Synthesis I. V. Borovlev et al. Paper

S_NH Arylamination of 3-Nitropyridine: A Competitive Formation of 2-Arylamino-5-nitropyridines and 2-Arylamino-5-nitrosopyridines

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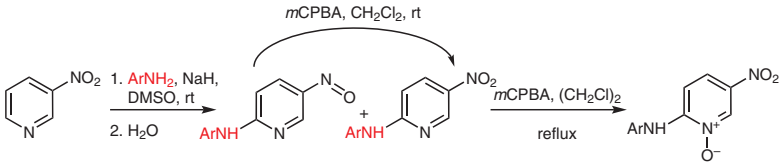

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Abstract Arylamination of 3-nitropyridine via the nucleophilic substitution of hydrogen leads to a mixture of 2-arylamino-5-nitropyridines and novel 2-arylamino-5-nitrosopyridines, with the latter as the major product. The proposed mechanism includes the formation of σ^H-adducts and their further aromatization proceeding either through an oxidative pathway or intramolecular Red/Ox pathway of the S_NH reaction. Moreover, we have shown that nitroso compounds can be selectively oxidized with *m*-chloroperbenzoic acid to give the corresponding nitro derivatives or their *N*-oxides, depending on the reaction temperature and the amount of oxidant.

Key words C–H functionalization, S_NH arylamination, 3-nitropyridine, metal-free synthesis

Aromatic and heteroaromatic amines are widely used as building blocks for various pharmaceuticals, drugs, agrochemicals, polymers, and materials.[1] Many methods for their synthesis employ halogenated starting materials under noncatalytic[2] or catalytic conditions.[3] This approach usually requires additional derivatization, that does not correspond the principle of atom economy.[4] Over the last few decades, significant progress in C–N bond formation through the activation of C–H bonds of aromatic and heteroaromatic compounds by transition metals has been achieved.[5] However, this approach cannot be applied to the synthesis of pharmaceuticals[6a] and organic dyes for solar cells[6b] as, for these purposes, metal traces are not tolerated.

Nucleophilic aromatic substitution of hydrogen (S_NH)[7] can be considered as an attractive alternative to the transition-metal approach. The S_NH methods include *cine*-, *tele*-, and vicarious nucleophilic substitution (VNS), which require a good leaving group presence in the substrate or in the reagent. Additionally, the oxidative nucleophilic substitution of hydrogen, which does not require any preparatory operations or expensive catalysts and ligands, can be used.[8] Its mechanism involves the formation of a σ^H adduct and its further aromatization in the presence of an oxidant (oxidative S_NH reaction).[9]

As the result of a cooperative electron-withdrawing effect of the nitro group and the N-heteroatom in the 3-nitropyridine molecule, the latter possesses strong electrophilic properties and can participate in different reactions with a variety of nucleophilic reagents. For example, oxidative amination of 3-nitropyridine employing liquid $NH_3/KMnO_4$ proceeded nonselectively, giving a mixture of three isomeric amino derivatives, the products of *ortho*- and *para*-substitution.[10] Additionally, the amination reactions of 3-nitropyridines with ammonia in aqueous $KMnO_4$ solution or $DMSO/KMnO_4$ were reported.[11] In these experiments, substitution at the position 6 of 3-nitropyridine was observed.

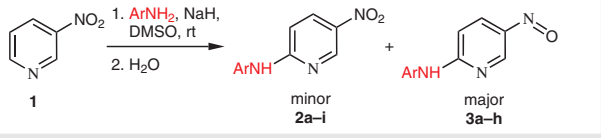
The oxidative S_NH alkylamination reaction of 3-nitropyridines has also been well-studied.[12] Usually, these reactions are performed employing an excess of alkyl- or dialkylamines in the presence of an oxidant. In 2010 Verbeeck and co-workers showed that such transformations in the presence of a complex oxidant, namely dipyridine silver permanganate $AgPy_2MnO_4$, are the most efficient.[12c] 3-Nitropyridines also participate in VNS reactions. For instance, amination reactions with hydroxylamine,[13a] 4-amino-1,2,4-triazole,[13a] *O*-methylhydroxylamine,[13b] and sulfenamides have been reported.[8b] VNS reactions with alkylamines and arylamines[8b,13c] have also been described, but they are less-well studied. Oxidative S_NH and VNS transformations usually proceeded regioselectively, affording the products of *para*-substitution towards the nitro group, exclusively.

The key features of S_NH arylamination are the inapplicability of amination and alkylamination protocols, due to the low nucleophilicity of arylamines, and their high susceptibility to oxidation. This is why the reactions of this type are almost unstudied. Until recently, there were only a few re-

ported examples of intermolecular arylamination: arylamination of 5-azacinnoline,[14] 1,2,4-triazines,[15] and 3-nitropyridines.[16,17] These experiments were performed in the presence of strong bases; in fact, arylamide anions acted as nucleophiles in these transformations.

Recently, we have demonstrated that even such weak N-nucleophiles as arylamino, acylamino, and carbamoyl amino groups, can be introduced into the 1,3,7-triazapyrene[18] and acridine[19] molecules via the S_NH process at room temperature. The reactions were performed, employing sodium hydride as the base in dry DMSO. This solvent is known to enhance the nucleophilicity of different anions. Hereby, the aim of the present work was to study the arylamination of 3-nitropyridine under the same conditions and to establish the scope of the reaction.

First, we performed the amination of 3-nitropyridine (**1**) with aniline as a model reaction. Sodium anilide (1.1 equiv) was prepared by the treatment of aniline with sodium hydride in dry DMSO at room temperature. Then, 3-nitropyridine (1.1 equiv) was added, and the reaction mixture was stirred under air (Table 1, Method A); complete conversion was observed in 15 minutes. Surprisingly, we could isolate two products with a similar structure. According to NMR and HRMS data, these compounds were *N*-(5-nitropyridin-2-yl)aniline (**2a**)[17] and new *N*-(5-nitrosopyridin-2-yl)aniline (**3a**) (Scheme 1, Table 1, entry 1). Increasing of the amount of aniline and NaH gave compounds **2a** and **3a** in higher yields with a predominance of the nitroso product **3a** (entries 2, 4, and 5). However, the reaction with 6 equivalents of sodium anilide resulted in the formation of a complex mixture of oligomerization products (entry 7). Heating the reaction mixture at 60 °C led to its decomposition. The use of 4 equivalents of sodium anilide at room temperature was found to be optimal.



Scheme 1 S_NH Arylamination of 3-nitropyridine

In 2011, Gulevskaya and co-workers reported that 3-nitropyridine has a dual role, as a substrate and an oxidant, in such reactions.[17] To examine, if 3-nitropyridine is the only oxidant in this reaction, or oxygen from the air is also involved, we performed the transformation under argon and

Table 1 Optimization of the Reaction Conditions for S_NH Phenylamination of 3-Nitropyridine (Method A, 15 min)

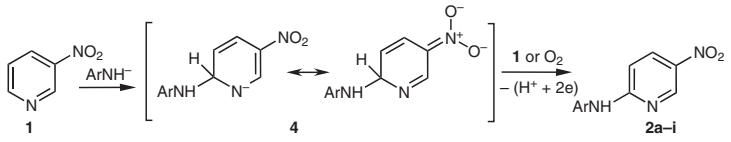
Entry	Aniline (equiv)	NaH (equiv)	Yields (%)[a]	
			2a	**3a**
1	1.1	1.1	16	8
2	2	2	16	22
3	2	2	9[b]	1.5[b]
4	3	3	16	31
5	4	4	22	33
6	4	4	25[c]	33[c]
7	6	6	–	–

[a] Isolated yields after column chromatography.
[b] The reaction was performed under argon.
[c] The reaction was performed with bubbling O_2.

obtained the both products in lower yields (Table 1, entry 3). On other hand, when the reaction was performed with bubbling oxygen, nearly the same outcome was observed (cf. entries 5 and 6). Thus, both 3-nitropyridine and oxygen could oxidize the σ^H adducts **4** into the nitro compound **2a** (Scheme 2). This is why the total yield of compounds **2a** and **3a**, which was calculated from the starting 3-nitropyridine, was low. It is known that oxygen can be an efficient oxidant only when anionic σ^H adducts are further deprotonated with a base; thus, actually, the corresponding dianion undergoes the oxidation[8d] (Scheme 2).

The reaction is accompanied by resinification, probably, due to the formation of some reduced products of 3-nitropyridine or due to the insufficient stability of intermediates **4**.

