DOI: 10.1002/ejoc.200600908

Phenylphosphoric Acid as a New Additive to Inhibit Olefin Isomerisation in Ruthenium-Catalysed Metathesis Reactions

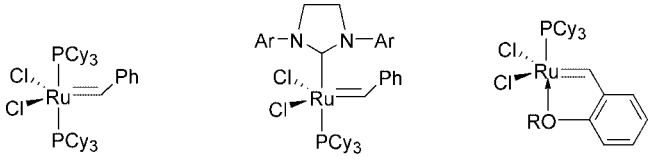
Nélida Gimeno,[a,b] Pilar Formentín,[a] Joachim H. G. Steinke,*[a] and Ramón Vilar*[a,b]

Keywords: Homogenous catalysis / Metathesis / Ruthenium / Alkenes / Ureas

A systematic study of the ruthenium-catalysed metathesis of alkenes containing hydrogen-bonding substituents (namely urea and thiourea groups) is presented. Under standard metathesis conditions, several of the substrates under study undergo alkene isomerisation instead of the targeted metathesis. However, in the course of these investigations it has been established that this unwanted isomerisation process can be suppressed by addition of phenylphosphoric acid to the reaction mixture. Some other potential isomerisation inhibitors (e.g. benzoic acid and salts of phosphoric acid) have been studied and their performance compared to that of phenylphosphoric acid. To extend the scope of phenylphosphoric acid, we also studied the metathesis of 1,3-diallylurea. Interestingly, not only did we observe the complete suppression of the isomerisation process, but also that it is possible to obtain instead of the ring-closing metathesis (RCM) product, ADMET oligomers resulting from the cross-metathesis of diallylurea at higher concentrations.

Introduction

Metal-catalysed alkene metathesis has been established as one of the most widely used organometallic transformations for carbon–carbon bond formation.[1–11] Initially, the scope and applications of this type of reaction was limited by the poor functional group tolerance that the catalysts had. However, over the past few years more robust, functionality-tolerant and highly reactive metathesis catalysts have been developed extending the scope of this transformation to a wide range of olefinic substrates. In particular, ruthenium-based catalysts developed by Grubbs[12–16] (e.g. **1** and **2** in Figure 1) and more recently by Hoveyda[17,18] (e.g. **3** in Figure 1) combine high-reactivity with very good tolerance to a wide range of functional groups.



1 **2** **3**

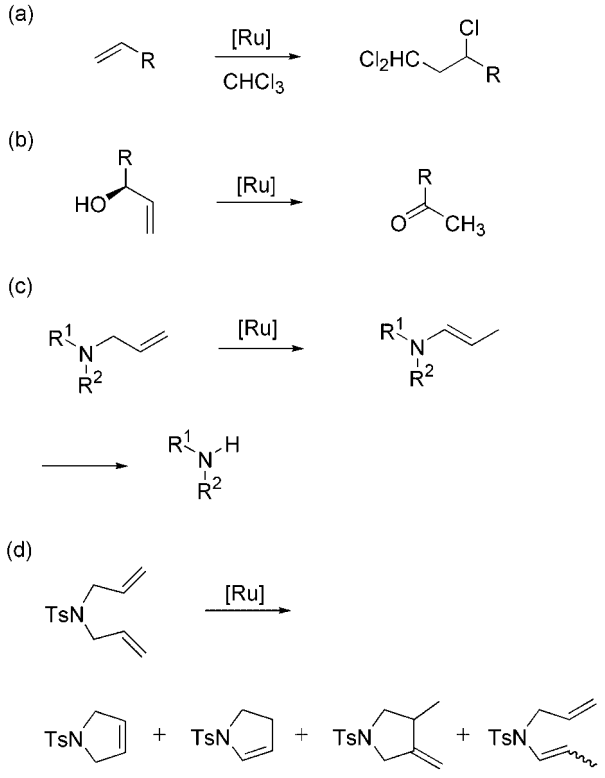
Figure 1. Selected examples of ruthenium-based catalysts for olefin metathesis.

[a] Department of Chemistry, Imperial College London, South Kensington, London SW7 2AZ, United Kingdom
E-mail: j.steinke@imperial.ac.uk
r.vilar@imperial.ac.uk
[b] Institute of Chemical Research of Catalonia (ICIQ), 43007 Tarragona, Spain

With the increased use of these ruthenium complexes in alkene metathesis, it has been found that several of them also catalyze other non-metathetic reactions (Scheme 1).[4,19–23] Although these reactions broaden the synthetic scope of the ruthenium-alkylidene catalysts, they can be troublesome if the metathesis products are the ones being sought.

