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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 iron oxide co-catalyst and hydroxylamine hydrochloride as amine source, up to 90% yield of aniline could be obtained with high selectivity. Further study shows that the overall reaction is pseudo-second order in 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 has been produced annually in massive amounts as a broadly used industrial material [1]. The current industrial method for aniline production is a two-step process: 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 mechanism [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 a 3-47 % yield of aniline with vanadium oxide catalysts under different conditions. Further developments were reported by Zhu et al. using sodium metavanadate as 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 (eq 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 of 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.

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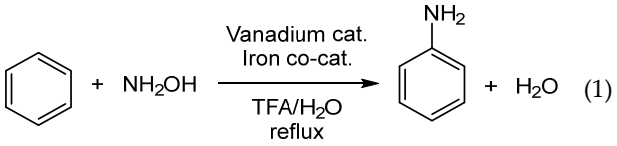


(1)

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 or GC2010 gas chromatograph equipped with a 30m × 0.25 mm (0.5 μ film) DB-WAXETR column. X-band EPR spectra were recorded on a Bruker EMXplus spectrometer 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.

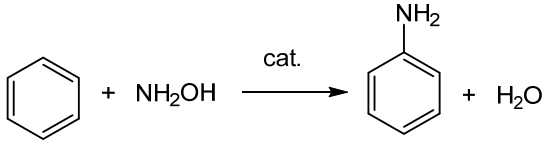
2.2. General procedure for amination reaction (Entry 6). To a 25 mL two-neck flask fitted with a reflux condenser was added 208.4 mg (3.00 mmol) of hydroxylamine hydrochloride, 11.0 mg sodium metavanadate $NaVO_3$ (0.09 mmol, 3% vs. hydroxylamine), 7.2 mg Fe_2O_3 (0.045 mmol, 1.5% vs. hydroxylamine), 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 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 by 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 Supporting Information.

3. Results

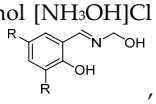
3.1. Identification of a vanadium catalytic system for aniline formation. Initial investigations of the amination of benzene using hydroxylamine hydrochloride were carried out by examining several vanadium compounds and transition metal oxidants as catalyst. Reactions were carried out under reflux open to the air. The compounds VO(OMe)(EIMP), $VO(acac)_2$, $NaVO_3$, $NaMoO_3$, 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]methyl]phenol). It was found that using an aqueous trifluoroacetic acid solvent mixture (TFA:H_2O, 4:1, v:v) resulted in superior yields of aniline, and that 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 indicated that the catalysts were activating the hydroxylamine toward 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.

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_2O	80	22
2	$VO(acac)_2$	1	-	N/A	AcOH:H_2O	80	trace
3	$NaVO_3$	1	Fe_2O_3	1.5	AcOH:H_2O	90	32
4	$NaVO_3$	3	-	N/A	TFA:H_2O	70	11
5	$NaVO_3$	1	Fe_2O_3	1	TFA:H_2O	100	96[c]
6	$NaVO_3$	3	Fe_2O_3	1.5	TFA:H_2O	100	85-40[d]
7	$NaVO_3$	3	Fe_2O_3	3	TFA:H_2O	r.t.	0
8[e]	$NaVO_3$	1	Fe_2O_3	1	TFA:H_2O	100-r.t.	21
9[f]	$NaVO_3$	3	Fe_2O_3	3	TFA	100	3
10	-	-	Fe_2O_3	3	TFA:H_2O	100	trace
11[g]	$NaVO_3$	3	Fe_2O_3	3	TFA:H_2O	100	53
12	V-cluster **A**	3	Fe_2O_3	3	TFA:H_2O	100	58
13[h]	V-cluster **A**	3	$FeSO_4$	3	TFA:H_2O	100	26
14	V-cluster **A**	50	-	N/A	TFA:H_2O	100	0
15	$Mn(acac)_2$	3	-	N/A	TFA:H_2O	100	0
16	$NaMoO_3$	3	-	N/A	TFA:H_2O	100	0
17	$NaMoO_3$	3	Fe_2O_3	3	TFA:H_2O	100	0

[a] Reaction time is 5 hours unless otherwise noted. The catalysts and 3.0 mmol $[NH_3OH]Cl$ were dissolved in 10mL 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-crystalized hydroxylamine per vanadium.

