Studies on Gas-phase Cyclometalations of $[ArNi(PPh_3)_n]^+$ (n = 1 or 2) by Electrospray Ionization Tandem Mass Spectrometry

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Gas-phase cyclometalation of $[ArNi(PPh_3)_n]^+$ (n = 1, 2) complexes have been studied by ESI-MS/MS. The electron-donating substituents of aromatic iodides in the *para* position were found to inhibit the cyclometalation process of losing ArH, while the electron-withdrawing substituents in the *para* position were found to enhance it. These results indicate that the cyclometalation process of losing ArH is favored by electron-deficient aromatic groups. In addition, the detailed dissociation pathways of the cationic nickel complexes were studied, and among these pathways, the process of aryl-aryl interchange was also found to proceed in ESI-MS/MS. (J Am Soc Mass Spectrom 2010, 21, 1265–1274) © 2010 American Society for Mass Spectrometry

Cyclometalation occurs when a ligand on an organo-metal complex undergoes an intramolecular metalation with concomitant formation of a chelate ring containing a metal-carbon bond [1]. This kind of transformation has attracted significant attention over the past three decades [2–7]. On the one hand, cyclometalation can be detrimental to a desired reaction course and can be prevented by a variety of techniques to improve catalytic efficiency of the metal complex. As cyclometalation methodology has been developed, a number of cyclometalated complexes were employed successfully in organic synthesis [8, 9], catalysis [10–12], and photochemistry [13–15]. Mechanisms for the cyclometalation associated with C–H bond cleavage have been proposed [16–21], and three related mechanisms for C–H bond cleavage are typically accepted: oxidative addition, electrophilic substitution, and multicentered pathways (such as σ-bond metathesis) [22–26]. The actual mechanisms that pertain for cyclometalation of a given metal complex are highly dependent on the exact nature of the metal complexes, identities of hydrocarbon substituents, solvents involved, and specific operating conditions [21]. As a result, a complete understanding and description of the general mechanism are still lacking, and more data are needed before we can fully describe critical reactivity patterns.

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The focus to date has been on the study of solution-phase cyclometalations, but gas-phase cyclometalations have recently received more attention [27–29]. Generally, gas-phase studies conducted with tandem mass spectrometry (MS/MS) on extremely small sample quantities can theoretically ascertain the propensity for a complex to undergo certain kinds of reactions. The energy conditions and dissociation pathways provide useful insights, with applicability to related solution-phase reactions [30–40]. Based on the gas-phase methodologies, Henderson and coworkers published their investigation of the cyclometalation of palladium(II) and platinum(II) diphosphine complexes $MCl_2(Ph_2P(CH_2)_5PPh_2)$ in 2004 [28]. More recently, Schwarz and coworkers explored the whole process of cyclometalation of 2,2′-bipyridine platinum(II) complexes in gas phase by a combination of gas-phase methodologies and theoretical calculations [29]. These successful studies of cyclometalation illustrated the unique value of MS/MS.

We previously employed electrospray ionization mass spectrometry (ESI-MS) to study the nickel-catalyzed cross-coupling reactions of substituted *o*-halobenzoates [41–43]. Under these conditions, key intermediates such as $[ArNi(L)]^+$ (L = ligand) were observed. To understand more about the $[ArNi(PPh_3)_2X]$ (X = halogen) complexes important in a variety of Ni-catalyzed cross-coupling and homo-coupling reactions involving aryl halides [44–46], MS/MS experiments was performed. Based on work previously carried out for $[ArPd(PPh_3)_2X]$ [47], we expected to observe the product ions $[PPh_3Ar]^+$ and $[PPh_4]^+$; however, the signal of

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Scheme 1. The cyclometalation observed for complex ions $[ArNi(PPh_3)]^+$.

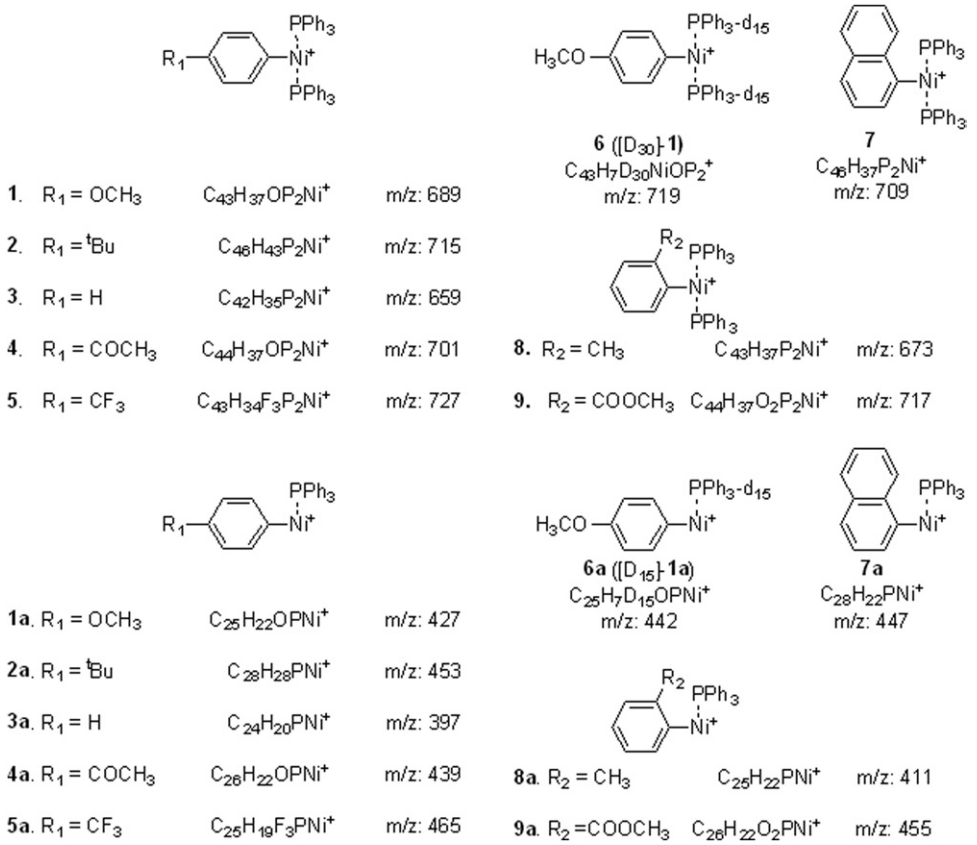
$[PPh_3Ar]^+$ and $[PPh_4]^+$ were not observed in this system. Rather, another interesting gas-phase fragmentation reaction of $[ArNi(PPh_3)]^+$ was noted: in a MS/MS experiment, the precursor ion $[ArNi(PPh_3)]^+$ yielded a product ion through the loss of Ar-H. We hypothesized that this product ion was formed through cyclometalation, as shown in Scheme **1**.

