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^{1}H and ^{13}C NMR spectral assignments of 18 novel polymethoxylated naphthochalcones bearing pyrazoline-1-carbothioamide groups

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Introduction

Plant-derived polyphenols are classified based on their carbon skeleton. Polyphenols with a C6–C3–C6 skeleton are called flavonoids and include flavones, flavanones, isoflavones, anthocyanins, and chalcones.[1] While most flavonoids have C3 with a closed ring, the chalcone C3 has an α,β-unsaturated carbonyl group so that the two benzene rings of the chalcone are connected through an open ring. Polyphenols bearing a pyrazoline moiety show various biological activities, including antimicrobial, anti-inflammatory, antitumor, and antidepressant activities.[2–4] Chalcones bearing a pyrazoline moiety instead of an α,β-unsaturated carbonyl group conserve the C6–C3–C6 skeleton and have a closed-ring C3 like other flavonoids. The anti-colorectal cancer activities and inhibitory effects on aurora B kinase of several chalcones bearing a pyrazoline moiety have been reported.[5] Polyphenols bearing a carbothioamide substituent at the N-1 of pyrazoline have antimicrobial, anticonvulsant, and antidepressant activities.[6,7] Therefore, combined chalcones bearing both a pyrazoline moiety and a carbothioamide substituent can be designed. Methoxylation increases the cell permeability and stability of many plant-derived polyphenols.[8] The previous works demonstrated that the position and number of methoxy groups alter the biological activities of polymethoxylated polyphenols.[9–11] To discover the potent polyphenols with antitumor activity, we designed and synthesized 18 novel polymethoxylated naphthochalcones bearing a pyrazoline-1-carbothioamide moiety (Fig. 1). The number of methoxy groups ranged from two to five. Their ^{1}H and ^{13}C nuclear magnetic resonance (NMR) data were assigned completely, and their molecular mass data were collected. This should help us identify the plant-derived polyphenols newly synthesized or isolated from the natural sources in the future.

Experimental

Syntheses

Typical synthetic procedures for the polymethoxylated naphthochalcones bearing a pyrazoline-1-carbothioamide moiety listed in Fig. 2 are summarized in Scheme 1. As a representative example, the synthetic procedure for derivative **1**, 5-(2,3-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-phenyl-pyrazoline-1-carbothioamide is described as follows. 2,3-dimethoxybenzaldehyde (**II**, 1.6 g, 10 mmol) was added to a solution of 1-hydroxy-acetonaphthone (**I**, 1.86 g, 10 mmol) in 50 ml of ethanol, and the temperature was adjusted to 4 °C in an ice bath. Five milliliters of 50% (w/v) aqueous KOH solution was added to the cooled reaction mixture, and the reaction mixture was stirred at room temperature for 48 h. The reaction mixture was poured into ice water and acidified with 6 N HCl. The resulting precipitate was filtered and washed with ethanol and used for the next reaction (**III**, yield 75%). Excess hydrazine monohydrate (1 ml of 64–65% solution, 13 mmol) was added to a solution of 1-hydroxy-naphthochalcone (**III**, 1.7 g, 5 mmol) in 30 ml of anhydrous ethanol, and the solution was refluxed for 6 h. The reaction mixture was cooled to room temperature to yield a solid that was then filtered.

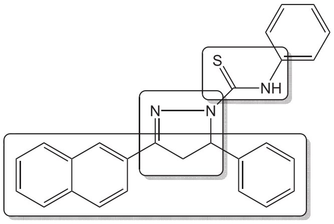

Figure 1. Chalcone bearing pyrazoline, carbothioamide, and naphthyl groups.

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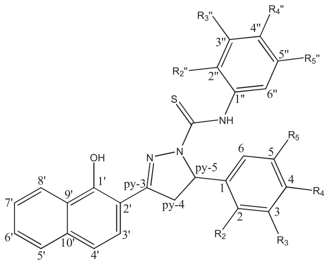
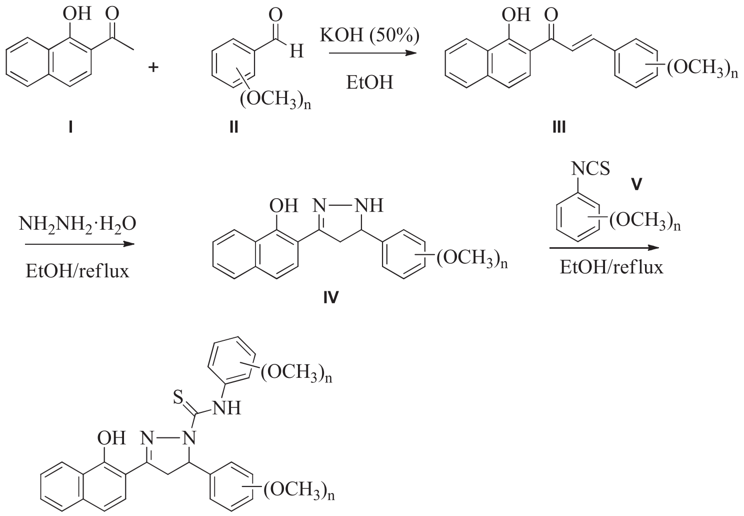


