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SPECIAL FEATURE SECTION: SAFETY OF CHEMICAL PROCESSES

Safety Highlights

Safety Notables: Information from the Literature

This is the fifth annual literature overview on safety issues which are of interest to process chemists and engineers to appear in *Organic Process Research & Development*. As in the previous years, this review will cover recent articles from the literature that address safety issues, common safety mistakes that seem to be repeated all too often, and major industrial accidents. This paper is not intended to be all-inclusive of the safety literature, nor should the information presented be used to make decisions regarding safety without reading the full text of the appropriate article. The intent is to give a flavor of the issues facing other chemists and engineers and how they are solving these problems.

Process Safety Begins in the Laboratory. Research and process development chemists have a key role in the safety of a chemical process throughout its life cycle. In an article written by Dennis Hendershot (*J. Chem. Health Saf.* **2007**, Jan/Feb, 25), the opportunities for these scientists to build safety into the fundamental chemistry of a process are outlined. These opportunities include

(1) developing alternative synthetic routes that use less hazardous starting materials and intermediates or less energetic reactions;

(2) utilizing catalysts that allow for less severe operating conditions or less reactive starting materials;

(3) if hazardous reagents or catalysts need to be used, immobilizing the hazard or running the reaction under dilute conditions should be examined;

(4) water should be used as solvent whenever possible, and other low hazard solvents should be examined;

(5) developing fast reactions that are easier to control.

The author quotes an anecdote that highlights how early consideration of safety can pay dividends. It is estimated that, relatively speaking, a safety problem eliminated by the use of inherent safety will cost $1 to fix in early research, $10 during the development of the process flow sheets, $100 during final detailed plant design, $1000 after the plant is built, and $10,000 after an incident has occurred.

A similarly themed article was written by A. A. Khan that highlighted the need for the evaluation of vulnerability in chemical operations before the process is run on scale (*Process Saf. Prog.* **2006**, *25*, 245). The required steps are outlined, and some major accidents are reviewed with potential lessons learned. The author states that safety evaluation of a chemical process needs to occur during the early process development studies and that all too often this evaluation is inadequate. Advice on the data needed for an adequate evaluation is given.

Green Chemistry. The concepts of Green Chemistry and how the field has grown to encompass the goal of sustainable development by reducing the adverse consequences of the substances that we use and generate was outlined in a special issue of *Chemical Reviews* (*Chem. Rev.* **2007**, *107*, 6). This issue, edited by István Horváth and Paul Anastas, contains several articles that could aid process chemists and engineers in designing potentially safer processes and/or processes that minimize environmental impact of the chemistry being run. One of the key areas of Green Chemistry is the replacement of hazardous solvents with environmentally benign solvents that will have limited or no impact on the health and the environment. In a review by Li *et al*. (*Chem. Rev.* **2007**, *107*, 2546), reactions of C-H bonds in water are discussed. Hundreds of reactions run in water are described which include oxidations, Aldol-type condensations and conjugate additions. Of course, the development of solvent-free processes is considered to be the best solution in Green Chemistry and this approach is described in a review by Walsh *et al*. In this article (*Chem. Rev.*, **2007**, *107*, 2503), a Green Chemistry approach to asymmetric catalysis in solvent-free and highly concentrated reactions is outlined. It was good to see that the authors mention that although the reactions in the review are Green in the sense that they are run in minimal or no solvent, there are risks in running these types of reactions. It is known that reactions that are conducted in the absence of solvent can rapidly generate heat and that a greater degree of care must be exercised when reactions are preformed at high concentration to avoid runaway reactions.

Design of Sparger Systems. Processes for the oxidation of carbon by molecular oxygen are widely used in the chemical industry to obtain products such as cyclohexanone from cyclohexane and terephthalic acid from *p*-xylene. Typically, air or air/oxygen mixtures are used, but even processes where pure oxygen is used can be found. In these processes, hazards can be found in the liquid phase, where uncontrolled reactions and thermal decomposition of the peroxides that may form can occur; or from an explosion in a coherent gas phase anywhere in the reactor. In an article written by Manfred Weber, some general aspects on the proper design of the sparger system for a cumene oxidation is described (*Process Saf. Prog.* **2006**, *25*, 326). The article summarizes all important parameters for the proper and safe design of a sparger system for large bubble columns used for these types of oxidations.

Comprehensive Project Design Review. In an article written by David Ayers (*Occup. Hazards* **2007**, *69*, 43), the steps to establishing a comprehensive project design review and process hazard review procedures are given. All too often projects begin or processes are brought online without a full

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understanding of the EH&S concerns. These concerns can be addressed through a stepwise approach of

(1) Kickoff meeting
(2) Documentation review
(3) New or modified construction review
(4) EH&S impact review
(5) Final process hazard review walk-through
(6) Punch list completion

The author goes into detail of what is expected at each step of the process. Although not an easy feat, the completion of a comprehensive project design review should ensure there are no hidden areas for employee injury or emergency response incidents, and the true cost of hazardous waste generation should be known.

