Collisionally Activated Dissociation of 1-Benzyloxypyridinium Cations.[1]

Alan R. Katritzky,* Zofia Dega-Szafran,‡ Clifford H. Watson, and John R. Eyler*
Department of Chemistry, University of Florida, Gainesville, FL 32611, USA

Eighteen pyridine-ring substituted *N*-benzyloxypyridinium cations all dissociate by two alternative pathways to give (A) a cation $C_7H_7^+$ and the substituted pyridine 1-oxide, and (B) a cation $C_7H_7O^+$ and the substituted pyridine. Appearance potentials (E_{app}) have been measured for both pathways; they are higher by 3–17 kcal mol^{-1} for the dominant pathway (A) than for (B).

The E_{app} values are compared with the ΔH_f values calculated by the AM1 method for reactants and products demonstrating extensive rearrangement in a product-like transition state (TS) for pathway (A) but not for (B). Both sets of E_{app} correlate roughly with $\Sigma\sigma$ for the pyridine ring substituents.

For the 4-dimethylamino derivatives, two additional homolytic pathways are found to give (C) a cation $Me_2NC_5H_4NO^{+\bullet}$ and (D) the 4-dimethylaminopyridine radical cation.

Pyridine 1-oxide and other heterocyclic *N*-oxides form quaternary salts on treatment with alkyl iodides, sulphates or sulphonates. This salt formation is hindered sterically by substituents in the α-position and hindered electronically by the presence of electron-withdrawing substituents in the α, β, or γ positions.[2] Quaternary salts of amine oxides are decomposed by base to yield the corresponding aldehyde and tertiary amine.[3–6]

The behaviour of a variety of biologically important pyridines and their quaternary salts and *N*-oxides upon electron impact, field ionization, and field desorption mass spectrometry has been described.[7–13] The fragmentation patterns depend considerably on the nature of the nitrogen substituents. However, there has been no previous detailed study of the fragmentation patterns of *N*-oxide quaternary salts. We now present the results of a study of the collisionally activated dissociation of laser-desorbed *N*-benzyloxypyridinium cations. The present work is an extension of previous studies on the collisionally activated dissociation of *N*-substituted pyridinium ions.[1,14]

Results and Discussion

We discuss in this paper the results of a study of eighteen 1-benzyloxypyridinium perchlorates, variously substituted in the pyridinium ring (Table 1).

Fragmentation Pathways.—Two distinct pathways were observed for the collisionally activated dissociation of all the R-substituted 1-benzyloxypyridinium perchlorates (**1**) (Scheme 1). The major pathway (A) yields the $C_7H_7^+$ ion, either benzyl (**3**) or tropylium (**4**) cation, and the R-substituted pyridine 1-oxide (**2**) (Table 2). The minor pathway (B) produces the $C_7H_7O^+$ ion, possibly benzyloxy (**6**), rearranged benzyloxy (**7**) or (**8**), or hydroxytropylium (**9**), cation and the R-substituted pyridine (**5**) (Table 3). The 4-dimethylamino derivatives (**1a**), (**1e**), and (**1h**), also showed two additional dissociation pathways (C) and (D) to produce the corresponding pyridine radical and *N*-oxide radical cations, respectively (Scheme 2 and Table 4).

Relative Dissociation Energies.—By plotting the relative kinetic energy *versus* the percentage of fragmentation $[Bz^+]/\{[RPyO^+Bz] + [Bz^+]\}$ or $[BzO^+]/\{[RPy^+] + [BzO^+]\}$ and extrapolating to zero dissociation, the appearance energies of the fragment ions were obtained.[1,14] Representative plots for three compounds for dissociation by both the pathways (A) and (B) of Scheme 1 are shown in Figure 1. The lines in Figure 1 were fitted by the linear least-squares method, and calculation of the *x*-intercepts gave, as described in the Experimental section, the appearance energies (E_{app}) for the respective fragments (Tables 2 and 3).

Calculations.—Enthalpies of formation were calculated for the R-substituted 1-benzyloxypyridinium (**1**) cations and for the benzyloxy cation and its isomers using the AM1 method.[15] Enthalpies of formation for the *C*-substituted pyridine 1-oxides, for the substituted pyridines, and for benzyl cation have been calculated previously in our laboratory.[14,16]

For 1-benzyloxypyridinium (**1r**), systematic calculations of the enthalpy of formation showed that, in the least energetic conformation, the dihedral angle between the phenyl and pyridinium rings is *ca.* 60° (Table 5). For the other pyridinium cations, a dihedral angle of 60° was used as the starting point for the calculations of their enthalpies of formation, but this angle was optimized in each case.

The calculated C–O and N–O bond lengths, and certain molecular angles are given in Table 6. The dihedral angles (γ) obtained by the AM1 method are very similar for the parent and for all the monosubstituted derivatives of 1-benzyloxypyridinium with methyl, 4-dimethylamino, or alkyloxy groups. However, a small but significant substituent effect on the dihedral angle was observed in di-and tri-methyl derivatives: 70.6° for (**1p**), 71.4° for (**1q**), and 72.1° for (**1m**). In general, steric hindrance at the α-position of the pyridinium ring increases the dihedral angle (γ).

The C(1)–C(2)–O bond angle (α) and the C(1)–O–N bond angle (β) depend only very slightly on the substituent in the pyridinium ring. The α-angle changed from 112.8° in (**1r**) to 114.1° in (**1e**). The β-angle also changes, from 118.6° in 2,4,6-trimethyl-(**1m**), and 118.8° in 2,6-dimethylpyridinium (**1p**) to 117.9° in 4-dimethylamino-(**1a**) and in 4-ethoxy-(**1c**) pyridinium.

The C–O and N–O bond lengths are almost constant at 1.467 ± 0.0015 and 1.330 ± 0.0012 Å, respectively.

Fragmentation to a Substituted Pyridine 1-Oxide and Benzyl Cation.—Using the ΔH_f values (Table 2) the theoretical enthalpies of dissociation $\Delta\Delta H_f$ for the process of pathway (A) on Scheme 1 were calculated using equation (1).

