

A ROMP-derived, polymer-supported chiral Schrock catalyst for enantioselective ring-closing olefin metathesis†

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A permanently polymer-immobilised version of Schrock's molybdenum catalyst was realised *via* polymerisation of chiral 5,5'-bis(norborn-5-ene-2-ylmethyleneoxymethyl)-3,3'-di-*tert*-butyl-6,6'-dimethylbiphen-2,2'-diol followed by reaction with the catalyst precursor Mo(N-2,6-*i*-Pr₂C₆H₃)(CHCMe₂Ph)(OSO₂CF₃)₂(CH₃OCH₂CH₂OCH₃); using this 5-, 6- and 7-membered heterocycles were synthesised *via* ring-closing metathesis (RCM) from (pro-)chiral substrates in high yields and ee with short reaction times; the catalyst shows low loss of molybdenum during RCM, and was easily separated and recycled.

Since the publication of the first metathesis catalysts, olefin metathesis has gained a strong position in synthetic organic and polymer chemistry.^{1–4} Especially the advent of well defined molybdenum and ruthenium catalysts paved the road for various applications in the synthesis of complex organic molecules.⁵ Ring-closing metathesis (RCM), ring-opening metathesis (ROM) and cross metathesis (CM) are now commonly used in various laboratories, predominantly since the catalysts themselves and key intermediates became commercially available. Recently, the development of chiral molybdenum catalysts gave access to the targeted synthesis of optically pure, and optically enriched organic molecules that would otherwise be difficult to prepare.⁶ Part of our current research focuses on the development and evaluation of heterogeneous molybdenum catalysts. Advantages of such catalysts include their simple removal from reaction mixtures, their reuse and a low metal content in the products of interests.

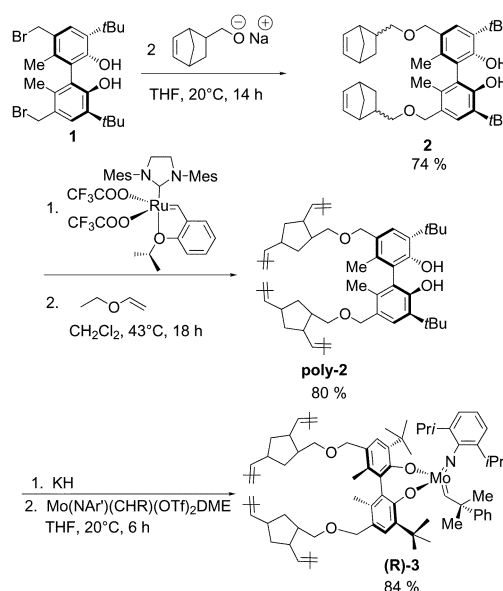
Recently, a number of immobilised metathesis catalysts have been reported.^{7–10} In the case of Ru-based catalysts, immobilisation can be accomplished *via* the alkylidene moiety,^{11–14} the phosphine¹⁵ and N-heterocyclic carbene (NHC),^{16–19} or by chlorine ligand exchange.^{20–25} Similarly, Mo-based metathesis catalysts ("Schrock catalysts") can in principle be immobilised either *via* the alkylidene, the imido or the alkoxide^{26,27} and phenoxide ligand. In contrast to systems immobilised *via* alkylidene, neither the imido nor the alkoxide ligand of a Schrock catalyst dissociates from the metal center in course of the catalytic cycle of a metathesis reaction. Recently, Schrock and Hoveyda described the synthesis of a polymer bound system obtained *via* free radical polymerisation.²⁸ In the present system, the molybdenum catalyst is incorporated into a polymer backbone prepared *via* ruthenium-catalysed ring-opening metathesis polymerisation (ROMP) of the norborn-2-ene-substituted chiral phenoxide (*R*)-5,5'-bis(norborn-5-ene-2-ylmethyleneoxymethyl)-3,3'-di-*tert*-butyl-6,6'-dimethylbiphen-2,2'-diol (**2**). For synthesis, (*R*)-5,5'-bis(bromomethyl)-3,3'-di-*tert*-butyl-6,6'-dimethylbiphen-2,2'-diol (**1**) was reacted with excess sodium norborn-5-ene-2-methanolate, thus yielding the polymerisable chiral phenol **2**.

Since **2** contains two protic phenol groups and protection-deprotection protocols were to be avoided, polymerisation had to be carried out using a ruthenium-derived catalyst. For ROMP

of **2** we examined a new type of initiator, Ru(OOCCF₃)₂(CH-*o*-*i*-Pr-O-C₆H₄)(IMesH₂).²¹ Synthesis of the gel-type support was carried out in methylene chloride using a molar ratio of **2** : initiator = 30 : 1, resulting in a support with a low degree of crosslinking. This directly translates into excellent swelling properties *e.g.* in benzene with a solvent uptake of 2000 wt.% (!). This value corresponds to a volume increase of 700%. Poly-**2** was finally deprotonated with potassium hydride and reacted with Mo(N-2,6-*i*-Pr₂C₆H₃)(CHCMe₂Ph)(OSO₂CF₃)₂DME to yield (*R*)-**3** in 84% yield (Scheme 1).

