Supplementary Information

Convergent and enantioselective syntheses of cytosolic phospholipase $\text{A}_2\alpha$ inhibiting $N$-(1-indazol-1-ylpropan-2-yl)carbamates

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2. Synthesis and characterization data of compound 2 S7
3. NMR-spectra of new compounds S12
4. Chiral separation of 4, (S)-4 and (R)-4 S33
1. Synthesis and characterization data of compound 4

![Chemical structures and reactions]

**1-Acetylindazole-5-carboxylic acid (6)**
A mixture of indazole-5-carboxylic acid (5) (2.2 g, 13.6 mmol) and acetic anhydride (44 ml) was heated under reflux for 2 h. After cooling overnight a solid precipitated, which was filtered off, washed with a mixture of diethyl ether and petroleum ether (1:1, v/v) and dried (2.33 g, 84%); mp 265-266 °C; 1H NMR (DMSO-D6): δ 2.73 (s, 3H), 8.17 (dd, 1H, J = 8.7 Hz and 1.6 Hz), 8.36 (d, 1H, J = 8.7 Hz), 8.50 – 8.52 (m, 1H), 8.58 – 8.59 (m, 1H); MS (EI): m/z (%) 204 (10) M⁺, 162 (100), 145 (51).

**tert-Butyl 1-acetylindazole-5-carboxylate (7)**
A solution of tert-butyl 2,2,2-trichloroacetimidate (4.97 g, 22.7 mmol) in dry cyclohexane (15 mL) was added dropwise under nitrogen to a solution of 6 (2.32 g, 11.4 mmol) in dry THF (30 mL). After addition of BF₃-etherate (227 µL), the mixture was stirred at room temperature for 2 h, treated with aqueous NaHCO₃-solution (5%) and
extracted exhaustively with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated. The residue was chromatographed on silica gel (hexane/ethyl acetate, 19:1) to yield 7 as a solid (2.62 g, 89%); mp 138-139 °C; ¹H NMR (CDCl₃): δ 1.63 (s, 9H), 2.80 (s, 3H), 8.17 – 8.21 (m, 2H), 8.41 – 8.42 (m, 1H), 8.44 – 8.47 (m, 1H); MS (EI): m/z (%) 260 (15) M⁺, 204 (50), 162 (100), 145 (73).

**tert-Butyl indazole-5-carboxylate (8)**
A solution of 7 (2.47 g, 9.49 mmol) in ethanol (100 mL) was treated with 1 M aqueous NaOH (40 mL). The mixture was stirred for at room temperature for 1 h. Then water was added and the pH value was adjusted to 4-5. The mixture was extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated to yield 8 as a solid (2.04 g, 98%); mp 156-157 °C; ¹H NMR (CDCl₃): δ 1.63 (s, 9H), 7.59 (d, 1H, J = 8.9 Hz), 8.11 (dd, 1H, J = 8.9 Hz and 1.5 Hz), 8.24 – 8.27 (m, 1H), 8.51 – 8.53 (m, 1H); MS (EI): m/z (%) 218 (25) M⁺, 162 (100), 145 (100).

**tert-Butyl 1-(oxiran-2-ylmethyl)indazole-5-carboxylate (9)**
To 8 (2.38 g, 10.9 mmol), powdered KOH (88%ig) (1.39 g, 21.8 mmol) and tetra-butylammonium bromide (352 mg, 1.09 mmol) was added epichlorohydrine (10 mL). The mixture was stirred at room temperature for 4 h, transferred onto a silica gel column, and eluted with hexane/ethyl acetate (19:1, 9:1, 8:2) to give 9 as a solid (1.38 g, 46%); mp 68-69 °C; ¹H NMR (CDCl₃): δ 1.62 (s, 9H), 2.54 – 2.58 (m, 1H), 2.84 – 2.88 (m, 1H), 3.36 – 3.42 (m, 1H), 4.47 (dd, 1H, J = 15.2 Hz and 5.5 Hz), 4.74 (dd, 1H, J = 15.2 Hz and 3.3 Hz), 7.49 (d, 1H, J = 8.9 Hz), 8.04 (dd, 1H, J = 8.9 Hz and 1.5 Hz), 8.11 (s, 1H), 8.43 – 8.45 (m, 1H); MS (EI): m/z (%) 274 (29) M⁺, 217 (66), 162 (100), 145 (34).

