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# Sodium Hydride Induced N-Arylation of Diisopropyl Azodicarboxylate by Aryl Trifluoromethanesulfonates

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Issa Yavari\* Majid Ghazanfarpour-Darjani Mohammad J. Bayat Alaleh Malekafzali

Department of Chemistry, University of Tarbiat Modares, P.O. Box 14115-175, Tehran, Iran yavarisa@modares.ac.ir

i-PrO<sub>2</sub>C<sup>N</sup>≈<sub>N</sub><sup>CO<sub>2</sub>i-Pr</sup> + ArOTf Cu<sub>2</sub>O, NaH, Lil .CO<sub>2</sub>i-Pr

13 examples; yields: 63-94%

Letter

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Abstract A method for intermolecular N-arylation of the anionic species derived from diisopropyl azodicarboxylate and sodium hydride by aryl trifluoromethanesulfonates, in the presence of a ligand-free copper(I) oxide catalyst at 80 °C in N,N-dimethylformamide, is reported. A variety of functionalized aryl triflouromethanesulfonates were efficiently coupled by this method.

Key words C-N cross-coupling, aryl trifluoromethanesulfonates, diisopropyl azodicarboxylate, copper(I) oxide

The past decade has witnessed significant progress in the development of cross-coupling reactions.<sup>1</sup> Transition metals are effective catalysts in cross-coupling reactions, particularly C-N bond-formation processes.<sup>2</sup> Several N-nucleophiles, such as amines, amides, hydrazines, and N-heterocycles, participate in C-N cross-coupling reactions,<sup>3-5</sup> and the application of other compounds as amination reagents have been developed.<sup>6,7</sup> Diisopropyl azodicarboxylate (DIAD) has been used as a suitable amination reagent for the preparation of hydrazides that can be subsequently deprotected to amines. However, this reaction has been limited to electron-rich aromatic systems.8-10

Recently, we reported effective systems for the coppercatalyzed coupling of aryl halides with the Mitsunobu reagent.<sup>11</sup> In this Letter, we describe C-N coupling of aryl triflates with the anionic adduct derived from DIAD and NaH. which constitutes a useful method for intermolecular Narylation with aryl trifluoromethanesulfonates (ArOTfs) in the presence of a ligand-free Cu<sub>2</sub>O catalyst and lithium iodide (Scheme 1).



Initial investigations show that 10 mol% of CuI could accomplish the transformation, and the desired coupling product was obtained in 45% yield, together with reduced DIAD in 20% yield. Phenyl trifluoromethanesulfonate, NaH, and DIAD were selected as prototypical reaction partners for the Cu<sub>2</sub>O-catalyzed coupling reaction. The optimized reaction conditions and catalyst system for this transformation involved phenyl trifluoromethanesulfonate (1 mmol), DIAD (1.2 mmol), NaH (1.2 mmol), Cu<sub>2</sub>O (10 mol%), and lithium iodide (1.0 mmol) in DMF (2 mL) at 80 °C (see Table 1).

Table 1 Optimization of Reaction Conditions for the Cu<sub>2</sub>O-Catalyzed Formation of Aryl Hydrazides<sup>a</sup>

Entry	Solvent	Additive	Yield (%)
1	DMSO	none	41
2	THF	none	15
3	MeCN	none	24
4	DMF	none	45
5	DMF	Lil	83
6	DMF	LiBr	69
7	DMF	LiOTf	74
8	DMF	Lil	76
9	DMF	KI	56

<sup>a</sup> Reactions conditions: phenyl trifluoromethanesulfonate (1.0 mmol), DIAD (1.2 mmol), NaH (1.2 mmol), Cu<sub>2</sub>O (0.10 mmol), additive (1.0 mmol), in solvent (2 mL) at 80 °C for 8 h under argon.

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In addition, 1,10-phenanthroline can be used as a unique ligand for the N-arylation with chlorobenzenes (Table 2). However, this conversion required higher catalyst loading (30 mol%) compared to those of aryl iodides, bromides, and triflates.

A series of substituted aryl O-triflates, as shown in Table 2, was subjected to the reaction conditions described above. Aryl O-triflates having electron-withdrawing, electron-releasing, and bulky groups on the aromatic ring, afforded moderate to good yields (Table 2).

 Table 2
 Reaction Scope for Aryl Sources

<i>i</i> -PrO <sub>2</sub> 0	N≈N <sup>∠CO<sub>2</sub>i-Pr</sup> + ArOTf 1 2	Cu <sub>2</sub> O, NaH, Lil DMF, 70 °C <sup>i</sup> ·PrO <sub>2</sub>	Ar I C <sup>N</sup> N <sup>CO2</sup> <sup><i>i</i>-Pr</sup> H <b>3</b>
Entry	Ar	Product	Yield (%) of <b>3</b>
1	Ph	3a	83
2	1-naphthyl	3b	80
3	4-MeC <sub>6</sub> H <sub>4</sub>	3c	79
4	2-MeC <sub>6</sub> H <sub>4</sub>	3d	72
5	3-MeC <sub>6</sub> H <sub>4</sub>	3e	80
6	4-MeOC <sub>6</sub> H <sub>4</sub>	3f	70
7	2-F <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	3g	63
8	3-F <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	3h	81
9	$4-NCC_6H_4$	3i	84
10	$2-O_2NC_6H_4$	Зј	67
11	$4-O_2NC_6H_4$	3k	94
12	2-thienyl	31	79
13	$2-CIC_6H_4$	3m	76

The optimized reaction conditions given above were compatible with the presence of functional groups such as CN, NO<sub>2</sub>, CF<sub>3</sub>, OMe, and halogens on the aromatic rings of the aryl halides and triflates. With iodobenzene as arylating reagent, the reaction could be carried out at 25 °C in the presence of Cu<sub>2</sub>O in DMF to achieve the desired product in 90% yield.

