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Application of combinatorial catalysis for the direct amination of benzene to aniline

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Abstract

High-throughput synthesis and screening methods have been developed for the direct amination of benzene to aniline using solid cataloreactants as oxidants. The discovery libraries consisted of hundreds of samples in the primary screen, and arrays of 24 catalysts in the secondary screen. Catalysts were prepared in multi-well batch reactors and screened in parallel for catalytic activity using modified TLC detection as a primary screen and fast serial GC detection as a secondary screen. Around 25,000 samples were screened in about a year. Promising hits identified in the high-throughput screens were successfully scaled up and optimized in conventional autoclaves. Novel cataloreactant systems consisting primarily of a noble metal and a reducible metal oxide have been discovered. Rh, Ir, Pd, and Ru were found to be suitable noble metal dopants. Ni and Co oxides were the only active and selective oxidants identified. Ni is the most active oxidant but requires a Mn dopant as a stabilizer to improve the regenerability, whereas Co is stable even at high regeneration temperatures. The best performing cataloreactants contain Rh or Ir as noble metals, NiO as an oxidant, and ZrO_2 or K–TiO_2 as carrier. An optimized cataloreactant, Rh/Ni–Mn/K–TiO_2 achieved stable 10% benzene conversion and >95% selectivity to aniline at 300 °C and 300 bar. Significantly, the cataloxidant can be regenerated repeatedly without a substantial loss of performance by reoxidation in air. Any noble metal oxides formed during regeneration are effectively reduced in situ during the next amination reaction.

Keywords: Amination; High-throughput; Cataloreactants

1. Introduction

Aniline is typically prepared by converting benzene to a derivative, such as nitrobenzene, phenol or chlorobenzene, and then converting the derivative to aniline. The direct amination of benzene (Fig. 1, Reaction I) has also been attempted [1–8]. One possible way to drive the thermodynamic equilibrium in the forward direction is to remove the hydrogen produced by reaction with lattice oxygen from solid reducible oxides (regenerable and reusable catalyst, the so-called ‘cataloreactant’, Reaction II) to form water. The most significant development in this area is the discovery of an efficient cataloreactant system

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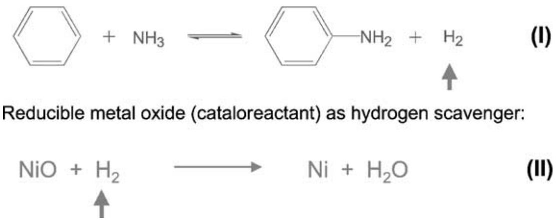

Fig. 1. General reaction scheme for the cataloreactant route for the direct amination of benzene to aniline. A reducible metal oxide is used as a hydrogen scavenger to drive the thermodynamic equilibrium to the right.

based on nickel/nickel oxide by DuPont [3]. In this case, a Ni/NiO/ZrO_2 cataloreactant at high pressure (∼300 bar) and high temperature (∼300 °C) showed a benzene conversion of about 13% for a reaction time of about 4 h in batch reactors. However, the Ni/NiO system is not sufficiently regenerable for a commercially attractive number of cycles without significant loss of activity.

2. Integrated workflow for high-throughput screening

The general screening strategy implemented at Symyx was based on three hierarchical screens. The primary screen was characterized by very high-throughput synthesis and screening in parallel batch reactors.[2] Aniline that was produced was detected in parallel using modified TLC methods. Identified hits were scaled up and further optimized in the secondary screen where conventional GC analysis was used for quantitative determination of benzene conversion and aniline selectivity. Confirmed leads were then further scaled up for regenerability and life time studies in conventional bench scale units (commercial Parr autoclave).

High-throughput batch reactor (HTBR) and high-pressure batch reactor (HPBR), cf., Fig. 2, with large numbers of wells in a rectangular or circular metal block were designed and built. The catalyst precursors were transferred to the reactor wells using Cavro robots, and the catalysts were prepared in situ in these reactor vials by a freeze drying method. Dry catalyst powders were then calcined at appropriate temperatures prior to reaction. Catalyst loading was typically 5 mg. The reactor vials were then filled with calculated amounts of benzene and ammonium carbonate. Parallel loading of ammonium carbonate was realized by a die block loaded with ammonium carbonate and a top punch. Ammonia was generated within the reactor vial by decomposing ammonium carbonate. After knife-edge sealing with an aluminum plate, the reactor block was heated to the required temperature whereby high pressure (200–300 bar) was generated in the sealed vials.

Following the reaction, the reactor block was cooled and the reaction product was analyzed by a modified TLC method.[3] An adsorption/optical detection method for the aniline yield has been developed which is based on aniline adsorption on a TLC plate and the selective conversion of trapped aniline with fluorescamine to a fluorescent derivative [9], cf., Fig. 3(a). The TLC plate was spray impregnated with the aniline sensor (150 ppm fluorescamine in excess CH_2Cl_2) followed by ambient drying. The fluorescence intensity showed a linear response to the amount of aniline over more than two orders of magnitude. The fluorescence was recorded in an imaging station equipped with a CCD camera, UV lamps, and luminescent filters, cf., Fig. 3(b).

