Electron Impact Studies. Part 116.[1] Mechanism of Keten Elimination from Acetanilide and Phenyl Acetate Radical Ions

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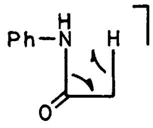
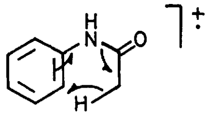
Ion cyclotron resonance studies show that the processes $M^{+\cdot} \longrightarrow (M - CH_2CO)^{+\cdot}$ from both the acetanilide and phenyl acetate molecular ions occur through four-membered transition states; the non-decomposing product ions from these processes correspond to the aniline and phenol ion radicals, respectively.

Kinetic isotope effects (k_H/k_D) for H–D transfer from p-RC_6H_4·NH·CO·CH_2·D increase (from 1.5 to 2.2 for decompositions in the first field-free region) with increasing σ^+ values of R. Kinetic energy releases occurring during the metastable decompositions $M^{+\cdot} \longrightarrow (M - CH_2CO)^{+\cdot}$ from p-RC_6H_4·NH·COMe increase with decreasing σ^+. A similar study with p-substituted phenyl acetates shows k_H/k_D to be small (1.2—1.3) and insensitive to changes in the *para*-substituent. Kinetic energy release is also relatively insensitive to the nature of the substituent. These results are rationalised in terms of transition state geometries.

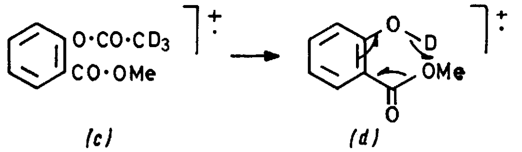
THE rearrangements $M^{+\cdot} \longrightarrow (M - CH_2CO)^{+\cdot}$ in the mass spectra of acetanilides and phenyl acetates have been the subject of a number of recent studies.[1-10] Considerations of steric effects upon the elimination of keten from substituted acetanilide molecular ions,[6] and of the observed isotope effect [7] for competing metastable transitions corresponding to $(M - CH_2CO)^{+\cdot} \longrightarrow [(M - CH_2CO) - HCN]^{+\cdot}$ from ${}^2H$-labelled *p*-chloroacetanilides, suggest a four- (*a*) rather than a six- (*b*) membered transition state for acetanilides. Evidence for a four-membered transition state during the elimination of keten from phenyl acetate molecular ions is given by the behaviour of the ion (*c*); this loses CD_2CO to yield (*d*) which decomposes characteristically by loss of MeOD.[10]



(*a*)



(*b*)



(*c*) (*d*)

The intensity of the rearrangement peak in the spectra of *meta*- and *para*-substituted acetanilides [4,5] and phenyl acetates [4,9] depends on the nature of the substituent. Correlations of this type [4,5,9] should however be viewed with caution in the light of critical reviews [11,12] of this technique.[13] The mechanistic issue is further clouded by a report [8] that the observed changes in appearance potential for the losses of CH_2CO from substituted acetanilides are due to changes in the number of degrees of freedom of the substituent rather than the influence of the substituent on the critical energy of the reaction.

In this study we seek to clarify the mechanism(s) for loss of keten from both acetanilide and phenyl acetate radical ions, by (*a*) determining the product ion structure in each case by ion cyclotron resonance, and (*b*) ascertaining the effect of the *para*-substituent on the transition state for each reaction by measuring (i) the primary deuterium isotope effect (k_H/k_D) for the hydrogen (deuterium) transfer reaction, and (ii) the kinetic energy released as translational energy of products for the appropriate metastable transition occurring in the first field-free region of the mass spectrometer.

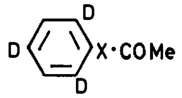
RESULTS AND DISCUSSION

Before undertaking an investigation of the nature of the transition state or of product ion structure, it is necessary to establish whether hydrogen scrambling between methyl and aryl hydrogen atoms (and NH where appropriate) competes with elimination of keten from the phenyl acetate and acetanilide ion radicals.