Although certain elegant gas-phase methodologies have been reported [48–52], to the best of our knowledge, little research has been conducted on the corresponding gas-phase chemistry. Our study furthers the investigation of this type of cyclonickelation, yielding new data on the gas-phase characteristics of Ni(II) complexes generated by electrospray ionization and probed using mass spectrometric dissociation techniques. The chemical structures for the specific compounds are shown in the Scheme **2**, using a referential numbering system to facilitate subsequent discussion. Compounds **1–9** are bisphosphine complexes, while **1a–9a** are monophosphine complexes. These experiments, together with labeling studies described below, provide evidence for the cyclometalation mechanism of PPh_3 ligands by a cationic Ni(II) center in the gas-phase. Data detailing the influence of the electronic effect of the functional groups in aromatic iodides on the cyclometalation are also presented.

Experimental

Materials and Sample Preparation

The starting materials $NiCl_2(PPh_3)_2$, tri(phenyl-d_{15}) phosphine (PPh_3-d_{15}), and all the aromatic iodides were purchased from Sigma-Aldrich Co. (St. Louis, MO, USA). The toluene and acetonitrile were HPLC-grade solvents from Merck Co. (Darmstadt, Germany). The complexes $ArNi(PPh_3)_2I$ were prepared by stirring a solution of ArI (0.005 mmol), $NiCl_2(PPh_3)_2$(0.005 mmol), and Zn (0.015 mmol) in freshly distilled dry toluene (2 mL) at room temperature under an atmosphere of argon [53, 54]. The deuterated complex (p-OCH_3-C_6H_4)$Ni(PPh_3$-$d_{15})_2I$ was prepared by stirring a solution of p-OCH_3-C_6H_4I (0.005 mmol), $NiCl_2(PPh_3$-$d_{15})_2$ (0.005 mmol), and Zn (0.015 mmol) in dry toluene (2 mL) at room temperature under an atmosphere of argon. Typically, 15 min after preparation, a 1-mL



Scheme 2. Structures of organonickel complex ions studied by ESI-MS/MS.

portion of each solution was taken from the reaction mixture and diluted with 99 mL CH_3CN; the diluted solution was immediately infused into the ESI source by a syringe pump at a flow rate of 10 $\mu L \cdot min^{-1}$ for the MS detection. Because the complexes are very sensitive to the air and easy to degenerate, one analysis generally lasts for 5 min.

Instrumentation

The experiments were performed in positive ion mode on a Thermo Finnigan TSQ Quantum Access triple quadrupole mass spectrometer (Thermo Finnigan, San Jose, CA, USA) equipped with a standard ESI ion source. The basic ESI conditions were ionized voltage, 3800 V; capillary offset, 37 V; and capillary temperature, 300 °C. The MS/MS experiments were carried out with argon as the collision gas. The collision energy ranged from 1 to 25 eV, depending on the ease of dissociation of the precursor ion. Data acquisition and analysis utilized the Xcalibur (ver. 2.0, Thermoquest Finnigan) software package. The instrument was calibrated with acetonitrile solutions of PEG400 and PEG800 before each experiment.

Results and Discussion

The gas-phase fragmentation reactions of the complex ions were studied and the relative mechanisms involved were proposed to proceed via several major pathways. We provided support for the cyclometalation in experiments with deuterium-labeled analogues of several species of interest. We also demonstrated the electronic effect of the aryl groups on the observed cyclometalation. The detailed data and the relative gas-phase chemistry are discussed below.

Fragmentation of Organonickel Complexes 1 and 1a

Observation of Cyclometalation

Isotopic distributions typical of nickel were observed in the ESI mass spectra of the complex ions $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3)_2]^+$ **1** and $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3)]^+$ **1a**. The largest peak in the isotopic cluster (**1** at *m/z* 689 and **1a** at *m/z* 427), was selected for further investigation by MS/MS.

