

Improved cross-metathesis of acrylate esters catalyzed by 2nd generation ruthenium carbene complexes

Grant S. Forman ^{*}, Robert P. Tooze

Sasol Technology Research Laboratory, Sasol Technology (UK) Limited, Purdie Building, North Haugh, St. Andrews, Fife KY16 9ST, Scotland, UK

Received 26 May 2005; accepted 15 July 2005

Available online 1 September 2005

Abstract

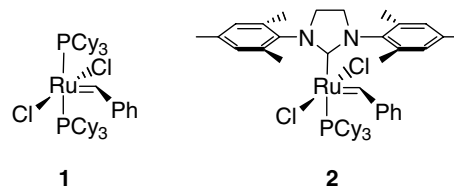
The performance of cross-metathesis reactions between acrylate esters and olefins catalyzed by Grubbs catalysts have been enhanced by the simple addition of *p*-cresol. For example, the efficiency of the cross metathesis reaction between methyl acrylate and 1-decene catalyzed by **2** was significantly increased by addition of *p*-cresol to the reaction mixture, resulting in increased product yields and *E/Z* ratios.

© 2005 Elsevier B.V. All rights reserved.

Keywords: Cross-metathesis; Grubbs catalyst; Acrylate; Carbene

N-heterocyclic carbenes (NHCs) have emerged as an important class of ligands for transition metals and are beginning to play a role in transition metal catalysis [1]. Nucleophilic carbene ligands are neutral two-electron donor ligands that have a negligible tendency towards π -back bonding, and as such they can be viewed as alternatives to phosphine ligands [2]. When complexed to middle or late transition metals, NHC's are relatively robust ligands in homogeneous catalysis [3], although reductive elimination of transition metal carbene complexes containing hydrocarbyl groups to form hydrocarbylimidazolium salts is also well documented [4]. A range of very active NHC containing catalysts have been reported in recent years [5a–i], the most prominent example being Grubbs 2nd generation olefin metathesis catalysts (**2**). Until the advent of this latter catalyst, the preparation of substituted olefins containing an electron-withdrawing functionality, such as α,β -unsaturated carbonyl compounds, through cross-

metathesis (CM) with terminal alkenes was a difficult task. These limitations were dramatically alleviated with the sterically demanding NHC containing complex **2** [6,7]. Despite these advances, many CM reactions between substituted olefins and terminal olefins require high catalyst loadings, and typically 1–5 mol.% catalyst has been employed in these reactions [7]. In these instances only 20–100 catalyst turnovers are possible, meaning the true efficiency of Ru–carbene **2** in these reactions remains uncertain.



We recently reported the addition of relatively low concentrations of phenol had a significant beneficial effect on self-metathesis (SM) reactions catalyzed by the 1st generation catalyst **1**. In addition, significant improvements in catalyst performance were observed

^{*} Corresponding author. Tel.: +44 1334 460938; fax: +44 1334 460939.

E-mail address: grant.forman@uk.sasol.com (G.S. Forman).



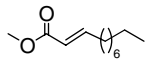


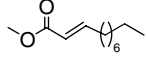


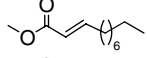


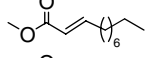
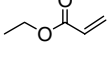

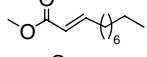


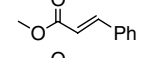


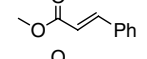


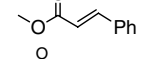

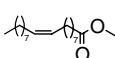
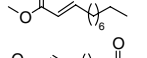


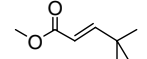


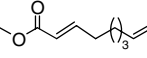
when phenol was added to CM reactions of methyl acrylate with 1-decene catalyzed by the NHC containing 2nd generation catalyst **2** [8]. Herein we report the efficiency of CM reactions between acrylate esters and terminal olefins catalyzed by **2** is increased by phenol addition, which allows reactions to be performed at lower catalyst loadings, a natural consequence of which is more economical processes.

