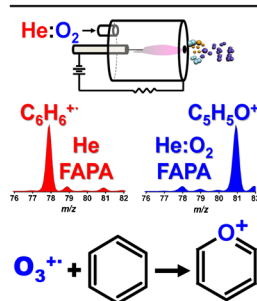


# Formation of Pirylium from Aromatic Systems with a Helium:Oxygen Flowing Atmospheric Pressure Afterglow (FAPA) Plasma Source

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**Abstract.** The effects of oxygen addition on a helium-based flowing atmospheric pressure afterglow (FAPA) ionization source are explored. Small amounts of oxygen doped into the helium discharge gas resulted in an increase in abundance of protonated water clusters by at least three times. A corresponding increase in protonated analyte signal was also observed for small polar analytes, such as methanol and acetone. Meanwhile, most other reagent ions (e.g.,  $O_2^{+}$ ,  $NO^+$ , etc.) significantly decrease in abundance with even 0.1% v/v oxygen in the discharge gas. Interestingly, when analytes that contained aromatic constituents were subjected to a He:O<sub>2</sub>-FAPA, a unique  $(M + 3)^+$  ion resulted, while molecular or protonated molecular ions were rarely detected. Exact-mass measurements revealed that these  $(M + 3)^+$  ions

correspond to  $(M - CH + O)^+$ , with the most likely structure being pyrylium. Presence of pyrylium-based ions was further confirmed by tandem mass spectrometry of the  $(M + 3)^+$  ion compared with that of a commercially available salt. Lastly, rapid and efficient production of pyrylium in the gas phase was used to convert benzene into pyridine. Though this pyrylium-formation reaction has not been shown before, the reaction is rapid and efficient. Potential reactant species, which could lead to pyrylium formation, were determined from reagent-ion mass spectra. Thermodynamic evaluation of reaction pathways was aided by calculation of the formation enthalpy for pyrylium, which was found to be 689.8 kJ/mol. Based on these results, we propose that this reaction is initiated by ionized ozone ( $O_3^{+}$ ), proceeds similarly to ozonolysis, and results in the neutral loss of the stable  $CHO_2^{\cdot}$  radical.

**Keywords:** Ion–molecule reactions, Ambient mass spectrometry, Pirylium formation, Mixed-gas plasma, Atmospheric-pressure glow discharge

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## Introduction

Helium is the most commonly used discharge gas in plasma-based ambient desorption/ionization (ADI) sources [1–6] due to the large reaction cross-section of excited helium species with atmospheric gases, such as  $N_2$  and  $H_2O$  [7], which lead to greater reagent-ion densities. Several other gases, such as nitrogen, argon, and air, also have been tested as plasma gases for ADI sources; however, helium provides the best sensitivity for most analytes regardless of discharge type or

geometry [5]. Apart from discharge-gas composition, several other operating parameters of these ionization sources also affect the plasma characteristics and lead to alternative ionization pathways. For instance, Cody [8] measured molecular ions for nonpolar and aliphatic compounds with a direct analysis in real time (DART) ionization source. The conditions for production of those spectra were that the grid-electrode potentials were increased by several hundred volts, the gas-heater temperature was elevated, and the source was positioned very close (*ca.* 3 mm) to the mass-spectrometer inlet. Badal et al. [9] demonstrated the ability to tune between charge-transfer and proton-transfer ionization mechanisms simply by changing the operating parameters of a flowing atmospheric pressure afterglow (FAPA) ionization source. In that work, it was observed that charge-transfer ionization was dominant when the

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discharge current was high and helium flow rate was low, whereas proton-transfer ionization dominated at lower discharge currents and higher plasma-gas flow rates.

Some groups have explored the utility of mixed gas plasmas to enhance the sensitivity for different analytes in ADI applications. For instance, Brewer et al. [10] observed 3-fold and 9-fold increases in molecular-ion signal for naproxen with a radiofrequency helium:oxygen atmospheric pressure glow discharge (APGD) source compared with pure helium and pure argon plasmas, respectively. In addition, they observed extensive fragmentation of analytes with the mixed-gas APGD, which produced spectra that were EI-database searchable. More recently, it has been shown that the addition of low mole fractions of molecular hydrogen to a helium dielectric-barrier discharge (DBD) can enhance protonated analyte-ion signal,  $(M + H)^+$ , up to 68 times for some analytes without a corresponding increase in chemical background [11, 12]. These studies demonstrate the diversity in chemistries that can be obtained from a range of plasma source configurations; simple modifications of discharge parameters or doping small amounts of molecular gases into the discharge can have profound effects on plasma chemistry and analyte ionization. Here, we explore the effects of O<sub>2</sub> addition on the gas-phase ion chemistry of a helium FAPA source. The FAPA source, which is based around a direct current (DC) APGD [4], provides a relatively simple, yet stable and robust, platform to probe and explore chemistries of pure and mixed gas plasmas [9, 13].

