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Synthesis and complete assignment of the ^{1}H and ^{13}C NMR signals of new acetamido and aminoflavonoid derivatives

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The complete ^{1}H and ^{13}C NMR assignment of 9 acetamidochalcones, 18 acetamidoflavones, 18 aminoflavones, 9 acetamidoflavonols and 9 aminoflavonols has been performed using one- and two-dimensional NMR techniques including COSY, HMQC and HMBC experiments. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: NMR; ^{1}H NMR; ^{13}C NMR; COSY; HMQC; HMBC; chalcones; flavones; flavonols

Introduction

Flavonoids, a family of polyphenolic compounds, are prominent plant secondary metabolites found in dietary components including fruits, vegetables, olive oil, tea and red wine.[1,2] Owing to their multiple biological activities, such as leishmanicidal,[3] anti-HIV,[4–6] antiviral,[7,8] antioxidant,[9,10] bactericidal,[11,12] anticancer[13,14] and cardioprotective[15], flavonoids synthetic pathways have attracted considerable attention.[16–18] In order to evaluate the potential anti-HIV and antiplasmodial activity of flavonoids compounds, we have started a medicinal chemistry program to highlight an SAR study of chalcone, flavone and flavonol derivatives with amino-substituents. Recently, synthesis and NMR data have been reported for flavones with amino groups in various positions of B ring.[19] In this paper, we present the synthesis and structural elucidation by 1D and 2D NMR experiments of flavonoids with acetamido or amino groups in position 6 of A ring and fluoro, trifluoromethyl and methoxy substituents in various positions of B ring.

Experimental

Synthesis

Chalcones (**1**) were obtained in 10 min with good yields (70–95%) from a modified Claisen–Schmidt condensation[20] of substituted benzaldehydes and 2-hydroxy-5-acetamidoacetophenone using lithium hydroxide in methanol under full-power microwave irradiation (MWI) (300 W). Chalcones were converted to flavonols (**3**)[21] by treatment with alkaline hydrogen peroxide for 24 h (40–70%). These flavonols were methylated using dimethyl sulphate to afforded 3-methoxyflavones (**4**).[22] Flavone derivatives (**2**) were obtained[23] by oxidative cyclisation of corresponding chalcone in DMSO with catalytic iodine in 90–95% yields during 30 min at full-power MWI. Deprotection of acetamido intermediates to the corresponding amino compounds (**5–7**) was done in ethanol and concentrated H_2SO_4 (9/1) under MWI for 30 min in quantitative yield.

NMR techniques

^{1}H and ^{13}C NMR experiments were performed at 300 K using a Bruker Avance DRX 300 spectrometer in a 5-mm QNP probe. Samples were dissolved in DMSO-d_6 solutions, and the central peak of solvent[24] ($\delta_H = 2.50$ ppm and $\delta_C = 39.5$ ppm) was used as internal standard. Resonance multiplicities for ^{13}C signals were established via the acquisition of DEPT spectra. All 2D spectra were acquired at 300 K on a Bruker Avance DRX 500 equipped with a Bruker CryoPlatform and a 5-mm cryo TXI probe. The temperature of the probe and preamplifier was 30 K. For 2D experiments Bruker microprograms using gradient selection (gs) were applied. COSY spectra[25] were obtained with an F_2 spectral width of 10 ppm and 2K data points and an F_1 spectral width of 256 t_1 increments with sine-bell windows in both dimensions. The HMQC spectra (inv4gs in the standard Bruker software) resulted from 256 × 1024 data matrix size with 32 scans per t_1, an inter-pulse delay of 3.2 ms and a 5 : 3 : 4 gradient combination.[26] The HMBC spectra[27] were measured using a pulse sequence (hmbcgs in the Bruker library) optimized on ^3J coupling values of 8 Hz (inter-pulse delay for the evolution of long-range coupling: 50 ms), and the same gradient ratio as described for the HMQC experiments. In this way direct responses (^{1}J couplings) were not completely removed.

Results and Discussion

The ^{1}H and ^{13}C assignments are presented in Tables 1–4. The compounds were grouped in seven different series: chalcones **1**,

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Table 1. ^{1}H NMR chemical shifts[a,b] for acetamidochalcones **1a–i**

Position	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**
H-3	6.96	6.96	6.96	6.96	6.96	6.96	6.97	6.96	6.97
H-4	7.71	7.69	7.71	7.71	7.71	7.70	7.71	7.71	7.70
H-6	8.17	8.28	8.14	8.19	8.14	8.11	8.18	8.10	8.11
H-α	7.77	7.84	7.72	7.64	7.79	7.74	7.73	7.83	7.79
H-β	7.77	8.04	7.79	7.79	7.85	7.82	7.78	7.93	7.89
H-2′	7.79	–	7.37	7.78	–	7.63	7.90	8.21	7.82
H-3′	7.47	7.13	–	7.04	7.34	–	7.32	–	8.01
H-4′	7.47	7.47	7.04	–	7.53	7.29	–	7.82	–
H-5′	7.47	7.05	7.37	7.04	7.32	7.50	7.32	7.69	8.01
H-6′	7.79	7.79	7.37	7.78	7.92	7.72	7.90	8.11	7.82
CH$_3$	2.03	2.05	2.02	2.04	2.08	2.02	2.03	2.02	2.02
NH	10.00	9.95	9.92	9.95	9.95	9.87	10.01	9.91	9.92
OH	11.70	11.93	11.71	11.98	11.57	11.63	11.73	11.60	11.50

