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RESEARCH ARTICLE

Gas Phase Decarbonylation and Cyclization Reactions of Protonated *N*-Methyl-*N*-Phenylmethacrylamide and Its Derivatives Via an Amide *Claisen* Rearrangement

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Abstract

Gas phase decarbonylation and cyclization reactions of protonated *N*-methyl-*N*-phenylmethacrylamide and its derivatives ($\mathbf{M}\cdot H^+$) were studied by electrospray ionization-tandem mass spectrometry (ESI-MS/MS). MS/MS experiments of $\mathbf{M}\cdot H^+$ showed product ions were formed by loss of CO, which could only occur with an amide *Claisen* rearrangement. Mechanisms for the gas phase decarbonylation and cyclization reactions were proposed based on the accurate *m/z* measurements and MS/MS experiments with deuterated compounds. Theoretical computations showed the gas phase *Claisen* rearrangement was a major driving force for initiating gas phase decarbonylation and cyclization reactions of $\mathbf{M}\cdot H^+$. Finally, the influence of different phenyl substituents on the gas phase *Claisen* rearrangement was evaluated. Electron-donating groups at the *para*-position of the phenyl moiety promoted the gas phase *Claisen* rearrangement to give a high abundance of fragment ions $[\mathbf{M} - CO + H]^+$. By contrast, electron-withdrawing groups on the phenyl moiety retarded the *Claisen* rearrangement, but gave a fragment ion at *m/z* 175 by loss of neutral radicals of substituents on the phenyl, and a fragment ion at *m/z* 160 by further loss of a methyl radical.

Key words: ESI-MS/MS, *N*-methyl-*N*-phenylmethacrylamides, Amide *Claisen* rearrangement reaction, Gas phase decarbonylation reaction, Gas phase cyclization reaction

Introduction

Tandem mass spectrometry provides extensive structural information about organic molecules, and is an important tool for mechanistic studies in gas phase organic chemistry [1–10]. Information about the energetics of gas phase reactions and fragmentation pathways can be investigated by adjusting the collision energy, the timescale of dissociation, and the collision gas. Recently, we reported many interesting gas phase reactions and related aromatic substitution rearrangement reactions, including benzyl migration [11], *Cope* rearrangement [11], *Smiles* rearrangement [12], metal cation catalyzed *Smiles* rearrangement [13, 14], gas phase rearrangement of the *p*-aminophenylsulfonyl cation [15], *sulfonyl-sulfinate* rearrangement [16], retro-*Michael* type fragmentation [17], and gas phase *Favorskii* rearrangement [18]. Certain analogies between reaction mechanisms in the gas phase and solution have been known for a long time [1–10, 19]. The reactivities and behaviors of ionic species in the gas phase and in solution can be correlated [12, 20–22], and there is a significant association between gas phase reactions and the analogous reactions in solution. Tandem mass spectrometry does not require large quantities of organic solvents and chemicals, and could be

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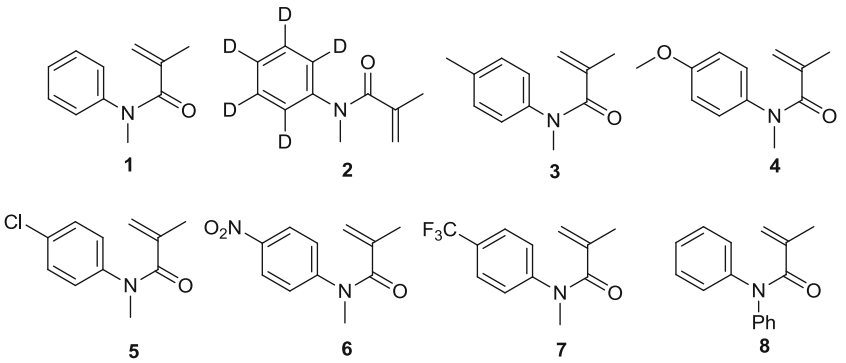


Scheme **1.** The structures of Compounds **1**–**8**

used as a high-throughput and green method to predict the chemical transformations of reactive compounds in solution.

As part of a continuing effort to study the gas phase rearrangement reactions, we studied the gas phase *Claisen* rearrangement reactions of protonated *N*-methyl-*N*-phenylmethacrylamide and its derivatives (Scheme 1 **1**–**8**) by ESI-MS/MS. These organic compounds have been used as reactive template substrates in palladium-catalyzed intramolecular oxidative aryltrifluoromethylation reaction and we have studied the reaction mechanism by ESI-MS [23]. Important Pd(IV) intermediates involved in the reaction were characterized by ESI-MS. Recently, further studies of gas phase reactions of these compounds showed their intrinsic intramolecular reactivities. These findings will aid development of analogous reactions in solution for synthetic chemistry.

The *Claisen* rearrangement [24] is a concerted [3,3] sigmatropic rearrangement reaction, which occurs in condensed and gas phases [25]. Gas phase *Claisen* rearrangements of protonated allyl phenyl ethers [26], protonated *N*-allylaniline [27], and protonated benzyloxy indoles have been investigated by mass spectrometry [28]. Similar gas phase *Claisen* rearrangement reactions have been reported in the dissociation process of radical cations formed by electron ionization mass spectrometry (EI-MS) [29–33]. Most of these gas phase *Claisen* rearrangement reactions of carbonyl compounds involve a CO-loss fragmentation pathway. In the present study, protonated *N*-methyl-*N*-phenylmethacrylamide and its derivatives (**1**·H^+–**8**·H^+) also gave fragment ions by loss of CO in MS/MS, and further in depth studies confirmed the occurrence of a gas phase amide *Claisen* rearrangement of **1**·H^+–**8**·H^+. Because of the close relationship between gas phase and solution reactions, we investigated the gas phase intrinsic reactivity of *N*-methyl-*N*-phenylmethacrylamide and its derivatives to explore their potential reactivity in novel reactions in solution.

