Simple Synthesis of *N*-Aryl-2-nitrosoanilines in the Reaction of Nitroarenes with Aniline Anion Derivatives

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Abstract: Anions generated from primary arylamines react with substituted nitrobenzenes to form σ^H-adducts, which, under basic reaction conditions, undergo transformation to *N*-aryl-2-nitrosoamines. Competitive substitution of reactive halogens in the nitroarenes, which is observed in certain cases, can be controlled by the solvent selected.

Key words: nucleophilic additions, arenes, amines, nitroso group

A fundamental reaction of nitroaromatic compounds with anionic nucleophiles is addition of the latter to the nitroarene ring at its activated positions with formation of σ-adducts.[1] Nucleophilic aromatic substitution (S_NAr) of halogens and some other leaving groups is a well-known result of the addition of the nucleophiles at positions occupied by such substituents. Formation of σ^H-adducts at unoccupied positions of the nitroarene, although usually faster, does not produce definite products until certain requirements are met. The presence of oxidizing agents in the reaction medium (oxidative nucleophilic substitution of hydrogen, ONSH)[1,2] or leaving groups in the nucleophile molecule (vicarious nucleophilic substitution, VNS)[3] are, among other, beneficial circumstances that allow the σ^H-adducts to convert into stable products. Another possible transformation of σ^H-adducts is the formal intramolecular redox process, resulting in substitution of hydrogen with parallel reduction of the nitro group to the nitroso group.[1a,4] In such reactions of carbanions, however, the so-formed substituted nitrosoarenes remain hypothetical intermediates as they were not isolated. Their formation was anticipated from the final products of subsequent transformations, usually leading to fused heterocycles.[4] As a rule, protic medium or the presence of Lewis acids are required for such reactions to occur. The Wohl–Aue reaction of anilines with nitroarenes in the presence of a base leading to phenazine derivatives is also believed to proceed via cyclization of nitroso compounds, although intermediate *N*-aryl-*o*-nitrosoanilines have not been detected.[5] On the other hand, when σ^H-adducts are formed in the position *para* to the nitro group the corresponding 4-nitrosodiarylamines can be obtained.[5b,6]

N-Aryl-2-nitrosoanilines have been reported in the literature in the photochemical rearrangements of *N*-acyl-*N*-(2-nitroaryl)anilines,[7a,b] in a few exceptional examples of the Fisher–Hepp rearrangement[7c,d] and in a complex mixture of products of the reaction of aryliminodimagnesium reagents with nitroarenes.[7e] One example of apparently direct C-nitrosation of 1,3,5-tris(phenylamino)benzene has also been reported.[7f] None of these reactions could be regarded as a useful method for practical synthesis.

In our preliminary communication we have shown that anions of arylamines react with substituted nitrobenzenes to form, after protonation with acetic acid, *N*-aryl-2-nitrosoanilines, which could be isolated in acceptable yields.[8]

Their convenient synthesis permits them to be considered as useful intermediates in organic synthesis and this was demonstrated by a few representative transformations: reduction to 2-(arylamino)anilines, acid-catalyzed cyclization to give substituted phenazines, and reaction with dimethyl malonate in the presence of potassium carbonate to give quinoxalin-2(1*H*)-one derivatives. Beneficial use of *N*-aryl-2-nitrosoanilines for the synthesis of these and other types of heterocyclic compounds, which are currently under investigation, prompted us to examine the title reaction from both a synthetic and a mechanistic point of view. During the preparation of this manuscript, an application of our method for the synthesis of some *N*-aryl-2-nitrosoanilines as *N*,*N*′-chelate ligands in rhenium complexes was reported.[9]

In this paper, we would like to present further examples of the reaction of arylamine anions with nitroarenes, exploring its scope and limitations. They were chosen with special regard to the orientation of the reaction (*ortho* and *para* positions in the nitroarene) and competition between the formation of nitrosoarenes and other possible processes that could be an effect of the nitroarene–aniline anion interactions under the applied conditions. The results, including those obtained earlier (entries 1–9), are collected in Table 1.

Initial examination of the selected base/solvent/quench systems was performed, which revealed important features of the reactions of preparative and mechanistic value. Formerly, searching for favorable conditions for the reaction, we found that the best yields of *N*-aryl-2-nitrosoanilines **3** were obtained when at least three equivalents of potassium *tert*-butoxide were used in the reaction, thus such an excess of the base was applied in the preparative experiments presented in the preliminary paper. This fact is, however, difficult to explain if **3** is formed, accord-

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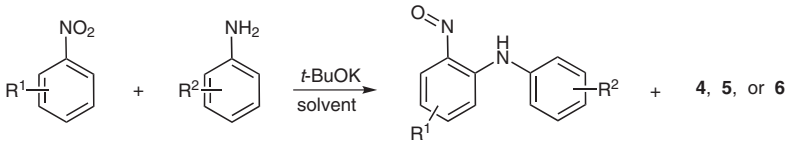
ing to our tentative supposition depicted in Scheme 1, via transformations of the protonated σ^H-adducts. An equimolar amount of the base seems to be sufficient for complete formation of the latter, and as a result also of the final product **3**. In order to clarify this discrepancy, additional experiments were performed.

