STUDY ON NMR SPECTRA OF SOME SECONDARY AMINES SYNTHESIZED FROM VANILLIN

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TÓM TẮT

NGHIÊN CỨU PHỔ CỘNG HƯỞNG TỪ HẠT NHÂN CỦA MỘT SỐ AMIN BẬC 2 ĐƯỢC TỔNG HỢP TỪ VANILLIN

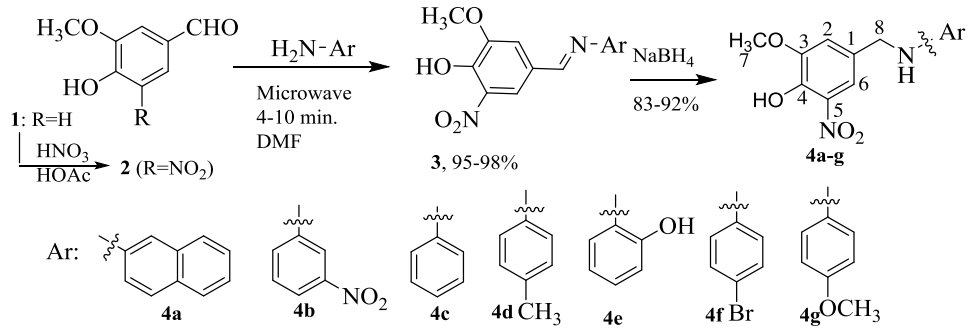
Tính chất phổ cộng hưởng từ hạt nhân của 7 amines được tổng hợp từ vanillin được nghiên cứu chi tiết. Mỗi nguyên tử hydro hoặc cacbon được quy kết chính xác từ phân tích phổ ^{1}H, ^{13}C NMR, HSQC và HMBC trên cơ sở độ chuyển dịch hóa học, hình dạng vân phổ, hằng số tương tác tách và tương tác giao trên các phổ cộng hưởng từ hai chiều.

1. INTRODUCTION

A secondary amine is a base that have exhibit various biological activities and is extensively applied in medicine such as hemolytic, necrotoxic, phytotoxic, antibiotic, insecticidal and antifungal activities of the fire ants' venom [1,2,3,4], anticonvulsant and neuroprotective properties [2, 5]. Mitoxantrone (trade name Novantrone) is an anthracenedione antineoplastic agent [6]. One of reasons making amines important is easy to convert to a salt that is water soluble so that it can be transported through the blood. Consequently, delivery of drug is convenient in most cases [7]. Therefore, understanding more about secondary amines and its spectral properties builds a full data about them being essential.

EXPERIMENTAL

Their ^{1}H and ^{13}C NMR spectra were recorded on FT-NMR Avance AV500 Spectrometer (Bruker, Germany) at 500 MHz and 125 MHz, respectively, using DMSO-*d*6 as solvent and TMS as an internal standard. Secondary amines were synthesized following [8] and Scheme 1.



2. RESULTS AND DISCUSSION

The assignments of protons and carbons were confirmed using ^{1}H NMR, ^{13}C NMR, HSQC and HMBC methods [9]. Our amines have a core numbered from 1 to 8 (Scheme 1) for analyzing spectra only (not for nomenclature). First of all, all protons and carbons of the core were assigned based on amine **4a** then inferred for other ones.