**tert-Butyl 1-[2-hydroxy-3-(4-octylphenoxy)propyl]indazole-5-carboxylate (10)**
A mixture of 9 (1.35 g, 4.92 mmol), 4-octylphenol (1.22 g, 5.91 mmol) and 4-dimethylaminopyridine (120 mg, 0.98 mmol) was heated with stirring at 120 °C for 2 h. The warm melt was dissolved in a small amount of toluene, and the solution was chromatographed on silica gel (hexane/ethyl acetate, 9:1) to yield 10 as a solid (1.73 g, 73%); mp 100-101 °C; ¹H NMR (CDCl₃): δ 0.87 (t, 3H, J = 6.9 Hz), 1.21-1.33 (m, 10H), 1.52 – 1.59 (m, 2H), 1.62 (s, 9H), 2.49 – 2.56 (m, 2H), 3.87 (dd, 1H, J = 9.6 Hz and 6.0 Hz),
3.99 (dd, 1H, $J = 9.6$ Hz and 5.3 Hz), 4.47 – 4.53 (m, 1H), 4.60 (dd, 1H, $J = 14.3$ Hz and 6.1 Hz), 4.69 (dd, 1H, $J = 14.2$ Hz and 4.1 Hz), 6.77 – 6.82 (m, 2H), 7.05-7.10 (m, 2H), 7.46 (d, 1H, $J = 8.9$ Hz), 8.01 (dd, 1H, $J = 8.9$ Hz und 1.5 Hz), 8.13 – 8.15 (m, 1H), 8.44 – 8.46 (m, 1H); MS (EI): $m/z$ (%) 480 (5) M+, 275 (30), 219 (100), 201 (34).

tert-Butyl 1-[2-(methanesulfonyloxy)-3-(4-octylphenoxy)propyl]indazole-5-carboxylate (11)

To 10 (1.67 g, 3.47 mmol) cooled in an ice bath was added dropwise a solution of methanesulfonyl chloride (597 mg, 5.21 mmol) in dry pyridine (15 mL). The mixture was stirred at room temperature for 3.5 h, poured into a mixture of water (10 mL), concentrated HCl (1 mL) and ice (20 g), adjusted to pH 3 with 10% HCl, and extracted exhaustively with CH₂Cl₂. The combined organic layers were washed with 10% aqueous HCl twice, dried (Na₂SO₄) and concentrated. The residue was chromatographed on silica gel (hexan/ethyl acetate, 9:1) to yield 11 as an oil (1.92 g, 99 %); $^1$H NMR (CDCl₃): δ 0.87 (t, 3H, $J = 6.8$ Hz), 1.22 – 1.33 (m, 10H), 1.52-1.59 (m, 2H), 1.62 (s, 9H), 2.51 – 2.56 (m, 2H), 2.65 (s, 3H), 4.17 (dd, 1H, $J = 10.8$ Hz and 5.8 Hz), 4.29 (dd, 1H, $J = 10.9$ Hz and 4.0 Hz), 4.84 (d, 2H, $J = 5.7$ Hz), 5.28 – 5.35 (m, 1H), 6.78 – 6.83 (m, 2H), 7.09 (d, 2H, $J = 8.9$ Hz), 7.55 (d, 1H, $J = 8.9$ Hz), 8.05 – 8.09 (m, 1H), 8.15 (s, 1H), 8.44 – 8.46 (m, 1H); MS (EI): $m/z$ (%) 558 (1) M⁺, 501 (20), 297 (100), 201 (61).

