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A re-examination of the mono-methoxy positional ring isomers of amphetamine, methamphetamine and phenyl-2-propanone

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Abstract

Recently, tablets inscribed with the Mitsubishi 3-diamond logo, and sold as 3,4-methylenedioxymethamphetamine (MDMA), were found to contain *p*-methoxymethamphetamine (PMMA), a compound with MDMA-like effects. Shortly after this first submission, similarly inscribed tablets were encountered containing both PMMA and *p*-methoxyamphetamine (PMA). This second tablet composition has been implicated in several recent deaths in the US. Because two other positions are available for mono-methoxy substitution on the phenyl ring, it is essential that the correct identification be made for these compounds. Analytical data are supplied to enable differentiation of these ring isomers as well as the ketones that serve as their precursors. Published by Elsevier Science Ireland Ltd.

Keywords: Methylenedioxymethamphetamine; *p*-Methoxymethamphetamine; *p*-Methoxyamphetamine

1. Introduction

Three recent deaths in suburban Chicago, IL and two deaths in the Orlando, FL area, have been attributed to the ingestion of 4-methoxyamphetamine (*p*-methoxyamphetamine, PMA) often in the form of small white tablets with an inscribed Mitsubishi 3-diamond logo. Autopsies conducted in connection with four other drug related deaths in the Orlando area identified PMA and additional illicit controlled substances in the postmortem examinations. Deaths from PMA in the US had been reported as far back as April 1973 in Kansas City, MO and Atlanta, GA [1]. Nine deaths from PMA also occurred in Canada between March and August 1973 [2]. From September 1995 through January 1997, 10 additional deaths from PMA were reported in Australia with six occurring in south Australia, three in Queensland, and one in western Australia [3]. In the early US and Canadian fatalities, drug users frequently believed what they were ingesting was 3,4-methylenedioxyamphetamine (MDA) often obtained in a powder form. In the Australian and recent American deaths, the ingested drug was typically thought by the user to be 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) and was usually consumed as capsules or tablets. The current American deaths all appear to be related to tablets with the Mitsubishi 3-diamond logo sold as the entactogen [4,5], MDMA. Similar tablets have been reported by the European Police Office (EUROPOL, The Hague, The Netherlands) as the putative cause of two fatalities in Denmark and one in Germany. Use of this logo on tablets is particularly insidious since the original formulation tablets having this logo did, in fact, contain MDMA. Dancesafe (http://www.dancesafe.org), an organization with an independent tablet analysis laboratory, has also reported that amphetamine was the sole active component in one version of this type of tablet. Recently, a new compound, 4-methoxymethamphetamine (*p*-methoxymethamphetamine, PMMA) [6], was identified as the only active ingredient in a new formulation of the Mitsubishi logo tablets. Additional formulations have also been reported including various mixtures which may contain any of the following ingredients, in various concentrations: amphetamine, PMA, PMMA, l-ephedrine, pseudoephedrine, 1-(4-methoxyphenyl)-2-propanol and a compound believed to be *N*,*N*-dimethyl-4-methoxyamphetamine. Unfortunately, composition of the tablets is indeterminate from their physical appearance so that the user has no reliable way of

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differentiating various formulations merely by visual observation. This fact is probably responsible in large part for the deaths in the Chicago area. Recent analysis of new submissions of 3-diamond logo tablets with a reddish colored appearance has shown them to be similar in composition to the multi-component white tablets involved in the Chicago fatalities.

In order to determine the physiological nature of a given compound (analeptic, analgesic, anorectic, entactogenic, hallucinogenic, soporific, etc.) without exposing human subjects to unknown consequences, drug discrimination studies are often used. Briefly, drug discrimination studies are conducted by training test animals, usually mice or rats, to differentiate the effect(s) of a ''training'' drug from those of a saline solution. When the test animals can reliably differentiate, or discriminate, the training drug from a saline solution, they may then be used to determine if the effects of a new compound mirror the effects of the training drug. If the animal's response to the new drug correlates with its response to the training drug, the tested compound is said to ''generalize'' to the training drug. A full discussion of drug discrimination procedures has previously been published [7,8].

In drug discrimination studies using rats [9,10], PMMA has been shown to generalize to MDMA, but not to amphetamine. The results of these studies indicate that the test animals equated the effects from PMMA to be like those from MDMA. Conversely, animals trained on amphetamine do not recognize an amphetamine-like effect from PMMA. Similar studies have shown that PMA has no MDMA-like character (effect) but rather has stimulant characteristics resembling a less potent amphetamine-like substance [11]. Although animal and human responses to a given drug do not always correlate [12,13], in this instance the absence of MDMA response in rats receiving PMA likely corresponds to the human physiological experience [13,14]. The lack of an MDMA effect from an ingested 3-diamond tablet containing only PMA may lead the drug user to believe the tablets merely have a lower concentration of MDMA than previously encountered 3-diamond tablets. Anticipating a physiological response that was not forthcoming, he/she may consume several tablets over a relatively short period of time (''piggy-backing'' or ''stacking'') in order to get the expected, but never achieved, MDMA response. Ultimately, such a procession of events would lead to a potentially fatal overdose.

Few reports of human studies with PMA exist [14,15]. Shulgin has reported [15] that at dosages of 40 mg or less, PMA is without peripheral or central effects, yet at 60–80 mg the effective dose for a psychotomimetic syndrome has been reached. This state is reached quite suddenly about an hour after ingestion, and results in an elevation of blood pressure. Shulgin further reports that PMA has a therapeutic index of about 2.5 and that as little as 150 mg may result in a fatal dose. The symptoms of an overdose include, extreme hyperthermia, respiratory depression, and convulsions. Virtually all of the subjects reported on by Cimbura [2] and Felgate et al. [3] had substantially elevated body temperatures at the time of death, with one fatality having registered a temperature of 115°F [3].

Although PMMA has typically been evaluated in drug discrimination experiments using rats [9,10,16,17], a single study with a human subject has been reported [14]. In this report, 110 mg produced an effect similar to an equivalent quantity of MDMA (100–120 mg) and lasted about 4 h. The drug discrimination studies indicated the potency of PMMA to be about three times that of MDMA. This difference in reported potency of PMMA between man and rat may be a species dependent phenomenon. In a previous study using mescaline and several of its analogs to evaluate the effectiveness of five species of test animals, the authors report that ''the dog may require two to four times as much of the substance (i.e. mescaline) as man to elicit a comparable response'' [18]. Similar quantitatively different results were reported with other animal species and varied depending on the drug tested.

The 2-methoxy isomer of methamphetamine (2-methoyxmethamphetamine, *o*-methoxymethamphetamine, OMMA) is currently available as a bronchodialator [19] but exhibits little [14] or no [20] stimulant activity. Virtually nothing has been reported about the activity of the 3-methoxymethamphetamine (*m*-methoxymethamphetamine, MMMA) isomer of PMMA. Each of the three mono-methoxy isomers of amphetamine shows central nervous system (CNS) stimulation in mice, but none of them approaches the potency of amphetamine itself [17].

From an analytical perspective, some information on the three mono-methoxy ring isomers of amphetamine [11,22,23] and methamphetamine [21–24] has previously been published. For forensic purposes, it is essential that an unequivocal identification of the ring position of the methoxy substituent on amphetamine or methamphetamine be made. With the renewed interest in PMA, and recent interest in PMMA, an update of the data acquired using older generation instrumentation, and a presentation of analytical data using more recent techniques, will be useful in forensic analysis.

2. Experimental

All six of the mono-methoxy compounds were prepared by catalytic hydrogenation in a Parr hydrogenation apparatus using the appropriate ketone (Aldrich Chemical Co., Milwaukee, WI), Raney Nickel, aqueous 28% ammonia or 40% methylamine, ethanol and hydrogen. The components were allowed to react for 8–12 h. The following purification process is somewhat tedious, but results in high purity products. For each synthesis, the Raney Nickel was removed and the clear filtrate mixed with a large volume of dilute aqueous sodium hydroxide. This solution was extracted four times with 25 ml of chloroform ($CHCl_3$), filtered through

Table 1
Melting points (mp, °C) and elemental analysis (%) for the listed compounds[a]

S. no.	Compound	mp (°C)	Elemental analysis of C, H, N, O	
			Found	Theory
1	2-MeoAmp HCl	110–112[b]	59.57, 8.03, 6.95, 8.09	59.55, 8.00, 6.94, 7.93
2	3-MeoAmp HCl	117.5–120[b]	59.45, 8.00, 6.88, 8.22	
3	4-MeoAmp HCl	206–207[b,c]	59.54, 8.00, 6.88, 8.14	
4	2-MeoMeth HCl	126–128[d,e]	61.40, 8.30, 6.43, 7.60	61.23, 8.43, 6.49, 7.42
5	3-MeoMeth HCl	98.5–101[d]	61.02, 8.40, 6.43, 7.45	
6	4-MeoMeth HCl	176.5–177[d,f]	61.41, 8.41, 6.46, 7.49	

[a] Keys — MeoAmp: methoxyamphetamine; MeoMeth: methoxymethamphetamine; HCl: hydrochloride.
[b] Bailey et al. [22] report 108–110°C for 2-MeoAmp, 115–116°C for 3-MeoAmp and 206–207°C for 4-MeoAmp.
[c] Shulgin and Shulgin [14] list 208–209°C for 4-MeoAmp.
[d] Bailey et al. [24] report 129–130.5°C for 2-MeoMeth, 88–90°C for 3-MeoMeth and 177–178°C for 4-MeoMeth.
[e] Merck Index [19] lists 129–131°C.
[f] Shulgin and Shulgin [26] list 177–178°C for 4-MeoAmp.

anhydrous sodium sulfate, and the extracts pooled. The chloroform was washed with five 75 ml portions of water to remove any free ammonia or methyl amine and the chloroform then filtered through anhydrous sodium sulfate. The chloroform solution was next extracted three times with 10 ml portions of dilute hydrochloric acid, leaving any unreacted, or reduced, ketone in the organic layer. The aqueous acid containing the methoxy amine was made basic with a dilute sodium hydroxide solution, extracted into ether, dried through anhydrous sodium sulfate and then isopropanolic hydrogen chloride added until just acidic to dampened universal pH paper. The solution was evaporated to dryness, dissolved in isopropanol and admixed with ether until turbidity resulted. Subsequently, the amine hydrochlorides precipitated from solution and were dried under low vacuum for 18 h. Melting points were determined using capillary tubes (1.6–1.8 mm × 90 mm) in a Hoover Unimelt apparatus. The resulting melting points are listed in Table 1. Elemental analysis was performed on each compound as the hydrochloride salt (Atlantic Microlab, Inc., Norcross, GA) and the actual and theoretical results presented in Table 1.

Presumptive tests (color tests, spot tests, field tests) are reported in Table 2. This method of testing used porcelain spot plates containing approximately 2–5 mg of each drug as the hydrochloride salt. Two to three drops of each reagent were applied to separate portions of the drug, and the short term response (5–10 s) noted and reported in Table 2. Solid phase infrared (IR) spectra (Fig. 1) were obtained using an ATI-Mattson Genesis Series Fourier Transform Infrared Spectrophotometer interfaced with a Dell Dimensions model XPS P90 computer. The IR spectra of the amines were acquired as the hydrochloride (HCl) salts in a potassium bromide (KBr) matrix while the IR spectra of the ketones were prepared using a thin film on a clear KBr disc. The gas phase IR spectra (Fig. 2) were recorded using a Hewlett-Packard (HP) model 5890 Series II gas chromatograph (GC) interfaced with an HP model 5965 infrared

Table 2
Color response for the listed compounds using some common reagents[a]

Hydrochloride	Marquis [29]	Mecke [30]	2° Amine [31]	Frohde [32][b]	Mandelin [33]	Liebermann [34]
Amphetamine	O(I)_Bn	NC	NR	NC	Bl/Gn[c]	O(I)
MDMA	Pr_Bk	Gn(I)_Bl(I)	Bl(D)	Bk	Bk[c]	Bk
2-MeoAmp	R_O	Ol/O	NR	O(P)	Gn/O[c]	Br(I)
3-MeoAmp	Pr	EGn_Gn	NR	NR	Gn/O_Gr[c]	Br
4-MeoAmp	NC	Ol(W)	NR	Gn(W)	Pk_R[c]	Pr/Br
2-MeoMeth	R_O	Ol/O	Bl	O(P)	Gn/O[c]	Br(D)
3-MeoMeth	Pr	EGn_Gn	Bl	NR	Pr(W)/Bl[c]	Br(D)
4-MeoMeth	NR	Ol(W)/Y	Bl	Gn(W)	Pk_R[c]	Pr/Br

[a] Keys — MDMA: 3,4-methylenedioxymethamphetamine; MeoAmp: methoxyamphetamine; MeoMeth: methoxymethamphetamine; (I): intense; W: weak; D: dark; P: pale; O: orange; R: red; Bl: blue; Br: brown; Bk: black; Pr: purple; Gn: green; EGn: emerald green; Gr: grey; Ol: olive green; Y: yellow; Pk: pink; NC: no change in reagent color; NR: no reaction, observed color is due to the reagent mix, i.e. pink for a negative secondary amine (2° amine) test, '/': mixture of colors or predominance of first color with streaks of the second color, 'underscore (_)': intermediate coloration of the two listed colors.
[b] Sodium molybdate, or ammonium molybdate, is more effective than molybdic acid.
[c] Mandelin's reagent is a yellow colored reagent and interpretation of color formation is more subjective than with colorless reagents.

detector (IRD). An HP Vectra XP/60 computer controlled the instrument. Chloroform solutions of the amines as free bases were injected into the GC–IRD to obtain vapor phase IR spectra.