Hazardous Material Compatibility Storage Guidelines. Inventory specialists rely upon a variety of sources to decide how best to store materials in a manner that prevents potential situations involving their hazardous materials inadvertently mixing in the workplace. A source that should be added to every warehouse managers' collection is an article written by Moder et al. (*Process Saf. Prog.* **2007**, *26*, 114), which outlines a hazardous material compatibility storage guideline and an abbreviated hazardous material compatibility storage tool . These systems, which are consistent with the Center for Chemical Process Safety, are described with easy to follow flowcharts and compatibility charts. A discussion on how these systems have been implemented in both existing and new facilities is given.

Phosgene Alternatives in the Synthesis of Isocyanates. Methyl *N*-phenyl carbamate is a key intermediate in the preparation of isocyanates, which are important reagents for the synthesis of many industrial chemicals. A common method for the production of methyl *N*-phenyl carbamate utilizes the highly toxic and corrosive chemical phosgene. The development of a novel nonphosgene approach to methyl *N*-phenyl and other carbamates was described in an article by Li et al. (*Green Chem.* **2007**, *9*, 527). The preparation of methyl *N*-phenyl carbamate from dimethyl carbamate and *N*,*N′*-diphenyl urea under mild conditions and atmospheric conditions are described. The paper also gives a good reference list for other alternatives for phosgene as an industrial reagent.

Outsourcing, Audits and Technology Transfer. The use of third party manufacturing vendors and the outsourcing of chemistry services continues to grow in the chemical industry. In two articles in the *Journal of Hazardous Materials*, this year topics surrounding the safety aspects of conducting work at off-site facilities were described. In the first article, the keys to effective third-party process safety audits were described (*J. Hazard. Mater.* **2007**, *142*, 574). The article is more written for the medium or small businesses that do not have the expertise or the resources to perform the compliance audits mandated by OSHA and the EPA and rely on third-party consultants to provide these services. However, the concepts apply to any safety audit that needs to be performed. In detail, the processes of planning for the audit, performance of the audit, and the follow-up after the audit are given. The paper also discusses the steps to improve the audit process and increase effectiveness whether performed by a third party or internally.

In the second article, the critical issues to be addressed in the transfer of hydrogen cyanide (HCN) manufacturing technology to a licensee is described (*J. Hazard. Mater.* **2007**, *142*, 677). Although HCN is a useful reagent for the manufacture of a wide variety of valuable industrial products, the compound's hazardous properties require process safety to be the highest priority. The process that was transferred has oxygen from air, ammonia, and natural gas reacting in a gas phase converter to product hydrogen cyanide, water, and combustion products.

$$NH_3 + CH_4 + 1.5\ O_2 \xrightarrow[\text{Pt/Rh}]{\text{1200 deg. C}} HCN + 3\ H_2O$$

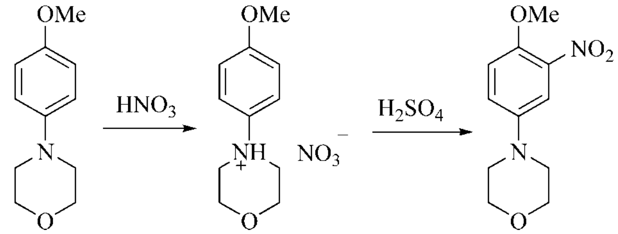
$$\Delta H = -482.3\ \text{kcal/mol HCN}$$

The article is not only a good resource to outline how to successfully and safely transfer a process from one manufacturing site to another, but it should be considered a must read for anyone considering making or using HCN in any process on scale.

Effective Use of DSC in Process Safety Analysis. Differential Scanning Calorimetry (DSC) is commonly used for thermal stability testing by process safety professionals. Researchers at Dow have summarized their 20 years of collective knowledge of DSC including routine screening, chemical compatibility, interpretation of peak shape, elimination of unnecessary testing, and estimation of reaction kinetics (*Process Saf. Prog.* **2007**, *26*, (1), 51). A hypothetical process is presented in order to demonstrate the testing strategy that would typically be applied at Dow. The authors note that testing should not be applied to every possible raw material, intermediate process stream, or mixtures of materials, and the decision to test or not to test should be made by qualified experts. They continue with a discussion of some common test conditions and data interpretation methods that they have found useful. Finally, the use of DSC to derive various kinetic models is discussed in some detail.