tert-Butyl 1-[2-azido-3-(4-octylphenoxy)propyl]indazole-5-carboxylate (12)

A solution of 11 (2.05 g, 3.67 mmol) and trimethylsilyl azide (723 µl, 5.45 mmol) in dry THF (50 mL) were treated under nitrogen with a 1 M solution of tetrabutylammonium fluoride in THF (5.5 mL). The mixture was stirred under reflux for 72 h. Then the solvent was distilled off and the residue chromatographed on silica gel (hexan/ethyl acetate, 49:1, 9:1) to yield 12 as an oil (1.21 g, 65 %); $^1$H NMR (CDCl₃): δ 0.87 (t, 3H, $J = 6.9$ Hz), 1.23 – 1.33 (m, 10H), 1.53 – 1.60 (m, 2H), 1.62 (s, 9H), 2.51 – 2.57 (m, 2H), 4.05 (dd, 1H, $J = 10.0$ Hz and 5.8 Hz), 4.37 (dd, 1H, $J = 10.0$ Hz and 4.4 Hz), 4.32 – 4.39 (m, 1H), 4.59 (dd, 1H, $J = 14.4$ Hz and 7.4 Hz), 4.71 (dd, 1H, $J = 14.5$ Hz and 5.3 Hz), 6.81 – 6.85 (m, 2H), 7.09 (d, 2H, $J = 8.5$ Hz), 7.48 (d, 1H, $J = 8.9$ Hz), 8.05 (dd, 1H, $J = 8.9$ Hz and 1.5 Hz), 8.17 (s, 1H), 8.46 (s, 1H); MS (EI): $m/z$ (%) 505 (4) M⁺, 463 (41), 407 (35), 244 (75), 216 (100), 175 (37).
**tert-Butyl 1-[2-amino-3-(4-octylphenoxy)propyl]indazole-5-carboxylate (13)**

A mixture of 12 (668 mg, 1.32 mmol), palladium (10%) on charcoal (130 mg) and dry THF (30 mL) was stirred under a balloon filled with H₂ at room temperature for 6 h. The reaction mixture was filtered through Celite, and the solvent was evaporated to yield 13 as an oil (620 mg, 98 %); ¹H NMR (400 MHz, CDCl₃): δ 0.87 (t, 3H, J = 6.9 Hz), 1.24 – 1.33 (m, 10H), 1.53 – 1.58 (m, 2H), 1.62 (s, 9H), 2.50 – 2.55 (m, 2H), 3.77-3.81 (m, 1H), 3.87 (dd, 1H, J = 9.3 Hz and 5.1 Hz), 3.92 (dd, 1H, J = 9.3 Hz and 5.2 Hz), 4.51 (dd, 1H, J = 14.2 Hz and 6.8 Hz), 4.63 (dd, 1H, J = 14.2 Hz and 5.5 Hz), 6.78 – 6.82 (m, 2H), 7.04 – 7.09 (m, 2H), 7.43 – 7.46 (m, 1H), 7.98 (dd, 1H, J = 8.9 Hz and 1.5 Hz), 8.12 – 8.12 (m, 1H), 8.43 – 8.44 (m, 1H); MS (EI): m/z (%) 479 (21) M⁺, 274 (18), 248 (100).

