

tone-sensitized irradiation of **4** in the presence of 3-methylindole (**7**) gave **8**²⁰ (66%), whereas direct irradiation of **4** and methyl indole-3-propionate (**9**) with 254-nm light resulted in the formation of **6** (60%) and **10**²¹ (15%).

Electrophilic substitution²² usually occurs predominantly at the 3 position of indoles, whereas radical reactions,²³ including several photoinduced reactions,²⁴ proceed less selectively to give mixture of 1-, 2-, 3-, 4-, and 6-substituted indoles. In the present case, however, the coupling reactions occurred exclusively on the 2 position of the indole molecules. The benzenoid ring was not attacked. Such a preferential attack on the 2 position has been observed in certain photoadditions²⁵ or in anodic cyanation,²⁶ where an electron-transfer process is believed to be involved.²⁷

Under conditions in which **1** reacted smoothly with **2**, both **1** and **4** were photochemically inert toward derivatives of other aromatic amino acids such as *N*-acetylhistidine methyl ester or *N*-acetyltyrosine methyl ester. Thus, the photochemical coupling reaction is *specific for tryptophan*. A similar coupling may take place between bromouracil-substituted DNA and tryptophyl residues in a protein. Thus, the coupling reactions reported here may serve as a useful model for the study of the lethal effects of UV light on cells. Moreover, because of its high selectivity, regioselectivity, and efficiency, the present reaction constitutes a useful synthetic method for the introduction of indolyl groups into the 5 position of uracil or uridine. Mechanistic aspects and other synthetic applications of this new type of photochemical coupling reactions are under study.

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- It is also known that various proteins are linked covalently to *normal* nucleic acids under the influence of UV light.^{5c,8}
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- Irradiation was done with a 100-W high-pressure mercury lamp using a glass filter (>300 nm) at ambient temperature.
- UV (acetonitrile) 260 nm (log ϵ 4.07), 328 (3.72); ¹H NMR (Me₂CO-d₆) δ 1.35 (s, 3 H), 1.55 (s, 3 H), 1.78 (s, 3 H), 3.24 (d, 2 H, J = 8 Hz), 3.59 (s, 3 H), 3.83 (d, 2 H, J = 6 Hz), 3.76-4.13 (2 H, NH and OH), 4.25 (td, 1 H, J = 6.0, 3.0 Hz), 4.78 (td, 1 H, J = 8.0, 8.0 Hz), 4.98 (dd, 1 H, J = 14.0, 2.4 Hz), 5.02 (dd, 1 H, J = 14.0, 3.0 Hz), 6.12 (d, 1 H, J = 2.4 Hz), 6.95-7.64 (m, 4 H), 7.69 (br d, 1 H, J = 8.0 Hz, NH), 8.22 (s, 1 H), 10.25 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 542.20036 (M⁺) (calcd for C₂₆H₃₀N₄O₈, 542.20124).
- Assignments are based on multiplicitities in the off-resonance decoupled spectrum and on chemical shifts in model compounds.
- Mp 222-224 °C dec; UV (acetonitrile) 264 nm (log ϵ 4.08), 288 (4.02), 337 (3.73); ¹H NMR (CDCl₃) δ 1.96 (s, 3 H), 3.32 (d, 2 H, J = 8 Hz), 3.36 (s, 3 H), 3.44 (s, 3 H), 3.62 (s, 3 H), 4.71 (td, 1 H, J = 8.0, 8.0 Hz), 6.64 (d, 1 H, J = 8 Hz, NH), 7.03-7.54 (m, 4 H), 8.09 (s, 1 H), 10.29 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 398.1592 (M⁺) (calcd for C₂₀H₂₂N₄O₅, 398.1590).
- Essentially the same result has been obtained in aqueous acetone.

- Quantum-yield measurement was carried out at 20 °C using benzophenone-benzhydrol actinometry.¹⁸ Potassium chromate in an aqueous solution of potassium carbonate was used to isolate the 313-nm region of the high-pressure mercury arc.
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- Photochemical debromination of 5-bromouracil by 254-nm light is well known.^{2b} See also J. M. Campbell, D. Schulte-Frohlinde, and C. von Sonntag, *Photochem. Photobiol.*, **20**, 465 (1974), and references therein.
- Mp 198-201 °C; UV (acetonitrile) 260 nm (log ϵ 3.95), 291 (3.98), 340 (3.72); ¹H NMR (CDCl₃) δ 2.31 (s, 3 H), 3.35 (s, 3 H), 3.38 (s, 3 H), 6.96-7.58 (m, 4 H), 7.94 (s, 1 H), 9.92 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 269.1142 (M⁺) (calcd for C₁₅H₁₅N₃O₂, 269.1164).
- Mp 59-60 °C; UV (acetonitrile) 264 (log ϵ 4.00), 282 (4.01), 332 (3.74); ¹H NMR (CDCl₃) δ 2.67-3.32 (m, 4 H), 3.45 (s, 3 H), 3.57 (s, 3 H), 3.67 (s, 3 H), 7.01-7.66 (m, 4 H), 8.07 (s, 1 H), 9.87 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 341.1354 (M⁺) (calcd for C₁₈H₁₈N₃O₄, 341.1374).
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Gas Phase Photodissociation of C₇H₇⁺

