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GAS-PHASE IONIC REACTIONS OF BENZYL AND METHOXIDE ANIONS

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Gas-phase reactions of benzyl and methoxide anions with alkyl formate and other esters were compared using Fourier transform io cyclotron resonance spectroscopy. Although these anions have similar basicities, in many cases the reaction pathways differ. © 1997 John Wiley & Sons, Ltd.

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INTRODUCTION

The purpose of this work was to investigate some reactivities of delocalized and localized ions by comparing benzyl and methoxide ions. We attempted to understand more completely the similarities and the differences in reactivity of delocalized and localized ions.

The reactivity of localized ions is often different from that of delocalized ions, both in the gas phase and in solution. This reactivity difference can be attributed, in part, to lack of concentration of charge, to the additional stability of the delocalized ion, to loss of conjugation in the transition state and to lack of synchronization of structural and electronic changes in the transition state.

This is an area of major interest which has been developed extensively.[1–4] The problem of the gas-phase reactivity of delocalized versus localized ions has been studied by DePuy *et al.*[5] and Brickhouse and Squires.[6] We have been interested in the reactivity of charge-delocalized ions, transacylation reactions and the structure and stability of various complex ions.[7–9] Many reactions of these ions, e.g. transacylation, are of major importance in organic synthesis and in biological systems and have been studied extensively in condensed- and gas-phase studies.[5, 10–15]

At least some of the comparisons between localized and delocalized ions can be made more effectively if the thermodynamics of the reactions are comparable. Previous studies[5] focused on the allyl ion, which is more basic than the methoxide ion. Benzyl and the methoxide anions have essentially the same gas-phase basicity. Prompted by our inability to make the benzyl anion–methanol complex in the gas phase, in spite of the fact that the methanol–methoxide complex anion in the gas phase is well known, we undertook a study of the relative behavior of benzyl anion and methoxide anion with substrates that have more than one product channel. In this paper we report our studies of the relative gas-phase reactivity of benzyl and methoxide anions in proton transfer vs transacylation and S_N2 vs transacylation reactions.

EXPERIMENTAL

Materials. NF_3 was obtained from Ozark Mahoning and toluene-2,3,4,5,6-d_5 from Isotec. All other chemicals were purchased from Aldrich. The samples were subjected to multiple freeze–pump–thaw cycles before introduction into the ion cyclotron resonance (ICR) cell.

Ion generation. Primary ions were generated by electron impact on neutral precursors. Fluoride ion was generated by dissociative electron capture of nitrogen trifluoride, NF_3:

$$NF_3 + e^- \longrightarrow F^- + NF_2$$

The oxide ion was generated from N_2O:

$$N_2O + e^- \longrightarrow O^{-\bullet} + N_2$$

Benzyl and deuterated benzyl anions were formed in two different ways:

$$C_6H_5CH_2SiMe_3 + F^- \longrightarrow C_6H_5CH_2^- + FSiMe_3$$

$$C_6D_5CH_3 + O^{-\bullet} \longrightarrow C_6D_5CH_2^- + OH^\bullet$$

ICR apparatus. All the experiments were performed with a Fourier transform IonSpec OMEGA ion cyclotron resonance (FT-ICR) spectrometer equipped with impulse excitation. Details of the experimental apparatus can be

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Table 1. Products from $C_6H_5CH_2^- + H\overset{O}{\overset{\|}{C}}—OR$

R	Product ions (%)				
	$H\overset{O}{\overset{\|}{C}}—O^-$	$C_6H_5\overset{-}{C}H\overset{O}{\overset{\|}{C}}H$	RO^-	$[ROHOR]^-$	$[C_6H_5CH_3OR]^-$
CH_3	0	100	0	0	0
C_2H_5[a]	0	53	0	47	0
$(CH_3)_3C$	0	15	38	47	0

[a] $C_6D_5CH_2^-$ was used in this experiment.

