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Ion/molecule reactions involving ionized toluene or ionized methyl benzoate and neutral methyl isocyanide

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Abstract

Ion/molecule reactions involving toluene and methyl isocyanide have been performed in a new rf-only hexapole collision cell recently installed in a large-scale tandem mass spectrometer. Among the various ionized products identified, indole derivatives have been characterized by collisional activation and result from the intermediacy of hydrogen-bridged radical cations and covalently bound dimers. Quantum theoretical computations support these experimental findings. A covalently bound dimer is also proposed in the ion/molecule reaction between ionized methyl benzoate and methyl isocyanide; such a dimer is nevertheless not detected due to the large exothermicity of the reaction leading to the ultimate products ascribed to *N*-methyl benzonitrilium ion, carbon dioxide and a methyl radical.

Keywords: Ion/molecule reaction; Toluene; Methyl benzoate; Methyl isocyanide; Quantum theoretical calculation

1. Introduction

Methyl isocyanide (CH_3NC, MIC) has proved to be an efficient neutral reagent for the identification of ions pertaining to the distonic [1] or distonoid [2] families. As the result of its relatively high ionization energy (11.24 eV) [3], charge exchange is usually not allowed and therefore structurally diagnostic reactions can take place. Moreover, due to its high dipole moment (3.85 D) [4], association with radical cations is expected to be highly favorable initiating a quite peculiar ion chemistry. A similar situation holds for the isomeric cyanide (CH_3CN) and the generation and the chemistry of acrylonitrile dimeric radical cations has been nicely described in a recent report [5].

In this context, we have studied the interaction of several ionized arenes with neutral MIC and the particular case of ionized toluene constitutes the principal aim of the present report. The results are thereafter extended to the reaction of ionized methyl benzoate with MIC.

2. Experimental

The spectra were recorded on a hybrid tandem mass spectrometer (Waters AutoSpec 6F, Manchester) combining six sectors of $cE_1B_1cE_2ccE_3B_2cE_4$ geometry (E_i stands for electric sector, B_i for magnetic sector, and c for conventional collision cells). Typical conditions have been reported elsewhere [6,7]. Recently, an rf-only hexapole collision cell (H_{cell}) has been installed inside the six-sector instrument between E_2 and E_3, replacing an rf-only quadrupole collision cell installed about 10 years ago [7]. This cell is longer (182 mm) and presents better focussing properties over a wider mass range resulting overall in a very significant gain in sensitivity. Moreover, a Pirani gauge has also been fitted allowing accurate measurement of the vacuum within the hexapole. Typically, the pressures used were in the 10^{-3} to 10^{-4} Torr range and were adjusted (and repro-

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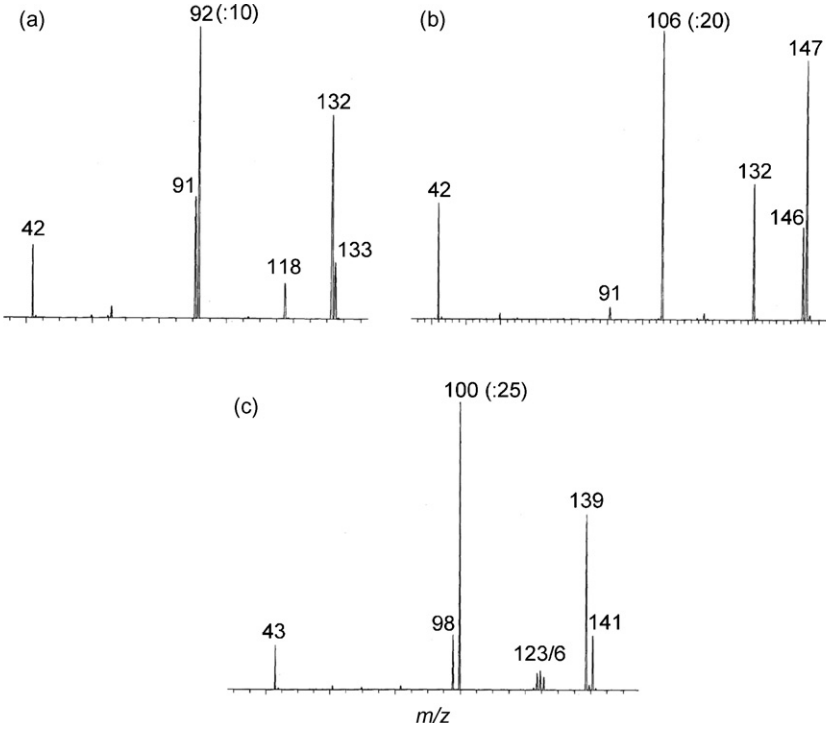


Fig. 1. Mass spectra of the ion/molecule reaction products between ionized toluene (a, *m/z* 92), ionized toluene-d_8 (b, *m/z* 100) or ionized ethyl benzene (c, *m/z* 106) and methyl isocyanide.

duced) using a Negretti needle valve. This cell allows, *inter alia*, the study of associative ion/molecule reactions [8]. Briefly, the experiments utilizing the hexapole consist of the selection of a beam of fast ions (8 keV) with the three first sectors ($E_1B_1E_2$), and the deceleration of these ions to approximately 5 eV kinetic energy, that is the voltage difference between the accelerating voltage and the floating voltage applied to the hexapole. Accurate control of this voltage is critical for maximizing the ion beam intensity and is defined by a 10-turn potentiometer, the same for the rf-voltage applied to the hexapole rods. The interaction between the ions and the reagent gas is thereafter realized in the H_{cell} and, after re-acceleration at 8 keV, all the ions generated in the hexapole are separated and mass measured by scanning the field of the second magnet. The high-energy collisional activation (CA) spectra of mass-selected ions generated in the H_{cell} can be recorded by scanning the field of E_4 after selection of the ions with E_3 and B_2.

Toluene, toluene-d_8, ethyl benzene, methyl benzoate and methyl-d_3 benzoate were commercially available and used without further purification. Methyl isocyanide was prepared according to a literature procedure [9].

