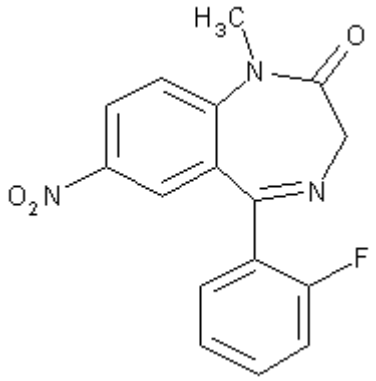
FLUNITRAZEPAM

Latest Revision: January 24, 2006



1. SYNONYMS

CFR:	Flunitrazepam
CAS #:	1622-62-4
Other Names:	5-(2-Fluorophenyl)-1,3-dihydro-1-methyl-7-nitro-2H-1,4-benzodiazepin-2-one Flunitrax Hipnosedon Hypnodorm Narcozep Noriel Ro 5-4200 Rohypnol Roipnol

2. CHEMICAL AND PHYSICAL DATA

2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Flunitrazepam	$C_{16}H_{12}FN_3O_3$	313.3	170

2.2. SOLUBILITY

Form	A	C	E	H	M	W
Flunitrazepam	S	PS	SS	SS	SS	I

A = acetone, C = chloroform, E = ether, H = hexane, M = methanol and W = water, VS = very soluble, FS = freely soluble, S = soluble, PS = sparingly soluble, SS = slightly soluble, VSS = very slightly soluble and I = insoluble

3. SCREENING TECHNIQUES

3.1. COLOR TESTS

REAGENT	COLOR PRODUCED
Walt's	Light green (green) solution
Janovsky	Violet

3.2. THIN LAYER CHROMATOGRAPHY

Visualization

Acidified iodoplatinate spray

COMPOUND	RELATIVE R_1 and COLOR	
	System TLC11	System TLC7
cocaine	0.8, purple	0.7, reddish brown
diazepam	1.0, red	1.0, reddish brown
flunitrazepam	1.0, light pink	1.0, reddish brown

3.3. GAS CHROMATOGRAPHY

Method FLU-GCS1

Instrument: Gas chromatograph operated in split mode with FID

Column: 100% dimethylpolysiloxane 30 m x 0.2 5mm x 0.25 µm

Carrier gas: Hydrogen at 1.9 mL/min

Temperatures: Injector: 265° C
Detector: 285°C
Oven program:
1) 120°C initial temperature for 1.0 min
2) Ramp to 270°C at 15°C/min
3) Hold final temperature for 4.0 min

Injection Parameters: Split Ratio = 25:1, 1 µL injected

Samples are to be dissolved in methylene chloride and filtered.

COMPOUND	RRT	COMPOUND	RRT
ephedrine	0.54	dextropropoxyphene	0.87
MDA	0.58	codeine	0.93
aspirin	0.58	morphine	0.94
MDMA	0.60	diazepam	0.94
guaifenesin	0.65	tetracosane	0.95
meprobamate	0.71	thorazine	0.97
methapyrilene	0.79	**flunitrazepam**	**1.00 (12.78 min)**
methocarbomal	0.80	heroin	1.01
cocaine	0.87		

3.4. HIGH PRESSURE LIQUID CHROMATOGRAPHY

Method FLU-LCS1

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5 µm ODS, 150 mm x 3.2 mm

Detector: UV, 210 nm

Flow: 1.0 mL/min

Injection Volume: 3.0 µL

Buffer: 4000 mL distilled water, 22.5 mL phosphoric acid adjust to pH 2.3 with triethylamine

Mobile Phase: Buffer/acetonitrile 50:50

Samples are to be dissolved in acetonitrile and filtered with a 0.45-micron filter.

COMPOUND	RRT	COMPOUND	RRT
flunitrazepam	**1.00 (6.20 min)**	diazepam	1.36

4. SEPARATION TECHNIQUE

Flunitrazepam is most often distributed in tablet form and may be isolated from tablet material by a chloroform, ether, or methanol wash.

Flunitrazepam has a dissociation constant (pK_a) of 1.8, and may be extracted from an aqueous alkaline solution using organic solvents.

5. QUANTITATIVE PROCEDURES

5.1. GAS CHROMATOGRAPHY

Method FLU-GCQ1

Internal Standard Stock Solution:
0.4 mg/mL tetracosane in methylene chloride.

Standard Solution Preparation:
Accurately weigh and prepare a standard solution of flunitrazepam at approximately 1.0 mg/mL using above internal standard stock solution.

