Methyl group transfer upon gas phase decomposition of protonated methyl benzoate and similar compounds

Rafał Frański*, Błażej Gierczyk, Maciej Zalas, Wojciech Jankowski and Marcin Hoffmann

Adam Mickiewicz University, Faculty of Chemistry, Umultowska 89B, 61-614 Poznań, Poland;

* - Author for correspondence, e-mail: franski@amu.edu.pl

Gas phase decompositions of protonated methyl benzoate and its conjugates have been studied by using electrospray ionization-collision induced dissociation-tandem mass spectrometry (ESI-CID-MS/MS). Loss of CO_2 molecule, thus transfer of methyl group, has been observed. In order to better understand this process the theoretical calculations have been performed. For methyl benzoate conjugates, it has been found that position of substituent affects the loss of CO_2 molecule, not the electron donor/withdrawing properties of the substituent. Therefore ESI-MS in positive ion mode may be useful for differentiation of isomers of methyl benzoate conjugates.

Keywords: methyl benzoate, electrospray ionization, tandem mass spectrometry, methyl salicylate, methylparaben

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jms.4069

Introduction

When upon gas phase decomposition of the given ion, a certain moiety migrates from one part of the ion to another it may complicate the interpretation of the product ion spectrum. As a consequence it may hamper the structural elucidations based on the obtained product ion spectrum. On the other hand, such intramolecular transfers are very interesting from the gas phase ion chemistry point of view, therefore there is a number of examples of detailed studies of such processes. The examples involve transfer of such moieties as amino,[1] halogen,[2,3] methoxy,[4] benzyl,[5-7] tosyl,[8] trimethylsilyl,[9] oxygen,[10] alkyl,[11] hydroxyl[12] and, as expected, most examples involve transfer of methyl group.[13-20]

Very recently, it has been observed that upon gas phase decomposition of protonated benzoic acid molecule (and similar compounds) transfer of two protons occurs, which leads to the formation of protonated benzene molecule. This process has been discussed in details by Attygalle and co-workers.[21] In this work we decided to check if upon gas phase decomposition of protonated methyl benzoate (and its conjugates) the transfer of methyl group can occur. As demonstrated further, although the methyl group is definitely less prone to transfer than proton, the process occurs. It also worth adding that the loss of CO_2 molecule has been also observed for metastable methyl benzoate molecular ion (obtained by electron ionization, EI), however, in the standard EI mass spectra (70 eV) this process has not been observed (http://webbook.nist.gov/chemistry/).[22]

Experimental

Methyl benzoate, methyl hydroxybenzoates (all isomers), methyl 2-fluorobenzoate, methyl 3-fluorobenzoate, phenyl benzoate, methyl 2-naphthoate were obtained from Sigma-Aldrich (Poznań, Poland) and used without purification.

Methyl 4-fluorobenzoate, methyl 1-naphthoate, methyl 2,6-dimethylbenzoate, methyl 2,6-dichlorobenzoate, ethyl benzoate and isotope labeled methyl benzoates ($C_6H_5COOCD_3$ and $C_6D_5COOCH_3$) were prepared by esterification of respective acids (acids were obtained from Sigma-Aldrich). The esterification procedures were as follows: 200 mg of acid was dissolved in 10 ml of methanol (Sigma-Aldrich). The obtained solution, after addition of 0.5 ml of thionyl chloride was heated under reflux for 1 h and concentrated on a rotary evaporator. The oily residue was dissolved in 5 ml of ethyl ether (Sigma-Aldrich), washed three times with saturated sodium bicarbonate (POCh) water solution, dried over anhydrous sodium sulfate (Chempur) and filtered. After solvent removal by evaporation on a rotary

evaporator the white-yellowish solid product was obtained. To synthesize isotopically labelled ester $C_6H_5COOCD_3$ the same procedure was used, but the acid, CD_3OD and thionyl chloride were used in smaller amounts i.e. 100 mg, 3 ml and 0,25 ml, respectively.

In order to synthetize methyl 2,6-dichlorobenzoate, different procedure was used. A portion of 200 mg of the acid was dissolved in 3 ml of thionyl chloride and stirred for 1 h. The solution obtained was evaporated on rotary evaporator and a portion of 5 ml of methanol was then dropwise added to the oily residue and the mixture were heated under reflux for 1 h and after that the product was isolated using above described procedure.

Product ion spectra were taken on a Waters/Micromass (Manchester, UK) Q-tof Premier mass spectrometer (software MassLynx V4.1, Manchester, UK). The sample solution of bilirubin was prepared in methanol/water 3/1 at concentrations about $2x10^{-5}$ mol/L. The sample solutions were infused into the ESI source by a syringe pump at a flow rate of 5 μL/min. The electrospray voltage was 2.7 kV and the cone voltage - 30 V. The source temperature was 80^{o}C and the desolvation temperature was 250^{o}C. Nitrogen was used as the cone gas and desolvating gas at the flow-rates of 0.8 and 13 L/min, respectively. Argon was used as a collision gas at the flow-rate 0.5 mL/min in the T-wave collision cell. This flow rate resulted in the collision cell pressure 0.3 Pa. Collision energy (CE, laboratory frame) was 5-20 eV. Only representative examples were selected for presentation, taking into account the abundances of fragment ions. The applied collision energy, the most important parameter for CID-MS/MS experiments, is indicated in each product ion spectrum shown. Because of a wide window (low resolution of the quadrupole analyzer), the selected ion beam and as a consequence the signals of fragment ions, contained isotope signals. The resolution of the second analyzer (time of flight analyzer) was 5000 - FWHM definition.

