Asymmetric Organocatalytic Epoxidation of α,β -Unsaturated Aldehydes with Hydrogen Peroxide

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Supporting Information

Contents:

- Experimental Section

General. The ^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm relative to CHCl_3 ($\delta = 7.26$) for ^1H NMR and relative to the central CDCl_3 resonance ($\delta = 77.0$) for ^{13}C NMR. Flash chromatography (FC) was carried out using Merck silica gel 60 (230-400 mesh). Optical rotation was measured on a Perkin-Elmer 241 polarimeter. NMR data of known compounds is in agreement with literature values.

Materials. Aldehydes **1a**, **1e-f**, and **1h-j** are commercially available and used as received. The organocatalyst **3** were prepared according to the published procedure.¹ Substrates **1b-d**² and **1g**³ were synthesized according to literature procedures. All solvents were of p. a. quality and used without further purification.

General Procedure for the Organocatalytic Epoxidation of α,β -Unsaturated Aldehydes. The catalyst (0.05 mmol, 10 mol %) was added at ambient temperature to a solution of the aldehyde (0.5 mmol) in CH_2Cl_2 (1.0 mL) followed by the addition of 35% H_2O_2 (aq.) (63 mg, 0.65 mmol, 1.3 equiv.). After 4 hours of reaction time the crude reaction mixture was passed through a silica gel FC column (ether/pentane) to give oxirane-2-carbaldehyde.

General Procedure for the NaBH_4 Reduction of Oxirane-2-Carbaldehyde. The crude reaction mixture, from the epoxidation of α,β -unsaturated aldehydes described above, was diluted with MeOH (1.0 mL) and cooled to 0 °C followed by addition of NaBH_4 (19 mg, 0.5 mmol). The mixture was then stirred for 10 min, quenched with sat. NH_4Cl and extracted with Et_2O . The organic layer was separated, dried over Na_2SO_4 and the solvent was removed. The crude product was purified by silica gel FC column (ether/pentane).

(2S,3R)-3-Phenyl-oxirane-2-carbaldehyde (2a): The title compound was prepared according to the general procedure described above. The spectroscopic data were in agreement with literature values.⁴ The ee was determined by GC on a Chrompak CP-Chirasil Dex CB-column. Temperature program: from 70 °C to 160° C at a rate of 10° C/min. R_t (min): 9.0 (major enantiomer); 9.1 (minor enantiomer). The absolute configuration was determined by optical rotation and compared with literature values.⁴ $[\alpha]^{25}_{\text{D}} -20.4$ ($c = 0.55$, CHCl_3).

(2S,3R)-3-(2-Nitro-phenyl)-oxirane-2-carbaldehyde (2b): The title compound was prepared according to the general procedure described above. ^1H NMR δ 9.30 (d, 1H, $J = 6.0$ Hz), 8.21 (dd, 1H, $J = 8.2, 1.4$ Hz), 7.82 (dd, 1H, $J = 8.2, 1.4$ Hz), 7.71 (dd, 1H, $J = 7.4, 1.5$ Hz), 7.68 (dd, 1H, $J = 8.2, 1.4$ Hz), 4.81 (d, 1H, $J = 2.1$ Hz), 3.32 (dd, 1H, $J = 6.0, 2.1$ Hz). ^{13}C NMR δ 194.3, 147.2, 133.2, 130.0, 128.1, 125.6, 123.6, 59.9, 53.7. The ee was determined after NaBH_4 reduction to the primary alcohol by HPLC on Daicel Chiralpak OJ and AS columns coupled in series, with hexane/*i*-PrOH (85:15) as the eluent: R_t (min): 26.4 (major enantiomer); 45.0 (minor enantiomer). $[\alpha]_D^{25} -29.7$ ($c = 1.3$, CHCl_3).

(2S,3R)-3-(2-Tolyl)-oxirane-2-carbaldehyde (2c): The title compound was prepared according to the general procedure described above. ^1H NMR δ 9.46 (d, 1H, $J = 6.0$ Hz), 7.44 (m, 4H), 4.53 (d, 1H, $J = 1.8$ Hz), 3.55 (dd, 1H, $J = 6.0, 1.8$ Hz), 2.60 (s, 3H). ^{13}C NMR δ 197.2, 136.2, 132.5, 130.1, 128.6, 126.4, 124.2, 62.0, 54.8, 18.7. The ee was determined after NaBH_4 reduction to the primary alcohol by HPLC on Daicel Chiralpak OJ and AS columns coupled in series, with hexane/*i*-PrOH (95:5) as the eluent: R_t (min): 24.8 (major enantiomer); 29.1 (minor enantiomer). $[\alpha]_D^{25} -160$ ($c = 1.0$, CHCl_3).