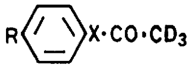
The appropriate decompositions of the ${}^2H$-labelled derivatives (1)—(4) in the ion source and the two field-free regions show that no H–D scrambling occurs between the methyl and phenyl units, *i.e.* the spectra of (1) and (2) show the ions $(M - CD_2CO)^{+\cdot}$, whereas

PhX·CO·CD_3

(1) X = O
(2) X = NH



(3) X = O
(4) X = NH



	R	X
(5)	MeO	O
(6)	NO_2	O
(7)	MeO	NH
(8)	NO_2	NH

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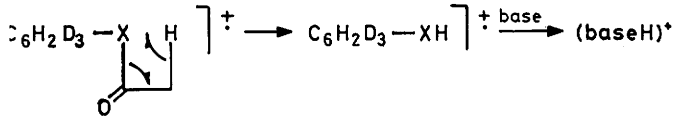
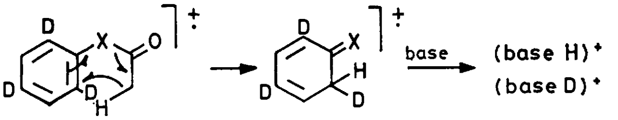
those of (3) and (4) exhibit the ions $(M - CH_2CO)^{+\bullet}$ only. The corresponding spectra of the *para*-substituted derivatives (5)—(8) show specific loss of CD_2CO, thus establishing that no hydrogen scrambling accompanies loss of keten from the systems under investigation.

(A) *Nature of the Transition State.*—Elimination of keten from the acetanilide and phenyl acetate molecular ions through four-centre states would yield the aniline and phenol radical ions, respectively, whereas reactions through six-membered transition states would give the imino and keto forms of the aniline and phenol species. Such ions can be distinguished by their differing abilities to transfer acidic protons to a suitable base in an ion cyclotron resonance (i.c.r.) cell.[14] This is illustrated for the labelled compounds (3) and (4) (X = O or NH, respectively) in Schemes 1 and 2. The [2,4,6-$^2H_3$]-aniline (or -phenol) ion should specifically transfer H^+ to the base (Scheme 1), whereas the imino (keto) form could transfer both H^+ and D^+ (Scheme 2).



SCHEME 1

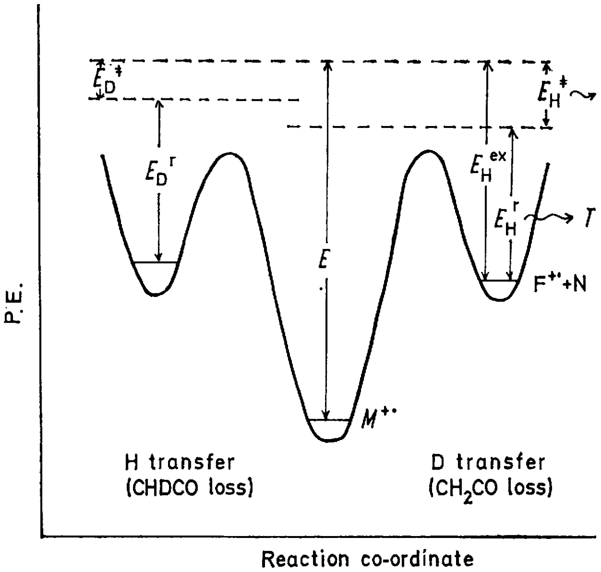


SCHEME 2

The base chosen was 3,4-lutidine (*cf.* ref. 14) and i.c.r. cell conditions were as follows: acetanilide (phenyl acetate) : 3,4-lutidine 10 : 1 (total pressure 5×10^{-6} Torr), electron beam energy 18 eV, and ion transit time[15] in the range 1×10^{-4} to 1×10^{-3} s (see below). The 3,4-lutidine molecular ion reacts with neutral lutidine to yield (base H)$^+$ (*cf.* ref. 14). When a large excess of acetanilide or phenyl acetate is present, the spectrum is again dominated by a peak due to (base H)$^+$, but in these cases it is almost exclusively produced by the reaction between the appropriate ion $(M - CH_2CO)^{+\bullet}$ and neutral base. The reacting species are determined by the cyclotron ejection technique.[16]