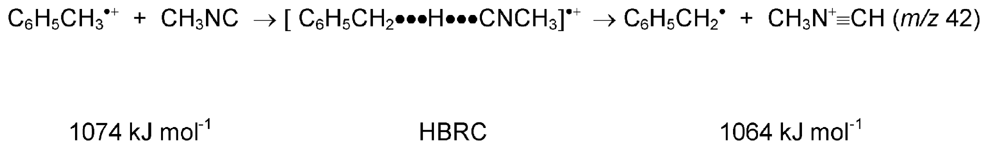
Quantum chemical calculations were carried out using the Gaussian 98 set of programs [10]. Structures were fully optimized using density functional theory with the hybrid B3LYP functional and the 6–311++G(d,p) basis set. The B3LYP/6-311++G(d,p) frequencies were scaled by 0.98 to evaluate the zero point vibrational contribution (ZPE) to the relative energies.

3. Results and discussion

3.1. Ion/molecule reactions of ionized toluene with neutral methyl isocyanide

The molecular ions of toluene (*m/z* 92) efficiently react with neutral methyl isocyanide (MIC) producing protonated MIC detected at *m/z* 42, see Fig. 1a. Based on available heats of formation [3], this proton transfer is calculated to be exothermic by 10 kJ mol^{-1} if the products are actually protonated MIC and a benzyl radical.

Such a reaction could proceed *via* an hydrogen-bridged radical cation (HBRC) as indicated in Scheme 1. One hydrogen of the methyl group of ionized toluene can be “solvated” by MIC yielding such an hydrogen-bridged radical cation. A subsequent carbon–hydrogen bond cleavage leaves the proton on the neutral with the highest proton affinity. The experimental [3] proton affinities of MIC and the benzyl radical are 843 and 833 kJ mol^{-1} respectively. These PA’s being quite similar, it is probable that



$$C_6H_5CH_3^{\bullet+} + CH_3NC \rightarrow [\, C_6H_5CH_2{\bullet\bullet\bullet}H{\bullet\bullet\bullet}CNCH_3]^{\bullet+} \rightarrow C_6H_5CH_2^{\bullet} + CH_3N^{+}{\equiv}CH\ (m/z\ 42)$$

1074 kJ mol^{-1} HBRC 1064 kJ mol^{-1}

Scheme 1.

$$[C_6H_5CH_2{\bullet}{\bullet}{\bullet}H{\bullet}{\bullet}{\bullet}CNCH_3]^{\bullet+} \rightarrow [C_6H_5CH_2CH{=}NCH_3]^{\bullet+} \rightarrow [C_6H_5CH_2C{\equiv}NCH_3]^{+}$$

HBRC CBD (*m/z* 133) CBD - $H^{\bullet}$ (*m/z* 132)

Scheme 2.

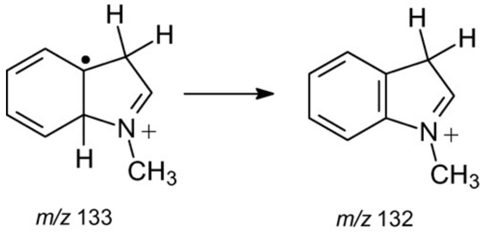
both reactions are in competition, but (re)formation of *m/z* 92 ions is in the present case a hidden reaction.

The peak at *m/z* 91 is already seen without the presence of MIC in the hexapole reaction cell and is attributed to a spontaneous loss of $H^{\bullet}$ from the metastable molecular ions. This observation is important because this reaction requires a critical energy of about 2.3 eV [12,13] and this excess of internal energy will explain why some endothermic ion/molecule reaction products are detected (*vide infra*).

The other competitive ion/molecule reaction generates *m/z* 133 ions which combine all the elements of toluene and MIC and, in fact, such a "dimer" could be the potential precursor of the other *m/z* 132 and 118 fragment ions by competitive hydrogen or methyl losses respectively. It cannot nevertheless be completely excluded that part of the *m/z* 132 ions could arise from ion/molecule reaction of the *m/z* 91 ions generated in moderate abundance by spontaneous dissociation of the toluene molecular ions, but it should however be noticed that the abundance of the *m/z* 91 ions is about 20 times lower than the abundance of the *m/z* 92 precursor ions. At this stage, we would suggest that the hydrogen-bridged species shown in Scheme 1 are partly isomerized into a covalently bound "dimer" (CBD) which further dissociates as shown in Scheme 2.

In Scheme 2, a carbon–carbon bond is created between the benzylic position and the isonitrile carbon atom with transfer of an hydrogen atom on this isonitrile carbon. The net result of this process is the formation of a *N*-methyl benzylimine structure (CBD in Scheme 2) which is certainly able to lose a hydrogen atom generating a nitrilium cation (*m/z* 132). The transition state in this process could be a three-membered CHC cyclic species bearing a positive charge. The CA spectrum of the *m/z* 132 ions is shown in Fig. 2a. The observation of an intense signal for $C_7H_7^+$ ions at *m/z* 91 is not unexpected for such a benzyl nitrilium connectivity.

When ionized ethyl benzene reacts with MIC, "dimerization" is again detected (*m/z* 147) together with consecutive losses of $H^{\bullet}$ and $CH_3^{\bullet}$, but no $C_2H_5^{\bullet}$ loss is observed (Fig. 1b), suggesting that the lost methyl radical originates from the MIC moiety. Compared to the lower homologue, relative intensities are nevertheless modified indicating an increased stability of the "dimer" and an easier loss of a methyl radical (compared to the $H^{\bullet}$ loss) perhaps because it originates at least partly from the ethyl group.



Scheme 3.

A deuterium labeled HBRC has been prepared by ion/molecule reaction starting with ionized toluene-d_8 and neutral MIC (Fig. 1c). The loss of an hydrogen atom mentioned above is cleanly replaced by a *specific* deuterium atom loss indicating that the methyl group of the isocyanide moiety is not involved at all in this cleavage. Methine deuterium loss from CBR with formation of *N*-methyl nitrilium ion could explain this specificity. An alternative mechanism could also be the intramolecular cyclisation of the imine radical cation and elimination of a ring hydrogen atom giving finally protonated *N*-methyl indole as shown in Scheme 3.

Surprisingly, the loss of a methyl radical observed for the unlabelled ions becomes much more complex for HBRC-d_8 and competitive elimination of CH_3, CHD_2, CH_2D and CD_3 radicals are now observed. This is in disagreement with the conclusion derived from the ethyl benzene/MIC experiment. Hydrogen/deuterium exchanges prior to dissociation are therefore occurring and then we have to consider various statistical situations as indicated in Table 1.

