A New Route to 4-Aminodiphenylamine via Nucleophilic Aromatic Substitution for Hydrogen: Reaction of Aniline and Azobenzene

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A new example of nucleophilic aromatic substitution for hydrogen is described which encompasses reacting aniline and azobenzene (**1**) in the presence of base under aerobic conditions to generate 4-(phenylazo)diphenylamine (**2**) in high yield. Monitoring the time course of the reaction under anaerobic conditions revealed that hydrazobenzene (**9**) was formed as an intermediate in the reaction in equal molar amounts as **2**. However, under aerobic conditions **9** was shown not to persist in the reaction mixture. The kinetic effect of isotopic substitution on this reaction was probed by competition experiments utilizing equal molar mixtures azobenzene-d_{10} and undeuterated material which gave a k_H/k_D of 4.6 ± 0.1. It was concluded from these studies that azobenzene was functioning as both the electrophile and oxidant in this reaction. Catalytic hydrogenation of **2** generates 4-aminodiphenylamine (4-ADPA) (**10**) and aniline. These reactions form the basis of a novel synthetic route to 4-ADPA which does not utilize halogenated intermediates or reagents and ultimately relies on O_2 as the terminal oxidant in the system.

The development of new environmentally favorable routes for the production of commercially relevant chemical intermediates and products is an area of considerable interest to the chemical processing industry. These synthetic routes will ideally focus on elimination of waste at the source and will require, in most cases, the discovery of new atomically efficient chemical reactions. In view of these emerging requirements, we have focused our attention on nucleophilic aromatic substitution for hydrogen (NASH) reactions as a means to generate aromatic amines without the need for halogenated materials or intermediates.[1] Of particular interest was the identification of novel synthetic strategies to 4-aminodiphenylamine (4-ADPA) (**10**) and its derivatives which are widely used as antioxidants in rubber products. Current processes for the manufacturing of 4-ADPA are heavily dependent on halogenated reagents which ultimately generate waste streams laden with inorganic salts and trace amounts of organic byproducts.[2] In pursuit of the these objectives, we recently have shown that the NASH reaction of aniline and nitrobenzene generates high yields of (4-nitrosophenyl)phenylamine and (4-nitrophenyl)phenylamine.[3] Catalytic hydrogenation of these intermediates produces 4-ADPA in a halogen-free process.[4]

The necessity for electron-withdrawing groups (EWG) in the activation of aromatic rings toward nucleophilic substitution is a well-established principle in organic chemistry. In the general case of nucleophilic aromatic substitution for halogen, a wide variety of EWG such as nitro,[5] (trifluoromethyl)sulfonyl,[6] and even phenylazo[7] have been shown to enhance the rate of S_NAr reactions. However, in the case of nucleophilic aromatic substitution for hydrogen, only nitroarenes have been successfully utilized[8] with the exception of a recent example where a diazonium salt was used to activate a substituted dicarboxylic acid toward intramolecular nucleophilic aromatic substitution.[9] We report here the first example of a nucleophilic aromatic substitution for hydrogen reaction that proceeds with an azo group as the activating electrophile. This reaction forms the basis for a novel route to 4-ADPA that does not require halogenated intermediates or reagents.

Results

The addition of strong bases, such as potassium *tert*-butoxide/18-crown-6 or tetramethylammonium hydroxide dihydrate ($(CH_3)_4N^+OH^-\cdot 2H_2O$) to mixtures of azobenzene (**1**) and aniline results in the formation of a dark purple solution. This reaction was allowed to stir for 12 h at 60–70 °C under a nitrogen blanket without the rigorous exclusion of O_2. Subsequent analysis of the reaction mixture by reverse phase HPLC indicated the single major product to be 4-(phenylazo)diphenylamine (**2**). Quenching of the reaction with methanol/water resulted in the precipitation of an orange solid which was recrystallized to give **2** in 96% yield on the basis of moles of **1** charged. Monitoring the time course of this reaction by HPLC revealed the intermediacy of hydrazobenzene (**9**) in the formation of **2** from aniline and azobenzene. It was evident from the analysis that as the reaction

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(1) (a) Riley, D. P.; Stern, M. K.; Ebner, J. Industrial Perspectives on the Use of Dioxygen: New Technology to Solve Old Problems in *The Activation of Dioxygen and Homogeneous Catalytic Oxidations*; Barton, D. H. R., Martell, A. E., Sawyer, D. T., Eds.; Plenum Press: New York, 1993. (b) Stern, M. K.; Cheng, B. K. *J. Org. Chem.* **1993**, *58*, 6883–6888.

(2) (a) Rondestvedt, C. S. *J. Org. Chem.* **1977**, *42*, 1786–1790. (b) A few of the numerous patents are listed: U.S. Patents 4 187 248, 4 683 332, 4 155 936, 4 670 595, 4 122 118.

(3) Stern, M. K.; Hileman, F. D.; Bashkin, J. K. *J. Am. Chem. Soc.* **1992**, *114*, 9237–9238.

(4) U.S. Patent 5 110 763.

(5) Terrier, F. Nucleophilic Aromatic Displacement: The Influence of the Nitro Group in *Organic Nitro Chemistry Series*; Feuer, H., Ed.; VCH Publishers, Inc.: 1991.

(6) Shein, S. M.; Ignatov, V. A.; Kozorez. L. A.; Chervatyuk, L. F. *Zh. Obshch. Khim.* **1967**, *37*, 114.

