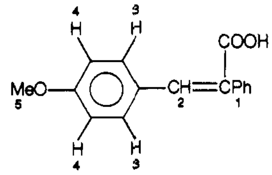
**Table II. Various Physical, Analytical, and Spectroscopic Data on Substrates**




| compd | mp, °C | Anal. calcd C | Anal. calcd H | Anal. found C | Anal. found H | recryst solv | IR,[a] cm$^{-1}$ C(---O)$_2^-$ asym | IR,[a] cm$^{-1}$ C(---O)$_2^-$ sym | $^1$H NMR,[b] ppm 5-H | 4-H | 3-H | 2-H | 1-H |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 354–355 | 73.16 | 4.50 | 73.28 | 4.66 | EtOH | 1600 | 1390 | | 7.15 | | 7.65 | 7.34 |
| 2 | 303–310 | 73.16 | 4.50 | 72.89 | 4.81 | EtOAc | 1552 | 1412 | | 7.23 | | 7.63 | 6.42 |
| 3 | 304–306 | 69.56 | 4.74 | 68.94 | 4.40 | EtOH | 1560 | 1390 | 3.63 | 6.52[d] | 6.88[d] | 7.59 | 7.18 |
| 4 | 294–296 | 69.56 | 4.74 | 68.70 | 4.76 | EtOH | 1570 | 1414 | 3.72 | 6.77[e] | 7.23[e] | 6.35 | 7.57 |
| 5 | 172–174 | | | | | benzene | | | | | | | |
| 6 | 192–194[c] | | | | | benzene | | | | | | | |

[a] IR spectra were recorded in KBr tablets on Unicam SP 200 instrument. [b] NMR spectra were recorded in $Me_2SO$ in the presence of $Me_4Si$ as internal standard on a JEOL C-60HL instrument. [c] 189–190 °C.[14] [d] $J_{4-3}$ = 9 Hz. [e] $J_{4-3}$ = 9 Hz.

evaporation of the resulting solution, the sodium salts were obtained by recrystallization from an appropriate solvent (see Table II). The yields were almost quantitative. Before use, the salts were dried at 120 °C and 0.1 torr for 2 h. Some data on the products are given in Table II.

**Catalyst Preparation.** Freshly prepared RNi was used in every experiment. The general method of preparation was as follows: 3 g of a 1:1 Ni–Al alloy (Carlo Erba Analyticals, Code 457675) was treated at 80 °C for 45 min with 60 mL of 20% NaOH solution. The resulting alloy was washed with 20 × 40 mL of distilled water.

**Catalyst Modification.** The modification involved a slight variation of the method of Izumi et al.[1] An aqueous solution (75 mL) of 1.6% D-TA (Janssen Chimica, No. T-10-9) and 10% NaBr was poured onto the catalyst prepared as above. After heating to 50 °C, the pH of the mixture was adjusted to 3.0 with 1 mL of NaOH. The mixture was kept at pH 3 and stirred intensively with a magnetic stirrer for 45 min, during the addition of an aqueous 5% D-TA + 10% NaBr solution, with continuous recording of the pH (Radiometer pH meter 22, Radelkis, Hungary). After treatment, the modifying solution was poured off the catalyst, which was then washed with 10 mL of water and 3 × 10 mL of absolute ethanol.

**Hydrogenation.** Hydrogenations were performed at 30 °C, in 20 mL of absolute ethanol, in a hydrogenation vessel operating at atmospheric pressure. The reaction vessel had a double wall. The reaction mixture was stirred magnetically. With the exception of **6**, the model compounds were hydrogenated with 100% conversion. After the uptake of the calculated quantity of hydrogen, the catalyst was filtered off, the filtrate was evaporated down, the residue was treated with dilute iced HCl and with ether (for **1**, **2**, and **5**) or EtOAc (for **3**, **4**, and **6**). The organic phase was separated, washed with 3 × 10 mL of water, dried over anhydrous $Na_2SO_4$, and evaporated, and the $[\alpha]^{20}_D$ value was determined (Polamat A, Carl Zeiss). The hydrogenated compounds obtained were checked for purity by means of their $^1$H NMR and IR spectra and elementary analysis. The results of the hydrogenation experiments are in Table I. The optical yields in the case of 2,3-diphenylpropionic acid were calculated via the values given for the optically pure modifications[15,16] through the formula $p = 100[\alpha]_{D\,measd}/[\alpha]_{D\,max}$. (*R*)-2,3-Diphenylpropionic acid has $[\alpha]^{25}_D$ −133.7° (*c* 0.4905, acetone). The $[\alpha]_D$ for the optically pure modification of 2-phenyl-3-(*p*-methoxyphenyl)propionic acid is unknown.

The aluminium[17] and nickel[18] contents of the filtered catalyst were dissolved in concentrated HCl, the solution was diluted to a definite volume with water, and titrimetric determinations were carried out. The reaction rates were calculated from the initial, linear section of the hydrogen consumption curves.

