Mechanism of the Methylene Transfer Reaction. C−C Activation and Reductive Elimination in One System. A DFT Study

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DFT calculations were employed to investigate the methylene transfer reaction mechanism in a model system related to the experimental Rh/PCP ligand system previously reported by us. The computationally established mechanism is in accordance with the experimental results. It was found to be a C−C reductive elimination/C−C oxidative addition sequence in which the C−C reductive elimination is the rate-determining step. The C−C activation reaction was found to take place by two different routes; both proceed through the initial formation of the η^2-arene complex **2**. In one pathway, C−C activation takes place from an agostic C−H complex intermediate, and in the other, it occurs from the η^2-arene complex directly. In both intermediates the C−C bond is predirected to the metal center. The methylene transfer reaction outcome is governed by thermodynamic factors. However, changing the thermodynamic factors might lead to the reverse methylene transfer reaction becoming kinetically accessible. The reverse reaction is relevant to the design of a potential catalytic methylene transfer system.

Introduction

Insertion of transition-metal complexes into C−C bonds in solution is a field of great current interest,[1−3] since it can lead to the development of new selective and efficient processes for the utilization of hydrocarbons. Thus, insight into the activation mechanism of strong C−C bonds and implementation of the mechanistic information in the development of catalytic systems are highly desirable goals. It is recognized that C−C bond activation is, in general, a less facile process than C−H activation, both thermodynamically and kinetically.[4,5] Thus, significant progress has been made in catalytic functionalization of hydrocarbons by C−H activation,[6] while only a few systems for the catalytic activation of nonstrained C−C bonds by metal complexes are known.[1]

We have demonstrated that it is possible to combine selective C−C bond oxidative addition with the activation of other strong bonds to form methylene transfer products.[3c,e,7] This unique transfer of a methylene group was shown to take place from the metal complex to organic moieties, such as benzene, silanes, and disilanes[7a] as well as to HCl[3c,7b] and H_2.[7c] Recently we have

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(1) For reviews on C−C bond activation, see: (a) Rybtchinski, B.; Milstein, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 870. (b) Murakami, M.; Ito, Y. In *Topics in Organometallic Chemistry*; Murai, S., Ed.; Springer-Verlag: New York, 1999; Vol. 3, pp 97−129. (c) van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759. (d) Rybtchinski, B.; Milstein, D. *Activation and Functionalization of C−H Bonds*; ACS Symp. Ser.; Oxford University Press: London, in press. (e) Lefebvre, F.; Thivolle-Cazat, J.; Dufaud, V.; Niccolai, G. P.; Basset, J.-M. *Appl. Catal. A* **1999**, *182*, 1. (f) Jun, C.-H.; Monn, C. W.; Lee, D.-Y. *Chem. Eur. J.* **2002**, *8*, 2423.

(2) Recent papers: (a) Albrecht, M.; Gossage, R. A.; Spek, A. L.; van Koten, G. *J. Am. Chem. Soc.* **1999**, *121*, 11898. (b) Edelbach, B. L.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **1999**, *18*, 4040. (c) Edelbach, B. L.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **1999**, *18*, 4660. (d) Zhang, X.; Carpenter, G. B.; Swigart, D. A. *Organometallics* **1999**, *18*, 4887. (e) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880. (f) Older, C. M.; Stryker, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 2784. (g) Ohki, Y.; Suzuki, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 3463. (h) Murakami, M.; Tsuruta, T.; Ito, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 2484. (i) Webster, C. E.; Hall, M. B. *Organometallics* **2001**, *20*, 5606. (j) Miller, J. A. *Tetrahedron Lett.* **2001**, *42*, 6991. (k) Muller, C.; Iverson, C. N.; Lachicotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **2001**, *123*, 9718. (l) Campora, J.; Gutierrez-Puebla, E.; Lopez, J. A.; Monge, A.; Palma, P.; del Rio, D.; Carmona, E. *Angew. Chem., Int. Ed.* **2001**, *40*, 3641. (m) Albrecht, M.; Spek, A. L.; van Koten, G. *J. Am. Chem. Soc.* **2001**, *123*, 7233. (n) Taw, F. L.; White, P. S.; Bergman, R. G.; Brookhart, M. *J. Am. Chem. Soc.* **2002**, *124*, 4192. (o) Jun, C.-H.; Monn, C. W.; Lee, H.; Lee, D.-Y. *J. Mol. Catal. A* **2002**, *189*, 145. (p) Jazzar, R. F. R.; Macgregor, S. A.; Mahon, M. F.; Richards, S. P.; Whittlesey, M. K. *J. Am. Chem. Soc.* **2002**, *124*, 4944. (q) Murakami, M.; Itahashi, T.; Ito, Y. *J. Am. Chem. Soc.* **2002**, *124*, 13976. (r) Mueller, C.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **2002**, *21*, 1975. (s) Bart, S. C.; Chirik, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 886. (t) Hinrichs, R. A.; Schroden, J. J.; Davis, H. F. *J. Am. Chem. Soc.* **2003**, *125*, 860. (u) Xi, Z. F.; Sato, K.; Gao, Y.; Lu, J. M.; Takahashi, T. *J. Am. Chem. Soc.* **2003**, *125*, 9568. (v) Taw, F. L.; Meller, A. H.; Bergman, R. G.; Brookhart, M. *J. Am. Chem. Soc.* **2003**, *125*, 9808.

