Supporting Information for Note Entitled

“A Novel One-Step Synthesis of 2-Substituted 6-Azaindoles from 3-Amino-4-picoline and Carboxylic Esters”

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General procedures: All reactions were performed in oven-dried glassware under nitrogen with magnetic stirring. All commercial reagents were used as received. Flash chromatography was performed using 230-400 mesh silica gel.

To a solution of 3-amino-4-picoline (0.88 g, 8.0 mmol) in anhydrous THF (30 mL) at -70 °C was added *sec*-BuLi (17.1 mL, 1.4 M in cyclohexane, 24.0 mmol). Then the reaction mixture was warmed to rt and stirred for 3 h. After cooled back to -70 °C, ethyl benzoate (0.36 g, 2.4 mmol) dissolved in THF (0.5 mL) was added in 5 min. The reaction mixture was stirred at -40 °C for 0.5 h and was quenched with MeOH (10 mL). The reaction was warmed to rt and stirred for 1 h. Half-saturated NH₄Cl aqueous solution (15 mL) was added and the aqueous layer was extracted with MTBE twice (30 mL each

extraction). The combined organic layer was washed with water once (40 mL) and brine once (40 mL) and dried over MgSO₄. Filtration and concentration gave a yellow solid which was further purified by flash chromatography (CH₂Cl₂/MeOH=9:1) to give desired product **3** (0.41 g, 88% yield) as a yellow solid (m.p.: 209-211 °C, Lit.^{1k,8}: 223-225 °C).

¹H NMR (DMSO-d₆, 400 MHz) δ 12.01 (s, 1H), 8.72 (s, 1H), 8.08 (d, *J*= 5.50 Hz, 1H), 7.91 (d, *J*= 7.24 Hz, 2H), 7.50 (m, 3H), 7.39 (m, 1H), 6.96 (s, 1H).

To a solution of 3-amino-4-picoline (1.08 g, 10.0 mmol) in anhydrous THF (40 mL) at -70 °C was added *sec*-BuLi (21.0 mL, 1.4 M in cyclohexane, 29.4 mmol). Then the reaction mixture was warmed to rt and stirred for 3 h. After cooled back to -70 °C, methyl 4-bromobenzoate (0.65 g, 3.0 mmol) dissolved in THF (0.5 mL) was added in 5 min. The reaction mixture was stirred at -30 °C for 0.5 h and was quenched with MeOH (10 mL). The reaction was warmed to rt and stirred for 1 h. Half-saturated NH₄Cl aqueous solution (15 mL) was added and the aqueous layer was extracted with MTBE twice (30 mL each extraction). The combined organic layers was washed with water once (40 mL) and brine once (40 mL) and dried over MgSO₄. Filtration and concentration gave a yellow solid which was further purified by flash chromatography (CH₂Cl₂/MeOH=95:5) to give desired product **4** (0.64 g, 78% yield) as a white solid (m.p.: 273-275 °C, Lit.⁸: 264-266 °C).

^1H NMR (DMSO- d_6 , 400 MHz) δ 12.09 (s, 1H), 8.76 (s, 1H), 8.10 (d, J = 5.52 Hz, 1H), 7.89 (d, J = 11.12 Hz, 2H), 7.72 (d, J = 11.08 Hz, 2H), 7.51 (d, J = 5.04 Hz, 1H), 7.02 (s, 1H).

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To a solution of 3-amino-4-picoline (0.88 g, 8.0 mmol) in anhydrous THF (30 mL) at -70 °C was added *sec*-BuLi (17.1 mL, 1.4 M in cyclohexane, 24.0 mmol). Then the reaction mixture was warmed to rt and stirred for 3 h. After cooled back to -70 °C, methyl 4-trifluoromethylbenzoate (0.50 g, 2.4 mmol) dissolved in THF (0.5 mL) was added in 5 min. The reaction mixture was stirred at -40 °C for 0.5 h and was quenched with MeOH (10 mL). The reaction was warmed to rt and stirred for 1 h. Half-saturated NH_4Cl aqueous solution (15 mL) was added and the aqueous layer was extracted with MTBE twice (30 mL each extraction). The combined organic layers was washed with water once (40 mL) and brine once (40 mL) and dried over MgSO_4 . Filtration and concentration gave a yellow solid which was further purified by flash chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ =9:1) to give desired product **5** (0.51 g, 80% yield) as a white solid (m.p.: 241-243 °C, Lit.⁸: 239-242 °C).

