



Denitrification Combined with Diazotization of Anilines and the Synthesis of 4'-Chlorobiphenyl-2,5-diamine and 1-Chloro-4-iodobenzene

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S Supporting Information

ABSTRACT: The diazotization of anilines in aqueous solution has been found to be highly useful as a key reaction step to achieve the denitrification of low-concentrated nitrogen dioxide in air. The diazonium salt from the wet scrubber—although obtained in highly diluted aqueous solution—was shown to be directly applicable in a radical Gomberg-Bachmann aryl–aryl coupling and a Sandmeyer iodination reaction.

INTRODUCTION

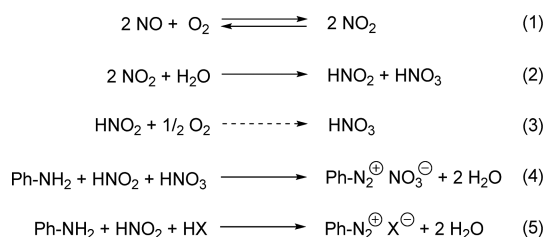
The denitrification of industrially produced waste gas¹ is today mainly achieved by selective catalytic (SCR)² or selective noncatalytic reduction (SNCR).³ The two major components, which are nitrogen monoxide and nitrogen dioxide, are thereby commonly reduced to dinitrogen through the use of ammonia as reductant. As ammonia needs to be added continuously to the gas stream as a function of the NO_x concentration, first to ensure complete conversion as well as to avoid major NH₃ slippage, such processes have difficulties in responding to rapidly changing NO_x concentrations.⁴ Denitrification systems relying on the absorption of NO_x into aqueous solutions, on the other hand, have to deal with the low solubility of nitrogen monoxide in water, which is commonly counterbalanced by the addition of a suitable oxidant such as hydrogen peroxide.⁵ In this way, NO is rapidly removed from the gas–solution equilibrium through oxidation to NO₂, and the absorption capabilities of the system are improved. Although efficient denitrification can be achieved for most industrial processes by the established standard techniques described above, these methods do not yet exploit the synthetic value of the nitrogen oxides, as only nitrogen or cheap bulk chemicals such as nitric acid or nitrate salts are obtained.⁶

Within our research directed toward the combination of denitrification with the synthesis of valuable fine chemicals, we first described a reaction sequence employing nitrogen monoxide for the synthesis of diversely ring-substituted aromatic amino acids.^{7,8} As this method later turned out to be limited to gas streams containing comparably high NO concentrations of at least 5 vol %, ^{8,9} we focused on improved recycling techniques being able to reliably convert lower concentrated and thus far more prevalent nitrogen dioxide at concentrations lower than 1 vol %.¹ In a first example, this could recently be achieved through the oxidative nitration of

styrenes in ethyl acetate.¹⁰ At the same time, our attention was drawn to aryldiazonium salts, mainly for two reasons. First, aromatic diazonium salts¹¹ are known to be highly versatile synthetic intermediates as they are associated with a number of prominent radical reactions¹² such as the Sandmeyer reaction,¹³ the Meerwein arylation,¹⁴ or the Gomberg-Bachmann reaction,¹⁵ as well as with important ionic transformations like Balz-Schiemann¹⁶ and Japp-Klingemann reactions,¹⁷ azo couplings,¹⁸ or syntheses proceeding via triazenes.¹⁹ More recently, this already broad variety has been expanded by palladium-catalyzed²⁰ as well as photocatalyzed reactions,²¹ and the number of industrial applications of diazonium salts has been increasing as well.²² The second reason for our interest was that diazonium salts can often be prepared in high yield through diazotization reactions using nitrite salts in the presence of acid.^{23,24} Due to the high reaction rates and the high degree of conversion, diazotizations are also applied as key steps in a number of analytical methods.²⁵

Assuming that the equilibrium between nitrogen monoxide and nitrogen dioxide in an oxygen-containing gas stream is largely shifted to the dioxide, as it is for example the case at lower temperatures,²⁶ the absorption of NO₂ in water would be quickly followed by disproportionation and the formation of equal amounts of nitrous and nitric acid (Scheme 1, 1 and 2).²⁷

Scheme 1. Reaction Steps Involved in the Diazotization of Aniline with Nitrogen Oxides in Air



As the resulting conditions in the aqueous solution are exactly those required for the diazotization of anilines, and this diazotization is moreover likely to proceed rapidly, the undesired oxidation of nitrous acid to nitric acid through oxygen from the gas stream can probably be overcome (Scheme 1, 3).²⁸ The overall sequence then leads to either

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diazonium nitrates or mixtures of diazonium salts, depending on the presence of an additional acid HX (Scheme 1, 4 and 5).

At this point, it is important to note that the diazotization of anilines with NO₂ has already been achieved in high and often even quantitative yield under carefully chosen conditions.²⁹ In extremely efficient gas–solid diazotizations of this type, the water produced in the reaction course remains as a part of the diazonium crystallites.³ Alternatively, diazonium salts can be obtained from acetanilides through reactions in condensed NO₂/N₂O₄ at temperatures around 5 °C.³¹ As these reactions have all been conducted in the absence of air, so that the concentration of the gaseous or liquid NO₂ in the reaction vessels did by far exceed the concentrations commonly present in waste gases, such direct diazotizations with NO₂ are yet difficult to apply as part of a recycling strategy.

In this article, we describe the diazotization of anilines in aqueous solution with low-concentrated nitrogen dioxide in air as well as the use of the resulting highly diluted diazonium salt solutions in Gomberg-Bachmann and Sandmeyer reactions.

RESULTS AND DISCUSSION

Optimization of Reaction Conditions on a Small Scale.

