Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Synthesis of Triphosphorous Bidentate Phosphine-Phosphoramidite Ligands and their Application in Highly Enantioselective Hydrogenation of *ortho*-Substituted Aryl Enamides

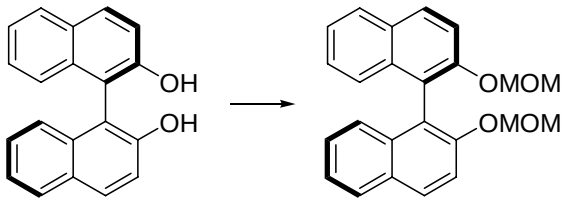
Weicheng Zhang and Xumu Zhang

Department of Chemistry, the Pennsylvania State University, University Park, PA 16802

All operations were carried out using standard Schlenk techniques unless mentioned otherwise. The degassed dry solvents are used for all experiments. Diphenylchlorophosphine, (1*S*, 1*S*′, 2*R*, 2*R*′)-Tangphos, and (*R*,*R*)-Et-DuPhos were purchased from Strem Inc., and all other chemicals were purchased from Aldrich or Acros Inc. The substrates were prepared according to literature.[1] NMR data were recorded on Bruker DPX-300, CDPX-300, and Avance-360 spectrometers. MS data were recorded on KRATOS mass spectrometer for LR-APCI and HR-APCI. Optical rotation was recorded on a Perkin-Elmer 241 polarimer. MM2 calculations were carried out with CAChe® program (CAChe Worksystem Pro version 6.1, Fujitsu Ltd.). Thin layer chromatography (TLC) was performed on EM reagents 0.25 mm silica 60-F plates. Column chromatography was performed using 200-400 mesh silica gel from Natland International Inc. Chiral GC analysis was carried out on Helwett-Parkard 6890 gas chromatography equipped with chiral capillary column (carrier gas: He at 1 mL/min). Chiral HPLC anaylsis was carried out on a Waters 600 chromatography at 25°C.

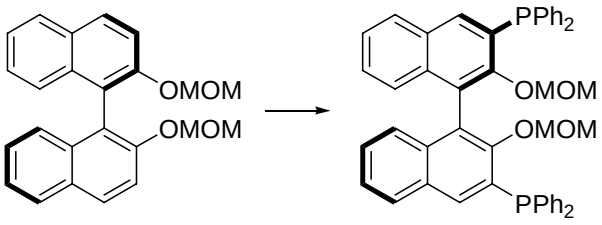
1. Synthesis and characterization of **1** (page S1-S4)

(a) (*R*)-2,2′-bis(methoxymethoxy)-1,1′-binaphthyl ((*R*)-BINOL-MOM)



The synthesis of (*R*)-BINOL-MOM followed literature procedure.[2]

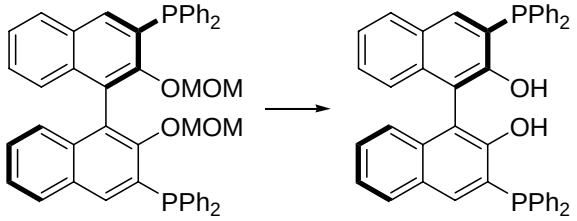
(b) (*R*)-2,2′-bis(methoxymethoxy)-3,3′-bis(diphenylphosphino)-1,1′-binaphthyl (**2**)



2

Toward a solution of BINOL-MOM (10 mmol, 3.744 g) in Et_2O (170 mL) charged into a flame-dried argon filled Schlenk flask was added *n*-BuLi (2.5M in hexane, 30 mmol, 12 mL) dropwise at room temperature, and stirred for 3 hours. THF (110 mL) was added and stirred for 1 hour. After the reaction mixture was cooled to 0°C, $ClPPh_2$ (30 mmol, 5.56 mL) was quickly added. The solution was stirred for 1 hour, and quenched with saturated aqueous NH_4Cl. The solvent was removed and the residue was dissolved in EtOAc and washed with water, brine, and dried with Na_2SO_4. After being concentrated, the product **2** was recrystallized from CH_2Cl_2/hexane as light yellow crystals. (5.18g, yield 70%) ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 2.75 (s, 6H), 4.68 (dd, 4H, J_1 = 18 Hz, J_2 = 3 Hz), 7.23-7.44 (m, 28H), 7.62-7.65 (d, 2H, J = 9 Hz). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 56.85, 56.91, 99.13, 99.23, 125.47, 126.41, 127.23, 128.44, 128.94, 128.96, 129.94, 129.06, 129.34, 129.39, 131.20, 133.22, 134.38, 134.49, 134.65, 134.76, 134.76, 136.88, 155.58. ^{31}P NMR (146 MHz, CD_2Cl_2): δ = -14.69 (s). HRMS ($M+Na^+$): calculated: 765.2300; found: 765.2279.