Arylamine anions bearing either electron-donating or electron-withdrawing substituents on the benzene ring, react with 3-nitropyridine under the same conditions to form a mixture of compounds **2** and **3** in different ratios, generally, with the predominance of the nitroso compound **3** (Scheme 1, Table 2, entries 3, 5, 7, and 9–12). The only exception was 4-nitroaniline, which afforded the nitro compound **2i** as the sole product even under an inert atmosphere (Table 2, entry 14). Obviously, the nitro group of this reagent is able to oxidize the corresponding σ^H adduct **4** in the final step of the transformation. Notably, the products of nucleophilic substitution at positions 2 and 4 of 3-nitropyridine were not detected. This can be explained by the instability of the corresponding σ^H adducts or their insuffi-

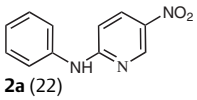
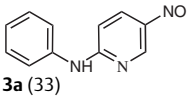
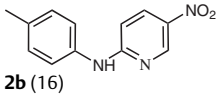
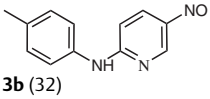
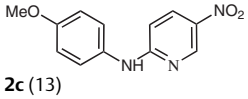
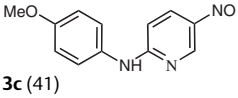
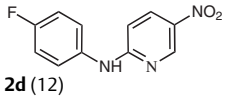
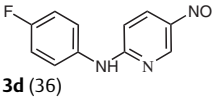
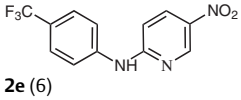
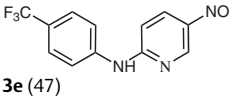
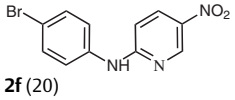
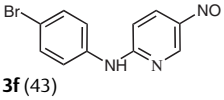
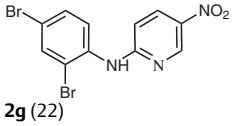
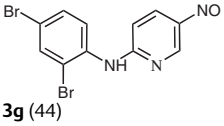
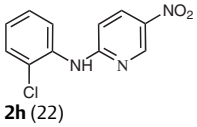
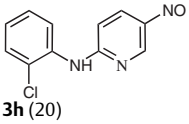
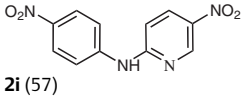


Scheme 2 Proposed pathway for the synthesis of nitro compounds **2a–i**

cient concentration in the reaction mixture. In the latter case, a stronger oxidant is required, which is not possible for a number of reasons (cf. with data[10]).

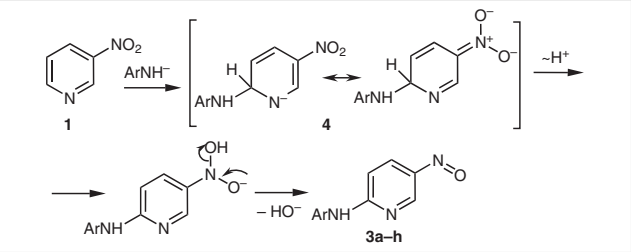
The formation of nitroso compounds from nitroarenes via the nucleophilic substitution is a well-known process.[8a] For example, anions of primary arylamines upon reaction with nitrobenzenes give *ortho*-σ^H-adducts which afford *N*-aryl-2-nitrosoanilines under basic conditions.[20] Interesting-

Table 2 Products of the S_N^H Arylamination Reaction of 3-Nitropyridine Using $ArNH_2$/NaH/DMSO at Room Temperature[a]

Entry	Amine	Method[b]	Yield (%)	
			2	**3**
1	$PhNH_2$	A	 **2a** (22)	 **3a** (33)
2	$PhNH_2$	B	**2a** (1)	**3a** (52)
3	$4\text{-}MeC_6H_4NH_2$	A	 **2b** (16)	 **3b** (32)
4	$4\text{-}MeC_6H_4NH_2$	B	**2b** (11)	**3b** (44)
5	$4\text{-}MeOC_6H_4NH_2$	A	 **2c** (13)	 **3c** (41)
6	$4\text{-}MeOC_6H_4NH_2$	B	**2c** (17)	**3c** (30)
7	$4\text{-}FC_6H_4NH_2$	A	 **2d** (12)	 **3d** (36)
8	$4\text{-}FC_6H_4NH_2$	B	**2d** (12)	**3d** (53)
9	$4\text{-}CF_3C_6H_4NH_2$	A	 **2e** (6)	 **3e** (47)
10	$4\text{-}BrC_6H_4NH_2$	A	 **2f** (20)	 **3f** (43)
11	$2,4\text{-}Br_2C_6H_3NH_2$	A	 **2g** (22)	 **3g** (44)
12	$2\text{-}ClC_6H_4NH_2$	A	 **2h** (22)	 **3h** (20)
13	$2\text{-}ClC_6H_4NH_2$	B	**2h** (7)	**3h** (14)
14	$4\text{-}NO_2C_6H_4NH_2$	A	 **2i** (57)	–
15	$4\text{-}NO_2C_6H_4NH_2$	B	**2i** (59)	–

[a] Isolated yields after column chromatography.
[b] Method A: one-time addition of 3-nitropyridine (1 equiv) to the solution of sodium arylamide (4 equiv) in DMSO, rt, 15 min; Method B: gradual addition of 3-nitropyridine (1 equiv) to a preformed solution of sodium arylamide (2 equiv) in DMSO, rt, 2.5 h.

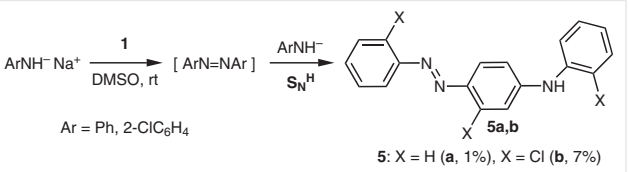
ly, the formation of both *ortho* and *para* σ^H adducts was observed, but only the *ortho* isomers of nitrosoanilines were isolated. According to the data reported by Wróbel and Kwast,[20b] *para* σ^H adducts can be oxidized to give the corresponding *N*-aryl-4-nitroanilines. The proposed mechanism for the synthesis of the nitroso compounds does not involve an external oxidant, which could be an alternative pathway for the aromatization of σ^H-adducts. The last step of the reaction proceeds as an intramolecular Red/Ox-process. The plausible mechanism for the formation of the nitroso compounds **3** is presented in Scheme 3.



Scheme 3 Proposed mechanism for the synthesis of compounds **3a–h**

Thus, the aromatization of σ^H adducts **4** can proceed according to 2 pathways, leading to the products of two competitive reactions with comparable rates. To the best of our knowledge, the intramolecular disproportionation of σ^H adducts with N-nucleophiles has not previously been described for 3-nitropyridine. It should be noted, the products of the condensation of anilines with nitroso compounds were not detected, and this can be explained by the fact that the compounds **3** formed inactive anions in the reaction mixture.

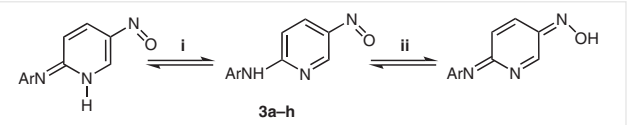
To minimize the consumption of 3-nitropyridine as an oxidant, we performed an additional experiment, where a diluted solution of 3-nitropyridine (1 equiv) in DMSO was slowly added (micro drops via a syringe) over 2.5 hours to the preformed solution of the aniline anion (2 equiv) in DMSO (Method B). In this experiment, the nitroso product **3a** was isolated in 52% yield, whereas the yield of the nitro compound **2a** was 1% (Table 1, cf. entries 1 and 2). Employing Method B, this tendency was observed for other arylamines as well. Moreover, the yields of nitro compounds **2b–d**,**h** were higher than those for **2a** (Table 2, entries 4, 6, 8). Notably, the yield of the sole product **2i** of the reaction with 4-nitroaniline was the same (entry 15). However, when a sixfold excess of sodium anilide was used, a complex mixture of reaction products was obtained. We were able to isolate only one side product, namely (*E*)-*N*-[4-(phenyldiazenyl)phenyl]aniline (**5a**)[21] (Scheme 4). The same reaction with 2-chloroaniline afforded previously unknown (*E*)-2-chloro-*N*-[3-chloro-4-(2-chlorophenyldiazenyl)phenyl]aniline (**5b**) under the same conditions.



Scheme 4 Proposed mechanism for the formation of byproducts **5a**,**b**

Although azobenzene can be generated via the aerobic oxidation of aniline under basic conditions,[22] without 3-nitropyridine, no formation of compound **5b** was observed. The structure of the product was established by X-ray crystal structure determination[23] (see the Supporting Information).

