Collisionally Activated Dissociation of Some Bulkily Substituted Pyridinium Cations, II[1)]

Substituent Effect on Appearance Potential

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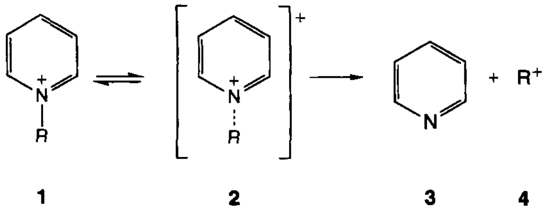
Collisionally activated dissociations (CADs) of various pyridine-ring substituted *N*-benzylpyridinium cations in the gas phase form the substituted pyridine and benzyl carbocation. Appearance energies (*AE*s) are estimated quantitatively from the appearance thresholds of the corresponding fragment ion from the laser-desorbed pyridinium cations. MO calculations predict that such unimolecular dissociation processes lead initially to ion-molecule pairs (IMPs): some such IMPs are of significantly lower energy than the fully dissociated products. The *AE*s have also been compared with the energy differences [$\Delta\Delta H_f = \Delta H_f(\mathrm{Py}) + \Delta H_f(\mathrm{R}^+) - \Delta H_f(\mathrm{Py}^+\mathrm{R})$] determined by AM1 calculations: in many cases these are quite close to the calculated energy differences; discrepancies are discussed.

The use of pulsed lasers to desorb involatile species[2)], often in conjunction with Fourier transform ion cyclotron resonance (FTICR) mass spectrometry[3–9)], has grown widely in recent years. The feasibility of desorbing and studying polymers[10)], biopolymers[11)], and a variety of other compounds[12–15)], has been demonstrated. Initial success in our laboratories[12,14,15)] with pyridinium ions suggested that this important class of charged species could be produced and studied in the gas phase by laser desorption (LD)FTICR mass spectrometry. We have previously demonstrated the applicability of this technique to examine the collisionally activated dissociation of laser-desorbed *N*-alkylpyridinium cations[1,16–18)]. In this paper we extend our investigation to include some sterically congested *N*-benzylpyridinium cations and study the mechanism of their dissociation by MO calculation.

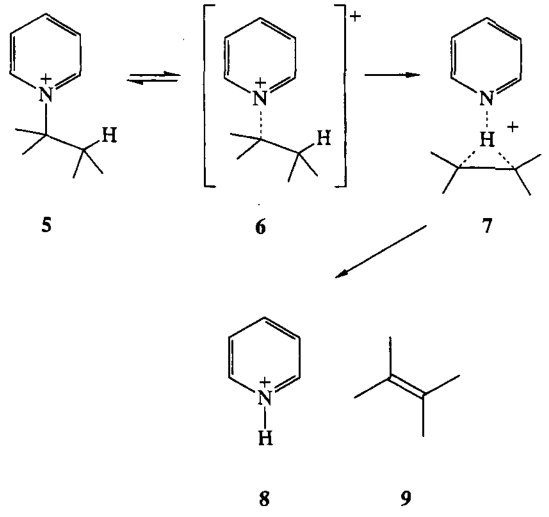
Fragmentation Pathways

Two distinct major pathways have been reported for the collisionally activated dissociation of *N*-alkylpyridinium cations[12–18)]. Compounds **1** in which R is an adamantyl, phenylethyl, benzyl, *p*-methoxybenzyl, or trityl group, yielded pyridine (**3**) and the corresponding carbocation **4** (Scheme 1). In addition, compound **5** may fragment by β-elimination to yield the pyridinium cation (**8**) and a strain-free olefin **9** (Scheme 2). Only in rare cases was homolytic fragmentation, to a pyridine radical cation and an allyl radical, encountered[1)].

Scheme 1. Fragmentation to pyridine and a carbocation



Scheme 2. Fragmentation to the pyridinium cation and an alkene



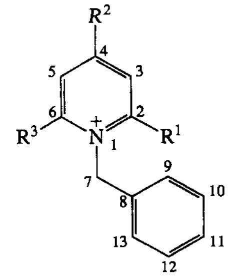
There is considerable evidence that alkylammonium cations undergo gas-phase unimolecular fragmentation via loose complexes[19–22)], and we have given evidence that such complexes (**2**, **6**) are involved in both fragmentation pathways (Schemes 1 and 2)[12,14,15)]. These complexes correspond to the ion-molecule pairs for which much evidence has been obtained in solution[23–25)] as well as in the gas phase[23)].

