

Article

Direct Aniline Formation with Benzene and Hydroxylamine

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Abstract: A single-step method for aniline formation was examined. Using a vanadate catalyst with an iron oxide co-catalyst and hydroxylamine hydrochloride as the amine source, an up to 90% yield of aniline was obtained with high selectivity. Further study showed that the overall reaction was pseudo-second order in terms of hydroxylamine concentration. Regioselective H-D exchange experiments suggest that the C-N bond formation step occurs via an irreversible electrophilic pathway. Based on all of the key observations, a mechanism is proposed.

Keywords: vanadium; catalysis; aniline; C-H activation

1. Introduction

Aniline is produced annually in massive amounts as a broadly used industrial material [1]. The current industrial method for aniline production is a two-step process: the nitration of benzene followed by catalytic hydrogenation of nitrobenzene [2]. The traditional aniline production method has proved to be economically efficient but not atom-efficient. Consequently, chemists have been interested in aniline production via direct benzene amination, with the ideal method combining ammonia and benzene with oxygen as the oxidant. A series of catalysts and conditions have been studied; however, these methods failed to provide high selectivity and yields of aniline [3,4].

To avoid the difficulty of cleavage of both an aromatic C-H bond and ammonia N-H bond in the same system, an alternative pathway is to use hydroxylamine as the amination reagent. This route has become increasingly attractive as new achievements have been reported on hydroxylamine production and the related mechanisms [5]. An example reported by Kuznetsova et al. in 2000 shows the possibility of aniline formation with hydroxylamine using a transition metal catalyst in acidic aqueous solution [6]. The reaction gives 3–47% yields of aniline with vanadium oxide catalysts under different conditions. Further developments were reported by Zhu et al. using sodium metavanadate as the catalyst in acetic acid aqueous solution [7]. After screening different conditions, the best combination of temperature, solvent, reaction time, and catalyst loading gave a 60–70% yield of aniline. In 2016, Chen and Yang reported a catalyst comprised of vanadium-containing molecular sieves that showed similar reactivity [8]. The above reports demonstrate that a vanadium salt is capable of catalyzing the direct amination reaction between hydroxylamine and benzene while still leaving ample room to improve the yield and selectivity.

To further improve benzene amination by hydroxylamine, a variety of vanadium complexes and co-catalysts were screened in our lab under a variety of reaction conditions (Equation (1)). Under optimized conditions, the yield was improved to over 90% with high selectivity. The loss of yield is a result of polymerization of the aniline product, leaving the potential for an even higher yield if this side reaction can be subverted. The change in vanadium oxidation state was also studied, along with the regioselectivity and the kinetic behavior of the system. Based on our observations and results, a new mechanism is proposed.



Citation: Liu, N.; Sleck, M.D.; Jones, W.D. Direct Aniline Formation with Benzene and Hydroxylamine. *Chemistry* **2023**, *5*, 2056–2067. <https://doi.org/10.3390/chemistry5040139>

Academic Editor: George O'Doherty

Received: 2 August 2023

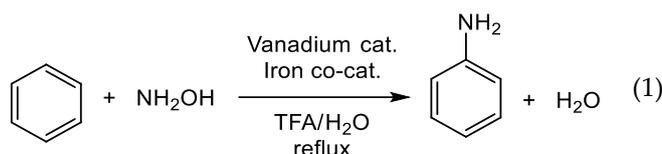
Revised: 18 September 2023

Accepted: 20 September 2023

Published: 23 September 2023



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2. Materials and Methods

2.1. General Considerations

Hydroxylamine hydrochloride and trifluoroacetic acid were obtained from Sigma-Aldrich Chemical Co. and used as received. Sodium metavanadate and iron oxide were obtained from Strem Chemicals, Inc. GC analysis was performed on a Shimadzu GC17A (Shimadzu U.S.A. Manufacturing, Inc., Canby, OR, USA) or GC2010 gas chromatograph equipped with a 30 m × 0.25 mm (0.5 μ film) DB-WAXETR column. X-band EPR spectra were recorded on a Bruker EMXplus spectrometer (Bruker BioSpin Corporation, Billerica, MA, USA) equipped with a 4119HS cavity and an Oxford ESR-900 helium flow cryostat. The instrument parameters for all samples were as follows: 5 K; 0.5 mW power; modulation amplitude 8 G; 9.38 GHz; modulation frequency 100 kHz.

