°C for 20 h. Water (0.5 mL) was added; titration with 0.1 N NaOH after 45 min indicated quantitative esterification. The recovered 2-phenylbutanoic acid (333 mg), $[\alpha]^{20}_D$ +1.39 ± 0.03° (*c* 6.6, C_6H_6), corresponded to an "optical yield"[16] of 4.3%. An identical determination using (+)-*p*-nitrobenzhydrol-*2,3,4,5,6-d*$_5$ [(+)-**6**] (175 mg), $[\alpha]^{20}_D$ +78.2° (*c* 1.1, $CHCl_3$), gave (+)-2-phenylbutanoic acid (346 mg), $[\alpha]^{20}_D$ +1.45 ± 0.03° (*c* 7.6, C_6H_6), "optical yield" 4.5%. On the basis of the Horeau model,[16,17] as applied to benzhydrols,[17] the *S* configuration[19] is tentatively assigned.[18]

(−)-Benzhydryl-*2,3,4,5,6-d*$_5$ Chloride (8). To a solution of (−)-**1** (352 mg, 1.86 mmol) in 2,6-lutidine (0.84 mL, 7.31 mmol) at −5 °C was added with stirring thionyl chloride (0.16 mL, 2.23 mmol). After 24 h at 5 °C the reaction mixture was extracted with hexane (5 × 6 mL), and the extracts were washed (H_2O), dried ($MgSO_4$), and concentrated to give 368 mg of a light brown oil, which was diluted with $CHCl_3$, passed through a Nuchar column (6 × 30 mm), distilled, and redistilled to give (−)-**8** (174 mg), $[\alpha]^{20}_D$ −0.21 ± 0.02° (*c* 14, $CDCl_3$) (cf. Table I for other rotations and Figure 2 for CD curve).

(−)-*p*-Nitrobenzhydryl Chloride.[12] (+)-*p*-Nitrobenzhydrol[12] (200 mg, 0.8 mmol), $[\alpha]^{20}_D$ +79.5° (*c* 1.3, $CHCl_3$) was dissolved in 2,6-lutidine (0.097 mL, 1.05 mmol) and the mixture cooled to −70 °C. Thionyl chloride (0.080 mL, 1.1 mmol) was added and the glassy mixture allowed to warm with stirring first to −40 °C and then to −20 °C over 1 h. The mixture was diluted with water (1 mL), extracted with hexane, and dried ($MgSO_4$), and the concentrated extracts were purified by preparative thin-layer chromatography (1:4 EtOAC–hexane) to give the chloride [121 mg, α^{20}_D +0.180 ± 0.002° (*c* 1.90, $CHCl_3$, *l* 1), $[\alpha]^{20}_D$ +9.8 ± 0.1° (*c* 1.9, $CHCl_3$)]. Rechromatography did not change this rotation significantly.[25] This experiment was repeated under the conditions used for converting (−)-**1** to (−)-**8**, namely, excess lutidine at −5 °C. The rotation of the resulting *p*-nitrobenzhydryl chloride was $[\alpha]^{20.0}_D$ +7.6 ± 0.1° (*c* 0.8, $CHCl_3$). Thus, inversion took place in these experiments using either equivalent amounts or excess lutidine in the absence of solvent, as well as with pyridine in $CHCl_3$ solvent.[12]

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(25) We obtained (+)-nitrobenzhydryl chloride with higher rotation, $[\alpha]^{20}_D$ +9.8 ± 0.1° (*c* 1.9, $CHCl_3$), than the maximum that was reported,[12] $[\alpha]^{20}_D$ −5.8° (*c* 1.0, $CHCl_3$). Our material was purified by preparative thin-layer chromatography while that reported in the literature was subjected to high vacuum distillation and probably underwent some racemization.

Notes

The Intramolecular Opening of the Oxirane Ring in Butyl 4,5-Anhydro-3,6-dideoxyhexaldonate

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Recently we reported a simple synthesis of racemic allomuscarine (**1**) from butyl (*E*)-2-hydroxyhex-4-enoate (**2**).[1] The crucial step of the synthesis involved the Lewis acid catalyzed intramolecular opening of the epoxide ring in

butyl 4,5-anhydro-3,6-dideoxyhexaldonate. From a mixture of epimeric epoxides **3** and **4** the ester **5** was obtained as the only product.

This paper returns to the intramolecular opening of the epoxide ring in **3** and **4** with the intention to explain the steric course of the reaction.