(3) Some recent papers on C−C activation from our groups: (a) Rybtchinski, B.; Milstein, D. *J. Am. Chem. Soc.* **1999**, *121*, 4528. (b) van der Boom, M. E.; Ben-David, Y.; Milstein, D. *J. Am. Chem. Soc.* **1999**, *121*, 6652. (c) van der Boom, M. E.; Kraatz, H.-B.; Hassner, L.; Ben-David, Y.; Milstein, D. *Organometallics* **1999**, *18*, 3873. (d) Gandelman, M.; Vigalok, A.; Konstantinovsky, L.; Milstein, D. *J. Am. Chem. Soc.* **2000**, *122*, 9848. (e) Cohen, R.; van der Boom, M. E.; Shimon, L. J. W.; Rozenberg, H.; Milstein, D. *J. Am. Chem. Soc.* **2000**, *122*, 7723. (f) Sundermann, A.; Uzan, O.; Milstein, D.; Martin, J. M. L. *J. Am. Chem. Soc.* **2000**, *122*, 7095. (g) Rybtchinski, B.; Oevers, S.; Montag, M.; Vigalok, A.; Rozenberg, H.; Martin, J. M. L.; Milstein, D. *J. Am. Chem. Soc.* **2001**, *123*, 9064. (h) Gandelman, M.; Shimon, L. J. W.; Milstein, D. *Chem. Eur. J.* **2003**, *9*, 4295.

(4) See, for instance: Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organo-transition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987.

(5) (a) Siegbahn, P. E. M.; Blomberg, M. R. A. *J. Am. Chem. Soc.* **1992**, *114*, 10548. (b) Blomberg, M. R. A.; Siegbahn, P. E. M.; Nagashima, U.; Wennerberg, J. *J. Am. Chem. Soc.* **1991**, *113*, 424.

(6) Recent reviews: (a) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507. (b) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633. (c) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698. (d) Crabtree, R. H. *Dalton* **2001**, 2437. (e) Jensen, C. M. *Chem. Commun.* **1999**, 2443.

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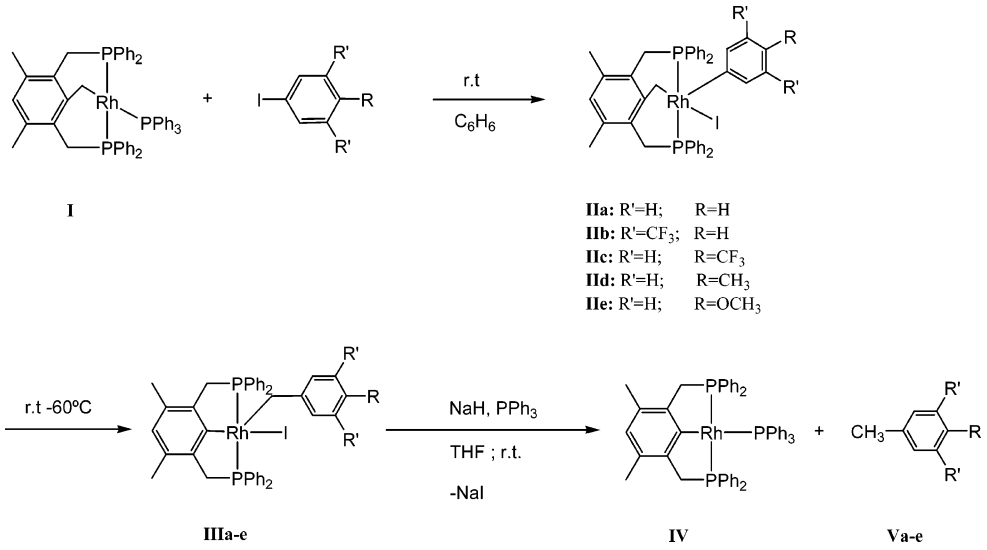
Scheme 1

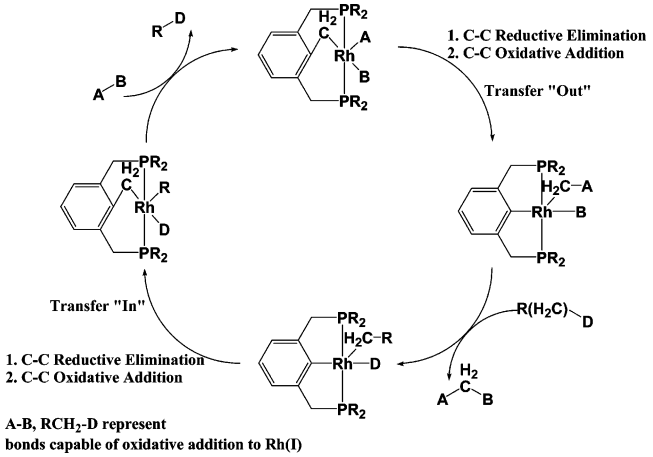


demonstrated an *intramolecular methylene transfer* reaction based on C−C activation, in which the transferred methylene moiety remains attached to the metal center (Scheme 1).[3e]

In this process, initial oxidative addition of aryl iodides to a PCP−CH_2−Rh^I complex occurs to form the aryl iodide Rh(III) compounds **IIa**−**e**, which upon mild heating undergo C−C activation to form the benzyl iodide complexes **IIIa**−**e**. This intramolecular process enabled the characterization of several stages in the methylene transfer reaction, which appeared to involve an unprecedented sequence of sp^2−sp^3 C−C bond reductive elimination and sp^2−sp^3 C−C bond activation reactions. We investigated the reaction kinetically and obtained activation parameters, which suggested that the C−C reductive elimination rather than the C−C oxidative addition is the rate-determining step of the sequence. However, only limited information about the reaction mechanism could be obtained due to the rapid C−C activation step, making the observation of intermediates unfeasible. It is highly desirable to develop a *catalytic* process in which a methylene unit will migrate from one compound by C−C activation and will be selectively incorporated into another compound. This may be possible on the basis of PCP complex methylene bridge transfer to various substrates (transfer "out") followed by its regeneration with another substrate (transfer "in"). A hypothetical catalytic methylene transfer cycle based on the PCP/Rh system is illustrated in Scheme 2.