2.2. General Procedure for Amination Reaction (Entry 6)

To a 25 mL two-neck flask fitted with a reflux condenser was added 208.4 mg (3.00 mmol) of hydroxylamine hydrochloride, 11.0 mg sodium metavanadate NaVO_3 (0.09 mmol, 3% vs. hydroxylamine), 7.2 mg Fe_2O_3 (0.045 mmol, 1.5% vs. hydroxylamine), 8 mL of trifluoroacetic acid, and 2 mL of water. The solution was stirred while heating to reflux until a clear light green solution formed, about 20 min. At this point, 0.82 g (10.5 mmol, 3.5 equiv) benzene was introduced and the reaction was refluxed for 5 h under an air atmosphere. For GC analysis, a syringe was used to collect a 0.1 mL aliquot of the reaction solution, which was neutralized with 1 mL 40% sodium hydroxide aqueous solution. The product was extracted with 10 mL of diethyl ether. All insoluble solid products were removed by filtration through cotton prior to examination via GC. For NMR analysis, a 1 mL sample of the reaction solution was neutralized with 40% sodium hydroxide solution, then extracted with diethyl ether and dried over MgSO_4 . The ether and the unreacted benzene were removed under vacuum to give aniline as a yellow liquid. Further details and yields are provided in Table 1 and in the Supplementary Materials.

Table 1. Aniline yields under different conditions ^a.

Entry	Catalyst	Catalyst Loading (%)	Co-Catalyst	Co-Catalyst Loading (%)	Solvent (4:1, v:v)	Temp. (°C)	Yield (%)
1	VO(OMe)-(EIMP) ^b	1	-	N/A	AcOH:H ₂ O	80	22
2	VO(acac) ₂	1	-	N/A	AcOH:H ₂ O	80	trace
3	NaVO ₃	1	Fe ₂ O ₃	1.5	AcOH:H ₂ O	90	32
4	NaVO ₃	3	-	N/A	TFA:H ₂ O	70	11
5	NaVO ₃	1	Fe ₂ O ₃	1	TFA:H ₂ O	100	96 ^c
6	NaVO ₃	3	Fe ₂ O ₃	1.5	TFA:H ₂ O	100	85–40 ^d
7	NaVO ₃	3	Fe ₂ O ₃	3	TFA:H ₂ O	r.t.	0
8 ^e	NaVO ₃	1	Fe ₂ O ₃	1	TFA:H ₂ O	100-r.t.	21
9 ^f	NaVO ₃	3	Fe ₂ O ₃	3	TFA	100	3

Table 1. Cont.

Entry	Catalyst	Catalyst Loading (%)	Co-Catalyst	Co-Catalyst Loading (%)	Solvent (4:1, v:v)	Temp. (°C)	Yield (%)
10	-	-	Fe ₂ O ₃	3	TFA:H ₂ O	100	trace
11 ^g	NaVO ₃	3	Fe ₂ O ₃	3	TFA:H ₂ O	100	53
12	V-cluster A	3	Fe ₂ O ₃	3	TFA:H ₂ O	100	58
13 ^h	V-cluster A	3	FeSO ₄	3	TFA:H ₂ O	100	26
14 ⁱ	V-cluster A	50	-	N/A	TFA:H ₂ O	100	0
15	Mn(acac) ₂	3	-	N/A	TFA:H ₂ O	100	0
16	NaMoO ₃	3	-	N/A	TFA:H ₂ O	100	0
17	NaMoO ₃	3	Fe ₂ O ₃	3	TFA:H ₂ O	100	0

^a Reaction time is 5 h unless otherwise noted. The catalysts and 3.0 mmol [NH₃OH]Cl were dissolved in 10 mL

solvent (0.3 M), then 0.94 mL benzene was injected; ^b EIMP: , R=H, t-Bu; ^c 6 mL solvent instead of 10 mL, product mixture contains solid polyaniline; ^d product mixture contains trace amount of polyaniline; ^e reacted at 100 °C for 30 min, then at room temperature for 48 h; ^f reaction in TFA solvent; ^g 1 equiv. of benzene. ^h reaction under nitrogen; ⁱ no hydroxylamine added, but cluster A contains 2 molecules of co-crystallized hydroxylamine per vanadium.

3. Results

3.1. Identification of a Vanadium Catalytic System for Aniline Formation

The initial investigations of the amination of benzene using hydroxylamine hydrochloride were carried out by examining several vanadium compounds and transition metal oxidants as catalysts. The reactions were carried out under reflux open to the air. The compounds VO(OMe)(EIMP), VO(acac)₂, NaVO₃, NaMoO₃, and Mn(acac)₂ were examined as catalysts in acetic acid/water solvent (4:1, v:v) at 1–3% catalyst loading (conditions similar to those reported previously [7], EIMP = 2-[(2-hydroxyethyl)imino]methylphenol). It was found that using an aqueous trifluoroacetic acid solvent mixture (TFA:H₂O, 4:1, v:v) resulted in superior yields of aniline, and that the addition of iron oxide resulted in even higher yields. GC analysis showed aniline formation with no other soluble byproducts. A black precipitate formed as the reactions approached completion that was identified as polyaniline (emeraldine salt, vide infra) [9].

