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Synthesis and Antimicrobial Activity of Hydroxyalkyl- and Hydroxyacyl-phenols and Their Benzyl Ethers☆

New phenolic compounds with hydrophilic side chains were prepared from 4-benzyloxybenzaldehyde and alkenyl magnesium bromides, followed by Sharpless dihydroxylation and hydrogenolytic removal of the benzyl group. The resulting compounds were tested in an agar diffusion assay against gram positive bacteria, gram negative bacteria, and against the fungi *Candida glabrata* and *Aspergillus niger.*

Keywords: Sharpless dihydroxylation; Antimicrobial activity; Hydroxyphenyl carbinols

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Introduction

Since 1867 phenols have been a well-known class of antimicrobial substances [1]. Derivatives of phenol, for instance thymol, and chlorophenol, are used as antiseptics, disinfectants, and preservatives. Alkyl substituents often increase the efficieny of antiseptic activity [2]. On the other hand, many natural products with antibiotic and antimycotic activity contain hydrophilic side chains, as do the new class of bengazoles [3].

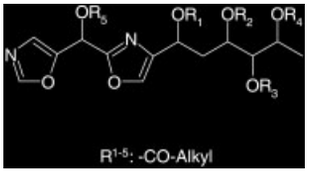

Figure 1

Hybrids of the two classes might be new potent phenolic antiseptics. Up to now, no phenolic derivatives with bengazole-type side chains have been synthesized and tested.

Investigations, results, and discussion

Following up this idea, 4-benzyloxybenzaldehyde (**1**) was subjected to Grignard reaction with vinyl-, allyl-, but-3-enyl-, pent-4-enyl-, and hex-5-enyl-magnesium bromide to give the racemic secondary alcohols **2** in good yields.

On the one hand, three of these racemic alcohols were hydrogenated with Pd/C to remove the benzyl protecting group. In the course of this reaction the double bond was also hydrogenated. One side reaction led to the alkylphenols **6**. The antimicrobial activity of the resulting (±)-hydroxyalkylphenols **3** was to be compared with the new more complex phenolic derivatives described below.

On the other hand, the double bond was dihydroxylated in a Sharpless dihydroxylation reaction [4] with α-AD mix ($(K_4[Fe(CN)_6]$, OsO_4, Na_2CO_3, $(DHQ)_2$-PHAL) to give the resulting (±)-dihydroxyketones **4**. The α-AD mix dihydroxylated the double bond and the secondary alcohol function was oxidised in the same reaction. The oxidation of the secondary alcohol depended on the presence of a surplus of α-AD mix. Under these conditions the α-AD mix showed no enantioselectivity. The resulting (±)-ketones were debenzylated to give the phenols **5** with trihydroxy side chain. During the hydrogenolysis of the protecting group the ketones were again reduced to the secondary alcohols, yielding diastereomeric mixtures of **5**.

The resulting compounds were tested in an agar diffusion assay (100 µg/disc) for their effects on the gram positive bacterium *Staphylococcus hominis,* the gram negative bacterium *Escherichia coli,* and the fungi *Aspergillus niger* and *Candida glabara* [5]. The potency of the substances was compared with the effects of clotrimazole (50 µg/disc) and tetracycline (50 µg/disc). Only the phenol ethers **2a**, **4a–e** showed poor activity against gram positive bacteria, gram negative bacteria, and the fungus *Aspergillus niger.*

Summing up, we could show that a bengazole-like side chain was not able to increase the antibiotic and antimycotic activity of phenols.

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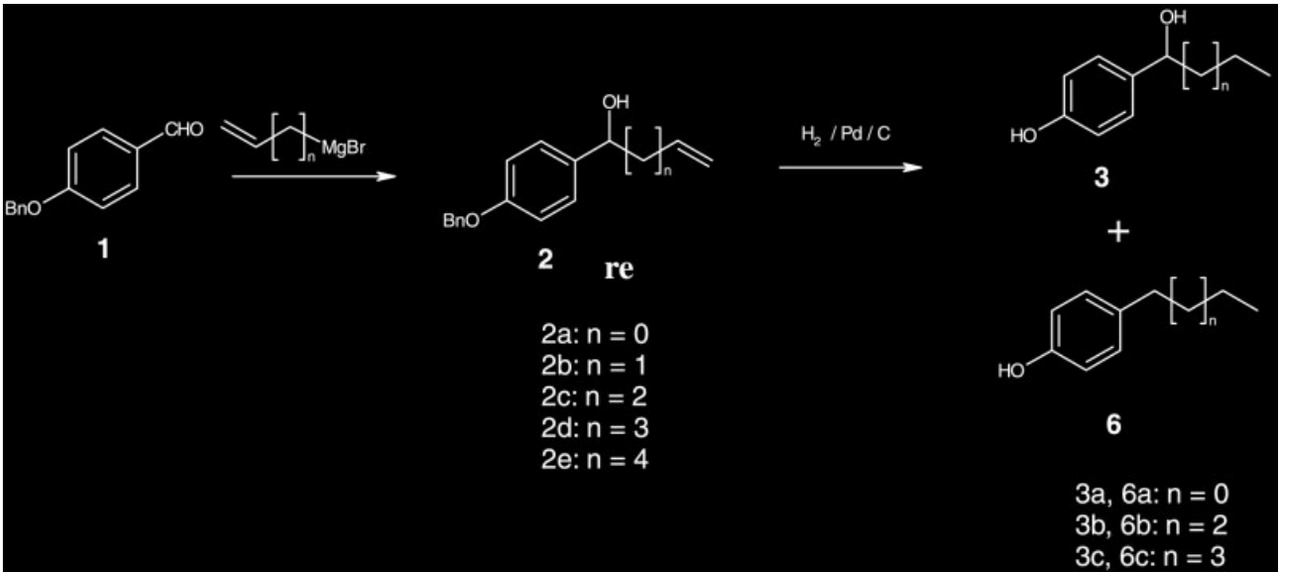