(c) (*R*)-3,3′-bis(diphenylphosphino)-1,1′-binaphthyl-2,2′-diol (**3**)

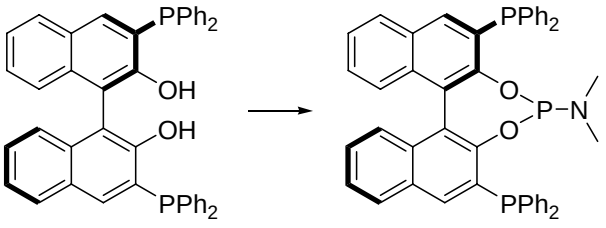


2 **3**

In a flame-dried argon filled Schlenk flask was charged **2** (400 mg, 0.539 mmol), MeOH (50 mL), and 10 drops of concentrated HCl (aqueous 35 wt%). The reaction mixture was stirred at 60°C for 1 hour. Then the solvent was removed, and the residue

was dissolved in EtOAc. Degassed saturated $NaHCO_3$ solution and brine were used to washed the solution. Then it was dried with Na_2SO_4. After being concentrated, it was purified through a short column of silica gel (eluent CH_2Cl_2) to afford the product **3** as white powder. (278 mg, 79% yield) ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 5.49 (s, 2H), 7.11-7.13 (m, 2H), 7.29-7.32 (m, 4H), 7.40-7.46 (m, 22H), 7.63-7.67 (m, 2H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 111.68, 111.70, 124.17, 124.47, 128.05, 128.87, 128.93, 129.03, 129.12, 129.43, 129.52, 129.74, 129.76, 134.08, 134.18, 134.30, 134.35, 134.56, 134.87, 153.88. ^{31}P NMR (146 MHz, CD_2Cl_2): δ = -17.43 (s). HRMS ($M+H^+$): calculated: 655.1956; found: 655.1926.

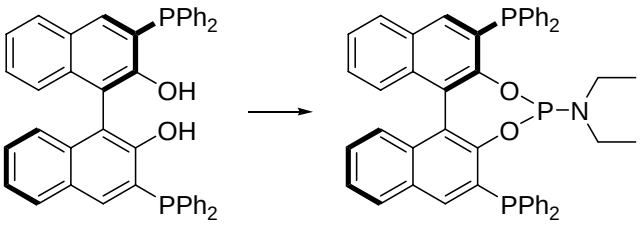
(d) (*R*)-*O*,*O*′-(3,3′-bis(diphenylphosphino)-1,1′-dinaphthyl-2,2′-diyl)-*N*,*N*-dimethylphosphorous amidite (**1a**)



3 **1a**

In a flame-dried argon filled Schlenk tube was charged **3** (563 mg, 0.86 mmol) and toluene (20 mL). Then hexamethylphosphorous triamide (HMPT, 0.2 mL, 1.12 mmol) was added. The reaction mixture was stirred at 110°C overnight. After being concentrated, the product was purified through a silica gel column (EtOAc/hexane = 1:15) to afford the product **1a** as white powder. (550.4 mg, yield 88%) ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 2.54 (d, J = 9.3 Hz), 7.24-7.46 (m, 28H), 7.61-7.68 (m, 2H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 35.77, 35.86, 36.01, 36.14, 122.63, 128.68, 128.74, 128.82, 128.84, 128.91, 128.98, 129.05, 129.08, 129.10, 129.20, 133.52, 133.78, 133.97, 134.23, 135.04, 135.32. ^{31}P NMR (146 MHz, CD_2Cl_2): δ = -16.98 (d, $J_{P\text{-}P}$ = 17.9 Hz), -12.62 (d, $J_{P\text{-}P}$ = 4.5 Hz), 149.53 (d, $J_{P\text{-}P}$ = 16.9 Hz). HRMS ($M+H^+$): calculated: 728.2037; found: 728.2014.