---

‡ *Permanent address:* Department of Chemistry, A. Mickiewicz University, 60780 Poznan, Poland.

Table 1. Preparation of R-substituted 1-benzyloxypyridinium perchlorates (**1**).

No.	R	M.p./°C	Yield (%)	Crystal form	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
(**1a**)	4-Dimethylamino[a]	85–87	21	prisms	$C_{14}H_{17}ClN_2O_5$	51.05	5.20	8.48	51.15	5.21	8.52
(**1b**)	4-Methoxy-2-methyl	128–129	98	needles	$C_{14}H_{16}ClNO_6$	51.18	4.90	4.20	51.00	4.89	4.27
(**1c**)	4-Ethoxy	152–153	85	needles	$C_{14}H_{16}ClNO_6$	51.12	4.88	4.19	51.00	4.89	4.25
(**1d**)	3,4-Dimethyl	117–118	71	needles	$C_{14}H_{16}ClNO_5$	53.63	5.13	4.43	53.60	5.14	4.46
(**1e**)	4-Dimethylamino-2-methyl	160–161	77	needles	$C_{15}H_{19}ClN_2O_5$	52.66	5.59	8.14	52.56	5.59	8.17
(**1f**)	2,6-Dimethyl-4-methoxy	197–198	66	needles	$C_{15}H_{18}ClNO_6$	52.45	5.26	4.05	52.41	5.28	4.07
(**1g**)	4-t-Butyl[b]	173–174	62	plates	$C_{16}H_{20}ClNO_5$	56.16	5.91	4.04	56.23	5.90	4.10
(**1h**)	2,6-Dimethyl-4-dimethylamino	211–212	70	plates	$C_{16}H_{21}ClN_2O_5$	53.91	5.94	7.80	53.86	5.93	7.85
(**1i**)	4-Methoxy	149–150	53	needles	$C_{13}H_{14}ClNO_6$	49.20	4.41	4.37	49.46	4.47	4.44
(**1j**)	3,5-Dimethyl	127–128	54	needles	$C_{14}H_{16}ClNO_5$	53.87	5.12	4.40	53.60	5.14	4.46
(**1k**)	4-Methyl[c]	126–127	64	needles	$C_{13}H_{14}ClNO_5$	52.17	4.67	4.59	52.10	4.71	4.67
(**1l**)	2-Methyl[c]	147–148	40	needles	$C_{13}H_{14}ClNO_5$	52.29	4.68	4.65	52.10	4.71	4.67
(**1m**)	2,4,6-Trimethyl	189–190	76	needles	$C_{15}H_{18}ClNO_5$	54.66	5.50	4.19	54.97	5.54	4.27
(**1n**)	3-Methoxy	122–124	32	needles	$C_{13}H_{14}ClNO_6$	49.28	4.43	4.36	49.46	4.47	4.44
(**1o**)	3-Methyl	98–99	35	needles	$C_{13}H_{14}ClNO_5$	52.18	4.67	4.59	52.10	4.71	4.67
(**1p**)	2,6-Dimethyl[d]	205–206	53	plates	$C_{14}H_{16}ClNO_5$	53.75	5.17	4.45	53.60	5.14	4.46
(**1q**)	2,4-Dimethyl[d]	143–144	81	needles	$C_{14}H_{16}ClNO_5$	53.57	5.12	4.40	53.60	5.14	4.46
(**1r**)	H[e]	116–117	70	needles	$C_{12}H_{12}ClNO_5$	50.49	4.18	4.89	50.45	4.23	4.90

[a] Previously known as the bromide, see ref. 4. [b] Previously known as the bromide, see ref. 3. [c] Previously known as the perchlorate, m.p. not quoted, see ref. 5. [d] Previously known as the bromide, see ref. 5. [e] Previously known as the bromide, see refs. 3, 6.

Table 2. Fragmentations of 1-benzyloxy-R-pyridinium cations (R–PyO$^+$Bz) (**1**) to the $C_7H_7{}^+$ cation (Bz$^+$) and substituted pyridine *N*-oxides (R–PyO).

No.	R	E_{app}(Bz$^+$)/ kcal mol^{-1}[a]	E_{int}(R–PyO$^+$)/ kcal mol^{-1} (350 K)[b]	E_{app}^{corr}(Bz$^+$)/ kcal mol^{-1} (350 K)[c]	ΔH_f/kcal mol^{-1} R–PyO$^+$Bz	ΔH_f/kcal mol^{-1} R–PyO[d]	$\Delta\Delta H_f{}^e$/kcal mol^{-1}[e] Benzyl	$\Delta\Delta H_f{}^e$/kcal mol^{-1}[e] Tropylium
(**1a**)	4-Dimethylamino	41	7	53	213	49	59	48
(**1b**)	4-Methoxy-2-methyl	38	7	50	167	−4	52	41
(**1c**)	4-Ethoxy	37	7	49	168	−3	52	41
(**1d**)	3,4-Dimethyl	38	6	49	199	25	49	38
(**1e**)	4-Dimethylamino-2-methyl	37	8	50	205	42	60	49
(**1f**)	2,6-Dimethyl-4-methoxy	30	8	43	160	−10	53	42
(**1g**)	4-t-Butyl	36	8	49	195	21	49	38
(**1h**)	2,6-Dimethyl-4-dimethylamino	35	9	49	198	36	60	50
(**1i**)	4-Methoxy	36	6	47	175	3	51	40
(**1j**)	3,5-Dimethyl	36	6	47	199	24	48	37
(**1k**)	4-Methyl	34	5	44	207	32	47	36
(**1l**)	2-Methyl	36	5	46	209	33	47	36
(**1m**)	2,4,6-Trimethyl	34	7	46	192	19	50	39
(**1n**)	3-Methoxy	34	6	45	180	2	45	34
(**1o**)	3-Methyl	31	5	41	208	32	46	35
(**1p**)	2,6-Dimethyl	30	6	41	202	27	48	37
(**1q**)	2,4-Dimethyl	31	6	42	200	25	49	38
(**1r**)	H	27	4	36	218	40	45	34