Full geometry optimizations and energy calculations were performed, within DFT framework at B3LYP/6-311++G(d,p).[23-25] level of theory because B3LYP (Becke, three-parameter, Lee-Yang-Parr) is one of the most popular functional and can be applied for many different systems.[22, 26-27] 6-311++G(d,p) basis set (augmented with diffuse and polarization functions) is recommended for calculations for simple molecules that include electronegative elements and for comparisons with experiment.[28] Wiberg bond indices[29] were calculated by Natural Bond Orbital (NBO) analyse[30, 31] for bonds between the aromatic or naphthyl ring and the carboxyl carbon atom. All quantum chemical calculations were performed with the GAUSSIAN 09.[32]

Results and Discussion

Figure 1 shows the product ion spectra of protonated methyl benzoate. As shown in Figure 1, at low collision energy (CE = 7 eV) the most abundant fragment ion is that formed by CO_2 loss. At higher collision energy this fragment ion is also abundant.

FIGURE 1

It can be taken for granted that the loss of CO_2 from protonated methyl benzoate leads to the formation of protonated toluene (m/z 93). In other words, upon gas phase decomposition of protonated methyl benzoate the transfer of methyl group occurs.

In the product ion spectra shown in Figure 1 there is also a peak at m/z 91, which corresponds to the well-known, stable, tropylium (benzylium) ion.[33] The ratio of tropylium ion/protonated toluene increases with increasing collision energy. At the higher collision energy there is also the phenylium ion at m/z 77 (Figure 1). It can be assumed that both tropylium ion and phenylium ion are formed from protonated toluene (by the loss of H_2 and CH_4 molecule, respectively,[34, 35]) although their direct formation from protonated methyl benzoate cannot be definitely excluded.

In supporting information there are product ion spectra obtained for deuterium labeled methyl benzoate (Figures 1s-4s) with brief discussion which confirm the interpretation shown in Figure 1.

Since the ion under this study is protonated methyl benzoate, thus it is reasonable to determine the protonation site of methyl benzoate. Our calculations showed that for methyl benzoate the most energetically favored protonated structure is obtained when the proton is attached to the oxygen atom of the carboxyl group (Scheme 1). According to results the structure in which the proton bonded to this oxygen atom is oriented towards the aromatic ring has lower energy than the structure with proton oriented in the opposite direction (the latter was of about 2.6 kcal/mol higher in energy).

SCHEME 1

It is reasonable that the first step of the CO_2 loss from protonated methyl benzoate is analogous to the first step of the CO_2 loss from protonated benzoic acid.[21] Namely, the proton attached to carbonyl oxygen atom is transferred to the *ortho* position of the aromatic ring (protonation at *ipso* position is less favored than protonation at *ortho* position, Scheme 1). It is also reasonable that the proton transfer is accompanied by the breaking of the C-C bond between benzene ring and ester group and then hydrogen is transferred to the *ipso* position. As a consequence, we deal with formation of the ion-neutral complex $C_6H_6^{\cdots}COOCH_3^+$. Dissociation of this complex leads to the formation of low abundant ion $[COOCH_3]^+$ at m/z 59 (Figure 1) or ion $[COOCD_3]^+$ at m/z 62 (supporting information, Figure 2s and 3s). However, the main process occurring for this complex is the transfer of methyl group to the benzene ring, the loss of CO_2 molecule, and formation of protonated toluene. Such process should not be affected sterically, therefore should be also observed for protonated methyl 2,6-dimethylbenzoate. And indeed, as shown in Figure 2, the loss of CO_2 molecule occurs for protonated methyl 2,6-dimethylbenzoate.

FIGURE 2

The product ion spectrum of protonated methyl 2,6-dimethylbenzoate shows that transfer of methyl group is not sterically affected. However the question is if the process can be affected by the electron effect and if yes in which way. As shown in Figure 3 the only process that occurred upon gas phase decomposition of protonated methyl 2,6-dichlorobenzoate is the formation of benzoyl ion (loss of a methanol molecule). It is clear that because of the electron effect of chlorine atoms the loss of CO_2 molecule (thus methyl group transfer) does not occur.

FIGURE 3

In order to better understand the electron effect, the product ion spectra were obtained for protonated methyl benzoate substituted at *ortho*, *met*a and *para* positions by both electron withdrawing and electron donor substituent. Figure 4 shows the product ion spectra of methyl fluorobenzoate isomers, while Figure 5 shows the product ion spectra of methyl hydroxybenzoates isomers. Fluorine is an electron withdrawing substituent and hydroxyl group is and electron donor substituent.[36]

FIGURE 4

FIGURE 5

As clearly shown in Figures 4 and 5, the loss of CO_2 molecule is an efficient process for *met*a isomers, whereas for *ortho* and *para* isomers it is of minor importance. In other words the position of substituent affects the loss of CO_2 molecule, not the electron donor/withdrawing properties of the substituent. It can be explained on the basis of respective resonance structures. For *ortho* and *para* isomers we can deal with structures containing positive charge on the substituent and double bond between aromatic ring and carboxyl carbon atom (supporting information, Scheme 1s). The loss of CO_2 molecule requires breaking of the bond between the aromatic ring and the carboxyl carbon atom. Formation of the structure for which this bond is double (thus stronger) prevents the breaking of this bond.