In summary, this synthesis offers a straightforward access to supported molybdenum catalysts from a commercially available metal complex. For the determination of the molybdenum loading, a direct measure of the effectiveness of heterogenisation, the polymer was digested in *aqua regia* and the Mo-content was determined by ICP-OES. Loadings of molybdenum up to 0.552 mmol g⁻¹ were obtained, corresponding to 55% conversion of all phenoxides. Since the polymer backbone is basically solely built from ligand, the catalyst loading achieved here is extraordinarily high compared to other supported systems, thus exceeding standard systems at least by a factor of 100.

In order to evaluate the activity of the polymer-supported catalyst in asymmetric olefin metatheses we first investigated the RCM reaction of allyldimethyl[3-methyl-1-(2-methylallyl)but-3-enyloxy]silane in CH₂Cl₂. The desired product was obtained in high yields (86%) and ee's (87%) within 2 h using 5.5 mol% (*R*)-**3**. Furthermore, no products resulting from dimerisation were observed by GC-MS. Encouraged by these results, we turned our attention to the synthesis of other medium-sized heterocycles. As substrates various oxygen, silicon or nitrogen bearing dienes and trienes were used (Table 1).



Scheme 1

† Electronic supplementary information (ESI) available: experimental procedures for immobilisation, analytical data, general description of setup for catalysis. See <http://www.rsc.org/suppdata/cc/b3/b306427a/>

Catalytic RCM reactions proceeded in high yields especially for (1-allyloxy)-2-methylallylbenzene. Even if only 3.3 mol% catalyst were used (see Table 1, entry 3), a yield of 75% was achieved. To reduce diffusion related phenomena, we initiated polymer swelling by using benzene as solvent. By this approach, an efficient access of the active molybdenum sites was guaranteed. Nevertheless, as reported by other groups, the use of amines as substrate (entries 4 and 5) gave poorer yields of desired product. This is rather attributed to the substitution pattern of the olefin than to catalyst immobilisation, since analogous homogeneous chiral catalysts give no appreciable increase in yield (see Table 1). Compared to the supported system derived *via* free radical polymerisation,²⁸ similar results were found using reduced amounts of catalyst and shorter reaction times (Table 1, entry 6), indicating improved accessibility of the catalytic sites.

Beside the ease of work up, reusability is another important feature of heterogeneous catalysts. Particularly for industrial applications, recyclable catalysts are highly desirable. We investigated the reusability of our catalyst in the RCM of allyldimethyl[3-methyl-1-(2-methylallyl)but-3-enyloxy]silane. The first catalytic cycle resulted in 97% product with 90% ee within 35 min. In the second cycle the catalyst gave 47% yield within 35 min. Though catalyst activity was notably diminished, the ee of the product was virtually unchanged (89% ee). In a third cycle, 52% yield and 95% ee were achieved in 270 min. As can be deduced from the data for ee and the GC-MS spectra, the supported catalyst does *not* react with the double bonds of the polymer backbone, as might be anticipated.

Another important point in heterogeneous catalysis is a low contamination of products with metals. All washings and filtered reaction mixtures were only slightly yellow colored. The catalyst was recovered after the third catalytic cycle in the

Table 1 (R)-3-promoted asymmetric RCM and desymmetrisation reactions

Substrate	Product	Cat. (mol%)	Yield (%)	Yield ^a (%)	ee	ee ^a
		3.4	97	86 ²⁹	90 ± 1	89 ²⁹
		3.3	61	—	95 ± 1	—
		3.3	75	56 ³⁰	25 ± 1	—
		5.2	22	21 ³¹	50 ± 5	45 ³¹
		2.8	16	35 ³¹	53 ± 5	47 ³¹
		4.0	96	97 ²⁸	90 ± 2	89 ²⁸

Entries 1–5: 30 min at 20 °C, 2 h at 45 °C, yields determined by GC-MS; entries 1,6: benzene, entries 2–5: CH₂Cl₂. Entries 1–3, 6: ee's determined by chiral GC-MS; entries 4–5: ee's determined by chiral HPLC.^a Homogeneous and free radical polymerisation-derived heterogeneous system.

RCM of allyldimethyl[3-methyl-1-(2-methylallyl)but-3-enyloxy]silane and digested in *aqua regia* by a microwave unit. From the filtered solution the molybdenum content was determined by ICP-OES. By comparison with the initial material a loss <5% of molybdenum within these three catalytic cycles was observed.

In summary, we presented a new polymer bound chiral molybdenum-based Schrock catalyst. This catalyst provides the possibility of transforming prochiral substrates into more complex molecules, *e.g.* unsaturated ring-systems. High yields as well as good enantioselectivity were attained. Beside the simplified work up of reaction mixtures, accomplishments were obtained concerning recyclability of the catalyst and the contamination of products with metal impurities.

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