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# Selective Photoinduced Reduction of Nitroarenes to *N*-Arylhydroxylamines

Michael G. Kallitsakis,* Dimitris I. Ioannou, Michael A. Terzidis, George E. Kostakis, and Ioannis N. Lykakis*

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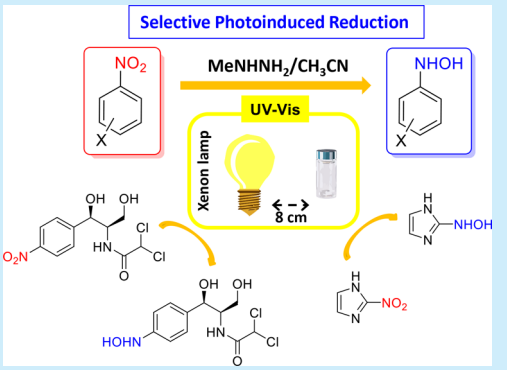
**ABSTRACT:** We report the selective photoinduced reduction of nitroarenes to *N*-arylhydroxylamines. The present methodology facilitates this transformation in the absence of catalyst or additives and uses only light and methylhydrazine. This noncatalytic photoinduced transformation proceeds with a broad scope, excellent functional-group tolerance, and high yields. The potential of this protocol reflects on the selective and straightforward conversion of two general antibiotics, azomycin and chloramphenicol, to the bioactive hydroxylamine species.




*N*-Arylhydroxylamines (*N*-AHA) are versatile organic molecules with useful applications as valuable intermediates in the synthesis of biologically active molecules, inhibitors of polymerization, and precursors for the synthesis of other organic fragments.[1] The selective reduction of nitroarenes is the most convenient protocol to obtain these attractive organic scaffolds; this transformation is promoted by zinc dust in either aqueous $NH_4Cl$, aluminum−amalgam, or even enzymatic biocatalysts.[1] However, these reagents are used in stoichiometric amounts, a significant drawback; thus, alternative methodologies have been developed. These alternative protocols involve heterogeneous catalytic systems (with Pt, Ru, Ni, Pd, Rh, Ir) and either molecular hydrogen[1,2] or hydrogen donor molecules including borohydrides[1,3a,b] or hydrazine hydrate[1,3c−e] (Scheme 1). The former protocol requires high pressures and temperatures, while the latter promotes this selective transformation under milder reaction conditions but the use of additives is necessary.

Light is the most abundant renewable energy source, and therefore, photochemistry has emerged as an efficient, green, eco-friendly approach to promote chemical transformations, especially organic reductive processes.[4] In this direction, the photoinduced reduction of nitroarenes has been achieved via photocatalytic hydrogenation or transfer hydrogenation processes.[5] To date, metal-based protocols, including transition-metal nanoparticles or complexes supported on active surfaces, promote the transformation of nitroarenes to the corresponding arylamines[6,7] or the corresponding azoxy- and azo-compounds (Scheme 1A).[8] Therefore, the selective photochemical synthesis of *N*-AHA from nitroarenes remains a significant challenge.

Given the importance of *N*-AHA in organic chemistry and inspired from metal-based[9,10] or photochemical[11] methodologies developed in our laboratory that facilitate the synthesis of interesting organic scaffolds,[10] we reasoned that it should be possible to develop a direct photoinduced reduction of nitroarenes to *N*-AHA with the use of methylhydrazine as hydrogen donor molecule (Scheme 1B). To the best of our knowledge, only specific examples with limited applicability on the photochemical reduction of 4-nitropyridine-1-oxide[12a] and *para*-X-substituted rich nitroarenes (X = H, Me, MeO)[12b−d] into the corresponding hydroxylamines in acidic alcoholic solvents have been reported.

In order to evaluate the photochemical reduction conditions, we used 4-nitrotoluene **1** as a probe molecule with different catalysts, hydrazine, or methyl hydrazine and MeOH or MeCN as solvents (Table S1). Inspired by metal-based selective reduction protocols of nitroarenes developed in our laboratory,[9] we initially studied the phototransformation of **1** in the presence of Cu(II) salts or complexes.[10a] In these cases, a mixture of the corresponding *N*-(*p*-tolyl)hydroxylamine **1a**, toluidine **1b**, and azoxy arene **1c** was obtained (Table S1,