(7) Miller, J. *Aromatic Nucleophilic Substitution*; Elsevier: Amsterdam, 1968.

(8) (a) Traynelis, V. J.; McSweeney, J. V. *J. Org. Chem.* **1966**, *31*, 243–247. (b) Makosza, M.; Winiarski, J. *Acc. Chem. Res.* **1987**, *20*, 282–289, and references therein. (c) Makosza, M.; Bialecki, M. *J. Org. Chem.* **1992**, *57*, 4784–4785. (d) Katritzky, A. R.; Laurenzo, K. S. *J. Org. Chem.* **1986**, *51*, 5039. (e) Katritzky, A. R.; Laurenzo, K. S. *J. Org. Chem.* **1988**, *53*, 3978. (f) Ayyangar, N. R.; Naik, S. N.; Srinivasan, K. V. *Tetrahedron Lett.* **1990**, 3217. (g) Davis, R. B.; Pizzini, L. C.; Benigni, J. D. *J. Am. Chem. Soc.* **1960**, *82*, 2913–2915. (h) Davis, R. B.; Pizzini, L. C. *J. Org. Chem.* **1960**, *25*, 1884–1888.

(9) Panetta, C. A.; Fang, Z.; Heimer, N. E. *J. Org. Chem.* **1993**, *58*, 6146–6147.

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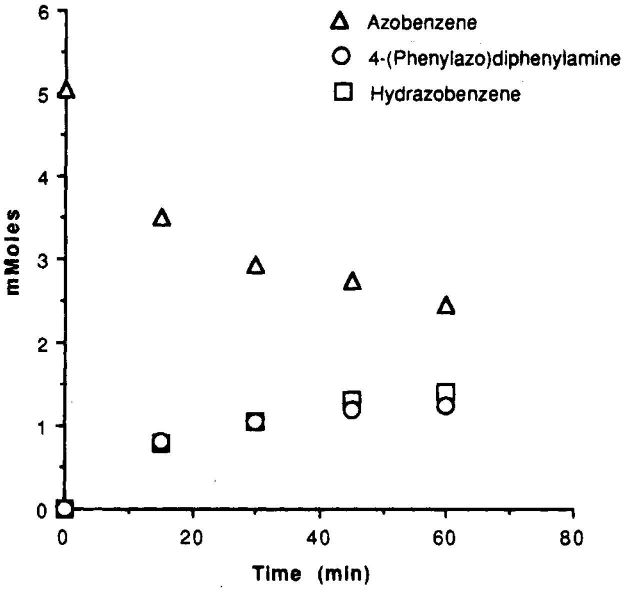


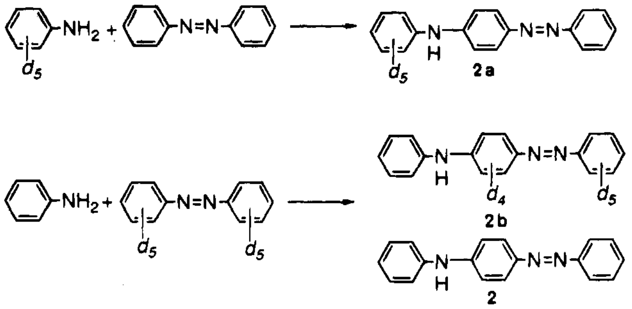
Figure 1. Time course of the reaction under anaerobic conditions monitoring the production of **2** and **9** and the consumption of **1** by HPLC chromatography.

Table 1. Effect of Water on the Yield of 4-(Phenylazo)diphenylamine (2)

mole ratio water:*tert*-butoxide	% yield[a] **2**
10	0
3	1
1	7
0.5	50

[a] Yields are based on moles of azobenzene charged and were determined by reverse-phase HPLC analysis as described in the Experimental Section. Reaction conditions: aniline (1.25 g), azobenzene (0.45 g), potassium *tert*-butoxide (0.55 g), and 18-crown-6 (0.65 g) were mixed with various amounts of water. The reactions were stirred at 80 °C for 2 h after which time they were analyzed by HPLC.

Scheme 1



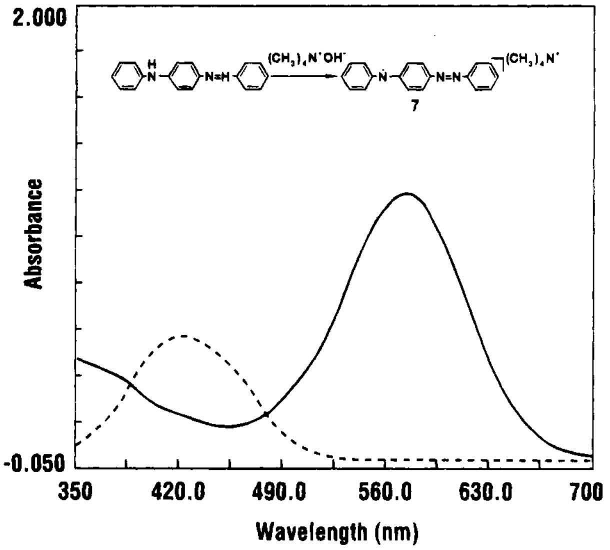


Figure 2. Visible electronic absorption spectra in DMSO of (- - -) authentic sample of **2** before addition of TMA(OH)·2H_2O, final [**2**] = 2.2 × 10^{-5}, λ_{max} = 424 nm, and (—) after addition of TMA(OH)·2H_2O to the DMSO solution of **2**, λ_{max} = 574 nm.

progressed, both hydrazobenzene and azobenzene were steadily consumed, generating **2** as the only major product. However, when an identical reaction was run under strictly anaerobic conditions, hydrazobenzene persisted in the reaction mixture and was formed concomitantly with **2** in equal molar amounts (Figure 1). As we have observed in other NASH reactions, the amount of water present in this reaction has a significant effect on the yield of **2** (Table 1).[1b,3] For optimal production of **2**, nearly anhydrous conditions must be maintained.