The utility of olefin metathesis in forming new C–C bonds has now been widely demonstrated in organic synthesis [9]. In particular, CM of acrylate esters with terminal olefins is a potential alternative to traditional Wittig and Heck-type C–C bond formation reactions [6,7]. Despite this, currently CM between α -carbonyl compounds, such as acrylate esters, with terminal olefins is relatively inefficient, requiring high catalyst loadings and extended reaction times. Recently Grubbs defined an acrylate ester as a Type II olefin, because it is capable of undergoing slow homodimerization [7]. In our hands however we were unable to detect (GC, GCMS) any

homodimers of methylacrylate in metathesis reactions catalyzed by **2**. This observation coupled with the lack of reactivity of methyl fumarate and the known [6] instability of β -carbonyl-carbene species of the type $[\text{Ru}] = \text{CH}(\text{CO})\text{R}$ suggests acrylate esters are more suitably classified as Type III olefins.

In an effort to make the CM reaction of acrylate esters with terminal olefins more efficient, a series of CM reactions between acrylate esters and olefins involving catalyst **2** and *p*-cresol (4-methylphenol) were performed, and the results are shown in Table 1. In this instance *p*-cresol (500 equivalents) was used for ease of handling, but results were found to be similar when phenol was used. Most reactions were performed at 50 °C and employed 2 equivalents of acrylate as cross-partner [10]. These results indicate that addition of phenol to acrylate CM reactions catalyzed by **2** has a positive effect on end conversions. For example, with 0.025 mol.% of catalyst **2**, the CM of methyl acrylate with 1-decene was achieved in 96% conversion after only 2 h

Table 1

Entry	CM Partner Y ^a	CM Partner Z ^a	Product(s) ^b	Cat (Mol %)	Ratio (Y:Z)	% Conv ^c	E/Z Ratio	% Conv. with 500 eq cresol ^c	E/Z Ratio
1				0.10 ^d	2:1	24	13:1	100	35:1
2				0.05	2:1	56	15:1	97	26:1
3				0.025	2:1	58	13:1	96	26:1
4				0.00625	2:1	47	15:1	71	16:1
5				0.05	2:1	43	14:1	95	22:1
6				0.025	2:1	24	>50:1	66	>50:1
7				0.00625	2:1	16	>50:1	57	>50:1
8				0.025	2:1	8	>50:1	40	>50:1
9				0.0125	4:1	45	11:1 10:1	82	25:1 32:1
10				0.10	10:1	11	>50:1	18	>50:1
11				0.025	4:1	5 ^e	11:1	24 ^f	13:1

^a Unless otherwise stated, reagents were purified by distillation and/or passing through a neutral alumina column.

^b Reactions performed at 50 °C for 2 h.

^c Determined by GC/GCMS.

^d Untreated 1-decene used.

^e 29% cyclohexene formed.

^f 66% cyclohexene formed.

with added *p*-cresol (500 equiv.), whereas only 58% conversion was obtained in the absence of *p*-cresol (Entry 3). A similar effect was observed for the CM of methyl acrylate with styrene (Entries 6–8). Additionally, the efficiency of CM reactions between methyl oleate and methyl acrylate was also increased with *p*-cresol addition (Entry 9). In certain instances the combination of catalyst **2** and phenols also appear to produce greater selectivity towards the desired product. For example, for the CM reaction between methyl oleate and methyl acrylate (Entry 9), in the absence of added *p*-cresol, 45% conversion was obtained with 87% selectivity towards end products, while with added *p*-cresol, 82% conversion was obtained with 95% selectivity towards products.

In most instances the *E/Z* ratio in reactions with added *p*-cresol is often significantly higher than for reactions with only catalyst **2**. For example, with 0.025 mol.% of catalyst **2**, the CM of methyl acrylate with 1-decene produced an *E/Z* ratio of 26:1 after only 2 h with added *p*-cresol (500 equiv.), whereas an *E/Z* ratio of only 13:1 was obtained in the absence of *p*-cresol (Entry 3). In this context, these results can be rationalized in terms of faster decomposition of catalyst **2** in the absence of *p*-cresol, preventing conversion of the sterically more accessible *cis*-isomer to the *trans*-product [8]. Addition of *p*-cresol appears to impart greater catalyst lifetime, which allows for continued reprocessing of the *cis*-product to the *trans*-product.

