Am. Chem. Soc., **104**, 6330 (1982).
11. M. Ciampolini, M. Micheloni, N. Nardi, F. Vizza, A. Buttafaba, L. Fabbrizzi, and A. Perotti, *J. Chem. Soc. Chem. Commun.*, 998 (1984).
12. K. Wieghardt, I. Talksdorf, and W. Herrmann, *Inorg. Chem.*, **24**, 1230 (1985).
13. I. Murase, K. Hamada, and S. Kida, *Inorg. Chim. Acta.*, **54**, 1174 (1981).
14. A. Buttafava, L. Fabbrizzi, A. Perotti, A. Poggi, and B. Seghi, *Inorg. Chem.*, **23**, 3917 (1984).
15. L. Fabbrizzi, F. Forlini, A. Perotti, and B. Seghi, *Inorg. Chem.*, **23**, 807 (1984).
16. L. Fabbrizzi, L. Montagna, A. Poggi, T. A. Kaden, and L. C. Siegfried, *J. Chem. Soc. Dalton Trans.*, 2631 (1987).
17. L. Fabbrizzi, L. Montagna, A. Poggi, T. A. Kaden, and L. C. Siegfried, *Inorg. Chem.*, **25**, 2671 (1986).
18. M. P. Suh, and S. -G. Kang, *Inorg. Chem.*, **27**, 2544 (1988).
19. S. -K. Jung, S. -G. Kang, and M. P. Suh, *Bull. Korean Chem. Soc.*, **10**, 362 (1989).
20. S. -G. Kang, S. -K. Jung, and J. K. Kweon, *Bull. Korean Chem. Soc.*, **11**, 431 (1990).
21. M. P. Suh, W. Shin, S. -G. Kang, M. S. Lah, and T. -M. Chung, *Inorg. Chem.*, **28**, 1602 (1989).
22. M. P. Suh, J. Choi, S. -G. Kang, and W. Shin, *Inorg. Chem.*, **28**, 1763 (1989).
23. M. P. Suh, S. -G. Kang, and T. -M. Chung, *Bull. Korean Chem. Soc.*, **11**, 206 (1990).
24. J. W. L. Martin, J. H. Timmons, A. E. Martell, and C. J. Wills, *Inorg. Chem.*, **19**, 2328 (1980).
25. N. F. Curtis, *J. Chem. Soc. Dalton Trans.*, 347 (1974).
26. R. W. Hay and D. P. Piplani, *J. Chem. Soc. Dalton Trans.*, 1956 (1977).
27. D. -T. Wu and C. -S. Chung, *Inorg. Chem.*, **25**, 3583 (1986).
28. E. Iwamoto, T. Yokoyama, S. Yamasaky, T. Yabo, T. Kumamaru, and Y. Yamamoto, *J. Chem. Soc. Dalton Trans.*, 1935 (1988) and references therein.
29. J. H. Cotes, D. A. Hadi, S. F. Linklon, H. W. Dodgen, and J. P. Hunt, *Inorg. Chem.*, **20**, 707 (1981).
30. R. W. Hay, B. Jeragh, B. Kaitner, and B. L. Ruhl, *J. Chem. Soc. Dalton Trans.*, 1531 (1982).

Conformational Analysis of Cyclooctanone: Evidence from ^{13}C Nuclear Magnetic Resonance

Miewon Jung*

Department of Chemistry, Sungshin Women's University, Seoul 136-742. *Received January 14, 1991*

The "frozen-out" ^{13}C-NMR spectrum of cyclooctanone conformer was detected at -150℃ and is reported for the first time. The stable conformation of cyclooctanone deduced by ^{13}C-NMR measurements was a unsymmetrical boat-chair conformation.

Introduction

Among medium rings the cyclooctanone is challenging substrates for conformational studies since early attempts to elucidate the conformation of cyclooctanone were not so successful.[1] Most of the information has been obtained by X-ray diffraction studies of crystalline compounds, molecular mechanics calculations, NMR measurements, and additionally from determinations of IR spectra, and dipole moments. There are limitations for most methods, such as X-ray methods requiring appropriate crystals for conformational analysis. Spectra of medium ring compounds by IR measurements are too complex for analysis (thus earier attemps by IR spectra led to incorrect interpretations.)[2] The diplole moment measurments are largely limited to compounds which have at least two polar groups. Among these methods for analysis of conformation NMR is powerful tool although even it has limitations.

