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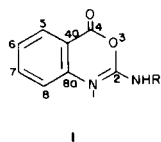
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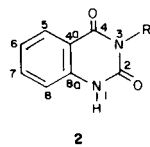
<sup>13</sup>C chemical shifts of nine *N*-substituted 2-amino-4*H*-3,1-benzoxazin-4-ones, the isomeric 3-substituted 2,4-(1*H*,3*H*)quinazolin-4-ones, and the parent compounds of the two series are reported. Support is provided for the endocyclic position of the C=N bond in the former series of compounds.

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As part of an investigation of methods of synthesis of fused ring heterocyclic compounds (1), we prepared a number of *N*-substituted 2-amino-4*H*-3,1-benzoxazin-4-ones and compared their infrared and proton nmr spectra with those of corresponding, 2-substituted 2,4-(1*H*,3*H*)quinazolin-4-ones (2). A review of the literature reveals an almost complete lack of information with regard to <sup>13</sup>C nmr spectra of such compounds (3). In this paper, we report on the <sup>13</sup>C chemical shift assignments of nine *N*-substituted 2-amino-4*H*-3,1-benzoxazin-4-ones (**1b-j**), the isomeric 3-substituted 2,4-(1*H*,3*H*)quinazolin-4-ones (**2b-j**), and the parent compounds of the two series (**1a,2a**).



1



2

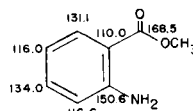
a, R = H

e, R = C<sub>6</sub>H<sub>5</sub>i, R = 3-ClC<sub>6</sub>H<sub>4</sub>b, R = CH<sub>3</sub>CH<sub>2</sub>f, R = 2-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>j, R = 4-ClC<sub>6</sub>H<sub>4</sub>c, R = CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>g, R = 3-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>

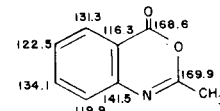
d, R = Cyclohexyl

h, R = 4-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>

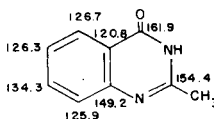
Of the two most downfield peaks in the spectrum of **1a** (both singlets in the off-resonance decoupled spectrum), the peak at 155.4 ppm, which is shifted upfield by 1-2 ppm for the *N*-alkyl derivatives **1b-d** and by 3-5 ppm for the *N*-aryl derivatives **1e-j**, is assigned to C-2. As a result, the other downfield peak (159.6 ppm), which remains essentially constant at *ca.*, 159 ppm for **1b-j**, must belong to the carbonyl carbon. Of the remaining two singlets in the off-resonance decoupled spectrum of **1a**, the one at 112.5 ppm is assigned to C-4a and the one at 151.0 ppm to C-8a by analogy to the assignments of methyl anthranilate (**3**) (**4**), 2-methyl-4*H*-3,1-benzoxazin-4-one (**4**) (**5**), 2-methyl-4-(3*H*)quinazolinone (**5**) (**6**), 2-benzyl-4-(3*H*)quinazolinone (**6**) (**6**), and 2,3-dimethyl-4-(3*H*)quinazolinone (**7**) (**6**). The signals at 127.9, 123.4, 136.4, and 122.7, all doublets in the off resonance decoupled spectrum, are assigned to the aromatic carbons C-5, C-6, C-7, and C-8, respectively (the C-6 and C-8 values may be interchanged) by analogy to **3-7**, as well as 2-methyl-3-phenyl-4-(3*H*)quinazolinone (**8**)



