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Degradation of Organic Cations under Alkaline Conditions

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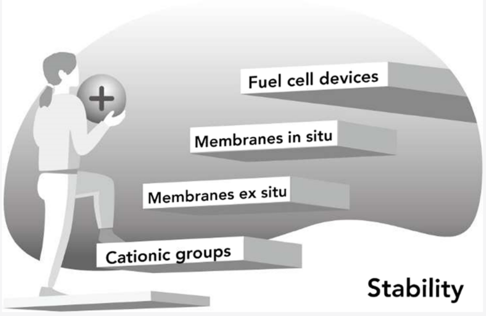
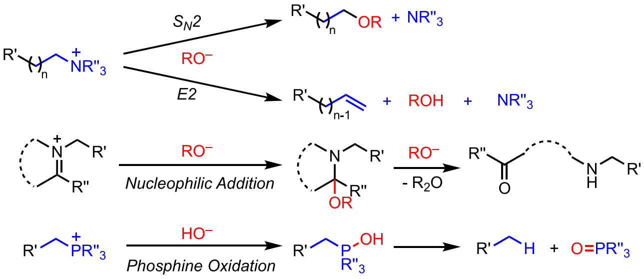
ABSTRACT: Understanding the degradation mechanisms of organic cations under basic conditions is extremely important for the development of durable alkaline energy conversion devices. Cations are key functional groups in alkaline anion exchange membranes (AAEMs), and AAEMs are critical components to conduct hydroxide anions in alkaline fuel cells. Previously, we have established a standard protocol to evaluate cation alkaline stability within KOH/CD$_3$OH solution at 80 °C. Herein, we are using the protocol to compare 26 model compounds, including benzylammonium, tetraalkylammonium, spirocyclicammonium, imidazolium, benzimidazolium, triazolium, pyridinium, guanidinium, and phosphonium cations. The goal is not only to evaluate their degradation rate, but also to identify their degradation pathways and lead to the advancement of cations with improved alkaline stabilities.



INTRODUCTION

During our long-term effort to develop durable alkaline anion exchange membranes (AAEMs), one of our major concerns is the alkaline stability of cationic functional groups in AAEMs.[1] The function of AAEMs is to transport hydroxide anions within clean energy conversion devices such as anion exchange membrane fuel cells (AEMFCs), alkaline water electrolyzers, electrodialyzers, and redox flow batteries.[2−4] Organic cations are key components in AAEMs as they serve as counterions of hydroxide anions and are covalently attached to polymeric backbones in AAEMs. However, as cations are vulnerable to strong nucleophiles and bases such as hydroxide, their alkaline stability is directly related to the life span of AAEMs.[5] Organic cations are common synthesis intermediates, and the reactions between them and bases have been well documented, including nucleophilic substitution (S$_N$2), Hofmann elimination (E2), ylide formation, Sommelet−Hauser rearrangement, and Stevens rearrangement.[6−8] Nevertheless, the cations in AAEMs need to remain intact for thousands of hours under high temperature (>80 °C) and high pH (>14) conditions. Hence, understanding cation degradation under alkaline conditions is key to designing better cationic candidates for AAEM applications. Some common degradation pathways are shown in Scheme 1. In general, all organic cations can undergo S$_N$2 at the α-position, and E2 can occur when β-hydrogens are present.[9] *N*-conjugated cations can also be attacked through nucleophilic addition to the C=N bonds.[8] Additionally, when oxygen-based nucleophiles react with phosphonium cations, Cahours−Hofmann reaction may occur to form phosphine oxide.[10]

Scheme 1. General Illustration of Cation Degradation Pathways under Alkaline Conditions



Model compound study is a common strategy to deconvolute cation decomposition in complicated polymeric AAEM systems, so that their degradation products, kinetics, and mechanisms can be unambiguously assigned using nuclear magnetic resonance (NMR) and high-resolution mass spectrometry (HRMS) techniques.[9−24] Although significant progress has been achieved over the past decade in enhancing the understanding of the cation alkaline stability, two major limitations still exist: inconsistent testing conditions and a lack of comparison among different classes of cations. It is broadly accepted that the cation stability studies need to be performed with concentrated base at high temperatures, although the choice of solvents differs. The reported solvent systems include water,[9,11−13] methanol,[14−18] anhydrous DMSO,[19,20] water/

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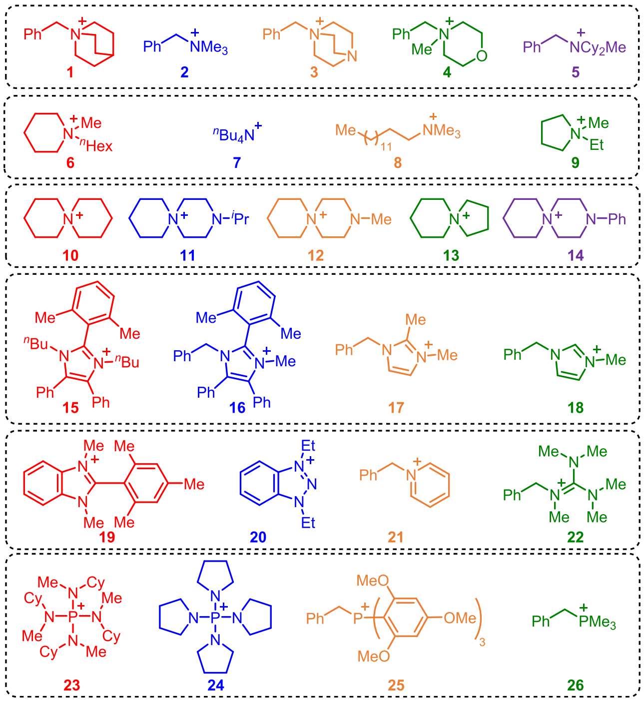
methanol cosolvent,[21−23] water/DMSO cosolvent,[24] and water/chlorobenzene phase transfer conditions.[10] One of the most comprehensive cation stability studies led by Marino and Kreuer tested a series of *N*-based cations in 6 M KOH aqueous solution at 160 °C,[9] and this report has pioneered a number of follow-up studies on piperidinium-functionalized AAEMs.[25−28] However, cation degradation in aqueous solution is relatively slow, and it is difficult to represent the low-hydration-level fuel cell operating conditions. As a result, organic solvents have been applied to lower the hydration levels of cations and accelerate their degradation. In our recent viewpoint, we discussed several important aspects to establishing a standard stability-evaluation protocol.[15] One of our characteristic conditions is the use of methanol-d_3 (CD_3OH) as the solvent, and its major advantages include the following: (1) good solvation of cations, (2) a potential fuel of AEMFCs, (3) accelerated degradation conditions in the presence of methoxide anions, (4) capability of avoiding H/D exchange, and (5) locking signals for ^{1}H NMR analysis.[15] Herein, 26 cations are divided into six groups (i.e. benzylammonium, tetraalkylammonium, spirocyclicammonium, imidazolium, other *N*-conjugated cations, and phosphonium) and are evaluated using our standard protocol (Chart 1). We are reporting on the detailed degradation rates and pathways for individual cations in KOH/CD_3OH at 80 °C to facilitate direct comparison of these different species.

