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Combined Synthetic/CD Strategy for the Preparation and Configurational Assignments of Model Acyclic 1,3-Polyols With a 1,2-Diol Terminal

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ABSTRACT Acyclic 1,3-polyols or skipped polyols are widely distributed in nature. Particularly skipped 1,3-polyols with a terminal 1,2-diol group are present in numerous antifungal polyene macrolides in various masked forms.' Although over 200 polyene macrolides are known, the planar structures of only about 40 have been determined, while those for which the full stereochemistry has been elucidated is less than ten. No simple method exists for configurational assignments of the 1,3-polyols moieties; moreover, this class of compounds are difficult to crystallize. In order to develop a general chiroptical method for structure determination of acyclic 1,3-polyols, we have combined a divergent synthetic approach with CD to prepare all possible stereoisomers of 1,2,4-triols, 1,2,4,6-tetrols and 1,2,4,6,8-pentols. The current set of reference polyols should be useful for setting up reference CD libraries and for model studies leading to a general method for configurational assignment of acyclic polyols. This strategy can be used to synthesize further extended members of acyclic 1,3-polyols and mixed 1,2/1,3-polyols which can be used for structural investigations of polyene macrolides and related compounds.

KEY WORDS: 1,3-skipped polyols, synthesis, absolute configuration, exciton coupling, Circular Dichroism, diastereomers separation

INTRODUCTION

The polyene macrolides, a large class of natural products with potent antiviral and antifungal activities, have been employed in antifungal therapy. They are characterized by the presence of a large 16- to 44-membered lactone ring containing 3–8 conjugated carbon-carbon bonds, a 1,2/1,3-polyol unit and often a sugar moiety[1,2] (Fig. 1). Since the discovery of the first polyene macrolide nystatin in 1950,[3] over 200 members have been reported. Although the planar structures of ca. 40 have been determined, the full stereochemistry has been elucidated for less than ten.[4–9] The main difficulties in their structural analysis arise from the presence of numerous stereogenic centers and high conformational flexibility, this latter property making them difficult to crystallize. Several general methods that have been developed for their structure determinations consist of chemical cleavage such as ozonolysis, hydrolysis of lactone, etc., to 1,2/1,3-polyol units which are then submitted to chemical/spectroscopic analysis. A recent study describes an NMR method for relative configurational assignments of 1,3-polyols.[10] Two reiterative methods also have been published for assignment of the absolute stereochemistry of 1,3-skipped polyols.[11–14] However, both depend on multistep chemical transformations followed by extensive NMR and/or CD measurements of benzoates, which make them difficult for microscale manipulations.

Recently we have developed a series of bichromophoric CD methods[15,16] for microscale configurational assignments of different acyclic polyols and aminopolyols, e.g. 1,2-polyols derived from sugars,[17,18] and the more complex cases represented by bacteriohopanepentols,[19] aminobacteriohopanes,[20–22] and sphingosines.[23] These CD studies clearly showed that with flexible compounds it is preferable to explore the exciton coupling between two different chromophores with more intense absorption than simple benzoates, and also to measure the CD in two solvents with different polarities. The resulting CD spectra yield more characteristic information and facilitate the structural assignments. Acyclic 1,3-skipped polyols, on the other hand, possess specific features arising from their planar zigzag conformations, and lead to simplified patterns in the CD of their acylates. Thus, structural assignments of 1,3-skipped polyols by CD raise new problems that need to be solved. We have recently given a short account aimed toward addressing these problems.[24] Namely, CD spectra were measured after converting the primary and secondary hydroxyl groups of model 1,2,4,6-tetrols into the 9-anthroate and *P*-methoxycinnamate, respectively; this was accompanied by a chemical ketalization step using *l*-menthone to differentiate 1,3-*syn* and *anti*-diols.[25] Although promising, the method required further experimental verifications with more model compounds. In these studies, all possible diastereomeric polyols up to pentols were required to secure a reference CD library in order to

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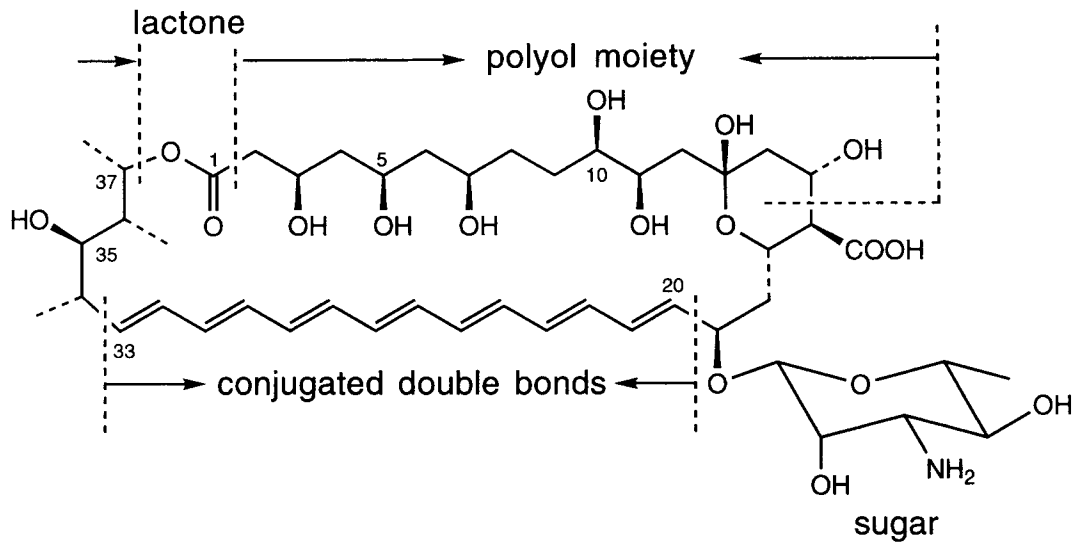
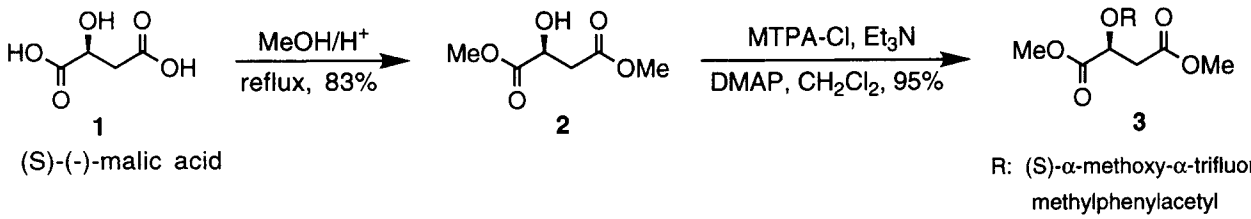


Fig. 1. Nystatin and the main structural subunits of polyene macrolides.



Scheme 1. Synthesis of Mosher's derivative 3.

delineate a common trend that could be used for configurational assignments of 1,3-polyols with a terminal 1,2-diol group.

In the following, a simple and general nonstereoselective synthetic procedure to create all possible stereoisomeric 1,3-polyols up to pentols, i.e., 1,2,4-triols, 1,2,4,6-tetrols, and 1,2,4,6,8-pentols, is described. Based on the synthetic strategy and the observed exciton coupled CD spectra of selected derivatives, the absolute configuration of each isomer was assigned unambiguously; these CD spectra also extend the reference 1,3-polyol CD library.[24]

MATERIALS AND METHODS

Enantiomeric Purity of (S)-(−)-Malic Acid

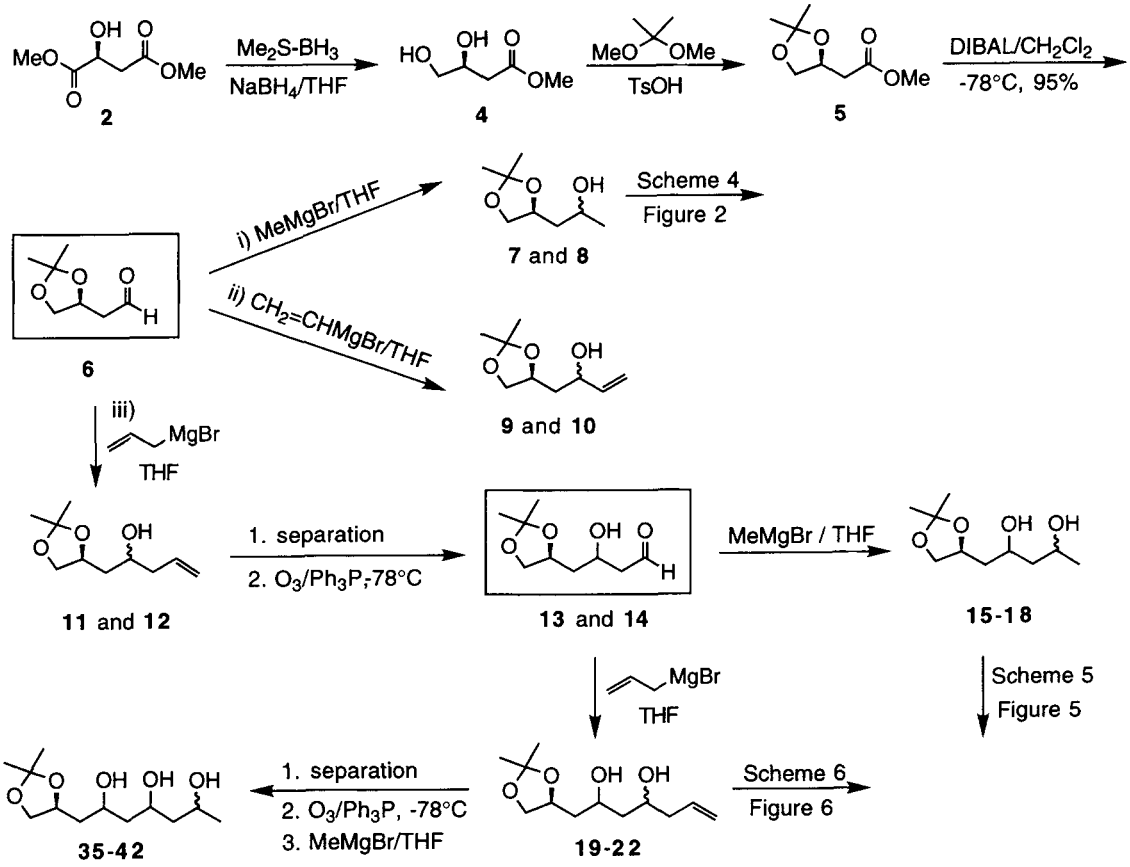
The model acyclic 1,3-polyols were synthesized from commercial (S)-(−)-malic acid **1**, the enantiomeric purity of the starting malic acid was confirmed by using Mosher's reagent. Dimethyl malate **2**, prepared by Fisher reaction in 83% yield, was reacted with Mosher's reagent to yield derivatized dimethyl malate **3** (Scheme 1). The enantiomeric purity of malic acid and the absence of any racemization during the Fisher reaction were checked by ^{1}H NMR of **3**.

1,2,4-Triols, 1,2,4,6-Tetrols, and 1,2,4,6,8-Pentols

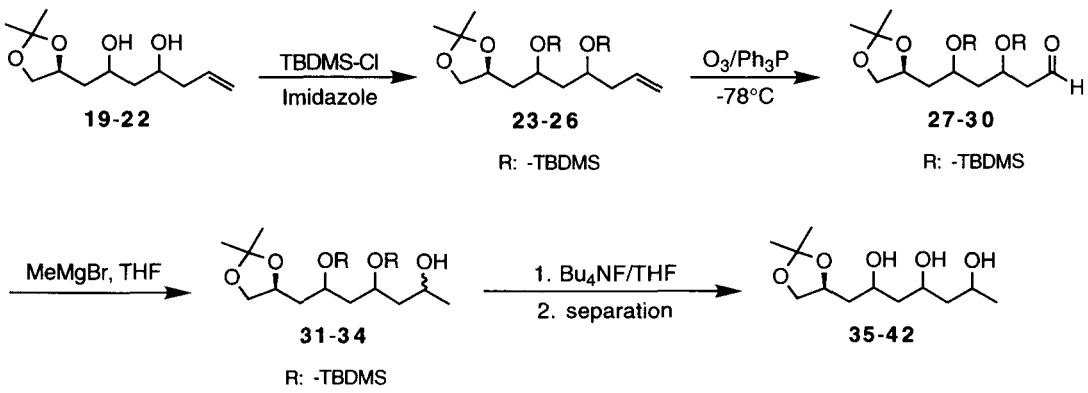
Dimethyl malate **2** was regioselectively converted to diol **4** by borane-dimethyl sulfide complex (BMS)[26] in the presence of catalytic amount of sodium tetrahydroborane (Scheme 2). Protection of diol **4** gave **5**, which was reduced with DIBAL to afford aldehyde **6**. This aldehyde was the chiral building block for the entire polyol series. Treatment of **6** with different Grignard reagents led to different polyols: (i) methyl magnesium bromide gave two model triols **7** and **8** in a 1:1 ratio; (ii) vinyl magnesium bromide gave two allylic triols **9** and **10** used for further 1,2-diol extensions;[27] and (iii) allyl magnesium bromide gave two homoallylic triols **11** and **12** used for further 1,3-diol extensions.