Epoxidation of the double bond in **2** with *m*-chloroperoxybenzoic acid afforded a mixture of two stereoisomeric epoxides **3** and **4** in a ratio of about 2:3.[2] The mixture was separated into pure components using GLC (cf. Experimental Section). The configuration lyxo and xylo was assigned to **3** and **4**, respectively, via correlation of **4** with allomuscarine at the later step of the synthesis.

The careful examination of the acid-catalyzed rearrangement of epoxides **3** and **4** led to the isolation of **5** and a mixture of diastereomeric compounds **6** and **7** (about 7% yield) and of an unidentified polymeric product (Scheme I). On the basis of analytical and spectral data (cf. Experimental Section), a structure of bicyclic ortho esters was assigned to **6** and **7**. The formation of an ortho ester is to our knowledge the first example of the intramolecular opening of the epoxide ring with an ester carbonyl group.[3]

The mixture of diastereomeric **6** and **7** without separation was hydrolyzed with aqueous acetic acid to give known lactones **11** and **12** in proportion of about 6:5, respectively. In ref 2, the configuration arabino was erroneously ascribed to the ribo lactone, and vice versa, the configuration ribo was erroneously ascribed to the arabino one.[4]

The intramolecular opening of the oxirane ring in **3** and **4** was followed by ^1H NMR using pure epoxides. The reactions were performed in $CDCl_3$ solution at −40 °C. The epoxide **4** in 10 min after the addition of the catalyst displayed signals due to **5** (significant prevalence) and to an unidentified ortho ester. On the other hand the epoxide **3** was found to be less reactive. It reacted in 1 h. The ^1H NMR spectrum of the postreaction mixture exhibited absorptions in regions characteristic for ortho esters and lacked signals due to the ester **5**. Examination of these reactions using TLC is fully consistent with observations

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(4) The correct assignment of configuration to all 3,6-dideoxyhexaldonolactones has been made by Lundt, I., Bock, K., and Pedersen, C., and will be published soon (personal communication).
(5) For the sake of simplicity all formulae in Scheme I refer to monosaccharide D series, although in fact they represent racemic compounds.

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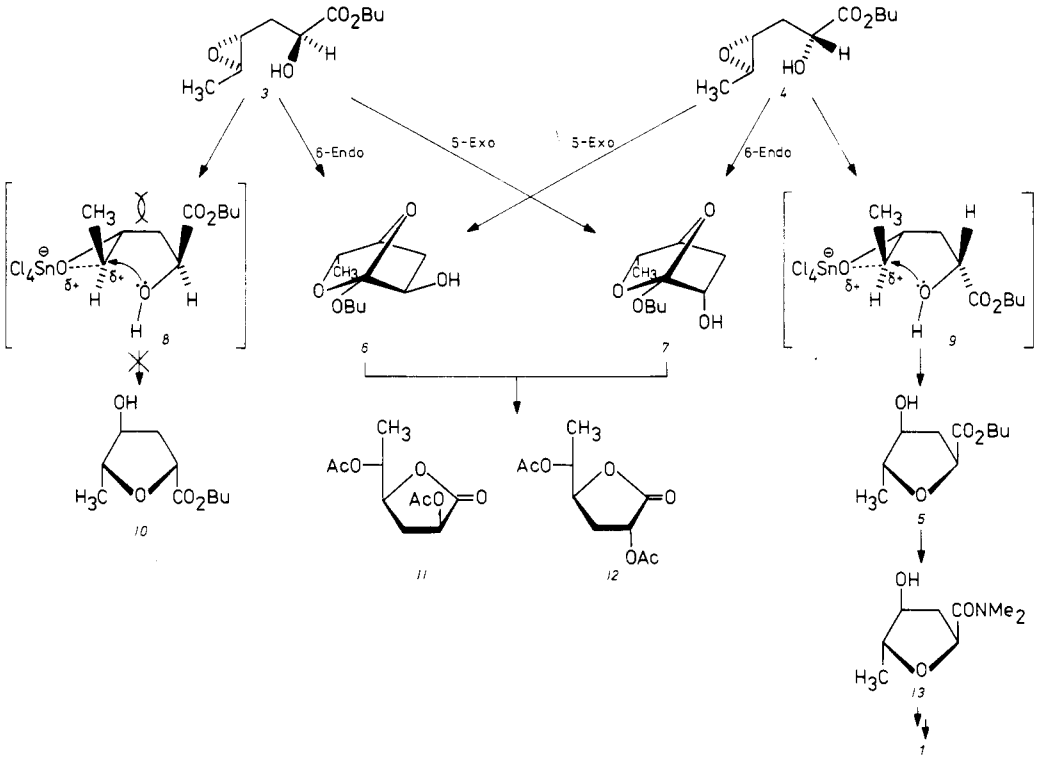
Scheme I[5]



drawn from NMR experiments.

