Control of H–C(sp³) Bond Cleavage Stoichiometry: Clean Reversible Alkyl Ligand Exchange with Alkane in $[LPt(Alk)(H)_2]^+$ (L = [2.1.1]-(2,6)-Pyridinophane)**

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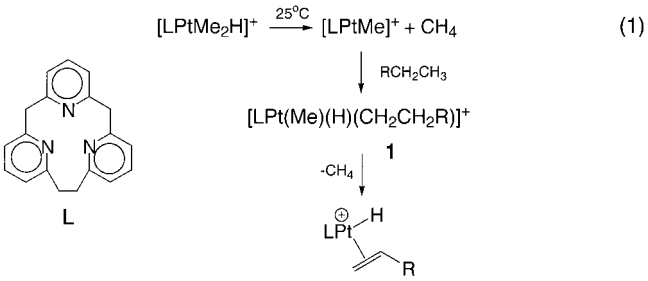
The ability of platinum compounds to activate methane catalytically in aqueous solution was first described more than 30 years ago.[1] Determining the mechanism of the Shilov reaction, which was considered to be an oxidative addition of an alkane to a platinum(II) center, remained challenging for over 25 years. First, increasingly persistent alkylhydridoplatinum(IV) complexes have been discovered,[2] and then the ability of platinum(II) species to add hydrocarbons to produce very stable platinum(IV) alkyl hydrides was demonstrated.[3]

Recent work[4] has shown that the transient $[LPtCH_3]^+$, where L is a ligand that cannot structurally accommodate the square-planar geometry preferred by four-coordinate Pt^{II} species and only modestly stabilizes the related octahedral alkane oxidative addition products, cleaves alkane C–H bonds. Here L is [2.1.1]-(2,6)-pyridinophane, and the transient is available according to Equation (1) in Scheme 1. This transient cleaves one substrate C–H bond, but methane is eliminated easily from the Pt^{IV} intermediate **1**; β-H elimination from the derived Pt^{II} alkyl compound then leads to net conversion of alkane to (coordinated) olefin, thus accomplishing a second substrate C–H bond cleavage.



Scheme 1. Synthesis of $[LPtMe]^+$ and reaction to give **1**.

To obtain alkane activation products different from the hydrido *olefin* complexes, we suggest here a modification of the starting dialkylhydridoplatinum(IV) complex to allow only an alkane *single* C–H bond activation event. For this we needed a species with a *single* alkyl ligand attached to a platinum(IV) center which will leave one hydride in the transient $[LPtX]^+$ (X = H) species. As a synthetic source of this transient, we initially considered whether $[LPtMe(H)_2]^+$ would selectively eliminate methane rather than H_2. The same question has been addressed recently for the complex $TpPtMeH_2$.[5] The free energies for methane and for H_2 elimination from $[LPtMe(H)_2]^+$ were calculated (DFT, PBE functional,[6] SBK basis set,[7] and program package Priroda[8]; Figure 1) and show that methane elimination is favored, both thermodynamically and kinetically,[9] by more than 13 kcal mol^{-1} relative to H_2 elimination. Due to the macrocycle constraints, Pt^{II} cannot achieve a planar four-coordinate geometry in $[LPtH]^+$ (Figure 1), and the best geometry is

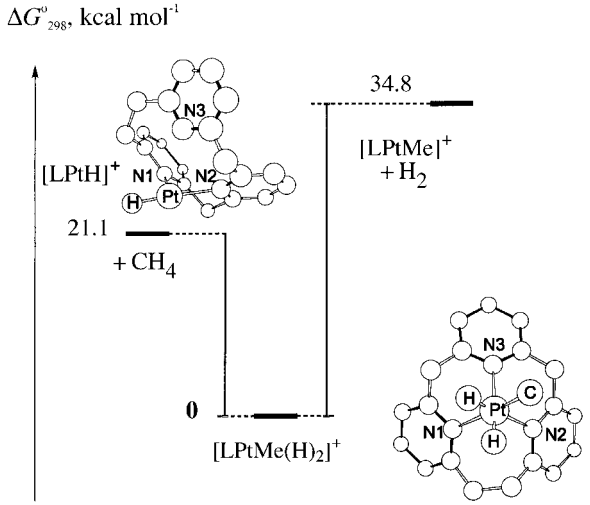
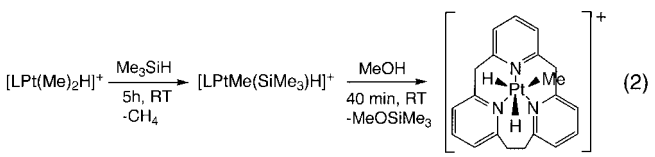


