Ethylphenidate: An Analytical Profile

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ABSTRACT: Spectroscopic and chromatographic data are provided for ethylphenidate, a relatively new internet-available compound, possessing CNS stimulant properties. Analytical data (infrared spectroscopy, mass spectrometry, and proton/carbon nuclear magnetic resonance spectroscopy) are presented.

KEYWORDS: ethylphenidate, methylphenidate analog, designer drugs, chemical analysis, forensic chemistry.

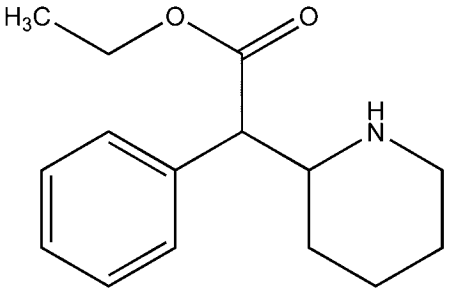


Figure 1 - Structural formula of ethylphenidate.

The sale of compounds touted as "legal highs" has recently flourished on the internet. Ethylphenidate (Figure 1) is currently one of many such compounds. However, although it is claimed to be legal, it may be considered to be an analog of the Schedule II controlled substance, methylphenidate [1]; ethylphenidate being an ethyl ester *vs*. methylphenidate being a methyl ester. Ethylphenidate is best known as a transesterification metabolite, after methylphenidate and ethanol are consumed together [2-5]. The synthesis and pharmacology of ethylphenidate enantiomers has also been recently studied [6]. Herein, an analytical profile is presented to assist forensic chemists who may encounter this substance in casework.

Experimental

Chemical, Materials, and Reagents

All solvents were distilled-in-glass products of Burdick and Jackson Labs (Muskegon, MI, USA). Methylphenidate HCl was obtained from the authentic reference collection of the DEA Special Testing and Research Laboratory. All other chemicals were of reagent-grade quality and products of Aldrich Chemical (Milwaukee, WI).

Synthesis

In accordance with Journal policy, exact experimental details are not provided. Methylphenidate HCl was hydrolyzed to ritalinic acid, which was subsequently esterified to ethylphenidate with ethanolic HCl (Figure 2).

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.

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 (GC). 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 at a scan rate of 2.59 scans/s. The GC was fitted with a 30 m x 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.

Nuclear Magnetic Resonance Spectroscopy (NMR)

Proton (^{1}H), carbon (^{13}C), and 2-dimensional NMR spectra were obtained on an Agilent VNMRS 600 MHz NMR using a 5 mm Protune broad band detection, variable temperature, pulse field gradient probe (Agilent, Palo Alto, CA). Samples were

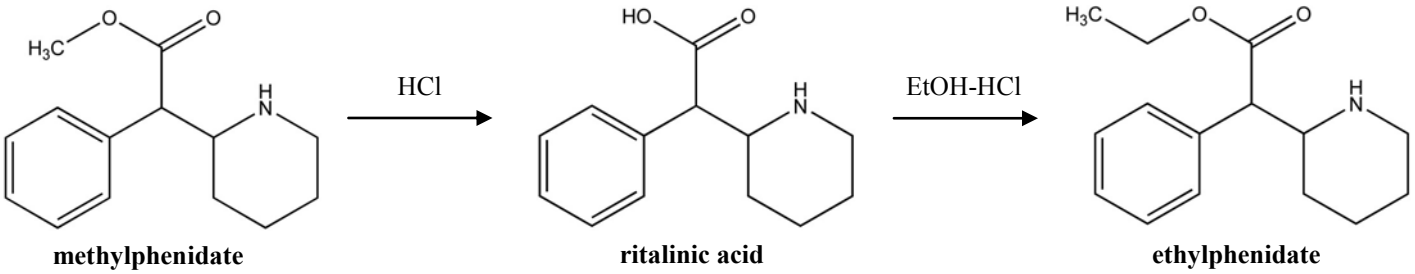


Figure 2 - Synthetic route for ethylphenidate.