Sample Preparation:
Accurately weigh an amount of sample into a volumetric flask and dilute with internal standard stock solution. If necessary, dilute the sample so the final concentration approximates the standard concentration.

Instrument: Gas chromatograph operated in split mode with FID

Column: 5% diphenyl/95% methyl siloxane 30 m x 0.25 µm film thickness

Carrier gas: Hydrogen at 3.5 mL/min

Temperatures: Injector: 285°C
Detector: 285°C

Oven program: 280°C isothermal

Injection Parameters: Split Ratio = 20:1, 2 µL injected

Typical Retention Time: Flunitrazepam: 4.0 min
Tetracosane: 1.9 min

Linear Range: 0.9 - 3.0 mg/mL

Repeatability: RSD less than 0.1%

Correlation Coefficient: 0.999

Accuracy: Error less than 1.3%

COMPOUND	RRT	COMPOUND	RRT
lorazepam	0.622	bromazepam	1.01
diazepam	0.768	prazepam	1.05
quazepam	0.776	nitrazepam	1.27
flunitrazepam	**1.00 (4.0 min)**	clonazepam	1.47

5.2. CAPILLARY ELECTROPHORESIS

Method FLU-CEQ1

Internal Standard Stock Solution:
0.2 mg/mL tetracaine in 1.0 N HCl.

Standard Solution Preparation:
Accurately weigh and prepare a standard solution of flunitrazepam at approximately 0.3 mg/mL using above internal standard stock solution. To improve the solubility of flunitrazepam, sonicate for five to ten minutes to insure complete dissolution.

Sample Preparation:
Accurately weigh an amount of sample into a volumetric flask and dilute with internal standard stock solution. If necessary, dilute the sample so the final concentration approximates the standard concentration.

Mode: Free zone

Column: 48.5 cm x 50 µm fused silica capillary

Run Buffer:	50 mM sodium phosphate buffer, pH 2.5
Detector:	UV, 210 nm
Voltage:	27 kV
Temperature:	25°C air cooled
Injection:	1 s hydrodynamic
Run Time:	12 min
Rinse Time:	2 min
Linear Range:	0.10 - 1.05 mg/mL
Repeatability:	RSD less than 0.9%
Correlation Coefficient:	0.999
Accuracy:	Error less than 5%

6. QUALITATIVE DATA

6.1. ULTRAVIOLET SPECTROPHOTOMETRY

SOLVENT	MAXIMUM ABSORBANCE (NM)
Methanol	252

See spectra on the following pages for FT-IR, Mass Spectrometry, Nuclear Magnetic Resonance, and Vapor Phase IR.

7. REFERENCES

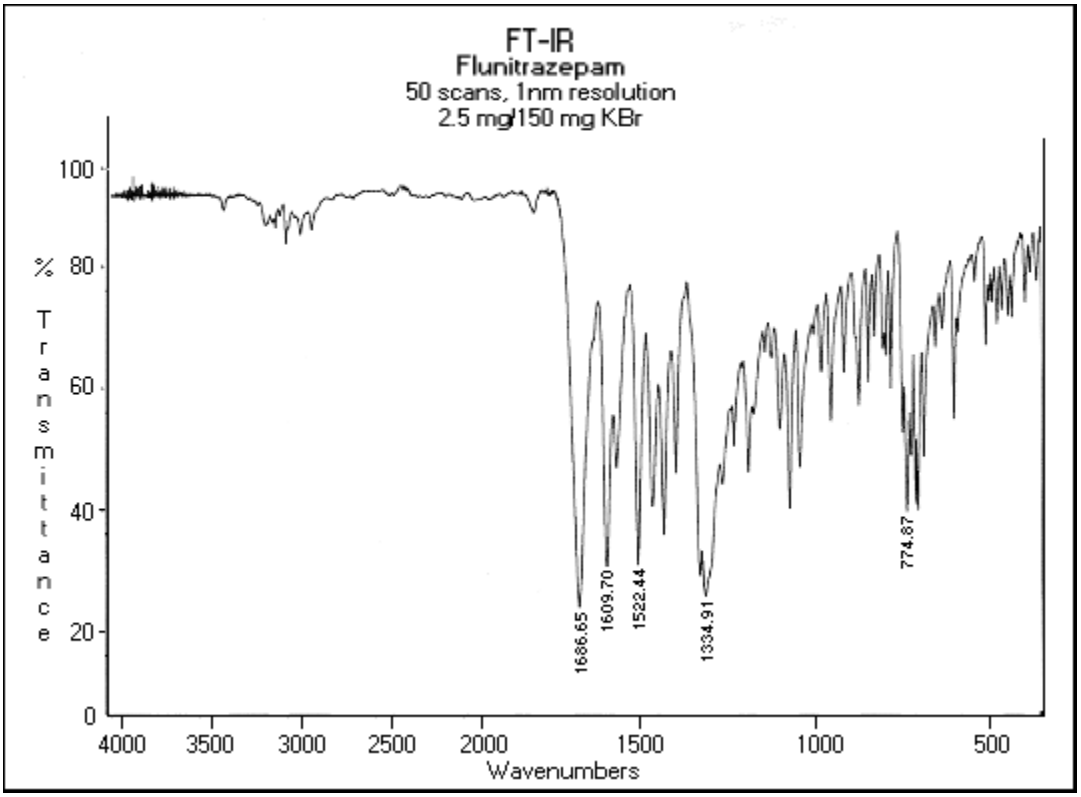
Clarke, E.G.C., *Isolation and Identification of Drugs, 2nd Edition*, The Pharmaceutical Press, 1986.

