Assignments of the Chemical Shifts of Carbon-13 Nuclear Magnetic Resonance Spectra of some 2-Methyl-3-(3,4-dimethoxy/dihydroxyphenylethyl)-4-quinazolones

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The ^{13}C nmr chemical shifts of a series of 2-methyl-3-(3,4-dimethoxy/dihydroxyphenylethyl)-4-quinazolones are reported. The carbon resonances have been assigned on the basis of chemical shift theory, intensity of the signals, multiplicities generated in SFORD spectra and the comparison with the structurally related compounds.

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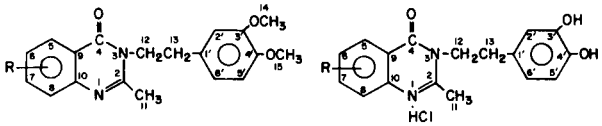
Earlier studies have reported the assignments of the various carbon resonances of methaqualone (1), 2-methyl-3-*ortho*-tolyl-4-quinazalone, which is a potent sedative, hypnotic and anticonvulsant drug (2), and some of its metabolites (3). Recent studies have been concerned with the synthesis of a series of 2-methyl-3-(3,4-dimethoxy/dihydroxyphenylethyl)-4-quinazolones **1-12** as possible antiparkinson agents (4). These observations prompted study of the chemical shifts of the ^{13}C nmr of **1-12** which could not only prove useful as a probe for their metabolic studies but would eliminate the preparation of radio labeled compounds. The present study deals with the assignments of the chemical shifts of the various carbon resonances of **1-12**.

The natural abundance ^{13}C nmr spectra of **1-12** were recorded on a JEOL FX-60 spectrometer operating at 15.00 kHz using deuterated dimethylsulfoxide as a solvent and tetramethylsilane as a reference. In all cases, a proton noise decoupled and a single-frequency off-resonance decoupled (SFORD) spectra were obtained. The proton noise decoupled spectrum gave the chemical shifts of the various carbon resonances and single-frequency off-resonance spectrum showed the multiplicity of the carbon resonances. The multiplicities generated in the SFORD spectra differentiated the methyl, methylene, methine and non-protonated carbon resonances, while in some cases the multiplicity was not clear due to very close chemical shifts. The proton noise decoupled and SFORD spectra of aniline hydrochloride **13** and 2-methyl-3-propyl-4-quinazolone hydrochloride **14** were also taken as reference model



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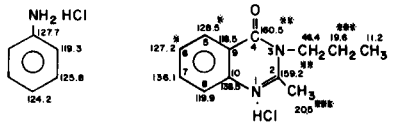

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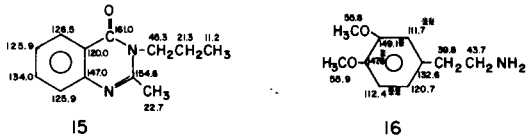

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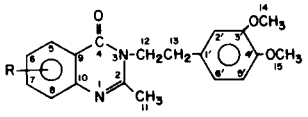
Table I

Carbon-13 Chemical Shifts of 2-Methyl-3-(3,4-dimethoxyphenylethyl)-4-quinazolones



