

Safe processes and high purity for a high-tech market

Dr Aline Devoille and Dr Marc Uerdingen of Novasep look at purification in the manufacture of electronic chemicals

Chemicals for the manufacture of electronic devices are currently in the spotlight and the way from bench to industrial production is paved with challenges. Electronic chemicals are often produced from highly energetic intermediates, raising a number of safety concerns. In addition, these compounds are required in very high and specific purity grades. A combination of safe and proven manufacturing practices and suitable purification processes is needed to provide the high quality chemicals needed in this high-tech market.

Safety first

N-heterocyclic compounds are widely used in electronic chemicals: in washing solutions for the lithographic process, as chelating agents for chemical mechanical planarisation (CMP) or in organic light-emitting diode (OLED) materials. The most common heterocycles are five-membered rings with several consecutive nitrogen atoms, like tetrazoles or oxadiazoles. This type of motif is typically generated by an azide reaction (Figure 1).¹

Azides, in particular small organic ones, are potentially hazardous, due to their explosive properties. They have to be handled carefully, especially at industrial scale. Safety criteria have to be defined early within the development of the production process. Specific equipment and good handling practices have to be implemented to operate under safe conditions.

As a first approach, basic considerations are to be taken into account: the basic guidelines stated by Peer are usually acknowledged as correct. Sodium azide, he states, "is relatively safe, especially in aqueous solution, unless

acidified to form HN_3 , which is volatile and highly toxic".²

In addition, hydrazoic acid is strongly shock-sensitive and it is critical to maintain its concentration in the gas phase below the point of condensation at any time during a given reaction. When generated *in situ*, it should be consumed quantitatively. Dilute aqueous solutions of hydrazoic acid (20% and lower) are not explosive and are safe to use, even at industrial scale.

Peer also states that, "for organic azides, the 'rule of six' is very useful: six carbons (or other atoms of about the same size) per energetic functional group (azide, diazo, nitro, etc.) provide sufficient dilution to render the compound relatively safe. Note that the presence of acetylenic groups or other energy producers with an azide makes for increased hazard."

"The decomposition of organic azides can be catalysed by certain transition metal species (especially those from the Fe and Co triads) and by strong acids [or bases] ... Azide groups attached directly to olefinic, aromatic or carbonyl moieties are much less stable and, other things being equal, more dangerous than aliphatic azides, the approximate activation energies for unimolecular loss of N_2 being 29 and 49 $\text{kcal}\cdot\text{mol}^{-1}$, respectively."

"For these reasons, azides should not be distilled or treated in a careless fashion. However, when common sense is employed, they can be prepared, stored and used without risk in the standard [small-scale] organic chemistry laboratory. We have never experienced a safety problem with these materials."²



Prochrom LC300 preparative HPLC column with Hipersep M chromatography system

These guidelines are also valid as a rough initial approach to industrial use of azides. However, theoretical considerations based exclusively on chemical structure analysis do not provide a reliable enough assessment of explosiveness. Experimental investigation is required to evaluate the hazard and to classify the compound according to the UN transport classification system.³

This classification determines the precaution required for handling and transportation. Thermal stability is assessed by differential scanning calorimetry, thermo-gravimetric analysis and the Koenen and Bonefire tests. Shock and friction tests assess the mechanical stability of the compound.

Samples are also tested for storage stability, detonation propagation (via the 2" steel tube test), self-decomposition and dust explosion (via the Hartmann tube test). Reaction calorimetry and reaction heat calculation investigations are also necessary to assess the hazards associated with a compound. Based on these experiments, sodium azide is classified as a 6.1 explosive compound and 1-H-tetrazole as a 1.1D.

Strong expertise and reference data collected over the years are necessary to determine the hazard class of a compound. These

