(1*R*,2*S*,3*S*,5*R*)-3-[(1*R*)-1-Methyl-3-oxobutyl]-3,6,6-trimethylbicyclo[3.1.1]hept-2-yl 2-Methylbutyrate (16). Into a solution of **15a** (131 mg, 0.45 mmol) in CH_2Cl_2 (10 mL) and MeOH (4 mL) was passed excess ozone at -78 °C for 1 h. After the excess ozone was removed by bubbling through with nitrogen gas for 30 min, dimethyl sulfide (280 mg, 4.5 mmol) was added. The mixture was stirred at -70 °C for 1 h and at room temperature for 12 h and concentrated. The residue was chromatographed (SiO_2; hexane-AcOEt, 7:1) to give 109 mg (75%) of **16** (R_f 0.51, Merck F 254; hexane-AcOEt, 5:1) and 31 mg of unidentified compound (R_f 0.34). **16**: bp 82-83 °C (0.02 mm); $[\alpha]^{26}_D$ +34.0° (*c* 1.5); IR (neat) 1720 (ester C=O), 1705 cm^{-1} (C=O); ^1H NMR (60 MHz) δ 0.82 (t, 3, CH_3), 0.87 (d, J = 6 Hz, 3, CH_3), 1.03 (s, 3, CH_3), 1.06 (d, J = 6 Hz, 3, CH_3), 1.18 (s, 6, CH_3), 1.20-3.00 (m, 12, CH_2, CH), 2.06 (s, 3, $COCH_3$), 3.14 (d, J = 4 Hz, 1, CH—O). Anal. Calcd for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.22; H, 10.68.

(1*R*,2*S*,3*S*,5*R*)-3-[(1*R*)-3-Hydroxy-1-methylbutyl]-3,6,6-trimethylbicyclo[3.1.1]heptan-2-ol (17a). To a suspension of $LiAlH_4$ (76 mg, 2.0 mmol) in ether (2 mL) was added a mixture of **16** (109 mg, 0.34 mmol) and 31 mg of unidentified compound obtained above in ether (5 mL) at 0 °C. The mixture was stirred at 2-5 °C for 1 h and at room temperature for 2 h, quenched with AcOEt (0.5 mL) and aqueous 5% $NaHCO_3$, and worked up in the usual manner to give 82 mg (76% yield from **15a**) of **17a**: mp 96-97 °C; $[\alpha]^{19}_D$ +27.0° (*c* 1.1); IR (Nujol) 3350 (OH), 3280 (OH), 1458, 1136, 1031 cm^{-1}; ^1H NMR (60 MHz) δ 0.94 (d, J = 7 Hz, 3, CH_3), 1.04, 1.11 (s, 6, CH_3), 1.17 (d, J = 7 Hz, 3, CH_3), 1.21 (s, 3, CH_3), 1.20-2.40 (m, 9, CH_2, CH), 2.87 (br s, 2, OH), 3.66-3.98 (m, 1, CH-O), 4.08 (d, J = 4 Hz, 1, CH-O). Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.75; H, 11.55.

(1*R*,3*S*,5*R*)-3-[(1*R*)-1-Methyl-3-oxobutyl]-3,6,6-trimethylbicyclo[3.1.1]heptan-2-one (17b). To a suspension of PCC (410 mg, 1.9 mmol) and AcONa (312 mg, 3.5 mmol) in CH_2Cl_2 (7 mL) was added a solution of **17a** (65 mg, 0.27 mmol) in CH_2Cl_2 (3 mL) at 0-5 °C. After being stirred at 0-5 °C for 1 h and at room temperature for 3 h, the mixture was worked up as described in the preparation of **11a** to give 62 mg (97%) of **17b**: bp 74-75 °C (0.025 mm) [lit.[6] mp 100 °C (0.1 mm)]; $[\alpha]^{15}_D$ +94.0° (*c* 0.5) (lit.[6] +120°); ^{13}C NMR δ 16.4 (q), 22.7 (q), 24.9 (q), 25.9 (t), 26.4 (q), 30.4 (q), 35.3 (d), 37.0 (t), 41.8 (d), 42.8 (s), 44.8 (s), 47.4 (t), 59.6 (d), 208.3 (s), 219.9 (s). IR and ^1H NMR spectral data were identical with those of an authentic specimen.[17]

(4*R*,4a*S*,6*R*)-4,4a,5,6,7,8-Hexahydro-6-(1-chloro-1-methylethyl)-4,4a-dimethyl-2(3*H*)-naphthalenone (Nootkatone Hydrochloride, 18). The diketone **17b** was converted to **18** by the literature method[6] in 77% yield: mp 84-85 °C (lit.[6] mp 84-85.5 °C); $[\alpha]^{16}_D$ +159.5° (*c* 0.43) (lit. +146°,[5b] +160°[6]); ^{13}C NMR δ 15.0 (q), 16.9 (q), 28.1 (t), 30.1 (q), 30.5 (q), 32.6 (t), 39.1 (s), 40.0 (t), 40.4 (d), 42.0 (t), 45.3 (d), 73.7 (s), 124.5 (s), 170.0 (d), 199.0 (s).

(4*R*,4a*S*,6*R*)-4,4a,5,6,7,8-Hexahydro-6-isopropenyl-4,4a-dimethyl-2(3*H*)-naphthalenone ((+)-Nootkatone, 1). The treatment of **18** with activated alumina in hexane at 60 °C for 24 h afforded a mixture of (+)-**1** and isonootkatone (91:1) in 76% yield by HPLC analysis (Waters Associates Model 6000A; μ-Porasil, 7.8 × 30 cm column; 10:1 hexane-AcOEt at 1.5 mL/min at room temperature): mp 29-30 °C (lit. mp 36-37,[1a] 28-30 °C[4b]); $[\alpha]^{15}_D$ +184° (*c* 0.94) (lit. +195.5°,[1a] +188°[6]). IR, ^1H NMR, ^{13}C NMR[20] spectral data were identical with those of the authentic sample of (+)-**1**.[21]

Registry No. **1**, 4674-50-4; **2a**, 38651-65-9; **2b**, 83198-84-9; **2c**, 29362-79-6; **3**, 73675-69-1; **4**, 83198-85-0; **5**, 83152-42-5; **6a**, 81550-51-8; **6b**, 83152-43-6; **7a**, 81550-52-9; **7b**, 81550-53-0; **7c**, 83152-44-7; **8a**, 81550-54-1; **8b**, 83152-45-8; **9**, 81550-55-2; **10a**, 81550-56-3; **10b**, 81550-57-4; **10c**, 83152-46-9; **11a**, 81550-58-5; **11b**, 83152-47-0; **11c**, 72521-65-4; **12**, 27621-99-4; **13**, 83152-48-1; **14**, 83152-49-2; **15**, 83152-50-5; **16**, 83152-51-6; **17a**, 81550-62-1; **17b**, 72453-41-9; **18**, 72453-44-2; dimethyl carbonate, 616-38-6.

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Regio- and Stereocontrolled Synthesis of Epoxy Alcohols and Triols from Allylic and Homoallylic Alcohols via Iodo Carbonates

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Received March 16, 1982

The regio- and stereoselective synthesis of cyclic iodo carbonates **1-10**, resulting from allylic and homoallylic alcohols, was investigated. These useful intermediates were easily hydrolyzed to epoxy alcohols **11-20** or triols **21-30**, depending on the polymeric reagent employed (Amberlyst A 26 in the OH^- or CO_3^{2-} form, respectively). Stereochemical assignments were carried out by ^{13}C NMR or ^1H NMR correlations and by conversion of the compounds to products of known stereostructures.

In connection with the total synthesis of macrolide antibiotics and polyether ionophores, there is increasing interest in methods for stereocontrolled double bond functionalization.[1] Recently Bartlett[2] achieved 1,3-asymmetric induction through the phosphate chain-extended epoxidation, Kishi[3] reported 1,4-asymmetric induction in the preparation of bis-homoallylic epoxy alcohols, and Still[4] showed that boranes may be used to hydroborate dienes to give diols with high 1,2, 1,3, and 1,4 remote asymmetric induction.

