Molecular Crystals and Liquid Crystals Science and Technology. Section A. Molecular Crystals and Liquid Crystals
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl19

Solid State NMR as a Tool to Differentiate Between the Enantiotopic Methyl Groups of Prochiral Guest Molecules in Tri-o-Thymotide Clathrates

Glenn A. Facey [a] & John A. Ripmeester [a]
[a] Steacie Institute for Molecular Science, National Research Council of Canada, Ottawa, CANADA, K1A 0R5
Version of record first published: 27 Oct 2006.

To cite this article: Glenn A. Facey & John A. Ripmeester (1992): Solid State NMR as a Tool to Differentiate Between the Enantiotopic Methyl Groups of Prochiral Guest Molecules in Tri-o-Thymotide Clathrates, Molecular Crystals and Liquid Crystals Science and Technology. Section A. Molecular Crystals and Liquid Crystals, 211:1, 167-175

To link to this article: http://dx.doi.org/10.1080/10587259208025816

Mol. Cryst. Liq. Cryst. 1992, Vol. 211, pp. 167–175
Reprints available directly from the publisher
Photocopying permitted by license only

Printed in the United States of America

SOLID STATE NMR AS A TOOL TO DIFFERENTIATE BETWEEN THE ENANTIOTOPIC METHYL GROUPS OF PROCHIRAL GUEST MOLECULES IN TRI-*O*-THYMOTIDE CLATHRATES

GLENN A. FACEY and JOHN A. RIPMEESTER
Steacie Institute for Molecular Science, National Research Council of Canada, Ottawa, CANADA, K1A 0R5.

(*Received July 11, 1991*)

Abstract Solid state ^{13}C CP/MAS and ^{2}H NMR are used to examine the tri-*o*-thymotide clathrates of 2-bromopropane, 2-propanol and dimethylsulfoxide. In all cases the enantiotopic methyl groups could be resolved.

Keywords: solid state NMR, tri-o-thymotide clathrates, 2-bromopropane, 2-propanol, dimethylsulfoxide, prochiral guests

INTRODUCTION

Tri-*o*-thymotide (TOT) is the cyclic triester of *o*-thymotic acid. It is most stable in either of two possible enantiomeric propeller conformations, P and M. These conformations are in dynamic equilibrium with one another in solution.[1,2] When recrystallized from organic solvents, containing hydrocarbon chains of less than five carbon atoms, TOT crystallizes into a cage clathrate structure.[3] The void spaces in the host network are occupied with guest solvent molecules. The ratio of host to guest is 2:1. Upon crystallization, TOT undergoes spontaneous optical resolution, such that all of the P propellers form one type of crystal and all of the M propellers form another.[4,5] Like the molecules themselves, the crystals and the void spaces therein, are dissymmetric. The dissymmetric cavities allow TOT to exhibit enantiomeric selectivity towards racemic guests.[6-11] The ability of single crystals of this material to include one enantiomer of a racemic pair in preference to the other has long been a topic of interest. Little attention, however, has been directed towards the TOT clathrates of prochiral guests.

Tetrahedral centres containing two identical substituents and two other unique substituents are prochiral centres.[12-14] Thus, the central atoms, A, of molecules with the general formula R_2-A-(X)(Y) are prochiral centres, and

such molecules are called prochiral molecules. If a molecular plane of symmetry, σ, bisecting the R-A-R bond angle exists, then the groups are enantiotopic; otherwise they are diastereotopic. As far as NMR spectroscopy is concerned, enantiotopic groups are chemical shift equivalent, or *isochronous*, in achiral or racemic media, whereas diastereotopic groups are chemical shift inequivalent or *anisochronous*. In chiral solvents, on the other hand, both enantiotopic and diastereotopic groups are anisochronous. Like chiral solvents, the chiral environment provided by the cages of TOT clathrates should also be able to discriminate between enantiotopic chemical groups.