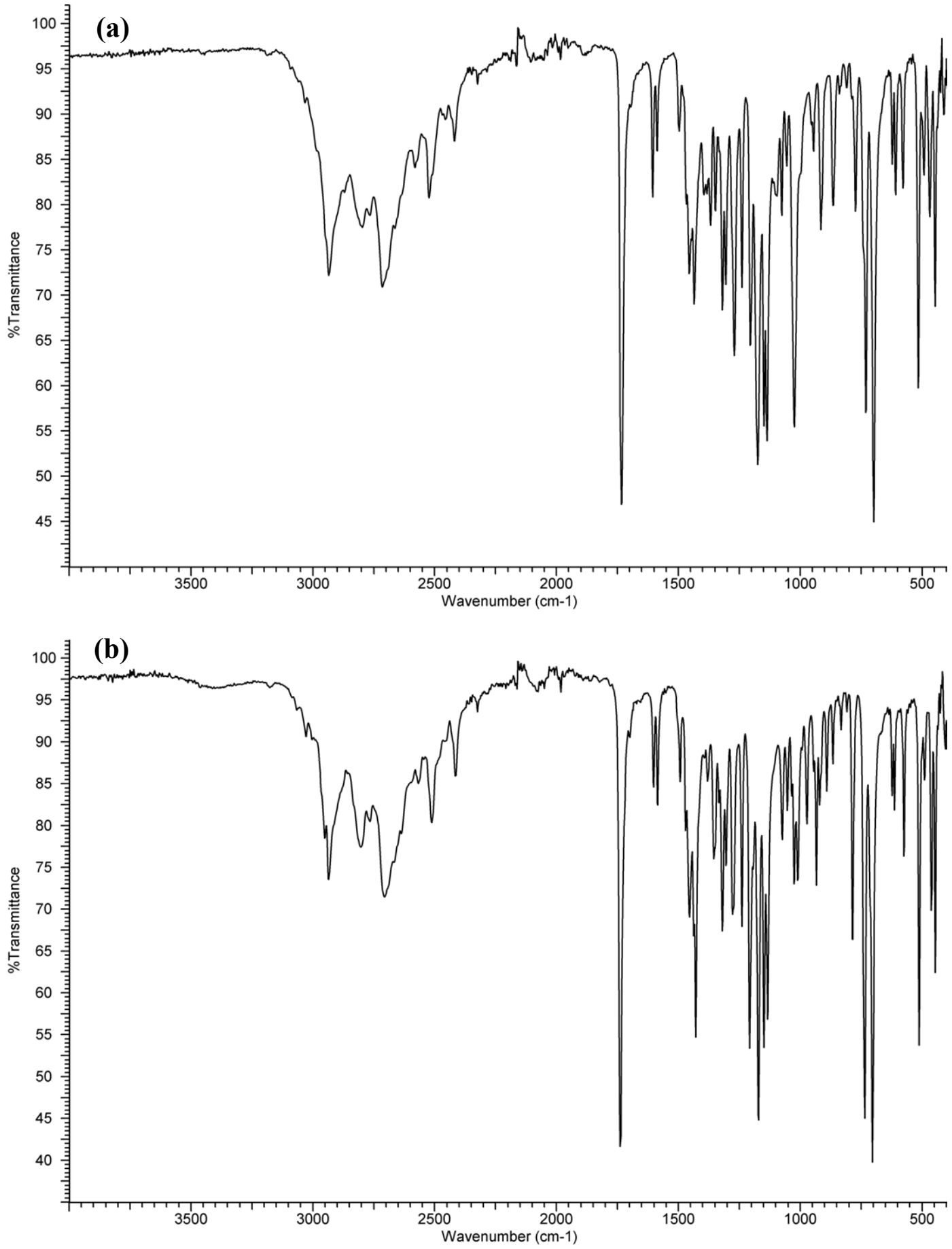
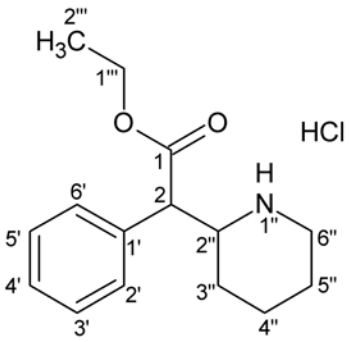


Figure 3 - Infrared spectra of (a) ethylphenidate HCl and (b) methylphenidate HCl.

Position	Carbon (ppm)	Proton (ppm, J)
1	171.8	-
2	54.0	4.32 (d, 9.7 Hz)
1'	134.3	-
2', 6'	128.5	7.28 (ad, 7.3 Hz, 2H)
3', 5'	129.2	7.35 (at, 7.3 Hz, 2H)
4'	128.3	7.33 (at, 7.3 Hz, 1H)
1''	-	8.69 (bs), 10.55 (bs)
2''	59.1	3.62 (aq, ~10.5 Hz)
3''	25.8	1.37 (m), 1.76 (m)
4''	21.9	1.81 (m), 2.11 (m)
5''	22.6	1.37 (m), 1.83 (m)
6''	45.6	2.92 (aq, ~12 Hz), 3.72 (bd, ~12 Hz)
1'''	62.4	4.29 (m)
2'''	13.9	1.20 (t,7.0 Hz)

