

Notes

Conformational Studies by Dynamic NMR. 73.¹ Conformational Enantiomers of Cyclohexene Oxide in the Solid State

Daniele Casarini*

Chemistry Department, University of Basilicata,
Potenza, Italy

Lodovico Lunazzi and Andrea Mazzanti*

Department of Organic Chemistry "A.Mangini", University
of Bologna, Risorgimento, 4, Bologna 40136, Italy

Gerald Simon

Varian GmbH, Darmstadt, Germany

Received November 22, 1999

The progress achieved in the instrumentation of high-resolution solid-state NMR spectrometers has allowed one to obtain detailed information about the dynamic processes occurring within organic molecules in the crystalline state. In particular, it has been shown that the rotational barriers are significantly higher (by a few kcal mol⁻¹) in the solid state than in solution,² due to the hindrance exerted by the crystal lattice upon the molecular motion. An analogous enhancement could be reasonably expected also for ring inversion. This is suggested by the observation that the related dynamic processes were observed at temperatures much higher than in solution, even though the corresponding free energies of activation (ΔG^\ddagger) were not measured in the crystalline state.³

We have recently obtained an example where the barrier for the inversion process of a six-membered ring had greatly increased in the solid state.⁴ For the ΔG^\ddagger value measured in crystalline dodecamethylcyclohexasilane, (Me₂Si)₆ is about 8 kcal mol⁻¹ higher than in solution (12.75 vs 4.85 kcal mol⁻¹). On the other hand, the free energies of activation measured for a number of ring inversions in inclusion compounds did not display

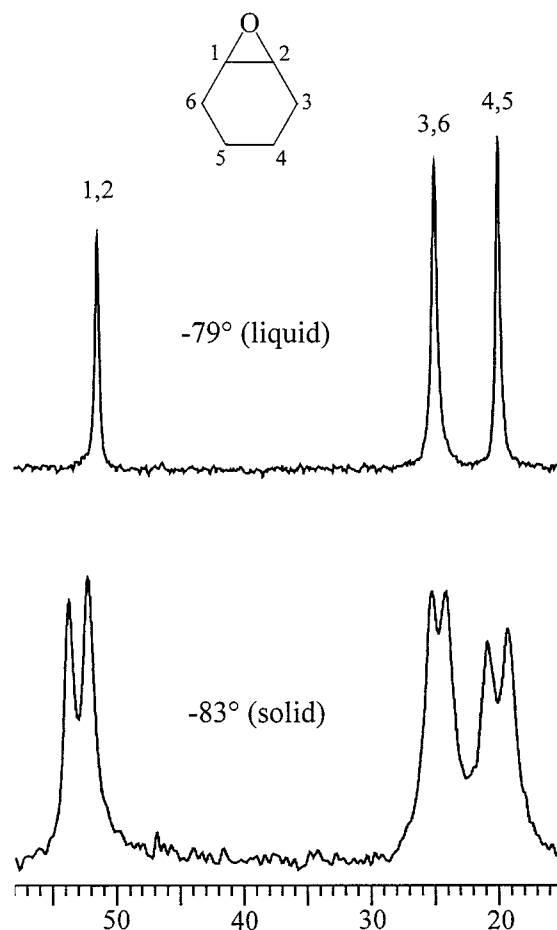


Figure 1. ¹³C spectrum (100.56 MHz) of cyclohexene oxide as a neat liquid (top) and CP-MAS spectrum of the same compound below the melting point (bottom).

substantial differences (less than 1 kcal mol⁻¹) with respect to those observed in solution.⁵

Recently, Pawar and Noe⁶ have measured the barrier ($\Delta G^\ddagger = 4.2$ kcal mol⁻¹) for the ring inversion of cyclohexene oxide [i.e., (CH₂CH₂CH)₂O] in solution (a 5:1:1 mixture of CHClF₂, CHCl₂F, and CHF₃ was used as solvent) by performing a line shape analysis of one of the three ¹³C lines, which splits into a doublet ($\Delta\delta = 2.2$ ppm) below -180 °C. The analogous splitting, expected to occur also for the other two lines, could not be revealed since the corresponding shift separations were too small. We found this molecule to be most appropriate for providing a second, additional case where enhancement of a ring inversion barrier in the solid state could possibly be observed.

(1) Part 72: Bonini, B. F.; Fochi, M.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2000**, *65*, 3200.

(2) Riddell, F. G.; Arumagam, S.; Anderson, J. E. *J. Chem. Soc., Chem. Commun.* **1991**, 1525. Barrie, P. J.; Anderson, J. E. *J. Chem. Soc., Perkin Trans. 2* **1992**, 2031. Riddell, F. G.; Arumagam, S.; Harris, K. D. M.; Rogerson, M.; Strange, J. H. *J. Am. Chem. Soc.* **1993**, *115*, 1881. Aliev, A. E.; Harris, K. D. M.; Apperley, D. C. *J. Chem. Soc. Chem. Comm.* **1993**, 251. Riddell, F. G.; Bernath, G.; Fülöp F. *J. Am. Chem. Soc.* **1995**, *117*, 2327. Casarini, D.; Foresti, E.; Lunazzi, L.; Mazzanti, A. *Chem. Eur. J.* **1999**, *5*, 3501. Lunazzi, L.; Mazzanti, A.; Casarini, D.; De Lucchi, O.; Fabris, F. *J. Org. Chem.* **2000**, *65*, 883.

