Supporting Information

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Alnuheptanoid B: A new Cyclic Diarylheptanoid from *Alnus japonica* Stem Bark

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2.5. Antioxidant Activity

The antioxidant activity was evaluated using 2,2'-diphenylpicrylhydrazyl (DPPH) assay as previously outlined (Mohamed et al. 2014a; Mohamed 2014b). 1 mL of the isolated compounds **1-5** (50 µM) was mixed with 1 mL of DPPH (4 mg was dissolved in 50 mL HPLC MeOH to obtain a concentration of 80 µg/mL) and allowed to stand for half an hour for any reaction to occur. The UV absorbance was recorded at 517 nm compared to DPPH in MeOH (blank). The experiment was performed in triplicate. The average absorption was recorded for each concentration. Propyl gallate was used as a standard antioxidant. The % free radical scavenging activity was calculated using the following formula:

$$\text{Antioxidant activity} = 100 \times \left(1 - \frac{\text{absorbance with compound}}{\text{absorbance of the blank}}\right)$$

2.6.2. Carrageenin-induced Rat Paw Edema

The anti-inflammatory activity was evaluated as previously described (Mohamed et al. 2014a, 2014c, 2015). Hind paw edema (skin edema) was induced by subplanter administration of 0.1 mL carrageenin (1 % w/v) in normal saline in the right hand paw of the rats. The inflamed animals were divided randomly into seven groups (6 for each); inflamed control group, inflamed treated with indomethacin (10 mg/kg, p.o, subcutaneously), and five groups of inflamed animals were treated with the tested compounds (**1**-**5**) individually (10 mg/kg, p.o, subcutaneously). The change in paw thickness in all tested animals was measured with Plethysmometer 7150 (UGO, Basil, Italy) at 0, 1, 2, 4, and 6 hr after carrageenin solution injection. The anti-inflammatory effect of the tested compounds was calculated in comparison to inflamed control group as shown in Table 2. The percentage of edema (inflammation) was calculated according to the following equation:

$$\text{Inhibition (\%)} = \frac{V_c - V_t}{V_c} \times 100$$

V_c = Volume of paw edema in control animals.

V_t = Volume of paw edema in treated animals.

