

The Characterization of Anastrozole

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ABSTRACT: The analysis and characterization of 2-[5-(1-cyano-isopropyl)-3-(1,2,4-triazolylmethyl)phenyl]-2-methylpropanenitrile (Anastrozole) is presented. Gas chromatography/mass spectrometry (GC/MS), Fourier-Transform nuclear magnetic resonance spectroscopy (FTNMR), and solid phase Fourier-Transform infrared (FTIR) spectroscopy data are presented.

KEYWORDS: anastrozole, GC/MS, NMR, FTIR, forensic chemistry

Anastrozole (Figure 1) is described as an aromatase inhibitor used in the treatment of breast cancer [1]. Anecdotal internet reports indicate that anastrozole is misused by males in the midst of an illicit steroid cycle to overcome production of excess estrogens [2]. Astra-Zeneca markets this particular drug in "Arimidex" preparations.

Experimental

Chemicals, Reagents, and Materials

All solvents were distilled-in-glass products of Burdick and Jackson Labs (Muskegon, MI). Anastrozole was obtained from Accustandard (New Haven, CT). All other chemicals were reagent grade quality and products of Aldrich Chemical (Milwaukee, WI).

Nuclear Magnetic Resonance (NMR) Spectroscopy:

¹H- and ¹³C-NMR spectra (Figures 2 and 3, respectively) were acquired on a Varian 400MR 400 MHz instrument using a AutoX 5 mm indirect detect pulse field gradient (PFG) probe at 26°C. (¹H parameters: Number of scans (nt) = 8, pulse width (pw) = 45°, relaxation delay (d1) = 1 s, acquisition time (at) = 2.6 s; ¹³C parameters: nt = 256, pw = 45°, d1 = 1 s, at = 1.3 s, proton decoupled). Spectra were processed using ACD/Labs *SpecManager* software (Advanced Chemistry Development Inc.©, Toronto, Canada). Anastrozole was prepared with CDCl₃ containing 0.05 wt % tetramethylsilane (TMS). Chemical shifts (δ) are reported in parts per million (ppm) using TMS (0.0 ppm) as the reference standard.

Fourier Transform Infrared Spectroscopy (FTIR):

The spectrum (Figures 4a and 4b) was acquired using a Thermo-Scientific iZ10 Spectrophotometer with a Golden Gate attenuated total reflectance (ATR) accessory. The spectrum was collected using 32 scans between 4000 cm⁻¹ and 400 cm⁻¹.

Gas Chromatography/Mass Spectrometry (GC/MS):

The spectrum (Figure 5) was acquired using an Agilent Model 6890N GC equipped with an Agilent Model 5973 quadrupole mass-selective detector (MSD). The MSD was operated using 70 eV electron ionization. The GC was fitted with a 30 m x 0.25 mm I.D. fused silica capillary column coated with 0.50 μm 35% phenyl, 65% dimethyl arylene siloxane (DB-35MS), and was operated in splitless mode. The injection port was maintained at 250°C. The oven temperature program was as follows: Initial temperature 90°C (1 minute), ramped to 300°C at 8°C per minute (final hold 10 minutes). Helium was used as a purge gas at a rate of 60 mL/second. Methanol was used as the solvent.

Discussion

The mass spectrum of anastrozole is fairly rich in detail yielding a m/z of 209 as the base peak with the second most abundant mass of 70 roughly half the intensity of the base. The mass spectrum readily indicates anastrozole's molecular ion at 293 mass units. The fragmentation of nitrile groups are indicated by the loss of 27 from the molecular ion as well [4]. The FTIR spectrum is very detailed with a number of sharp bands in the fingerprint region that should enable relative ease