[a] Corrected for energy spread in ions and neutrals, as discussed in ref. 1 (values ±8 kcal mol^{-1}). [b] Estimated as described in ref. 1. [c] For the process R–PyO$^+$Bz (350 K) $\longrightarrow$ RPyO (350 K) + Bz$^+$ (350 K). Internal energy of Bz$^+$ (350 K) = 5 kcal mol^{-1} has been added to the sum of the previous two columns (error ±8 kcal mol^{-1}). [d] From ref. 16. [e] $\Delta\Delta H_f$ from equation (1), ΔH_f(benzyl) = 223;[14] ΔH_f(tropylium) = 212 kcal mol^{-1}.[14]

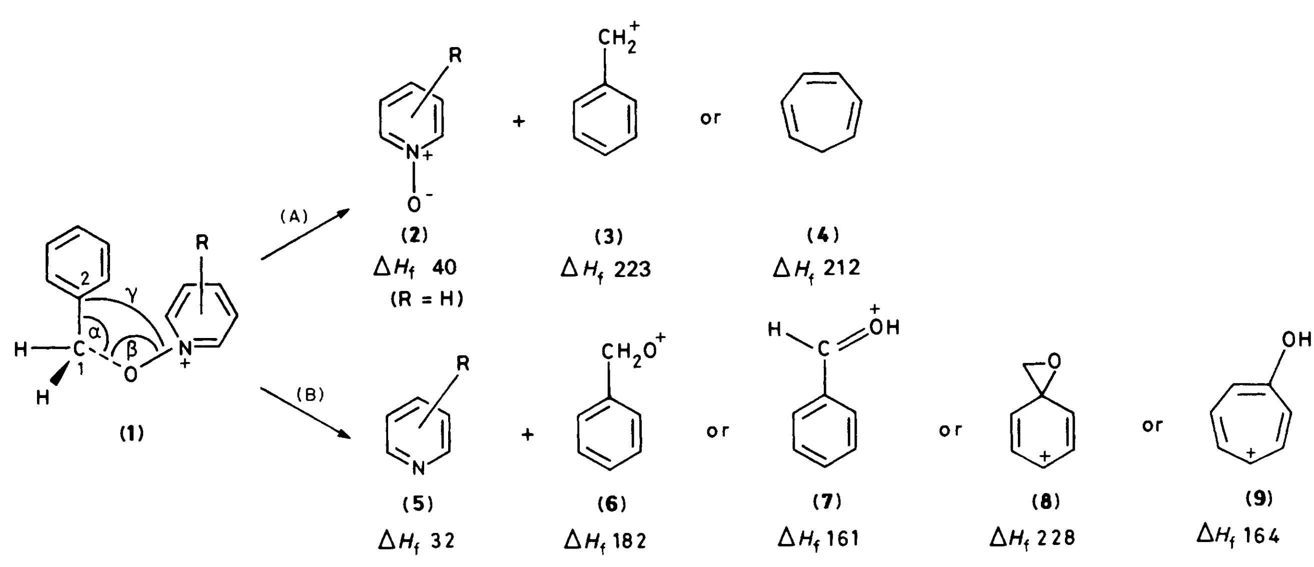
$$\Delta\Delta H_f = [\Delta H_f(\text{R–PyO}) + \Delta H_f(\text{Bz}^+)] - \Delta H_f(\text{R–PyO}^+\text{Bz}) \quad (1)$$

Two structures for $C_7H_7{}^+$ have been considered, unrearranged benzyl cation (**3**) and tropylium cation (**4**). The appearance potentials are plotted against their $\Delta\Delta H_f$ values in Figure 2. In all cases the appearance potentials occur at lower, often considerably lower, values than would be expected for a dissociation process without any rearrangement of the cation. However they are all at higher, or within experimental error of, the values expected for a dissociation process which occurred with rearrangement of the benzyl to give a tropylium cation. This is strong evidence that such rearrangement occurs within a molecular complex before the transition state is reached. Similar conclusions were previously reached for the dissociation of certain 1-benzylpyridinium cations.[14]

The appearance energies for breaking the O–C bond to give the substituted pyridine increase as a function of the electron-donating ability of the pyridine ring substituents. Although the effects of 2-methyl and 2,6-dimethyl substitution appear to vary in the 4-methoxy and 4-dimethylamino series, within each series the E_{app} values are identical within the experimental error. We find roughly the order:

$$\text{4-NMe}_2 > \text{4-MeO} > \text{4-alkyl} > \text{3-MeO} \sim \text{3-Me} > \text{H}$$

This order is in agreement with the expected stabilization of the 1-benzyloxy cation by electron donation from the substituent.



Scheme 1.

Table 3. Fragmentations of 1-benzyloxy-R-pyridinium cations (R–PyO$^+$Bz) (**1**) to $C_7H_7O^+$ cation (BzO$^+$) and substituted pyridines (R–Py).

