Tetrahedron Letters No. 42, pp 4331 - 4334, 1972. Pergamon Press. Printed in Great Britain.

NMR INVESTIGATION OF RING INVERSION IN A CYCLOHEPTANONE DERIVATIVE

Maurice St-Jacques and Cambyse Vaziri
Department of Chemistry, University of Montreal
Montreal, Quebec, Canada.

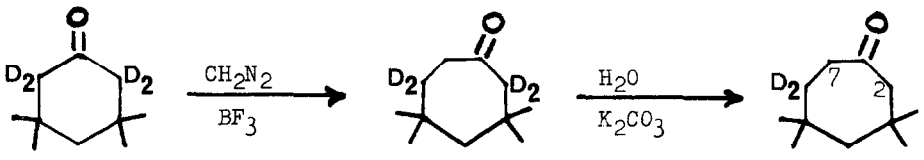
(Received in USA 29 August 1972; received in UK for publication 19 September 1972)

Seven membered carbocyclic molecules are reputed to have rather low barriers to ring inversion presumably because of a low energy demanding pseudorotation (1). For example, it was reported that the barrier to interconversion of the cycloheptane twist-chair is too small for measurement by ^{19}F nmr spectroscopy whereas the presence of a gem-dimethyl group raises the barrier to pseudorotation such that 1,1-difluoro-4,4-dimethylcycloheptane was found to have an energy of activation of about 6 kcal/mole (2). Recent work has also shown that cycloheptene has a very low free energy of activation ($\Delta G^{\neq}$) of 5,0 kcal/mole at -165° (3). We wish to report that altough cycloheptanone still undergoes very rapid ring inversion on the nmr time scale at -170°, its derivative, 3,3,5,5-tetramethylcycloheptanone, has a significantly higher barrier to inversion.

For reasons that will soon become apparent, it was necessary to prepare the deuterated derivative 3,3,5,5-tetramethyl-6,6-dideuteriocycloheptanone (1) by the sequence of reactions described below. Ring expansion of 3,3,5,5-tetramethyl-2,2,6,6-tetradeuteriocyclohexanone (2)(4) with diazomethane in the presence of boron trifluoride etherate (5) produced 3* which was readily

* Carbon and hydrogen analysis of the nondeuterated analog of 3 or 1 as well as the mass spectrum of 1 are in accord with the proposed structure. The pmr spectra were recorded on a JEOL JNM-4H-100 spectrometer as previously described (3).

transformed into 1 by exchange in water.



2 3 1

Figure 1 shows a series of 100 MHz deuterium decoupled pmr spectra of the C_2 and C_7 methylene protons of 1 (5% solution in chlorodifluoromethane) at various temperatures. A comparison with 3 reveals that, at high temperature, the signal at δ 2.362 is due to the C_7 methylene protons while that at δ 2.437 is associated with the C_2 methylene group. As the temperature is gradually decreased, only the low field singlet splits into an AB quartet below -138°, the coalescence temperature. Analysis of the spectrum at -155° gives a chemical shift difference ($\Delta\upsilon$) of 90.4 Hz and a geminal coupling constant (^2J) of -10.1 Hz. A computer simulation of this spectral change with the DNMR-2 program (6) shows that ^2J is essentially equal to the observed separation of each doublet.

The rate constant for ring inversion was estimated to be 202 sec^{-1} at -138° and application of standard equations (7) led to a $\Delta G^{\neq}$ of 6.3 kcal/mole.

It is noteworthy to emphasize that the signals of the methyl groups (two singlets), the C_4 methylene and C_7 methylene groups did not change on going to -170°. The use of deuterium labelling in 1 has proved essential to a clear-cut observation of the spectral change illustrated in Figure 1.

Under ideal circumstances, interpretation of the low temperature spectrum generally reveals the characteristic geometry of the stable conformation. But since the large number of accidental chemical shift coincidences greatly limit the information obtained from the spectrum at -155°, it is difficult to distinguish unambiguously between chair or twist-chair conformations containing the carbonyl and methyl groups at various locations. The large difference in $\Delta\upsilon$ characteristic of the protons in each of the C_2 and C_7 methylene groups

suggests that they are not distributed symmetrically about the carbonyl group. Calculations by Allinger and coworkers (8) on the preferred location of the carbonyl group on the cycloheptanone twist-chair are not of much help in choosing the proper conformation.

It therefore appears premature to speculate on this complex subject and we reserve our comments until such time when we have succeeded in preparing other cycloheptanone derivatives whose $\Delta\upsilon$ and ^2J parameters for methylene protons α to the carbonyl group, once understood, should provide a means of determining the geometry of the stable conformation of cycloheptanone derivatives in solution.

We acknowledge financial support from the National Research Council of Canada and the Quebec Ministry of Education.