found elsewhere.[10–12] Briefly, the ICR system consists of a $2 \times 2 \times 2$ in cubic cell, constructed from six stainless-steel plates mounted on Vespel rods. Ions were trapped with magnetic fields in the range 0·6–0·8 T. Neutral samples were admitted to the high-vacuum can by means of Varian leak valves. Typical operating pressures were between 10^{-7} and 10^{-6} Torr (1 Torr = 133·3 Pa). The kinetic energy of the incident electrons was controlled by varying the potential applied to the filament and the bias on the trapping plates. Typical operating current and voltage for the filament were 2–3 A and 1–3 V, respectively. Standard notched ejection techniques were used to remove unwanted ions from the detection region of the ICR cell and thereby isolate the ions of itnerest. All experiments were carried out at a temperature estimated to be 350 K.[10]

Data collection. The duty cycle involved fluoride or oxide ion formation for 20–40 ms followed by ejection of free electrons for 40 ms. After a short time delay (*ca.* 30–50 ms), fluoride (or oxide) ion was ejected. Products were analyzed 1000–1500 ms after ejection. The ratio of the product ions changes slightly with the delay time. At very early delay times few products are produced, and therefore the signal-to-noise ratio is not good. At long delay times, differential ion loss becomes a problem. Taking data at the intermediate time range (1000–1500 ms) minimizes the error. The ratios in this range are relatively constant. For each data point, multiple scans (200–500) were averaged to obtain reproducible ion abundances, and multiple data points were averaged at each pressure. The data collection was repeated at a variety of pressures of the neutrals. The ratio of the product ions varied on different days within 5%

RESULTS

The reactions between benzyl anion and methyl, ethyl and *tert*-butyl formate were investigated. The results are shown in Table 1. In the experiment with ethyl formate the resulting ethoxide–ethanol complex ion formed as a secondary reaction product has the same $m/z = 91$ as the benzyl anion. We used deuterated benzyl anion to distinguish between the products. The amount of the products, including the alcohol–alkoxide ion, is not expected to be affected significantly by the use of the deuterated toluene to generate $C_6D_5CH_2^-$.

The reactions between benzyl anion and methyl benzoate, methyl trifluoroacetate, methyl acetate and methyl cyanoformate were studied and the reaction products are shown in Table 2. The major product in the reaction with the methyl acetate was deprotonation at the α-carbon and is not shown

Table 2. Products from $C_6H_5CH_2^- + R\overset{O}{\overset{\|}{C}}—OCH_3$

R	Product ions (%)		
	$R\overset{O}{\overset{\|}{C}}–O^-$	R^-	$C_6H_5\overset{-}{C}H\overset{O}{\overset{\|}{C}}R$
H	0	0	100
C_6H_5	13	0	87
CN	25	75	0
CF_3	37	26	37[a]

[a] $C_6H_5CHCOCF_3^-$ (18%) and $C_6H_5CHCOOCH_3^-$ (19%).

Table 3. Products from $CH_3O^- + R\overset{O}{\overset{\|}{C}}—OCH_3$

R	Product ions (%)			
	$R\overset{O}{\overset{\|}{C}}—O^-$	R^-	CH_3O^-	$[CH_3OHOCH_3]^-$
H	5	0	0	95
C_6H_5[a]	28	0	72	0
CN	63	37	0	0
CF_3[b]	90	10	0	0

[a] Ref. 13.
[b] Ref. 14.

in the table. In the reaction with methyl trifluoroacetate, both $C_6H_5CHCOCF_3^-$ and $C_6H_5CHCOOCH_3^-$, formed in comparable amounts, are listed in the appropriate column. More details about the mechanism are provided in the Discussion section.

Table 3 lists the products for the reactions of methoxide with corresponding neutral compounds. Some of these reactions have been reported previously.

DISCUSSION

The goal of this work was to study the chemical reactivity of a delocalized ion (benzyl anion) in reactions that have multiple channels available, and to compare it with a localized ion (methoxide anion) with similar basicity. The first part of this section examines the occurrence of proton transfer reactions versus transacylations while the second part examines the competition between S_N2 and transacylations.