Complex ion **1** primarily yielded the product ion **A** at *m/z* 581 and **B** at *m/z* 611 corresponding to loss of $CH_3OC_6H_5$ and benzene, respectively (Figure 1). These fragmentations were different from the typical pathway of losing the ligand, and seemed to be analogous to the pathways of losing small neutral molecules such as ketene, CO_2, HCOOH, and so on [55–59]. The loss observed here of $CH_3OC_6H_5$ from $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3)_2]^+$ suggests that the C–H bond of the PPh_3 ligand was activated, and that the resulting cyclometalation product was produced in the form of ion **A**. The origin of the hydrogen in the dissociated $CH_3OC_6H_5$ molecule was further explored in the deuterium-labeling experiments, which would be discussed below. The dissociation pattern related to loss of benzene that results in ion **B** has been reported in the palladium system [47, 60]. The structure of ion **B** is difficult to be assigned only from the MS/MS result, one possible transformation from $[ArNi(PPh_3)_2]^+$ to $[PhNi(PPh_3)(PPh_2Ar)]^+$ (Ar = p-CH_3O-C_6H_4) might ex-

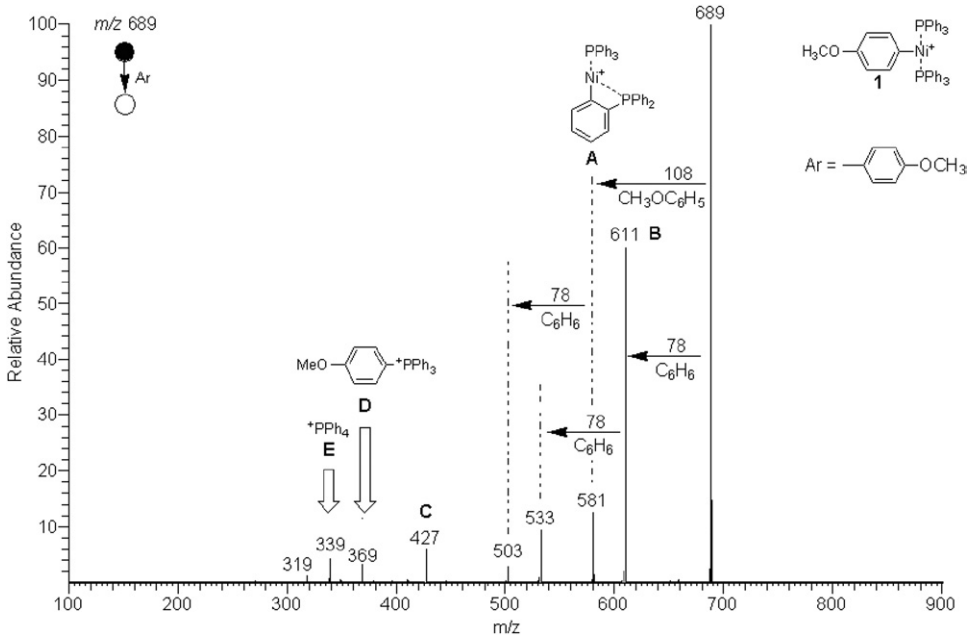
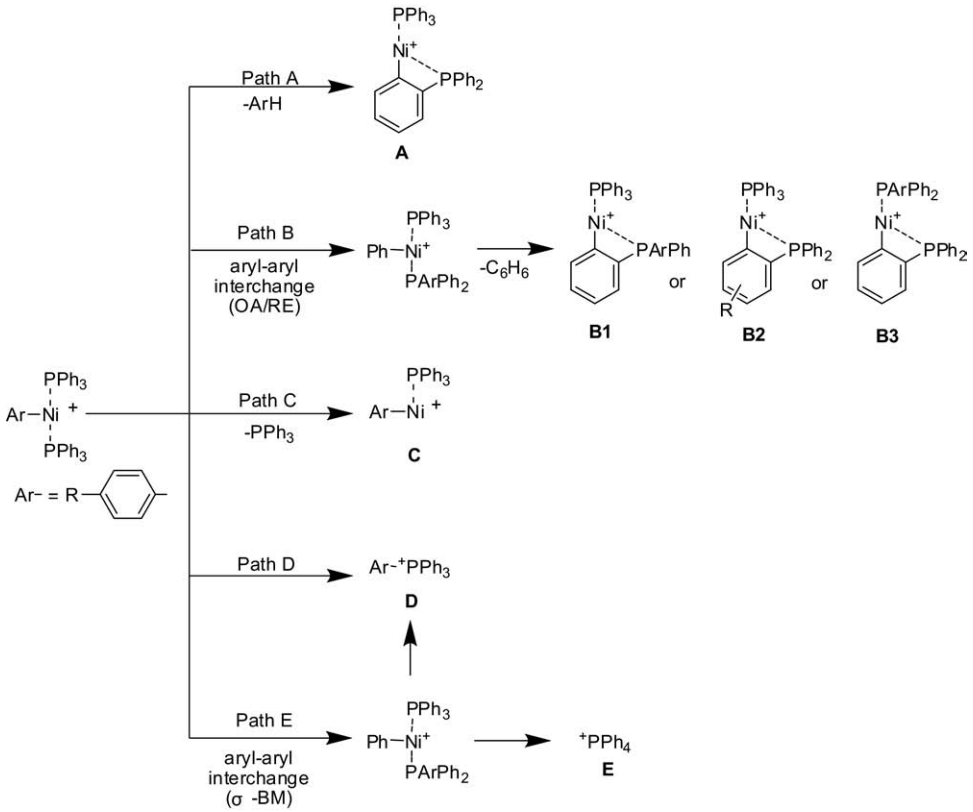


Figure 1. ESI-(+)-MS/MS spectrum for Complex **1** at *m/z* 689.



