# Effects of Substituents on NMR Chemical Shifts and Mass Fragmentation Patterns of 1-Aryl-3-phenylpropanes

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The <sup>1</sup>H and <sup>13</sup>C chemical shifts and the mass spectral fragmentation patterns of 1-aryl-3-phenylpropanes with *m*- or *p*-substituents (H, NO<sub>2</sub>, Br, Cl, OCH<sub>3</sub>, CH<sub>3</sub>) were studied. The electronic effects of the substituents seemed to be transmitted by the through-space as well as by a through-bond mechanism, resulting in an inverse correlation in the plot of the chemical shift values of *i*-C vs. the Hammett  $\sigma$  values. The mass spectra showed the substituted benzyl fragments as the base peaks when the substituents were electron donating, whereas the benzyl fragment was observed as the base peaks with the electron-withdrawing substituents.

Keywords: Chalcone, Reduction, 1,3-Diarylpropane, Correlation of chemical shift with Hammett  $\sigma$  value

### Introduction

The effect of substituents on the physical and chemical properties of compounds is perhaps one of the most frequently considered concepts in organic chemistry. A number of common and important relationships between the substituent groups and the physicochemical properties have been developed. Linear free energy relationship, the so-called the Hammett equation, is probably the most widely applied relationship. This equation was originally derived to relate the acidities of the substituents. There are countless reports where the principle is applied in the investigation of the organic reaction mechanism.<sup>1</sup>

The concept has been extended to rationalize the nuclear magnetic resonance (NMR) chemical shifts. The empirical substituent constants have been derived by relating the observed values of chemical shift and the electronic nature of the substituents.<sup>2</sup> Such methodology was applied to make comparison of the NMR properties of the five-membered heterocyclic aromatic compounds, which led to the calculation of the aromaticity indices of the heterocycles.<sup>3</sup>

Recently, we have been interested in the transmission of the electronic effect of the substituent that should result in the shift in the NMR spectra. For example, in our previous report we studied the transmission of the electronic effect of the substituent in the benzene ring on the chemical shift of <sup>1</sup>H and <sup>13</sup>C with the system of the chalcones (1).<sup>4</sup> The two aryl rings are linked by the three sp<sup>2</sup>-hybridized carbon atoms of the enone moiety. Then, it seemed natural to investigate the transmission of the electronic effect of the substituent in one ring to another through three sp<sup>3</sup>-hybridized carbon atoms. The ideal system should be the derivatives of 1-(*m*- or *p*-substituted)phenyl-3-phenylpropane (2).

The structure of 2 can be considered as a methylene bonded to an unsubstituted benzyl and an m- or a psubstituted benzyl group. The substituted and the unsubstituted benzyl groups should affect each other on the physicochemical properties such as the chemical shifts in the NMR spectra and the fragmentation pattern in the mass spectra. We report the results of our study on the effect of the substituents on the one benzyl group to the other unsubstituted benzyl group that appeared in the NMR and the mass spectra of 2.

### **Results and Discussion**

Synthesis. First we had to synthesize the compounds 2a**k**. There are, in general, two approaches to achieving the synthesis of 2 in the literature: coupling the arylpropane derivatives with aryl derivatives, and the stepwise reduction of the chalcones 1. However, there is no report of preparing 2a-k using one set of reaction conditions. For example, the synthesis of the unsubstituted 1,3-diphenylpropane (2d) was done by the reduction of the chalcone 1d with NaBH<sub>4</sub>/  $Pd(OAc)_2$  in  $CHCl_3^5$  or with triethylsilane and trifluoroacetic acid,<sup>6</sup> by the coupling of 3-phenylpropyl halides with phenylmagnesium halides,<sup>7</sup> by the high-pressure hydrogenation of 1,3-diphenylpropene,<sup>8</sup> or by the desulfurization of benzo[*b*]thiophene derivatives.<sup>9</sup> Other 1,3-diphenylpropane derivatives reported in the literature are p-NO<sub>2</sub> (2k),<sup>10</sup> p-Br (2g),<sup>6,11,12</sup> *m*-Br (2i),<sup>13</sup> *p*-OCH<sub>3</sub> (2a),<sup>5,8,9,14</sup> and *p*-CH<sub>3</sub> (2b).<sup>6,15</sup> The use of triethylsilane and trifluoroacetic acid in CCl<sub>4</sub> solution has been reported for the preparation of 2g (82% yield), 2a (82%), and 2d (80%) with the ratio of the substrate (1):HSiEt<sub>3</sub>:CF<sub>3</sub>CO<sub>2</sub>H = 1:3:10, and the reaction conditions of stirring at 50 °C for 6 h.<sup>6</sup> But we were unable to reproduce the yields, and the major products were substituted 1,3-diphenylpropan-1-ols.