**Acknowledgment.** We gratefully acknowledge MTA and NSF support for the US/Hungarian collaboration. We also acknowledge the support provided for this research by the Hungarian Academy of Sciences (Grant No. 319/82/1.3) and the Ministry of Culture (Grant No. 40/1981). We express our thanks to Dr. G. B. Bartók for the microanalyses, to Dr. J. T. Kiss for the IR recordings, and to Dr. G. Dombi for the $^1$H NMR recordings.

**Registry No.** **1**, 15352-96-2; **2**, 15352-97-3; **3**, 106319-21-5; **4**, 106319-22-6; **5**, 91-48-5; **6**, 13938-24-4; (*R*)-$C_6H_5CH_2CHPhCO_2H$, 17040-62-9; (−)-4-$H_3COC_6H_4CH_2CHPhCO_2H$, 106319-23-7.

(15) Pettersson, K. *Ark. Kemi* **1954**, *7*, 339.
(16) Watson, M. B.; Youngson, G. W. *J. Chem. Soc. C* **1968**, 258.
(17) Sajó, I. *Acta Chim. Hung.* **1955**, *6*, 251.
(18) Kinnunen, J.; Merikanto, B. *Chem. Anal.* **1954**, *43*, 13.

# Stereochemistry and Synthetic Applications of the Products of Yeast Reduction of 3-Hydroxy-3-methyl-5-phenylpent-4-en-2-one

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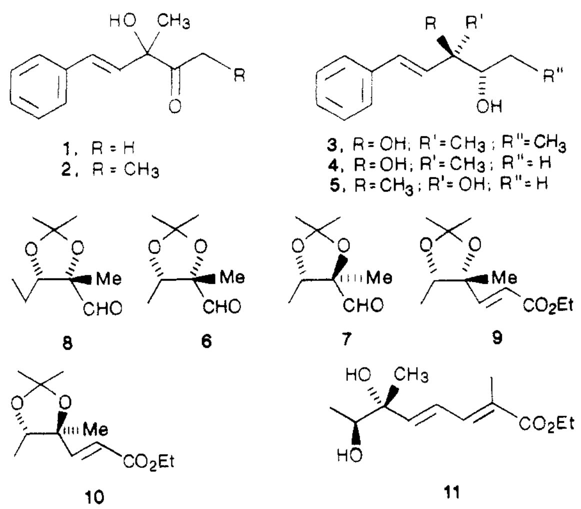
*Received August 6, 1986*

In recent years a growing number of chiral intermediates complementary or alternative to the components of the "pool of chirality"[1] have been produced by microbial transformations or by use of purified enzymes and have been used successfully in the synthesis of natural products. Among this set of compounds, species containing in a relatively small carbon framework chiral centres of type RR′CHOH or/and RR′R″CH are prominent and, due to its commercial availability and synthetic flexibility, bakers' yeast is the most widely used microbial system for making them.[2]

(1) Seebach, D.; Kalinowski, H. O. *Nachr. Chem. Tech.* **1976**, *24*, 415. Fischli, A. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Salle und Sauerlander: Frankfurt am Main, 1980; Vol. 2, p 269.
(2) For recent representative examples of the use of purified enzymes and microbial transformations in organic synthesis, see: *Enzymes in Organic Synthesis*; CIBA Foundation Symposium 111; Pitman: London, 1985. *Enzymes as Catalysts in Organic Synthesis*; Schneider, M. P., Ed.; Nato ASI Series; D. Reidel Publishing Co., 1986; Series C, Vol. 178.

Chart I




Recently,[3] during a study of the structural limitations for acceptability of a substrate by the multienzymatic system involved in the conversion of $C_6$–$C_3$, aromatic $\alpha$,-$\beta$-unsaturated aldehydes into $C_6$–$C_5$, (2*S*,3*R*) methyl diols of bakers' yeast, we carried out the reduction of the $\alpha$-hydroxy-$\alpha$-methyl ketones **1** and **2**. We observed that, whereas **2** affords (3*S*,4*R*)-**3** in ca. 15% yield as supported by its conversion into the known aldehyde **8**, methyl ketone **1** gave rise in ca. 80% yield to a ca 1:1 mixture of diastereoisomeric diols, whose optical purity and absolute configuration remained undetermined. We now assign the 2*S*,3*R* and 2*S*,3*S* absolute configurations depicted in **4** and **5** to the latter materials and, in further support of the significance to organic synthesis of the microbial transformations of nonconventional substrates as sources of chirality, we describe some applications of **4** and **5** and their derivatives to the synthesis of chiral substances of quite different type.

In work designed to establish the absolute configuration of **4** and **5**, the latter were converted into the isopropylidene derivatives, yielding in turn on treatment with ozone, the aldehydes **6** and **7** as a mixture which was directly converted into **9**, $[\alpha]^{20}_D$ −4.6° (*c* 4, $CHCl_3$), and **10** $[\alpha]^{20}_D$ +45° (*c* 1, $CHCl_3$), in 25% and 54% overall yield from **4** + **5**. These substances were identical in every respect, including optical rotation, with the products prepared during the synthesis of (+)-citreodiol **11** in five steps from L-rhamnose.[4] The latter carbohydrate-based synthesis of **9** and **10** requires as key intermediate a sugar enone retaining only one of the chiral centers of the starting 6-deoxy sugar. The above correlation thus allows the assignment of the 2*S*,3*R* and 2*S*,3*S* stereochemistry depicted in **4** and **5**, respectively, to the products of yeast reduction of **1**.