For example, Snapper has reported that complex **1** catalyses the addition of chloroform to alkenes [see reaction (a) in Scheme 1],[24] while Hoye and Zhao have shown that in the presence of ruthenium catalysts allyl alcohols are degraded to ketones [see reaction (b) in Scheme 1].[25]

One of the most common non-metathetic reactions catalysed by ruthenium-carbene complexes is the isomerisation of alkenes [see reactions (c) and (d) in Scheme 1]. Although this type of reaction has been successfully used to synthesise a wide range of organic products[26–28] and as a means for deprotecting allylic amines[29,30] and amides[31] [see reaction (c) in Scheme 1], it is a problem when the product targeted is the one resulting from metathesis. Although the exact mechanism of this side-reaction has not yet been established, several studies indicate that ruthenium hydride species, either formed in situ by decomposition of the catalyst or present as impurities in the original catalyst, are responsible for the isomerisation process.[21,22,32–35] Due to the problems that this reaction can pose, several studies have been carried out to find ways to suppress it. For example, Nolan and Prunet reported in 2002 that tricyclohexylphosphane oxide inhibits isomerisation of specific olefinic substrates.[35] More recently, Grubbs has compared the effect that different additives have in the distribution of products from metathesis and isomerisation. For example, species



Scheme 1. Non-metathetic reactions catalysed by ruthenium complexes.

such as 2,6-dichloro-1,4-benzoquinone and tetrafluoro-1,4-benzoquinone were shown to suppress completely olefin isomerisation of various olefins.[36] Acetic acid has also shown to prevent isomerisation of alkenes but its scope seems to be limited to specific substrates. In a recent paper Meyer has reported that tin(II) chloride and bromide salts enhance the metathesis performance of catalyst **1** inhibiting, as well, the isomerisation.[37]

We have particular interest in using alkene metathesis to synthesise compounds that have hydrogen-bonding groups which can potentially act as molecular receptors for anionic species. Consequently we have engaged in studying the best catalysts and experimental conditions required to perform this transformation on urea- and amide-substituted alkenes (see Figure 2).

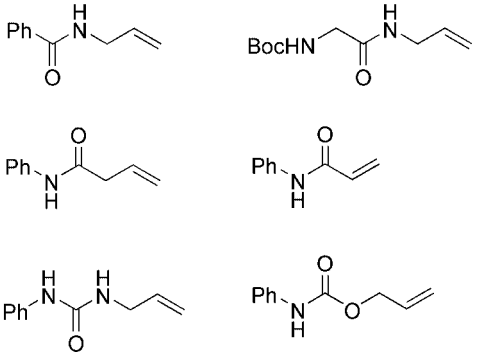
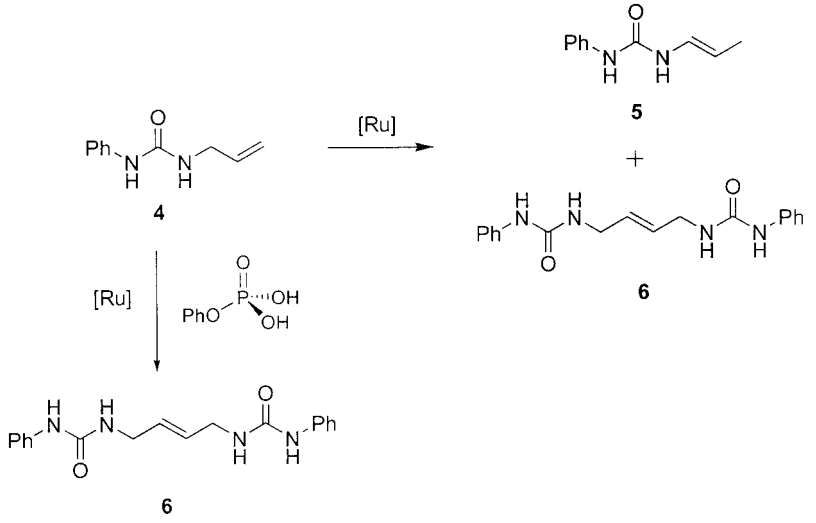


Figure 2. Functionalized alkene substrates under study.

As we reported in a preliminary communication, under previously reported "standard" experimental conditions for alkene metathesis, **1** and **2** catalyze mainly the isomerisation of the urea- and amide-substituted alkenes and not their metathesis.[38] Since for our aims this is an unwanted reaction, we investigated conditions under which the reaction would mainly give the metathesis products. Interestingly, we found that upon addition of phenylphosphoric acid, P(=O)(OPh)(OH)$_2$, the course of the reaction changes favouring the formation of the metathesis products while the isomerisation process is completely suppressed (Scheme 2).

