bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxaldehyde, 117370-71-5; 2-methoxybicyclo[2.2.1]hept-5-ene-2-*endo*-dimethoxymethane, 117370-72-6; bicyclo[2.2.1]hept-5-ene-(*E*)-[(trimethylsilyl)oxy]-2-methylene, 117370-73-7; bicyclo[2.2.1]hept-5-ene-(*Z*)-[(trimethylsilyl)oxy]-2-methylene, 117370-74-8; 4-methoxy-4-(dimethoxymethyl)cyclohexene, 117370-75-9; *N*-(methoxycarbonyl)-2-oxocycloheptanamine, 117370-78-2; 4-hydroxy-4-(dimethoxymethyl)cyclohexene, 117370-81-7; 2-hydroxybicyclo[2.2.1]hept-5-ene-2-carboxaldehyde, 117370-86-2; *N*,*O*-bis(methoxycarbonyl)-*N*-(2-methoxyallyl)hydroxylamine, 117370-90-8.

The Chemistry of L-Ascorbic and D-Isoascorbic Acids. 2. *R* and *S* Glyceraldehydes from a Common Intermediate[1]

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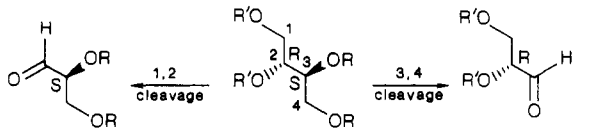
(*R*)- and (*S*)-glyceraldehyde and glycerol derivatives have been prepared from (2*R*,3*S*)-1,2-*O*-isopropylidenebutane-1,2,3,4-tetrol. (2*R*,3*S*)- and (2*S*,3*S*)-1,2-*O*-benzylidenebutane-1,2,3,4-tetrol have been prepared and cleaved to give (*R*)- and (*S*)-1,2-*O*-benzylideneglyceraldehydes and -glycerols. The conservation of chirality and conversion to PAF analogues are also demonstrated.

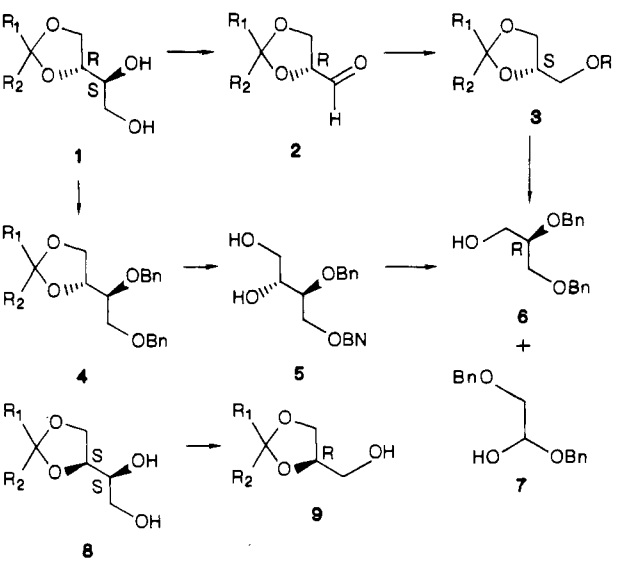
(*R*)- and (*S*)-glyceraldehyde and glycerol derivatives are common building blocks for a number of chiral natural[2] and synthetic[3] products. The enantiomers are usually prepared by degradative methods of the proper starting materials,[4] or, in the case of glycerols, by exchange of substituents between the oxygens at C-1 and C-3.[5] The latter procedure for inversion of chirality is rather lengthy and requires selective blocking of a primary hydroxyl group in a 1,2-diol system, a process that is not always totally selective and proceeds in variable yields.[5,6] More recently the use of enzymes has been reported for the preparation of chiral glycerols that have been suitably protected for further synthetic manipulations.[7] This paper describes a novel and simple approach for the preparation of (*R*)- and (*S*)-glyceraldehydes and glycerols from a *single* compound that contains both chiral centers, and in high yields. Also reported is a practical approach to the hitherto unknown (*R*)- and (*S*)-1,2-*O*-benzylideneglyceraldehydes, which are readily converted to the corresponding glycerol derivatives.

Conceptually both (*R*)- and (*S*)-glyceraldehyde derivatives can be prepared by selective cleavage of either the C-1, C-2 or C-3, C-4 bonds in a properly protected, and thus chiral, (2*R*,3*S*)-butane-1,2,3,4-tetrol derivative (Scheme I).

Scheme I



Scheme II[a]



[a] Bn = $CH_2C_6H_5$. **a** series: $R_1 = R_2 = CH_3$. **b** series: $R_1 = H$; $R_2 = C_6H_5$.

