A highly enantioselective intramolecular Heck reaction with a monodentate ligand
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General procedures All reactions were performed under an argon atmosphere using standard Schlenk-type techniques. Solvents for the AHR and amines were distilled prior to use. All reagents were purchased from commercial suppliers and used as received unless otherwise noted. L**4** and L**4** were synthesized according to a method previously reported. Column chromatography was performed using Kieselgel 60 (230–400 mesh).

1H and 13C NMR spectra were recorded on a Varian Gemini 200 or Varian 300 spectrometer in CDCl3. Chemical shifts are given in ppm (reference δc for 1H NMR and δc for 13C NMR). Mass spectra were recorded on an AEI MS-902 MS.

4-(2-iodo)benzoylphenoquinone (4): 6.8 g (27 mmol) of (2-iodo)benzoylchloride, 14.9 g (135 mmol) of hydroquinone and 6.6 g (40.5 mmol) of K2CO3 were dissolved in 100 ml of acetone and stirred under reflux overnight. The mixture was cooled to room temperature and the salts were removed by filtration. The remaining solution was evaporated and the residue was dissolved in CHCl3. The precipitated hydroquinone was removed by filtration. After evaporation of the CHCl3, the remaining oil was suspended in MeOH, after which the diether 4a precipitated (0.65 g, 4.5%). Another filtration and evaporation yielded the pure mono-ether 4 as an orange oil (5.9 g, 91%).

1H NMR δ = 7.97 (m, 1H), 6.72 (d, J = 9 Hz, 2H), 6.82 (d, J = 9 Hz, 2H), 7.26, (m, 1H), 7.40 (m, 2H), 7.84 (m, 1H). 13C NMR δ = 137.95 (d), 138.14 (s), 148.74 (s), 151.78 (s). HRMS calcd for C14H1102, 325.980, found 325.980.

1,4-di-(2-iodo)benzoylbenzene (4a): m.p. 119.6-122.3 °C. 1H NMR δ = 4.95 (s, 4H), 6.88 (s, 4 H), 6.99 (m, 2H), 7.38 (m, 2H), 7.46 (m, 2H), 7.81 (m, 2H). 13C NMR δ = 74.52 (t), 97.15 (s), 115.89 (d), 123.84 (d), 126.81 (d), 129.39 (d), 139.12 (s), 152.90 (s). HRMS calcd for C14H1102, 341.924, found 341.923.

4-(2-iodo)benzoyl-4-methoxy cyclohexa-2,5-dien-2-one (1) To a stirred solution of 5.0 g (15.3 mmol) of 4-(2-iodo)benzoylphenoquinone 4 in dry MeOH (10 ml) was added over 30 min a solution of 5.0 g (15.3 mmol) phenyl-iodo-diaceata (PIDA) in MeOH (50 ml). After 17h at ambient temperature, the mixture was diluted with water (150 ml) and extracted with EtO (3x 50 ml). The combined organic layers were extracted with 2N NaOH (50 ml), brine (50 ml), dried on Na2SO4 and evaporated. The remaining oil was purified by column chromatography (SiO2, Hexane:EtOAc = 8:1), yielding the product as a yellow solid (4.5 g, 83%. m.p. 39.7-41.4 °C). 1H NMR δ = 3.9 (s, 3H), 4.58 (s, 2H), 6.22 (d, J = 6Hz, 2H), 6.85 (d, J = 6 Hz, 2H), 6.94 (m, 1H), 7.38 (m, 2H), 7.67 (d, J = 4 Hz, 1H). 13C NMR δ = 50.78 (q), 68.81 (q), 119.75 (s), 119.78 (s), 128.27 (d), 128.39 (s), 128.60 (d), 129.10 (d), 139.65 (s), 143.16 (d), 185.04 (s). HRMS calcd for C14H10OJ3, 355.991, found 355.992.

General procedure for the AHR: 0.033 mmol of Pd(OAc)2, and 0.066 mmol of L**4**-1 or 0.099 mmol of L**4**-2 were dissolved under Ar in 3 ml of dry and degassed solvent (see Table 1) and heated under reflux for 1-2 h, until a clear yellow solution was obtained. 1.2 mmol of base, the additive and ethylene (3.3 mmol) of 1 were added and the mixture was refluxed for 48 h. The solvent was evaporated and the crude product was purified by column chromatography (SiO2, Pet. Ether 40/60 : EtOAc = 9:1).
2-iodo-3-methyl-benzoic acid (7) 4.6 g (20.6 mmol) of 2-amino-3-methylbenzoic acid was dissolved in 15 ml of conc. HCl at 0°C. After 15 min, the mixture was diluted with 10 g of ice and a solution of 21 mmol (1.45 g) of NaNO2 in 10 ml of H2O was added slowly. After 10 min, the orange solution was poured into a solution of 13.3 g (10.0 mmol) I2 in 30 ml of H2O and stirring was continued for 16 h. The mixture was extracted with diethyl ether (3 x 100 ml) and dried on Na2SO4. Evaporation of the solvent yielded the product as a yellow oil. (2.0 g, 62%).

