

In the particular reaction studied — cyclization of a heteroatom-tethered 1,6-enyne — two diastereomeric products are possible. Calculations showed that the transition state in the rate-determining step of the reaction was highly charge-polarized. Importantly, in the two transition states leading to the two different diastereomers this polarization was in opposite directions, suggesting that the reaction could be selective if this polarization is biased. The calculations suggested that addition of an electron-withdrawing substituent (such as a halogen) to one end of the substrate enyne would provide the necessary bias, and improve both the reactivity and the diastereoselectivity of the reaction.

Baik, Evans and co-workers then challenged their computational work by preparing substrates with halogen substituents. They confirmed both the increased reactivity — the reaction no longer requires heating — and diastereoselectivity. The halogen substituent used as the bias does remain in the reaction product, but it provides a useful ‘handle’ for further reactions.

CATALYSIS

Silver lining to CH₄ activation

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Converting methane — which typically makes up over 80% of natural gas — into more useful chemicals would allow better exploitation of this low-cost feedstock. The carbon–hydrogen bonds of alkanes are relatively strong and inert, however, and this is even more pronounced with methane. Although a few processes have been reported, activating a C–H methane bond has remained notoriously difficult. The volatility of methane and its poor solubility in organic solvents have also prevented the use of strategies developed for other alkanes. Now, a team from four institutions in France and Spain have circumvented these problems by carrying out the reaction in supercritical carbon dioxide.

Previously, highly electrophilic silver complexes with perhalogenated borate ligands were shown to catalyse the insertion of carbenes — species in which a carbon atom bears two non-bonding electrons — into primary and secondary C–H bonds. But this approach has not been successful with methane, because carbenes preferably react with any other C–H bond in the reaction medium. This did not occur with supercritical carbon dioxide, in which three silver complexes with perfluorinated indazole borates catalysed the activation of methane.

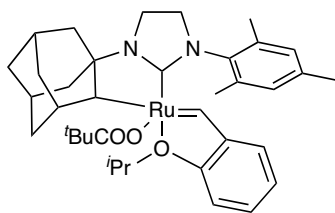
Supercritical carbon dioxide efficiently dissolved methane and the carbene precursor (N₂=CHCO₂Et). Despite the limited solubility

of the catalysts, the species reacted to form ethyl propionate (CH₃–CH₂CO₂Et). This reaction also activated a C–H bond in ethane — more easily than that in methane — and in pentane. The researchers propose a mechanism based on a dinitrogen elimination and subsequent insertion in a C–H bond of the resulting metal carbene species.

METATHESIS

Insist on *cis*

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Carbon–carbon bond formation is one of the most important processes in organic synthesis because it enables chemists to construct a vast array of molecular frameworks in a controlled fashion. The olefin metathesis reaction, in which two carbon atoms are stitched together through the formation of a double bond, has proved to be a particularly useful way to do this. One longstanding challenge, however, has been the inability to selectively make *Z*-alkenes (usually *cis*-isomers) with this reaction.

Although some tungsten- and molybdenum-based catalysts for the olefin metathesis reaction have recently been shown to produce *Z*-alkenes with a very high degree of selectivity, the well-known family of ruthenium-derived catalysts have not been so successful in this regard. Now, Bob Grubbs and Koji Endo from the California Institute of Technology have shown that ruthenium complexes with a chelating *N*-heterocyclic carbene (NHC) ligand are active olefin metathesis catalysts and can, in some cases, produce *Z*-alkenes with very high selectivity. In these systems, the NHC is not only bonded to the metal centre through the carbene carbon atom (as is usually the case in these compounds), but also through one of its side-chains following intramolecular C–H bond activation.

When the side-chain on the NHC ligand bonded to the ruthenium centre is a bulky adamantyl group, the catalyst was found to produce at least 90% of the *Z*-alkene product in cross-metathesis reactions between two different olefin coupling partners. The catalyst, which can be made in a series of simple steps and is tolerant of water in the reaction medium, offers a convenient route to the stereocontrolled synthesis of olefins.

blogroll

MicKIE mouse

Introducing some artistry, and could you isotopically fatten a mouse?

“What would happen, hypothetically, if a baby mouse could grow up eating only deuterated food and water? Could you make an unusually heavy mouse?” asked Sharon Neufeldt in an entertaining post on her ‘I can has science?’ blog (<http://go.nature.com/OmRAfV>).

Assuming that the elemental make-up of a mouse is pretty similar to that of a human, Neufeldt estimates it would be 10% heavier — but not “a fat mouse, just a more dense mouse.” Of course, those readers familiar with the kinetic isotope effect and cellular function will realize that the poor, if hypothetical, heavy mouse would not last long with all its hydrogen atoms swapped for deuterium. As Neufeldt discusses, “a carbon–deuterium bond can be 6.5 times slower to break than a carbon–hydrogen bond”, which could have pretty drastic consequences to your mouse “cells won’t be able to function properly and [the mouse] will start to die.”

But what about enriching the mouse with ¹³C? The smaller kinetic isotope effect might help the mouse’s health, but the weight gain wouldn’t be anywhere near as striking at a mere 1.5%. Neufeldt also points out another flaw in her plan: it would cost over \$600 a day to feed her mouse on commercially available ¹³C-labelled glucose. At that price, she said she might as well treat the mouse to three meals a day at her favourite French restaurant.

One of the most positive and publicly visible uses of chemistry has to be in art conservation and restoration so it’s great to see that *Chemical & Engineering News*’ Sarah Everts has launched a new blog on this topic, called Artful Science (<http://cenblog.org/artful-science/>). Posts have so far covered topics as different as the chemistry behind fading blue pigments, the isotope techniques used to discover whether the influx of South American silver really did cause the ‘Price Revolution’, and using DNA from ancient Maori cloaks to track feather trade routes.