Experimental

Chemicals and Materials

Compounds **1**–**8** were synthesized and verified by NMR, IR, and MS [23]. All sample solutions were prepared in CH_3CN (0.1 mg/mL).

ESI Triple Quadrupole Mass Spectrometer Experiments

The ESI-MS and subsequent MS/MS experiments were performed on a Finnigan TSQ Quantum Access triple-quadrupole mass spectrometer (Thermo Fisher Scientific, Waltham, MA, USA) equipped with a standard ESI ion source. Nitrogen was used as the sheath gas and auxiliary gas, and argon as the collision gas. The basic ESI conditions were as follows: vacuum, 2.8×10^{-6}Torr; spray voltage, 3800 V; capillary temperature, 270 °C; sheath gas pressure, 20 arbitrary units; and auxiliary gas pressure, 5 arbitrary units. The collision energy depended on the dissociation capability of the precursor ions. Data acquisition and analysis were carried out with the Xcalibur software package

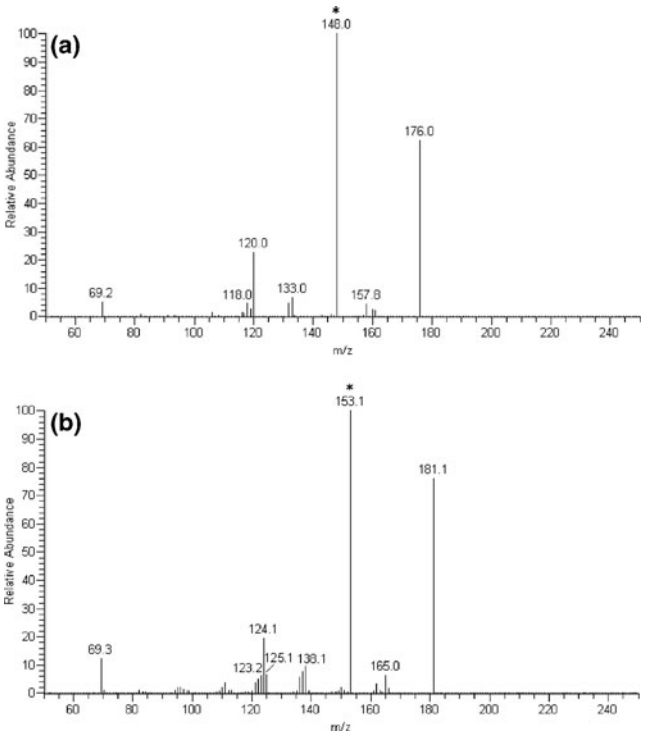


Figure 1. ESI-MS/MS spectra of (**a**) **1**·H^+ at *m/z* 176; (**b**) **2**·H^+ at *m/z* 181. The peaks marked with an asterisk are the gas phase decarbonylation and cyclization reaction product ions of **1**·H^+ and **2**·H^+

Table 1. Comparison of the ESI Q-TOF MS Results and the Theoretical *m/z* Values for the Product ions of **1**·H$^+$ in ESI-MS/MS

Possible elemental compositions	Detected *m/z* values	Theoretical *m/z* values	Relative error (ppm)
$C_{11}H_{14}NO^+$	176.1069	176.1070	0.6
$C_{10}H_{14}N^+$	148.1120	148.1121	0.7
$C_9H_{11}N^+$	133.0888	133.0886	–1.5
$C_8H_{10}N^+$	120.0812	120.0808	–3.3
$C_4H_5N^+$	69.0338	69.0335	–4.3

(ver. 2.0; Thermo Fisher Scientific). The injection speed was 10 μL/min.

Accurate m/z Measurements of Product Ions from 1·H$^+$ by ESI-Q-TOF MS

Accurate *m/z* measurements of product ions from **1**·H$^+$ were performed on an Agilent 6538 UHD accurate-mass quadrupole time-of-flight (Q-TOF) LC/MS system (Agilent Technologies, Santa Clara, CA, USA). The system was controlled by Agilent MassHunter workstation software for Q-TOF LC/MS (ver. B.04.00; Agilent Technologies). ESI-MS/MS experiments were performed in positive ion mode with the capillary voltage set at 4000 V and fragmentor voltage at 125 V. The desolvent temperature was 350 °C, and the drying gas (N_2) flow rate was 8 L/min. The collision gas (N_2) was set at 5 psi. The ESI Q-TOF MS was tuned and calibrated with TOF Tuning Mix solution and TOF Reference Mix solution (Agilent Technologies), respectively. The CH_3CN solution of **1** was injected at 10 μL/min.

