as absorbance at 362 nm as a function of time. After three superimposible traces were recorded, a Polaroid photograph of the oscilloscope screen was taken. Pseudo-first-order rate constants were calculated from these photographs by using a least-squares line fitting computer program.

One reservoir syringe of the spectrophotometer was filled with a solution of thiol and pyridine (if any) in acetonitrile. The other syringe was filled with a solution of tetrabutylammonium triiodide and tetrabutylammonium tetrafluoroborate in the same solvent. The two solutions were simultaneously injected into a 2.0-cm path length cell. Maximum mixing time with this cell is 2 ms. The syringes, mixing chamber, and cell were thermostated at 25.0 ± 0.1 °C with a Brinkmann Instrument Lauda Type K-2/R thermostat.

Linear regression of the effect of changes in [I⁻] and k_{obsd} (Table I, lines 5-8) yields the following correlations: A, slope = -0.9, coefficient of correlation = 0.998; B, slope = -0.9, coefficient of correlation = 0.995; C, slope = -0.9, coefficient of correlation = 0.98; D, slope = -1.0, coefficient of correlation = 0.990. These reactions are thus inverse first order in iodide. Linear regression of the thiol dependence of k_{obsd} (Table I, lines 1-4; Table II, lines 1-4) yield the following: A, slope = 1.0, coefficient of correlation = 0.98; B, slope = 2.0, coefficient of correlation = 0.997; D, slope = 1.0, coefficient of correlation = 0.99993. The reactions of A and D are first order in thiol. Compound B is second order in B. The thiol dependence of C was not studied.

Infrared Measurements. Measurements were made with a Perkin-Elmer Model 180 spectrophotometer.

Electrochemical Oxidations. Electrochemical oxidations were carried out by cyclic voltammetry. A Princeton Applied Research Model 173 potentiostat, Model 175 universal program-mer, Model 178 electrometer, and Model RE 0074 X-Y recorder were used. Sample preparation was carried out under a nitrogen atmosphere in a Kewaunee Scientific Equipment drybox. Kodak electrochemical grade tetrabutylammonium perchlorate was the supporting electrolyte in acetonitrile (Burdick and Jackson Laboratories, Inc.).

A three-compartment electrochemical cell consisted of two outer compartments containing a silver reference electrode (Ag|0.1 M AgNO₃ in CH₃CN) and a platinum counterelectrode. The platinum working electrode was cleaned in 10 M HNO₃, heated in a flame, and oven-dried before each experiment.

Reaction Products. Products were determined by titration of 5 mmol of thiol in 50 mL of CH₃CN with 2.6 mmol of I₂ in 50 mL of CH₃CN. The titration continued until the I₂ had been consumed by the thiol. The end point was determined by the slight retention of the yellow color from excess iodine.

The resulting solutions were extracted three times into CHCl₃ following neutralization of the pyridinium salts with an aqueous solution of 1 M NaOH. The solvent was removed with a rotary evaporator, yielding the products. Mass spectra and data obtained from a Varian 90 MHz NMR spectrometer are consistent with disulfides being the reaction products in each case.

Registry No. A, 2044-28-2; B, 2127-05-1; C, 4410-99-5; D, 1322-36-7; I₂, 7553-56-2; pyridine, 110-86-1.

Gas-Phase Dieckmann Ester Condensation Characterized by Mass Spectrometry/Mass Spectrometry

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Negative-ion mass spectra obtained by chemical ionization show signals which correspond in mass-to-charge ratio to the products of the title reaction. Collision-induced dissociation of these ions and comparison of the resulting spectra with those of authentic compounds confirm this assignment. Charge-inversion spectra and isotopic labeling both provide further evidence for analogous mechanisms for the Dieckmann reaction in the gas phase and in solution. A closely related gas-phase reaction, not observed in solution, is cyclization of diesters bearing α-alkyl substituents by elimination of a molecule of dialkyl ether. This apparently represents a new type of fragmentation reaction in closed-shell negatively charged ions. The newer mass spectral methods used here not only provide a rapid means of uncovering such variants in the course of reaction but also allow the direct characterization of species which occur only as transient reaction intermediates in the condensed phase.