*Spectral Data of Compounds **1**, **2**, **4**, and **5***

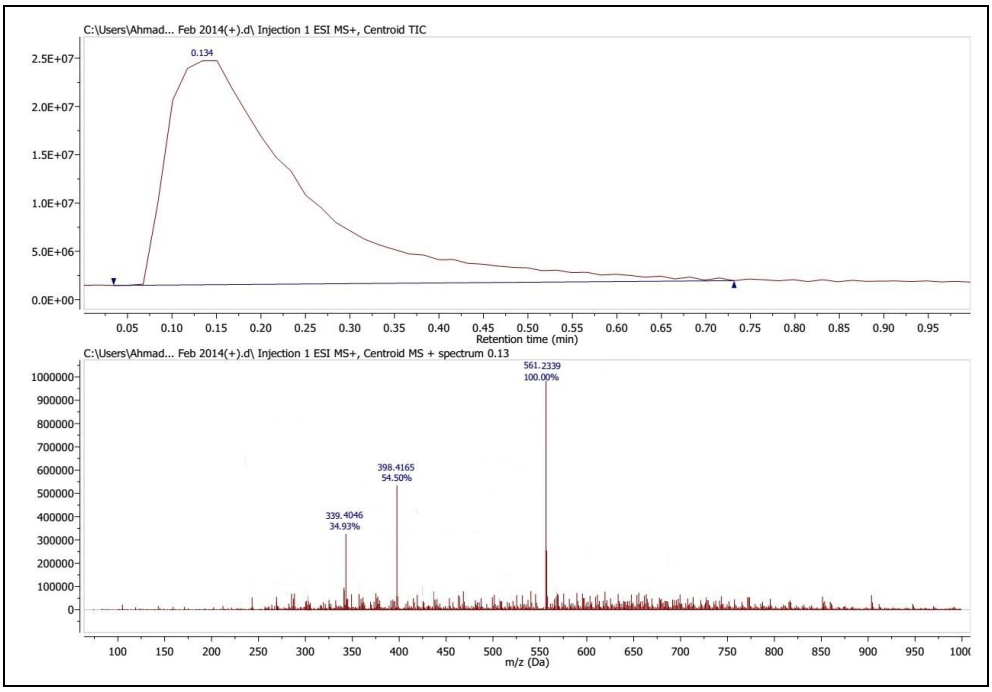
Myricanone (**1**): White needles (22.1 mg); m.p. 191-192 °C; UV (MeOH) λ_{max}: 215.0, 258.0, 295.0 nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.72 (2H, m, H-7), 1.94 (2H, m, H-8), 1.87 (2H, m, H-9), 2.77 (2H, m, H-10), 2.81 (2H, m, H-12), 3.03 (2H, m, H-13), 7.05 (1H, dd, *J* = 6.6, 2.0 Hz, H-15), 6.88 (1H, d, *J* = 6.6 Hz, H-16), 6.74 (1H, d, *J* = 2.0 Hz, H-18), 6.60 (1H, s, H-19), 3.98 (3H, s, 4-OCH_3), 3.81 (3H, s, 3-OCH_3), 7.66 (1H, brs, 17-OH), 5.91 (1H, brs, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 125.4 (s, C-1), 123.1 (s, C-2), 145.9 (s, C-3), 138.7 (s, C-4), 147.8 (s, C-5), 123.0 (s, C-6), 26.8 (t, C-7), 24.4 (t, C-8), 21.8 (t, C-9), 46.1 (t, C-10), 213.6 (s, C-11), 42.5 (t, C-12), 28.8 (t, C-13), 132.4 (s, C-14), 128.9 (d, C-15), 116.9 (d, C-16), 151.7 (s, C-17), 132.4 (d, C-18), 128.9 (d, C-19), 61.3 (q, 3-OCH_3), 61.4 (q, 4-OCH_3); ESIMS: *m*/*z* 357 $[M + H]^+$.

(+)-*S*-Myricanol (**2**): White needles (14.8 mg); m.p. 103-104 °C; $[\alpha]_D$ +38.5 (*c* 0. 5, $CHCl_3$); UV (MeOH) λ_{max}: 221.0, 259.0, 295.0 nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.55 (1H, m, H-7A), 1.93 (1H, m, H-7B), 2.78 (1H, m, H-8A), 1.92 (1H, m, H-8B), 1.69 (1H, m, H-9A), 1.55 (1H, m, H-9B), 1.90 (1H, m, H-10A), 1.54 (1H, m, H-10B), 4.08 (1H, m, H-11), 2.33 (1H, m, H-12A), 1.72 (1H, m, H-12B), 2.94 (2H, m, H-13), 7.08 (1H, dd, *J* = 7.0, 1.5 Hz, H-15), 6.91 (1H, d, *J* = 7.0 Hz, H-16),

