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

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Abstract: Method of variable-temperature of ^{1}H-NMR as well as ^{13}C-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 H_{14} and H_{13} located at 293K on ^{1}H-NMR spectrum but the calculated activation rotation-energy was 13.38 kcal/mole. Meanwhile, the coalescence temperature of H_{12} and H_{15} was at 313K on ^{1}H-NMR spectrum but the activation rotation-energy was 13.74 kcal/mole. Additionally, the coalescence temperature of C_{13} and C_{14} on 13C-NMR spectrum was also at 333K as well as the calculated activation rotation-energy was 14.66 kcal/mole.
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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 ^{1}H-NMR and ^{13}C-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 ^{o}C 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. ^{1}H and ^{13}C NMR spectra were recorded on the Bruker 500 MHz NMR spectrometers in DMF-d^{7}.

3. Results and Discussion

3-1. ^{1}H-NMR spectrum analysis

The C_9-C_{10} 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.

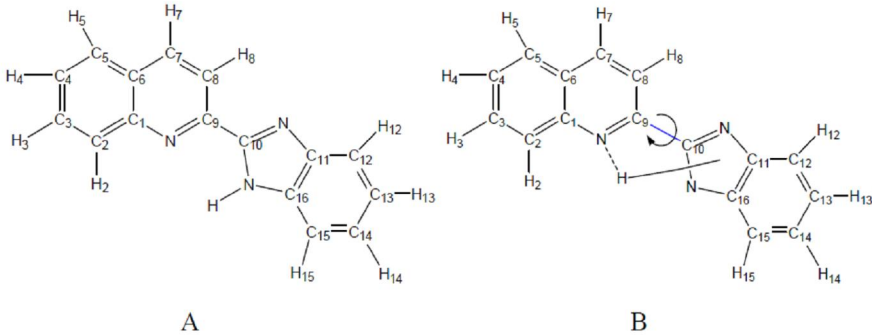

Figure 1. (A) Structure of benzimidazol-2-yl-quinoline, (B) Rotation of benzimidazol-2-yl-quinoline

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_5, d), 8.15 ppm (H_7, d),7.93 ppm (H_3+H_{12}, m), 7.77ppm (H_{15}+H_4, m), 7.41 ppm, (H_{13}, t), 7.35 ppm, (H_{14}, t).