Derivative	R_2	R_3	R_4	R_5	$R_{2''}$	$R_{3''}$	$R_{4''}$	$R_{5''}$	Mass (calcd./found)	Name
1	OCH_3	OCH_3	H	H	H	H	H	H	482.1538/482.1514*	5-(2,3-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-phenyl-pyrazoline-1-carbothioamide
2	OCH_3	OCH_3	H	H	H	H	OCH_3	H	512.1644/512.1631*	5-(2,3-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(4-methoxyphenyl)-pyrazoline-1-carbothioamide
3	OCH_3	OCH_3	H	H	OCH_3	H	H	H	514.1801/514.1798	5-(2,3-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(2-methoxyphenyl)-pyrazoline-1-carbothioamide
4	OCH_3	OCH_3	H	H	H	OCH_3	H	H	514.1801/514.1815	5-(2,3-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(3-methoxyphenyl)-pyrazoline-1-carbothioamide
5	OCH_3	OCH_3	H	H	OCH_3	H	OCH_3	H	542.1750/542.1746*	5-(2,3-dimethoxyphenyl)-*N*-(2,4-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-pyrazoline-1-carbothioamide
6	OCH_3	OCH_3	H	H	H	OCH_3	OCH_3	OCH_3	574.2012/574.2050	5-(2,3-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(3,4,5-trimethoxyphenyl)-pyrazoline-1-carbothioamide
7	OCH_3	H	OCH_3	H	H	H	H	H	482.1538/482.1540*	5-(2,4-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-phenyl-pyrazoline-1-carbothioamide
8	OCH_3	H	OCH_3	H	OCH_3	H	H	H	514.1801/514.1825	5-(2,4-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(2-methoxyphenyl)-pyrazoline-1-carbothioamide
9	OCH_3	H	OCH_3	H	H	OCH_3	H	H	512.1644/512.1618*	5-(2,4-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(3-methoxyphenyl)-pyrazoline-1-carbothioamide
10	OCH_3	H	OCH_3	H	H	H	OCH_3	H	514.1801/514.1790	5-(2,4-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(4-methoxyphenyl)-pyrazoline-1-carbothioamide
11	OCH_3	H	OCH_3	H	OCH_3	H	OCH_3	H	542.1750/542.1733*	*N*,5-bis(2,4-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-pyrazoline-1-carbothioamide
12	OCH_3	H	OCH_3	H	H	OCH_3	OCH_3	OCH_3	572.1855/572.1827*	5-(2,4-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(3,4,5-trimethoxyphenyl)-pyrazoline-1-carbothioamide
13	H	OCH_3	H	OCH_3	H	H	H	H	484.1695/484.1693	5-(3,5-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-phenyl-pyrazoline-1-carbothioamide
14	H	OCH_3	H	OCH_3	OCH_3	H	H	H	514.1801/514.1854	5-(3,5-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(2-methoxyphenyl)-pyrazoline-1-carbothioamide
15	H	OCH_3	H	OCH_3	H	OCH_3	H	H	514.1801/514.1794	5-(3,5-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(3-methoxyphenyl)-pyrazoline-1-carbothioamide
16	H	OCH_3	H	OCH_3	H	H	OCH_3	H	514.1801/514.1706	5-(3,5-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(4-methoxyphenyl)-pyrazoline-1-carbothioamide
17	H	OCH_3	H	OCH_3	OCH_3	H	OCH_3	H	544.1906/544.1846	*N*-(2,4-dimethoxyphenyl)-5-(3,5-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-pyrazoline-1-carbothioamide
18	H	OCH_3	H	OCH_3	H	OCH_3	OCH_3	OCH_3	574.2012/574.2056	5-(3,5-dimethoxyphenyl)-3-(1-hydroxynaphthalen-2-yl)-*N*-(3,4,5-trimethoxyphenyl)-pyrazoline-1-carbothioamide

* denotes a negative molecular ion. The others were collected as positive molecular ions.

Figure 2. Structures, names, and mass data of polymethoxylated naphthochalcones **1–18** bearing pyrazoline-1-carbothioamide moieties.



Scheme 1. The procedure used to prepare polymethoxylated naphthochalcones **1–18** bearing pyrazoline-1-carbothioamide moieties.

The crude solid was purified by recrystallization from ethanol to afford pure pyrazoline (**IV**, yield 86%, mp 127–128 °C). Phenyl isothiocyanate (**V**, 68 mg, 0.5 mmol) and pyrazoline (**IV**, 174 mg, 0.5 mmol) were dissolved in 15 ml of anhydrous ethanol, and the reaction mixture was refluxed for 2 h. After cooling to room temperature, the resulting solid was filtered and purified by recrystallization in ethanol to give a pure compound of **1** (yield 80%, mp 212–214 °C). The other derivatives were synthesized using similar methods.