A plausible mechanism for the formation of products  $3^{12}$  is given in Scheme 2. The copper complex 4, formed from 1 and Cu<sub>2</sub>O, undergoes a reduction reaction with NaH to generate the salt 5. This salt is attacked by aryl trifluoromethanesulfonate 2 to afford aryl hydrazide 3.



In conclusion, we have described a novel system for the copper-catalyzed N-arylation of diisopropyl azodicarboxylate in good to excellent yields. This system operates under mild enough conditions and tolerates a wide array of functional groups. Using this procedure iodobenzene was selectively coupled with diisopropyl azodicarboxylate in the presence of bromobenzene and benzene O-triflates.

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- (12) **Typical Procedure for the Preparation of Aryl Hydrazides 3** To a stirred solution of DIAD (1.2 mmol) in DMF (2 mL) at 0 °C, NaH (0.05 g, 1.2 mmol) was added in portions over 20 min. Then, the aryl 0-triflate (1.0 mmol), Lil (134 mg, 1mmol), and Cu<sub>2</sub>O (15 mg, 0.1 mmol) were added to the reaction mixture, which was stirred at 80 °C for 8 h under N<sub>2</sub>. The reaction was cooled and quenched by adding CH<sub>2</sub>Cl<sub>2</sub> (2 mL) and sat. aq NH<sub>4</sub>Cl (3 mL). The mixture was stirred for an additional 30 min, and two layers were separated. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 2 mL), the combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. The residue was purified by chromatography (silica gel; hexane–EtOAc, 3:1) to give the product.

Spectroscopic analyses of all derivatives except  ${\bf 3d}$  and  ${\bf 3m}$  have been reported.  $^{11}$ 

### Diisopropyl 1-o-Tolylhydrazine-1,2-dicarboxylate (3d)

Yellow solid; mp 101–103 °C; yield: 0.21 g (72%). IR (KBr):  $v_{max}$  = 3242, 1541, 1518, 1330, 1140 cm<sup>-1</sup>. <sup>1</sup>H NMR (500.1 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.16 (6 H, d, <sup>3</sup>J = 7.1 Hz, 2 Me), 1.25 (6 H, d, <sup>3</sup>J = 7.0 Hz, 2 Me), 2.33 (3 H, s, Me), 4.97–4.99 (2 H, m, 2 CHO), 7.06 (1 H, br s, NH), 7.19–7.22 (3 H, m, 3 CH), 7.44 (1 H, d, <sup>3</sup>J = 7.8 Hz, CH). <sup>13</sup>C NMR (125.7 MHz, CDCl<sub>3</sub>):  $\delta$  = 21.1 (2 Me), 21.4 (2 Me), 26.1 (Me), 68.9 (CHO), 70.1 (CHO), 113.1 (CH), 119.2 (CH), 126.3 (CH), 129.2 (CH), 130.9 (C), 140.5 (C), 155.7 (C=O), 156.1 (C=O). MS: *m/z* (%) = 294 (4 [M<sup>+</sup>], 235 (57), 192 (42), 177 (40), 133 (100), 102 (76), 58 (34), 44 (28). Anal. Calcd (%) for C<sub>15</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub> (294.35): C, 61.21; H, 7.53; N, 9.52. Found: C, 59.89; H, 7.59; N, 9.59.

# Diisopropyl 1-(2-Chlorophenyl)hydrazine-1,2-dicarboxylate (3m)

Colorless solid; mp 103–106 °C; yield 0.24 g (76%). IR (KBr):  $v_{max}$  = 3286, 1564, 1518, 1332, 1136 cm<sup>-1</sup>. <sup>1</sup>H NMR (500.1 MHz,

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 $\begin{array}{l} {\rm CDCl}_3{\rm ):} \; \delta = 1.13 \; (6 \; {\rm H}, \; {\rm d}, \; {}^3J = 6.9 \; {\rm Hz}, \, 2 \; {\rm Me}), \; 1.26 \; (6 \; {\rm H}, \; {\rm d}, \; {}^3J = 7.0 \\ {\rm Hz}, \, 2 \; {\rm Me}), \; 4.98 - 5.01 \; (2 \; {\rm H}, \; {\rm m}, \, 2 \; {\rm CHO}), \; 7.17 \; (1 \; {\rm H}, \; {\rm br} \; {\rm s}, \; {\rm NH}), \; 7.46 - \\ 7.53 \; (2 \; {\rm H}, \; {\rm m}, \, 2 \; {\rm CH}), \; 7.62 - 7.67 \; (2 \; {\rm H}, \; {\rm m}, \, 2 \; {\rm CH}), \; {}^{13}{\rm C} \; {\rm NMR} \; (125.7 \\ {\rm MHz}, \; {\rm CDCl}_3{\rm ):} \; \delta = \; 21.9 \; (2 \; {\rm Me}), \; 22.3 \; (2 \; {\rm Me}), \; 70.1 \; ({\rm CHO}), \; 71.0 \\ ({\rm CHO}), \; 123.8 \; ({\rm CH}), \; 128.1 \; ({\rm CH}), \; 131.6 \; ({\rm CH}), \; 132.6 \; ({\rm CH}), \; 133.0 \; ({\rm C}), \end{array}$ 

139.4 (C), 154.3 (C=O), 156.0 (C=O). MS: m/z (%) = 314 (1) [M<sup>+</sup>], 225 (12), 212 (53), 197 (45), 152 (100), 102 (64), 111 (12), 58 (35), 44 (19). Anal. Calcd (%) for C<sub>14</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>4</sub> (314.76): C, 53.42; H, 6.08; N, 8.90. Found: C, 53.79; H, 6.04; N, 8.98.

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