The reactions between the ions $(M - CH_2CO)^{+\bullet}$ [from (3) and (4)] and 3,4-lutidine specifically yield (base H)$^+$ ions. No (base D)$^+$ component was detected. A similar reaction between the ion $(M - CD_2CO)^{+\bullet}$ ion from phenyl [$^2H_3$]acetate (1) and 3,4-lutidine produces only a (base D)$^+$ species. The ion $(M - CD_2CO)^{+\bullet}$ from the [$^2H_3$]acetanilide (2) (in this case $PhNHD^{+\bullet}$) reacts with neutral base to yield (base H)$^+$ and (base D)$^+$ in the ratio 2.4 : 1 (*i.e.* $k_H/k_D = 2.4$) at a transit time of 1×10^{-3} s. Finally, it has been noted in one instance[17] that enol ⟶ keto tautomerism can be detected if long transit times (*e.g.* 10^{-3} s) are used in the i.c.r. cell. The experiments described above were repeated with a number of transit times between 1×10^{-4} and 1×10^{-3} s; no alteration was noted in any case, *i.e.* neither imino ⟶ amino, nor keto ⟶ enol conversion was detected. We conclude that the non-decomposing product ions correspond to the aniline and phenol radical ions, respectively, and that both rearrangements are likely to proceed through four-membered transition states [see (*a*) and Scheme 1].

(B) *Deuterium Isotope Effects and Kinetic Energy Releases.*—(i) para-*Substituted acetanilides.* Kinetic isotope effects can be expressed as differences and ratios of isotopic zero point energies and ratios of partition functions between reactant and transition state.[18] The Figure illustrates the general case for competitive H• and D• transfer followed by loss of some neutral species N. Because of the differences in zero point energies associated with C–H and C–D bonds, the internal energy of the activated complex for H• transfer is greater than that for D• transfer and, as a consequence, the deuterium isotope effect [k_H(transfer)/k_D(transfer)] will be greater than unity. In addition, the isotope effect *increases* as the internal energy (E) of the decomposing ion $M^{+\bullet}$ *decreases*. Kinetic isotope effects can also be expressed in terms of the changes in vibrational frequencies at the reaction site in proceeding along the



Potential energy diagram for H• and D• transfer for a molecular ion $M^{+\bullet}$ of internal energy E with subsequent loss of a neutral molecule N (see ref. 27 for a full description); $E_D^‡$ represents the excess energy of the transition state due to loss of CHDCO (H transfer); $E_H^‡$ represents the excess energy of the transition state due to loss of CH_2CO (D transfer)

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[17] J. R. Hass, M. M. Bursey, D. G. I. Kingston, and H. P. Tannenbaum, *J. Amer. Chem. Soc.*, 1972, **94**, 5095.

[18] R. A. More O'Ferrall, in 'Proton Transfer Reactions,' eds. E. F. Caldin and V. Gold, Halsted Press, New York, 1975, ch. 8.

reaction co-ordinate.[19,20] It would therefore be expected that a change in the *para*-substituent of an acetanilide should affect the nature of the transition state for keten elimination, thus producing a change in the deuterium isotope effect. Increased bonding in the transition state leads to a ' tighter ' transition state ($\Delta S^\ddagger < 0$) and hence a lower isotope effect.

Deuterium isotope effects can be very large for positive ion decompositions[21] [if the internal energy of $M^{+\cdot} = E - E_H^\ddagger$ (Figure), $k_H/k_D = \infty$], but in general $k_H/k_D < 10$.[22] A *maximum* estimate of the magnitude of the deuterium isotope effects for loss of keten from substituted acetanilide molecular ions can be obtained from theoretical calculations for hydrogen transfer reactions in model systems.[23,24] For the symmetrical hydrogen transfer system $A \cdots H \cdots B$, k_H/k_D decreases markedly as the angle between $A \cdots H$ and $H \cdots B$ decreases.[23] When the angle is 90° (as in a four-membered transition state) $k_H/k_D = 2.3$. This value is obtained only when H is equidistant from A and B. When H is closer to either A or B (*i.e.* when the transition state more closely resembles either reactant or product), lower isotope effects are expected.[24] Isotope effects are therefore expected to be relatively small in the acetanilide system.

