

## Methyl Substitution Effects on $^1\text{H}$ and $^{13}\text{C}$ NMR Data of Methoxyflavones

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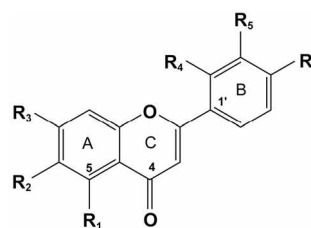
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Flavones are very common in nature and consist of a large group of plant metabolites.<sup>1,2</sup> They have biological effects in numerous mammalian cell systems, which have led to interest in their possible role in human health and disease. Methoxyflavones, also found in natural sources, have recently been shown to be cancer chemopreventive agents. The methylation of flavone results in the enhanced metabolic stability and membrane permeability in the intestine/liver due to increased hydrophobicity, thus improving oral bioavailability.<sup>3</sup>

Methoxyflavones have been identified using a number of instrumental analyses. Among these analyses, nuclear magnetic resonance (NMR) spectroscopy is one of the most powerful tools available to determine the composition of unknown compounds based on the changes in chemical shifts caused by the number or position of substituents. Although methylation may not cause drastic change of chemical shifts even in protons, the complete NMR data of methoxyflavones can help us identify derivatives isolated from natural products. In the present study, we report the complete  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of 21 methoxyflavones: five monomethoxyflavones, ten dimethoxyflavones, five trimethoxyflavones, and one tetramethoxyflavone (Fig. 1). However, NMR data of nine methoxyflavone derivatives have previously been reported.<sup>4-11</sup> As a result, the complete  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of 12 methoxyflavones were determined here.

Among 12 unpublished methoxyflavones, we reported the interpretation of NMR data of 6,2',4'-trimethoxyflavone (**17**) in detail here as a representative of them. Eighteen  $^{13}\text{C}$  peaks were observed in the  $^{13}\text{C}$  NMR spectrum and the peaks between 50 and 60 ppm suggested the presence of methoxy carbons. In addition, the most downfield shifted peak at 176.8 ppm was assigned to C-4. In heteronuclear multiple bonded connectivities (HMBC), it was long-range coupled to two  $^1\text{H}$  peaks at 6.90 and 7.41 ppm which were attached directly to two  $^{13}\text{C}$  peaks at 109.4 and 104.6 ppm, respectively. Because the former proton showed a long-ranged coupling with the carbon at 160.3 ppm, it should be assigned to H-3. Subsequently,  $^1\text{H}$  at 7.41 ppm was identified as H-5. Moreover, the  $^{13}\text{C}$  peak at 160.3 ppm was determined to be C-2. Another  $^{13}\text{C}$  peak showing a long-ranged coupling with H-5 at 156.4 ppm was proved to be C-6. Additionally, the carbon peak at 123.7 ppm which was long-range coupled with H-3 was identified as C-10. Furthermore, the methine carbons at 120.0 and 123.0 ppm were directly attached to

two  $^1\text{H}$  at 7.68 and 7.39 ppm, respectively. These protons were correlated with each other in correlated spectroscopy (COSY), thus they could be assigned to H-7 and/ or H-8. Since the former was long-range coupled to C-10, it should be H-8. On the other hand, the  $^{13}\text{C}$  peak at 150.5 ppm was long-range coupled to H-7, so it was considered to be C-9. Also, three aromatic proton signals ascribed to those of ring B were observed at 6.76, 6.73, and 7.93 ppm. Among them, two signals at 6.73 and 7.93 ppm were correlated with each other in COSY spectrum, and they were assigned to H-5' and/ or H-6', respectively. Because the latter showed weak



