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THE GAS-PHASE PINACOL REARRANGEMENT AND RELATED REACTIONS IN ORGANIC CATIONS GENERATED BY CHEMICAL IONISATION

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Abstract—Reactions which simulate acid catalysed rearrangements in solution have been demonstrated in organic cations generated by chemical ionisation in the mass spectrometer. The pinacol-pinacolone rearrangement has been shown to occur following protonation of various pinacols with $C_4H_9^+$. In related reactions, a number of aldehydes, $RC(R_1R_2)\cdot CHO$, following protonation in the gas-phase, undergo rearrangement to the protonated ketones, $HC(R_1R_2)\cdot CO\cdot R$. All the above rearrangements have been demonstrated via Collision-Induced Dissociation (CID) in the third field-free region of a triple-sector mass spectrometer, followed by Mass-analysed-Ion-Kinetic-Energy (MIKE) spectrometry.

INTRODUCTION

The utilisation of electron-impact mass spectrometry as a tool for structural elucidation of organic molecules is of course a consequence of the relationship between the structure of the neutral molecule and the fragmentation pattern of the molecular ion in the mass spectrometer. In many cases the facile cleavage of certain bonds in the molecular ion is readily interpretable and predictable on the basis of experience from reactions in solution chemistry. However, there are other instances where unimolecular reactions in the mass spectrometer are not obviously related to reactions in solution. This is due to the facts that: (1) molecular ions in the mass spectrometer are radical ions, not normally found in solution and (2) reactions in solution often involve more than one molecular species, one of which may be a solvent molecule.

With the advent of Ion Cyclotron Resonance (ICR) and Chemical Ionisation (CI) mass spectrometry it became possible to simulate, in the gas-phase, some bimolecular reactions of even-electron ions found in solution, free from solvent interactions. In particular, studies of equilibrium reactions either in the ICR cell,[1,2] or in a high-pressure ion source,[3,4] have yielded gas-phase acidities and basicities of organic species which reveal conclusions of fundamental importance in mechanistic organic chemistry.

The decomposition of even-electron ions generated by CI is not usually extensive and this presents problems when investigating correlations with decomposition reactions in solution. However, the availability of Collision-Induced Dissociation (CID) and Mass-analysed-Ion-Kinetic-Energy (MIKE) Spectroscopy have enabled the decompositions of such low-energy ions, generated in a CI source, to be observed in a field-free region of a mass spectrometer. For example, the mechanism of the Fischer indole synthesis has been investigated in the gas-phase by identifying the collision-induced decompositions of the deamination product of protonated acetone phenylhydrazone.[5] Similarly, the pinacol-pinacolone rearrangement was observed in the mass spectrometer.[5] The positions of ethylation and protonation on a variety of substrate amines have also been investigated by such methods.[6]

The present study provides further illustrations of the combined techniques of chemical ionisation and collision-induced dissociation in the simulation of well-known solution reactions in the mass spectrometer. Two related types of reaction are investigated: (1) the pinacol-pinacolone rearrangement, involving both aliphatic and aromatic species and (2) the rearrangement of some protonated aldehydes to isomeric protonated ketones[7] via 1,2-alkyl or -aryl migrations.

RESULTS

A. *The pinacol rearrangement.* The occurrence in the gas-phase of this well-known acid-catalysed rearrangement has already been demonstrated for pinacol itself.[5] The present paper extends the investigation to aromatic and alicyclic pinacols. The purpose of the study was twofold: (1) to demonstrate the general occurrence of this reaction and (2) to determine the migratory aptitude of different groups during the rearrangements.

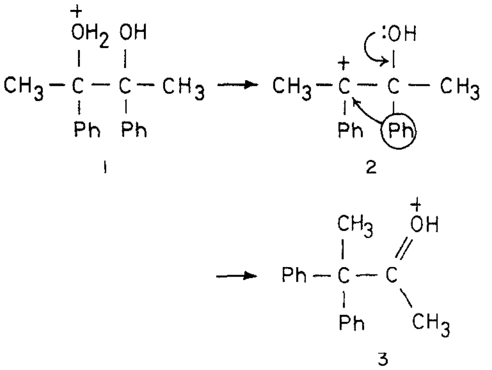
The rearrangement of the protonated pinacol compound **1** was investigated in a high pressure isobutane ion-source. No MH^+ ions were observed in the normal mass spectrum, the highest mass ions being found at m/z 225 (MH^+-H_2O) corresponding to structure **2**. In sulphuric acid solution, ion **2** rearranges to form the isomeric protonated ketone **3**, via migration of a phenyl group. The isobutane chemical ionisation spectrum of ketone **3** exhibits an abundant MH^+ ion. Accordingly the ions at m/z 225 were selected by the magnet for collision-induced dissociation both from the substrate pinacol **1** and its rearrangement product **3**. The isomeric, alternative pinacolone product **4**, which would result from a

