Cationic Au(I)-Catalyzed Cycloisomerization of *N*-(2-Alkynylphenyl)indolines for the Construction of Indolobenzazepine Skeleton

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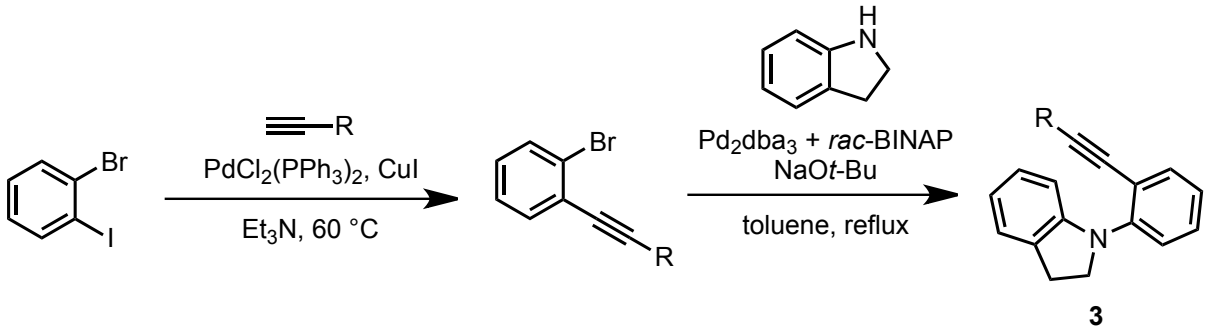
(1) General synthetic scheme of 1-(2-(2-alkynyl)phenyl)-1*H*-indoline derivatives (3)

Sonogashira coupling was conducted under the literature conditions[1]: A dry Schlenk tube was charged with 1-bromo-2-iodobenzene (1.0 eq.), $PdCl_2(PPh_3)_2$ (5 mol%), CuI (5 mol%), alkyne (1.5 eq.), and triethylamine (0.25 M) was added to the reaction vessel. The reaction mixture was then stirred at room temperature for 8 h. The bromides were purified by a short column and were subjected to the next Pd-catalyzed amination without isolation.

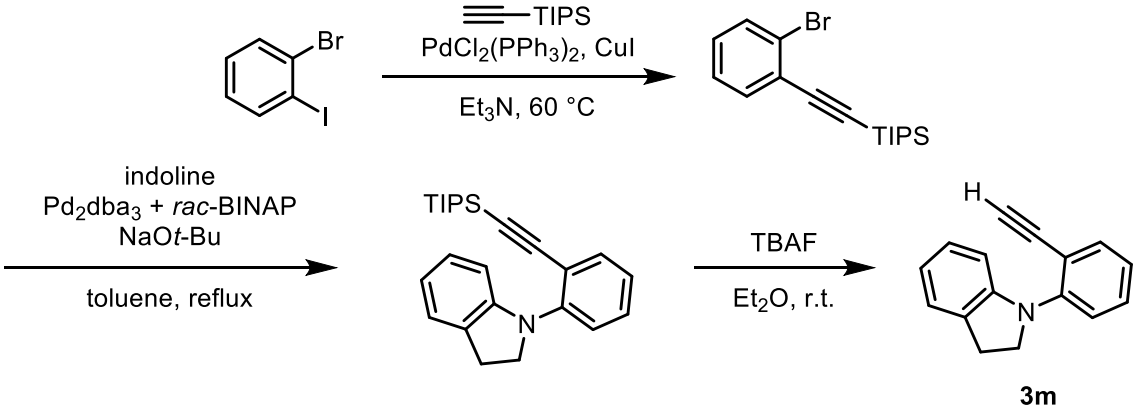
Then Pd-catalyzed amination was conducted under the literature conditions[2]: A dry Schlenk tube was charged with crude product (1.0 eq.), Pd_2dba_3 (2 mol%), *rac*-BINAP (4 mol%), NaO*t*-Bu (1.3 eq.), and toluene (0.25 M). The solution was stirred at 125 °C (bath temperature) for 24 h. After cooling, it was filtered by silica gel and the solvents were removed. Then, the residue was purified by flush column chromatography on silica gel to give desired indoline derivatives **3**.



