Asymmetric intramolecular C-H insertions of aryldiazoacetates

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Supporting Information

Experimental conditions and spectral data for **7, 10-13**

Experimental Section.

The ^{1}H and ^{13}C NMR spectra were run at either 300, 400 or 500 and 75 or 125 MHz in $CDCl_3$, unless otherwise noted. Mass spectral determinations were carried out at 70 eV., and IR spectra were obtained using a Nicolet Impact series 420 IR.

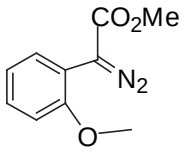
Glassware was oven-dried at >100 °C prior to use. Hexanes were distilled over sodium with triglyme and benzophenone and degassed bubbling argon for at least 5 min before the reaction was started . Reactions were performed under an atmosphere of argon. Low temperatures were maintained by use of a Neslab Cryocool immersion cooler.

Column chromatography was carried out on ICN silica gel 60 (230-400 mesh). Commercially available reagents were used without additional purification unless noted, and p-Acetamida benzenesulfonyl azide (*p*-ABSA) was prepared by the literature procedure[1].

General Procedure for the Synthesis of Methyl Aryldiazoacetates.

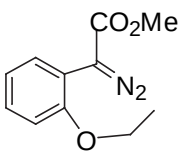
Methyl arylacetate (1 eq, 5-100 mmol) and *p*-ABSA (1.2 eq) were dissolved in CH_3CN and cooled to 0 °C under argon atmosphere. DBU (1.2 eq) was added, and the ice bath was removed. The reactional mixture was stirred for 24 h at 24 °C. The mixture was quenched with saturated NH_4Cl and the water layer was extracted with diethyl ether (3x). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was triturated with 50% of diethyl ether / petroleum ether, the solid was filtered off and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (5% diethyl ether / petroleum ether).

Methyl 2–Methoxyphenyldiazoacetate (7a).



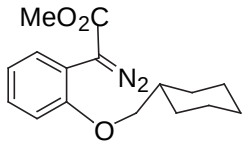
Yellow oil, 75% yield. ^{1}H NMR (300 MHz) δ 7.59 (d, *J* = 8.1 Hz, 1 H), 7.29 (t, *J* = 8.1 Hz, 1 H), 7.05 (t, *J* = 7.8 Hz, 1 H), 6.93 (d, *J* = 8.1 Hz, 1 H), 3.91 (s, 3 H), 3.88 (s, 3 H). ^{13}C NMR (75 MHz) δ 52.5, 56.1, 111.4, 121.7, 129.2, 130.7, 156.0, 165.5 (C = N_2 signal missing). IR (neat) 2952, 1742, 1435, 1274, 1249 cm^{-1}. HRMS calcd for C_{10} $H_{10}N_2O_3$, 206.0691, found, 206.0692.

Methyl 2–Ethoxyphenyldiazoacetate (7b).



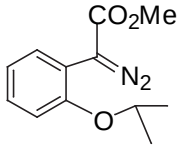
Yellow oil, 70% yield. ^{1}H NMR (300 MHz) δ 7.77 (t, *J* = 7.8 Hz, 1 H), 7.45 (t, *J* = 8.0 Hz, 1 H), 7.21 (t, *J* = 8.2 Hz, 1H), 7.09 (t, *J* = 7.8 Hz, 1 H), 4.27 (q, *J* = 7.0 Hz, 2H), 4.04 (s, 3H), 1.64 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (75 MHz) δ 15.1, 52.5, 64.5, 112.0, 113.9, 121.5, 128.9, 130.6, 155.2, 167.2 (C = N_2 missing). IR (neat) 2981, 2951, 1739, 1455, 1248 cm^{-1}. HMRS calcd for C_{11} $H_{12}N_2O_3$ 220.0834, found, 220.0833.

Methyl 2–(Hydroxymethyl)cyclohexanephenyldazoacetate (7c).



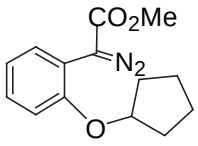
Yellow oil, 75% yield. ^{1}H NMR (500 MHz) δ 7.58 (t, *J* = 7.8 Hz, 1 H), 7.34 (t, *J* = 8.0 Hz, 1 H), 7.01 (t, *J* = 7.8 Hz, 1 H), 6.95 (t, *J* = 8.1 Hz, 1 H), 3.97 (s, 3 H), 3.89 (d, *J* = 6.2 Hz, 1 H), 1.85 (m, 6 H), 1.22 (m, 5 H). ^{13}C NMR (125 MHz) δ 26.4, 26.9, 30.5, 38.3, 52.5, 74.6, 111.9, 114.6, 121.3, 129.0, 130.6, 155.3, 167.1 (C = N_2 missing). IR (neat) 2929, 2852, 2098, 1720, 1602, 1205, 1342 cm^{-1}. HRMS calcd for C_{16} $H_{20}N_2O_3$, 288.1460, found, 288.1461.

