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Photoreduction of nitro arenes by formic acid in acetonitrile at room temperature

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Abstract

The formic acid-mediated photoreduction of aromatic nitro compounds in room temperature acetonitrile solutions was investigated. This mild photoreduction can be accomplished in high yield, with wide functional group tolerance and short reaction times (30 min to 1 h), and allows a very clean method for the conversion of nitro arenes to amines. Also, the photoreduction, as a convenient, versatile and general method, applies efficiently to polycyclic and heterocyclic nitro arenes.

Nitro compounds are important building blocks in organic synthesis[1] and routinely serve as precursors to amines. A vast number of nitroaromatics are commercially available or easily prepared.[2] Reduction of nitro aromatics to the corresponding amines is a synthetically important transformation,[3] both in industry and academic laboratories, particularly when a molecule has several other reducible functionalities. Numerous methods has been developed for the reduction of nitro compounds to amines,[4] including those that involve hydrogenation, electron transfer, and hydride reductions. Nevertheless, chemists continue to seek[5] or call upon[6] new protocols to carry out such reductions.

The search for new nitro reduction methods has largely ignored the potential of formic acid under ultra-violet wavelength irradiation as a reducing agent. Although successful thermal reduction of nitro arenes with HCOOH in the presence of Zn or 10% Pd–C has been reported.[6e,f] Photoredox reactions of nitro benzenes have been deeply reviewed and two different reaction pathways could be addressed: (1) electron transfer and (2) hydrogen abstraction. The former is favored in highly polar solvents, for example, acidic and alkaline media, while the latter is favored in neutral alcoholic media.[7–10] The photoreduction of aromatic nitro compounds in acidic media (HCl, H_2SO_4, and $HClO_4$) has been studied from a mechanistic point of view and the product distribution of the photoreaction has been also analyzed.[9–21]

In view of the lack of information regarding the synthetic potential of the photoreduction of aromatic nitro compounds using organic acids instead of mineral acids, herein we now present our study on the photoreduction of a variety of nitro arenes by formic acid in acetonitrile solution, which resulted in a convenient, versatile, and a highly optimized procedure to synthesize amino arenes in one reaction step and in good to excellent chemical yield.

To begin, we simply subjected nitrobenzene (**1a**) to our photoreduction conditions. Gratifyingly, these conditions afforded aniline (**2a**) within 30 min. To build from this result, the photoreduction of **1a** was screened against different concentrations of formic acids, formate sources, solvents, atmosphere, and different excitation wavelengths.

In the absence of formic acid no amine formation was seen after 1 day of irradiation. Instead, as the concentration of formic acid is increased, the efficiency of the photoreduction of nitrobenzene increases. The reactions were run

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formic acid free but in the presence of ammonium formate and potassium formate in acetonitrile water (9:1) mixture (enhancement of formate salts solubilities). No aniline was obtained after 5 h of irradiation but the addition of formic acid from 0.01 to 0.1 M to the reaction mixture provided the formation of aniline in around 60–75 min in fairly good yield (53–65%). Thus, the use of formic acid in the absence of formate sources is the optimized condition of photoreduction of nitrobenzene giving aniline in high yield (98.3%).

Changing the reaction solvent dramatically affected the reaction efficiency. Solvents such as methanol, isopropanol, and acetonitrile water (1:1) mixture need a longer irradiation time (4–8 h) to reach a comparable chemical yield as obtained in neat acetonitrile. The reactions run in DMF and THF showed to fail as reaction solvents. Therefore, acetonitrile is the optimal solvent used for the photoreduction and provides the polar media for photoinduced electron-transfer processes.[22]

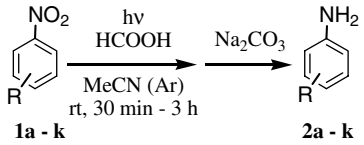
Nitro arenes populate the triplet excited state efficiently under continuous excitation (ϕ_T higher than 0.50) [22,23] and this excited state is most likely to be n,π^* or π,π^* depending on the nature of the aromatic nucleus (benzenic, naphthalenic or heterocyclic moiety) and on the substituents attached to the nitro aromatic compounds.[24,25] Molecular oxygen (triplet ground state, $^3O_2$) quenches efficiently the lowest triplet excited states of nitro aromatic compounds and no photoreaction takes place under oxygen atmosphere.[24,26] Therefore, the photoreactions were run under Argon atmosphere (bubbling the solutions during 20 min before irradiation).

