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離子阱串聯質譜儀於自身離子/分子反應的研究與其應用在 同分異構物的區別之新方法的研發

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中文摘要:

離子阱串聯質譜儀於自身離子/分子反應的研究與其應用在同分異構物的區別之新方法的研發

自身離子/分子反應為本實驗室在離子阱質譜儀中開發出來的一種反應[1]。它是利用一些化合物本身具有可產生一些特殊反應活性的碎片離子與中性的化合物分子本身進行有選擇性的自身離子/分子反應。本反應打破傳統的化學游離方式，不須加入任何會誘發化學游離反應（Chemical Ionization）之化學游離試劑，而分析物本身可產生有選擇性之自身化學游離反應。此方法在離子阱質譜儀中，利用自身分子的碎片，研發具有選擇性的自身離子/分子反應[1-3]，這種新型態的反應有三項重要優點：(1)因不須使用任何化學游離試劑，方便、快速且經濟。(2)有選擇性的反應所產生的特性質譜峰可以提供新的鑑定質譜圖之方法。(3)開發出新型態的離子/分子反應。本研究計劃的內容如下：1.在離子阱串聯質譜儀中研發結合氣相層析法，選擇性的自身離子/分子反應及串聯質譜技術的新方法以區別同分異構物 2.多巴胺在內部游離式離子阱質譜儀中自身離子/分子反應的反應機構的研究 3.比較自身離子/分子反應圖譜與電子撞擊法、化學游離法的差異；在這計劃中，除了自身離子/分子反應在一些含氮化合物或藥物觀察到非常珍貴的穩定 $[M+13]^+$ 及 $[M+27]^+$ 自身離子/分子反應的產物離子，這些離子在以往文獻中均為不容易穩定生成，但卻具有做為重要鑑定功能的離子，在本計劃中，我們利用離子阱質譜儀的特殊技術包括碰撞活化解離與 isolation 的技術，另外再加上理論計算的輔助，探討這些特殊離子生成的反應機構與途徑，離子的結構訊息等。本計劃中亦開發連結氣相層析質譜儀與自身離子/分子反應，碰撞活化解離技術，能量解離質譜等技術以開發一種用來區別許多同分異構物的方法。

關鍵詞：離子阱質譜儀，化學游離法，串聯質譜，選擇性自身離子/分子反應、時間解離質譜、能量解離質譜、碰撞活化解離

Study of Self-Ion/Molecule Reactions in Ion Trap Mass Spectrometer and its applications in isomer Differentiation

Abstract

In this project, we present a new method of applying the nature of Self-Chemical Ionization reaction to perform Self-Ion / Molecule Reactions (SIMR) in two different types of ion trap instruments in the

gas-phase. The advantages of the SIMR include providing a rapid, economic, easy to use and efficient method for generating SIMR spectra having the capability for identification in ion trap mass spectrometry. Furthermore, novel application for isomer differentiation based on SIMR in both external and internal source ion trap mass spectrometers is demonstrated in this project too. Since no chemical reagent is needed to perform selective ion/molecule reactions, it is very convenient, easy to use and economic. This study open a new way for identification compounds in ion trap mass spectrometry based on the SIMR. The contribution of these projects is to discover a new kind of gas-phase analytical application method involving the use of SIMR in the future.

Keywords: Ion Trap Mass Spectrometry, Self-Ion/Molecule Reactions, collisionally activated dissociation (CAD), energy resolved mass spectrometry (ERMS).

Introduction

Although Self-Chemical Ionization reaction (SCI) has been observed since last decade, only a few studies have been discussed this phenomenon systematically. Previous work has first demonstrated the possibility of applying the nature of Self-Chemical Ionization (SCI) to perform the Selective Self-Ion/molecule Reactions (SSIMR) for three crown ethers in both the external and internal ion trap mass spectrometers [1]. In this study, we continue to further apply this method to perform SIMR in the ion trap mass spectrometer for many compounds. We found that if the parameters that affect the SCI reactions such as reaction time, electronic beam energy and analyte concentration can be strictly controlled, the SIMR spectra can be very reproducible. Based on this feature, the SIMR method was developed [1-3]. The SIMR employs fragment ions from molecules which can produce low mass fragment ions, and in turn can serve as proton-transfer reagent ions or undergo secondary ion/molecular reactions to produce adduct ions. SIMR is a new kind of reaction pattern, which can be used for the trap-type of mass spectrometers.

