Ion–molecule reactions of benzoyl ions in a quadrupole ion trap mass spectrometer

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Studies using quadrupole ion trap mass spectrometry show that gas phase benzoyl ions, of the type $[C_6X_5CO]^+$ (X = H, F, 4-Me, 4-Bu^t) undergo selective ion–molecule reactions with compounds containing hydroxy groups. The formation of $[M + C_6X_5CO]^+$, $[M - H]^+$ and $[M - OH]^+$ products is determined by the hydroxy group environment in agreement with the known thermochemistry of these ions and a molecular modelling study of the electrophilic addition. Storing the benzoyl ion at higher values of the ion trap q_z parameter during the reaction reduces adduct ion intensity, due to an increased rate of dissociation of the adduct. Substitution of the benzoyl ion with fluorine or a methyl group modifies the electrophilic character of the benzoyl ion, allowing the selectivity of its reactions to be controlled. Reaction of $[C_6H_5CO]^+$ and $[C_6F_5CO]^+$ with unsaturated compounds yielded the corresponding adduct ions, whilst the formation of adduct and $[M - Cl]^+$ product ions was observed only for the reaction of $[C_6F_5CO]^+$ with chlorine-containing molecules. The potential of the benzoyl ion and substituted benzoyl ions as selective chemical ionisation reagents is illustrated for the product related intermediates of 2-(8-phenyloctyl)benzaldehyde separated by GC.

Introduction

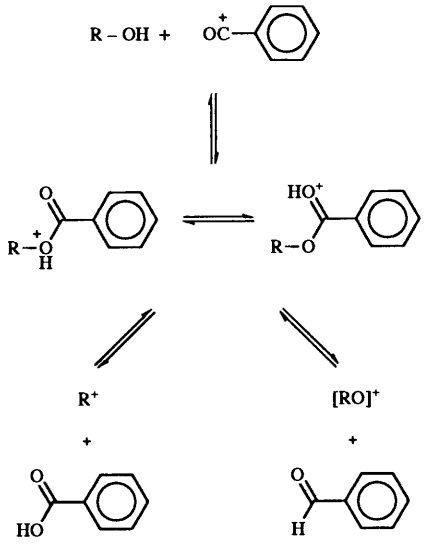
Gas phase ion–molecule reactions of the benzoyl ion have attracted considerable interest. Reactions in the pressure and time regimes of the mass spectrometer using ion cyclotron resonance (ICR) and quadrupole instruments have been reported for simple amines,[1] ammonia,[2] dienes[3] and 1,3-dioxolanes.[4] The chemistry of the benzoyl ion has also been studied in the 90–650 Torr pressure range for reaction periods of 15–20 months. In these experiments, the reactant ion was generated by β decay of [1,4-$^3H_2$]benzene in the presence of a large excess of carbon monoxide and neutral products were identified by radio GC and HPLC.[5,6] The benzoyl ion has been characterised through these reactions as a mild, selective electrophile, preferring n-type nucleophile centres of the substrate rather than π-type centres, which undergoes benzoylation of phenol, aniline and anisole.[7] NMR studies on substituted benzoyl cations[8–10] have shown that electron donating substituents such as 4-CH_3O and 4-CH_3 increase charge delocalisation into the aryl ring, whilst electron withdrawing groups such as 4-F and 4-CF_3 have the opposite effect, increasing the electrophilic nature of the benzoyl ion.

Reactions involving hydroxy functional groups have been reported for the gas phase nitrosonium ion, NO^+,[11] the trimethylsilyl ion, $(Me)_3Si^+$,[12,13] the boron-containing cations, $[MeOBOMe]^+$ and $[MeBMe]^+$,[14] and the dimethyl ether derived ion, $[MeOCH_2]^+$.[15] However, the selectivity of all these ions for hydroxy groups is limited by their reactivity towards a variety of other functional groups, such as ketones, ethers and carboxylic acids.[16–18]

We have recently reported preliminary studies on the reaction of the benzoyl ion with the hydroxy functional group.[19] In this paper, we describe an ion trap mass spectrometric study of the selectivity of the ion–molecule reactions of benzoyl ions of the type $[C_6X_5CO]^+$ (X = H, F, 4-Me, 4-Bu^t) with hydroxy and other functional groups. The influence of experimental conditions such as helium buffer gas pressure and the ion trap q_z parameter on benzoyl ion reactivity have been investigated. The potential of the benzoyl ion as a selective chemical ionisation reagent is demonstrated by its reactions with the product related intermediates of 2-(8-phenyloctyl)benzaldehyde (POB),[20] the precursor of SK & F104353[21] (SmithKline Beecham), a peptidoleukotriene antagonist, following GC separation.