In the absence of hydrogen exchange (entry 1 in Table 1), one expects the occurrence of a single peak at *m/z* 126 or 123. Given the results obtained for ionized ethyl benzene (*vide supra*), a single loss of ${}^{\bullet}CH_3$ appeared more likely and this is actually not the case. If a complete scrambling occurs (entry 2), the loss of

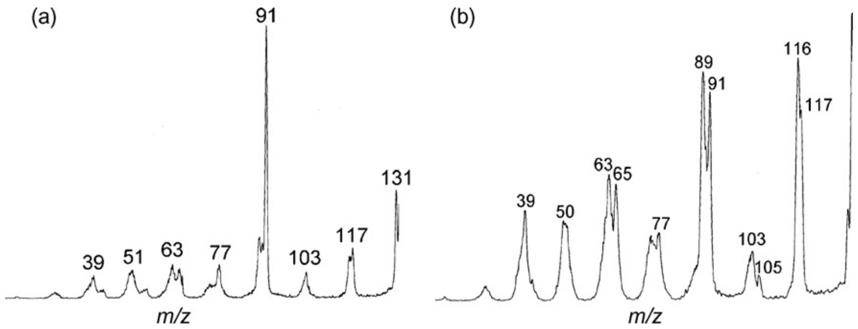


Fig. 2. CA spectrum of the *m/z* 132 ions generated by ion/molecule reactions between ionized toluene and neutral methyl isocyanide.

Table 1
Predicted abundance ratios for methyl losses from the “dimer”

		Loss of CH_3 *m*/*z* 126	Loss of CH_2D *m*/*z* 125	Loss of CHD_2 *m*/*z* 124	Loss of CD_3 *m*/*z* 123
1	Absence of hydrogen exchange	1 or –	–	–	– or 1
2	Complete scrambling	1	24	84	56
3	Partial scrambling between methyl hydrogen and ring deuterium	1	15	30	10
4	Partial scrambling between methyl hydrogen and methyl deuterium	1	9	9	1
5	Experimental results	9	12	11	1

$^{\bullet}CH_3$ should be of very low intensity and that is certainly also not the case (see entry 5). The same conclusion can be drawn for partial scrambling (entries 3 and 4).

The situation is therefore certainly more complex and, given the data of Table 1, one would suggest that two methyl loss mechanisms are at least competing. One mechanism is responsible for the specific loss of CH_3 and the second methyl loss is occurring after hydrogen exchange between both the methyl groups. That could explain the similar abundances in entries 4 and 5 of Table 1 except for the increased intensity of the *m*/*z* 126 peak. It is suggested that this specific fragmentation could be ascribed to a covalently bound complex while non-specific methyl losses requires probably the intermediacy of hydrogen bound radical cations. Extensive hydrogen rearrangements have been shown to occur frequently in alkyl aromatics as summarized in recent reports [13].

Support for this can be found in the CA spectrum of the *m*/*z* 133 ions shown in Fig. 3. The intense peak of interest is noticed at *m*/*z* 92 which could be ascribed to an ion–neutral complex $[C_7H_8{\bullet}{\bullet}{\bullet}CNCH_3]^{\bullet+}$ dissociating by loss of neutral isocyanide. This preferential loss of MIC is in keeping with the relative ionization energies of toluene (8.82 eV) and methyl isocyanide (11.24 eV). Compared to the other fragmentations, this peak moreover presents a narrower profile (small kinetic energy release) again in agreement with the formation of a non-covalently bound “dimer” [14]. Most of the other peaks, in particular the charge stripping peak at *m*/*z* 66.5, are however more likely ascribed to a covalently bound “dimer”.

The CA spectrum of Fig. 3b features a base peak for the loss of $D^{\bullet}$ (not shown) and also a surprisingly quite complex dissociation pattern. One peak of interest is noticed at *m*/*z* 100 ($C_7D_8^{\bullet+}$) which could be ascribed to the dissociation of an ion–neutral complex (INC) $[C_7D_8{\bullet}{\bullet}{\bullet}CNCH_3]^{\bullet+}$ bound dimer (formation of ionized perdeuterated toluene). The other peaks, in particular the charge stripping peak at *m*/*z* 70.5 are again more likely ascribed to a covalently bound “dimer”.

By using a linked B/E scan procedure (Fig. 3c), it becomes evident that an hydrogen/deuterium exchange has occurred and analysis of the peaks in the *m*/*z* 94–100 region suggests that other HBRC complexes such as $[C_7HD_7{\bullet}{\bullet}{\bullet}CNCH_2D]^{\bullet+}$, $[C_7H_2D_6{\bullet}{\bullet}{\bullet}CNCHD_2]^{\bullet+}$, $[C_7H_3D_5{\bullet}{\bullet}{\bullet}CNCD_3]^{\bullet+}$ are co-generated. This is also evident in the *m*/*z* 122–126 region (methyl