Herein, we report a more detailed study on the use of phenylphosphoric acid as isomerisation inhibitor probing the influence of reaction time, temperature and stoichiometry and nature of the additive (salt form, counterion effects) on product distribution. Furthermore we have extended the scope of this compound as an additive to favour metathesis using a wider range of substrates.



Scheme 2. Reactions showing isomerisation vs. metathesis for 1-allyl-3-(phenyl)urea (**4**).

Results and Discussion

Phenylphosphoric Acid as An Isomerisation Inhibitor in Olefin Metathesis

In order to gain a deeper insight into the competition between isomerisation and metathesis of substituted olefins, the reaction shown in Scheme 2 was investigated. The results of these investigations are summarised in Table 1. Under standard metathesis conditions the reaction of **4** with 10 mol-% of **2** yields a mixture of isomerisation (55%) and metathesis (33%) products (compound **5** and **6** respectively, see Entry 1 in Table 1). However, upon addition of $P(=O)(OPh)(OH)_2$ (see Entry 2) the isomerisation is completely suppressed and the only product obtained is **6** (cross-metathesis product). To investigate whether the amount of additive or the temperature of the reaction would have an effect on the product distribution, the above reaction was repeated with ten times less phenylphosphoric acid (5%) and at a lower temperature (10 °C). As can be seen in Entry 3, the reduction in both temperature and amount of additive had very little effect on the distribution of products. This indicates that the isomerisation process can be inhibited completely (and hence only the cross-metathesis product obtained) by carrying out the reaction at low temperature and with as little as 5% of phenylphosphoric acid additive.

As indicated above, the exact mechanism by which Grubbs' catalyst **2** promotes alkene isomerisation is not yet known. Several studies have shown that ruthenium hydride species, either formed in situ by decomposition of the catalyst or present as impurities in the original catalyst, are responsible for the isomerisation. Consequently, species capable of reacting with the ruthenium hydride complexes could in principle be effective additives to inhibit this unwanted process. It is then possible that $P(=O)(OPh)(OH)_2$ inhibits the isomerisation process of allyl(phenyl)urea (and other allylic substrates as shown in our preliminary communication[38]) by reacting with any potential ruthenium hydride species present in the reaction mixture.

In order to have a better understanding of the isomerisation-inhibition process, several reactions were carried out. We first studied whether the mono-triethyl ammonium salt of phenylphosphoric acid (see Entries 4 and 5) would still inhibit alkene isomerisation. To our surprise, this additive not only inhibited isomerisation but also alkene metathesis (at both 10 and 40 °C). It has been shown by others[39] that some hydrochloride salts of amines are compatible with ruthenium-based metathesis catalysts. It was hence surprising that in the current study complete de-activation of the catalytic species was observed. A possible explanation for this could be that under the experimental conditions of this specific reaction, the amine/ammonium equilibrium plays a role in the deactivation of the catalyst (e.g. presence of free amine). In order to investigate this hypothesis, the reaction was repeated using the mono-tetraethyl ammonium salt $[P(=O)(OPh)(OH)(O)][NEt_4]$ as additive (see Entry 6). In this case, no metathesis product was obtained while 80% alkene isomerisation was observed. These observations suggest that $P(=O)(OPh)(OH)_2$ inhibits olefin isomerisation by acting as an acidic additive and also that catalyst **2** is not tolerant to $[HNEt_3]^+$.

To explore whether the isomerisation of allyl(phenyl)urea would be inhibited by a different acid, the reaction was repeated in the presence of benzoic acid (see Entry 7). As expected, alkene isomerisation was suppressed and the metathesis product **6** was formed in a reasonable yield of 43%. This is also consistent with previous reports in which acetic acid has shown to inhibit the isomerisation of certain alkenes.[36]

Once we had shown the importance of the acidic protons of the additives for the inhibition of alkene isomerisation, it was of interest to evaluate whether or not other known inhibitors would work for our substrate [i.e. allyl(phenyl)-urea]. Grubbs has recently shown that quinones can act as effective additives in ruthenium-catalysed metathesis reactions.[36] Consequently, 2,6-dichloro-1,4-benzoquinone was added to the reaction of **2** with substrate **4**. This reaction yielded the metathesis product **6** in 54% yield and no isomerisation product was formed. This result shows that 2,6-dichloro-1,4-benzoquinone (Entry 8 in Table 1) and our phosphate monoester $P(=O)(OPh)(OH)_2$ (Entries 2 and 3 in Table 1) are essentially equally effective as isomerisation inhibitor; an interesting result given the high effectiveness of the former as demonstrated by Grubbs[36] for other substrates.