In the case of the secondary screen, 24 reactions were effected in parallel at high pressure (HPBR), as shown in Fig. 4. The volume of the reactor vessel was 0.5 ml. A programmable oven was adapted for loading the reactors with liquid benzene at lower than ambient temperature to prevent evaporative loss. A volume of gaseous ammonia was then loaded by further lowering the reactor temperature using liquid N_2. A parallel gas-loading device was developed for condensing ammonia gas in multi-reactors simultaneously. Commercially available VCR fittings were slightly modified as reaction vessels. The fittings can be reused while the gaskets are commercially available. The reactor vessel was compatible with the GC/MS's auto-sampler. After reaction and removal of the gaseous reactants, the vessel could be loaded on the GC/MS sampler directly for product analysis, cf., Fig. 4. In situ synthesis also became possible. The HPBR was capable of carrying out reactions at ∼300 bar and at temperatures up to ∼500 °C. The catalyst loading in this case varied

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[2] US Patent 5,985,356. Additional patents pending.

[3] Patents pending.

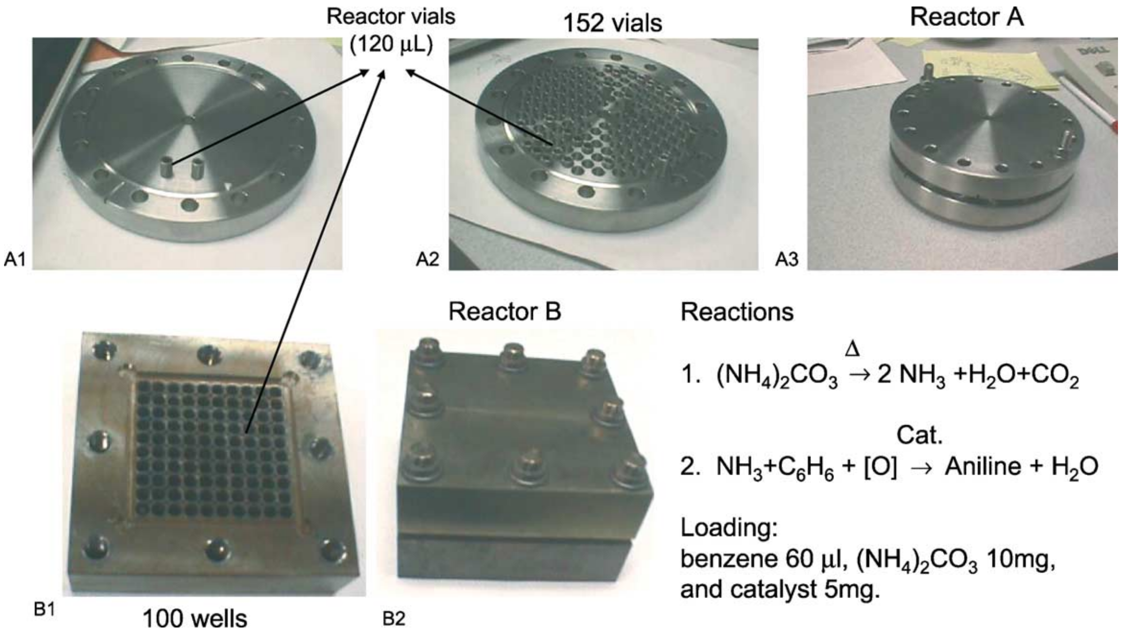

Fig. 2. HTBR used as primary screen for the discovery of aniline cataloreactants. Circular (15 × 10) and square (10 × 10) arrays are shown. The sample throughput can further be improved by using multiple reactor blocks at the same time or by increasing the number of wells in the block.

between 30 and 180 mg, and the ammonia to benzene ratio was maintained at about 4. Typically, the reaction time was about 4 h. When the reaction was complete, the vials were cooled and the product was diluted with methylene chloride for analysis using GC/MS. Fig. 4 provides details of the HPBR vessel design and part of the workflow.

Catalyst libraries for primary and secondary screening were synthesized in situ by using Symyx' proprietary Library Studio® and Impressionist™ software.[4] The metal precursor solutions (metal acetylacetonate solutions in acetic acid, aqueous metal nitrate solutions, metal oxalates in aqueous oxalic acid solutions, etc.) were dispensed automatically by robots, and the catalysts were prepared by subsequent drying and calcination steps. A typical post-synthesis treatment involved a drying step at 110 °C and calcination in air at 450 °C for 4 h. Sol–gel techniques, wet impregnation techniques of pre-loaded carriers or freeze drying methods were employed. More details can be found elsewhere [10,11].

A useful parameter for characterizing the catalyst loading for a batch reaction is the weight ratio of the total amount of ammonia+benzene to the total amount of the catalyst ("reactant to catalyst ratio"). The R/C ratio preferably ranges from about 0.5:1 to about 10:1, in each case by weight. The reaction conditions are then specified by T, p, reaction time, R/C ratio, and ammonia/benzene ratio.

