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# Constituents of *Gastrodia elata* and Their Neuroprotective Effects in HT22 Hippocampal Neuronal, R28 Retinal Cells, and BV2 Microglial Cells

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**List of Supporting Information**

**S1.** $^{1}$H and $^{13}$C NMR spectral data of compounds **4–19**.

4-[[4-(ethoxymethyl)phenoxy]methyl]phenol (**4**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 7.26 (2H, d, $J$ = 8.0 Hz, H-2, H-6), 7.26 (2H, d, $J$ = 8.0 Hz, H-2′, H-6′), 6.92 (2H, d, $J$ = 8.0 Hz, H-3′, H-5′), 6.76 (2H, d, $J$ = 8.0 Hz, H-3, H-5), 4.93 (2H, s, $H_2$-7), 4.44 (2H, s, $H_2$-7′), 3.53 (2H, q, $J$ = 7.0 Hz, $\underline{CH_2}CH_3$), 1.23 (3H, t, $J$ = 7.0 Hz, $CH_2\underline{CH_3}$);; $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 129.0 (C-1), 129.7 (C-2, 6), 115.6 (C-3, C-5), 155.9 (C-4), 70.0 (C-7), 130.8 (C-1′), 129.6 (C-2′, C-6′), 115.0 (C-3′, C-5′), 158.6 (C-4′), 72.6 (C-7′), 65.7 ($\underline{CH_2}CH_3$), 15.3 ($CH_2\underline{CH_3}$).

Gastrol A (**5**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, $CD_3COCD_3$) $\delta$ : 7.34 (2H, d, $J$ = 8.5 Hz, H-2″, 6″), 7.31 (2H, d, $J$ = 8.5 Hz, H-2, H-6), 7.23 (2H, d, $J$ = 8.5 Hz, H-2′, H-6′), 7.01 (2H, d, $J$ = 8.5 Hz, H-3, H-5), 6.89 (2H, d, $J$ = 8.5 Hz, H-3″, H-5″), 6.85 (2H, d, $J$ = 8.5 Hz, H-3′, H-5′), 5.03 (2H, s, $H_2$-7″), 4.48 (2H, s, $H_2$-7), 4.46 (2H, s, $H_2$-7′); $^{13}$C NMR (125 MHz, $CD_3COCD_3$) $\delta$ : 132.0 (C-1), 130.2 (C-2, C-6), 115.5 (C-3, C-5), 159.5 (C-4), 72.0 (C-7), 130.6 (C-1′), 130.4 (C-2′, C-6′), 115.9 (C-3′, C-5′), 157.8 (C-4′), 72.3 (C-7′), 129.2 (C-1″), 130.4 (C-2″, C-6″), 116.1 (C-3″, 5″), 158.2 (C-4″), 70.5 (C-7″).

Bis(4-hydroxyphenyl)methane (**6**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 6.96 (4H, d, $J$ = 8.5 Hz, H-2, H-6, H-2′, H-6′), 6.68 (4H, d, $J$ = 8.5 Hz, H-3, H-5, H-3′, H-5′), 3.74 (2H, s, $H_2$-7); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 134.4 (C-1, C-1′), 130.9 (C-2, C-6, C-2′, C-6′), 116.2 (C-3, C-5, C-3′, C-5′), 156.6 (C-4, C-4′), 41.3 (C-7).

4-Hydroxybenzyl vanillyl ether (**7**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 7.17 (2H, d, $J$ = 8.5 Hz, H-2, H-6), 6.91 (1H, d, $J$ = 1.5 Hz, H-2′), 6.77 (1H, dd, $J$ = 8.0, 1.5 Hz, H-6′), 6.77 (1H, d, $J$ = 8.0 Hz, H-5′), 6.76 (2H, d, $J$ = 8.5 Hz, H-3, H-5), 4.41 (2H, s, $H_2$-7′), 4.41 (2H, s, $H_2$-7), 3.84 (3H, s, 3′-$OCH_3$); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 131.2 (C-1), 131.1 (C-2, 6), 116.3 (C-3, 5), 158.5 (C-4), 72.9 (C-7), 130.5 (C-1′), 113.2 (C-2′), 149.2 (C-3′), 147.6 (C-4′), 116.1 (C-5′), 122.5 (C-6′), 73.1 (C-7′), 56.6 (3′-$OCH_3$).

Bis(4-hydroxybenzyl)ether (**8**) exhibited following data: colorless oil; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 7.16 (4H, d, $J$ = 8.5 Hz, H-2, H-6, H-2′, H-6′), 6.76 (4H, d, $J$ = 8.5 Hz, H-3, H-5, H-3′, H-5′), 4.40 (4H, s, $H_2$-7, $H_2$-7′); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 130.5 (C-1, C-1′), 131.1 (C-2, C-6, C-2′, C-6′), 116.3 (C-3, C-5, C-3′, C-5′), 158.7 (C-4, C-4′), 72.9 (C-7, C-7′).

2,4-Bis(4-hydroxybenzyl)phenol (**9**) exhibited following data: brownish amorphous powder; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 6.99 (2H, d, $J$ = 8.5 Hz, H-2′, H-6′), 6.92 (2H, d, $J$ = 8.5 Hz, H-2″, H-6″), 6.80 (1H, d, $J$ = 2.0 Hz, H-2), 6.78 (1H, dd, $J$ = 8.0, 2.0 Hz, H-5), 6.66 (1H, d, $J$ = 8.0 Hz, H-6), 6.66 (2H, d, $J$ = 8.5 Hz, H-3′, H-5′), 6.66 (2H, d, $J$ = 8.5 Hz, H-3″, H-5″), 3.78 (2H, s, $H_2$-7′), 3.69 (2H, s, $H_2$-7″); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 154.4 (C-1), 133.9 (C-2), 132.1 (C-3), 134.6 (C-4), 128.4 (C-5), 116.1 (C-6), 129.7 (C-1′), 131.0 (C-2′, C-6′), 116.2 (C-3′, C-5′), 156.4 (C-4′), 35.9 (C-7′), 134.3 (C-1″), 130.8 (C-2″, C-6″), 116.1 (C-3″, C-5″), 156.5 (C-4″), 41.4 (C-7″).

Gastrodigenin (**10**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 7.16 (2H, d, $J$ = 8.5 Hz, H-2, H-6), 6.76 (2H, d, $J$ = 8.5 Hz, H-3, H-5), 4.39 (2H, s, $H_2$-7); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 130.4 (C-1), 131.1 (C-2, C-6), 116.3 (C-3, C-5), 158.5 (C-4), 72.8 (C-7).

4-Hydroxybenzyl ethyl ether (**11**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, $CDCl_3$) $\delta$ : 7.10 (2H, d, $J$ = 8.0 Hz, H-2, H-6), 6.72 (2H, d, $J$ = 8.0 Hz, H-3, H-5), 4.42 (2H, s, $H_2$-7), 3.53 (2H, q, $J$ = 7.0 Hz, $\underline{CH_2}CH_3$), 1.22 (3H, t, $J$ = 7.0 Hz, $CH_2\underline{CH_3}$); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ : 130.2 (C-1), 129.9 (C-2, C-6), 115.5 (C-3, C-5), 155.7 (C-4), 72.7 (C-7), 65.7 ($\underline{CH_2}CH_3$), 15.3 ($CH_2\underline{CH_3}$).

Gastrodin (**12**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 7.28 (2H, d, $J$ = 8.5 Hz, H-2, H-6), 7.08 (2H, d, $J$ = 8.5 Hz, H-3, H-5), 4.89 (1H, d, $J$ = 7.5 Hz, Glc H-1), 4.54 (2H, s, $H_2$-7), 3.89 (1H, dd, $J$ = 12.0, 2.0 Hz, Glc $H_2$-6a), 3.70 (1H, dd, $J$ = 12.0, 5.0 Hz, Glc $H_2$-6b), 3.46-3.37 (4H, Glc H-2, H-3, H-4, H-5); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 136.8 (C-1), 129.6 (C-2, C-6), 117.8 (C-3, C-5), 158.7 (C-4), 65.0 (C-7), 102.6 (Glc C-1), 75.1 (Glc C-2), 78.3 (Glc C-3), 71.6 (Glc C-4), 78.2 (Glc C-5), 62.7 (Glc C-6).

4-Hydroxybenzaldehyde (**13**) exhibited following data: brownish amorphous powder; $^{1}$H NMR (500 MHz, $CD_3OD$) $\delta$ : 9.76 (1H, s, C$\underline{H}$O) 6.96 (2H, d, $J$ = 8.5 Hz, H-2, H-6), 6.68 (2H, d, $J$ = 8.5 Hz, H-3, H-5); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 130.4 (C-1), 133.6 (C-2, C-6), 117.1 (C-3, C-5), 165.5 (C-4), 193.0 ($\underline{C}$HO).

3,5-Dimethoxybenzoic acid-4-*O*-$\beta$-D-glucopyranoside (**14**) exhibited following data: white amorphous powder; $^{1}$H NMR (500 MHz, DMSO-$d_6$) $\delta$ : 7.22 (2H, s, H-2, H-6), 5.11 (1H, d, $J$ = 7.0 Hz,

Glc H-1), 3.59-3.06 (6H, Glc H-2, H-3, H-4, H-5, $H_2$-6), 3.80 (6H, s, 3-$OCH_3$, 5-$OCH_3$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ : 136.0 (C-1), 116.9 (C-2, C-6), 161.9 (C-3, C-5), 147.6 (C-4), 176.8 (COOH), 111.6 (Glc C-1), 83.9 (Glc C-2), 87.1 (Glc C-3), 79.6 (Glc C-4), 86.3 (Glc C-5), 70.5 (Glc C-6), 66.0 (3-$OCH_3$, 5-$OCH_3$).

Parishin E (**15**) exhibited following data: yellowish oil; $^1$H NMR (500 MHz, $CD_3OD$) $\delta$ : 7.31 (2H, d, $J$ = 8.5 Hz, H-2′, H-6′), 7.08 (2H, d, $J$ = 8.5 Hz, H-3′, H-5′), 5.06 (2H, d, $J$ = 2.5 Hz, $H_2$-7′), 4.91 (1H, d, $J$ = 7.5 Hz, Glc H-1), 3.89 (1H, dd, $J$ = 12.0, 2.0 Hz, Glc $H_2$-6a), 3.70 (1H, dd, $J$ = 12.0, 5.5 Hz, Glc $H_2$-6b), 3.47-3.30 (4H, Glc, H-2, H-3, H-4, H-5), 2.96 (1H, d, $J$ = 15.5 Hz, $H_2$-3a), 2.92 (1H, d, $J$ = 16.0 Hz, $H_2$-1a), 2.85 (1H, d, $J$ = 15.5 Hz, $H_2$-3b), 2.79 (1H, d, $J$ = 16.0 Hz, $H_2$-1b); $^{13}$C NMR (125 MHz, $CD_3OD$) $\delta$ : 44.2 (C-1), 75.1 (C-2), 44.5 (C-3), 131.4 (C-1′), 131.0 (C-2′, C-6′), 117.9 (C-3′, C-5′), 159.2 (C-4′), 67.4 (C-7′), 102.4 (Glc C-1), 75.1 (Glc C-2), 78.3 (Glc C-3), 71.6 (Glc C-4), 78.2 (Glc C-5), 62.7 (Glc C-6), 171.5 (COOR), 173.9 (COOH), 177.1 (COOH).

Adenosine (**16**) exhibited following data: white amorphous powder; $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ : 8.35 (1H, s, H-8), 8.14 (1H, s, H-2), 7.37 (2H, br s, $NH_2$), 5.88 (1H, d, $J$ = 6.0 Hz, H-1′), 5.46 (1H, br d, $J$ = 6.0 Hz, 2′-OH), 5.45 (1H, br dd, $J$ = 7.5, 4.5 Hz, 5′-OH), 5.20 (1H, br d, $J$ = 4.5 Hz, 3′-OH), 4.61 (1H, ddd, $J$ = 6.0, 6.0, 5.0 Hz, H-2′), 4.14 (1H, ddd, $J$ = 5.0, 4.5, 3.0 Hz, H-3′), 3.96 (1H, ddd, $J$ = 3.5, 3.5, 3.0 Hz, H-4′), 3.67 (1H, ddd, $J$ = 12.0, 4.5, 3.5 Hz, $H_2$-5′a), 3.55 (1H, ddd, $J$ = 12.0, 7.5, 3.5 Hz, $H_2$-5′b); $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ : 152.3 (C-2), 149.0 (C-4), 119.3 (C-5), 156.1 (C-6), 139.9 (C-8), 87.9 (C-1′), 73.4 (C-2′), 70.6 (C-3′), 85.8 (C-4′), 61.6 (C-5′).