Separation of diastereomers **11** and **12**, followed by ozonolysis yielded, respectively, aldehydes **13** and **14**, which were used as building blocks for further polyol elongations. After separation, treatment of **13** and **14** with methyl magnesium bromide gave four model tetrols **15/16** and **17/18**, respectively. For further preparation of 1,2,4,6,8-pentols, allyl magnesium bromide was reacted with **13** and **14** to give homoallyl tetrols **19/20** and **21/22**, which after a further cycle of diastereomer separation/ozonolysis/Grignard addition yielded the eight reference pentols **35–42**.

In the synthesis of model pentols (or higher homologous polyols) the final acetonide protected polyols are quite polar and water soluble. In order to improve the hydrophobicity of the intermediates and to facilitate the workup procedure after the Grignard addition, protecting/deprotecting steps were used in the final stage of the pentol synthesis (Scheme 3). Protection of tetrols **19–22** by TBDMS afforded **23–26**.



Scheme 2. Synthesis of 1,3-polyols with 1,2-diol terminal, Part 1.

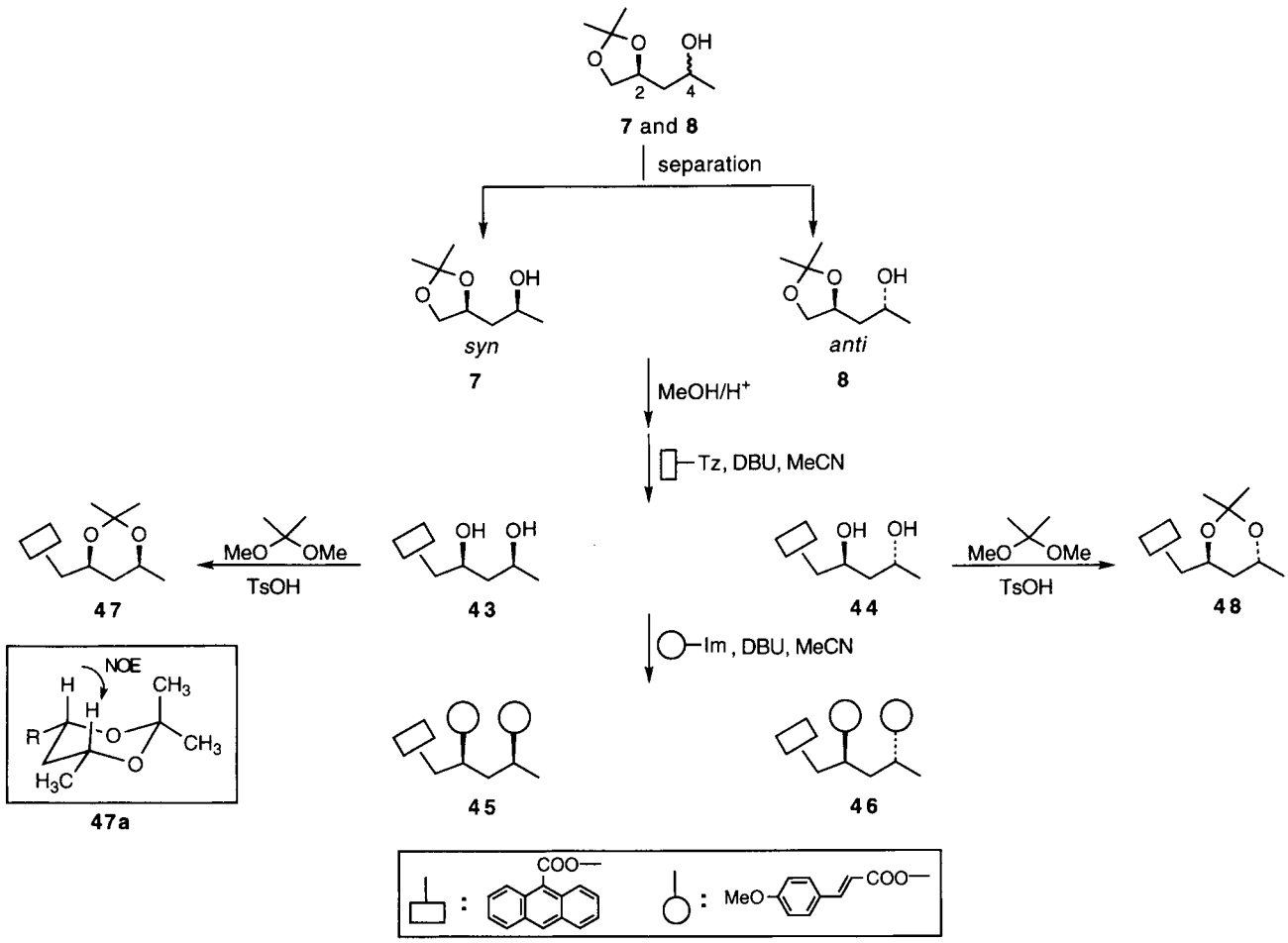


Scheme 3. Synthesis of 1,3-polyols with 1,2-diol terminal, Part 2.

Ozonolysis followed by Grignard addition led to **31–34**; treatment of **31–34** with tetrabutylammonium fluoride followed by diastereomer separation afforded model pentols **35–42**.

Mono- and Bichromophoric Polyol Derivatives

After separation of the diastereomeric pair **7/8** and acetonide cleavage, the model triols were converted into corresponding bichromophoric derivatives **45** and **46** by selective anthroylation of the primary alcohol with 9-anthroyl tetrazole to diols **43/44** which were then treated with *P*-methoxycinnamoyl imidazole (Scheme 4). For NMR studies, diols **43/44** were converted into 1-anthroate-2,4-acetonide triols **47** and **48** (Scheme 4). Prior to stereochemical analysis by CD, reference tetrols **15–18** were converted into corresponding dicinnamates **49–52** (Scheme 5). Similarly, with the view of assigning the absolute configurations, the homoallylic tetrols **19–22** and pentols **35–42** were converted into corresponding dibenzoates **53–56** and tribenzoates **57–64**, respectively, by dimethylaminobenzoylation (Scheme 6).



Scheme 4. Derivatization of 1,2,4-triols.

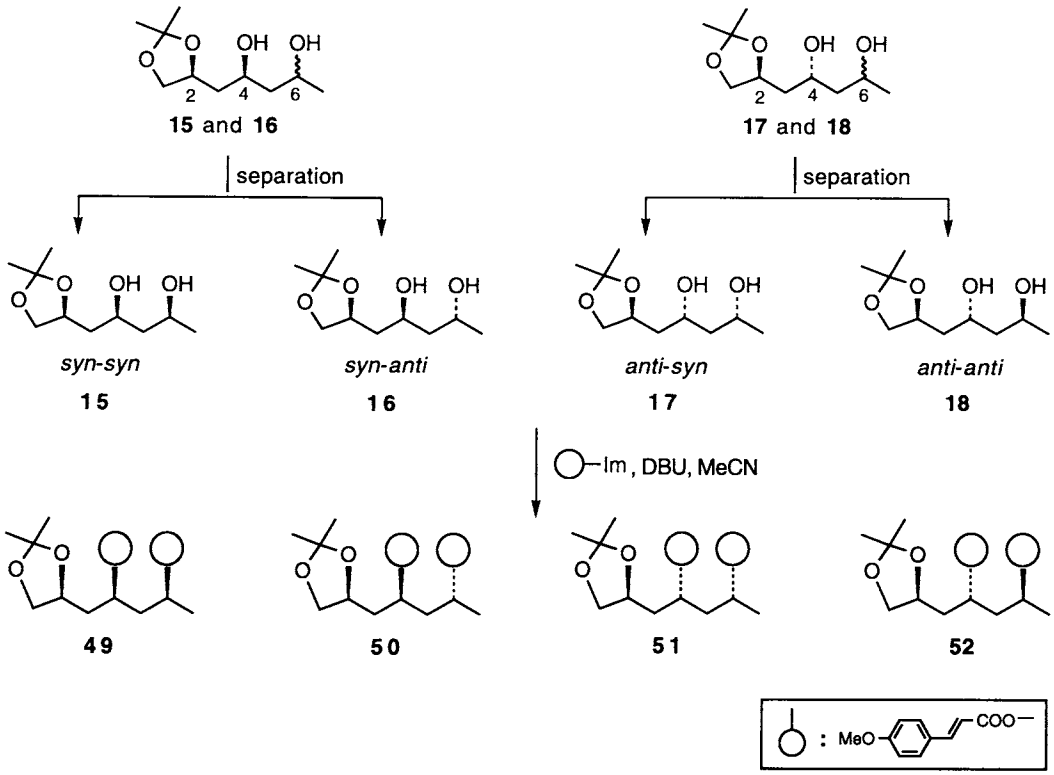
RESULTS AND DISCUSSION

Over the past 25–30 years the exciton chirality method has been extensively applied to absolute configurational assignment of rigid cyclic compounds.[15] More recently, its utility has also been proven for acyclic and conformational flexible molecule.[13,14,16–24,28] Although the exciton coupling between identical chromophores, e.g., benzoates, have been successfully used in both cyclic and acyclic series, recent data point out that coupling between different chromophores is more useful in acyclic cases because they give CD spectra which uniquely represent their stereochemistry.[20–22,29]

Recently, two types of exciton chromophores were introduced to selectively derivatize hydroxyl groups in acyclic 1,2-polyols and 1,2,4,6-tetrols: 9-anthroate (Anth) for the terminal primary hydroxyl and *p*-methoxycinnamate (Cin) for secondary hydroxyls. It was found that in all anthroate/cinnamate derivatives, the sign of the 252 nm Cotton effect (CE) originating from the intense coupling between the 1-anthroate and the 2-methoxycinnamate, reflects the C-2 configuration. Namely, a positive CE at 252 nm (positive shorter wavelength counterpart of negative couplet) shows that the transition moments of 1-anthroate and 2-cinnamate are coupled in an anticlock-wise sense as shown in Figure 2 for **45** and **46**, both having S configuration.[29] Thus, the sign of this anthroate/cinnamate coupling is independent of the configurations at remaining chiral centers. This regularity is found to be true for all 1,2- and 1,3-polyols containing 1,2-diol moiety.[20–22,30,31]

However, the remaining cinnmate/cinnamate exciton couplets bear specific features for each type. The "fingerprint" region ca. 280–320 nm results from the 1,2- and 1,3-cinnamate/cinnamate (Cin/Cin) couplings. The CDs of coupled cinnamate groups for 1,2- and 1,3-diacylates are shown in Figure 3. In acyclic 1,2-dicinnamates (Fig. 3a) the amplitudes (A value) are much smaller than was found for cyclic 1,2-dicinnamates (A value ca. 70–100).[30,31] The A values of −34 for 1,2-*syn* and −7.3 for 1,2-*anti* reflect the population of the three staggered conformations (Fig. 4). In 1,2-*syn*-derivatives, **S-1** predominates. However, in 1,2-*anti*-derivatives, the most stable form **A-3** shows no exciton coupling while the remaining two forms **A-1** and **A-2** are of opposite chirality, thus leading to weak couplets.

The difference between *syn*/*anti* cinnamate/cinnamate couplings becomes more profound in the 1,3 case. The large exciton splitting seen in the 1,3-*anti*-dicinnamate (A = −71, Fig. 3b) appears as a very distinctive unique characteristic for 1,3-*anti* stereochemistry due to the closer distance between



Scheme 5. Chromophoric derivatization of 1,2,4,6-tetrols.

the two chromophores and conformational stability of this unit. Harada and co-workers[28] found that an acyclic 1,3-*anti*-dibenzoate adopts a planar zigzag form in its most stable conformation and exhibits a strong positive or negative CD exciton couplet corresponding to the sign of the screw sense between the two gauche oriented chromophores. While the most stable form of the 1,3-*syn* analog also adopts a zigzag conformation, in this case the coupling between the cinnamate transition moments does not lead to split Cotton effects because of their achiral parallel orientation.

To summarize, the CD spectra of 1,3-polyols display clear differences from those of 1,2-polyols: (i) as compared to 1,2-acylates, the 1,3-*syn* and 1,3-*anti* pair-wise interactions give rise to more distinctive CD patterns, the discrimination from each other being unambiguous based on the profound difference in A values; (ii) the higher conformational stability of 1,3-polyols chain leads to less complicated CD spectra and more facile analysis of experimental CD data based on the principle of pair-wise additivity.