3. Lead discovery and development of new catalyst concept

A large number of catalyst libraries consisting of binary, ternary, and quaternary compositions were synthesized and screened in the HTBR. The screening protocol included oxidants (reducible metal oxides), noble metals, carriers, and dopants. The most significant discovery from this primary screen was the identification of noble metals as active amination catalysts as may be seen in Fig. 5. The library consisting of NiO and rhodium oxide (supported on a ZrO_2–Nb_2O_5–Ta_2O_5 ternary) showed large yields of aniline, whereas the library without rhodium oxide

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[4] European Patent EP 1080435. Additional patents pending.

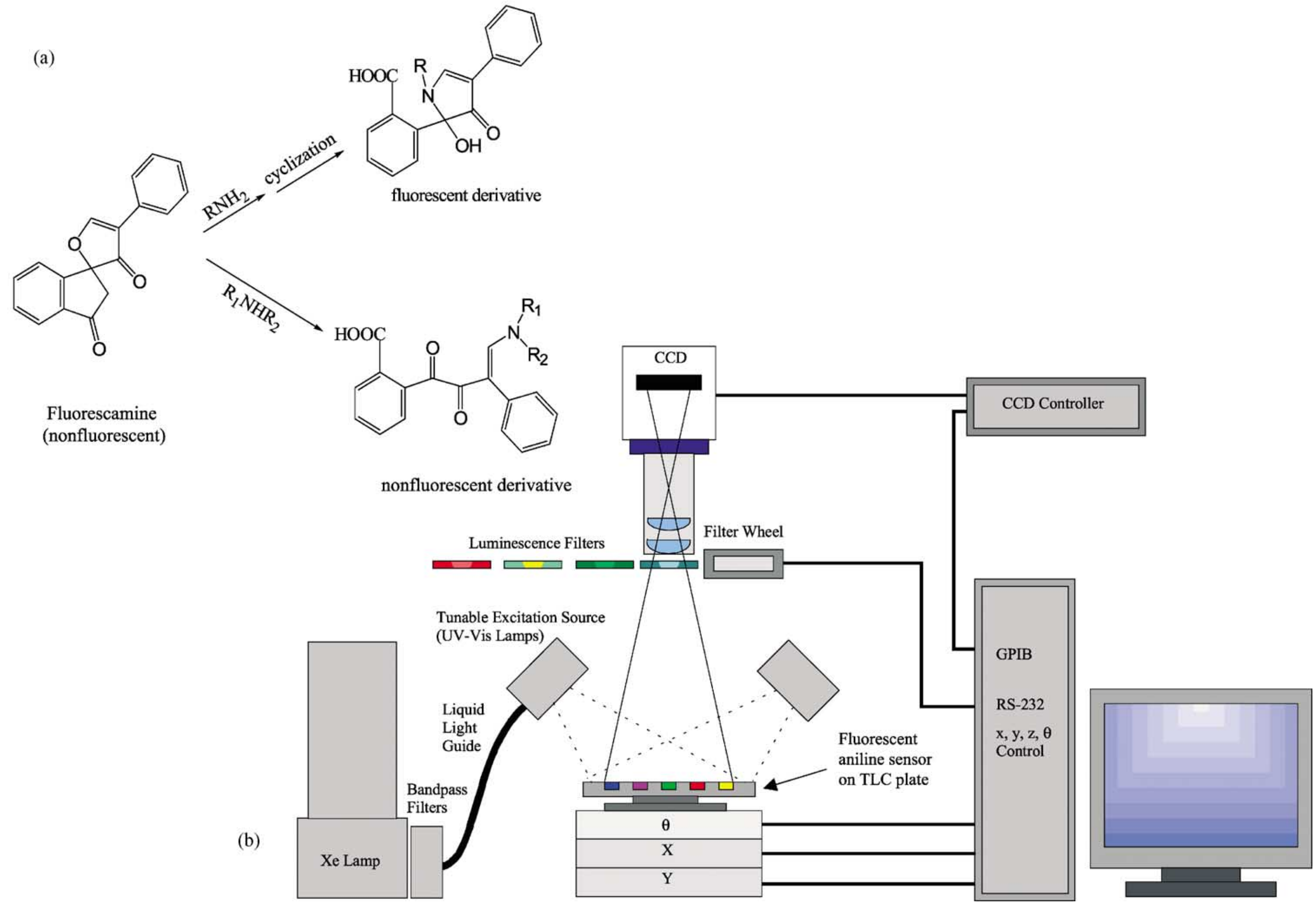

Fig. 3. Parallel TLC detection of aniline with the selective fluorescent dye fluorescamine (patents pending). (a) Aliquots of the reaction mixture are spotted onto a silica TLC plate which is then uniformly sprayed with a diluted solution of fluorescamine (150 ppm) in CH_2Cl_2, followed by ambient drying. The nonfluorescent dye selectively reacts with primary amines to a fluorescent cyclic derivative whereas the reaction with secondary amines leads to nonfluorescent derivatives. The porous and acidic silica layer is an efficient absorbent to trap aniline, and a chromatographic development of the TLC plates is not required. (b) The fluorescence signals are then recorded in an automated imaging station equipped with CCD camera, UV lamps, and luminescent filters. Integral signal intensities were calculated by averaging over the spot sizes. The calibration curve shows that the fluorescence intensity response is directly proportional to the amount of aniline produced by the reaction.

