Strong reduction of hydroxylamine accumulation in the catalytic hydrogenation of nitroarenes by vanadium promoters

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The accumulation of hydroxylamines during the catalytic hydrogenation of several aromatic nitro compounds could be reduced from > 40% to < 1% by the addition of catalytic amounts of vanadium promoters, resulting in a faster reaction and purer products.

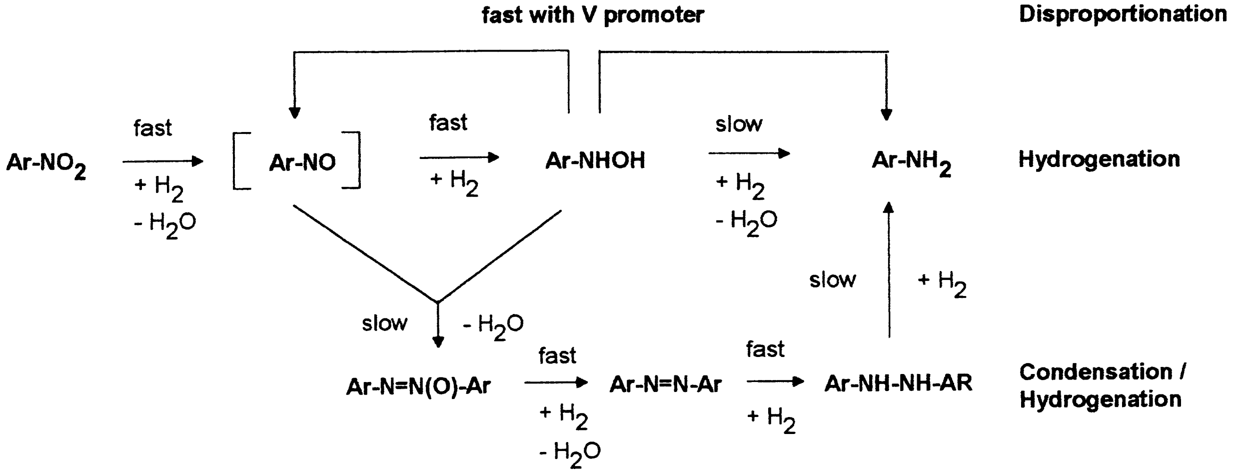
Keywords: catalytic hydrogenation, aromatic nitro compounds, nitroarenes, hydroxylamine accumulation, vanadium promoter

1. Introduction

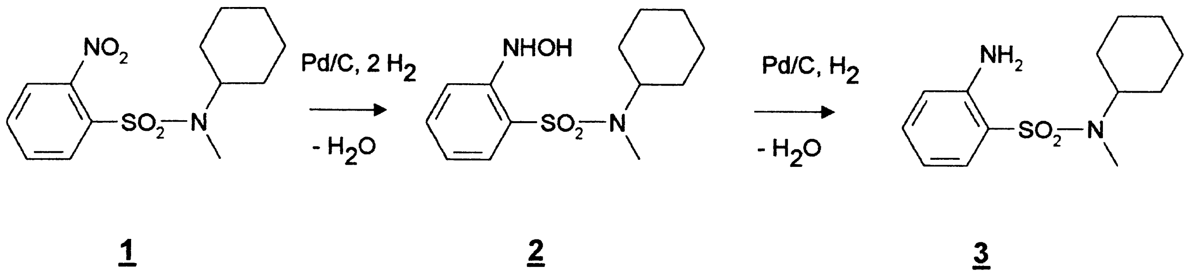
The catalytic hydrogenation of aromatic nitro compounds is industrially important, e.g., for the production of dyes and whiteners, or agrochemical and pharmaceutical intermediates [1]. The reaction proceeds via several intermediates [2]. The most important is the corresponding hydroxylamine species (scheme 1 and [3]). Nitro compounds with electron-withdrawing substituents, e.g., sulfonamide or halogen, accumulate arylhydroxylamines in large amounts during the reaction. This is especially critical when the hydrogenation is carried out in batch reactors at low or medium temperature. Hydroxylamines are problematic in many respects. They are often thermally unstable and can disproportionate with a strong exotherm, causing heavy explosions [4]. They are also known as potent carcinogens and therefore are hazardous in case of interrupted or incomplete hydrogenation [5]. Hydroxylamine accumulation can cause poor product quality because condensation with the nitroso compound leads to the formation of colored azo or azoxy products (lower part of scheme 1). The maximum concentration of hydroxylamines is notoriously difficult to predict [6]; therefore, the product quality can differ from batch to batch. Even though some technical and chemical approaches exist to solve this problem [7], better solutions are clearly needed. The work presented here shows that vanadium promoters can solve the hydroxylamine problem in many cases [8].