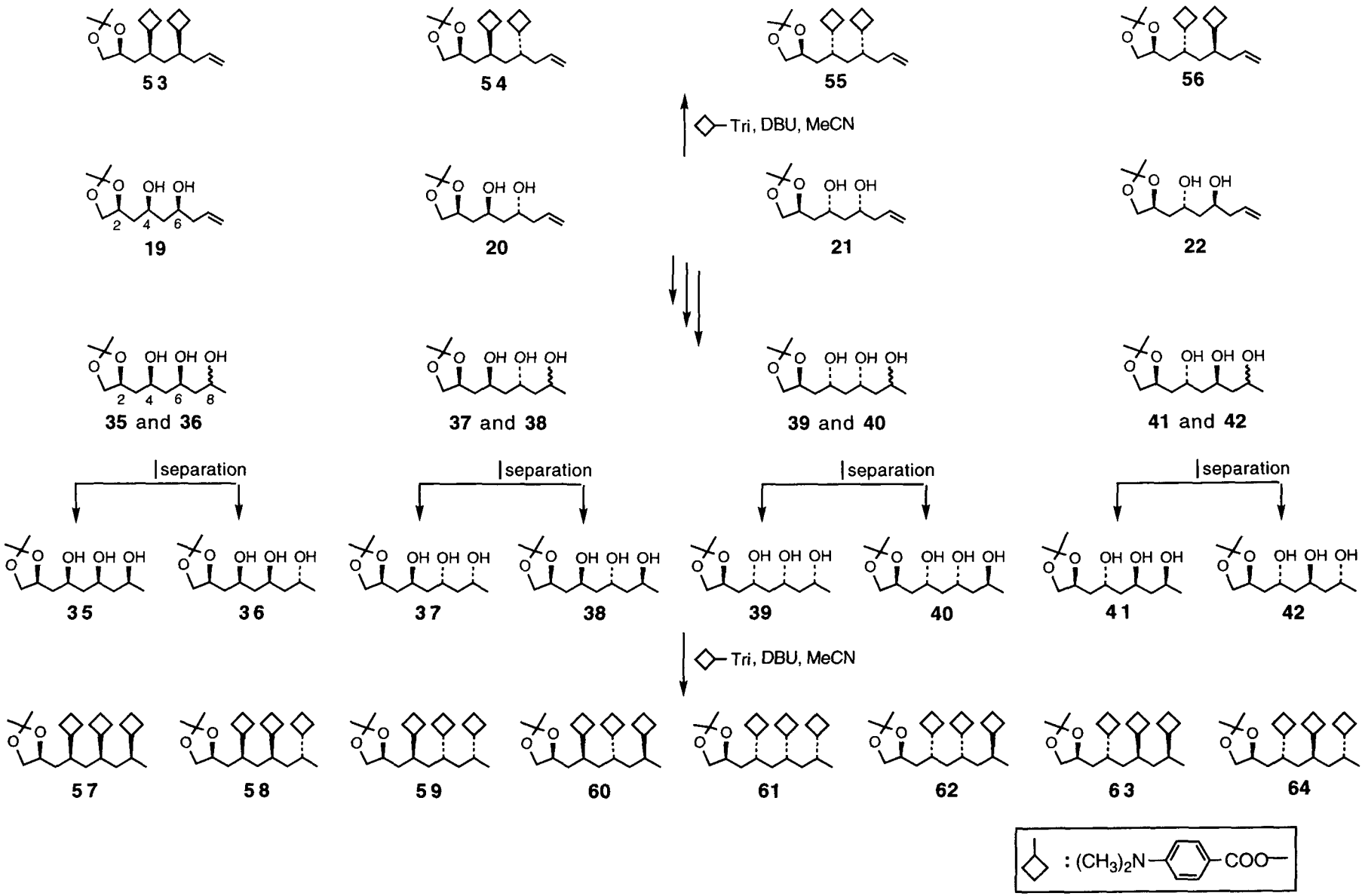
Accordingly, the exciton coupling CD curves of acylated 1,3-polyols can be simply represented by one of two characteristic shapes rather than by numerous reference curves: (i) distinctive negative or positive exciton couplet if the polyol contains odd number of 1,3-*anti* moieties, or (ii) very weak mono or bisignate CD when an even number of 1,3-*anti* and/or all 1,3-*syn* moieties are present.

In this study two types of chromophores have been chosen for the secondary hydroxyl groups. *P*-Methoxycinnamate was initially used because this chromophore has large ϵ (23 400) at long wavelength (λmax 306 nm) in MeCN and the derivatization yield is high (~95%). However, from the CD standpoint, this chromophore is not ideal since it is not symmetric. Moreover, this chromophore is light sensitive due to isomerization of the double bond.[32] Subsequently it was found that the dimethylaminobenzoate chromophore is more suited in view of its large ϵ (30 400) at 309 nm (which is close to the absorption band of cinnamate, Fig. 3b) and has symmetric structure, stability and high yield of formation, ca. 90%. Therefore in the latter part of this work, the *P*-dimethylaminobenzoate chromophore (DAB) was used instead of *P*-methoxycinnamate (Cin). The CD spectra of 1,3-*anti*-cinnamate/cinnamate (Cin/Cin) and dimethylaminobenzoate/dimethylaminobenzoate (DAB/DAB) exciton couplings are displayed in Figure 3b; the DAB/DAB couplet with A value of −85 is stronger than the corresponding Cin/Cin (A = −71) thus improving the CD sensitivity.

Since the synthetic polyol pairs (e.g., **7/8, 15/16** and **35/36** etc.) could not unambiguously be differentiated by NMR spectroscopy, we used a simple and practical approach for determining the absolute configurations based on the combination of synthetic strategy and exciton coupled CD.

1,2,4-Triols

The stereochemistry of 1,2,4-triols **7** and **8** was determined simply from the CD spectra of their bichromophoric derivatives **45** and **46** (Fig. 2). The 252 nm band results primarily from exciton coupling between the 1-Anth/2-Cin chromophores. The contribution from the 1-Anth/4-Cin couplet to 252 nm are much weaker. The clear positive CE shows the S-configuration for C-2. In the 280–320 nm region, deriv-



Scheme 6. Chromophoric derivatization of 1,2,4,6-homoallylic tetrols and 1,2,4,6,8-pentols.

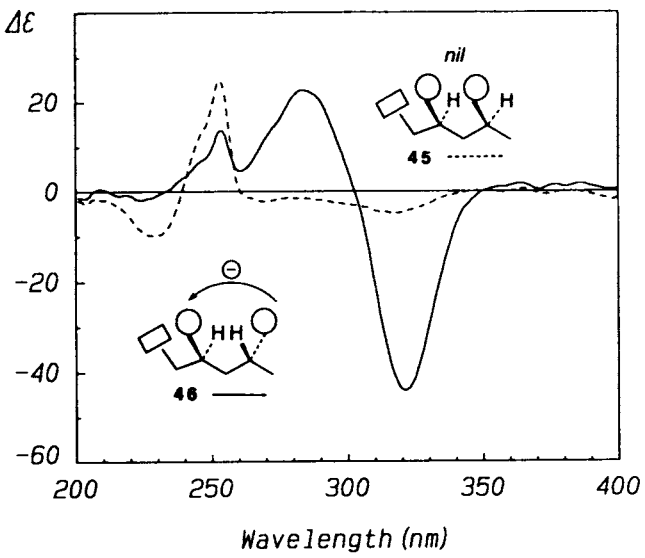


Fig. 2. CD spectra and λ_{ext} nm/$\Delta\varepsilon$ values of 1,2,4-triol anthroate/cinnamate derivatives **45** and **46** in MeCN. **45:** 252 (+25), 317 (−4.9); **46:** 253 (+13.7), 283 (+22.7), 320 (−44.1).

ative **46** shows a strong negative Cin/Cin coupling which accounts for the 1,3-*anti* stereochemistry, while in **45**, the absence of Cin/Cin couplet in the 280–320 nm region leads to a 1,3-*syn* configuration. Therefore, the configurations of **7** and **8** are established as **2S,4S** and **2S,4R**, respectively.

This CD assignment was confirmed by NMR (Scheme 4). In **47**, the acetonide of 1,3-*syn* isomer **7**, the 2-H and 4-H (axial/axial) exhibited a strong NOE, while the corresponding protons in 1,3-*anti* isomer **48** are 1,3-axial/equatorial and showed no NOE.

1,2,4,6-Tetrols and 1,2,4,6,8-Pentols

The synthetic scheme used in the synthesis of model tetrols divides the four diastereomers into two groups: *syn-syn/syn-anti* and *anti-syn/anti-anti* (Scheme 5). Each group contains one diastereomer with an odd number of 1,3-*anti* moiety which after derivatization should give rise to a strong positive or negative CD spectrum depending on the chirality of C-4 and C-6. Therefore the *nil* and strong negative Cin/Cin coupling is correlated with the group *syn-syn* (**15** or **49**) and *syn-anti* (**16** or **50**), respectively, whereas in the other group, the *nil* and strong positive Cin/Cin coupling is associated with *anti-syn* (**17** or **51**) and *anti-anti* (**18** or **52**) isomers, respectively (Fig. 5).

The stereochemistry of the four homoallylic tetrols (**19–22**) were determined in a similar manner (Scheme 6). Each of the homoallylic tetrols was used as precursor for the synthesis of pentols **35–42**. From the CD spectra of the derivatives of four pentol groups and their parent tetrols, the configuration of all pentols was easily assigned (Fig. 6 and 7). Their CD spectra followed the trend already discussed without exception. Each pair displayed one very weak and one strong bisignate CD curve, depending on the chiral twist between the hydroxyl groups.

On Figure 7 is shown schematically, the general synthetic and configurational strategy for 1,3-skipped polyols. In this approach, the polyols were synthesized from (S)-(−)-malic acid. The absolute configuration at C-2 was first established, thus decreasing the number of possible configurations in 1,2,4-triols from four to two; in 1,2,4,6-tetrols from eight to four and in 1,2,4,6,8-pentols from sixteen to eight. The tree can be further extended to hexols, heptols, etc. Also by using different Grignard reagents, the positions of hydroxyl groups can be controlled.[27] According to the present synthetic approach summarized in Scheme 2, each Grignard reaction step readily gives rise to almost equal amounts of the next higher diasteromeric pair.

Diastereomer Separation

During the synthesis, it was found that the THF/CH_2Cl_2 combination was a good solvent system for diastereomeric separation of polyol pairs by flash chromatography on silica gel, e.g., 5% THF/CH_2Cl_2 for triol pairs **7/8** and **11/12**; 12% THF/CH_2Cl_2 for tetrol pairs **15/16, 17/18, 19/20, 21/22** and 50% THF/CH_2Cl_2 for pentol pairs **35/36, 37/38, 39/40, 41/42**. The conventional solvent system used for free and acylated polyols, MeOH/CH_2Cl_2, was not suited for diastereomeric separation in the present series. It is believed that THF probably forms a "complex" more readily with one isomer than with the other, thus leading to a better separation in THF/CH_2Cl_2 than in other systems. Also from the tree in Figure 7, it was found that in the 1,3-diol pair resulting from elongation of a particular precursor, it was always the *syn*-isomer that had a larger Rf value than the corresponding *anti*-isomer. Namely, in Scheme 6, in the pair **35** (*syn-syn-**syn***)/**36** (*syn-syn-**anti***) derived from **19** (*syn-syn*), the former diastereomer has the larger Rf value.

CONCLUSION

A combination of a divergent synthetic strategy with microscale exciton coupled CD has led to the preparation of all possible stereoisomers of 1,2,4-triols, 1,2,4,6-tetrols and 1,2,4,6,8-pentols. This approach can be used for the synthesis of further extended acyclic 1,3-polyols and mixed 1,2/1,3-polyols with a terminal C-1/C-2 diol.[26] The current set of reference polyols with established configurations should be useful for setting up a reference CD library and for model studies to develop a general method for configurational assignment of acyclic polyols. These aspects are currently under study.