The temperature programmed GC retention time (RT) data were acquired using an HP 6890 GC with a flame ionization detector (FID) and a J & W, DB-1 coated capillary column (Table 3). An HP Kayak XA computer controlled

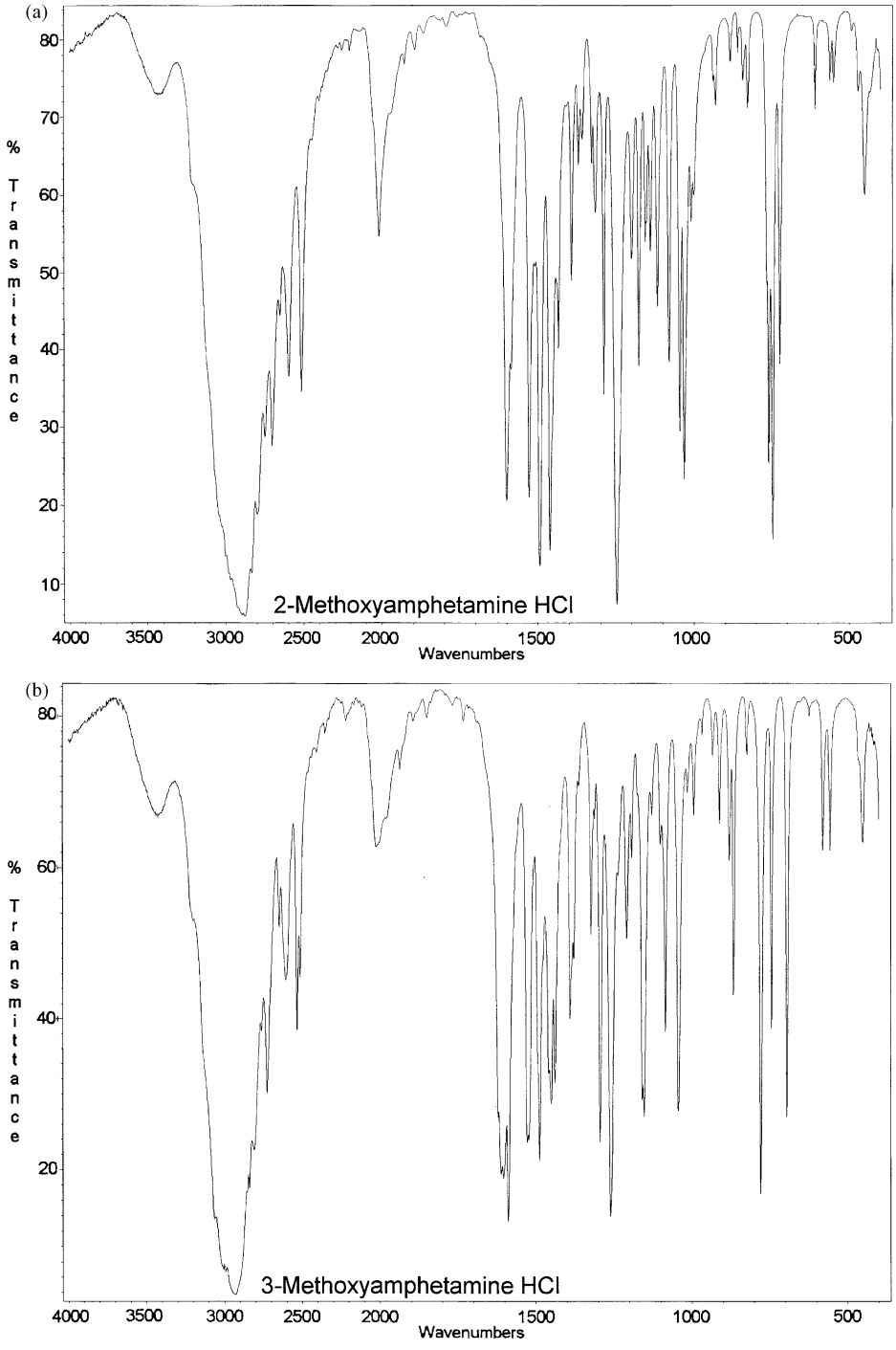
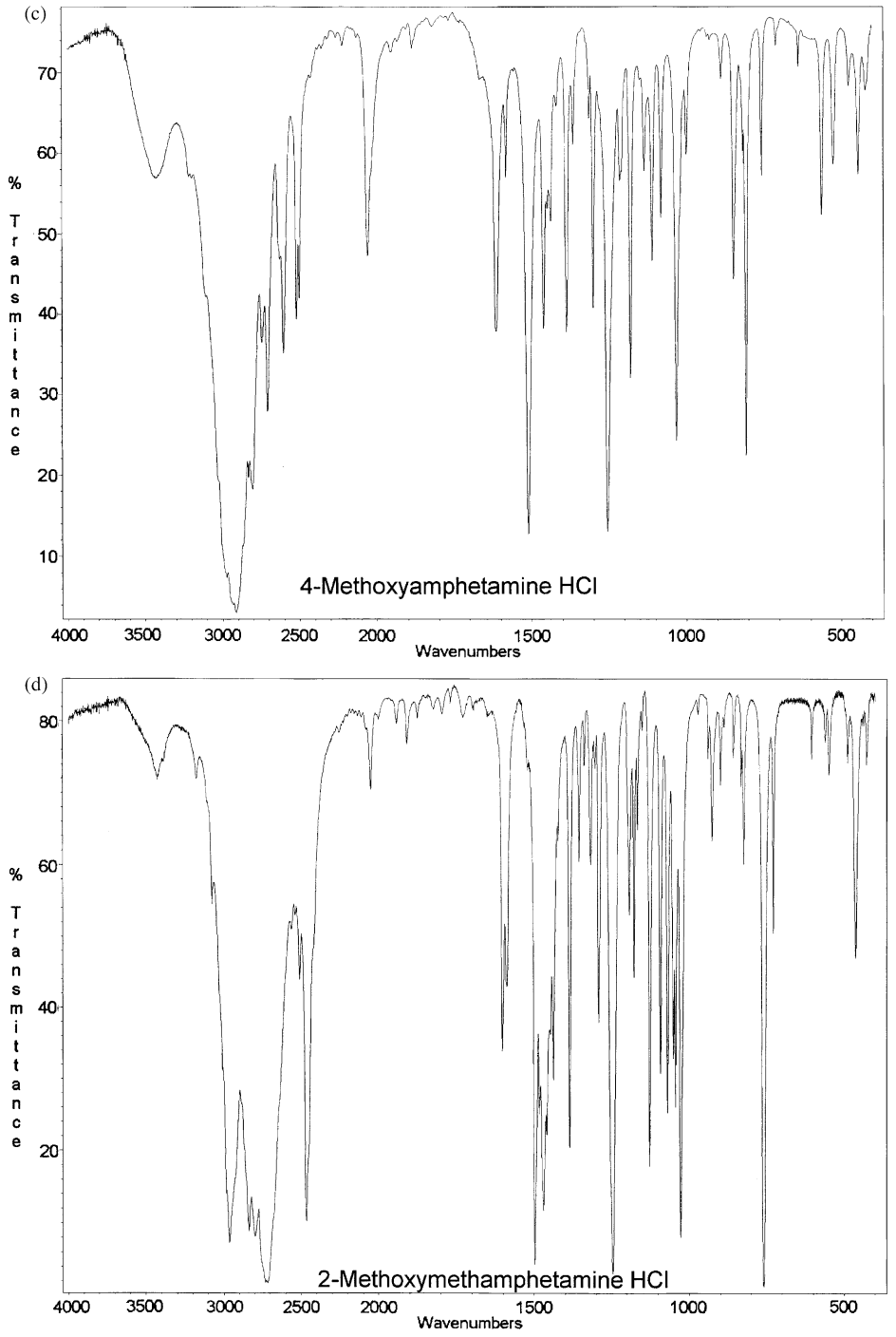


Fig. 1. Infrared spectra of the 2-, 3-, and 4-methoxy amines as the hydrochloride salts and the ketone precursors as neat liquids.



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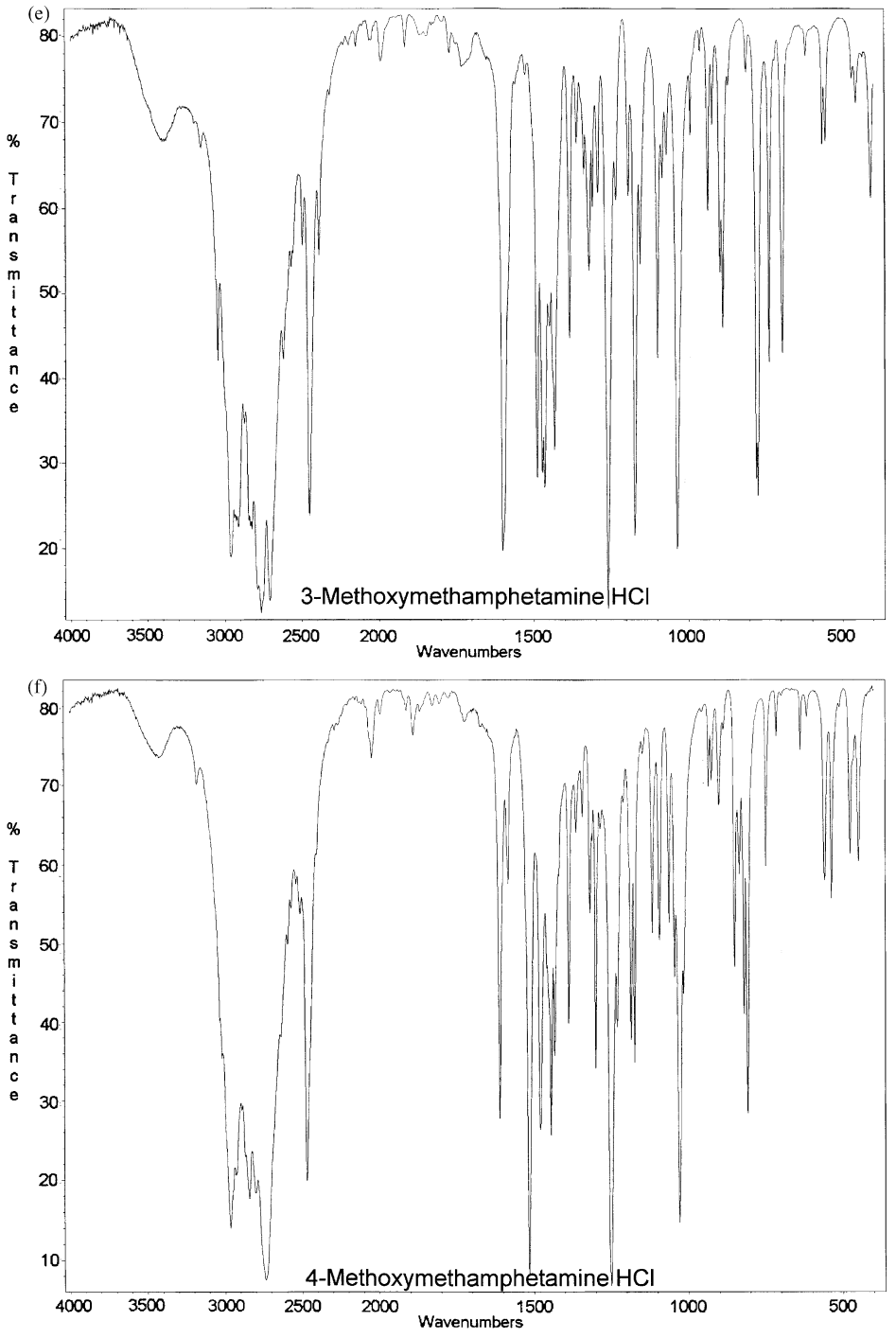

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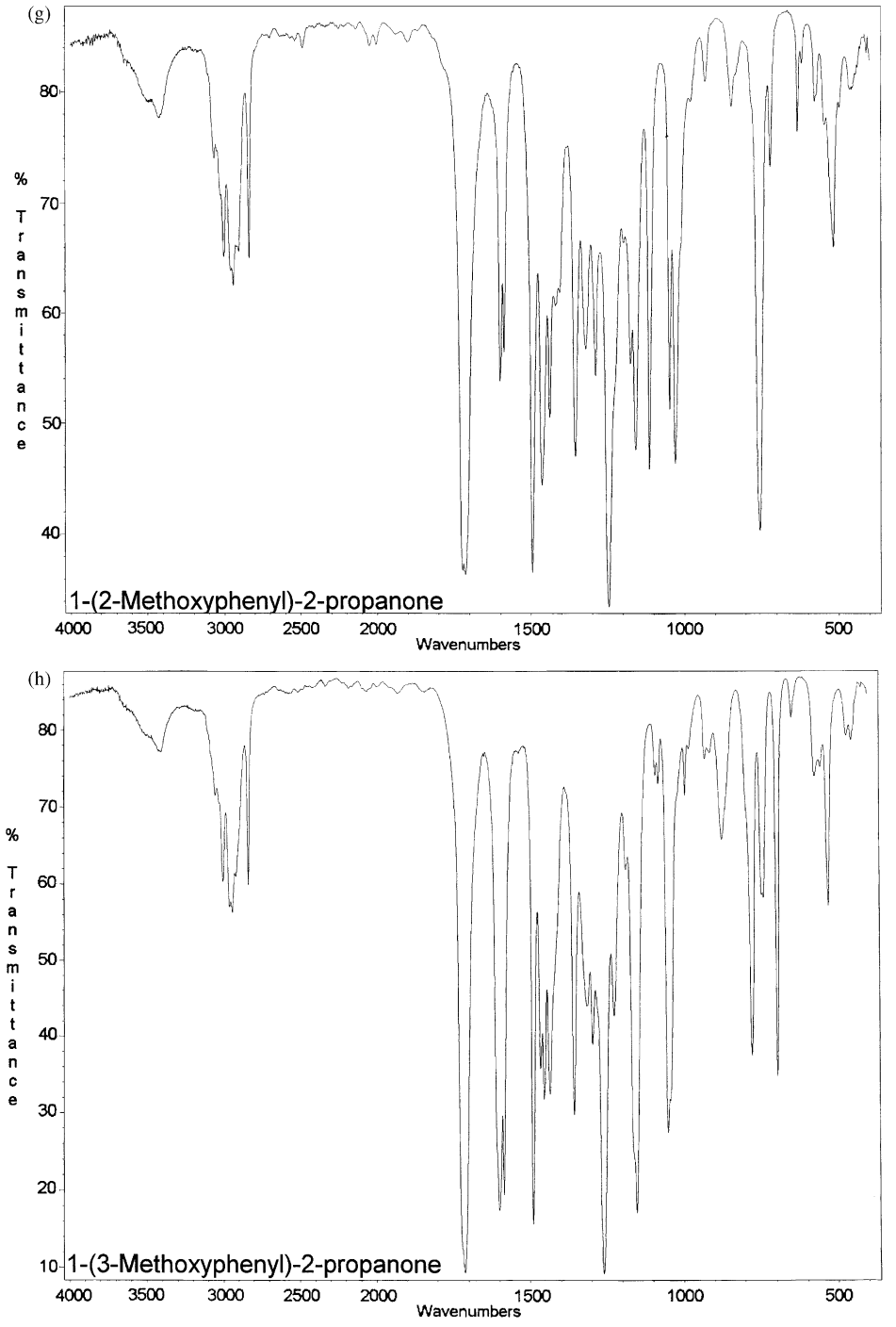

