change in apparent extinction coefficients that accompanies complex formation.

In Table II are the extinction coefficients obtained for the complexes. For a given complex at a given wavelength, these extinction coefficients tend to change monotonically with increasing strength of complexation. This is shown by the log-log plots of extinction coefficients vs. equilibrium constants per hydroxy group for formation of the complexes shown in Figure 4. This sort of observation has been made previously.[14] It suggests that there is more proton transfer in the complexes formed with larger equilibrium constants. Because of the different ways in which the hydroxy group is linked to the chromophore that is responsible for the UV absorption, no simple relationship is expected between the slopes of the lines for the different phenols.

We do not wish to imply that all the relationships suggested in the figures would describe the results adequately over an indefinite range of the variables. This would require such improbable constants as smaller equilibrium constants for more acidic phenols than for closely related phenols of weaker acidity. The straight lines shown are presumably just approximations to the long gradual curves that would be required to describe the results over an infinite range of the variables.

(14) Cf. Joesten, M. D.; Schaad, L. J. *Hydrogen Bonding*; Marcel Dekker: New York, 1974, Section 4.IV. Vinogradov, S. N.; Linnell, R. H. *Hydrogen Bonding*; Van Nostrand Reinhold: New York, 1971; Sections 3-5, 4-8, 5-10.

Notes

Bakers' Yeast Mediated Synthesis of 4-Deoxy-D-*lyxo*-hexopyranose (4-Deoxy-D-mannose)

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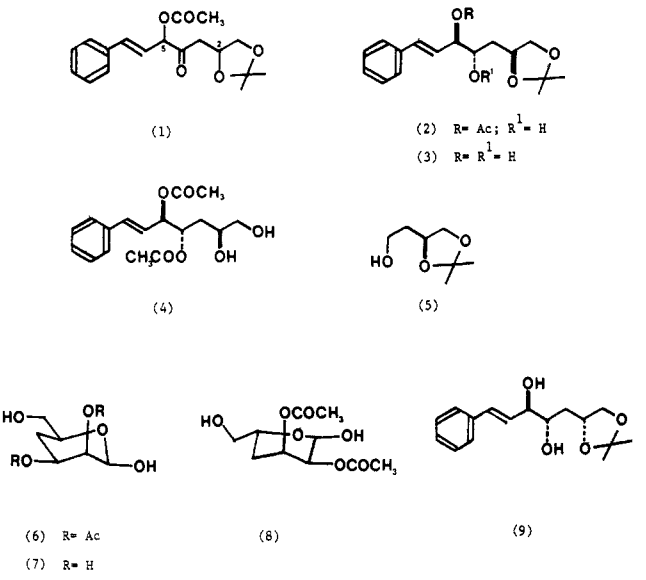
Received July 10, 1986

Recently,[1] in a study of the substrate specificity of the multienzymatic conversion by bakers' yeast of C_6–C_3 aromatic α,β-unsaturated aldehydes to C_6–C_5, 2*S*,3*R* methyl 2,3-diols, we obtained from a series of racemic α-hydroxy ketones, a set of synthetically useful anti and syn chiral diols. We observed high stereospecificity in the carbonyl reduction, but the ratios of the two diastereoisomers, as the result of a kinetic resolution, were strongly dependent on structural features of the substrate. In order to obtain more information on the acceptability of nonnatural substrates by synthetically useful enzymes[2] we extended our investigation to diastereoisomeric α-acetoxy ketones bearing in β'- and γ'-positions of the alkyl side chain two oxygen substituents, and we now report on the results that eventually led to a straightforward synthesis of 4-deoxy-D-*lyxo*-hexopyranose (**7**) and of the 4,7-dideoxy-D-heptose derivative **15**.

Thus, yeast treatment of the racemic α-acetoxy ketone **1**, obtained as a ca. 1:1 mixture of diastereoisomers starting from protected 3-bromopropane-1,2-diol, 1,3-dithiane, and cinnamaldehyde,[3] afforded the 2*S*,4*S*,5*R* carbinol **2** as a major transformation product in ca. 20% yield, 70% of starting material being recovered. The stereochemical assignment of product **2** was made as follows (Chart I). Basic hydrolysis of the carbinol fraction gave crude material from which crystalline **3**, mp 111–112 °C, separated in 85% yield. The latter on HIO_4 oxidation followed by

Chart I



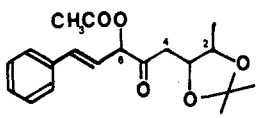
$NaBH_4$ reduction afforded optically pure **5**, characterized as the crystalline 3,5-dinitrobenzoate.[4] Furthermore, the diacetate diol **4**, prepared in 80% yield from **3** on acetylation followed by controlled acidic hydrolysis, afforded on ozonolysis and Ph_3P treatment the diacetate **6**, converted in turn into 4-deoxy-D-*lyxo*-hexopyranose (**7**), $[\alpha]^{20}_D$ +28° (*c* 1, H_2O) (lit.[5] $[\alpha]^{20}_D$ +29.5°), in ca. 47% overall yield from **4**.