The next synthetic application of **4** and **5** is in the aminodeoxy sugar field. For some years now we have been using (2*S*,3*R*)-5-phenylpent-4-ene-2,3-diol (**4**, without the C-3 methyl group), prepared by fermenting bakers' yeast from cinnamaldehyde, as starting material in the synthesis of L-daunosamine and its configurational isomers[5] and more recently of 2,4,6-trideoxy-4-amino-L-*lyxo*-hexose.[6] The glycoside **24**, derived from the latter aminodeoxy sugar and adriamycinone shows quite interesting antitumor activity as compared with that of the isomeric naturally occurring adriamycin **25**.[7] Accordingly, it seemed worthwhile to evaluate the activity profile of the 4'-*C*-methyl analog of **24** which we thought might be prepared via the required intermediate **23** from **4** by using the above-mentioned[6] procedure. We therefore started from the mixture of aldehydes **6** and **7**, in the expectation of being able to effect separation at some stage of the sequence. The reaction scheme involves the preparation from **6** of the 4,5-*erythro* material **12**. Studies with racemic **6** (prepared from (*E*)-2-methylbutenoic acid via tungstate-catalyzed anti hydroxylation, followed by protection as methyl ester–isopropylidene derivative and DIBAH reduction) indicated that diallylzinc affords racemic **12** in 95:5 ratio with the 4,5-*threo* diastereoisomer, in agreement with Felkin's[8] mode of addition. The stereochemistry of the adduct **12** is based on its conversion, via acid-catalyzed deprotection and ozonolysis, into 2,6-dideoxy-4-*C*-methyl-*ribo*-hexose (**16**), as indicated by $^1$H NMR studies on the $\alpha$-ethyl glycoside. The axial orientation of the OH-3 group is suggested from the values of the vicinal coupling constants $J(2_e,3)$ and $J(2_a,3)$ of 3.2 and 3.4 Hz, respectively. The configuration at the quanternary carbon C-4 was established on the basis of the NOE enhancement of the H-2a proton (3%) upon irradiation of the Me-4 group.

When allylmagnesium bromide is added to **6**, product **12** is accompanied by ca. 15% of the 4,5-*threo* material. Thus, the adducts **12** and **13**, obtained from the mixture **6** + **7** on reaction with diallylzinc, on sequential treatment with 4-toluenesulfonyl chloride in pyridine and aqueous methanolic $CF_3COOH$ afforded oily **14**, $[\alpha]^{20}_D$ +8.68°, and **15**, an oil which solidified on standing, $[\alpha]^{20}_D$ − 30.15°, after separation by column chromatography. The tosylates of these compounds afforded the epoxy alcohols **17** and **18**, which gave in turn via **19** and **20** the cyclic products **21** and **22**, bearing the correct configuration and the required functionalities for direct conversion into the required aminodeoxy sugar derivative(s). This was achieved for the L-*lyxo* isomer **23** starting from **21**, whereas the conversion of **22** into the *ribo* isomer was not performed because the yield in the N-debenzylation of **22** remained unacceptably low. The structure of **23** was deduced from the analysis of the $^1$H NMR spectrum which showed a mixture of the $\alpha$ and $\beta$ anomers in ca. 7:3 ratio. The configuration at C-3 is apparent from the values of the vicinal coupling constants $J$(2e,3) and $J$(2a,3) of 11.8 and 4.7 Hz which are typical of an axial–axial and an equatorial–axial proton arrangement, respectively. The configuration at the quaternary carbon C-4 was established by selective irradiation of the amide proton which produced a positive NOE effect of 3% on the H-2a hydrogen and no enhancement for the H-3 and H-5 protons (−$NHCOCF_3$ group axially oriented).

In conclusion we have shown that yeast reduction of **1** and **2** affords functionalized chiral synthons which can be used in the synthesis of natural products. Further synthetic application of the chirons obtained from **1** and **2** will be reported in due course.

