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SUPPLEMENTARY INFORMATION (7 Pages)

Asymmetric C-H Oxidation of *vic* Diols to α-Hydroxy Ketones by a Fructose-Derived Dioxirane: Electronic Effects on the Enantioselectivity of Oxygen Transfer

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Experimental Section

General Methods. ^{1}H- and ^{13}C-NMR spectra were measured on a Brucker AC 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz) spectrometer with TMS as internal standard. *J* values are given in Hz. IR spectra were recorded on a Perkin-Elmer 1600 FT-IR spectrophotometer. HPLC was conducted on a Kontron (Eching/München) analytic HPLC instrument with Kontron HPLC pumps (Model 322) and a Rheodyne 7725 injector (maximum sample volume: 20 μL). Enantiomers were detected by a tunable absorbance detector (Kontron, Model UVIKON 720 LC micro) at 220 or 254 nm. The optical rotations were on-line detected by a CHRALYZER® (IBZ Meßtechnik, Hannover) polarimetric detector. Enantiomers were separated on a Chiralcel OD-H or a Chiralcel OB-H column (0.46 cm ϕ × 25 cm) from the Daicel Chemical Industries, Co Ltd. (Exton, PA, USA). Elemental analyses were carried out by the Microanalytical Division of the Institute of Inorganic Chemistry, University of Würzburg. Melting points were taken on a Büchi B-545 apparatus and are not corrected. TLC analyses were conducted on precoated silical-gel foils Polygram SIL G/UV$_{254}$ (40 × 80 mm) from Macherey & Nagel (Düren, Germany). Spots were identified on UV-light exposure and/or by iodine vapor. Silical gel (63-200 μm, Woelm) was used for column chromatography. 4,4'-Difluorobenzil, 2,2'-dichlorobenzil and 4,4'-dibromobenzil were commercial products of Aldrich and Lancaster and were used as received. DMD solutions[1b] and the fructose-derived ketone **1**[12c] were prepared according to the literature procedure. 4,4'-Dimethylbenzil,[23] 4,4'-dimethoxybenzil[23] and 4,4'-dichlorobenzil[24] were prepared from the corresponding benzoins, which were again obtained from the corresponding benzaldehyde derivatives.[25] 4,4'-Dicyanobenzil was prepared by oxidation of *d,l*-**2g** with excess amounts of DMD. The *meso* diols **2a-g** and **2i** were prepared by reduction of the corresponding benzils with $NaBH_4$,[26]

while *meso*-**2h**[27] was made available from *trans*-4,4'-dinitrostilbene epoxide by acid-catalyzed ring-opening reaction. The *d,l*-**2a** and **2b** derivatives were obtained by isomerization of *meso*-**2a** and *meso*-**2b**.[28] The derivatives *d,l*-**2d**, *d,l*-**2e**, *d,l*-**2f** and *d,l*-**2g** were synthesized by reduction of the corresponding aldehydes with $TiCl_3$ in CH_2Cl_2.[29] Attempts to prepare the diol *d,l*-**2c** by the above-mentioned methods failed. The diastereomeric diols *erythro*-**2j**, *cis*-**2k**, *trans*-**2k** and *trans*-**2l** were obtained from the corresponding epoxides according to literature procedure.[30] The *threo*-**2j** substrate was prepared from *trans*-β-methylstyrene[31] and the *cis*-**2l** from 1,2-dihydronaphthalene.[32] The *cis*-**4a**, *cis*-**4c**, *trans*-**4a** and *trans*-**4c** cases were prepared by ketalization of the corresponding diols.[33] The racemic samples of the α-hydroxy ketones **3**, if not commercially available, were obtained by DMD oxidation of the corresponding *vic* diols. All of the α-hydroxy ketones **3**, except for **3g**, are known compounds.

Preparation of *cis*-4,5-Bis(4-methoxyphenyl)-2,2-dimethyl-1,3-dioxolane (*cis*-4b): To a solution of *meso*-**2b** (1.21 g, 5.0 mmol) in 2,2-dimethoxypropane (10 mL) and benzene (20 mL) was added *p*-toluenesulfonic acid (60 mg) and the mixture was refluxed for 16 h. After cooling to room temperature (ca 20 °C), the mixture was taken up in ether (100 mL), washed with saturated aqu. $NaHCO_3$ (2 × 15 mL), and dried over $MgSO_4$. The solvent was evaporated (20 °C/14 mbar) and the residue was purified by silical-gel chromatography (deactivated with 1% Et_3N) to give a pale yellow oil. After Kugel-Rohr distillation, 0.99 g (70%) product was obtained as colorless oil which was crystallized out on standing as colorless needles, m.p. 56.3 °C. ^{1}H NMR ($CDCl_3$): δ 1.73 (s, 3 H), 1.94 (s, 3 H), 2.33 (s, 6 H), 5.60 (s, 2 H), 7.02 (s, 8 H); ^{13}C NMR ($CDCl_3$): δ 21.1 (q), 24.6 (q), 26.9 (q), 81.3 (d), 108.4 (s), 126.9 (d), 128.2 (d), 134,7 (s), 136.5 (s); IR ($CHCl_3$) 3619, 3022, 2895, 1694, 1608, 1519, 1478, 1424, 1229, 1208 cm^{-1}. Anal. Calcd. for $C_{19}H_{22}O_2$ (282.4): C, 80.82; H, 7.85. Found: C, 80.97; H, 7.62.

