

Characterization of Eleven 2,5-Dimethoxy-*N*-(2-methoxybenzyl)phenethylamine (NBOMe) Derivatives and Differentiation from their 3- and 4-Methoxybenzyl Analogues - Part I

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ABSTRACT: The characterization of eleven 2,5-dimethoxy-*N*-(2-methoxybenzyl) phenethylamine (NBOMe) derivatives and their 3- and 4-methoxybenzyl analogues via mass spectrometry and infrared spectrometry is presented. Analytical data is presented to differentiate these positional isomers.

KEYWORDS: hallucinogens, NBOMe, 25H-NBOMe, 25B-NBOMe, 25C-NBOMe, 25D-NBOMe, 25E-NBOMe, 25I-NBOMe, 25N-NBOMe, 25P-NBOMe, 25T2-NBOMe, 25T4-NBOMe, 25T7-NBOMe, designer drugs, synthesis, characterization, forensic chemistry.

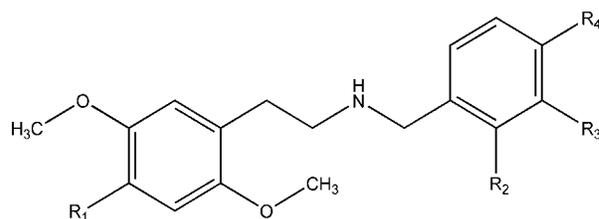
A number of highly potent hallucinogenic phenethylamine derivatives have been encountered by law enforcement within the past year. These designer drugs are commonly referred to as “NBOMe” compounds; their structures are depicted in Figure 1 (compounds **1**, **4**, **7**, **10**, **13**, **16**, **19**, **22**, **25**, **28**, and **31**). They are *N*-(2-methoxy)benzyl derivatives of the “2C compounds” (2,5-dimethoxyphenethylamines with various substituents at C-4), first made popular as a result of their publication in PIHKAL [1]. The NBOMe series was first investigated by Heim and co-workers [2] as agonists for the 5-HT_{2A} serotonin receptors that are associated with hallucinogenic activity, and later by Braden *et al.* as “superpotent” agonists for those receptors [3]. Although there have been no scientific studies on the potency of these derivatives, several illicit drug-related Internet websites recommend sub-milligram (microgram) doses, on par with LSD. Violent physical/mental episodes and deaths have been attributed to the abuse of these compounds [4, 5]. The NBOMe compounds are illicitly distributed as either uncut powders or diluted to sub-milligram doses laced into perforated blotter paper. Due to their extreme potency, forensic chemists must take great care to prevent accidental self-dosing during routine chemical analysis.

Except for three NBOMe derivatives [6], there currently is little or no spectroscopic or spectrometric data in the literature on these compounds. Herein, we report the synthesis, characterization, and differentiation of 11 commonly encountered 2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine (NBOMe) derivatives from their 3- and 4-methoxybenzyl analogues (Figure 1) via mass spectrometry and infrared spectroscopy. Nuclear magnetic resonance spectroscopy of these compounds will be the subject of a later report.

Experimental

Chemicals, Reagents, and Materials

All solvents were distilled-in-glass products of Burdick and Jackson Labs (Muskegon, MI). 2,5-Dimethoxy-4-bromophenethylamine, 2,5-dimethoxy-4-chlorophenethylamine, 2,5-dimethoxy-4-methylphenethylamine, 2,5-dimethoxy-4-



Compound	R ₁	R ₂	R ₃	R ₄
25H-NB2OMe (1)	H	OCH ₃	H	H
25H-NB3OMe (2)	H	H	OCH ₃	H
25H-NB4OMe (3)	H	H	H	OCH ₃
25B-NB2OMe (4)	Br	OCH ₃	H	H
25B-NB3OMe (5)	Br	H	OCH ₃	H
25B-NB4OMe (6)	Br	H	H	OCH ₃
25C-NB2OMe (7)	Cl	OCH ₃	H	H
25C-NB3OMe (8)	Cl	H	OCH ₃	H
25C-NB4OMe (9)	Cl	H	H	OCH ₃
25D-NB2OMe (10)	CH ₃	OCH ₃	H	H
25D-NB3OMe (11)	CH ₃	H	OCH ₃	H
25D-NB4OMe (12)	CH ₃	H	H	OCH ₃
25E-NB2OMe (13)	C ₂ H ₅	OCH ₃	H	H
25E-NB3OMe (14)	C ₂ H ₅	H	OCH ₃	H
25E-NB4OMe (15)	C ₂ H ₅	H	H	OCH ₃
25I-NB2OMe (16)	I	OCH ₃	H	H
25I-NB3OMe (17)	I	H	OCH ₃	H
25I-NB4OMe (18)	I	H	H	OCH ₃
25N-NB2OMe (19)	NO ₂	OCH ₃	H	H
25N-NB3OMe (20)	NO ₂	H	OCH ₃	H
25N-NB4OMe (21)	NO ₂	H	H	OCH ₃
25P-NB2OMe (22)	CH ₂ CH ₂ CH ₃	OCH ₃	H	H
25P-NB3OMe (23)	CH ₂ CH ₂ CH ₃	H	OCH ₃	H
25P-NB4OMe (24)	CH ₂ CH ₂ CH ₃	H	H	OCH ₃
25T2-NB2OMe (25)	CH ₃ CH ₂ S	OCH ₃	H	H
25T2-NB3OMe (26)	CH ₃ CH ₂ S	H	OCH ₃	H
25T2-NB4OMe (27)	CH ₃ CH ₂ S	H	H	OCH ₃
25T4-NB2OMe (28)	(CH ₃) ₂ CHS	OCH ₃	H	H
25T4-NB3OMe (29)	(CH ₃) ₂ CHS	H	OCH ₃	H
25T4-NB4OMe (30)	(CH ₃) ₂ CHS	H	H	OCH ₃
25T7-NB2OMe (31)	CH ₃ (CH ₂) ₂ S	OCH ₃	H	H
25T7-NB3OMe (32)	CH ₃ (CH ₂) ₂ S	H	OCH ₃	H
25T7-NB4OMe (33)	CH ₃ (CH ₂) ₂ S	H	H	OCH ₃

Figure 1 - Structural formulas.

ethylphenethylamine, 2,5-dimethoxy-4-iodophenethylamine, 2,5-dimethoxy-4-nitrophenethylamine, 2,5-dimethoxy-4-propylphenethylamine, 2,5-dimethoxy-4-ethylthiophenethylamine, 2,5-dimethoxy-4-isopropylthiophenethylamine, and 2,5-dimethoxy-4-propylthiophenethylamine were obtained from the reference materials collection maintained at this laboratory. 2,5-Dimethoxyphenethylamine and all other chemicals were of reagent-grade quality and products of Sigma-Aldrich Chemical (Milwaukee, WI).

Synthesis of NBOMe compounds (1-33)

In accordance with *Journal* policy, exact experimental details are not provided, but are outlined in Figure 2 for 2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine **1**. Briefly, the appropriate 4-substituted 2,5-dimethoxyphenethylamine was condensed with the appropriate methoxy-substituted benzaldehyde, and then reduced with NaBH₄ to provide the desired product. All compounds were converted to their HCl ion-pairs with ethereal HCl.

Gas Chromatography/Mass Spectrometry (GC/MS)

Mass spectra were obtained on an Agilent Model 5975C quadrupole mass-selective detector (MSD) that was interfaced with an Agilent Model 7890A gas chromatograph. The MSD was operated in the electron ionization (EI) mode with an ionization potential of 70 eV, a scan range of 34-600 amu, and a scan rate of 2.59 scans/s. The GC was fitted with a 30 m x

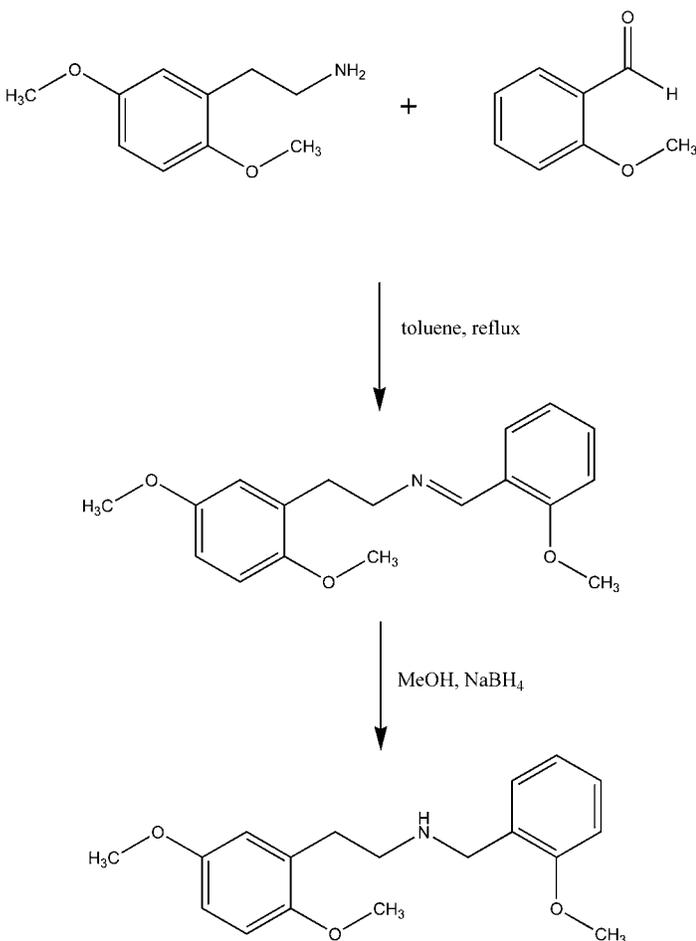


Figure 2 - Synthetic scheme for 2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine **1** (25H-NB2OMe).

Table 1 - Gas chromatographic retention times (min) for the NBOMe compounds^a.

Compound	2-OMe	3-OMe	4-OMe
25H-NBOMe	24.84	25.34	25.66
25B-NBOMe	28.00	28.60	28.90
25C-NBOMe	26.91	27.54	27.85
25D-NBOMe	25.40	25.92	26.21
25E-NBOMe	26.08	26.61	26.89
25I-NBOMe	29.31	29.80	30.20
25N-NBOMe	29.55	30.21	30.45
25P-NBOMe	27.01	27.47	27.75
25T2-NBOMe	29.51	29.99	30.25
25T4-NBOMe	29.54	30.01	30.26
25T7-NBOMe	30.41	30.89	31.14

^aConditions given in the experimental section.

0.25 mm ID fused-silica capillary column coated with 0.25 μm 100% dimethylpolysiloxane, DB-1 (J & W Scientific, Rancho Cordova, CA). The oven temperature was programmed as follows: Initial temperature, 100°C; initial hold, 0.0 min; program rate, 6°C/min; final temperature, 300°C; final hold, 5.67 min. The injector was operated in the split mode (21.5:1) at 280°C. The MSD source was operated at 230°C.

Infrared Spectroscopy (FTIR)

Infrared spectra were obtained on a Thermo-Nicolet Nexus 670 FTIR equipped with a single bounce attenuated total reflectance (ATR) accessory. Instrument parameters were: Resolution = 4 cm⁻¹; gain = 8; optical velocity = 0.4747; aperture = 150; and scans/sample = 16.

Results and Discussion

For the purposes of this article and clarity, abbreviations of the ensuing compounds will include the 4-substitution as commonly given for the 2C moiety + the *N*-benzyl addition (i.e., 2C-B = 25B-NB), and also include the position of the methoxy-substitution (i.e., 2-methoxy = 2OMe) on the benzyl moiety. Therefore 2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine **1** = 25H-NB2OMe, 2,5-dimethoxy-*N*-(3-methoxybenzyl)phenethylamine **2** = 25H-NB3OMe, and 2,5-dimethoxy-*N*-(4-methoxybenzyl)phenethylamine **3** = 25H-NB4OMe. The three 4-bromo derivatives are abbreviated 25B-NB2OMe **4**, 25B-NB3OMe **5**, and 25B-NB4OMe **6**. This nomenclature is also utilized for compounds **7-33**, as illustrated in Figure 1.

GC/MS Differentiation of the NBOMe methoxybenzyl positional isomers (2-OMe vs. 3-OMe vs. 4-OMe)

GC retention times for all 33 NBOMe compounds are presented in Table 1. All amines were injected as their free bases and were found to be relatively high boiling, late eluting compounds. The three methoxybenzyl positional isomers for each of the NBOMe compounds were resolved in the described

system. The elution order (retention time) was as followed: 4-Methoxybenzyl > 3-methoxybenzyl > 2-methoxybenzyl for each NBOMe series.

Mass spectra for compounds **1-33** are given in Figures 3-13. In general, all compounds produced a base peak ion at m/z 121 due to cleavage of the benzyl moiety and an ion at m/z 150 due to *alpha*-cleavage of the phenethylamine moiety. All 2-methoxybenzyl substituted compounds (**1**, **4**, **7**, **10**, **13**, **16**, **19**, **22**, **25**, **28**, and **31**) produced a tropylium ion at m/z 91 at significantly greater relative abundance than their corresponding 3- and 4-methoxybenzyl substituted analogues. Although Zuba and Sekula [6] did not report molecular ions for underivatized **10** or **13**, we obtained molecular ion data for all 33 compounds. The relative abundances of the molecular ions were extremely low, however, and ranged from 0.05 to 1.0%.

25H-NB2OMe 1, 25H-NB3OMe 2, and 25H-NB4OMe 3 (Figure 3)

Compound **1** is differentiated from **2** and **3** by the relative abundances of m/z 91 (**1** = 30%, **2** = 12%, and **3** = 5%) and the relative abundances of m/z 150 and m/z 152 (m/z 150/152: **1** = 7.1, **2** = 2.1, and **3** = 1.2). Further delineation of **1** was observed by comparing ions at m/z 268 and m/z 270 (m/z 268/270: **1** = 0.8, **2** = 2.2, and **3** = 2.1). Compound **1** also produced a significant M-2 ion at m/z 299, relative to the molecular ion (m/z 299 > m/z 301), while **2** and **3** had more intense molecular ions (m/z 301 > m/z 299).

25B-NB2OMe 4, 25B-NB3OMe 5, and 25B-NB4OMe 6 (Figure 4)

Each compound produced molecular ions at m/z 379 and m/z 381, and at fragment ions m/z 199 and m/z 201, consistent with the relative abundance ratios expected for bromine substitution. All three compounds were differentiated by the relative abundances of fragment ions found at m/z 91 and m/z 150 (m/z 150/91: **4** = 2.2, **5** = 7.1, and **6** = 5.8). Although the m/z 150/91 ratio for **5** and **6** were somewhat similar, the relative abundance for m/z 150 produced by **5** was 73%, compared to 38% for **6**.

25C-NB2OMe 7, 25C-NB3OMe 8, and 25C-NB4OMe 9 (Figure 5)

All three compounds were differentiated by the relative abundances of fragment ions found at m/z 91 (tropylium) and m/z 150 (m/z 150/91: **7** = 1.6, **8** = 6.1, and **9** = 5.3). Although the m/z 150/91 ratio for **8** and **9** were similar, the relative abundance for m/z 150 produced by **8** was 46%, compared to 24% for **9**. Compound **7** also produced a significant M-2 ion at m/z 333, relative to the first chlorine isotope molecular ion (m/z 333 > m/z 335), while **8** and **9** had a more intense chlorine isotope at m/z 335 (m/z 335 \geq m/z 333).

25D-NB2OMe 10, 25D-NB3OMe 11, and 25D-NB4OMe 12 (Figure 6)

The tropylium ion (m/z 91) abundances were **10** = 28%, **11** = 13%, and **12** = 7%. Further delineation was also observed by the relative abundances of the fragment ions produced at m/z 150 and m/z 166 (m/z 150/166: **10** = 1.8, **11** = 0.9, and **12** = 0.3).

25E-NB2OMe 13, 25E-NB3OMe 14, and 25E-NB4OMe 15 (Figure 7)

The tropylium ion (m/z 91) abundances were **13** = 28%, **14** = 13%, and **15** = 6%. Further delineation was also observed by the relative abundances of the fragment ions produced at m/z 150 and m/z 180 (m/z 150/180: **13** = 1.8, **14** = 1.0, and **15** = 0.3).

25I-NB2OMe 16, 25I-NB3OMe 17, and 25I-NB4OMe 18 (Figure 8)

The tropylium ion (m/z 91) abundances were **16** = 29%, **17** = 11%, and **18** = 4%. Further delineation was also observed by the relative abundances of the fragment ions produced at m/z 150 (**16** = 62%, **17** = 75%, and **18** = 39%) and m/z 278 (**16** = 2%, **17** = 12%, and **18** = 5%).

25N-NB2OMe 19, 25N-NB3OMe 20, and 25N-NB4OMe 21 (Figure 9)

The tropylium ion (m/z 91) abundances were **19** = 34%, **20** = 13%, and **21** = 5%. The ratio for the relative abundances of m/z 91 and m/z 150 also differentiated the three compounds (m/z 150/91: **19** = 1.2, **20** = 4.2, and **21** = 3.3).

25P-NB2OMe 22, 25P-NB3OMe 23, and 25P-NB4OMe 24 (Figure 10)

The tropylium ion (m/z 91) abundances were **22** = 26%, **23** = 12%, and **24** = 8%. The ratio for the relative abundances of m/z 150 and m/z 194 also differentiated the three compounds (m/z 150/194: **22** = 2.1, **23** = 1.1, and **24** = 0.4). All three compounds produced a significant M-2 ion at m/z 341.

25T2-NB2OMe 25, 25T2-NB3OMe 26, and 25T2-NB4OMe 27 (Figure 11)

The tropylium ion (m/z 91) abundances were **25** = 25%, **26** = 10%, and **27** = 4%. The ratio for the relative abundances of m/z 150 and m/z 212 also differentiated the three compounds (m/z 150/212: **25** = 1.5, **26** = 0.9, and **27** = 0.3). All three compounds produced a significant M-2 ion at m/z 359.

25T4-NB2OMe 28, 25T4-NB3OMe 29, and 25T4-NB4OMe 30 (Figure 12)

The tropylium ion (m/z 91) abundances were **28** = 24%, **29** = 9%, and **30** = 4%. The ratio for the relative abundances of m/z 150 and m/z 226 also differentiated the three compounds (m/z 150/226: **28** = 1.9, **29** = 1.1, and **30** = 0.3). All three compounds produced a significant M-2 ion at m/z 373.

25T7-NB2OMe 31, 25T7-NB3OMe 32, and 25T7-NB4OMe 33 (Figure 13)

All three propyl derivatives could be differentiated by the tropylium ion relative abundances, which were nearly identical to **28-30** (see above). The ratio for the relative abundances of m/z 150 and m/z 226 also differentiated the three compounds (m/z 150/226: **31** = 1.6, **32** = 1.0, and **33** = 0.2). All three compounds produced a significant M-2 ion at m/z 373. The propyl derivatives **31-33** can be easily differentiated from their corresponding isopropyl analogues **28-30** by the ratios of the relative abundances of m/z 183 and m/z 226, where m/z 226/183 ~ 11 for **31-33** and ~3 for **28-30**.

