Activity and selectivity control in the synthesis of alicylic amines.

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Introduction

Heterogeneous catalysis for the production of Fine Chemicals and Pharmaceutical intermediates is often a complex area of three-phase reaction. The influences on the reaction selectivity and activity are many and varied. Alicyclic amines are important for use in pesticides, plasticizers, explosives, inhibitors of metal corrosion, sweetening agents and as intermediates in the pharmaceutical industry. Whilst there is a relatively extensive literature concerning the hydrogenation of aniline itself, relatively few reports are extant of studies of the hydrogenation of substituted anilines [1-3]. In this study we have examined how the reaction activity and selectivity can be controlled with a knowledge of the reaction mechanism and correct choice of catalyst, solvent and temperature.

Materials and Methods

The catalysts used throughout the study were a series of 2.5% w/w Rh/SiO_2 prepared by incipient wetness by Johnson Matthey using silica powders supplied by Grace Davison Catalysts. The metal dispersions were determined by hydrogen chemisorption. The STR experiments were carried out using a Buchi autoclave stirred tank reactor. Typically 2 g of pre-reduced catalyst was added with 300 ml of solvent to the reaction vessel and an *in situ* reduction carried out at 328 K for 30 minutes. 0.0196 moles *p*-toluidine (Sigma-Aldrich) or 4-*t*-butylaniline were dissolved in 50 ml of solvent and, immediately after the *in situ* reduction, injected into the reaction vessel and stirred to allow mixing. The vessel was pressurised to 2 barg with H_2, the stirrer speed set to 1000 r.p.m. and the progress of the reaction monitored by the uptake of H_2 and by gas chromatographic analysis of samples of the reaction mixture at regular time intervals.

Results and Discussion

Higher reaction temperatures increased the rate of hydrogenation and decreased the cis/trans ratio of products in line with kinetic and thermodynamic expectations. When catalysts with different metal crystallite sizes were tested it was found that as metal crystallite size increased so did the Turn-Over Frequency (TOF). This unusual antipathetic particle size effect suggests hydrogenation is preferred at plane face/terrace sites rather than edge or corner sites. The rate of hydrogenation for both 4-methylaniline and 4-*tert*-butylaniline tended to zero at ~0.35nm (Figure 1).

The rate of 4-methylaniline and 4-tert-butylaniline hydrogenation was monitored in polar primary and secondary alcohols and non-polar solvents. The reaction rates varied by an order of magnitude depending on the solvent used, with the maximum reaction rate achieved when using propan-2-ol. The 'hydrogen-donor' characteristics of polar secondary alcohols may provide an additional source of hydrogen. The ratio of cis/trans isomers is proportional to the dielectric constant of the solvent. As dielectric constant increases the polarity of the solvent also increases. This affects the relative thermodynamic stability not of the final products but of the partially hydrogenated enamine and imine intermediates.

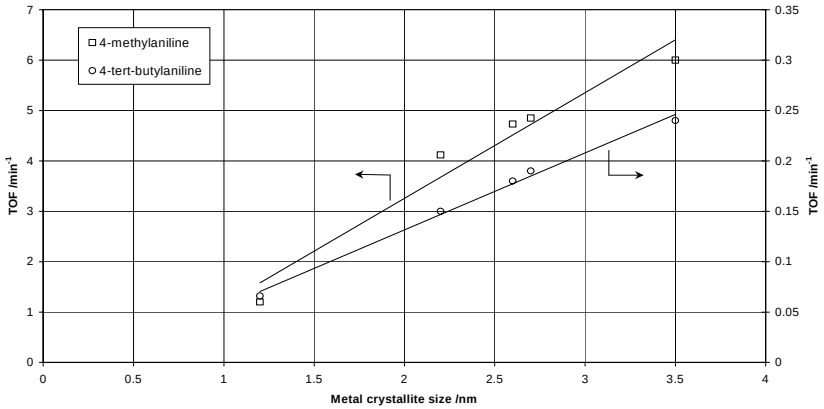

Figure 1. Antipathetic particle size effect.

The imines hydrogenate to the respective *cis* isomer. Analysis of the reaction kinetics revealed that the system deactivated. This was shown to be a function of the amount of product in the system. The primary amine product is a stronger base (pKa 3.5) than the starting aromatic amines (pKa ~ 10) and inhibits reactant adsorption, hence deactivating the system.

Significance

The antipathetic particle size effect coupled to the effects of solvents and the products show the need for a thorough understanding of the catalytic system. Once such an understanding is in place the activity and stereoselectivity of the system can be controlled to optimize the desired reaction products.

References

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