



V. Aggarwal

The author presented on this page has published more than **25 articles** in *Angewandte Chemie* in the last 10 years, most recently: "Highly Diastereoselective and Enantiospecific Allylation of Ketones and Imines Using Borinic Esters: Contiguous Quaternary Stereogenic Centers": J. L.-Y. Chen, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2014**, *53*, 10992–10996; *Angew. Chem.* **2014**, *126*, 5604–5607.

Varinder K. Aggarwal

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Education:	1980–1983 BA, University of Cambridge 1983–1986 PhD with Dr. Stuart Warren, University of Cambridge 1986–1988 Postdoctoral position with Prof. Gilbert Stork, Columbia University
Awards:	1997 Royal Society of Chemistry (RSC) Hickinbottom Fellowship; 1999 RSC Corday Morgan Prize and Medal; Novartis Lectureship; Liebig Lectureship, Gesellschaft Deutscher Chemiker (GDCh; German Chemical Society); 2007 RSC/GDCh Alexander Todd/Hans Krebs Lectureship; RSC Tilden Lectureship; 2009 RSC Stereochemistry Award; SCI Award for Process Research (GSK-AZ-Pfizer); 2012 elected Fellow of the Royal Society; 2013 RSC Perkin Award
Current research interests:	Our group interests lie in the field of organic chemistry, focusing especially on stereoselective synthesis, mechanistic studies, and total synthesis of natural and non-natural products. The aim of our research is to design and develop new synthetic tools, allowing ultimately for the efficient and rapid synthesis of complex targets and biologically relevant compounds. Our current focus is in the field of organoboron chemistry, since boron seems to possess a unique ability to orchestrate many processes cleanly and with high stereochemical fidelity.
Hobbies:	Running; coach and organizer for my son's under-15 soccer team; cycling; table tennis; yoga

My favorite author (fiction) is ... V. S. Naipaul (*A House for Mr. Biswas*).

I would have liked to have discovered ... the zipper—brilliant, flexible, versatile, and essential. Simple, yet intricate.

The best advice I have ever been given is ... "Be careful, Varinder, don't go off the rails" (when I was a teenager; from my physics teacher, Mr. Thompson).

The worst advice I have ever been given was ... "You should get a proper job."

If I could go back in time and do any experiment, it would be ... Fleming's discovery of penicillin. A chance observation, but brilliant recognition that something strange had occurred and warranted further investigation. Another example of how fortune favors the prepared mind.

I can never resist ... cantuccini biscotti with vin santo—it reminds me of Italy and the Italian students I have had.

The most amusing chemistry adventure in my career was ... asking four distinguished academics, with considerable weight of intellect, to get out of my car as it struggled to get up the hill in Sheffield on a winter's day at the end of the Sheffield Stereochemistry Conference in the mid-1990s.

My top three films of all time are ... *Fitzcarraldo*, *Ran*, *Downfall*.

My favorite song of music is ... *You Belong to Me* by Kate Rusby; makes me think of my children.

The most significant scientific advance of the last 100 years has been ... the contraceptive pill—it has transformed society.

If I could have dinner with three famous scientists from history, they would be ... Hooke, Lavoisier, and Satyendra Bose.

And I would ask them ... about their relationships with fellow scientists (Hooke with Newton) and the challenges of doing science in politically challenging times.

I chose chemistry as a career because ... I drifted there, but then I hoisted the sails.

My best investment was ... my road bike (second hand, £150, works beautifully, and I have done thousands of miles on it).

If I were not a scientist, I would be ... a foreign journalist. They have to really know the culture and understand the people in order to make sense of what is going on. It is not that far removed from doing research in chemistry.

Has your approach to publishing your results changed since the start of your career?

Not really. I like papers to be informative and educational as I continuously learn from teachers I have never met, but whose papers are beautifully written and highly scholastic.

What do you think the future holds for your field of research?

The field of synthesis is in decline because many people think it is a mature subject and that we can make any molecule we want. That is almost certainly true if one had access to unlimited manpower. However in the real world we don't have unlimited resources, and synthesis continues to be highly labor-intensive because of the challenges it presents. Unless the molecule is very simple, it is not possible to go into the lab and make it within a short period of time. Stork had a "Rule of

Seven"—"However long you think a synthesis will take, multiply it by seven". Take (–)-sparteine as an example. When we first began our research, it was cheap and readily available but now costs upwards of £250 per gram. In fact the (+)-isomer is now less expensive than the (–)-isomer! If synthesis was mature, this useful small-molecule ligand would be available at much lower cost. The training one gets in synthesis also serves society in major ways as the scientists gain an appreciation of molecular structure, reactivity, and physical-organic principles—all of which are critical across a diverse range of industries. If appreciation and funding of synthesis continues to decline, society will suffer as a result. When Stork's Rule of Seven becomes a Rule of One then I would call synthesis a mature science, but until then it needs to be supported.