Atmospheric-pressure plasmas are well-suited for gas-phase chemistry as they efficiently produce excited species, ions, and electrons over a broad range of energies. These species can lead to unique chemical reactions through ion–molecule and ion–ion reactions. For example, production of phenol via oxidation of aromatic systems has commonly been observed with atmospheric pressure chemical ionization (APCI) with a DC corona discharge, though this reaction and the resulting products are commonly viewed as a nuisance in mass - spectrometric analyses [14]. In addition, a number of unique chemical reactions have been demonstrated with alternating current (AC) dielectric barrier discharges (DBDs). In 2009, Na et al. [15] reported the Birch reduction of benzene to 1,4-cyclohexadiene with a DBD-based low-temperature plasma (LTP). They observed dihydrogenation of benzene and other arenes when introduced to the discharge region of the LTP. More recently, a single-step nitrogen-atom insertion between carbon–carbon bonds of saturated alkanes has been shown with gas-phase reactant ions, such as N<sub>3</sub><sup>+</sup>, generated in microdischarges in nitrogen gas at atmospheric pressure [16]. Furthermore, Zhang et al. [17] observed the replacement of a carbon atom with a nitrogen atom in the benzene ring via a reaction with plasma-produced reactants. In this case, the reaction was observed when benzene was introduced directly into the discharge of an LTP probe operated with air, N<sub>2</sub>, or even NO-doped N<sub>2</sub> as the discharge gas.

In this work, we show a unique chemical modification of aromatic systems with an oxygen-doped helium-FAPA (He:O<sub>2</sub>-FAPA). Specifically, when aromatic ring-containing analytes

were subjected to a He:O<sub>2</sub>-FAPA, a unique  $(M + 3)^+$  ion was always produced; it was found that these ions correspond to  $(M - CH + O)^+$ . These ions were confirmed to be pyrylium-based through exact mass and tandem mass spectrometry measurements. The utility of rapid gas-phase pyrylium-ion formation is also demonstrated through S<sub>N</sub>2 chemistry with ammonia. Lastly, a potential mechanism and likely reactant species that cause aryl-to-pyrylium conversion will be discussed.

## Experimental

### Reagents

All reagents used were analytical grade. Ultra-high purity helium (99.999%) and a helium/oxygen mixture (80%/20%) were obtained from Airgas (Radnor, PA, USA). Biphenyl was purchased from ACROS Organics (Morris Plains, NJ, USA), while benzene, 1,3,5-trimethylbenzene, 2,4,6-trimethylpyrylium tetrafluoroborate, acetaminophen, and benzene-d<sub>6</sub> were purchased from Sigma-Aldrich (St. Louis, MO, USA).

### Ionization Source

The FAPA used here was of a pin-to-plate geometry as described by Shelley et al. [18]. Briefly, an atmospheric pressure glow discharge (APGD) was sustained between a stainless-steel pin cathode and brass plate anode. The electrodes were held in place inside a quartz discharge chamber. Discharge species (*e.g.*, excited species, ions, and electrons) interact with atmospheric gases and analytes as they exit a 1.6-mm hole in the anode plate. A high DC potential (*ca.* - 550 V) was applied to the pin electrode from a custom-built high-voltage power supply (Prosolia Inc., Indianapolis, IN, USA), capable of providing up to 30 mA at - 2000 V. The circuit was completed by connecting the anode to the ground terminal of the power supply. The APGD of the FAPA was operated in a current controlled mode with 20-mA of current. The flow rate of helium was controlled with a mass flow controller (model C50L-AL-DD-2-PV2-V0-SCR; Sierra Instruments Inc., Monterey, CA, USA) whereas another mass flow controller (model C50L-AL-DD-2-PV2-V0-SCR; Sierra Instruments Inc.) was used to control the flow rate of helium/oxygen mixture. The gas flows were mixed in a T-junction connected to the discharge chamber. The accuracy and precision of the flow controller used for the helium/oxygen mixture dictated the smallest fraction of oxygen that could be reproducibly introduced into the discharge, which was 0.1%. The source was mounted onto a manual xyz translation stage (PT3; Thorlabs Inc., Newton, NJ, USA) for precise alignment of the ion source with the mass spectrometer inlet. Volatile analytes, such as acetone, methanol, and benzene, were introduced to the FAPA afterglow through a fused-silica capillary with nitrogen as a carrier gas. Solid analytes were introduced to the FAPA with the glass probe fixed on a one-dimensional translation stage (PT1; Thorlabs Inc., Newton, NJ, USA), similar to previous arrangements [19, 20].