Results and discussion

A general scheme for the reaction of isolated benzoyl ions of the type $[C_6X_5CO]^+$ with hydroxy-containing compounds in the quadrupole ion trap is shown in Scheme 1 (X = H). The three



Scheme 1

main products of the benzoylation reaction are the $[M + C_6X_5CO]^+$ adduct ion, $[M - OH]^+$ resulting from hydroxy abstraction and $[M - H]^+$ from hydride abstraction. The formation of adduct and hydroxy abstraction products is illustrated by the mass spectrum resulting from the reaction of $[C_6H_5CO]^+$ with 2-methylpropan-2-ol, [Fig. 1(*a*)]. The spectrum shows a strong $[M + 105]^+$ adduct ion at *m/z* 179 (100%) and a weak $[M - OH]^+$ ion at *m/z* 57 (4%) (Scheme 2). A fragmentation product of the adduct, $[C_6H_5C(OH)_2]^+$, is

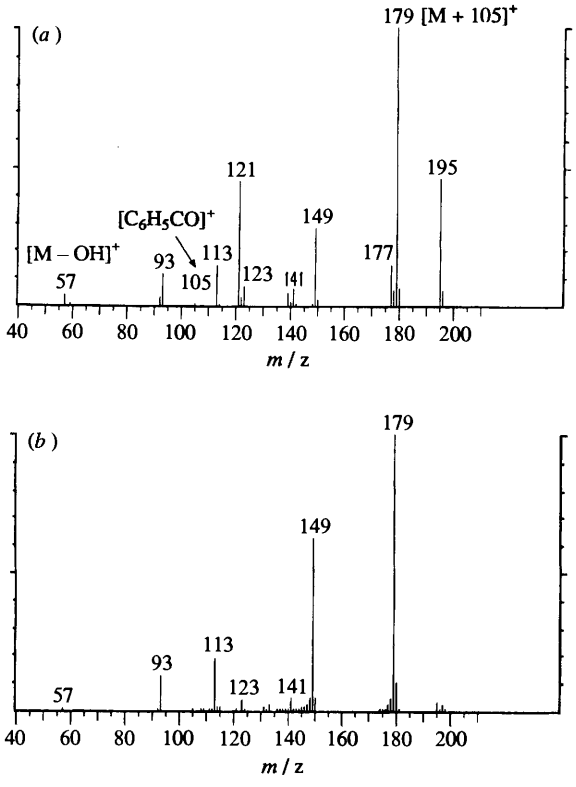
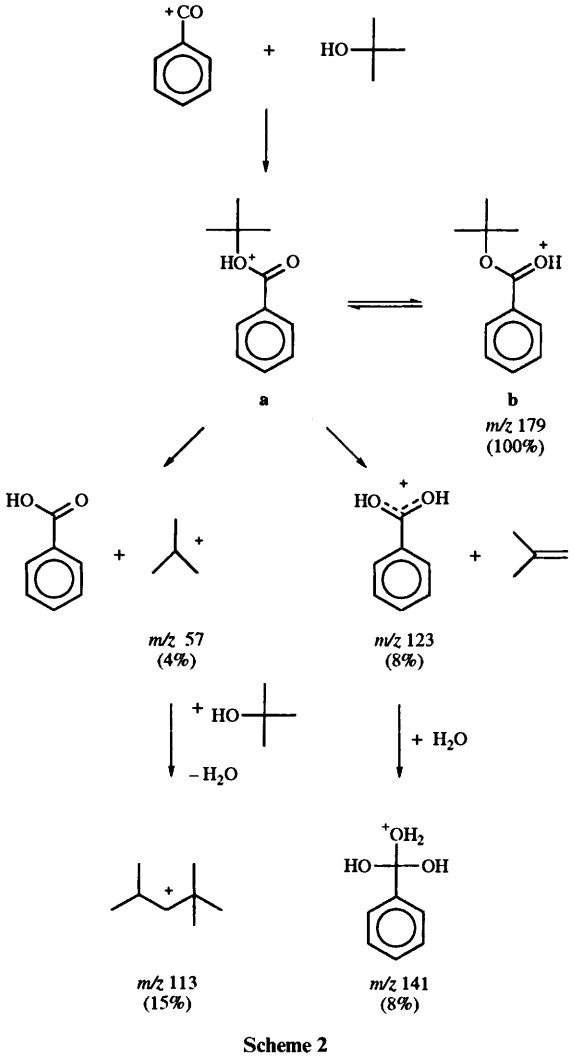
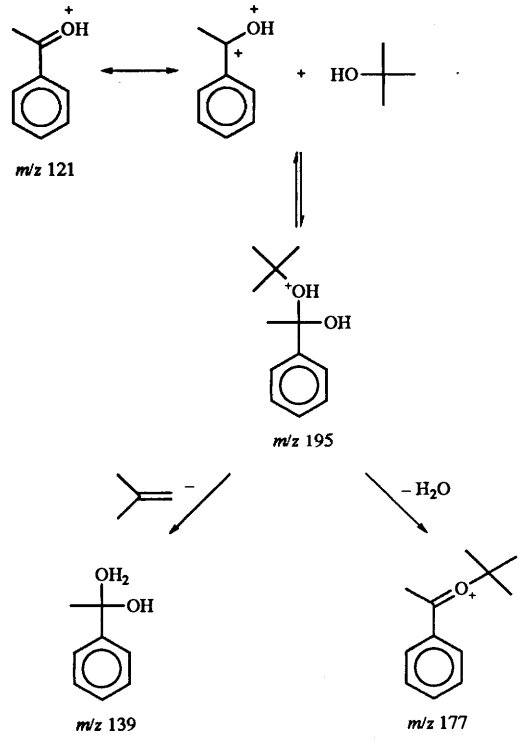