Therefore, several attempts were made for the synthesis of **2a–k** from the chalcones (**1**) using one set of conditions, employing triethylsilane and trifluoroacetic acid, as shown in Scheme 1. After the countless trials of the reaction conditions, we were able to find the most effective conditions for the complete conversion of **1** to **2**, namely heating the mixture of **1**: Et<sub>3</sub>SiH:CF<sub>3</sub>CO<sub>2</sub>H = 1:8:16 by mole for 5 h in a sealed tube at 80 °C. The reaction time could be reduced to 1 h by employing a huge excess of the reagents, but that does not seem to be economical. The isolated yields of **2a–k** were over 80% after the column chromatography (silica gel, hexane:EtOAc = 9:1). The <sup>1</sup>H and <sup>13</sup>C NMR spectroscopic data are listed in Tables 1 and 2, respectively.

**Correlations of NMR Chemical Shifts with Hammett**  $\sigma$ **.** Quantitative analysis of the electronic effects of the substituents on the benzene ring on the rate or equilibrium constants that take place at the side chain has usually been made by the Hammett correlation. Such an approach can also be applied to the variation of the chemical shift values.<sup>16</sup> The analysis is typically done by the single substituent parameter (SSP) and dual substituent parameter (DSP) approaches, which are represented by Eqs. (1) and (2), respectively.<sup>17</sup>

$$\delta_{\rm Z} - \delta_{\rm H} = \rho \sigma \tag{1}$$

$$\delta_{\rm Z} - \delta_{\rm H} = \rho_{\rm I} \sigma_{\rm I} + \rho_{\rm R} \sigma_{\rm R} \tag{2}$$



Z :**a**, *p*-OCH<sub>3</sub>; **b**, *p*-CH<sub>3</sub>; **c**, *m*-CH<sub>3</sub>; **d**, H; **e**, *m*-OCH<sub>3</sub>, **f**, *p*-Cl; **g**, *p*-Br; **h**, *m*-Cl; **i**, *m*-Br; **j**, *m*-NO<sub>2</sub>, **k**, *p*-NO<sub>2</sub>

Scheme 1. Synthesis of 1-aryl-3-phenylpropanes.

DSP provides the information on the magnitudes of the inductive and resonance effects of the substituent, respectively. We have found that the correlations of the <sup>1</sup>H and <sup>13</sup>C chemical shifts vs. the Hammett  $\sigma$  values using SSP analysis are fair to good, as shown in Figure 1. The slopes ( $\rho$ ) and the correlation coefficients (r) from similar plots are listed in Table 3.

As shown in Table 3, the proton chemical shift values did not show any meaningful correlation with the  $\sigma$  values. On the other hand, the values of the <sup>13</sup>C showed a significant correlation (r = 0.950-0.984) with 2-C, *i*-C, *o*-C, and *p*-C, but no correlation was apparent with 1-C and *m*-C. 3-C showed only a trend in the correlation. There was absolutely no correlation with 1-C (r = 0.247), which is the benzylic carbon atom directly bonded to the benzene ring having the substituents. This is in contrast to the general notion that the electronic effect would be most efficiently transmitted to it. The observation is consistent with similar phenomena observed in the *m*- or *p*-substituted phenethyl compounds<sup>18</sup> and in the benzyl esters.<sup>19</sup>