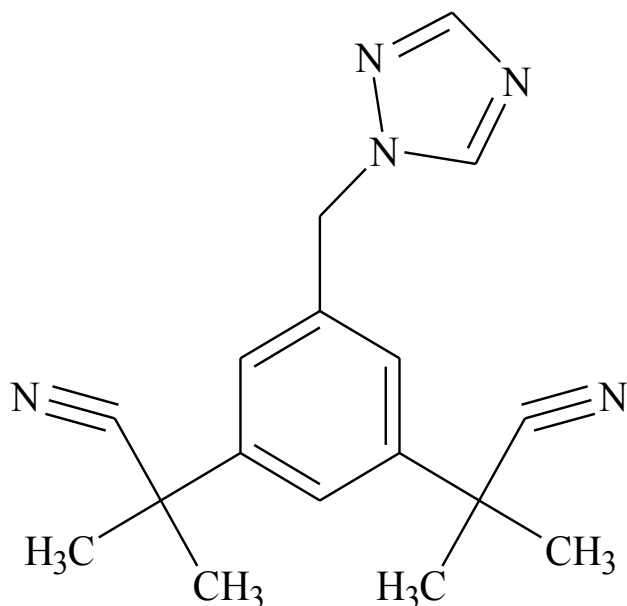


Figure 1 - Anastrozole.

Chemical Formula/CAS Number: C₁₇H₁₉N₅ / [120511-73-1]

Molecular Weight: 293.35 amu

Melting Point: 81-82°C [1]

Solubility: Deionized Water: sparingly soluble; Methanol, Acetone, Ethanol, and Tetrahydrofuran: freely soluble; Acetonitrile: very soluble [3]