## Experimental Section

**General Methods.** $^1$H NMR spectra were determined on Varian EM 390 (90 Mhz) and on Bruker CXP (300 MHz) spec-

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(4) Shizuri, Y.; Nishiyama, S.; Imai, D.; Yamamura, S.; Furukawa, H.; Kawai, K.; Okada, N. *Tetrahedron Lett.* **1984**, *25*, 4771.
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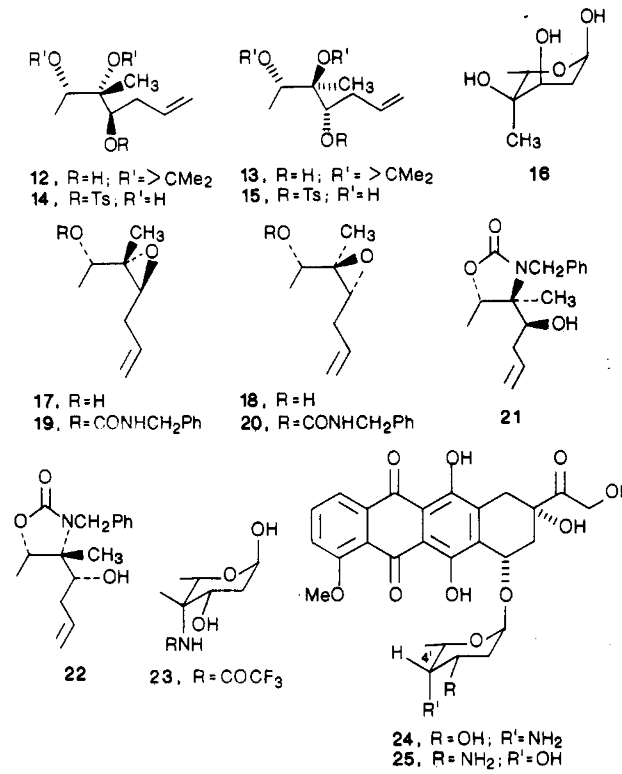
(6) Fronza, G.; Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G. *Carbohydr. Res.* **1985**, *136*, 115.
(7) Brit. App. 8508079 (March 28, 1985) to Farmitalia-C. Erba.
(8) Chêrest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199.

**Chart II**




trometers. Chemical shifts are expressed in ppm (δ) relative to internal $Me_4Si$. All NMR spectra were recorded in $CDCl_3$ unless otherwise stated. Optical rotations were recorded on a Jasco Dip 181 digital polarimeter. Specific rotation values refer to 20 °C. Purification of products was performed by flash chromatography on silica gel (Merck 60, 0.04–0.063 mm) eluting with mixture of *n*-hexane and ethyl acetate. Analytical samples were prepared by bulb-to-bulb distillation under reduced pressure. Melting points are uncorrected.

**3-Hydroxy-3-methyl-5-phenylpent-4-en-2-one (1).** To 400 mL of a 1 M **2-lithio-2-methyl-1,3-dithiane** THF solution (prepared from 0.4 mol of **2-methyl-1,3-dithiane**, and 42 mL of a 10.5 M solution of *n*-BuLi at −40 °C), was added 58.4 g (0.4 mol) of benzalacetone diluted in 100 mL of dry THF at −60 °C under nitrogen. After 3 h the temperature was raised to −25 °C and the reaction mixture was left under stirring at the same temperature for 3 h. The reaction was quenched with 5 mL of MeOH, 5 mL of acetone, and 100 mL of water and was then diluted with 300 mL of ethyl acetate. The residue obtained upon evaporation of the organic solvent was chromatographed on 400 g of silica gel to give 89.5 g (0.32 mol) (80% yield) of **2-methyl-2-(1-hydroxy-1-methyl-3-phenylprop-2-en-1-yl)-1,3-dithiane** as an oil which solidified on standing: $^1$H NMR (δ) 1.52 (3 H, s), 1.81 (3 H, s), 1.95 (2 H, m), 2.85 (5 H, m), 6.58 (1 H, d), 6.78 (1 H, d) and 7.35 (5 H, m). Anal. Calcd for $C_{15}H_{20}OS_2$: C, 64.27; H, 7.19. Found: C, 64.26; H, 7.22. To a solution of 25 g (0.089 mol) of the above product in 650 mL of 30% aqueous THF were added 38.5 g (0.178 mol) of HgO and 25.3 g (0.178 mol) of $BF_3{\cdot}Et_2O$ under vigorous stirring at room temperature. The reaction mixture was left to stir for 2 h and then poured in 1 L of ethyl ether, filtered, and washed with 200 mL of 5% $NaHCO_3$ aqueous solution. The aqueous phase was extracted with ethyl ether (2 × 150 mL). The oily residue obtained upon purification by flash chromatography gave 12.7 g (0.067 mol) (75% yield) of 1, as an oil: $^1$H NMR δ 1.52 (3 H, s), 2.25 (3 H, s), 4.12 (1 H, sb), 6.23 (1 H, d), 6.8 (1 H, d), 7.35 (5 H, m). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.72; H, 7.48.