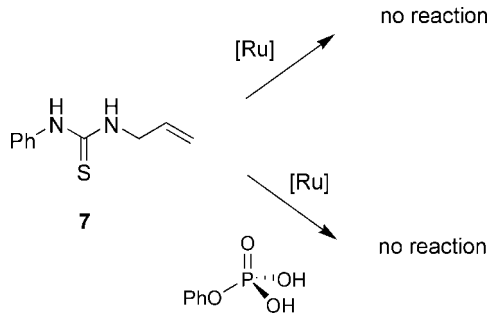
Table 1. Summary of the conditions employed and the results obtained for the different ruthenium-catalysed reactions of 1-allyl-3-phenylurea **4**.

Entry[a]	Additive	Amount of additive (% with respect to the urea)	Temp. [°C]	% yield[b] of **6**	% yield[b] of **5** (*E*/*Z*)[c]	% yield[b] of **4**
1	–	–	40	33	55 (1:1)	10
2	$P(=O)(OPh)(OH)_2$	50	40	56	–	30
3	$P(=O)(OPh)(OH)_2$	5	10	50	–	50
4	$[P(=O)(OPh)(OH)(O)][NHEt_3]$	50	40	–	–	100
5	$[P(=O)(OPh)(OH)(O)][NHEt_3]$	50	10	–	–	100
6	$[P(=O)(OPh)(OH)(O)][NEt_4]$	50	10	–	80 (1:15)	20
7	PhCOOH	5	10	43	–	57
8	2,6-dichloro-1,4-benzoquinone	10	40	54	–	46

[a] All reactions were carried out in CH_2Cl_2 using 10 mol-% of **2**. [b] Reaction time 16 h. [c] Isomerisation product **5** was obtained as an *E*/*Z* mixture. The proportions of each isomer are shown in brackets.

Reactions of Complex 2 with 1-Allyl-3-(phenyl)thiourea (7)

In order to potentially expand the scope of phenylphosphoric acid as inhibitor for olefin isomerisation when using Grubbs' catalyst, olefinic substrates carrying other types of hydrogen bonding receptor groups were studied. Interestingly, when **2** was added to a solution of allyl(phenyl)thiourea in the absence of phenylphosphoric acid (using analogous conditions to the ones described for the urea substrate – Entry 1 in Table 1) no reaction was observed even after 18 h (Scheme 3).



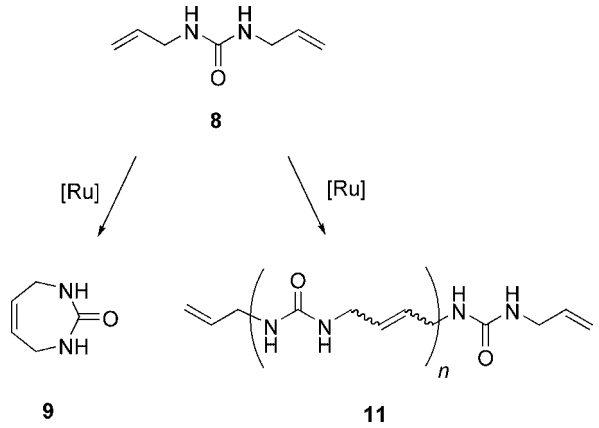
Scheme 3. Attempted reaction between **2** and 1-allyl-3-(phenyl)-thiourea.

Analysis of the reaction mixture by ^{1}H NMR spectroscopy indicated that the only species present was starting material. The same result was obtained when the reaction was repeated in the presence of 50% phenylphosphoric acid at 40 °C. These observations suggest that the thiourea group somehow interferes with the catalytic ruthenium species for both metathesis and isomerisation of the alkene. A possible explanation for this behaviour could be the strong coordinating ability of thiourea groups towards the metal centre. There are several examples previously reported of ruthenium complexes with thiourea groups as ligands.[40,41]

To elucidate whether the thiourea was indeed coordinating to the metal centre, a 1:1 mixture of **2** and allyl(phenyl)-thiourea was prepared and monitored by ^{31}P NMR spectroscopy. After ca. 1 h it was observed that 7 new dominant singlets (plus several more small peaks) appeared between δ = 25.3 and 33.9 ppm; although one of these resonances could be associated with the original Grubbs' catalyst (δ = 31.4 ppm) the appearance of so many new ^{31}P NMR signals, indicates that **2** readily reacts with allyl(phenyl)thiourea to yield a wide range of phosphorus-containing products. Due to the large amount of products in this mixture and the fact that no alkene metathesis (or even isomerisation) was observed when using **7** as substrate, it was decided not to continue the investigation of metathesis with thiourea-containing alkenes.