Scheme S1.

(2) Synthetic scheme of *N*-(2-ethynylphenyl)indoline (3m)

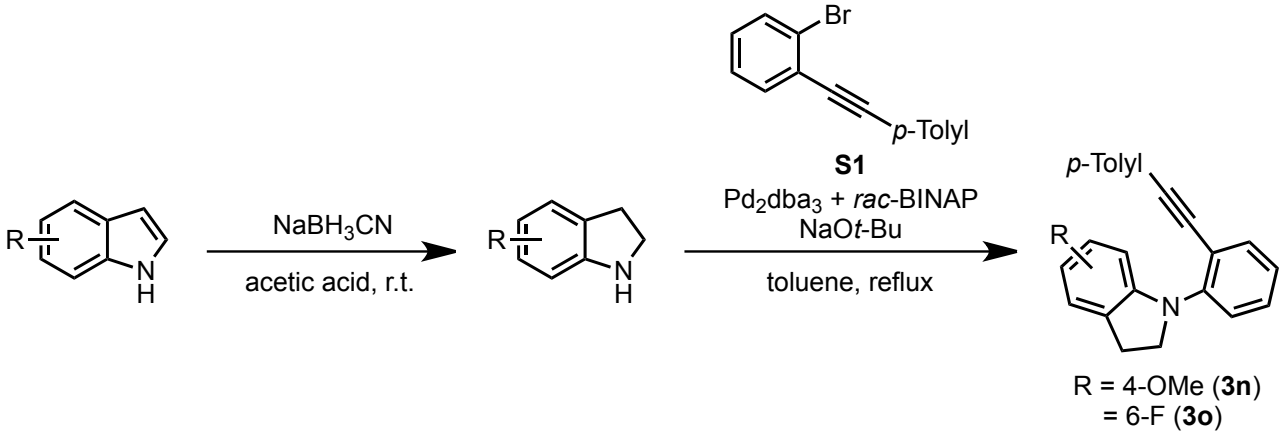
At the first step, Sonogashira coupling of 1-bromo-2-iodobenzene with triisopropylsilylacetylene was conducted under the reported conditions.[3] A dry Schlenk tube was charged with 2-bromo-1-iodobenzene (0.5 mmol), $PdCl_2(PPh_3)$ (0.01 mmol), CuI (0.02 mmol), triisopropylsilylacetylene (0.75 mmol), and triethylamine (1.0 ml). The solution was stirred at 60 ℃ (bath temperature) for 24 h. After cooling, the obtained bromide was purified by a short column and was subjected to the next Pd-catalyzed amination without complete isolation: Pd-catalyzed amination was conducted under the same condition as the latter step in Scheme S1, and the crude products were subjected to the next desilylation[4]: A dry schlenk tube was charged with triisopropylsilylalkyne (0.29 mmol), tetrabutylammoniumfluoride (0.34 mmol), and diethylether (1.16 ml). The solution was stirred at room temperature for 5 min, and it was filtered by silica gel and the solvents were removed. Then the residue was purified by PTLC to give **3m** (60.6 mg, 68% in three steps).



Scheme S2.

(3) Synthetic scheme of substituted indoline derivatives (3n and 3o)

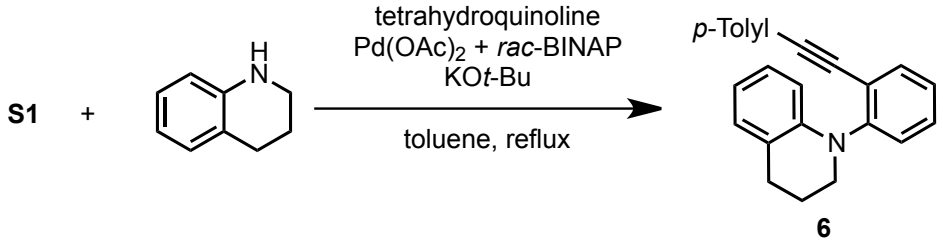
At the first step, 6-fluoroindoline was prepared via hydrogenation of the corresponding substituted indoles[5]: A dry Schlenk tube was charged with 6-fluoroindole (0.5 mmol), $NaBH_3CN$ (1.0 mmol), and acetic acid (0.2 ml). The solution was stirred at room temperature for 2 h, and then quenched by 5 ml of 2M NaOH aq, and the organic materials were extracted by CH_2Cl_2. The combined organic layer was washed with brine, and dried over Na_2SO_4. After removal of solvent, the crude products were purified by PTLC (hexane/ethyl acetate = 5/1) to give 6-fluoroindoline (39.5 mg, 57%). Then Pd-catalyzed amination proceeded under the same conditions as the latter step of scheme S1 to give **3n** (23.4 mg, 18% in two steps). 4-Methoxyindoline derivative **3o** was synthesize under the same condition as above (77.1 mg, 62% in two steps).