Structure



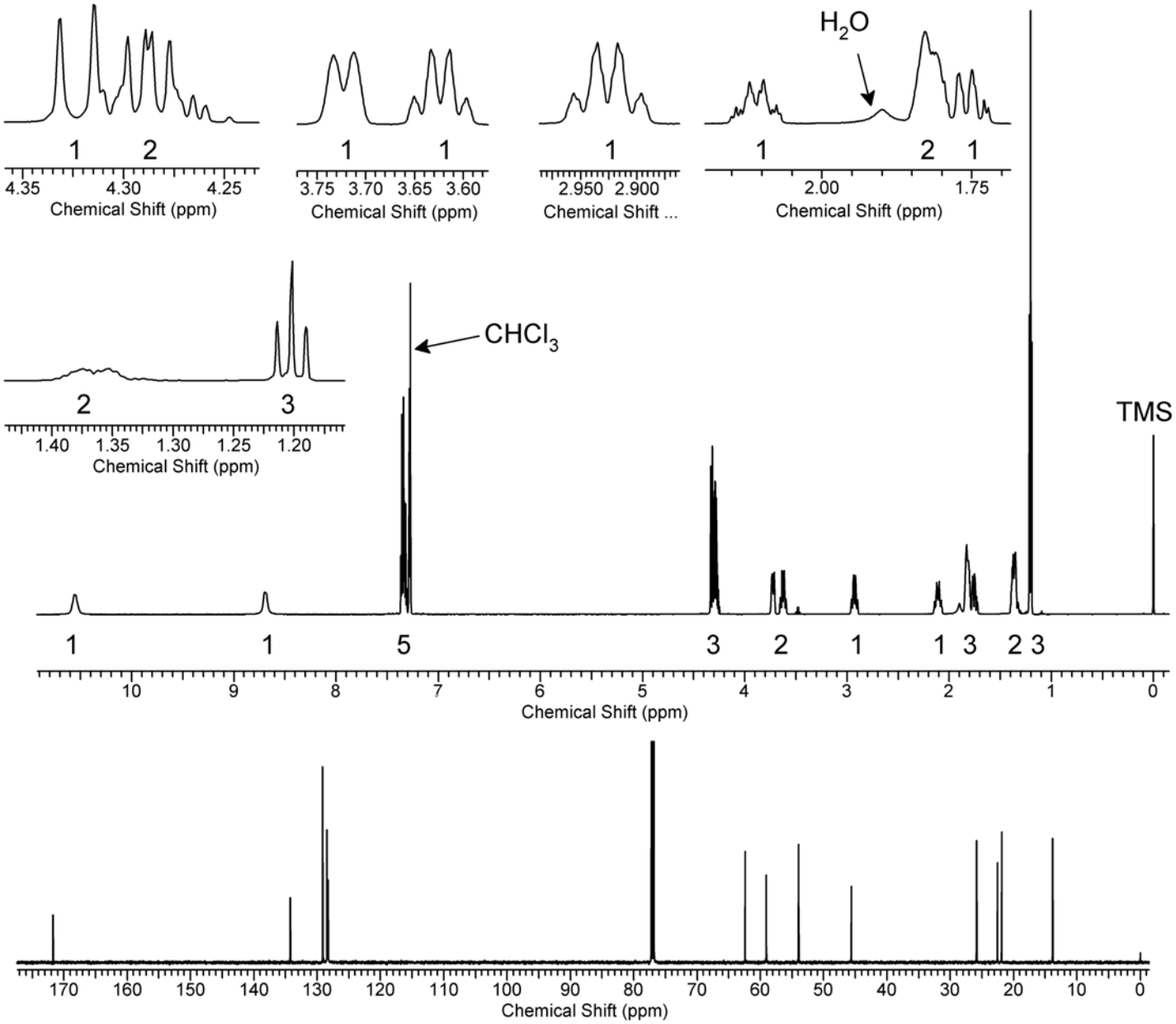


Figure 4 - ^{1}H and ^{13}C NMR spectra and associated data for ethylphenidate HCl in $CDCl_3$. Proton abbreviations: ad = apparent doublet, aq = apparent quartet, at = apparent triplet, bd = broad doublet, bs = broad singlet, d = doublet, m = multiplet, t = triplet.