An electrospray ionization source (HESI-II probe, Thermo Scientific, San Jose, CA, USA) was used to generate comparison mass spectra and product ion mass spectra of 2,4,6-trimethylpyrylium tetrafluoroborate. A 0.4 mM solution of 2,4,6-trimethylpyrylium tetrafluoroborate was prepared in a methanol:water mixture (50%:50%). The flow rate was set to 5  $\mu$ L/min. Sheath gas flow rate, sweep gas flow rate, and auxiliary gas flow rate all were set to zero. The ESI source voltage was 5.0 kV.

### Mass Spectrometry

Low resolution and tandem mass spectra were acquired with Thermo LTQ XL linear ion trap mass spectrometer (Thermo Scientific, San Jose, CA, USA), while a Thermo Exactive Plus mass spectrometer (Thermo Scientific, Bremen, Germany) was used for exact mass measurements. The LTQ XL mass spectra were collected in positive ionization mode with a maximum injection time of 100 ms and three microscans per spectrum. Capillary temperature was maintained at 275 °C. For reagent-ion measurements, capillary and tube lens voltages were held at 2 and 31 V, respectively, whereas, higher mass-to-charge detection was done with capillary and tube lens voltages of 15 and 65 V, respectively. High resolution mass spectra were also collected in positive ionization mode with inlet capillary temperature, capillary voltage, and S-lens rf level of 320 °C, 0 V, and 50%, respectively.

### Pyrylium Enthalpy Calculations

The enthalpy of formation for pyrylium was determined with energies derived from ab initio density functional theory (DFT) calculations. The Becke's three parameter hybrid DFT/HF method with Lee-Yang-Parr's correlation functional (B3LYP) was used for structural optimization and energy calculation obtained using Gaussian09. An isodesmic reaction scheme shown in Supplementary Figure S-1 was used to calculate the enthalpy of formation for pyrylium. The molecular structures of benzene, furan, cyclopentadienyl anion, and pyrylium were prepared using B3lyp/3-21G theoretical model using thermochemical data from the literature [21–23]. An HF/6-31G\* optimization was performed and the resultant geometries and orbitals were used as the input for geometric optimization and frequency analysis with B3lyp/6-31+G\*, which provided a zero-point-energy (ZPE) for the isodesmic reaction. The optimized structures were then used to calculate the electronic energy using B3lyp/6-311++G(d, p). The resulting total energies were calculated using the sum of the electronic energy and corrected ZPE, using a correction coefficient of 0.75.

## Results and Discussion

To preliminarily gauge the effects of adding oxygen to a helium FAPA source, less than 1.0% v/v of oxygen was added to the helium directly prior to the FAPA discharge. Reagent- and analyte-ion populations produced with He:O<sub>2</sub>-FAPA were

monitored in the low-mass range of the mass spectrum. Most notably, addition of even a small amount of oxygen to the discharge increased the abundance of the protonated water dimer ( $[\text{H}_2\text{O}]_2\text{H}^+$ ) by 3.4 times (*cf.* Figure 1) with no notable elevation in chemical background signals; under certain source conditions, signal for protonated water dimer increased by more than 19-fold over a He-FAPA. It is also important to note that all detected protonated water clusters (i.e.,  $n = 2, 3, 4,$  and  $5$ ) exhibited the same trend upon addition of oxygen to the FAPA plasma gas (*cf.* Supplementary Figures S-2 and S-3). Protonated water clusters are important reagent ions in ADI-MS analyses as proton-transfer ionization is efficient for many organic analytes and leads to little molecular fragmentation. Maximum production of protonated water clusters was found to occur with 0.1% v/v oxygen in helium (*cf.* Figure 1, red trace). A similar increase in signal was also observed for polar analytes such as acetone (*cf.* Figure 1, blue trace) and methanol (*cf.* Supplementary Figure S-4) with an enhancement in  $[\text{MH}]^+$  signal of up to 4.5 and 12.5 times, respectively.

Though the exact processes that lead to increased protonated water cluster signals is unknown at this time, some possible reasons can be deduced from the literature. For instance, it is known that  $\text{O}_2^+$  can directly lead to the formation of protonated water clusters via ion–molecule and clustering reactions [24]. Though the conditions used in that study differ from those of a He:O<sub>2</sub>-FAPA, the same reactions could occur in the open air afterglow region where plasma species, including  $\text{O}_2^+$ , mix with room air.