Sir:

The C₇H₇⁺ cation continues to present a challenging structural problem to mass spectroscopists. Extensive mass spectroscopic¹⁻⁴ and ion photodissociation⁵ results using specifically labeled precursors (²H, ¹³C) show that hydrogen and carbon scrambling occur to a large degree in the formation and fragmentation of C₇H₇⁺. Such results are suggestive of the symmetrical tropylium ion (I). On the other hand, ions having



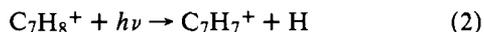
enough internal energy to fragment will undoubtedly undergo molecular rearrangement prior to dissociation and therefore may not reflect the ground state structure or stability of the ion. Studies utilizing collisional activation (CA) or collision induced dissociation (CID) techniques, generally believed to yield ground-state structural information, have indicated that C₇H₇⁺ obtained from toluene, for example, is a mixture of isomers possibly undergoing interconversion.⁶ These techniques, however, by their very nature may also promote scrambling prior to dissociation and detection and, in addition, sample ions that may have lifetimes only on the order of 10⁻⁵ s.

The most convincing evidence for the long-lived existence of more than one cyclic isomer of C₇H₇⁺ in the gas phase comes from ion-molecule reaction studies using ion cyclotron resonance (ICR) spectroscopy.⁷⁻⁹ Shen et al.⁷ concluded from

deuterium-labeling experiments that the $C_7H_7^+$ ions generated from toluene which undergo



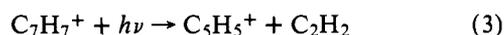
have the benzyl structure (II). At the pressures employed in this study, the time between collisions was several milliseconds yielding a lower limit for the lifetime of the cation on that order. More recently, elegant time resolved studies utilizing ICR demonstrated that $C_7H_7^+$, generated photochemically⁸ from toluene radical cation via



and directly from toluene and several of its derivatives by electron impact,⁹ exists as two distinct populations, one reactive (benzyl) and one unreactive (hypothesized as tropylium), both of which maintain their structural integrities on the order of seconds. Using this methodology Ausloos et al.⁹ reported, for example, that $C_7H_7^+$ ions generated from toluene at electron energies above 25 eV consist of ~40% tropylium and ~60% benzyl cation, while $C_7H_7^+$ ions generated from benzyl chloride above 25 eV consist of ~10% tropylium and ~90% benzyl cation.

In reinvestigating the photochemistry of the toluene system (i.e., $C_7H_7^+$, $C_7H_8^+$, and $C_8H_9^+$), our main objective was to obtain *direct* evidence for the structure of the unreactive $C_7H_7^+$ ions. The solution absorption spectrum of the tropylium ion¹⁰ has a maximum at ~275 nm (Figure 1) at which wavelength the photon energy is well in excess of the estimated 57 kcal/mol required for conversion of tropylium to benzyl cation.¹¹ A change in reactivity of the unreactive ions could therefore be expected to occur upon irradiation in this wavelength region. Monitoring the change in reactivity as a function of wavelength would yield information about the absorption spectrum of the unreactive species and hence information about its ground-state structure.

Quite unexpectedly, dissociation of $C_7H_7^+$ to $C_5H_5^+$



was observed. This reaction has not been previously observed despite the numerous photodissociation studies reported in the literature in which $C_7H_7^+$ has been present as a product ion.^{5,8,12-14} Figure 1 compares the gas phase photodissociation spectrum of $C_7H_7^+$ with the solution absorption spectrum¹⁰ of the tropylium ion. The gas phase spectrum was obtained by monitoring the appearance of $C_5H_5^+$ while continuously ejecting $C_7H_8^+$ to prevent reaction 2. An ICR¹⁵ was utilized for these studies in conjunction with a Schoeffel 3.5-kW mercury-xenon arc lamp and 0.25-m monochromator set for a resolution of 10 nm. Other conditions for this experiment included an electron energy of 17 eV, a neutral gas pressure of $\sim 1 \times 10^{-7}$ Torr, and a trapping time of 1.5 s. Under similar conditions, $C_7H_7^+$ generated from benzyl chloride at 70 eV yielded the identical photodissociation spectrum shown in Figure 1, with >50% of the ions observed to photodissociate. These results show conclusively that the photodissociation spectrum arises from $C_7H_7^+$ ions which undergo reaction 1 and, thus, the spectrum is associated with the benzyl ion. Furthermore, as shown in Figure 1, the photodissociation spectrum differs significantly from the solution spectrum, having an absorption maximum at longer wavelengths (290 ± 10 nm) as well as being considerably broader. This difference cannot be attributed to just a solvent effect, since the solvent would be expected to broaden the solution spectrum relative to the gas phase spectrum. While the presence of tropylium ion *cannot* be ruled out by these results, the photodissociation spectrum indicates the presence of an ion other than tropylium and is consistent with the benzyl cation whose spectrum is predicted to have a maximum at 290 nm.¹⁶ The absence of a band in the photodissociation spectrum in Figure 1 at longer