The photoreduction of **1a** was also carried out at two different wavelengths, 254 and 313 nm, and aniline (**2a**) was obtained in 98.3% and 95.0% yield, respectively. This result means that the lowest triplet excited state, which is most likely to be n,π^* excited state, is the photo reactive excited state.[24] Thus, our optimal conditions were determined to be the first conditions examined, namely, 0.01–0.05 mmol of nitro arene, *hv* (254 or 313 nm) and 0.5–1.0 M of formic acid in acetonitrile (25 mL) under Argon atmosphere at room temperature. To the best of our knowledge, this is the first example of a photoreduction of nitro compounds in the presence of an organic acid. Also, the procedure is much simpler, milder, and selective than any other photo induced reduction of nitro arenes.[9,20,27]

Substrate screening of a variety of nitro-substituted arenes and heteroarenes was thus initiated. In practice, this photoinduced reduction scheme is also applicable to a wide variety of nitrobenzene derivatives with different electron-releasing and electron-withdrawing substituents in *para*-position (Scheme 1). In all cases, the yields are high (75–100%; see Table 1). Chemoselectivity is observed for the photo reaction, so the nitro group is photoreduced in the presence of reducible groups: nitrile and carbaldehyde groups. Selectivity of the photo reaction is also observed. Thus, photoreduction of *p*-dinitro-(**1b**) and *m*-dinitrobenzene (**1c**) gives the corresponding anilines (**2b** and **2c**) in 100% and 98% yield, respectively, in 30–60 min of irradiation. Longer period of irradiation time (2–4 h) provided a significant formation of the 1,3-diamino- and 1,4-diaminobenzene in 30–50% yield. Chemoselectivity of *p*-chloride- and *p*-bromo nitrobenzenes are not observed. Instead, aniline is formed in 70% yield as the main photoproduct along with significant amounts of the corresponding *p*-chloro- and *p*-bromoanilines (10–15% yield). This behavior is attributed to the photochemically dehalogenation of the *p*-chloro- and *p*-bromo nitro arenes from their lowest triplet excited state through a C–X (X: Cl; Br) homolytic cleavage.[28]

The photolysis of nitro arenes with electron-releasing groups in *para* position, such as, hydroxy (**1g**), methoxy (**1i**), and thiomethoxy (**1h**) groups, requires a longer period of photolysis time (240–300 min). However, the corresponding *p*-substituted anilines (**2g**–**h**) are obtained in good chemical yields. This behavior is due to a charge transfer excited state, which is more stable than the lowest triplet excited state, and disfavors the photoinduced electron transfer process that is the photoreduction driving-force.[24] In the cases of *p*-nitroaniline (**1j**) and *p*-nitro-*N*,*N*-dimethylaniline (**1k**) the photo reduction takes place efficiently and the corresponding anilines (**2j**–**k**) are formed in good chemical yields (Table 1). The protonation process of the amino group, which avoid a charge transfer excited state, favors the photoinduced electron transfer process. The presence of a weak releasing group in *para*-position, like the methyl group (**1f**), does not affect in a significant extent the photo-

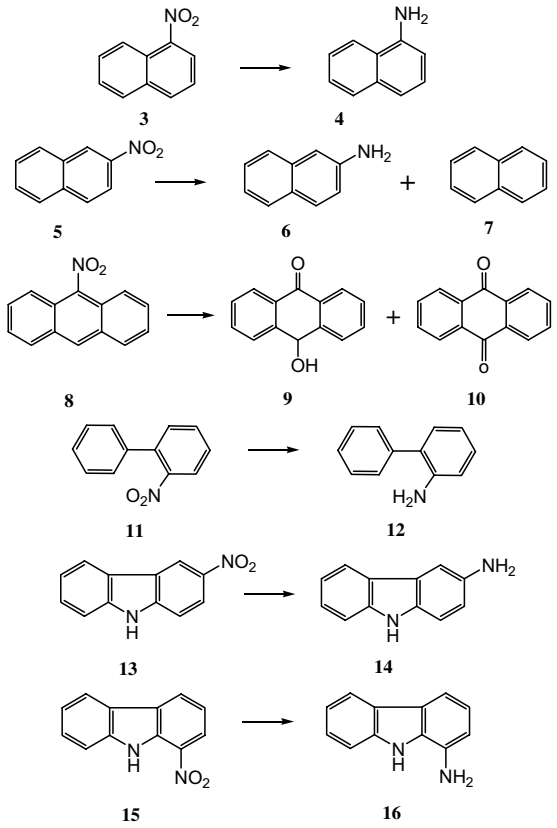
Table 1
Photoreduction of functionalized nitro arenes with formic acid[a]



