New Reactivity from $(PCy_3)_2Cl_2Ru{=}CHPh$: A Mild Catalyst for Kharasch Additions

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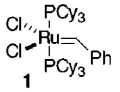
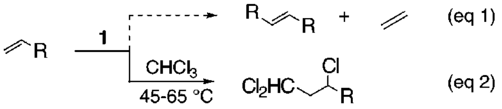
The availability of new olefin metathesis catalysts[1] has led to the emergence of several new, important methods for small molecule synthesis.[2] The widely used Grubbs' ruthenium catalyst[3] **1**, for example, has played a pivotal role in the development of synthetically useful transformations, such as ring-closing, ring-opening, and cross metatheses.[4] Within the context of these recent advancements, we wish to report some unexpected reactivity from this popular olefin metathesis catalyst (**1**).[5]

During an investigation of novel, metathesis-active ruthenium complexes,[6] we isolated a product derived not from olefin metathesis (eq 1) but from a metal-catalyzed addition of $CHCl_3$ across an alkene (eq 2). An investigation of this chemistry led to the discovery that **1** is an efficient and mild catalyst for the Kharasch addition of $CHCl_3$ across olefins.[7]



1



In contrast to AIBN- or peroxide-promoted addition of halocarbons to alkenes, transition-metal complexes have demonstrated higher chemo- and regioselectivity for similar transformations.[8] Ruthenium, in particular, has played a prominent role in Kharasch chemistry with $Cl_2Ru(PPh_3)_3$ (**2**)[9] displaying some of the highest efficiency and versatility for halocarbon activation and addition to alkenes.[10] Accordingly, we compared the reactivity of ruthenium carbene **1** with other known Kharasch addition catalysts.

The ability of complex **1** to catalyze the Kharasch addition of $CHCl_3$ across various olefins is contrasted to catalyst **2** in Table 1. While higher temperatures (>120 °C) and prolonged reaction times (>8 h) have usually been required in previously reported Kharasch additions, exposure of styrene to chloroform (10 equiv) in the presence of alkylidene **1** (2.5 mol %) for only 2 h at 65 °C resulted in a quantitative yield of addition product **4** (entry 1). The same reaction conditions with $Cl_2Ru(PPh_3)_3$ (**2**) provided <5% of **4**. Not surprisingly, 1-octene (**5**) underwent an olefin metathesis, as well as a Kharasch addition of $CHCl_3$ (entry 2). These results indicate that, in $CHCl_3$, readily metathesizable olefins, such as unhindered alkenes, are susceptible to both reaction pathways.

With this in mind, less metathesis-active substrates were subjected to conditions that facilitate Kharasch additions (5−7.5 mol % **1**, 10 equiv of $CHCl_3$, 65 °C)[11] and were compared to results obtained with catalyst **2**. In all cases, alkylidene **1** provided significantly greater reactivity than catalyst **2** (entries 1−7). For instance, as illustrated in entry 3, in the presence of catalyst **1**, $CHCl_3$ adds across methyl acrylate (**7**) in 84% yield, whereas with catalyst **2**, less than 5% of **8** is observed. As seen in entries 4−6, complex **1** catalyzes the intermolecular addition of $CHCl_3$ to 1,1-disubstituted substrates. While these additions were slower than with monosubstituted olefins, they proceeded in synthetically useful yields. To the best of our knowledge, this intermolecular addition of $CHCl_3$ to these types of olefins have not been previously reported; this is presumably due to substrate polymerization under the typically harsh reaction conditions. Entry 7 indicates that the ruthenium-catalyzed addition could not be extended to a 1,2-disubstituted substrate, even under forcing conditions.