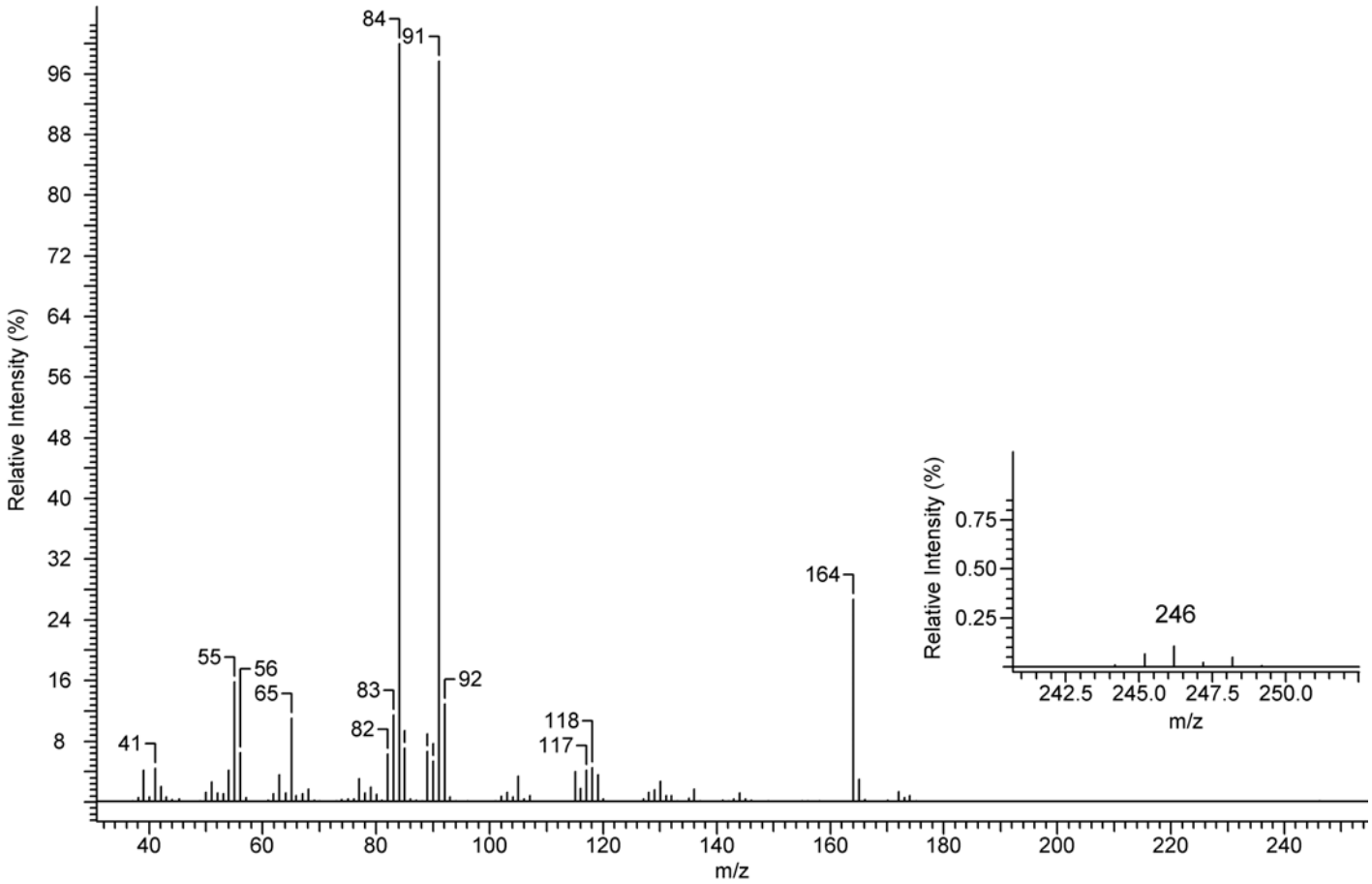


Figure 5 - Electron ionization mass spectrum of ethylphenidate.

dissolved in deuterochloroform ($CDCl_3$) containing 0.03% v/v tetramethylsilane (TMS) as the 0 ppm reference compound. The sample temperature was maintained at 26°C. Standard Agilent pulse sequences were used to acquire ^1H, proton-decoupled ^{13}C, and gradient versions of HSQC and HMBC spectra. Data processing was performed using software from Agilent and Applied Chemistry Development (ACD/Labs, Toronto, Canada). Structure elucidation and the prediction of ^1H and ^{13}C spectra was accomplished using ACD/Labs software.

Discussion

The FTIR spectrum of ethylphenidate HCl is remarkably similar to that of methylphenidate HCl (Figure 3). Only minor differences in some absorbance patterns can be discerned. Therefore, the use of a complementary spectroscopic/ spectrometric method is recommended. The ^1H and ^{13}C NMR of ethylphenidate (Figure 4) clearly distinguish it from methylphenidate due to the presence of the ethyl ester proton pattern (4.29 ppm ^1H multiplet CH_2, and 1.20 ppm triplet CH_3) instead of the methoxy singlet. The mass spectrum of ethylphenidate (Figure 5) gives a very weak M-1 ion at *m/z* 246 with major ions at *m/z* 84 (piperidinium ion; base peak) and *m/z* 91 (tropylium ion). An ion at *m/z* 164 is the complementary ion (ethyl phenylacetate moiety) from loss of the piperidine fragment (analogous to *m/z* 150 for methylphenidate; methyl phenylacetate moiety).

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