Figure 1. DFT-calculated Gibbs free energy [kcal mol^{-1}] of methane versus dihydrogen elimination from $[LPtMe(H)_2]^+$. Selected bond lengths [Å]: $[LPtH]^+$: Pt-N1 1.991, Pt-N2 2.173, Pt-N3 2.985; $[LPtMe(H)_2]^+$: Pt-N1 2.243, Pt-N2 2.243, Pt-N3 2.222.

three-coordinate T-shaped, with only 14 valence electrons. The out-of-plane pendant N3 atom interacts negligibly with the Pt^{II} center, and the longer distance of Pt to N2 than to N1 shows the *trans* influence of hydride.[10] Based on the energies in Figure 1, we expected to develop reversible alkane single C–H bond activation chemistry with a $[LPtH]^+$ transient; this is unprecedented for Pt^{II}.

The synthesis of $[LPtMe(H)_2]^+$,[11] as its $[BAr^F_4]^-$ salt (Ar^F = 3,5-$(CF_3)_2C_6H_3$), is summarized in Equation (2) (> 98% yield based on NMR data, relative to signal for BAr^F_4; yield of isolated product 85%). The new dihydridoplatinum(IV) com-



plex is air- and water-stable and can be recrystallized from a warm water–methanol mixture. No decomposition of this complex as a solid is observed at room temperature for at least two months. According to ^1H and ^{13}C NMR data, the

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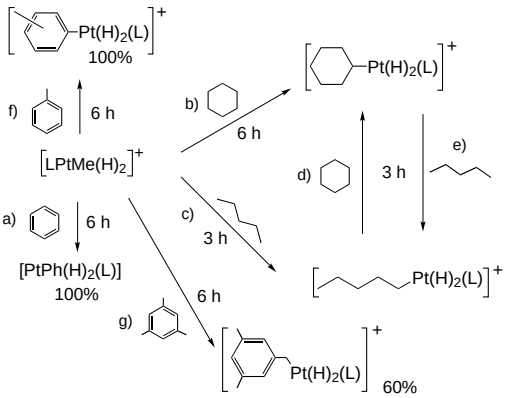
$[LPtMe(H)_2]^+$ ion is unsymmetrical. The ^1H NMR spectrum shows two separate resonance signals for nonequivalent hydrido ligands at $\delta = -20.37$ (s, $^1J_{Pt,H} = 1318$ Hz) and -19.32 ppm (s, $^1J_{Pt,H} = 1276$ Hz) (CD_2Cl_2, 21 °C), two sets of signals with an AX pattern for the ligand methylene bridges, three triplets for *para* protons of pyridine residues in a 1:1:1 ratio, and six doublets for the corresponding *meta* protons of equal intensity.

When $[LPtMe(H)_2]^+$ was heated in a solution of dichloromethane containing benzene (50 vol %) in a sealed NMR tube at 86 °C, the NMR signals of the methyl ligand and both hydride ligands of the starting complex gradually disappear and two new hydride resonance signals appear at $\delta = -19.24$ (s, $^1J_{Pt,H} = 1349$ Hz) and -18.13 ppm (s, $^1J_{Pt,H} = 1307$ Hz) (CD_2Cl_2, 21 °C). Over 6 h, the starting complex transforms almost quantitatively into the dihydridophenylplatinum(IV) complex of the same low symmetry as its methyl predecessor (Scheme 2a) (> 98 % yield based on NMR data, relative to signal for BAr^F_4; yield of isolated product 80 %).



Scheme 2. Reactions of $[LPtMe(H_2)]^+$. See text for details.

