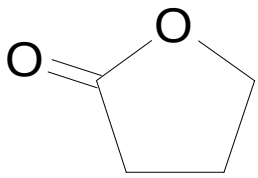

gamma-butyrolactone

1. SYNONYMS

CFR:	*Gamma*-butyrolactone
CAS #:	96-48-0
Other Names:	GBL Butyrolactone *Gamma*-hydroxybutyric acid lactone 3-Hydroxybutyric acid lactone 4-Hydroxybutanoic acid lactone 1,2-Butanolide 1,4-Butanolide Dihydro-2(3H)-furanone

2. CHEMICAL AND PHYSICAL DATA

Gamma-butyrolactone (GBL) is a precursor in the manufacture of *gamma*-hydroxybutyric acid (GHB). In aqueous solution, GBL undergoes a hydrolysis reaction and exists in equilibrium with GHB. This solution chemistry is strongly dependent upon solution pH, as well as other factors, and is discussed in detail in the GHB monograph.

***2.1.* CHEMICAL DATA**

Form	Chemical Formula	Molecular Weight (g/mole)	Melting Point (°C)
GBL	$C_4H_6O_2$	86.09	-42

***2.2.* SOLUBILITY**

Form	A	C	E	H	M	W
GBL	VS	VS	VS	SS	VS	VS

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

TEST	COLOR PRODUCED
Cobalt Thiocyanate	Blue Lake

Relatively pure samples of GBL produce a blue phase below the red reagent solution, which slowly dissipates as GBL dissolves into solution. Other organic liquids (e.g., ethanol, acetone) may also produce a blue color, but appear differently as the entire solution develops blue. 1,4-Butanediol, as well as aqueous solutions of GBL, fail to produce a color change. An alternative procedure entailing a toluene extraction has been developed for aqueous solutions of GBL (Morris, 1999), but may be difficult to interpret. Recently the hydroxamic acid test has been reported as an effective presumptive test for GBL with less false positives (Morris, 2005).

3.2. CRYSTAL TESTS

There are no reliable crystal tests currently available for GBL.

3.3. GAS CHROMATOGRAPHY

Method GBL-GCS1

GBL is soluble in either methylene chloride or chloroform, and readily extracts from aqueous solutions for gas chromatographic analysis (see Section 4, Separation Techniques).

Sample Preparation:
Dissolve or extract the sample into methylene chloride or chloroform. Dry the extract solutions over a column of drying agent.

Instrument:	Gas chromatograph with electron-impact mass selective detector
Column:	100% polydimethylsiloxane, 12.0 m x 0.20 mm x 0.33µm film thickness
Carrier gas:	Helium at 1.0 mL/min
Temperatures:	Injector: 250°C Transfer line: 280°C Oven program: 70°C initial temperature for 1.20 min Ramp to 280°C at 15°C/min Hold final temperature for 5.00 min
Injection parameters:	Split Ratio = 50:1, 1 µL injected

COMPOUND	RRT
GBL	**1.00**
GHB·TMS_2	3.00

3.4. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Method GBL-LCS1

Sample Preparation:
Dissolve or dilute (if necessary) in mobile phase and filter (0.45 µm).

Instrument: High performance liquid chromatograph with diode array detector

Column: 5 µm ODS Hypersil, 4.6 mm x 100 mm

Detector: UV, 215 nm

Flow: 0.75 mL/min

Injection Volume: 5 µL

Buffer: 10 mM NaH_2PO_4 adjusted to pH 3 with H_3PO_4

Mobile Phase: Buffer:methanol (80:20)

COMPOUND	RRT
GHB	0.92
GBL	1.00

Method GBL-LCS2

GBL may be identified in aqueous solutions by LC-MS employing an ammonium acetate buffer (see the electrospray mass spectrum of GBL). The electrospray (+) mass spectrum exhibits one prominent peak due to an ammonium ion complex with GBL (104 amu), and a weaker peak for a protonated GBL species (87 amu). The spectrum may also display an artifact peak for the sodium ion complex with GBL (109 amu) if a sodium salt is present in the sample.

Standard Solution Preparation:
Prepare the standard solution of GBL (5-10 mg per mL) in methanol.