The methyl groups of substituted isopropyl groups are enantiotopic if the C2 substituent has a mirror plane bisecting the CH_3-C-CH_3 bond angle. Thus, the methyl groups of 2-bromopropane are enantiotopic. The methyl groups of 2-propanol are enantiotopic if the torsion angle, H-O-C2-H is fixed at either 0° or 180° or, if there is fast rotation about the C-O bond. Otherwise the methyl groups are diastereotopic. The methyl groups of dimethylsulfoxide are enantiotopic. The lone electron pair on the sulfur atom can be considered to be situated on a mirror plane bisecting the C-S-C bond angle.

EXPERIMENTAL

Tri-*o*-thymotide was prepared from *o*-thymotic acid according to the literature.[15] The crude product was recrystallized twice from acetone and dried in an oven at 150° for 48 hours to remove the enclathrated acetone.

Dimethylsulfoxide-d_6 and 2-propanol-(1,3-d_6) were purchased from MSD isotopes. 2-Bromopropane-(1,3-d_6) was prepared from 2-propanol-(1,3-d_6) by the action of PBr_3.[16,17]

The TOT clathrates of 2-bromopropane, 2-bromopropane-(1,3-d_6), 2-propanol, dimethylsulfoxide and dimethylsulfoxide-d_6 were prepared by recrystallization of TOT in the neat guest material followed by evaporation of the guest at room temperature. Due to low solubility and small quantity of

guest, the TOT clathrate of 2-propanol-(1,3-d_6) was prepared at slightly elevated temperature and pressure. TOT (~300 mg) and 2-propanol-(1,3-d_6) (2.5 g) were placed in a heavy walled glass tube. The contents of the tube were frozen with liquid nitrogen and the tube was evacuated. Two freeze-pump-thaw cycles were carried out and the tube was then sealed with a torch with the contents frozen and under vacuum. It was allowed to warm to room temperature, then placed in an oven at ~ 100°C for 19 days. After being removed from the oven, the tube was allowed to cool to room temperature. the contents were then frozen with liquid nitrogen and the tube was opened. After thawing, the mixture was placed in a petri dish where the excess guest was allowed to evaporate, leaving the clathrate.

All NMR experiments were conducted on a Bruker CXP 180 pulse spectrometer at resonance frequencies of 27.6 MHz for ^2H and 45.3 MHz for ^{13}C. The ^{13}C NMR data were collected using the CP/MAS technique[18-22] with a pulse sequence to suppress the first order spinning sidebands.[23] The $\pi/2$ pulses were 3.8 μsec. The cross polarization time was set at 3 msec and the repetition time was 2 sec. Spinning rates were typically between 3 and 4 kHz. The dipolar dephasing technique[24,25] was used for the spectrum indicated in figure 1, with a dipolar dephasing time of 40 μsec. The quadrupolar echo pulse sequence[26] was used to obtain the ^2H NMR spectra. The $\pi/2$ pulses were 3 μsec, the delay between pulses was set at 35 μsec and the repetition time was 2 sec.

RESULTS AND DISCUSSION

The ^{13}C CP/MAS NMR spectra of TOT / 2-bromopropane, TOT / 2-propanol and TOT / dimethylsulfoxide are shown in figure 1. The most intense resonances in the spectra are due to the TOT host while those marked with asterisks are due to the guest materials. The insets are expansions of the methyl resonances of the guests. They appear as doublets for both the 2-

bromopropane and the 2-propanol. The chemical shift differences between the components of the doublets are 0.4 ppm and 0.2 ppm for 2-bromopropane and 2-propanol, respectively. There is no such splitting for the methyl resonances of dimethylsulfoxide.