Nuclear Magnetic Resonance Spectra

The synthetic polymethoxylated naphthochalcones bearing a pyrazoline-1-carbothioamide moiety except derivatives **3** and **8** were dissolved in deuterated dimethyl sulfoxide, and derivatives **3** and **8** were dissolved in deuterated chloroform. The ^{1}H and ^{13}C chemical shifts of the deuterated solvent were referenced to tetramethylsilane. Nuclear magnetic resonance samples were prepared at approximately 50 mM and transferred to a 2.5-mm NMR tube for spectral analysis. All NMR experiments were carried out on an Avance 400 spectrometer system (9.4 T; Bruker, Karlsruhe, Germany) at 25 °C. For the one-dimensional (1D) ^{1}H NMR spectra, the relaxation delay, 90° pulse, spectral width, number of data points, and digital resolution were 1 s, 11.8 µs, 5555 Hz, 32 K, and 0.339 Hz/point, respectively. For the ^{13}C NMR spectra, the respective parameters were 3 s, 15.0 µs, 20 964 Hz, 64 K, and 0.640 Hz/point. For two-dimensional (2D) experiments, such as correlation spectroscopy (COSY), heteronuclear multiple-quantum correlation (HMQC), and heteronuclear multiple-bond correlation (HMBC), all data points ($t_2 \times t_1$) were acquired with 2 K × 256.[12] The long-range coupling time for HMBC was 70 ms. Zero-filling of 2 K and the sine-squared bell window function were applied before Fourier transformation using XWin-NMR (Bruker).[13,14] All NMR data were analyzed using Sparky.[15]

General Experimental Procedures

To confirm the structures of the 18 derivatives, high-resolution electron impact ionization mass spectrometry was performed on a JMS700 spectrometer (JEOL, Tokyo, Japan) at the Korea Basic Science Institute at Daegu, Korea.

Results and discussion

All of the polymethoxylated naphthochalcones bearing a pyrazoline-1-carbothioamide moiety shown in Fig. 2 are novel. The number of methoxy groups ranged from two to five. The procedure used to assign the NMR data of derivative **3** was as follows. The ^{13}C peak shifted the farthest downfield was

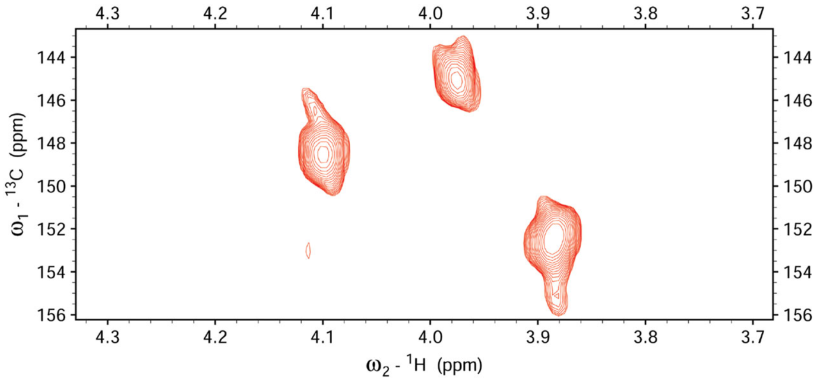


Figure 3. The partial HMBC spectrum of derivative **3** collected in deuterated chloroform. Long-range coupling between C-2″ (148.7 ppm) and 2″-OMe (4.10 ppm), and C-2 (145.0 ppm) and 2-OMe (3.98 ppm), and C-3 (152.5 ppm) and 3-OMe (3.88 ppm).

170.8 ppm and was assigned as thioketone. The next farthest downfield ^{13}C peak was 158.0 ppm and was determined to be the C-3 of pyrazoline (named C-py-3). It was long-range coupled to four ^{1}H peaks at 3.39, 4.02, 6.36, and 7.23 ppm in the HMBC spectrum. Because the two protons at 3.39 and 4.02 ppm are attached to the carbon at 42.4 ppm directly in HMQC, they were assigned as the methylene protons of H-py-4. The ^{1}H peak at 6.36 ppm is one-bond correlated with the ^{13}C peak at 57.6 ppm, which is the second upfield shifted peak excluding the methoxyl groups, so it is H-py-5. The remaining proton, 7.23 ppm, should be H-3′. The proton and carbon peaks contained in the naphthalene group were determined based on the correlations of the COSY and HMBC spectra. The two carbons at 145.0 and 118.1 ppm were long-range coupled to H-py-5, so the former was assigned as C-2 and the latter as C-6. H-py-4 showed long-range coupling with two ^{13}C peaks at 107.6 and 134.8 ppm in the HMBC. Because the former was already determined to be C-2′ based on the correlations of the COSY and HMBC spectra, the carbon at 134.8 ppm was assigned as C-1. The three proton peaks at 6.82, 6.86, and 7.01 ppm were correlated with each other in the COSY spectrum, so they are H-4, H-5, or H-6. Based on the interpretation of the COSY and HMBC spectra, they were assigned as H-6, H-4, and H-5, respectively. Because the ^{13}C peak at 152.5 ppm showed long-range coupling with the ^{1}H peak at 7.01 ppm (H-5), it was identified as C-3. Because the two carbons at 128.1 and 148.5 ppm were long-range coupled to H-5″ and H-4″, respectively, they were assigned as C-1″ and C-2″, respectively. C-2″ showed long-range couplings with two protons at 7.11 and 8.98 ppm. They may be H-4″ and/or H-6″. While the former shows doublet of doublet of doublet (ddd), the latter does doublet of doublet (dd). Therefore, two protons at 7.11 and 8.98 ppm were assigned H-4″ and H-6″, respectively. Because four protons at 6.98, 7.00, 7.11, and 8.98 showed cross peaks in the COSY spectrum, they should be H-3″, H-4″, H-5″, and/or H-6″. H-4″ and H-6″ were determined as mentioned previously already; thus, two protons at 6.98 and 7.00 ppm could be assigned to be H-3″ and/or H-5″. C-1″ was long-range coupled with the ^{1}H peak at 6.98 ppm in the HMBC spectrum. Therefore, it should be H-3″. As a result, the remaining proton at 7.00 ppm was determined to be H-5″. Derivative **3** contains three methoxy groups. As shown in Fig. 3, three peaks in the partial HMBC spectrum provide information about three methoxy groups. The ^{1}H peaks at 3.88, 3.98, and 4.10 ppm can be assigned as 3-OMe, 2-OMe, and 2″-OMe, respectively. Likewise, the two ^{1}H peaks at 9.72 and 10.82 ppm show long-range coupling peaks, as shown in Fig. 4A and 4B, in which the former peak is coupled to C-2″ and C-6″ and the latter peak is coupled to C-1′, C-2′, and C-9′. Therefore, they are NH and OH, respectively. These assignments agreed with the reported results.[16] The important correlations obtained from the COSY and HMBC spectra of derivative **3** are shown in Fig. 5. The NMR data for the other derivatives were determined in a similar manner. Their complete ^{1}H and ^{13}C NMR data are listed in Tables 1 and 2, respectively. For reference, the ^{1}H and ^{13}C NMR spectra are provided as supporting information.