Fig. 1 Reaction of the benzoyl ion with 2-methylpropan-2-ol, without (*a*) and with (*b*) pulsed-valve introduction of acetophenone



Scheme 2

observed at *m/z* 123 arising from loss of butene and this ion reacts further with water to yield the ion at *m/z* 141. The $[M - OH]^+$ ion forms an adduct with 2-methylpropan-2-ol, which dehydrates to form the $[C_8H_{17}]^+$ alkyl ion at *m/z* 113. These processes were confirmed by isolation of the $[M - OH]^+$ and $[C_6H_5C(OH)_2]^+$ ions, followed by reaction with the appropriate neutral. A protonated dimer ion of 2-methylpropan-2-ol is present in the spectrum at *m/z* 149, together with a product ion at *m/z* 93. The proton bound dimer ion has also been observed in an FT-ICR study of the proton transfer reactions of 2-methylpropan-2-ol.[22] Acetophenone, which is present in the trap as the precursor for the $[C_6H_5CO]^+$ ion, is readily protonated to form $[C_6H_5C(OH)Me]^+$ (*m/z* 121) and this ion undergoes competing reactions with 2-methylpropan-2-ol, leading to the formation of ions at *m/z* 195 (M + 121), 177 (M + 121 – H_2O) and 139 (M + 121 – butene) (Scheme 3). Pulsed introduction of acetophenone into



Scheme 3

the quadrupole ion trap *via* a pulsed valve (5 ms wide band width) virtually eliminates these side reactions, since most of the neutral acetophenone is pumped away before the end of the benzoyl ion isolation period, allowing a clear distinction between product ions arising from protonated acetophenone and those from the benzoyl ion [Fig. 1(*b*)].

The variation of product ion intensities for the reaction of the benzoyl ion with 2-methylpropan-2-ol over reaction times of up to 110 ms is shown in Fig. 2. A rapid decrease in $[C_6H_5CO]^+$ ion intensity occurs within the first 50 ms. The *m/z* 179 adduct ion intensity reaches a maximum during this period and then gradually decreases. There is no significant increase in fragment ion intensity to account for the loss of the adduct ion, which may arise because of proton transfer to acetophenone, since the intensity of protonated acetophenone rapidly increases at longer reaction times. This explanation is supported by the observation that if the $[M + 105]^+$ ion is isolated and held in the trap for a few milliseconds, protonated acetophenone (*m/z* 121) appears in the spectrum. The $[M - OH]^+$ hydroxy abstraction ion (*m/z* 57) decreases over the reaction time since it reacts with 2-methylpropan-2-ol to produce *m/z* 113, which increases initially and then levels off at reaction times greater than 50 ms. The principal fragment ion (*m/z* 123) decreases

Table 1 Product ions observed for the reaction of $[C_6H_5CO]^+$ with some hydroxy containing compounds (% relative abundance)

Compound	$[M + 105]^+$	$[M - OH]^+$	$[M - H]^+$	Other ions
2-Methylpropan-2-ol	179 (100%)	57 (4%)	—	113 (15%) 123 (8%), 141 (3%)
Butan-2-ol	179 (55%)	—	73 (21%)	123 (100%), 129 (23%) 147 (13%), 131 (11%)
Butan-1-ol		no reaction		
Cyclohexanol	—	—	99 (100%)	—
Benzhydrol	—	167 (100%)	—	—
Benzyl alcohol	—	91 (100%)	—	197 (19%), 181 (17%) 169 (8%), 211 (6%)
Pentafluorobenzyl alcohol		no reaction		
Phenol		no reaction		
trans-Cyclopentane-1,2-diol	207 (71%)	—	—	189 (100%), 67 (16%)
cis-Cyclopentane-1,2-diol		no reaction		
Flutriafol[a]	406 (26%)	284 (100%)	—	
Fluconazole[b]	411 (100%)	289 (43%)	—	248 (12%)
4-(2-Hydroxyethyl)-2-oxoindole	282 (23%)	160 (100%)	—	

[a] 1-(2-Fluorophenyl)-1-(4-fluorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanol. [b] 2-(2,4-Difluorophenyl)-1,3-bis(1*H*-1,2,4-triazol-1-yl)propan-2-ol.