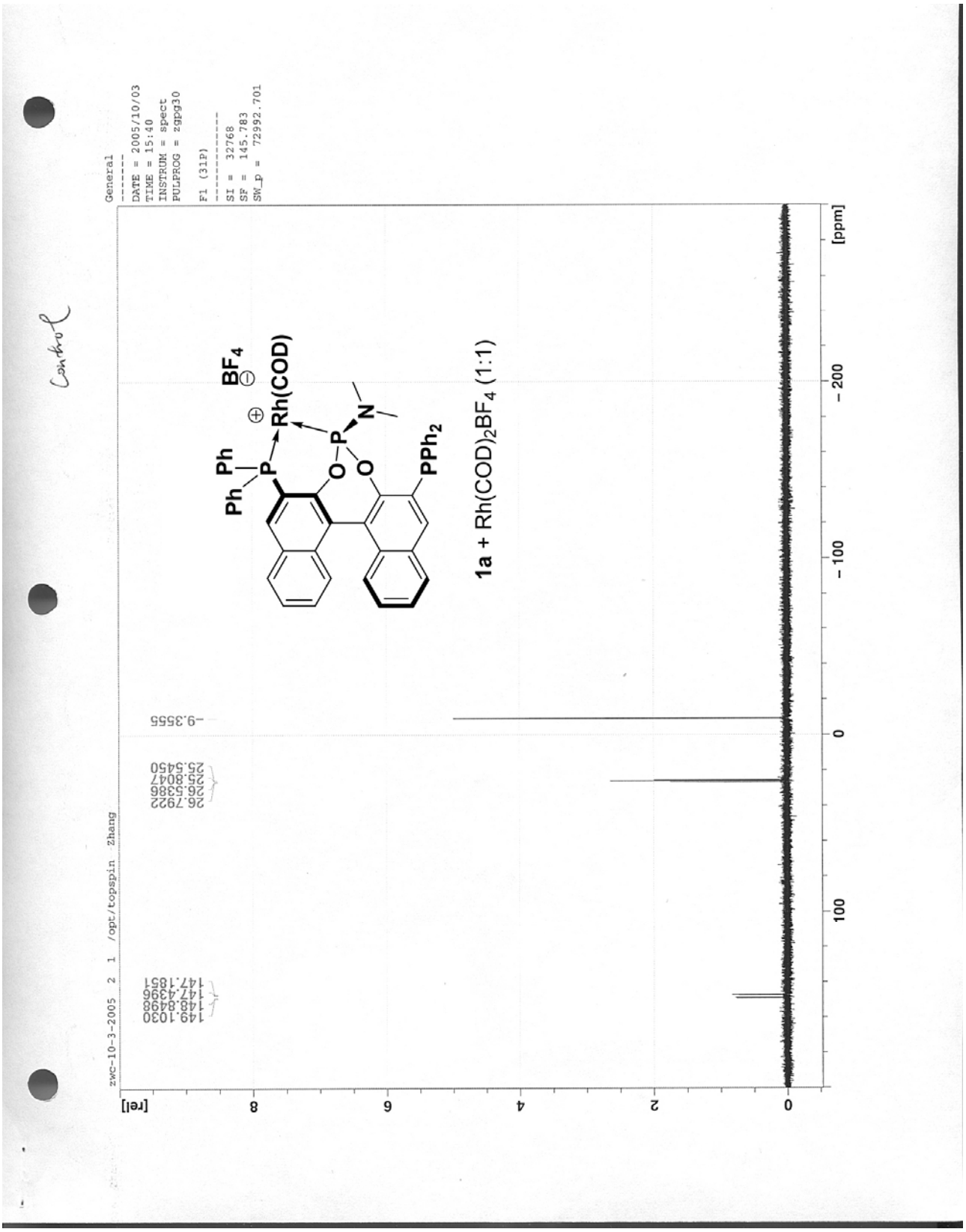
(e) (*R*)-*O*,*O*′-(3,3′-bis(diphenylphosphino)-1,1′-dinaphthyl-2,2′-diyl)-*N*,*N*-diethylphosphorous amidite (**1b**)



3 **1b**

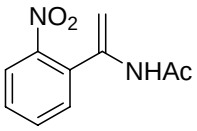
In a flame-dried argon filled Schlenk tube was charged **3** (253 mg, 0.39 mmol) and toluene (10 mL). Then hexaethylphosphorous triamide (HEPT, 0.15 mL, 0.54 mmol) was added. The reaction mixture was stirred at 110°C overnight. After being concentrated, the product was purified through a silica gel column (EtOAc/hexane = 1:10) to afford the product **1b** as white powder. (234 mg, yield 80%) ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 0.92 (t, J = 7.1 Hz), 2.95 (m, 4H), 7.22-7.51 (m, 28H), 7.59-7.67 (m, 2H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 15.39, 15.44, 15.49, 40.27, 40.32, 40.56, 40.61, 124.87, 128.64, 128.73, 128.77, 128.83, 128.87, 129.03, 129.06, 129.09, 129.13, 133.55, 133.82, 134.00, 134.28, 134.99, 135.27, 137.07. ^{31}P NMR (146 MHz, CD_2Cl_2): δ = -13.05 (d, $J_{P\text{-}P}$ = 30.3 Hz), -11.43 (s), 150.57 (d, $J_{P\text{-}P}$ = 30.1 Hz). HRMS ($M+H^+$): calculated: 756.2350; found: 756.2328.