Because ionic species have long been known to be the reactive intermediates responsible for the conversion of nonionic reactants to nonionic products in many condensed-phase organic reactions, gas-phase analogues of well-known organic reactions have frequently been a target for investigation by mass spectrometry. Typical of early electron-impact studies of this nature were those on anchimeric assistance in processes analogous to solvolytic reactions,[1] intramolecular cyclizations which amount to nucleophilic aromatic substitution,[2] Wagner-Meerwein rearrangements,[3] and rearrangement reactions which correspond to thermolytic processes.[4] These studies were limited in two particular ways: first, the great body of reactions which are not unimolecular was excluded from examination, and second, evidence for the structures of the ions under study was indirect and relied on a considerable knowledge of fragmentation behavior under electron-impact conditions. These two limitations have subsequently been lifted: first, ion/molecule reactions can be investigated by various experimental means, including chemical ionization (CI),[5] flowing afterglow,[6] and ion cyclotron

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resonance (ICR) spectroscopy,[7] and, second, collision-induced dissociation (CID) or collisional activation (CA) of mass-selected ions serves as one of several sensitive means of characterizing ion structures.[8]

This study employs the potent combination[9] of chemical ionization with collisional activation to investigate the base-catalyzed Dieckmann condensation.[10] Enolate anion formation in the gas phase is effected by using OH$^-$ reagent ions.[11] The course of the Dieckmann condensation is checked against that in solution, particularly insofar as the appearance of corresponding products is concerned. The key to product identification lies in the tandem technique of mass spectrometry/mass spectrometry (MS/MS).[12] In this method, a particular ion, generated in the reaction vessel (here a chemical ionization source), is extracted and separated from its congeners before being characterized via the mass spectrum of its reaction products (here, products of collision-induced dissociation are used).

As in earlier and somewhat similar studies[13] on the acid-catalyzed Fischer indole synthesis, a specific objective of this work is to assess the capabilities of the available methods for studying organic reaction mechanisms in the gas phase. Experiments follow classical approaches to mechanism determination in the particulars of product structural characterization, isotope labeling, and diversion of the predicted course of the reaction by appropriate modification of the reagents. These features are also evident from related studies such as those of the gas-phase Beckmann rearrangement[14] and the Michael addition.[15] Alternative mass spectrometric approaches, particularly the use of ion cyclotron resonance spectroscopy and drift-tube methods, also continue to provide increasingly detailed insights into organic reaction mechanisms. Noteworthy illustrations are provided by a meticulous study of the Claisen condensation[16] and by the carbanion chemistry reported recently by the groups of DePuy[17] and McDonald.[18] The present approach uses MS/MS to isolate and characterize the ion of interest from a complex mixture of reactants, products, and intermediates.

Scheme I. Proposed Similarity between the Solution-
and Gas-Phase Mechanisms of the Dieckmann
Condensation for Dimethyl Adipate
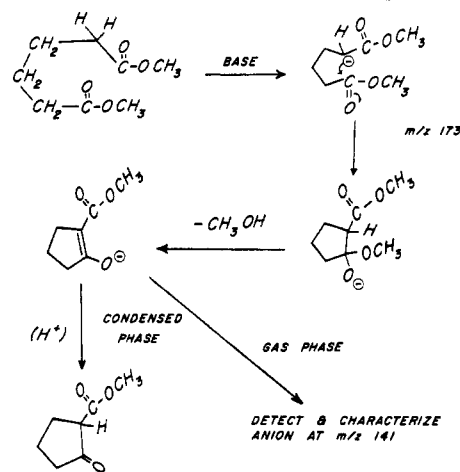
Experimental Section

Experiments were performed on a mass-analyzed ion kinetic energy spectrometer (MIKES)[19] equipped with a chemical ionization source.[20] The MS/MS spectra were obtained by setting the magnetic sector to pass to the second field-free region of the mass spectrometer only ions of the mass-to-charge ratio of interest. These ions were collisionally excited and the products of subsequent dissociation monitored via an electric sector scan. All MS/MS spectra were acquired with the instrument under computer control.[21]

Typical operating conditions were as follows: source pressure, approximately 0.3 torr as measured by an MKS Baratron capacitance manometer; electron ionizing energy, 500 eV; accelerating potential, 7 kV. The reagent gas mixture use to generate the negative ions was isobutane/nitrous oxide in an approximate ratio of 5:1, which produces a mixture of reagent ions including OH$^-$, CN$^-$, H$_2$O·OH$^-$, and N$_2$O·OH$^-$.[22] All MS/MS spectra were obtained with air as the collision gas at an indicated pressure of (2-3) $\times$ 10^{-5} torr as measured by a Bayard-Alpert ionization gage (2-3 mtorr estimated collision cell pressure, corresponding to single collision conditions).