Derivative	Nomenclature	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	R <sub>6</sub>
1	5-Methoxyflavone	OMe	H	H	H	H	H
2	6-Methoxyflavone	H	OMe	H	H	H	H
3	7-Methoxyflavone	H	H	OMe	H	H	H
4	2'-Methoxyflavone	H	H	H	OMe	H	H
5	3'-Methoxyflavone	H	H	H	H	OMe	H
6	5,2'-Dimethoxyflavone	OMe	H	H	OMe	H	H
7	5,3'-Dimethoxyflavone	OMe	H	H	H	OMe	H
8	5,4'-Dimethoxyflavone	OMe	H	H	H	H	OMe
9	6,2'-Dimethoxyflavone	H	OMe	H	OMe	H	H
10	6,3'-Dimethoxyflavone	H	OMe	H	H	OMe	H
11	7,2'-Dimethoxyflavone	H	H	OMe	OMe	H	H
12	7,3'-Dimethoxyflavone	H	H	OMe	H	OMe	H
13	7,4'-Dimethoxyflavone	H	H	OMe	H	H	OMe
14	2',4'-Dimethoxyflavone	H	H	H	OMe	H	OMe
15	3',4'-Dimethoxyflavone	H	H	H	H	OMe	OMe
16	6,2,3'-Trimethoxyflavone	H	OMe	H	OMe	OMe	H
17	6,2,4'-Trimethoxyflavone	H	OMe	H	OMe	H	OMe
18	7,2,3'-Trimethoxyflavone	H	H	OMe	OMe	OMe	H
19	7,2,4'-Trimethoxyflavone	H	H	OMe	OMe	H	OMe
20	7,3,4'-Trimethoxyflavone	H	H	OMe	H	OMe	OMe
21	5,6,7,4'-Tetramethoxyflavone (scutellarein tetramethyl ether)	OMe	OMe	OMe	H	H	OMe

**Figure 1.** Structures and nomenclatures of methoxyflavone derivatives 1-21

long-ranged coupling with C-2, it was assigned to H-6'. Consequently, the remaining proton at 6.76 ppm should be H-3'. Among undetermined three carbons, the most upfield

shifted carbon was determined to be C-1'. In order to distinguish between C-2' and C-4', first of all, 2'-OMe and 4'-OMe were determined using the nuclear Overhauser enhan-