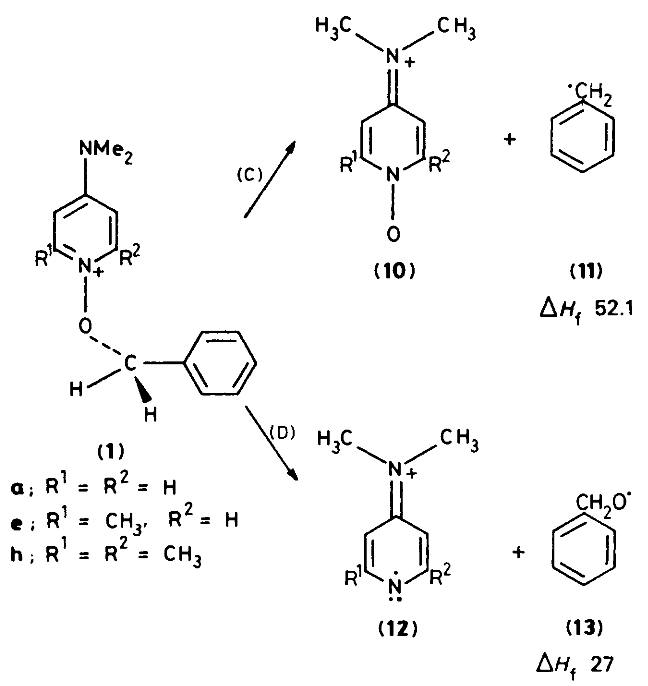
No.	R	E_{app}(BzO$^+$)/ kcal mol^{-1} [a]	E_{int}(RPy)/ kcal mol^{-1} (350 K) [b]	E^{cor}_{app}(BzO$^+$)/ kcal mol^{-1} (350 K) [c]	ΔH_f (R–Py)/ kcal mol^{-1} [d]	$\Delta\Delta H_f$/kcal mol^{-1} [e] Linear (**6**)	Linear (**7**)	Spiro (**8**)	Tropylium (**9**)
(**1d**)	3,4-Dimethyl	35	5	46	17	0	−21	46	−18
(**1g**)	4-t-Butyl	30	7	43	14	0	−21	47	−18
(**1m**)	2,4,6-Trimethyl	30	6	42	12	2	−19	48	−16
(**1e**)	4-Dimethylamino-2-methyl	26	7	39	33	10	−11	56	−8
(**1f**)	2,6-Dimethyl-4-methoxy	25	7	38	−19	4	−17	50	−14
(**1a**)	4-Dimethylamino	24	6	36	40	9	−12	55	−9
(**1q**)	2,4-Dimethyl	25	5	36	18	0	−21	47	−18
(**1c**)	4-Ethoxy	24	6	36	−12	2	−19	48	−16
(**1l**)	2-Methyl	25	4	35	26	−1	−22	45	−19
(**1i**)	4-Methoxy	24	5	35	−6	1	−20	47	−17
(**1k**)	4-Methyl	25	4	35	24	−1	−22	45	−19
(**1n**)	3-Methoxy	24	5	35	−6	−4	−24	43	−22
(**1j**)	3,5-Dimethyl	23	5	34	16	−1	−22	45	−19
(**1b**)	4-Methoxy-2-methyl	22	6	34	−13	2	−19	49	−16
(**1p**)	2,6-Dimethyl	22	5	33	20	0	−21	46	−18
(**1r**)	H	22	3	31	32	−3	−24	43	−22
(**1o**)	3-Methyl	21	4	31	24	−2	−23	44	−20

[a] Corrected for energy spread in ions and neutrals, as discussed in ref. 1 (values ±8 kcal mol^{-1}). [b] Estimated as described in ref. 1. [c] For the process RPyO$^+$Bz (350 K)$\rightarrow$RPyO (350 K) + Bz$^+$ (350 K). Internal energy of Bz$^+$ (350 K) = 5 kcal mol^{-1} has been added to the sum of the previous two columns (error ±8 kcal mol^{-1}). [d] From ref. 16. [e] From equation (2); ΔH_f(BzO$^+$) (**6**) = 182 kcal mol^{-1}; ΔH_f(BzO$^+$) (**7**) = 161; ΔH_f(BzO$^+$) (**8**) = 228 kcal mol^{-1}; ΔH_f(Tropylium-OH)$^+$ (**9**) = 164 kcal mol^{-1}.

Table 4. Fragmentation of some 1-benzyloxy-4-dimethylaminopyridiniums to radical cations.

No.	R	Pathway (C) [(**10**)] *m/z*	E_{app}/ kcal mol^{-1} [a]	E_{int}/ kcal mol^{-1} [b]	E^{corr}_{app}/ kcal mol^{-1} [c]	ΔH_f/ kcal mol^{-1}	Pathway (D) [(**12**)] *m/z*	E_{app}/ kcal mol^{-1} [a]	E_{int}/ kcal mol^{-1} [b]	E^{corr}_{app}/ kcal mol^{-1} [d]	ΔH_f/ kcal mol^{-1}
(**1a**)	4-Dimethylamino	138	38	6	49	222	122	22	5	33	228
(**1e**)	4-Dimethylamino-2-methyl	152	33	7	45	213	136	32	7	45	220
(**1h**)	2,6-Dimethyl-4-dimethylamino	166	24	8	37	204	150	14	7	27	212

[a] Corrected for energy spread in ions and neutrals, as discussed in ref. 1 (values ±8 kcal mol^{-1}). [b] Estimated as described in ref. 1. [c] For the process RPyO$^+$Bz (350 K)$\rightarrow$(**10**) (350 K) + $C_7H_7^{\cdot}$ (350 K). Internal energy of $C_7H_7^{\cdot}$ (350 K) = 5 kcal mol^{-1} has been added to the sum of the previous two columns (error ±8 kcal mol^{-1}). [d] For the process RPyO$^+$Bz (350 K)$\rightarrow$(**12**) (350 K) + $C_7H_7O^{\cdot}$ (350 K). Internal energy of $C_7H_7O^{\cdot}$ (350 K) = 6 kcal mol^{-1} has been added to the sum of the previous columns (error ±8 kcal mol^{-1}).



Scheme 2.