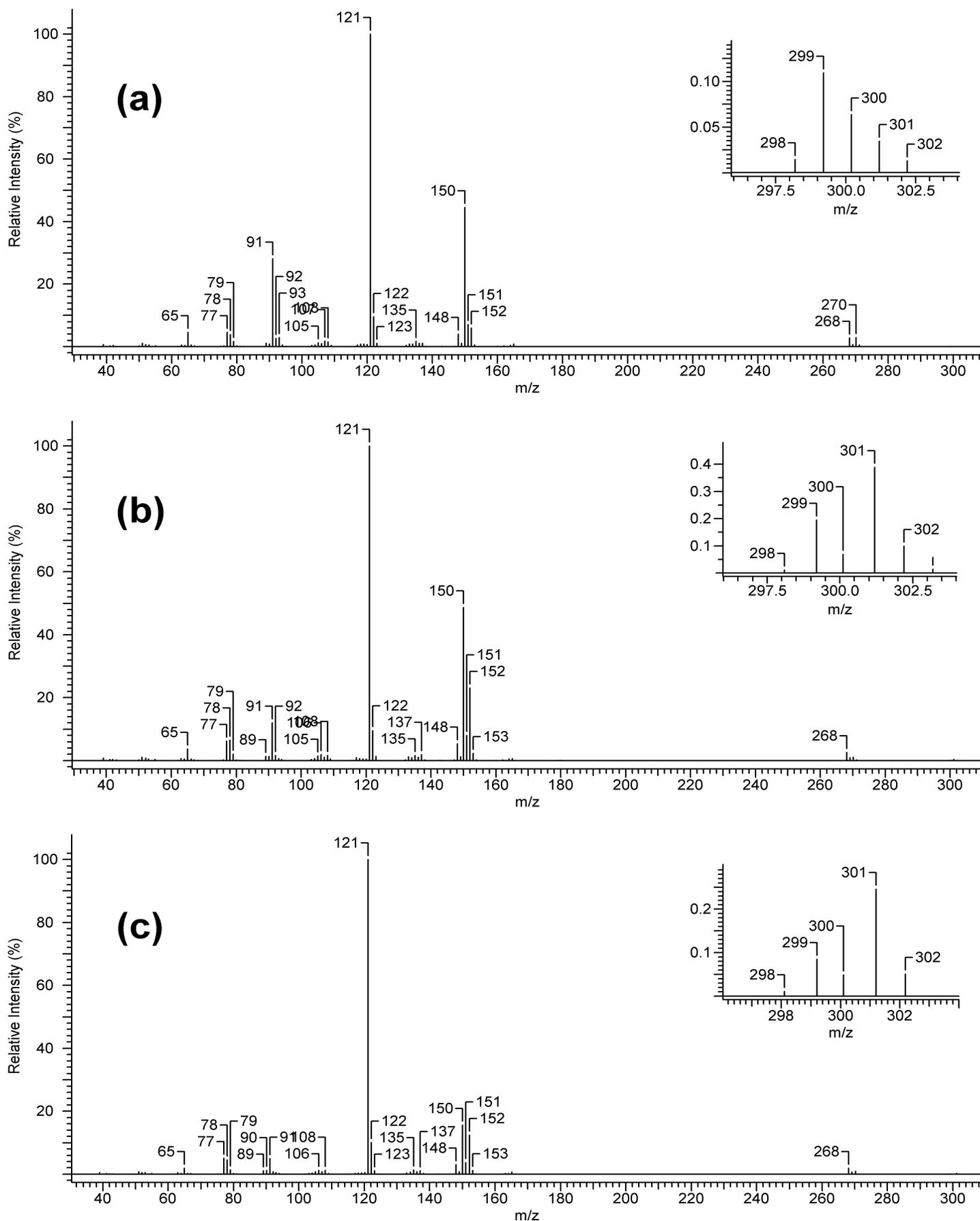


Figure 3 - Mass spectra of (a) 2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine (25H-NB2OMe) **1**, (b) 2,5-dimethoxy-*N*-(3-methoxybenzyl)phenethylamine (25H-NB3OMe) **2**, and (c) 2,5-dimethoxy-*N*-(4-methoxybenzyl)phenethylamine (25H-NB4OMe) **3**.

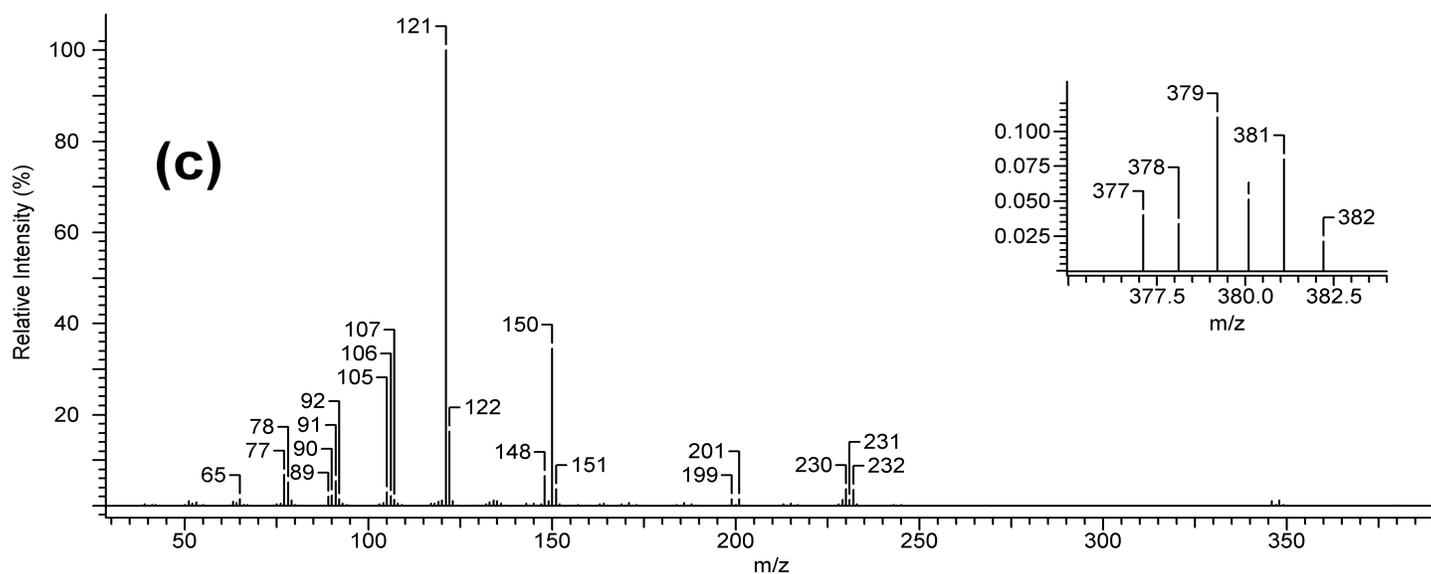
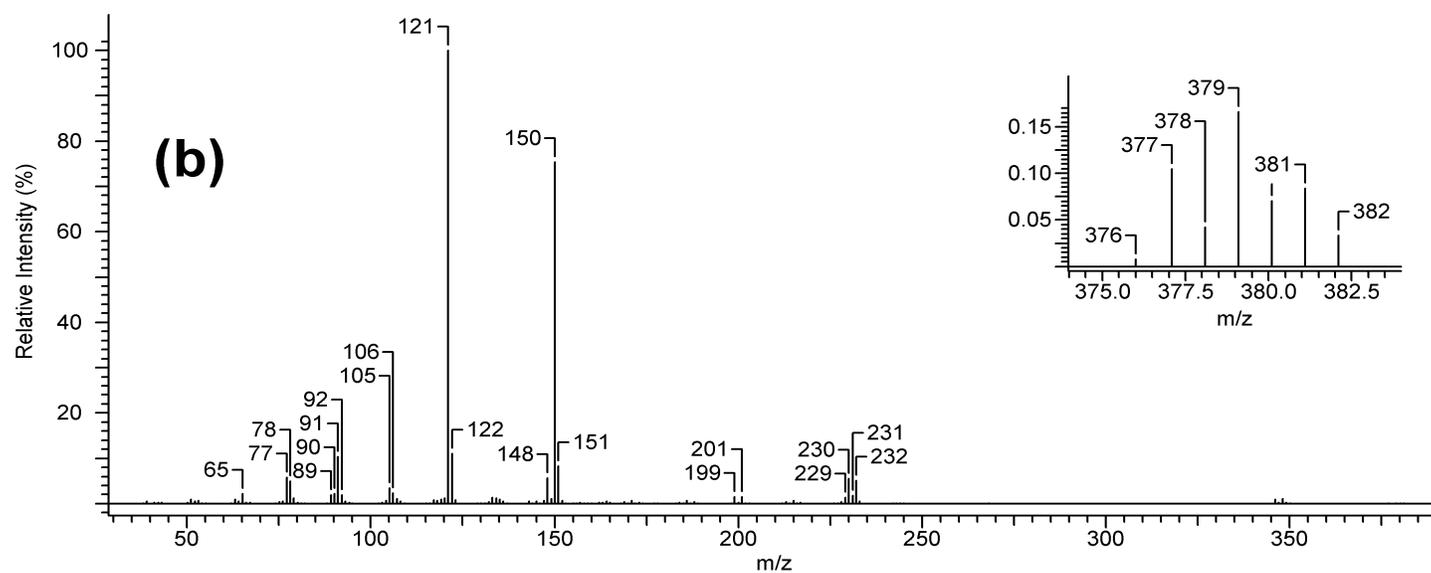
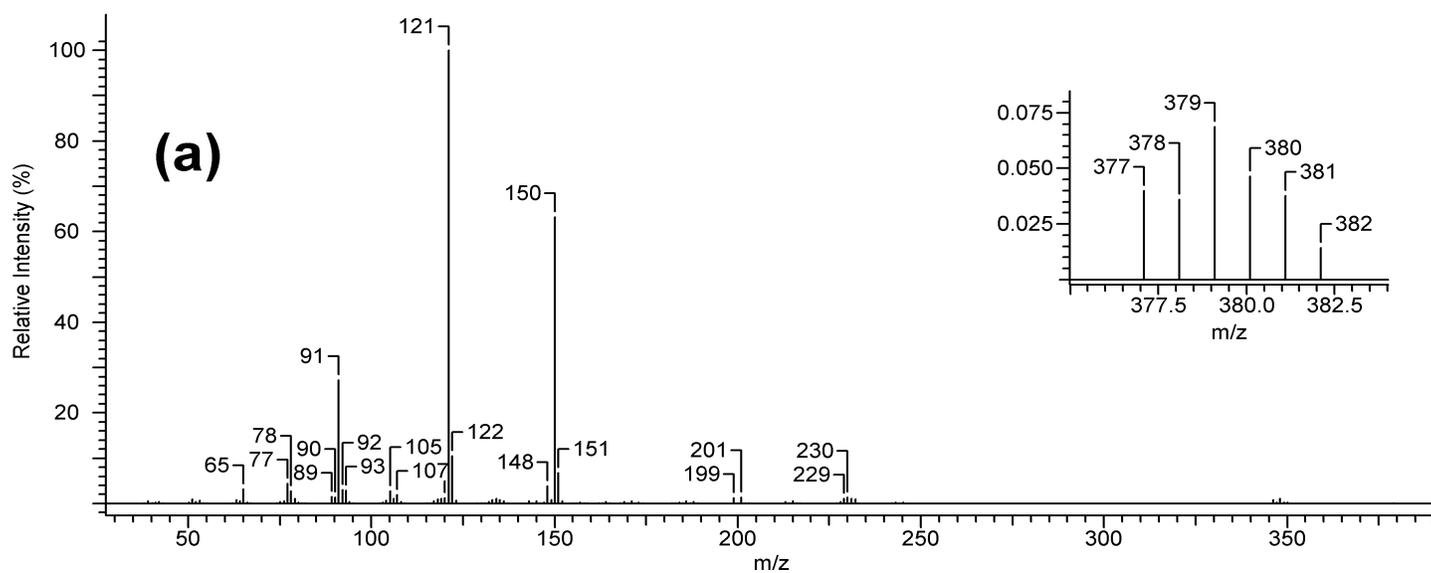


Figure 4 - Mass spectra of (a) 2,5-dimethoxy-4-bromo-*N*-(2-methoxybenzyl)phenethylamine (25B-NB2OMe) **4**, (b) 2,5-dimethoxy-4-bromo-*N*-(3-methoxybenzyl)phenethylamine (25B-NB3OMe) **5**, and (c) 2,5-dimethoxy-4-bromo-*N*-(4-methoxybenzyl)phenethylamine (25B-NB4OMe) **6**.

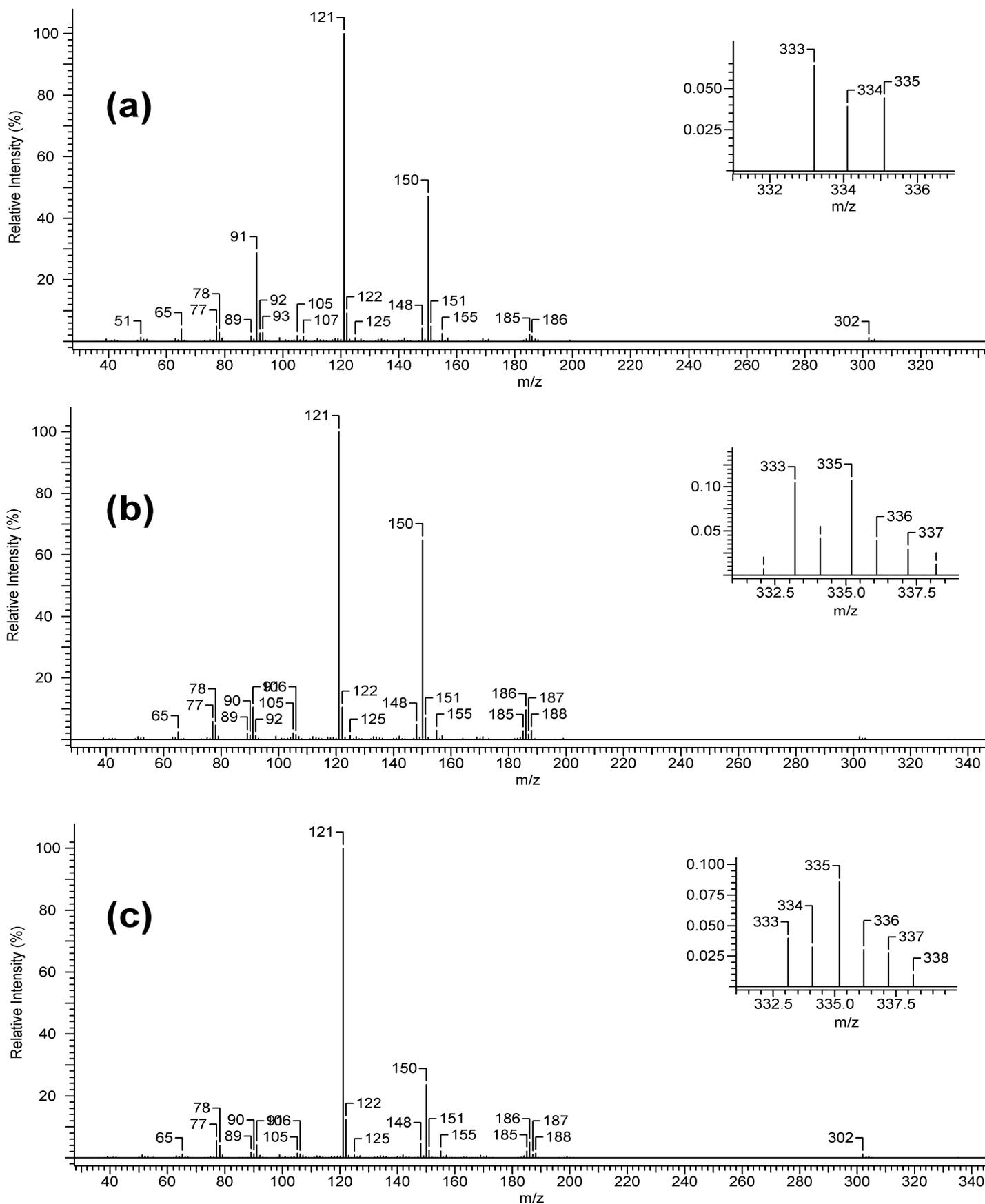


Figure 5 - Mass spectra of (a) 2,5-dimethoxy-4-chloro-*N*-(2-methoxybenzyl)phenethylamine (25C-NB2OMe) **7**, (b) 2,5-dimethoxy-4-chloro-*N*-(3-methoxybenzyl)phenethylamine (25C-NB3OMe) **8**, and (c) 2,5-dimethoxy-4-chloro-*N*-(4-methoxybenzyl)phenethylamine (25C-NB4OMe) **9**.

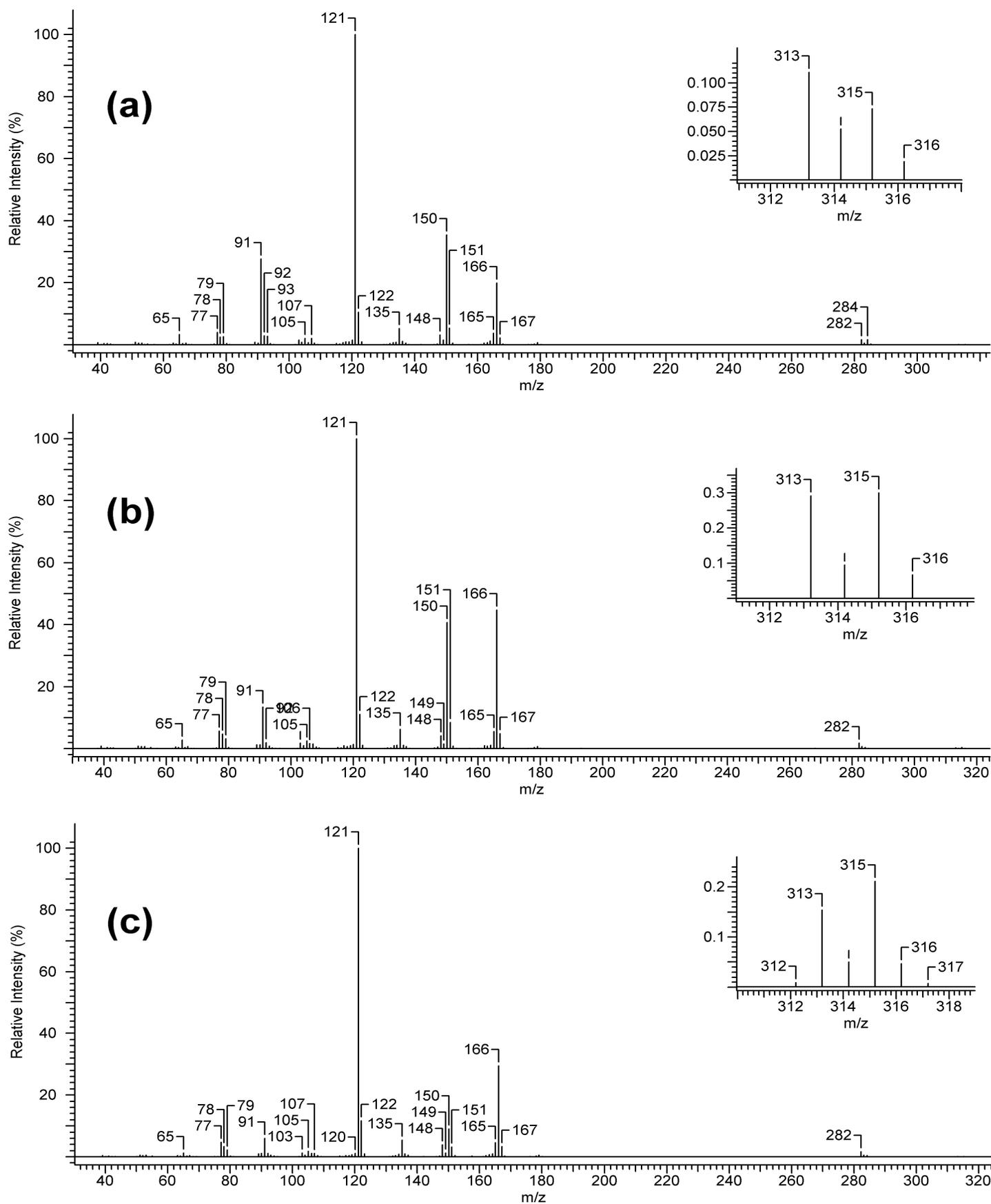


Figure 6 - Mass spectra of (a) 2,5-dimethoxy-4-methyl-*N*-(2-methoxybenzyl)phenethylamine (25D-NB2OMe) **10**, (b) 2,5-dimethoxy-4-methyl-*N*-(3-methoxybenzyl)phenethylamine (25D-NB3OMe) **11**, and (c) 2,5-dimethoxy-4-methyl-*N*-(4-methoxybenzyl)phenethylamine (25D-NB4OMe) **12**.