The minor diastereoisomer (10%) which accompanied **2** in the yeast treatment of **1** was assigned the 2*R*,4*S*,5*R* stereochemistry depicted in **9**. This compound from the mother liquors of crystalline **3** was also converted into a diacetate diol and afforded on ozonolysis 2,3-diacetyl-4-deoxy-D-*lyxo*-hexopyranose (**6**) and a ribo isomer **8**, $[\alpha]^{20}_D$ −18° (*c* 1, MeOH), in ca. 1.5:1 ratio. The latter 4-deoxy sugar was assigned the L absolute configuration because the *S* alcohol **5** from the mixture eventually yielding **6** and **8** resulted of ca. 0.3% ee.[6]

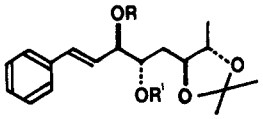
(1) Fuganti, C.; Grasselli, P.; Servi, S.; Spreafico, F.; Zirotti, C.; Casati, P. *J. Org. Chem.* **1984**, *49*, 4087.
(2) *Enzymes in Organic Synthesis*; Pitmann: London, 1985.
(3) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231.
(4) Meyers, A. I.; Lawson, J. P. *Tetrahedron Lett.* **1982**, *26*, 4961.
(5) Rasmussen, J. R. *J. Org. Chem.* **1980**, *45*, 2725.

0022-3263/87/1952-2086$01.50/0

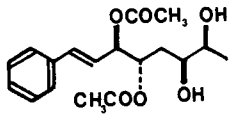
Chart II



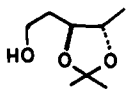
(10)



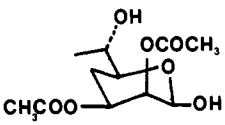
(11) R= Ac; R^1= H
(12) R= R^1= H



(13)



(14)



(15)

The α-acetoxy ketone **10** behaves similarly on yeast reduction and gave a single carbinol **11** in 20% yield, in addition to 70% unreacted starting material.[7] The crystalline diol **12**, mp 93–95 °C, obtained in 80% yield from **11** on basic hydrolysis, was assigned the 2*S*,3*S*,5*S*,6*R* configuration on the basis of the following evidence (Chart II). Sequential treatment of **12** with HIO_4 and $NaBH_4$ gave rise to (3*S*,4*S*)-**14**, $[\alpha]^{20}_D$ −14.5° (see below) in 60% yield. Furthermore, the diacetylated diol **13** on ozonolysis and Me_2S treatment, afforded the 4,7-dideoxy-D-heptose derivative **15**, $[\alpha]^{20}_D$ +3° (*c* 1, MeOH, equilibrium), in 25% overall yield from **12**.

Apparently the absolute configuration at C-3 determines which of the components of the racemic mixture **10** is accepted as a substrate by the enzyme(s) involved in the reduction of the C-5 carbonyl. Indeed a 1:1 mixture of diastereoisomeric **10** prepared from L-threonine[8] and thus showing the 2*R*,3*R*,6*R*,*S* absolute configuration, was not reduced even after long incubation with large amounts of yeast. The diastereomeric mixture **10** from L-threonine after sequential $NaBH_4$ reduction, basic hydrolysis and HIO_4–$NaBH_4$ treatment, gave the enantiomer of the C-5 alcohol **14**, $[\alpha]^{20}_D$ 15.2°, thus allowing the assignment of the 2*S*,3*S* stereochemistry to **12**.

Thus, in the enzymic reduction of the carbonyl group of the α-acetoxy ketones **1** and **10**, hydrogen addition takes place onto the *re* face of the (5*R*) and (6*R*) enantiomers, respectively, but the rate of reduction is higher for the diastereoisomeric form containing a $\beta'S$ oxygen-substituted carbon atom. In chemical terms these results represent a transformation which leads to enantiomerically pure products possessing a useful array of chiral centers and functionalities and from which the deoxy sugar derivatives **6**, **8**, and **15** have been prepared in a direct manner.

Further synthetic applications of the C_6 and C_7 aldehydes prepared by ozonolysis of fully protected forms of **3** and **13** will be reported shortly.

Experimental Section

General Methods. ^1H NMR spectra were determined on a Varian EM-390 (90 MHz) and on a Bruker CXP (300 MHz) instrument. Chemical shifts are in ppm (δ) relative to internal Me_4Si. *J* values are given in hertz. Optical rotations were recorded on a Jasco DIP-181 digital polarimeter. Purification of products was performed by flash chromatography on silica gel (Merck 60, 0.040–0.063 mm) with mixtures of hexane and ethyl acetate. Analytical samples were prepared by bulb-to-bulb distillation under reduced pressure. Melting points are uncorrected.