[a] In ppm from TMS; DMSO-*d6* as solvent.
[b] ^{1}H resonances in the substituents (in ppm): **2b**, OCH$_3$ 3.93; **2c**, OCH$_3$ 3.81; **2d**, OCH$_3$ 3.82.

Table 2. ^{13}C NMR chemical shifts[a,b] for acetamidochalcones **1a–i**

Position	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**
C-1	121.46	120.93	121.39	120.89	121.47	121.46	121.26	121.68	121.78
C-2	156.93	157.17	156.93	157.10	156.52	156.95	156.74	156.85	156.60
C-3	117.90	117.83	117.86	117.69	117.75	117.87	117.68	117.87	117.86
C-4	128.22	129.41	128.29	128.08	127.93	128.52	128.10	128.54	128.27
C-5	131.35	131.27	131.27	131.03	131.26	131.23	131.12	131.24	131.31
C-6	121.17	120.56	121.23	120.89	120.72	121.46	121.11	121.48	121.28
C-β′	193.06	193.22	193.13	192.89	192.45	193.00	192.81	192.93	192.66
C-α	122.94	122.41	123.26	119.57	125.46	125.34	122.69	125.28	126.04
C-β	144.30	139.51	144.28	144.55	135.68	142.66	142.87	142.17	141.79
C-1′	134.66	122.82	136.06	127.03	122.21	137.24	122.69	135.89	138.70
C-2′	129.29	158.69	113.97	130.84	161.05	114.96	131.18	125.36	129.43
C-3′	128.99	112.03	159.87	114.61	116.28	162.67	116.15	130.08	126.05
C-4′	131.13	132.69	116.93	162.13	132.83	117.66	163.57	127.08	130.27
C-5′	128.99	120.90	130.29	114.61	125.16	131.28	116.15	130.29	126.05
C-6′	129.29	127.97	121.44	130.84	129.87	121.46	131.18	132.67	129.43
CO	168.35	168.22	168.28	168.13	168.13	168.29	168.13	168.28	168.24
CH$_3$	23.92	23.85	23.88	23.72	23.74	23.84	23.70	23.85	23.85

[a] In ppm from TMS; DMSO-*d6* as solvent.
[b] ^{13}C resonances in the substituents (in ppm) and $^nJ_{C,F}$ (in Hz): **1b**, OCH$_3$ 55.83; **1c**, OCH$_3$ 55.50; **1d**, OCH$_3$ 55.45; **1e**, $^1J_{C-2',F} = 252.0$, $^2J_{C-1',F} = 11.3$, $^2J_{C-3',F} = 21.9$, $^3J_{C-4',F} = 8.3$, $^3J_{C-6',F} = 2.1$, $^3J_{C-\beta,F} = 3.0$, $^4J_{C-\alpha,F} = 6.0$; **1f**, $^1J_{C-3',F} = 243.0$, $^2J_{C-2',F} = 21.9$, $^2J_{C-4',F} = 21.1$, $^3J_{C-1',F} = 7.5$, $^3J_{C-5',F} = 7.5$, $^4J_{C-\beta,F} = 3.0$, $^5J_{C-\alpha,F} = 3.0$; **1g**, $^1J_{C-4',F} = 249.0$, $^2J_{C-3',F} = 21.9$, $^3J_{C-2',F} = 9.8$; **1h**, CF$_3$ 124.20, $^1J_{C,F} = 270.0$, $^2J_{C-3',F} = 31.7$, $^3J_{C-2',F} = 4.2$, $^3J_{C-4',F} = 4.2$; **1i,** CF$_3$ 124.09, $^1J_{C,F} = 269.0$, $^2J_{C-4',F} = 32.1$, $^3J_{C-3',F} = 3.8$.

acetamidoflavones **2**, acetamidoflavonols **3**, methoxy-3 acetamidoflavonols **4**, aminoflavones **5**, aminoflavonols **6** and methoxy-3 aminoflavonols **7** (Fig. 1). The A ring protons, which were easily assigned on the basis of chemical shifts and multiplicity, enabled the assignment by direct correlation (HMQC) of carbons to which they are directly attached. HMBC experiments were then performed to establish long-range H/C correlations. Based on these experiments, the three quaternary carbon signals C-9 (C-2 for chalcones), C-10 (C-1 for chalcones) and C-6 (C-5 for chalcones) could be readily assigned. For the **1a–1i** derivatives, the complete assignment of the C ring protons required the unambiguous determination of the very near H-α and H-β resonances which were assigned based on the HMQC results, since C-β is more deshielded than C-α.[28]