Volatile samples were leaked into the source as vapors from liquid reservoirs. These samples were routinely degassed by several freeze–pump–thaw cycles. Less volatile samples were introduced into the source via a direct-insertion probe. Those samples which were available commercially were used without additional purification. The ethyl methyl adipate, dimethyl-d_3 adipate,[23] 2-methyl-2-carbethoxycyclohexanone, 6-methyl-2-carbethoxycyclohexanone, and diethyl 2-methylpimelate[24] were all prepared according to literature procedures. All of the synthesized materials were purified by vacuum distillation and yielded boiling points in good accord with reported values. The mass spectra of these compounds showed no evidence of unreacted starting material.

Results and Discussion

The Dieckmann condensation is initiated in solution by the abstraction of an acidic proton from a molecule of a dicarboxylic acid ester by a suitable base (Scheme I). Upon formation of the stable enolate anion, the intramolecular Claisen condensation proceeds very readily. A similar situation is likely to occur in the mass spectrometer

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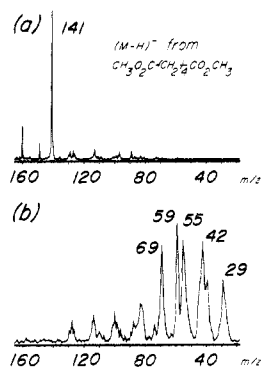(24) Vul'fson, N. S.; Zaretskii, V. I. *J. Gen. Chem. USSR (Engl. Transl.)* 1958, *28*, 365.

Figure 1. (a) Negative MS/MS (fragment ion) spectrum of m/z 173⁻, deprotonated dimethyl adipate (reaction intermediate). (b) Positive fragment ion (charge inversion) spectrum of the mass-selected m/z 173⁻ ions.

under negative chemical ionization (NCI) conditions. It is well-known that esters yield reasonably abundant [M − H]⁻ anions in NCI.[22] It is therefore conceivable that under such conditions the enolate anion of the dicarboxylic ester which is initially generated will behave similarly to its condensed-phase analogue.

The negative chemical ionization mass spectrum of dimethyl adipate shows an ion of moderate abundance at m/z 173⁻ ([M − H]⁻) along with the signal of greatest intensity in the spectrum at m/z 141⁻ (corresponding to elimination of neutral methanol from the [M − H]⁻ ion). The appearance of this very intense signal at the appropriate mass-to-charge ratio suggests that the elimination of methanol in the ion source results in a product ion of considerable stability. Such stability can be accounted for by resonance stabilization in the proposed 2-carbomethoxycyclopentanone structure of the enolate fragment ion. If the proposed structure can be confirmed, then this is evidence that the gas-phase intramolecular Claisen condensation proceeds in a manner which is analogous to that which occurs in the condensed phase.

To more closely examine the chemical behavior of the [M − H]⁻ ion, free of any interferences which may be present in the source of the mass spectrometer, the deprotonated molecule at m/z 173⁻ was mass selected and transmitted to the second reaction region of the MS/MS instrument. The fragment ions which resulted from the collision-induced dissociations of the parent ions were then monitored by scanning the electric sector. The spectrum obtained is shown in Figure 1a. Loss of 32 daltons (nominally CH₃OH) from the deprotonated molecule is the major decomposition process and substantiates the origin of the large signal at the same mass (m/z 141⁻) in the NCI mass spectrum. However, Figure 1a is noticeably devoid of structurally diagnostic fragmentations. This MS/MS data is therefore not sufficient to establish the structure of the [M − H]⁻ ion. Limited fragmentation in negative ion MS/MS spectra has been noted previously,[25,26] and for this reason it has become standard practice to record both the negatively and positively charged fragments derived from a selected negative parent ion. The latter, a charge-inversion spectrum, is shown in Figure 1b for m/z 173⁻, the conjugate base of dimethyl adipate. This spectrum shows fragment ions, particularly at the low masses, which are characteristic of the proposed cyclopentanone structure (e.g., the fragment ions at m/z 55⁺ and m/z 29⁺
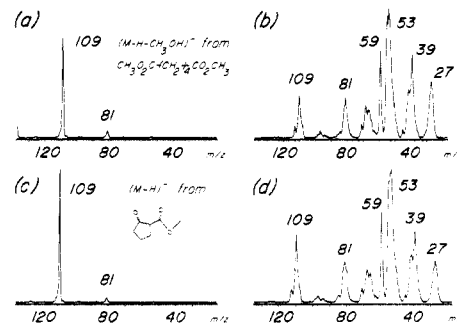

