ANALYSIS OF NMR SPECTRA OF SUBSTITUTED 4-AZIDO-2-METYLQUINOLINES

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TÓM TẮT

PHÂN TÍCH PHỔ NMR CỦA CÁC HỢP CHẤT 4-AZIDO-2-METYLQUINOLIN THẾ

Các 4-azido-2-metylquinolin thế khác nhau đã được tổng hợp bằng phản ứng của dẫn xuất 4-cloro-2-metylquinolin thế tương ứng. Phổ ^{1}H và ^{13}C NMR của các hợp chất azide đã ghi và được thảo luận. Các tín hiệu cộng hưởng từ trong phổ NMR của chúng chỉ ra mối quan hệ giữa cấu trúc và vị trí của nhóm thế. Các kiểu ghép cặp spin-spin đã phản ánh các kiểu thế khác nhau ở vòng benzen của quinolin.
Keyword(s): 4-azido-2-metylquinoline, 4-cloro-2-metylquinoline.

1. INTRODUCTION

The compounds containing azido group have particular importance in organic synthesis, and itself have biological activity. The azido derivatives are one of two important precursors in the synthesis of heterocylic aromatic ring 1,2,3-triazole through click reaction with alk-1-ynes [1-6].

The synthetic method of substituted 4-azido-2-metylquinolines **3a-j** has been reported previously [7]. In this article, we announced that those 4-azido derivatives were synthesized by reaction of corresponding 4-chloro ones with sodium azide in DMF as solvent. There are several discussions herein about the influence of structural factors to the positions of resonance signals in their ^{1}H and ^{13}C NMR spectra of these azido derivatives.

II. EXPERIMENTAL PART

Substituted 4-azido **3a-j** (*Scheme 1*) were synthesized in bellow procedure [7] from 2-metylquinolin-4-ones **1a-j**, respectively, through corresponding 4-chloroquinoline derivatives [8]. Their ^{1}H and ^{13}C NMR spectra was

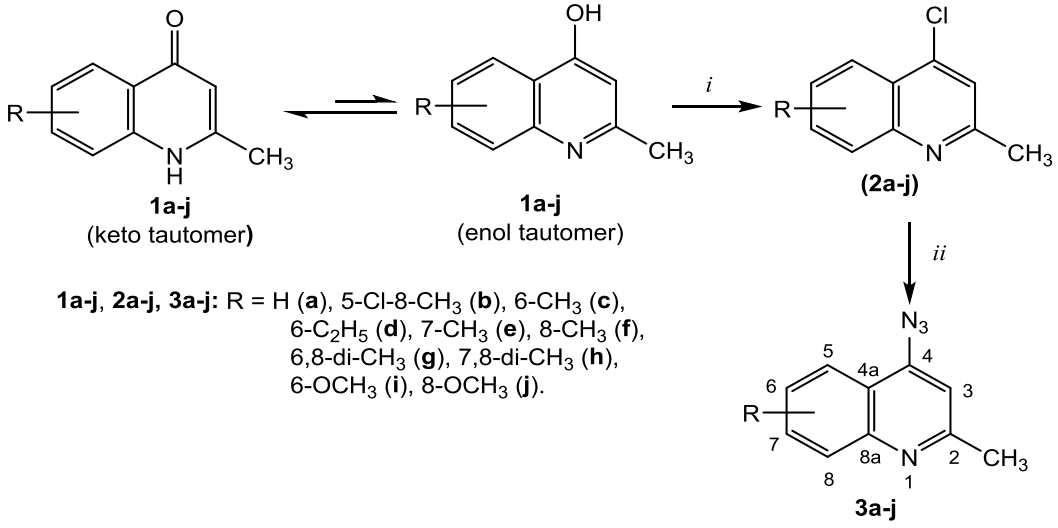
recorded on FT-NMR Avance AV500 Spectrometer (Bruker, Germany) at 500.13 MHz and 125.77 MHz, respectively, using DMSO-d_6 as solvent and TMS as an internal standard. Spectral data of ^{1}H and ^{13}C NMR were summarized in Tables 1 and 2.