Instrument: High performance liquid chromatograph with atmospheric pressure ionization electrospray mass selective detector

Column: 5 µm Aqua C18, 100 mm x 4.6 mm

Detector: Scan mode, positive ion
Capillary voltage: 3000 V
Fragmentor: 30 eV
Nebulizer pressure: 60 psig
Drying gas flow: 13.0 L/min
Drying gas temperature: 350°C

Flow: 1.500 mL/min

Injection Volume: 5 μL

Buffer: 20 mM CH_3COONH_4 (~ pH 7.5)

Mobile Phase: 100% Buffer

Typical Retention Times: GHB: 2.00 min
1,4-Butanediol: 5.44 min
GBL: 6.46 min

COMPOUND	RRT
GHB	0.310
1,4-Butanediol	0.842
GBL	1.000

3.5. NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

Method GBL-NMRS1

Relatively pure samples of GBL or GBL isolated by extraction may be prepared in deuterium oxide (D_2O) or deuterated chloroform ($CDCl_3$). Simple aqueous solutions may be diluted in D_2O.

Sample Preparation:
Dissolve relatively pure samples of GBL in D_2O with the internal reference standard 2,2-dimethyl-2-silylpentane-5-sulfonate (DDS) or in $CDCl_3$ with the internal reference standard tetramethylsilane (TMS). Dilute aqueous solutions in D_2O with DDS. Filter all preparation solutions before analysis.

Instrument: Nuclear magnetic resonance spectrometer

Probe: 5-mm dual channel, room temperature

Parameters: ^1H NMR:
Observation frequency: 300 MHz
Pulse angle: 30^o
Acquisition time: 1.998 s
Spectral window: 4500 Hz
Filter bandwidth: 2250 Hz

Delay: 0 - 1 s
Frequency offset: 0 Hz
Number of transients: 16

^{13}C NMR:
Observation frequency: 75 MHz
Pulse angle: 45^{o}
Acquisition time: 1.706 s
Spectral window: 18761.7 Hz
Filter bandwidth: 9500 Hz
Delay: 0 s
Frequency offset: 0 Hz
Number of transients: 512 (minimum)
Proton decoupler: on
Decoupler modulation frequency: 3233 Hz

4. SEPARATION TECHNIQUES

Relatively pure samples of GBL may be examined directly by infrared spectroscopy for the identification of GBL. GBL can be separated from aqueous solutions by a liquid-liquid extraction using methylene chloride or chloroform. Since aqueous solutions containing GBL may also contain GHB, aqueous samples should also be examined for the presence of GHB (see GHB Monograph).

GBL is efficiently extracted from most aqueous solutions with methylene chloride (the partition coefficient is approximately 4.5). The extraction effectively separates GBL from any GHB (Chappell, Meyn and Ngim, 2004) since the free acid and common dissolved salts of GHB remain in the original aqueous solution due to their high polarity and water solubility. Following the extraction, the extract solution is dried over a column of anhydrous sodium sulfate (or other suitable drying agent) to remove residual water. The extract solution may be examined by GC-MS to identify GBL. Alternatively, a relatively pure residue of GBL can be recovered by evaporation of the solvent. A clear, oily liquid will remain, which may be examined neat by infrared spectroscopy (see transmission and attenuated total reflection infrared spectra of GBL).

5. QUANTITATIVE PROCEDURES

Relatively pure liquid samples of GBL may be quantified by gas chromatography and reported as a purity. Aqueous solutions of GBL should be quantified by liquid chromatography and reported as a concentration.

5.1. GAS CHROMATOGRAPHY

Method GBL-GCQ1

Standard Solution Preparation:
Prepare a standard solution of GBL in methylene chloride or chloroform at approximately 1.0 mg per mL.

Internal Standard Solution Preparation:
Prepare a solution of *n*-decane in methylene chloride or chloroform at approximately 0.7 mg per mL.

Sample Preparation:

Accurately weigh an amount of sample into a volumetric flask and dilute with methylene chloride or chloroform (same solvent as standard and internal standard solutions). If necessary, dilute the sample to a final concentration approximately equal to that of the standard (and within the linear range of the method).

