

NMR Spectral Studies of Some Six–Membered and Seven–Membered Saturated Heterocyclic Compound t[3]–Ethyl-r[2],c[7]-Diphenylhomopiperazin–5–One

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Abstract

Some six and seven membered saturated hetero cyclic compounds were prepared. ^1H NMR were recorded in $\text{DMSO} - d_6$. The chemical shifts were compared with those in CDCl_3 . The COSY, NOESY and ^{13}C - ^1H correlation spectra had been recorded to assign the signals unambiguously. The coupling constant of benzylic proton with one of the vicinal proton was found to be zero. The buffering effect of alkyl groups was also studied. The chemical shift values, area of the signals, multiplicity, COSY and NOESY spectra were used to assign the signals. Further COSY and NOESY and $^{13}\text{C} - ^1\text{H}$ correlation spectra were also used. The solvent effect, concentration effect, and temperature effect were also studied using $\text{DMSO} - d_6$ and CDCl_3 . α -effect, and polar nature of the neighbouring group were also studied.

Keywords: Assignment, Correlation, Chemical shift, Isopropyl, Multiplets, NOE, Peak, Signal

1. Introduction

Ever since Barton pointed out the importance of conformational analysis, there has been a rapid development in the conformational analysis of various systems. Nuclear magnetic resonance spectroscopy is a powerful tool for such analysis. ^1H , ^{13}C , ^{15}N , ^{17}O and ^{33}S are the nuclei used for analysis.^{1–15} Nowadays 2-D -NMR spectroscopy is also used for structural diagnosis.

2. ^1H NMR Spectroscopy

The important measurables in the ^1H NMR spectra are Chemical Shifts and Constants.

2.1 ^1H Chemical Shift

Chemical shift of a proton is affected by the electron density around it; the higher the electron density, the higher the field of absorption. The chemical shift s for CH_3I ,

CH_3Br , CH_3Cl , and CH_3F are 2.16, 2.68, 3.05 and 4.26 ppm respectively. The values are in line with the inductive effects of the halogen atoms¹⁶.

2.2 Proton-Proton Coupling Constants

Coupling constants are of immense use in configurational and conformational studies. Vicinal coupling constant between two protons depends on their relative positions. For example, in 1,2 – disubstituted ethenes, the vicinal coupling constant between the olefinic protons is always larger for trans isomer 12 than for cis isomer 13¹.

Sesquiterpene ether [-] kessane[25] was isolated from *valeriana officinalis*²; *heracleum dissectum*³ *bothriochloa intermedia*⁴. *B. bladhi* and various *Sonecia* species⁵. Lankhorst et al.⁶ have recorded 600 MHz spectrum of 25. From the observed vicinal coupling constants the conformations of the cyclopentane and cycloheptane rings in 25 have been assigned.

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3. ¹³C NMR Spectroscopy

3.1 ¹³C Chemical Shift

¹³C chemical shift depends on many factors. Lambert et al.⁷ have studied the effect of heteroatom in mono-heterocyclohexanes 26 on the shifts of ring carbons. The α - shift is a steep function of the electronegativity of the heteroatom X. An increase by one unit in electronegativity produces a downfield shift of about 50 ppm. However, the effect of hetero atom electronegativity on β and γ carbons is small.

3.2 ¹³C- ¹H Coupling Constants

The ¹³C- ¹H-coupling constants are useful parameters in the study of organic molecules.

One bond coupling constant $^1J_{CH}$ is given by equation 9,^{8,9} where %s represents the percentage 's' character of the carbon hybrid orbital participating in the C-H bond

4. Two - Dimensional NMR Spectroscopy

In one dimensional NMR spectrum, the abscissa corresponds to the frequency axis and ordinate gives the intensities of the signals. In a two dimensional NMR spectrum, both the abscissa and the ordinate are frequency axes, with the intensities constituting a third.

5. Homonuclear Correlation Spectroscopy [HOMOCOSY]

In this type of spectrum, ¹H chemical shifts along both frequency axes are correlated with each other. The ¹H spectrum appears along the diagonal as contours responding peak intensities. The off-diagonal contours are the cross peaks. A horizontal line drawn from a cross peak will intercept a contour on the diagonal, and a vertical line from the same cross peak will intercept another contour on the diagonal with which the first diagonal contour is coupled. Thus, we can assign signals unambiguously.

6. Scope of the Present Investigation

In the present study, DAERM method and Altona's equation are used to calculate torsional angles from the

reported proton - proton vicinal coupling constants of the following compounds:

$$r(2),c(6) - \text{diphenoxan-4-one} \quad (41)$$

$$t(3)\text{-Methyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (42)$$

$$t(3)\text{-Ethyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (43)$$

$$t(3)\text{-isopropyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (44)$$

$$3,3\text{-dimethyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (45)$$

$$N\text{-Methyl-t}(3)\text{-Methyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (46)$$

A method is proposed to find whether the vicinal coupling in a -CHX - CH₂ - system represents a single conformation or an equilibrium between two or more conformations. This method is applied in conformational analysis of the following compounds:

$$N\text{-Phenylcarbamoyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (53)$$

$$N\text{-Phenylcarbamoyl-t}(3) - \text{methyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (54)$$

$$N\text{-Phenylcarbamoyl-t}(3) - \text{ethyl-r}(2),c(6) - \text{diphenylpiperidin-4-one} \quad (55)$$

N-Phenylcarbamoyl-t(3) - isopropyl-r(2),c(6) - diphenylpiperidin-4-one (NOSEY spectra have been recorded for 59 and 60.