2. Experimental

Materials. Benzenesulfonamide-N-cyclohexyl-N-methyl-2-nitro **1** (structures see scheme 2) was supplied by R. Zeller from the Ciba dyestuffs division. All other



Scheme 1. Reaction network of nitroarene hydrogenation.



Scheme 2. Catalytic hydrogenation, structure of model substrate, hydroxylamine intermediate and final product.

reagents and solvents were obtained from commercial suppliers and used without further purification.

Benzenesulfonamide-N-cyclohexyl-N-methyl-2-hydroxylamino: **2** was synthesized according to ref. [9]. M.p. 100–102°C. 1-H NMR (400 MHz, $CDCl_3$): 8.60 ppm (s, 1H), 7.70 (d, 1H), 7.40–7.55 (m, 2H), 6.90–7.00 (dd, 1H), 5.15 (s, 1H), 4.65–4.80 (m, 1H), 2.75 (s, 3H), 0.95–1.80 (m, 10H).

Screening of metal salts. To 10 mg **2** dissolved in 1 ml methanol in a 2 ml glass vial, 2–3 mg metal salt were added. The vial was closed and heated to 65°C for about 60 min. TLC was used to identify the products and to estimate the rate of the reaction.

Catalytic disproportionation. 1 g **2** was refluxed for 3 h with 3–5 mol% of the salt in methanol in a round bottom flask. NMR was used to identify the products after evaporation of the methanol.

Catalytic hydrogenation. 77 g of nitro compound **1** were dissolved in 111 ml THF in an 0.3 ℓ steel autoclave. 530 mg of 5% Pd/C (Johnson Matthey 87L), 1.2 ml acetic acid and 0.006 mol% metal salt relative to **1** were added. The reaction was run at 120°C and 20 bar H_2. Samples were taken at about 22, 44 and 66% hydrogen uptake. Analysis of the samples as well as of the final product was carried out by NMR after evaporation of the solvent.

3. Results and discussion

It was speculated that if a metal ion or complex can increase the disproportionation rate of a given hydroxylamine, then such a promoter might also suppress accumulation thereof. Hydroxylamine **2** was chosen as a model because it is relatively stable and because the corresponding aniline **3** is an important intermediate for a reactive dye. A broad screening of more or less methanol soluble metal salts was carried out. 100 metal salts spanning the whole periodic table were screened. Eleven thereof showed a very fast and fourteen a fast decomposition of the hydroxylamine **2**, mainly to nitroso, azoxy and amine products. The most active were the salts of Ag, Ce, Co, Cu, Cr, Fe, Hg, Mn, Mo, Re, Ru, Ti, Tl, Th and V. These salts can often also act as disproportionation catalysts for H_2O_2. All metals have in common that more than one oxidation state is easily accessible. In some cases, the oxidation state of the metal (e.g., with iron) or the counter ion (e.g., with manganese) also had an influence on the rate of decomposition, but no clear trend was seen.