**tert-Butyl 1-{3-(4-octylphenoxy)-2-[(phenoxycarbonyl)amino]propyl}indazole-5-carboxylate (14)**

A solution of 13 (74 mg, 0.15 mmol) and ethyl(diisopropyl)amine (31 mg, 0.18 mmol) in dry THF (7 mL) was treated dropwise under stirring with a solution of phenyl chloroformate (28 mg, 0.18 mmol) in dry THF (5 mL). The mixture was stirred at room temperature for 45 min. Then the solvent was distilled off and the residue purified by chromatography on silica gel (hexane/ethyl acetate, 9:1) to yield 14 as an oil (87 mg, 94 %); ¹H NMR (CDCl₃): δ 0.87 (t, 3H, J = 6.8 Hz), 1.23 – 1.32 (m, 10H), 1.52 – 1.59 (m, 2H), 1.61 (s, 9H), 2.50 – 2.56 (m, 2H), 3.81 (dd, 1H, J = 9.7 Hz and 6.2 Hz), 4.05 – 4.10 (m, 1H), 4.49 – 4.57 (m, 1H), 4.73 (dd, 1H, J = 14.4 Hz and 5.8 Hz), 4.87 (dd, 1H, J = 14.4 Hz and 5.1 Hz), 6.11 (d, 1H, J = 8.0 Hz), 6.82 (d, 2H, J = 8.5 Hz), 7.04 – 7.10 (m, 4H), 7.20 (t, 1H, J = 7.4 Hz), 7.33 – 7.38 (t, 2H, J = 7.9 Hz), 7.54 (d, 1H, J = 8.8 Hz), 7.99 (d, 1H, J = 8.8 Hz), 8.14 (s, 1H), 8.44 (s, 1H); MS (EI): m/z (%) 599 (2) M⁺, 506 (33), 450 (40), 244 (100), 201 (36).

**1-{3-(4-Octylphenoxy)-2-[(phenoxycarbonyl)amino]propyl}indazole-5-carboxylic acid (4)**

A solution of 14 (84 mg, 0.14 mmol) in dry CH₂Cl₂ (10 mL) cooled in an ice bath was treated with trifluoroacetic acid (1.3 g). The mixture was stirred at room temperature for 12 h, concentrated and chromatographed on silica gel (hexane/ethyl acetate/acetic acid, 8:2:0.1) to yield 4 as a solid (69 mg, 91 %); mp 183-184 °C; ¹H NMR (DMSO-Đ₆): δ 0.83 (t, 3H, J = 6.8 Hz), 1.17 – 1.28 (m, 10H), 1.45 – 1.54 (m, 2H), 2.45-2.49 (m, 2H),
4.02-4.11 (m, 2H), 4.25 – 4.34 (m, 1H), 4.60 (dd, 1H, $J = 14.4$ Hz and 7.5 Hz), 4.70 (dd, 1H, $J = 14.4$ Hz and 5.2 Hz), 6.78 (d, 2H, $J = 8.0$ Hz), 6.85 (d, 2H, $J = 8.5$ Hz), 7.09 (d, 2H, $J = 8.5$ Hz), 7.12 – 7.17 (m, 1H), 7.25 – 7.31 (m, 2H), 7.65 (d, 1H, $J = 8.8$ Hz), 7.95 (d, 1H, $J = 8.8$ Hz), 8.08 (d, 1H, $J = 8.5$ Hz), 8.21 (s, 1H), 8.38 (s, 1H); HRMS (ESI): (M-H) calculated: 542.2660, found: 542.2660.
2. Synthesis and characterization data of compound 2

**tert-Butyl 2,2-dimethyl-4-[(4-octyloxy)methyl]oxazolidine-3-carboxylate (29)**

To a solution of 4-octylphenol (1.40 g, 6.79 mmol) in dry DMF (20 mL) was added sodium hydride (60% dispersion in mineral oil) (0.260 g, 6.5 mmol). The mixture was stirred at room temperature for about 30 min until no further development of hydrogen could be observed. A solution of racemic tert-butyl 2,2-dimethyl-4-[(tosyloxy)methyl]oxazolidine-3-carboxylate (27) (2.50 g, 6.49 mmol) in DMF (20 mL) was added dropwise and the mixture was heated at 70°C for about 3 h. After addition of water (80 mL), the reaction mixture was exhaustively extracted with ethyl acetate. The combined organic phases were dried with Na$_2$SO$_4$, concentrated and chromatographed on silica gel (hexane/ethyl acetate, 19:1) to yield 29 as an oil (1.84 g, 68%). The $^1$H NMR and $^{13}$C NMR spectral data were identical with those of (S)-29. HRMS (APCI, direct probe) $[M+H]^+$ calculated: 420.3108, found: 420.3112.
**tert-Butyl [1-hydroxy-3-(4-octylphenoxy)propan-2-yl]carbamate (30)**