Instrument: Gas chromatograph with flame-ionization detector

Column: 100% polydimethylsiloxane, 15.0 m x 0.20 mm x 0.33µm film thickness

Carrier gas: Helium at 1.0 mL/min

Temperatures: Injector: 180°C
Detector: 270°C
Oven program:
80°C initial temperature for 1.50 min
Ramp to 90°C at 15°C/min
Hold final temperature for 0.80 min

Injection parameters: Split Ratio = 30:1, µL injected

Typical Retention Time: GBL: 1.30 min
n-Decane: 2.44 min

Linear Range: 0.25 – 2.04 mg/mL

Repeatability: RSD less than 3.0%

Correlation Coefficient: 0.9999

Accuracy: Error less than 5.0%

COMPOUND	RRT
GBL	1.00
n-decane (ISDT)	1.88

5.2. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Method GBL-LCQ1

Standard Solution Preparation:
Prepare a standard solution of GBL in water at approximately 1.0 mg per mL.

Sample Preparation:
Accurately weigh or pipette an amount of sample into a volumetric flask and dilute with water. If necessary, dilute the sample to a final concentration approximately equal to that of the standard (and within the linear range of the method). Filter the sample (0.45 µm).

Instrument:	High performance liquid chromatograph with diode array detector
Column:	5 μm Aqua C18, 100 mm x 4.6 mm; 25°C
Detector:	UV, 195 nm (450 nm reference)
Flow:	1.0 mL/min
Injection Volume:	2 μL
Buffer:	25 mM KH_2PO_4, pH 6.5
Mobile Phase:	100% Buffer
Typical Retention Time:	GHB: 3.30 min GBL: 8.90 min
Linear Range:	0.32 - 5.04 mg/mL
Repeatability:	RSD less than 3.0%
Correlation Coefficient:	0.9998
Accuracy:	Error less than 5.0%

COMPOUND	**RRT**
GHB	0.371
GBL	1.000

6. QUALITATIVE DATA

See spectra on the following pages for Infrared Spectroscopy, Mass Spectrometry, and Nuclear Magnetic Resonance.

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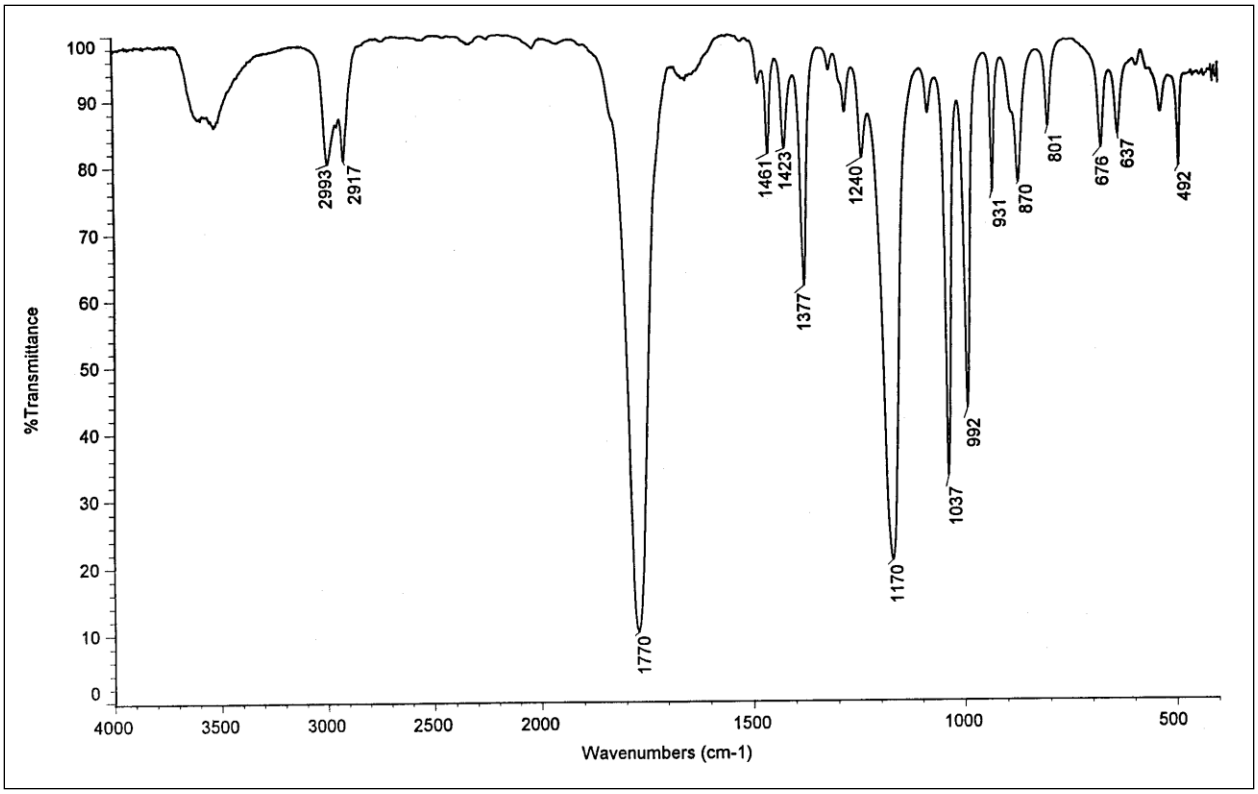
Vose, J., Tighe, T., Schwartz, M. and Buel, E. “Detection of *Gamma*-Butyrolactone (GBL) as a Natural Component of Wine”. *J. Forensic Sci.*, 2001, Vol. 46, No. 5, pp. 1164-7.

