Microencapsulation of a Metathesis Catalyst

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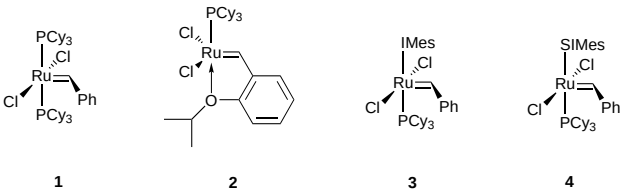
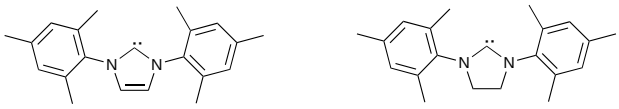
Abstract: Microencapsulation of the saturated *N*-heterocyclic carbene metathesis catalyst **4** in polystyrene gives a material that is catalytically active, and is easily recovered and reused.

Keywords: alkenes; catalysis; metathesis; microencapsulation; polymer



1 **2** **3** **4**



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The development of well-defined catalysts for the alkene metathesis reaction has led to this key carbon-carbon bond-forming reaction taking centre stage in a range of imaginative approaches to complex target molecules and in many new ventures in polymer chemistry and materials science.[1] Whilst the ruthenium complex **1** has proven to be an excellent metathesis catalyst precursor in many contexts, some problems associated with reactivity and recovery have been identified and are now starting to be addressed.

At a molecular level, the chelate complex **2**[2] and the *N*-heterocyclic carbene complexes **3**[3] and **4**[4] have enhanced catalyst reactivity/recovery profiles compared to catalyst **1**. The main area of endeavour with respect to recovery, however, is catalyst immobilisation on supports. All of the ligand types on catalysts **1** – **4** have now been used to make immobilised metathesis catalysts. In a seminal paper, Grubbs attached the progenitor of catalyst **1** to polystyrene through its phosphine ligands.[5] More recently Barrett immobilised catalysts **1** and **3** by metathesising their phenylcarbene ligands with vinylpolystyrene.[6] Subsequently, Nolan attached catalysts **1**, **3**, and **4** to a macroporous vinylpolystyrene in the same manner to give several effective immobilised catalyst systems.[7] Complex **2** has been immobilised on dendrimers,[8] on poly(ethylene glycol),[9] and on polystyrene[10] via a range of sophisticated linkers terminating in a chelating arylcarbene ligand. Complexes of type **4** have been immobilised onto polystyrene[11] and monolithic supports[12] *via* the heterocyclic carbene ligand, and catalyst **1** has been immobilised by the exchange of a chloride ligand with the polystyrene-supported silver salt of a carboxylic acid.[13]

In all of the systems described above, the metathesis pre-catalysts are immobilised onto their supports using covalent or co-ordinate bonds, which will be subsequently broken during the operation of the catalytic cycle. Microencapsulation is a technique used in medicine and pharmacy which has been applied recently to chemical catalysis, in particular to Lewis acid catalysis,[14] osmium tetraoxide-catalysed oxidations,[15] and palladium-catalysed carbon-carbon bond-forming reactions.[16] In this approach the catalyst of interest is merely enveloped in a polymer film to render it recoverable and reusable. As this is potentially a relatively easy and economic route to catalyst immobilisation and recycling, we thought it would be of interest to determine whether or not it would be possible to microencapsulate a metathesis catalyst and still retain catalytic activity. As a result of our studies, we report herein the first microencapsulation of a metathesis catalyst and the catalytic activity of the resulting material.

After some experimentation, catalyst **4** and polystyrene were found to be the partners of choice for envelopment using the following optimised procedure. Polystyrene was dissolved in cyclohexane, a process facilitated by warming to 50 °C. After cooling to room temperature, catalyst **4** was added to the polystyrene solution to give a purple mixture which became a purple viscous solution on stirring for an hour at room temperature. After cooling the viscous solution to 0 °C, which led to further thickening, slow addition of methanol resulted in the precipitation of a purple solid. Washing with methanol and drying gave microencapsulated **4** as a purple powder. A scanning electron microscopy (SEM) micrograph of the powder revealed the presence of polystyrene-enveloped microparticles across the polymer surface, and energy-dispersive X-ray (EDX) dif-

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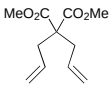
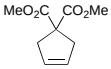
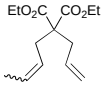
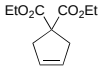
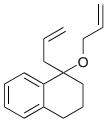
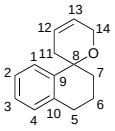
Table 1. Ring-closing metathesis using catalyst **4** microencapsulated in polystyrene.[a]

Entry	Substrate	Product	Run	Yield [%][b]	Ref.
1			1	92	[17]
2			2	71	
3			3	52	
4			4	40	
5			1	82	[18]
6			1	89	
7			1	90	[19]
8			1	84	

[a] All reactions run in water/methanol (4:1) using 0.5 mmol of substrate and 2.4 mol % of ruthenium catalyst microencapsulated in polystyrene.
[b] Isolated yield after column chromatography.

fraction analysis of these particles indicated that the particles contained ruthenium, phosphorus, and chlorine. Ruthenium analysis (ICP-AES) of the powder indicated that 87% of the catalyst had been enveloped, a value consistent with the value obtained by weighing the polymer before and after catalyst envelopment (90%).