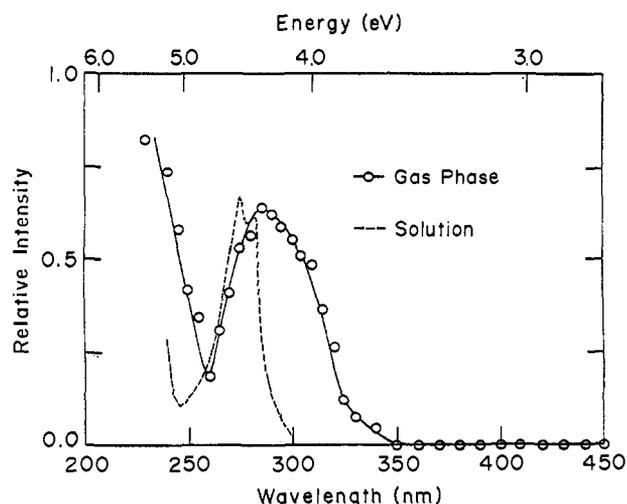


Figure 1. Comparison of the gas phase photodissociation spectrum of $C_7H_7^+$ to the solution absorption spectrum of tropylium ion. The relative intensities of the two spectra are not directly comparable.

wavelengths, predicted¹⁶ for the benzyl cation to occur at 412 nm and observed for benzyl ion¹⁷ and several of its α -carbon- and ring-substituted derivatives in solution,^{16,18,19} can be attributed to the thermodynamics of reaction 3. The heats of formation of the ions involved in process 3 are not known precisely. In particular, $\Delta H_f(C_5H_5^+)$ varies over some 50 kcal/mol.²⁰ Using $\Delta H_f(\text{benzyl}) = 211$,²¹ $\Delta H_f(C_2H_2) = 54$,²⁰ and $\Delta H_f(C_5H_5^+) = 254$ kcal/mol (the lowest reported value of which we are aware),²⁰ the thermodynamic threshold for process 3 is calculated to occur at 295 nm (97 kcal/mol). Calculation assuming tropylium or using larger values for $\Delta H_f(C_5H_5^+)$ would lead to a threshold at even shorter wavelengths. Alternatively, the threshold observed in Figure 1 at 350 nm (82 ± 5 kcal/mol) can be used to estimate an upper limit of $\Delta H_f(C_5H_5^+) \leq 239 \pm 5$ kcal/mol. Finally, these results would also be consistent with $\Delta H_f(C_7H_7^+) \geq 226 \pm 5$ kcal/mol, within the range of a number of earlier estimates for $\Delta H_f(\text{benzyl})$.^{9,20}

These results exhibit a novel photochemical reaction of $C_7H_7^+$ associated with the "reactive" form of the ion (where "reactive" corresponds to those ions which undergo reaction 1) and are consistent with the benzyl cation. Previous ICR photodissociation studies^{5,8,12-14} of the toluene system limited to the wavelength range $\lambda \geq 400$ nm would fail to observe reaction 3.²² Time-resolved studies are currently underway to quantitatively determine population makeup of $C_7H_7^+$ ions generated from different neutral precursors. These studies will complement rather than duplicate ion-molecule reaction studies since (1) there is disagreement⁹ between the ion-molecule reaction results and previous determinations by other methods for which the photodissociation method would yield important new evidence; (2) time-resolved photodissociation studies could conceivably uncover new populations of ions within the existing "reactive" and "unreactive" categories, presently not known; (3) a wider variety of species may be studied for which characteristic reactions are unknown (e.g., halo- and alkyl-substituted species); and (4) the photodissociation spectra will ultimately yield a direct handle on the structures of the species involved and their UV absorption spectra, the latter providing an important comparison with solution spectra.

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- (22) For a one-photon process, reaction 3 will not be observed for $\lambda > 400$ nm. Using laser irradiation (4545–5145 Å), we have observed a two-photon process in which $C_7H_7^+$ dissociates to $C_5H_5^+$. These results will be reported elsewhere.