The twelve most reactive metal salts for decomposition were also tested in catalytic amounts. With eight of them, **2** showed a fast reaction (table 1). In all cases but one (Re), $\geqslant 88\%$ of the starting material was transformed to azoxy, nitroso and aniline product, indicating that most promoters mainly catalyzed the disproportionation of **2**. However, the amount of aniline formed varied considerably from 3% (CuCl) to 71% ($Tl(NO_3)_3$). CuCl obviously catalyzed the oxidation and $Tl(NO_3)_3$ the reduction of the hydroxylamine as well. Oxygen and methanol probably were the oxidant and the reductant, respectively. $CuCl_2 \cdot 2H_2O$ on the other hand acted only as disproportionation catalyst. Ag, Ce, Mn and Ti salts showed slow or no reaction, and with Re, unidentified by-products were formed.

The active disproportionation promoters were tested in catalytic hydrogenation (scheme 2). Figure 1 depicts the most important results obtained. The results show that the addition of promoters, especially of vanadium salts, had a dramatic effect on the course of the hydrogenation. The maximum level of hydroxylamine accumulation decreased from > 40% to less than 1% with NH_4VO_3 or V/Pd/C. Other metal salts like $VOSO_4$ and V_2O_5 also reduced the hydroxylamine level but were less

Table 1

Product composition in mol% of starting material after reaction of **2** with 3–5 mol% metal salt (methanol, reflux, 3 h, product analysis by NMR)

Metal salt	2	Azoxy	Nitroso	Amine
NH_4VO_3	0	30	23	46
$FeBr_2$	0	25	21	53
$Co(NO_3)_2 \cdot 6H_2O$	0	16	28	58
CuCl	3	31	60	3
$ReCl_3$ [a]	6	36	3	6
$CuCl_2 \cdot 2H_2O$	8	38	11	38
Mo(acetylacetonate)$_2$	8	37	9	34
$Tl(NO_3)_3$	11	18	4	71
no additive	89	0	0	9

[a] 39% unidentified products.