We have recently reported the preparation of (2*S*,3*S*)-1,2-*O*-isopropylidenebutane-1,2,3,4-tetrol from 5,6-*O*-isopropylidene-L-ascorbic acid.[8] Other chiral butanetetrols are accessible from either D- or L-tartaric acids.[9] However, the isomeric (2*R*,3*S*)-1,2-*O*-isopropylidene- and -benzylidenebutane-1,2,3,4-tetrols, which are derivable

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0022-3263/88/1953-6005$01.50/0

from *meso* tartaric acid, have only been recently prepared from D-isoascorbic acid.[10] Although the chemistry of L-ascorbic acid has been thoroughly studied,[11] that of its C-5 isomer, D-isoascorbic acid, remains relatively unexplored.[12]

The preparation of the key synthons (2*R*,3*S*)-1,2-*O*-isopropylidenebutane-1,2,3,4-tetrol (**1a**) and the 1,2-*O*-benzylidene derivative (**1b**) have already been described.[10] (*S*)-1,2-*O*-isopropylideneglycerol (**3a**, R = H) was obtained from **1a** by periodate cleavage followed by borohydride reduction.[13] Similarly, (*R*)-1,2-di-*O*-benzylglycerol (**6**)[14] was derived from (2*S*,3*R*)-1,2-di-*O*-benzylbutane-1,2,3,4-tetrol (**5**).[10]

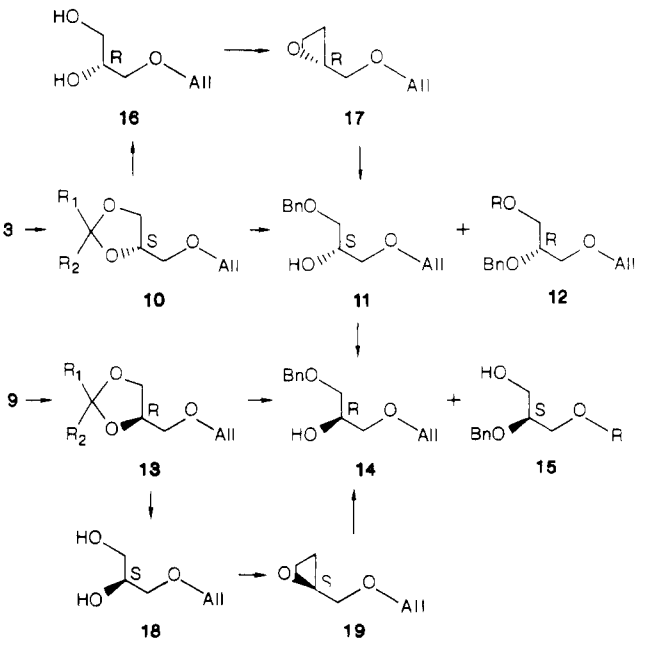
Our attention was next focused on the preparation of (2*S*)- and (2*R*)-2,3-*O*-benzylideneglyceraldehydes, two compounds that have not been previously reported. In addition to sharing the synthetic utility of the 2,3-*O*-isopropylidene analogues, they offer the added advantages associated with the chemistry of the benzylidene ring. While oxidative cleavage with *N*-bromosuccinimide[15] furnishes the 3-bromo-2-benzoate ester (glyceraldehyde numbering), reduction with a variety of reagents leads primarily to the 3-*O*-benzyl ether.[9b,16] Thus, selective manipulations of the hydroxyl group at C-2 become feasible, a feature that is not possible with the isopropylidene ring where both hydroxyl groups are deprotected simultaneously.

Scheme II depicts the preparation of (2*R*)-2,3-*O*-benzylideneglyceraldehyde (**2b**) and the (2*S*)- and (2*R*)-benzylideneglycerols **3b** (R = H) and **9b**, respectively.[17] Periodate cleavage[18] of **1b** followed by extraction with methylene chloride gave a very viscous material whose ^{1}H NMR spectrum showed a minor amount of the desired aldehyde. However when the product was distilled, the distillate proved to be the desired aldehyde, obtained as a diastereomeric mixture, showing typical aldehyde and benzylidene resonances in the ^{1}H NMR spectrum. As is the case with the isopropylidene analogue, this aldehyde is also unstable on standing, as suggested by a gradual reduction of the aldehydic proton resonance and a change in its consistency from a free flowing liquid to a viscous oil. Attempts to prepare **2b** by the lead tetraacetate method were not successful. This is probably due to acid hydrolysis of the benzylidene ring as indicated by the formation of benzaldehyde.

