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Surprising Differences of Alkane C-H Activation Catalyzed by Ruthenium Nanoparticles: Complex Surface-Substrate Recognition?

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The activation of C–H bonds of alkanes remains a major challenge for chemistry. In a series of deuteration experiments with D_2 in contact with bis-(diphenylphosphino) butane (dppb) stabilized ruthenium nanoparticles (liquid substrates, 60 °C, 6 bar D_2) we have observed a surprisingly large reactivity of cyclopentane as compared to cyclohexane and other alkanes. DFT calculations using a ligand-free $Ru_{13}H_{17}$ model cluster as catalyst indicate oxidative C–H cleavage of the bound substrates as rate limiting reaction step. They also indicate similar binding and activation enthalpies of reactions of cyclopentane and cyclohexane.

The activation of inert C–H bonds of alkane chains is one of the major challenges for chemists. What nature achieves with high efficiency in enzymatic conversions[1] is still nearly not feasible in technical reactions, namely regio- and stereo selective activation of alkanes. The highest value in mastering this field of catalysis refers to the world's crude oil reserves, which constitute up to 50% alkanes.[2] If a C–H bond in an alkane could be regarded as a precursor to a hydroxyl-, carboxy- or an amine group for example, the large alkane fraction in the crude oil would feed the pool of industrial base chemicals. Thus, heterogeneous catalysis has long studied the activation of hydrocarbons on metal surfaces with typical reactions such as alkane hydrogenolysis. In these studies, H/D exchange has been used as a test of reactivity of the hydrocarbons. In this respect, when explicitly mentioned no real difference in reactivity was found for cyclohexane and cyclopentane.[3,4,5,6] In solution, the research field of C–H activation in alkanes was established by the pioneering work of Shilov *et al.*[7] and was tackled mostly by organometallic chemistry since then.[8]

Whereas previous C–H activation studies employed homogeneous catalysis, some of us have explored the use of transition metal Ru-nanoparticles separated by organic protecting ligands as homogeneous and heterogeneous catalysts.[9,10,11] Recently, transition metal nanoparticles have also been created on well-defined metal surfaces and studied with respect to their catalytic activity.[12] Ligand separated nanoparticles catalyze a number of chemical reactions, e.g. hydrogenation of olefins and C–C activation.[13] In combined ^1H gas phase and solid state ^2H NMR studies[14,15] some of us have shown that these particles contain surface hydrogens, which can be replaced by deuterons by exposure to D_2 gas, resulting in the release of HD. However, it was also observed that CH_2 groups of organic ligands such as hexadecylamine (HDA) were partially deuterated, a process which could only take place via C–H activation.

As H/D exchange is almost isoenergetic to the insertion of functional groups[16] it can be used in heterogeneous catalysis as a straightforward test for C–H bond activation.[17] Recently some of us demonstrated that Ru nanoparticles could also catalyze in organic or aqueous solvents the site- and stereo selective deuteration of a variety of aza compounds.[18,19] In the present study we explore the C–H activation potential of Ru nanoparticles towards alkanes via H/D exchange and discovered much to our surprise a large difference of reactivity between cyclopentane and cyclohexane.

We choose bis-(diphenylphosphino) butane (dppb) stabilized ruthenium nanoparticles as heterogeneous catalyst (Scheme 1), a system which is synthetically well established and can be regarded as a prototype for a hybrid of a heterogeneous and homogeneous catalyst. We first studied cyclopentane and cyclohexane as model substrates, since methylene groups in cyclic alkanes are the most reactive ones towards C–H activation.[20] We then expanded our investigation to *n*-pentane, *n*-octane and *iso*-pentane as representatives for linear and branched alkanes. We chose heterogeneous liquid-solid reaction conditions by bringing the MNPs, synthesized as described previously,[21,22,23] in direct contact with the liquid substrates as

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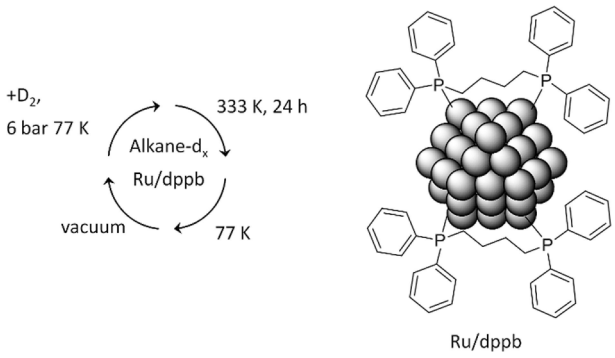