*S*-(4-Hydroxybenzyl) glutathione (**17**) exhibited following data: white amorphous powder; $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ : 7.09 (2H, d, $J$ = 8.5 Hz, H-2‴, H-6‴), 6.69 (2H, d, $J$ = 8.5 Hz, H-3‴, H-5‴), 4.50 (1H, dd, $J$ = 9.0, 5.0 Hz, H-2′), 3.71 (1H, d, $J$ = 2.5 Hz, $H_2$-2″a), 3.63 (1H, d, $J$ = 2.5 Hz, $H_2$-2″b), 3.63 (2H, s, $H_2$-7‴), 3.40 (1H, t, $J$ = 6.5 Hz, H-2), 2.78 (1H, dd, $J$ = 14.0, 5.0 Hz, $H_2$-3′a), 2.55 (1H, dd, $J$ = 14.0, 9.0 Hz, $H_2$-3′b), 2.32 (2H, m, $H_2$-4), 1.93 (1H, br dt, $J$ = 6.5, 6.5 Hz, H-3); $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ : 171.7 (C-1), 53.1 (C-2), 26.8 (C-3), 31.5 (C-4), 170.9 (C-5), 170.7 (C-1′), 52.2 (C-2′), 33.0 (C-3′), 170.6 (C-1″), 41.2 (C-2″), 128.1 (C-1‴), 129.9 (C-2‴, C-6‴), 115.1 (C-3‴, C-5‴), 156.3 (C-4‴), 34.8 (C-7‴).

Palmitic acid ethyl ester (**18**) exhibited following data: yellowish waxy-like; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ : 4.10 (2H, q, $J$ = 7.0 Hz, $CH_2CH_3$), 2.26 (2H, t, $J$ = 7.5 Hz, $H_2$-2), 1.60 (2H, m, $H_2$-3), 1.28-1.22 (24H, br m, $H_2$-4, $H_2$-5, $H_2$-6, $H_2$-7, $H_2$-8, $H_2$-9, $H_2$-10, $H_2$-11, $H_2$-12, $H_2$-13, $H_2$-14, $H_2$-15) 1.23 (3H, t, $J$ = 7.0 Hz, $CH_2CH_3$), 0.86 (3H, t, $J$ = 7.0 Hz, $H_3$-16); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ : 174.2 (C-1), 34.6 (C-2), 25.2 (C-3), 29.4 (C-4), 29.6 (C-5), 30.0, 30.0, 29.9, 29.9, 29.9, 29.8, 29.7 (C-6, C-7, C-8, C-9, C-10, C-11, C-12), 29.5 (C-13), 32.2 (C-14), 22.9 (C-15), 14.3 (C-16), 60.4 ($CH_2CH_3$), 14.5 ($CH_2CH_3$).

Linoleic acid ethyl ester (**19**) exhibited following data: colorless oil; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ : 5.33 (4H, m, H-9, H-10, H-12, H-13), 4.13 (2H, q, $J$ = 7.0 Hz, $CH_2CH_3$), 2.75 (2H, t, $J$ = 6.5 Hz, $H_2$-11), 2.26 (2H, t, $J$ = 7.5 Hz, $H_2$-2), 2.02 (4H, br dt, $J$ = 7.0, 7.0 Hz, $H_2$-8, $H_2$-14), 1.60 (2H, br m, H-3), 1.36-1-29 (14H, br m, $H_2$-4, $H_2$-5, $H_2$-6, $H_2$-7, $H_2$-15, $H_2$-16, $H_2$-17), 1.23 (3H, t, $J$ = 7.0 Hz, $CH_2CH_3$), 0.87 (3H, t, $J$ = 7.0 Hz, $H_3$-18); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ : 174.1 (C-1), 34.6 (C-2), 31.7 (C-3), 29.8, 29.6, 29.4, 29.3, 29.3, 25.2, 22.8 (C-4, C-5, C-6, C-7, C-15, C-16, C-17), 27.4 (C-8), 128.1 (C-9), 130.4 (C-10), 25.8 (C-11), 130.3 (C-12), 128.2 (C-13), 27.4 (C-14), 14.3 (C-18), 60.4 ($CH_2CH_3$), 14.5 ($CH_2CH_3$).

143 **Table S1.** Screening of all isolated compounds for protective effects against HT22 cell death caused
144 by glutamate-induced toxicity.

| Compound | Concentration (μM) | Cell viability (%) | Compound | Concentration (μM) | Cell viability (%) |
|---|---|---|---|---|---|
| | 5.6 | 38.27 ± 5.96 | | 5.6 | 22.14 ± 2.82 |
| **1** | 16.6 | 33.62 ± 3.90 | **2** | 16.6 | 22.88 ± 3.46 |
| | 50.0 | 71.48 ± 6.68 | | 50.0 | 72.26 ± 7.41 |
| | 5.6 | 37.94 ± 3.77 | | 5.6 | 120.02 ± 2.41 |
| **3** | 16.6 | 51.75 ± 3.28 | **4** | 16.6 | 95.83 ± 14.01 |
| | 50.0 | 25.20 ± 2.20 | | 50.0 | 53.17 ± 0.12 |
| | 5.6 | 110.34 ± 2.78 | | 5.6 | 22.51 ± 1.90 |
| **5** | 16.6 | 110.34 ± 2.71 | **6** | 16.6 | 25.71 ± 2.71 |
| | 50.0 | 98.02 ± 0.78 | | 50.0 | 26.28 ± 9.32 |
| | 5.6 | 24.33 ± 4.86 | | 5.6 | 32.68 ± 1.32 |
| **7** | 16.6 | 32.69 ± 2.03 | **8** | 16.6 | 32.47 ± 3.60 |
| | 50.0 | 85.61 ± 10.78 | | 50.0 | 100.35 ± 1.49 |
| | 5.6 | 31.79 ± 9.05 | | 5.6 | 22.72 ± 1.82 |
| **9** | 16.6 | 20.67 ± 4.07 | **10** | 16.6 | 19.13 ± 3.92 |
| | 50.0 | 17.37 ± 2.18 | | 50.0 | 23.79 ± 0.19 |
| | 5.6 | 30.78 ± 4.96 | | 5.6 | 32.42 ± 1.45 |
| **11** | 16.6 | 27.67 ± 9.04 | **12** | 16.6 | 28.60 ± 2.89 |
| | 50.0 | 24.90 ± 3.26 | | 50.0 | 23.07 ± 1.12 |
| | 5.6 | 21.75 ± 8.62 | | 5.6 | 22.86 ± 10.6 |
| **13** | 16.6 | 20.21 ± 0.72 | **14** | 16.6 | 24.10 ± 3.53 |
| | 50.0 | 20.07 ± 0.43 | | 50.0 | 20.16 ± 1.47 |
| | 5.6 | 34.32 ± 3.65 | | 5.6 | 37.70 ± 0.96 |
| **15** | 16.6 | 33.15 ± 3.21 | **16** | 16.6 | 59.00 ± 6.08 |
| | 50.0 | 23.59 ± 0.90 | | 50.0 | 76.25 ± 5.31 |
| | 5.6 | 33.95 ± 6.46 | | 5.6 | 45.92 ± 3.18 |
| **17** | 16.6 | 54.24 ± 18.69 | **18** | 16.6 | 57.65 ± 4.64 |
| | 50.0 | 27.75 ± 1.21 | | 50.0 | 50.30 ± 6.46 |
| | 5.6 | 30.32 ± 6.53 | **DMSO** | - | 100.00 ± 2.00 |
| **19** | 16.6 | 31.50 ± 6.60 | **Glu** | 5 mM | 44.62 ± 2.00 |
| | 50.0 | 19.65 ± 1.92 | **NAC** | 1 mM | 102.40 ± 0.95 |

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146 **Table S2.** Screening of all isolated compounds (50 μM) for protective effects on R28 cell death
147 caused by $H_2O_2$ induced toxicity.
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| No | Cell viability (%) | No | Cell viability (%) | No | Cell viability (%) |
|---|---|---|---|---|---|
| **1** | 7.99 ± 0.13 | **2** | 79.88 ± 0.59 | **3** | 53.47 ± 3.14 |
| **4** | 31.60 ± 3.47 | **5** | 55.27 ± 0.18 | **6** | 76.13 ± 0.04 |
| **7** | 82.66 ± 2.49 | **8** | 40.88 ± 4.19 | **9** | 19.75 ± 9.86 |
| **10** | 53.07 ± 2.87 | **11** | 49.41 ± 9.92 | **12** | 52.01 ± 2.52 |
| **13** | 54.10 ± 1.33 | **14** | 53.99 ± 6.32 | **15** | 55.90 ± 2.22 |
| **16** | 58.30 ± 3.37 | **17** | 57.64 ± 4.14 | **18** | 54.49 ± 5.13 |
| **19** | 12.91 ± 4.62 | **DMSO** | 100.00 ± 3.22 | **Glu (5 mM)** | 50.77 ± 0.02 |
| **NAC (1 mM)** | 96.70 ± 0.95 | | | | |

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**Table S3.** Screening of all isolated compounds for inhibitory effects of nitric oxide production on LPS treated BV2 cell lines.

| Compound | Concentration (μM) | Litrite (μM) | Compound | Concentration (μM) | Litrite[a] (μM) |
|---|---|---|---|---|---|
| **1** | 0.2 | 27.91 ± 3.09 | **2** | 0.2 | 30.80 ± 0.33 |
| | 1.8 | 27.52 ± 1.66 | | 1.8 | 25.88 ± 0.22 |
| | 16.6 | 29.47 ± 2.21 | | 16.6 | 27.91 ± 0.44 |
| | 50.0 | 25.17 ± 3.65 | | 50.0 | 28.77 ± 0.11 |
| **3** | 0.2 | 28.84 ± 0.66 | **4** | 0.2 | 28.30 ± 1.21 |
| | 1.8 | 27.13 ± 0.66 | | 1.8 | 27.91 ± 0.88 |
| | 16.6 | 26.73 ± 0.99 | | 16.6 | 23.53 ± 0.00 |
| | 50.0 | 25.48 ± 0.77 | | 50.0 | 20.09 ± 1.10 |
| **5** | 0.2 | 26.34 ± 1.55 | **6** | 0.2 | 29.86 ± 0.99 |
| | 1.8 | 25.88 ± 2.65 | | 1.8 | 23.77 ± 0.11 |
| | 16.6 | 25.56 ± 0.66 | | 16.6 | 25.95 ± 0.11 |
| | 50.0 | 23.38 ± 1.10 | | 50.0 | 30.02 ± 0.11 |
| **7** | 0.2 | 28.92 ± 0.77 | **8** | 0.2 | 28.76 ± 1.21 |
| | 1.8 | 25.41 ± 1.33 | | 1.8 | 27.36 ± 0.11 |
| | 16.6 | 26.97 ± 0.44 | | 16.6 | 27.67 ± 0.33 |
| | 50.0 | 26.03 ± 1.10 | | 50.0 | 28.06 ± 1.99 |
| **9** | 0.2 | 27.52 ± 0.33 | **10** | 0.2 | 27.91 ± 1.32 |
| | 1.8 | 29.08 ± 0.33 | | 1.8 | 25.95 ± 1.43 |
| | 16.6 | 27.98 ± 2.10 | | 16.6 | 26.97 ± 0.22 |
| | 50.0 | 9.94 ± 2.78 | | 50.0 | 27.36 ± 3.87 |
| **11** | 0.2 | 29.16 ± 1.33 | **12** | 0.2 | 27.83 ± 0.77 |
| | 1.8 | 22.98 ± 0.11 | | 1.8 | 27.20 ± 1.44 |
| | 16.6 | 23.92 ± 0.99 | | 16.6 | 26.66 ± 0.88 |
| | 50.0 | 26.11 ± 1.44 | | 50.0 | 25.95 ± 0.99 |
| **13** | 0.2 | 30.64 ± 0.55 | **14** | 0.2 | 27.44 ± 0.44 |
| | 1.8 | 22.59 ± 0.22 | | 1.8 | 24.55 ± 1.88 |
| | 16.6 | 22.83 ± 0.11 | | 16.6 | 23.84 ± 1.10 |
| | 50.0 | 26.81 ± 0.00 | | 50.0 | 23.22 ± 0.22 |
| **15** | 0.2 | 27.98 ± 0.77 | **16** | 0.2 | 29.47 ± 2.21 |
| | 1.8 | 27.83 ± 0.55 | | 1.8 | 26.73 ± 0.77 |
| | 16.6 | 24.39 ± 1.21 | | 16.6 | 25.95 ± 2.10 |
| | 50.0 | 26.81 ± 0.88 | | 50.0 | 24.47 ± 1.77 |
| **17** | 0.2 | 32.20 ± 0.11 | **18** | 0.2 | 32.13 ± 2.65 |
| | 1.8 | 29.10 ± 2.65 | | 1.8 | 27.91 ± 1.10 |
| | 16.6 | 26.11 ± 2.32 | | 16.6 | 26.19 ± 0.66 |
| | 50.0 | 25.56 ± 1.77 | | 50.0 | 26.03 ± 0.88 |
| **19** | 0.2 | 34.16 ± 1.44 | **DMSO** | - | 2.91 ± 0.22 |
| | 1.8 | 29.08 ± 2.54 | | | |
| | 16.6 | 26.97 ± 2.65 | **LPS** | 1 μg/ml | 32.43 ± 0.44 |
| | 50.0 | 25.95 ± 1.44 | | | |