In contrast to nitro products **2**, in the ^{1}H NMR spectra of nitroso compounds **3** in DMSO-d_6, we observed broad proton signals of the pyridine ring. Additionally, ^{13}C NMR spectra of compounds **3c**,**d**,**e**,**h** demonstrated an incomplete set of signals at room temperature, which can be explained by the prototropic tautomerism of the nitroso compounds **3a–h** in DMSO-d_6 (Scheme 5).



Scheme 5 Prototropic tautomerism of nitroso compounds **3** in DMSO-d_6

In contrast, in the ^{1}H NMR spectra of the products **3** at 60 °C, we observed narrow proton signals. Moreover, a complete set of signals of the pyridine ring was found in the ^{13}C NMR spectra of the compounds **3c**,**d**,**e**,**h** at 60 °C. Apparently, the tautomerization rate at room temperature for these compounds is rather slow on an NMR timescale.

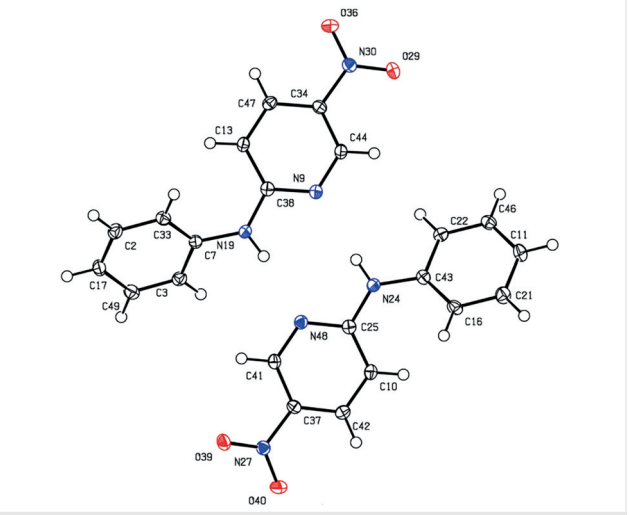


Figure 1 ORTEP diagram of nitro compound **2a**

The structures of the compounds **2a** (Figure 1) and **3a** (Figure 2) were confirmed by X-ray determination.[23]

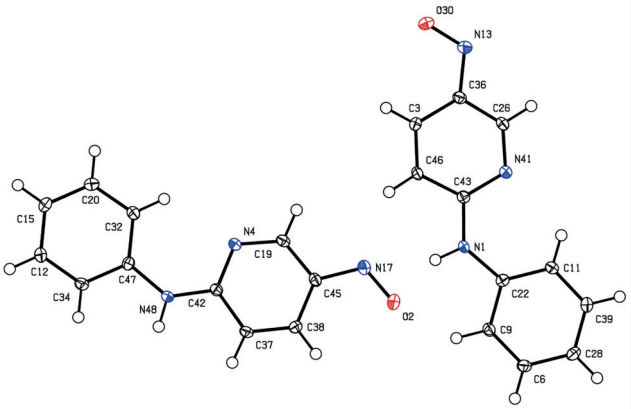
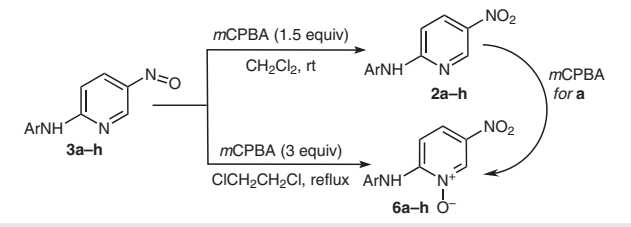


Figure 2 ORTEP diagram of nitroso compound **3a**

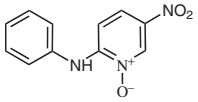
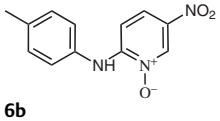
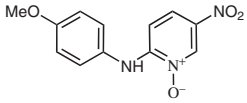
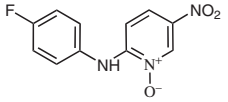
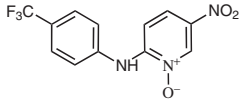
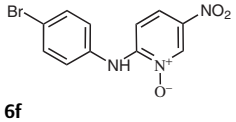
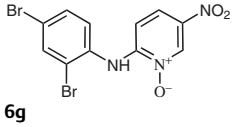
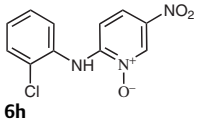
For further studies of these related compounds, we tried to transform the nitroso derivatives **3a–h** into the nitro products **2a–h**. The reaction was performed in dichloromethane solution at room temperature, using *m*-chloroperbenzoic acid (*m*CPBA) as an oxidant. The corresponding nitro compounds **2a–h** were obtained in 53–80% yields (Scheme 6). However, when *N*-(5-nitrosopyridin-2-yl)arylamines **3a–h** were refluxed with an excess of the same oxidant in the 1,2-dichloroethane, the reaction proceeded further, leading to new *N*-(5-nitro-1-oxypyridin-2-yl)arylamines **6a–h** in moderate yields (Scheme 6, Table 3). Obviously, the nitroso group of compounds **3** is more easily oxidized than the pyridine nitrogen.



Scheme 6 Oxidation of nitroso and nitro compounds with *m*-chloroperbenzoic acid

Oxidation of nitro compound **2a** under same conditions also gave the corresponding *N*-oxide **6a** (Scheme 6). The formation of *N*-oxides **6a–h** can take place due to the electron-donor effect of the substituent at the 2-position of the pyridine ring. Thus, no reaction was observed using 3-nitropyridine as the starting compound. We also failed to obtain the *N*-oxide from the nitro compound **2i** even using a large excess of oxidant. The structure of *N*-oxide **6b** was confirmed by X-ray crystal structure determination[23] (see the Supporting Information).

Table 3 Synthesis of *N*-(5-Nitropyridin-2-yl)arylamines **2** and *N*-(5-Nitro-1-oxypyridin-2-yl)arylamines **6**

Entry	Starting compound	Product	Yield[a] (%)
1	**3a**	**2a**	78
2	**3a**		40
3	**2a**	**6a**	41
4	**3b**	**2b**	73
5	**3b**		56
6	**3c**	**6b**	
7	**3c**	**2c**	76
			44
8	**3d**	**6c**	
9	**3d**	**2d**	67
			40
10	**3e**	**6d**	
11	**3e**	**2e**	80
			45
12	**3f**	**6e**	
13	**3f**	**2f**	53
			39
14	**3g**	**6f**	
15	**3g**	**2g**	71
			41
16	**3h**	**6g**	
17	**3h**	**2h**	78
			40
		6h	

[a] Isolated yields after column chromatography.

In summary, we have shown that sodium arylamides can be used as nucleophiles in S_NH reactions with 3-nitropyridine, affording new 2-arylamino-5-nitrosopyridines along with the expected 2-arylamino-5-nitropyridines. Aromatization of σ^H-adducts, which are formed in the first step of the reaction, proceeds via two possible pathways. Thus, an oxidative S_NH process, in which both 3-nitropyridine and atmospheric oxygen act as oxidants, affords nitro compounds. Alternatively, an intramolecular Red/Ox process, which is well-known for VNS reactions, gives the corresponding nitroso derivatives. The first example of the synthesis of nitroso compounds via attack on the *para*-position to the nitro group by the arylamide anion is described. Finally, we have demonstrated that nitroso compounds can be transformed into the corresponding nitro products or their *N*-oxides, depending on the reaction temperature and the amount of *m*-chloroperbenzoic acid. The obtained products represent versatile precursors for valuable pyridine derivatives.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance HD 400 spectrometer in the solvent indicated relative to residual DMSO signals[24] or TMS as internal standard when $CDCl_3$ was used as solvent. HRMS were registered on a Bruker UHR-TOF Maxis™ Impact instrument using the DART technique (carrier gas He, 300 °C). IR spectra were recorded on a Shimadzu IRTracer-100. All melting points were determined in glass capillaries using REACH Devices RD-MP and Electrothermal IA 9200 instruments and are uncorrected. The identity of the compounds prepared by various methods was established by comparison of their IR spectra. The progress of the reactions was monitored by TLC using Silufol UV-254 silica gel plates; petroleum ether = PE. *m*-Chloroperbenzoic acid containing 77% of active ingredient (abcr GmbH & Co. KG) and NaH as 60% w/w dispersion in mineral oil was used as such (Merck). Other commercially available chemicals were used also without additional purification.