In no case was aniline or an organometallic product seen when these metal compounds were treated with benzene in the absence of hydroxylamine, which indicates that the catalysts were activating the hydroxylamine towards reaction with benzene, rather than the other way around. Table 1 shows the different catalysts, conditions, and additives tested. The most efficient (and inexpensive) system involved both sodium vanadate and iron oxide as co-catalysts.

After testing a variety of conditions, it was observed that all vanadium complexes showed similar performance during the reaction, suggesting that the ligands simply dissociate under the strong acidic reaction conditions. Changing the iron:vanadium ratio only slightly influenced the aniline yield. Keeping the amounts of solvent and catalyst constant, a decrease in hydroxylamine concentration led to less polymerization, but at the expense of the yield of aniline. Increasing the reaction time also resulted in a drop in aniline yield due to the polymerization reaction.

Although the net reaction is a straightforward bimolecular dehydration reaction, the observation of multiple color changes as the reaction progressed indicates a more complicated process. To maximize the aniline yield, the catalysts were first reacted with hydroxylamine to form the active species followed by addition of benzene. From the clear initial reaction solution, a black solid was observed at the end of the reaction. The black solid was confirmed to be polyanilinium trifluoroacetate via infrared spectroscopy. The spectrum matches that of protonated polyaniline as reported by Stejskal [10] with an additional peak at 1666 cm⁻¹ for the trifluoroacetate counterion. The polymer was removed before determining the yield of aniline using GC. Thus, the mass balance was not complete from the GC analysis. A trace amount of *N*-phenyl-*p*-phenylenediamine was observed in the GC spectrum, which is consistent with the formation of polyaniline. A trace amount of

phenol was also observed in the GC spectrum as a side product. No bis-aminated product was observed.

To gain insight into the mechanism, our first effort was to attempt to isolate intermediates from the reaction. A blue vanadium(IV) cluster (**A**) was crystallized from the reaction solution prior to the addition of benzene (Figure 1). The structure of **A** shows two symmetry-related octahedral $[\text{V}^{\text{IV}}\text{O}(\text{O}_2\text{CCF}_3)_4(\text{H}_2\text{O})]^{2-}$ complexes bridged by sodium ions. There are also three additional waters (one attached to Na^+ , two outer sphere), two hydroxylammonium cations, and one trifluoroacetate anion in the asymmetric unit, which balance the charge of the V^{IV} complex. The co-crystallized hydroxylammonium trifluoroacetate indicate that vanadium is not further reduced to vanadium(III) even with excess hydroxylamine present at room temperature. However, upon heating the blue solution with hydroxylamine, the change of color from blue to green indicates the possibility of vanadium(IV) reduction to vanadium(III). No decomposition was observed after the crystal was exposed to air for several months. When cluster **A** was used to replace sodium metavanadate as the catalyst in a 1:1 vanadium ratio, similar observations and aniline yields were obtained under the same reaction conditions. These observations support that the initial step is the reduction of vanadium(V) to vanadium(IV) by hydroxylamine. A related complex, $\text{Na}_4(\text{VO})_2(\text{CF}_3\text{CO}_2)_8(\text{THF})_6(\text{H}_2)_2$, was structurally characterized by Cotton [11].

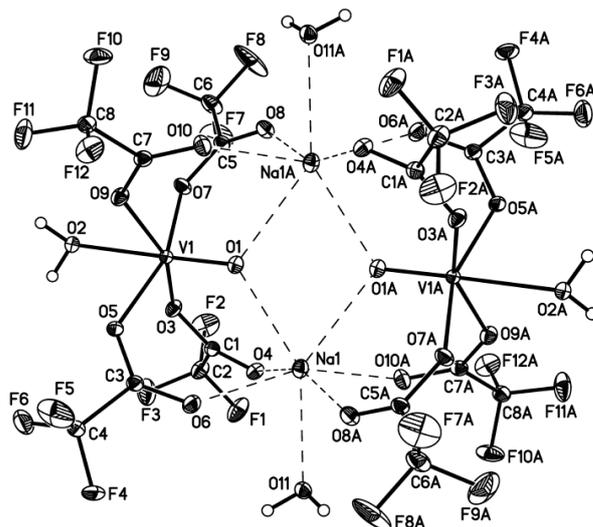


Figure 1. Crystal structure of vanadium cluster **A**, $[\text{Na}_2(\text{VO})_2(\text{O}_2\text{CCF}_3)_8(\text{OH}_2)_4]^{2-}$, omitting exogenous $[\text{O}_2\text{CCF}_3]^-$, $[\text{NH}_3\text{OH}]^+$, and H_2O . The complete formula of the crystalline material in the unit cell is $[\text{NH}_3\text{OH}]_4[\text{Na}_2(\text{VO})_2(\text{O}_2\text{CCF}_3)_8(\text{OH}_2)_4][\text{O}_2\text{CCF}_3]_2 \cdot 4\text{H}_2\text{O}$.