1,2-(Isoproylidenedioxy)-5-acetoxy-7-phenylhept-6-en-4-one (1). To 200 mL of 1 M 2-lithio-1,3-dithiane THF solution at −78 °C under N_2 was added 39 g (0.2 mol) of 1,2-(isopropylidenedioxy)-3-bromopropane (prepared from 3-bromo-1,2-propanediol, 2,2-dimethoxypropane, and PTSA) in 50 mL of THF during 30 min. The temperature was raised to −40 °C for 16 h. After that time the reaction mixture was treated with 15 mL of MeOH and subsequently poured into 200 mL of ice–water. The mixture was extracted with Et_2O (3 × 150 mL). The organic phase was washed with 50 mL of 5% K_2CO_3 and dried (Na_2SO_4) and the solvent evaporated. The residue was purified by flash chromatography, yielding 7 g of 1,3-dithiane and 28 g (60%) of 2-[2,3-(isopropylidenedioxy)propyl]-1,3-dithiane as an oil, which solidified on standing: ^1H NMR ($CDCl_3$) δ 3.98–4.52 (3 H, m, C*H*S_2, OC*H*CHO), 3.58 (1 H, dd, *J* = 6.0 and 7.5, OCHC*H*'O), 2.70–3.00 (4 H, m, 2 SCH_2), 1.42 (3 H, s, CH_3). To a solution of 23.4 g (0.1 mol) of the latter product in 100 mL of THF under N_2 at −78 °C was added 6.5 mL of 16 M *n*-BuLi in hexane. The reaction mixture was maintained 12 h at −40 °C and then treated with 13.2 g (0.1 mol) of cinnamaldehyde. After 5 h, usual workup afforded 31 g (85%) of 2-[2,3-(isopropylidenedioxy)propyl]-2-(1-hydroxy-3-phenyl-2-propenyl)-1,3-dithiane as an oil, which solidified on standing: ^1H NMR ($CDCl_3$) δ 7.24–7.52 (5 H, m, Ph), 6.73 (1 H, d, PhC*H*=, *J* = 15.5), 6.48 (1 H, dd, =C*H*C), 6.10 (1 H, d, C*H*COMe, *J* = 6.0), 4.58 (1 H, m, C*H*O), 4.23 (1 H, t, OCH*H*', *J* = 6.0), 3.57 (1 H, t, OCH*H*'), 2.40–3.40 (8 H, m, 4-CH_2), 2.18 (3 H, s, COCH_3), 1.40 (3 H, s, CH_3), 1.38 (3 H, s, CH_3).

The latter material (31 g, 0.085 mol) in 80 mL of dry pyridine was treated dropwise with 80 mL of Ac_2O at room temperature. After 12 h the reaction mixture was evaporated to dryness under vacuum, and the residue in 600 mL of THF–H_2O (7:3) was treated under stirring at 23 °C with 36.5 g (0.17 mol) of HgO and 21.2 mL (0.17 mol) of BF_3·Et_2O for 4 h. The reaction mixture was diluted with 200 mL of H_2O and extracted with Et_2O (3 × 150 mL). The organic phase was washed with 5% $NaHCO_3$ solution (3 × 100 mL), dried (Na_2SO_4), and evaporated. The yellow residue was chromatographed on 200 g of silica gel, yielding 19 g (80%) of product **1** as a thick oil. Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.82; H, 6.93. ^1H NMR ($CDCl_3$) (mixture of two diastereoisomers) δ 7.13–7.46 (5 H, m, Ph), 6.83 (1 H, d, PhC*H*=, *J* = 15.5), 6.14 (1 H, dd, =C*H*C, *J* = 8.0), 5.63 and 5.58 (1 H, d, C*H*OAc), 4.47 (1 H, m, C*H*O), 4.19 (1 H, m, OCH*H*'), 3.55 (1 H, m, OCH'H), 3.12 and 3.06 (1 H, dd, COC*H*H', *J* = 17.5, *J* = 5.5), 2.72 and 2.64 (1 H, dd, COCH*H*', *J* = 7.5), 2.19 and 2.20 (3 H, s, COCH_3), 1.39, 1.37, 1.34, and 1.33 (6 H, s, 2 CH_3).

2,3-(Isopropylidenedioxy)-6-acetoxy-8-phenyloct-7-en-5-one (10). To a stirred solution of 29 g (0.2 mol) of *trans*-2,2,5-trimethyl-1,3-dioxolane-4-methanol[7] and 58 g (0.22 mol) of triphenylphosphine in 100 mL of CH_2Cl_2 was added portionwise 39 g (0.22 mol) of *N*-bromosuccinimide, while the temperature was maintained below 30 °C. After 1 h at 23 °C, the solvent was evaporated, and the residue was distilled at 20 mmHg to give 30 g (72%) of *trans*-4-(bromomethyl)-2,2,5-trimethyl-1,3-dioxolane, mp 70 °C. Starting from (4*S*,5*S*)-*trans*-2,2,5-trimethyl-1,3-dioxolane-4-methanol,[8] (4*R*,5*S*)-4-(bromomethyl)-2,2,5-trimethyl-1,3-dioxolane was obtained in similar fashion: $[\alpha]^{20}_D$ −9° (*c* 1, $CHCl_3$). The synthesis of racemic and optically active **10** proceeds from the above bromo derivatives as previously indicated for **1**. Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.65; H, 7.28. Found: C, 68.54; H, 7.22 ^1H NMR ($CDCl_3$) δ 7.28–7.52 (5 H, m, Ph), 6.86 (1 H, d,

(6) The mother liquors from which **3** had crystallized clearly contain **3** and **9** in a 1.5:1 ratio. If this mixture is sequentially treated as described for pure **3**, **6** and **8** are eventually obtained in the above ratio. Alternatively **3** and **9** are converted into **5** in which the *S* absolute configuration still predominates, but the *ee* is now of only 0.3%. Since **3** and **9** are epimers at C-2 which becomes C-5 in the two hexopyranoses, one of the two compounds **6** and **8** belongs to the D series and the other to the L series.