Chart 1. Cations explored in this study. The six groups represent some of the most common cations in AAEMs.



RESULTS AND DISCUSSION

With the previously established alkaline stability protocols,[15] the organic cations were subjected to 1 M or 2 M KOH/CD_3OH solution at 80 °C for 30 days with an internal standard (3-(trimethylsilyl)-1-propanesulfonic acid sodium salt, NaDSS) in sealed NMR tubes. The decomposition processes were frequently monitored by ^{1}H NMR analysis to assign the decomposition products and the dominating degradation pathways. The results of the kinetics of all the tested cations are shown in Figure 1 (1 M conditions) and Figure 2 (2 M conditions). As a side note, we have previously reported the stability studies of some of the cations under KOH/CD_3OH conditions,[10,14,29] while herein we are using the data to provide a systematic comparison and discussion. Additionally, control experiments have also been performed to confirm that the internal standard NaDSS is sufficiently stable under alkaline conditions (Figure S74).

Benzylammonium cations (Scheme 2) have been the focus of study in AAEMs over the past two decades. Cations such as BTMA (**2**) are not only straightforward to incorporate in AAEMs, but also lack *β*-hydrogens and therefore cannot degrade through Hofmann elimination. However, numerous reports have pointed out that these benzylammonium cations are not stable under alkaline conditions.[9,11,12,29,30] Five benzylammonium model compounds (**1**−**5**) were evaluated using our protocol, and the results are shown in Scheme 2 (also see Figures 1A and 2A). BTMA (**2**) degraded via an S_N2 mechanism, and a nucleophilic attack at the benzylic position was more favored than at the methyl position to produce ether and tertiary amine products.[14] When cyclohexyl groups were applied to derivatize BTMA into *N*-benzyl-*N*-cyclohexyl-*N*-methylcyclohexanaminium (**5**), we observed less than 1% cation remaining after five days (Scheme 2). This result contrasts with a previous report by Bae and Mohanty,[11] wherein cyclohexyl substituents improved cation stability in water. This is possibly because the cation with more hydrophobic substituents is better solubilized in methanol, and the strong steric interference in **5** also increases its ground state energy.[31] Using our protocol, only benzyl methyl ether and *N*,*N*-dicyclohexylmethylamine were detected by ^{1}H NMR spectroscopy after the stability study. *N*-Benzylmorpholinium (**4**), which contains an ether functional group, has been hypothesized to have increased conductivity and alkaline stability due to its expanded hydration sphere surrounding the organic cations.[32] However, **4** degraded completely over 20 days under 1 M KOH/CD_3OH conditions, mostly through benzylic S_N2 attack to produce *N*-methylmorpholine and benzyl methyl ether (Scheme 2). Notably, a small amount of vinyl ether degradation product was also detected. This is likely because the adjacent oxygen atom increases the acidity of the *β*-hydrogens in morpholinium, resulting in a higher relative rate of Hofmann elimination.[33] Bicyclic ammonium cations derivatized from DABCO (1,4-diazabicyclo[2.2.2]octane) are also common motifs in AAEMs,[34] while faster degradation of *N*-benzyl DABCO (**3**) than BTMA was observed under our KOH/methanol conditions (Scheme 2). Both the benzylic and the ring-opening S_N2 attack were identified through the analysis of the ^{1}H NMR spectrum, and the latter pathway was favored in a 2:1 ratio likely due to the release of ring strain. HRMS was applied to further identify the proposed CD_3O^- ring-opened product, as methanol-d_3 was used as the reaction media (Figure S17). *N*-Benzylquinuclidinium (**1**) is a similar bicyclic ammonium cation as *N*-benzyl DABCO that has been applied in AAEMs,[35] but has a methine at the bridgehead in place of a nitrogen atom. This substitution resulted in significantly improved alkaline stability, with 67% of the original cation remaining after 1 M KOH/CD_3OH for 30 days (Scheme 2). Similar to **3**, the degradation pathways yielded the ring-opened products, benzyl methyl ether and quinuclidine. The ring-opening reaction was slightly preferred (ca. 1.3:1)