[1] Secreted nitric oxide levels were determined by Griess reagent. [2] 1 μg/mL of LPS was used in NO production and cell viability assay. The % values are representative relative cell viabilities compared with DMSO treated cell growth (negative control, 100% value)

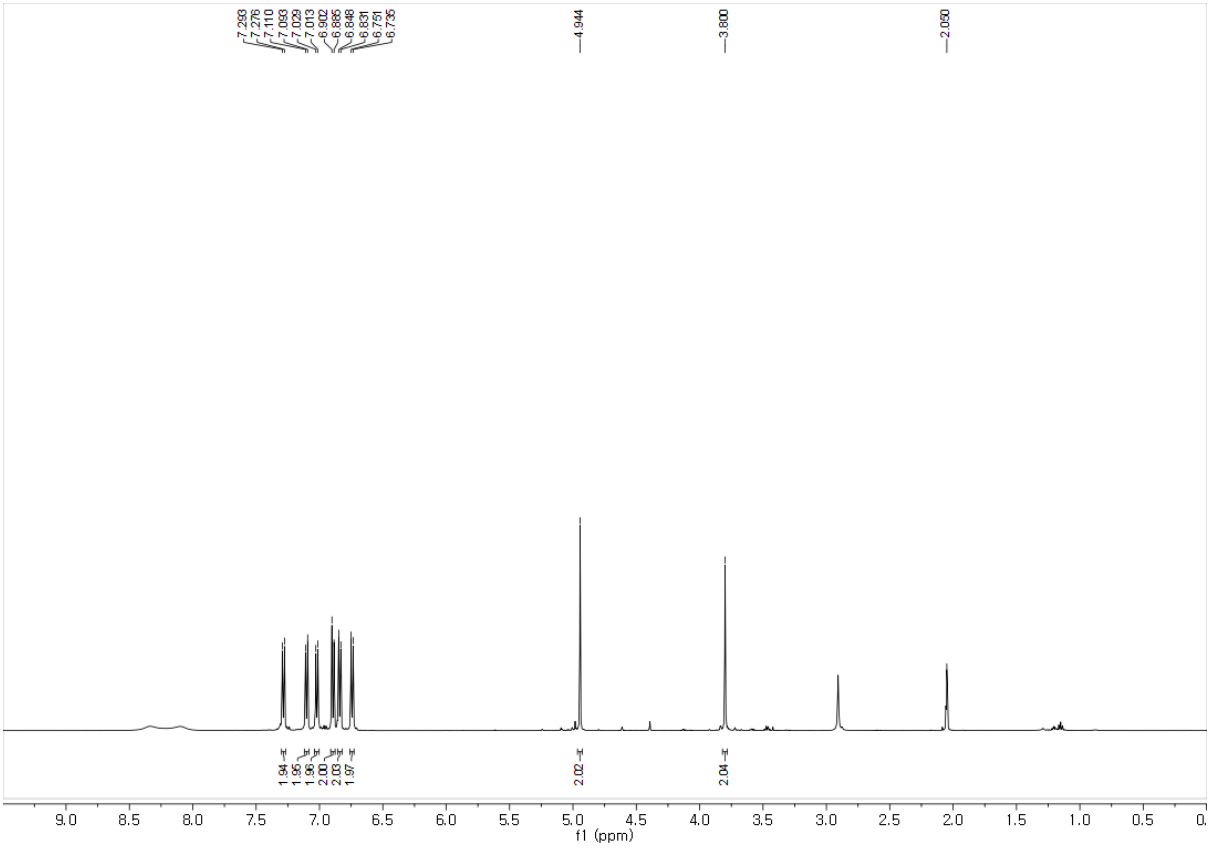



**Figure S1.** The $^{1}H$ NMR spectrum of compound **1** (500 MHz, $CD_3COCD_3$).

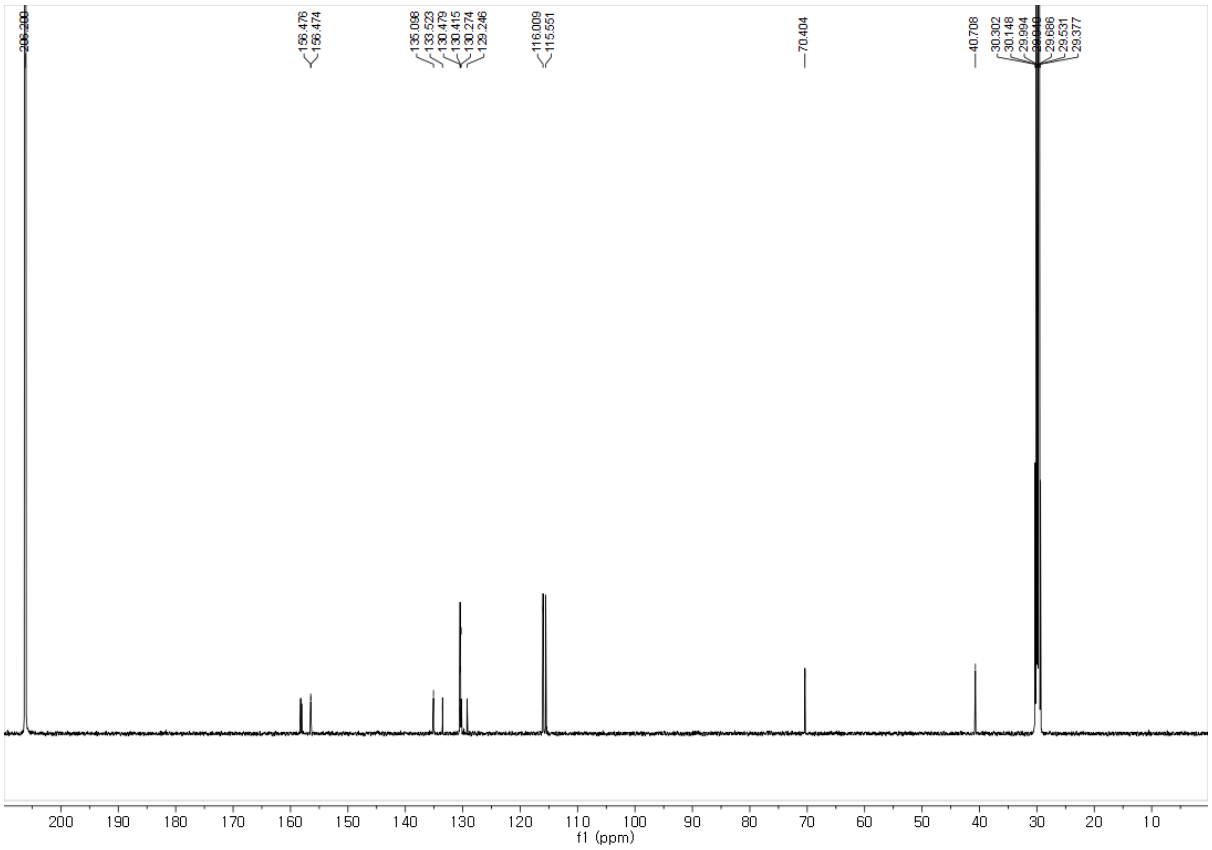



**Figure S2.** The $^{13}C$ NMR spectrum of compound 1 (125 MHz, $CD_3COCD_3$).

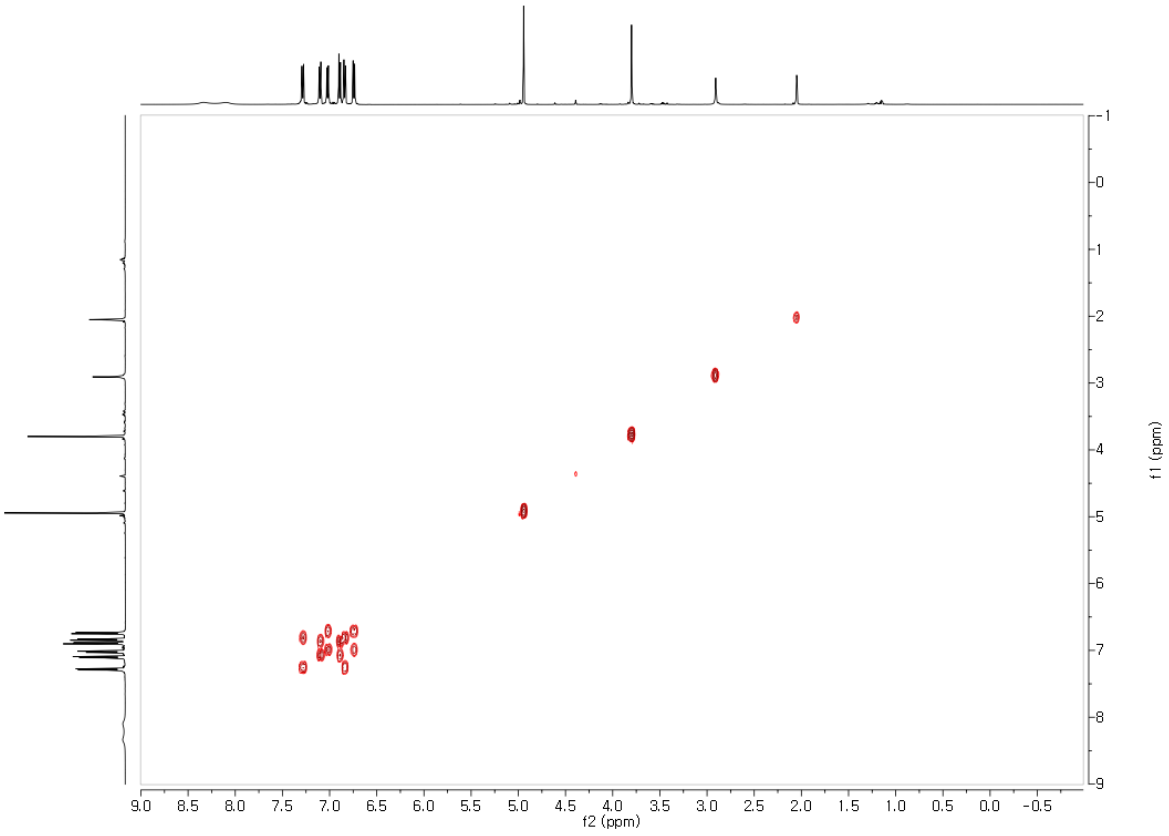



**Figure S3.** The $^{1}H$-$^{1}H$ COSY NMR spectrum of compound **1** (500 MHz, $CD_3COCD_3$).

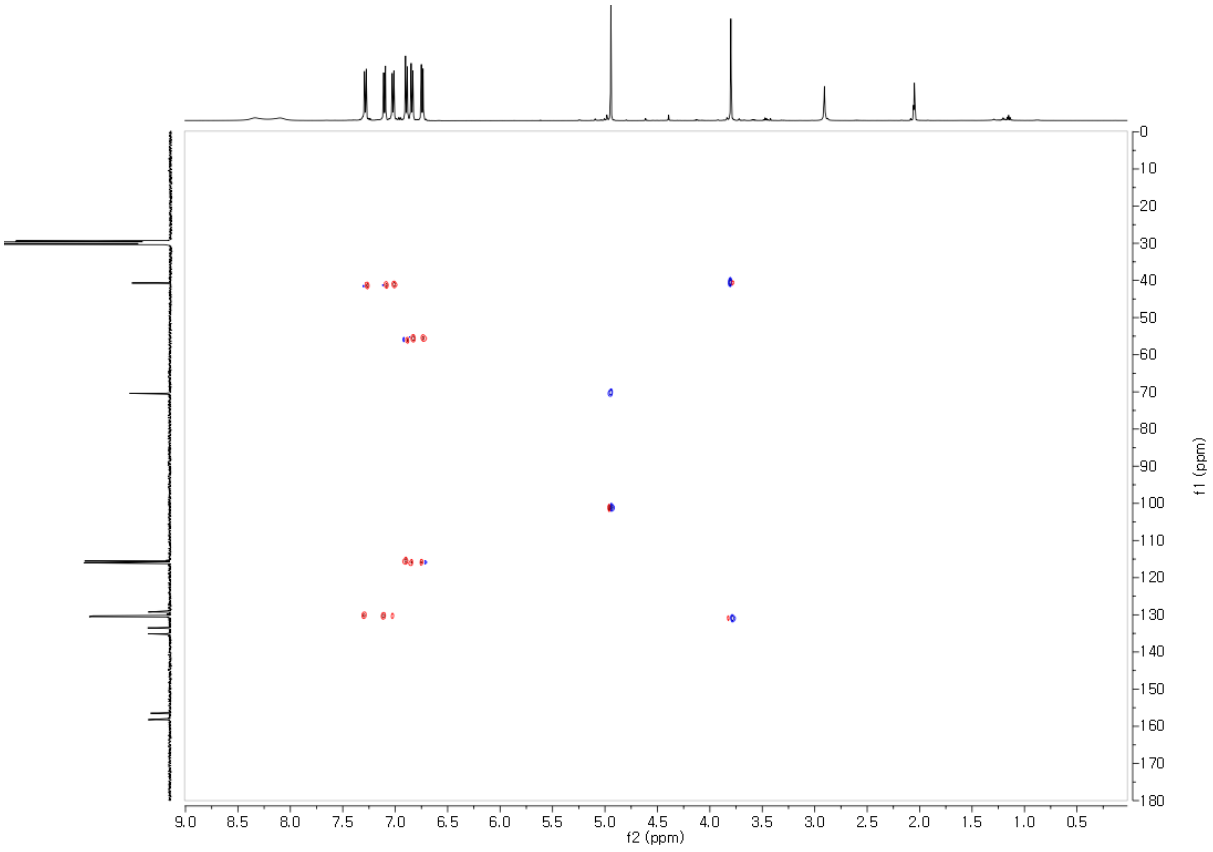



**Figure S4.** The HSQC NMR spectrum of compound **1** (500 MHz, $CD_3COCD_3$).

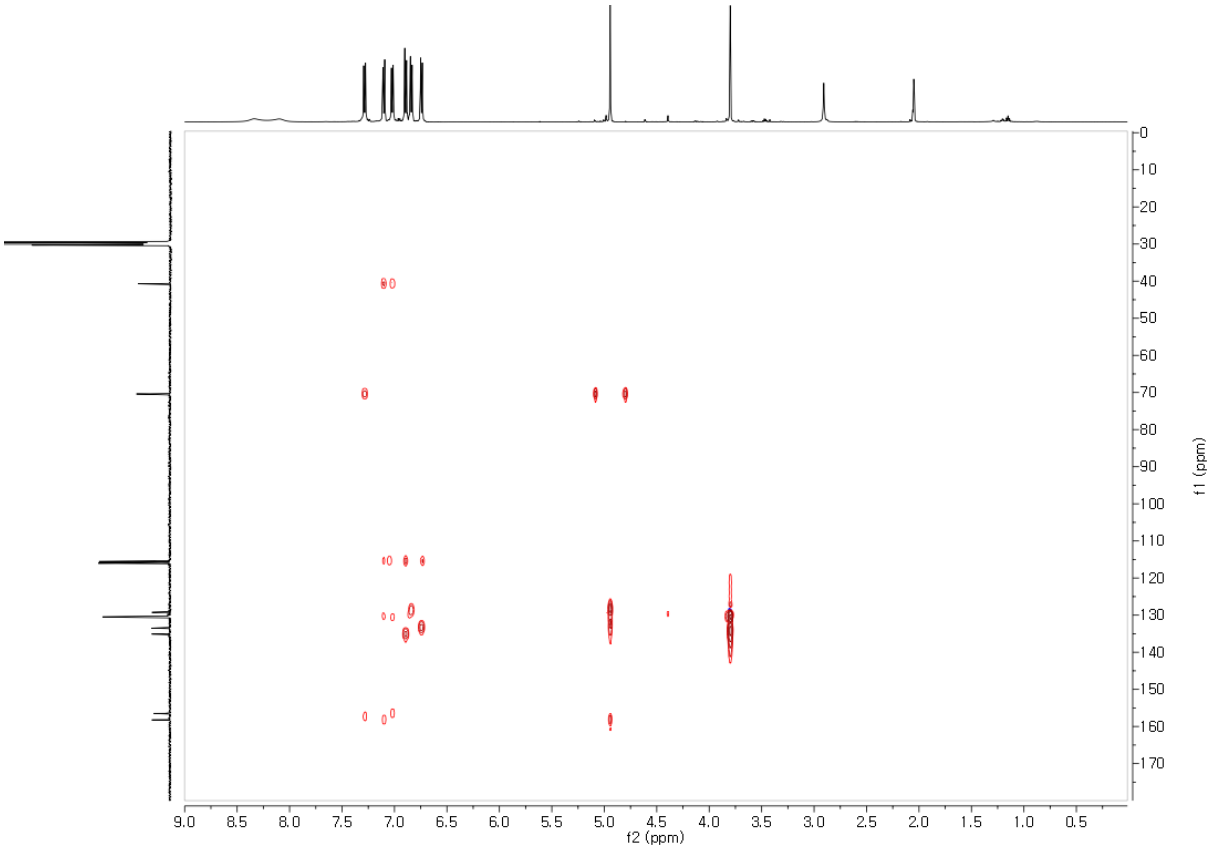



**Figure S5.** The HMBC NMR spectrum of compound **1** (500 MHz, $CD_3COCD_3$).

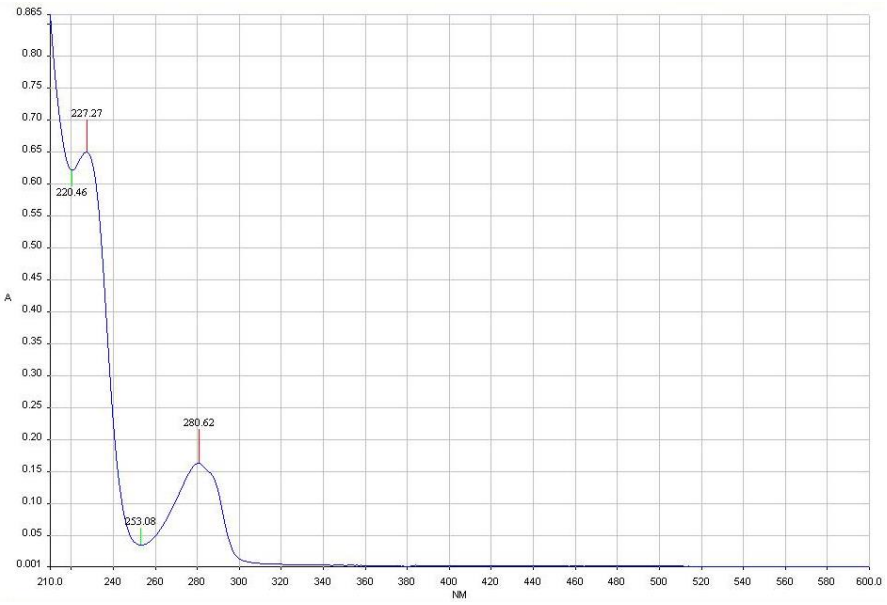