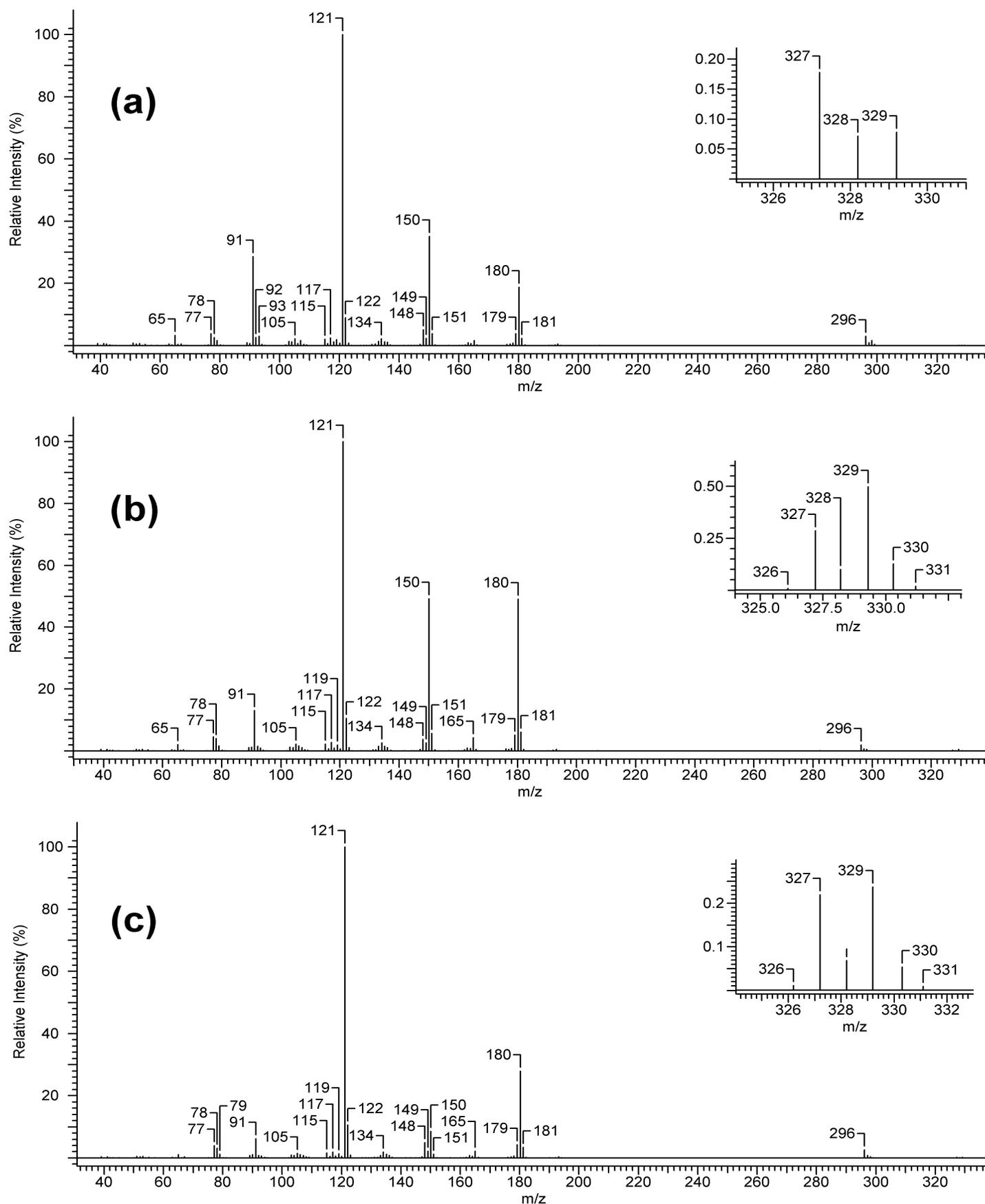


Figure 7 - Mass spectra of (a) 2,5-dimethoxy-4-ethyl-*N*-(2-methoxybenzyl)phenethylamine (25E-NB2OMe) **13**, (b) 2,5-dimethoxy-4-ethyl-*N*-(3-methoxybenzyl)phenethylamine (25E-NB3OMe) **14**, and (c) 2,5-dimethoxy-4-ethyl-*N*-(4-methoxybenzyl)phenethylamine (25E-NB4OMe) **15**.

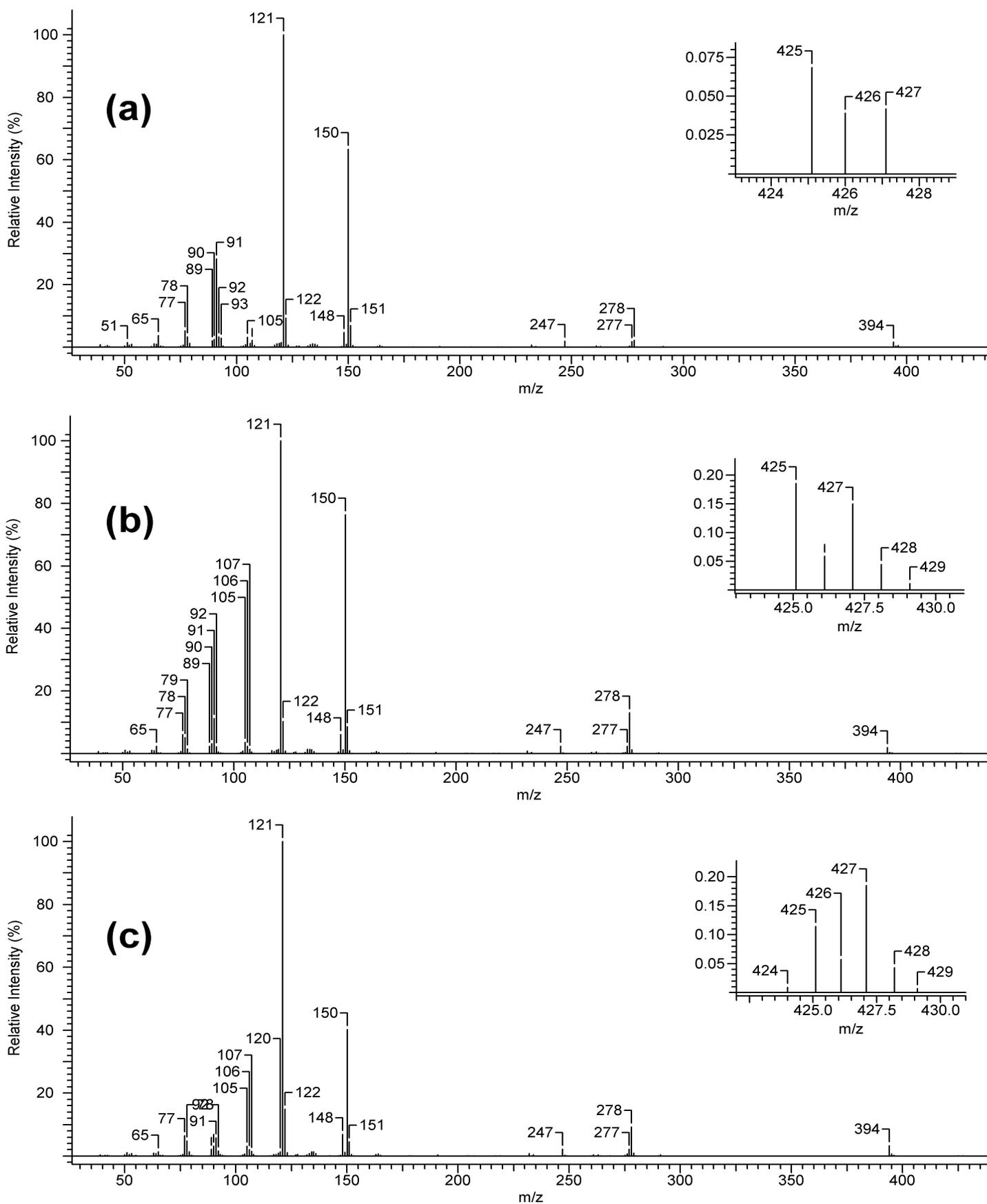


Figure 8 - Mass spectra of (a) 2,5-dimethoxy-4-iodo-*N*-(2-methoxybenzyl)phenethylamine (25I-NB2OMe) **16**, (b) 2,5-dimethoxy-4-iodo-*N*-(3-methoxybenzyl)phenethylamine (25I-NB3OMe) **17**, and (c) 2,5-dimethoxy-4-iodo-*N*-(4-methoxybenzyl)phenethylamine (25I-NB4OMe) **18**.

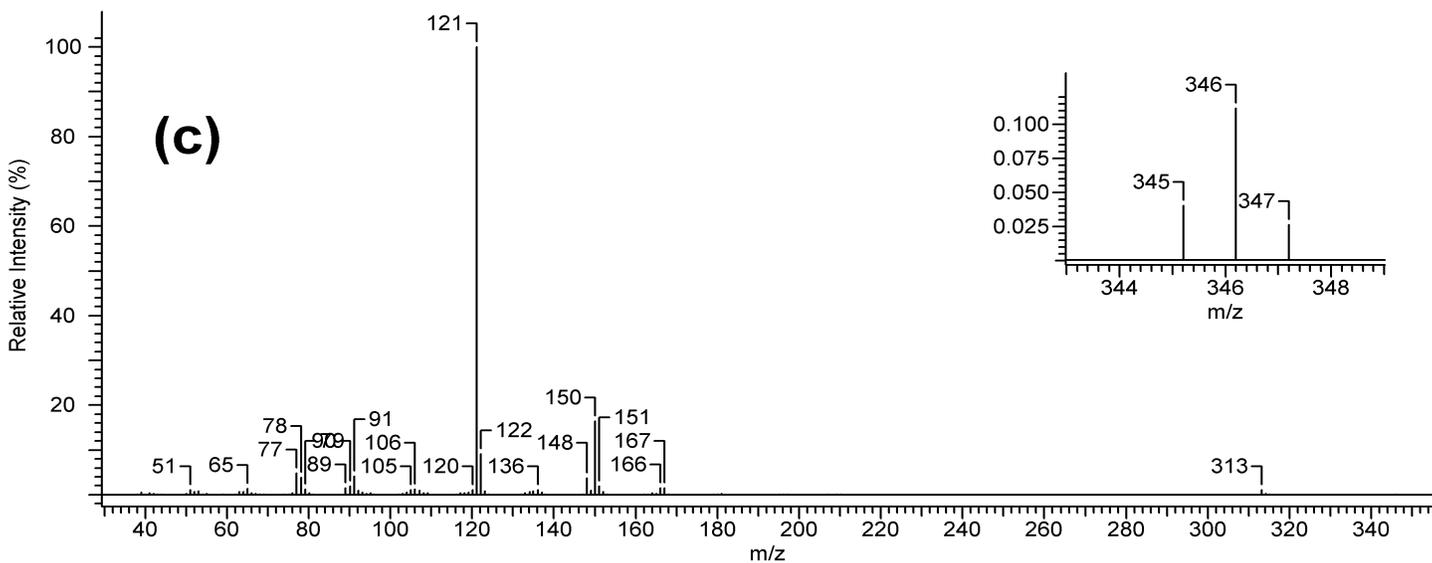
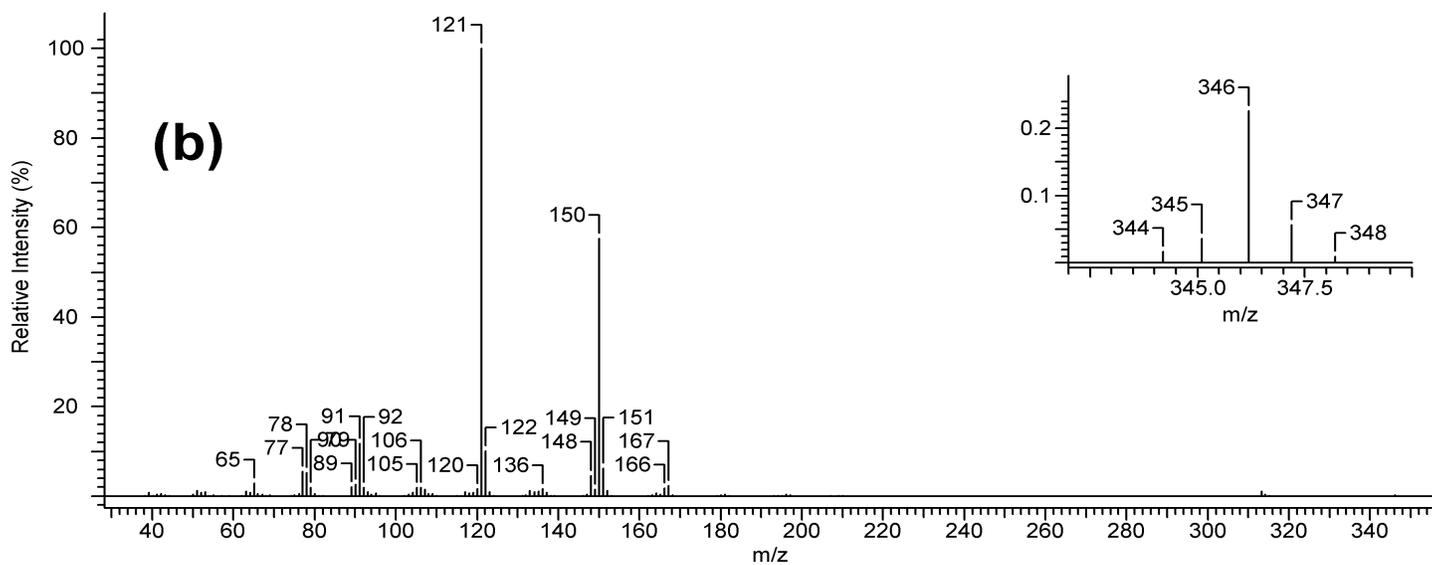
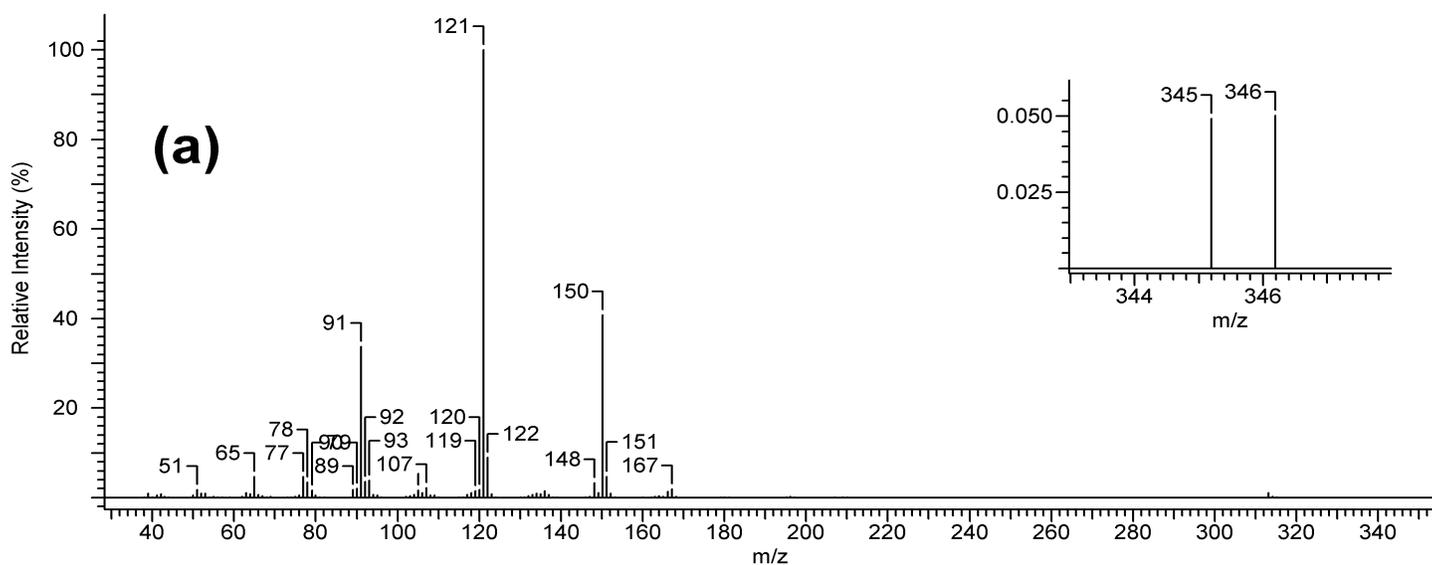


Figure 9 - Mass spectra of (a) 2,5-dimethoxy-4-nitro-*N*-(2-methoxybenzyl)phenethylamine (25N-NB2OMe) **19**, (b) 2,5-dimethoxy-4-nitro-*N*-(3-methoxybenzyl)phenethylamine (25N-NB3OMe) **20**, and (c) 2,5-dimethoxy-4-nitro-*N*-(4-methoxybenzyl)phenethylamine (25N-NB4OMe) **21**.