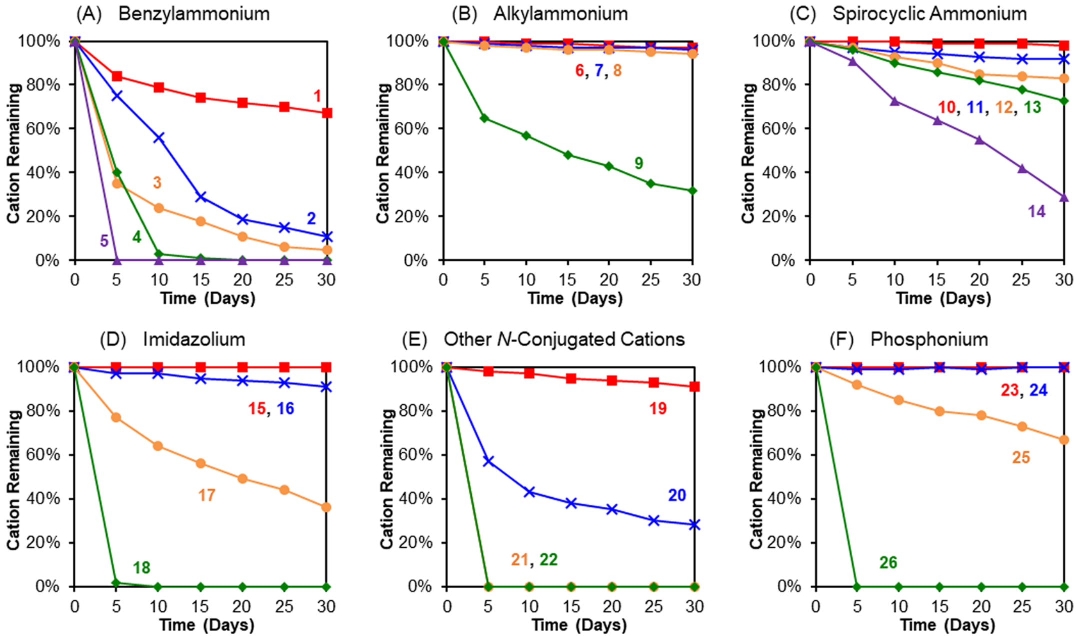


Figure 1. Alkaline stability results for cations **1**−**26** under 1 M KOH/CD_3OH conditions.

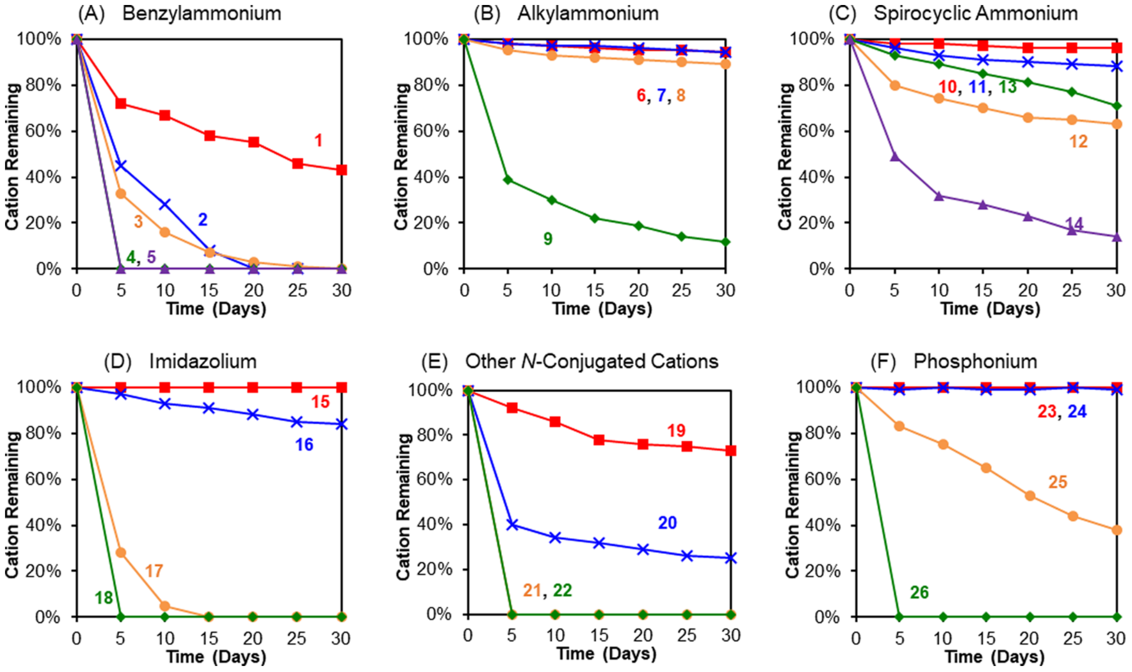


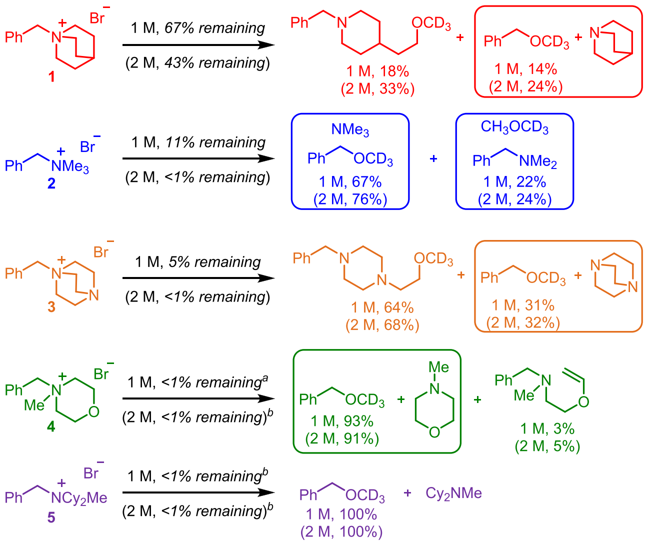
Figure 2. Alkaline stability results for cations **1**−**26** under 2 M KOH/CD_3OH conditions.

and the isotope labeled product was also observed by HRMS (Figure S11).