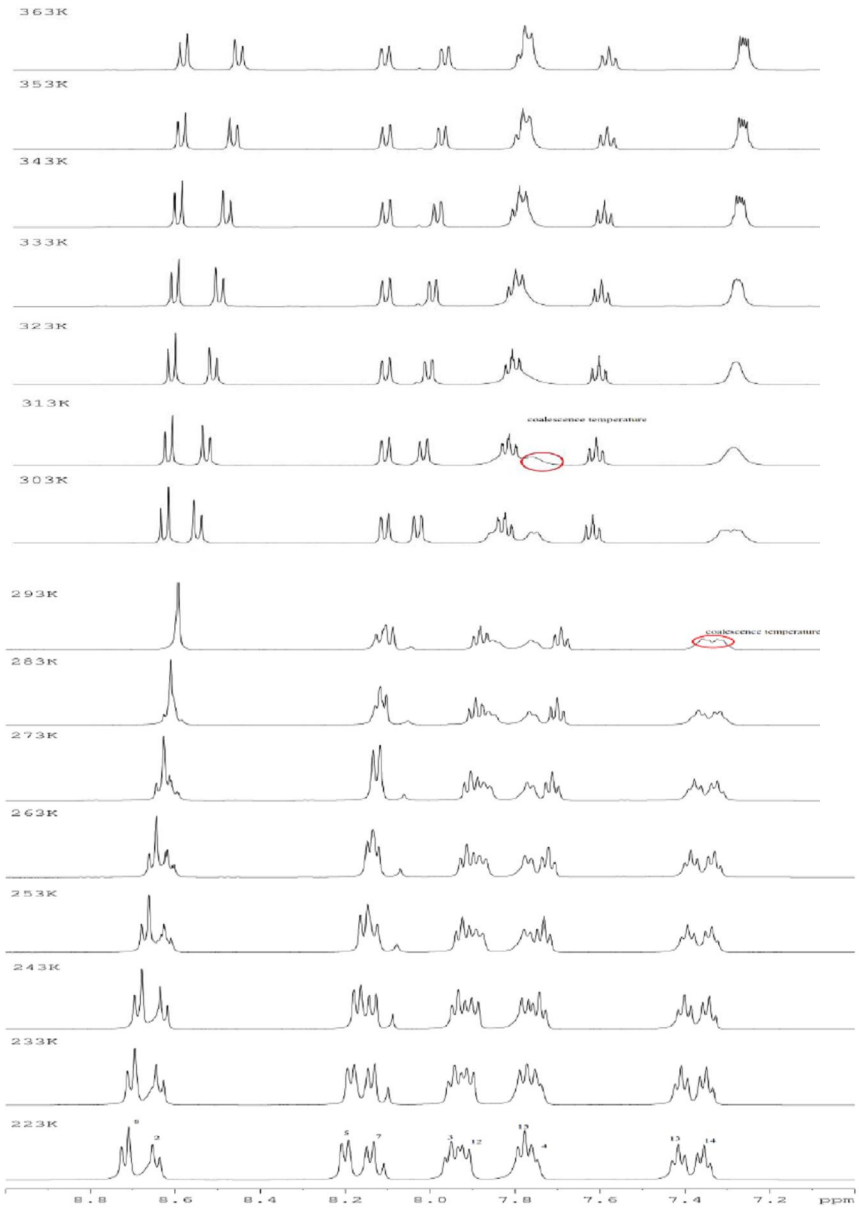

Figure 2. Variable-temperature ^{1}H-NMR of benzimidazol-2-yl-quinoline

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 ($\Delta G = 0.00457 T_C \left(9.97 + \log\left(\frac{T_C}{\Delta\delta} \right) \right)$, coalescence temperature (Tc) [8] is the combination temperature of 2 peaks where Δδ 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_{12} and H_{15} cannot be distinguished. As the temperature rises to 313K, the speed of rotation starts to increase. It makes the chemical-shift of H_{12} and H_{15} being overlapped. As Figure 2 is high variable temperature of ^{1}H-NMR. Here the activation energy of rotation is 13.74kcal/mole. So 313K should be the coalescence temperature of H_{12} and H_{15}. $H_{9\text{-}10}$ and $H_{12\text{-}15}$ 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. ^{13}C-NMR spectrum analysis