¹H NMR spectra have been recorded for t(3)-methyl-r(2),c(7)-diphenylhomopiperazin-5-one (61), t(3)-ethyl-r(2),c(7)-diphenyl homopiperazin-5-one (62) and t(3)-isopropyl-r(2),c(7)-diphenyl homopiperazin-5-one (63) have been recorded at 500MHz in DMSO- d₆. The various chemical shifts and coupling constants have been extracted. These values are compared with those in CDCl₃. The solvent effect is discussed.

¹H NMR spectra have been recorded for compound 62 at 300K and 333K. The temperature effect is discussed. ¹H NMR spectra have been recorded for compound 63 at 300K and 333K. The temperature effect is discussed.

COSY, NOESY and ¹³C - ¹H correlation spectra have been recorded for compounds 61-63. These are used to assign the signals unambiguously.

7. Result and Discussion

t[3] - Ethyl -r[2],c[7]- diphenylhomopiperazin -5 - one[62]

^1H NMR spectrum of 62 in DMSO $-d_6$ at 500 MHz is shown in Plate – 7. The NOESY spectrum has also been recorded, and this is shown in Plate – 8

7.1 Assignment of Signals

The triplet at 0.72 ppm corresponds to three protons and has a coupling constant of 7.3 Hz. Obviously, this is due to the methyl proton. The multiplet at 1.41 ppm corresponds to two protons. This must be due to CH_2 of ethyl group.

There are two peaks for the ortho aromatic protons at 8.06 and 7.96 ppm. Each of these peaks corresponds to 2 protons. These are due to ortho protons of the phenyl rings at C- 2 and C- 7. For other aromatic protons, a multiplet is seen at 7.58 ppm. This corresponds to six protons.

In the NOESY spectrum shown in Plate – 8, the CH_2 of ethyl group at 1.41 ppm shows weak NOE with the peak at 3.79 ppm. Therefore, it should be due to H-3.

The ortho aromatic proton signal at 8.05 ppm gives NOE with the peak at 3.79 ppm. Therefore, this signal is due to the ortho protons at C -3. The other ortho aromatic proton signal at 7.96 ppm gives NOE with the peak at 3.90 ppm. Therefore, the peak at 3.90 ppm is due to H- 6a.

The ortho aromatic protons at C -2 can only show NOE with H – 3 and H-2. Similarly, the ortho aromatic protons at C -7 can show NOE with H – 6a and H -7. The ortho aromatic protons at 8.05 ppm show NOE with the proton at 4.88 ppm. Therefore, the signal at 4.88 ppm is due to H -2.

The ortho protons at 7.96 ppm show NOE with proton at 5.11 ppm. Therefore, the signal at 5.11 ppm should be

Table 1. The chemical shift values⁶ in DMSO $-d_6$ and CDCl_3 , 114

Proton	DMSO - d_6 [ppm]	CDCl_3 [ppm]
NH(amino)	11.31[d]	2.02[s]
NH (lactum)	10.09[d]	5.90[s]
Aromatic	8.05[d] 7.96[d] 7.58[m]	7.32[m]
H - 7	5.11[s]	4.11[d]
H- 2	4.88[t]	3.77[d]
H - 6 _a	3.90[t]	3.15[q]
H - 3	3.79[s]	3.66[m]
H - 6 _c	2.82[d]	2.65[d]
CH_2 (Et)	1.41[m]	1.11[m]
CH_3 (Et)	0.72[t]	0.85[t]

Table 2. The chemical shift values of different carbons⁶

Carbon	Chemical shift [ppm]
Ipsso	136.6
	135.7
	130.4
Aromatic	130.2
	129.7
	129.6
C - 2	64.2
C - 7	60.4
C - 3	52.8
C - 6	46.1
CH_2 (Et)	18.5
CH_3 (Et)	11.7

due to H -7. This is because the ethyl group at C -3 should give upfield shift to H -2.

8. References

1. Thomas WA. Nuclear magnetic resonance spectroscopy. Annu Rev. 1968; 1:43.
2. Bladon P. Nuclear magnetic resonance spectroscopy. Annu Rev. 1969; 2:1.
3. Thomas WA. Nuclear magnetic resonance spectroscopy. Annu. 1970; 3:91.
4. Anet FAL, Anet R. Determination of organic structure from physical methods. Nachol FC, editor. New York: Academic Press. 1971; 3:343.
5. Anet FAL, Anet R. Dynamic nuclear magnetic resonance spectroscopy. Jackman LM, Cotton FA, editor. New York: Academic Press. 1975; 3:543.
6. Lukas G. Bull Soc Chem. 1972; 351.
7. Tanable M. Biosynthesis. Geissman TA, editor. Special-ist periodical reports. London: The Chemical Society; 1973.
8. Lambert JB, Featherman SI. Chem Rev. 1975; 611.
9. Levy GC, Nelson GL. Carbon - 13 nuclear magnetic resonance for organic chemists. New York: Wiley - Interscience, New York; 1972.
10. Hore PJ, J Magn Reson. 1985; 561.
11. Stothers JB. Carbon - 13 NMR Spectroscopy. New York: Academic Press; 1972.
12. Wasylshen RE, Schaefer T. Can J Chem. 1973; 51:3087.
13. Eliel EL, Manoharan M. Magn Reson Chem. 1985; 23:225.
14. Crandall JK, Centeno MA. J Org Chem. 1979; 44:1183.
15. Crandall JK, Centeno MA, Brreson S. J Org Chem. 1979; 44:1186.