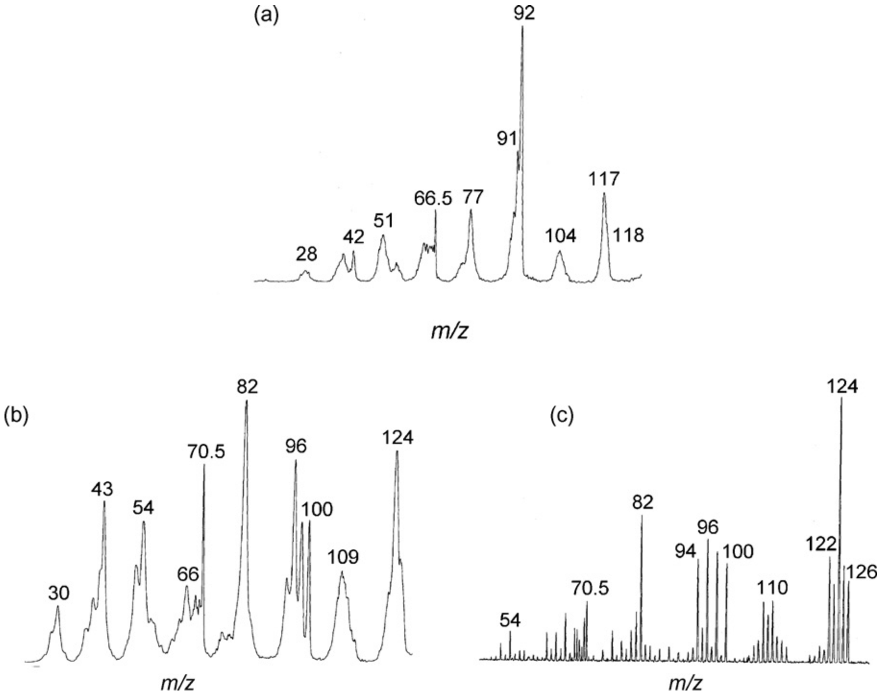


Fig. 3. CA spectrum (air collision gas) of the *m*/*z* 133 ions generated by ion/molecule reaction of ionized toluene with methyl isocyanide (a). The same spectra of the *m*/*z* 141 ions for the ion/molecule reaction of ionized toluene-d_8 with methyl isocyanide (E-scan, b) and (B/E scan, c).

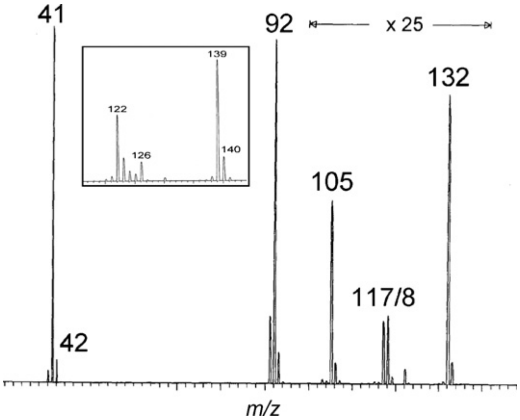


Fig. 4. Mass spectrum recorded after reaction of ionized MIC with neutral toluene in the hexapole collision cell. The inset shows the *m/z* 120–140 region of the mass spectrum recorded after reaction of ionized MIC with neutral toluene-d_8.

Table 2
Peaks observed when mass-selected methyl isocyanide ions react with neutral toluene

m/z	Possible attribution
132	Loss of $H^{\bullet}$ from a non-observed “dimer”
118	Loss of $CH_3^{\bullet}$ from the “dimer”
117	Loss of $CH_3^{\bullet}$ and $H^{\bullet}$ from the “dimer”
105	Possible loss of CHN from *m/z* 132 (not discussed in this work)
92	Charge exchange reaction; toluene molecular ions
91	Spontaneous loss of $H^{\bullet}$ from *m/z* 92
42	Hydrogen atom transfer to ionized methyl isocyanide
41	Mass-selected methyl isocyanide ions
40	Collision induced dissociation (loss of $H^{\bullet}$) from *m/z* 41

and methane losses). In contrast, such exchange is not observed for the *m/z* 82 cation corresponding to perdeuterated phenyl cations, $C_6D_5^+$. Again, we would suggest that the specific formation of the phenyl cations originates from covalently bound dimers. Mechanisms will be presented in the second part of this paper which concerns reactions between ionized MIC and neutral toluene.

3.2. Ion/molecule reactions of ionized methyl isocyanide with neutral toluene

Relative permutation of the charge, i.e., reaction of ionized methyl isocyanide with neutral toluene in the rf-only hexapole collision cell, modifies significantly the mass spectrum shown in Fig. 1a, see Fig. 4 and Table 2. This is not unexpected as the dipole moment of toluene (0.36 D) is largely much lower than the dipole moment of methyl isocyanide (3.85 D).

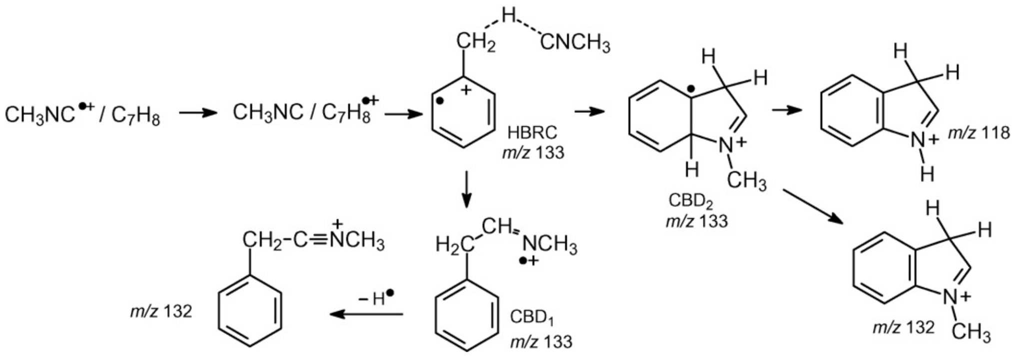
The major reaction is the charge exchange process allowed by the relative ionization energies (*vide supra*) and producing toluene radical cations (*m/z* 92). This reaction is exothermic by 233 kJ mol^{-1}, a value high enough to explain the consecutive formation of $C_7H_7^+$ cations (*m/z* 91) plus $H^{\bullet}$ that requires 216 kJ mol^{-1} [3].

The peak at *m/z* 42 corresponding to protonated MIC could arise from an hydrogen atom transfer from neutral toluene to ionized MIC. Thermochemical data indicates here again a large exothermicity amounting to 243 kJ mol^{-1}: $CH_3NC^{\bullet+} + CH_3C_6H_5$ (1307 kJ mol^{-1}) $\rightarrow CH_3N^+CH + {}^{\bullet}CH_2C_6H_5$ (1064 kJ mol^{-1}).

In the higher mass region, formation of a “dimer” is observed but with a very low intensity. Most of the ions seen at *m/z* 133 are due in fact to the isotopic peak of *m/z* 132 resulting from an hydrogen loss. The CA spectrum of these *m/z* 132 ions is shown in Fig. 2b; it is distinctively different from the spectrum shown in Fig. 2a and strong analogies are found with the spectrum of protonated *N*-methyl indole (not shown). We suggest that a mixture of isomeric species are indeed generated, the benzyl *N*-methyl nitrilium and the protonated indole structures already presented in Schemes 3 and 4 respectively.

