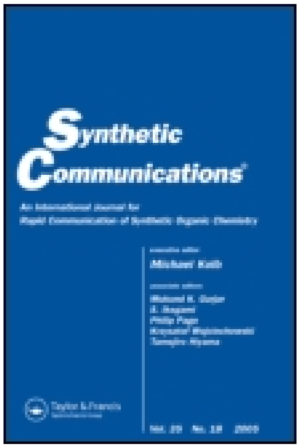

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HYPERVALENT IODINE IN SYNTHESIS. 77. AN EFFICIENT METHOD FOR THE SYNTHESIS OF *N*-ARYLINDOLES BY THE COPPER-CATALYZED *N*-ARYLATION OF INDOLE WITH DIARYLIODONIUM SALTS

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ABSTRACT

N-arylindoles were prepared in good yields by copper-catalyzed *N*-arylation of indole with diaryliodonium salts.

In continuation of our interest in exploring the utility of transition metal-catalyzed arylation reaction,[1] we examined *N*-arylation of indole with diaryliodonium salts in the presence of copper catalyst (Scheme 1). The results are summarized in Table 1.

We found that copper-catalyzed *N*-arylation of indole with diaryliodonium salts could proceed smoothly at 140–150°C and gave *N*-arylindoles in good yields. Compared with the traditional Ullmann reaction[2]

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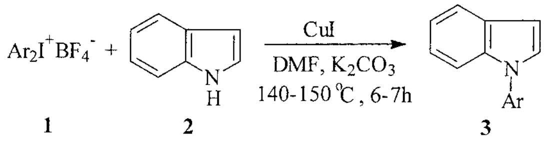

Scheme 1.

Table 1. Copper-Catalyzed *N*-Arylation of Indole

Entry	$Ar_2I^+BF_4^-$	Copper Catalyst	Product	Yield[a] (%)
1	$Ph_2I^+BF_4^-$ **1a**	$Cu(OAc)_2$	**3a**	52
2	**1a**	$Cu(acac)_2$	**3a**	83
3	**1a**	CuI	**3a**	83
4	$(p\text{-Tol})_2I^+BF_4^-$ **1b**	CuI	**3b**	87
5	$(p\text{-ClC}_6H_4)_2I^+BF_4^-$ **1c**	CuI	**3c**	92
6	$(p\text{-CH}_3OC_6H_4)_2I^+BF_4^-$ **1d**	CuI	**3d**	80
7	$(p\text{-BrC}_6H_4)_2I^+BF_4^-$ **1e**	CuI	**3e**	81
8	$(m\text{-NO}_2C_6H_4)_2I^+BF_4^-$ **1f**	CuI	**3f**	76
9	$(p\text{-CH}_3CONH\,C_6H_4)_2I^+BF_4^-$ **1g**	CuI	**3g**	72

[a] Yield of isolated pure product.

(190–210°C), the reaction temperature was lower greatly. Furthermore, stoichiometric copper powder was not needed. Among the tested copper catalysts including CuI, $Cu(OAc)_2$ and $Cu(acac)_2$, though each of them can catalyze this reaction, CuI is the most effective and practical. Several diaryliodonium salts with various substituents such as methyl, chloro, methoxy, bromo, nitro and acetamido groups were tested. It was found that the reaction is general for these substrates.

In conclusion, we provide an effective synthesis for *N*-arylindoles by copper-catalyzed *N*-arylation of indole with diaryliodonium salts. It has some advantages over others[3–10] such as mild reaction conditions, simplicity of procedure, using nonpoisonous, accessible reagents and good yields.

EXPERIMENTAL

Melting points were uncorrected. ^{1}H NMR data were recorded on Avance 400 spectrometer using $CDCl_3$ as the solvent with TMS as an internal standard. IR spectra were determined on Vector 22 infrared spectrometer with KBr pallet. MS spectra were recorded on HP5859B mass spectrometer. Elemental analyses were performed on EA1110.

General procedure for preparation of *N*-arylindoles. A mixture of diaryliodonium salt **1** (1 mmol), indole **2** (1 mmol), K_2CO_3 (3 mmol), CuI (10 mol%) and DMF (5 ml) was stirred under a nitrogen atmosphere at 140–150°C for 6–7 h. After cooling, the reaction mixture was diluted with saturated NH_4Cl aqueous (20 ml), and extracted with diethyl ether (3 × 15 ml). The combined organic layer was washed with brine, dried over anhydrous sodium sulfate. After removal of the solvent under vacuum, the residue was chromatographed on silica gel plate using petroleum ether for **3a**–**3e**, c-hexane/ethyl acetate (20 : 1) for **3f** and *c*-hexane/ethyl acetate (1 : 1) for **3g** as a developer to give pure product.