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

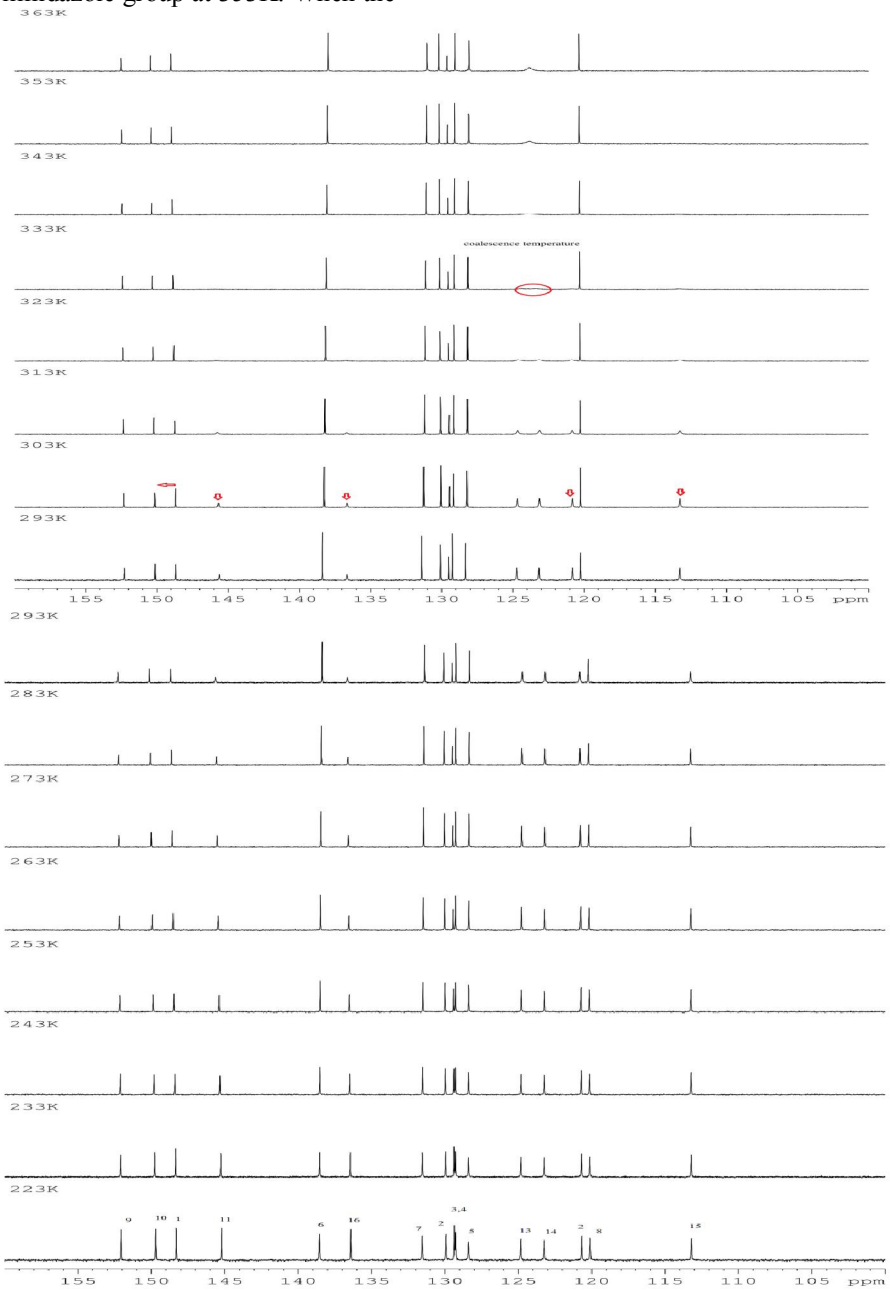

Figure 3. Variable-temperature 13C-NMR of benzimidazol-2-yl-quinoline. (below) low temperature, (top) high temperature

When the temperature is 223K, the spectrum of ^{13}C-NMR is as follows: 151.5 ppm(C_9), 149.9 ppm(C_{10}), 149.3ppm (C_1), 145.1 ppm(C_{11}), 138.7 ppm (C_6), 136.8 ppm (C_{16}), 131.8 ppm (C_7), 130.0 ppm (C_2), 129.3 ppm (C_3), 129.2 ppm (C_4), 125.0 ppm (C_{13}), 123.2 ppm (C_{14}), 121.9 ppm (C_{12}), 120.1 ppm (C_8), 113.2 ppm (C_{15}). As in Figure 3 (top), C_{12} and C_{13} are in down field but C_{14} and C_{15} are in up filed. As the temperature rises from 223K to 293K, the intensity of C (C_{11}, C_{16}, C_{13}, C_{14}, C_{12}, C_{15}, C_{10}) is reducing in benzylimidazole group. However, the reducing rate of C_{10} is relatively less than other locations of C. The effect from rotation to the C_{10} 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 benzylimidazole group. By solving Gutowsky- Holm equation, rotation of C_{13} and C_{14} in benzylimdazole group is about 14.66kcal/mole. Moreover, the intensity peaks of C_{11}, C_{16}, C_{12} and C_{15} start getting broad at 313K, and the peak disappeared at 323K. Even when the temperature goes up to 363K, the peaks of C_{11}, C_{16}, C_{12} and C_{15} are all invisible. The chemical-shift of C_{11}, C_{16}, C_{12} and C_{15} parts too far to be combined into a new peak at 363K. In contrary, the chemical-shift of C_{13} and C_{14} 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 C_{10} would be moved to downfield when the density of peak was affected by raising temperature and closer C_9. 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 C_{10} increases for the part of N_1- C_{10}-N_2 carrying with negative charge and causing chemical-shift of C_{10} at up field. But the rotation rate goes up as the temperature rising and some parts of negative charges fell over slowly on $N_1$and N_2. C_{10} carrying with negative charge can turn into quaternary-C from tertiary-C. Meanwhile, the chemical-shift of C_{10} 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.

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