^1H NMR (DMSO- d_6 , 400 MHz) δ 12.21 (s, 1H), 8.78 (s, 1H), 8.13 (d, J = 8.00 Hz, 2H), 8.11 (d, J = 5.48 Hz, 1H), 7.86 (d, J = 8.60 Hz, 2H), 7.53 (d, J = 5.44 Hz, 1H), 7.13 (s, 1H).

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To a solution of 3-amino-4-picoline (1.08 g, 10.0 mmol) in anhydrous THF (40 mL) at -70 °C was added *sec*-BuLi (21.0 mL, 1.4 M in cyclohexane, 29.4 mmol). Then the reaction mixture was warmed to rt and stirred for 3 h. After cooled back to -70 °C, methyl 2-naphthoate (0.56 g, 3.0 mmol) dissolved in THF (0.5 mL) was added in 5 min. The reaction mixture was stirred at -30 °C for 0.5 h and was quenched with MeOH (10 mL). The reaction was warmed to rt and stirred for 16 h. Half-saturated NH₄Cl aqueous solution (15 mL) was added and the aqueous layer was extracted with MTBE twice (30 mL each extraction). The combined organic layer was washed with water once (40 mL) and brine once (40 mL) and dried over MgSO₄. Filtration and concentration gave a yellow solid which was further purified by flash chromatography (CH₂Cl₂/MeOH=9:1) to give desired product **6** (0.58 g, 79% yield) as a white solid (m.p.: 246-248 °C, Lit.^{1k}: 263-264 °C).

¹H NMR (DMSO-d₆, 400 MHz) δ 12.21 (s, 1H), 8.79 (s, 1H), 8.50 (s, 1H), 8.10 (m, 3H), 7.98 (t, *J*= 6.84 Hz, 2H), 7.57 (m, 3H), 7.14 (s, 1H).

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Commercially available 3-amino-4-picoline (1.32 g, 12.0 mmol) was dissolved in

anhydrous THF (44 mL) in a dry flask under nitrogen. The solution was cooled to -78 °C and a solution of *s*-BuLi (1.4 M in cyclohexane, 26 mL, 36.0 mmol) was added in 10 min. The solution was warmed to rt, stirred at that temperature for 3 h, and cooled to -78 °C. The ester (0.67 g, 4.8 mmol) was added and the resulting mixture was stirred at -78 °C for 1 h. Methanol (20 mL) was added in 5 min and the solution was warmed up to room temperature and stirred for 1 h. A half-saturated NH₄Cl aqueous solution (30 mL) was added and the organic residue was extracted with MTBE (3 x 50 mL). The combined organic extract was dried over MgSO₄ and the solvent was evaporated under vacuum. The oil was purified by silica gel chromatography (50% hexanes/ethyl acetate to 100% ethyl acetate then MeOH) to give 0.38 g of **7** (44% yield) as an off-white powder (m.p.: 185-189 °C, Lit.⁸: 218-220 °C).

¹H NMR (DMSO-d₆, 400 MHz) δ 11.91 (s, 1H), 8.70 (s, 1H), 8.28 (s, 1H), 8.07 (d, *J*= 5.32 Hz, 1H), 7.82 (t, *J*= 1.80 Hz, 1H), 7.46 (d, *J*= 5.32 Hz, 1H), 7.04 (d, *J*= 1.76 Hz, 1H), 6.74 (s, 1H).

