Communication

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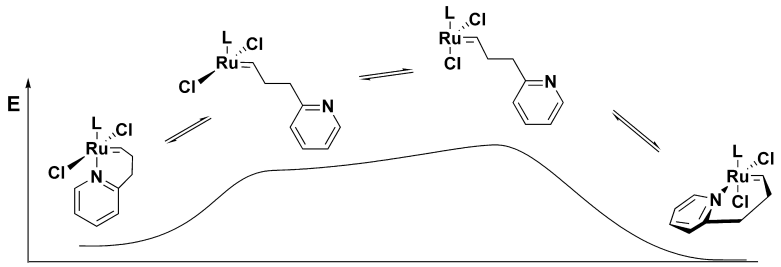
J. Am. Chem. Soc., **2005**, 127 (35), 12218-12219• DOI: 10.1021/ja051796a • Publication Date (Web): 16 August 2005



Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

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The Isomerization Equilibrium between Cis and Trans Chloride Ruthenium Olefin Metathesis Catalysts from Quantum Mechanics Calculations

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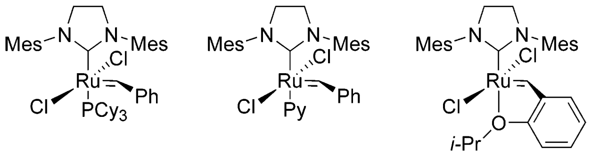
Olefin metathesis has become a powerful synthetic tool for carbon−carbon bond-forming transformations, important to fields of synthetic chemistry spanning from natural products to commercial polymeric materials.[1] Since the discovery of functional group tolerant and highly active catalysts by Grubbs (**1**),[2] the design of new systems has focused on optimizing products for specific applications.[3] These catalytic systems generally initiate by loss of a neutral ligand, usually trans to the N-heterocyclic carbene.[4] Recently, this initiation step has been improved by replacing strongly coordinating phosphines with weakly bound oxygen- or nitrogen-containing ligands.[5] These ruthenium catalysts bearing more labile groups have had great success as fast-initiating versions (**2** and **3**) of the widely used second generation Grubbs catalysts.[6] On the other hand, slow-initiating systems are useful particularly in ring-opening metathesis polymerization (ROMP) resin formulations where the gel-times need to be sufficiently long to allow for handling or molding (Figure 1).



1 **2** **3**

Figure 1.

Grubbs and Schrodi recently reported the synthesis of **4** as a slow initiating highly active ROMP catalyst.[7] Furthermore, they found that it undergoes a conformation change into **5,** which is even a slower initiating catalyst. Interestingly, mixtures of these two isomers provide intermediate initiation latencies.

Computational modeling studies on the nature of the mechanism of olefin metathesis[8] have concluded that the chloride ligands remain in the trans geometry throughout the catalytic cycle. In contrast, Grubbs and co-workers found that in enantioselective metathesis experiments, the major product is inconsistent with expectations from a trans chloride intermediate.[9] They proposed that a *cis*-chlororuthenium intermediate must be present in the mechanism of enantioselective ring-closing metathesis and deduced its geometry on the basis of the observed major products.

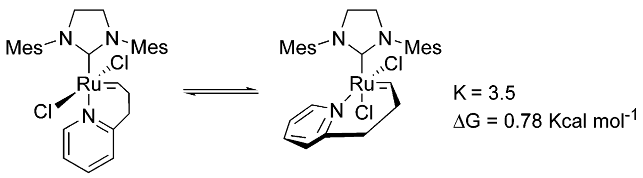
To understand these phenomena and the apparent disagreement between theory and experiment, we carried out extensive QM studies to establish the structures and thermodynamics of the equilibrium between **4** and **5**.

All calculations were performed using density functional theory (DFT) with the B3LYP hybrid functional [as implemented in Jaguar 5.5 (release 11)].[10] B3LYP utilizes both exact Hartree−Fock (HF) exchange and nonlocal corrections (generalized gradient approximation) to the Slater local exchange functional. We used the Becke three-parameter functional (B3) with the Becke nonlocal gradient correction,[11] the Vosko−Wilk−Nusair exchange functional,[12] and the local and nonlocal correlation functional of Lee, Yang, and Parr (LYP).[13] This flavor of density functional theory produces good descriptions of reaction profiles for transition metal-containing compounds.[14] The 1s−3d core electrons of the ruthenium atom were described with the Hay and Wadt core-valence relativistic effective-core-potential (ECP) leaving the outer 16 electrons (4s, 4p, 4d, 5s, etc.) to be treated explicitly (denoted as LACVP in Jaguar).[15] All electrons were considered for all other atoms with the 6-31G** basis set.[16] To determine whether use of this modest basis set might affect the results, we also carried out calculations with the same geometries, but used the 6311G**++ basis.

Every structure was optimized both for gas phase and for solvent [using the Poisson−Boltzmann (PBF) continuum approximation].[17] For each optimized structure, we calculated the analytic Hessian to obtain the vibrational frequencies, which in turn were used to obtain the zero-point energies and free energy corrections to 313 K. The free energies at 0 K are quoted here, but the 313 K results are in the Supporting Information. For the stable compounds we started with X-ray crystallographic structures,[7] while reaction intermediates were obtained by modifying fully converged structures.