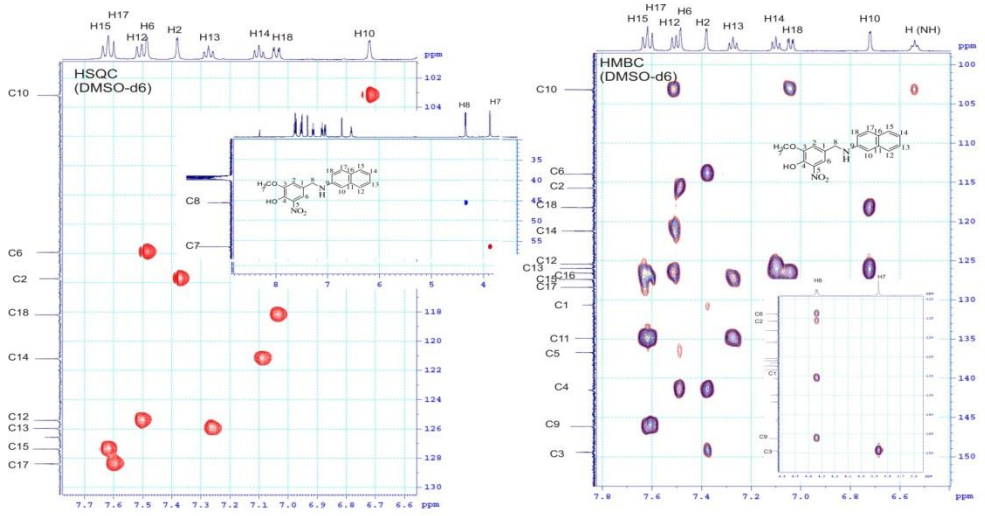
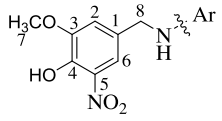


Figure 1. HSQC and HMBC spectra of 4a

Assignments protons and carbons of the core were listed in table 1 and 2. In the ^{1}H and ^{13}C NMR spectra of amine **4a**, H7/C7 and H8/C8 were easily identified at strong field. The blue color of the cross peak of H8 at δ 4.33 ppm (d, *J*6.0, 2H) and C8 at δ 45.6 ppm on the HSQC spectrum indicating that H8 and C8 belonging to >CH_2 group that coupled with proton of >NH group with coupling constant about 5-6 Hz. On the HMBC spectrum showed a cross peak of H7 at δ 3.87 ppm (s, 3H) and C3 at δ 149.4 ppm that was interacted with H2 δ 7.38 (d, *J*2.0, 1H) but H6 7.48 ppm (d, *J*2.0, 1H) did not. Therefore, H2 and H6 were distinguished. Consequently, C2 δ 115.7 ppm and C6 113.9 ppm were indicated as well. The peak at δ 141.5 ppm on the ^{13}C NMR spectrum must be for C4 due to both H2 and H6 had cross peaks with. C1 at δ 130.6 ppm was also assigned

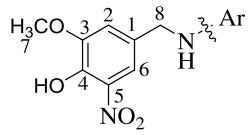
because it had a cross peak with H8 (small picture) and H2. C5 was confirmed at δ 136.7 ppm due to it had a cross peak with H6. One of the most important peaks was at around 5.7 – 6.2 ppm indicating the new proton formed with reduction reaction with $NaBH_4$. It was an exchangeable proton so its signal was changed depending on amines and condition recording spectra. In some cases (**4a**, **4b**, **4c** and **4f**) this peak was a triple with coupling constant about 5.5-6.0 Hz indicating its vicinal location with H8 ($>CH_2$), other cases (**4d**, **4e** and **4g**), it was a broad peak. Another observation was that a peak at about δ 10.22 ppm was for proton of phenolic hydroxyl group. ^{1}H NMR spectrum of compound **4e** showed another resonance signal at δ 9.15 ppm (s, 1H) was for proton of another OH group. ^{1}H NMR and ^{13}C NMR data were listed in table 1 and 2 that were inferred from similarity of the core and NMR analysis of compound **4a** then were checked with HMBC spectra for each compound. Table 1 showed that chemical shifts of H2, H6, H7 and H8 were not much different that agreed with the fact that the core was quite far from the changed part. Similarly, chemical shifts of C1÷C8 were retained stably as well.