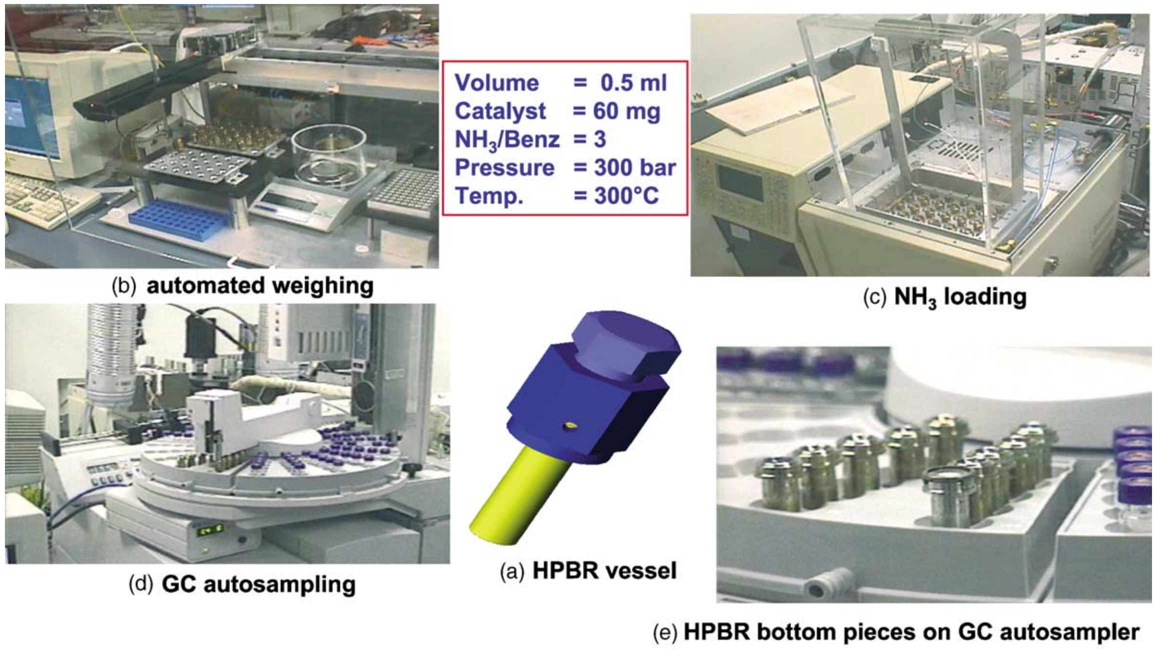

Fig. 4. HPBRs (6 × 4) used as secondary screen for scale-up and optimization of HTBR hits. Sample loading, reactant loading, weighing steps, and GC analysis are all automated. The reactor vessels are weighed after each loading step as well as at the end of the reaction to ensure the absence of leakage. Arrays of 6 × 4 vessels form a catalyst library and are processed simultaneously. During reaction, HPBR arrays are agitated on a rocker in a static oven. (a) Single HPBR vessel with VCR fitting. Volume = 0.5 ml, catalyst loading = 60 mg, NH_3/benzene ratio = 3, pressure = 300 bar, reaction temperature = 300 °C. (b) Automated weighing. A Cavro robot places the individual reactors from the HPBR array onto the scale. (c) NH_3 loading by condensing gaseous NH_3 into the HPBR vessels which are mounted on a modified GC oven and cooled with liquid nitrogen. (d) and (e) Array of HPBR bottom pieces on GC auto-sampler. After reaction, excess methylene chloride is added to the reaction mixture in the vessels and the catalyst particles are settled at the bottom allowing a clear solution for GC analysis and avoiding contamination of the sampler/injector. Prior to analysis, the vessels are covered by a septum with knife-edge seal.

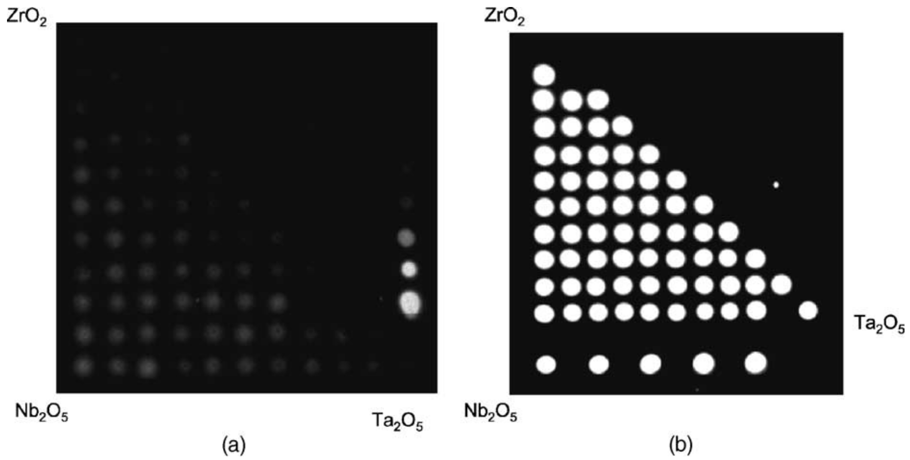

Fig. 5. Discovery of Rh/Ni as a new cataloreactant in HTBR (300 °C for 4 h reaction time) (patent pending). (a) 20% Ni loaded on zirconia–niobia–tantalia carriers. Without Rh the NiO is inactive. (b) 5% Rh and 20% Ni loaded. With Rh high activity for aniline formation is observed. The spots in the last row are spotted aniline standards.

