Attractive Noncovalent Interactions in the Mechanism of Grubbs Second-Generation Ru Catalysts for Olefin Metathesis
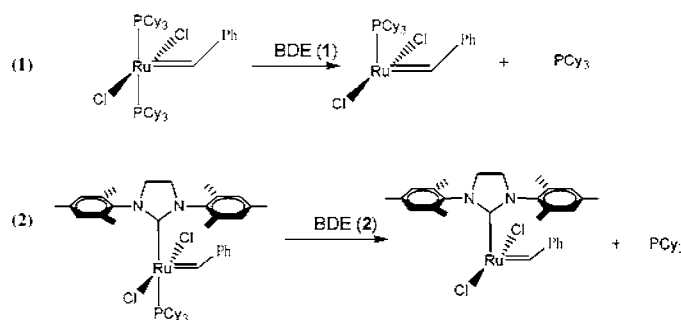
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ABSTRACT

Second-generation ruthenium carbenoid catalysts for olefin metathesis are a hundred to a thousand times more active than first-generation catalysts, despite a slower initiation step. A new density functional capable of treating medium-range correlation energy shows that the relative rates of generation of the catalyst are determined by attractive noncovalent interactions.

Grubbs' second-generation Ru metathesis catalysts[1–5] are a hundred to a thousand times more active than first-generation Ru metathesis catalysts, and they also exhibit greater thermal and chemical stability.[1–3] The catalysts are illustrated in Figure 1. The difference is the substitution of one of the phosphine ligands, usually tricyclohexylphospine, PCy_3, of the bisphosphine first-generation precatalyst by a *N*-heterocyclic carbene (NHC), usually 1,3-dimesityl-4,5-dihydro-2-ylidene, henceforth denoted H_2IMes. Liquid-phase mechanistic studies established that olefin metathesis with these 16-electron (five-coordinate) Ru precatalysts proceeds by phosphine dissociation to generate the 14-electron (four-coordinate) active species. A surprising discovery[6,7] (later confirmed in the gas phase[8]) was that phosphine dissociation in $(PCy_3)_2Cl_2Ru{=}CHPh$ (**1**) is faster than that in (H_2IMes)-
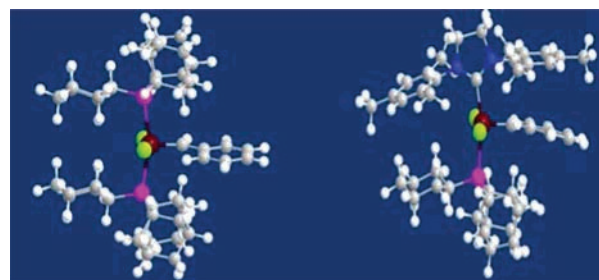

Figure 1. First-generation (left) and second-generation (right) Grubbs catalysts for olefin metathesis.

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(PCy$_3$)Cl$_2$Ru=CHPh (**2**), so that the rate of generation of active species does not correlate with catalytic activity. The effect on initiation of changing the solvent from toluene to CH$_2$Cl$_2$ was the same for **1** and **2**, so the substituent effect does not depend on solvent. Since the reverse association reaction is believed to be barrierless,[9] the relative dissociation rates are attributed to a smaller Ru−P bond dissociation energy (BDE) in **1** than in **2** (Scheme 1). Understanding the

Scheme 1. First Step: Generation of the Catalyst from the Precatalysts
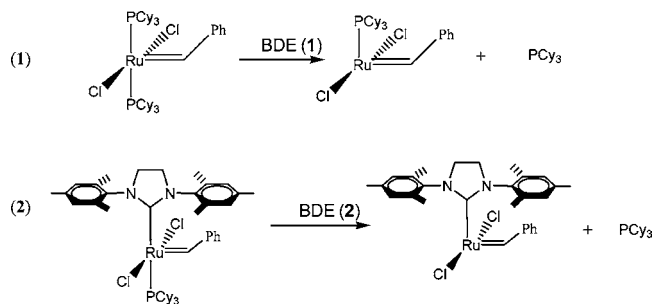
factors that control catalyst initiation is critical to rational ligand-design strategies for new catalysts.[10,11]