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 indicated 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, black solid was observed at the end of the reaction. The black solid was confirmed to be polyanilinium trifluoroacetate by 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 is removed before determining the yield of aniline by GC. Thus, the mass balance is 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 is also observed in the GC spectrum as a side product. No bis-aminated product is 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 $[V^{IV}O(O_2CCF_3)_4(H_2O)]^{2-}$ complexes bridged by sodium ions. There are also 3 additional waters (one attached to Na^+, two outer sphere), 2 hydroxylammonium cations, and 1 trifluoroacetate anion in the asymmetric unit, which balance the charge of the V^{IV} complex. The co-crystallized hydroxylammonium trifluoroacetate indicated 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 is 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, $Na_4(VO)_2(CF_3CO_2)_8(THF)_6(H_2))_2$ has been structurally characterized by Cotton.[11]

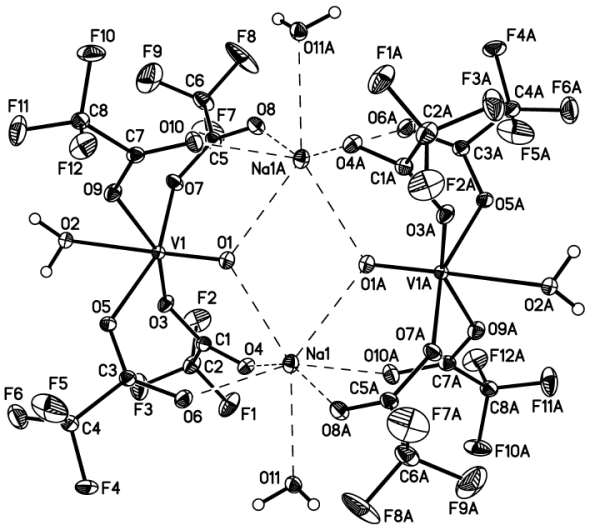


Figure 1. Crystal structure of vanadium cluster **A**, $[Na_2(VO)_2(O_2CCF_3)_8(OH_2)_4]^{2-}$, omitting exogenous $[O_2CCF_3]^-$, $[NH_3OH]^+$, and H_2O. The complete formula of the crystalline material in the unit cell is $[NH_3OH]_4[Na_2(VO)_2(O_2CCF_3)_8(OH_2)_4][O_2CCF_3]_2\ 4H_2O$.

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-crystalized 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 is coordinating with hydroxylamine or benzene, it is believed that iron is playing 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 aniline is observed, the yield is about half of that observed under an atmosphere of air, and polyaniline formation is only observed when the sample is 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 literature spectra. 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 are 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 is seen, suggesting that any such species must be short-lived in the reaction.

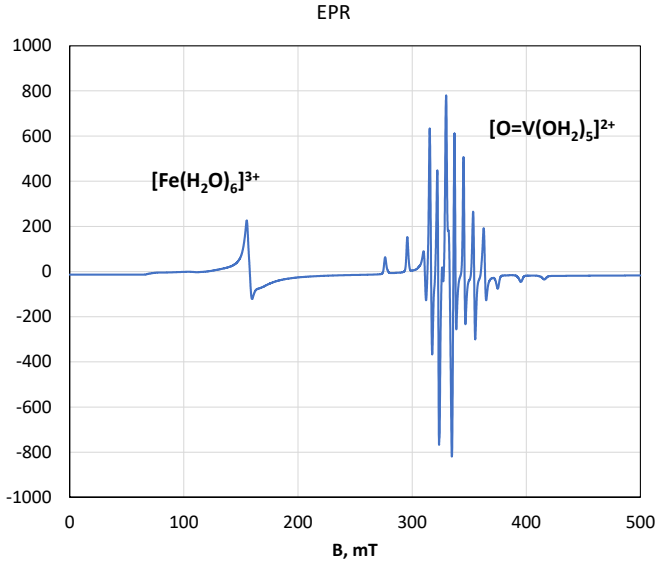


Figure 2. EPR spectrum at 5 K of the reaction mixture from Table 1, Entry 6, after 45 min.

3.2. Kinetic and mechanistic study. The variation of reaction yields in Table 1 led us to become interested in the kinetics of the reaction. To best avoid the polymerization, 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 occurs, 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 of 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.

