Variable-temperature NMR studies of benzimidazol-2-yl-quinoline

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Abstract: Method of variable-temperature of 1H-NMR as well as 13C-NMR can be used to determine the location of coalescence temperature on the NMR spectrum. To solve the Gutowsky-Holm equation, the activation rotation-energy can be computed. Hence, for the synthesized compound of benzimidazol-2-yl-quinoline, we observed the coalescence temperature of H14 and H13 located at 293K on 1H-NMR spectrum but the calculated activation rotation-energy was 13.38 kcal/mole. Meanwhile, the coalescence temperature of H12 and H15 was at 313K on 1H-NMR spectrum but the activation rotation-energy was 13.74 kcal/mole. Additionally, the coalescence temperature of C13 and C14 on 13C-NMR spectrum was also at 333K as well as the calculated activation rotation-energy was 14.66 kcal/mole.


Key words: NMR spectrum, Gutowsky-Holm equation

1. Introduction

Natural anti-cancer compounds, for instance, berberine, cryptolepine and camptothecin are basically poly-ring structured. Neidle et al. (2003) reported the mechanism of the anti-cancer for some of poly-ring compounds may have the stability if combining with DNA, such as Imidazole ring. Compounds with benzimidazole group can be bonded to DNA’s minor groove [1-5]. The temperature and the rotation energy of the molecules can be observed through Variable-temperature NMR [6-7]. For molecule planar structure, when it does not free to rotate at the temperature below the bearing range of DNA, the structure can be easier bonding to DNA. This report demonstrates the temperature and energy of benzimidazol-2-yl-quinoline in rotation via using variable temperature of 1H-NMR and 13C-NMR.

2. Material and Methods

Quinoline-2-carboxylic acid (20 mmol, 3.4634 g), 1,2-phenylenediamine (20 mmol, 2.1628 g), and polyphosphoric acid (PPA, 20 ml) were added to a flask. The mixture was heated at 200 ºC for 4 h. After cooling to room temperature, the residue was slowly added to deionized water (500 ml) with stirring. The solid was collected by suction filtration and purified by column chromatography using ethyl acetate/hexane (1:1) as eluent. Colorless crystals of benzimidazol-2-yl-quinoline were obtained in 85% yield. 1H and 13C NMR spectra were recorded on the Bruker 500 MHz NMR spectrometers in DMF-d7.

3. Results and Discussion

3-1. 1H-NMR spectrum analysis

The C9-C10 bond is a single bond of benzimidazol-2-yl-quinoline. At the low temperature, single bond would not free rotate but compose to be stable conformational molecule which is shown in Figure 1.

Figure 1. (A) Structure of benzimidazol-2-yl-quinoline, (B) Rotation of benzimidazol-2-yl-quinoline

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In Figure 2, it depicts that the characteristic of variable-temperature of $^1$H-NMR at low temperature. When the temperature is below 263K, benzimidazol-2-yl-quinoline is a stable conformational molecule.

The spectra of $^1$H-NMR is listed as follows: 8.72 ppm (H$_8$, d), 8.63 ppm (H$_2$, d), 8.20 ppm (H$_6$, d), 8.15 ppm (H$_7$, d), 7.93 ppm (H$_3$+H$_12$, m), 7.77 ppm (H$_15$+H$_4$, m), 7.41 ppm (H$_{13}$, t), 7.35 ppm (H$_{14}$, t).