We have also performed the calculations for protonated methyl fluoro- and hydroxybenzoates conjugates. Analogously as for unsubstituted methyl benzoate, the most energetically favored protonated structures are those with the proton attached to the oxygen atom of the carboxyl group (supporting information, Schemes 2s-7s). Furthermore, for the favored structures, the calculated Wiberg bond indices for bonds between the aromatic ring and the carboxyl carbon atom, for *meta* isomers are slightly lower than for *ortho* and *para* isomers (supporting information, Schemes 2s-7s).

It has to be added that besides fluorine and hydroxyl groups other groups can influence the loss of CO_2 molecule from respective protonated methyl benzoates**.** In order to minimize other effects than the electron one we have decided to check the influence of fluorine and hydroxyl moieties. For example, for an amino group, which has stronger electron donor properties than a hydroxyl group[36], we could deal with its protonation instead of protonation of carbonyl oxygen atom. For a nitro group, which has stronger electron withdrawing properties than fluorine[36], we would deal with its decomposition namely with the loss of NO molecule,[37] and this process may compete with the loss of CO_2 molecule.

If it is true that that the efficiency of the loss of CO_2 molecule can be explained on the basis of respective resonance structures, for methyl naphthoate isomers we should deal with different efficiencies of the loss of CO_2 molecule. And indeed, as shown in Figure 6 for methyl 2-naphthoate, the loss of CO_2 molecule is definitely more efficient than for methyl 1-

naphthoate. It may be explained on the basis of respective resonance structures (supporting information, Scheme 8s and 9s).

FIGURE 6

We have also performed the calculations for protonated methyl naphthoates. Analogously as for the other compounds discussed above, the most energetically favored structures were obtained when the proton was attached to the oxygen atom of the carboxyl group (supporting information, Scheme 10s and 11s). Furthermore, for the favored structures, the calculated Wiberg bond indices for bonds between the naphthyl ring and the carboxyl carbon atom, for methyl 2-naphthoate are slightly lower than for methyl 1-naphthoate (supporting information, Scheme 10s and 11s).

We have also checked if the loss of CO_2 molecule can occur for other esters of benzoic acid (other than methyl ester). In other words, we wanted to answer the question if any other moiety than that of methyl can be transferred to the aromatic ring upon gas phase decomposition of protonated ester. As shown in supporting information (Figure 5s and 6s), for protonated ethyl benzoate and protonated phenyl benzoate, the loss of CO_2 molecule does occur. Thus, the moiety other than methyl one are not transferred to the aromatic ring.

Methyl *para*-hydroxybenzoate has a number of practical applications e.g. as a food preservative (it is called methylparaben and is coded under the number E218). ESI-MS coupled with liquid chromatography, usually in negative ion mode, has been used for its analysis in various samples.[38-42] Methyl *ortho*-hydroxybenzoate (methyl salicylate) has been found in various natural sources usually by using electron ionization (EI) mass spectrometry coupled with gas chromatography.[43-46] It is worth adding that EI mass spectra of all methyl hydroxybenzoate isomers are very similar (http://webbook.nist.gov/chemistry/), which may cause a problem with their correct identification.[43] As shown in Figure 5, the product ion spectra of all methyl hydroxybenzoate isomers are substantially different. Therefore ESI-MS in positive ion mode may be useful for their identification. Obviously it requires more detailed analytical studies.

Conclusions

The loss of CO_2 molecule, thus transfer of a methyl group, occurs upon gas phase decompositions of protonated methyl benzoate and its conjugates, as demonstrated by the

respective product ion spectra. It is reasonable that this process occurs through the ion-neutral complex. For methyl benzoate conjugates, it is the substituent position that affects the process, not its electron donor/withdrawing properties. Therefore, the product ion spectra of the protonated molecules may be useful for differentiation of isomers of methyl benzoate conjugates.

Acknowledgments

This research was supported in part by PL-Grid Infrastructure.

References

[1] Z.-Y. Ju, Y. Ye, S.-B. Zhong, R.-Y. Zou, X.-C. Liao, Y.-F. Zhao. A novel rearrangement in ESI-MS^n of spirocyclic pentaerythritol di(phosphate monoamides) *Int. J. Mass Spectrom.* **2008**, *273*, 31.

[2] Y. Chai, X. Xiong, L. Yue, Y. Jiang, Y. Pan, X. Fang. Intramolecular halogen transfer via halonium ion intermediates in the gas phase. *J. Am. Soc. Mass Spectrom.* **2016**, *27*, 161.

[3] N. Picazas-Márquez, M, Sierra, C. Nova, J.M. Moreno, N. Aboitiz, G. de Rivas, M.A. Sierra, R. Martínez-Álvarez, E. Gómez-Caballero. GC-MS Study of Mono- and bishaloethylphosphonates related to schedule 2.B.04 of the chemical weapons convention: the discovery of a new intramolecular halogen transfer. *J. Am. Soc. Mass Spectrom.* **2016**, *27*, 1510.