(7) Hatch, R. P.; Shringarpure, J.; Weinreb, S. *J. Org. Chem.* **1978**, *43*, 4172.

(8) Fronza G.; Fuganti, C.; Grasselli, P.; Marinoni, G. *Tetrahedron Lett.* **1979**, 3883.

PhC*H*=, J = 15.5), 6.18 (1 H, dd, =C*H*CH, J = 7.0), 5.72 (1 H, d, C*H*OAc), 3.63–4.12 (2 H, m, C*H*O), 2.83 (1 H, dd, CH*H*′, J = 16.5, J = 6.0), 2.62 (1 H, dd, CH*H*′, J = 4.5), 2.22 (3 H, s, COCH_3), 1.40 (3 H, s, CH_3), 1.28 (3 H, d, CH_3, J = 6.0).

Yeast Reduction. In a 10-L glass jar a mixture was made up composed of 1 kg of commercial bakers' yeast and 0.6 kg of D-glucose in 5 L of tap water at 28/30 °C. As the fermentation started, 19 g of the α-acetoxy ketone **1** in 50 mL of EtOH was added from a dropping funnel during 10 min. After 12 h at 25–28 °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 through flash chomatography to give ca. 13.3 g (70%) of unreacted α-acetoxy ketone **1** and ca. 3.8 g (20%) of **2** as a yellowish oil: ^{1}H NMR ($CDCl_3$) (mixture of stereoisomers) δ 7.2–7.5 (5 H, m, Ph), 6.72 (1 H, d, PhC*H*=, J = 15.5), 6.23 and 6.17 (1 H, dd, =C*H*C, J = 8.0), 5.40 and 5.18 (1 H, dd, C*H*OAc, J = 3.5), 3.90–4.50 (3 H, m, C*H*O), 3.54 (1 H, m, C*H*O), 2.12 and 2.10 (3 H, s, COCH_3), 1.60–2.12 (2 H, m, CH_2), 1.43, 1.40, 1.37, and 1.32 (6 H, s, 2 CH_3).

In analogous way the reduction of the α-acetoxy ketone **10** was effected, affording the hydroxy acetate as a brownish oil in 20% yield.

4-Deoxy-D-*lyxo*-hexopyranose (7) and 2,3-Diacetyl-4-deoxy-L-*ribo*-hexopyranose (8). To a solution of 3.8 g (0.012 mol) of **2** in 20 mL of MeOH was added at 23 °C 2 mL of 2 N NaOH with stirring. After 12 h the reaction mixture was concentrated to ca. 10 mL, diluted with 10 mL of 20% NaCl solution, and extracted twice with 80-mL portions of ethyl acetate. The organic phase was washed with 2 × 20 mL of 5% NaCl solution, dried, and evaporated. The residue (2.7 g) separated from hexane–ethyl acetate 2.3 g (85%) of the crystalline diol **3**: mp 111–112 °C; $[\alpha]^{20}_D$ +10.8° (c 1, $CHCl_3$). Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.95; H, 7.92. ^{1}H NMR ($CDCl_3$) δ 7.27–7.5 (5 H, m, Ph), 6.68 (1 H, d, PhC*H*=, J = 16.0), 6.24 (1 H, dd, =C*H*C, J = 6.5), 3.86–4.52 (4 H, m, C*H*O), 3.56 (1 H, t, C*H*O, J = 6.0), 2.86 (2 H, br, OH), 1.73 (2 H, t, CH_2, J = 6.0), 1.42 (3 H, s, CH_3), 1.36 (3 H, s, CH_3).

To a solution of 5.56 g (0.02 mol) of the diol **3** in 50 mL of CH_2L_2 and 20 mL of dry pyridine was added 20 mL of acetic anhydride. After 12 h at 23 °C, the reaction mixture was evaporated to dryness, and the residues was purified by flash chromatography to afford 6.9 g (95%) of the diacetate as an oil: $[\alpha]^{20}_D$ +21.4° (c 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.12–7.50 (5 H, m, Ph), 6.70 (1 H, d, PhC*H*=, J = 15.5), 6.10 (1 H, dd, =C*H*C, J = 6.5), 5.63 (1 H, dd, =CHC*H*OAc, J = 3.0), 5.27 (1 H, m, AcOC*H*CH$_2$), 3.90–4.30 (2 H, m, C*H*O), 3.53 (1 H, m, C*H*′O), 1.72–2.10 (2 H, m, CH_2), 2.10 (3 H, s, COCH_3), 2.12 (3 H, s, COCH_3), 1.40 (3 H, s, CH_3).