Figure 2. (a) Negative MS/MS spectrum of m/z 141⁻, the gas-phase reaction product for the condensation of dimethyl adipate. (b) Charge-inversion spectrum of the same m/z 141⁻ ions. (c) Negative fragment ion spectrum of m/z 141⁻, the conjugate base of 2-carbomethoxycyclopentanone (conventionally synthesized Dieckmann condensation product). (d) corresponding charge-inversion spectrum of m/z 141⁻ (see Figure 2c).
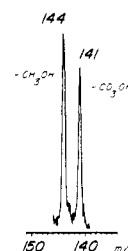

Figure 3. Portion of the negative MS/MS spectrum of m/z 176⁻ (deprotonated dimethyl adipate-d_3) illustrating the competitive elimination of labeled (CD₃OH) vs. unlabeled (CH₃OH) methanol. The appearance of these two signals confirms the identity of the elimination product as that of an alcohol molecule originating from the ester functinality of the original substrate.

constitute the two most intense signals in the electron-impact mass spectrum of cyclopentanone itself). Since both MS/MS spectra in Figure 1 result from the deprotonated molecule, in solution a nonisolable entity, these two spectra demonstrate one of the unique capabilities of MS/MS and lend valuable supporting evidence to the structural conclusions to be drawn later.

At this point, analysis of the reaction product was undertaken. While many of the experimental methods for studying gas-phase ion/molecule reaction products yield only mass-to-charge ratio information, MS/MS allows a direct comparison of the fragment ion spectra obtained from the gas-phase reaction product with those generated from various authentic compounds. In Figure 2 the MS/MS spectra of the [M − H − CH₃OH]⁻ elimination product of dimethyl adipate and the conjugate base of 2-carbomethoxycyclopentanone are compared. The excellent agreement between the two charge-inversion spectra is a good indication of the validity of the proposed mechanism seen in Scheme I.[27] Although there are relatively few fragments present, the agreement between the respective negative ion spectra is important and adds further support to this conclusion.
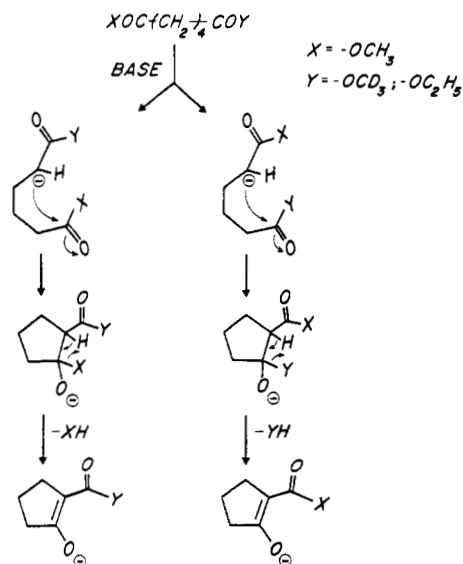
Confirmation that the dominant negative fragment ion generated from the [M − H]⁻ ion of dimethyl adipate indeed arises by methanol elimination was obtained by introducing dimethyl-d_3 adipate into the source of the mass

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(27) What the data show is the identity of the ion structure(s) generated from the Dieckmann product and from the authentic compound. A direct demonstration of structure is not possible, and one relies on the assumption that the conjugate base of 2-carbomethoxycyclopentanone preserves the structure of the neutral molecule. This argument also implies that the cyclization of the [M − H]⁻ ion occurs through carbon and not through oxygen which would yield a product of different structure.

Scheme II. Verification of the Proposed Reaction
Pathway through Chemical Modification of the Reaction
Substrate (Isotopic Incorporation and Functional
Group Variation)