[4] Y. Chen, Y. Yin, X. Sun, X. Liu, H. Wang, Y. Zhao. A novel rearrangement in electrospray ionization multistage tandem mass spectrometry of amino acid ester cyclohexyl phosphoramidates of AZT. *J. Mass Spectrom.* **2005**, *40*, 636.

[5] H. Sun, Y. Chai, X. Xu, Y. Pan. Intramolecular benzyl cation transfer in the fragmentation of Cinchona alkaloid-based quaternary ammonium cations. *Int. J. Mass Spectrom.* **2013**, *335*, 16.

[6] F. Li, X. Zhang, H. Zhang, K. Jiang. Gas-phase fragmentation of the protonated benzyl ester of proline: intramolecular electrophilic substitution versus hydride transfer. *J. Mass Spectrom.* **2013**, *48*, 423.

[7] Z. Yan, B. Tounge, G.W. Caldwell. An unusual intramolecular transfer of the fluorobenzyl cation between two remote amidic nitrogen atoms induced by collision in the gas phase. *Rapid Commun. Mass Spectrom.* **2012**, *26*, 49.

[8] S. Wang, L. Yu, Y. Wu, C. Guo, N. Zhang, K. Jiang. Gas-phase fragmentation of protonated *N*,2-diphenyl-*N'*-(*p*-toluenesulfonyl)ethanimidamides: tosyl cation transfer versus proton transfer. *J. Am. Soc. Mass Spectrom.* **2015**, *26*, 1428.

[9] D. Tsikas. GC–ECNICI-MS/MS of eicosanoids as pentafluorobenzyl-trimethylsilyl(TMS) derivatives: Evidence of CAD-induced intramolecular TMSether-to-ester rearrangement using carboxy-^{18}O-labelled eicosanoidsand possible implications in quantitative analysis. *J. Chromatogr.* B **201**7, *1047*, 185.

[10] J. Paulose, J. Cyriac, G. Mathai, D. Giblin, M.L. Gross. Protonated N-alkyl-2-nitroanilines undergo intramolecular oxidationof the alkyl chain upon collisional activation. *Int. J. Mass Spectrom.* **2017**, *413*, 75.

[11] J.C. Reepmeyer. Direct intramolecular gas-phase transfer reactions during fragmentation of sildenafil and thiosildenafil analogs in electrospray ionization mass spectrometry. *Rapid Commun. Mass Spectrom.* **2009**, *23*, 927.

[12] L. Svilar, V. Stankov-Jovanovic, M. Stadler, H. Nedev, J.-Cl. Tabet. Distinctive gas-phase fragmentation pathway of themitorubramines, novel secondary metabolites from *Hypoxylon fragiforme*. *Rapid Commun. Mass Spectrom.* **2012**, *26*, 2612.

[13] A.-C. Almstrand, C. Johnson, R.C. Murphy. Evidence for an N-methyl transfer reaction in phosphatidylcholines with a terminal aldehyde during negative electrospray ionization tandem mass spectrometry. *Anal. Bioanal. Chem.* **2015**, *407*, 5045.

[14] P.R. Tiller, C. Raab, C.E.C.A. HOP. An unusual fragmentation mechanism involving the transfer of a methyl group. *J. Mass Spectrom.* **2001**, *36*, 344.

[15] L. Yue, C. Guo, Y. Chai, X. Yin, Y. Pan. Gas-phase reaction: alkyl cation transfer in the dissociation of protonated pyridyl carbamates in mass spectrometry. *Tetrahedron* **2014**, *70*, 9500.

[16] J. Cui, X. Gao, A. Fan, S. Zhang, Y. Liu, P. Xua, Y. Zhao. Identification of amino acid phosphorodiamidates of antiviral nucleosides using electrospray ionisation tandem mass spectrometry. *Eur. J. Mass Spectrom*. **2011**, *17*, 187.

[17] X. Gao, G. Zhu, Z. Zeng, W. Chen, Z. Lin, Y. Liu, P. Xu, Y. Zhao. A novel methyl migration to the phosphoryl group with the formation of cyclic aminoacylphosphoramidates in electrospray ionization tandem mass spectra of amino

acid ester phosphoramidates of antiviral nucleosides. *Rapid Commun. Mass Spectrom.* **2011**, *25*, 1061.

[18] L. Xiong, L. Ping, B. Yuan, Y. Wang. Methyl group migration during the fragmentation of singly charged ions of trimethyllysine-containing peptides: precaution of using MS/MS of singly charged ions for interrogating peptide methylation. *J. Am. Soc. Mass Spectrom.* **2009**, *20*, 1172.

[19] X. Zhang, S. Yao, Y. Guo. Intramolecular methyl migration in the protonated *N*,*N*'-dimethylpropane-1,3-diamine and *N*,*N*'-dimethylethane-1,2-diamine. *Int. J. Mass Spectrom.* **2008**, *270*, 31.

[20] D.J. Lavorato, L.M. Fell, G.A. McGibbon, S. Sen, J.K. Terlouw, H. Schwarz. Identifying ylide ions and methyl migrations in the gas phase: the decarbonylation reactions of simple ionized N-heterocycles. *Int. J. Mass Spectrom.* **2000**, *195/196*, 71.