A solution of 6.9 g (0.019 mol) of the diacetyl derivative of **3** in 50 mL of THF at 23 °C with stirring was treated with 10 mL of a 1% methanolic solution of HCl for 6 h. The reaction mixture was diluted with 50 mL of Et_2O and 10 mL of 5% $NaHCO_3$ solution and extracted twice with 50-mL portions of ethyl acetate. The residue obtained upon evaporation of the solvent was purified by flash chromatography, yielding 5.22 g (85%) of the diacetate diol **4**, as an oil: $[\alpha]^{20}_D$ +29.2° (c 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.22–7.52 (5 H, m, Ph), 6.70 (1 H, d, PhC*H*=, J = 15.5), 6.12 (1 H, dd, =C*H*CH, J = 7.0), 5.56 (1 H, dd, =CHC*H*OAc, J = 3.0), 5.36 (1 H, m, AcOC*H*CH$_2$), 3.30–3.82 (3 H, m, C*H*OH and CH_2OH), 2.82 (2 H, br, OH), 2.16 (3 H, s, COCH$_3$), 2.12 (3 H, s, COCH_3), 1.50–1.95 (2 H, m, CH_2).

Ozonized oxygen was passed through a solution of 5.2 g (0.016 mol) of **4** in 30 mL of CH_2Cl_2 at −40 °C until the absorption was completed. Then N_2 was passed through, and with stirring at −20 °C, 4.2 g (0.016 mol) of triphenylphosphine was added portionwise. After standing at 23 °C for 12 h, the reaction mixture was evaporated, the residue was taken up with ca. 30 mL of Et_2O, and the warm solution was treated with petroleum ether (40–60 °C) until cloudy. The precipitate which separated after 12 h at 4 °C was filtered and washed with a cold mixture of Et_2O–petroleum ether. The residue obtained on evaporation of the solvent was purified by flash chromatography to give ca. 3 g of 2,3-diacetyl-4-deoxy-D-*lyxo*-hexopyranose (**6**) containing ca. 10–15% of triphenylphosphine oxide: ^{1}H NMR ($CDCl_3$) δ (α anomer; just after the dissolution of the sample, only traces of the β-anomer could be detected) 1.69 (H-4e, J(3,4e) = 5.2, J(5,4e) = 2.6, J(4e,4a) = 12.2), 1.83 (H-4a, J(3,4a) = 12.0, J(5,4a) = 12.0), 2.01 and 2.13 (2 COCH$_3$, s), 3.59 (H-6, J(6,6′) = 11.8, J(5,6) = 6.2), 3.63 (H-6′, J(5,6′) = 3.8), 4.20 (H-5), 4.83 (OH-1, br s), 5.11 (H-2, J(1,2) = 2.1, J(2,3) = 3.2), 5.22 (H-1), 5.36 (H-3). The structural assignment of compound **6** is based on the values of the vicinal coupling constant. The calculated values for the α-lyxo configuration ($^4C_1$ (D) conformation) derived from a statistical treatment of the vicinal coupling constants for hexopyranoses were[10] J(1,2) = 1.8, J(2,3) = 3.1, J(3,4e) = 4.9, J(3,4a) = 12.0, J(4a,5) = 12.0, and J(4e,5) = 2.6, which are in good agreement with the reported data.

A solution of the above mixture in 20 mL of dry methanol was treated 16 h with 20 mL of 3% HCl in methanol at 23 °C. The residue obtained upon evaporation of the solvent under vacuum below 40 °C was taken up with 25 mL of water, extracted with 10 mL of toluene, and treated with 1 g of Amberlite IR 120 (H^+ form) and the mixture refluxed for 24 h. Workup of the reaction as indicated[5] afforded ca. 1.4 g (47%) of 4-deoxy-D-*lyxo*-hexopyranose (**7**): $[\alpha]^{20}_D$ +28° (c 1, H_2O, equilibrium) (lit.[5] $[\alpha]^{20}_D$ +29.5°). The mother liquors from several preparations of **3** were pooled, converted into the 4,5-diacetyl 1,2-diol, and ozonized, as above, to give in 1.5:1 ratio, after separation by flash chromatography, product **6** and 2,3-diacetyl-4-deoxy-L-*ribo*-hexopyranose (**8**) as an oil: $[\alpha]^{20}_D$ −18° (c 1, MeOH, 3 h, equilibrium); ^{1}H NMR ($CDCl_3$) δ (β anomer) 1.77 (H-4e, J(3,4e) = 3.2, J(4a,4e) = 14.6, J(5,4e) = 3.2), 1.85 (H-4a, J(3,4a) = 3.2, J(5,4a) = 10.8), 2.07 and 2.12 (2 COCH$_3$, s), 3.58 (H-6, J(6,6′) = 12.0, J(5,6) = 6.4), 3.71 (H-6′, J(5,6′) = 3.0), 4.01 (H-5), 4.68 (H-2, J(1,2) = 8.3, J(2,3) = 3.2, 5.07 (H-1), 5.48 (H-3). Calculated values of the vicinal coupling constants for the β-ribo configuration ($^1C_4$ (L) conformation) were[10] J(1,2) = 8.3, J(2,3) = 3.1, J(3,4e) = 3.1, J(3,4a) = 2.6, J(5,4e) = 2.6, and J(5,4a) = 11.2.

