

Increasing Productivity with Automated Flash Purification

Rice University Customer Case

By Sarah Moran



During a recent trip to Houston, Texas, I was able to stop in at Dr. László Kürti's lab at Rice University and speak with him and one of his graduate students, Nicole Behnke, to learn about their recent projects, how they use the Isolera™, and learn some interesting chemistry along the way. Sitting inside his office with dozens of textbooks and reference books lining the walls, we dug into the thinking behind the science.

The scientists, left to right: Dr. László Kürti, graduate student Kaitlyn Lovato, Ph.D. Padmanabha Venkatesh Kattamuri, and graduate student Nicole Behnke. Not Pictured: Ph.D. Zhe Zhou, Ph.D. Juha Siitonen, Ph.D. Yaojia Jiang, Ph.D. Pyeong-Seon Kim.

You might recognize László Kürti from your organic chemistry classes where his first textbook titled "*Strategic Applications of Named Reactions in Organic Synthesis*" is widely used by both undergraduate and graduate students, and by professional chemists in research laboratories worldwide.

Can you tell me how you integrate flash chromatography into your everyday activities?

Nicole Behnke: We use the Isolera flash chromatography system for almost everything we do. It's really convenient to put your material onto a column and be able to do other tasks while it

runs – the ability to do two things at once is my favorite part. I can have a column running while doing something else like setting up another reaction or taking notes, so I can be more productive.

László Kürti: Luckily Nicole hasn't had to do a ton of manual columns, but take me for example, I did my Ph.D. at University of Pennsylvania from 2001–2006. We didn't have such a system and used only manual columns. When I look back, I calculated that 50% of my time as a Ph.D. was spent baby-sitting columns. I'm good at utilizing my time, so I read lots of literature

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references for my named reaction book while those columns were running. I'm pretty sure that from all the manual column-packing back then, I now have un-removable silica in my lungs! That's something I want to highlight: the air in the lab is much cleaner and the hazard lower because the silica is contained in the Biotage cartridges.

Is clean air one of your main reasons for choosing pre-packed columns?

LK: That's one reason why I bought several Isolera units. I also wanted to have my group work efficiently, and I can tell you that the lab's productivity has increased considerably as a result of these machines and columns. It's well-known that when I was starting my career at UT Southwestern (2010–2015) I had only three group members, and we published many papers with lots of structurally diverse substrates and products. It's because of the two Isolera units that we were able to be so productive. People could do, as Nicole pointed out, multiple things at the same time and not have to focus on just collecting fractions of purified compounds. The Isolera is great too because it tells you which compound is in which test tube.

So how has your productivity increased?

LK: By at least a factor of two, and that's a conservative estimate. If the separation is clear-cut, then it's easy to run a few separations a day. We can run three or four columns a day, which is a good, busy day for the students. I also put a lot of emphasis on people having enough time to think about their projects. We should do more than just execute reaction sequences and purify the resulting compounds. In the meantime, we need to think deeply about multiple aspects of our projects and Biotage allows us to do this. In essence, the Isolera is a labor saving device. Thinking almost moves to the backburner when you get too busy. You always need the quiet time. This allows you to diversify your daily activities if you have Biotage.



Nicole Behnke at the workstation. “We were able to make around 60 substrates and used our Isolera for every single one of those purifications.”

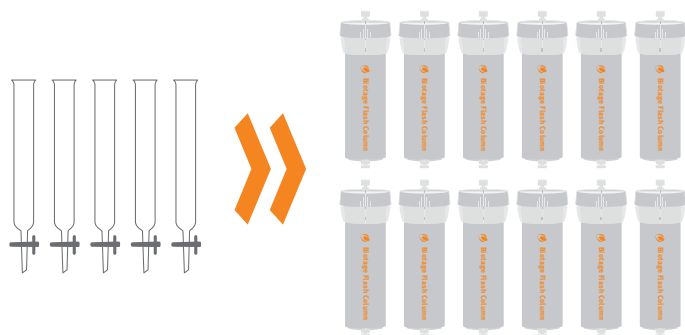
Nicole, you just published a paper. Can you describe what it is about?