We have demonstrated that a reverse transfer reaction can take place from our methylene transfer products **IIIa**−**e** (Scheme 1) by a succession of C−C reductive elimination and C−H activation.[3e] To develop conditions for catalysis, the detailed mechanism of the methylene transfer reaction should be elucidated. We describe here a computational DFT study of the methylene transfer reaction in the (PCP−CH_2)Rh(Ar)(X) system that sheds light on this unique process, which involves C−C activation and reductive elimination in a single system.

Scheme 2



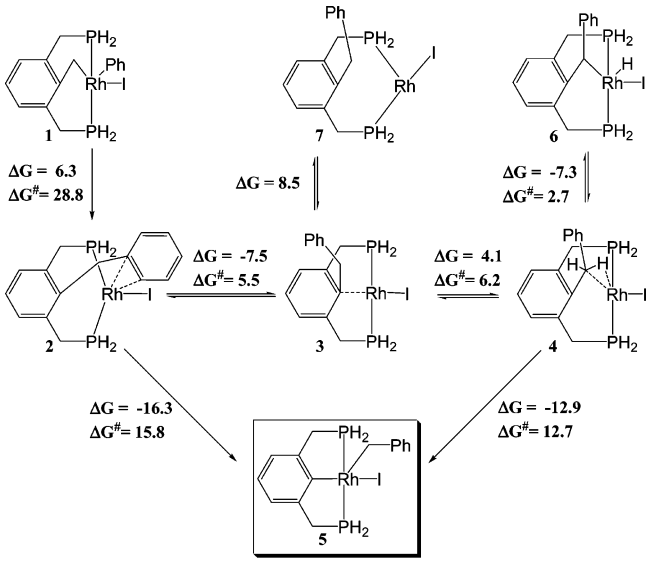
Results

Density functional theory (DFT) using the Gaussian98 program package[8] was used to calculate the structures and energies of the intermediates and transition states involved in the methylene transfer sequence. The computational model for the experimental system is the Rh(Ph)[$CH_2C_6H_3(CH_2PH_2)_2$](I) complex (**1**, Scheme 3). It has H instead of Ph substituents on the bischelating phosphine ligand and no Me substituents in the chelate aromatic ring.[9] All the calculations were performed at the mPW1k/SDB-cc-pVDZ//mPW1k/SDD level of theory (for details see Computational Methods).

(7) (a) Gozin, M.; Aizenberg, M.; Liou, S.-Y.; Weisman, A.; Ben-David, Y.; Milstein, D. *Nature* **1994**, *370*, 42. (b) van der Boom, M. E.; Kraatz, H. B.; Ben-David, Y.; Milstein, D. *Chem. Commun.* **1996**, 2167. (c) Liou, S.-Y.; van der Boom, M. E.; Milstein, D. *Chem. Commun.* **1998**, 687.

(8) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery Jr, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.11; Gaussian, Inc. Pittsburgh, PA, 2001.

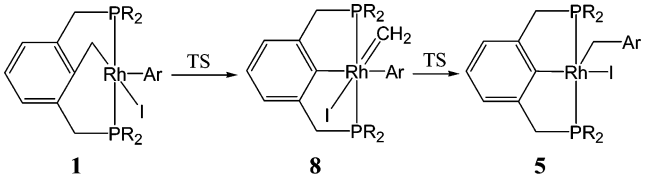
Scheme 3



The results of the calculations are summarized in Scheme 3. Relative energies for the optimized geometries at the mPW1k/SDD level and for the single-point calculations at the mPW1k/SDB-cc-pVDZ level are described for E_{tot} and G_{298} in the Supporting Information.

The methylene transfer sequence starts with C−C reductive elimination in complex **1**. The barrier found for the C−C reductive elimination step is rather high ($\Delta G^{\ddagger}$ = 28.8 kcal/mol) and corresponds to the 23 kcal/mol barrier found experimentally.[3e] We attribute the discrepancy to the limitations of our computational model.[10] This process has the highest barrier of the whole methylene transfer sequence, in good agreement with our experimental results. The reductive elimination leads to the formation of complex **2**, which is an "open" chelate complex stabilized by an η^2-arene coordination to the Ph moiety. There are two competing pathways that start from intermediate **2**, both leading to the C−C activated complex **5**, and a pathway involving the formation of C−H activated complex **6**. In the first route complex **2** oxidatively adds the $C_{ipso}-C_{CH_2}$ bond to give **5** with a barrier of 15.8 kcal/mol. In the second route complex **2** is first converted to the η^1-arene complex **3** (with a lower barrier of $\Delta G^{\ddagger}$ = 5.5 kcal/mol), which is then transformed to the C−H agostic complex **4** with a low barrier of 6.2 kcal/mol. The C−H agostic complex **4** is capable of both C−H and C−C activation. The C−C activation results in the formation of the most stable thermodynamic product, **5**; however, the barrier to form the C−H activated complex **6** is much lower (2.7 kcal/mol for C−H vs 12.7 kcal/ml for C−C activation).[11]

Scheme 4



Nevertheless, as the back reaction barrier (for C−H reductive elimination) is relatively low ($\Delta G^{\ddagger}_{C-H,RE}$ = 10.0 kcal/mol), it is conceivable that *reversible* C−H activation leading to the formation of **6** takes place, while the C−C activation process leading to **5** is the thermodynamically preferable reaction. No transition state directly connecting **3** and **5** was found. Such a direct transition state connecting between similar η^1-arene and C−C activation PCP complexes was found computationally by Cao and Hall for the Ir−PCP system.[12] However, for the analogous Rh−PCP system, no such transition state was found in the calculations by Hall, but rather a stepwise mechanism similar to that found in our study. In our previous study on C−C and C−H oxidative mechanism in the Rh−PCP system[3f] we have also found a local minimum corresponding to an η^1-arene intermediate; however, it was not directly involved in the C−C bond activation, similarly to the system reported here. It should be noted that although an open 14e intermediate was located (**7**; Scheme 3), no direct involvement of this high-energy intermediate in the methylene transfer sequence was found. Nonetheless, this unsaturated open intermediate might be generated reversibly from complexes such as **2**−**4** (although no transition states were found for these transformations).

