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^{1}H and ^{13}C NMR spectral assignments of novel flavonoids bearing benzothiazepine

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Introduction

Benzothiazepine is a heterocyclic compound containing nitrogen and sulfur. A variety of derivatives can be designed by modifying the positions of the double bond and benzene ring. 2,3-Dihydro-1,5-benzothiazepine (also known as 2,3-dihydro[*b*][1,4]thiazepine) derivatives show diverse biological activities, including inhibitory effects on alpha-glucosidase, urease, cholinesterase, and butyrylcholinesterase, and agonistic activity toward the transient receptor potential ankyrin 1 (TRPA1) receptor (Fig. 1(A)).[1–4] When two benzene rings are attached at the C-2 and C-4 positions, 2,4-diphenyl-2,3-dihydro-1,5-benzothiazepine containing a C6-C3-C6 skeleton can be derived (Fig. 1(B)). Flavonoids are found in various plants as their secondary metabolites and are composed of C6-C3-C6 skeletons (Fig. 1(C)).[5,6] Because methoxylation and naphthalenyl groups can increase cellular compartmentation and cell permeability,[7,8] we designed and synthesized methoxylated 4-(1-hydroxy-naphthalen-2-yl)-2-phenyl-2,3-dihydro-1,5-benzothiazepine derivatives (Fig. 1(D)). However, flavonoids bearing a benzothiazepine skeleton have rarely been reported,[2,3] even though their design and synthesis are of interest because of their biological diversity. Furthermore, because the ^{1}H and ^{13}C NMR, and high resolution mass spectrometric (HR/MS) data can be used as references for further study, herein, we report the NMR and MS data of 27 novel flavonoids bearing benzothiazepine skeletons.

Experimental

Syntheses

All of the benzothiazepine derivatives (**1-27**) were synthesized as shown in Scheme 1. The typical procedure for the synthesis of benzothiazepine **20** is described as follows. To a stirred solution of 2′-hydroxy-4,5-dimethoxyacetophenone (**I**, 5 mmol, 980 mg) and 4-methoxy-1-naphthaldehyde (**II**, 5 mmol, 930 mg) in ethanol (50 ml) was added an aqueous solution of KOH (50% w/v, 5 ml), and the mixture was stirred at room temperature for 24 h. Ice-water was added to the mixture, which was acidified with 3 N HCl to pH = 3, to form a precipitate. The precipitate was filtered and washed with water and methanol successively to give a chalcone compound (**III**, yield: 40%, MP: 181–184 °C). 2-Aminothiophenol (**IV**, 1.2 mmol, 150 mg, d: 1.17 g/ml) was added to a solution of the chalcone (**III**, 1 mmol, 364 mg) in 15 ml of ethanol containing a catalytic amount of gallium (III) trifluoromethanesulfonate. The reaction mixture was refluxed at 85 °C for 6 h. After cooling the reaction mixture to room temperature, a precipitate is formed. The resulting solid was filtered and washed with ethanol and was recrystallized from ethanol to form the pure benzothiazepine compound (**20**, yield: 67%, MP: 213–221 °C).

NMR spectra

The synthesized benzothiazepines were prepared in deuterated chloroform ($CDCl_3$), apart from derivative **27**, which was dissolved in deuterated dimethyl sulfoxide (DMSO-d_6), with concentrations of approximately 50 mM, and transferred into 2.5 mm NMR tubes for the NMR experiments. All NMR spectroscopic data were collected using an Avance 400 spectrometer (9.4 T; Bruker, Karlsruhe, Germany) at room temperature. The chemical shifts were referenced to TMS. The parameters for the ^{1}H and ^{13}C NMR experiments were as follows: the relaxation delay, 90° pulse, spectral width, number of data points, and digital resolution were set to 1 and 3 s, 11.8 and 15.0 μs, 5500 and 20 000 Hz, 32 and 64 K, and 0.340 and 0.640 Hz/point, respectively. The parameters for the distortionless enhancement by polarization transfer (DEPT) experiments were the same as those for ^{13}C NMR. The data points of the two dimensional experiments, including correlation spectroscopy (COSY), heteronuclear multiple quantum coherence (HMQC), and heteronuclear multiple bond connectivity (HMBC), were set to 2 K × 256 ($t_2 \times t_1$). The long-range coupling times for HMBC were set to 40 and 70 ms. The detailed experimental methods were the same as those previously reported.[9]

General experimental procedures

To obtain the HR/MS data of the benzothiazepine derivatives, ultra performance liquid chromatography (UPLC)-hybrid quadrupole-time-of-flight mass spectrometry was carried out on a Waters Acquity

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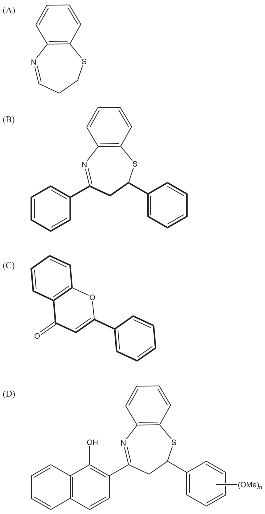


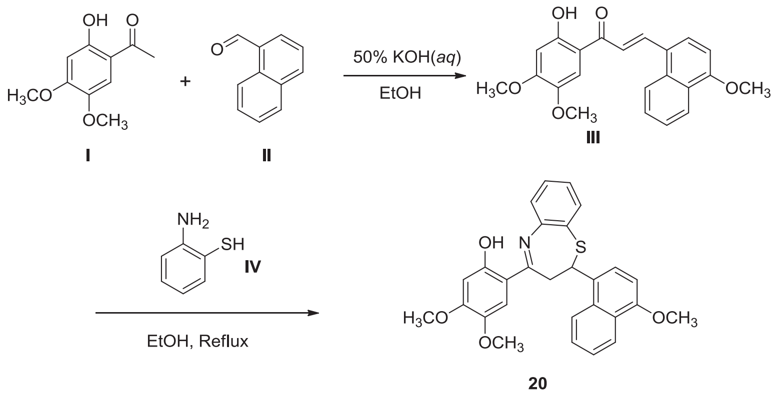
Figure 1. (A) 2,3-Dihydro-1,5-benzothiazepine (also known as 2,3-dihydro [*b*][1,4]thiazepine), (B) 2,4-diphenyl-2,3-dihydro-1,5-benzothiazepine, (C) flavone, and (D) methoxylated 4-(1-hydroxy-naphthalen-2-yl)-2-phenyl-2,3-dihydro-1,5-benzothiazepine.

