Results and Discussion

Fragmentation of compounds in EI mode was studied by GC/HRMS with an Agilent 7890A chromatograph connected with a tandem quadrupole-time-of-flight accurate-mass detector (Agilent 5975 C tandem quadrupole/TOF detector). For chromatographic separation, an HP 5ms capillary column (30.0 m × 0.25 mm × 0.25 μm, 5992475-433) was used. The oven temperature was maintained at 70 °C for 1 min then programmed at 15 °C/min to 290 °C which was maintained for 15 min. The injector temperature was 280 °C, and the interface temperature 290 °C. Helium in constant flow-mode was used as carrier gas; the flow rate was 1.0 ml/min. The mass detector was equipped with an EI source (70 eV). The quadrupole detector was adjusted for total ion current in MS mode and for the isolation of the precursor ions with a window of m/z 1.3 in MS/MS mode. Collision-induced dissociation (CID) spectra were recorded at collision energy in the range of 5–20 eV in a hexapole collision cell filled with nitrogen (99.999%). The accurate mass detector (TOF) was operated in extended dynamic range (GSD). The results of fragmentation were evaluated on the basis of analogues of known phenethylamines of 2C family, some derivatives of amphetamine and other NBOMEs. Electron-donating groups in para-position of benzene ring in NBOMEs favor the rearrangement, which is evidenced by higher intensity of corresponding peaks of radical cations in mass spectra of such compounds.

In fragmentation of benzylcyclohexadienyl radical cation (ion A in figure, for compound 1) is considered in the literature by mass spectrometry as the most probable mechanism of rearrangement of alkyl benzenes. At the same time, it is assumed that when both ortho-positions in the benzene ring are substituted, the rearrangement does not take place because of steric hindrance. In fact, most of β-phenethylamines, including those with a tert-butyl and 2,3-methylenedioxy substituent, which is described in the literature, demonstrate the same rearrangement, containing at least one free ortho-position in benzene ring. In this respect, 2,4,6-TMPEA-NBOMe presents a surprising example of the rearrangement with both substituted ortho-positions. It is difficult to rationalize, why McLafferty rearrangement is so efficient in the case of compound 1. Because the steric hindrance due to two methoxy groups in ortho-positions is rather pronounced, one may speculate about ipso-substitution in this highly activated benzene ring. Alternatively, one may propose that rather electron-donating substituent in the substituted ring than steric effects play the major role in the rearrangement. Anyway, the presence of three highly electron donating methoxy groups in the ortho-positions and para-positions favors the McLafferty rearrangement.

For deuterated compound 6, corresponding C6H4D2O+ (m/z 184.1050) ion is formed. Tandem mass spectrometric experiments (MS/MS) in CID mode have shown that the directions of further fragmentation of C6H4D2O+ (m/z 182.0937) radical cation are typical for methoxy derivatives of benzene and involve elimination of the hydroxyl group, CH3 and CHD radicals or formyldehyde molecule.

Fragmentation of bis-trifluoroacetyl compound 5 is essentially similar to that of compounds 3 and 4.

Experimental

Main directions of fragmentation of compounds 1–4 in EI elucidated by means of high resolution and tandem mass spectrometry are shown in figure below.

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