The inset in Fig. 4 shows part of the mass spectrum recorded after reaction of ionized MIC with neutral toluene-d_8 in the hexapole collision cell. It is clear from this spectrum that the $D^{\bullet}$ loss (*m/z* 139) from the residual *m/z* 141 ions is largely favored over $H^{\bullet}$ loss (*m/z* 140, mainly the isotope peak of *m/z* 141). That was also the case in the previous experiments (*vide supra*). Other peaks are more difficult to interpret: losses of CH_3 and CD_3 are indicated by the peaks at *m/z* 126 and 123, but some H/D exchange must occur as indicated by peaks at *m/z* 125 and 124. The peak at *m/z* 122 corresponds to a loss of C, H, D_3.

On the basis of the analysis of collisional activation spectra (Fig. 5a), it is found that the *m/z* 118 ions generated in the ion/molecule reactions have clearly the structure of protonated indole. These ions result from the demethylation of a covalently bound dimer.



Scheme 4.

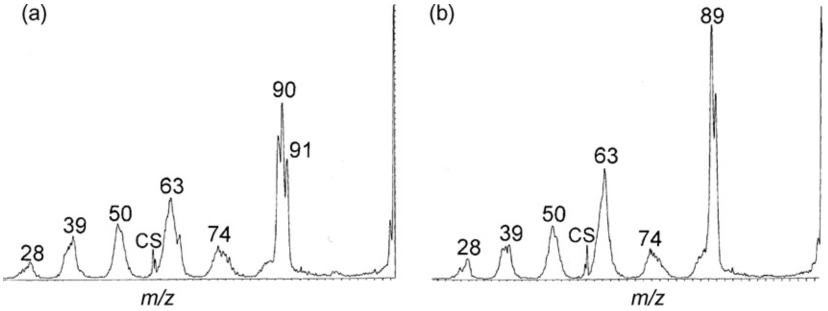


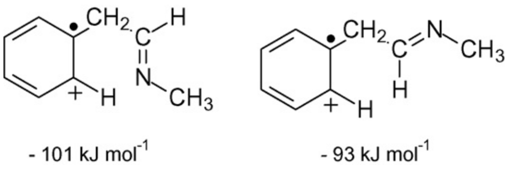
Fig. 5. CA spectra (nitrogen collision gas) of (a) *m/z* 118 ions and (b) *m/z* 117 ions generated by ion/molecule between mass-selected methyl isocyanide ions and neutral toluene.

In order to accommodate all these experimental results, we propose the following sequence of events (Scheme 4): (a) the ion–neutral complex MIC$^{\bullet+}$/toluene undergoes charge exchange into an isomeric complex MIC/toluene$^{\bullet+}$ with a stabilization energy of 233 kJ mol^{-1}; (b) this complex is isomerized into an hydrogen-bridged radical cation, then into covalently bound dimers; (c) the excess energy allows two distinct reaction channels giving a mixture of imine radical cations (CBD$_1$) and its product of cyclisation CBD$_2$; (d) the consecutive loss of a hydrogen atom from these ions yields a mixture of *N*-methyl nitrilium ions and protonated *N*-methylindole; (e) CBD$_1$ is not expected to lose easily a methyl group and thus demethylation proceeds *via* CBD$_2$ giving finally protonated indole.

Given the higher internal energy available when ionized methyl isocyanide reacts with neutral toluene, the *m/z* 118 ions could react further by hydrogen loss producing indole radical cations at *m/z* 117. Again, this is unambiguously proved by analysis of the appropriate CA spectrum (Fig. 5b). The same reaction is not accessible starting with MIC/toluene$^{\bullet+}$ due to the lower energy imparted to the "dimers". Calculated relative energies at the B3LYP level of theory have been used to support the proposed mechanisms and are summarized in the potential energy diagram presented later in this paper (see Scheme 7).

3.3. Theoretical considerations

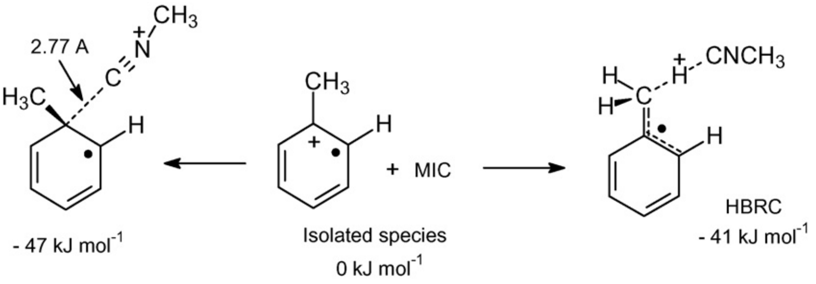
Ionization of toluene, i.e., removal of one π electron, yields *m/z* 92 molecular ions which can be formulated as indicated in Scheme 5 with the positive charge localized on the ring carbon atom bearing the methyl group (a tertiary carbocation) and the radical delocalized over five ring carbon atoms ("extended" allylic conjugation).



Scheme 6.

In such an electronic configuration, the benzylic hydrogen atoms are acidified by hyperconjugation and it is not unexpected that a strong ion–dipole interaction occurs with the high dipole moment of methyl isocyanide (3.85 D) giving *in fine* a hydrogen-bridged radical cation calculated to be more stable than the separated partners by −41 kJ mol^{-1} (Scheme 6). In fact, we have also found that another kind of ion–neutral complex linking the isonitrile carbon of MIC to the *ipso* position of ionized toluene is also a minimum on the potential energy surface (see Fig. 6a) lying 47 kJ mol^{-1} lower in energy than the isolated reagents. Such an intermediate collapses into a pure covalently bound dimer found at −59 kJ mol^{-1} which presents a plane of symmetry perpendicular to the ring (see Fig. 6b). As such a kind of ion is expected to lead to *N*-methyl benzonitrilium ions by methyl loss rather to indole ions, they were consequently not further considered. The occurrence of such intermediates will nevertheless be reconsidered in the final part of the paper where the reactivity of ionized methyl benzoate toward MIC was investigated.

Given the fact that it has been experimentally shown that benzyl *N*-methyl nitrilium ions (*m/z* 132) are, *at least partly*, generated in the ion/molecule process, it is suggested that the hydrogen-bridged radical cation is further isomerized into a covalently bound dimer having the benzyl *N*-methyl formimine



Scheme 5.