**Table 1.** The  $^1\text{H}$  chemical shifts of 21 methoxyflavone derivatives 1-21

$\delta$ of $^1\text{H}$ (J, Hz)										
position	1	2	3	4	5	6	7	8	9	10
3	6.83 (s)	7.02 (s)	6.92 (s)	6.91 (s)	7.08 (s)	6.77 (s)	6.87 (s)	6.73 (s)	6.90 (s)	6.96 (s)
5		7.44 (d, 2.8)	7.91 (d, 8.8)	8.03 (dd, 1.7, 7.9)	8.05 (dd, 7.9, 1.6)	-	-	-	7.41 (d, 3.1)	7.40 (d, 3.1)
6	6.97 (d, 8.4)	-	7.03 (dd, 8.8, 2.4)	7.46 (ddd, 1.0, 7.9, 8.0)	7.50 (m)	6.98 (dd, 8.4)	6.97 (d, 8.4)	6.97 (d, 8.4)	-	-
7	7.68 (dd, 8.4, 8.4)	7.43 (d, 7.0)	-	7.78 (ddd, 1.7, 7.1, 8.0)	7.83 (m)	7.68 (dd, 8.4, 8.4)	7.67 (dd, 8.4, 8.4)	7.66 (dd, 8.4, 8.4)	7.37 (dd, 3.1, 9.1)	7.38 (dd, 8.8, 3.1)
8	7.25 (m)	7.76 (m)	7.26 (d, 2.4)	7.67 (d, 8.0)	7.80 (m)	7.21 (d, 8.4)	7.26 (d, 8.4)	7.24 (d, 8.4)	7.63 (d, 9.1)	7.70 (d, 8.8)
2'	8.03 (dd, 2.0, 7.6)	8.10 (dd, 1.9, 7.6)	8.05 (m)	-	7.60 (m)	-	7.53 (dd, 1.8, 2.2)	7.98 (d, 9.0)	-	7.54 (d, 2.0)
3'	7.54 (m)	7.59 (m)	7.55 (m)	7.21 (d, 8.3)	-	7.24 (d, 8.4)	-	7.08 (d, 9.0)	7.21 (dd, 0.9, 8.1)	-
4'	7.56 (m)	7.60 (m)	7.56 (m)	7.54 (ddd, 1.7, 7.6, 8.3)	7.17 (dd, 2.5, 8.1)	7.55 (ddd, 8.4, 7.4, 1.7)	7.13 (ddd, 0.8, 2.2, 8.0)	-	7.54 (ddd, 1.7, 7.7, 8.1)	7.14 (dd, 8.2, 2.0)
5'	7.54 (m)	7.59 (m)	7.55 (m)	7.11 (dd, 7.6, 7.6)	7.49 (m)	7.14 (m)	7.45 (dd, 8.0, 8.0)	7.08 (d, 9.0)	7.12 (ddd, 0.9, 7.7, 7.8)	7.45 (dd, 8.0, 8.0)
6'	8.03 (dd, 2.0, 7.6)	8.10 (dd, 1.9, 7.6)	8.05 (m)	7.88 (dd, 1.7, 7.6)	7.67 (m)	7.89 (dd, 7.8, 1.7)	7.60 (ddd, 0.8, 1.8, 8.0)	7.98 (d, 9.0)	7.88 (dd, 1.7, 7.8)	7.670 (dd, 8.0, 2.0)
5-OMe	3.86 (s)	-	-	-	-	3.86 (s)	3.86 (s)	3.86 (s)	-	-
6-OMe	-	3.87 (s)	-	-	-	-	-	-	3.86 (s)	3.85 (s)
7-OMe	-	-	3.90 (s)	-	-	-	-	-	-	-
2'-OMe	-	-	-	3.90 (s)	-	3.92 (s)	-	-	3.92 (s)	-
3'-OMe	-	-	-	-	3.87 (s)	-	3.85 (s)	-	-	3.86 (s)
4'-OMe	-	-	-	-	-	-	-	3.84 (s)	-	-