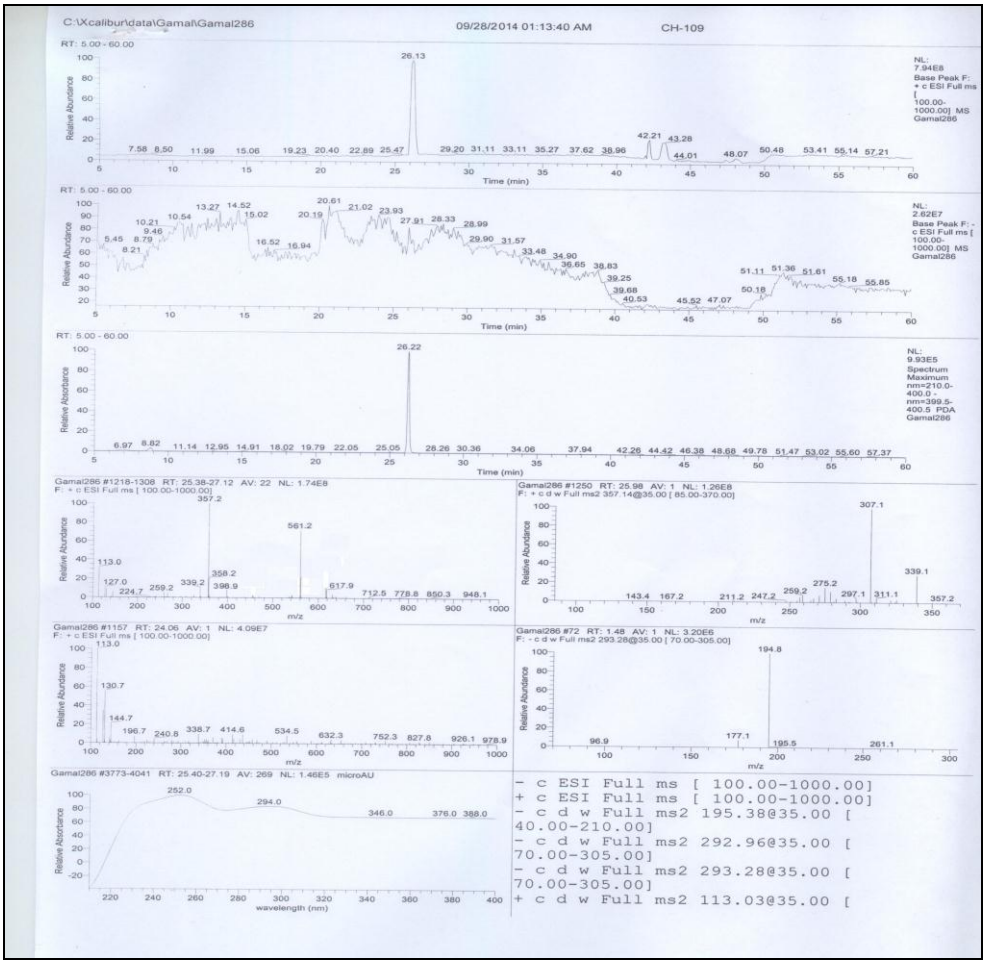
7.17 (1H, d, J = 1.5 Hz, H-18), 6.90 (1H, s, H-19), 3.99 (3H, s, 4-OCH_3), 3.87 (3H, s, 3-OCH_3), 7.70 (1H, brs, 17-OH), 5.90 (1H, brs, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 124.7 (s, C-1), 122.6 (s, C-2), 145.8 (s, C-3), 138.6 (s, C-4), 147.7 (s, C-5), 123.4 (s, C-6), 25.7 (t, C-7), 25.4 (t, C-8), 23.0 (t, C-9), 39.4 (t, C-10), 68.6 (d, C-11), 34.7 (t, C-12), 26.9 (t, C-13), 130.6 (s, C-14), 129.9 (d, C-15), 116.8 (d, C-16), 151.4 (s, C-17), 133.1 (d, C-18), 129.4 (d, C-19), 61.3 (q, 3-OCH_3), 61.4 (q, 4-OCH_3); ESIMS: m/z 359 $[M + H]^+$.