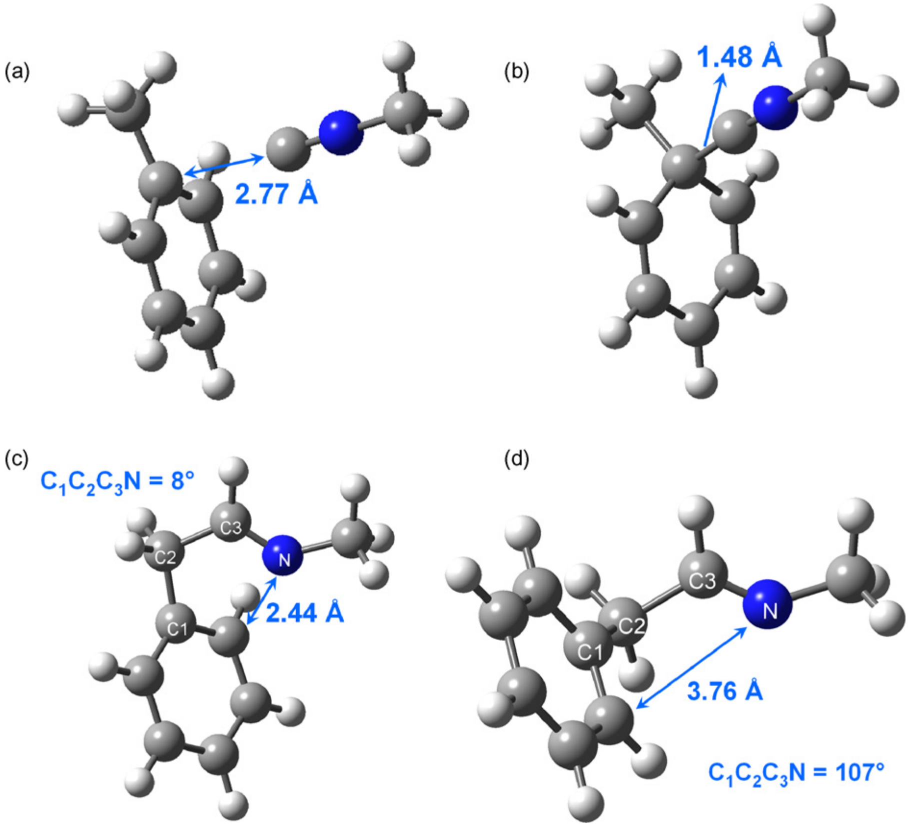
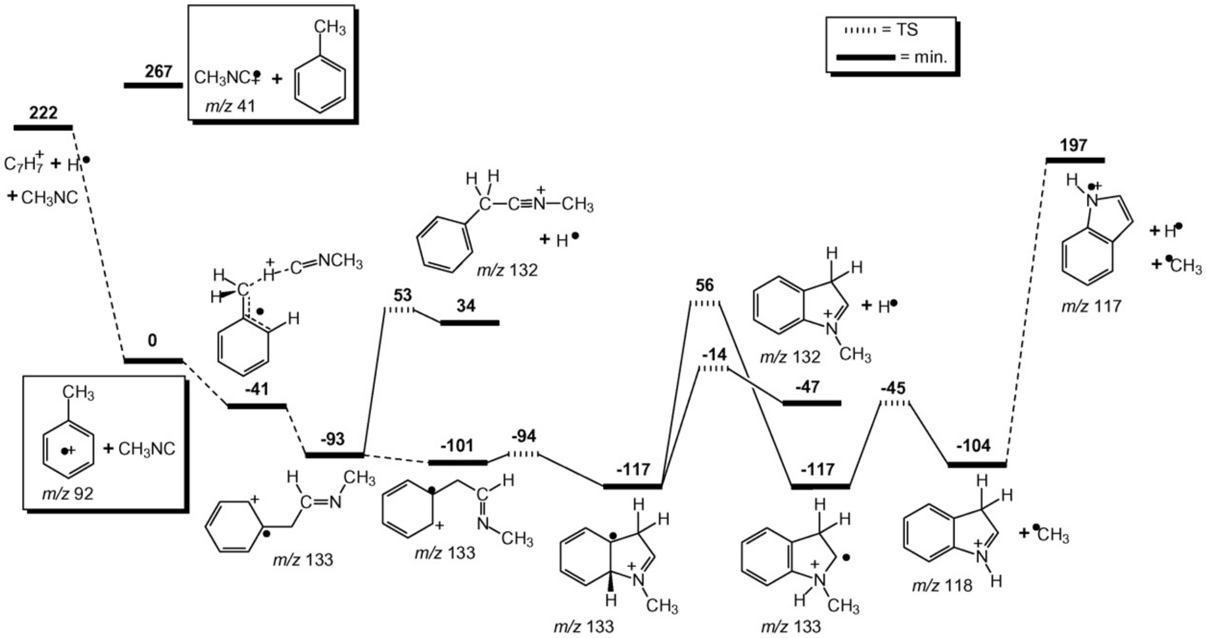


Fig. 6. Optimized structures of (a) an ion–neutral complex linking ionized toluene and MIC, (b) a covalently bound dimer linking ionized toluene and MIC at the *ipso* position and of (c and d) two conformations of ionized *N*-methyl benzylimine presenting the *E* configuration (*m*/*z* 133).

connectivity, BnCH=NMe (Bn = benzyl). At the moment, we do not have theoretical evidence to support such an isomerization, but we would like to suggest that the transition state involved should be a three-membered, positively charged, ring having therefore a partial aromatic character. Carbon–carbon bond formation concerted with an hydrogen migration simulates in fact a carbene insertion reaction within a carbon–hydrogen single bond.



Scheme 7. Proposed potential energy surface and calculated relative energies summarizing the genesis of the products detected in the ion/molecule reactions of ionized toluene with MIC. All values expressed in kJ mol^{-1} relative to isolated ionized toluene plus neutral MIC.

$$C_6H_5CH_3^{\bullet+} + CH_3NC \rightarrow [\,C_6H_5CH_2{\bullet\bullet\bullet}H{\bullet\bullet\bullet}CNCH_3]^{\bullet+} \rightarrow C_6H_5CH_2^{\bullet} + CH_3N^{+}{\equiv}CH\ (m/z\ 42)$$

1074 kJ mol^{-1} HBRC 1064 kJ mol^{-1}

Scheme 8. Major ion/molecule reaction products of isomeric $C_8H_8O_2^{\bullet+}$ radical cations with neutral methyl isocyanide [15].

