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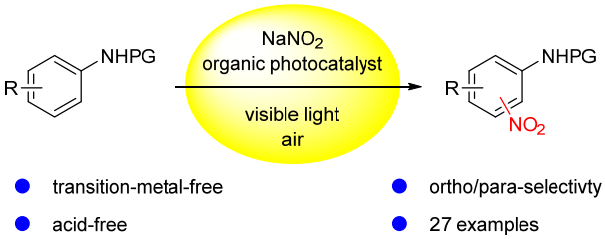
Visible light mediated nitration of protected anilines

Simon J. S. Düsel and Burkhard König*

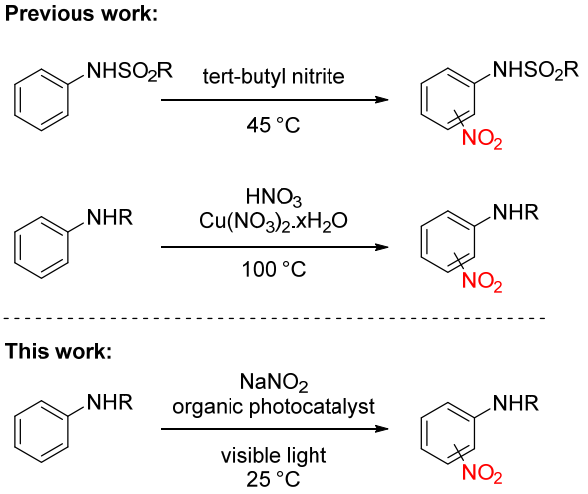
Faculty of Chemistry and Pharmacy, University of Regensburg, D-93040 Regensburg, Germany

The photocatalytic nitration of protected anilines proceeds with riboflavin tetraacetate as organic photoredox catalyst. Sodium nitrite serves as NO_2-source in the visible-light driven room temperature reaction. Various nitroanilines are obtained in moderate to good yields without the addition of acid or stoichiometric oxidation agents. The catalytic cycle is closed by aerial oxygen as the terminal oxidant.



Introduction

Nitroanilines are an important class of compounds that are used as precursors in the synthesis of dyes, pigments and drugs.[1] The classic nitration process of arenes requires harsh reaction conditions with high temperature and strong acids. Milder methods that allow the presence of sensitive functional groups were therefore developed.[2] *Tert*-butyl nitrite was shown to be a potent nitration reagent at slightly elevated temperatures for the nitration of aromatic sulfonamides.[3] However, differently protected anilines (e.g. amides) can only be obtained at high temperatures using copper catalysis.[4] Many recently reported methods require transition metal catalysts or stoichiometric amounts of oxidants.[5-10] Furthermore, nitration methods that work for a variety of functional groups are scarce. In this regard the work of Carretero is an exception, as they present a versatile copper catalyzed procedure for differently protected anilines with HNO_3 as NO_2-source, though temperatures of 100 °C are required (Scheme 1).[11] This motivated us to develop a room temperature nitration protocol that works for a broad range of differently protected anilines without the use of transition metals or acids. Many photoredox catalyzed reactions can be performed at room temperature.[12-16] Moreover, such radical reactions open new pathways for substitution and for C-H functionalization reactions.[17-20] Metal contamination can be avoided by using organic photocatalysts, which are typically of low cost.[21]



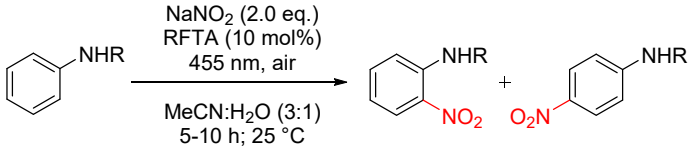
Scheme 1. Recent methods for the nitration of protected anilines

Results and Discussion

We started our investigations with sodium nitrite as NO_2-source. To our delight, blue light irradiation with riboflavin tetraacetate (RFTA) as photocatalyst allowed the nitration of N-Boc-aniline.[22-24] To solubilize the nitrite salt and the organic starting material, a 3 : 1 mixture of acetonitrile and water was used. The reaction progress was monitored by TLC and GC-FID analysis, showing that after complete conversion of the starting material slow degradation of the often colored products occurs. Therefore, the reaction time was adjusted for every compound. Anilines are typically protected as (PhNHR) carbamide (R = Boc, Cbz, Fmoc), sulfonamide (R = Ts, Ms) and amide (Ac, Bz). We therefore investigated our method on these substances (Table 1) and obtained moderate to good yields. The oxidation potentials of the anilines reside in the rage of +1.7 V to +1.9 V (vs SCE in pure MeCN), but for the sulfonamide species a second oxidation

peak (+1.91 V for **5a**; +1.89 V for **6a**) was measured indicating that further oxidation to an undesired species can be the origin of the diminished yield.[25] The para-product was obtained as the major regioisomer in all experiments. Fmoc protected aniline (**7a**) is not suitable for this method, as this substrate is poorly soluble in the used solvent mixture. Furthermore, deprotection and undesired side reactions occur for this substrate.