3,5-Dinitrobenzoate of (3*S*)-3,4-(Isopropylidenedioxy)-butan-1-ol. To a stirred solution of 2.1 g (0.01 mol) of $HIO_4 \cdot 2H_2O$ in 40 mL of dry THF at 23 °C was added all at once 2.8 g (0.01 mol) of **3** in 10 mL of THF. After 2 min, 2 drops of ethylene glycol were added, and the reaction mixture was diluted with 100 mL of Et_2O and 25 mL of 5% $NaHCO_3$. The acqueous phase was extracted twice with 50-mL portions of Et_2O. The organic phase was concentrated to ca. 10 mL, diluted with 10 mL of ethanol, and treated at 23 °C with 1 g of $NaBH_4$ portionwise. After 12 h, addition of 10 mL of 15% NaCl solution, extraction with Et_2O, and evaporation of the organic phase left an oil, which was dissolved in 20 mL of dry pyridine and treated at 0 °C with 4.6 g (0.02 mol) of 3,5-dinitrobenzoyl chloride. After 24 h at 23 °C the reaction mixture was poured in ice-water and extracted with ethyl acetate, and the organic phase was washed with 100 mL of cold 1% HCl and 100 mL of 5% $NaHCO_3$, dried, and evaporated. The oily residue was purified by flash chromatography to give the 3,5-dinitrobenzoate of benzyl alcohol (2.2 g 72%) and the 3,5-dinitrobenzoate of (3*S*)-**5** (2.1 g, 60%): mp 62–63 °C (absolute ethanol); $[\alpha]^{20}_D$ −13.6° (c 1.5, $CHCl_3$) (lit.[4] $[\alpha]^{20}_D$ −13.7°).[9] When the above sequence of reactions was performed on a lot of mother liquors of **3** yielding on ozonolysis **6** and **8** in 1.5:1 ratio, the α value of the 3,5-dinitrobenzoate of **5** was −4.5°.

2,3-Diacetyl-4,7-dideoxy-D-heptose (15). The carbinol fraction **11**, obtained in the yeast reduction of **10**, afforded, on basic hydrolysis as above, crystalline **12**, mp 93–95 °C (hexane), $[\alpha]^{20}_D$ −1.2° (c 1, $CHCl_3$), in 80% yield: ^{1}H NMR ($CDCl_3$) δ 7.18–7.53 (5 H, m, Ph), 6.70 (1 H, d, PhC*H*=, J = 15.5), 6.27 (1 H, dd, =C*H*CH, J = 6.0), 4.30 (1 H, dd, =CHC*H*, J = 4.5), 3.67–4.15 (3 H, m, C*H*OH and C*H*O), 2.80 (1 H, br, OH), 2.45 (1 H, br, OH), 1.70 (2 H, m, CH_2), 1.42 (6 H, s, 2 CH_3), 1.26 (3 H, d, CH_3, J = 5.8).

The 5,6-diacetyl 2,3-diol **13**, $[\alpha]^{20}_D$ −64° (c 1, $CHCl_3$), prepared from **12** as above, was ozonized to give in ca. 70% yield the oily 2,3-diacetyl-4,7-dideoxy-D-heptose derivative **15**: $[\alpha]^{20}_D$ +3° (c 1, MeOH, 1 h, equilibrium). Anal. Calcd for $C_{11}H_{18}O_7$: C, 50.37; H, 6.92. Found: C, 50.42; H, 6.89. ^{1}H NMR ($CDCl_3$) δ (α anomer) 1.02 (CH$_3$-6, J(6,CH$_3$) = 6.3), 1.57 (H-4e, J(3,4e) = 5.0 J(4a,4e) = 12.0, J(5,4e) = 2.5), 1.81 (H-4a, J(3,4a) = 12.1, J(5,4a) = 11.8), 1.71 and 1.74 (2 COCH$_3$, s), 3.62 (H-6, J(5,6) = 6.8), 3.78 (H-5), 5.18 (H-1, J(1,2) = 1.9), 5.43 (H-2, J(2,3) = 3.0), 5.56 (H-3). The

(9) The oily residue obtained on evaporation of the mother liquors shows $[\alpha]^{20}_D$ −13.2°.

calculated values[10] of the vicinal coupling constants for the α-configuration are the same reported for compound 6.

(3*S*,4*S*)-3,4-(Isopropylidenedioxy)pentan-1-ol (14). The periodate oxidation of the diol 12 and the subsequent $NaBH_4$ reduction were performed as indicated above for the conversion of 3 into 5. Benzyl alcohol was removed from the reaction mixture by hydrogenolysis to toluene in the presence of 10% Pd/C with H_2 in ethanol at 23 °C and 2 atm. (3*S*,4*S*)-14, as an oil, was obtained in 45% overall yield from 12: $[\alpha]^{20}_D$ −14.5° (*c* 1, $CHCl_3$). When (2*R*,3*R*,6*RS*)-10 was reduced with $NaBH_4$ in isopropyl alcohol, followed by basic treatment, a mixture of 5,6-syn and 5,6-anti diols was obtained. Sequential treatment of the mixture with $HIO_4 \cdot 2H_2O$ and $NaBH_4$ gave (3*R*,4*R*)-14: $[\alpha]^{20}_D$ +14.9° (*c* 1, $CHCl_3$).

