Mechanism of C−H Bond Activation of Alkyl-Substituted Benzenes by Cationic Platinum(II) Complexes

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While all methyl- and ethyl-substituted benzenes react with diimine Pt(II) methyl cations to give η^3-benzyl products, they do not all get there by the same pathway. For toluene and *p*-xylene, isotopic labeling shows that initial activation occurs at aryl positions with subsequent intermolecular conversion to the benzyl product. For ethylbenzene and 1,4-diethylbenzene, initial activation takes place exclusively at aryl C−H bonds, and conversion to the η^3-benzyl product takes place via intramolecular isomerization. Only in the most extreme case of steric crowding—the reaction of a bulky diimine platinum methyl cation (Ar = Mes) with triethylbenzene—does direct activation of the ethyl group become preferred to aryl activation.

Introduction

Selective C−H bond activation and functionalization is a long-standing and current goal in organic and organometallic chemistry.[1] In most cases to date, obtaining useful selectivities requires the assistance of directing groups.[2−5] In the absence of such direction, previous research has suggested that initial C−H bond activation is kinetically not very selective—less selective than hydrogen abstraction by radicals, for example—although reversible activation often leads to selective formation of products as a consequence of thermodynamic stability.[6−10] We have been examining reactivity patterns of alkyl-substituted benzenes, to identify factors controlling kinetic and thermodynamic preferences for activation of aryl vs alkyl C−H bonds.

Much of our work on the detailed mechanism of C−H bond activation has involved platinum methyl cations $[(NN)PtMe(solv)]^+$ (**2**),[10−12] where (NN) represents a bidentate diimine ligand and (solv) = trifluoroethanol (TFE). **2** is obtained by protonolysis of platinum dimethyl **1** in TFE with either $HBF_4{\cdot}OH_2$[11] (which affords an

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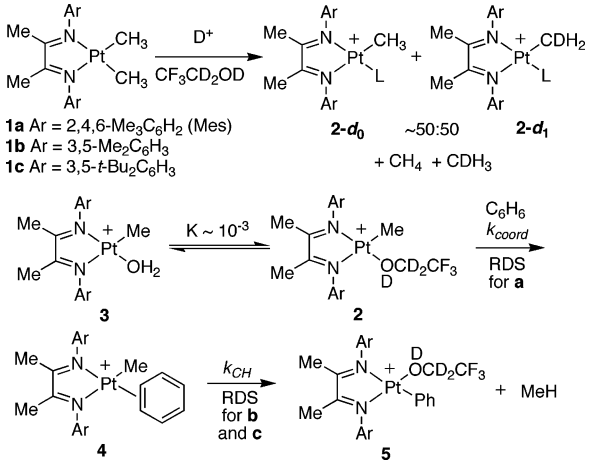
Scheme 1

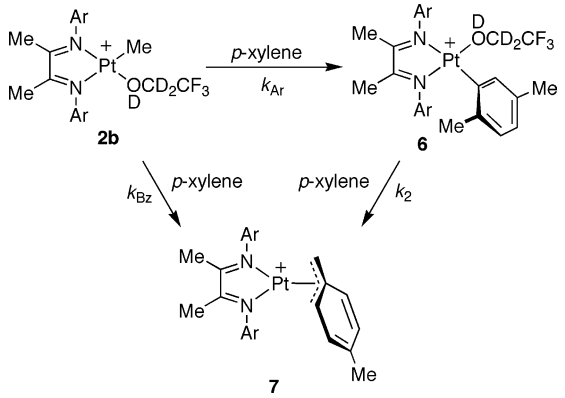


equilibrium mixture with aquo complex **3**)[10a,12] or $B(C_6F_5)_3$ (which produces acid by coordinating to trifluoroethanol),[13,14] yielding anhydrous **2**. In either case, if deuterated solvent is used, **2** is formed as a mixture of two isotopologs,[15,16] as shown in Scheme 1. (In subsequent schemes we will represent this mixture simply as Pt-Me.)

Platinum methyl cation **2** reacts with benzene to form phenyl complex **5** via benzene π-complex **4**.[12] Kinetics studies indicate that the identity of the rate-determining step depends on the degree of steric crowding: for relatively congested complexes with 2,6-disubstituted aryl substituents (Ar) on the diimine ligand, as for **2a** (Ar = mesitylene), coordination of benzene is rate limiting, whereas in the absence of *ortho* substitution (as for **2b** and **2c**), C−H bond activation becomes the slowest step (Scheme 1).[10a]

Anhydrous **2** reacts with alkyl-substituted benzenes (*p*-xylene, mesitylene, *p*-diethylbenzene) to form η^3-benzyl complexes as the sole final products, the apparent result of selective benzylic C−H bond activation.[10b,17] Kinetics experiments revealed that the reaction of **2b** with *p*-xylene involves competing direct benzylic activation to give η^3-complex **7** and aryl C−H bond activation

Scheme 2

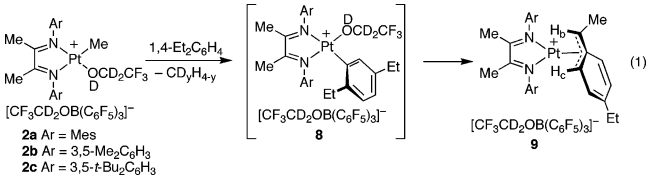


of *p*-xylene by **2b** to give **6**; the latter occurs about twice as fast. A subsequent, slower intermolecular reaction converts **6** to **7** (Scheme 2).[10b]

The present work seeks to extend these patterns to other methyl- and ethyl-substituted benzenes. Questions of interest include the following: Is an η^3-complex always the thermodynamic product? Do aryl and benzylic activation always compete? What are the relative reactivities of methyl and ethyl C−H bonds? For ethylbenzenes, is there direct secondary C−H bond activation of the benzylic methylene group? We show through the use of isotopic labeling and other experiments that while the η^3-complex is apparently always thermodynamically favored, there is *not* one single common pathway for getting there; rather the detailed mechanism depends on the steric nature of both the platinum diimine ligand and the substrate in an unexpectedly complex manner.

Results and Discussion

1,4-Diethylbenzene: Reactivity and Products. Extensive studies of reactivity and product properties were performed using 1,4-diethylbenzene as substrate, both because symmetry provides (relatively) straightforward interpretation and for comparison to the baseline *p*-xylene case. Irrespective of the steric nature of platinum methyl cation **2**, η^3-complex **9** was the sole final product obtained from the reaction of **2** with 1,4-diethylbenzene (eq 1, Figure 1). For less bulky diimine ligands (**2b**, **2c**), an intermediate aryl complex **8** could be observed by ^{1}H NMR spectroscopy before complete conversion to the η^3-complex, analogous to the behavior of *p*-xylene. In contrast when a sterically bulky aryl group was employed (**2a**), only the disappearance of starting cation and formation of product could be detected. Qualitatively, the rate of the reaction depended on the identity of the diimine aryl group: the half-life for the reaction (with 2.5 equiv of substrate) was less than 1 h for **2b** or **2c** but around 8 h for **2a**.