Table 1. The CID/MIKE spectra for the m/z 225 ion formed from 1, 3 and 4

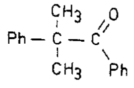
Precursor	Reacting ion	Product ions and relative intensities (%) m/z: 210	207	193	181	179	165	147	119	105	91	77	43
1	$MH^+ - H_2O$	7	3	-	25	6	18	100	9	15	4	5	5
3	MH^+	6	3	-	20	5	15	100	7	13	4	5	5
4	MH^+	14	8	8	6	2	5	100	8	20	4	6	-

methyl group migration was also employed as a check. The relevant CID/MIKE spectra are shown in Table 1.

The spectra from precursors **1** and **3** are almost identical. This confirms that the reaction sequence **1** → **3** has occurred. The main collision-induced reaction (loss of C_6H_6) is not diagnostic of detailed structural features but the formation of m/z 181, probably corresponding to $MePh_2C^+$, is indicative of structure **3** as the main decomposing species.



The protonated molecular ion of ketone **4** exhibits a different CID/MIKE spectrum from that of the m/z 225 ions formed from **1** and **3** (Table 1). The most prevalent reaction remains the elimination of C_6H_6 to form m/z 147 but the minor peaks exhibit quite different abundance ratios. In particular, the relative intensities of the structurally diagnostic ions at m/z values 181 ($MePh_2C^+$), 119 (Me_2PhC^+), 105 ($PhCO^+$) and 43($MeCO^+$) are informative. The abundance ratio, m/z 181 : m/z 119 changes from approximately 2.8 for precursors **1** and **3** to approximately 0.7 for precursor **4**. Similarly, the m/z 43 ion is almost totally absent from the spectrum of **4**, whereas the relative abundance of m/z 105 is greater compared with its abundance in the spectra from **1** and **3**. These results therefore indicate that the m/z 225 ions from structures **1** and **3** are dissimilar to those formed from structure **4** and the differences are interpretable in terms of the precursor ion structures.



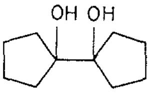
$$Ph-\overset{CH_3}{\underset{CH_3}{C}}-C(=O)Ph$$

4

The conclusions from the results in Table 1 are as follows: (1) the pinacol–pinacolone rearrangement occurs in the gas-phase for ion **1**, (2) preferential migration of the phenyl group occurs during this rearrangement to yield an ion corresponding to protonated ketone **3**, not protonated ketone **4**. However, the MH^+ ion from **4** shows some characteristics of partial isomerisation to **3** prior to collision-induced decomposition (and vice-versa).

The gas-phase pinacol rearrangement has also been investigated for the pinacol **5**. This rearrangement presents the interesting possibility of formation of a spirocyclic ion via a rearrangement in the mass spectrometer. Accordingly, the CID/MIKE spectra were investigated for the ions at m/z 153 formed following chemical ionisation of compounds **5** (MH^+-H_2O), **6**, **7** and **8** (all MH^+). Compounds **7** and **7**, isomeric with **6** were employed as a check for differences between spectra. Fig. 1(a) shows the CID/MIKE spectrum for m/z 153 (MH^+-H_2O) formed from compound **5**. The spectrum for the same ion from compound **6** (MH^+ in this case) is identical to that shown in Fig. 1(a). The identity of these two spectra establishes that the acid-catalysed rearrangement of the pinacol **5** to the protonated pinacolone product **6** takes place in the gas-phase.

To serve as a check that the above conclusions are valid and that the identity of CID/MIKE spectra can be used in this case as a criterion for structural identity, the spectra of protonated **7** and **8** (closely related isomers of **6**) were obtained. Figures 1(b) and 1(c) show the spectra of m/z 153 from **7** and **8** respectively. Despite undergoing many common transitions, the ions yielding the spectra shown in Fig. 1 clearly possess different structures. The main transition in all the spectra is the loss of H_2O to yield the m/z 135 ion. This is a common fragmentation reaction of protonated aliphatic ketones.[8] However there are several notable differences in relative abundances of fragment ions between the three spectra.