N-(5-Nitropyridin-2-yl)arylamines 2a–i and *N*-(5-Nitrosopyridin-2-yl)arylamines 3a–h; General Procedures

Method A: To a solution of the arylamine (2 mmol) in anhyd DMSO (2 μL), NaH (2 mmol) was added at rt. When H_2 bubbling ceased, 3-nitropyridine **1** (0.5 mmol) was added. The mixture was stirred vigorously at rt for 0.25 h. Then it was poured onto well-milled ice (~50 g). Upon reaching rt, the solution was acidified with dil HCl to pH ~7. The precipitate obtained was filtered off, washed with water, and dried. The crude products were separated by column flash chromatography (silica gel, CH_2Cl_2/PE 1:1 then CH_2Cl_2) to give a first yellow fraction (CH_2Cl_2/PE 1:1) and then a second yellow-green fraction (CH_2Cl_2). After evaporation of the solvent, the corresponding nitro **2** and nitroso compounds **3** were obtained from the first and the second fractions, respectively. In the case of nitro compound **2i**, the separation was performed by elution with CH_2Cl_2 collecting the second yellow fraction. The products were then purified by recrystallization from an appropriate solvent.

Method B: To a solution of the arylamine (1 mmol) in anhyd DMSO (1.5 μL), NaH (1 mmol) was added at rt. When H_2 bubbling ceased, the solution of 3-nitropyridine **1** (0.5 mmol) in DMSO (1.5 μL) was added gradually by micro drops via a syringe over 2.5 h with vigorous stirring. Then it was poured onto well-milled ice (~50 g). Upon reaching rt, the solution was acidified with dil HCl to pH ~7. The precipitate obtained was filtered off, washed with water, and dried. The separation of nitro **2** and nitroso compounds **3** was performed as indicated in Method A.

N-(5-Nitropyridin-2-yl)aniline (2a)

Yellow solid; yield: 24 mg (22%, Method A); 1.08 mg (1%, Method B); mp 138–139 °C (CH_2Cl_2) (Lit.[17] 135–136 °C).

IR (thin film): 3235, 3035, 2939, 1582, 1547, 1464, 1328 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.13 (br s, 1 H, NH), 9.03 (d, *J* = 2.8 Hz, 1 H, H-6 Py), 8.29 (dd, *J* = 9.3, 2.8 Hz, 1 H, H-4 Py), 7.70 (d, *J* = 7.9 Hz, 2 H, H-2′,6′ Ph), 7.36 (br t, *J* = 7.9 Hz, 2 H, H-3′,5′ Ph), 7.08 (br t, *J* = 7.4 Hz, 1 H, H-4′ Ph), 6.91 (d, *J* = 9.3 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.0, 146.0, 139.4, 136.1, 132.5, 128.9, 123.2, 120.2, 110.0.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}N_3O_2$: 216.0768; found: 216.0766.

N-(5-Nitrosopyridin-2-yl)aniline (3a)

Dark green solid; yield: 33 mg (33%, Method A); 51.7 mg (52%, Method B); mp 167–168 °C (CH_2Cl_2).

IR (thin film): 3294, 3205, 3042, 1588, 1526 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.50 (br s, 1 H, NH), 9.78 (br s, 1 H, H-6 Py), 7.82 (d, *J* = 7.9 Hz, 2 H, H-2′,6′ Ph), 7.41 (br t, *J* = 7.9 Hz, 2 H, H-3′,5′ Ph), 7.12 (br t, *J* = 7.4 Hz, 1 H, H-4′ Ph), 7.07 (br s, 1 H, H-4 Py), 6.82 (d, *J* = 9.2 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.9, 159.2, 138.9, 129.0 (2 C), 124.1, 120.9, 111.19, 111.15.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}N_3O$: 200.0818; found: 200.0802.

4-Methyl-*N*-(5-nitropyridin-2-yl)aniline (2b)

Yellow solid; yield: 18 mg (16%, Method A); 12.6 mg (11%, Method B); mp 140–141 °C (CH_2Cl_2).

IR (thin film): 3227, 3178, 3030, 2921, 1594, 1581, 1540, 1330 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.05 (br s, 1 H, NH), 9.01 (d, *J* = 2.8 Hz, 1 H, H-6 Py), 8.26 (dd, *J* = 9.3, 2.8 Hz, 1 H, H-4 Py), 7.57 (d, *J* = 8.3 Hz, 2 H, H-2′,6′ C_6H_4), 7.17 (d, *J* = 8.3 Hz, 2 H, H-3′,5′ C_6H_4), 6.85 (d, *J* = 9.3 Hz, 1 H, H-3 Py), 2.28 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.1, 146.1, 136.8, 135.8, 132.4, 129.3 (2 C), 120.4, 109.6, 20.5.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{12}N_3O_2$: 230.0924; found: 230.0905.

4-Methyl-*N*-(5-nitrosopyridin-2-yl)aniline (3b)

Dark green solid; yield: 34 mg (32%, Method A); 47 mg (44%, Method B); mp 170–171 °C (CH_2Cl_2).

IR (thin film): 3232, 3023, 2930, 1600, 1571, 1532, 1506 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.45 (br s, 1 H, NH), 9.75 (br s, 1 H, H-6 Py), 7.69 (br d, 2 H, H-2′,6′ C_6H_4), 7.22 (d, *J* = 8.3 Hz, 2 H, H-3′,5′ C_6H_4), 7.05 (br s, 1 H, H-4 Py), 6.77 (d, *J* = 9.3 Hz, 1 H, H-3 Py), 2.31 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.2, 161.4, 159.6, 136.8, 133.8, 134.0, 130.1, 129.9, 121.5, 21.0.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{12}N_3O$: 214.0975; found: 214.0970.

4-Methoxy-*N*-(5-nitropyridin-2-yl)aniline (2c)

Dark red solid; yield: 16 mg (13%, Method A); 21 mg (17%, Method B); mp 162–163 °C (CH_2Cl_2).

IR (thin film): 3230, 3180, 2923, 1598, 1549, 1510, 1328 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.00 (br s, 1 H, NH), 8.99 (d, *J* = 2.8 Hz, 1 H, H-6 Py), 8.24 (dd, *J* = 9.3, 2.8 Hz, 1 H, H-4 Py), 7.56 (d, *J* = 8.9 Hz, 2 H, H-3′,5′ C_6H_4), 6.95 (d, *J* = 8.9 Hz, 2 H, H-2′,6′ C_6H_4), 6.79 (d, *J* = 9.3 Hz, 1 H, H-3 Py), 3.75 (s, 3 H, OCH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.2, 155.6, 146.3, 135.5, 132.4, 132.2, 122.4, 114.1 (2 C), 55.2.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{12}N_3O_2$: 246.0873; found: 246.0870.

4-Methoxy-*N*-(5-nitrosopyridin-2-yl)aniline (3c)

Black solid; yield: 47 mg (41%, Method A); 34 mg (30%, Method B); mp 158–159 °C (CH_2Cl_2).

IR (thin film): 3218, 3000, 2825, 1600, 1505 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$, 20 °C): δ = 9.62 (br s, 1 H, NH), 7.53 (br s, 1 H, H-6 Py), 7.25 (d, *J* = 8.8 Hz, 2 H, H-3′,5′ C_6H_4), 7.04–6.97 (m, 1 H, H-4 Py), 6.91 (d, *J* = 8.8 Hz, 2 H, H-2′,6′ C_6H_4), 6.47 (d, *J* = 9.2 Hz, 1 H, H-3 Py), 3.78 (s, 3 H, OCH_3).

^1H NMR (400 MHz, DMSO-d_6, 60 °C): δ = 10.25 (br s, 1 H, NH), 9.63 (br s, 1 H, H-6 Py), 7.67 (d, *J* = 8.9 Hz, 2 H, H-3′,5′ C_6H_4), 7.08 (dd, *J* = 8.9, 1.6 Hz, 1 H, H-4 Py), 6.99 (d, *J* = 8.9 Hz, 2 H, H-2′,6′ C_6H_4), 6.73 (d, *J* = 9.3 Hz, 1 H, H-3 Py), 3.79 (s, 3 H, OCH_3).

^{13}C NMR (100 MHz, DMSO-d_6, 60 °C): δ = 160.8, 159.6, 159.1, 156.1, 131.6, 122.8, 119.4, 114.1, 110.1, 55.1.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{12}N_3O$: 230.0924; found: 230.0914.

4-Fluoro-*N*-(5-nitropyridin-2-yl)aniline (2d)

Orange solid; yield: 14 mg (12%, Method A); 14 mg (12%, Method B); mp 188–189 °C (CH_2Cl_2).

