Supporting Information

“Alkenes as Ketol Surrogates – A New Approach Towards Enantiopure Acyloins“

Bernd Plietker*

Organische Chemie II, Fachbereich Chemie,

Universität Dortmund,

Otto-Hahn-Str. 6, D-44221 Dortmund.

e-mail: plietker@pop.uni-dortmund.de

General Remarks. Ethyl acetate was purified by distillation over CaCl_2 prior to use. RuCl_3 was obtained from Aldrich. A stock solution (0.1 M) was prepared calculating with $\text{RuCl}_3(\text{H}_2\text{O})_2$ and dissolving the catalyst (2.44 g, 10 mmol) in 100 mL water. The deep brown solution can be stored on the bench for weeks without loss of activity. Flash-chromatography was done on silica 60 (230-400 mesh) using head pressure by means of compressed air. Infrared spectra (IR) were recorded as a thin film between KBr-plates. The instrument used was a Bruker IFS 66 FT-IR spectrophotometer. Proton (^1H NMR, 400 MHz) and carbon (^{13}C NMR, 100.6 MHz) nuclear magnetic resonance spectra were recorded in chloroform(d -1) and referenced to the solvent signal. The instrument used was a Bruker DRX 400.

General Procedure for the asymmetric dihydroxylation. A 50 mL round-bottomed flask equipped with a magnetic stirring bar was charged with 5.6 g AD-mix- α and methanesulfonylamide (380 mg, 4 mmol). *tert*-Butanol (20 mL) and water (20 mL) was added and the slurry was stirred at room temperature until all solids dissolved. The orange solution was cooled to 0 °C. The olefin (4 mmol) was added in one portion. The mixture was kept at 0 °C with vigorous stirring until TLC showed complete conversion. Sat. Na_2SO_3 -solution (20 mL) was added and the reaction was allowed to warm up within 1 h. Phases were separated, the aqueous layer was extracted with ethyl acetate (3 x 40 mL). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuum. The resulting crude product was further purified via flash-chromatography.

(5*S*,6*S*)-Decane-5,6-diol (6).^[1] (563 mg, 3.24 mmol, 81 %). Colourless solid. m.p. 50 °C. *R*_f. 0.56 (5:1 pentane / ethyl acetate). HPLC (bisbenzoate, Chiralcel AD, heptane / 2-propanol (99.8 : 0.2), flow: 1mL/min, 215 nm): *t*₁ = 7.1, *t*₂ = 9.6). [α]_D (*c* 0.9, CHCl₃): +31.1. ¹H NMR (400 MHz, CDCl₃). δ 3.37-3.39 (m, 2*H*), 2.12 (s, 2*H*), 1.28-1.50 (m, 12*H*), 0.90 (t, *J* = 7.1 Hz, 6*H*) ppm. ¹³C NMR (100 MHz, CDCl₃). δ 74.5, 33.3, 27.7, 22.7, 14.1 ppm. IR (KBr). ν 3409 (s), 2954 (s), 2932 (s), 2858 (m), 1465 (m), 1147 (m), 1073 (m) cm⁻¹.

(1*S*,2*S*)-1,2-Diphenyl-ethane-1,2-diol (7).^[1] (762 mg, 3.56 mmol, 89 %). Colourless solid. m.p. 150 °C. *R*_f. 0.36 (3:1 pentane / ethyl acetate). HPLC (Chiralcel OJ, heptane / 2-propanol (90 : 10), flow: 1mL/min, 215 nm): *t*₁ = 14.9, *t*₂ = 16.8. [α]_D. 95.1 (*c* 1.1, EtOH). ¹H NMR (400 MHz, CDCl₃). δ 7.16-7.23 (m, 6*H*), 7.08-7.10 (m, 4*H*), 4.67 (s, 2*H*), 3.02 (s, 2*H*) ppm. ¹³C NMR (100 MHz, CDCl₃). δ 139.9, 128.0, 127.9, 127.0, 79.2 ppm. IR (KBr). ν 3499 (s), 3395 (s), 2895 (m), 1452 (m), 1198 (s), 1044 (s), 777 (s), 705 (s), 696 (s), 519 (m) cm⁻¹.

