POSITIVE-ION, NEGATIVE-ION AND SURFACE IONIZATION MASS SPECTRA OF MPTP AND ITS DERIVATIVES

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原　　報

POSITIVE-ION, NEGATIVE-ION AND SURFACE IONIZATION MASS SPECTRA OF MPTP AND ITS DERIVATIVES

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MPTP 及び類似化合物の正イオン・負イオン及び表面電離マススペクトル

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Summary

Positive-ion electron impact (PIEI), positive-ion chemical ionization (PICI), negative-ion chemical ionization (NICI) and surface ionization (SI) mass spectra of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), 1-methyl-4-(2-pyrrolylphenyl)-1,2,3,6-tetrahydropyridine, 1-methyl-4-(3-methoxyphenyl)-1,2,3,6-tetrahydropyridine and 1-methyl-4-(2-isopropylphenyl)-1,2,3,6-tetrahydropyridine, have been presented, and each fragmentation mode has been analyzed. In the PIEI mode, molecular ions appeared in all four compounds and three of them constituted the base peaks. In the PICI modes, intense $[M]^+$ and $[M+1]^+$ ions were observed; $[M]^+$ ions were the base peaks for all compounds. In common with both PIEI and PICI modes, cleavages between the two ring structures were found. In the NICI mode, $[M-1]^-$ peaks constituted the base peaks, but were much less intense than in other modes. In the SI mode, single and intense $[M-3]^+$ peaks appeared; these peaks are probably due to aromatization of the *N*-methyltetrahydropyridine ring. The detection limits for four compounds, obtained by total ion monitoring, in the PIEI, PICI, NICI and SI modes were 2.1−7.9, 29−85, 99−3500, 0.33−1.1 pmol on-column, respectively.

Key words: MPTP; 1-Methyl-4-(3-methoxyphenyl)-1,2,3,6-tetrahydropyridine; Mass spectrometry; Negative-ion chemical ionization; Surface ionization organic mass spectrometry

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Introduction

In early 1980's, MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), an impurity of a meperidine analogue, 1-methy-4-phenyl-4-propionoxypiperidine (MPPP), was found to be a cause of parkinsonian symptoms for MPPP abusers in the US [1,2]. Since then, MPTP-induced parkinsonism has been regarded as a good model in human and non human primates [3]; biological activities of many analogues of MPTP have been also tested [4,5]. In this paper, positive-ion electron impact (PIEI), positive-ion chemical ionization (PICI) and negative-ion chemical ionization (NICI) mass spectra of MPTP, and its derivatives, such as 1-methyl-4-(2-pyrrolylphenyl)-1,2,3,6-tetrahydropyridine (MPyPTP), 1-methyl-4-(3-methoxyphenyl)-1,2,3,6-tetrahydropyridine (3' OCH_3-MPTP), and 1-methyl-4-(2-isopropylphenyl)-1,2,3,6-tetrahydropyridine (2' IP-MPTP), have been presented, and each fragmentation mode has been analyzed. Some years ago, a surface ionization organic mass spectrometer (SIOMS) was developed [6, 7]; we have also presented surface ionization (SI) mass spectra of the above compounds on an SIOMS in the positive mode.

Experimental

Materials

MPTP-HCl was purchased from Research Biochemical International (Natric, MA, USA). 3' OCH_3-MPTP oxalate, MPyPTP oxalate and 2' IP-MPTP oxalate were synthesized in the Department of Chemistry, Virginia Polytechnic and State University [4, 8]. A DB-5MS fused silica capillary column (30 m×0.32 mm i.d., film thickness 0.25 μm) was obtained from J&W Scientific (Folsom, CA, USA). Other chemicals used were of analytical grade.

Conditions of gas chromatography (GC) / mass spectrometry (MS)

Mass spectra in the PIEI, PICI, NICI and SI modes were recorded on a QP-5050A mass spectrometer coupled to a GC-17A gas chromatograph (Shimadzu Corp., Kyoto) with a computer-controlled data analysis system. The detailed instrumentation of the SIOMS has been described elsewhere [9].