Experimental

All experiments were carried out in both external and internal source ITMS (Finnigan MAT GCQ and Varian Saturn 2000 GC/MS) under the EI, SIMR and CI modes. DME was applied as the CI reagent gas. The electronic energy was 70 eV for EI. No CI reagent was used in the SIMR. Both ITMS instruments were operated in the mass selective instability

mode. Solutions of compounds were prepared at concentrations of 1×10^{-3} to 1×10^{-5} g/ml. One μL of the solution was introduced to the ion source of ITMS via a gas chromatograph (GC). For experiments performed in the external source ITMS (Finnigan MAT GCQ, San Jose, CA, USA), the temperature of the ion source was set at 200°C . The ion injection time was 25 msec. For experiments undertaken in the internal source ITMS (Saturn 2000, Varian, Walnut Creek, CA, USA), the selective ejection chemical ionization (SECI) was used to perform both DME CI and SIMR experiments. The ionization time was controlled by the automatic reaction control (ARC). The temperatures of trap, transfer line and manifold were 120°C , 240°C and 80°C , respectively. QISMS (Varian) research version software was used to implement the various RF voltage sequences. The ITMS was connected by a heated transfer line to a Varian 3800 model GC equipped with split/splitless injection and programmable on-column injector. O, m, p-xylene isomers were introduced to the ITMS by GC via a 1079 injection port. A 30m DB5-MS capillary column with an internal diameter of 0.25mm and a film thickness of $0.25 \mu\text{m}$ was used to introduce xylene isomers under the following conditions: injector temperature 200°C , injection volume $1 \mu\text{L}$ (splitless injection); temperature program, 1 min at 50°C then $50^\circ\text{C}/\text{min}$ to 200°C . The spectra acquisition was achieved for the mass range m/z 10-650 at 1 sec/scan. For CAD experiments, the collisional activation time was 20 msec. Signal width for selection of the parent ions was 1 u. The collision energy was varied from 0.5 to 0.6 V.

Results and Discussion

This study introduces a novel reaction pattern termed Self - Ion / Molecule Reactions (SIMR) in both external and internal source Ion Trap Mass Spectrometers (ITMS). The SIMR employs fragment ions from molecules which can produce low mass fragment ions, and in turn can serve as proton - transfer reagent ions or undergo secondary ion/molecular reactions to produce adduct ions. Up to date, the methyne addition products ($[\text{M}+13]^+$ ions) have been observed for several nitrogenated compounds including aza-crown ethers [1], aniline [4], dopamine [5] and xylene isomers [6] from SIMR in the ITMS. While the xylene isomers are the first three compounds that can produce the methyne addition ions in SIMR for non-nitrogenated compounds. Combining isolation experiments, isotopic labeling and semi-empirical calculations, the reaction mechanism for formation of $[\text{M}+\text{CH}]^+$ ions of compounds can be determined. Selective self-ion/molecule reaction product ions were produced between the oxygenated and nitrogenated crown ethers. For the oxygenated crown ethers, Self-Ion/Molecule

Reactions lead to the formation of the protonated ions, adduct ions of fragments ($[M+F]^+$) and $[M+H_3O]^+$, while the nitrogenated crown ethers produce $[M+H]^+$, $[M+CH]^+$ and $[M+C_2H_3]^+$ ions.

This study also presents a novel, simple and rapid procedure for isomer differentiation by combining gas chromatograph (GC), SIMR, and tandem mass technique (MS/MS) in an ITMS. SIMR product ions were produced from four isomers. For aniline, SSIMR induces the formation of the molecular ion, $[M+H]^+$, $[M+CH]^+$, adduct ions of fragments ($[M+F]^+$, where F represents fragment ions) and $[2M-H]^+$; 2 and 3-picoline produces $[M+H]^+$, $[2M-H]^+$ and $[M+F]^+$, while the 5-hexynenitrile produces $[M+H]^+$, $[M+F]^+$ and $[2M+H]^+$ ions.

The advantages of the SIMR include providing a rapid, economic, easy to use and efficient method for generating SIMR spectra having the capability for identification in the ITMS. The applicability of SIMR for isomer discrimination is better than electronic ionization (EI) and dimethyl ether chemical ionization (DME CI) in the ITMS since no CI reagent, metal ions or internal standards were required to perform SIMR.

