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Editorial

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Metal Contamination: When the Contaminant May Be the Actual Catalyst

Those who work in the fine chemicals, agrochemicals and pharmaceutical industries are used to analysing final products for metal contamination, but we do not always analyse our metallic reagents and catalysts to make sure that the metal present is "what it says on the tin". A recent alert from the laboratories of Steve Buchwald and Carsten Bolm (*Angew. Chem., Int. Ed.* **2009**, *48*, 5586−5587) warns of the role of metal contaminants in catalysis by iron salts. In our Highlights from the Literature section we have often suggested that chemists consider iron catalysts for many reactions, but some have found the results not so reproducible. It was noticed by chemists in two groups, at MIT and Aachen, that catalyst activity depended on the metal salt purity and even more so on its commercial source.

In a collaborative investigation, they have now established that the outcome of iron-catalysed reactions can be affected by traces of metal contaminants (particularly copper), hence, the importance of the commercial source of the reagent. Thus, in some reactions use of 99.99% pure ferric chloride led to lower yields than when 98% pure salt was used. Addition of 5 ppm cuprous oxide to the 99.99% pure ferric chloride restored the yield. However, it was also found that the cuprous oxide in the absence of iron also catalysed the reaction (e.g., arylation of a pyrrazole).

A few years ago there was a similar story, when a publication on metal-free Suzuki reactions was subsequently shown to be due to traces of precious metal in the sodium salt used in the reaction. Similar tales are heard about Simmons−Smith and other reactions. There must be hundreds of anecdotes in industry where changing the source of metal has caused problems. I remember one incident more than 30 years ago when I was scaling up a copper-catalysed Meerwein reaction of diazonium salts, where high yields of 95% were occasionally obtained with some samples of copper salts, when the norm was often 50−60%. Investigation of this anomaly led eventually to a highly cost-effective process.

So the message is clear. Trace metals can have tremendous importance in catalysis, and when changing the source of reagent and its specification/quality, one should be aware of these dangers. An increase in quality does not necessarily mean a better reaction yield or faster catalyst. Be warned!

We are now accepting papers for the Special Feature Section on Genotoxic Impurities, which will appear in issue 4 of 2010. This is a hot topic at present as evidenced by recent papers and correspondence in *Organic Process Research & Development*. The deadline for receipt of submissions is January 31, 2010. I look forward to receiving your manuscripts.

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Editor

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