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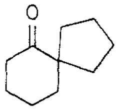

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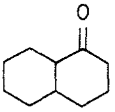

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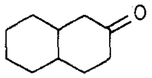

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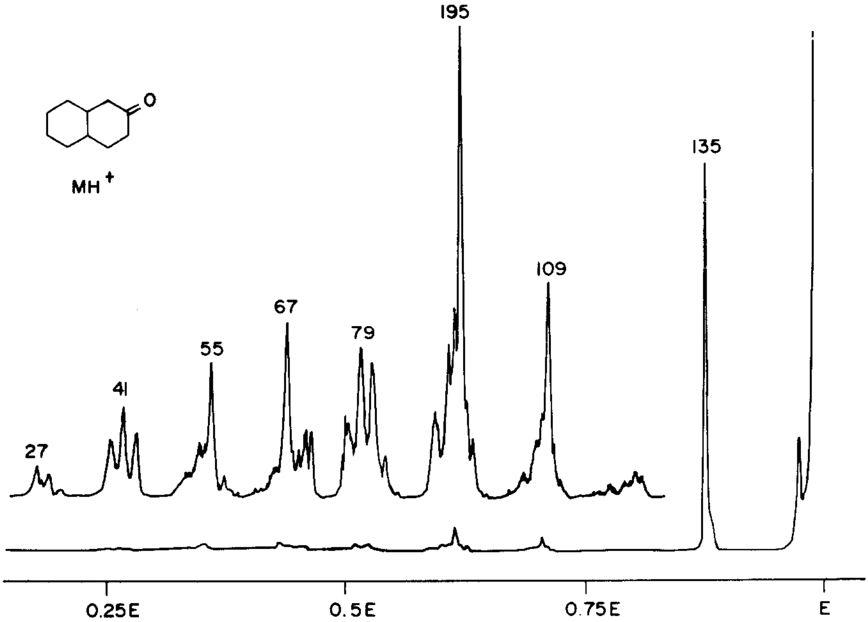
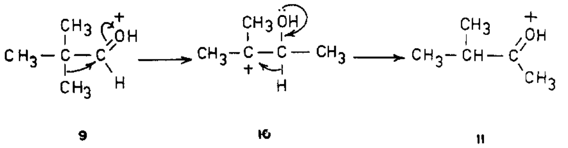


Fig. 1(c).

Fig. 1. The CID/MIKE spectra of m/z 153 from the pinacol (**5**) ($[MH\text{-}H_2O]^+$) and the decalones (**7**) and (**8**) (both MH^+). The spectrum of the protonated ketone (**6**) is identical to that shown in Fig. 1(a) and is therefore not reproduced here.

Table 2. The CID/MIKE spectra for the m/z 87 ion as shown in structures **9** and **11**. The transition to m/z 69 occurs also as a unimolecular reaction of metastable ions

Precursor	Reacting ion	Product ions and relative intensities (%) m/z: 71	69	57	45	43	41
9	MH^+	90	100	20	25	65	30
11	MH^+	100	90	20	25	75	34



The above conclusion does not necessarily imply that the decomposing ions possess structure **11**. In fact, in an analogous but simpler situation, it has been shown from consideration of reaction energetics that protonated acetone rearranges to protonated propanal prior to unimolecular decomposition.[10]

The analogous reaction to that demonstrated above has been investigated for a series of aromatic aldehydes and ketones, in order to determine the generality of the reaction. For example, the 1,2-migration of a phenyl group in the protonated diphenylacetaldehyde molecule **12** would yield protonated deoxybenzoin **14** via the intermediate **13**. The CID/MIKE spectra of these ions (m/z 197), produced by chemical ionisation with isobutane, have therefore been measured and the spectrum of the aldehyde, **12**, is shown in Fig. 2. The spectrum produced under the same conditions for the protonated isomeric ketone, **14**, was almost identical to that shown in Fig. 2, the only difference being a reduced intensity of m/z 168.

The above results strongly indicate that isomerisation between ions **12** and **14** occurs via interchange of a phenyl group and an H atom. The carbonium ion **13** is a feasible intermediate for this reaction and can be generated by protonation of stilbene oxide **15**. The CID/MIKE spectrum of **15**, produced by isobutane chemical ionisation, has therefore been measured and found to be identical to that of protonated deoxybenzoin **14**. This spectrum supports the isomerisations shown for ions **12**–**15** and further verifies the generality of this type of reaction.