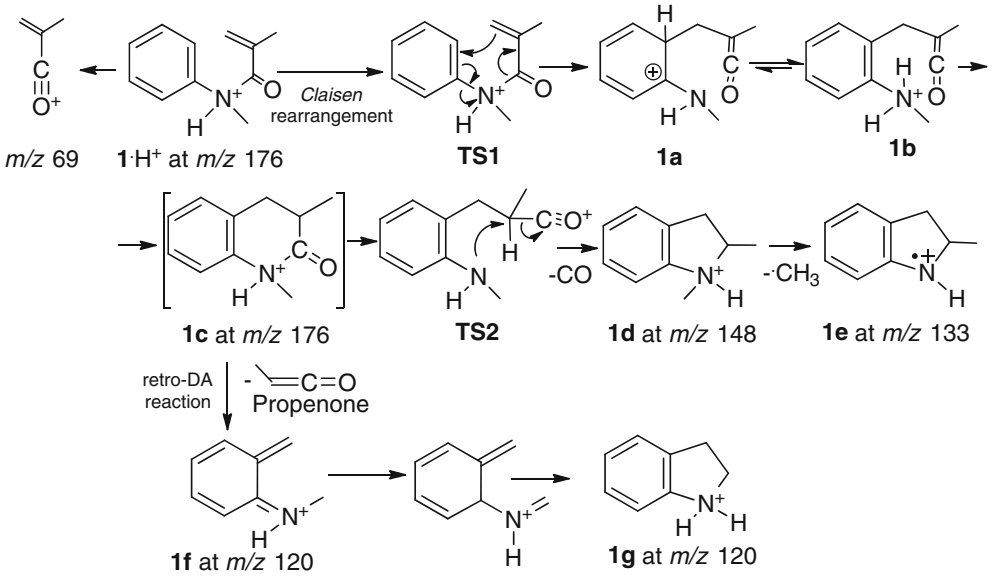
Theoretical Computation Methods

The structures of the ions in the fragmentation pathways of **1**·H$^+$ at *m/z* 176 to protonated 1,2-dimethylindoline (**1d**) at *m/z* 148, were optimized by the density functional theory (DFT) with B3LYP (Gaussian 03; Gaussian Inc., Wallingford, CT, USA) with the standard 6-311 G (d,p) basis set [34]. The Gibbs free energies were calculated using the optimized geometries and frequency calculations. The structures of two transition states (**TS1** and **TS2**) were optimized and subjected to vibration frequency analysis by ab initio restricted Hatree-Fock method with Spartan molecular modeling software (PC Spartan Pro. ver. 1.0.7; Wavefunction Inc., Irvine, CA, USA) using the STO-3 G basis set [35]. Then the Gibbs free energy of the two transition states (**TS1** and **TS2**) were calculated by DFT-B3LYP 6-311 G (d,p) with Gaussian 03. The Gibbs free energy of CO was taken into consideration during these calculations.

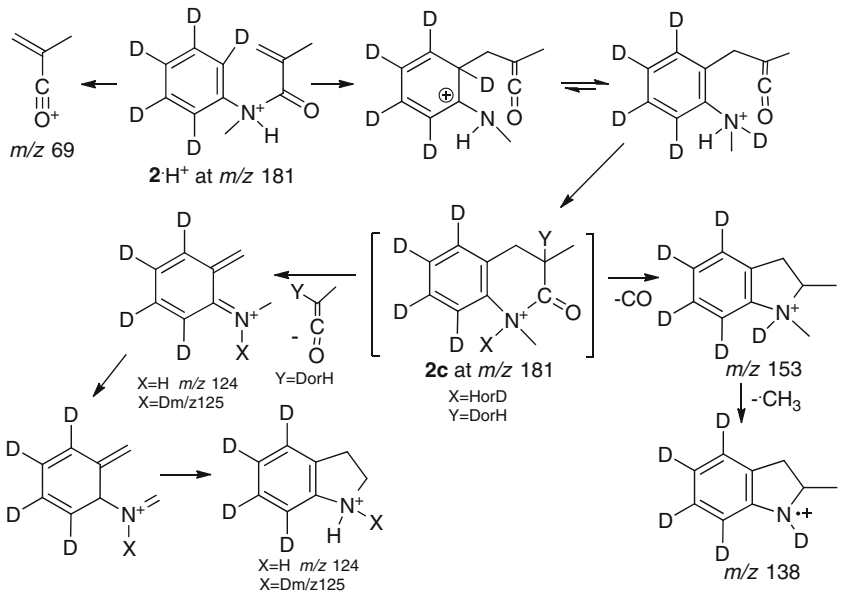
Results and Discussion

Gas Phase Amide Claisen Rearrangement Reactions of Protonated N-Methyl-N-Phenylmethacrylamide and Its Derivatives

As a continuation of mass spectrometry investigations of gas phase rearrangement reactions, we explored the gas phase rearrangement reactions of protonated *N*-methyl-*N*-phenylmethacrylamide and its derivatives. The full scan ESI mass spectra of these compounds gave clear and intense signals for **M**·H$^+$, and the in-source decay fragment ions of **M**·H$^+$ were similar to the product ions of **M**·H$^+$ in MS/MS. With a collision energy of 18 eV, the ESI-MS/MS spectra of **1**·H$^+$ at *m/z* 176 and **2**·H$^+$ at *m/z* 181 were shown in Figure 1. It should be noted that Compound **2** is d_5-labeled Compound **1**. ESI-MS/MS of **1**·H$^+$ at *m/z* 176 gave a primary product ion at *m/z* 148 and other low intensity product ions at *m/z* 133 and 120, and (2-methylallylidyne)oxonium at *m/z* 69 (Figure 1a).



