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Direct formation of aromatic C–N bonds. Regioselective amination of *m*-dinitrobenzene via fluoride promoted nucleophilic aromatic photosubstitution for hydrogen

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Abstract

Useful yields are achieved in the regioselective direct formation of anilines and aromatic amides through hydrogen nucleophilic aromatic photosubstitution of *m*-dinitrobenzene with primary amines and amides, promoted by fluoride anion. © 1999 Elsevier Science Ltd. All rights reserved.

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The development of new environmentally favorable routes for the production of commercially relevant chemical intermediates and products is an area of considerable interest. These synthetic routes will require, in most cases, the discovery of new atomically efficient chemical reactions. In view of these requirements, we have focused our attention on nucleophilic aromatic substitution for hydrogen reactions (NASH)[1] as a means to generate functionalized aromatics without the need for halogenated materials or intermediates.[2] NASH reactions formally require the replacement of a hydride ion, and they happen 'spontaneously' consuming part of the starting material in the oxidation of the anionic σ-complex, or they are promoted by the addition of external oxidants. Low yields (with few exceptions)[3] and lack of generality are the main drawbacks of these synthetic procedures.[1] In addition, some of the substances used as oxidants, such as permanganate, are hazardous in their own right. We have recently shown[2] that by the use of UV irradiation (to help the redox step) and fluoride anion (to activate the nucleophile in an essentially neutral medium),[4] useful yields of *C*-arylated ketones, esters and nitriles could be achieved.

Several different methods for the direct amination of nitrobenzenes that do not require chlorobenzenes have been reported. Perhaps the most synthetically useful of these is vicarious nucleophilic substitution for hydrogen (VNS).[5] In spite of the fact that this method gives rise to reasonable yields of aminated nitrobenzenes,[6] the requirement of an auxiliary leaving group still persists. Recently Stern et al.[7] have described the direct amination of nitrobenzene with aniline and amides in useful yields. However, simple

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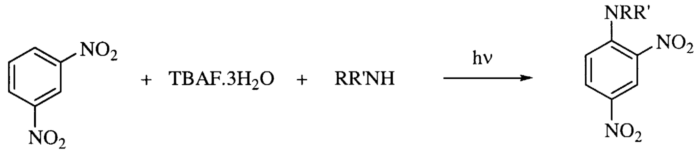
aliphatic amines failed. We wish to report here the photochemically induced direct coupling of amines and amides with *m*-dinitrobenzene, promoted by fluoride anion.

Table 1
Photoreactions of *m*-DNB with amines and amides in the presence of TBAF

Exp.	Nucleophile	Conditions[a]	Recovered m-DNB(%)	**1** Yield(%)[b]
1	$PhNH_2$	DMF, 3 h, r.t., hν	---	54
2	$CH_3(CH_2)_3NH_2$	DMF, 4h, r.t., hν	16	52
3	$CH_3(CH_2)_5NH_2$	DMF, 5h, r.t., hν	9	47
4	$PhCH(CH_3)NH_2$	DMF, 3h, r.t., hν	15	36
5	Morpholine	DMF, 4h, r.t., hν	7	17
6	Piperidine	DMF, 4h, r.t., hν	16	6
7	$CH_3(CH_2)_3CHNHCH_3$	DMF, 4h, r.t., hν	12	6
8	CH_3CONH_2	DMF, 3h, r.t. hν	15	47
9	$PhCONH_2$	DMF, 5h, r.t., hν	---	47

[a]Excess of nucleophile (5 eq.). No precautions with the presence of oxygen were taken. 5 eq. of FTBA.$3H_2O$. 125W Medium pressure Hg lamp with pyrex filter. [b]Preparative yields based on non-recovered starting material.

In Table 1 (Scheme 1), the photoreactions (UV light, pyrex filter) of *m*-dinitrobenzene (*m*-DNB) with amines and amides, in the presence of TBAF, are described. No reaction is produced in the absence of irradiation or in the absence of TBAF. At variance with what happens with carbon nucleophiles,[2] no precautions with the presence of oxygen are needed, and irradiation with visible light did not lead to products. The yields when primary amines or amides are used range from fair to good considering the starting material is also acting as an oxidant in the process, and the experimental procedure is extremely simple. Curiously enough, secondary amines give poor yields (experiments 5, 6 and 7). Extensive decomposition of the reaction mixture is observed in these cases. Also at variance to the reaction with carbon nucleophiles,[2] the photoreaction is totally regioselective, the product resulting from attack at the C-4 in *m*-DNB being the only one that is now produced.



1

Scheme 1.

As far as we know, the experiments reported in Table 1 are the first examples of nucleophilic aromatic photosubstitution of hydrogen with nitrogen nucleophiles. In addition, experiments 8 and 9 constitute a formal ‘chlorine free’ new route to 2,4-dinitroaniline through hydrolysis of the obtained aromatic amides (or treatment of the amides with methanolic ammonia).[7b] Mechanistic studies are currently in progress and a full account will be published in the near future.

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