Scheme 1. Deuteration experiments performed of alkanes with 6 bar D_2 and Ru/dppb nanoparticles as catalyst using different batch reaction cycles.

well as gaseous D_2 and omitted a solvent. Mild conditions were used (333 K, 1 or 2 ml liquid alkane in a total volume of 95 mL and 6 bar D_2 gas). Generally, several batch cycles were performed, during typically 24 h. After each cycle the samples were frozen to 77 K and the hydrogen gas mixture removed *in vacuo* and fresh D_2 gas added for a new reaction cycle at 333 K. At the end, mass spectra were taken to analyze the progress of alkane deuteration. The results are assembled in Table 1.

Fast deuteration of cyclopentane and slow deuteration of other alkanes. The isotopomer fraction patterns obtained from mass spectra of cyclopentane after 1, 3 and 5 reaction cycles are depicted in Figure 1a to 1c. The spectra show in addition to the mole peak of the substrate cyclopentane-d_0 (mass 70 *m/z*) additional peaks of partially deuterated isotopologues, up to cyclopentane-d_{10}. After 3 batch cycles (Figure 1b), cyclopentane-d_0 still dominates, but a significant amount of cyclopentane-d_2 is formed. We also conducted an experiment with 2 ml substrate with only one batch cycle, but with a reaction time of 6 days (Figure 1a). It resulted in an exchange of only 6.3% of the hydrogen atoms, where the initial dominance of cyclopentane-d_1 was gone. After 5 batch cycles (Figure 1c), cyclopentane-d_4 becomes the dominant species. Thus, an excellent deuteration fraction of 40% is achieved in relatively mild conditions.

Previously, for H/D exchange of cyclopentane on metal surfaces a preference for the formation of the d_5-isotopologue was observed where all hydrogen atoms of one side the cyclopentane ring are exchanged.[24,25,26] The finding of the dominance of cyclopentane-d_2 in the initial reaction stages

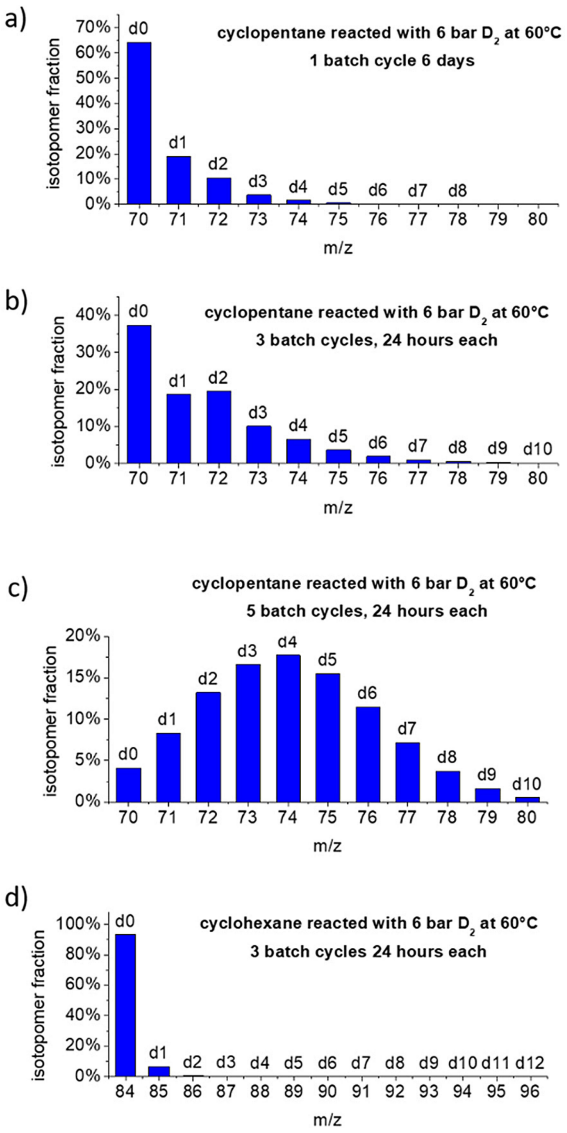


Figure 1. Isotopomer fraction patterns obtained from mass spectra for deuteration experiments on the substrates cyclopentane (a-c) and cyclohexane (d).

indicates then that the incorporation of two deuterons is more probable than of one deuteron. This means that in the case of Ru-nanoparticles two C–H bonds can be activated during a

Table 1. Deuterium fractions of selected liquid alkanes after reaction with D_2 in contact with Ru/dppb nanoparticles.

