Electronic Supplementary Material (ESI) for Chemical Science.

Highly Efficient Enantioselective Liquid Liquid Extraction of 1,2-Amino-Alcohols via SPINOL Based Phosphoric Acid Hosts.

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Contents

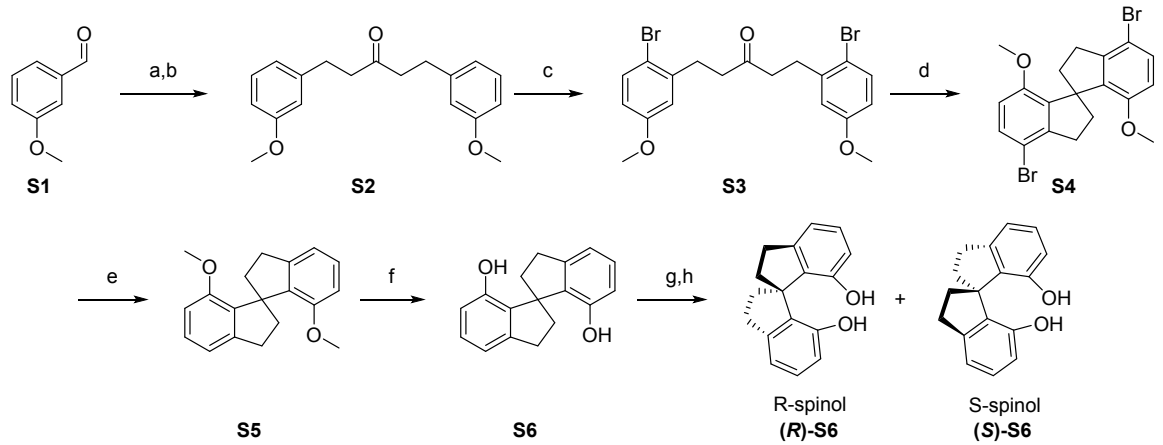
1. General info:

Chromatography: Merck silica gel type 9385 230-400 mesh, TLC: Merck silica gels 60, 0.25 mm. Conversions of the reactions were determined by TLC unless otherwise stated. Components were visualized by UV and potassium permanganate staining. Mass spectra were recorded on an AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+). ^{1}H- and ^{13}C-NMR were recorded on a Varian AMX400 (400 and 101 MHz, respectively) or a Varian VXR300 (300 and 75 MHz, respectively) using $CDCl_3$ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26 for ^{1}H, δ 77.0 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. All reactions were carried out under nitrogen or argon atmosphere in either oven dried round bottom flasks (gram scale or above) or oven dried sealed tubes (sub-gram scale) using standard Schlenk techniques. Diethyl ether, tetrahydrofuran, dichloromethane and toluene were used from the solvent purification system (MBRAUN SPS systems, MB-SPS-800). All catalysts, ligands, reagents and other solvents were purchased from commercial sources and used as received without further purification unless otherwise stated, except organo-lithium reagents which were titrated before use using diphenylacetic acid. When needed degassing of solvents was performed via the freeze, pump, thaw technique. SFC measurements were performed on a Waters Thar SFC system on a Chiralpak IA using as conditions 85% CO_2 / 15% CH_3OH, 150 bar, 4 mL/min. RP-HPLC measurements were performed on a Shimadzu SIL-20A with a CTO-20AC column oven and LC-20AD pumps on a CROWNPAK® CR(-) chiral column (Daicel, Japan) equipped with a guard column. Calibration curves were prepared in the concentration range employed for the determination of the distribution. Uncertainties were typically

lower than 2.0%. General HPLC conditions for enantiomeric separation of aryl-1,2- and aryl-2,1-amino alcohols: Perchloric acid solutions (pH =1,5 or pH =1) flow = 1.0 ml/min were used as eluent, with exception of serine (**8**), phenylalanine (**16**), homoserine (**17**), 3-amino-3-phenyl-1-propanol (**19**) and normethaneprhrine (**24**) where flow of 0,5 ml/min was applied. Column temperature was set at 20°C, with exception of 3-aminoisobuteric acid (**18**), where 0°C was applied.

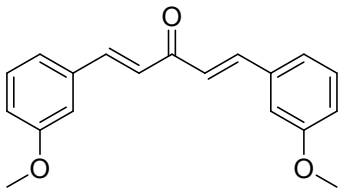
2. General synthetic route towards (*R*)- and (*S*)- 2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol (Spinol).

Spinol was synthetized as follows according to the method described by Birman *et al.*[1] with minor modifications, all spectroscopic data matching, and was resolved according to method described by Deng and Ye with minor modifications.[2]



Scheme 1: Synthetic route towards (*R*)- and (*S*)-spinol. Reaction conditions: a) Me_2CO, NaOH, 50% EtOH-H_2O, r.t, 60%. b) Raney Ni, H_2, Me_2CO, r.t 95% c) Br_2, pyridine, DCM, 0°C. 95% d) SiO2-SOOH, r.t, neat, 65%. e) ^nBuLi, THF, -78°C, 95%. f) BBr_3, DCM, -78°C, 85%. g) N-Benzylcinchonidinium chloride, toluene, reflux. h) HCl, (R)-spinol 90%, >99% ee, (S)-spinol 80%, >99% ee.

S1: 1,5-bis(3-methoxyphenyl)penta-1,4-dien-3-one



A solution of *m*-anisaldehyde (10.0 g, 73.4 mmol, 2 equiv) and acetone (2.70 ml, 36.8 mmol, 1 equiv) in ethanol (20 ml) was added dropwise to a solution of NaOH (7.5 g, 190 mmol, 2.5 equiv) in 120 ml

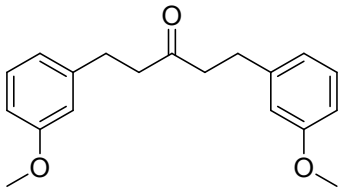
[1] V. B. Birman, A. L. Rheingold, K.-C. Lam, *Tet. Asym.* **1999**, *10*, 125-131.
[2] J.-H. Zhang, J. Liao, X. Cui, K.-B. Yu, J. Zhu, J.-G. Deng, S.-F. Zhu, L.-X. Wang, Q.-L. Zhou, L. W. Chung, T. Ye, *Tet. Asym.* **2002**, *13*, 1363-1366

of ethanol/H2O (1:1, 0.25 M) at 0 °C. The mixture was stirred for 3 h, then diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, and purified by FCC (PE/AcOEt, 9/1) to give 6.6 g of 1,5-bis(3-methoxyphenyl)pentan-3-one (62% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 16 Hz, 2H), 7.34 (t, *J* = 8 Hz, 2H), 7.22 (d, *J* = 8 Hz, 2H), 7.13 (s, 2H), 7.07 (d, *J* = 16 Hz, 2H), 6.97 (dd, *J* = 8, 2 Hz, 2H), 3.86 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 189.0, 160.0, 143.3, 136.2, 130.0, 125.7, 121.1, 116.4, 113.3, 55.4.

S2: 1,5-bis(3-methoxyphenyl)pentan-3-one

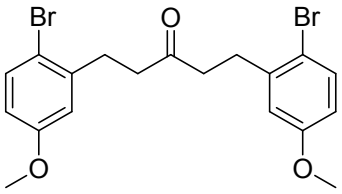


A solution of 1,5-bis(3-methoxyphenyl)penta-1,4-dien-3-one (20.0 g, 68 mmol, 1 equiv) in acetone (200 ml, 0.35 M) was stirred with Raney Ni (2 g) under an atmosphere of hydrogen at rt under very vigorous stirring (1500 rpm, large stir bar, formation of a big vortex) for 1h, if the stirring is not strong enough the reaction will take up to 48 h to complete. The suspension was filtered on celite (AcOEt) and concentrated under vacuum to give 19.65 g clean 1,5-bis(3-methoxyphenyl)pentan-3-one (95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (t, J = 8 Hz, 2H), 6.75-6.69 (m, 6H), 3.78 (s, 6H), 2.86 (t, *J* = 8 Hz, 4H), 2.71 (t, *J* = 8 Hz, 4H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 209.0, 159.6, 142.6, 129.4, 120.6, 114.1, 111.4, 55.1, 44.4, 29.8.

S3 1,5-bis(2-bromo-5-methoxyphenyl)pentan-3-one

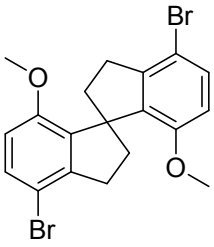


Crude 1,5-bis(3-methoxyphenyl)pentan-3-one (19.65 g, 66 mmol, 1 equiv) was dissolved in CH_2Cl_2 (220 ml, 0.3 M total), pyridine (15.95 ml, 198 mmol, 3 equiv.) was added, and the mixture was cooled to 0 °C. A solution of bromine in CH_2Cl_2 (10% v/v, 8.5 ml, 165 mmol, 2.5 equiv.) was added drop wise. The reaction mixture was allowed to warm to rt and stirred until the starting material had disappeared (by NMR, 3h). The mixture was diluted with DCM, washed with aqueous $NaHSO_3$ to remove excess bromine, then with HCl 1M and water, dried over Na_2SO_4 and concentrated under vacuum to give 30.5 g of 1,5-bis(2-bromo-5-methoxyphenyl)pentan-3-one (95% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 9 Hz, 2H), 6.77 (d, *J* = 3 Hz, 2H), 6.63 (dd, *J* = 9, 3 Hz, 2H), 3.78 (s, 6H), 2.96 (t, *J* = 8 Hz, 4H), 2.72 (t, J = 8 Hz, 4H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 208.6, 159.1, 141.3, 133.5, 116.3, 114.8, 113.8, 55.6, 42.7, 30.7.

S4: 4,4'-dibromo-7,7'-dimethoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]

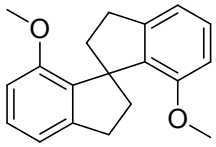


To a solution of 1,5-bis(2-bromo-5-methoxyphenyl)pentan-3-one (5g, 11.45 mmol, 1 equiv) in DCM (112ml, 0.1M) at 0°C was added 50g of silica-sulfuric acid.[3] The red suspension was evaporated to dryness at room temperature to avoid degradation of the substrate and left to stand for 3 hours after which the brownish solid was filtered over a pad of silica with DCM and concentrated *in vacuo*. The residue was which was recrystallized in hexane to yield to give 3.25g of 4,4'-dibromo-7,7'-dimethoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.6 Hz, 2H), 6.52 (d, *J* = 8.6 Hz, 2H), 3.52 (s, 6H), 3.14-2.84 (m,42H), 2.40-2.26 (m, 2H), 2.23-2.07 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 144.8, 138.0, 130.3, 110.8, 110.5, 61.9, 55.4, 55.4, 37.9, 33.2.

S5: 7,7'-dimethoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]



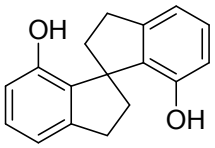
To a solution of crude 4,4'-dibromo-7,7'-dimethoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (7.5 g, 17.2 mmol, 1 equiv) in THF (170 ml, 0.1 M) cooled to -78 °C was added n-BuLi (1.6 M in hexanes, 45 ml, 68.8 mmol, 4 equiv) and stirred for 1 h. The reaction mixture was then quenched with 10 ml of ethanol and returned to r.t and most of the THF was removed under vacuum. The remaining solution was diluted in DCM and washed with water and dried over Na_2SO_4. The thus obtained 4.6g of 7,7'-dimethoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (96%) proved to be >95% pure by 1H-NMR and was used as such in the next, if needed it can be recrystallized in hexanes.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (t, *J* = 7.7 Hz, 2H), 6.87 (dd, *J* = 7.7 Hz, 2H), 6.63 (d, *J* = 8.1 Hz, 2H), 3.54 (s, 6H), 3.13-2.92 (m, 4H), 2.43-2.28 (m, 2H), 2.25-2.08 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 145.3, 136.8, 127.5, 116.7, 108.5, 59.1, 55.1, 55.1, 38.7, 31.5.

[3]M. A. Zolfigol, *Tetrahedron*,**2001**, *57*, 9509-9511

3: Spinol

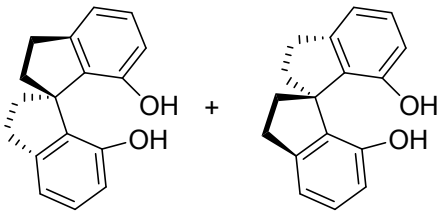


To a solution of 7,7'-dimethoxy-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (6.43 g, 23.0 mmol, 1 equiv) in DCM (115 ml, 0.2 M) cooled to -78 °C, is added slowly BBR_3 (neat, 5.0 ml, 52 mmol, 2.3 equiv)and the reaction mixture is slowly returned to room temperature overnight. The reaction mixture is then diluted with DCM and a few milliliters of water carefully added, when the excess of BBR_3 is quenched the mixture is washed with $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated under vacuum. The residue is purified by FCC (PE/AcOEt , 9/1) and if needed recrystallized from hexanes to give 4.9 g clean spinol (84%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18 (t, *J* = 7.7 Hz, 2H), 6.90 (dd, *J* = 7.4, 1.0 Hz, 2H), 6.68 (d, *J* = 8.1 Hz, 2H), 4.59 (brs, 2H), 3.34-2.89 (m, 4H), 2.43-2.26 (m, 2H), 2.26-2.12 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 153.0, 146.0, 130.6, 130.1, 117.9, 114.5, 57.6, 37.6, 31.4.

3': S/R-spinol



R-spinol S-spinol

To a solution of racemic spinol in toluene is added N-Benzylcinchonidinium chloride. The suspension is heated to reflux for 1.5 h and then returned to room temperature. The white solid is filtered on a sintered funnel to afford the S-spinol/ N-Benzylcinchonidinium chloride complex and the filtrate evaporated to afford R-spinol.

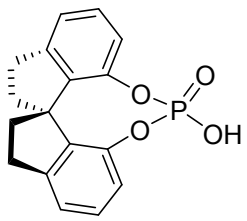
The complex is suspended in AcOEt and HCl 1M is added till the pH reaches 3 (stable over 5 minutes, going lower than pH 2 will cause degradation). The organic layer is separated, washed with brine, dried over Na_2SO_4, and concentrated under vacuum. The residue is filtered on a pad of silica (AcOEt) to remove any trace salts remaining, concentrated and recrystallized from hexanes to give pure (S)-(-)-spinol (78% yield, >99% ee).