Because benzyl S_N2 degradation is a major issue for benzylammonium cations, some recent reports have demonstrated that ammonium cations without benzyl substituents, such as tetraalkylammonium cations, have better alkaline stability, although β-hydrogen atoms are present in these cations.[9,36−39] We tested four different tetraalkylammonium model cations (**6**−**9**) using the standard protocol (Scheme 3 and Figures 1B and 2B). Both tetrabutylammonium (**7**) and tetradecyltrimethylammonium (**8**) have significantly enhanced alkaline stability (96 and 94% cation remaining, respectively). The 4% observed degradation products of **7** came from Hofmann elimination (Scheme 3). The major degradation pathway of **8** was nucleophilic demethylation, and only 1% Hofmann elimination was detected (Scheme 3).[40] A comparison of **8** with BTMA (**2**) clearly shows the improvement of alkaline stability achieved by replacing the benzyl substituent with a long alkyl chain. These observations suggest that Hofmann elimination in alkylammonium cations is much slower than nucleophilic substitution of benzyl and methyl groups under alkaline conditions. Cyclic ammonium cations are proposed to have even better alkaline stability than long alkyl chains because Hofmann elimination can be conformationally disfavored.[9,25−28] As follows, piperidinium cation (**6**) showed 97% cation remaining after 1 M KOH/

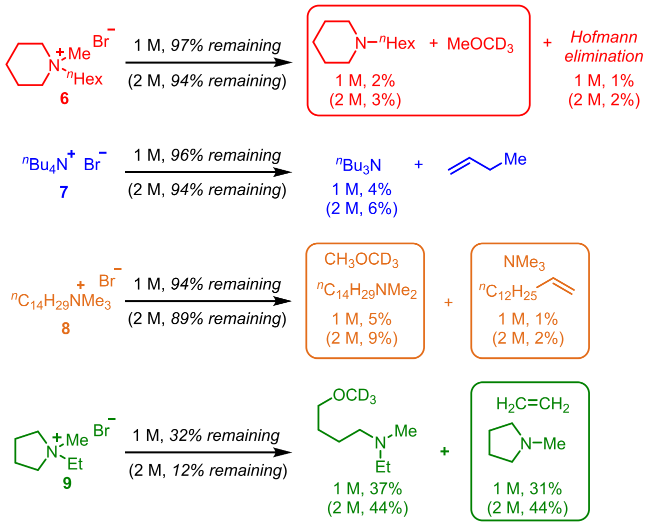
CH_3OH for 30 days (Scheme 3). Both demethylation and Hofmann elimination products were identified in the degradation mixture, but due to their low concentrations, it was difficult to identify whether the Hofmann elimination occurred on the hexyl chain or the piperidinium ring.[26] In contrast, pyrrolidinium cation (**9**) exhibited faster degradation, leaving just 33% of cation remaining after 1 M KOH/CH_3OH treatment for 30 days (Scheme 3).[29] Two comparative degradation pathways were identified from the ^1H NMR analysis, including methoxide S_N2 ring-opening attack and Hofmann elimination generating pyrrolidine and ethylene. The proposed ring-opened product was confirmed by HRMS (Figure S35). The advantages of this protocol are highlighted by the alkaline-stability studies of these ammonium cations,[15] as volatile compounds such as ethylene, dimethyl ether, and trimethylamine can be easily detected in the sealed NMR tubes.

Scheme 2. Stability Results of Benzylammonium Cations (1−5) Under 1 M and 2 M KOH/CD_3OH 80 °C Conditions. Numbers in Parentheses Indicate 2 M KOH/CD_3OH

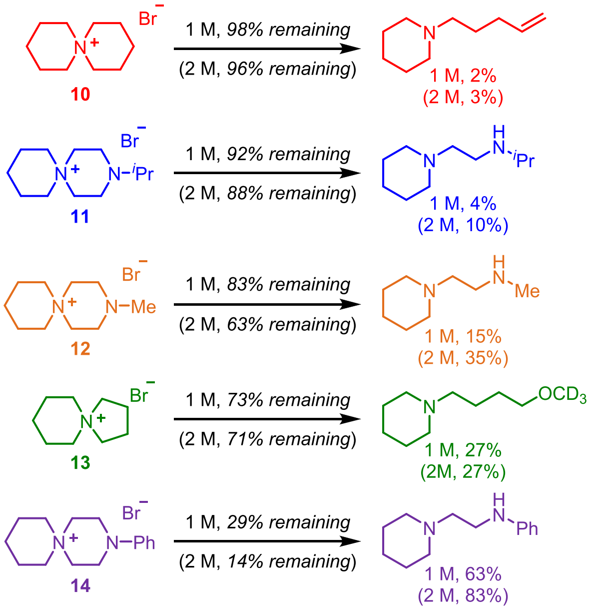


[a] 20 days. [b] 5 days.

Scheme 3. Stability Results of Tetraalkylammonium Cations (6−9) Under 1 M and 2 M KOH/CD_3OH 80 °C Conditions. Numbers in Parentheses Indicate 2 M KOH/CD_3OH

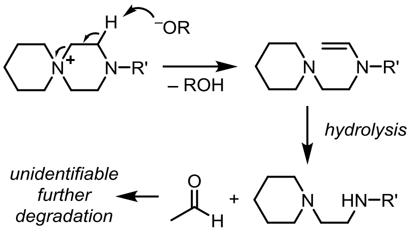


Scheme 4. Stability Results of Spirocyclic Ammonium Cations (10−14) Under 1 M and 2 M KOH/CD_3OH 80 °C Conditions. Numbers in Parentheses Indicate 2 M KOH/CD_3OH