8. ADDITIONAL RESOURCES

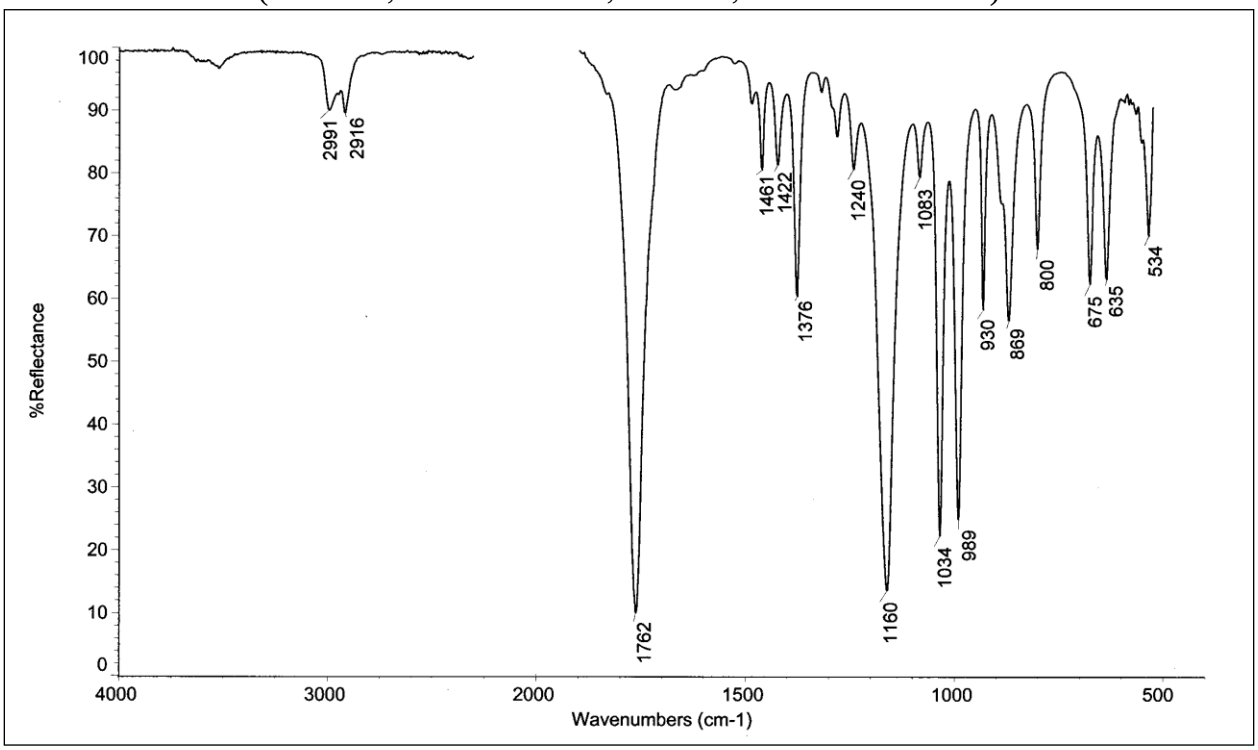
Forendex

Wikipedia

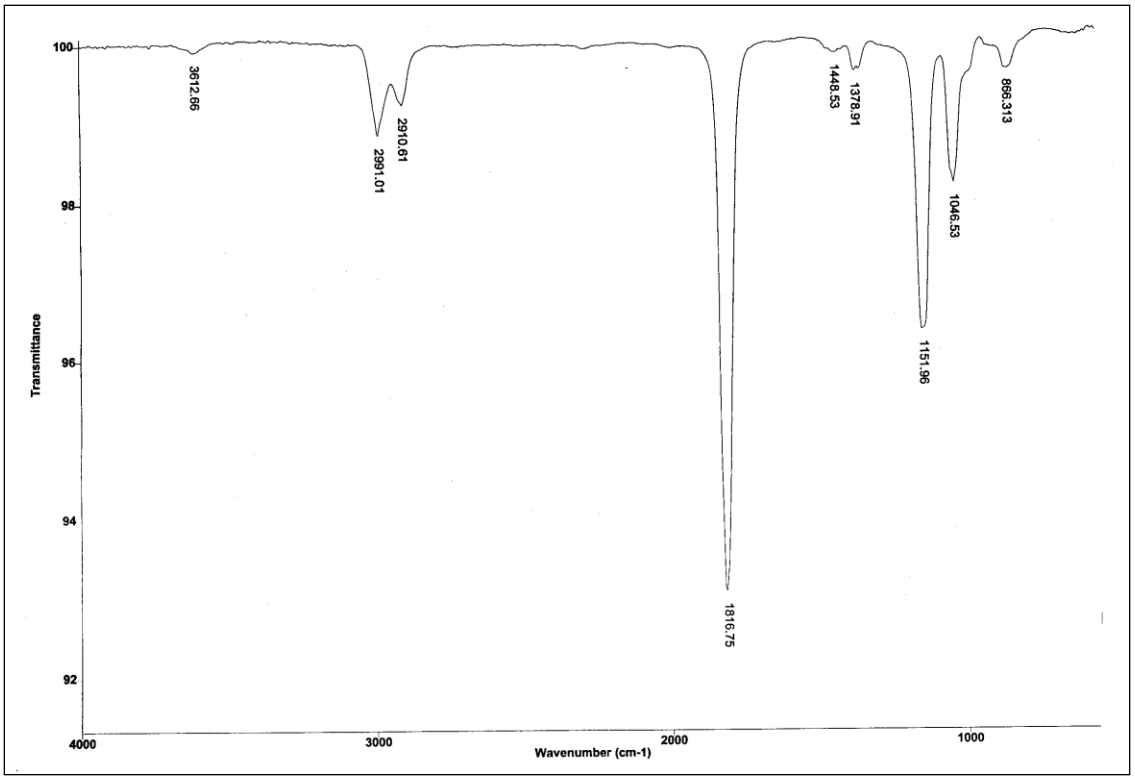
Transmission Infrared Spectroscopy: *Gamma*-Butyrolactone, (sample neat between KBr disks)
16 scans, 4.0 cm^{-1} resolution