The 18 derivatives can be placed in three groups: **1–6** (2,3-dimethoxy groups), **7–12** (2,4-dimethoxy groups), and **13–18** (3,5-dimethoxy groups). The ^{13}C chemical shifts of py-3 are in the order derivatives **7–12** (high frequency) > **1–6** > **13–18** (low frequency). For C-py-4 and C-py-5, derivatives **13–18** are in the high-frequency group, and derivatives **7–12** are in the low-frequency group. The ^{13}C chemical shifts of thioketone, C-1′ and C-1″, do not differ. The ^{1}H chemical shifts of py-5 are in the order derivatives **1–6** (high frequency) > **7–12** > **13–18** (low frequency). While the ^{1}H chemical shifts of H-py-4a are in the order derivatives **13–18** > **1–6** > **7–12**, those of H-py-4b are in the order **1–6** > **13–18** > **7–12**. For the proton chemical shifts of the carbothioamide group, derivatives **7–12** are observed at a lower frequency than derivatives **1–6** and **13–18**. The chemical shifts of all of the hydroxyl protons are observed at approximately 10.5 ppm, but because derivatives **3** and **8** were dissolved in chloroform, their hydroxyl groups are found at 10.8 ppm. These findings will help us identify new naphthochalcones bearing pyrazoline-1-carbothioamide moieties in the future.

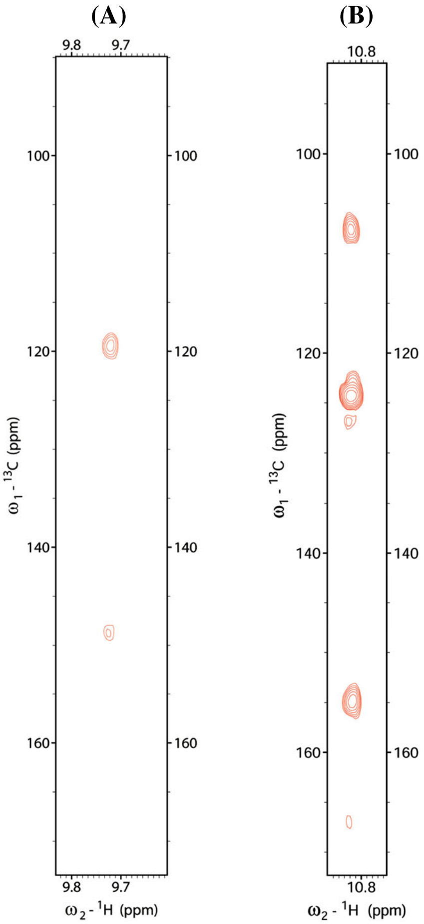


Figure 4. The partial HMBC spectrum of derivative **3** collected in deuterated chloroform. (A) Long-range coupling between NH (9.72 ppm) and C-6″ (119.5 ppm)/C-2″ (148.5 ppm) and (B) long-range coupling between OH (10.82 ppm) and C-2′ (107.6 ppm)/C-9′ (124.3 ppm)/C-1′ (154.8 ppm).

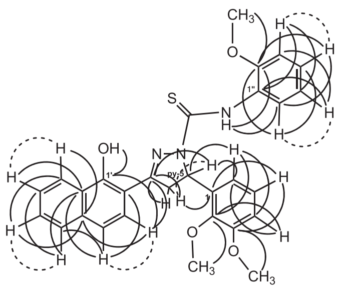


Figure 5. The important correlations obtained from the COSY (dot lines) and HMBC (solid lines) spectra of derivative **3**.