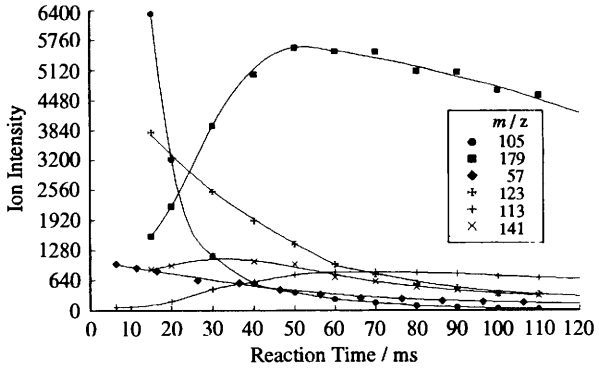


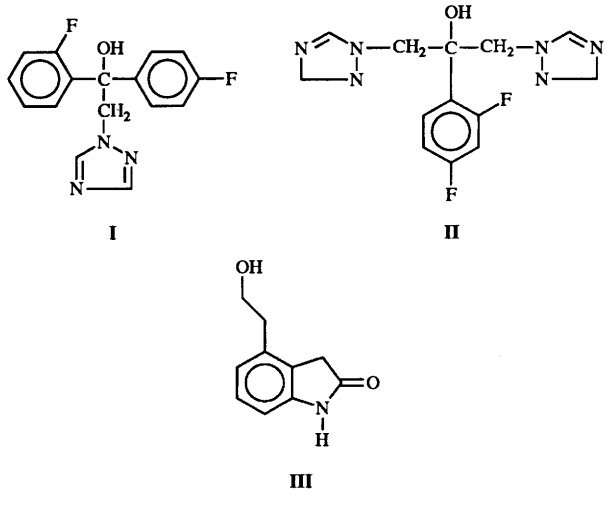
Fig. 2 Ion intensity *vs.* reaction time for the reaction between $[C_6H_5CO]^+$ and 2-methylpropan-2-ol

throughout the reaction times, as does the product of its reaction with water, *m/z* 141, probably as a result of a deprotonation reaction with acetophenone.

The reaction products of $[C_6H_5CO]^+$ with a selection of hydroxy containing compounds in the ion trap are summarised in Table 1. Butan-2-ol reacts to produce the characteristic $[M + 105]^+$ adduct ion and an $[M - H]^+$ ion resulting from hydride abstraction, but not the $[M - OH]^+$ ion observed for 2-methylpropan-2-ol. No reaction is observed with butan-1-ol. The other aliphatic alcohol studied, cyclohexanol, yielded only the $[M - H]^+$ ion on reaction with $[C_6H_5CO]^+$. In contrast, the aromatic benzyl alcohol and benzhydrol (diphenylmethanol) both produce strong $[M - OH]^+$ hydroxy abstraction ions, with no adduct formation or hydride abstraction observed, but benzoylation of phenol does not occur in the trap. These reactions are consistent with the known thermochemistry of the benzoyl ion. The formation of benzoic acid from $[C_6H_5CO]^+$ is strongly exothermic ($\Delta H_f \sim -999$ kJ mol^{-1} under standard conditions) and the reaction to form $[M - OH]^+$ from the neutral precursor might therefore be expected to be favoured so long as hydroxy abstraction is endothermic by less than this amount. Hence, the $[C_7H_7]^+$ ion is observed as the only product for the reaction of the $[C_6H_5CO]^+$ ion with benzyl alcohol since this reaction is exothermic ($\Delta H_r = -24$ kJ mol^{-1}). However, the $[C_4H_9]^+$ ion is not formed from the reaction of the benzoyl ion with butan-1-ol or butan-2-ol, since both these reactions are endothermic ($\Delta H_r = +125$ and $+62$ kJ mol^{-1}, respectively), as is that for phenol ($\Delta H_r = +292$ kJ mol^{-1}). A weak $[Bu^t]^+$ ion is detected following the reaction with 2-methylpropan-2-ol, even though the overall reaction is slightly endothermic ($\Delta H_r = +6$ kJ mol^{-1}). The reaction leading to the appearance of the $[M - H]^+$ from butan-2-ol, is also calculated to be slightly endothermic ($\Delta H_r = +8$ kJ mol^{-1}), taking the formation of benzaldehyde from $[C_6H_5CO]^+$ to be exothermic by 742 kJ mol^{-1}. However the effective temperature of an ion in the quadrupole ion trap is a complex function of the trap temperature and the applied radio frequency voltages and this will influence these weakly endothermic reactions.[23]

trans-Cyclopentane-1,2-diol reacts with $[C_6H_5CO]^+$ to produce a strong $[M + 105]^+$ adduct ion (71%), which dehydrates to yield the base peak ion at *m/z* 189 (Table 1). In contrast, *cis*-cyclopentane-1,2-diol does not react because the configuration of the *cis*-isomer favours intramolecular hydrogen bonding between the hydroxy groups which prevents adduct formation with the benzoyl ion. The electrophilic addition reaction therefore provides a simple method to distinguish between these isomeric forms.

There is no reaction between $[C_6H_5CO]^+$ and pentafluorinated benzyl alcohol, as the strong withdrawing effect of the fluorine atoms causes the lone pairs on the oxygen to be less available for bonding. Flutriafol (**I**) (a broad-spectrum systemic



I **II**

III

fungicide, Zeneca, UK), fluconazole (**II**) (an anti-fungal drug, Pfizer, UK) and 4-(2-hydroxyethyl)-2-oxoindole (**III**) (an intermediate in the production of Ropinirole, an anti-Parkinson's drug, SB, UK) all produce strong $[M - OH]^+$ ions (Table 1), as expected for hydroxy-containing compounds with an adjacent aromatic ring. Adduct ions are also formed between $[C_6H_5CO]^+$ and the nitrogen-containing compounds **I**–**III**. These observations on the reactivity of the range of hydroxy-containing compounds listed in Table 1, suggest that the $[C_6H_5CO]^+$ ion interacts with the hydroxy functional

group in a specific and predictable way, making it a potentially useful probe for the presence and chemical environment of hydroxy groups.