My 5 top papers:

1. "Practical and Highly Selective Sulfur Ylide Mediated Asymmetric Epoxidations and Aziridinations Using an Inexpensive, Readily Available Chiral Sulfide. Application to the Total Synthesis of Quinine and Quinine": O. Illa, M. Arshad, A. Ros, E. M. McGarrigle, V. K. Aggarwal, *J. Am. Chem. Soc.* **2010**, *132*, 1828–2830.

After a 15-year-long odyssey of trying to find the ideal sulfide that was both easily accessible and gave high enantioselectivities, Ona Illa made the breakthrough. She discovered a really simple sulfide, made in one step from elemental sulfur and limonene, which gave very high *ee* values in epoxidation and aziridination. It is hard to imagine a sulfide that is easier to access on scale for this type of transformation. The referees' reports on the paper were the best I have ever had and I received a number of complimentary e-mails on the work too.

2. "Enantiodivergent conversion of chiral secondary alcohols into tertiary alcohols": J. L. Stymiest, V. Bagutski, R. M. French, V. K. Aggarwal, *Nature* **2008**, *456*, 778–782.

This paper opened up a whole new platform of research for us. It is one of the few methods available for making tertiary boronic esters with high enantioselectivity and has recently been scaled up to 24 kg by Keith Fandrick at Boehringer Ingelheim.

3. "Stereocontrolled organocatalytic synthesis of prostaglandin PGF_{2α} in seven steps": G. Coulthard, W. Erb, V. K. Aggarwal, *Nature* **2012**, *489*, 278–281.

This paper describes the proline-catalysed aldol dimerization of succinaldehyde to make a bicyclic enal in high enantioselectivity, which was only four steps away from PGF_{2α}. In Sorensen's beautifully written accompanying article he commented "Few chemists, even those of adventurous spirit, would have believed that a useful synthesis of the hemiacetal could be achieved through the direct pairing of two molecules of succinaldehyde." Graeme Coulthard had an adventurous

spirit but more importantly showed a tenacity and doggedness to make this difficult reaction work.

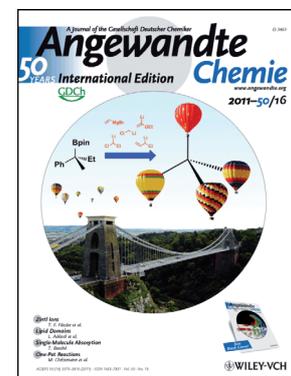
4. "Assembly-line synthesis of organic molecules with tailored shapes": M. Burns, S. Essafi, J. R. Bame, S. P. Bull, M. P. Webster, S. Balieu, J. W. Dale, C. P. Butts, J. N. Harvey, V. K. Aggarwal, *Nature* **2014**, *513*, 183–188.

Since we first reported in 2009 of being able to do three to four consecutive homologations of boronic esters without the need for intermediate purification, I have dreamt about making complex molecules iteratively. With the right reagents (and excellent co-workers) we were finally able to do nine iterations with only a single purification. Furthermore, depending on the configuration of the substituents that were added, the molecule adopted either a linear or a helical conformation. Absolutely beautiful.

5. "On the Importance of Leaving Group Ability in Reactions of Ammonium, Oxonium, Phosphonium, and Sulfonium Ylides": V. K. Aggarwal, J. N. Harvey, R. Robiette, *Angew. Chem. Int. Ed.* **2005**, *44*, 5468–5471; *Angew. Chem.* **2005**, *117*, 5604–5607.

In this paper we looked at a broad set of ylide reactions and found that reactivity is to a large part determined by the leaving-group ability of the corresponding onium group. For example, the literature on phosphorus ylides is vast, but they only participate in one main reaction, namely the Wittig reaction. Their limited reactivity is because phosphines are poor leaving groups. In contrast, sulfur ylides are more versatile and engage in many different types of reactions because sulfides are good leaving groups. Recognition that leaving-group ability is the dominant factor across a range of fundamental and important transformations brought about a general understanding of the factors involved in the different chemical processes. We are often seeking unifying themes that link together unconnected, disparate observations, and here we had one.

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The work of V. Aggarwal has been featured on the cover of *Angewandte Chemie*:

"Enantioselective Construction of Quaternary Stereogenic Centers from Tertiary Boronic Esters: Methodology and Applications": R. P. Sonawane, V. Jheengut, C. Rabalakos, R. Larouche-Gauthier, H. K. Scott, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2011**, *50*, 3760–3763; *Angew. Chem.* **2011**, *123*, 3844–3847.