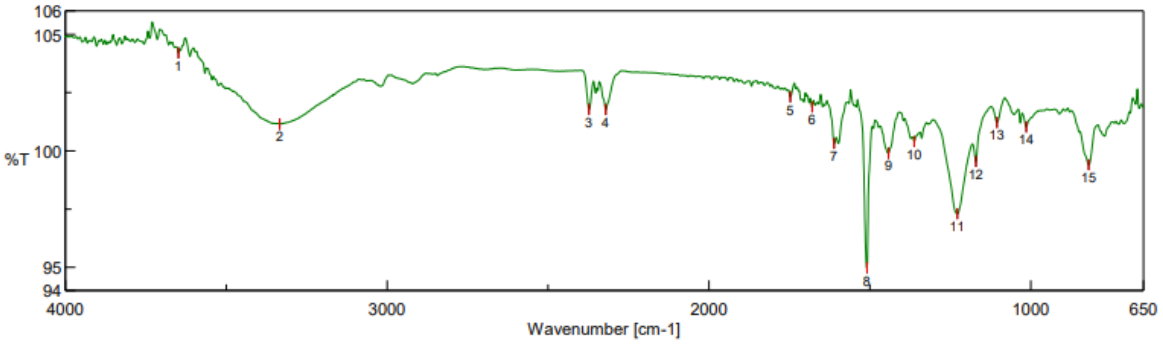



**Figure S6.** The UV spectrum of compound 1 ($CH_3OH$, c=1.6 × $10^{-5}$ M).




[ Result of Peak Picking ]

| No. | Position | Intensity | No. | Position | Intensity | No. | Position | Intensity |
|---|---|---|---|---|---|---|---|---|
| 1 | 3648.66 | 104.195 | 2 | 3334.32 | 101.142 | 3 | 2372.98 | 101.777 |
| 4 | 2320.91 | 101.772 | 5 | 1747.19 | 102.315 | 6 | 1679.69 | 101.887 |
| 7 | 1611.23 | 100.316 | 8 | 1509.03 | 94.9727 | 9 | 1442.49 | 99.8964 |
| 10 | 1362.46 | 100.389 | 11 | 1228.43 | 97.2937 | 12 | 1170.58 | 99.5382 |
| 13 | 1105.01 | 101.215 | 14 | 1014.37 | 101.023 | 15 | 820.563 | 99.4001 |

**Figure S7.** The IR spectrum of compound **1** [using the attenuated total reflection (ATR) sampling technique].

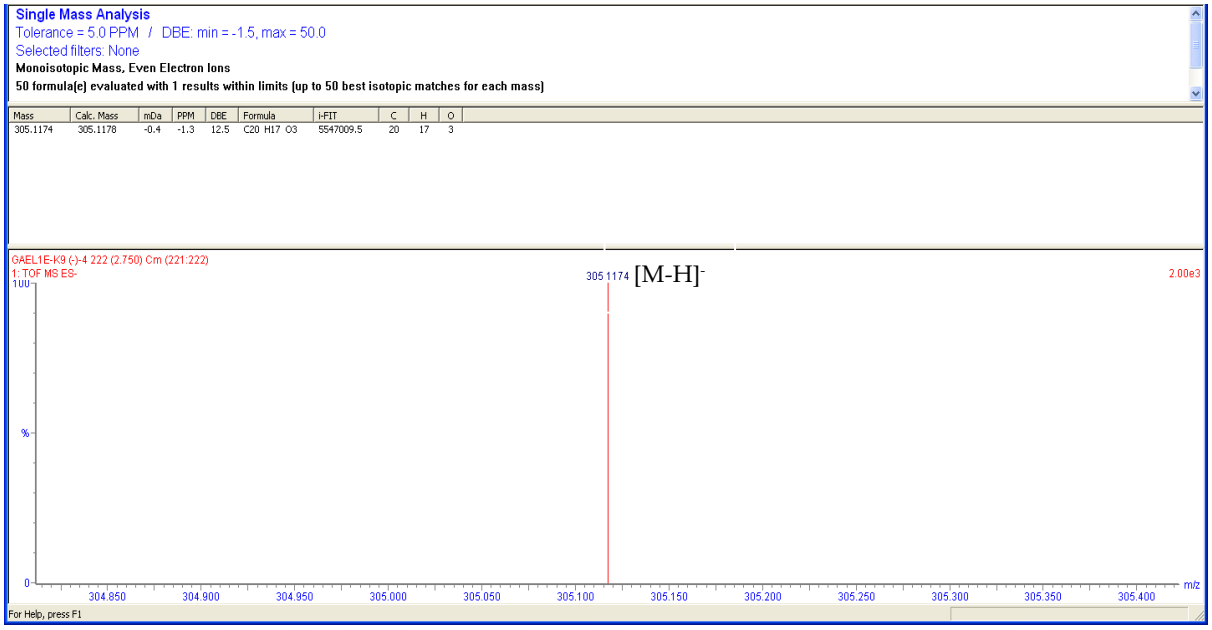



**Figure S8.** The HRESIMS spectrum of compound **1** (*m*/*z* 305.1174 [M – H]⁻; calcd for $C_{20}H_{17}O_3$, 305.1178).