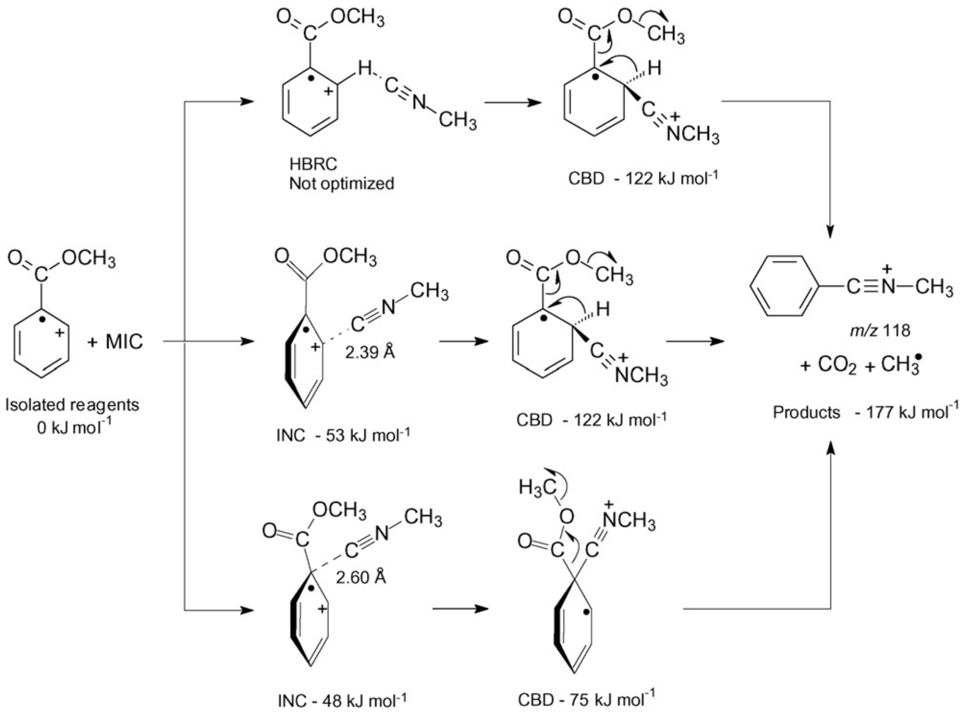
Due to the presence of the imine double bond, two geometrical isomers can exist in the *E* or *Z* configurations. We have estimated the relative energies of the *E* geometrical isomers, expected to be less hindered and therefore more stable than the *Z* configurations, considering two distinct conformations obtained by rotation around the CH_2–CH single bond (Scheme 7, see also Fig. 6c and d for geometrical parameters). The relative energies are found to be optimized at −101 and −93 kJ mol^{-1} respectively as indicated in Scheme 7. Considering that one ring π electron is involved, the greater stability of the most hindered *E* conformer could be, if the energy difference is significant, due to some favorable interaction between the cationic site and the lone pair of electrons at the imine nitrogen.

In fact, such imine radical cations are expected to lose the methine hydrogen forming a nitrilium product ion plus the hydrogen atom. This final level is calculated to lie at +34 kJ mol^{-1} with a low-lying transition state located at +53 kJ mol^{-1}. That such an endothermic process could occur in our experimental conditions is not unexpected because the reactive *m*/*z* 92 ions are not thermalized and are formed within the ion source with a broad internal energy distribution extending certainly up to 2.3 eV, i.e., the (appearance) energy [11,12] required for the observation in the mass spectrum of the *m*/*z* 91 ions resulting from metastable *m*/*z* 92 ion decomposition within the hexapole reaction cell (see Scheme 7).

As ionized indole derivatives are also detected among the products, another covalently bound dimer is probably co-generated. As shown in the formula before, the imine radical cation must adopt an appropriate configuration (around the C=N double bond) and an appropriate conformation (around de CH_2–CH single bond) to allow intramolecular cyclisation into a bicyclic species to occur. Its relative energy is estimated to be −117 kJ mol^{-1}. A low transition state energy for this cyclisation process has been found at −94 kJ mol^{-1}: this allows competition between the simple cleavage of the imine ion and the rearrangement–cyclisation reaction (Scheme 7).

Direct loss of a hydrogen atom from this intermediate should produce protonated *N*-methyl indole at an energy level of −47 kJ mol^{-1} with a low-lying transition state energy of −14 kJ mol^{-1}. Another reaction channel, namely the loss of a methyl group giving *m*/*z* 118 ions, could be due to an initial 1,2-hydrogen shift from carbon to nitrogen giving a distonic ylid species also (fortuitously) localized at −117 kJ mol^{-1} with a transition state energy of +56 kJ mol^{-1} and followed by a methyl loss with a final total relative energy of −104 kJ mol^{-1} and a transition state energy of −45 kJ mol^{-1}.

In the reaction of ionized MIC with neutral toluene, similar species as those described above are also produced. The major difference is the thermochemistry of the reaction. Vertical charge exchange allowed by the relative ionization energies of toluene



Scheme 9.

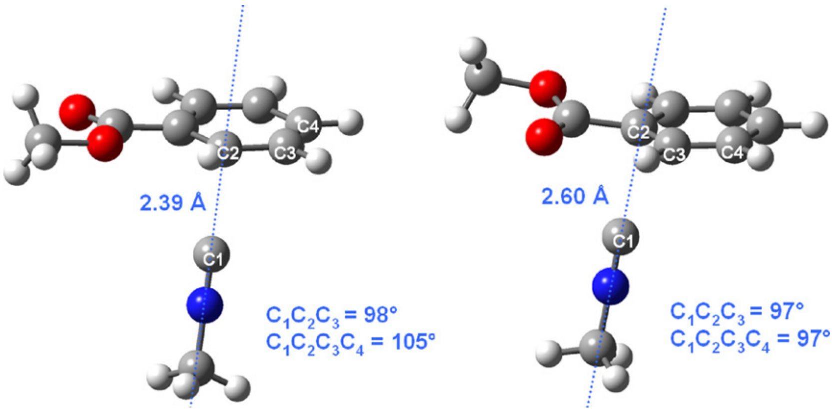


Fig. 7. Optimized structures of ion–neutral complexes involving interaction between *ortho* or *ipso* ring carbon atoms of ionized methyl benzoate and the isonitrile carbon atom (*m*/*z* 177).

and MIC produces the $C_7H_8^{\bullet+}$/MIC complex with an excess energy of at least 267 kJ mol^{-1}. That could explain why *m*/*z* 133 ions are no longer observed and also explain why a peak at *m*/*z* 117 is now observed. The loss of a hydrogen atom from protonated indole (*m*/*z* 132) requiring about 300 kJ mol^{-1} is now energetically accessible.