Myricanone 5-*O*-β-D-glucopyranoside (**4**): White amorphous powder (15.3 mg); UV (MeOH) λ_{max}: 220.0, 251.0, 294.0 nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 2.81 (2H, m, H-7), 1.75 (2H, m, H-8), 1.51 (2H, m, H-9), 2.63 (2H, m, H-10), 2.74 (2H, m, H-12), 2.84 (2H, m, H-13), 6.95 (1H, dd, J = 6.6, 1.7 Hz, H-15), 6.71 (1H, d, J = 6.6 Hz, H-16), 6.45 (1H, d, J = 1.7 Hz, H-18), 6.35 (1H, s, H-19), 4.79 (1H, d, J = 7.6 Hz, H-1`), 3.19 (1H, m, H-2`), 3.06 (1H, m, H-3`), 3.16 (1H, m, H-4`), 3.24 (1H, m, H-5`), 3.61 (1H, m, H-6`A), 3.43 (1H, m, H-6`B), 5.03 (1H, brs, 2`-OH), 4.93 (1H, d, J = 4.3 Hz, 3`-OH), 4.09 (1H, d, $J$ = 4.3 Hz, 4`-OH), 5.28 (1H, d, J = 3.5 Hz, 5`-OH), 4.34 (1H, t, $J$ = 4.6 Hz, 6`-OH), 3.81 (3H, s, 4-OCH_3), 3.75 (3H, s, 3-OCH_3), 8.91 (1H, brs, 17-OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_H 128.9 (s, C-1), 128.0 (s, C-2), 148.5 (s, C-3), 145.3 (s, C-4), 148.7 (s, C-5), 126.1 (s, C-6), 27.1 (t, C-7), 24.2 (t, C-8), 21.2 (t, C-9), 45.1 (t, C-10), 213.2 (s, C-11), 41.7 (t, C-12), 28.0 (t, C-13), 130.7 (s, C-14), 128.3 (d, C-15), 115.5 (d, C-16), 152.3 (s, C-17), 133.2 (d, C-18), 128.5 (d, C-19), 103.4 (d, C-1`), 74.0 (d, C-2`), 77.0 (d, C-3`), 69.9 (d, C-4`), 76.4 (d, C-5`), 61.0 (t, C-6`), 60.1 (q, 3-OCH_3), 60.9 (q, 4-OCH_3); ESIMS: m/z 519 $[M + H]^+$, 357 $[(M + H)\text{-Glu}]^+$.