Theoretical analysis of these systems requires the inclusion of dynamic electron correlation for a reliable description of bond breaking and noncovalent interactions. This makes reliable wave function theory prohibitively expensive. Even applications of the more affordable density functional theory (DFT) have usually involved truncated ligands, which makes it impossible to assess the stereoelectronic effects reliably. However, a few calculations involve untruncated DFT calculations of the full 16-electron complexes.[9,12−14] DFT, however, is only as reliable as the functional that is employed, and functionals used in previous work on transition metal catalysts suffer from well-known deficiencies. Especially serious among these for the present application are difficulties in validation,[15] imperfect treatment of dynamic correlation effects on noncovalent interactions,[15,16] sometimes large errors for metal−ligand bond energies (especially for the functionals that are most accurate for organic thermochemistry),[15,17,18] and an unbalanced treatment of sterically branched hydrocarbon fragments.[15,19−23]

Apparently as a result of inaccurate functionals, the DFT calculations are unable to account for the difference between the bond dissociation energies of **1** and **2**, ΔBDE $\equiv$ BDE-(**1**) − BDE(**2**). The experimental work is discussed elsewhere[6,7,9] and leads to a best estimate of the difference of bond dissociation energies of −3.4 kcal/mol, but the four most complete previous DFT values are +1.4, +2.3, +1.8, and +1.9 kcal/mol.[9,24] An insightful attempt to correct for the imperfect treatment of attractive noncovalent interactions by molecular mechanics increased the bond strengths by ~13 kcal/mol, but only changed ΔBDE to +2.2 kcal/mol, which does not resolve the cause of the discrepancy.[9] A recent review[15] suggests that "similar effects occur more broadly when studying large transition metal complexes", and that the absence of dispersion-like interactions in DFT can account for large errors in bond energies.[15] Our understanding of organometallic catalysts requires identifying the physical elements that must be included in a predictively reliable theory.

Recently[25] a new density functional called M06-L has been developed that includes a more reliable treatment of medium-range correlation energy. This was accomplished by designing new functional forms for the exchange and correlation functionals that reduce unphysical self-correlation[15] errors and that are optimized for a diverse data set including barrier heights and noncovalent interactions, both of which are sensitive to medium-range correlation energy. The M06-L functional was especially recommended for applications to organometallics because it largely overcomes the difficulty mentioned above that the functionals that are best for organic chemistry are often very inaccurate for transition metal bond energies.[25−27] The M06-L functional has been shown to be reasonably accurate for attractive noncovalent interactions at distances where the densities of the two fragments overlap appreciably, even though it does not include the correct long-range dipole−dipole limit of dispersion forces in the non-overlapping region.[25]

We have now applied the M06-L density functional and the popular B3LYP,[29−32] BP86,[29,33] and PW91[34] functionals along with two more recent (but older than M06-L) high-

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quality functionals, PBEh[35,36] and TPSSh,[37,38] to the Ru benzylidene compounds **1** and **2** employing a double-ζ-quality (DZQ) basis set[17,39] and a triple-ζ-quality (TZQ) basis set[17,39] explained elsewhere. In some cases we also included a counterpoise correction[28] (CP) for basis set superposition error. The results are listed in Table 1.

Table 1. Bond Dissociation Energies (kcal/mol) for the Grubbs Catalysts

method[a]	BDE(**1**)	BDE(**2**)	ΔBDE
exptl			-3.4 ± 2[b]
M06-L/TZQ	36.1	40.2	-4.1
M06-L/TZQ-CP[c]	34.2	38.2	-4.0
M06-L/DZQ	41.7	45.2	-3.5
M06-L/DZQ-CP[c]	38.3	41.7	-3.4
B3LYP/DZQ	19.0	17.4	1.6
B3LYP/DZQ-CP[c]	15.6	14.0	1.7
BP86/DZQ	20.0	18.8	1.2
PW91/DZQ	26.1	25.7	0.4
PBEh/DZQ	28.9	28.1	0.8
TPSSh/DZQ	24.6	23.5	1.1
remove RuCl$_2$[d]			
M06-L/DZQ	9.9	14.4	-4.5
B3LYP/DZQ	-4.5	-8.0	3.5

[a] See the Supporting Information for the geometries. [b] As inferred from experiment,[6,7,9] but see text for comments on the difference between the experiment (finite temperature, condensed-phase enthalpy of activation) and the calculation (equilibrium bond dissociation energy). [c] These results are corrected for the basis set superposition error by the counterpoise[28] approach. [d] We removed the Ru^{2+} cation and the two Cl$^-$ anions from the complexes, without reoptimizing the geometries of either the original complexes or their dissociation products