Proton transfer vs transacylation

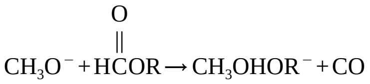
The reactivity difference between delocalized and localized ions in proton transfer and transacylations has been studied previously in related systems. DePuy *et al.*[5] performed an extensive study in which various charge-localized and charge-delocalized ions were allowed to react with methyl formate, and found that there is a significant difference in the reactivity of these two classes. Charge-localized ions reacted to give mainly α-elimination, whereas charge-delocalized ions reacted exclusively at the carbonyl group. Pioneering work by Riveros and co-workers[15,16] on alkyl formate reactions with alkoxides and by Johlman and Wilkins[17] on hydroxide–alkyl formate systems showed that when different pathways are available, α-elimination is a major pathway. Brickhouse and Squires[6] have also shown that there are significant differences in the reactivity of charge localized and delocalized ions with 6,6-dimethylfulvene. Localized ions gave mainly proton abstraction, whereas delocalized ions gave mainly addition.

We report here the reactivity of delocalized benzyl anion towards various formates and the comparison with the reactions of methoxide anion. Although the Riveros reaction, equation (1), is the major reaction pathway for methoxide,[11,15,16] Table 1 shows that in the reaction between benzyl anion and various formates, no S_N2 or Riveros reaction products were observed. For ethyl and especially *tert*-butyl formate, we observe secondary Riveros reaction products:

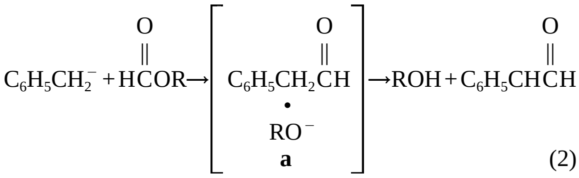
$$C_6H_5CH_2^- + HCOOR \rightarrow OR^- + C_6H_5CH_2CHO$$

$$RO^- + HCOOR \rightarrow ROHOR^- + CO$$

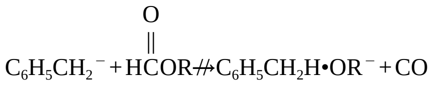
Equations (2)–(4) illustrate possible reaction pathways for the benzyl anion with alkyl formates. As shown in equation (2), the transacylation reaction actually gives an enolate ion product resulting from the proton transfer reaction by the alkoxide ion in the complex **a**. *t*-BuO$^-$ is also observed when benzyl anion reacts with *tert*-butyl formate because *t*-BuO$^-$ is sterically bulky, and therefore the proton transfer in the product complex is not efficient.



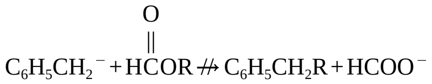
$$CH_3O^- + H\overset{\overset{O}{\|}}{C}OR \rightarrow CH_3OHOR^- + CO \qquad (1)$$



$$C_6H_5CH_2^- + H\overset{\overset{O}{\|}}{C}OR \rightarrow \left[\begin{array}{c} C_6H_5CH_2\overset{\overset{O}{\|}}{C}H \\ \bullet \\ RO^- \\ \mathbf{a} \end{array}\right] \rightarrow ROH + C_6H_5CH\overset{\overset{O}{\|}}{C}H \qquad (2)$$

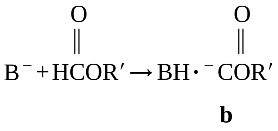


$$C_6H_5CH_2^- + H\overset{\overset{O}{\|}}{C}OR \nrightarrow C_6H_5CH_2H\bullet OR^- + CO \qquad (3)$$

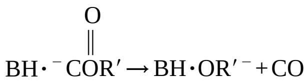


$$C_6H_5CH_2^- + H\overset{\overset{O}{\|}}{C}OR \nrightarrow C_6H_5CH_2R + HCOO^- \qquad (4)$$

The Riveros reaction is thought to occur via a proton transfer of the formate proton, decarbonylation and formation of the complex ion product[5] [Equations (5) and (6)].



$$B^- + H\overset{\overset{O}{\|}}{C}OR' \rightarrow \underset{\mathbf{b}}{BH\cdot{}^-\overset{\overset{O}{\|}}{C}OR'} \qquad (5)$$