Methyl 2–*iso*–Propoxyphenyldiazoacetate (7d).



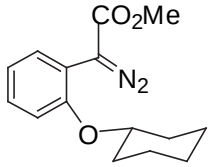
Yellow oil, 72% yield. ^{1}H NMR (300 MHz) δ 7.75 (t, *J* = 8.1 Hz, 1 H), 7.41 (t, *J* = 8.1 Hz, 1 H), 7.18 (t, *J* = 8.2 Hz, 1 H), 7.09 (t, *J* = 8.2 Hz, 1 H), 4.79 (hept, *J* = 6.0 Hz, 1H), 4.04 (s, 3 H), 1.56 (d, *J* = 6.0 Hz, 6 H). ^{13}C NMR (75 MHz) δ 22.4, 52.4, 71.1, 113.4, 121.3, 128.8, 129.2, 130.8, 154.1, 165.5 (C = N_2 missing). IR (neat) 2978, 2951, 1099, 1743, 1704, 1599, 1492, 1339, 1249 cm^{-1}.

Methyl 2–Cyclopentyloxyphenyldiazoacetate (7e).



Yellow oil, 70% yield. ^{1}H NMR (400 MHz) δ 7.62 (t, *J* = 8.0 Hz, 1 H), 7.24 (t, *J* = 8.1 Hz, 1 H), 7.02 (t, *J* = 8.1 Hz, 1 H), 6.93 (t, *J* = 7.8 Hz, 1 H), 4.87 (qt, *J* = 6.0 Hz, 1 H), 3.95 (s, 3 H), 1.82 (m, 8 H). ^{13}C NMR (125 MHz) δ 24.6, 33.4, 52.5, 80.4, 113.1, 121.1, 126.2, 128.7, 130.7, 154.3, 165.8 (C = N_2 missing). IR (neat) 2953, 2097, 1742, 1704, 1598, 1492, 1455, 1434, 1345, 1248 cm $^{-1}$. HRMS calcd for C_{14} $H_{16}N_2O_3$, 260.11877, found, 260.1181.

Methyl 2–Cyclohexyloxyphenyldiazoacetate (7f).



Yellow oil, 64% yield. ^{1}H NMR (400 MHz) δ 7.59 (t, *J* = 8.0 Hz, 1 H), 7.23 (t, *J* = 8.1 Hz, 1 H), 7.12 (t, *J* = 8.1 Hz, 1 H), 6.92 (t, *J* = 7.8 Hz, 1 H), 4.91 (m, 1 H), 3.84 (s, 3 H), 1.99 (m, 2H), 1.82 (m, 2H), 1.57 (m, 3H), 1.39 (m, 4 H). ^{13}C NMR (125 MHz) δ 23.8, 25.6, 31.8, 52.2, 74.2, 113.1, 120.9, 128.5, 129.8, 131.2, 154.2, 165.4 (C = N_2 missing). IR (neat) 2936, 2858, 2097, 1743, 1703, 1493, 1451, 1435, 1347, 1251 cm^{-1}. HRMS calcd for C_{15} $H_{18}N_2O_3$, 274.1317, found, 274.1323.

General Procedure for C-H insertion reactions.

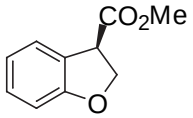
Procedure A:

Methyl arydiazoacetate (1 mmol) in hexanes (10 mL) was added, by syringe pump for 3 h, to a solution of Rh_2(*S*--DOSP)$_4$ **1a** (0.01 mmol, 1 mol %) (in 5 mL of hexanes). The solution was stirred at –50 °C for 72 h (at 25 ^{0}C for 2 h for compound **7a**) and the solvent was removed under reduced pressure. The crude mixture was purified by chromatography on silica gel (diethyl ether and petroleum ether, 1:20),to give the benzofurans below.