The white solid obtained from the filtrate is filtered on a pad of silica (AcOEt) to remove any trace salts remaining, concentrated and recrystallized from hexanes to give pure (R)-(+)-spinol (68% yield, >99% ee).

3. Synthesis of Spinol based phosphoric acids

The following spinol based phosphoric acids and intermediates leading to these were synthesized according to the procedures reported by List et all.[4]

SPA 1: (S)-12-hydroxy-4,5,6,7-tetrahydrodiindeno[7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide



To a solution of (S)-spinol (50 mg, 0.20 mmol, 1 equiv) in pyridine (1.3 ml, 0.15 M) was added $POCl_3$ (56 µl, 0.6 mmol, 3 equiv). The mixture was then stirred for 6 hours before dioxane/water was added

[4] Müller, S. (2012). The Catalytic Asymmetric Fischer Indolization and Beyond. Thesis, Universitätsverlag, Köln.

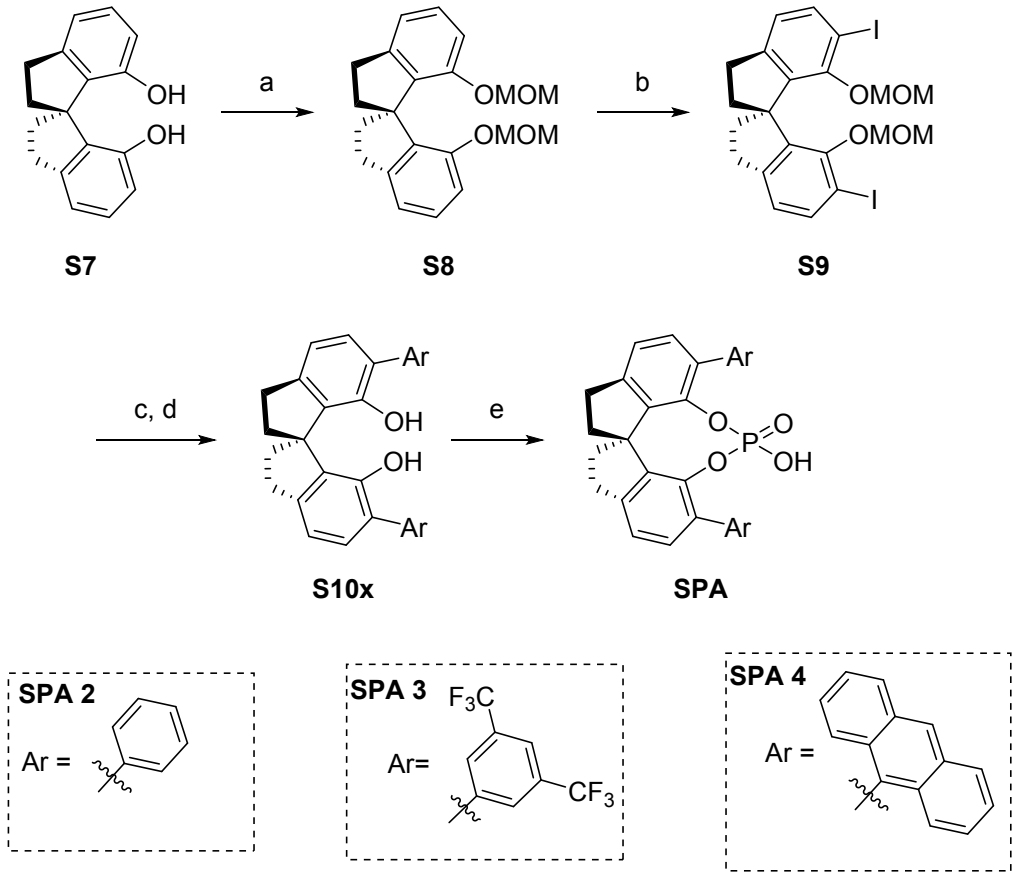
(4/1 V:V 1 ml) and the mixture heated to 100°C for 3 hours. The mixture was then returned to r,t, diluted with AcOEt, washed twice with 5 M HCl, brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by FCC (DCM/MeOH, 0-5%) to give 12 mg clean (S)-12-hydroxy-4,5,6,7-tetrahydrodiindeno[7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide (20%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (dt, *J* = 14.8, 7.4 Hz, 4H), 7.04 (d, *J* = 7.7 Hz, 2H), 3.21-2.99 (m, 2H), 2.83 (dd, *J* = 16.0, 7.7 Hz, 2H), 2.27 (dd, *J* = 12.0, 6.3 Hz, 2H), 2.14-1.94 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 145.5, 139.3, 128.7, 122.9, 121.5, 59.3, 38.3, 30.6.

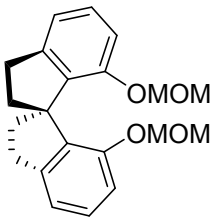
^{31}P (162MHz, $CDCl_3$) δ -11.25.

General scheme for the synthesis of phosphoric acids SPA 2-4



Scheme 1: Synthetic route towards SPA 2-4. Reaction conditions: a) NaH, THF then MOMCl r.t 85%. b) ^{n}BuLi, TMEDA, TBME, then I_2 r.t 70%, c) for **S10a** and **S10b** $ArB(OH)_2$, $Pd(PPh_3)_4$, K_2CO_3, THF, MeOH, H_2O reflux; for **S10c** $ArB(OH)_2$, $Pd(PPh_3)_4$, K_3PO_4, DME, reflux. d) HCl, dioxane, reflux. e) $POCl_3$, pyridine, reflux then dioxane, H_2O reflux or Na_2CO_3, H_2O, reflux

S8: (R)-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]

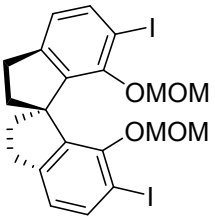


A solution of R-spinol (970 g, 3.8 mmol, 1 equiv) in THF (5ml) is slowly added to a suspension of NaH (60% in mineral oil, 828 mg, 19 mmol, 5 equiv) in THF (8ml) and the resulting mixture stirred for 3 h. MOMCl (0.72 ml, 9.5 mmol, 2.5 equiv) in THF (10ml) is then added at 0°C and the reaction stirred at r.t overnight. The reaction mixture is then diluted with AcOEt and the excess NaH quenched with a little water, washed with NH_4Cl, brine, dried over Na_2SO_4 and concentrated under vacuum. The residue is purified by FCC (PE/AcOET, 95/5) to give 1.1 g clean 7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (85%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (t, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 7.5, 1 Hz, 2H), 6.74 (d, *J* = 8.1 Hz, 2H), 4.88 (d, *J* = 6.4 Hz, 2H), 4.82 (d, *J* = 6.4 Hz, 2H), 3.20-2.94 (m, 10H), 2.56-2.40 (m, 2H), 2.27-2.14 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 153.5, 145.7, 137.6, 127.6, 117.7, 111.3, 93.4, 59.5, 55.5, 39.2, 31.8

S9: (R)-6,6'-diiodo-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]

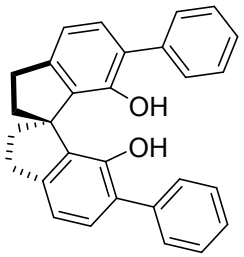


To a solution of (R)-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (1.1 g, 3.23 mmol, 1 equiv) and TMEDA (1.46 ml, 9.96 mmol, 3 equiv) in THF (32 ml, 0.1 M) cooled to -78 °C is added n-BuLi (1.4 M, 9 ml, 12.94 mmol, 4 equiv). The reaction mixture is then stirred 6 h at r.t before being cooled to -78 °C again. I_2 (3.28 g, 12.94 mmol, 4 equiv) in THF (20ml) is added and the reaction mixture stirred overnight at r.t. The reaction mixture is then diluted with DCM and washed with $NaHSO_3$, water and brine, dried over Na_2SO_4 and concentrated under vacuum. The residue is then purified by FCC (PE/DCM, 90/10-70/30) to give 6,6'-diiodo-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (70%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.0 Hz, 2 H), 6.78 (d, *J* = 8.0 Hz, 2H), 4.85 (d, *J* = 5.1 Hz, 2H), 4.63 (d, *J* = 5.1 Hz, 2H), 3.07-2.87 (m, 10 H), 2.58-2.36 (m, 2 H), 2.25-2.09 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 154.2, 146.8, 143.5, 138.8, 122.6, 99.3, 89.0, 61.1, 57.0, 39.4, 31.0.

S10a: (R)-6,6'-diphenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol

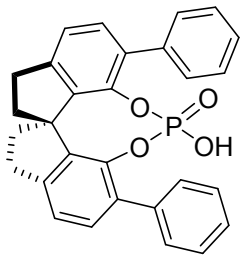


A solution of (R)-6,6'-diiodo-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (200 mg, 0.33 mmol, 1 equiv) and phenyl boronic acid (165 mg, 1.35 mmol, 4 equiv) in THF/MeOH (25:1 V/V, 6.6 ml, 0.05 M) was degassed once. Then K_2CO_3 (270 mg, 1.98 mmol, 6 equiv) in water (1ml) and $Pd(PPh_3)_4$ (52 mg, 0.05 mmol, 15%) was added and the mixture degassed twice more. The reaction mixture was then heated to reflux for 24 hours before being cooled to r.t, diluted with DCM and washed with water, brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was dissolved in dioxane (3 ml, 1M) and HCl (37%, 10% V/V) was added. The mixture was stirred under vigorous stirring at 80 °C for 2 h before being diluted with DCM, washed with $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by FCC (PE/Et_2O, 95/5) to give 78 mg of clean (R)-6,6'-diphenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol (59% two steps).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.3 Hz, 4H), 7.41 (t, *J* = 7.5 Hz, 4H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.20 (d, *J* = 7.6 Hz, 2H), 6.95 (d, *J* = 7.6 Hz, 2H), 5.07 (s, 2H), 3.22-2.97 (m, 4H), 2.54-2.28 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.6, 145.4, 137.6, 132.2, 130.7, 129.4, 128.7, 127.3, 127.1, 117.5, 58.6, 38.00, 31.3.

SPA 2: (R)-12-hydroxy-1,10-diphenyl-4,5,6,7-tetrahydrodiindeno[7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide



To a solution of (R)-6,6'-diphenyl-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol (60 mg, 0.15 mmol, 1 equiv) in pyridine (0.5 ml, 0.3 M) was added $POCl_3$ (41µl, 0.45 mmol, 3 equiv) and the mixture was heated to 80°C for 24 h. After this the mixture was cooled to r.t and water (0.3 ml) was added and the mixture heated to 80°C for another 4 h. After cooling to r.t the mixture was acidified to pH 1 (HCl 5M), diluted with DCM and washed with water and brine and concentrated under

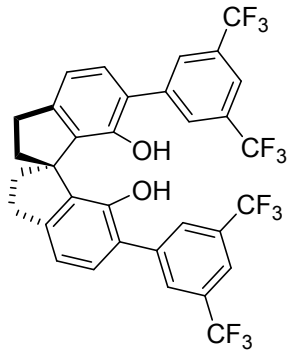
vaccum. The residue was purified by FCC (DCM/MeOH 0-5%) before being dissolved in DCM and washed twice with HCl (4M) then water before being concentrated under vacuum and co-evaporated with toluene. This gave 40 mg of (R)-12-hydroxy-1,10-diphenyl-4,5,6,7-tetrahydrodiindeno[7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide (59%)

^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$): δ 7.46- 7.36 (m, 4H), 7.19 (ddd, *J* = 10.1, 5.9, 2.1 Hz, 6H), 7.16-7.05 (m, 4H), 3.03 (ddd, *J* = 17.2, 11.4, 6.7 Hz, 2H), 2.87-2.73 (m, 2H), 2.25 (dd, *J* = 12.0, 6.5 Hz, 2H), 2.11 (dd, *J* = 11.5, 8.6 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3/CD_3OD$): δ 151.9, 148.9, 147.2, 144.7, 141.1, 136.8, 136.0, 134.39, 133.2, 129.1, 66.5, 45.2, 36.8.

^{31}P NMR (162 MHz, $CDCl_3/CD_3OD$): δ -10.80.

S10b: (R)-6,6'-bis(3,5-bis(trifluoromethyl)phenyl)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol



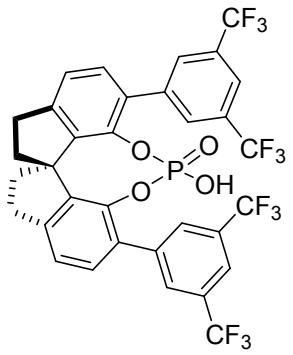
A solution of 6,6'-diiodo-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (200 mg, 0.33 mmol, 1 equiv) and 3,5-Bis(trifluoromethyl)phenylboronic acid (350 mg, 1.35 mmol, 4 equiv) in THF/MeOH (25:1 V/V, 6.6 ml, 0.05 M) was degassed once. Then K_2CO_3 (270 mg, 1.98 mmol, 6 equiv) in water (1ml) and $Pd(PPh_3)_4$ (52 mg, 0.05 mmol, 15%) was added and the mixture degassed twice more. The reaction mixture was then heated to reflux for 24 hours before being cooled to r.t, diluted with DCM and washed with water, brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was dissolved in dioxane (3 ml, 1M) and HCl (37%, 10% V/V) was added. The mixture was stirred under vigorous stirring at 80 °C for 2 h before being diluted with DCM, washed with $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by FCC (PE/Et_2O, 95/5) to give 98 mg of clean (R)-6,6'-bis(3,5-bis(trifluoromethyl)phenyl)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol (44% two steps).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 1.6 Hz, 4H), 7.88-7.67 (m, 2H), 7.30 (d, *J* = 7.7 Hz, 2H), 7.05 (d, *J* = 7.7 Hz, 2H), 4.93 (s, 2H), 3.15 (dt, *J* = 8.5, 4.7 Hz, 4H), 2.47 (ddd, *J* = 13.1, 6.6, 2.5 Hz, 2H), 2.37 (ddd, *J* = 13.1, 10.4, 8.9 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 150.0, 147.2, 139.8, 131.8, 131.6 (q, *J* = 33.1 Hz), 130.8, 129.6 (d, *J* = 3.4 Hz), 124.8, 123.5 (q, *J* = 272.6 Hz). 120.9 (quint, *J* = 3.1 Hz), 118.7, 58.1, 37.8, 31.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.88.