Table 1. ^{1}H NMR spectral data of the core [δ (ppm), J (Hz)]



	H2	H6	H7	H8	H (NH)	H (OH)
4a	7.38 (d, *J*2.0, 1H)	7.48 (d, *J*2.0, 1H)	3.87 (s, 3H)	4.33 (d, *J*6.0, 2H)	6.54 (t, *J* 6.0, 1H)	10.22 (s, 1H)
4b	7.34 (d, *J* 2.0, 1H)	7.45 (d, *J* 2.0, 1H)	3.86 (s, 3H)	4.32 (d, *J* 6.0, 2H)	6.45 (t, *J* 6.0, 1H)	10.29 (s, 1H)
4c	7.31 (d, *J* 1.5, 1H)	7.42 (d, *J*1.5, 1H)	3.85 (s, 3H)	4.22 (d, *J* 6.0, 2H)	6.22 (t, *J* 6.0, 1H)	10.22 (br, 1H)
4d	7.30 (d, *J* 1.5, 1H)	7.41 (d, *J* 2.0, 1H)	3.85 (s, 3H)	4.19 (d, *J* 5.0, 2H)	6.01 (br, 1H)	10.20 (br, 1H)
4e	7.32 (d, *J*1.5, 1H)	7.40 (d, *J*1.5, 1H)	3.84 (s, 3H)	4.26 (d, *J*6.0, 2H)	5.37 (br, 1H)	10.21 (br, 1H) 9.25 (s, 1H)
4f	7.26 (s, 1H)	7.40 (s, 1H)	3.84 (s, 3H)	4.20 (d, *J*6.0, 2H)	6.45 (t, *J* 5.5, 1H)	10.20 (br, 1H)
4g	7.30 (d, *J* 2.0, 1H)	7.42 (d, *J*2.0, 1H)	3.85 (s, 3H)	4.16 (d, *J* 6.0, 2H)	5.82 (br, 1H)	10.15 (br, 1H)

Table 2. ^{13}C NMR spectral data of the core [δ (ppm)]



	C1	C2	C3	C4	C5	C6	C7	C8
4a	130.6	115.7	149.4	141.5	136.7	113.9	56.5	45.6
4b	129.9	115.6	149.4	141.5	136.6	113.9	56.5	45.3
4c	131.0	115.7	149.4	141.4	136.6	113.7	56.5	45.5
4d	131.2	115.5	149.3	141.3	136.6	113.7	56.5	45.8
4e	131.5	115.5	149.3	141.3	136.8	113.5	56.5	45.7
4f	131.2	115.3	149.6	142.0	136.5	113,8	56.4	45.4
4g	131.3	115.5	149.3	141.2	136.6	113,8	56.2	46.4

The aromatic moieties of amines were definitely different. The naphthnyl group or amine **4a** was shown in Figure 1 and table 3 and 4. The resonance signal of H8 at δ 4.33 ppm (d, *J* = 6.0 Hz, 2H) was a starting point to assign protons and carbons on the aromatic moieties. ^{1}H NMR soectrum of amine **4a** had got a peak at δ 146.1 ppm that was for C9 as the HMBC spectrum of amine **4a** had got a cross peak with H8. Interestingly, H15 and H17 made a pseudo triplet peak at δ 7.61 ppm with coupling constant value about 9.0 Hz. In fact, the resonance signal at δ 7.61 ppm (t, *J* 9.0, 1H) was for H17 because H17 had a cross peak with C9 meanwhile H15 could not. The HSQC of amine **4a** had got a cross peak between H17 and C17, therefore, the resonance signal at δ 128.4 ppm was for C17 respectively. The peak at δ 134.9 ppm was for C11; another one at δ 127.3 ppm was for C15 since both had cross peaks with H17. Double checking on the HSQC of amine **4a**, the resonance signal at δ 7.62 ppm (d, *J*9.5, 1H) was for H15 when it had an interaction with C15. Similarly, H13 was at δ 7.27 ppm (td, *J*8.0, 1.5, 1H) and C13 was at δ 125.9 ppm. Basing on a cross peak with proton of >NH group, the resonance signal at δ 103.1 ppm was for C10 and a doublet peak at δ 6.72 (d, *J*1.5, 1H) was assigned for H10. Doing the same manner, C18 was at δ 118.2ppm; H18 was at δ 6.04 (dd, *J*8.5, 2.0, 1H); H12 was at δ 7.51 (d, *J*8.5, 1H); C12 was at δ 125.4 ppm; H14 was at δ 7.10 (td, *J*8.0, 1.0, 1H); C14 was at δ 121.2 ppm. Other ^{1}H NMR and ^{13}C NMR data of aromatic part of other amines **4b-g** were listed in table 3 and 4.