IR (thin film): 3351, 3259, 3164, 2925, 1627, 1549, 1508, 1326 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.14 (br s, 1 H, NH), 9.02 (d, *J* = 2.7 Hz, 1 H, H-6 Py), 8.28 (dd, *J* = 9.3, 2.7 Hz, 1 H, H-4 Py), 7.74–7.68 (m, 2 H, H-3′,5′ C_6H_4), 7.24–7.18 (m, 2 H, H-2′,6′ C_6H_4), 6.86 (d, *J* = 9.3 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.9, 158.1 (d, $^1J_{C,F}$ = 158.1 Hz), 146.0, 136.1, 135.8, 132.6, 122.1 (d, $^3J_{C,F}$ = 7.8 Hz), 115.5 (d, $^2J_{C,F}$ = 22.2 Hz), 109.9.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9FN_3O_2$: 234.1100; found: 234.1094.

4-Fluoro-*N*-(5-nitrosopyridin-2-yl)aniline (3d)

Brown solid; yield: 39 mg (36%, Method A); 57.5 mg (53%, Method B); mp 201–202 °C (CH_2Cl_2).

IR (thin film): 3225, 3049, 2923, 2852, 1600, 1502 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6, 20 °C): δ = 10.53 (br s, 1 H, NH), 9.77 (br s, 1 H, H-6), 7.87–7.80 (m, 2 H, H-3′,5′ C_6H_4), 7.30–7.21 (m, 2 H, H-2′,6′ C_6H_4), 7.10–7.06 (m, 1 H, H-4 Py), 6.78 (d, *J* = 9.2 Hz, 1 H, H-3 Py).

^1H NMR (400 MHz, DMSO-d_6, 60 °C): δ = 10.35 (br s, 1 H, NH), 9.68 (d, *J* = 2.0 Hz, 1 H, H-6 Py), 7.82 (dd, *J* = 9.1 Hz, $J_{C,F}$ = 5.0 Hz, 2 H, H-3′,5′ C_6H_4), 7.23 (d, *J* = 9.1 Hz, $J_{C,F}$ = 2.3 Hz, 2 H, H-2′,6′ C_6H_4), 7.12 (dd, *J* = 9.3, 2.0 Hz, 1 H, H-4 Py), 6.79 (dd, *J* = 9.3 Hz, $J_{C,F}$ = 0.3 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6, 60 °C): δ = 159.8 (d, $^1J_{C,F}$ = 187.7 Hz), 159.6, 159.1, 157.2, 135.1, 122.8 (d, $^3J_{C,F}$ = 7.9 Hz), 119.5 (d, $^4J_{C,F}$ = 2.4 Hz), 115.2 (d, $^2J_{C,F}$ = 22.3 Hz), 110.6.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9FN_3O$: 218.0724; found: 218.0726.

***N*-(5-Nitropyridin-2-yl)-4-(trifluoromethyl)aniline (2e)**

Yellow solid; yield: 8.5 mg (6%, Method A); mp 137–138 °C (CH_2Cl_2).

IR (thin film): 3344, 3231, 3098, 1589, 1552, 1520, 1360 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.45 (br s, 1 H, NH), 9.09 (d, *J* = 2.8 Hz, 1 H, H-6 Py), 8.37 (dd, *J* = 9.3, 2.8 Hz, 1 H, H-4 Py), 7.96 (d, *J* = 8.5 Hz, 2 H, H-3′,5′ C_6H_4), 7.71 (d, *J* = 8.5 Hz, 2 H, H-2′,6′ C_6H_4), 7.01 (d, *J* = 9.3 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.5, 145.6, 143.3, 137.0, 132.9, 124.5 (q, $^1J_{C,F}$ = 269.7 Hz), 126.1 (q, $^3J_{C,F}$ = 3.8 Hz), 122.5 (q, $^2J_{C,F}$ = 31.8 Hz), 119.3, 111.2.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_9F_3N_3O_2$: 284.0641; found: 284.0643.

***N*-(5-Nitrosopyridin-2-yl)-4-(trifluoromethyl)aniline (3e)**

Dark green solid; yield: 63 mg (47%, Method A); mp 171–172 °C (CH_2Cl_2).

IR (thin film): 3299, 3184, 3088, 1590, 1516, 1501 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6, 20 °C): δ = 10.75 (br s, 1 H, NH), 9.88 (br s, 1 H, H-6 Py), 8.10 (d, *J* = 8.6 Hz, 2 H, H-3′,5′ C_6H_4), 7.77 (d, *J* = 8.6 Hz, 2 H, H-2′,6′ C_6H_4), 7.12 (br d, *J* = 8.7 Hz, 1 H, H-4 Py), 6.91 (d, *J* = 9.2 Hz, 1 H, H-3 Py).

^1H NMR (400 MHz, DMSO-d_6, 60 °C): δ = 10.58 (br s, 1 H, NH), 9.77 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 8.07 (d, *J* = 8.6 Hz, 2 H, H-3′,5′ C_6H_4), 7.73 (d, *J* = 8.6 Hz, 2 H, H-2′,6′ C_6H_4), 7.17 (dd, *J* = 9.2, 2.4 Hz, 1 H, H-4 Py), 6.92 (d, *J* = 9.2 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6, 60 °C): δ = 160.5, 158.6, 157.9, 142.6, 125.8 (q, ^3J = 11.3 Hz), 124.2 (q, ^1J = 269.6 Hz), 123.2 (q, ^2J = 95.7 Hz), 120.0, 119.6, 111.6.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_9F_3N_3O$: 268. 0708; found: 268. 0692.

4-Bromo-*N*-(5-nitropyridin-2-yl)aniline (2f)

Pale brown solid; yield: 29 mg (20%, Method A); mp 148–149 °C (CH_2Cl_2/PE).

IR (thin film): 3348, 3219, 3138, 2921, 2850, 1620, 1581, 1536, 1358 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.22 (br s, 1 H, NH), 9.05 (d, *J* = 2.7 Hz, 1 H, H-6 Py), 8.31 (dd, *J* = 9.3, 2.8 Hz, 1 H, H-4 Py), 7.71 (d, *J* = 8.9 Hz, 2 H, H-3′,5′ C_6H_4), 7.53 (d, *J* = 8.9 Hz, 2 H, H-2′,6′ C_6H_4), 6.92 (d, *J* = 9.3 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.6, 145.8, 138.9, 136.4, 132.6, 131.6, 121.7, 114.5, 110.6.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9{}^{79}BrN_3O_2$: 293.9873; found: 293.9873.

4-Bromo-*N*-(5-nitrosopyridin-2-yl)aniline (3f)

Brown solid; yield: 60 mg (43%, Method A); mp 185–186 °C (CH_2Cl_2).

IR (thin film): 3297, 3196, 3013, 2925, 2851, 1604, 1581, 1524 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.57 (br s, 1 H, NH), 9.81 (br s, 1 H, H-6 Py), 7.84 (d, J = 8.8 Hz, 2 H, H-3′,5′ C_6H_4), 7.59 (d, J = 8.8 Hz, 2 H, H-2′,6′ C_6H_4), 7.10–7.05 (m, 1 H, H-4 Py), 6.83 (d, J = 9.2 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.8, 158.8, 138.4, 131.7, 122.5, 115.5, 111.6.

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{11}H_9{}^{79}BrN_3O$: 277.9924; found: 277.9928.

2,4-Dibromo-*N*-(5-nitropyridin-2-yl)aniline (2g)

Yellow solid; yield: 41 mg (22%, Method A); mp 162–163 °C (CH_2Cl_2/PE).

IR (thin film): 3356, 3079, 2919, 2854, 1607, 1568, 1528, 1349 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.75 (br s, 1 H, NH), 8.93 (d, J = 2.8 Hz, 1 H, H-6 Py), 8.32 (dd, J = 9.3, 2.8 Hz, 1 H, H-4 Py), 7.97 (d, J = 1.5 Hz, 1 H, H-3′ C_6H_3), 7.65–7.58 (m, 2 H, H-5′,6′ C_6H_3), 6.90 (d, J = 9.3 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.6, 145.9, 136.7, 136.6, 134.9, 133.1, 131.3, 129.2; 120.4, 118.3, 109.2.

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{11}H_8{}^{49}Br_2N_3O_2$: 371.8978; found: 371.8974.

2,4-Dibromo-*N*-(5-nitrosopyridin-2-yl)aniline (3g)

Green solid; yield: 78 mg (44%, Method A); mp 189–190 °C (CH_2Cl_2).