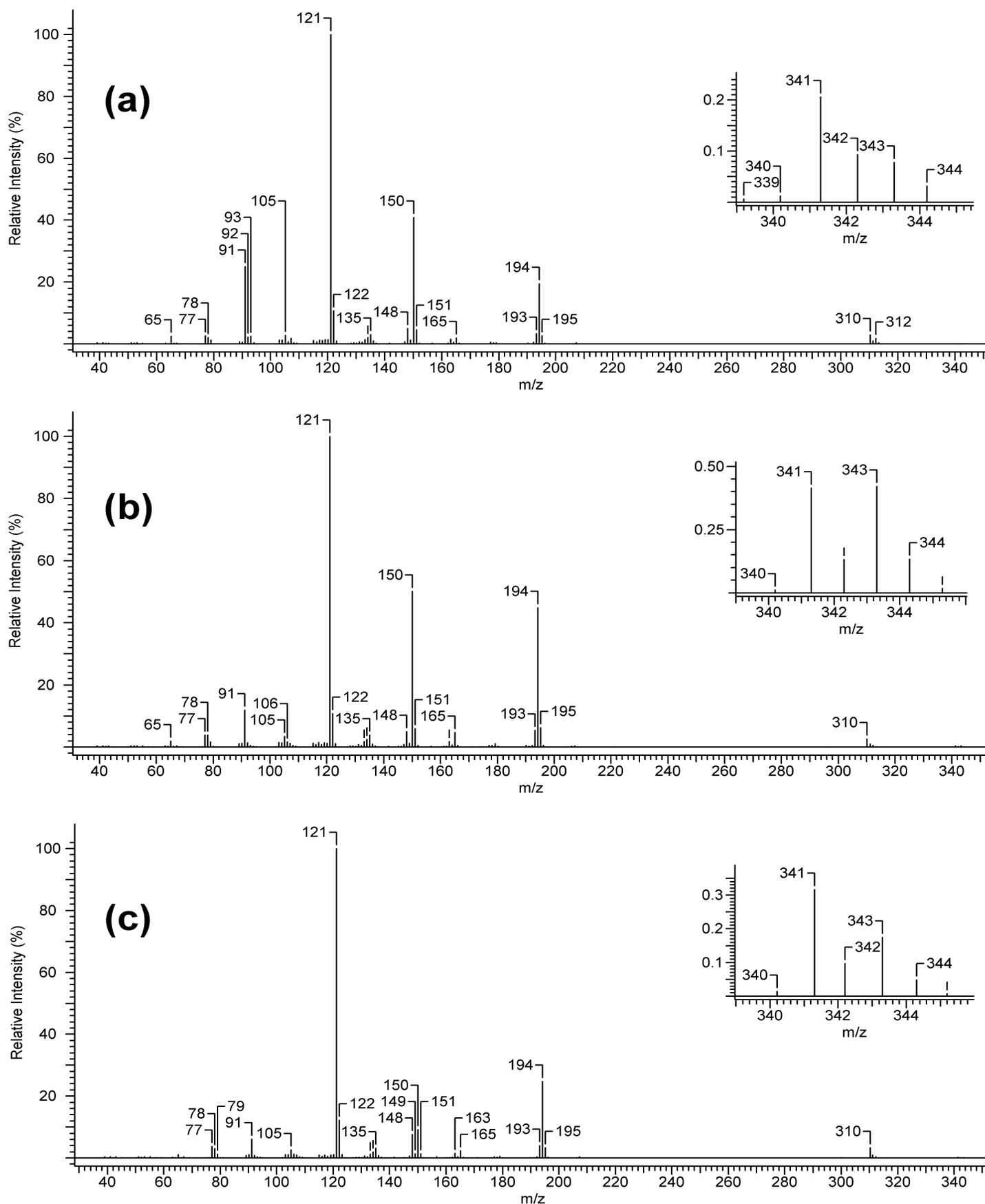


Figure 10 - Mass spectra of (a) 2,5-dimethoxy-4-propyl-*N*-(2-methoxybenzyl)phenethylamine (25P-NB2OMe) **22**, (b) 2,5-dimethoxy-4-propyl-*N*-(3-methoxybenzyl)phenethylamine (25P-NB3OMe) **23**, and (c) 2,5-dimethoxy-4-propyl-*N*-(4-methoxybenzyl)phenethylamine (25P-NB4OMe) **24**.

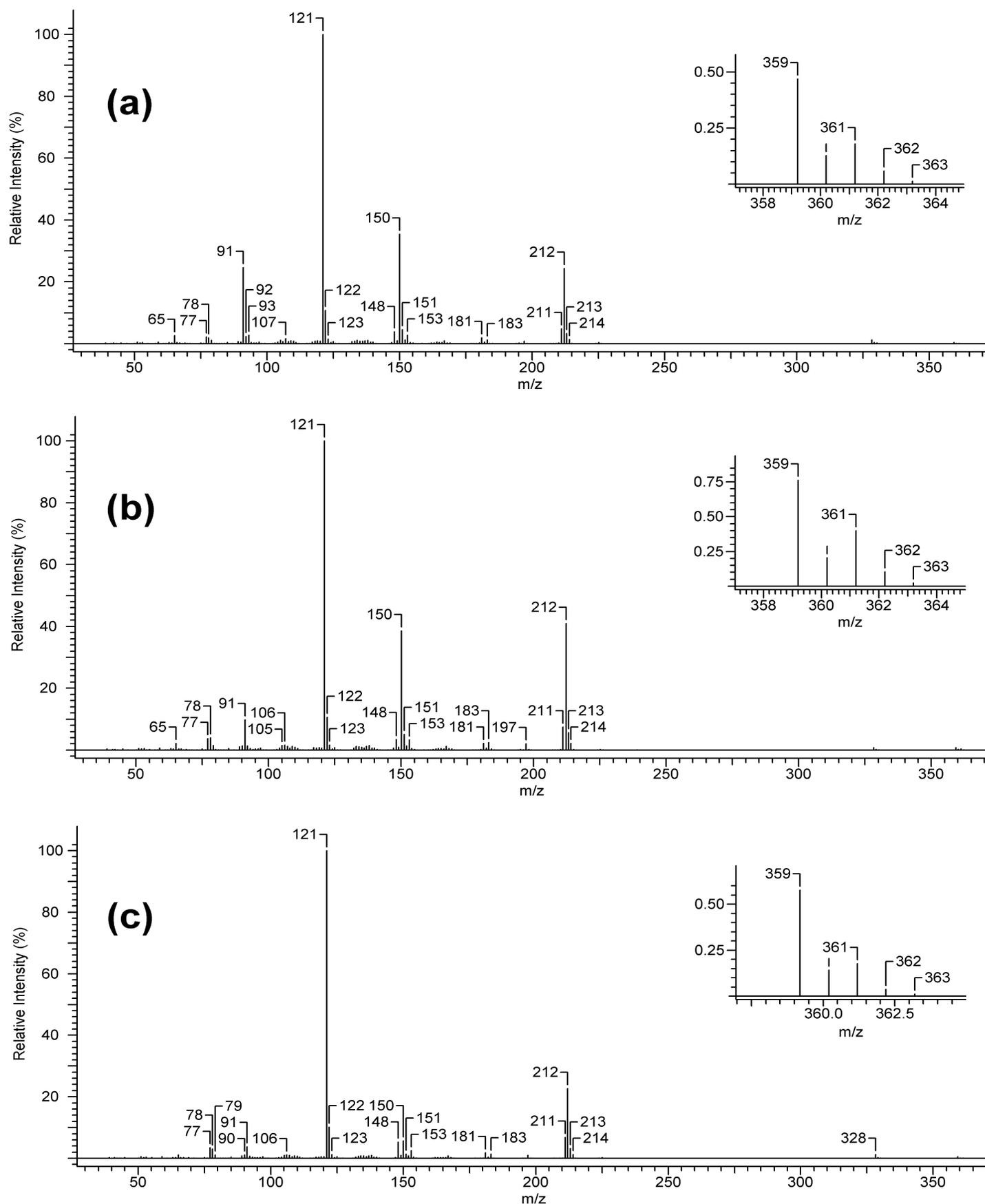


Figure 11 - Mass spectra of (a) 2,5-dimethoxy-4-ethylthio-*N*-(2-methoxybenzyl)phenethylamine (25T2-NB2OMe) **25**, (b) 2,5-dimethoxy-4-ethylthio-*N*-(3-methoxybenzyl)phenethylamine (25T2-NB3OMe) **26**, and (c) 2,5-dimethoxy-4-ethylthio-*N*-(4-methoxybenzyl)phenethylamine (25P-NB4OMe) **27**.

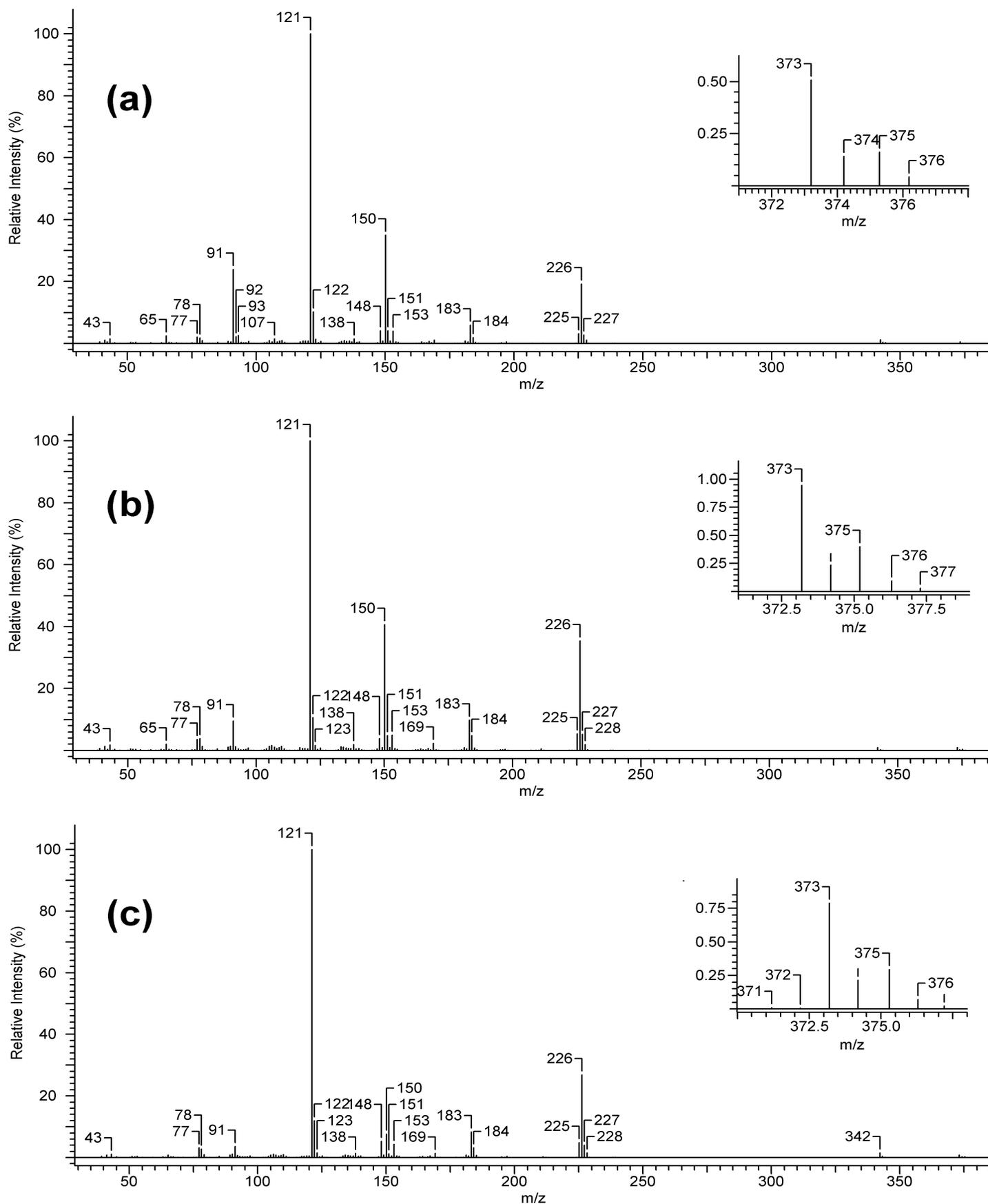


Figure 12 - Mass spectra of (a) 2,5-dimethoxy-4-isopropylthio-*N*-(2-methoxybenzyl)phenethylamine (25T4-NB2OMe) **28**, (b) 2,5-dimethoxy-4-isopropylthio-*N*-(3-methoxybenzyl)phenethylamine (25T4-NB3OMe) **29**, and (c) 2,5-dimethoxy-4-isopropylthio-*N*-(4-methoxybenzyl)phenethylamine (25T4-NB4OMe) **30**.

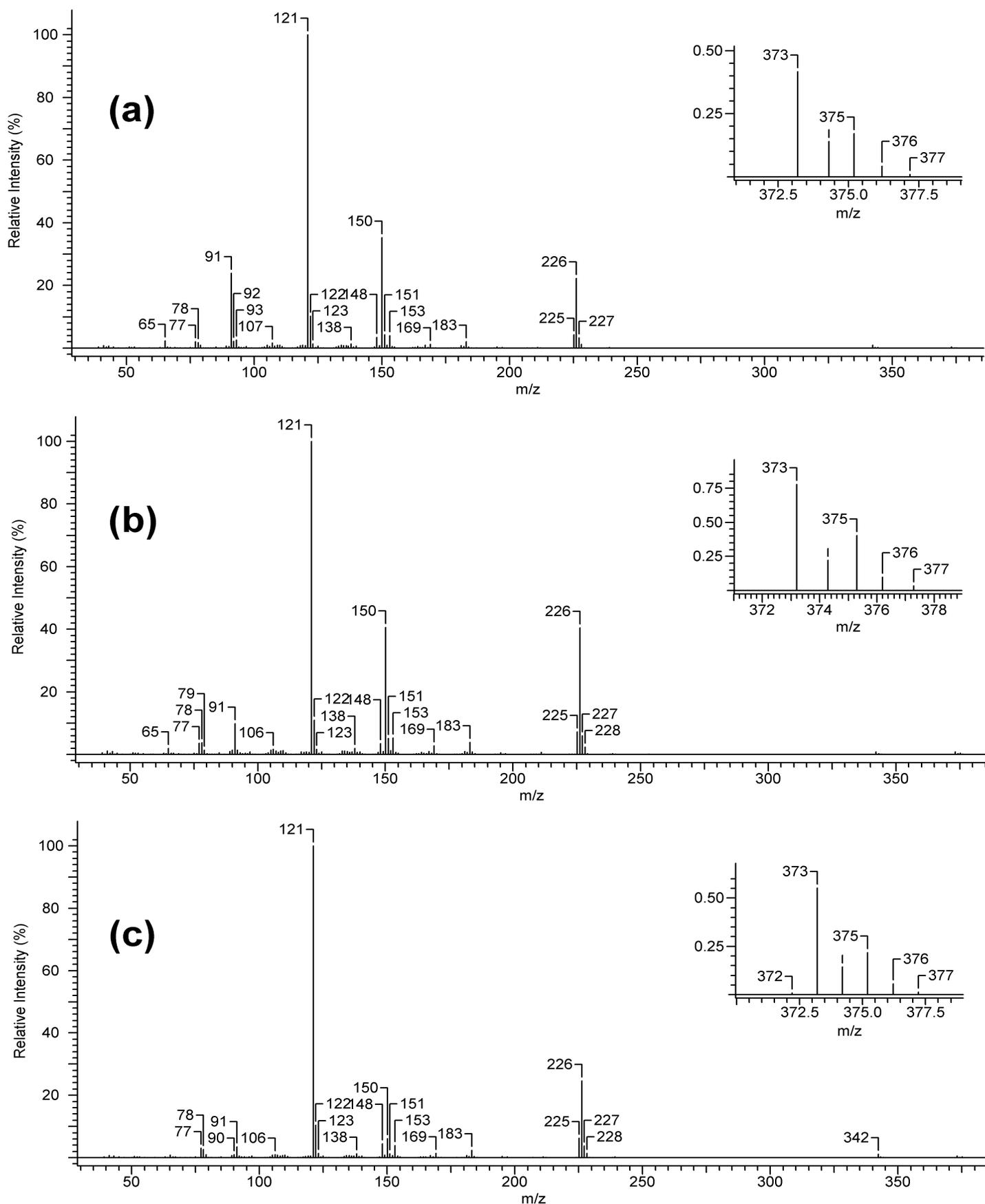


Figure 13 - Mass spectra (a) 2,5-dimethoxy-4-propylthio-N-(2-methoxybenzyl)phenethylamine (25T7-NB2OMe) **31**, (b) 2,5-dimethoxy-4-propylthio-N-(3-methoxybenzyl)phenethylamine (25T7-NB3OMe) **32**, and (c) 2,5-dimethoxy-4-propylthio-N-(4-methoxybenzyl)phenethylamine (25T7-NB4OMe) **33**.

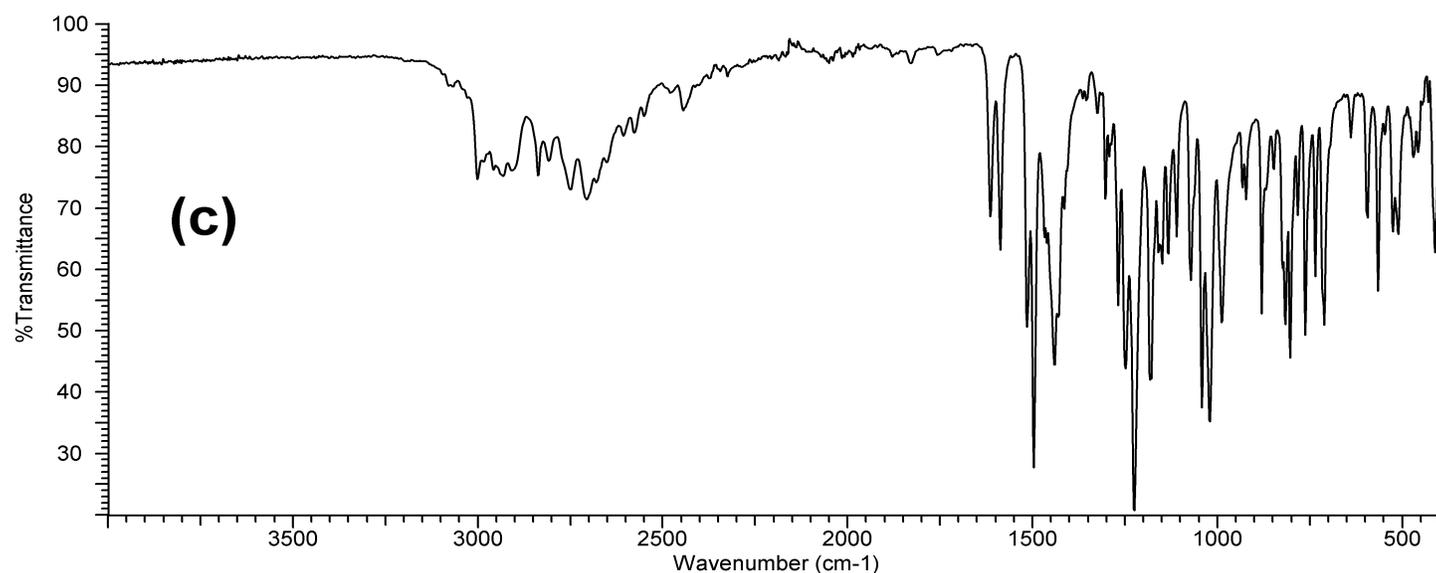
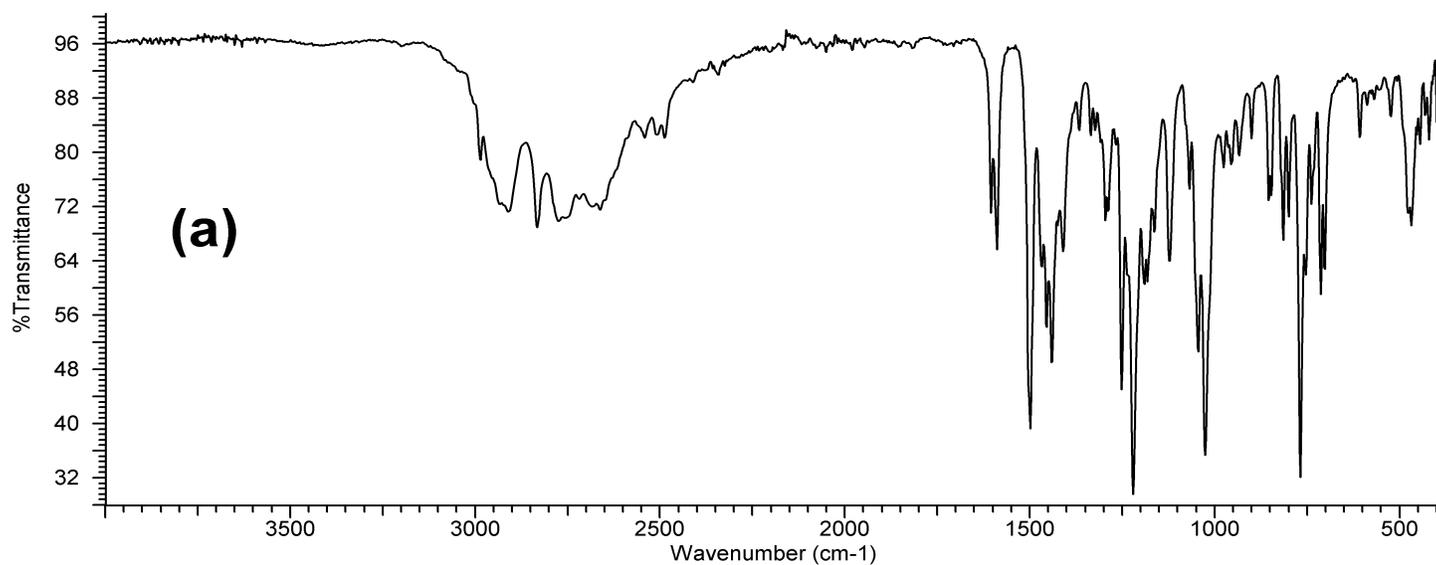


Figure 14 - FTIR spectra of (a) 2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine HCl (25H-NB2OMe) **1**, (b) 2,5-dimethoxy-*N*-(3-methoxybenzyl)phenethylamine HCl (25H-NB3OMe) **2**, and (c) 2,5-dimethoxy-*N*-(4-methoxybenzyl)phenethylamine HCl (25H-NB4OMe) **3**.