The behaviour of the benzoyl ion towards a number of carboxylic acids (4-chlorobenzoic acid, phenylacetic acid, isobutyric acid), ethers (anisole, diphenyl ether, ethyl phenyl ether), ketones (benzophenone, acetophenone), amines (diethylamine, benzylamine, butylamine, *sec*-butylamine, *tert*-butylamine, aniline) and molecules containing a carbon–carbon double bond {styrene and dienstrol [4,4′-(diethylideneethylene)diphenol]} has also been investigated. Amines and molecules containing a carbon–carbon double bond reacted with the $[C_6H_5CO]^+$ ion in the lower pressure regime (*ca.* 10^{-3} Torr) of the quadrupole ion trap mass spectrometer,[24] but none of the acids, ketones or ethers yielded ionic products. This is in contrast to the reactivity of the benzoyl ion with anisole, which has been reported in the 90–650 Torr region.[7] This difference in reactivity probably arises because of the slow rate of collisional stabilisation of the excited adduct ion relative to the dissociation of the adduct that occurs inside the ion trap, the dominant process in this case being the dissociation of the adduct to yield the reactants. At much higher pressures (*e.g.* 760 Torr) the rate of collision cooling of the excited adduct ion population exceeds that of the reverse reaction, making back dissociation the less favoured pathway.

Molecular modelling studies of the electrophilic addition of $[C_6H_5CO]^+$ to 2-methylpropan-2-ol suggest that the adduct formed initially (**a**, Scheme 2) is unstable, since no energy minima could be found. However, rearrangement to **b**, which has the proton on the carbonyl oxygen, gave a stable adduct. The formation of adduct **b** with 2-methylpropan-2-ol was calculated to be exothermic by 85 kJ mol^{-1}, whilst production of $[M - OH]^+$ from this adduct was calculated to be endothermic by 93 kJ mol^{-1}. These observations support the view that formation of the $[M - OH]^+$ ion proceeds preferentially *via* adduct ion **a** and that this pathway competes with formation of the more stable adduct ion, **b**. This is further supported by a comparison of the collisionally activated dissociation (CAD)[25] tandem mass spectrum of the *m*/*z* 179 ion formed by the reaction of the benzoyl ion with 2-methylpropan-2-ol, with the spectrum of the $[M + H]^+$ ion of *tert*-butyl benzoate generated by ammonia chemical ionisation of the parent compound, which is also expected to have the structure **b**. Both precursor ions yielded the *m*/*z* 123 product ion *via* the loss of butene, suggesting that **b** is the most likely structure of the *m*/*z* 179 ion, whilst the *m*/*z* 57 ion expected from structure **a** was not observed. The reaction of $[C_6H_5CO]^+$ with hydroxy-deuteriated 2-methylpropan-2-ol, $(CH_3)_3COD$, produced a 1:3 intensity ratio for the deuteriated and undeuteriated $[M + 105]^+$ adduct ions, indicating that proton transfer might not be a simple rearrangement, but may involve an intermolecular exchange *via* a third body.

The formation of the rearranged carbonyl-protonated product analogous to **b** for the benzoylation of benzyl alcohol was calculated from molecular modelling data to be exothermic by 102 kJ mol^{-1} and production of $[M - OH]^+$ from this rearranged ion was calculated to be endothermic by 110 kJ mol^{-1}. The transfer of the hydroxy group must therefore occur rapidly following electrophilic addition of the benzoyl ion, since $[M - OH]^+$ is the only product ion observed for benzyl alcohol. The formation of the rearranged carbonyl protonated adduct with butan-1-ol was calculated to be exothermic by 95 kJ mol^{-1} but the electrophilic addition production was also not detected for the reaction with the benzoyl ion. Generation of the $[M - OH]^+$ and $[M - H]^+$ ions from the stable adduct were calculated to be endothermic by 112 and 95 kJ mol^{-1}, respectively, and these ions were likewise not detected. These observations are explained if the rearrangement to the more stable adduct is less favoured than the dissociation pathway for the electrophilic addition product of butan-1-ol.

Ion trap operating conditions were observed to have a considerable influence on the reactions of the benzoyl ion. The effect of helium pressure on the stability of the adduct was investigated at three different helium pressures, 1×10^{-4}, 8×10^{-5} and 5×10^{-5} Torr (uncorrected ion gauge reading) for the reaction of 2-methylpropan-2-ol with the benzoyl ion. At a helium pressure of 1×10^{-4}, the adduct ion intensity was observed to increase (11% higher), relative to the intensity at 3×10^{-5} Torr. Decreased fragmentation was also observed at this higher helium pressure, 4% less relative to the fragment intensity at 8×10^{-5} Torr. At the lowest helium pressure of 5×10^{-5} Torr, decreased adduct ion intensity was observed (21% less relative to adduct ion intensity at 8×10^{-5} Torr) and increased fragmentation (8% higher relative to fragment ion intensity at 8×10^{-5} Torr). The adduct therefore appears to be more efficiently collisionally stabilised at higher helium pressures, resulting in an increased intensity of the adduct ion and less fragmentation. These observations are consistent with the differing reaction pathways noted earlier for the interaction of the benzoyl ion with anisole in the ion trap and 90–650 Torr pressure regimes.