**Yeast Reduction of 1.** In a 10-L glass jar a mixture was made up composed of 1 kg of commercial bakers' yeast and 0.5 kg of D-glucose in 5 L of tap water at 35 °C. As the fermentation started, 20 g (0.105 mol) of 1 in 50 mL of EtOH was added dropwise during 10 min. After 12 h at 25 °C, 1 kg of Celite was added, the reaction mixture was filtered on a large Buchner funnel, the solid pad was washed with 1 L of ethyl acetate, and the filtrate was extracted twice with 1.5-L portions of ethyl acetate. The organic phase, once dried, was evaporated, leaving a residue which was purified on silica gel to give 16 g (0.084 mol) (80% yield) of an inseparable mixture of 4 and 5: oil, $[\alpha]_D$ +14.5° (*c* 1, $CHCl_3$); $^1$H NMR δ 1.2 (3 H, d), 1.34 (3 H, s), 2.42 (2 H, 2 OH, b), 3.78 (1 H, m), 6.29 and 6.33 (1 H, d), 6.72 (1 H, d), 7.35 (5 H, m). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.95; H, 8.40.

**(4*R*,5*S*)- and (4*S*,5*S*)-4-(2-Carbethoxyethenyl)-2,2,4,5-tetramethyl-1,3-dioxolane (9 and 10).** Twenty grams (0.104 mol) of the diastereoisomeric mixture of 4 and 5 was dissolved in 200 mL of dry benzene and 21.7 g (0.208 mol) of 2,2-dimethoxypropane and 100 mg (0.5 mmol) of 4-toluenesulfonic acid were added at 23 °C. The reaction mixture was heated at reflux for 3 h, cooled, and diluted with 200 mL of ethyl acetate. The organic solution was washed witth 100 mL of saturated solution of $NaHCO_3$, dried, and evaporated under reduced pressure. Purification by chromatography gave 20.5 g (0.088 mol) (85% yield) of the protected diols, $[\alpha]_D$ +30° (*c* 1, $CHCl_3$). Ozonized oxygen was passed through a solution of 20 g (0.086 mol) of the above product in 200 mL of dry $CH_2Cl_2$ at −40 °C until the absorption was complete. Nitrogen was then flushed through for 20 min and a solution of 24.9 g (0.095 mol) of triphenylphosphine in 50 mL of dry $CH_2Cl_2$ was added dropwise at the same temperature. After 1 h at −40 °C and 5 h at 23 °C, two volumes of petroleum ether were added to precipitate the triphenylphosphonium oxide. The solution was chilled and filtered, the filtrate was washed with petroleum ether, and the combined organic solvents were evaporated in vacuum at low temperature to give the mixture of the aldehydes 6 + 7 which was used directly without further purification. To the mixture of the aldehydes 6 + 7 in 150 mL of dry benzene were added 31.7 g (0.088 mol) of (carbethoxymethylene)triphenylphosphorane and 100 mg (0.8 mmol) of benzoic acid, and the solution was heated at reflux for 2 days. The solvent was evaporated under reduced pressure and the residue purified on silica gel. Elution with hexane–ethyl acetate (9:1) gave first the anti diastereoisomer 9 (4.6 g (0.02 mol) (25% yield), $[\alpha]_D$ −4.6° (*c* 4, $CHCl_3$); $^1$H NMR δ 1.23 (3 H, d), 1.32 (3 H, t), 1.42 (3 H, t), 1.45 (3 H, s), 1.54 (3 H, s), 4.07 (1 H, q), 4.22 (2 H, q), 6.07 (1 H, d), 6.90 (1 H, d). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.11; H, 8.87.] and then the syn diastereoisomer 10 [5.2 g (0.023 mol) (54% yield), $[\alpha]_D$ +45° (*c* 1, $CHCl_3$); $^1$H NMR δ 1.23 (3 H, s), 1.26 (3 H, d), 1.3 (3 H, t)), 1.4 (3 H, s), 1.48 (3 H, s), 4.03 (1 H, q), 4.2 (2 H, q), 6.08 (1 H, d), 6.88 (1 H, d). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.13; H, 8.87.] A higher yield (45%) of the anti diastereoisomer 9 was obtained by carrying out the Wittig reaction on the deprotected diastereoisomeric mixture of the aldehydes 6 + 7 and reprotecting the intermediate $C_6$ unsaturated diol esters to separate the two diastereoisomers 9 and 10.

**(4*S*,5*S*)- and (4*R*,5*S*)-4-(1(*RS*)-Hydroxybut-3-en-1-yl)-2,2,4,5-tetramethyl-1,3-dioxolane (12 and 13).** To a solution of diallylzinc, prepared by addition of 54 g (0.4 mol) of anhydrous zinc chloride in 200 mL of dry ethyl ether at 0 °C to allylmagnesium bromide, obtained in turn from 48.4 g (0.4 mol) of allyl bromide and 11.7 g (0.48 mol) of Mg in 500 mL of dry ether was added the mixture of the aldehydes 6 and 7, derived from 40 g (0.21 mol) of the diastereoisomeric diols 4 and 5, at −78 °C under nitrogen. After being stirred for 3 h at the same temperature, the reaction mixture was quenched with 100 mL of a saturated solution of $NH_4Cl$, and the ethereal solution was separated. Concentration in vacuo gave 25 g (0.125 mol) of an inseparable mixture of 12 and 13 (60% yield from 4 + 5): $^1$H NMR δ 1.09–1.48 (12 H, 4$CH_3$, overlapped signals), 2–2.5 (3 H, m, $CH_2$-3, OH), 3.55–4.15 (2 H, m, H-4, H-6), 4.99–5.3 (2 H, m, $CH_2$-1), 5.6–6.13 (1 H, m, H-2). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.95; H, 10.08.