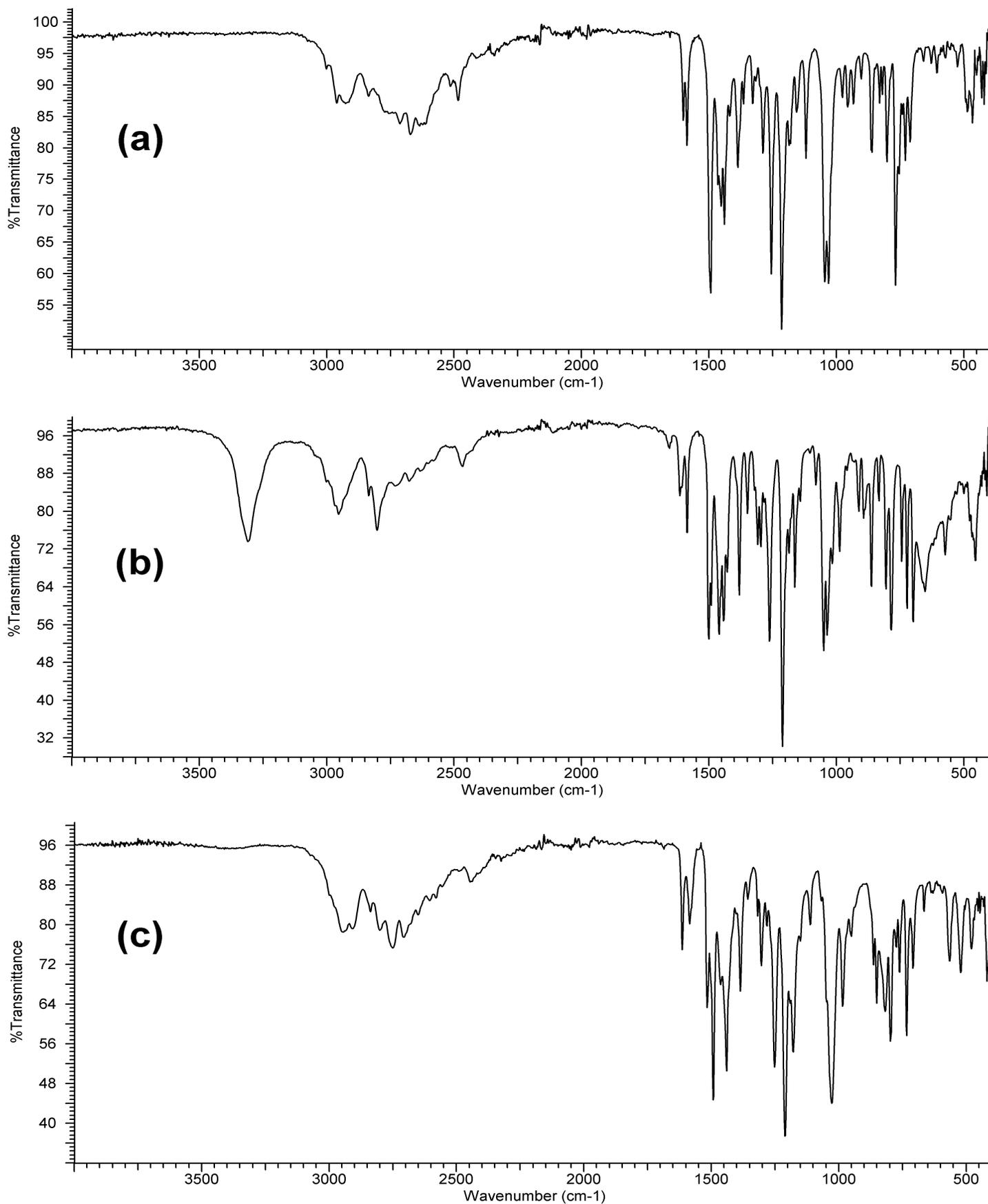


Figure 15 - FTIR spectra of (a) 2,5-dimethoxy-4-bromo-*N*-(2-methoxybenzyl)phenethylamine HCl (25B-NB2OMe) **4**, (b) 2,5-dimethoxy-4-bromo-*N*-(3-methoxybenzyl)phenethylamine HCl (25B-NB3OMe) **5**, and (c) 2,5-dimethoxy-4-bromo-*N*-(4-methoxybenzyl)phenethylamine HCl (25B-NB4OMe) **6**.

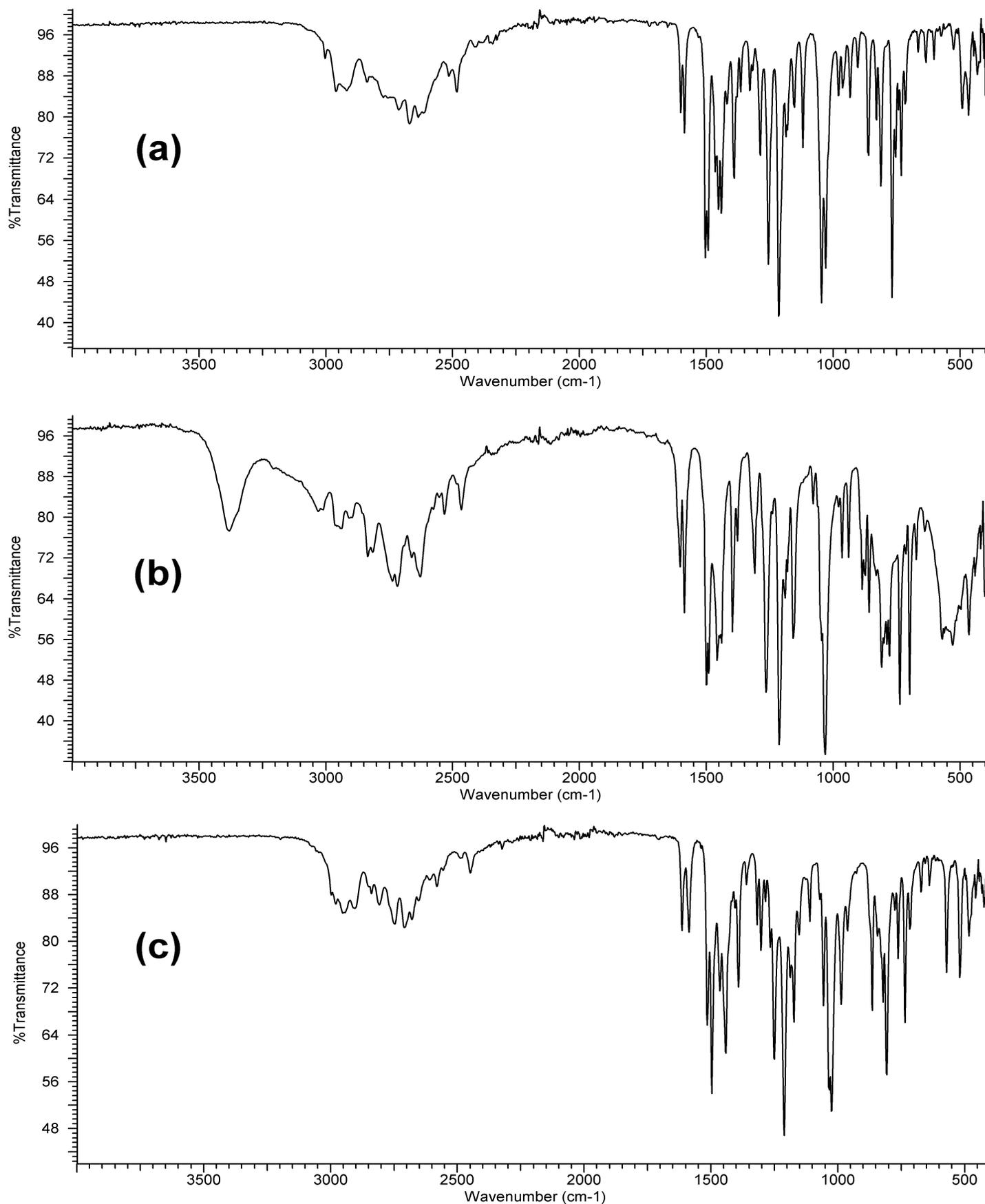


Figure 16 - FTIR spectra of (a) 2,5-dimethoxy-4-chloro-*N*-(2-methoxybenzyl)phenethylamine HCl (25C-NB2OMe) **7**, (b) 2,5-dimethoxy-4-chloro-*N*-(3-methoxybenzyl)phenethylamine HCl (25C-NB3OMe) **8**, and (c) 2,5-dimethoxy-4-chloro-*N*-(4-methoxybenzyl)phenethylamine HCl (25C-NB4OMe) **9**.

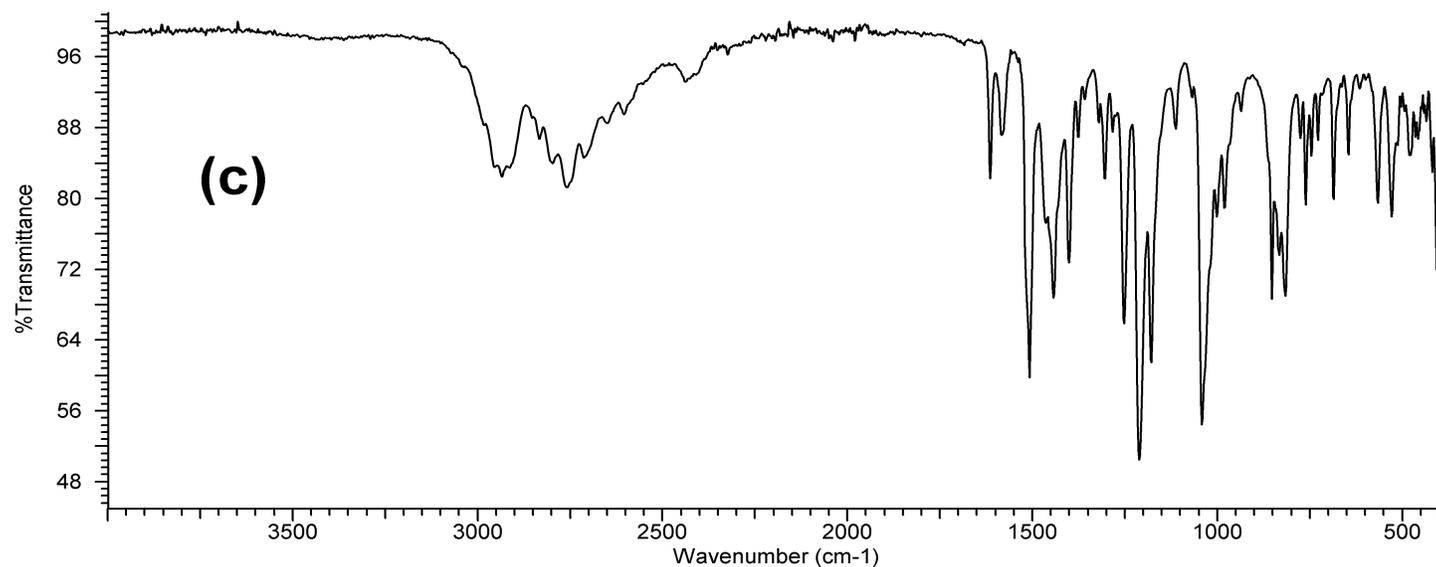
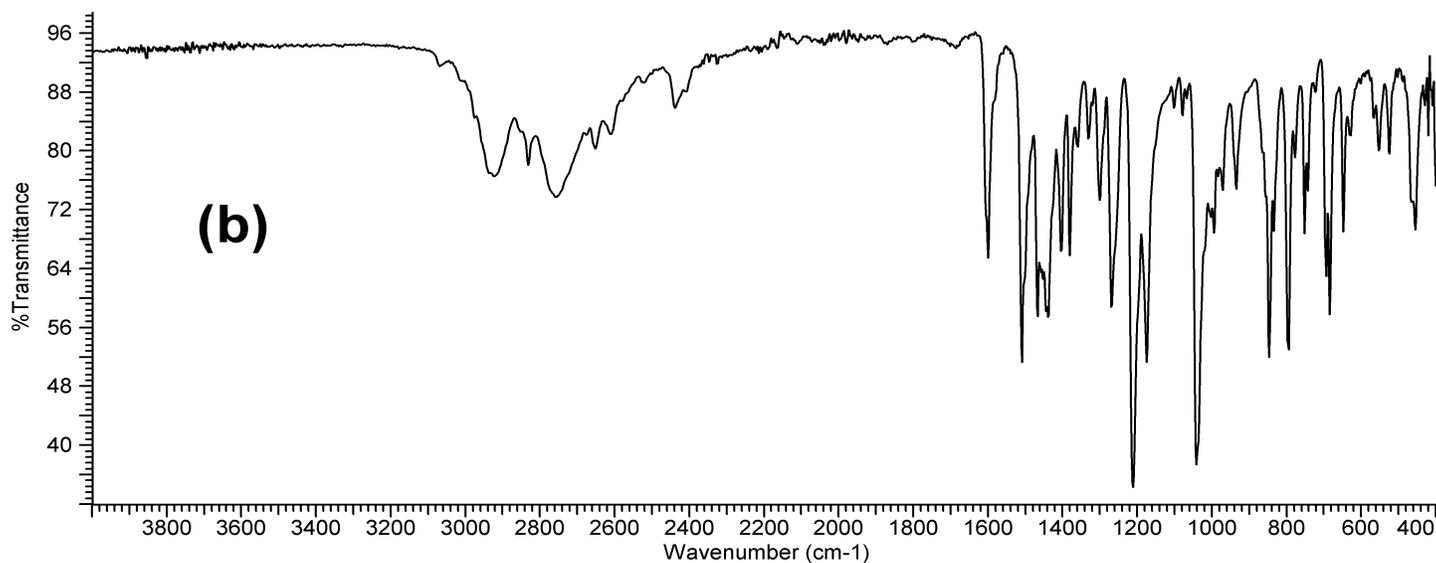
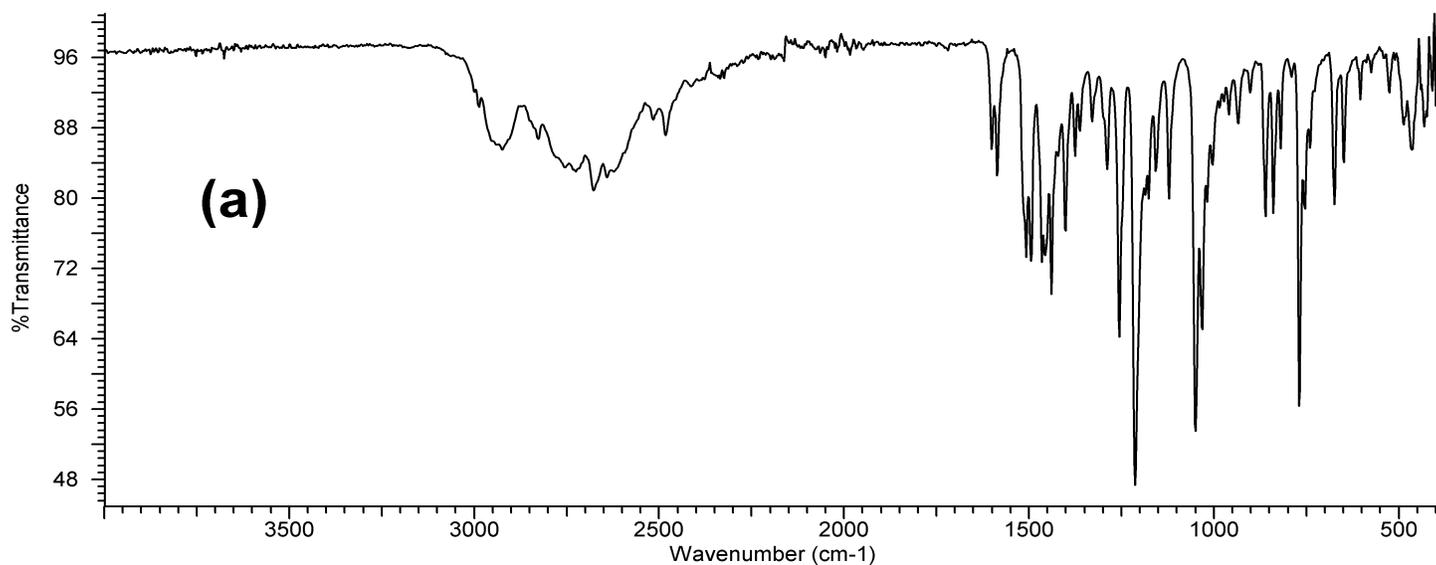


Figure 17 - FTIR spectra of (a) 2,5-dimethoxy-4-methyl-*N*-(2-methoxybenzyl)phenethylamine HCl (25D-NB2OMe) **10**, (b) 2,5-dimethoxy-4-methyl-*N*-(3-methoxybenzyl)phenethylamine HCl (25D-NB3OMe) **11**, and (c) 2,5-dimethoxy-4-methyl-*N*-(4-methoxybenzyl)phenethylamine HCl (25D-NB4OMe) **12**.