Substrate	Boiling point [k]	Substrate volume [ml]	Batch cycles	Reaction time	Deuterium fraction[a] [%]	Average number of D
Cyclopentane		1	3	24 h	16.2	1.6
Cyclopentane	322.4	1	5	24 h	40.2	4.0
Cyclopentane		2	1	6 d	6.2	0.6
Cyclohexane	353.9	1	3	24 h	0.65	0.08
n-Pentane	309.3	1	3	24 h	0.80	0.1
iso-Pentane	301.0	1	3	24 h	0.48	0.06
n-Octane	398.8	1	3	24 h	0.76	0.14

[a] Approximate values not corrected for the presence of ^{13}C. For further reaction conditions, see text.

single substrate binding process to surface Ru. That could lead to the formation of CD_2 groups or to two separate CD groups.

In the case of the other substrates, *n*-pentane, *n*-octane, *iso*-pentane, cyclohexane, the number of batch cycles was reduced to three for convenience, as this is sufficient to obtain information about the catalytic activity. Compared to cyclopentane, for all the other alkanes, very low turnovers are observed and at best a single deuterium atom is incorporated (Table 1). As an example, the details of the mole peak part of the mass spectrum of the cyclohexane experiment are depicted in Figure 1d.

This much more efficient deuteration of cyclopentane compared to the other alkanes was very surprising: Under energetic considerations such a difference is not to be expected since all C–H bonds in alkanes have comparable cleavage energies between 402 and 439 kJ/mol.[27,28] In particular, cyclopentane (395–403 kJ/mol) and cyclohexane (400 kJ/mol) are quite similar with respect to C–H bond dissociation energies.[29] Considering the general reactivity order for H/D exchange in alkanes, which attributes the highest activity to C–H groups in cycloalkanes,[20] one would anticipate a similar reactivity of cyclopentane and cyclohexane.

To exclude trivial causes of the effect, we first checked the boiling points of the substrates included in Table 1, but no influence on the deuterium fraction achieved could be established. Next, we investigated the deuteration of cyclopentane and cyclohexane under fully inert conditions (1 ml liquid alkanes in a total volume of 90 mL containing 4 bar D_2 gas, oxygen free environment) to exclude that a reaction of the catalyst with spurious oxygen or other impurities present in the solvent or the atmosphere of the glove box accounts for the different efficiencies in deuteration. The obtained isotopomer patterns in Figure S1a,c clearly show that the difference in the deuteration efficiency is reproducible under inert conditions (333 K, 4 bar D_2, degassed substrates). As further shown in Figure S1b,d, although the conversion to higher deuterated isotopomers increases with increasing temperature from 333 K to 373 K, the pronounced difference between cyclopentane and cyclohexane is still present. These results show that the different deuteration efficiencies are of general nature and not the result of a spurious presence of oxygen. Finally, we investigated the influence of the stabilizing dppb ligand on the deuteration of alkanes by comparing the Ru/dppb catalyst with ruthenium nanoparticles supported on Siralox (R), which contain no stabilizing ligand system. As shown in Figure S2, also for this catalyst system the pronounced difference between cyclopentane and cyclohexane is present, suggesting that the stabilizing ligand system has no significant influence on the deuteration efficiency of ruthenium nanoparticles.