One of the notable phenomena is that the <sup>13</sup>C correlation has the negative  $\rho$  values for 2-C and *i*-C. Similar observations were made in the *m*- and *p*-substituted chalcones (1) in our previous report,<sup>1</sup> and the values are listed in Table 3 for the purpose of comparison. The three carbon atoms that connect the two benzene rings in the chalcone system are sp<sup>2</sup>-hybridized, which is striking contrast to the present system of sp<sup>3</sup>-hybridized carbon atoms. Apparently, the electronic effect of the substituent seems to transmit more efficiently through the sp<sup>2</sup>-C, which is evidenced by the larger absolute  $\rho$  values (-121.42 for  $\alpha$ -C of 1 vs. -64.60 for 2-C of 2). The negative  $\rho$  value observed in 1 was explained by the  $\pi$  polarization mechanism.<sup>19</sup> Obviously, such mechanism cannot be applied to the present system in which the linkers are all sp<sup>3</sup>-hybrized.

The inverse correlation of 2-C in **2** may be explained by the transmission of the electronic effect alternating like a wave.<sup>20</sup> The alternation of substituent-induced charges was suggested as a general phenomenon for carbon atoms in  $\pi$ 

**Table 1.** <sup>1</sup>H-NMR chemical shift values of **2a–2k** in chloroform-*d* (in  $\delta$ ).

	1-H	2-H	3-Н	<i>о</i> -Н	<i>m</i> -H	<i>р-</i> Н	2′-Н	3-Н	4′-H	5′-H	6′-H
a	2.60	1.95	2.66	7.20	7.30	7.19	7.12	6.85		6.85	7.12
a	2.64	1.96	2.67	7.21	7.30	7.20	7.12	7.09		7.09	7.12
a	2.64	1.98	2.68	7.21	7.30	7.19	7.01		7.01	7.19	7.01
d	2.67	1.99	2.67	7.21	7.30	7.20	7.21	7.30	7.20	7.30	7.21
a	2.65	1.97	2.67	7.19	7.29	7.23	6.75		6.75	7.29	7.19
f	2.65	1.97	2.67	7.21	7.32	7.22	7.14	7.28		7.28	7.14
g	2.52	1.85	2.56	7.09	7.21	7.11	6.97	7.31		7.31	6.97
h	2.55	1.87	2.57	7.10	7.21	7.09	7.09		7.12	7.11	6.97
i	2.63	1.96	2.66	7.19	7.30	7.20	7.35		7.33	7.15	7.11
j	2.60	1.93	2.68	7.11	7.22	7.13	7.96		7.97	7.36	7.43
k	2.67	1.92	2.59	7.10	7.22	7.13	7.25	8.06		8.06	7.25

<sup>a</sup>CH<sub>3</sub> signal in δ: 2a 3.87; 2b 2.34; 2c 2.31; 2e 3.82.

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Table 2	2. <sup>13</sup> C-NMR chemic	al shift values of <b>2a</b>	<b>-2k</b> in chloroform-	d (in ppm).			
	1-C	2-C	3-C	i-C	<i>o</i> -C	<i>m</i> -C	<i>р-</i> С
a	34.93	33.60	35.80	142.79	128.71	128.86	126.12
b	35.41	33.47	35.86	142.80	128.70	128.87	126.12
c	35.81	33.40	35.94	142.67	128.71	128.87	126.14
d	35.86	33.37	35.86	142.71	128.72	128.87	126.15
e	35.84	33.23	35.88	142.68	128.72	128.86	126.16
f	35.14	33.25	35.71	142.11	130.19	128.81	126.25
g	35.19	33.18	35.70	142.40	128.77	128.84	126.26
h	35.48	33.10	35.74	142.36	128.78	128.84	126.27
i	35.46	33.12	35.74	142.06	128.78	128.84	126.28
j	35.66	32.97	35.38	141.94	128.81	128.86	126.42
k	35.68	32.85	35.65	141.91	128.81	128.86	126.44
	1'-C	2'-C	3'-C	4'-C	5'-C	6'-C	
a	134.78	129.72	114.14	158.14	114.14	129.72	
a	139.62	128.74	129.41	135.56	129.41	128.74	
a	142.78	129.69	138.25	126.90	128.62	125.86	
d	142.71	128.72	128.87	126.15	128.87	128.72	
a	160.03	114.63	144.36	111.43	129.66	121.30	
f	141.11	130.19	128.81	131.85	128.81	130.19	
g	141.63	130.63	131.77	119.67	131.77	130.63	
h	144.74	128.98	134.48	127.06	129.96	126.37	
i	142.34	131.90	122.82	129.30	130.28	127.52	
j	144.65	123.65	148.75	121.45	129.58	135.15	
k	150.61	129.61	124.05	146.76	124.05	129.61	

