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In situ recognition of molecular chirality by mass spectrometry Hydration effects on differential stability of homo- and heterochiral dimethyltartrate clusters

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Abstract

We explored a possibility of using atmospheric pressure ionization techniques like corona discharge chemical ionization and surface thermoionization for distinguishing the chiral chemical compounds *in situ*. In both cases of ionization techniques we used home built ion sources coupled with non-modified ThermoFinnigan interfaces. For the proof-of-principle demonstration of recognition of molecule chirality *in situ* we used dimethyltartrate as a model chiral substance. We demonstrated that both ionization methods produce dimers and trimers of the dimethyltartrate molecules with pronounced chiral discrimination effects. In the case of corona discharge ionization we detected H_3O^+ and H_2O^+ based dimers and trimers. K^+ based dimers and trimers dominated the mass spectra in the case of thermoionization. Homochiral domination in the potassiumated dimers and H_2O^+ based dimers can be attributed to inherited chirality effect from the trimers. We showed that addition of the water molecules to dimers strongly influenced the effect of chirality on dimer stability by making heterochiral dimer more stable than homochiral in case of addition of one water molecule and removing the influence of chirality on dimers stability by addition of two or more water molecules. The experimental observations agree well with the results of the quantum chemical calculation obtained for dimers containing different number of water molecules.

Keywords: Recognition of chirality; Atmospheric pressure ionization; Thermoionization

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1. Introduction

Feasibility of recognition of the molecular chirality by mass spectrometry has been demonstrated by many groups [1]. In the combination with "kinetic method" [2] it has been applied to solve even some practical problems of controlling chiral purity of drugs [3]. One of the most intriguing and challenging problems for chiral recognition is the detection of the chiral asymmetry in extraterrestrial conditions to answer the question of the origin of homochirality on Earth. There were a lot of discussions about a possibility to detect chiral polarization of molecular sediments on the surface of the Saturn's satellite—Titan [4]. Successful Cassini-Huygens mission to Titan has increased the interest to this subject and further investigations will be undertaken including analyses of the chirality of the organic compounds on its surface. Two other objects of the Solar system: Mars and Europa are considered to be likely to contain organic compounds as well, but to our knowledge there are no nearest plans to investigate their surfaces for the

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Abbreviations: DMT, dimethyltartrate; CI, chemical ionization; ESI, electrospray ionization; MALDI, matrix-assisted laser desorbtion/ionization; AP, atmospheric pressure; APCI, atmospheric pressure chemical ionization; CID, collision induced dissociation

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presence of chiral polarization. Harsh conditions on the Titan's surface put strong limitations on the choice of the methodology for *in situ* analyses of the chirality of the organic compounds. Earlier we have already discussed the potential strategies for recognition of chirality of the organic compounds on the Titan's surface [5]. We made a conclusion, that the mass spectrometry is the most adequate technique for this purpose because of its high sensitivity and a possibility for direct identification of the analyzed molecules. Another important practical application of such technique of chiral recognition would be analysis of the chiral purity of the drugs. The possibility of performing analyses under the atmospheric pressure makes this approach especially attractive.

Intrinsically, mass spectrometry provides achiral property of an ion—that is mass to charge ratio. However, the analysis of the molecular chirality becomes possible by analyzing ion–molecular complexes. Homochiral and heterochiral complex usually have different stability. This property allows to distinguish those complexes and to determine their relative abundances. Ion–molecular complexes can be formed by a number of ionization techniques including CI, MALDI and ESI. Those three methods can be used at the near atmospheric pressure, so that only ionized part of the analyte is introduced into the analyzer and they need only low pumping capacity of mass spectrometer vacuum system. Among those three methods, the CI is the most simple and robust. The most simple implementation of CI is atmospheric pressure CI (APCI) caused by corona discharge. It is quite possible to monitor ion–molecular complexes in APCI conditions. For example in water containing atmosphere water clusters $H^+(H_2O)_n$ with n up to 50 dominates mass spectrum at room temperature (see below).