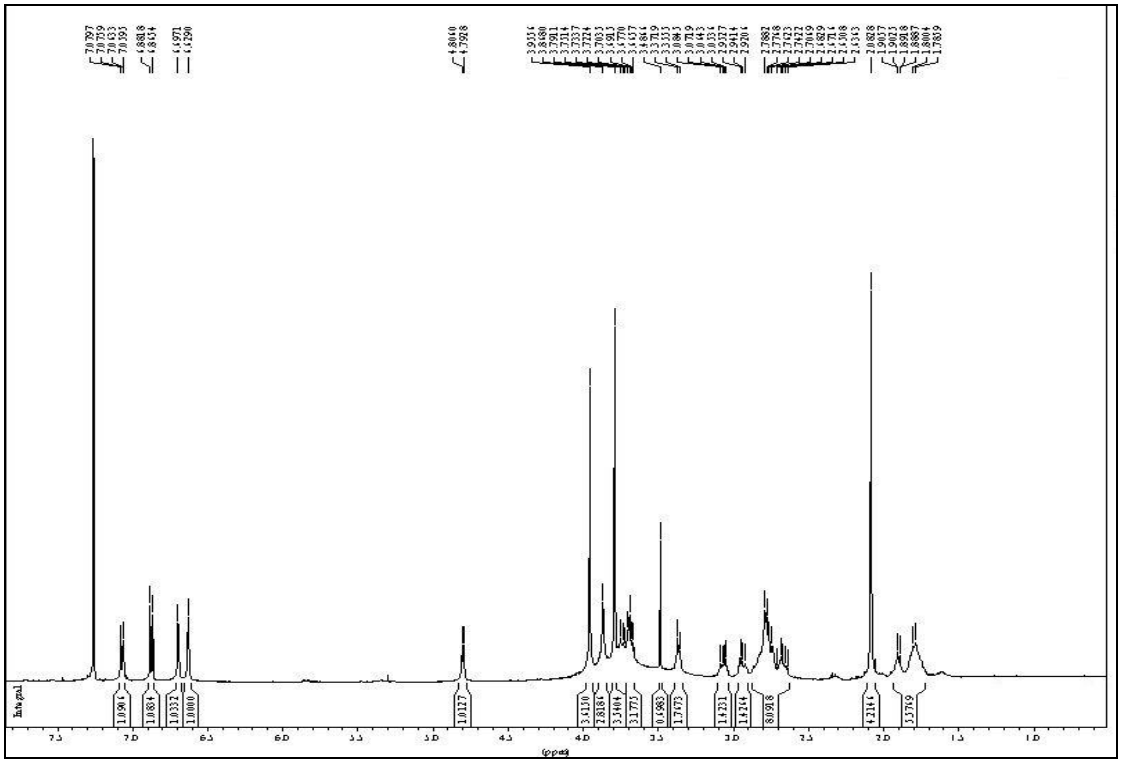
(+)-*S*-Myricanol 5-*O*-β-D-glucopyranoside (**5**): White amorphous powder (18.9 mg); $[\alpha]_D$ +82.3 (*c* 0. 5, CH_3OH); UV (MeOH) λ_{max}: 231.0, 253.0, 294.0 nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 2.54 (2H, m, H-7), 2.71 (2H, m, H-8), 1.28 (1H, m, H-9A), 1.21 (1H, m, H-9B), 1.63 (1H, m, H-10A), 1.35 (1H, m, H-10B), 3.95 (1H, m, H-11), 2.09 (1H, m, H-12A), 1.49 (1H, m, H-12B), 2.83 (1H, m, H-13A), 2.78 (1H, m, H-13B), 6.96 (1H, dd, J = 6.6, 1.5 Hz, H-15), 6.74 (1H, d, J = 6.6 Hz, H-16), 6.92 (1H, brs, H-18), 6.60 (1H, s, H-19), 4.84 (1H, d, J = 7.6 Hz, H-1`), 3.04 (1H, m, H-2`), 3.06 (1H, m, H-3`), 3.17 (1H, m, H-4`), 3.23 (1H, m, H-5`), 3.58 (1H, m, H-6`A), 3.42 (1H, m, H-6`B), 5.03 (1H, d, $J$ = 2.5 Hz, 2`-OH), 4.93 (1H, d, J = 4.1 Hz, 3`-OH), 4.41 (1H, d, $J$ = 3.8 Hz, 4`-OH), 5.22 (1H, d, J = 3.5 Hz, 5`-OH), 3.36 (1H, t, $J$ = 4.6 Hz, 6`-OH), 3.81 (3H, s, 3-OCH_3), 3.83 (3H, s, 4-OCH_3), 8.91 (1H, brs, OH), 4.41 (1H, d, J = 3.8 Hz, OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 128.4 (s, C-1), 128.0 (s, C-2), 148.3 (s, C-3), 145.1 (s, C-4), 148.8 (s, C-5), 126.0 (s, C-6), 25.8 (t, C-7), 26.0 (t, C-8), 22.5 (t, C-9), 39.3 (t, C-10), 66.5 (d, C-11), 34.4 (t, C-12), 26.8 (t, C-13), 129.4 (s, C-14), 129.1 (d, C-15), 115.6 (d, C-16), 152.0 (s, C-17), 134.6 (d, C-18), 129.5 (d, C-19), 103.9 (d, C-1`), 74.0 (d, C-2`), 77.1 (d, C-3`), 69.9 (d, C-4`), 76.5 (d, C-5`), 60.9 (t, C-6`), 60.1 (q, 3-OCH_3), 60.8 (q, 4-OCH_3); ESIMS: m/z 521 $[M + H]^+$, 359 $[(M + H)\text{-Glu}]^+$.



