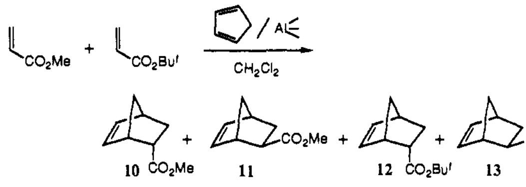
quently, MAD can be utilized both as an effective Lewis acid for endo selectivity and as a stereocontroller for asymmetric induction.

Furthermore, chemoselective Diels–Alder reaction of a mixture of *tert*-butyl and methyl acrylates with cyclopentadiene appears feasible in the presence of MAD. Here, only small amounts of the *tert*-butyl acrylate–cyclopentadiene endo adduct **12** were detected (ratio of **10–13**, 94:3:3:0), indicating the virtually complete discrimination of two different acrylate carbonyls with MAD.



MAD : 95% (94 : 3 : 3 : 0)
Et_2AlCl : 72% (32 : 1 : 67 : 0)
heat : 88% (43 : 20 : 28 : 9)

In conclusion, the exceptionally bulky MAD, in addition to its Lewis acidic character, has been proven to play a crucial role in synthetically promising discrimination of two different fumarate carbonyls, thereby achieving remarkably high regioselectivity, endo selectivity, and diastereoselectivity in the Diels–Alder reactions of unsymmetrical fumarates hitherto not observable with ordinary Lewis acids. This methodology not only provides a conceptually new mode of carbonyl discrimination but also meets versatile synthetic demands due to continuous, yet extensive developments of stereoselective Diels–Alder reactions in organic synthesis.

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(8) The absolute configuration of the cycloadducts **6–9** was correlated to the known (5*S*,6*S*)-5,6-bis(hydroxymethyl)-2-norbornene: Horton, D.; Machinami, T. *J. Chem. Soc., Chem. Commun.* **1981**, 88.

Enantiospecific Synthesis via Sequential Diastereofacial and Diastereotopic Group Selective Reactions: Enantiodivergent Synthesis of *syn*-1,3-Polyols

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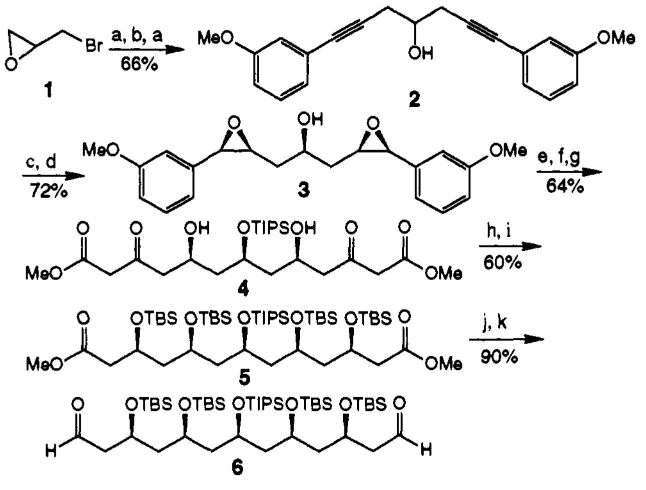
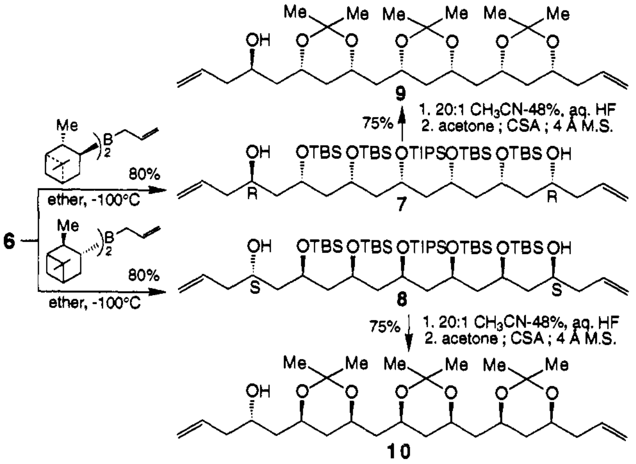
Transformation of meso molecules into chiral, nonracemic products relies mainly on monofunctionalization of the enantiotopic termini by the use of hydrolytic enzymes[1] or some recently developed nonenzymatic chemical reactions,[2] which operate through diastereofacial selective reactions controlled by *both* substrate and reagent. Herein, we describe a different approach via two simultaneous *exclusively* reagent-controlled diastereofacial selective reactions at both termini and subsequent terminal differentiation via a diastereotopic group selective reaction.[3] This strategy has been applied to an enatiodivergent synthesis of *syn*-1,3-polyol chains from a meso precursor.