In recent papers we have described a novel functionalization of double bonds of allylic and homoallylic alcohols.[5-7]

We report here further developments of our process, concerning the regio- and stereoselective synthesis of epoxy

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(2) (a) Bartlett, P. A.; Jernstedt, K. K. *J. Am. Chem. Soc.* **1977**, *99*, 4829. (b) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3.
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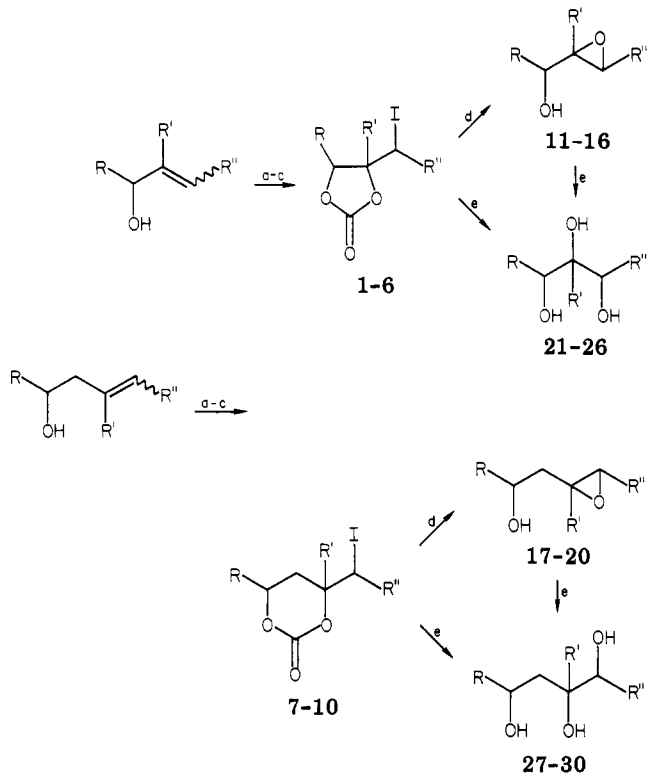
Scheme I[a,b]



[a] R, R', and R'' = H or alkyl. [b] (a) *n*-BuLi; (b) CO_2; (c) I_2, THF; (d) Amberlyst A 26 OH^- form, methanol, room temperature; (e) Amberlyst A 26 CO_3^{2-} form, refluxing benzene.

alcohols and triols starting from the corresponding cyclic iodo carbonates, obtained through a 1,2- and 1,3-asymmetric induction in both cyclic and acyclic systems. Five- and six-membered cyclic iodo carbonates of allylic and homoallylic alcohols are respectively obtained by treatment of lithium alkoxides with carbon dioxide, followed by iodocyclization.[5] The successive hydrolyses[6,7] afford either epoxy alcohols or triols, depending upon the reaction conditions. The steps of this synthesis are outlined in Scheme I.

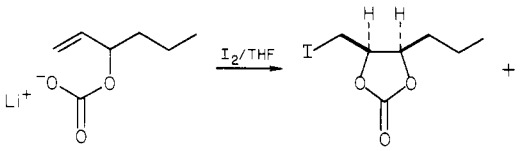
Results and Discussion

(A) Iodo Carbonates. The iodolactonization reaction is a versatile and highly stereoselective process, as demonstrated by Bartlett[8] and Corey.[9] As part of our studies in the synthesis of natural compounds by means of cyclofunctionalization reactions proceeding via an intermediate iodonium,[10] we carried out the iodocyclization of lithium alkenyl carbonates,[5] prepared in quantitative yield by bubbling CO_2 into a THF solution of lithium alkoxides at room temperature for 1 h. These carbonates can be isolated by performing the reaction in dry ether and were characterized by IR spectroscopy ($\nu_{C=O}$ 1750–1805 cm^{-1}). The iodocyclization reaction was carried out in homogeneous THF solution at room temperature by adding 2.2 equiv[11] of I_2 dissolved in THF to the carbonate. The cyclic iodo carbonates were obtained in good yield. The reaction seems to have a wide applicability toward either allylic or homoallylic primary, secondary, and tertiary alcohols: the results are summarized in Table I.

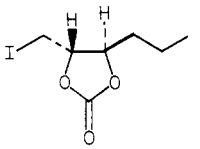
This useful procedure functionalizes C=C double bonds with total regioselection: allylic alcohols give five-membered rings and homoallylic alcohols give six-membered rings, exclusively. Moreover, the reaction shows high stereoselection with the iodo carbonates **2**, **5**, **6**, **9**, and **10**, obtained from 2(*E*)-octen-4-ol, 2-cyclohexen-1-ol, 3,7-dimethyl-1,6-octadien-3-ol (linalool), 4-penten-2-ol, and 4-methyl-4-penten-2-ol, respectively, while lower selectivity is observed in the cases of 1-hexen-3-ol and 2-methyl-1-hepten-3-ol (iodo carbonates **1** and **3**). The diastereomeric ratios were determined by VPC analysis (see Experimental Section). The stereostructures of cyclic iodo carbonates **1–3** were established by conversion into the corresponding epoxy alcohols (see section B), whose configuration was assigned by comparison with authentic samples (prepared according to the literature[12,13]) and confirmed by ^1H NMR analysis.

The diastereomeric ratios of the epoxy alcohols recovered after hydrolysis always corresponded to the ratio of the iodo carbonate starting material.

The diastereomeric ratio of the iodo carbonate **1** was determined by ^1H NMR spectroscopy. The pure diastereomers isolated by silica gel chromatography were selectively irradiated at the iodomethyl and methylene groups, and the resonances for the C-3 and C-4 protons were used to determine the ratio of the cis/trans isomer (40:60) by assigning the lower field resonances to the cis configuration.[14]



cis-**1** (40%)



trans-**1** (60%)

For the iodo carbonate **2**, having a diastereomeric ratio of 7:93, the trans stereostructure of the major isomer was established by conversion to the corresponding epoxy alcohol; the assignment was confirmed by the ^1H NMR chemical shifts of the C-3 and C-4 protons of the ring, which were in agreement with a trans configuration.[14]

The cyclic iodo carbonates **1** and **3** were also obtained by treatment of the corresponding alkenyl methyl carbonates with I_2 in acetonitrile[8] either at room temperature or under reflux. Although an increase of the trans isomer was observed, under these conditions the reaction occurred at a much slower rate and with lower yields. In fact, the ester **31** furnished **1** in 60% yield, the cis/trans ratio being 20:80, while the ester **32** gave **3** in 40% yield, the cis/trans ratio being 52:48.

The stereostructrures for iodo caronbates **5**, **6**, **9**, and **10** were assigned by ^1H NMR spectroscopy.

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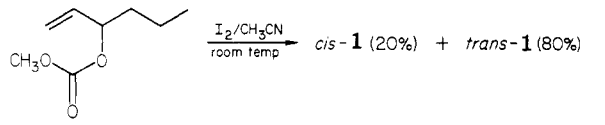

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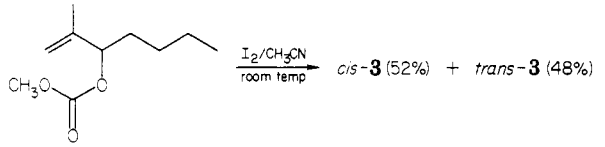
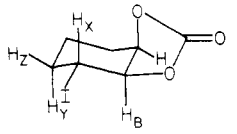


32

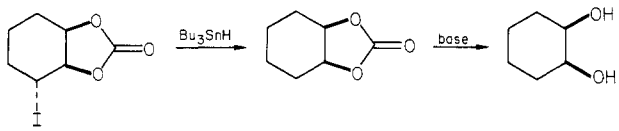
The stereostructure of the iodo carbonate **5** (99:1 dia-



5

stereomeric ratio) was determined by ^{1}H NMR (100 MHz) and confirmed by suitable reactions. The diagnostic feature is the H_X resonance which appears as a multiplet (eight lines) with J = 10.0, 7.0, and 4.0 Hz. After irradiation at the methylene protons H_Y and H_Z, this resonance appeared as a rough doublet with J = 10.0 Hz, in full agreement with an axial–axial coupling constant between H_X and H_B. The remaining coupling constants are thus assigned as the axial–axial and the axial–equatorial coupling constants of H_X with methylene protons.