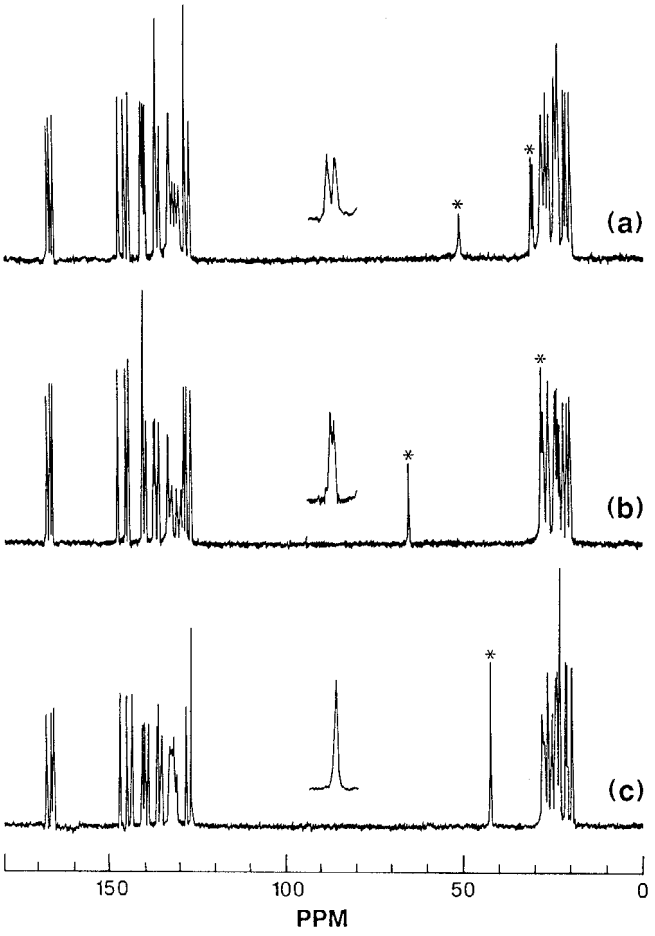

FIGURE 1: ^{13}C CP/MAS NMR spectra of the TOT clathrates of: (a), 2-bromobutane; (b), 2-propanol and (c), dimethylsulfoxide. The insets are expansions of the methyl group resonances of the guest molecules. For (b), the inset was taken from a spectrum acquired under dipolar dephasing conditions to eliminate overlap with the spectrum of the TOT host.

In the case of 2-bromopropane the two methyl groups are enantiotopic and the methyl group resonances are therefore anisochronous due to the chiral environment provided by the TOT cages. If it is assumed that the hydroxyl group of the enclathrated 2-propanol is free to rotate fast on the msec time scale, then one can conclude that the splitting of the methyl resonance, in this case, is also due to the enantiotopic groups. If for some reason the OH group is locked into a single conformation the observed splitting must result from the diastereotopic relationship between the methyl groups. Since the inner walls of the TOT cages are lined primarily with alkyl protons, there is little, if any, chance of hydrogen bonding to occur between the host and guest. Guest - guest interactions are also expected to be small since the guest molecules are self contained in TOT cages. For these reasons, it seems unlikely that the hydroxyl group would be held rigidly into a single conformation. The splitting must therefore be due to the enantiotopic relationship between the methyl groups.

The ^{13}C methyl resonances of TOT enclathrated dimethylsulfoxide are unresolved, however; the molecular symmetry dictates an enantiotopic relationship between them. The resonance splitting must therefore be too small to be observed. It should be noted that the methyl groups of pure solid dimethylsulfoxide, which have been shown to be inequivalent by both crystallographic[27,28] and NMR[29] methods, also give rise to the same ^{13}C chemical shielding parameters.[19]

The solid state ^2H NMR spectra of TOT / 2-bromopropane-(1,3-d_6), TOT / 2-propanol-(1,3-d_6) and TOT / dimethylsulfoxide-d_6 at 213 K are shown in figure 2 along with fast motional limit lineshape simulations.[30-32] The parameters of the simulations are given in table I. In all cases the ^2H NMR spectra can be represented with a 1:1 sum of two component spectra, one for each methyl group in the molecule. The methyl groups are not only anisochronous but also have different mobilities. The ^2H NMR spectrum for a methyl group rotating at a rate greater than or ~ 10^7 Hz is typically axially symmetric with an inner splitting of ~ 42 kHz. All of the components of the

