Analytical and Bioanalytical Chemistry (2023) 415:5855–5856
https://doi.org/10.1007/s00216-023-04887-1

ANALYTICAL CHALLENGE

Bridged bicyclic molecule NMR challenge

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Accepted: 25 July 2023 / Published online: 11 October 2023

We would like to invite you to participate in the Analytical Challenge, a series of puzzles to entertain and challenge our readers. This special feature of "Analytical and Bioanalytical Chemistry" has established itself as a truly unique quiz series, with a new scientific puzzle published every 3 months. Readers can access the complete collection of published problems with their solutions on the ABC homepage at http://www.springer.com/abc. Test your knowledge and tease your wits in diverse areas of analytical and bioanalytical chemistry by viewing this collection.

In the present challenge, bicyclic molecules are the topic. And please note that there is a prize to be won (a Springer book of your choice up to a value of €100 — given to one winner selected randomly). Please read on.

Meet the challenge

As the name implies, a bicyclic molecule contains two joined rings [1]. Bridged bicyclic structures occur widely in many biologically important natural molecules such as borneol and camphor. Indeed, such molecules are object of high interest in organic chemistry and drug discovery owing to their attractive pharmacokinetic properties.

A common challenge for NMR scientists concerning bridged bicyclic molecules is the determination of the relative orientation of substituents in such molecules, as shown in Fig. 1.

The standard and likely the most convenient approach to NMR structure elucidation of such substances is the NOESY experiment to observe NOE correlations of protons neighboring the substituent group R with the protons of the nearby CH_2 groups belonging to either the short bridge (for *endo* isomer) or the long bridge (for *exo* isomer) of the bicycle.

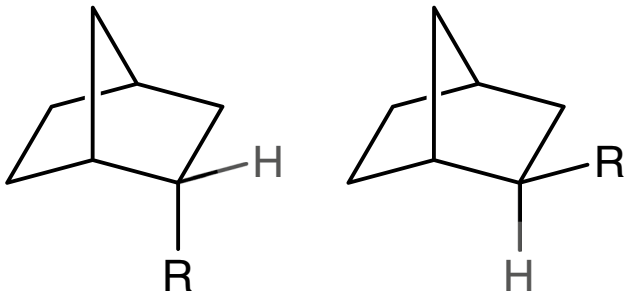

Fig. 1 Example of a bicyclo[2.2.1]alkane having *endo*-oriented (left) and *exo*-oriented (right) substituent

But there is often a simpler way for the structure elucidation of such molecules, especially if the short bridge contains a heteroatom. In such cases, the spin-coupling picture of the protons located at the bridgehead positions becomes simpler.

The challenge

A colleague obtained two isomers of a bridged bicyclic compound (Fig. 2). But time is short! All we have before setting up next batch of overnight reactions are the ^{1}H-NMR spectra of these isomers in chloroform-d_3 (Fig. 3).

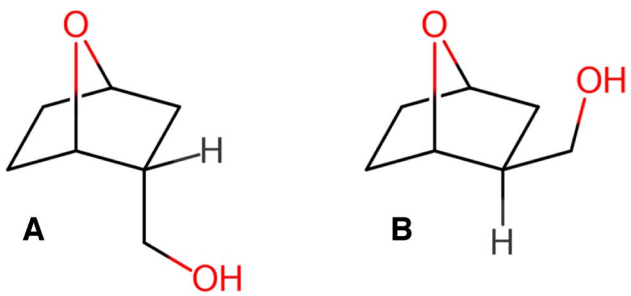

Fig. 2 Structures of two bridged bicyclic isomers **A** (*endo* isomer) and **B** (*exo* isomer)