3.4. Ion/molecule reaction between ionized methyl benzoate and neutral methyl isocyanide

It has been previously shown that methyl benzoate molecular ions (*m*/*z* 136) efficiently react with neutral MIC to produce mainly secondary ion species at *m*/*z* 118 suggested to be the *N*-methyl benzonitrilium ions (Ph–C≡N$^+$Me). This behavior contrasts with the reactivity of isomeric $C_8H_8O_2^{\bullet+}$ species as shown in Scheme 8 [15].

Based on the results obtained on the toluene/MIC system, one suggests now that the first step consists of the generation of an ion–neutral complex which is further isomerized into a covalently bound intermediate before fragmentation. The first situation considered was the occurrence of an hydrogen-bridged radical cation as the initial step followed by isomerization into a covalently bound dimer as depicted in Scheme 9. At the level of theory used, such a “dimer” is indeed found 122 kJ mol^{-1} more stable than the isolated reagents, but all the attempts to localize the hydrogen-bridged radical cation precursor failed.

We have therefore considered the possible occurrence of other kinds of ion–neutral complexes and found that this is effectively the case if the isonitrile carbon center is approaching carbon atoms of the benzene ring. For instance, a “dimer” with a 2.39 Å distance (see Fig. 7) between the *ortho* carbon and the isonitrile carbon is indeed found to be a minimum on the potential energy surface with an energy of −53 kJ mol^{-1} relative to the isolated species. Carbon–carbon bond completion into a CBD has a total exothermicity of 122 kJ mol^{-1} which is certainly high enough to allow a subsequent [1,2] hydrogen migration initiating decarboxylation and methyl loss as indicated in Scheme 9. It has been reported that the combination of carbon dioxide and a methyl radical is more stable than a $CH_3O–C^{\bullet}(=O)$ methoxy acyl radical by 79 kJ mol^{-1} [16].

In fact, a more direct route could also involve the interaction between the isonitrile carbon and the *ipso* position of the ring of ionized methyl benzoate. Such an intermediate complex with a carbon–carbon bond distance of 2.60 Å is also found to be a minimum on the potential energy surface and lies −48 kJ mol^{-1} lower in energy than the isolated species. Carbon–carbon bond formation leads to an intermediate similar to the species proposed in radical cation mediated aromatic substitution reactions [17]. For instance, the reaction between neutral ammonia and ionized chlorobenzene leads to the displacement of the chlorine atom with the production of anilinium ions. The overall process is calculated to be exothermic with only low energy transition states explaining why the initially formed encounter complex or its *ipso*-adduction product were not detected (ion cyclotron resonance experiments) [1].

Whatever the mechanism involved, the overall exothermicity of the complete process is calculated to be −177 kJ mol^{-1}. We believe that the behavior described above for the chlorobenzene/ammonia system applies also here and it is thus reasonable to assume that this amount of energy is high enough to lead to the products. As a direct consequence, *m*/*z* 177 “dimeric” ions

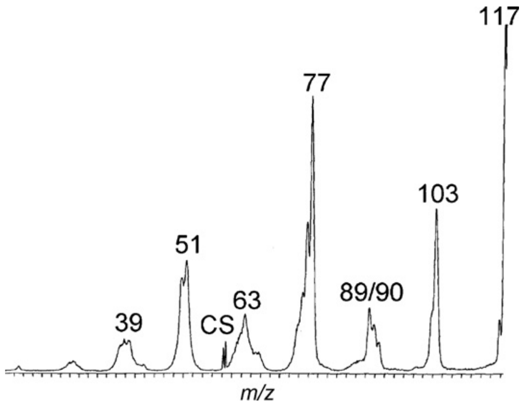


Fig. 8. CA spectrum (nitrogen collision gas) of the *m*/*z* 118 ions generated by ion/molecule reaction of ionized methyl benzoate with methyl isocyanide. The same spectrum is obtained if the *m*/*z* 118 ions are generated by ion/molecule reaction of benzonitrile with dimethyl chloronium ions in methyl chloride chemical ionization conditions.

are not expected to be an observable species in our experimental setup and this is in agreement with the experiment.

The proposed mechanism is also supported by labeling (methyl-d_3 benzoate) experiments that indicate that the lost methyl originates specifically from the ester function. Moreover, the *N*-methyl benzonitrilium structure of the so-formed ions (*m*/*z* 118) is clearly indicated by the identical CA spectra of these ions and the reference ions formed by ion/molecule reaction between dimethyl chloronium ions ($CH_3Cl^+CH_3$) and neutral benzonitrile. This reaction is indeed supposed to transfer a methyl cation at nitrogen and the presence of intense peaks at *m*/*z* 103 and 77 in the CA spectrum supports the formation of this mono-substituted benzenic structure (see Fig. 8).

4. Conclusions

Ionized toluene and neutral methyl isocyanide have been observed to form "dimeric" radical cations when allowed to react in an hexapole collision cell inserted within a field free region of a large-scale sector mass spectrometer. The unusual formation and dissociation of such ions has been interpreted on the basis of the occurrence of hydrogen-bridged radical cations and covalently bound dimers. Finally, ionized indoles (protonated *N*-methyl indole, protonated indole and indole molecular ions) have been identified among the products. Calculated relative energies at the B3LYP level of theory have been used to support the proposed mechanisms. The main product of the ion/molecule reaction between ionized methyl benzoate and methyl isocyanide has been identified as the *N*-methyl benzonitrilium ion and a mechanism again supported by theoretical considerations is presented.

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