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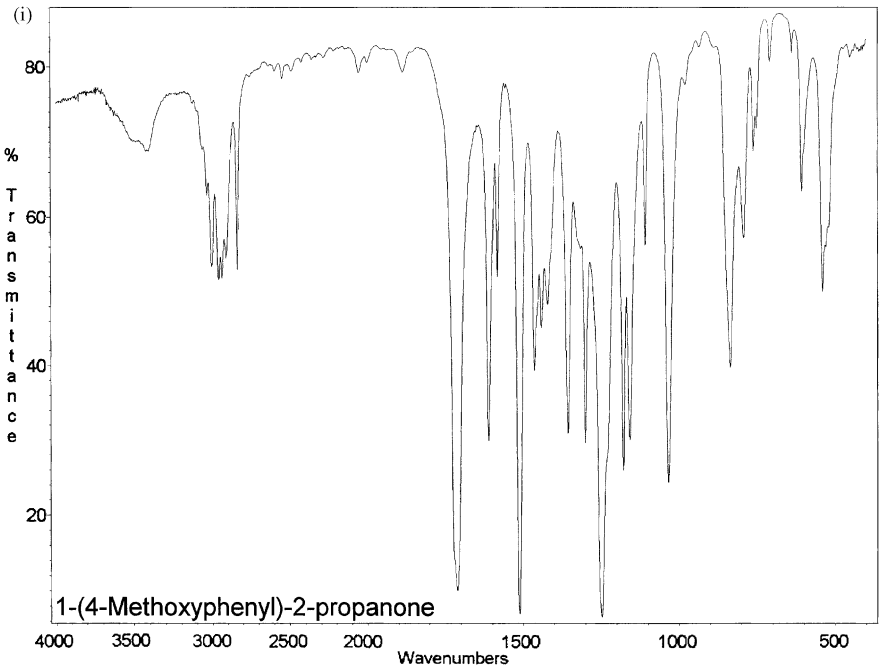


Fig. 1. (*Continued*).

Table 3
Retention times (RT, min) for the listed compounds[a]

S. no.	Compound	GLC1[b]	GLC2[c]
1	2-Methoxyamphetamine	3.05	4.65
2	3-Methoxyamphetamine	3.49	5.35
3	4-Methoxyamphetamine	3.62	5.60
4	2-Methoxymethamphetamine	3.73	5.69
5	3-Methoxymethamphetamine	4.36	6.68
6	4-Methoxymethamphetamine	4.62	7.07
7	2′-Methoxyphenyl-2-propanone	2.99	4.78
8	3′-Methoxyphenyl-2-propanone	3.24	5.25
9	4′-Methoxyphenyl-2-propanone	3.48	5.64
10	*N*-acetyl-2-methoxyamphetamine	9.99	10.86
11	*N*-acetyl-3-methoxyamphetamine	10.26	11.14
12	*N*-acetyl-4-methoxyamphetamine	10.39	11.29
13	*N*-acetyl-2-methoxymethamphetamine	10.47	11.39
14	*N*-acetyl-3-methoxymethamphetamine	10.64	11.58
15	*N*-acetyl-4-methoxymethamphetamine	10.84	11.75
16	Propiophenone[d]	1.58	2.61
17	Tridecane[d]	2.87	3.90
18	Pseudoephedrine[d]	3.52	6.14

[a] Propiophenone, tridecane, and pseudoephedrine included as RT references.

[b] J & W, DB-1; 15 M × 320 μM × 0.25 μM; HP 6890 GC; FID detector; 120°C for 8 min; rate 30°C/min; final temperature 240°C; final time 0.0; gas type: helium; split ratio 11.0:1 ml/min; split flow 24.2 ml/min; total flow 29.2 ml/min; linear velocity 47 cm/s; makeup flow (N_2) 35.0 ml/min.

[c] HP-5MS 5% phenyl methyl siloxane; 30 M × 250 μM × 0.25 μM; HP 6890 GC; MSD 5973 detector; 130°C for 8 min; rate 30°C/min; final temperature 250°C; final time 0.0; initial helium carrier flow 1.0 ml/min; linear velocity 38 cm/s; split ratio 100:1 ml/min; split flow 99.6 ml/min; total flow 103.5 ml/min.

[d] Compounds included as RT references.

program execution through a windows NT interface. Additional GC data and electron impact (EI) mass spectra (Fig. 3) were acquired from an HP model 5973 mass selective detector (MSD) interfaced with an HP 6890 GC containing a HP-5MS 5% phenyl methyl siloxane coated capillary column. Programming was controlled with a Windows 95-based HP Vectra XA computer. *N*-acetyl (amide) mass spectra (Fig. 4) were acquired by adding two drops of acetic anhydride directly to the original chloroform solutions of the bases and re-injecting the mixtures using the original parameters listed in Table 3. Proton nuclear magnetic resonance (pNMR) spectra (Fig. 5) were recorded using a Varian

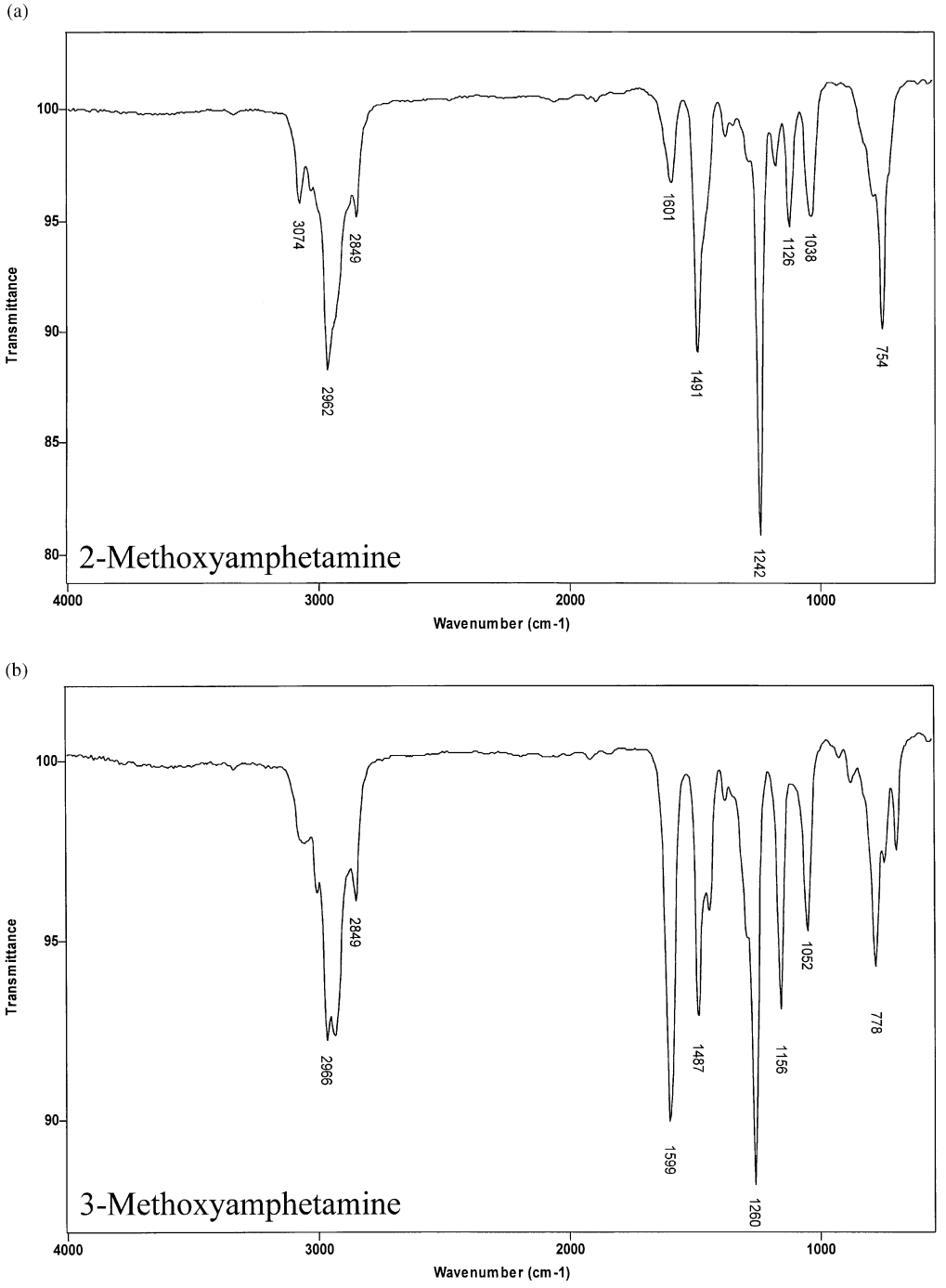
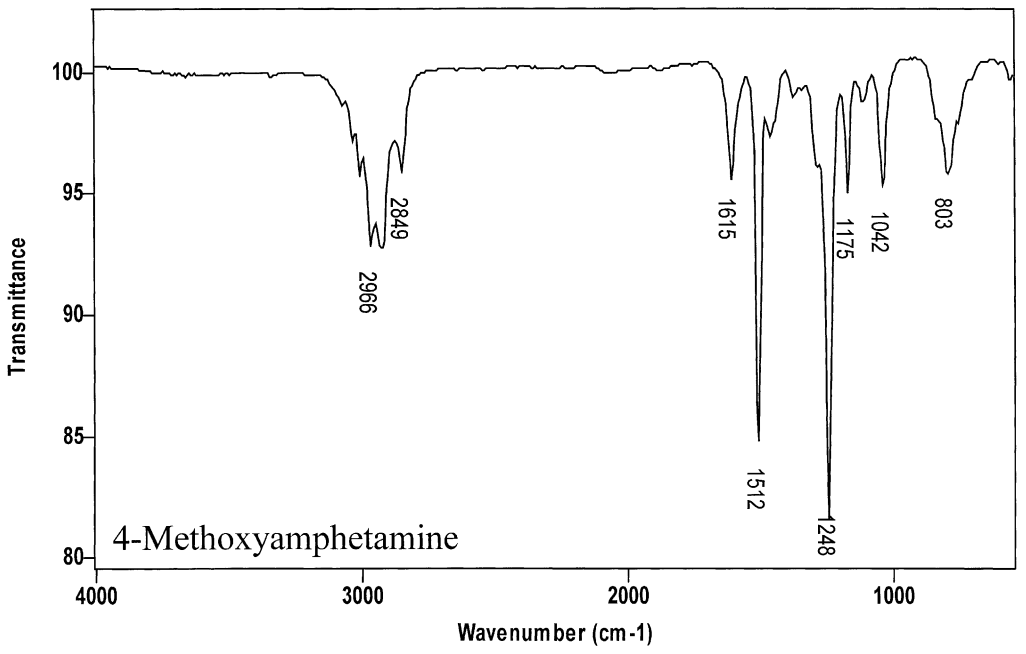
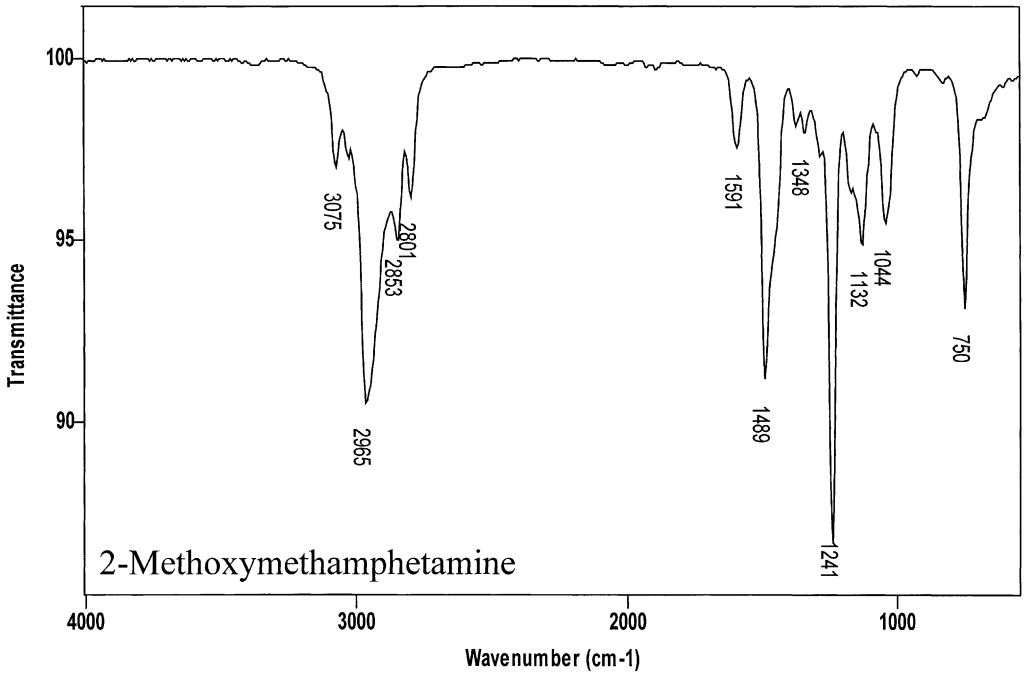


Fig. 2. Vapor phase infrared spectra of the free base 2-, 3-, and 4-methoxy amines and the ketone precursors.

