Solvent-controlled switch of selectivity between sp^2 and sp^3 C–H bond activation by platinum(II)†

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By merely changing the solvent, two different cyclometalated platinum complexes resulted from either sp^2 or sp^3 C–H bond activation can be prepared selectively. For example, the reaction of L1 with K_2PtCl_4 in MeCN gave exclusively kinetic product 1a, while the reaction in AcOH was thermodynamically controlled and produced predominantly 1b.

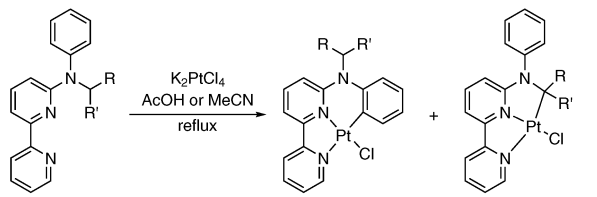
The activation of unactivated C–H bonds by transition metals tackles one of the most challenging chemical transformations and has enormous potential in chemical industry.[1] The C–H activation by platinum salts is among the earliest and most extensively investigated processes.[2] Cyclometalation, an intramolecular version of C–H activation, has played a significant role in understanding the mechanistic details in the C–H activation process.[3] On the other hand, cyclometalated platinum compounds have demonstrated their unique applications in various areas from catalysis[4] to organoelectronic[5] and biological[6] fields. Control of selectivity is one of the most important issues in chemical synthesis. It is generally recognized that an aromatic C–H bond is more reactive toward activation by platinum complexes,[2b] but a recent study showed that there exists a delicate balance between sp^2 and sp^3 C–H bond activation in the reported platinum(II) complex system.[3d] Here we report a *solvent-controlled switch of selectivity* between sp^2 and sp^3 C–H bond activation[7] by K_2PtCl_4 (Table 1). Such a degree of solvent-manipulated control over the selectivity in the sp^2 and sp^3 C–H bond activation is rarely seen in the literature.[7a] To the best of our knowledge, this is the first report on a high degree of solvent-controlled switch of selectivity between sp^2 and sp^3 C–H bond activation by a platinum complex. It should be noted that a solvent-controlled C–C *vs.* C–H bond activation by a cationic rhodium complex has been reported.[8]

When ligand **L1** and K_2PtCl_4 in acetic acid were refluxed for 24 hours, a new compound was formed cleanly as revealed by the TLC analysis of the reaction mixture. In principle, with chelation to the bipyridine, the cyclometalation could be directed to either the *N*-phenyl ring (**1a**) or the methyl group (**1b**), namely, sp^2 *vs.* sp^3 C–H activation. One would expect the cyclometalation to occur at one of the *ortho* positions of the *N*-phenyl ring since the sp^2 C–H is considered to be more reactive. However, the new products were identified as predominantly **1b** (96%) formed from the activation of a C–H bond of the methyl group and **1a** was presented as a minor (4%) product (Table 1). The metalation position can be easily identified by examining the proton NMR spectrum of the product, which showed that the signal of the methyl group in the ligand disappeared and a new singlet peak appeared at 5.42 ppm displaying a platinum satellite with the coupling constant of 40 Hz ($^2J_{Pt-H}$).

When the methyl group was replaced with an ethyl (**L2**) or an isopropyl group (**L3**), **2b** and **3b** were obtained,‡ respectively (Table 1). No formation of **3a** by the sp^2 C–H activation was detected. The proton NMR of **2b** showed a quartet at 5.88 ppm displaying a platinum satellite ($^2J_{Pt-H}$ 48 Hz) and a doublet at 1.40 ppm, indicating a metalation at the CH_2 carbon of the *N*-ethyl group. The proton NMR of **3b** displayed a singlet at 1.48 ppm ($^3J_{Pt-H}$ 17.5 Hz) assigned to the methyl signal of the *N*-isopropyl group. The CH signal from the ligand disappeared as the hydrogen was removed by cycloplatination.

Surprisingly, when the reaction of **L1** with K_2PtCl_4 was carried out in acetonitrile, a complete switch of the selectivity from sp^3 to sp^2 C–H bond activation was achieved and **1a** was produced exclusively (Table 1). No products resulting from the sp^3 C–H activation were detected. The reaction of **L2** and **L3** gave predominantly **2a** and **3a**, respectively. The selectivity for **3a** was moderate, but the pure isomer could be isolated by just one recrystallization from dichloromethane–hexane.

Table 1 The reactions of **L1–L3** with K_2PtCl_4 in different solvents



	In AcOH			In MeCN		
Product	*t*/h	Ratio[a]	Yield[b]	*t*/h	Ratio[a]	Yield[b]
1a : **1b**	24	4 : 96	73%	72	100 : 0	73%
2a : **2b**	48	3 : 97	63%	48	93 : 7	70%
3a : **3b**	48	0 : 100	38%	72	70 : 30	36%

[a] Isomeric ratio determined by proton NMR spectra of the crude products. [b] Isolated yield of the pure major isomer.