Most of the ^{1}H and ^{13}C chemical shift assignmentsof the B ring resonances were achieved, in a straightforward manner, on the basis of signal intensities, chemical shift considerations,[29] magnitude of ^{n}J (C,F) and ^{n}J (H,F) coupling constants and long-range correlation peaks (^{3}J couplings) from the methoxy protons. The complete assignment of the other ring B resonances was based on the analysis of the COSY, HMQC and HMBC spectra. Finally, some of aminoflavones or aminoflavonols (**5g, 5i, 6c, 6g, 6i, 7d** and**7e**) were studied either as chlorhydrates or as a mixture of neutral and protonated species.

Table 3. ^{1}H NMR chemical shifts[a,b,c] for acetamido-(**2–4**) and amino(**5–7)** flavonoid derivatives

Position	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**
H-3	7.00	6.84	7.03	6.90	6.70	7.06	6.97	7.18	7.15
H-5	8.34	8.30	8.33	8.31	8.31	8.31	8.31	8.32	8.35
H-7	7.96	7.89	7.95	7.94	7.93	7.93	7.94	7.96	7.97
H-8	7.75	7.64	7.75	7.72	7.65	7.73	7.71	7.80	7.78
H-2′	8.10	–	7.58	8.04	–	7.94	8.14	8.40	8.31
H-3′	7.60	7.20	–	7.12	7.42	–	7.40	–	7.94
H-4′	7.58	7.52	7.16	–	7.62	7.43	–	7.96	–
H-5′	7.60	7.10	7.48	7.12	7.40	7.61	7.40	7.81	7.94
H-6′	8.10	7.85	7.67	8.04	7.97	7.92	8.14	8.39	8.31
CH_3	2.09	2.06	2.09	2.08	2.07	2.09	2.08	2.08	2.09
NH	10.27	10.23	10.31	10.27	10.26	10.27	10.26	10.28	10.30
NH_2	–	–	–	–	–	–	–	–	–
OH	–	–	–	–	–	–	–	–	–
OCH_3	–	–	–	–	–	–	–	–	–
Atom	**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**
H-3	–	–	–	–	–	–	–	–	–
H-5	8.42	8.46	8.45	8.41	8.48	8.45	8.44	8.42	8.44
H-7	7.90	7.86	7.92	7.88	7.88	7.92	7.91	7.91	7.90
H-8	7.71	7.58	7.73	7.71	7.62	7.73	7.71	7.76	7.73
H-2′	8.19	–	7.75	8.19	–	8.02	8.27	8.54	8.40
H-3′	7.55	7.19	–	7.12	7.42	–	7.40	–	7.92
H-4′	7.51	7.49	7.09	–	7.59	7.33	–	7.85	–
H-5′	7.55	7.08	7.47	7.12	7.37	7.60	7.40	7.80	7.92
H-6′	8.19	7.46	7.77	8.19	7.75	8.07	8.27	8.46	8.40
CH_3	2.08	2.10	2.09	2.09	2.10	2.10	2.08	2.08	2.09
NH_2	–	–	–	–	–	–	–	–	–
NH	10.30	10.27	10.27	10.26	10.28	10.27	10.35	10.25	10.26
OH	9.53	8.87	9.45	9.40	9.36	9.39	9.51	9.93	9.98
OCH_3	–	–	–	–	–	–	–	–	–
Atom	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**	**4h**	**4i**
H-3	–	–	–	–	–	–	–	–	–
H-5	8.37	8.42	8.38	8.36	8.42	8.36	8.37	8.37	8.37
H-7	7.94	7.92	7.94	7.93	7.94	7.93	7.92	7.94	7.95
H-8	7.67	7.59	7.72	7.70	7.64	7.70	7.69	7.72	7.70
H-2′	8.02	–	7.57	8.05	–	7.83	8.21	8.32	8.22
H-3′	7.56	7.19	–	7.14	7.43	–	7.40	–	7.94
H-4′	7.58	7.54	7.16	–	7.63	7.41	–	7.94	–
H-5′	7.56	7.09	7.50	7.14	7.40	7.62	7.40	7.82	7.94
H-6′	8.02	7.49	7.62	8.05	7.73	7.89	8.21	8.31	8.22
CH_3	2.08	2.08	2.10	2.09	2.10	2.08	2.09	2.09	2.08
NH_2	–	–	–	–	–	–	–	–	–
NH	10.28	10.29	10.27	10.29	10.30	10.26	10.26	10.28	10.28
OH	–	–	–	–	–	–	–	–	–
OCH_3	3.81	3.81	3.82	3.79	3.77	3.83	3.81	3.84	3.83
Atom	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**[c]	**5h**	**5i**[c]
H-3	6.87	6.76	6.91	6.78	6.93	6.95	7.08	7.06	7.08
H-5	7.13	7.14	7.14	7.08	7.11	7.11	7.82	7.13	7.36
H-7	7.09	7.08	7.10	7.06	7.09	7.07	7.63	7.11	7.29
H-8	7.51	7.45	7.53	7.47	7.46	7.52	7.87	7.57	7.65
H-2′	8.05	–	7.55	8.00	–	7.91	8.20	8.35	8.29
H-3′	7.58	7.22	–	7.10	7.44	–	7.45	–	7.93
H-4′	7.57	7.54	7.12	–	7.63	7.42	–	7.94	–
H-5′	7.58	7.12	7.47	7.10	7.41	7.61	7.45	7.80	7.93
H-6′	8.05	7.84	7.62	8.00	7.96	7.91	8.20	8.36	8.29
CH_3	–	–	–	–	–	–	–	–	–