It should be noted that the efficiency of CM reactions catalyzed by **2** using acrylonitriles, 1,1-disubstituted olefins, allyl acetate and methyl-1-penten-3-ol do not appear to be significantly enhanced by phenol addition. In this instance the positive effect of phenol appears to be specific to CM reactions involving acrylate esters. Interestingly, β -carbonyl-carbene species of the type $[\text{Ru}] = \text{CH}(\text{CO})\text{R}$ are known to be highly unstable [6], and decompose rapidly compared to alkylidene complexes of unfunctionalised olefins. On the basis of these observations, Grubbs has proposed that β -carbonyl-carbene species are not involved in cross-metathesis and are not responsible for the bulk of product formation. We have also failed to detect propagating species of the type $[\text{Ru}] = \text{CH}(\text{CO})\text{R}$ by ^1H NMR in the presence and absence of *p*-cresol. We have previously shown by NMR studies and DFT calculations that interaction of phenol with catalyst **1** is capable of altering the relative rates of phosphine loss and rebinding, activating the carbene carbon for reaction with olefinic substrate and hemilabile stabilization of the key 14-electron intermediate species. In this instance it is not possible to delineate which effect described above is contributing to the aforementioned beneficial catalyst performance, although it appears from the relative amounts of *E*- and *Z*- isomers formed from the reactions depicted in Table 1 that *p*-cresol addition is giving rise to a longer lived catalyst.

In summary, this report has shown that the activity and lifetime of CM reactions between acrylate esters and terminal olefins catalyzed by **2** can be enhanced by the simple addition of phenols such as *p*-cresol. This system gives rise to higher conversions and greater *E/Z* selectivity compared to reactions where only **2** is used, and a natural consequence of the greater catalyst efficiency described above is lower catalyst loadings and more economical metathesis processes. Studies aimed at further increasing the efficiency of Ru-carbene metathesis catalysts and applying them to industrially relevant applications are ongoing.