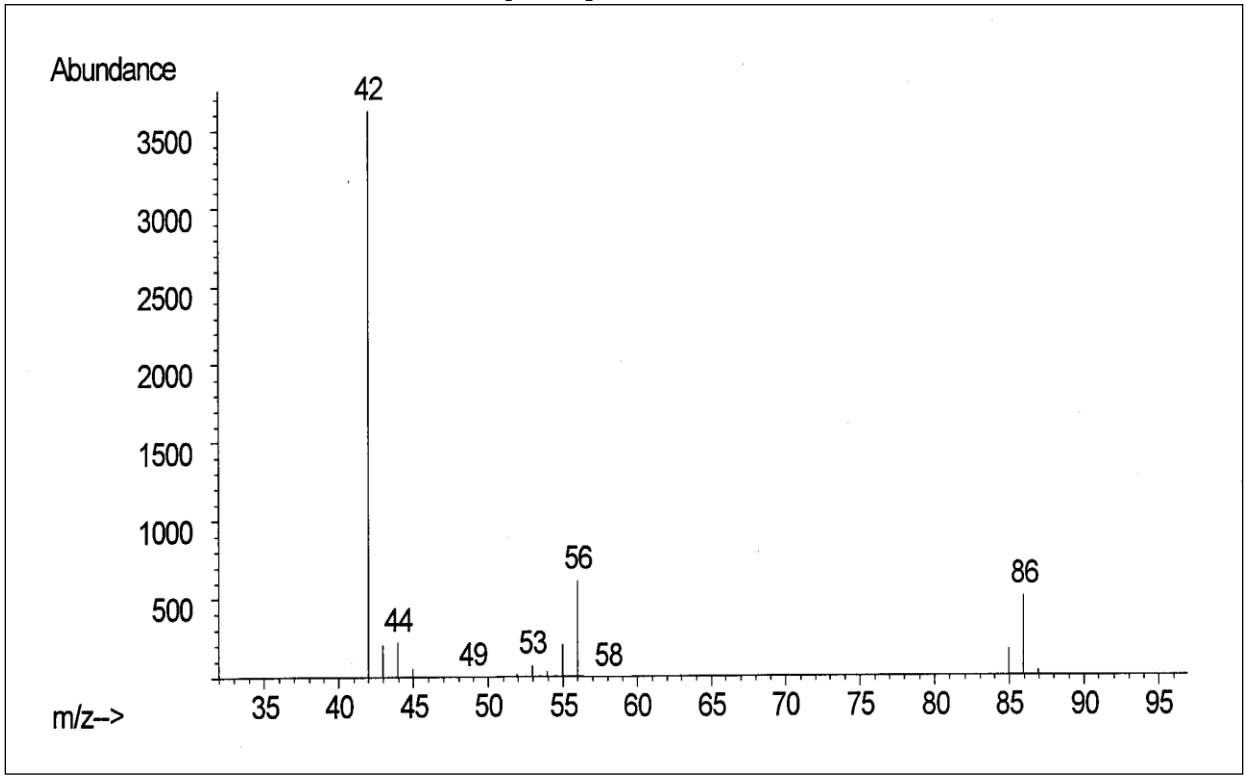
IR (ATR): *Gamma*-Butyrolactone
(3-bounce, diamond device, 16 scans, 4.0 cm^{-1} resolution)