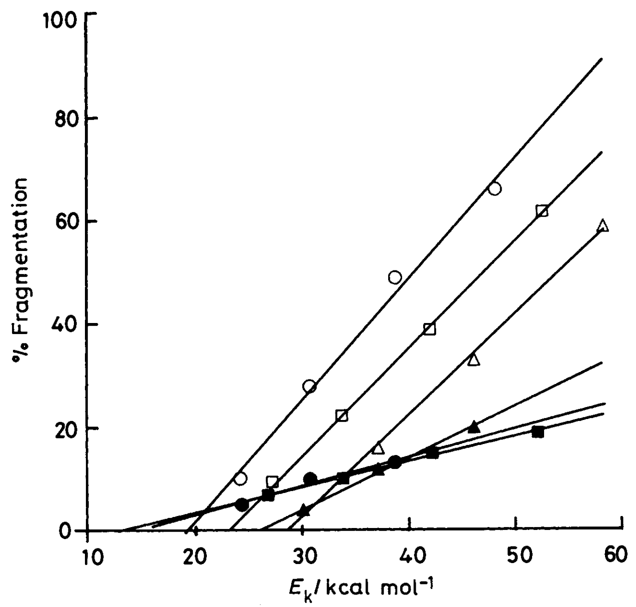


Figure 1. Correlation between the centre of motion relative kinetic energy available *via* CAD and the relative abundance of benzyl cation (Bz) (△, □, ○) and benzyloxy cation (BzO^+) (▲, ■, ●) found by the dissociation of R-substituted 1-benzyloxypyridinium cations: (**1d**), R = 3,4-Me_2; (**1o**), R = 3-Me; and (**1r**), R = H, respectively.

Fragmentation to a Substituted Pyridine and Benzyloxy Cation.—The theoretical heats of dissociation $\Delta\Delta H_f$ for the pathway (B) on Scheme 1 were calculated by AM1 using equation (2).

$$\Delta\Delta H_f = [\Delta H_f(\text{R-Py}) + \Delta H_f(\text{BzO}^+)] - \Delta H_f(\text{R-PyO}^+\text{Bz}) \quad (2)$$

Four structures were considered for the cation $C_7H_7O^+$: linear benzyloxy (**6**), protonated benzaldehyde (**7**), spiro (**8**), and hydroxytropylium (**9**). Clearly, enough energy is present to release unrearranged $PhCH_2O^+$, and although rearrangement before the transition state to (**7**) or to (**9**) [but not to (**8**)] is conceivable, it is not required by these energetics (Table 3).

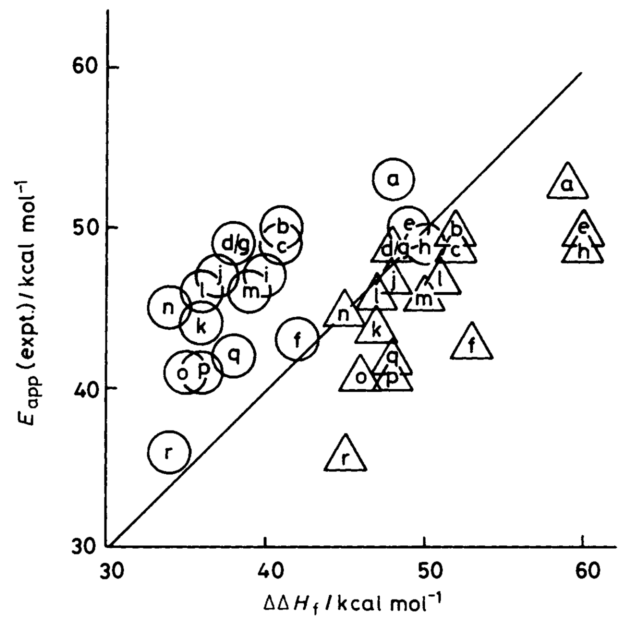


Figure 2. Plot of measured appearance energies (E_{app}) against calculated enthalpies of formation ($\Delta\Delta H_f$) of R-PyO$^+$Bz ⟶ R-PyO + Bz^+: ○, simple cation; △, tropylium cation; data from Table 2.

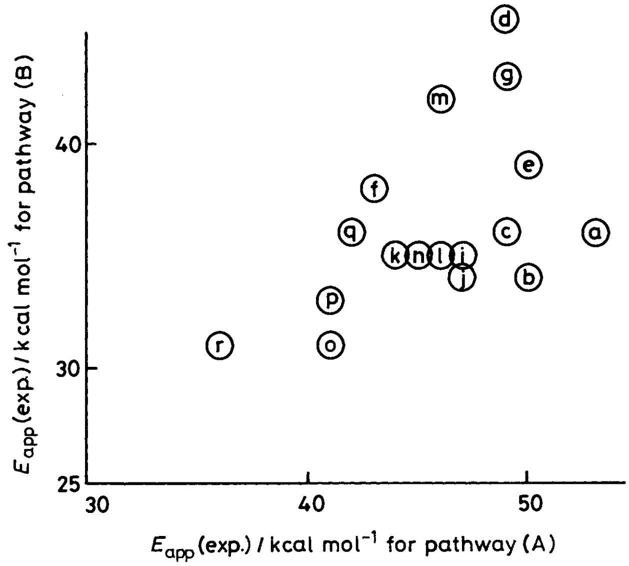


Figure 3. Plot of E_{app} for pathway (B) *vs.* E_{app} for pathway (A) for compounds not substituted in the 2-position.

Table 5. The enthalpies of formation calculated by the AM1 method for 1-benzyloxypyridinium (**1r**).

Dihedral angle/°	ΔH_f/kcal mol^{-1}
0	221
45	218
60	218
90	219
120	221
180	221

The E_{app} for pathway (B) of Scheme 1 are from 3 to 17 kcal mol^{-1} lower than those for pathway (A) (*cf.* Tables 2 and 3). This is in general a reflection of the much larger C–O than N–O

Table 6. Bond distances/Å and angles/° in R-substituted 1-benzyloxypyridine cations (**1**) in the gas phase.