SPA 3: (R)-1,10-bis(3,5-bis(trifluoromethyl)phenyl)-12-hydroxy-4,5,6,7-tetrahydrodiindeno[7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide



To a solution of (R)-6,6'-bis(3,5-bis(trifluoromethyl)phenyl)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol (98 mg, 0.145 mmol, 1 equiv) in pyridine (0.5 ml, 0.3 M) was added $POCl_3$ (40µl, 0.44 mmol, 3 equiv) and the mixture was stirred for 24 h. A second dose of $POCl_3$ (40µl, 0.44 mmol, 3 equiv) was added and the mixture stirred till full consumption of the starting material. After this water (0.3 ml) was added very carefully (strong exothermic reaction) and the mixture was diluted with DCM and acidified to pH 1 (HCl 5M), washed with water and brine and concentrated under vaccum. The residue was dissolved in THF (10 ml) and 1 ml of saturated Na_2CO_3 was added. The mixture was heated to 70 °C till full consumption of the intermediate (18h) before being returned to r.t, diluted with DCM and washed twice with HCl (4M), brine and concentrated under vaccum. The residue was purified by FCC (Toluene/DCM 0-100%) before being dissolved in DCM and washed twice with HCl (4M) then water before being concentrated under vacuum and co-evaporated with toluene. This gave 96.6 mg of (R)-1,10-bis(3,5-bis(trifluoromethyl)phenyl)-12-hydroxy-4,5,6,7-tetrahydrodiindeno[7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide (90%)

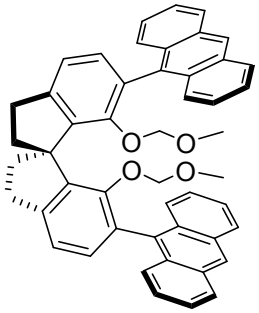
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.65 (m, 4H), 7.46 (s, 2H), 7.26 (dd, *J* = 7.6, 1.3 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 2H), 3.24-3.10 (m, 2H), 2.99 (dd, *J* = 16.3, 7.8 Hz, 2H), 2.37 (dd, *J* = 12.1, 6.4 Hz, 2H), 2.29-2.16 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 147.2 (d, *J* = 2.3 Hz), 141.6 (d, *J* = 7.9 Hz), 140.6 (d, *J* = 3.5 Hz), 139.5, 132.2 (d, *J* = 3.8 Hz), 131.2 (q, *J* = 33.1 Hz), 130.7, 129.5, 123.3 (q, *J* = 272.7 Hz), 123.2, 120.6 (quint, *J* = 3.6 Hz), 59.9, 38.5, 30.5.

^{31}P NMR (162 MHz, $CDCl_3$): δ -10.60

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.76.

S10c': (1R,6r,6's)-6,6'-di(anthracen-9-yl)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol

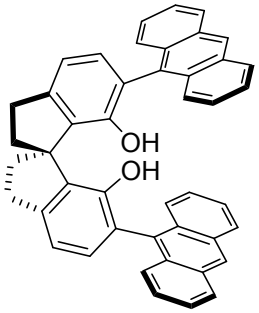


A solution of 6,6'-diiodo-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (300 mg, 0.51 mmol, 1 equiv) and 9-anthracyl boronic acid (457 mg, 2.03 mmol, 4 equiv) and K_3PO_4 (861 mg, 4.06 mmol, 8 equiv) in DME (5.0 ml, 0.1 M) was degassed once via *freeze-pump-thaw*. $Pd(PPh_3)_4$ (54 mg, 0.051 mmol, 0.1 equiv) was added and the mixture degassed via the same method twice more. The reaction mixture was then heated to 85 °C for 48 hours before being cooled to r.t, diluted with DCM and then washed with water, brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by FCC (Hexane/Toluene/iPrOH 94/5/1) to give 196 mg clean (1R,6r,6's)-6,6'-di(anthracen-9-yl)-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (55% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.49 (s, 2H), 8.10-8.02 (d, *J* = 7.5 Hz, 2H), 7.98 (t, *J* = 8.4 Hz, 4H), 7.61 (dd, *J* = 8.9, 1.1 Hz, 2H), 7.45 (dddd, *J* = 18.0, 8.0, 6.5, 1.4 Hz, 4H), 7.23-7.09 (m, 4H), 7.05 (d, *J* = 7.5 Hz, 2H), 6.21 (ddd, *J* = 8.8, 6.5, 1.2 Hz, 2H), 4.39 (d, *J* = 5.8 Hz, 2H), 3.84 (d, *J* = 5.8 Hz, 2H), 3.28 (ddd, *J* = 15.8, 10.7, 7.9 Hz, 2H), 3.20 -3.04 (m, 2H), 2.65 (td, *J* = 11.6, 11.1, 9.0 Hz, 2H), 2.52 (s, 8H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 154.1, 145.5, 141.8, 134.5, 132.6, 131.6, 131.31, 130.7, 130.2, 128.7, 128.6, 127.8, 127.5, 127.0, 126.8, 126.1, 125.7, 125.5, 125.1, 119.9, 98.6, 60.1, 56.3, 39.0, 31.4.

S10c : (1R,6r,6's)-6,6'-di(anthracen-9-yl)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol



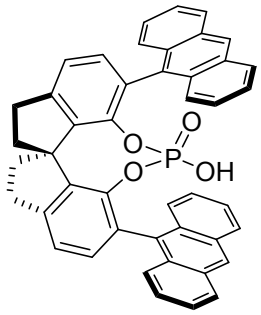
A solution of (1R,6r,6's)-6,6'-di(anthracen-9-yl)-7,7'-bis(methoxymethoxy)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene] (196 mg, 0.28 mmol, 1 equiv) was dissolved in dioxane (3 ml, 0.1 M) and HCl (37%, 10% V/V) was added. The mixture was stirred under vigorous stirring at 80 °C for 2 h. The mixture was then cooled to room temperature, diluted with DCM, washed with $NaHCO_3$, brine, dried over

Na_2SO_4 and concentrated under vacuum. The residue was purified by FCC (dry loaded on silica, PE/AcOEt, 7/3) to give 71 mg of clean (S)-6,6'-di(anthracen-9-yl)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol (41%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 2H), 8.12-8.03 (m, 2H), 8.00 (d, *J* = 8.5 Hz, 2H), 7.81 (dd, *J* = 8.7, 1.2 Hz, 2H), 7.48 (ddd, *J* = 8.3, 6.5, 1.3 Hz, 2H), 7.41 (ddd, *J* = 8.1, 6.6, 1.4 Hz, 2H), 7.33 (dd, *J* = 8.9, 1.1 Hz, 2H), 7.30-7.24 (m, 2H), 7.08 (d, *J* = 7.5 Hz, 2H), 7.00 (d, *J* = 7.5 Hz, 2H), 6.48 (ddd, *J* = 8.8, 6.5, 1.2 Hz, 2H), 4.59 (s, 2H), 3.33-3.20 (m, 2H), 3.15 (ddd, *J* = 16.0, 8.5, 2.3 Hz, 2H), 2.67-2.49 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 150.7, 145.7, 133.3, 131.6, 131.5, 131.4, 131.0, 130.9, 130.7, 128.6, 128.1, 127.3, 126.5, 126.1, 125.8, 125.4, 125.2, 122.6, 116.9, 58.8, 38.3, 31.6.

SPA 4: (1r,5aR,10s,12S)-1,10-di(anthracen-9-yl)-12-hydroxy-4,5,6,7-tetrahydrodiindeno [7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide



To a solution of 6,6'-di(anthracen-9-yl)-2,2',3,3'-tetrahydro-1,1'-spirobi[indene]-7,7'-diol (71 mg, 0.12 mmol, 1 equiv) in pyridine (1.17 ml, 0.1 M) was added at 0°C $POCl_3$ (55µl, 0.59 mmol, 5 equiv) and the mixture was stirred at 80°C for 24 h after which a precipitate had formed. The reaction was returned to r.t and dioxane (2 ml) was added followed by water (0.6 ml). The reaction was then heated to 100°C for 48 h after which the precipitate had dissolved. The reaction mixture is then returned to r.t, diluted with DCM and washed with HCl (4M) and water before being concentrated under vacuum. The residue was purified by FCC (DCM, Acetone, AcOH 90/9/1) before being dissolved in DCM and washed twice with HCl (4M) then water before being concentrated under vacuum and co-evaporated with toluene. After 48h of drying under high vacuum 70 mg of(1r,5aR,10s,12S)-1,10-di(anthracen-9-yl)-12-hydroxy-4,5,6,7-tetrahydrodiindeno [7,1-de:1',7'-fg][1,3,2]dioxaphosphocine 12-oxide (89%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (s, 2H), 7.84-7.69 (m, 4H), 7.70-7.58 (m, 2H), 7.38-7.26 (m, 6H), 7.28-7.17 (m, 4H), 7.13 (t, *J* = 7.7 Hz, 2H), 7.00 (t, *J* = 7.5 Hz, 2H), 3.45-3.23 (m, 2H), 3.23-2.86 (m, 2H), 2.57 (dd, *J* = 12.0, 6.3 Hz, 2H), 2.52-2.30 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 146.0, 144.1, 144.0, 140.3, 140.3, 133.3, 132.1, 131.3, 130.7, 130.6, 130.2, 130.2, 129.6, 128.5, 128.0, 128.0, 127.3, 126.4, 125.8, 124.6, 124.6, 122.3, 60.2, 38.9, 30.4. (Extra signals due to ^{31}P couplings depending on apodisation factor)

^{31}P (121 MHz, $CDCl_3$) δ -11.77.

4. General procedures for ELLE experiments.

GP 1) General procedure for biphasic batch extraction experiments

All extraction experiments were conducted in 2 ml auto-sampler vials with crimp cap seals equipped with stirrbars. In a standard experiment, a solution of the racemic guest (0.4ml, indicated concentration) dissolved in a phosphate buffer solution (buffer strength 0.1 M, indicated pH) was carefully added to a solution of the corresponding host in the indicated solvent (0.4 ml, 1.0 mM). The two-phasic system was then cooled to the indicated temperature and stirred at 900 rpm for 16 hours. The phases were then allowed to separate over a period of 2 minutes. The aqueous phase was removed and an aliquot injected into a reverse phase HPLC for determination of the ee, distribution and α_{op}. All extraction experiments were carried out *in triplo* and with a simultaneous blank reaction (concentration of host = 0.0 mM).

GP 2) General procedure for the U-tube reactor experiments

To a U-shaped reactor vessel (Figure 7a, inner diameter = 1.0 cm) equipped with a stirrbar, was added a solution of SPA 4 in chloroform (10 ml, 0.5 mM). The vessal the solution was cooled to 6°C and both the feeding phase (5 ml of a 2 or 20.0 mM solution of racemic phenylglycinol dissolved in a phosphate buffer solution (buffer strength 0.1 M) pH= 5.0) and the receiving phase (5ml of a HCl solution in doubly distilled water such as pH = 2.0) were added simultaneously to respectfully the right and left legs of the U-tube. Stirring was set to 900 rpm and aliquots of 0.2 ml were removed from the receiving phase at given intervals. Each aliquot was replaced by an equal amount of fresh receiving phase.

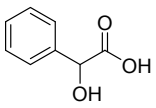
GP 3) General procedure for the triphasic reactor system experiments

To a tube-shaped reactor vessel, as described in Figure 7b (inner diameter = 0.9 cm), equipped with a stirrbar and overhead stirrer, was added the first host phase comprised of a solution of SPA 4 in chloroform (3 ml, 1.0 mM). The vessal was cooled to 6°C and then was carefully added so as no mixing of phases could be observed in the following order, the feeding phase (5 ml of a 2.0 mM solution of racemic phenylglycinol dissolved in a phosphate buffer solution (buffer strength 0.1 M) pH= 5.0) and the second host phase comprised of a solution of SPA 4 in toluene (3 ml, 1.0 mM). Stirring was set at a rate of 900 rpm so as all three phases were stirred but no mixing occurred and was left for 16 hours. The organic phases were removed from the reactor and each independently extracted with a 3 ml of a solution of HCl in doubly distilled water pH = 2.0. The extracted aqueous phases were sampled for measuring in reverse phase HPLC.

5. Enantioselectivities, distributions and α_{op} for all experiments

Guest Screening for SPA 1-4

All extractions on guests **5-19** were run according to GP 1 and with the following parameters: guest solution concentration set to 2 mM, host solution solvent being chloroform, vessel temperature set to 6 °C, buffer pH set to 5.0.