TABLE 1

Deuterium isotope effects and energetics for loss of keten from molecular ions of *para*-substituted acetanilides (all energies in eV)

	k_H/k_D [a]												
Subst.	Source	1st FFR	σ_p^+	$T_{50\%}$ [b]	ΔH_f (M) [c]	A.P. ($F^{+\cdot}$) [d,e]	I.P. (F) [d,e]	ΔH_f (F) [c,e]	E_{excess} [f]	T/E_{excess}	Kinetic shift [i]	E^r	T/E^r
HO			−0.92	0.015									
MeO	1.17	1.5	−0.78	0.017	−2.46	10.7	7.8	−0.47	1.5	0.011	1.10	0.42	0.04
Me	*g*	1.65	−0.31	0.010	−1.12	10.6	8.1	+0.73	1.3	0.008	0.94	0.33	0.03
H	1.72	2.2	0	0.013	−0.85	10.8 [8b]	7.7	+1.00	1.9	0.007	0.7	1.06	0.01
Cl	1.31	1.8	0.11	0.010 5	+0.73	10.6	8.1	+2.59	1.3	0.008			
MeCO	1.50	2.1	0.50 [h]	0.009	−2.99	10.6	8.2	−0.69	0.8	0.011 5			
NO_2	1.65	2.1	0.79	0.008	−0.28	10.4	8.9	+0.67	1.2	0.007	0.23	1.05	0.007

[a] Errors ±0.02 (source); ±0.1 (FFR). [b] Error ±0.001 eV. [c] Error ±0.04 eV mol^{-1}. [d] Error ±0.2 eV. [e] J. L. Franklin, J. G. Dillard, H. M. Rosenstock, J. T. Herron, K. Draxl, and F. H. Field, ' Ionization Potentials, Appearance Potentials, and Heats of Formation of Gaseous Positive Ions ' U.S. Dept. of Commerce, National Bureau of Standards, Washington, 1969. [f] ΔH_f (CH_2CO) = −0.635 eV mol^{-1} (footnote *e*). [g] Calculation not possible because of the process ($M - CH_2CO)^{+\cdot} - H\cdot$. [h] σ Value. [i] Calc. from ref. 8*a*.

The deuterium isotope effects (calculated from peak abundances) obtained for losses of CH_2CO and CHDCO from the molecular ions of p-$RC_6H_4\cdot NH\cdot CO\cdot CH_2D$ in both the ion source and the first field-free region, are listed in Table 1. Deuterium isotope effects greater than unity are noted in all cases, indicating that the hydrogen transfer occurs in the rate-determining step. No distinction can be made between a concerted process, and a stepwise process in which the first step involves a slow hydrogen transfer. The isotope effect increases as the substituent becomes more electron-withdrawing (*e.g.* $k_H/k_D = 1.5$ and 2.1 in the first field-free region for MeO and NO_2, respectively), and the maximum value obtained is close to the theoretical value[23] (see above). The values obtained for acetanilide itself are high, and have been checked on a number of occasions. We do not know whether this is simply an anomalous result; or whether it reflects a true Westheimer effect,[24] *i.e.* where the transferring H is equidistant between N and C for the acetanilide case, closer to N for electron-donating substituents (' product-like ' transition state), and *fractionally* closer to C for electron-withdrawing substituents (' reactant-like ' transition state). Whatever the reason for this high value it does not affect the general conclusion that bonding in the transition state for keten elimination is stronger (tighter transition state) for electron-donating substituents than it is for electron-withdrawing substituents.

When a metastable ion fragments unimolecularly, kinetic (translational) energy (T) is released in the centre of mass, and the resulting range of kinetic energies can be used to calculate the value of T.[25,26] It has been proposed[27,28] that ion kinetic energy peak width at half height ($T_{50\%}$) is a reasonable measure of the average value of kinetic energy release, and this parameter has been used for the determination of ion structure[29] and in studies of energy partitioning.[30,31] Rearrangement reactions yield a range of T values, including some values in excess of 1 eV, since rearrangement reactions often proceed through ' tight ' transition

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states from which energy is not readily partitioned into active internal modes.[32]