[21] S. Xu, J. Pavlov, A.B. Attygalle. Collision-induced dissociation processes of protonated benzoic acid and related compounds: competitive generation of protonated carbon dioxide or protonated benzene. *J. Mass Spectrom.* **2017**, *52*, 230.

[22] N. Dechamps, R. Flammang, P. Gerbaux, P.-C. Nam, M.-T. Nguyen. Decarboxylation of metastable methyl benzoate bolecular ions. *J. Am. Soc. Mass Spectrom.* **2006**, *17*, 807.

[23] P.J. Stephens, F.J. Devlin, C.F. Chabalowski, M.J. Frisch, Ab Initio calculation of vibrational absorption and circular dichroism spectra using density functional force fields. *J. Phys. Chem.* **1994**, *98*, 11623.

[24] K. Kim, K.D. Jordan. Comparison of density functional and MP2 calculations on the water monomer and dimer. *J. Phys. Chem.* **1994**, *98*, 10089.

[25] T. Clark, J. Chandrasekhar, G.W. Spitznagel, P.V.R. Schleyer. Efficient diffuse function-augmented basis sets for anion calculations. III. The 3-21+G basis set for first-row elements, Li–F. *J. Comput. Chem.* **1983**, *4*, 294.

[26] J. Miao, W. Xu, B. Zhu, Y. Gao, Ti12Xe: A twelve-coordinated Xe-containing molecule. *Phys. Lett. A* **2017**, *381*, 2363.

[27] D.R. Glowacki, W.J. Rodgers, R. Shannon, S.H. Robertson, J.N. Harvey. Reaction and relaxation at surface hotspots: using molecular dynamics and the energy-grained master equation to describe diamond etching. *Phil. Trans. R. Soc. A* **2017**, *375*, 20160206.

[28] R. Krishnan, J.S. Binkley, R. Seeger, J.A. Pople. Self-consistent molecular orbital methods. XX. A basis set for correlated wave functions. *J. Chem. Phys.* **1980**, *72*, 650.

[29] K.B. Wiberg. Application of the pople-santry-segal CNDO method to the cyclopropylcarbinyl and cyclobutyl cation and to bicyclobutane. *Tetrahedron* **1968**, *24*, 1083.

[30] J.P. Foster, F. Weinhold. Natural hybrid orbitals. *J. Am. Chem. Soc.* **1980**, *102*, 7211.

[31] F. Weinhold, A.E. Reed. Natural bond orbital analysis of near-Hartree-Fock water dimer. *J. Chem. Physics.* **1983**, *78*, 4066.

[32] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery, Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, N.J. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox. Gaussian 09, Revision A.1, Gaussian, Inc., Wallingford, CT, 2009.

[33] E.-L. Zins, C. Pepe, D. Rondeau, S. Rochut, N. Gallandc, J.-C. Tabet. Theoretical and experimental study of tropylium formation from substituted benzylpyridinium species *J. Mass. Spectrom.* **2009**, *44*, 12.

[34] D. Schröder, H. Schwarz, P. Milko, J. Roithová. Dissociation routes of protonated toluene probed by infrared spectroscopy in the gas Phase**.** *J. Phys. Chem. A* **2006,** *110*, 8346.

[35] O. Dopfer, J. Lemaire, P. Maître, B. Chiavarino, M.E. Crestoni, S. Fornarini. IR spectroscopy of protonated toluene: Probing ring hydrogen shifts in gaseous arenium ions. *Int. J. Mass Spectrom.* **2006**, *249-250*, 149.

[36] C. Hansch, A. Leo, R.W. Taft. A survey of hammett substituent constants and resonance and field parameters. *Chem. Rev.* **1991**, *97*, 165.

[37] K. Levsen, H.-M. Schiebel, J.K. Terlouw, K.J. Jobst, M. Elend, A. Preiß, H. Thiele, A. Ingendoh. Even-electron ions: a systematic study of the neutral species lost in the dissociation of quasi-molecular ions. *J. Mass Spectrom.* **2007**, *42*, 1024.

[38] J. Lv, L. Wang, X. Hu, Z. Ta, Y. Yang. Rapid determination of 10 parabens in spices by high performance liquid chromatography-mass spectrometry. Anal. Lett. **2012**, *45*, 1960.

[39] I. González-Mariño, J.B. Quintana, I. Rodríguez, R. Cela. Simultaneous determination of parabens, triclosan and triclocarban in water by liquid chromatography/ electrospray ionisation tandem mass spectrometry. *Rapid Commun. Mass Spectrom.* **2009**, *23*, 1756.

[40] S. Lu, S. Gong, S. Ma, X. Zeng, Z. Yu, G. Sheng, J. Fu. Determination of parabens in human urine by liquid chromatography coupled with electrospray ionization tandem mass spectrometry. *Anal. Methods.* **2014**, *6*, 5566.

[41] R. Rodríguez-Gómez, N. Dorival-García, A. Zafra-Gómez, F.J. Camino-Sánchez, O. Ballesteros, A. Navalón. New method for the determination of parabens and bisphenol A inhuman milk samples using ultrasound-assisted extraction andclean-up with dispersive sorbents prior to UHPLC–MS/MS analysis. *J. Chromatogr*. B **2015**, *992*, 47.