<sup>a</sup>CH<sub>3</sub> signal in ppm 2a 55.67; 2b 21.42; 2c 21.84; 2e 55.55.



**Figure 1.** Correlation between  $\sigma$  and <sup>13</sup>C chemical shift differences  $\delta_Z - \delta_H$  of 2-C and *i*-C in **2** in 0.1 M-chloroform-*d*.

systems.<sup>21</sup> Apparently, such a phenomenon also seems to take place through the sp<sup>3</sup>-hybridized carbon skeleton, as shown by a negative  $\rho$  and the best *r* (0.984) value observed in the present system.

Such a rationale should raise a question as to why the  $\rho$  value of *i*-C is negative. Furthermore, the magnitude of the

 $\rho$  value of *i*-C (-90.31) is the largest in spite of the separation of the two rings by --CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-- chain. The observation may be explained by the mode of the transmission of substituent electronic effect not only through bonding but also through space, as shown in Figure 2. The two benzene rings may be partially stacked by the  $\pi$ - $\pi$  interaction, as shown in the Newman projection like **I**.

Such an arrangement in space may facilitate the transmission of the substituent effect through the interaction of the p orbitals. The largest magnitude of the  $\rho$  and the good correlation coefficient values for the *i*-C may be the result of such an interaction.

The close array of the two rings may also be the cause for the negative  $\rho$  value for 3-C, although the value of r (0.745) may only imply a trend. The H atom bonded to 3-C and the ortho carbon atom of the benzene ring having the substituents may be close comprising a six-membered ring, as shown in **II**. If this is the case, the meta substituents may be considered para to the carbon atom and the para substituents should become meta. In order to examine the plausibility of such a rationale, the values of  $\sigma_m$  and  $\sigma_p$  for each substituent were replaced with the values of  $\sigma_p$  and  $\sigma_m$ , respectively. The results of calculations after the exchange are listed in Table 3 in italic.

It is interesting to note that the correlation coefficient for 3-H was improved dramatically from 0.135 to 0.773 after exchange of  $\sigma_p$  and  $\sigma_m$ . Furthermore, the correlation for 3-

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C was also improved from 0.745 to 0.896. On the other hand, 2-C showed a decreased correlation, changing the r value from 0.984 to 0.727.

The idea that the substituent effect of one ring can be transmitted by the through-space mechanism may be supported by examining the substituent chemical shift corrections for the arylpropyl group. Such a calculation is possible by averaging the values for the series. The results are listed in Table 4 along with the values reported in the literature for CH<sub>3</sub>—, CH<sub>3</sub>CH<sub>2</sub>—, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>— and C<sub>6</sub>H<sub>5</sub>— groups.<sup>22</sup> In general, phenyl group is considered as an electron-withdrawing substituent, which causes downfield shift of <sup>1</sup>H and <sup>13</sup>C signals in the benzene ring to which it is linked with some minor exceptions of *p*-H and *o*-C. On the other hand, alkyl groups are known to cause upfield shift of all H and C signals except *i*-C, as shown in Table 4. Table 4 clearly shows that the signals of the protons in the phenyl ring of **2a–2k** shift upfield with a minor exception ( $\Delta\delta$  0.01) of *m*-H, and those of the <sup>13</sup>C shift to

downfield except *p*-C. Especially, the magnitude of the shift for the *i*-C (14.08 ppm) is far greater than that for the alkyl groups (9.2–11.7 ppm). Comparison of the magnitudes of the values for the arylpropyl and phenyl groups is more striking because the benzene ring separated by the three sp<sup>3</sup>-hybridized carbon atoms shows a much larger



Figure 2. Illustration of the through-space transmission of the substituent effect.