Reaction of Complex 2 with 1,3-Diallylurea (8)

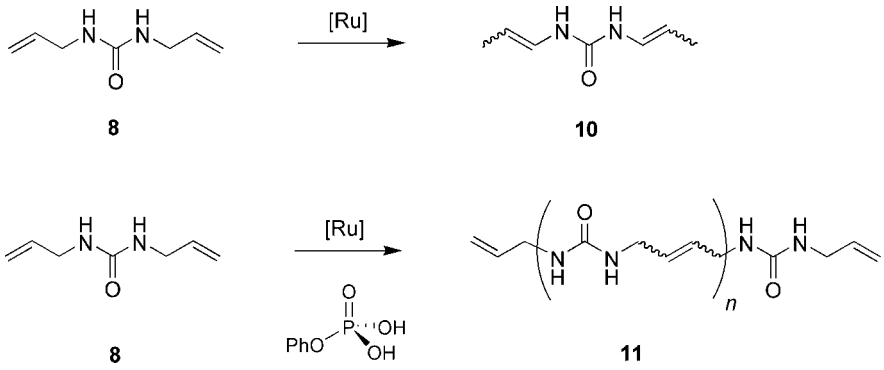
As a further determinant for the scope of our additive we investigated the ability of phenylphosphoric acid to act as isomerisation inhibitor and potential reaction template. We chose the conversion of 1,3-diallylurea (**8**) to either the cyclic urea **9** or potentially leading to an ADMET-type oligomerisation **11** using **2** as metathesis catalyst (see Scheme 4).



Scheme 4. Using Grubbs' catalyst **2**, the 1,3-diallylurea (**8**) could in principle give the ring-closing metathesis product **9** or the ADMET-type oligomerisation **11**.

The reaction was first carried out in the absence of phenylphosphoric acid under analogous conditions to those used for allyl(phenyl)urea (see Entry 1, Table 1). 1,3-Diallylurea (**8**) was dissolved in CH_2Cl_2 and complex **2** added to the solution. The reaction mixture was stirred overnight at 40 °C after which time the solvent was evaporated under reduced pressure. The ^{1}H NMR spectrum of the crude mixture showed signals at δ = 5.86, 5.17 and 3.79 ppm corresponding to the starting material plus a series of resonances at δ = 6.56, 4.97 and 4.57 ppm which can be assigned to product **10** (see Scheme 5). This species, resulting from isomerisation of **8**, has itself three different *cis-trans* isomers (namely *EE*, *EZ* and *ZZ*) which have been previously characterised by ^{1}H NMR spectroscopy.[42] On the basis of this, it was possible to assign the resonances corresponding to the olefinic protons of **10** and calculate that the proportion of **8** which isomerised to **10** was ca. 50% (by ^{1}H NMR spectroscopy). Since the latter di-olefinic species has been previously characterised and our main interest is on metathesis processes (not observed here), we decided not to isolate the isomerisation product **10**. It should also be mentioned that no traces of the RCM product **9** (which has been previously synthesised via a different route and its ^{1}H NMR spectrum reported) could be detected.

The reaction of **8** with catalyst **2** was then repeated in the presence of phenylphosphoric acid to suppress the isomerisation process. When a 3.6 mM solution of **8** was stirred for about 12 h at 40 °C neither isomerisation nor any metathesis product occurred, the starting material was completely recovered. However, when the reaction was repeated (under identical reaction conditions), with a 10-times higher concentration of diallylurea, a white precipitate formed (23 mg corresponding to 50% conversion of the starting material). This product was isolated by filtration and washed with dichloromethane. The ^{1}H NMR spectrum of both the precipitate and the solution showed that no alkene isomerisation to **10** or RCM of the di-olefin to yield **9** had



Scheme 5. In the presence of catalyst **2**, 1,3-diallylurea (**8**) isomerises to **10**. When the same reaction is carried out in the presence of phenylphosphoric acid, the isomerisation is suppressed favouring a metathetical process to yield the oligomeric urea species **11**. The formation of the ring-closing metathesis product **9**, was not observed in any of these experiments.

taken place. Instead, the characterisation of the isolated solid was consistent with a cross-metathesis process (ADMET) (see Scheme 5).

The ^{1}H NMR spectrum of the isolated precipitate showed it to be a mixture of oligomeric species with the general formula shown in Scheme 5 (species **11**). Two broad signals at δ = 5.96 (3.5 H) and 5.49 (2.5 H) ppm, a multiplet at δ = 5.79 (1 H) ppm and a doublet of doublets at δ = 5.04 (2 H) ppm were present in the ^{1}H NMR spectrum. The two broad signals are consistent with a mixture of oligomers where the signal at δ = 5.96 ppm corresponds to the urea NH protons and the one at δ = 5.49 ppm corresponds to the olefinic protons resulting from cross-metathesis (for comparison, the –CH=CH– protons in **6** – see Scheme 2 – appear at δ = 5.62 ppm). The two double doublets at δ = 5.01 and 5.09 ppm, respectively, are consistent with the H_2C=CHR protons and the doublet of doublet of triplets at δ = 5.79 ppm corresponds to the single vinylic end-group proton (H_2C=C*H*R) which would be expected for a linear oligomeric species **11**. The relative integration between the terminal olefinic protons and those corresponding to the central 1,2-disubstituted double bond, were suitable for end-group analysis and indicate that the average degree of oligomerisation of **11** is 4. The ^{13}C NMR spectroscopic data also confirmed the proposed oligomeric structure, with resonances corresponding to terminal and 1,2-disubstituted allyl groups and a carbonyl peak at δ = 158.09 ppm (163.2 ppm for **8**).

