The Green Chemistry Institute Pharmaceutical Roundtable (GCIPR) Reagent Guides

What do the Reagent Guides Hope to Achieve?

In line with the GCIPR core values, these guides aim to assist chemists in making informed decisions regarding the most sustainable reagent for the transformation to hand. They follow on from the concept of the Reagent guides introduced by Pfizer.

The guides are compiled by enthusiastic industrial multidisciplinary chemists who have scaled many of the methods.

While the guides are designed to promote green chemistry, they also aim to be a convenient reference and, as such, are not limited to only those reagents considered ‘green’.

Good green chemistry requires the chemist to look across a range of factors before making the best choice. With the inclusion of information such as atom efficiency, ecotoxicology/toxicology profiles, safety issues, waste products, sustainable feedstocks etc – we hope these guides give obvious promotion of some reagents over others. However a holistic approach is encouraged – i.e if a ‘greener’ reagent gives a much lower yield or requires multiple steps the overall benefit may be limited (i.e higher footprint in the wider context) in contrast to an initially less green reagent.


Oxidation to Aldehyde and Ketone example

TEMPO-Bleach oxidation

Mechanism + Description

As a precursor for TEMPO, NaOCl is often used as a co-oxidant which generates NaCl as a by-product. But or tetroxone are often added as a promoter.

General Comments

A common terminal oxidant is bleach (NaOCl) which is often employed with a Bromide or borate co-catalyst. Reactions in water of highpurity reactions are often helped by the addition of a phase transfer catalyst.

Key References

- Production of Aldehydes by Continuous Bleach Oxidation of Alcohols

Relevant Scale up examples

8 Guides Now Publicly Available...

Bromination
Fluorination
Chlorination
Iodination
Metals Removal
Chiral Hydrogenation
Oxidation to Acids
Suzuki Rxn
Buchwald-Hartwig Rxn

More Guides Coming

Green Review

1. Atom efficiency (byproducts Met)
Generally good – the removal of H, generates NaCl ($\text{NaCl}$) as a by-product.

2. Safety Concerns
All TEMPO oxidations are exothermic and may present delayed exotherms. Compatibility of NaOCl with other reaction components needs to be considered.

3. Toxicity and environmental/aquatic impact
Generally low when used catalytically, the major concerns arising from the co-oxidant. Nitrooxy radicals like TEMPO and the hydroxylamine intermediates in the oxidation cycle give positive structural alerts as potent genotoxic impurities (PGI).

4. Cost, availability & sustainable feedstocks
The cost of TEMPO has fallen over time and is now available in bulk. Other analogs are less commercially available and much more expensive – but sometimes display greater activity. The solvation of TEMPO comes from acetone and amine.

5. Sustainability implications
With good optimisation of catalytic loading, and a low molecular weight terminal oxidant like NaOCl, this oxidation is a good choice. The major concern would be the solvent used. Many initial publications used dichloromethane, but later work has shown more sustainable solvents can be used – see references.

The American Society of Chemistry Green Chemistry Institute Pharmaceutical Roundtable (ACS GCIPR)

The roundtable was formed in 2005. Its mission is to catalyze the implementation of green chemistry and green engineering in the global pharmaceutical industry.

The activities of the ACS GCIPR reflect the joint belief that the pursuit of green chemistry and green engineering is imperative for a sustainable business and world environment. The ACS GCIPR aims to achieve its mission through 4 strategic priorities:

- Inform and Influence the Research Agenda
- Tools for Innovation
- Education Resource
- Global Collaboration

The roundtable is currently made up of 12 globally leading pharmaceutical companies and 1 associate member.

www.reagentguides.com