(*R*)- and (*S*)-1,2-*O*-benzylideneglycerols **9b** and **3b** (R = H) were also directly prepared from tetrols **8b** and **1b**, respectively, without isolation of the aldehyde.[13]

In order to evaluate their synthetic utility and to determine whether or not any racemization had taken place,

Scheme III[a]



[a] All = $CH_2CH{=}CH_2$; Bn = $CH_2C_6H_5$. **a** series: $R_1 = R_2 = CH_3$. **b** series: R_1 = H; $R_2 = C_6H_5$.

glycerols **3b** (R = H) and **9b** were first allylated and then subjected to the transformations outlined in Scheme III. When allyl ethers **10b** and **13b** were treated with either LAH/$AlCl_3$[16] or $NaCNBH_3$/TMSCl[19] they underwent regioselective ring opening to give enantiomeric glycerols **11** and **14**, respectively, as regioisomeric mixtures (5.5:1) with **12** (R = H) and **15** (R = allyl).[20] The ^{1}H NMR spectrum clearly showed two types of benzyl protons, a singlet (δ 4.46 major) and an AB quartet (δ 4.56, minor). One minor isomer (**12**, R = H) was easily separated as its trityl derivative (**12**, R = Tr) by column chromatography. Attempts to reverse the regioselective ring cleavage were only partially successful when diborane was used as the reducing agent.[21] Treatment of (*S*)-1-*O*-benzyl-2,3-*O*-benzylideneglycerol (**3b**, R = Bn) with a 5-fold excess of diborane·THF complex, at refluxing temperature for a period of 48 h, resulted in the formation of a 55:45 mixture of (*R*)-2,3-di-*O*-benzylglycerol (**6**) and the optically inactive 1,3-di-*O*-benzyl isomer (**7**, Scheme II).

That no racemization had taken place during periodate cleavage is demonstrated both spectroscopically and chemically. A high-resolution ^{1}H NMR spectrum for compound **6** showed two separate resonances for the benzyl protons. A singlet at δ 4.46 for the primary and an AB quartet centered at δ 4.58, J = 12 Hz assigned to the secondary. The addition of (+)Eu(hfc)$_3$ in concentrations of 2.0, 4.0, and 8.0 mM to a 0.1 M solution of **6** caused, as expected, a greater downfield shift of the AB quartet than the singlet without doubling of resonance lines. Had any racemization occurred, two sets of AB quartets would have been expected. Indeed, when this experiment was repeated on racemic **6**, two distinct AB quartets were observed for the *R* and *S* enantiomers. Similar results were also obtained with compound **10a**.

Further evidence for chiral integrity is demonstrated by the conversion of the isopropylidene ethers **10a** and **13a**

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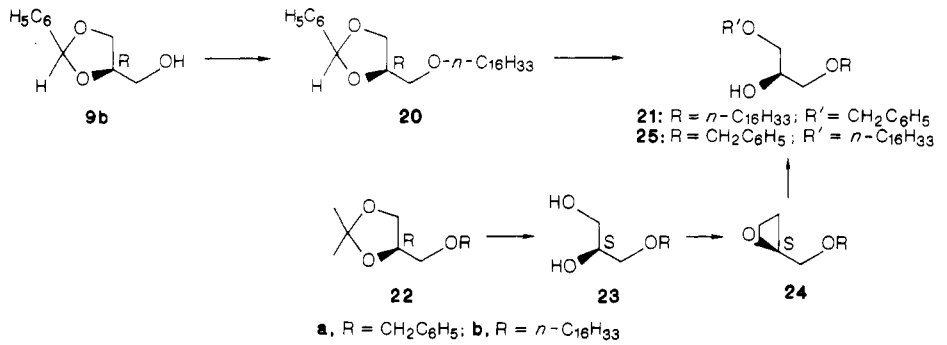
Scheme IV



to **11** and **14**, respectively. Thus, acid hydrolysis of **10a** and **13a**[6a] followed by epoxide formation[22] furnished (*S*)- and (*R*)-allylglycidols **17** and **19**, respectively. Regiospecific[23] ring opening of these epoxides with benzylate ion gave enantiomers **11** and **14**. Finally, inversion[22] of configuration of **11** furnished **14**. The equal but opposite rotations obtained for all enantiomeric pairs listed in Scheme III offer ample evidence that chiral integrity was always maintained.

Enantiomeric glycerols are useful chirons in phospholipid syntheses.[24] Of special and recent interest is the preparation of enantiomeric analogues of the platelet activating factors (PAF).[25] Minor modifications of the synthetic sequences outlined in Scheme III allowed the preparation of useful chirons for PAF analogues. These are shown in Scheme IV.

Alkylation of **9b** with hexadecyl mesylate furnished ether **20** in high yield. As was the case with **13b**, reduction of **20** with $LAH/AlCl_3$ furnished glycerol **21** as the major product in an isomeric mixture (7:1) with **15** (R = *n*-$C_{16}H_{33}$). This is based on ^1H NMR analysis, which showed two types of benzyl protons, a singlet at δ 4.5 (major) and an AB quartet at δ 4.61 ppm (minor), both integrating for a total of two protons. No attempts were made to separate them. The enantiomers **21** and **25** were also prepared from (*R*)-1,2-*O*-isopropylideneglycerol. Thus, alkylation of **22** (R = H) with benzyl bromide and hexadecyl mesylate furnished the corresponding ethers **22a**[26] and **22b**, respectively. Acid hydrolysis of these compounds to the corresponding glycerols **23a**[26] and **23b**[6b] followed by epoxide formation[22] gave glycidol ethers **24a**[27] and **24b**. Regiospecific ring opening[23] of **24a** with sodium hexadecylate and **24b** with sodium benzylate furnished enantiomers **25** and **21**, respectively. The conversion of these intermediates to PAF analogues will be reported elsewhere.