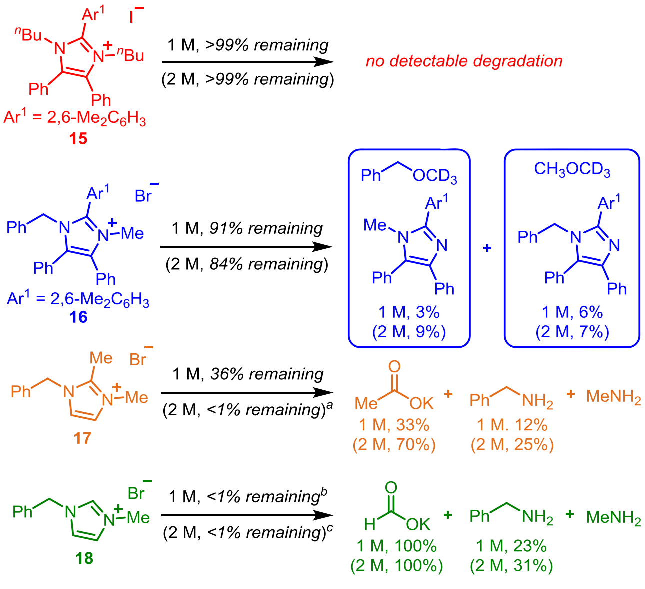
It is proposed that spirocyclic piperidinium cations have even better alkaline stability than simple piperidinium,[9,41,42] and thus we also tested spirocyclic cations (Scheme 4 and Figures 1C and 2C). Only 2% cation degradation was detected for **10** under 1 M KOH/CD_3OH conditions with Hofmann elimination as the major degradation pathway. Consistent with the trend of pyrrolidinium **9** versus piperidinium **6**, we observed faster degradation for spirocyclic cation **13** than for **10**. In the case of five-membered ring, **13** mostly degraded through S_N2 ring-opening attack (Scheme 4). In addition, another challenge related to spirocyclic piperidinium is how to tether the cation onto polymers, as Jannasch and co-workers envisioned that the substituents on piperidinium cations would rigidify the rings and decrease the stability.[41] Thus, spirocyclic piperizinium is a potential candidate, as the tertiary amine could act as a linker (**11**, **12**, and **14** in Scheme 4).[43] However, faster degradation than **10** was detected, and a plausible pathway is shown in Scheme 5. It is proposed that the extra nitrogen atom accelerated the ring-opening Hofmann elimination, and the resultant enamine intermediate hydrolyzed

Scheme 5. Proposed Major Degradation Pathways for Piperizinium Cations



thereafter (Scheme 5). As a result, the steric hindrance around the nitrogen atoms played important roles on alkaline stability, and the *i*-Pr substituted cation **11** showed significantly better alkaline stability than cations **12** and **14**.

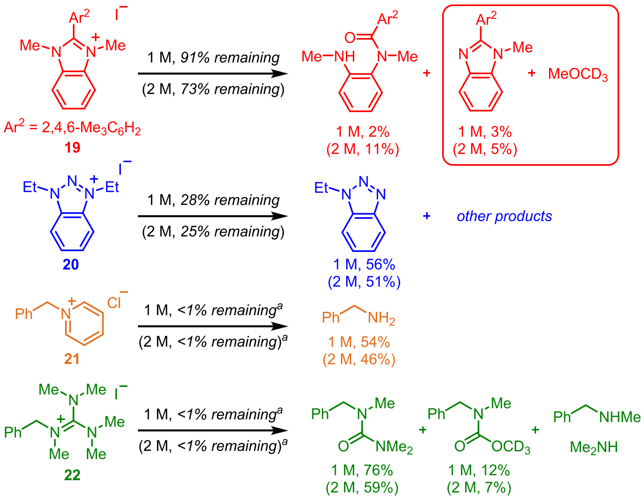
Scheme 6. Stability Results of Imidazolium Cations (15−18) under 1 M and 2 M KOH/CD$_3$OH 80 °C Conditions. Numbers in Parentheses Indicate 2 M KOH/CD$_3$OH



^{a}15 days. ^{b}10 days. ^{c}5 days.

In addition to ammonium cations, *N*-conjugated cations have also been incorporated into a variety of AAEMs.[20,21,44,45] These cations can potentially demonstrate higher chemical stabilities, because the positive charge is delocalized and stabilized by resonance; however, *N*-conjugated cations have additional degradation pathways, and judicious design is required to improve their alkaline stability (Scheme 6 and Figures 1D and 2D).[31] For example, 1-benzyl-3-methylimidazolium (**18**) showed no evidence of degradation products from S_N2 of benzyl or methyl groups by ^{1}H NMR analysis, while it decomposed into benzyl amine, methyl amine, formate salt, and hydrated glycolaldehyde (Scheme 6). This observation is consistent with recent imidazolium decomposition studies by Pellerite et al. under slightly different conditions,[13] and the degradation is likely initiated by nucleophilic addition to the C2 position (N−$\underline{\text{C}}$=N) followed by complete enamine and amide hydrolysis (Scheme 1).[31] When the C2 position was substituted with a methyl group (**17**), the degradation was slower, but the degradation products were similar (Scheme 6).[13,46] Model compound **16** was designed to block the C2 position from nucleophilic attack by incorporating a bulky 2,6-dimethylphenyl substituent.[14] The alkaline stability of **16** was significantly higher, and only degradation products from S_N2 attack on the benzyl and methyl groups were identified without ring-opening/imidazolium-hydrolysis products (Scheme 6). When the labile benzyl and methyl groups were replaced by *n*-butyl groups, the imidazolium cations (**15**) became extremely stable under our KOH/CD$_3$OH conditions, and no degradation products could be detected by ^{1}H NMR spectroscopy (Scheme 6).[14] It is noteworthy that Hofmann elimination of the *n*-butyl groups can be the major degradation pathway of cation **15** under more aggressive KOH/anhydrous DMSO conditions.[19,20] The results summarized in Scheme 6 highlight the impact of substituent choice on the alkaline stability of *N*-conjugated cations.

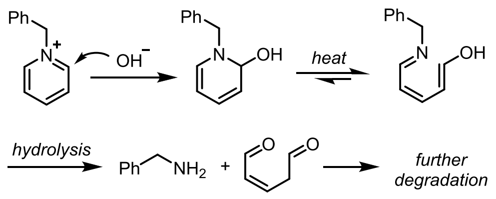
Scheme 7. Stability Results of Non-Imidazolium *N*-Conjugated Cations (19−22) Under 1 M and 2 M KOH/CD$_3$OH 80 °C Conditions. Numbers in Parentheses Indicate 2 M KOH/CD$_3$OH



^{a}5 days.