Results and Discussion

We have previously reported[16] that the parent *N*-benzylpyridinium cation **10a** underwent CAD and had a corrected appearance energy (*AE*) of 45 kcal mol^{-1}. As the AM1-calculated energy for the dissociation of this cation to pyridine and the benzyl cation is almost identical (44.5 kcal mol^{-1})[26], we concluded that the coincidence of *AE*s with calculated dissociation energies [$\Delta\Delta H_f(\mathrm{Py/R^+})$ values; Table 1,2 and Eq. (1)] could serve as a tool to predict relative $C-N^+$ bond strengths.

$$\Delta\Delta H_f = \Delta H_f(\mathrm{Py}) + \Delta H_f(\mathrm{R^+ \text{ or } T^+}) - \Delta H_f(\mathrm{Py^+R}) \qquad (1)$$

Scheme 3



10	R^1=R^2=R^3
a	H
b	Me

11	R^1 (R^2=R^3=Ph)
a	ß-naphthyl
b	2'-styryl
c	H
d	2-pyridyl
e	α-naphthyl
f	2-(1,4-dimethylphenyl)
g	iPr
h	Ph

Table 1. Energetics, part I. – ΔH_f[kcal mol^{-1}] of the fragmentation of the pyridinium cations **11a–h**

Compd.	E_{app} of R^{+} [a]	Internal Energy (350 K)[b]		Corrected Appearance Energy (350 K)[c]	ΔH_f (AM1)[33]	
		R^+	$Py_{(sub)}$		Py^+R	Py
11a	33	5	13	51	303.1	131.7
11b	40	5	13	58	296.0	126.9
11c	31	5	10	46	256.6	85.3
11d	35	5	12	52	297.8	124.8
11e	38	5	13	56	304.3	133.8
11f	38	5	14	57	270.5	99.8
11g	33	5	14	52	241.0	68.8
11h	41	5	12	49	285.0	113.2

[a] Corrected for energy spread in ions and neutral, see ref.[16]. – [b] Calculated or estimated as discussed in ref.[16]. – [c] For the process Py^+R (350 K) → Py (350 K) + R^+ (350 K); internal energy of the cation (column 3) and of the substituted pyridine (column 4) (both at 350 K) is added to the E_{app} (column 2).

The alternative pathway (yielding the tropylium cation) seems to be much less probable, as the AM1 method predicts a much lower $\Delta\Delta H_f$ value (32.8 kcal mol^{-1}; Table 2) for this dissociation. The latter is outside the combined error range of both the methods applied; in general the measured *AE*s are accurate within 5 kcal mol^{-1}. The similarity of the structures **10a,b** and **11a–h** discussed herein and their dissociation products makes it probable that errors in calculated absolute ΔH_f values for the individual species partially cancel in the $\Delta\Delta H_f$ values. Nevertheless, the very close agreement between the experimental and theoretical estimated energy differences for e.g. **10a** could in part be fortuitous.

The substitutional pattern of the compounds measured varies considerably (Scheme 3).

Table 2. Energetics, part II. – $\Delta\Delta H_f$ [kcal mol^{-1}] of the fragmentations including transition states (TS) and ion molecule pairs (IMPs)

Compd.[a]	*AE*	TS	$\Delta\Delta H_f$(AM1)[33]		
			IMP	Py/R^+ [b]	Py/T^+ [b]
10a	45	35.4	34.8	44.5	32.8
11a	51	36.7	35.8	50.8	39.1
11b[c]	58	–[d]	49.7	53.0	41.3
11c	46	38.5	38.2	50.7	39.0
11d	52	35.0	32.9	49.0	37.3
11e	56	37.3	36.5	51.6	39.9
11f	57	37.0	36.3	51.5	39.8
11g	52	38.4	37.7	49.9	38.2
11h	49	36.8	35.9	50.2	38.5

[a] All values refer to most stable conformations; therefore, the values of **10b** are not included (see paragraph iii). – [b] See Equation (1); R^+: benzyl cation (ΔH_f = 222.1 kcal mol^{-1}); T^+: tropylium cation (ΔH_f = 210.5 kcal mol^{-1}). – [c] (*E*) configuration. – [d] As the reaction coordinate is very flat for $C-N^+$ distances around 2–3 Å, the TS could not be localized (NS01A routine).

