Comparing *Grubbs*-, *Werner*-, and *Hofmann*-Type (Carbene)ruthenium Complexes: The Key Role of Pre-Equilibria for Olefin Metathesis

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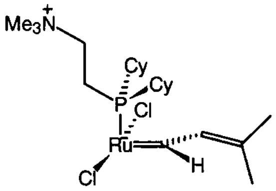
A gas-phase comparison of intrinsic olefin metathesis rates for (carbene)ruthenium complexes by means of electrospray-ionization tandem mass spectrometry reveals a reversal of the reactivity trends observed in solution. The solution-phase ordering of reactivity is accordingly attributed to a more favorable pre-equilibrium, producing the metathesis-active species in the case of the *Hofmann*- and *Werner*-type complexes relative to those of the *Grubbs* type.

Introduction. – Since the initial observation of homogeneous olefin metathesis catalyzed by organometallic complexes [1], there have been a wide range of mechanistic studies aimed at elucidating the structural factors controlling reactivity and selectivity in this novel reaction [2]. Particular attention in recent years had been paid to (carbene)ruthenium complexes because of their tolerance of polar functionality, wide substrate acceptance, and availability as well-defined complexes [3–8]. Moreover, their ease-of-use in applications has led to the widespread adoption of (carbene)-ruthenium complexes in organic synthesis and polymer chemistry [9]. Recent work of *Hofmann* and co-workers involves a variation on the basic structure – cationic (carbene)ruthenium complex with *cis*-phosphines – that exhibit much higher ring-opening metathesis polymerization (ROMP) reactivity in solution than had been reported for any other Ru system [6]. The mechanistic origins of the enhanced reactivity, on the other hand, remain to be unraveled. A well-grounded explanation would be, without doubt, crucial to any attempt to design more active catalysts *de novo*. We report a gas-phase comparison of a series of complexes representing the activated forms of the *Grubbs* and *Hofmann* (carbenes)ruthenium complexes in which the intrinsic metathesis activity can be determined. The systematic comparison shows that the higher reactivity of the *Hofmann* complexes in solution derives from a more favorable pre-equilibrium – the activation step – in the *Hofmann* systems, rather than from higher intrinsic reactivity in the metathesis step.

Experimental. – The instrument and general techniques have been previously described [10][11]. The preparation of $[(RCy_2P)(Cl)_2Ru{=}CH{-}CH{=}CMe_2]^+$ (**1**, Cy = cyclohexyl, R = 2-(trimethylammonium)ethyl) in the gas phase was achieved as reported previously by *Chen* and co-workers [10] for the analogous benzylidene complex. Complex **2**, $[(Cy_3P)_2(Cl)Ru{=}CH{-}CH{=}CMe_2]^+$ (or its carbyne hydride isomer, *vide infra*), was prepared by electrospraying a 10^{-5} M solution of $[(Cy_3P)_2(Cl)_2Ru{=}CH{-}CH{=}CMe_2]$ in CH_2Cl_2, in which a small extent of heterolysis is sufficent to produce the ions needed for electrospray. The cationic *Hofmann* carbene complex **3**, $\{[(t\text{-}Bu)_2P(CH_2)P(t\text{-}Bu)_2](Cl)Ru{=}CH{-}CH{=}CMe_2)\}^+$, was prepared by electrospray in CH_2Cl_2 of the corresponding dimeric dicationic triflate salt, synthesized as previously reported [6], under conditions comparable to those for **2**. The isotopic pattern in the mass spectrum under high resolution confirmed that the species produced in the electrospray was the monomeric cation rather than the dimeric dication with the same *m*/*z* ratio.



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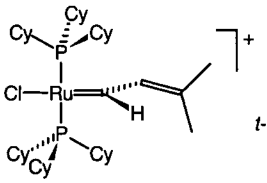

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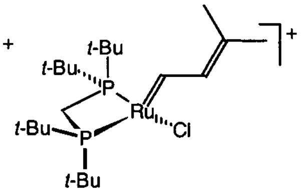

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The reactivity of complexes **1**–**3** was probed by the reaction of the mass-selected cationic complexes with but-1-ene in the second octopole of the modified *Finnigan-MAT TSQ-7000* tandem mass spectrometer. The relative reactivities were determined by the extent of reaction, measured by integrated peak intensities for reactant and product ions, at a standard collision energy (nominally 1.0 eV in the laboratory frame) and standardized pressure of but-1-ene (*ca.* 14 mTorr, uncorrected reading on a *Pirani* gauge). Each reported reaction efficiency is the average of 10 independent measurements for which 95% confidence limits were computed by means of a *t*-distribution.