EXPERIMENTAL

General

Solvents used for reactions were reagent grade. Anhydrous solvents were freshly distilled (THF from Na/benzophenone; CH_2Cl_2 and acetonitrile from CaH_2). Unless otherwise mentioned, reagents were obtained from commercial sources and were used as such. Moisture sensitive reactions were carried out in oven-dried glassware under argon atmosphere. Thin-layer chromatography (TLC) was used for monitoring reactions, by using Analtech Silica Gel GHLF

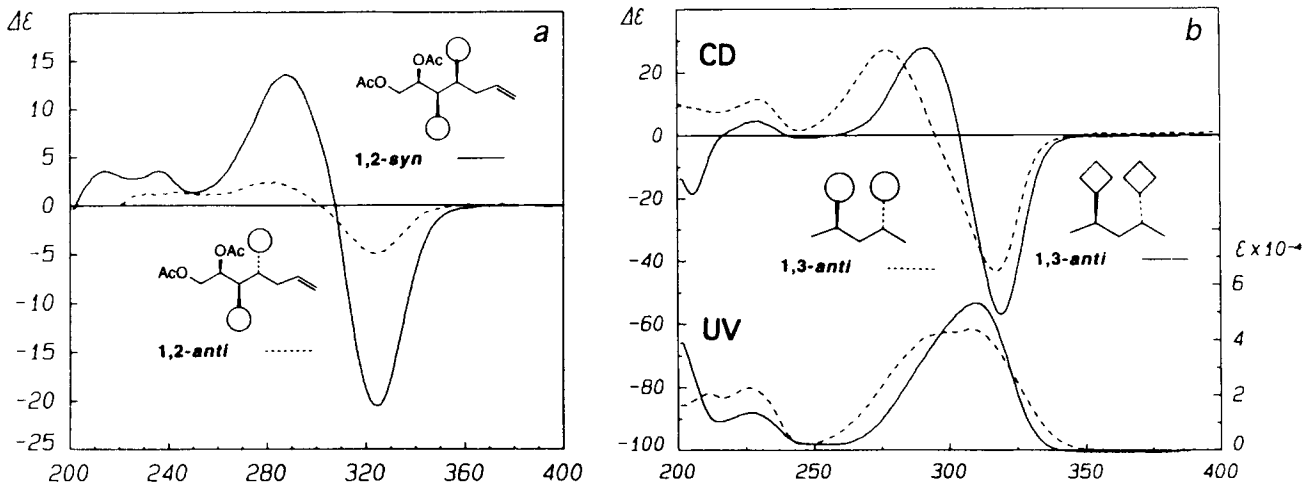


Fig. 3. CD spectra and λ_{ext} nm/$\Delta\epsilon$ values of model 1,2- and 1,3-diol cinnamate and benzoate derivatives in MeCN.

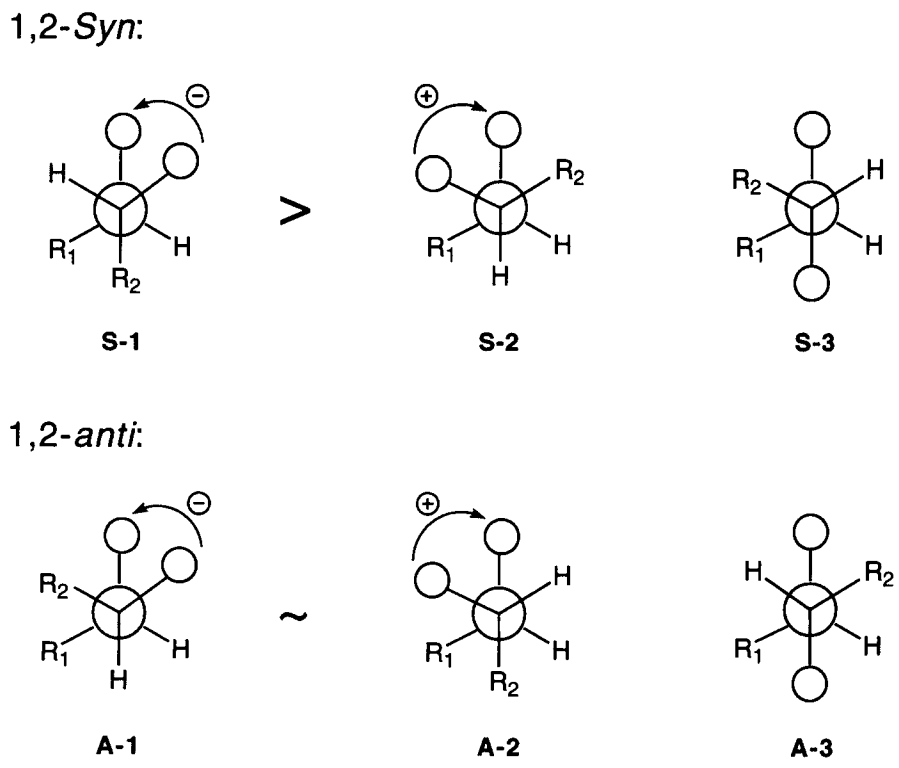


Fig. 4. Staggered conformations of 1,2-*syn*- and 1,2-*anti*-diol derivatives.

plates (250 nm thick). ICN silica gel (32–63 mesh) was employed for flash chromatography.

All ^1H NMR spectra were recorded in $CDCl_3$ on a Varian VXR 400 MHz spectrometer and are reported in parts per million (δ) relative to $CHCl_3$ (7.24 ppm) as an internal reference, with coupling constants (J) reported in hertz (Hz). Low-resolution and high-resolution FAB mass spectra were measured on a JOEL JMS-DX 303 HF mass spectrometer using glycerol matrix and Xe ionizing gas. CI mass spectra were measured on NERMAG R10-10 spectrometer with NH_3 as ionizing gas. UV-VIS and CD spectra were recorded in acetonitrile solutions on a Perkin-Elmer Lambda 4B UV/VIS spectrophotometer and JASCO J-720 spectropolarimeter respectively. Smoothing and other manipulation of spectra were carried out with software developed in house: DFT (Discrete Fourier Transform) procedure for smoothing.

(S)-(−)-Dimethyl-malate (2) (S)-(−)-Malic acid (41 g, 0.25 mol) was dissolved in 3% HCl-MeOH solution prepared by adding 14 ml of acetyl chloride to 270 ml of MeOH. The solution was left to stand at room temperature overnight and

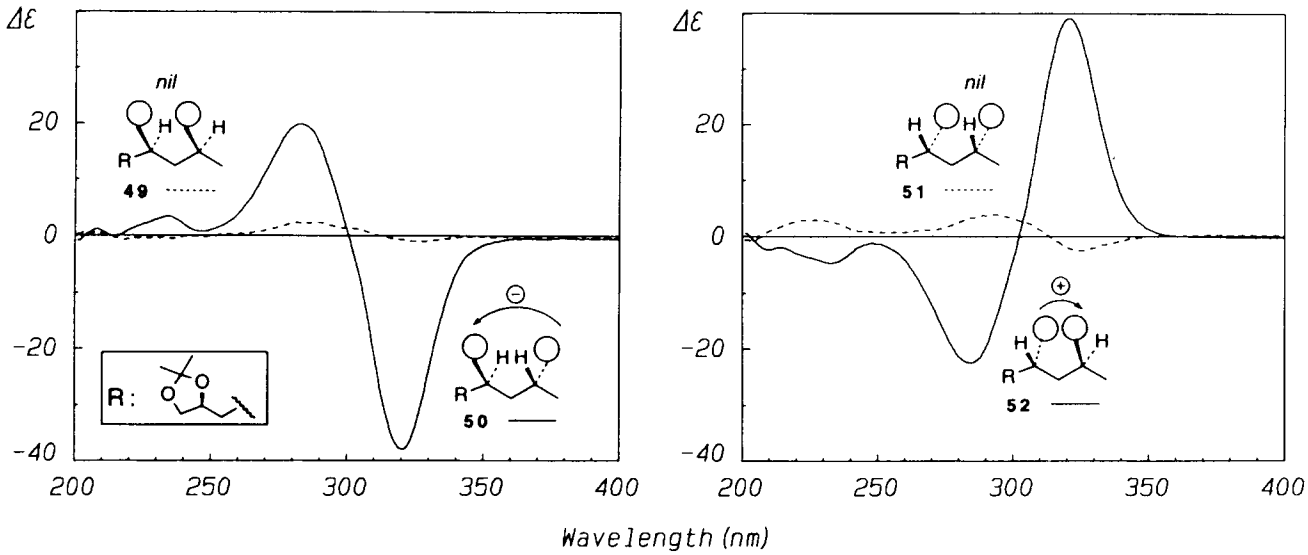


Fig. 5. CD spectra and λ_{ext} nm/Δε value of 1,2,4,6-tetrol cinnamate derivatives **49–52** in MeCn. **49:** 289 (+2.4), 327 (−0.9); **50:** 281 (+19.8), 319 (−37.9); **51:** 291 (+4.0), 323 (−2.5); **52:** 283 (−22.4), 319 (+39.2).

then concentrated *in vacuo*. The residue was distilled (b.p. 100°C–102°C, 3 mmHg) to give 43 g (88%) of **2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.54–4.88 (m, 1H), 3.81 (s, 3H), 3,71 (s, 3H), 2.88 (dd, J = 16.5, 4.5 Hz, 1H), 2.81 (dd, J = 16.5, 6.9 Hz, 1H); M.S.: *m/z* 163 $(M + 1)^+$.

(S)-(−)-2-*O*-[(S)-α-Methoxy-α-trifluoro-methylphenyl-acetyl]-dimethyl-malate (3) To a solution of **2** (4 mg, 24.7 μmol) in dry CH_2Cl_2 (1 ml) was added (S)-α-methoxy-α-trifluoro-methylphenylacetyl chloride (9 μl, 49.3 μmol), Et_3N (7 μl, 50.3 μmol) and catalytic amount of DMAP. The reaction was stirred for 30 minutes at 0°C and concentrated. The residue was purified by silica gel flash chromatography (EtOAc/Hexane, 1:1) to give 8.9 mg of **3** in 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.56 (m, 2H), 7.43–7.38 (m, 3H), 5.71 (dd, J = 9.1, 3.7 Hz, 1H), 3.76 (s, 3H), 3.70 (s, 3H), 3.55 (s, 3H), 3.04–2.88 (m, 2H); M.S.: *m/z* 379 $(M + 1)^+$.

(2S)-1,2-Dihydroxy-butanoate (4) To a solution of **2** (43 g, 0.27mol) in dry THF (550 ml) was added borane-dimethyl sulfate complex (27 mL, 0.27 mol). After 30 minutes, $NaBH_4$ (0.4 g, 12 mmol) was added. The reaction mixture was stirred at room temperature for 30 minutes followed by addition of methanol (170 ml). After stirring for another 30 minutes at room temperature, the reaction mixture was concentrated *in vacuo* and distilled (bp 158°C, 0.3 mmHg) to give 32 g **4** as colorless oil in 90% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (m, 1H), 4.10 (m, 1H), 3.66 (s, 3H), 3.64 (m, 1H), 2.67 (dd, J = 16.4, 6.2 Hz, 1H), 2.51 (dd, J = 16.4, 6.8 Hz, 1H); M.S.: *m/z* 135 $(M + 1)^+$.

(2S)-1,2-(*O*-Isopropylidene-dihydroxy)-butanoate (5) To a solution of **4** (10 g, 0.07 mol) in 2,2-dimethoxy propane (200 ml) was added *p*-TsOH (0.3 g). The mixture was stirred at room temperature overnight, then neutralized with $NaHCO_3$ and filtered. The filtrate was concentrated, diluted with 200 mL ether and washed with brine. After drying over $MgSO_4$ and evaporation of the solvents, the crude product was distilled (b.p. 62°C, 0.3 mmHg) to give 11.2 g of **5** in 85% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (pentet, J = 6.5 Hz, 1H), 4.13 (dd, J = 8.4, 6.0 Hz, 1H), 3.67 (s, 3H), 3.62 (dd, J = 8.4, 6.4 Hz, 1H), 2.68 (dd, J = 16.9, 6.4 Hz, 1H), 2.50 (dd, J = 16.9, 7.0 Hz, 1H), 1.42 (s, 3H), 1.30 (s, 3H); M.S.: *m/z* 175 $(M + 1)^+$.

(2S)-1,2-*O*-Isopropylidene-4-butanal-1,2-diol (6) To a solution of **5** (5.2 g, 30 mmol) in dry CH_2Cl_2 (180 ml) was added DIBAL (40 ml, 1.0 M in CH_2Cl_2) at −78°C under Ar. After stirring at −78°C for 20 minutes, the reaction mixture was quenched with CH_3OH (10 ml) and poured into a mixture of saturated sodium potassium tartrate aqueous solution (200 ml) and ether (200 ml). After stirring at room temperature for 2 hours, the aqueous layer was separated and extracted with 3 × 100 ml ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give **6** as a colorless oil (4.1 g, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 4.52 (pentet, J = 8.5 Hz, 1H), 4.18 (dd, J = 11.1, 8.1 Hz, 1H), 3.58 (dd, J = 11.1, 8.9 Hz, 1H), 2.85 (dd, J = 23.0, 8.7 Hz, 1H), 2.74 (dd, J = 23.0, 8.2 Hz, 1H), 1.44 (s, 3H), 1.34 (s, 3H); M.S.: *m/z* 145 $(M + 1)^+$.

