Supporting Information
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Supporting Information

Development of an amino acid/hydroxy oxime dual catalyst system for highly stereoselective direct asymmetric aldol reactions on water

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**General:** Infrared (IR) spectra were recorded on a Termo Fisher Nicolet 6700 FT-IR spectrometer, $\nu_{max}$ in cm$^{-1}$. Bands were characterized as broad (br), strong (s), medium (m), or weak (w). Melting Points were measured on Stuart SMP$_3$ Melting Point Apparatus (The temperature was not corrected). $^1$H NMR spectra were recorded on a Bruker Avance 500 (500 MHz) spectrometer. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance resulting from incomplete deuterium incorporation as the internal standard (CDCl$_3$: $\delta$ 7.26 ppm). Data were reported as follows: chemical shift, multiplicity ($s$ = singlet, $d$ = doublet, $q$ = quartet, br = broad, $m$ = multiplet), and coupling constants (Hz), integration. $^{13}$C NMR spectra were recorded on a Bruker Avance 500 (125.8 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl$_3$: $\delta$ 77.16 ppm). High-resolution mass spectrometry was performed on an Agilent 6520 Accurate-Mass Q-TOF LC/MS (positive mode). Optical rotations were measured on a Perkin-Elmer 341 Polarimeter ($d = 546$ nm, Hg lamp, $1$ dm cell). The enantiomeric excess was determined by Agilent 1260 infinity series HPLC (Chiral Technologies Chiralpak AS-H column (4.6 mm x 250 mm)) in comparison with authentic racemic materials. All the reactions were carried out under an atmosphere of air in a closed system. Chemicals and solvents were either purchased puriss p. A. from commercial suppliers or were purified by standard techniques. Aluminum sheet silica gel plates (Fluka 60 F254) were used for thin-layer chromatography (TLC), and the compounds were visualized by irradiation with UV light (254 nm) or by treatment with a solution of phosphomolybdic acid (25 g), Ce(SO$_4$)$_2$·H$_2$O (10 g), conc. H$_2$SO$_4$ (60 mL), and H$_2$O (940 mL), followed by heating. Purification of the product was carried out by flash column chromatography using silica gel (Fluka 60, particle size 0.040-0.063 mm).

**General procedure of the asymmetric aldol reaction for screening:** To a mixture of catalyst O-(tert-Butyldimethylsiloxy)-L-threonine 5g (5.83 mg, 0.025 mmol, 20 mol%, 0.2 equiv), oxime 6c (3.2 mg, 0.025 mmol, 20 mol%, 0.2 eq) and cyclohexanone 2 (0.128 mL, 1.25 mmol, 10 eq) were added 4-nitrobenzaldehyde 3 (18.87 mg, 0.125 mmol, 1 eq) and H$_2$O (0.128 mL). The mixture was vigorously stirred at room temp until completion of the reaction (monitored by crude NMR). Diastereoselectivity and conversion were determined from the $^1$H NMR of the crude analysis. The product was purified by silica gel column chromatography. (PE/EtOAc: 2:1) to give the pure aldol product 4 as a colourless oil (28.5 mg, 92% yield). The enantiomeric excess was determined by chiral phase-HPLC analysis.
(2S)-2-[(R)-hydroxy-(4-nitrophenyl)methyl] cyclohexanone 4\(^1\)

\[
\text{H NMR (500 MHz, CDCl}_3\text{): } \delta 8.21 (m, 2H), 7.50 (m, 2H), 4.89 (dd, } J=8.4, 3.1 \text{ Hz, 1H), 4.07 (d, } J=3.1 \text{ Hz, 1H), 2.59 (m, 1H), 2.47 (m, 1H), 2.37 (m, 1H), 2.12 (m, 1H), 1.83 (m, 1H), 1.67 (m, 1H), 1.56 (m, 2H), 1.38 (m, 1H); } ^{13}\text{C NMR (125.8MHz, CDCl}_3\text{): } \delta 214.7, 148.5, 147.5, 127.9, 123.5, 73.9, 57.2, 42.7, 30.8, 27.7, 24.7; R_f = 0.57 (PE:EtOAc = 2:1); [\alpha]^{20}_D = +12.6(c =1.00, CHCl_3) \text{ for an enantiomeric enriched sample (98% ee). From HPLC analysis enantiomeric purity was determined in comparison with authentic racemic material (AS column, 90/10 hexanes/i-PrOH, 1.0 mL/min, 254 nm); } t_r (\text{major enantiomer}) = 46.34 \text{ min, } t_r (\text{minor enantiomer}) = 56.53
\]