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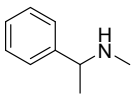

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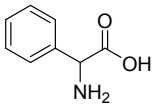

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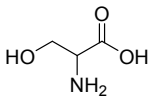

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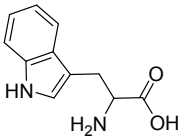

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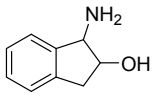

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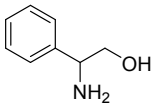

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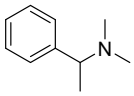

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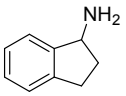

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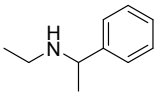

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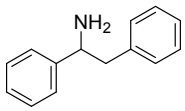

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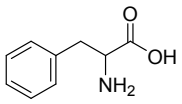

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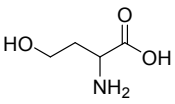

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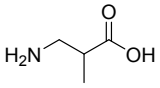

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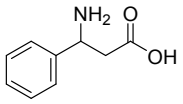


19

Compound	SPA 2				SPA 3				SPA 4			
	ee%	Ds	Dr	α_{op}	ee%	Ds	Dr	α_{op}	ee%	Ds	Dr	α_{op}
5	--	--	--	--	--	--	--	--	--	--	--	--
6	2	--	--	--	2	--	--	--	--	--	--	--
7	6	--	--	--	7	--	--	--	--	--	--	--
8	--	--	--	--	--	--	--	--	--	--	--	--
9	--	--	--	--	2	--	--	--	--	--	--	--
10	18	1.276	3.414	2.7	5	--	--	--	--	--	--	--
11	40	0.452	2.315	5.1	33	1.276	3.414	2.7	37	0.0284	0.9889	34.8
12	--	--	--	--	--	--	--	--	--	--	--	--
13	1	--	--	--	1	--	--	--	--	--	--	--
14	3	--	--	--	1	--	--	--	--	--	--	--
15	10	--	--	--	7	--	--	--	--	--	--	--
16	--	--	--	--	--	--	--	--	--	--	--	--
17	--	--	--	--	--	--	--	--	--	--	--	--
18	--	--	--	--	--	--	--	--	--	--	--	--
19	--	--	--	--	--	--	--	--	--	--	--	--

Temperature Screening on 11 with SPA 2,4

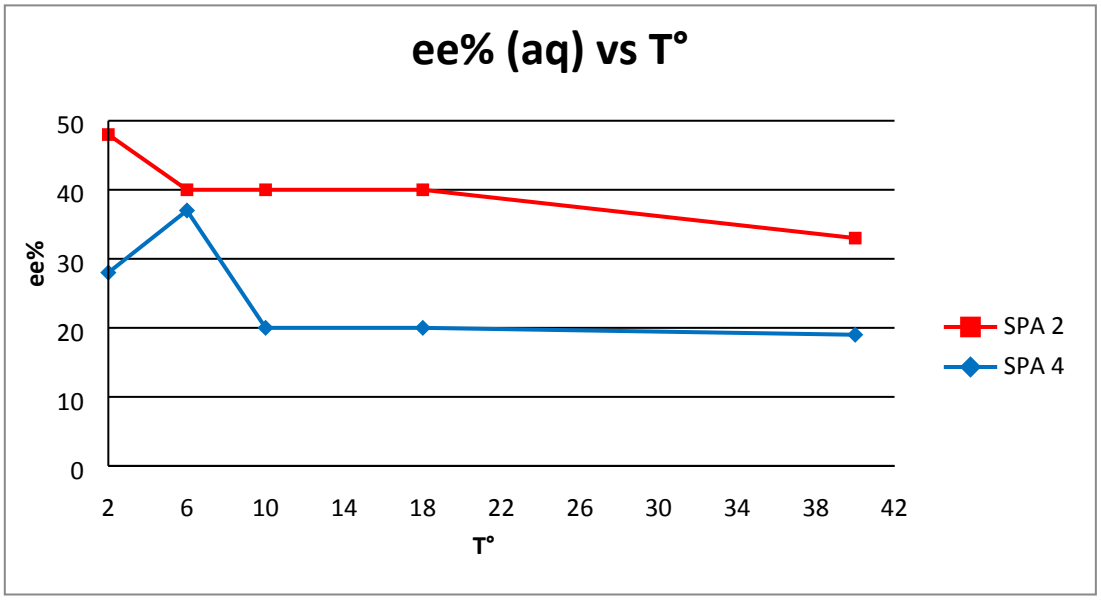
All extractions were run on guest **11** according to GP 1 and with the following parameters: guest solution concentration set to 2 mM, host solution solvent being chloroform, vessel temperature set to as indicated, buffer pH set to 5.0.

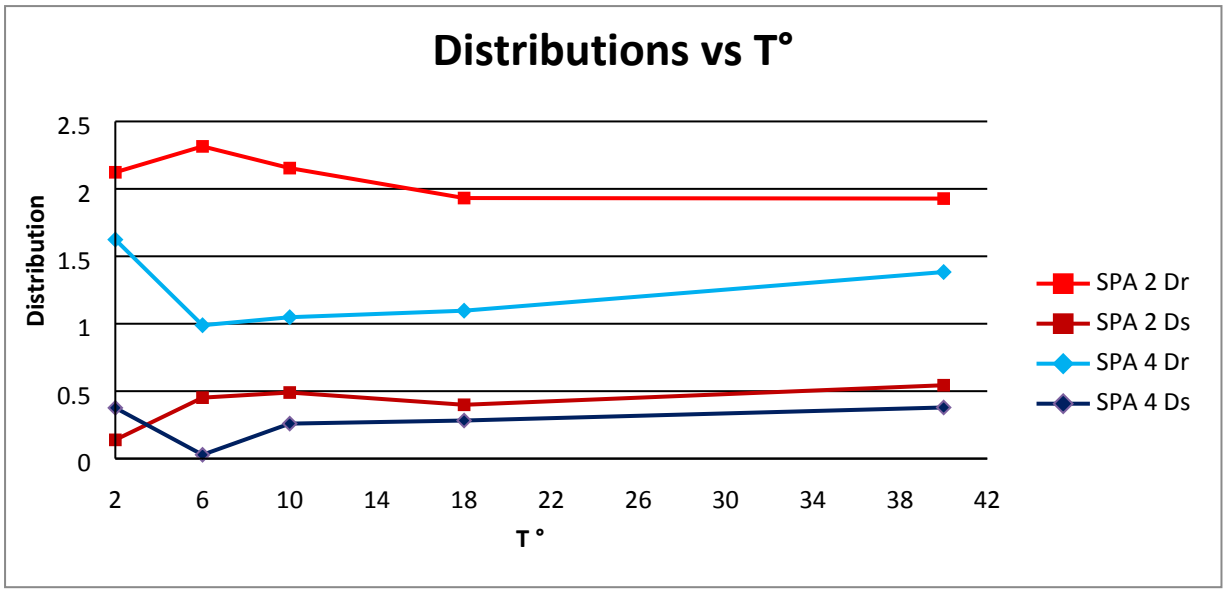
For SPA 2

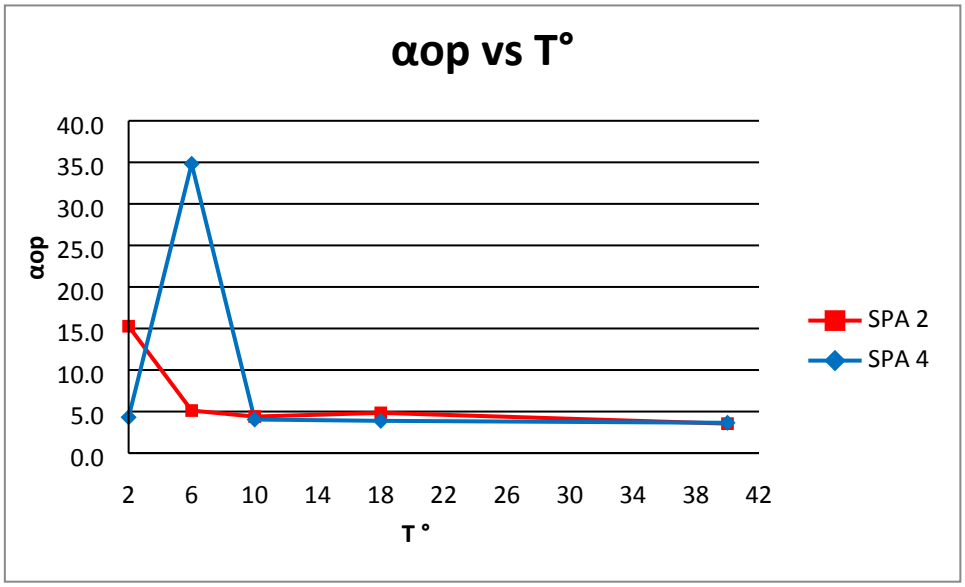
T°	ee% (aq)	D_S	D_R	α_{op}
2°C	48	0.139	2.123	15.273
6 °C	40	0.452	2.315	5.122
10 °C	40	0.490	2.154	4.396
18 °C	40	0.399	1.932	4.842
40 °C	33	0.544	1.928	3.544

For SPA 4

T°	ee% (aq)	D_S	D_R	α_{op}
2°C	28	0.376	1.624	4.315
6 °C	37	0.0284	0.9889	34.820
10 °C	20	0.259	1.048	4.041
18 °C	20	0.282	1.097	3.884
40 °C	19	0.379	1.383	3.649





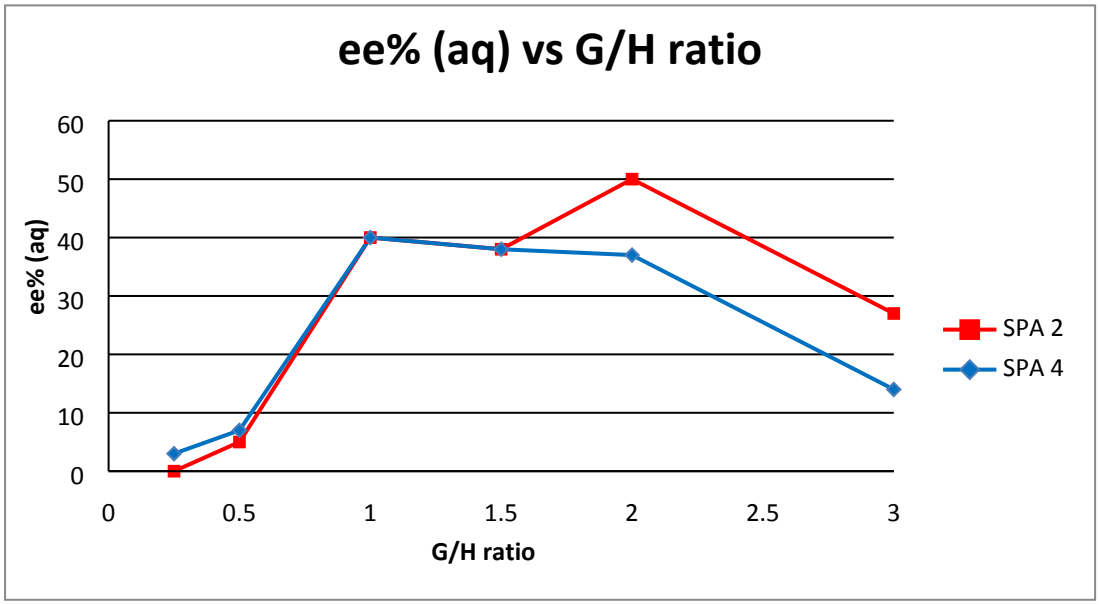


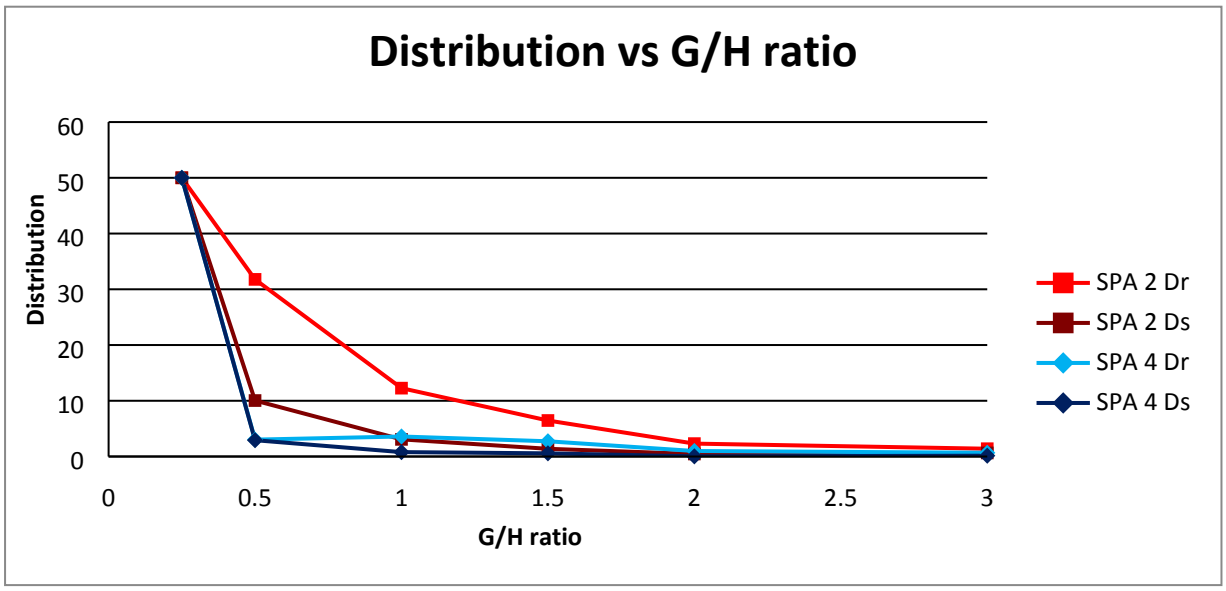
Guest to Host Screening on 11 with SPA 2,4

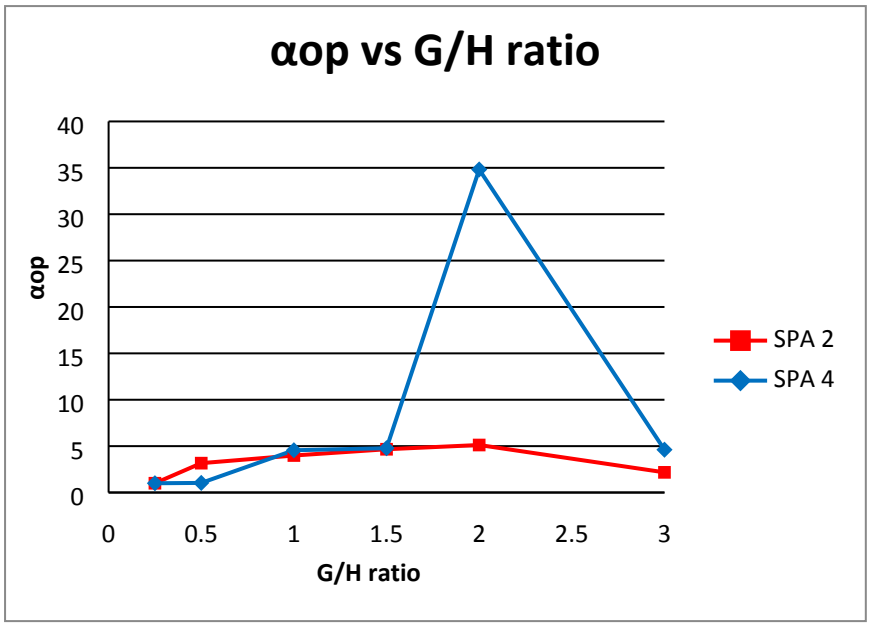
All extractions were run on guest **11** according to GP 1 and with the following parameters: guest solution concentration set as indicated, host solution solvent being chloroform, vessel temperature set to 6 °C, buffer pH set to 5.0. When values become extreme they are marked n.a as unreliable. For use in the graphs they were arbitrarily set to: ee% = 0, Ds/Dr = 50, α_{op} = 1