Table 1 Photocatalytic nitration of differently protected anilines



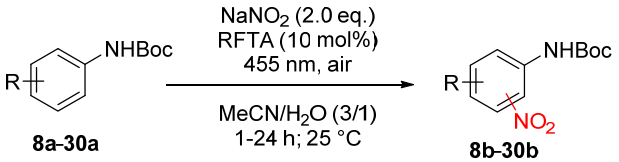
1a-7a **1b-7b** **1c-7c**

Entry	Compound	R =	E_{ox} (V)	Time (h)	yield[b] (%)	
					1b-7b	**1c-7c**
1	**1a**	Boc	1.75	10	41	45
2	**2a**	Cbz	1.70	6	36	43
3	**3a**	Bz	1.83	8	28	41
4	**4a**	Ac	1.75	10	28	33
5	**5a**	Ts	1.77	5	37	50
6	**6a**	Ms	1.74	8	25	35
7	**7a**	Fmoc	1.87	8	>10	>10[c]

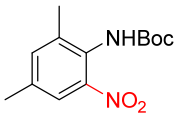
[a] Reaction conditions: Aniline **1a-7a** (0.2 mmol), sodium nitrite (0.4 mmol), RFTA (10 mol%) in a mixture of acetonitrile (3 mL) and water (1 mL) distributed over 4 glass vials irradiated from the bottom side with a blue LED at 25 °C. [b] Isolated yields. [c] inseparable mixture, no full conversion.

The scope was expanded to differently N-Boc protected anilines (Table 2), as this class of compounds is, in contrast to sulfonamides, not well represented in the recent nitration literature. The reaction times vary between 1 h and 24 h. For electron-rich methoxy-substituted derivatives **13a**-**15a** good yields and complete conversion to the *ortho* and *para* regioisomers are achieved after a maximum of 6 h. Phenacetin (**17a**), a former used acetylated drug, is nitrated with a yield of 52% after 6 h, while for longer reaction times dinitration and degradation can be observed for this compound. Alkynes are tolerated, but vinyl anilines are not stable under the oxidative conditions. Partial oxidation of the double bond as well as vinylic NO_2 addition and polymerization were observed for **12a**. The reaction time for less activated anilines as halogenated anilines or aminobenzoic acid derivatives increases to 8 h - 10 h. Only for *para* halogenated compounds **20b** and **21b** a small amount of *ipso*-substituted nitration product **1c** is obtained.[26] The yield drastically decreases when this method is applied to very electron deficient heterocycles. For compound **29a** and **30a** more than 90% of the starting material can be reisolated. The oxidation potential of the excited catalyst is too low for the oxidation of these compounds.[27] For compounds **8a**-**28a** neither large amounts of starting material nor any specific side products could be isolated. It is known that unprotected anilines easily polymerize upon oxidation.[28,29] Related degradation pathways must be taken into account for the herein presented compounds that provided lower yield.

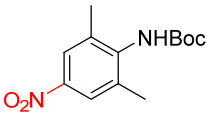
Table 2 Nitration of N-Boc-anilines

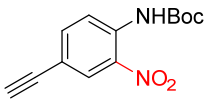


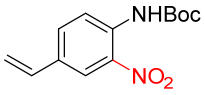
8a-30a **8b-30b**

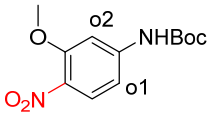

8b 81% (72%[a])

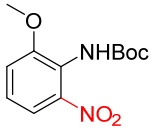

9b 60%

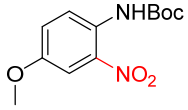

10b 27%

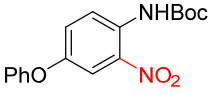

11b 71%

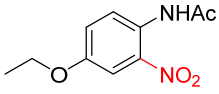

12b 15%

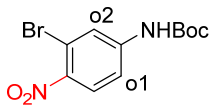

13b 90% (p:o[1]:o[2] = 4.2:2.8:1)

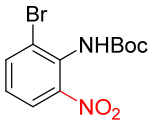

14b 62% (o:p = 1.4:1)

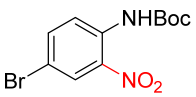

15b 69%

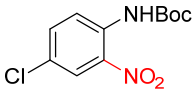

16b 61%

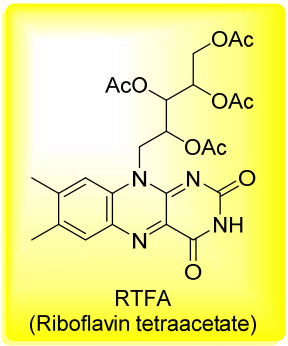

17b 52%[b]

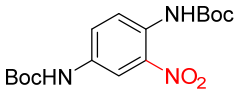

18b 59% (p:o[1]:o[2] = 2:1:1)

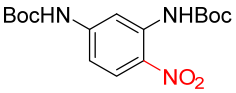

19b 27% (o:p = 1.7:1)

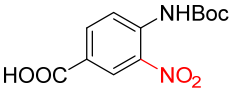

20b 80% (o:p = 3:1)[c]

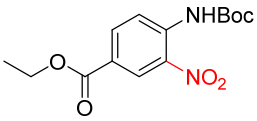

21b 80% (o:p = 7:1)[c]