**2,6-Dideoxy-4-*C*-methyl-DL-*ribo*-hexose (16).** Racemic 12 (8 g, 0.04 mol) (prepared from sodium tungstate catalyzed hydroxylation of (*E*)-2-methylbutenoic acid, esterification in MeOH/HCl of the diol, protection of the intermediate diol ester with 2,2-dimethoxypropane, DIBAH reduction to racemic 6, and subsequent addition of diallylzinc) was dissolved in 40 mL of EtOH and 40 mL of 20% aqueous acetic acid; the mixture was heated at reflux for 3 h and evaporated to give 5.4 g (0.034 mol) (85% yield) of **4,5,6-trihydroxy-5-methylhept-1-ene.** The latter material was ozonized in MeOH at -40 °C. To the resulting solution was added 2.2 g (0.035 mol) of dimethyl sulfide, and the mixture was left at the same temperature for 2 h and then refluxed for 3 h. Evaporation of the solvent and purification gave 4 g (0.025 mol) (72% yield) of **16**. Anal. Calcd for $C_7H_{14}O_4$: C, 51.84; H, 8.70. Found: C, 51.83; H, 8.68. For a better NMR interpretation, **16** was converted into the ethyl glycoside by dissolving 0.1 g of the sugar in 10 mL of EtOH/HCl (5%) and leaving the reaction mixture at 25 °C for 3 h. Ethyl glycoside of **16**: $^1$H NMR δ 4.87 (1 H, dd, H-1, $J(1,2_e)$ = 1.5, $J(1,2_a)$ = 3.4 Hz), 3.87 (1 H, q, H-5, $J$(5,Me) = 6.5 Hz), 3.83 (1 H, d, OH-3, $J$(3,OH) = 9.5 Hz), 3.75 (1 H, m, -C$HH'$CH$_3$, $J$(H,H') = 9.5, $J$(H,CH$_3$) = 7.0 Hz), 3.59 (1 H, dt, H-3, $J(3,2_e)$ = 3.2, $J(3,2_a)$ = 3.4 Hz), 3.44 (1 H, m, -CH$H'CH_3$, $J$(H', CH$_3$) = 7.0 Hz), 2.99 (1 H, s, OH), 2.08 (1 H, m, H-2$_e$, $J(2_e,2_a)$ = 14.3 Hz), 1.99 (1 H, m, H-2$_a$), 1.23 (3 H, t, -CHH'$CH_3$), 1.25 (3 H, d, CH$_3$-5), 1.11 (3 H, s, CH$_3$-4).

**(2*S*,3*S*,4*R*)- and (2*S*,3*R*,4*S*)-2,3-Dihydroxy-3-methyl-4-(tosyloxy)hept-6-ene (14 and 15).** To a solution of 20 g (0.1 mol) of **12** and **13** in 100 mL of dry pyridine was added 57.2 g (0.3 mol) of 4-toluenesulfonyl chloride in one portion at 0 °C, and the reaction mixture was left at 23 °C for 2 days. The solution was poured into 200 mL of ice-water and the aqueous phase extracted with ethyl acetate (2 × 50 mL). The combined organic phases were washed with water (4 × 100 mL), dried, and evaporated in vacuo at 35 °C. The crude oil was purified on silica gel to give 14.2 g (0.04 mol) (40% yield) of the inseparable diastereoisomeric tosylates; 14 g of the latter mixture was hydrolyzed in 50 mL of EtOH and 50 mL of 30% aqueous $CF_3COOH$ for 12 h at 25 °C. The solvent was evaporated under reduced pressure at 35 °C and the residue, diluted in 100 mL of ethyl acetate, was washed with water (2 × 50 mL). The organic solvent was evaporated to give an oil which was purified by flash chromatography (eluent hexane–ethyl acetate, 1:1) to give first **15** [3.5 g (0.011 mol), oil, $[\alpha]_D$ -30.15° (*c* 1, CHCl$_3$); $^1$H NMR δ 1.0 (3 H, s), 1.19 (3 H, d), 2.05–2.50 (2 H, m), 2.42 (3 H, s), 2.70 (2 H, 2 OH, s), 4.02 (1 H, q), 4.62–5.00 (3 H, m), 5.57 (1 H, m), 7.32 (2 H, d), 7.80 (2 H, d). Anal. Calcd for $C_{15}H_{22}O_5S$: C, 57.31; H, 7.06. Found: C, 57.28; H, 7.05.] and then **14** [5 g (0.016 mol), oil, $[\alpha]_D$ +8.68° (*c* 1, CHCl$_3$); $^1$H NMR δ 1.22 (3 H, s), 1.26 (3 H, d), 2.48 (3 H, s), 2.67 (2 H, m), 2.30–2.70 (2 H, m), 3.50 (1 H, q), 4.70–5.15 (3 H, m), 5.69 (1 H, m), 7.33 (2 H, d), 7.83 (2 H, d). Anal. Calcd for $C_{15}H_{22}O_5S$: C, 57.31; H, 7.06. Found: C, 57.79; H, 7.05.].