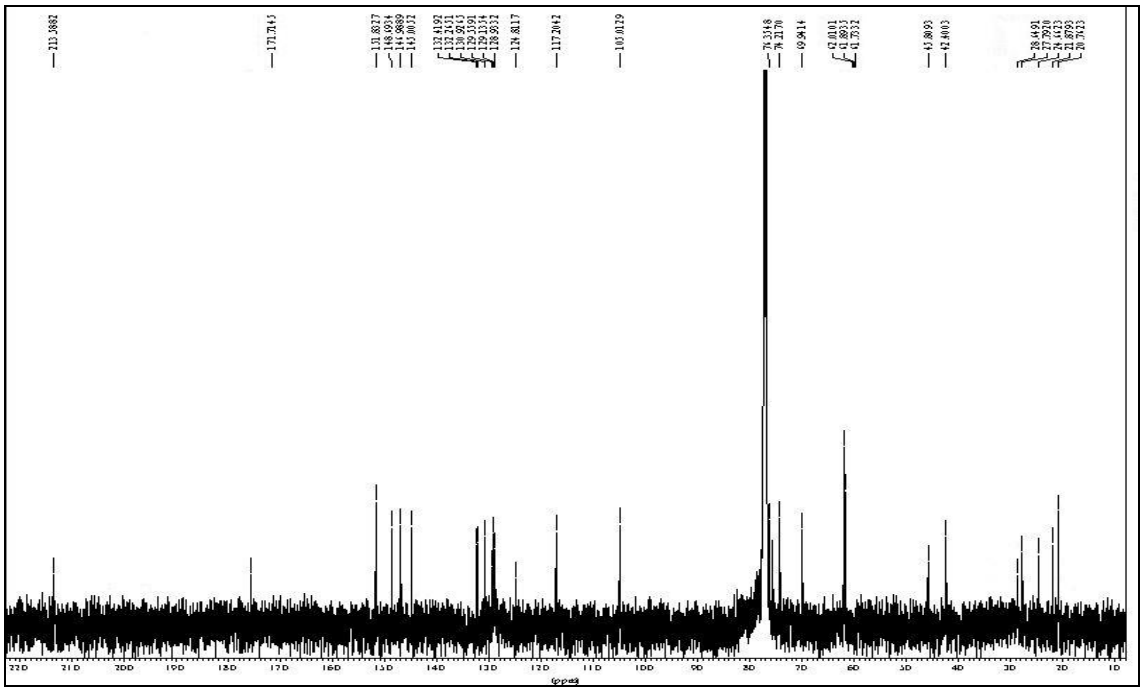
S1: HRESI-MS spectrum of compound **3**



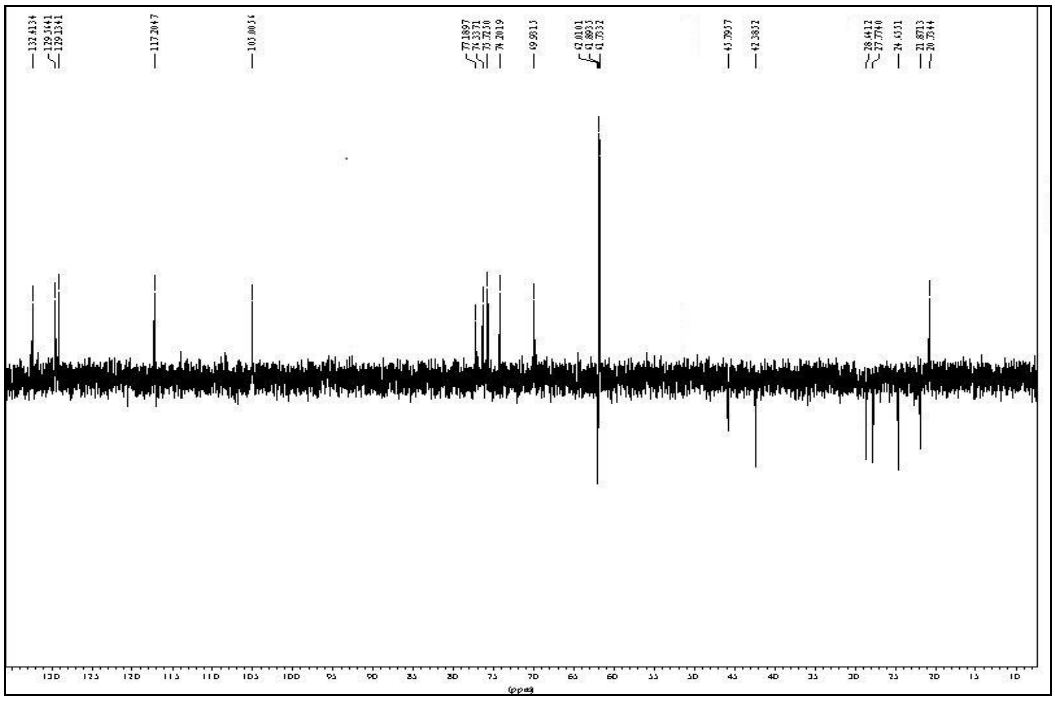
