Highly Efficient and Recyclable Polymer-Bound Catalyst for Olefin Metathesis Reactions

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Abstract: Polymer supported ruthenium alkylidene catalysts **6** and **8** have been prepared and for the first time applied to cross metathesis reactions with electron deficient alkenes. These robust complexes are re-usable, highly active and tolerate a wide variety of functional groups.

Key words: alkenes, carbene complexes, metathesis, ruthenium, solid phase synthesis

In the last decade, olefin metathesis catalysed by well-defined transition metal alkylidene complexes such as **1**–**4** (Figure 1) has emerged as a powerful tool for C–C coupling reactions in organic synthesis.[1] However, these homogeneous catalysts are rarely recoverable after the reaction. Given the high cost of ruthenium alkylidene complexes, the recyclability of the catalyst is therefore of great importance. The introduction of a chelating *o*-isopropoxybenzylidene ligand[2] instead of the traditional tricyclohexylphosphine moiety (see catalysts **3** and **4**), has enabled catalyst recovery by column chromatography. A more fundamental approach involves the immobilisation of the catalyst on a solid support. This can allow the isolation of the catalyst from the reaction solution by simple filtration and so is ideal for recycling purposes.

Several examples of immobilisation have been described. The first of these was the immobilisation of **1** via the phosphine ligand, affording a long-lived but relatively inactive catalyst.[3] Later, binding of the styrene moiety to the polymer support was accomplished by Barrett.[4] This so-called "boomerang" catalyst displayed a similar activity in ring closing metathesis (RCM) reactions to its homogeneous analogue **1**. The considerable advantages associated with the replacement of one trialkylphosphine with the sterically demanding and more Lewis-basic IMes[5] ligand have recently been exploited in polymer-bound variants of **2**.[6,7] Similarly, the enhanced recoverability of **3** demonstrated by Hoveyda has led to an immobilised catalyst[8] which displays high activity even after multiple runs.

There are numerous examples of RCM promoted by polymer-bound catalysts in the literature. However, cross metathesis (CM) presents a greater challenge because of both selectivity and the longer lifetimes required for the alkylidene intermediates. Efficient cross-couplings by poly-

mer bound catalysts have not yet been reported. We have found that **4** serves as an exceptionally stable and active catalyst for CM reactions in which one of the olefins is electron deficient, such as methyl vinyl ketone, methyl acrylate and even acrylonitrile.[9] In view of this high stability, activity, and recyclability we were interested in the properties of polymer bound versions of **4**, particularly in CM reactions of this type. Herein we describe the immobilisation of **4**, both via the IMes and chelating styrene ligands. The activity and recoverability of these catalysts in both CM and RCM reactions are also reported.
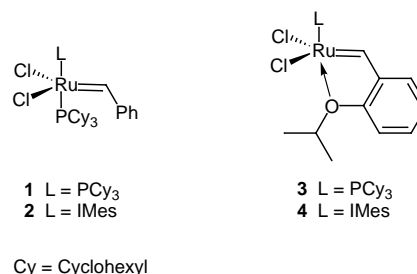
Figure 1 Ruthenium alkylidene complexes for metathesis

In line with earlier work in our laboratories,[7] we attached the IMes ligand to a Merrifield resin via an ether linkage. Imidazolium chloride **5** was first converted to the corresponding *t*-butoxy addition product, subsequent addition of 2 equivalents of **3** followed by heating gave **6** as a green resin (Scheme 1). The catalyst loading (0.70 mmolg^{-1}) was determined by ruthenium analysis (XFA) and by mass balance of the polymer. A catalyst bound to the polymer via the styrene ligand was also prepared. We wished to increase the distance between the alkylidene and the polymer support, and so a Wang resin (loading 0.72 mmolg^{-1}) was preferred in order to obtain a higher accessibility to the metal centre. 2-Isopropoxy-5-hydroxystyrene[8] was coupled to Wang resin in a Mitsunobu reaction to give ligand **7** in quantitative yield (as determined by mass balance). Subsequent ligand exchange with **2** facilitated by CuCl as a phosphine scavenger[2] afforded immobilised catalyst **8** as a deep green resin[10] (Scheme 1) with an initial ruthenium loading of 0.35 mmolg^{-1}, as determined by both ruthenium elemental analysis and mass balance.

Immobilisation via the IMes ligand

Immobilisation via the styrene ligand
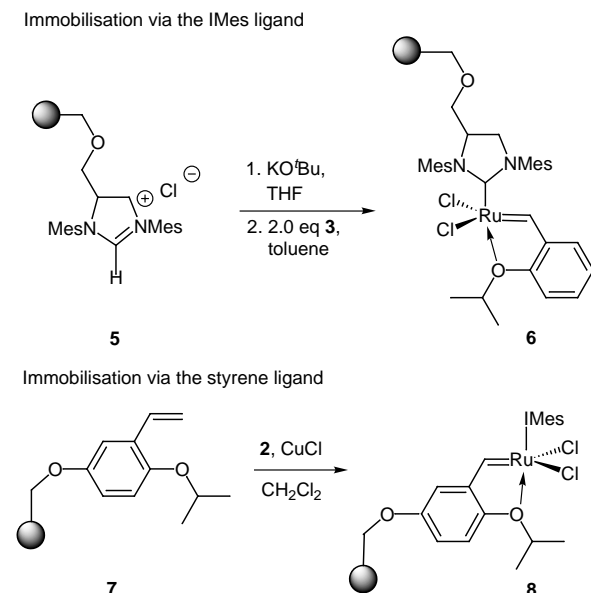
Scheme 1

In order to test the metathesis activity of **6** and **8**, the RCM of diallyltosylamine was investigated. We found that ring-closing of this substrate with either catalyst was quantitative even after 4 runs under standard conditions (CH_2Cl_2, 0.1 M, 45 °C).