Figure 2

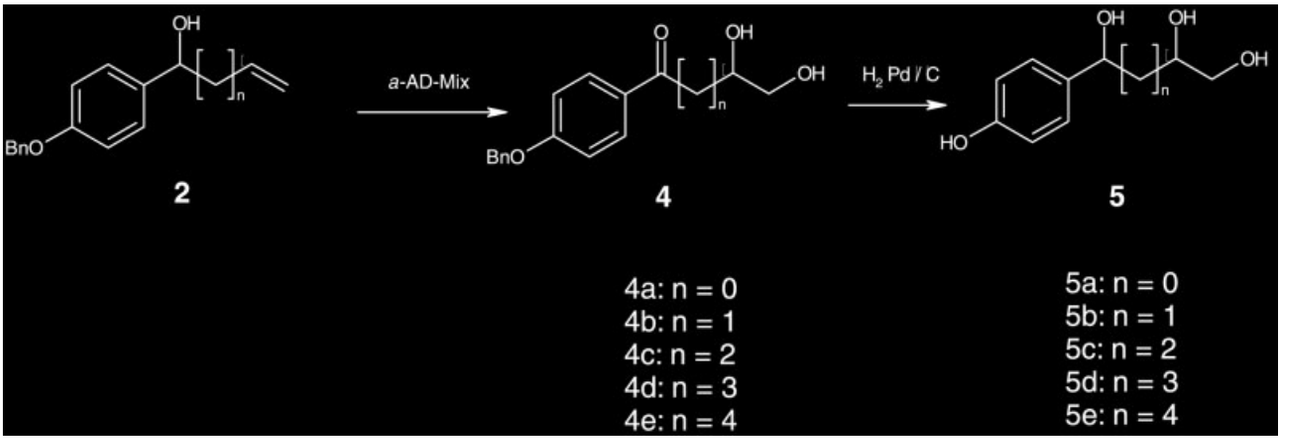

Figure 3

Table 1. Antimicrobial activity in the agar diffusion assay (substances: 100 µg/disk, references: 50 µg/disk (Cl: clotrimazole, Te: tetracycline), zone of inhibition: diameter in mm).

Microorganism	**2a**	**2b**	**2c**	**2d**	**2e**	**3a**	**3b**	**3c**	**4a**	**4b**	**4c**	**4d**	**4e**	**5a**	**5b**	**5c**	**5d**	**5e**	**Cl**	**Te**
Aspergillus niger	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	20	0
Candida glabrata	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	35	0
Escherichia coli	7	0	0	0	0	0	0	0	6	7	7	7	7	0	0	0	0	0	13	21
Staphylococcus hominis	8	0	0	6	6	0	0	0	6	6	6	6	6	0	0	0	0	0	10	21

Acknowledgement

We wish to thank Prof. Dr. Franz Bracher for kind support.

Experimental

Elemental analysis: Heraeus CHN-Rapid, IR Spectra: Perkin-Elmer FT-IR Paragon 1000, MS: Hewlett Packard MS-Engine; Electron ionisation (EI) 70 eV, chemical ionisation (CI) with CH_4 (300 eV); NMR (400 MHz): Jeol GSX 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz); Melting points: Büchi Melting Point B-540 (not corrected); flash column chromatography (FCC): silica gel 60 (230–400 mesh, E. Merck, Darmstadt). The diastereomeric ratio was determined by ^{13}C-NMR.

(±)-4-Benzyloxyphenylalkenols **2a–e**

Magnesium (14.0 mmol) was suspended in 5 mL dry THF, then 5 mL of a solution of alkenyl bromide (10.5 mmol) in dry THF was added. After stirring for one hour the suspension was heated under reflux for one hour. The solution of the Grignard reagent was taken up in a syringe and it was added to a solution of 1.5 g (7 mmol) 4-benzyloxybenzaldehyde (**1**) in 5 mL dry THF. The mixture was stirred for two hours and heated for one hour under reflux. Then the mixture was quenched with 10 mL saturated aqueous NH_4Cl solution and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated. The residue was purified by FCC (hexane/ethyl acetate 4:1).