Table 1. ^{1}H nuclear magnetic resonance chemical shifts of polymethoxylated naphthochalcones **1–18** bearing pyrazoline-1-carbothioamide moieties, where py denotes pyrazoline and the multiplicity and coupling constants are given in parentheses

Position	1	2	3	4	5	6	7	8	9
H-py-4a	3.26(dd, 18.0, 3.6)	3.23(dd, 18.0, 3.6)	3.39(dd, 17.7, 4.1)	3.25(dd, 18.0, 3.6)	3.24(dd, 17.9, 3.6)	3.26(dd, 18.0, 3.5)	3.22(dd, 17.8, 3.1)	3.33(dd, 17.7, 3.6)	3.21(dd, 17.9, 3.1)
H-py-4b	4.16(dd, 18.0, 11.7)	4.13(dd, 18.0, 11.7)	4.02(dd, 17.7, 11.4)	4.14(dd, 18.0, 11.7)	4.13(dd, 17.9, 11.9)	4.15(dd, 18.0, 11.8)	4.06(dd, 17.8, 11.3)	3.94(dd, 17.7, 11.4)	4.05(dd, 17.9, 11.3)
H-py-5	6.25(dd, 11.7, 3.6)	6.23(dd, 11.7, 3.6)	6.36(dd, 11.4, 4.1)	6.26(dd, 11.7, 3.6)	6.17(dd, 11.9, 3.6)	6.27(dd, 11.8, 3.5)	6.18(dd, 11.3, 3.1)	6.28(dd, 11.4, 3.6)	6.18(dd, 11.3, 3.1)
NH	10.50(s)	10.39(s)	9.72(s)	10.45(s)	9.95(s)	10.39(s)	10.44(s)	9.69(s)	10.40(s)
H-3	—	—	—	—	—	—	6.60(d, 2.3)	6.49(d, 2.4)	6.60(d, 2.3)
H-4	6.95(dd, 8.3, 1.1)	6.94(d,m, 1.7)	6.86(dd, 8.2, 1.2)	6.94(dd, 8.2, 1.2)	6.93(dd, 8.2, 1.5)	6.95(dd, 8.2, 1.1)	—	—	—
H-5	7.01(dd, 8.3, 7.6)	6.99(d,m, 7.7)	7.01(dd, 8.2, 7.5)	7.00(dd, 8.2, 7.5)	6.99(dd, 8.2, 7.5)	7.01(dd, 8.2, 7.5)	6.47(dd, 8.5, 2.3)	6.42(dd, 8.5, 2.4)	6.47(dd, 8.5, 2.3)
H-6	6.65(dd, 7.6, 1.1)	6.64(dd, 7.7, 1.7)	6.82(dd, 7.5, 1.2)	6.65(dd, 7.5, 1.2)	6.65(dd, 7.5, 1.5)	6.65(dd, 7.5, 1.1)	6.90(d, 8.5)	7.10(d, 8.5)	6.90(d, 8.5)
H-3′	7.55(d, 8.8)	7.53(d, 8.7)	7.23(d, 8.7)	7.54(d, 8.8)	7.53(d, 8.8)	7.57(d, 8.7)	7.53(d, 8.8)	7.25(d, 8.7)	7.53(d, 8.8)
H-4′	7.45(d, 8.8)	7.45(d, 8.7)	7.38(d, 8.7)	7.45(d, 8.8)	7.44(d, 8.8)	7.45(d, 8.7)	7.44(d, 8.8)	7.37(d, 8.7)	7.44(d, 8.8)
H-5′	7.89(dd, 6.8, 1.7)	7.88(d,m, 6.8)	7.79(dd, 6.9, 1.6)	7.89(d,m, 6.9)	7.53(d,m, 6.9)	7.89(d,m, 6.9)	7.88(dd, 6.8, 1.3)	7.79(dd, 6.9, 1.5)	7.88(dd, 6.8, 1.7)