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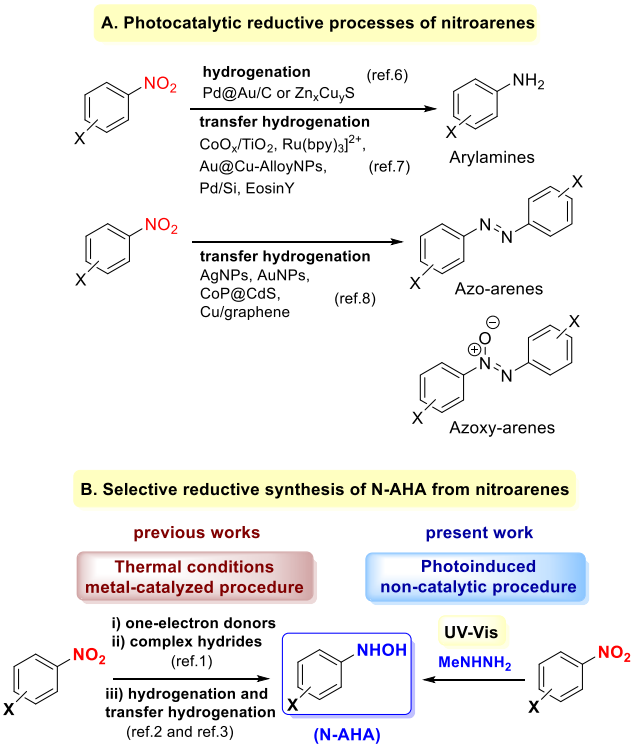
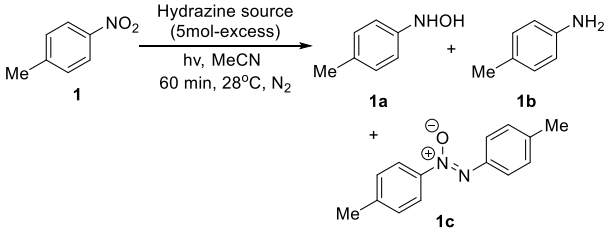
**Scheme 1. Photo- and Thermal-Catalytic Reductive Processes of Nitroarenes**




entries 1 and 2), while under thermal conditions we observed that no reaction takes place (Table S1, entry 3). Similar results were also observed in the reactions with Co(II) salts and complexes, as catalysts, in MeOH or MeCN (Table S1, entries 4−6) and 9,10-dicyanoanthracene, and rose bengal, as conventional photosensitizers (Table S1, entries 7 and 8). The reaction in the absence of any catalyst but in the presence of hydrazine hydrate (Table S1, entries 9 and 10) yields a mixture of products, with amine **1b** as the major product.

Surprisingly, when we incorporated methylhydrazine in the absence of any catalyst, **1a** was selectively formed in quantitative yield, and the product could be isolated by a simple filtration over a short pad of silica, thus omitting chromatographic purification (Table 1, entry 1). To gain better insight and rationalize this unexpected result, we performed a set of reactions. We found that phenylhydrazine also promotes the selective formation of hydroxylamine **1a**, but at a lower isolated yield (Table 1, entry 2); 1,1-dimethylhydrazine performs poorly (Table 1, entry 3), whereas the use of 1,2-diphenylhydrazine, 4-nitrophenylhydrazine, *p*-toluenesulfonylhydrazine, or hydrazine hydrate suppresses the formation of **1a** (Table 1, entries 4−7). The addition of water (20 $\mu$L, 0.2% v/v) with methylhydrazine did not affect the transformation of **1** to **1a** (Table 1, entry 8), whereas under $H_2$ atmosphere (balloon) no photochemical conversion of **1** was accomplished (Table 1, entry 9). Further control experiments revealed that the reaction does not proceed in the absence of methylhydrazine or light (Scheme S1) with the use of a cutoff filter at 420 nm or upon white LED irradiation (Table 1, entries 10−13). Moreover, a smaller amount of methylhydrazine (3 or 4 molar excess) or a shorter reaction time (15 or 30 min) leads to the formation of **1a** in moderate yield (Table 1, entries 14−17). On the contrary, the use of methylhydrazine, in 10 molar excess, or prolonged reactions afforded **1a** in quantitative yields