(2S,4S)- and (2S, 4R)-1,2-*O*-Isopropylidene-pentane-1,2,4-triols (7) and (8) To a solution of **6** (1.3 g, 9.0 mmol) in dry THF (20 ml) at −20°C was added methyl magnesium bromide (4.5 ml, 13.5 mmol, 3.0 M in ether). The reaction mixture was stirred at room temperature for 2 hours and then quenched with saturated NH_4Cl aqueous solution. After extraction with ether (3 × 20 ml), drying over $MgSO_4$, filtration, and concentration, the crude product was subjected to flash chromatography on silica gel (5%, THF/CH_2Cl_2) to give 0.65 mg of **7** and 0.62 mg of **8** in overall 88% yield: ^{1}H NMR **7** (400 MHz, $CDCl_3$) δ 4.38–4.30 (m, 1H), 4.07 (dd, J = 8.3, 6.4 Hz, 1H), 4.06–3.99 (m, 1H), 3.57 (dd, J = 8.3, 7.4 Hz, 1H), 1.72–1.65 (m, 2H), 1.43 (s, 3H), 1.33 (s, 3H), 1.21 (d, J = 6.5 Hz, 3H); M.S.: *m/z* 161 $(M + 1)^+$; ^{1}H NMR **8** (400 MHz, $CDCl_3$) δ 4.28–4.11 (m, 1H), 4.08 (dd, J = 8.6, 6.7 Hz, 1H), 4.05–3.96 (m, 1H), 3.54 (dd, J = 8.6, 7.6 Hz,

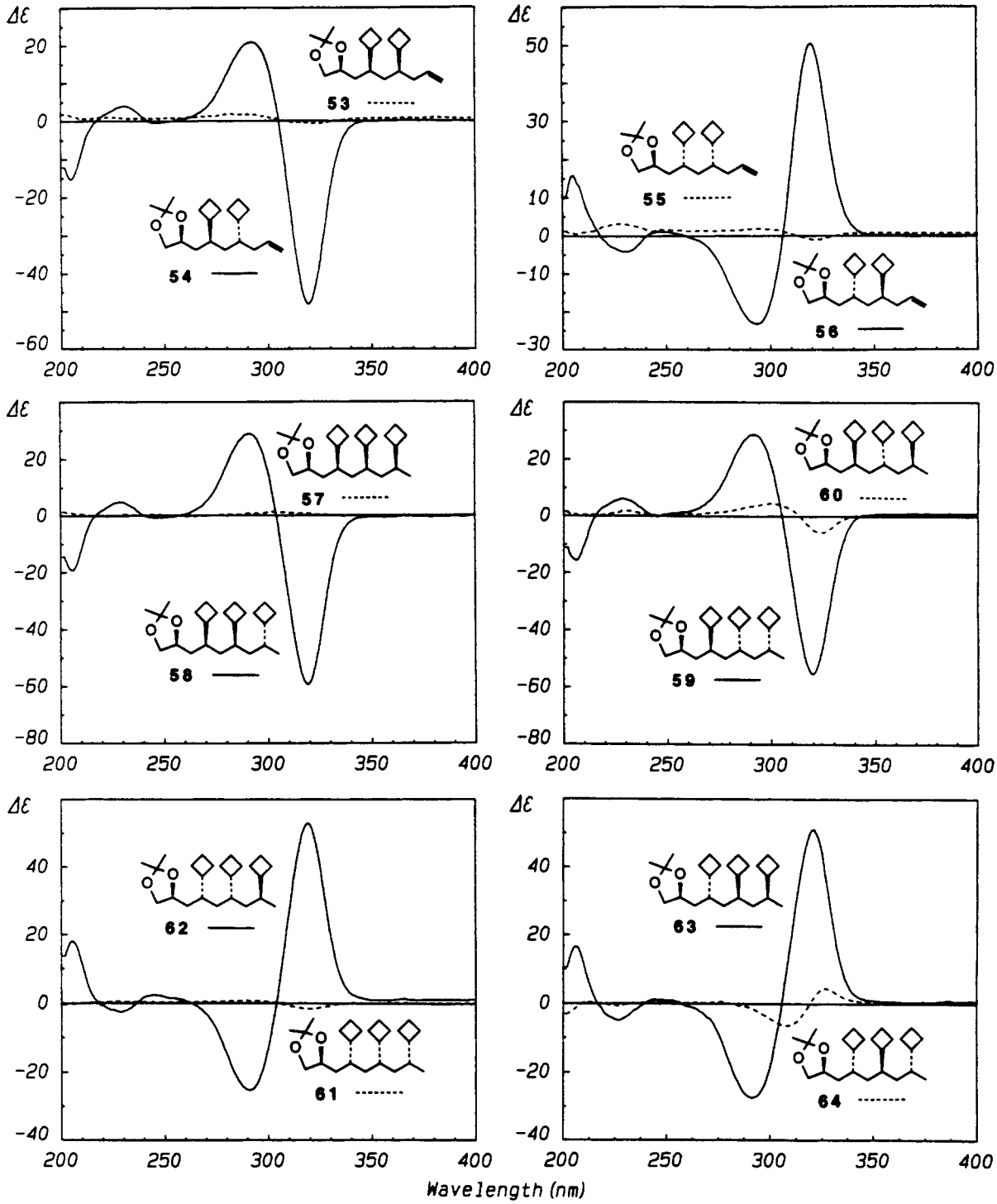


Fig. 6. CD spectra and λ_{ext} nm/$\Delta\epsilon$ values of cinnamate derivatives of 1,2,4,6-homoallylic tetrols **53–56** and 1,2,4,6,8-pentols **57–64** in MeCn. **53:** 289 (+1.1), 324 (−1.4); **54:** 291 (+21), 318 (−48.2); **55:** 298 (+1.1), 321 (−1.8); **56:** 292 (−23.1), 319 (+50.5); **57:** 301 (+1.3); **58:** 291 (+28.8), 319 (−59.2); **59:** 291 (+28.8), 319 (−55); **60:** 298 (+4.6), 322 (−5.6); **61:** 287 (+0.8), **62:** 318 (+53.2), 298 (−25.3); **63:** 290 (−27.3), 320 (+51);**64:** 308 (−6.3), 326 (+4.4).

1H), 1.66–1.62 (m, 2H), 1.44 (s, 3H), 1.34 (s, 3H), 1.27 (d, J = 6.3 Hz, 3H); M.S.: *m/z* 161 $(M + 1)^+$.

(2S,4S)- and (2S, 4R)-1,2-*O*-Isopropylidene-6-heptene-1,2,4-triols (11) and (12) To a solution of **6** (4.1 g, 28.5 mmol) in dry THF (60 ml) at −20°C was added allyl magnesium bromide (57 ml, 57 mmol, 1.0 M in ether). The reaction mixture was stirred at room temperature for 2 hours and then quenched with saturated NH_4Cl aqueous solution. After extraction with ether (3 × 20 ml), drying over $MgSO_4$, filtration, and evaporation of the solvents, the crude product

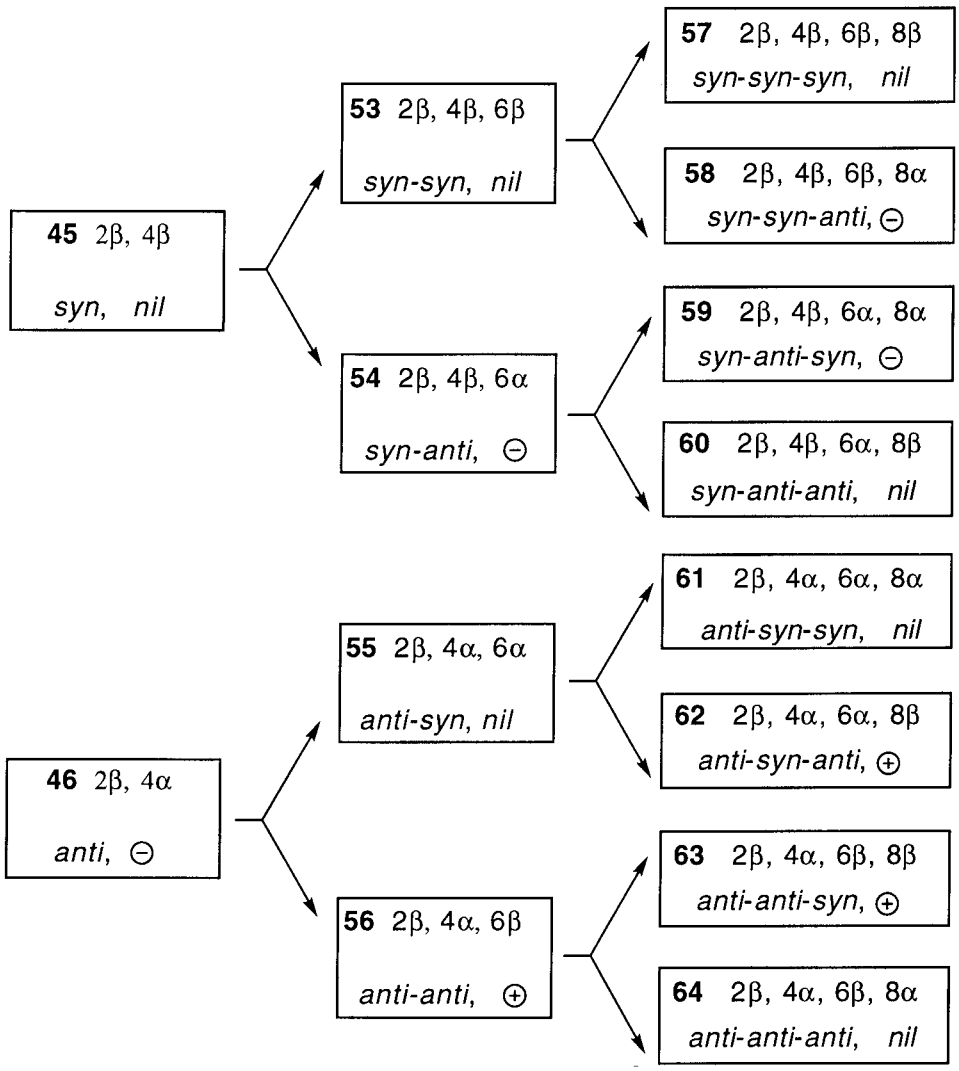


Fig. 7. General synthetic and configurational strategy for 1,3-skipped polyols.

was subjected to flash chromatography on silica gel (5%, THF/CH_2Cl_2) to give 2.4 mg of **11** and 2.1 mg of **12** in overall 85% yield: ^{1}H NMR **11** (400 MHz, $CDCl_3$) δ 5.89–5.78 (m, 1H), 5.13–5.08 (m, 2H), 4.31–4.22 (m, 1H), 4.09 (dd, J = 8.0, 5.9 Hz, 1H), 3.93–3.84 (m, 1H), 3.56 (dd, J = 8.0, 6.1 Hz, 1H), 2.31–2.27 (m, 2H), 1.78–1.55 (m, 2H), 1.44 (s, 3H), 1.32 (s, 3H); M.S.: *m/z* 187 $(M + 1)^+$; ^{1}H NMR **12** (400 MHz, $CDCl_3$) δ 5.88–5.76 (m, 1H), 5.18–5.11 (m, 2H), 4.38–4.32 (m, 1H), 4.09 (dd, J = 8.1, 5.8 Hz, 1H), 3.93–3.85 (m, 1H), 3.58 (dd, J = 8.1, 6.3 Hz, 1H), 2.35–2.17 (m, 2H), 1.79–1.62 (m, 2H), 1.46 (s, 3H), 1.34 (s, 3H); M.S.: *m/z* 187 $(M + 1)^+$.

Representative procedure for ozonolysis and Grignard addition (Method A): (2S, 4S, 6S)- and (2S, 4S, 6R)-1,2-*O*-Isopropylidene-heptane-1,2,4,6-tetrols (15) and (16) Compound **11** (0.8 g, 4.3 mmol) in CH_2Cl_2 (40 ml) and CH_3OH (10 ml) was treated with ozone at −78°C until the solution turned blue. The reaction mixture was then bubbled with O_2 until colorlessness before triphenylphosphine (1.4 g, 5.3 mmol) was added. The mixture was warmed up to room temperature and concentrated to give the crude aldehyde **13** without any further purification. To a solution of this aldehyde **13** in dry THF (4 ml) at −20°C was added methyl magnesium bromide (2.8 ml, 8.4 mmol, 3.0 M in ether). After stirring for 2 hours at room temperature, the reaction mixture was quenched with saturated NH_4Cl aqueous solution. After extraction with ether (3 × 10 ml), drying over $MgSO_4$, filtration and evaporation of the solvents, the crude product was purified and separated by flash chromatography on silica gel (12% THF/CH_2Cl_2) to give 337 mg of **15** and 318 mg of **16** in overall 75% yield: ^{1}H NMR **15** (400 MHz, $CDCl_3$) δ 4.29–4.23 (m, 1H), 4.10–4.02 (m, 3H), 3.54 (t, J = 7.6 Hz, 1H), 1.73–1.61 (m, 2H), 1.59–1.49 (m, 2H), 1.43 (s, 3H), 1.31 (s, 3H), 1.17 (d, J = 6.4 Hz, 3H); HRMS calcd for $C_{10}H_{20}O_4$ (M + 1) 205.1440, found 205.1433; ^{1}H NMR **16** (400 MHz, $CDCl_3$) δ 4.31–4.25 (m, 1H), 4.20–4.16 (m, 1H), 4.15–4.07 (m, 2H), 3.56 (t, J = 8.0 Hz, 1H), 1.81–1.60 (m, 4H), 1.44 (s, 3H), 1.32 (s, 3H), 1.21 (d, J = 6.4 Hz, 3H); HRMS calculated for $C_{10}H_{20}O_4$ (M + 1) 205.1440, found 205.1432.