H-6′	7.61 (ddd, 8.3, 6.8, 1.4)	7.61 (ddd, 8.3, 6.8, 1.5)	7.59 (ddd, 8.6, 6.9, 1.7)	7.61 (ddd, 8.4, 6.9, 1.6)	7.60(m)	7.61 (ddd, 8.4, 6.9, 1.6)	7.61 (ddd, 8.2, 6.8, 1.4)	7.59 (ddd, 8.6, 6.9, 1.7)	7.60(ddd, 8.4, 6.8, 1.5)
H-7′	7.58 (ddd, 8.3, 7.4, 1.7)	7.58 (dd,m, 8.3, 6.8)	7.57 (ddd, 8.6, 6.8, 1.6)	7.58 (dd,m, 8.4, 6.9)	7.57(m)	7.58 (dd,m, 8.4, 7.1)	7.57 (ddd, 8.2, 6.9, 1.3)	7.56 (ddd, 8.6, 6.8, 1.5)	7.57(ddd, 8.4, 6.8, 1.5)
H-8′	8.34(dd, 7.4, 1.4)	8.34(dd, 6.8, 1.5)	8.48(dd, 6.8, 1.7)	8.34(d,m, 6.9, 1.6)	8.33(d,m, 7.5)	8.35(dd, 7.1, 1.6)	8.33(dd, 6.9, 1.4)	8.47(dd, 6.8, 1.7)	8.34(dd, 6.8, 1.5)
H-2″	7.48(dd, 8.5, 1.0)	7.32(d, 8.8)	—	7.16(dd, 2.0, 1.7)	—	6.89(s)	7.50(d,m, 1.4)	—	7.17(dd, 2.2, 2.2)
H-3″	7.36(dd, 8.5, 7.4)	6.92(d, 8.8)	6.98(dd, 8.0, 1.2)	—	6.63(d, 2.6)	—	7.36(dd, 8.4, 7.4)	6.97(dd, 8.1, 1.2)	—
H-4″	7.19(dd, 7.4, 1.0)	—	7.11 (ddd, 8.0, 7.8, 1.6)	6.76(dd,m, 8.2, 2.0)	—	—	7.18(dd, 7.4, 1.4)	7.09 (ddd, 8.1, 7.8, 1.6)	6.76(ddd, 8.3, 2.2, 0.8)
H-5″	7.36(dd, 8.5, 7.4)	6.92(d, 8.8)	7.00(m)	7.26(dd, 8.2, 8.0)	6.51(dd, 8.7, 2.6)	—	7.36(dd, 8.4, 7.4)	6.98(dd,m, 8.0, 1.2)	7.26(dd, 8.3, 8.0)
H-6″	7.48(dd, 8.5, 1.0)	7.32(d, 8.8)	8.98(dd, 8.0, 1.6)	7.10 (dd,m, 8.0, 1.7)	7.36(d, 8.7)	6.89(s)	7.50(d,m, 1.4)	8.99(dd, 8.0, 1.6)	7.11(ddd, 8.0, 2.2, 0.8)
2-OCH$_3$	3.84(s)	3.83(s)	3.98(s)	3.84(s)	3.81(s)	3.85(s)	3.81(s)	3.76(s)	3.81(s)
3-OCH$_3$	3.81(s)	3.80(s)	3.88(s)	3.80(s)	3.79(s)	3.81(s)	—	—	—
4-OCH$_3$	—	—	—	—	—	—	3.72(s)	3.82(s)	3.72(s)
2″-OCH$_3$	—	—	4.10(s)	—	3.79(s)	—	—	4.07(s)	—
3″-OCH$_3$	—	—	—	3.76(s)	—	3.77(s)	—	—	3.76(s)
4″-OCH$_3$	—	3.76(s)	—	—	3.77(s)	3.67(s)	—	—	—
5″-OCH$_3$	—	—	—	—	—	3.77(s)	—	—	—
1′-OH	10.54(br s)	10.51(br s)	10.82(br s)	10.52(br s)	10.48(br s)	10.54(br s)	10.51(br s)	10.84(br s)	10.57(br s)