Several experiments were performed to examine the nature of the species responsible for the Kharasch addition chemistry. Both tricyclohexylphosphine and tricyclohexylphosphine oxide were treated with styrene (10 equiv) and $CHCl_3$ (100 equiv) and heated (65 °C) under inert atmo-

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[1] (a) Couturier, J.-L.; Paillet, C.; Leconte, M.; Basset, J.-M.; Weiss, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *34*, 628−631. (b) Nugent, W. A.; Feldman, J.; Calabrese, J. C. *Tetrahedron* **1995**, *117*, 8992−8998. (c) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Reagan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875−3886. (d) Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 9858−9859.

[2] For recent reviews on the use of olefin metathesis in synthesis, see: (a) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−2056. (b) Fürstner, A. *Top. Catal.* **1997**, *4*, 285−299. (c) Armstrong, S. K. *J. Chem. Soc., Perkins Trans. 1* **1998**, 371−387. (d) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413−4450. For specific examples, see: (e) Snapper, M. L.; Tallarico, J. A.; Randall, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 1478−1479. (f) Harrity, J. P. A.; La, D. S.; Cefalo, D. R.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 2343−2351. (g) Cuny, G. D.; Cao, J.; Hauske, J. R. *Tetrahedron Lett.* **1997**, *38*, 5237−5240. (h) Schneider, M. F.; Lucas, N.; Velder, J.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 257−259. (i) Fürstner, A.; Langemann, K. *J. Am. Chem. Soc.* **1997**, *119*, 9130−9136. (j) Yang, Z.; He, Y.; Vourloumis, D.; Vallberg, H.; Nicolaou, K. C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 166−168. (k) Meng, D.; Su, D.-S.; Balog, A.; Bertinato, P.; Sorenson, E. J.; Danishefsky, S. J.; Zheng, Y.-H.; Chou, T.-C.; He, L.; Horwitz, S. *J. Am. Chem. Soc.* **1997**, *119*, 2733−2714. (l) Kim, S.-H.; Figueroa, I.; Fuchs, P. L. *Tetrahedron Lett.* **1997**, *38*, 2601−2604. (m) Winkler, J. D.; Stelmach, J. E.; Axten, J. *Tetrahedron Lett.* **1996**, *36*, 4317−4318. (n) Barret, A. G. M.; Baugh, S. P. D.; Gibson, V. C.; Giles, M. R.; Marshall, E. L.; Procopiou, P. A. *Chem. Commun.* **1997**, 155−159. (o) Crimmins, M. T.; King, B. W. *J. Org. Chem.* **1996**, *61*, 4192−4193.

[3] Fluka's 1998 "Reagent of the Year".

[4] (a) Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426−5427. (b) Martin, S. F.; Wagman, A. S. *Tetrahedron Lett.* **1995**, *36*, 1169−1170. (c) Huwe, C. M.; Blechert, S. *Tetrahedron Lett.* **1995**, *36*, 1621−1624. (d) Randall, M. L.; Tallarico, J. A.; Snapper, M. L. *J. Am. Chem. Soc.* **1995**, *117*, 9610−9611. (e) Schneider, M. F.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 411−412. (f) Crowe, W. E.; Zhang, Z. J. *J. Am. Chem. Soc.* **1993**, *115*, 10998−10999. (g) Crowe, W. E.; Goldberg, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 5162−5163. (h) Brümmer, O.; Rückert, A.; Blechert, S. *Chem.*−*Eur. J.* **1997**, *3*, 441−446. Also see ref 2.

[5] Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039−2041.

[6] Tallarico, J. A.; Bonitatebus, P. J.; Snapper, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 7157−7158.