**Table 1. Hydrazine Evaluation in the Photoinduced Reduction of 1**




| | | relative yields[b] (%) | | | |
|---|---|---|---|---|---|
| A/A | hydrazines[a] | **1** | **1a** | **1b** | **1c** |
| 1 | $MeNHNH_2$ | | >99 | | |
| 2 | $PhNHNH_2$ | 32 | 68 | | |
| 3 | $Me_2NNH_2$ | 5 | 32 | | 63 |
| 4 | PhNHNHPh | 100 | | | |
| 5 | $4\text{-}NO_2PhNHNH_2$ | 100 | | | |
| 6 | $TsNHNH_2$ | 100 | | | |
| 7 | $NH_2NH_2{\cdot}H_2O$ | | 23 | 48 | 29 |
| 8[c] | $MeNHNH_2$ | | 95 | 5 | |
| 9 | $H_2$ bubbling | 100 | | | |
| 10 | | 100 | | | |
| 11[d] | $MeNHNH_2$ | 100 | | | |
| 12[e] | $MeNHNH_2$ | 100 | | | |
| 13[f] | $MeNHNH_2$ | 100 | | | |
| 14 | $MeNHNH_2$ (3 mol-excess) | 26 | 65 | | 9 |
| 15 | $MeNHNH_2$ (4 mol-excess) | 15 | 85 | | |
| 16 | $MeNHNH_2$ (10 mol-excess) | | 95 | 5 | |
| 17 | $MeNHNH_2$(15 min) | 45 | 55 | | |
| 18 | $MeNHNH_2$(30 min) | 16 | 84 | | |
| 19 | $MeNHNH_2$(300 min) | | 100 | | |

[a]Conditions: **1** (0.2 mmol), hydrazine source (1 mmol), MeCN (1 mL), 60 min. [b]Relative yields of products measured by the appropriate proton signals from the $^1H$ NMR of the crude reaction mixture. [c]20 $\mu$L(0.2% v/v) of $H_2O$ was added in the reaction mixture. [d]In the absence of light at 28 and 70 °C for 1 h, respectively. [e]Irradiation with a cutoff filter at 420 nm, $t$ = 1 h. [f]Irradiation using white LED, 11 W, for 24 h.

(Table 1, entries 18 and 19). The last set of reactions included the use of other various hydrogen donor molecules, i.e., hydrosilanes, boranes, ammonium formate, or formic acid and isopropyl alcohol, which did not facilitate the selective reduction (Table S2).

Interestingly, the reaction, except acetonitrile, takes place in a variety of solvents including ethanol, isopropyl alcohol, dimethyl carbonate, tetrahydrofuran, 1,2-dichloroethane, and toluene (Table S3, entries 1−8). The reaction in ethyl acetate showed lower selectivity (Table S3, entry 9) with significant amounts of toluidine **1b** and azoxyarene **1c**. No reaction occurs in water (Table S3, entry 10), but the use of a solvent mixture $H_2O/CH_3CN$ (1:1) promotes the reduction as well as the formation of **1b** (Table S3, entry 11).[13]

After establishing the optimum conditions, we assessed the scope of the protocol toward various nitroarenes and focused on different variations. Remarkably, this photoinduced protocol shows a broad functional group tolerance, and a series of nitroarenes (**1**−**22**) yielded the desired corresponding *N*-AHA (**1a**−**22a**) in excellent isolated yields (Scheme 2). The chemoselective reduction of the nitro group, in the presence of other reducible functional groups, is a very challenging task; however, this protocol leads to the selective and sole reduction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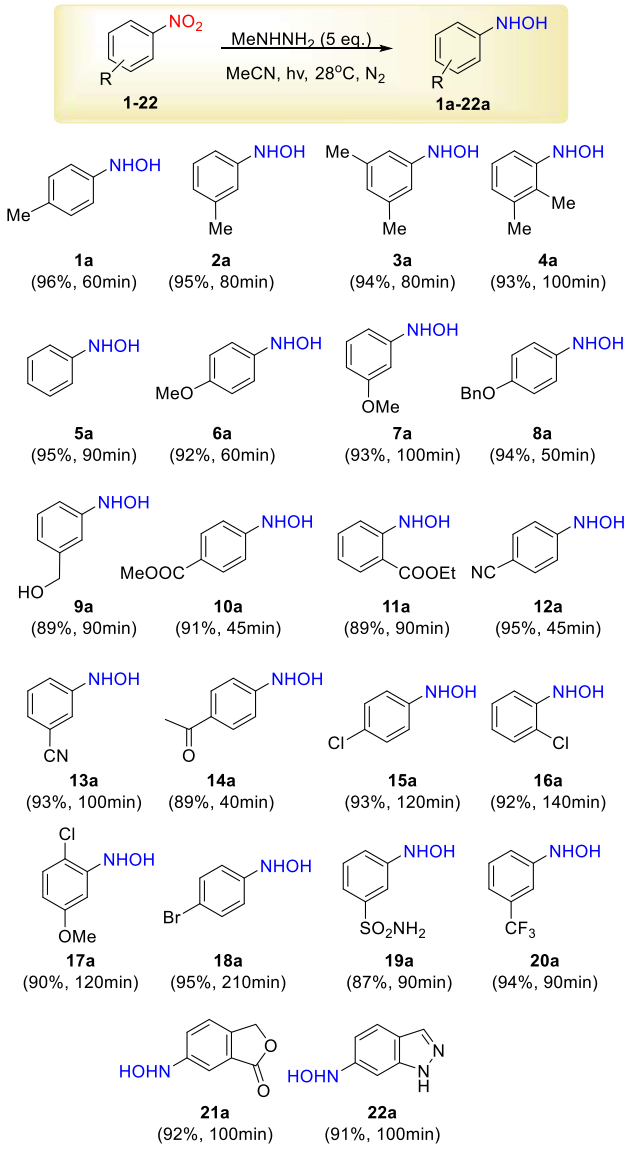
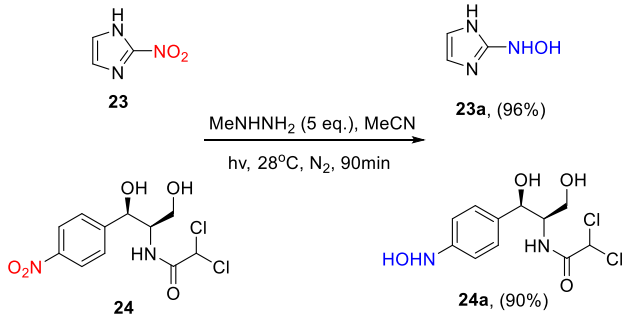
**Scheme 2. Photoinduced Synthesis of Various *N*-AHA Using Methylhydrazine**