(2S, 4R, 6R)- and (2S, 4R, 6S)-1,2-*O*-Isopropylidene-heptane-1,2,4,6-tetrols (17) and (18) 338 mg of **17** and 311 mg of **18** were prepared from 800 mg of **12** in 74% yield

by the procedure described in method A. ^{1}H NMR **17** (400 MHz, $CDCl_3$) δ 4.35 (pentet, J = 6.4 Hz, 1H), 4.11–4.07 (m, 3H), 3.57 (t, J = 8.0 Hz, 1H), 1.74–1.80 (m, 2H), 1.59–1.56 (m, 2H), 1.45 (s, 3H), 1.33 (s, 3H), 1.21 (d, J = 6.4 Hz, 3H); HRMS calcd for $C_{10}H_{20}O_4$ (M + 1) 205.1440, found 205.1432; ^{1}H NMR **18** (400 MHz, $CDCl_3$) δ 4.35 (pentet, J = 6.0 Hz, 1H), 4.22–4.14 (m, 2H),4.09 (dd, J = 8.0, 6.0 Hz, 1H), 3.60 (t, J = 8.0 Hz, 1H), 1.84–1.60 (m, 4H), 1.45 (s, 3H), 1.33 (s, 3H), 1.25 (d, J = 6.4 Hz, 3H); HRMS calculated for $C_{10}H_{20}O_4$ (M + 1) 205.1440, found 205.1431.

(2S, 4S, 6S)- and (2S, 4S, 6R)-1,2-*O*-Isopropylidene-8-nonene-1,2,4,6-tetrols (19) and (20) 2.4 g of **19** and 2.2 g of **20** were prepared from 5.4 g of **11** in 70% yield by the procedure described in method A. ^{1}H NMR **19** (400 MHz, $CDCl_3$) δ 5.92–5.72 (m, 1H), 5.14–5.11 (m, 1H), 5.09 (bs, 1H), 4.28 (m, 1H), 4.10 (dd, J = 8.1, 5.9 Hz, 2H), 3.93 (m, 1H), 3.57 (t, J = 8.0 Hz, 1H), 2.27–2.23 (m, 2H), 1.75–1.65 (m, 2H), 1.63–1.56 (m, 2H), 1.43 (s, 3H), 1.36 (s, 3H); M.S.: *m/z* 231 $(M + 1)^+$; ^{1}H NMR **20** (400 MHz, $CDCl_3$) δ 5.85–5.75 (m, 1H), 5.15 (d, J = 8.6 Hz, 1H), 5.11 (s, 1H), 4.35–4.27 (m, 1H), 4.25–4.18 (m, 1H), 4.12 (dd, J = 8.1, 6.0 Hz, 1H), 4.04–3.97 (m, 1H), 3.58 (t, J = 8.0 Hz, 1H), 2.32–2.25 (m, 2H), 1.84–1.62 (m, 4H), 1.44 (s, 3H), 1.38 (s, 3H); M.S.: *m/z* 231 $(M + 1)^+$.

(2S, 4R, 6R)- and (2S, 4R, 6S)-1,2-*O*-Isopropylidene-8-nonene-1,2,4,6-tetrols (21) and (22) 2.2 g of **21** and 2.1 g of **22** were prepared from 5.1 g of **12** in 69% yield by the procedure described in method A. ^{1}H NMR **21** (400 MHz, $CDCl_3$) δ 5.88–5.75 (m, 1H), 5.14 (bs, 1H), 5.10 (bs, 1H), 4.38–4.31 (m, 1H), 4.09 (dd, J = 8.0, 5.8 Hz, 2H), 3.97–3.90 (m, 1H), 3.56 (t, J = 7.9 Hz, 1H), 2.28–2.21 (m, 2H), 1.74–1.69 (m, 2H), 1.62–1.55 (m, 2H), 1.42 (s, 3H), 1.37 (s, 3H); M.S.: *m/z* 231 $(M + 1)^+$; ^{1}H NMR **22** (400 MHz, $CDCl_3$) δ 5.89–5.77 (m, 1H), 5.19–5.15 (m, 1H), 5.13 (bs, 1H), 4.40–4.39 (m, 1H), 4.23–4.15 (m, 1H), 4.09 (dd, J = 8.0, 6.4 Hz, 1H), 4.04–3.96 (m, 1H), 3.60 (t, J = 8.0 Hz, 1H), 2.32–2.25 (m, 2H), 1.85–1.64 (m, 4H), 1.43 (s, 3H), 1.36 (s, 3H), M.S.: *m/z* 231 $(M + 1)^+$.

Representative procedure for silylation (Method B): (2S, 4S, 6S)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonene-1,2,4,6-tetrol (23) To a solution of compound **19** (0.50 g, 2.2 mmol) in DMF (2 mL) was added *tert*-butyldimethylsilyl chloride (0.85 g, 5.7 mmol) and imidazole (0.75 g, 11.0 mmol). The reaction mixture was stirred at 35–45°C overnight. After extraction with ether (3 × 10 ml), filtration and concentration, the crude product was purified by flash chromatography on silica gel (5% Hexane/EtOAc) to give 0.9 g of **23** in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90–5.70 (m, 1H), 5.10 (bs, 1H), 5.00 (bs, 1H), 4.22–4.14 (m, 1H), 4.07–4.00 (m, 1H), 3.95–3.90 (m, 1H), 3.85–3.79 (m, 1H), 3.48 (t, J = 7.8 Hz, 1H), 2.26–2.17 (m, 2H), 1.85–1.80 (m, 2H), 1.72–1.60 (m, 2H), 1.38 (s, 3H), 1.33 (s, 3H), 0.88 (bs, 18H), 0.04 (bs, 12H); M.S.: *m/z* 459 $(M + 1)^+$.

Compounds **24–26** were synthesized from **20–22**, respectively, using the same procedure (Method B).

(2S, 4S, 6R)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonene-1,2,4,6-tetrol (24) ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92–5.71 (m, 1H), 5.08 (bs, 1H), 5.01 (bs, 1H), 4.25–4.12 (m, 1H), 4.08–4.02 (m, 1H), 3.92–3.79 (m, 2H), 3.47 (t, J = 7.8 Hz, 1H), 2.29–2.17 (m, 2H), 1.94–1.80 (m, 1H), 1.65–1.60 (m, 3H), 1.39 (s, 3H), 1.34 (s, 3H), 0.87 (bs, 18H), 0.05 (bs, 12H); M.S.: *m/z* 459 $(M + 1)^+$.

(2S, 4R, 6R)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonene-1,2,4,6-tetrol (25) ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89–5.71 (m, 1H), 5.10–5.00 (m, 2H), 4.22–4.15 (m, 1H), 4.05–3.84 (m, 2H), 3.78–3.72 (m, 1H), 3.49–3.44 (m, 1H), 2.28–2.15 (m, 2H), 1.81–1.63 (m, 2H), 1.60–1.45 (m, 2H), 1.39 (s, 3H), 1.33 (s, 3H), 0.88 (bs, 18H), 0.07 (s, 3H), 0.06 (bs, 9H); M.S.: *m/z* 459 $(M + 1)^+$.

(2S, 4R, 6S)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonene-1,2,4,6-tetrol (26) ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87–5.77 (m, 1H), 5.07 (bs, 1H), 5.04 (bs, 1H), 4.21–4.15 (m, 1H), 4.03 (dd, J = 7.8, 5.9 Hz, 1H), 3.89–3.82 (m, 1H), 3.80–3.75 (m, 1H), 3.47 (t, J = 7.8 Hz, 1H), 2.27–2.15 (m, 2H), 1.83–1.76 (m, 1H), 1.74–1.67 (m, 1H), 1.60–1.51 (m, 2H), 1.39 (s, 3H), 1.33 (s, 3H), 0.88 (bs, 18H), 0.07 (bs, 6H), 0.06 (bs, 6H); M.S.: *m/z* 459 $(M + 1)^+$.

Representative procedure for ozonolysis (Method C): (2S, 4S, 6S)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonanal-1,2,4,6-tetrol (27) Compound **23** (0.6 g, 1.3 mmol) in CH_2Cl_2 (40 ml) and CH_3OH (10 ml) was treated with ozone at −78°C until the solution turned blue. The reaction mixture was then bubbled with O_2 until colorlessness before triphenylphosphine (0.4 g, 1.5 mmol) was added. The mixture was warmed up to room temperature and concentrated to give the crude aldehyde which was purified by flash chromatography on silica gel (15% EtOAc/Hexane) to give 0.53 mg of **27** in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (bs, 1H), 4.36–4.30 (m, 1H), 4.22–4.16 (m, 1H), 4.05 (dd, J = 7.9, 5.8 Hz, 1H), 3.95–3.91 (m, 1H), 3.49 (t, J = 7.8 Hz, 1H), 2.62–2.47 (m, 2H), 1.88–1.65 (m, 4H), 1.39 (s, 3H), 1.34 (s, 3H), 0.88 (bs, 18H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H), M.S.: *m/z* 461 $(M + 1)^+$.

Aldehydes **28–30** were synthesized from **24–26**, respectively, using the same procedure (Method C).

(2S, 4S, 6R)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonanal-1,2,4,6-tetrol (28) ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (bs, 1H), 4.30–4.23 (m, 1H), 4.19–4.12 (m, 1H), 4.05–3.99 (m, 1H), 3.93–3.88 (m, 1H), 3.44 (t, J = 7.8 Hz, 1H), 2.57–2.50 (m, 2H), 1.88–1.60 (m, 4H), 1.37 (s, 3H), 1.31 (s, 3H), 0.85 (bs, 18H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); M.S.: *m/z* 461 $(M + 1)^+$.

(2S, 4R, 6R)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonanal-1,2,4,6-tetrol (29) ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (bs, 1H), 4.26–4.23 (m, 1H), 4.20–4.17 (m, 1H), 4.04 (dd, J = 7.7, 5.9 Hz, 1H), 4.00–3.96 (m, 1H), 3.46 (t, J = 8.0 Hz, 1H), 2.66–2.48 (m, 2H), 1.86–1.70 (m, 2H), 1.66–1.52 (m, 2H), 1.38 (s, 3H), 1.33 (s, 3H), 0.88 (bs, 9H), 0.87 (bs, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H); M.S.: *m/z* 461 $(M + 1)^+$.

(2S 4R, 6S)-1,2-*O*-Isopropylidene-4,6-bis(*tert*-butyldimethylsilyl)-8-nonanal-1,2,4,6-tetrol (30) ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (bs, 1H), 4.28–4.09 (m, 2H), 4.08–3.97 (m, 1H), 3.76–3.62 (m, 1H), 3.44 (t, J = 8.0 Hz, 1H), 2.54–2.48 (m, 2H), 1.80–1.60 (m, 4H), 1.38 (s, 3H), 1.35 (s, 3H), 0.88 (bs, 18H), 0.05 (bs, 12H); M.S.: *m/z* 461 $(M + 1)^+$.

Representative procedure for Grignard addition and desilylation (Method D): (2S, 4S, 6S, 8S)- and (2S,4S, 6S, 8R)-1,2-*O*-Isopropylidene-nonane-1,2,4,

6,8-pen-tols (35) and (36) To a solution of **27** (1.0 g, 2.2 mmol) in dry THF (10 ml) at −20°C was added methyl magnesium bromide (1.0 mL, 3.0 mmol, 3.0 M in ether). After stirring for 2 hours at room temperature, the reaction mixture was quenched with saturated NH_4Cl aqueous solution. After extraction with ether (3 × 10 ml), drying over $MgSO_4$, filtration and evaporation of the solvents, the crude product was obtained for the desilylation without any further purification. To a solution of above product in THF (2 ml) was added tetrabutylammonium fluoride (5.0 mL, 5.0 mmol, 1.0 M in THF). The reaction was stirred at room temperature for 5 hours. After the solvent was removed under reduced pressure, the residue was column chromatographed on silica gel (50% THF/CH_2Cl_2) to give 206 mg of **35** and 209 mg of **36** in overall 77% yield. ^{1}H NMR **35** (400 MHz, $CDCl_3$) δ 4.31–4.25 (m, 1H), 4.17–4.07 (m, 4H), 3.59–3.55 (m, 1H), 1.69–1.50 (m, 6H), 1.43 (s, 3H), 1.36 (s, 3H), 1.23 (d, J = 6.3 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$; ^{1}H NMR **36** (400 MHz, $CDCl_3$) δ 4.63–4.60 (m, 1H), 4.18–4.09 (m, 4H),3.57 (t, J = 8.1 Hz, 1H), 1.80–1.61 (m, 6H), 1.43 (s, 3H), 1.37 (s, 3H), 1.22 (d, J = 6.3 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$.