Procedure B:

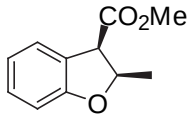
Methyl arydiazoacetate (1 mmol) in methylene chloride (10 mL) was added, by syringe pump for 3 h, to a solution of Rh_2(*S*-biTISP)$_2$ (**8**) or **9** (0.01 mmol, 1 mol %) in 5 mL of methylene chloride. The solution was stirred at –50 °C for 72 h and the solvent was removed under reduced pressure. The crude mixture was purified by chromatography on silica gel (diethyl ether and petroleum ether, 1:20), to give the benzofurans below.

2,3-Dihydrobenzofuran-3-carboxylic Acid Methyl Ester (10a)[4].



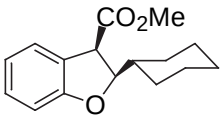
Colorless oil, 98% yield; >2% ee (determined by HPLC: OD, 1.0 mL/min, 0.5% *i*-Pr-OH in hexanes; T_R = 12.0 min and 15.5 min)[6a] (65% yield; 43% ee)[6b] (70% yield; 63% ee)[6c] $[\alpha]^{25}_D$ = -8.76^0, (c 0.69 $CHCl_3$)[6c]. ^{1}H NMR (300 MHz)[A] δ 7.39 (d, *J* = 8.1 Hz, 1 H), 7.21 (t, *J* = 7.8 Hz, 1 H), 6.91 (t, *J* = 8.1 Hz, 1H), 6.85 (d, *J* = 8.1 Hz 1H), 4.97 (dd, *J* = 6.6 Hz and 3.0 Hz, 1 H), 4.69 (t, *J* = 9.3 Hz, 1 H), 4.37 (dd, *J* = 6.6 Hz and 2.7 Hz, 1 H), 3.81 (s, 3 H), ^{13}C NMR (75 MHz) δ 47.3, 52.8, 72.7, 110.2, 120.9, 124.4, 125.6, 129.7, 160.0, 171.9.

2-Methyl-2,3-dihydrobenzofuran-3-carboxylic Acid Methyl Ester (11b and 12b).



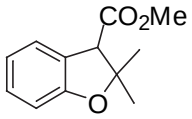
Colorless oil, 85% yield of diastereomers combined **11b** and **12b**; ratio 4:1, respectively; 65% yield of major diastereomer **11b**; 60% ee[6a] of major product, (determined by HPLC: OD, 1.0 mL/min, 0.5% *i*-Pr-OH in hexanes; T_R = 8.3 min and 12.8 min), (50% yield of major diastereomer **11b** and 53% ee)[6b], (70% yield and 45% ee of major diastereomer **11b**) [6c]. $[\alpha]^{25}_{D}$ = -1.14^0, (c 2.1 $CHCl_3$)[6a] and $[\alpha]^{25}_{D}$ = +3.61^0 (c 1.88. $CHCl_3$) [6c]. ^{1}H NMR (500 MHz) δ 7.22 (m, 2 H), 6.92 (t, *J* = 8.1, 1 H), 6.84 (d, *J* = 8.1 Hz, 1 H), 5.09 (m, 1 H), 4.31, (d, *J* = 9.0 Hz, 1 H), 3.76 (s, 3 H), 1.47 (d, *J* = 7.0 Hz, 3 H). ^{13}C NMR (125 MHz) δ 16.8, 52.1, 52.2, 81.8, 110.2, 121.1, 125.5, 125.9, 129.6, 160.1, 171.3. IR (neat) 2959, 2930, 2873, 1728, 1462, 1275, 1123, 1072 cm^{-1}. HRMS calcd for C_{11} $H_{12}O_3$, 192.0813, found, 192.0811.

2-Cyclohexyl-2,3-dihydrobenzofuran-3-carboxylic Acid Methyl Ester (11c).



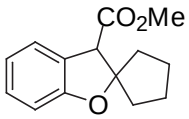
Colorless crystal (mp 88-90 ^{0}C), 80% yield of major diastereomer **11c**; 95% de and 63% ee (determined by HPLC: OJ, 0.5 mL/min, 0.5% *i*-Pr-OH in hexanes; T_R = 8.7 min and 10.5 min), (22% yield and 60% ee of major diastereomer **11c**)[6b], (35% yield and 35% ee of major diastereomer **11c**)[6c]. $[\alpha]^{25}_{D}$ = - 1.67^0, (c 1.5 $CHCl_3$)[6a]. ^{1}H NMR (500 MHz) δ 7.22 (m, 2 H), 6.88 (m, 2 H), 4.44 (dt, *J* = 8.0 Hz and 1.5 Hz, 1 H), 4.16 (d, *J* = 8.0 Hz 1H), 3.71 (s, 3 H), 2.17 (m, 1 H), 2.01 (m, 1 H), 1.77 (m, 4 H), 1.21 (m, 5 H). ^{13}C NMR (125 MHz) δ 25.6, 25.9, 26.5, 29.7, 30.4, 39.0, 50.3, 52.2, 90.3, 110.3, 121.0, 125.0, 126.6, 129.7, 160.2, 171.6. IR (neat) 2926, 2853, 1724, 1597, 1480, 1239 cm^{-1}. HRMS calcd for C_{16} $H_{20}O_3$, 260.1412, found, 260.1431.