References

- [1] A.J. Arduengo, R.L. Harlow, M. Kline, *J. Am. Chem. Soc.* 113 (1991) 361.
- [2] (a) D. Bourissou, O. Guerret, F.P. Gabl ai, G. Bertrand, *Chem. Rev.* 100 (2000) 39;
(b) R.W. Alder, in: G. Bertrand (Ed.), *Carbene Chemistry: From Fleeting Intermediates to Powerful Reagents*, Marcel Dekker, New York, 2002, p. 153 (Chapter 5).
- [3] W.A. Herrmann, *Angew Chem., Int. Ed.* 41 (2002) 1290.
- [4] D.S. McGuinness, N. Saendig, B.F. Yates, K.J. Cavell, *J. Am. Chem. Soc.* 123 (2001) 4029, and references cited therein.
- [5] (a) T. Weskamp, W.C. Schattenmann, M. Speigler, W.A. Herrmann, *Angew Chem., Int. Ed.* 37 (1998) 2490;
(b) T. Weskamp, F.J. Kohl, W. Hieringer, D. Gleich, W.A. Herrmann, *Angew. Chem., Int. Ed.* 38 (1999) 2416;
(c) L. Ackermann, A. F urstner, T. Weskamp, F.J. Kohl, W.A. Herrmann, *Tetrahedron Lett.* 40 (1999) 4787;
(d) T. Weskamp, F.J. Kohl, W.A. Herrmann, *J. Organomet. Chem.* 582 (1999) 362;
(e) U. Frenzel, T. Weskamp, F.J. Kohl, W.C. Schattenmann, O. Nuyken, O.W.A. Herrmann, *J. Organomet. Chem.* 586 (1999) 263;
(f) M. Scholl, T.M. Trnka, J.P. Morgan, R.H. Grubbs, *Tetrahedron Lett.* 40 (1999) 2247;
(g) M. Scholl, S. Ding, C.W. Lee, R.H. Grubbs, *Org. Lett.* 1 (1999) 953;
(h) J. Huang, E.D. Stevens, S.P. Nolan, J.L. Petersen, *J. Am. Chem. Soc.* 121 (1999) 2674;
(i) L. Jafarpour, J. Huang, E.D. Stevens, S.P. Nolan, *Organometallics* 18 (1999) 3760.
- [6] A.K. Chatterjee, J.P. Morgan, M. Scholl, R.H. Grubbs, *J. Am. Chem. Soc.* 122 (2000) 3783.
- [7] A.K. Chatterjee, T.-L. Choi, D.P. Sanders, R.H. Grubbs, *J. Am. Chem. Soc.* 125 (2003) 11360.
- [8] G.S. Forman, A.E. McConnell, R.P. Tooze, W.J. van Rensburg, W.H. Meyer, M.M. Kirk, C.L. Dwyer, D.W. Serfontein, *Organometallics*. (2005) in press.
- [9] (a) M. Schuster, S. Blechart, *Angew Chem., Int. Ed.* 109 (1997) 2037;
(b) A. F urstner, *Top. Catal.* 4 (1997) 285;
(c) S.K. Armstrong, *J. Chem. Soc. Perkin Trans.* 1 (1998) 371;
(d) R.H. Grubbs, S. Chang, *Tetrahedron* 54 (1998) 4413;
(e) A.J. Phillips, A.D. Abell, *Aldrichim. Acta* 32 (1999) 75;
(f) C.L. Kingsbury, S.J. Mehrman, J.M. Takacs, *Curr. Org. Chem.* 3 (1999) 497;
(g) A. F urstner, *Angew Chem. Int. Ed.* 39 (2000) 3012;
(h) M.R. Buchmeiser, *Chem. Rev.* 100 (2000) 1565;
(i) G.R. Cook, *Curr. Org. Chem.* 4 (2000) 869;
(j) L. Yet, *Chem. Rev.* 100 (2000) 2963;

- (k) R. Roy, S.K. Das, J. Chem. Soc., Chem. Commun. (2000) 519;
- (l) M.E. Maier, Angew. Chem., Int. Ed. 39 (2000) 2073;
- (m) G.W. Coates, J. Chem. Soc., Dalton Trans. (2002) 467;
- (n) S. Mecking, A. Held, F.M. Bauers, Angew. Chem., Int. Ed. 41 (2002) 544;
- (o) S.J. Connon, S. Blechert, Angew. Chem., Int. Ed. 42 (2003) 1900;
- (p) J.C. Mol, J. Mol. Cat. A: Chem. 213 (2004) 39–45;
- (q) R.H. Grubbs, D.M. Lynn, in: Aqueous-Phase Organometallic Catalysis, 2nd ed., 2004, p. 550;
- (r) D. Astruc, New J. Chem. 29 (2005) 42.

[10] Representative procedure: A 250 mL three-necked round bottom flask was fitted with a dry-ice reflux condenser, thermometer and septum. A needle was inserted through the septum and connected

to a gas supply via a needle valve to ensure a slow and steady stream of argon through the reaction solution. Methyl acrylate (8.7 mL, 97 mmol), 1-decene (9.0 mL, 48 mmol) and *p*-cresol (2.5 g, 23 mmol) were added to the reaction vessel and the reaction was heated to 50 °C. Catalyst **2** (40 mg, 0.048 mmol) was weighed into an aluminum weighing tray and added to the reaction mixture. Samples were taken at regular intervals via syringe through the septum. Samples were analyzed by GC with a Pona column and by GCMS with an MDN column. The residue was concentrated under reduced pressure to remove excess methyl acrylate. The material obtained in this way was subjected to flash chromatography (2:1 hexane/CH₂Cl₂ elution) which afforded, after concentration of the appropriate fractions, the cross-metathesis product as a colourless oil (8.2 g, 86%).