Commercially available 3-amino-4-picoline (1.32 g, 12.0 mmol) was dissolved in anhydrous THF (44 mL) in a dry flask under nitrogen. The solution was cooled to -78 °C and a solution of *s*-BuLi (1.4 M in cyclohexane, 26 mL, 36.0 mmol) was added in 10 min. The solution was warmed to rt, stirred at that temperature for 3 h, and cooled to -78 °C. The ester (0.75 g, 4.8 mmol) was added and the resulting mixture was stirred at -78 °C for 1 h. Methanol (20 mL) was added in 5 min and the solution was warmed up to room temperature and stirred for 1 h. A half-saturated NH₄Cl aqueous solution (30 mL) was

added and the organic residue was extracted with MTBE (3 x 50 mL). The combined organic extract was dried over MgSO₄ and the solvent was evaporated under vacuum. The oil was purified by silica gel chromatography (50% hexanes/ethyl acetate to 100% ethyl acetate then MeOH) to give 0.52 g of **8** as an off-white powder (54% yield).

See *Experimental Section* for characterization data for this new compound.

To a solution of 3-amino-4-picoline (1.08 g, 10.0 mmol) in anhydrous THF (40 mL) at -70 °C was added *sec*-BuLi (21.0 mL, 1.4 M in cyclohexane, 29.4 mmol). Then the reaction mixture was warmed to rt and stirred for 3 h. After cooled back to -70 °C, methyl acetate (0.22 g, 3.0 mmol) dissolved in THF (0.5 mL) was added in 5 min. The reaction mixture was stirred at -30 °C for 0.5 h and was quenched with MeOH (10 mL). The reaction was warmed to rt and stirred for 1 h. Half-saturated NH₄Cl aqueous solution (15 mL) was added and the aqueous layer was extracted with MTBE twice (30 mL each extraction). The combined organic layers was concentrated gave a colorless oil which was further purified by flash chromatography (CH₂Cl₂/MeOH=9:1) to give desired product **9** (0.13 g, 33% yield) as a colorless solid (m.p.: 171-174 °C, Lit.⁷: 185 °C).

¹H NMR (MeOH-d₄, 400 MHz) δ 8.60 (s, 1H), 8.01 (d, *J*= 5.84 Hz, 1H), 7.55 (d, *J*= 5.84 Hz, 1H), 6.37 (s, 1H), 2.54 (s, 3H).

Commercially available 3-amino-4-picoline (1.32 g, 12.0 mmol) was dissolved in anhydrous THF (44 mL) in a dry flask under nitrogen. The solution was cooled to -78 °C and a solution of *s*-BuLi (1.4 M in cyclohexane, 26 mL, 36.0 mmol) was added in 10 min. The solution was warmed to rt, stirred at that temperature for 3 h, and cooled to -78 °C. The ester (0.79 g, 4.8 mmol) was added and the resulting mixture was stirred at -78 °C for 1 h. Methanol (20 mL) was added in 5 min and the solution was warmed up to room temperature and stirred for 1 h. A half-saturated NH₄Cl aqueous solution (30 mL) was added and the organic residue was extracted with MTBE (3 x 50 mL). The combined organic extract was dried over MgSO₄ and the solvent was evaporated under vacuum. The oil was purified by silica gel chromatography (50% hexanes/ethyl acetate to 100% ethyl acetate then MeOH) to give 0.60 g of **10** as an off-white powder (57% yield).

See *Experimental Section* for characterization data for this new compound.

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To a solution of 3-amino-4-picoline (1.08 g, 10.0 mmol) in anhydrous THF (40 mL) at -70 °C was added *sec*-BuLi (21.0 mL, 1.4 M in cyclohexane, 29.4 mmol). Then the reaction mixture was warmed to rt and stirred for 3 h. After cooled back to -70 °C, methyl trimethylacetate (0.35 g, 3.0 mmol) dissolved in THF (0.5 mL) was added in 5 min. The reaction mixture was stirred at -30 °C for 1 h and was quenched with MeOH (10 mL). The reaction was warmed to rt and stirred for 1 h. Half-saturated NH₄Cl aqueous solution (15 mL) was added and the aqueous layer was extracted with MTBE twice (30 mL each extraction). The combined organic layers was washed with water once (40 mL) and brine