Examination of the CID/MIKE spectra of protonated diphenylacetaldehyde **12**, deoxybenzoin **14** and stilbene oxide **15** leaves little doubt concerning the decomposing structure following collision. The three major ions formed are m/z 105 ($PhCO^+$), m/z 91 ($C_7H_7^+$) and m/z 77 ($C_6H_5^+$). These decompositions are wholly consistent with fragmentations from protonated deoxybenzoin **14**. In particular it is inconceivable that protonated diphenylacetaldehyde **12** would yield either the $C_6H_5CO^+$ or $C_7H_7^+$ ions via a direct decomposition. The only minor inconsistency in the spectra of **12**, **14** and **15** is the occurrence of a small peak at m/z 168 in the aldehyde spectrum **12**. The loss of 29 mass units (CHO?) in this reaction may be accommodated by partial protonation on a phenyl ring.

The results above, for two sets of compounds, therefore, establish that the pinacol-pinacolone rearrangement occurs in the gas-phase in the absence of solvent. Furthermore, the intramolecular nature of the reaction in solution[9] is confirmed for the gas-phase reaction. However, it should be noted that the occurrence of the rearrangement does not in itself imply that the protonated pinacolone is the only product ion undergoing collision-induced dissociation. There may be a distribution of decomposing ions.

B. *Isomerisation of protonated aldehydes and ketones.* It has been known for some time that certain aldehydes may undergo rearrangement in acid media. For example, protonated pivaldehyde **9** undergoes rearrangement in acid solution to generate protonated methyl isopropyl ketone **11**, probably via the tertiary carbonium ion intermediate **10**.[7]

Accordingly ions **9** and **11** have been generated in the gas-phase by chemical ionisation from the respective carbonyl compounds, to determine whether these protonated molecular ions rearrange to common structures. The abundances of ions in the relevant CID/MIKE spectra are shown in Table 2. The two spectra are closely similar, thus demonstrating that **9** rearranges to **11**, or *vice-versa*. Incidentally, these spectra also bear a close resemblance to that of the $[M-CH_3]^+$ ion (structure **11**) generated by electron-impact from 2,3-dimethylbutan-2-ol.

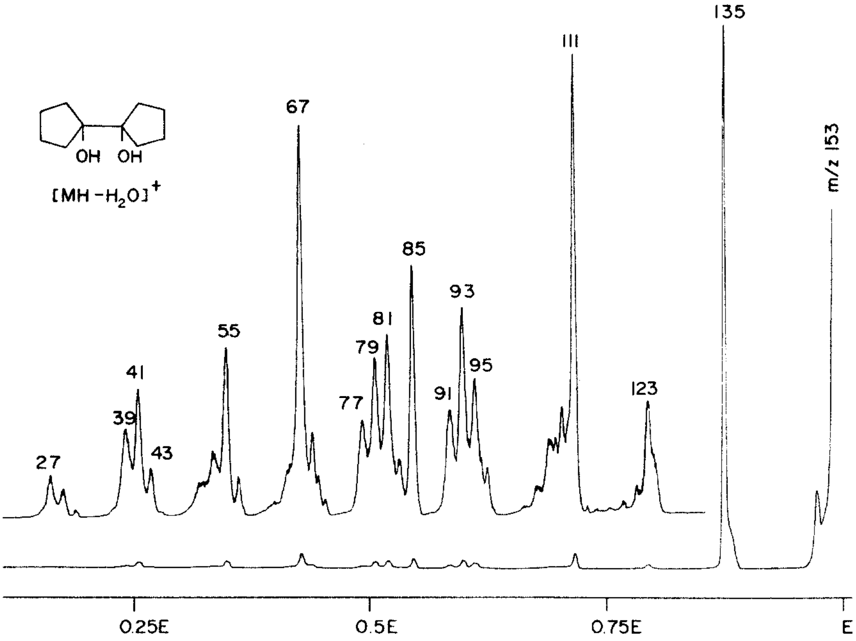


Fig. 1(a).