Compared with the parent cation **10a**, all the compounds except **10b** bear phenyl groups at C-4 and C-6 of the pyridinium moiety. Compound **11c** starts with this pattern. The cations **11a, b, d–h** represent derivatives with C-2 substituents of different steric and electronic demands: alkyl-, aryl-, and (α-β)alkenyl groups.

The experimentally determined *AE* values of compounds **11a–h** (Table 2) vary within the range of 46 to 58 kcal mol^{-1}, the AM1-calculated dissociation energies from 49 to 53 kcal mol^{-1}. In general, low (high) *AE* values correlate with low (high) $\Delta\Delta H_f$ values (Table 2). Considering the experimental accuracy of the *AE* measurements and the AM1-calculated energies (see above) the quality of this correlation is acceptable. With the single exception of the 2,4,6-trimethyl derivative **10b** (*AE* = 41 kcal mol^{-1}; $\Delta\Delta H_f(\mathrm{Py/R^+})$ = 49 kcal mol^{-1}), differences between experimental and calculated results are within 5 kcal mol^{-1}.

A main objective of the present work was to obtain further insights into the fragmentation processes. This includes the discussion of the energetics and structural properties of the cations before and after their collision with argon. Therefore, we performed AM1 calculations to simulate the complete dissociation pathways of compounds **10a, b** and **11a–h**. The results are summarized and discussed below.

AM1 Calculation of the Dissociation Pathways (Formation of the Benzyl Cation)

The energy profiles for the dissociation of cations **10a** and **11a–h** reveal an almost identical shape and are characterized by the existence of very weakly stabilized IMPs. The activation energy for the IMP formation do not vary significantly (35–39 kcal mol^{-1}). This "similarity" of the IMPs is also reflected in the corresponding energy gaps between the transition states (TS) and the completely dissociated moieties. The IMP/TS differences vary between 1 and 2 kcal mol^{-1}, those of the IMP/dissociated products between 9 and 15 kcal mol^{-1}.

The extent of C–N bond distances to which significant interaction between the benzyl cation and the respective pyridine moiety occurs is remarkable (ca. 2–9 Å). The total energy of the systems remains almost constant within this range and at greater distances rises smoothly to that of the energetic sum of the dissociated products (Figure 1). Significantly, the energies of all TSs and IMPs are less than those of the corresponding completely dissociated products.

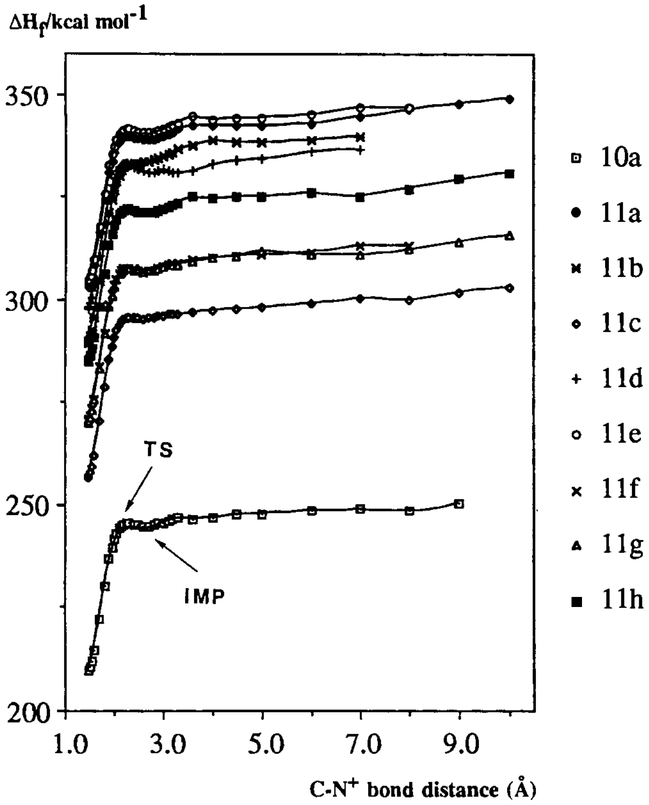


Figure 1. Energy profiles of the C–N$^+$ bond cleavage, formation of the benzyl cation and pyridinium derivatives from the most stable conformation of **10a** and **11a–h** (ΔH_f vs. C–N$^+$ bond distance); for **10b** see paragraph iii

As expected, the *AEs* measured by using moderately energized argon atoms give information only on the complete dissociation. Attempted correlation of *AE* vs TS or *AE* vs IMP energies reveal no reliable correlation. As variations between TS and IMP energies are small (see above) and the total energies of the dissociated products are always above these values, this lack of correlation is understandable. The relation between *AE* and $\Delta\Delta H_f(\mathrm{Py/R^+})$ values is thus the only important one.