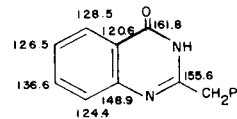
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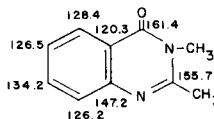
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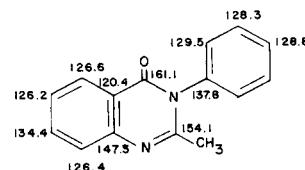
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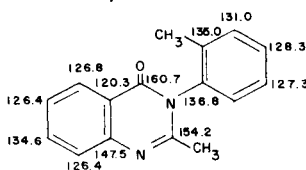
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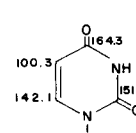
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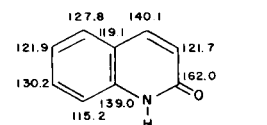
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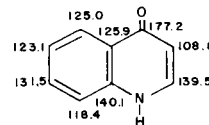
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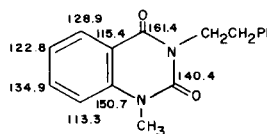
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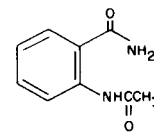
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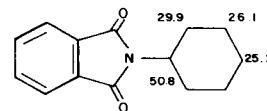
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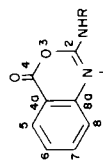


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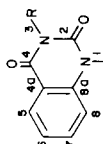
Table I  
<sup>13</sup>C Chemical Shifts of 2-Amino-4*H*-3,1-benzoxazin-4-ones (**1**) (a)



Compound No.	R	Benzoxazinone Ring								Benzene Ring of R					ArCH <sub>3</sub>			Aliphatic R		
		C-2	C-4	C-4a	C-5	C-6(b)	C-7	C-8(b)	C-8a	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'	C-1'	C-2'	C-3'	C-4'	
<b>1a</b>	H	155.4	159.6	112.5	127.9	123.4	136.4	122.7	151.0											
<b>1b</b>	CH <sub>3</sub> CH <sub>2</sub>	154.0	159.5	112.6	128.0	123.8	136.4	122.6	150.8											
<b>1c</b>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>	154.1	159.4	112.5	127.8	123.7	136.2	122.4	150.8											
<b>1d</b>	Cyclohexyl	153.2	159.3	112.4	127.7	123.6	136.3	122.4	150.7											
<b>1e</b>	C <sub>6</sub> H <sub>5</sub>	150.6	159.0	113.7	127.9	123.9	136.4	122.9	149.4	138.1	119.6	128.5	124.4							
<b>1f</b>	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	152.5	159.5	113.4	128.2	124.1	136.7	123.6	150.1	135.5 (138.7)	133.1 (128.9)	130.5 (129.1)	126.1 (b) (124.4)	126.3 (b) (125.4)	125.9 (b) (119.6)	17.9				
<b>1g</b>	3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	150.6	159.0	113.7	127.9	123.9	136.4	123.7	149.4	137.9 (138.1)	120.2 (120.2)	137.8 (b) (137.8)	124.4 (125.0)	128.3 (128.5)	116.8 (116.5)	21.1				
<b>1h</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	150.7	159.2	113.8	128.1	124.5	136.7	124.0	149.6	135.5 (135.0)	119.7 (119.6)	129.2 (129.1)	132.1 (133.7)							
<b>1i</b>	3-ClC <sub>6</sub> H <sub>4</sub>	150.1	158.7	113.9	127.9	124.3	136.5	122.5	148.8	139.5 (139.1)	118.8 (119.8)	133.1 (134.9)	124.5 (124.6)	130.0 (129.5)	117.7 (117.6)					
<b>1j</b>	4-ClC <sub>6</sub> H <sub>4</sub>	150.3	158.8	113.8	127.9	124.4	136.5	124.2	149.0	137.0 (136.1)	120.9 (120.6)	128.4 (128.7)	126.7 (130.8)							

(a) Values in parentheses are calculated. (b) These values may be interchanged.