Registry No. 1 (isomer 1), 106976-80-1; 1 (isomer 2), 106976-81-2; 2, 106976-84-5; 3, 106976-85-6; 3 (diacetate), 106976-86-7; 4, 106976-87-8; 5 (3,5-dinitrobenzoate), 85287-65-6; 6, 106976-88-9; 7, 74164-24-2; 8, 106976-89-0; 9 (5-acetate), 107034-98-0; 10 (racemic isomer 1), 106976-83-4; 10 (racemic isomer 2), 107035-00-7; 10 (2*R*,3*R*,6*R*), 107035-01-8; 10 (2*R*,3*R*,6*S*), 107034-99-1; 10 (2*S*,3*S*,6*R*), 107035-02-9; 10 (2*S*,3*S*,6*S*), 107035-03-0; 11, 106976-90-3; 12, 106976-91-4; 13, 106976-92-5; 14 (3*S*,4*S*), 106987-87-5; 14 (3*R*,4*R*), 106987-88-6; 15, 106976-93-6; 2-lithio-1,3-dithiane, 36049-90-8; 1,2-(isopropylidenedioxy)-3-bromopropane, 34637-20-2; 3-bromo-1,2-propanediol, 34637-21-3; 2-[2,3-(isopropylidenedioxy)propyl]-1,3-dithiane, 106976-78-7; cinnamaldehyde, 104-55-2; 2-[2,3-(isopropylidenedioxy)propyl]-2-(1-hydroxy-3-phenyl-2-propenyl)-1,3-dithiane (isomer 1), 106976-79-8; 2-[2,3-(isopropylidenedioxy)propyl]-2-(1-hydroxy-3-phenyl-2-propenyl)-1,3-dithiane (isomer 2), 106976-94-7; *trans*-2,2,5-trimethyl-1,3-dioxolane-4-methanol, 81739-14-2; *trans*-4-(bromomethyl)-2,2,5-trimethyl-1,3-dioxolane, 106976-82-3; (4*S*,5*S*)-*trans*-2,2,5-trimethyl-1,3-dioxolane-4-methanol, 85249-45-2; (4*R*,5*S*)-4-(bromomethyl)-2,2,5-trimethyl-1,3-dioxolane, 107034-97-9; 3,5-dinitrobenzoyl chloride, 99-33-2.

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Synthesis and pK_a Values of 4,5-Dinitro-1,8-biphenylenediol[1]

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Received September 10, 1986

1,8-Biphenylenediol has been shown to use its two hydroxy groups to form hydrogen bonds to the same oxygen atom.[2-4] Because the hydrogen bonding ability of structurally similar acids increases with their increasing acidity[5] more acidic derivatives of 1,8-biphenylenediol are of interest. Since ortho and para nitro substituents are among the strongest electron withdrawers of common substituents and since an ortho nitro substituent could give complications from internal hydrogen bonding, we have prepared 4,5-dinitro-1,8-biphenylenediol (1) and determined its ionization constants.

Experimental Section

2,3-Dichloro-4-nitroanisole. A mixture of 8.47 g (48 mmol) of 2,3-dichloroanisole, 7.64 g (58 mmol) of nitronium tetrafluoroborate, and 400 mL of glacial acetic acid was kept at 90–110 °C for 1 h and then stirred at room temperature for 12 h. The reaction mixture was poured into 500 mL of water and extracted with ether. The combined organic layers were washed with water and sodium carbonate solution and dried with magnesium sulfate. Removal of the solvent gave 8.0 g of brownish viscous oil, which was chromatographed with 35:1 petroleum ether–ethyl acetate to give three fractions, of which the last was 1.76 g (17% yield) of 2,3-dichloro-4-nitroanisole: ^1H NMR (acetone-d_6, 90 MHz) δ 8.17 (d, J = 9 Hz, 1 H, H-5), 7.32 (d, 1 H, H-6), 4.09 (s, 3 H, OCH_3); mass spectrum, m/z 222 (M^+). An analytical sample was recrystallized three times from hexane to give pale yellow prisms: mp 81–82 °C.

Anal. Calcd for $C_7H_5O_3Cl_2N$: C, 37.87; H, 2.27; Cl, 31.94; N, 6.31. Found: C, 38.05; H, 2.33; Cl, 31.62; N, 6.23.

2,3-Dichloro-6-nitroanisole and 2,3-Dichloro-4,6-dinitroanisole. The first fraction in the chromatography just described was 0.4 g of a mixture of starting 2,3-dichloroanisole and 2,3-dichloro-6-nitroanisole: ^1H NMR (acetone-d_6, 90 MHz) δ 7.90 (d, J = 9 Hz, 1 H, H-5), 7.59 (d, 1 H, H-4), 4.05 (s, 3 H, OCH_3): mass spectrum, m/z 222 (M^+).