That **2** was indeed formed via a NASH reaction and not by condensation of aniline with (4-nitrosophenyl)phenylamine, as recently observed by Marletta,[10] was confirmed by a series of deuterium-labeling experiments (Scheme 1). Thus, when aniline-d_5 (99% isotopically enriched) was reacted with azobenzene, only 4-(phenylazo)diphenylamine-d_5 (**2a**) was produced, as is evident by electron impact mass spectral analysis showing a molecular ion with m/z = 278. When the identical reaction was carried out using azobenzene-d_{10} and undeuterated aniline, the corresponding 4-(phenylazo)diphenylamine-d_9 (**2b**) was observed (m/z = 282). This ion showed the loss of $C_6D_5N_2^+$ to give an intense fragment ion at m/z = 172 corresponding to $C_6H_5NHC_6D_4^+$, which is consistent with our structural assignment. A small amount of **2** (<5%) was also detected (m/z = 273) and was attributed to the aerobic oxidation of aniline to azobenzene under the reaction conditions.

The highly colored nature of the reaction mixture is typical of all the NASH reactions which we have studied.[1b,3] In these examples the colored species were identified as the salts of the dehydronated amine products. Unfortunately, attempts to isolate the $(CH_3)_4N^+$ salt of **2** were unsuccessful due to the formation of extremely hygroscopic solids which were difficult to isolate and characterize. However, it was possible to monitor the reaction by UV–vis spectroscopy. Under the reaction conditions, a new band appeared at λ_{max} = 574 nm that was not present in either mixtures of aniline and azobenzene in the absence of $(CH_3)_4N^+OH^-$ or in mixtures of aniline and $(CH_3)_4N^+OH^-$ or azobenzene and $(CH_3)_4N^+OH^-$ alone. An identical spectrum was obtained when $(CH_3)_4N^+OH^-$ was added to a DMSO solution of **2** indicative of the *in situ* formation of its $(CH_3)_4N^+$ salt **7** (Figure 2). We conclude from this data that the initial product of the reaction is the anion of **2** with either a potassium or tetramethylammonium counter ion depending on the reagents employed.

In an effort to further probe the critical oxidation step, the kinetic effect of isotopic substitution was determined by competition reactions utilizing deuterated and undeuterated azobenzene. Thus, equal molar amounts of

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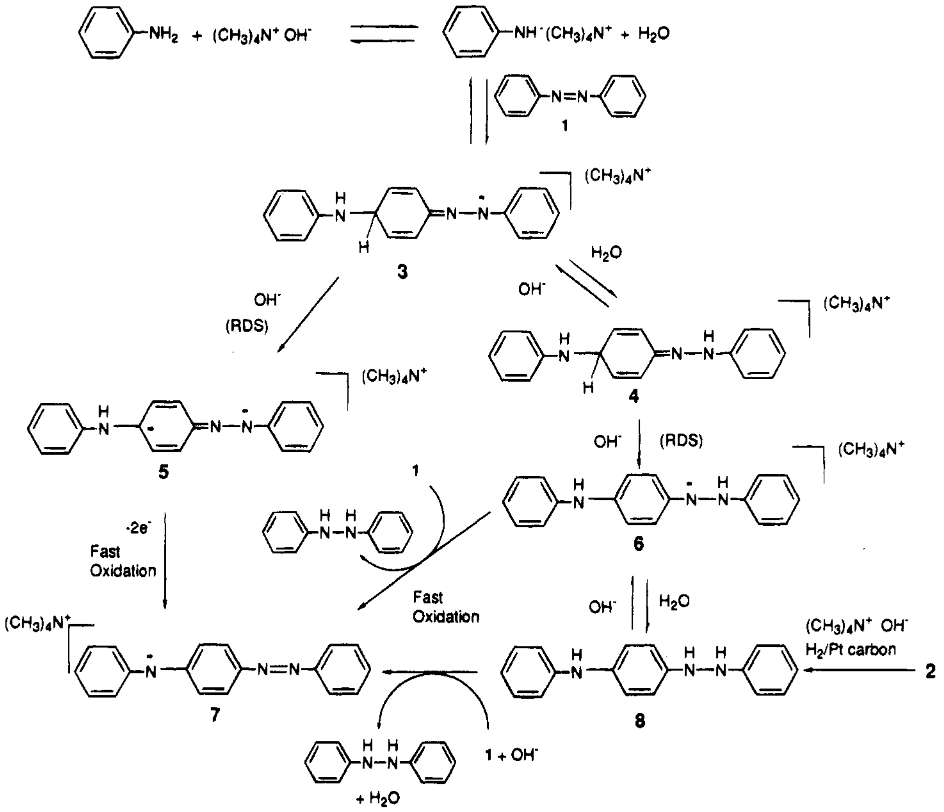
(10) It has been observed that the reaction of aniline and superoxide can produce (4-nitrosophenyl)phenylamine, which can further condense with another molecule of aniline to generate **2**. See: (a) Frimer, A. A.; Aljadeff, G.; Ziv, J. *J. Org. Chem.* **1983**, *48*, 1700–1705. (b) Stuehr, D. J.; Marletta, M. A. *J. Org. Chem.* **1985**, *50*, 694–696.