Scheme 3. The main dissociation pathways of **1–5** (OA/RE: oxidative addition/reductive elimination; σ-BM: σ-bond metathesis).

plain the formation of ion **B** by the loss of benzene (Scheme 3). The MS/MS spectrum of complex ion **1** also contains fragment ions at *m/z* 533 and 503. We suggest that the signal at *m/z* 533 is produced by loss of two molecules of benzene from the precursor ion **1**, while the signal at *m/z* 503 arises from the loss of one molecule of $CH_3OC_6H_5$ and one molecule of benzene from the precursor ion **1**. The ion **C** at *m/z* 427 is the phosph-

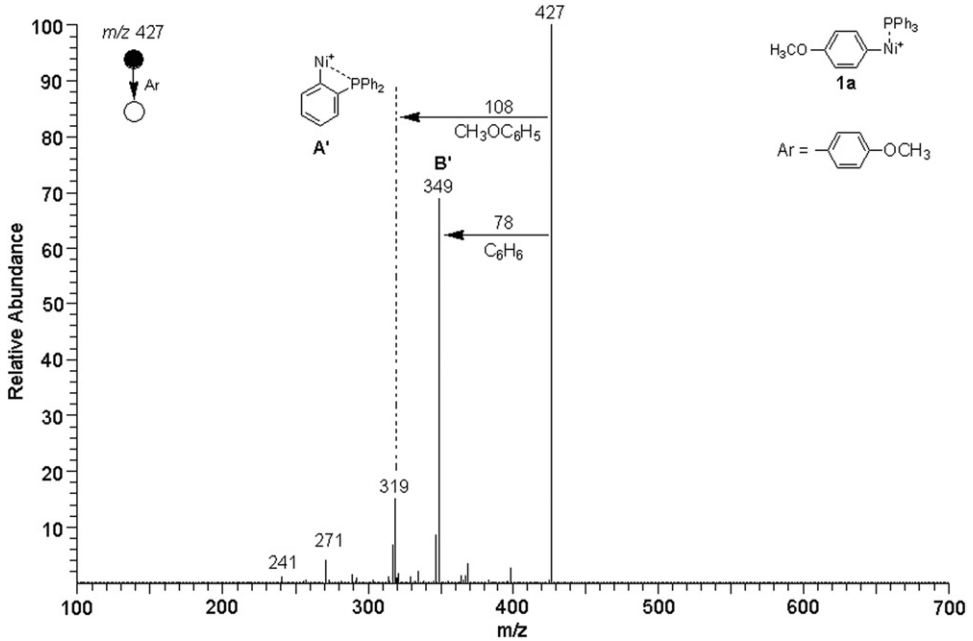
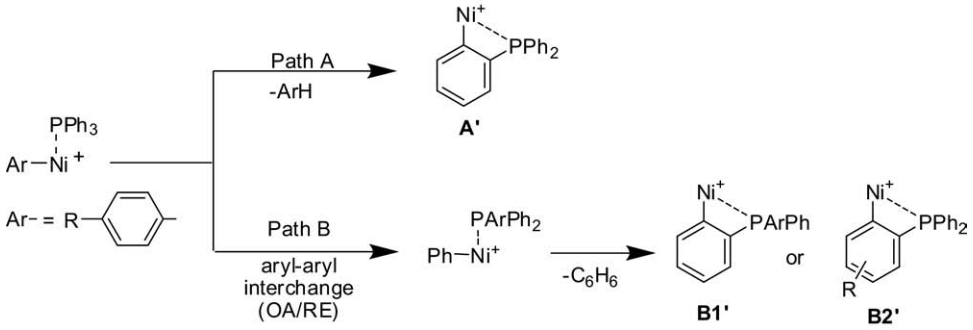


Figure 2. ESI-(+)-MS/MS spectrum for Complex **1a** at *m/z* 427.



Scheme 4. The main dissociation pathways of **1a–5a**. (OA/RE: oxidative addition/reductive elimination).

ine dissociation product of ion **1**, and the product ion **C** might have the same structure with **1a**. Additionally, the product ions **D** $[(p\text{-}CH_3O\text{-}C_6H_4)PPh_3]^+$ and **E** $[PPh_4]^+$ were observed with lower intensities. The product ion **D** at *m/z* 369 may be produced through reductive elimination of $[ArNi(PPh_3)_2]^+$. The dissociation pattern that produces ion **E** at *m/z* 339 can be explained by phenyl migration from PPh_3 to the metal center, a pattern also observed in the aforementioned palladium experiments [47].

The MS/MS spectrum of complex ion $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3)]^+$ **1a** is relatively simple: dissociation pathways of **1a** at *m/z* 427 were analogous to that of **1**, giving the corresponding fragment ions **A′** at *m/z* 319 and **B′** at *m/z* 349 by losing $CH_3OC_6H_5$ and benzene, respectively (Figure 2). **A′** at *m/z* 319 was also suggested to be the cyclometalation product ion. The structure of ion **B′** is also difficult to be assigned only from the MS/MS result, one possible transformation from $[ArNi(PPh_3)]^+$ to $[PhNi(PPh_2Ar)]^+$ (Ar = p-CH_3O-C_6H_4) might explain the formation of ion **B** by the loss of benzene (Scheme 4).