Although aryl activation products were not observed in the reaction of 1,4-diethylbenzene with the crowded

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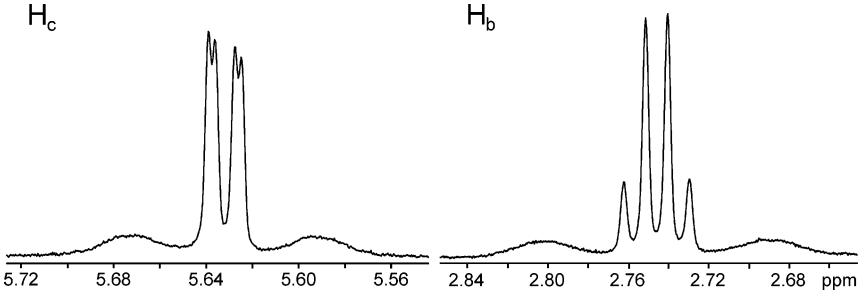
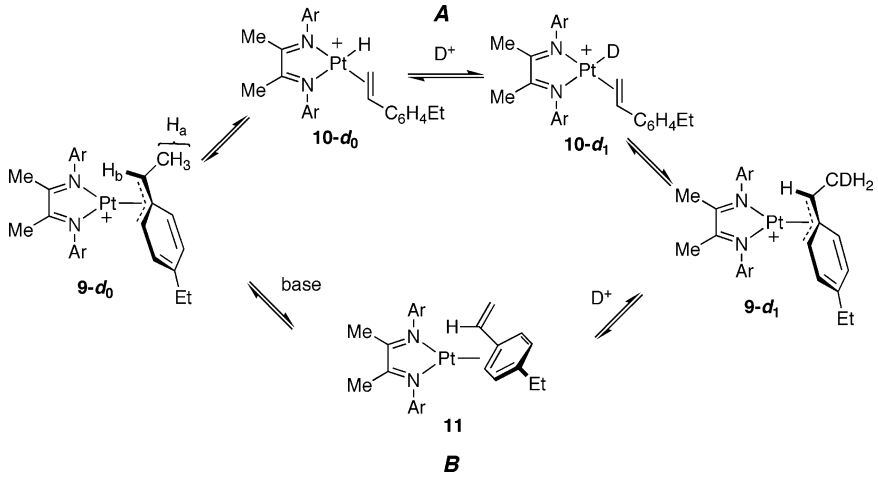
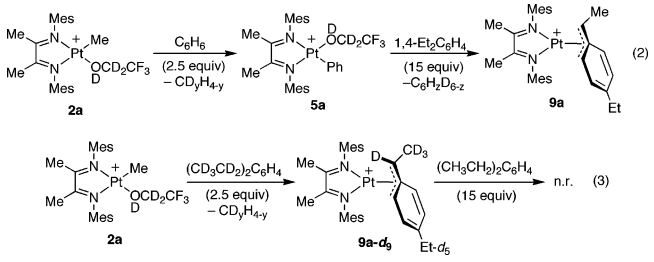


Figure 1. Diagnostic ^{1}H NMR peaks for **9a**, showing ^{195}Pt satellites[10b]

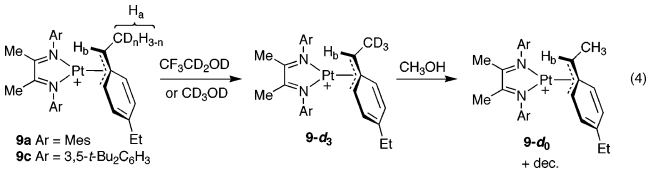
Scheme 3



platinum methyl cation **2a**, exposure of platinum phenyl cation **5a** to an excess of diethylbenzene resulted in the clean formation of the η^3-complex **9a** (eq 2). Aryl C−H bond activation thus appears to be reversible under these reaction conditions, but formation of the product η^3-benzyl complex is irreversible: **9a-**d_9 does not react with an excess of 1,4-diethylbenzene-d_0 (eq 3).[18]



While the η^3-complexes are resistant to further C−H bond activation, they do undergo slow isotope exchange with solvent at the methyl (H_a) position (eq 4). For example, after reaction of **2a** with 1,4-diethylbenzene, the methyl-H_a resonance for **9a** appeared as a doublet at 0.30 ppm in the ^{1}H NMR. In CF_3CD_2OD solution this resonance slowly became a multiplet as it lost intensity and eventually disappeared. No other signal's intensity was affected. Addition of methanol-d_4 increased the rate of isotope exchange. For smaller 3,5-disubstituted diimine ligands, exchange was competitive with C−H activation: after complete reaction, η^3-complex **9c** exhibited a multiplet at 0.30 ppm instead of the expected doublet. This isotope exchange at H_a was reversible: removal of the deuterated solvent and replacement with methanol-d_0 resulted in reappearance of the doublet, along with some concomitant decomposition (see below).



Two possible mechanisms for isotope exchange can be envisioned: β-hydride elimination or direct deprotonation (Scheme 3). β-Hydride elimination (path *A*) from **9** would generate an ethylstyrene-hydride-Pt(II) complex **10-**d_0, which could exchange with solvent to afford **10-**d_1. 2,1-Insertion of 4-ethylstyrene into **10-**d_1 would regenerate the benzyl product. The insertion would have to be completely regioselective[19] since the signal intensity of H_b remains unchanged. In the Brönsted acid−base mechanism (path *B*), deprotonation would generate ethylstyrene-Pt(0) complex **11**, which would reprotonate with D^+, giving exchange solely at

(18) This experimental result was not unique to complex **9a**: the η^3-complexes formed from reaction with *p*-xylene and ethylbenzene did not react further with excess different isotopologs of the starting substrate either.

(19) The insertion of styrene into related palladium hydride complexes typically occurs somewhat regioselectively, but not with complete selectivity. For leading references, see: (a) Iggo, J. A.; Kawashima, Y.; Liu, J.; Hiyama, T.; Nozaki, K. *Organometallics* **2003**, *22*, 5418−5422. (b) Nozaki, K.; Komaki, H.; Kawashima, Y.; Hiyama, T.; Matsubara, T. *J. Am. Chem. Soc.* **2001**, *123*, 534−544. (c) Milani, B.; Anzilutti, A.; Vicentini, L.; Sessanta o Santi, A.; Zangrando, E.; Geremia, S.; Mestroni, G. *Organometallics* **1997**, *16*, 5064−5075. (d) Brookhart, M.; Rix, F. C.; DeSimone, J. M.; Barborak, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 5894−5895. (e) Barsacchi, M.; Consiglio, G.; Medici, L.; Petrucci, G.; Suter, U. W. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 989−991.

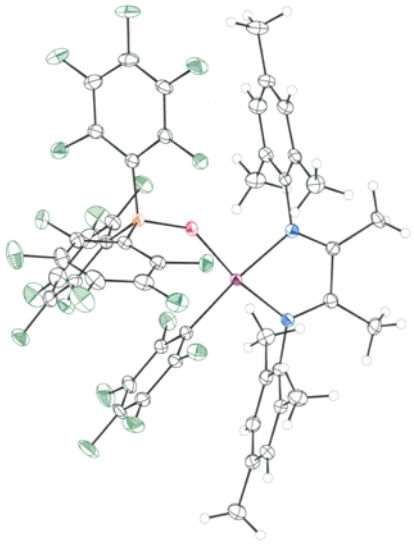
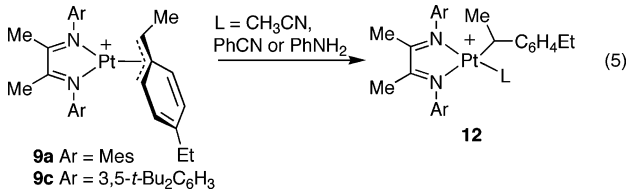


Figure 2. X-ray structure of **13a**.

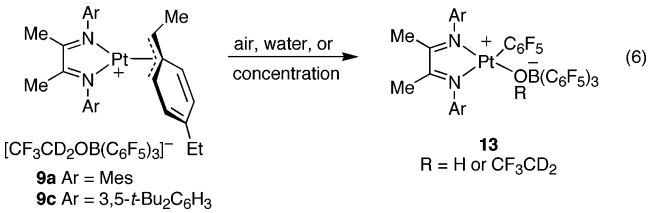
the methyl position. The latter appears more likely,[20] but the former cannot be ruled out at this time.