Table 3. (*Continued*)

Atom	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**[c]	**5h**	**5i**[c]
NH_2	5.53	5.55	5.55	5.44	5.55	5.61		5.52	
NH	–	–	–	–	–	–	–	–	–
OH	–	–	–	–	–	–	–	–	–
OCH_3	–	–	–	–	–	–	–	–	–
Atom	**6a**	**6b**	**6c**[c]	**6d**	**6e**	**6f**	**6g**[c]	**6h**[c]	**6i**[c]
H-3	–	–	–	–	–	–	–	–	–
H-5	7.18	7.18	7.36	7.12	7.16	7.15	7.88	7.39	7.71
H-7	7.10	7.05	7.24	7.06	7.07	7.10	7.60	7.27	7.49
H-8	7.48	7.33	7.59	7.45	7.39	7.50	7.84	7.63	7.76
H-2′	8.17	–	7.74	8.15	–	7.98	8.26	8.52	8.41
H-3′	7.55	7.16	–	7.10	7.35	–	7.42	–	7.93
H-4′	7.50	7.49	7.08	–	7.58	7.32	–	7.85	–
H-5′	7.55	7.06	7.47	7.10	7.35	7.59	7.42	7.80	7.93
H-6′	8.17	7.44	7.78	8.15	7.73	8.04	8.26	8.45	8.41
CH_3	–	–	–	–	–	–	–	–	–
NH_2	5.55	5.45		5.44	5.48	5.53			
NH	–	–	–	–	–	–	–	–	–
OH		8.54			8.72			9.75	
OCH_3	–	–	–	–	–	–	–	–	–
Atom	**7a**	**7b**	**7c**	**7d**[c]	**7e**	**7f**	**7g**	**7h**	**7i**
H-3	–	–	–	–	–	–	–	–	–
H-5	7.21	7.06	7.12	7.40	7.33	7.12	7.12	7.14	7.12
H-7	7.13	7.01	7.07	7.27	7.19	7.08	7.06	7.09	7.09
H-8	7.48	7.44	7.46	7.59	7.46	7.48	7.44	7.51	7.47
H-2′	8.00	–	7.53	8.03	–	7.81	8.28	8.30	8.21
H-3′	7.58	7.28	–	7.13	7.42	–	7.40	–	7.92
H-4′	7.57	7.46	7.12	–	7.64	7.40	–	7.93	–
H-5′	7.58	7.03	7.47	7.13	7.39	7.61	7.40	7.82	7.92
H-6′	8.00	7.42	7.57	8.03	7.73	7.87	8.28	8.30	8.21
CH_3	–	–	–	–	–	–	–	–	–
NH_2	5.53	5.51	5.51	–	–	5.51	5.51	5.56	5.54
NH	–	–	–	–	–	–	–	–	–
OH	–	–	–	–	–	–	–	–	–
OCH_3	3.78	3.83	3.78	3.78	3.78	3.80	3.77	3.82	3.80

[a] In ppm from TMS; DMSO-*d6* as solvent.

[b] ^{1}H resonances in the substituents (in ppm): **2b**, OCH_3 3.79; **2c**, OCH_3 3.82; **2d**, OCH_3 3.85; **3b**, OCH_3 3.79; **3c**, OCH_3 3.82; **3d**, OCH_3 3.85; **4b**, OCH_3 3.75; **4c**, OCH_3 3.85; **4d**, OCH_3 3.86; **5b**, OCH_3 3.90; **5c**, OCH_3 3.86; **5d**, OCH_3 3.85; **6b**, OCH_3 3.78; **6c**, OCH_3 3.83; **6d**, OCH_3 3.83; **7b**, OCH_3 3.78; **7c**, OCH_3 3.82; **7d**, OCH_3 3.85.

[c] Recorded as an hydrochloride.