The first series of experiments was carried out to get insights into the feasibility of the overall sequence starting with the conversion of nitrogen monoxide, which is the main product in most combustion processes, to nitrogen dioxide at room temperature in air.²⁶ After absorption of NO₂ into an acidic aqueous solution of 4-chloroaniline, disproportionation would give nitric as well as nitrous acid, from which the latter can be expected to lead to diazotization. The results obtained from these initial experiments are summarized in Table 1.

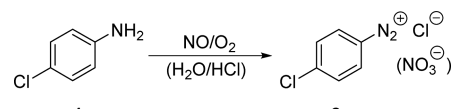
By gradually lowering the amount of nitrogen monoxide introduced into the reaction vessel from 4.0 to 0.1 equiv per aniline **1a**, three trends became apparent. First, full conversion of the aniline **1a** to the diazonium salt **2a** could already be

achieved with the theoretically required amount of 2.0 equiv NO (entries 4–6), and second, an excess NO did not lead to any degradation of the diazonium ions (entries 1–3). Third, byproducts were also not observed in reactions with lower concentrated NO (entries 7–11). Although these reactions with substoichiometric amounts of NO could only lead to an incomplete conversion of the aniline, the percentage of NO incorporated into the diazonium ion always reached or was close to the theoretical value of 50%. Particular reactions in this series showed that the volume of the reaction mixture can be reduced (entry 5), that the reaction time can be shortened to 10 min (entries 6 and 9), and that a stepwise addition of small amounts of NO is possible, too (entry 11). After having obtained these initial results, the diazotization appeared to be highly favorable for implementing the desired recycling strategy for nitrogen monoxide, as the reaction had turned out to be robust at low as well as at high concentrations of NO and NO₂. The formation of the diazonium salts can thus be expected to proceed as a clean reaction independent of the NO/NO₂ concentration in the gas phase. Little or no negative influence on the diazotization can also be anticipated from the two major components usually observed in industrial waste gases besides NO and NO₂,^{1b} which are hydrochloric acid and sulfur dioxide. Hydrochloric acid is present in the reaction mixture anyway, and for SO₂, an additional experiment showed that the quantitative yield of **2a** was not reduced when the reaction reported in entry 6 (Table 1) was conducted in the presence of 5% SO₂ relative to the combined amount of NO and NO₂.

Since it is known that diazotization reactions can strongly depend on the substitution pattern of the aniline's aromatic core,³² a number of substituted anilines were evaluated under the previously developed reaction conditions (Table 2).

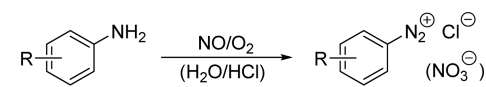
Among the halogenated anilines **1a–1f** (entries 1–6), only 4-iodoaniline (**1f**) (entry 6) gave a remarkably lower yield, which can to some extent be attributed to the nucleophilic substitution of the iodine atom for chlorine, thus leading to 4-chlorophenyldiazonium chloride (**2a**) as a side product.³³ The

Table 1. Investigation of Reaction Conditions on a Small Scale^a

				
entry	NO (equiv)	reaction time (min)	diazotization (%) ^{b,c} [max. %]	percentage of NO inc. in 2a
1	4.0	120	100 [100]	
2	3.0	120	100 [100]	
3	2.3	120	100 [100]	
4	2.0	120	100 [100]	50
5	2.0	120 ^d	100 [100]	50
6	2.0	10	100 [100]	50
7	1.0	120	46 [50]	46
8	1.0	30	50 [50]	50
9	1.0	10	45 [50]	45
10	0.1	120	4.9 [5.0]	49
11	3 × 0.1	3 × 120	15 [15]	50

^aStandard conditions: 4-Chloroaniline (**1a**) (1 mmol), NO (see table), H₂O (12 mL), 1 N HCl (4 mL), rt, 250 mL round-bottom flask. ^bYields determined by ¹H NMR using maleic acid as an internal standard (after the concentration of the reaction mixture in vacuo). ^cDiazonium salt partially detected as triazene in reactions with incomplete diazotization. ^dReaction in H₂O (6 mL) and 1 N HCl (2 mL).

Table 2. Substrate Scope^a

			
entry	aniline 1 : R	yield ^b 2 (%)	side product
1	1a : 4-Cl	2a (quant.)	
2	1b : 3-Cl	2b (quant.)	
3	1c : 2-Cl	2c (quant.)	
4	1d : 4-F	2d (quant.)	
5	1e : 4-Br	2e (88)	2a (12)
6	1f : 4-I	2f (71)	2a (4)
7	1g : 4-Me	2g (95)	
8	1h : 4-OH	2h (quant.)	
9	1i : 4-CN	2i (91) ^d	
10	1j : 4-NO ₂	2j (quant.) ^c	
11	1k : H	2k (19) ^d	diverse

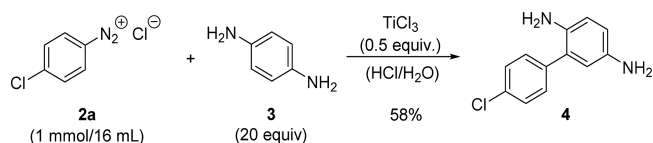
^aReaction conditions: Aniline (1 mmol), NO (2 mmol), H₂O (12 mL), 1 N HCl (4 mL), rt, 1/2 h, 250 mL round-bottom flask. ^bYields determined by ¹H NMR using maleic acid as internal standard (after concentration of the reaction mixture in vacuo). ^cExperiment conducted in 2 N HCl (20 mL). ^dIncomplete conversion, remaining starting material observed.