(3R,4S)-1,3-bis[(tert-butyl(dimethyl)silyl)oxy]-4-hydroxy-octadecan-2-one (9)

\[
\text{C}_{13}\text{H}_{27}\text{OH}OOTBS
\]

\[
\text{C}_{13}\text{H}_{27}\text{OH}OOTBS
\]

Colorless oil, yield 132mg (0.242 mmol, 55%); dr (Syn:anti) = 19:1; [\alpha]^{20}_D = +3.1^o (c = 1.0, CHCl_3); R_f = 0.41 (PE:EtOAc = 10:1); IR(neat): 2924 (s), 2853 (s), 1734 (C=O), 1463(m), 1388 (w), 1361(w), 1252(m), 1096(m), 1005(w), 938(w), 834(s), 776(s), 733(w), 674(w). \(^1\text{H NMR (500 MHz, CDCl}_3\text{): } \delta 4.50 (d, } J=18.4 \text{ Hz, 1H), 4.45 (d, } J=18.4 \text{ Hz, 1 H), 4.30 (d, } J=2.8 \text{ Hz, 1H), 3.77 (m, 1H), 2.16 (d, } J=9.8 \text{ Hz, 1H), 1.47 (m, 2H), 1.35-1.20 (m, 24H), 0.94 (s, 9H), 0.90 (s, 9H), 0.86 (t, } J=7.0 \text{ Hz, 3H), 0.09 (s, 9H), 0.06 (s, 3H). } ^{13}\text{C NMR(125.8 MHz, CDCl}_3\text{): } \delta 210.5, 79.2, 73.2, 68.6, 34.1, 32.1, 29.85, 29.84, 29.82, 29.79, 29.71, 29.6, 29.5, 25.99, 25.96, 25.89, 22.85, 18.6, 18.3, 14.2, -4.6, -4.9, -5.2, -5.3; HRMS (ESI\(^+\)) [M+H]\(^+\) Calcd for C\(_{30}\)H\(_{65}\)O\(_4\)Si\(_2\): 545.4416, found: 545.4420.
(3R,4S)-1,3,4-tris[(tert-butyl(dimethyl)silyl)oxy]octadecan-2-one (10)

Colourless oil, yield 118 mg (0.179 mmol, 90%); [α]$_D^{20}$ = -2.8° (c = 0.59, CHCl$_3$); R$_f$ = 0.43 (PE:EtOAc = 15:1); IR (neat): 2925 (s), 2854 (s), 1736 (C=O), 1471 (m), 1462 (m), 1361 (w), 1252 (m), 1111 (m), 1004 (w), 938 (w), 833 (s), 773 (s), 673 (w). $^1$H NMR (500 MHz, CDCl$_3$): δ 4.61 (d, $J$ = 18.9 Hz, 1H), 4.46 (d, $J$ = 18.9 Hz, 1H), 4.17 (d, $J$ = 3.3 Hz, 1H), 3.80 (m, 1H), 1.67 (m, 1H), 1.43-1.19 (m, 25H), 0.95 (s, 9H), 0.93 (s, 9H), 0.91 (s, 9H), 0.89 (t, $J$ = 6.7 Hz 3H), 0.15 (s, 3H), 0.09 (m, 9H), 0.05 (s, 3H), 0.04 (s, 3H). $^{13}$C NMR (125.8 MHz, CDCl$_3$): δ 208.7, 79.1, 75.0, 69.1, 34.3, 32.89, 32.09, 31.94, 29.86, 28.94, 29.82, 29.80, 29.73, 29.71, 29.69, 29.5, 26.1, 26.04, 26.0, 25.90, 25.85, 22.8, 18.7, 18.3, 14.3, -4.2, -4.4, -4.5, -4.9, -5.0, -5.2; HRMS (ESI$^+$) [M+H]$^+$ Calcd for C$_{36}$H$_{79}$O$_4$Si$_3$: 659.5281, found: 659.5283.