The structure of **A** shows no vanadium–nitrogen bond, suggesting the activation of hydroxylamine is through an oxidation process instead of metal coordination. The crystal structure also shows co-crystallized hydroxylammonium trifluoroacetate in a 2:1 ratio to vanadium in the cluster, which suggests that the cluster is the active species during the reaction. However, the reaction of the cluster and benzene (3.5 equiv. vs hydroxylammonium in the cluster as determined by elemental analysis of nitrogen) with no additional hydroxylamine produced no aniline. This result argues against the cluster as the active intermediate.

To explore the possibility that there could be a V-Fe cluster in solution, the vanadium(IV) crystalline material (**A**) was treated with iron oxide. The iron oxide precipitated separately from the solution with no reaction. Finding no evidence that iron coordinated with hydroxylamine or benzene, it is believed that iron played a role as an electron shuttle between vanadium and hydroxylamine. To confirm this possibility, the reaction was tested under oxygen-free conditions using a nitrogen atmosphere with the vanadium(IV) cluster **A** and FeSO_4 . While the aniline was observed, the yield was about half of that observed under an atmosphere of air, and polyaniline formation was only observed when the sample was

neutralized. We conclude that vanadium(V) is not necessary for aniline formation, which is consistent with the hypothesis that vanadium(IV) can be further reduced to vanadium(III) during the reaction. Thus, the observations strongly suggest that hydroxylamine was activated when it was oxidized during reduction of V^V to give an active intermediate. The observation of polymerization suggests that an intermediate in forming the aniline product is the aniline radical cation, which becomes the chain initiator to produce polyaniline.

In an effort to observe an intermediate in the reaction, a reaction was run using the conditions of entry 6 in Table 1. After 45 min, a 0.3 mL aliquot was transferred to an EPR tube and freeze-quenched in liquid nitrogen. The EPR spectrum was immediately recorded, as shown in Figure 2. Two species can be readily identified by comparison to spectra in the literature. The iron appears as $[Fe(H_2O)_6]^{3+}$ at $g = 4.24$ as a result of the Fe_2O_3 being hydrolyzed in the strongly acidic aqueous solvent [12]. The other species appearing near $g = 2.0$ is identical to that reported for $[O=V(H_2O)_5]^{2+}$ [13]. Consequently, the metals were seen in their resting states as Fe(III) and V(IV), indicating that the vanadium is indeed reduced by hydroxylamine in the experiment. No evidence for a nitrogen- or carbon-based radical was seen, suggesting that any such species must be short-lived in the reaction.

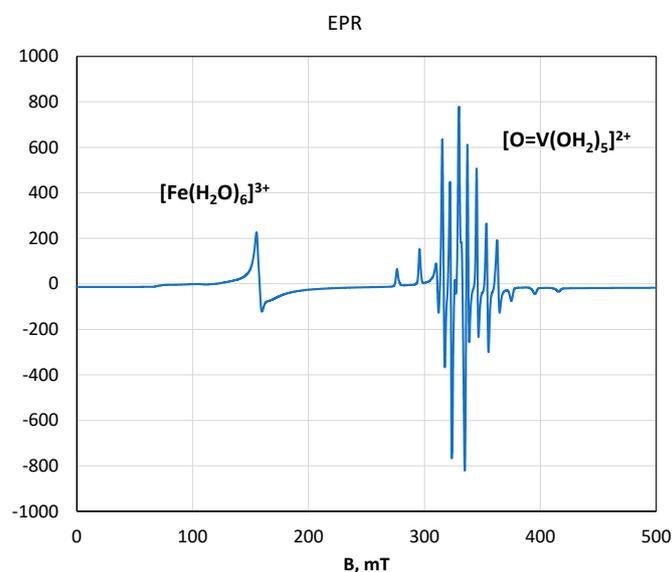


Figure 2. EPR spectrum at 5 K of the reaction mixture from Table 1, Entry 6, after 45 min.

3.2. Kinetic and Mechanistic Study

The variation in reaction yields in Table 1 led us to become interested in the kinetics of the reaction. To best avoid polymerization, the kinetic experiments were performed with lower substrate concentrations. To prevent the formation of solid polyaniline (Table 1, entry 5), the concentration of hydroxylamine was varied over a range below 0.4 M. The brown color of the product solution still indicated that some polymerization occurred, which limited the quality of the kinetic data. Plots of the yield of aniline vs. time for various initial conditions are shown in Table 2 and Figure 3.

Table 2. Effect of variation in hydroxylamine concentration ^a.