		Distance		Angle		
No.	R	C–O	N–O	C(2)–C(1)–O α	C(1)–O–N β	C(2)–C(1)–O–N γ
(**1a**)	4-Dimethylamino	1.465	1.328	112.9	117.9	−65.9
(**1b**)	4-Methoxy-2-methyl	1.466	1.332	113.7	118.1	−66.0
(**1c**)	4-Ethoxy	1.466	1.330	113.0	117.9	−64.1
(**1d**)	3,4-Dimethyl	1.467	1.330	113.0	118.1	−63.0
(**1e**)	4-Dimethylamino-2-methyl	1.468	1.329	114.1	118.2	−64.7
(**1f**)	4-Methoxy-2,6-dimethyl	1.466	1.331	114.0	118.4	−67.4
(**1g**)	4-t-Butyl	1.469	1.330	113.0	118.1	−60.4
(**1h**)	4-Dimethylamino-2,6-dimethyl	1.465	1.329	114.0	118.4	−69.8
(**1i**)	4-Methoxy	1.467	1.329	113.0	118.0	−63.6
(**1j**)	3,5-Dimethyl	1.468	1.332	112.9	118.1	−63.9
(**1k**)	4-Methyl	1.468	1.330	113.1	118.1	−63.7
(**1l**)	2-Methyl	1.468	1.331	113.0	118.2	−63.6
(**1m**)	2,4,6-Trimethyl	1.467	1.332	113.7	118.6	−72.1
(**1n**)	3-Methoxy	1.470	1.332	112.9	118.1	−63.5
(**1o**)	3-Methyl	1.468	1.332	112.9	118.1	−64.5
(**1p**)	2,6-Dimethyl	1.468	1.332	113.7	118.8	−70.6
(**1q**)	2,4-Dimethyl	1.469	1.330	112.9	118.4	−71.4
(**1r**)	H	1.470	1.331	112.8	118.2	−63.2

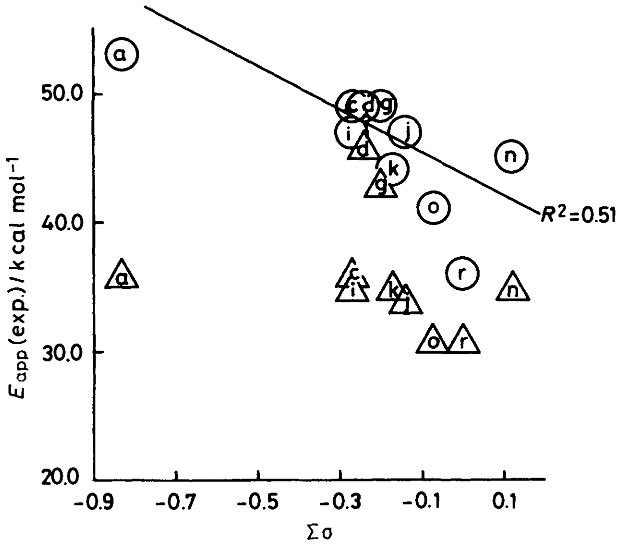
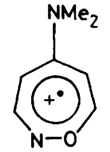
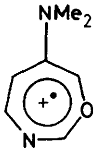


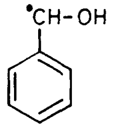
Figure 4. Plot of E_{app} for pathway (A), ○, and pathway (B), △ *vs.* Σσ for compounds not substituted in the 2-position; σ constants taken from D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420; data from Tables 2 and 3.



(**14**)
ΔH_f 232 kcal mol^{-1}



(**15**)
ΔH_f 20 kcal mol^{-1}



(**16**)

bond energy: thus $\Sigma\Delta H_f$ for (pyridine 1-oxide + tropylium cation) is 251 kcal mol^{-1} while $\Sigma\Delta H_f$ for (pyridine + hydroxytropylium cation) is only 196 kcal mol^{-1} (see Scheme 1). This would suggest differences in E_{app} between pathways (A) and (B) of around 50 kcal mol^{-1}. This is a much larger difference than found experimentally, indicating a transition state close to reactants for pathway (B), but close to products for pathway (A), and emphasizing the extensive rearrangement in the transition state for pathway (A) but not (B).

The difference between the E_{app} for pathway (A) and (B) is least for compounds substituted α to the pyridinium *N*-atom.

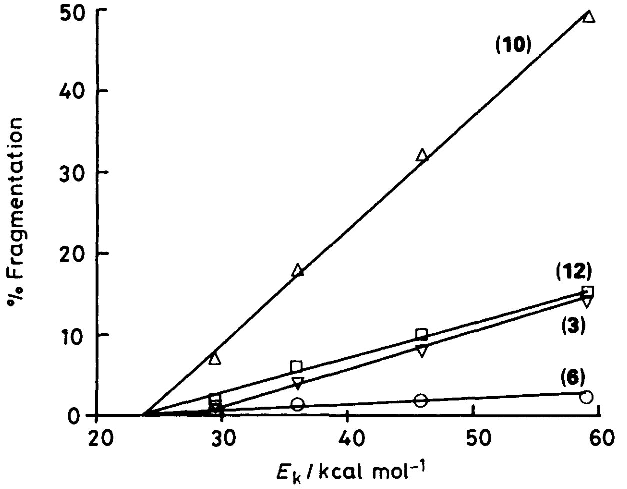


Figure 5. Correlation between the centre of motion relative kinetic energy available *via* CAD and the relative abundance of fragment ions for the dissociation of 1-benzyloxy-4-dimethylamino-2-methylpyridinium perchlorate (**1e**) [pathways (A)–(D)]: (**3**) benzyl cation, ▽; (**6**) benzyloxy cation, ○; (**10**) 4-dimethylamino-2-methylpyridine *N*-oxide radical cation, △, and (**12**) 4-dimethylamino-2-methylpyridine radical cation, □.

For the other compounds no correlation is found between E_{app} for pathways (A) and (B) (Figure 3). For pathway (A), the E_{app} values in turn correlated roughly with Σσ, showing that, as is to be expected, the pyridine cation is stabilized by electron-donating substituents (Figure 4). No significant correlation with Σσ is found for pathway (B).