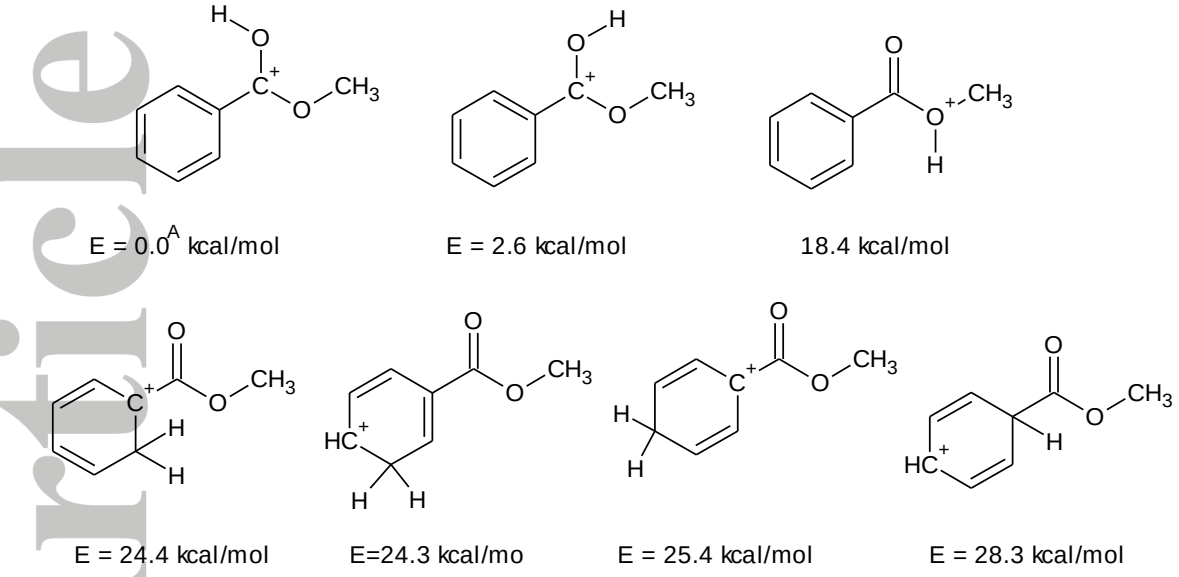
[42] L. Ren. J. Fang, G. Liu, J. Zhang, Z. Zhu, H. Liu, K. Lin, H. Zhang, S. Lu. Simultaneous determination of urinary parabens, bisphenol A, triclosan, and 8-hydroxy-2′-deoxyguanosine by liquid chromatography coupled with electrospray ionization tandem mass spectrometry. *Anal. Bioanal. Chem.* **2016**, *408*, 2621.

[43] T.K. Jayasekara, P.C. Stevenson, S.R. Belmain, D.I. Farman D.R. Hall. Identification of methyl salicylate as the principal volatile component in the methanol extract of root bark of *Securidaca longepedunculata* Fers. *J. Mass Spectrom.* **2002**, *37*, 577.

[44] Y. Kuwahara, M. Morita, Y. Ichiki, T. Tanabe, Y. Asano. 1-Phenyl-2-pentanone and methyl salicylate: new defense allomone components and their content shift during ontogenetic development of the millipede *Nedyopus tambanus mangaesinus* (Polydesmida: Paradoxosomatidae). *Appl. Entomol. Zool.* **2017**, *52*, 447.

[45] R.H.C. Nébié, R.T. Yaméogo, A. Bélanger, F.S. Sib. Salicylate de méthyle, constituant unique de l'huile essentielle de l'écorce des racines de *Securidaca longepedunculata* du Burkina Faso. *C. R. Chimie* **2004**, *7*, 1003.

[46] C. Deng, X. Zhang, W. Zhu, J. Qian. Gas chromatography-mass spectrometry with solid-phase microextraction method for determination of methyl salicylate and other volatile compounds in leaves of *Lycopersicon esculentum*. *Anal. Bioanal. Chem.* **2004**, *378*, 518.



Scheme 1. Investigated types of protonation patterns of methyl benzoate.

E - relative energy, ^{A} - absolute energy baseline: -460.593103 [hartree].

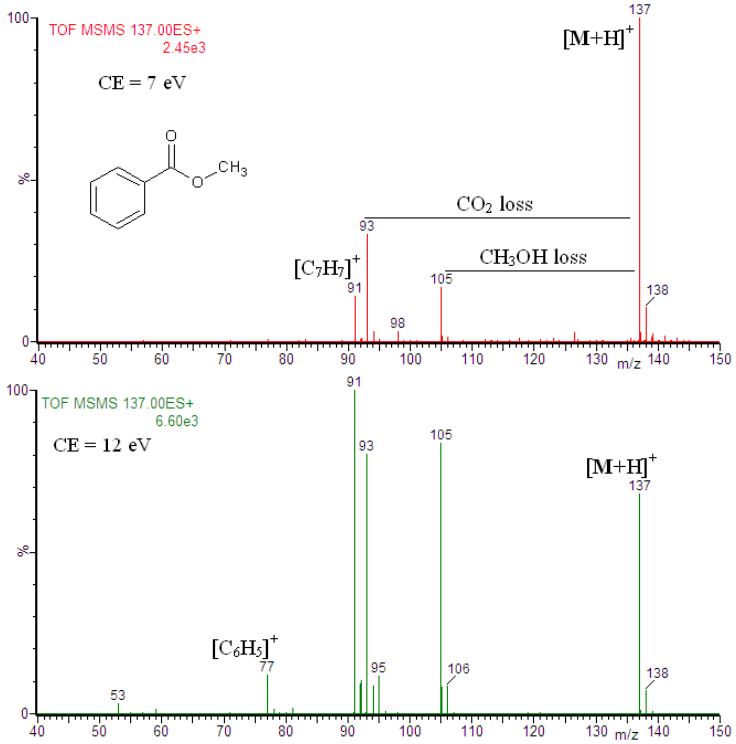


Figure 1. Product ion spectra of protonated methyl benzoate.