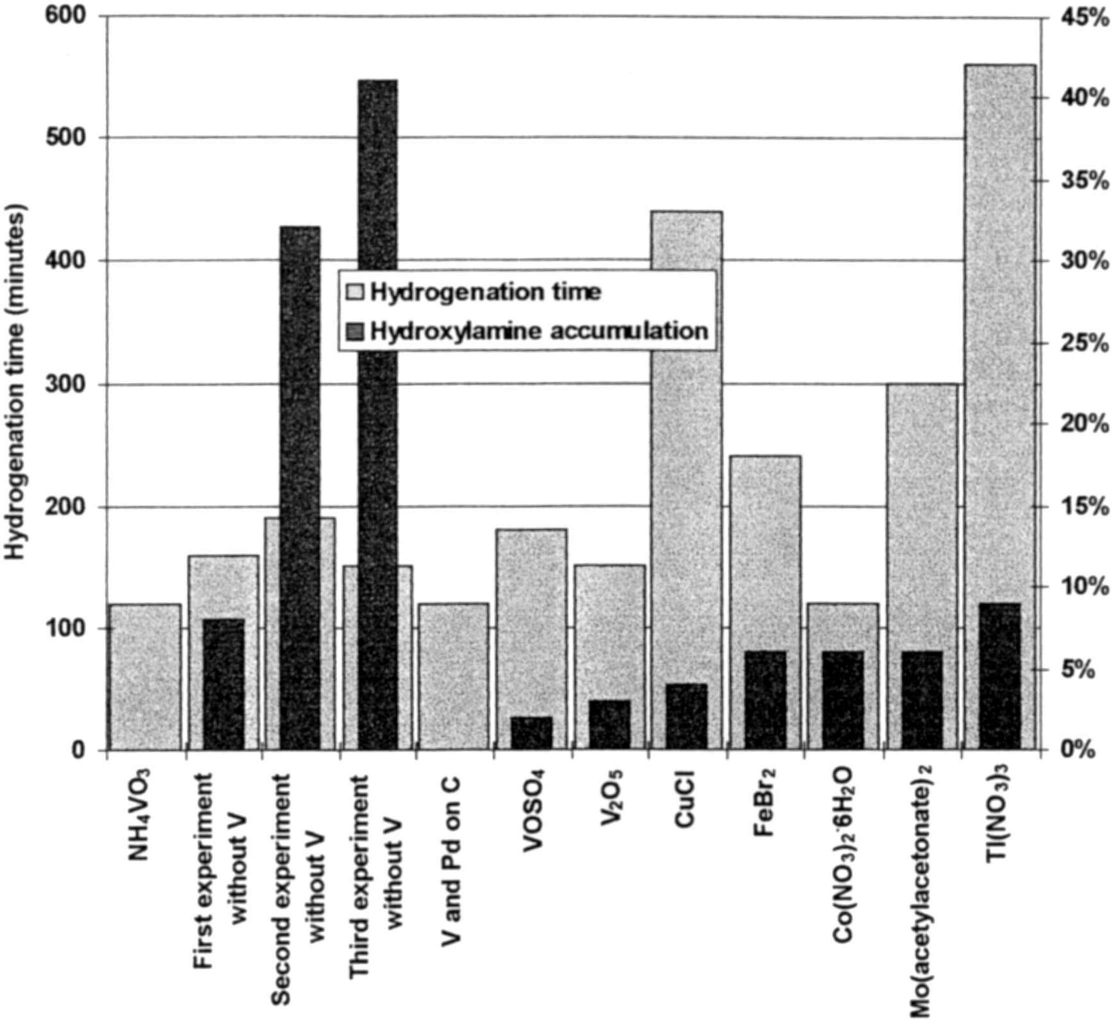


Figure 1. Hydrogenation of nitroarene **1**. Effect of additives on the maximum hydroxylamine accumulation (always observed after 66% hydrogen uptake) and the time needed for 100% conversion. Product analysis by NMR.

effective. In addition, the hydrogenation reaction in presence of vanadium salts was faster than without. Except for $Co(NO_3)_2 \cdot 6H_2O$, all other additives led to longer reaction times and all of them were less effective in reducing accumulation of **2**. Products obtained with efficient promoters were whiter (cleaner) than the ones without. This indicates that the amount of colored condensation products was also reduced.

Surprisingly, these effects were achieved by just adding vanadium salts to the hydrogenation mixture. It is interesting to note that the steel autoclave used in the catalytic hydrogenation showed a "memory effect". Thus, an experiment without the addition of a vanadium promoter still showed considerably less accumulation if the experiment before was run with a V-promoter. Despite of careful cleaning; only the third run in the same reaction vessel showed hydroxylamine levels similar to the runs without vanadium salts.

It is also possible to impregnate a Pd/C catalyst with a vanadium salt. The use of other catalysts like Pt/C is feasible too. This flexibility makes it easy to apply the promoters in production processes. Examples are multiton hydrogenations of **1**, 2-nitro-2′,4,4′-tricholorodiphenyl ether, or 1-chloro-2,4-dinitrobenzene. Deactivation of the Pt or Pd catalysts by vanadium salts was observed in rare cases. By first depositing the V-promoter on charcoal, the problem could be partially solved.

Mechanistic consideration. While there are no details available on the mode of action of the co-catalysts, we can speculate what their function might be. Catalytic hydrogenations of aromatic nitro compounds with a stable hydroxylamine intermediate often have two distinct kinetic phases. First, the nitro compound is reduced rapidly, primarily to the corresponding hydroxylamine. Then, the hydroxylamine is reduced to the corresponding aniline at a much lower rate. With vanadium promoters, the second phase is less pronounced or disappears. This suggests a mechanism which could be called a "catalytic by-pass": The hydroxylamine is not directly hydrogenated to the corresponding aniline but disproportionates rapidly (upper part of scheme 1). The nitroso intermediate then re-enters the catalytic cycle, and as a consequence, the amine formation is accelerated. During various hydrogenations, we never observed nitroso intermediate. This apparent contradiction to the above proposed mechanism can be explained by the strong adsorption and fast hydrogenation reaction of the nitroso compound [10]. This means that this intermediate either never leaves the catalyst surface or is adsorbed very quickly and is therefore not observed.

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