Monitoring the Role and Metabolism of 13C-Hyperpolarized Steroids and Nonsteroidal Anti-Inflammatory Drugs via Parahydrogen-Enhanced MRI

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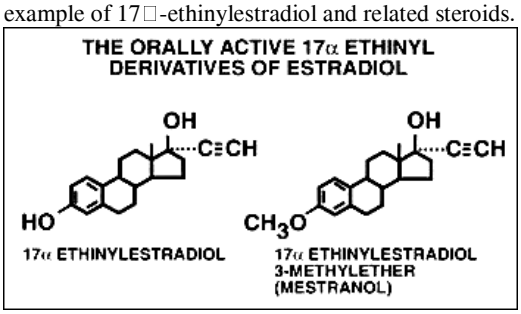
Introduction

The class of drugs known as **N**on**S**teroidal **A**nti-**I**nflammatory **D**rugs is typically refered to as NSAIDs. This nomenclature was chosen to differentiate them from steroids, the other major class of anti-inflammatory drugs. Steroids play a vital role in the human body; however, since their concentrations are very low, their role and actions are very difficult to investigate in situ via conventional analytical techniques. This constraint is even more true in particular for all those methods, which provide visual information. Apart from techniques of nuclear medicine, which require radioactively labeled compounds, MRI has some potential, but only if a considerable enhancement of its monitoring sensitivity is accomplished. A concept, which shows some promise is to use sufficiently hyperpolarized compounds that are accessible using either optical approaches via hyperpolarized rare gases or chemically via Parahydrogen Induced Polarization (PHIP).[1]

Results

Via this latter concept we have been able to ^{13}C-hyperpolarize 1-vinyl-1-hydroxycyclopentane, the para-hydrogenation product of a simple model compound for steroids, namely 1-ethinyl-1-hydroxycyclopentane, which mimics the D ring for example of 17□-ethinylestradiol and related steroids.



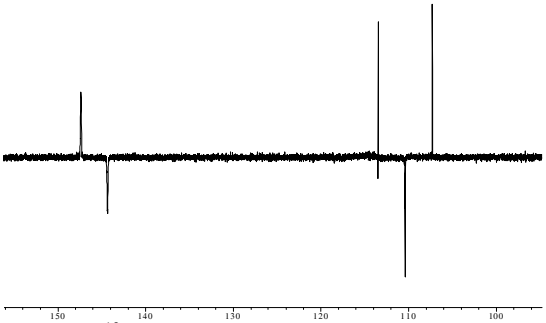
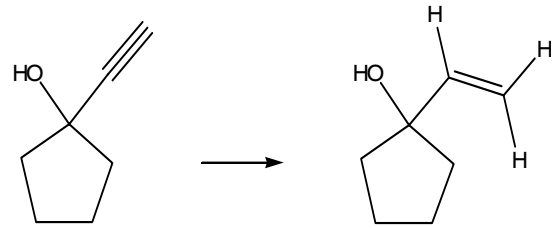


Figure 1: ^{13}C-hyperpolarized 1-vinyl-1-hydroxy-cyclo-Pentane obtained via parahydrogenation of 1-ethinyl, 1-hydroxycyclopentane using a cationic catalyst.



Hydrogenation of 1-ethinyl-1-hydroxycyclopentane

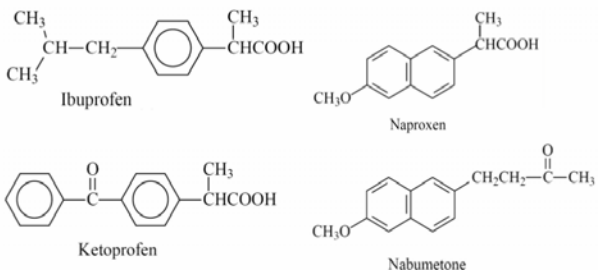


Figure 2: NSAIDs that can be hyperpolarized from suitable precursors via PHIP. To hyperpolarize ibuprofen, three alternatives exist, namely either starting from the correspondingly substituted phenylacrylic acid or from a phenylpropionic acid with an unsaturated side chain.

Discussion and Conclusions

The NSAIDs of the phenylalkynoic acid series listed below can be obtained in both ^{1}H- or ^{13}C-hyperpolarized as well. However, since the most significant aspect of NSAID distribution[2] is plasma protein binding, the consequences of that for the decay of the hyperpolarization has to be studied in vivo. Their plasma protein binding poses potential to study their interaction with other drugs that bind with albumin at the same sites.

References

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2.) Mehanna, AS, Am. J. Pharmaceut. Edu., **67**, 2 (**2003**), article 63