In contrast to the protonated water clusters, the abundance of nearly all other FAPA reagent ions, including  $\text{NO}^+$ ,  $\text{HCO}^+$ , and  $\text{O}_2^+$ , dramatically decreased with the smallest fraction of oxygen added to the discharge gas, 0.1% v/v (*cf.* Supplementary Figure S-5). The one exception to this behavior was the ion signal at  $m/z$  48, which increased by *ca.* five times with 0.1% v/v oxygen added to the discharge (*cf.* Supplementary Figure S-6). While accurate mass measurements were not possible with the available instrumentation, the two most likely species to appear at  $m/z$  48 for this system are  $\text{O}_3^+$  and  $(\text{NO} + \text{H}_2\text{O})^+$ .

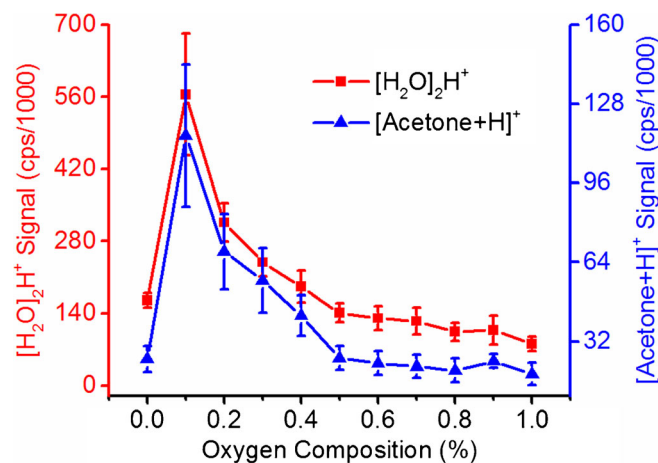


Figure 1. Protonated water dimer ( $[\text{H}_2\text{O}]_2\text{H}^+$ ) (red) and protonated acetone (blue) signals as a function of percent oxygen composition in the helium-based FAPA

Because the trend in Supplementary Figure S-6 is much different than that for the NO<sup>+</sup>, we rationalize that the majority of the ions detected at this mass are O<sub>3</sub><sup>+</sup>. This observation is somewhat surprising given that O<sub>3</sub><sup>+</sup> is known to readily react with O<sub>2</sub> to form O<sub>2</sub><sup>+</sup> [25].

Desorption/ionization of analytes containing aromatic constituents exhibited significant chemical modification of the aromatic system when a He:O<sub>2</sub>-FAPA was used. With a helium-FAPA, these analytes were detected as molecular or pseudo-molecular ions (M<sup>+</sup> or MH<sup>+</sup>, respectively). When these analytes were desorbed/ionized with a He:O<sub>2</sub>-FAPA, all these species produced a mass spectral peak corresponding to (M+3)<sup>+</sup> (cf. Figure 2, Supplementary Figures S-7 and S-8). Exact mass measurements showed that the ion corresponding to (M+3)<sup>+</sup> from benzene (C<sub>6</sub>H<sub>6</sub>) at *m/z* 81.033 has an elemental composition of C<sub>5</sub>H<sub>5</sub>O<sup>+</sup>. The most stable and probable structure for such an elemental composition is that of pyrylium. Similar to the results obtained with benzene, (M+3)<sup>+</sup> ions corresponding to (M – CH + O)<sup>+</sup> were detected when biphenyl (C<sub>12</sub>H<sub>10</sub>), aniline (C<sub>6</sub>H<sub>7</sub>N), acetaminophen (C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>), naphthalene (C<sub>10</sub>H<sub>8</sub>), anthracene (C<sub>14</sub>H<sub>10</sub>), and 1,3,5-trimethylbenzene (C<sub>9</sub>H<sub>12</sub>) were introduced to the He:O<sub>2</sub>-FAPA, which demonstrates that pyrylium derivatives can be formed from a variety of aromatic-containing precursors. Though the finding that aryl rings can be converted into pyrylium species is surprising, this (M+3)<sup>+</sup> feature has been shown in APCI mass spectra of benzene produced in air [14, 26]. Unfortunately, though the mass-spectral peaks are labeled as C<sub>5</sub>H<sub>5</sub>O<sup>+</sup>, there is no discussion of this ion in the text.

To aid in the confirmation of the formation of pyrylium from benzene as well as to devise potential reaction mechanisms, mass spectra of deuterated benzene (C<sub>6</sub>D<sub>6</sub>) were also acquired with a He-FAPA and a He:O<sub>2</sub>-FAPA (cf. Figure 3). With a He-FAPA, the molecular cation (M<sup>+</sup>), *m/z* 84.0842 were detected for deuterated benzene, whereas (M+2)<sup>+</sup>, *m/z* 86.0650, ions were recorded with a He:O<sub>2</sub>-FAPA. Exact mass measurement showed that these (M+2)<sup>+</sup> ions correspond to (M – CD + O)<sup>+</sup> with an elemental composition of C<sub>5</sub>D<sub>5</sub>O<sup>+</sup>. These findings align with spectra obtained for previously presented aromatic systems with a He:O<sub>2</sub>-FAPA in that a ring-opening – ring-closing reaction

results in the removal of CH (or, in this case, CD) from an aryl ring. The lack of hydrogen atoms in the deuterated pyrylium product indicates that the mechanism does not involve replacement or removal of aromatic hydrogens, other than the one on the leaving group.