UPLC system (Waters Corp., Milford, MA) with the help of Prof. Choong Hwan Lee at Konkuk University, Korea.[10] All HR/MS data were collected as M + H ions, except for derivatives **5**, **8**, **16**, and **19**, which were collected in M − H ion mode. Melting points, ultraviolet/visible (UV/VIS) spectra in chloroform, and infrared (IR) spectra were measured using Mel-Temp II (LabX, Midland, ON, Canada), a 50-Conc UV-Visible spectrophotometer (Varian), and FT-IR 4200 (JASCO, Easton, MD) with ATR (Attenuated Total Reflection, ATR PR0450-S), respectively.

Results and discussion

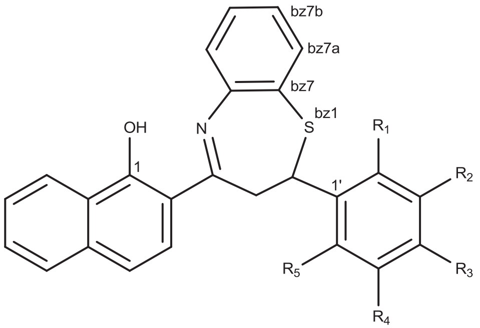
All of the synthesized benzothiazepines are listed in Table 1. The procedure used to assign the NMR data of derivative **8**, (*E*)-2-(2-(2,3,4-trimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl) naphthalen-1-ol was as follows: 28 carbon peaks were observed in the ^{13}C NMR spectrum. Of them, only one methylene peak at 36.1 ppm was observed in the DEPT experiments, which was the benzothiazepine-3 carbon (named C-bz3). Two protons at 2.95 and 3.54 ppm were directly attached to C-bz3 in the HMQC spectrum. As a proton peak at 5.48 ppm was correlated with the two protons above in the COSY spectrum, it was assigned as H-bz2. Six protons at 7.18, 7.51, 7.59, 7.63, 7.73, and 8.55 ppm were correlated with each other; therefore, they belonged to the naphthalenyl group. Based on the interpretation of the COSY, HMQC, and HMBC spectra, the carbons and protons of the naphthalenyl group were determined. Likewise, four protons at 7.25, 7.39, 7.49, and 7.73 ppm were correlated with each other and were assigned to H-bz7b, H-bz6a, H-bz6b, and H-bz7a, respectively, with the help of the COSY, HMQC, and HMBC experimental data. Because the carbon peak at 172.0 ppm was long-range coupled to H-bz2 in the HMBC spectrum, it was determined to be C-bz4. Two ^{13}C peaks at 146.4 and 125.9 ppm showed long-range coupling to H-bz6b and H-bz7b, respectively, in the HMBC spectrum, and were assigned to C-bz6 and C-bz7, respectively. The ^{13}C peak at 129.3 ppm was long-range coupled to the H-bz3 protons and was, thus, attributed to C-1′. This carbon showed long-range coupling with the proton peak at 6.65 ppm; therefore, this proton was H-5′. As a result, the ^{13}C peak at 121.5 ppm could be assigned to C-6′. Three methoxy carbons and protons were determined by long-range couplings in the HMBC spectrum at 56.2 (2′-OCH_3), 61.0 (3′-OCH_3), and 61.5 ppm (4′-OCH_3). The complete assignments of the ^{1}H and ^{13}C signals of derivative **8**, (*E*)-2-(2-(2,3,4-trimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl) naphthalen-1-ol, are listed in Tables 2 and 3, respectively. The important correlations obtained from the COSY and HMBC spectra of derivative **8** are shown in Fig. 2. The NMR data of the other benzothiazepine derivatives were interpreted using the same procedure as for derivative **8**. The complete assignments of the ^{1}H and ^{13}C NMR data for all derivatives are listed in Tables 2 and 3, respectively. For reference, the ^{1}H and ^{13}C NMR spectra and HR/MS spectrometric data are provided as Supplementary Information.

As listed in Table 1, the 27 benzothiazepine derivatives can be classified into three groups: **1–11**, **12–21**, and **22–27**. The only difference between derivative **12** with derivative **22** is the presence of a 1-naphthalenyl group in the former and 2-naphthalenyl group in the latter. The carbon chemical shifts of C-3, C-5, C-8, C-9, and C-10 in the naphthalenyl group showed differences greater than 1 ppm. Both C-bz2 and C-bz3 of derivative **12** are shielded more than those of derivative **22**. The proton chemical shifts of H-5, H-7, H-8, H-bz2, and H-bz3 showed differences greater than 0.1 ppm. Derivatives containing a 1-naphthalenyl group (**12–21**) tended to show more shielded carbon and deshielded proton chemical shifts than derivatives containing a 2-naphthalenyl group (**22–27**), especially for bz2. For bz7, the average values of the carbon chemical shifts in derivatives **1–11**, **12–21**, and **22–27** were 126.1, 125.2, and 124.7 ppm, respectively. That is, the carbon chemical shifts of 2-naphthalenyl-



Scheme 1. Procedure for the preparation of benzothiazepines **1–27**.

Table 1. Structures and names of benzothiazepines **1–27**, and their high resolution mass data. HR/MS data were collected in $[M+H]^-$ mode. * denotes HR/MS data collected in $[M\text{-}H]^-$ mode. bz and str represent benzothiazepine and strong, respectively



Derivative	R$_1$	R$_2$	R$_3$	R$_4$	R$_5$	Mass (calcd./ found)	Name	Melting point/°C	Color	UV λ_{max}/ nm	IR/cm^{-1}
1	OCH$_3$	H	H	H	H	411.1293/ 412.1396	(*E*)-2-(2-(2-methoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	178–181	yellow	280	3047 (C-H, str. aromatic), 1578 (C = N, str.), 744 (C-S-C, str.)
2	OCH$_3$	OCH$_3$	H	H	H	441.1399/ 442.1524	(*E*)-2-(2-(2,3-dimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	192–196	yellow	280	3049 (C-H, str. aromatic), 1575 (C = N, str.), 768 (C-S-C, str.)
3	H	H	H	H	H	381.1187/ 382.1277	(*E*)-2-(2-phenyl-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	204–206	yellow	280	3049 (C-H, str. aromatic), 1599 (C = N, str.), 758 (C-S-C, str.)
4	H	OCH$_3$	H	H	H	411.1293/ 412.1367	(*E*)-2-(2-(3-methoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	175–177	yellow	280	3049 (C-H, str. aromatic), 1588 (C = N, str.), 781 (C-S-C, str.)
5	H	H	OCH$_3$	H	H	411.1293/ 410.1232*	(*E*)-2-(2-(4-methoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	193–197	yellow	280	3054 (C-H, str. aromatic), 1607 (C = N, str.), 745 (C-S-C, str.)
6	OCH$_3$	H	OCH$_3$	H	H	441.1399/ 442.1468	(*E*)-2-(2-(2,4-dimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	204	yellow	280	3059 (C-H, str. aromatic), 1590 (C = N, str.), 794 (C-S-C, str.)
7	H	OCH$_3$	H	OCH$_3$	H	441.1399/ 442.1474	(*E*)-2-(2-(3,5-dimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	154–156	yellow	280	3046 (C-H, str. aromatic), 1590 (C = N, str.), 749 (C-S-C, str.)
8	OCH$_3$	OCH$_3$	OCH$_3$	H	H	471.1504/ 470.1437*	(*E*)-2-(2-(2,3,4-trimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	192–193	yellow	280	3054 (C-H, str. aromatic), 1582 (C = N, str.), 755 (C-S-C, str.)
9	OCH$_3$	H	OCH$_3$	OCH$_3$	H	471.1504/ 472.1548	(*E*)-2-(2-(2,4,5-trimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	168–170	yellow	280	3054 (C-H, str. aromatic), 1584 (C = N, str.), 756 (C-S-C, str.)
10	OCH$_3$	H	OCH$_3$	H	OCH$_3$	471.1504/ 472.1603	(*E*)-2-(2-(2,4,6-trimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	214–218	yellow	280	3059 (C-H, str. aromatic), 1585 (C = N, str.), 746 (C-S-C, str.)
11	H	OCH$_3$	OCH$_3$	H	H	441.1399/ 442.1485	(*E*)-2-(2-(3,4-dimethoxyphenyl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)naphthalen-1-ol	200	yellow	280	3049 (C-H, str. aromatic), 1599 (C = N, str.), 754 (C-S-C, str.)

