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Synthesis and Characterization of Some *N*-Aryl-4-nitroimidazoles as Potential Insensitive Energy Materials

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N-Aryl derivatives of 4-nitroimidazole have been synthesized under CuI/TBAB catalytic system in excellent yields, using KOH as base in DMF solvent.

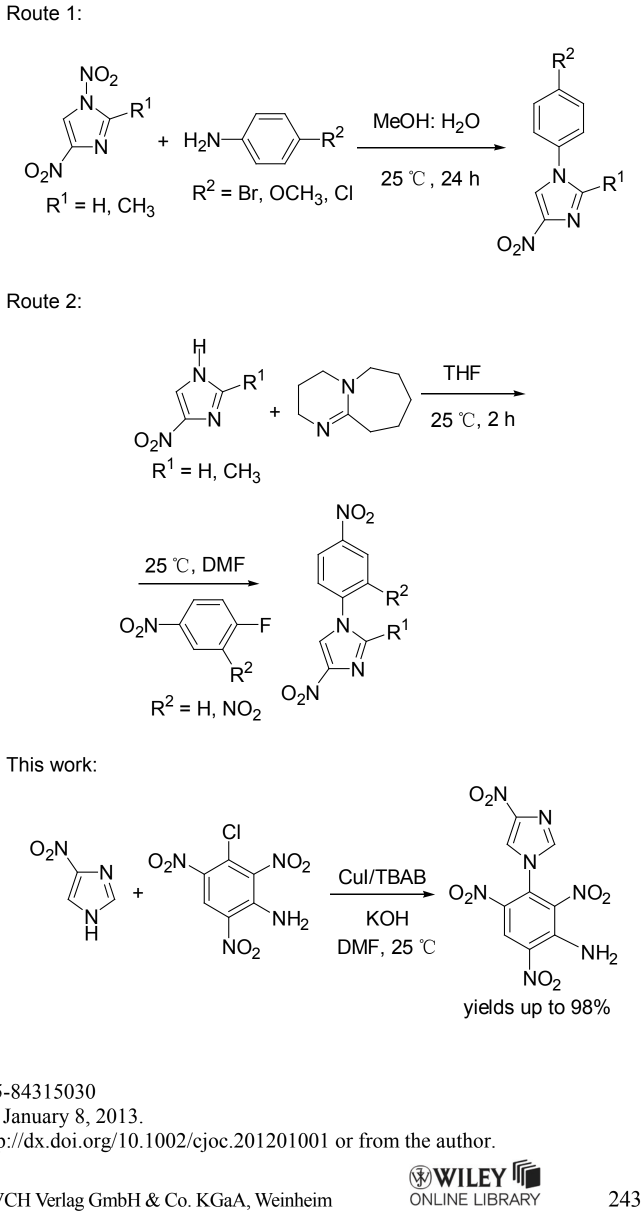
Keywords organic chemistry, synthesis, CuI-catalyzed, *N*-arylation, 4-nitroimidazole

Introduction

The synthesis and development of new, insensitive energetic materials that contain aromatic nitrogen-containing heterocyclic core units have attracted attention due to their more favorable elemental composition with relatively higher energetic performance in regard to oxygen balance, density, and other thermodynamic properties when compared to their carbon-only analogous aromatic compounds.[1-7] It is with this background and in continuation of our program aimed at synthesis of new nitroimidazole-based energetic materials that we have undertaken the synthesis of *N*-aryl-*C*-nitroimidazoles.

It has been reported in the literature[8] that when 1,4-dinitroimidazole reacted with anilines in aqueous methanol at ambient temperature, degenerated ring transformation occurred, thereby providing 1-aryl-4-nitroimidazoles, in high yields, containing electron-donating or relatively weak electron-withdrawing substituents like OH, OR, R, Cl, Br, COOR *etc.* in aryl group. Very weak nucleophiles (*e.g.* 2,4-dinitroaniline) do not react with 1,4-dinitroimidazole (Scheme 1, Route 1). In order to introduce 2,4-dinitrophenyl substituent on the pyrrole type nitrogen atom in C-nitro-1H-azoles, Searcey and co-workers[9] utilized tetraalkyl ammonium salts of nitroimidazoles to react with halo compounds. Walczak and co-workers[8] used a reaction of 1-fluoro-2,4-dinitro- or 1-fluoro-4-nitrobenzene accordingly with nitroazole-1,8-diaza-bicycle[5.4.0]-7-undecenium salts (Scheme 1, Route 2). Dissolution of 4-nitroimidazole (4-NI) in DMF and treatment with picryl fluoride at ambient temperature, followed by quenching in water, afforded 4-nitro-1-picrylimidazole in 68% yield.[10] All of these either used active fluoride compounds as substrate or had a low yield, chloride compounds are little reported. In the past few years, a wide number of protocols for the experimentally simple transition metal-catalyzed *N*-arylation of free (NH)-imidazoles with aryl