Pentol acetonides **37–42** were synthesized from **28–30**, respectively, using the same procedure (Method D).

(2S, 4S, 6R, 8R)-1,2-*O*-Isopropylidene-nonane-1,2, 4,6,8-pentols (37) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.33–4.26 (m, 1H), 4.24–4.17 (m, 1H), 4.15–4.07 (m, 3H), 3.58 (t, J = 6.3 Hz, 1H), 1.80–1.62 (m, 6H), 1.43 (s, 3H), 1.36 (s, 3H), 1.20 (d, J = 6.3 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$.

(2S, 4S, 6R, 8S)-1,2-*O*-Isopropylidene-nonane-1,2, 4,6,8-pentols (38) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34–4.26 (m, 1H), 4.24–4.09 (m, 4H), 3.58 (dd, J = 8.1, 7.2 Hz, 1H), 1.83–1.54 (m, 6H), 1.42 (s, 3H), 1.36 (s, 3H), 1.23 (d, J = 6.3 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$.

(2S, 4R, 6R, 8R)-1,2-*O*-Isopropylidene-nonane-1,2, 4,6,8-pentols (39) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38–4.32 (m, 1H), 4.19–4.07 (m, 4H), 3.58 (t, J = 7.8 Hz, 1H),1.75–1.52 (m, 6H), 1.42 (s, 3H), 1.36 (s, 3H), 1.20 (d, J = 6.2 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$.

(2S, 4R, 6R, 8S)-1,2-*O*-Isopropylidene-nonane-1,2, 4,6,8-pentols (40) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38–4.33 (m, 1H), 4.28–4.22 (m, 1H), 4.20–4.14 (m, 2H), 4.09 (dd, J = 8.1, 6.1 Hz, 1H), 3.58 (t, J = 8.1 Hz,1H), 1.80–1.60 (m, 6H), 1.43 (s, 3H), 1.36 (s, 3H), 1.23 (d, J = 6.2 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$.

(2S, 4R, 6S, 8S)-1,2-*O*-Isopropylidene-nonane-1,2, 4,6,8-pentols (41) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38–4.31 (m, 1H), 4.25–4.17 (m,2H), 4.11–4.08 (m, 2H), 3.59 (t, J = 7.8 Hz, 1H), 1.84–1.62 (m, 6H), 1.42 (s, 3H), 1.36 (s, 3H), 1.22 (d, J = 6.1 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$.

(2S, 4R, 6S, 8R)-1,2-*O*-Isopropylidene-nonane-1,2, 4,6,8-pentols (42) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40–4.29 (m, 2H), 4.24–4.13 (m, 2H), 4.10 (dd, J = 8.1, 6.0 Hz, 1H), 3.60 (t, J = 7.8 Hz, 1H), 1.85–1.54 (m, 6H), 1.42 (s, 3H), 1.37 (s, 3H), 1.25 (d, J = 6.3 Hz, 3H); M.S.: *m/z* 249 $(M + 1)^+$.

Bichromophoric derivatization of triol acetonides 7 and 8 to 45 and 46. (2S, 4S)- and (2S, 4R)-1-*O*-anthroyl-2,4-di-(*O*-*P*-methoxycinnamoyl)-pentane-1,2,4-triol (45) and (46)

i) Acetonide cleavage: To a methanolic solution (0.5 ml) of triol acetonide **7** (10 mg, 62.5 μmol) was added 2–3 drops of acetyl chloride. The mixture was stirred for 2 h. The solvent was removed under reduced pressure and the residue was dried overnight *in vacuo*. The triol so obtained was subjected to anthroylation without further purification.

ii) Anthroylation To the above triol in acetonitrile (2 mL) was added 9-anthroyltetrazole (34.4 mg, 125 μmol) and DBU (18.7 μl, 125 μmol). The reaction mixture was stirred at room temperature for 8 hours and concentrated. The yellow residue was purified by silica gel flash chromatography (3% MeOH/CH_2Cl_2) to give 10.1 mg of **43** in 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.05 (m, 4H), 7.53 (m, 4H), 4.63 (dd, J = 11.3, 3.6 Hz, 1H), 4.52 (dd, J = 11.3, 7.0 Hz, 1H), 4.33 (m, 1H), 4.13 (m, 1H), 1.72 (m, 2H), 1.24 (d, J = 6.2 Hz, 3H); M.S.: *m/z* 325 $(M + 1)^+$.

(2S, 4R)-1-*O*-anthroyl-pentane-1,2,4-triol (44) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.05 (m, 4H), 7.51 (m, 4H), 4.67 (dd, J = 11.4, 3.7 Hz, 1H), 4.57 (dd, J = 11.3, 7.3 Hz, 1H), 4.40 (m, 1H), 4.22 (m, 1H), 1.78 (m, 1H), 1.68 (m, 1H), 1.27 (d, J = 6.2 Hz, 3H); M.S.: *m/z* 325 $(M + 1)^+$.

iii) Cinnamoylation To **43** (5 mg, 15.4 μmol) in acetonitrile (2 ml) was added *P*-methoxycinnamoyl imidazole (10.7 mg,46.2 μmol) and DBU (7 μl, 46.8 μmol). The reaction mixture was stirred at room temperature in the dark for 4 hr. After the solvent was removed, the residue was purified by silica gel flash chromatography (EtOAc/Hexane, 1:3) to give 8.9 mg of **45** in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.10–7.97 (m, 4H), 7.68 (d, J = 16.0 Hz, 1H), 7.63 (d, J = 16.0 Hz, 1H), 7.49–7.37 (m, 8H), 6.86 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 6.34 (d, J = 16.0 Hz, 1H), 6.27 (d, J = 16.0 Hz, 1H), 5.59–5.52 (m, 1H), 5.28–5.18 (m, 1H), 4.94 (dd, J = 11.9, 3.2 Hz, 1H), 4.74 (dd, J = 11.9, 5.2 Hz, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 2.22–2.07 (m, 2H), 1.36 (d, J = 6.2 Hz, 3H); HRMS calcd for $C_{40}H_{36}O_8$ 644.2410, found 644.2438.

(2S, 4S)-1-*O*-anthroyl-2,4-di-(*O*-*P*-methoxycinnamoyl)-pentane-1,2,4-triol (46) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.12–7.97 (m, 4H), 7.67 (d, J = 16.0 Hz, 1H), 7.60 (d, J = 16.0 Hz, 1H), 7.49–7.35 (m, 8H), 6.85 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.33 (d, J = 16.0 Hz, 1H), 6.26 (d, J = 16.0 Hz, 1H), 5.62–5.52 (m, 1H), 5.25–5.15 (m, 1H), 4.93 (dd, J = 11.9, 3.5 Hz, 1H), 4.73 (dd, J = 11.9, 5.1 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 2.18–2.08 (m, 2H), 1.36 (d, J = 6.3 Hz, 3H); HRMS calcd for $C_{40}H_{36}O_8$ 644.2410, found 644.2426.

Preparation of acetonides 47 and 48. (2S, 4S)-1-*O*-anthroyl-2,4-*O*-isopropylidene-pentane-1,2,4-triols (47) To a solution of **43** (5 mg, 15.4 μmol) in 2,2-dimethoxy propane (2 ml) and acetone (2 ml) was added *P*-TsOH (catalytic amount). After the reaction mixture was stirred at room temperature for 2 h, it was passed through a small basic alumina column and concentrated for purification by preparative TLC (silica gel,EtOAc/Hexane 3:7) to give 5.3 mg **47** in 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.18 (d, J = 8.8 Hz, 4H), 8.03 (d, J = 8.4 Hz, 4H), 7.51 (m, 4H), 4.65 (dd, J = 11.3, 3.4 Hz, 1H), 4.56 (dd, J = 11.4, 6.8 Hz, 1H), 4.40 (m, 1H), 4.08 (m, 1H), 1.70 (m, 2H), 1.52 (s, 3H), 1.51 (s, 3H), 1.22 (d, J = 6.1 Hz, 3H); M.S.: *m/z* 365 $(M + 1)^+$.

(2S, 4R)-1-*O*-anthroyl-2,4-*O*-isopropylidene-pentane-1,2,4-triols (48) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.17 (d, J = 8.7 Hz, 4H), 8.03 (d, J = 8.3 Hz, 4H), 7.51 (m, 4H), 4.68–4.58 (m, 2H), 4.34 (m, 1H), 4.04 (m, 1H), 1.72

(m, 2H), 1.50 (s, 3H), 1.42 (s, 3H), 1.23 (d, J = 6.3 Hz, 3H); M.S.: *m/z* 365 $(M + 1)^+$.

Preparation of di-*P*-methoxycinnamates 49–52. (2S, 4S, 6S)-1,2-*O*-Isopropylidene-4,6-di-(*O*-*P*-methoxycinnamoyl)-heptane-1,2,4,6-tetrol (49) To **15** (10 mg, 50 μmol) in acetonitrile (1 ml) was added *P*-methoxycinnamoyl imidazole (46.4 mg, 200 μmol) with 29 μl (200 μmol) of DBU. The mixture was stirred at room temperature in the dark for 4 h and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (EtOAc/Hexane 3:7) to give 22 mg of **49** in 85% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 16.0 Hz, 1H), 7.61 (d, J = 16.0 Hz, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 6.28 (d, J = 16.0 Hz, 1H), 6.26 (d, J = 16.0 Hz, 1H), 5.25–5.13 (m, 2H), 4.19 (pentet, J = 6.4 Hz, 1H), 4.09 (dd, J = 8.0, 6.0 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.57 (t, J = 7.2 Hz, 1H), 2.19–2.01 (m, 2H), 1.92–1.84 (m, 2H), 1.43 (s, 3H), 1.33 (d, J = 4.4 Hz, 3H), 1.27 (s, 3H); HRMS calcd for $C_{30}H_{36}O_8$ (M + 1) 525.2488, found 525.2464.

(2S, 4S, 6S)-1,2-*O*-Isopropylidene-4,6-di-(*O*-*P*-methoxycinnamoyl)-heptane-1,2,4,6-tetrol (50) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 16.0 Hz, 1H), 7.58 (d, J = 16.0 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.25 (d, J = 16.4 Hz, 1H), 6.24 (d, J = 16.4 Hz, 1H), 5.24 (m, 1H), 5.15 (m, 1H), 4.19 (pentet, J = 6.4 Hz, 1H), 4.10 (dd, J = 8.0, 6.0 Hz, 1H), 3.82 (s, 6H), 3.60 (t, J = 7.2 Hz, 1H), 2.10–2.00 (m, 2H), 1.90–1.83 (m, 2H), 1.43 (s, 3H), 1.33 (d, J = 6.0 Hz, 3H), 1.29 (s, 3H); HRMS calcd for $C_{30}H_{36}O_8$ (M + 1) 525.2488, found 525.2463.

(2S, 4R, 6R)-1,2-*O*-Isopropylidene-4,6-di-(*O*-*P*-methoxycinnamoyl)-heptane-1,2,4,6-tetrol (51) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 16.0 Hz, 1H), 7.61 (d, J = 16.0 Hz, 1H), 7.43 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 6.28 (d, J = 16.0 Hz, 1H), 6.26 (d, J = 16.0 Hz, 1H), 5.27 (m, 1H), 5.15 (m, 1H), 4.15 (pentet, J = 6.8 Hz, 1H), 4.02 (dd, J = 8.0, 6.0 Hz, 1H), 3.83 (s, 6H), 3.54 (t, J = 8.0 Hz, 1H), 2.15 (pentet, J = 7.6 Hz, 1H), 2.02–1.96 (m, 1H), 1.92–1.85 (m, 2H), 1.41 (s, 3H), 1.33 (d, J = 6.4 Hz, 3H), 1.27 (s, 3H); HRMS calcd for $C_{30}H_{36}O_8$ 525.2488, found 525.2463.