Thermolysis of $[LPtMe(H)_2]^+$ in 1:1 mixtures of cyclohexane or *n*-pentane (Scheme 2b and c, respectively) and CD_2Cl_2 used as a solvent also cleaved C–H bonds. After $[LPtMe(H)_2]^+$ had been heated for 3–6 h at 86 °C, new dihydrido alkyl complexes $[LPt(Alk)(H)_2]^+$ were obtained in 80 % (Alk = cyclohexyl; Cy) yield (based on NMR data, relative to signal for BAr^F_4) or 70 % (Alk = *n*-amyl; *n*-Am) yield (based on NMR data, relative to signal for BAr^F_4). The less than quantitative yield is due to side reactions with dichloromethane. In each case, two new hydride resonance signals appeared together with characteristic multiplets of methylene and methine protons in the α-position to the platinum center, along with their corresponding platinum satellites (see Supporting Information). No significant amounts of dihydrido *sec*-pentyl isomers were observed in the case of *n*-pentane even after longer time (20 h at 86 °C), thus indicating the high thermodynamic (see below) selectivity of the transient $[LPtH]^+$ species towards primary alkane C–H bonds. Both cyclohexyl and *n*-pentyl dihydrides have been isolated, recrystallized from a warm water–methanol mixture, and further characterized by ^{13}C NMR spectroscopy.

Why do these reactions stop at Pt^{IV} alkyl compounds, rather than proceeding to the Pt^{II} hydrido olefin products (Scheme 1) produced when the reactive transient is $[LPtMe]^+$? The reason is precisely the same as why $[LPtMe(H)_2]^+$ loses methane, not H_2: the strong energetic preference against H_2 loss shown in Figure 1.

Figure 1, together with the electronic similarly of $[LPtR(H)_2]^+$ when R = methyl, amyl, or cyclohexyl, suggests that the alkane cleavage shown in Scheme 2 should be reversible, to regenerate $[LPtH]^+$. The reversibility of alkyl ligand exchange at a platinum(IV) center at 86 °C has been shown by two experiments in which either *n*-amyl- or cyclohexyldihydridoplatinum(IV) complexes were heated at this temperature with a 1:1 mixture of the other related hydrocarbon and CD_2Cl_2. In the case of $[LPt(n\text{-}Am)(H)_2]^+$ the conversion was complete in 3 h with 60 % yield of $[LPtCy(H)_2]^+$ (Scheme 2d). Free *n*-pentane was detected in the course of this reaction. Some of the starting compound decomposed to form unidentified products presumably derived from reaction with CD_2Cl_2. Similarly, $[LPtCy(H)_2]^+$ reacted completely with *n*-pentane in 3 h to form $[LPt(n\text{-}Am)(H)_2]^+$ in 50 % yield (Scheme 2e). Since these hydrocarbyl exchange reactions of secondary (Cy) and primary alkyl compounds are complete within 3 h we can conclude that this time is sufficient to bring *n*-pentane to equilibrium with corresponding isomeric primary and secondary pentyl dihydrides. Therefore, the observed selectivity of *n*-pentane C–H bond cleavage (see above) reflects thermodynamic, not kinetic selectivity of transient $[LPtH]^+$.

To learn more about the regioselectivity of transient $[LPtH]^+$ we studied the reactivity of $[LPtMe(H)_2]^+$ towards toluene and mesitylene, two other aromatic hydrocarbons that offered both saturated and aromatic C–H bonds. Both react cleanly in the course of 3–6 h at 86 °C in 1:1 hydrocarbon–CD_2Cl_2 mixtures with $[LPtMe(H)_2]^+$ to produce new platinum(IV) hydrocarbyl dihydrides (Scheme 2f and g, respectively). Toluene traps the transient efficiently and gives rise to two distinct products in a 2:1 ratio. Their hydrides resonate at $\delta = -19.28$ (s, $^1J_{Pt,H} = 1350$ Hz) and -18.17 ppm (s, $^1J_{Pt,H} = 1310$ Hz) for the major isomer and $\delta = -19.30$ (s, $^1J_{Pt,H} = 1351$ Hz) and -18.19 ppm (s, $^1J_{Pt,H} = 1308$ Hz) for the minor isomer. Two distinct methyl groups of the tolyl ligands integrate as 3H each relative to their hydride resonance signals. According to the pattern of aryl resonance signals, the major product is the *meta*-tolyl isomer, $[LPt(m\text{-}Tol)(H)_2]^+$. The minor product is assigned as the *para*-tolyl isomer. Neither an *ortho* isomer nor a product of methyl C–H bond cleavage is observed. It is usual[12] that aromatic C–H bonds are preferred in oxidative addition to a metal center. Mesitylene, however, gives a single reaction product which is obtained in poorer yield (60 %, based on NMR data, relative to the signal for BAr^F_4) than alkanes (Scheme 2g). In this case new hydride resonance signals appear at $\delta = -20.13$ (s, $^1J_{Pt,H} = 1334$ Hz) and -19.20 ppm (s, $^1J_{Pt,H} = 1290$ Hz). Aromatic protons show two broadened singlets, $\delta = 6.62$ (br s, 1H; *para*-CH) and 6.73 ppm (br s, 2H; *ortho*-CH); two singlets integrate as two equivalent methyl groups (2.16; s, 6H) and as a platinum-bound methylene group with characteristic platinum satellites at $\delta = 3.46$ ppm (apparent s, $^1J_{Pt,H} =$ 110 Hz, 2H). These data are consistent with the formulation of the reaction product as $[LPt(CH_2\text{-}3,5\text{-}Me_2C_6H_3)(H)_2]^+$.