2,2-Dimethyl-2,3-dihydro-benzofuran-3-carboxylic Acid Methyl Ester (13d)[5].



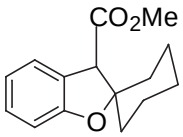
Colorless oil, 98% yield; 94% ee[6a] (determined by HPLC: OJ, 0.5 mL/min, 0.5% *i*-Pr-OH in hexanes; T_R = 8.6 min and 9.1 min), (48% yield and 68% ee)[6b], (57% yield and 65% ee)[6c]. $[\alpha]^{25}_D$ = +31.2^0, (c 1.2. $CHCl_3$)[6a] and $[\alpha]^{25}_D$ = -11.6^0 (c 2.4. $CHCl_3$)[6c].^{1}H NMR (500 MHz) δ 7.24 (m, 2 H), 6.91 (t, J = 8.1 Hz, 1 H), 6.80 (d, J = 8.1 Hz, 1H), 4.09 (s, 1 H), 3.78 (s, 3 H), 1.65 (s, 3 H), 1.41 (s, 3 H), ^{13}C–NMR (125 MHz) δ 23.5, 29.1, 52.3, 58.1, 88.3, 110.2, 120.8, 125.2, 126.5, 129.5, 159.1, 171.4.

2,2-spirocyclopentyl-2,3-dihydrobenzofuran-3-carboxylic Acid Methyl Ester (13e).



Colorless oil, 78% yield; 90% ee (determined by HPLC: OJ, 0.5 mL/min, 0.5% *i*-Pr-OH in hexanes; T_R = 8.4 min and 9.8 min). $[\alpha]^{25}_D$ = +6.83, (c 1.0 $CHCl_3$)[6a]. ^{1}H-NMR (300 MHz) δ 7.41(m, 2 H), 7.08 (t, J = 8.1 Hz, 1 H), 6.98 (d, J = 8.0 Hz, 1 H), 4.39 (s, 1 H), 3.93 (s, 3 H), 2.04 (m, 8 H). ^{13}C–NMR (75 MHz) δ 34.9, 40.7, 52.6, 55.8, 98.9, 110.6, 120.9, 125.9, 126.1, 139.8, 159.5, 172.1. IR (neat) 2953, 2872, 2115, 1743, 1598, 1492, 1246 cm^{-1}. HRMS calcd for $C_{14}H_{16}O_3$, 232.1099, found, 232.1091.

2,2-spirocyclohexyl-2,3-dihydrobenzofuran-3-carboxylic Acid Methyl Ester (13f).



Colorless oil, 10% yield; 80% ee (determined by HPLC: OJ, 0.5 mL/min, 0.5% *i*-Pr-OH in hexanes; T_R = 7.9 min and 8.3 min). $[\alpha]^{25}_D$ = +7.29^0, (c 0.9 $CHCl_3$)[6a]. ^{1}H NMR (300 MHz) δ 7.20 (m, 2 H), 6.89 (t, J = 7.5 Hz, 1 H), 6.83 (d, J = 8.0 Hz, 1 H), 3.98 (s, 1 H),

3.76 (s, 1 H), 1.72 (m, 10 H). ^{13}C NMR (75 MHz) δ 22.5, 22.8, 25.3, 32.13, 37.8, 52.3, 58.1, 89.7, 110.4, 120.6, 125.5, 126.2, 129.4, 159.2, 171.6. IR (neat) 2936, 2872, 2117, 1732, 1597, 1482, 1244 cm^{-1}. HRMS calcd for C_{15} $H_{18}O_3$, 246.1257, found, 246.1277.

Bibliography

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6. a) When **1a** was the catalyst; b) when **8** was the catalyst c) when **9** was the catalyst.