An alternative mechanism for the C−C reductive elimination/C−C activation sequence of the methylene transfer process was also addressed. In this mechanism an initial C−C cleavage step generates an intermediate methylidene complex, which could then insert into the Rh−Ar bond, resulting in the formation of **5** (Scheme 4). Calculation of the intermediate methylidene complex **8** (or its isomer with the methylidene moiety in a position cis to the iodine ligand) resulted in a high-energy compound, which is 60 kcal/mol (or 43 kcal/mol for the cis-iodine isomer) higher than the thermodynamic product **5**. These complexes are higher in energy than any of the intermediates and transition states involved in the methylene transfer sequence depicted in Scheme 3. Thus, complex **8** is not expected to be formed under the experimental reaction conditions, ruling out the possibility for the methylidene mechanism in the methylene transfer reaction.

Our computational results are in good agreement with our experimental findings. Thus, complex **5**, which is an analogue of the experimental thermodynamic products, complexes **IIIa**−**e** (see Scheme 1), is the thermodynamically most stable product, in accordance with the experimental observations. C−C reductive elimination was found to be the rate-limiting step in both the experimental and computational studies.

(9) Steric effects may have some influence on the mechanism of the methylene transfer reaction. However, the Ph substituents are not considered to be especially sterically demanding. They may impose lower electron density on the metal than in the case of H substituents, which might somewhat reduce the barriers involved in reductive elimination processes and increase the barriers of C−C and C−H activation. However, the difference is not expected to be significant (see ref 12 for example) and will not change the overall mechanism. Overall, good agreement with the experimental system was observed (see in the text).

(10) This barrier is expected to decrease when Ph substituents are introduced to the ligand system, as a result of a reduced electron density on the Rh center (due to the electron-withdrawing nature of the Ph substituents) that would favor reductive elimination.

(11) In addition, there are two C−H bonds available for C−H activation vs only one C−C bond in the C−C activation, making the C−H activation route even more favorable.

(12) Cao, Z. X.; Hall, M. B. *Organometallics* **2000**, 19, 3338.

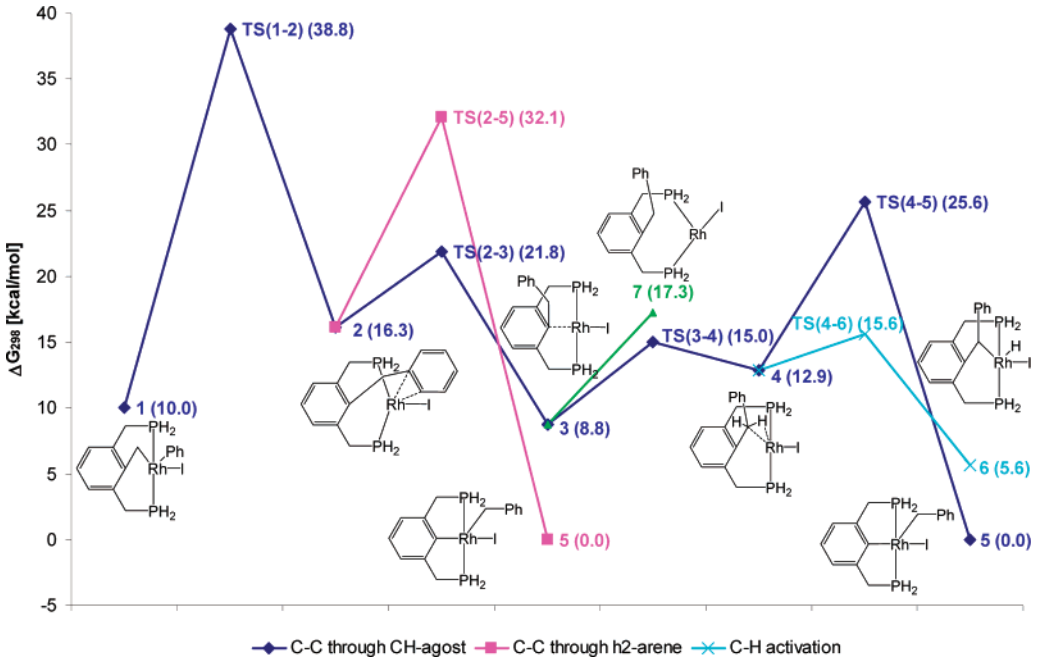


Figure 1. Relative free energies (ΔG_{298}) of the methylene transfer intermediates and transition states at the mPW1k/SDD/mPW1k/SDB-cc-pVDZ level of theory.