Scheme 2



azobenzene-d_{10} and unlabeled material were reacted with aniline and $(CH_3)_4N^+OH^-\cdot 2H_2O$ under anaerobic conditions. The isolated product was analyzed by mass spectrometry to determine the proportion of **2** and **2b** generated. Triplicate analysis of the competition experiment revealed an average k_H/k_D value of 4.6 ± 0.1.

Product **2** can be converted to 4-ADPA in high yield by catalytic hydrogentation under a variety of neutral or acidic conditions. Typically the reaction was conducted with aniline as solvent using either Pt/carbon or PtO_2 catalysts under 100 psig (6.9 bar) H_2 at 70 °C and was complete when the theoretical 2 equiv of H_2 per mol of **2** charged was consumed.

Several different mechanistic pathways for the formation of **2** can be suggested that are consistent with the observed isotope effect. One potential pathway invokes the intermediacy of 4-(phenylhydrazo)diphenylamine (**8**) or its anion (**6**) which can be generated via a series of monoanion intermediates from σ-complex **3** (Scheme 2). Alternately, initial formation of dianion intermediate **5** must also be considered in light of the proposal of Guthrie[11a] that dianions are involved in the NASH reaction of alkoxides and nitrobenzene. We suspected that characterization of **5** would be difficult if not impossible due to its expected instability. However, it was possible to generate **8** directly by catalytic hydrogenation of **2** under *basic* conditions (Scheme 2), providing an opportunity to test if **8** was a viable intermediate in the reaction sequence. Shown in Figure 3 is the hydrogen consumption for the reduction of **2** and an equal molar amount of $(CH_3)_4N^+OH^-$ in aniline. The reaction is rapid and terminates after 1 equiv of H_2 is consumed per mol of **2** charged which is consistent with the *in situ* production of **8** or **6**. Addition of azobenzene to this freshly prepared solution of **8** under anaerobic conditions resulted in the generation of hydrazobenzene in 75% yield.

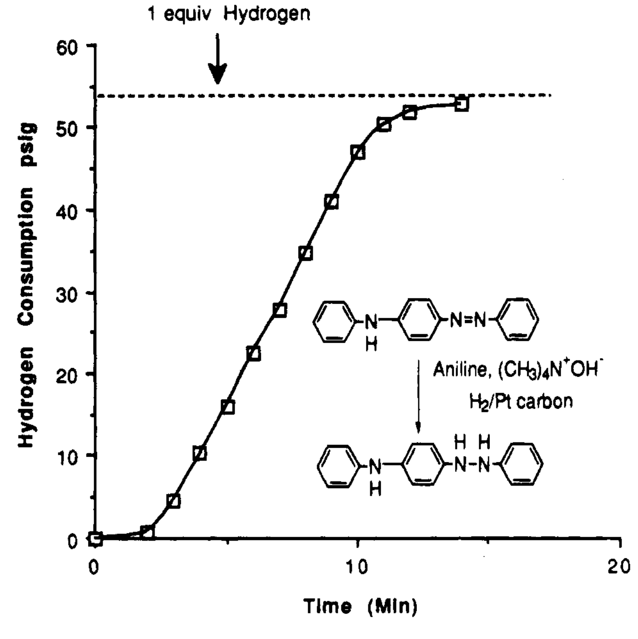
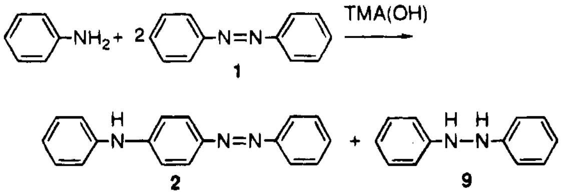


Figure 3. Plot of hydrogen consumption (psig) vs time for the conversion of **2** to **8**.

Discussion

The coupling of aniline and azobenzene to produce **2** is a unique example of a NASH reaction in that the phenylazo moiety functions as the EWG to activate the phenyl ring toward nucleophilic attack. Like other NASH reactions, the formal oxidation of a σ-complex intermediate is required for product formation. Our studies[1b,3,4] and the work of others[11] have clearly demonstrated that in the case of nitroarenes the nitro group can serve efficiently as the oxidant. The observation that hydrazobenzene is formed as an intermediate in this reaction, and that under anaerobic conditions it is generated in equal molar amounts as product, indicates that azobenzene must be functioning as the oxidant in this system. However, on the basis of the reaction stoichiometry (eq 1), there is a requirement for hydrazobenzene to be oxidized back to azobenzene for the observed yields of **2** to be achieved.



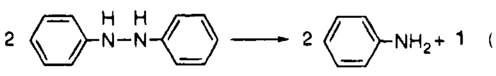
(1)

Any mechanism proposed to explain the oxidative conversion of **3** to products must take into consideration the observed kinetic isotope effect. One possibility is direct dehydronation of **3** generating dianion **5** which is rapidly oxidized to products (Scheme 2). A mechanism similar to this has been proposed by Guthrie in the NASH reaction of *tert*-butoxide and nitrobenzene.[11a] In this case, a k_H/k_D value of 4 was also observed and a mechanism was forwarded that required the dehydronation of a σ-complex intermediate. Guthrie concluded that the dianion mechanism for oxidation of σ-complex intermediates most likely would be restricted to aromatic nitro compounds since it was unlikely that other functional groups would provide the required stabilization. Accordingly, one would expect the intermediacy of dianion species would be even less likely with an azo group as the activating electrophile.