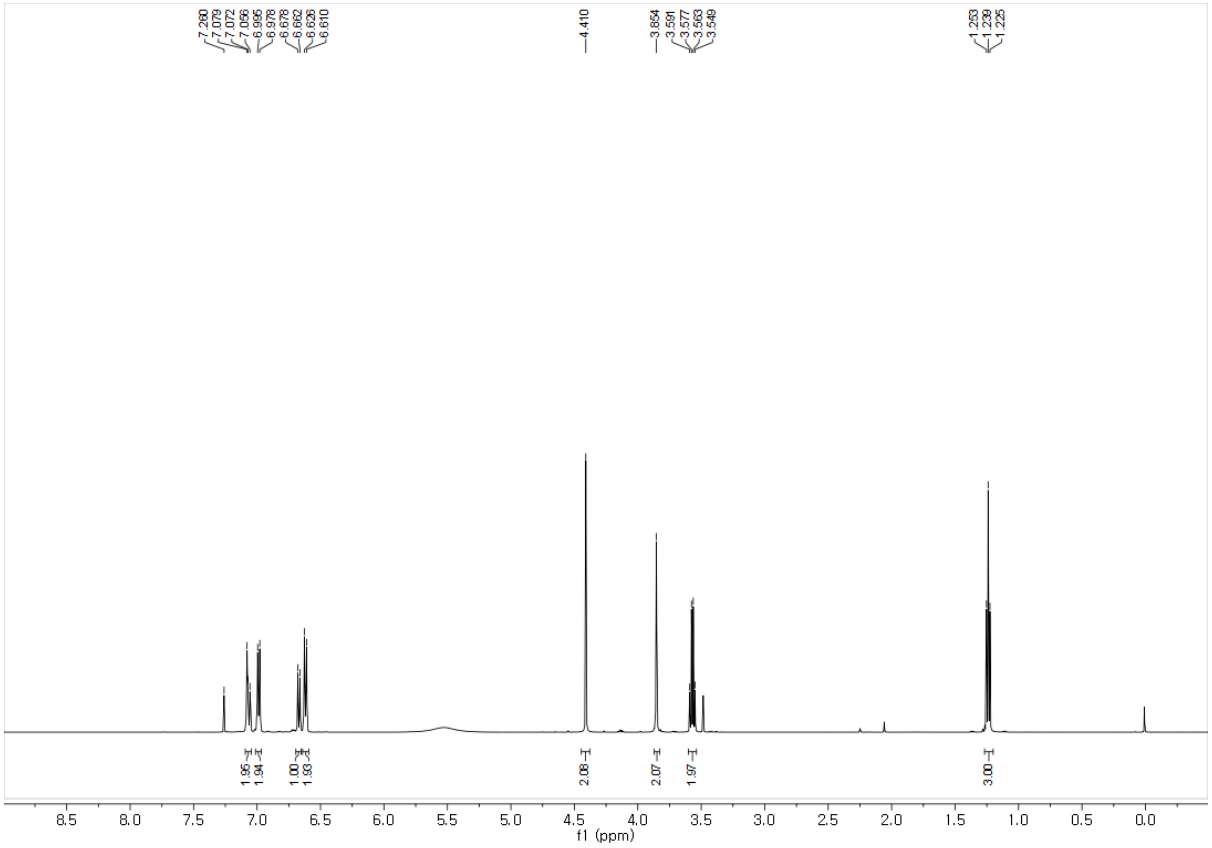



**Figure S9.** The $^{1}H$ NMR spectrum of compound **2** (500 MHz, $CDCl_3$).

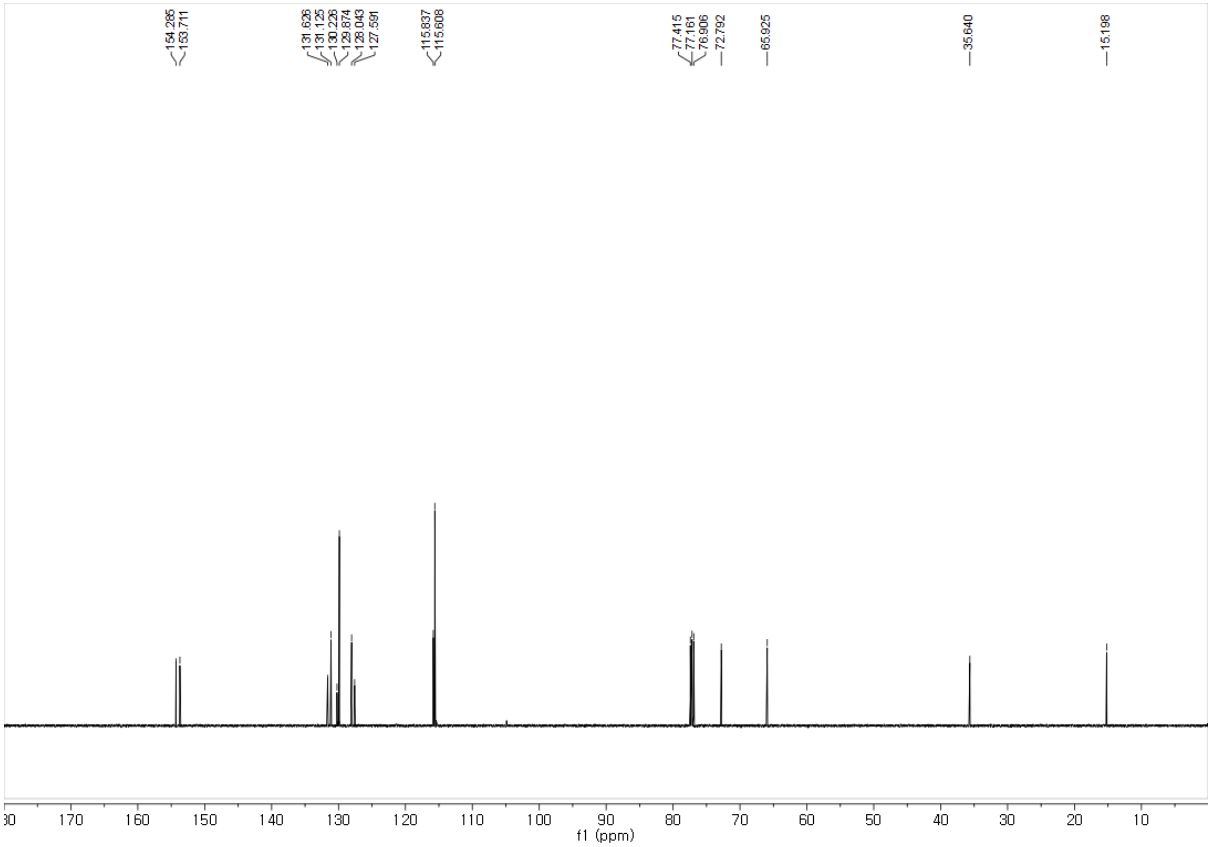
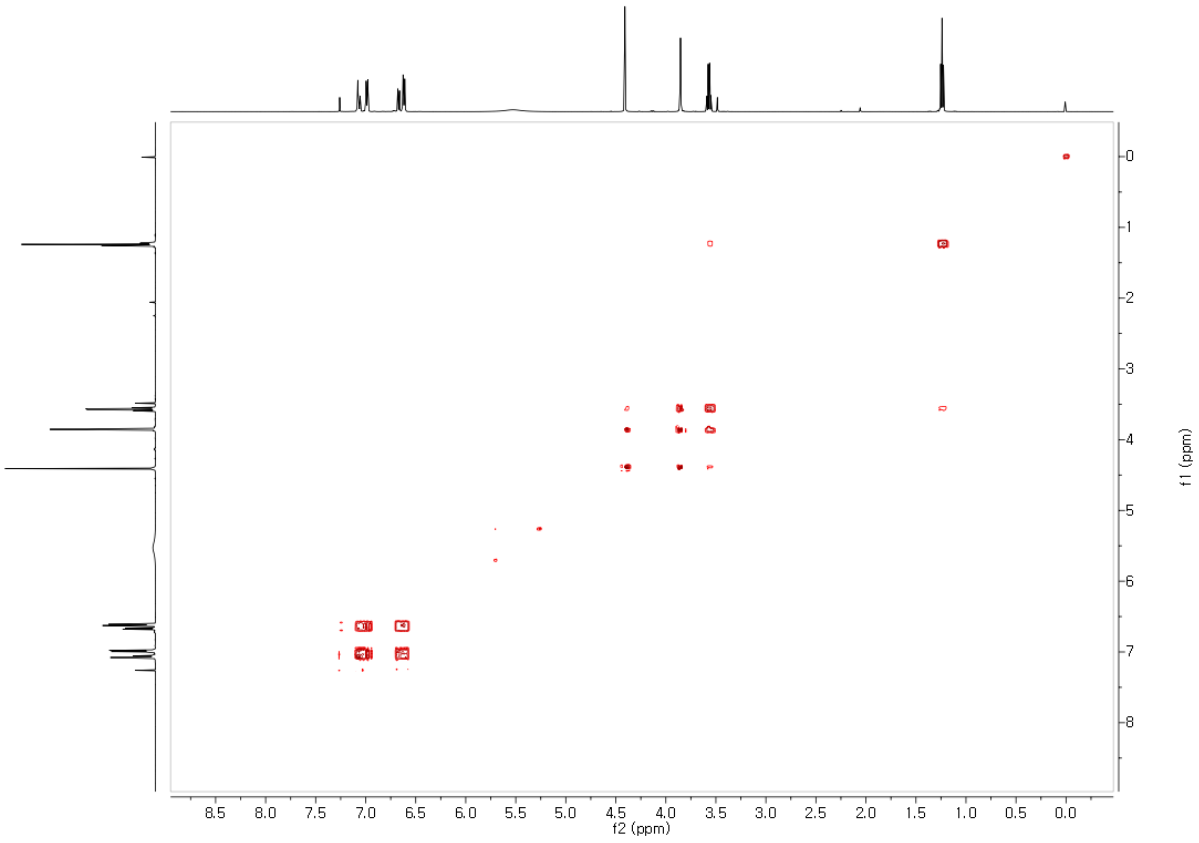



**Figure 10.** The $^{13}C$ NMR spectrum of compound **2** (125 MHz, $CDCl_3$).




188

189 **Figure S11.** The $^{1}H$-$^{1}H$ COSY NMR spectrum of compound **2** (500 MHz, $CDCl_3$).