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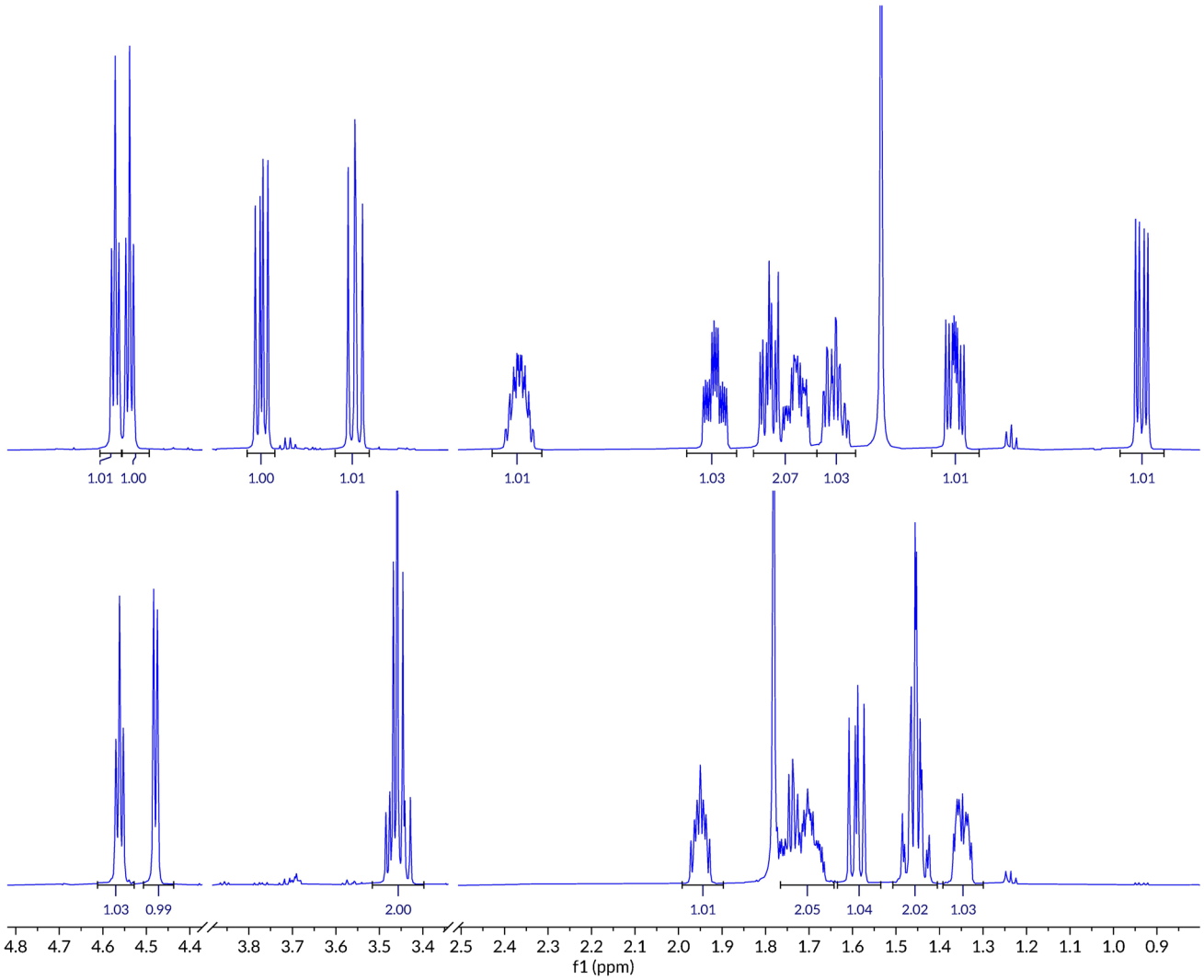

Fig. 3 600 MHz. ^{1}H-NMR spectra of substances **A** and **B** in $CDCl_3$

Using only these two ^{1}H-NMR spectra without peak-picking and detailed multiplet analysis, try to determine which spectrum (top and bottom) corresponds to which isomer. Explain your reasoning. A hint: find the key difference in the spin-coupling patterns, not the chemical shifts!

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Michael B. Smith, "Organic chemistry: an acid—base approach". Boca Raton: CRC Press, Taylor & Francis Group; 2011. https://books.google.com/books?id=gKPtYs0jyMcC.

We invite our readers to participate in the Analytical Challenge by solving the puzzle above. Please send the correct solution to abc@springer.com by January 1, 2024. Make sure you enter "Bridged bicyclic molecule NMR challenge" in the subject line of your e-mail. The winner will be notified by e-mail, and their name will be published on the "Analytical and Bioanalytical Chemistry" homepage at http://www.springer.com/abc and in the journal (volume 416/issue 9) where readers will find the solution and a short explanation.

The next Analytical Challenge will be published in 416/1, January 2024. If you have enjoyed solving this Analytical Challenge you are invited to try the previous puzzles on the ABC homepage.