IR (thin film): 3253, 3156, 3077, 1607, 1515 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.17 (br s, 1 H, NH), 9.66 (br s, 1 H, H-6 Py), 8.00 (s, 1 H, H-3′ C_6H_4), 7.68–7.63 (m, 2 H, H-5′,6′ C_6H_3), 7.11 (br d, J = 7.9 Hz, 1 H, H-4 Py), 6.81 (d, J = 9.2 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.2, 159.9, 136.3, 134.9 (2C), 131.3 (2C), 129.9, 120.9, 119.1, 110.0.

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{11}H_8{}^{79}Br_2N_3O$: 355.9029; found: 355.9021.

2-Chloro-*N*-(5-nitropyridin-2-yl)aniline (2h)

Yellow solid; yield: 27 mg (22%, Method A); 9 mg (7%, Method B); mp 130–131 °C (CH_2Cl_2).

IR (thin film): 3404, 3177, 3099, 2937, 1600, 1575, 1530, 1365 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.78 (br s, 1 H, NH), 8.94 (d, J = 2.8 Hz, 1 H, H-6 Py), 8.31 (dd, J = 9.3, 2.8 Hz, 1 H, H-4 Py), 7.70 (dd, J = 7.8, 1.5 Hz, 1 H, H-3′ C_6H_4Cl), 7.55 (dd, J = 8.0, 1.3 Hz, 1 H, H-6′ C_6H_4Cl), 7.39 (ddd, J = 6.7, 8.0, 1.5 Hz, 1 H, H-5′ C_6H_4Cl), 7.27 (ddd, J = 7.8, 6.7, 1.3 Hz, 1 H, H-4′ C_6H_4Cl), 6.88 (d, J = 9.3 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.8, 145.9, 136.4, 135.6, 133.0, 129.9, 128.3, 127.7, 127.3, 126.9, 109.0.

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{11}H_9N_3O_2{}^{35}Cl$: 250.0378; found: 250.0380.

2-Chloro-*N*-(5-nitrosopyridin-2-yl)aniline (3h)

Green solid; yield: 23 mg (20%, Method A); 16.3 mg (14%, Method B); mp 121–122 °C (CH_2Cl_2).

IR (thin film): 3242, 3148, 3077, 1601, 1514, 1503 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$, 20 °C): δ = 9.81 (br s, 1 H, NH), 8.16 (d, J = 8.1 Hz, 1 H, H-3′ C_6H_4), 7.63 (br s, 1 H, H-6 Py), 7.49 (dd, J = 8.0, 1.0 Hz, 1 H, H-6′ C_6H_4), 7.35–7.32 (m, 1 H, H-4′ C_6H_4), 7.18–7.14 (m, 1 H, H-5′ C_6H_4), 7.13 (br d, J = 8.4 Hz, 1 H, H-4 Py), 6.68 (d, J = 9.1 Hz, 1 H, H-3 Py).

^{1}H NMR (400 MHz, DMSO-d_6, 60 °C): δ = 10.02 (br s, 1 H, NH), 9.59 (br s, 1 H, H-2 Py), 7.76 (d, J = 8.0 Hz, 1 H, H-3′ C_6H_4), 7.58 (dd, J = 8.1, 1.2 Hz, 1 H, H-6′ C_6H_4), 7.43 (ddd, J = 8.0, 7.6, 1.2 Hz, 1 H, H-4′ C_6H_4), 7.32 (ddd, J = 8.1, 7.6, 1.4 Hz, 1 H, H-5′ C_6H_4), 7.15 (dd, J = 9.2, 2.0 Hz, 1 H, H-4 Py), 6.79 (d, J = 9.2 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6, 60 °C): δ = 161.0, 160.0, 158.3, 135.1, 129.6, 128.7, 127.6, 127.5, 127.2, 120.1, 109.4.

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{11}H_9N_3O^{35}Cl$: 234.0429; found: 234.0435.

4-Nitro-*N*-(5-nitropyridin-2-yl)aniline (2i)

Yellow solid; yield: 74 mg (57%, Method A); 77 mg (59%, Method B); mp 272–273 °C (EtOH).

IR (thin film): 3347, 3237, 3093, 1594, 1577, 1555, 1394, 1315 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.71 (br s, 1 H, NH), 9.13 (d, J = 2.0 Hz, 1 H, H-6 Py), 8.43 (dd, J = 9.1, 2.0 Hz, 1 H, H-4 Py), 8.24 (d, J = 8.9 Hz, 2 H, H-3′,5′ C_6H_4), 8.01 (d, J = 8.9 Hz, 2 H, H-2′,6′ C_6H_4), 7.08 (d, J = 9.1 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.0, 146.1, 145.3, 141.3, 137.6, 133.1, 125.1, 118.6, 112.0.

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{11}H_9N_4O_4$: 261.0618; found: 261.0617.

Side-Products 5a,b; General Procedure

To a solution of the aniline or *o*-chloroaniline (3 mmol) in anhyd DMSO (1.5 mL), NaH (3 mmol) was added at rt. When H_2 bubbling ceased, a solution of 3-nitropyridine (0.5 mmol) in DMSO (1.5 mL) was added gradually by micro drops via a syringe over 2.5 h with vigorous stirring. Then it was poured onto well-milled ice (~50 g). Upon reaching rt, the solution was acidified with dilute HCl to pH ~7. The aqueous solution was extracted with CH_2Cl_2 (3 × 10 mL) and the solvent was distilled off on a rotary evaporator under reduced pressure. The dried residue was purified by flash chromatography (silica gel, CH_2Cl_2) collecting the first orange fraction.

(*E*)-*N*-[4-(Phenyldiazenyl)phenyl]aniline (5a)

Orange solid; yield: 3 mg (1%); mp 80–81 °C (PE) (Lit.[21] 80–81 °C).

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{18}H_{16}N_3$: 274.1339; found: 274.1350.

(*E*)-2-Chloro-*N*-[3-chloro-4-(2-chlorophenyldiazenyl)phenyl]aniline (5b)

Orange solid; yield: 26 mg (7%); mp 142–143 °C (PE).

IR (thin film): 3404, 3065, 2921, 2854, 1601, 1581, 1512, 1418, 1340 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.93 (s, 1 H, NH), 7.73 (d, J = 9.0 Hz, 1 H), 7.68 (dd, J = 7.8, 1.4 Hz, 1 H), 7.63 (dd, J = 7.7, 2.0 Hz, 1 H), 7.58 (dd, J = 8.1, 1.2 Hz, 1 H), 7.53–7.44 (m, 3 H), 7.39 (ddd, J = 8.2, 7.7, 1.3 Hz, 1 H), 7.23 (ddd, J = 8.0, 7.8, 1.4 Hz, 1 H), 7.03 (d, J = 2.3 Hz, 1 H), 6.96 (dd, J = 9.0, 2.4 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.6, 148.3, 140.4, 137.7, 137.0, 133.4, 131.8, 130.7, 130.5, 128.3, 128.1, 127.7, 126.1, 125.2, 119.0, 117.7, 114.5, 114.0.

HRMS (DART): m/z [M + H]$^+$ calcd for $C_{18}H_{13}N_3Cl_3$: 376.0170; found: 376.0171.

N-(5-Nitropyridin-2-yl)arylamines 2a–h from *N*-(5-Nitrosopyridin-2-yl)arylamines 3a–h; General Procedure

A solution of *m*CPBA (1.5 mmol) and *N*-(5-nitrosopyridin-2-yl)arylamine **3** (1 mmol) in CH_2Cl_2 (5 mL) was stirred at rt for 0.5 h. After evaporation of the solvent, the crude products were separated by column flash chromatography (silica gel, benzene then benzene/EtOAc) to give a first colorless fraction (benzene) and then a second yellow fraction (benzene/EtOAc 5:1). *N*-(5-Nitropyridin-2-yl)arylamines **2a–h** were obtained from the second fraction.

N-(5-Nitropyridin-2-yl)aniline (2a)

Yield: 168 mg (78%).

4-Methyl-*N*-(5-nitropyridin-2-yl)aniline (2b)

Yield: 167 mg (73%).

4-Methoxy-*N*-(5-nitropyridin-2-yl)aniline (2c)

Yield: 186 mg (76%).

4-Fluoro-*N*-(5-nitropyridin-2-yl)aniline (2d)

Yield: 156 mg (67%).

N-(5-Nitropyridin-2-yl)-4-(trifluoromethyl)aniline (2e)

Yield: 226 mg (80%).

4-Bromo-*N*-(5-nitropyridin-2-yl)aniline (2f)

Yield: 155 mg (53%).

2,4-Dibromo-*N*-(5-nitropyridin-2-yl)aniline (2g)

Yield: 263 mg (71%).

2-Chloro-*N*-(5-nitropyridin-2-yl)aniline (2h)

Yield: 194 mg (78%).