DFT calculations have identified two feasible C−C activation pathways resulting in the formation of **5**: a direct route proceeding through intermediate **2** with a barrier of 15.8 kcal/mol and a route involving a reversible C−H activation (through the η^1-arene complex **3** and the η^2_{CH} complex **4**). This path, involving the formation of the C−H agostic complex **4**, has a lower barrier for C−C activation (12.7 kcal/mol). However, since both barriers for C−C activation (**2** → **5**, $\Delta G^{\ddagger}$ = 15.8 kcal/mol; **4** → **5**, $\Delta G^{\ddagger}$ = 12.7 kcal/mol) are relatively low and comparable for both routes, it is conceivable that both of them can take place. *All productive pathways were found to proceed through complex* ***2****, which is a key intermediate in the methylene transfer reaction*. Complex **2** is a conceptually new precursor for C−C oxidative addition. It directs the C−C bond to the metal center through an η^2_{C-C}-arene coordination rather than through an η^2_{C-H} one and is unique for the system containing a benzyl C−C bond. It should be noted that η^2_{C-C}-arene complexes were suggested to be the initial reactants in C−H σ-bond activation reactions.[13]

All pathways that can take place in the methylene transfer sequence are described in Figure 1.

It should be noted that, on the basis of our DFT study, C−C oxidative addition can take place in forward reactions **2** → **5** ($\Delta G^{\ddagger}$ = 15.8) and **4** → **5** ($\Delta G^{\ddagger}$ = 12.7) or the reverse reaction **2** → **1** ($\Delta G^{\ddagger}$ = 22.5 kcal/mol). Nevertheless, although the C−C oxidative addition reaction **2** → **1** is kinetically possible, since **5** (rather than **1**) is the thermodynamically most stable product in the methylene transfer sequence (**1** → → **5**), it is the only product that can be observed in agreement with our experimental results.[3e] The barriers for C−C reductive elimination are higher than those for its microscopic reverse reaction, C−C activation. They are similar for the forward direction ($\Delta G^{\ddagger}$ = 28.8 kcal/mol for **1** → **2**) and for the reverse direction ($\Delta G^{\ddagger}$ = 25.6 kcal/mol for **5** → **4** or $\Delta G^{\ddagger}$ = 32.1 kcal/mol for **5** → **2**).

Each single barrier involved in both forward and reverse processes is reachable for our system (Figure 1). However, the *effective* barrier for the reverse reaction **5**→**1** is the highest barrier of the pathway relative to the lowest energy point, hence the effective free energy for **5**→**1** is 38.8 kcal/mol. Thus, reverse methylene transfer reaction will not take place unless **5** is less thermodynamically stable than **1**. This conclusion is important for the design a catalytic system for the methylene transfer reaction (vide infra).

Structures of the Complexes

The structures of all intermediates relevant to the methylene transfer mechanism are illustrated in Figure 2.

Two structural isomers were found for complex **1** (Figure 2). One has a Ph ligand in a position trans to the empty coordination site (**1**), and the other has an iodine trans to the empty coordination site (**1-iso**). Complex **1** is the analogue of the experimentally observed complex **IIa** (Scheme 1)[3e] and is 17.4 kcal/mol lower in energy than the complex **1-iso** (probably due to the trans effect of the Ph ligand being greater than that of I). In comparison of the structure of **1** to the analogous experimental X-ray structure of **IIa**, it can be seen that the Rh−C_{CH_2} bond distances are similar in the two complexes (2.075 vs 2.069 Å in the X-ray structure), as are the Rh−C_{CH_2}−C_{ipso} bond angles (88.8 vs 90.2° in the X-ray structure). This similarity between the calculated and the experimental structures implies that our model system closely parallels the experimental system.

(13) (a) Jones, W. D.; Feher, F. J. *Acc. Chem. Res.* **1989**, *22*, 91. (b) Belt, S. T.; Duckett, S. B.; Helliwell, M.; Perutz, R. N. *J. Chem. Soc., Chem. Commun.* **1989**, 928. (c) Belt, S. T.; Dong, L.; Duckett, S. B.; Jones, W. D.; Partridge, M. G.; Perutz, R. N. *J. Chem. Soc., Chem. Commun.* **1991**, 266. (d) Chin, R. M.; Dong, L.; Duckett, S. B.; Partridge, M. G.; Jones, W. D.; Perutz, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 7685. (e) Johansson, L.; Tilset, M.; Labinger, J. A.; Bercaw, J. E. *J. Am. Chem. Soc.* **2000**, *122*, 10846. (f) Reinartz, S.; White, P. S.; Brookhart, M.; Templeton, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 12724.