General Procedure for the Asymmetrization of *meso* Diols: To a solution of *meso* diol **2** (0.10 mmol), ketone **1** (77.48 mg, 0.30 mmol) and Bu_4NHSO_4 (1.5 mg, 4.0 μmol) in 1.5 mL CH_3CN was added at 0 °C 1.0 mL of 0.05 M $Na_2B_4O_7$ in 4×10^{-4} M aqueous Na_2EDTA while stirring. Solutions of Curox® (92.0 mg, 0.15 mmol) and K_2CO_3 (87.0 mg, 0.63 mmol) in 0.65 mL of 4×10^{-4} M aqueous Na_2EDTA were added simultaneously by means of separate syringes within 2 h. The mixture was further stirred for 1 h and then diluted with H_2O (20 mL), extracted with ether (3 × 20 mL), washed with H_2O (2 × 10 mL), and dried over $MgSO_4$. After removal of the solvent (20 °C/20 mbar), the residue was purified by silica-gel

chromatography to give the recovered ketone **1** (40-60% yield) and benzoin **3** in 80-95% yield (based on conversion) with an ee value of 17-60% for the *R* enantiomer.

General Procedure for Kinetic Resolution of *rac* Diols: To a solution of *d,l* diol **2** (0.10 mmol), ketone **1** (77.48 mg, 0.30 mmol) and Bu_4NHSO_4 (1.5 mg, 4.0 μmol) in 1.5 mL of CH_3CN was added at 0 °C 1.0 mL of 0.05 M $Na_2B_4O_7$ in 4×10^{-4} M aqueous Na_2EDTA while stirring. Solutions of Curox® (46.0 mg, 0.075 mmol) and K_2CO_3 (44.0 mg, 0.315 mmol) in 0.33 mL of 4×10^{-4} M aqueous Na_2EDTA were added simultaneously by means of separate syringes over 2 h. The mixture was further stirred for 1 h and then worked up as described above to give the (*S*)-**3** with an ee value of 61-75%.

Derivation of 4,4'-Dichlorobenzoin (3e) and 4,4'-Dibromobenzoin (3f) for Determination of ee Values: The enantiomerically enriched α-hydroxy ketone **3e** or **3f** was dissolved in acetic anhydride (0.5 mL) and pyridine (0.3 mL) was added while stirring. The mixture was stirred at *ca.* 20 °C for 2 h, then diluted with 20 mL of H_2O, and extracted with ether (3 × 10 mL). The combined organic phases were washed successively with saturated $NaHCO_3$ solution (10 mL), H_2O (2 × 10 mL), and dried over $MgSO_4$. After removal of the solvent (20 °C/ 20 mbar), the ee value of the acetate was determined by chiral HPLC analysis.

General Procedure for Oxidation of Acetals: To a solution of *cis*-**4** (0.10 mmol), ketone **1** (77.48 mg, 0.30 mmol) and Bu_4NHSO_4 (1.5 mg, 4.0 μmol) in 3.0 mL of 1:2 (v/v) CH_3CN/DMM (dimethoxymethane) at 0 °C was added 2.0 mL of 0.05 M $Na_2B_4O_7$ in 4×10^{-4} M aqueous Na_2EDTA while stirring. Solutions of Curox® (276.0 mg, 0.45 mmol) and K_2CO_3 (260.0 mg, 1.89 mmol) in 1.5 mL of 4×10^{-4} M aqueous Na_2EDTA were added simutaneously by means of separate syringes within 3.5 h. The mixture was further stirred for 1.5 h and then worked up as described above. The ee value of the product **3** was determined directly on the crude product.