N-(5-Nitro-1-oxypyridin-2-yl)arylamines 6a–h; General Procedure

A solution of *m*CPBA (0.6 mmol) and *N*-(5-nitrosopyridin-2-yl)arylamine **3** (0.2 mmol) or nitro compound **2a** (0.2 mmol) in 1,2-dichloroethane (10 mL) was refluxed for 1 h. After evaporation of the solvent, the crude products were separated by column flash chromatography (silica gel, benzene then benzene/EtOAc) to give a first maize yellow fraction (benzene), and then a second yellow fraction (benzene/EtOAc, 10:1). *N*-(5-Nitro-1-oxypyridin-2-yl)arylamines **6a–h** were obtained from the second fraction.

N-(5-Nitro-1-oxypyridin-2-yl)aniline (6a)

Pale brown solid; yield: 18.5 mg (40% from **3a**), 19 mg (41%, **2a**); mp 176–177 °C (benzene/PE).

IR (thin film): 3074, 1624, 1564, 1499, 1329, 1274 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.33 (br s, 1 H, NH), 9.11 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 8.02 (dd, *J* = 9.5, 2.4 Hz, 1 H, H-4 Py), 7.47 (dd, *J* = 7.4, 7.3 Hz, 2 H, H-3′,5′ Ph), 7.41 (d, *J* = 7.4 Hz, 2 H, H-2′,6′ Ph), 7.29 (t, *J* = 7.3 Hz, 1 H, H-4′ Ph), 7.09 (d, *J* = 9.5 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.3, 136.9, 135.1, 134.0, 129.6, 126.1, 124.0, 123.3, 105.1.

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{10}N_3O_3$: 232.0717; found: 232.0737.

4-Methyl-*N*-(5-nitro-1-oxypyridin-2-yl)aniline (6b)

Pale brown solid; yield: 27 mg (56%); mp 171–172 °C (benzene/PE).

IR (thin film): 3170, 3152, 1624, 1573, 1326, 1271 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.25 (br s, 1 H, NH), 9.09 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 8.00 (dd, *J* = 9.5, 2.4 Hz, 1 H, H-4 Py), 7.27 (s, 4 H, C_6H_4), 7.01 (d, *J* = 9.5 Hz, 1 H, H-3 Py), 2.33 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.5, 135.7, 134.8, 134.2, 134.0, 130.1, 124.1, 123.3, 104.9, 20.6.

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{12}N_3O_3$: 246.0873; found: 246.0880.

4-Methoxy-*N*-(5-nitro-1-oxypyridin-2-yl)aniline (6c)

Orange solid; yield: 23 mg (44%); mp 173–174 °C (benzene/PE).

IR (thin film): 3075, 1618, 1563, 1499, 1328, 1275 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.19 (br s, 1 H, NH), 9.08 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 7.99 (dd, *J* = 9.6, 2.4 Hz, 1 H, H-4 Py), 7.31 (dd, *J* = 8.9, 3.3 Hz, 2 H, H-2′,6′ C_6H_4), 7.03 (dd, *J* = 8.9, 3.3 Hz, 2 H, H-3′,5′ C_6H_4), 6.89 (d, *J* = 9.6 Hz, 1 H, H-3 Py), 3.78 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.7, 152.9, 134.6, 133.9, 129.4, 126.1, 123.3, 114.8, 104.7, 55.4.

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{12}N_3O_4$: 262.0822; found: 262.0820.

4-Fluoro-*N*-(5-nitro-1-oxypyridin-2-yl)aniline (6d)

Brown solid; yield: 20 mg (40%); mp 251–252 °C (benzene/PE).

IR (thin film): 3190, 3131, 1631, 1580, 1500, 1330, 1274 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.32 (br s, 1 H, NH), 9.11 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 8.01 (dd, *J* = 9.5, 2.4 Hz, 1 H, H-4 Py), 7.47–7.41 (m, 2 H, H-3′,5′ C_6H_4), 7.35–7.28 (m, 2 H, H-2′,6′ C_6H_4), 7.00 (d, *J* = 9.5 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.1 (d, $^1J_{C,F}$ = 241.8 Hz), 152.6, 135.1, 134.0, 133.2, 126.3 (d, $^3J_{C,F}$ = 8.6 Hz), 123.3, 116.4 (d, $^2J_{C,F}$ = 22.6 Hz), 105.0.

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_9FN_3O_3$: 250.0622; found: 250.0630.

N-(5-Nitro-1-oxypyridin-2-yl)-4-(trifluoromethyl)aniline (6e)

Yellow solid; yield: 27 mg (45%); mp 187–188 °C (benzene/PE).

IR (thin film): 3075, 1614, 1569, 1508, 1320, 1275 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 10.57 (br s, 1 H, NH), 9.15 (d, *J* = 2.3 Hz, 1 H, H-6 Py), 8.04 (dd, *J* = 9.5, 2.3 Hz, 1 H, H-4 Py), 7.81 (d, *J* = 8.4 Hz, 2 H, H-3′,5′ C_6H_4), 7.64 (d, *J* = 8.4 Hz, 2 H, H-2′,6′ C_6H_4), 7.34 (d, *J* = 9.5 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.6, 141.8, 136.1, 134.2, 126.6 (q, $^3J_{C,F}$ = 3.7 Hz), 124.2 (q, $^1J_{C,F}$ = 270.1 Hz), 125.5 (q, $^2J_{C,F}$ = 31.9 Hz), 123.4, 123.0, 106.2.

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_9F_3N_3O_3$: 300.0591; found: 300.0591.

4-Bromo-*N*-(5-nitro-1-oxypyridin-2-yl)aniline (6f)

Pale brown solid; yield: 24 mg (39%); mp 211–212 °C (benzene/PE).

IR (thin film): 3071, 1619, 1563, 1327, 1274 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.37 (br s, 1 H, NH), 9.12 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 8.01 (dd, *J* = 9.5, 2.4 Hz, 1 H, H-4 Py), 7.64 (d, *J* = 8.6 Hz, 2 H, H-2′,6′ C_6H_4), 7.38 (d, *J* = 8.6 Hz, 2 H, H-3′,5′ C_6H_4), 7.14 (d, *J* = 9.5 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.0, 136.5, 135.4, 134.0, 132.4, 125.9, 123.2, 118.2, 105.5.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9{}^{79}BrN_3O_3$: 309.9813; found: 309.9823.

2,4-Dibromo-*N*-(5-nitro-1-oxypyridin-2-yl)aniline (6g)

Yellow solid; yield: 32 mg (41%); mp 208–209 °C (benzene/PE).

IR (thin film): 3076, 1621, 1565, 1329, 1274 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.17 (br s, 1 H, NH), 9.13 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 8.09 (d, *J* = 2.1 Hz, 1 H, H-3′ C_6H_3), 8.00 (dd, *J* = 9.4, 2.4 Hz, 1 H, H-4 Py), 7.72 (dd, *J* = 8.5, 2.1 Hz, 1 H, H-5′ C_6H_3), 7.47 (d, *J* = 8.5 Hz, 1 H, H-6′ C_6H_3), 6.68 (d, *J* = 9.4 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.0, 135.7, 135.6, 135.1, 134.0, 132.2, 130.0, 123.1, 122.2, 120.6, 105.8.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_8{}^{79}Br_2N_3O_3$: 387.8927; found: 387.8932.

2-Chloro-*N*-(5-nitro-1-oxypyridin-2-yl)aniline (6h)

Pale brown solid; yield: 21 mg (40%); mp 162–163 °C (benzene/PE).

IR (thin film): 3085, 1619, 1566, 1329, 1267 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.21 (br s, 1 H, NH), 9.13 (d, *J* = 2.4 Hz, 1 H, H-6 Py), 8.02 (dd, *J* = 9.4, 2.4 Hz, 1 H, H-4 Py), 7.68 (dd, *J* = 7.8, 1.2 Hz, 1 H, H-3′ C_6H_4Cl), 7.54 (dd, *J* = 7.7, 1.7 Hz, 1 H, H-6′ C_6H_4Cl), 7.49 (dd, *J* = 7.5, 7.8 Hz, 1 H, H-4′ C_6H_4Cl), 7.42 (dd, *J* = 7.7, 7.5 Hz, 1 H, H-5′ C_6H_4Cl), 6.64 (d, *J* = 9.4 Hz, 1 H, H-3 Py).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.2, 135.5, 134.0, 133.9, 130.5, 130.0, 128.9, 128.7, 128.3, 123.2, 105.5.

HRMS (DART): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9{}^{35}ClN_3O_3$: 266.0327; found: 266.0327.