REFERENCES

1. R. Knorr, C. Ganter and J.D. Roberts, Angew. Chem. (Int. Ed.), 6, 556 (1967).
2. J.D. Roberts, Chem. in Britain, 2, 529 (1966).
3. M. St-Jacques and C. Vaziri, Can. J. Chem., 49, 1256 (1971).
4. M. St-Jacques, M. Bernard and C. Vaziri, Can. J. Chem., 48, 2386 (1970).
5. F.A.L. Anet, M. St-Jacques and G.N. Chmurny, J. Am. Chem. Soc., 90, 5843 (1968)
6. G. Binsch, J. Am. Chem. Soc., 91, 1304 (1969).
7. D. Kost, E.H. Carlson and M. Raban, Chem. Comm., 656 (1971), and references cited therein.
8. N.L. Allinger, M.T. Tribble and M.A. Miller, Tetrahedron, 28, 1173 (1972).

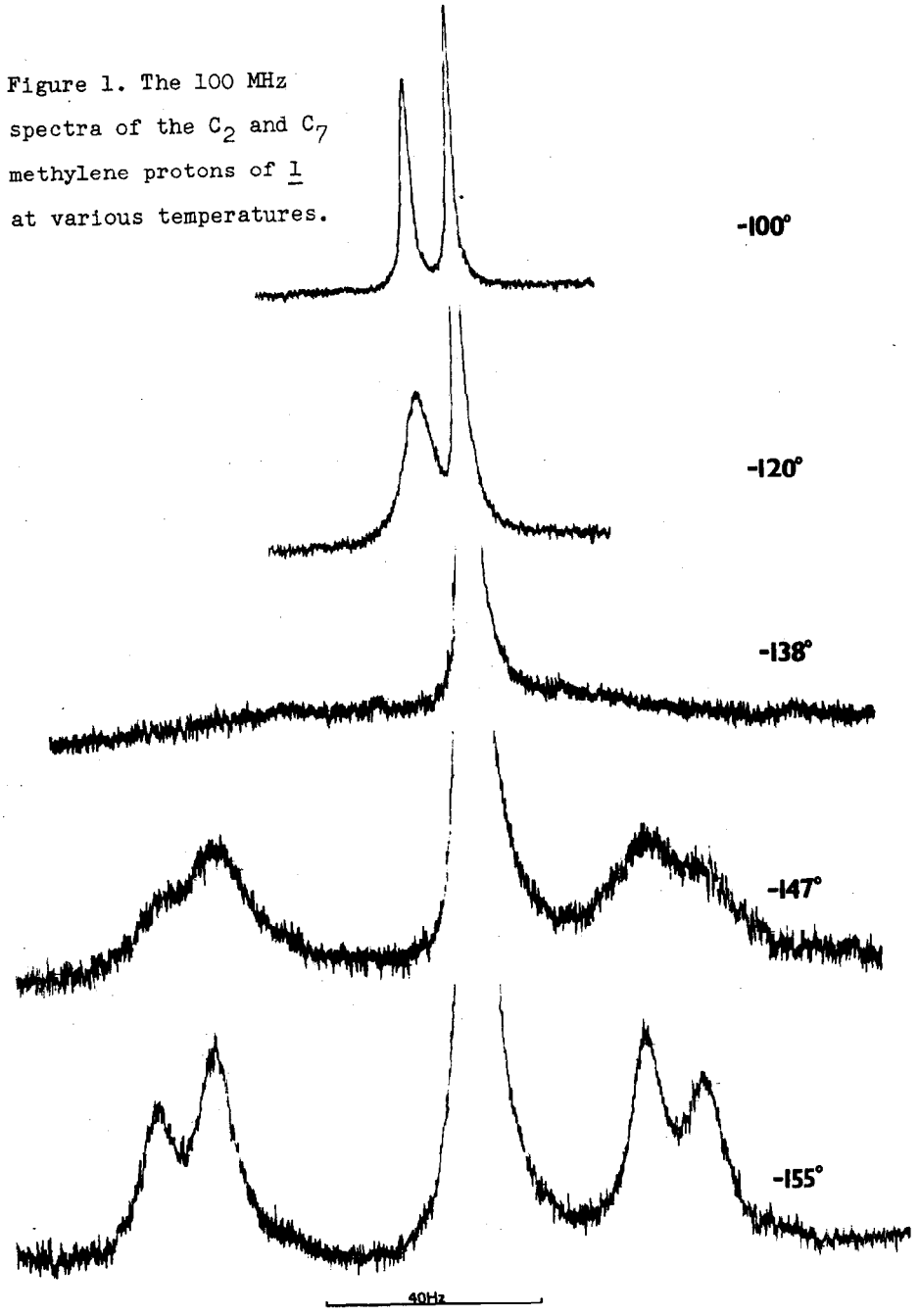


Figure 1. The 100 MHz spectra of the C_2 and C_7 methylene protons of 1 at various temperatures.