(2S, 4R, 6S)-1,2-*O*-Isopropylidene-4,6-di-(*O*-*P*-methoxycinnamoyl)-heptane-1,2,4,6-tetrol (52) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 16.0 Hz, 2H), 7.36 (d, J = 7.6 Hz, 4H), 6.79 (d, J = 8.8 Hz, 4H), 6.24 (d, J = 16.0 Hz, 1H), 6.23 (d, J = 16.0 Hz, 1H), 5.26 (m, 1H), 5.19 (m, 1H), 4.14 (m, 1H), 4.03 (dd, J = 8.0, 6.0 Hz, 1H), 3.81 (s, 6H), 3.55 (t, J = 8.0 Hz, 1H), 2.14–2.07 (m, 2H), 1.97–1.93 (m, 2H), 1.43 (s, 3H), 1.33 (d, J = 4.8 Hz, 3H), 1.29 (s, 3H); HRMS calcd for $C_{30}H_{36}O_8$ (M + 1) 525.2488, found 525.2464.

Preparation of dimethylaminobenzoates 53–64. (2S, 4S, 6S)-1,2-*O*-Isopropylidene-4,6-di-(*O*-dimethylaminobenzoyl)-8-nonene-1,2,4,6-tetrol (53) To **19** (10 mg, 44 μmol) in acetonitrile (1 ml) was added dimethylaminobenzoyl triazole (28.1 mg, 130 μmol) with 19 μl (130 μmol) of DBU. The mixture was stirred at room temperature overnight and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (EtOAc/Hexane 1:1) to give 20 mg of **53** in 88% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d's, J = 8.9 Hz, 4H), 6.60 (d's, J = 8.8 Hz, 4H), 5.84–5.74 (m, 1H), 5.32–5.27 (m, 2H), 5.14–5.08 (m, 2H), 4.20–4.16 (m, 1H), 4.00 (dd, J = 8.0, 5.9 Hz, 1H), 3.56 (t, J = 7.8 Hz, 1H), 3.00 (bs, 12H), 2.44–2.40 (m, 2H), 2.15–1.84 (m, 4H), 1.38 (s, 3H), 1.31 (s, 3H); HRMS calcd for $C_{30}H_{40}N_2O_6$ 524.2886, found 524.2892.

(2S, 4S, 6R)-1,2-*O*-Isopropylidene-4,6-di-(*O*-dimethylaminobenzoyl)-8-nonene-1,2,4,6-tetrol (54) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.9 Hz, 2H), 7.82 (d, J = 8.9 Hz, 2H), 6.58 (d, J = 8.5 Hz, 4H), 5.86–5.77 (m, 1H), 5.32–5.21 (m, 2H), 5.12–5.06 (m, 2H), 4.24–4.17 (m, 1H), 4.08 (dd, J = 8.1, 5.8 Hz, 1H), 3.56 (t, J = 8.0 Hz, 1H), 3.02 (s, 6H), 3.01 (s, 6H), 2.48 (t, J = 6.7 Hz, 2H), 2.17–2.09 (m, 3H), 1.96–1.89 (m, 1H), 1.36 (s, 3H), 1.30 (s, 3H); HRMS calcd for $C_{30}H_{40}N_2O_6$ 524.2886, found 524.2902.

(2S, 4R, 6R)-1,2-*O*-Isopropylidene-4,6-di-(*O*-dimethylaminobenzoyl)-8-nonene-1,2,4,6-tetrol (55) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d's, J = 8.9 Hz, 4H), 6.65 (d, J = 8.8 Hz, 2H), 6.64 (d, J = 8.9 Hz, 2H), 5.85–5.75 (m, 1H), 5.39–5.33 (m, 1H), 5.28–5.23 (m, 1H), 5.10–5.03 (m, 2H), 4.15–4.11 (m, 1H), 3.95 (dd, J = 7.9, 5.8 Hz, 1H), 3.51 (t, J = 7.9 Hz, 1H), 3.04 (bs, 12H), 2.49–2.45 (m, 2H), 2.25–2.17 (m, 1H), 2.10–2.00 (m, 2H), 1.97–1.87 (m, 1H), 1.37 (s, 3H), 1.32 (s, 3H); HRMS calcd for $C_{30}H_{40}N_2O_6$ 524.2886, found 524.2913.

(2S, 4R, 6S)-1,2-*O*-Isopropylidene-4,6-di-(*O*-dimethylaminobenzoyl)-8-nonene-1,2,4,6-tetrol (56) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.9 Hz, 2H), 7.78 (d, J = 8.8 Hz, 2H), 6.54 (d's, J = 8.9 Hz, 4H), 5.87–5.77 (m, 1H), 5.33–5.25 (m, 2H), 5.12–5.04 (m, 2H), 4.19–4.14 (m, 1H), 3.98 (dd, J = 8.0, 5.8 Hz, 1H), 3.54 (t, J = 7.7 Hz, 1H), 3.00 (s, 6H), 2.99 (s, 6H), 2.47 (t, J = 6.0 Hz, 2H), 2.22–2.05 (m, 2H), 2.03 (t, J = 6.4 Hz, 2H), 1.37 (s, 3H), 1.32 (s, 3H); HRMS calcd for $C_{30}H_{40}N_2O_6$ 524.2886, found 524.2896.

(2S, 4S, 6S, 8S)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl)-nonane-1,2,4,6,8-pentol (57) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92–7.88 (m, 6H), 6.63 (d, J = 8.6 Hz, 6H), 5.43–5.25 (m, 3H), 4.19–4.13 (m, 1H), 4.02 (dd, J = 8.0, 5.8 Hz, 1H), 3.48 (t, J = 7.8 Hz, 1H), 3.03 (s, 6H), 3.02 (s, 6H), 3.01 (s, 6H), 2.31–2.22 (m, 2H), 2.11–2.04 (m, 2H), 2.00–1.95 (m, 1H), 1.98–1.84 (m, 1H), 1.32 (s, 3H), 1.28 (d, J = 6.2 Hz, 3H), 1.25 (s, 3H); HRMS calcd for $C_{39}H_{51}N_3O_8$ 689.3676, found 689.3670.

(2S, 4S, 6S, 8R)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl)-nonane-1,2,4,6,8-pentol (58) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 9.0 Hz, 2H), 7.85 (d, J = 9.0 Hz, 2H), 7.75 (d, J = 9.0 Hz, 2H), 6.67–6.62 (m, 6H), 5.42–5.36 (m, 1H), 5.35–5.31 (m, 1H), 5.21–5.16 (m, 1H), 4.23–4.18 (m, 1H), 4.04 (dd, J = 8.1, 5.8 Hz, 1H), 3.52 (t, J = 7.6 Hz, 1H), 3.03 (s, 6H), 3.02 (s, 6H), 2.98 (s, 6H), 2.36–2.29 (m, 1H), 2.24–2.17 (m, 1H), 2.13–2.00 (m, 3H), 1.95–1.90 (m, 1H), 1.37 (s, 3H), 1.34 (d, J = 6.2 Hz, 3H), 1.29 (s, 3H); HRMS calculated for $C_{39}H_{51}N_3O_8$ 689.3676, found 689.3682.

(2S, 4S, 6R, 8R)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl)-nonane-1,2,4,6,8-pentol (59) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 9.0 Hz, 2H), 7.82 (d, J = 9.0 Hz, 2H), 7.72 (d, J = 9.0 Hz, 2H), 6.60 (d, J = 9.0 Hz, 2H), 6.55 (d, J = 9.0 Hz, 2H), 6.44 (d, J = 9.0 Hz, 2H), 5.39–5.34 (m, 1H), 5.29–5.25 (m, 2H), 4.20–4.13 (m, 1H), 4.03 (dd, J = 8.1, 5.8 Hz, 1H), 3.52 (t, J = 7.7 Hz,

1H), 3.01 (s, 6H), 2.99 (s, 6H), 2.97 (s, 6H), 2.34–2.23 (m, 2H), 2.14–2.00 (m, 2H), 1.99–1.86 (m, 2H), 1.35 (d, J = 6.1 Hz, 3H), 1.34 (s, 3H), 1.28 (s, 3H); HRMS calculated for $C_{39}H_{51}N_3O_8$ 689.3676, found 689.3680.

(2S, 4S, 6R, 8S)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl-nonane-1,2,4,6,8-pentol (60) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.9 Hz, 2H), 7.79 (d, J = 8.9 Hz, 2H), 7.75 (d, J = 8.9 Hz, 2H), 6.55 (d, J = 8.9 Hz, 2H), 6.53 (d, J = 8.9 Hz, 2H), 6.48 (d, J = 8.9 Hz, 2H), 5.33–5.19 (m, 3H), 4.21–4.15 (m, 1H), 4.05 (dd, J = 8.1, 5.9 Hz, 1H), 3.53 (t, J = 7.7 Hz, 1H), 3.00 (bs, 12H), 2.98 (s, 6H), 2.29–2.22 (m, 1H), 2.17–2.08 (m, 4H), 1.96–1.89 (m, 1H), 1.34 (s, 3H), 1.33 (d, J = 6.0 Hz, 3H), 1.29 (s, 3H); HRMS calculated for $C_{39}H_{51}N_3O_8$ 689.3676, found 689.3670.

(2S, 4R, 6R, 8R)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl)-nonane-1,2,4,6,8-pentol (61) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.88 (m, 6H), 6.64–6.62 (m, 6H), 5.42–5.33 (m, 2H), 5.26 (dd, J = 12.8, 6.0 Hz, 1H), 4.14–4.07 (m, 1H), 3.91 (dd, J = 8.0, 5.9 Hz, 1H), 3.45 (t, J = 7.7 Hz, 1H), 3.03 (s, 6H), 3.02 (s, 6H), 3.01 (s, 6H), 2.31–2.23 (m, 1H), 2.11–1.97 (m, 3H), 1.91–1.84 (m, 1H), 1.30 (s, 3H), 1.28 (d, J = 6.2 Hz, 3H), 1.23 (s, 3H); HRMS calculated for $C_{39}H_{51}N_3O_8$ 689.3676, found 689.3675.

(2S, 4R, 6R, 8S)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl)-nonane-1,2,4,6,8-pentol (62) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 9.0 Hz, 2H), 7.84 (d, J = 9.0 Hz, 2H), 7.75 (d, J = 9.0 Hz, 2H), 6.64 (d, J = 8.9 Hz, 2H), 6.61 (d, J = 8.9 Hz, 2H), 6.51 (d, J = 8.9 Hz, 2H), 5.42–5.32 (m, 2H), 5.20–5.15 (m, 1H), 4.17–4.11 (m, 1H), 3.94 (dd, J = 8.0, 5.9 Hz, 1H), 3.49 (t, J = 7.7 Hz, 1H), 3.02 (s, 6H), 3.01 (s, 6H), 2.98 (s, 6H), 2.34–2.20 (m, 2H), 2.09–1.90 (m, 4H), 1.33 (s, 3H), 1.32 (d, J = 6.0 Hz, 3H), 1.27 (s, 3H); HRMS calculated for $C_{39}H_{51}N_3O_8$ 689.3676, found 689.3681.

(2S, 4R, 6S, 8S)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl)-nonane-1,2,4,6,8-pentol (63) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 9.0 Hz, 2H), 7.80 (d, J = 9.0 Hz, 2H), 7.71 (d, J = 9.0 Hz, 2H), 6.62 (d, J = 9.0 Hz, 2H), 6.55 (d, J = 9.0 Hz, 2H), 6.45 (d, J = 9.0 Hz, 2H), 5.43–5.36 (m, 1H), 5.30–5.23 (m, 2H), 4.17–4.11 (m, 1H), 3.94 (dd, J = 8.0, 5.9 Hz, 1H), 3.48 (t, J = 7.8 Hz, 1H), 3.02 (s, 6H), 3.00 (s, 6H), 2.97 (s, 6H), 2.34–2.26 (m, 2H), 2.22–2.17 (m, 2H), 2.02–1.93 (m, 2H), 1.35 (s, 3H), 1.33 (d, J = 6.0 Hz, 3H), 1.29 (s, 3H); HRMS calculated for $C_{39}H_{51}N_3O_8$ 689.2676, found 689.3678.

(2S, 4R, 6S, 8R)-1,2-*O*-Isopropylidene-4,6,8-tri-(*O*-dimethylaminobenzoyl)-nonane-1,2,4,6,8-pentol (64) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 9.0 Hz, 2H), 7.77 (d, J = 9.0 Hz, 2H), 7.74 (d, J = 9.0 Hz, 2H), 6.60 (d, J = 9.0 Hz, 2H), 6.53 (d, J = 9.0 Hz, 2H), 6.51 (d, J = 9.0 Hz, 2H), 5.35–5.27 (m, 2H), 5.23–5.19 (m, 1H), 4.19–4.12 (m, 1H), 3.97 (dd, J = 8.0, 5.9 Hz, 1H), 3.51 (t, J = 7.7 Hz, 1H), 3.01 (s, 6H), 2.99 (s, 6H), 2.98 (s, 6H), 2.22–2.00 (m, 6H), 1.36 (s, 3H), 1.34 (d, J = 6.2 Hz, 3H), 1.29 (s, 3H); HRMS calculated for $C_{39}H_{51}N_3O_8$ 689.3676, found 689.3680.

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