For the conformational analysis of cyclooctanone, Anet's group did an ^1H-NMR study of cyclooctanone at low temperature to freeze out a stable conformation. But they did not deduce stable conformation because of the complexity of the alkyl region in the ^1H-NMR spectrum.[3] They also reported the ^1H and ^{13}C-NMR spectra of the C_9-C_{16} cycloalkanones with changing temperature form -80℃ to -170℃, but they did not report a variable temperature ^{13}C-NMR study of cyclooctanone.[4] ^{13}C-NMR has been successfully utilized in the study of molecular conformation in solution when one deals with stable conformers or molecules where rapid interconversion occurs at ambient temperature.

^{13}C-NMR spectra are obtained in the present work at various temperature from 20℃ to -150℃ in order to find the chemical shifts at the temperature at which the dynamic process can be "frozen-out" on the NMR time scale and cyclooctanone can be observed as a stable conformation.

Experimental

Synthesis of Cyclooctanone-2,2,8,8,D_4. Cyclooctanone-2,2,8,8-D_4 was prepared from cyclooctanone (6.3 g, 0.05 mol) by heating it with D_2O (3.6 g, 0.18 mol) and NaOD (from 0.1 g Na) and freshly dried THF (5 ml) for 4 h.[5] The mixture was saturated with NaCl, the organic phase was seperated and the aqueous phase was combined, dried with

Table 1. ^{13}C-NMR Chemical Shifts of Cyclooctanone at Various Temperatures

Temp. (℃)[a]	Chemical shifts (ppm)[b]				
	C-1	C-2,8	C-3,7	C-4,6	C-5
22.0	214.20	42.04	26.03	27.82	25.08
−20.5	214.29	42.03	26.04	27.82	24.90
−58.5	215.07	42.06	25.99	27.72	24.78
−90.3	216.53	42.13	26.00	27.61	24.74
−125.0	217.78	[c]	[c]	[c]	25.45
−148.5	217.83	45.67	31.66	30.17	25.25
		39.76	21.98	26.26	

[a]The ^{13}C-NMR spectra were obtained in $CFCl_3$ from 22℃ to −90.3℃ and in CF_2Cl_2 from −125℃ to −148.5℃. [b]Chemical shifts were referenced by $CFCl_3$ (115.70 ppm) and CF_2Cl_2 (126.30 ppm). [c]The signals were broadened and overlapped at this temperature.

Na_2SO_4, filtered, and evaporated. After three such exchange treatments, the cyclooctanone was isolated, distilled (5.3 g, 81%, bp 70℃, at 3 mm), and shown to be 96% deuterated at C_2 and C_8 by NMR spectroscopy.

^{13}C-NMR ($CDCl_3$): 217.71 (s, C_1), 40.91 (p, J_{CD}=19.5 HZ, C_2, C_8). 26.82 (s, C_4, C_6), 25.19 (s, C_3, C_7), 24.44 ppm (s, C_5).

^{13}C-NMR Mesurements of Cyclooctanone. Both proton coupled and decoupled ^{13}C spectra were obtained to determine multiplicities and aid signal assignments. The ^{13}C was measured with narrow spectral width to afford good digital resolution (*ca* 0.001 ppm/point). Temperature was controlled during acquisition of spectra recorded while temperature varied by more than ± 1℃ were discarded. All chemical shifts reported were referenced to Me_4Si (0.00 ppm) either directly for ^{1}H-NMR spectra or indirectly for ^{13}C spectra by using solvent signals for reference: $CDCl_3$(77.00 ppm) as a triplet, CF_2Cl_2 (126.30 ppm) as a triplet, $CFCl_3$ (115.70 ppm) as a doublet.

^{13}C-NMR spectra of unlabeled and labeled cyclooctanone samples were recorded from 20℃ to −150℃ at every 20℃ interval and the entire spectra were measured with a width of 20000 Hz anf 65000 data points. The solvents used were $CFCl_3$ (from 20℃ to 90℃) and CF_2Cl_2 (from −120℃ to −150℃).

Results and Discussion

The chemical shifts at various temperatures are listed in Table 1. Carbonyl and C-5(δ) carbons were easily assigned by the chemical shift and peak intensity in the room temperature ^{13}C-NMR spectrum. The chemical shift of the carbonyl carbon is expected to occur in the most downfield position in the ^{13}C-NMR spectrum, and its peak intensity as a quaternary carbon is expected to be weak. The peak intensity of the C-5(δ) carbon is weaker than that of the other methylene carbons because it has no equivalent methylene carbon. The most deshielded peak in the alkyl region is assigned to C-2 and C-8, since the carbonyl group exerts the greatest deshielding effect on the α carbons.