The η^3-bonding in **9** is not affected by the presence of oxygen Lewis bases such as Et_2O, MeOH, or H_2O. Better ligands, such as the nitrogen Lewis bases acetonitrile, benzonitrile, and aniline, are able to displace the benzene ring π-bond to form η^1-complexes **12** (eq 5), as revealed by significant differences in the ^{1}H NMR of **12**: the diagnostic Pt−H coupling for the H_c of **9** was no longer visible and its peak was shifted downfield.[21]



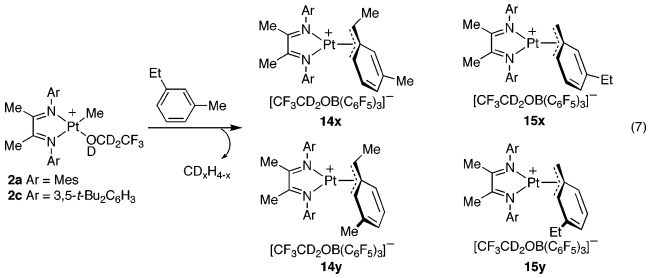
(5)

9 decomposes gradually, especially upon concentration or exposure of η^3-complex to water or air, to form **13**, resulting from aryl transfer from the counterion (eq 6). No **13** was observed spectroscopically during reaction of **2a** (Ar = Mes) with 1,4-diethylbenzene to form η^3-complex **9a**, but it was found as a competitive byproduct, in up to 20−30% yield, at low substrate concentrations, with a sterically less congested complex (**2c**) or substrate (ethylbenzene). The structure of **13a** (R = H) was determined crystallographically (Figure 2).[22,23]



(6)

Regioselectivity of Benzyl C−H Bond Activation: Methyl vs Ethyl Substituents. η^3-Complexes were obtained as sole final products from *all* the methyl- and/or ethyl-substituted benzenes studied. We further examined how the Pt center discriminates between substituents in mixed (methyl-ethyl) benzenes. In addition to the issue of regioselectivity, there is also the possibility of constitutional isomerism, depending on the nature of the substrate, because the η^3-benzyl structures appear to be nonfluxional on the NMR time scale.[10b] This is illustrated for the case of 3-ethyltoluene in eq 7, where products derived from both ethyl (**14**) and methyl (**15**) C−H bond activation were observed, each existing in two isomeric forms (denoted as **x** and **y**; we have no way of knowing which is which).



(7)

Both the regioselectivity of benzylic C−H bond activation and the isomeric selectivity of the resulting η^3-complex appear to depend on the steric natures of both the diimine ligand and the substrate, although the dependence is not completely straightforward (Table 1). In general we found a range from a slight preference to a substantial preference for ethyl activation, except for the case of the bulkiest diimine ligand (Ar = Mes) and substrate (3,5-dimethylethylbenzene), where activation of the methyl C−H bond was preferred by 13:87 (entry 1). With the less sterically encumbered substrate 4-ethyltoluene, the selectivity of C−H bond activation was reversed to give a strong preference for activation of the ethyl C−H bond (entry 2), a preference eroded only slightly for the *ortho*- or *meta*-analogues (entries 3 and 4). In most cases where constitutional isomerism is possible there is a strong preference for one isomer, with the exception of the products of ethyl activation of 3-ethyltoluene.

There appears to be a general preference for ethyl activation, with some reversals, most notably for the reaction of the most crowded complex with the trisubstituted arene (entry 1). However, a steric model clearly cannot explain *all* the behavior; for example, note the lower proportion of ethyl activation in entries 7, 8, 11, and 12 (smaller ligands) compared to entries 3 and 4. Since ethyl- and methyl-substituted benzenes react by different mechanisms (see below), the absence of any straightforward trend may not be surprising. In any case, the fact that ligand control of selectivity *can* be obtained is encouraging and suggests the possibility of useful transformations, such as asymmetric C−H activation, with the appropriate ligand choice.

Experiments with Regiospecifically Isotopically Labeled Substrates: General Comments. Although reaction of platinum methyl cations **2** with alkyl-substituted benzenes always leads to η^3-complexes as

(20) When deuterated alcohols more Lewis basic than TFE-d_3 were employed, isotope exchange was observed in the backbone methyl groups of the diimine ligand; see ref 10a.

(21) The crystal structure of an analogous (η^1-benzyl)(CH_3CN) complex from *p*-xylene has been determined; see ref 10b.

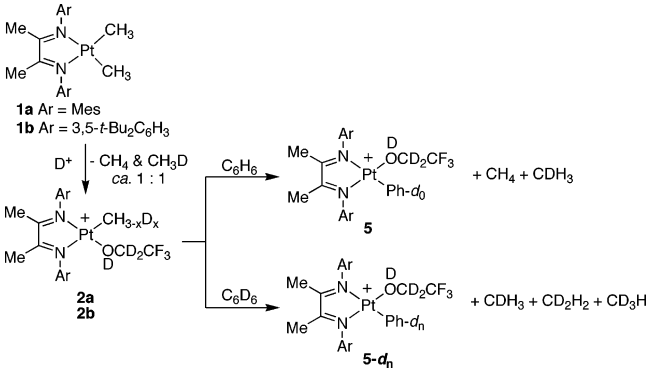
(22) Refer to the Supporting Information for crystallographic data.

(23) Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 248006.

Table 1. Comparison of Regioselectivity of C−H Bond Activation

Entry	L_nPtMe^+	substrate	regiosel. of ethyl:methyl activation	x : y in ethyl activation product	x : y in methyl activation product
1	**2a**		13:87	n.a.	>95:5
2	**2a**		87:13	n.a.	n.a.
3	**2a**		79:21	66:33	93:7
4	**2a**		78:22	>95:5	84:16
5	**2b**		20:80	n.a.	>95:5
6	**2b**		78:22	n.a.	n.a.
7	**2b**		51:49	50:50	79:21
8	**2b**		69:31	>95:5	76:24
9	**2c**		55:45	n.a.	>95:5
10	**2c**		79:21	n.a.	n.a.
11	**2c**		47:53	52:48	70:30
12	**2c**		54:46	>95:5	>95:5

Scheme 4



final product, the mechanism by which they are reached is far from clear. In some cases competitive aryl C−H activation may be observed, but failure to observe such species does not necessarily imply they are not intermediates. Evidence bearing on this question may be obtained from reactions of regiospecifically isotopically labeled substrates, followed by analysis of isotope distribution in the liberated methane, recovered substrate, and η^3-benzyl product.

The composition of methane isotopologs indicates the site of initial activation, as illustrated in Scheme 4 for the reaction of benzene with platinum methyl cation **2**. Activation of a C−H bond results in only two isotopologs of methane, CH_4 and CDH_3 (recall that a mixture of **2**-d_0 and **2**-d_1 is generated in the protonolysis of the starting platinum dimethyl complex).[16] In contrast, when a substrate C−D bond is activated, all four isotopologs of methane are generated.

In the latter case, multiple deuterium incorporation into methane occurs because dissociation of methane from the σ-complex **16** is slower than the reversible C−H bond cleavage/formation reactions via platinum hydride **17** (Scheme 5), in most cases leading to complete or near-complete statistical scrambling among the positions in **5** and methane.[10a,12,24] Additional incorporation of deuterium can be effected by isotope exchange between platinum hydride **17** and solvent. This latter process is influenced by basicity of reaction media and is at most a minor contributor unless a more basic medium, such as methanol, is employed.[10a]

Isotopic exchange in unreacted substrate can arise from two routes. The process outlined in Scheme 5 scrambles isotopes between substrate and the Pt-bound methyl group (and perhaps with solvent as well); hence, if substrate coordination and activation are reversible, exchanged substrate would be released, accompanied by exchange in the methyl group of unreacted **2**. The other route is a secondary reaction such as that seen for *p*-xylene (Scheme 2); for the case of deuterated methyl groups and undeuterated benzene ring (or the reverse) the conversion of **6** to **7** would change the isotope at one aromatic position. An additional possibility would be via the exchange with solvent at C_a of **9** (eq 4), but since other evidence indicates formation of η^3-benzyl product is completely irreversible (see above), this would not be expected to lead to any exchange in free substrate.