190

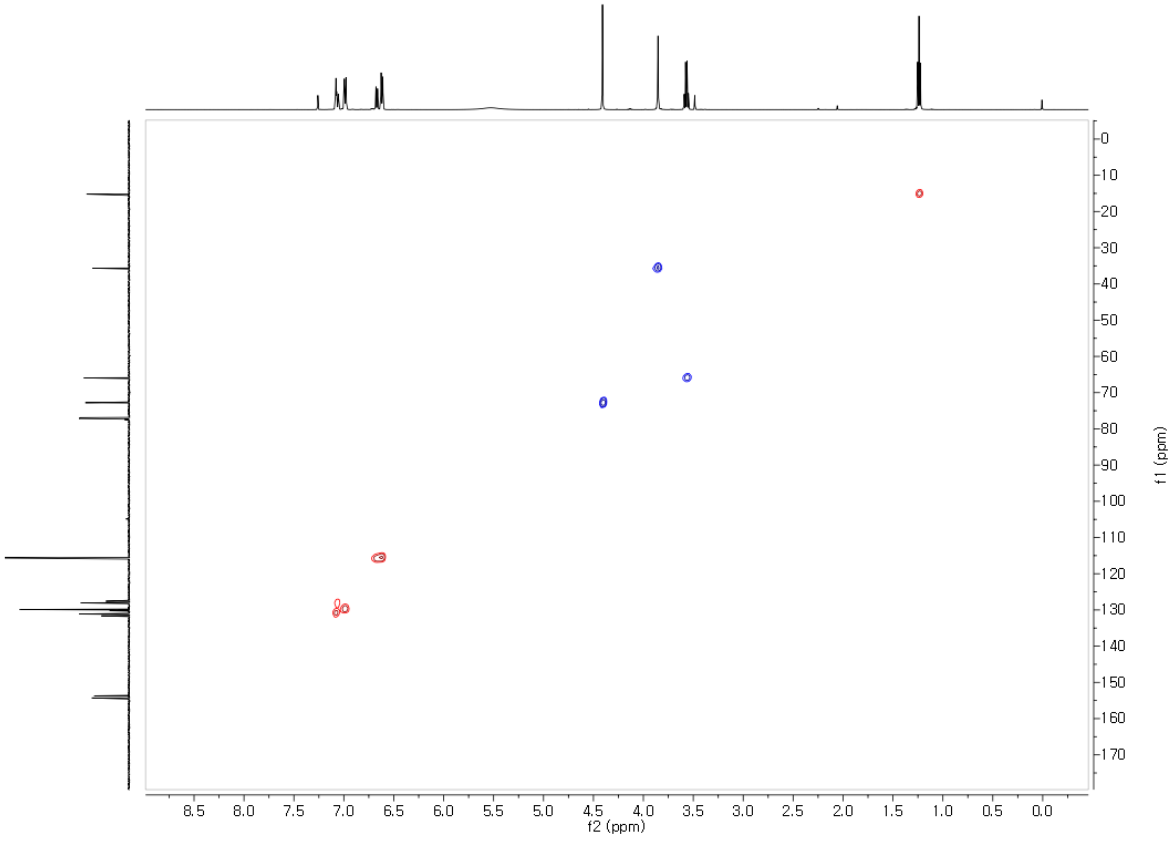
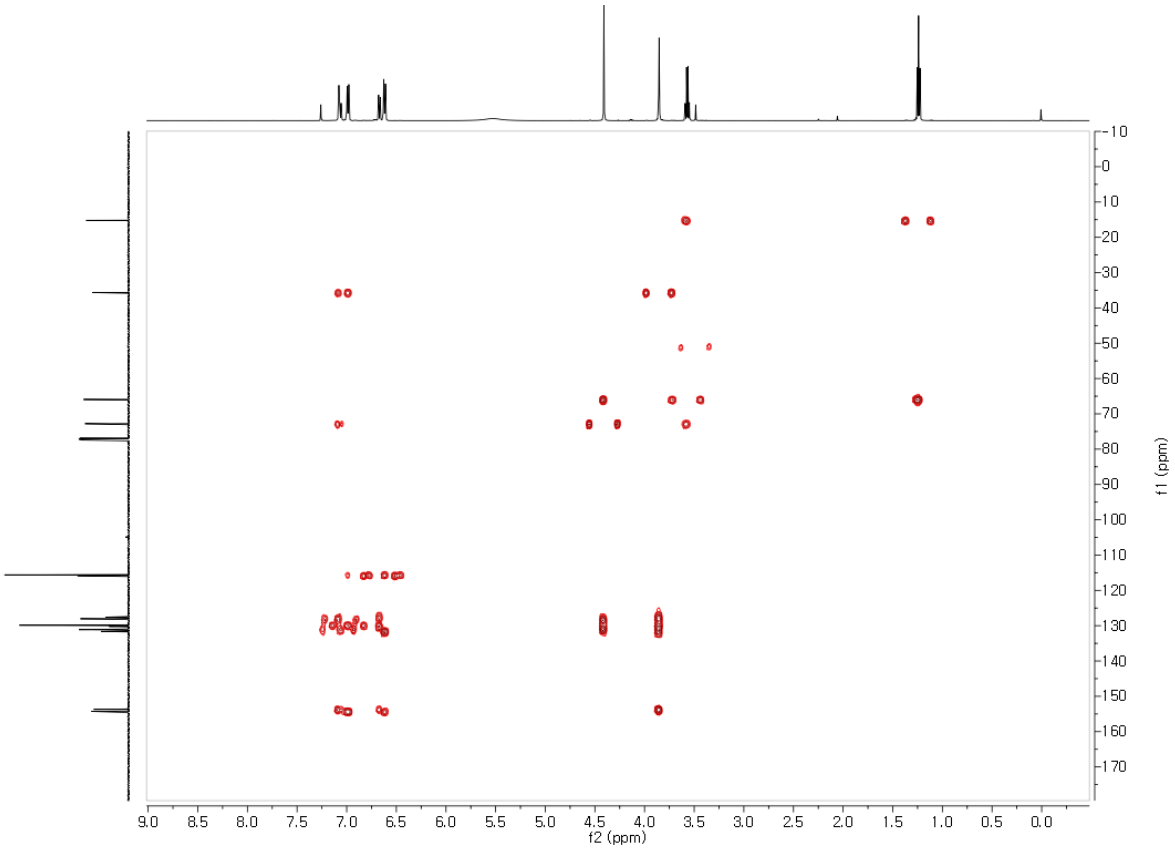


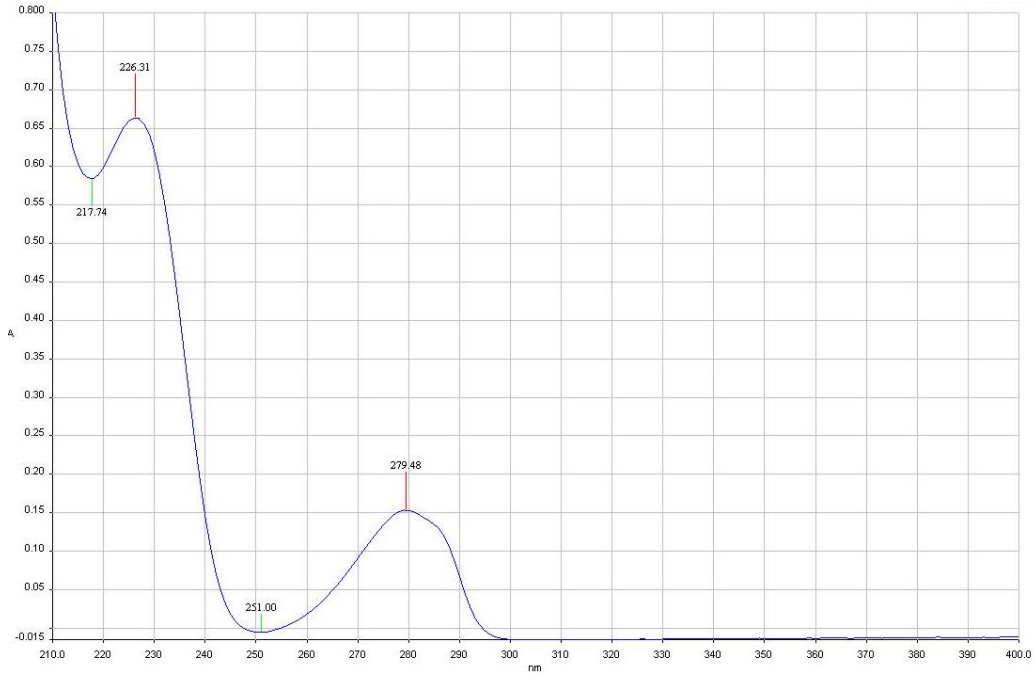

**Figure S12.** The HSQC NMR spectrum of compound **2** (500 MHz, $CDCl_3$).




194

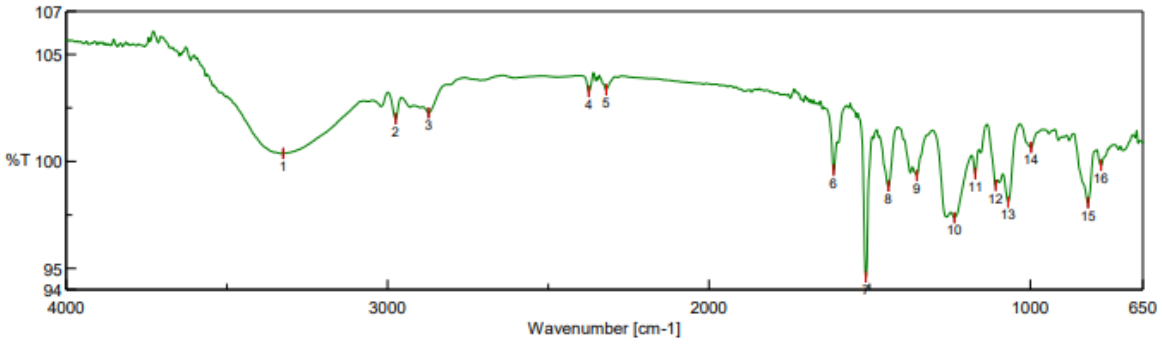
195 **Figure S13.** The HMBC NMR spectrum of compound **2** (500 MHz, $CDCl_3$).

196




197

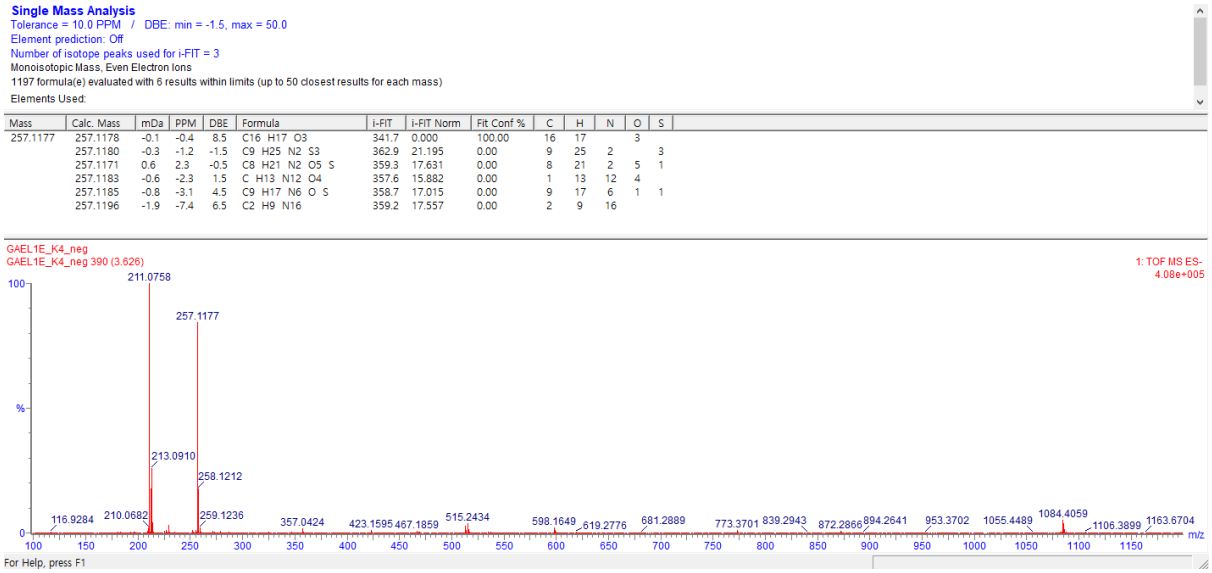
198 **Figure S14.** The UV spectrum of compound **2** ($CH_3OH$, c=1.9 × $10^{-5}$ M).




[ Result of Peak Picking ]

| No. | Position | Intensity | No. | Position | Intensity | No. | Position | Intensity |
|---|---|---|---|---|---|---|---|---|
| 1 | 3324.68 | 100.355 | 2 | 2974.66 | 101.982 | 3 | 2872.45 | 102.262 |
| 4 | 2373.94 | 103.259 | 5 | 2319.95 | 103.336 | 6 | 1612.2 | 99.5903 |
| 7 | 1511.92 | 94.5818 | 8 | 1441.53 | 98.8363 | 9 | 1352.82 | 99.3367 |
| 10 | 1236.15 | 97.3676 | 11 | 1171.54 | 99.4209 | 12 | 1107.9 | 98.8775 |
| 13 | 1069.33 | 98.0915 | 14 | 997.982 | 100.653 | 15 | 820.563 | 98.0665 |
| 16 | 780.065 | 99.8064 | | | | | | |

**Figure S15.** The IR spectrum of compound **2** [using the attenuated total reflection (ATR) sampling technique].



**Single Mass Analysis**
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
1197 formula(e) evaluated with 6 results within limits (up to 50 closest results for each mass)
Elements Used:

| Mass | Calc. Mass | mDa | PPM | DBE | Formula | i-FIT | i-FIT Norm | Fit Conf % | C | H | N | O | S |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 257.1177 | 257.1178 | -0.1 | -0.4 | 8.5 | C16 H17 O3 | 341.7 | 0.000 | 100.00 | 16 | 17 | | 3 | |
| | 257.1180 | -0.3 | -1.2 | -1.5 | C9 H25 N2 S3 | 362.9 | 21.195 | 0.00 | 9 | 25 | 2 | | 3 |
| | 257.1171 | 0.6 | 2.3 | -0.5 | C8 H21 N2 O5 S | 359.3 | 17.631 | 0.00 | 8 | 21 | 2 | 5 | 1 |
| | 257.1183 | -0.6 | -2.3 | 1.5 | C H13 N12 O4 | 357.6 | 15.882 | 0.00 | 1 | 13 | 12 | 4 | |
| | 257.1185 | -0.8 | -3.1 | 4.5 | C9 H17 N6 O S | 358.7 | 17.015 | 0.00 | 9 | 17 | 6 | 1 | 1 |
| | 257.1196 | -1.9 | -7.4 | 6.5 | C2 H9 N16 | 359.2 | 17.557 | 0.00 | 2 | 9 | 16 | | |



**Figure S16.** The HRESIMS spectrum of compound **2** (*m*/*z* 257.1177 [M – H]⁻; calcd for $C_{16}H_{17}O_3$, 257.1178).