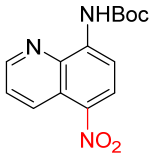


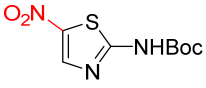

22b 58%

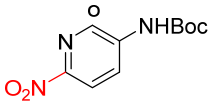

23b 76% (p:o = 4:1)

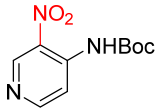

24b 52%


25b 33%


26b 52% (p:o = 1.2:1)


27b 25 %

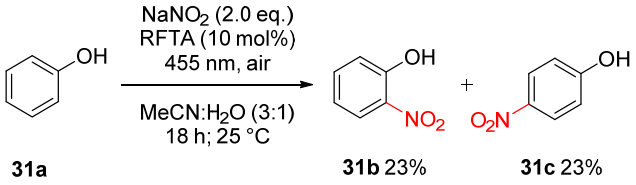

28b 21% (p:o = 1.3:1)


29b 0%


30b 0%

Reaction conditions: Aniline **8a-30a** (0.2 mmol), sodium nitrite (0.4 mmol), RFTA (10 mol%) in a mixture of acetonitrile (3 mL) and water (1 mL) distributed over 4 glass vials irradiated from the bottom side with a blue LED at 25 °C for 1-24 h. Isolated yields. The major isomer is shown.[a]Reaction of **8a** (0.2 mmol) was performed in a single vial. [b] N-Acetylated starting material. [c]*para*-Isomer obtained by *ipso*-substitution of the halide atom.

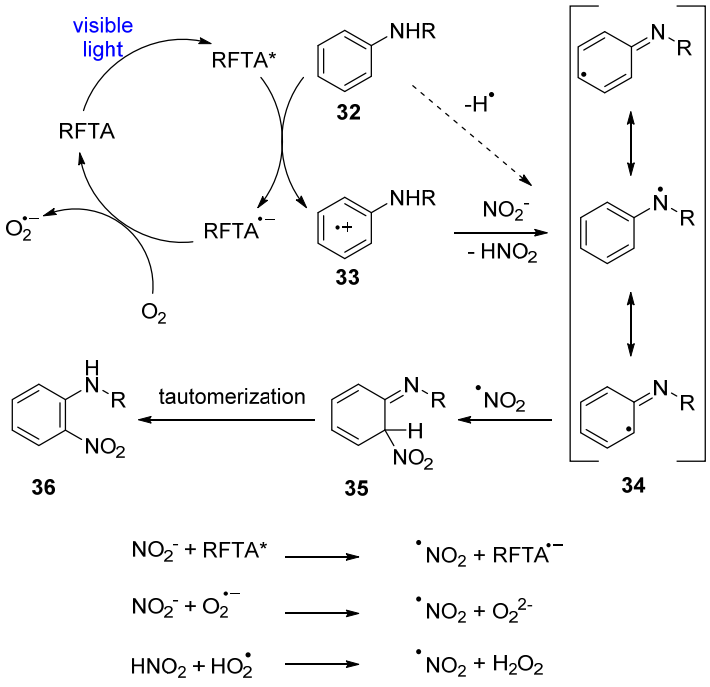
Most of the obtained products absorb light in the same spectral region as the photocatalyst. A sufficient light input into the reaction mixture was achieved using a low concentration (0.05 M) of the aniline. For each compound four separate reaction vials were used in parallel and combined before workup to ensure a good light penetration into the reaction mixture. Applying a segmented flow system did not provide satisfying results. The herein described method was also used for the nitration of phenol (Scheme 2), yielding 46% of nitrophenol (**31b** + **31c**). A likely rational explanation for the diminished product yield is the known tendency of the intermediate phenoxyradicals to polymerize.[30-33] (For variation of the reaction conditions, see Supporting information, Tables S1 and S2).



Scheme 2 Photocatalytic nitration of phenol

Reaction conditions: Phenol (**31a**) (0.05 mmol), sodium nitrite (0.1 mmol), RFTA (10 mol%) in a mixture of acetonitrile (0.75 mL) and water (0.25 mL), irradiated with a blue LED at 25 °C. Yields determined by analytical HPCL with naphthalene as internal standard.

In Scheme 3 we propose a mechanism of the photo-nitration. The non-photocatalyzed parts of the mechanistic proposal are in agreement with literature reports.[3,4,11] The photocatalyst, after excitation, oxidizes the aniline derivative **32**.[34,35] The acidity of radical cations increases compared to the neutral compound and therefore the consecutive formation of the stabilized radical **34** via loss of a proton can occur.[36,37] Nitrogen dioxide as a persistent radical species is formed via different pathways and is able to react with **34**.[38,39] After rearomatization, the desired para- and ortho-regioisomeric substitution products are obtained. Direct H-abstraction from **32** by reactive oxygen species as alternative or additional route to the amidyl radical **34** cannot be excluded at this stage of the investigation. In 2010 Ivanov et al. reported a photo induced electron transfer from the nitrite anion to excited riboflavin, confirmed by fluorescence quenching experiments.[40] We find emission quenching for the acetylated derivative of the dye by sodium nitrite. However, in contrast to Ivanov's observation, we observe dynamic quenching (Stern-Volmer constant K_{SV} = 14.1 mol^{-1}) of the emission of RFTA upon addition of $NaNO_2$ in an acetonitrile-water solvent mixture (Figure 1). Dynamic emission quenching of RFTA by aniline **1a** (K_{SV} = 11.3 mol^{-1}) supports the oxidation of the arene as a key step of the proposed mechanism.