(c)



(d)



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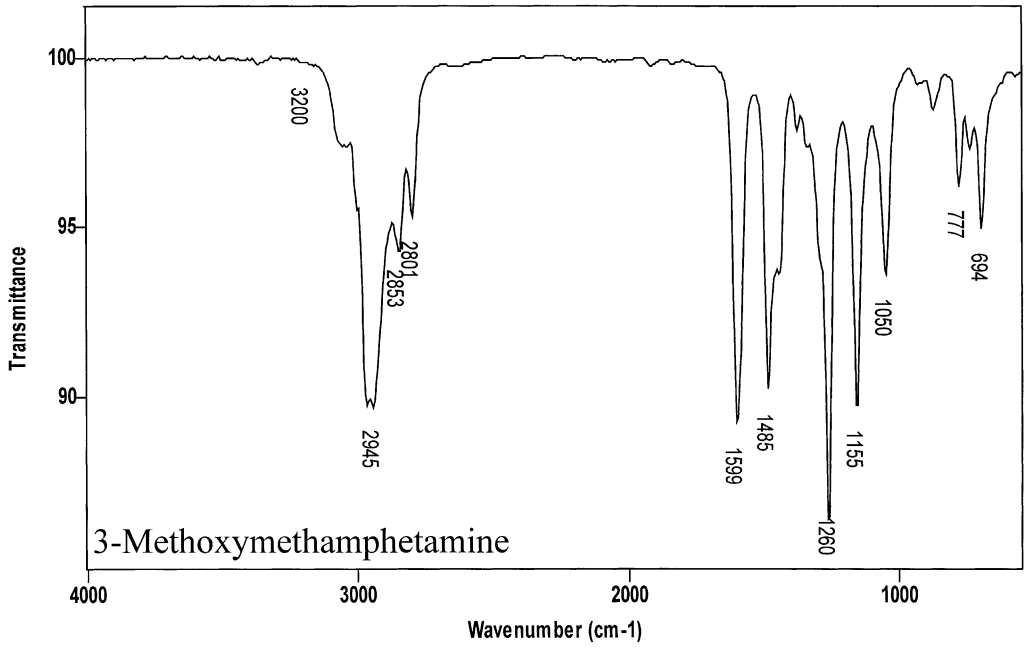

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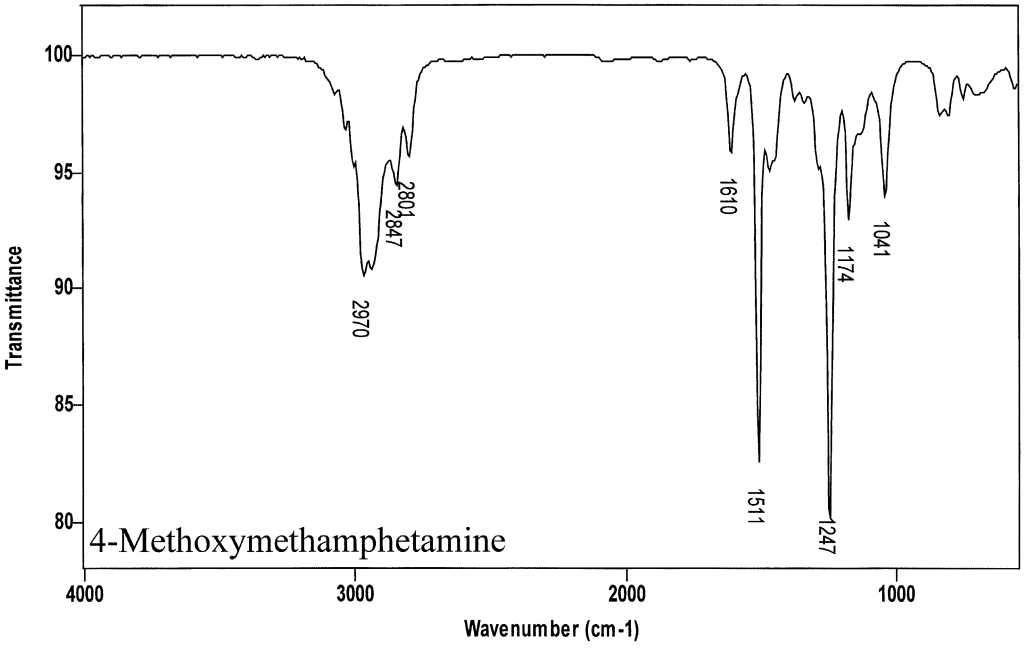

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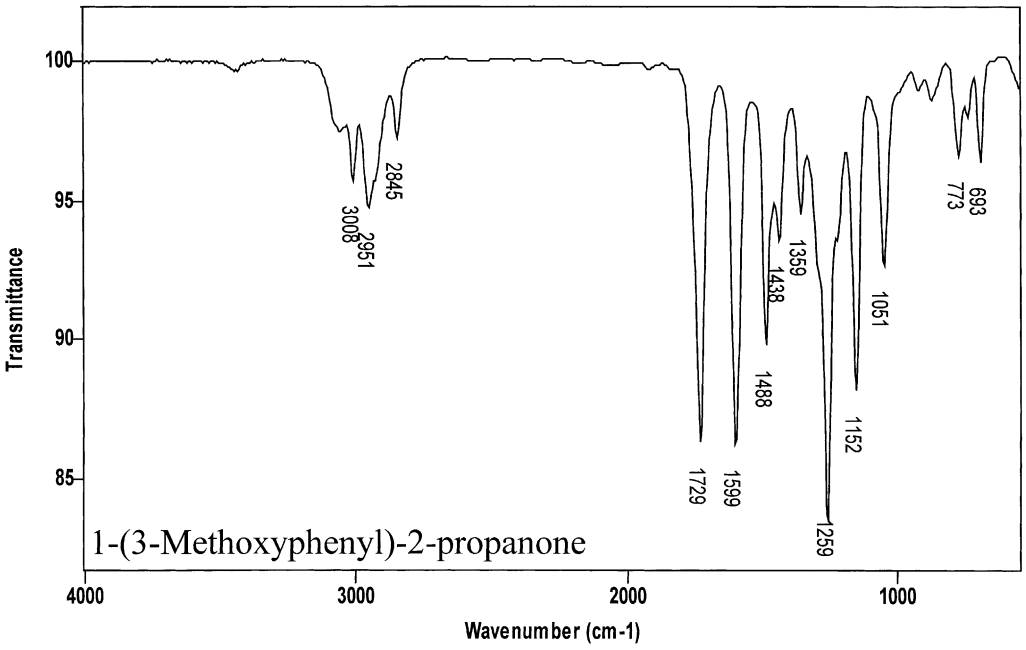

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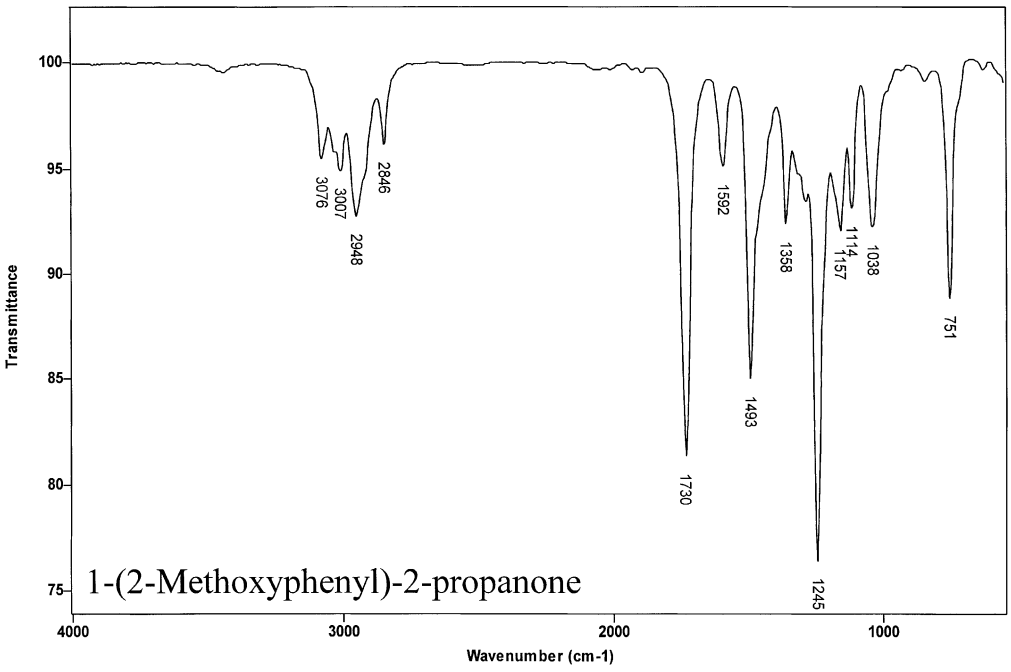

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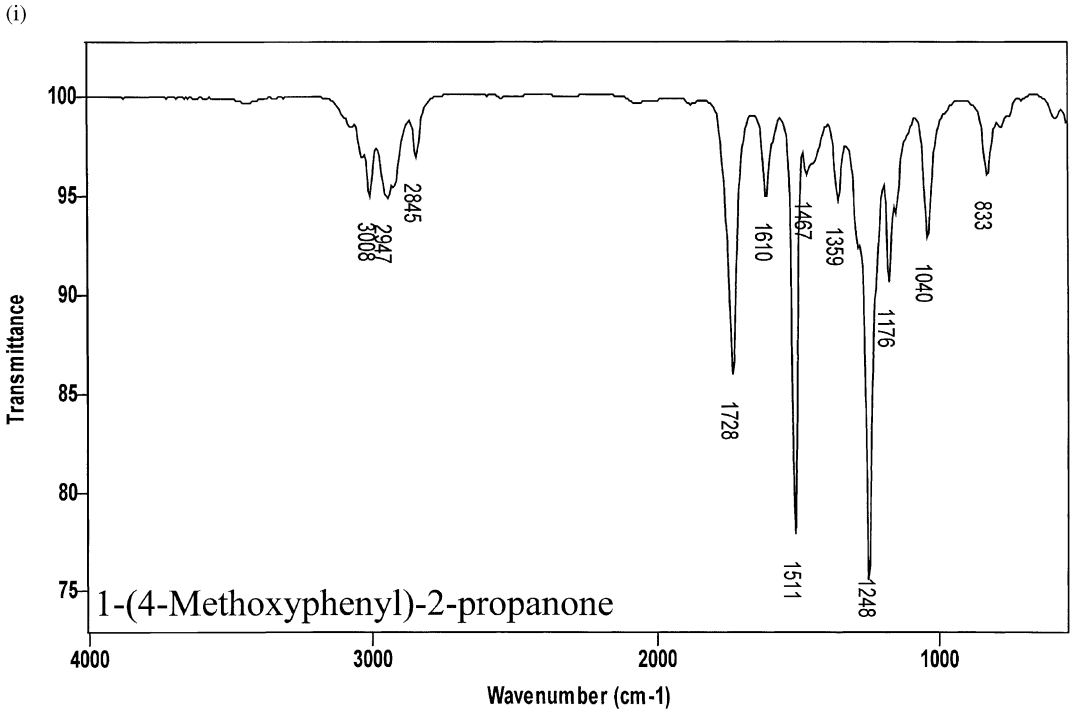


Fig. 2. (*Continued*).

Gemini 300 Fourier transform nuclear magnetic resonance (FTNMR) spectrometer. The six amines were extracted from basic aqueous solutions into deuterochloroform ($CDCl_3$). The free base solutions were then passed through a bed of anhydrous sodium sulfate directly into 5 mm NMR sample tubes. The ketones were dissolved directly in $CDCl_3$. Tetramethylsilane served as an internal chemical shift standard ($\delta + 0.00$ ppm) at 20°C (ambient) with a 300 MHz observation frequency.

3. Results and discussion

Six ring substituted methoxyphenylisopropylamines and their three ketone precursors were examined by a variety of instrumental and chemical techniques that are representative of the wide spectrum of instrumental and analytical methods available to forensic drug laboratories. The results of each category of testing are discussed below.

3.1. Melting points and elemental analysis

The determination of melting point ranges is a standard method for indicating purity of compounds. Sharp small ranges of 1–3°C indicate a pure compound, while wide ranges show evidence of impurities being present. Likewise, elemental analyses providing values close to the theoretical are an indicator of high purity compounds. Melting points and elemental analysis of experimental compounds are shown in Table 1.