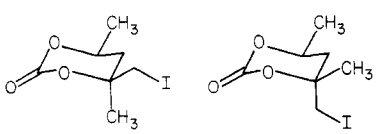
Moreover, alkaline hydrolysis of the cyclic carbonate resulting from reaction of iodo carbonate **5** with tri-*n*-butyl tin hydride affords *cis*-cyclohexane-1,2-diol.[15]



5

The diastereomeric ratio for iodo carbonate **6** was 80:20; the relative stereochemistry of the two isomers was elucidated on the basis of the ^{1}H NMR spectrum. The tertiary methyl resonance occurs at 1.40 ppm for the minor component and at 1.43 ppm for the major one. Since the isomer with the methyl group cis to a bulky substituent in five-membered cyclic carbonates has an upfield absorption, we attribute the cis configuration to the major component and the trans configuration to the minor one.[16]

A high stereoselection was also observed in the iodocyclization of the carbonate resulting from 4-methyl-4-penten-2-ol. The diastereomeric ratio for iodo carbonate **10** was 94:6. In the ^{1}H NMR spectrum of the major com-



cis-10 *trans*-10

ponent we observed the resonances for the secondary methyl at 4.43 ppm, for the tertiary methyl at 1.64 ppm, and for the iodomethyl at 3.40 ppm, while the spectrum of the minor component showed the resonances for the same groups at 1.42, 1.60, and 3.44 ppm. Since the axial methyl resonance is generally observed at lower field than the equatorial one in six-membered rings,[17] we accordingly assign the cis configuration to the major component and the trans configuration to the minor one. Moreover, this assignment agrees with our previous results for the similar iodo carbonate **9**.[5]

(B) Epoxy Alcohols. Cyclic iodo carbonates were converted into the corresponding epoxy alcohols by treatment with a resin (Amberlyst A 26, OH^- form[18]). The reaction was performed in methanol at room temperature and was complete after 2 h. The resin was then filtered off, and the product, after evaporation of the methanol, was practically pure (see Table I). The hydrolysis proceeds with retention of the stereostructure present in the starting iodo carbonate. In fact, *cis*-**1** and *trans*-**1** iodo carbonates, isolated by silica gel chromatography, afforded exclusively the epoxy alcohols *erythro*-**11** and *threo*-**11**, respectively. The stereostructures and the diastereomeric ratio for these products were determined by a VPC comparison with a mixture prepared by epoxidation of 1-hexen-3-ol with *t*-BuOOH/$VO(acac)_2$.[12] Analogously, the *cis*-**3** and *trans*-**3** iodo carbonates gave the *erythro*-**13** and *threo*-**13** epoxy alcohols, respectively.

The same diastereomeric ratio of the iodo carbonate **2** was observed for the corresponding epoxy alcohol **12** (7:93 erythro/threo).

The assigned stereochemistry of epoxy alcohols **15** and **19** was confirmed by comparison of their ^{13}C NMR spectra with that of a known mixture obtained by epoxidation of the corresponding alcohols with MCPBA[13] or *t*-BuOOH/$VO(acac)_2$,[12] respectively.

Only 40% yield was observed in the conversion of iodo carbonate **6** into the epoxy alcohol **16**, and the diastereomeric ratio of the starting iodo carbonate remains unchanged in the reaction product. The main component of the reaction mixture was 3,7-dimethyl-3-hydroxy-6-octen-2-one.

(C) Triols. Both iodo carbonates and epoxy alcohols were easily hydrolyzed to the corresponding triols in good yield by treatment with carbonate ion supported on Amberlyst A 26, an anion-exchange resin.[7] The reaction was carried out in refluxing benzene and was complete after 6 h. The results are summarized in Table II, where the yields of triols are referred to the hydrolysis of epoxy alcohol. The direct conversion of iodo carbonates to triols also occurred in good yield, except for **6**. The diastereomeric ratios of triols were determined by VPC analysis.

The reaction proceeded through the corresponding intermediate epoxy alcohol, as shown by TLC analysis. When both the iodo carbonate and epoxy alcohol disappeared, the resin was filtered off, and the triol, which remained adsorbed on the Amberlyst A 26, was recovered by washing with methanol. This procedure avoids difficulties connected with an aqueous workup, due to the high solubility of the products in water.

The hydrolysis proceeded with a total retention at chiral centers present in the starting material. An exception to this generalization is the iodo carbonate **2**, which gave a 60:20:20 diastereomeric mixture with unassigned stereostructure.

The pure isolated epoxy alcohols *erythro*-**11** and *threo*-**11** afforded *erythro*-**21** and *threo*-**21** triols, respectively, and their stereostructures were determined by comparison with authentic samples of diastereomers,

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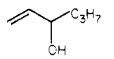
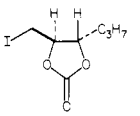
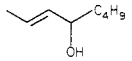
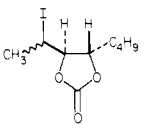
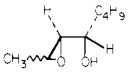
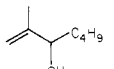
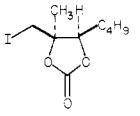
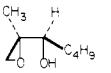
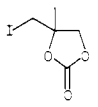
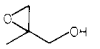
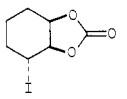
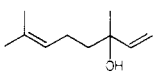
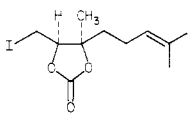
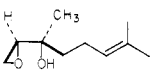
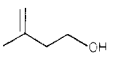
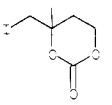
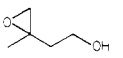
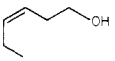
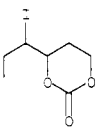
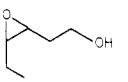
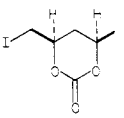
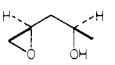
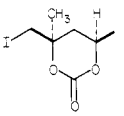
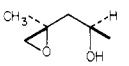
Table I. Epoxidation of Allylic and Homoallylic Alcohols through Cyclic Iodo Carbonates

alcohol	iodo carbonate (major isomer)	total yield,[a] %	product distribution (cis/trans)[b]	epoxy alcohol (major isomer)	total yield,[a] %	product distribution (erythro/threo)[b]
	 1	83 70[c]	40:60 20:80	 11	88	40:60
	 2	85	7:93	 12	91	7:93
	 3	81 60[c]	60:40 52:48	 13	85	60:40
	 4	85		 14	85	
	 5	67	99:1	 15	90	99:1
	 6	90	80:20	 16	40	80:20
	 7	82		 17	92	
	 8	80		 18	90	
	 9	80	95:5	 19	90	95:5
	 10	90	94:6	 20	91	94:6

[a] Isolated yields of chromatographed products. [b] Determined by VPC (see Experimental Section). [c] Iodocyclization performed on alkenyl methyl carbonate.

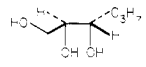
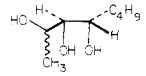
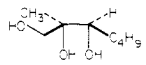
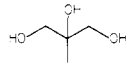
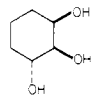
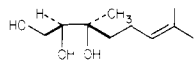
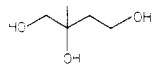
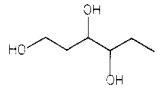
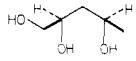
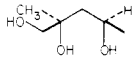
prepared from (*E*)- and (*Z*)-2-hexen-1-ol by treatment with *t*-BuOOH/OsO_4.[19] The stereostructures of triols *erythro*-**23** and *threo*-**23** were determined in the same manner.