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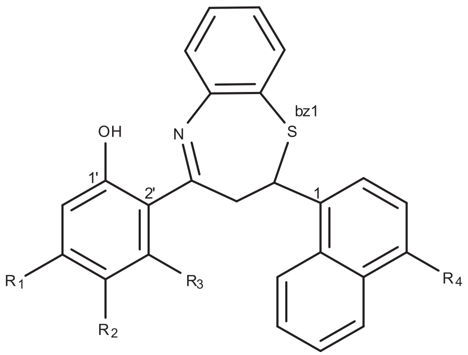
Table 1. (Continued)



Derivative	R_1	R_2	R_3	R_4	Mass (calcd./found)	Name	Melting point/°C	Color	UV λ_{max}/nm	IR/cmx^{-1}
12	H	H	H	H	381.1177/ 382.1274	(*E*)-2-(2-(naphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	188–190	lemon	275	3052 (C-H, str. aromatic), 1594 (C = N, str.), 753 (C-S-C, str.)
13	OCH_3	OCH_3	H	H	441.1399/ 442.1477	(*E*)-4,5-dimethoxy-2-(2-(naphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	208–212	lemon	290	3051 (C-H, str. aromatic), 1607 (C = N, str.), 768 (C-S-C, str.)
14	OCH_3	H	OCH_3	H	441.1399/ 442.1462	(*E*)-3,5-dimethoxy-2-(2-(naphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	190–194	pale-yellow	300	3051 (C-H, str. aromatic), 1604 (C = N, str.), 765 (C-S-C, str.)
15	OCH_3	H	H	H	411.1293/ 412.1367	(*E*)-5-methoxy-2-(2-(naphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	195–197	pale-yellow	290	3058 (C-H, str. aromatic), 1593 (C = N, str.), 772 (C-S-C, str.)
16	H	OCH_3	H	H	411.1293/ 410.1293*	(*E*)-4-methoxy-2-(2-(naphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	176–179	pale-yellow	275	3059 (C-H, str. aromatic), 1594 (C = N, str.), 768 (C-S-C, str.)
17	H	OCH_3	H	OCH_3	441.1399/ 442.1484	(*E*)-4-methoxy-2-(2-(4-methoxynaphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	184–187	pale-yellow	275	3067 (C-H, str. aromatic), 1575 (C = N, str.), 756 (C-S-C, str.)
18	H	H	OCH_3	OCH_3	441.1399/ 442.1446	(*E*)-3-methoxy-2-(2-(4-methoxynaphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	180–184	pale-yellow	285	3065 (C-H, str. aromatic), 1590 (C = N, str.), 731 (C-S-C, str.)
19	H	H	H	OCH_3	411.1293/ 410.1217*	(*E*)-2-(2-(4-methoxynaphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	192–193	lemon	275	3064 (C-H, str. aromatic), 1590 (C = N, str.), 756 (C-S-C, str.)
20	OCH_3	OCH_3	H	OCH_3	471.1504/ 472.1561	(*E*)-4,5-dimethoxy-2-(2-(4-methoxynaphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	213–221	pale-yellow	290	3049 (C-H, str. aromatic), 1590 (C = N, str.), 761 (C-S-C, str.)
21	OCH_3	H	H	OCH_3	441.1399/ 442.1472	(*E*)-5-methoxy-2-(2-(4-methoxynaphthalen-1-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	186–188	yellow	285	3073 (C-H, str. aromatic), 1590 (C = N, str.), 754 (C-S-C, str.)

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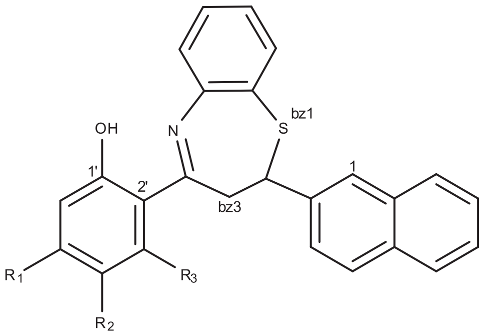
Table 1. (Continued)



Derivative	R_1	R_2	R_3	Mass (calcd./found)	Name	Melting point/°C	Color	UV λ_{max}/nm	IR/cm^{-1}
22	H	H	H	381.1187/ 382.1267	(*E*)-2-(2-(naphthalen-2-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	170–174	lemon	270	3049 (C-H, str. aromatic), 1592 (C = N, str.), 749 (C-S-C, str.)
23	OCH_3	OCH_3	H	441.1399/ 442.1488	(*E*)-4,5-dimethoxy-2-(2-(naphthalen-2-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	190–194	lemon	280	3054 (C-H, str. aromatic), 1610 (C = N, str.), 740 (C-S-C, str.)
24	OCH_3	H	H	411.1293/ 412.1378	(*E*)-5-methoxy-2-(2-(naphthalen-2-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	184–186	lemon	285	3047 (C-H, str. aromatic), 1603 (C = N, str.), 741 (C-S-C, str.)
25	OCH_3	H	OCH_3	441.1399/ 442.1469	(*E*)-3,5-dimethoxy-2-(2-(naphthalen-2-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	196–197	yellow	285	3045 (C-H, str. aromatic), 1590 (C = N, str.), 752 (C-S-C, str.)
26	H	H	OCH_3	411.1293/ 412.1394	(*E*)-3-methoxy-2-(2-(naphthalen-2-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	171–173	yellow	280	3052 (C-H, str. aromatic), 1590 (C = N, str.), 736 (C-S-C, str.)
27	H	OCH_3	H	411.1293/ 412.1361	(*E*)-4-methoxy-2-(2-(naphthalen-2-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol	174	yellow	275	3051 (C-H, str. aromatic), 1592 (C = N, str.), 740 (C-S-C, str.)