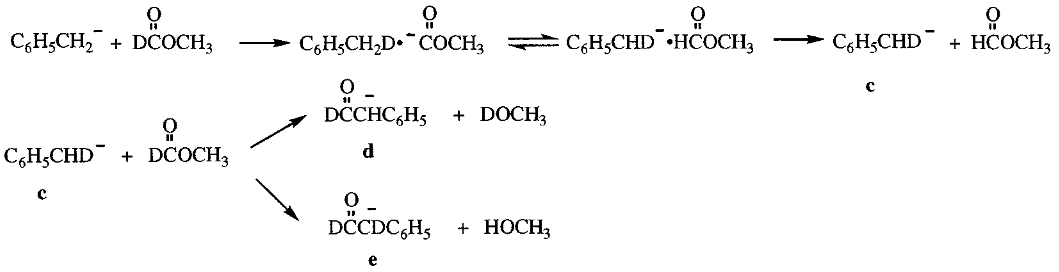


$$BH\cdot{}^-\overset{\overset{O}{\|}}{C}OR' \rightarrow BH\cdot OR'^- + CO \qquad (6)$$

For the reaction of benzyl anion with formates we did not observe a complex ion of the type $BH\cdot OR'^-$. In contrast, methoxide ion, with a similar basicity to benzyl anion, reacts with methyl formate and gives the complex ion shown in equation (1). We do not observe $BH\cdot OR'^-$ either because the proton transfer [equation (5)] does not occur or because the decarbonylation reaction [equation (6)] does not occur.

In order to find out if reaction (6) occurs, we performed calculations at the MP2/6–31+G*//6–31+G* level, which show that the stability of the toluene–methoxide complex relative to separated methoxide plus toluene is about 10–15 kcal mol^{-1}.[18] The stability of the complex of methoxide–methanol is significantly greater, and therefore the lack of a thermodynamic driving force might be a major factor why the second step [equation (6)], does not occur.

To see if reaction (5) occurs independently of reaction (6), we studied the reaction of benzyl ion with deuterated methyl formate. If reaction (5) is reversible and reaction (6) does not occur, we would see proton exchange and observe scrambling of the hydrogens. Scheme 1 shows the possible



Scheme 1

products from the simple dissociation, **c**, or from proton transfer followed by transacylation and subsequent proton transfer, **d** and **e**. Since products **c** and **e** are not observed (**d** can also be produced from transacylation of $C_6H_5CH_2^-$ with $DCOOCH_3$ followed by a deprotonation; this will be discussed later), the proton transfer does not occur. This is consistent with our previous observation that a significant barrier exists in the reaction between benzyl anion and toluene.[8, 10] The more basic allyl anion was allowed to react with methyl formate in a similar experiment. We did not observe any scrambling of deuterium, and therefore we infer that proton transfer is slow even in this more exothermic reaction.

The overall reaction to give transacylation is approximately 10% efficient. Proton transfer does not compete with transacylation. Since proton transfer is not observed within our detection limits, we infer that proton transfer [equation (5)], must be less than 1% efficient. This is may be an important reason why the Riveros reaction does not occur for the benzyl anion. Even though we posit an intermediate **b** [equation (5)], it is possible that the Riveros reaction is actually concerted. In any event, proton transfer does not occur. Based on the discussion above, we conclude that in the reaction with various formates, when both competing channels, proton transfer and transacylation, are available and are slightly exothermic, the transacylation dominates for delocalized ions, whereas the proton transfer dominates for localized ions. Thus, benzyl, a softer base than methoxide, reacts with the carbonyl group, which is a softer acid than H, whereas the harder methoxide reacts with the hard acid H.[19]

Proton transfer reactions of benzyl anion were studied in reactions in which this channel becomes more exothermic. When benzyl ion reacts wtih methyl acetate it does only proton transfer, and only $^-CH_2COOCH_3$ is observed, similar to the reaction of methoxide ion.[13]

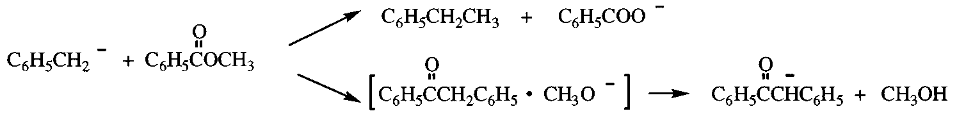
In summary, for reactions of benzyl and methoxide anion with various formates, two competing pathways are available. When the proton transfer channel is not very exothermic, the transacylation dominates for the delocalized anion whereas proton transfer reaction dominates for the localized anion. When the proton transfer becomes sufficiently exothermic, as in the methyl acetate reaction, the proton transfer product dominates for both delocalized and localized anions.