3.2. Presumptive tests

Presumptive tests (i.e. field tests, color tests) can be of significant value in gathering information about an unknown at the beginning stage of analysis. These tests indicate a positive result by formation of a color that is characteristic of a class of compounds (i.e. functional groups). By using a select assortment of color reagents, it is often possible to narrow the identity of an unknown sample to a small number of compounds. Six presumptive tests (Table 2) are presented here to help in identifying mono-methoxy substituted amphetamine analogs. The Marquis test presents the most striking example of the value of presumptive testing. By using the Marquis test in combination with the secondary amine test (2° amine test, nitroprusside test) the probable identity of the eight compounds in Table 1 can be ascertained. In practice, the lack of response to the Marquis and secondary amine tests, as observed with the 4-methoxy amines, would trigger the use of an additional combination of field tests, some of which are given in Table 2. Mecke's reagent is particularly useful for presumption of 3,4-methylenedioxyamphetamine (MDA) and its *N*-substituted analogs since it yields an emerald green color that *instantly* turns to an intense Prussian blue in the presence of these compounds. Tablets or powders which contain mixtures of

drugs can provide confusing results. A given set of color responses to a combination of field test reagents only serves as an indicator of what may be identified by further specific analysis.

3.3. Gas chromatography

Two types of column coating, DB-1 and HP-5MS were examined using several compounds as retention time

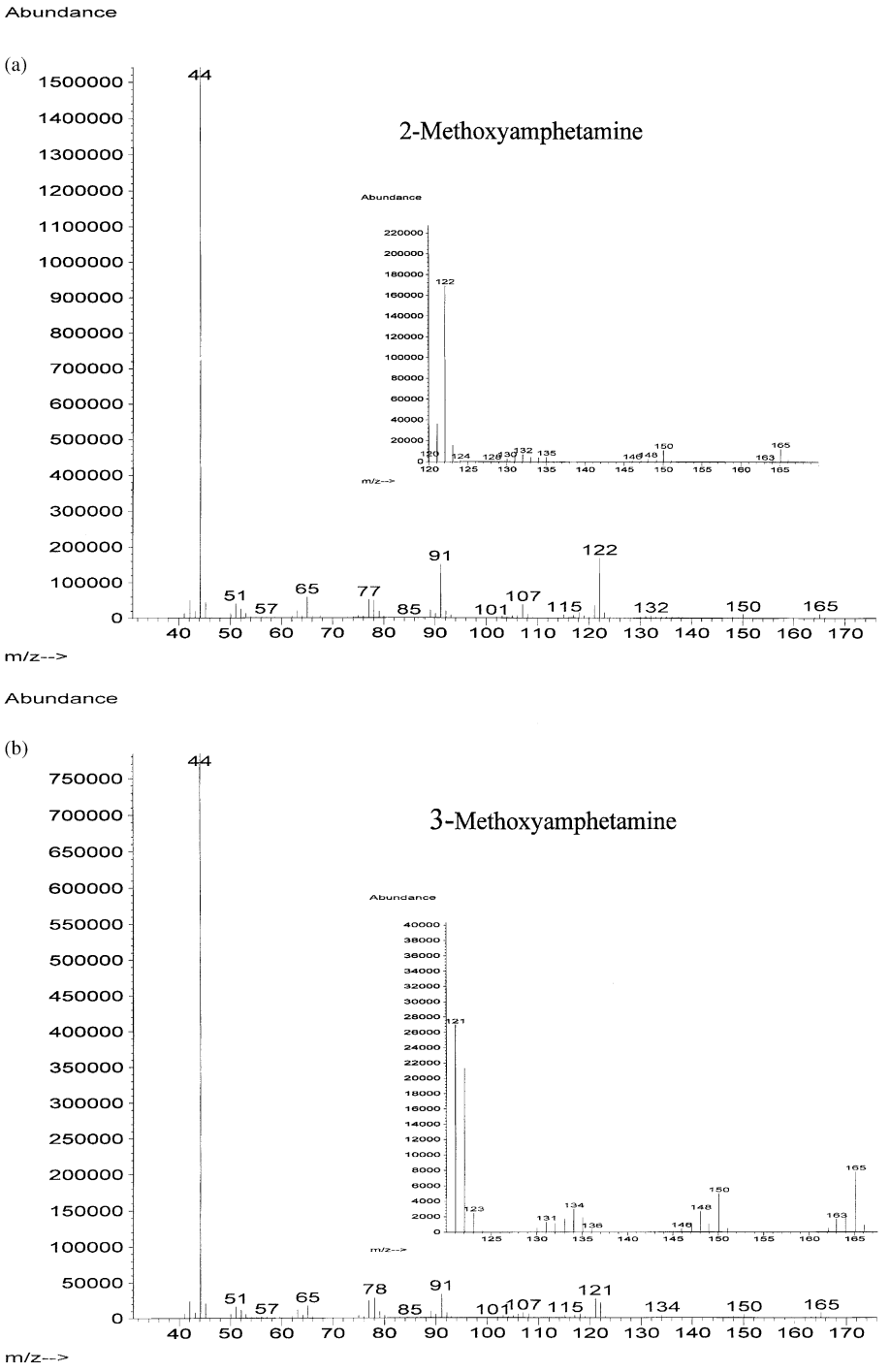
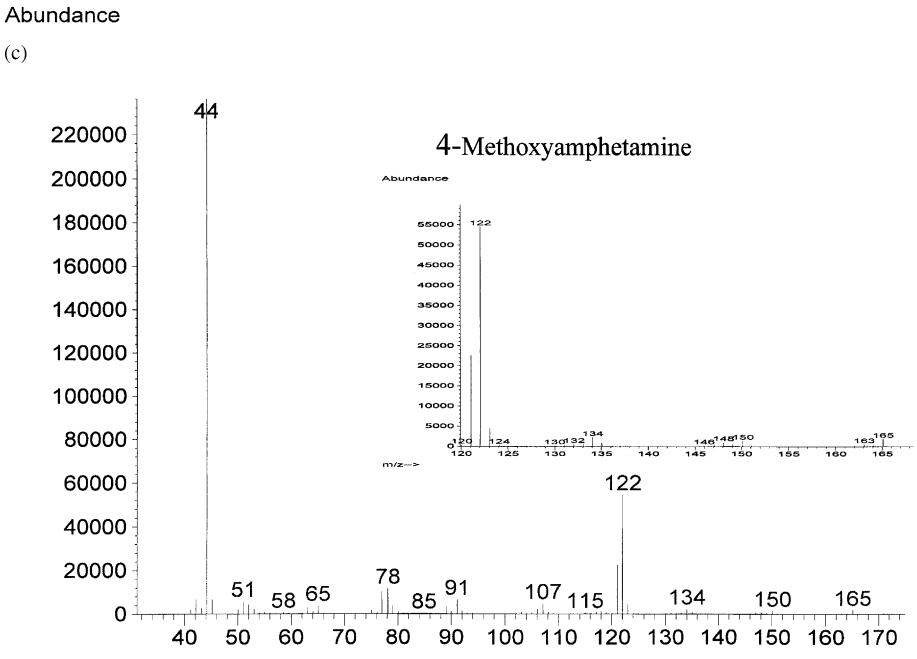
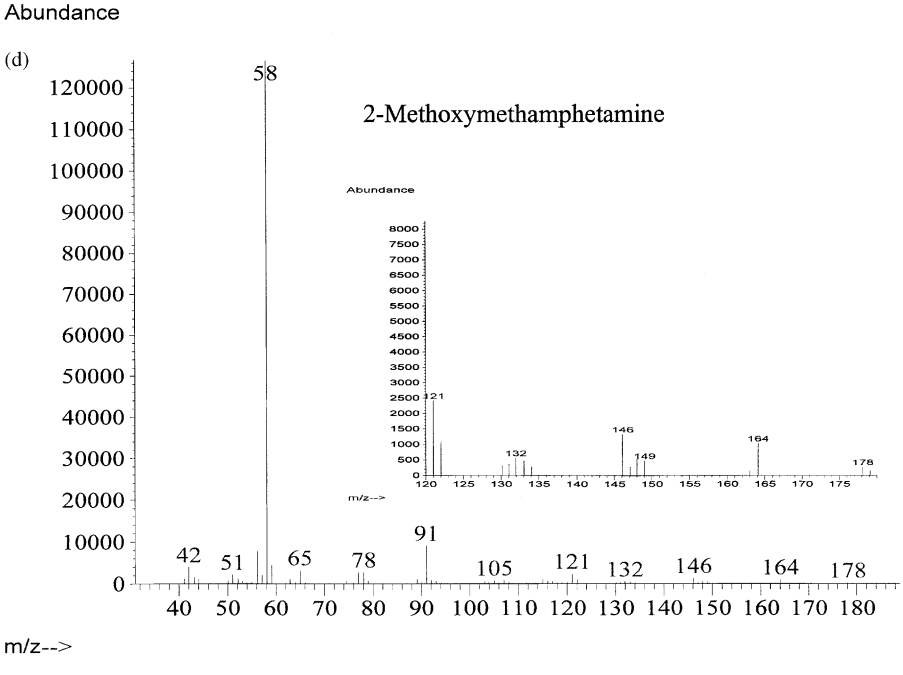


Fig. 3. Electron impact (EI) mass spectra of the free base 2-, 3-, and 4-methoxy amines and their ketone precursors.





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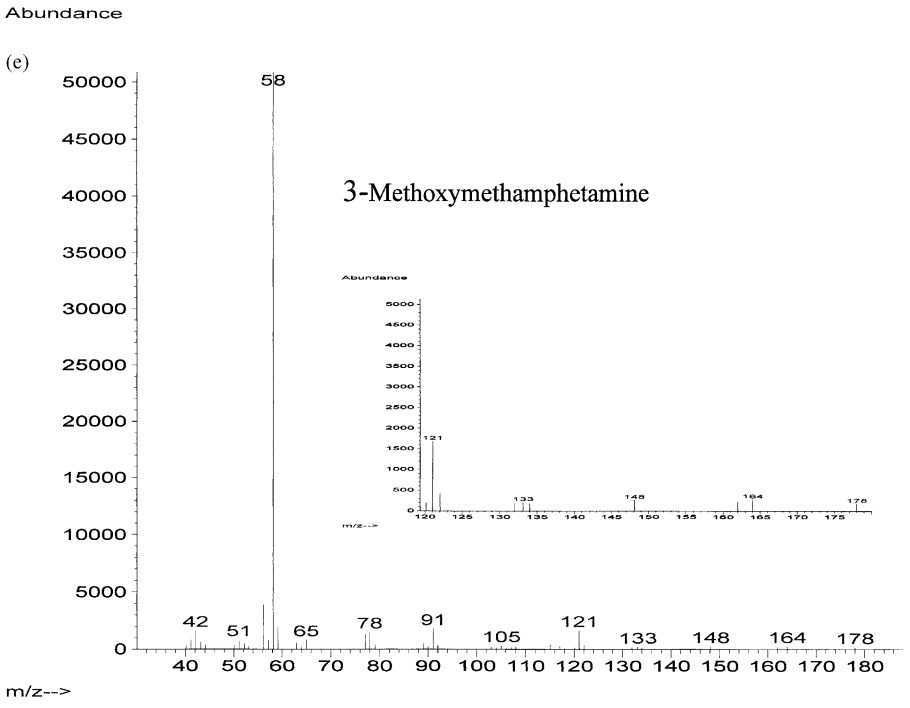