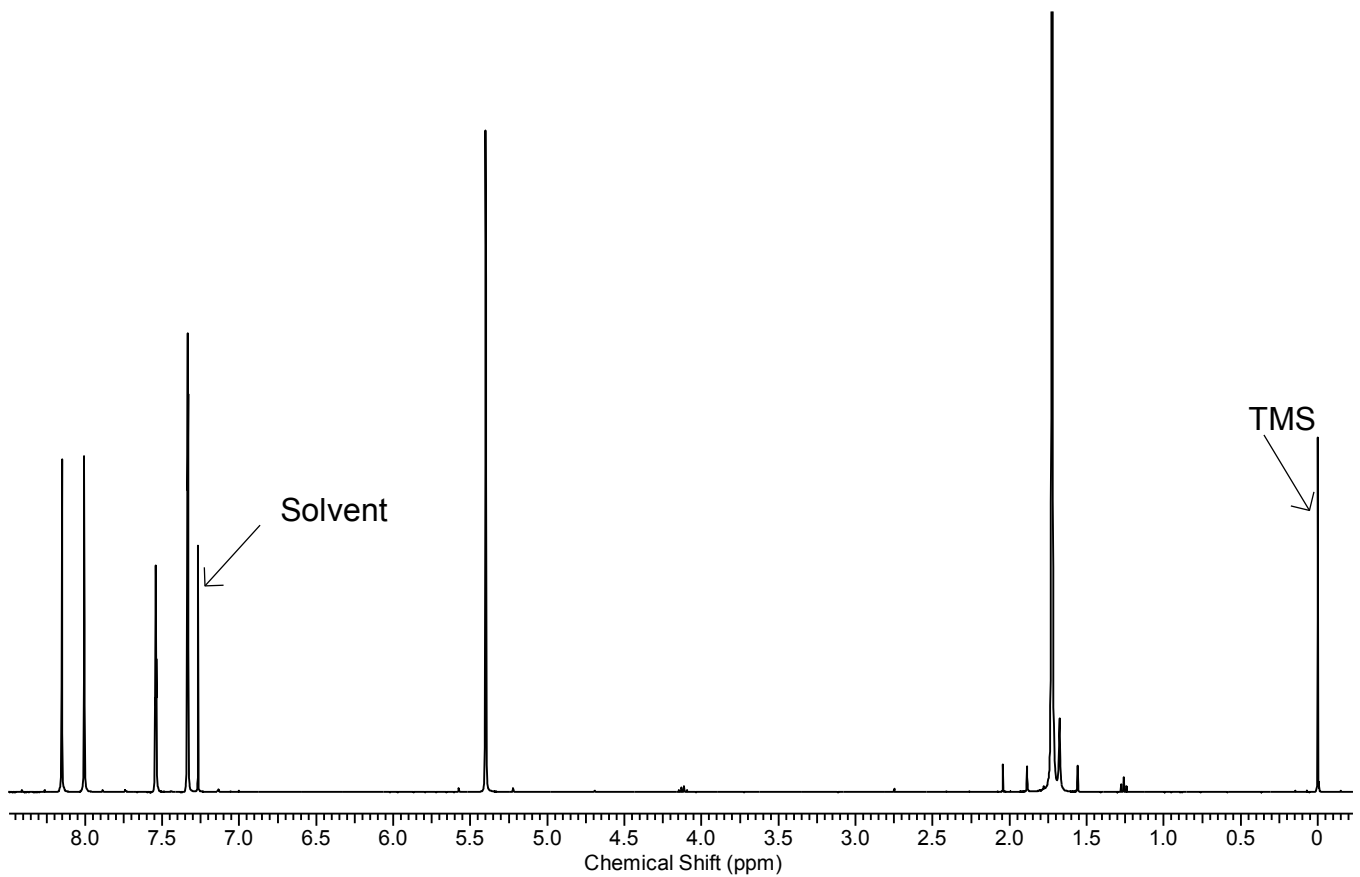


Figure 2 - ^1H NMR spectrum of anastrozole.

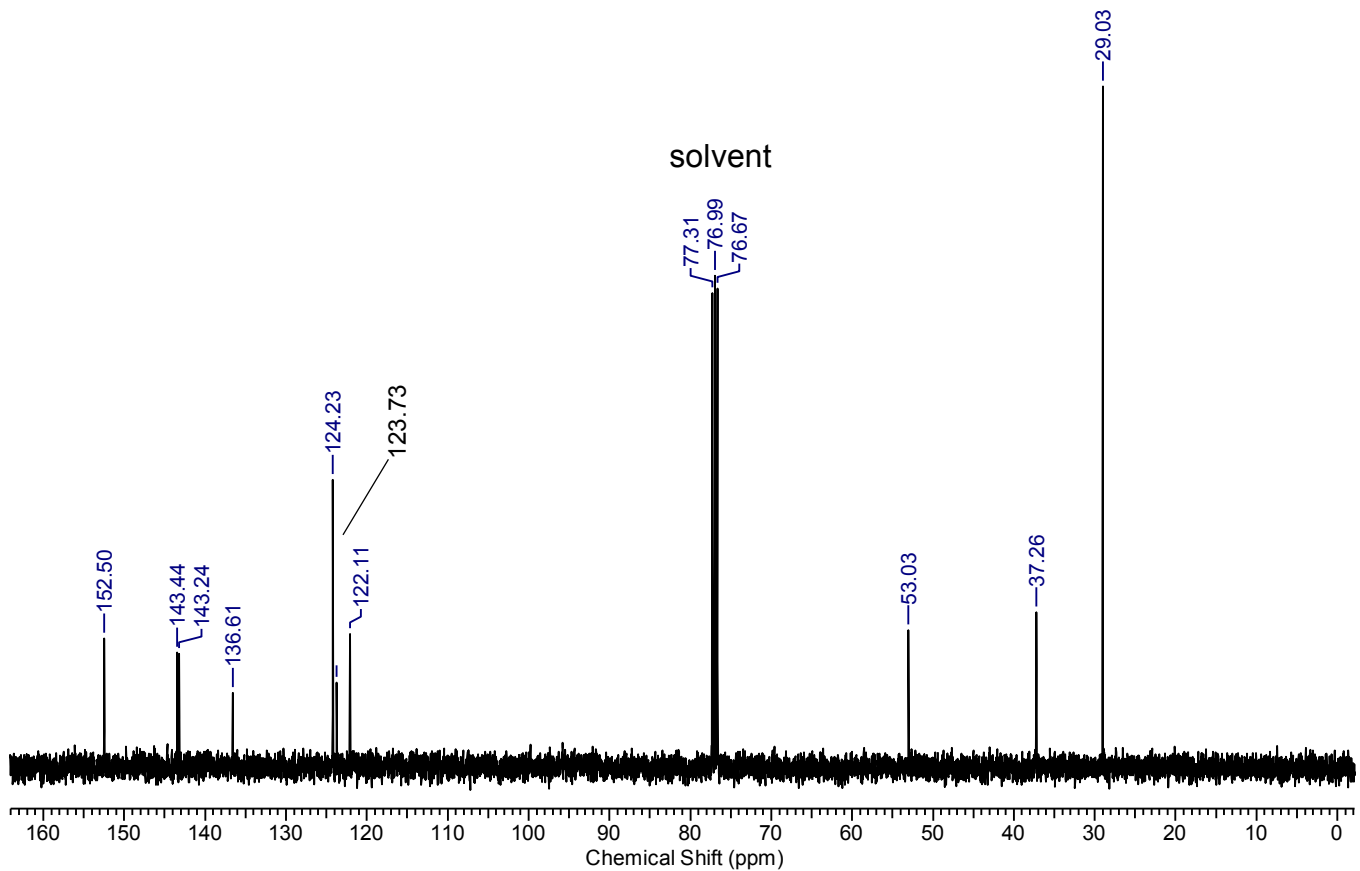


Figure 3 - ^{13}C NMR spectrum of anastrozole.