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The structures of the complexes **3a** and **3b** were further confirmed by single crystal X-ray structure determination (Fig. 1). The complex **3b** displays a planar coordination geometry. The *N*-phenyl group is nearly perpendicular to the coordination plane, which is to minimize the steric interaction with the isopropyl and bipyridyl groups. The complex **3a** has a N^N*C coordination geometry featuring a fused five–six-membered metallacycle, where N*C denotes a six-membered and N^N denotes a five-membered chelation to the platinum.[5b,9] In contrast to **3b**, the tridentate chelating ligand in **3a** is not planar and the *N*-phenyl group is significantly bent with respect to the rest of the coordination geometry (for different views of the geometry of **3a** and **3b**, see Fig. S1 in ESI†). This geometric distortion from desired square planar structure of Pt(II) complexes is likely the result of the steric hindrance caused by the isopropyl group, since in a similar five–six-membered platinacycle where all three N-substituents are either phenyl or pyridine rings, the coordination geometry is closer to a square plane.[9]

Our next focus is to unveil the underlying factors responsible for this interesting selectivity in intramolecular C–H bond activation. We reasoned that the reaction in acetic acid may be thermodynamically controlled while the reaction in acetonitrile may be kinetically controlled. We accept the general notion of preference of sp^2 C–H bond activation, however, the complex formed through sp^3 C–H bond activation may be more stable than that through the sp^2 C–H activation because of the formation of a five-membered chelate. Five-membered metal chelation is generally considered to be more stable than the chelation of other sizes in coordination complexes.[10] Another major contributing factor is steric interaction of the pendent *N*-alkyl group with the tridentate chelating ligand. In complexes **1b–3b**, the pendent *N*-phenyl group can adopt a perpendicular orientation relative to the coordination plane to minimize the steric interaction.

The thermodynamic control of the reaction in acetic acid was furthered supported by the isomerization of **1a**. When isomerically pure **1a** was refluxed in acetic acid, the isomerization to **1b** proceeded slowly and toward near completion after 3 days (**1b** : **1a** = 96 : 4). This isomerization is likely taking place *via* acid-assisted cleavage of the Pt–C(sp^2) bond in **1a** followed by the activation of the methyl C–H bond by the platinum center, which gives the complex **1b**. When refluxing **1b** in acetonitrile, even in the presence of HCl or acetic acid, no isomerization to **1a** was detected.

When the reaction of **L1** with K_2PtCl_4 was carried out in AcOD, a high degree of deuterium incorporation was found at the *ortho* positions of the *N*-phenyl ring and the methylene group, along with partial H/D exchange detected on the pyridine ring as shown in Scheme 1. The H/D exchange at the *ortho*-position of the *N*-phenyl ring and the methylene group may be interpreted by reversible bipyridine-directed cycloplatination reaction. The H/D exchange on the pyridine ring is likely attained through the bidentate cyclometalation of the bipyridine ligand.[11] When the isomerization of **1a** was carried out in AcOD, a similar level of H/D exchange at the *ortho* position of the *N*-phenyl ring and the methylene group in the product **1d** was detected. There was no H/D exchange observed at the position of the bipyridine ring (Scheme 1).

A high degree of multiple D incorporation at the *ortho* positions of the *N*-phenyl ring and the methylene group would suggest that equilibrium might be readily established between the sp^2 and sp^3 C–H bond activation. However, when **1b** was refluxed in AcOD, interestingly, no H/D exchange was detected at the *ortho* position of the phenyl ring whereas a 90% D incorporation into the methylene group was observed (Scheme 1, **1e**). These observations suggest that the barrier for the cleavage of the C–Pt bond of **1b** by AcOD may be too high for the reversed process leading to the formation of **1a** to occur. The kinetic barrier for the sp^2 C–H bond activation must be very small so that a rapid equilibrium between **L1** and **1a** can be established and a high degree of D scrambling at the *ortho* position of the phenyl ring in the reaction of **L1** and

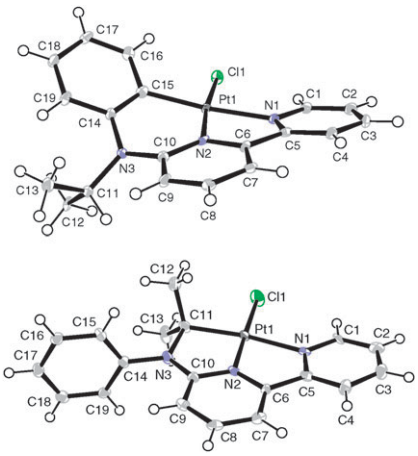
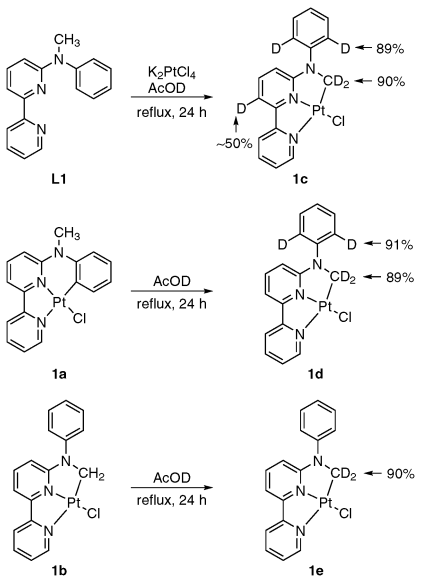