The formation of pyrylium species was further confirmed via product ion scans of the [M+3]<sup>+</sup> ion of 1,3,5-trimethylbenzene produced with He:O<sub>2</sub>-FAPA at *m/z* 123. This spectrum was compared with the tandem mass spectrum obtained from a commercially available 2,4,6-trimethylpyrylium tetrafluoroborate salt, which was ionized with electrospray ionization. Both product-ion spectra exhibited a base peak at *m/z* 95, corresponding to C<sub>6</sub>H<sub>7</sub>O<sup>+</sup>, as the major fragment (cf. Figure 4). Furthermore, both spectra contained minor fragment ions at *m/z* 93, 105, and 108. The MS<sup>3</sup> spectra of the major fragment ion at *m/z* 95 were acquired for both the plasma-synthesized product and the commercial salt and found to be quite similar with a major fragment at *m/z* 67, corresponding to C<sub>5</sub>H<sub>7</sub><sup>+</sup>, and minor fragments at *m/z* 77, 91, and 93 (cf. Supplementary Figure S-9). The similarity between mass spectra obtained for the plasma-synthesized product and a commercial trimethylpyrylium salt, as well as the unique elemental composition of the species formed by He:O<sub>2</sub>-FAPA, confirm that pyrylium was formed via the reaction between aromatic systems and a plasma-generated reactant species.

Based on the results presented above, it is clear that ring-opening – ring-closing steps must occur to form pyrylium from the aryl structure. Although at this time the exact mechanism of pyrylium formation has not been probed in great detail, some information on the potential reactants and processes can be inferred from these findings as well as the literature. First, the reaction occurs very rapidly and goes to completion on a mass spectrometric timescale (i.e., tens of milliseconds). As such, the plasma-produced reactant is almost certainly a positive ion, which would serve to lower the activation barrier of the reaction and speed up an otherwise slow reaction. A list of potential oxygen-containing reactant ions can be formulated from the background mass spectrum of the He:O<sub>2</sub>-FAPA (cf. Supplementary Figure S-10). Potential reactant ions determined from this mass spectrum include NO<sup>+</sup>, O<sub>2</sub><sup>+</sup>,

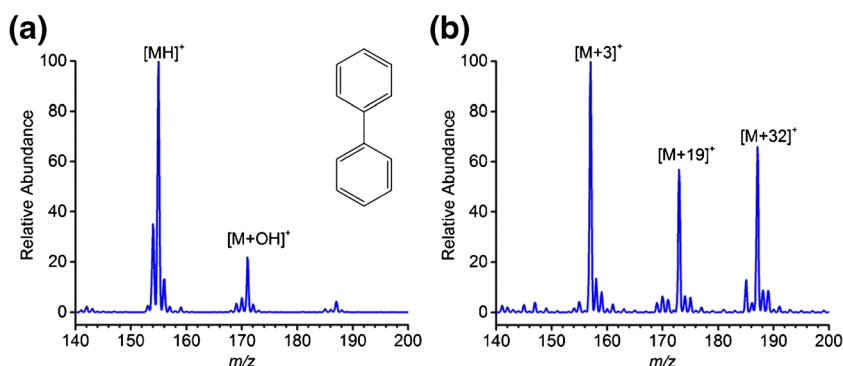
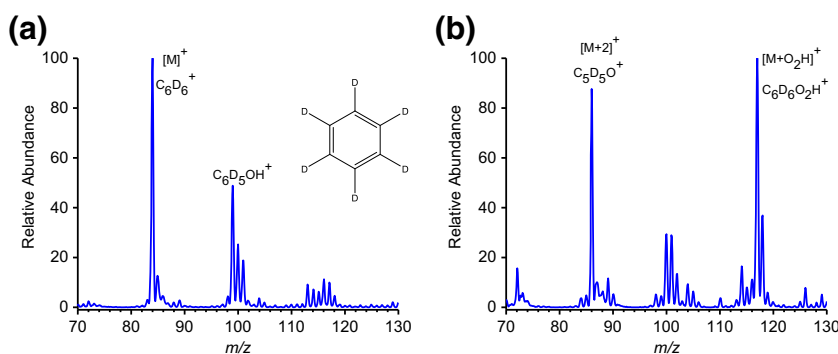