The effect of varying the kinetic energy of the benzoyl ion was studied for the product ion distribution of the reaction with 2-methylpropan-2-ol. The kinetic energy of ions in the quadrupole radio frequency field of an ion trap is related to their q_z value, given by eqn. (1), where V is the applied radio

$$q_z = -4eV/mr_0^2\Omega^2 \quad (1)$$

frequency voltage amplitude, e is the charge on the ion, m is the mass of the ion, r_0 is the internal radius of the trap ring electrode and Ω is the angular frequency of the radio frequency field. Ions having a larger q_z value will possess greater kinetic energy and storing the benzoyl ion at a high q_z value during the reaction period therefore 'heats' the reactant, allowing the effect on the benzoyl ion and product abundances to be studied.

Increasing the q_z of the benzoyl ion resulted in a decrease in the relative rate of the reaction, illustrated in Fig. 3 by the slopes of the lines for ln [**I**] *vs.* time at three different q_z values (at a q_z of 0.17 the line deviates from linearity at reaction times below 30 ms, but the reason for this is not clear). The faster rate of decrease in the $[C_6H_5CO]^+$ intensity at low q_z is accompanied by a corresponding increase in the $[M + 105]^+$ adduct ion intensity. These spectral changes may be attributed to a decreased rate of formation of the adduct. Increasing the q_z value of the benzoyl ion during the reaction period is therefore less favourable for adduct and product ion formation.

The reactions of the substituted benzoyl ions $[C_6X_5CO]^+$ (X = H, F, 4-Me or 3,5-di-*tert*-butyl) were investigated in the quadrupole ion trap to determine the influence of substitution on the relative reactivities of these ions and the observed ionic products. Table 2 shows the product ion abundances for the reactions of these substituted benzoyl ions with some oxygenated compounds. $[C_6F_5CO]^+$ is a much stronger electrophile than $[C_6H_5CO]^+$ because of the electron-withdrawing properties of the fluorine substituents. This causes the ion to be significantly more reactive, forming an $[M - OH]^+$ ion with isobutyric acid and an $[M + 195]^+$ adduct ion with diphenyl ether and phenol, as well as the expected reaction products with benzyl alcohol and 2-methylpropan-2-ol. In the reaction with 2-methylpropan-2-ol, increased intensity for the $[M - OH]^+$ ion was observed compared with the $[C_6H_5CO]^+$ ion. In contrast, $[3,5\text{-}(Bu^t)_2C_6H_5CO]^+$ is a much weaker electrophile, because of the electron-donating properties of the *tert*-butyl groups. This results in the ion being unreactive towards all of the oxygenated compounds in Table 2. The $[4\text{-}CH_3C_6H_4CO]^+$ and $[C_6H_5CO]^+$ ions show reactivities which are intermediate between the pentafluoro- and di-*tert*-butyl-substituted ions, with the $[4\text{-}CH_3C_6H_4CO]^+$ the weaker

Table 2 Product ions observed for the reactions of substituted benzoyl ions (% relative abundance)

Compound	$[C_6F_5CO]^+$	$[C_6H_5CO]^+$	$[4\text{-}CH_3C_6H_4CO]^+$	$[(C_4H_9)_2C_6H_3CO]^+$
2-Methylpropan-2-ol	$[M + 195]^+$ (33%) $[M - OH]^+$ (7%) $[C_6F_5CO_2H]^+$ (100%)	$[M + 105]^+$ (100%) $[M - OH]^-$ (4%)	$[M + 119]^+$ (20%) $[M + 119 - C_4H_8]^+$ (100%)	no reaction
Benzyl alcohol	$[M - OH]^+$ (100%)	$[M - OH]^+$ (100%)	$[M - OH]^+$ (100%)	no reaction
Phenol	$[M + 195]^+$ (100%)	no reaction	no reaction	no reaction
Isobutyric acid	$[M - OH]^+$ (100%)	no reaction	no reaction	no reaction
Diphenyl ether	$[M + 195]^+$ (100%)	no reaction	no reaction	no reaction

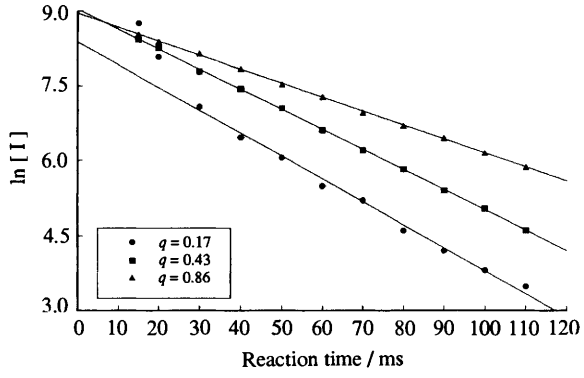


Fig. 3 ln [I] for $[C_6H_5CO]^+$ ion intensity *vs.* reaction time at three different q_z values

electrophile of the two because of the electron donating properties of the methyl group.