same side product **2a** was also found in the diazotization of 4-bromoaniline (**1e**) (entry 5), which however proceeded much cleaner than the analogous reaction of **1f**. Donor as well as acceptor substituted anilines **1h–1j** were well-tolerated, as evidenced by the high yields reached with the 4-hydroxy, the 4-cyano, and 4-nitro derivatives of aniline (entries 8–10). The worst result was found in the diazotization of unsubstituted aniline **1k** (entry 11), which was the only reaction of this series leading to a number of side-products and a major amount of unconverted starting material. The comparison with 4-methylaniline (**1g**) (entry 7) is hereby interesting, as the large difference in yield between the two reactions (c.f. entries 7 and 11) cannot be due to a significantly different activation of the aromatic core, but has to be some special effect of the additional methyl group. A plausible explanation is the facilitated formation of charge-transfer complexes of phenyl-diazonium ions with aniline, leading to a sluggish reaction in contrast to all other pairs of substituted anilines and diazonium ions, for which packing and aggregation is less favorable.³⁴

To complete this study, the diazotization of four anilines (**1g**: R = Me, **1h**: R = OH, **1i**: R = 4-CN, **1j**: R = 4-NO₂) under the conditions of Table 2 was followed by TLC to get an insight into a possible dependence of the reaction rate on the substitution pattern. No difference in rate could be observed among the anilines **1g**, **1i**, and **1j**, whereas the diazotization of **1h** proceeded more slowly. We therefore assume that the rate-limiting step in the reaction of electron-deficient (c.f. **1i** and **1j**) and electron-neutral anilines (c.f. **1g**) is the uptake of NO₂ into the solution followed by rapid diazotization, while diazotization of donor-substituted anilines (c.f. **1h**) is slower and thus rate-limiting.

As the access to diazonium salts from anilines and low concentrated dioxide had now also turned out as reliable and broadly applicable, we conducted one preliminary small-scale experiment on the envisaged biaryl synthesis (Scheme 2). For

Scheme 2. Small-Scale Synthesis of Aminobiphenyl 4 with 2a from NO-Based Diazotization



this purpose, a solution of diazonium salt **2a** prepared in one of the above shown flask reactions (Table 2, entry 1) was used in a titanium(III)-mediated coupling to 1,4-phenylenediamine.^{35–37} Key questions thereby were whether negative effects would be observed due the unconventionally high dilution for radical aryl–aryl coupling reactions (1 mmol of diazonium salt in 16 mL of water)^{38,39} or the presence of nitric acid in the reaction mixture (c.f. Scheme 1), which could lead to an undesired consumption of the reductant titanium(III)-chloride. In the particular experiment, and in line with earlier optimizations,³⁶ the solution of **2a** obtained from the NO-based diazotization, was added slowly over 7 min to another solution containing an excess of 1,4-phenylenediamine (**3**) and substoichiometric titanium(III)-chloride⁴⁰ in dilute hydrochloric acid. After workup and purification by column chromatography, the desired biphenyl diamine **4** was obtained in 58% yield.^{41,42}

Having shown the suitability of diluted diazonium salt solutions for radical aryl–aryl couplings as well as the

compatibility of nitric acid with a titanium(III)-mediated reaction, we turned to investigate the two-step sequence from nitrogen oxides to biphenyldiamine **4** on a larger scale.

In general, biphenyls represent an important group of compounds with many fields of industrial application.⁴³ Biphenyldiamine **4** in particular has been described as an additive for hair colorants,^{42a} as a structural motif in polymers,^{42b} and as well as a central building block for pharmaceuticals^{42c} and agrochemicals.^{36a}

Scaling up and Reactions in a 10 L Wet Scrubber. First scaling up attempts were made with a 700 mL washing flask containing the aniline **1a** in dilute hydrochloric acid (see Supporting Information). By bubbling a gas stream (1.0 vol % NO₂ in air, ca. 10 mL/min) through this solution in a way that ca. 50 cm in length had to be passed, only conversions lower than 10% of the aniline **1a** could be reached with three equivalents of nitrogen dioxide in air being applied over the whole reaction time of 30 min. The comparably short contact time as well as the insufficient contact surface between gas and solution within the washing flask setup appeared to be plausible explanations for the low conversions.⁴⁴

In the next series of experiments, and with the special focus to increase both contact time and surface, a 10 L wet scrubber was used (Figure 1, see also Supporting Information for

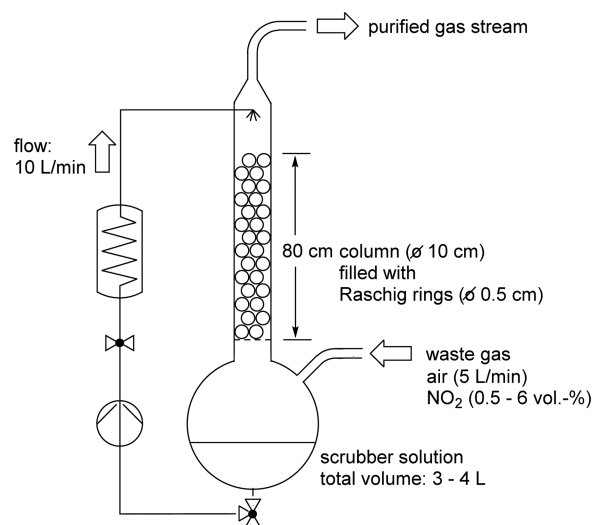


Figure 1. Setup for diazotization reactions in a 10 L wet scrubber.

setup).^{45a} The scrubber solution again contained aniline **1a** (100 mmol) in dilute hydrochloric acid and a stream of NO₂ in air (0.5–6 vol %, ca. 5000–60 000 ppm, 5 L/min) was passed through the scrubber for at least 22 min.⁴⁶ The gas stream was thereby not bubbled through the scrubber solution but got in contact with it when passing in counterstream through the column filled with Raschig rings.