Scheme 1 Synthesis scheme of *N*-aryl-4-nitroimidazoles



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halides has been described,[11,12] but nitroimidazoles are little reported. Nitroimidazoles have been used as antifungal, antibacterial, antiviral, antitumor drugs and their intermediates[8,13] and recently as high energy materials, respectively.

In this work, we utilize chloronitroarenes to react with 4-nitroimidazoles under the catalytic system CuI/TBAB, which gives *N*-aryl-4-nitroimidazoles in excellent yields. This is a new and practical route to synthesis of nitroimidazole-based energetic materials.

Experimental

A general procedure for the preparation of *N*-aryl-4-nitroimidazoles

A mixture of 4-nitroimidazole (**1a** 0.45 g, 4 mmol), KOH (0.22 g, 4 mmol) and DMF (15 mL) was stirred at ambient temperature for 1 h, followed by CuI/TBAB (0.03 g/0.06 g, 0.16 mmol/0.19 mmol), then chloronitroarene (**1b**, **2b**, **3b**, **4b**, **5b**, 4 mmol) was added in small lots with stirring. The contents were kept stirring for 2—4 h at room temperature. The reaction mixture was poured onto ice-water mixture. The precipitations were collected and dried on air, recrystallized from acetone/methol, giving **1c**—**5c**, respectively.

1-(2',4'-Dinitrophenyl)-4-nitroimidazole (1c)

Yield: 80%; m.p. 150—152 ℃ (153—154 ℃[8]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 9.01 (d, J=2.5 Hz, 1H), 8.91 (d, J=1.15 Hz, 1H), 8.79 (dd, J=2.5, 8.7 Hz, 1H), 8.30 (d, J=1.15 Hz, 1H), 8.19 (d, J=8.7 Hz, 1H).

1-(2',4',6'-Trinitrophenyl)-4-nitroimidazole (2c)

Yield: 83%; m.p. 280—282 ℃ (286—287 ℃[10]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 9.37 (s, 2H), 8.86 (d, J=1.45 Hz, 1H), 8.29 (d, J=1.45 Hz, 1H).

1-(3'-Amino-2',4',6'-trinitrophenyl)-4-nitro-imidazole (3c)

Yield: 98%; m.p. 246—248 ℃; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 9.12 (s, 1H), 8.76 (d, J=1.3 Hz, 1H), 8.75 (s, 2H), 8.18 (d, J=1.3 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 122.63, 126.33, 127.96, 129.63, 137.93, 147.31. MS (ESI) m/z: 337.86 (M–H). Structure of this product was established unambiguously via single crystal X-ray crystallography (Figure 1). Selected X-ray data:[14] crystal system, monoclinic; space group, $P2_1/N$; volume, 1302.1 A^3; Z, 4; density, 1.73 g/cm^3.

1-(3',5'-Diamino-2',4',6'-trinitrophenyl)-4-nitro-imidazole (4c)

Yield: 83%; m.p. 296—298 ℃; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.77 (d, J=1.3 Hz, 1H), 8.18 (d, J=1.3 Hz, 1H), 8.21 (s, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 121.09, 121.69, 123.26, 129.29, 137.03, 138.81, 141.21, 146.24, 147.23. Anal. calcd for $C_9H_6N_8O_8$: C 30.52, H 1.71, N 31.64; found C 30.48, H 1.76, N 31.62. MS (ESI) m/z: 352.86 (M–H).

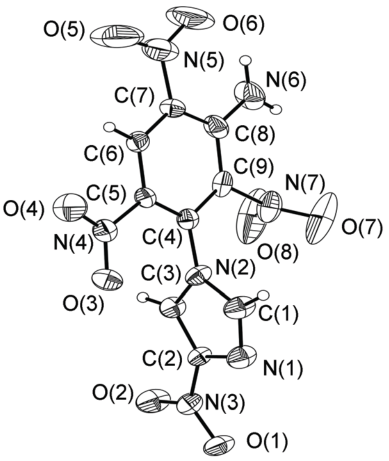


Figure 1 ORTEP view of **3c**.