Attempts to sort out assignments of the other methylene carbon peaks at room temperature led to use of the specifically deuterated cyclooctanone. In the case of C-2 deuteration, for example, the assignment of chemical shifts of all methylene carbons was easily achived. The assignments can be explained by the following: (1) complete deuteration on the C-2 and C-8 positions gives rise to splitting of the ^{13}C signal at 41.47 ppm from a singlet to a pentet and to reduced signal intensity; (2) C-3 and C-7, C-4 and C-6 carbons are assigned according to the different intrinsic isotope shifts. The pairs of nondeuterated methylene are differently shielded by the intrinsic isotope effect with the larger effect expected for C-3 and C-7 carbons. The upfield isotope shift on the signal at 26.03 ppm was 0.194 ppm, which is larger than that on the signal at 27.79 ppm (0.094 ppm) in the ^{13}C-NMR spectrum of a 2:1 mixture of cyclootanone-2,2,8,8-D_4 (2) and

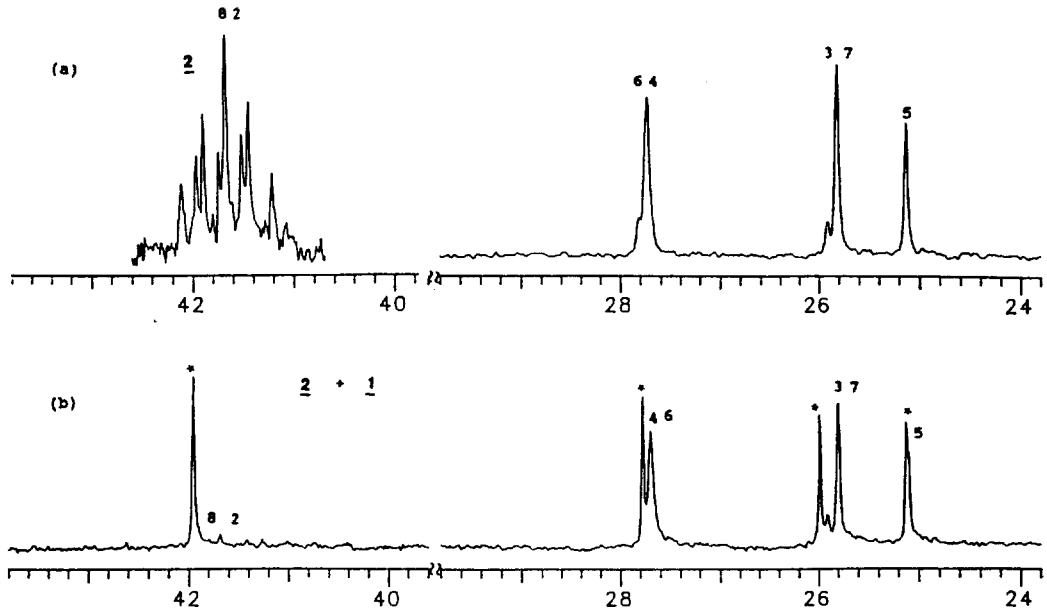

Figure 1. (a) The ^{13}C NMR Spectrum of Cyclooctanone-2,2,8,8-D_4 (2) at 18.5~, (b) The ^{13}C NMR Spectrum of a 2:1 Mixture of Cyclooctanone-2,2,8,8-D_4 (2) and Cyclooctanone (1) at 18.5~ (asterisks indicate peaks of unlabeled cyclooctanone).