Physical and Spectroscopic Data

***N*-Phenylindole 3a.** Oil (lit[2(c)] oil). ^{1}H NMR δ_H 6.67 (m, 1H), 7.20 (m, 2H), 7.33 (m, 2H), 7.49 (m, 4H), 7.55 (m, 1H), 7.68 (m, 1H). IR ν_{max}/cm^{-1} 1597, 1515, 1498, 1457, 1332, 1234, 1213, 1136, 774, 742, 696.

***N*-(4-Methylphenyl)indole 3b:** Oil (lit[2(c)] oil). ^{1}H NMR δ_H 2.42 (s, 3H), 6.65 (m, 1H), 7.15 (m, 1H), 7.20 (m, 1H), 7.29 (m, 3H), 7.37 (m, 2H), 7.52 (m, 1H), 7.68 (m, 1H). IR ν_{max}/cm^{-1} 1519, 1458, 1334, 1234, 1213, 1135, 822, 762, 741.

***N*-(4-Chlorophenyl)indole 3c.** M.p. 66–67°C (lit[2(c)] m.p. 64–66°C). ^{1}H NMR δ_H 6.69 (m, 1H), 7.20 (m, 2H), 7.29 (m, 1H), 7.43–7.52 (m, 5H), 7.68 (m, 1H). IR ν_{max}/cm^{-1} 1592, 1516, 1492, 1331, 1233, 1211, 1132, 1088, 1011, 831, 762, 737.

***N*-(4-Methoxyphenyl)indole 3d.** M.p. 56–58°C (lit[2(c)] m.p. 57–58°C). ^{1}H NMR δ_H 3.88 (s, 3H), 6.65 (m, 1H), 7.03 (m, 2H), 7.15–7.20 (m, 2H), 7.27 (m, 1H), 7.39 (m, 2H), 7.44 (m, 1H), 7.68 (m, 1H). IR ν_{max}/cm^{-1} 1611, 1517, 1457, 1333, 1301, 1248, 1213, 1179, 1134, 1105, 835, 762, 747.

***N*-(4-Bromophenyl)indole 3e.** M.p. 64–65°C (lit[9] m.p. was not reported). ^{1}H NMR δ_H 6.69 (m, 1H), 7.17 (m, 1H), 7.24 (m, 1H), 7.29 (m, 1H), 7.39 (m, 2H), 7.51 (m, 1H), 7.63 (m, 2H), 7.68 (m, 1H). IR ν_{max}/cm^{-1} 1588, 1516, 1491, 1455, 1334, 1310, 1233, 1211, 1133, 1101, 1072, 1009, 828, 762, 738, 722. MS *m*/*z* 271 (M^+, 100), 273 ($M^+ + 2$, 98.14). Anal. Calcd for $C_{14}H_{10}BrN$: C, 61.79; H, 3.70; N, 5.14. Found: C, 61.56; H, 3.74; N, 5.28.

***N*-(3-Nitrophenyl)indole 3f.** M.p. 65–67°C (lit[2(b)] m.p. 67–68°C). ^{1}H NMR δ_H 6.76 (m, 1H), 7.24 (m, 1H), 7.29 (m, 1H), 7.38 (m, 1H), 7.59 (m, 1H), 7.71 (m, 2H), 7.87 (m, 1H), 8.19 (m, 1H), 8.40 (m, 1H). IR ν_{max}/cm^{-1} 1607, 1534, 1487, 1455, 1349, 1236, 1211, 1137, 742.

***N*-(4-Acetamidophenyl)indole 3g.** M.p. 161–162°C. ^{1}H NMR δ_H 2.23 (s, 3H), 6.67 (m, 1H), 7.16–7.21 (m, 2H), 7.29 (m, 1H), 7.38 (s, 1H, N-H), 7.45 (m, 2H), 7.51 (m, 1H), 7.64–7.69 (m, 3H). IR ν_{max}/cm^{-1} 3243, 3052, 1659, 1612, 1519, 1461, 1415, 1371, 1316, 1266, 1236, 1215, 1139, 1014, 969, 840, 764, 744. MS *m*/*z* 250 (M^{+}, 100). Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.62; H, 5.68; N, 11.27.

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