The potential of these benzoyl ions as selective chemical ionisation reagents was investigated for the reactions of $[C_6H_5CO]^+$, $[4\text{-}CH_3C_6H_4CO]^+$ and $[C_6F_5CO]^+$ with the product-related intermediates of 2-(8-phenyloctyl)benzaldehyde (POB) (the precursor of SK & F104353, a peptidoleukotriene antagonist). Fig. 4(*a*) illustrates the total ion current observed for the EI GC–MS analysis of these intermediates. The products of the ion–molecule reactions of the benzoyl ions with these intermediates in the ion trap are shown in Fig. 4(*b*)–(*d*). In each case residual precursor was removed from the trap by resonance ejection prior to the spectral acquisition scan. The benzoyl ion reacts with only four components of the mixture; benzyl alcohol, 7-phenylheptene, bibenzyl and 7-phenylheptyl alcohol [Fig. 4(*b*)]. Both hydroxy-containing compounds react to produce an $[M - OH]^+$ hydroxy abstraction ion as expected for these aromatic alcohols (Table 1). 7-Phenylheptene forms an $[M + 105]^+$ adduct ion and bibenzyl undergoes a side reaction, which leads to the formation of $M^{+\bullet}$ by charge exchange. The selective ionisation reactions of the $[C_6H_5CO]^+$ ion thus greatly simplify the chromatogram and allow some assignment of functionality.

The reactions of the pentaflurobenzoyl ion, a much stronger electrophile than $[C_6H_5CO]^+$, are illustrated in Fig. 4(*c*). The greater reactivity of this ion is apparent from the larger number of components which undergo ionising reactions. Benzyl alcohol yields product ions as before, and 7-phenylheptyl alcohol produces $[M - OH]^+$, $[M + 195 - H_2O]^+$ and fragment ions from the hydroxy abstraction ion. However, the greater electrophilicity of the $[C_6F_5CO]^+$ ion also results in formation of an $[M - Cl]^+$ chloride abstraction ion from the reaction with benzyl chloride. Similarly, 7-phenylheptyl chloride produces an $[M + 195]^+$ adduct and an $[M - H]^+$ ion. The reaction with *o*-tolualdehyde produces an adduct ion at *m/z* 315, an $[M - OH]^+$ hydroxy abstraction ion and an $[M - H]^+$ hydride abstraction ion. An ion at *m/z* 119 is produced from the reaction with 7-phenylheptene, which is assigned to $[M + 195 - C_6F_5COC_4H_7]^+$. $[M + 195]^+$, $[M + 195 - H_2O]^+$ and $M^{+\bullet}$ are also all formed from the reaction with bibenzyl.

Fig. 4(*d*) illustrates the reactions of the 4-methylbenzoyl ion, a weaker electrophile than $[C_6H_5CO]^+$, with the product-related intermediates of POB. Only one reaction is observed, with benzyl alcohol to produce the characteristic $[M - OH]^+$ ion. These observations confirm that the electrophilic nature of the benzoyl ion is strongly influenced by variation of the ring substituents, allowing its selectivity to be controlled. The ion–molecule chemistry of the benzoyl ion therefore has potential as a selective chemical ionisation technique in structural and trace analysis with product ion distributions allowing functional group assignment.

Conclusion

The $[C_6X_5CO]^+$ ions react within the pressure and time regimes of the quadrupole ion trap mass spectrometer with compounds containing a hydroxy functionality to yield characteristic $[M + C_6X_5CO]^+$, $[M - OH]^+$ and $[M - H]^+$ products. Product distributions are determined by the structure of the hydroxy compound, making it a potentially useful probe for establishing the presence and chemical environment of hydroxy groups. The benzoyl ions also undergo reactions with alkenes resulting in adduct formation. Storing the benzoyl ion at a low q_z value during the reaction period, as well as at increased pressure, stabilises adduct formation. The gas-phase chemistry of the benzoyl ions in the quadrupole ion trap is strongly influenced by the substituents on the phenyl ring.

Experimental

Experiments were performed using a quadrupole ion trap mass spectrometer (Finnigan MAT ITMS, San Jose, CA), operated at 120 °C. All chemicals were obtained from Aldrich Chemical Co. (Dorset, UK), except *tert*-butyl benzoate (TCI, Japan), and used without further purification. Liquid samples were introduced *via* a leak valve (Meggitt Avionics, Portsmouth, UK) and solid samples on a solids probe. The product related intermediates of POB were obtained from SmithKline Beecham R & D (Tonbridge, UK) and introduced using a Varian 3400 gas chromatograph coupled to the quadrupole ion trap. The capillary column used to separate the components was a 30 m × 0.25 mm id DB17 column (J & W Scientific, California, USA). The GC conditions were as follows: injector temperature, 280 °C; transfer line, 250 °C; 1 mm^3 splitless injection (split flow at 30 cm^3 min^{-1}); helium head pressure, 15 psi. The column oven temperature was 40 °C for 1 min, raised to 280 °C at 20 °C min^{-1} and held for 10 min.

In a typical experiment, the benzoyl ion was generated as an electron ionisation fragment of acetophenone, isolated using

