

DIV-CC-NNN

Azides Manipulation: Danger is not our Middle Name

M. Zuffo, a G. Razzetti, L. Simons, C. Stewart, B. Loertscher B. Loertscher B. Loertscher B. Loertscher B. Loertscher B. Baranzate, Italy

Bipharma Inc, 4502 Campus Dr, Kalamazoo, US

michela.zuffo@dipharma.com

Azides play a pivotal role in organic synthesis, as they allow to introduce a variety of key functional groups in synthetic scaffolds of interest. These include amines, triazoles, tetrazoles, isocyanates, etc. 1,2 Regardless of azides role in the synthesis -whether only azide-based reagents are used or the azide moiety is also present in the resulting product- this type of chemistry generally involves significant safety risks. 3 Main concerns are linked to azides general toxicity and explosivity. In addition to this, each azide bears the potential to form hydrazoic acid (HN₃) upon decomposition, which is even more dangerous than its precursors. 4

Despite these caveats, azides are often manipulated, especially at small and medium scale, with insufficient precautions and knowledge about the involved risks. ^{5,6} At Dipharma, we have extensive experience in the safety evaluation for scale-up of chemical processes involving azides, with multi-ton productions per year of various intermediates and APIs exploiting this type of chemistry. In this presentation, we will provide a general overview about the dos and don'ts in azides manipulation based on this expertise. These will cover the main incompatibilities, some rule-of-thumbs to evaluate the dangers that may be encountered and some strategies to tame the highlighted dangers. These will be supported by tailored examples from our product portfolio, giving a taste of the chemical space that can be accessed at scale when making good use of azides chemistry.

References:

[1] S. Bräse; C. Gil; K. Knepper; V.N. Zimmermann, Angew. Chem Int. Ed. 2005, 44, 5188 – 5240.

[2] E. F. V. Scriven; K. Turnbull, Chem. Rev. 1988, 88 (2), 297 – 368

[3] J.-P. Hagenbuch, Chimia, 2003, 57 (12), 773 - 776

[4] J. Wiss, C. Fleury, C. Heuberger, U. Onken, M. Glor, OPRD 2007, 11 (6), 1096-1103

[5] N. P. Peet, P. Weintraub, «Azide explosions discussed further,» C&EN, 14 March 1994

[6] V. J. Hruby, L. Boteju, G. Li, «Explosion with sodium azide,» C&EN, p. 2, 11 October 1993.