Table 1. (Continued)

Position	10	11	12	13	14	15	16	17	18
H-py-4a	3.20(dd, 17.8, 3.1)	3.21(dd, 17.8, 3.0)	3.21(dd, 17.8, 3.1)	3.38(dd, 18.0, 3.1)	3.40(dd, 18.0, 3.1)	3.37(dd, 18.1, 3.2)	3.36(dd, 18.0, 3.0)	3.37(dd, 18.0, 3.1)	3.37(dd, 18.0, 3.1)
H-py-4b	4.05(dd, 17.8, 11.3)	4.04(dd, 17.8, 11.2)	4.05(dd, 17.8, 11.3)	4.12(dd, 18.0, 11.4)	4.12(dd, 18.0, 11.4)	4.11(dd, 18.1, 11.4)	4.10(dd, 18.0, 11.4)	4.10(dd, 18.0, 11.4)	4.11(dd, 18.0, 11.4)
H-py-5	6.17(dd, 11.3, 3.1)	6.11(dd, 11.2, 3.0)	6.18(dd, 11.3, 3.1)	6.09(dd, 11.4, 3.1)	6.04(dd, 11.4, 3.1)	6.08(dd, 11.4, 3.2)	6.06(dd, 11.4, 3.0)	6.04(dd, 11.4, 3.1)	6.08(dd, 11.4, 3.1)
NH	10.35(s)	9.91(s)	10.34(s)	10.50(s)	10.11(s)	10.46(s)	10.39(s)	10.00(s)	10.40(s)
H-2	—	—	—	6.38(d, 2.1)	6.39(s,m)	6.37(d, 2.1)	6.36(d, 2.2)	6.38(d, 2.0)	6.38(d, 2.1)
H-3	6.60(d, 2.3)	6.59(d, 2.3)	6.60(d, 2.3)	—	—	—	—	—	—
H-4	—	—	—	6.40(d,m, 2.1)	6.39(s,m)	6.39(dd, 2.2, 2.1)	6.39(dd, 2.2, 2.2)	6.39(d,m, 2.0)	6.40(dd, 2.1, 2.1)
H-5	6.47(dd, 8.5, 2.3)	6.46(dd, 8.5, 2.3)	6.47(dd, 8.5, 2.3)	—	—	—	—	—	—
H-6	6.89(d, 8.5)	6.88(d, 8.5)	6.91(d, 8.5)	6.38(d, 2.1)	6.39(s,m)	6.37(d, 2.2)	6.36(d, 2.2)	6.38(d, 2.0)	6.38(d, 2.1)
H-3′	7.52(d, 8.8)	7.52(d, 8.8)	7.54(d, 8.8)	7.55(d, 8.8)	7.54(d, 8.8)	7.54(d, 8.8)	7.54(d, 8.8)	7.53(d, 8.8)	7.55(d, 8.8)
H-4′	7.44(d, 8.8)	7.43(d, 8.8)	7.45(d, 8.8)	7.46(d, 8.8)	7.46(d, 8.8)	7.45(d, 8.8)	7.44(d, 8.8)	7.45(d, 8.8)	7.46(d, 8.8)
H-5′	7.88(dd, 6.7, 1.3)	7.87(m)	7.89(dd, 6.8, 1.4)	7.89(m)	7.89 (dd, 6.9, 1.4)	7.90(dd, 6.9, 1.3)	7.88(d, 6.9)	7.88(dd, 6.9, 1.4)	7.89(dd, 6.9, 1.5)
H-6′	7.60(ddd, 8.1, 6.7, 1.3)	7.60(m)	7.60 (ddd, 8.3, 6.8, 1.5)	7.61(m)	7.61 (ddd, 8.2, 6.9, 1.4)	7.61 (ddd, 8.4, 6.9, 1.5)	7.61(m)	7.61 (ddd, .8.3, 6.9, 1.5)	7.62 (ddd, 8.3, 6.9, 1.5)
H-7′	7.57(ddd, 8.1, 6.9, 1.3)	7.56(m)	7.58 (ddd, 8.3, 6.9, 1.4)	7.58(m)	7.57(m)	7.58(ddm, 6.8, 1.3)	7.57(m)	7.57 (ddd, 8.2, 6.9, 1.4)	7.59 (ddd, .8.3, 6.7, 1.5)
H-8′	8.33(dd, 6.9, 1.3)	8.32(m)	8.34(dd, 6.9, 1.5)	8.34(m)	8.35(dd, 7.7, 1.3)	8.34(dd, 6.8, 1.5)	8.33(m)	8.33(dd, 6.9, 1.5)	8.35(dd, 6.7, 1.5)
H-2″	7.34(d, 8.8)	—	6.90(s)	7.50(d,m, 8.4)	—	7.17(dd, 2.2, 2.2)	7.33(d, 8.9)	—	6.89(s)
H-3″	6.93(d, 8.8)	6.64(d, 2.6)	—	7.37(dd, 8.4, 7.4)	7.09(dd, 8.3, 1.0)	—	6.92(d, 8.9)	6.64(d, 2.6)	—
H-4″	—	—	—	7.19(dd, 7.4, 1.3)	7.22 (ddd, 8.3, 7.6, 1.4)	6.76 (ddd, 8.3, 2.2, 0.7)	—	—	—
H-5″	6.93(d, 8.8)	6.52(dd, 8.7, 2.6)	—	7.37(dd, 8.4, 7.4)	6.95 (ddd, 7.8, 7.6, 1.0)	7.27(dd, 8.3, 7.9)	6.92(d, 8.9)	6.53(dd, 8.7, 2.6)	—
H-6″	7.34(d, 8.8)	7.41(d, 8.7)	6.90(s)	7.50(d,m, 8.4)	7.72(dd, 7.8, 1.4)	7.11 (ddd, 7.9, 2.2, 0.7)	7.33(d, 8.9)	7.35(d, 8.7)	6.89(s)
2-OCH_3	3.81(s)	3.81(s)	3.80(s)	—	—	—	—	—	—
3-OCH_3	—	—	—	3.72(s)	3.72(s)	3.71(s)	3.71(s)	3.72(s)	3.71(s)
4-OCH_3	3.73(s)	3.72(s)	3.72(s)	—	—	—	—	—	—
5-OCH_3	—	—	—	3.72(s)	3.72(s)	3.71(s)	3.71(s)	3.72(s)	3.71(s)
2″-OCH_3	—	3.81(s)	—	—	3.85(s)	—	—	3.80(s)	—
3″-OCH_3	—	—	3.77(s)	—	—	3.76(s)	—	—	3.77(s)
4″-OCH_3	3.76(s)	3.78(s)	3.67(s)	—	—	—	3.76(s)	3.78(s)	3.67(s)
5″-OCH_3	—	—	3.77(s)	—	—	—	—	—	3.77(s)
1′-OH	10.54(br s)	10.49(br s)	10.56(br s)	10.51(br s)	10.49(br s)	10.51(br s)	10.46(br s)	10.45(br s)	10.52(br s)

Table 2. ^{13}C NMR chemical shifts of polymethoxylated naphthochalcones **1–18** bearing pyrazoline-1-carbothioamide moieties, where py denotes pyrazoline