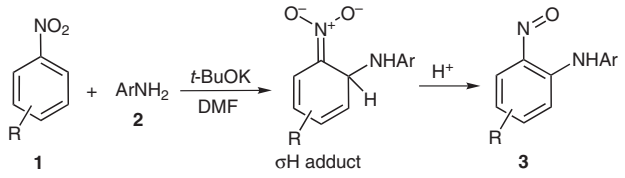
Table 1 Synthesis of *N*-Aryl-2-nitrosoanilines **3** in the Reaction of Nitroarenes **1** with Aniline Derivatives **2**[a]



1 2 3

Entry	R^1	R^2	Solvent	Procedure, time (min)[b]	Nitrosoaniline	Yield[c] (%)	Other products[d]
1[e]	4-Cl	4-Cl	DMF	A, 3	**3a**[f]	64	
2[e]	4-Cl	4-OEt	DMF	A, 3	**3b**	66	
3[e]	4-Cl	3,4-Cl_2	DMF	A, 3	**3c**	55	
4[e]	4-Cl	4-Me	DMF	A, 3	**3d**[f]	56	
5[e]	2,4-Cl_2	4-Cl	DMF	A, 3	**3e**	55	**4e** (19)
6[e]	4-OMe	4-Me	DMF	A, 5	**3f**[f]	72	
7[e]	4-Cl-2-CF_3	4-Cl	DMF	A, 3	**3g**	30	
8[e]	4-Cl-2-OMe	4-OEt	DMF	A, 5	**3h**[g]	60	
9[e]	4-OMe	4-Br	DMF	A, 3	**3i**	33	
10	4-Cl	2,6-Me_2	DMF–THF	B, 10	**3j**	84	
11	2,4-Cl_2	2,6-Me_2	DMF–THF	C	**3k**	60	
12	2,4-Cl_2	4-OEt	DMF–THF	A, 60	**3l**	47	**4l** (8)
13	H	4-Cl	DMF	B, 15	**3m**	36	**5m** (13)
14	H	4-Cl	THF	B, 60	**3m**	63	
15	2-Cl-4-OMe	4-OEt	DMF	A, 5	**3n**	34	**4n** (17)
16	4-OMe[h]	4-Cl	DMF–THF	C	**3o**	56	
17	4-F	2,6-Me_2	DMF	C	**3p**	14	**5p** (70)
18	4-F	2,6-Me_2	THF	C	**3p**	67	
19	4-F	4-Cl	DMF	B, 5	**3q**	33	**5m** (37)
20	4-F	4-Cl	THF	B, 15	**3q**	66	**5m** (4)
21	2-NH_2-5-NO_2	4-Cl	DMF	C	**3r/3s**[i]	41/12	
22	2-Cl	4-Cl	THF	B, 30	**3t**	43	**4t** (15)
23	4-Cl	H[j]	DMF–THF	A, 15	**3u**	0	**6** (32/60)[k]

[a] Numbering of R group positions corresponds to starting materials **1** and **2**.
[b] Reaction conditions. A: –60 °C, 5–60 min, quenched with AcOH at –60 °C; B: –60 °C, 10–60 min, then poured into acidified H_2O; C: –60 °C, 5 min, warmed to r.t. then poured into acidified H_2O.
[c] Isolated yield.
[d] The structures shown on Figure 1. Yields (%) in parentheses.
[e] Reported in the preliminary communication.[8]
[f] Compounds fully characterized in the preliminary communication.[8] See also ref.[9]
[g] This compound was earlier described erroneously as 2-chloro-4-methoxy isomer.[8]
[h] 1-Nitro-4-methoxynaphthalene.
[i] Two isomers, the structures shown on Figure 1.
[j] *N*-Methyl compound.
[k] Yields of the reactions with an equimolar amount or with a 2-fold excess of 1-chloro-4-nitrobenzene, respectively.



Scheme 1 Formation of nitrosoanilines **3**

In order to use convenient gas chromatography analysis of the reaction mixtures, 2,6-dimethylaniline was chosen for the model reaction with nitroarenes. *N*-Aryl-2-nitrosoanilines are quite stable compounds and they can be stored at room temperature for extended periods without detectable degradation. However, they were found to be unstable at higher temperatures and, thus, monitoring of their formation by gas chromatography was impossible. Fortunately, nitrosoanilines derived from 2,6-dimethylaniline showed much higher thermal stability, for which both steric hindrance in the vicinity of the nitroso group and/or the presence of substituents at *ortho* positions in the *N*-aryl moiety that prevent potential cyclization processes, could be responsible. Thus, 1-chloro-4-nitrobenzene was reacted with 2,6-dimethylaniline in *N*,*N*-dimethylformamide at –60 °C using various amounts of potassium *tert*-butoxide and the yield of 5-chloro-*N*-(2,6-dimethylphenyl)-2-nitrosoaniline (**3j**) formed was measured by gas chromatography using internal standards. All reactions were performed by adding the nitroarene to a solution of 2,6-dimethylaniline and potassium *tert*-butoxide, so an excess of the base/anilide was maintained during the addition of 1-chloro-4-nitrobenzene.

The reaction was first conducted on a preparative scale using three equivalents of potassium *tert*-butoxide (Table 1, entry 10), nitrosoaniline **3j** was isolated in 84% yield, characterized, and used to prepare the calibration mixtures.

It was found, that the yield of **3j** was strongly depended on the amount of the base used and after 10 minutes of the reaction the yields, which did not change noticeably when the reaction was continued, were 32%, 68%, and 92% at one, two, and three equivalents of potassium *tert*-butoxide, respectively.

Another important observation was made: **3j** was produced in the reaction not only when the reaction mixture was acidified with acetic acid at low temperatures, as practiced previously, but also when it was quenched by pouring into dilute hydrochloric acid, dilute acetic acid, aqueous ammonium chloride solution, or even into water, followed by neutralization. Importantly, the chromatographically determined yields of **3j** were virtually equal in each case.

Moreover, when the reaction mixture was allowed to warm up to room temperature for a period of one hour then quenched, **3j** was obtained in a yield only slightly lower than that obtained when the reaction was finished at –60 °C. It is not expected that the σ^H-adducts would be stable at room temperature.