**Table 3.** Slopes  $\rho$  (in Hz) and the correlation coefficients *r* for the plots of the chemical shift difference values  $\delta_Z - \delta_H$  vs. the Hammett substituent constants  $\sigma$ .<sup>*a,b*</sup>

$1^{c}$			2							
			From <sup>1</sup> H-	NMR data	From <sup>13</sup> C-NMR data					
	ρ	r		ρ	r		ρ	r		
C=0	-142.66	0.573	1-H	43.52 27.90	0.731 0.507	1-C	22.73 -20.07	0.247 0.218		
α-C	-121.42	0.844	2-H	13.39 9.95	0.515 0. <i>306</i>	2-C	-64.60 -47.73	0.984 0.727		
β-C	268.96	0.994	3-Н	1.90 17.52	0.135 <i>0.773</i>	3-C	-33.35 -40.12	0.745 <i>0</i> .896		
i-C	-77.66	0.993				<i>i</i> -C	-90.31 -83.65	0.975 <i>0.904</i>		
<i>о</i> -С	35.99	0.995	<i>о</i> -Н	-9.25 -8.78	0.777 <i>0.738</i>	<i>o</i> -C	11.87 11.17	0.950 <i>0.894</i>		
<i>m</i> -C	19.42	0.986	<i>m</i> -H	1.25 1.22	0.330 <i>0.324</i>	<i>m</i> -C	1.34 <i>–1.37</i>	0.357 <i>0.367</i>		
<i>р</i> -С	89.04	0.993	<i>р-</i> Н	4.91 0.839	0.598 <i>0.102</i>	<i>р-</i> С	33.11 <i>31.01</i>	0.976 <i>0.914</i>		

<sup>*a*</sup> The numbers in italic indicate the values obtained by exchanging  $\sigma_m$  and  $\sigma_p$ .

 $^{\it b}$  The  $\sigma$  values are taken from Ref. 16.

<sup>c</sup> The values are taken from Ref. 4.

**Table 4.** Calculated substituent parameters for *m*- and *p*-substituted 3-arylpropyl group on the chemical shifts of the protons and carbons in the benzene ring.

Substituent	<i>о</i> -Н	<i>m</i> -H	<i>р</i> -Н	i-C	<i>o</i> -C	<i>m</i> -C	<i>р</i> -С
Z-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -	-0.09	0.01	-0.09	14.08	0.38	0.35	-2.26
CH <sub>3</sub> - <sup><i>a</i></sup>	-0.20	-0.12	-0.21	9.2	0.7	-0.1	-3.0
CH <sub>3</sub> CH <sub>2</sub> — <sup>a</sup>	-0.14	-0.05	-0.18	11.7	-0.6	-0.1	-2.8
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> — <sup>a</sup>	b	b	b	10.3	-0.2	0.1	-2.7
$C_6H_5-a$	0.22	0.06	-0.04	9.6	-1.6	0.5	0.5

<sup>*a*</sup> From Ref. 22.

<sup>b</sup> Data unavailable.

Article

Mass Spectral Fragmentation Patterns. The throughspace transmission of the substituent effect seems to be consistent with the fragmentation pattern in the mass spectra of 2. The m/z values of the major fragments and their relative intensities are listed in Table 5.

As mentioned earlier, the unique structural characteristic of 2 is the presence of the substituted benzyl and the unsubstituted benzyl groups linked by a CH<sub>2</sub> group. Therefore, the notable fragments should be those listed in Scheme 2.

The nitro compounds 2j and 2k showed very similar fragmentation patterns. Because of the strong electronwithdrawing nature of the nitro group, the major bond cleavage is expected to take place between 2-C and 3-C, resulting in the formation of III and IX.

Similarly, the base peak was III when the electronwithdrawing groups were present at the meta position as for 2i and 2h. On the other hand, 2e and 2c showed the base peaks derived from the McLafferty rearrangement. The cleavage of 1-C-2-C bond may be facilitated by the electron-donating substitution at the meta position, as shown in Scheme 3.