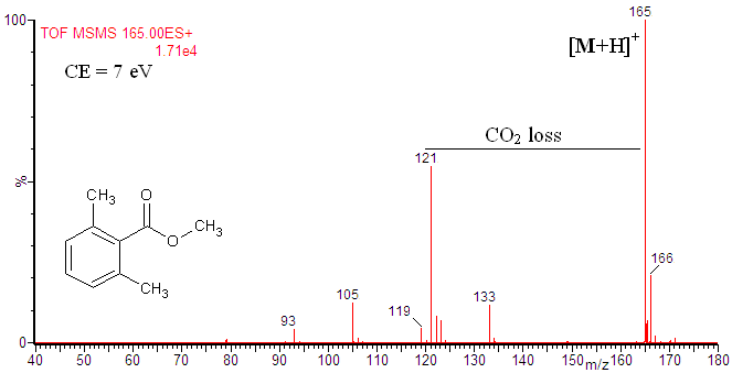


Figure 2. Product ion spectrum of protonated methyl 2,6-dimethylbenzoate.

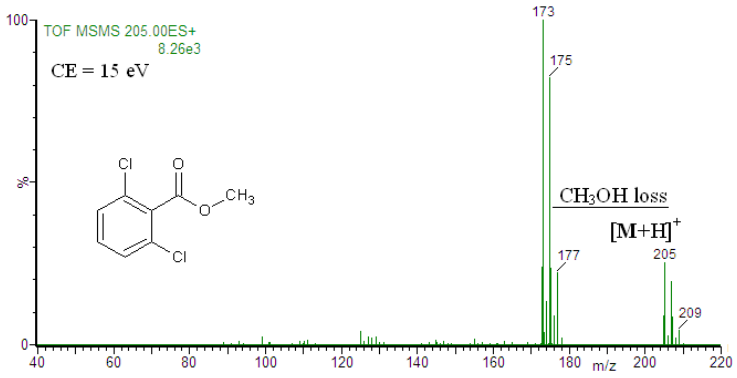


Figure 3. Product ion spectrum of protonated methyl 2,6-chlorobenzoate.

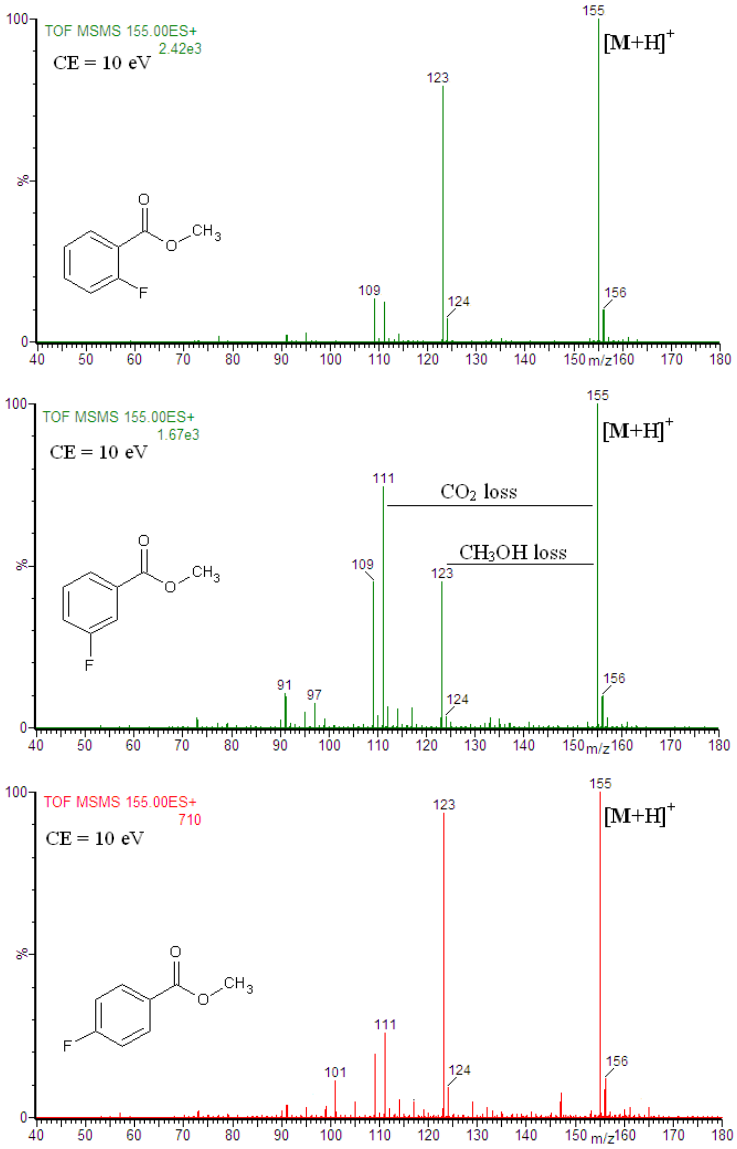


Figure 4. Product ion spectra of protonated methyl fluorobenzoates isomers.