Figure 2. Mass spectra of biphenyl obtained with a He-FAPA (a) and He:O<sub>2</sub>-FAPA containing 0.1% oxygen (b). Both spectra were acquired with 1.0 L/min total gas flow rate and 20 mA discharge current





**Figure 3.** Mass spectra of benzene-D<sub>6</sub> obtained with a He-FAPA (a) and He:O<sub>2</sub>-FAPA with 0.1% oxygen (b). Both spectra were obtained with 1.0 L/min total gas flow rate and 20 mA discharge current

O<sub>3</sub><sup>+</sup>, HCO<sup>+</sup>, and H<sub>3</sub>O<sup>+</sup>, which could react with the aromatic analyte as shown in Reaction 1:



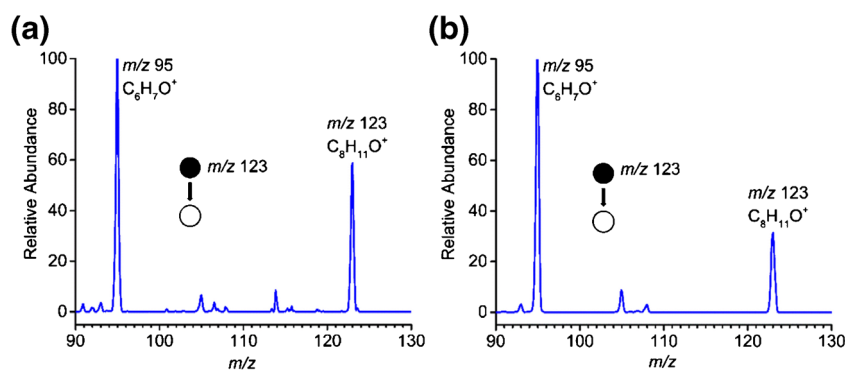
where RO<sup>+</sup>=NO<sup>+</sup>, O<sub>2</sub><sup>+</sup>, O<sub>3</sub><sup>+</sup>, HCO<sup>+</sup>, or H<sub>3</sub>O<sup>+</sup>.

To the best of our knowledge, the standard enthalpy of formation ( $\Delta H_f^\circ$ ) of pyrylium has not been experimentally or computationally determined. To gain a better understanding of the energetics of the possible reactions taking place, the  $\Delta H_f^\circ$  was calculated, with density functional theory, from the isodesmic reaction between pyrylium and the cyclopentadienyl anion (*cf.* Supplementary Figure S-10). The total energies provided by Gaussian contain the sum of electronic and thermal enthalpies, which allow the calculation of the enthalpy of the reaction. The enthalpy of the reaction is determined by taking the difference of the sum of reactants and the products. From this approach, the enthalpy of formation for pyrylium was determined to be 689.8 kJ/mol.

Because benzene has a lower enthalpy of formation than pyrylium, the pyrylium formation reaction would only proceed if a stable neutral loss product was formed from the reaction. Based on the above list of possible reactant ions, the corresponding neutral loss products would be HCN, HCO, HCO<sub>2</sub>, C<sub>2</sub>H<sub>2</sub>, and CH<sub>4</sub>, respectively. This reaction would only proceed if the enthalpy of reaction ( $\Delta H_{rxn}$ ) is negative. Based on the calculated value of  $\Delta H_f^\circ$  for pyrylium and the literature values of  $\Delta H_f^\circ$  for all other reactants, Hess's law was used to calculate  $\Delta H_{rxn}$  for each possible reactant (*cf.* Table 1).

From the values presented in Table 1, it is clear that ionized ozone, O<sub>3</sub><sup>+</sup>, is the most energetically favorable reactant to convert benzene to pyrylium. However, it is also energetically possible for NO<sup>+</sup> and O<sub>2</sub><sup>+</sup> to lead to pyrylium-ion formation. A number of selected ion flow tube (SIFT) MS studies have examined gas-phase reactions between atmospheric plasma cations, including NO<sup>+</sup> and O<sub>2</sub><sup>+</sup>, and benzene, toluene, or ethylbenzene [28–30]. The dominant reactions in every case were non-dissociative charge-transfer ionization, which produced molecular cations (M<sup>+</sup>). In fact, no pyrylium, or any other oxygen-containing products, were detected in any of those cases. Furthermore, these charge-transfer reactions were found to proceed at or very near the collision rate. Thus, it seems unlikely that reactions between NO<sup>+</sup> or O<sub>2</sub><sup>+</sup> and benzene would lead to pyrylium-ion formation.