An alternate mechanism for the production of **7** from **3** would be through 4-(phenylhydrazo)diphenylamine intermediates **8** or **6** (Scheme 2). This mechanism requires azobenzene to be a competent oxidant of either **8** or **6** since hydrazobenzene is observed as an intermediate in the reaction under both aerobic and anaerobic conditions. Our studies into the generation of **8** via hydrogenation revealed it to be extremely oxygen sensitive. For instance, HPLC analysis of a freshly prepared solution of **8** showed only a single peak corresponding to **2**, indicating that **8** was rapidly oxidized during sampling or analysis. Although **8** could not be directly characterized, several lines of evidence support its formation by direct hydrogenation of **2**. First, only 1 equiv of H_2 is consumed in the reduction of **2** in the presence of $(CH_3)_4N^+OH^-$ while 2 equiv of H_2 is consumed when the hydrogenation is conducted under neutral or acidic conditions where **2** is completely converted to 4-ADPA. Second, hydrogenation reactions of aniline solutions of azobenzene under basic conditions generate hydrazobenzene and also stop when 1 equiv of H_2 is consumed.[12] The observation that hydrazobenzene is formed when a freshly prepared solution of **8** is treated with azobenzene supports the intermediacy of 4-(phenylhydrazo)diphenylamine species in the formation of **2** from aniline and azobenzene and rules out the need to invoke the direct oxidation of dianion **5**.

On the basis of these results, we propose the following mechanistic scheme for the formation of **7** from aniline and azobenzene (Scheme 2). Dehydronation of aniline by base to generate the anilide anion is most likely the first step in the reaction and is responsible for the dramatic sensitivity of the reaction to water. A similar dehydronation has been proposed in the reaction of aniline and nitrobenzene and reflects the requirement for a more potent nucleophile in these reactions than the neutral amine.[3] Attack of the anilide anion at the *para* position of azobenzene generates the expected σ-complex intermediate[13] **3** which can undergo a series hydronation/dehydronation steps to form intermediate **4**. Dehydronation of **4** is rate limiting with the subsequent formation of **6** or **8** that is rapidly oxidized by a second equivalent of azobenzene, generating **7** and hydrazobenzene.

Two reasonable mechanisms can be proposed for the regeneration of azobenzene from the hydrazo species. It is known that hydrazobenzene can disproportionate under basic conditions with the stoichiometry shown in eq 2.[14] While at first this seems like an attractive mechanism, a careful analysis of the overall reaction stoichiometry reveals that it is impossible to generate **2** in 96% yield if the disproportionation pathway is the only method for the formation of azobenzene.[15] However, it was our concern that ruling out the disproportionation mechanism solely on the basis of this analysis may be premature. If a second route for the generation of azobenzene was operating concurrently with the disproportionation of hydrazobenzene, it may be possible to achieve higher than the theoretical yields of **2**. For instance, it is known that azobenzene can be generated by the aerobic oxidation of aniline under basic conditions.[16] If this reaction was indeed occurring to a significant extent, it would still be possible for disproportionation to be the predominant route for recycling hydrazobenzene with the higher yield of **2**, resulting from the augmentation of azobenzene production from the aerobic oxidation of aniline.



(2)

This scenario was ruled out by revisiting the isotopic labeling experiments which utilized azobenzene-d_{10} and undeuterated aniline. If in fact the disproportionation

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[11] (a) Guthrie, R. D.; Nutter, D. E. *J. Am. Chem. Soc.* **1982**, *104*, 7478–7482. (b) Zimmerman, W. Z. *Physiol. Chem.* **1935**, 233, 257. (c) King, T. J.; Newall, C. E. *J. Chem. Soc.* **1962**, 367. (d) Foster, R.; Mackie, R. K. *Tetrahedron*, **1962**, *18*, 1131. (e) Bunnett, J. F.; Zahler, R. E. *Chem. Rev.* **1951**, *49*, 273. (f) Stahly, G. B. *J. Org. Chem.* **1985**, *50*, 3091. (g) Davis, R. B.; Pizzini, L. C.; Benigni, J. D. *J. Am. Chem. Soc.* **1960**, *82*, 2913–2915. (h) Davis, R. B.; Pizzini, L. C. *J. Org. Chem.* **1960**, *25*, 1884–1888. (i) Treston, A.; Blakeley, R. L.; Zerner, B. *J. Chem. Soc., Chem. Commun.* **1980**, 394–395. (j) Rajanbabu, T. V.; Reddy, G. S.; Fukunaga, T. *J. Am. Chem. Soc.* **1985**, *107*, 5473. (k) Wohl, A. *Chem. Ber.* **1903**, *36*, 4135.

[12] We have hydrogenated azobenzene under basic conditions in the same apparatus and monitored hydrogen uptake and product formation. A similar hydrogen uptake curve as shown in Figure 3 was observed for azobenzene with the reaction stopping at hydrazobenzene. Others have reported on the difficulty of hydrogenating hydrazobenzene to aniline under basic conditions. See: (a) Lunn, G.; Sansone, E. B.; Kefer, L. K. *Environ. Sci. Technol.* **1981**, *17*, 240–243. (b) Ho, T.-L.; Olah, G. A. *Synthesis* **1977**, 169–170.