Table 4. ^{13}C NMR chemical shifts[a,b,c] for acetamido-(**2–4**) and amino(**5–7**) flavonoid derivatives

Position	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**
C-2	162.34	160.47	162.15	162.14	159.50	160.81	161.40	160.60	160.62
C-3	106.42	112.52	106.72	105.00	111.10	107.11	106.32	107.50	107.84
C-4	176.98	177.02	177.08	176.86	176.93	177.02	176.92	177.04	176.99
C-5	113.01	112.94	113.01	113.13	113.11	112.95	113.00	112.96	112.94
C-6	136.79	136.67	136.82	136.69	137.12	136.89	136.80	136.94	136.96
C-7	125.56	125.54	125.61	125.40	125.97	125.64	125.55	125.70	125.78
C-8	119.01	118.96	119.10	118.91	119.24	119.08	118.99	119.21	119.12
C-9	151.49	151.76	151.51	151.46	151.84	151.41	151.43	151.49	151.47
C-10	123.50	123.25	123.51	123.35	123.47	123.47	123.40	123.51	123.50
C-1′	131.21	119.99	132.64	123.35	119.24	133.61	127.80	132.48	135.19
C-2′	126.29	157.58	111.50	128.19	160.23	113.18	128.98	122.90	127.17

Table 4. *(Continued)*

Position	2a	2b	2c	2d	2e	2f	2g	2h	2i
C-3′	129.11	111.09	159.73	114.61	117.10	162.44	116.21	129.99	125.95
C-4′	131.74	132.86	117.59	162.50	133.89	118.50	164.11	128.08	131.27
C-5′	129.11	120.76	130.31	114.61	125.37	131.21	116.21	130.33	125.95
C-6′	126.29	129.15	118.60	128.19	129.75	121.42	128.98	130.33	127.17
CO	168.55	168.58	168.64	168.61	168.80	168.59	168.56	168.61	168.61
CH_3	23.98	24.01	24.02	24.01	24.18	24.00	23.98	24.01	23.99
Atom	**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**
C-2	145.25	147.00	144.86	145.65	143.36	143.39	144.28	143.11	143.41
C-3	138.87	138.81	138.97	138.05	139.22	139.32	138.66	139.44	140.04
C-4	172.96	172.56	172.94	172.62	172.61	172.97	173.00	172.95	172.65
C-5	112.77	112.71	112.71	112.81	112.72	112.59	112.63	112.57	112.76
C-6	136.05	135.89	136.09	136.06	136.08	136.10	136.01	136.07	136.32
C-7	125.74	125.26	125.76	125.43	125.57	125.81	125.55	125.73	126.02
C-8	119.08	118.89	119.05	118.98	118.95	118.99	118.90	119.04	119.21
C-9	150.76	151.05	150.68	150.62	151.05	150.58	150.55	150.59	150.82
C-10	121.48	122.06	121.37	121.26	121.96	121.31	121.37	121.36	121.53
C-1′	130.02	119.94	132.65	124.43	118.97	134.05	128.00	132.45	135.58
C-2′	127.75	157.13	113.46	129.53	159.18	114.24	130.37	123.96	128.31
C-3′	128.68	111.96	159.25	113.22	116.17	162.03	115.62	129.33	125.59
C-4′	131.34	131.75	115.31	160.58	132.48	116.65	162.60	126.03	130.50
C-5′	128.68	120.15	129.77	113.22	124.40	130.55	115.62	129.78	125.59
C-6′	127.75	131.06	120.10	129.53	131.22	121.31	130.37	131.10	128.31
CO	168.84	168.56	168.82	168.70	168.61	168.67	168.62	168.55	168.76
CH_3	24.09	24.02	24.05	24.17	24.03	23.99	24.00	23.98	24.19
Atom	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**	**4h**	**4i**
C-2	140.42	140.85	140.53	139.75	141.19	140.94	140.43	140.85	141.27
C-3	154.79	155.65	154.57	154.79	152.09	153.25	154.18	152.99	153.23
C-4	173.70	173.39	173.71	173.47	173.51	173.92	174.32	173.76	173.98
C-5	112.85	112.92	112.83	112.89	113.08	112.98	113.96	112.80	112.98
C-6	136.39	136.37	136.40	136.30	136.71	136.65	136.10	136.55	136.73
C-7	125.56	125.47	125.60	125.40	125.88	125.89	126.05	125.73	126.01
C-8	118.89	118.92	119.00	118.81	119.12	119.20	118.92	119.09	119.22
C-9	150.62	151.04	150.61	150.49	151.14	150.75	150.91	150.64	150.83
C-10	123.69	124.08	123.67	123.66	124.16	123.83	123.74	123.74	123.91
C-1′	130.52	119.70	131.72	122.64	118.78	132.83	126.70	132.22	134.68
C-2′	128.20	156.89	113.76	130.00	159.35	115.11	130.38	124.69	129.29
C-3′	128.63	111.74	159.17	114.17	116.28	162.13	115.32	129.47	125.72
C-4′	130.78	132.08	116.33	161.17	133.18	117.86	163.50	127.22	130.49
C-5′	128.63	120.25	129.83	114.17	124.84	131.00	115.32	129.97	125.72
C-6′	128.20	130.44	120.52	130.00	131.27	124.62	130.38	131.60	129.29
CO	168.55	168.60	168.57	168.85	168.79	168.78	168.95	168.63	168.82
CH_3	24.01	24.01	23.98	23.98	24.16	24.16	23.85	24.10	24.19
OCH3-3	59.66	59.66	59.69	59.45	60.06	59.89	59.61	59.76	60.06
Atom	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**[c]	**5h**	**5i**[c]
C-2	161.70	159.91	161.48	161.82	157.72	160.13	161.86	160.07	160.34
C-3	105.77	112.48	106.08	105.01	110.24	106.43	106.56	106.98	107.46
C-4	177.14	177.13	177.16	177.03	176.89	177.18	176.35	177.34	176.98
C-5	105.24	105.30	105.31	104.38	104.72	104.83	115.81	105.31	108.75
C-6	146.23	145.95	145.85	146.55	146.85	146.72	133.34	146.57	142.06
C-7	121.91	121.96	122.07	121.45	121.94	121.88	127.47	122.26	124.06
C-8	119.03	118.96	119.11	118.83	119.01	119.08	120.32	119.38	119.59
C-9	148.08	148.45	148.21	147.81	148.09	147.47	153.09	148.25	149.80
C-10	124.23	123.99	124.23	124.18	124.05	124.23	123.85	124.43	124.17
C-1′	131.60	120.49	133.01	123.78	120.10	134.05	127.60	133.02	135.40
C-2′	126.11	157.41	111.31	127.98	159.58	112.99	129.14	122.82	130.95