Scheme 3 Mechanistic proposal

Carretero showed that N,N-disubstitued anilines do not react under their conditions, postulating Cu(II) as the oxidizing species, as the formation of the amidyl radical **34** is not possible.[11] This was also observed during our investigations, N,N-disubstituted anilines do not yield nitration products. (See Supporting information, Table S3)

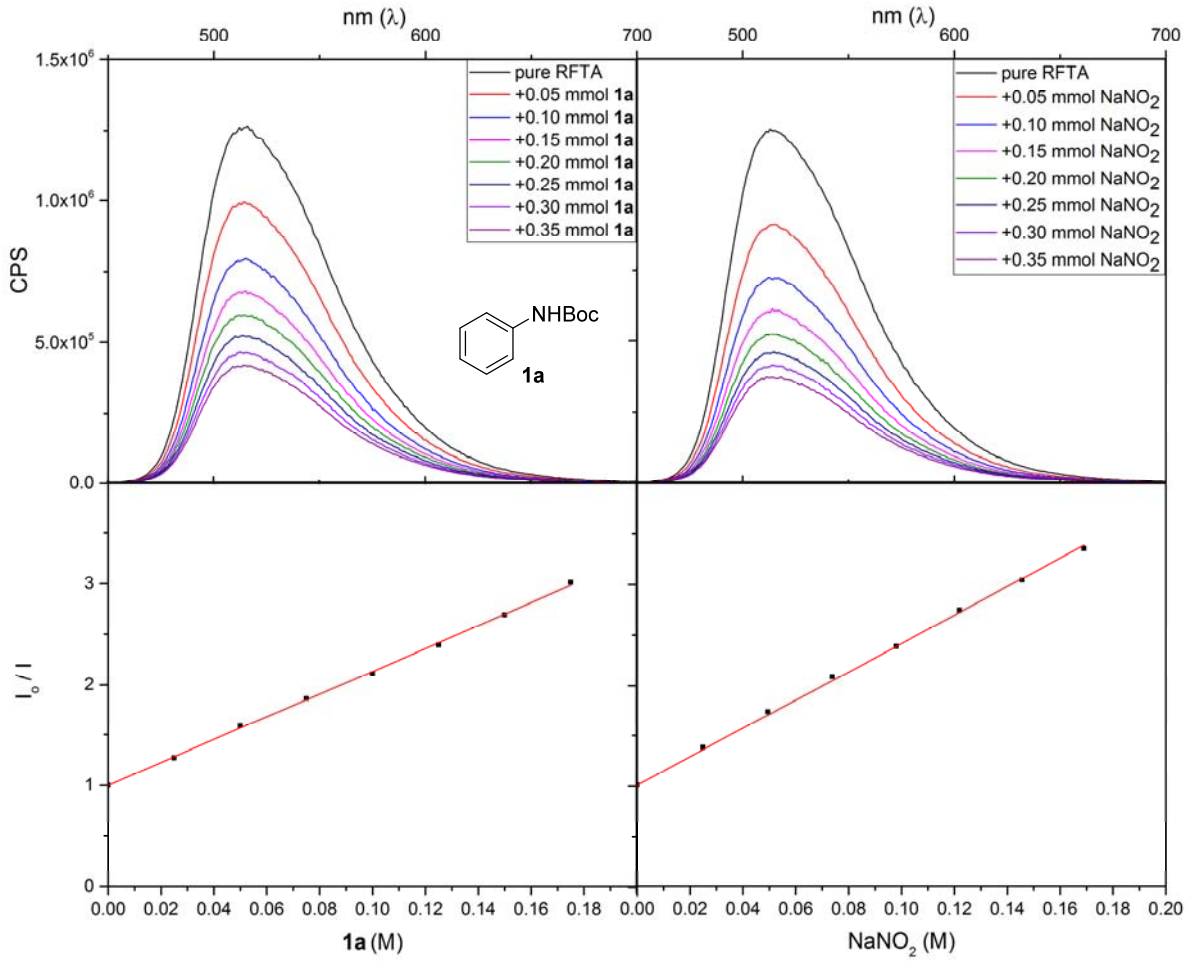
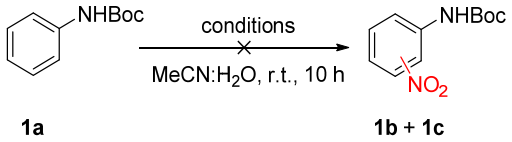


Figure 1 Fluorescence quenching of RFTA (10 µM in a 3 : 1 mixture of MeCN : H_2O) upon titration with N-Boc-aniline (1a) and $NaNO_2$.