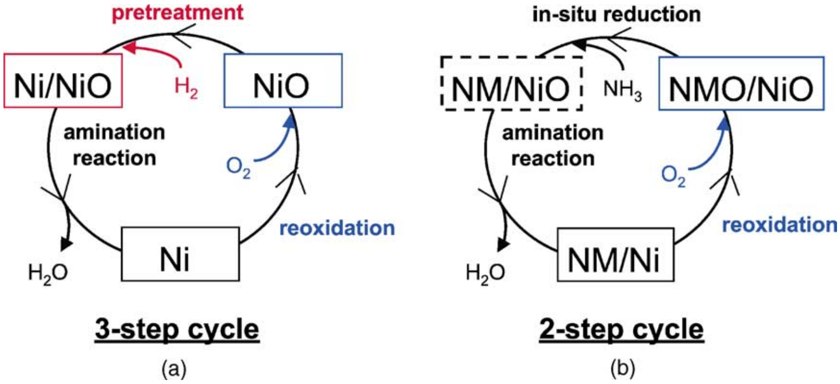

Fig. 6. Prior art and new Symyx concepts for dual-function cataloreactants (dehydrogenation function and hydrogen scavenging function) (patent pending). (a) In the prior art the active Ni sites (metallic Ni) are produced externally by a hydrogen pre-reduction step ($NiO + H_2 = Ni/NiO$). The ratio Ni/NiO is critical for the catalytic performance. (b) In the present case the active noble metal centers are produced by in situ reduction by ammonia. All the Ni is initially in the oxide form and available for H_2 scavenging but part of the NiO oxidant is eventually reduced to the metallic state in the course of the reaction thus forming new dehydrogenation centers in addition to the noble metal centers.

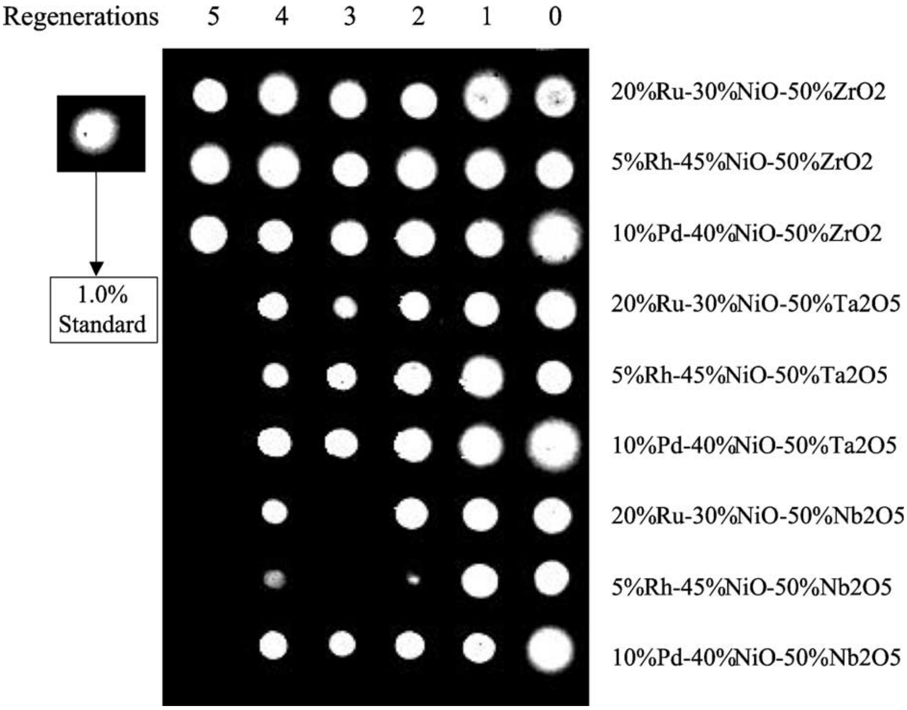

Fig. 7. Cataloreactants are regenerated in the primary screen. Comparison of (Ru, Rh, Pd)/NiO/(ZrO_2, Ta_2O_5, Nb_2O_5) cataloreactants. The noble metal/NiO/carrier systems are active even after 4–5 cycles of regeneration.

showed hardly a trace of aniline. These catalysts were not pre-reduced by hydrogen and therefore the Ni only containing catalysts were not active. In the case of the NiO–RhO system, rhodium oxide was reduced in situ by ammonia to metallic rhodium, which in turn initiates the amination process. The oxygen atoms of NiO are used to extract the released hydrogen atoms. In order to achieve similar functions with only Ni-containing catalysts, it is necessary that some of the NiO be reduced to nickel metal by hydrogen prior to the reaction. Unlike rhodium oxide, NiO is not reduced by ammonia. This discovery eliminated time-consuming catalyst preparation steps. Thus it was realized that the previous three-step cycle could be replaced by a simpler and more robust two-step cycle where the hydrogen pretreatment is replaced by an in situ reduction of the noble metal oxide by ammonia, as illustrated in Fig. 6.