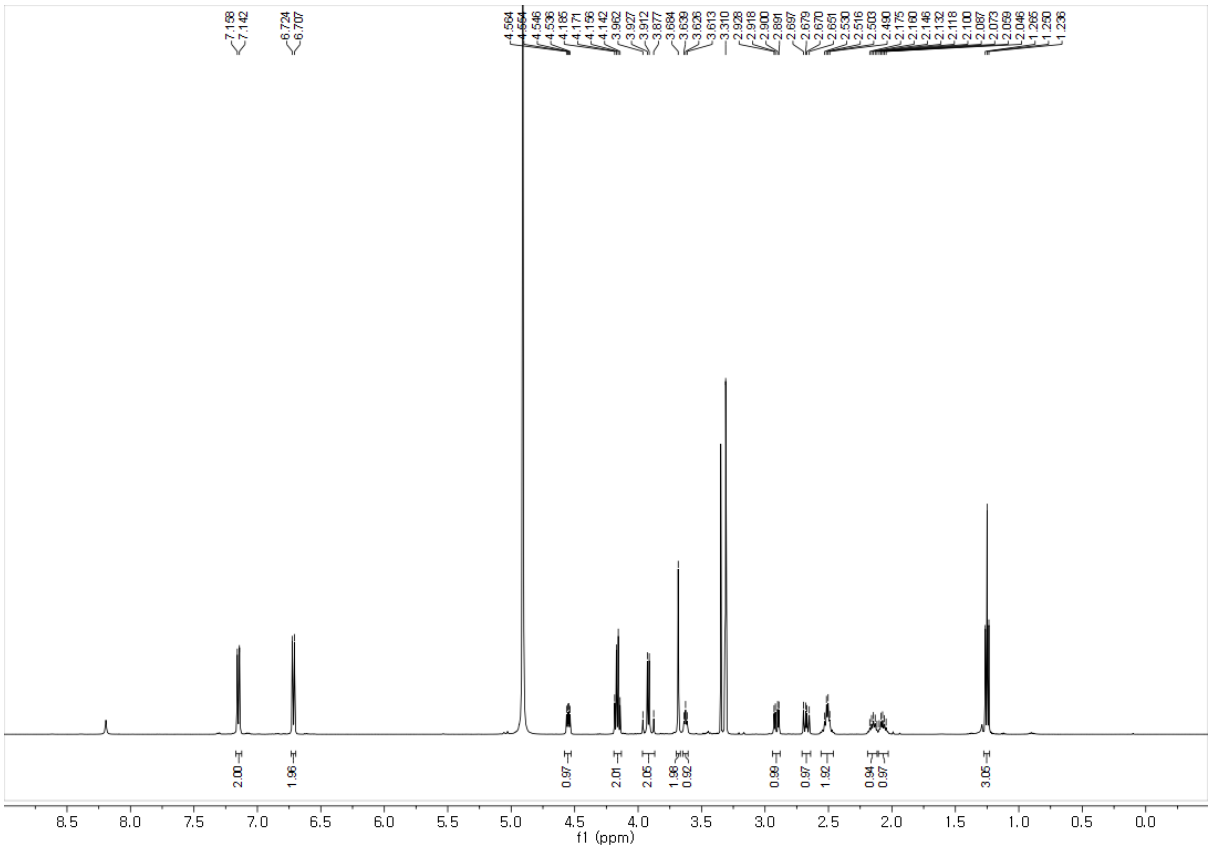
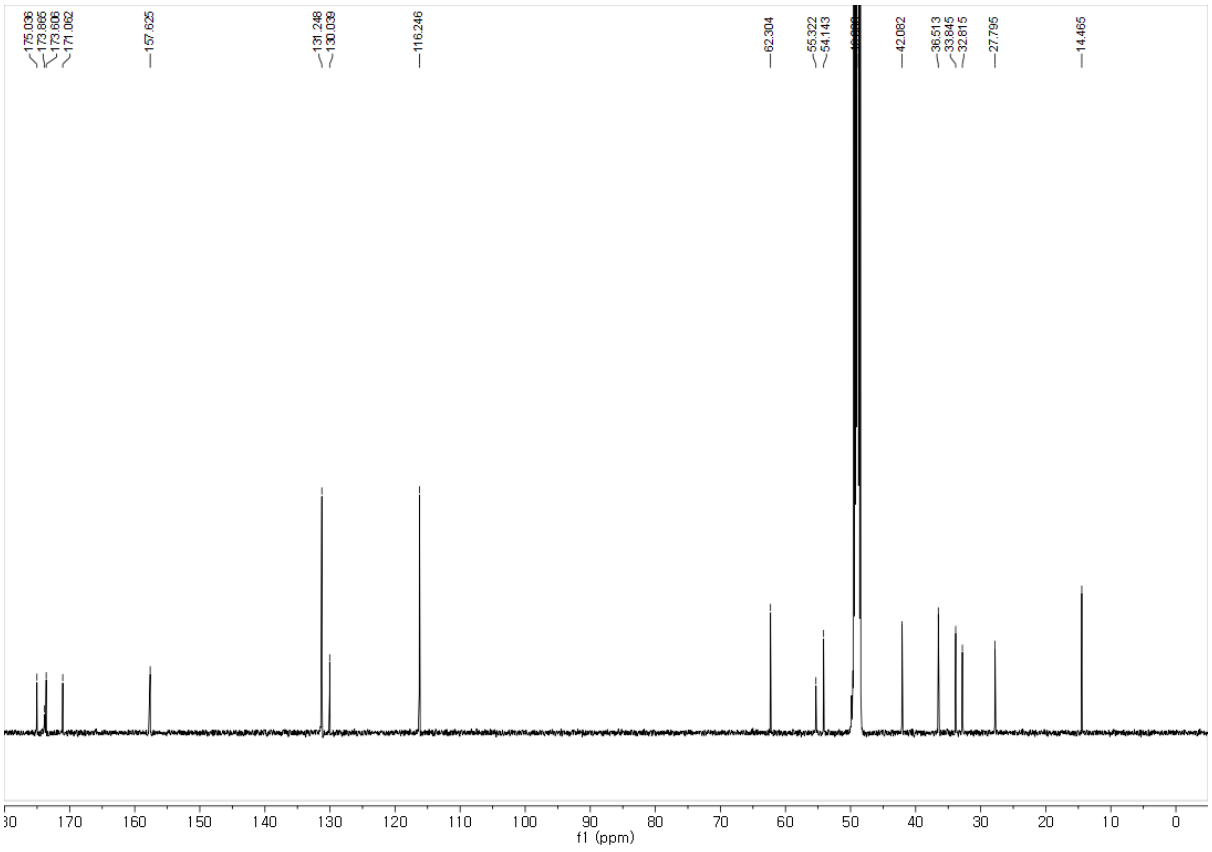


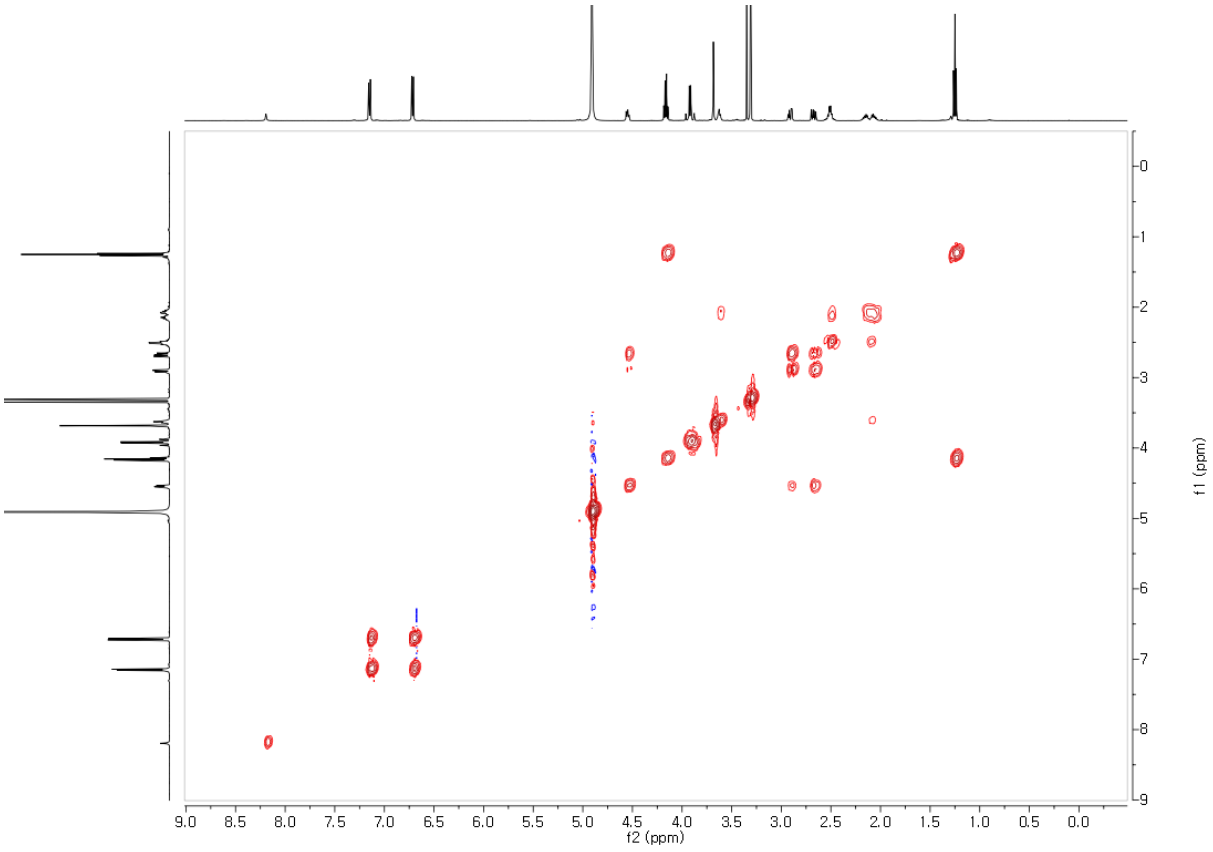

**Figure S17.** The $^{1}H$ NMR spectrum of compound **3** (500 MHz, $CD_3OD$).




210

211 **Figure S18.** The $^{13}C$ NMR spectrum of compound **3** (125 MHz, $CD_3OD$).

212




213

214 **Figure S19.** The $^{1}H$-$^{1}H$ COSY NMR spectrum of compound **3** (500 MHz, $CD_3OD$).