Ratio guest/SPA 2	guest mmol	host mmol	ee%	Ds	Dr	α_{op}
0.25	0.25	1	0	n.a	n.a	n.a
0.5	0.5	1	5	10.041	31.776	3.165
1	1	1	40	3.075	12.265	3.989
1.5	1.5	1	38	1.385	6.46	4.664
2	2	1	50	0.452	2.315	5.122
3	3	1	27	0.643	1.398	2.174

Ratio guest/SPA 4	guest mmol	host mmol	ee%	Ds	Dr	α_{op}
0.25	0.25	1	0	n.a	n.a	n.a
0.5	0.5	1	7	3.030	2.927	1.035
1	1	1	40	0.788	3.592	4.555
1.5	1.5	1	38	0.572	2.733	4.777
2	2	1	37	0.0284	0.9889	34.820
3	3	1	14	0.146	0.674	4.615







pH Screening on 11 with SPA 2,4

All extractions were run on guest **11** according to GP 1 and with the following parameters: guest solution concentration 2 mM, host solution solvent being chloroform, vessel temperature set to 6 °C, buffer pH set as indicated. When values become extreme they are marked n.a as unreliable. For use in the graphs they were they were arbitrarily set to: ee% = 0, Ds/Dr = 0, α_{op} = 1

For SPA 2

pH	ee% (aq)	D_R	D_S	α_{op}
2	0	n.a	n.a	1
3	7	0.124	0.038	3.263
3.7	21	0.651	0.163	3.994
4.5	23	0.817	0.2	4.085
5	40	2.315	0.452	5.122
5.5	27	0.987	0.245	4.029
6.5	33	1.046	0.275	3.804
7.5	17	1.932	1.237	1.562
8.4	39	133.574	61.328	2.178
9.6	44	83.834	27.162	3.086
10.6	31	22.779	12.6	1.808
11.1	17	13.219	9.926	1.332
12	5	10.424	10.153	1.027

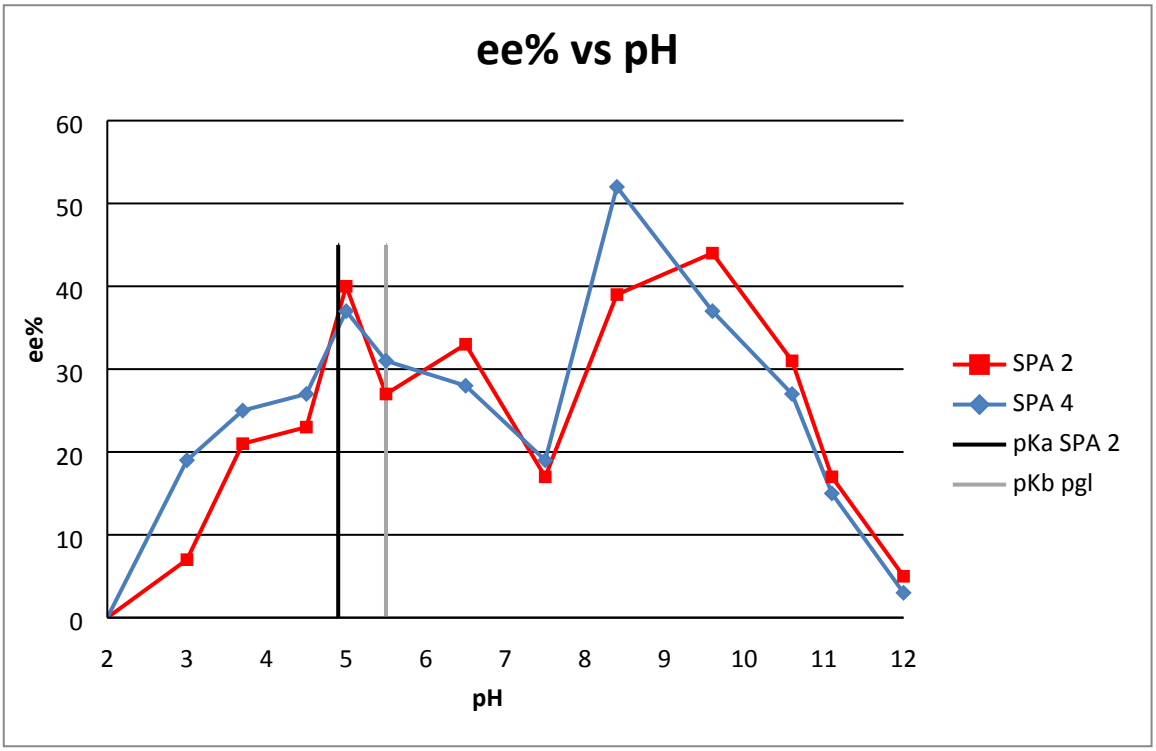
For SPA 4

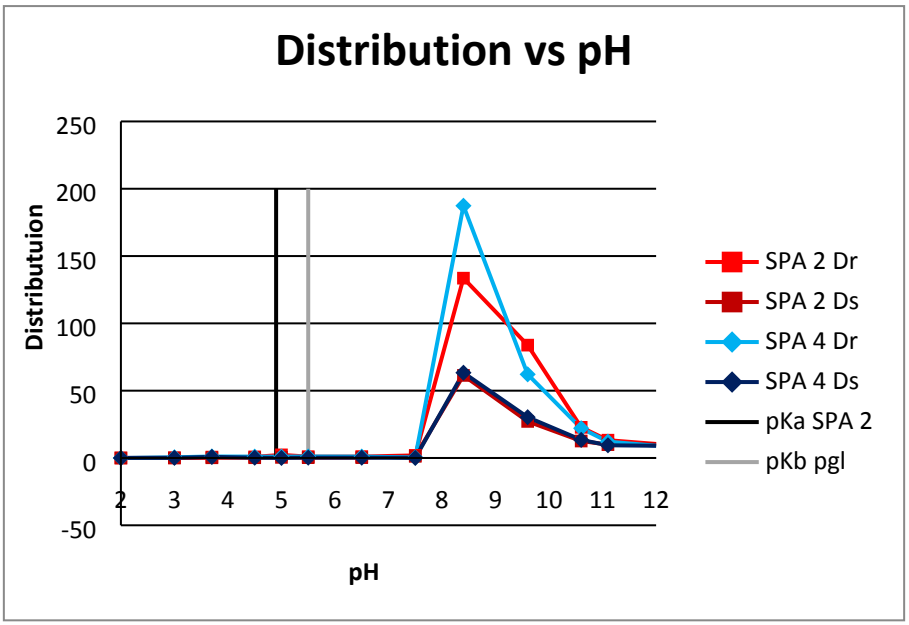
pH	ee% (aq)	D_R	D_S	α_{op}
2	0	n.a	n.a	1
3	19	0.51	0.107	4.766
3.7	25	1.123	0.798	1.407

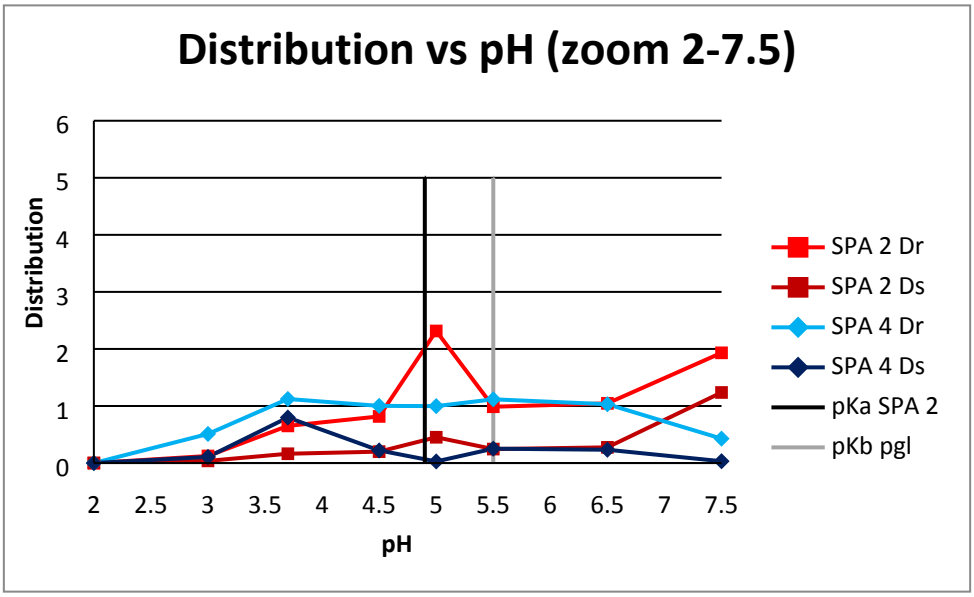
4.5	27	1.002	0.221	4.534
5	37	0.9889	0.0284	34.820
5.5	31	1.117	0.252	4.433
6.5	28	1.031	0.233	4.425
7.5	19	0.428	0.032	13.375
8.4	52	187.367	63.332	2.958
9.6	37	62.139	30.293	2.051
10.6	27	22.072	13.455	1.640
11.1	15	12.161	9.444	1.288
12	3	9.084	9.069	1.002

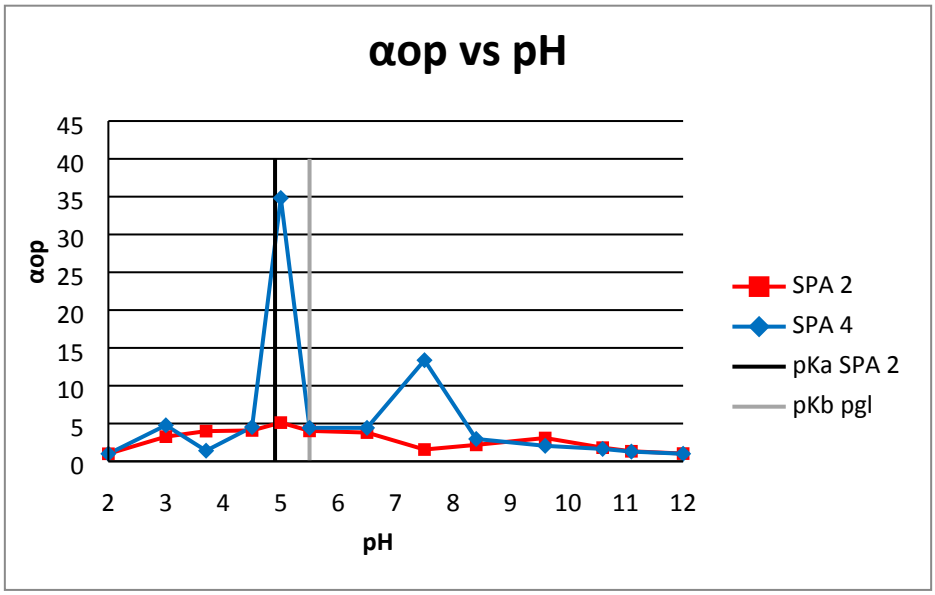
When run without buffer:

Initial Solution pH	ee% (aq)	D_R	D_S	α_{op}
9	37	1.812	0.322	5.620




Distribution vs pH
Distributuion
250
200
150
100
50
0
-50
2 3 4 5 6 7 8 9 10 11 12
pH
SPA 2 Dr
SPA 2 Ds
SPA 4 Dr
SPA 4 Ds
pKa SPA 2
pKb pgl


Distribution vs pH (zoom 2-7.5)
Distribution
6
5
4
3
2
1
0
2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5
pH
SPA 2 Dr
SPA 2 Ds
SPA 4 Dr
SPA 4 Ds
pKa SPA 2
pKb pgl


αop vs pH
αop
45
40
35
30
25
20
15
10
5
0
2 3 4 5 6 7 8 9 10 11 12
pH
SPA 2
SPA 4
pKa SPA 2
pKb pgl

Solvent Screening on 11 with SPA 2,4

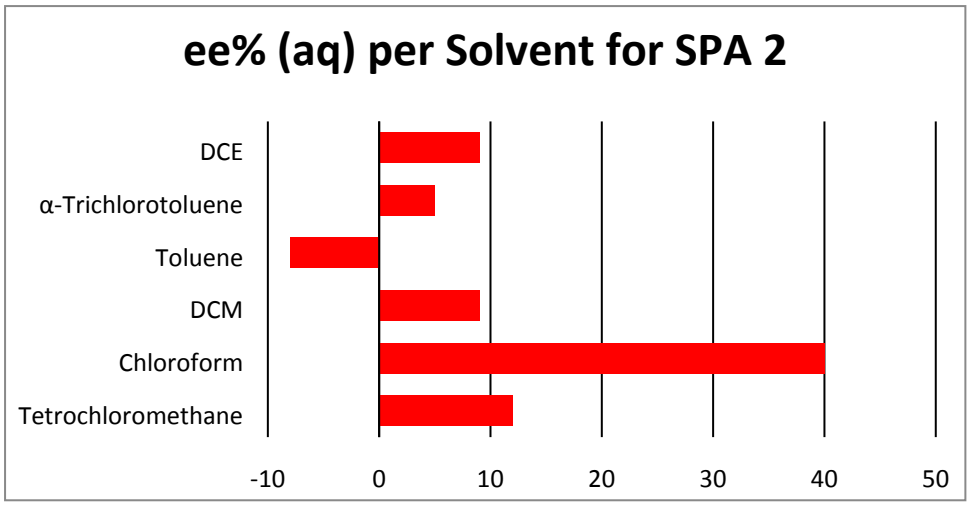
All extractions were run on guest **11** according to GP 1 and with the following parameters: guest solution concentration 2 mM, host solution solvent as indicated, vessel temperature set to 6 °C, buffer pH set to 5.0. For SPA 4 in chlorobenzene distributions are expressed as $*10^2$