S_N2 *vs transacylations*

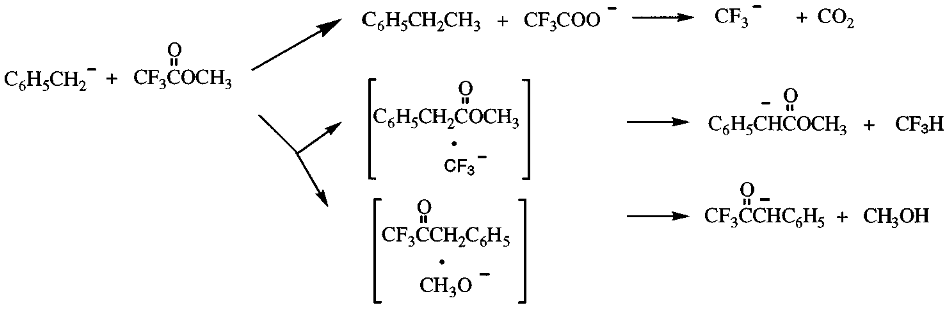
We studied the reactions of benzyl anion with various carbonyl substrates and the products observed are shown in Table 2. The RCO_2^- clearly originates from the S_N2 channel, whereas $C_6H_5CHCOR^-$ originates from the transacylation channel, followed by a deprotonation. The R^- products might be formed either from the S_N2 channel, upon decomposition of the carboxylate ion, or through the transacylation channel, upon dissociation of the ion–molecule complex. Examining Table 2, we see that except in the reaction with methyl formate, the S_N2 pathway is observed in every other case. Transacylation is observed unambiguously in every reaction, except in the reaction with methyl cyanoformate.

When benzyl anion was allowed to react with methyl benzoate, transacylation was the dominant pathway. Scheme 2 illustrates the two competing pathways for benzyl anion, transacylation and S_N2 reactions.

In the reaction with methyl trifluoracetate, the products of several additional pathways were observed. The S_N2 channel produced CF_3COO^-, which accounts for at least 37% of the products. Transacylation resulted in two different enolate ions, shown in Scheme 3, and accounts for 37% of the products. Two possible sources for the CF_3^- ion which was observed (26%) could be the decomposition of

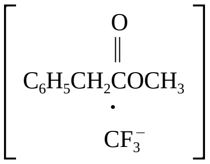


Scheme 2



Scheme 3

the S_N2 product, CF_3COO^-, or transacylation. Our previous work on the IR decomposition of fluorine-containing ions[20,21] and work by McDonald and Chowdhury[14] on the gas-phase reactions of methyl trifluoroacetate suggest that CF_3COO^- formed in a highly exothermic reaction can decompose to form CF_3^- and CO_2. We think that the CF_3^- originates from the decomposition of the CF_3COO^-, and is not formed from the dissociation of the transacylation complex ion:



$$\left[\begin{array}{c} \overset{O}{\overset{\|}{C_6H_5CH_2COCH_3}} \\ \bullet \\ CF_3^- \end{array}\right]$$

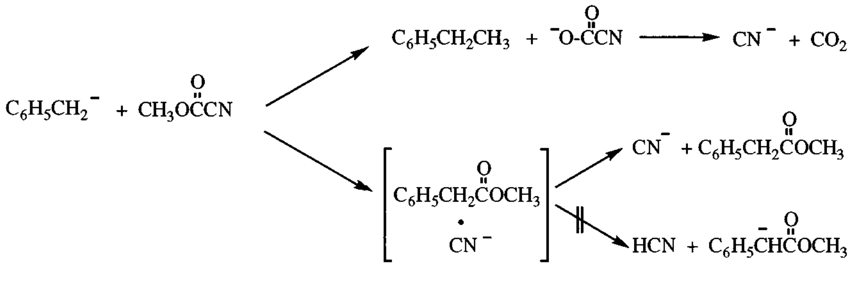
We showed previously[22,23] that in the transacylation reactions of enolate anions with trifluoroacetyl chloride, a proton transfer occurs within the addition–elimination complex before the complex falls apart. Furthermore, the CF_3^- group is not bulky and we expect that the proton transfer should be efficient. Similar products for the reaction of the allyl anion with methyl trifluoroacetate have been observed by McDonald and Chowdbury.[14] We therefore conclude that the S_N2 channel acounts for 63% of the products and the transacylation for 37% of the products.