215

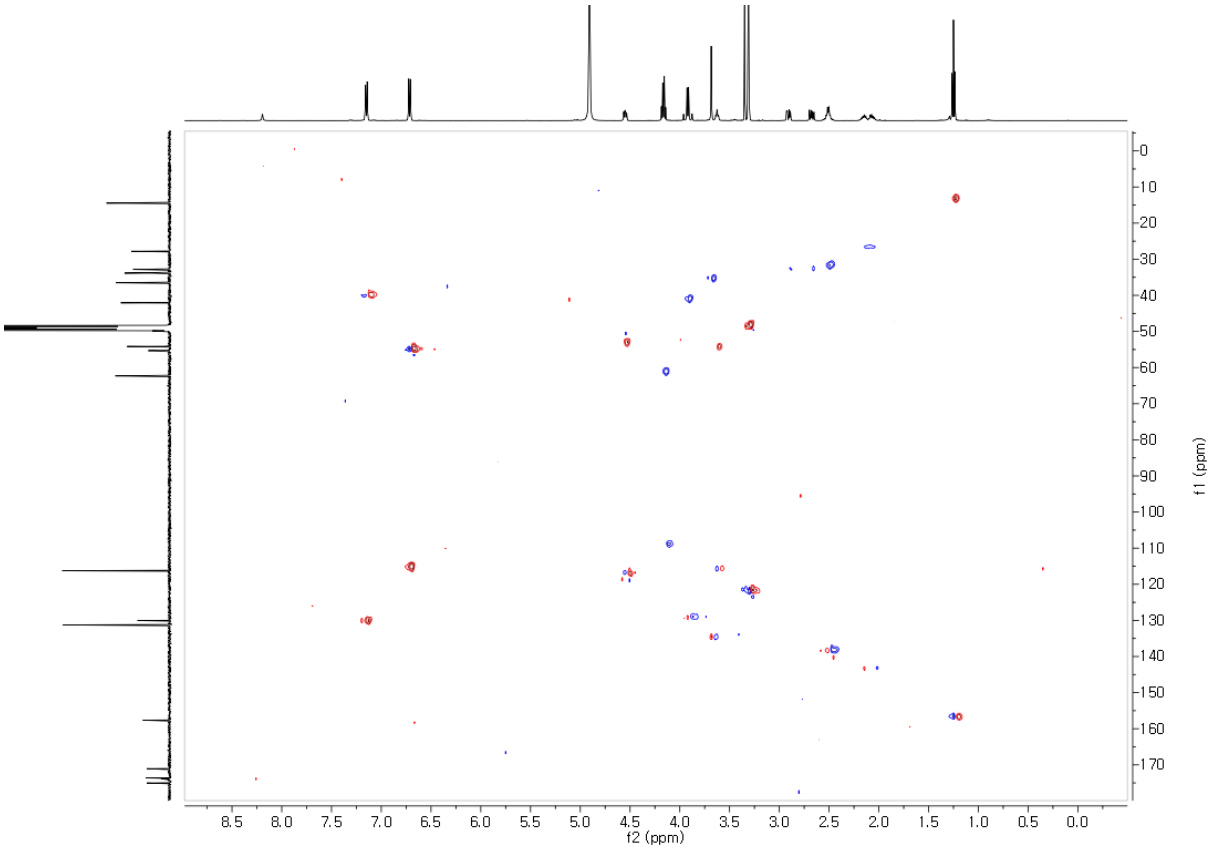



**Figure S20.** The HSQC NMR spectrum of compound **3** (500 MHz, $CD_3OD$).

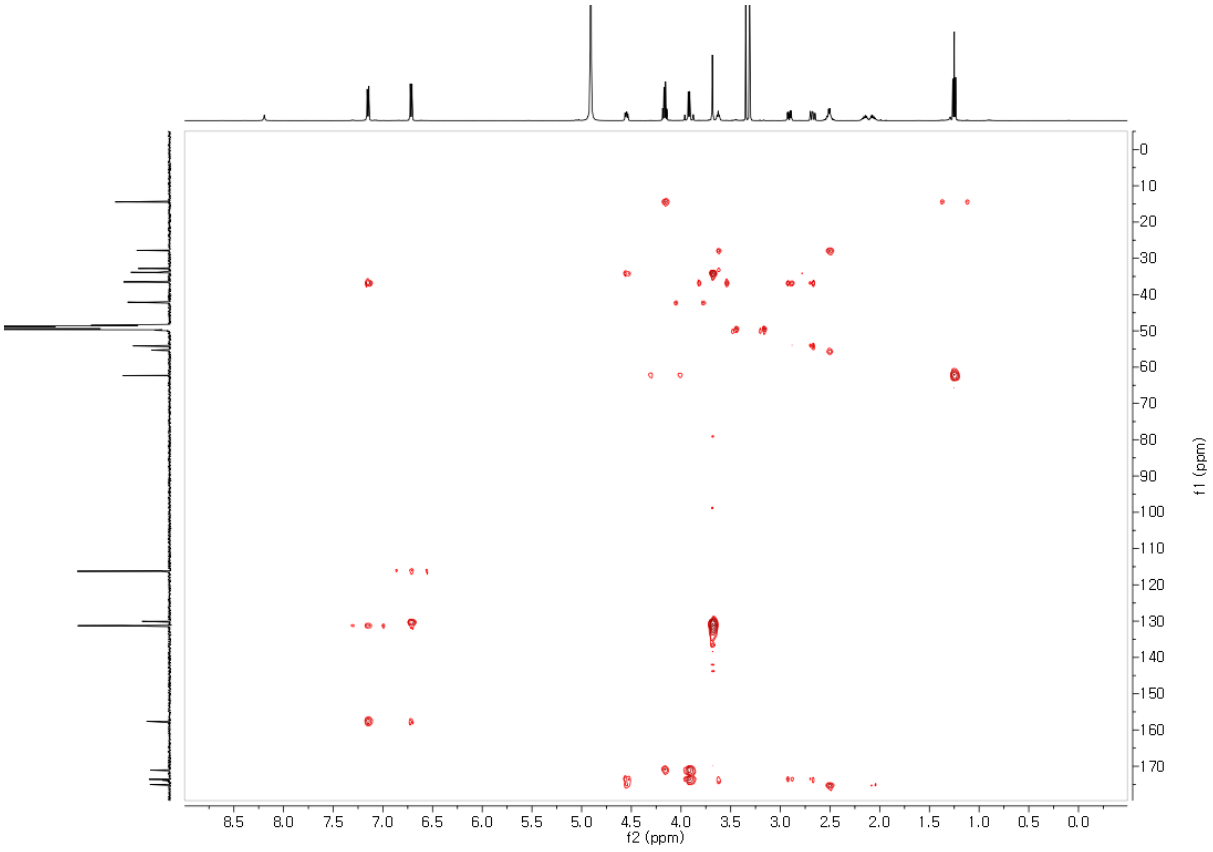



**Figure S21.** The HMBC NMR spectrum of compound **3** (500 MHz, $CD_3OD$).

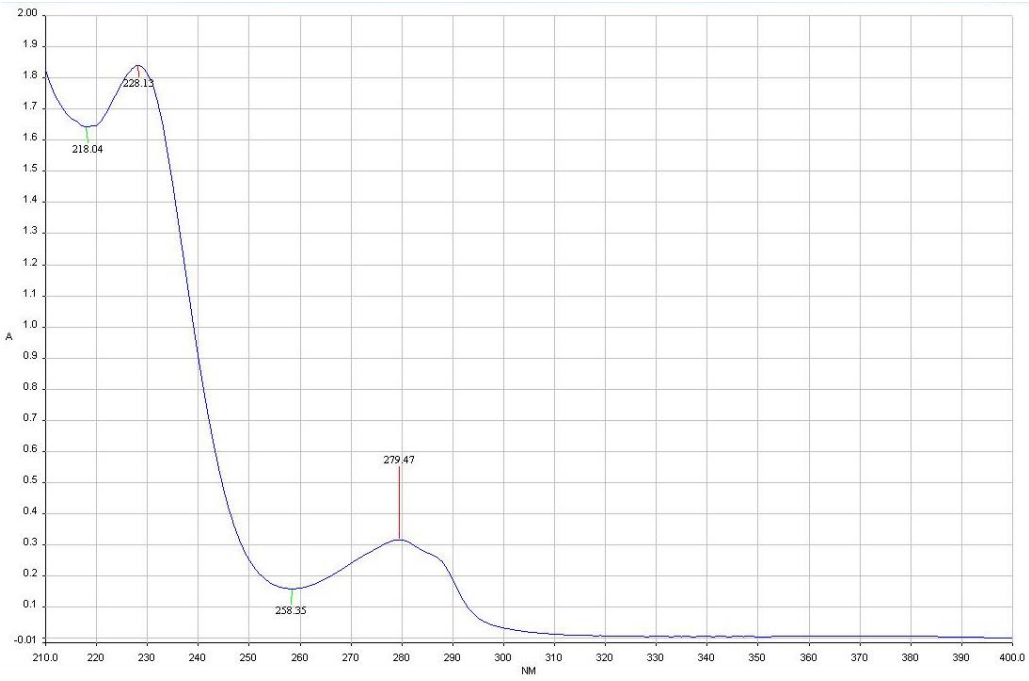
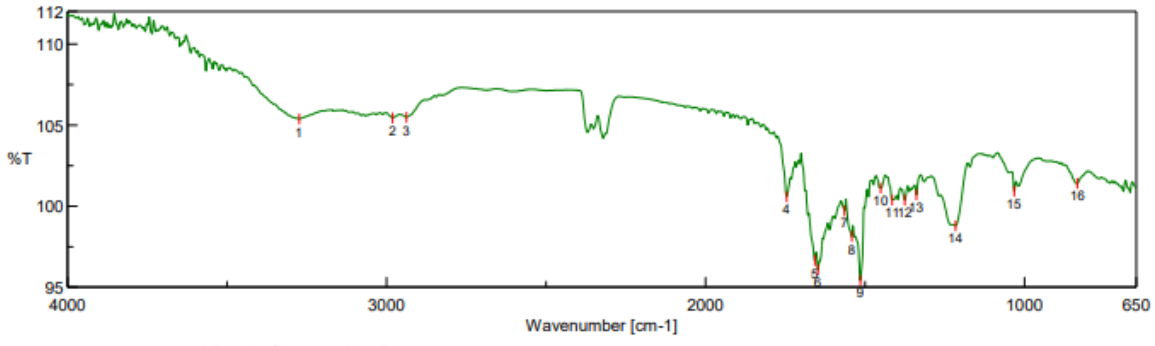



**Figure S22.** The UV spectrum of compound **3** ($CH_3OH$, c=1.1 × $10^{-5}$ M).




[ Result of Peak Picking ]

| No. | Position | Intensity | No. | Position | Intensity | No. | Position | Intensity |
|---|---|---|---|---|---|---|---|---|
| 1 | 3273.57 | 105.367 | 2 | 2981.41 | 105.429 | 3 | 2938.02 | 105.465 |
| 4 | 1746.23 | 100.575 | 5 | 1657.52 | 96.6456 | 6 | 1647.88 | 96.0796 |
| 7 | 1564.95 | 99.7024 | 8 | 1541.81 | 98.1301 | 9 | 1514.81 | 95.4064 |
| 10 | 1451.17 | 101.103 | 11 | 1415.49 | 100.378 | 12 | 1375.96 | 100.364 |
| 13 | 1339.32 | 100.697 | 14 | 1216.86 | 98.7768 | 15 | 1032.69 | 100.914 |
| 16 | 835.026 | 101.395 | | | | | | |

225

226 **Figure S23.** The IR spectrum of compound **3** [using the attenuated total reflection (ATR) sampling
227 technique]..

228

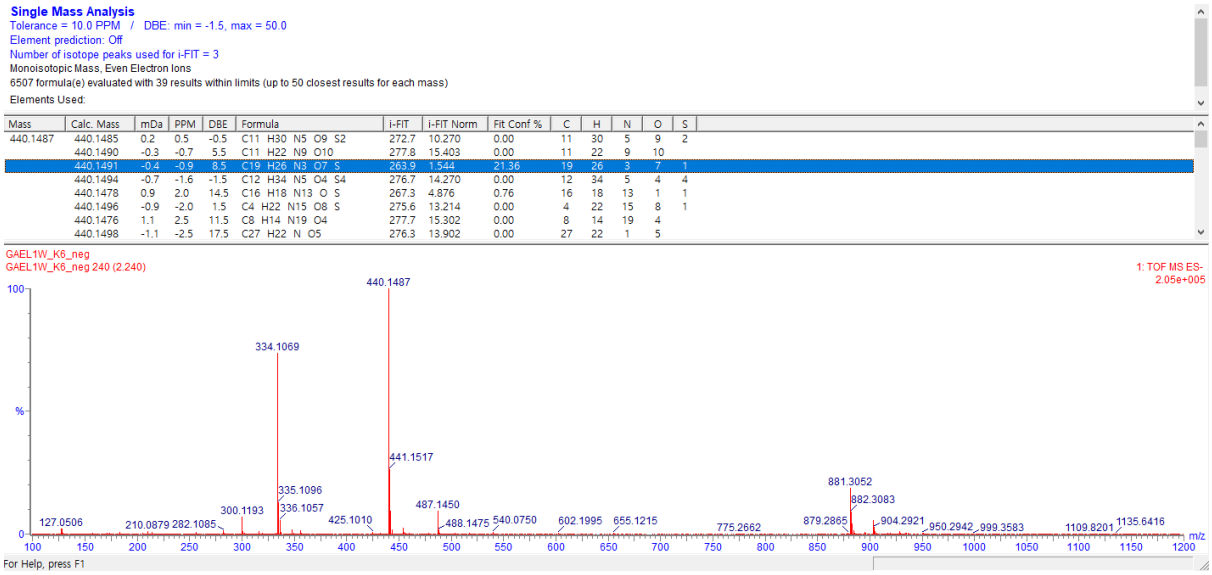



**Figure S24.** The HRESIMS spectrum of compound **3** (*m*/*z* 440.1487 [M – H]⁻; calcd for $C_{19}H_{26}N_3O_7S$, 440.1491).