NB: We took α -bromo amides and α -bromo carboxylic acids and looked to form a carbon-oxygen bond, which makes hindered ethers. We were able to make around 60 substrates and used our Isolera for every single one of those purifications. We had a broad range of compounds including primary, secondary and tertiary alcohols, phenols, and compounds with sulfur, and created carbon-oxygen or carbon-sulfur bonds. We used the Isolera for every compound and had very good separation for all of the products and very high yields, which were in the 90% range.

Also in that project, we did kind of a mini medicinal chemistry project where we made an analog to a PAR-1 antagonist and purified all of intermediates with the Isolera. Even though these intermediates had a little more complicated structure than usual, the Isolera handled it well and had good separation for all of those compounds. Most of the products in this project were very UV active and the Isolera did a great job separating them and indicating which test tubes each of these compounds ended up in. For each class of compounds we build a custom method, so for carboxylic acid products we had a particular method and for carboxamides we had another. The custom-tailored methods seemed to work universally well in all of our purifications during this project.

When you're doing a project of this scale, how important is the reliability of the instrument?

NB: It's always important. We performed this synthesis on a 0.2 mmol scale, so it was really important to get off as much product from the column as we could. It makes a big difference in the isolated yields if you have loss at these small scales. For this project, reliability was particularly important.



Doubled productivity. With Isolera™ and pre-packed flash columns, Dr. Kürti's lab runs more than twice as many samples than during the days of manually packed columns.



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What do you consider when you are looking into what instruments to use?

NB: Right now, the project that my fellow graduate student Kaitlyn Lovato and I are working on involves products that are polar and stick to the silica gel. It is very hard to find good methods for the purification of these compounds. Until about two months ago when I started this new project, I used the Isolera in every project.

LK: The particular Isolera unit that Nicole and Dr. Zhe Zhou work on is one I brought over with me from UT Southwestern – this unit is now 9 years old and still works like a Swiss watch. I'm very grateful to Biotage for their support when I moved to Rice. We now have a total of six machines.

What would be your favorite things about using the Isolera?

NB: Efficiency and productivity, being able to do two things at once.

LK: Convenience, because you can just reach in the drawer and pick up the particular column you need and decide whether to inject the sample on the top or on a Samplet for dry loading.

NB: I think the majority of us do dry loading about 90% of the time.

LK: Our Isolera units do not use much solvent, therefore we never have spills. We have never lost any material.

After our interview completed, Nicole took me into the lab where she adjusted an experiment currently running and then walked me through to describe different stations and on-going projects. I left with an even better understanding of organic chemistry and what drives performance in an organic chemistry lab.



EUROPE

Main Office: +46 18 565900
Toll Free: +800 18 565710
Fax: +46 18 591922
Order Tel: +46 18 565710
Order Fax: +46 18 565705
order@biotage.com
Support Tel: +46 18 56 59 11
Support Fax: +46 18 56 57 11
eu-1-pointsupport@biotage.com

NORTH & LATIN AMERICA

Main Office: +1 704 654 4900
Toll Free: +1 800 446 4752
Fax: +1 704 654 4917
Order Tel: +1 704 654 4900
Order Fax: +1 434 296 8217
ordermailbox@biotage.com
Support Tel: +1 800 446 4752
Outside US: +1 704 654 4900
us-1-pointsupport@biotage.com

JAPAN

Tel: +81 3 5627 3123
Fax: +81 3 5627 3121
jp_order@biotage.com
jp-1-pointsupport@biotage.com

CHINA

Tel: +86 21 68162810
Fax: +86 21 68162829
cn_order@biotage.com
cn-1-pointsupport@biotage.com

KOREA

Tel: +82 31 706 8500
Fax: +82 31 706 8510
korea_info@biotage.com
kr-1-pointsupport@biotage.com

INDIA

Tel: +91 22 4005 3712
india@biotage.com

Distributors in other regions
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