SUPPORTING INFORMATION

Double Parallel Dynamic Resolution through Lipase-Catalyzed Asymmetric Transformation

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Table of contents

General methods

Reagents were obtained from commercial suppliers and used as received. Lipase PS "Amano" IM (EC 3.1.1.3) was purchased from Amano Enzyme Inc. ^{1}H and ^{13}C NMR data were recorded on a Bruker Avance 400 (100) MHz and/or a Bruker Avance 500 (125) MHz, respectively. Chemical shifts are reported as δ values (ppm) with $CDCl_3$ (^{1}H NMR δ7.26, ^{13}C NMR δ77.0) as an internal standard. *J* values are given in Hertz (Hz). Analytical high performance liquid chromatography (HPLC) with chiral stationary phase was performed on an HP-Agilent 1110 Series controller and a UV detector, using a Daicel Chiralpak OJ column (4.6 × 250 mm, 10 µm). Solvents for HPLC use were of spectrometric grade. Thin layer chromatography (TLC) was performed on precoated Polygram® SIL G/UV 254 silica plates (0.20 mm, Macherey-Nagel), visualized with UV-detection. Flash column chromatography was performed on silica gel 60, 0.040-0.063 mm (SDS).

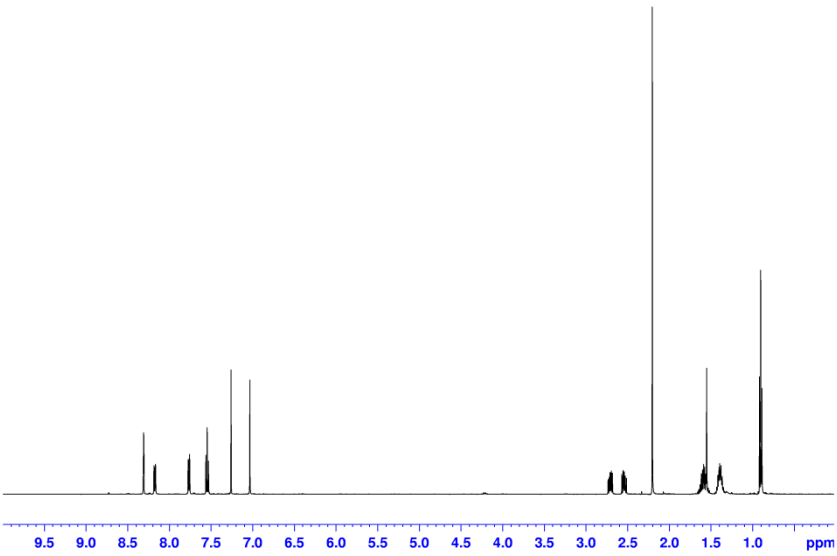
Generation of dynamic systems and lipase-catalyzed asymmetric transformation

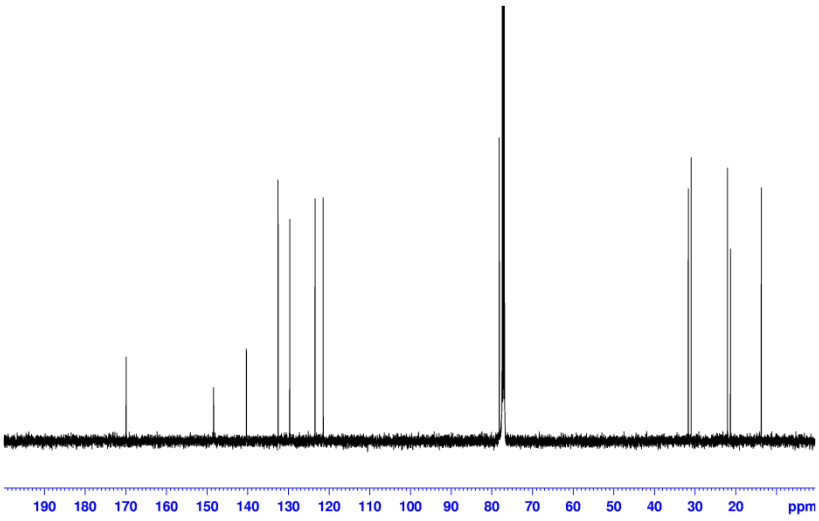
The dynamic systems were generated by adding 1 equiv of each aldehyde (**1**, **2** and **3**, 0.1 mmol), together with 1 equiv of 2-nitropropane **A** (0.1 mmol), 1-butanethiol **B** (0.1 mmol) and TEA (0.5 mmol) in the specific dry solvent (0.6 mL). After addition of phenyl acetate (3 equiv, 0.3 mmol), the solution was transferred to a 1.5 mL sealed-cap vial containing PS-IM and ground 4 Å molecular sieves (20 mg), dried for 2 days before use, under argon atmosphere at RT or 0 °C. ^{1}H NMR was used to follow the reaction process until completion. For complex systems, work-up and column purification were necessary before chiral analysis. The reaction mixture was filtered to remove PS-IM, and the solvent removed by evaporation. The crude product was dissolved in CH_2Cl_2, and the solution was extracted with water and brine. Drying over $MgSO_4$, filtration and evaporation provided a yellow oil, which was purified by flash column chromatography using hexanes/EtOAc (25:1, v/v) as eluent. For similar systems but with only one aldehyde as starting material, the crude reaction mixtures were directly sampled and analyzed by ^{1}H NMR and HPLC.