At the M06-L/TZQ-CP level of theory, we obtain ΔBDE $= -4.0$ kcal/mol, in good agreement with experiment. This shows the importance of medium-range correlation energy for the description of large transition metal complexes. Table 1 shows that M06-L gives larger BDEs for both **1** and **2** with the DZQ basis set than the TZQ basis set, but the CP correction brings the results closer. Furthermore, all four M06-L calculations, with and without the CP correction, give very similar values for ΔBDE, in the range -3.4 to -4.1 kcal/mol, and the negative sign is the right trend. The BP86, PW91, PBE0, and TPSSh functionals are better than the most popular functional, B3LYP, but they share the same flaw as B3LYP for the prediction of the ΔBDE trend.

Although the goal of this work is to provide insight into the factors responsible for the previously unexplained trend in the rate of the first step in the catalytic mechanism, it is also interesting to look at the magnitude of the BDEs. With our better basis set and CP corrections these are 11 ± 2 kcal/

mol larger than the enthalpy of activation inferred[7] from experiment in toluene. It has previously been estimated[12] that the gas-phase electronic values would be lowered 2 kcal/mol by solvent effects and $3-4$ kcal/mol by vibrational effects. The remaining deviation of 6 ± 3 kcal/mol is not unreasonably large for simulating such a complex system. Solvent effects are expected to be more important for the absolute bond dissociation enthalpies than for their difference, and in several similar systems they have been estimated to be even larger, even as large as 13 kcal/mol,[12] which would more than account for the remaining discrepancy. An accurate treatment of solvent effects must account for the competition between cavitation, dispersion, and electrostatic effects[40] and would be an interesting subject for future study.

For the binding of the 14-electron active catalyst to an ethylene molecule, M06-L/DZQ gives a binding energy of 18.8 kcal/mol for the second-generation catalyst, which is 5.1 kcal/mol stronger than that for the first-generation catalyst. These results are consistent with the interpretation of Sanford et al.[6,7] that the second generation catalysts are more catalytically efficient, despite dissociating phospine relatively inefficiently, because coordination of olefin to the 14-electron species is more facile in the NHC complexes than in the bis-phosphine ones. More complete mechanistic studies[13,41] have identified other important features in the full catalytic cycle.

The success of the M06-L density functional in explaining the difference between first- and second-generation Grubbs catalysts allows us to use it to obtain insight into the origin of the substituent effect on bond energy and hence on the kinetics of the key step by which catalyst is generated from precatalyst. In particular we can assess the role of non-covalent interactions. To do this we removed the Ru^{2+} cation and the two Cl$^-$ anions from the complexes, without reoptimizing the geometries of either the original complexes or their dissociation products. The change in energy upon dissociation of the remaining moieties may now be fairly ascribed to noncovalent interactions. With the M06-L functional, we obtain dissociation energies of 14.4 and 9.9 kcal/mol, respectively, for the demetalized **1** and **2**, with a difference of -4.5 kcal/mol. This explains the sign of the ΔBDE value of the original complexes. The positive BDEs, even in the absence of Ru, show that the noncovalent interactions between the large ligands are attractive. However, the B3LYP functional gives a negative BDE and the wrong ΔBDE trend for demetalized **1** and **2**. This is consistent with results for test suites[17,25,42,43] on which we have found that M06-L is more accurate than the other functionals considered above for both noncovalent interaction energies and metal–ligand bond energies.

We conclude that noncovalent attractive interactions between the large ligands in the precatalysts play a decisive role in the effect of ligand variation on the mechanism and activity of ruthenium-based olefin metathesis. The roles of

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covalent and dative electronic effects (electron-donating effects) and noncovalent repulsive interactions (steric effects)[11,13,41,44−59] have been widely discussed, but the noncovalent attractive interactions have been ignored (except for the insightful, pioneering work of Tsipis et al.,[9] mentioned above, that does not agree with experiment because the densiy functionals used in that study are inaccurate for medium-range correlation energy). The ability of new density functionals to analyze and accurately model such attractive interactions due to medium-range correlation energy opens new possibilities for computer-aided catalyst design.

Supporting Information Available: Computational details and Cartesian coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

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