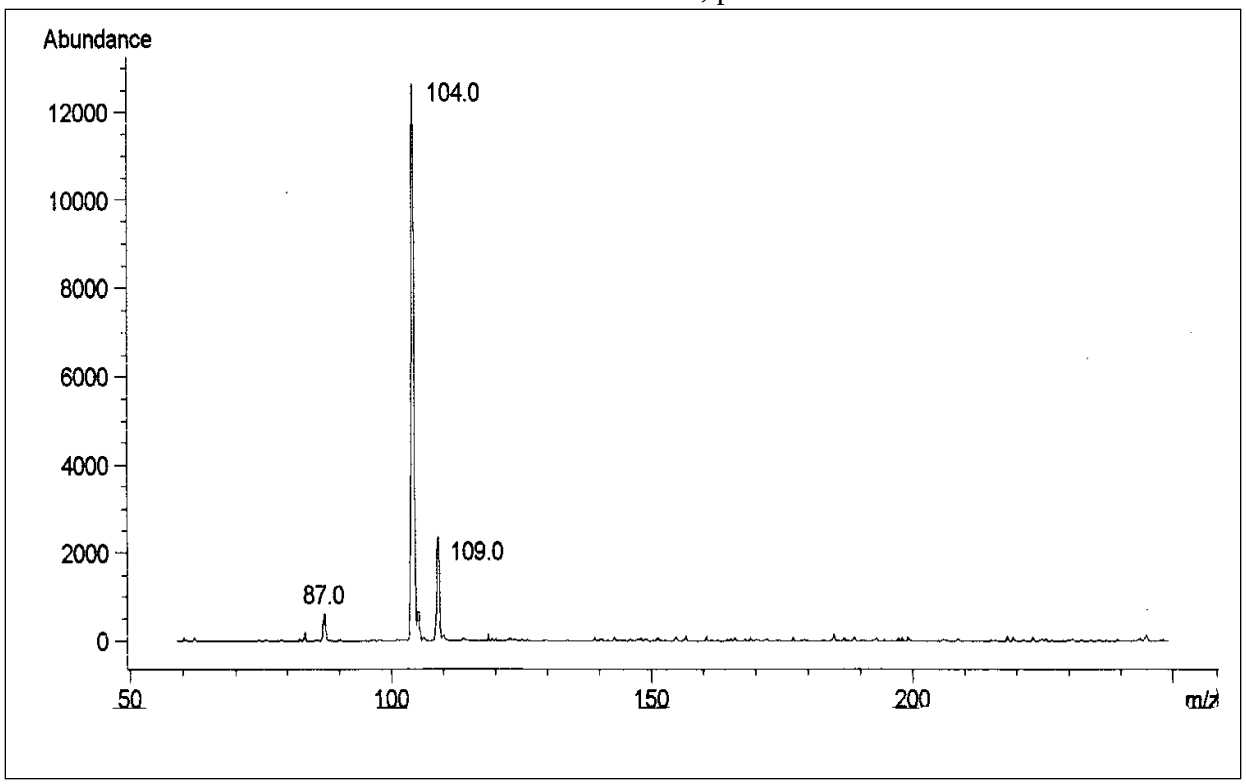
IR (Transmission Vapor): *Gamma*-Butyrolactone
8.0 cm^{-1} resolution