Unfortunately, studies on reactions involving O<sub>3</sub><sup>+</sup>, particularly those with organic molecules, are more sparse. Similar to NO<sup>+</sup> and O<sub>2</sub><sup>+</sup>, the ionization energy of ozone, 12.53 eV, is appreciably higher than that of benzene, 9.24 eV, which indicates that non-dissociative charge-transfer ionization could be a possible reaction pathway. Perhaps surprisingly, it has been noted that some exothermic non-dissociative charge-transfer reactions with ozone ion proceed more slowly than the collision rate, which implies that other more favorable reactions pathways exist in these scenarios. Unique behavior of O<sub>3</sub><sup>+</sup> has been noted for reactions with smaller, atmospherically relevant species. For instance, dissociative oxidation products (*cf.* Reaction 2) have been observed for species of lower ionization potential than ozone [31–33]. Theoretical modeling



**Figure 4.** Tandem MS of [M+3]<sup>+</sup> ion produced from 1,3,5-trimethylbenzene with He:O<sub>2</sub>-FAPA (0.1% oxygen) (a) and 2,4,6-trimethylpyrylium with electro spray ionization (ESI) source (b)

**Table 1.** Plasma-Generated Reactant Ions and the Corresponding Neutral-Loss Products, along with Their Respective Standard Enthalpies of Formation, which Could be Responsible for the Conversion of Benzene to Pirylium. The Standard Enthalpy of Formation for Benzene and Pirylium is 82.9 kJ/mol [27] and 689.8 kJ/mol, respectively

Possible reactant ion	$\Delta H_{f, reactant}^{\circ}$ (kJ/mol)	Neutral-loss product	$\Delta H_{f, product}^{\circ}$ (kJ/mol)	$\Delta H_{rxn}$ (kJ/mol)
H <sub>3</sub> O <sup>+</sup>	449.2 <sup>b</sup>	CH <sub>4</sub>	-74.87 <sup>a</sup>	82.8
HCO <sup>+</sup>	824.0 <sup>a</sup>	C <sub>2</sub> H <sub>2</sub>	226.73 <sup>a</sup>	9.6
NO <sup>+</sup>	986.6 <sup>b</sup>	HCN	135.14 <sup>a</sup>	-244.6
O <sub>2</sub> <sup>+</sup>	1164 <sup>b</sup>	HCO <sup>•</sup>	43.51 <sup>a</sup>	-513.2
O <sub>3</sub> <sup>+</sup>	1352 <sup>b</sup>	HCO <sub>2</sub> <sup>•</sup>	-221.8 <sup>b</sup>	-967.2

<sup>a</sup>Values obtained directly from NIST Webbook [27]

<sup>b</sup>Values calculated from the data available in NIST webbook [27]

of this reaction revealed that it proceeds through a stable, although short-lived, five-member ring intermediate.



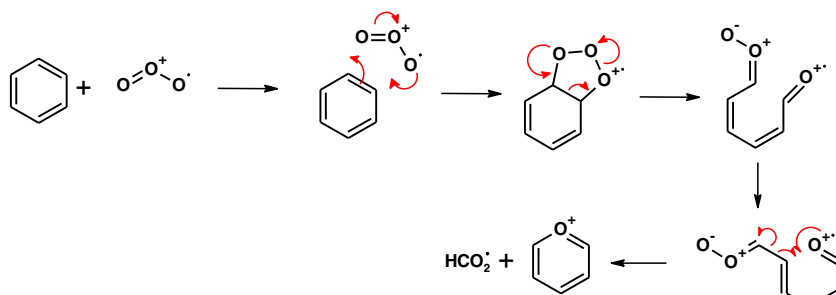
The calculated enthalpies of reactions from Table 1 show that ozone ion, O<sub>3</sub><sup>+</sup>, would be the most energetically favorable reactant ion to convert benzene to pyrylium. To further support this hypothesis, ion signal at *m/z* 48 was found to increase by 5-fold when oxygen was added to the helium-FAPA discharge (*cf.* Supplementary Figure S-6); in fact, O<sub>3</sub><sup>+</sup> was the only reagent ion, other than protonated water clusters, found to increase in abundance with the addition of oxygen to the plasma gas.

Based on the information above in conjunction with the O<sub>3</sub><sup>+</sup> reaction literature, a possible mechanism for this pyrylium formation reaction from O<sub>3</sub><sup>+</sup> is shown in Scheme 1. The first step of the reaction is similar to ozonolysis of alkenes where a five-member ring containing three oxygen atoms is formed as an intermediate. As was shown in the reaction between O<sub>3</sub><sup>+</sup> and SCO [32], the stability of this intermediate would favor dissociative charge-transfer and lead to a faster reaction rate than non-dissociative charge-transfer. A ring-opening step, which leads to separation of oxygen atoms, is followed by a radical-driven ring closure resulting in the neutral loss of HCO<sub>2</sub><sup>•</sup>. Future studies will aim to more systematically study this reaction pathway, the associated energetics, and the seemingly ubiquitous nature of aryl-to-pyrylium conversion.