Acetic acid (2*S*,3*S*)-2,3-dihydroxy-3-phenyl-propyl ester (8).^[2] (496 mg, 2.36 mmol, 59 %). Colorless oil. *R*_f. 0.38 (1:1 pentane / ethyl acetate). HPLC (Chiralcel OD-H, heptane / 2-propanol (97 : 3), flow: 1mL/min, 215 nm): *t*₁ = 28.8, *t*₂ = 34.0. [α]_D. -75.6 (*c* 0.9, CHCl₃). ¹H-NMR (400 MHz, CDCl₃). δ 7.28-7.38 (m, 5*H*), 4.58 (d, *J* = 6.4 Hz, 1*H*), 4.04 (m, 1*H*), 3.91 (m, 2*H*), 2.86 (br. s., 2*H*), 2.02 (s, 3*H*). ¹³C-NMR (100 MHz, CDCl₃). δ 140.1, 128.8, 128.5, 127.2, 126.7, 74.6, 74.1, 65.3, 20.9 ppm. IR (film). ν 3418 (s), 3032 (w), 2900 (w), 1723 (s), 1381 (m), 1244 (s), 704 (s) cm⁻¹.

(1*S*,2*S*)-Chloro-1-phenyl-propane-1,2-diol (9).^[3] (634 mg, 3.40 mmol, 85 %). Colourless oil. *R*_f. 0.26 (3:1 pentane / ethyl acetate). HPLC (Chiralcel OD-H, heptane / 2-propanol (97 : 3), flow: 1mL/min, 215 nm): *t*₁ = 32.1, *t*₂ = 35.2. [α]_D. +3.1 (*c* 1.0, EtOH). ¹H NMR (400 MHz, CDCl₃). δ 7.31-7.37 (m, 5H), 4.69 (d, *J* = 6.8 Hz, 1*H*), 3.87 (ddd, *J* = 6.8, 5.6, 4.0 Hz, 1*H*), 3.53 (dd, *J* = 11.6, 4.0 Hz, 1*H*), 3.45 (dd, *J* = 11.6, 5.6 Hz, 1*H*) ppm. ¹³C NMR (100 MHz, CDCl₃). δ 139.9, 128.8, 128.6, 126.7, 75.5, 74.8, 46.2 ppm. IR (KBr). ν 3394 (s), 1454 (m), 1197 (m), 1058 (m), 764 (m), 702 (m) cm⁻¹.

(1*R*,2*S*)-1-Phenyl-3-(phenylsulfonyl)propane-1,2-diol (10).^[4] (1.09 g, 3.76 mmol, 94 %). White solid. m.p. 133 °C. *R*_f. 0.48 (3:2 pentane / ethyl acetate). HPLC (Chiralcel OD-H, heptane / 2-propanol (90 : 10), flow: 1mL/min, 215 nm): *t*₁ = 28.3, *t*₂ = 31.0. [α]_D. +15.0 (*c* 1.2, CHCl₃). ¹H-NMR (400 MHz, CDCl₃). δ 7.80-7.84 (m, 2*H*), 7.49-7.65 (m, 3*H*), 7.20-7.30 (m, 5*H*), 4.56 (d, *J* = 6.0 Hz, 1*H*), 4.24 (ddd, *J* = 9.4, 6.0, 2.0 Hz, 1*H*), 3.25 (dd, *J* = 14.6, 9.4 Hz, 1*H*), 3.21 (dd *J* = 14.6, 0.2 Hz, 1*H*), 2.60 (s, 2*H*) ppm. ¹³C-NMR (100 MHz, CDCl₃). δ 139.2, 139.0, 134.2, 129.5, 128.9, 128.7, 128.0, 126.9, 70.5, 58.8, 37.1 ppm. IR (KBr). ν 3521 (s), 3064 (w), 3028 (w), 2976 (w), 2942 (w), 2925 (w), 1168 (s), 1147 (m), 1084 (m) cm⁻¹.