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. The ^1H NMR spectra were recorded on a Varian EM-390 and Bruker AM300 spectrometers. The chemical shifts are expressed in parts per million with respect to tetramethylsilane. Silica gel (Merck, grade 60, 230–400 mesh, 60A) suitable for column chromatography was purchased from Aldrich. Thin-layer chromatography was run on precoated (0.2 mm) silica gel 60 F-254 plates manufactured by EM Laboratories, Inc., and short-wave ultraviolet light (254 nm) was used to detect the UV absorbing spots. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. Optical rotations were determined on a Perkin-Elmer 141 polarimeter at 25 °C.

(*R*)-1,2-*O*-Benzylideneglyceraldehyde (2b). To a stirred solution of $NaHCO_3$ (5 mg) in water (10 mL) was added (2*R*,3*S*)-1,2-*O*-benzylidenebutane-1,2,3,4-tetrol (**1b**, 1.0 g, 4.76 mmol). The reaction mixture was cooled in an ice bath, and a solution of $NaIO_4$ (1.08 g, 5.05 mmol) in water (10 mL) was added dropwise over a period of 10 min. The reaction mixture was stirred further in the ice bath for 15 min. Extraction with CH_2Cl_2 (5 × 10 mL), drying over anhydrous $MgSo_4$, filtration, and evaporation of the solvent yielded a viscous oil (0.79 g, 93%). Vacuum distillation (0.1 mm, 175 °C) furnished the free-flowing aldehyde: ^1H NMR ($CDCl_3$) δ 3.46–4.73 (m, 3), 5.83 and 5.93 (s, 1), 7.16–7.53 (m, 5), 9.6–9.76 (d, 1, *J* = 7.0 Hz).

(*S*)-1,2-*O*-Isopropylideneglycerol (3a, R = H). The procedure outlined in ref 13 was followed giving the product in 70% yield: $[\alpha]_D$ +13.68° (neat) [lit.[13] $[\alpha]_D$ +15.14° (neat)].

(*S*)-1,2-*O*-Benzylideneglycerol (3b, R = H). The same procedure used for the preparation of **3a** (R = H) was followed to give the product in 85% yield.

(*S*)-1,2-*O*-Benzylidene-3-*O*-benzylglycerol (3b, R = Bn). Sodium hydride (1.0 g, in 60% mineral oil, 41.7 mmol) was washed three times with hexane and suspended in dry DMF (30 mL). To this suspension a solution of **3b** (R = H, 3.41 g, 18.9 mmol) in dry DMF (15 mL) was added over a period of 5 min, and the reaction mixture was stirred at room temperature for 10 min. Benzyl bromide (3.4 g, 19.9 mmol) was then added, and the reaction mixture was stirred at room temperature for 4 h. The excess NaH was destroyed by careful addition of water (5 mL). More water (50 mL) was added, and the product was extracted with ether. The organic layer was washed with water (7 × 25 mL), dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness to give the crude product as an oil. Purification by column chromatography on silica gel, eluting with hexane/EtOAc (9:1, v/v), furnished the product (4.0 g, 78.2%) as two diastereoisomers: ^1H NMR ($CDCl_3$) δ 3.45–3.65 (m, 2), 3.65–4.15 (m, 2), 4.15–4.35 (m, 1), 4.51 (q_{AB}, 2, *J* = 15 Hz), 5.72 (s, $^1/_2$), 5.88 (s, $^1/_2$), 6.93–7.67 (m, 10) [Lit.[15] δ 3.45–4.16 (m, 4), 4.33 (m, 1), 4.56 (s, 1), 4.58 (s, 1), 5.8 (s, $^1/_2$), 5.93 (s, $^1/_2$), 7.22–7.62 (m, 5), 7.28 (s, 5). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.5; H, 6.6. Found: C, 75.67; H, 6.68.