of the nitro group to the corresponding hydroxylamine in the presence of carboxyl, cyano, and carbonyl groups (**10a**−**14a**). Interestingly, under the present protocol, no reductive dehalogenated process occurs,[14] and the corresponding halogenated aromatic *N*-AHA **15a**−**18a** species are formed in excellent yields. To further identify the limitations of the present light-driven procedure, heterocyclic substrates such as 6-nitrophthalide (**21**) and 6-nitro-1*H*-indazole (**22**) were reduced, giving quantitatively the corresponding hydroxylamines **21a** and **22a**, respectively. On the other hand, no reduction was observed with 1-nitrohexane even after 120 min of irradiation, a result that supports the necessity of an aromatic ring to facilitate this transformation. A lab-scale reaction was also performed using **1** (1 mmol) and $MeNHNH_2$ (5 mmol) in 3 mL of $CH_3CN$, and the corresponding N-AHA **1a** was isolated after 2 h irradiation time in 87% yield.

Given the simplicity of the present protocol, when compared with already known methodologies,[2,3] we reasoned that the approach would be applicable for the synthesis of a series of biologically interesting molecules. Thus, aiming to expand the scope of this protocol in pharmaceutical relevant molecules, we attempted a direct photoinduced reduction of two antibiotics: azomycin (**23**) and chloramphenicol (**24**).[15] The hydroxylamine and/or nitroso derivatives of **23** were found to exhibit high potential for the treatment of latent tuberculosis (i.e., imidazole derivatives are also designed to intercalate with intracellular nucleophiles including DNA) and treatment of several bacterial infections. At the same time, the corresponding derivatives of **24** were used as an eye ointment to treat conjunctivitis.[15a] To the best of our knowledge, the already known protocols that yield **23a** and **24a** involve metal-based, electrochemical, and biosynthetic processes[16] with significant drawbacks such as low yields, difficulty in handling and separation of the mixture of several unstable products. Notably, the present simple methodology provides easy, clean, and straightforward access to the corresponding *N*-AHA **23a** and **24a** in high isolated yields 96% and 90%, respectively, within 90 min (Scheme 3).