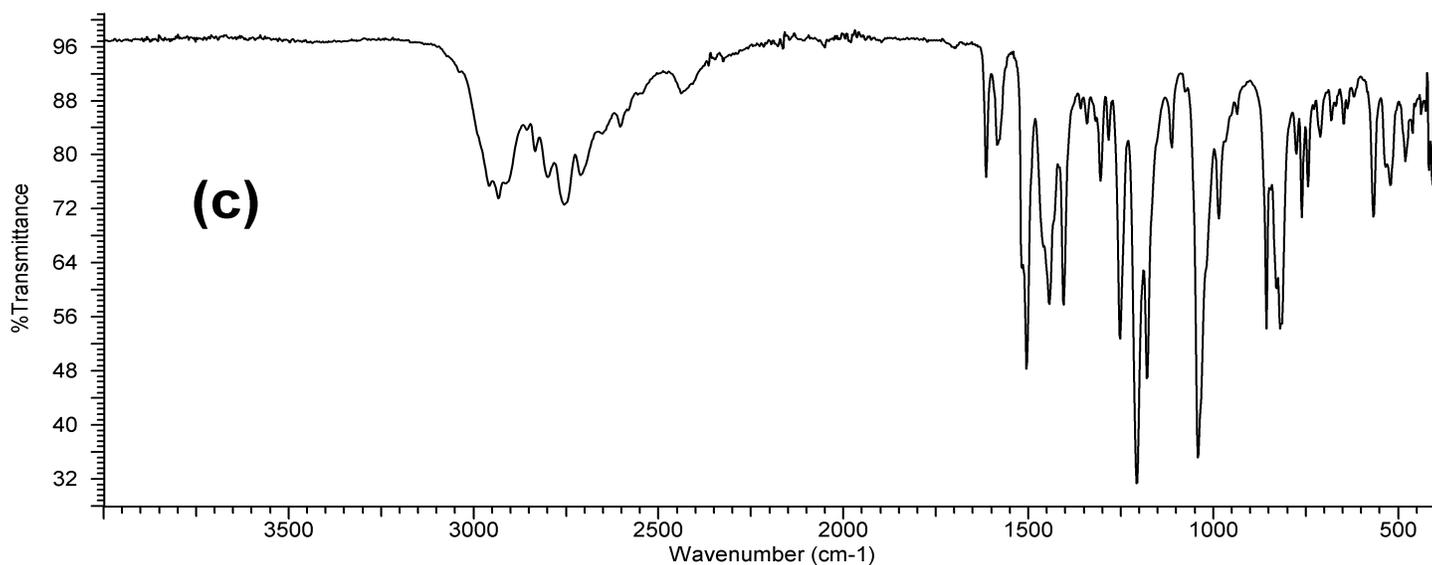
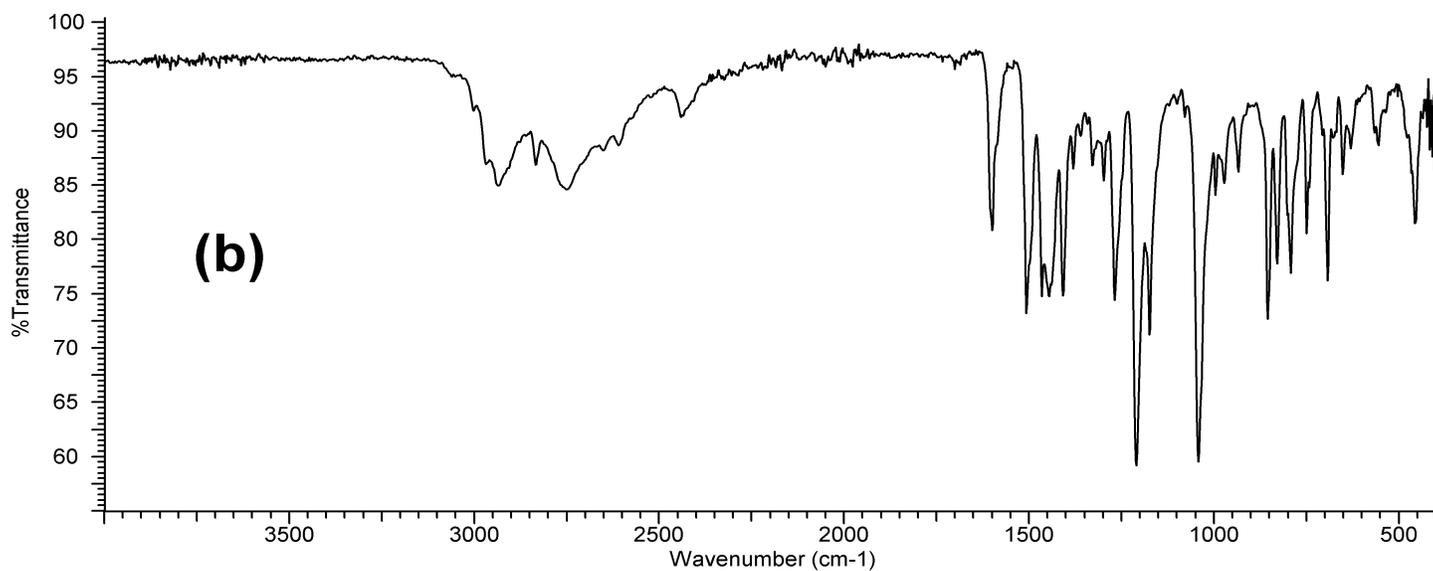
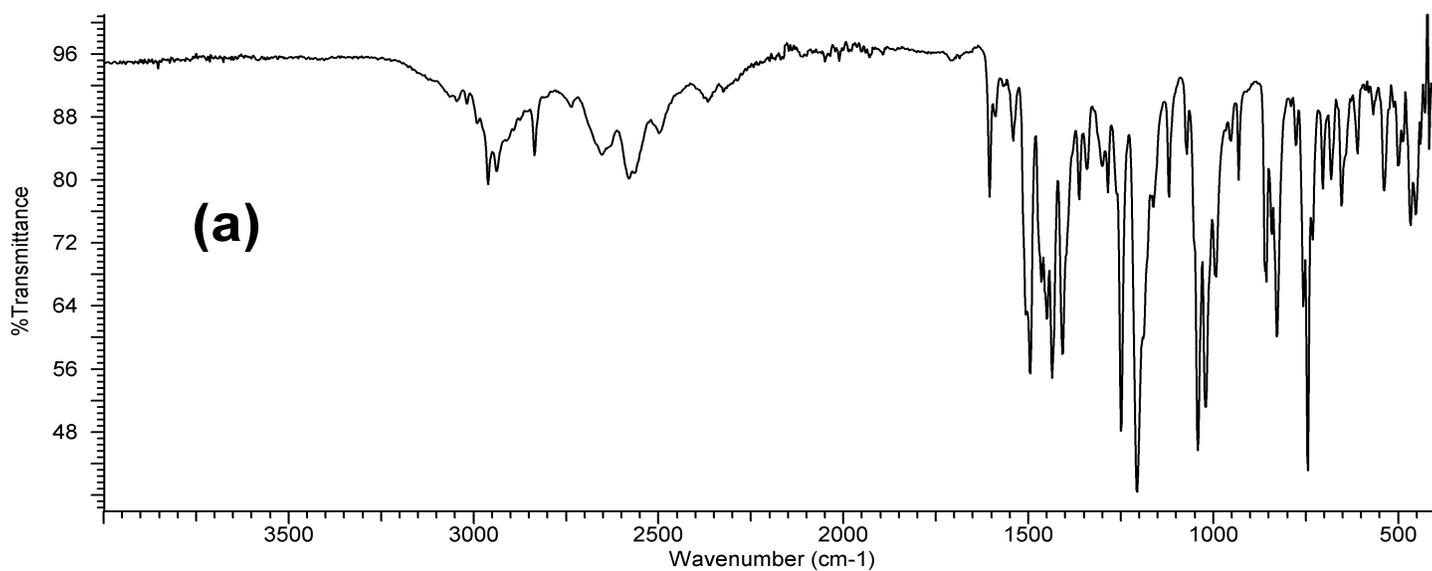


Figure 18 - FTIR spectra of (a) 2,5-dimethoxy-4-ethyl-*N*-(2-methoxybenzyl)phenethylamine HCl (25E-NB2OMe) **13**, (b) 2,5-dimethoxy-4-ethyl-*N*-(3-methoxybenzyl)phenethylamine HCl (25E-NB3OMe) **14**, and (c) 2,5-dimethoxy-4-ethyl-*N*-(4-methoxybenzyl)phenethylamine HCl (25E-NB4OMe) **15**.

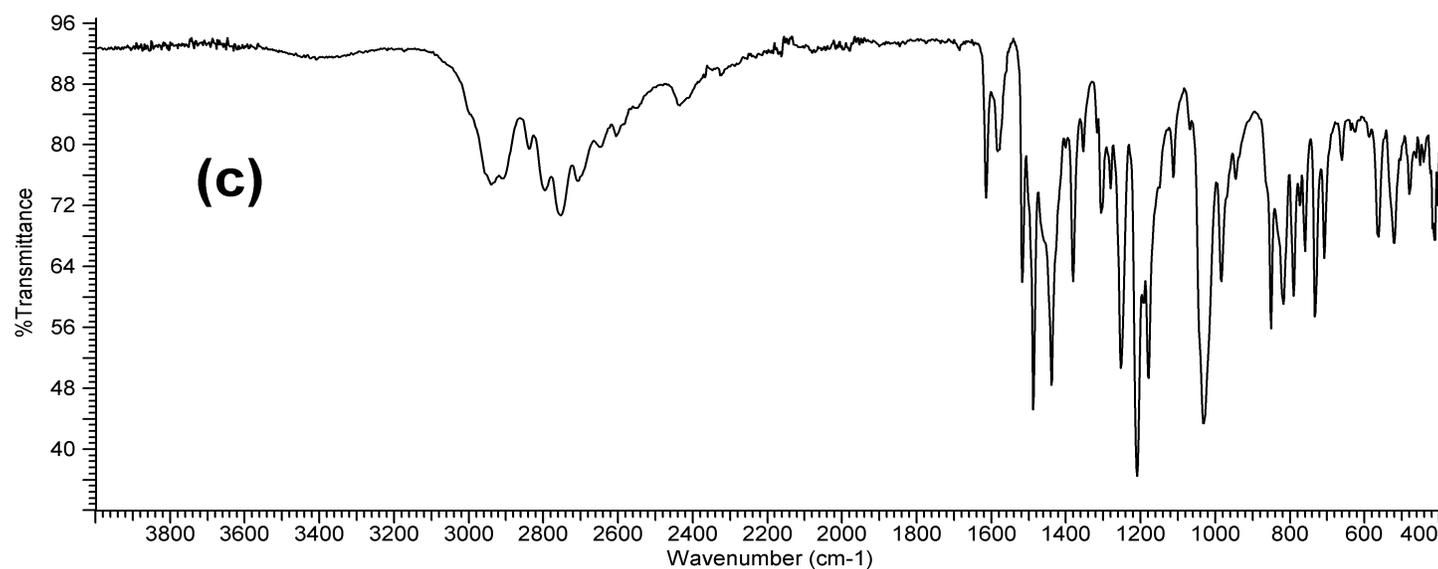
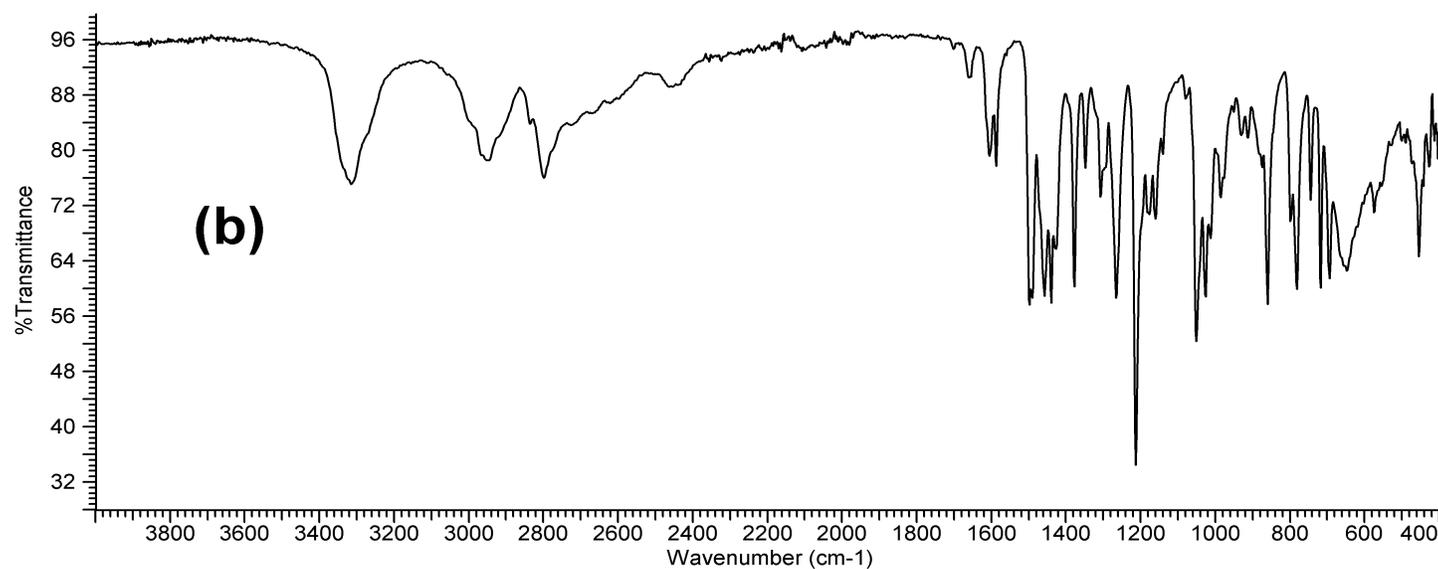
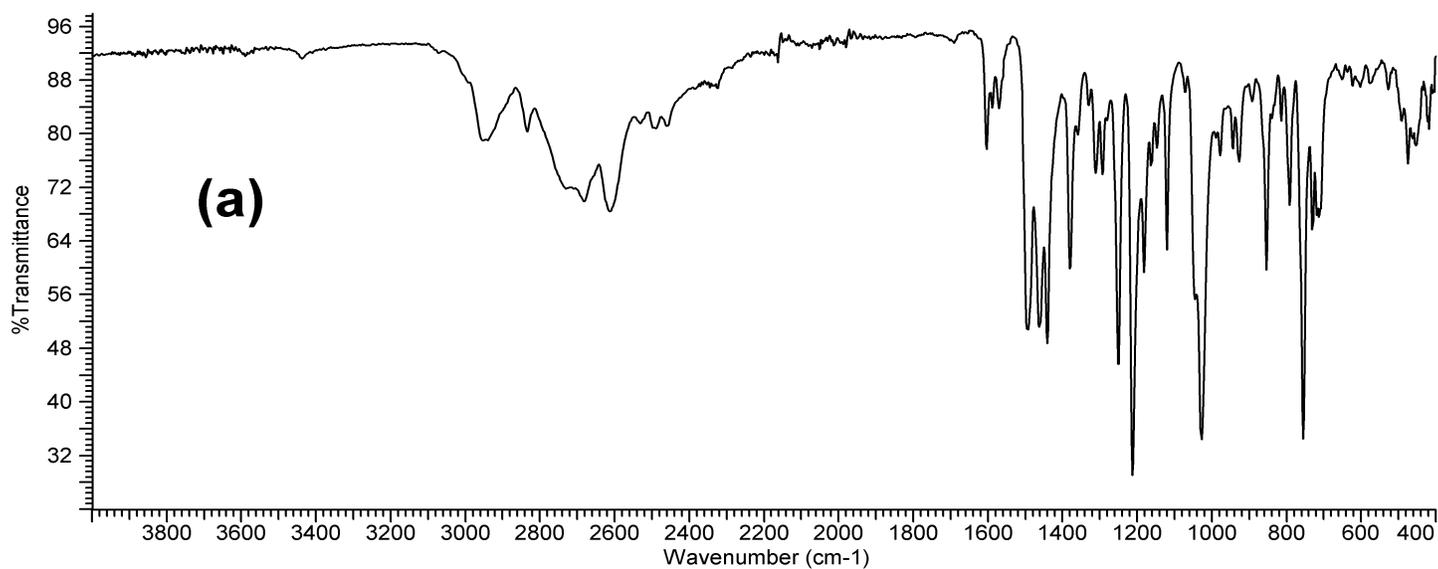


Figure 19 - FTIR spectra of (a) 2,5-dimethoxy-4-iodo-*N*-(2-methoxybenzyl)phenethylamine HCl (25I-NB2OMe) **16**, (b) 2,5-dimethoxy-4-iodo-*N*-(3-methoxybenzyl)phenethylamine HCl (25I-NB3OMe) **17**, and (c) 2,5-dimethoxy-4-iodo-*N*-(4-methoxybenzyl)phenethylamine HCl (25I-NB4OMe) **18**.

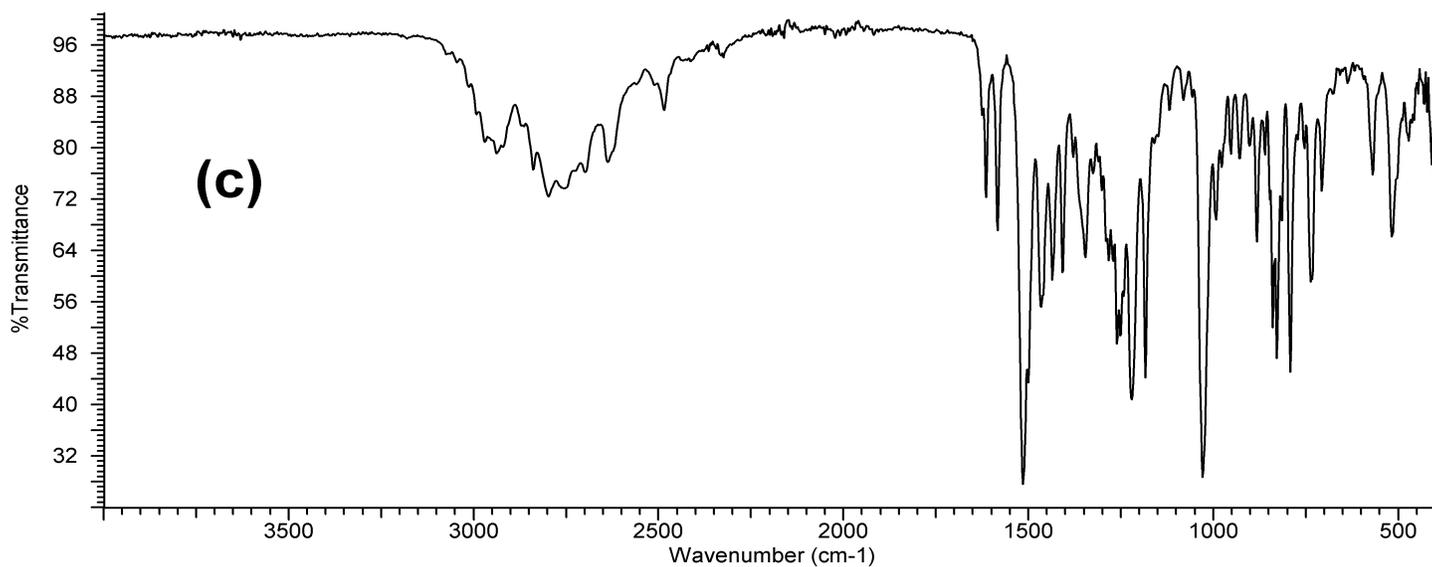
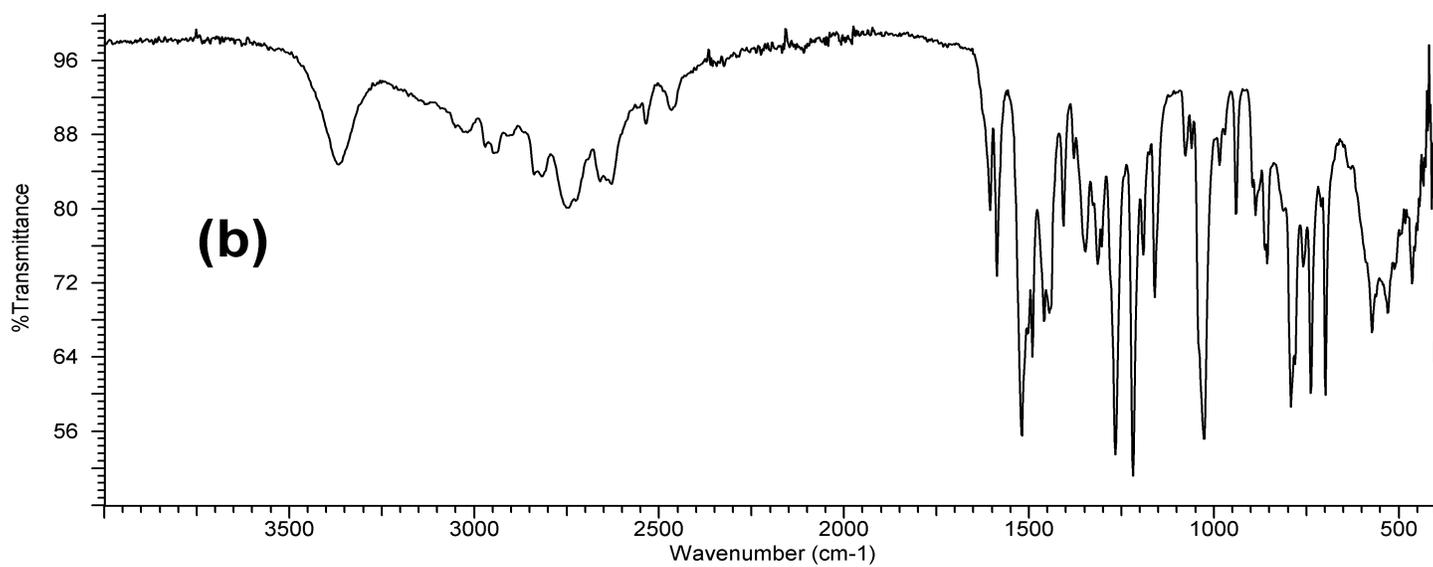
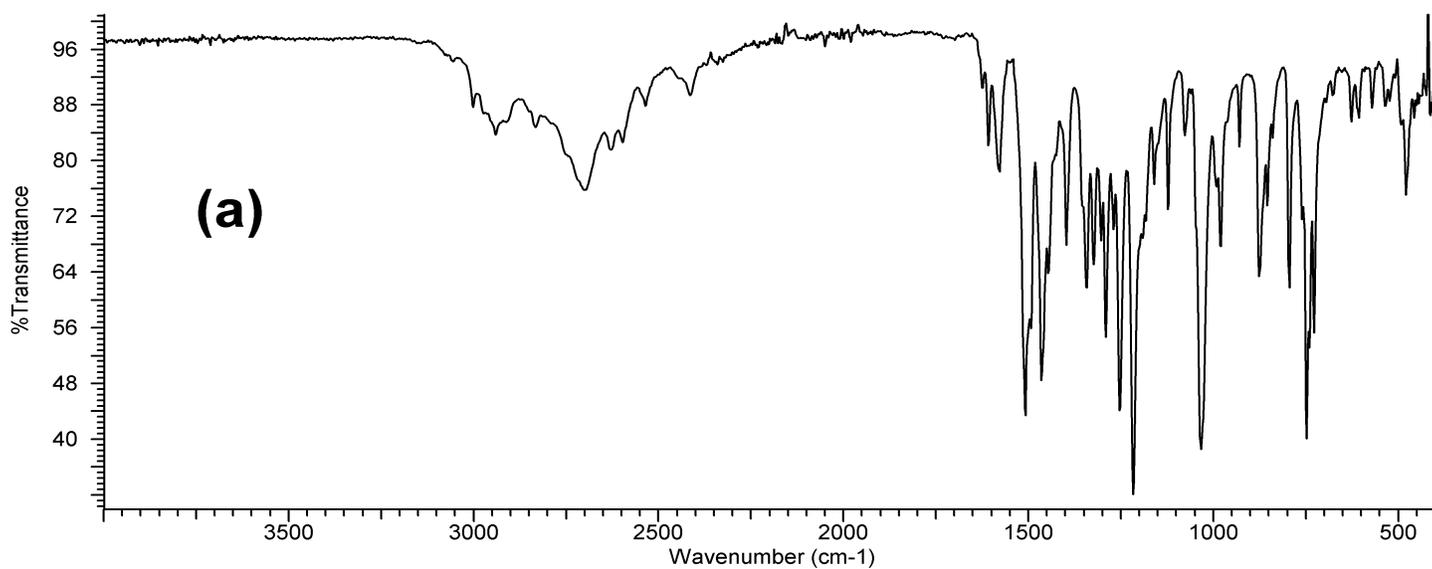