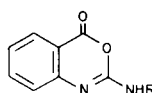
Table II  
<sup>13</sup>C Chemical Shifts of 2,4-(1*H*,3*H*)Quinazoliniones (**2**) (a)



Compound No.	R	Quinazolinione Ring								Benzene Ring of R					ArCH <sub>3</sub>			Aliphatic R		
		C-2	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'	C-1'	C-2'	C-3'	C-4'	
<b>2a</b>	H	150.1	162.6	114.3	126.8	122.1	134.6	115.2	140.7											
<b>2b</b>	CH <sub>3</sub> CH <sub>2</sub>	149.8	161.5	113.8	127.1	122.1	134.5	114.9	139.3											
<b>2c</b>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>	150.1	161.7	113.8	127.2	122.0	134.4	114.9	139.3											
<b>2d</b>	Cyclohexyl	150.1	162.2	114.1	127.3	122.1	134.5	114.7	139.4											
<b>2e</b>	C <sub>6</sub> H <sub>5</sub>	150.2	162.1	114.3	127.5	122.4	135.0	115.2	139.8	135.7	129.0	128.7	128.0							
<b>2f</b>	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	149.9	162.0	114.2	127.8	122.7	135.0	115.5	140.1	135.2 (136.3)	135.9 (b) (138.3)	129.0 (129.3)	128.5 (128.0)	126.7 (125.6)	129.3 (129.0)	17.2				
<b>2g</b>	3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	150.2	162.2	114.3	127.6	122.4	134.9	115.3	139.8	135.7 (135.7)	129.5 (129.6)	128.6 (138.0)	129.1 (128.6)	128.7 (128.7)	20.8					
<b>2h</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	150.1	162.0	114.2	127.4	122.2	134.7	115.1	139.7	133.0 (132.6)	128.6 (129.0)	129.1 (137.2)	137.2 (137.3)							
<b>2i</b>	3-ClC <sub>6</sub> H <sub>4</sub>	149.9	162.0	114.2	127.4	122.4	135.1	115.2	139.8	137.1 (136.7)	129.2 (129.2)	129.2 (135.1)	128.1 (128.2)	128.7 (129.7)	128.0 (b) (127.0)					
<b>2j</b>	4-ClC <sub>6</sub> H <sub>4</sub>	149.9	162.0	114.2	127.4	122.4	135.0	115.2	139.7	132.7 (133.7)	130.9 (130.0)	128.7 (128.9)	134.5 (134.4)							

(a) Values in parentheses are calculated. (b) These values may be interchanged.

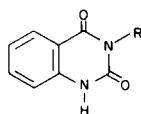
Table III  
Substituent Chemical Shift Increments (ppm)  
for the 4*H*-3,1-Benzoxazin-4-on-2-ylamino Group (a) (b)



	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'
CH <sub>3</sub> CH <sub>2</sub>	30.0	8.4				
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>	27.3	5.7	-5.5	0.2		
Cyclohexyl	22.0	4.2	-3.4	-2.7		
C <sub>6</sub> H <sub>5</sub>	9.6	-8.9	0.0	-4.1		
2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	6.4	-4.7	1.4	-2.4	0.9	-2.6
3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	9.4	-8.9	0.0	-4.7	-0.2	-8.6
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	10.1	-8.8	0.1	-5.7		
3-ClC <sub>6</sub> H <sub>4</sub>	10.0	-9.9	-1.8	-4.2	0.5	-8.8
4-ClC <sub>6</sub> H <sub>4</sub>	10.5	-8.6	-0.3	-8.2		

(a) Based on Chemical shifts of carbon atoms of ethane (5.7 ppm), butane (13.1, 24.9 ppm), cyclohexane (27.6 ppm), benzene (28.5 ppm) (20), and substituent chemical shift increments for CH<sub>3</sub> and Cl (18). (b) Primed numbers refer to carbon atoms of group R.