**Scheme 3. Application of the Present Methodology to the Selective Photo-reduction of the Antibiotics Azomycin 23 and Chloramphenicol 24**




Regarding the mechanism of this photochemical transformation, it is essential to note that the addition of an equimolar amount of 9,10-dicyanoanthracene (9,10-DCA, 0.2 mmol) retards the reaction process (**1a** in 45% and **1c** in 22%); however, the presence of 0.2 mmol of 1,3,5-trimethoxybenzene (TMB) does not affect the reaction conversion (**1a** in 90%) significantly (Scheme S3). In the same context, the addition of the radical inhibitor TEMPO in an equimolar amount did not suppress the reaction, which suggests that a free radical pathway is not predominate in this photochemical transformation (Scheme S3). These results support a possible proton-coupled electron transfer (PCET) process between the excited form of the nitroarene and the methylhydrazine; however, a hydrogen atom transfer (HAT) cannot be excluded.[17]

No formation of the *N*-AHA **5a** was observed during the photochemical reaction of the corresponding azoxy- (**5c**), azo- (**5e**), and hydrazobenzene (**5d**) under the same conditions and in the absence or in the presence of 0.2 mmol of $H_2O$ as additive (Scheme S4). This result supports the presence of a direct route of the reduction process.

In addition, the photoinduced reaction between **5** and methylhydrazine was monitored by UV−Vis spectroscopy (Figure S1); the formation of the corresponding *N*-AHA **5a** was observed as the only product.

Of note is that the reaction of nitrosobenzene **5f** with 5, 3, 2, or even 1 equiv of methylhydrazine at 28 °C in $CD_3CN$ yields,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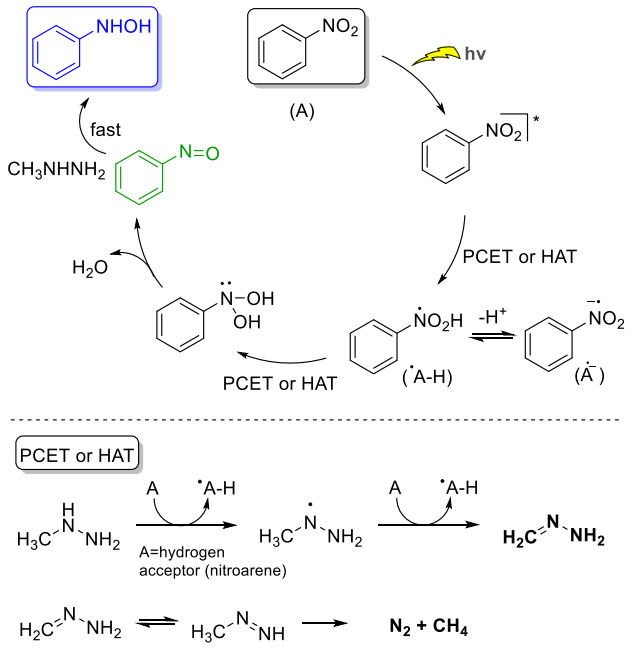
within 15 min, **5a** in >85% yield (Table S9), proven by direct $^1$H NMR monitoring. This result supports the, possible, in situ formation of a nitrosoarene intermediate, which is transformed into the corresponding hydroxylamine in the presence of methylhydrazine through a nonphotochemical pathway, although an electrochemical reductive pathway[18] can also take part during the photoreaction.

It is well-known that hydrazine hydrate produces harmless side products such as nitrogen and water under photoirradiation.[19] Thus, for examining the possibility of decomposition, we performed a set of photoreductions using methylhydrazine and phenylhydrazine, accordingly. In the former, a significant amount of methane was measured using a gas chromatography−thermal conductivity detector (GC−TCD) (Scheme S5); however, in the presence of phenylhydrazine, a significant amount of benzene was verified by $^1$H NMR spectroscopy during the photochemical reduction of **1** into **1a** (Scheme S6). Moreover, the corresponding hydrazone of formaldehyde, a decomposition product of methylhydrazine, was identified in the reaction mixture by $^1$H NMR spectroscopy (Figure S2).[19a] These results indicate the presence of a radical degradation process of the methylhydrazine in the presence or absence of the nitroarene,[17,20] and support further the necessity of methylhydrazine molar excess based on nitroarene amount.

Based on these experimental data, we envisage a plausible mechanistic pathway shown in Scheme 4. The first step

**Scheme 4. Plausible Mechanism for the Photoinduced Synthesis of *N*-Phenylhydroxylamine from Nitrobenzene**




involves the excitation of nitrobenzene ($PhNO_2$*), followed by a PCET or HAT pathway, between $PhNO_2$* and methylhydrazine, to give $PhN\dot{O}_2H$ and $PhN\dot{O}_2^-$ radicals in an equilibrium form. Preliminarily kinetic studies performed in $CD_3CN$ and monitored directly by $^1$H NMR, showed a faster reduction for the electron-withdrawing substituted nitroarene (4-MeOOC, **10**) against the electron-donating substituted nitroarenes (4-Me, **1** and 4-MeO, **6**) (Figures S3−S5). This result may support the formation of the above-proposed radicals. Then the $PhN\dot{O}_2H$, through a second PCET or HAT process with methylhydrazine, is transformed to *N*-phenyldihydroxylamine ($PhN(OH)_2$) and subsequently to the nitrosobenzene intermediate, after the loss of a water molecule, which can be directly reduced to the desired *N*-phenylhydroxylamine (PhNHOH) through a nonphotochemical process (Scheme 4).[19,20] Although this is a plausible mechanistic pathway, theoretical calculations and electrochemical studies are in progress to support this hypothesis.

