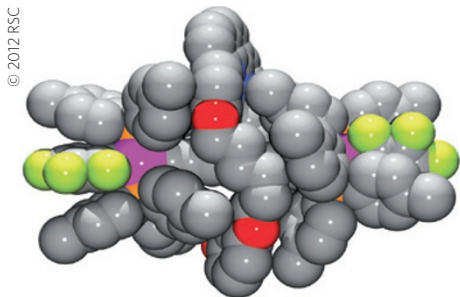


INTERLOCKED MOLECULES

Protecting polyynes

Chem. Commun. **48**, 7562–7564 (2012)

Org. Lett. **14**, 3424–3426 (2012)



Polyynes are compounds in which linear chains of *sp*-hybridized carbon atoms are held together with alternating single and triple bonds. Not only have the somewhat unusual composition and structure of these carbon-rich materials attracted the interest of chemists for many years, but they also represent discrete examples of the proposed one-dimensional allotrope of carbon known as carbyne.

As long ago as the 1970s, synthetic chemists were able to make polyynes

containing up to 16 acetylenic units, but these reactive species would readily polymerize if not kept in dilute solutions. More recently, it has been found that placing bulky groups at each end of the carbon chain results in stable compounds that can be isolated.

The calming influence of the end groups on the reactivity of polyynic chains only extends so far, however, and as the chains get longer, alternative approaches to modulate their behaviour are going to be required. Now, two research teams have independently shown how polyynic chains can be ‘insulated’ by encircling them with a macrocycle to produce interlocked molecules known as rotaxanes.

John Gladysz and co-workers from Texas A&M University coupled together pairs of butadiyne building blocks — each with a bulky platinum-based group at one end — in the presence of a 33-membered macrocyclic ring to give a tetrayne-based rotaxane. In a process that is referred to as ‘active templating’, a copper ion bound to the macrocycle mediates the coupling of the two terminal alkynes.

Using the same macrocycle and a similar copper-mediated coupling approach, a

team of researchers led by Harry Anderson at the University of Oxford and Rik Tykwinski at the University of Erlangen-Nuremberg, were able to make a series of polyynic rotaxanes comprising 4, 6 or 10 acetylenic units. In this case, however, the polyynic chains were capped with ‘super-trityl’ groups rather than metal-based complexes. Anderson, Tykwinski and co-workers then went on to demonstrate that the environment around the polyynic chain could be influenced by binding a metal ion to the phenanthroline group of the macrocycle. SC

DNA REPLICATION

High fidelity

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DNA provides the blueprint for life, therefore the importance of its accurate replication cannot be underestimated. This is the job of DNA polymerases, a family of enzymes that take template strands of DNA and co-ordinate the creation of complementary strands, making sure that the correct nucleotide is incorporated at each step. The breathtaking accuracy of the process (1 error for every 10^5 – 10^8 nucleotides added) is reliant

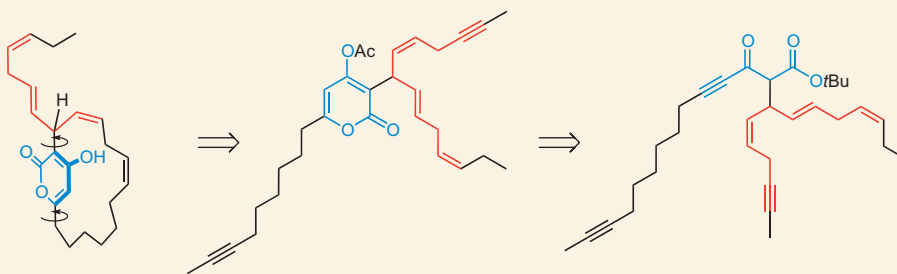
NATURAL PRODUCTS

Sensitive synthesis

Angew. Chem. Int. Ed. **51**, 6929–6933 (2012)

Three of the most common justifications for total-synthesis campaigns are (i) as tests for newly developed synthetic methodology, (ii) the interesting biological activity of the natural products and (iii) the presence of synthetically challenging or unusual carbon skeletons in the structure. A rare example now reported by Alois Fürstner and co-workers from the Max-Planck-Institut für Kohlenforschung in Mülheim, Germany includes elements of all three.

Neurymenolide A was first isolated from a species of red algae found in the South Pacific. It exhibits activity against both methicillin- and vancomycin-resistant bacteria — so the structure could be important in the generation of new drug targets. Fürstner and co-workers, however, were most interested in the unusual structure, which contains a 4-hydroxypyronone as part of a macrocycle (pictured). Restricted rotation of this moiety (blue) in combination with the single stereocentre (of unknown configuration) means that the compound



exists as a mixture of two diastereomers that interconvert on a timescale of several hours.

The key feature of any synthesis of this target is that the skipped polyene array (red) is likely to isomerize easily to the energetically more favourable conjugated system — so identification of a mild synthetic method was important. Fürstner and co-workers first developed a mild gold-catalysed method for the construction of 4-hydroxypyronones. To construct the natural product, however, it was necessary to use the new cyclization method on a substrate containing no less than six carbon-carbon

multiple bonds. Furthermore, the electrophilic catalyst must react fastest at the least electron-rich alkyne.

Following formation of the desired pyrone, the macrocycle was formed using a molybdenum alkyne metathesis catalyst previously developed by the Fürstner group. The selectivity of this catalyst for reaction with two methyl-alkynes in the presence of three other alkenes is remarkable. The synthesis was completed by a selective reduction of the alkyne resulting from this metathesis and a final deprotection to remove an acetyl group introduced during pyrone formation. SD