reportedly taken to overcome the strain associated with the final 5,6 ring system, and was first proposed by Al Mourabit and co-workers in considering plausible biosynthetic pathways to phakellin and related tetracyclic PIAs[7]. The process is also highly reminiscent of one recently employed by the Du Bois group in their elegant synthesis of saxitoxin[8,9].

The ambiphilic reactivity of 2-aminoimidazoles enables them to participate as both nucleophiles and electrophiles through tautomerization (Fig. 1c). This reactivity had first been suggested by Potier and Al Mourabit in the context of a possible biosynthetic pathway to tetracyclic PIAs[10]. The Baran team made clever use of these precedents in postulating and implementing the successful transannular closure used to form the last two rings of palau'amine. Another highlight of the synthesis is the strategic use of a silver(II) oxidant, methodology that was developed in the course of this group's previous synthetic studies towards the axinellamines, and one that minimizes redox adjustments and enabled installation of the labile carbinolamine late in the synthesis.

The laboratory synthesis of palau'amine also raises interesting questions regarding its biosynthesis. The reported failed attempts to directly form the final two rings using biomimetic oxidative cyclizations are provocative. Is it possible that strategies such as these — involving medium-sized ring formation followed by transannular ring closure — are common in natural product biosynthesis? Indeed, there are numerous postulated examples of such ring contractions involving transannular Diels–Alder processes of macrocycles[1,2]. These questions will hopefully inspire chemists to explore the pathways and enzymes involved in the biosynthesis of these structurally complex alkaloids.

Although the first chemical synthesis of racemic palau'amine has been achieved (in 25 steps with an overall yield of 0.0015%), the story of palau'amine's synthesis and biological properties — as with similar structurally intriguing and challenging natural products — is just beginning. Certainly, the ability to access these compounds and, in particular, design derivatives in optically active form, will pave the way for broader and more detailed biological studies. Furthermore, palau'amine and related PIAs will undoubtedly continue to inspire new synthetic strategies and synthetic methods in the future. ❐

Daniel Romo is in the Department of Chemistry at Texas A&M University, College Station, Texas 77842, USA. e-mail: romo@tamu.edu

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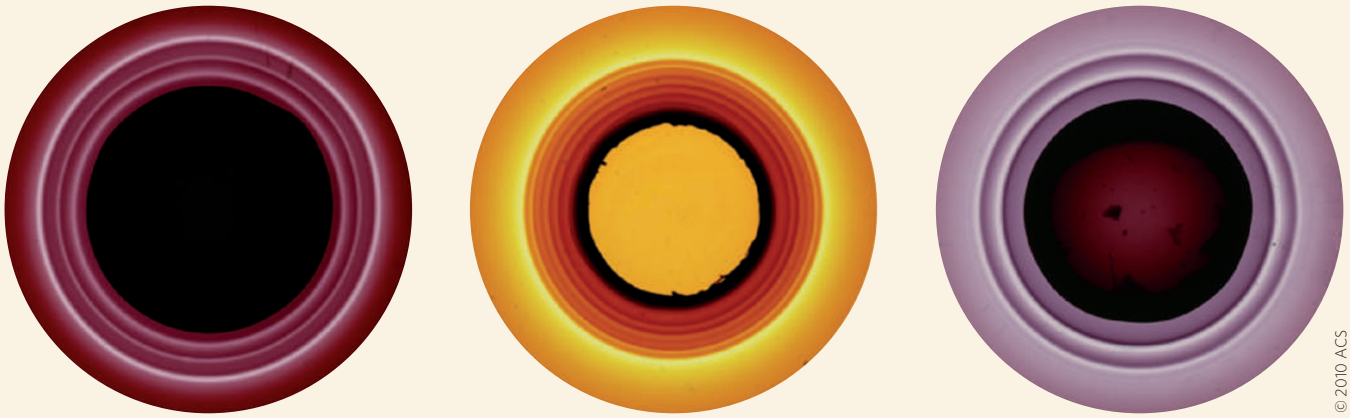
LIESEGANG RINGS

Nanoparticles ring the changes



Liesegang rings are circular patterns formed by ions precipitating in well-defined areas, rather than a single place, of a gel. They are, however, formed by a relatively small number of combinations of species and supports. Most of the species are ionic and offer little chance to tune their properties such as size or solubility, so the rings are generally not controllable.

Now, Bartosz Grzybowski and colleagues from Northwestern University have used metallic nanoparticles covered with positively or negatively charged molecules to create more predictable Liesegang rings (pictured; *J. Am. Chem. Soc.* **132,** 58–60; 2010). A sheet of agarose gel was soaked in a solution of similarly charged nanoparticles. A disc was then cut from the middle of the sheet and filled with a solution of the oppositely charged nanoparticles. As these diffuse through the gel over a day or more, they form rings of precipitate of equal amounts of nanoparticles of both polarities.

Although the nanoparticle system is similar to traditional Liesegang-type ones, they form by different mechanisms, with precipitation of ions governed by the solubility product of the salts, but nanoparticle aggregation works in a different way. Grzybowski and colleagues developed a model that uses diffusion and aggregation coefficients to predict the trends in spacing between the rings.

NEIL WITHERS

The original version of this story first appeared on the Research Highlights section of the *Nature Chemistry* website.