(±)-1-(4-Benzyloxyphenyl)propenol (**2a**)

From 1.5 g (7.0 mmol) 4-benzyloxybenzaldehyde (**1**) and 1.3 g (10.5 mmol) vinyl bromide. Yield: 1.1 g (65%) as a white solid, mp: 60.3 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm): = 1.97 (s, 1H, OH), 5.05 (s, 2H, CH_2), 5.14 (d, *J* = 6 Hz, 1H, CH), 5.18 (ddd, *J* = 11.0 Hz, *J* = 1.5 Hz, *J* = 1.5 Hz, 1H, HC=), 5.32 (ddd, *J* = 17.0 Hz, *J* = 1.5 Hz , *J* = 1.5 Hz, 1H, HC=), 6.03 (ddd, *J* = 6.0, Hz, *J* = 11.0 Hz, *J* = 17.0 Hz, 1H, –CH=), 7.0 (d, *J* = 8.0 Hz, 2H, aromat. CH), 7.3 (d, *J* = 8.0 Hz, 2H, aromat. CH), 7.31–7.44 (m, 5H, aromat. CH). ^{13}C-NMR ($CDCl_3$), δ (ppm) = 70.14 (CH_2), 74.96 (CH), 114.88 (H_2C=), 115.00 (2 aromat. CH), 127.53 (2 aromat. CH), 127.79 (2 aromat. CH), 128.06 (2 aromat. CH), 128.68 (aromat. CH), 135.20 (quart. C), 137.04 (quart. C), 140.43 (CH=), 158.51 (quart. C). MS (EI): *m/z* (%) = 240 (M+, 100), 185 (30), 149 (60). IR (KBr) ν (cm^{-1}) = 3349, 2909, 1638, 1611, 1511, 1421, 1248, 1170, 848, 745. Calcd.: C: 79.97 H: 6.71 Found: C: 80.32 H: 6.88. $C_{16}H_{16}O_2$ (240.3)

(±)-1-(4-Benzyloxyphenyl)but-3-enol (**2b**)

From 1.5 g (7.0 mmol) 4-benzyloxybenzaldehyde (**1**) and 9.0 mL commercially available allylmagnesium bromide solution (1 M in THF). Yield: 1.3 g (75%) as a white solid, mp: 68.4 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 2.49 (ddd, *J* = 7.0 Hz, *J* = 7.0 Hz, *J* = 1.3 Hz, 2H, CH_2), 4.67 (dt, *J* = 6.4 Hz, *J* = 2.1 Hz, 1H, CH), 5.06 (s, 2H, CH_2O), 5.10–5.18 (m, 2H, H_2C=), 5.80 (ddt, *J* = 7.0 Hz, *J* = 10.0 Hz, *J* = 17.2 Hz, 1H, –CH=), 6.96 (d, *J* = 8.6 Hz, 2H, aromat. CH), 7.28 (d, *J* = 8.6 Hz, 2H, aromat. CH), 7.29–7.45 (m, 5H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 43.85 (CH_2), 70.11 (CH_2O), 73.05 (CH), 114.82 (2 aromat. CH), 118.28 (=CH_2), 127.19 (2 aromat. CH), 127.55 (2 aromat. CH), 128.04 (aromat. CH), 128.68 (2 aromat. CH), 134.73 (–CH=), 140.43, (quart. C), 141.04 (quart. C), 162.27 (quart. C). MS (CI) *m/z* = 255 (M^+ + 1, 2), 237 (100), 213 (20), 185 (15), 147 (21). IR (NaCl film) ν cm^{-1}) = 3321, 3073, 2937, 1640, 1610, 1584, 1512, 1454, 1386, 1333, 1301, 1243, 1174, 1016, 908, 862. Calcd.: C: 80.28 H: 7.13 Found: C: 80.36 H: 7.13. $C_{17}H_{18}O_2$ (254.3).

(±)-1-(4-Benzyloxyphenyl)pent-4-enol (**2c**)