Fragmentation of Organonickel Complexes 6 and 6a

Tracing the Origin of Protons in the Dissociated $CH_3OC_6H_5$ with Deuterium Labeling

To investigate further the origin of the hydrogen in the $CH_3OC_6H_5$ molecule that dissociated from the precursor ions, MS/MS experiments were performed on deuterium-labeled analogues of **1** and **1a**: complex **6** $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3\text{-}d_{15})_2]^+$ and **6a** $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3\text{-}d_{15})]^+$, respectively. Ion **6** at *m/z* 719 fragmented to yield product ions **A–d$_{29}$** at *m/z* 610 by loss of $CH_3OC_6H_4D$ (Figure 3),) and ion **6a** at *m/z* 442 fragmented to yield product ions **A–d$_{14}$** at *m/z* 333 by

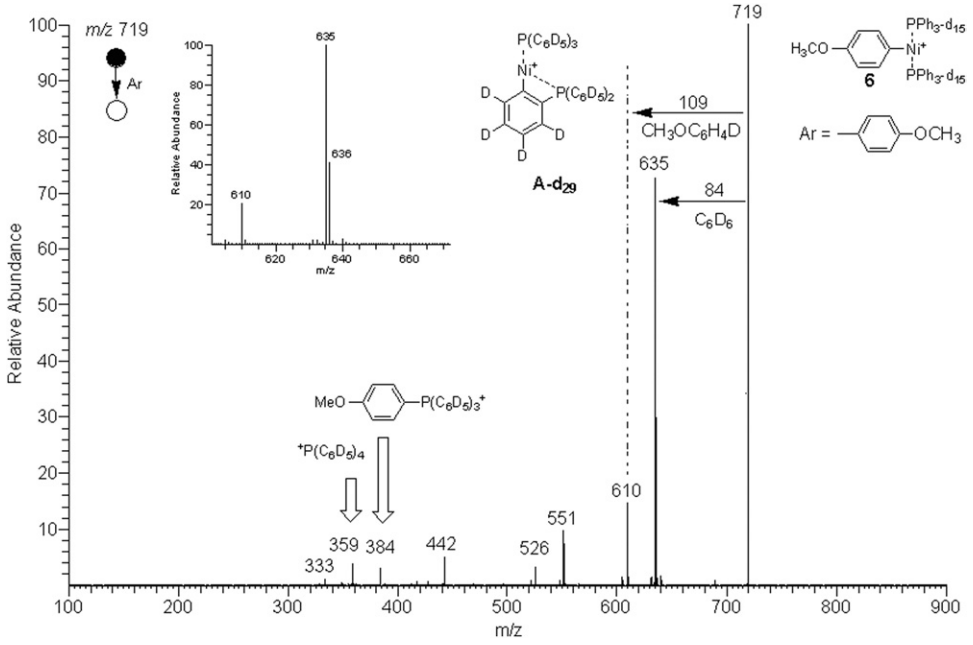


Figure 3. ESI-(+)-MS/MS for Complex **6** at *m/z* 719. Inset: the enlargement of the region between *m/z* 600 and 650.

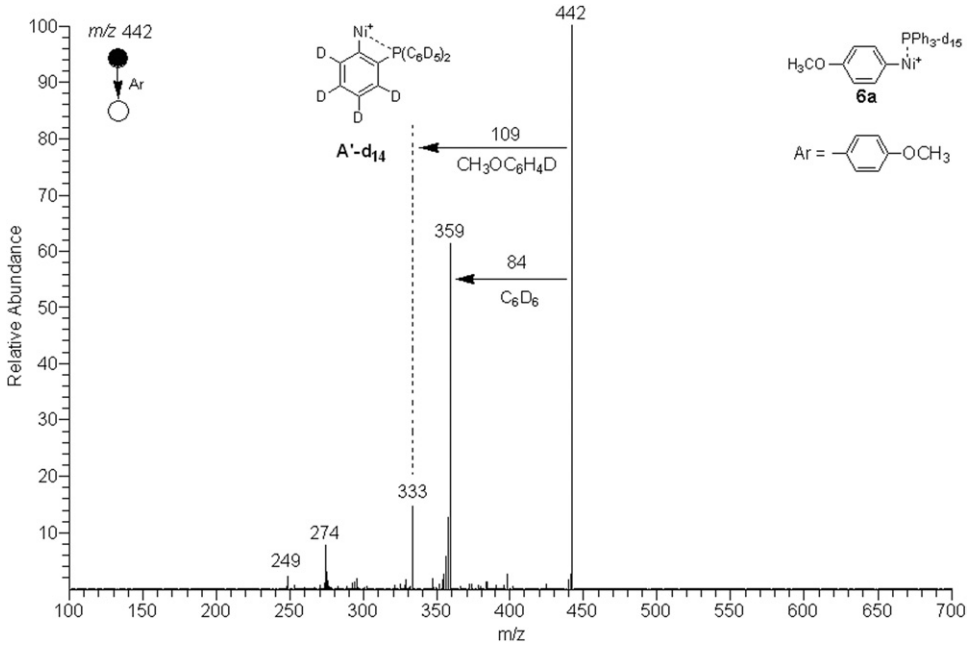


Figure 4. ESI-(+)-MS/MS for Complex **6a** at *m/z* 442.

loss of $CH_3OC_6H_4D$ (Figure 4). These results all suggest that the scrambled hydrogen in the neutral loss of $CH_3OC_6H_5$ originates from the phenyl groups of the triphenylphosphine ligand. These experimental findings also give support to the possibility of the gas-phase cyclometalation of **1** and **1a** during MS/MS.