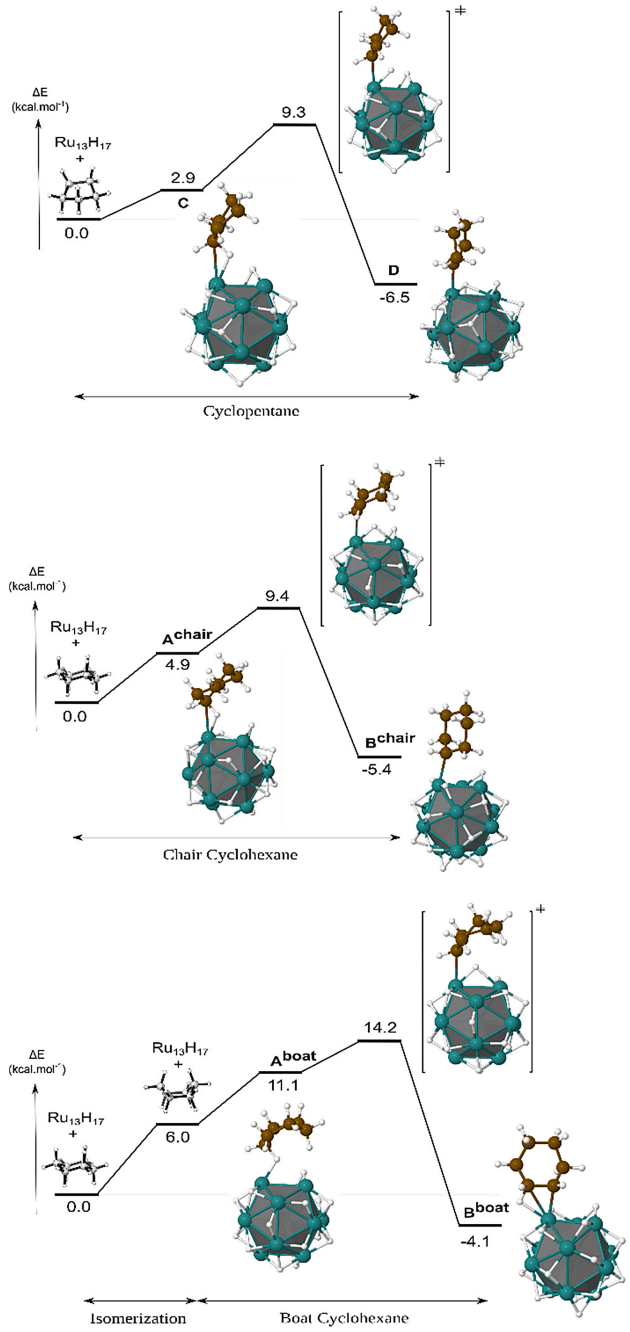
Thermodynamic or kinetic reaction control? In the experiment with 2 mL cyclopentane that was performed with only one batch cycle and a reaction time of 6 days (Table 1) we noticed that the thermodynamic equilibrium was not yet reached. Assuming a statistical equilibrium, a deuterium fraction of about 18% is to be expected in a system with 2 mL cyclopentane (21.1 mmol, 211 eq. H) and 6 bar D_2 in 95 mL (23.4 mmol, 46.8 eq. D). It can, therefore, be concluded that the different substrate reactivities are not caused by equilibrium isotope effects. Thus, the results are kinetically controlled. Furthermore, it can be concluded that the low reactivity of cyclohexane is not a consequence of diffusion problems caused by molecular size. Preliminary experiments performed on toluene, which exhibits a similar calculated van der Waals volume as cyclohexane (toluene = 98.9/cyclohexane = 101.9 Å^3),[30] indicate a much larger reactivity towards deuteration, i.e. toluene can readily access the surface and react. Thus, the ligand sphere of the particle does not act as a steric- or diffusion limiting barrier.

Reaction mechanism. To identify the rate limiting step in the C–H activation the generally accepted reaction mechanism for the activation of alkanes by metal complexes is adapted in Scheme S1 to the case of alkane deuteration by transition metal nanoparticles.

In the first step (see Scheme S1a), surface hydride of the latter – which contain a large number of defects such as edges, apexes and steps[31] that offer coordinatively unsaturated metal atoms – are deuterated releasing HD when they are exposed to D_2 gas.[15] In the second step, the alkane substrate forms a σ-complex with surface Ru atoms and transfers an H from C to Ru (Scheme S1b) corresponding to an oxidative cleavage of a surface alkyl. As surface H/D exchange is fast,[15] there is a great chance that in the backward reaction a D is transferred to C. Finally, the deuterated product is released from the surface.

