SUPPORTING INFORMATION

Enantioselective Rhodium-Catalyzed Addition of Arylboronic Acids to Trifluoromethyl Ketones

Sébastien L. X. Martina,[a] Richard B. C. Jagt,[a] Johannes G. de Vries,*[b] Ben L. Feringa,*[a] Adriaan J. Minnaard*[a]

[a] *Department of Organic and Molecular Inorganic Chemistry, Stratingh Institute, University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands*

[b] *DSM Pharmaceutical Products - Advanced Synthesis & Catalysis, P.O. box 18, 6160 MD Geleen, The Netherlands*

General remarks: All air- and moisture-sensitive manipulations were carried out under a dry nitrogen atmosphere using standard Schlenk techniques. ^{1}H NMR and ^{19}F NMR spectra were recorded on a Varian 400 (400 and 376 MHz, respectively). ^{13}C NMR spectra were recorded on a Varian 300 (75 MHz). Chemical shifts (δ) are quoted in ppm using residual solvent as internal standard (δ_C 77.16 and δ_H 7.26 for $CDCl_3$). For ^{19}F-NMR an external reference was used (α,α,α-trifluorotoluene: -63.8 ppm). Mass spectra (HRMS) were recorded on an AEI MS-902. Optical rotations were measured on a Schmidt and Haensch Polartronic MH8. $Rh(acac)(C_2H_4)_2$ was purchased from Strem and used without further purification. All other chemicals were purchased from Acros or Aldrich and used as received. Flash chromatography was performed using silica gel 60 Å (Merck, 230-400 mesh). Ligand (*S*)-**L** was prepared according to a literature procedure.[1]

Enantioselective Catalytic Addition Reactions

General Procedure for Table 1. In a flame dried Schlenk tube under a nitrogen atmosphere, $Rh(acac)(C_2H_4)_2$ (2.30 mg, 9 μmol, 5 mol%) and ligand (*S*)-**L** (10.16 mg, 22 μmol, 12.5 mol%) were dissolved in MTBE (2.5 mL). After 10 min at 25 °C, 2,2,2-trifluoroacetophenone **1a** or **1b** (0.178 mmol) was added, followed by the addition of 3 equiv arylboronic acid (0.534 mmol). After stirring for 20 h at reflux temperature, the mixture was quenched with a 12.5 % aqueous ammonia solution and extracted with EtOAc. The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Products **3a-j** were purified by flash chromatography using eluent conditions reported for TLC (*vide infra*).

Table 1, entry 1: 2,2,2-trifluoro-1-(4-methoxyphenyl)-1-phenyl-1-ethanol (3a). Yield: 50% (colourless oil). TLC conditions: (hexane/ethylacetate = 90/10) R_f 0.25. ^{19}F NMR ($CDCl_3$) δ = -75.87; ^{1}H NMR ($CDCl_3$) δ = 7.52-7.48 (m, 2H), 7.42-7.34 (m, 5H), 6.90-6.85 (m, 2H), 3.81 (s, 3H), 2.86 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 159.76, 139.67, 131.68, 128.95, 128.94, 128.70, 128.34, 127.53, 125.52 (q, J_{CF} = 284 Hz), 79.35 (q, J_{CF} = 28 Hz), 55.38. HRMS calculated for $C_{15}H_{13}O_2F_3$: *m/z* 282.0867, found: 282.0889; The ee was determined by chiral HPLC on a DAICEL AD

column with heptane/2-propanol = 90/10. Retention times: 6.3 and 7.2 min. 68% ee. $[\alpha]_D$ = +2.2 (c = 9.84, $CHCl_3$).

Table 1, entry 2 and entry 5: 2,2,2-trifluoro-1-(4-chlorophenyl)-1-phenyl-1-ethanol (3b). Yield for entry 2: 28% (colourless oil). Yield for entry 5: 90% (colourless oil). TLC conditions: (hexane/ethyl acetate = 90/10) R_f 0.32. ^{19}F NMR ($CDCl_3$) δ = -75.84; ^{1}H NMR ($CDCl_3$) δ = 7.50-7.31 (m, 9H), 2.87 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 139.15, 137.82, 134.94, 129.09, 129.05, 128.59, 128.54, 127.39, 125.25 (q, J_{CF} = 284 Hz), 79.31 (q, J_{CF} = 29 Hz). HRMS calculated for $C_{14}H_{10}OF_3{}^{37}Cl$: *m/z* 288.0343, found: 288.0362; The ee was determined by chiral HPLC on a DAICEL AD column with heptane/2-propanol = 90/10. Retention times: 4.7 and 5.1 min. 68% ee for entry 1. 79% ee for entry 5. $[\alpha]_D$ = +13.3 (c = 6.93, $CHCl_3$).

