Conformational analysis of glycerol using ^{1}H NMR spectroscopy

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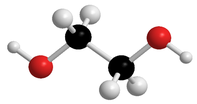
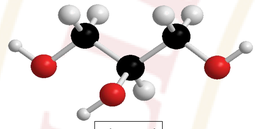
Abstract

The conformational preferences of 1,2,3-propanetriol (glycerol) in a variety of solvents were determined through the use of vicinal ^{1}H-^{1}H NMR coupling constants. The study of glycerol is of interest because of the unexpectedly high ~80%:20% gauche:anti conformational preference observed for the vicinal hydroxyl groups in the related compound 1,2-ethanediol (ethylene glycol). This high gauche hydroxyl preference in ethylene glycol has been attributed to hyperconjugative $\sigma_{C\text{-}H} \rightarrow \sigma^*_{C\text{-}OH}$ interactions. A similar gauche hydroxyl preference may be expected in glycerol, however its greater rotational freedom may also allow for intramolecular hydrogen bonding between the C-1 and C-3 hydroxyl groups. Due to uncertainty in the stereospecific assignment of $J_{1,3}$ and $J_{2,3}$, this research currently yields two contrasting sets of results for the nine conformations of glycerol. The correct set of results will be determined through the isotopic synthesis of *rac*-(2*SR*,3*RS*)-1,1,3-trideuterio-1,2,3-propanetriol, and the observation of only H-1, H-3, and $J_{1,3}$ (in progress).

Ethylene Glycol versus Glycerol

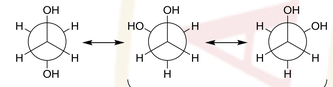


ethylene glycol



glycerol

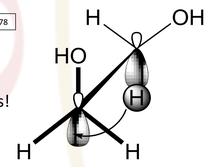
The vicinal OH groups of ethylene glycol exhibit a surprisingly high % gauche.



12-20 % anti OH | 80-88% gauche OH

Pachler, K. G. R.; Wessels, P. L. *J. Mol. Struct.* **1970**, *6*, 471-478

Why? Intramolecular hydrogen bonding – No!
Hyperconjugation between $\sigma_{C\text{-}H} \rightarrow \sigma^*_{C\text{-}OH}$ – Yes!

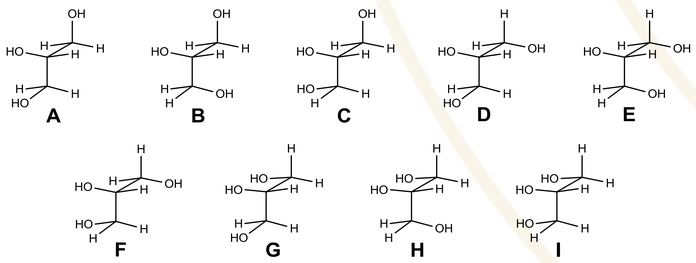


Patterson, K. A.; Stein, R. S.; Drake, M. D.; Roberts, J. D. *Magn. Reson. Chem.* **2005**, *43*, 225-230

Hyperconjugation is a donation of electron density from an electron rich orbital into a coplanar electron deficient orbital. The result is stabilization.

Will glycerol, with its three vicinal OH groups, exhibit similar conformational preferences as ethylene glycol?

The Nine Conformations of Glycerol

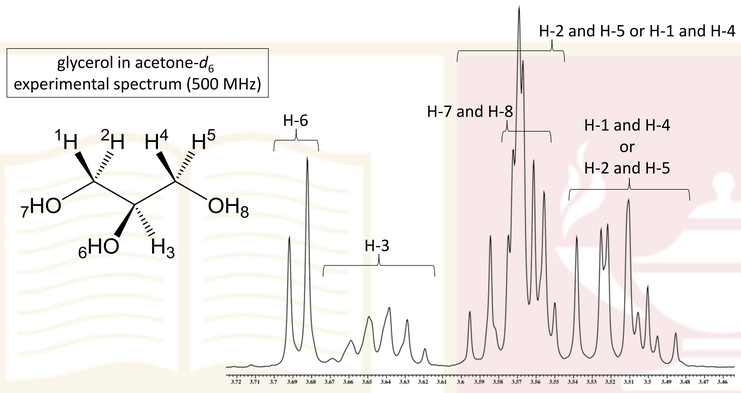


Potential Conformational Influences in Glycerol

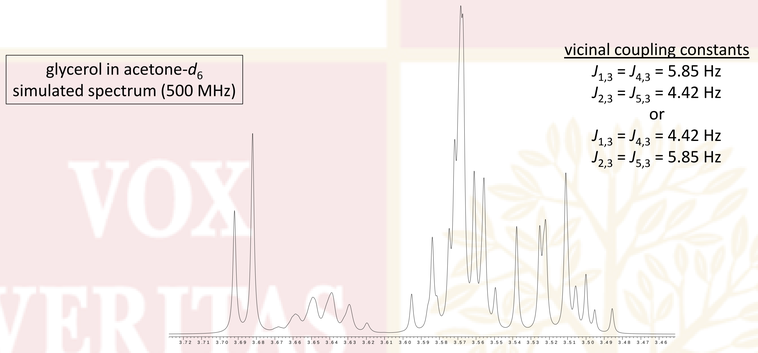
1. Steric bulk of vicinal substituents – not expected to be important.
2. Coulombic repulsion of lone pair electrons – would favor **E**
3. Intramolecular hydrogen bonding between vicinal OH groups – would favor **A**, **C**, **G**, **I**
4. Role of solvent – may affect potential intramolecular hydrogen bonding.
   – polarity of solvent may affect conformer polarity.
5. Hyperconjugation: preference for gauche OH groups expected – would favor **A**, **C**, **G**, **I**