Results and Discussion. – The efficiencies of the gas-phase olefin-metathesis reactions of complexes **1**–**3** are shown in the *Table*. In each case, the metathesis reaction, if observed, was clean, giving the corresponding (propylidene)ruthenium complex. In some cases, adduct ions, corresponding to the olefin π-complex, were also observed in small amounts. The efficiencies, which, under the standardized conditions, are a measure of relative reaction rate are expressed as the fraction of reactant ions converted to the product. While the absolute efficiency is instrument-dependent, the relative efficiencies are meaningful as a measure of the rate. Moreover, measurements with norbornene instead of but-1-ene gave parallel trends; the but-1-ene data are given because, for acyclic metathesis, the π-complex and the metathesis product can be unambiguously distinguished by mass alone. The trends with a range of various structural alterations have been observed and will be discussed in a more extensive report.

Table. *Reaction Efficiencies and Relative Metathesis Rates for the Carbene Complexes* **1**–**3** *with But-1-ene in the Gas Phase*

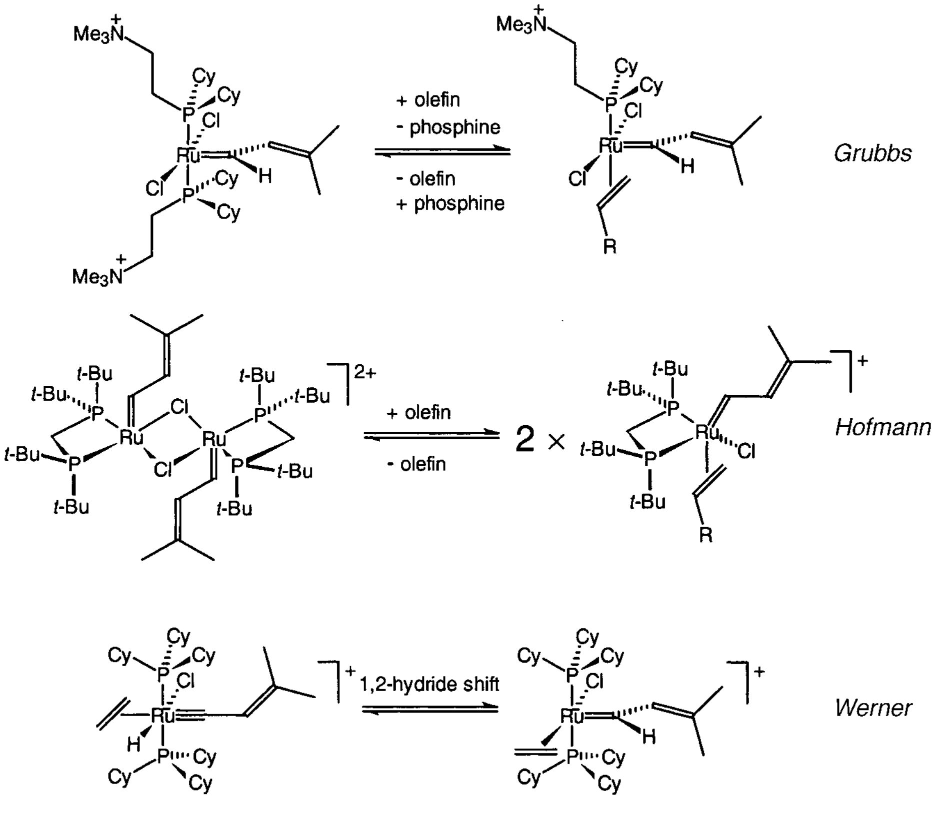
Complex	But-1-ene [mTorr]	π-Complex	Metathesis product	Rel. rate
1	13.4 ± 0.1	$(7.4 \pm 2.5) \times 10^{-5}$	$(1.88 \pm 0.02) \times 10^{-1}$	41
2	13.6 ± 0.3	$(1.0 \pm 0.1) \times 10^{-5}$	$(0.00 \pm 0.01) \times 10^{-4}$	0.0
3	14.0 ± 0.1	$(8.5 \pm 1.0) \times 10^{-5}$	$(4.59 \pm 0.09) \times 10^{-3}$	1.0

The solution-phase reactivity of complexes that form **1**–**3** as active species has been evaluated by ROMP of cycloalkenes. Because the *Grubbs* system [4] was the first and best characterized, it has served as the benchmark for comparisons by the others. The *Hofmann* carbenes, formed in solution by dissociation of the dicationic dimers [6], catalyze the ROMP of cyclooctene at least by two orders of magnitude faster under standardized conditions than $[(Cy_3P)_2(Cl)_2Ru{=}CHPh]$, the benchmark *Grubbs* system, and even the second-generation *Grubbs* catalysts [12]. Similarly, the cationic

Ru complex from *Werner* [7], which presumably rearranges to a carbene complex *in situ*, is reported to catalyze ROMP of cyclooctene twenty-times faster than the benchmark *Grubbs* system. However, the mechanistic origin of the improved solution-phase reactivity of both the *Hofmann* and *Werner* systems could not be unambiguously assigned to any single effect, electronic or steric, based on the solution-phase experiments and quantum-chemical calculations [10][13] alone.