The MS conditions were: interface temperature, 260℃; ionization current, 60 μA; in the PIEI mode, electron energy 70 eV and detector voltage 1.5 kV; in the PICI and NICI modes, electron energy 200 eV, detector voltage 2.0 kV, reagent gas methane and chamber pressure about 5×10^{-3} Pa; in the SI mode, filament current 1.6 A and chamber pressure of oxygen $2-3\times10^{-3}$ Pa.

The GC conditions were: column temperature, 100−280℃ (1 min hold at 100℃, 5℃/min up to 155℃, 20℃/min up to 280℃); injection temperature, 250℃; and helium flow rate, 1.8

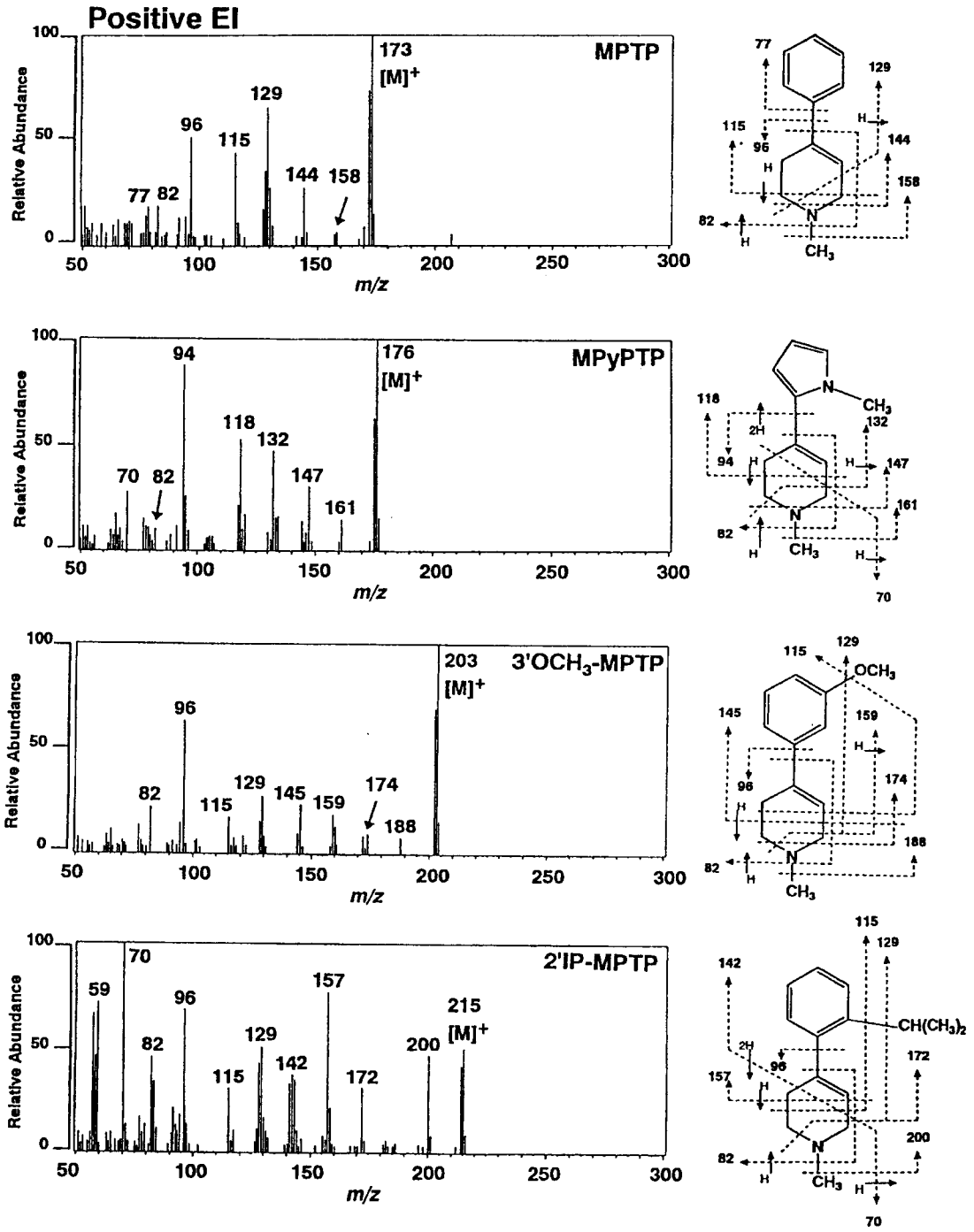

Fig. 1. PIEI mass spectra of MPTP, 1-methyl-4-(2-pyrrolylphenyl)-1,2,3,6-tetrahydropyridine (MPyPTP), 1-methyl-4-(3-methoxyphenyl)-1,2,3,6-tetrahydropyridine (3' OCH_3-MPTP) and 1-methyl-4-(2-isopropylphenyl)-1,2,3,6-tetrahydropyridine (2' IP-MPTP), and their probable fragmentation modes.