[7] (a) Kharasch, M. S.; Jensen, E. V.; Urry, W. H. *Science* **1945**, *102*, 128. (b) Kharasch, M. S.; Jensen, E. V.; Urry, W. H. *J. Am. Chem. Soc.* **1945**, *67*, 1864−1865. (c) Kharasch, M. S.; Jensen, E. V.; Urry, W. H. *Ibid.* **1946**, *68*, 154−155. (d) Kharasch, M. S.; Jensen, E. V.; Urry, W. H. *Ibid.* **1945**, *67*, 1626. (e) Kharasch, M. S.; Jensen, E. V.; Urry, W. H. *Ibid.* **1947**, *69*, 1100−1105. (f) Kharasch, M. S.; Reinmuth, O.; Urry, W. H. *Ibid.* **1947**, *69*, 1105−1110. For reviews of transition metal-promoted radical addition reactions, see: (g) Minisci, F. *Acc. Chem. Res.* **1975**, *8*, 165−171. (h) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519−564.

[8] For copper-promoted reactions, see: Asscher, M.; Vofsi, D. *J. Chem. Soc.* **1963**, 3921−3927. For molybdenum-promoted reactions, see: Davis, R.; Groves, I. F. *J. Chem. Soc., Dalton Trans. 1* **1987**, 1515−1520. For iron-promoted reactions, see: Elzinga, J.; Hogeeven, H. *J. Org. Chem.* **1980**, *45*, 3957−3969. For palladium-promoted reactions, see: Tsuji, J.; Sato, K.; Nagashima, H. *Chem. Lett.* **1981**, 1169−1170.

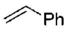
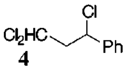
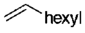
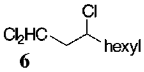
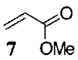
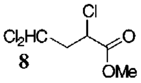
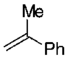
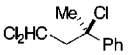
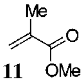
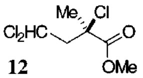
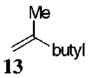
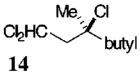
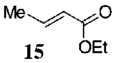
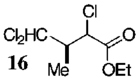
[9] For an early example of an intermolecular Kharasch addition catalyzed by Ru, see: Matsumoto, H.; Nakano, T.; Nagai, Y. *Tetrahedron Lett.* **1973**, *51*, 5147−5150.

[10] (a) Lee, G. M.; Parvez, M.; Weinreb, S. M. *Tetrahedron* **1988**, *44*, 4671−4678. (b) Grigg, R.; Devlin, J.; Ramasubbu, A.; Scott, R. M.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1515−1520. (c) Lee, G. M.; Weinreb, S. M. *J. Org. Chem.* **1990**, *55*, 1281−1285 and references therein.

[11] The use of as little as 3 equiv of chloroform results in similar reactivity with slightly lower yields.

10.1021/jo982349z CCC: $18.00

Table 1. Kharasch Additions with Complexes 1 and 2

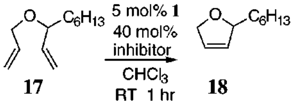
entry	substrate	product	catalyst	yield	time
(1)	 **3**	 **4**	**1** **2**	100% <5%	2 h[b]
(2)	 **5**	 **6**	**1** **2**	25%[e] 0%	2 h[b]
(3)	 **7**	 **8**	**1** **2**	84% <5%	4 h[d]
(4)	 **9**	 **10**	**1** **2**	85% 0%	12 h[c]
(5)	 **11**	 **12**	**1** **2**	90% 0%	12 h[c]
(6)	 **13**	 **14**	**1** **2**	63% 0%	12 h[c]
(7)	 **15**	 **16**	**1** **2**	<10% 0%	24 h[c]

[a] Catalyst **1** = $Cl_2Ru(PCy_3)_2CHPh$; catalyst **2** = $Cl_2Ru(PPh_3)_3$. [b] 2.5 mol % of catalyst. [c] 7.5 mol % of catalyst. [d] 5.0 mol % of catalyst. [e] Plus mainly 7-tetradecene.

sphere (Ar). These conditions resulted only in recovered starting material, indicating that the phosphine alone is not responsible for the observed reactivity. In fact, excess phosphine has an inhibitory affect on the Kharasch reactivity of **1**. The addition of 10 mol % of PCy_3 with 5.0 mol % of **1** leads to <5% of **4**, even after 18 h of heating (65 °C).[12] This finding suggests that, like olefin metathesis, catalyst activation through phosphine dissociation may play a role in the Kharasch chemistry.[13] Catalyst **1** was also subjected to typical reaction conditions with styrene as substrate under an O_2 atmosphere, and as before, no Kharasch addition products (i.e., <2%) were observed. These data imply that oxidative modification of ruthenium does not facilitate the addition chemistry.