Scheme S3.

(4) Synthetic scheme of 1-(2-(2-(4-methylphenyl)ethynyl)phenyl)-1,2,3,4-tetrahydroquinoline (6)

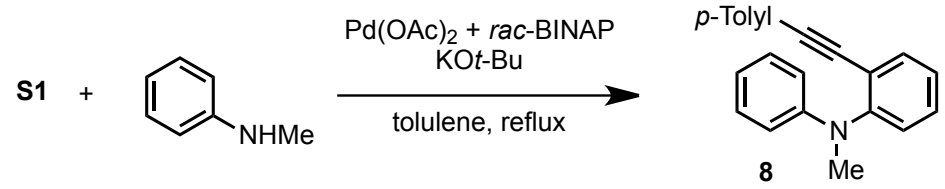
Pd-catalyzed amination was conducted in a dry Schlenk tube, which was charged with **S1** (0.36 mmol), tetrahydroquinoline (0.43 mmol), $Pd(OAc)_2$ (0.018 mmol), *rac*-BINAP (0.020 mmol), K*t*-BuO (0.50 mmol), and toluene (0.66 ml). The solution was stirrd at 100 °C for 24 h, and it was filtered by silica gel and the solvents were removed. Then the residue was purified by flash column chromatography (hexane/toluene = 5/1) to give desired product **6** (66.6 mg, 57%).



Scheme S4.

(5) Synthetic scheme of *N*-methyl-*N*-phenyl-2-(2-(4-methylphenyl)ethynyl)benzenamine (8)

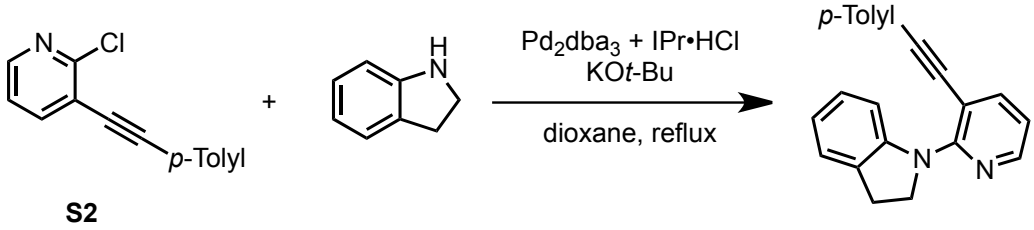
The preparation of **8** was the same as Scheme S4 using *N*-methylaniline instead of tetrahydroquinoline, and desired **8** was obtained (99.6 mg, 72%).



Scheme S5.

(6) Synthetic scheme of 1-(3-(2-(4-methylphenyl)ethynyl)pyridin-2-yl)indoline (3p)

In this scheme, **S2** was synthesized under the reported conditions[7]. Next Pd-catalyzed amination was conducted under the reported conditions: A dry schlenk tube was charged with **S2** (0.5 mmol), indoline (0.56 mmol), Pd_2dba_3 (0.005 mmol), IPr·HCl (0.02 mmol), KO*t*-Bu (0.75 mmol) and 1.5 ml of dioxane. The solution was stirred at 110 °C (bath temperature) for 5 h, and then it was filtered by silica gel. After removal of solvent, desired **3p** was obtained (75.1 mg, 48%).



Scheme S6.

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