To confirm the postulated reaction mechanism, further experiments (Table 3) were performed. For entries 2-7 no product formation was detected by GC analysis. As oxygen is considered necessary to regenerate the ground state of the catalyst, the reaction was performed under inert atmosphere (entry 1), which drastically decreased the yield. Only traces (less than 5% of **1b** + **1c**) were detected. This can be explained as 10 mol% of the catalyst in its oxidized form are present at the beginning, which after reduction cannot be regenerated. The visible-light activated photocatalyst is essential, as the reaction does not proceed in the dark or without catalyst under blue light irradiation. The role of hydrogen peroxide (entry 4) was investigated, as this is the main byproduct of the described reaction. No product formation was observed upon addition of hydrogen peroxide. Nitration of the aniline derivative via peroxynitrite was not considered as relevant.[41-43] The addition of TEMPO (entry 5) completely stops the reaction, indicating a radical mechanism. Nevertheless, it has to be noted that TEMPO itself can be photocatalytically oxidized.[44] Pyrazole and Br^- were reported to be sufficient nucleophiles that can react with photocatalytically generated aromatic radical cations.[45-47] In our case only degradation of **1a** (which also occurs, if only **1a** and catalyst, but no $NaNO_2$ is present in the reaction mixture), but no formation of any adducts was observed. In difference to the mechanism postulated by Liang et al.[7], direct nucleophilic addition of the nitrite anion to the aniline radical cation **33** is likely to be excluded for the herein reported process.

Table 3 Control experiments



1a **1b** + **1c**

Entry	Change from standard conditions[a]
1	under N_2 atmosphere[b]
2	no light
3	no catalyst
4	no catalyst; with 3 eq. H_2O_2
5	addition of 2 eq. TEMPO
6	2 eq. NaBr instead of $NaNO_2$
7	2 eq. pyrazole instead of $NaNO_2$

[a]Standard conditions: N-Boc-Aniline **1a** (0.05 mmol), sodium nitrite (0.1 mmol), RFTA (10 mol%) in a 3:1 mixture of MeCN:H_2O (1 mL) irradiated with 455 nm LED at 25 °C for 10 h. Analyzed by GC-FID; in general no product formation detected. [b] minor traces of the desired product were detected.

CONCLUSIONS

In conclusion, protected anilines were photocatalytically nitrated. All reactions are performed at room temperature without the addition of transition metals or stoichiometric oxidation reagents. Sodium nitrite is used as a cost-effective nitration reagent that is easily stored and handled. The reactions were performed under air employing a mixture of acetonitrile and water as solvent. Many functional groups are tolerated by the reaction.

EXPERIMENTAL SECTION

General information: Unless stated all reagents and solvents were purchased from commercial suppliers and used without further purification. Thin layer chromatography (TLC) was performed on Merck silica gel plates 60 F_{254} and visualization was accomplished by irradiation at 254 nm. Gas chromatography coupled with a flame ionization detector (GC-FID) was performed using a capillary column (length: 30 m; diam. 0.25 mm; film: 0.25 µ) with He gas as carrier. All products were purified by automated flash chromatography (Biotage® Isolera™ Spektra One) using a mixture of petroleum ether (PE) and ethyl acetate as eluent and silica gel of type 60 M (40-63 µm, 230-440 mesh) by Merck as stationary phase. High-resolution mass spectra (HRMS) were obtained using a time-of-flight mass analyzer. IR spectra were measured on an Agilent Cary 630 spectrometer at room temperature. UV-Vis absorption spectra were measured in acetonitrile on an Agilent Cary 100 spectrometer at 25 °C with a quartz cuvette (4×10 mm). Fluorescence spectra were measured on a Horiba Scientific Fluoromax-4 spectrometer at room temperature with a quartz cuvette (10×10 mm) using 2 mL of RFTA solution (10 µM). Aliquots of pure solid compound **1a** or a solution of $NaNO_2$ (5.0 M; 10 µL) were added for quenching experiments. ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ or Acetone-d_6 using Bruker Avance 400 and 300 MHz spectrometers with the solvent residual peaks as the internal standard.[48]. HPLC analysis was performed with an Agilent 1220 Infinity LC (column: Phenomenex Luna 3 µM C18(2) 100 Å, 150 x 2.00 mm; flow: 0.3 mL/min at 30 °C; solvent A: MilliQ water with 0.05 % vol. TFA; solvent B: MeCN) and naphthalene as internal standard. Electrochemical studies were carried out with a three-electrode setup under argon atmosphere in MeCN containing 0.1 M tetra-n-butylammonium tetrafluoroborate using ferrocene/ferrocenium (Fc/Fc+) as an internal reference.[49] Photochemical reactions were performed with 455 nm LEDs (OSRAM Oslon SSL 80 royal-blue. λ = 455 nm (± 15 nm), 3.5 V, 700 mA). Riboflavin tetraacetate (RFTA) was prepared by acetylation of riboflavin after a literature known procedure.[50] Protected anilines were commercially available or prepared by standard procedures.[6,51-55]

General procedure for the photocatalytic nitration of protected anilines. The aniline derivative **1a**-**30a** (0.05 mmol) and RFTA (2.7 mg, 0.005 mmol) were dissolved in acetonitrile (0.75 mL) and added to a glass vial (size 5 mL). A freshly prepared solution of sodium nitrite (6.9 mg, 0.1 mmol) in water (0.25 mL) was added. The vial was closed with a septum and a syringe needle (Ø=1 mm) was inserted

to provide air supply. The reaction vial was placed in a custom-built cooling system at 25 °C and irradiated under stirring with a 455 nm LED through the glass bottom (0.5 cm distance to LED). The reaction progress was monitored by TLC or GC-FID and the reaction was stopped, when all starting material was consumed, or no further progress was detected. Four equal reaction mixtures were united and the solvent was removed at reduced pressure. Subsequently the products were purified by automated silica gel flash column chromatography.