*General procedure for synthesis of substituted 4-azido-2-metylquinolines **3a-j**:*

To the solution of appropriate substituted 4-chloro-2-metylquinoline **2a-j** (10 mmol) in DMF (20 mL) in 100 ml round-bottomed flask was added sodium azide (15 mmol). A few crystals of KI then were added as catalyst. The obtained mixture was refluxed with stirring on water-bath at 50°C for 20 hours. Solvent DMF was removed completely in vacuum to obtained brown solids. Water was added to dissolve inorganic salts. Separated solid substance was filtered on Büchner funnel, washed well with water, and dried in air. The compounds were purified by recrystallization from ethanol: toluene (9: 1) obtained crystals or solids. The yields of products **3a-j** were 78–97%.

III. RESULTS AND DISCUSSION

The selected ^{1}H and ^{13}C NMR spectral data of substituted 4-azido-2-metylquinolines **3a-j** were listed in Table 1 and 2. From Tables 1 and 2 it's shown that protons and carbon-13 atoms in these molecules have proper resonance signals in corresponding spectral regions which are characteristic for each type of atoms.



Scheme 1: Synthesis path for substituted 4-azido-2-metylquinolines. Reaction conditions: (i) $POCl_3$, 70°C until dissolved, then 90°C, 1 hr; (ii) NaN_3, DMF, 50°C, 20 hrs.

The signal was located in region at δ=10.61−10.36 ppm in ^{1}H NMR spectra that belonged to NH bond in initial quinolin-4-ones **1a-j** disappeared in ^{1}H NMR spectra of the corresponding azido derivatives **3a-j**.

Simultaneously, in ^{13}C NMR spectra, the chemical shift of the metyl group on position 2 of azido derivatives **3a-j** was shifted downfield more than that in corresponding 4(1*H*)-quinoline-4-one derivatives **1a-j** respectively, from δ=20.3−15.6 ppm (of **1a-j**) [8] to δ=25.7−24.5 ppm (of **3a-j**, *Table 2*). The reason of these changes is that the anisotropic influence of heteroaromatic ring (pyridine ring) was more powerful than double bond of alkene in quinoline-4-ones **1a-j** that was non-heteroaromatic ring [8]. Proton H-3 of the pyridine moiety in compounds **3a-j** had resonance signal at δ=7.47−6.90 in singlet because this proton had not magnetic interactions with any other protons in quinoline ring. In compared with compounds **1a-j**, it is found that the corresponding signal of proton H-3 was located in upfield region (δ=5.95−5.81 ppm, in singlet, *Table 1*). This event demonstrated that aromatic pyridine moiety in compounds **3a-j** also affected to position of resonance signal of proton H-3 and made it to shift to downfield region by the anisotropic effect of this heteroaromatic ring.

Chemical shifts of both carbon atoms C-2 and C-8a were most affected by electronegative nitrogen atom in ring quinoline; these resonance signals located in range of δ = 159.6−157.2 ppm and δ=149.3−144.6 ppm, respectively (*Table 2*). Metyl substituent on position 2 of quinoline ring had chemical shift in region of δ = 2.51−2.67 ppm in singlet. Metyl substituent on position 6 had signal at δ = 2.46−2.63 ppm; metyl group on position 7 had signal at δ = 2.43 ppm; metyl group on position 8 had signal at δ = 2.42−2.63 ppm. Methoxy group on position 6 had chemical shift at δ = 3.88 ppm, on position 6 had δ = 3.94 ppm. All these signals were in singlet. Ethyl substituent on position 6 had two signals at δ = 2.77 in quartet and δ = 1.25 ppm in triplet that belonged to Metylene and metyl groups, respectively. The coupling constant in this case was J = 7.55 Hz that was typical for alkane protons.

In case of compound **3c** (R=6-F) each signal of protons H-5, H-7 and H-8 was splitted further due to magnetic interactions between each of these protons and fluorine atom. The coupling constants for these magnetic interactions were J_{HF} = 9.6 Hz (for H-5); J_{HF} = 3.0 Hz (for H-7) and J_{HF} = 5.25 Hz (for H-8). Carbon atoms in benzene component of quinoline ring also had similarly coupling interactions, i.e., between C-4a with J_{CF} = 36.5 Hz, C-5 with J_{CF} = 94 Hz, C-6 with J_{CF} = 10 Hz, C-7 with J_{CF} = 101.5 Hz and C-8 with J_{CF} = 21 Hz.

In short, the structures of substituted 4-azido-2-metylquinolines has been confirmed from the spectral data discussed above.