Entry	$[NH_3OHCl]$, M	$[NaVO_3]$, mM	cat. Loading, %
1 ^b	0.170	6.0	3.6
2	0.247	6.0	2.4
3	0.295	6.0	2.0
4 ^c	0.408	4.0	1.0
5	0.184	5.5	3.0

^a Reactions carried out with 1:1 $NaVO_3:Fe_2O_3$ in 10 mL 4:1 TFA: H_2O at 100 °C and 0.6 M benzene; ^b 0.5 M benzene; ^c 1.4 M benzene.

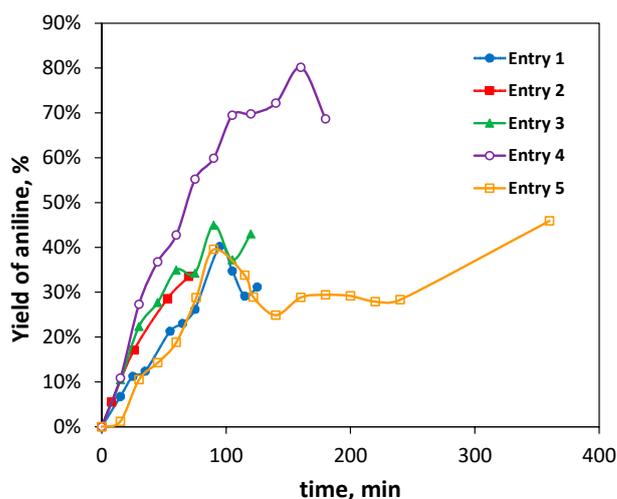


Figure 3. Aniline yield under different initial conditions over time. All experiments are under reflux at 100 °C in 4:1 TFA:H₂O. Mol. ratio NaVO₃: Fe₂O₃ = 1:1.

In these reactions, a decrease in the yield of aniline was observed after a certain time of reaction, which can be associated with the polymerization that occurs only after substantial formation of aniline. A similar decrease in yield was noted in previous reports, but there was no accounting for this decrease other than “experimental error” [7]. When plotting the calculated concentration of hydroxylamine versus time (from the formation of aniline), it is observed that the point at which the disappearance of hydroxylamine stops is strongly correlated with the point at which the aniline concentration decreases, ~60 min (Figure 4). A possible explanation for this is that there are two competing pathways. When the concentration of hydroxylamine is sufficiently low, the effective reduction potential is not high enough to form the active vanadium(IV) intermediate. At the point where the aniline concentration decreases, the pathway switches from vanadium-catalyzed aniline production by oxidizing hydroxylamine to vanadium-catalyzed aniline polymerization [14–16]. The polymerization process consumes aniline at a faster rate than it is produced, but then slows due to the consumption of aniline. This leads to a drop in yield followed by an increase as the aniline production continues. It is worth noting that once the polymerization started, the mass balance of benzene to aniline was poor since some material was lost to polyaniline formation. Therefore, only the data points before the drop in aniline formation were considered for useful kinetic analysis.

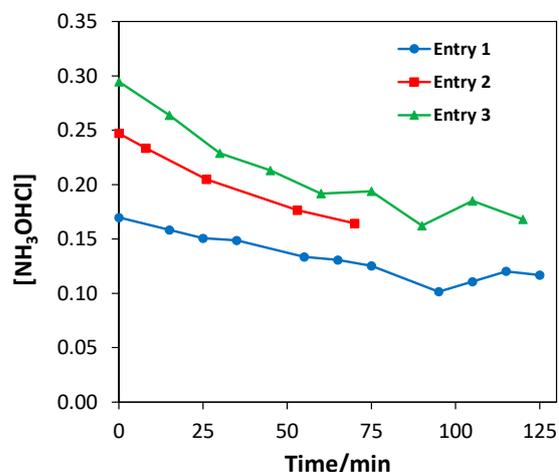


Figure 4. Hydroxylamine concentration vs. time. Hydroxylamine concentration was calculated from measured aniline concentration quantitative conversion without side reactions up to the time where polyaniline formed (~60 min). $[\text{NH}_2\text{OH}]_t = [\text{NH}_2\text{OH}]_0 - [\text{aniline}]_t$.

To analyze the data, the kinetic method reported by Burés was used to determine the reaction order in hydroxylamine [17]. Product concentrations over time were plotted under different initial hydroxylamine concentrations while the concentration of catalyst remained unchanged (Table 2, entries 1–3, Figure 5). The effective concentration of benzene was limited by low solubility in the aqueous reaction solution and was therefore considered to be constant. When plotting the data according to the variable time normalization analysis, hydroxylamine shows second-order kinetic dependence. Plotting $1/[\text{aniline}]$ vs. time for each data set shows good linear behavior, indicating that the reaction is the overall second order in hydroxylamine concentration (Figure 6). The order of vanadium catalyst was not determined due to the significant change in yield when changing the catalyst loading.