The ^1H NMR spectrum of the triol **25**, obtained from epoxy alcohol **15** in a diastereomeric ratio of 99:1, was used to assign the stereostructure: the resonances observed were in complete agreement with those reported in the literature[20] for the DL (1,2/3) diastereomer, and the assignment was further confirmed by the melting point.[20]

(19) Sharpless, K. B.; Akashi, K. *J. Am. Chem. Soc.* **1976**, *98*, 1986.

(20) McCasland, G. E.; Naumann, M. O.; Durham, L. J. *J. Org. Chem.* **1966**, *31*, 3079.

Table II. Hydrolysis of Epoxy Alcohols by means of Carbonate Ion on Polymeric Support

epoxy alcohol	triol (major isomer)	total yield,[a] %	product distribution (erythro/threo)[b]
11	 **21**	80	40:60
12	 **22**	85	*c*
13	 **23**	78	60:40
14	 **24**	80	
15	 **25**	85	99:1
16	 **26**	90	80:20
17	 **27**	84	
18	 **28**	83	
19	 **29**	81	95:5
20	 **30**	84	94:6

[a] Isolated yield of chromatographed products. [b] Determined by VPC (see Experimental Section). [c] A mixture of three diastereomers, in a relative ratio of 60:20:20, is obtained.

The stereostructure of the major component of the triol **29**, obtained from epoxy alcohol **19**, was determined by conversion into *erythro*-2,4-pentanediol, identified by its ^{1}H NMR spectrum and by comparison with an authentic sample.[21]

Triols **26** and **30** were obtained from epoxy alcohols **16** and **20**, respectively, and the diastereomeric ratio was the same as that observed in the starting epoxy alcohol. Since it seemed reasonable to assume that hydrolysis occurs with stereostructure retention, it was possible to assign the erythro configuration to the major isomer.

Conclusions

The results presented here constitute an interesting approach to the regio- and stereocontrolled functionalization of the C=C double bond. In fact, we observed that the six-membered-ring iodo carbonate formation, in the cyclization of carbonates obtained from homoallylic alcohols, occurs with high stereoselection. This behavior is in qualitative agreement with the 1,3-interaction, present in the cyclic iodo carbonate, which forces both substituents into the equatorial positions, giving almost exclusively the cis isomer.

The cyclization of carbonates obtained from allylic alcohols always led to a five-membered ring which generally directed the bulky vicinal substituents in the trans position. In fact, with an allylic alcohol having an internal C=C double bond, high sterelselection was obtained in the corresponding iodo carbonate **2**, since the CH_3CHI group is bulky and favors a trans relationship. On the contrary, a cis/trans mixture of iodo carbonates was obtained in the functionalization of a terminal double bond. The lower stereoselection resulting for the iodo carbonate **1** could be due to the smaller CH_2I group (with respect to the CH_3CHI present in **2**). In the case of iodo carbonate **3** the comparable size of the CH_3 and CH_2I substituents is probably unable to induce the preferential formation of one isomer.

The present study also provides a simple method for preparing epoxy alcohols and triols. The hydrolysis of cyclic iodo carbonates generally occurs in good yields, giving products with defined configuration. In fact, from the cis iodo carbonates were obtained erythro epoxy alcohols and triols, while from trans iodo carbonates only threo epoxy alcohols and triols were recovered.

Experimental Section

The starting materials were obtained from commercial suppliers and were used without purification. Tetrahydrofuran (THF) was distilled from $LiAlH_4$ or sodium/benzophenone immediately prior to use. All reactions involving organometallic reagents were conducted under an argon atmosphere. Melting points (Pyrex capillary) are uncorrected. IR spectra were determined with a Perkin-Elmer Model 710B infrared recording spectrophotometer. ^{1}H NMR spectra were determined on the following spectrometers: Perkin-Elmer R-12-B (60 MHz) and Varian XL-100 (100 MHz). ^{13}C NMR spectra were measured at 25.14 MHz with a Varian XL-100 spectrometer. ^{1}H NMR chemical shifts are expressed in parts per million downfield from internal tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate. Mass spectra were obtained with a double-focusing Varian MAT 112 at an ionizing voltage of 70 eV. Mass spectral data are tabulated as m/e values. Analytical vapor-phase chromatography (VPC) was carried out on a Carlo Erba capillary gas chromatograph (Fractovap 4160) equipped with a SE-52 flexible glass capillary column (25 m × 0.3 mm i.d.; carrier gas He, p_{He} = 0.6 kg/cm^2). Chromatograms, peak areas, and retention times were obtained by using a Perkin-Elmer Sigma 10 data processor. Thin-layer chromatography was performed on silica gel HF_{254} (Merck) and column chromatography on silica gel (Merck, 0.05–0.20 mesh). *n*-Butyllithium was purchased from Fluka as a 1.8 M solution in *n*-hexane.

General Procedure for Preparation of Iodo Carbonates 1–10. To a solution of allylic or homoallylic alcohol (30 mmol) in dry THF (50 mL) under argon at room temperature was added *n*-BuLi (19.0 mL of a 1.8 M solution in *n*-hexane), and the mixture was stirred for 1 h at room temperature. CO_2 was then bubbled into the solution at 0 °C and the mixture allowed to stand at room temperature for 1 h under a CO_2 stream. To the carbonate so obtained was added I_2 (16.7 g, 66 mmol) dissolved in THF (70 mL), and the mixture was stirred for 12 h. Ethyl acetate (100 mL) was then added and the organic phase washed with $Na_2S_2O_3$ solution until the iodine color disappeared. After extraction and drying (Na_2SO_4), the solvent was evaporated in vacuo and the residue chromatographed on a silica gel column. The iodo carbonates **1–10** were separated by elution with cyclohexane/ethyl acetate (80:20). The results are summarized in Table I.

3-(Iodomethyl)-4-*n*-propyl-2,5-dioxacyclopentanone (1): colorless oil; IR (film) 1800 ($\nu_{C=O}$) cm^{-1} VPC (100 °C for 5 min and then to 240 °C at 10 °C/min) gave a cis/trans ratio of 40:60;

(21) Cazaux, L.; Maroni, P. *Bull. Soc. Chim. Fr.* **1972**, 780.

cis isomer t_R = 11.86; ^1H NMR ($CDCl_3$) δ 1 (t, 3 H, CH_3), 1.25–2 (m, 4 H, CH_2), 3.4 (d, 2 H, CH_2I, J = 5 Hz), 4.6–5.3 (m, 2 H, CH–O). Trans isomer: t_R = 11.28; ^1H NMR ($CDCl_3$) δ 1 (t, 3 H, CH_3), 1.25–2 (m, 4 H, CH_2), 3.45 (d, 2 H, CH_2I; J = 5 Hz), 4.2–4.65 (m, 2 H, CH–O); MS, m/e 270 (M^+), 156, 142, 128, 82.

Anal. Calcd for $C_7H_{11}O_3I$: C, 31.11; H, 4.10. Found: C, 31.01; H, 4.04.

3-(1-Iodoethyl)-4-*n*-butyl-2,5-dioxacyclopentanone (2): colorless oil; IR (film) 1800 ($\nu_{C=O}$) cm^{-1}; VPC (100 °C for 5 min and then to 240 °C at 10 °C/min) gave a cis/trans ratio of 7:93; cis isomer t_R = 12.05, trans isomer t_R = 11.84; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, CH_3), 1.1–1.65 (m, 6 H, CH_2), 2 (d, 3 H, CH_3; J = 7 Hz), 3.95–4.65 (complex pattern, 3 H, CHI, 2 CH–O); MS, m/e 298 (M^+), 170, 156, 142, 128, 110, 70.

Anal. Calcd for $C_9H_{15}O_3I$: C, 36.24; H, 5.07. Found: C, 36.15; H, 5.01.