once (40 mL) and dried over MgSO₄. Filtration and concentration gave a yellow solid which was further purified by flash chromatography (CH₂Cl₂/MeOH=95:5) to give desired product **11** (0.40 g, 77% yield) as a yellow solid (m.p.: 201-203 °C, Lit.⁷: 204 °C). ¹H NMR (DMSO-d₆, 400 MHz) δ 11.42 (s, 1H), 8.83 (s, 1H), 8.02 (d, *J*= 5.56 Hz, 1H), 7.41 (d, *J*= 5.28 Hz, 1H), 6.23 (s, 1H), 1.37 (s, 9H).

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Commercially available 3-amino-4-picoline (1.32 g, 12.0 mmol) was dissolved in anhydrous THF (44 mL) in a dry flask under nitrogen. The solution was cooled to -78 °C and a solution of *s*-BuLi (1.4 M in cyclohexane, 26 mL, 36.0 mmol) was added in 10 min. The solution was warmed to rt, stirred at that temperature for 3 h, and cooled to -78 °C. The ester (1.0 g, 4.8 mmol) was added and the resulting mixture was stirred at -78 °C for 1 h. Methanol (20 mL) was added in 5 min and the solution was warmed up to room temperature and stirred for 1 h. A half-saturated NH₄Cl aqueous solution (30 mL) was added and the organic residue was extracted with MTBE (3 x 50 mL). The combined organic extract was dried over MgSO₄ and the solvent was evaporated under vacuum. The oil was purified by silica gel chromatography (50% hexanes/ethyl acetate to 100% ethyl acetate then MeOH) to give 0.78 g of **12** as an off-white powder (64% yield).

See *Experimental Section* for characterization data for this new compound.

13

Commercially available 3-amino-4-picoline (1.32 g, 12.0 mmol) was dissolved in anhydrous THF (44 mL) in a dry flask under nitrogen. The solution was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *s*-BuLi (1.4 M in cyclohexane, 26 mL, 36.0 mmol) was added in 10 min. The solution was warmed to rt, stirred at that temperature for 3 h, and cooled to $-78\text{ }^{\circ}\text{C}$. The ester (0.67 g, 4.8 mmol) was added and the resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 1 h. Methanol (20 mL) was added in 5 min and the solution was warmed up to room temperature and stirred for 1 h. A half-saturated NH_4Cl aqueous solution (30 mL) was added and the organic residue was extracted with MTBE (3 x 50 mL). The combined organic extract was dried over MgSO_4 and the solvent was evaporated under vacuum. The oil was purified by silica gel chromatography (50% hexanes/ethyl acetate to 100% ethyl acetate then MeOH) to give 0.42 g of **13** as an off-white powder (48% yield).

See *Experimental Section* for characterization data for this new compound.

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To a solution of 3-amino-4-picoline (1.08 g, 10.0 mmol) in anhydrous THF (40 mL) at $-70\text{ }^{\circ}\text{C}$ was added *sec*-BuLi (21.0 mL, 1.4 M in cyclohexane, 29.4 mmol). Then the reaction mixture was warmed to rt and stirred for 3 h. After cooled back to $-70\text{ }^{\circ}\text{C}$, lactone (0.64 g, 3.0 mmol) dissolved in THF (0.5 mL) was added in 5 min. The reaction mixture was stirred at $-30\text{ }^{\circ}\text{C}$ for 1.5 h and was quenched with MeOH (10 mL). The

reaction was warmed to rt and stirred for 1 h. Half-saturated NH_4Cl aqueous solution (15 mL) was added and the aqueous layer was extracted with MTBE twice (30 mL each extraction). The combined organic layers was washed with water once (40 mL) and brine once (40 mL) and dried over MgSO_4 . Filtration and concentration gave a yellow oil which was further purified by flash chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}=85:15$) to give desired product **14** (0.51 g, 56% yield) as a yellow solid.

See *Experimental Section* for characterization data for this new compound.