

SYNLETT Spotlight 2

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Metathesis. The Schrock and Grubbs Catalysts

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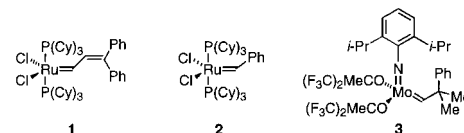
Brian A. Chauder was born in Cape Breton, Nova Scotia. He received a B.Sc. degree from Acadia University and his M.Sc. from the University of Waterloo (1998). His Ph.D. studies in synthetic methodology and total synthesis are currently in progress with Professor Victor Snieckus at Queen's University.



A cursory glance at the current synthetic literature attests to the explosion in the application of metathesis.¹ The ring-closure metathesis (RCM) is the most widely used concept and the Grubbs ruthenium alkylidenes **1** and **2** and the Schrock molybdenum alkylidene **3** are the exclusive catalysts. All three catalysts are reactive with a diverse range of substrates, are tolerant of many functional groups (e.g. ROH, RCOR, RCHO, RCONR₂) and are effective in RCMs from simple 5-, 6-, 7-membered to 17-membered carbo- and hetero-cyclic arrays. Although the Schrock catalyst is the most reactive, it has a narrower functional group tolerance (e.g. incompatible with ROH and RCO₂H groups). In a further contrast, the Schrock catalyst promotes RCM of di-, tri- and even tetra-substituted alkenes whereas the Grubbs catalysts are successful for only di-

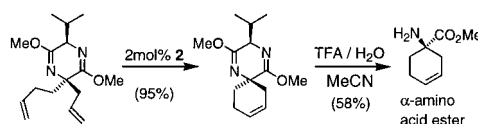
substituted alkenes (Ene-yne RCM is an exception²). Typical RCM conditions are high dilution (10 – 50 mM) and slow substrate addition, especially when competitive polymerization is observed.

Preparation: The Grubbs catalysts are easy to prepare³ (orange-brown solids) and are stable to air for up to 2 weeks (extreme case, 1 year) unlike the Schrock catalyst which must be used in a refrigerated glove box.⁴

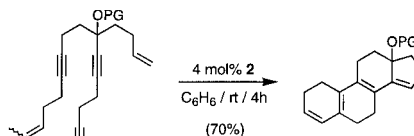


Abstracts

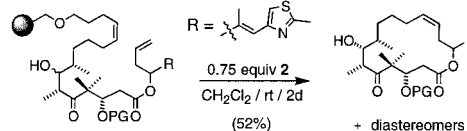
The venerable Schoellkopf amino acid synthesis followed by RCM gives, *via* spirocyclic systems, conformationally restricted α -amino esters which would otherwise be difficult to prepare in optically active form.⁵



Part-steroid structures are conveniently prepared by positioning an acetylenic relay between two olefinic side chains to effect an iterative RCM.⁶ An ene-yne metathesis strategy also comprises a key step in the total synthesis of the natural product stemoamide.⁷



Indicative of the times, solid state RCMs are being pursued,⁸ e.g. in the total synthesis of epothilone A.⁹ The precursor to the natural product was cyclized and cleaved from the resin in one step; in this process, the metal carbene becomes immobilized on the resin and cannot be reused.



References

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