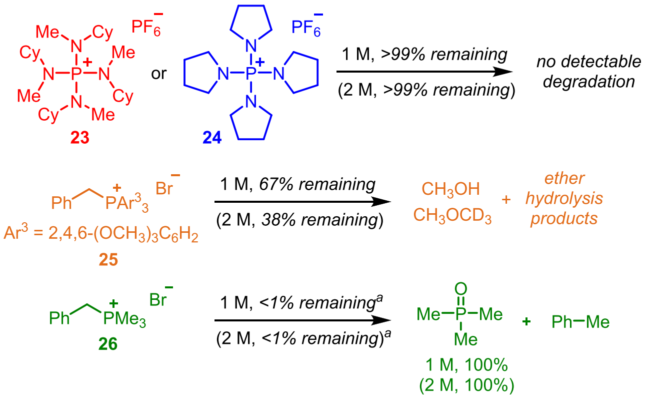
Other types of *N*-conjugated cations, including benzimidazolium, benzotriazolium, pyridinium, and guanidinium, have also been studied using our standard protocol (Scheme 7 and Figures 1E and 2E). Holdcroft and coworkers have prepared a series of benzimidazolium-functionalized AAEMs of which model compound **19** is a representative example.[47,48] The C2 position is substituted by a 2,4,6-trimethylphenyl group to inhibit nucleophilic attack, which is the same strategy for imidazolium cation **15**. However, hydroxide can still initiate nucleophilic ring-opening attack and demethylation of **19**, indicating that benzimidazolium is not as alkaline stable as the corresponding penta-substituted imidazolium cations (Scheme 7).[31,49] When the C2 position of imidazolium is replaced by a nitrogen atom, the cation turns into a triazolium.[50] We subjected benzotriazolium **20** under the KOH/CD$_3$OH conditions and observed deethylation as the major degradation product at a much faster rate than imidazolium **15** and benzimidazolium **19** (Scheme 7). The benzotriazole product was confirmed by HRMS, but we are currently unable to confidently assign the degradation mechanism, as neither ethylene nor ethanol was observed in comparative amount, while a broad range of unidentifiable peaks were present throughout the ^{1}H NMR spectra after alkaline stability studies (Figure S61). Pyridinium is another common cyclic *N*-conjugated cation, yet model compound **21** degraded rapidly in 1 M KOH/CD$_3$OH with benzyl amine as the only identifiable degradation product (Scheme 7). The proposed degradation mechanism is shown in Scheme 8, which includes nucleophilic aromatic attack on pyridinium, 6π-electrocyclic ring opening, and sequential hydrolysis.[51] Rapid hydrolysis was also observed when noncyclic *N*-conjugated cation, guanidinium (**22**), was treated with standard alkaline conditions, and several hydrolysis intermediates were identified by ^{1}H NMR analysis (Scheme 7).[52] The degradations of **21** and **22** are both initiated by nucleophilic addition on the iminium carbon,

Scheme 8. Proposed Major Degradation Pathways for Pyridinium Cations



rather than nucleophilic substitution on the methyl or benzyl groups. These results suggest that one fundamental strategy for enhanced alkaline stability is to increase the steric hindrance and prohibit the potential nucleophilic attack on the electrophilic sp^2 carbon centers, and this is exactly what Zhang et al. recently revealed in their systematic alkaline stability studies of various guanidinium derivatives.[16]

Scheme 9. Stability Results of Phosphonium Cations (23−26) Under 1 M and 2 M KOH/CD_3OH 80 °C Conditions. Numbers in Parentheses Indicate 2 M KOH/CD_3OH



[a] 5 days.

Phosphorus is a neighboring member of nitrogen in Group 15 elements, thus its corresponding cation, phosphonium, has also been involved in various AAEM structures (Scheme 9 and Figures 1F and 2F).[53−55] In comparison to BTMA (**2**), benzyltrimethylphosphonium cation **26** degraded much faster via a distinct mechanism (Scheme 9). Rather than S_N2 attack, degradation was initiated by the nucleophilic attack of hydroxide on the phosphorous center, leading to phosphine oxidation (Cahours-Hofmann reaction, also see Scheme 1).[2] The observed degradation products are toluene and trimethylphosphine oxide.[22] As reported by Yan et al, phosphine oxidation can be inhibited by integrating bulky and electron-rich aromatic rings (**25**).[22] Neither phosphine oxidation nor nucleophilic benzyl substitution were detected by ^1H NMR analysis when **25** was treated with KOH. Instead, the methoxy substituents on the aromatic ring were attacked by both methoxide and hydroxide, giving rise to ether hydrolysis products (Scheme 9).[22] To further improve the alkaline stability of phosphonium cations, the phosphorous atom can be substituted by four amino groups to give tetrakisaminophosphonium cations like **23** and **24**, which are elegantly stabilized by both resonance and steric hindrance. Under our standard KOH/CD_3OH protocol conditions, neither bulky **23** nor hydrophilic **24** showed detectable degradation (Scheme 9). It is noteworthy that with even harsher alkaline treatment (i.e., 2 M KOH/2-(2-methoxyethoxy)ethanol at 160 °C or 50 wt % NaOH/H_2O phase-transfer in chlorobenzene at 100 °C), both tetrakisaminophosphonium cations would degrade mostly through Cahours−Hofmann phosphine oxidation.[10]