The results obtained under various conditions are summarized in Table 3. The initial attempt with a total amount of 200 mmol NO₂ in the gas stream showed that, in the wet scrubber, this theoretical amount of NO₂ (c.f. Scheme 1, 2) necessary for complete diazotization is not fully, but nearly sufficient to achieve full conversion of the aniline **1a** (entry 1). In all following experiments, we therefore increased the amount of NO₂ in air to 300 mmol. In the first series of variations (entries 2–4), the addition time of NO₂ (300 mmol) was prolonged from 22 to 269 min which was useful to study the

Table 3. Diazotization in 10 L Wet Scrubber under Various Conditions^a

$\text{1a} \xrightarrow[\text{(H}_2\text{O/HCl)}]{\text{NO}_2} \text{2a}$

1a (100 mmol) **2a**

Entry	NO ₂ (mmol)	Addition time (min)	NO ₂ in air (vol.-%)	Solvents 1N HCl/H ₂ O (L/L)	Diazotization (%) ^b
1	200	22.4	4.00	0.8/3.2	94
2	300	22.4	6.00	0.8/3.2	100
3	300	67.2	2.00	0.8/3.2	100
4	300	269	0.50	0.8/3.2	100
5	300	22.4	6.00	0.6/2.4 ^c	100
6	300	22.4	6.00	0.5/3.5	100
7	300	22.4	6.00	0.3/3.7	100
8	300	22.4	6.00	0.12/3.88	96 ^d

^aStandard conditions: Stream of NO₂ in air (5 L/min) passed through wet scrubber filled with a solution of 4-chloroaniline (100 mmol) in H₂O, 1 N HCl at rt. ^bYields determined by ¹H NMR using maleic acid as an internal standard (after concentration in vacuo). ^cTotal amount of solvent reduced to 3 L. ^dFormation of a yellow precipitate <2%.

diazotization at three different NO₂ concentrations of 6, 2, and 0.5 vol % (ca. 60 000, 20 000, and 5000 ppm). In all cases, complete diazotization and no byproduct formation were observed. Further on, the content of hydrochloric acid in the scrubber solution was gradually decreased from 8 equiv (entry 2) over 6, 5, and 3 to finally 1.2 equiv per aniline **1a** (entries 5–8). Only in the last experiment with the lowest concentration of hydrochloric acid (entry 8), diazotization was incomplete, and the precipitation of a small amount of an insoluble yellow product (<2%) in the scrubber was noticed. This points to the fact that an aqueous scrubber solution containing only 4-chloroanilinium hydrochloride without a certain excess of hydrochloric acid is not suitable. In a single experiment (entry 5), we also reduced the total volume of the scrubber solution

from 4 to 3 L, which did not lead to any negative effects on the diazotization.

With regard to an application of the NO-based diazotization reaction as a new method for denitrification of waste gases, we measured the NO and NO₂ concentrations in the gas stream after passage through the scrubber.^{45b} Due to the limited detection ranges of the sensor for NO (max. 3000 ppm) and NO₂ (600 ppm), both concentrations could not be directly determined in the ingoing gas stream. For this reason, a technique of generating NO₂ from copper powder and concentrated nitric acid was selected for the experiments, as this method is known to produce NO₂ nearly quantitatively, in high purity and along with only small amounts of NO.^{46,47a} As nitrogen dioxide thus certainly represents the by far major nitric oxide component in the gas stream, the following discussion of the results is focused on NO₂. The labeling of the concentration curves for NO₂ in Figure 2 does directly correspond to the experiments and entries in Table 3 (see Supporting Information for the two-dimensional version of Figure 2).

Regarding the NO₂ concentrations after passage through the scrubber, it became obvious that the diazotization reaction of **1a** had indeed been able to largely remove nitrogen dioxide from the gas stream in all experiments. Over the time of the actual addition (entries 1, 2, and 5–8: 22.4 min, entry 3: 67.2 min, entry 4: 269 min), the measured NO₂ concentrations all remained lower than 200 ppm. In the experiment with the lowest NO₂ concentration of 0.5 vol % (ca. 5000 ppm, entry 4), which is still above the values observed in most industrially produced waste gases,^{1b} the wet scrubber led to a reduction of the NO₂ concentration to less than 110 ppm over a time span of 250 min. Despite the simple conditions used, these values are already close to the current maximum emission value allowed for NO_x in the European Union, which is 100 ppm.^{1b} The other experiments using higher NO₂ concentrations and short addition times of 22 min (entries 1, 2, and 5–8) also demonstrate the efficacy of the absorption system, as the initial concentration of 6 vol % of NO₂ (ca. 60 000 ppm) could be reduced to 250 ppm. The concentration values recorded for NO₂ in the period (ca. 20 min) after the actual addition, in

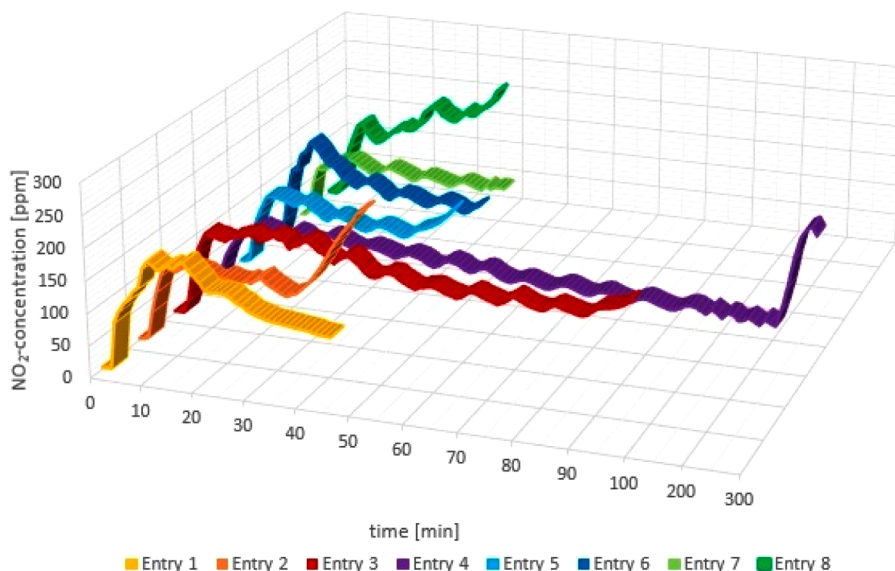
**Figure 2.** NO₂ concentrations measured after passage through wet scrubber.