(*R*)-1,2-Di-*O*-benzylglycerol (6). Method A. Tetrol **5**[10] was cleaved as for **3a** (R = H) to give the product in 64% yield: $[\alpha]_D$ +0.64° (neat) [lit.[14] $[\alpha]_D$ +3.8° (neat)].[28]

Method B. To a stirred solution of **3b** (R = Bn, 0.5 g, 1.85 mmol)[15] in THF (8 mL) was added a solution of BH_3·THF (1M, 7 mL) under nitrogen atmosphere, and the reaction mixture was refluxed for 48 h. After cooling, excess reagent was decomposed

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(28) The discrepancy in these rotations cannot be explained. The chemical purity of **6** was confirmed by elemental analysis (Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.15; H, 7.39). Enantiomeric purity was demonstrated by the chiral shift reagent study. Furthermore, compound **6** was prepared by the same procedure from the 2*S*,3*S* diastereomer of **5**[10] and was found to have the same rotation.

by the addition of water (1.5 mL). The solvent was evaporated, and the residue was extracted with $CHCl_3$ (3 × 10 mL), and the organic phase was backwashed with water (3 × 5 mL) and dried over anhydrous $MgSO_4$. Removal of $CHCl_3$ under reduced pressure gave a crude product, which was purified by silica gel column chromatography, eluting with hexane/EtOAc (6.7:1, v/v) to give compound **7** in 22.4% yield: ^1H NMR ($CDCl_3$) δ 2.6 (br s, 1, D_2O exchangeable), 3.5 (d, 4, J = 6 Hz), 3.7–4.05 (m, 1), 4.45 (s, 2), 7.3 (s, 5). The spectrum was identical with that of a sample prepared according to a literature procedure.[23] Futher elution gave compound **6** in 27.4% yield.

(2*S*,3*S*)-1,2-*O*-Benzylidenebutane-1,2,3,4-tetrol (8b). The same procedure to obtain **1b**[10] was followed by starting with L-ascorbic acid to give the compound **8b** in 31.6% overall yield. The ^1H NMR spectrum of **8b** was identical with that of **1b**. Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.78; H, 6.70.

(*R*)-1,2-*O*-Benzylideneglycerol (9b). Benzylidene **8b** was cleaved as described earlier for **3a** (R = H). The product was obtained in 88% yield.

(*S*)-1-*O*-Allyl-2,3-*O*-isopropylideneglycerol (10a). To a stirred suspension of NaH (50% in mineral oil, 28.8 g, 0.6 mol, previously washed three times with hexane) in dry DMF (350 mL) was added dropwise a solution of **3a** (R = H) (33.0 g, 0.25 mol) in dry DMF (100 mL) at room temperature. Stirring was continued for 0.5 h. Allyl bromide (47.6 mL, 0.54 mol) was added dropwise over a period of 20 min, and the resulting mixture was stirred overnight at room temperature. Water (12 mL) was carefully added, and the mixture was poured into water (1.0 L). Extraction with Et_2O (4 × 200 mL), backwashing with water (10 × 100 mL), drying over anhydrous $MgSO_4$, filtration, and evaporation of the solvent gave the product (37.2 g, 86%). The pure sample was obtained by distillation (0.1 mm, 50 °C): $[\alpha]_D$ +22.8° (neat) [lit.[6a] $[\alpha]_D$ +23.21° (neat)].

(*S*)-1-*O*-Allyl-2,3-*O*-benzylideneglycerol (10b). This was obtained from **3b** (R = H) by following the procedure for **10a**. The pure product was obtained by column chromatography, eluting with hexane/EtOAc (9:1, v/v) in 86% yield: ^1H NMR ($CDCl_3$) δ 3.3–4.6 (m, 7), 4.9–5.4 (m, 2), 5.6–6.2 (m, 2), 7.13–7.56 (m, 5). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.64; H, 7.12.

(*S*)-1-*O*-Allyl-3-*O*-benzylglycerol (11). Method A. Benzyl alcohol (6.7 mL), (*S*)-1-*O*-allyglycidol (**17**, 2 g, 17.5 mmol), and *tert*-butyl alcohol (75 mL) were added successively to a solution of NaOH (0.75 g, 18.7 mmol) in water (0.75 mL) at room temperature. The reaction mixture was stirred vigorously for 3 h under reflux, diluted with water (15 mL), and extracted with Et_2O (3 × 20 mL). The ether extract was washed with brine solution (2 × 5 mL) and dried over anhydrous $MgSO_4$. The ether and excess benzyl alcohol were removed under reduced pressure leaving the product as an oil (2.9 g, 76%). An analytical sample was obtained by vacuum distillation (0.2 mm, 120–25 °C): $[\alpha]_D$ −0.74° (*c* 1.79, EtOH); ^1H NMR ($CDCl_3$) δ 2.85 (br s, 1, D_2O exchangeable), 3.32–3.54 (m, 4), 3.80–4.03 (m, 3), 4.45 (s, 2), 4.95–5.30 (m, 2), 5.55–6.04 (m, 1), 7.25 (s, 5). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.27; H, 8.10. Found: C, 70.21; H, 7.84.