A solution of 29 (1.75 g, 4.17 mmol) in diethyl ether (12.5 mL) and methanol (12.5 mL) was treated with concentrated HCl (4 mL) and stirred at room temperature for 12 h. After evaporation of the solvent in vacuo the intermediate 2-amino-3-(4-octylphenoxy)propan-1-ol hydrochloride was yielded as a white solid (1.31 g, 99%); mp 181-182°C; ¹H NMR (400 MHz, DMSO-D₆): δ 0.80 – 0.91 (m, 3H), 1.16 – 1.33 (m, 10H), 1.46 – 1.58 (m, 2H), 2.48 – 2.52 (m, 2H), 3.41 – 3.52 (m, 1H), 3.59 – 3.76 (m, 2H), 4.06 (dd, J = 10.3 Hz and 6.4 Hz, 1H), 4.14 (dd, J = 10.3 Hz and 4.6 Hz, 1H), 5.39 (t, J = 5.1 Hz, 1H), 6.88 (d, J = 8.6 Hz, 2H), 7.11 (d, J = 8.5 Hz, 2H), 8.22 (s, broad, 3H); ¹³C NMR (101 MHz, DMSO-D₆): δ = 13.9, 22.1, 28.6, 28.8, 31.2, 31.2, 34.2, 51.7, 58.5, 65.2, 114.5, 129.2, 135.0, 155.9; HRMS (APCI, direct probe) [M+H]⁺ calculated: 280.2271, found: 280.2286.

To a solution of 2-amino-3-(4-octylphenoxy)propan-1-ol hydrochloride (1.30 g, 4.12 mmol) in diethyl ether (18 mL) and methanol (7 mL) were added triethylamine (1.06 g, 10.5 mmol) and di-tert-butyl dicarbonate (0.91 g, 4.17 mmol) at 0°C. The mixture was stirred for 12 h. Then the mixture was concentrated and chromatographed on silica gel (hexane/ethyl acetate, 7:3) to yield 30 as an oil (1.50 g, 96%). The ¹H NMR and ¹³C NMR spectral data were identical with those of (R)-30. HRMS (APCI, direct probe) [M+H]⁺ calculated: 380.2795, found: 380.2774.

**2-[(tert-Butoxycarbonyl)amino]-3-(4-octylphenoxy)propyl 4-methylbenzenesulfonate (31)**

A solution of 30 (1.45 g, 3.82 mmol) in CH₂Cl₂ (20 mL) was added dropwise to a solution of tosyl chloride (1.46 g, 7.66 mmol) and 4-dimethylaminopyridine (0.234 g, 1.92 mmol) in CH₂Cl₂ (20 mL). The mixture was treated with triethylamine (0.77 g, 7.61 mmol) and stirred for 12 h. The reaction mixture was washed three times with 1 M KHSO₄ and with brine, dried over Na₂SO₄, concentrated and chromatographed on silica gel (hexane/ethyl acetate, 9:1 to 8:2) to yield 31 as an oil (2.01 g, 99%). The ¹H NMR and ¹³C NMR spectral data were identical with those of (S)-31. HRMS (ESI+) [M+H]⁺ calculated: 534.2884, found: 534.2873.
Allyl 1-[2-[(tert-butoxycarbonyl)amino]-3-(4-octylphenoxy)propyl]indole-5-carboxylate (35)