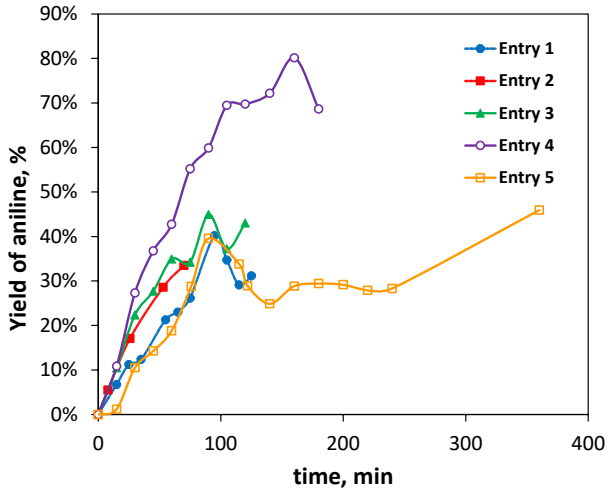


Figure 3. Aniline yield under different initial conditions over time. All experiments are under reflux at 100 °C in 4:1 TFA:H_2O. Mol. ratio $NaVO_3$: Fe_2O_3 = 1:1.

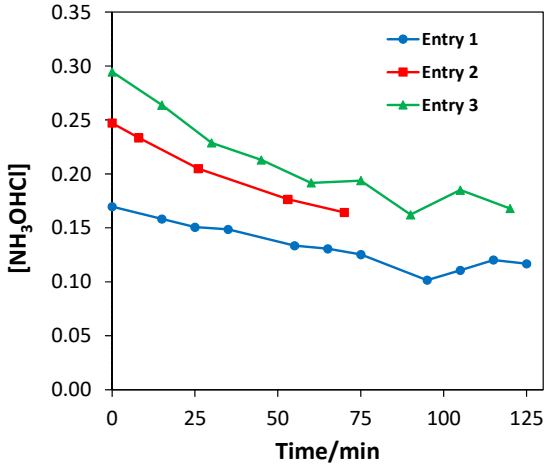


Figure 4. Hydroxylamine concentration vs. time. Hydroxylamine concentration is calculated from measured aniline concentration quantitative conversion w/o side reactions up to the time where polyaniline forms (~60 min). $[NH_2OH]_t = [NH_2OH]_0 - [aniline]_t$

In these reactions, a *decrease* in yield of aniline is 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 will not be 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 is poor since some material is lost to polyaniline formation. Therefore, only the data points before the drop in aniline formation were considered for useful kinetic analysis.

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 is limited by the low solubility in the aqueous reaction solution and is therefore considered to be constant. When plotting the data according to the variable time normalization analysis, hydroxylamine shows a second order kinetic dependence. Plotting 1/[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.

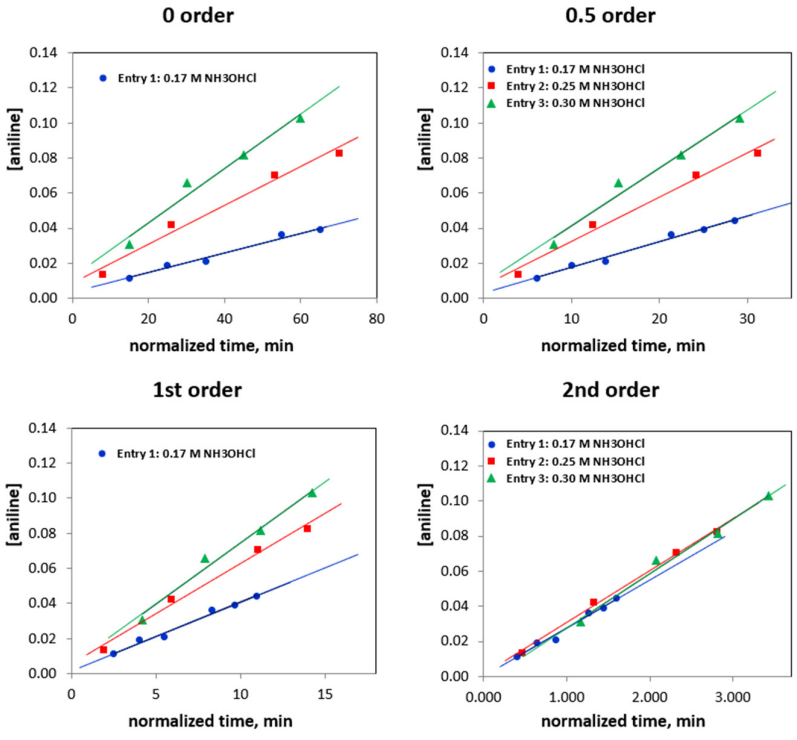


Figure 5. Variable time normalization analysis of aniline concentration. Data points from experiments differing only in hydroxylamine concentration will overlay only when the x-axis is the time integral of the hydroxylamine concentration raised to the correct power. Entries 4 and 5 are not included because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