$XOC(CH_2)_4COY$

$X = -OCH_3$
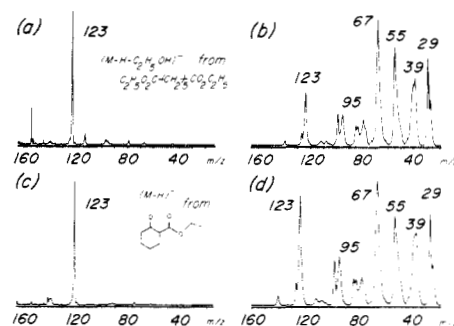$Y = -OCD_3 ; -OC_2H_5$

Figure 4. (a) Product analysis of m/z 169⁻, the gas-phase reaction product for the condensation of diethyl pimelate (negative MS/MS spectrum). (b) Charge-inversion spectrum of m/z 169⁻, the ethanol elimination product of protonated diethyl pimelate. (c) Negative MS/MS spectrum of m/z 169⁻ from the authentic 2-carbethoxycyclohexanone. (d) Corresponding charge-inversion spectrum of m/z 169⁻ (see Figure 4c).
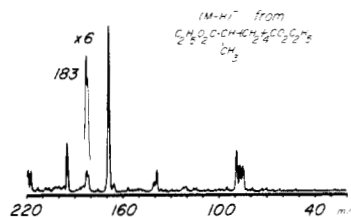

Figure 5. Negative MS/MS spectrum of m/z 229⁻, the conjugate base of diethyl 2-methylpimelate (reaction intermediate), illustrating the major gas-phase decomposition processes.

spectrometer. This symmetrical molecule is expected to undergo the cyclization–elimination process with equal probability from either terminus of the molecule. In the absence of a kinetic isotope effect the elimination of the labeled vs. unlabeled methanol should occur equally as judged by the fragments observed in both the mass spectrum and in the MS/MS spectrum of the conjugate base m/z 176⁻ ([M – H]⁻ of dimethyl-d_3 adipate). The experimental results, seen in Figure 3, confirm this expectation. The small preference shown for CH₃OH elimination can be accounted for in part by instrumental discrimination in favor of the more massive fragment and in part by the influence of a secondary isotope effect. The former effect should be on the order of 2–5%[28] while the latter is more difficult to estimate although reasonably large values have been reported for some metastable and collision-induced dissociation reactions.[29]

Following established methods of investigating reaction mechanisms, a structural variation in the reactants was introduced so as to alter the course of the reaction in a controlled fashion, as depicted in Scheme II. The substrate was changed from dimethyl adipate to the mixed ester, ethyl methyl adipate. The results of this change are predictable in light of the loss of symmetry within the molecule, and a distribution of products associated with methanol vs. ethanol elimination is expected. The measured ratio of m/z 141⁻ to 155⁻ in the negative MS/MS spectrum of m/z 187⁻ ([M – H]⁻ of ethyl methyl adipate) was very close to that expected.[28] Apparently any steric or electronic effects associated with reaction of the ethyl as opposed to the methyl ester are small.

To further test the hypothesis of the occurrence of the Dieckmann condensation in the gas phase, we examined yet another substrate. Much like the adipic acid ester, diethyl pimelate undergoes a cyclization–elimination reaction in solution to yield 2-carbethoxycyclohexanone. As in the previous example, the NCI mass spectrum of diethyl pimelate displays a signal due to the conjugate base [M – H]⁻ at m/z 215⁻ and a very intense signal at m/z 169⁻

(corresponding to [M – H – C₂H₅OH]⁻). Examination of the negative ion MS/MS spectrum of m/z 215⁻ (the deprotonated substrate) shows the expected peak at m/z 169⁻ ([M – H – C₂H₅OH])[30] as well as that at m/z 123⁻ ([M – H – 2C₂H₅OH]⁻) as the two main loss processes. Verification of the structure of the product ion was again accomplished by direct comparison of fragment ion spectra obtained from (1) the [M – H – C₂H₅OH]⁻ cyclization–elimination product as generated in the ion source from neutral diethyl pimelate and (2) the m/z 169⁻ ion formed directly by proton abstraction from neutral 2-carbethoxycyclohexanone. Again, there is complete agreement in both the negative and positive (charge inversion) fragment ion spectra (Figure 4).

As first noted by Vul'fson and Zaretskii in their reinvestigation of the original work of Dieckmann,[24] when the dicarboxylic ester is substituted at a position adjacent to one of the carbonyl functionalities, the possibility exists that more than one product may be formed upon cyclization, and in all cases the thermodynamically more stable enolate anion dominates and therefore dictates the structure of the final product. This particular variation of the reaction can be carried out by simply changing from diethyl pimelate to the substituted diethyl 2-methylpimelate. Of the two possible products, only the 6-methyl-2-carbethoxycyclohexanone was reported to be formed. Even when synthesized by alternative routes, the other product, 2-methyl-2-carbethoxycyclohexanone, isomerizes under the reaction conditions.[31] This observation led to the conclusion that the expected statistical ring closure from either terminus of the symmetrical diethyl pimelate is significantly perturbed by the presence

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(29) McLafferty, F. W.; McAdoo, D. J.; Smith, J. S.; Kornfeld, R. J. Am. Chem. Soc. 1971, 93, 3720.