Scheme **2.** Proposed rearrangement/fragmentation pathways of **1**·H$^+$ in ESI-MS/MS



Scheme **3.** Proposed rearrangement/fragmentation pathways of **2**·H$^+$ in ESI-MS/MS

Table 1 shows the accurate masses of the proposed product ions from **1**·H$^+$ at *m/z* 176 by ESI-Q-TOF MS. These results supported the proposed structures of the product ions of **1**·H$^+$. As shown in Figure 1, the product ion at *m/z* 148 from **1**·H$^+$ and product ion at *m/z* 151 from **2**·H$^+$ were formed by gas phase decarbonylation reactions, which require skeleton rearrangement. The proposed fragmentation pathways of **1**·H$^+$ at *m/z* 176 and **2**·H$^+$ at *m/z* 181 are shown in Schemes 2 and 3, respectively. According to these reaction schemes, the product ions of **1**·H$^+$ or **2**·H$^+$ could be divided into the following two categories: (1) fragment ions of **1**·H$^+$ and **2**·H$^+$ without rearrangement before the *Claisen* reaction, such as the ion at *m/z* 69, which is a typical fragment ion of **1**·H$^+$-**8**·H$^+$; (2) fragment ions of rearranged **1**·H$^+$ or **2**·H$^+$, such as the product ions at *m/z* 148, 133, and 120 from **1**·H$^+$ and the product ions at *m/z* 153, 138 and 124 from **2**·H$^+$. The major product ions of **1**·H$^+$ or **2**·H$^+$ were the fragment ions of rearranged **1**·H$^+$ or **2**·H$^+$, which suggests they have high gas phase *Claisen* rearrangement reactivity.

The major driving force of the decarbonylation of **1**·H$^+$ is a *Claisen* rearrangement. Gas phase *Claisen* rearrangement of **1**·H$^+$ first produces ketene intermediate **1a** by breaking the amide N-C bond via **TS1**, and **1a** then rearranges to **1b**

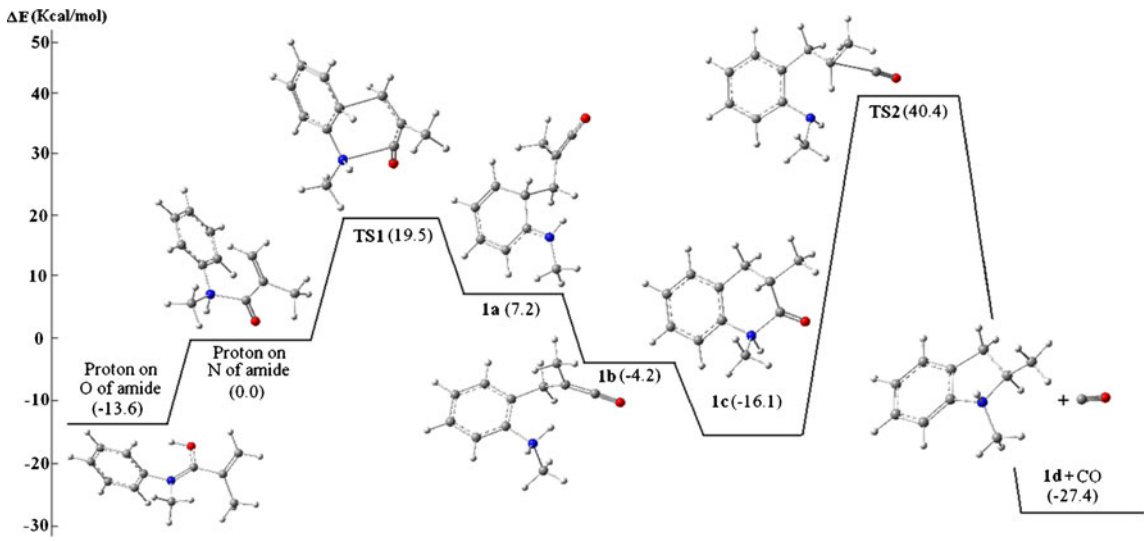


Figure 2. DFT B3LYP 6-311 G (d,p) optimized structures and relative Gibbs free energies of the ions along the multistep fragmentation pathways of **1**·H$^+$ at *m/z* 176 to **1d** at *m/z* 148. This involved a gas phase *Claisen* rearrangement via the transition state **TS1**, and finally **1c** dissociated to the **1d** ion at *m/z* 148 by loss of CO through **TS2.** The relative Gibbs free energy of **1**·H$^+$ at *m/z* 176 (protonation on *N* atom of amide) was set at 0 kcal/mol