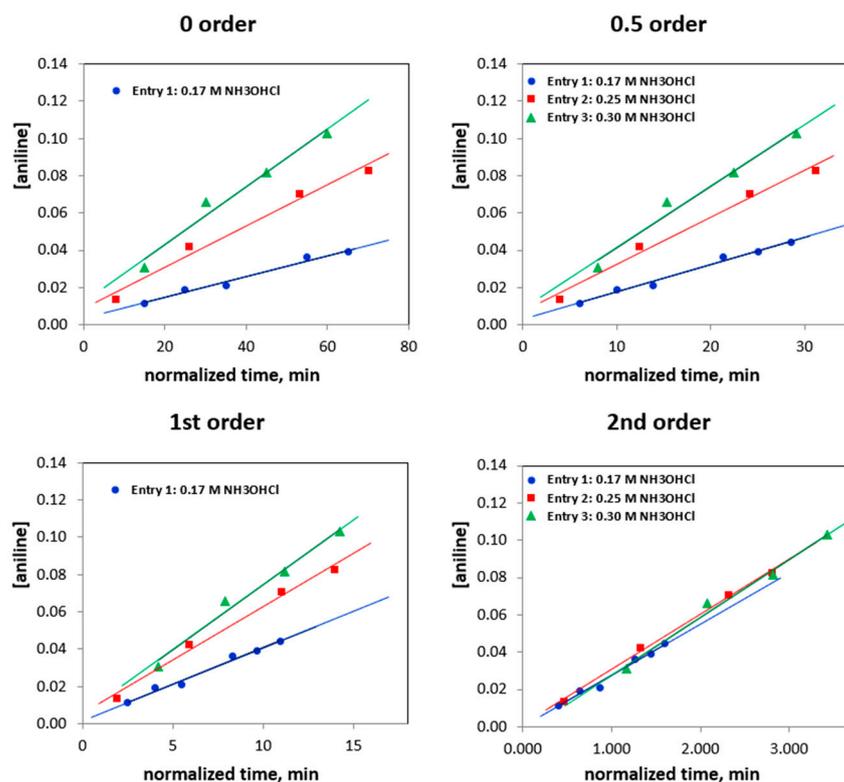


Figure 5. Variable time normalization analysis of aniline concentration. Data points from experiments differing only in hydroxylamine concentration overlay only when the x-axis is the time integral of the hydroxylamine concentration raised to the correct power. Entries 4 and 5 are not included because of different catalyst concentrations.

To gain insight into the activation of the benzene C-H bond, the use of C_6D_6 for aniline formation was examined (Scheme 1). The product was characterized using GC-MS to determine the number of protons exchanged in the process (Table 3). C_6D_6 and hydroxylamine were mixed with the catalysts in H_2O and TFA. The product observed initially had a highest $m/z = 98$ corresponding to $C_6D_5NH_2$, along with a highest fragment peak of $m/z = 71$, arising from loss of HCN where the carbon lost was the ipso carbon [18]. As the reaction proceeded, the major isotopomer had $m/z = 97$, corresponding to $C_6HD_4NH_2$ with a highest fragment peak of 70 after 2 h. After 5 h, the highest mass peak was $m/z = 95$ ($C_6H_3D_2NH_2$), with a highest fragment peak of $m/z = 68$. The H/D exchange continued at room temperature at a slower rate. The decrease in the molecular weight of the product to $m/z = 95$ strongly indicates H-D exchange of the aromatic ring, where at most three deuteriums were replaced by hydrogens. When looking at the benzene peak in the above GCMS experiments, no H/D exchange was observed, which also proved that the formation of the C-N bond was not reversible.

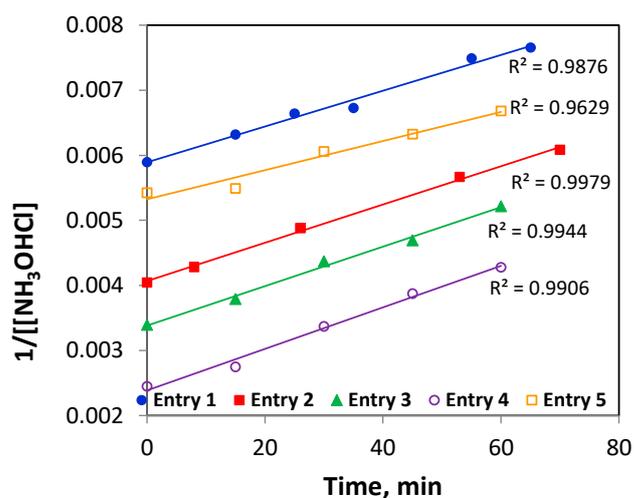
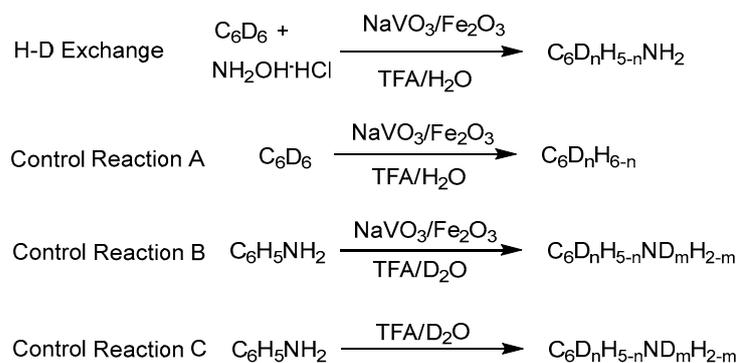