Figure 20 - FTIR spectra of (a) 2,5-dimethoxy-4-nitro-*N*-(2-methoxybenzyl)phenethylamine HCl (25N-NB2OMe) **19**, (b) 2,5-dimethoxy-4-nitro-*N*-(3-methoxybenzyl)phenethylamine HCl (25N-NB3OMe) **20**, and (c) 2,5-dimethoxy-4-nitro-*N*-(4-methoxybenzyl)phenethylamine HCl (25N-NB4OMe) **21**.

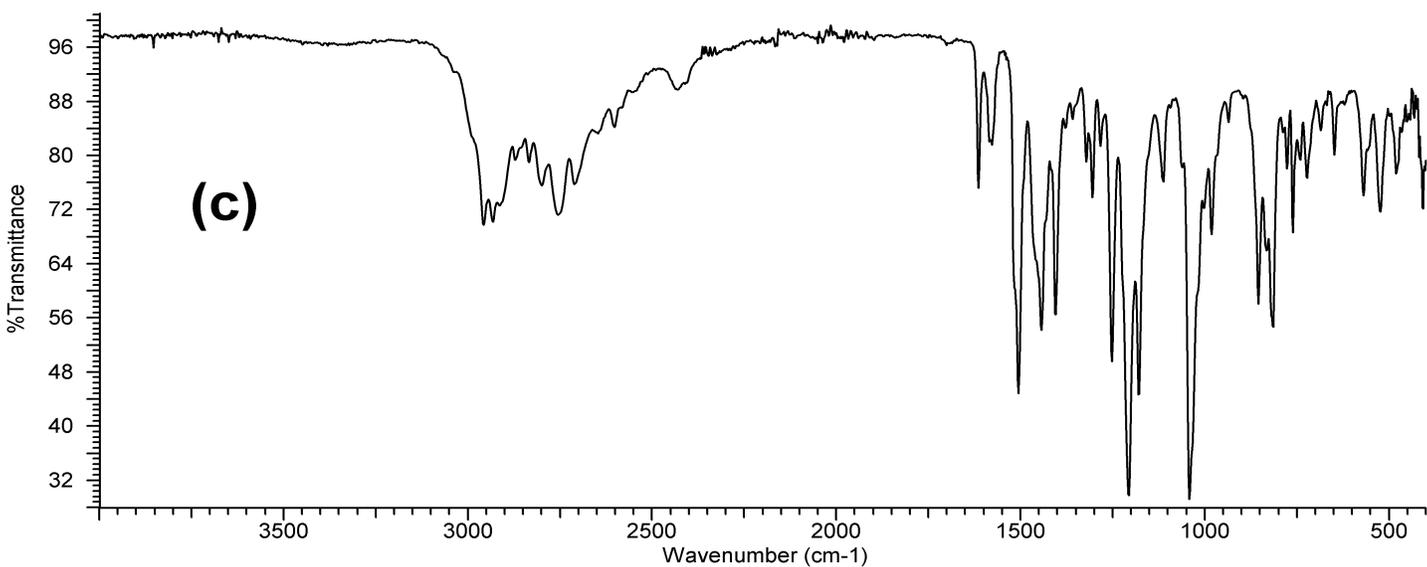
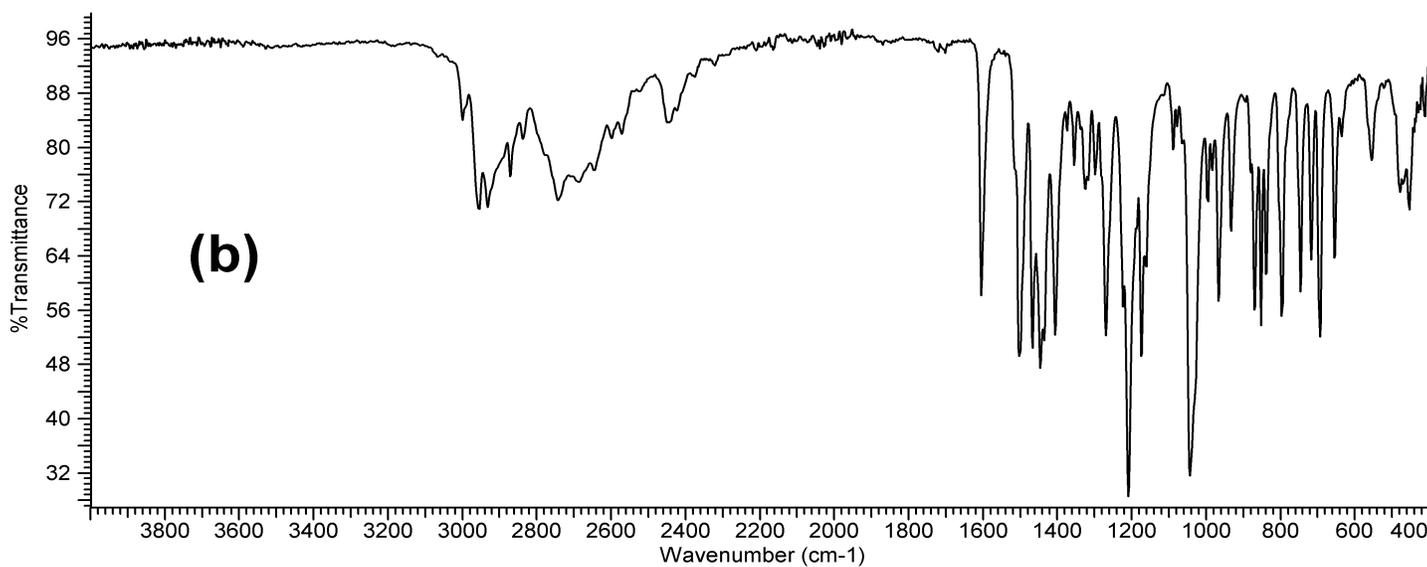
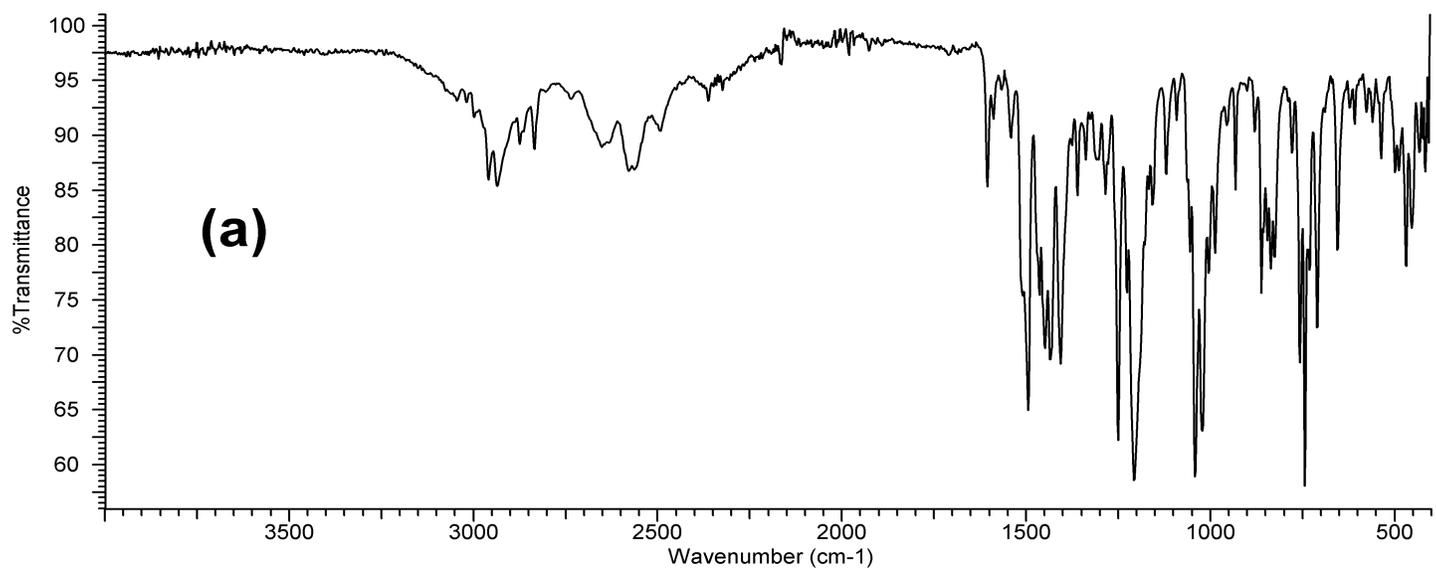


Figure 21 - FTIR spectra of (a) 2,5-dimethoxy-4-propyl-*N*-(2-methoxybenzyl)phenethylamine HCl (25P-NB2OMe) **22**, (b) 2,5-dimethoxy-4-propyl-*N*-(3-methoxybenzyl)phenethylamine HCl (25P-NB3OMe) **23**, and (c) 2,5-dimethoxy-4-propyl-*N*-(4-methoxybenzyl)phenethylamine HCl (25P-NB4OMe) **24**.

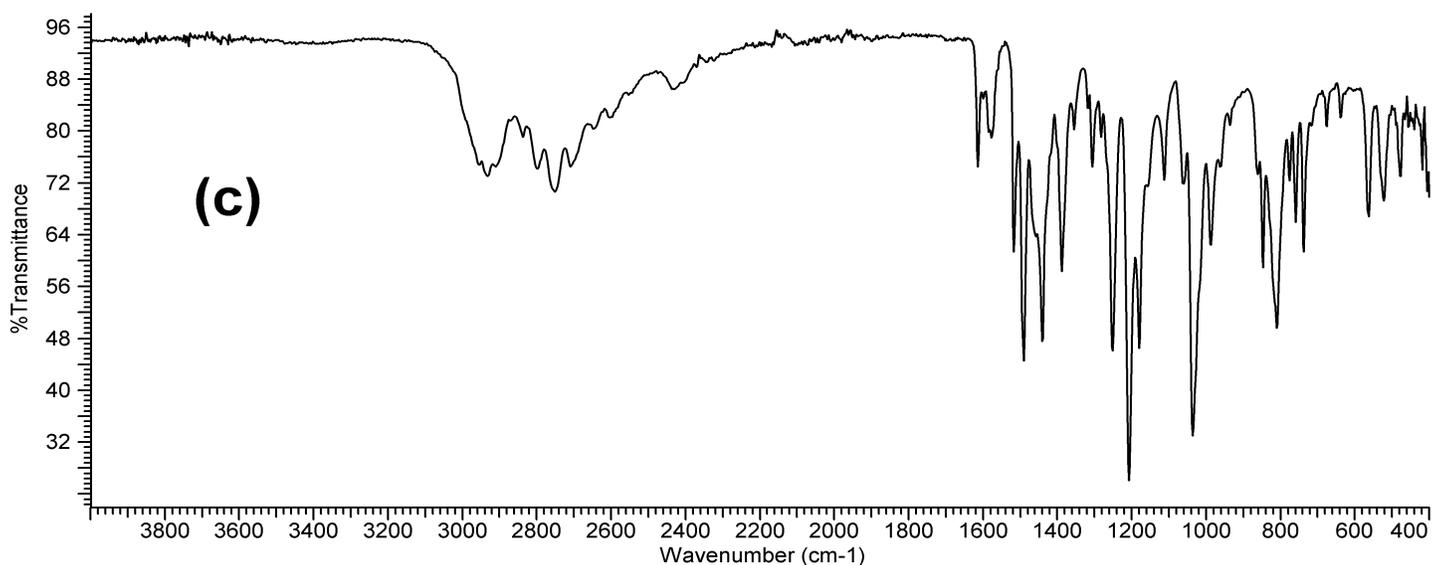
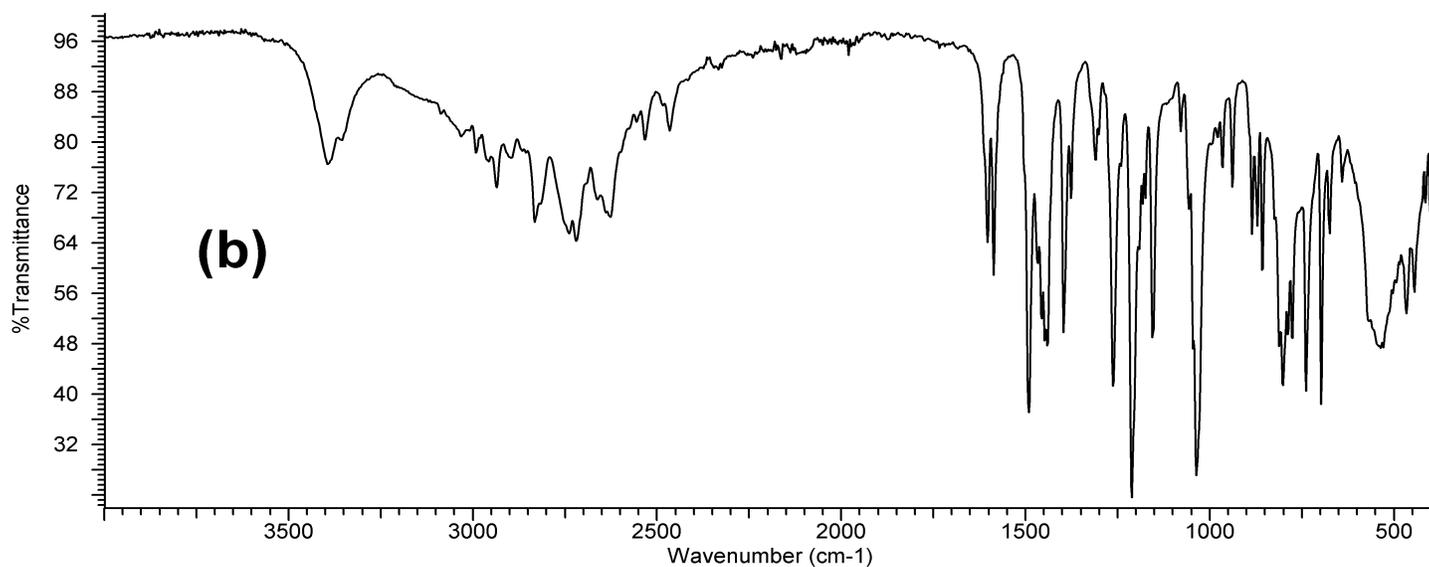
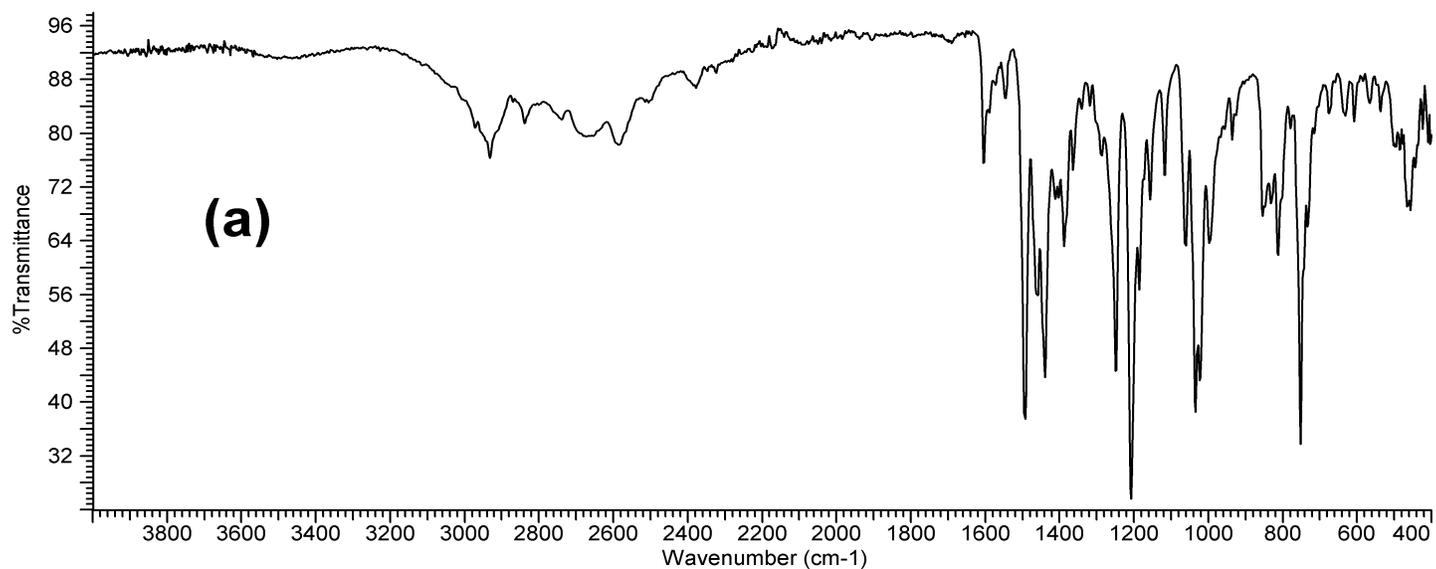


Figure 22 - FTIR spectra of (a) 2,5-dimethoxy-4-ethylthio-*N*-(2-methoxybenzyl)phenethylamine HCl (25T2-NB2OMe) **25**, (b) 2,5-dimethoxy-4-ethylthio-*N*-(3-methoxybenzyl)phenethylamine HCl (25T2-NB3OMe) **26**, and (c) 2,5-dimethoxy-4-ethylthio-*N*-(4-methoxybenzyl)phenethylamine HCl (25T2-NB4OMe) **27**.