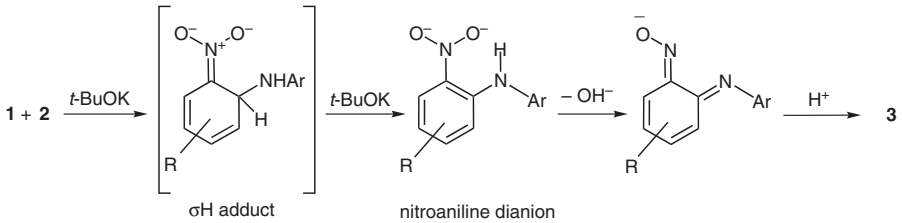
All the observations above indicate that the reaction is more complex and that Scheme 1 does not reflect the actual course of the reaction. They suggest that the final product is formed in the reaction mixture prior to the final quench, the latter being nothing more than protonation of the anionic form of the nitrosoaniline. Thus, the base is also involved in the reaction step leading to the nitrosoarene, possibly as depicted in Scheme 2.

A more detailed examination of the mechanistic aspects of the reaction is in progress and will be published elsewhere.

Most of the reactions under investigation were complete in 5–15 minutes after mixing of the reagents at –60 °C. For certain substrates, however, when the reaction mixture was allowed to warm up to room temperature, the yields were noticeably higher. Essentially, two solvents, *N*,*N*-dimethylformamide and tetrahydrofuran, were used for their different polarity. Usually, the reactions carried out in tetrahydrofuran required a longer time to go to completion. Occasionally a *N*,*N*-dimethylformamide–tetrahydrofuran (2:1) mixture was applied for its behavior at low temperatures, much better than that of *N*,*N*-dimethylformamide itself near its freezing point, while maintaining dipolar properties of the latter.

The results collected in Table 1 show, that the reaction has quite general character. Numerous anilines **2** enter the reaction, provided their acidity allows for effective deprotonation by potassium *tert*-butoxide and, on the other hand, nucleophilicity of their anions is sufficient for efficient addition to the nitroarene. The choice of anilines, however, seems to be limited to primary ones. *N*-Methylaniline reacted readily with 1-chloro-4-nitrobenzene, but the expected nitrosoaniline was not isolated. Instead, the ONSH product of *ortho* hydrogen with the aniline was formed (Table 1, entry 23).

The results seem to be in accord with the revised mechanistic scheme, indicating that in the absence of the hydro-



Scheme 2 Revised scheme of the formation of nitrosoanilines from the σ^H-adducts

gen atom at the *ortho* amino group, formation of the nitroso group becomes problematic, or much slower than the competitive oxidation of the intermediate dianion. The oxidation process occurs most probably by means of the starting nitroarene, as the yield of **6** can be significantly improved when an excess of **2** is used.

Nitrobenzene and its substituted derivatives enter the reaction with selectivity that is strongly dependent on the substituents as well as on the solvent used. Nitroarenes substituted in the *para* position formed 2-nitrosoanilines efficiently, and formation of ONSH products at the *ortho* position was not observed. However, when the nitroarene possesses halogen atoms, or other leaving group at another activated position of the aromatic ring (*ortho* or *para* to the nitro group), substitution of this group with anilide (S_NAr) can be a serious competing reaction. It is known, that addition of nucleophiles to the aromatic ring occurs, as a rule, much faster to the activated unsubstituted carbon atom than to that substituted with potential leaving groups, including even the most reactive halogens.[1] This statement was frequently confirmed in carbanion chemistry, but in cases of hetero nucleophiles, the rule seems to be less rigid. In the reactions of substituted nitroarenes with aniline anions, competitive S_NAr substitution of chlorine was observed only when it was located at the position *ortho* to the nitro group (entries 5, 12, 15, and 22). In the reaction of 4-chloroaniline with 2,4-dichloro-1-nitrobenzene in *N*,*N*-dimethylformamide or *N*,*N*-dimethylformamide–tetrahydrofuran mixture, the nitrosoaniline **3e** was the major product and only *ortho* halogen was replaced by the anilide to give **4e**. Changing the order of addition of the reagents, the solvent from *N*,*N*-dimethylformamide to tetrahydrofuran, and also the amount of the base, had little influence on the products ratio **3e/4e**, which varied from 3.2 to 4.6 depending on particular reaction conditions.

Reaction of more sterically demanding 2,6-dimethylaniline with 2,4-dichloro-1-nitrobenzene led to the nitrosoarene **3k** almost exclusively (entry 11). Substitution of fluorine is much easier, thus it is observed also when the halogen is located in the *para* position (entries 17–20). 1-Fluoro-4-nitrobenzene reacted with the anion of 4-chloroaniline yielding both nitrosoaniline **3q** and S_NAr product **5m** in ratio 0.9. Impressive increase of this ratio to 16 was achieved by changing the solvent used from *N*,*N*-dimethylformamide to tetrahydrofuran. The latter is known to promote nucleophilic addition of carbanions and other anionic nucleophiles selectively to the *ortho* position in nitroarenes.[3]

Analogous reaction of 1-fluoro-4-nitrobenzene with 2,6-dimethylaniline carried out in *N*,*N*-dimethylformamide or *N*,*N*-dimethylformamide–tetrahydrofuran gave mainly substitution of the *para*-fluorine substituent (**3p/5p** 0.2), which again proves the importance of steric hindrance in the formation of σ^H-adducts, in this case due to the two adjacent methyl groups in the 2,6-dimethylaniline. On the other hand, in the same reaction carried out in tetrahydrofuran the nitroso product **3p** was formed exclusively (Table 1, entry 18).

When both, *ortho* and *para* positions in the nitroarene are unsubstituted, σ^H-adducts at both these positions can be formed. In highly polar, aprotic solvents, addition of nucleophiles at the *ortho* position is usually faster than at the *para* position,[1,10] but when the equilibration of the σ^H-adducts take place, formation of the products of the reaction at *para* position could also be expected. Indeed, in the reaction of nitrobenzene with anion of 4-chloroaniline in *N*,*N*-dimethylformamide formation of σ^H-adducts at both positions occurred, but only the *ortho* isomer of nitrosoaniline **3m** was isolated. The σ^H-adducts formed at the *para* position underwent an oxidation reaction, leading to the corresponding 4-nitrodiarylamine **5m**. In tetrahydrofuran, the latter was not observed and **3m** was formed exclusively in good yield (entries 13 and 14). This seems to confirm the anticipated role of the hydrogen atom at the *ortho* amino group in the transformation of σ^H-adducts into nitrosoanilines (Scheme 2).