The kinetic energy T released in the decomposition of a metastable ion can arise from the excess energy $E^{\ddagger}$ and the reverse activation energy E^{r} (see Figure)[33,34] both of which are partitioned among internal modes. A comparison of T or T/E_{excess} (when T and E_{excess} are large $T/E_{\text{excess}} \simeq T^{r}/E^{r}$)[30] for the metastable peaks arising from loss of keten from *para*-substituted acetanilide molecular ions should yield information regarding the relative 'tightness' of each transition state. The value of E_{excess} can be calculated from the expression (i)[30] (*cf.* Figure), and an *approximate* reverse activation

$$E_{\text{excess}} = \text{A.P.}(\text{F}^{+\cdot}) - \text{I.P.}(\text{F}) + \Delta H_{f}(\text{M}) - \Delta H_{f}(\text{F}) - \Delta H_{f}(\text{N}) \quad \text{(i)}$$

energy (for metastable transitions) by the expression[35] $E^{r} \simeq E_{\text{excess}}$ − kinetic shift. Values of $T_{50\%}$, T/E_{excess}, and T/E^{r} are listed in Table 1 for the acetanilides, as are the various parameters required for their determination. All measured T values were corrected for the contribution from the main beam width at the appropriate accelerating potential.

All T values are small (ranging from 4 to 0.7% of the reverse activation energy), with peak shapes approximating to gaussian and containing no fine structure. This indicates (i) that only one mechanism is involved in each case, and (ii) that E^{r} and $E^{\ddagger}$ are readily partitioned among active oscillators. As T values are small there will be contributions to T from both E^{r} and $E^{\ddagger}$, but since we are concerned with the *relative* change in T with the substituent, this problem will not affect the argument. The values of T, T/E_{excess}, and T/E^{r} all increase as the electron-donating ability of the substituent increases. In other words, the 'tightness' of the transition state increases with increasing electron-donating power of the substituent, a conclusion in agreement with results from the kinetic isotope study.

(ii) para-*Substituted phenyl acetates.* The results of a similar study of *para*-substituted phenyl acetates are listed in Table 2. We were unable to calculate T/E^{r} values for this series since kinetic shift values are not available, and also as the procedure used for the combustion measurements resulted in partial hydrolysis of the acetates to the appropriate phenol. T/E^{r} values in this series are not essential, since T shows no systematic variation with changing substituent (see below).

Small deuterium isotope effects (1.2—1.3 in the first field-free region) are observed for loss of keten from *para*-substituted phenyl acetate molecular ions, and the values are insensitive to changes in the electronic nature of the substituent. The operation of an isotope effect again indicates that the hydrogen transfer occurs in the rate-determining step. Kinetic energy release values are small, with peak profiles being approximately gaussian and containing no fine structure. There is no clear correlation between T and the σ^{+} value of the substituent. The only firm statement that can be made is that the substituent affects the transition state for elimination of keten from phenyl acetate less than it does for acetanilide molecular ions.

TABLE 2

Deuterium isotope effects and kinetic energy release values for loss of keten from molecular ions of *para*-substituted phenyl acetates[a]

	k_{H}/k_{D}			
Subst.	Source	1st FFR	σ_{p}^{+}	$T_{50\%}$
MeO	1.17	1.25	−0.78	0.007
Me	1.14	1.2	−0.31	0.004
H	1.16	1.2	0	0.003
Cl	1.18	1.3	0.11	0.004
CHO	1.08	*b*	0.22	0.005
MeCO	1.13	*b*	0.50	0.004
NO_2	1.09	1.2	0.79	0.008

[a] Errors as indicated in Table 1. [b] Not measurable owing to overlapping transitions.

The reason for the difference between the two systems can be rationalised using Westheimer's model.[24] In the acetanilide case, a progressive increase in the electron density on N gives a stronger N···H bond in the transition state, resulting in smaller isotope effects and larger kinetic energy releases (in the limiting case of a highly asymmetric transition state, the isotope effect would become unity[24]). If the NH is replaced by the more electronegative O, the asymmetry will be increased because of the formation of the stronger O···H bond in the transition state. The transition state stretching frequency will then approach the product stretching frequency, thus yielding small isotope effects.[19,20] In addition, the larger bond force constants in the transition state for phenyl acetate (bond energy of O–H is greater than that of N–H by 0.64 eV mol^{-1}) would also contribute to smaller isotope effects. In conclusion, the asymmetry of the transition state may therefore account for the reduced influence of the *para*-substituent on both the isotope effect and the kinetic energy release in the phenyl acetate system.