The second fraction was 0.3 g (2% yield) of 2,3-dichloro-4,6-dinitroanisole: ^1H NMR (acetone-d_6, 90 MHz) δ 8.65 (s, 1 H, H-5), 4.13 (s, 3 H, OCH_3).

2,2′-Diiodo-6,6′-dimethoxy-3,3′-dinitrobiphenyl (3). A mixture of 10.5 g (22.5 mmol) of 2,2′-diiodo-6,6′-dimethoxybiphenyl (2), 17.95 g (135 mmol) of nitronium tetrafluoroborate, and 265 mL of glacial acetic acid was refluxed for 1.2 h. The cooled mixture was poured into 500 mL of water and extracted with ether. The combined organic layers were washed with 150 mL of water, sodium carbonate solution, sodium bisulfite solution, and water and then dried with magnesium sulfate. Evaporation of the solvent gave 12.4 g of reddish solid that was chromatographed on silica gel with 3:1 hexane–ethyl acetate to give 4.49 g (8.08 mmol, 36%) of yellow crystalline 3. Three recrystallizations from chloroform–hexane gave crystals: mp 202.5–203 °C; R_f 0.32 (2:1 hexane–ethyl acetate); IR (KBr) 1565, 1340 (NO_2) cm^{-1}; ^1H NMR (acetone-d_6, 90 MHz) δ 8.09 (d, J = 9 Hz, 2 H, H-4,4′), 7.37 (d, 2 H, H-5,5′), 3.81 (s, 6 H, OCH_3); mass spectrum, m/z 556 (M^+).

Anal. Calcd for $C_{14}H_{10}O_6N_2I_2$: C, 30.24; H, 1.81; N, 5.04; I, 45.64. Found: C, 30.45; H, 1.94, N, 4.88; I, 45.06.

2,2′-Diiodo-6,6′-dimethoxy-3-nitrobiphenyl, 2,2′-Diiodo-6,6′-dimethoxy-5-nitrobiphenyl, 2,2′-Diiodo-6,6′-dimethoxy-3,5′-dinitrobiphenyl, and 2,2′-Diiodo-6,6′-dimethoxy-3,3′,5,5′-tetranitrobiphenyl. Other products from the preceding reaction were obtained by column and/or preparative thin layer chromatography and identified from the following evidence. All the R_f values are in 2:1 hexane–ethyl acetate.

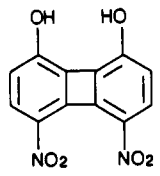
A 7% yield (0.83 g) of 2,2′-diiodo-6,6′-dimethoxy-3-nitrobiphenyl: R_f 0.52; ^1H NMR (acetone-d_6, 90 MHz) δ 8.03 (d, J = 9 Hz, 1 H, H-4), 7.67–7.46 (dd, $J_{3',4'}$ = 6 Hz, $J_{3',5'}$ = 3 Hz, 1 H, H-3′), 7.38–7.18 (m, 3 H, H-4′, H-5, H-5′), 3.86 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3); mass spectrum, m/z 511 (M^+), 384 ($M^+ - I$).

A 4% yield (0.5 g) of 2,2′-diiodo-6,6′-dimethoxy-5-nitrobiphenyl: R_f 0.70; ^1H NMR (acetone-d_6, 90 MHz) δ 8.01 (d, J = 9 Hz, 1 H, H-4), 7.75–7.15 (m, 4 H, H-3, H-3′, H-4′, H-5′), 3.80 (s, 3 H, OCH_3), 3.59 (s, 3 H, OCH_3); mass spectrum, m/z 511 (M^+).

A 32% yield (4.0 g) of 2,2′-diiodo-6,6′-dimethoxy-3,5′-dinitrobiphenyl: R_f 0.47; ^1H NMR (acetone-d_6, 90 MHz) δ 8.19–8.00 (m, 2 H, H-4, H-4′), 7.78 (d, J = 9 Hz, 1 H, H-3′), 7.45 (d, J = 9 Hz, 1 H, H-5), 3.95 (s, 3 H, OCH_3), 3.62 (s, 3 H, OCH_3); mass spectrum, m/z 556 (M^+), 429 ($M^+ - I$).

A trace of 2,2′-diiodo-6,6′-dimethoxy-3,3′,5,5′-tetranitrobiphenyl: R_f 0.67; ^1H NMR (acetone-d_6, 90 MHz) δ 8.65 (s, 2 H, H-4,4′), 3.80 (s, 6 H, OCH_3); mass spectrum, m/z 519 ($M^+ - I$).

1,8-Dimethoxy-4,5-dinitrobiphenylene (4). A solution of 500 mg (0.90 mmol) of 3 in 50 mL of dry dimethylformamide was



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(1) This investigation was supported in part by Grant No. CHE-8114770 from the National Science Foundation. Abstracted in part from the Ph.D. Dissertation of K. Ahn, The Ohio State University, 1986.
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