In conclusion, we present an efficient methodology that selectively reduces nitroarenes to the corresponding *N*-AHA. The cooperation of nitroarenes and methylhydrazine orchestrates a light-driven, in situ generation of nitrosoarenes which yields *N*-AHA in a fast and clean manner. The protocol has a broad scope, excellent functional group tolerance, absence of byproducts, while other reducible functional groups remain intact. The present photoinduced reduction methodology is simple and applies to the bioactive molecules azomycin and chloramphenicol, giving rise to a plausible approach for a series of pro-drug molecules, thus opening new research avenues with high synthetic and biological impact.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01367.

General procedures, mechanistic studies, and NMR spectra (PDF)

## ■ AUTHOR INFORMATION


### Corresponding Authors

**Michael G. Kallitsakis** − *Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki 54124, Greece*; Email: kallitsos29@gmail.com

**Ioannis N. Lykakis** − *Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki 54124, Greece*; orcid.org/0000-0001-8165-5604; Email: lykakis@chem.auth.gr

### Authors

**Dimitris I. Ioannou** − *Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki 54124, Greece*

**Michael A. Terzidis** − *Department of Nutritional Sciences & Dietetics, International Hellenic University, 57400 Thessaloniki, Greece*

**George E. Kostakis** − *Department of Chemistry, School of Life Sciences, University of Sussex, Brighton BN1 9QJ, U.K.*; orcid.org/0000-0002-4316-4369

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c01367


### Notes

The authors declare no competing financial interest.

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## REFERENCES

(1) *The Chemistry of Hydroxylamines, Oximes and Hydroxamic Acids*; Rappoport, Z., Liebman, J. F.; John Wiley & Sons, Ltd., 2009.

(2) (a) Boymans, E. H.; Witte, P. T.; Vogt, D. *Catal. Sci. Technol.* **2015**, *5*, 176−183. (b) Rong, Z.; Du, W.; Wang, Y.; Lu, L. *Chem. Commun.* **2010**, *46*, 1559−1561. (c) Takenaka, Y.; Kiyosu, T.; Choi, J.-C.; Sakakura, T.; Yasuda, H. *Green Chem.* **2009**, *11*, 1385−1390.

(3) (a) Doherty, S.; Knight, J. G.; Backhouse, T.; Summers, R. J.; Abood, E.; Simpson, W.; Paget, W.; Bourne, R. A.; Chamberlain, T. W.; Stones, R.; Lovelock, K. R. J.; Seymour, J. M.; Isaacs, M. A.; Hardacre, C.; Daly, H.; Rees, N. H. *ACS Catal.* **2019**, *9*, 4777−4791. (b) Prakash, P.; De Masi, D.; Geertsen, V.; Miserque, F.; Li, H.; Namboothiri, I. N. N.; Gravel, E.; Doris, E. *Chemistry Select* **2017**, *2*, 5891−5894. (c) Jawale, D. V.; Gravel, E.; Boudet, C.; Shah, N.; Geertsen, V.; Li, H.; Namboothiri, I. N. N.; Doris, E. *Chem. Commun.* **2015**, *51*, 1739−1742. (d) Hojczyk, K. N.; Feng, P.; Zhan, C.; Ngai, M.-Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 14559−14563. (e) Shil, A. K.; Das, P. *Green Chem.* **2013**, *15*, 3421−3428.

(4) (a) Kou, J.; Lu, C.; Wang, J.; Chen, Y.; Xu, Z.; Varma, R. S. *Chem. Rev.* **2017**, *117*, 1445−1514. (b) Capaldo, L.; Ravelli, D. *Eur. J. Org. Chem.* **2017**, *2017*, 2056−2071. (c) Friedmann, D.; Hakki, A.; Kim, H.; Choi, W.; Bahnemann, D. *Green Chem.* **2016**, *18*, 5391−5411.