Table 4. Conditions for Biaryl Synthesis: Change in the Equivalents of Acid per 1,4-Phenylenediamine (3) in the Reaction Course^{a,b}

Entry (cf. Table 3)	HCl in scrubber solution (mol)	HCl added to 3 (mol)	HCl added with TiCl ₃ (mol)	Acid content at start (mol)	Acid content at end (mol)	Variation of acid/ phenylenediamine varies from (equiv) ^[a]
1	0.8	0.75	0.15	0.9	1.6	1.8 - 3.2
2	0.8	0.75	0.15	0.9	1.65	1.8 - 3.3
3	0.8	0.0	0.15	0.15	0.9	0.3 - 1.8
4	0.8	0.0	0.15	0.15	0.9	0.3 - 1.8
5	0.6	0.0	0.15	0.15	0.7	0.3 - 1.4
6	0.5	0.0	0.15	0.15	0.6	0.3 - 1.2
7	0.3	0.0	0.15	0.15	0.4	0.3 - 0.8
8	0.12	0.0	0.15	0.15	0.21	0.3 - 0.42

^aValues calculated for a virtual 100 mmol reaction scale (use of total solution volume of 4 L from wet scrubber for aryl–aryl coupling reaction). ^bFor reaction conditions, see the [Experimental Section](#).

which only air was passed through the scrubber, indicate that NO₂ may be liberated to some extent from the scrubber solution by the stream of air after a certain time, thus leading to a rise in some of the concentration curves.

In contrast to the effective removal of NO₂ from the gas stream, which gave comparable results for all eight experiments (Figure 2), the removal of NO appeared to depend more on the acidity of the scrubber solution. With the least acidic scrubber solution (entry 8), comparably high values for NO of up to 400 ppm were measured, while other experiments in this series gave NO concentrations in the range of 120–200 ppm.^{47b} These values are however difficult to discuss, since the NO concentration in the gas stream before entry into the scrubber could not be determined.^{47a,c} With regard to the fact that only small amounts of NO were most probably generated in comparison to NO₂ (see above), these values nevertheless show that the absorption system based on diazotization is better suited for the removal of NO₂, which can in turn be rationalized by the far lower solubility of NO in aqueous solutions (see [Introduction](#)). A control experiment in which NO₂ in the ingoing gas stream was replaced by NO (300 mmol added over 22.4 min)⁴⁶ led to an unexpectedly effective removal of NO from the gas stream with maximum values of 210 ppm (NO) and 120 ppm (NO₂) after passage through the scrubber. Nevertheless, only 80% of the aniline 1a could be converted to 2a in this attempt, resulting in no byproducts other than the unreacted aniline. In agreement with the assumptions made above, this finding suggests that in the case of NO a longer premixing time of the nitrogen oxides and the stream of air is required to increase the amount of NO₂ relative to NO. This simple modification can then be expected to lead not only to good denitrification for NO, but also to an again full conversion of the aniline, as it was commonly achieved with NO₂.

In the next step, the diazonium salts obtained from the diazotization reactions conducted in the wet scrubber (Table 3) were used for the synthesis of 4'-chlorobiphenyl-2,5-diamine (4). A preliminary series of experiments thereby indicated that the titanium(III)-mediated biaryl synthesis can as well be

performed with partially diazotized anilines, which is due to the fact that protonated 1,4-phenylenediamine (3) is a far better aryl radical acceptor than the protonated 4-chloroaniline (1a) remaining from the incomplete diazotization step (see [Supporting Information](#)). From these reactions, it could also be deduced that a reduction of the excess of 1,4-phenylenediamine (3) from 20 to 5 equiv is tolerated with an only slight decrease in yield (c.f. [Scheme 2](#)). Furthermore, reaction temperatures should not exceed room temperature, and an argon atmosphere as well as the presence of titanium(III)-chloride⁴⁰ were found to lead to a cleaner product formation.

For these reasons, the scaling up experiments summarized in Table 4 were conducted with 5 equiv of 1,4-phenylenediamine (3), under argon atmosphere and at room temperature. It is thus important to note that the overall conditions were in two ways less favorable than those used in the coupling reaction shown in [Scheme 2](#), as the diazonium salt was even further diluted (100 mmol/4000 mL from scrubber vs. 1 mmol/16 mL from flask experiment), and the excess of the phenylenediamine 3 was reduced by a factor of 4. Besides studying the feasibility of radical aryl–aryl coupling reactions under such unusual and rather unfavorable conditions,³⁸ we aimed to determine the ideal acid concentration for the formation of biphenyl 4 from 2a and 3. The background thereby was that the reactivity of 1,4-phenylenediamine (3) as an acceptor for aryl radicals is on the one hand enhanced by low acid concentrations, as this leaves the amino groups more or less unprotonated, so that they can act as strongly donating and activating substituents.⁴⁸ On the other hand, a low amount of acid and insufficient protonation could allow side-reactions of 3 and 2a such as azo coupling and triazene formation.⁴⁹

Whereas the amount of acid per 1,4-phenylenediamine (3) at the start of the addition of 2a can readily be determined from the amount of hydrochloric acid that comes with the reductant titanium(III)-chloride (TiCl₃ used as solution in 3 N HCl) and from what was deliberately added in some of the experiments (entries 1 and 2), the final amount further includes such values as the acid from the scrubber solution, acid consumption during diazotization, and acid formation from NO₂ disproportionation.