■ CONCLUSION

A standard protocol to analyze cation alkaline degradation in CD_3OH has been reported, and herein, we use the protocol to understand the degradation mechanisms of 26 cations under the same set of conditions. Their alkaline stability trend can be summarized as follows. For ammonium cations, benzyl nucleophilic substitution would dominate when available, while S_N2 elsewhere and Hofmann elimination are also valid degradation pathways. For *N*-conjugated cations, S_N2 and Hofmann elimination are less problematic than nucleophilic addition to the iminium carbon centers. For these compounds, the steric hindrance plays an important role in improving the alkaline stability. Further hydrolysis and rearrangement are also common for *N*-conjugated cations. For phosphonium cations, Cahours−Hofmann phosphine oxidation is a unique, yet rapid degradation route, thus sterically bulky substituents near the phosphorous can significantly decelerate this pathway. Attention needs to be made when using electron-rich aromatic substituents on phosphorous, as ether hydrolysis will likely occur under alkaline conditions. Tetrakisaminophosphonium is one of the most stable scaffolds as organic cations. The power of this protocol is underscored by the broad scope of cations and the clear degradation mechanism assignment. We are also delighted to notice that this protocol has been used by the Swager group and the Tang group to identify new cation candidates (i.e., pyrazolium[17] and cobaltocenium,[18] respectively) for AAEMs. More recently, Mustain et al. prepared AEMFCs assembled with alkyltrimethylammonium-functionalized AAEMs and ionomers,[56] which outperformed previous BTMA-based ones,[57] and it was the first AEMFC to meet the US Department of Energy requirements to operate stably at current density of 600 mA cm^{-2} for 2000 hours.[56] With the alkaline-stable cations in hand and their possible degradation pathways in mind, our future goal is to install these cations into polymeric structures to develop durable AAEMs and fuel cell devices for green energy conversion applications.

■ EXPERIMENTAL SECTION

Methods and Instruments. ^1H and ^{13}C NMR spectra were recorded on a Bruker 400, Varian INOVA 500 or 600 MHz instrument at 22 °C with shifts reported relative to the residual solvent peak (CD_3OD or CD_3OH); 3.31 ppm (^1H) and 49.00 ppm (^{13}C). Electrospray ionization−high-resolution mass spectrometry (ESI-HRMS) analyses were performed on a Bruker 9.4 T solariX Fourier-transform ion cyclotron resonance mass spectrometry (FT-ICR-MS) instrument. Direct analysis in real time—high-resolution mass spectrometry (DART-HRMS) analysis—was performed on a Thermo Scientific Exactive Orbitrap MS system equipped with an Ion Sense DART ion source.

Solvent Suppression Procedure. Quantitative ^1H NMR spectra for model compound stability studies were acquired in CD_3OH to (1) prevent unwanted hydrogen/deuterium exchange in model compounds and degradation products and (2) improve the solubility of model compounds and degradation products.[29,58,59] The −OH signal in CD_3OH was suppressed by presaturation with a 2 second presaturation delay and continuous wave irradiation with decoupler field strength ($\gamma B1$) of 113 Hz (equivalent to a presaturation power of 9). Spectra were acquired over a spectral width of −1 to 14 ppm with 60 s relaxation delay and nominal 90° excitation pulse. Sixteen scans were averaged for each analysis. NMR spectra were processed using MestReNova Version 14.0.0-23239 (Mestrelab Research S.L). Whittaker smoother baseline correction was applied, and linear correction was used for all integrals. Note that residual signals between 5.5 and 6.5 ppm often derive from solvent suppression and shift depending on sample pH.

Chemicals. 3-(Trimethylsilyl)-1-propanesulfonic acid sodium salt (NaDSS) (TCI Chemicals), methanol-d_3 (Acros), methanol-d_4 (Cambridge Isotope Laboratories), potassium hydroxide (Mallinckrodt), tetrabutylammonium bromide (**7**), and tetradecyltrimethylammonium bromide (**8**) (Sigma-Aldrich) were all used as received. The model compounds were prepared according to literature procedures: 1-benzylquinuclidin-1-ium bromide (**1**);[60] benzyltrimethylammonium bromide (**2**);[14] 1-benzyl-1,4-diazabicyclo[2.2.2]octan-1-ium bromide (**3**);[61] 4-benzyl-4-methylmorpholin-4-ium bromide (**4**);[61] *N*-benzyl-*N*-cyclohexyl-*N*-methylcyclohexanaminium bromide (**5**);[11] 1-hexyl-1-methylpiperidin-1-ium bromide (**6**);[62] 1-ethyl-1-methylpyrrolidin-1-ium bromide (**9**);[63] 6-azaspiro[5.5]undecan-6-ium bromide (**10**);[9] 5-azaspiro[4.5]decan-5-ium bromide (**13**);[42] 1,3-di-*n*-butyl-2-(2,6-dimethylphenyl)-4,5-diphenylimidazolium iodide (**15**);[14] 1-benzyl-2-(2,6-dimethylphenyl)-3-methyl-4,5-diphenylimidazolium (**16**);[14] 1-benzyl-2,3-dimethylimidazolium bromide (**17**);[14] 1-benzyl-3-methylimidazolium bromide (**18**);[14] 1,3-dimethyl-2-mesityl-1*H*-benzimidazolium iodide (**19**);[64] 1-benzylpyridin-1-ium chloride (**21**);[65] *N*-[bis(dimethylamino)methylene]-*N*-methyl-1-phenylmethanaminium iodide (**22**);[66] tetrakis[cyclohexyl(methyl)amino]phosphonium hexafluorophosphate (**23**),[67] tetrakis(pyrrolidin-1-yl)phosphonium hexafluorophosphate (**24**);[10] benzyl-tris(2,4,6-trimethoxyphenyl)-phosphonium bromide (**25**);[68] and benzyltrimethylphosphonium bromide (**26**).[69]

General Model Compound Synthesis Procedure. A modified literature procedure was used.[9] To a predried 50 mL Teflon-lined seal-tube was added K_2CO_3 (2.4 mmol, 1.2 equiv). The flask was left under vacuum for 10 min, and then refilled with N_2. This process was repeated three times, followed by the addition of the corresponding nucleophile (2.0 mmol, 1.0 equiv), alkyl halide, and MeCN (10 mL). The tube was then sealed under N_2 and warmed up to 80 °C, and the reaction was maintained under stirring at 80 °C for 16 h. After cooling to 22 °C, the mixture was diluted with CH_2Cl_2 and filtered through cotton. The filtrate was then concentrated and triturated in Et_2O to afford the model compounds as white solids.