3-(Iodomethyl)-3-methyl-4-*n*-butyl-2,5-dioxacyclopentanone (3): colorless oil; IR (film) 1800 ($\nu_{C=O}$) cm^{-1}; VPC (100 °C for 5 min and then to 240 °C at 10 °C/min) gave cis/trans ratio of 60:40; cis isomer t_R = 12.58; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, CH_3), 1.15–2 (m, 6 H, CH_2), 1.65 (s, 3 H, CH_3), 3.35 (s, 2 H, CH_2I), 4.4 (t, 1 H, CH–O). Trans isomer: t_R = 12.48; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, CH_3), 1.1–1.9 (m, 6 H, CH_2), 1.55 (s, 3 H, CH_3), 3.4 (s, 2 H, CH_2I), 4.45 (t, 1 H, CH–O); MS m/e 298 (M^+), 170, 158, 142, 128, 110, 70.

Anal. Calcd for $C_9H_{15}O_3I$: C, 36.24; H, 5.07. Found: C, 36.16; H, 4.99.

3-(Iodomethyl)-3-methyl-2,5-dioxacyclopentanone (4): white crystals; mp 71 °C; IR (Nujol) 1805 ($\nu_{C=O}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (s, 3 H, CH_3), 3.45 (s, 2 H, CH_2I), 4.35 (AB q, 2 H, CH_2O); MS, m/e 242 (M^+), 142, 127, 100, 86.

Anal. Calcd for $C_5H_7O_3I$: C, 24.8; H, 2.91. Found: C, 24.1; H, 2.87.

4-Iodo-1,3-dioxahexahydroindan-2-one (5): white crystals; mp 69 °C; IR (Nujol) 1800 ($\nu_{C=O}$) cm^{-1}. VPC (100 °C for 5 min and then to 240 °C at 10 °C/min) gave a 7a,3a-cis, 3a,4-trans/7a,3a-trans, 3a,4-trans ratio of 99:1. 7a,3a-Cis, 3a,4-trans isomer: t_R = 9.46; ^1H NMR ($CDCl_3$) δ 1.2–3.25 (m, 6 H, CH_2), 4–4.35 (m, 1 H, CHI), 4.6–5.0 (m, 2 H, CH–O). 7a,4a-Trans, 4a,4 trans isomer: t_R = 9.28; MS, m/e 268 (M^+), 141, 127, 97.

Anal. Calcd for $C_7H_9O_3I$: C, 31.35; H, 3.38. Found: C, 31.26; H, 3.31.

3-(Iodomethyl)-4-methyl-4-(4-methyl-3-penten-1-yl)-2,5-dioxacyclopentanone (6): colorless oil; IR (film) 1800 ($\nu_{C=O}$) cm^{-1}. VPC (100 °C for 5 min and then to 240 °C at 10 °C/min) gave a cis/trans diastereomer ratio of 80:20. Cis isomer: t_R = 10.45; ^1H NMR ($CDCl_3$) δ 1.43 (s, 3 H, CH_3), 1.6, 1.68 (2 s, 6 H, CH_3), 1.5–2.4 (m, 4 H, CH_2), 3.30 (AB q, 2 H, CH_2I, J_{AB} = 8 Hz), 4.71 (t, 1 H, CH–O, J = 8 Hz), 5.20 (t, 1 H, CH=C, J = 6 Hz). Trans isomer: t_R = 10.29; ^1H NMR ($CDCl_3$) δ 1.40 (s, 3 H, CH_3), 1.6, 1.68 (2 s, 6 H, CH_3), 1.5–2.4 (m, 4 H, CH_2), 3.30 (AB q, 2 H, CH_2I, J_{AB} = 8 Hz), 4.75 (t, 1 H, CH–O, J = 8 Hz), 5.20 (t, 1 H, CH=C, J = 6 Hz); MS, m/e 324 (M^+), 196, 184, 154, 136, 128, 110, 94.

Anal. Calcd for $C_{11}H_{17}O_3I$: C, 40.74; H, 5.28. Found: C, 40.67; H, 5.21.

3-(Iodomethyl)-3-methyl-2,6-dioxacyclohexanone (7): white crystals; mp 79 °C; IR (Nujol) 1750 ($\nu_{C=O}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65 (s, 3 H, CH_3), 2.1–2.5 (m, 2 H, CH_2), 3.45 (s, 2 H, CH_2I), 4.45 (t, 2 H, CH_2–O, J = 6 Hz); MS, m/e 256 (M^+), 169, 129, 127, 115.

Anal. Calcd for $C_6H_9O_3I$: C, 28.13; H, 3.54. Found: C, 28.07; H, 3.47.

3-(1-Iodoprop-1-yl)-2,6-dioxacyclohexanone (8): colorless oil; IR (film) 1750 ($\nu_{C=O}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, CH_3), 1.2–1.5 (m, 2 H, CH_2), 2.1–2.5 (m, 2 H, CH_2), 4.1–4.6 (complex m, 4 H, CH_2–O, CH–O, CHI); MS, m/e 270 (M^+), 141, 127.

Anal. Calcd for $C_7H_{11}O_3I$: C, 31.11; H, 4.10. Found: C, 31.04; H, 4.05.

3-(Iodomethyl)-5-methyl-2,6-dioxacyclohexanone (9): colorless oil; IR (film) 1750 ($\nu_{C=O}$) cm^{-1}. VPC (100 °C for 5 min and then to 240 °C at 10 °C/min) gave a cis/trans ratio of 95:5. Cis isomer: t_R = 10.21; ^1H NMR ($CDCl_3$) δ 1.45 (d, 3 H, CH_3, J = 6 Hz), 1.7 (dt, 1 H, H_A, J_{AB} = 12.5 Hz, J_{AX} = 11.5 Hz), 2.4 (dt, 1 H, H_B, J_{AB} = 12.5 Hz, J_{BX} = 3 Hz), 3.45 (d, 2 H, CH_2I, J = 5 Hz), 4.2–4.5 (complex m, 2 H, CH–O). Trans isomer: t_R = 9.75; MS, m/e 256 (M^+), 128, 127, 87.

Anal. Calcd for $C_6H_9O_3I$: C, 28.13; H, 3.54. Found: C, 28.04; H, 3.47.

3-(Iodomethyl)-3,5-dimethyl-2,6-dioxacyclohexanone (10): IR (Nujol) 1750 ($\nu_{C=O}$) cm^{-1}; VPC (100 °C for 5 min and then to 240 °C at 10 °C/min) gave a cis/trans ratio of 94:6. Cis isomer: t_R = 11.58; white crystals; mp 109 °C; ^1H NMR ($CDCl_3$) δ 1.43 (d, 3 H, CH_3, J = 6 Hz), 1.64 (s, 3 H, CH_3), 1.8–2.4 (m, 2 H, CH_2), 3.40 (s, 2 H, CH_2I), 4.3–4.9 (m, 1 H, CH–O). Trans isomer: t_R = 10.86; colorless oil; ^1H NMR ($CDCl_3$) δ 1.42 (d, 3 H, CH_3, J = 6 Hz), 1.60 (s, 3 H, CH_3), 1.8–2.9 (m, 2 H, CH_2), 3.44 (s, 2 H, CH_2I), 4.2–4.9 (m, 1 H, CH–O); MS, m/e 270 (M^+), 184, 141, 127, 85.

Anal. Calcd for $C_7H_{11}O_3I$: C, 31.11; H, 4.10. Found: C, 31.02; H, 4.05.

General Procedure for Preparation of Alkenyl Methyl Carbonates 31 and 32. The allylic or homoallylic alcohol (30 mmol) was dissolved in dry ether (30 mL) containing Et_3N (3.4 g, 33 mmol), and CH_3OCOCl (2.8 g, 30 mmol) in dry ether (10 mL) was added at 0 °C under stirring. After 1 h the mixture was diluted with water and extracted with ether. The organic layer was washed (3 N HCl, 10% aqueous $NaHCO_3$ solution, water), dried (Na_2SO_4), and evaporated in vacuo. After removal of the solvent, the residue was purified by silica gel chromatography; and after elution with hexane/ether (90:10), alkenyl methyl carbonates **31** and **32** were obtained in 95% yield.