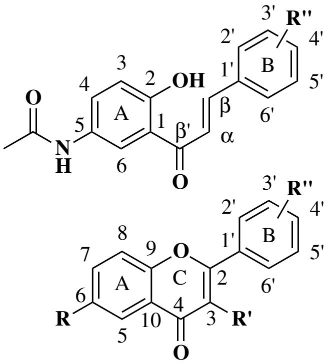
Table 4. (*Continued*)

Atom	5a	5b	5c	5d	5e	5f	5g[c]	5h	5i[c]
C-3′	129.08	110.52	159.69	114.51	116.88	162.47	116.31	130.11	125.98
C-4′	131.60	132.51	117.24	161.82	132.29	118.16	164.25	127.92	129.25
C-5′	129.08	120.76	130.22	114.51	125.17	131.20	116.31	130.31	125.98
C-6′	126.11	129.06	118.40	127.98	129.45	122.26	129.14	130.48	130.95
Atom	**6a**	**6b**	**6c[c]**	**6d**	**6e**	**6f**	**6g[c]**	**6h[c]**	**6i[c]**
C-2	144.49	146.36	144.46	144.89	142.76	142.80	144.85	143.09	143.58
C-3	138.27	138.21	138.60	137.41	138.57	138.71	138.80	139.35	140.04
C-4	172.66	172.41	172.58	173.28	172.41	172.71	172.43	172.88	172.91
C-5	104.43	104.22	112.63	104.21	104.14	103.94	115.70	108.11	113.08
C-6	145.46	145.73	131.58	145.82	145.95	145.96	132.48	141.61	135.48
C-7	122.49	121.95	125.71	122.06	122.27	122.54	127.24	124.42	126.58
C-8	118.93	118.82	119.95	118.79	118.85	118.96	120.23	119.67	120.17
C-9	147.47	147.79	148.72	147.19	147.75	147.26	152.09	149.14	151.22
C-10	122.12	122.81	121.96	122.06	122.70	122.06	121.86	122.21	122.08
C-1′	129.60	120.35	132.78	124.05	119.30	133.93	127.74	132.81	135.48
C-2′	127.50	157.10	113.29	129.22	159.15	113.99	130.30	124.07	128.39
C-3′	128.49	111.92	159.16	114.01	116.11	162.02	115.71	129.51	125.70
C-4′	131.71	131.51	115.06	160.24	132.22	116.28	162.73	126.13	129.50
C-5′	128.49	120.10	129.64	114.01	124.36	130.55	115.71	130.00	125.70
C-6′	127.50	131.02	119.34	129.22	131.19	123.40	130.30	131.27	128.39
Atom	**7a**	**7b**	**7c**	**7d[c]**	**7e[c]**	**7f**	**7g**	**7h**	**7i**
C-2	140.04	141.06	140.27	139.59	140.68	140.48	140.00	140.37	140.81
C-3	154.33	155.64	154.14	154.58	151.58	152.69	153.48	152.41	152.66
C-4	173.62	174.48	173.85	173.33	173.20	173.83	173.81	173.68	173.91
C-5	105.55	107.06	104.55	108.96	107.19	104.55	104.59	104.28	104.49
C-6	144.91	143.93	146.50	140.91	143.47	146.45	146.54	146.48	146.67
C-7	122.56	122.30	122.24	123.95	123.43	122.41	122.24	122.25	122.53
C-8	119.00	118.80	119.13	119.31	119.19	119.16	119.07	119.08	119.17
C-9	147.69	149.25	147.32	149.03	148.74	147.32	147.30	147.19	147.69
C-10	124.46	125.06	124.66	122.83	124.69	124.64	124.68	124.56	124.75
C-1′	130.56	120.25	132.31	124.32	118.85	133.22	127.60	131.97	135.07
C-2′	128.11	157.04	113.84	129.94	160.60	114.98	130.90	124.55	129.16
C-3′	128.62	111.22	159.31	114.17	116.07	162.12	115.92	129.41	125.69
C-4′	130.85	131.60	116.22	161.10	132.84	117.56	163.31	126.97	130.19
C-5′	128.62	120.17	129.95	114.17	124.58	130.93	115.92	129.65	125.69
C-6′	128.11	130.39	120.58	129.94	131.03	124.47	130.90	132.11	129.16
OCH_3-3	59.61	60.13	59.78	59.44	59.83	59.81	59.76	59.72	60.01