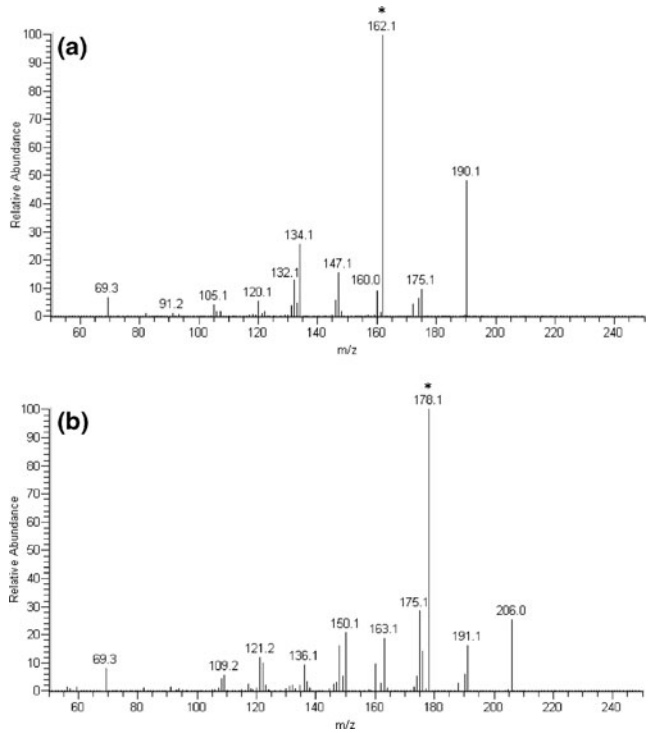
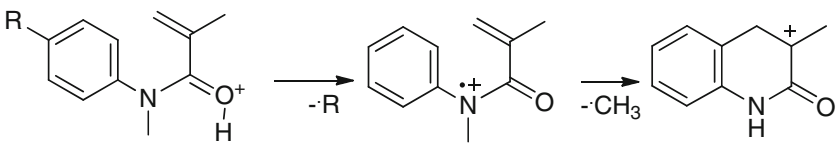


Figure 3. ESI-MS/MS spectra of (**a**) **3**·H$^+$ at *m/z* 190; (**b**) **4**·H$^+$ at *m/z* 206. The peaks marked with asterisks are the gas phase decarbonylation and cyclization reaction product ions of **3**·H$^+$ and **4**·H$^+$

by hydrogen migration [36] (Scheme 2). Ion **1b** undergoes intramolecular hydrogen rearrangement and cyclocondensation via attack of an amine at the ketene to intermediate **1c**, which has a dihydroquinolinone structure. Intermediate **1c** dissociates to the major product ion protonated 1,2-dimethylindoline (**1d**) at *m/z* 148 by expulsion of neutral CO and to protonated indoline (**1 g**) at *m/z* 120 by loss of neutral propenone via gas phase retro *Diels-Alder* (DA) reaction.

ESI-MS/MS of **2**·H$^+$ showed similar a product ion at *m/z* 153, which confirmed the mechanism of the decarbonylation process described above. The formation of a product ion at *m/z* 125 from **2**·H$^+$ at *m/z* 181 proved that the gas phase *Claisen* rearrangement process produced a mobile deuterium cation from the deuterium labeled phenyl moiety. The gas phase retro-DA reaction of **2c** at *m/z* 181 mainly gave a product ion at *m/z* 124 because of the proton/amine interaction was stronger than that with deuterium cation (Scheme 3). Thus, decarbonylation of **1**·H$^+$ and **2**·H$^+$ involved simultaneous breaking of C–N and C–C bonds and formation of C–C and C–N bonds. The gas phase intramolecular dissociation process of **1**·H$^+$ was an interesting gas phase synthesis of protonated indoline and 1,2-dimethylindoline.

The theoretical results could be used to study the formation mechanism of product ion **1d** at *m/z* 148 from **1**·H$^+$ at *m/z* 176 via the gas phase amide *Claisen* rearrangement. The structures of **1a**–**1d** and **TS1**–**TS2** were optimized and shown in Figure 2. The theoretical computations showed two possible original structures and their relative Gibbs free energies for **1**·H$^+$ at *m/z* 176 because of different protonation sites (Figure 2). When the relative Gibbs free energy of the precursor ion **1**·H$^+$ at *m/z* 176 with protonation of the *N* atom on the amide was set at 0 kcal/mol, the structure of **1**·H$^+$ at *m/z* 176 with protonation of the O atom on the amide had a lower Gibbs free energy (–13.6 kcal/mol, Figure 2). Protonation of the *N* atom on the amide facilitated the gas phase *Claisen* rearrangement of **1**·H$^+$ by readily breaking the C–N bond and forming a new C–C bond to **1a**. This had a relative Gibbs free energy of 7.2 kcal/mol and occurred via a six-membered ring transition state, **TS1**. The energy barrier of this *Claisen* rearrangement was 19.5 kcal/mol. Aromatization of **1a** by hydrogen migration gave a more stable structure for **1b** with a relative Gibbs free energies of –4.2 kcal/mol. Then, the intermediate **1c** is formed as described above. Intermediate **1c** is stable and contains a six-membered ring, its relative Gibbs free energy is –16.1 kcal/mol. Finally, **1c** dissociates to form the major product ion, protonated 1,2-dimethylindoline (**1d**) at *m/z* 148, by loss of CO via a six-membered ring transition state, **TS2**. The theoretical computations show that hydrogen bonding stabilizes the structure of **TS2**. The energy barrier for the decarbonylation reaction of **1c** is 56.5 kcal/mol. The schematic potential energy surface (in kcal/mol) of this gas phase reaction is shown in



3·H$^+$ at *m/z* 190,R=CH_3
4·H$^+$ at *m/z* 206,R=OCH_3
5·H$^+$ at *m/z* 210,R= ^{35}Cl
5·H$^+$ at *m/z* 212,R= ^{37}Cl
6·H$^+$ at *m/z* 221,R=NO_2
7·H$^+$ at *m/z* 244,R=CF_3