The isotopic composition of liberated methane and unconverted substrate was determined by ^{1}H NMR spectroscopy and mass spectrometry, respectively. For convenience, the methane formed during the initial protonolysis of **1** (a roughly equimolar mixture of CH_4 and CH_3D) was not separated, so that the measurement represents the sum of that sample and the methane formed during substrate activation (Scheme 4). The ratio of peak intensities for $[M + 1]^+/[M]^+$ (for D replacing H) or $[M - 1]^+/[M]^+$ (for H replacing D) provides an estimate of the extent of exchange in recovered free substrate; a value of 1,[25] for example, would indicate that a replacement has occurred in about half the molecules. Mass spectrometry can determine not only the extent but also the location of exchange, since most substrates exhibit two identifiable mass fragments: the parent ion ($[M]^+$) and the fragment ($[M - Me]^+$). If a ratio for the parent peak is the same as the corresponding ratio in $[M - Me]^+$, then the exchange must be exclusively on the arene ring; if they differ, some or all of the exchange is on the methyl group. Because of the different pathways available for multiple H−D substitution, which complicates quantitative analysis of these measurements, the discussion will be mostly qualitative.

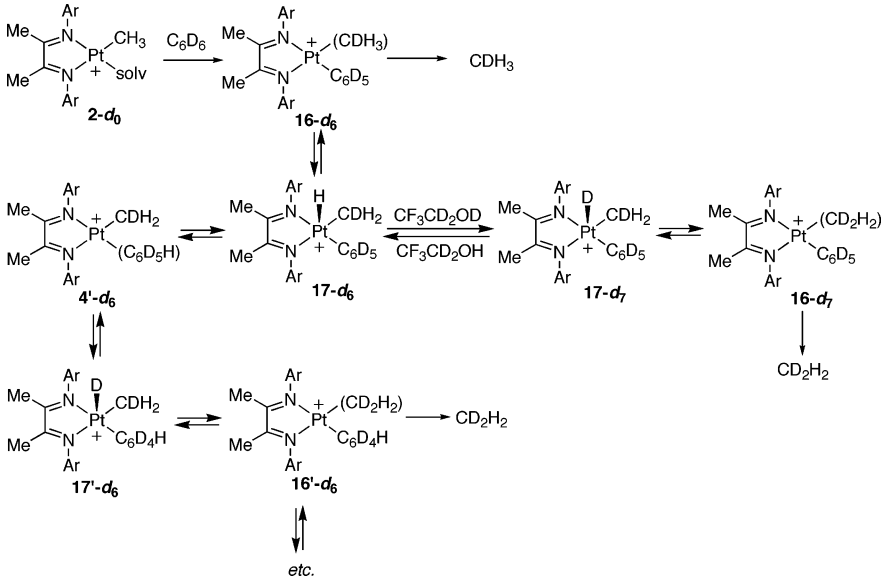
Evidence of isotope migration within final η^3-benzyl products can also provide information on steps following initial activation. As we shall see, such observations apply only to ethyl-substituted benzenes.

Examination of Methyl-Substituted Benzene Isotopologs. The results for reactions between variously labeled methyl-substituted benzenes and platinum methyl cations **2** (eq 8) are shown in Table 2. Let us first look in detail at the findings for the various toluene

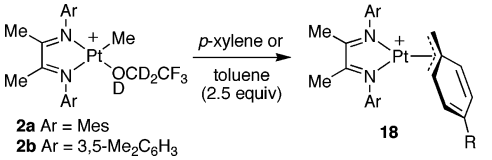
(24) For leading reports on the role of σ-complexes in C−H activation, see: (a) Mobley, T. A.; Schade, C.; Bergman, R. G. *J. Am. Chem. Soc.* **1995**, *117*, 7822−7823. (b) Stahl, S. S.; Labinger, J. A.; Bercaw, J. E. *J. Am. Chem. Soc.* **1996**, *118*, 5961−5976. (c) Bromberg, S. E.; Yang, H.; Asplund, M. C.; Lian, T.; McNamara, B. K.; Kotz, K. T.; Yeston, J. S.; Wilkens, M.; Frei, H.; Bergman, R. G.; Harris, C. B. *Science* **1997**, *278*, 260−263. (d) Geftakis, S.; Ball, G. E. *J. Am. Chem. Soc.* **1998**, *120*, 9953−9954. (e) Janak, K. E.; Parkin, G. *J. Am. Chem. Soc.* **2003**, *125*, 6889−6891. (f) Castro-Rodriguez, I.; Nakai, H.; Gantzel, P.; Zakharov, L. N.; Rheingold, A. L.; Meyer, K. *J. Am. Chem. Soc.* **2003**, *125*, 15734−15735. (g) Lawes, D. J.; Geftakis, S.; Ball, G. E. *J. Am. Chem. Soc.* **2005**, *127*, 4134−4135.

(25) There will be some $[M - 1]^+$ or $[M - 1]^+$ intensity resulting from fragmentation, natural abundance ^{13}C, etc.; all values (Tables 2, 3, 5) are corrected for the values observed in unexchanged substrates.

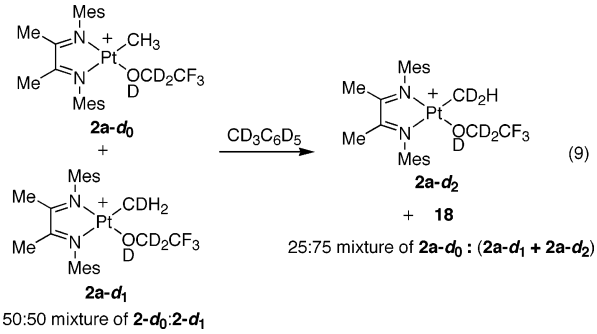
Scheme 5. Mechanisms for Multiple Methane Isotopolog Formation



isotopologs reacting with **2a** (entries 1−4).[26] The methane isotopolog distribution depends *only* on the aryl labeling: if the aryl positions are protonated, CH_4 and CH_3D are obtained in about 3:1 ratio, while if the aryl positions are deuterated, all four methane isotopologs are observed. This indicates that the initial site of C−H activation is exclusively the arene sites. We would expect scrambling between the five aryl positions and three Pt-Me positions to be rapid, analogous to the benzene case shown in Schemes 4 and 5. The Pt-Me consists of about 1:1 CH_3 and CH_2D, so the methane liberated by reaction with aryl-protonated toluenes should be predominantly (∼15/16) CH_4 (neglecting any isotope effects); when combined with the 1:1 mixture of CH_4 and CH_3D obtained in protonolysis, the overall ratio should be close to 3:1 CH_3:CH_2D. In contrast, aryl-deuterated toluenes should give a preponderance of deuterated methanes, as observed.