Table 1   Cross Metathesis with Electron Deficient Olefins

EWG	Conversion (%)[a] using **6**	Conversion (%)[a] using **8**
CN	15	98
$COCH_3$	68	97
CO_2CH_3	96	97
$CON(CH_3)_2$	42	40
$CONH^iPr$	-	96
CHO	-	86

[a] Determined by ^1H NMR spectroscopy

Unexpectedly, this relatively high activity towards RCM displayed by **6** did not translate to CM. As can be seen from the results outlined in Tables 1, **8** displayed a much improved activity towards CM involving electron deficient alkenes. More gratifying was the excellent catalyst recoverability in these reactions. For instance the CM of **9** with methyl vinyl ketone[11] was quantitative after each of 5 consecutive runs (Table 2). It must be noted however, that longer reaction times were required with each run.

Similar results were obtained using methyl acrylate as the electron deficient partner. Furthermore, with the exception of acrylonitrile and acrolein, which gave *E/Z* ratios of 1:3 and 1:1 respectively, all cross couplings gave *E/Z* ratios in the order of >20:1.

Table 2   Recycling Results for the CM of **9** with Methyl Vinyl Ketone Catalysed by **8**

| Run	Reaction time	Conversion (%)[a]
1	4	100
2	4	100
3	12	100
4	20	100
5	43	100

[a] Determined by ^1H NMR spectroscopy

To demonstrate the robust nature and general synthetic applicability of **8** in these CM processes, coupling reactions between methyl vinyl ketone (chosen as representative of electron deficient alkenes) and substrates containing various functional groups were carried out (Figure 2). In all cases excellent yields of cross-product[12] (≥ 90%) were obtained. At first glance, the differences in CM activity between **6** and **8** could be rationalised in terms of the relative Lewis basicity of the chelating isopropoxy group. One would expect a tighter Ru–O bond in **8** (thus stabilising the intermediate alkylidenes in metathesis processes), due to the presence of the a *para* electron donating ether group. However, this was discounted by a comparison of the CM activity of homo- and heterogeneous catalysts **4**, **6**, **17** and **18** (Scheme 2 and Figure 3). In a variety of CM reactions, no significant change in reactivity was detected between the bisisopropoxy catalysts and their parent analogues.

Since it has been demonstrated[13] that metathesis reactions promoted by **2** proceed via a dissociative mechanism involving 14 electron intermediates, it seems likely that the superior activity of **8** in CM reactions of this type can be attributed to the ability of this pre-catalyst to dissociate in solution, giving a homogeneous active species, whereas the active species derived from **6** remain immobilised, and so suffer from the same diffusion related disadvantages previously reported by Grubbs.[3] This difference is most clearly seen in CM reactions involving the highly electron deficient acrylonitrile; pre-catalyst **8** gives excellent conversion, while with **6**, decomposition of the short-lived electron deficient intermediates may be competitive with metathesis, resulting in a poor yield of cross product. This would also explain why little difference between **6** and **8** is seen with respect to RCM activity, as there is only one substrate and so diffusion and intermediate lifetimes are less important.

10 (>98)   **11** (90)

12 (>98)   **13** (89)

14 (97)   **15** (94)

16 (94)
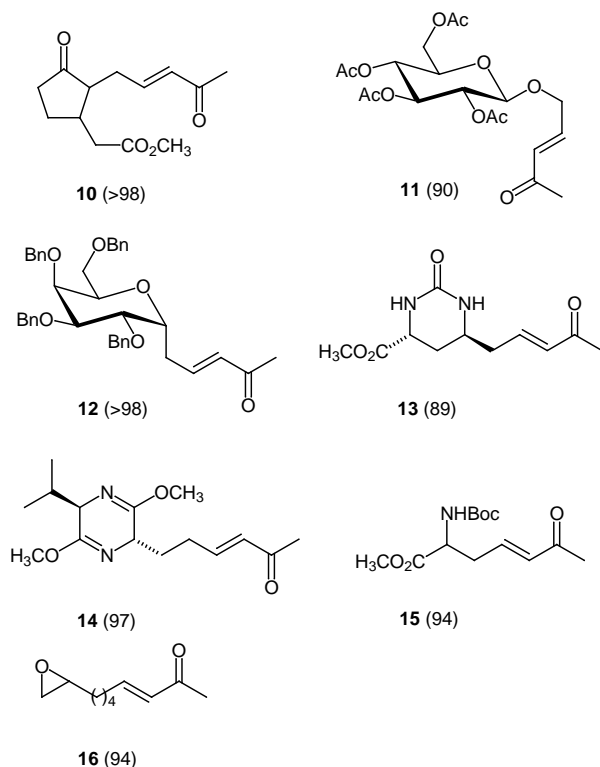
Figure 2 Products (% conversion) of CM reactions with methyl vinyl ketone