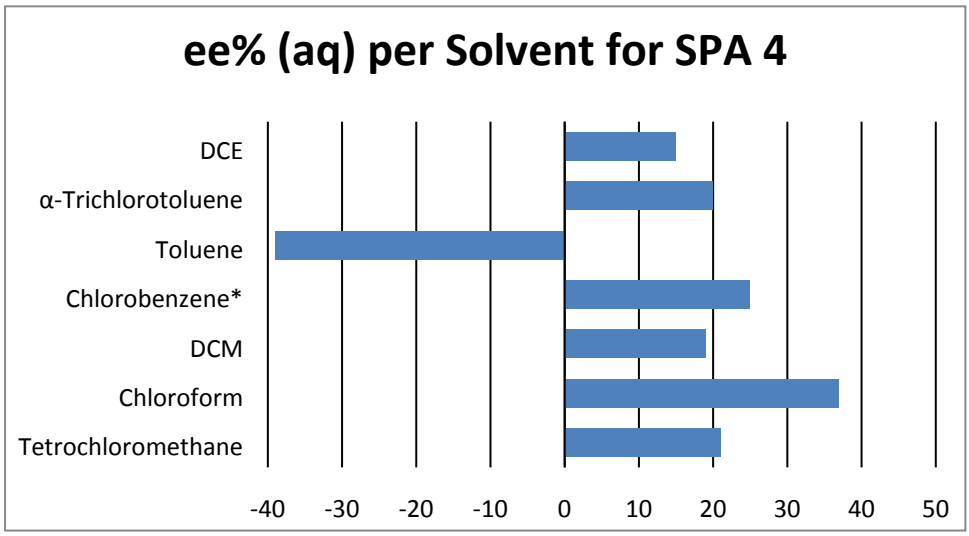
For SPA 2

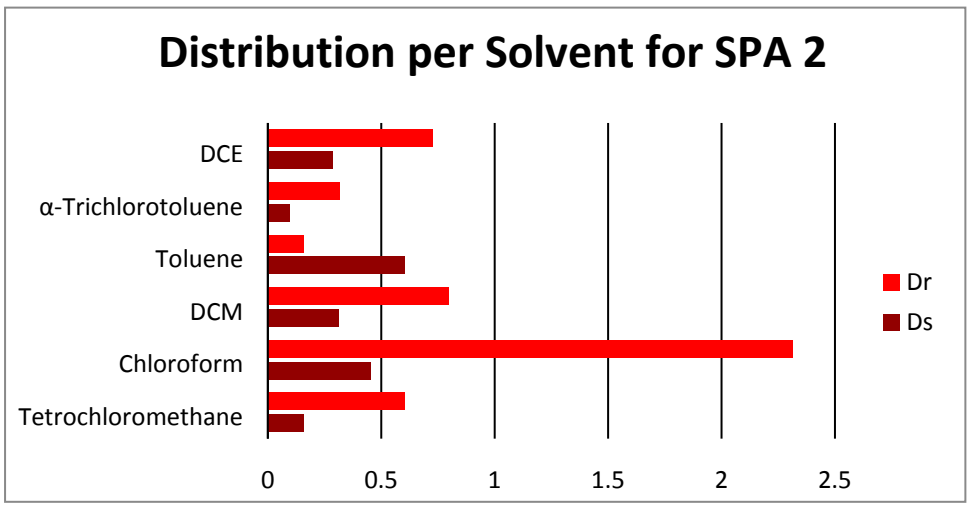
Solvent	ee% (aq)	D_S	D_R	α_{op}
Tetrochloromethane	12	0.156	0.601	3.853
Chloroform	40	0.452	2.315	5.122
DCM	9	0.31	0.797	2.571
Toluene	-8	0.601	0.156	3.853
α-Trichlorotoluene	5	0.094	0.315	3.351
DCE	9	0.287	0.727	2.533

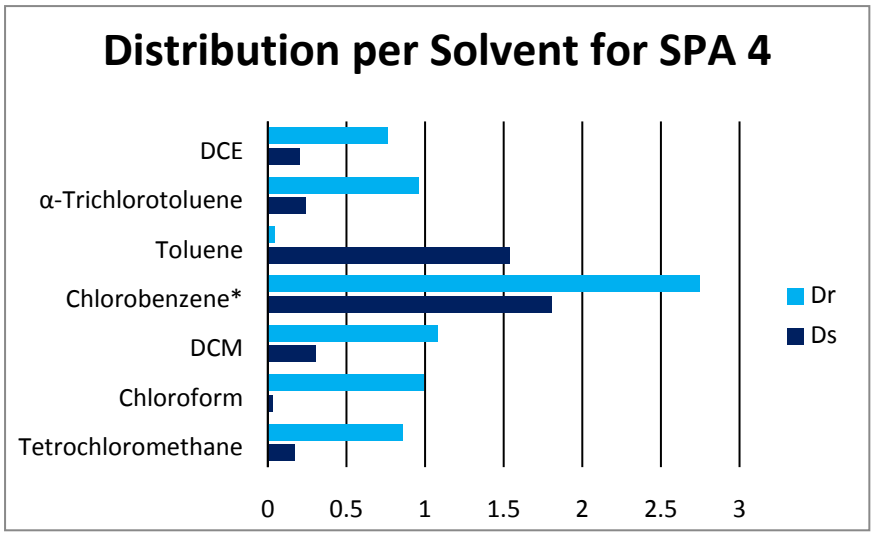
For SPA 4

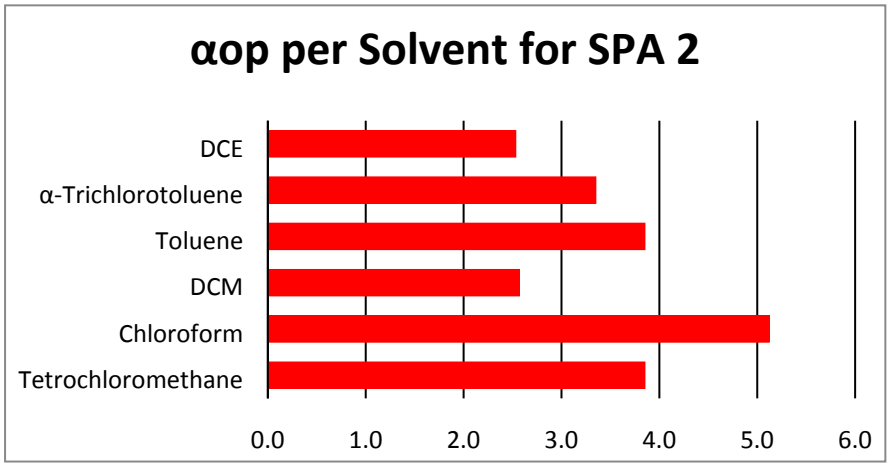
Solvent	ee% (aq)	D_S	D_R	α_{op}
Tetrochloromethane	21	0.168	0.859	5.113
Chloroform	37	0.0284	0.9889	34.820
DCM	19	0.307	1.081	3.521
Chlorobenzene	25	180.4	274.8	1.523
Toluene	-39	1.538	0.044	34.955
α-Trichlorotoluene	20	0.239	0.957	4.004
DCE	15	0.2	0.763	3.815

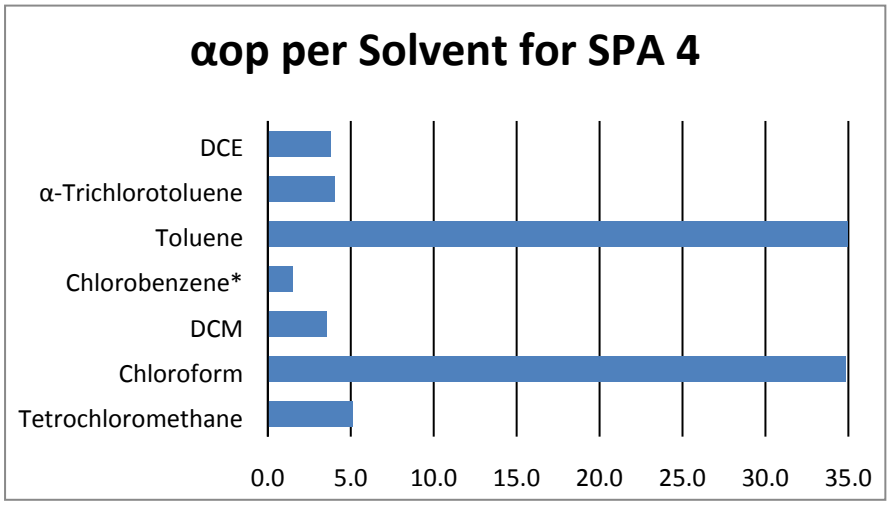

ee% (aq) per Solvent for SPA 2
DCE
α-Trichlorotoluene
Toluene
DCM
Chloroform
Tetrochloromethane
-10
0
10
20
30
40
50


ee% (aq) per Solvent for SPA 4
DCE
α-Trichlorotoluene
Toluene
Chlorobenzene*
DCM
Chloroform
Tetrochloromethane
-40
-30
-20
-10
0
10
20
30
40
50


Distribution per Solvent for SPA 2
DCE
α-Trichlorotoluene
Toluene
DCM
Chloroform
Tetrochloromethane
0
0.5
1
1.5
2
2.5
Dr
Ds

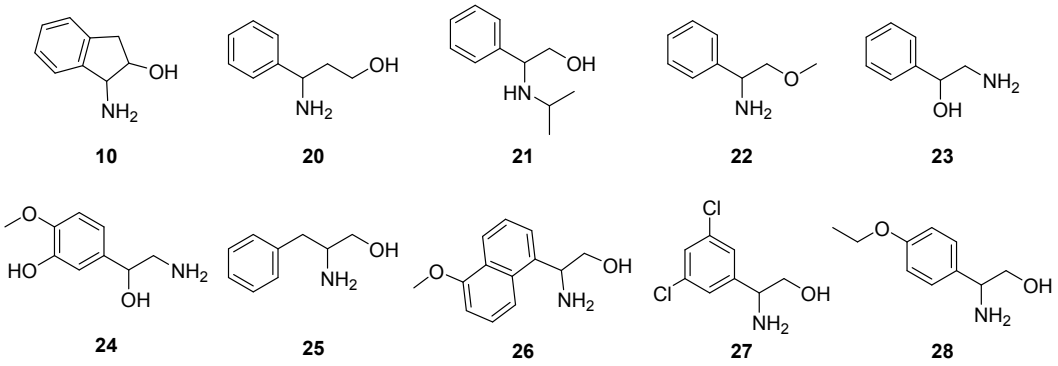

Distribution per Solvent for SPA 4
DCE
α-Trichlorotoluene
Toluene
Chlorobenzene*
DCM
Chloroform
Tetrochloromethane
0
0.5
1
1.5
2
2.5
3
Dr
Ds


αop per Solvent for SPA 2
DCE
α-Trichlorotoluene
Toluene
DCM
Chloroform
Tetrochloromethane
0.0
1.0
2.0
3.0
4.0
5.0
6.0


αop per Solvent for SPA 4
DCE
α-Trichlorotoluene
Toluene
Chlorobenzene*
DCM
Chloroform
Tetrochloromethane
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0

Amino-Alcohol Screening with SPA 2,4

All extractions were run on the corresponding guest according to GP 1 and with the following parameters: guest solution concentration 2 mM, host solution solvent as chloroform, vessel temperature set to 6 °C, buffer pH set to 5.0.



Compound	ee% (aq)		D_S		D_R		α_{op}	
	SPA 2	SPA 4	SPA 2	SPA 4	SPA 2	SPA 4	SPA 2	SPA 4
10	18	rac	1.276	n.a	3.414	n.a	2.7	n.a
20	rac	rac	n.a	n.a	n.a	n.a	n.a	n.a
21	rac	rac	n.a	n.a	n.a	n.a	n.a	n.a
22	rac	rac	n.a	n.a	n.a	n.a	n.a	n.a
23	8	11	0.400	0.419	0.345	0.276	1.2	1.5
24	20	9	0.377	0.438	1.163	0.854	3.1	2.0
25	1	6	0.394	0.315	0.423	0.389	1.1	1.2
26	n.a	n.a	n.a	n.a	n.a	n.a	n.a	n.a
27	7	8	0.346	0.345	0.969	0.726	2.8	2.1
28	57	60	0.346	0.365	1.13	1.014	3.3	2.8

pH Screening on 28 with SPA 2,4

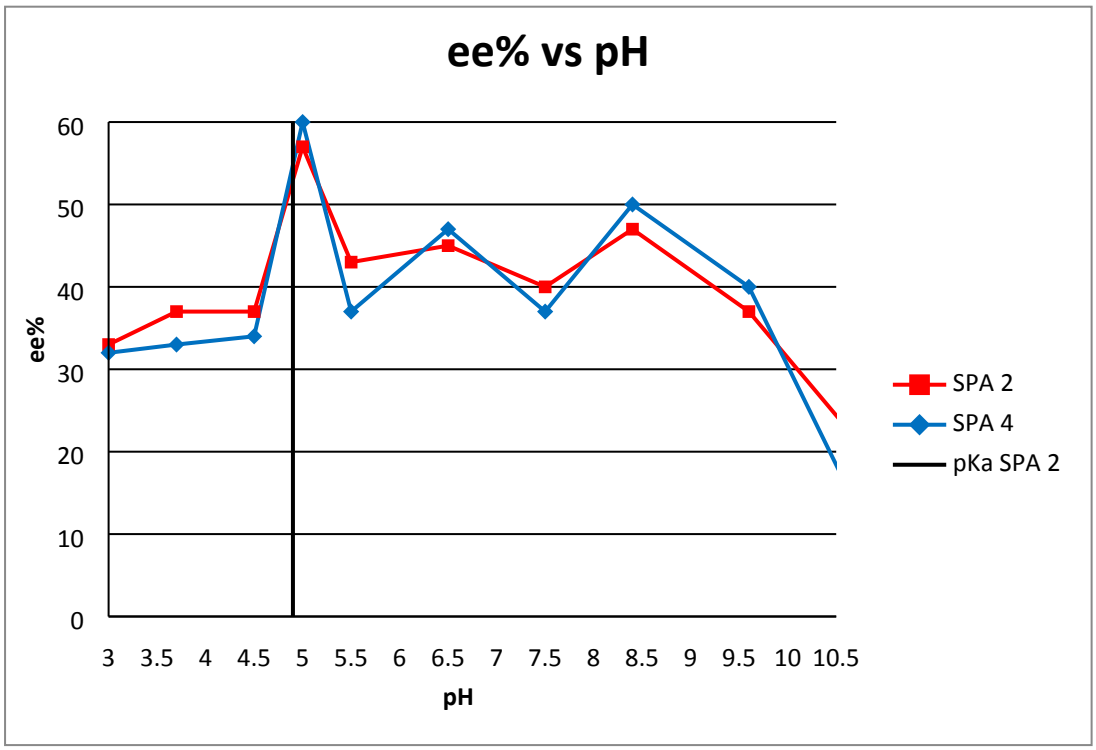
All extractions were run on guest **28** according to GP 1 and with the following parameters: guest solution concentration 2 mM, host solution solvent being chloroform, vessel temperature set to 6 °C, buffer pH set as indicated.