The extent of isotope exchange in free substrate depends on whether the aryl and benzylic positions have the same or opposite isotopes. In the first case, exchange will result from the above scrambling process followed by loss of toluene, either by reversible activation (i.e., loss of benzene from **4**) or by secondary reaction (as in Scheme 2). Consider entry 1: since **2** contains on average half a D per Pt, and the reaction was carried out with 2.5 equiv of substrate per Pt, full statistical scrambling would place a D in about 1/4 of the substrate present at the completion of reaction, in rough agreement with the observed values, which correspond to exchange in 1/5 of the molecules. Evidence for some reversible aryl C−H bond activation was obtained from monitoring the reaction progress using ^{1}H NMR spectroscopy: formation of additionally deuterated platinum methyl cation **2a** before its consumption was observed, but only when alkyl-substituted benzenes deuterated in aryl positions, such as toluene-d_5, were employed as substrates (eq 9). The platinum methyl isotopologs **2a**-d_1 and **2a**-d_2 were increased by about 25% at 60% conversion.[27]



What happens if the aryl and methyl positions of toluene have opposite labels? In the sequential mechanism shown (for *p*-xylene) in Scheme 2, initially formed Pt-aryl **6** reacts with the benzylic position of a second molecule of substrate to give the η^3-complex **7**. In the case of toluene, the isotopolog distribution for liberated methane indicates that *all* of the reaction follows this route. Hence, for this case, we would expect that *every* product-forming event will be accompanied by liberation of an aryl-exchanged molecule of toluene, and the extent of exchanged free substrate should be much higher. The exact level of exchange is difficult to calculate, as it involves not only this mechanism along with the scrambling described in the preceding paragraph, but also the extent to which exchanged molecules liberated at low conversion levels can re-react with another molecule of **2**. Qualitatively, though, it is clear from Table 2 (compare entries 3 and 4 to 1 and 2) that the observations agree well with this model.

(26) With the sterically smaller platinum methyl complex **2c** (Ar = 3,5-di-*tert*-butylbenzene), similar trends were observed. For presentation of these data, refer to the Supporting Information.

(27) The distribution of platinum methyl cation isotopologs was estimated from comparison of the Pt-Me resonance with an aryl proton resonance. See the Supporting Information for more details.

Table 2. Examination of Methyl-Substituted Benzene Isotopologs

				MS analysis of recovered substrate[b]			
entry	L_nPtMe^+	substrate	CH_4:CDH_3:CD_2H_2:CD_3H[a]	$[M+1]^+/[M]^+$	$[M-1]^+/[M]^+$	$[(M+1)-Me]^+/[M-Me]^+$	$[(M-1)-Me]^+/[M-Me]^+$
1	**2a**	$CH_3C_6H_5$	76:24:0:0	0.26		n.a.	n.a.
2	**2a**	$CD_3C_6D_5$	19:36:32:13		0.25	n.a.	n.a.
3	**2a**	$CH_3C_6D_5$	18:42:32:8		1.09	n.a.	n.a.
4	**2a**	$CD_3C_6H_5$	75:25:0:0	0.85		n.a.	n.a.
5	**2a**	1,4-$(CH_3)_2C_6D_4$	27:39:26:8		0.13		0.13
6	**2a**	1,4-$(CD_3)_2C_6H_4$	62:34:4:<1	0.37		0.39	
7	**2b**	1,4-$(CH_3)_2C_6D_4$	15:32:35:18		0.33		0.34
8	**2b**	1,4-$(CD_3)_2C_6H_4$	64:31:4:1	0.34		0.38	

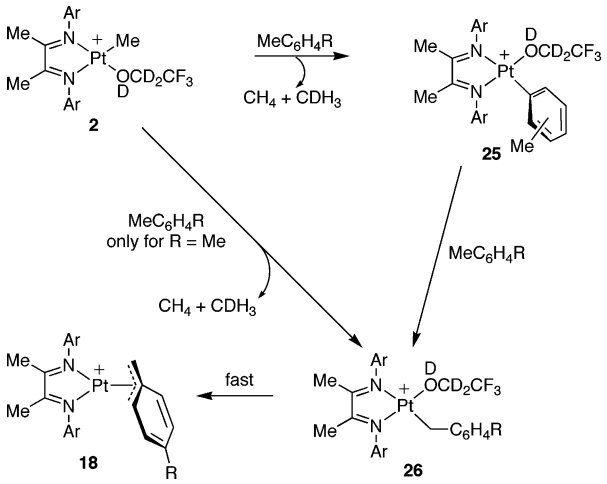
[a] The reported ratio includes the methane isotopologs produced from the protonation of the starting platinum dimethyl complex as determined using ^{1}H NMR spectroscopy. [b] Ion ratios corrected by corresponding values for unexchanged starting substrate.

The findings for xylene isotopologs are less clear, as expected from the fact that initial activation involves competition between the aryl and benzyl positions.[10b] Consistent with that earlier finding, *both* *p*-xylene-α,α,α,α′,α′,α′-d_6 and *p*-xylene-d_4 led to all four isotopologs of methane (entries 5−8), confirming that initial benzylic C−H bond activation is competitive with aryl C−H bond activation. Quantitatively, the degree of incorporation of label from benzylic positions appears initially to be less than expected: for **2b**, aryl C−H bond activation had been reported to proceed only twice as fast as benzylic CH_3 bond activation. Again, though, any calculation is complicated by the factors discussed above, the possibility of differential kinetic isotope effects (previously a KIE of 4.0 was found for aryl C−H bond activation only),[10b] and the further likelihood that reversible C−H activation applies *only* to aryl, not benzyl, positions; once a benzyl position has reacted, it is probable that the adjacent benzene π-bond coordinates immediately and prevents further scrambling (if benzyl C−H bond activation were reversible, the resultant η^3-benzyl complex could be exchanged with a different isotopolog, which was not observed; see above).[18] This factor would increase (possibly very substantially) the relative incorporation of H or D into liberated methane from aryl rather than benzyl positions. Isotope exchange in recovered substrate is (qualitatively) in agreement: comparison of the parent and (parent minus methyl) peaks shows clearly that all such exchange takes place in aryl, not benzylic, positions.

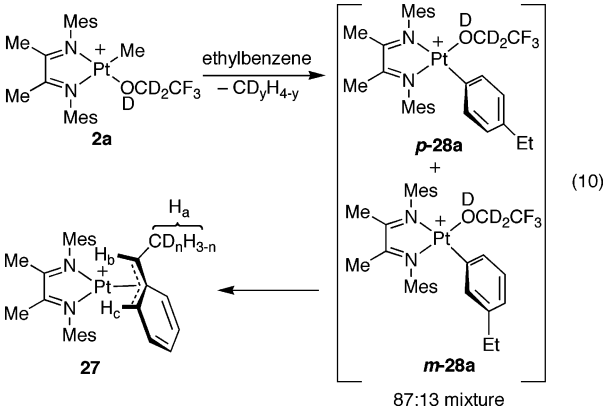
To summarize, these data suggest that the mechanism of C−H bond activation of methyl-substituted benzenes is dependent on the steric nature of the substrate (Scheme 6). Direct benzylic C−H bond activation to form **26** is competitive with aryl C−H bond activation only when the aryl sites are sterically congested, as in *p*-xylene. For the more accessible aryl C−H bonds in toluene, aryl C−H activation occurs rapidly. The activation of the benzylic methyl C−H bond presumably occurs via the corresponding σ-complex. Formation of this σ-complex could occur directly between reaction of platinum aryl complex **25** and the benzylic methyl C−H bond or more likely from initial π-coordination followed by migration to the σ-complex. Upon formation of the benzylic platinum(II) species **26**, the complex relaxes rapidly to η^3-product **18**, a thermodynamic well.

Examination of Ethyl-Substituted Benzene Isotopologs. Formation of η^3-complexes from the reaction of **2a**[26] with ethyl-substituted benzene isotopologs was investigated in the same manner. For ethylbenzene,

Scheme 6



results of analysis of the methane isotopologs and recovered substrate are shown in Table 3 and are mostly analogous to those found for toluene substrates. The methane isotopolog ratio depends only on the isotope in the aryl positions, and recovered ethylbenzene shows low levels of exchange, in the aryl positions only, arising from scrambling with D in the starting Pt methyl group. No participation of label in the ethyl group could be observed (entries 4−6). Together, these results show that initial C−H bond activation occurs exclusively at the sterically accessible aryl C−H bonds. By following the reaction progress using ^{1}H NMR spectroscopy, a mixture (87:13) of intermediate platinum aryl complexes (**28**) can be observed, presumably corresponding to activation of *para*- and *meta*-aryl C−H bonds (eq 10).