3,5-Di-(4'-nitroimidazole)-2,4,6-trinitro-benzenamine (5c)

Yield: 75%; m.p. 235—238 ℃; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.85 (s, 1H), 8.78 (s, 1H), 8.54 (s, 2H), 8.27 (s, 1H), 8.22 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 121.51, 123.16, 126.30, 130.83, 134.87, 137.34, 139.04, 169.84. Anal. calcd for $C_{12}H_6N_{10}O_{10}$: C 32.01, H 1.34, N 31.11; found C 31.96, H 1.31, N 31.12. MS (ESI) m/z: 448.82 (M–H).

Results and Discussion

4-NI reacted with 1-chloro-2,4-dinitrobenzene (**1b**) in DMF using pyridine as base, no reaction occurred at room temperature. Rising the temperature (80 ℃), we just obtained hydrolysis product. However, hydrolysis occurred when 4-NI reacted with picryl chloride (**2b**) at room temperature. Using inorganic base such as K_2CO_3 and KOH, the results were unchanged. Fortunately, we got **3c** in moderate yield (65%) when 4-NI reacted with **3b** in DMF under KOH condition, comparing to the virtually quantitative yield (98%) when under CuI/TBAB catalysis, which can actually avoid the self-reaction of **3b** (Table 1).

Table 1 The results under different conditions^a

Substrate	Procedure modification	Yield^b/%
1b	Without CuI/TBAB, reaction at r.t. or 80 ℃ using pyridine as base	No reaction or Hydrolysis
	Under CuI/TBAB, reaction at r.t.	80
2b	Without CuI/TBAB, reaction at r.t.	Hydrolysis
	Under CuI/TBAB, reaction at r.t.	83
3b	Without CuI/TBAB, reaction at r.t.	65
	Under CuI/TBAB, reaction at r.t.	98

^{a} All reactions carried out using KOH as base unless otherwise stated; ^{b} Isolated yield.

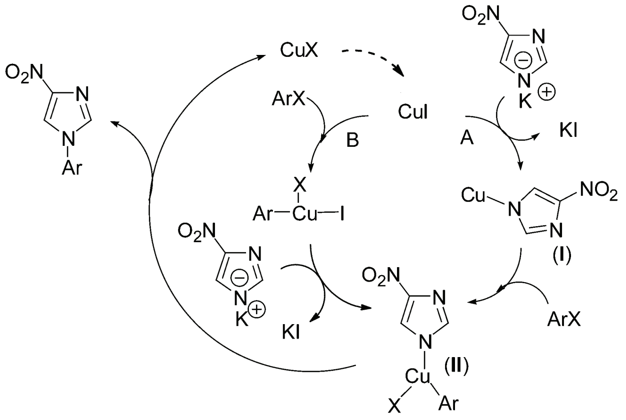
4-NI and 3-chloro-2,4,6-trinitro-benzenamine (**3b**) were used as model substrates to optimize the reaction conditions. Effects of parameters such as catalyst, base, and additive were studied (Table 2). In our initial experiment, **3b** (1 equiv.) was treated with 4-NI (1 equiv.) in DMF at room temperature for 2 h in the presence of KOH (1 equiv.); only moderate yield of **3c** was obtained (Table 2, Entry 1). Adding TBAB to the reaction led to only a slight increase of yield (Table 2, Entry 2), but a good yield was obtained in the presence of CuI (Table 2, Entry 3). It was found that CuI/TBAB catalyst with KOH afforded an excellent yield (98%) whereas K_2CO_3 gave moderate yields (69%) and $KHCO_3$ showed equal activity as NaOH (84% and 80%, respectively) (Table 2, Entries 4, 7—9). Other copper compounds (CuO and $Cu(OAc)_2$) were also evaluated but proved inferior to CuI (Table 2, Entries 5 and 6).

Table 2 Optimization of conditions for the synthesis of *N*-aryl-*C*-nitroimidazoles[a]

Entry	Catalyst	Additive	Base	Yield[b]/%
1	—	—	KOH	65
2	—	TBAB	KOH	70
3	CuI	—	KOH	84
4	CuI	TBAB	KOH	98
5	CuO	TBAB	KOH	71
6	$Cu(OAc)_2$	TBAB	KOH	61
7	CuI	TBAB	NaOH	80
8	CuI	TBAB	K_2CO_3	69
9	CuI	TBAB	$KHCO_3$	84

[a] Reaction condition: 4-NI (4 mmol), base (4 mmol), **3b** (4 mmol), Cat. (0.16 mmol), TBAB (0.19 mmol), DMF (10 mL); [b] Isolated yield.