Table 1. Selected ^{1}H NMR spectra of substituted 4-azido-2metylquinolines [δ (ppm), multicity, J(Hz)]

R	H-3	H-5	H-6	H-7	H-8	Metyl groups
H (a)	7.28,s	7.91,d, 7.25	7.52,t, 7.45	7.74,td, 1.25, 6.95	7.89,d, 8.15	2.62, 2-CH_3
5-Cl-8-Me (b)	7.47,s	-	7.56,d, 7.5	7.50,d, 7.5	-	2.63, 2- CH_3; 2.67, 8-CH_3
6-F (c)	7.44,s	7.60,dd, 2.75*	-	7.68,td, 9.25*	7.98,dd, 9.25*	2.65, 2-CH_3
6-Me (d)	7.27,s	7.67	-	7.57,d, 7.5	7.79,d, 7.5	2.61, 2-CH_3; 2.46, 6-CH_3
6-Et (e)	7.29,s	7.70	-	7.61,dd, 1.5, 8.5	7.82,d, 8.5	2.67 2-CH_3; 2.77,q,7.55; 6-**CH_2**CH_3,; 2.62, 1.25,t, 7.55, 6-CH_2**CH_3**
8-Me (f)	7.19,s	7.79,d, 8.5	7.58,dd,2.0, 8.5	7.78,m	-	2.50, 2-CH_3; 2.67, 8-CH_3
6,8-diMe (g)	7.29,s	7.44	-	7.54	-	2.67 2-CH_3; 2.63, 6-CH_3; 2.42, 8-CH_3
7,8-diMe (h)	7.26,s	7.69,d, 8.5	7.34,d, 8.5	-	-	2.65 2-CH_3; 2.63, 8-CH_3; 2.43, 7-CH_3
6-OMe (i)	7.31,s	7.21,d, 2.80	-	7.38,dd, 2.85, 9.15	7.82,d, 9.20	3.88, 6-OCH_3; 2.61 2-CH_3
8-OMe (j)	6.90,s	7.13,d, 8.0	7.37,t, 8.5	7.52,d, 9.5	-	3.94, 8-OCH_3; 2.51 2-CH_3

***** H-5 J_{HF} = 9.6 Hz; H-7 J_{HF} = 3.0 Hz; H-8 J_{HF} = 5.25 Hz

Table 2. ^{13}C NMR spectra of substituted 4-azido-2metylquinolines (δ,ppm)

R	C-2	C-3	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	Metyl groups
H (a)	159.60	110.43	145.61	122.13	126.16	119.75	130.77	128.64	148.63	25.25, 2-CH_3
5-Cl-8-Me (b)	158.91	113.26	145.34	117.00	130.43	125.59	128.88	136.24	149.26	25.22, 2-CH_3; 18.88, 8-CH_3
6-F (c)	160.73	111.34	145.83	131.66*	105.92*	159.23*	120.71*	145.35*	158.78	25.16, 2-CH_3
6-Me (d)	158.56	110.42	144.97	120.93	119.67	135.72	132.84	128.42	147.20	25.12,2-CH_3; 21.59, 6-CH_3
6-Et (e)	158.62	110.41	145.10	119.70	119.59	141.81	131.77	128.62	147.46	8.61,6-**CH_2**CH_3; 25.16,2-CH_3); 15.78,6-CH_2**CH_3**
8-Me (f)	159.81	110.71	147.84	127.94	122.05	121.21	134.02	137.39	147.85	24.51, 2-CH_3; 21.55, 8-CH_3
6,8-diMe (g)	157.31	110.24	145.09	119.60	118.80	135.10	132.93	135.92	146.21	25.54,2-CH_3; 21.63,6-CH_3; 18.30,8-CH_3
7,8-diMe (h)	158.12	109.25	145.73	117.92	118.90	128.69	133.59	138.27	147.50	25.73,2-CH_3; 20.77,7-CH_3; 13.66,8-CH_3
6-OMe (i)	157.26	120.53	144.34	122.99	100.32	156.81	110.72	130.32	144.60	1, 55.92,6-OCH_3; 24.95,2-CH_3
8-OMe (j)	157.16	126.32	140.09	123.53	115.38	126.87	108.77	155.83	146.79	56.05,8-OCH_3; 25.54,2-CH_3

* C-4a, J_{CF} = 36.5 Hz, C-5, J_{CF} = 94 Hz, C-6, J_{CF} = 10 Hz, C-7, J_{CF} = 101.5 Hz, C-8, J_{CF} = 21 Hz

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