(2S,3S,4S)-N-benzyl-1,3,4-tris[(tert-butyl(dimethyl)silyl)oxy]octadecan-2-amine (11)

Colorless oil, yield 106 mg (0.141 mmol, 90%) as a. [α]$_D^{20}$ = -7.6° (c = 1.35, CHCl$_3$); R$_f$ = 0.22 (PE:EtOAc = 30:1); IR (neat): 3346 (br s), 2952 (m), 2925 (s), 2853 (s), 1462 (m), 1388 (w), 1360 (w), 1250 (s), 1089 (s), 1005 (w), 937 (w), 831 (s), 811 (m), 773 (s), 730 (w), 696 (w), 669 (w). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.33 (m, 2H), 7.29 (m, 2H), 7.20 (m, 1H), 3.88 (d, $J$ = 12.7 Hz, 1H), 3.84 (m, 1H), 3.73 (d, $J$ = 12.6 Hz, 1H), 3.69 (m, 1H), 3.62 (m, 2H), 2.81 (td, $J$ = 13.2, 6.6, 2.2 Hz, 1H), 1.61 (m, 1H), 1.41 (m, 1H), 1.35-1.20 (m, 25H), 0.90 (s, 9H), 0.88 (m, 12H), 0.80 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.06 (m, 6H), 0.05 (s, 3H), 0.03 (s, 3H); $^{13}$C NMR (125.8 MHz, CDCl$_3$): δ 141.4, 128.7, 128.3, 126.7, 76.3, 73.5, 64.5, 61.6, 53.4, 32.1, 31.5, 29.9, 29.86, 29.83, 29.76, 29.71, 29.5, 26.8, 26.2, 26.0, 25.9, 22.85, 18.5,
18.2, 18.0, 14.3, -3.7, -4.2, -4.4, -4.6, -4.9, -5.1; HRMS (ESI$^+$) [M+H]$^+$ Calcd for C$_{43}$H$_{88}$NO$_3$Si$_3$: 750.6067, found: 750.6070.

(2S,3S,4S)-2-Aminooctadecane-1,3,4-triol (D-lyx0-Phytosphingosine (1)$^4$

![Chemical Structure](image)

White solid, yield 36 mg (0.114 mmol, 64%); m.p. 106-107$^\circ$C (lit$^2$).104-105$^\circ$C, lit$^3$.104.5-105.5$^\circ$C ); $[\alpha]_D^{20} = -9.5 \quad (c = 0.96, \text{pyridine}) \quad \{\text{lit}^2[a]_D^{25} = -6.4 \quad (c = 1.0, \text{pyridine}) \}$; R$_f$ = 0.17 (CHCl$_3$: CH$_3$OH: NH$_4$OH = 30:10:1); IR(neat): 3346 (br s), 2922 (s), 2852 (m), 2360 (m), 2341 (w), 1733 (w), 1586 (w), 1464 (m), 1102 (s). $^1$H NMR (500 MHz, pyridine-$d_5$): δ 4.33 (m, 2H), 4.24 (m, 1H), 4.10 (m, 1H), 3.73 (m, 1H), 2.02 (m, 1H), 1.88 (m, 1H), 1.72 (m, 1H), 1.56 (m, 1H), 1.45-1.15 (m, 22H), 0.85 (t, $J = 6.3$ Hz, 3H). $^{13}$C NMR (125.28 MHz, pyridine-$d_5$): δ 74.4, 72.0, 64.2, 56.7, 34.6, 32.1, 30.2, 30.1, 30.0, 29.9, 29.6, 26.7, 22.9, 14.3; HRMS (ESI$^+$) [M+H]$^+$ Calcd for C$_{18}$H$_{40}$NO$_3$: 318.3003, found: 318.3005.

Reference:

$^1$H NMR spectrum of compound 4 in CDCl₃.
HPLC spectrum of compound 4 comparing with racemic.
$^1$H NMR spectrum of compound 9 in CDCl$_3$. 
$^{13}$C NMR spectrum of compound 9 in CDCl$_3$. 

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IR spectrum of compound 9 (neat)
$^1$H NMR spectrum of compound 10 in CDCl$_3$. 
$^{13}$C NMR spectrum of compound 10 in CDCl$_3$. 

![Diagram of the 13C NMR spectrum of compound 10 in CDCl$_3$.]
No search results for the selected spectrum!
$^1$H NMR spectrum of compound 11 in CDCl$_3$. 
$^{13}$C NMR spectrum of compound 11 in CDCl$_3$. 

![Image of 13C NMR spectrum]
No search results for the selected spectrum!
$^1$H NMR spectrum of compound 1 in pyridine-$d_5$. 
$^{13}$C NMR spectrum of compound 1 in pyridine-$d_5$. 
IR spectrum of compound 1 (neat).
Mass spectrum of compound 1

### Qualitative Compound Report

**Data File:** QH-mzML

**Sample Name:** QH-21-006

**Instrument Name:** Instrument 1

**Acq Method:** NA

**Comment:** NA

### Compound Table

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### MS Zoomed Spectrum

**Compound 1:** Scan (0.330-0.676 min, 10 Scans) GFM 0.00869 Subtract 360.25370 (M+H)

### MS Spectrum Peak List

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