From 1.5 g (7.0 mmol) 4-benzyloxybenzaldehyde (**1**) and 1.4 g (10.5 mmol) but-3-enyl bromide. Yield: 1.03 g (55%) as a white solid, mp: 62.8 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 1.70–1.96 (m, 2H, CH_2), 2.03–2.19 (m, 2H, CH_2), 4.65 (m, 1H, CH), 4.95–5.08 (m, 2H, =CH_2), 5.07 (s, 2H, CH_2O), 5.84 (ddt, *J* = 2.4 Hz, *J* = 14.8 Hz, *J* = 27.2 Hz, 1H, –CH=), 6.96 (d, *J* = 9.3 Hz, 2H, aromat. CH), 7.27 (d, *J* = 9.3 Hz, 2H, aromat. CH), 7.34–7.43 (m, 5H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 30.23 (CH_2), 38.06 (CH_2), 70.12 (CH_2O), 73.74 (CH), 114.87 (2 aromat. CH), 114.94 (H_2C=), 127.26 (2 aromat. CH), 127.55 (2 aromat. CH), 128.06 (aromat. CH), 128.68 (2 aromat. CH), 132.06 (quart. C), 137.10 (–CH=), 138.30 (quart. C), 158.37 (quart. C). MS (CI) *m/z* = 267 (M^- – 1, 7), 251 (100), 213 (20), 185 (15), 161 (25). IR (KBr) ν (cm^{-1}) = 3335, 2933, 1684, 1605, 1509, 1465, 1454, 1362, 1242, 1005, 825, 700. Calcd.: C: 80.56 H: 7.51 Found: C: 80.13 H: 7.44. $C_{18}H_{20}O_2$ (268.4).

(±)-1-(4-Benzyloxyphenyl)hex-5-enol (**2d**)

From 1.5 g (7.0 mmol) 4-benzyloxybenzaldehyde (**1**) and 1.6 g (10.5 mmol) pent-4-enyl bromide. Yield: 1.28 g (65%) as a white solid, mp: 62.8 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 1.35–1.49 (m, 2H, CH_2), 1.64–1.85 (m, 2H, CH_2), 2.06 (m, 2H, CH_2), 4.61 (m, 1H, CH), 4.93–5.01 (m, 2H, =CH_2), 5.06 (s, 2H, CH_2), 5.77 (m, 1H, –CH=), 6.95 (d, *J* = 8.6 Hz, 2H, aromat. CH), 7.25 (d, *J* = 8.6 Hz, 2H, aromat. CH), 7.30–7.43 (m, 5H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 25.24 (CH_2), 33.68 (CH_2), 38.46 (CH_2), 70.12 (CH_2O), 74.22 (CH), 114.76 (=CH_2), 114.80 (2 aromat. CH), 127.24 (2 aromat. CH), 127.56 (2 aromat. CH), 128.06 (aromat. CH), 128.68 (2 aromat. CH), 137.07 (quart. C), 137.31 (quart. C), 138.68 (–CH=), 158.33 (quart. C). MS (CI) *m/z* = 283 (M^+ + 1, 5), 265 (100), 213 (10), 185 (15), 175 (15). IR (KBr) ν (cm^{-1}) = 3309, 3063, 2915, 2860, 1600, 1519, 1240, 1020, 840, 700. Calcd.: C: 80.28 H: 7.13 Found: C: 80.56 H: 7.05. $C_{19}H_{22}O_2$ (282.4).

(±)-1-(4-Benzyloxyphenyl)hept-6-enol (**2e**)

From 1.5 g (7.0 mmol) 4-benzyloxybenzaldehyde (**1**) and 1.7 g (10.5 mmol) hex-5-enyl bromide. Yield: 1.45 g (70%) as a white solid, mp: 51 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 1.20–1.75 (m, 4H, CH_2), 1.81 (m, 2H, CH_2), 2.04 (m, 2H, CH_2), 4.60 (m, 1H, CH), 4.95 (m, 2H, =CH_2), 5.06 (s, 2H, CH_2O), 5.78 (m, 1H, –CH=), 6.95 (d, *J* = 8.8 Hz, 2H, aromat. CH), 7.25 (d, *J* = 8.8 Hz, 2H, aromat. CH), 7.27–7.45 (m, 5H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 25.38 (CH_2), 28.78 (CH_2), 33.66 (CH_2), 38.77 (CH_2), 70.00 (CH_2O), 74.19 (CH), 114.34 (H_2C=), 114.72 (2 aromat. CH), 127.13 (2 aromat. CH), 127.44 (2 aromat. CH), 127.94 (aromat. CH), 128.56 (2 aromat. CH), 136.96 (quart. C), 137.26 (quart. C), 138.84 (–CH=), 158.20 (quart. C). MS (EI) *m/z* = 296 (M^+, 2), 213 (35), 91 (100). IR (KBr) ν (cm^{-1}) = 3321, 2926, 2854, 1641, 1513, 1454, 1241, 1017, 743, 696. Calcd.: C: 81.04 H: 8.16 Found: C: 81.27 H: 8.16. $C_{20}H_{24}O_2$ (296.4).

(±)-4-Hydroxyphenylcarbinols **3a–c**

1.0 mmol of the 4-benzyloxyphenyl alcohol 2 was dissolved in 15 mL methanol and 20 mg Pd/C was added. The suspension was stirred under H_2 atmosphere for 10 hours. Then the catalyst was filtered off and the solvent was evaporated.