***tert*-Butyl (2,4-dimethyl-6-nitrophenyl)carbamate (8b)**. According to the general procedure, after 24 h **8b** was isolated as yellow solid (43.1 mg, 0.162 mmol, 81%) using a gradient of 2% to 10% EtOAc/PE for silica gel flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.29 (s, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 137.4, 136.8, 136.0, 127.7, 123.0, 81.3, 28.2, 20.7, 18.7. UV-Vis (ε, L·mol^{-1}·cm^{-1}): 268 nm (2949), 320 (1598). FT-IR (cm^{-1}, neat, ATR): 3118, 2978, 1700, 1532. HRMS (+ESI) *m/z:* Calcd for $C_{13}H_{18}N_2O_4Na$ 289.1159 [M + Na]$^+$; Found 289.1167. Mp: 140-142 °C.

***tert*-Butyl (2,6-dimethyl-4-nitrophenyl)carbamate (10b)**. According to the general procedure, after 24 h **10b** was isolated as yellow solid (14.3 mg, 0.054 mmol, 27%) using a gradient of 2% to 9% EtOAc/PE for silica gel flash column chromatography.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 2H), 6.01 (s, 1H), 2.36 (s, 6H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, CDC_3l) δ 145.7, 140.2, 136.8, 123.2, 81.1, 28.2, 18.8. UV-Vis (ε, L·mol^{-1}·cm^{-1}): 290 nm (7793). FT-IR (cm^{-1}, neat, ATR): 3244, 2926, 1685, 1502. HRMS (+ESI) *m/z:* Calcd for $C_{13}H_{18}N_2O_4Na$ 289.1159 [M + Na]$^+$; Found 289.1164.

***tert*-Butyl (4-ethynyl-2-nitrophenyl)carbamate (11b)**. According to the general procedure, after 5.5 h **11b** was isolated as yellow solid (37.0 mg 0.141 mmol, 71%) using a gradient of 2% to 7% EtOAc/PE for silica gel flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.56 (m, 1H), 8.31 (m, 1H), 7.66 (m, 1H), 3.10 (s, 1H), 1.54 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.9, 138.8, 136.2, 135.3, 129.5, 120.6, 115.9, 82.3, 81.1, 78.4, 28.2. UV-Vis absorption (ε, L·mol^{-1}·cm^{-1}): 373 nm (3284). FT-IR (cm^{-1}, neat, ATR): 3388, 3287, 2983, 2929, 1729, 1503. HRMS (+ESI) *m/z:* Calcd for $C_{13}H_{14}N_2O_4Na$ 285.0846 [M + Na]$^+$; Found 285.0852. Mp: 112-113 °C.

***tert*-Butyl (2-nitro-4-vinylphenyl)carbamate (12b)**. According to the general procedure, after 1 h **12b** was isolated as yellow solid (8.1 mg, 0.031 mmol, 15%) using a gradient of 2% to 5% EtOAc/PE for silica gel flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 8.52 (m, 1H), 8.18 (m, 1H), 7.66 (m, 1H), 6.66 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.77 (d, *J* = 17.6 Hz, 1H), 5.34 (d, *J* = 10.9 Hz, 1H), 1.54 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 136.0, 135.2, 134.2, 133.0, 131.8, 123.3, 120.8, 115.4, 80.0, 28.2. UV-Vis absorption (ε, L·mol^{-1}·cm^{-1}): 258 nm (25766), 380 (3016). FT-IR (cm^{-1}, neat, ATR): 3355, 2926, 1729, 1512. HRMS (+ESI) *m/z:* Calcd for $C_{13}H_{16}N_2O_4Na$ 287.1002 [M + Na]$^+$; Found 287.1003. Mp: 64-67 °C.