Table IV  
Substituent Chemical Shift Increments (ppm) for the  
2,4-(1*H*,3*H*)Quinazolin-3-yl Group



R	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'
CH <sub>3</sub> CH <sub>2</sub>	29.2	7.1				
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>	26.5	4.6	-5.3	0.3		
Cyclohexyl	25.2	0.7	-1.7	-2.6		
C <sub>6</sub> H <sub>5</sub>	7.2	0.5	0.2	-0.5		
3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	6.1	-1.9	1.4	0.0	1.3	0.8
3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	7.2	0.4	0.5	-0.5	0.2	0.7
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	7.6	0.1	0.0	-0.6		
3-ClC <sub>6</sub> H <sub>4</sub>	7.6	0.5	-2.1	-0.6	0.6	1.5
4-ClC <sub>6</sub> H <sub>4</sub>	6.2	1.4	0.0	-0.4		

(a) Based on chemical shifts of carbon atoms of ethane (5.7 ppm), butane (13.1, 24.9 ppm), cyclohexane (27.6 ppm), benzene (128.5 ppm) (20), and substituent chemical shift increments for CH<sub>3</sub> and Cl (18). (b) Primed numbers refer to carbon atoms of group R.

and 2-methyl-3-(2-methylphenyl)-4-(3*H*)quinazolinone (9) (5).

Of the four singlets in the off-resonance decoupled spectrum for **2a**, the ones at 150.1 and 162.6 ppm are assigned to C-2 and C-4 carbonyl carbon atoms, respectively, by analogy to uracil (**10**) (6). The other two singlets at 114.3 and 140.7 ppm, are taken to represent the resonances of C-4a and C-8a, by analogy to the assignments of **10**, 2-quinolone (**11**) (7), and 4-quinolone (**12**) (8). The doublets at 126.8, 122.1, 134.6, and 115.2 ppm are attributed to C-5, C-6, C-7, and C-8, respectively, on the basis of the assignments of **11** and **12**, as well as 1-methyl-3-(2-phenylethyl)-2,4-(1*H*,3*H*)quinazolin-3-ylidene (**13**) (9). Furthermore, if *N*-acetyl-2-aminobenzamide (**14**) is taken as a rough

model of **2a**, use of the substituent parameters for -CONH<sub>2</sub> and -NHC(=O)CH<sub>3</sub> (**10**) allows estimation (11) of the chemical shifts of C-5 through C-8. The values thus obtained, 127.6, 122.6, 131.4, and 118.3 ppm, compare reasonably well with the respectively assigned experimental chemical shifts.

In examining the spectra of **1b-j** and **2b-j**, following recognition of the signals corresponding to the carbon atoms of the benzoxazinone, or quinazolin-2(1*H*)-one moiety, the remaining resonances are assigned to the carbon atoms of group R. For **1b** and **2b**, the assignments of the aliphatic carbons are obvious, whereas for **1c,d** and **2c,d** they are made on the basis of the corresponding values for *n*-butylamine (**12**) and cyclohexylamine (**13**). In the case of **2d**, recognition of the signals of the cyclohexyl carbon atoms is further facilitated by the corresponding values observed for *N*-cyclohexylphthalimide (**15**) (14).

In the spectrum of **1e**, the phenyl group carbon atoms are represented by the following resonances (multiplicity in the off-resonance decoupled spectrum indicated in parentheses): 138.1 (s), 128.5 (d), 124.4 (d), and 119.6 (d) ppm. The first signal obviously corresponds to C-1' (*cf.*, chemical shift of the corresponding carbon atom of acetanilide: 138.2 ppm) (15), whereas the one at 124.4 ppm, which is of lower intensity than the other two doublets, belongs to C-4'. The signals at 119.6 and 128.5 ppm are attributed respectively to C-2' and C-3', since an amino substituent is known to shield the *ortho*, but leave the *meta* carbon practically unaffected (16). On the basis of these values and 128.5 ppm as the chemical shift of the benzene carbons, the 4*H*-3,1-benzoxazin-4-on-2-ylamino group substituent parameters are calculated (11) as +9.6, -8.9, 0.0, and -4.1 ppm for C-1', C-2', C-3', and C-4', respectively, of the benzene ring.