4. Primary and secondary screening

Primary screening was targeted to identify the best oxidant, benzene/ammonia activator, and support for the cataloreactant. A performance comparison of Ru, Rh, Pd activators and zirconia, niobia, tantalia supports with NiO as oxidant is exemplified in Fig. 7. The studies showed that Ni oxide is the best oxidant, followed by Co oxide. Subsequent screening showed that both zirconia and titania were good carriers for dispersing the active catalyst components. However, it was realized that titania had to be doped with about 0.5 wt.% potassium to neutralize acidic surface sites.

Four-component libraries consisting of noble metal/oxidant/metal dopant/carrier were then synthesized and screened in the HPBR. Typical results are shown in Fig. 8. As observed in the primary screen, it may be seen that Rh is more active than Pd, zirconia is a better carrier than silica, and NiO is the best oxidant. Both Mn and Ce are also slightly active but unselective. The activity can be modified further to some extent by the nature of the metal dopant, however, the total activity is predominantly due to the NiO oxidant. Thus the trends seen in the primary screen could be confirmed in the secondary screen where more traditional catalyst samples were used (impregnation of shaped carriers).

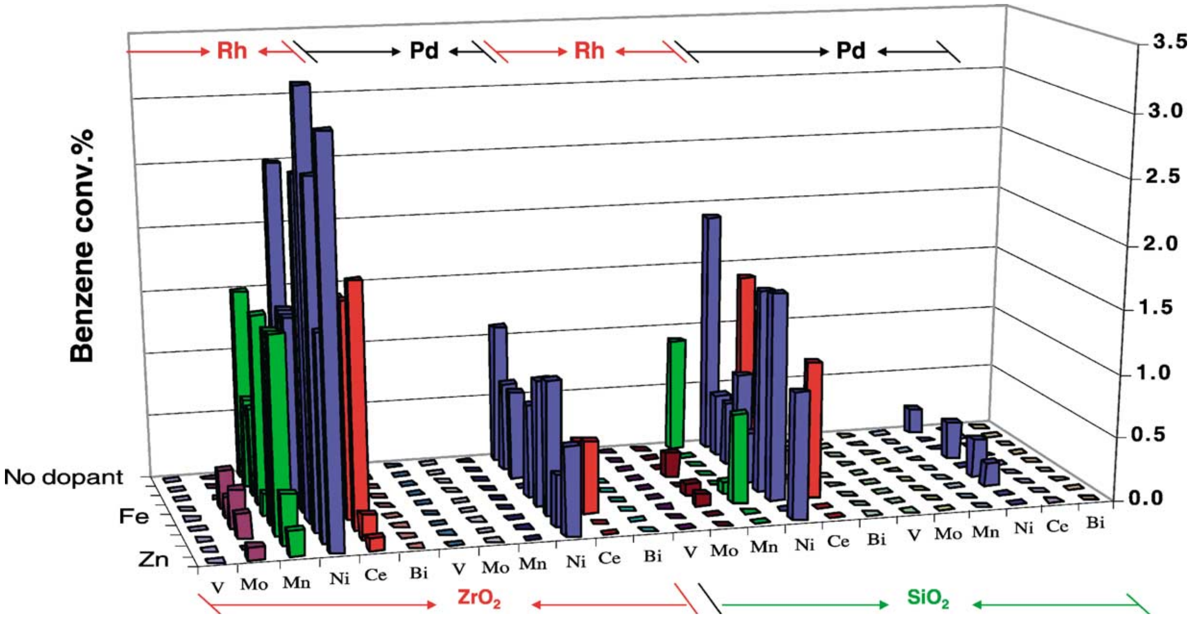

Fig. 8. Example of four-component library (Rh, Pd)–M_1–M_2–(ZrO_2, SiO_2) for screening of oxidants (V, Mo, Mn, Ni, Ce, Bi) and dopants (V, Cr, Mn, Fe, Co, Ni, Cu, Zn) in HPBR (300 °C for 4 h GC analysis). Among the carriers, zirconia is better than silica, and among the oxidants, NiO is by far the best. The activity can further be modified by metal dopants (patent pending).