According to Baldwin rules,[6] predictions for the opening of three-membered ring to form cyclic structures lie between those for tetrahedral and trigonal systems, generally prefering exo modes. Hence 5-endo ring closure, which is represented here by the formation of a tetrahydrofuran ring from **3** and **4** should be disfavored. Epoxides **3** and **4** under a variety of basic conditions, e.g., *t*-BuOK in THF or DBU in a nonpolar solvent, did not form the furanoid ring and remained unchanged; hence, Baldwin rules were obeyed. Nucleophilic opening in acidic medium, used by us, suggests, however, the carbocationic-type process which does not generally follow Baldwin rules.[6,7] The reaction proceeds through the transition state where both partial bonds are longer than usual, borderline S_N2, or in the extreme through S_N1-type ring opening.[8] The process involved the coordination of the epoxide oxygen atom by the Lewis acid, causing subsequently a partial positive charge at the C-5 carbon atom or formation of the intimate ion pairs **8** and **9** (Scheme I). Rapid trapping of the intermediate **9** by the OH group produces stereospecifically **5** with the inversion at the C-5. It could be assumed that the additional syn quasi-1,3-interaction between the methyl group and butoxycarbonyl in the hypothetical transition state prohibited the formation of the five membered furanoid ring. The fact that **3** does not produce **10** might also be explained by the instability of the product **10** to the reaction conditions.

The competitive intramolecular reaction leading to the formation of ortho esters **6** and **7** occurred probably through a similar mechanism. In this case the carbocationic intermediate is trapped by the ester carbonyl group. Both racemic ortho esters can be obtained either from **3** or from **4** depending on the site of the positive charge (C-4 or C-5 carbon atom) at the carbocationic intermediate. Therefore the ratio of lactones **11** and **12** obtained after hydrolysis of **6** and **7** can not be directly connected with the composition of starting epoxides without additional investigations using optically pure compounds **3** and **4**.

The ester **5** was subsequently transformed into allomuscarine via sequence of reactions published earlier.[1]

Experimental Section

^1H NMR spectra were recorded in $CDCl_3$ solutions with a JEOL JNM-4H-100 and a Bruker 500 spectrometers (Me_4Si, 0 ppm). ^{13}C NMR spectra were obtained on a Varian CFT-20 spectrometer in $CDCl_3$ solutions (Me_4Si, 0 ppm). IR spectra were recorded on a Unicam SP-200 spectrophotometer. Melting points are uncorrected. TLC was performed on Merck DC Alufolien (Kieselgel 60 F-254) and column chromatography with silica gel Merck (230–400 mesh).

As the catalyst, stannic chloride solution in CH_2Cl_2 (1 mmol/1 mL) was employed.

Butyl 4,5-Anhydro-3,6-dideoxy-DL-*lyxo*- and -DL-*xylo*-hexaldonate (**3** and **4**). To a solution of *m*-chloroperoxybenzoic acid (28.0 g, 0.16 mol) in $CHCl_3$ (250 mL) was added anhydrous sodium acetate (20.0 g). The mixture was stirred, cooled with water, and treated slowly with **2** (12.4 g, 0.07 mol). Subsequently the mixture was stirred at room temperature for 7 days. After the disappearance of the substrate (TLC; 5:5:0.5 v/v hexane–Et_2O–MeOH) the mixture was cooled to 0 °C and filtered. The solution was washed with 5% aqueous NaOH at 0 °C and ice–water, dried, evaporated, and distilled at 112–115 °C (0.5 torr) to give **3** and **4** (10.0 g, 80%). GLC (10% XE 60 on Gas Chrom Q; 3 m × 4 mm; 150 °C; N_2, 60 mL/min) showed four epoxides: **3** and **4** (90%) in a 4.5:5.5 ratio derived from trans ester **2** and two DL-ribo and DL-arabino (10%) in proportion of about 1:1 derived from cis ester. Repeating preparative GLC (4-m, 6-mm internal diameter column filled with chromosorb Q coated with 10% XE 60; flow rate, 80 mL/min; 155 °C), of 50-mg portions, allowed the separation of 1 g of the mixture. **3** (0.18 g) and **4** (0.27 g) were obtained as pure isomers.

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(9) The crystallization from hexane–AcOEt enhanced the content of the major component.

