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Does the Dieckmann Condensation Occur in the Gas Phase?

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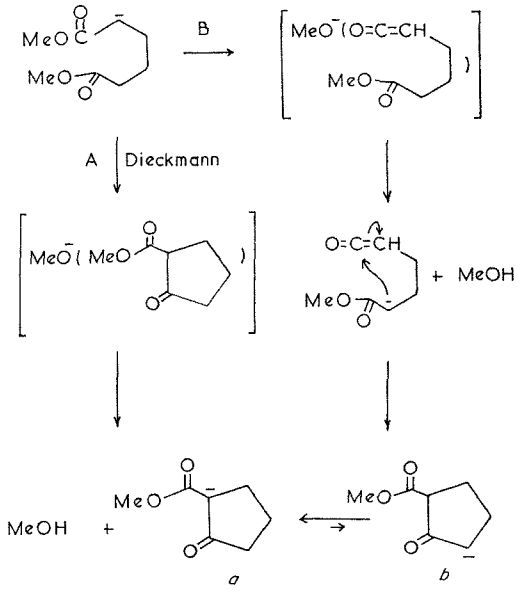
Burinsky and Cooks[1] have reported that deprotonated dimethyl adipate eliminates methanol via a gas-phase Dieckmann condensation. This is in contrast to the behaviour of simple methyl ester enolates which lose MeOH by a different mechanism, e.g. $MeOCO\bar{C}HCH_2R \rightarrow [Me\bar{O}(OCCHCH_2R)] \rightarrow O{=}C{=}CH\bar{C}HR + MeOH$. Evidence is presented which supports the Dieckmann mechanism for adipates. For example, $MeOCO\bar{C}(Me)CH_2CH_2CD(Me)CO_2Me$ should eliminate MeOD in a Dieckmann condensation, but MeOH by the alternative mechanism outlined above. Experimentally, MeOD is lost exclusively. Similarly, $MeOCO\bar{C}DCH_2CH_2C(Me)_2CO_2Me$ also loses MeOD, consistent with a Dieckmann process

INTRODUCTION

In 1982, Burinsky and Cooks[1] reported the gas-phase Dieckmann condensation of deprotonated adipates; this was followed by a later report by McDonald and Chowdhury on a cognate system.[2]

The gas-phase Dieckmann condensation could, in principle, be either concerted or stepwise; we represent it as the stepwise process A shown in Scheme 1. However, enolate ions derived from simple esters do not fragment in this way upon collisional activation; rather, they fragment through an ion complex of the type shown in the first step of route B (Scheme 1).[3–5] Subsequent deprotonation followed by cyclization could yield *b*, which should be convertible to Dieckmann product *a* under conditions of collisional activation (cf. Ref. 5).

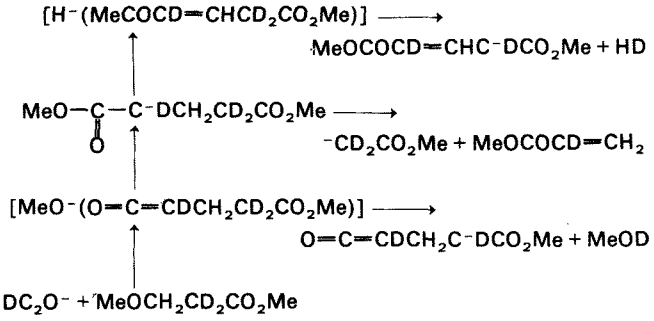


Scheme 1

In this paper we investigate the fragmentations of a number of deuterium- and methyl-substituted adipates in order to differentiate between the two mechanistic pathways shown in Scheme 1.