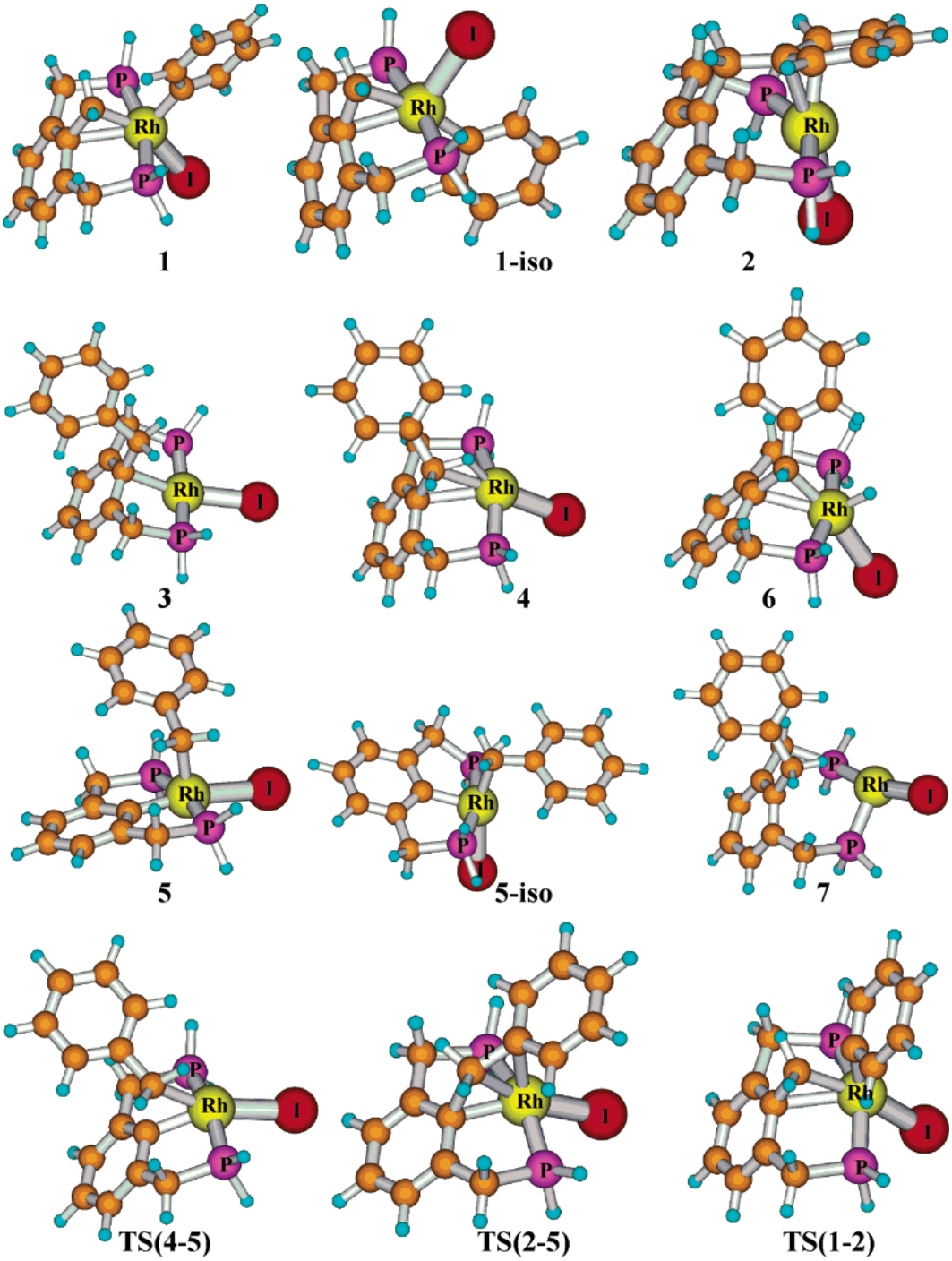


Figure 2. Structures of the intermediate complexes found for the methylene transfer reaction sequence.

The η^1-arene complex **3** has a relatively short Rh−C_{ipso} bond (2.3 Å) compared to that in complex **2** (2.9 Å), and it reveals a slight distortion in the chelate aromatic ring which could be attributed to arenium character. The Rh−C_{ipso} bond in **3** (2.3 Å) is much longer than that in **5** (2.0 Å), and dearomatization is not significant, as indicated by the bond lengths and angles. The Wiberg bond index obtained from a natural bond order (NBO) calculation confirms that there is an interaction between the Rh center and the C_{ipso} atom; thus, Rh−C_{ipso} is a true bond (for Wiberg index values see the Supporting Information). The Rh−C_{ipso} bond length and the slight dearomatization of the ring is similar to that found by us for the cationic σ-arenium species.[14] The Rh−C_{CH_2} distance in **3** is 3.0 Å therefore, there is no C−C agostic type coordination to the Rh center. Analogous η^1-arene complexes were previously found computationally by us[3f] as well as by Cao and Hall[12] in similar Rh and Ir/PCP systems. In our study no direct C−C cleavage was found to take place from **3**, as in the case for Rh/PCP system in the calculations by us[3f] and by Cao and Hall.[12]

No η^2-arene coordination to the chelate aryl was found. All attempts to find an η^2-arene intermediate converged to the η^1-arene complex **3**. However, in the search for the analogous η^1-arene complex of the external aryl (rather than that of the chelate aryl), only the

(14) Vigalok, A.; Rybtchinski, B.; Shimon, L. J. W.; Ben-David, Y.; Milstein, D. *Organometallics* **1999**, *18*, 895.

η^2-complex **2** was found. It should be noted that η^2-arene coordination to the chelate aryl was computationally found in bis-chelating PCN[15] and PCO[3g] systems and in the monochelating PC system.[16] To the best of our knowledge, complex **2** is a new computationally found intermediate for C−C oxidative addition. It is an open chelate stabilized by η^2 coordination to the reductively eliminated arene ring. The Rh−CH_2 distance in **2** is 3.1 Å; therefore, it cannot be regarded as a π-benzyl complex but rather as an η^2 complex with Rh−C_{aryl} distances of 2.2 and 2.4 Å and corresponding bond orders. The Rh- - -C_{ipso} distance in **2** is relatively long (2.9 Å), and no interaction is observed between the Rh and C_{ipso} atoms on the basis of the NBO calculation. In the C−H agostic complex **4**, however, the Rh- - -C_{ipso} distance is much shorter (2.5 Å), which may explain the lower kinetic barrier for C−C oxidative addition proceeding via **4**. No C−C agostic interaction was found in **4**. The methylene C−H bond, which is coordinated to the metal, is longer than the C−H bond which is not coordinated to the metal (1.16 vs 1.09 Å, respectively); thus, this is a true agostic C−H bond (indicated also by NBO analysis).[17] Similar C−H agostic PCP complexes were previously found by us[3f] and by Cao and Hall[12] to be the intermediates for C−C activation.