(±)-1-(4-Hydroxyphenyl)propanol (**3a**)

From 150 mg (0.6 mmol) of **2a**. Yield: 70 mg (77 %) as a colourless oil.

^{1}H-NMR (d_6-acetone) δ (ppm) = 0.77 (t, *J* = 7.4 Hz, CH_3), 1.61 (m, 1 H, CH_2), 1.71 (m, 1 H, CH_2), 4.40 (t, *J* = 6.8 Hz, 1 H, CH), 6.70 (d, *J* = 8.5 Hz, 2 H, aromat. CH), 7.05 (d, *J* = 8.5 Hz, 2 H, aromat. CH). ^{13}C-NMR (d_6-acetone) δ (ppm) = 10.21 (CH_3), 31.83 (CH_2), 75.44 (CH), 115.13 (2 aromat. CH), 127.05 (2 aromat. CH), 136.09 (quart. C), 156.12 (quart. C). All data were in full accordance with the values given in [8]. $C_9H_{12}O_2$ (152.19).

(±)-1-(4-Hydroxyphenyl)pentanol (**3b**)

From 150 mg (0.5 mmol) of **2c**. Yield: 65 mg (72 %) as a colourless oil.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 0.87 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.33 (m, 4 H, CH_2), 1.70 (m, 1 H, CH_2), 1.82 (m, 1 H, CH_2), 4.60 (t, *J* = 6.7 Hz, 1 H, CH), 6.77 (d, *J* = 8.6 Hz, 2 H, aromat. CH), 7.18 (d, *J* = 8.6 Hz, 2 H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 13.99 (CH_3), 22.54 (CH_2), 28.01 (CH_2), 38.43 (CH_2), 74.55 (CH), 115.45 (2 aromat. CH), 127.41 (2 aromat. CH), 136.55 (quart. C), 155.19 (quart. C). MS (EI) *m/z* = 180 (M^+, 5), 123 (100). Calcd.: C: 73.30 H: 8.95 Found: C: 72.95 H: 8.91. $C_{11}H_{16}O_2$ (180.25). All data were in full accordance with those given in [6].

(±)-1-(4-Hydroxyphenyl)hexanol (**3c**)

From 760 mg (2.7 mmol) of **2d**. Yield: 510 mg (96 %) as a colourless oil.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 0.88 (t, *J* = 8.2 Hz, 3 H, CH_3), 1.15–1.79 (m, 6 , CH_2), 4.53 (dd, *J* = 7.5 Hz, *J* = 13.5 Hz, 1 H, CH), 6.79 (d, *J* = 8.9 Hz, 2 H, aromat. CH), 7.18 (d, *J* = 8.9 Hz, 2 H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 14.32 (CH_3), 23.18 (CH_2), 39.66 (CH_2), 74.26 (CH), 115.71 (2 aromat. CH), 128.11 (2 aromat. CH), 137.54 (quart. C), 156.83 (quart. C). MS (EI) *m/z* = 176 (M^+ – 18, 15), 137 (40), 107 (100). IR (KBr) ν (cm^{-1}) = 3333, 3024, 2956, 2931, 1614, 1598, 1454, 1240, 1171, 1109, 1005, 949, 895. $C_{12}H_{18}O_2$ (194.28).

(±)-4-Benzyloxyphenyldihydroxyalkanones **4a**–**e**

1.0 mol of the alkene **2a**–**e** was dissolved in 20 mL of a mixture of *tert*-butanol and water (1:1) and 2.0 g α-AD mix were added. The suspension was cooled to 0 °C and stirred for 12 hours. Then it was quenched with 20 mL 10 % Na_2SO_3 solution and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were evaporated. The residue was purified by FCC (ethyl acetate).

(±)-1-(4-Benzyloxyphenyl)-2,3-dihydroxypropan-1-one (**4a**)

From 200 mg (0.8 mmol) of **2a** and 2.0 g α-AD mix. Yield: 140 mg (65 %) as a white solid, mp: 140.1 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 3.82 (dd, *J* = 5.1 Hz, *J* = 11.3 Hz, 1 H, CH), 3.96 (dd, *J* = 3.8 Hz, *J* = 11.3 Hz, 1 H, CH), 5.19 (m, 1 H, CH), 5.26 (m, 2 H, CH_2O), 7.09 (d, *J* = 8.9 Hz, 2 H, aromat. CH), 7.24–7.60 (m, 5 H, aromat. CH), 7.99 (d, *J* = 8.9 Hz, 2 H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 65.95 (CH_2O), 71.16 (CH_2O), 75.57 (CH), 115.88 (2 aromat. CH), 128.60 (2 aromat. CH), 129.09 (2 aromat. CH), 129.56 (aromat. CH), 132.06 (2 aromat. CH), 133.20 (quart. C), 164.60 (quart. C), 210.31 (CO). MS (CI) *m/z* = 273 (100), 243 (70), 211 (75). IR (KBr) ν (cm^{-1}) = 3376, 2925, 1672, 1605, 1575, 1509, 1453, 1381, 1244, 1176, 1122, 1056, 1019, 974. Calcd.: C: 70.58 H: 5.92 Found: C: 70.70 H: 6.17. $C_{16}H_{16}O_4$ (274.3).