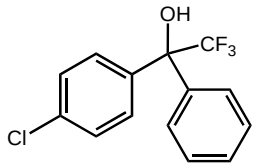


Table 1, entry 3: 2,2,2-trifluoro-1-(4-chlorophenyl)-1-(4-methoxyphenyl)-1-ethanol (3c). Yield: 96% (yellow oil). TLC conditions: (hexane/ethylacetate = 95/5) R_f 0.35. ^{19}F NMR ($CDCl_3$) δ = -76.03; ^{1}H NMR ($CDCl_3$) δ = 7.44-7.31 (m, 6H), 6.90-6.85 (m, 2H), 3.81 (s, 3H), 2.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 159.94, 138.04, 134.84, 131.31, 129.11, 128.85, 128.48, 125.32 (q, J_{CF} = 285 Hz), 113.90, 79.06 (q, J_{CF} = 29 Hz), 55.44. HRMS calculated for $C_{15}H_{12}OF_3{}^{37}Cl$: *m/z* 318.0453, found: 318.0452. The ee was determined by chiral HPLC on a Chiralcel OB-H column with heptane/2-propanol = 90/10. Retention times: 10.0 and 11.0 min. 68% ee. $[\alpha]_D$ = +13.7 (c = 11.23, $CHCl_3$).

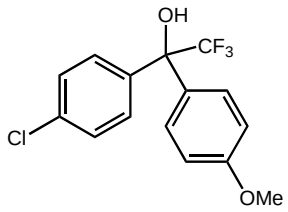
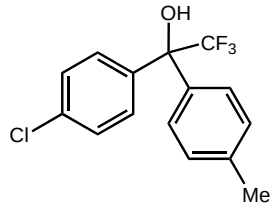
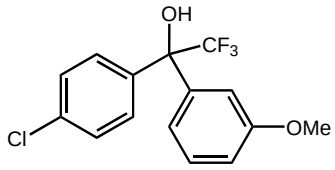


Table 1, entry 4: 2,2,2-trifluoro-1-(4-chlorophenyl)-1-(4-methylphenyl)-1-ethanol (3d). Yield: 91% (colourless oil). TLC conditions: (hexane/ethylacetate = 95/5) R_f 0.51. ^{19}F NMR ($CDCl_3$) δ = -75.95; ^{1}H NMR ($CDCl_3$) δ = 7.43 (d, 2H, J_{CF} = 8.4 Hz), 7.37-7.31 (m, 4H), 7.18 (d, 2H, J_{CF} = 8.4 Hz), 2.85 (s, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ = 139.03, 137.91, 136.30, 134.84, 129.29, 129.11, 128.48, 127.28, 125.27 (q, J_{CF} = 284 Hz), 79.17 (q, J_{CF} = 29 Hz), 21.21. HRMS calculated for $C_{15}H_{12}OF_3{}^{35}Cl$: *m/z* 300.0529, found: 300.0516. The ee was determined by chiral HPLC on a DAICEL AD column with heptane/2-propanol =



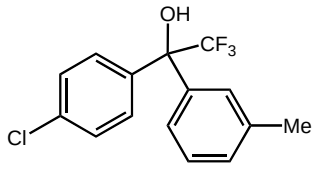
90/10. 83% ee. Retention times: 15.0 and 17.5 min. 83% ee. $[\alpha]_D$ = +15.9 (c = 8.43, $CHCl_3$).

Table 1, entry 6: 2,2,2-trifluoro-(4-chlorophenyl)-1-(3-methoxyphenyl)-1-ethanol (3e). Yield: 94% (colourless oil). TLC



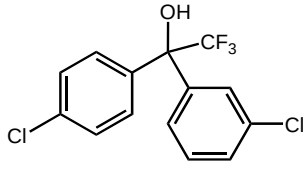
conditions: (hexane/ethylacetate = 95/5) R_f 0.28. ^{19}F NMR ($CDCl_3$) δ = -75.83; ^{1}H NMR ($CDCl_3$) δ = 7.40 (d, 2H, J_{CF} = 8.4 Hz), 7.32-7.22 (m, 3H), 7.10-6.99 (m, 2H), 6.87 (ddd, 1H, J_{CF} = 8.0, 2.4, 1.2 Hz), 3.75 (s, 3 H), 2.88 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 159.63, 140.58, 137.62, 134.94, 129.63, 129.00, 128.54, 125.15 (q, J_{CF} = 284 Hz), 114.14, 113.61, 79.17 (q, J_{CF} = 29 Hz), 55.44. HRMS calculated for $C_{15}H_{12}O_2F_3{}^{37}Cl$: *m/z* 318.0448, found: 318.0460; The ee was determined by chiral HPLC on a DAICEL AD column with heptane/2-propanol = 85/15. Retention times: 4.8 and 5.4 min. 71% ee. $[\alpha]_D$ = +8.5 (c = 9.62, $CHCl_3$).

