Organic Process Research & Development

Editorial

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Green Chemistry is Good Process Chemistry

One of the aims of good process chemistry should be to minimise the amount of waste products in manufacture. Chemists and engineers can achieve this in several ways, but one excellent way is to minimise the amount of solvent used in a chemical process, first ensuring that this does not, in itself, lead to increased hazards. After all, solvents are very useful as a heat sink in exothermic processes.

Choosing the solvent for a chemical process is a complex issue, and all chemists have their own favorite solvent which they like to use in the laboratory. However, when it comes to manufacture, the choice should be much more limited (for toxicity and environmental reasons as much as cost), and there have been a number of recent publications which have listed solvents and prioritised them in terms of "greenness". See for example Dunn, P. J. ref 1 and Jimenez-Gonzales, C.; Constable, D. J. C. ref 2.

Over the last 18 months, the Editorial Advisory Board of *Organic Process Research & Development* (OPRD) have discussed the use of certain, less environmentally friendly solvents in published papers, and we have been given information through presentations from the ACS Green Chemistry Pharmaceutical Round Table on this subject. We are still surprised, for example, at the continued use of benzene in university laboratories—a solvent which is virtually banned in industry (at least in Western Europe), although still in use as an important raw material for aromatic compounds. Other undesirable solvents such as chloroform regularly appear in journal articles, even occasionally in OPRD in the past.

We have decided, therefore, to take the lead in encouraging chemists and engineers to minimise the use of certain solvents such as benzene, carbon tetrachloride, chloroform, dichloroethane, HMPA, carbon disulfide, and other environmentally harmful solvents by changing our editorial policy with regard to papers containing reactions and processes using these solvents. Here are some extracts from the 2012 Scope and Editorial Policy, found in Information for Authors under Submission & Review at the OPRD home page, http://pubs.acs.org/journal/oprdfk.

> *"The journal encourages researchers to consider the environmental consequences of the way in which they perform their experiments and to minimize waste."*
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> and
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> *"From 2012 the policy on use of organic solvents has been changed to discourage scientists from using particular solvents and to encourage them to seek alternatives wherever possible; papers containing **strongly undesirable solvents** (e.g., benzene, carbon tetrachloride, chloroform, HMPA, carbon disulfide, etc.) will only be considered if accompanied by an analysis of alternatives or if a convincing justification for such use is presented."*

The journal also encourages authors to carry out calculations which give performance metrics related to environmental impact and green chemistry principles, and the following statement is now included in the scope and policy of the journal.

> *"Thus submissions including quantitative measures of green chemistry performance such as mass intensity/efficiency, atom economy, and E-factor are particularly welcome."*

I note that several recent papers, particularly from certain companies such as GSK and Pfizer, have already included such calculations of green chemistry performance. Regretably, many papers, whilst demonstrating excellent synthetic chemistry, still show a disregard for the amount of waste, particularly aqueous and solvent waste, produced on a kilogram scale. Too often the processes are more what we would expect to see in university or medicinal chemistry laboratories, where little attempt has been made to optimise the workup to minimise the number of unit operations, particularly solvent extractions and washings, and the amount of solvent used in each operation. The editors encourage all authors to consider these issues before submitting their papers to OPRD, and we warn that **authors risk having papers rejected unless environmental impact and green chemistry principles are considered.**

We hope that in doing this we can encourage chemists in university and discovery chemistry, as well as process chemistry, to become more aware of alternatives to toxic and environmentally harmful solvents and to use simple alternatives wherever possible (see below), and to teach students to minimise the amount of solvent (and aqueous waste, too) in reactions and especially workups as an important principle of good practical chemistry. After all, green chemistry is just good process chemistry.

Table 1 is adapted from the Dunn reference quoted earlier.[1] The only quibble I have is that I prefer isopropyl acetate to ethyl acetate as an extraction solvent since the relatively high solubility of EtOAc in water (and water in EtOAc) means that the aqueous waste is contaminated with more organic material, thus making it harder to dispose of—and also product could be lost in the aqueous layer!

Table 1. Solvent replacements (as used at Pfizer)

undesirable solvent	alternative
hexane and pentane	heptane
DIPE or diethyl ether	2-MeTHF or TBME
dioxane or DME	2-MeTHF or TBME
chloroform, dichloroethane	dichloromethane
DMF, DMA, or NMP	acetonitrile
pyridine	triethylamine
dichloromethane (extractions)	ethyl acetate, TBME, 2-MeTHF, toluene
dichloromethane (chromatography)	ethyl acetate/heptane
benzene	toluene

Thus, in conclusion, the policy of OPRD on the use of undesirable solvents is now strictly defined to encourage use of alternatives where possible. Perhaps we should also change the front cover of OPRD from red to green?

Trevor Laird, Editor

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REFERENCES

(1) Dunn, P. J. *Pharmaceutical Process Development*; Blacker, J. A., Williams, M. T., Eds.; Royal Society of Chemistry: London, 2011; Chapter 6.

(2) Jimenez-Gonzales, C.; Constable, D. J. *Green Chemistry and Engineering: A Practical Approach*; Wiley: New York, 2011.