計劃成果自評:

After one year's hard working by the young people and me in our group, we already published several SCI journals for this project. The information is provided below:

1. Hui-Fen Wu*, Wen-Feng Wu, Comparing differentiation of xylene isomers by electronic ionization, chemical ionization and Self-Ion/Molecule Reactions and the first observation of methyne addition ions for xylene isomers in Self-Ion/Molecule Reactions for non-nitrogenated compounds, Rapid Communications in Mass Spectrometry, 2003, 17, in press (SCI).
2. Hui-Fen Wu*, Chien-Hung Chen, Li-Chi Lu, Probing the Reaction Mechanisms of Self - Ion/Molecule Reaction for Dopamine in an Ion Trap Mass Spectrometer, Rapid Communications in Mass Spectrometry, 2003, 17, 1479-1482 (SCI).
3. Hui-Fen Wu* and Pei-Yi Lin, Probing the Effects of Reagent Gas Pressure and Ion Source Temperature for Dimethyl Ether Chemical Ionization of Tricyclic Antidepressants in an External Source Ion Trap

Mass Spectrometer, J. Chin. Chem. Soc., 2003/12, 50, in press (SCI).

4. Hui-Fen Wu* and Yu-Jie Chuan, Isomer Differentiation by Combining Gas Chromatography, Selective Self-Ion/ Molecule Reaction and Tandem Mass Spectrometry in an Ion Trap Mass Spectrometer, Rapid Communications in Mass Spectrometry, 2003, 17,1030-1036 (SCI).
5. Hui-Fen Wu*, Yen-Ren Chen, Bin-Wei Lai, Novel observation of total ion chromatogram (TIC) splitting under positive chemical ionization in an external source Ion Trap Mass Spectrometer, Journal of Mass Spectrometry, 2003, 38,458-459 (SCI).

Besides, we also demonstrated part of the results in the conferences as below:

1. 楊志浩，吳慧芬,利用頂空式固相微萃取法/氣相層析離子阱串聯質譜儀偵測水中二甲苯及研發以自身離子/分子反應進行同分異構物鑑別之新方,2002年10月25-27,中油,中國化學會年會, paper No.P-AN-047.
2. Hui-Fen Wu*, Wen-Feng Wu and Li-Chi Lu, Probing the Reaction Mechanism for Methylene Addition Reaction of O, M, P-Xylenes in the Self-Ion/ Molecule Reactions and Differentiation of Xylene Isomers by Several Ion Trap Mass Spectrometric Techniques. 2002年10月25-27, 中油,中國化學會年會, paper No.P-AN-046.
3. Hui-Fen Wu*, Shan-Min Huan, Chan-Fu Wu and Mon-Tin Wu, 2002, Molecular Modelling and Electrospray Mass Spectrometry for Probing Host-Guest Interaction of Metal Ions with Bis[(benzo-15-crown-5)-15-ylmethyl]pimelate. 2002年10月25-27, 中油,中國化學會年會, paper No.P-AN-044.
4. Hui-Fen Wu*, Chien-Hung Chen and Bin-Wei Lai, Unusual Adduct Ions Attachment in Negative Chemical Ionization and Collisionally

Activated Dissociation in an Ion Trap. 2002 年 10 月 25-27, 中油,中國化學會年會, paper No.P-AN-045.

5. Hui-Fen Wu* and Yu-Jie Chuan, A Novel Method for Isomer Differentiation by Combining Gas Chromatograph, Selective Self-Ion/Molecule Reaction and Tandem Mass Technique (GC/SSIMR/MS/MS) in an Ion Trap Mass Spectrometer. 50th ASMS Conference on Mass Spectrometry and Allied Topics, Orlando, FL, ThPQ351. 2002 年 6 月 2-6

6. Bin-Wei Lai, Hui-Fen Wu*, Self-Ion/ Molecule Reactions for Negative Ions (SIMRNI) in an External Source Ion Trap Tandem Mass Spectrometer, 2002 年 5/10,分析技術研討會,弘光技術學院, B8.

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1. Hui-Fen Wu and Ming-Yi Ho, Selective Self - Ion / Molecule Reactions in Both External and Internal Source Ion Trap Mass Spectrometers, *Rapid Communications in Mass Spectrometry*, 2001, 15, 1309-1316.
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3. Hui-Fen Wu*, Chien-Hung Chen, Yu-Jie Chuang, Hsiao-Wei Li and Wen-Fon Wu, 2001 年 10 月 20-21, Study of Self - Ion/Molecule Reactions in Bench-top Ion Trap Mass Spectrometer,第二屆兩岸分析化學會議,北京,清華大學, China, P215.
4. H.-F. Wu and Y.-J. Chuan, *Rapid Commun. Mass Spectrom.*, 2003, 17, 1030.
5. H.-F. Wu, C.-H. Chen, L.-C. Lu, *Rapid Commun. Mass Spectrom.*, 2003, 17, 1479.
6. H.-F. Wu, W.-F. Wu, *Rapid Commun. Mass Spectrom.*, 2003, 17, in press.