Table 1, entry 7: 2,2,2-trifluoro-(4-chlorophenyl)-1-(3-methylphenyl)-1-ethanol (3f). Yield: 91% (colourless oil). TLC



conditions: (hexane/ethylacetate = 95/5) R_f 0.50. ^{19}F NMR ($CDCl_3$) δ = -75.79; ^{1}H NMR ($CDCl_3$) δ = 7.43 (d, 2H, J_{CF} = 8.4 Hz), 7.36-7.24 (m, 5H), 7.21-7.17 (m, 1H), 2.87 (s, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ = 139.13, 138.43, 137.85, 134.86, 129.81, 129.11, 128.51, 128.46, 127.96, 125.24 (q, J_{CF} = 285 Hz), 123.33, 79.25 (q, J_{CF} = 29 Hz), 21.71. HRMS calculated for $C_{15}H_{12}OF_3{}^{35}Cl$: *m/z* 300.0529, found: 300.0525. The ee was determined by chiral HPLC on a DAICEL AD column with heptane/2-propanol = 85/15. Retention times: 3.9 and 4.2 min. 76% ee. $[\alpha]_D$ = +15.7 (c = 16.81, $CHCl_3$).

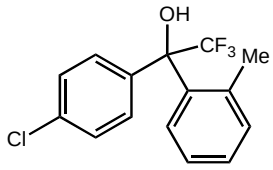
Table 1, entry 8: 2,2,2-trifluoro-(4-chlorophenyl)-1-(3-chlorophenyl)-1-ethanol (3g). Yield: 52% (colourless oil). TLC



conditions: (hexane/ethylacetate = 90/10) R_f 0.30. ^{19}F NMR ($CDCl_3$) δ = -75.90; ^{1}H ($CDCl_3$) δ = 7.51-7.28 (m, 8H), 2.91 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 140.89, 137.27, 135.32, 134.71, 129.81, 129.32, 128.96, 128.93, 128.82, 127.75, 125.70, 125,66, 124.97 (q, J_{CF} = 284 Hz), 123.33, 78.99 (q, J_{CF} = 29 Hz). HRMS calculated for $C_{14}H_9OF_3{}^{35}Cl_2$: *m/z* 319.9982, found: 319.9992.

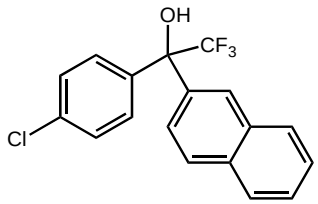
The ee was determined by chiral HPLC on a DAICEL AD column with heptane/2-propanol = 90/10. Retention times: 4.4 and 4.7 min. 83% ee. $[\alpha]_D$ = -7.2 (c = 9.75, $CHCl_3$).

Table 1, entry 9: 2,2,2-trifluoro-(4-chlorophenyl)-1-(2-methylphenyl)-1-ethanol (3h). Yield: 40% (colourless oil). TLC



conditions: (hexane/ethylacetate = 90/10) R_f 0.40. ^{19}F NMR ($CDCl_3$) δ = -75.62; ^{1}H ($CDCl_3$) δ = 7.70-7.66 (m, 1H), 7.36-7.24 (m, 6H), 7.19-7.15 (m, 1H), 2.80 (s, 1H), 1.96 (s, 3H); ^{13}C NMR ($CDCl_3$) δ = 138.72, 136.65, 134.73, 133.64, 129.34, 129.24, 128.30, 127.07 (q, J_{CF} = 3.8 Hz), 125.17 (q, J_{CF} = 285 Hz), 123.75, 80.19 (q, J_{CF} = 28 Hz), 21.46. HRMS calculated for $C_{15}H_{12}OF_3{}^{37}Cl$: *m/z* 302.0499, found: 302.0501. The ee was determined by chiral HPLC on a DAICEL AD column with heptane/2-propanol = 90/10. Retention times: 3.7 and 4.1 min. 50% ee. $[\alpha]_D$ = +45.5 (c = 7.83, $CHCl_3$).

Table 1, entry 10: 2,2,2-trifluoro-(4-chlorophenyl)-1-(2-naphthyl)-1-ethanol (3i). Yield: 69% (colourless oil). TLC



conditions: (hexane/ethylacetate, 90/10) R_f 0.30. ^{19}F NMR ($CDCl_3$) δ = -75.53; ^{1}H NMR ($CDCl_3$) δ = 8.08 (s, 1H), 8.00-7.81 (m, 3H), 7.57-7.42 (m, 5H), 7.35 (d, 2H, J = 8.4 Hz), 3.00 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 137.66, 136.20, 135.03, 133.20, 132.69, 129.21, 128.80, 128.61, 128.03, 127.69, 126.83, 126.57, 125.95, 124.98, 125.32 (q, J_{CF} = 285 Hz), 79.50 (q, J_{CF} = 28 Hz). HRMS calculated for $C_{18}H_{12}OF_3{}^{35}Cl$: *m/z* 336.0529, found: 336.0513. The ee was determined by chiral HPLC on a Chiralcel OD column, heptane/2-propanol = 85/15. Retention times: 5.3 and 6.9 min. 76% ee. $[\alpha]_D$ = +40.6 (c = 12.2, $CHCl_3$).

References

(1) Bernsmann, H.; Van den Berg, M.; Hoen, R.; Minnaard, A. J.; Mehler, G.; Reetz, M. T.; De Vries, J. G.; Feringa, B.L. *J. Org. Chem.* **2005**, *70*, 943.