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Thus, 1,3,5-trimethylbenzene fails to react with sterically inaccessible aromatic C–H bonds but prefers activation of less hindered saturated C–H bonds. The only precedent for such selectivity of mesitylene oxidative addition to a platinum atom is the d^{10} transient $[Pt(Cy_2PC_2H_4PCy_2)]$.[13,14] At the same time, formation of mixtures of isomeric aryl- and benzylplatinum(II) complexes as products of methylarene activation with platinum(II) complexes is known.[15]

Thus, the influence of X = H versus X = Me in transient $[LPtX]^+$ is controlled by both the thermodynamics and kinetics of the reductive elimination of the resulting $[LPtH(R)X]^+$. When X = Me, methane elimination is accessible, but when X = H, H_2 elimination is energetically inaccessible, resulting in a Pt^{IV} product and only a single alkane C–H bond cleaved. In short, the number of methyl groups in the $[LPt(Me)_nH_{3-n}]^+$ precursor dictates the number of alkane substrate C–H bonds that can be altered. This controllable production of alkane-derived $[Pt^{IV}(alkyl)]$ or $[Pt^{II}(olefin)]$ complexes may prove valuable in subsequent efforts to derivatize and effect net production of functionalized organic products from alkanes.

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[9] Activation barriers, not shown in Figure 1, fully support this claim; they will be reported later.

[10] Transient $[LPtH]^+$ might also be expected to be accessible by ethane elimination from $[LPtMe_2H]^+$, but DFT calculations show a lower ΔG^0_{298} for methane than for ethane elimination, +11 versus +16 kcal mol^{-1}, respectively.

[11] For a conversion of $[CpFe(\eta^2\text{-}HSiEt_3)]$ to $[CpFe(\eta^2\text{-}H_2)]$ and Et_3SiOMe by methanolysis see: E. Scharrer, S. Chang, M. Brookhart, *Organometallics* **1995**, *14*, 5686 – 5694.

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Directing Otherwise Incompatible Reactions in a Single Solution by Using DNA-Templated Organic Synthesis**

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General methods for translating amplifiable information carriers such as DNA into synthetic molecules may enable the evolution of non-natural molecules through iterated cycles of translation, selection, and amplification that are currently available only to proteins and nucleic acids. During the process of developing such a method, we recently discovered that DNA templates can sequence-specifically direct a broad range of chemical reactions without any apparent structural requirements.[1,2] The generality of DNA-templated synthesis together with appropriate linker and purification strategies enabled the first multistep small-molecule syntheses programmed by DNA templates,[3] which raised the possibility of using this approach to generate synthetic small-molecule libraries of useful complexity.

DNA-templated synthesis[4–24] can generate products individually linked to oligonucleotides that both encode and direct their syntheses.[1–3] This feature may enable reaction modes useful for library construction that are not available through current synthetic approaches. Present synthesis methodology, for example, cannot differentiate functional groups of similar reactivity on different molecules within the same solution even though such differentiation would enable diversification to take place without the effort or constraints associated with spatial separation. Here we report that DNA oligonucleotides can simultaneously direct several different types of synthetic reactions within the same solution, even though the reactants involved would be cross-reactive and therefore incompatible under traditional synthesis conditions. Our findings represent a new mode of reaction made possible by DNA-templated synthesis and may enable the one-pot diversification of synthetic library precursors into products of multiple reaction types.

The ability of DNA templates to mediate diversification by using different types of reaction without spatial separation was first tested by preparing three oligonucleotide templates of different DNA sequences (**1a**–**3a**) functionalized at their 5′-ends with maleimide groups and three oligonucleotide reagents (**4a**–**6a**) functionalized at their 3′-ends with an amine, thiol, or nitroalkane group, respectively. The DNA sequences of the three reagents each contained a different 10-base annealing region that was complementary to ten bases

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