(±)-1-(4-Benzyloxyphenyl)-3,4-dihydroxybutan-1-one (**4b**)

From 150 mg (0.6 mmol) of **2b** and 2.0 g α-AD mix. Yield: 100 mg (58 %) as a white solid mp: 90.0 °C.

^{1}H-NMR (d_4-methanol) δ (ppm) = 3.10 (d, *J* = 5.9 Hz, 2 H, CH_2), 3.55 (d, *J* = 5.9 Hz, 2 H, CH_2O), 4.22 (tt, *J* = 5.9 Hz, *J* = 5.9 Hz, 1 H, CH), 5.15 (s, 2 H, CH_2O), 7.06 (d, *J* = 8.8 Hz, 2 H, aromat. CH), 7.24–7.25 (m, 5 H, aromat. CH), 7.97 (d, *J* = 8.8 Hz, 2 H, aromat. CH). ^{13}C-NMR (d_4-methanol) δ (ppm) = 41.63 (CH_2), 65.59 (CH_2O), 69.84 (CH_2O), 68.97 (CH), 114.41 (2 aromat. CH), 127.48 (2 aromat. CH), 127.77 (aromat. CH), 127.98 (quart. C), 128.26 (2 aromat. CH), 130.74 (2 aromat. CH), 138.01 (quart. C), 164.37 (quart. C), 199.59 (CO). MS (CI) *m/z* = 287 (M^+ + 1, 20), 269 (40), 227 (100). IR (KBr) ν (cm^{-1}) = 3376, 2925, 1676, 1602, 1509, 1254, 1174, 1016, 821. Calcd.: C: 71.31 H: 6.34 Found: C: 70.97 H: 6.38 $C_{17}H_{18}O_4$ (286.3).

(±)-1-(4-Benzyloxyphenyl)-4,5-dihydroxypentan-1-one (**4c**)

From 200 mg (0.8 mmol) of **2c** and 2.0 g α-AD mix. Yield: 135 mg (57 %) as a white solid, mp: 80.1 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 1.20 (m, 2 H, CH_2), 1.81 (m, 2 H, CH_2), 3.06 (dd, 1 H, CH), 3.42 (dd, 1 H, CH), 3.59 (dd, 1 H, CH), 3.61 (m, 1 H, CH), 5.06 (s, 2 H, CH_2), 6.93 (d, *J* = 8.8 Hz, 2 H, aromat. CH), 7.19–7.35 (m, 5 H, aromat. CH), 7.89 (d, *J* = 8.8 Hz, 2 H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 27.17 (CH_2), 34.44 (CH_2), 66.81 (CH_2O), 70.15 (CH_2O), 71.73 (CH), 73.89 (CH), 74.38 (CH), 114.33 (2 aromat. CH), 127.01 (2 aromat. CH), 127.47 (2 aromat. CH), 128.26 (2 aromat. CH), 128.70 (aromat. CH), 131.99 (quart. C), 136.20 (quart. C), 162.99 (quart. C), 199.59 (CO). MS (CI) *m/z* (%) = 301 (M^+ + 1, 10), 283 (20), 91 (100). IR (KBr) ν (cm^{-1}) = 3364, 2925, 1676, 1601, 1509, 1454, 1379, 1302, 1254, 1168, 1016, 916, 862. Calcd.: C: 71.98 H: 7.71 Found: C: 71.88 H: 7.53. $C_{18}H_{20}O_4$ (300.4)

(±)-1-(4-Benzyloxyphenyl)-5,6-dihydroxyhexan-1-one (**4d**)

From 250 mg (1.3 mmol) of **2d** and 2.0 g α-AD mix. Yield: 175 mg (42 %) as a white solid: mp: 120.6 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 1.18 (m, 2 H, CH_2), 1.44 (m, 2 H, CH_2), 1.80 (m, 2 H, CH_2), 3.40 (dd, *J* = 11.2, Hz, *J* = 8.1 Hz, 1 H, CH), 3.59 (dd, *J* = 3.4 Hz, *J* = 11.2 Hz, 1 H, CH), 3.64 (m, 1 H, CH), 5.07 (s, 2 H, CH_2), 6.94 (d, *J* = 10.0 Hz, 2 H, aromat. CH), 7.23–7.38 (m, 5 H, aromat. CH), 7.88 (d, *J* = 10.0 Hz, 2 H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 19.81 (CH_2), 32.71 (CH_2), 37.76 (CH_2), 66.71 (CH_2O), 70.14 (CH_2O), 71.65 (CH), 114.61 (aromat. CH), 127.46 (aromat. CH), 128.25 (aromat. CH), 128.70 (aromat. CH), 130.35 (aromat. CH), 136.15 (quart. C), 162.67 (quart. C), 199.41 (CO). MS (CI): *m/z* (%) = 315 (M^+ + 1, 100), 297 (50), 249 (55). IR (NaCl film) ν (cm^{-1}) = 3289, 2923, 1675, 1602, 1508, 1455, 1413, 1377, 1303, 1253, 1172, 1109, 1051, 1009, 916. Calcd.: C: 72.59 H: 7.05 Found: C: 72.47 H: 7.52. $C_{19}H_{22}O_4$ (314.4).

