Long-lived states of magnetically inequivalent protons in aliphatic chains of nonchiral molecules

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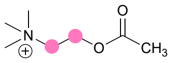
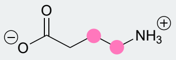
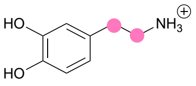
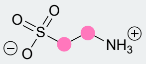
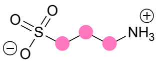
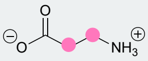
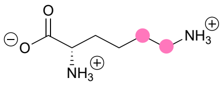
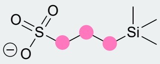
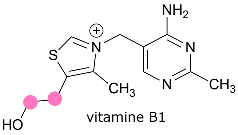
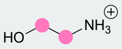
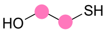
Introduction

Long-lived states (LLS) are population imbalances between nuclear singlet and triplet states and can have lifetimes T_{LLS} much longer than the longitudinal relaxation time T_1, as they are immune to intrapair dipole-dipole relaxation. [1]

In order to create an LLS within a molecule the two nuclei of the spin pair have to be either chemically or magnetically inequivalent. For protons of a methylene group, chemical inequivalence can be given by the vicinity to a chiral center. Magnetic inequivalence results from different out-of-pair *J*-couplings - a condition which is often fulfilled in aliphatic chains comprised of adjacent methylene units. These chains often form spin systems of the type AA'MM'(XX'), allowing the population of LLS in many compounds for which such states have not previously been observed.

Observation of Long-lived states in molecules containing adjacent methylene units

Long lived states were observed in many compounds containing a short aliphatic chain. Methylene groups for which it was possible to observe a LLS signal upon irradiation at the respective chemical shift are indicated in pink.

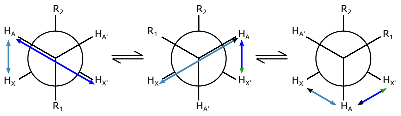
compound	**T_{LLS}*/T_1**	**compound**	**T_{LLS}*/T_1**
 acetylcholine	2.9	 γ-aminobutyric acid (GABA)	4.1
 dopamine	5.9	 taurine	5.7
 homotaurine	5.4	 β-alanine	4.4
 L-lysine	3.6	 sodium trimethylsilyl-propanesulfonate (DSS)	5.4
 vitamine B1	5.0	 ethanolamine	2.5
 beta-mercaptoethanol	4.5	 butanol	4.0

● - LLS of CH_2 group accessible by SLIC

*longest LLS lifetime within the molcule used for ratio T_{LLS}/T_1

In some cases, the "accessibility" and the duration of τ_{SLIC} were observed to be dependent on environmental factors such as pH.

⟶ The magnitude of magnetic inequivalence is dependent on the populations of the rotational conformers, which can be influenced by steric hindrance of bulky residues, electrostatic interactions between charges, etc.



Acknowledgements

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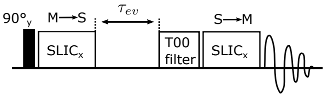
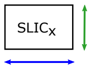
Method

Long-lived states were excited using the spinlock-induced crossing (SLIC) pulse sequence [2]:



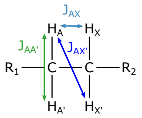
Two selective spinlocking pulses (SLIC pulses) are used to transfer population from a triplet to the singlet state (**M**agnetization ⟶ **S**inglet) and back (**S**inglet ⟶ **M**agnetization) for observation.

The ideal values for the SLIC pulse duration τ_{SLIC} and amplitude ν_{SLIC} are dependent on the *J*-couplings of the spin system and were adjusted experimentally for efficient population of the LLS. Typical values for ν_{SLIC} were 25 - 29 Hz; typical values for τ_{SLIC} were between about 100 and 900 ms.



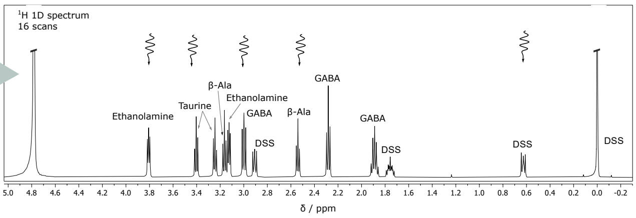
$$\nu_{SLIC} = 2|J_{intra}| = 2\left(\frac{|J_{AA'} + J_{XX'}|}{2}\right)$$

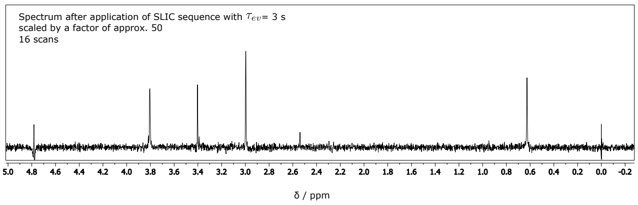
$$\tau_{SLIC} = \frac{1}{\sqrt{2}|\Delta J|} = \frac{1}{\sqrt{2}|J_{AX} - J_{AX'}|}$$



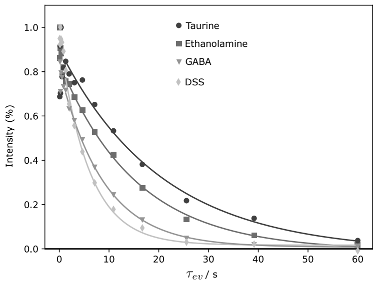
Simultaneous T_{LLS} measurement of several compounds in a mixture

Phase modulation of the SLIC pulse and the use of averaged values for SLIC duration and amplitude allowed simulaneous creation of LLS on several molecules, as well as the measurement of the lifetimes T_{LLS}.





Decay curves for the measurement of T_{LLS}



T_{LLS} (Taurine) = 20.6 ± 2.3 s

T_{LLS} (Ethanolamine) = 15.4 ± 0.7 s

T_{LLS} (GABA) = 8.9 ± 0.3 s

T_{LLS} (DSS) = 5.9 ± 0.5 s

Conclusion

- Long-lived states (LLS) between protons of a methylene group can be excited in aliphatic segments of molecules due to magnetic inequivalence. A chiral center in the vicinity of the methylene group is not needed, opening up a broad scope of possible substrates for the preparation of LLS.
- LLS were created and characterized in twelve compounds in which LLS have not previously been observed.
- Creation of LLS and measurement of T_{LLS} was possible for 4 compounds at the same time.

References

[1] M. Carravetta, M. H. Levitt, *J. Am. Chem. Soc.* **2004**, *126*, 6228–6229.
[2] S. J. DeVience, R. L. Walsworth, M. S. Rosen, *Phys. Rev. Lett.* **2013**, *111*, 173002.