Scheme 4. Proposed dissociation pathways of **3**·H$^+$–**7**·H$^+$ to product ion at *m/z* 175 by loss of neutral radical ·R and further to product ion at *m/z* 160 by loss of ·CH_3 in ESI-MS/MS

Figure 2. The conversion of $\mathbf{1}\cdot H^+$ at *m/z* 176 (protonation on *N* atom of the amide) to **1d** at *m/z* 148 and CO is a multistep and highly exothermic process (by 27.4 kcal/mol). This gas phase rearrangement of $\mathbf{1}\cdot H^+$ at *m/z* 176 to **1d** at *m/z* 148 by loss of CO is thermodynamically feasible, which is in agreement with the MS/MS experimental results of $\mathbf{1}\cdot H^+$ at *m/z* 176.

The Influence of Electronic Effects of Phenyl Substituents on the Gas Phase Amide Claisen Rearrangement

To investigate the effects of phenyl substituents on the *Claisen* rearrangement, derivatives of **3**–**8** with various substituent groups (Scheme 1) were analyzed by ESI-MS/MS. Compounds **3** and **4** contained the electron-donating groups methyl and methoxy, respectively. MS/MS of $\mathbf{3}\cdot H^+$ at *m/z* 190 and $\mathbf{4}\cdot H^+$ at *m/z* 206 gave fragment ions $[\mathbf{M} - CO + H]^+$ with high relative abundance at *m/z* 162 and 178, respectively, which were formed by loss of CO (Figure 3). The CO loss can be explained by a *Claisen* rearrangement analogous to that with compound **1**. However, small amounts of a fragment ion at *m/z* 175 formed by loss of a neutral radical $\cdot OCH_3$, and an ion at *m/z* 160 formed by further loss of the methyl radical $\cdot CH_3$, were detected in the MS/MS of $\mathbf{4}\cdot H^+$ (Scheme 4). Table 2 summarizes the substituent effects of $\mathbf{1}\cdot H^+$–$\mathbf{8}\cdot H^+$ on the gas phase *Claisen* rearrangement in terms of the peak ratio $[\mathbf{M} - CO + H]^+/\mathbf{M}\cdot H^+$. The $[\mathbf{M} - CO + H]^+/\mathbf{M}\cdot H^+$ ratio of $\mathbf{4}\cdot H^+$ at *m/z* 206 was 3.8, and was higher than that of $\mathbf{3}\cdot H^+$ at *m/z* 190 (2.1) because of the higher electron-donating ability of the methoxy group compared to the methyl group. Electron-donating groups, such as OCH_3, which promote the gas phase *Claisen* rearrangement and increase the relative abundance of product ions of $[\mathbf{M} - CO + H]^+$, and only small amounts of product ions at *m/z* 175 and 160 will form (Scheme 4).

With an electron-withdrawing substituent (R), such as Cl, NO_2, or CF_3, $\mathbf{M}\cdot H^+$ could undergo a new type of fragmentation to give a fragment ion at *m/z* 175 formed by loss of neutral radical ·R, and finally to an ion at *m/z* 160 formed by loss of $\cdot CH_3$ (Scheme 4). Compared with the MS/

Table 2. Summary of Substituent Effects on the Gas Phase *Claisen* Rearrangement in Terms of the Peak Ratio $[\mathbf{M} - CO + H]^+/\mathbf{M}\cdot H^+$

Compounds	R groups	Ratios of $[\mathbf{M} - CO + H]^+/\mathbf{M}\cdot H^+$
1	–H	1.6
2[a]	–D	1.3
3	$-CH_3$	2.1
4	$-OCH_3$	3.8
5	–Cl	1.8
6	–NO2	0.6
7	–CF3	0.1
8[b]	–H	0.6

Compounds **1**–**7** had a methyl group on the *N* atom and had different *para*-substituents on the phenyl moiety (R group, Scheme 1)
[a]Compound **2** was a d_5-labeled isomer of Compound **1**
[b]Compound **8** had a phenyl group on the *N* atom

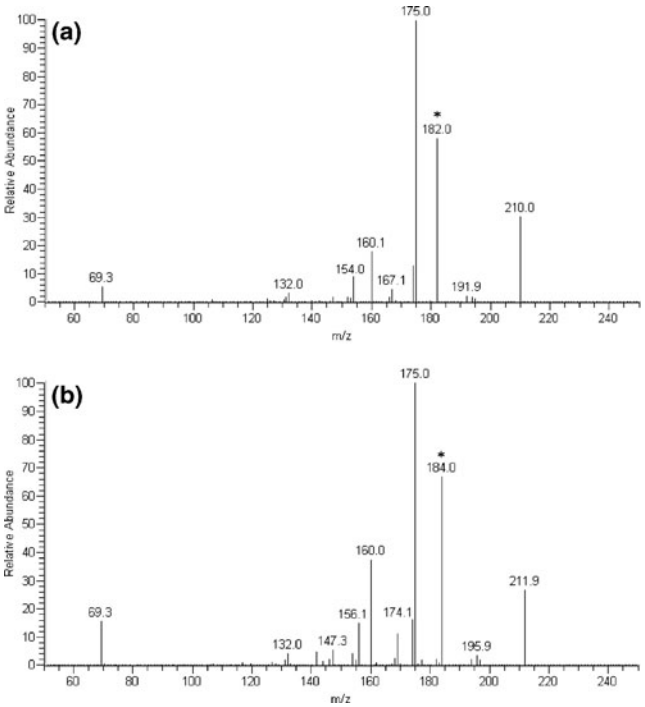


Figure 4. ESI-MS/MS spectra of (**a**) $\mathbf{5}\cdot H^+$ at *m/z* 210 (containing ^{35}Cl); (**b**) $\mathbf{5}\cdot H^+$ at *m/z* 212 (containing ^{37}Cl). The peaks marked with asterisks are the gas phase decarbonylation and cyclization reaction product ions of $\mathbf{5}\cdot H^+$