Synthesis of racemic compound 4B

3-nitrobenzaldehyde **1** (30.2 mg, 0.2 mmol) was dissolved in CH_2Cl_2 (0.6 mL), after which 1-butanethiol (21.6 µL, 0.24 mmol), TEA (83.4 µL, 0.6 mmol) and acetic anhydride (56.7 µL, 0.6 mmol) were added to the solution. The reaction mixture was stirred at RT for 2 d. After neutralization with 1M HCl solution, the reaction solution was extracted with CH_2Cl_2 (2 mL × 3), dried over $MgSO_4$, filtered, and the solvent evaporated under vacuum. The crude product was further purified using column chromatography (hexane/EtOAc, 10:1 (v/v)) providing compound **4B** (10.6 mg) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$, 25 ^{o}C) δ 0.90 (t, J=7.4, H, CH_3), 1.39 (m, 2H, CH_2), 1.59 (m, 2H, CH_2), 2.20 (s, 3H, CH_3), 2.54 (m, 1H, CH_2), 2.71 (m, 1H, CH_2), 7.03 (s, 1H, CH), 7.55 (t, J=7.9, 1H, CH), 7.77 (d, J=7.9, 1H, CH), 8.18 (d, J=7.9, 1H, CH), 8.30 (s, 1H, CH); ^{13}C NMR (125 MHz, $CDCl_3$, 25 ^{o}C) δ 13.7, 21.3, 22.0, 31.0, 31.7, 78.2, 121.5, 123.5, 129.7, 132.5, 140.4, 148.5, 169.9.

^{1}H NMR-, ^{13}C NMR-spectra of product **4B**

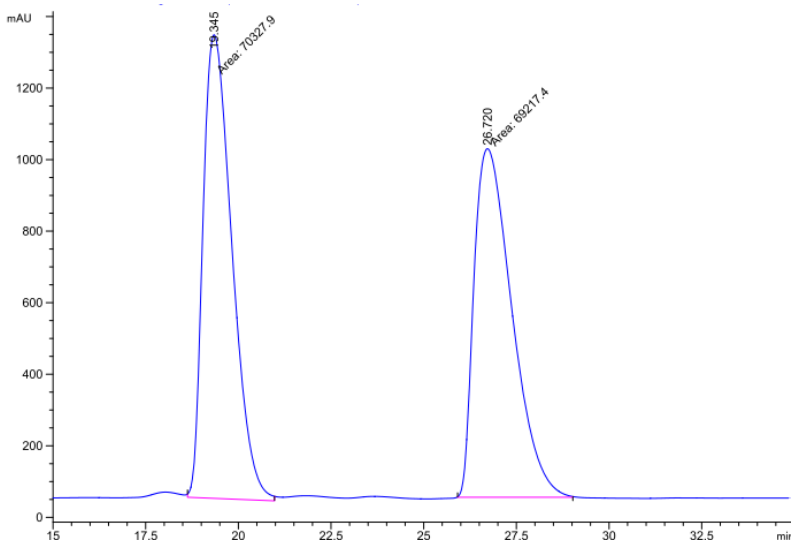




HPLC analyses

The enantiomeric purity of product **4B** from the dynamic systems was determined by analytical HPLC using a Daicel Chiralpak OJ column. Analyses were carried out at 298 K and 210 nm for 40 min, using hexane:^{i}PrOH (90:10, v/v) as mobile phase.

a) Racemic mixture of **4B.**



b) Product **4B** separated from dynamic system.