Two structural isomers were found for complex **5** (Figure 2): one with the benzyl ligand trans to an empty coordination site (**5**) and an isomer with the chelate ring trans to an empty coordination site (**5-iso**). The energies of these two structures differ by 1.5 kcal/mol, **5-iso** being more stable. This could result from the preference of an sp^2 carbon to be trans to an empty coordination site rather than to an iodide, as the trans effect of an sp^2 carbon is expected to be stronger than that of an sp^3 carbon. We considered complex **5** for the mechanism description, since it is more comparable to the X-ray structure found for the analogous experimental complex **IIIc**,[3e] and only transition states leading to **5** (but not to **5-iso**) were located in our calculations. Complexes **5** and **5-iso** are the most stable complexes in the computational model system. The reason for complex **5** thermodynamic preference over complex **1** could be the higher stability of five-membered rings chelate vs six-membered rings.

The open chelate complex **7** is a higher energy compound. It has a T-shaped geometry with the two phosphine arms cis to each other and an iodine ligand trans to one phosphine. This complex is not an intermediate for C−C cleavage. It demonstrates distances between the Rh center and the carbons relevant in C−C activations (3.3 and 3.5 Å) that are longer than in other intermediates.

The transition state geometries for C−C reductive elimination **TS(1−2)** and C−C cleavage **TS(2−5)** are very similar (Figure 2). The major differences between them are the bond distances of the C−C bonds that are being formed or activated.[18] In **TS(1−2)** the forming C_{Ar}−C_{CH_2} bond is 1.8 Å, whereas in **TS(2−5)** the same bond is 1.5 Å. In the same way, the activated C_{CH_2}−C_{ipso} bond in **TS(2−5)** is 1.8 Å, whereas the same bond in **TS(1−2)** is 1.5 Å. The Rh−C_{CH_2} distance is 2.3 Å for both **TS(1−2)** and **TS(2−5)**. This geometric similarity between the two transition states reflects the similarity of the bonds that are being activated and formed: namely sp^2−sp^3 aryl−benzyl C−C bonds in both transition states. Significantly, the geometry for the C−C cleavage transition state **TS(4−5)** is very different from that of **TS(2−5)**, reflecting the different geometry of the intermediate from which the C−C activation step takes place. This signifies the importance of predirection of the C−C bond toward the metal center required for C−C bond activation, rather than specific transition state geometry.

Discussion

Calculations found two feasible routes for C−C activation in the studied model system. The first route, involving formation of the η^1-arene and C−H agostic intermediates, was computationally suggested by Cao and Hall for similar Rh systems.[12] A similar mechanism involving formation of a C−H agostic intermediate as a precursor for C−C activation was also suggested by us for several analogous systems.[3f,g] It should be noted that while in Rh systems a C−H agostic complex similar to **4** was found computationally, no such intermediate was found for the analogous Ir/PCP system, in which the C−C cleavage reaction was suggested to take place directly from the η^1-arene complex (similar to **3**).[12] No direct transformation was found to take place from **2** to **4**. Thus, the formation of an η^1-arene complex promotes the low-energy C−C cleavage path and it is critical for C−H activation.

The second route for C−C cleavage found in our calculations follows a C−C cleavage reaction taking place from the "open" η^2 complex **2**. This direct route was not found computationally before and thus is a conceptually new path for a C−C oxidative addition process in our systems. The alternative activation of a C−C bond without precoordination of the metal to an adjacent C−H bond raises the possibility for designing a system with more favorable C−C vs C−H competing aptitudes. We previously reported on a 14e intermediate (which does not involve η^{2}_{C-C}-arene coordination) that was directly observed to undergo aryl−Me oxidative addition at low temperature.[3d]

It should be noted that C−C oxidative addition, in contrast to C−H oxidative addition, was not found to take place from an agostic C−C intermediate; thus, there is no direct coordination of the bond to be cleaved to the metal as in the C−H activation reaction. However, predirection of the C−C bond toward the metal is required. In our model system it is either η^2 coordination or a C−H agostic bond that is necessary for bringing the C−C bond into close proximity to the metal, making the C−C cleavage step possible by two different routes. The importance of such predirection for the cleavage of C−C bonds was recently demonstrated in the PCO system both experimentally and theoretically.[3g]

To design a catalytic methylene transfer reaction, the reverse C−C reductive elimination/C−C activation sequence **5** → → **1** should be considered. The effective barrier for the process **5** → → **1** either through complex **4** (**5** → **4** → **3** → **2** → **1**) or directly through complex **2** (**5**

(15) Sundermann, A.; Uzan, O.; Martin, J. M. L. *Organometallics* **2001**, *20*, 1783.
(16) Rybtchinski, B.; Cohen, R.; Ben-David, Y.; Martin, J. M. L.; Milstein, D. *J. Am. Chem. Soc.* **2003**, *125*, 11041.
(17) Hall, C.; Perutz, R. N. *Chem. Rev.* **1996**, *96*, 3125.
(18) This is best illustrated by following the imaginary frequencies for the transition states in MOLDEN.

→ **2** → **1**) is too high to allow this reverse reaction to take place (38.8 kcal/mol), although each individual step in the reverse reaction seems to be kinetically accessible, especially when considering the longer path **5** → **4** → **3** → **2** →**1**. However, provided that the thermodynamics are favorable, this pathway might be also kinetically accessible. If the stability of **5** is lower than that of **1**, it will result in a lower effective barrier for the reverse process.[19] Thus, on the basis of our study, the reversibility of the methylene transfer sequence might be achievable, provided that a proper thermodynamic design would result in a lower effective barrier for the process. Efforts toward the catalytic methylene transfer system based on our computational study are currently underway in our laboratories.