Experiments to probe further the catalytic role of ruthenium were also conducted. For example, one possibility is that a minor impurity in complex **1** affects the observed reactivity. Along these lines, intermediates in the synthesis of alkylidene **1** were tested for Kharasch activity. Complexes $(Ph_3P)_2Cl_2RuCHPh$ and $Cl_2Ru(PPh_3)_3$ (**2**) with and without additional trialkylphosphines showed little activity (<5% conversion).

Detailed studies of ruthenium complex **2** suggest that halocarbon addition occurs through a radical-based pathway within the coordination sphere of the metal.[14] If this mechanism holds true for carbene **1**, radical scavengers should selectively influence intermediates in the catalytic cycle of the Kharasch addition. Along these lines, the addition of either 2,6-di-*tert*-butyl-4-methylphenol (BHT) or galvinoxyl to alkylidene **1** were found to severely limit the formation of the expected Kharasch product (**3** → **4**) without significantly affecting metathesis activity (**17** → **18**, eq 3).[15] Whereas the specific structures and events in the catalytic cycle are unclear for complex **1**, these results support the ruthenium-mediated, radical nature of the reaction.



17 **18**

% yield of **18**	
no inhibitor	82%
BHT	79%
galvinoxyl	68%

(eq 3)

In light of these observations and with the interest of developing new synthetic opportunities for metatheses, this divergence in reactivity is noteworthy. Numerous examples of the RCM of macrocycles and trisubstituted olefins, as well as the ROMP of sterically demanding or low-strain monomers, have appeared recently in the literature,[16] very often requiring more forceful reaction conditions. It is of importance to note that with alkylidene **1** the higher temperatures and the use of chlorinated hydrocarbon solvents, such as chloroform, could lead to anomalous metathesis results from competing Kharasch chemistry.

In summary, Grubbs' ruthenium benzylidene complex **1** catalyzes the chemo- and regioselective addition of chloroform across mono- and 1,1-disubstituted olefins. In comparison to previously described ruthenium-based Kharasch catalysts, the mild conditions under which complex **1** affects the addition of $CHCl_3$ are particularly noteworthy. The factors defining this reactivity and applications to other known Kharasch-type reactions are currently under investigation.

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Supporting Information Available: Experimental details for the syntheses and characterizations of compounds **6**−**14** (9 pages).

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(12) The reaction was complete within 2 h in the absence of excess phosphine.

(13) (a) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887−3897. (b) Aagaard, O. M.; Meier, R. J.; Buda, F. *J. Am. Chem. Soc.* **1998**, *120*, 7174−7182.

(14) (a) Bland, W. J.; Davis, R.; Durrant, J. L. A. *J. Organomet. Chem.* **1985**, *280*, 397−406. (b) Matsumoto, H.; Nikaido, T.; Nagai, Y. *Tetrahedron Lett.* **1975**, *11*, 899−902. (c) Matsumoto, H.; Nikaido, T.; Nagai, Y. *J. Org. Chem.* **1978**, *43*, 1734−1736. Also see ref 10.

(15) Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J Am. Chem. Soc.* **1993**, *115*, 9856−9857.

(16) (a) Miller, S. J.; Blackwell, H. E.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 9606−9614. (b) Maier, M. E.; Langenbacher, D.; Rebien, F. *Liebigs Ann.* **1995**, 1843−1848. (c) Lynn, D. M.; Kanaoka, S.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 784−790.