4,4'-Dimethylbenzoin[16] **(3b)**: ^1H NMR ($CDCl_3$): δ 2.28 (s, 3 H), 2.35 (s, 3 H), 4.57 (d, J = 6.0, 1 H), 5.90 (d, J = 6.0, 1 H), 7.10-7.24 (m, 6 H), 7.82 (d, J = 8.2, 2 H); ^{13}C NMR ($CDCl_3$): δ 21.1 (q), 21.6 (q), 75.8 (d), 127.6 (d), 129.2 (d), 129.3 (d), 129.7 (d), 130.9 (s), 136.3 (s), 138.3 (s), 144.7 (s), 198.5 (s).

4,4'-Dimethoxybenzoin[16] **(3c)**: ^{1}H NMR ($CDCl_3$): δ 3.75 (s, 3 H), 3.88 (s, 3H), 4.59 (d, J = 6.0, 1 H), 5.85 (d, J = 6.0, 1 H), 6.81-6.88 (m, 4 H), 7.22-7.26 (m, 2 H), 7.82-7.93 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ 55.2 (q), 55.4 (q), 75.2 (d), 113.9 (d), 114.4 (d), 126.2 (s), 129.0 (d), 131.5 (d), 131.8 (s), 159.6 (s), 163.9 (s), 197.3 (s).

4,4'-Difluorobenzoin[16] **(3d)**: ^{1}H NMR ($CDCl_3$): δ 4.46 (d, J = 5.6, 1 H), 5.83 (d, J = 5.6, 1 H), 6.90-7.05 (m, 4 H), 7.19-7.26 (m, 2 H), 7.82-7.89 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ 75.3 (d), 115.9 (d, $J_{C\text{-}F}$ = 8.4), 116.4 (d, $J_{C\text{-}F}$ = 8.2), 129.5 (d, $J_{C\text{-}F}$ = 8.4), 131.9 (d, $J_{C\text{-}F}$ = 9.4), 134.7 (s), 134.8 (s), 161.9 (d, $J_{C\text{-}F}$ = 161.5), 166.9 (d, $J_{C\text{-}F}$ = 170.4), 197.1 (s).

4,4'-Dichlorobenzoin[16] **(3e)**: ^{1}H NMR ($CDCl_3$): δ 4.46 (d, J = 6.0, 1 H), 5.80 (d, J = 6.0, 1 H), 7.14-7.32 (m, 6 H), 7.72-7.76 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ 75.4 (d), 129.0 (d), 129.1 (d), 129.4 (d), 130.4 (d), 131.4 (s), 134.7 (s), 137.1 (s), 140.6 (s), 197.4 (s).

4,4'-Dibromobenzoin[16] **(3f)**: ^{1}H NMR ($CDCl_3$): δ 4.52 (d, J = 5.5, 1 H), 5.85 (d, J = 5.5, 1 H), 7.12-7.20 (m, 2 H), 7.43-7.47 (m, 2 H), 7.52-7.57 (m, 2 H), 7.71-7.76 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ 75.5 (d), 122.9 (s), 129.3 (d), 129.5 (s), 130.4 (d), 131.8 (s), 132.1 (d), 132.3 (d), 137.5 (s), 197.5 (s).

4,4'-Dicyanobenzoin (3g): ^{1}H NMR ($CDCl_3$): δ 4.44 (d, J = 5.9, 1 H), 5.99 (d, J = 5.9, 1 H), 7.44 (d, J = 8.3, 2 H), 7.64 (d, J = 8.3, 2 H), 7.73 (d, J = 6.8, 2 H), 7.97 (d, J = 6.8, 2 H); ^{13}C NMR ($CDCl_3$): δ 76.0 (d), 113.0 (s), 117.3 (s), 117.6 (s), 118.0 (s), 128.3 (d), 129.3 (d), 132.7(d), 133.1 (d), 136.2 (s), 142.7 (s), 197.1 (s); IR ($CHCl_3$): 3472, 2978, 2402, 2235, 1729, 1691, 1521, 1478, 1230, 1207 cm^{-1}. Anal. Calcd. for $C_{16}H_{10}N_2O_2$ (262.3): C, 73.27; H, 3.84; N, 10.68; Found: C, 73.00; H: 3.77; N, 10.66.

2,2'-Dichlorobenzoin[34] **(3i)**: ^{1}H NMR ($CDCl_3$): δ 5.61 (s, 1 H), 6.35 (s, 1 H), 7.17-7.26 (m, 8 H).