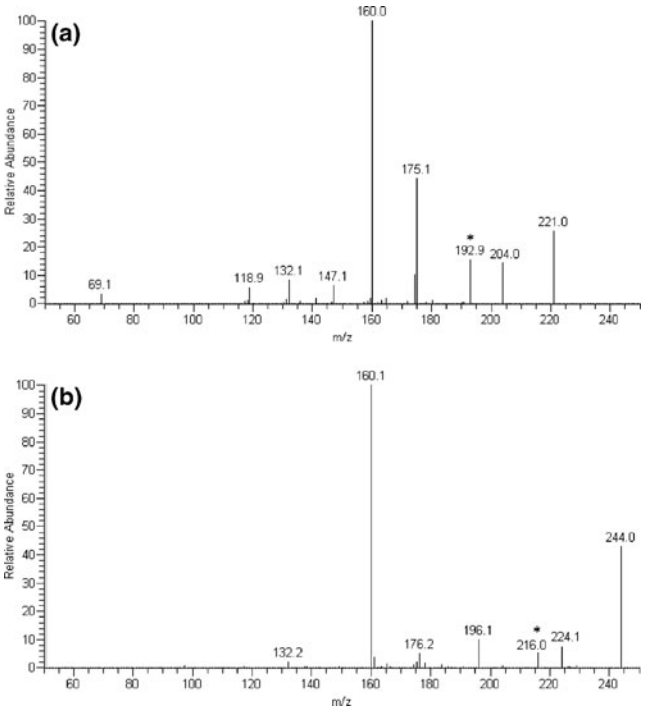


Figure 5. ESI-MS/MS spectra of (**a**) $\mathbf{6}\cdot H^+$ at *m/z* 221; (**b**) $\mathbf{7}\cdot H^+$ at *m/z* 244. The peaks marked with asterisks are the gas phase decarbonylation and cyclization reaction product ions of $\mathbf{6}\cdot H^+$ and $\mathbf{7}\cdot H^+$

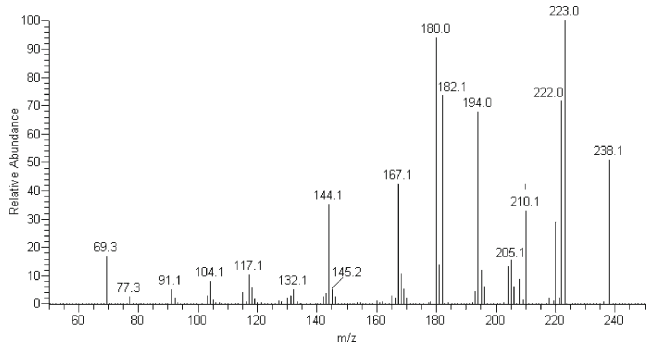


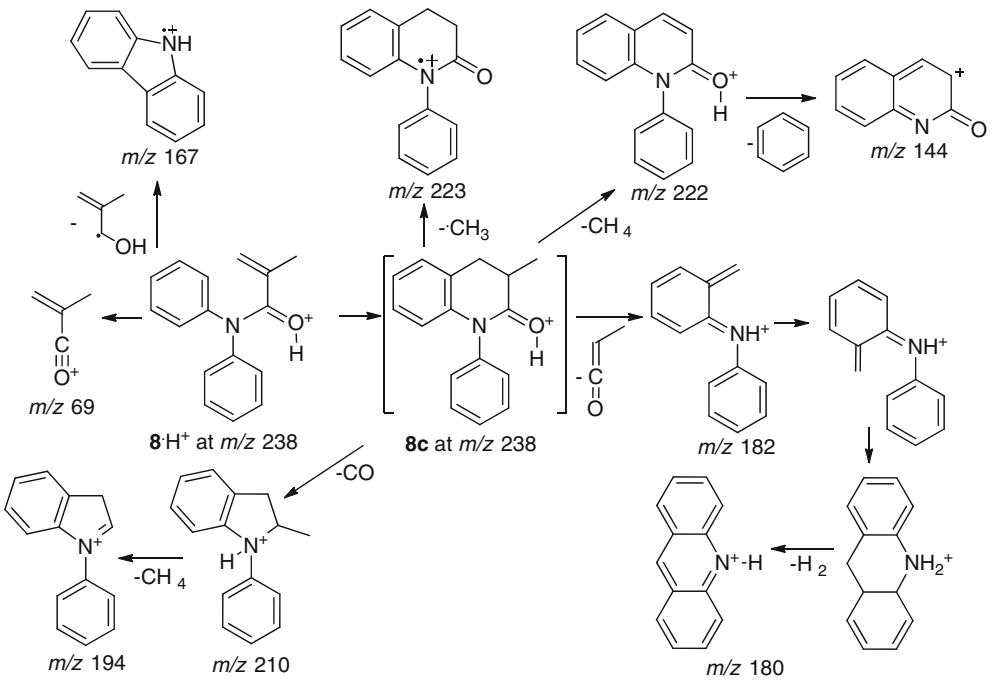
Figure 6. ESI-MS/MS spectrum of **8**·H$^+$ at *m/z* 238. The peaks marked with asterisks are the gas phase decarbonylation and cyclization reaction product ion of **8**·H$^+$