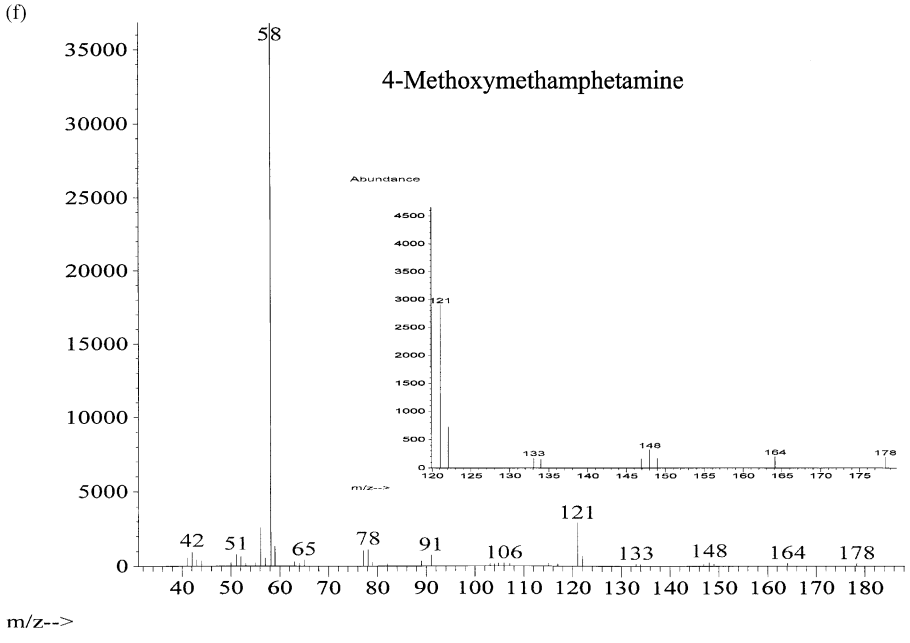

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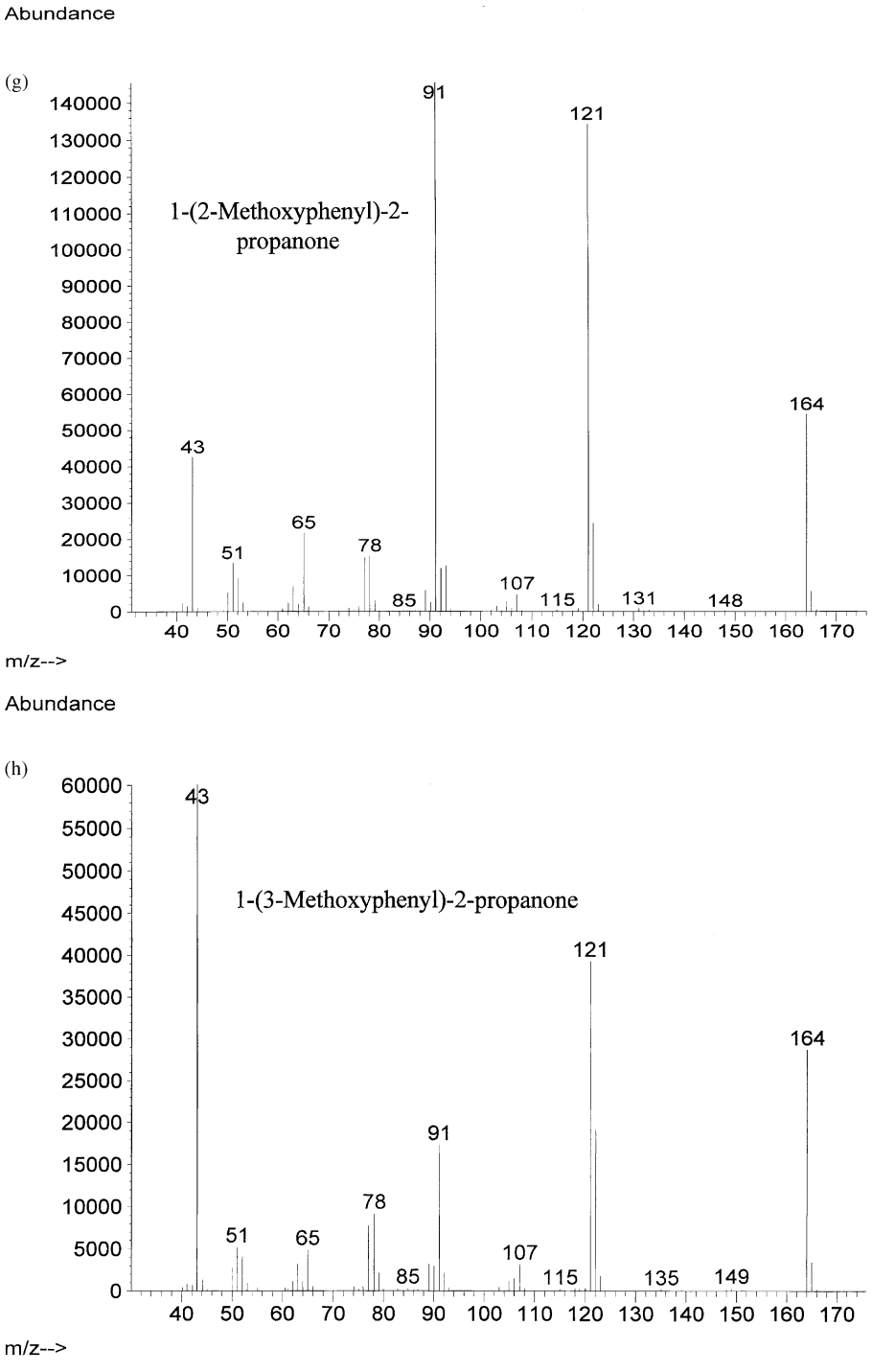


Fig. 3. (*Continued*).

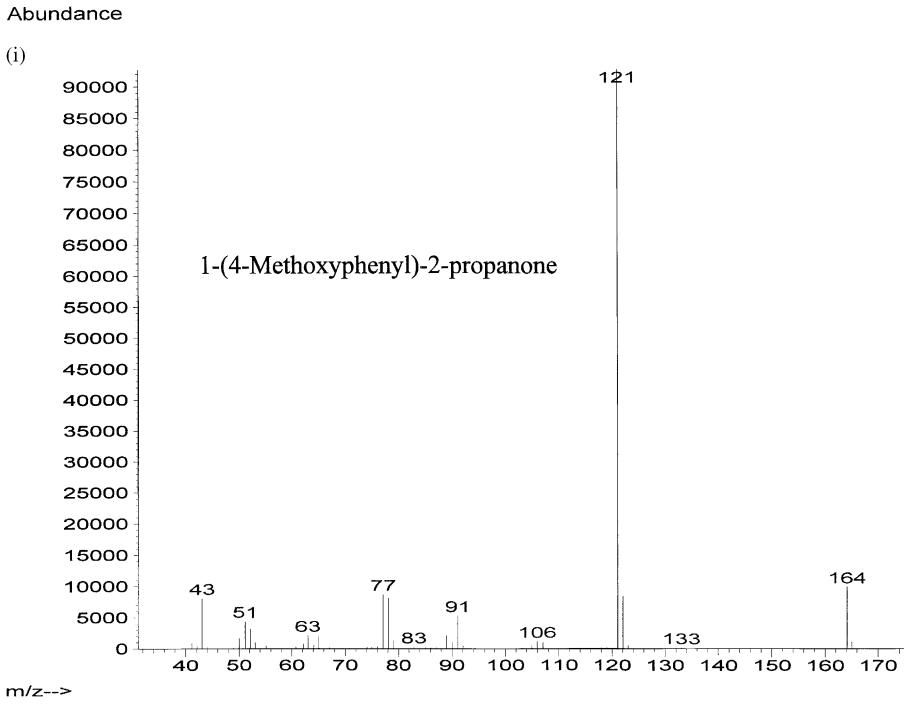


Fig. 3. (*Continued*).

reference standards (Table 3). No two compounds co-elute on either column type.

3.4. Infrared spectrometry

Infrared spectra of each of the six mono-methoxy amines as the hydrochloride salt are presented along with spectra of the three ketone precursors used in the synthesis of these ring substituted amines (Fig. 1). Each of these compounds is easily differentiated by solid phase IR. The gas phase IR spectra (Fig. 2) lack the fine structure associated with the solid phase spectra and differentiation of these compounds by vapor phase IR often entails closer scrutiny. As GC eluates, the vapor phase IR spectra have the advantage of representing very pure compounds that do not suffer from solid-state IR complications such as polymorphism and multiple hydrated forms.

3.5. Mass spectrometry

The electron impact mass spectra of all nine compounds are presented in Fig. 3. The amine hydrochlorides were extracted from pH 12–13 basic aqueous solutions into chloroform, dried through a column of anhydrous sodium sulfate, and subsequently introduced into the GC–MS as the free bases. The amines show very small molecular ions (M^+) typical of phenethylamines, and insets of the enhanced masses above 120 Da are provided for the six amines. The addition of several drops of acetic anhydride to each of the previously extracted amines (free bases in $CHCl_3$) allows formation of their respective acetamides when injected into the hot injection port of the GC. This technique provides an additional mass spectrum (Fig. 4) of each amine as its *N*-acetyl derivative and also gives an accompanying retention time. The acetylated compounds retain their base peaks (B) and acquire a B + 42 fragment and an M + 42 molecular ion. The liquid ketones were dissolved directly in $CHCl_3$ and their mass spectra are included in Fig. 3.

3.6. Proton nuclear magnetic resonance

The pNMR spectra of the 2-, 3-, and 4-methoxyamphetamines can readily be distinguished from the 2-, 3-, and 4-methoxymethamphetamines by the chemical shift of the N–CH_3 group appearing between 2.6 and 2.7 ppm. The multiplets between 7.0 and 7.6 allow differentiation of the *ortho* (2-), *meta* (3-), and *para* (4-) ring positions of the methoxy group for both the amines and the ketones.

3.7. Tablet extraction

A suitable number of tablets should be screened before mixing or grinding to determine if the tablets exhibit a similar composition [25]. If necessary, the tablets should be segregated based on these results and then ground into a fine powder, mixed with water, filtered, and admixed with a sodium hydroxide solution. The solutions may then be extracted with a water immiscible solvent, such as

chloroform and used directly for mass spectrometry or, if the tablets appear to be single entity, converted to the hydrochloride salt for infrared spectroscopy. For tablets that appear to be single entity, or have a relatively large concentration of one component, a chloroform dry wash will extract the hydrochloride salt directly and permit a direct acquisition of the infrared spectrum. In a similar manner, phosphates and sulfates can often be dry extracted using methanol or ethanol. If salt form preservation is not required, phosphates and sulfates can be extracted from basic aqueous

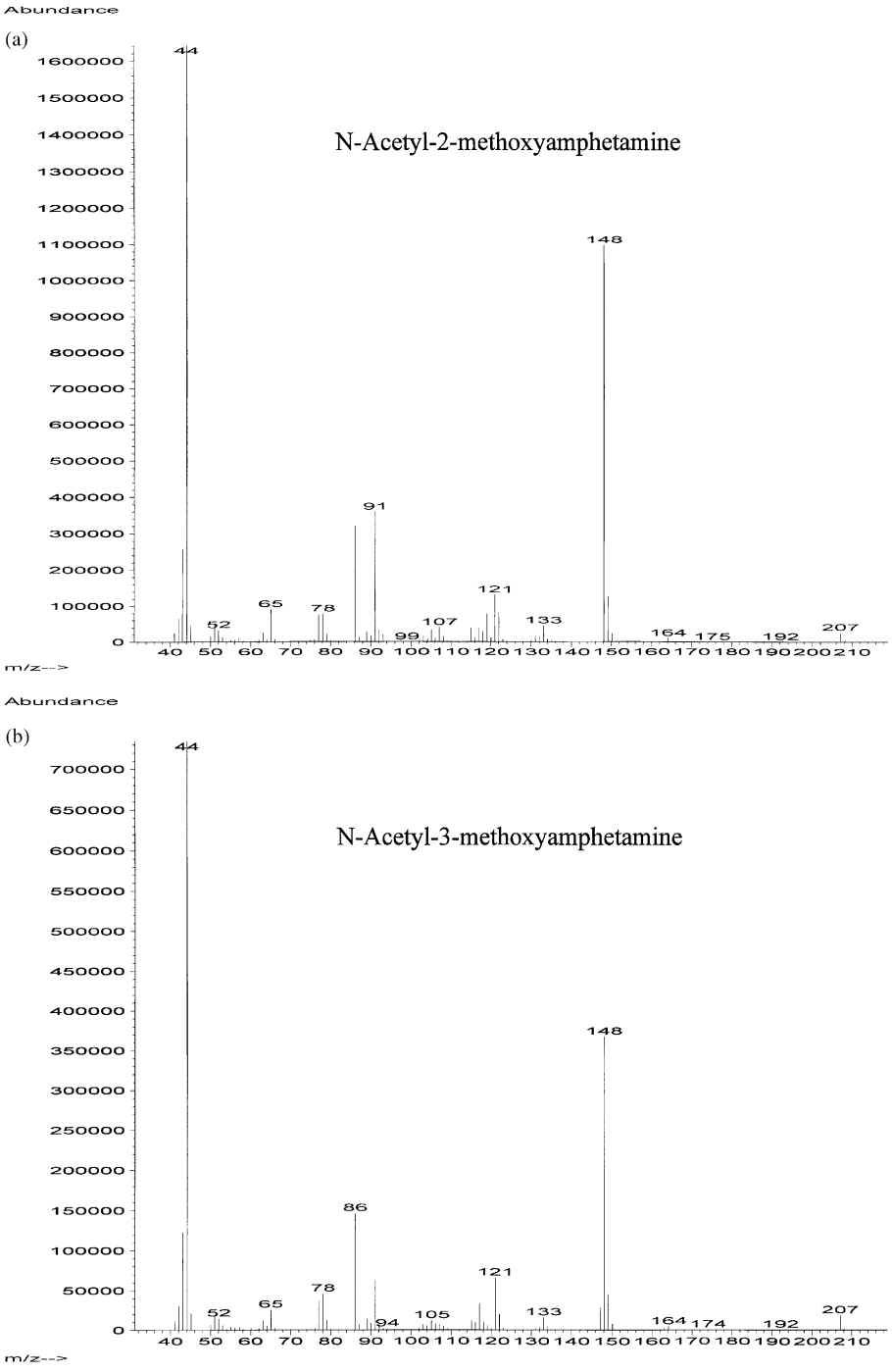
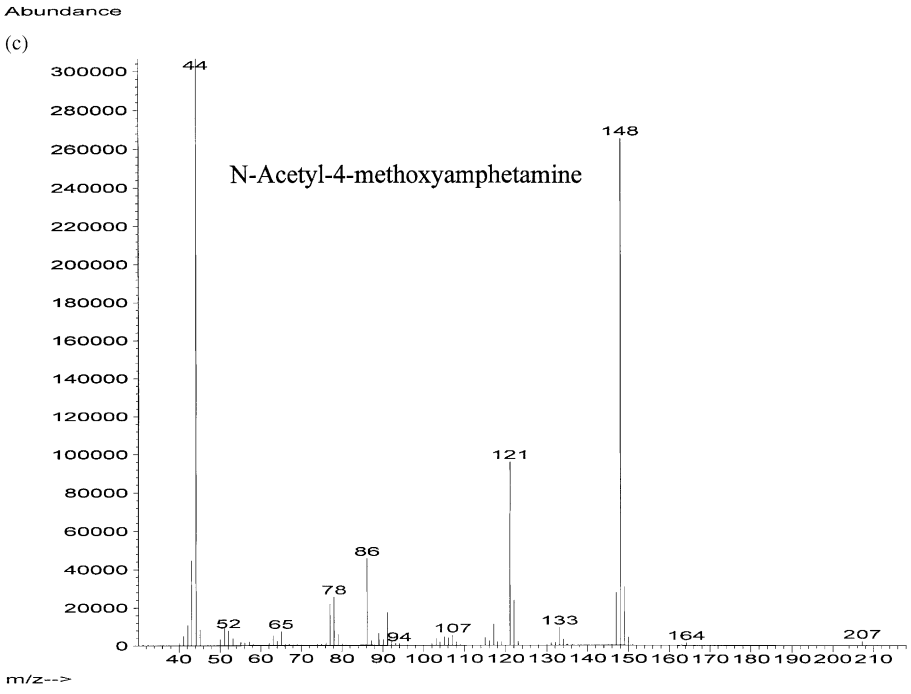


Fig. 4. Electron impact (EI) mass spectra of the 2-, 3-, and 4-methoxy amines as their *N*-acetyl derivatives (acetamides).