(1-Hexen-3-yl) methyl carbonate (31): colorles oil; IR (film) 1750 ($\nu_{C=O}$) cm^{-1}; ^1H NMR (CCl_4) δ 0.95 (t, 3 H, CH_3), 1.1–1.9 (m, 4 H, CH_2), 3.8 (s, 3 H, OCH_3), 4.8–6.1 (complex pattern, 4 H, $CH=CH_2$, CH–O); MS, m/e 158 (M^+), 115, 99, 59.

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. found: C, 60.68; H, 8.86.

(2-Methyl-1-hepten-3-yl) methyl carbonate (32): colorless oil; IR (film) 1750 ($\nu_{C=O}$) cm^{-1}; ^1H NMR (CCl_4) δ 0.95 (t, 3 H, CH_3), 1.1–1.8 (m, 6 H, CH_2), 1.7 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 4.85 (m, 1 H, CH–O), 4.9 (s, 2 H, $CH_2=C$); MS, m/e 186 (M^+), 130, 111, 56.

Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.41; H, 9.68.

General Procedure for Preparation of Iodo Carbonates from Alkenyl Methyl Carbonates. To a solution of alkenyl methyl carbonate (10 mmol) in THF (20 mL) was added iodine (5 g, 20 mmol) dissolved in THF (50 mL), and the mixture was stirred for 5 h. Then ethyl acetate (50 mL) was added, and the organic phase was washed with $Na_2S_2O_3$ solution until the iodine color disappeared. After extraction and drying (Na_2SO_4), the solvent was evaporated in vacuo and the residue purified by silica gel chromatography; after elution with hexane/ethyl acetate (80:20), iodo carbonates were obtained. Yields are reported in Table I.

Preparation of Amberlyst A 26 in the OH^- Form. A 1 N NaOH solution (100 mL) was added under argon at room temperature to 10 g of Amberlyst A 26 (Rohm and Haas) in the chloride form (average capacity ~3.7 mequiv/g) and the suspension stirred for 1 h. The NaOH solution was then discarded, and the resin was washed with water (100 mL) and then with methanol (200 mL) while stirring. The reagent can be used directly but must be prepared under an inert atmosphere, since it is CO_2 sensitive, and stored at 0 °C to avoid decomposition.

Hydrolysis of Iodo Carbonates. Synthesis of Epoxy Alcohols 11–20. A solution of the iodo carbonate (10 mmol) in methanol (20 mL) was added under argon at room temperature to a stirred suspension of the resin Amberlyst A 26 in the OH^- form (6 g, ~22 mequiv) and stirring continued for 2 h. The resin was then filtered off and washed with methanol (40 mL). The organic solution was evaporated in vacuo, and the epoxy alcohols **11–20** were obtained practically pure. The results are summarized in Table I.

1,2-Epoxy-3-hexanol (11): colorless oil; VPC (60 °C) gave an erythro/threo diastereomeric ratio of 40:60. Erythro isomer: t_R = 2.60; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H, CH_3), 1.2–1.8 (m, 4 H, CH_2), 2.55–3 (m, 3 H, $\overline{CH_2–CHO}$), 2.9 (br s, 1 H, OH), 3.4–3.9 (m,

1 H, CHOH). Threo isomer: t_R = 2.65; ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 3 H, CH_3), 1.2–1.9 (m, 4 H, CH_2), 2.5–3.2 (m, 3 H, $\overline{CH_2-CHO}$), 2.9 (br s, 1 H, OH), 3.5–4 (m, 1 H, CHOH); MS, *m/e* 116 (M^+), 98, 74, 56.

Anal. Calcd for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 61.97; H, 10.36.

2,3-Epoxy-4-octanol (12): colorless oil; VPC (60 °C for 5 min and then to 240 °C at 10 °C/min) gave an erythro/threo diastereomeric ratio of 7:93. Erythro isomer, t_R = 6.39. Threo isomer: t_R = 6.57; ^{1}H NMR ($CDCl_3$) δ 0.9 (t, 3 H, CH_3), 1.15–1.7 (m, 6 H, CH_2), 1.35 (d, 3 H, CH_3), 2.55–3.2 (m, 2 H, $\overline{CH-CHO}$), 3.2–3.6 (m, 1 H, CHOH), 3.35 (br s, 1 H, OH); MS, *m/e* 87 ($M^+ - C_4H_9$), 82, 71, 69, 58, 57.

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.56; H, 11.12.

1,2-Epoxy-2-methyl-3-heptanol (13): colorless oil; VPC (70 °C) gave an erythro/threo diastereomeric ratio of 60:40. Erythro isomer: t_R = 5.15; ^{1}H NMR ($CDCl_3$) δ 0.9 (t, 3 H, CH_3), 1.1–1.8 (m, 6 H, CH_2), 1.3 (s, 3 H, CH_3), 2.7 (dd, 2 H, $\overline{C-CH_2O}$), 3.4–3.7 (m, 1 H, CHOH), 3.6 (br s, 1 H, OH). Threo isomer: t_R = 6.02; ^{1}H NMR ($CDCl_3$) δ 0.9 (t, 3 H, CH_3), 1.1–1.8 (m, 6 H, CH_2), 1.3 (s, 3 H, CH_3), 2.65 (dd, 2 H, $\overline{C-CH_2O}$), 3.1–3.45 (m, 1 H, CHOH), 3.6 (br s, 1 H, OH); MS, *m/e* 87 ($M^+ - C_4H_9$), 85, 71, 58.

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.57; H, 11.13.

2,3-Epoxy-2-methyl-1-propanol (14): colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 3 H, CH_3), 2.75 (AB q, 2 H, $\overline{CH_2-CO}$, J = 5 Hz), 3.75 (d, 2 H, CH_2OH, J = 2 Hz), 6 (br s, 1 H, OH); MS, *m/e* 88 (M^+), 57 ($M^+ - CH_2OH$), 42, 31.

Anal. Calcd for $C_4H_8O_2$: C, 54.53; H, 9.15. Found: C, 54.46; H, 9.08.

2,3-Epoxycyclohexan-1-ol (15): colorless oil; VPC (60 °C) gave a cis/trans diastereomeric ratio of 99:1. Cis isomer: t_R = 2.10; ^{1}H NMR ($CDCl_3$) δ 1.3–2 (m, 6 H, CH_2), 3.35 (br s, 2 H, $\overline{CH-CHO}$), 3.85 (br s, 1 H, OH), 4.05 (m, 1 H, CHOH); ^{13}C NMR δ 67.6, 55.8, 55.2, 28.2, 22.9, 19.3. Trans isomer: t_R = 2.34; no peaks attributable to trans isomer could be seen in the ^{13}C NMR spectrum; MS, *m/e* 114 (M^+), 96 ($M^+ - H_2O$), 55, 41.

Anal. Calcd for $C_6H_{10}O_2$: C, 63.13;, H, 8.83. Found: C, 63.07; H, 8.77.

1,2-Epoxy-3,7-dimethyl-6-octen-3-ol (16): colorless oil; VPC (70 °C) gave an erythro/threo diastereomeric ratio of 80:20. Erythro isomer: t_R = 7.20; ^{1}H NMR ($CDCl_3$) δ 1.2 (s, 3 H, CH_3), 1.35–1.9 (m, 8 H, CH_2 and CH_3), 1.9–2.4 (m, 2 H, CH_2), 2.25 (br s, 1 H, OH), 2.15–3.1 (m, 3 H, $\overline{CH-CH_2O}$), 5.2 (t, 1 H, CH=C, J = 7 Hz). Threo isomer: t_R = 8.11; MS, *m/e* 170 (M^+), 152 ($M^+ - H_2O$), 127, 109, 83, 69, 55, 43.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.48; H, 10.59.

3,4-Epoxy-3-methyl-1-butanol (17): colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.4 (s, 3 H, CH_3), 1.9 (t, 2 H, CH_2, J = 6 Hz), 2.6–2.9 (m, 2 H, $\overline{CH_2-CO}$), 2.85 (br s, 1 H, OH), 3.8 (t, 2 H, CH_2OH, J = 6 Hz); MS, *m/e* 102 (M^+), 87 ($M^+ - CH_3$), 84 ($M^+ - H_2O$), 71, 57, 55.