2. ^{31}P-NMR spectrum of [Rh(COD)**1a**]BF_4 (page S5)



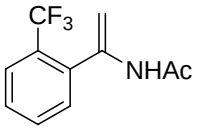
3. Characterization of new compounds **4l**, **4m**, **5l**, and **5m** (page S6-S7)

(1) *N*-(1-(2-nitrophenyl)ethyl)acetamide **4l**



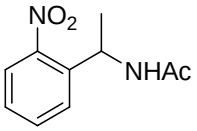
^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.94 (s, 3H), 4.76 (s, 1H), 5.54 (s, 1H), 7.31 (s, 1H), 7.48-7.54 (m, 2H), 7.60-7.65 (m, 2H), 7.87-7.90 (m, 1H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 23.93, 104.68, 124.31, 129.72, 132.13, 133.41, 133.63, 139.26, 148.48, 168.89. HRMS ($M+Na^+$): calculated: 229.0589, found: 229.0571.

(2) *N*-(1-(2-trifluruomethylphenyl)ethyl)acetamide **4m**



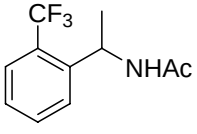
^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.99 (s, 3H), 4.70 (s, 1H), 5.90 (s, 1H), 6.80 (s, 1H), 7.47-7.71 (m, 4H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 24.26, 103.88, 122.68, 126.31, 126.48, 126.55, 126.62, 126.69, 128.23, 128.63, 129.02, 131.98, 132.33, 137.81, 137.84, 139.49, 169.04. HRMS ($M+Na^+$): calculated: 252.0612, found: 252.0614.

(3) *N*-Acetyl-1-(2-nitrophenyl)ethylamine **5l**



^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.49 (d, *J* = 7.0 Hz, 3H), 1.90 (s, 3H), 5.37-5.42 (m, 1H), 6.38 (s, br, 1H), 7.39-7.42 (m, 1H), 7.50-7.60 (m, 2H), 7.81-7.85 (m, 1H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 21.75, 23.09, 46.22, 124.78, 128.23, 128.29, 133.68, 139.63, 139.64, 169.61. $[\alpha]_D^{20}$ = -117.2° (GC 98.2% ee, *c* 0.85, $CHCl_3$). HRMS ($M+ Na^+$): calculated: 231.0746, found: 231.0751.

(4) *N*-Acetyl-1-(2-trifluruomethylphenyl)ethylamine **5m**

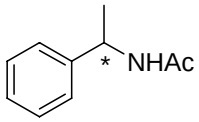


^{1}H NMR (300 MHz, CD_2Cl_2): δ = 1.40 (d, *J* = 6.9 Hz, 3H), 1.90 (s, 3H), 5.31-5.35 (m, 1H), 6.60 (s, br, 1H), 7.33-7.39 (m, 1H), 7.54-7.56 (m, 2H), 7.62-7.65 (m, 1H). ^{13}C NMR

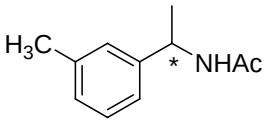
(75 MHz, CD_2Cl_2): δ = 23.22, 23.37, 46.12, 46.15, 46.18, 46.22, 126.11, 126.19, 126.27, 126.35, 126.72, 127.21, 127.44, 127.54, 132.81, 132.82, 144.19, 144.21, 169.50. $[\alpha]_D^{20}$ = +71.7° (GC 94.2% ee, *c* 0.71, $CHCl_3$). HRMS ($M+Na^+$): calculated: 254.0769, found: 254.0774.

