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Palladium-Catalyzed Direct *Ortho*-Nitration of Azoarenes Using NO_2 as Nitro Source

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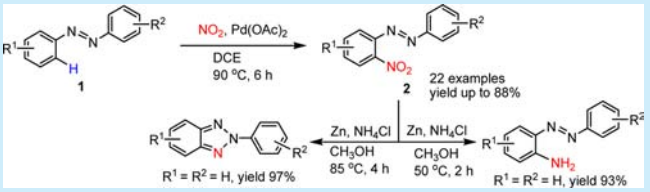
Supporting Information

ABSTRACT: A palladium-catalyzed direct *ortho*-nitration reaction of azoarenes was developed in which NO_2 was used as both nitro source and oxidant for the first time. The nitration products were converted into *o*-aminoazoarenes or benzotriazole derivatives by a simple reduction.



Azoarenes are an important class of synthetic coloring agents in the dye industry. The role of the structural factors, such as the number of azo moieties, the nature of the aromatic ring, and the nature, position, and number of substituents on dye properties have been intensively studied.[1] The character of the light-driven reversible isomerization between their *cis* and *trans* forms makes them excellent candidates to modulate the relative movement of different moieties;[2] therefore, azoarenes are widely used in many newly rising areas of science, such as photochemical molecular switch, supermolecular chemistry of host−guest recognition, self-assembly liquid crystal material, analysis of biomedical imaging, and chemical and light-driven molecular motors.[3] A review for the synthesis of azoarenes is available.[4] In the past decade, transition-metal-catalyzed chelation-assisted inert C−H bond functionalization has become a remarkable strategy in the construction of a variety of carbon−carbon or carbon−heteroatom bonds with features of step-economics and green chemistry.[5] With this concept, a series of modifications to azoarenes were developed, e.g., Pd-catalyzed *ortho*-acylation using aldehydes, α-oxocarboxylic acids or toluene derivatives as the acyl sources,[6] Rh-catalyzed annulation with alkynes,[7] Rh-catalyzed C−H bond addition of azoarenes to aldehydes and subsequent formation of indazoles,[8] Rh-catalyzed amidation with *N*-sulfonyl azides,[9] Pd-catalyzed *ortho*-alkoxylation with alcohols,[10] and Ru-catalyzed alkenylation of azoxybenzenes with alkenes.[11]

It is well-known that the nitro group can affect the properties of the organic compounds by its strong electron-withdrawing character. Nitro compounds are also key materials for preparing dyes, plastics, explosives, pharmaceuticals, and many other useful compounds.[12] Several transition-metal-catalyzed chelation-assisted *ortho*-nitrations of aromatic C−H bonds have been reported for the synthesis of this class of compounds in recent years.[13] Very recently, a direct metal-free nitro-carbocyclization of activated alkenes was also described.[14] Still, to establish a cheap, efficient, and atom-economic nitration method is a significant challenge. Continuous interest in developing convenient routes for the construction of carbon−carbon and carbon−heteroatom bonds prompted us to study such a nitration protocol. Now we report the palladium-catalyzed direct *ortho*-nitration to azoarenes, in which NO_2 as a "clean" nitro source was first used in the transition metal-catalyzed C−H bond functionalization. The nitration products were converted into *o*-amino azoarenes or benzotriazole derivatives by a simple reduction.

We performed our study with the direct *ortho*-nitration of azobenzene (**1a**), and the results are assembled in Table 1. $NaNO_2$ (2 equiv) was initially selected as the nitro source. Without the catalyst, the reaction could not take place at all (entry 1). Thus, $Pd(OAc)_2$ (10 mol %) was employed as the catalyst. An oxidant was also essential to this transformation. In the presence of oxone or $K_2S_2O_8$, the reaction gave the desired product **2a** in 42% and 10% yield in 12 h, respectively (entries 2 and 3), while the addition of 3 equiv of HOAc increased the yield to 80% when $K_2S_2O_8$ was used (entry 4). We then used NO_2 as the nitro source. To our delight, compared with $NaNO_2$, the nitration with NO_2 to **1a** gave the corresponding product **2a** in a higher yield of 85% in 6 h (entry 5). Without the oxidant, a similar yield of 87% was obtained (entry 6). NO_2 was then selected for our present nitration reaction. Several solvents (CH_3CN, dioxane, toluene, and DCE) were tested, and DCE gave the best results (entries 6−9). The screening of the reaction temperature was also carried out and the suitable temperature was proved to be 90 °C (entries 6 and 10).