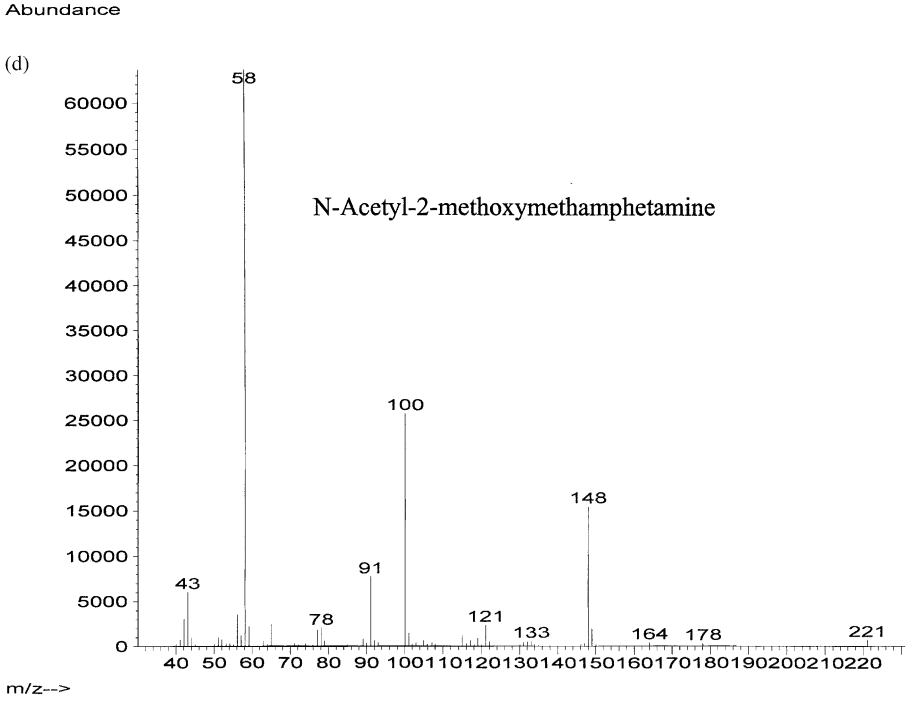


Fig. 4. (*Continued*).

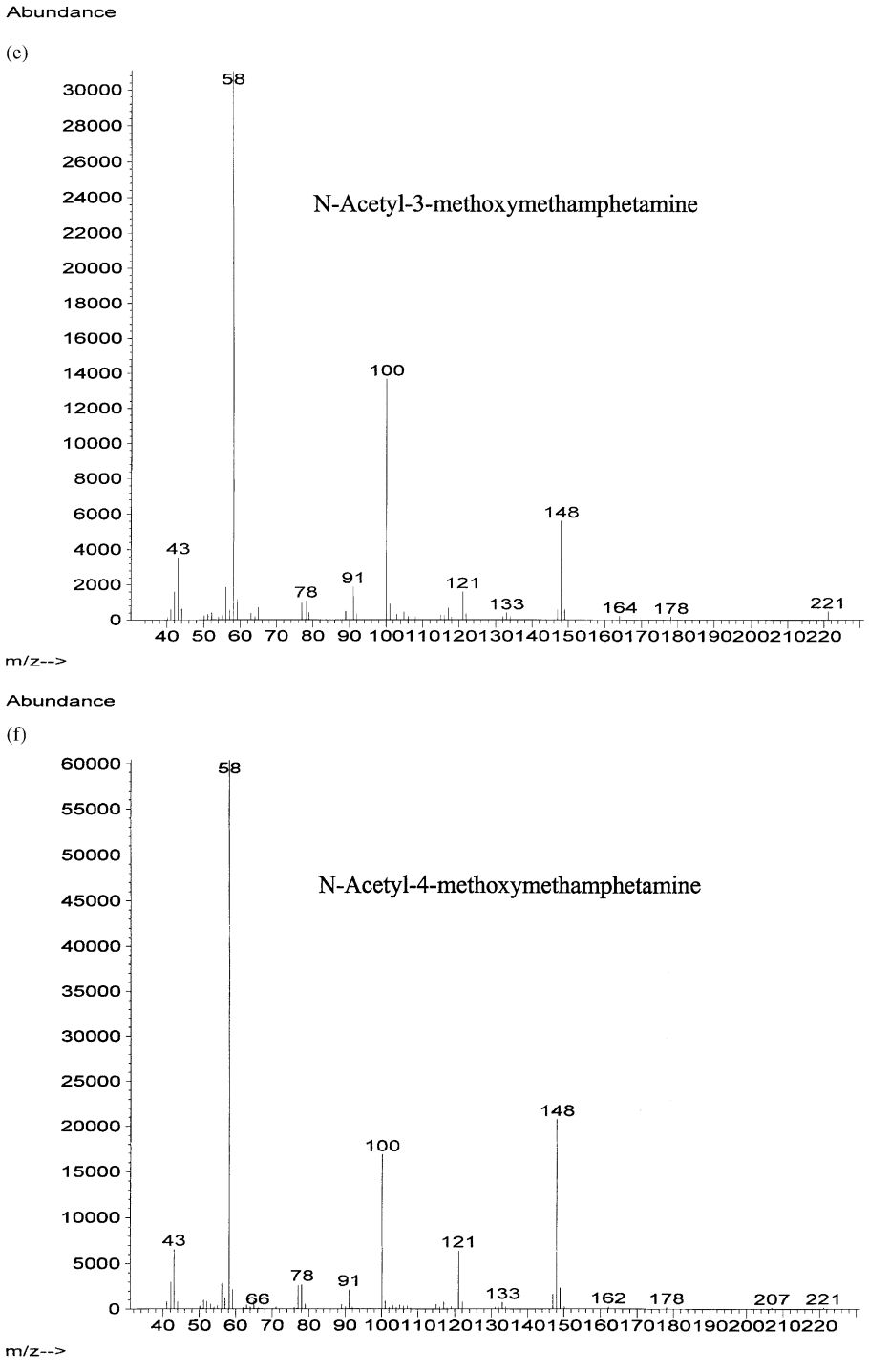


Fig. 4. (*Continued*).

solutions with an appropriate solvent, followed by conversion to the hydrochloride salt with hydrogen chloride gas or hydrochloric acid in 2-propanol.

3.8. Clandestine synthesis

The method of clandestine synthesis of PMA and PMMA is currently in question. A wide variety of techniques is available that uses the commercially available 4-methoxy ketone as the precursor [26,27]. At the present time, there are no reports of the clandestine synthesis of the 2-, or 3-methoxy amines. Kirkbride et al. recently published a ''fingerprint'' of by-products for determining if the Leuckart procedure has been used in the synthesis of PMA [28]. Because mixtures containing both PMA and PMMA have been identified in the 3-diamond tablets, the question arises whether this combination was intentionally prepared by mechanically mixing the products of two separate syntheses,

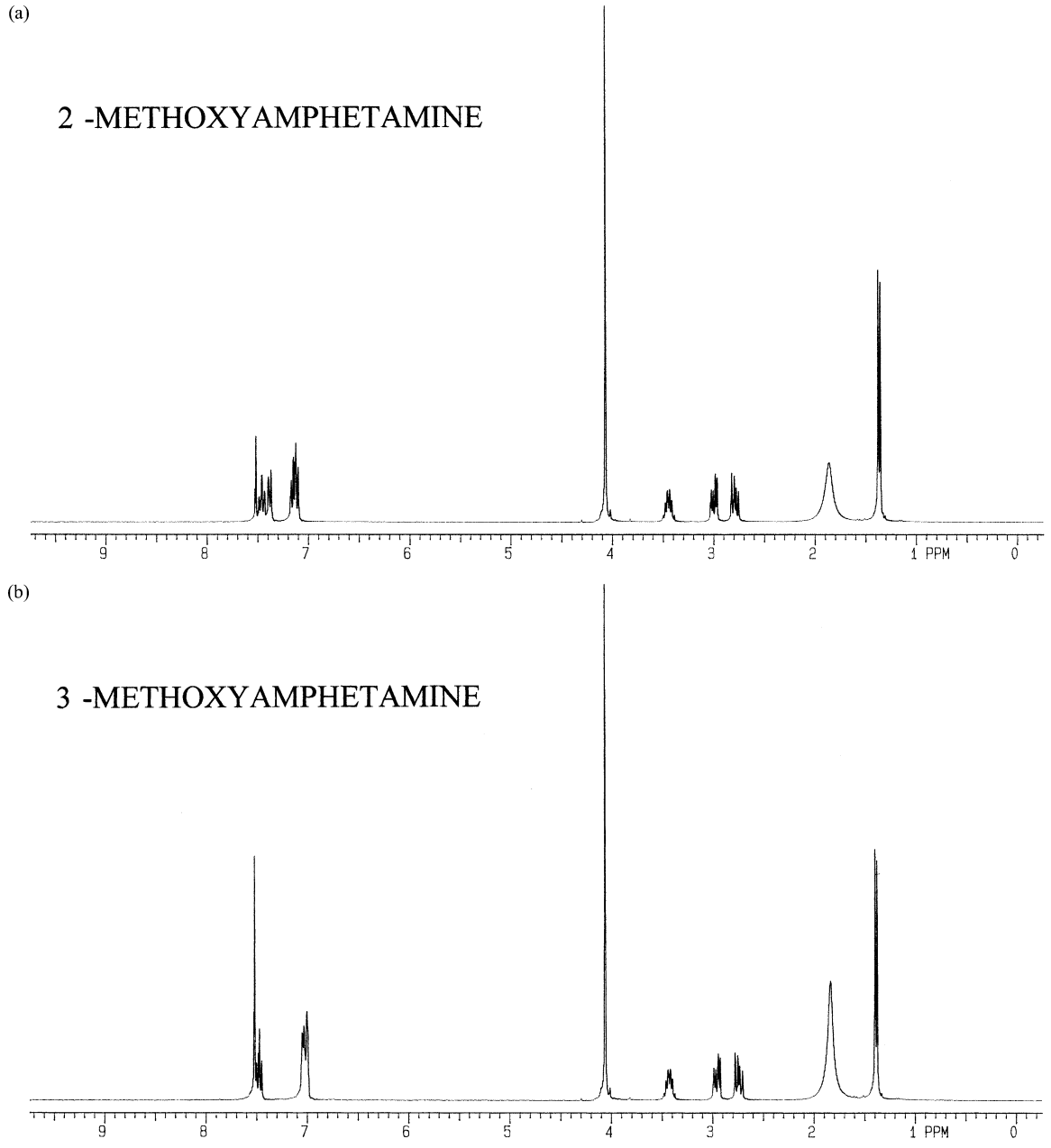
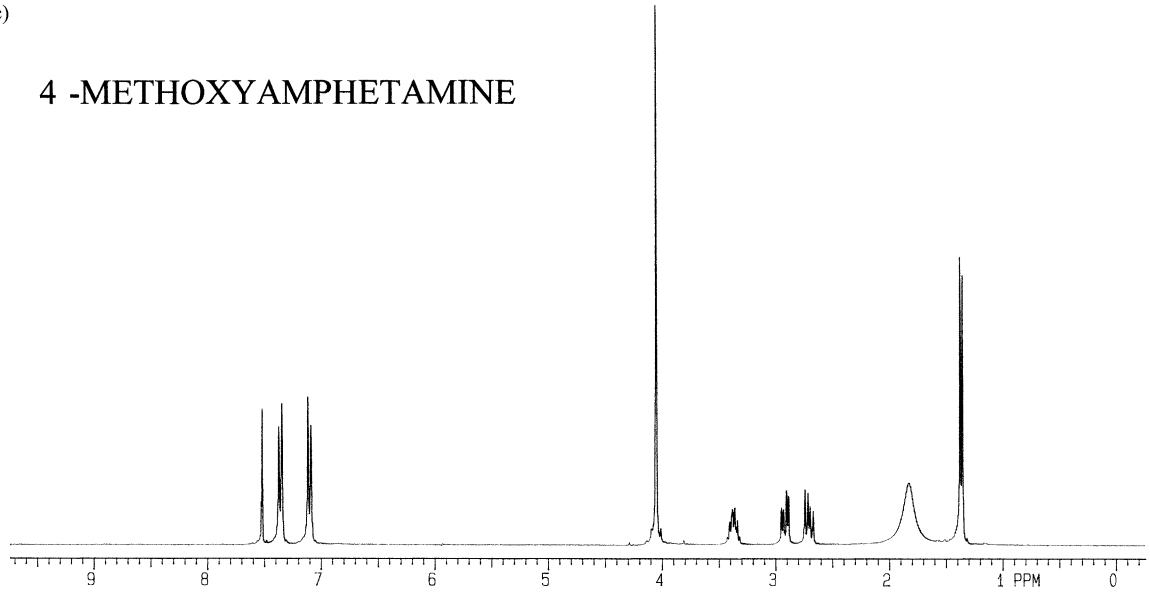


Fig. 5. pNMR spectra of the 2-, 3-, and 4-mono-methoxy amines as free bases and their ketone precursors in deuterochloroform.