[a] In ppm from TMS; DMSO-*d6* as solvent.

[b] ^{13}C resonances in the substituents (in ppm) and $^{n}J_{C,F}$ (in Hz): **2b**, OCH_3 55.98; **2c**, OCH_3 55.49; **2d**, OCH_3 55.56; **2e**, $^{1}J_{C-2',F} = 248.0$, $^{2}J_{C-1',F} = 14.3$, $^{2}J_{C-3',F} = 22.6$, $^{3}J_{C-4',F} = 6.8$, $^{4}J_{C-3,F} = 8.3$; **2f**, $^{1}J_{C-3',F} = 246.0$, $^{2}J_{C-2',F} = 23.4$, $^{2}J_{C-4',F} = 21.1$, $^{3}J_{C-1',F} = 7.5$, $^{3}J_{C-5',F} = 8.3$, $^{4}J_{C-6',F} = 2.1$; **2g**, $^{1}J_{C-4',F} = 250.0$, $^{2}J_{C-3',F} = 22.6$, $^{3}J_{C-2',F} = 9.8$; **2h**, CF_3 123.42, $^{1}J_{C,F} = 270.0$, $^{2}J_{C-3',F} = 31.7$, $^{3}J_{C-2',F} = 3.8$, $^{3}J_{C-4',F} = 3.8$; **2i,** CF_3 124.88, $^{1}J_{C,F} = 272.0$, $^{2}J_{C-4',F} = 32.4$, $^{3}J_{C-3',F} = 3.8$; **3b**, OCH_3 55.76; **3c**, OCH_3 55.36; **3d**, OCH_3 55.53; **3e**, $^{1}J_{C-2',F} = 251.0$, $^{2}J_{C-1',F} = 14.3$, $^{2}J_{C-3',F} = 21.1$, $^{3}J_{C-4',F} = 9.0$; **3f**, $^{1}J_{C-3',F} = 242.0$, $^{2}J_{C-2',F} = 24.1$, $^{2}J_{C-4',F} = 20.4$, $^{3}J_{C-1',F} = 8.9$, $^{3}J_{C-5',F} = 8.3$; **3g**, $^{1}J_{C-4',F} = 247.0$, $^{2}J_{C-3',F} = 21.0$, $^{3}J_{C-2',F} = 8.0$; **3h**, CF_3 123.42, $^{1}J_{C,F} = 270.0$, $^{2}J_{C-3',F} = 31.7$, $^{3}J_{C-2',F} = 3.8$, $^{3}J_{C-4',F} = 3.8$; **3i,** CF_3 124.68, $^{1}J_{C,F} = 272.0$, $^{2}J_{C-4',F} = 32.4$, $^{3}J_{C-3',F} = 3.8$; **4b**, OCH_3 55.68; **4c**, OCH_3 55.29; **4d**, OCH_3 55.41; **4e**, $^{1}J_{C-2',F} = 249.0$, $^{2}J_{C-1',F} = 14.3$, $^{2}J_{C-3',F} = 21.1$, $^{3}J_{C-4',F} = 6.8$; **4f**, $^{1}J_{C-3',F} = 243.0$, $^{2}J_{C-2',F} = 23.4$, $^{2}J_{C-4',F} = 21.1$, $^{3}J_{C-1',F} = 8.3$, $^{3}J_{C-5',F} = 7.5$, $^{4}J_{C-6',F} = 3.0$; **4g**, $^{1}J_{C-4',F} = 252.0$, $^{2}J_{C-3',F} = 21.9$, $^{3}J_{C-2',F} = 9.0$; **4h**, CF_3 123.42, $^{1}J_{C,F} = 270.0$, $^{2}J_{C-3',F} = 32.4$, $^{3}J_{C-2',F} = 3.8$, $^{3}J_{C-4',F} = 3.8$; **4i,** CF_3 124.81, $^{1}J_{C,F} = 272.0$, $^{2}J_{C-4',F} = 32.4$, $^{3}J_{C-3',F} = 3.8$; **5b**, OCH_3 55.92; **5c**, OCH_3 55.43; **5d**, OCH_3 55.49; **5e**, $^{1}J_{C-2',F} = 253.0$, $^{2}J_{C-1',F} = 9.8$, $^{2}J_{C-3',F} = 21.9$, $^{3}J_{C-4',F} = 