(±)-1-(4-Benzyloxyphenyl)-6,7-dihydroxyheptan-1-one (**4e**)

From 500 mg (1.7 mmol) of **2e** and 2.0 g α AD mix. Yield: 510 mg (90 %) as a white solid mp: 145 °C.

^{1}H-NMR ($CDCl_3$) δ (ppm) = 1.24–1.75 (m, 6 H, CH_2), 2.88 (t, *J* = 7.1 Hz, 2 H, CH_2), 3.36 (m, 2 H, CH), 3.54 (m, 1 H, CH), 5.08 (s, 2 H, CH_2), 6.96 (d, *J* = 8.8 Hz, 2 H, aromat. CH), 7.36 (m, 5 H, aromat. CH), 7.89 (d, *J* = 8.8 Hz), 2 H, aromat. CH). ^{13}C-NMR ($CDCl_3$) δ (ppm) = 29.12 (CH_2), 30.23 (CH_2), 37.80 (CH_2), 43.78 (CH_2), 69.75 (CH_2O), 73.02 (CH_2O), 75.08 (CH), 117.74 (2 aromat. CH), 130.12 (2 aromat. CH), 130.46 (2 aromat. CH), 130.96 (aromat. CH), 131.57 (2 aromat. CH), 139.94 (quart. C), 140.20 (quart. C), 167.56 (quart. C), 204 (CO). MS (CI): *m/z* (%)

= 329 (M^+ + 1, 40), 313 (100), 213 (85). IR (NaCl film): ν (cm^{-1}) = 3367, 2935, 1677, 1600, 1510, 1454, 1377, 1240, 1173, 1015, 911. Calcd.: C: 73.15 H: 7.37 Found: C: 72.75 H: 7.38. $C_{20}H_{24}O_4$ (328.4).

4-Hydroxyphenylalkanetriol **5a–e**

0.5 mmol of the benzyloxy derivatives were dissolved in 15 mL methanol and 20 mg Pd/C was added. The suspension was stirred for 10 h under H_2 atmosphere. Then the catalyst was filtered off and the solvent was evaporated. The residue was purified by FCC (ethyl acetate/methanol).

1-(4-Hydroxyphenyl)propane-1,2,3-triol (diastereomeric mixture) (**5a**)

From 200 mg (0.7 mmol) of **4a**. Yield: 84 mg (65%) as a white solid.

^{1}H-NMR (d_3-acetonitrile) δ (ppm) = 3.42–3.73 (m, 3H, CH), 4.57 (d, *J* = 6.2 Hz, 1H, CH), 6.87 (d, *J* = 8.4 Hz, 2H, aromat. CH), 7.29 (d, *J* = 8.4 Hz, 2H, aromat. CH).

^{13}C-NMR (d_3-acetonitrile) δ (ppm) = 63.98 (CH_2O), 75.30 (CH), 75.70 (CH), 115.37 (2 aromat. CH), 128.93 (2 aromat. CH), 134.26 (quart. C), 156.91 (quart. C). MS (CI) *m*/*z* = 167 (M^+ + 1–18, 100), 149 (70), 107 (48). IR (NaCl film) ν (cm^{-1}) = 3358, 1613, 1514, 1449, 1238, 1027, 825, 530. Calcd.: C: 58.69 H: 6.57 Found: C: 58.94 H: 6.58. $C_9H_{12}O_4$ (184.2). Diastereomeric ratio: 1:1.

4-(4-Hydroxyphenyl)butane-1,2,4-triol (diastereomeric mixture) (**5b**)

From 80 mg (0.28 mmol) of **4b**. Yield: 20 mg (36%) as a yellow oil.

^{1}H-NMR (d_4-methanol) δ (ppm) = 1.71–1.90 (m, 2H, CH_2), 2.54–3.48 (m, 3H, CH, CH_2O), 4.68 (m, 1H, CH), 6.64 (m, 2H, aromat. CH), 7.09 (m, 2H, aromat. CH). ^{13}C-NMR (d_4-methanol) δ (ppm) = 42.81 (CH_2), 43.24 (CH_2), 66.92 (CH_2O), 67.38 (CH_2O), 70.34 (CH), 71.18 (CH), 71.60 (CH), 73.21 (CH), 116.01 (2 aromat. CH), 116.24 (2 aromat. CH), 128.06 (2 aromat. CH) 128.52 (2 aromat. CH), 136.74 (quart. C), 137,71 (quart. C), 157,61 (quart. C), 157,71 (quart. C). MS (CI) *m*/*z* = 181 (M + 1–18, 100)163 (55), 147 (55), 121 (85). IR (NaCl film) ν (cm^{-1}) = 3349, 2940, 1614, 1599, 1514, 1238, 1056, 835. Calcd.: C: 60.59 H: 7.12 Found: C: 60.41 H: 7.05. $C_{10}H_{14}O_4$ (198.2). Diastereomeric ratio: 1:1.3.