Scheme I[a]



[a] (a) 2-MeOPhCCLi, $BF_3·OEt_2$, THF, −78 °C; (b) powdered KOH, Et_2O; (c) H_2, Ni_2B, EtOH (aqueous); (d) $VO(O\text{i-}Pr)_3$ (catalytic), *t*-BuOOH, CH_2Cl_2; (e) TIPSOTf, Et_3N, CH_2Cl_2; (f) Li, NH_3 (liquid), THF, *t*-BuOH; (g) O_3, MeOH, −78 °C, then PPh_3; (h) $MeOBEt_2$, $NaBH_4$, THF/MeOH, −78 °C; (i) TBSOTf, Et_3N, CH_2Cl_2; (j) $LiEt_3BH$, THF, 0 °C; (k) $(ClCO)_2$, DMSO, CH_2Cl_2, −78 °C, then Et_3N.

Scheme II



The two-directional synthesis of a *meso-syn*-1,3-polyol[4,5] is depicted in Scheme I. Achiral carbinol **2** was prepared by sequential homologations of epibromohydrin with lithium 3-methoxyphenylacetylide.[6] Controlled hydrogenation of **2**,[7] followed by stereoselective epoxidation[8] afforded bisepoxide **3** with diastereofacial selectivity of 15:1.[9] Silylation of **3**, followed by dissolving metal–ammonia reduction[10] and ozonolysis, revealed

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(4) For a discussion of the two-directional chain synthesis strategy, see: Schreiber, S. L. *Chem. Scr.* **1987**, *27*, 563.

(5) For a recent review of synthesis of 1,3-polyols, see: Oishi, T.; Nakata, T. *Synthesis* **1990**, 635.

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(8) Mihelich, E. D.; Daniels, K.; Eickhoff, D. *J. Am. Chem. Soc.* **1981**, *103*, 7690.

(9) The ratio is based on the pure major product and combination of the undesired minor isomers isolated by silica gel chromatography as determined by weight.

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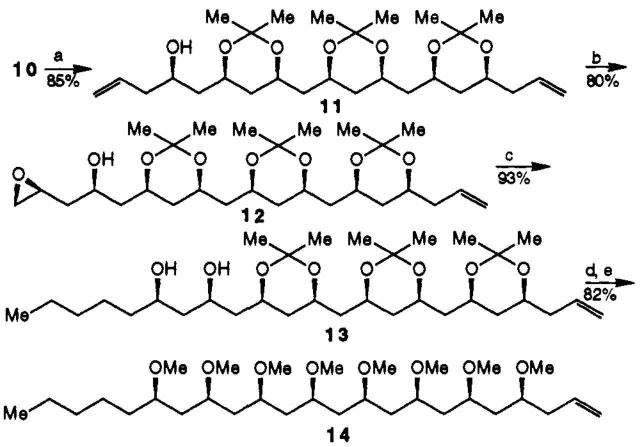
Scheme III[a]



[a] (a) DEAD, Ph_3P, $PhCO_2H$, THF, then NaOH; (b) $VO(O\textit{i}\text{-}Pr)_3$ (catalytic), *t*-BuOOH, CH_2Cl_2; (c) $(\textit{n}\text{-}Bu)_2CuLi$, Et_2O, −20 °C; (d) MeOH, *p*-TsOH (catalytic); (e) KH, MeI, THF.

the ketoester functionalities to give **4**. Simultaneous chelation controlled reduction[11] of both of the hydroxy ketone moieties in **4** afforded the *all-syn*-pentaol derivative with a 12:1 syn/anti ratio,[9] which was silylated to provide **5**. Subsequent reduction/oxidation provided *meso*-dialdehyde **6**.