We now discuss the alternative fragmentation which results in the formation of the tropylium ion. The stability of the tropylium cation is greater than that of the benzyl cation (−11.7 kcal mol^{-1}), and thus the overall dissociation energies [$\Delta\Delta H_f(\mathrm{Py/T^+})$ and $\Delta\Delta H_f(\mathrm{Py/R^+})$ values; Table 2] differ correspondingly.

AM1 Calculation of the Benzyl to the Tropylium Cation Rearrangement

As demonstrated by Dewar's MINDO/3 calculations[27], this arrangement requires the intermediate formation of the CH_2-containing 1,3,5-cycloheptatrienyl (CHT) cation (ΔH_f = 240.9 kcal mol^{-1}) followed by a 1,2-hydride shift to give the tropylium cation. In the MINDO/3 approximation the CHT lies 20.5 kcal mol^{-1} above the benzyl cation, the hydrogen migration requires another 12.2 kcal mol^{-1}, and thus the corresponding activation barrier was estimated[27] as 32.7 kcal mol^{-1}. This value is just within the "critical" region which could be accessible under the CAD experiment. As the final formation of the tropylium cation is overall exothermic, based on the published MINDO/3 calculations[27], we previously postulated[16] that there could be sufficient energetic gain so that tropylium dissociation would compete with dissociation to the benzyl cation.

Following Dewar's approach, we re-calculated the important intermediates and transition states of this rearrangement[28] by using the AM1 hamiltonian. Important results are summarized here (complete reaction pathway calculations are available on request).

According to AM1, the CH_2-containing cycloheptatrienyl cation (ΔH_f = 274.7 kcal mol^{-1}) lies 52.6 kcal mol^{-1} above the benzyl cation, and the 1,2-hydride migration requires an activation energy of 16.6 kcal mol^{-1}, corresponding to an overall activation energy for the benzyl to the tropylium cation rearrangement of 69.2 kcal mol^{-1}. This barrier is too high to be surmountable in the course of our CAD experiments even if the rearrangement were to start before complete dissociation occured. Thus, on the energy hypersurface the cationic portion of the IMP already possesses the electronic character of a "naked" benzyl cation necessary for the benzyl-tropylium rearrangement. The energy required for the ring expansion and hydrogen migration added to that of the IMP would lead for benzylpyridinium (**10a**) to some 105 kcal mol^{-1} above its ground state energy[29]. Hence, the AM1 model stringently favors the benzyl cation dissociation pathways summarized in Table 2 and Figure 1 over dissociation to the tropylium cation.

Influence of Substituents of the Pyridinium Moiety

Interpretations are based on the most stable conformations of the respective starting cations and dissociation products.

i) *The 2-Aryl-Substituted Derivatives* **11a, d–f, h**: Both the CAD-measured *AEs* and the AM1-calculated values indicated increased stability for the 2-aryl-substituted analogues **11a–h** as compared to the parent cation **10a**. By contrast in solution compound **11h** undergoes nucleophilic substitution of the pyridinium moiety much more easily than **10a**[23,24]. We believe that this discrepancy is explained by solvent effects, which better stabilize the small cation **10a**. In solution, S_N2-type reactions are generally observed[30]. In the gas phase these 2-substituents together with 6-phenyl group cause increased charge delocalization of the pyridinium ring system, and this outweighs the (destabilizing) steric interaction of the C-2/C-6 substituents with the *N*-benzyl moiety. This interpretation is supported by the data for the cation **11b**.

ii) *The Cation* **11b**: Both the experimental *AEs* and the AM1-calculated ΔH_f indicate that the pyridinium cation **11b** is the most stable one considered in this paper. For the 2-aryl derivatives (**11a**, **d**–**f**, **h**) the optimized geometries indicate that π conjugation (though still active) is reduced due to significant non-coplanarity of aryl/pyridinium ring moieties. By contrast in the most stable conformation of **11b** the 2-[(*E*)-styryl] substituent is completely coplanar with the pyridinium ring explaining its greater stability.