17   **18**
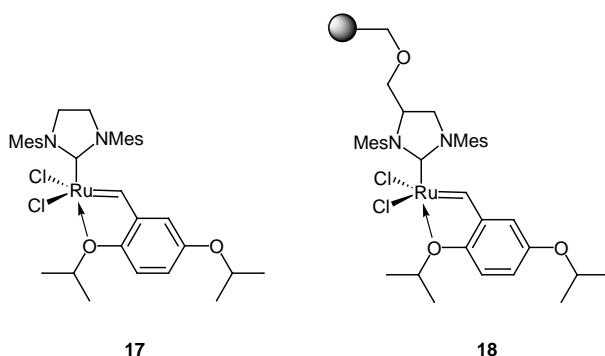
Figure 3 Isopropoxy analogues of **4** and **6**

The affinity of the active species derived from **4** or **8** for ligand **7** was also tested. A CM reaction promoted by **4** was carried out in the presence of **7**. After removal of the products and residual amounts of **4** by repeated washing, the remaining solid phase material exhibited RCM activity, showing that pre-catalyst **8** is not just a latent source of the homogeneous active species, but is verifiably recyclable. In order to better understand the cause of the superior stability of **8** in these reactions, fundamental mechanistic studies are underway in our laboratories. Progress along these lines will be reported in due course.

In summary, we have presented two novel immobilised ruthenium alkylidene catalysts (**6** and **8**), which display excellent activity in olefin metathesis reactions. For the first time, CM with highly electron deficient alkenes such as acrylonitrile promoted by a polymer-bound catalyst has

been described. The high efficiency and recoverability of these species make them attractive and more economical alternatives to their homogeneous counterparts.
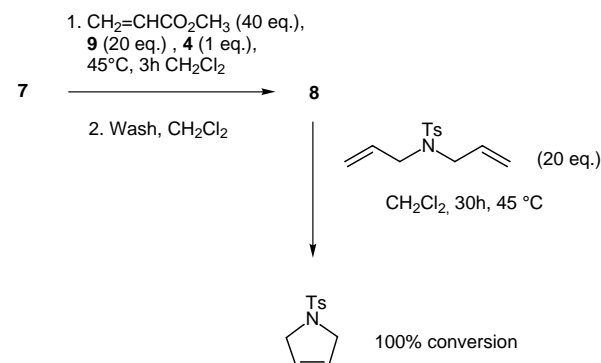
Scheme 2

Acknowledgement

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(10) Procedure for the preparation of **8**: To a suspension of **7** (573 mg, 0.354 mmol) in CH_2Cl_2 (9 mL) were added **2** (330 mg,

0.390 mmol) and CuCl (38.6 mg, 0.390 mmol), the resulting red mixture was heated under reflux for 3 h. The reaction mixture was transferred to a separatory funnel and the phosphine salts were removed. The solvent was then removed by filtration and the resin washed with CH_2Cl_2 until the washings were colourless and then three times with Et_2O. The resin was dried under high vacuum and stored at 4 °C.

(11) General procedure for CM with **6** or **8**: To a solution of **9** (0.1 mmol) and the electron deficient alkene (0.2 mmol) in CH_2Cl_2 (5 mL) was added **6** or **8** (0.005 mmol) under N_2 and the resulting suspension was heated under reflux for 4–43 h. After filtration, the solvent was removed in vacuo and the yield determined by ^{1}H NMR spectroscopy. After washing

three times with CH_2Cl_2 the catalyst was suitable for immediate re-use.

(12) All new compounds were fully characterised. Selected data for **13**: ^{1}H NMR (400 MHz, CDCl$_3$, ppm): 6.72 (1 H, dt, J = 18.7 Hz), 6.18 (1 H, d, J = 18 Hz), 5.94 (2 H, bs), 5.14 (1 H, t, 5 Hz), 3.76 (3 H, s), 3.56 (1 H, m), 2.43 (2 H, m), 2.28 (3 H, s), 2.19 (1 H, m, Hz), 1.94 (1 H, m). ^{13}C NMR (125 MHz, CDCl$_3$, ppm): 197.8, 171.6, 155.9, 141.0, 134.4, 52.8, 51.0, 47.0, 38.5, 28.l7, 27.3. HRMS (EI)) $C_{11}H_{16}N_2O_4$ [(M+H)$^+$] 241.1188. Found 241.1191. R_f 0.5 (2:1 MTBE / MeOH). IR (cm^{-1}): 3239, 3093, 2953, 2855, 1736, 1671, 1507, 1437, 1363, 1314, 1256, 1215, 1175, 1026, 988, 763.

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