(5) (a) Nabid, M. R.; Nazaru, N.; Asadi, S.; Heravi, M. M.; Sedghi, R. *Curr. Org. Chem.* **2016**, *20*, 696−734. (b) Kadam, H. K.; Tilve, S. G. *RSC Adv.* **2015**, *5*, 83391−83407.

(6) Recent photocatalytic hydrogenation processes: (a) Hao, C.-H.; Guo, X.-N.; Sankar, M.; Yang, H.; Ma, B.; Zhang, Y.; Tong, X.; Jin, G.; Guo, X.-Y. *ACS Appl. Mater. Interfaces* **2018**, *10*, 23029−23036. (b) Yu, Z.; Chen, Z.; Chen, Y.; Peng, Q.; Lin, R.; Wang, Y.; Shen, R.; Cao, X.; Zhuang, Z.; Li, Y. *Nano Res.* **2018**, *11*, 3730−3738.

(7) Recent photocatalytic transfer hydrogenation processes: (a) Amanchi, S. R.; Kumar, K. V. A.; Lakshminarayana, B.; Satyanarayana, G.; Subrahmanyam, C. *New J. Chem.* **2019**, *43*, 748−754. (b) Todorov, A. R.; Aikonen, S.; Muuronen, M.; Helaja, J. *Org. Lett.* **2019**, *21*, 3764−3768. (c) Piggott, E. K.; Hope, T. O.; Crabbe, B. W.; Jalbert, P.-M.; Orlova, G.; Hallett-Tapley, G. L. *Catal. Sci. Technol.* **2017**, *7*, 5758−5765. (d) Xiao, Q.; Sarina, S.; Waclawik, E. R.; Jia, J.; Chang, J.; Riches, J. D.; Wu, H.; Zheng, Z.; Zhu, H. *ACS Catal.* **2016**, *6*, 1744−1753. (e) Tsutsumi, K.; Uchikawa, F.; Sakai, K.; Tabata, K. *ACS Catal.* **2016**, *6*, 4394−4398. (f) Yang, X.-Y.; Chen, B.; Zheng, L.-Q.; Wu, L.-Z.; Tung, C.-H. *Green Chem.* **2014**, *16*, 1082−1086.

(8) (a) Chen, G.-J.; Xin, W.-L.; Wang, J.-S.; Cheng, J.-Y.; Dong, Y.-B. *Chem. Commun.* **2019**, *55*, 3586−3589. (b) Mondal, B.; Mukherjee, P. S. *J. Am. Chem. Soc.* **2018**, *140*, 12592−12601. (c) Xu, Y.; Chen, Y.; Fu, W.-F. *ACS Omega* **2018**, *3*, 1904−1911. (d) Chaiseeda, K.; Nishimura, S.; Ebitani, K. *ACS Omega* **2017**, *2*, 7066−7070. (e) Guo, X.; Hao, C.; Jin, G.; Zhu, H.-Y.; Guo, X.-Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 1973−1977. (f) Zhu, H.; Ke, X.; Yang, X.; Sarina, S.; Liu, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 9657−9661.

(9) (a) Iordanidou, D.; Zarganes-Tzitzikas, T.; Neochoritis, C. G.; Dömling, A.; Lykakis, I. N. *ACS Omega* **2018**, *3*, 16005−16013. (b) Papadas, I. T.; Fountoulaki, S.; Lykakis, I. N.; Armatas, G. S. *Chem. - Eur. J.* **2016**, *22*, 4600−4607. (c) Andreou, D.; Iordanidou, D.; Tamiolakis, I.; Armatas, G. S.; Lykakis, I. N. *Nanomaterials* **2016**, *6*, 54−65. (d) Fountoulaki, S.; Daikopoulou, V.; Gkizis, P. L.; Tamiolakis, I.; Armatas, G. S.; Lykakis, I. N. *ACS Catal.* **2014**, *4*, 3504−3511. (e) Gkizis, P. L.; Stratakis, M.; Lykakis, I. N. *Catal. Commun.* **2013**, *36*, 48−51.

(10) (a) Kallitsakis, M.; Loukopoulos, E.; Abdul-Sada, A.; Tizzard, G. J.; Coles, S. J.; Kostakis, G. E.; Lykakis, I. N. *Adv. Synth. Catal.* **2017**, *359*, 138−145. (b) Andreou, D.; Kallitsakis, M. G.; Loukopoulos, E.; Gabriel, C.; Kostakis, G. E.; Lykakis, I. N. *J. Org. Chem.* **2018**, *83*, 2104−2113.