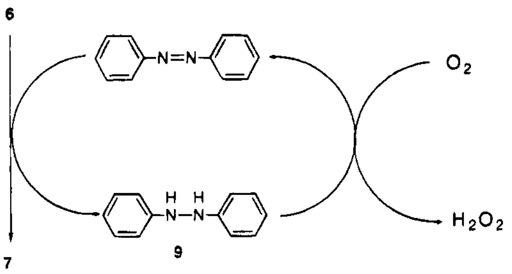
[13] (a) Buncel, E. *Supplement F: The Chemistry of Amino, Nitroso, and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: London, 1982; Part 2, Chapter 27. (b) Jackson, C. L.; Boos, W. F. *Am. Chem. J.* **1898**, *20*, 444. (c) Jackson, C. L.; Gazzolo, F. H. *Am. Chem. J.* **1900**, *23*, 376. (d) Meisenheimer, J. *Ann. Chem.* **1902**, *323*, 205. (e) Buncel, E.; Webb, J. G. K. *Can. J. Chem.* **1972**, *50*, 129. (f) Buncel, E.; Webb, J. G. K. *Can. J. Chem.* **1974**, *52*, 630. (g) Buncel, E.; Webb, J. G. K. *Tetrahedron Lett.* **1976**, 4417. (h) Buncel, E.; Webb, J. G. K.; Wiltshire, J. F. *J. Am. Chem. Soc.* **1977**, *99*, 4429. (i) Buncel, E.; Jarrel, H.; Leung, H. W.; Webb, J. G. K. *J. Org. Chem.* **1974**, *39*, 272. (j) Spear, R. J.; Norris, W. P.; Read, R. W. *Tetrahedron Lett.* **1983**, 1555. (k) Strauss, M. J. *Chem. Rev.* **1970**, *70*, 667.

[14] Heesing, A.; Schinke, U. *Chem. Ber.* **1977**, *110*, 2867–2871.

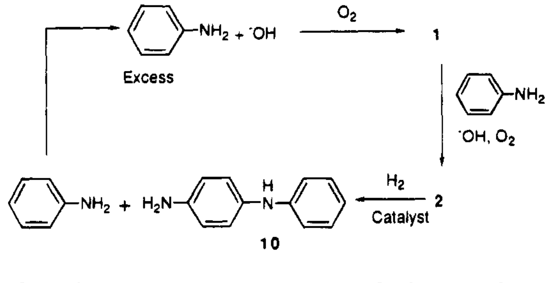
[15] A 66% yield of **2** is the theoretical limit if all the hydrazobenzene is converted to azobenzene via a disproportionation reaction.

[16] Jeon, S.; Sawyer, D. T. *Inorg. Chem.* **1990**, *29*, 4612–4615.

Scheme 3



Scheme 4

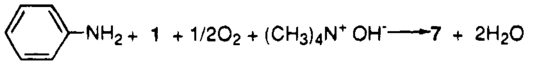


of hydrazobenzene was occurring with the simultaneous oxidation of aniline to azobenzene, aniline-d_5 would have to be observed in the reaction along with significant quantities of **2**. The mass spectral analysis of the reaction mixture showed no aniline-d_5 and only trace amounts of **2** (<5%). The predominant product of the reaction was **2b**. We conclude from this data that regeneration of azobenzene from hydrazobenzene in this process does not proceed via a disproportionation mechanism.

An alternate mechanism for the regeneration of azobenzene that is consistent with all the observed experimental findings is the aerobic oxidation of hydrazobenzene under basic conditions (Scheme 3).[17] The H_2O_2 coproduced by this process would be expected to be unstable to the reaction conditions and decompose ultimately to give water, O_2, and hydroxide ion (eq 3).[16] This mechanism

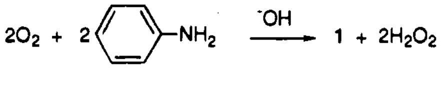
$$\mathrm{HOOH} + \mathrm{HOO}\cdot \longrightarrow \mathrm{H_2O} + \mathrm{O_2}^{-} + \mathrm{HO}\cdot \longrightarrow \mathrm{H_2O} + \mathrm{O_2} + {}^{-}\mathrm{OH} \quad (3)$$

successfully explains the observed instability of the hydrazobenzene when the reaction is run without the exclusion of O_2 and its persistence when strictly anaerobic conditions are maintained. Furthermore, the complete recycling of hydrazobenzene by this pathway is consistent with the near quantitative yield of **2** observed in the reaction. The balanced chemical equation (eq 4) derived from the reactions shown in Schemes 2 and 3 and eq 3 is consistent with the observed stoichiometry and requirement for the aerobic oxidation of hydrazobenzene.