Reaction of 4-chloroaniline with 2,4-dinitroaniline (entry 21) required an additional equivalent of base, since the latter is a strong N–H acid, thus under basic conditions exists in an anionic form. Nevertheless, due to the two nitro groups present in the aromatic ring it retains significant electrophility. The structure of the ring exhibits cyclohexadienoid character, originated from strong conjugation of the negatively charged amine nitrogen with the nitro groups. Thus, the addition of nucleophiles occurs as a rule selectively at C3, i.e. at a position between the nitro groups.[11] The reaction with 4-chloroaniline also follows this rule, even so two isomeric nitroso compounds were obtained depending on the nitro groups reduced (entry 21). The structure of the main product **3r** shown in Figure 1 was confirmed by standard ^1H and ^{13}C NMR spectra, but those taken for the minor product **3s** were not diagnostic due to extremely broad signals of protons and carbon atoms of the nitrosoaromatic ring, thus, the structure of **3s** remains tentative.

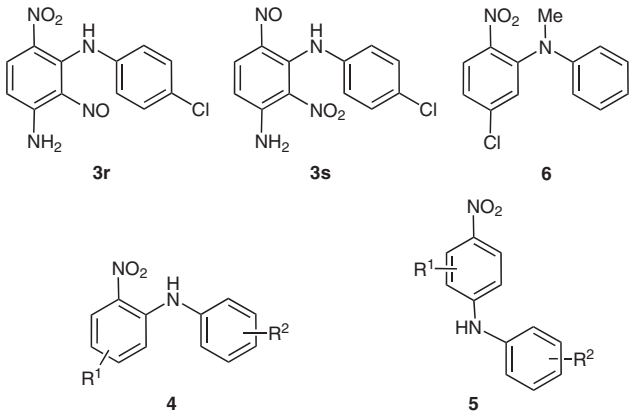


Figure 1

In summary, the nucleophilic substitution of *ortho* hydrogen in nitroarenes with anions of aniline derivatives carried out at low temperature in *N*,*N*-dimethylformamide or tetrahydrofuran leads to *N*-aryl-substituted *ortho*-nitrosoanilines in acceptable yields. This simple, one-step procedure, starting with easily available materials, seems to be, so far, the only convenient method of practical synthesis of such bifunctional compounds, which are potentially useful building blocks, suitable for synthesis of many types of nitrogen heterocyclic structures. Our investigation on this, so far unexplored, field are now in progress.

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker (500 MHz) (500 MHz for ^{1}H and 125 MHz for ^{13}C spectra), Varian-NMR-vnmrs600 (600 MHz for ^{1}H spectra) and a Varian Mercury 400 (400 MHz for ^{1}H and 100 MHz for ^{13}C spectra) instruments at 298 K or 233 K in the case of **3e**. Mass spectra (EI, 70 eV) were obtained on an AMD-604 spectrometer. Silica gel Merck 60 (230–400 mesh) was used for column chromatography. THF was distilled from Na/benzophenone ketyl prior to use. DMF was dried over CaH_2, distilled and stored over molecular sieves.

2-Chloro-4-(trifluoromethyl)-1-nitrobenzene,[12] 4-chloro-2-methoxy-1-nitrobenzene,[13] were obtained according to the literature. All other reagents are commercially available.

N-Aryl-2-nitrosoanilines 3; General Procedures

Procedure A: To a cooled soln of *t*-BuOK (6 mmol, 672 mg) in the specified solvent (12 mL) was added dropwise at –60 °C a soln of aniline **1** (2 mmol), then nitroarene **2** (2 mmol) in the appropriate solvent (2 mL each). The mixture was stirred at this temperature for 5–60 min (Table 1), and a cooled mixture of AcOH (1.5 mL) and DMF (1.5 mL) was added in 1 portion. The cooling bath was removed and the mixture was allowed to reach r.t., then it was poured into H_2O (ca. 50 mL) and extracted with EtOAc. The extract was washed with H_2O and brine and dried (Na_2SO_4). After evaporation, the crude product mixture was subjected to column chromatography (silica gel, hexane–EtOAc, hexane–CH_2Cl_2, or hexane–benzene).

Procedure B: The reaction was carried out and worked up according to the procedure A, except that after stirring of the reaction mixture at –60 °C for the time specified (Table 1), the mixture was poured into dilute aq HCl (ca. 50 mL) and extracted with EtOAc.

Procedure C: The reaction was carried out and worked up according to the procedure A, except that after 5 min of stirring of the reaction mixture at –60 °C the cooling bath was removed and the mixture was allowed to reach r.t., then it was poured into dilute aq HCl (ca. 50 mL) and extracted with EtOAc.

Products **3a**, **3d**, and **3f** were fully characterized in the preliminary communication,[8] and also in ref.[9]

5-Chloro-*N*-(4-ethoxyphenyl)-2-nitrosoaniline (3b)

Brown solid; mp 106–107 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, *J* = 7.1 Hz, 3 H), 4.06 (q, *J* = 7.1, 2 H), 6.88–6.98 (m, 4 H), 7.11–7.18 (m, 2 H), 8.66 (br s, 1 H), 12.10 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7, 63.7, 114.4, 115.5, 118.3, 126.7, 128.4, 134.3 (br), 141.9 (br), 144.5, 154.9, 157.9.

MS (EI): *m*/*z* (%) = 276 (18), 261 (33), 259 (100), 233 (34), 231 (84), 216 (29), 154 (29).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{14}H_{13}{}^{35}ClN_2O_2$: 276.0666; found: 276.0658.