Homolytic Fragmentations of 1-*Benzyloxy*-4-*dimethylaminopyridiniums*.—Formation of aromatic amine radical cations and pyridine radical cations is well recognized,[17–20] and substituent effects have been discussed.[21] The kinetics of formation of free benzyl radicals in solution and the effect of substituents have been reported by Dinçtürk *et al.*[22,23]

Four distinct pathways (A)–(D) for the collisionally activated dissociation of R-substituted 4-dimethylaminopyridinium (**1a**) and (**1e**), and three pathways (A), (C), and (D) for (**1h**) were observed (Schemes 1 and 2). Representative plots of the relative kinetic energy against the relative abundance of all four of

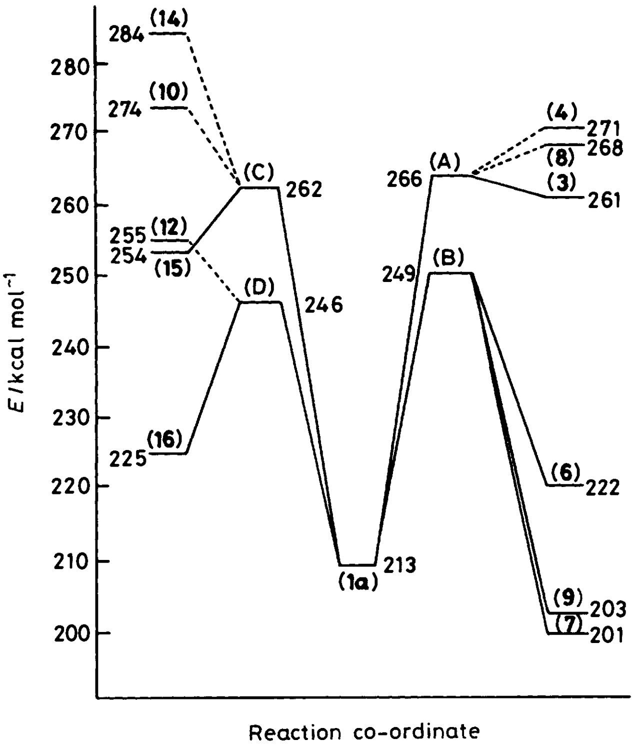


Figure 6. Energy profile for the dissociation of the 1-benzyloxy-4-dimethylaminopyridinium cation (**1a**) by pathways (A)–(D).

the fragment ions for 1-benzyloxy-2-methyl-4-dimethylaminopyridinium (**1e**) are shown in Figure 5.

In pathway (C) benzyl radical (**11**) and a cation $Me_2NC_5H_4$-$NO^{+\cdot}$ (**10**) are found: AM1 calculations show that extensive rearrangement of (**10**) occurs. The first rearrangement postulated (14)[24] has an even higher ΔH_f (232 kcal mol^{-1}). However, product (**15**) has the required lower energy (ΔH_f 202 kcal mol^{-1}). Rearrangement of type (**10**) ⟶ (**15**) is known in the photochemistry of pyridine 1-oxide.[25]

In pathway (D) benzyloxy radical (**13**) and 4-dimethylaminopyridinium radical cation (**12**) are found: AM1 calculations indicate that the products have $\Sigma\Delta H_f$ greater than the TS (see Figure 6) and therefore that rearrangement occurs to give (**16**).

The appearance potentials for the dissociation processes of Scheme 2 are given in Table 4. The appearance potentials decrease on going from (**3**) to (**10**), and from (**12**) to (**6**), and an energy diagram is deduced by combining the experimental and theoretical results (Figure 6).

It is of interest that the collisionally activated dissociation of the 4-dimethylamino derivatives gives the pyridinium 1-oxide radical ion (**10**) as the major product, even though its formation involves the greatest rearrangement.

Experimental

Measurements.—All mass spectrometric studies were carried out using a Nicolet FT/MS-1000 Fourier transform ion cyclotron mass spectrometer equipped with a 3 T superconducting magnet. Gas-phase pyridinium ions were produced by laser desorption using a pulsed CO_2 laser. Ions were trapped for 1 s prior to CAD to allow any energetically 'hot' ions time to cool *via* unreactive collisions. Argon was used as the collision gas for CAD results presented. For details of the experimental set up and analysis of data see ref. 14.

Calculations of the Enthalpies of Formation.—Calculations were performed by the AM1 method[15] using the MOPAC program with complete geometry optimization (version 3.0)[26] on a MicroVAX II computer. Standard bond lengths and bond angles were taken as the starting points. Planarity of the phenyl and pyridine rings, and C_{2v} symmetry of pyridine rings were assumed, but the conformations of, *e.g.*., CH_3, OCH_3, OC_2H_5, and $N(CH_3)_2$ groups were optimized.

Calculations of the Fenthalpies of Formation.—Calculations were performed by the AM1 method[15] using the MOPAC program with complete geometry optimization (version 3.0)[26] on a MicroVAX II computer. Standard bond lengths and bond angles were taken as the starting points. Planarity of the phenyl and pyridine rings, and C_{2v} symmetry of pyridine rings were assumed, but the conformations of, *e.g.*, CH_3, OCH_3, OC_2H_5, and $N(CH_3)_2$ groups were optimized.

Relative Dissociation Energies.—Recent studies have shown[27] that the usual infinite parallel-plate capacitor approximation[28,29] overestimates ion kinetic energies by 48%. This correction has been made to all kinetic energies reported in this paper. By plotting the centre of mass (CM) kinetic energy *versus* the percentage fragmentation (intensity of fragment ion/sum of the intensities for all ions) for each fragmentation pathway and extrapolating to zero dissociation, estimates of the appearance energies were made. The data shown in Figures 1 and 5 were fitted using a weighted least-squares method,[30] and calculation of the x-intercepts gave appearance energy (E_{app}) estimates for the respective fragments (Tables 2 and 3). The weighted least-squares fit accounted for errors in both the kinetic-energy spread[31] and the percentage fragmentation. The values calculated for the x-intercepts were corrected by the method of Chantry[32] to produce 'best estimates' for the fragment ions' appearance energies. This procedure for obtaining appearance energies was tested by comparing results using n-butylbenzene and nitrobenzene with known E_{app} values.[33,34] Based on these comparisons an error estimate of 8 kcal mol^{-1} for the E_{app} values quoted in this paper was obtained.