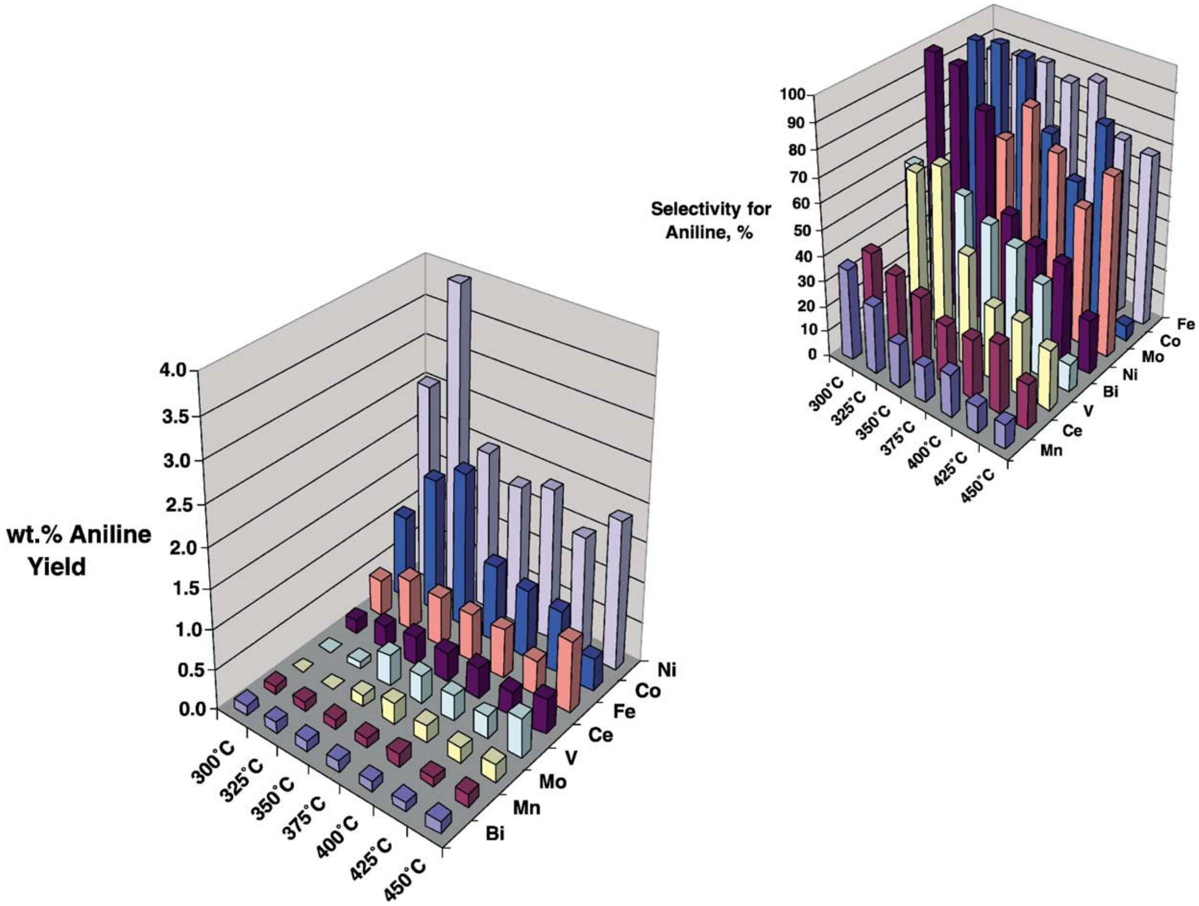

Fig. 9. Activity and selectivity of metal oxide oxidants in the temperature range of 300–450 °C. NiO is the most active oxidant. Co oxide and Fe oxide show some activity at higher temperatures. The composition of the catalysts is 2 wt.% Rh and 20 wt.% M based on the weight of the ZrO_2 support (Norton XZ 16075), where M is the oxidant metal chosen from V, Mo, Mn, Co, Ni, Ce, Bi, and Fe. They were made by serial aqueous impregnation with metal salts (mostly nitrates)/drying at 120 °C followed by a single calcination at 380 °C for 4 h in air (patent pending).

Various cataloreactants with constant metal oxide content (20 wt.% metal) were screened at different temperatures in the HPBR. Typical results are shown in Fig. 9. At all temperatures in the range 300–450 °C, Ni was the best cataloreactant with 4% maximum aniline yield at 325 °C; Co was the second best oxidant with 2% maximum aniline yield at 350 °C; and Fe was third best with 0.9% aniline yield at 450 °C. Aniline production and/or selectivity was relatively lower for Mn, Bi, Mo, V, and Ce up to 450 °C.

We found that regenerability of bulk cataloreactants can be successfully studied in situ in the HPBR. After the amination reaction the catalysts were reoxidized in air at 450–475 °C for 2–4 h. Although Ni can be oxidized to NiO at around 300 °C, it was necessary to heat the catalyst to 475 °C to burn off the coke deposits on its surface. The regeneration studies showed that the catalysts slowly lost their activity from cycle to cycle reaching about 50% of their initial activity after five regenerations. A search for stabilizers showed that Mn when present in small amounts renders the Ni-based cataloreactants fully regenerable. A Ni/Mn ratio of 10 is adequate for efficient regeneration of the catalysts. It is believed that small amounts of Mn prevent Ni particle agglomeration during high temperature regeneration and keep the Ni dispersion high.