In benzylimidazole, H$_{12}$ and H$_{13}$ were located at down field but H$_{15}$ and H$_{14}$ at up field for N$_1$ is an electron-donating amine group and N$_2$ is electron-withdrawing imine group. So H$_{15}$ and H$_{14}$ have relative high electron density compares to H$_{12}$ and H$_{13}$ which located at down field. As the temperature rises to 293K, the single bond of C$_9$-C$_{10}$ starts to rotate slowly. The activation rotation-energy is strong enough to make the chemical-shift of H$_{13}$ and H$_{14}$ being overlapped and leads to a phenomenon of broad (Figure 2). According to Gutowsky-Holm equation ($\Delta G = 0.00457T_c \left(9.97 + \log \left(\frac{T_c}{\Delta \delta}\right)\right)$), coalescence temperature ($T_c$) [8] is the combination temperature of 2 peaks where $\Delta \delta$ is the difference between the two peaks as the chemical-shift. The coalescence temperature of H$_{14}$ and H$_{13}$ is located at 293K. It activation rotation-energy is 13.38
kcal/mole. However, at this temperature, H\textsubscript{12} and H\textsubscript{15} cannot be distinguished. As the temperature rises to 313K, the speed of rotation starts to increase. It makes the chemical-shift of H\textsubscript{12} and H\textsubscript{15} being overlapped. As Figure 2 is high variable temperature of \textsuperscript{1}H-NMR. Here the activation energy of rotation is 13.74kcal/mole. So 313K should be the coalescence temperature of H\textsubscript{12} and H\textsubscript{15}. H\textsubscript{9,10} and H\textsubscript{12,15} intensity would be enhanced as the temperature goes up. The H of pyridine group may not even be affected into change on benzylimidazole group at 353K. When the temperature goes up to 363K, the broad are appeared of pyridine group. The observation results should be affected on the fast rotation of benzylimidazole group. Because of the limited NMR machine, we are only to be able to work up to 363K.

3-2. \textsuperscript{13}C-NMR spectrum analysis

A stable conformational molecule has been formed at low temperature. Figure 3 shows the \textsuperscript{13}C-NMR spectrum at low variable temperature. Temperature control is from 223K to 293K.

![Figure 3. Variable-temperature 13C-NMR of benzimidazol-2-yl-quinoline. (below) low temperature, (top) high temperature](image-url)
When the temperature is 223K, the spectrum of $^{13}$C-NMR is as follows: 151.5 ppm(C9), 149.9 ppm(C10), 149.3 ppm(C11), 145.1 ppm(C12), 138.7 ppm (C6), 136.8 ppm (C16), 131.8 ppm (C7), 130.0 ppm (C2), 129.3 ppm (C3), 129.2 ppm (C4), 125.0 ppm (C13), 123.2 ppm (C14), 121.9 ppm (C15), 120.1 ppm (C8), 113.2 ppm (C13). As in Figure 3 (top), C12 and C13 are in down field but C14 and C15 are in up filed. As the temperature rises from 223K to 293K, the intensity peaks of C16 of pyridine and H of imidazole ring would be made moved to downfield when the density of peak was reducing in benzimidazole group. However, the reducing rate of C10 is relatively less than other locations of C. The effect from rotation to the C10 is thus smaller because it is the pivot point of rotation. From the spectrum of high variable temperature of $^{13}$C-NMR (As figure 3 below), we could know the coalescence temperature is located at 333K of benzimidazole group. By solving Gutowsky- Holm equation, rotation of C13 and C14 in benzimidazole group is about 14.66kcal/mole. Moreover, the intensity peaks of C11, C16, C12 and C15 start getting broad at 313K, and the peak disappeared at 323K. Even when the temperature goes up to 363K, the peaks of C11, C16, C12 and C15 are all invisible. The chemical-shift of C11, C16, C12 and C15 parts too far to be combined into a new peak at 363K. In contrary, the chemical-shift of C13 and C14 is less apart from each other. Therefore, a new peak has been combined at 323K and its intensity is increased by raising temperature. The chemical-shift of C10 would be moved to downfield when the density of peak was affected by raising temperature and closer C9. The N of pyridine and H of imidazole ring would be made strong interaction with each other which may cause part of N carrying with positive charges. However, the electron density of C10 increases for the part of N1, C10-N2 carrying with negative charge and causing chemical-shift of C13 at up field. But the rotation rate goes up as the temperature rising and some parts of negative charges fell over slowly on N1 and N2. C10 carrying with negative charge can turn into quaternary-C from tertiary-C. Meanwhile, the chemical-shift of C10 would have moved toward downfield.

**4. Conclusions**

The benzimidazol-2-yl-quinoline was synthesized and we found the lowest coalescence temperature under 293K and activation rotation-energy was 13.8kcal/mole. The investigation turns out that the compounds benzimidazol-2-yl-quinoline potentially at 293K can be easy bonded with DNA.

**Acknowledgements**

This research was supported by the National Science Council of the Republic of China.

**References**