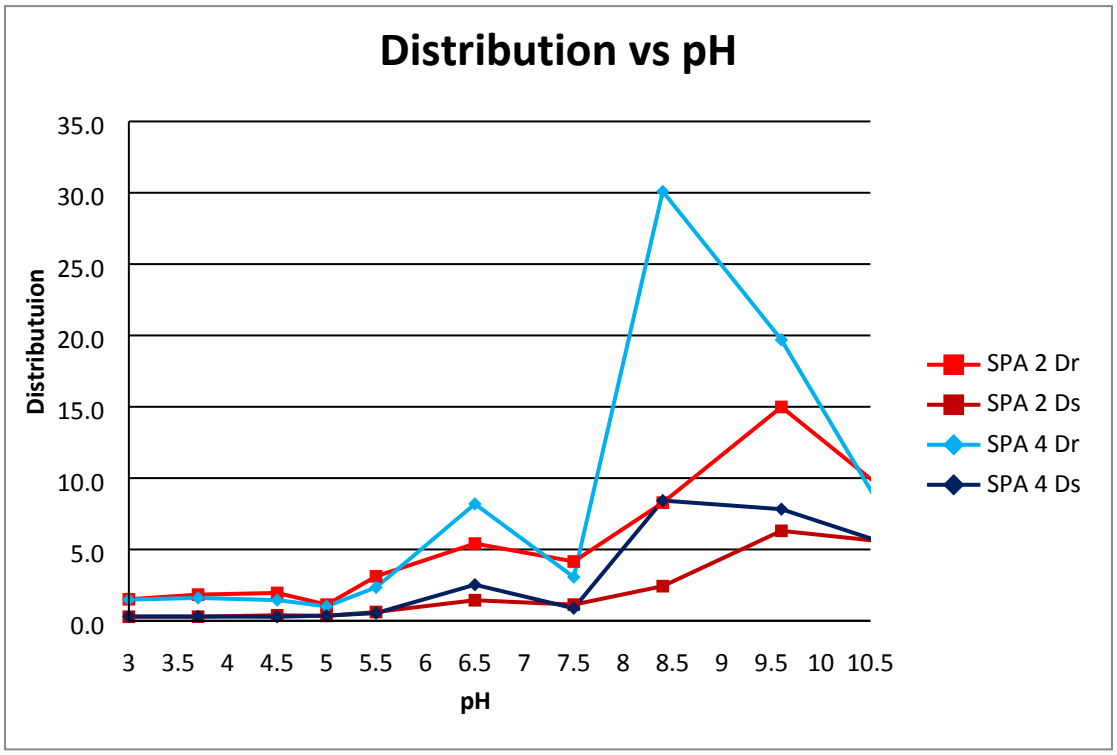
For SPA 2

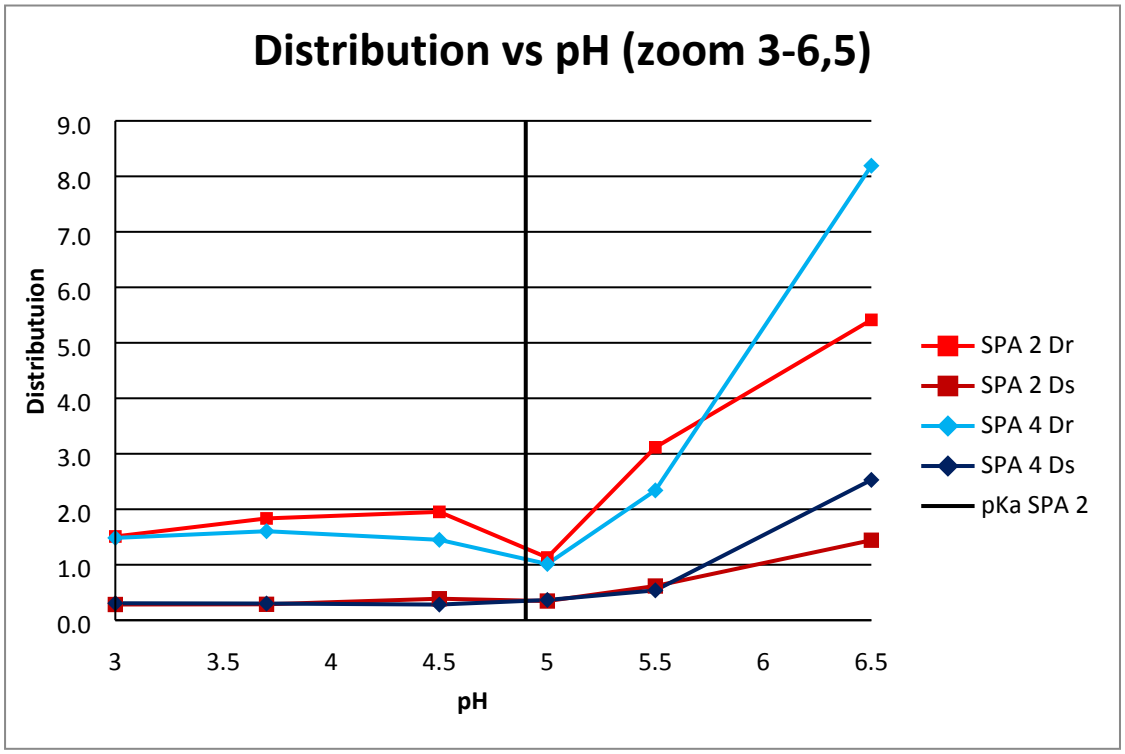
pH	ee% (aq)	D_R	D_S	α_{op}
3	33	1.510	0.283	5.325
3.7	37	1.835	0.287	6.391
4.5	37	1.953	0.388	5.034
5	57	1.130	0.346	3.266
5.5	43	3.116	0.617	5.053
6.5	45	5.413	1.442	3.754
7.5	40	4.156	1.134	3.666
8.4	47	8.279	2.429	3.409
9.6	37	14.988	6.306	2.377
10.6	23	9.396	5.577	1.685

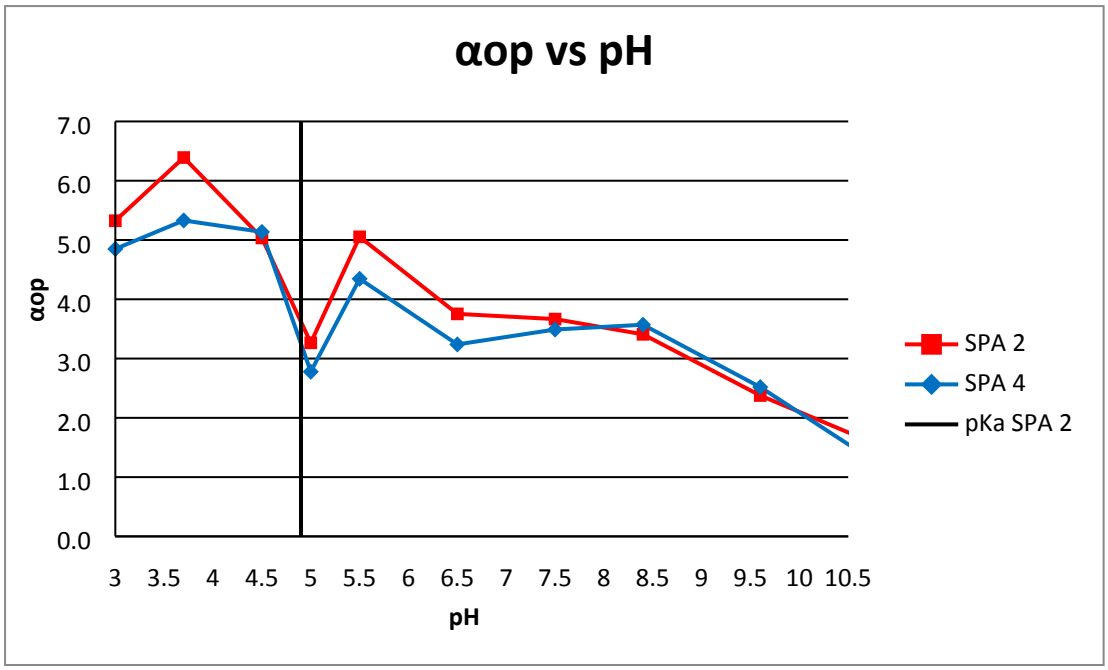
For SPA 4

pH	ee% (aq)	D_R	D_S	α_{op}
3	32	1.484	0.306	4.849
3.7	33	1.604	0.301	5.330
4.5	34	1.449	0.282	5.136
5	60	1.014	0.365	2.778
5.5	37	2.340	0.539	4.346
6.5	47	8.192	2.529	3.239
7.5	37	3.064	0.878	3.490
8.4	50	30.092	8.428	3.571
9.6	40	19.695	7.822	2.518
10.6	16	8.026	5.551	1.446



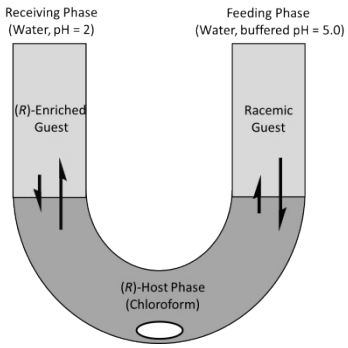

Distribution vs pH
Distributuion
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8 8.5 9 9.5 10 10.5
pH
SPA 2 Dr
SPA 2 Ds
SPA 4 Dr
SPA 4 Ds


Distribution vs pH (zoom 3-6,5)
Distributuion
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
3 3.5 4 4.5 5 5.5 6 6.5
pH
SPA 2 Dr
SPA 2 Ds
SPA 4 Dr
SPA 4 Ds
pKa SPA 2



U-tube

U-tube experiments where run on **11** according to GP 2.



With 2 mM feeding phase

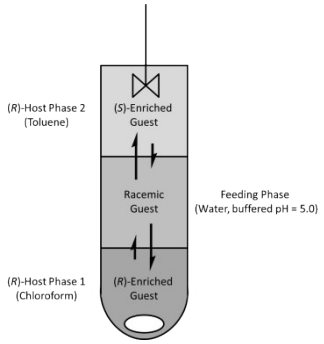
Aliquot	Extraction Time	ee% Receiving Phase
1	1 h	41
2	2 h	35
3	3 h	29
4	72 h	9

With 20 mM feeding phase

Aliquot	Extraction Time	ee% Receiving Phase
1	10 min	50
2	20 min	52
3	1 h	52
4	2 h	55
5	3 h	50
6	4 h	47
7	24 h	29

Tri-phase reactor

Tri-phase experiments where run on **11** according to GP 3.



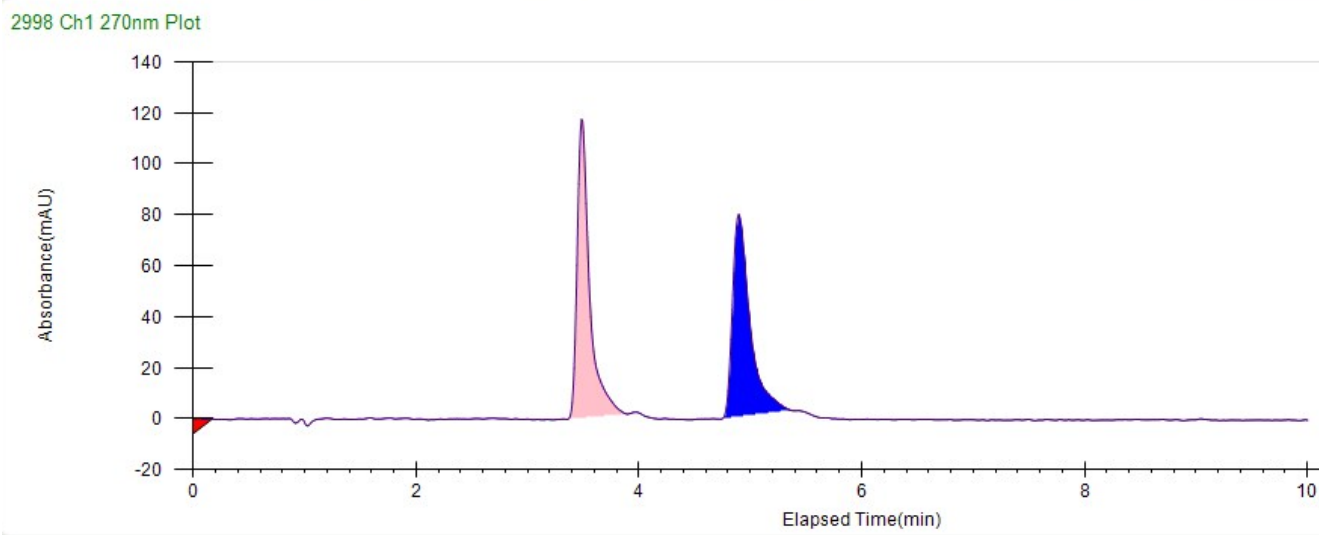
Solvent	ee% (aq)
(*R*)-host phase 1	41
(*R*)-host phase 2	-48

A control back-extraction was run to measure how much 11 could be recovered from the organic phase by acidic wash. This showed that over 98% of **11** present in the organic phase could be recuperated making the observed HPLC values reliable.