We chose a reaction with the Brown reagents,[12] (+)- or (−)-diisopinylcampheyl allyl borane (Ipc_2BAll) to convert the C_s symmetric **6** into either antipode of the enlongated product (Scheme II). As we expected, dialdehyde **6** underwent additions with (+)-Ipc_2BAll or (−)-Ipc_2BAll to provide either **7** ($[a]_D^{25}$ +22.8, *c* 3.3, $CHCl_3$) or **8** ($[a]_D^{25}$ −23.0, *c* 3.4, $CHCl_3$), respectively, with high diastereoselectivity (>15:1).[9] The enantiomeric excess **7** and **8** were determined to be >98% based upon ^1H NMR analysis of their corresponding Mosher ester derivatives.[13] It is remarkable that a single enantiomeric reagent introduced two new stereocenters and determined the absolute stereochemistry at five preexisting stereocenters. Inspired by the chemistry of "ancillary stereocontrol"[14] and "diastereoselective resolution"[2i,15] involving acetonide groups as messengers to deliver stereochemical information in 1,3-diol systems, we examined a diastereotopic group selective acetonide formation as a means of terminal differentiation present in **7** and **8**. Desilylation of **7** or **8** and treatment with a catalytic amount of camphorsulfonic acid in acetone resulted in selective formation of tris(acetonide) **9** or **10** engaging the six *syn*-hydroxyl groups.[16] The excellent diastereotopic group selectivity (15:1)[9] in this transformation can be rationalized by the thermodynamic preference for a *syn*-1,3-acetonide over an *anti*-1,3-acetonide due to 1,3-diaxial interaction of methyl groups encountered in the latter.

For synthetic application of this strategy, we chose a novel isotactic polymethoxy-1-alkene **14**, isolated from the tolytoxin-producing blue-green algae *Tolypothrix conglutinata var. colorata* Ghose[17] and *Scytonema burmanicum*[18] (Scheme III). Mitsunobu inversion[19] of **10** provided **11**. Subjecting **11** to the V^{5+} catalyzed epoxidation conditions[8] resulted in a 5:1 diastereomeric mixture of epoxides with the desired compound **12** as the predominant product. Separation of **12** from its diastereomer by HPLC and subsequent *n*-butylcuprate opening of the epoxide afforded **13** with all of the required stereocenters. Finally, deprotection and methylation accomplished the synthesis of octamethoxy-1-tricosene **14**.

In conclusion, we have demonstrated an enantiodivergent synthesis of *syn*-1,3-polyols from a meso precursor via a exclusively reagent-controlled diastereofacial selective allylation reaction.[20] The diastereotopic group selective reactions can provide a solution to the problem of terminus differentiation. Studies toward synthesis of *anti*-1,3-polyols are underway and will be reported in the future.

Acknowledgment. We are grateful to Professor S. L. Schreiber and Dr. M. T. Goulet for helpful discussions on this subject. We thank Drs. M. Bernstein and L. A. Trimble for NMR measurement and Ms. C. Li for mass spectra on several intermediates. We also thank Dr. D. Dubé for his critical reading of this manuscript.

Supplementary Material Available: Spectral data for **2–6**, **8**, **10**, and **14** (3 pages). Ordering information is given on any current masthead page.

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Cryptoclastic Diastereotopism: NMR Evidence for the Chirotopicity of the Methyl Group in (α-Deuterio-*o*-chlorotoluene)chromium Tricarbonyl

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On the basis of symmetry arguments, the hydrogens of a chirotopic methylene group CH_2XY^* reside in diastereotopic environments.[2] This chirotopicity commonly manifests itself as an AB pattern in the ^1H NMR spectrum of the molecule.[3] However, except for α-deuterio-1,2-dimethylpiperidine (**1**),[4] no such AB pattern has been observed when X or Y is deuterium.[5] In **1**, the diastereotopicity is enhanced by "a strong conformational (rotomeric) preference as well as the existence of widely different magnetic environments at the sites occupied by the methylene protons".[4]

The rotational preference in **1** stems from an orbital interaction between the lone pair on N and the σ^* orbital of the α-CH bond and from the propensity for D to occupy the strongest binding site.[8] The ability of arene-bound metals to accelerate the solvolysis of α-halo aromatics and the increased acidity of alkyl protons α to a metal–arene system point to a significant interaction between the orbitals of the metal and those of the α carbon.[9] If the

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