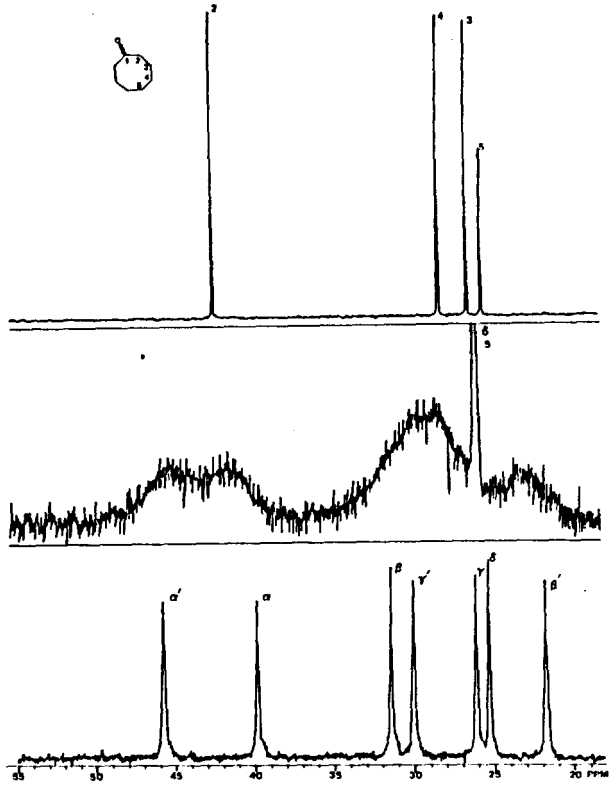

Figure 2. ^{13}C-NMR spectra of cyclooctanone at various temperature.
(a) 5 peaks are present in a ^{13}C-NMR spectum due to rapid equilibrium at 22℃ (only the H peaks in the alkyl region are shown). (b) Equivalent methylene carbons are broadened except carbonyl and C-5 carbons at −125℃. (c) 8 carbon peaks are well resolved since exchange is slow enough at −148.5℃

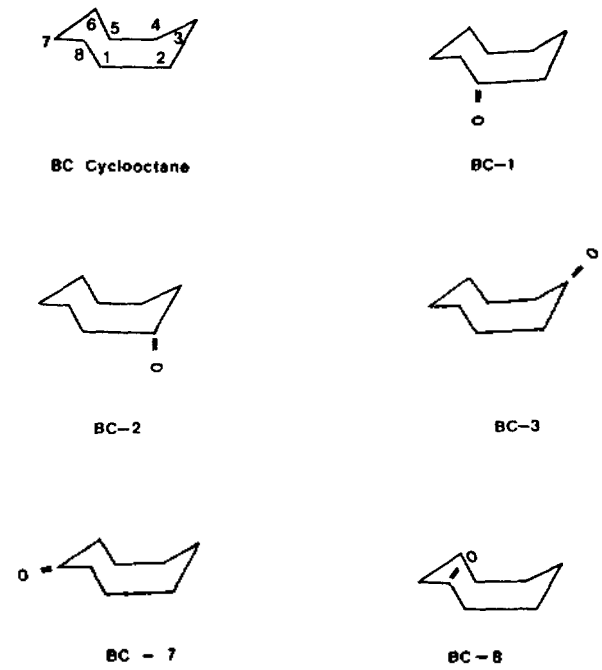

Figure 3. Boat-chair cyclooctanone conformations from replacement of methylene group by carbonyl group.

cyclooctanone (1) as shown in Figure 1 (The isotopically shifted signals are somewhat broader than those for unlabeled cyclooctanone, presumably due to unresolved coupling to deuterium). Thus, the 26.03 ppm signal is assigned to C-3 and C-7 carbons and 27.79 ppm to C-4 and C-6. The remaining signal is for the δ carbon (C-5) which shows no resolved isotope effect. The ^{13}C signal assignments of cyclooctanone by deuterium substitution agree with those of silverstein.[6]

The structure of cyclooctanone on the NMR time scale at room temperature was known as a conformational average having net C_{2v} symmetry which has two planes and an axis of symmetry as in the plannar representation of cyclooctanone.[7] The C_{2v} symmetry can be explained by any combination of rapidly intercoverted conformers.

The ^{1}H-decoupled ^{13}C spectrum of cyclooctanone above −58.5℃ in Table 1 has sharp singlet signals, shows brodening at −90℃ in the signal at 26.0 ppm, has broad signals also at 28.50 and 43.00 ppm at −125℃, and finally has eight sharp resonance signals at −150℃. The ^{13}C-NMR spectra of cyclooctanone at several temperatures are shown in Figure 2 for comparison. The ^{13}C signals for cyclooctanone at −125 ℃ were broad except for the carbonyl and δ carbons; the rate of exchange was starting to slow down at this temperature but the ^{13}C signals were still broadened due to not having reached the point of slow dynamic process at this temperature. Since a dynamic process is slow enough on the NMR time scale, previously averaged methylene carbons show seperate signals at low temperature.

The ^{13}C signals of the low temperature ^{13}C-NMR spectrum at −148.5℃ can be readily assigned since the averaged methylene signals at room temperature will split symmetrically to upfield and downfield directions from the original position. For instance, the most deshielded pair at 39.76 and 45.67 ppm (C-2 and C-8) can be assigned to α and α′ carbons, among the eigtht methylene carbons, get the greatest deshilding effect due to the carbonyl group. The signals at 31.66 and 21.98 ppm can be assigned to β and β′ (C-3 and C-7) in the low temperature ^{13}C-NMR spectrum because the ^{13}C signal of β carbons appear at the averaged position (26.03 ppm) at room temperature. The peaks or γ and γ′ carbons (C-4 and C-6) are assigned at 30.17 and 26.26 ppm in the low temperature ^{13}C-NMR spectrum which are averaged at 27.82 ppm in the room temperature NMR spectrum. The signals of carbonyl and δ (C-5) carbons were not split at low temperature. Thus, carbonyl carbons, C-1 (217.83 ppm) and C-5 (25.25 ppm) can be fixed.