In striking contrast to the toluene case, though, there is *no* additional exchange in recovered substrate when

Table 3. Examination of Ethylbenzene Isotopologs

			MS analysis of recovered substrate[b]			
entry	substrate	CH_4:CDH_3:CD_2H_2:CD_3H[a]	$[M+1]^+/[M]^+$	$[M-1]^+/[M]^+$	$[(M+1)-Me]^+/[M-Me]^+$	$[(M-1)-Me]^+/[M-Me]^+$
1	$CH_3CH_2C_6H_5$	76:24:0:0	0.21		0.20	
2	$CD_3CD_2C_6D_5$	12:35:41:12		0.23		0.22
3	$CH_3CH_2C_6D_5$	14:37:38:11		0.22		0.23
4	$CH_3CD_2C_6H_5$	73:27:0:0	0.22		0.21	
5[c]	$CH_3CD_2C_6H_5$	100:0:0:0	0		0	
6	$CD_3CH_2C_6H_5$	73:27:0:0	0.19		0.19	

[a] The reported ratio includes the methane isotopologs produced from the protonation of the starting platinum dimethyl complex as determined using ^{1}H NMR spectroscopy. [b] Ion ratios corrected by corresponding values for unexchanged starting substrate. [c] CF_3CH_2OH employed as solvent.

Table 4. Examination of Ethylbenzene Isotopologs

		% deuterium in **27**		
entry	substrate	H_a	H_b	H_c
1	$CH_3CH_2C_6H_5$	18	0	0
2	$CD_3CD_2C_6D_5$	>95	>95	>95
3	$CH_3CH_2C_6D_5$	64	0	44
4	$CH_3CD_2C_6H_5$	47	>95	trace
5	$CD_3CH_2C_6H_5$	46	0	66

the aryl and ethyl groups (at the methyl and/or methylene position) are oppositely labeled (entries 3−6). This result implies that conversion of **28** to **27** does not involve reaction with a second molecule of ethylbenzene, but rather some alternate pathway. It further implies that the exchange that was found for recovered substrate is due to reversible aryl C−H activation alone, in agreement with the observation of additional deuteration of unreacted **2**, at partial reaction, when the aryl ring was deuterated.

How then does the conversion of **28** to **27** take place? The pattern of isotope exchange in the product η^3-complexes (Table 4) is highly informative on this question. A small amount of isotope exchange at H_a was always seen, irrespective of the isotopolog of ethylbenzene, as a consequence of exchange with deuterated solvent (see above). Substantial isotope exchange between the aryl H_c and methyl H_a positions was evident, whenever these two positions contained different labels in the starting ethylbenzene isotopolog. Exchange *into* H_b was never observed, nor from H_b into H_c (entry 4), but exchange *from* H_b into H_a was seen, as revealed by comparing entries 1 and 4. The process effecting this exchange must precede exchange of H_a with solvent; otherwise, significant amounts of D would show up at the aryl position H_c in entries 1 and 4.

A mechanism that can account for these data is shown in Scheme 7. As with toluene, initial activation occurs exclusively, and reversibly, at an aryl C−H bond in ethylbenzene, resulting in NMR-detectable amounts of both ***p*-28** and ***m*-28**. It is not clear whether interconversion between ***p*-28**, ***m*-28**, and ***o*-28** occurs bimolecularly or through an intramolecular migration. Unlike toluene, however, conversion to η^3-complex **27** must be intramolecular, not intermolecular (to explain the absence of additional exchange in recovered substrate for entries 3−6 in Table 3). We propose this occurs through the *ortho*-ethylphenyl complex ***o*-28**, which undergoes a series of rapid and reversible steps: intramolecular C−H activation at the methyl position to give platinum(IV) metallocycle **29**;[28] reductive elimination to β-phenethyl platinum(II) complex **30**; and β-hydrogen elimination to styrene complex **31**. Instead of reverting to **30** (1,2-insertion), **31** can alternatively undergo *irreversible* 2,1-insertion to form a benzylic structure, α-phenethyl platinum(II) complex **32**, which would rapidly relax to the η^3-product **27**.[29] This sequence would scramble label between positions H_c and H_a and would also move label from H_b to H_a, but would never move label into H_b. The fact that less label is transferred from H_b to H_c than to H_a suggests that **31** goes to **32** at least as fast, or perhaps somewhat faster, than it reverts to **30**.

Results for 1,4-diethylbenzene isotopologs (eq 11, Table 5) are generally consistent with this mechanism, but exhibit some interesting differences. As above, introduction of D from substrate into methane was observed only when 1,4-diethylbenzene-d_4 was employed as substrate (entry 4), implying that a platinum aryl complex is formed before subsequent rearrangement to the η^3-complex, although in this case no intermediates can be detected by NMR spectroscopy. In contrast to the ethylbenzene case, however, the recovered substrate showed only very small amounts of exchange, suggesting that aryl activation is *not* reversible, but that rearrangement to η^3-benzyl is relatively much faster. Since an aryl product from 1,4-diethylbenzene must have Pt *ortho* to an ethyl group, Scheme 7 would indeed predict just such behavior: not only is the aryl product always in the right configuration to undergo oxidative addition of a methyl C−H bond, but also one would expect slower aryl C−H activation as a consequence of crowding (see below).[30] ^{1}H NMR spectroscopy of the product η^3-complex again shows exchange between H_a and H_c (entries 3 and 4).

(11)

With 1,3,5-triethylbenzene isotopologs (Table 6) we see an effect of the steric environment of platinum methyl cation **2** on the selectivity of initial C−H bond

(28) For a recent report of a similar rearrangement from an *ortho*-arylmetal complex to an η^3-complex via a palladocycle, see: Jones, G. D.; Anderson, T. J.; Chang, N.; Brandon, R. J.; Ong, G. L.; Vicic, D. A. *Organometallics* **2004**, *23*, 3071−3074.

(29) A similar β-hydride elimination followed by a 2,1-methylstyrene insertion to afford an analogous Pd-η^3-benzyl complex was proposed by Brookhart and co-workers; see ref 17b.

(30) When a sterically smaller ligand was employed (Ar = 3,5-dialkylbenzene), substantially more isotope exchange was observed in the recovered 1,4-diethylbenzene isotopologs.