RESULTS AND DISCUSSION

The Dieckmann condensation occurs *in solution* whenever the enolate anion of a bis ester can form a cyclic five- or six-membered β-keto ester.[6] Dimethyl glutarate does not undergo the Dieckmann condensation in solution because the formation of a four-membered β-keto ester is thermodynamically unfavourable. It is of interest, therefore, to examine the collisional activation (CA) mass spectrum of deprotonated dimethyl glutarate. The CA mass spectrum of the $[M - D^+]^-$ ion of D_4-dimethyl glutarate is shown in Fig. 1. The four competitive fragmentations rationalized in Scheme 2 are characteristic of ester enolate ions. It is of interest that the loss of MeOD† is a minor process; this is in marked



Scheme 2

† The possibility that loss of MeOD occurs by a 'Dieckmann' condensation seems unlikely but cannot be completely excluded on the available evidence. The more likely mechanism is analogous to that shown in Scheme 2 for succinate enolates.

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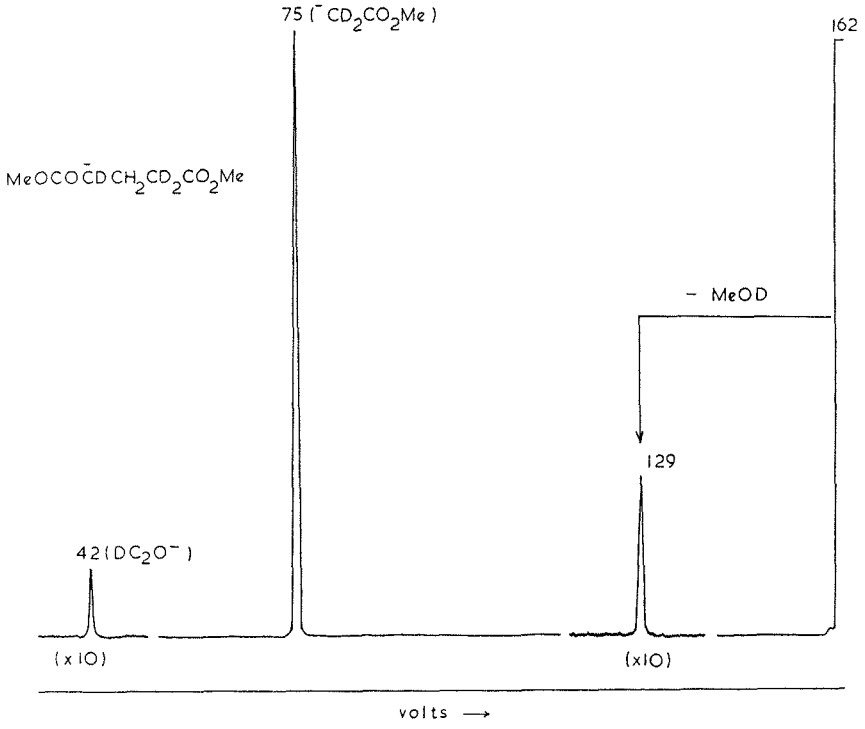
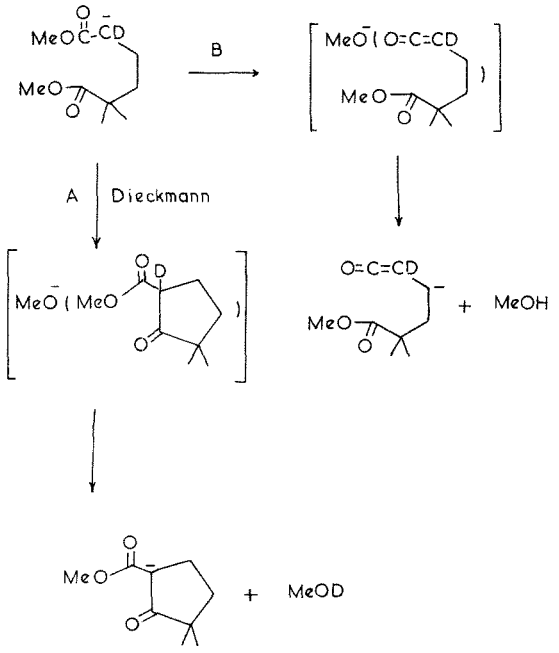


Figure 1. CA mass spectrum of the $[M - D^+]^-$ ion of dimethyl d_4-glutarate. For experimental conditions see Experimental section.