(1*S*,2*S*)-3-Benzyloxy-1-phenyl-propane-1,2-diol (11).^[5] (836 mg, 3.24 mmol, 81 %). Colourless solid. m.p. 61 °C. *R*_f. 0.28 (3:1 pentane / ethyl acetate). HPLC (Chiralcel OJ, heptane / 2-propanol (95 : 5), flow: 1mL/min, 215 nm): *t*₁ = 56.2, *t*₂ = 75.9. [α]_D. -8.2 (*c* 1.1, CHCl₃). ¹H-NMR (400 MHz, CDCl₃). δ 7.31-7.36 (m, 10*H*), 4.72 (d, *J* = 5.5 Hz, 1*H*), 4.54 (d, *J* = 12.0 Hz, 1*H*), 4.47 (d, *J* = 12.0 Hz, 1*H*), 3.83 (m, 1*H*), 3.50 (dd, *J* = 9.5, 3 Hz, 1*H*),

3.42 (dd, $J = 9.5, 5.5$ Hz, $1H$), 3.11 (s, $1H$), 2.83 (s, $1H$) ppm. ^{13}C -NMR (100 MHz, $CDCl_3$). δ 141.9, 139.1, 130.0, 129.9, 129.5, 129.4, 129.3, 128.1, 76.3, 76.2, 75.1, 72.5 ppm. IR (KBr). ν 3415 (s), 3031 (w), 3030 (w), 2876 (w), 1495 (m), 1118 (s), 1026 (s), 737 (s), 700 (s) cm^{-1} .

General Procedure for the Mono Oxidation. A 100-mL round-bottomed flask equipped with magnetic stirring bar and overpressure valve was charged with $NaHCO_3$ (420 mg, 5.0 mmol). A 0.1 M aqueous solution of $RuCl_3$ (200 μ L, 0.02 mmol) was added and the suspension was diluted with 1.8 mL H_2O , 12 mL CH_3CN and 12 mL ethyl acetate. Oxone[®] (6.14 g, 10 mmol) was added in one portion to the resulting brownish suspension (gas evolution!). When the color turned bright yellow the diol (2 mmol) was added in one portion. The reaction was followed by TLC. After complete conversion the mixture was poured onto 30 mL sat. $NaHCO_3$ - and 30 mL sat. Na_2SO_3 -solution. Phases were separated and the aqueous layer was extracted with ethyl acetate (3 x 30 mL). After drying the combined organic layer over Na_2SO_4 and evaporation of the solvent in vacuum the oily crude product was purified by flash-chromatography.

1-Hydroxy-octan-2-one (2).^[6] (271 mg, 1.88 mmol, 94 %). Colorless oil. R_f 0.36 (5 : 1 pentane / ethyl acetate). 1H NMR (400 MHz, $CDCl_3$). δ 4.21 (s, $2H$), 3.14 (s, $1H$), 2.37 (t, $J = 7.6$ Hz, $2H$), 1.61 (m, $2H$), 1.21 – 1.38 (m, $6H$), 0.85 (t, $J = 6.8$ Hz, $3H$). ^{13}C NMR (100 MHz, $CDCl_3$). δ 210.0, 68.2, 38.5, 31.5, 28.9, 23.8, 22.5, 14.1. IR (film). ν 3426 (br), 2957 (s), 2930 (s), 2859 (s), 1722 (s), 1059 (m).

2-Hydroxy-1-phenyl-ethanone (12).^[7] (248 mg, 1.82 mmol, 91 %). White solid. m.p. 88 °C. R_f 0.57 (5:1 pentane / ethyl acetate). 1H NMR (400 MHz, $CDCl_3$). δ 7.92 (d, $2H$), 7.62 (dd, $1H$), 7.52 (dd, $2H$), 4.88 (s, $2H$), 3.52 (s, $1H$). ^{13}C NMR (100 MHz, $CDCl_3$). δ 199.8, 135.8, 134.8, 130.4, 129.2, 66.9. IR (KBr). ν 3430 (s), 3390 (s), 1683 (s), 1236 (m), 688 (m).