Compound No	R	Chemical Shift (ppm)																			
		C-2	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	C-11	C-12	C-13	C-14	C-15	R
1	H	155.2	161.3	126.3	126.3	134.4	126.3	120.8 (a)	147.7 (b)	130.7	112.7 (c)	148.8 (b)	147.1 (b)	112.1 (c)	120.1 (a)	22.7	45.8	33.1	55.6 (d)	55.3 (d)	
2	6-Cl	156.0	160.5	125.3	130.7	134.8	129.0	121.4 (a)	145.9	130.7	112.8 (b)	148.9 (c)	147.9 (c)	112.3 (b)	121.0 (a)	22.9	46.3	33.1	55.8 (d)	55.7 (d)	
3	7-Cl	156.7	160.5	128.3	126.6 (a)	138.9	125.7 (a)	118.8	148.1 (b)	130.6	112.7 (c)	148.8 (b)	147.7 (b)	112.0 (c)	120.8	22.9	46.0	33.1	55.4	55.4	
4	6-I	156.3	160.1	134.6	91.1	142.9	128.9	121.9 (a)	146.4 (b)	130.7	112.8 (c)	148.9 (b)	147.7 (b)	112.3 (c)	121.0 (a)	23.0	46.3	33.1	55.7	55.7	
5	6-CH_3	154.1	161.1	126.4 (a)	135.9 (b)	135.7 (b)	125.4 (a)	119.8 (c)	145.1	130.7	112.7 (d)	148.8 (e)	147.7 (e)	112.0 (d)	120.8 (c)	22.6	45.7	33.3	55.6 (f)	55.3 (f)	20.9
6	8-CH_3	153.9	161.4	123.7	125.7	134.5 (a)	134.5 (a)	119.8 (b)	145.4	130.6	112.5 (c)	148.7 (d)	147.6 (d)	112.0 (e)	120.7 (b)	23.0	45.7	33.1	55.2	55.2	16.9

(a,b,c,d,e,f) May be interchanged in the same compound.

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compounds for comparative evaluation. The chemical shifts of the various signals in the proton noise decoupled spectra of **1-12** have been assigned on the basis of the chemical shift theory, multiplicities observed on SFORD spectra, signal intensity and comparison with the corresponding carbon chemical shift of the model compounds.

The proton noise decoupled spectrum of aniline hydrochloride gave as expected four signals. The singlet at 127.7 ppm is assigned to the carbon directly attached to the amino group. The three doublets centered at 119.3, 125.8 and 124.2 ppm are assigned to the *ortho, meta* and *para* carbons, respectively, on the basis of the signal intensity and the chemical shift theory. These results have indicated that a significant downfield shift at *ortho* and *para* carbons and upfield shifts at *ipso* and *meta* carbons are associated with aniline hydrochloride as compared to aniline (5).

The chemical shifts of the various carbon resonances of **14** are represented on the structure of **14**. The four singlets in the downfield region at 160.5, 159.2, 138.5 and 118.5 ppm are assigned to C-4, C-2, C-10 and C-9, respectively, where C-2 and C-4 may be interchanged. The doublets centered at 128.5, 127.2, 136.1 and 119.9 ppm are attributed to the carbon resonances of C-5, C-6, C-7 and C-8, respectively. However, the doublets at C-5 and C-6 may be interchanged. These assignments have been made on the basis of the chemical shift theory and comparing the corresponding carbon chemical shifts of **13** and **15** (1). The remaining signals of **14** have been assigned by comparing the chemical shifts of **15** and multiplicities observed in SFORD spectrum.

2-Methyl-3-(3,4-dimethoxyphenylethyl)-4-quinazolones (**1-6**)

The chemical shifts of the various carbon resonances of **1-6** are represented in Table I. The two quartets centered at about 23 ppm and 55 ppm are assigned to the carbon resonances of C-11 and both C-14 and C-15, respectively, on the basis of the chemical shift theory. Since a nitrogen atom attached to aliphatic carbon causes more downfield shift than the aromatic ring, the two signals at about 33 ppm and 46 ppm, whose multiplicity in SFORD spectra are not clear due to close chemical shifts of dimethylsulfoxide, are assigned to C-13 and C-12, respectively. In the case of **5**, the signal at 20.9 ppm is assigned to the carbon of methyl group present at position 6 of the quinazolone moiety while in **6** the signal at 16.9 ppm is attributed to the carbon of methyl group attached to position 8 of the quinazolone moiety.