(30) The fact that the pimelate conjugate base loses two molecules of alcohol while the adipate loses juse one is not significant. Loss of the second alcohol from the adipate is observed (Figure 2) under appropriate conditions of energization.

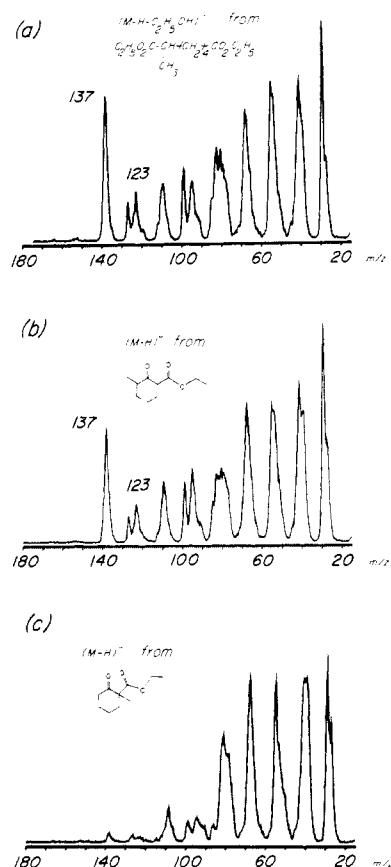(31) Vul'fson, N. S.; Zaretskii, V. I. J. Gen. Chem. USSR (Engl. Transl.) 1959, 29, 2704.

Figure 6. (a) Charge-inversion spectrum of m/z 183⁻, the ethanol elimination product of deprotonated diethyl 2-methylpimelate (gas-phase reaction product). (b) Product analysis of the conjugate base of authentic 6-methyl-2-carbethoxycyclohexanone (charge-inversion spectrum of m/z 183⁻). (c) Positive fragment ion (charge inversion) spectrum of m/z 183⁻ from deprotonated 2-methyl-2-carbethoxycyclohexanone.

of the methyl substituent. That is, the methyl substituent destabilizes the tertiary carbanion by steric hindrance to solvation.

This same experimental variation was explored in the gas phase with the introduction of diethyl 2-methylpimelate into the chemical ionization source of the MIKE spectrometer. As expected, there did appear in the mass spectrum an ion of significant intensity at m/z 183⁻ ([M − H − C_2H_5OH]⁻) along with an ion of moderate intensity at m/z 229⁻ ([M − H]⁻). In agreement with previous results, the MS/MS spectrum of the deprotonated molecule (Figure 5) showed as one of the favored decomposition processes loss of 46 daltons (nominally C_2H_5OH) to yield an ion at m/z 183⁻. Analysis of this product ion was accomplished by recording both negative and positive fragment ion spectra and comparing them to the corresponding spectra obtained for authentic compounds representing both of the possible isomers in question. As seen in Figure 6, a comparison of the charge-inversion spectra of the reaction product with the two substituted cyclic ketones leads to the conclusion that the ions generated from (1) diethyl 2-methylpimelate and (2) 6-methyl-2-carbethoxy-cyclohexanone are structurally indistinguishable. On the other hand, the spectrum of the Dieckmann product differs significantly from that of the conjugate base of the isomeric cyclization product 2-methyl-2-carbethoxycyclohexanone. Important features of these spectra which support this conclusion include the prominence of the peaks at m/z 137⁺, 127⁺, and 123⁺ for both the reaction product ([M − H − C_2H_5OH]⁻ from diethyl 2-methylpimelate) and the 6-methyl-2-carbethoxycyclohexanone as compared to the

Table I

m/z	% rel abundance	
	[M + H − CH_3OH]⁺ from dimethyl adipate	[M + H]⁺ from 2-carbomethoxy-cyclopentanone
115	34	
111	100	100
97	4	>1
83	10	5
73	9	
59	7	>1
55	18	7
41	5	2

m/z	% rel abundance	
	[M + H − C_2H_5OH]⁺ from diethyl pimelate	[M + H]⁺ from 2-carbethoxy-cyclohexanone
153	13	1
143	13	45
135	8	
125	100	100
115	5	3
97	13	9
69	10	9
55	7	9

effective absence of these signals in the spectrum of the 2-methyl-2carbethoxycyclohexanone. On the face of it, the gas-phase reaction parallels that in solution even to the extent that the thermodynamically favored enolate (5, Scheme III) is formed preferentially. However, the appearance of m/z 169⁻ as the base peak in the fragment ion spectrum of the deprotonated substrate (Figure 5) establishes that the reaction does not in fact parallel that in solution; rather, one observes cyclization products derived from both of the alternative enolate ions 2 and 3.