tert*-Butyl (2-nitro-4-phenoxyphenyl)carbamate (16b)**. According to the general procedure, after 6 h **12b** was isolated as orange solid (40.2 mg, 0.122 mmol, 61%) using an isocratic mixture of 1% EtOAc/PE for silica gel flash column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.49 (s, 1H), 8.52 (m, 1H), 7.78 (m, 1H), 7.41 – 7.29 (m, 3H), 7.20 – 7.12 (m, 1H), 7.00 (m, 2H), 1.54 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 152.4, 151.4, 136.5, 131.5, 130.1, 126.9, 124.2, 122.5, 118.9, 114.8, 81.8, 28.2. UV-Vis absorption (ε, L·mol^{-1}·cm^{-1}): 383 nm (3502). FT-IR (cm^{-1}, neat, ATR): 3369, 2926, 1726, 1510. HRMS (+ESI) *m/z:* Calcd for $C_{17}H_{18}N_2O_5Na$ 353.1108 [M + Na]$^+$; Found 353.1115. Mp: 81-81 °C.tert*-Butyl (3-bromo-4-nitrophenyl)carbamate (18b-p)**, ***tert*-Butyl (5-bromo-2-nitrophenyl)carbamate (18b-o^1)** and ***tert*-Butyl (3-bromo-2-nitrophenyl)carbamate (18b-o^2)**. According to the general procedure, after 8 h **18b-p**, **18b-o^1** and **18b-o^2** were isolated as yellow solids (**18b-p** 9.4 mg, 0.030 mmol, 15%. **18b-o^1** 9.4 mg, 0.030 mmol, 15%. **18b-o^2** 18.3 mg, 0.058 mmol, 29%) using a gradient of 2% to 15% EtOAc/PE for silica gel flash column chromatography. Spectral data for **18b-p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.0 Hz, 1H), 7.90 (d, *J* = 2.3 Hz, 1H), 7.38 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.74 (s, 1H), 1.53 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.60, 143.60, 143.09, 127.36, 123.35, 116.52, 116.45, 82.34, 28.20. HRMS (+ESI) *m/z:* Calcd for $C_{11}H_{13}BrN_2O_4Na$ 338.9951 [M + Na]$^+$; Found 338.9954. Spectral data for **18b-o**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.85 (d, *J* = 2.1 Hz, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.21 (dd, *J* = 9.0, 2.1 Hz, 1H), 1.55 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.85, 136.83, 134.47, 131.35, 127.00, 125.10, 123.25, 82.46, 28.18.HRMS (+ESI) *m/z:* Calcd for $C_{11}H_{13}BrN_2O_4Na$ 338.9951 [M + Na]$^+$; Found 338.9948. Spectral data for **18b-o^2:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.36 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.34 – 7.31 (m, 1H), 1.51 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 133.0, 132.2, 128.1, 121.3, 114.2, 82.3, 28.2. UV-Vis absorption (ε, L·mol^{-1}·cm^{-1}): 275 nm (2607). FT-IR (cm^{-1}, neat, ATR): 3417, 2929, 1737, 1490. HRMS (+ESI) *m/z:* Calcd for $C_{11}H_{13}BrN_2O_4Na$ 338.9951 [M + Na]$^+$; Found 338.9978.

***tert*-Butyl (2-bromo-6-nitrophenyl)carbamate (19b-o)** and **tert-Butyl (2-bromo-4-nitrophenyl)carbamate (19b-p)**. According to the general procedure, after 10 h **19b-o** and **19b-p** were isolated as yellow solids (**19b-o** 10.5 mg, 0.033 mmol, 17%. **19b-p** 6.3 mg, 0.020 mmol, 10%) using a gradient of 3% to 5% EtOAc/PE for silica gel flash column chromatography. Spectral data for **19b-o**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 – 8.39 (m, 2H), 8.18 (m, 1H), 7.32 (s, 1H), 1.56 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5, 142.3, 142.3, 128.0, 124.2, 118.2, 111.0, 82.7, 28.2. UV-Vis absorption (L·mol^{-1}·cm^{-1}): ε_{318} = 12161. FT-IR (cm^{-1}, neat, ATR): 3408, 2930, 1729, 1504. HRMS (+ESI) *m/z:* Calcd for $C_{11}H_{13}BrN_2O_4Na$ 338.9951 [M + Na]$^+$; Found 338.9949. Spectral data for **19b-p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (m, 1H), 7.82 (m, 1H), 7.18 (m, 1H), 6.95 (s, 1H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3, 137.1, 130.2, 125.9, 124.7, 120.9, 82.7, 28.1. UV-Vis absorption (ε, L·mol^{-1}·cm^{-1}): 307 nm (1787). FT-IR (cm^{-1}, neat, ATR): 3157, 2986, 1700, 1532. HRMS (+ESI) *m/z:* Calcd for $C_{11}H_{13}BrN_2O_4Na$ 338.9951 [M + Na]$^+$; Found 338.9952.

Di-*tert*-butyl (2-nitro-1,4-phenylene)dicarbamate (22b). According to the general procedure, after 8.5 h **12b** was isolated as orange solid (41.2 mg, 0.117 mmol, 58%) using a gradient of 2% to 8% EtOAc/PE for silica gel flash column chromatography.^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.45 (s, 1H), 8.44 (m, 1H), 8.33 (d, *J* = 2.6 Hz, 1H), 7.51 (m, 1H), 6.68 (s, 1H), 1.52 (d, *J* = 3.6 Hz, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5, 152.4, 136.1, 132.9, 131.0, 126.1, 121.5, 114.8, 81.7, 28.3, 28.2. UV-Vis absorption (ε, L·mol^{-1}·cm^{-1}): 248 nm

(29040), 397 nm (2822).FT-IR (cm^{-1}, neat, ATR): 3386, 2978, 1726, 1517. HRMS (+ESI) *m/z:* Calcd for $C_{16}H_{23}N_3O_6Na$ 376.1479 [M + Na]$^+$; Found 376.1483. Mp: 160-162 °C.