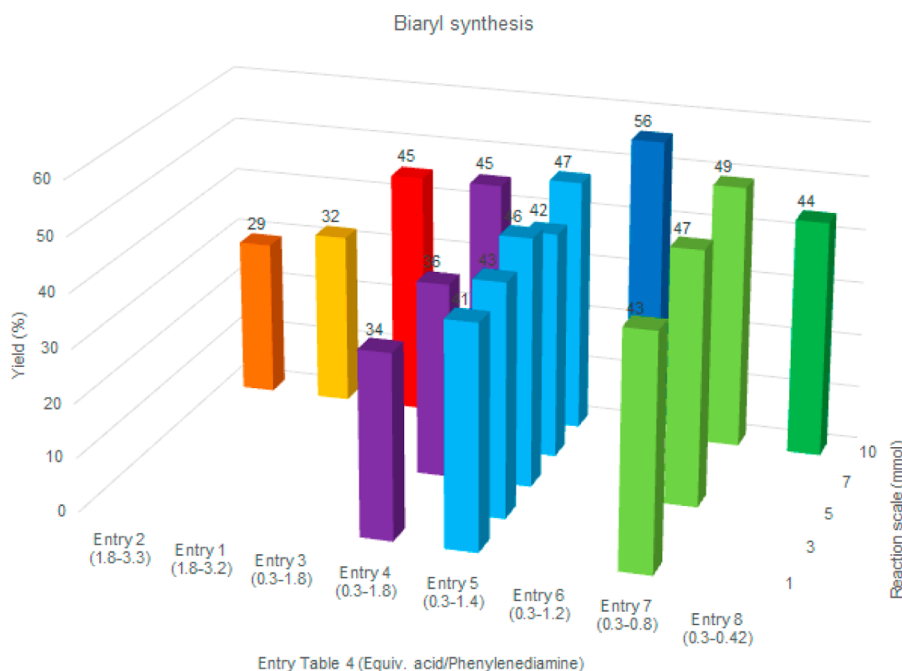


Figure 3. Yields for 4'-chlorobiphenyl-2,5-diamine (**4**) using solutions of diazonium salt **2a** from the wet scrubber experiments.⁵⁰

The final column in Table 4 contains the important range over which the amount of acid per phenylenediamine **3** changes over the time the diazonium salt is added (for detailed calculation, see Supporting Information). The entries 1–8 in Table 4 again correspond to those in Table 3, Figure 2, and Figure 3.

Figure 3 summarizes the yields obtained from a series of aryl–aryl coupling experiments conducted with the diazonium salt solutions from the wet scrubber. The different reaction scales in the range of 1–10 mmol for the diazonium salt **2a** correspond to solution volumes of 40–400 mL from the scrubber.

Solutions of **2a**, which were used for biaryl syntheses on different scales (entries 4, 5, and 7), generally led to slightly increased yields at larger reaction scales. Most importantly, however, the synthetic results confirm the above made assumption that phenylenediamine **3** has to be roughly monoprotonated to be able to act efficiently as radical scavenger, but not to be susceptible to side-reactions such as azo coupling or triazene formation.⁴⁹ The optimized conditions (Table 3, entry 6) were further used for an experiment on a 50 mmol scale, so that two liters of the diazonium salt solution were added to the diamine **3** and titanium(III)-chloride. After purification by column chromatography biphenyl **4** was obtained in 46% isolated yield (5.03 g). Moreover, an improved workup procedure could be developed, which allows isolation of biphenyl **4** in very good purity only through stepwise extraction of the crude reaction mixture (see Experimental Section).

As a second application besides radical biaryl synthesis, we investigated the suitability of the diazonium chloride **2a**, as it was obtained from the wet scrubber (Table 3, entry 6), for Sandmeyer reactions. The results from the series of experiments aiming at the synthesis of 1-chloro-4-iodobenzene (**5**) are summarized in Table 5.

As determined by internal standard, the best yield for iodobenzene **5** (88%) was obtained from a reaction of **2a** with three equivalents of potassium iodide at 50 °C (entry 2).⁵¹ Purification of the crude product by column chromatography

Table 5. Conditions for Sandmeyer Reactions

entry	variation of reaction conditions	yield ^{b,c} 5 (%)
1	<i>a</i>	45
2	50 °C	88
3	NaI (3.0 equiv)	70
4	KI (1.5 equiv)	58
5	KI (3 equiv) + I ₂ (1 equiv)	61

^aStandard conditions: **2a** (10 mmol in 400 mL), KI (3 equiv), rt, 1/2 h. ^bYields of **5** determined by ¹H NMR using maleic acid as an internal standard (after concentration of the reaction mixture in vacuo). ^cIn all reactions chlorobenzene was observed as the only side product.

confirmed this result and led to an identical yield of 88%, which corresponds to 2.09 g on the 10 mmol reaction scale. In all reactions (entries 1–5), chlorobenzene resulting from hydrogen abstraction by the aryl radical could be identified as the only side-product.¹² The conversion of **2a** into the iodide **5** is particularly valuable due to its metal-free nature, the possibility to recycle the excess iodide from the reaction mixture,⁵² and the manifold options to employ aryl iodides in transition metal-catalyzed coupling reactions.⁵³

In summary, we have shown that the removal of nitrogen dioxide from air can be efficiently coupled with the diazotization of a variety of aniline derivatives. With further experiments in a 10 L wet scrubber, this strategy featuring in particular the so far unexploited combination of denitrification and diazotization was demonstrated to be well applicable to streams of low-concentrated nitrogen dioxide in air. Although the resulting diazonium salt was obtained as a highly diluted aqueous solution, it could successfully be applied in a radical aryl–aryl coupling reaction leading to 4'-chlorobiphenyl-2,5-diamine as well as in a Sandmeyer iodination reaction providing 4-chloro-1-iodobenzene. Further studies focus on the behavior

of diversely substituted anilines as part of the absorption system in the wet scrubber as well as on the application of the corresponding diazonium salts in other radical and nonradical transformations.

