SYNLETT Spotlight 2

Metathesis. The Schrock and Grubbs Catalysts

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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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