$\delta$ of $^1\text{H}$ (J, Hz)											
position	11	12	13	14	15	16	17	18	19	20	21
3	6.86 (s)	6.98 (s)	6.84 (s)	6.92 (s)	7.03 (s)	6.74 (s)	6.90 (s)	6.69 (s)	6.83 (s)	6.95 (s)	6.70 (s)
5	7.94 (d, 8.8)	7.93 (d, 8.8)	7.92 (d, 8.8)	8.03 (dd, 1.7, 7.8)	8.03 (dd, 1.5, 7.9)	7.42 (m)	7.41 (m)	7.94 (d, 8.8)	7.90 (d, 8.8)	7.92 (d, 8.8)	-
6	7.06 (dd, 8.8, 2.4)	7.06 (dd, 2.4, 8.8)	7.04 (dd, 8.8, 2.4)	7.47 (ddd, 1.0, 7.0, 7.8)	7.48 (ddd, 1.5, 6.8, 7.9)	-	-	7.05 (dd, 2.4, 8.8)	7.02 (dd, 2.4, 8.8)	7.05 (dd, 2.4, 8.8)	-
7	-	-	-	7.80 (ddd, 1.7, 7.0, 8.3)	7.80 (m)	7.38 (dd, 3.2, 8.8)	7.39 (m)	-	-	-	-
8	7.25 (d, 2.4)	7.32 (d, 2.4)	7.28 (d, 2.4)	7.72 (dd, 1.0, 8.3)	7.78 (m)	7.66 (d, 8.8)	7.68 (d, 8.5)	7.18 (d, 2.4)	7.21 (d, 2.4)	7.32 (d, 2.4)	7.20 (s)
2'	-	7.60 (m)	8.04 (dd, 8.9, 2.0)	-	7.59 (d, 2.1)	-	-	-	-	7.59 (d, 2.2)	8.01 (d, 9.0)
3'	7.25 (d, 8.3)	-	7.10 (dd, 8.9, 2.0)	6.76 (m)	-	-	6.76 (d, 2.4)	-	6.73 (m)	-	7.10 (d, 9.0)
4'	7.57 (ddd, 8.3, 7.4, 1.7)	7.16 (dd, 2.5, 8.1)	-	-	-	7.30 (dd, 2.0, 8.2)	-	7.27 (dd, 2.0, 8.2)	-	-	-
5'	7.15 (dd, 7.8, 7.4)	7.48 (dd, 8.1, 8.1)	7.10 (dd, 8.9, 2.0)	6.75 (dd, 2.3, 8.0)	7.12 (d, 8.5)	7.22 (dd, 7.5, 8.2)	6.73 (dd, 2.4, 8.5)	7.23 (dd, 7.4, 8.2)	6.70 (d, 2.4)	7.12 (d, 8.4)	7.10 (d, 9.0)
6'	7.93 (dd, 7.8, 1.7)	7.66 (m)	8.04 (dd, 8.9, 2.0)	7.94 (d, 8.0)	7.70 (dd, 2.1, 8.5)	7.35 (dd, 2.0, 7.5)	7.93 (d, 8.5)	7.36 (dd, 2.0, 7.4)	7.92 (d, 8.4)	7.69 (dd, 2.2, 8.4)	8.01 (d, 9.0)
5-OMe	-	-	-	-	-	-	-	-	-	-	3.80 (s)
6-OMe	-	-	-	-	-	3.86 (s)	3.86 (s)	-	-	-	3.77 (s)
7-OMe	3.91 (s)	3.92 (s)	3.91 (s)	-	-	-	-	3.90 (s)	3.90 (s)	3.93 (s)	3.95 (s)
2'-OMe	3.93 (s)	-	-	3.94 (s)	-	3.81 (s)	3.94 (s)	3.82 (s)	3.93 (s)	-	-
3'-OMe	-	3.87 (s)	-	-	3.89 (s)	3.87 (s)	-	3.87 (s)	-	3.90 (s)	-
4'-OMe	-	-	3.85 (s)	3.87 (s)	3.85 (s)	-	3.87 (s)	-	3.86 (s)	3.86 (s)	3.90 (s)

ced spectroscopy (NOESY) experiment. Importantly, an nOe cross peak between H-3 and the  $^1\text{H}$  peak at 3.94 ppm was observed, thus it was assigned to 2'-OMe proton which was directly attached to the  $^{13}\text{C}$  peak at 56.1 ppm in heteronuclear multiple quantum coherence (HMQC). Since 2'-OMe proton showed weak long-ranged coupling with the  $^{13}\text{C}$  peak at 159.4 ppm, it should be assigned to C-2'. Subsequently, the carbon peak at 163.1 ppm should be C-4'. Furthermore, the  $^1\text{H}$  peak at 3.87 ppm was long-range coupling to C-4', thus it was 4'-OMe proton. Apparently, one remaining undetermined proton at 3.86 ppm must be 6-OMe proton. In order to confirm this result, the NOESY spectrum was carefully interpreted. Importantly, an nOe peak was observed between H-5 and 6-OMe proton and the complete assignments of  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of 6,2',4'-trimethoxyflavone are listed in Tables 1 and 2, respectively. Like 6,2',4'-trimethoxyflavone, NMR data of 20 methoxyflavone derivatives were assigned and their assignments are also listed in Tables 1 and 2.