Method B: LAH/$AlCl_3$. To a stirred solution of compound **10b** (1.0 g, 4.5 mmol) in Et_2O/CH_2Cl_2 (1:1, 35 mL) was added LAH (0.86 g, 21.6 mmol), and the mixture was heated to boiling. To this solution $AlCl_3$ (2.45 g, 18.4 mmol) in Et_2O (10 mL) was slowly added over a period of 15 min. Refluxing was continued for 3 h. After cooling, excess LAH was decomposed by the addition of EtOAc (20 mL) followed by water (20 mL). Alumina was filtered off, and the ether solution was washed with water (3 × 30 mL), dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness to give the crude product (0.87 g) as a mixture of **11** and **12** (R = H). A portion of this mixture (0.2 g, 0.9 mmol), trityl chloride (0.25 g, 0.89 mmol), pyridine (2 mL), CH_2Cl_2 (6 mL), and 4A molecular sieves (1 g) was stirred at room temperature for 24 h. Excess solvent was removed under reduced pressure, and the residue, thus obtained, was extracted with Et_2O (5 × 10 mL). The ether extracts were combined, washed with water (3 × 10 mL), and dried over anhydrous $MgSO_4$. Removal of Et_2O under diminished pressure gave a crude product, which consisted of **11** and **12** (R = Tr). Separation by silica gel column chromatography eluting with hexane/EtOAc (4:1, v/v) gave **12** (R = Tr, 27 mg): $[\alpha]_D$ −6.83° (*c* 2.02, EtOH); ^1H NMR ($CDCl_3$) δ 3.21 (m, 2), 3.45–3.76 (m, 3), 3.76–4.0 (m, 2), 4.61 (s, 2), 4.8–5.3 (m, 2), 5.5–6.0 (m, 1), 6.95–7.55 (m, 20). Anal. Calcd for $C_{32}H_{32}O_3$: C, 82.72; H, 6.94. Found: C, 82.62; H, 7.11.

Further elution furnished compound **11** (103 mg, 51.5%): $[\alpha]_D$ −0.73° (*c* 3.46, EtOH). The ^1H NMR spectrum was identical with that of the same compound obtained by method A.

(*R*)-1-*O*-Allyl-2-*O*-benzylglycerol (12, R = H). A solution of **12** (R = Tr, 0.24 g, 0.51 mmol) in 80% acetic acid (3.5 mL) was refluxed for 1 h. After evaporation of the solvent, left over acid was neutralized with $NaHCO_3$ (10%, 5 mL), and the aqueous layer was extracted with CH_2Cl_2. Drying over anhydrous $MgSO_4$, filtration, and evaporation of the solvent gave an oil. Purification by column chromatography on silica gel, eluting with hexane/EtOAc (6:1, v/v), furnished the product (77 mg, 67.3%): $[\alpha]_D$ −3.16° (*c* 1.38, EtOH); ^1H NMR ($CDCl_3$) δ 2.23 (br s, 1, D_2O exchangeable), 3.4–3.8 (m, 5), 3.85–4.05 (m, 2), 4.6 (q_{AB}, 2, J = 12 Hz), 5.0–5.4 (m, 2), 5.6–6.1 (m, 1), 7.3 (s, 5). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.19; H, 8.13.

(*R*)-1-*O*-Allyl-2,3-*O*-isopropylideneglycerol (13a). This compound was prepared from **9a** by following the same procedure used to obtain **10a** from **3a** (R = H) in 86.5% yield: $[\alpha]_D$ −22.0° (neat) [lit.[6a] for the *S*-isomer: $[\alpha]_D$ +23.21° (neat)].

(*R*)-1-*O*-Allyl-2,3-*O*-benzylideneglycerol (13b). This compound was prepared from **9b** via the same procedure used to obtain **10a** from **3a** (R = H) in 84% yield after purification of the crude product by silica gel column chromatography, eluting with hexane/EtOAc (9:1, v/v). The ^1H NMR spectrum of **13b** was identical with that of **10b**. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.68; H, 7.30.

(*R*)-1-*O*-Allyl-3-*O*-benzylglycerol (14). Method A. The procedure and yield are identical to method A used to prepare compound **11**: $[\alpha]_D$ +0.74° (*c* 3.53, EtOH). The ^1H NMR spectrum of **14** was identical with that of **11**.

Method B: Identical to method B for the preparation of **11** in 79.2% yield.

Method C. Compound **11** (0.22 g, 1.0 mmol), triphenylphosphine (0.4 g, 1.5 mmol), and benzoic acid (0.18 g, 1.5 mmol) were dissolved in dry benzene (2 mL). To this stirred solution was added dropwise a solution of diisopropyl azodicarboxylate (DIAD, 0.3 mL, 1.5 mmol) in dry benzene (0.5 mL) at room temperature. After the addition was complete, the reaction mixture was stirred for 24 h. Evaporation of benzene gave a residue, which was purified by silica gel column chromatography with hexane/EtOAc (97:3, v/v) as eluent. The benzoate ester obtained (0.25 g) was hydrolyzed with NaOH (57 mg) in MeOH (1.25 mL) and water (0.25 mL) at room temperature. Evaporation of the solvents followed by extraction of the residue with Et_2O provided **14** (0.15 g, 70%): $[\alpha]_D$ +0.72° (*c* 2.63, EtOH).