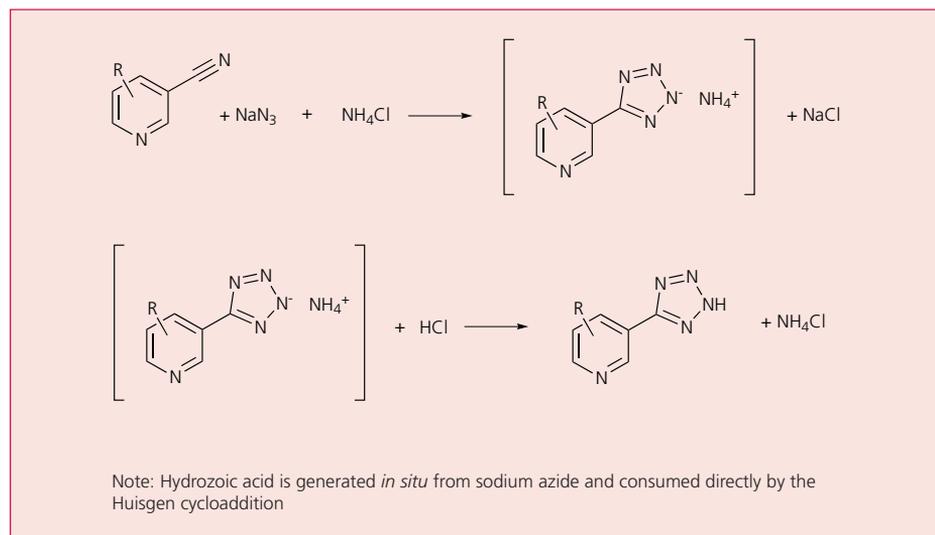


Figure 1 - Reaction of a cyano compound with hydrazoic acid in a 1,3-dipolare cycloaddition

qualifications are also needed to design and operate safe processes. Only companies with long track record in hazardous chemistry, notably historical producers of explosives, have the knowledge and experience to produce or use high energy materials on large scale.

Purity is key

Electronic chemicals are typically needed as ultra-pure compounds, since even trace impurities can heavily impact the performance of the material. In addition, the market is tending towards ever more stringent purity requirements and increasingly seeks advanced purification technologies for intermediates and final products alike.

High purity can have different significance for different applications. For example, chemicals for OLED manufacturing are required in high absolute purity of >99.999%. Even though the chemical structures of potential impurities are known, their effect on performance remains unknown. Very strict and constant impurity profiles are thus demanded.

By contrast, semiconductor materials can tolerate lower relative purity of 99.9%+ but it is critical to avoid specific impurities, including metals such as copper. The purity required can be so high that the accuracy of current analytical methods is not sufficient to validate a batch and a physical performance test is also needed. As a result, the monitoring and correction of industrial processes is very challenging.

The achievement of the desired purity needs to be anticipated very early in the process development. The whole production process demands extremely robust processes so as to ensure a constant quality and impurity profile over time. Several methods can be considered to purify the final product and the choice often results from a cost-purity balance.

Sublimation is still the method of choice to reach high purity. This physical property also allows the use of chemical vapour deposition, which is widespread in the industry. However, it suffers from poor efficiency at large scale - only a few percentage points of the product actually gets deposited for small organic molecules.

With printed electronics gaining momentum, thin films tend to be produced via printed ink-jet technology, which requires liquid organic formulations. Organic molecules rarely undergo sublimation and alternative purification methods are required.

Most of the time, heat-stable liquid substances are **distilled**, provided that their boiling point is reasonably low, while solid compounds are **crystallised**. Since electronic chemicals are often small molecules, the impurities are usually structurally very different from the desired molecule and exhibit different physico-chemical behaviour. If a crystallisation is possible, it is usually very selective and leads to high purity.

In some cases, distillation or crystallisation are very difficult or even impossible and **flash chromatography** is implemented as a quick, versatile approach to high purity organic

chemicals: impurities can be eliminated and ultra-high purity can be reached, even from very complex mixtures. However, this technology is often seen as expensive, tedious and inefficient at production scale.

The electronics industry rarely considers **preparative HPLC** to solve these challenging purifications, despite the numerous successful examples of production-scale HPLC in the fine chemicals, pharmaceuticals and food industries. Preparative HPLC is well suited to moderate to medium scales (up to 1 tonne) and is based on the same principle as analytical HPLC: a solute is injected and separated through a column packed with small-sized particles at an elevated flow rate.

For large-scale purification purposes, the use of the stationary phase is optimised and the productivity is improved by injecting larger

quantities of crude product - the column is overloaded to reach the minimum acceptable resolution between peaks - and stacking injections: a new injection is carried out before all products of the previous injection have been collected.

Whilst flash chromatography can be well suited to capture or silica filtration steps, HPLC offers strong potential in challenging industrial purifications. It is robust and highly predictable and it offers direct linear scale-up (see *box story*). The potential for chromatography in a given separation is assessed by screening stationary phases and operating conditions.

Lithographic chemicals

Demand for chemicals for electronic applications has increased significantly in recent years and it became a major market for fine



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■ Industrial HPLC v flash

HPLC is two to five times more efficient than flash chromatography: the increased flow rate - and therefore the operating pressure - affords narrower peaks, better resolution, and very fine separations. A single path is typically sufficient to obtain very high purity. The product is consistently collected at the required purity as a single fraction, thanks to an automated collection system.

HPLC benefits from a linear scale-up, up to one million-fold, and results at large scale are reliably predicted from a limited number of sub-gram experiments.¹⁰ Appropriate process development leads to highly reproducible and robust processes for consistent impurity profiles batch after batch.

Another important difference between flash chromatography and HPLC lies in the stationary phase. The phases developed for HPLC are well-characterised, small particle (10-20 µm) media. Their spherical shape and narrow size distribution enhances efficiency.