■ EXPERIMENTAL SECTION

General Experimental Section. Solvents and reagents were used as received. ^1H NMR spectra were recorded on 360 and 600 MHz spectrometers using CDCl_3 and $\text{DMSO}-d_6$ as solvents referenced to TMS (0 ppm), CHCl_3 (7.26 ppm), or $\text{DMSO}-d_6$ (2.50 ppm). Chemical shifts are reported in parts per million (ppm). Coupling constants are in Hertz (J Hz). The following abbreviations are used for the description of signals: s (singlet), d (doublet), dd (double doublet), t (triplet), q (quadruplet), m (multiplet). ^{13}C NMR spectra were recorded at 91 and 151 MHz in CDCl_3 using CDCl_3 (77.0 ppm) as a standard. Mass spectra were recorded using electron impact (EI) or electron spray ionization (ESI). Analytical TLC was carried out on Merck silica gel plates using short wave (254 nm) UV light to visualize components. Silica gel (Kieselgel 60, 40–63 μm) was used for flash column chromatography.

General Procedure 1 (Table 1). In a 250 mL round-bottom flask equipped with a balloon for pressure equilibration, nitrogen monoxide (0.10–4.00 mmol) was added by syringe to a mixture of 4-chloroaniline (**1a**) (1.00 mmol, 128 mg) in a mixture of water and 1 N HCl (3:1 v/v, 16 mL). After vigorous stirring at room temperature, the reaction mixture was concentrated under reduced pressure and analyzed by ^1H NMR spectroscopy.

General Procedure 2 (Table 2). In a 250 mL round-bottom flask equipped with a balloon for pressure equilibration, nitrogen monoxide (45 mL, ca. 2.0 mmol) was added by syringe to a solution of the aniline derivative (1.00 mmol) in a mixture of water and 1 N HCl (3:1 v/v, 16 mL). After vigorous stirring for 30 min at room temperature, the reaction mixture was concentrated under reduced pressure and analyzed by ^1H NMR spectroscopy. The reaction rates of the anilines were compared by TLC with a identical reaction setup. Full conversion was observed for **1g**, **1i**, and **1j** after 2 min, for **1h** after 6 min.

General Procedure 3 (Table 3 and Figure 2). A stream of nitrogen dioxide (generated by slow addition of copper powder (0.5 equiv) to concentrated nitric acid (2.0 equiv)) in air (0.5, 2, 4, or 6 vol % NO_2 , total flow: ca. 5 L/min) was passed through a 10 L wet scrubber (for pictures see [Supporting Information](#)) containing 4-chloroaniline (**1a**) (12.8 g, 100 mmol) in a mixture of water and 1 N HCl (see [Table 3](#)) over a time of 22.4, 67.2, or 269 min (see [Table 3](#)) at room temperature. After the NO_2 generation was finished, the air flow through the scrubber was maintained for another 38 min. The content of NO_2 in the outgoing gas stream was measured over the time of NO_2 generation and for further 23 min.

For the control reaction, nitrogen monoxide (300 mmol, ca. 6.72 L) was generated by the slow addition of potassium iodide (300 mmol, 49.8 g, dissolved in 300 mL water) to a mixture sodium nitrite (300 mmol, 20.7 g) and diluted sulfuric acid (ca. 10%, 1.5 L) over 22.4 min.

General Procedure 4 (Scheme 2). A 16 mL aliquot of the 0.062 M solution of 4-chlorophenyl diazonium chloride (**2a**) (ca. 1 mmol) was added dropwise by syringe pump to a vigorously stirred solution of 1,4-phenylenediamine (**3**) (2.16 g, 20.0 mmol) in degassed water (10 mL) and hydrochloric acid

(7 mL, 3 N HCl) and titanium(III)-chloride (0.5 mmol, 0.5 mL, ca. 1 M solution in 3 N HCl) over a period of 7 min under argon. After the addition was complete, the mixture was left to stir for 10 more minutes, and a solution of sodium hydroxide (4.0 g) and sodium sulfite (4.0 g) in water (40 mL) was added. After extraction with diethyl ether (3 \times 100 mL), the combined organic phases were washed with satd. aqueous sodium chloride and dried over sodium sulfate. Concentration in vacuo and purification by column chromatography (*n*-hexane/ethyl acetate 8:1) gave the biphenyl-2,5-diamine **4**.

General Procedure 5 (Table 4 and Figure 3). A 400 mL aliquot of the 0.025 M solution of 4-chlorophenyl diazonium chloride (**2a**) (ca. 10 mmol, obtained as described in [General Procedure 3](#)) was added by dropping funnel to a vigorously stirred solution of 1,4-phenylenediamine (**3**) (5.40 g, 50.0 mmol) in degassed water (100 mL) and titanium(III)-chloride (5.0 mmol, 5.0 mL, ca. 1 M solution in 3 N HCl) over a period of 7 min under argon. In the case that additional hydrochloric acid (25 mL, 75 mmol, 3 N HCl, see entries 1 and 2, [Table 4](#)) was added to **3** before the addition of **2a**, the amount of water was reduced to 75 mL. For reactions on smaller scales (1, 3, 5, and 7 mmol of **2a**), the amounts of all reagents and solvents were reduced accordingly.

After the addition of **2a** was complete, the mixture was left to stir for 15 more minutes, and a solution of sodium hydroxide (20.0 g) and sodium sulfite (20.0 g) in water (400 mL) was added. After extraction with diethyl ether (3 \times 100 mL), the combined organic phases were washed with saturated aqueous sodium chloride and dried over sodium sulfate. Concentration in vacuo and purification by column chromatography (*n*-hexane/ethyl acetate 8:1) gave 4'-chlorobiphenyl-2,5-diamine (**4**).