(*R*)-1-*O*-Allylglycerol (16). Activated amberlite IR-120 plus (64.3 g, activated by stirring it with 30 mL of concentrated HCl for 0.5 h, filtered, and washed with water) was added to a solution of **10a** (37.2 g, 0.22 mol) in 95% ethanol (600 mL). The reaction mixture was stirred at room temperature for 20 h. Filtration, evaporation of the solvent, dissolution of the residue in ether, drying over anhydrous $MgSO_4$, and evaporation gave the crude product. This was purified on a silica gel column, eluting with a mixture of hexane/EtOAc (3:2, v/v) to obtain **16** (24.4 g, 85.5%): $[\alpha]_D$ +5.3° (neat) [lit.[6a] $[\alpha]_D$ +6.45° (neat)].

(*R*)-1-*O*-Allylglycidol (17). Compound **16** (24.4 g, 0.18 mmol) was dissolved in dry benzene (560 mL), and triphenylphosphine (56.3 g, 0.21 mol) was added. The reaction mixture was boiled without a condenser to $^3/_4$ of its original volume and cooled to room temperature. Diethyl azodicarboxylate (DEAD, 35.3 mL, 0.22 mol) was added, and the reaction mixture was stirred at room temperature for 1 h. Removal of benzene followed by vacuum distillation of the residue (0.4 mm, 43 °C) furnished the product (12.5 g, 59.3%): $[\alpha]_D$ −10.19° (*c* 2.59, EtOH); ^1H NMR ($CDCl_3$) δ 2.36–2.9 (m, 2), 2.83–3.8 (m, 3), 3.9–4.16 (m, 2), 5.0–5.46 (m, 2), 5.5–6.1 (m, 1). Anal. Calcd for $C_6H_{10}O_2$: C, 63.21; H, 8.84. Found: C, 63.31; H, 8.71.

(*S*)-1-*O*-Allylglycerol (18). This compound was obtained from **13a** via the same procedure used to obtain **16** from **10a** in 85% yield: $[\alpha]_D$ −6.18° (neat) [lit.[6a] for the *R* isomer $[\alpha]_D$ +6.45° (neat)].

(*S*)-1-*O*-Allylglycidol (19). This compound was obtained from **18** via the same procedure used to obtain **17** from **16**: $[\alpha]_D$

+9.6° (c 0.94, EtOH). The ^{1}H NMR spectrum of **19** was identical with that of **17**.

(*R*)-1,2-*O*-Benzylidene-3-*O*-hexadecylglycerol (20). Sodium hydride (0.13 g, in 50% mineral oil, 2.7 mmol) was washed three times with hexane and suspended in dry DMF (10 mL). To this suspension was added a solution of **9b** (0.31 g, 1.7 mmol) in dry DMF (5 mL) over a period of 5 min, and the reaction mixture was stirred at room temperature for 10 min. Hexadecyl mesylate (0.59 g, 1.8 mmol) was then added, and the reaction mixture was stirred at 70 °C for 2.5 h. After cooling, excess NaH was destroyed by careful addition of water (0.5 mL), and the product was extracted with Et_2O. The organic layer was washed with water (7 × 25 mL), dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness to give the crude product as an oil. Purification by column chromatography on silica gel, eluting with hexane/EtOAc (9:1, v/v), furnished **20** (0.49 g, 72%): mp 42–45 °C; ^{1}H NMR ($CDCl_3$) δ 0.83 (t, 3, J = 6 Hz), 1.23 (br s, 28), 3.35–3.65 (m, 4), 3.66–4.5 (m, 3), 5.75 and 5.86 (s, 1), 7.15–7.6 (m, 5). Anal. Calcd for $C_{26}H_{44}O_3$: C, 77.18; H, 10.96. Found: C, 77.03; H, 11.03.

(*R*)-1-*O*-Benzyl-3-*O*-hexadecylglycerol (21). Method A. This compound was prepared from **24b** via the same procedure used to obtain compound **11** by method A, in 77% yield: mp 36–38 °C; $[\alpha]_D$ −0.84° (c 1.91, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.83 (t, 3, J = 6 Hz), 1.23 (s, 28), 2.76 (d, 1, J = 4.5 Hz, D_2O exchangeable), 3.3–3.67 (m, 6), 3.8–4.1 (m, 1), 4.5 (s, 2), 7.26 (s, 5). Anal. Calcd for $C_{26}H_{46}O_3$: C, 76.80; H, 11.40. Found: C, 77.02; H, 11.12.