The presence of different oligomers in the product **11** (see Scheme 5) was confirmed by FAB(+) mass spectrometry which showed peaks at 253 a.m.u. (species with n = 1), 365 a.m.u. (species with n = 2) and 477 a.m.u. (species with n = 3). No evidence for the formation of cyclic species was found by neither mass spectrometry nor NMR spectroscopy.

Interestingly, the ^{31}P{^{1}H} NMR spectrum of a DMSO solution of the isolated solid (that contains **11**) showed a singlet at δ = –5.6 ppm indicating the presence of phenylphosphoric acid in the sample. Further inspection of the ^{1}H NMR spectrum of **11** revealed signals in the aromatic region (three broad resonances at δ = 7.29, 7.14 and 7.07 ppm with a relative integration ratio of 2:2:1) which we also associated to phenylphosphoric acid. The relative integration between these signals and those corresponding to the terminal olefinic protons of **11** is approximately 1:4. The presence of phenylphosphoric acid in the precipitate (even if in relatively small amounts) suggests a strong association between this compound and the oligourea species **11**. It is well established that urea groups and phosphate groups interact strongly via hydrogen bonding,[43,44] hence it is not unexpected that **11** binds phenylphosphoric acid, though it does not explain the complete lack of reactivity under more dilute reaction conditions. Further studies will need to be carried out to determine the extent of interaction between these two species and whether this can be used more generically to guide the outcome of the metathesis reaction of 1,3-diallylurea and related hydrogen bonding receptor motifs.

Conclusions

We have identified in more detail the scope of phenylphosphoric acid acting as an effective inhibitor of unwanted alkene isomerisation using Grubbs' catalyst **2** for metathetical reactions. Our data supports a likely mechanism of action involving the reaction between the most acidic proton of the additive and hydrido ruthenium complexes (which could catalyse isomerisation) present in the reaction mixture. We have also shown that phenylphosphoric acid inhibits the isomerisation of diallylurea groups. This has allowed us to prepare oligomeric polyureas in an ADMET process using Grubbs' catalyst **2**. Interestingly the phenylphosphoric additive co-precipitates with the oligomers which may be the result of a strong association between the phosphoric acid group and the urea receptor motif and could have implications for hydrogen bond-controlled templating of metathesis processes. Experiments to clarify the levels of involvement of the additive are being targeted.

Experimental Section

General: All manipulations were carried out under purified and dry nitrogen or argon using standard Schlenk-line techniques unless otherwise stated. Solvents were dried from the appropriate drying

agent, degassed and stored under nitrogen. All commercially available solid starting materials were not further purified. All liquid starting materials were dried with molecular sieves and thoroughly degassed by freeze pump thaw prior to use. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded with a Bruker Avance 400 or Bruker Avance 500 spectrometer and referenced to residual ^{1}H and ^{13}C signals of the solvents or 85% H_3PO_4 as an external standard (^{31}P). 1,3-diallylurea and 2,6-dichloro-1,4-benzoquinone were purchased from Sigma Aldrich. Phenylphosphoric acid was purchased from TCI Europe. 1-Allyl-3-phenylurea (**4**)[45] and 1-allyl-3-(phenyl)thiourea (**7**)[46] were synthesised following reported procedures.

Cross Metathesis of Allyl(phenyl)urea: The following general procedure was employed for the metathesis of the allylurea (further details regarding some of the experimental conditions are provided in Table 1). To a solution of allyl(phenyl)urea (61.5 mg, 0.4 mmol) in dry and degassed CH_2Cl_2, a solution of Grubbs' catalyst **2** (37.3 mg, 0.04 mmol, 10 mol-% corresponding to a concentration of catalyst of 2 mM) in the same solvent was added. The resulting mixture was stirred overnight at the corresponding temperature (see Table 1). The formation of a white precipitate (corresponding to the metathesis product **6**) was observed in the course of the reactions. This solid was isolated by filtration and washed several times with hexane. The solvent from the remaining filtrate was evaporated under reduced pressure to yield a brown oil. This crude was purified by silica gel column chromatography using CH_2Cl_2/ethyl acetate [9:1 (v/v)] as eluent.