Position	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
C-py-3	158.0	157.7	158.0	157.9	157.5	157.9	158.3	158.3	158.3	158.1	158.0	158.2	157.7	157.5	157.7	157.5	157.3	157.7
C-py-4	42.6	42.4	42.4	42.5	42.6	42.5	42.1	42.0	42.0	42.0	42.2	42.0	43.1	43.4	43.1	43.0	43.2	43.0
C-py-5	58.3	58.3	57.6	58.3	58.3	58.2	58.1	57.5	58.1	58.1	58.0	58.1	62.0	61.8	62.0	62.0	61.9	62.0
C = S	173.6	174.1	170.8	173.4	174.4	173.3	173.6	170.8	173.4	174.1	174.4	173.4	173.9	173.8	173.6	174.3	174.9	173.6
1	136.0	136.1	134.8	135.9	136.1	136.0	121.7	120.7	121.7	121.8	121.9	121.7	144.9	144.8	144.8	145.0	145.0	144.9
2	145.0	145.0	145.0	145.0	145.1	145.0	156.8	160.0	156.8	156.8	156.8	156.9	103.4	103.4	103.4	103.4	103.3	103.5
3	152.6	152.6	152.5	152.6	152.6	152.6	98.9	98.7	98.9	98.9	98.9	98.9	160.7	160.7	160.7	160.7	160.6	160.7
4	111.8	111.7	111.3	111.8	111.7	111.8	159.8	156.6	159.8	159.7	159.7	159.8	98.1	98.1	98.1	98.1	98.1	98.1
5	123.9	123.9	123.8	123.9	123.8	123.9	104.4	103.4	104.4	104.3	104.3	104.4	160.7	160.7	160.7	160.7	160.6	160.7
6	117.7	117.8	118.1	117.7	117.7	117.7	126.4	127.0	126.4	126.3	126.3	126.6	103.4	103.4	103.4	103.4	103.3	103.5
1′	153.6	153.1	154.8	153.2	153.2	153.3	153.3	154.8	153.3	153.2	153.4	153.1	153.3	153.2	153.3	153.6	153.2	153.2
2′	109.0	109.0	107.6	109.0	109.1	109.0	109.0	107.9	109.0	109.0	109.1	109.1	108.9	109.1	108.9	108.9	109.0	109.0
3′	125.7	125.7	123.9	125.7	125.6	125.7	125.6	123.9	125.6	125.6	125.6	125.6	125.6	125.5	125.6	125.6	125.5	125.6
4′	119.0	119.2	119.3	119.2	119.2	119.1	119.2	119.2	119.2	119.2	119.1	119.3	119.2	119.3	119.2	119.1	119.2	119.3
5′	127.5	127.5	127.1	127.5	127.5	127.5	127.5	127.0	127.5	127.5	127.5	127.5	127.5	127.5	127.5	127.5	127.5	127.5
6′	128.2	128.1	128.0	128.2	128.1	128.1	128.1	128.0	128.1	128.1	128.1	128.1	128.2	128.2	128.2	128.2	128.1	128.2
7′	125.9	126.0	125.5	126.0	125.9	125.9	126.0	125.5	126.0	125.9	125.9	126.0	126.0	126.0	126.0	126.0	126.0	126.0
8′	122.9	122.8	123.0	122.9	122.9	122.9	122.9	123.0	122.8	122.8	122.9	122.8	122.9	122.9	122.9	122.9	122.9	122.9
9′	124.4	124.2	124.3	124.3	124.3	124.4	124.3	124.1	124.3	124.2	124.3	124.2	124.3	124.3	124.3	124.4	124.3	124.3
10′	134.9	134.8	135.0	134.9	134.8	134.9	134.9	134.9	134.9	134.8	134.8	134.9	134.9	134.9	134.9	134.9	134.9	134.9
1″	139.8	132.7	128.1	140.9	121.8	135.6	139.9	128.2	141.0	132.8	121.8	134.8	139.8	128.5	140.9	132.7	121.7	134.8
2″	126.1	127.8	148.5	111.5	154.8	103.6	126.0	148.5	111.4	127.8	154.8	103.7	126.0	153.4	111.4	127.7	155.0	103.6
3″	128.0	113.2	109.4	158.9	98.9	152.1	128.0	109.4	158.9	113.2	98.9	152.1	128.0	111.6	159.0	113.2	98.9	152.1
4″	125.0	156.8	123.6	110.4	158.4	134.8	124.9	123.5	110.3	156.7	158.4	135.6	125.1	126.6	110.4	156.8	158.5	135.5
5″	128.0	113.2	120.0	128.6	104.0	152.1	128.0	120.0	128.6	113.2	104.0	152.1	128.0	119.9	128.7	113.2	104.0	152.1
6″	126.1	127.8	119.5	118.1	128.7	103.6	126.0	119.5	118.0	127.8	128.6	103.7	126.0	126.8	117.9	127.7	128.9	103.6
2-OCH$_3$	59.6	59.6	59.8	59.6	59.6	59.6	55.6	54.9	55.6	55.6	55.6	55.6	—	—	—	—	—	—
3-OCH$_3$	55.6	55.6	55.2	55.6	55.6	55.6	—	—	—	—	—	—	55.1	55.1	55.1	55.1	55.1	55.1
4-OCH$_3$	—	—	—	—	—	—	55.1	55.1	55.1	55.1	55.2	55.1	—	—	—	—	—	—
5-OCH$_3$	—	—	—	—	—	—	—	—	—	—	—	—	55.1	55.1	55.1	55.1	55.1	55.1
2″-OCH$_3$	—	—	55.5	—	55.7	—	—	55.5	—	—	55.7	—	—	55.7	—	—	55.6	—
3″-OCH$_3$	—	—	—	55.1	—	55.8	—	—	55.1	—	—	55.8	—	—	55.1	—	—	55.8
4″-OCH$_3$	—	55.2	—	—	55.3	60.0	—	—	—	55.2	55.3	60.0	—	—	—	55.2	55.3	60.1
5″-OCH$_3$	—	—	—	—	—	55.8	—	—	—	—	—	55.8	—	—	—	—	—	55.8

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