**(2*S*,3*S*,4*S*)-2-Hydroxy-3-methyl-3,4-epoxyhept-6-ene (17).** **14** (4.5 g, 14 mmol) in 50 mL of dry MeOH was stirred at 25 °C with 6 g of finely powdered anhydrous potassium carbonate for 3 h. The reaction mixture was diluted with 150 mL of ethyl ether and washed with water (2 × 50 mL). The residue, purified by flash chromatography, gave 1.85 g (13 mmol) (92% yield) of **17**: oil, $[\alpha]_D$ +8.2° (*c* 0.5, CHCl$_3$); $^1$H NMR δ 1.2 (3 H, d), 1.33 (3 H, s), 2.22 (1 H, OH, m), 2.32 (2 H, m), 3.13 (1 H, t), 3.78 (1 H, q), 5.00–5.30 (2 H, m), 5.87 (1 H, m). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.58; H, 9.91.

**(2*S*,3*R*,4*R*)-2-Hydroxy-3-methyl-3,4-epoxyhept-6-ene (18).** The 2*S*,3*R*,4*R* diastereoisomer derived from **15** had the following: $[\alpha]_D$ -4.5° (*c* 0.5 CHCl$_3$); $^1$H NMR δ 1.21 (3 H, d), 1.32 (3 H, s), 2.06 (1 H, OH, m), 2.32 (2 H, m), 3.00 (1 H, t), 3.51 (1 H, q), 5.00–5.53 (2 H, m), 5.85 (1 H, m). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.58; H, 9.92.

***N*-Benzylurethane 19.** To a stirred solution of 1.8 g (12.7 mmol) of the epoxy alcohol **17** in 25 mL of dry $CH_2Cl_2$ were added 6 g (76 mmol) of dry pyridine and 3.9 g (19.5 mmol) of (4-nitrophenyl)chloroformate. Once the alcohol **17** disappeared (TLC), a solution of 8.5 g (79 mmol) of benzylamine in 20 mL of dry $CH_2Cl_2$ was added. After being stirred for a further 30 min, the reaction mixture was diluted with ethyl ether (100 mL) and washed with water (3 × 20 mL) and brine (1 × 20 mL). The organic layer was dried and concentrated in vacuo and pyridine was distilled off by azeotropic distillation with toluene, yielding a faintly yellowish oil. The crude product was purified by flash chromoatography, giving 2.6 g (9.5 mmol) (75% yield) of **19**, oil which resulted devoid of optical activity: $^1$H NMR δ 1.28 (3 H, s), 1.29 (3 H, d), 2.12–2.50 (2 H, m), 3.03 (1 H, t), 4.33 (2 H, d), 4.60 (1 H, q), 4.80–5.30 (3 H, m), 5.82 (1 H, m), 7.31 (5 H, m). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69. Found: C, 69.80; H, 7.65.

**Cyclic Urethane 21.** To a solution of 2.6 g (9.5 mmol) of **19** in 30 mL of anhydrous THF at -10 °C was added 1.1 g (9.8 mmol) of potassium *tert*-butylate under stirring. The reaction mixture was left under stirring for 1 h and the temperature was raised to 5 °C. The solution was poured into 20 mL of ice/water and extracted with ethyl acetate (2 × 50 mL). The solvent, on evaporation, left 2.3 g (8.5 mmol) (90% yield) of **21**, again devoid of optical activity: $^1$H NMR δ 1.23 (3 H, s), 1.31 (3 H, d), 1.80–2.30 (3 H, m), 3.48 (1 H, dd), 4.30 and 4.56 (2 H, AB system), 4.62 (1 H, q), 4.90–5.20 (2 H, m), 5.72 (1 H, m), 7.32 (5 H, m). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69. Found: C, 69.78; H, 7.65.