To our knowledge surface thermoionization being one of the oldest and well characterized techniques of positive and negative ion production in high vacuum has never been used as a method of ionization at atmospheric pressure. In this paper we characterized APCI by corona discharge and AP surface thermoionization as methods for *in situ* determination of enantiomeric composition by direct probing of the analyte vapors. As a model substance we used dimethyltartrate. This substance has two chiral centers. It is solid at room temperature and has vapor pressure of about 10^{-6} Torr. It has strong effect of chirality in the formation of protonated dimers and trimers. Also the thermodynamics and kinetics of their cluster formation is well characterized [6–9]. To distinguish between left and right forms of DMT molecules we labeled left form of the DMT by substituting both methyl groups with deuterated ones. It has been shown before that this substitution does not affect the stability of the protonated DMT cluster.

2. Instruments

For the detection of the corona discharge ionization source products we used ThermoFinnigan SSQ 710C single quadrupole and ThermoFinnigan LCQ DECA-XP ion trap mass spectrometers. For detection of the surface thermoionization products we used Only ThermoFinnigan LCQ DECA-XP. In the case of liquid samples it is possible to do both ESI and APCI without modification of the standard ThermoFinnigan ion sources. For API of gas samples we introduce a simple modification by adding a corona discharge needle on one holder and heated wire of NiCr alloy on the other. The corona discharge was ignited by high voltage from the standard API ion source.

2.1. Ionization source

2.1.1. Corona discharge source

The home built corona discharge API source is shown on Fig. 1. It is similar to what was described earlier [10]. The source consists of a tungsten wire tip approximately 10 μm in diameter, producing a discharge in a point-to-plane geometry with the 500 μm i.d. stainless steel heated inlet capillary of the mass spectrometer. The corona discharge is located in a volume between the tip and capillary inlet. The tip-to-capillary distance can be varied and was chosen to support stable corona. Voltages ranging from 2 to 4 kV were applied to the tip using a ThermoFinnigan (formerly Finnigan MAT, San Jose, CA) electrospray ionization power supply through a 1 GΩ (Caddock Electronics, Riverside, CA) resistor placed in series with the tip that acts to limit and stabilize the discharge current. A point-to-plane corona discharge is used to produce primary ions, which ionize the trace organic vapors through a series of ion–molecule reactions. It is well known that in the corona discharge source working in positive ion mode a rapid sequence of ion–molecule reactions occurs to form a series of protonated water molecular clusters of the type $(H_2O)_nH^+$ [11]. Fig. 2 shows a typical example of a mass spectrum of laboratory air. It was measured at room temperature of desolvating capillary using ThermoFinnigan SSQ 710C single quadrupole mass spectrometer. As we can see corona discharge ionization method gives mass spectra, which are sensitive not only to proton affinities in the positive ionization mode and electron affinity in the negative mode, but also sensitive to thermo-chemistry of complex formation. Peak $H^+(H_2O)_{21}$ in water cluster series corresponding to the structure of enhanced stability dominates in the mass spectrum. These protonated clusters are formed in the chain of ion molecular reactions started from $N_2{}^+$ and $O_2{}^+$ ions, formed in corona discharge, which then were converted into H_2O^+ giving H_3O^+, the last two ions serve

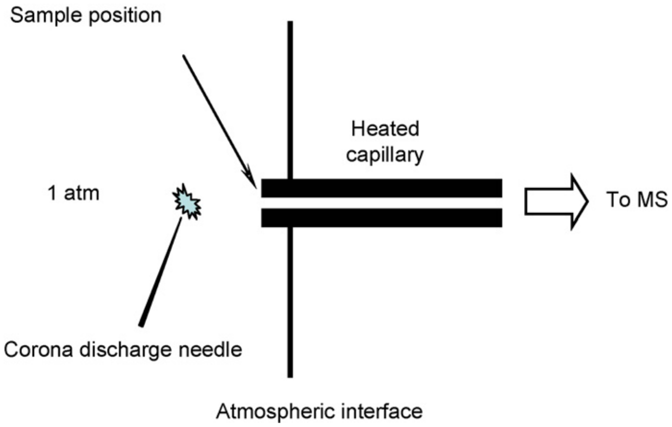

Fig. 1. Corona discharge source setup.