Di-tert-butyl (4-nitro-1,3-phenylene)dicarbamate (23b-p) and Di-tert-butyl (2-nitro-1,3-phenylene)dicarbamate (23b-o). According to the general procedure, after 8.5 h **23b-p** and **23b-o** were isolated as yellow solids (**23b-p** 42.9 mg, 0.121 mmol, 61%. **23b-o** 10.8 mg, 0.031 mmol, 15%) using a gradient of 0% to 5% EtOAc/PE for silica gel flash column chromatography. Spectral data for **23b-p**: ^{1}H NMR (400 MHz, CDC_3) δ 9.95 (s, 1H), 8.35 (m, 1H), 8.18 (d, *J* = 9.4 Hz, 1H), 7.43 (m, 1H), 6.99 (m, 1H), 1.52 (d, *J* = 7.2 Hz, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3, 151.8, 145.8, 137.5, 130.5, 128.0, 111.1, 107.3, 81.9, 81.9, 28.2. UV-Vis absorption (ε, $L{\cdot}mol^{-1}{\cdot}cm^{-1}$): 253 nm (10153), 348 nm (13715). FT-IR (cm^{-1}, neat, ATR): 3322, 2985, 1737, 1704, 1543. HRMS (+ESI) *m/z:* Calcd for $C_{16}H_{23}N_3O_6Na$ 376.1479 [M + Na]$^+$; Found 376.1479. Spectral data for **23b-o**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 2H), 7.91 (m, 2H), 7.46 (m, 1H), 1.51 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 134.5, 134.2, 130.9, 115.8, 81.9, 28.2. UV-Vis absorption (ε, $L{\cdot}mol^{-1}{\cdot}cm^{-1}$): 347 nm (2828). FT-IR (cm^{-1}, neat, ATR): 3403, 2927, 1733, 1483. HRMS (+ESI) *m/z:* Calcd for $C_{16}H_{23}N_3O_6Na$ 376.1479 [M + Na]$^+$; Found 376.1480. Mp: 92-93 °C.

***tert*-Butyl (4-nitrothiazol-2-yl)carbamate (27b**). According to the general procedure, after 24 h **27b** was isolated as yellow solid (12.3 mg, 0.050 mmol, 25%) using a gradient of 5% to 30% EtOAc/PE for silica gel flash column chromatography.^{1}H NMR (400 MHz, CDC_3) δ 8.21 (d, *J* = 0.8 Hz, 1H), 1.61 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 151.8, 143.0, 140.2, 84.7, 28.1. UV-Vis absorption (ε, $L{\cdot}mol^{-1}{\cdot}cm^{-1}$): 343 nm (14698), 433 nm (2121). FT-IR (cm^{-1}, neat, ATR): 3161, 2923, 1726, 1488. HRMS (+ESI) *m/z:* Calcd for $C_8H_{11}N_3O_4SNa$ 268.0362 [M + Na]$^+$; Found 268.0365. Mp: 148 °C (decomposition).

***tert*-Butyl (6-nitropyridin-3-yl)carbamate (28b-p)** and ***tert*-Butyl (2-nitropyridin-3-yl)carbamate (28b-o)**. According to the general procedure, after 8.5 h **23b-p** and **23b-o** were isolated as pale yellow solids (**23b-p** 5.8 mg, 0.024 mmol, 12%. **23b-o** 4.3 mg, 0.018 mmol, 9%) using a gradient of 10% to 25% EtOAc/PE for silica gel flash column chromatography. Spectral data for **23b-o**: ^{1}H NMR (400 MHz, CDC_3) δ 9.38 (s, 1H), 9.06 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.23 (dd, *J* = 4.2, 1.5 Hz, 1H), 7.64 – 7.56 (m, 1H), 1.55 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0, 141.1, 132.2, 130.6, 130.1, 82.7, 28.2. UV-Vis absorption (ε, $L{\cdot}mol^{-1}{\cdot}cm^{-1}$): 310 nm (6607) FT-IR ($cm^{-1}$, neat, ATR): 3255, 2982, 1730, 1519. HRMS (+ESI) *m/z:* Calcd for $C_{10}H_{13}N_3O_4$ 240.0979 [M + H]$^+$; Found 240.0979. Spectral data for **23b-p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.6 Hz, 1H), 8.38 – 8.32 (m, 1H), 8.25 (d, *J* = 8.9 Hz, 1H), 7.04 (s, 1H), 1.54 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 151.69, 140.47, 137.60, 126.62, 119.27, 82.78, 28.17. HRMS (+ESI) *m/z:* Calcd for $C_{10}H_{13}N_3O_4$ 240.0979 [M + H]$^+$; Found 240.0982.

ASSOCIATED CONTENT

Supporting information

The Supporting Information is available free of charge available on the ACS Publications website.

Image of the photoreactor employed for the reactions. Optimization tables for the photocatalytic nitration reactions. UV-Vis absorption spectra. IR spectra. ^{1}H and ^{13}C NMR spectra.

AUTHOR INFORMATION

*B.K.: e-mail, Burkhard.Koenig@ur.de; fax, (+49)-941-943-1717; phone, (+49)-943-4575.

ORCID

Burkhard König: 0000-0002-6131-4850

Notes

The authors declare no competing financial interest.

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