Table 2. ^{1}H NMR chemical shifts of benzothiazepines **1–27**, where bz denotes benzothiazepine, and multiplicity and coupling constants are given in parentheses. s, d, m, and br denote singlet, doublet, multiplet, and broad, respectively

Position	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
H-bz2	5.57(dd, 12.6, 4.4)	5.54(dd, 12.6, 4.4)	5.06(dd, 12.1, 4.7)	4.92(dd, 12.0, 4.7)	5.05(dd, 11.8, 4.8)	5.49(dd, 12.4, 4.4)	4.97(dd, 11.7, 4.8)	5.45(dd, 12.3, 4.5)	5.55(dd, 11.8, 4.7)
H-bz3a	2.92(dd, 13.0, 12.6)	2.94(dd, 13.0, 12.6)	3.11(dd, 13.3, 12.1)	3.00(dd, 13.3, 12.0)	3.10(dd, 13.3, 11.8)	2.91(dd, 13.1, 12.4)	3.12(dd, 13.4, 11.7)	2.92(dd, 13.0, 12.3)	2.89(dd, 13.0, 11.8)
H-bz3b	3.57(dd, 13.0, 4.4)	3.55(dd, 13.0, 4.4)	3.50(dd, 13.3, 4.7)	3.40(dd,13.3, 4.7)	3.47(dd, 13.3, 4.8)	3.52(dd, 13.1, 4.4)	3.48(dd, 13.4, 4.8)	3.51(dd, 13.0, 4.5)	3.51(dd, 13.0, 4.7)
H-bz6a	7.36(dd, 7.9, 1.4)	7.36(dd, 7.9, 1.4)	7.37(dd, 7.9, 1.4)	7.27(dd, 7.9, 1.3)	7.38(dd, 8.0, 1.4)	7.36(dd, 7.9, 1.4)	7.36(dd, 7.9, 1.3)	7.36(dd, 7.9, 1.4)	7.36(dd, 7.9, 1.4)
H-bz6b	7.46(ddd, 7.9, 7.6, 1.4)	7.478(ddd, 7.9, 7.6, 1.4)	7.495(ddd, 7.9, 7.4, 1.3)	7.39(ddd, 7.9, 7.5, 1.4)	7.493(ddd, 8.0, 7.6, 1.3)	7.46(ddd, 7.9, 7.5, 1.3)	7.48(ddd, 7.9, 7.3, 1.2)	7.46(ddd, 7.9, 7.7, 1.4)	7.47(ddd, 7.9, 7.6, 1.4)
H-bz7b	7.23(ddd, 7.7, 7.6, 1.4)	7.24(ddd, 7.7, 7.6, 1.4)	7.24(ddd, 7.7, 7.4, 1.4)	7.14(ddd, 7.7, 7.5, 1.3)	7.24(ddd, 7.7, 7.6, 1.4)	7.22(ddd, 7.7, 7.5, 1.4)	7.23(ddd, 7.5, 7.3, 1.3)	7.22(ddd, 7.7, 7.7, 1.4)	7.23(ddd, 7.7, 7.6, 1.4)
H-bz7a	7.73(dd, 7.7, 1.4)	7.74(dd, 7.7, 1.4)	7.66(dd, 7.7, 1.3)	7.57(dd, 7.7, 1.4)	7.65(dd, 7.7, 1.3)	7.71(dd, 7.7, 1.3)	7.68(dd, 7.5, 1.2)	7.697(dd, 7.7, 1.4)	7.73(dd, 7.7, 1.4)
H1	—	—	—	—	—	—	—	—	—
H2	—	—	—	—	—	—	—	—	—
H3	7.64(d, 9.0)	7.68(d, 9.1)	7.40(d, 9.1)	7.31(d, 9.0)	7.39(d, 9.1)	7.61(d, 9.0)	7.39(d, 9.0)	7.60(d, 9.0)	7.58(d, 9.1)
H4	7.15(d, 9.0)	7.16(d, 9.1)	7.11(d, 9.1)	7.02(d, 9.0)	7.10(d, 9.1)	7.13(d, 9.0)	7.11(d, 9.0)	7.15(d, 9.0)	7.127(d, 9.1)
H5	7.70(dd, 8.2, 1.5)	7.71(dd, 8.1, 1.2)	7.69(dd, 8.1, 1.3)	7.60(dd, 8.0, 1.5)	7.70(dd, 8.1, 1.3)	7.67(dd, 8.1, 1.1)	7.69(dd, 8.1, 1.1)	7.694(dd, 8.1, 1.2)	7.69(dd, 8.1, 1.2)
H6	7.57(ddd, 8.2, 7.0, 1.5)	7.57(ddd, 8.1, 6.8, 1.3)	7.57(ddd, 8.1, 6.9, 1.3)	7.48(ddd, 8.0, 7.0, 1.3)	7.58(ddd, 8.1, 6.8, 1.4)	7.56(ddd, 8.1, 7.0, 1.1)	7.57(ddd, 8.1, 7.0, 1.3)	7.56(ddd, 8.1, 6.9, 1.4)	7.56(ddd, 8.1, 6.9, 1.3)
H7	7.48(ddd, 8.3, 7.0, 1.5)	7.489(ddd, 8.2, 6.8, 1.2)	7.495(ddd, 8.2, 6.9, 1.3)	7.40(ddd, 8.2, 7.0, 1.5)	7.493(ddd, 8.2, 6.8, 1.3)	7.48(ddd, 8.1, 7.0, 1.1)	7.49(ddd, 8.2, 7.0, 1.1)	7.48(ddd, 8.2, 6.9, 1.2)	7.48(ddd, 8.2, 6.9, 1.2)
H8	8.53(dd, 8.3, 1.5)	8.52(dd, 8.2, 1.3)	8.52(dd, 8.2, 1.3)	8.42(dd, 8.2, 1.3)	8.52(dd, 8.2, 1.4)	8.52(dd, 8.1, 1.1)	8.51(dd, 8.2, 1.3)	8.52(dd, 8.2, 1.4)	8.51(dd, 8.2, 1.3)
H2′	—	—	7.34(m)	6.81(d, 1.1)	7.26(ddd, 8.7, 3.1, 2.2)	—	6.49(d, 2.2)	—	—
H3′	6.91(dd, 8.2, 1.0)	—	7.34(m)	—	6.85(ddd, 8.7, 3.0, 2.0)	6.49(d, 2.3)	—	—	6.52(s)
H4′	7.27(ddd, 8.2, 7.6, 1.6)	6.86(dd, 8.1, 1.3)	7.30(m)	7.27(dd, 7.9, 1.3)	—	—	6.38(dd, 2.2, 2.2)	—	—
H5′	6.94(ddd, 7.6, 7.6, 1.0)	7.04(dd, 8.1, 7.8)	7.34(m)	7.15(dd, 8.0, 7.9)	6.85(ddd, 8.7, 3.0, 2.0)	6.45(dd, 8.4, 2.3)	—	6.62(d, 8.7)	—
H6′	7.55(dd, 7.6, 1.6)	7.15(d, 7.8, 1.3)	7.34(m)	6.73(ddd, 8.0, 1.3, 1.1)	7.26(ddd, 8.7, 3.1, 2.2)	7.42(d, 8.4)	6.49(d, 2.2)	7.18(d, 8.7)	7.126(s)
