Organic Process Research & Development

Organic Process Research & Development **2003**, *7*, 225

Editorial

Dangers of the Unknown

I must have had the future safety issue of *Organic Process Research & Development* (OPRD) on my mind whilst I was browsing through a remarkable book entitled *Fluorine Chemistry at the Millenium −Fascinated by Fluorine*, edited by Eric Banks (Elsevier, 2000), since most of the chapters I chose to read had a safety theme. The dangers of scale-up are illustrated by the following account from Darryl D. Desmarteau of Clemson University!

He needed $S_2O_6F_2$ for some work on the fluorosulphate radical and therefore scaled up the reaction of SO_3 and F_2 to 900 g using a catalytic reactor. The temperature controller was not working too well and when this happens a significant by-product, $FOSO_2F$, arises. As a result, the 900 g of $S_2O_6F_2$ produced also gave 200 g of this by-product which was separated and collected in a cold trap, then transferred to a metal cylinder and allowed to warm to room temperature. He then went for a couple of beers with a friend before returning to the lab. About 2 h later, judging that the compound had warmed, he removed the cylinder and laid it on its side in the fume hood and labeled it. He was just reaching to pick it up when the cylinder exploded with incredible force, instantly removing the chemist's left-hand and part of the forearm, and also part of his right-hand. The face shield and safety glasses were destroyed and his wristwatch was embedded in the ceiling!

The chemist said that from this he learnt two lessons:

(1) It's what you do not know that will get you (i.e. forewarned is forearmed).

(2) If he had had two more beers, he may not have lost his hand, since the explosion may have occurred before he returned to the lab!

As you can maybe guess from the tone of the above, the chemist described this incident in a light-hearted way. He continued doing chemistry for many years with a prosthetic device for a left-hand (most useful for handling hot objects!). He also raced cars for a hobby, not letting his disability prevent him from doing anything he wanted. A remarkable story.

The other chapter, which fascinated me, was from William J Middleton formerly of DuPont. Whilst working on Freon refrigerants he came across some extremely toxic fluorine compounds such as perfluoropinacol, prepared from hexafluoroacetone. A single drop of perfluoropinacol on the skin of a guinea pig is sufficient to kill it. Middleton had made over 500 g before this was realised. It was only by good fortune and excellent hygiene practices by DuPont employees that no one was poisoned by this material before it was ultimately destroyed. So fluorine compounds can be amongst the least toxic (e.g., blood substitutes) and the most toxic, too.

On the subject of extreme toxicity, a presentation by Jared Randall of Procter and Gamble, at a recent Organic Process R & D symposium in New Orleans, described a highly toxic but very minor impurity in a batch of drug substance, which failed the Ames test. After discussion with the FDA the specification for this impurity was set at 0.0000070%! Since the compound was a late eluter in the HPLC (∼60 min, if I remember correctly), it was very easy to miss at the low level required for carcinogenicity. Hopefully, more details of this project will appear in future editions of the journal.

I hope these stories have made you more aware of the dangers of the unknown. For our safety issue in Nov/Dec 2003, you can prevent the "dangers of the unknown" by publishing details of compounds you have worked on and found to be toxic, unstable, explosive, or difficult to handle. Don't keep this information to yourself—publish it in OPRD. Letters to the editor on safety topics are also very welcome.

Trevor Laird
Editor

OP034047R

10.1021/op034047r CCC: $25.00
Published on Web 04/26/2003