Additionally, the loss of C_6D_6 was also observed at *m/z* 635 in Figure 3 and at the same time a high intensity peak at *m/z* 636 (see inset in Figure 3) was also noted, which suggests that the pathway of losing C_6HD_5 from the precursor ion exists during the fragmentation and that the proton in the lost molecule of C_6HD_5 should come from the aromatic group (see Scheme S6, which can be found in the electronic version of this article). This finding supports the hypothesis that the pathway of losing benzene involves an interchange between the aryl group and the phenyl group of the PPh_3 ligand; that is to say, a transformation from $[ArNi(PPh_3)_2]^+$ to $[PhNi(PPh_3)(PPh_2Ar)]^+$ takes place before fragmentation/dissociation. This transformation process was known as the aryl-aryl interchange [62], thus this concept was applied in the below discussion.

Fragmentation of $[ArNi(PPh_3)_2]^+$ 1–5

The ESI mass spectra of the complexes $ArNi(PPh_3)_2I$ with substitutions in the *para* position display isotopic distributions anticipated for the nickel-containing ions $[ArNi(PPh_3)_2]^+$ **2–5.** In MS/MS experiments performed on the largest of the nickel isotope peaks, dissociation patterns similar to those of ion **1** were found. The major fragmentation pathways are proposed and summarized in Scheme 3.

For ions $[ArNi(PPh_3)_2]^+$ **1–5**, there are five possible fragmentation pathways, among which paths A and B are dominant (Scheme 3). Path A is proposed to be a process of cyclometalation, which may proceed via γ-C–H bond activation by nickel(II), a process of oxidative addition-reductive elimination or σ-bond metathesis, to yield the product ion **A** by loss of ArH. Based on the information derived from the deuterium labeling experiments described above and relative literatures [47, 60–62], Path B is suggested to be a two step process of first aryl-aryl interchange and then cyclometalation. That is to say, the ions **B1, B2,** and **B3** may be generated from $[PhNi(PPh_3)(PArPh_2)]^+$ which is produced by phenyl migration from the triphenylphosphine ligand to the nickel center by cleavage of the phosphorus-phenyl bond. Path C, involving loss of one molecule of triphenylphosphine, is the most common fragmentation for many metal complex ions. Path D possibly proceeds primarily through reductive elimination of $[ArNi(PPh_3)_2]^+$ to produce the ion $[PPh_3Ar]^+$, and Path E is thought to proceed via the aryl-aryl interchange, with subsequent reductive elimination of this nickel-phenyl complex to yield a product ion $[PPh_4]^+$. As for

Table 1. Primary product ions and ratios of their intensities from fragmentation of complex ions 1-5 under identical collision conditions

Complexes	Precursor ion	Product ion A	Product ion B	I(A)/I(B)[a]	SD (n = 9)
1	689	581	611	0.15	0.03
2	715	581	637	0.17	0.01
3	659	581	581	–[b]	–[b]
4	701	581	623	0.25	0.01
5	727	581	649	0.30	0.01

[a]The collision energy ranged from 1 to 18 eV, the average ratio was calculated.
[b]The ratio could not be calculated for this single product ion.

Table 2. Primary product ions and ratios of their intensities from fragmentation of complex ions 1a–5a under identical collision conditions

Complexes	Precursor ion	Product ion A	Product ion B	I(A′)/ I(B′)[a]	SD (n = 9)
1a	427	319	349	0.17	0.07
2a	453	319	375	0.18	0.06
3a	397	319	319	–[b]	–[b]
4a	439	319	361	0.42	0.06
5a	465	319	387	0.45	0.07

[a]The collision energy ranged from 1 to 20 eV, the average ratio was calculated.
[b]The ratio could not be calculated for this single product ion.

the difference of Path B and E, it's proposed that Path B and E involves an oxidative addition/reductive elimination process and a σ-bond metathesis pathway, respectively [51–52].

To investigate this feature of gas-phase C–H bond activation of PPh_3 further, the MS/MS experimental results for $[ArNi(PPh_3)_2]^+$ were studied in detail. Interestingly, the pathway that involves the loss of ArH to yield ion **A** competes with the pathway that features the loss of benzene to produce ion **B**: through the experiments performed over the same collision energy range, we found the ratio of intensities of product ions **A** and **B** was altered when the substitution groups of aromatic moiety changed from electron-donating groups to electron-withdrawing groups (Table 1). The trend can be observed clearly in the data summarized in Table 1.

Apparently the extend of giving product ion **A** increases by the presence of electron-withdrawing substituents such as the trifluoromethyl group in ion **5**, while the extend of giving product ion **A** decreases by the presence of electron-donating substituents such as the butyl group in ion **2**. These results give evidence for the electrophilic character of the nickel center, which is consistent with the previous studies of C–H bond activation of nickel center in solution [63–65].

Fragmentation of $[ArNi(PPh_3)]^+$ 1a–5a

For the unsaturated complexes ions $[ArNi(PPh_3)]^+$ **1a–5a**, two main fragmentation pathways were proposed and showed in Scheme 4: Pathway A that involves loss of ArH to yield ion **A′** competes with Pathway B that features the loss of benzene to produce ion **B′**.