(2S,3R)-3-(4-Chloro-phenyl)-oxirane-2-carbaldehyde (2d): The title compound was prepared according to the general procedure described above. ^1H NMR δ 9.18 (d, 1H, $J = 6.0$ Hz), 7.35 (d, 2H, $J = 8.4$ Hz), 7.22 (d, 2H, $J = 8.4$ Hz), 4.15 (d, 1H, $J = 1.9$ Hz), 3.39 (dd, 1H, $J = 6.0, 1.9$ Hz). ^{13}C NMR δ 196.8, 135.3, 133.0, 129.3 (2C), 127.3 (2C), 63.1, 56.3. The ee was determined after NaBH_4 reduction to the primary alcohol by HPLC on Daicel Chiralpak OJ with hexane/*i*-PrOH (99:1) as the eluent: R_t (min): 54.6 (major enantiomer); 64.9 (minor enantiomer). $[\alpha]_D^{25} -37$ ($c = 1.0$, CHCl_3).

(2S,3R)-3-Ethyl-oxirane-2-carbaldehyde (2e): The title compound was prepared according to the general procedure described above. The ee was determined by GC on a Chrompak CP-Chirasil Dex CB-column. Temperature program: from 70 $^{\circ}\text{C}$ to 150 $^{\circ}\text{C}$ at a rate of 10 $^{\circ}\text{C}/\text{min}$. R_t (min): 2.92 (major enantiomer); 3.01 (minor enantiomer). The yield was determined after NaBH_4 reduction to the primary alcohol and its spectroscopic data were in agreement with literature values.⁵

(2S,3R)-3-Isopropyl-oxirane-2-carbaldehyde (2f): The title compound was prepared according to the general procedure described above. ^1H NMR δ 9.02 (d, 1H, J = 6.3 Hz), 3.18 (dd, 1H, J = 6.3, 1.8 Hz), 3.05 (dd, 1H, J = 6.7, 1.9 Hz), 2.60 (app. octet, 1H, J = 6.7 Hz), 1.07 (d, 1H, J = 6.7 Hz), 0.99 (d, 1H, J = 6.7 Hz). ^{13}C NMR δ 198.6, 61.7, 58.1, 29.9, 18.9, 18.0. The ee was determined by GC on a Chropak CP-Chirasil Dex CB-column. Temperature program: from 70 °C to 100° C at a rate of 10° C/min. R_t (min): 3.72 (major enantiomer); 3.80 (minor enantiomer). $[\alpha]^{25}_{\text{D}}$ -42 (c = 1.0, CHCl_3).

(2S,3R)-3-Benzyloxymethyl-oxirane-2-carbaldehyde (2g): The title compound was prepared according to the general procedure described above. The spectroscopic data were in agreement with literature values.⁶ The ee was determined by GC on a Chropak CP-Chirasil Dex CB-column. Temperature program: from 100 °C to 160° C at a rate of 10° C/min, isotherm for 10 min. R_t (min): 11.7 (major enantiomer); 11.8 (minor enantiomer). The absolute configuration was determined by optical rotation and compared with literature values, $[\alpha]^{25}_{\text{D}}$ -34.7 (c = 1.0, CHCl_3).⁶

(2S,3S)-3-Formyl-oxirane-2-carboxylic acid ethyl ester (2h): The title compound was prepared according to the general procedure described above. ^1H NMR δ 9.05 (d, 1H, J = 6.3 Hz), 4.23 (m, 2H), 3.75 (d, 1H, J = 1.8 Hz), 3.75 (dd, 1H, J = 6.8, 1.8 Hz), 1.34 (t, 3H, J = 7.3 Hz). ^{13}C NMR δ 195.0, 166.1, 62.6, 57.5, 50.8, 14.0. The ee was determined by GC on a Chropak CP-Chirasil Dex CB-column. Temperature program: from 70° C to 85° C at a rate of 5° C/min, isotherm for 20 min. R_t (min): 17.1 (major enantiomer); 19.6 (minor enantiomer). $[\alpha]^{25}_{\text{D}}$ -33 (c = 0.7, CHCl_3).

(2S)-3,3-Dimethyl-oxirane-2-carbaldehyde (2i): The title compound was prepared according to the general procedure described above. After NaBH_4 reduction and esterification of the corresponding alcohol with *p*-nitro-benzoylchloride the ee was determined by HPLC on Daicel Chiralpak AD column with hexane/*i*-PrOH (90:10) as the eluent: R_t (min): 13.8 (major enantiomer); 12.4 (minor enantiomer). The absolute configuration was determined by optical rotation and compared with literature values, $[\alpha]^{25}_{\text{D}}$ +6.6 (c = 0.48, CHCl_3).⁷ The yield was

determined after NaBH₄ reduction to the primary alcohol and its spectroscopic data were in agreement with literature values.⁸

3-Methyl-3-(4-methyl-pent-3-enyl)-oxirane-2-carbaldehyde (2j): The title compound was prepared according to the general procedure described above. The spectroscopic data were in agreement with literature values.⁹ The ee was determined after NaBH₄ reduction to the primary alcohol by HPLC on Daicel Chiralpak AS column with hexane/*i*-PrOH (98:2) as the eluent: R_t major diastereoisomer (min): 17.4 (major enantiomer); 12.6 (minor enantiomer); R_t minor diastereoisomer (min): 11.5 (major enantiomer); 19.5 (minor enantiomer).

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