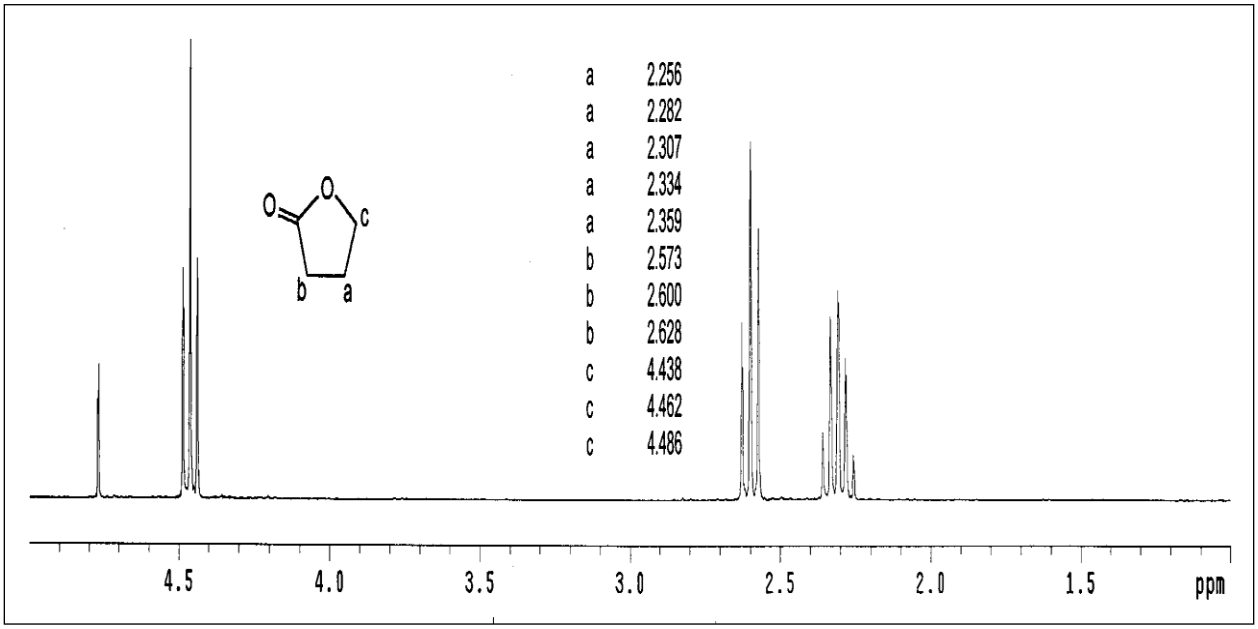
Mass Spectrometry (EI): *Gamma*-Butyrolactone
quadrupole detector



Mass Spectrometry (Electrospray (+)): *Gamma*-Butyrolactone
0.02 M ammonium acetate, pH 7.5 buffer



Nuclear Magnetic Resonance (^{1}H): *Gamma*-Butyrolactone 300 MHz
D_2O with DDS



Nuclear Magnetic Resonance (^{13}C): *Gamma*-Butyrolactone 75 MHz
D_2O with DDS