Direct One Pot Synthesis of Phenanthrenes via Suzuki-Miyaura Coupling/Aldol Condensation Cascade Reaction

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SUPPORTING INFORMATION

Experimental details and spectroscopic data for compounds 1b, 2b, 3, 4a-q, 8a-d, 10, and 11. This material is available free of charge via the Internet at http://pubs.acs.org
General

All reactions were conducted in oven-dried microwave glassware by using Biotage Initiator EXP™ microwave reactor under an atmosphere of dry nitrogen. All solvents were purified before use unless otherwise indicated. Toluene was distilled from CaH₂. All other reagents were used without further purification.

Aryl bromides, 1a₁ and 1c₂ were prepared by the coupling of 2-bromophenylacetic acid with methylamine and benzylamine, respectively. 1d₃ and 1k₄ were prepared by following the literature methods. Phenylacetates 5 1e and 1f were prepared by reaction of 2-bromophenylacetic acid in the presence of catalytic p-toluenesulfonic acid, in methanol and in ethanol, respectively. Compounds 1g-1j, 1l, 2a, 2c, 7, and 6a-d were obtained from commercial sources and used without further purification.

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F₂₅₄ glass plates precoated with a 0.2 mm thickness of silica gel. The TLC plates were visualized by shortwave (254 nm) or longwave (360 nm) UV light, potassium permanganate or ceric ammonium molybdate stain. Flash chromatography on Kieselgel 60 (230400 mesh) silica gel was performed using a CombiFlash Companion system. Preparative HPLC normal phase separations were performed using a Shimadzu HPLC system composed of two LC-8A pumps, a CTO-10A column oven and injector, a SPD-10A detector, and a SCL-10A system controller.

FT-IR spectra were recorded as neat samples using a Travel IR Portable spectrometer. Melting points were determined on a Uni-Melt capillary melting point apparatus and are uncorrected. GC/MS spectra were measured on a Shimadzu spectrometer. $^1$H NMR and spectra were obtained at 300 MHz on a Varian Gemini 300 instrument using CDCl$_3$ as solvent. $^1$H NMR assignment abbreviations are the following: singlet (s), doublet (d), triplet (t), quartet (q), broad singlet (bs), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). $^{13}$C NMR spectra were measured at 75.5 MHz or 125 MHz using CDCl$_3$ as an internal reference.

2-(2-Bromo-4-methoxyphenyl)-N-methylacetamide (1b). To a solution of (2-bromo-4-methoxy)phenylacetic acid (1.0 g, 4.08 mmol) in 10 mL of CH$_2$Cl$_2$ was added methylamine (0.23 mL, 40 wt% in H$_2$O, 2.7 mmol) and EDCI (0.78 g, 4.08 mmol). The mixture was stirred at room temperature for 2 h and quenched with H$_2$O (10 mL). The resulting two phases were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL). The combined organic layers washed with brine and dried over MgSO$_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (50% → 80% EtOAc/hexanes) to provide acetamide 1b (683 mg) in 65% yield as a white solid: mp 98–100°C; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.24 (d, 1H, $J = 8.5$ Hz), 7.14 (d, 1H, $J = 2.6$ Hz), 6.86 (dd, 1H, $J = 8.5$, 2.6 Hz), 5.53 (bs, 1H), 3.79 (s, 1H), 3.64 (s, 1H), 2.77 (d, 3H, $J = 4.8$ Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 170.9, 159.7, 132.3, 127.0,
125.4, 118.6, 114.3, 55.8, 43.2, 26.7; IR (neat) 3288, 1650, 1496, 1255, 1029 cm\(^{-1}\); MS (EI) \(m/z\) M\(^+\) for C\(_{10}\)H\(_{12}\)BrNO\(_2\) calcd 258, found 258 (M\(^+\), 2), 200 (83), 198 (78), 178 (100), 150 (10), 121 (20).

![Chemical Structure](image)

4,5-Dimethoxy-2-formylphenylboronic acid (2b). The literature procedure\(^6\) was used to prepare the title compound (51% yield for two steps), which was obtained as a white solid: mp 200–202\(^\circ\)C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 9.78 (s, 1H), 8.03 (s, 2H), 7.82 (s, 1H), 7.38 (s, 1H), 4.05 (s, 3H), 4.01 (s, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 196.8, 153.4, 150.5, 133.7, 120.9, 120.8, 56.5, 56.3; MS (EI) \(m/z\) M\(^+\) for C\(_9\)H\(_{11}\)BO\(_2\) calcd 210, found 210 (M\(^+\), 58), 209 (29), 179 (29), 166 (100).

SpinWorks 2.4: khy-iv-o25-1

SpinWorks 2.4: khy-iv-o25c

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processed size: 65536 complex points
number of scans: 322

file: C:\Users\Documents\Scripps\SPECTRO\573\khy-iv-o25c.png
transmitter freq.: 75.424064 MHz
processed size: 65536 complex points
number of scans: 322