Application of SepaFlash® Cartridges in the Purification of Diazo Compounds

Application R&D Center

Recently, the research group of Dr Andre Charette from University of Montreal published a new work [1] on the famous chemical journal ***Angewandte Chemie International Edition***. In their work, they utilized the continuous flow system for the safe and quick synthesis of nonstabilized alkyl diazo compounds.

Diazo compounds are a powerful and versatile class of reagents in organic synthesis, as they are precursors of either highly reactive carbenes, carbenoids, or carbocations, thus enabling formal C-H, C-C, and C-X bond insertions as well as various cycloadditions. However, the drawbacks of this species including sensitivity, explosivity and toxicity are still hindering their common use in laboratories, especially on large scale. In Dr Charette's group, continuous flow technology was employed to tackle the above mentioned issues. The continuous flow system can overcome the three main drawbacks of nonstabilized diazoalkanes synthesis: 1) precise control of the production conditions to limit degradation; 2) easy purification by the use of insoluble solid reagents to avoid the handling of the diazo solution; and 3) on-demand direct consumption of the reactive materials at the output of the reactor, thus circumventing the risks associated with

storage of toxic and unstable reagents. Figure 1 shows the experimental setup of alkyl diazo compounds synthesis on a continuous flow system.

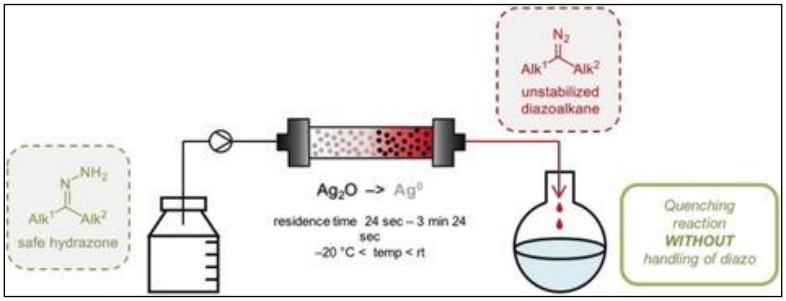

Figure 1. The brief schematic of the experimental setup of alkyl diazo compounds synthesis on a continuous flow system (Reproduced from the website of *Angewandte Chemie International Edition*).

To demonstrate the suitability of the method for safe and convenient large-scale production of unstabilized diazoalkanes, a scale-up synthesis of a furyl-alkyl diazoalkane was conducted. As shown in Figure 2, 8.5 mmol of the furan diazo compound **2q** was produced over 60 minutes, and it was consumed in line in a [3+2] cycloaddition. Purifications by flash chromatography were performed on an automated flash chromatography system companion using pre-packed SepaFlash® silica columns from Santai Technologies. The gradient was from 0% ethyl acetate and hexanes to 100% ethyl acetate. The flash purification afforded the desired product **3q** as a yellow oil, with the weight of 1.71 g as well as the yield of 76%.

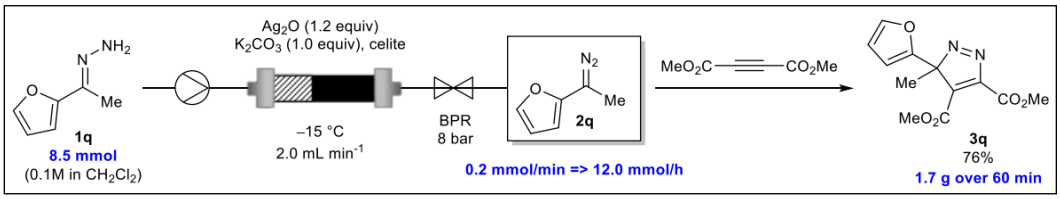

Figure 2. Scale-up synthesis of a furyl-alkyl diazoalkane (Reproduced from the supporting information of Ref. 1).

In Dr Charette's group, several kinds of SepaFlash® silica columns were utilized for the purification of synthetic products, including Standard Series (40 – 63 μm UltraPure irregular silica) and HP Series (25 μm and 15 μm High-capacity spherical silica). The high-capacity spherical silica has 40% higher surface area, doubling the loading capacity of lower surface area silica. Besides, HP series silica columns have the following features:

- HP series flash columns are spin-welded and allow for higher pressure of up to 400 psi.

- Spherical silica provides improved performance without increasing the backpressure.
- This series provide Luer-Lok in and Luer-Lok out flexibility for convenient column stacking which makes the column resolution even better.
- Available adapters for HP series columns facilitate compatibility with any flash system on the market.

Please find more ordering information and specifications of HP series silica columns in the following tables.

High-capacity spherical silica, 25 µm, 50 Å (NEW Product)
(surface area 700 m^2/g, pH 5.0–8.0, loading capacity 0.1–30%)

Item Number	Column Size	Sample Size	Units/Box	Flow Rate (mL/min)	Cartridge Length (mm)	Cartridge ID (mm)	Max. Pressure (psi/bar)
SW-2102-004-SP(H)	4 g	4 mg–1.2 g	20	15-30	113.8	12.4	400/27.5
SW-2102-012-SP(H)	12 g	12 mg–3.6 g	18	25-50	134.8	21.4	400/27.5
SW-2102-025-SP(H)	25 g	25 mg–7.5g	12	25-50	184.0	21.4	400/27.5
SW-2102-040-SP(H)	40 g	40 mg–12 g	12	30-60	184.4	26.7	400/27.5
SW-2102-080-SP(H)	80 g	80 mg–24 g	10	40-80	257.4	31.2	350/24.0
SW-2102-120-SP(H)	120 g	120 mg–36 g	10	45-90	261.5	38.6	300/20.7
SW-2102-220-SP(H)	220 g	220 mg–66 g	6	60-120	223.5	61.4	300/20.7
SW-2102-330-SP(H)	330 g	330 mg–99 g	5	60-120	280.2	61.4	250/17.2

• Compatible with all flash chromatography systems, for example ISCO, Biotage, Yamazen, etc.

High-capacity spherical silica, 15 µm, 50 Å (NEW Product)
(surface area 700 m^2/g, pH 5.0–8.0, loading capacity 0.1–30%)

Item Number	Column Size	Sample Size	Units/Box	Flow Rate (mL/min)	Cartridge Length (mm)	Cartridge ID (mm)	Max. Pressure (psi/bar)
SW-2103-004-SP(H)	4 g	4 mg–1.2 g	20	15-30	113.8	12.4	400/27.5
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References

1. P. Rulliere, G. Benoit, E. M. D. Allouche, A. B. Charette, Safe and Facile Access to Nonstabilized Diazoalkanes Using Continuous Flow Technology, *Angew. Chem. Int. Ed.* **2018**, 57, 5777–5782.

For further information on detailed specifications of SepaBean™ machine, or the ordering information on SepaFlash® series flash cartridges, please visit our website:

www.velocityscientific.com.au