Preparation of R-Substituted 1-*Benzyloxypyridinium perchlorates* (**1a–r**).—To the corresponding R-substituted pyridine 1-oxide (0.005 mol) in nitromethane or chloroform (5 cm^3) was added the benzyl bromide (0.85 g, 0.005 mol). The mixture was stirred at 20 °C for 12 h. Dilution with diethyl ether (30 cm^3) precipitated the crude R-substituted 1-benzyloxypyridinium bromide. This was dissolved in ethanol (3 cm^3) and aqueous 70% perchloric acid was gradually added. The perchlorate separated and was recrystallized from ethanol. The m.p., isolated yields of pure products, and elemental analysis are given in Table 1. The structures of the salts were established by ^1H, ^{13}C NMR and mass spectroscopy.

Acknowledgements

We thank Professor M. Szafran for advice and help with the MO calculations and the Polish Academy of Sciences for financial support [Z.D-S. Project CPBP 01.12.8.5]. J. R. E. and C. H. W. acknowledge the Office of Naval Research for partial support.

References

1 For related work see A. R. Katritzky, C. H. Watson, Z. Dega-Szafran, and J. R. Eyler, *J. Am. Chem. Soc.*, 1990, **112**, 2479.
2 A. R. Katritzky and J. M. Lagowski, 'Chemistry of the Heterocyclic *N*-Oxides,' Academic Press, London, New York, 1971.
3 R. E. Manning and F. M. Schaefer, *Tetrahedron Lett.*, 1975, 213.
4 S. Mukaiyama, J. Inanaga, and M. Yamaguchi, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 2221.

5 V. J. Traynelis and J. P. Kimball, *J. Org. Chem.*, 1975, **40**, 2365.
6 W. Feely, W. L. Lehn, and V. Boekelheide, *J. Org. Chem.*, 1957, **22**, 1135.
7 D. A. Brent, D. J. Rouse, M. C. Sammons, and M. M. Bursey, *Tetrahedron Lett.*, 1973, 4127.
8 G. W. Wood and P. Y. Lau, *Org. Mass. Spectrom.*, 1975, **10**, 1147.
9 H. J. Veith, *Org. Mass. Spectrom.*, 1976, **11**, 629.
10 C. N. McEwen, S. F. Layton, and S. K. Taylor, *Anal. Chem.*, 1977, **49**, 922.
11 E. Larsen, H. Egsgaard, and H. Holmen, *Org. Mass. Spectrom.*, 1978, **13**, 417.
12 P. Ellingsen, G. Hvistendahl, and K. Undheim, *Org. Mass. Spectrom.*, 1978, **13**, 455.
13 B. Nowak-Wydra and M. Szafran, *Pol. J. Chem.*, 1982, **56**, 941.
14 A. R. Katritzky, C. H. Watson, Z. Dega-Szafran, and J. R. Eyler, *J. Am. Chem. Soc.*, 1990, **112**, 2471.
15 J. M. S. Dewar, E. G. Zoebisch, E. F. Healy, and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.
16 B. Nogaj, E. Dulewicz, B. Brycki, A. Hrynio, P. Barczynski, Z. Dega-Szafran, M. Szafran, P. Koziol, and A. R. Katritzky, *J. Phys. Chem.*, **94**, 1279.
17 Y. L. Chow, in 'Reactive Intermediates,' ed. R. A. Abramovitch, Plenum Press, New York, London, 1980, vol. 1, p. 151.
18 K. C. Bass and P. Nababsing, in 'Advances in Free-Radical Chemistry,' ed. G. H. Williams, Academic Press, New York, London, 1972, vol. 4, p. 1.
19 A. J. Bard, A. Ledwith, and H. J. Shine, in *Adv. Phys. Org. Chem.*, 1976, **13**, 156.
20 C. J. M. Stirling, 'Radicals in Organic Chemistry,' Oldbourne Press, London, 1965.
21 G. Leroy, D. Peeters, M. Sana, and C. Wilante, in 'Substituent Effects in Radical Chemistry, eds. H. G. Viehe, Z. Janousek, and R. Merenyi, D. Reidel Publ. Co., Dordrecht, Boston, Lancaster, Tokyo, 1986, p. 1.
22 S. Dinçtürk, R. A. Jackson, M. Townson, H. Agirbas, N. C. Billingham, and G. March, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1121.
23 S. Dinçtürk and R. A. Jackson, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1127.
24 S. T. Reid, *Adv. Heterocycl. Chem.*, eds. A. R. Katritzky and A. J. Boulton, Academic Press, New York, London, 1970, vol. 11, p. 1.
25 G. W. H. Cheeseman and E. S. G. Werstiuk, *Adv. Heterocycl. Chem.*, eds. A. R. Katritzky and A. J. Boulton, Academic Press, New York, London, 1978, vol. 22, p. 367.
26 J. J. P. Stewart, MOPAC Program Package, *QCPE*, 1983, No. 455.
27 P. B. Grosshans, P. Shields, and A. G. Marshall, *J. Am. Chem. Soc.*, in press.
28 M. Bensimon and R. Houriet, *Int. J. Mass Spectrom. Ion Proc.*, 1986, **72**, 93.
29 R. B. Cody, R. C. Burnier, and B. S. Freiser, *Anal. Chem.*, 1982, **54**, 843.
30 J. A. Irvin and T. I. Quickenden, *J. Chem. Ed.*, 1983, **60**, 711.
31 W. T. Huntress, Jr., M. M. Mosesman, and D. D. Elleman, *J. Chem. Phys.*, 1971, **54**, 843
32 P. J. Chantry, *J. Chem. Phys.*, 1971, **55**, 2746.
33 T. Baer, O. Dutuit, H. Mestdagh, and C. Rolando, *J. Phys. Chem.*, 1988, **92**, 5674.
34 M. Panczel, and T. Baer, *Int. J. Mass Spectrom. Ion Proc.*, 1984, **58**, 43.

Paper 9/00845D
Received 21*st December* 1989
Accepted 19*th March* 1990