2′-OCH$_3$	3.92(s)	3.95(s)	—	—	—	3.89(s)	—	3.84(s)	3.89(s)
3′-OCH$_3$	—	3.89(s)	—	3.65(s)	—	—	3.73(s)	3.91(s)	—
4′-OCH$_3$	—	—	—	—	3.79(s)	3.79(s)	—	4.01(s)	3.88(s)
5′-OCH$_3$	—	—	—	—	—	—	3.73(s)	—	3.73(s)
1-OH	16.74(s)	16.67(s)	16.76(s)	16.65(s)	16.76(s)	16.75(s)	16.72(s)	16.74(s)	16.73(s)
Position	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
H-bz2	5.87(dd, 13.2, 3.7)	5.05(dd, 11.0, 5.0)	5.95(dd, 12.3, 4.3)	6.01(dd, 10.5, 4.8)	6.13(dd, 12.4, 4.0)	5.90(dd, 12.1, 4.3)	5.99(dd, 11.6, 4.5)	5.93(dd, 11.3, 4.5)	6.16(dd, 12.4, 4.1)
H-bz3a	3.26(dd, 12.9, 3.7)	3.12(dd, 13.3, 11.0)	3.27(dd, 13.0, 12.3)	3.18(dd, 13.3, 10.5)	3.24(dd, 12.4, 12.1)	3.24(dd, 13.1, 12.1)	3.25(dd, 13.1, 11.6)	3.19(dd, 13.1, 11.3)	3.25(dd, 12.4, 12.2)
H-bz3b	3.57(dd, 13.2, 12.9)	3.46(dd, 13.3, 5.0)	3.51(dd, 13.0, 4.3)	3.37(dd, 13.3, 4.8)	3.72(dd, 12.1, 4.0)	3.43(dd, 13.1, 4.3)	3.45(dd, 13.1, 4.5)	3.42(dd, 13.1, 4.5)	3.67(dd, 12.2, 4.1)
H-bz6a	7.35(dd, 7.8, 1.5)	7.37(dd, 7.9, 1.4)	7.34(dd, 7.9, 1.4)	7.29(dd, 7.9, 1.4)	7.30(dd, 7.4, 1.4)	7.31(dd, 7.9, 1.3)	7.33(dd, 7.9, 1.3)	7.32(dd, 7.9, 1.3)	6.71(dd, 7.9, 1.3)
H-bz6b	7.57(ddd, 7.8, 7.4, 1.5)	7.49(ddd, 7.9, 7.7, 1.4)	7.49(ddd, 7.9, 7.6, 1.4)	7.47(ddd, 7.9, 7.7, 1.4)	7.46(ddd, 7.6, 7.4, 1.5)	7.47(ddd, 7.9, 7.7, 1.3)	7.49(ddd, 7.9, 7.7, 1.5)	7.48(ddd, 7.9, 7.7, 1.4)	7.47(ddd, 7.9, 7.5, 1.4)
H-bz7b	7.22(ddd, 7.7, 7.4, 1.5)	7.23(ddd, 7.7, 7.6, 1.4)	7.18(ddd, 7.6, 7.6, 1.4)	7.19(ddd, 7.7, 7.7, 1.4)	7.15(ddd, 7.6, 7.3, 1.4)	7.16(ddd, 7.8, 7.7, 1.3)	7.20(ddd, 7.7, 7.7, 1.3)	7.19(ddd, 7.7, 7.7, 1.3)	7.15(ddd, 7.9, 7.5, 1.3)
H-bz7a	7.62(dd, 7.7, 1.5)	7.66(dd, 7.6, 1.4)	7.57(dd, 7.6, 1.4)	7.66(dd, 7.7, 1.4)	7.41(dd, 7.3, 1.5)	7.55(dd, 7.8, 1.3)	7.63(dd, 7.7, 1.5)	7.62(dd, 7.7, 1.4)	7.32(dd, 7.9, 1.4)
H1	—	—	—	—	—	—	—	—	—
H2	—	—	7.59(d, 7.5)	7.786(d, 7.7)	7.47(d, 7,5)	7.58(d, 7.5)	7.68(d, 7.5)	7.58(d, 8.1)	7.48(d, 8.1)
H3	7.54(d, 9.0)	7.34(d, 9.0)	7.406(dd, 8.2, 7.5)	7.40(dd, 7.7, 7.7)	7.37(dd, 7.7, 7.5)	7.40(dd, 8.2, 7.5)	7.41(dd, 8.2, 7.5)	6.73(d, 8.1)	6.71(d, 8.1)
H4	7.10(d, 9.0)	7.08(d, 9.0)	7.80(d, 8.2)	7.786(d, 7.7)	7.77(d, 7.7)	7.79(d, 8.2)	7.80(d, 8.2)	—	—
H5	7.68(dd, 8.3, 1.5)	7.68(dd, 8.1, 1.5)	7.91(dd, 8.3, 1.3)	7.90(dd, 7.3, 2.0)	7.89(dd, 8.0, 1.5)	7.90(dd, 8.0, 1.3)	7.90(dd, 7.9, 1.5)	8.36(dd, 8.3, 1.5)	8.36(dd, 8.3, 1.3)
H6	7.47(ddd, 8.3, 6.9, 1.5)	7.57(ddd, 8.1, 7.0, 1.3)	7.54(ddd, 8.3, 6.9, 1.3)	7.52(ddd, 7.3, 5.7, 2.4)	7.52(ddd, 8.0, 6.8, 1.2)	7.53(ddd, 8.0, 6.8, 1.2)	7.53(ddd, 7.9, 6.8, 1.2)	7.52(ddd, 8.3, 6.9, 1.2)	7.52(ddd, 8.3, 6.9, 1.3)
H7	7.41(ddd, 8.4, 6.9, 1.5)	7.48(ddd, 8.2, 7.0, 1.5)	7.60(ddd, 8.5, 6.9, 1.3)	7.55(ddd, 7.2, 5.7, 2.0)	7.57(ddd, 8.4, 6.8, 1.5)	7.59(ddd, 8.4, 6.8, 1.3)	7.57(ddd, 8.3, 6.8, 1.5)	7.58(ddd, 8.3, 6.9, 1.5)	7.60(ddd, 8.4, 6.9, 1.3)
H8	8.52(dd, 8.4, 1.5)	8.51(dd, 8.2, 1.3)	8.04(dd, 8.5, 1.3)	8.07(dd, 7.2, 2.4)	8.13(dd, 8.4, 1.2)	8.02(d, 8.4)	8.07(dd, 8.3, 1.2)	7.99(dd, 8.3, 1.2)	8.08(dd, 8.4, 1.3)
H1′	—	—	—	—	—	—	—	—	—
H2′	—	6.88(d, 2.0)	—	—	—	—	—	—	—
H3′	6.12(s)	—	7.56(dd, 8.2, 1.4)	6.71(s)	—	7.41(d, 8.9)	6.98(dd, 1.4, 1.4)	6.94(dd, 1.6, 1.6)	—
H4′	—	—	6.87(ddd, 8.2, 7.1, 1.1)	—	5.93(d, 2.4)	6.41(dd, 8.9, 2.6)	—	—	7.30(d, 8.2)
H5′	6.12(s)	6.85(dd, 8.2, 2.0)	7.409(ddd, 8.3, 7.1, 1.4)	—	—	—	7.03(d, 1.4)	7.02(d, 1.6)	7.29(dd, 8.2, 8.1)