Of 21 methoxyflavone derivatives, NMR data of eight derivatives have been previously reported. Six of them (10, 11, 13, 14, 15, 21) were determined by Freeman *et al.*,<sup>6</sup> Pelter *et al.*,<sup>7</sup> Gaydou *et al.*,<sup>8</sup> Inuma *et al.*,<sup>9</sup> Terani *et al.*,<sup>10</sup> and Horie *et al.*,<sup>11</sup> and the remaining three (16, 17, 19) were identified by us.<sup>12-14</sup> In the present study, we found some discrepancies in the NMR data obtained in two of the former cases. In the case of 2',4'-dimethoxyflavone (14), two signal peaks at 124.5 and 124.3 ppm were assigned to C-5 and C-6, respectively in the previous data,<sup>8</sup> whereas the signals at C-5 and C-6 were determined to be 124.7 and 125.2 ppm, respectively in our data. Since the  $^1\text{H}$  peak at 8.03 ppm

which attached to the  $^{13}\text{C}$  peak at 124.7 ppm showed a long-ranged coupling with C-4, it should be C-5. On the other hand, the  $^{13}\text{C}$  peak at 125.2 was long-range coupled to H-8, thus it should be C-6. In addition, two signal peaks at 160.9 and 162.7 ppm in the previous data were determined to be C-4' and C-2, respectively, whereas they were determined to be 163.2 and 160.6 ppm in our data and identified as C-4' and C-2, respectively. According to our study, the former carbon showed long-ranged coupling with H-3', H-5', and H-6', therefore it should be C-4'. On the other hand, the latter carbon showed long-ranged coupling with H-3 and H-6' in HMBC, thus it should be C-2. Moreover, additional signal peaks at 109.9 and 112.2 ppm were assigned to C-1' and C-3, respectively in the previous data, whereas those peaks appeared at 112.3 and 110.2 ppm and were determined to be C-1' and C-3, respectively in our data. Because the singlet  $^1\text{H}$  peak at 6.92 ppm was directly attached to the  $^{13}\text{C}$  peak at 110.2 ppm, the carbon was determined to be C-3. The  $^{13}\text{C}$  peak at 112.3 ppm was long-range coupled to H-3, H-3', and H-5', therefore it should be C-1'. Like 2',4'-dimethoxyflavone, the previous NMR data of 3',4'-dimethoxyflavone (15) showed some differences with our data.<sup>9</sup> Signal peaks at 123.3, 123.7, 124.6, and 125.0 ppm were assigned to C-1', C-10, C-6, and C-5, respectively in the previous data, whereas those peaks at 123.29, 123.32, 124.7, and 125.3 ppm were determined to be C-10, C-1', C-5, and C-6, respectively in our data. In addition, the  $^{13}\text{C}$  peak at 123.29 ppm was long-range coupled to H-8, H-6, and H-3, thus it should be C-10. Since the  $^{13}\text{C}$  peak at 123.32 ppm showed long-ranged coupling with H-2' and H-5', it should be C-1'. Moreover, the  $^1\text{H}$  peak at 8.03 ppm which was attached to