Conclusions

The mechanism for the methylene transfer reaction in the (H−PCP−CH_2)Rh(Ph)(I) model system was investigated computationally. The calculations support the experimental conclusion that the rate-determining step in the methylene transfer sequence is the initial C−C reductive elimination rather than the C−C activation step. Two routes were found for the C−C activation process taking place after the formation of the η^2 arene complex **2**, which is a key intermediate participating in all pathways found for the reaction. One route, which is lower in energy, proceeds through the η^1 complex **3**, which is converted to the agostic C−H complex **4** that is an intermediate for the C−C bond oxidative addition. The other route is going directly from the "open" η^2_{CC}-arene complex **2** to the C−C activated complex **5**. This is a new computational result regarding the C−C activation mechanism that emphasizes the importance of predirection of the metal toward the C−C bond and identifies a new directing mechanism. The reverse sequence for C−C reductive elimination and C−C activation, **5** → **1**, was also considered. Changing the thermodynamic propensities in the system might lead to a change in the effective barrier of the reverse process, resulting in a thermodynamically and kinetically accessible reaction relevant to the design of a catalytic methylene transfer system.

Computational Methods

All calculations were carried out using the Gaussian 98 program, revision A.11,[8] running on a mini-farm of Pentium IV Xeon 1.7/2.0 GHz PC's running Red Hat Linux 7.2 in our group and on the Faculty of Chemistry Linux PC Farm.

The mPW1k (modified Perdew-Wang 1-parameter for kinetics) exchange-correlation functional of Truhlar and co-workers[20] was employed in conjunction with the SDD and SDB-cc-pVDZ basis sets (see below). This functional is based on the Perdew−Wang exchange functional[21] with Adamo and Barone's modified enhancement factor[22] and the Perdew−Wang correlation functional.[21] A larger percentage of Hartree−Fock exchange has been introduced[20] to circumvent the underestimated barrier heights typical of standard exchange-correlation functionals. It has been shown[20,23−25] that this functional generally yields much more reliable reaction barrier heights than B3LYP or other "conventional" exchange-correlation functionals, especially when transition metals are involved.[25,27]

The SDD basis set is the combination of the Huzinaga−Dunning double-ζ basis set on lighter elements with the Stuttgart−Dresden basis set−relativistic effective core potential (RECP) combination[26] on the transition metals. The SDB-cc-pVDZ basis set combines the Dunning cc-pVDZ basis set[27] on the main-group elements with the Stuttgart−Dresden basis set−RECP combination[28] on the transition metals, with an f-type polarization exponent taken as the geometric average of the two f exponents given in the Appendix to ref 28.

The energetics for our final reaction profiles obtained from the mPW1k functional with SDD basis set were validated by single-point energy calculations, using the SDD reference geometries, with the extended SDB-cc-pVDZ basis set.

Geometry optimizations for minima were carried out using the standard Schlegel algorithm[29] in redundant internal coordinates until in the neighborhood of the solution and then were continued using analytical second derivatives.[30] Optimizations for transition states were carried out with an initial guess for the transition state being generated from manual manipulation of the geometry using MOLDEN.[31] In cases where this approach failed to converge, we used analytical second derivatives at every step.

Zero-point and RRHO (rigid rotor−harmonic oscillator) thermal corrections (to obtain ΔS and ΔG values at 298.15 K) were obtained from the unscaled computed frequencies.

Where necessary, the Grid = UltraFine combination, i.e., a pruned (99 590) grid in the integration and gradient steps and a pruned (50 194) grid in the CPKS (coupled perturbed Kohn−Sham) steps, was used as recommended in ref 32.

For interpretative purposes, atomic partial charges and Wiberg bond indices[33] were obtained by means of a natural population analysis (NPA)[34] at the mPW1k/SDD level.

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Supporting Information Available: A table giving *xyz* coordinates of all computed structures and a figure giving Wiberg indices for complexes **2**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) In the experimental system, a similar pathway to the latter (leading to a C−H activation product) was shown to take place in a related PCP system.[3e]

(20) Lynch, B. J.; Fast, P. L.; Harris, M.; Truhlar, D. G. *J. Phys. Chem. A* **2000**, *104*, 4811.
(21) Perdew, J. P.; Chevary, J. A.; Vosko, S. H.; Jackson, K. A.; Perderson, M. R.; Singh, D. J.; Fiolhais, C. *Phys. Rev. B* **1992**, *46*, 6771.
(22) Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664.
(23) (a) Parthiban, S.; de Oliveira, G.; Martin, J. M. L. *J. Phys. Chem. A* **2001**, *105*, 895. (b) Lynch, B. J.; Truhlar, D. G. *J. Phys. Chem. A* **2001**, *105*, 2936.
(24) Iron, M. A.; Lo, H. C.; Martin, J. M. L.; Keinan, E. *J. Am. Chem. Soc.* **2002**, *124*, 7041.
(25) Iron, M. A.; Sundermann, A.; Martin, J. M. L. *J. Am. Chem. Soc.* **2003**, *125*, 11430.
(26) Dolg, M. In *Modern Methods and Algorithms of Quantum Chemistry*; Grotendorst, J., Ed.; John von Neumann Institute for Computing: Jülich, Germany, 2000; Vol. 1, pp 479−508.
(27) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007.
(28) Martin, J. M. L.; Sundermann, A. *J. Chem. Phys.* **2001**, *114*, 3408.
(29) (a) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214. (b) Peng, C.; Ayala, P. Y.; Schlegel, H. B.; Frisch, M. J. *J. Comput. Chem.* **1996**, *17*, 49.
(30) Stratmann, R. E.; Burant, J. C.; Scuseria, G. E.; Frisch, M. J. *J. Chem. Phys.* **1997**, *106*, 10175.
(31) Schaftenaar, G. Molden 3.6, 1999. URL: http://www.cmbi.kun.nl/~schaft/molden/molden.html.
(32) Martin, J. M. L.; Bauschlicher, C. W.; Ricca, A. *Comput. Phys. Commun.* **2001**, *133*, 189.
(33) Wiberg, K. B. *Tetrahedron* **1968**, *24*, 1083.
(34) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.