Figure 6. Second-order rate law approximation for aniline formation reactions under different initial conditions (first 60–70 min).



Scheme 1. H-D exchange reactions.

Table 3. GC-MS results for H-D exchange reactions.

Reaction	Reaction Time	Peak (<i>m/z</i>)	Relative Intensity (%)	Number of Atoms Exchanged (D→H)
H-D exchange	2 h	95	18.1	1
		96	62.6	
		97	100	
		98	79.4	
		99	4.5	
H-D exchange	5 h	94	11.9	3
		95	100	
		96	65.1	
		97	20.3	
Control A	5 h	84	100	0
		93	69.0	
		94	100	
		95	64.7	
Control B	5 h	96	16.0	1
		93	100	
		94	85.2	
		95	30.1	
Control C	5 h	96	4.8	0
		93	100	
		94	85.2	

Although H-D exchange of benzene is known to occur in the presence of TFA and water under specific conditions [19], a control reaction (Scheme 1, A) showed no MS peak at $m/z = 83$ (C_6D_5H), suggesting that the reaction conditions in this work were not sufficient for benzene H-D exchange. Control reactions B and C rule out the possibility of aniline aromatic C-H activation by the catalyst system. The minor MS peaks at $m/z = 95$ and 96 are considered as H-D exchange of the amine group through protonation and deprotonation and cannot be used to prove that H-D exchange has occurred on the aromatic ring. In conclusion, the catalyst system does not activate aromatic C-H bonds of aniline or benzene in the absence of NH_2OH . This conclusion supports our hypothesis that the key step of aniline formation is hydroxylamine activation.

To understand the regioselectivity of H-D exchange, the 1H NMR spectrum of the aniline produced by the reaction of C_6D_6 and NH_2OH in TFA/ H_2O was examined. In the aromatic region, only two singlets are observed at δ 6.51 (1 H, para-substituted) and 6.58 (2 H, ortho-substituted). A singlet at δ 5.01 ppm corresponds to the amine group. Only the in-situ-produced aniline underwent aromatic H-D exchange at the para- and ortho- positions under these conditions, which leads to the assumption of an aniline radical cation intermediate.

Surprisingly, high yields were not obtained when applying the same system to other aromatic substrates (Table 4). Toluene gave a combined yield of 33% for para- and ortho-substituted products. Trifluorotoluene only gave a trace amount of meta-trifluoromethyl aniline. Naphthalene gave 1-naphthylamine as the only product with a yield of 31%. Chlorobenzene and fluorobenzene gave <10% yield. Phenol, anisole, aniline, styrene, and pyridine gave no amination product under the same conditions. It is possible that the formation of an iron(III)-phenol complex in aqueous solution prevents phenol and anisole (which decomposes to phenol under such strongly acidic conditions) from reacting with hydroxylamine. However, an experiment using sodium vanadate as the catalyst without the addition of iron co-catalyst still gave no amination product. Considering that iron-benzene complexes are not usually observed other than in charge-transfer reactions [20–22], the explanation of how iron increases the yield of benzene amination is not understood.

Table 4. Aniline formation for other aromatic substrates ^a.

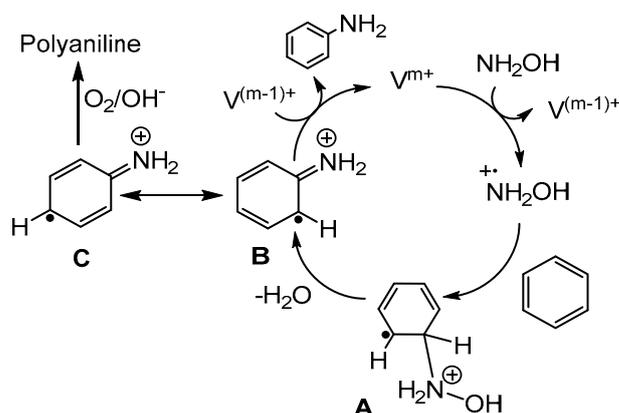
Substrate	Yield (%)
Toluene	33
Trifluorotoluene	trace
Naphthalene	31
Chlorobenzene	7%
Fluorobenzene	trace
Phenol	0
Anisole	0
Aniline	0
Styrene	0
Pyridine	0