(11) (a) Tzirakis, M. D.; Lykakis, I. N.; Orfanopoulos, M. *Chem. Soc. Rev.* **2009**, *38*, 2609−2621. (b) Symeonidis, T. S.; Athanasoulis, A.; Ishii, R.; Uozumi, Y.; Yamada, Y. M. A.; Lykakis, I. N. *ChemPhotoChem.* **2017**, *1*, 479−484.

(12) (a) Kaneko, C.; Yamada, S.; Yokoe, I.; Hata, N.; Ubukata, Y. *Tetrahedron Lett.* **1966**, *7*, 4729−4733. (b) Hashimoto, S.; Sunamoto, J.; Fujii, H.; Kano, K. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1249−1251. (c) Hashimoto, S.; Kano, K. *Tetrahedron Lett.* **1970**, *11*, 3509−3512. (d) Hashimoto, S.; Kano, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 549−553.

(13) A further set of experiments with electron-withdrawing and electron-donating substituted nitroarenes was performed in MeOH and MeCN, and the results are summarized in Tables S4−S8.

(14) (a) Marin, M.; Miranda, M. A.; Marin, M. L. *Catal. Sci. Technol.* **2017**, *7*, 4852−4858. (b) Sakamoto, H.; Imai, J.; Shiraishi, Y.; Tanaka, S.; Ichikawa, S.; Hirai, T. *ACS Catal.* **2017**, *7*, 5194−5201.

(15) (a) Kumar, P. *Pharmacology and Therapeutics for Dentistry*, 7th ed.; Elsevier, 2017, 457−487. (b) Qu, Y.; Spain, J. C. *Environ. Microbiol.* **2011**, *13*, 1010−1017. (c) Singh, R.; Manjunatha, U.; Boshoff, H. I.; Ha, Y. H.; Niyomrattanakit, P.; Ledwidge, R.; Dowd, C. S.; Lee, I. Y.; Kim, P.; Zhang, L.; Kang, S.; Keller, T. H.; Jiricek, J.; Barry, C. E., 3rd *Science* **2008**, *322*, 1392−1395.

(16) (a) McClelland, R. A.; Panicucci, R.; Rauth, A. M. *J. Am. Chem. Soc.* **1987**, *109*, 4308. (b) Corbett, M. D.; Chipko, B. R. *Antimicrob. Agents Chemother.* **1978**, *13*, 193−198. (c) Lu, H.; Chanco, E.; Zhao, H. *Tetrahedron* **2012**, *68*, 7651−7654. (d) Jakubec, P.; Urbanova, V.; Medrikova, Z.; Zboril, R. *Chem. - Eur. J.* **2016**, *22*, 14279−14284.

(17) Selected reports on the photochemistry of nitroarenes: (a) Wubbels, G. G.; Snyder, E. J.; Coughlin, E. B. *J. Am. Chem. Soc.* **1988**, *110*, 2543−2548. (b) Döpp, D.; Topics, D. *Top. Curr. Chem.* **1975**, *55*, 49−85. (c) Frolov, A. N.; Kuznetsova, N. A.; Eltsov, A. V. *Russ. Chem. Rev.* **1976**, *45*, 1024−1034. (d) Cu, A.; Testa, A. C. *J. Am. Chem. Soc.* **1974**, *96*, 1963−1965. (e) Barltrop, J. A.; Bunce, N. J.; Thomson, A. *J. Chem. Soc. C* **1968**, 1467−1474. (f) Hurley, R.; Testa, A. C. *J. Am. Chem. Soc.* **1966**, *88*, 4330−4332.

(18) (a) Steudel, E.; Posdorfer, J.; Schindler, R. N. *Electrochim. Acta* **1995**, *40*, 1587−1594. (b) Huang, Y.; Lessard, J. *Electroanalysis* **2016**, *28*, 2716−2727.

(19) Selected reports on the photochemical decomposition of hydrazine: (a) Lambert, C. E.; Shank, R. C. *Carcinogenesis* **1988**, *9*, 65−70. (d) Hawkins, W. G.; Houston, P. L. *J. Phys. Chem.* **1982**, *86*, 704−709. (g) Arvis, M.; Devillers, C.; Gillois, M.; Curtat, M. *J. Phys. Chem.* **1974**, *78*, 1356−1360. (h) Stief, L. J.; DeCarlo, V. J. *J. Chem. Phys.* **1966**, *44*, 4638−4639.

(20) King, D. M.; Bard, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 419−423.



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