Table 3. ^{1}H NMR spectral data of the aromatic part [δ (ppm), J (Hz)]

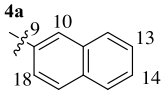
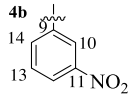
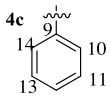
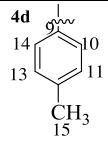
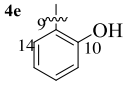
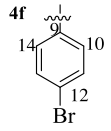
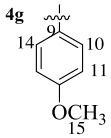
	H10	H11	H12	H13	H14	H15	H17	H18
4a 	6.72 (d, *J*1.5, 1H)	-	7.51 (d, *J*8.5, 1H)	7.27 (td, *J*8.0,1.5, 1H)	7.10 (td, *J*8.0, 1.0, 1H)	7.62 (d, *J*9.5, 1H)	7.61 (d, *J* 9.0, 1H)	6.04 (dd, *J*8.5, 2.0, 1H)
4b 	7.39 (t, *J*2.0, 1H)	-	7.01 (d,q *J*8.5, 1.0, 1H)	7.32 (t, *J*8, 1H)	7.35 (d,q, *J*8.0, 1.0, 1H)	-	-	-
4c 	6.57 (d, *J*7.5, 1H)	7.04 (t, *J*7.5, 1H)	6.52 (t, *J*7.5, 1H)	7.04 (t, *J*7.5, 1H)	6.57 (d, *J*7.5, 1H)	-	-	-
4d 	6.49 (d, *J*8.5, 1H)	6.66 (d, *J*8.0, 1H)	-	6.66 (d, *J*8.0, 1H)	6.49 (d, *J*8.5, 1H)	2.12 (s, 3H)	-	-
4e 	-	6.39 (dd, *J*8.5,1.5, 2H)	6.55 (td, *J*7.5,1.0, *1*H)	6.39 (dd, *J*8.5,1.5, 2H)	6.66 (dd, *J*8.5 1.5, 1H)	-	-	-
4f 	6.54 (d, *J*9.0, 1H)	7.17 (d, *J*9.0, 1H)	-	7.17 (d, *J*9.0,1H)	6.54 (d, *J*9.0,1H)	-	-	-
4g 	6.53 (dd, *J*7.5, 2.5,1H)	6.68 (dd, *J* 7.5, 2.5, 1H)	-	6.68 (dd, *J*7.5, 2.5, 1H)	6.53 (dd, *J*7.5, 2.5,1H)	3.61 (s, 3H)	-	-

Table 4. ^{13}C NMR spectral data of the aromatic part [δ (ppm)]

	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18
4a	146.1	103.1	134.9	125.4	125.9	121.2	127.3	126.5	128.4	118.2
4b	149.3	118.5	148.7	129.8	110.2	105.8	-	-	-	-
4c	148.3	112.3	128.8	116.0	128.8	112.3	-	-	-	-
4d	146.0	112.5	129.2	124.4	129.2	112.5	20.0	-	-	-
4e	144.1	136.6	110.2	119.5	116.9	113.6	-	-	-	-
4f	147.5	114.3	131.3	106.6	131.3	114.3	-	-	-	-
4g	142,4	113.4	114.5	150.8	114.5	113.4	56.5	-	-	-

3. CONCLUSIONS

In conclusion, all protons and carbons of seven secondary amines were assigned exactly based on ^{1}H NMR, ^{13}C NMR, HSQC and HMBC spectral analysis. Resonance signals of proton

(H2, H6, H7 and H8) and corresponding carbons (C1÷C8) also retained stably since they were far from different aromatic parts.

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