Improved Workup Procedure. After the addition of **2a** to **3** and TiCl_3 was complete, the resulting mixture was left to stir for further 15 min, and it was then extracted with ethyl acetate (3 \times 100 mL) to remove unpolar side products. Due to the acidic conditions, the biphenyl diamine **4** as well as unreacted 1,4-phenylenediamine (**3**) were protonated and remained in the aqueous phase. Subsequently, a solution of sodium hydroxide (20.0 g) and sodium sulfite (20.0 g) in water (400 mL) was added to the aqueous phase. After extraction with diethyl ether (3 \times 100 mL), the combined organic phases were washed with saturated aqueous sodium chloride and dried over sodium sulfate. Due to the low solubility of phenylenediamine **3** in diethyl ether only trace amounts of **3** were extracted from the aqueous phase. The purity of **4** reached with this procedure is comparable to the purity previously observed after column chromatography.

General Procedure 6 (Table 5). Potassium iodide (30 mmol, 4.98 g) was added to a 400 mL aliquot of the 0.025 M solution of 4-chlorophenyl diazonium chloride (**2a**) (ca. 10 mmol, obtained as described in [General Procedure 3](#)), and the solution was stirred for 30 min. After extraction with diethyl ether (3 \times 200 mL), the combined organic phases were washed with saturated aqueous sodium chloride and dried over sodium sulfate. After concentration in vacuo the yield of 1-chloro-4-iodobenzene (**5**) was determined by ^1H NMR using maleic acid as an internal standard. Purification of **5** was achieved through column chromatography (100% diethyl ether).

4-Chlorobenzenediazonium Chloride (2a**).**⁵⁴ Prepared according to GP 1–3. ^1H NMR (360 MHz, $\text{DMSO}-d_6$): δ (ppm) = 8.12 (d, J = 9.3 Hz, 2 H), 8.76 (d, J = 9.3 Hz, 2 H).

3-Chlorobenzenediazonium Chloride (2b).⁵⁵ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 8.01 (t, *J* = 8.3 Hz, 1 H), 8.38 (ddd, *J* = 1.0 Hz, *J* = 2.0 Hz, *J* = 8.3 Hz, 1 H), 8.70 (ddd, *J* = 1.0 Hz, *J* = 2.0 Hz, *J* = 8.3 Hz, 1 H), 8.92 (t, *J* = 2.0 Hz, 1 H).

2-Chlorobenzenediazonium Chloride (2c).⁵⁶ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 7.93–8.00 (m, 1 H), 8.20 (dd, *J* = 1.0 Hz, *J* = 8.3 Hz, 1 H), 8.29 (ddd, *J* = 1.6 Hz, *J* = 7.6 Hz, *J* = 8.3 Hz, 1 H), 8.93 (dd, *J* = 1.6 Hz, *J* = 8.3 Hz, 1 H).

4-Fluorobenzenediazonium Chloride (2d).⁵⁴ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 7.90 (dd, *J* = 8.3 Hz, *J* = 9.4 Hz, 2 H), 8.87 (dd, *J* = 4.5 Hz, *J* = 9.4 Hz, 2 H).

4-Bromobenzenediazonium Chloride (2e).⁵⁴ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 8.26 (d, *J* = 9.2 Hz, 2 H), 8.62 (d, *J* = 9.2 Hz, 2 H).

4-Iodobenzenediazonium Chloride (2f).⁵⁷ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 8.37 (d, *J* = 9.0 Hz, 2 H), 8.43 (d, *J* = 9.0 Hz, 2 H).

4-Methylbenzenediazonium Chloride (2g).⁵⁷ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 2.57 (s, 3 H), 7.80 (d, *J* = 8.3 Hz, 2 H), 8.58 (d, *J* = 8.3 Hz, 2 H).

4-Hydroxybenzenediazonium Chloride (2h).⁵⁸ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 7.27 (d, *J* = 9.3 Hz, 2 H), 8.50 (d, *J* = 9.3 Hz, 2 H).

4-Cyanobenzenediazonium Chloride (2i).⁵⁴ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 8.47 (d, *J* = 9.1 Hz, 2 H), 8.91 (d, *J* = 9.1 Hz, 2 H).

4-Nitrobenzenediazonium Chloride (2j).⁵⁶ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 8.71 (d, *J* = 9.3 Hz, 2 H), 8.96 (d, *J* = 9.3 Hz, 2 H).

Benzenediazonium Chloride (2k).⁵⁴ Prepared according to GP 2. ¹H NMR (360 MHz, DMSO-*d*₆): δ (ppm) = 7.94–8.02 (m, 2 H), 8.18–8.31 (m, 1 H), 8.63–8.74 (m, 2 H).

4'-Chlorobiphenyl-2,5-diamine (4).^{36a} Prepared according to GP 4 and GP 5. *R*_f = 0.5 (EtOAc) [UV]. ¹H NMR (600 MHz, CDCl₃): δ (ppm) = 3.42 (bs, 4 H), 6.52 (d, *J* = 2.5 Hz, 1 H), 6.60 (dd, *J* = 2.5 Hz, *J* = 8.5 Hz, 1 H), 6.64 (d, *J* = 8.5 Hz, 1 H), 7.37–7.41 (m, 4 H). ¹³C NMR (151 MHz, CDCl₃): δ (ppm) = 116.8 (CH), 117.4 (CH), 117.9 (CH), 127.7 (C_q), 128.9 (2 × CH), 130.4 (2 × CH), 133.1 (C_q), 135.9 (C_q), 137.9 (C_q), 137.9 (C_q). HRMS (EI) calculated for C₁₂H₁₁ClN₂ [H⁺]: 219.0684, found: 219.0679. The analytical data are in agreement with those reported in ref 36a.

1-Chloro-4-iodobenzene (5).⁵⁹ Prepared according to GP 6. ¹H NMR (600 MHz, CDCl₃): δ (ppm) = 7.09 (d, *J* = 8.7 Hz, 2 H), 7.61 (d, *J* = 8.7 Hz, 2 H).

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.oprd.5b00298.

Additional experimental procedures, ¹H NMR spectra of biaryl 4, characterization data for byproducts, and pictures of 10 L wet scrubber and NO_x gas sensor (PDF)

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Notes

The authors declare no competing financial interest.

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