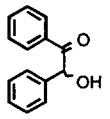
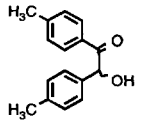
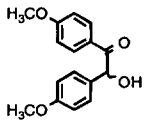
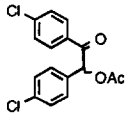
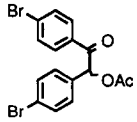
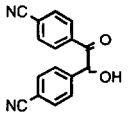
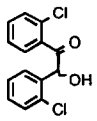
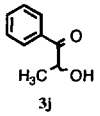
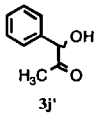
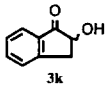
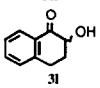
2-Hydroxy-1-phenyl-1-propanone[17] **(3j)**: ^{1}H NMR ($CDCl_3$): δ 1.45 (d, J = 7.0, 3 H), 3.59 (br.s, 1 H, OH), 5.16 (q, J = 7.0, 1 H), 7.46-7.62 (m, 3 H), 7.90-7.94 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ 22.3 (q), 69.3 (d), 128.6 (d), 128.8 (d), 133.3 (s), 134.0 (d), 202.3 (s).

1-Hydroxy-1-phenyl-2-propanone[17] **(3j')**: ^{1}H NMR ($CDCl_3$): δ 2.08 (s, 3 H), 3.60 (br.s, 1 H, OH), 5.09 (s, 1 H), 7.26-7.42 (m, 5 H); ^{13}C NMR ($CDCl_3$): δ 25.2 (q), 80.1 (d), 127.3 (d), 128.7 (d), 129.0 (d), 137.9 (s), 207.1 (s).

2-Hydroxy-indan-1-one[17] **(3k)**: ^{1}H NMR ($CDCl_3$): δ 3.01 (d-d, J_1 = 16.6, J_2 = 5.0, 1 H), 2.04 (br.s, 1 H, OH), 3.58 (d,d, J_1 = 16.6, J_2 = 7.8, 1 H), 4.55 (d,d, J_1 = 7.8, J_2 = 5.0, 1 H), 7.37-7.55 (m, 2 H), 7.60-7.68 (m, 1 H), 7.77 (d, J = 7.7, 1 H); ^{13}C NMR ($CDCl_3$): δ 35.1 (t), 74.3 (d), 124.5 (d), 126.8 (d), 128.0 (d), 134.0 (s), 135.9 (d), 150.9 (s), 206.5 (s).

2-Hydroxy-3,4-dihydro-2*H*-naphthalen-1-one[17] **(3l):** ^{1}H NMR ($CDCl_3$): δ 2.03 (m, 1 H), 2.52 (m, 1 H), 3.01 (m, 1 H), 3.14 (m, 1 H), 3.96 (br. s, 1 H, OH), 4.37 (d-d, J_1 = 13.4, J_2 = 5.5, 1 H), 7.26-8.04 (m, 4 H).

Table 1. HPLC Conditions and Retention Times for the Enantiomers of the α-Hydroxy Ketones **3**[a]

3	eluent	flow rate (mL/min)	UV detection (nm)	Rt (min)	config	Rt (min)	config
 **3a**	90:10 n-hexane / 2-propanol	0.6	220	22.4	*S*(+)	32.2	*R*(-)
 **3b**	95:5 n-hexane / 2-propanol	0.6	220	22.7	*S*(+)	30.2	*R*(-)
 **3c**	90:10 n-hexane / 2-propanol	0.6	220	16.2	*S*(+)	20.2	*R*(-)
 **3d**	95:5 n-hexane / 2-propanol	0.6	220	26.4	*S*(+)	28.7	*R*(-)
 (ref 35)	90:10 n-hexane / 2-propanol	0.5	254	13.6	*R*(-)[b]	15.5	*S*(+)[b]
 (ref 36)	90:10 n-hexane / 2-propanol	0.5	254	17.4	*R*(-)[b]	20.4	*S*(+)[b]
 **3g**	80:20 n-hexane / ethanol	0.5	254	36.4	*R*(+)[c]	39.1	*S*(-)[c]
 **3i**	90:10 n-hexane / 2-propanol	0.5	220	27.5	*S*(+)[c]	36.1	*R*(-)[c]
 **3j**	90:10 n-hexane / 2-propanol	0.6	220	12.8	*S*(-)	14.3	*R*(+)
 **3j'**	90:10 n-hexane / 2-propanol	0.6	220	16.9	*S*(+)	19.3	*R*(-)
 **3k**	90:10 n-hexane / 2-propanol	0.5[d]	220	30.5	*R*(-)	43.9	*S*(+)
 **3l**	90:10 n-hexane / 2-propanol	0.5[d]	220	25.9	*R*(+)	31.6	*S*(-)

[a]On a Chiralcel OD-H column, unless otherwise indicated. [b]Assigned according to the configuration of the corresponding α-hydroxy ketone. [c]Tentatively assigned. [d]On a Chiralcel OB-H column.

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