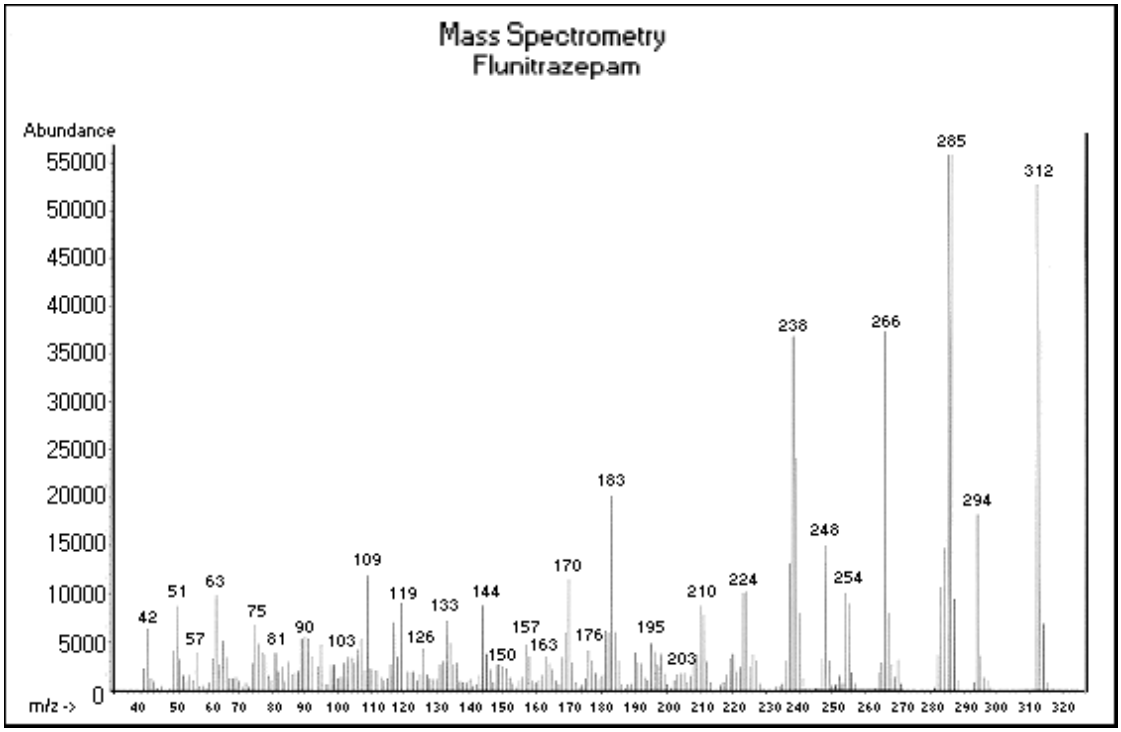
Budavari, S., *The Merck Index, 12th Edition*, Merck and Co., Inc., 1996, p. 702.