5-Chloro-*N*-(3,4-dichlorophenyl)-2-nitrosoaniline (3c)

Red solid; mp 155 °C subl. (hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (m, 2 H), 7.14 (d, *J* = 8.4, 2.5 Hz, 1 H), 7.38 (d, *J* = 2.5 Hz, 1 H), 7.51 (d, *J* = 8.4 Hz, 1 H), 8.66 (br s, 1 H), 11.60 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$):[14] δ = 114.0, 119.6, 124.0, 126.5, 130.5, 131.5, 133.8, 136.2, 145.0, 154.9.

MS (EI): *m*/*z* (%) = 302 (10), 301 (11), 300 (11), 299 (10), 285 (97), 283 (100), 271 (24), 269 (25), 237 (23), 235 (36), 200 (31).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_7{}^{35}Cl_3N_2O$: 299.9624; found: 299.9630.

3,5-Dichloro-*N*-(4-chlorophenyl)-2-nitrosoaniline (3e)

Brown crystals; mp 183 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.90 (d, *J* = 2.0 Hz, 1 H), 7. 09 (d, *J* = 2.0 Hz, 1 H), 7.14–7.19 (m, 2 H), 7.40–7.45 (m, 2 H), 12.68 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.8, 119.7, 126.7, 130.2, 133.1, 133.8, 134.2, 144.9, 146.9, 150.9.

MS (EI): *m*/*z* (%) = 302 (21), 301 (8), 300 (22), 285 (96), 283 (100), 271 (38), 269 (39), 237 (31), 235 (48).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_7{}^{35}Cl_3N_2O$: 299.9624; found: 299.9612.

3-Chloro-*N*-(4-chlorophenyl)-2-nitroso-5-(trifluoromethyl)aniline (3g)

Red solid; mp 110–112 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15–7.19 (m, 2 H), 7.19–7.21 (m, 1 H), 7.28 (d, *J* = 1.9 Hz, 1 H), 7.44–7.47 (m, 2 H), 12.51 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.1 (q, J_{C-F} = 4.3 Hz), 115.1 (q, J_{C-F} = 4.3 Hz), 122.4 (q, J_{C-F} = 272.6 Hz), 126.6, 130.3, 132.0, 133.4, 134.0, 138.6 (q, J_{C-F} = 32.8 Hz), 147.1, 151.5.

MS (EI): *m*/*z* (%) = 336 (9), 334 (14), 319 (64), 317 (100), 303 (34), 269 (37).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_7{}^{35}Cl_2F_3N_2O$: 333.9887; found: 333.9874.

5-Chloro-*N*-(4-ethoxyphenyl)-3-methoxy-2-nitrosoaniline (3h)

Brown solid; mp 156–157 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (t, *J* = 7.0 Hz, 3 H), 4.05 (t, *J* = 7.0 Hz, 2 H), 4.12 (s, 3 H), 6.26 (d, *J* = 1.8 Hz, 1 H), 6.48 (d, *J* = 1.8 Hz, 1 H), 6.90–6.94 (m, 2 H), 7.09–7.14 (m, 2 H), 13.24 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7, 56.8, 63.7, 99.4, 106.2, 115.4, 126.8, 128.3, 135.8, 146.8, 148.2, 157.9, 163.7.

MS (EI): *m*/*z* (%) = 308 (25), 306 (72), 289 (100), 261 (75), 246 (42), 232 (14).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{15}H_{15}{}^{35}ClN_2O_3$: 306.0771; found: 306.0781.

N-(4-Bromophenyl)-5-methoxy-2-nitrosoaniline (3i)

Dark green solid; mp 138 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H), 6.36 (br s, 1 H), 6.62 (br d, *J* = 8.2 Hz, 1 H), 7.1–7.2 (m, 2 H), 7.5–7.6 (m, 2 H), 8.59 (br d, *J* = 8.2 Hz, 1 H), 12.76 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.9, 93.8, 109.4, 119.6, 126.4, 132.8, 136.2, 136.5, 143.1, 153.8, 167.2.

MS (EI): *m*/*z* (%) = 308 (27), 306 (28), 291 (97), 289 (100), 227 (17), 182 (30), 154 (40).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{11}{}^{79}BrN_2O_2$: 306.0004; found: 305.9989.

5-Chloro-*N*-(2,6-dimethylphenyl)-2-nitrosoaniline (3j)
Yellow-green solid; mp 55–58 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.10 (s, 6 H), 6.30 (d, *J* = 1.7 Hz, 1 H), 6.93 (d, *J* = 7.5 Hz, 1 H), 7.14–7.18 (m, 2 H), 7.19–7.23 (m, 1 H), 8.78 (br s, 1 H), 11.75 (br s, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 18.0, 114.1, 118.3, 128.2, 128.8, 133.2, 134.6 (br), 135.9, 142.3 (br), 144.9, 155.0.

MS (EI, 70 eV): *m*/*z* (%) = 260 (2) [M$^+$], 245 (100), 228 (7).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{13}{}^{35}ClN_2O$: 260.0716; found: 260.0722.

3,5-Dichloro-*N*-(2,6-dimethylphenyl)-2-nitrosoaniline (3k)
Dark solid; mp 92–95 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08 (s, 6 H), 6.24 (d, *J* = 2.0 Hz, 1 H), 7.02 (d, *J* = 2.0 Hz, 1 H), 7.15–7.18 (m, 2 H), 7.20–7.25 (m, 1 H), 12.46 (br s, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.0, 113.9, 118.9, 128.5, 128.9, 132.7, 135.6, 135.7, 144.9, 146.5, 151.0.

MS (EI, 70 eV): *m*/*z* (%) = 294 (8) [M$^+$], 279 (100), 248 (7), 228 (10), 214 (6).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}{}^{35}Cl_2N_2O$: 294.0327; found: 294.0335.