To a solution of allyl indol-5-carboxylate (0.743 g, 3.69 mmol) in dry DMF (10 mL) was added sodium hydride (60% dispersion in mineral oil) (0.148 g, 3.70 mmol). The mixture was stirred at room temperature for about 30 min until no further development of hydrogen could be observed. A solution of 31 (1.80 g, 3.37 mmol) in DMF (10 mL) was added dropwise and the mixture was heated at 80°C for about 3 h. After addition of water (50 mL), the reaction mixture was extracted with ethyl acetate. The combined organic phases were dried with Na₂SO₄, concentrated and chromatographed on silica gel (hexane/ethyl acetate, 9:1) to yield 35 as a white solid (0.965 g, 51%); mp 104-105°C; ¹H NMR (400 MHz, CDCl₃): δ 0.85 – 0.92 (m, 3H), 1.21 – 1.36 (m, 10H), 1.46 (s, 9H), 1.52 – 1.64 (m, 2H), 2.51 – 2.60 (m, 2H), 3.73 (dd, J = 9.7 Hz and 1.7 Hz, 1H), 3.87 (dd, J = 9.6 Hz and 3.7 Hz, 1H), 4.25 – 4.36 (m, 1H), 4.36 – 4.50 (m, 2H), 4.84 (dt, J = 5.4 Hz and 1.4 Hz, 2H), 5.10 (d, J = 8.4 Hz, 1H), 5.28 (dq, J = 10.5 Hz and 1.3 Hz, 1H), 5.42 (dq, J = 17.2 Hz and 1.4 Hz, 1H), 6.00 – 6.14 (m, 1H), 6.56 (d, J = 3.2 Hz, 1H), 6.79 (d, J = 8.6 Hz, 2H), 7.06 – 7.14 (m, 3H), 7.51 (d, J = 8.8 Hz, 1H), 7.90 (dd, J = 8.7 Hz and 1.5 Hz, 1H), 8.39 (s, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 14.3, 22.8, 28.5, 29.4, 29.4, 29.6, 31.8, 32.0, 35.2, 46.5, 50.1, 65.3, 66.2, 80.3, 103.7, 109.4, 114.4, 117.8, 121.8, 123.6, 124.1, 128.2, 129.6, 129.9, 132.9, 136.3, 139.1, 155.4, 156.1, 167.4; HRMS (APCI, direct probe) [M+H]⁺ calculated: 563.3479, found: 563.3522.

Allyl 1-[2-amino-3-(4-octylphenoxy)propyl]indole-5-carboxylate (36)

A solution of 35 (0.750 g, 1.33 mmol) in CH₂Cl₂ (15 mL) was treated with trifluoroacetic acid (2 mL) and stirred at room temperature for 2 h. Then the reaction mixture was evaporated and the residue was treated with ethyl acetate and washed with 2 M aqueous NaOH solution. The aqueous layer was extracted three times with ethyl acetate. The combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure to yield 36 as an oil (0.611 g, 99%). ¹H NMR (400 MHz, DMSO-D₆): δ 0.77 – 0.88 (m, 3H), 1.13 – 1.31 (m, 10H), 1.49 (p, J = 7.1 Hz, 2H), 2.45 (d, J = 7.7 Hz, 2H), 3.39 (p, J = 5.7 Hz, 1H), 3.74 (d, J = 5.4 Hz, 2H), 4.19 (dd, J = 14.2 Hz and 6.8 Hz, 1H), 4.34 (dd, J = 14.2 Hz and 5.8 Hz, 1H), 4.77 (dt, J = 5.3 Hz and 1.5 Hz, 2H), 5.25 (dq, J = 10.5 Hz and 1.5 Hz, 1H), 5.38 (dq, J = 17.2 Hz and 1.7 Hz, 1H), 6.05 (ddt, J = 17.3 Hz, 10.6 Hz and 5.3 Hz, 1H), 6.60 (d, J = 3.1 Hz, 1H), 6.80 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 3.2 Hz, 1H), 7.57 (d, J = 8.7 Hz, 1H),
7.71 (dd, \( J = 8.7 \) Hz and 1.7 Hz, 1H), 8.26 (d, \( J = 1.6 \) Hz, 1H); \(^{13}\)C NMR (101 MHz, DMSO-\( D_6 \)): \( \delta = 13.9, 22.1, 28.6, 28.7, 28.8, 31.2, 31.3, 34.2, 49.3, 51.0, 64.5, 70.2, 102.3, 110.0, 114.3, 117.5, 120.3, 121.9, 123.0, 127.6, 129.1, 131.3, 133.1, 134.5, 138.7, 156.4, 166.3; HRMS (APCI, direct probe) [\( M+H \)]\(^{+}\) calculated: 463.2955, found: 463.2968