**Table 2.** The  $^{13}\text{C}$  chemical shift of 21 methoxyflavone derivatives 1-21

	$\delta$ of $^{13}\text{C}$																				
position	1*	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2	160.0	162.3	162.1	160.5	162.3	157.9	159.7	160.1	160.2	162.1	160.2	161.8	162.3	160.6	162.7	161.3	160.3	161.0	159.9	162.3	160.3
3	108.4	106.1	106.8	111.5	107.2	113.0	108.6	106.9	110.8	106.4	111.5	107.0	105.2	110.2	105.7	110.4	109.4	111.2	110.0	105.6	106.1
4	176.4	176.8	176.4	177.1	177.1	176.5	176.4	176.4	176.9	176.9	176.4	176.4	176.3	177.1	177.0	176.6	176.8	176.3	176.5	176.4	175.6
5	159.1	104.7	126.1	124.7	124.7	159.0	159.0	159.0	104.5	104.7	126.1	126.0	126.1	124.7	124.7	104.6	104.6	126.2	126.0	126.1	151.6
6	107.2	156.6	114.6	125.2	125.5	107.0	107.2	107.2	156.4	156.6	114.6	114.6	114.5	125.2	125.3	156.6	156.4	114.7	114.3	114.5	139.7
7	134.2	123.2	163.8	134.1	134.3	134.1	134.2	134.1	123.0	123.3	163.8	163.8	163.7	134.1	134.0	123.3	123.0	163.9	163.7	163.7	157.4
8	110.0	120.1	100.9	118.4	118.6	109.9	110.0	109.9	119.8	120.2	100.8	100.9	100.9	118.4	118.5	120.1	120.0	100.8	100.7	100.9	97.3
9	157.6	150.4	157.5	155.8	155.6	157.7	157.5	157.5	150.6	150.4	157.7	157.4	157.4	155.8	155.6	150.6	150.5	157.7	157.5	157.4	153.9
10	113.8	124.0	117.1	123.1	123.3	113.5	113.7	113.7	123.7	124.0	116.9	117.0	117.1	123.1	123.29	123.8	123.7	117.0	116.8	117.1	112.0
1'	130.8	131.2	131.2	119.8	132.5	119.4	132.2	122.9	120.0	132.6	119.9	132.5	123.3	112.3	123.32	126.0	112.4	125.9	112.3	123.4	123.0
2'	126.0	126.3	126.1	157.6	111.5	157.5	111.1	127.8	157.5	111.5	157.5	111.3	128.0	159.5	109.4	147.1	159.4	147.1	159.3	109.4	127.8
3'	129.0	129.1	129.0	112.4	159.7	112.4	159.6	114.5	112.3	159.7	112.5	159.6	114.5	99.1	149.0	153.0	99.0	153.0	99.0	149.0	114.5
4'	131.5	131.7	131.6	132.8	117.6	132.6	117.4	161.9	132.6	117.5	132.7	117.3	162.0	163.2	151.9	115.8	163.1	115.8	163.0	151.8	161.9
5'	129.0	129.1	129.0	120.7	130.2	120.7	130.1	114.5	120.6	130.2	120.7	130.1	114.5	106.3	111.7	124.5	106.2	124.5	106.1	111.7	114.5
6'	126.0	126.3	126.1	129.1	118.6	128.8	118.3	127.8	129.0	118.5	129.0	118.4	128.0	130.4	119.9	120.6	130.3	120.5	130.1	119.7	127.8
5-OMe	56.1	-	-	-	-	56.1	56.1	56.1	-	-	-	-	-	-	-	-	-	-	-	-	61.8
6-OMe	-	55.7	-	-	-	-	-	-	55.6	55.5	-	-	-	-	-	55.7	55.7	-	-	-	61.0
7-OMe	-	-	56.0	-	-	-	-	-	-	-	56.0	56.0	55.5	-	-	-	-	56.1	56.0	56.1	56.4
2'-OMe	-	-	-	55.9	-	55.9	-	-	55.8	-	55.9	-	-	56.1	-	60.6	56.1	60.5	56.3	-	-
3'-OMe	-	-	-	-	55.4	-	55.4	-	-	55.7	-	55.4	-	-	55.8	56.0	-	56.0	-	55.9	-
4'-OMe	-	-	-	-	-	-	-	55.5	-	-	-	-	56.0	55.7	55.7	-	55.6	-	55.6	55.7	55.5

the  $^{13}\text{C}$  peak at 124.7 ppm was long-range coupled to C-4, C-7, and C-9, thus the carbon should be C-5. Because the  $^1\text{H}$  peak at 7.48 ppm which was attached to the  $^{13}\text{C}$  peak at 125.3 ppm showed long-ranged coupling with C-5, C-7, and C-8, the carbon should be C-6.

Regardless of the substituents at A-ring, no significant alteration was observed in the  $^{13}\text{C}$  chemical shifts of B-ring based on the elucidation of the  $^{13}\text{C}$  chemical shifts of methoxyflavones. Likewise, the substitution at B-ring did not cause a change in the  $^{13}\text{C}$  chemical shifts at A-ring. As a result, a combination of the  $^{13}\text{C}$  chemical shifts of methoxyflavones examined in the present study can help us predict the chemical shifts of a methoxyflavone with unknown  $^{13}\text{C}$  chemical shifts.