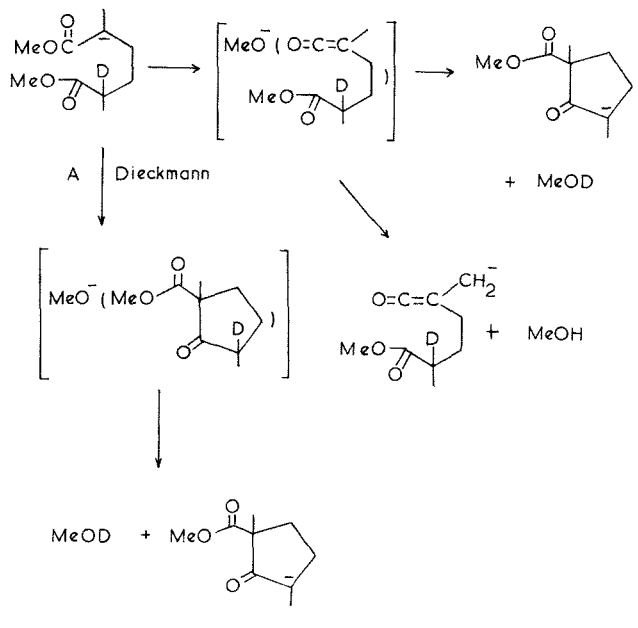
contrast to the behaviour of methyl malonate and succinate enolates, where loss of methanol produces the base peak of the CA mass spectrum.[5]

Reaction of dimethyl glutarate with HO^- yields only an $[M - H^+]^-$ ion. In contrast, the analogous reaction with dimethyl adipate gives a small peak corresponding to $[M - H^+]^-$ and a pronounced $[M - H^+]^-$ – MeOH peak. The latter ion has a CA mass spectrum identical (within experimental error) to that of authentic *a* (Scheme 1), formed by deprotonation of 1-carbomethoxycyclopentanone. The same result was obtained earlier by Cooks,[1] but the spectra obtained in this study are somewhat different from those observed earlier (see Table 1 and cf. Ref. 1).

In order to investigate the mechanism of the 'Dieckmann' condensation of adipates, we have measured the CA mass spectra of the two deuterium-labelled dimethyl dimethyladipate anions, shown in Schemes 3 and 4. If the deuterated anion shown in Scheme 3 decomposes via Dieckmann route A, MeOD should be eliminated specifically. If, on the other hand, route B is preferred, Dieckmann condensation cannot occur because of the blocked *gem*-dimethyl position and

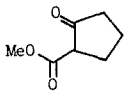
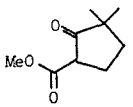
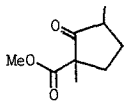


Scheme 3



Scheme 4

Table 1. CA mass spectra of $[M - H^+]^-$ – MeOH ions from adipates and of the corresponding deprotonated Dieckmann products

		Loss							Formation			
Ion	Precursor	H·	H_2	Me·	H_2O	MeOH	MeOH + H_2	HCO_2Me	$[CH_2{=}C(Me)CO_2]^-$	$[CH_2{=}CHCO_2]^-$	$[HC_2O]^-$	MeO^-
$[M - H^+]^-$ – MeOH	$MeCO_2(CH_2)_4CO_2Me$	20	10	0.4	0.1	100		4		0.5	0.15	0.2
$[M - H^+]^-$		20	11	0.5	0.2	100		4		0.5	0.1	0.2
$[M - H^+]^-$ – MeOH	$MeCO_2C(Me)_2(CH_2)_3CO_2Me$	25		21		100	34	49				6
$[M - H^+]^-$		28		20		100	37	53				5
$[M - H^+]^-$ – MeOH	$MeCO_2CH(Me)(CH_2)_2CH(Me)CO_2Me$	16		5		93		100	16			
$[M - H^+]^-$		16		6		96		100	16			

MeOH will be eliminated. No $[M - D^+]^-$ ion is observed for this system; the only peak observed is an $[M - D^+]^-$ – MeOD species. In addition, reaction of $MeOCO(CH_2)_3CMe_2CO_2Me$ with HO^- yields an $[M - H^+]^-$ – MeOH ion whose CA spectrum is very similar to that of deprotonated 1-carbomethoxy-3,3-dimethylcyclopentanone (see Table 1). Thus in this case the experimental evidence points to the exclusive operation of the Dieckmann condensation.

