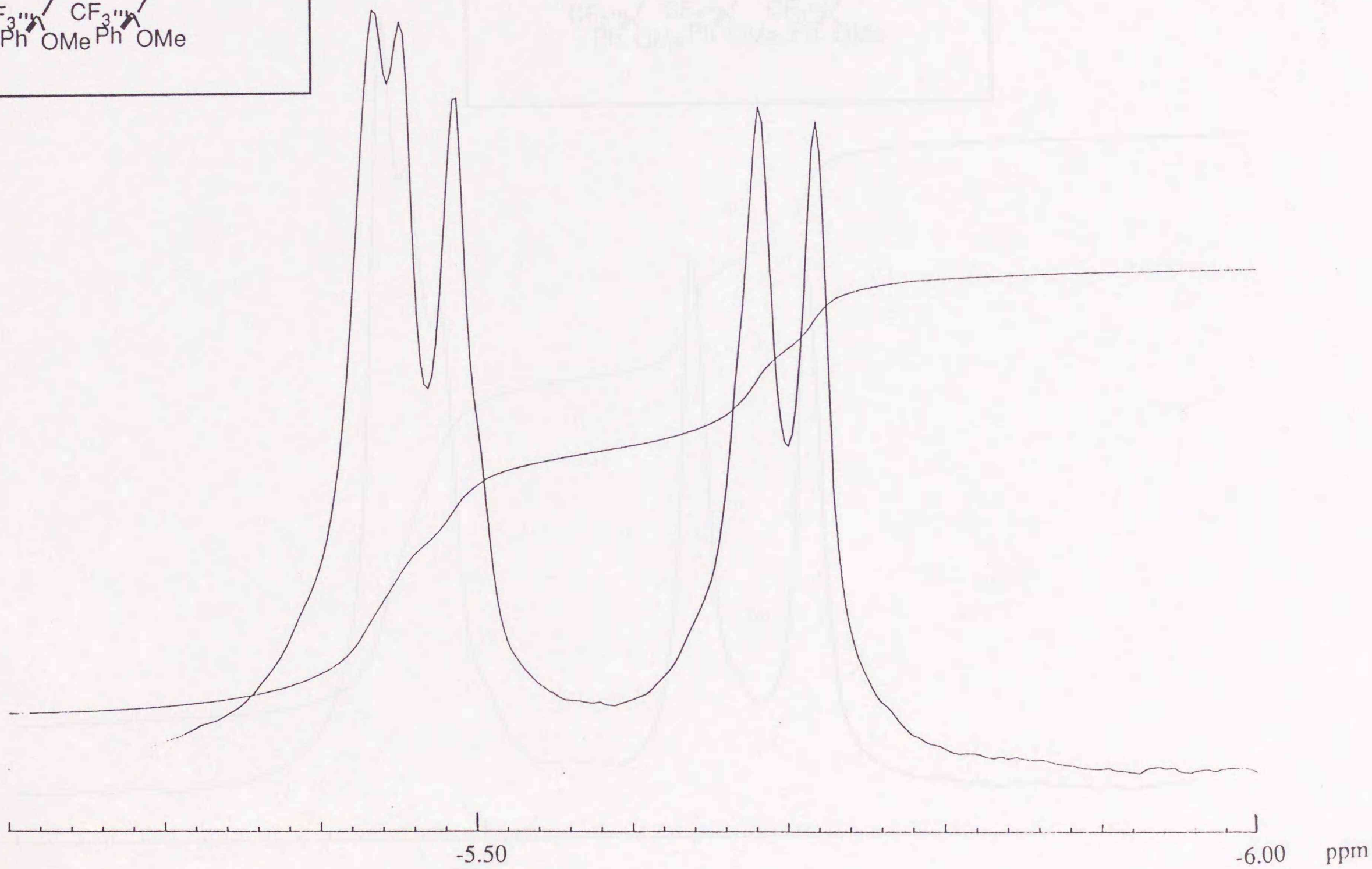

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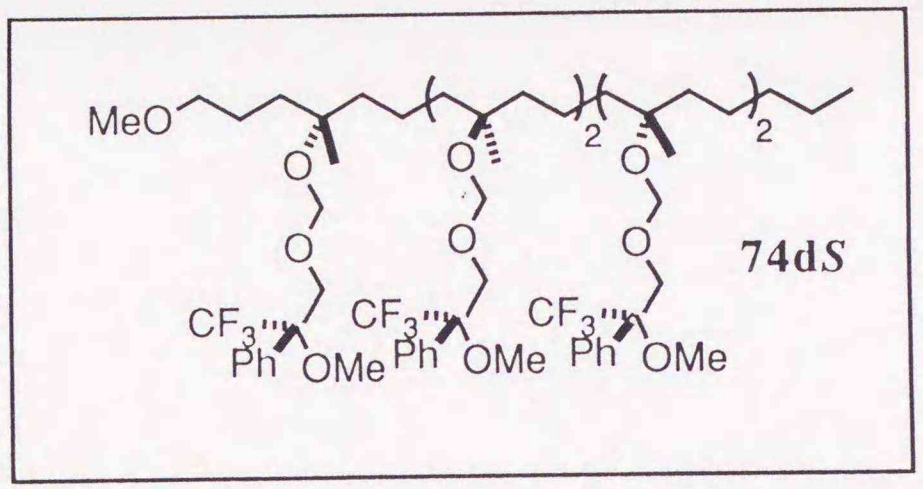