6. Spectroscopic data

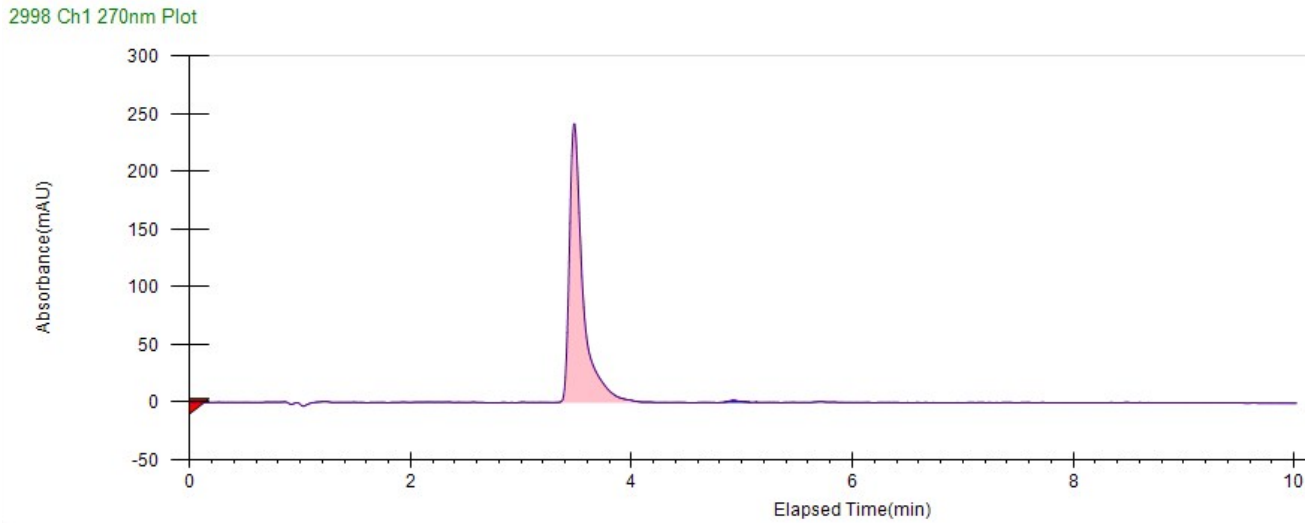
SFC traces

Racemic Spinol.



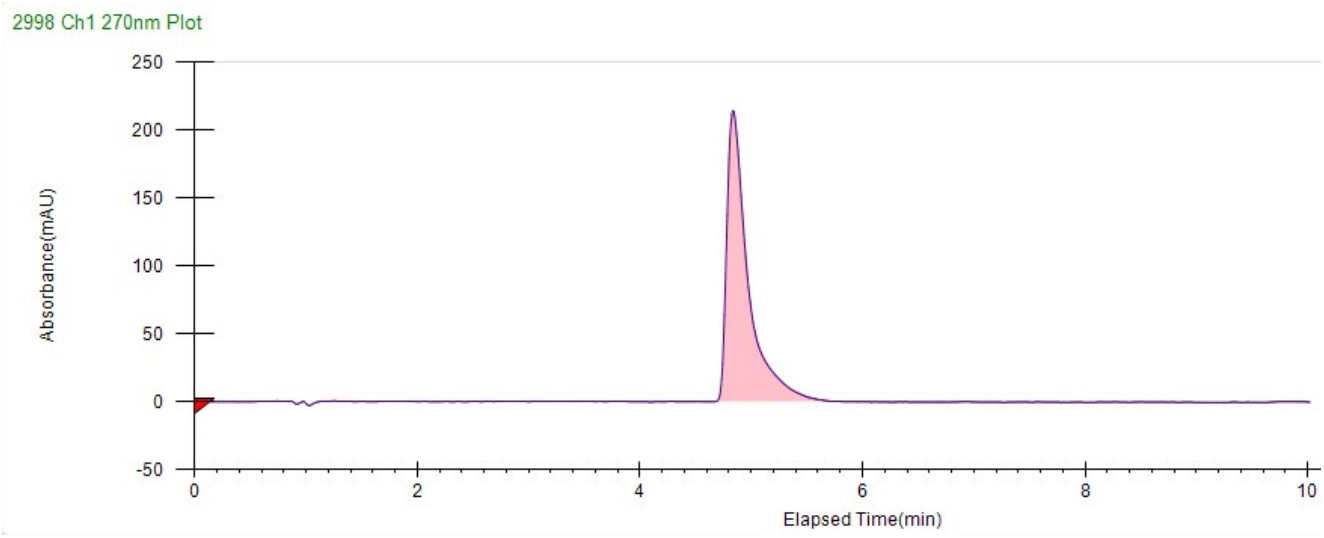
Peak Name	Area Percent	Area	Retention Time	Height
Peak1	51.2775	899.1879	3.48 min	117.1581
Peak2	48.7225	854.3828	4.89 min	79.1378

(R)-Spinol



Peak Name	Area Percent	Area	Retention Time	Height
Peak1	99.2586	2044.3708	3.48 min	241.4377
Peak2	0.7414	15.2711	4.92 min	1.7468

(S)-Spinol



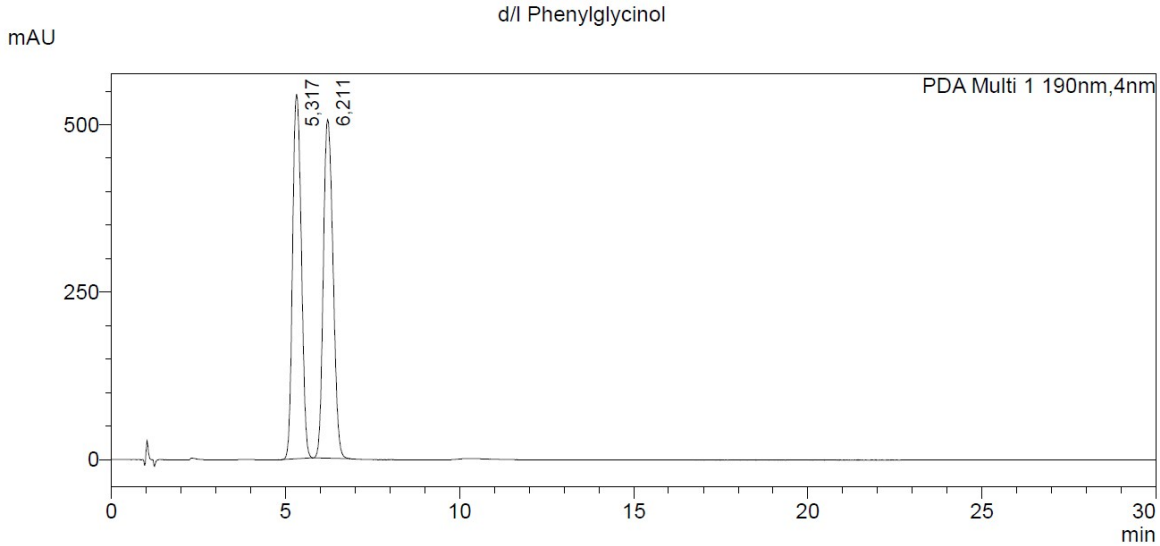
Peak Name	Area Percent	Area	Retention Time	Height
Peak1	100	2861.7142	4.83 min	214.2427

HPLC traces

Only Key Traces for each compound are shown. Broad peak at approximatively 50 min is the phosphate buffer.

11: Phenylglycinol

Racemic phenylgycinol

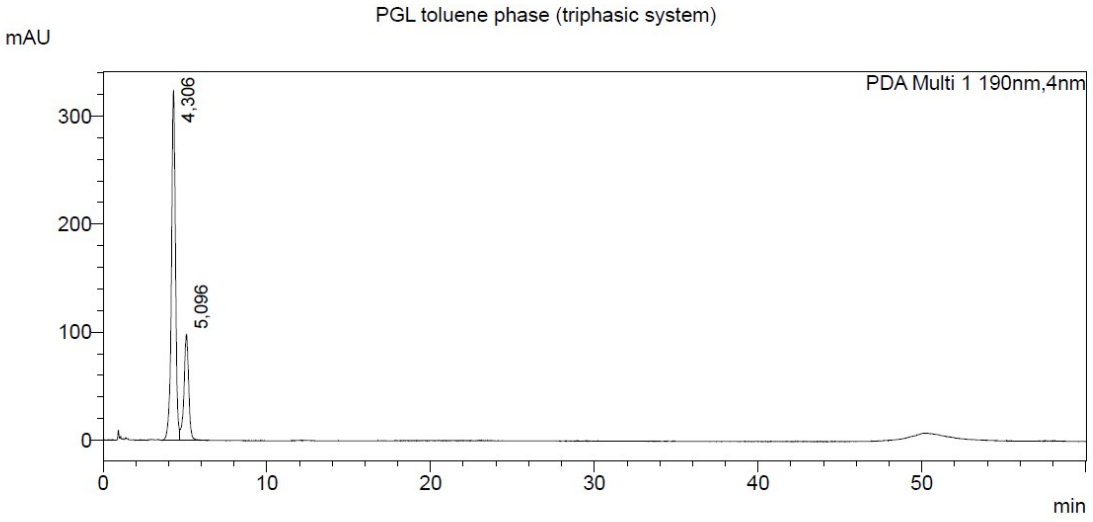


<Peak Table>

PDA Ch1 190nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5,317	9491796	543615	49,273		M	
2	6,211	9771870	505205	50,727		M	
Total		19263665	1048820				

Triphasic resolution system, (*R*)-host phase 2

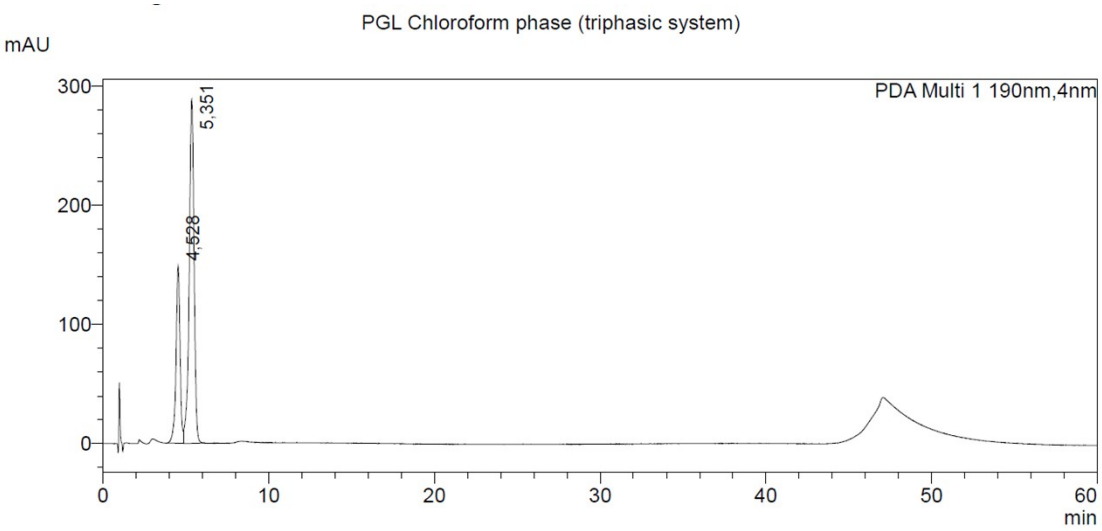


<Peak Table>

PDA Ch1 190nm

Peak#	Ret. Time	Area	Height	Area%
1	4,306	5565733	323060	74,233
2	5,096	1931890	97967	25,767
Total		7497623	421027	100,000

Triphasic resolution system, (*R*)-host phase 1

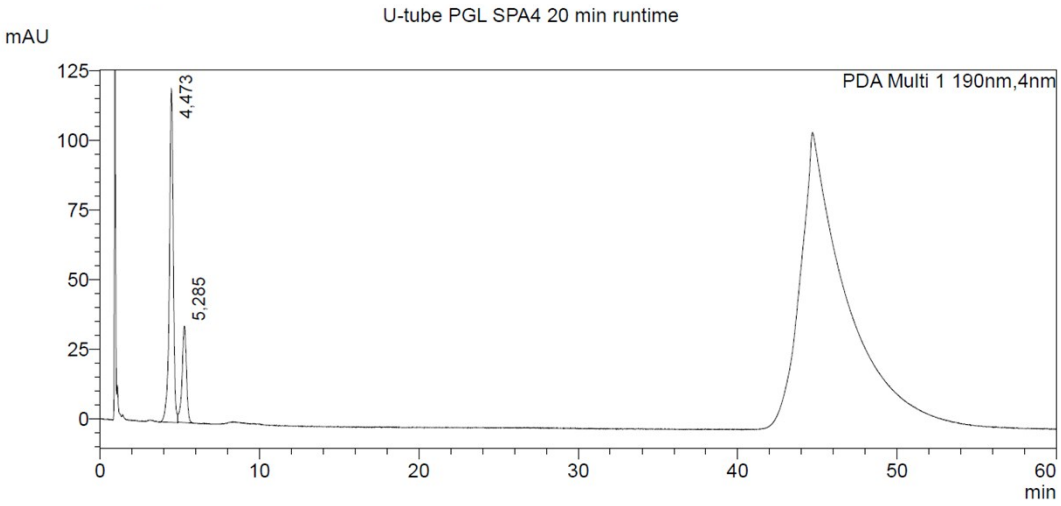


<Peak Table>

PDA Ch1 190nm

Peak#	Ret. Time	Area	Height	Area%
1	4,528	2515577	148818	29,935
2	5,351	5887977	288990	70,065
Total		8403555	437808	100,000

U-tube receiving phase (pH = 1,5)



<Peak Table>

PDA Ch1 190nm

Peak#	Ret. Time	Area	Height	Area%
1	4,473	2023406	119879	75,127
2	5,285	669910	34718	24,873
Total		2693316	154597	100,000

NMR