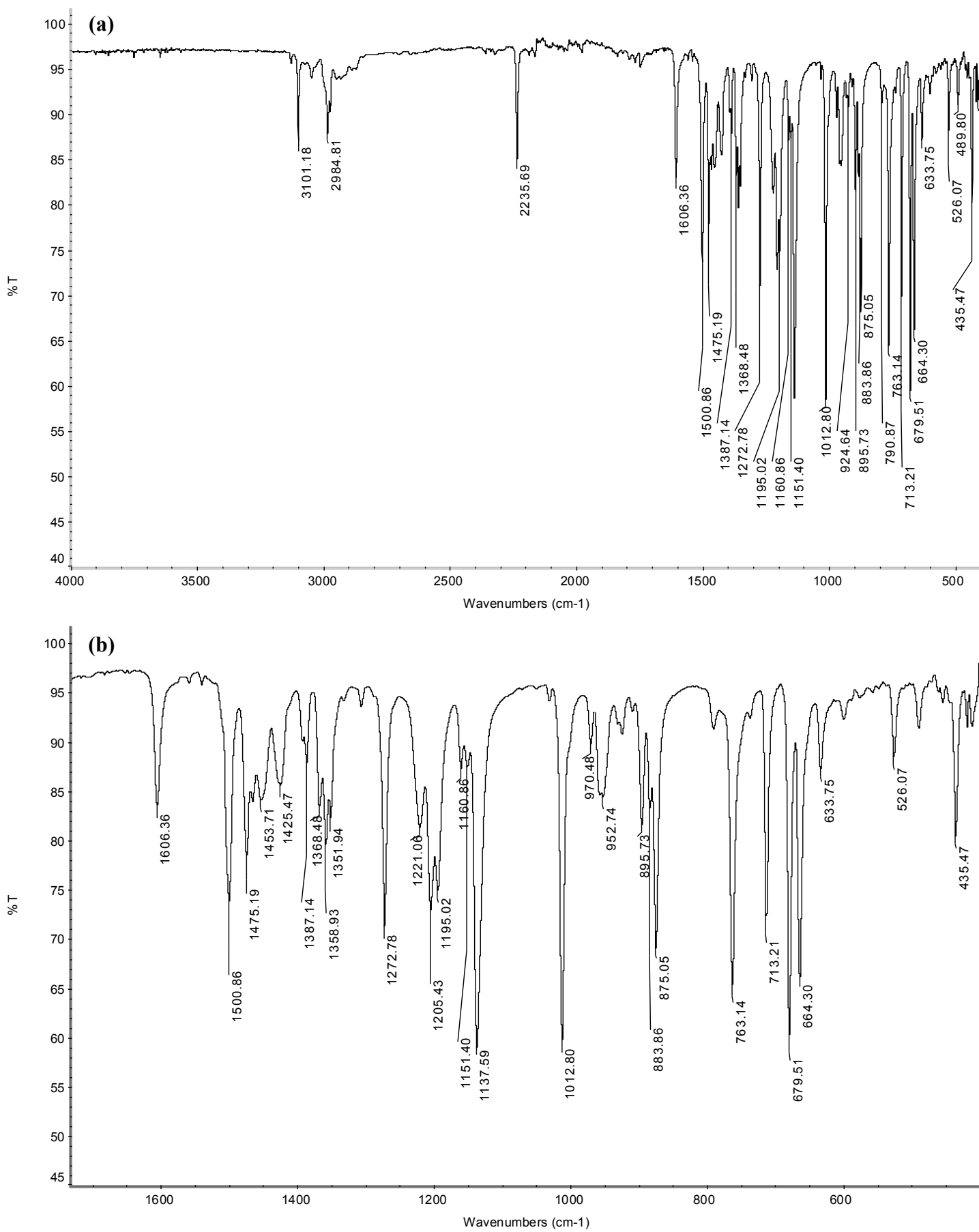


Figure 4 - FTIR of anastrozole: (a) full spectrum, (b) fingerprint region expanded.