When the substituted group was changed from methoxyl to trifluoromethyl, the ratio for the unsatura-

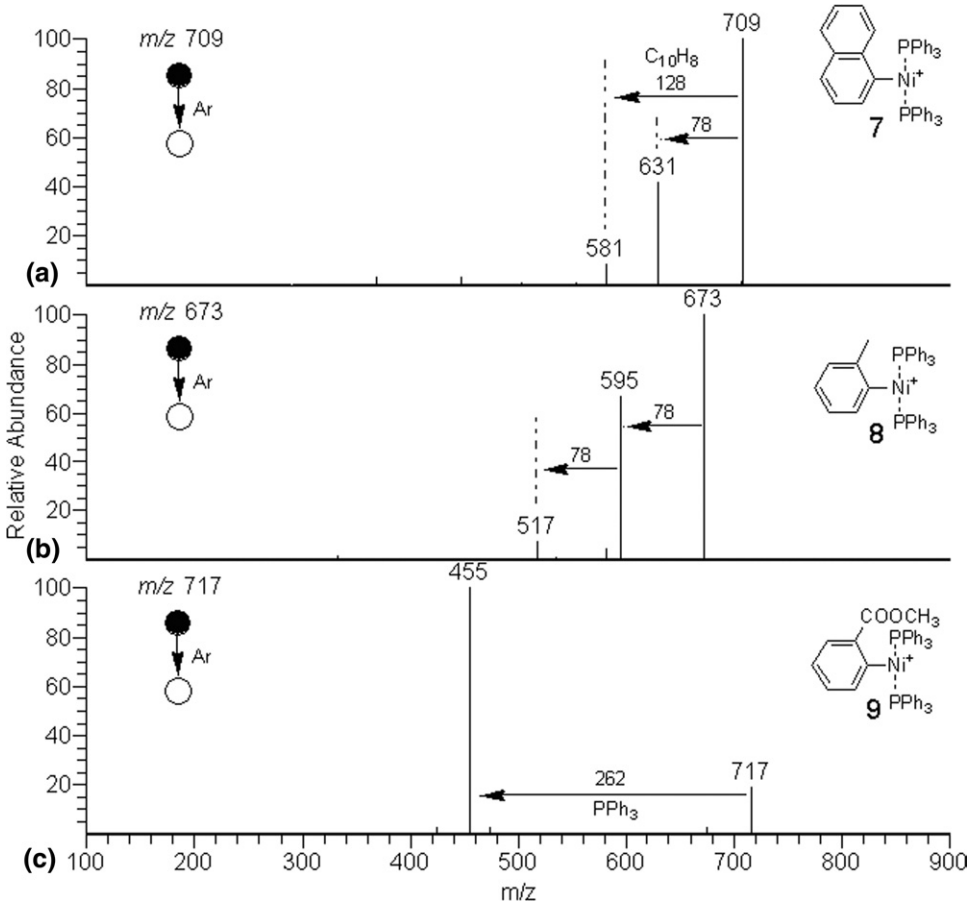


Figure 5. ESI-(+)-MS/MS for Complex **7** at *m/z* 709, Complex **8** at *m/z* 673, and Complex **9** at *m/z* 717.

ted complex ion $[ArNi(PPh_3)]^+$ subsequently changes form 0.17 to 0.45 (Table 2), these results suggest that the pathway of losing ArH is promoted by electron-withdrawing substituents on the aromatic ring, which is consistent with the trend of $[ArNi(PPh_3)_2]^+$ discussed above. In addition, the comparison between ion $[ArNi(PPh_3)]^+$ and $[ArNi(PPh_3)_2]^+$ was made. Taking complex ions $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3)]^+$ and $[(p\text{-}CH_3O\text{-}C_6H_4)Ni(PPh_3)_2]^+$ as an example, the ratio of the former (0.17) is greater than that of the latter (0.15). Because the ions with one phosphine are less hindrance than those with two phosphines, it is suggested that the less hindrance environment was better for the pathway of losing ArH in these systems.

Fragmentation of $[ArNi(PPh_3)_2]^+$ **7**, **8**, *and* **9**

When the position of substituents on the aromatic iodine was *ortho* instead of *para*, less fragmentation pathways were observed in the MS/MS experiments of $[ArNi(PPh_3)_2]^+$ (Figure 5). For ion **7** $[(C_{10}H_7)Ni(PPh_3)_2]^+$ at *m/z* 709 and **8** $[(o\text{-}CH_3\text{-}C_6H_4)Ni(PPh_3)_2]^+$ at *m/z* 673, the signals at *m/z* 581 were small and the pathway of losing ArH was unfavored. Based on these comparisons, the pathway of losing ArH for **8** was found to be more inhibited than that of **7**.

For ion **9** $[(o\text{-}COOCH_3\text{-}C_6H_4)Ni(PPh_3)_2]^+$ at *m/z* 717, the only fragmentation pathway observed was the dissociation of one PPh_3 ligand, suggesting the distinctive influence of *ortho*-substitution of carboxymethyl. A similar effect of the *ortho*-substitution of carboxymethyl was observed in the coupling of naphthol [66], which indicates the participation of *ortho*-ester in binding to the metal center. For ion **9**, we postulate that the coordination of *ortho*-carboxymethyl to nickel weakens the Ni-PPh_3 bonding, which facilitates the leaving of one PPh_3 ligand. This phenomenon is also accordance with the fact that in liquid-phase *ortho*-substitution of carboxymethyl in the ArI was found to facilitate coupling reaction [67].

