



B18 A NMR Study of the Stability of Gamma-Butyrolactone (GBL) in Water

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The goals of this presentation are to present to the forensic community the results of a study concerning the rate of GBL hydrolysis to gamma-hydroxybutyric acid (GHB) over time and as a function of initial GBL concentration (5% to 90%). Attendees will gain an appreciation of the value of ^1H NMR for studying the conversion of GBL to GHB over time.

The increased use of GBL as an alternative to salts of the club drug gamma-hydroxybutyric acid (GHB) and the subsequent increase in sample submissions to forensic laboratories for analysis has required the forensic chemist to use a variety of analytical tools for proper identification. The most useful technique to identify these compounds and to observe their chemical interconversion, especially in liquid samples, appears to be ^1H NMR. Most importantly, ^1H NMR is minimally invasive with respect to the sample matrix which allows for direct observation of the chemistry without chemically altering the compounds or promoting interconversion.

The ^1H NMR analysis of a recent submission of the product "Verve 5.0" revealed that the GBL partially hydrolyzed into GHB (the free acid). Upon further investigation, this process of hydrolysis was confirmed when an authenticated pure standard sample of GBL (several months old) used for identification of GBL was also found to contain GHB free acid, the hydrolysis product of GBL. To better understand this instability of GBL in aqueous media, the hydrolysis of GBL to GHB in deuterium oxide was studied by ^1H NMR over a one year time period. During this same time, the pH of the GBL solutions was also measured and compared to the conversion data. The rate of hydrolysis was revealed to be a function of and inversely proportional to the initial GBL concentration. At lower GBL concentrations, measurable hydrolysis occurs within days. At higher GBL concentrations, measurable hydrolysis takes several months to occur. This hydrolysis is accompanied by a concomitant decrease in pH; however, there does appear to be an induction period during which the pH decreases without any measurable GHB formation. This induction period occurs from neutral to approximately pH 4-5. The pK_a of GHB stated in the literature is 4.71, which is within this pH induction range. The chemical shifts of GBL and GHB signals observed in the ^1H NMR spectra change as a function of initial GBL concentration, but not as a function of pH. At lower GBL concentrations, equilibrium is reached at a pH of 2-3 and approximately 25% hydrolysis. Quantitative data were calculated from integration of the NMR signals. High Performance Liquid Chromatography (HPLC) was used to confirm the presence of multiple chemical species. The conversion of GBL to GHB was measured by simple integration of the areas from the methylene triplets furthest downfield (directly bonded to oxygen). All signals appear at unique chemical shifts and all splitting follows simple first order principles. The rate of hydrolysis of GBL is a function of the initial GBL concentration and the extent of hydrolysis can be correlated with the concomitant decrease in pH. ^1H NMR has proven to be an ideal technique to observe this chemical process.

GBL, GHB Free Acid, NMR Spectrometry