**2,4,6-Trideoxy-4-(trifluoroacetamido)-4-*C*-methyl-L-*lyxo*-hexose (23).** To a solution of **21**, 2.3 g (8.5 mmol) in dry THF at -78 °C, was added dropwise liquid $NH_3$ (ca. 15 mL), followed portionwise by Li (ca. 1 g) until the solution became deep blue. The solution was then stirred at -78 °C for 3 h, solid $NH_4Cl$ and a few drops of MeOH were added until the solution became colorless, the mixture was left at 25 °C for 1 h and filtered, and the solution was evaporated under vacuum. The residue was eluted from a short column of silica gel with ethyl acetate to give 0.56 g (3 mmol) (35% yield) of debenzylated **21**, an oil which solidified on standing: $[\alpha]_D$ -29.36° (*c* 0.5, CHCl$_3$); $^1$H NMR δ 1.22 (1 H, s), 1.36 (1 H, d), 1.68 (1 H, OH), 2.08–2.33 (2 H, m), 3.58 (1 H, m), 4.69 (1 H, q), 5.17 (2 H, m), 5.80 (2 H, m). Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.16. Found: C, 58.34; H, 8.13. A solution of the above material, 0.5 g (2.7 mmol) in 5 mL of EtOH and 5 mL of water containing 0.2 g (8 mmol) of LiOH, was boiled under reflux for 2 h, and then concentrated under reduced pressure, and the crude residue was taken up with 100 mL of boiling ethyl acetate and filtered. The oily residue (0.4 g) was dissolved in dry $CH_2Cl_2$ (5 mL) and stirred at 0 °C with 10 mL of trifluoroacetic anhydride. After 3 h the mixture was taken to dryness, dissolved in 25 mL of MeOH, and treated with 25 mg of sodium methoxide. The mixture was boiled for 3 h. After cooling, the solution was neutralized with $CH_3COOH$, concentrated under vacuum, and diluted with 30 mL of ethyl acetate. The organic phase was washed with water (10 mL) and evaporated to give 0.6 g of an oil. The above material in 50 mL of dry MeOH was ozonized at -40 °C; decomposition of the intermediate ozonide with dimethyl sulfide, as above, gave 0.28 g (1.1 mmol) (40% yield) of **23**: oil, $[\alpha]_D$ +33.5° (*c* 0.5, MeOH, 24 h); $^1$H NMR (α anomer) δ 6.58 (1 H, s, NH$_4$), 5.32 (1 H, dd, H-1, $J(1,2_e)$ = 1.0, $J(1,2_a)$ = 4.0 Hz), 4.11 (1 H, q, H-5, $J$(5-Me) = 6.6 Hz), 4.00 (1 H, dd, H-3, $J(3,2_e)$ = 4.6, $J(3,2_a)$ = 11.8 Hz), 2.04 (1 H, m, H-2$_e$, $J(2_e,2_a)$ = 13.5 Hz), 1.68 (1 H, m, H-2$_a$), 1.57 (3 H, s, CH$_3$-4), 1.17 (3 H, d, CH$_3$-5); (β anomer) δ 6.65 (1 H, s, NH), 4.82 (1 H, dd, H-1, $J(1,2_e)$ = 2.6, $J(1,2_a)$ = 9.8 Hz), 3.65 (1 H, dd, H-3, $J(3,2_e)$ = 4.7, $J(3,2_a)$ = 11.8 Hz), 2.19 (1 H, m, H-2$_e$, $J(2_e,2_a)$ = 13.0 Hz), 1.54 (1 H, m, H-2$_a$), 1.56 (3 H, s, CH$_3$-4), 1.24 (3 H, d, CH$_3$-5).

***N*-Benzylurethane 20.** Following the same conditions used to prepare **19** from **18**, **20** could be obtained in 73% yield: $[\alpha]_D$ +9.3° (*c* 0.5, CHCl$_3$); $^1$H NMr δ 1.26 (3 H, d), 1.32 (3 H, s), 2.20–2.50 (2 H, m), 2.92 (1 H, t), 4.37 (2 H, d), 4.68 (1 H, q), 5.81 (1 H, m), 7.33 (5 H, m). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69. Found: C, 69.77; H, 7.70. Similarly product **22** was prepared from **20**, but its debenzylation proceeded with ca. 10% yield.

**Acknowledgment.** We thank Mrs. R. Bernardi for GC analysis. This work has been financially supported by Piano Finalizzato CNR Chimica Fine e Secondaria.

**Registry No.** **1**, 92010-40-7; **4**, 106544-28-9; **4** (isopropylidene protected), 106544-30-3; **5**, 106544-29-0; **5** (isopropylidene protected), 106622-87-1; **6**, 106622-88-2; (±)-**6**, 106544-44-9; **7**, 106622-89-3; **9**, 106544-31-4; **10**, 106622-90-6; **12**, 106544-32-5; (±)-**12**, 106622-97-3; **12** (tosylate), 106544-35-8; **13**, 106622-91-7; **13** (tosylate), 106622-93-9; **14**, 106622-94-0; **15**, 106544-36-9; **16**, 106544-34-7; **16** (ethyl glycoside), 106622-92-8; **17**, 106544-37-0; **18**, 106622-95-1; **19**, 106544-38-1; **20**, 106622-96-2; **21**, 106544-39-2; **21** (debenzylated), 106544-40-5; **22**, 106544-43-8; **23** (α anomer), 106544-41-6; **23** (β anomer), 106544-42-7; 2-lithio-2-methyl-1,3-dithiane, 27969-97-7; 2-methyl-1,3-dithiane, 6007-26-7; benzalacetone, 122-57-6; 2-methyl-2-(1-hydroxy-1-methyl-3-phenylprop-2-en-1-yl)-1,3-dithiane, 106544-27-8; (carbethoxymethylene)triphenylphosphorane, 1099-45-2; 4,5,6-trihydroxy-5-methylhept-1-ene, 106544-33-6.