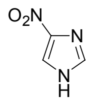
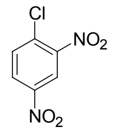
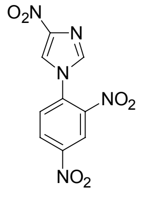
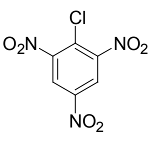
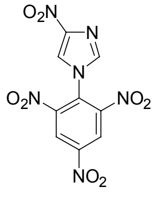
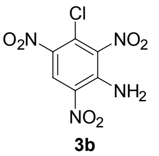
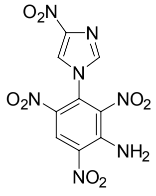
Scheme 2 The possible catalytic cycle driven by CuI



As described in Scheme 2, we have formulated a possible catalytic cycle for the copper catalyzed *N*-arylation of nitro-imidazole based on the previously reported mechanism.[11] There are two ways to lead to the intermediate (**II**) which undergoes a reductive elimination to provide the target product and to regenerate the $Cu^{(I)}$. First way described as A: Chelation of $Cu^{(I)}$ with potassium salt of 4-NI occurs to form the (**I**) and the subsequent oxidative addition of the (**I**) with aryl chloride leads to the intermediate (**II**); Another way described as B: Oxidative addition of $Cu^{(I)}$ with aryl chloride leads to the $Cu^{(III)}$, then chelation of it with potassium salt of 4-NI occurs to form the intermediate (**II**). To confirm the possible catalytic cycle, we designed the following reactions (Table 4).

It showed that the product of the reaction of 4-NI, KOH and CuI (Table 4, Entry 2, corresponding to A) gave equal activity as CuI (Table 1, Entries 3, 7, and 9);

Table 3 Preparation of some *N*-aryl-4-nitroimidazoles

Entry	Nitroimidazole	Substrate	Product	Yield/%
1	 **1a**	 **1b**	 **1c**	80
2	**1a**	 **2b**	 **2c**	83
3	**1a**	 **3b**	 **3c**	98

Continued

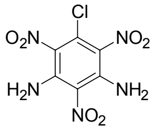
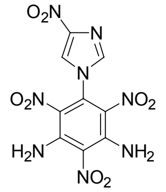
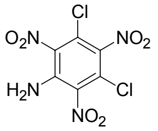
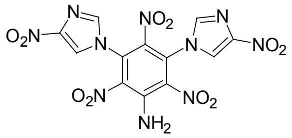
Entry	Nitroimidazole	Substrate	Product	Yield/%
4	**1a**	 **4b**	 **4c**	83
5	**1a**	 **5b**	 **5c**	75

Table 4 The results under different conditions to confirm the possible catalytic cycle[a]

	Procedure and result
1	without CuI, yield 70%
2	Separating the product of the reaction of 4-NI, KOH, CuI and then using it as the catalyst, yield 80%
3	making ArX and CuI react first, then adding salt of 4-NI, yield 65%
4	under CuI, yield 98%

[a] Using **1c** as the substrate and TBAB as the additive.

Table 5 Some explosive properties of new compounds

	Density/(g/cm^3)	Oxygen balance/%	VOD/(km/s)	Impact sensitivity (H_{50})/cm
3c	1.73	–59	7.58	109
4c	—	–59	7.72	167
5c	—	–60	7.62	103

however, when we changed the order of adding materials (Table 4, Entry 3, corresponding to B), the yield decreased to 65%, the same as no catalyst and additive (Table 1, Entry 1). Thus, we believed that the possible catalytic cycle was carried out by the way A.

The impact sensitivity of new compounds was calculated according to the reference.[15] VOD was calculated theoretically with the help of the reference [16].

Conclusions

In summary, we have investigated and established that the CuI/TBAB catalytic system is efficient and has a good yield for preparation of *N*-aryl-4-nitroimidazole as potential insensitive energy materials, using chloronitroarene as substrate.

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[14] Complete crystallographic information files for compound **3c** has been deposited with the Cambridge Crystallographic Data Center as supple-mentary publications CCDC 883593. Copies of this data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ (UK); Tel.: (+44) 1223-336-408, Fax: (+44) 1223-336-033, or E-mail: deposit@ccdc. cam. ac. uk.

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