Method B: LAH/$AlCl_3$. To a stirred solution of compound **20** (0.25 g, 0.6 mmol) in Et_2O:CH_2Cl_2 (10 mL, 1:1) was added LAH (0.12 g, 3.2 mmol), and the mixture was heated to boiling. To this solution $AlCl_3$ (0.34 g, 2.5 mmol) in Et_2O (5 mL) was slowly added over a period of 15 min. Refluxing was continued for 2 h. After cooling, excess LAH was decomposed by the addition of EtOAc (4 mL) followed by water (5 mL). Alumina was filtered off, and the ether solution was washed with water (3 × 5 mL), dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness to give the crude product 0.23 g. Filtration on silica gel with $CHCl_3$ provided **21** (0.22 g, 84%).

(*R*)-1,2-*O*-Isopropylidene-3-*O*-hexadecylglycerol (22b). This compound was prepared from **9a** via the same procedure used to obtain **20** from **9b**, in 89% yield as an oil: $[\alpha]_D$ −7.34° (c 3.89, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 3, J = 6 Hz), 1.23 (s, 28), 1.3 (s, 3), 1.4 (s, 3), 3.35–4.35 (m, 7). Anal. Calcd for $C_{22}H_{44}O_3$: C, 74.10; H, 12.44. Found: C, 74.09; H, 12.43.

(*S*)-1-*O*-Hexadecylglycerol (23b). This was obtained from **22b** via the same procedure used to obtain **16** from **10a**, in 74% yield: mp 64 °C (lit.[6b] mp 62.5–63.5 °C); $[\alpha]_D$ +2.83° (c 0.6, $CHCl_3$) [lit.[6b] $[\alpha]_D$ +3.1° (c 1.0, $CHCl_3$)].

(*S*)-1-*O*-Benzylglycidol (24a). This compound was obtained from **23a** via the same procedure used to obtain **17** from **16**, in 72.3% yield: $[\alpha]_D$ +11.8° (neat) [lit.[26] $[\alpha]_D$ +13.9° (neat)].

(*S*)-1-*O*-Hexadecylglycidol (24b). The same procedure for obtaining **17** was applied to **24b**. However this product was obtained by filteration of the crude reaction mixture on a silica gel column with hexane/EtOAc (9:1, v/v) in 72% yield: mp 37 °C; $[\alpha]_D$ +4.96° (c 1.74, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 3, J = 6 Hz), 1.25 (s, 28), 2.53 (dd, 1, J = 2.5 and 5.0 Hz), 2.83 (dd, 1, J = 4.2 and 5.0 Hz), 3.0–3.23 (m, 1), 3.25–3.8 (m, 4). Anal. Calcd for $C_{19}H_{38}O_2$: C, 76.45; H, 12.83. Found: C, 76.68; H, 12.61.

(*S*)-1-*O*-Benzyl-3-*O*-hexadecylglycerol (25). Epoxide **24a** was ring opened with sodium hexadecylate as outlined for obtaining compound **11** from **17** by method A. The product was obtained in 69% yield: mp 36–38 °C; $[\alpha]_D$ +0.95° (c 2.95, EtOH). The ^{1}H NMR spectrum of **25** was identical with that of **21**.

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Vinylic Organoboranes. 11. A Highly Stereospecific and Regiospecific Synthesis of Trisubstituted Alkenes via Organoboranes

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A highly stereospecific synthesis of trisubstituted alkenes using (*E*)- and (*Z*)-2-(1-substituted-1-alkenyl)-1,3,2-dioxaborinanes is presented. (*E*)-2-(1-Substituted-1-alkenyl)-1,3,2-dioxaborinanes (**1**), as described previously, readily react with organolithium or Grignard reagents in diethyl ether at −78 °C to form the corresponding "ate" complexes. Treatment of these "ate" complexes with iodine in methanol induces the migration of the alkyl group from boron to the adjacent carbon, followed by a base-induced deiodoboronation to afford stereodefined trisubstituted alkenes in good yields (50–82%) and in excellent stereochemical purities (≥97%). Similarly, (*Z*)-2-(1-substituted-1-alkenyl)-1,3,2-dioxaborinanes (**2**), easily obtainable by a previous procedure, react with organolithium or Grignard reagents, followed by treatment with iodine and base, to produce the stereoisomeric trisubstituted alkenes in good yields (65–82%) and in excellent isomeric purities (≥97%). These two procedures provide a convenient route to any of the six possible trisubstituted alkenes, $R^1CH{=}CR^2R^3$.

Introduction

The synthesis of trisubstituted alkenes of defined stereochemistry has attracted considerable attention in recent years because many biologically active compounds occurring in nature possess the structural skeleton of trisubstituted alkenes.[2] Application of organoboranes to the stereospecific synthesis of (*Z*)-disubstituted[3] and

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