(Continues)

Table 2. (Continued)

Position	10	11	12	13	14	15	16	17	18
H6′	—	6.79(d, 8.2)	7.10(dd, 8.3, 1.1)	6.57(s)	6.20(d, 2.4)	6.58(d, 2.6)	7.03(d, 1.4)	7.02(d, 1.6)	6.39(d, 8.1)
4-OCH_3	—	—	—	—	—	—	—	3.97(s)	3.97(s)
2′-OCH_3	3.67(br s)	—	—	—	—	—	—	—	—
3′-OCH_3	—	3.86(s)	—	—	3.83(s)	—	—	—	3.69(s)
4′-OCH_3	3.81(s)	3.73(s)	—	3.54(s)	—	—	3.63(s)	3.60(s)	—
5′-OCH_3	—	—	—	3.91(s)	3.63(s)	3.85(s)	—	—	—
6′-OCH_3	3.67(br s)	—	—	—	—	—	—	—	—
1-OH	16.79(s)	16.78(s)	—	—	—	—	—	—	—
1′-OH	—	—	14.54(s)	15.01(s)	16.81(s)	15.10(s)	14.07(s)	14.08(s)	15.74(s)
Position	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**
H-bz2	5.88(dd, 12.1, 4.3)	5.95(dd, 9.9, 4.9)	5.83(dd, 11.8, 4.2)	5.21(dd, 12.5, 4.6)	5.24(dd, 10.8, 5.0)	5.05(dd, 12.3, 4.6)	5.39(dd, 12.6, 4.2)	5.48(dd, 12.6, 4.4)	5.51(dd, 12.3, 4.7)
H-bz3a	3.24(dd, 13.0, 12.1)	3.16(dd, 13.2, 9.9)	3.20(dd, 13.1, 11.8)	3.21(dd, 13.1, 12.5)	3.19(dd, 13.3, 10.8)	3.03(dd, 13.1, 12.3)	3.04(dd, 12.6, 12.2)	3.07(dd, 12.6, 12.2)	3.09(dd, 13.2, 12.3)
H-bz3b	3.48(dd, 13.0, 4.3)	3.34(dd, 13.2, 4.9)	3.40(dd, 13.1, 4.2)	3.47(dd, 13.1, 4.6)	3.33(dd, 13.3, 5.0)	3.28(dd, 13.1, 4.6)	3.71(dd, 12.2, 4.2)	3.67(dd, 12.2, 4.4)	3.65(dd, 13.2, 4.7)
H-bz6a	7.34(dd, 7.9, 1.4)	7.28(dd, 7.7, 1.4)	7.30(dd, 7.8, 1.4)	7.33(dd, 7.9, 1.4)	7.30(dd, 7.9, 1.4)	7.18(dd, 7.9, 1.3)	7.28(dd, 7.9, 1.2)	7.31(dd, 7.9, 1.4)	7.39(dd, 7.8, 1.3)
H-bz6b	7.483ddd, 7.9, 7.6, 1.5)	7.45(ddd, 7.7, 7.7, 1.4)	7.45(ddd, 7.8, 7.5, 1.4)	7.49(ddd, 7.9, 7.6, 1.4)	7.47(ddd, 7.9, 7.6, 1.4)	7.37(ddd, 7.9, 7.8, 1.4)	7.43(ddd, 7.9, 7.6, 1.4)	7.49(ddd, 7.9, 7.7, 1.4)	7.59(ddd, 7.8, 7.6, 1.3)
H-bz7b	7.18(ddd, 7.9, 7.6, 1.4)	7.18(ddd, 7.7, 7.7, 1.4)	7.15(ddd, 7.5, 7.5, 1.4)	7.23(ddd, 7.7, 7.6, 1.4)	7.18(ddd, 7.7, 7.6, 1.4)	7.08(ddd, 7.8, 7.7, 1.3)	7.20(ddd, 7.7, 7.6 1.2)	7.22(ddd, 7.7, 7.5, 1.4)	7.29(ddd, 7.7, 7.6, 1.3)
H-bz7a	7.57(dd, 7.9, 1.5)	7.65(dd, 7.7, 1.4)	7.55(dd, 7.5, 1.4)	7.66(dd, 7.7, 1.4)	7.64(dd, 7.7, 1.4)	7.51(dd, 7.7, 1.4)	7.65(dd, 7.7, 1.4)	7.66(dd, 7.5, 1.4)	7.62(dd, 7.7, 1.3)
H1	—	—	—	7.70(d, 2.0)	7.72(d, 2.2)	7.57(d, 1.9)	7.68(d, 2.1)	7.69(d, 1.8)	7.85(d, 1.5)
H2	7.476(d, 8.1)	7.69(d, 8.1)	7.49(d, 8.1)	—	—	—	—	—	—
H3	6.72(d, 8.1)	6.72(d, 8.1)	6.72(d, 8.1)	7.45(dd, 8.6, 2.0)	7.469(dd, 8.4, 2.2)	7.32(dd, 8.7, 1.9)	7.42(dd, 8.5, 2.1)	7.43(dd, 8.5, 1.8)	7.48(dd, 8.6, 1.5)
H4	—	—	—	7.81(d, 8.6)	7.79(d, 8.4)	7.68(d, 8.7)	7.79(d, 8.5)	7.82(d, 8.5)	7.89(d, 8.6)
H5	8.37(dd, 8.3, 1.4)	8.35(dd, 8.0, 1.6)	8.35(dd, 8.2, 1.2)	7.79(dd, 8.7, 2.1)	7.76(dd, 9.2, 2.2)	7.67(d, 8.7)	7.78(d, 8.5)	7.82(d, 8.7)	7.84(d, 9.1)
H6	7.53(ddd, 8.3, 6.8, 1.4)	7.51(ddd, 8.0, 6.8, 1.2)	7.52(ddd, 8.2, 6.9, 1.1)	7.54(ddd, 8.7, 6.9, 2.1)	7.468(ddd, 9.2, 6.6, 2.2)	7.35(ddd 8.7, 6.8, 1.7)	7.47(ddd, 8.5, 6.8, 2.1)	7.50(ddd, 8.7, 6.9, 1.8)	7.51(ddd, 9.1, 7.7, 2.3)
H7	7.61(ddd, 8.4, 6.8 1.4)	7.56(ddd, 8.3, 6.8, 1.6)	7.60(ddd, 8.1, 6.9, 1.2)	7.47(ddd, 8.5, 6.8, 2.2)	7.45(ddd, 9.3, 6.6, 2.2)	7.33(ddd, 8.5, 6.8, 1.8)	7.47(ddd, 8.5, 6.8, 1.5)	7.48(ddd, 8.5, 6.9, 1.8)	7.51(ddd, 8.6, 7.7, 1.5)
H8	7.97(dd, 8.4, 1.4)	7.99(dd, 8.3, 1.2)	7.95(dd, 8.1, 1.1)	7.80(dd, 8.5, 2.2)	7.81(dd, 9.3, 2.2)	7.66(dd,8.5, 1.8)	7.80(d, 8.5)	7.84(d, 8.5)	7.89(d, 8.6)
H1′	—	—	—	—	—	—	—	—	—
H2′	—	—	—	—	—	—	—	—	—
H3′	7.54(dd, 8.2, 1.2)	6.65(s)	7.39(d, 8.9)	7.63(dd, 8.2, 1.5)	6.82(s)	7.39(d, 8.9)	—	—	7.30(d, 3.0)
H4′	6.85(ddd, 8.2, 7.0, 1.1)	—	6.40(dd, 8.9, 2.5)	6.91(ddd, 8.2, 7.3, 1.2)	—	6.34(dd, 8.9, 2.6)	5.97(d, 2.4)	6.70(dd, 8.3, 1.0)	—
H5′	7.40(ddd, 8.3, 7.0, 1.2)	—	—	7.41(ddd, 8.3, 7.3, 1.5)	—	—	—	7.30(dd, 8.3, 8.3)	7.11(dd, 9.0, 3.0)
H6′	7.09(dd, 8.3, 1.1)	6.55(s)	6.56(d, 2.5)	7.09(dd, 8.3, 1.2)	6.57(s)	6.41(d, 2.6)	6.19(d, 2.4)	6.43(dd, 8.3, 1.0)	6.96(d, 9.0)
4-OCH_3	3.98(s)	3.95(s)	3.98(s)	—	—	—	—	—	—
3′-OCH_3	—	—	—	—	—	—	3.87(s)	3.93(s)	—
4′-OCH_3	—	3.49(s)	—	—	3.60(s)	—	—	—	3.71(s)
5′-OCH_3	—	3.90(s)	3.84(s)	—	3.91(s)	3.72(s)	3.84(s)	—	—
1′-OH	14.55(s)	15.05(s)	15.15(s)	14.50(s)	14.96(s)	15.05(s)	16.72(s)	15.69(s)	13.75(s)