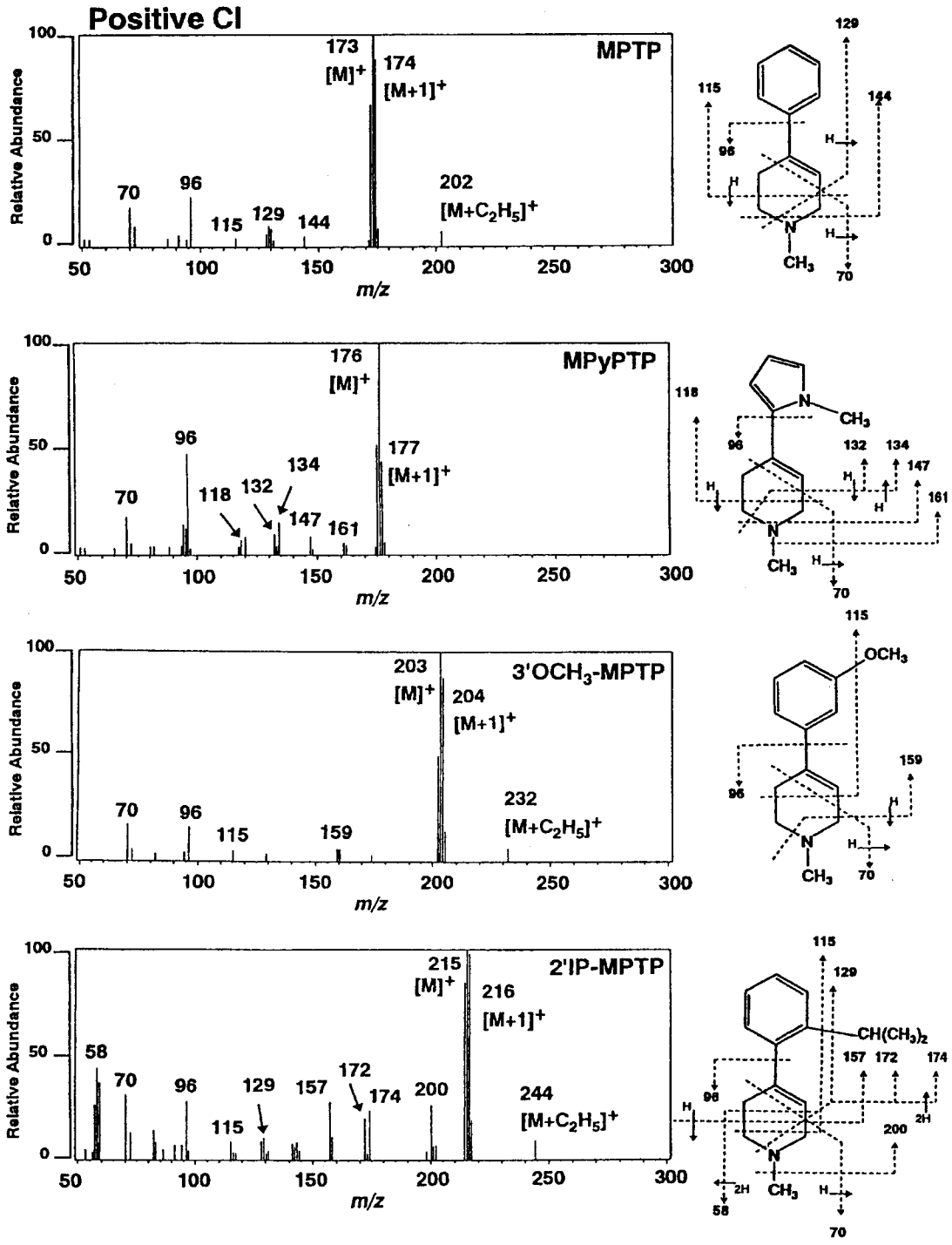

Fig. 2. PICI mass spectra of MPTP, MPyPTP, 3' OCH_3-MPTP and 2' IP-MPTP, and their probable fragmentation modes.

