446g Development of Efficient and Robust Nitro Reduction Process: Catalyst Selection and Thermo-Kinetic Understanding

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The catalytic hydrogenation of aromatic nitro compounds is important for the production of pharmaceutical intermediates. Successful development and scale-up of this complex exothermic process involves an understanding of the complex interplay between the kinetics as well as hydrodynamics and mass transfer. The nitro-reduction proceeds via several intermediates of which the hydroxylamine species may be the most significant. Hydroxylamines are problematic not only owing to the fact that they are thermally unstable, can disproportionate (with a strong exotherm) and are potent carcinogens, but they also can undergo condensation with the nitroso intermediate leading to the formation of colored azo or azoxy products. In this study, it was demonstrated that with a proper choice of catalyst, it is possible to reduce the hydroxylamine accumulation and thereby eliminate the potential color issue. The process also has potential leaching issues due to the limitation on the choice of the solvent due to solubility and consideration of subsequent process issues. The approach taken to overcome this issue by modifying the catalyst or changing the support for the catalyst will be discussed. Finally, a coherent picture of underlying phenomena was obtained using data obtained by a in-line monitoring, reaction calorimetry and hydrogen uptake measurement