5-(4-Hydroxyphenyl)pentane-1,2,5-triol (diastereomeric mixture) (**5c**)

From 150 g (0.5 mmol) of **4c**. Yield: 67 mg (63%) as a colourless oil.

^{1}H-NMR (d_4-methanol) δ (ppm) = 1.2–1.93 (m, 4H, CH_2), 3.48 (m, 3H, CH, CH_2), 4.52 (m, 1H, CH), 6.83 (d, *J* = 8.8 Hz, 2H, aromat. CH), 7.89 (d, *J* = 8.8 Hz, 2H. aromat. CH). ^{13}C-NMR (d_4-methanol) δ (ppm) = 28.24 (CH_2), 34.20 (CH_2), 66.38 (CH_2O), 72.32 (CH), 74.11 (CH), 115.11 (2 aromat. CH), 127.38 (2 aromat. CH), 132.37 (quart. C), 162.73 (quart. C). Calcd.: C: 60.59 H: 7.12 Found: C: 60.37 H: 7.28. $C_{11}H_{16}O_4$ (212.2). Diastereomeric ratio: 1:1.

6-(4-Hydroxyphenyl)hexane-1,2,6-triol (diastereomeric mixture) (**5d**)

From 100 mg (0.3 mmol) of **4d**. Yield: 43 mg (60%) as a colourless oil.

^{1}H-NMR (d_4-methanol) δ (ppm) = 1.29 (m, 2H, CH_2), 1.40–1.69 (m, 2H, CH_2), 1.69–2.00 (m, 2H, CH_2), 3.51 (m, 2H, CH_2), 3.66 (m, 1H, CH), 6.88 (d, *J* = 8.8 Hz, 2H, aromat. CH), 7.92 (d, *J* = 8.8 Hz, 2H, aromat. CH). ^{13}C-NMR (d_4-methanol) δ (ppm) = 20.74 (CH_2), 32.62 (CH_2), 37.62 (CH_2), 66.24 (CH_2O), 71.86 (CH), 71.89 (CH), 73.61 (CH), 114.93 (2 aromat. CH), 128.69 (quart. C), 130.52 (2 aromat. CH), 162.43 (quart. C). MS (CI) *m*/*z* = (225, M^- – 1, 100), 207 (55). Calcd.: C: 63.70 H: 8.02 Found: C: 64.00 H: 8.00. $C_{12}H_{18}O_4$ (226.3). Diastereomeric ratio: 1:1.

7-(4-Hydroxyphenyl)hepane-1,2,7-triol (diastereomeric mixture) (**5e**)

From 200 mg (0.6 mmol) of **4e**. Yield: 110 mg (75%) as a colourless oil.

^{1}H-NMR (d_6-acetone) δ (ppm) = 1.15–1.39 (m, 6H, CH_2), 1.40–1.70 (m, 2H, CH_2), 3.32 (dd, *J* = 6.8 Hz, *J* = 10.8 Hz, 1H, CH), 3.41 (dd, *J* = 4.1 Hz, *J* = 10.8 Hz, 1H, CH), 3.52 (m, 1H, CH), 4.49 (t, *J* = 7.2 Hz, 1H, CH), 5.55 (s, 1H, OH), 6.73 (d, *J* = 8.5 Hz, 2H, aromat. CH), 7.11 (d, *J* = 8.5 Hz, 2H, aromat. CH). ^{13}C-NMR (d_6-acetone) δ (ppm) = 25.53 (CH_2), 26.00 (CH_2), 33.46 (CH_2), 39.61 (CH_2), 66.52 (CH_2O), 71.84 (CH), 73.23 (CH), 114.86 (2 aromat. CH), 127.14 (2 aromat. CH), 137.12 (quart. C), 156.35 (quart. C). MS (CI) *m*/*z* = (223, M^+ – 17,100), 187 (20), 107 (60). IR (NaCl film) ν (cm^{-1}) = 3320, 2924, 2854, 1597, 1512, 1454, 1245, 1164, 1066, 828, 735, 698. Calcd.: C: 64.98 H: 8.39 Found: C: 64.64 H: 8.83. $C_{13}H_{20}O_4$ (240.3). Diastereomeric ratio: 1:1.

References

☆ Dedicated to Prof. Dr. E. Reimann on occasion of his 65th birthday.

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