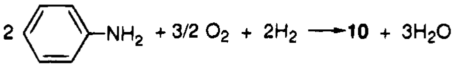
(4)

The ability to prepare **2** in high yield from the reaction of aniline and azobenzene forms the basis of a new route for the production of 4-ADPA (Scheme 4). Hydrogenation of **2** generates the desired product and a mole of aniline which can be recycled. It is also important to point out that azobenzene is the product of the aerobic oxidation of aniline (eq 5).[16] Thus, it is possible to envision a route



(5)

to 4-APDA which is based on aniline, uses O_2 as the oxidizing agent, and produces water as the only byproduct. Accordingly, the net equation (eq 6) for the overall process would be



(6)

In conclusion, the reaction between aniline and azobenzene is a new example of nucleophilic aromatic substitution for hydrogen that has the unprecedented characteristics of using an azo group both as the activating electrophile and as an intermediate oxidant. In addition, this series of reactions demonstrates a novel synthetic route to 4-ADPA that ultimately utilizes O_2 as the terminal oxidant, eliminates the need for halogenated reagents and intermediates, and generates water as the major byproduct in the synthesis of this important aromatic amine.

Experimental Section

General Procedures. Reactions were monitored by reversed-phase HPLC using biphenyl as the internal standard. A Waters 600 series HPLC equipped with a Vydac 201HS54 (4.6 × 250 mm) column with UV detection at 254 nm was employed in all the analysis. Elution gradient: initial conditions = 75% A and 25% B, flow rate 1.5 mL/min; 0–35 min, 20% A and 80% B; 35–40 min, 100% B; 40–45 min, 100% B. Solvent A = water, solvent B = 40% methanol in acetonitrile. Solvents were rigorously purged with oxygen-free helium to allow for the quantitation of 1,2-diphenylhydrazine. Under these conditions the following retention times were observed: *trans*-azobenzene (35.5 min), 1,2-diphenylhydrazine (27 min), 4-(phenylazo)diphenylamine (40.5 min), 2-(phenylazo)diphenylamine (43.5 min), biphenyl (33.1 min). Low-resolution mass spectral analyses were carried out by electron impact (EI) and methane chemical ionization (CI-CH_4) on a Finnigan 4500 system equipped with a Teknivent Vector Two data system. High-resolution mass spectral analyses were carried out on a Finnigan MAT Model 90. Biphenyl, 1,2-diphenylhydrazine, 18-crown-6, 4-(phenylazo)diphenylamine, potassium *tert*-butoxide, nitrobenzene-d_5, and aniline-d_5 were purchased from Aldrich Chemical Co. All were used without further purification. Azobenzene, which was contaminated with small amounts of azoxybenzene, was purchased from Eastman Kodak and was purified by chromatography on basic alumina (toluene:petroleum ether 1:4). Tetramethylammonium hydroxide pentahydrate (Aldrich) was converted to the dihydrate by lyophilization overnight. The extent of hydration of the resulting salt was determined by standard titration techniques.

Preparation of 4-(Phenylazo)diphenylamine (2) Using *tert*-Butoxide. To a stirred solution of aniline (5 mL, 52 mmol) were added azobenzene (1.8 g, 10 mmol), potassium *tert*-butoxide (2.24 g, 20 mmol), 18-crown-6 (2.64 g, 10 mmol), and biphenyl (0.55 g, 3.5 mmol). The reaction was stirred at 70 °C for 12 h under a nitrogen blanket without any precautions to rigorously exclude oxygen. Analysis of the reaction mixture by HPLC showed a 98% yield of 4-(phenylazo)diphenylamine based on azobenzene. Methylene chloride (25 mL) was added to the reaction mixture which was then washed with water. The organic layer was separated and dried over $MgSO_4$. The crude product was chromatographed on silica (9:1 hexane:ethyl acetate) to obtain 2.6 g (96% yield based on azobenzene) of the desired product as an orange-yellow powder which co-

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(17) Calderwood, T. S.; Sawyer, D. T. *J. Am. Chem. Soc.* **1984**, *106*, 7185–7186.

eluted on HPLC with an authentic sample of **2**. Chemical ionization high-resolution mass spectrometry: observed M + H 274.1306, calculated 274.1344 Δmmu = −3.841.

Preparation of 2 Using Tetramethylammonium Hydroxide. A 25% aqueous solution of tetramethylammonium hydroxide (10 mL, 27 mmol) was subjected to vacuum distillation at 60 °C to remove water. When a solid precipitate began to form, aniline (5 mL, 52 mmol) and azobenzene (1.8 g, 10 mmol) were added. The solution was stirred for 8 h at 60 °C under vacuum (20 Torr) to remove water after which time 10 mL of 90% methanol was added. The resulting precipitate was filtered under suction to obtain a crude product. Recrystallization from 90% methanol afforded 2.6 g of 4-(phenylazo)diphenylamine as an orange-yellow solid in 96% yield based on azobenzene. Similar yields of 4-(phenylazo)diphenylamine are obtained if TMA(OH)·$2H_2O$ is initially used as the source of hydroxide.

Reaction of Aniline and Azobenzene under Anaerobic Conditions. Azobenzene (0.92 g, 5 mmol), potassium *tert*-butoxide (1.12 g, 10 mmol), 18-crown-6 (1.4 g, 5.3 mmol), and biphenyl (0.1 g, 0.6 mmol) were mixed in 10 mL of rigorously degassed aniline in an argon-filled controlled-atmosphere drybox. The reaction was stirred at 60 °C during which time aliquots were removed at various times. Each sample was dissolved in oxygen-free methanol and subjected to routine HPLC analysis to determine the yield of 1,2-diphenylhydrazine and 4-(phenylazo)diphenylamine (Figure 1).