A paper describing the DSC data for benzotriazole and 1,2,3-triazole highlights the importance of careful experimental technique when applying the results to process safety analysis (*Tetrahedron Lett.* **2007**, *48*, 1233). Workers at Merck KGaA report the exothermic decomposition energy of benzotriazole and 1,2,3-triazole as 1590 and 2600 J/g, respectively. Katritzky and co-workers reported the values as 547 and 126 J/g (*Tetrahedron Lett.* **2006**, *47*, 7653). The researchers at Merck KGaA suggest that the discrepancy may be due to the difference in sample cell since they used sealed high pressure stainless steal pans, and Katritzky *et al*. used sealed aluminum pans. Process safety professionals typically use high pressure crucibles in order to avoid endothermic evaporation that could mask an exotherm.

A Novel Nitration Process. Nitration is a common chemical transformation that is typically accompanied by a large heat of reaction for the desired reaction and potentially hazardous decomposition side-reactions. Researchers from Roche Carolina Inc. have reported a novel nitration of 4-(4-methoxyphenyl)-morpholine through use of the corresponding nitric acid salt (*Org. Process Res. Dev.* **2007**, *11*, 861).



The direct nitration of 4-(4-methoxyphenyl)morpholine was problematic due to overnitration in the presence of excess nitric acid, among other processing issues. Attempts to carefully control the stoichiometry were not successful. Therefore, the isolated nitrate salt was prepared in order to ensure a 1:1 ratio of nitric acid to substrate in the subsequent nitration. Nitration was achieved by adding a methylene chloride solution of the nitrate salt to concentrated sulfuric acid. The authors discuss optimization of the nitration conditions, including an interesting observation regarding regioselectivity. A process safety analysis was performed including heat of reaction measurements and thermal stability testing by accelerating rate calorimetry (ARC).

Large Scale Performic Acid Oxidation. A research group at Pfizer reported the oxidation of a thioacetate to a sulfonic acid using performic acid (*Org. Process Res. Dev.* **2007**, *11*, 762). Since the rate of decomposition of performic acid becomes hazardous even at subambient temperatures, the process was carefully designed to avoid significant accumulation of the peracid. RC1 testing showed that addition of 30 wt % aqueous hydrogen peroxide to an acetic acid solution of the thioacetate was highly exothermic but resulted in low thermal accumulation. The peracid oxidation was chosen in order to avoid the need for a quench involving metal counterions and, therefore, the excess peroxide was quenched by transferring the completed reaction mixture to a slurry of G-60 Darco. A disadvantage of this quench is the generation of oxygen gas, which was purged from the reactor using a rapid nitrogen sweep. The authors describe several safety considerations and engineering controls that were considered prior to scale-up, including tank preparation, the hydrogen peroxide charge, quench of the excess peroxide, and isolation of the product. The process was run five times on 30–35 kg scale without incident.

Scale-Down Approach to Process Safety and Optimization. Process development chemists and engineers typically carry out laboratory experiments designed to mimic the conditions that will be experienced upon scale-up to production vessels. Stoessel and Zufferey (*Inst. Chem. Eng. Symp. Ser.* **2007**, *153*, paper 113, 1) have reported the use of a modified RC1 in order to mimic the exact temperature course of an industrial reactor at laboratory scale. To understand the dynamics of the industrial reactors, water or toluene was heated and cooled in the plant reactors at different fill levels and stirring speeds, and the solvent and jacket temperatures were recorded. This data was used to generate numerical simulation models of the plant reactor dynamics. With this model in hand, experiments in the modified RC1 could be forced to track the temperature profiles that would be predicted on-scale. The validity of the technique was demonstrated by comparing the temperature profiles and selectivity for an oxidation reaction run in both the modified RC1 and in a 630 L vessel.

Explosion and Decomposition Characteristics of Hydrazoic Acid. Hydrazoic acid is a volatile, toxic compound that is formed in many azide processes due to the presence of small amounts of protic species. Last year, researchers from Novartis Pharma AG developed an online IR method to determine levels of hydrazoic acid in the headspace (*Org. Process Res. Dev.* **2006**, *10*, 349). This year, the same group has reported on the lower decomposition limit (LDL) of hydrazoic acid in a nitrogen atmosphere as a function of temperature and total initial pressure (*Org. Process Res. Dev.* **2007**, published ASAP, DOI 10.1021/op7000645). They report that hydrazoic acid explodes with more violence than propane in air, and it has a low minimum ignition energy of <1 mJ. The LDL drops as a function of increasing the total initial pressure, but there is no significant correlation with temperature. They also found that small partial pressures of solvents such as ethyl acetate and xylene efficiently inhibit explosion but warn that a detailed risk analysis is necessary for all processes involving hydrazoic acid.