For the reactions carried out in the presence of P(=O)(OPh)-(OH)$_2$, [P(=O)(OPh)(O)(OH)][NHEt$_3$], [P(=O)(OPh)(O)(OH)]-[NEt$_4$], benzoic acid or 2,6-dichloro-1,4-benzoquinone, the additive was mixed with the corresponding olefinic substrate in CH_2Cl_2 and the catalyst was then added to this mixture. For additive/alkene ratios employed, see Table 1 and sections 2.2–2.3.

Reaction of 1,3-Diallylurea with 2 and Phenylphosphoric Acid. Low Concentration: To a solution of 1,3-diallylurea (50.0 mg, 0.4 mmol) and phenylphosphoric acid (31.3 mg, 0.2 mmol) in 100 mL of dry and degassed CH_2Cl_2, a solution of Grubbs' catalyst **2** (30.5 mg, 0.04 mmol, 10 mol-% corresponding to a concentration of catalyst of 2 mM) in the same solvent was added. The resulting mixture was stirred overnight at 40 °C. The organic solvent was evaporated after this time and an orange oil obtained. Only starting material was recovered.

Reaction of 1,3-Diallylurea with 2 and Phenylphosphoric Acid. High Concentration: To a solution of 1,3-diallylurea (50.0 mg, 0.4 mmol) and phenylphosphoric acid (31.3 mg, 0.2 mmol) in 10 mL of dry and degassed CH_2Cl_2, a solution of Grubbs' catalyst **2** (30.5 mg, 0.04 mmol, 10 mol-% corresponding to a concentration of catalyst of 2 mM) in the same solvent was added. The resulting mixture was stirred overnight at 40 °C. The formation of a white precipitate (corresponding to the metathesis oligomeric product **11**) was observed in the course of the reaction. This solid was isolated by filtration and washed several times with dichloromethane. Yield: (23 mg corresponding to 50% conversion of the starting material). ^{1}H NMR ([D$_6$]DMSO, 400 MHz): δ = 3.60 (m, 6 H, CH_2), 5.04 (m, 2 H, CH=CH_2), 5.49 (br. s, 2 H, C*H*=), 5.79 (m, 1 H, C*H*=CH$_2$), 5.96 (br. s, 3 H, N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO, 400 MHz): δ = 41.02 (NH–*CH$_2$*–CH=CH), 42.12 (NH–*CH$_2$*–CH=CH$_2$), 114.75 (*CH$_2$*=CH), 128.89 [*CH*=CH (*trans*)], 129.60 (*CH*=CH *cis*), 137.31 (NH–CH$_2$–*CH*=CH$_2$), 158.09 [NH*C*(O)NH] ppm. {MS (FAB+): 253 a.m.u. (species where n = 1), 365 a.m.u. (species where n = 2) and 477 a.m.u. (species where n = 3)}.

Acknowledgments

We thank the Ministerio de Educación y Ciencia of Spain (grant CTQ2004-04103/BQU) and the Institut Català d'Investigació Química (ICIQ Foundation) for financial support and the European Union for a Marie Curie Fellowship (P. F.).