Fragmentation of $[ArNi(PPh_3)]^+$ **7a**, **8a**, *and* **9a**

As the monophosphine complexes $[ArNi(PPh_3)]^+$ **7a** and **8a** is less crowded than the bisphosphine complexes $[ArNi(PPh_3)]^+$ **7** and **8**. It was thought that the pathway of losing ArH would be more favored for these monophosphine complexes. However, in MS/MS of ions **7a** $[(C_{10}H_7)Ni(PPh_3)]^+$ at *m/z* 447 and **8a** $[(o\text{-}CH_3\text{-}C_6H_4)Ni(PPh_3)]^+$ at *m/z* 411 (Figure 6), the fragment ion at *m/z* 319 by loss of ArH could not be observed clearly, indicating this pathway was more inhibited than that of **7**

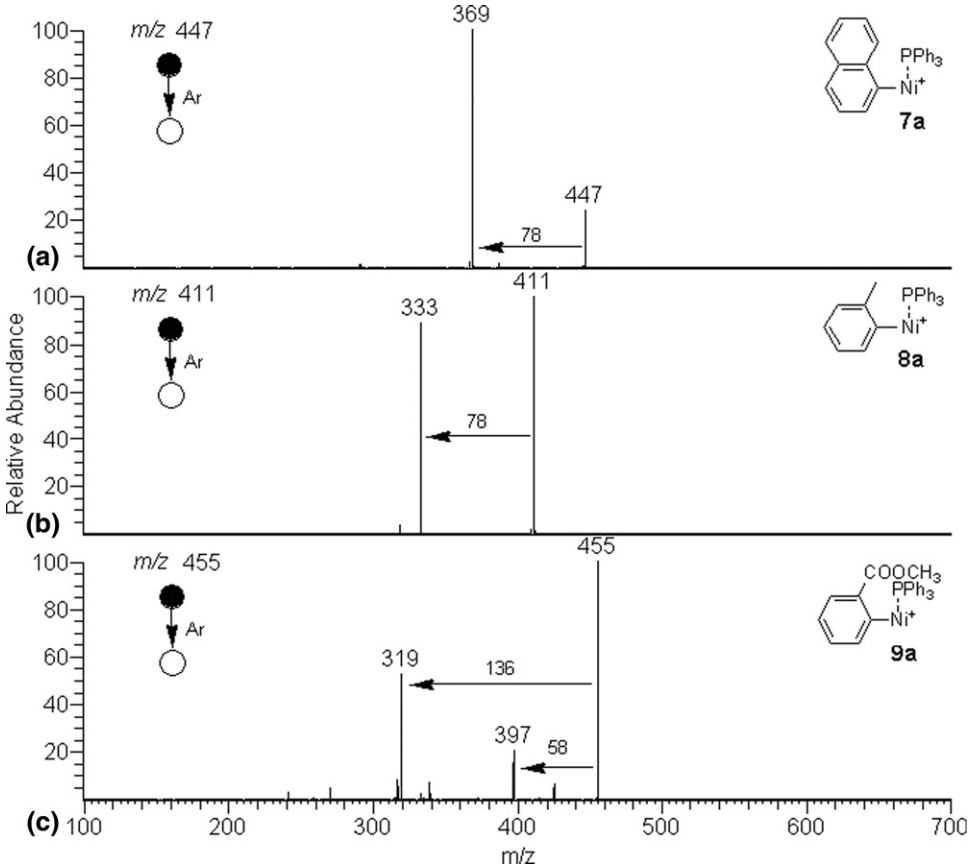


Figure 6. ESI-(+)-MS/MS for Complex **7a** at *m/z* 447, Complex **8a** at *m/z* 411, and Complex **9a** at *m/z* 455.

and **8**. It seems that a different mechanism operated for the dissociation of monophosphine complexes $[ArNi(PPh_3)]^+$. For ion **9a** $[(o\text{-}COOCH_3\text{-}C_6H_4)Ni(PPh_3)]^+$, the pathway of losing $C_6H_5COOCH_3$ was the primary fragmentation. The less steric hindrance of complex (monophophine coordination), the electron-withdrawing group (the *ortho*-group of carboxymethyl), or both might account for the observation fragmentation of **9a**. Further studies and experiments are needed to explain the detailed reaction mechanism of the gas-phase chemistry for those ions.

Conclusions

In conclusion, our MS/MS studies of cationic organonickel complexes $[ArNi(PPh_3)_n]^+$ (n = 1, 2) provide insights into the cyclometalation reactions promoted by Ni(II) in the gas phase. In the competitive fragmentation pathways related to the loss of Ar-H or benzene, the Ar-H was determined to form primarily from the Ni-bonded Ar group together with one hydrogen atom from the PPh_3 ligand, which is the evidence for the presence of a cyclometalation mechanism. Deuterium-labeling experiments further confirmed the existence of this process in the dissociation. Deuterium-labeling experiments also provided supports for the aryl-aryl interchange of complex ions of $[ArNi(PPh_3)_2]^+$. Additionally, in summarizing the dissociation pathways for $[ArNi(PPh_3)_n]^+$ ions, we found that the pathway of losing ArH is favored when the functional groups on the aromatic halides are electron-withdrawing. Our results highlight the importance of the electrophilicity of the metal center in the context of gas-phase cyclometalation, which correlates well with the mechanism of liquid-phase C–H bond activation.

Acknowledgments

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Appendix A Supplementary Material

Supplementary material associated with this article may be found in the online version at doi:10.1016/j.jasms.2010.03.040.

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