

ALKENE STEREOCHEMISTRY

Inverting isomers

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The *cis*–*trans* isomerization of alkenes is perhaps the first type of stereochemistry most chemistry students encounter. Methods for the synthesis of alkenes often afford one of the two isomers selectively. For example, the classical Wittig reaction with an unstabilized ylide favours production of a *cis*-alkene. But what does the synthetic chemist do if the isomer produced is not the one they desire? Photochemical isomerization can enable *trans* to *cis* conversions and metal catalysis can offer a route in the opposite direction, but there are few general methods that operate under mild conditions. Now, a serendipitous discovery by Geoffrey Coates and his graduate students Jessica Lamb and Aran Hubbell at Cornell University has led to the development of a

general route for the isomerization of alkenes through sequential epoxidation–deoxygenation.

The Coates group has had a long-standing interest in epoxide carbonylation reactions to generate β -lactone products. “We typically employ catalysts with cobalt tetracarbonyl anions for these reactions and had begun to explore the use of other metals,” explains Coates. But the use of a manganese pentacarbonyl anion provided a surprising result: selective deoxygenation and catalyst turnover under CO pressure. “The carbonylation reactions were observed to proceed by a stereo-invertive mechanism, so we hypothesized that, if combined with a diastereoselective alkene epoxidation, this deoxygenation reaction might

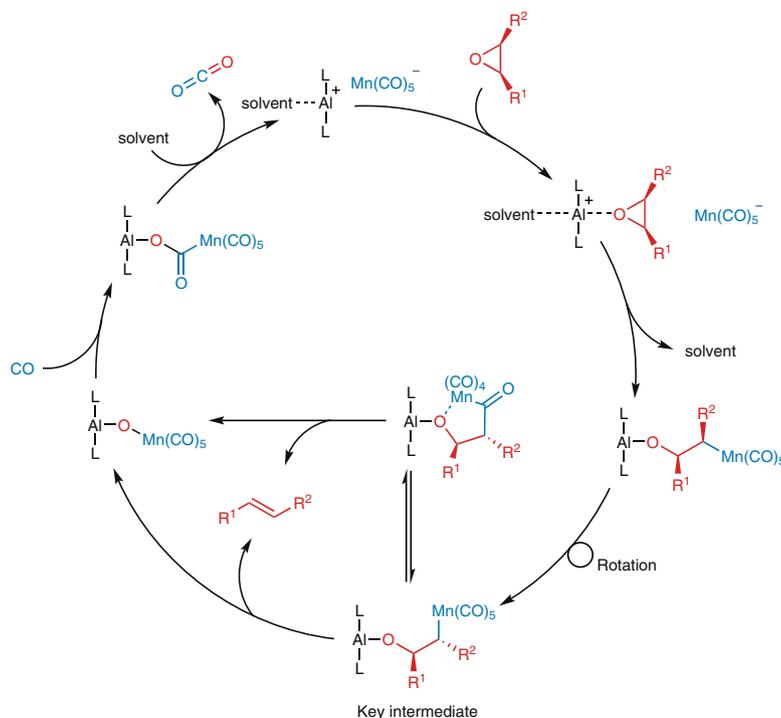
enable a useful alkene isomerization,” he continues.

The proposed reaction mechanism for conversion of a *cis*-epoxide into a *trans*-alkene is pictured. The epoxide is activated by the Lewis acidic portion of the catalyst followed by nucleophilic attack of the manganese pentacarbonyl anion and loss of a ligated solvent to produce a ring-opened intermediate with inverted stereochemistry. The inverted alkene can be produced either by a direct β -oxygen elimination or by CO insertion to first form an acyl manganese intermediate. In both cases, the oxygen-bridged aluminium–manganese complex that is formed reacts with CO to eventually regenerate the active catalyst and turnover the cycle. A third possible pathway, involving formation of a β -lactone followed by decarboxylation, was ruled out.

The reaction enables the conversion of both *cis*-alkenes into *trans*-olefins and *trans*-olefins into *cis*-alkenes. “We were surprised by the differences in rate between *cis*- and *trans*-epoxide deoxygenation,” says Coates. “We were able to exploit this to resolve a diastereomeric mixture of epoxides, generating a *trans*-alkene and leaving behind unreacted *trans*-epoxide.”

In the future, the team hopes to exploit their method to perform late-stage stereochemical inversion in complex molecule synthesis. To do that, they will first aim to get a more thorough understanding of the mechanism so that their reaction can tolerate more complex and heavily substituted epoxides. “We also hope to develop catalysts for deoxygenation of alicyclic *cis*-epoxides as this would provide a route to generate cyclic *trans*-alkenes,” says Coates.

Stephen G. Davey



Credit: Adapted with permission from Lamb, J. R. et al. *J. Am. Chem. Soc.* **142**, 8029–8035 (2020), ACS

ORIGINAL ARTICLE Lamb, J. R. et al. Carbonylative, catalytic deoxygenation of 2,3-disubstituted epoxides with inversion of stereochemistry: an alternative alkene isomerization method. *J. Am. Chem. Soc.* **142**, 8029–8035 (2020)