1a - k **2a - k**

Substrate	R	Irradiation time (min)	Yield (**2a**–**k**) (%)
1a	H	35	98
1a[b]	H	30	95
1a[c]	H	15 h	No reaction
1a[d]	H	300	No reaction
1b	4-NO_2	60	100
1c[e]	**3**-NO_2	30	98
1d	**4**-CN	75	96
1e	4-CHO	65	77
1f	4-Me	25	81
1g	4-OH	310	79
1h	4-SMe	300	75
1i	4-OMe	250	82
1j	4-NH_2	145	85
1k	4-NMe_2	135	91

[a] Reaction conditions: 0.10–0.50 mmol of substituted-nitro arene, formic acid (1.0 M), excitation wavelength: 254 nm, quartz vessel, degassed MeCN (50 mL), under Ar, room temperature.
[b] Excitation wavelength: 313 nm.
[c] Potassium formate (0.5 M), formic acid free, solvent: MeCN–H_2O (9:1).
[d] Standard condition, non-Argon degassed solution.
[e] *m*-Dinitrobenzene.



Scheme 1. Photoreduction of polycyclic nitro arenes and heterocyclic nitro arenes with formic acid.

reduction of the nitro group and *p*-toluidine (**2f**) is obtained in 81% yield.

Extension of the methodology to nitro-substituted polynuclear aromatics and heteroaromatics afforded the expected amines in high yields, but not without some nuances. 1-Nitronaphthalene (**3**) was photoreduced, in our standard conditions, giving **4** in 94% yield (80 min of irradiation). 2-Nitronaphthalene (**5**) was easily photoreduced in 15 min to 2-aminonaphthalene (**6**) but significant amounts of naphthalene (**7**) was formed (17%). Irradiation of 1-nitro- and 2-nitronaphthalene at 254 and 366 nm, respectively, produces the expectable amino derivatives in good chemical yields (see Table 2) indicating that the lowest triplet excited state (π,π^* electronic transition)[15,16,19,25,30a] is the photo reactive excited state. 9-Nitroanthracene (**8**) was not photoreduced in our standard conditions to the corresponding amino derivative while 9-hydroxy-10-anthraquinone (**9**) and 9,10-anthraquinone (**10**) were formed in 62% and 38% yield, respectively. The Barton reaction, a photoinduced isomerization of the nitro group to the nitrite group, takes place and accounts for the formation of the quinones above mentioned.[29] In contrast to the aforementioned polynuclear aromatics, *o*-nitrobiphenyl (**11**) is reduced to the corresponding amino derivative **12** in 89% yield (see Table 2) without modification of the standard conditions. Likewise, 1-nitrocarbazole (**13**) and 3-nitrocarbazole (**15**), as examples of nitro heterocyclic arenes, are

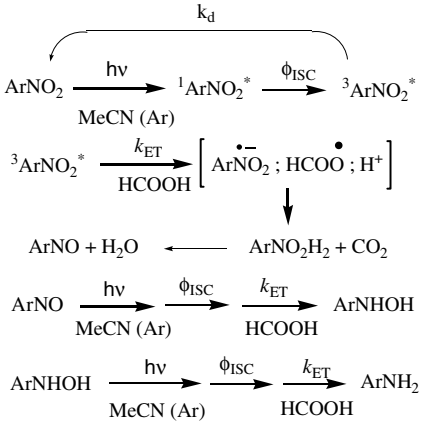
Table 2
Photoreduction of polycyclic and heterocyclic nitro arenes with formic acid[a]

Substrate	Irradiation time (min)	Yield (aminoarene) (%)
3	79	94 (**4**)
3[b]	55	75 (**4**)
3[c]	120	64 (**4**)
5	15	82 (**6**), 15 (**7**)
5[c]	15	83 (**6**); 17 (**7**)
8	120	62 (**9**); 38 (**10**)
11	30	89 (**12**)
13	35	95 (**14**)
15	45	96 (**16**)

[a] Reaction conditions: 0.10–0.50 mmol of nitro arene, formic acid (1.0 M), excitation wavelength: 313 nm, unless indicated otherwise, quartz vessel, degassed MeCN (50 mL), under Ar, room temperature.
[b] Excitation wavelength: 254 nm.
[c] Excitation wavelength: 366 nm.

easily reduced to the corresponding amine derivatives, **14** and **16**, respectively, in good chemical yields and in 45 min according to our standard conditions (see Table 2).