Scheme 7. Proposed Mechanism for Formation of η^3-Complex 27

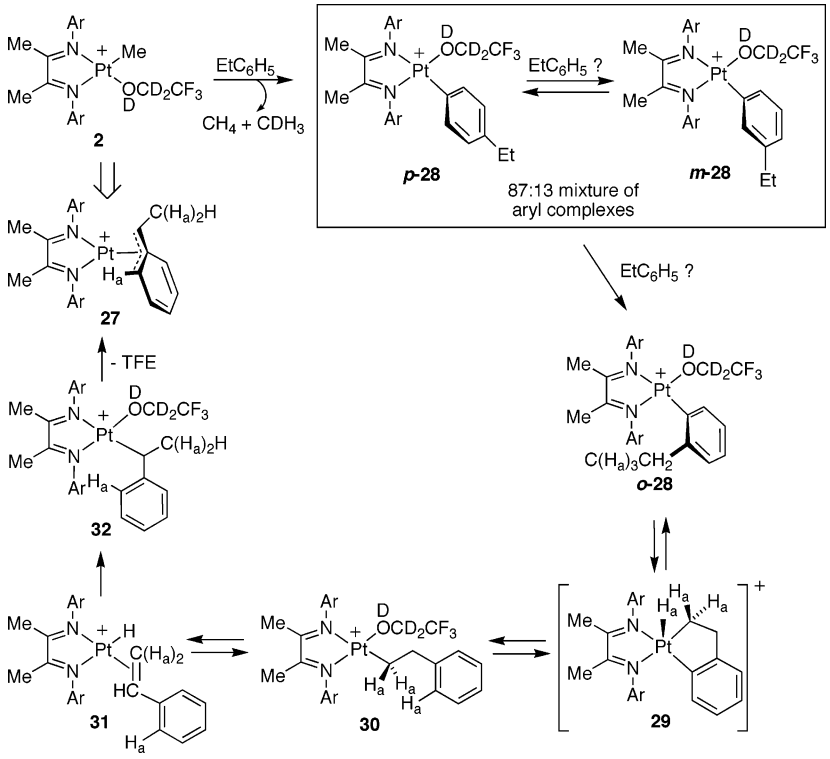


Table 5. Examination of 1,4-Diethylbenzene Isotopologs

			MS analysis of recovered substrate[b]				% deuterium in **9**		
entry	substrate	CH_4:CDH_3: CD_2H_2:CD_3H[a]	$[M+1]^+/[M]^+$	$[M-1]^+/[M]^+$	$[(M+1)-Me]^+/[M-Me]^+$	$[(M-1)-Me]^+/[M-Me]^+$	H_a	H_b	H_c
1	$(CH_3CH_2)_2C_6H_4$	69:31:0:0	0.08		0.08		16	0	12
2[c]	$(CH_3CH_2)_2C_6H_4$	100:0:0:0	≪0.01		≪0.01		n.a.	n.a.	n.a.
3	$(CD_3CD_2)_2C_6H_4$	70:30:0:0	0.02		0.02		87	0	84
4	$(CH_3CH_2)_2C_6D_4$	21:45:28:6		0.19		0.20	73	0	27

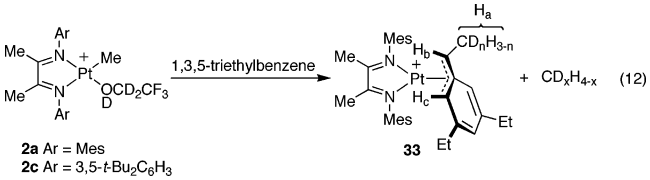
[a] The reported ratio includes the methane isotopologs produced from the protonation of the starting platinum dimethyl complex as determined by ^{1}H NMR spectroscopy. [b] Ion ratios corrected by corresponding values for unexchanged starting substrate. [c] CF_3CH_2OH was employed as the solvent.

Table 6. Examination of 1,3,5-Triethylbenzene Isotopologs

				% deuterium in **33**		
entry	substrate	L_nPtMe^+	CH_4:CDH_3: CD_2H_2:CD_3H[a]	H_a	H_b	H_c
1	$(CH_3CH_2)_3C_6H_3$	**2c**	69:31:0:0	16	0	0
2	$(CD_3CD_2)_3C_6H_3$	**2c**	64:36:0:0	85	0	75
3	$(CH_3CH_2)_3C_6D_3$[c]	**2c**	24:46:24:6	41	0	55
4	$(CH_3CH_2)_3C_6H_3$	**2a**	66:34:0:0	6	0	7
5	$(CD_3CD_2)_3C_6H_3$	**2a**	30:49:18:3	>95	0	0
6	$(CH_3CH_2)_3C_6D_3$[c]	**2a**	46:40:13:1	0	0	90[c]

[a] The reported ratio includes the methane isotopologs produced from the protonation of the starting platinum dimethyl complex. [b] $\Delta([M+1]^+/[M]^+)$ measured. [c] $Et_3C_6D_3$ is 94% deuterated.

activation. For both **2a** and **2c** the product was consistently the η^3-complex **33** (eq 12). Analysis of methane isotopologs reveals that for the sterically smaller complex **2c** aryl C−H bond activation is the exclusive initial step (entries 1 and 2), although again no intermediate aryl complex can be detected. The expected exchange between positions H_a and H_c was observed (entries 2 and 3). In contrast, direct activation of the ethyl group appears to be the dominant path for bulkier **2a**, as revealed by the extensive deuteration of methanes in entry 5 as well as the virtual absence of isotope exchange between positions in entries 5 and 6. (The appearance of some multiply deuterated methane in entry 6 indicates that some competitive aryl activation may take place as well.) In the absence of substrates with partially labeled ethyl groups, it is not possible to determine whether the initial activation takes place at the methyl position, followed by isomerization as in Scheme 7, or at the methylene position.



Comparative Reactivities

Rate constants for reactions of di- and triethylbenzene with **2a** are compared to those for several related reactions in Table 7. Comparison of entries 1 and 4 shows that the bulkier ligand with Ar = mesityl slows the benzene reaction by nearly 2 orders of magnitude. The different KIE values were previously interpreted in terms of a change in RDS, benzene coordination being rate-limiting for **2a**, but C−H activation for **2c**.[10a] Ethyl substitution on benzene retards the reaction rate only

Table 7. Comparison of Rate Constants for Various Alkyl-Substituted Benzenes and Steric Nature of Diimine Ligands

entry	L_nPtMe^+	substrate	k ($M^{-1}\cdot s^{-1}$), 20 °C	k_H/k_D
1	**2a**	benzene	$4.1(4) \times 10^{-4}$	1.1[a]
2	**2a**	1,4-diethylbenzene	$2.4(2) \times 10^{-4}$	0.9,[b] 0.9[c]
3	**2a**	1,3,5-triethylbenzene	$1.3(1) \times 10^{-4}$	3.0,[d] 1.1[e]
4[f]	**2b**	benzene	$1.6(2) \times 10^{-2}$	1.8
5[f]	**2b**	*p*-xylene (Ar CH)	$4.0(13) \times 10^{-3}$	4.0
6[f]	**2b**	*p*-xylene (benzyl CH_3)	$2.0(9) \times 10^{-3}$	0.8

[a] From ref 10a. [b] 1,4-Diethylbenzene-d_{10} (25 °C). [c] 1,4-Diethylbenzene-d_4 (25 °C). [d] 1,3,5-Triethylbenzene-d_{15} (40 °C). [e] 1,3,5-Triethylbenzene-d_3 (40 °C). [f] From ref 10b.

slightly: diethylbenzene reacted nearly half as fast as benzene (entry 2), while triethylbenzene slowed the rate further but only by another factor of 2 (entry 3). The shift from initial aryl activation for diethylbenzene to primarily side-chain activation for triethylbenzene (see above) is accompanied by a significant KIE for deuteration in the ethyl groups, but not in the aryl positions. This result may also suggest that the RDS has been changed from coordination to oxidative addition of the ethyl C−H bond. It should be noted, though, that for the reactions of *p*-xylene with **2a** (entries 5 and 6) the opposite result was found: deuteration of aryl positions gave a significant KIE, while deuteration of the methyl groups did not.[10b] We do not at this time have a fully satisfying interpretation of that observation.