MS spectrum of **1**·H$^+$, the relative abundance of fragment ions [**M** − CO + H]$^+$ at *m/z* 182 from **5**·H$^+$ decreased significantly (Figure 4). Because Cl substituent on phenyl group is not a strong electron-withdrawing group [37], the peak ratio of [**M** − CO + H]$^+$/**M**·H$^+$ of **5**·H$^+$ is 1.8 (Figure 4a), which has no significant difference with that of **1**·H$^+$ (1.6). Meanwhile the fragment ion at *m/z* 175 formed by loss of a neutral radical of the substituent ·Cl was the major fragment ion of **5**·H$^+$ at *m/z* 210 containing ^{35}Cl and *m/z* 212 containing ^{37}Cl. This confirmed the proposed dissociation pathways of **M**·H$^+$ with different substituents (R groups) by loss of a neutral radical of the substituent (Scheme 4).

With a strong electron withdrawing group, such as NO_2 or CF_3, on the phenyl group, only a small amount of fragment ions [**M** − CO + H]$^+$ at *m/z* 193 and 216 formed by loss of CO from **6**·H$^+$ at *m/z* 221 and **7**·H$^+$ at *m/z* 244, respectively (Figure 5). According to Table 2, the [**M** − CO + H]$^+$/**M**·H$^+$ ratios of **6**·H$^+$ (0.6) and **7**·H$^+$ (0.1) were much lower than that of **1**·H$^+$ (1.6) because of the stronger electron-withdrawing groups (NO_2 and CF_3) they contained. The major fragment ions of **6**·H$^+$ and **7**·H$^+$ were ion at *m/z* 175 formed by loss of neutral substituent radicals (·NO_2 or ·CF_3), and ion at *m/z* 160 formed by further loss of ·CH_3, in similar dissociation pathways to **5**·H$^+$. An electron-withdrawing substituent on the phenyl group retarded the gas phase *Claisen* rearrangement in solvent free conditions. Meanwhile **6**·H$^+$ at *m/z* 221 gave a fragment ion at *m/z* 204 formed by loss of ·OH, and **7**·H$^+$ at *m/z* 244 gave a fragment ion at *m/z* 224 formed by loss of HF. These are the typical fragmentation pathways of compounds containing NO_2 or CF_3. The peak for the fragment ion at *m/z* 175 from **7**·H$^+$ at *m/z* 244 was extremely low. The fragment ion at *m/z* 176 was formed by loss of 2HF from the *Claisen* rearrangement fragment ion at *m/z* 216, which was formed by loss of CO from **7**·H$^+$ at *m/z* 244.

Previous studies showed that the reaction rates of the *Claisen* rearrangement in solution were slightly dependent on the substitution group effect, with electron-donating groups increasing the rate and electron-withdrawing groups decreasing the rate [37, 38]. Our results for the substitution group effect were consistent with these studies. The only difference was that the effect on the reaction rate was larger in solvent free conditions than in solution.

The methyl group on the *N* atom was changed to a phenyl group in compound **8**. The decarbonylation reaction initiated by the *Claisen* rearrangement produced [**8** − CO + H]$^+$ at *m/z* 210, and [**8** − CO–CH_4 + H]$^+$ at *m/z* 194 was formed by



Scheme **5.** Proposed rearrangement/fragmentation pathways of **8**·H$^+$ in ESI-MS/MS

further loss of CH_4. However, these were not the major dissociation pathways of $\mathbf{8}\cdot H^+$ (Figure 6), and some new interesting rearrangement processes occurred. The proposed formation pathways of product ions from $\mathbf{8}\cdot H^+$ in ESI-MS/MS are shown Scheme 5. The six-membered ring intermediate **8c** is proposed as an important intermediate to form various fragment ions. The strong conjunction effect of the phenyl group could explain formation of the various fragment ions with ring structures, such as the ions at *m/z* 223, 222, 144, 194, 182, 180, and 167 (Scheme 5).

Conclusion

This investigation of the gas phase decarbonylation and cyclization of protonated *N*-methyl-*N*-phenylmethacrylamides via an amide *Claisen* rearrangement provides important insight into the intrinsic gas phase reactivity of these compounds and the origin and mechanism of the gas phase amide *Claisen* rearrangement reaction. Electron-donating groups on the phenyl moiety promoted the gas phase *Claisen* rearrangement to give a high abundance of fragment ions $[\mathbf{M} - CO + H]^+$. By contrast, electron-withdrawing groups on the phenyl moiety retarded the *Claisen* rearrangement and gave fragment ion at *m/z* 175 by loss of neutral radicals of the phenyl substituents and fragment ion at *m/z* 160 by further loss of $\cdot CH_3$. This report of the intrinsic reactivity of these compounds (**1**–**8**) to form indoline derivatives is novel, and could be used to investigate new solution phase chemical transformations of these reactive compounds to indoline derivatives.

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