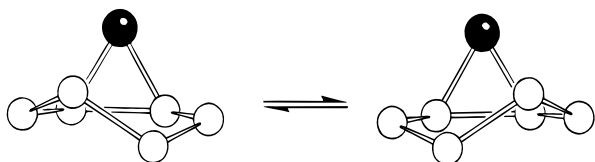
(3) Buchanan, G. W.; Kirby, R. A.; Ripmeester, J. A.; Ratcliffe, C. I. *Tetrahedron Lett.* **1987**, *28*, 4783. Buchanan, G. W.; Morat, C.; Ratcliffe, C. I.; Ripmeester, J. A. *J. Chem. Soc., Chem. Comm.* **1989**, 1306.

(4) Casarini, D.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **1998**, *63*, 9125.

(5) Müller, K. *J. Phys. Chem.* **1992**, *96*, 5733. Müller, K. *Magn. Reson. Chem.* **1992**, *30*, 228. Aliev, A. E.; Harris, K. D. M. *J. Am. Chem. Soc.* **1993**, *115*, 6369. Müller, K. *Magn. Reson. Chem.* **1995**, *33*, 113. Nordon, A.; Harris, R. K.; Yeo, L.; Harris, K. D. M. *Chem. Commun.* **1997**, 961. O'Leary, B. M.; Grotzfeld, R. M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 11701.

(6) Pawar, D. M.; Noe, E. A. *J. Am. Chem. Soc.* **1998**, *120*, 1485.

Scheme 1



Although cyclohexene oxide is a liquid at ambient temperature, it freezes at $-81\text{ }^{\circ}\text{C}$, so that a solid-state spectrum can be obtained below this temperature. A differential scanning calorimetric determination did show that the only observed phase change occurs at the melting point. The CP-MAS spectrum of crystalline $(\text{CH}_2\text{CH}_2\text{-CH})_2\text{O}$ is reported in Figure 1 (bottom trace). The three sharp lines, due to the three pairs of dynamically equivalent (homotopic) carbons in the liquid phase (Figure 1, upper trace), split into equally intense doublets separated by 1.54, 1.12, and 1.57 ppm for the carbons in positions 1 and 2, 3 and 6, and 4 and 5, respectively. These values are similar to that of the separation detected in solution.⁶ The doublets observed at low temperature in the solid state NMR spectrum are a consequence of the fact that the ring inversion process, which reversibly exchanges the half-chair conformer⁶ with its enantiomeric form (Scheme 1), has been made slow in the NMR timescale. In each enantiomer, the six carbon atoms are diastereotopic, thus accounting for the six lines CP-MAS spectrum.

It is important to stress that, contrary to the case of dodecamethylcyclohexasilane,⁴ the three lines split into six *as soon as the compound becomes solid*, and in a reversible manner become three as soon as the compound melts. In other words, the expected coalescence of each pair of lines cannot be experimentally detected in the solid state since it occurs at a temperature higher than the melting point. As a consequence, only the lower limit for the ΔG^\ddagger value in the crystalline phase can be obtained in the present case.

For this purpose, we performed a computer line shape analysis of the six signals and observed that the theoretical coalescence point is reached when using a rate constant of $95 \pm 5\text{ s}^{-1}$. This corresponds to a free energy

of activation of 9.1 kcal mol^{-1} at $-81\text{ }^{\circ}\text{C}$, if a transmission coefficient of $1/2$ is used in the Eyring equation,⁷ as is customary for ring-inversion processes.^{6,8} Since such a coalescence could not be observed in the temperature range where the compound is still solid, the exchange of the two enantiomers (Scheme 1) in the crystalline phase requires a barrier certainly higher than 9.1 kcal mol^{-1} . From this result, it can therefore be concluded that the barrier has been enhanced by more than 5 kcal mol^{-1} with respect to the value measured in solution.

This experiment convincingly confirms that the inversion processes of six-membered rings display barriers much greater in the solid than in solution, the effect being even larger than that observed for the rotation processes.

Experimental Section

The commercially available cyclohexene oxide was purified by distillation before the use. The liquid sample was tightly sealed in 5 mm zirconia rotor, spun at the magic angle with a speed of about 4 kHz in a spectrometer (Varian, Inova 400) operating at 100.56 MHz for ^{13}C . The cooling was achieved by means of a flow of dry nitrogen, precooled in a heat exchanger immersed in liquid nitrogen and the temperature calibrated by observing the melting point of the compound (measured as $-81 \pm 1\text{ }^{\circ}\text{C}$ in the DSC experiment) within the spectrometer. The mixing time was 1 ms, the recycling time 10 s, the pulse width $5\text{ }\mu\text{s}$, and the number of transients 16. The chemical shifts were measured, by replacement, with respect to the methyl signal of hexamethylbenzene (17.3 ppm). The line shape simulation was performed by making use of a PC version of the DNMR 6 program.⁹ The DSC determination was obtained with a scanning rate of 5 degrees per minute, heating from -135 ° to $-40\text{ }^{\circ}\text{C}$.

Acknowledgment. Financial support has been received from MURST, Rome (national project "Stereo-selection in Organic Synthesis"), and from the University of Bologna (Finanziamento d'Ateneo 2000–2002).

JO991800Z

(7) The use of an unitary coefficient would yield a ΔG^\ddagger equal to 9.3 kcal mol^{-1} .

(8) Sandström, J. *Dynamic NMR Spectroscopy*, Academic Press: London, 1982; p 105.

(9) QCPE Program no. 633, Indiana University, Bloomington, IN.