In several studies, Ball *et al.*[32,33,34] have elucidated the structures of σ-complexes of cyclohexane, cyclopentane and *n*-pentane with Re fragments by NMR spectroscopy. They observed very similar structures of the C–H-Re moiety. Moreover, DFT calculations indicated similar free energies of activation of H transfer from C to Re.[35] That is in line with previous DFT calculations of the pathway of deuteration of compounds with amino groups using Ru-nanoparticles.[18,19]

To check whether the oxidative cleavage of the σ-complex is the rate limiting step also in the deuteration of alkanes by RuNP we have carried out DFT calculations at the DFT-PBE level of theory. Thus, the C–H activation of the cyclopentane and of the two more stable conformations of cyclohexane (twist-boat and chair) has been studied using a 0.5 nm ruthenium cluster with 1.4 H atoms per Ru surface atom ($Ru_{13}H_{17}$) as RuNP model. The same strategy has also been successfully used in previous studies to shed light both on the enantiospecific C–H activation of an isopropylamine using RuNPs as catalysts[19] and to compare the C–C vs. C–H activation of ethane at the surface of RuNPs.[36] In all cases (Scheme 2), the C–H activation reaction begins by the formation of an adduct ($\mathbf{A}^{chair}$, $\mathbf{A}^{boat}$ and **C**) that exhibits a so-called agostic interaction, i.e., a three-center two electron bond between a C–H bonding orbital of one of the CH_2 groups lifted out of the plane of the ring and an empty metal orbital. The increase of the C–H bond length by around 0.07 Å, independently of the reactant, is indicative of the formation of this agostic interaction. For the chair cyclohexane and cyclopentane it is worth noting that the C–H bond activation is a kinetically very accessible process with the same activation barrier of ~9.4 kcal/mol. From a thermodynamic point of view, the C–H bond breaking is also very similar and



Scheme 2. C–H activation pathway for twist-boat cyclohexane, chair cyclohexane and cyclopentane at Ru cluster surface.

slightly favored, between −5.4 and −6.5 kcal/mol. The C–H bond activation barrier in the twist boat conformation of cyclohexane was found to be 14.2 kcal/mol which is somewhat larger than calculated for the other species. That difference may be attributed to the intrinsic isomerization cost between the chair and twist-boat conformations.

Unfortunately, we were not able in this study to explore whether different contributions to the binding and/or activation entropies are responsible for the different reactivity of cyclopentane with respect to the other alkanes. That could arise from a different reduction of the number of molecular configurations in the σ-complexes and the transition states with respect to the unbound states. Such a "ligand configurational entropy" has been demonstrated in the case of binding of small flexible molecules to proteins.[37] This reduction of the configurational space is symbolized schematically in Scheme S1b for the binding and the reaction of the central C–H group of *n*-pentane to Ru. In other words, in the transition state of the oxidative cleavage only certain molecular conformations may be reactive. That circumstance depends both on the properties of the substrate molecules as well as on the details of the configuration of the catalytic Ru atoms and the adjacent organic stabilizing ligands. However, ligand configurational entropy contributions may not play the decisive part of the different reactivity of cyclopentane and of the other alkanes.

Thus, our calculations derived for "ideal" alkane/$Ru_{13}H_{17}$ model systems indicate similar binding and activation enthalpies of C–H activation of cyclopentane and cyclohexane. It was not possible in the present study to explore whether different binding and activation entropies which could arise from a different conformational entropy decrease upon binding is the cause. Anyway, it might be possible that there are no major differences in these entropy terms.

As the differences between the C–H activation of cyclopentane and the other alkanes by RuNP are well reproducible, we have to conclude that the latter exhibit a specifically enhanced reactivity for cyclopentane which can, however, not be explained in terms of the "ideal" alkane/RuNP model. That means that the "real" nanoparticles do not only contain a complex surface with many defects and disordered ligands but also provide the possibility of specific intra- and intermolecular primary and secondary interactions with substrates resulting in different reactivities for different substrates. In a way, the real RuNP behave in a similar way as substrate recognizing enzymes.

In conclusion, the liganded Ru-surface exhibits a specific recognition for cyclopentane whose origin is not yet understood but must arise from a complex interplay of various intra- and intermolecular surface-substrate interactions, perhaps accompanied by different tunneling rates, owing to conformational changes in the course of the transfer reaction. Thus, the observation of the structure-dependent C–H activation of alkanes by RuNP opens up a lot of new questions and challenging tasks for the future, in particular the vision of preferentially catalyzing certain reactions by suitable modifications of the nanoparticle-ligand interface.

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Conflict of Interest

The authors declare no conflict of interest.

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