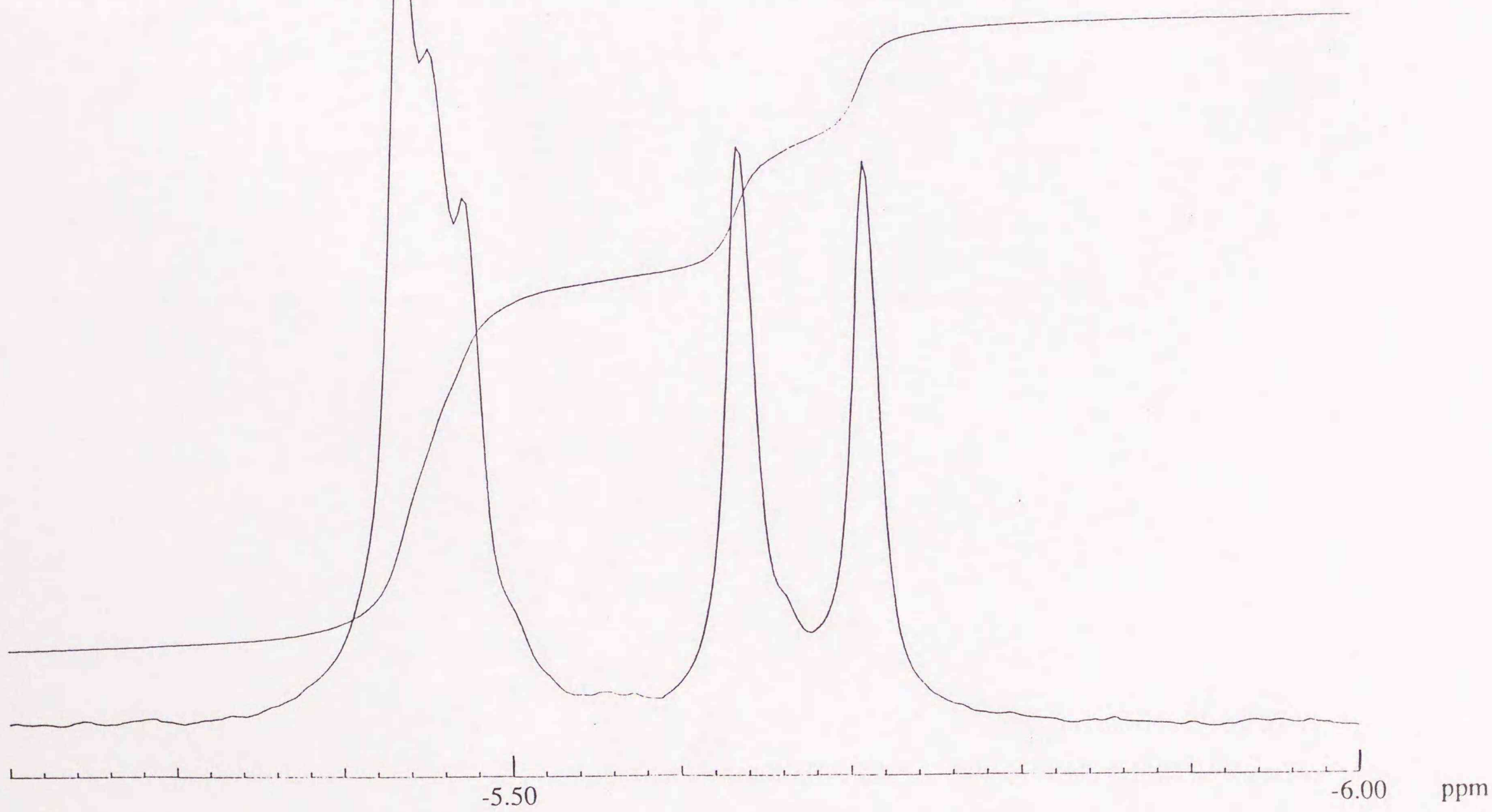
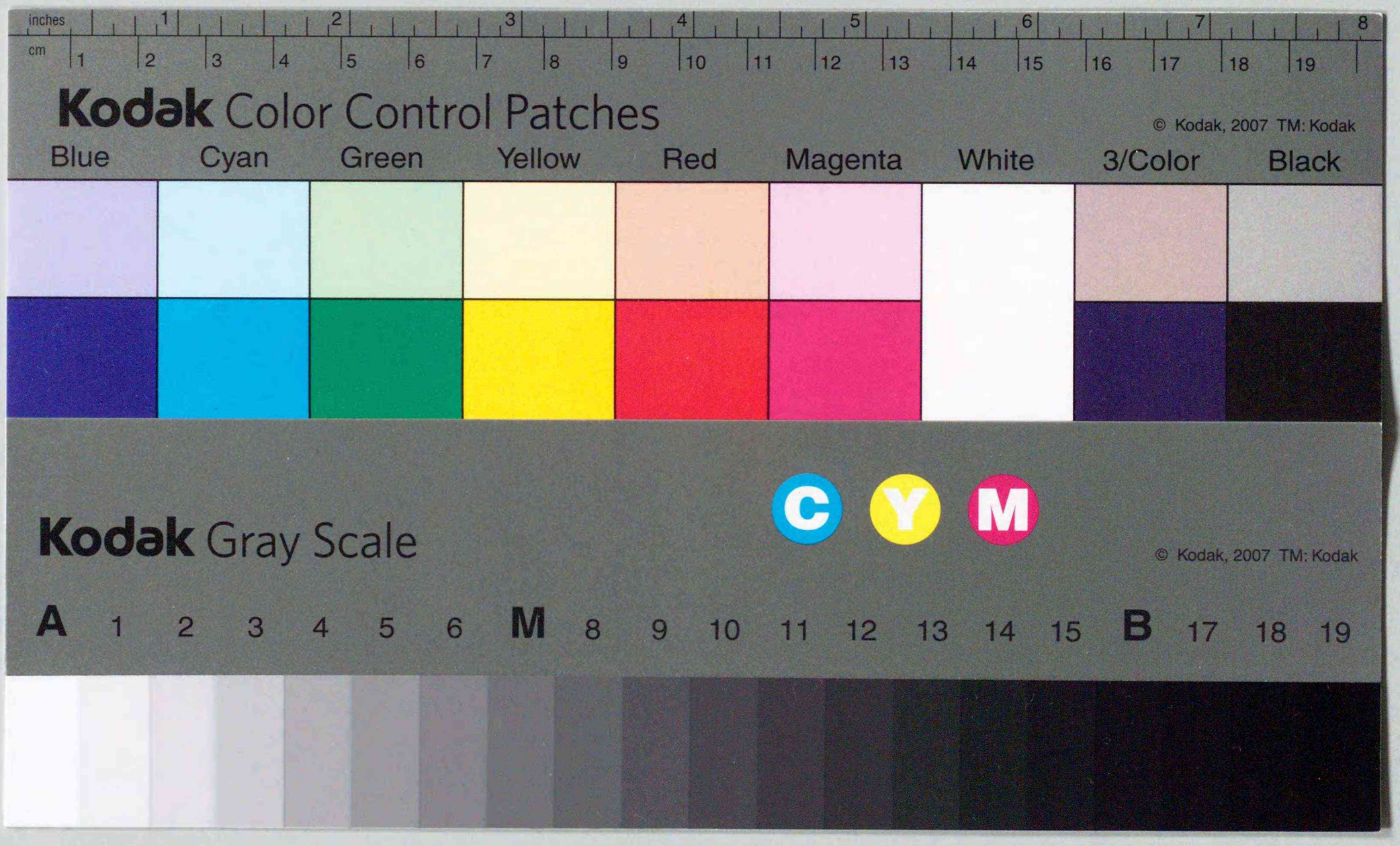


74dS

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Yellow
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A 1 2 3 4 5 6 M 8 9 10 11 12 13 14 15 B 17 18 19