Table 3. ^{13}C NMR chemical shifts of benzothiazepines **1–27**, where bz denotes benzothiazepine

Position	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
C-bz2	52.7	52.3	59.1	55.4	55.5	52.6	55.5	52.4	52.6
C-bz3	35.3	36.3	36.8	36.7	37.0	35.5	36.6	36.1	36.0
C-bz4	172.2	172.1	171.5	171.5	171.4	172.1	171.5	172.0	172.1
C-bz6	146.4	146.6	146.3	146.3	146.1	146.3	146.3	146.4	146.4
C-bz6a	125.5	125.6	125.6	125.6	125.5	125.5	125.6	125.5	125.6
C-bz6b	130.0	130.2	130.3	130.3	130.2	129.9	130.4	130.1	130.1
C-bz7b	126.7	126.8	126.9	126.9	126.9	126.7	126.9	126.7	126.7
C-bz7a	135.7	135.7	135.6	135.5	135.6	135.7	135.5	135.6	135.4
C-bz7	126.3	125.8	125.8	125.8	125.7	125.6	125.7	125.9	126.4
C1	168.7	168.4	168.7	168.6	168.8	168.8	168.6	168.5	168.7
C2	110.3	110.3	110.1	110.1	110.1	110.3	110.1	110.3	110.3
C3	124.4	124.3	124.0	124.0	125.5	124.4	124.0	124.3	124.5
C4	117.0	119.0	117.2	118.6	117.1	116.9	117.2	117.1	117.0
C5	127.4	127.4	127.4	127.4	127.4	127.4	127.4	127.4	127.4
C6	129.7	129.7	129.8	129.8	129.8	129.7	129.8	129.7	129.7
C7	125.6	125.6	125.7	125.7	126.9	126.5	125.9	125.6	125.6
C8	125.1	125.0	125.1	125.0	125.1	125.1	125.0	125.0	125.0
C9	128.0	127.9	127.9	127.9	130.0	127.8	127.9	127.9	127.9
C10	136.9	136.9	136.8	136.8	136.8	136.9	136.8	136.8	136.9
C1′	131.6	137.3	143.7	145.2	136.0	124.3	145.8	129.3	123.0
C2′	155.5	144.9	128.3	112.2	127.5	156.6	104.6	149.9	149.7
C3′	110.6	152.7	129.1	160.0	114.3	98.7	161.2	142.0	97.4
C4′	129.1	111.9	126.4	117.2	159.5	160.7	99.9	153.5	149.4
C5′	121.0	124.6	129.1	130.1	114.3	104.5	161.2	107.5	143.2
C6′	127.2	117.2	128.3	113.5	127.5	128.0	104.6	121.5	111.7
2′-OCH_3	55.7	61.3	—	—	—	55.7	—	56.2	56.5
3′-OCH_3	—	56.0	—	59.0	—	—	59.2	61.0	—
4′-OCH_3	—	—	—	—	58.7	55.6	—	61.5	56.4
5′-OCH_3	—	—	—	—	—	—	59.2	—	56.7
6′-OCH_3	—	—	—	—	—	—	—	—	—
Position	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
C-bz2	48.6	56.0	54.6	54.7	53.4	54.3	54.9	55.0	54.0
C-bz3	33.1	36.9	35.2	36.0	39.7	35.1	35.7	35.8	40.3
C-bz4	172.4	171.5	173.7	172.3	172.9	172.8	173.3	173.3	173.8
C-bz6	144.9	146.2	149.1	149.1	147.6	149.1	149.3	149.2	148.2
C-bz6a	125.4	125.6	125.9	125.8	126.0	125.8	125.7	125.8	125.8
C-bz6b	129.6	130.3	130.2	130.1	130.0	130.1	130.2	130.0	129.9
C-bz7b	126.1	126.8	126.6	126.2	126.2	126.1	126.6	126.5	126.2
C-bz7a	135.4	135.4	135.6	135.4	135.6	135.5	135.5	135.5	135.6
C-bz7	128.4	126.2	125.0	124.5	125.7	125.0	125.0	125.2	125.3
C1	169.9	168.9	138.8	138.4	140.0	138.8	138.6	130.5	130.9
C2	112.6	110.2	123.4	125.3	123.0	123.4	123.9	123.3	123.1
C3	124.4	124.2	125.7	125.8	125.7	125.6	125.9	103.4	103.5
C4	116.5	117.1	128.7	128.7	128.2	128.6	128.7	155.5	155.2
C5	127.3	127.4	129.5	129.6	129.3	129.4	129.5	124.2	123.2
C6	128.9	129.8	126.2	126.1	126.1	126.2	126.2	125.5	126.1
C7	125.3	125.7	127.0	126.9	126.6	126.9	126.9	127.4	127.1
C8	125.1	125.1	122.5	122.0	122.8	122.5	122.3	122.1	122.6
C9	129.2	128.0	129.9	129.9	129.9	129.9	129.9	130.8	132.0
C10	136.9	136.8	134.2	134.1	134.2	134.2	134.2	126.1	126.1
C1′	110.0	136.0	163.1	160.6	168.6	164.3	157.2	157.2	160.6