Anal. Calcd for $C_5H_{10}O_2$: C, 58.80; H, 9.87. Found: C, 58.72; H, 9.84.

3,4-Epoxy-1-hexanol (18): colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.1 (t, 3 H, CH_3), 1.3–2 (m, 4 H, CH_2), 2.75–4 (m, 2 H, $\overline{CH-CHO}$), 3.15 (br s, 1 H, OH), 3.85 (t, 2 H, CH_2OH, J = 6 Hz); MS, *m/e* 116 (M^+), 85 ($M^+ - CH_2OH$), 59, 57, 41.

Anal. Calcd for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 61.98; H, 10.36.

4,5-Epoxy-2-pentanol (19): Colorless oil; VPC (60 °C) gave an erythro/threo diastereomeric ratio of 95:5. Erythro isomer: t_R = 2.42; ^{1}H NMR ($CDCl_3$) δ 1.25 (d, 3 H, CH_3, J = 6 Hz), 1.5–1.9 (m, 2 H, CH_2), 2.6 (br s, 1 H, OH), 2.4–2.95 (m, 2 H, $\overline{CH_2-CHO}$), 2.95–3.3 (m, 1 H, $\overline{CH_2-CHO}$), 4.1 (m, 1 H, CHOH); ^{13}C NMR δ 23.4, 41.5, 46.8, 50.3, 66.0. Minor peaks attributable to the threo isomer (t_R = 2.55) were seen in the ^{13}C NMR spectrum at δ 23.8, 41.6, 47.1, 50.2, and 65.4. From the peak ratio the erythro/threo ratio was confirmed as being 95:5: MS, *m/e* 102 (M^+), 87 ($M^+ - CH_3$), 84 ($M^+ - H_2O$), 83, 57, 45.

Anal. Calcd for $C_5H_{10}O_2$: C, 58.80; H, 9.87. Found: C, 58.73; H, 9.83.

4,5-Epoxy-4-methyl-2-pentanol (20): colorless oil; VPC (70 °C) gave an erythro/threo diastereomeric ratio of 94:6. Erythro isomer: t_R = 2.70; ^{1}H NMR ($CDCl_3$) δ 1.2 (d, 3 H, CH_3, J = 6 Hz), 1.4 (s, 3 H, CH_3), 1.5–2.4 (m, 2 H, CH_2), 2.7 (d, 2 H, $\overline{CH_2-CO}$), 3.7 (br s, 1 H, OH), 3.6–4.4 (m, 1 H, CHOH). Threo isomer: t_R = 2.92; MS, *m/e* 116 (M^+), 59, 57, 40.

Anal. Calcd for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 61.96; H, 10.37.

Preparation of Amberlyst A 26 in CO_3^{2-} Form. A 1 M solution of sodium carbonate (900 mL) was slowly percolated through a column filled with Amberlyst A 26 (15 g; Rohm and Haas) in the chloride form (average capacity ~3.7 mequiv/g) until a negative test for chloride ion in the eluent was obtained. The resin was then washed with methanol and ether and dried in vacuo for 2 h at room temperature. This reagent was stored for 1 month at room temperature without loss of reactivity.

Hydrolysis of Epoxy Alcohols. Synthesis of Triols 21–30. Amberlyst A 26 in the carbonate form (8 g, ~30 mequiv) was added to a stirred solution of the epoxy alcohol (10 mmol) in benzene (20 mL) and the suspension refluxed for 6 h. The resin was then filtered off and the benzene solution discarded. After successive washing of the resin with methanol (50 mL) and evaporation in vacuo of the solvent, the pure triols were obtained. The results are summarized in Table II.

1,2,3-Hexanetriol (21): colorless oil; VPC (65 °C) gave an erythro/threo diastereomeric ratio of 40:60. Erythro isomer, t_R = 2.96. Threo isomer: t_R = 2.86; ^{1}H NMR (D_2O) δ 1 (t, 3 H, CH_3), 1.2–1.8 (m, 4 H, CH_2), 3.75 (m, 4 H, CHOH, CH_2OH); MS, *m/e* 103 ($M^+ - CH_2OH$), 91, 85, 73, 61, 43, 31, 30.

Anal. Calcd for $C_6H_{14}O_3$: C, 53.71; H, 10.52. Found: C, 53.65; H, 10.47.

2,3,4-Octanetriol (22): colorless oil; VPC (65 °C for 5 min and then to 240 °C at 10 °C/min) gave a diastereomeric mixture of unassigned configuration in a 60:20:20 ratio (t_R = 6.35, 5.80, and 5.26, respectively); ^{1}H NMR (CD_3COCD_3) δ 0.9 (t, 3 H, CH_3), 1.1–1.8 (m, 6 H, CH_2), 1.25 (t, 3 H, CH_3), 3–4.2 (m, 3 H, CHOH), 3.85 (br s, 3 H, OH); MS, *m/e* 117 ($M^+ - CH_3CHOH$), 100, 81, 69.

Anal. Calcd for $C_8H_{18}O_3$: C, 59.23; H, 11.18. Found: C, 59.16; H, 11.14.

2-Methyl-1,2,3-heptanetriol (23): colorless oil; VPC (90 °C) gave an erythro/threo diastereomeric ratio of 60:40. Erythro isomer: t_R = 9.00; ^{1}H NMR (CD_3COCD_3) δ 0.9 (t, 3 H, CH_3), 1.15–1.7 (m, 6 H, CH_2), 3.3–3.9 (m, 3 H, CH_2OH, CHOH), 3.85 (br s, 3 H, OH). Threo isomer: t_R = 9.32; ^{1}H NMR (CD_3COCD_3) δ 0.9 (t, 3 H, CH_3), 1.1 (s, 3 H, CH_3), 1.15–1.7 (m, 6 H, CH_2), 3.5 (m, 3 H, CH_2OH, CHOH), 3.85 (br s, 3 H, OH); MS, *m/e* 131 ($M^+ - CH_2OH$), 113, 105, 87, 75.

Anal. Calcd for $C_8H_{18}O_3$: C, 59.23; H, 11.18. Found: C, 59.17; H, 11.13.

2-Methyl-1,2,3-propanetriol (24): colorless oil; ^{1}H NMR (D_2O) δ 1.15 (s, 3 H, CH_3), 3.45 (s, 4 H, CH_2OH); MS, *m/e* 91 ($M^+ - CH_3$), 75 ($M^+ - CH_2OH$), 57, 32, 31, 30.

Anal. Calcd for $C_4H_{10}O_3$: C, 45.27; H, 9.50. Found: C, 45.20; H, 9.46.

1,2,3-Cyclohexanetriol (25): white crystals; VPC (90 °C) gave a mixture of DL (1,2/3) and meso (1,3/2) (99:1) compounds. DL (1,2/3) isomer: t_R = 9.81; mp 124 °C (lit.[20] mp 125 °C); ^{1}H NMR (D_2O) δ 1.35–2.1 (m, 6 H, CH_2), 3.43 (dd, 1 H, CHOH), 3.7 (m, 1 H, CHOH), 4.03 (m, 1 H, CHOH). Meso (1,3/2) isomer: t_R = 9.94; MS, *m/e* 114 ($M^+ - H_2O$), 96 ($M^+ - 2\ H_2O$), 86, 83, 70, 58, 57, 43.

Anal. Calcd for $C_6H_{12}O_3$: C, 54.53; H, 9.15. Found: C, 54.47; H, 9.11.