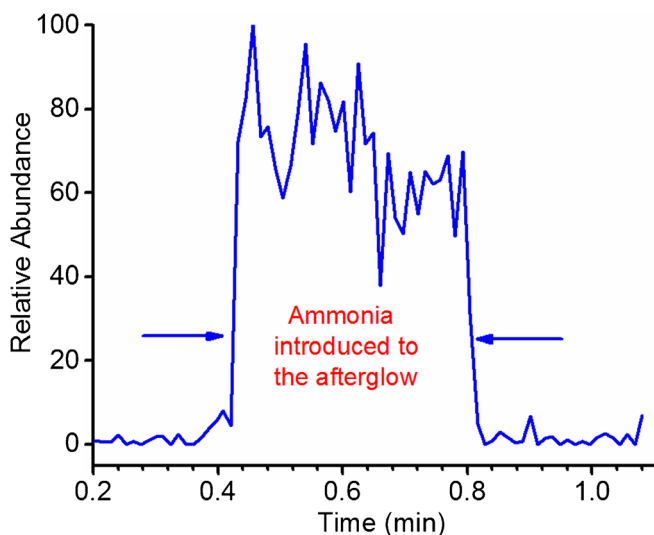
Pyrylium-based species have been synthesized in a variety of fashions and used for diverse applications, particularly as pigments and fluorophores [34–38]. However, pyrylium synthesis typically requires at least one carbonyl derivative (aldehyde,

ketone, acid, or ester) along with a catalyst and suitable solvents such as acetone and ethers [34]. In addition, the reaction mixture needs to be refluxed for several hours under high temperatures [34]. Although synthetic routes for formation of substituted pyrylium species can have yields as high as 65% [34], synthesis of pyrylium is a significantly more challenging task due to the propensity for nucleophilic attack. Here, with a He:O<sub>2</sub>-FAPA, conversion of aromatic systems to pyrylium is rapid (within a few milliseconds), and relatively efficient with a yield of 45%. In this case, the yield was calculated by dividing the pyrylium ion signal by all other ion signals related to the aromatic analyte based on exact mass measurements.

One important use of pyrylium-based compounds is as a reagent for the synthesis of molecules with strong aromatic character due to the fact that pyrylium is readily attacked by even moderate nucleophiles. In particular, pyrylium is often reacted with ammonia and primary amines to form pyridine and pyridinium derivatives [37]. Because of their high reactivity via nucleophilic attack, we explored the ability to create pyridinium species from plasma-synthesized pyrylium. Specifically, the fast and efficient production of pyrylium in the gas phase was used to convert ammonia and benzene into pyridine with He:O<sub>2</sub> FAPA. Ammonia rapidly reacts with pyrylium to produce protonated pyridine. The abundance of *m/z* 80, which corresponds to protonated pyridine, was monitored with continuous introduction of benzene to the afterglow of He:O<sub>2</sub>-FAPA. A significant increase in *m/z* 80 was observed when ammonia was introduced to the afterglow (*cf.* Figure 5), which was not observed with a helium-only FAPA. Exact mass measurement of *m/z* 80 produced from benzene and ammonia with He:O<sub>2</sub> FAPA corresponded to the protonated pyridine, which showed that the pyrylium produced



**Scheme 1.** Likely mechanism of pyrylium formation from benzene with plasma-produced ozone radical ion serving as the other reactant



**Figure 5.** Chronogram of  $m/z$  80 when benzene was constantly introduced to the afterglow of a He:O<sub>2</sub>-FAPA with ammonia introduced in between

from benzene and He:O<sub>2</sub>-FAPA were rapidly converted to protonated pyridine due to fast reaction with ammonia. These results show that benzene can be directly and efficiently converted to pyridine with He:O<sub>2</sub>-FAPA. In the future, we aim to expand this gas-phase ion chemistry to form more complex products as well as to scale-up and collect reaction products.

## Conclusion

The effects of oxygen addition to a helium FAPA source were explored. Unique chemical modification of aromatic systems to produce pyrylium was observed with He:O<sub>2</sub>-FAPA. Formation of pyrylium was confirmed by exact mass measurement, tandem mass spectrometry, and detection of an isotopically labeled compound. Furthermore, rapid production of pyrylium was used to convert benzene to pyridine. Pyrylium rapidly reacts with primary amines as well. The application of this method of rapid pyrylium generation could be used for such amine modifications, which will be the focus of future studies.

The enhancement of protonated water clusters and acetone on oxygen addition to He-FAPA showed that sensitivity for different analytes can be enhanced with different gas compositions. Utility of addition of other molecular gasses to the He-FAPA will also be studied in future.

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