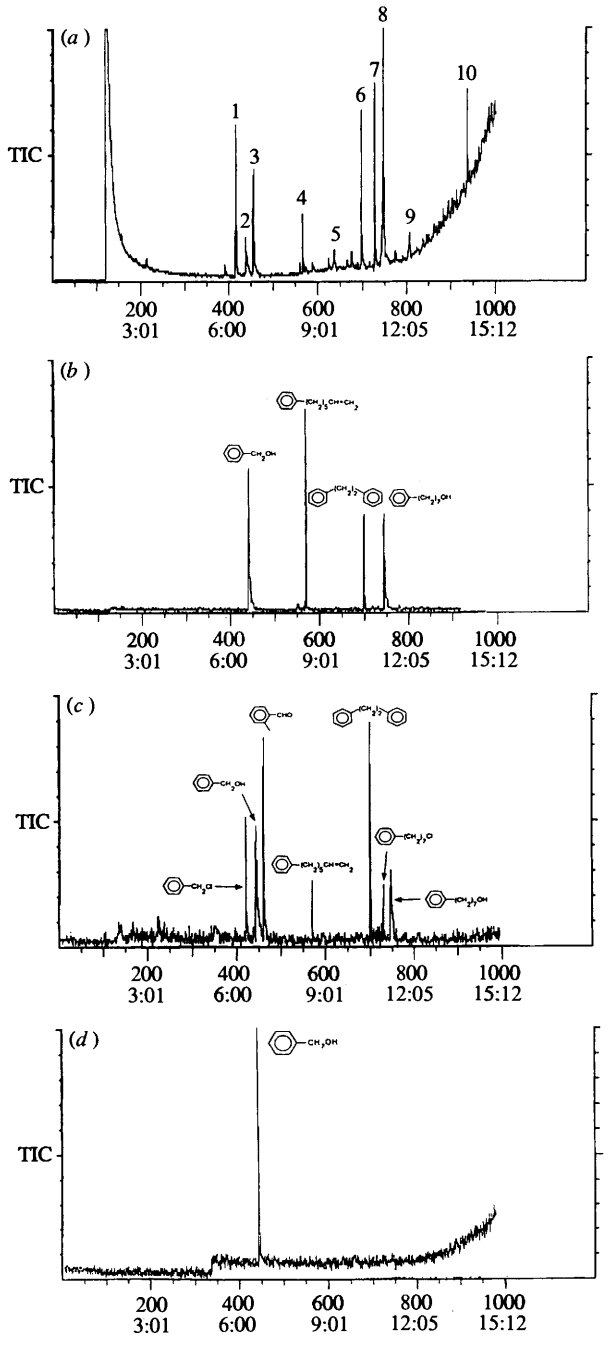


Fig. 4 (*a*) Total ion current (TIC) trace for the EI GC–MS of product related intermediates of POB. Elution order: 1 = benzyl chloride, 2 = benzyl alcohol, 3 = *o*-tolualdehyde, 4 = 7-phenylheptene, 5 = SB205268, 6 = bibenzyl, 7 = 7-phenylheptyl chloride, 8 = 7-phenylheptyl alcohol, 9 = 1,10-dichlorodecane, 10 = diphenyloctane. (*b*) TIC for the products of the reactions of $[C_6H_5CO]^+$ with the product related intermediates of POB. (*c*) TIC for the products of the reactions of $[C_6F_5CO]^+$ with the product related intermediates of POB. (*d*) TIC for the products of the reactions of $[4\text{-}MeC_6H_4CO]^+$ with the product related intermediates of POB.

resonance hole isolation,[26] and allowed to react with neutral sample vapour for 10–110 ms. Reaction times were varied using key sequences[27] to increase automatically the reaction time. Total reaction times were calculated from the end of the benzoyl ion isolation period, taking into account electron multiplier warm-up and the time taken to eject the benzoyl ion. For ions lighter than the benzoyl ion, the total reaction time was calculated up to the time taken to eject those ions. Slight changes to the ionisation time were needed to ensure similar initial benzoyl ion intensities were present at the different q_z values of 0.17, 0.43 and 0.86.

Pulsed valve introduction of reagent was carried out using a modified automobile fuel injector (Bosch, part no. 02EAC 4866) and a simple power supply was designed and built to drive the valve. For pulsed introduction of acetophenone, the pulsed valve was positioned inside the vacuum manifold, just above the ion trap, which was assembled without the Teflon spacers between the ring and end cap electrodes to aid removal of the neutral acetophenone. The time taken for the acetophenone to be removed from inside the trap was calculated by introducing a pulse of acetophenone, followed by a variable delay before electron ionisation of residual sample. The resulting $[C_6H_5CO]^+$ intensity gave an indication of how much neutral sample vapour was still resident inside the trap. These experiments established that the acetophenone concentration in the ion trap fell to 10% of the peak pulse concentration within 5 ms of the start of the pulse.

The $[C_6F_5CO]^+$ and $[4\text{-}MeC_6H_4CO]^+$ ions were generated as EI fragments from 2′,3′,4′,5′,6′-pentafluoroacetophenone and 4′-methylacetophenone respectively. The $[3,5\text{-}(Bu^t)_2C_6H_3CO]^+$ ion was generated as an ammonia CI fragment of 3′,5′-di-*tert*-butylbenzoic acid. Reagent pressure was 2×10^{-6} Torr and sample pressures were typically 5×10^{-6} Torr. Helium bath gas pressure was maintained at 1×10^{-4} Torr (uncorrected). All pressures were measured by the ion trap vacuum chamber ion gauge.

Thermochemical data were taken from references 28 and 29 unless otherwise stated. Molecular modelling was carried out on a Silicon Graphics 4D35 Personal Iris machine using the VAMP programme (version 4.5),[30] with the PM3 hamiltonian,[31] using the 'PRECISE' keyword. Final geometries were characterised as true minima by the absence of negative eigenvalues in the Hessian matrix.

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