3,5-Dichloro-*N*-(4-ethoxyphenyl)-2-nitrosoaniline (3l)
Brown solid; mp 79–81 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, *J* = 7.0 Hz, 3 H), 4.05 (q, *J* = 7.0 Hz, 2 H), 6.86 (d, *J* = 2.0 Hz, 1 H), 6.92–6.97 (m, 2 H), 6.99 (d, *J* = 2.0 Hz, 1 H), 7.08–7.13 (m, 2 H), 12.87 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7, 63.8, 114.3, 115.6, 118.8, 126.9, 127.6, 135.5, 144.4, 146.2, 150.7, 158.2.

MS (EI, 70 eV): *m*/*z* (%) = 310 (35) [M$^+$], 293 (99), 265 (100), 251 (39), 217 (39), 188 (30).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}{}^{35}Cl_2N_2O_2$: 310.0276; found: 310.0287.

***N*-(4-Chlorophenyl)-2-nitrosoaniline (3m)**
Brown solid; mp 102–105 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.04 (app. t, *J* = 7.5 Hz, 1 H), 7.12 (app. d, *J* = 8.4 Hz, 1 H), 7.20–7.23 (m, 2 H), 7.36–7.40 (m, 3 H), 8.71 (br s, 1 H), 11.83 (br s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$):[14] δ = 114.8, 118.2, 125.9, 129.8, 131.6, 135.8, 138.0, 156.7.

^{13}C NMR (125 MHz, 233 K, $CDCl_3$): δ = 114.5, 118.3, 125.8, 129.6, 131.3, 131.6, 134.7, 138.5, 140.7, 156.0.

MS (EI, 70 eV): *m*/*z* (%) = 232 (10) [M$^+$, 215 (100), 201 (35), 179 (6), 167 (41), 139 (10).

HRMS (EI): *m*/*z* calcd for $C_{12}H_9{}^{35}Cl\ N_2O$: 232.0403; found: 232.0397.

3-Chloro-*N*-(4-ethoxyphenyl)-5-methoxy-2-nitrosoaniline (3n)
Yellow-green solid; mp 130–137 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, *J* = 7.0 Hz, 3 H), 3.74 (s, 3 H), 4.05 (q, *J* = 7.0 Hz, 2 H), 6.13 (d, *J* = 2.5 Hz, 1 H), 6.39 (d, *J* = 2.5 Hz, 1 H), 6.91–6.95 (m, 2 H), 7.11–7.16 (m, 2 H), 13.57 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7, 56.0, 63.7, 92.8, 110.4, 115.4, 126.8, 128.5, 140.0, 146.0, 149.5, 157.9, 166.7.

MS (EI, 70 eV): *m*/*z* (%) = 306 (62) [M$^+$], 289 (74), 261 (100), 246 (31), 218 (18).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{15}{}^{35}ClN_2O_3$: 306.0771; found: 306.0761.

***N*-(4-Chlorophenyl)-4-methoxy-1-nitrosonaphthalen-2-amine (3o)**
Dark-green solid; mp 166–169 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (s, 3 H), 6.13 (s, 1 H), 7.15–7.22 (m, 2 H), 7.40–7.45 (m, 2 H), 7.45–7.50 (m, 1 H), 7.59–7.65 (m, 1 H), 7.98 (dd, *J* = 8.1, 0.7 Hz, 1 H), 8.80 (dd, *J* = 8.1, 0.7 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.2, 90.4, 121.6, 122.9, 123.0, 125.5, 127.0, 129.8, 130.8, 132.1, 133.8, 137.9, 144.4, 147.0, 165.2.

MS (EI, 70 eV): *m*/*z* (%) = 312 (100) [M$^+$], 295 (44), 281 (17), 266 (22).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{13}{}^{35}ClN_2O_2$: 312.0666; found: 312.0655.

***N*-(2,6-Dimethylphenyl)-5-fluoro-2-nitrosoaniline (3p)**
Dark-green solid; mp 75–77 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 6 H), 5.91 (dd, $J_{C\text{-}C}$ = 2.2 Hz, $J_{C\text{-}F}$ = 11.5 Hz, 1 H), 6.70 (br s, 1 H), 7.12–7.23 (m, 3 H), 8.87 (br s, 1 H), 11.93 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.0, 99.3 (d, $J_{C\text{-}F}$ = 25.8 Hz), 107.1 (d, $J_{C\text{-}F}$ = 24.0 Hz), 128.14, 128.8, 133.3, 135.8, 137.2 (br), 144.6 (br), 154.8, 168.2 ($J_{C\text{-}F}$ = 264.7 Hz).

MS (EI, 70 eV): *m*/*z* (%) = 244 (2) [M$^+$], 229 (100), 212 (4), 198 (9).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{13}FN_2O$: 244.1012; found: 244.1020.

***N*-(4-Chlorophenyl)-5-fluoro-2-nitrosoaniline (3q)**
Green crystals; mp 125–128 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68 (dd, $J_{C\text{-}C}$ = 2.2 Hz, $J_{H\text{-}F}$ = 11.5 Hz, 1 H), 6.72–6.80 (m, 1 H), 7.18–7.22 (m, 2 H), 7.38–7.43 (m, 2 H), 8.70 (br s, 1 H), 12.06 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$):[12] δ = 99.6 (d, $J_{C\text{-}F}$ = 25 Hz), 107.8 (d, $J_{C\text{-}F}$ = 25 Hz), 126.1, 130.0, 132.3, 135.1, 144.5 (br), 154.8, 168.1 ($J_{C\text{-}F}$ = 263 Hz).

MS (EI, 70 eV): *m*/*z* (%) = 250 (5) [M$^+$], 233 (100), 219 (41), 198 (8), 184 (38).