[1] K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4490–4527.
[2] D. J. Wallace, *Angew. Chem. Int. Ed.* **2005**, *44*, 1912–1915.
[3] J. Mulzer, E. Oehler, *Top. Curr. Chem.* **2004**, *13*, 269–366.
[4] B. Schmidt, J. Hermanns, *Top. Organomet. Chem.* **2004**, *13*, 223–267.
[5] R. H. Grubbs, *Tetrahedron* **2004**, *60*, 7117–7140.
[6] A. D. Piscopio, J. E. Robinson, *Curr. Opin. Chem. Biol.* **2004**, *8*, 245–254.
[7] A. Deiters, S. F. Martin, *Chem. Rev.* **2004**, *104*, 2199–2238.
[8] J. C. Mol, *J. Mol. Catal. A* **2004**, *213*, 39–45.
[9] M. A. Leeuwenburgh, G. A. van der Marel, H. S. Overkleeft, *Curr. Opin. Chem. Biol.* **2003**, *7*, 757–765.
[10] R. R. Schrock, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2003**, *42*, 4592–4633.
[11] E. N. Guidry, S. J. Cantrill, J. F. Stoddart, R. H. Grubbs, *Org. Lett.* **2005**, *7*, 2129–2132.
[12] T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18–29.
[13] C. W. Bielawski, R. H. Grubbs, *Angew. Chem. Int. Ed.* **2000**, *39*, 2903–2906.
[14] J. P. Morgan, R. H. Grubbs, *Org. Lett.* **2000**, *2*, 3153–3155.
[15] A. K. Chatterjee, J. P. Morgan, M. Scholl, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 3783–3784.
[16] P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100–110.
[17] A. H. Hoveyda, D. G. Gillingham, J. J. Van Veldhuizen, O. Kataoka, S. B. Garber, J. S. Kingsbury, J. P. A. Harrity, *Org. Biomol. Chem.* **2004**, *2*, 8–23.
[18] J. S. Kingsbury, J. P. A. Harrity, P. J. Bonitatebus Jr., A. H. Hoveyda, *J. Am. Chem. Soc.* **1999**, *121*, 791–799.
[19] B. Schmidt, *Angew. Chem. Int. Ed.* **2003**, *42*, 4996–4999.
[20] B. Schmidt, *Eur. J. Org. Chem.* **2003**, 816–819.
[21] B. Schmidt, *J. Org. Chem.* **2004**, *69*, 7672–7687.
[22] B. Schmidt, *Chem. Commun.* **2004**, 742–743.
[23] B. Alcaide, P. Almendros, *Chem. Eur. J.* **2003**, *9*, 1258–1262.
[24] J. A. Tallarico, L. M. Malnick, M. L. Snapper, *J. Org. Chem.* **1999**, *64*, 344–345.
[25] T. R. Hoye, H. Zhao, *Org. Lett.* **1999**, *1*, 1123–1125.
[26] D. Finnegan, B. A. Seigal, M. L. Snapper, *Org. Lett.* **2006**, *8*, 2603–2606.
[27] M. Arisawa, Y. Terada, M. Nakagawa, A. Nishida, *Angew. Chem. Int. Ed.* **2002**, *41*, 4732–4734.
[28] A. E. Sutton, B. A. Seigal, D. F. Finnegan, M. L. Snapper, *J. Am. Chem. Soc.* **2002**, *124*, 13390–13391.
[29] B. Alcaide, P. Almendros, J. M. Alonso, *Chem. Eur. J.* **2003**, *9*, 5793–5799.
[30] B. Alcaide, P. Almendros, J. M. Alonso, A. Luna, *Synthesis* **2005**, 668–672.
[31] B. Alcaide, P. Almendros, J. M. Alonso, *Chem. Eur. J.* **2006**, *12*, 2874–2879.
[32] S. H. Hong, M. W. Day, R. H. Grubbs, *J. Am. Chem. Soc.* **2004**, *126*, 7414–7415.
[33] B. Schmidt, *Eur. J. Org. Chem.* **2004**, 1865–1880.
[34] D. V. McGrath, R. H. Grubbs, *Organometallics* **1994**, *13*, 224–235.
[35] D. Bourgeois, A. Pancrazi, S. P. Nolan, J. Prunet, *J. Organomet. Chem.* **2002**, *643–644*, 247–252.
[36] S. H. Hong, D. P. Sanders, C. W. Lee, R. H. Grubbs, *J. Am. Chem. Soc.* **2005**, *127*, 17160–17161.
[37] W. H. Meyer, A. E. McConnell, G. S. Forman, C. L. Dwyer, M. M. Kirk, E. L. Ngidi, A. Blignaut, D. Saku, A. M. Z. Slawin, *Inorg. Chim. Acta* **2006**, *359*, 2910–2917.

[38] P. Formentin, N. Gimeno, J. H. G. Steinke, R. Vilar, *J. Org. Chem.* **2005**, *70*, 8235–8238.
[39] G. C. Fu, S. T. Nguyen, R. H. Grubbs, *J. Am. Chem. Soc.* **1993**, *115*, 9856–9857.
[40] S. D. Robinson, A. Sahajpal, J. W. Steed, *Inorg. Chim. Acta* **2000**, *306*, 205–210.
[41] B. G. Olby, S. D. Robinson, *Inorg. Chim. Acta* **1989**, *165*, 153–162.
[42] S. Krompiec, M. Pigulla, N. Kuznik, M. Krompiec, B. Marciniec, D. Chadyniak, J. Kasperczyk, *J. Mol. Catal. A* **2005**, *225*, 91–101.
[43] P. D. Beer, P. A. Gale, *Angew. Chem. Int. Ed.* **2001**, *40*, 486–516.
[44] P. A. Gale, *Coord. Chem. Rev.* **2000**, *199*, 181–233.
[45] L. A. Tsoi, A. D. Salimbaeva, B. D. Abiyurov, *Zh. Org. Khim.* **1983**, *19*, 2605–2609.
[46] J. C. Pascal, H. Pinhas, F. Laure, D. Dumez, A. Poizot, *Eur. J. Med. Chem.* **1990**, *25*, 81–85.

Received: October 18, 2006
Published Online: December 19, 2006