(S)-6-Hydroxy-decan-5-one (13).^[8] (306 mg, 1.78 mmol, 89 %). Colorless oil. R_f 0.52 (5:1 pentane / ethyl acetate). HPLC (Chiralcel OJ, heptane / 2-propanol (99.5 : 0.5), flow: 1mL/min, 205 nm): $t_1 = 7.7$, $t_2 = 8.3$. $[\alpha]_D +3.3$ (c 0.9, CHCl_3). ^1H NMR (400 MHz, CDCl_3). δ 4.16 (dd, $J = 5.6, 2.8$ Hz, 1H), 3.42 (s, 1H), 2.45 (m, 2H), 1.81 (m, 2H), 1.26 – 1.66 (m, 8H), 0.91 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3). δ 214.0, 77.8, 39.0, 34.9, 28.4, 23.9, 15.3, 15.2. IR (film). ν 3480 (br), 2958 (s), 2873 (m), 1712 (s), 1466 (m), 1045 (m).

(S)-2-Hydroxy-1,2-diphenyl-ethanone (14).^[9] (390 mg, 1.84 mmol, 92 %). White solid. m.p. 137 °C. R_f 0.57 (3:1 pentane / ethyl acetate). HPLC (Chiralcel OD, heptane / 2-propanol (90 : 10), flow: 1mL/min, 254 nm): $t_1 = 9.4$, $t_2 = 12.9$. $[\alpha]_D +117.0$ (c 1.0, acetone). ^1H NMR (400 MHz, CDCl_3). δ 7.92 (d, 2H), 7.27 – 7.56 (m, 8H), 5.92 (s, 1H), 4.56 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3). δ 200.4, 140.5, 135.4, 130.6, 130.5, 130.3, 130.2, 130.0, 129.2, 77.6. IR (KBr). ν 3379 (br), 2932 (w), 1679 (s), 1206 (m), 1092 (m), 755 (s), 704 (s), 511 (s).

Acetic acid (S)-2-hydroxy-3-oxo-3-phenyl-propyl ester (15).^[5] (370 mg, 1.78 mmol, 89 %). Colorless oil. R_f 0.52 (3:1 pentane / ethyl acetate). HPLC (Chiralcel OD-H, heptane / 2-propanol (97 : 3), flow: 1mL/min, 254 nm): $t_1 = 25.9$, $t_2 = 34.8$. $[\alpha]_D +6.7$ (c 1.2, CHCl_3). ^1H NMR (400 MHz, CDCl_3). δ 7.94 (dd, 2H), 7.62 (ddd, 1H), 7.49 (dd, 2H), 5.28 (dd, $J = 5.9, 3.2$ Hz, 1H), 4.53 (dd, $J = 11.6, 3.2$ Hz, 1H), 4.09 (dd, $J = 11.6, 5.9$ Hz, 1H), 3.93 (s, 1H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3). δ 198.5, 170.9, 134.6, 133.5, 129.2, 128.7, 72.1, 66.9, 30.2. IR (film). ν 3463 (br), 3064 (w), 2957 (w), 2856 (w), 1742 (s), 1688 (s), 1378 (m), 1235 (s), 1047 (m), 702 (m).

3-Chloro-(*S*)-2-hydroxy-1-phenylpropan-1-one (16). (325 mg, 1.76 mmol, 88 %). Colorless oil. R_f 0.59 (3:1 pentane / ethyl acetate). HPLC (Chiralcel OD-H, heptane / 2-propanol (97 : 3), flow: 1mL/min, 254 nm): $t_1 = 17.9$, $t_2 = 19.4$. $[\alpha]_D$. -2.5 (c 0.8, CHCl_3). ^1H NMR (400 MHz, CDCl_3). δ 7.91 (d, $J = 7.5$ Hz, 2H), 7.67 (t, $J = 7.5$ Hz, 1H), 7.54 (t, $J = 7.5$ Hz, 2H), 5.36 (t, $J = 3.5$ Hz, 1H), 4.05 (s, 1H), 3.94 (dd, $J = 11.5, 3.5$ Hz, 1H), 3.77 (dd, $J = 11.5, 3.5$ Hz, 1H), ^{13}C NMR (100 MHz, CDCl_3). δ 197.9, 134.5, 133.4, 129.2, 128.5, 72.6, 47.4. IR (film). ν 3455 (br), 1680 (s), 1598 (m), 1450 (m), 1293 (s), 1098 (s), 705 (m). HRMS; calc. for $[\text{C}_9\text{H}_9\text{O}_2\text{Cl}]$: 184.61926; found: 184.61935