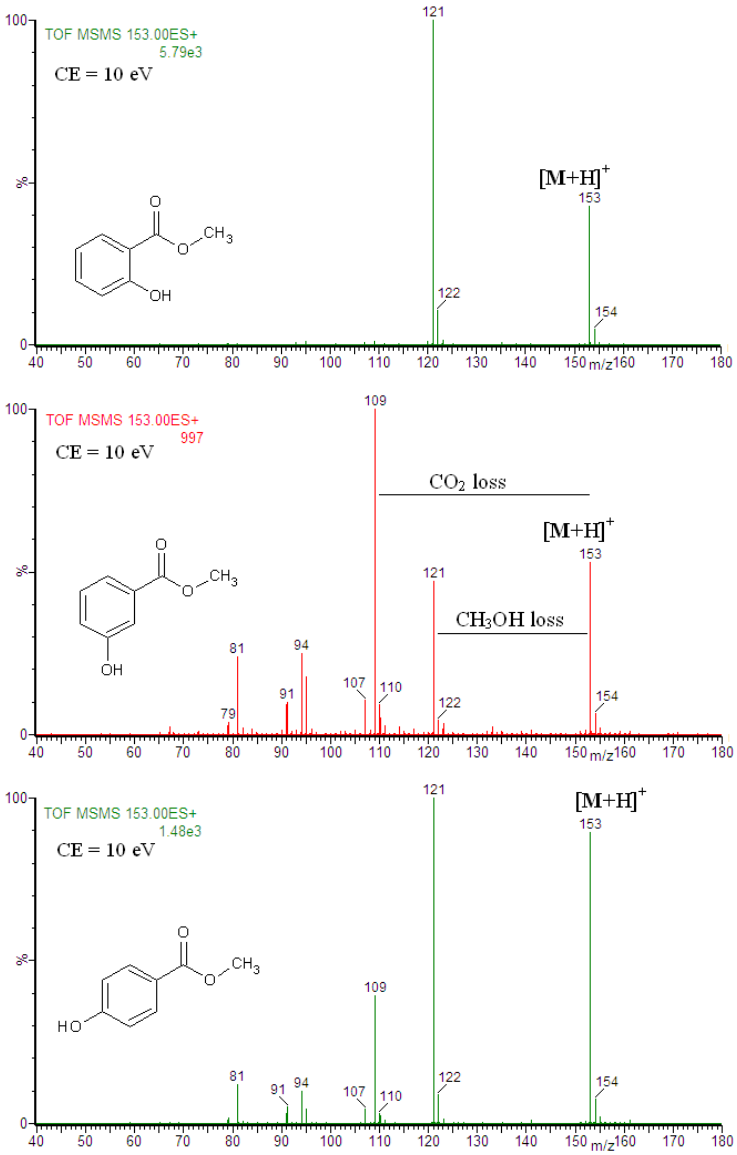


Figure 5. Product ion spectra of protonated methyl hydroxybenzoates isomers.

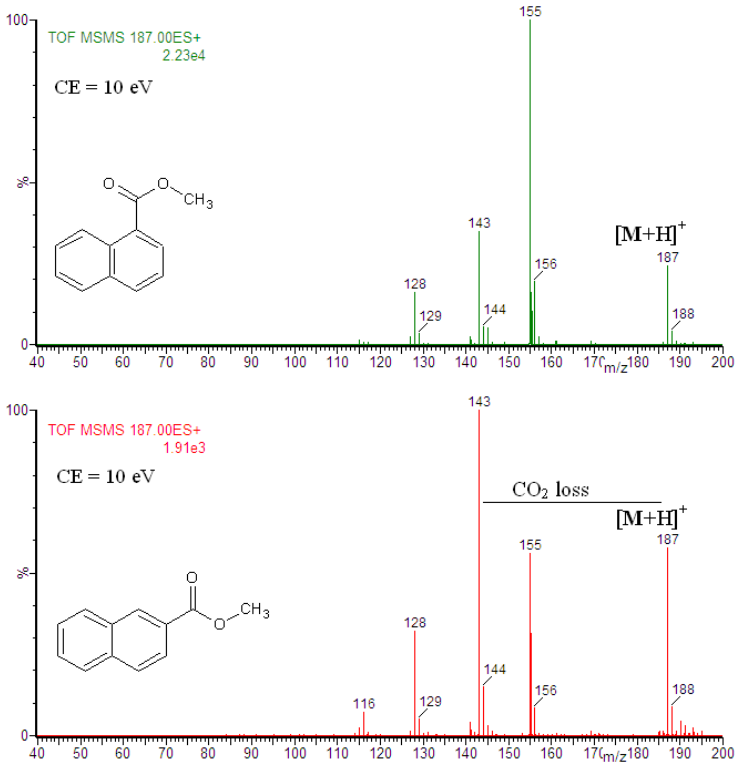


Figure 6. Product ion spectra of protonated methyl naphthoate isomers.