The reaction products of benzyl anion and methyl cyanoformate are shown also in Table 2, and the different pathways are illustrated in Scheme 4. The S_N2 channel which produces $NCCO_2^-$ accounts for at least 25% of the products. No enolate ion is observed, since CN^- is not basic enough to deprotonate the methyl phenylacetate in the resulting complex. No products from CH_3O^- loss are observed; these channels are energetically unfavorable with respect to the loss of CN^-. The CN^- can arise either from the decomposition of the $NCCO_2^-$, i.e. from the S_N2 channel, or from the dissociation of the complex ion, produced in the transacylation. Since the dissociation of the complex is exothermic, we cannot distinguish which channel produces the CN^-, but based on the trifluoroacetate decomposition, we think that the CN^- is formed mainly through the S_N2 channel. If this is the case, the S_N2 channel could account for up to 100% of the products.

In summary, from Table 2, we observe that the better the leaving group, the more S_N2 products we see. If we compare transacylation with the S_N2 reaction for the series HCOOMe, PhCOOMe, CF_3COOMe, the S_N2 channel accounts for an increasing amount of the products. The S_N2 channel is also dominant for NCCOOMe.

The products of the reactions of the methoxide with various carbonyl substrates are shown in Table 3. The RCO_2^- products originate from the S_N2 channels, the $[CH_3OHOCH_3]^-$ originates from the α-elimination and the CH_3O^- originates from the transacylation. The R^- products might be formed either from the S_N2 channel upon decomposition of the carboxylate ion, or through the transacylation channel upon the dissociation of the ion–molecule complex. Examining Table 3, we see that the S_N2 pathway is observed in every case.

When methoxide anion was allowed to react with methyl



Scheme 4

benzoate, S_N2 (28%) and transacylation products (72%) were observed.[13] In the reaction of methoxide and methyl trifluoroacetate, the S_N2 channel accounts for at least 90% of the products.[14] In the reaction with methyl cyanoformate, we observed that methoxide produced 63% $NCCO_2^-$ via the S_N2 channel, but this channel probably accounts for as much as 100% of the products, since the CN^- is formed mainly via the S_N2 channel similar to the benzyl anion.

From Table 3, we find that when methoxide reacts with the series HCOOMe, PhCOOMe, CF_3COOMe, as the leaving group become better more of the S_N2 product is observed. Transacylation is observed unambiguously only when the carboxylate ion cannot decompose to form R^- ion.

If we compare the reactivity of methoxide and benzyl anions, we find that in the reaction with methyl benzoate the methoxide produces more of the S_N2 product, 28% compared with 13%. Similarly, for methyl trifluoroacetate, methoxide reacts at least 90% via the S_N2 channel, which for the benzyl ion is no more than 63%. With the methyl cyanoformate both compounds react mainly through the S_N2 channel.

CONCLUSION

We have addressed the similarities and differences of delocalized and localized ions by studying reactions of benzyl anion and comparing them with those of methoxide ion, which has the same basicity. We find that in the reaction with alkyl formates benzyl anion gives only transacylation, in contrast to methoxide, which reacts exclusively via proton transfer. From deuterium exchange experiments we find that proton transfer is inhibited for benzyl anion. This is consistent with previous experiments which have shown that there is a significant barrier to proton transfer for conjugated ions in many proton transfer reactions.[8] We confirm previous observations that there is a difference in the proton transfer reactivity of delocalized and localized ions in reactions which are slightly exothermic. However, if the proton transfer becomes sufficiently exothermic, such as in the reaction of benzyl ion with methyl acetate, the proton transfer dominates, similarly to methoxide anion.

In the reaction of benzyl ion with methyl benzoate, methyl cyanoformate and methyl trifluoroacetate, both S_N2 and transacylation are observed, similarly to methoxide. The better the leaving group, the more of the S_N2 products are observed.

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