Isotopic Labeling Experiments. Reaction of Aniline-d_5 and Azobenzene. Azobenzene (0.36 g, 1.9 mmol), potassium *tert*-butoxide (0.45 g, 4.0 mmol), 18-crown-6 (0.55 g, 2 mmol), and aniline-d_5 (2.0 g, 20.4 mmol) were stirred at 80 °C under nitrogen for 12 h. The reaction was quenched with 0.5 mL of glacial acetic acid and 2 mL of ethyl acetate. The organic phase was washed with water and dried over $MgSO_4$. Electron impact mass spectral analysis of the reaction product showed a peak at *m/z* = 278 consistent with the assignment of the product as 4-(phenylazo)diphenylamine-d_5.

Reaction of Aniline and Azobenzene-d_{10}. Azobenzene-d_{10} (0.36 g, 1.87 mmol), potassium *tert*-butoxide (0.45 g, 4.0 mmol), 18-crown-6 (0.55 g, 2 mmol), and aniline (2.0 g, 21.5 mmol) were stirred at 80 °C under nitrogen for 12 h. The reaction was quenched with 0.5 mL of glacial acetic acid and 2 mL of ethyl acetate. The organic phase was washed with water and dried over $MgSO_4$. Electron impact mass spectral analysis of the reaction product showed a peak at *m/z* = 282 consistent with the assignment of the product as 4-(phenylazo)diphenylamine-d_9.

Preparation of Azobenzene-d_{10}. A modification of the method of Bigelow was used.[18] A suspension of nitrobenzene-d_5 (2.5 g, 19.5 mmol), Zn dust (2.65 g), NaOH powdered (3.25 g, 81.2 mmol), 7.5 mL of water, and 25 mL of methanol was stirred at reflux under nitrogen for 12 h. The solid was filtered hot and water was added to the filtrate to cause precipitation. The resulting yellow solid was filtered and dried under suction. The yellow solid, which is a mixture of 1,2-diphenylhydrazine and azobenzene, was stirred in 50 mL of ether with 3 g of AgO at room temperature for 1 h. The solution was filtered and the filtrate was concentrated under vacuum to yield 1.5 g (80%). Analysis of the orange solid by electron impact mass spectrometry showed a peak at *m/z* = 192 consistent with the desired product.

Determination of k_H/k_D by Competition Studies. Aniline (1.5 mL, 4.0 mmol) was mixed with azobenzene-d_0 (0.18 g, 1 mmol), azobenzene-d_{10} (0.19 g, 1 mmol), and tetramethylammonium hydroxide dihydrate (0.8 g, 6.2 mmol) in an argon-filled controlled-atmosphere drybox. The solution was stirred at 53 °C for 12 h. A portion of the reaction was removed, dissolved in ethyl acetate, and washed with water until the deep purple color changed to orange. The organic layer was separated and dried over $MgSO_4$. The solution was analyzed by chemical ionization mass spectrometry to obtain the ratio of 4-(phenylazo)diphenylamine-d_0 (M + H = 274, average integration area 22223) and 4-(phenylazo)diphenylamine-d_9 (M + H = 283, average integration area 4784).

Preparation of 4-(Phenylhydrazo)diphenylamine (8) via Hydrogenation of 2. 4-(Phenylazo)diphenylamine (5.0 g, 18.3 mmol) (97% purity, Aldrich), 170 mL of aniline, $(CH_3)_4N^+OH^-$ (6.66 g of 25% aqueous solution, 18.3 mmol), and Pt/carbon catalyst (2 g wet weight, Calsicat 120) were charged into a 300-mL stainless steel autoclave (Autoclave Engineers) equipped with a sealless magnetic stirrer and Type J thermocouple. Hydrogen was fed into the autoclave from a 120-mL reservoir charged with 600 psig H_2. The autoclave was maintained at a pressure of 200 psig via a controlling regulator placed between the reservoir and the autoclave. The pressures in both the reservoir and the autoclave were simultaneously measured with Validyne pressure transducers and were continuously recorded on a Molytek data logger. Hydrogen consumption was calculated from the measured drop in reservoir pressure. At a volume of 120 mL, a pressure drop of 3 psi in the reservoir equals approximately 1 mmol of hydrogen.

Hydrogen uptake began upon initiation of stirring (1500 rpm) at a temperature of 23 °C. Hydrogen uptake ceased when the reservoir pressure dropped 53 psig (calculated theoretical uptake: 53.97 psig), after which time stirring was stopped. The autoclave was vented while still maintaining a H_2 pressure (~1 atm) and azobenzene (3.33 g, 18.3 mmol) dissolved in 20 mL of degassed aniline was injected. The reaction was stirred gently for 1 min and was sampled via syringe for immediate HPLC analysis. Only three products were observed from the analysis, **2**, azobenzene (0.83 g, 4.57 mmol), and hydrazobenzene (2.5 g, 13.7 mmol, 75% yield based on azobenzene charged).

Preparation of 4-Aminodiphenylamine (10) via Hydrogenation of 2. A solution containing 4-(phenylazo)diphenylamine (0.30 g, 1.0 mmol), 10 mL of aniline, biphenyl (0.073 g, 0.4 mol), and 200 mg of PtO_2 was charged in a hydrogenation flask and was reacted under 100 psig hydrogen at 70 °C for 12 h. The solution was filtered and subjected to HPLC analysis which showed complete conversion of starting material to 4-aminodiphenylamine.

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(18) Bigelow, H. E.; Robinson, D. B. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. 3, p 103.