3,7-Dimethyl-6-octene-1,2,3-triol (26). VPC (120 °C) gave an erythro/threo diastereomeric ratio of 80:20. Erythro isomer: t_R = 10.02; white crystals; mp 44 °C; ^{1}H NMR (CD_3COCD_3) δ 1.15 (s, 3 H, CH_3), 1.3–1.8 (m, 8 H, CH_2 and CH_3), 1.8–2.4 (m, 2 H, CH_2), 3.3–4 (m, 3 H, CHOH, CH_2OH), 4.8 (br s, 3 H, OH), 5.25 (t, 1 H, C=CH, J = 6 Hz). Threo isomer: t_R = 10.20; MS, *m/e* 170 ($M^+ - H_2O$), 152 ($M^+ - 2\ H_2O$), 127, 109, 83, 69, 55, 43.

Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63.72; H, 10.68.

2-Methyl-1,2,4-butanetriol (27): colorless oil; ^1H NMR (CD_3COCD_3) δ 1.15 (s, 3 H, CH_3), 1.73 (t, 2 H, CH_2, J = 6 Hz), 3.4 (s, 2 H, CH_2OH), 3.75 (t, 2 H, CH_2OH, J = 6 Hz), 3.95 (br s, 3 H, OH); MS, m/e 89 ($M^+ - CH_2OH$), 87, 75, 71, 69, 57, 31.

Anal. Calcd for $C_5H_{12}O_3$: C, 49.98; H, 10.07. Found: C, 49.93; H, 10.04.

1,3,4-Hexanetriol (28): colorless oil; ^1H NMR (CD_3COCD_3) δ 1 (t, 3 H, CH_3, J = 6 Hz), 1.25–1.85 (m, 4 H, CH_2), 3.1–3.9 (m, 2 H, CHOH), 3.7 (t, 2 H, CH_2OH, J = 6 Hz), 4.55 (br s, 3 H, OH); MS, m/e 103 ($M^+ - CH_2OH$), 71, 43, 31, 30.

Anal. Calcd for $C_6H_{14}O_3$: C, 53.71; H, 10.52. Found: C, 53.68; H, 10.49.

1,2,4-Pentanetriol (29): colorless oil; VPC (70 °C) gave an erythro/threo diastereomeric ratio of 95:5. Erythro isomer: t_R = 2.40; ^1H NMR (D_2O) δ 1.2 (d, 3 H, CH_3), 1.65 (t, 2 H, CH_2), 3.4–4.3 (complex pattern, 4 H, CH_2OH, CHOH). Threo isomer: t_R = 2.51; MS, m/e 89 ($M^+ - CH_2OH$), 87, 71, 69, 31, 30.

Anal. Calcd for $C_5H_{12}O_3$: C, 49.98; H, 10.07. Found: C, 49.93; H, 10.04.

2-Methylpentane-1,2,4-triol (30): colorless oil; VPC (90 °C) gave an erythro/threo diastereomeric ratio of 94:6. Erythro isomer: t_R = 4.27; ^1H NMR (CD_3COCD_3) δ 1.15 (d, 3 H, CH_3, J = 6 Hz), 1.2 (s, 3 H, CH_3), 1.4–1.6 (m, 2 H, CH_2), 2.2 (br s, 3 H, OH), 3.4 (d, 2 H, CH_2OH), 3.8–4.4 (m, 1 H, CHOH). Threo isomer: t_R = 4.41; MS, m/e 103 ($M^+ - CH_2OH$), 85, 75, 59, 57.

Anal. Calcd for $C_6H_{14}O_3$: C, 53.71; H, 10.52. Found: C, 53.67; H, 10.48.

Acknowledgment. We are grateful to the National Research Council (Centro di Studio per la Fisica delle Macromolecole) for financial support.

Registry No. *cis*-1, 83134-75-2; *trans*-1, 83134-76-3; 2, 83134-77-4; *cis*-3, 83134-78-5; *trans*-3, 83134-79-6; 4, 78947-98-5; 5 (isomer 1), 83134-80-9; 5 (isomer 2), 83134-81-0; *cis*-6, 83134-82-1; *trans*-6, 83134-83-2; 7, 78947-95-2; 8, 78947-94-1; *cis*-9, 82770-18-1; *trans*-9, 82770-17-0; *cis*-10, 83134-84-3; *trans*-10, 83134-85-4; *erythro*-11, 83134-86-5; *threo*-11, 83134-87-6; 12, 4798-68-9; *erythro*-13, 53837-93-7; *threo*-13, 53837-92-6; 14, 872-30-0; *cis*-15, 26828-72-8; *trans*-15, 26828-73-9; *erythro*-16, 29428-56-6; *threo*-16, 29428-57-7; 17, 59954-67-5; 18, 67663-02-9; *erythro*-19, 83134-88-7; *threo*-19, 83134-89-8; *erythro*-20, 83134-90-1; *threo*-20, 83134-91-2; *erythro*-21, 83134-92-3; *threo*-21, 64446-63-5; 22, 36283-98-4; *erythro*-23, 83134-93-4; *threo*-23, 83134-94-5; 24, 25245-58-3; *dl*-25, 13302-87-9; *meso*-25, 2630-65-1; *erythro*-26, 83134-95-6; *threo*-26, 83134-96-7; 27, 62875-07-4; 28, 83134-97-8; *erythro*-29, 83212-31-1; *threo*-29, 83212-32-2; *erythro*-30, 83134-98-9; *threo*-30, 83134-99-0; 31, 83135-00-6; 32, 83135-01-7; 1-hexen-3-ol, 4798-03-2; (*E*)-2-octen-4-ol, 20125-81-9; 2-methyl-1-hepten-3-ol, 13019-19-7; 2-methyl-2-propen-1-ol, 513-42-8; 2-cyclohexen-1-ol, 822-67-3; linalool, 78-70-6; 3-methyl-3-buten-1-ol, 763-32-6; (*Z*)-3-hexen-1-ol, 928-96-1; 4-penten-2-ol, 625-31-0; 4-methyl-4-penten-2-ol, 2004-67-3.

Synthetic Studies of the Thieno[3,2-*d*]pyrimidine *C*-Nucleoside Isostere of Inosine[1]

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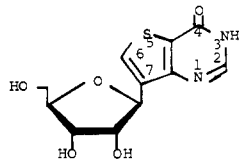
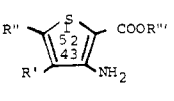
Received May 3, 1982

Synthesis of the thieno[3,2-*d*]pyrimidine *C*-nucleoside isostere of inosine 1β was achieved via a two-step ring closure of C-4 ribosylated methyl 3-aminothiophene-2-carboxylate 11β or, more efficiently, by reaction of 3-aminothiophene-2-carboxamide 14β with triethyl orthoformate. Intermediates 11β and 14β were obtained from common synthetic precursor 3 by reaction with methyl 2-mercaptoacetate or 2-mercaptoacetamide, respectively, and cyclization in base. The corresponding derivatives in the α series were made by identical procedures to confirm all structural assignments.

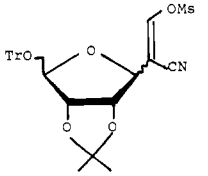
As part of an ongoing program concerned with the synthesis and biological evaluaton of *C*-nucleoside analogues of the natural purine nucleosides, we reported recently the synthesis of several pyrrolo[3,2-*d*]pyrimidine (9-deazapurine) *C*-nucleosides.[2,3] We report here the synthesis of 7-β-D-ribofuranosylthieno[3,2-*d*]pyrimidin-4-(3*H*)-one (1β), the first member of a structurally related, new class of *C*-nucleosides and an isostere of inosine and of formycin B.[4]



1β



2



3

The synthesis of a thieno[3,2-*d*]pyrimidine system was first reported by Gompper et al.[5] A more systematic investigation of this class of heterocycles by several investigators[6-8] was made possible by the development of a practical and versatile approach to their most common synthetic precursors, the 3-amino-2-carbalkoxythiophenes 2 by reaction of α,β-dichloropropionitriles with 2-mercaptoacetate esters in base.[9] Continued interest in these thienopyrimidines has been generated mainly by the wide spectrum of pharmacological activity discovered for

(1) This investigation was supported by funds from the National Cancer Institute, DHHS (Grants CA-08748, -18856, and -24634) and from the American Cancer Society (Grant CH-169).

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