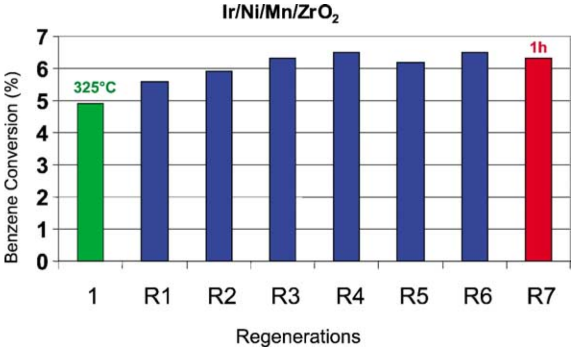

Fig. 10. The performance of the Ir lead Ir/Ni/Mn/ZrO_2 (0.5% Ir, 18% Ni, 1.5% Mn) in the tertiary screen (Parr bomb). Reaction conditions: 350 °C, 300 bar for 2 h at a reactant/catalyst ratio of 0.83 and a NH_3/benzene ratio of 3 (first run at 325 °C reaction temperature, eighth run after seven regenerations for 1 h reaction time). Reoxidation at 475 °C for 2 h in air. The Ir lead is found to be completely regenerable even after seven cycles of regeneration (patent pending).

Compared to Rh, Ir is relatively less active at a given temperature. To achieve the same aniline productivity, Ir containing cataloreactants need to be heated to a slightly higher temperature. Our studies show that Ir requires about 25 °C higher temperatures than Rh to achieve comparable aniline production rates, as shown in Fig. 10. This activity ranking also parallels their ammonia decomposing ability. Rh is active in decomposing ammonia even at 300 °C, while Ir decomposes it to a lesser extent at this temperature. Since higher reaction temperatures are desirable as they favor the kinetics as well as the thermodynamics of amination, high temperature Ir leads might have the potential for further improvements.

5. Regenerability

The (Rh, Ir)/(Ni/Mn, Co) cataloreactant systems are regenerable by air oxidation (reoxidation of metal oxide, burn off of coke) without any additional pretreatments. An optimized Rh-based catalyst comprising Rh (about 1.25% Rh), Ni oxide (about 15% Ni), Mn oxide (about 1.5% Mn) on a K–TiO_2 carrier (0.5% K), with all percentages by weight relative to the weight of the support, was repeatedly evaluated for the amination reaction in the tertiary screen (Parr bomb) at 325 °C and 300 bar for 2 h (NH_3/benzene = 6 and $R/C = 1$). After isolation, the catalyst was dried at 110 °C for 1 h, and then regenerated by reoxidation in air in a calcination oven at 475 °C for about 1 h. The catalyst enables benzene conversions in excess of 10% to be consistently obtained which is close to the maximum, thermodynamically allowed limit. Additionally, in each case, the aniline selectivity was greater than 95%, cf., Fig. 11. At temperatures in excess of ∼330 °C, Ni promotes coking (increased toluene formation) while Rh catalyses ammonia decomposition (into H_2 and N_2).

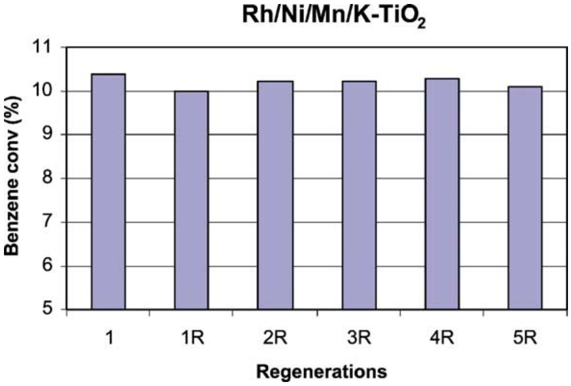

Fig. 11. The performance of the optimized Rh lead Rh/Ni/Mn/K–TiO_2 (0.5% K, 15% Ni, 1.5% Mn, 1.25% Rh) in the tertiary screen (Parr bomb). Reaction conditions: 325 °C, 300 bar for 2 h at a reactant/catalyst ratio of 1 and a NH_3/benzene ratio of 6. Reoxidation at 475 °C for 2 h in air. A benzene conversion of over 10% and an aniline selectivity of over 95% have been achieved (patent pending).

6. Discussion

Combinatorial approaches have been employed to identify cataloreactants containing noble metals and reducible metal oxides that are advantageous with respect to benzene conversion, aniline selectivity, and catalyst regenerability.[5] The best oxidants identified were Ni and Co oxide. Fe oxide was also selective but much less active. Other reducible metal oxides were unselective. All the noble metals (in combination with Ni or Co oxide) showed some activity and high aniline selectivity, with Rh and Ir being the most

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[5] Patent pending.

active and selective. Pd and Ru were found to be slightly less selective. Pt-containing cataloreactants are not fully regenerable, i.e., these systems lose their activity from cycle to cycle. The selectivity to aniline was very high for Ni- and Co-based catalysts reaching about 90–95% in most cases. Very small amounts of toluene and biphenyl were detected as side products. The cobalt oxide system can be regenerated as such and requires no additional dopants like Mn in the NiO based cataloreactant. In addition, cobalt oxide based cataloreactants can be regenerated by heating to very high temperature (~500 °C) which potentially allows shorter reoxidation times and higher space time yields. Re-oxidizing NiO at temperatures above 475 °C results in a loss of activity of the cataloreactant.

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