The minimized structures match the crystallographic data accurately, with bond distances within 0.05 Å and bond angles within 4° (structural details in the Supporting Information). The largest variations are observed for the pyridyl and chloride ligands. Some differences may be due to packing effects in the crystal. We conclude that B3LYP provides a good description of the molecular structures of these systems. We find that in the gas phase, the cis geometry (**5**) is 6.8 kcal less favorable than the trans analogue (**4**). However, when the solvation correction is included with methylene chloride as a model solvent ($\epsilon = 9.1$, solvent radius = 2.34 Å), we find that the cis chloride structure (**5**) is favored by 0.7 kcal (Scheme 1). Therefore, the calculations suggest that the product ratio of **5**:**4** should be 76:24. This result is extremely close to the experimental value of 78:22 suggesting that cis is more stable by 0.78 kcal. Concerned with the solvent dependence of the relative stability of both isomers, we calculated the energy difference in benzene as a model solvent ($\epsilon = 2.3$, solvent radius = 2.60 Å) and found that in this media, the trans chloride isomer is more stable by 2.0 kcal, leading to 96% of **4**. This is consistent with experiment,

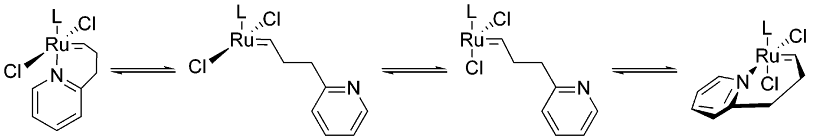
Scheme 1. Isomerization Equilibrium Observed Experimentally in Dichloromethane at 40 °C



4 **5**

10.1021/ja051796a CCC: $30.25 © 2005 American Chemical Society

Scheme 2. Proposed Isomerization Mechanism with Relative Free Energies (kcal mol^{-1}) Calculated at 0 K; Two Basis Sets Were Used[a]



		4	**4_d**	**5_d**	**5**
Gas phase	631G**	0	14.95	23.03	6.78
	6311G**++	0	14.64	22.07	8.17
Solvent phase	631G**	0	13.55	18.83	-1.12
	6311G**++	0	11.67	17.62	-0.70

[a] Solvent phase energies were determined using methylene chloride as model solvent ($\epsilon = 9.1$, solvent radius = 2.34 Å).

since **5** is not observed when benzene is used as a solvent.[18] Furthermore, we predict that a higher ratio of cis product can be obtained if the isomerization reaction is performed in a more polar solvent than methylene chloride.[19]

This strong dependence on solvent polarity results from the enormous difference in the dipole moment from the wave functions of the complexes: 1.5 D for **4** and 12.4 D for **5**. This difference arises from the polarity in Ru−Cl bonds, which cancel in the trans geometry. This marked difference in polarity translates to very different solvation energies (calculated as 14.8 and 22.7 kcal for **4** and **5** respectively in methylene chloride as model solvent), which increases the relative stability of the cis chloride structure (**5**).

It has been shown[4,8] that the metathesis initiation rate is determined by the barrier leading to the formation of the active 14-electron complex. Therefore, to investigate the difference in experimental metathesis initiation rates,[7] we calculated the dissociation energy of the pyridyl ligand from both products. Starting from the tetracoordinate trans chloride structure (**4**), we suggest that the pyridyl ligand dissociates to allow migration of one chloride group to occupy the position trans to the NHC ligand. This cis chloride structure (**5_d**) is then trapped by the pendant pyridyl ligand previously dissociated. As presented in Scheme 2, the solution dissociation energy of the pyridyl ligand from the cis geometry (**5** to **5_d**) is 18 kcal, which is 6 kcal higher than that from **4** to **4_d** (12 kcal). Therefore, the difference in the initiation rates of **4** and **5** is due to the relatively higher dissociation energy of compound **5**.

Summarizing, we analyzed the mechanism of cis−trans isomerization of chloride ligands in ruthenium metathesis catalysts using QM, leading to geometries close to X-ray crystallography. In addition we calculate that the cis form is 1.1 kcal *more stable* than trans in methylene chloride, in excellent agreement with the experimental value of 0.78 kcal. In benzene, we calculate that **4** is 2 kcal *less stable* than **5**, also in agreement with experiment since it is not isolated. This suggests that the product ratios could be shifted from either mostly trans to mostly cis by merely replacing solvents. We suggest intermediates in the isomerization mechanism that account for the difference in initiation rates of the parent compounds.

Acknowledgment. The facilities of the Materials and Process Simulation Center are supported by ONR-DURIP, ARO-DURIP, MURI-ARO, MURI-ONR, DOE (ASC, FETL), NSF (CHE), NIH, Aventis Pharma, ChevronTexaco, Nissan Corp., Berlex Biopharma, and Beckman Institute.

Supporting Information Available: Tables of geometries, ZPE corrections, and absolute energies of structures **4**, **5**, **4d**, and **5d**; a detailed comparison of the most representative structural features of the calculated structures and the reported crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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JA051796A