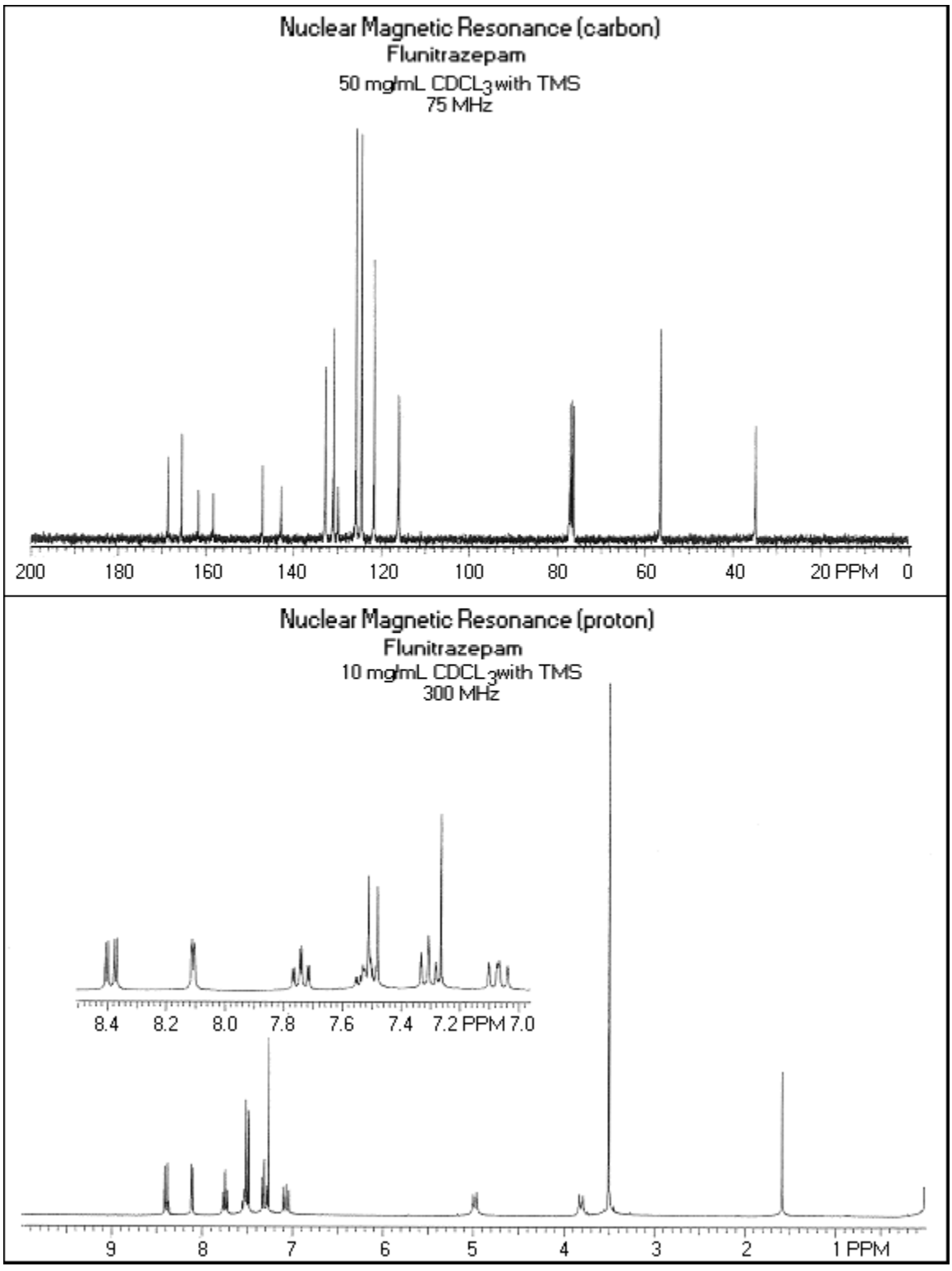
8. ADDITIONAL RESOURCES

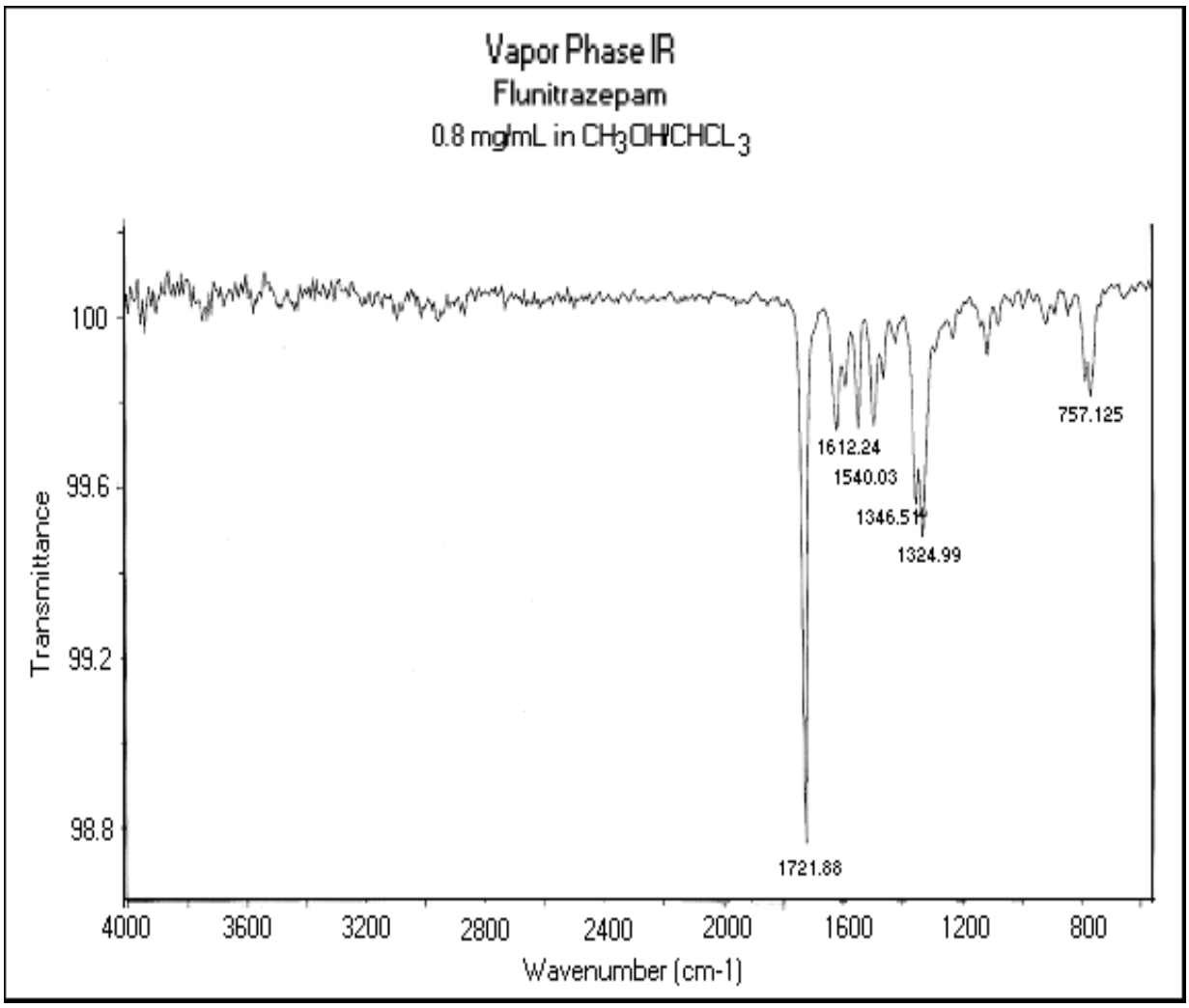
Forendex

Wikipedia


FT-IR
Flunitrazepam
50 scans, 1nm resolution
2.5 mg/150 mg KBr
% Transmittance
100
80
60
40
20
0
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers
1686.65
1609.70
1522.44
1334.91
774.87


Mass Spectrometry
Flunitrazepam
Abundance
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
m/z ->
42
51
63
57
75
81
90
103
109
119
126
133
144
150
157
163
170
176
183
195
203
210
224
238
248
254
266
285
294
312


Nuclear Magnetic Resonance (carbon)
Flunitrazepam
50 mg/mL CDCL3 with TMS
75 MHz
200
180
160
140
120
100
80
60
40
20 PPM
0
Nuclear Magnetic Resonance (proton)
Flunitrazepam
10 mg/mL CDCL3 with TMS
300 MHz
8.4
8.2
8.0
7.8
7.6
7.4
7.2 PPM
7.0
9
8
7
6
5
4
3
2
1 PPM


Vapor Phase IR
Flunitrazepam
0.8 mg/mL in CH3OH/CHCL3
Transmittance
100
99.6
99.2
98.8
1721.88
1612.24
1540.03
1346.51
1324.99
757.125
4000
3600
3200
2800
2400
2000
1600
1200
800
Wavenumber (cm-1)