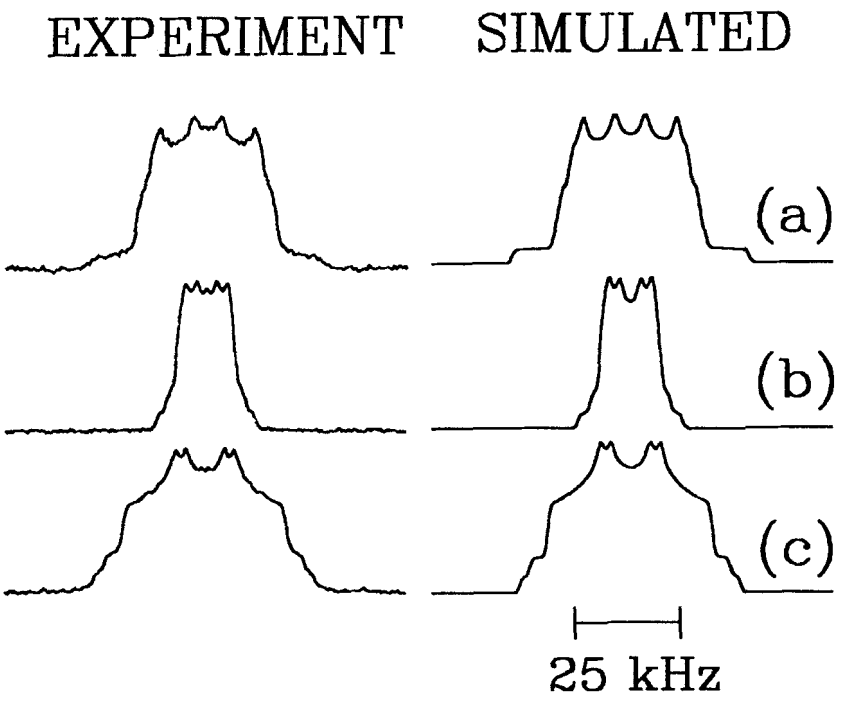

FIGURE 2: Solid state ^2H NMR spectra and fast motional lineshape simulations of the TOT clathrates of: (a), 2-bromopropane-(1,3-d_6); (b), 2-propanol-(1,3-d_6) and (c), dimethylsulfoxide-d_6 at 213 K.

TABLE I Parameters for ^2H NMR lineshape simulations

	e^2Qq/h (kHz)	η
TOT / 2-Bromopropane-(1,3-d_6)	25.0	0.429
	39.3	0.200
TOT / 2-Propanol-(1,3-d_6)	13.3	0.490
	17.2	0.171
TOT / Dimethylsulfoxide-d_6	34.6	0.565
	38.4	0.490

spectra in figure 2 are narrower than this, indicating that additional molecular motions are augmenting the fast methyl group rotations. These additional motions must also occur at a rate, fast on the NMR time scale (~ 10^7 Hz). Since the line widths and shapes are different for each of the three guest molecules, one must conclude that the molecules undergo quite different molecular motions. Also, since each spectrum is the sum of two equal intensity components, the molecular motions experienced by each guest molecule must treat each of the two methyl groups differently. A detailed description would require more experimentation.

CONCLUSION

The dissymmetric cages of tri-*o*-thymotide clathrates provide a suitable chiral environment to allow the differentiation of enantiotopic methyl groups of small guest molecules by solid state NMR techniques. In this respect TOT behaves as a "solid state chiral chemical shift reagent". In some cases where the ^{13}C methyl resonances accidentally overlap, the methyl groups can be differentiated by solid state ^2H NMR. The molecular motions, experienced by the TOT enclathrated guest molecules, treat the enantiotopic methyl groups differently.