C2′	161.0	109.8	118.6	110.3	103.9	112.2	118.2	118.3	110.2
C3′	90.8	149.1	128.6	110.1	161.9	129.9	112.1	112.2	164.6
C4′	161.0	149.3	118.8	141.9	90.7	107.2	152.0	151.9	101.0
C5′	90.8	111.2	133.9	154.7	164.5	165.0	121.3	121.2	133.4
C6′	161.0	118.5	119.0	101.7	94.9	102.0	119.6	119.5	111.7
4-OCH_3	—	—	—	—	—	—	—	55.9	55.8
2′-OCH_3	55.6	—	—	—	—	—	—	—	—
3′-OCH_3	—	59.2	—	—	55.7	—	—	—	55.7
4′-OCH_3	55.6	56.2	—	56.5	—	—	56.0	55.7	—
5′-OCH_3	—	—	—	56.2	55.6	55.6	—	—	—
6′-OCH_3	55.6	—	—	—	—	—	—	—	—
Position	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**
C-bz2	54.7	54.8	54.4	60.4	60.2	59.8	59.8	60.3	59.3
C-bz3	35.2	36.2	35.2	36.8	37.0	36.5	41.5	42.1	36.1
C-bz4	173.7	172.5	172.9	173.3	172.1	172.2	172.6	173.5	174.0
C-bz6	149.0	149.0	149.0	149.0	149.0	148.6	147.5	148.1	149.7

(Continues)

Table 3. (Continued)

Position	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**
C-bz6a	125.8	125.7	125.7	125.9	125.8	125.5	125.8	125.7	125.5
C-bz6b	130.0	130.0	130.0	130.2	130.2	129.9	130.0	130.0	130.5
C-bz7b	126.5	126.1	126.1	126.6	126.2	126.1	126.1	126.2	126.7
C-bz7a	135.5	135.4	135.5	135.4	135.3	135.1	135.4	135.4	135.1
C-bz7	125.2	125.6	125.3	124.4	124.9	124.3	126.2	124.6	123.5
C1	130.8	130.1	130.8	124.5	125.0	124.2	124.3	126.0	124.3
C2	123.7	123.4	123.7	141.1	140.6	140.8	142.3	142.2	140.9
C3	103.3	103.5	103.3	124.6	124.7	124.2	124.6	124.3	124.7
C4	155.5	155.5	155.5	129.2	129.1	129.7	129.0	129.0	128.5
C5	123.3	124.8	123.3	127.9	127.9	127.8	128.1	127.9	127.9
C6	125.5	125.4	125.4	126.7	126.7	126.4	126.5	126.6	126.5
C7	127.4	127.3	127.4	126.4	126.5	126.1	126.2	126.4	126.2
C8	122.3	121.9	122.3	128.2	128.1	128.8	127.9	128.1	127.6
C9	130.8	130.9	130.9	133.3	133.3	133.0	133.4	133.4	132.7
C10	126.1	126.1	126.1	133.2	133.2	132.8	133.0	133.0	132.5
C1′	163.0	160.6	165.8	163.0	160.7	164.0	168.4	160.6	155.8
C2′	118.6	110.2	112.2	118.5	110.0	117.8	104.0	110.1	118.0
C3′	128.6	110.4	129.9	128.6	111.3	127.6	161.9	164.5	113.2
C4′	118.8	141.9	107.1	118.8	141.9	106.9	90.7	101.0	151.6
C5′	133.8	154.6	164.3	133.9	154.9	165.3	164.5	133.5	121.1
C6′	118.9	101.6	102.0	118.9	101.7	101.7	94.8	111.8	118.5
4-OCH_3	55.7	55.7	55.7	—	—	—	—	—	—
3′-OCH_3	—	—	—	—	—	—	55.8	55.9	—
4′-OCH_3	—	56.4	—	—	57.0	—	—	—	55.6
5′-OCH_3	—	56.2	55.6	—	56.2	55.4	55.6	—	—

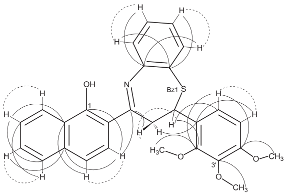


Figure 2. Important correlations obtained from the COSY (dotted lines) and HMBC (solid lines) spectra of derivative **8**.

benzothiazepines (**12–27**) are more shielded than those of 4-naphthalenyl-benzothiazepines (**1–11**). On the contrary, in the cases of C-bz4 and C-bz6, the carbon chemical shifts of 2-naphthalenyl-benzothiazepines (**12–27**) are more deshielded than those of 4-naphthalenyl-benzothiazepines (**1–11**). For H-bz3a, the proton chemical shifts of 2-naphthalenyl-benzothiazepines (**12–27**) are more deshielded than those of 4-naphthalenyl-benzothiazepines (**1–11**). These results can be used as a reference for identifying new benzothiazepine derivatives in the future.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's website.