Using the optimized reaction conditions, we then explored the substrate scope of this Pd-catalyzed *ortho*-nitration of azoarenes. The results are summarized in Scheme 1. For the symmetrical azoarenes, the substrates with a range of substituents on the benzene ring were tested. The results revealed that the reaction had good compatibility with several

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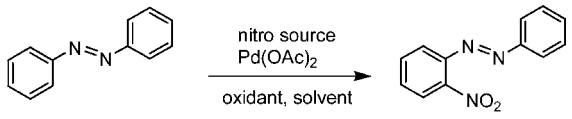
Table 1. Optimization of the Reaction Conditions[a]



1a 2a

entry	nitro source (equiv/atm)	oxidant (equiv)	solvent	yield[b] (%)
1[c]	$NaNO_2$ (2)	$K_2S_2O_8$ (3)	DCE	0
2	$NaNO_2$ (2)	oxone (3)	DCE	42
3	$NaNO_2$ (2)	$K_2S_2O_8$ (3)	DCE	10
4[d]	$NaNO_2$ (2)	$K_2S_2O_8$ (3)	DCE	80
5	NO_2 (1)	$K_2S_2O_8$ (3)	DCE	85
6	NO_2 (1)		DCE	87
7	NO_2 (1)		CH_3CN	54
8	NO_2 (1)		dioxane	18
9	NO_2 (1)		toluene	45
10[e]	NO_2 (1)		DCE	65

[a]Unless otherwise specified, the reactions were carried out in a sealed tube in the presence of azobenzene (**1a**) (0.5 mmol), $NaNO_2$ (2 equiv), or NO_2 (1 atm), $Pd(OAc)_2$ (10 mol %), and oxidant (3 equiv) in 2 mL of solvent at 90 °C for 12 h (using $NaNO_2$) or 6 h (using NO_2). [b]Isolated yield. [c]Without catalyst. [d]CH_3COOH (3.0 equiv) was added. [e]At 70 °C.

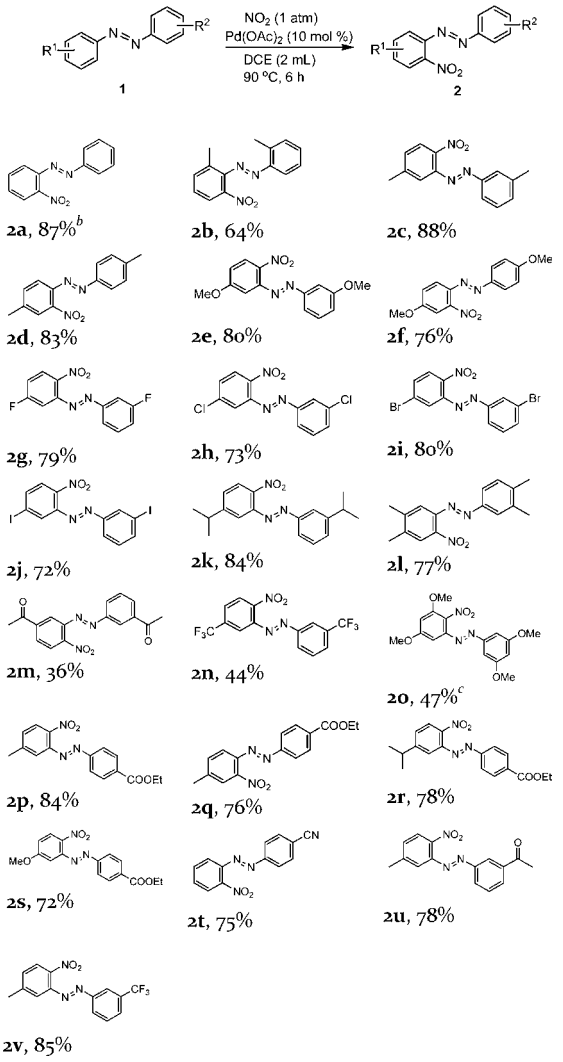
functional groups, and the presence of alkyl, methoxyl, and halo groups did not evidently affect the transformation. For most substrates with these groups, high yields were obtained under the standard reaction conditions (**2c**–**l**), and only the *ortho*-substituted azobenzene gave the moderate yield because of the steric effect (**2b**). However, with some electron-withdrawing groups, such as acyl, trifluoromethyl showed inhibiting effect to the reaction (**2m**,**n**). Surprisingly, azobenzene with two electron-donating groups (OCH_3) also gave lower yield (**2o**). It is interesting that this C–H nitration of azoarenes with meta substituents showed excellent regioselectivity. In any case, the nitration occurred at the position para to the meta substituents.