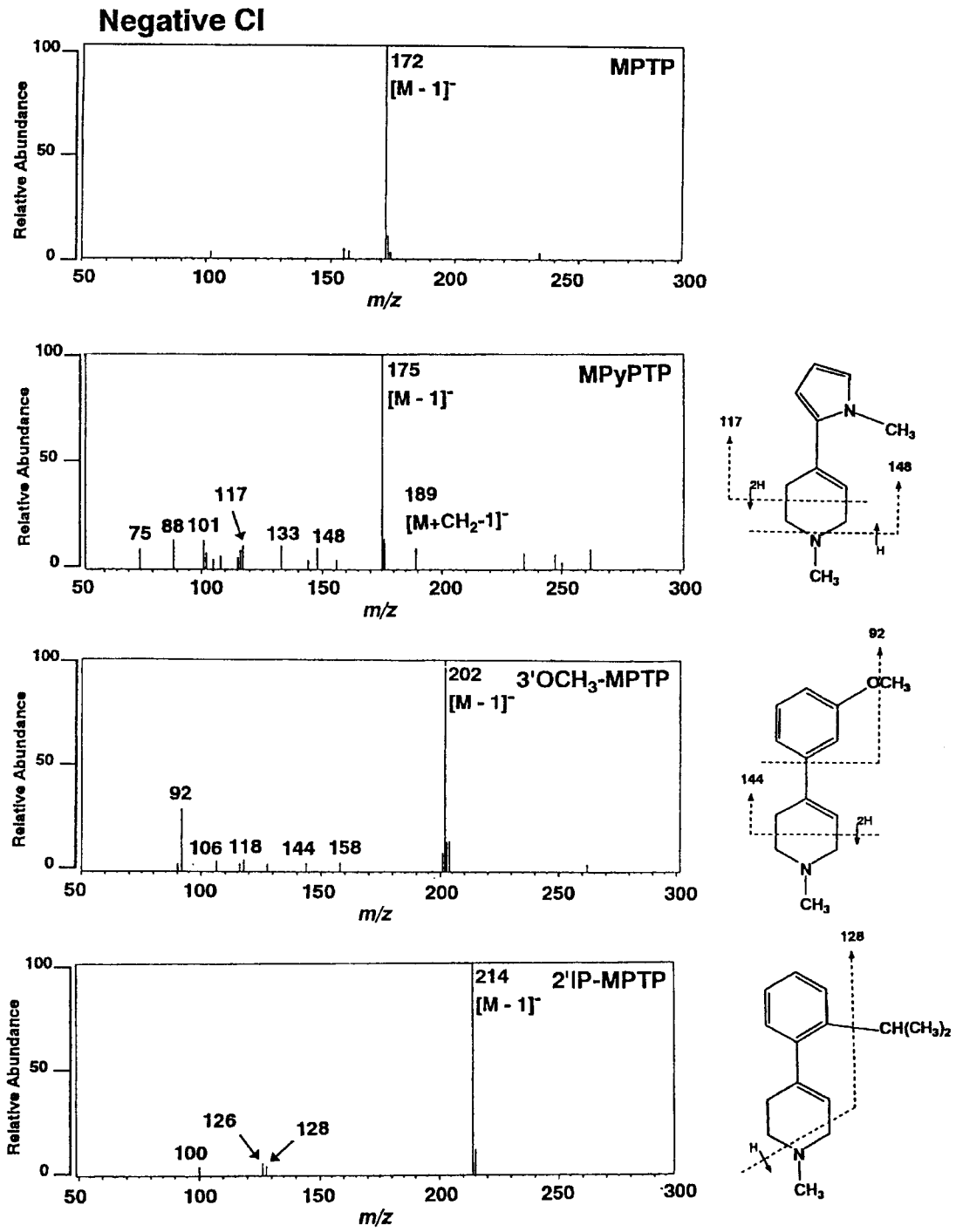

Fig. 3 . NICI mass spectra of MPTP, MPyPTP, 3' OCH_3-MPTP and 2' IP-MPTP, and their probable fragmentation modes.