Venting of Low Pressure Hydrogen Gas. The venting of hydrogen gas is an inevitable consequence of its use in industrial processes. With the potential for hydrogen to be used as a fuel carrier, the need for safer venting techniques will only increase in the coming years. A thorough review of the literature on this subject was written this year by G. R. Astbury (*Process Saf. Environ. Prot.* **2007**, *7*, 289). The article provides detailed analysis of the literature as well as a discussion on the pros and cons of various venting techniques available. There is also a decision tree provided for establishing appropriate venting regimes, which is a valuable tool to have on hand.

Inherently Safer Technology. Trevor Kletz in his book on plant design (*Plant Design for Safety*; Hemisphere Publishing Corporation: New York, 1991) stated, "The essence of inherently safer approach to plant design is the avoidance of hazards rather than their control by added-on protective equipment." This year, as usual, many articles were published that discussed the principles of inherently safer design of chemical processes and process plants. In fact, there is one written by Trevor Kletz himself, which appears immediately after this review. For an overview on this topic, please see the well written full review of inherently safer design by Dennis Hendershot (*Process Saf. Prog.* **2006**, *25*, 98).

In a paper written by Mannan (*J. Loss Prev. Process Ind.* **2007**, *20*, 79), the integration of Dow's fire and explosion index into process design and optimization is discussed. The concept was to add a safety metric, in this case the fire and explosion index, into the parameters for designing a piece of equipment or a new process. The authors outline how to reduce the safety parameter into a mathematical expression, show that there is a possibility for this expression to be integrated into the process design, and present that general idea that any safety metric can be integrated into the design of industrial processes. The final result is the optimum economic and inherently safer design for the reactor and distillation column system.

The lack of formal integration between process design stages with risk and consequence estimation is a hurdle to designing inherently safe process plants. To help close this gap, a new tool named integrated risk estimation tool (iRET) has been developed (*J. Loss Prev. Process Ind.* **2006**, *19*, 409). The authors give good background on the other tools that exist and then walk the reader through the framework of the iRET. This method provides a systematic methodology and technology to design an inherently safer plant. The overview of designing a safer plant was also the topic of an article written by Phil Leckner (*Chem. Eng.* **2006**, December 30). The author walks the reader through the stages needed to complete basic process engineering and then into the detailed process engineering required. An emphasis on performing a process safety analysis on both the process and the instrumentation and control systems is given. He also gives advice on how to implement a management of change procedure to ensure that all the work to design a safer process is not lost when a change is discussed.

A real-life example of choosing an inherently safer process option was outlined in an article by Karen Study of Rohm and Haas Company (*J. Hazard. Mater.* **2007**, *142*, 771). In the paper, a project to supply ammonia to a catalytic reactor was reviewed. The article is interesting in that what the team thought was going to be the inherently safer option at the start of the process did not turn out to be so in the final design. One of the conclusions is that there is not a single metric that can be considered as the "correct" metric for selecting one inherently safer design over another option. There is always a tradeoff.

Mining the Web for Safety Information. The following is a list of Web sites that the authors find useful for finding information on process safety and hazard analysis. If any readers have additions to this list, we would be most interested in seeing them and perhaps including them in next year's review.

(1) A list of pertinent safety Web sites for educational materials for universities and industry has been provided by Joesph Louvar and Dennis Hendershot (*Process Saf. Prog.* **2007**, *26*, 85).

(a) http://www.sache.org – Web site for the Safety and Chemical Engineering Education program

(b) http://www.csb.gov – Web site for the United States Chemical Safety and Hazards Investigation Board

(c) http://www.aiche.org – Web site for the American Institute of Chemical Engineers (in particular please see http://www.aiche.org/ccps/)

(2) http://www.nationalboard.org/nationalboard/Default.aspx – Web site for the National Board of Boiler and Pressure Vessel Inspectors. The National Board of Boiler and Pressure Vessel Inspectors was created in 1919 to promote greater safety to life and property through uniformity in the construction, installation, repair, maintenance, and inspection of boilers and pressure vessels. The National Board membership oversees adherence to codes involving the construction and repair of boilers and pressure vessels.

(3) http://www.genevac.co.uk/safe-evaporation/ – This site maintains several technical guides and articles on the safe evaporation of corrosive solutions.

(4) http://www.chemsoc.org/networks/gcn/ – Web site of the Green Chemistry Network (GCN). The main aim of the GCN is to promote awareness and facilitate education, training and practice of Green Chemistry in industry, commerce, academia and schools.

(5) http://www.safetynet.de/ – The European Safety management Group has a Web site dedicated to the distribution of safety information.

(6) http://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report – This Web site, operated by the EPA, contains basic information about the health and environmental hazards of 101 mass-produced chemicals.

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