A series of unsymmetrical azoarenes were then employed for this *ortho*-nitration reaction (**2p**–**v**). For every substrate, the reaction took place exclusively on the benzene ring with an electron-donating group in moderate to good yields, which further indicated that an electron-rich benzene ring was favorable to the reaction.

Using the *ortho*-nitration product as the reactant, a further transformation was studied. As shown in Scheme 2, 2-nitroazobenzene (**2a**) was selected as the substrate, Zn power was employed as a reducer, and NH_4Cl was used as additive. In methanol, a reduction product 2-aminoazobenzene (**3a**) was obtained at 50 °C after 2 h in 93% yield. However, when the reaction temperature was raised to 85 °C, a reductive cyclization product 2-phenyl-2*H*-benzo[*d*][1,2,3]triazole (**4a**) was generated in an excellent yield of 97% after 4 h.

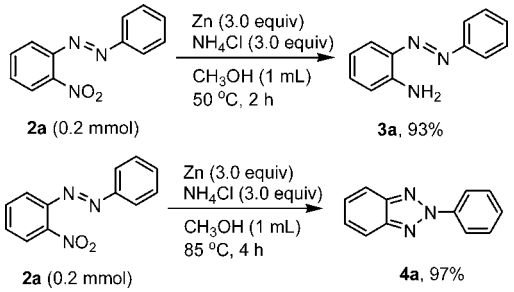
For understanding the mechanism of this palladium-catalyzed nitration of the C(sp^2)–H bond, we determined the components of the gas generated from the reaction under a limited amount of NO_2 and air via GC–FTIR. From the mixture, NO and N_2O were detected, which suggested that NO_2 may also act as an oxidant except as the nitro source in this transformation. Based on this assumption and the related transition-metal-catalyzed *ortho*-nitration reactions of the reported C(sp^2)–H bond,[13] a possible mechanism is proposed (Scheme 3). First, the coordination of azo in azobenzene to $Pd(OAc)_2$ formed a cyclopalladated intermediate **A**; this

Scheme 1. Results of the Nitration Reaction of Azobenzene[a]



[a]Reaction conditions: **1** (0.5 mmol), $Pd(OAc)_2$ (10 mol %), NO_2 (1 atm), and the DCE (2 mL) in a sealed tube at 90 °C for 6 h. [b]Isolated yields. [c]At 100 °C.

Scheme 2. Reduction of *Ortho*-Nitration Product of Azobenzene



intermediate then underwent chelation with NO_2 to form a Pd^{III} intermediate **B**. The oxidation of **B** by another NO_2 generated the Pd^{IV} intermediate **C**. Finally, the reductive elimination of **C** leads to the nitration product **2** with regeneration of Pd^{II} to start the next cycle.

In summary, we have developed a simple method for the direct *ortho*-nitration of azoarenes via a Pd-catalyzed azo group

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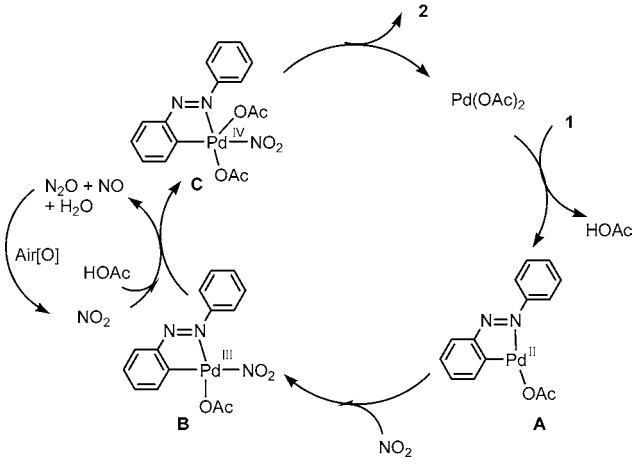
Scheme 3. Proposed Mechanism for Pd-Catalyzed Nitration of C(sp^2)−H Bond



directed sp^2 C−H bond activation using NO_2 as the nitro source. The reaction exhibited good functional group tolerance, and a series of azobenzene derivatives with either electron-donating or electron-withdrawing groups were nitrated directly and efficiently. The nitration products were reduced to *o*-aminoazoarenes or benzotriazole derivatives by zinc. This protocol provided a convenient and atom-economic route for the syntheses of 2-nitroazoarenes and related compounds and therefore is an important extension of the chemistry of azo compounds.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and full characterization for all compounds; copies of ^{1}H NMR and ^{13}C NMR for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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