The isomeric deuterated dimethyl dimethyladipate enolate ion shown in Scheme 4, could, in principle, react in one of four ways. It could either follow the Dieckmann condensation (route A), but in this case the intermediate ion complex must eliminate MeOD. If, in contrast route B is followed, then (i) cyclization may effect elimination of MeOD, or (ii) elimination of a proton α to the ketene unit (two possibilities, one shown in Scheme 4) would result in specific loss of MeOH. No $[M - D^+]^-$ ion is observed for this system; the only peak observed is $[M - D^+]^-$ – MeOD. Finally, reaction of $MeOCOC(Me)CH_2CH_2C(Me)CO_2Me$ with HO^- yields an $[M - H^+]^-$ – MeOH ion whose CA spectrum is very similar to that of deprotonated 1-carbomethoxy-1,3-dimethylcyclopentanone (see Table 1). Thus again, the experimental evidence points to the operation of a gas-phase Dieckmann condensation in this case.

In conclusion, the experimental evidence presented in this paper supports the earlier report by Burinsky and Cooks[1] that elimination of methanol from the dimethyl adipate enolate ion occurs by a facile Dieckmann condensation.

EXPERIMENTAL

CA mass spectra were recorded on a VG ZAB 2HF mass spectrometer operating in the negative chemical ionization (CI) mode.[7] All slits were fully open to obtain maximum sensitivity and to minimize energy-resolution effects. The CI slit was used in the ion source: ionizing energy 70 eV (tungsten filament); ion source temperature 180 °C; accelerating voltage 7 kV. Reactant HO^- ions were used for deprotonating unlabelled adipates and 1-carbomethoxycyclopentanones; DO^- was used for all deuterium-labelled substrates. Reactant HO^- (or DO^-) ions were formed from H_2O (or D_2O) using 70 eV electrons.[8] The indicated source pressure of H_2O (or D_2O) was 5×10^{-4} Torr. The adipate or carboethoxycyclopentanone pressure (the substrate was introduced through the septum inlet at 180 °C) was 5×10^{-7} Torr. The *estimated* total pressure in the source is 10^{-1} Torr. The pressure of He in the second collision cell was 2×10^{-7} Torr measured by an ion gauge situated between the electric sector and the second collision cell. This produced a decrease in the main beam signal of ~10% and thus corresponds essentially to single-collision conditions.

Dimethyl glutarate was a commercial product. Dimethyl adipate,[9] dimethyl 1,4-dimethyladipate[10] and dimethyl 1,1-dimethyladipate[11] were prepared by standard methods. The labelled compounds

$MeOCOCD_2CH_2CD_2CO_2Me$,
$MeOCOCD_2CH_2CH_2CD_2CO_2Me$,
$MeOCOCD(Me)CH_2CH_2CD(Me)CO_2Me$
$MeOCOCD_2CH_2CH_2CMe_2CO_2Me$

and were prepared from the appropriate unlabelled precursor by MeOD/NaOMe exchange in a sealed tube at 90 °C for 16 h (deuterium incorporation >95% in each case (d_2 or d_4 as appropriate), as shown by positive ion mass spectrometry and ^1H nuclear magnetic resonance). 1-Carbomethoxycyclopentan-2-one[12] and 1-carbomethoxy-1,3-dimethylcyclopentan-2-one[13] were prepared by Dieckmann condensation[12,14] of the appropriate adipates.

1-Carbomethoxy-3,3-dimethylcyclopentan-2-one was prepared by the standard Dieckmann condensation[12,14] from dimethyl 1,1-dimethyladipate. The yield was 39%, b.p. 110 °C/18 mm; C 63.35, H 8.5; $C_9H_{14}O_3$ requires C 63.5, H 8.3%.

Acknowledgement

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