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Supporting Information

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References

(1) (a) Travis, A. S. In *The Chemistry of Anilines, Part 2*; Rappoport, Z., Ed.; Wiley: Chichester, **2007**, Chap. 13, 715. (b) Corey, E. J.; Czako, B.; Kurti, L. *Molecules and Medicine*; Wiley: Hoboken, **2007**. (c) Gangopadhyay, P.; Radhakrishnan, T. P. *Chem. Mater.* **2000**, *12*, 3362. (d) Bag, B.; Bharadwaj, P. K. *J. Phys. Chem. B* **2005**, *109*, 4377.

(2) (a) Terrier, F. *Modern Nucleophilic Aromatic Substitution*; Wiley-VCH: Weinheim, **2013**. (b) Gorelik, M. V.; Efros, L. S. *Osnovy Khimii i Tekhnologii Aromaticheskikh Soedinenii (Principles of the Chemistry and Technology of Aromatic Compounds)*; Khimia: Moscow, **1992**.

(3) de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, **2004**, 2nd ed..

(4) (a) Arends, I.; Sheldon, R.; Hanefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, **2007**. (b) Constable, D. J. C.; Dunn, P. J.; Hayler, J. D.; Humphrey, G. R.; Leazer, J. L.; Linderman, R. J.; Lorenz, K.; Manley, J.; Pearlman, B. A.; Wells, A.; Zaks, A.; Zhang, T. Y. *Green Chem.* **2007**, *9*, 411. (c) Utepova, I. A.; Trestsova, M. A.; Chupakhin, O. N.; Charushin, V. N.; Rempel, A. A. *Green Chem.* **2015**, *17*, 4401. (d) Xu, J.; Wei, Z.; Li, J. *Chin. J. Org. Chem.* **2012**, *32*, 1208.

(5) (a) Tsang, W. C. P.; Zheng, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 14560. (b) Kim, J. Y.; Cho, S. H.; Joseph, J.; Chang, S. *Angew. Chem. Int. Ed.* **2010**, *49*, 9899. (c) Kim, J. Y.; Park, S. H.; Ryu, J.; Cho, S. H.; Kim, S. H.; Chang, S. *J. Am. Chem. Soc.* **2012**, *134*, 9110. (d) Kim, J.; Kim, S. H.; Chang, S. *Chem. Eur. J.* **2013**, *19*, 7328. (e) Ryu, J.; Shin, K.; Park, S. H.; Kim, J. Y.; Chang, S. *Angew. Chem. Int. Ed.* **2012**, *51*, 9904.

(6) (a) Verbitskiy, E. V.; Cheprakova, E. M.; Slepukhin, P. A.; Kravchenko, M. A.; Skornyakov, S. N.; Rusinov, G. L.; Chupakhin, O. N.; Charushin, V. N. *Eur. J. Med. Chem.* **2015**, *97*, 225. (b) Verbitskiy, E. V.; Cheprakova, E. M.; Subbotina, J. O.; Schepochkin, A. V.; Slepukhin, P. A.; Rusinov, G. L.; Charushin, V. N.; Chupakhin, O. N.; Makarova, N. I.; Metelitsa, A. V.; Minkin, V. I. *Dyes Pigm.* **2014**, *100*, 201.

(7) Chupakhin, O. N.; Charushin, V. N.; van der Plas, H. C. *Nucleophilic Aromatic Substitution of Hydrogen*; Academic Press: San Diego, **1994**.

(8) (a) Mąkosza, M.; Wojciechowski, K. *Top. Heterocycl. Chem.* **2014**, *37*, 51. (b) Mąkosza, M.; Białecki, M. *J. Org. Chem.* **1998**, *63*, 4878. (c) Mąkosza, M. *Chem. Soc. Rev.* **2010**, *39*, 2855. (d) Mąkosza, M.; Wojciechowski, K. *Chem. Rev.* **2004**, *104*, 2631. (e) Chupakhin, O. N.; Charushin, V. N. *Tetrahedron Lett.* **2016**, *57*, 2665. (f) Mąkosza, M. *Synthesis* **2017**, *49*, 3247.

(9) (a) van der Plas, H. C. *Adv. Heterocycl. Chem.* **2004**, *86*, 1. (b) Charushin, V. N.; Chupakhin, O. N. *Top. Heterocycl. Chem.* **2014**, *37*, 1. (c) Gulevskaya, A. V.; Pozharskii, A. F. *Top. Heterocycl. Chem.* **2014**, *37*, 179. (d) Mattijs, B.; Maes, B. U. W. *Adv. Organomet. Chem.* **2017**, *67*, 401.

(10) Wozniak, M.; Baranski, A.; Szpakiewicz, B. *Liebigs Ann. Chem.* **1991**, 875.

(11) (a) Bakke, J. M.; Svensen, H. *Tetrahedron Lett.* **2001**, *42*, 4393. (b) Bakke, J. M. *J. Heterocycl. Chem.* **2005**, *42*, 463.

(12) (a) Szpakiewicz, B.; Wozniak, M. *J. Prakt. Chem.* **1999**, *341*, 75. (b) Gulevskaya, A. V.; Maes, B. U. W.; Meyers, C.; Herrebout, W.; van der Veken, B. J. *Eur. J. Org. Chem.* **2006**, 5305. (c) Verbeeck, S.; Herrebout, W. A.; Gulevskaya, A. V.; van der Veken, B. J.; Maes, B. U. W. *J. Org. Chem.* **2010**, *75*, 5126.

(13) (a) Bakke, J. M.; Svensen, H.; Trevisan, R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 376. (b) Seko, S.; Miyake, K. *Chem. Commun.* **1998**, 1519. (c) Katritzky, A. R.; Laurenzo, K. S. *J. Org. Chem.* **1986**, *51*, 5039.

(14) Budyka, M. F.; Terent'ev, P. B.; Kost, A. N. *Chem. Heterocycl. Compd.* **1978**, *14*, 663.

(15) Garnier, E.; Audoux, J.; Pasquinet, E.; Suzenet, F.; Poullain, D.; Lebret, B.; Guillaumet, G. *J. Org. Chem.* **2004**, *69*, 7809.

(16) Patriciu, O.-I.; Finaru, A.-L.; Sandulescu, I.; Guillaumet, G. *Synthesis* **2007**, 3868.

(17) Gulevskaya, A. V.; Tyaglivaya, I. N.; Verbeeck, S.; Maes, B. U. W.; Tkachuk, A. V. *ARKIVOC* **2011**, *(ix)*, 238.

(18) (a) Borovlev, I. V.; Demidov, O. P.; Saigakova, N. A.; Amangasieva, G. A. *Eur. J. Org. Chem.* **2014**, 7675. (b) Borovlev, I. V.; Demidov, O. P.; Kurnosova, N. A.; Amangasieva, G. A.; Avakyan, E. K. *Chem. Heterocycl. Compd.* **2015**, *51*, 170. (c) Borovlev, I. V.; Demidov, O. P.; Amangasieva, G. A.; Avakyan, E. K.; Kurnosova, N. A. *ARKIVOC* **2016**, *(iii)*, 58.

(19) (a) Demidov, O. P.; Borovlev, I. V.; Amangasieva, G. A.; Avakyan, E. K. *Chem. Heterocycl. Compd.* **2016**, *52*, 104. (b) Borovlev, I. V.; Demidov, O. P.; Amangasieva, G. A.; Avakyan, E. K. *Tetrahedron Lett.* **2016**, *57*, 3608.

(20) (a) Wróbel, Z.; Kwast, A. *Synlett* **2007**, 1525. (b) Wróbel, Z.; Kwast, A. *Synthesis* **2010**, 3865. (c) Kwast, A.; Stachowska, K.; Trawczynski, A.; Wróbel, Z. *Tetrahedron Lett.* **2011**, *52*, 6484. (d) Wróbel, Z.; Stachowska, K.; Grudzień, K.; Kwast, A. *Synlett* **2011**, 1439. (e) Ayyangar, N. R.; Naik, S. N.; Srinivasan, K. V. *Tetrahedron Lett.* **1990**, *31*, 3217.

(21) Stern, M. K.; Cheng, B. K.; Hileman, F. D.; Allman, J. M. *J. Org. Chem.* **1994**, *59*, 5627.

(22) Jeon, S.; Sawyer, D. T. *Inorg. Chem.* **1990**, *29*, 4612.

(23) CCDC 1540375 (**5b**; crystal from PE), CCDC 1543237 (**2a**; crystal from CH_2Cl_2), CCDC 1543224 (**3a**; crystal from PE/CH_2Cl_2, 1:1), and CCDC 1575585 (**6b**; crystal from EtOAc) contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

(24) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.