^a Reaction conditions: To a 25 mL two-neck flask fitted with a reflux condenser was added 208.4 mg (3.00 mmol) of hydroxylamine hydrochloride, 11.0 mg sodium metavanadate $NaVO_3$ (0.09 mmol, 3% vs. hydroxylamine), 7.2 mg Fe_2O_3 (0.045 mmol, 1.5% vs. hydroxylamine), 8 mL of trifluoroacetic acid, and 2 mL of water. The solution was stirred while heating to reflux until a clear light green solution formed, about 20 min. At this point, 10.5 mmol (3.5 equiv) substrate was introduced and the reaction refluxed for 5 h under an air atmosphere.

3.3. Mechanistic Proposal

Reviewing all the results above, the mechanism shown in Scheme 2 fits all the key observations. First, only vanadium is necessary for the amination reaction; iron does no more than support the reaction. Second, vanadium(V) and vanadium(IV) catalysts have similar performance for both yields and processes, with both reducing to V(III) at the initiation of the reaction. Third, the C-N bond formation step is irreversible. After the C-N bond formation step, the intermediate undergoes an aromatic H-D exchange reaction. In the last stage, the reaction product polymerizes in the strongly acidic environment in

the presence of oxygen but does not polymerize under nitrogen until being neutralized (Scheme 2). The reaction exhibits second-order behavior in hydroxylamine, leading to a hypothesis that the reduction is only triggered when two molecules of hydroxylamine are coordinated to the vanadium center together. The selectivity of aniline H-D exchange and amination of other aromatic substrates comply with the classic rules of electrophilic aromatic substitution, suggesting that the active intermediate behaves as an electrophile rather than a nucleophile.



Scheme 2. Proposed mechanism. Intermediate A, B, and C are not observed directly. B and C undergo radical H-D exchange at para- and ortho- positions.

This mechanism suggests that other sources of NH_2^+ should also work. The same reaction as in Table 1, Entry 6 was carried out using methoxyamine hydrochloride (MeONH_3Cl) in place of hydroxylamine hydrochloride. However, no aniline was observed via GC.

Other possibilities for the mechanism include acylation of the hydroxylamine to make $[(\text{CF}_3\text{CO}_2)\text{NH}_3]^+\text{Cl}^-$, which could act as an electrophilic source of NH_2 . There is precedent in the literature for the direct acylation of hydroxylamine on oxygen rather than nitrogen [23], so this species could lose a proton and then deliver NH_2^+ to the arene (electrophilic amination). This pathway would not require vanadium, however, which is contraindicated by Entry 10 in Table 1. In addition, the acylation of hydroxylamine would have to be competitive with protonation to form $[\text{NH}_3\text{OH}]^+$ under the highly acidic conditions employed in these experiments, which favor $[\text{NH}_3\text{OH}]^+$ as the dominant species. Note that the X-ray structure of A displays two $[\text{NH}_3\text{OH}]^+$ cations and a $[\text{CF}_3\text{CO}_2]^-$ anion within the asymmetric unit. Therefore, for hydroxylamine to be involved in the reaction, $[(\text{CF}_3\text{CO}_2)\text{NH}_3]^+$ would have to be present in equilibrium with its deprotonated form for the mechanism in Scheme 2 to apply.

4. Conclusions

In summary, a vanadium–iron catalytic system to produce aniline directly from benzene in high yield was developed. Using hydroxylamine as the amination reagent, no oxidant was needed for this transformation. This system is currently limited to unsubstituted benzene as the substrate since the other aromatic compounds only exhibit low yields or are not reactive in the system. Based on kinetic study and H/D exchange experiments, a new mechanism is proposed that could help develop the next generation of catalysts for aniline formation.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/chemistry5040139/s1>, detailed experimental procedures, summary of X-ray structural determination of A [24,25].

Author Contributions: Conceptualization, N.L., M.D.S. and W.D.J.; methodology, N.L. and M.D.S.; formal analysis, N.L. and W.D.J.; investigation, N.L. and M.D.S.; writing and editing, N.L. and W.D.J.; supervision, project administration, funding acquisition, W.D.J. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the National Science Foundation under the CCI Center for Enabling New Technologies through Catalysis, CHE-1205189.

Data Availability Statement: Accession Code CCDC #2283056 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Acknowledgments: W.D.J. acknowledges the assistance in obtaining X-ray structures by William W. Brennessel at the X-ray Crystallographic Facility of the Department of Chemistry at the University of Rochester.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Dedication: This manuscript is dedicated to the contributions of Professor Masahiro Miura for his contributions to catalytic chemistry and π -conjugated molecule synthesis.

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