(*S*)-2-Hydroxy-1-phenyl-3-(phenylsulfonyl)propan-1-one (17).^[10] (505 mg, 1.74 mmol, 87 %). Yellow oil. R_f 0.59 (5:1 pentane / ethyl acetate). HPLC (Chiralcel OD-H, heptane / 2-propanol (90 : 10), flow: 1.2 mL/min, 254 nm): $t_1 = 24.3$, $t_2 = 26.4$. $[\alpha]_D$. $+22.9$ (c 1.0, CHCl_3). ^1H NMR (400 MHz, CDCl_3). δ 7.95 (dd, 4H), 6.56 – 7.67 (m, 6H), 5.60 (dd, $J = 10.0, 1.2$ Hz, 1H), 3.57 (dd, $J = 14.8, 1.2$ Hz, 1H), 3.29 (dd, $J = 14.8, 10.0$ Hz, 1H), 2.95 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3). δ 236.3, 197.4, 139.6, 134.9, 134.2, 132.3, 129.4, 129.1, 128.5, 68.7, 61.2. IR (KBr). ν 3451 (br), 3064 (m), 1694 (s), 1692 (s), 1310 (s), 1151 (m), 1024 (m), 737 (m).

3-Benzyloxy-(*S*)-2-hydroxy-1-phenylpropan-1-one (18). (389 mg, 1.52 mmol, 76 %). White solid. m.p. 39 °C. R_f 0.51 (3 : 1 pentane / ethyl acetate). HPLC (Chiralcel OJ, heptane / 2-propanol (95 : 5), flow: 1mL/min, 215 nm): $t_1 = 56.2$, $t_2 = 75.9$. $[\alpha]_D$. $+21.9$ (c 1.6, CHCl_3). ^1H NMR (400 MHz, CDCl_3). δ 7.90 (d, $J = 7.5$ Hz, 2H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.49 (t, $J = 7.5$ Hz, 2H), 7.27-7.36 (m, 1H), 7.22 (m, 2H), 7.13 (m, 2H), 5.21 (t, $J = 4$ Hz, 1H), 4.51 (d, J

= 12.5 Hz, 1H), 4.44 (d, J = 12.5 Hz, 1H), 3.81 (dd, J = 10.5, 4 Hz, 1H), 3.76 (dd, J = 10.5, 4 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3). δ 199.7, 137.8, 134.1, 129.0, 128.8, 128.5, 128.2, 127.8, 127.7, 73.9, 73.7, 72.8. IR (KBr). ν 3464 (br), 3062 (m), 3030 (m), 2864 (m), 1685 (s), 1452 (s), 1235 (s), 1104 (s), 740 (m), 699 (s). HRMS; calc. for $[\text{C}_{16}\text{H}_{16}\text{O}_3]$: 256.10995; found: 256.10987.

Literature:

- [1] C. Döbler, G. M. Mehlretter, U. Sundermeier, M. Beller, *J. Am. Chem. Soc.* **2000**, *122*, 10289.
- [2] E. N. Jacobsen, I. Marko, W. S. Mungall, G. Schröder, K. B. Sharpless, *J. Am. Chem. Soc.* **1988**, *110*, 1968.
- [3] K. P. M. Vanhessche, Z.-M. Wang, K. B. Sharpless, *Tetrahedron Lett.* **1994**, *35*, 3469.
- [4] P. Duppau, R. Epple, A. A. Thomas, V. V. Fokin, K. B. Sharpless, *Adv. Synth. Catal.* **2002**, *344*, 421.
- [5] T. K. M. Shing, E. K. W. Tam, V. W.-F. Tai, I. H. F. Chung, Q. Jiang, *Chem. Eur. J.* **1996**, *2*, 50.
- [6] Y. Tamura, T. Yakura, J.-I. Haruta, Y. Kita, *Tetrahedron Lett.* **1985**, *26*, 3837.
- [7] B.-S. Koo, C. K. Lee, K.-J. Lee, *Synth. Commun.* **2002**, *32*, 2115.
- [8] N. S. Srinivasan, D. G. Lee, *Synthesis* **1979**, 520.
- [9] P. M. Cullis, G. Lowe, *J. Chem. Soc., Perkin Trans. I* **1981**, 2317.
- [10] B. Plietker, *J. Org. Chem.* **2003**, *68*, 7123.

7