Abundance

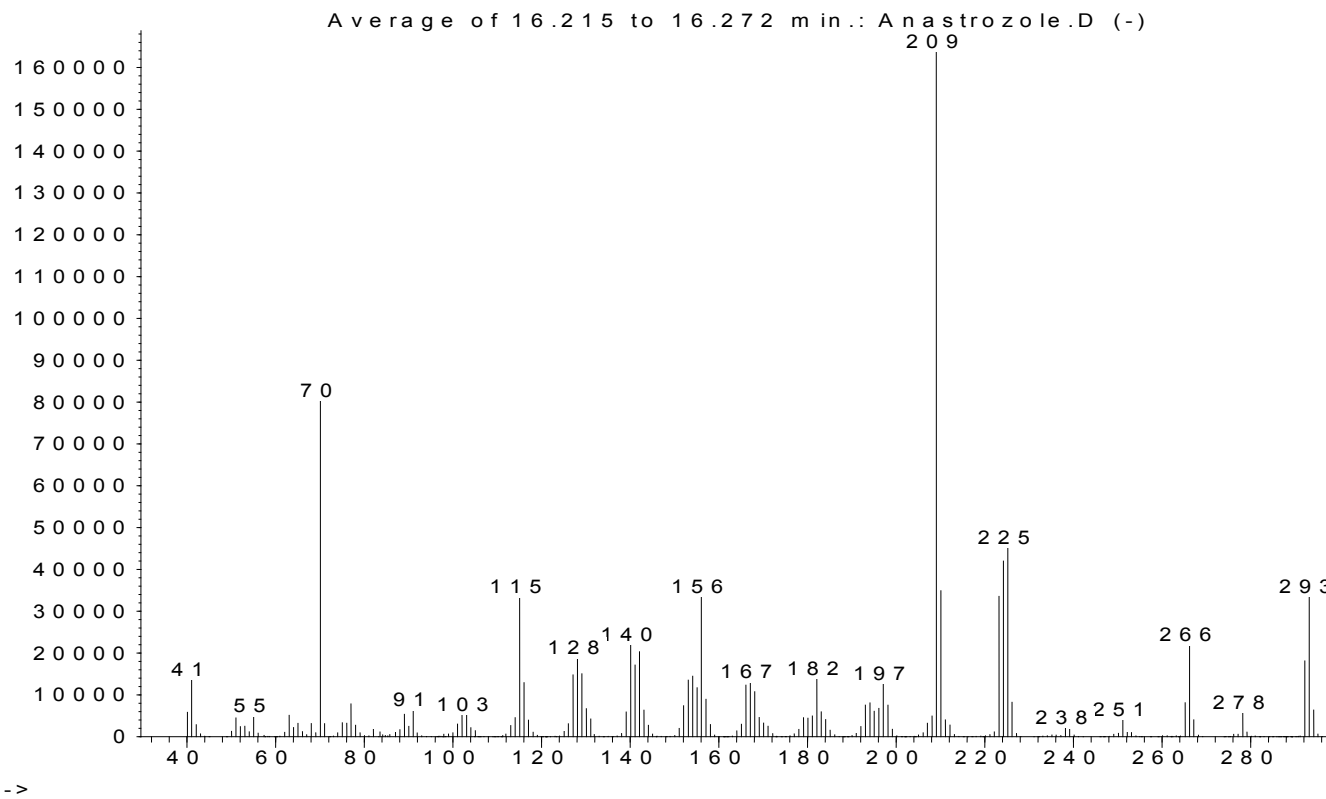


Figure 5 - Mass spectrum of anastrozole.

for identification and discrimination. The NMR spectra of anastrozole is abundant in both proton and carbon observations enabling confirmation of the structure as well.

References:

1. Merck Index. 12th ed. Merck: Whitehouse Station, NJ, 2007, 667.

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3. Physician's Desk Reference 61st ed. (2007), Montvale, NJ: Thompson PDR.
4. Smith RM. Understanding Mass Spectra., Wiley-Interscience, 2004, p. 122.