The position to which the proton transfers for the McLafferty rearrangement is para from the substituents in **2e** and **2c**. The *m*-OCH<sub>3</sub> group is electron withdrawing ( $\sigma$ 0.12). But the rearrangement should take place at the para position from the OCH<sub>3</sub> group, as shown in Scheme 4.

Apparently, the through-space interaction of the electronic effect of the substituent seems to be parallel in trend to the chemical shift and the fragmentation pattern. Then, it is understandable that the rearrangement takes place from the substituted benzylic proton to the unsubstituted benzyl ring forming IX in case of the presence of the electronwithdrawing group (2f-k). When the electron-donating group is at the para position (2a, 2b), the base peak is VI because the substituent would make the benzyl cation more stable.

In conclusion, the 1-aryl-3-phenylpropane system is an excellent model for the support of the through-space transmission of the electronic effect of a substituent. Such phenomenon, in addition to the through-bond transmission, should play an important role in the correlation of the  $^{13}C$ chemical shift with the Hammett  $\sigma$  values and the mass spectral fragmentation.



Scheme 2. Mass fragmentation patterns of 2.



Scheme 3. Dependence of the mass fragmentation on the electronic nature of the substituent.

VI

121 (100)

105 (100)

105 (35)

91 (53)

121 (9)

125 (29)

169 (18)

125 (13)

169 (7)

136 (12)

136(1)

	$M^+$	III	IV	
a	226 (55)	(14)	135 (4)	

(46)

(43)

(53)

(19)

(60)

(63)

(100)

(100)

(100)

(100)

119 (42)

119 (21)

105 (49)

135 (4)

139 (16)

183 (15)

139 (14)

183 (8)

150 (83)

150 (49)

Table 5. Mass spectral data of 2a-2k, m/z (%).

210 (100)

210 (62)

196 (65)

226 (39)

230 (74)

274 (51)

230 (87)

274 (58)

241 (100)

241 (51)

b

с

d

e

f

g h

i

j k

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v

(7)

(81)

(35)

(49)

(7)

(43)

(49)

(39)

(44)

(100)

(100)

VIII

122 (13)

106 (71)

106 (100)

92 (100)

122 (100)

126 (13)

170 (7)

126 (61)

170 (42)

137 (41)

137 (31)

IX

(6)

(61)

(26)

(100)

(100)

(100)

(66)

(79)

(100)

(100)

(7)



Scheme 4. McLafferty cleavage observed in 2e.

#### Experimental

NMR spectra were recorded on a Bruker DPX-400 FT NMR spectrometer (Rheinstetten, Germany) in the Central Lab of Kangwon National University at 400 MHz for <sup>1</sup>H and 100 MHz for <sup>13</sup>C and were referenced to tetramethylsilane. Mass spectra were obtained using a JEOL JMS-700 mass spectrometer (Akishima, Japan) at 20 eV. The solution for the NMR spectrum was prepared by dissolving the appropriate amount of **2** in a 1-mL volumetric flask to make the concentration 0.1 M in chloroform-*d*. A portion (0.6 mL) of the solution was transferred into a 5-mm NMR tube, and the spectrum was obtained at 20 °C.

Preparations of *m*- or *p*-substituted chalcones (1) were carried out from the commercially available benzaldehydes and acetophenones by following the procedures in the literature.<sup>23</sup>

Reduction of *m*- and *p*-substituted chalcones (1) to 1,3diarylpropanes (2). An illustrative procedure for the conversion of 1d to 2d is as follows: A mixture of 1d (110 mg, 0.53 mmoles), Et<sub>3</sub>SiH (0.70 mL, 4.38 mmoles), and CF<sub>3</sub>CO<sub>2</sub>H (0.65 mL, 8.53 mmoles) in a sealed tube was stirred at 80 °C for 5 h. The resulting liquid was poured into dichloromethane (50 mL) and washed with 1M NaOH (3 × 20 mL) and water (10 mL), successively. The organic layer was dried over MgSO<sub>4</sub> and then evaporated, yielding a viscous liquid, which was chromatographed (silica gel, EtOAc:hexane = 1:9) to obtain the pure product 2d in 70% yield.