3: ^{1}H NMR 0.9–1.8 (m, 7 H, C_3H_7), 1.38 (d, 3 H, CH_3), 1.91 (dt, 1 H, $J_{3,3'}$ = 14.5, $J_{2,3}$ + $J_{3,4}$ = 12.5 Hz, H-3), 2.22 (dt, 1 H, $J_{2,3'}$ + $J_{3',4}$ = 8.7 Hz, H-3'), 2.98 (m, 2 H, H-4,5), 4.30 (t, 2 H, OCH_2), 4.45 (dd, 1 H, $J_{2,3}$ + $J_{2,3'}$ = 10.7 Hz, H-2) ppm.

4: ^{1}H NMR 0.9–1.8 (m, 7 H, C_3H_7), 1.39 (d, 3 H, H-3,3'), 2.99 (m, 2 H, H-4,5), 4.26 (t, 2 H, OCH_2), 4.46 (t, 1 H, $J_{2,3}$ + $J_{2,3'}$ = 12.7 Hz, H-2) ppm.

Anal. Calcd for (the mixture of epoxides) $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.1; H, 8.90.

Butyl 2,5-Anhydro-3,6-dideoxy-DL-*arabino*-hexaldonate (5). A solution of the mixture of epoxides 3 and 4 (0.5 g, 2.47 mmol) in dry CH_2Cl_2 (15 mL) was cooled to −40 °C and treated under dry argon with SnCl, in CH_2Cl_2 (2 mL). After 1 h Et_3N (0.5 mL) was added to neutralize the solution. The mixture was diluted with 20 mL of CH_2Cl_2, washed with saturated $NaHCO_3$ and water, and dried and the solvent evaporated. The oily residue was separated on a silica gel column with hexane–Et_2O–MeOH (10:5:0.5 v/v) as eluent (flash chromatography). Two fractions were obtained: a less polar one, the mixture of 6 and 7 (0.025 g, 5%), and a more polar one, 5 (0.20 g, 40%).

The mixture of 6 and 7: colorless crystals; IR (Nujol) 3500 cm^{-1}, no carbonyl absorption was observed; ^{1}H NMR (signals of the major isomer[7]) 0.9–1.7 (m, 7 H, C_3H_7), 1.31 (d, 3 H, CH_3), 1.84 (ddd, 1 H, J = 11.1, 3.3, and 13.6 Hz, H-3), 2.08 (ddd, 1 H, J = 4.8, 3.0 and 13.6 Hz, H-3'), 3.4–3.8 (m, 4 H, OCH_2, H-2,5), 4.02 (t, 1 H, $\sum|J|$ = 6.1 Hz, H-4) ppm; ^{13}C NMR (the assignments of lines to diastereomers are based on ^{13}C line intensities and should be considered as tentative) [major component] 13.86, 19.40, 31.70, 59.78 (butyl), 17.62 (CH_3), 34.60 (CH_2), 67.37, 70.51, 73.30 (C-2,4,5), 106.20 (C-1), [minor component] 13.81, 19.40, 31.60, 59.84 (butyl), 17.92 (CH_3), 34.60 (CH_2), 67.14, 70.40, 73.42 (C-2,4,5), 105.44 (C-1) ppm.

Anal. Calcd for (the mixture) $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.5; H, 9.2.

Acetate of the mixture of 6 and 7: ^{1}H NMR (signals of the major component[7]) 0.9–1.7 (m, 7 H, C_3H_7), 1.21 (d, 3 H, CH_3), 1.91 (ddd, 1 H, J = 11.4, 3.0, and 13.4 Hz, H-3), 2.04 (s, 3 H, OAc), 2.15 (ddd, 1 H, J = 3.2, 6.1, and 13.4 Hz, H-3'), 3.4–3.8 (m, 3 H, OCH_2, H-5), 3.95 (t, 1 H, $\sum|J|$ = 5.8 Hz, H-4), 4.87 (m, 1 H, H-2) ppm.

Anal. Calcd for (a mixture) $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.8; H, 8.4.

5: colorless oil; bp 120 °C [0.2 torr (air bath)]; IR (film) 3500, 1735 cm^{-1}; ^{1}H NMR 0.9–1.7 (m, 7 H, C_3H_7), 1.20 (d, 3 H, J = 6.5 Hz, CH_3), 2.09 (dt, 1 H, $J_{2,3}$ = 3.6 Hz, $J_{3,4}$ = 3.2 Hz, $J_{3,3'}$ = 13.7 Hz, H-3), 2.49 (ddd, 1 H, $J_{2,3'}$ = 9.0 Hz, $J_{3',4}$ = 6.1 Hz, H-3'), 3.97 (m, 1 H, $J_{4,5}$ = 2.9 Hz, H-4), 4.16 (t, 2 H, OCH_2), 4.19 (dq, 1 H, H-5) ppm; ^{13}C NMR 13.66, 19.04, 30.54, 65.27 (butyl), 19.25 (C-6), 37.82 (C-3), 75.77 (C-4), 76.73 (C-5), 83.88 (C-2), 174 (C-1) ppm.

Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.3; H, 9.1.

Acetate of 5: IR (film) 1740 cm^{-1}; ^{1}H NMR 0.9–1.9 (m, 7 H, C_3H_7), 1.28 (d, 1 H, J = 6.7 Hz, CH_3), 2.08 (s, 3 H, OAc), 2.26 (dt, 1 H, $J_{2,3}$ = 3.6 Hz, $J_{3,4}$ = 2.7 Hz, $J_{3,3'}$ = 14.1 Hz, H-3), 2.60 (ddd, 1 H, $J_{2,3'}$ = 9.2 Hz, $J_{3',4}$ = 6.6 Hz, H-3'), 4.18 (t, 2 H, OCH_2), 4.30 (dq, 1 H, $J_{4,5}$ = 3.2 Hz, H-5), 4.61 (dd, 1 H, H-2), 4.85 (m, 1 H, H-4) ppm.

Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.9; H, 8.1.

The experiment performed in a NMR test tube was as follows: A solution of the epoxide 3 or 4 (30 mg) in $CDCl_3$ (0.5 mL) at −40 °C was treated with $SnCl_4$ in the same solvent to make the substrate:catalyst ratio equal to 4:1. The spectra were recorded 10, 30, and 60 min after mixing the substrate with $SnCl_4$.

2,5-Di-*O*-acetyl-3,6-dideoxy-DL-*arabino*- and -DL-*ribo*-aldonolactones (11 and 12). A solution of a mixture of 6 and 7 (0.1 g, 0.5 mmol) in 50% aqueous AcOH (2 mL) was refluxed for 6 h and then the solvent evaporated to dryness under reduced pressure. The oily residue was acetylated with Ac_2O and pyridine. Solvents were removed under diminished pressure, and the residue was purified on a silica gel column to give a mixture of lactones 11 and 12 (0.5 g, 87%) in proportion of about 5.5:4.5, respectively.

2,5-Anhydro-3,6-dideoxy-*N*,*N*-dimethyl-DL-*arabino*-hexaldonamide (13). A solution of 5 (0.20 g, 1 mmol) in 20% methanolic dimethylamine (5 mL) was heated at 80 °C in a steel bomb for 24 h. The solution was evaporated and purified by chromatography to give 13 (0.12 g, 69%); mp 74–75 °C; IR (KBr) 3350, 1640 cm^{-1}; ^{1}H NMR 1.17 (d, 1 H, J = 6.5 Hz, CH_3), 2.22 (d, 1 H, $J_{3,3'}$ = 14.0 Hz, H-3), 2.32 (ddd, 1 H, $J_{2,3'}$ = 8.6 Hz, $J_{3',4}$ = 6.2 Hz, H-3'), 3.97 (dd, 1 H, $J_{4,OH}$ = 10.6 Hz, H-4), 4.22 (dq, $J_{4,5}$ = 1.6 Hz, H-5), 4.96 (dd, 1 H, $J_{2,3}$ = 1.8 Hz, H-2) ppm.

Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.3; H, 9.0; N, 8.0.

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Synthesis of 4-Methyl- and 4,4-Dimethyl-1,3-dioxin-2(4*H*)-one and Related Enol Carboxylates

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Recently we had occasion to examine the synthesis of derivatives of 1,3-dioxin-2(4*H*)-one (**1a**). Although numerous alkenyl carboxylates and acyclic alkenyl carbonate esters[1] are well documented, **1a** and simple derivatives are unknown. Indeed we were concerned that the paucity of information on **1** may well have resulted from instability as a result of facile decomposition via a retro–Diels–Alder reaction. Recently, Trost reported the synthesis of **2** using the reflux of the selenoxide derived from **3a** in 1,2-dichloroethane and norbornadiene as a key step.[2] Herein we report a method for the facile synthesis of **1b**, **1c**, and three related acyclic analogues **10a**, **10b**, and **10c** (Chart I).

Results and Discussion

2-Methyl-3-buten-2-ol was converted into **4a** (58%) by sequential reaction with diphenyl diselenide–benzeneselininic acid[3] and carbonyl diimidazole[4] in toluene solution. It was essential that **4a** was purified by rapid chromatography on silica to prevent partial isomerization on the column to give **3b**. On ozonolysis[5] in dichloromethane solution at −78 °C, **4a** was converted into the corresponding selenoxide which on warming up to 0 °C in the presence of pyridine smoothly underwent syn elimination[4] to produce the cyclic enol carbonate **1b**. In contrast to the slow

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