Further examination of Figure 5 suggests an explanation. Although the ion at m/z 183⁻ has been shown to be structurally indistinguishable from the expected solution-phase reaction product, the most intense fragment ion in the negative MS/MS spectrum of the reaction intermediate (the [M − H]⁻ ion at m/z 229⁻) occurs at m/z 169⁻ and corresponds to what must be the most favorable gas-phase decomposition reaction of the deprotonated diethyl 2-methylpimelate, loss of methyl ethyl ether. This seems to be the direct result of abstraction of a methine hydrogen to form a tertiary carbanion (3 in Scheme III). On this basis the two structurally different forms of [M − H]⁻ react to give different products, viz., 2 → 5 and 3 → 4. The elimination of a neutral ether molecule represents an unexpected rearrangement–fragmentation of an enolate. Nevertheless, proof of the occurrence of this ether elimination variant of the Dieckmann condensation was found by comparison of the spectrum of the ether elimination product with that of the authentic enolate ion given previously in Figure 4d. An excellent match was recorded. Enhanced stability of the tertiary enolate 3 in the gas phase vis-à-vis solution follows from the well-known role of alkyl substituents in stabilizing charge in the gas phase.[32]

In the course of this study it was observed that the *protonated* diesters also undergo alcohol elimination, a well-known reaction of esters under positive chemical ionization conditions.[33] This process might occur by cyclization–elimination in the diesters and so represent an
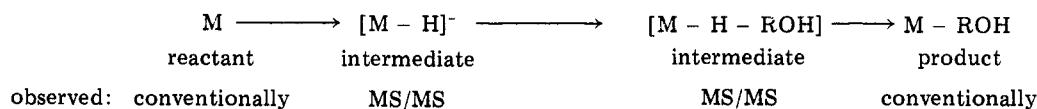
(32) Bartmess, J. E.; McIver, R. T., Jr. "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, Chapter 11.

(33) (a) Herman, J. A.; Harrison, A. G. *Can. J. Chem.* **1981**, *59*, 2133. (b) Benoit, F. M. Harrison, A. G. *Org. Mass Spectrom.* **1978**, *13*, 128.

Scheme III.[a] Comparison and Contrast of Classical and Gas-Phase Cyclization of Diethyl 2-Methylpimelate (1)