With regard to mechanism, the findings herein and from other studies[30] led us to surmise that these photoreductions advance via nitroso and then hydroxylamine intermediates.[25] The precise method by which these intermediates are formed and subsequently reduced is not entirely clear. To rationalize the reaction mechanism according to our experimental evidence, we propose that the photoreduction of nitro arenes is initiated by a PET reaction. A simplified mechanism for this reaction is shown in Scheme 2. Charge transfer following excitation gives the nitro arene anion radical and formyl radical. Abstraction of hydrogen from the solvent and proton transfer produces the nitroso arene hydrate intermediate that loses a molecule of water to give the nitroso arene intermediate. Subsequently, the PET reaction takes place over the nitroso arene and the hydroxylamine arene, which are more reactive than the nitro arene, to give the corresponding amino arene. Our ongoing assessments of such possibilities will be reported later in terms of time-resolved spectroscopy characterization of



Scheme 2. Proposed reaction mechanism.

triplet species and ion-radical transients formed by a PET reaction of nitro arenes.

In summary, formic acid-mediated photoreduction in neat acetonitrile at room temperature, rapidly and mildly reduce nitro-substituted arenes, polynuclear nitro arenes, and nitro heteroarenes to their corresponding amines in good to high yields. The photoreduction is initiated through a PET process and at different excitation wavelength. This method exhibit good functional group compatibility, show chemoselectivity on *m*- and *p*-dinitrobenzene and can be considered as a general and wide useful methodology. Finally, the method is inexpensive, with simple work-up and does not need the use of mediated-metals reduction agents.

General method for the synthesis of substituted anilines: The photoreactions were carried out by using a final volume of 3 mL of 0.05 M acetonitrile solutions of the nitro arenes in the presence of 0.5 M formic acid. The solutions were contained in rubber-stoppered quartz tubes provided with a stir bar. These were exposed to four 15 W lamps (Applied Photophysics) of different wavelength emissions: 254, 313, and 366 nm while a steam of dry argon saturated with the appropriate solvent was passed in the solution through a needle. To the photolyzed solution 1 mL of water and an excess of solid Na_2CO_3 were added and two layers were formed. The organic layer was separated, dried with Na_2SO_4 and filtered-off. This organic solution was then subjected to chromatographic analysis. The products formed were determined by capillary GC (HP-1 or HP-5) on the basis of calibration curves in the presence of cyclododecane as the internal standard after appropriate work-up of the solution. Nitro arenes **1**–**11** and their photoproducts were purchased from Aldrich Co. and Mallinkrodt. Compounds **13**–**16** were prepared according to published procedure.[31]