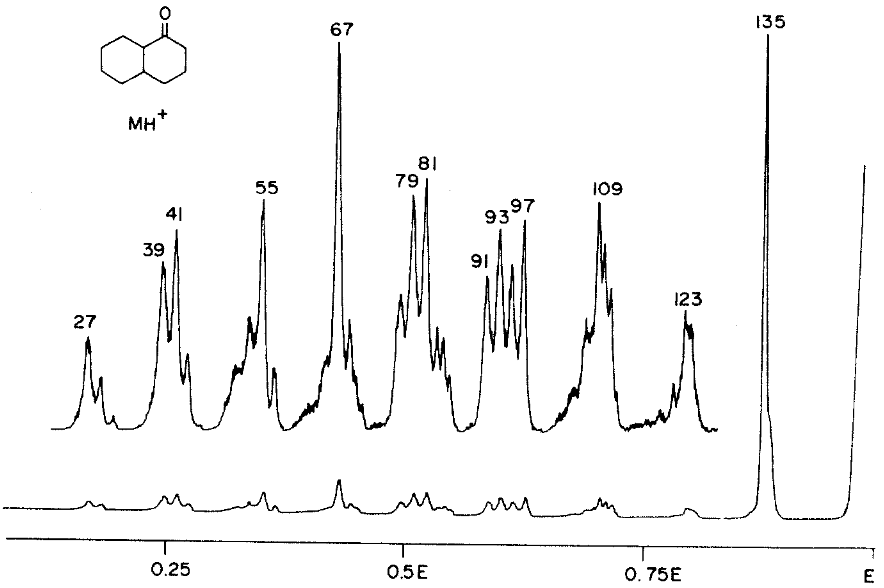


Fig. 1(b).

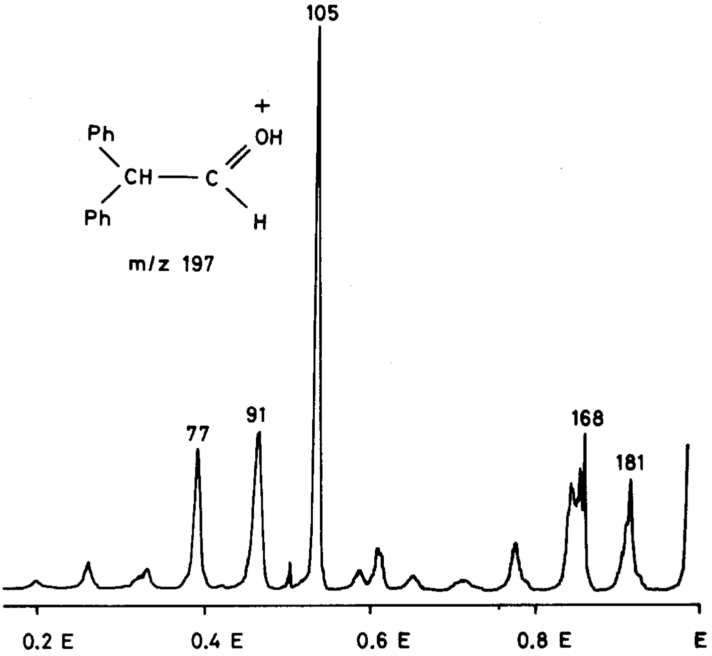
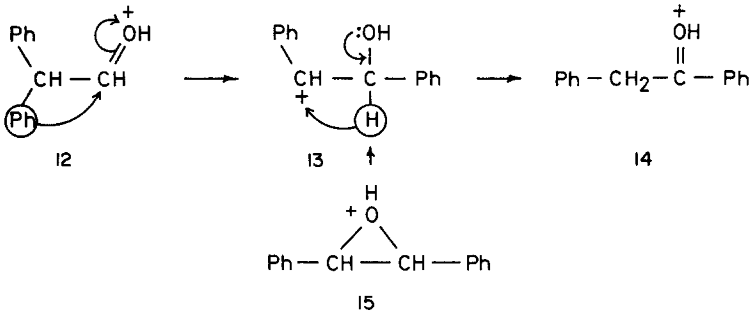
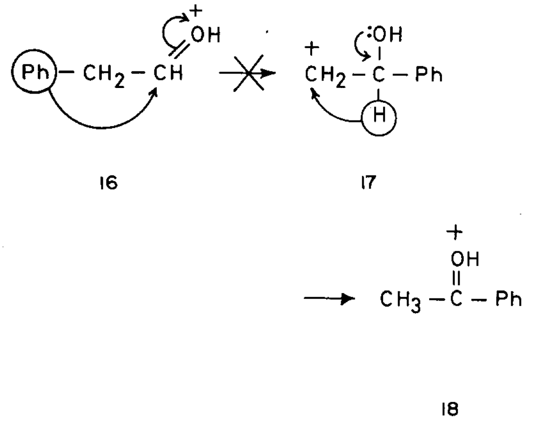


Fig. 2. The CID/MIKE spectra of m/z 121 (MH^+) from diphenylacetaldehyde (12).