Fig. 1 ORTEP representation of molecules **3a** (top) and **3b** (bottom). Selected bond lengths (Å) and angles (°): **3a**: Pt(1)–C(15) 1.997(5), Pt(1)–N(1) 2.091(4), Pt(1)–N(2) 2.000(4), Pt(1)–Cl(1) 2.310(1), C(15)–Pt(1)–N(1) 167.32(18), N(2)–Pt(1)–Cl(1) 173.54; **3b**: Pt(1)–C(11) 2.026(6), Pt(1)–N(1) 2.115(5), Pt(1)–N(2) 1.944(5), Pt(1)–Cl(1) 2.3029(15), C(11)–Pt(1)–N(1) 163.1(2), N(2)–Pt(1)–Cl(1) 178.26 (14).



Scheme 1 Reaction of **L1** with K_2PtCl_4, isomerization of **1a**, and H/D exchange of **1b** in AcOD.

Table 2 The product ratio for the reactions of **L1** with K_2PtCl_4 in mixed solvents

AcOH–MeCN (48 h)		AcOH : MeCN (v/v, 80 : 20)	
AcOH : MeCN (v/v)	**1a** : **1b**	Time/h	**1a** : **1b**
50 : 50	100 : 0	10	69 : 31
70 : 30	70 : 30	20	58 : 42
80 : 20	45 : 55	40	25 : 75
90 : 10	26 : 74	80	5 : 95

isomerization of **1a** in AcOD could be achieved. The H/D at the methylene group may proceed through a dual agostic interaction.[3d]

In acetonitrile, the stronger solvent coordinating ability[12] may deactivate the platinum center toward more difficult sp^3 C–H bond activation, but not toward the sp^2 C–H activation. The results for the reaction of **L1** suggested that the barrier for the sp^2 C–H activation is much smaller than that of sp^3 C–H activation, so the kinetic product was obtained exclusively. However, with the increase of bulkiness of the *N*-alkyl group (methyl to ethyl to isopropyl), the steric demand for the reorganization of the ligand for the sp^2 C–H activation is increased and the difference in the activation barrier between sp^2 and sp^3 C–H activation is decreased, so the formation of **3b** becomes competitive (Table 1). To further explore the solvent effect on the reaction, we carried out the reaction of **L1** with K_2PtCl_4 in a mixture of acetonitrile and acetic acid and the results are summarized in Table 2. With 50 : 50 (v/v) of acetic acid and acetonitrile as the solvent, the reaction (90 °C, 48 h) still gave exclusively the sp^2 C–H bond activation product **1a**. However, when the amount of acetic acid was further increased, the reaction under the same conditions (90 °C, 48 h) produced a mixture of **1a** and **1b** with decreasing ratio of **1a** to **1b**. Furthermore, the product distribution was found to be time-dependent. For example, in 80 : 20 (v/v) of acetic acid and acetonitrile under reflux conditions, the product ratio of **1a** to **1b** at reaction time from 10 to 80 hours was decreased from 69 : 31 to 5 : 95 (Table 2). These results demonstrated that the formation of **1a** was kinetically controlled and *the solvent played a crucial role in controlling the chemical kinetics* involved in this reaction.

In summary, we have demonstrated that selective formation of cyclometalated platinum complexes through either the sp^2 or the sp^3 C–H bond activation can be readily achieved by simply switching the solvent. This remarkable solvent-controlled switch of selectivity not only offers an excellent method to control the product formation but also provides an interesting system for probing some important mechanistic issues associated with the transition metal-assisted C–H bond activations.

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Notes and references

‡ It is noteworthy that the reaction of **L2** also produced a small amount of **1b** as a byproduct (**1b** : **2b** = 7 : 93). The formation of **1b** must involve the cleavage of the sp^3 C–C bond of the ethyl group. In the reaction of the **L3**, byproducts resulting from the cleavage of C (isopropyl)–N bond were produced but neither **2b** nor **1b** was identified. When the methyl group of **L1** was replaced with a tertiary butyl group, the reaction of the resultant ligand under the same reaction conditions produced only the products associated with the cleavage of the C (*tert*-butyl)–N bond. The C–C and C–N bond cleavages are currently under investigation and will be reported in the future.

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