3-Isopropyl-3,6-diazaspiro[5.5]undecan-6-ium bromide (11). According to the general procedure, 1-isopropylpiperazine (2.0 mmol, 1.0 equiv), 1,5-dibromopropane (2.0 mmol, 1.0 equiv), K_2CO_3 (2.4 mmol, 1.2 equiv), and 10 mL MeCN were used to synthesize the title compound **11** as white solid (466 mg, 84% yield). **^{1}H NMR (400 MHz, CD_3OD):** δ 3.57−3.45 (m, 8H), 2.91−2.76 (m, 5H), 1.96−1.84 (m, 4H), 1.79−1.66 (m, 2H), 1.10 (d, *J* = 6.5 Hz, 6H); **^{13}C{^{1}H} NMR (100 MHz, CD_3OD):** δ 60.8 (br), 60.3, 55.3, 43.0, 22.6, 20.4, 18.8; **HRMS (ESI)** *m*/*z*: [M − Br]$^+$ Calcd for $C_{12}H_{25}N_2$: 197.2012; Found 197.2011.

3-Methyl-3,6-diazaspiro[5.5]undecan-6-ium bromide (12). According to the general procedure, 1-methylpiperazine (2.0 mmol, 1.0 equiv), 1,5-dibromopropane (2.0 mmol, 1.0 equiv), K_2CO_3 (2.4 mmol, 1.2 equiv), and 10 mL MeCN were used to synthesize the title compound **12** as white solid (256 mg, 51% yield). **^{1}H NMR (400 MHz, CD_3OD):** δ 3.61−3.45 (m, 8H), 2.77 (t, *J* = 5.3 Hz, 4H), 2.40 (s, 3H), 1.91 (p, *J* = 6.0 Hz, 4H), 1.78−1.67 (m, 2H); **^{13}C{^{1}H} NMR (100 MHz, CD_3OD):** δ 60.7 (br), 59.7, 48.6, 45.2, 22.6, 20.4; **HRMS (ESI)** *m*/*z*: [M − Br]$^+$ $C_{10}H_{21}N_2$ 169.1699; Found 169.1699.

3-Phenyl-3,6-diazaspiro[5.5]undecan-6-ium bromide (14). According to the general procedure, 1-phenylpiperazine (2.0 mmol, 1.0 equiv), 1,5-dibromopropane (2.0 mmol, 1.0 equiv), K_2CO_3 (2.4 mmol, 1.2 equiv), and 10 mL MeCN were used to synthesize the title compound **14** as white solid (280 mg, 45% yield). **^{1}H NMR (400 MHz, CD_3OD):** δ 7.29 (t, *J* = 7.7 Hz, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.92 (t, *J* = 7.3 Hz, 1H), 3.70 (t, *J* = 5.2 Hz, 4H), 3.58 (t, *J* = 5.8 Hz, 4H), 3.51 (t, *J* = 5.2 Hz, 4H), 1.95 (p, *J* = 6.0 Hz, 4H), 1.76 (p, *J* = 6.1 Hz, 2H); **^{13}C{^{1}H} NMR (100 MHz, CD_3OD):** δ 150.9, 130.3, 122.1, 117.6, 60.6, 59.7, 43.8, 22.6, 20.4; **HRMS (ESI)** *m*/*z*: [M − Br]$^+$ Calcd for $C_{15}H_{23}N_2$: 231.1856; Found 231.1856.

1,3-Diethyl-1*H*-benzo[*d*][1,2,3]triazol-3-ium iodide (20). According to the general procedure, benzotriazole (2.0 mmol, 1.0 equiv), ethyliodide (4.4 mmol, 2.2 equiv), K_2CO_3 (2.4 mmol, 1.2 equiv), and 10 mL MeCN were used to synthesize the title compound **20** as white solid (298 mg, 49% yield). **^{1}H NMR (400 MHz, CD_3OD):** δ 8.36−8.28 (m, 2H), 8.03−7.96 (m, 2H), 5.07 (q, *J* = 7.3 Hz, 4H), 1.79 (t, *J* = 7.3 Hz, 6H); **^{13}C{^{1}H} NMR (100 MHz, CD_3OD):** δ 136.2, 132.3, 114.8, 48.6, 14.3; **HRMS (ESI)** *m*/*z*: [M − I]$^+$ Calcd for $C_{10}H_{14}N_3$: 176.1182; Found 176.1183.

Model Compound Study Procedures. Stock solutions of basic methanol were prepared by dissolving KOH (1 M or 2 M) and 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt (0.0250 M) in CD_3OH.[15,29] For example, a 1 M solution was prepared by dissolving KOH (142 mg, 2.51 mmol) and NaDSS (13.6 mg, 0.0625 mmol) in 2.50 mL of CD_3OH. The model compound (0.05 M for 1 M KOH and 0.03 M for 2 M KOH) was dissolved in the methanol solution (0.50 mL) and passed through a glass wool plug into an NMR tube. The NMR tube was flame-sealed and analyzed by ^{1}H NMR spectroscopy for the initial time point. Integration of a selected signal in the model compound relative to a signal related to 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt provided the initial quantity of model compound. The tube was heated in an oil bath at 80 °C. At specified time points, every 5 days, the tubes were removed, cooled to room temperature, and analyzed by ^{1}H NMR spectroscopy to determine the quantity of model compound remaining (^{1}H NMR spectra are provided). The ^{1}H NMR spectra of **15**, **16**, **23**, and **24** under standard protocol conditions (1 M and 2 M KOH in CD_3OH at 80 °C for 30 days) were previously reported.[10,14] The final cation percentage remaining results were covered in our previous *viewpoint*.[15]

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02051.

Expanded data table, NMR and HRMS spectra, and degradation product assignment (PDF).

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Notes

The authors declare the following competing financial interest(s): K.M. Hugar and G.W. Coates are cofounders of Ecolectro, and hold an equity stake in the company.

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