$$H_5C_2O_2CCH(CH_3)-(CH_2)_4-CO_2C_2H_5$$
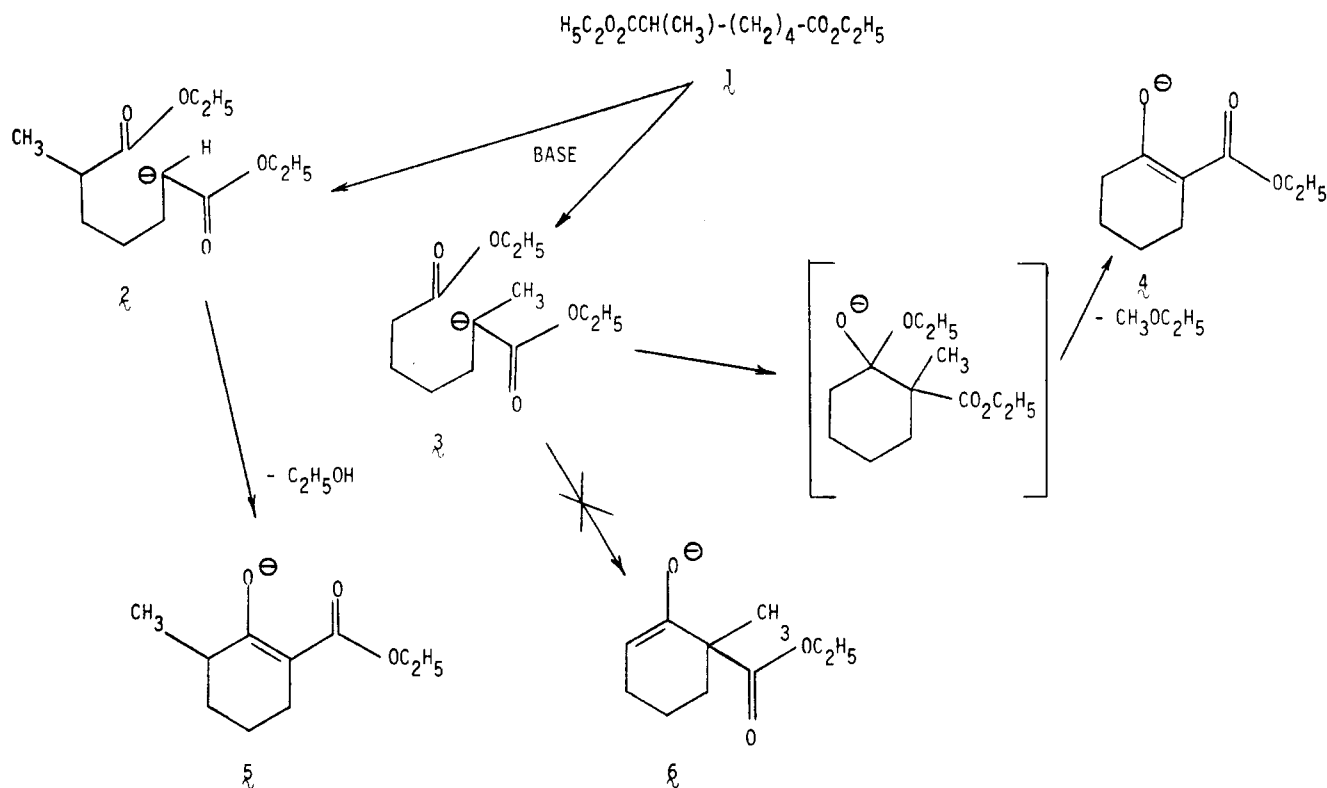
[a] In solution **5** is formed exclusively, due to preferential formation of **2** or rapid interconversion of **6** to **5**. Similarly, gas-phase results also indicate the pathway **1 → 2 → 5**, however, only as a minor process. Because of differences in anion stability in the gas phase and in solution, the dominant gas-phase process is indicated to be **1 → 3 → 4**.

Scheme IV

$$M \longrightarrow [M - H]^- \longrightarrow [M - H - ROH] \longrightarrow M - ROH$$

	reactant	intermediate	intermediate	product
observed:	conventionally	MS/MS	MS/MS	conventionally

acid–catalyzed analogue of the Dieckmann reaction. Comparison of MS/MS spectra of the alcohol elimination products and the corresponding cyclic keto esters (Table I) established that this was *not* the case. This example further strengthens confidence in the structural methods used in this paper.

Conclusion

There exists a gas-phase version of the Dieckmann reaction which is mechanistically analogous to the solution reaction. The evidence for this comes from carbanion selection and structural characterization; similarities can extend to product distributions even when various products of different enthalpy are possible. The complementary nature of the methods used to investigate the condensed- and gas-phase reactions is illustrated for the condensation of a diester, M, to yield the cyclic keto ester, M – ROH (Scheme IV). The role of MS/MS in characterizing reaction intermediates is evident in this comparison.

In the solution-phase version of the Dieckmann condensation the deprotonated molecule is the reaction intermediate and is the precursor of all product molecules formed in the reaction. However, the situation in the gas phase is distinctly different. The ions formed via proton abstraction may or may not be intermediates of the reaction, depending on their internal energy, with this quantity being determined by the energy transferred upon ionization and the extent of collisional stabilization. Consequences of a population of ions of various energies which are not in equilibrium with each other include the existence of several reaction channels and their associated products for the conjugate bases (gas-phase enolate ions) of these molecules. The postulated existence of multiple reaction channels accounts for the appearance of unexpected products in the negative fragment ion spectrum of the [M – H]⁻ ion of diethyl 2-methylpimelate.

This study, which represents the first detailed application of MS/MS to reactions occurring through negatively charged intermediates, employs concepts which should be capable of generalization and of wider application. Charge inversion, a most powerful analytical[12] and ion structural[26] procedure, is used here in a mechanistic investigation.