HRMS (EI): *m*/*z* calcd for $C_{12}H_8{}^{35}ClFN_2O$: 250.0309; found: 250.0300.

3-Amino-*N*-(4-chlorophenyl)-6-nitro-2-nitrosoaniline (3r)
Dark brown solid; mp 210–211 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.39 (d, *J* = 9.7 Hz, 1 H), 7.13–7.18 (m, 2 H), 7.27–7.31 (m, 2 H), 8.05 (d, *J* = 9.7 Hz, 1 H), 8.66 (br s, 1 H), 10.41 (br s, 1 H), 11.01 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$):[14] δ = 109.4, 119.8, 122.3, 124.3, 127.5, 128.7, 135.4, 141.8, 148.0.

MS (EI, 70 eV): *m*/*z* (%) = 292 (5) [M$^+$], 291 (6), 275 (100), 258 (87), 240 (19), 228 (17), 215 (12).

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{12}H_8ClN_4O_3$: 291.0279; found: 291.0271.

3-Amino-*N*-(4-chlorophenyl)-2-nitro-6-nitrosoaniline (3s)
Brown solid; mp 230–245 °C.

^{1}H NMR (400 MHz, DMSO-d_6):[14] δ = 6.54 (br s, 1 H), 7.13–7.21 (m, 2 H), 7.32–7.40 (m, 2 H), 8.32 (br s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$):[14] δ = 110.4, 122.3, 129.0, 152.6.

MS (EI, 70 eV): *m*/*z* (%) = 292 (34) [M$^+$], 291 (34), 275 (100), 259 (24), 258 (23), 257 (70), 244 (19), 227 (33).

HRMS (EI): *m*/*z* calcd for $C_{12}H_9ClN_4O_3$: 292.0363; found: 292.0356.

3-Chloro-*N*-(4-chlorophenyl)-2-nitrosoaniline (3w)
Red solid; mp 134–136 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.96 (d, *J* = 8.8 Hz, 1 H), 7.08 (d, *J* = 7.4 Hz, 1 H), 7.18 (d, *J* = 8.5 Hz, 2 H), 7.25–7.30 (m, 1 H), 7.39 (d, *J* = 8.5 Hz, 2 H), 12.72 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 114.7, 119.0, 126.5, 129.9, 132.5, 133.1, 134.9, 138.6, 145.3, 152.5.

MS (EI, 70 eV): *m*/*z* (%) = 266 (19) [M$^+$], 249 (100), 235 (36), 201 (37).

HRMS (EI): *m*/*z* calcd for $C_{12}H_8{}^{35}Cl_2N_2O$: 266.0014; found: 266.0020.

5-Chloro-*N*-(4-chlorophenyl)-2-nitroaniline (4e)
Yellow solid; mp 158–159 °C (Lit.[15] 158–158.5).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.96 (dd, *J* = 9.2, 2.2 Hz, 1 H), 7.09 (d, *J* = 2.2 Hz, 1 H), 7.20–7.24 (m, 2 H), 7.40–7.45 (m, 2 H), 8.17 (d, *J* = 9.2 Hz, 1 H), 9.47 (br s, 1 H).

MS (EI, 70 eV): *m*/*z* (%) = 282 (100) [M$^+$], 248 (25), 235 (20), 201 (34).

HRMS (EI): *m*/*z* calcd for $C_{12}H_8{}^{35}Cl_2N_2O_2$: 291.9963; found: 281.9972.

5-Chloro-*N*-(4-ethoxyphenyl)-2-nitroaniline (4l)
Yellow solid; mp 128–131 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (t, *J* = 7.0 Hz, 3 H), 4.07 (q, *J* = 7.0 Hz, 2 H), 6.66 (dd, *J* = 9.2, 2.2 Hz, 1 H), 6.93–6.99 (m, 3 H), 7.15–7.20 (m, 2 H), 8.14 (d, *J* = 9.2 Hz, 1 H), 9.44 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 63.8, 115.0, 115.7, 117.2, 127.3, 128.0, 130.1, 130.9, 142.5, 145.2, 157.8.

MS (EI, 70 eV): *m*/*z* (%) = 292 (100) [M$^+$], 263 (58), 230 (14), 217 (18), 182 (12).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{13}{}^{35}Cl\ N_2O_3$: 292.0614; found: 292.0603.

***N*-(4-Ethoxyphenyl)-5-methoxy-2-nitroaniline (4n)**
Yellow solid; mp 135–137 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.44 (t, *J* = 7.0 Hz, 3 H), 3.70 (s, 3 H), 4.07 (t, *J* = 7.0 Hz, 2 H), 6.28 (dd, *J* = 9.5, 2.6 Hz, 1 H), 6.33 (d, *J* = 2.6 Hz, 1 H), 6.92–6.96 (m, 2 H), 7.18–7.21 (m, 2 H), 8.16 (d, *J* = 9.5 Hz, 1 H), 9.64 (br s, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.8, 55.6, 63.7, 96.9, 106.1, 115.5, 126.9, 127.2, 128.9, 130.8, 147.0, 157.4, 165.6.

MS (EI, 70 eV): *m*/*z* (%) = 288 (100) [M$^+$], 259 (63), 226 (11).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{16}N_2O_4$: 288.1110; found: 288.1118.

***N*-(4-Chlorophenyl)-2-nitroaniline (4u)**
Orange crystals; mp 143–144 °C (EtOH) (Lit.[16] 142–144 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (ddd, *J* = 8.6, 7.0, 1.2 Hz, 1 H), 7.17 (dd, *J* = 8.6, 1.2 Hz, 1 H), 7.21–7.24 (m, 2 H), 7.36–7.41 (m, 3 H), 8.21 (dd, *J* = 8.6, 1.5 Hz, 1 H), 9.40 (br s, 1 H).

MS (EI, 70 eV): *m*/*z* (%) = 248 (100), M$^+$, 214 (27), 201 (30), 167 (26).