ACKNOWLEDGEMENT

We gratefully acknowledge the financial support of NSERC.

REFERENCES

1. W.D. Ollis and I.O. Sutherland, J. Chem. Soc. Chem. Comm., 402 (1966).

2. A.P. Downing, W.D. Ollis and I.O. Sutherland, J. Chem. Soc., 24 (1970).

3. D. Lawton and H.M. Powell, J. Chem. Soc., 2339 (1958).

4. H.M. Powell, Nature, 170, 155 (1952).

5. A.C.D. Newman and H.M. Powell, J. Chem. Soc., 3747 (1952).

6. R. Arad-Yellin, B.S. Green, M. Knossow and G. Tsoucaris, J. Am. Chem. Soc., 105, 4561 (1983).

7. R. Arad-Yellin, B.S. Green and M. Knossow, J. Am. Chem. Soc., 102, 1157 (1980).

8. R. Gerdil and J. Allemand; Helv. Chim. Acta., 63, 1750 (1980).

9. R. Gerdil, Topics in Curr. Chem., 140, 71 (1987).

10. J.A. Ripmeester and N.E. Burlinson, J. Am. Chem. Soc., 107, 3713 (1985).

11. G. Facey and J.A. Ripmeester, J. Chem. Soc. Chem. Comm., 1585 (1990).

12. W.B. Jennings, Chem. Rev., 75, 307 (1975).

13. K.R. Hanson, J. Am. Chem. Soc., 88, 2731 (1966).

14. K. Mislow and M. Raban, Top Stereochem., 1, 1 (1967).

15. W. Baker, B. Gilbert and W.D. Ollis, J. Chem. Soc., 1443 (1952).

16. C.R. Noller and R. Adams, J. Am. Chem. Soc., 48, 1080 (1926).

17. G.K. Helmkamp, C.D. Joel and H. Sharman, J. Org. Chem., 21, 844 (1956).

18. A. Pines, M.G. Gibby and J.S. Waugh, J. Chem. Phys., 56, 1776 (1972).

19. A. Pines, M.G. Gibby and J.S. Waugh, Chem. Phys. Lett., 15, 373 (1972).

20. A. Pines, M.G. Gibby and J.S. Waugh, J. Chem. Phys., 59, 569 (1973).

21. E.R. Andrew, Int. Rev. Phys. Chem., 1, 195 (1981).

22. For an overall review and a comprehensive list of references see: C.A. Fyfe, Solid State NMR for Chemists, C.F.C. Press, Guelph (1983).

23. M.A. Hemminga and P.A. de Jager, J. Magn. Reson., 51, 339 (1983).

24. S.J. Opella and M.H. Frey, J. Am. Chem. Soc., 101, 5854 (1979).

25. L.B. Alemany, D.M. Grant, T.D. Alger and R.J. Pugmire, J. Am. Chem. Soc., 105, 6697 (1983).

26. J.H. Davis, K.R. Jeffrey, M. Bloom, M.I. Valic and T.P. Higgs, Chem. Phys. Lett., 42, 390 (1976).

27. M.A. Viswamitra and K.K. Kannan, Nature, 209, 1016 (1966).

28. R. Thomas, C.B. Shoemaker and K. Eriks, Acta. Crystallogr, 21, 12 (1966).

29. J.A. Ripmeester, Can. J. Chem., 59, 1671 (1981).

30. N. Bloembergen and T.S. Rowland, Phys. Rev., 55, 1679 (1965).

31. N. Bloembergen and T.S. Rowland, Acta Metallurgica, 1, 731 (1953).

32. M. Mehring, NMR Basic Principles and Progress: High Resolution NMR Spectroscopy of Solids, Chapt 1, Edd. P. Diehl, E. Fluck, R. Kosfeld; Springer-Verlag, New York (1976).