Modern stationary phases are widely recognised to be stable and robust. Yet, these criteria are tested at laboratory scale for each purification, because they are directly impacted by the operating conditions (product

corrosiveness, nature of the eluent, operating pressure, etc.). Regeneration or back-flush steps can be necessary and a good process optimisation maximises the lifetime of the phase.

As a rule of thumb, HPLC requires five to ten times less stationary phase than flash chromatography because its use is optimised and the volumes required are lower; bed lengths rarely exceed 20-30 cm.

While the mobile phase is often renewed for each batch in flash chromatography, it can easily be reused for hundreds of cycles with HPLC: a six-month to one-year lifetime is normally a given and phase durability exceeding five years are commonly observed for mild condition separations. Production costs are also limited by very efficient solvent recycling (over 99%) at industrial scale.

In terms of productivity, industrial HPLC separations usually reach around 2-10 kg of pure product produced per kg of stationary phase per day, affording productions in the range of few kilograms to hundreds of tonnes/year with costs potentially in the low range of hundreds of Euros/kg of pure product.

chemicals. These compounds include finishing agents for wafers, lithographic processes, chemicals for printed electronics, etc. The use of different N-heterocycles and reactive azides is discussed below, together with the specific grades required.

Tetrazoles with specific substitutions are used at different stages in the **lithographic process**, a key step in the production of microchips. Thione- or mercapto-substituted tetrazoles can be used as precursors in the production of UV-resists: the loss of dinitrogen and heteroatom sulphur from them is photo-triggered, leading to the corresponding carbodiimide. This compound then reacts further with free carboxylic acid to form the UV resists.⁴

Thione- and mercapto-substituted tetrazoles are also used in washing solution for the lithographic printed plate.⁵ Their ability to complex with silver enables metallic compounds to be captured and recovered on a filter. This prevents silver suspension in the washing solution from causing turbidity or the release of silver into the environment. In addition, ink receptivity and printing endurance are reported to be remarkably improved.

Both of these applications require high purity. In particular, metal traces have to be strictly avoided in thin film applications to ensure a high quality of film. As a result, starting materials used in the production of tetrazoles have to be purified, usually by conventional methods.

A stringent equipment cleaning process also has to be implemented to meet the low ppm or even ppb specifications for metal or halide traces. The final product may need to be further purified, typically by successive washing steps,

to remove metal traces and inorganic salts and by chromatography or crystallisation to discard organic impurities.

CMP & tetrazoles

Tetrazoles are good chelating agents, due to their high affinity for metals, especially copper. Substituted and non-substituted tetrazoles (like 1-H-tetrazole) play a crucial role in formulations for **CMP**. This technology achieves a planar and homogeneous surface down to atomic scale by combining chemical and mechanical forces.⁶ It is typically used for semiconductor wafers or metal stripes.

The CMP process requires high purity grades: only very low levels of organic solvents and particles are tolerated. Due to the difficulty of reducing the VOC content down to the ultra-low ppm level, the use of organic solvent should be kept to a minimum in the synthesis and washing process.

Since tetrazoles are explosive, their formulation requires special care for the product to be handled and transported in a non-explosive form. Novasep has developed a safe formulation of 1-H-tetrazole using water as a phlegmatising agent which does not interact with the CMP formulation or the substrate itself.

1-H-tetrazole can also be substituted for a less reactive compound. For instance, 5-phenyl-1-H-tetrazole is a safe copper-passivating agent for low-pH in CMP or etching formulations.⁷

OLED chemicals

OLED technology is currently gaining momentum over liquid crystal display

technology. Recent advances, especially in the area of printing, are opening up applications for larger devices, such as TVs.

OLED screens have a multi-layer structure and heterocycles are involved in the composition of several of them. Amongst the chemicals involving hazardous chemistry, dimeric, dendrimeric and polymeric oxadiazoles are widely investigated as electron transport material, due to their π -stacking abilities.⁸ An example of a very efficient synthetic approach to oxadiazoles is illustrated by the reaction of 1,3-dicyanobenzene with 3-(1,2,4-triazol-5-yl)-benzotrile.⁹

Chemicals used for OLED materials are typically required in >99.999% purity; the impact on the efficiency of a given impurity and the combined impact of various impurities present in the different layers can be significant and has to be eliminated. The most commonly used materials are organic compounds, which are purified by sublimation and deposited by sublimation and ink-jet processes. In particular, the light-emitting layer is composed of highly conjugated organic dyes. Chromatography can be a method of choice to discard organic impurities and reach ultra-high purity.

In the light of the complex syntheses involved, the purity required and the high added value of electronic chemicals, preparative HPLC is an efficient and cost-effective option to consider for complex purifications. In addition, the high reactivity of some chemicals or starting materials calls for advanced safety precautions. As a result, the production of many electronic chemicals would benefit from partnerships with experts in purification and/or hazardous chemistry.

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