HRMS (EI): *m*/*z* calcd for $C_{12}H_9{}^{35}ClN_2O_2$: 248.0353; found: 248.0347.

4-Chloro-*N*-(4-nitrophenyl)aniline (5m)
Pale brown crystals; mp 182–183 °C (Lit.[17] 180–181 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.91–6.94 (m, 2 H), 7.13–7.17 (m, 2 H), 7.33–7.37 (m, 2 H), 8.11–8.15 (m, 2 H).

MS (EI, 70 eV): *m*/*z* (%) = 248 (100) [M$^+$], 218 (22), 167 (72).

5-Chloro-2-nitro-*N*-methyl-*N*-phenylaniline (6)
Oil (Lit.[18] 50–53 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.31 (s, 3 H), 6.80–6.84 (m, 2 H), 7.13 (dd, *J* = 9.1, 2.2 Hz, 1 H), 7.20–7.25 (m, 3 H), 7.32 (d, *J* = 2.2 Hz, 1 H), 7.76 (d, *J* = 8.8 Hz, 1 H).

MS (EI, 70 eV): *m*/*z* (%) = 262 (73) [M$^+$], 245 (39), 215 (100), 180 (30).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{11}{}^{35}ClN_2O_2$: 262.0509; found: 262.0502.

References

(1) (a) Terrier, F. *Nucleophilic Aromatic Displacement, The Influence of the Nitro Group*; Verlag Chemie: Weinheim, **1991**. (b) Chupakhin, O. N.; Charushin, V. N.; van der Plas, H. C. *Nucleophilic Aromatic Substitution of Hydrogen*; Academic Press: San Diego, **1994**. (c) Mąkosza, M. *Russ. Chem. Bull.* **1996**, *45*, 491.

(2) (a) Mąkosza, M.; Staliński, K. *Pol. J. Chem.* **1999**, *73*, 151. (b) Mąkosza, M.; Staliński, K. *Tetrahedron* **1998**, *54*, 8797. (c) Mąkosza, M.; Staliński, K. *Chem. Eur. J.* **2001**, *7*, 2025. (d) Adam, W.; Mąkosza, M.; Zhao, C. G.; Surowiec, M. *J. Org. Chem.* **2000**, *65*, 1099.

(3) (a) Mąkosza, M.; Winiarski, J. *Acc. Chem. Res.* **1987**, *20*, 282. (b) Mąkosza, M.; Wojciechowski, K. *Liebigs Ann./ Recl.* **1997**, 1805. (c) Mąkosza, M.; Kwast, A. *J. Phys. Org. Chem.* **1998**, *11*, 341.

(4) (a) Wróbel, Z. *Tetrahedron Lett.* **1997**, *38*, 4913. (b) Wróbel, Z. *Tetrahedron* **1998**, *54*, 2607. (c) Wróbel, Z. *Eur. J. Org. Chem.* **2000**, 521. (d) Wróbel, Z. *Pol. J. Chem.* **1998**, *72*, 2384. (e) Wróbel, Z. *Synlett* **2004**, 1929.

(5) (a) Wohl, A.; Aue, W. *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 2442. (b) Wohl, A. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 4135. (c) Serebryanyi, S. B. *Uk. Khim. Zh. (Russ. Ed.)* **1955**, *21*, 350.

(6) (a) Stern, M. K.; Hileman, F. D.; Bashkin, J. K. *J. Am. Chem. Soc.* **1992**, *114*, 9237. (b) Beska, E.; Toman, P.; Fiedler, K.; Hronec, M.; Pinter, J. US 6388136, **2002**.

(7) (a) Fasani, E.; Pietra, S.; Albini, A. *Heterocycles* **1992**, *33*, 573. (b) Fasani, E.; Mella, M.; Albini, A. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2689. (c) Fischer, O.; Hepp, E. *Justus Liebigs Ann. Chem.* **1889**, *255*, 145. (d) Titova, S. P.; Arinich, A. K.; Gorelik, M. V. *J. Org. Chem. USSR (Eng. Transl.)* **1986**, 1407. (e) Okubo, M.; Inatomi, Y.; Taniguchi, N.; Imamura, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3581. (f) Jin, D.; Mandenhall, D. *Tetrahedron Lett.* **1996**, *37*, 4881.

(8) Wróbel, Z.; Kwast, A. *Synlett* **2007**, 1525.

(9) Wirth, S.; Wallek, A. U.; Zernickel, A.; Feil, F.; Sztiller-Sikorska, M.; Lesiak-Mieczkowska, K.; Bräuchle, C. h.; Lorenz, I.-P.; Czyż, M. *J. Inorg. Biochem.* **2010**, *104*, 774.

(10) Mąkosza, M.; Lobanova, O.; Kwast, A. *Tetrahedron* **2004**, *60*, 2577.

(11) Mąkosza, M.; Voskresensky, S.; Białecki, M.; Kwast, A. *Pol. J. Chem.* **1999**, *73*, 1969.

(12) Tsui, K.; Nakamura, K.; Konishi, N.; Okumura, H.; Matsuo, M. *Chem. Pharm. Bull.* **1992**, *40*, 2399.
(13) Barluenga, J.; Fananas, F. J.; Sanz, R.; Fernandez, Y. *Chem. Eur. J.* **1965**, 397.
(14) Some signals very broad or invisible.
(15) Kottenhahn, A. P.; Seo, E. T.; Stone, H. W. *J. Org. Chem.* **1963**, *28*, 3114.
(16) Cross, B.; Williams, J. P.; Woodall, R. E. *J. Chem. Soc. C* **1971**, 2085.
(17) Johnson, H. W. Jr.; Iwata, Y. *J. Org. Chem.* **1971**, *36*, 1921.
(18) Hunziker, F.; Kunzle, F.; Schmutz, J. *Helv. Chim. Acta* **1966**, *49*, 244.