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Energy Partitioning in Unimolecular Decomposition. Isotope Effects on the Kinetic Energy Release in the Loss of H₂ from (CH₂=OH)⁺

Sir:

There now exists a very large body of data concerning the translational energies released in unimolecular decompositions of gaseous ions, much of which has been obtained from analysis of metastable peak shapes.¹ This energy originates from excess energy (i.e., internal energy in excess of the activation energy), and from the reverse activation energy. The excess energy may be partitioned statistically; however, there is conclusive evidence that the proportion of the reverse activation energy partitioned as translation varies quite considerably from reaction to reaction.^{1,2} The purpose of this paper is to show how a dynamical approach to the partition of reverse activation energy elegantly explains the large deuterium isotope effects on energy release in the elimination of H₂ from (CH₂=OH)⁺³ (see Table I). It has been pointed out previously that these

Table I. Isotope Effects on Experimental and Calculated Energy Releases

	Exptl ^a	Calcd
(CH ₂ =OH) ⁺ → (CHO) ⁺ + H ₂	1	1
(CH ₂ =OD) ⁺ → (CHO) ⁺ + HD	1.15	1.25
(CD ₂ =OH) ⁺ → (CDO) ⁺ + HD	0.89	0.77
(CD ₂ =OD) ⁺ → (CDO) ⁺ + D ₂	1.04	0.98

^a Values taken from ref 3. Similar results were obtained in our laboratory.

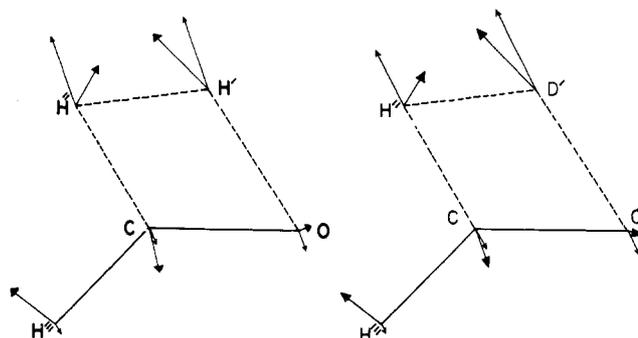


Figure 1. The compositions in terms of mass-weighted atomic displacements of the transition-state reaction coordinate (heavy arrows) and the product separation coordinate (light arrows) for (a) (CH₂=OH)⁺ and (b) (CH₂=OD)⁺. These displacements are proportional to the mass-weighted velocities, and to the square root of kinetic energy.

isotope effects cannot be attributed to zero point energy effects,⁴ nor are they readily explained by considering merely transition-state structure.⁵

From the point of view of reaction dynamics, two aspects of the partition of reverse activation energy can be distinguished: first, initial storage of kinetic energy in product modes determined by the local compositions of the reaction coordinate between transition state and products and, second, subsequent partial redistribution of this energy if the reaction coordinate is curved. To treat this partitioning, we consider simply the composition of the reaction coordinate at the transition state in terms of mass-weighted atomic displacements,⁶ and compare this composition with that of a translation separating the products. The more closely these two composite motions correspond to each other, the larger, we suggest, will be the proportion of reverse activation energy partitioned as translation.^{7,8} The transition-state atomic motions are normalized and expressed as a 3*N* dimensional unit vector.⁹ This unit vector is projected onto the 3 dimensional subspace of product separation coordinates, and the square of the length of the projection taken as a measure of the proportion of energy released in translation.⁹

This approach neglects redistribution of kinetic energy once it has appeared in a particular mode; however, it also underestimates the extent to which energy is initially stored in modes effecting product separation. The success of the approach depends upon the extent to which these factors compensate for each other.

The atomic motions of the transition-state reaction coordinates have been calculated for the loss of H₂ from (CH₂=OH)⁺, HD from (CH₂=OD)⁺, HD from (CD₂=OH)⁺, and D₂ from (CD₂=OD)⁺ (see Figure 1). The MINDO/3 molecular orbital method^{10,15} has been employed, and the potential energy surface has been searched to locate the saddlepoint.¹¹ The proportions of the reverse activation energy appearing as translation have been obtained using the approach discussed above, and the results satisfactorily reproduce the trend of the experimental isotope effects¹² (Table I).

Figure 1 illustrates how the significant contributions to the translational energy release arise from H' and H''. Only these atoms show large displacements in similar directions in both the transition state and product separation. The contribution of H' is twice as large as that of H'', again as might be evident from Figure 1, and the trend of the calculated isotope effects (Table I) reflects the effect of isotopic substitution on the contribution from the atom at the H' position. The changes in the contribution from the H'' position upon substitution in fact oppose the overall isotope effects (Table I), but these changes are masked by the much larger changes in the H' contribution.