2-iodo-3-methylbenzylalcohol (8) 3.6 g (13.7 mmol) of 2-iodo-3-methyl benzoic acid was dissolved in 100 ml of dry THF. 2.08 g (55 mmol) of NaBH4 was added at 0°C, which a solution of 3.5 g (13.7 mmol) I2 in 50 ml of dry THF was added dropwise. The mixture was stirred for 16 h at ambient temperature, was then treated with 200 ml 1N HCl solution, and extracted with diethyl ether (3 x 100 ml). The combined organic layers were washed with brine and dried on Na2SO4. Evaporation of the solvent yielded the product as a cream solid. (3.1 g, 86%).

2-iodo-3-methylbenzylchloride (9) 3.0 g (12.1 mmol) of the 2-iodo-3-methylbenzylalcohol and 13.0 mmol of Et3N (1.31 g) were dissolved in 100 ml of dry CH2Cl2. Slowly, 12.7 mmol (1.50 g) of 2-iodo-3-methylbenzylalcohol was dissolved in 100 ml of dry THF. 2.08 g (55 mmol) of NaBH4 was added at 0°C, which a solution of 3.5 g (13.7 mmol) I2 in 50 ml of dry THF was added dropwise. The mixture was stirred for 16 h at ambient temperature, was then treated with 200 ml 1N HCl solution, and extracted with diethyl ether (3 x 100 ml). The combined organic layers were washed with brine and dried on Na2SO4. Evaporation of the solvent yielded the product as a yellow oil. (1.2 g, 75%). 1H NMR δ 2.27 (s, 3H), 7.05 (m, 3H), 10.76 (bs, COOH). 13C NMR δ 29.21 (q), 99.25 (s), 126.41 (d), 127.24 (d), 138.79 (s), 140.57 (s), 141.83 (d), 183.58 (s). HRMS calcd. for C15H15O3I 370.007, found 370.005.

4a-methoxy-10-methyl-4lf-benzo[c]chromen-2(6H)-one (12) AHR was performed using monodentate ligand L*-2, Pd(OAc)2, CHCl3, as a solvent and Cy2MeN as a base, resulting in 52% conv. after refluxing for 48h. E.e. 75%. E.e. determination on HPLC DAICEL OD column, Heptane: iPrOH = 95: 5, rt 10.9 min, 35.94 min. 1H NMR δ 2.2. (s, 3H), 3.42 (s, 3H), 4.93 (dd, J = 13, 78 Hz, 2H), 6.35 (d, J = 9 Hz, 1H), 6.43 (s, 1H), 6.86 (d, J = 9Hz, 1H), 7.08 (m, 3H). 13C NMR δ 20.91 (t), 53.67 (q), 67.81 (q), 124.81 (d), 126.32 (d), 127.91 (d), 131.43(d), 134.83 (d), 135.19 (s), 137.22 (s), 138.68 (d), 147.83 (d), 153.14 (s), 184.55 (s).

4-(2-iodo-3-methylbenzyl)oxy]-4-methoxy-2,5-cyclohexadien-1-one (11) 1.51 g (4.44 mmol) 4-(2-iodo-3-methyl benzyl)oxy]phenol was dissolved in 10 ml of MeOH. A solution of 4.5 mmol (1.45 g) of PIDA in 25 ml of MeOH was added dropwise at ambient temperature. The mixture was stirred overnight and was then diluted with 100 ml of H2O and extracted with diethyl ether (3 x 100 ml). The combined organic layers were dried on Na2SO4, and the solvent was removed by evaporation, yielding a brown oil. The crude product was purified by column chromatography (SiO2, Hexane:EtOAc, 5:1), yielding the product as a yellow oil. (1.2 g, 75%). 1H NMR δ 2.24 (s, 3H), 3.41 (s, 3H), 4.63 (s, 2H), 6.25 (d, J = 10Hz, 2H), 6.88 (d, J = 10 Hz, 2H), 7.18 (m, 3H). 13C NMR δ 27.45 (q), 49.34 (q), 68.34 (t), 91.30 (s), 103.28 (s), 124.30 (d), 126.52 (d), 127.59 (d), 128.40 (d), 138.79 (s), 140.57 (s), 141.83 (d), 183.58 (s). HRMS calcd. for C26H26O1J 370.007, found 370.005.