**Allyl 1-{3-(4-octylphenoxy)-2-[(phenoxy carbonyl)amino]propyl}indole-5-carboxylate (37)**

To a solution of 36 (0.300 g, 0.65 mmol) in dry THF (10 mL) was added dropwise at 0 °C triethylamine (99 µL, 0.71 mmol) followed by phenyl chloroformate (90 µL, 0.72 mmol). The mixture was stirred at room temperature for 2 h, concentrated and chromatographed on silica gel (hexane/ethyl acetate, 9:1 to 8:2) to yield 37 as a solid (0.213 g, 56%); mp 93-94°C; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 0.86 – 0.93 \) (m, 3H), 1.23 – 1.38 (m, 10H), 1.59 (p, \( J = 7.4 \) Hz, 2H), 2.58 (t, \( J = 7.6 \) Hz, 2H), 3.84 (dd, \( J = 9.7 \) Hz and 2.5 Hz, 1H), 3.98 (dd, \( J = 9.8 \) Hz and 3.5 Hz, 1H), 4.39 – 4.61 (m, 3H), 4.84 (dt, \( J = 5.5 \) Hz and 1.5 Hz, 2H), 5.28 (dq, \( J = 10.5 \) Hz and 1.4 Hz, 1H), 5.43 (dq, \( J = 17.2 \) Hz and 1.6 Hz, 1H), 5.69 (d, \( J = 8.1 \) Hz, 1H), 6.07 (ddt, \( J = 17.2 \) Hz, 10.5 Hz and 5.5 Hz, 1H), 6.59 (dd, \( J = 3.2 \) Hz and 0.8 Hz, 1H), 6.84 (d, \( J = 8.5 \) Hz, 2H), 7.08 – 7.18 (m, 5H), 7.19 – 7.28 (m, 1H), 7.39 (dd, \( J = 8.5 \) Hz and 7.3 Hz, 2H), 7.55 (d, \( J = 8.7 \) Hz, 1H), 7.91 (dd, \( J = 8.7 \) Hz and 1.6 Hz, 1H), 8.42 (d, \( J = 1.6 \) Hz, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta = 14.3, 22.8, 29.4, 29.4, 29.6, 31.8, 32.0, 35.2, 46.2, 50.8, 65.3, 65.9, 103.9, 109.4, 114.4, 117.9, 121.7, 122.0, 123.7, 124.2, 125.8, 128.2, 129.6, 129.7, 129.8, 132.8, 136.6, 139.0, 150.8, 154.5, 156.0, 167.3; HRMS (ESI+) [\( M+H \)]\(^{+}\) calculated: 583.3166, found: 583.3137

**1-{3-(4-Octylphenoxy)-2-[(phenoxy carbonyl)amino]propyl}indole-5-carboxylic acid (2)**

To a solution of 37 (0.170 g, 0.29 mmol) in dry THF (20 mL) was added under nitrogen tetrakis(triphenylphosphine)palladium(0) (0.034 g, 0.029 mmol). Nitrogen was bubbled through the solution for 10 min. Then acetic acid (0.5 mL) was added. The mixture was stirred at room temperature for 6 h, concentrated and chromatographed on silica gel (hexane/ethyl acetate/acetic acid, 8:2:0.2) to yield 2 as a solid (0.132 g, 83%); mp 160-
161°C. The $^1$H NMR and $^{13}$C NMR spectral data were identical with those already published for 2. HRMS (ESI+) $[M+H]^+$ calculated: 543.2853, found: 543.2875
3. NMR-spectra of new compounds