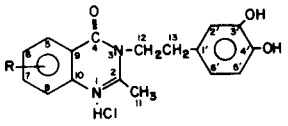
The signals observed in downfield region in the proton noise decoupled spectra of **1-6** are due to C-2, C-4 and aromatic carbon resonances. The carbon resonances of C-1′, C-2′, C-3′, C-4′, C-5′ and C-6′ have been assigned by considering the effect of the methoxy groups present at position 3 and 4 on ethylbenzene (6). These results have been compared with the corresponding carbon chemical shifts of **16** (6). The singlets near 161 ppm and 155 ppm are assigned to C-2 and C-4, respectively, and these are in agreement with the corresponding carbon chemical shifts of **15** (1). The assignments of the carbon resonances of C-5 to C-10 in **1** have been made by comparing the chemical shifts of **15** (1). In the case of **2-6**, the carbon resonances of C-5 to C-10 have been assigned by considering the effects of chloro, iodo or methyl group on the chemical shifts of C-5 to C-10 in **1**. These assignments are in agreement with their respective calculated values.

2-Methyl-3-(3,4-dihydroxyphenylethyl)-4-quinazolone Hydrochlorides (**7-12**).

The chemical shifts of the various carbon resonances of **7-12** are recorded in Table II. The farthest upfield quartet centered at about 20 ppm is assigned to C-11. The other two upfield signals of about 32 ppm and 47 ppm are attributed to the carbon resonances of C-13 and C-12, respectively. These assignments have been made directly

Table II

Carbon-13 Chemical Shifts of 2-Methyl-3-(3,4-dihydroxyphenylethyl)-4-quinazolone Hydrochlorides



Compound No	R	Chemical Shift (ppm) C-2	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	C-11	C-12	C-13	R
7	H	158.9 (a)	160.5 (a)	128.6 (b)	127.2	136.2	119.7	118.5	138.4	128.4 (b)	115.9 (c)	145.4	144.2	116.3 (c)	120.1	19.5	46.8	32.2	
8	6-Cl	158.4 (a)	159.8 (a)	126.0	132.4	135.9	123.5	119.6	138.8	128.4	115.9 (b)	145.4	144.2	116.3 (b)	120.2	20.0	46.8	32.2	
9	7-Cl	158.8 (a)	160.4 (a)	129.0	128.4	141.5	119.4	117.7	140.1	128.4	115.9 (b)	145.4	144.1	116.2 (b)	120.7	20.3	46.7	32.2	
10	6-I	158.3 (a)	159.1 (a)	134.9	92.9	144.0	124.0	119.7	140.0	128.4	115.8 (b)	145.3	144.0	116.2 (b)	120.6	20.5	46.7	32.4	
11	6-CH_3	158.9 (a)	159.2 (a)	126.3	137.2	137.2	119.6	118.5	138.5	128.5	115.9 (b)	145.4	144.1	116.3 (b)	120.7	20.0 (c)	46.6	32.4	20.9 (c)
12	8-CH_3	158.1 (a)	160.2 (a)	124.6	127.4	136.3	132.0	119.4 (b)	140.1	128.8	116.0 (c)	145.5	144.2	116.4 (c)	119.7 (b)	21.3	46.8	32.7	17.7

(a,b,c) May be interchanged in the same compound.

by comparison with the corresponding carbon chemical shifts of **1-6**. The signals due to the carbon of the methyl group attached to quinazolone moiety at position 6 in **11** and 8 in **12** have been represented by the chemical shifts observed at 20.9 and 17.7 ppm, respectively.

The carbon resonances of C-1′, C-2′, C-3′, C-4′, C-5′ and C-6′ have been assigned by considering the effects of the hydroxyl groups on the chemical shifts of ethyl benzene. The assignments of the chemical shifts of the various carbon resonances of the quinazolone ring in **7** have been made on the basis of the comparison with the corresponding carbon chemical shifts of **14**. The assignment of carbon resonances of the quinazolone ring in **8-12** have been made by considering the effect of chloro, iodo or methyl group on the chemical shift of the quinazolone ring carbons in **7**. The values of these assignments have been found to correspond well with their calculated values.

EXPERIMENTAL

The ^{13}C nmr spectra of **1-14** were obtained on a JEOL FX-60 spectrometer operating at 15.00 KHz. The compounds were run in 10 mm tube using deuterated dimethylsulfoxide (30% w/v) as internal lock and solvent and tetramethylsilane as a reference. The spectrometer setting used during the experiments was the spectral width of 4 KHz and the pulse width of 12 μ seconds (60°).

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