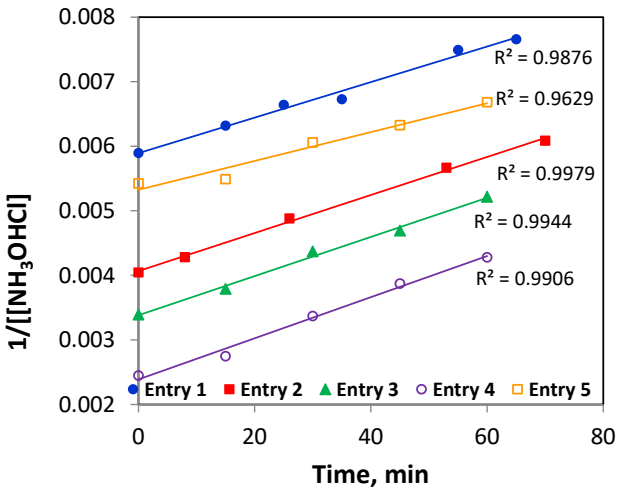


Figure 6. Second order rate law approximation for aniline formation reactions under different initial conditions (first 60-70 min).

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 by 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 is the ipso carbon [18]. As the reaction proceeded, the major isotopomer has m/z = 97, corresponding to $C_6HD_4NH_2$ with a highest fragment peak of 70 after 2 hours. After 5 hours, 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 3 deuteriums are replaced by hydrogens. When looking at the benzene peak in the above GCMS experiments, no H/D exchange is observed, which also proved the formation of the C-N bond is not reversible.

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 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 undergoes aromatic H-D exchange at 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.

Scheme 1. H-D exchange reactions.

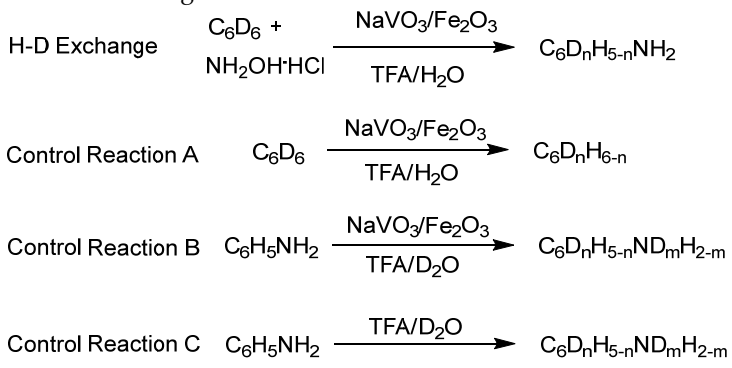


Table 3. GC-MS results for H-D exchange reactions

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

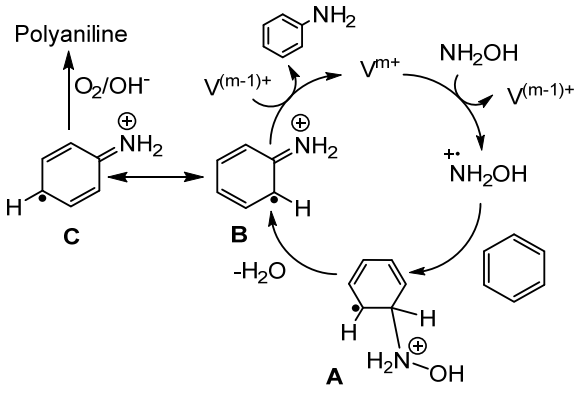
Table 4. Aniline formation for other aromatic substrates[a]

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 minutes. At this point, 10.5 mmol (3.5 equiv) substrate was introduced and the reaction refluxed for 5 hours 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 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 by GC.

Other possibilities for the mechanism include acylation of the hydroxylamine to make $[(CF_3CO_2)NH_3]^+Cl^-$ which could act as an electrophilic source of NH_2. There is literature precedent for 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, acylation of hydroxylamine would have to be competitive with protonation to form $[NH_3OH]^+$ under the highly acidic conditions employed in these experiments, which favor $[NH_3OH]^+$ as the dominant species. Note that the X-ray structure of **A** displays two $[NH_3OH]^+$ cations and a $[CF_3CO_2]^-$ anion within the asymmetric unit. Therefore, for hydroxylamine to be involved in the reaction, $[(CF_3CO_2)NH_3]^+$ would have to be present in equilibrium with its deprotonated form for the mechanism in Scheme 2 to apply.

4. Conclusion

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

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, detailed experimental procedures, summary of X-ray structural determination of **A**. .

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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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