In the spectrum of **2e**, the signals derived from the phenyl group carbon atoms are at 128.0 (d), 128.7 (d), 129.0 (d), and 135.7 (s) ppm. Of these, the singlet at 135.7 ppm belongs to C-1', whereas the doublet at 128.0 ppm to C-4', because of its smaller intensity compared to the remaining two signals. To differentiate between C-2' (129.0 ppm) and C-3' (128.7 ppm), use is made again of the fact that a benzene ring substituent affects very little the chemical shift of the *meta* carbon (16). There is good agreement between these assignments and those recently made for the phenyl group carbons of 2-methyl-3-phenyl-4-(3*H*)quinazolinone (**8**) (5). Upon calculation, as before (11), of the 2,4-(1*H*,3*H*)quinazolin-3-yl group substituent parameters, the values of +7.2, +0.5, +0.2, and -0.5 ppm are respectively obtained for C-1', C-2', C-3', and C-4', of the benzene ring.

The thus calculated chemical shift increments (17) for the 2,4-(1*H*,3*H*)quinazolin-3-yl and the 4*H*-3,1-benzoxazin-4-on-2-ylamino groups have been used in combination with the corresponding methyl, or chloro substituent

parameters (18) to estimate the chemical shifts of the aromatic carbon atoms of group R in **1f-j** and **2f-g**. These estimated values, together with the relative intensities of peaks and the multiplicities of signals in the off-resonance decoupled spectra, have led to assignments of chemical shifts for C-1' through C-6' of these compounds. As shown in Tables I and II, the assigned, experimental chemical shifts agree well with the calculated values for **1g-j** and **2g-j**, but less so for **1f** and **2f**. The latter discrepancies are not surprising, in view of the fact that substituent chemical shift effects are not quite additive when substituents on a benzene ring are *ortho* with regard to each other (19). It is noteworthy that there is good agreement between the assigned chemical shifts of C-1' through C-6' of **2f** and the corresponding values of 2-methyl-3-(2-methylphenyl)-4-(3*H*)quinazolinone (**9**) recently reported (5).

A comparison of the chemical shifts of C-8a in the two series of compounds reveals that the signals of this carbon atom appear at a field lower by about 10 ppm for **1** than for **2**. This is consistent with the expected deshielding of C-8a by the electron withdrawing effect of the pyridine-type N-1 in compounds **1** (6) and strengthens the belief that these compounds exist (at least in solution) in the amino form shown, rather than the tautomeric imino structure with an exocyclic C=N bond (2).

On the basis of the assigned, experimental chemical shifts of C-1' through C-6' of **1b-j** and **2b-j**, substituent parameter values have been calculated (11,20) for the 4*H*-3,1-benzoxazin-4-on-2-ylamino and 2,4-(1*H*,3*H*)quinazolin-3-yl groups and are shown in Table III and IV. It is interesting to note that, in contrast to the former, the latter group exerts practically no shielding effect on the *o*- and *p*-carbons of the benzene ring. This is very likely due to the depletion of electron density on the quinazolinone N-3 atom by the electron withdrawing effect of the two flanking carbonyl groups.

#### EXPERIMENTAL

The <sup>13</sup>C spectra were recorded at 34° on a Varian FT-80A instrument using 5 mm. tubes, solutions in hexadeuteriodimethyl sulfoxide, concen-

trations of the order of 1 mole %, and the solvent as internal reference. All chemical shifts are reported in ppm downfield from tetramethylsilane by adding 39.6 ppm to the chemical shifts with respect to DMSO-d<sub>6</sub>. The measurement conditions were as follows: frequency 20 MHz, tip angle 44°, pulse repetition time 0.5 sec., spectral width 5000 Hz, and 16000 data points for the Fourier transform.

Acknowledgement.

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