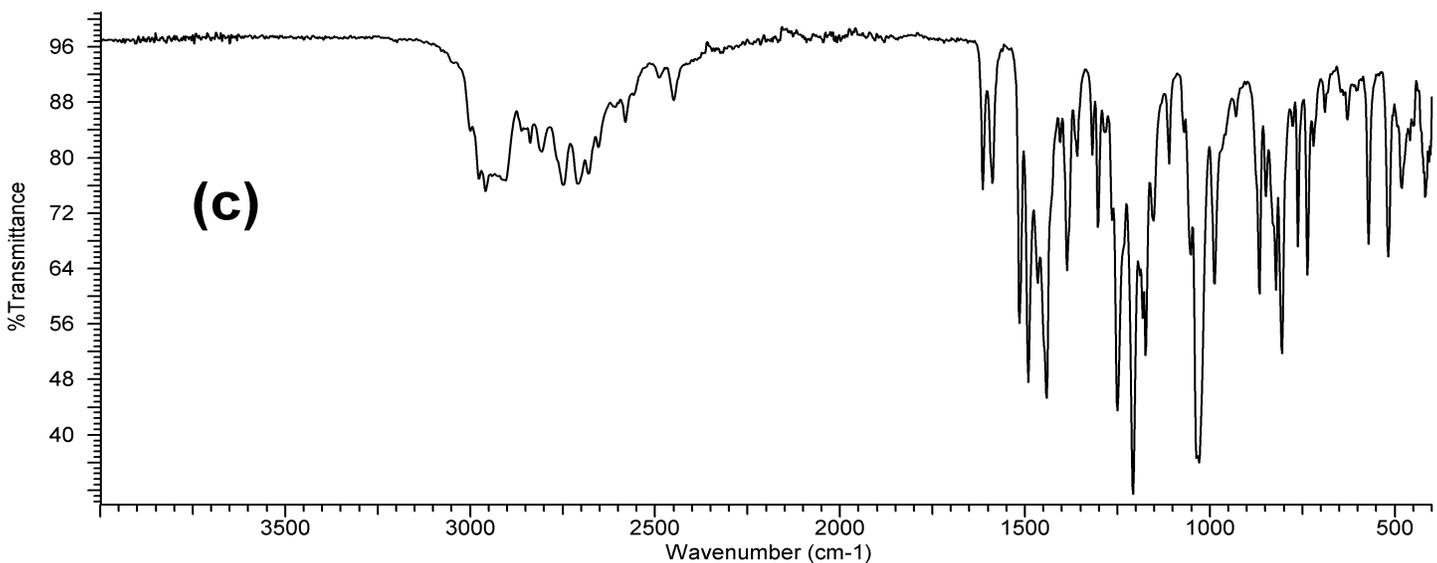
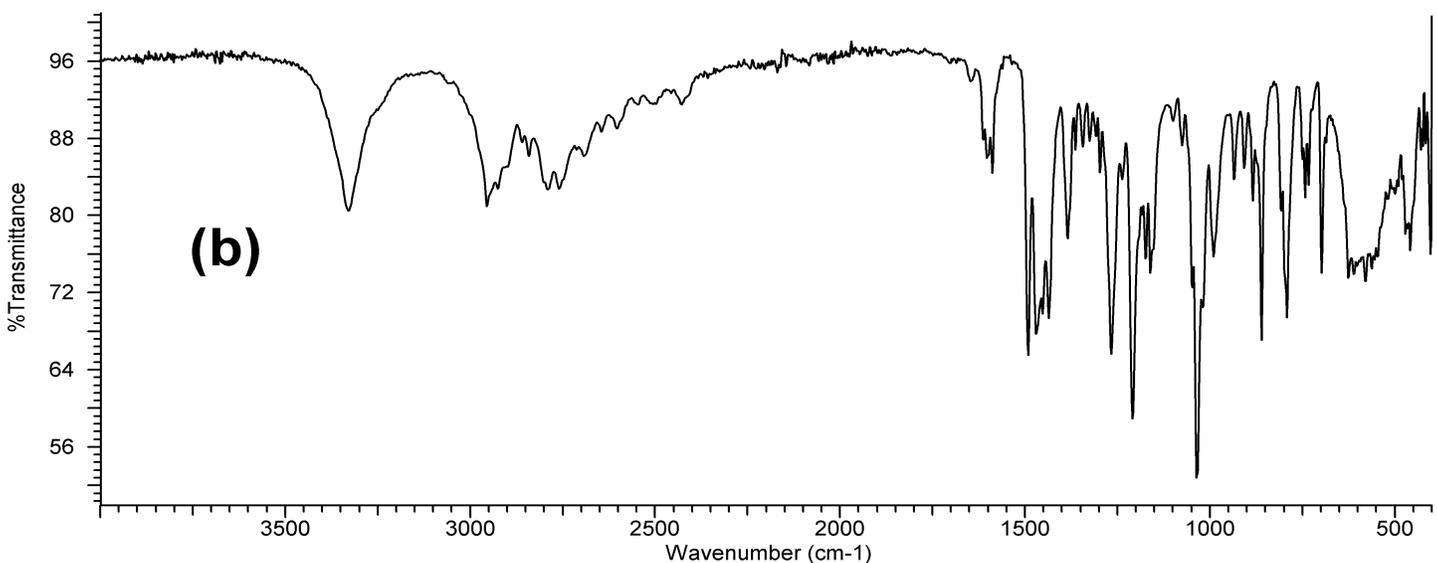
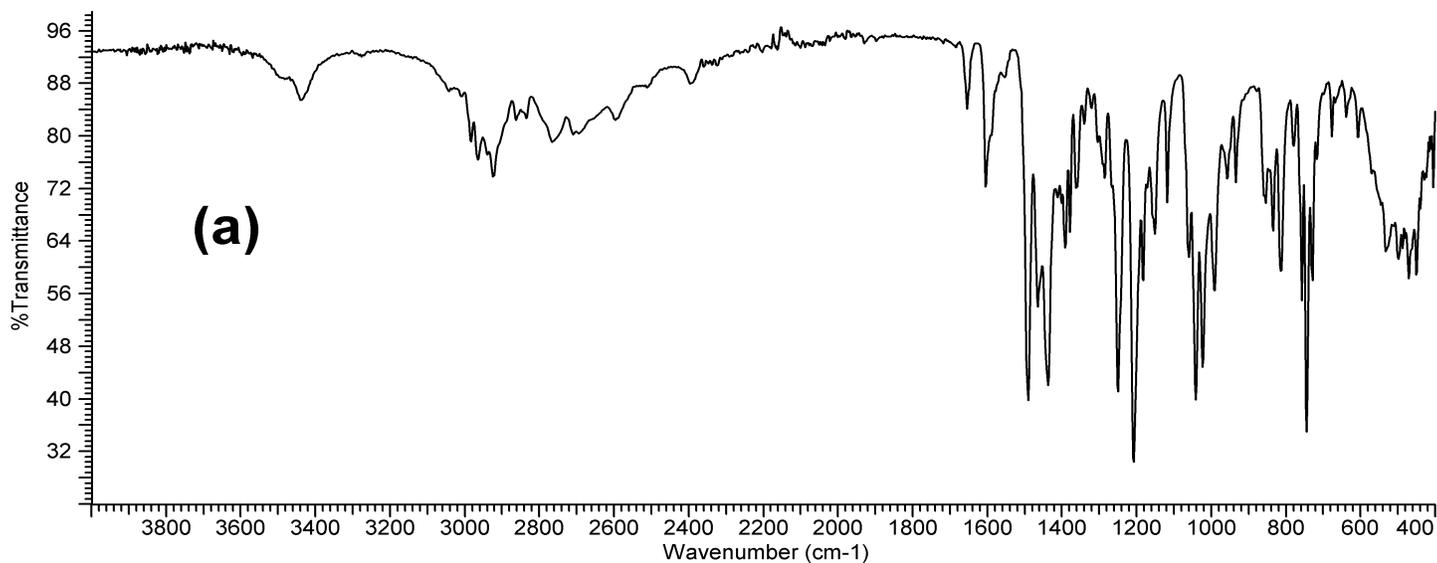


Figure 23 - FTIR spectra of (a) 2,5-dimethoxy-4-isopropylthio-*N*-(2-methoxybenzyl)phenethylamine HCl (25T4-NB2OMe) **28**, (b) 2,5-dimethoxy-4-isopropylthio-*N*-(3-methoxybenzyl)phenethylamine HCl (25T4-NB3OMe) **29**, and (c) 2,5-dimethoxy-4-isopropylthio-*N*-(4-methoxybenzyl)phenethylamine HCl (25T4-NB4OMe) **30**.

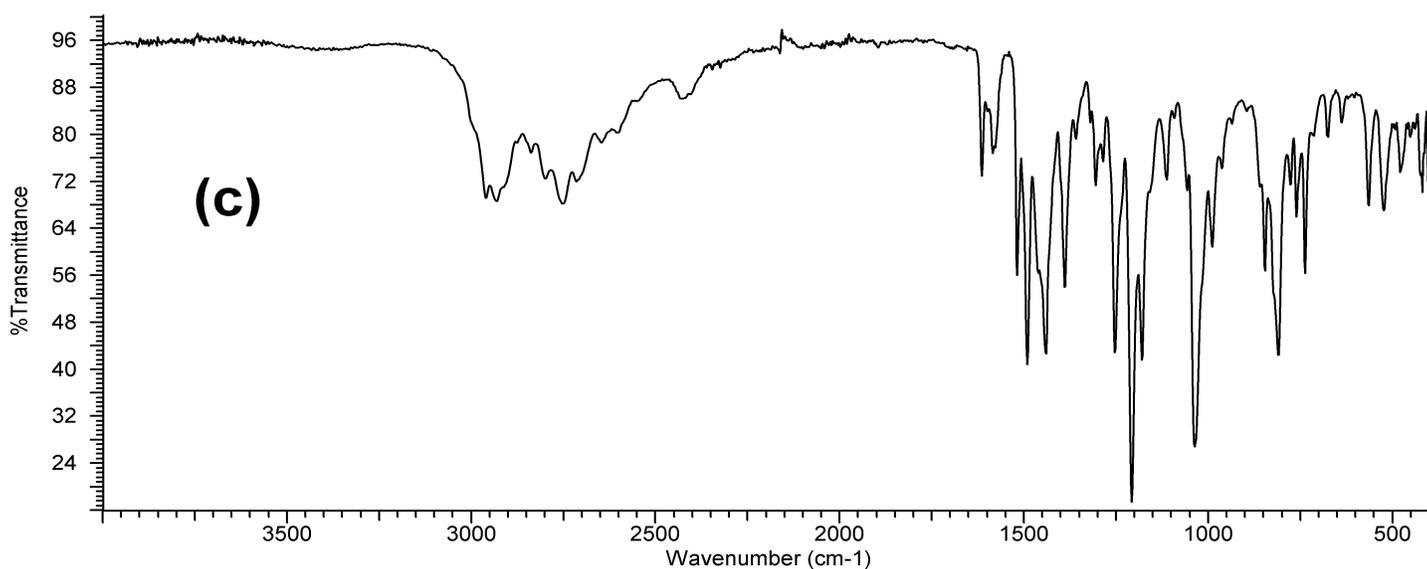
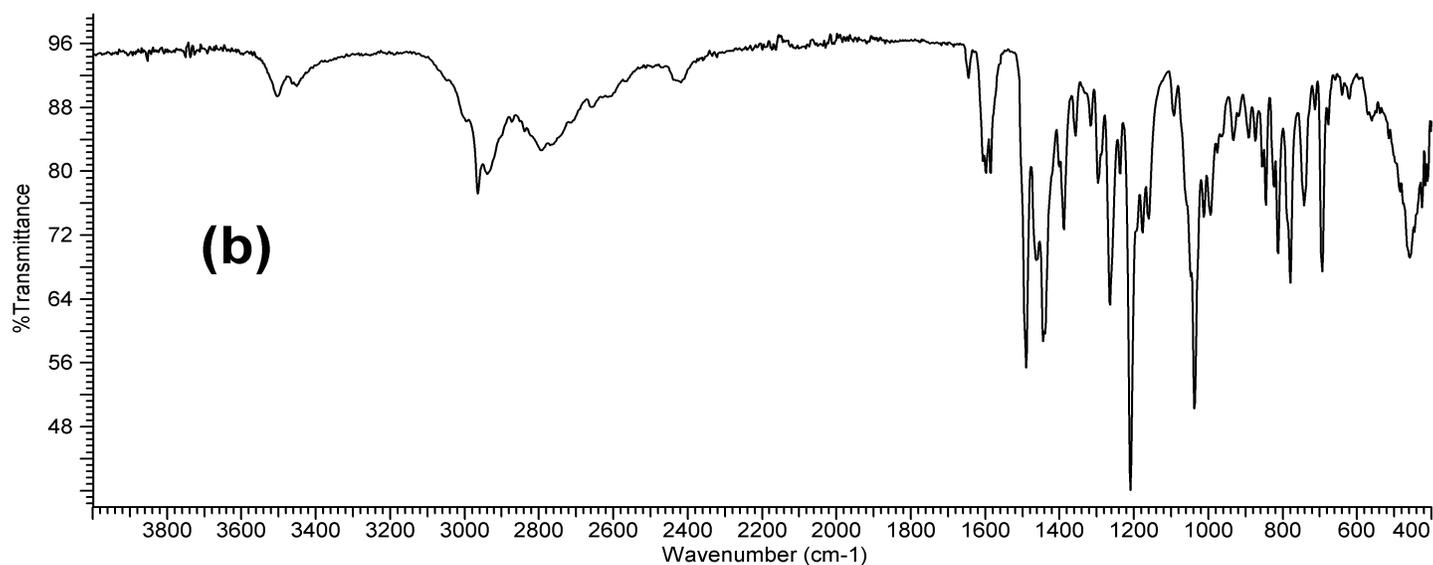
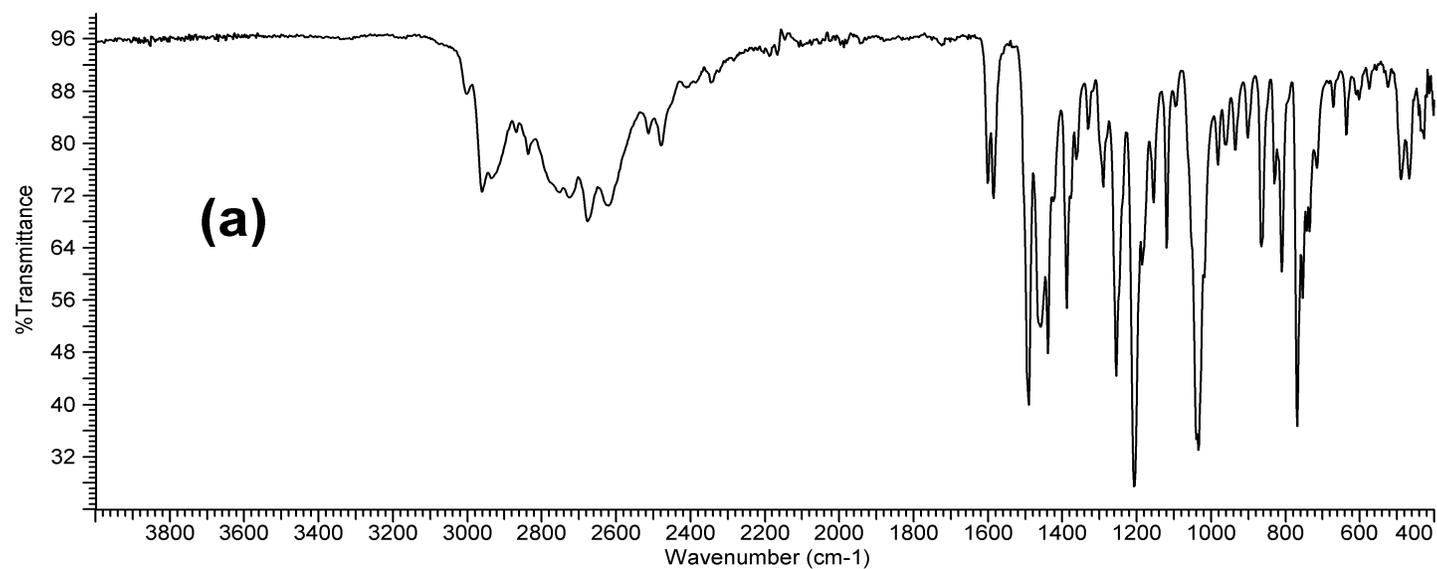


Figure 24 - FTIR spectra of (a) 2,5-dimethoxy-4-propylthio-*N*-(2-methoxybenzyl)phenethylamine HCl (25T7-NB2OMe) **31**, (b) 2,5-dimethoxy-4-propylthio-*N*-(3-methoxybenzyl)phenethylamine HCl (25T7-NB3OMe) **32**, and (c) 2,5-dimethoxy-4-propylthio-*N*-(4-methoxybenzyl)phenethylamine HCl (25T7-NB4OMe) **33**.

FTIR Differentiation of the NBOMe methoxybenzyl positional isomers (2-OMe vs. 3-OMe vs. 4-OMe)

FTIR spectra for compounds **1-33** as the HCl ion-pairs are given in Figures 14-24. Each compound exhibited characteristic secondary amine HCl ion-pair absorbances between 2500-3000 cm^{-1} . Although each compound produced somewhat similar spectra, characteristic differences were observed between 400-1600 cm^{-1} , where each compound could be easily differentiated. Six of the 3-methoxybenzyl analogues (**5**, **8**, **17**, **20**, **26**, and **29**) exhibited an apparent H_2O stretching band at approximately 3150-3350 cm^{-1} . The band could not be diminished even upon vacuum drying of the samples.

Conclusions

Each of the differing 4-substituted 2,5-dimethoxy-*N*-(2-methoxybenzyl) phenethylamines were distinguished from their 3- and 4-methoxybenzyl analogues via mass spectrometry and infrared spectroscopy.

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