Acknowledgments. We thank Dr. Gary Kwong for help in preparing the manuscript. This research was supported by 2015 Research Grant from the Kangwon National University (No. 520150200).

#### References

- For example, F. A. Carroll, *Perspectives on Structure and Mechanism in Organic Chemistry*, 2nd ed., John Wiley & Sons, New York, NY, **2010**, p. 385.
- H. Gunther, *NMR Spectroscopy*, 2nd ed., John Wiley & Sons, New York, NY, **1995**, p. 102.
- K. O. Jeon, J. H. Jun, J. S. Yu, C. K. Lee, J. Heterocyclic Chem. 2003, 40, 763.

- For example,H. S. H. Lee, H. J. Jeon, J. S. Yu, C. K. Lee, Bull. Korean Chem. Soc. 2010, 31, 1689.
- K. A. De Castro, S. Oh, J. Yun, J. K. Lim, G. An, D. K. Kim, H. Rhee, *Synth. Commun.* 2009, *39*, 3509.
- D. N. Kursanov, N. M. Loim, V. A. Baranova, L. V. Moiseva, L. P. Zalukaev, Z. N. Parnes, *Synthesis* 1973, 7, 420.
- K. Nakata, C. Feng, T. Tojo, Y. Kobayashi, *Tetrahedron Lett.* 2014, 55, 5774.
- S. Kumar, L. C. S. Reddy, Y. Kumar, A. Kumar, B. K. Singh, V. Kumar, S. Malhotra, M. K. Pandey, R. Jain, R. Thimmulappa, S. K. Sharma, A. K. Prasad, S. Biswal, E. V. Eycken, A. L. DePass, S. V. Malhotra, B. Ghosh, V. S. Parmar, Arch. Pharm. Chem. Life Sci. 2012, 345, 368.
- R. Royer, P. Demerseman, J.-P. Lechartier, A. Cheutin, J. Org. Chem. 1962, 27, 3808.
- 10. G. A. Molander, C.-S. Yun, Tetrahedron 2002, 58, 1465.
- 11. C. Matthias, D. Kuck, Croat. Chem. Acta 2009, 82, 7.
- 12. J. Barluenga, M. Tomas-Gamasa, F. Aznar, C. Valdes, *Nat. Chem.* **2009**, *1*, 494.
- B. A. Ellsworth, W. Meng, M. Patel, R. N. Girotra, G. Wu, P. M. Sher, D. L. Hagan, M. T. Obermeier, W. G. Humphreys, J. G. Robertson, A. Wang, S. Han, T. L. Waldron, N. N. Morgan, J. M. Whaley, W. N. Washburn, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 4770.
- G. A. Molander, O. A. Argintaru, I. Arom, S. D. Dreher, *Org. Lett.* 2010, 12, 5783.
- 15. H. Pines, J. Shabtai, J. Org. Chem. 1961, 26, 4220.
- H.-O. Kalinowski, S. Berger, S. Braun, *Carbon-13 NMR Spectroscopy*, John Wiley & Sons, New York, NY, 1984, p. 311.
- 17. D. J. Craik, R. T. C. Brownlee, Prog. Phys. Org. Chem. 1983, 14, 1.
- L. F. Blackwell, P. D. Buckley, K. W. Jolley, Aust. J. Chem. 1976, 29, 2423.
- J. Bromilow, R. T. C. Brownlee, D. J. Craik, P. R. Fiske, J. E. Rowe, M. Sadek, *J. Chem. Soc. Perkin Trans. II* 1981, 753.
- G. K. Hamer, I. R. Peat, W. F. Raynolds, *Can. J. Chem.* 1973, 51, 897.
- 21. C. N. Robinson, G. E. Stablein, C. D. Slater, *Tetrahedron* **1990**, *46*, 335.
- E. Pretsch, P. Buhlmann, C. Affolter, *Structure Determination* of Organic Compounds, 3rd ed., Springer, Berlin, 2000, p. 97 and 182.
- 23. S. Bhagat, R. Sharma, D. M. Sawant, L. Sharma, A. K. Chakraborti, *J. Mol. Cat. A* **2006**, *244*, 20.