(c)



(d)

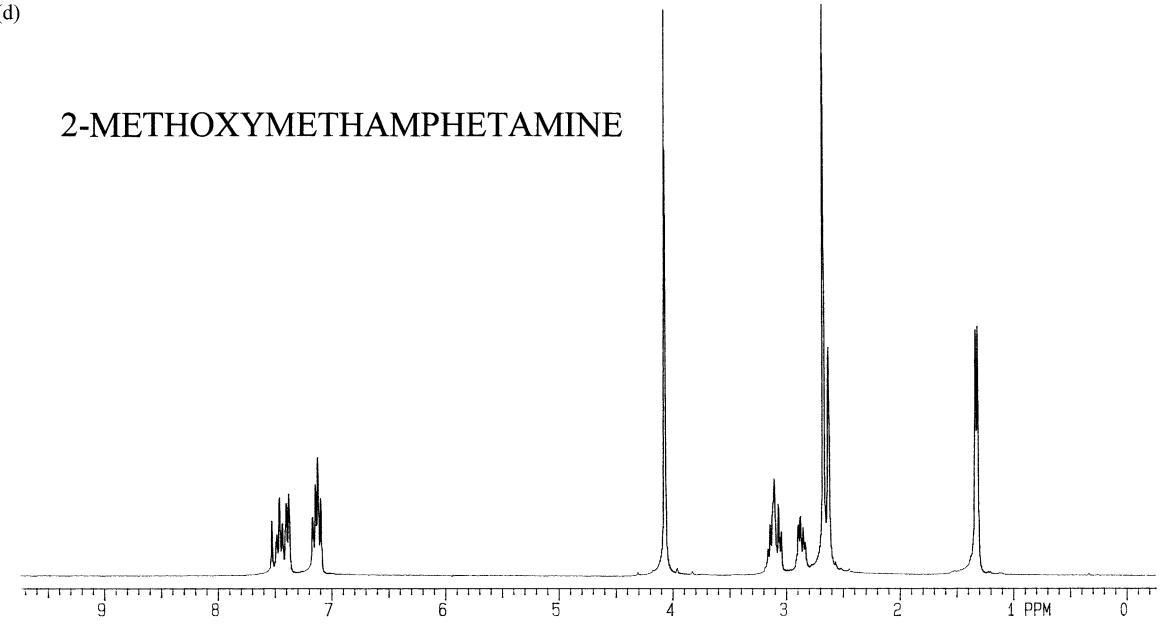


Fig. 5. (*Continued*).

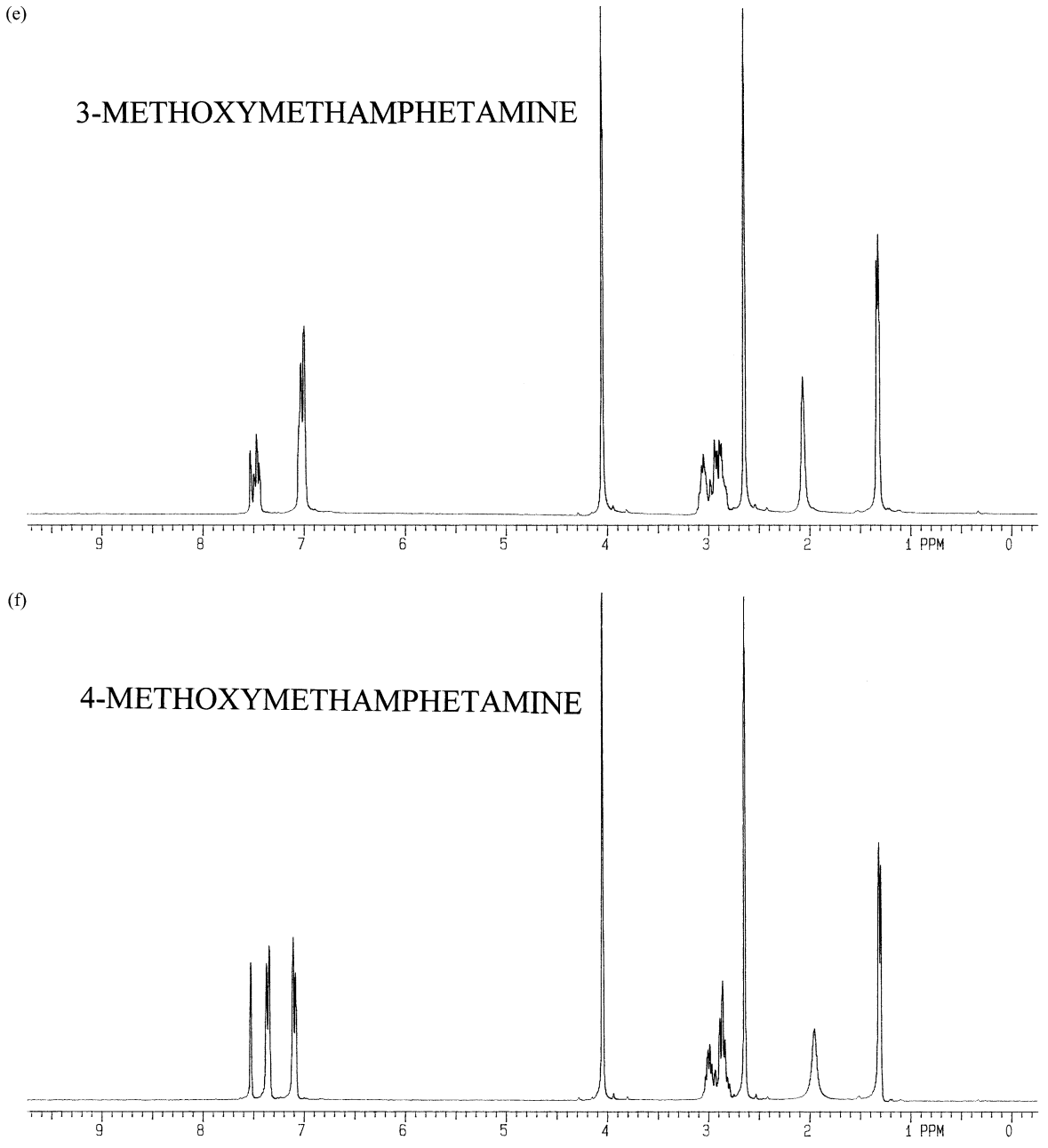


Fig. 5. (*Continued*).

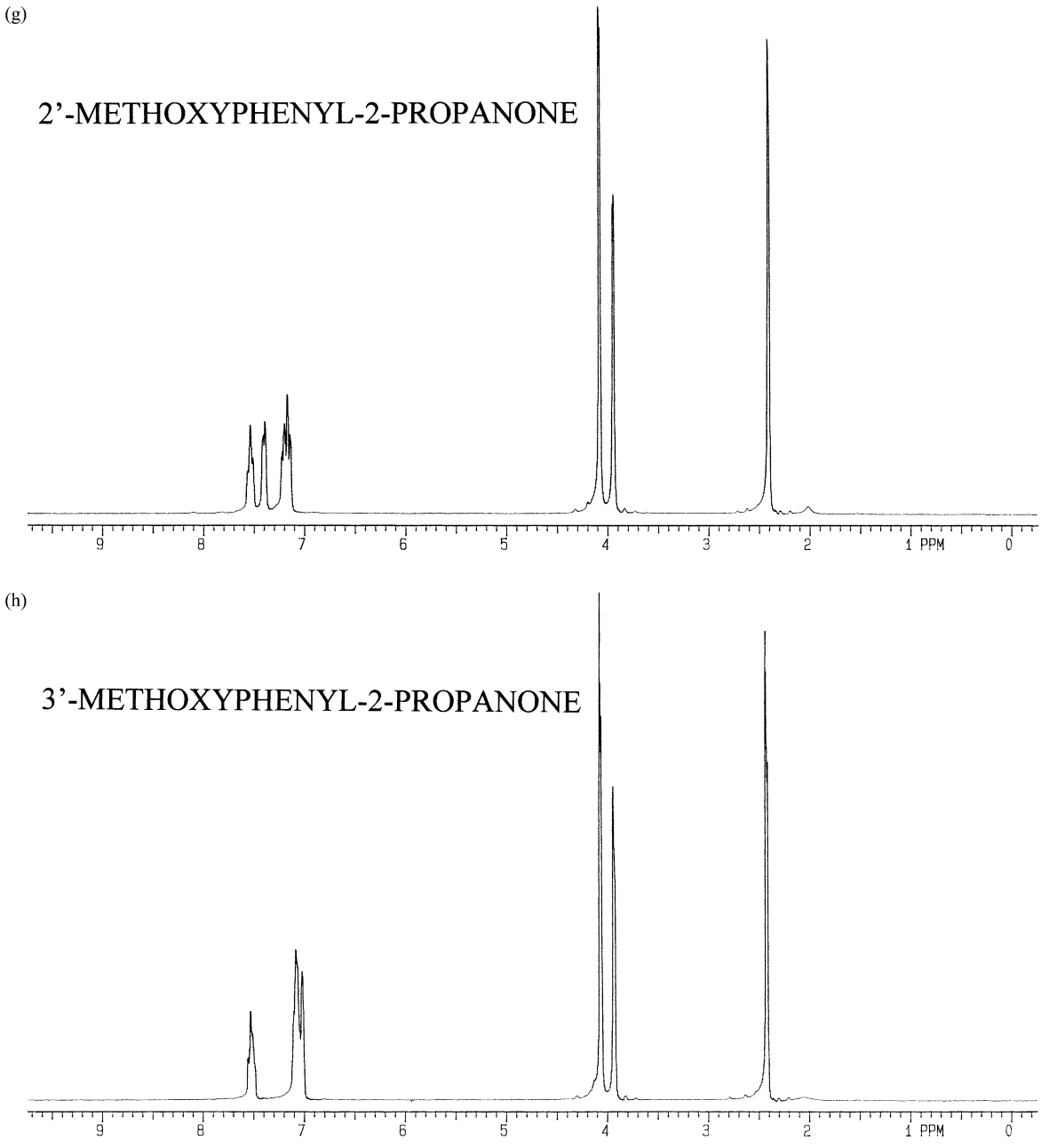


Fig. 5. (*Continued*).

(i)

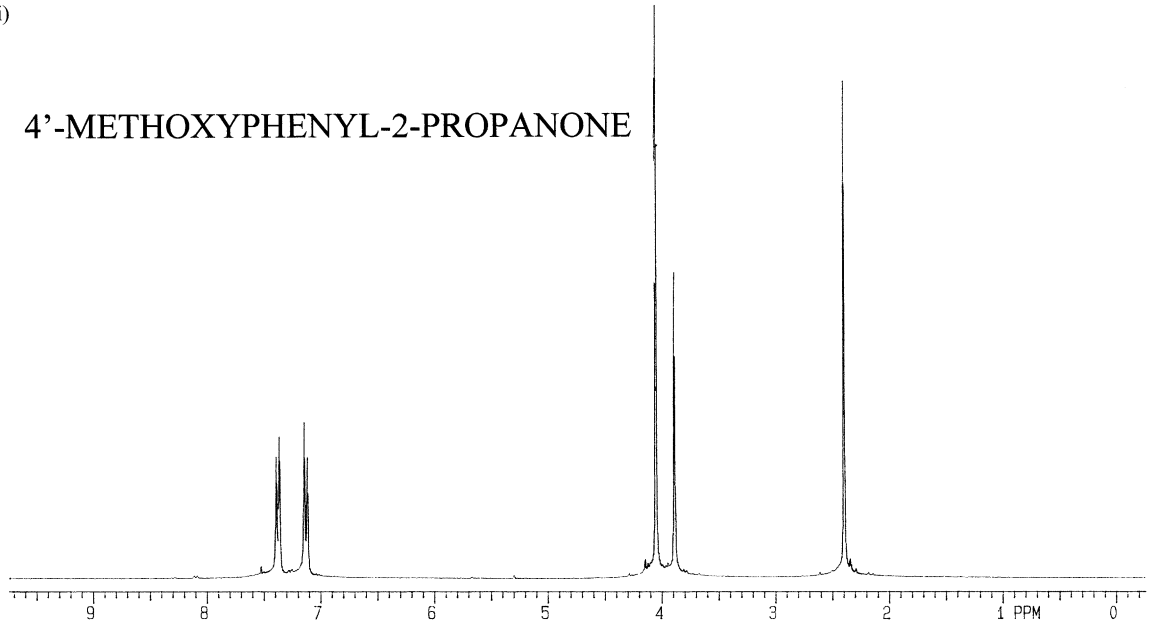


Fig. 5. (*Continued*).

or whether it occurred unintentionally as a result of a synthesis process that used impure (or clandestinely manufactured) methylamine. The later case is due to chance, the former due to design with the intent of mixing a weak stimulant (PMA) with a strong entactogen (PMMA) in an attempt to produce a product that mimics the effects of MDMA.

4. Conclusion

The varying composition of Mitsubishi 3-diamond tablets has undoubtedly contributed to recent deaths in Europe, suburban Chicago and, most likely, Florida. PMA has been determined, primarily through drug discrimination studies, to be a weak stimulant with no entactogen (MDMA-like) component, while PMMA has no stimulant aspect but is a strong entactogen. Tableted mixtures of PMA/PMMA may be the result of synthesis with impure chemicals or may be an attempt to mix the components to achieve an MDMA-like effect. Unequivocal identification of the six mono-methoxy phenylisopropylamines, and the three ketones that serve as precursors, can be made using a variety of analytical techniques.

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