Method

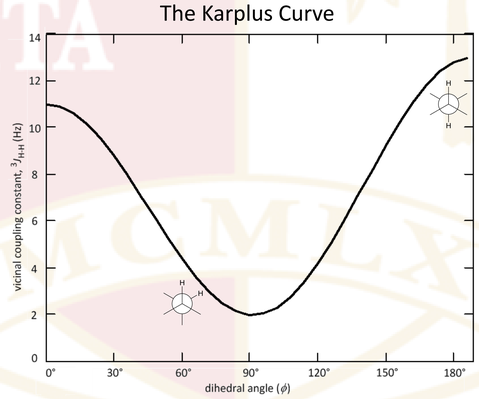
1. ^{1}H NMR spectra of glycerol in a variety of deuterated solvents are acquired using a 500 MHz NMR spectrometer.



2. The experimental NMR spectrum is then duplicated on a computer using gNMR 4.1 NMR simulation software.



3. The vicinal ^{1}H-^{1}H coupling constants extracted from gNMR 4.1 are then used to calculate conformational percentages by way of a Karplus-like relationship between the coupling constants and the dihedral angle.



- Treatment of the observed $^3J_{H\text{-}H}$ constants as a weighted average of calculated $^3J_{H\text{-}H}$ constants, for a particular staggered dihedral angle, allows us to convert the observed $^3J_{H\text{-}H}$ values into conformer percentages.
- Instead of the Karplus equation, we will use the semi-empirical Altona equation which allows for more specificity in the substituents present and the solvent used.

Altona equation: $$^3J_{H-H} = 14.63\cos^2(\phi) - 0.78\cos(\phi) + 0.60 + \sum_i \lambda_i \times \left\{0.34 - 2.31\cos^2\left[s_i(\phi) + 18.4|\lambda_i|\right]\right\}$$

Altona, C.; Francke, R.; de Haan, R.; Ippel, J. H.; Daalmans, G. J.; Hoekzema, A. J. A. W.; van Wijk, J. *Magn. Reson. Chem.* **1994**, *32*, 670-678

Results

Conformational Percentages

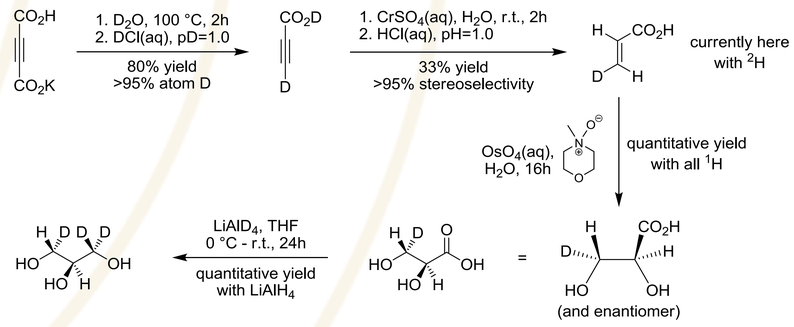
solvents	dielectric constant	% A	% B	% C	% D	% E	% F	% G	% H	% I
D_2O	79	5	11	6	11	28	14	6	14	7
methanol	33	12	15	8	15	18	9	8	9	5
ethanol	25	14	16	8	16	17	9	8	9	4
isopropyl alcohol	18	14	14	9	14	15	9	9	9	6
tert -butyl alcohol	13	16	15	9	15	14	9	9	9	5
DMSO	47	12	14	8	14	17	10	8	10	6
acetonitrile	38	7	11	9	11	17	13	9	13	10
acetone	21	6	11	7	11	21	14	7	14	9
THF	8	10	12	10	12	13	11	10	11	10
chloroform	5	5	10	7	10	21	15	7	15	10
1,4-dioxane	2	9	15	6	15	26	10	6	10	4

- However, uncertainty in the NMR peak assignments for H-1/H-4 and H-2/H-5 leads to uncertainty in the assignment of $J_{1,3}$ and $J_{2,3}$.
- Switching the values of $J_{1,3}$ and $J_{2,3}$ gives vastly different conformational results.

Conformational Percentages When Switching $J_{1,3}$ and $J_{2,3}$

Solvents	Dielectric constant	% A	% B	% C	% D	% E	% F	% G	% H	% I
D_2O	79	28	12	13	12	5	6	13	6	6
methanol	33	17	15	9	15	14	8	9	8	5
ethanol	25	16	16	8	16	15	8	8	8	4
isopropyl alcohol	18	13	14	9	14	16	10	9	10	6
tert -butyl alcohol	13	12	15	8	15	18	10	8	10	6
DMSO	47	15	15	9	15	14	9	9	9	6
acetonitrile	38	17	12	13	12	8	9	13	9	9
acetone	21	21	12	13	12	7	7	13	7	8
THF	8	13	12	11	12	11	10	11	10	10
chloroform	5	22	11	14	11	6	7	14	7	9
1,4-dioxane	2	22	17	8	17	13	6	8	6	3

Current Work – Synthesis to Identify $J_{1,3}$ and $J_{2,3}$



When completed, we should only observe H-1, H-3, and $J_{1,3}$

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