9.1$, $^{3}J_{C-2,F} = 3.0$, $^{4}J_{C-3,F} = 9.0$; **5f**, $^{1}J_{C-3',F} = 242.0$, $^{2}J_{C-2',F} = 23.3$, $^{2}J_{C-4',F} = 20.4$, $^{3}J_{C-1',F} = 8.9$, $^{3}J_{C-5',F} = 8.3$; **5g**, $^{1}J_{C-4',F} = 250.0$, $^{2}J_{C-3',F} = 22.6$, $^{3}J_{C-2',F} = 9.0$; **5h**, CF_3 124.05, $^{1}J_{C,F} = 270.0$, $^{2}J_{C-3',F} = 30.2$, $^{3}J_{C-2',F} = 3.8$, $^{3}J_{C-4',F} = 3.8$; **5i,** CF_3 124.81, $^{1}J_{C,F} = 272.0$, $^{2}J_{C-4',F} = 32.4$, $^{3}J_{C-3',F} = 3.8$. **6b**, OCH_3 55.71; **6c**, OCH_3 55.25; **6d**, OCH_3 55.36; **6e**, $^{1}J_{C-2',F} = 251.0$, $^{2}J_{C-1',F} = 14.3$, $^{2}J_{C-3',F} = 21.8$, $^{3}J_{C-4',F}$ 8.6, $^{3}J_{C-5',F}$ 3.5; **6f**, $^{1}J_{C-3',F} = 243.0$, $^{2}J_{C-2',F} = 24.1$, $^{2}J_{C-4',F} = 20.4$, $^{3}J_{C-1',F} = 8.3$, $^{3}J_{C-5',F} = 8.3$; **6g**, $^{1}J_{C-4',F} = 249.0$, $^{2}J_{C-3',F} = 22.0$, $^{3}J_{C-2',F} = 8.0$, $^{4}J_{C-1',F} = 2.5$, **6h**, CF_3 123.42, $^{1}J_{C,F} = 270.0$, $^{2}J_{C-3',F} = 31.7$, $^{3}J_{C-2',F} = 3.8$, $^{3}J_{C-4',F} = 3.8$; **6i,** CF_3 124.81, $^{1}J_{C,F} = 272.0$, $^{2}J_{C-4',F} = 32.4$, $^{3}J_{C-3',F} = 3.8$; **7b**, OCH_3 55.47; **7c**, OCH_3 55.44; **7d**, OCH_3 55.43; **7e**, $^{1}J_{C-2',F} = 250.0$, $^{2}J_{C-1',F} = 14.3$, $^{2}J_{C-3',F} = 21.1$, $^{3}J_{C-4',F} = 7.5$; **7f**, $^{1}J_{C-3',F} = 243.0$, $^{2}J_{C-2',F} = 24.1$, $^{2}J_{C-4',F} = 20.3$, $^{3}J_{C-1',F} = 8.3$, $^{3}J_{C-5',F} = 7.5$, $^{4}J_{C-6',F} = 3.0$; **7g**, $^{1}J_{C-4',F} = 250.0$, $^{2}J_{C-3',F} = 21.9$, $^{3}J_{C-2',F} = 9.0$, $^{4}J_{C-1',F} = 3.0$; **7h**, CF_3 123.42, $^{1}J_{C,F} = 270.0$, $^{2}J_{C-3',F} = 32.4$, $^{3}J_{C-2',F} = 3.8$, $^{3}J_{C-4',F} = 3.8$; **7i,** CF_3 124.81, $^{1}J_{C,F} = 272.0$, $^{2}J_{C-4',F} = 32.4$, $^{3}J_{C-3',F} = 3.8$.

[c] Recorded as an hydrochloride.



1

2-7

R' \ R	NHCOCH$_3$	NH$_2$
H	**2**	**5**
OH	**3**	**6**
OCH$_3$	**4**	**7**

R''	
H	**a**
2-OCH$_3$	**b**
3-OCH$_3$	**c**
4-OCH$_3$	**d**
2-F	**e**
3-F	**f**
4-F	**g**
3-CF$_3$	**h**
4-CF$_3$	**i**

Figure 1. Structures of chalcone, flavone and flavonol derivatives **1–7** (numbering from Ref. [28]).

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