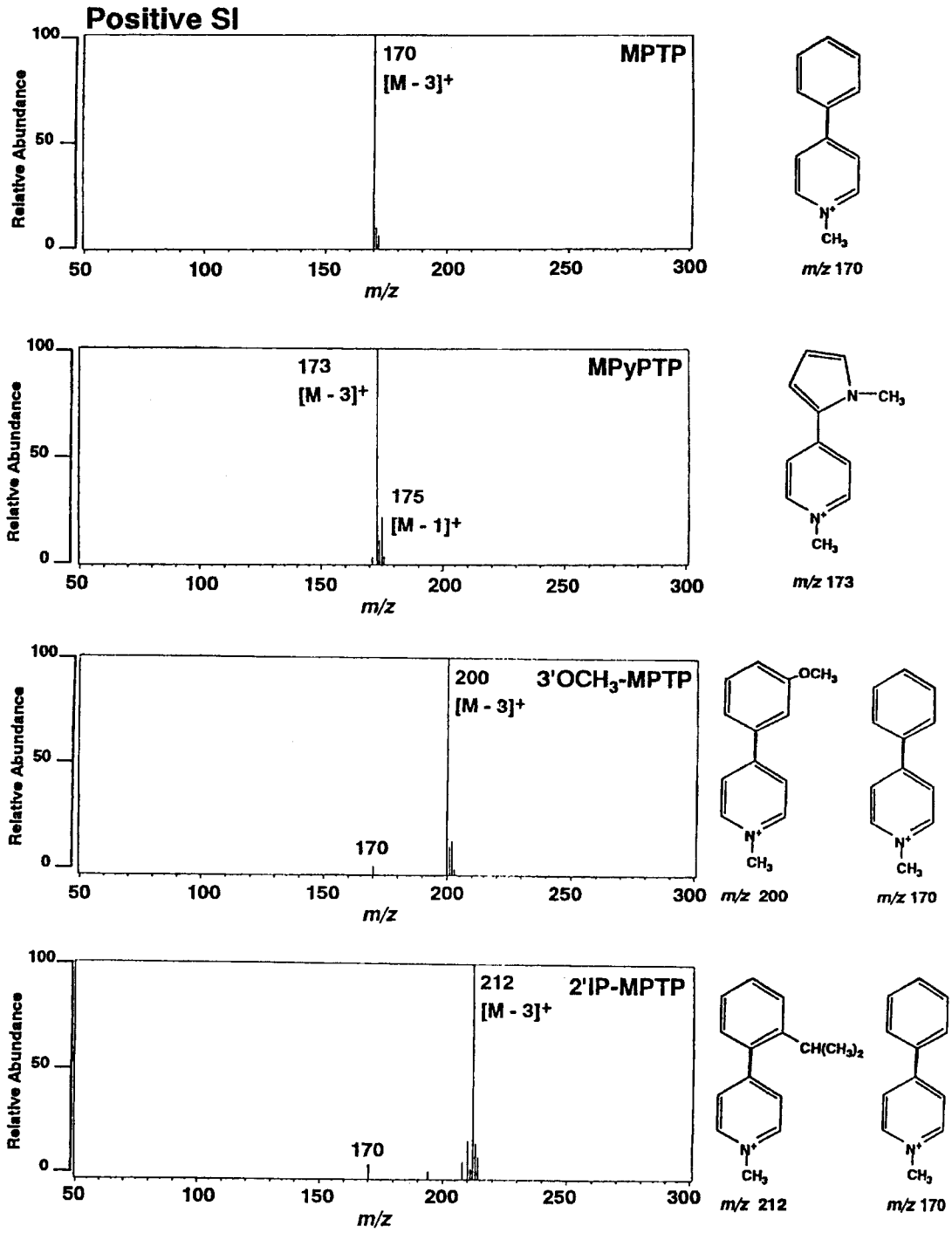

Fig. 4. SI mass spectra of MPTP, MPyPTP, 3' OCH_3-MPTP and 2' IP-MPTP, and their probable fragmentation modes.

ml/min. The samples were injected in the splitless mode and the splitter was opened after 1 min. Each compound was dissolved in methanol and a 1-μl aliquot of it was subjected to GC/MS analysis.

Results and discussion

PIEI, PICI, NICI and SI mass spectra of four compounds and each probable fragmentation mode are shown in Figs. 1—4.

In PIEI mass spectra (Fig. 1), molecular ions appeared for all four compounds; they constituted the base peaks for MPTP, MPyPTP and 3' OCH_3-MPTP. There were characteristic ions observed at m/z 94 or 96, which are formed by cleavage between the two ring structures.

In PICI mass spectra (Fig. 2), all compounds showed intense peaks of $[M]^+$ and $[M+1]^+$; the $[M]^+$ ions constituted the base peaks. In MPTP, 3' OCH_3-MPTP and 2' IP-MPTP, small peaks of $[M+C_2H_5]^+$ were observed. Fragment peaks of m/z 70 and 96 appeared in common for the four compounds.

In NICI mass spectra, $[M-1]^-$ peaks constituted the base peaks in all four compounds (Fig. 3), but their absolute intensities were much smaller than those in other modes. Small fragment peaks, many of which were not identifiable, were observed for MPyPTP and 3' OCH_3-MPTP.

The SI mode gave almost single $[M-3]^+$ peaks in all four compounds (Fig. 4). For explanation of the $[M-3]^+$ peaks, aromatization of the *N*-methyltetrahydropyridine ring is most probable (Fig. 4). Similar phenomena were observed by Fujii and other researchers [10, 11].

To check sensitivity of the present GC/MS methods, the intensities of peaks, obtained by total ion monitoring, were compared with each other in the four modes. The detection limits for four compounds in the PIEI, PICI, NICI and SI modes were 2.1—7.9, 29—85, 990—3500, 0.33—1.1 pmol on-column, respectively.

The present study has revealed that the SI mode is most suitable to quantitate MPTP and related compounds with high sensitivity; it can be applied for monitoring their concentrations in body fluids and tissues after administration of small amounts of them.

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