### Experimental Section

Twenty-one *O*-methylated flavone derivatives were purchased from INDOFINE chemical company, Inc. (Hillsborough, NJ, USA). These chemicals supplied from the company at the purity of 98% were used for the NMR experiments without further purification.

All NMR experiments were carried out on a Bruker Avance 400 spectrometer system (9.4 T, Karlsruhe, Germany) at 298 K as previously described.<sup>12,13</sup> The concentrations of the samples were approximately 50 mM in  $\text{DMSO-}d_6$ . Sixteen transients were acquired for  $^1\text{H}$  NMR experiments with a 1 s relaxation delay using  $90^\circ$  pulse of  $10.2 \mu\text{s}$ , the spectral width of 6,000 Hz, and 32 K data points. A spectral width of 20,000 Hz,  $90^\circ$  pulse of  $10.3 \mu\text{s}$ , and 64 K data points were used for the  $^{13}\text{C}$  NMR and distortionless enhancement by polarization transfer (DEPT) experiments. All two-dimensional spectra were collected with  $2 \text{ K} \times 256$ . The delay for long-ranged coupling in HMBC and the mixing time for the NOESY experiments were 70 ms and 1s,

respectively. Prior to Fourier transformation, 2 K zero filling and sine-squared bell window functions were applied using XWIN-NMR (Bruker).<sup>14</sup> All NMR data are provided as supporting information.

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### References

1. Dixon, R. A.; Steele, C. L. *Trends Plant Sci.* **1999**, *4*, 394.
2. Koes, R. E.; Quattrocchio, F. *Mol. JNM. BioEssays* **1994**, *16*, 123.
3. Dixon, R. A.; Paiva, N. L. *Plant Cell* **1995**, *7*, 1085.
4. Moon, B. H.; Lee, Y. S.; Ahn, J. H.; Lim, Y. H. *Magn. Reson. Chem.* **2006**, *44*, 99.
5. Park, Y. H.; Lee, Y. U.; Kim, H. J.; Lee, Y. S.; Yoon, Y. A.; Moon, B. H.; Chong, Y. H.; Ahn, J. H.; Shim, Y. H.; Lim, Y. H. *Bull. Korean Chem. Soc.* **2006**, *27*, 1537.
6. Freeman, P. W.; Murphy, S. T.; Nemorin, J. E.; Taylor, W. C. *Aust. J. Chem.* **1981**, *34*, 17.
7. Pelter, A.; Ward, R. S.; Gray, T. I. *J. Chem. Soc. Perkin Trans.* **1976**, *23*, 2475.
8. Gaydou, E. M.; Bianchini, J. P. *Bull. Soc. Chem. (France)* **1978**, *II*, 43.
9. Iinuma, M.; Matsuura, S.; Kusuda, K. *Chem. Pharm. Bull.* **1980**, *28*, 708.
10. Terani, B.; Makhani, K. R. *Tetrahedron* **1976**, *32*, 565.
11. Horie, T.; Ohtsuru, Y.; Shibata, K.; Yamashita, K.; Tsukayama, M.; Kawamura, Y. *Phytochemistry* **1998**, *47*, 865.
12. Moon, B. H.; Lee, Y. S.; Ahn, J. H.; Lim, Y. H. *Magn. Reson. Chem.* **2005**, *43*, 858.
13. Yang, H. J.; Kang, K. R.; Lim, Y. H. *Magn. Reson. Chem.* **2003**, *41*, 223.
14. Moon, J. K.; Rhee, S. K.; Kim, J. H.; Kim, G. B.; Yun, H. S.; Chung, B. J.; Lee, S. S.; Lim, Y. H. *Bull. Korean Chem. Soc.* **2003**, *23*, 1545.