The reactivity of microencapsulated **4** was initially examined using a standard test substrate, *N*,*N*-diallyltosylamide. After some experimentation, the solvent system of choice was identified as a 4:1 mixture of water and methanol (polystyrene is significantly soluble in less polar solvents). A mixture of substrate and encapsulated **4** (2.4 mol % of ruthenium) in H_2O/MeOH (4:1; catalyst **4** is active in this solvent system) was thus heated at 50 °C for 1.5 h, after which time the mixture was cooled to room temperature and an excess of MeOH added to ensure complete extraction of product from the polystyrene. Filtration returned the microencapsulated catalyst, and this was dried and used in subsequent runs. The filtrate was evaporated to give the ring-closing metathesis product in quantitative mass yield. The metathesis product was 99% pure by high-field ^{1}H and ^{13}C NMR spectroscopy and ruthenium analysis indicated that it was contaminated by 540 ppm ruthenium as a result of leaching from the polymer. Column chromatography removed the trace impurities and gave an isolated yield of 92% (Table 1, Entry 1). The microencapsulated catalyst could be recycled and was found to retain significant activity over four cycles (Table 1, Entries 1 – 4) – addition of styrene or 1-hexene had no significant effect on the recycling profile. Several other dienes also gave high yields of ring-closing metathesis products under the conditions described above (Table 1, Entries 5 – 8).

In summary, we have microencapsulated a metathesis catalyst for the first time, and demonstrated that the resulting material is catalytically active and may be easily recovered and reused. The activity and recycling properties of the microencapsulated catalyst, whilst not as good as the optimised Nolan macroporous vinylpolystyrene system,[7] are remarkably similar to the other immobilised metathesis catalysts reported to date,[5,6,8–13] all of which require more expensive and/or lengthy syntheses, and use chemical bonds to initially anchor the metathesis catalyst to its support.

Experimental Section

Encapsulation of 4

Polystyrene (0.5 g, M_w *ca.* 280,000) was added to cyclohexane (10 mL) and heated at 50 °C until the polymer completely dissolved. The solution was then cooled to room temperature and catalyst **4** (0.080 g) was added to give a purple mixture. Stirring at room temperature for 1 h gave a purple viscous solution that was slowly cooled to 0 °C during which time the solution became more viscous. Slow addition of methanol (40 mL) and standing for 1 h at room temperature led to the formation of a purple solid. Washing with methanol (2 × 20 mL) and drying under vacuum overnight gave microencapsulated **4** as a purple powder; yield: 0.572 g. Ru content (ICP-AES) = 0.72%.

Metathesis Reactions

The metathesis substrate (0.5 mmol) and microencapsulated **4** [0.080 g (**4**, 0.010 g, 0.012 mmol, 2.4 mol %)] were added to a mixture of water and methanol (4:1, 2.5 mL). The mixture was heated at 50 °C for 1.5 h, cooled, and then treated with methanol (5 mL) and stirred for a further 15 min. The catalyst was collected by filtration, dried, and used for subsequent reactions. The filtrate was concentrated to give the product as an oil or solid. Traces of impurities were removed by column chromatography.

Data for the Product of Entry 8, Table 1

Colourless oil. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 1.70 – 1.80 (m, 1H, 7-H), 1.85 – 2.05 (m, 2H, 6-H), 2.10 – 2.20 (m, 1H, 7-H), 2.20 – 2.30 (m, 1H, 5-H or 11-H), 2.50 – 2.60 (m, 1H, 5-H or 11-H), 2.70 – 2.95 (m, 2H, 5-H or 11-H), 4.15 (dd, 1H, *J* = 17 Hz,

1.5 Hz,14-H), 4.25 (dd, 1H, $J = 17$ Hz, 4 Hz, 14-H), 5.80 (dt, 1H, $J = 10$ Hz, 1.5 Hz, 12-H), 5.85 – 5.95 (m, 1H, 13-H), 7.00 (d, 1H, $J = 6.5$ Hz, 4-H), 7.10 – 7.25 (m, 2H, H-2 and H-3), 7.45 (d, 1H, $J = 6$ Hz, H-1); ^{13}C NMR ($CDCl_3$, 90.6 MHz): $\delta = 19.8$ (6-C), 29.8, 31.4, 36.0 (5-C, 7-C, 11-C), 61.4 (14-C), 72.1 (8-C), 123.9, 125.6, 126.1, 127.1, 127.3, 128.7 (1-C, 2-C, 3-C, 4-C, 12-C, 13-C), 137.1, 141.1 (9-C, 10-C); IR ($CHCl_3$): $\nu = 2940$ (C-H), 3015 (C-H), 1677 (C=C) cm^{-1}; MS (EI): m/z (%) = 200 (37) $[M]^+$, 146 (52), 118 (40), 86 (26), 84 (100); HR-MS: calcd.: 200.12012; found: 200.12007.

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