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References and notes

1. Ono, N. *The Nitro Group in Organic Synthesis*; Wiley-VCH: New York, 2001.
2. Olah, G. A.; Malhotra, R.; Narane, S. C. In *Nitration: Methods and Mechanisms*; Fever, H., Ed.; Wiley-VCH: New York, 1989.
3. Ehernkanfer, R.; Ram, S. *Tetrahedron Lett.* **1984**, *25*, 3415.
4. (a) Kabalka, G. W.; Varma, R. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 8, pp 363–379; (b) Larock, R. C. *Comprehensive Organic Transformations: A Guide to Functional Group Preparation*, 2nd ed.; Wiley-VCH: New York, 1999; pp 821–828.
5. (a) Adams, J. P. *J. Chem. Soc., Perkin Trans.* 1 **2002**, 2586–2597; (b) Tafesh, A. M.; Weiguny, J. *Chem. Rev.* **1996**, *96*, 2035–2052.
6. For selected examples of newly developed nitro reductions being employed by others, see: (a) McLaughlin, M. A.; Barnes, D. M. *Tetrahedron Lett.* **2006**, *47*, 9095–9097; (b) Jacobsen, M. F.; Moses, J. E.; Adlington, R. M.; Baldwin, J. E. *Org. Lett.* **2005**, *7*, 641–644; (c) Camerel, F.; Ulrich, G.; Zeissel, R. *Org. Lett.* **2004**, *6*, 4171–4174; (d) Berque-Bestel, I.; Soulier, J. L.; Giner, M.; Rivail, L.; Langlois, M.; Siesie, S. *J. Med. Chem.* **2003**, *46*, 2606–2620; (e) Channe Gowda, D.; Mahesh, B.; Gowda, Sh. *Indian J. Chem., Sect. B* **2001**, *40B*, 75–77; (f) Channe Gowda, D.; Gowda, Sh. *Indian J. Chem., Sect. B* **2000**, *39B*, 709–711.
7. Chow, Y. L. *The Chemistry of Amine, Nitroso and Nitro Compounds and their Derivatives*; Wiley: New York, 1982; Part I, Supplement F, Chapter 6.
8. (a) Frolov, A. N.; Kuznetsova, N. A.; Eltov, A. V. *Russ. Chem. Rev.* **1976**, *45*, 1024; (b) Akiyama, K.; Ikegani, Y.; Ikenoue, T.; Tero-Kubota, S. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3269.
9. Wubbels, G. G.; Jordan, J. W.; Mills, N. S. *J. Am. Chem. Soc.* **1973**, *95*, 1281.
10. Cu, A.; Testa, A. C. *J. Am. Chem. Soc.* **1974**, *96*, 1963.
11. Letsinger, R. L.; Wubbels, G. G. *J. Am. Chem. Soc.* **1966**, *88*, 5041.
12. Hurley, R.; Testa, A. C. *J. Am. Chem. Soc.* **1966**, *88*, 4330.
13. Hurley, R.; Testa, A. C. *J. Am. Chem. Soc.* **1967**, *89*, 6917.
14. Hashimoto, S.; Sunamoto, J.; Fujii, H.; Kano, K. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1249.
15. Hurley, R.; Testa, A. C. *J. Am. Chem. Soc.* **1968**, *90*, 1949.
16. Trotter, W.; Testa, A. C. *J. Phys. Chem.* **1970**, *74*, 845.
17. Cu, A.; Testa, A. C. *J. Phys. Chem.* **1973**, *77*, 1487.
18. Hashimoto, S.; Ueda, K.; Kano, K. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 1102.
19. Cu, A.; Testa, A. C. *J. Phys. Chem.* **1975**, *79*, 644.
20. Wubbels, G. G.; Snyder, E. J.; Coughlin, E. B. *J. Am. Chem. Soc.* **1988**, *110*, 2543.
21. Fukuzumi, S.; Tokuda, Y. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 831.
22. Turro, N. J. *Modern Molecular Photochemistry*; The Benjamin Cummings Pushing Company: CA, 1978.
23. Murov, S. L.; Carmicheal, I.; Hug, G. L. *Handbook of Photochemistry*, 2nd ed.; Marcel Dekker: New York, 1993.
24. Nakagaki, R.; Mutai, K. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 261–274.
25. Döpp, D. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. H., Song, P.-S., Eds.; CRC Press: Boca Ratón, Florida, 1995; pp 1019–1062, Section I, Chapter 81.
26. (a) Görner, H.; Döpp, D. *J. Photochem. Photobiol., A* **2003**, *159*, 219–225; (b) Görner, H. *J. Photochem. Photobiol., A* **1999**, *126*, 15–21.
27. Wubbles, G. G.; Letsinger, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 6698–6706.
28. Bunce, N. J. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. H., Song, P.-S., Eds.; CRC Press: Boca Ratón, Florida, 1995; pp 1181–1192, Section I, Chapter 86.
29. (a) Mahdavi, F.; Bruton, T. C.; Li, Y. *J. Org. Chem.* **1993**, *58*, 744–746; (b) Chapman, O. L.; Heckert, D. C.; Reasoner, W.; Thackaberry, S. P. *J. Am. Chem. Soc.* **1966**, *88*, 5550.
30. (a) Görner, H.; Döpp, D. *J. Chem. Soc., Perkin Trans. 2* **2002**, 120–125; (b) Frolov, A. N.; Kuznetsova, N. A.; Eltsov, A. V.; Rtishcher, I. *Zh. Org. Khim.* **1973**, *9*, 963–973.
31. Bonesi, S. M.; Ponce, M. A.; Erra-Basells, R. *J. Heterocycl. Chem.* **2004**, *41*, 161–171.