From the reaction efficiencies, it is immediately evident that the gas-phase reactivity of **1** is more than forty-times higher than that of **3**. With the assumption that these gas-phase reactivities are mirrored in solution, the difference in ordering between gas-phase and solution can only be explained by a more favorable pre-equilibrium in the case of **3**, when the reaction occurs in solution (*Scheme*). In the *Hofmann* system, catalytically active species **3** are formed from dinuclear precursors, which undergo more-facile dissociation and less-facile reassociation due to their cationic nature than related neutral bimetallic congeners [13].

Scheme



The olefin complexes of the active species are formed in solution from reservoir species in a reversible step preceding the actual metathesis, which kinetically manifests itself as a depression of the observed rate by the equilibrium constant for the reversible reaction, be it ligand exchange or some other kinetic process. The present analysis does not allow a judgment as to whether ligand exchange is associative or dissociative. It should be noted that, for the *Grubbs* carbenes, there has been no direct observation of the metathesis-active species in solution, although indirect evidence from kinetics [4] or trapping [14][15] has established the presence and importance of a (carbene)(monophosphine)ruthenium complex that is formed *in situ*¹). For the *Hofmann* carbenes, a cationic monomeric (carbene)ruthenium has been isolated and fully characterized as the MeCN adduct [16], consistent with our suggestion that the pre-equilibrium is, in general, favorable for this class of carbene complex. The present gas-phase study, by concentrating on the metathesis-active species, separates the effects of the pre-equilibrium from those due to electronic and/or steric influences in the active complexes themselves. The dramatic reversal of order in the reactivity going from solution to the gas phase is a clear indication that the pre-equilibrium plays a decisive role in the solution-phase rates.

In light of the comparison of **1** and **3**, the comparison of **1** and the cation formed by chloride dissociation from $[(Cy_3P)_2(Cl)_2Ru{=}CH{-}CH{=}CMe_2]$, depicted as **2**, is also very informative. *Werner* isolates, in the solid state, a (carbyne)(hydrido)ruthenium complex [7] $[(solv)(Cy_3P)_2(H)(Cl)Ru{\equiv}CMe]^+\ BF_4^-$ (solv = solvent molecule), which is then used in solution as a ROMP catalyst. While a carbene complex could not be observed by ^{1}H-NMR in solution – only the carbyne is seen – the metathesis reaction presumably proceeds through the intermediacy of a carbene complex formed by an intramolecular 1,2-hydride shift in the carbyne complex. In our experiment, **2** shows no measurable gas-phase metathesis reactivity at all, which would be consistent with the present discussion if one postulates that the ion produced in the gas-phase experiment has the *Werner*-type carbyne rather than carbene structure **2**, and that the necessary 1,2-hydride shift (*Scheme*), while possible, is thermodynamically unfavorable in both gas and condensed phase²). For **1** and **3**, by gas-phase experiments, the intrinsic metathesis rates are measured; **2** differs from the other two species in that the unfavorable pre-equilibrium is present in both the gas-phase and solution-phase reactions. Accordingly, the ion **2**, assumed to be carbyne-hydride isomer, should show a much reduced apparent reactivity in the gas phase, which pushes the reaction efficiency below the level that can be reliably measured in this particular experiment. An important effect of the constrained *cis*-orientation of the phosphines in the *Hofmann* carbene series is the tilting of the carbyne/carbene equilibrium in favor of the carbene [16]. Given that the previous work by the *Chen* group showed that electronic effects on the metathesis step itself, while amenable to a *Hammett*-type linear-free-energy analysis, were nevertheless relatively modest, *i.e.*, $\rho \approx 0.7$, one can surmise that the greatest opportunity for further activity improvement within the (carbene)ruthenium system is to work on the pre-equilibria.

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¹) Interestingly, *Grubbs* has reported (IV. International Symposium, SFB 347, Universität Würzburg, September 20–22, 2000) that high phosphine dissociation rates (as measured in solution by NMR) correlate with low catalyst activities and *vice versa*. These studies indicate that slow phosphine reassociation, competing with olefin capture, causes enhanced catalyst activity.

²) For **2**, *m*/*z* as measured by MS experiments, of course, does not unambiguously prove the hydride carbyne structure. Other species lacking metathesis activity cannot be rigorously excluded.

Conclusion. – Direct comparison of the activated forms of the *Grubbs* and *Hofmann* (carbene)ruthenium metathesis catalysts has established that the intrinsic gas-phase reactivity of the *Grubbs* catalysts is much higher than that for the *Hofmann* complexes. This situation is reversed in solution by a much more favorable pre-equilibrium for the latter. Similarly, the complexes of *Werner*, which show a high activity in solution, are slow to react in the gas phase because an unfavorable pre-equilibrium is still present in the gas phase for that complex. Optimization of solution-phase metathesis rates should, therefore, focus on improvement in the step that actually precedes the metathesis itself, because, as this study shows, these effects can span orders of magnitude and are primarily responsible for the extraordinarily high solution-phase ROMP rates in the *Hofmann* systems.

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