1-[3-(4-Octylophenoxy)-2-[(phenoxy carbonyl)amino]propyl]indole-5-carboxylic acid (2)
1-[3-(4-Octylphenoxy)-2-[(phenoxy-carbonyl)amino]propyl]indazole-5-carboxylic acid (4)
Allyl indazole-5-carboxylate (15)
Allyl 1-(oxiran-2-ylmethyl)indazole-5-carboxylate (16)
Allyl 1-(3-azido-2-hydroxypropyl)indazole-5-carboxylate (17)
Allyl 1-(3-amino-2-hydroxypropyl)indazole-5-carboxylate hydrochloride (18)
Allyl 1-{3-[(tert-butoxycarbonyl)amino]-2-hydroxypropyl}indazole-5-carboxylate (19)
Allyl 1-\{(tert-butoxycarbonyl)amino\}-2-(tosyloxy)propyl\}indazole-5-carboxylate (20)
Allyl 1-[[1-(tert-butoxycarbonyl)aziridine-2-yl]methyl]indazole-5-carboxylate (21)
Allyl 1-{2-[(tert-butoxycarbonyl)amino]-3-(4-octyloxy)propyl}indazole-5-carboxylate (22)
Allyl 1-[2-amino-3-(4-octylphenoxy)propyl]indazole-5-carboxylate (23)
Allyl 1-{3-(4-octylphenoxy)-2-[(phenoxycarbonyl)amino]propyl}indazole-5-carboxylate (24)
tert-Butyl 2,2-dimethyl-4-[(4-octyloxy)methyl]oxazolidine-3-carboxylate (29)
**t*ert-Butyl (1-hydroxy-3-(4-octylphenoxy)propan-2-yl)carbamate (30)**

<table>
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S25
2-[(tert-Butoxycarbonyl)amino]-3-(4-octylphenoxy)propyl 4-methylbenzenesulfonate (31)
(S)-tert-Butyl 4-(((S)-(allyloxy)carbonyl)indazole-1-yl)methyl)-2,2-dimethyloxazolidine-3-carboxylate ((S)-32)
(S)-Allyl 1-[2-((tert-butoxycarbonyl)amino)-3-hydroxypropyl]indazole-5-carboxylate ((S)-33)
$(S)$- Allyl 1-\([2-\{(\text{tert-butoxycarbonyl})\text{amino}\]-3-(tosyloxy)propyl\}indazole-5-carboxylate $(S)$-34
Allyl 1-[(tert-butoxycarbonyl)amino]-3-(4-octylphenoxy)propyl]indole-5-carboxylate (35)
Allyl 1-[2-amino-3-(4-octylphenoxy)propyl]indole-5-carboxylate (36)
Allyl 1-{3-(4-octylphenoxy)-2-[(phenoxycarbonyl)amino]propyl}indole-5-carboxylate (37)
4. Chiral separation of 4, (S)-4 and (R)-4

1-[3-(4-Octyphenoxy)-2-[(phenoxy carbonyl) amino]propyl]indazole-5-carboxylic acid (4)
(S)-1-[3-(4-Octylophenoxy)-2-[(phenoxycarbonyl)amino]propyl]indazole-5-carboxylic acid ((S)-4)

Report date: 26.02.2014 16:11:19
Printed by: Wally Haneveld
Ident: TS0128
Analysis from: 23.01.2014 21:00:48
File: 14013315348
Run operator: Wally Haneveld
Analysis number: 15530
SAMPLE:
Vial number: 9
Volume: 20.0 µl
Dilution: 1.00
Amount: 1.0000
COLUMN:
Size: 2.0 x 60 mm
Number: 5.0 µm
ELUENT:
Flow: 1.00 mL/min
Temperature: 30.0°C
Pressure: 4.5 MPa

Quantitation method: Custom

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BÜCHROFF Chromatography GmbH
(R)-1-[3-(4-Octylphenoxy)-2-[(phenoxycarbonyl)amino]propyl]indazole-5-carboxylic acid ((R)-4)