iii) *The Cation* **10b**: The *AE* value (41 kcal mol^{-1}) differs significantly from the AM1-calculated dissociation energy (49 kcal mol^{-1}). The former value shows **10b** to be the least stable cation of this series. It is not unreasonable to expect that the hyperconjugative stabilization of three methyl groups should be close to that of three partly π-decoupled phenyl groups (cation **11h**). This interpretation is again supported by considerations of the most stable conformation of **10b** and **11h**. As the *AE* value of **10b** is surprisingly low, we calculated conformations of **10b**, varying both the $N-CH_2$ and the CH_2–phenyl dihedral angles [D1: C-8/C-7/N-1/C-2 and D2: C-9/C-8/C-7/N-1; Scheme 3]. Two characteristic minima are found: One represents the most stable conformer (ΔH_f = 184.7 kcal mol^{-1}; D1 = 76.6°; D2 = 55.1°), the other (ΔH_f = 188.8 kcal mol^{-1}; D1 = 0.0°; D2 = 93.7°) is 4.1 kcal mol^{-1} more energetic. As expected, the energy of the dissociated 2,4,6-trimethylpyridine shows no significant dependence on the rotations of the methyl groups.

Based upon the above considerations, the calculated dissociation energy of the less stable conformer **10b** decreases to 45 kcal mol^{-1}. This improved agreement with the observed *AE* value suggests that in some cases a higher energy conformer determines the dissociation pathway in laser desorption.

Conclusion

Most of our *AE* values parallel the corresponding calculated dissociation energies of the pyridinium cations resulting from their most stable conformations. A discrepancy between the experimental and observed energy difference for **10b** stimulated the use of AM1 to seek a theoretical interpretation which indicates that observed *AEs* may depend on the cation conformation. The experimentally determined *AEs* respond to the electronic influence of substituents at the pyridinium moiety.

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Experimental

All mass-spectrometric studies were carried out by using a Nicolet FT/MS-1000 Fourier transform ion cyclotron mass spectrometer equipped with a 3-Tesla superconducting magnet. Gas-phase pyridinium ions were produced by direct laser desorption using a CO_2 laser. Ions formed by laser desorption were trapped for one second prior to CAD to allow time for thermal reactions of any energetically "hot" ions. Argon, at a pressure of 1 × 10^{-5} Torr, was used as the collision gas. Details of the experimental setup and data analysis procedures have been previously described[16–18].

All calculations were carried out by using version 4 and 5 of the MOPAC package[31–33]. Geometries were completely optimized with the stopping criteria defined by the "PRECISE" option. In all cases trial geometries were generated by using the MMX force field incorporated in PCMODEL[33]. The lowest energy conformations for each of the ions **10a**, **b** and **11a**–**h** were used as input to MOPAC and the most stable conformation for each at the semi-empirical level used in subsequent studies. The dissociation pathways of these cations were followed by extending the $C-N^+$ bond lengths while minimizing the energy of the system with respect to all remaining geometrical variables. In all cases the approximate transition states located in this way were refined by using the local (Erlangen) implementation[32] of Powell's NS01A subroutine, rather than the default optimizer in the standard version of MOPAC. In each case diagonalization of the Cartesian force constant matrix revealed the required single negative eigenvalue characteristic of a genuine transition state (saddle point).

Preparation of N-Benzylpyridinium Salts: Compounds used here have been previously prepared in our laboratory: *N*-benzylpyridinium bromide (**10a**)[16], *N*-benzyl-2,4,6-trimethylpyridinium perchlorate (**10b**)[37a], *N*-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate (**11h**)[34], and *N*-benzyl-2,4-diphenyl-6-substituted pyridinium tetrafluoroborates **11a**–**g**[35–37b].

CAS Registry Numbers

10a: 15519-25-2 / **10b**: 46504-11-4 / **11a**: 86018-87-3 / **11b**: 137122-33-9 / **11c**: 80560-54-9 / **11d**: 81765-06-2 / **11e**: 86018-84-0 / **11f**: 86018-77-1 / **11g**: 89021-40-9 / **11h**: 56524-87-9 / benzyl cation: 6711-19-9 / tropylium cation: 26811-28-9

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[1] Part 30 in the series "Kinetics and Mechanisms of Nucleophilic Displacement with Heterocycles as leaving Groups"; for part I and 29 see: A. R. Katritzky, Z. Dega-Szafran, C. H. Watson, J. R. Eyler, *J. Chem. Soc., Perkin Trans. 2* **1990**, 1051.

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