4. Chiral GC and HPLC conditions for the determination of ee (page S7-S9)

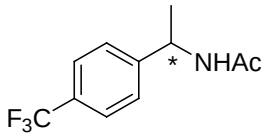
(1) *N*-Acetyl-1-phenylethylamine (**5a**): GC, β-dex 390, 150°C, t_S = 22.8 min, t_R = 23.8 min



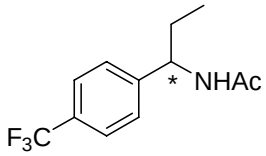
(2) *N*-Acetyl-1-(3-methylphenyl)ethylamine (**5b**): GC, β-dex 390, 140°C, t_S = 51.3 min, t_R = 54.9 min



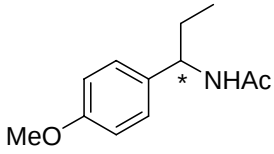
(3) *N*-Acetyl-1-(4-trifluoromethylphenyl)ethylamine (**5c**): GC, β-dex 390, 150°C, t_S = 30.8 min, t_R = 32.4 min



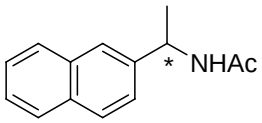
(4) *N*-Acetyl-1-(4-trifluoromethylphenyl)propylamine (**5d**): GC, β-dex 390, 160°C, t_S = 23.4 min, t_R = 24.7 min



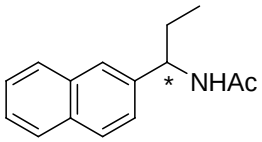
(5) *N*-Acetyl-1-(4-methoxyphenyl)propylamine (**5e**): HPLC, (*R*,*R*)-Poly Whelk-0 from Regis Technologies Inc., 1 mL/min, *i*PrOH/hexane = 90:10, t_S = 12.37 min, t_R = 35.78 min



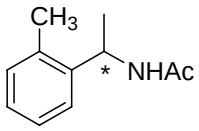
(6) *N*-Acetyl-1-(2-naphthyl)ethylamine (**5f**): HPLC, (*R*,*R*)-Poly Whelk-0 from Regis Technologies Inc., 1 mL/min, *i*PrOH/hexane = 70:30, t_S = 5.78 min, t_R = 50.03 min



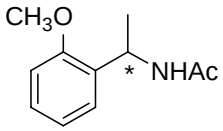
(7) *N*-Acetyl-1-(2-naphthyl)propylamine (**5g**): HPLC, (*R*,*R*)-Poly Whelk-0 from Regis Technologies Inc., 1 mL/min, *i*PrOH/hexane = 80:20, t_S = 6.82 min, t_R = 59.90 min



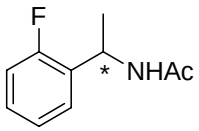
(8) *N*-Acetyl-1-(2-methylphenyl)ethylamine (**5h**): GC, γ-dex 225, 140°C, t_S = 54.6 min, t_R = 58.7 min



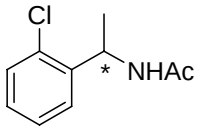
(9) *N*-Acetyl-1-(2-methoxyphenyl)ethylamine (**5i**): GC, γ-dex 225, 150°C, t_S = 45.2 min, t_R = 47.1 min



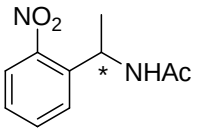
(10) *N*-Acetyl-1-(2-fluorophenyl)ethylamine (**5j**): GC, γ-dex 225, 150°C, t_S = 21.2 min, t_R = 26.8 min



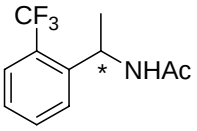
(11) *N*-Acetyl-1-(2-chlorophenyl)ethylamine (**5k**): GC, γ-dex 225, 150°C, t_S = 53.8 min, t_R = 62.5 min



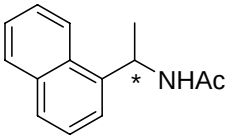
(12) *N*-Acetyl-1-(2-nitrophenyl)ethylamine (**5l**): GC, γ-dex 225, 170°C, t_{minor} = 48.8 min, t_{major} = 51.6 min



(13) *N*-Acetyl-1-(2-trifluromethylphenyl)ethylamine (**5m**): GC, γ-dex 225, 150°C, t_{minor} = 22.5 min, t_{major} = 23.9 min



(14) *N*-Acetyl-1-(1-naphthyl)ethylamine (**5n**): GC, γ-dex 225, 180°C, t_S = 54.9 min, t_R = 60.0 min



[1] (a) M. J. Burk, G. Casy, N. B. Johnson, *J. Org. Chem.* **1998**, *63*, 6084. (b) Z. Zhang, G. Zhu, Q. Jiang, D. Xiao, X. Zhang, *J. Org. Chem.* **1999**, *64*, 1774. (c) van den Berg, M.; Haak, R. M.; Minnaard, A. J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *Adv. Synth. Catal.* **2002**, *344*, 1003.
[2] M. Shi, C.-J. Wang, *Tetrahedron: Asymmetry* **2002**, *13*, 2161.