EXPERIMENTAL

Mass spectra were determined with a modified[36] Hitachi–Perkin-Elmer RMU 7D spectrometer. Compounds were introduced at 150 °C through an all-glass inlet system. Decompositions in the first field-free region were monitored using the metastable focusing technique.[37] Kinetic energy release curves were determined as described previously[38] using an automatic hV scanning unit in conjunction with the RMU 7D spectrometer. Each kinetic energy release value listed in Tables 1 and 2 is an average of six determinations.

I.c.r. spectra were measured at 18 eV by magnetic field

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[32] Ref. 26, pp. 70 and 104—122.

[33] C. E. Klotz, *J. Chem. Phys.*, 1964, **41**, 117.

[34] R. Taubert, *Z. Naturforsch.*, 1964, **19a**, 911.

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[38] J. H. Bowie, S. G. Hart, and T. Blumenthal, *Internat. J. Mass Spectrometry Ion Phys.*, 1976, **22**, 7.

modulation with a Dynaspec ICR 9 spectrometer modified to allow computer control of all drift voltages, and direct reading of the ion-transit time.[15] Typical operating conditions with the square three-section cell were $\omega_c/2\pi = 153.7$ kHz, emission current 0.2 μA, ion current in range 10^{-11}—10^{-12} A, and transit times in the range 1×10^{-4}—1×10^{-3} s. 3,4-Lutidine was introduced through one of the dual inlet ports at room temperature. Acetanilide was admitted to the cell by the direct probe (no heat applied to probe, cell temperature 40 °C). Phenyl acetate was adsorbed on diatomaceous earth, the mixture placed in the direct probe, and the phenyl acetate admitted to the cell with both cell and probe maintained at room temperature (20 °C). Ionisation and appearance potential measurements were determined with the ICR 9 spectrometer using the semilogarithmic plot method [39] with krypton as standard.

Standard heats of formation were obtained using a Mahler–Cook stainless-steel bomb calorimeter of 300 ml capacity. Duplicate results were obtained in all cases.

A general procedure (below) was used to prepare the following known compounds; acetanilides, *p*-HO,[40] *p*-MeO,[41] *p*-Me,[42] H,[43] *p*-Cl,[44] *p*-COMe,[45] *p*-NO_2;[44] phenyl acetates, *p*-MeO,[46] *p*-Me,[47] H,[48] *p*-Cl,[49] *p*-CHO,[50] *p*-COMe,[51] and *p*-NO_2.[52]

A mixture of the appropriate aniline or phenol (1 g), acetyl chloride (0.6 g), and pyridine (0.7 g) was stirred in anhydrous diethyl ether (20 cm^3) at 0 °C for 30 min. Water (10 cm^3) was added and the ethereal layer separated, dried ($MgSO_4$), and evaporated to give the crude product which was purified by thick-layer chromatography on Merck Kieselgel G–HF254 (1 : 1) [ethyl acetate–benzene (2 : 3)]. Products were further purified by either crystallisation or distillation, and their purity was checked by g.l.c. Yields for purified products were in the range 50—80%.

The [α-$^2H_1$]acetanilides (Table 1) and phenyl [$^2H_1$]acetates (Table 2) corresponding to the above unlabelled compounds were prepared by the general method (above) using [α-$^2H_1$]acetyl chloride ($^2H_0$ 1%, $^2H_1$ 99%).[53,54]

The [$^2H_3$]-derivatives (1), (2), and (5)—(8) were prepared [42] in quantitative yield by using the appropriate aniline or phenol with [$^2H_6$]acetic anhydride.

The [2,4,6-$^2H_3$]-derivatives (3) and (4) were prepared by the reactions between acetyl chloride and [2,4,6-$^2H_3$]aniline ($^2H_2$ 4%, $^2H_3$ 96%) [55] and [2,4,6-$^2H_3$]phenol ($^2H_2$ 3%, $^2H_3$ 97%),[56] respectively.

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