Conclusions

While all methyl- and ethyl-substituted benzenes react with Pt(II) cation **2** to give η^3-benzyl products, they do *not* all get there by the same pathway. For toluene and *p*-xylene, initial activation at aryl positions is evidenced by the buildup of NMR-detectable amounts of aryl-platinum complexes during the course of the reaction, with subsequent conversion to the benzyl product.[10b] Isotopic labeling studies in the present work reveal that the latter conversion is intermolecular, involving reaction with a second molecule of substrate, and that there is competitive initial activation at the benzyl position for *p*-xylene but *not* for toluene, presumably a consequence of greater crowding in the former. Previous findings from kinetics experiments agree with this conclusion.[10b]

For ethylbenzene and 1,4-diethylbenzene, isotopic labeling shows that initial activation takes place exclusively at aryl C−H bonds, although the intermediate aryl complexes are detectable only for the former, and that conversion to the η^3-benzyl product takes place via intramolecular isomerization rather than secondary reaction with additional substrate. Comparison of 1,4-diethylbenzene to *p*-xylene suggests that direct C−H activation of a substituted benzylic methylene C−H bond is disfavored relative to that of a benzylic methyl, presumably a result of the increased steric interactions present for activation of a secondary C−H bond, and that activation at the nonbenzylic methyl position is not competitive either, despite the steric retardation of reaction at the aryl positions. Only in the most extreme case of steric crowding—the reaction of bulky **2a** with triethylbenzene—does direct activation of the ethyl group become preferred to aryl activation, although which ethyl position is reactive cannot be determined from available data.

While the accessibility of multiple pathways for the same overall transformation will unquestionably make it difficult to predict selectivity patterns, the fact that preferences for activation of different C−H bonds can be so strongly affected by the steric properties of substrate and activating complexes is encouraging for the larger program of designing selective C−H activation processes for useful organic synthetic goals.

Experimental Section

General Procedures. ^1H NMR and ^{13}C NMR spectra were recorded at ambient temperature using Varian 600 or 300 spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. Mass spectra were acquired on a Finnigan LCQ ion trap or Agilent 5973 Network mass selective detector and were obtained by peak matching. All reactions were carried out under an atmosphere of nitrogen in glassware that had been oven-dried. Unless otherwise noted, all reagents were commercially obtained and, where appropriate, purified prior to use. Tris(pentafluorophenyl)borane [$B(C_6F_5)_3$] was purified by sublimation (90 °C, 0.5 mmHg). Trifluoroethanol-d_3 was dried over 3 Å molecular sieves for at least 5 days and then vacuum distilled onto $B(C_6F_5)_3$. After 6 h, the trifluoroethanol-d_3 was vacuum distilled and stored in a valved reaction vessel. The platinum dimethyl complexes were synthesized following earlier reported procedures.[10b,14] Trifluoroethanol-d_3, $B(C_6F_5)_3$, and platinum dimethyl complexes were stored in a Vacuum Atmospheres nitrogen atmosphere drybox. A representative procedure and diagnostic characterization of an η^3-complex (**9a**) are included below. For procedures and characterization of other new complexes, refer to the Supporting Information.

Representative Preparation and Characterization of an η^3-Complex. To a light orange solution of platinum methyl cation **2a** (prepared by dissolving 0.010 g of platinum dimethyl complex **1a** (0.018 mmol) and 0.017 g of $B(C_6F_5)_3$ (0.033 mmol) in 0.700 mL of trifluoroethanol-d_3) was added 0.056 mL of 1,4-diethylbenzene (0.36 mmol). The progress of the reaction was monitored periodically using ^1H NMR spectroscopy. After 14 h, the reaction mixture was heated to 45 °C. After 13 h, the reaction mixture was cooled and ^1H NMR spectroscopy analysis revealed complete consumption of **2a** and formation of η^3-product **9a** (in situ characterization data): ^1H NMR (600 MHz, CF_3CD_2OD) δ 7.13 (s, 1H), 7.12 (s, 1H), 7.06 (s, 1H), 6.96 (AB splitting, 1H), 6.91 (s, 1H), 6.05 (s, 1H), 6.05 (d, J = 5.8 Hz, 1H), 5.62 (d, J = 6.0 Hz, J_{PtH} = 46 Hz, 1H), 2.76 (q, J = 6.6 Hz, J_{PtH} = 66 Hz, 1H), 2.37 (s, 3H), 2.34 (s, 6H), 2.18 (s, 3H), 2.16 (m, 1H), 2.07 (m, 1H), 1.96 (s, 3H), 1.89 (s, 3H), 1.85 (s, 3H), 1.46 (s, 3H), 1.03 (t, J = 7.2 Hz, 3H), 0.32 (d, J = 6.6 Hz, 3H).

The η^3-complex could also be prepared with BF_4^-, a more robust counterion. To a suspension of platinum dimethyl **1a** (0.092 g, 0.15 mmol) in 8 mL of CF_3CH_2OH was added 0.032 mL of a 54 wt % solution of HBF_4 in Et_2O (0.19 mmol). Upon homogeneity, 0.065 mL of 1,4-diethylbenzene (0.42 mmol) was added to the reaction solution. After 6 days at 25 °C, the reaction mixture was warmed to 45 °C. After 18 h, the reaction mixture was cooled to 25 °C and was concentrated in vacuo. The resulting red residue was redissolved in 5 mL of methanol and concentrated in vacuo to afford 0.180 g of a dark red residue: ^1H NMR (600 MHz, CD_2Cl_2) δ 7.11 (s, 1H), 7.10 (s, 1H), 7.04 (s, 1H), 6.92 (s, 1H), 6.91 (s, 1H), 6.90 (s, 1H), 5.99 (d, J = 6.0 Hz, 1H), 5.63 (dd, J = 7.0, 1.8 Hz, J_{PtH} = 38 Hz, 1H), 2.75 (q, J = 6.6 Hz, J_{PtH} = 48 Hz, 1H), 2.39 (s, 3H), 2.37 (s, 3H), 2.36 (s, 3H), 2.21 (s, 3H), 2.14 (m, 1H),[a] 2.45 (m, 1H),[a]

2.01 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.46 (s, 3H), 1.03 (t, J = 7.8 Hz, 3H), 0.30 (d, J = 6.6 Hz, 3H); ^{13}C NMR (150.8 MHz, CD_2Cl_2) δ 180, 177, 143.4, 143.2, 141, 140.7, 140, 138, 135.0, 134.9, 130.22, 130.15, 129.9, 129.8, 129.7, 129, 128, 127, 116 (b), 112, 42, 29, 19.5, 19.3, 18.8, 18, 17.73, 17.68, 17.3, 16.7, 14, 12; IR (KBr pellet) 2968, 1610, 1386, 1059, 851 cm^{-1}; HRMS (FAB) m/z calcd for $C_{32}H_{41}N_2Pt^+$ $(M - BF_4)^+$ 648.2918, found 648.2932. [a]Identified using 2D NMR COSY experiment.

General Comments on Isotopolog Experiments. A light orange solution of platinum methyl cation **2a** (prepared by dissolving 0.010 g of platinum dimethyl complex **1a** (0.018 mmol) and 0.017 g of $B(C_6F_5)_3$ (0.033 mmol) in 0.700 mL of trifluoroethanol-d_3) was analyzed using ^{1}H NMR spectroscopy. At this time the amount of deuterium incorporation into the Pt-Me resonance was determined by comparison of its peak area to the average peak area of both the aryl protons and methyl groups present on the diimine ligand. After spectroscopic analysis, 2.5 equiv of substrate was added. The progress of the reaction was monitored periodically using ^{1}H NMR spectroscopy. After 10 h, the reaction mixture was heated to 45 °C. After 13 h, the reaction mixture was cooled and ^{1}H NMR spectroscopy analysis revealed complete consumption of the aryl complexes and formation of η^3-product. The amount of deuterium incorporation into the η^3-product was determined by comparison of the average signal intensity of the methyl groups present on the diimine ligand with the resonances associated with H_a, H_b, and H_c, respectively. The methane isotopolog distribution was also determined using ^{1}H NMR spectroscopy analysis (0.10−0.15 ppm). After spectroscopic analyses, the reaction mixture was filtered through SiO_2, and the resulting clear filtrate, containing recovered substrate, was analyzed by GC-MS.

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Supporting Information Available: Detailed experimental procedures, characterization data, integrated rate laws, tables of GC-MS isotope exchange, and X-ray diffraction data for **12** are available free of charge via the Internet at http://pubs.acs.org.

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