The above rearrangement, 12 → 14, incorporates as an intermediate the secondary carbonium ion 13, in which the positive charge is stabilised by the remaining phenyl group. However, if phenyl acetaldehyde is employed as the substrate for protonation, then the possibility arises that the rearrangement to protonated acetophenone via a phenyl migration (16 → 18) might be precluded due to the high energy of the primary carbonium ion 17. In order to test the occurrence of this rearrangement, the CID/MIKE spectra of protonated phenylacetaldehyde and acetophenone were compared as indicated previously.



The spectra (Fig. 3) show that the two species of ions have totally different structures. Hence no rearrangement has taken place. The spectrum of protonated acetophenone contains intense peaks at m/z 43(CH_3CO^+) and 105 ($PhCO^+$) which are almost absent in the spectra of protonated phenylacetaldehyde. Conversely, the spectrum of the latter ion includes prominent peaks at m/z 91 ($C_7H_7^+$) and 103 $(MH\text{-}H_2O)^+$ which are characteristic of the structure of the parent ion.

The results demonstrated here therefore indicate that the rearrangement (16 → 18) is precluded due to the high energy barrier for isomerisation of 16 to the primary carbonium ion 17. The protonated molecular ions 16 and 18 preferentially retain their structures prior to collision-induced dissociation rather than isomerising to common structures.

CONCLUSIONS

It has been shown that two types of acid-catalysed rearrangement known to occur in solution can be simulated in low-energy protonated molecular ions produced by chemical ionisation in the gas-phase. In one case where a rearrangement did not occur the high energy of

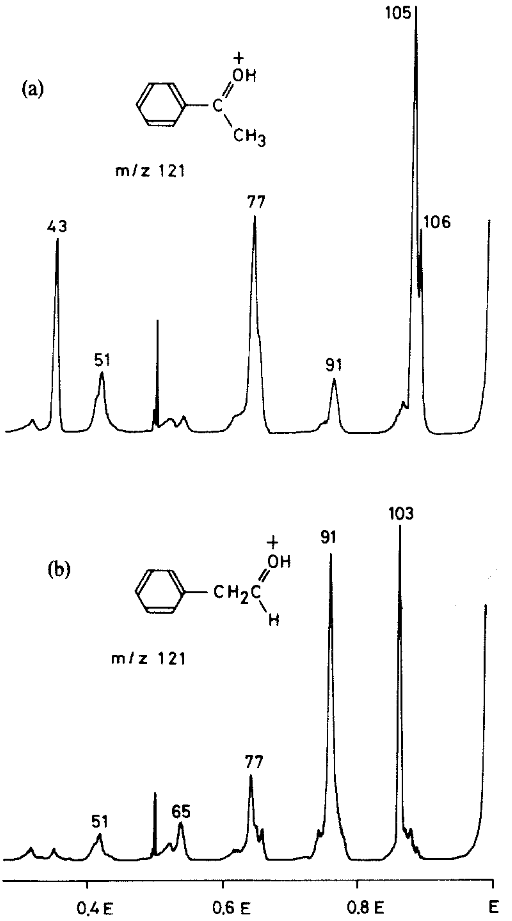


Fig. 3. The CID/MIKE spectra of m/z 121 (MH^+) from (a) acetophenone **18** and (b) phenylacetaldehyde **16**.

the prospective intermediate precludes a phenyl-group migration.

The utilisation of the combined techniques of chemical ionisation mass spectrometry and collision-induced dissociation to simulate reactions occurring in solution also opens up the intriguing possibility that a variety of solution reactions could be predicted on the basis of reactions occurring in the mass spectrometer.

EXPERIMENTAL

Measurements were performed on an AEI MS-902 mass spectrometer, modified for the observation of collision-induced dissociations by the addition of a second electrostatic analyser following the magnet.[11] Collision-induced decompositions occurred in the third field-free region (between the magnet and the second electric sector) and MIKE spectra were observed by scanning the voltage of this second electrostatic analyser. Air was used as the collision gas at a pressure not greater than 10^{-4} torr. The accelerating voltage was 9 kV.

A chemical ionisation source (dual EI/CI) supplied by Mass Spectrometry Services Ltd. was used to generate the protonated molecular ions. Isobutane was employed as the reagent gas, the source pressure being regulated to obtain the best MH^+ concentration (or $[MH^+-H_2O]$ concentration for the substituted pinacols). The electron energy was 100 eV.

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