The carbonyl and δ carbon lines remained unchanged at all temperature in agreement with the presence of a single kind of conformation (a chiral conformation and its mirror image are taken to be the same kind of conformation). On the other hand, the α, β, γ carbon resonances are split into 1:1 doublets (actually pairs of singlet) at −148.5℃ as shown in Figure 2. The splitting of signals is consistent with presence of a single boat-chair conformation which lacks C_2 or C_s symmetry (*i.e.*, no axis, or no plane of symmetry coincident with the Cδ-C=O plane). If the conformation had any symmetry elements, no change would occur in the ^{13}C-NMR spectrum even at low temperature since the presence of symmetry would result in identical resonances for equivalent

methylene carbons interchanged by a symmetry operation. Nuclei interchanged by a symmetry operation have the same chemical and electronic environments.[8] Figure 3 shows the five possible types of boat-chair cyclooctanone resulting from replacement of a CH_2 in cyclooctane. Replacement of a CH_2 that lies on the symmetry element gives a structure which retains the symmetry. Thus, replacement of CH_2 by CO at C-3 or C-7 gives BC-3, BC-7 which still has C_s symmetry. However, BC-1, BC-2, and BC-8 are all unsymmetrical boat-chair (C_1 point group). Replacement at the remaining positions (not shown in Figure 3) generates structures which are enantiomeric with BC-1, BC-2 and BC-8: BC-1 and BC-5, BC-2, and BC-4, and BC-8 and BC-6 are enantiomeric pairs. If the cyclooctanone existed as crown or BC-3 or BC-7 conformation in Figure 3, the signal of α, β, and γ could not be seperated simply be lowering the temperature.

Another interesting result is that the difference of chemical shift for the C-3, C-7 pair (β and β′ environments) is the largest of the methylene pairs, which can be explained by the location of the carbonyl group in the BC-1 boat-chair conformation. The location of carbonyl group in either the BC-3 or BC-7 conformers would generate a plane of symmetry, *i.e.*, the C_s symmetry group, and thus no seperation of C-3 and C-7 would occur at low temperature. The location of the carbonyl in either the BC-2 or BC-8 conformers creates unsymmetrical boat-chair conformers, but the chemical shift seperation between C-3 and C-7 would not be as large as the seperation for BC-1 conformer. According to the calculations of strain energy done by Allinger *et al.*,[9] the cyclooctanone boat-chair conformation has the lowest conformational strain energy among the possible conformations since the carbonyl group remains at favorable site (position 1 or 5) to relieve nonbonded interactions and eclipsing strain present in cyclooctane.[10]

From these results, the existence of a single kind of conformation which must be unsymmetrical (boat-chair conformation) is evident, which is consistent Allinger's MM2 force field calculation. Several cyclooctanone derivatives and related compounds had their structures determined by X-ray diffraction. Most of these compounds had boat-chair conformations.[11]

References

1. N. G. Allinger and S. Greenberg, *J. Am. Chem. Soc.*, **81**, 5733 (1951).
2. M. Hanack, "Conformation Theory"; Academic Press, New York (1965).
3 F. A. L. Anet, M. St. Jacques and P. M. Henricks, *Intrascience Chem. Rep.*, **4**, 251 (1970).
4. F. A. L. Anet, A. K. Cheng, and J. Krane, *J. Am. Chem. Soc.*, **95**, 7877 (1973).
5. F. C. Brown and G. J. Boxter, *Aust. J. Chem.*, **31**, 327 (1978).
6. R. M. Silverstein, G. C. Bassler and T. C. Morrill "Spectrometric Identification of Organic Compounds", 4th ed., John Wiley & Sons, New York, p. 257 (1981).
7. F. A. L. Anet "Conformational Analysis: Scope and Present Limitation", Academic Press, p. 15 (1971).
8. E. B. Whipple, G. N. Chmurny, and G. C. Andrews, *Org. Mag. Reson.*, **15**, 324 (1981).
9. N. L. Allinger, M. T. Tribble, and M. A. Miller, *Tetrahedron*, **28**, 1173 (1972).
10. F. A. L. Anet, M. St. Jacques, P.M. Henricks, A. K. Cheng, J. Krane, and L. Wong, *Tetrahedron*, **30**, 1629 (1974).
11. H. B. Burgi and J. D. Dunitz, *Helv. Chem. Acta.*, **49**, 2492 (1966).