S2: ESI-MS spectrum of compound **3**



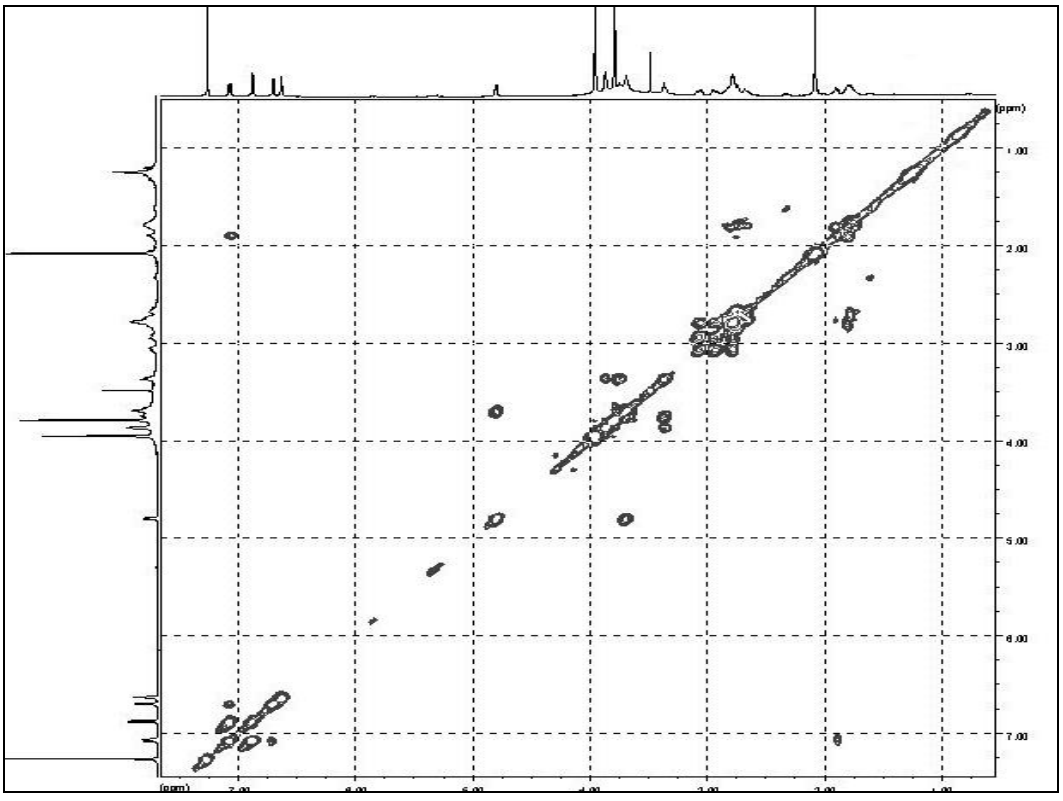
S3: ^{1}H NMR spectrum of compound **3** (400 MHz, $CDCl_3$).



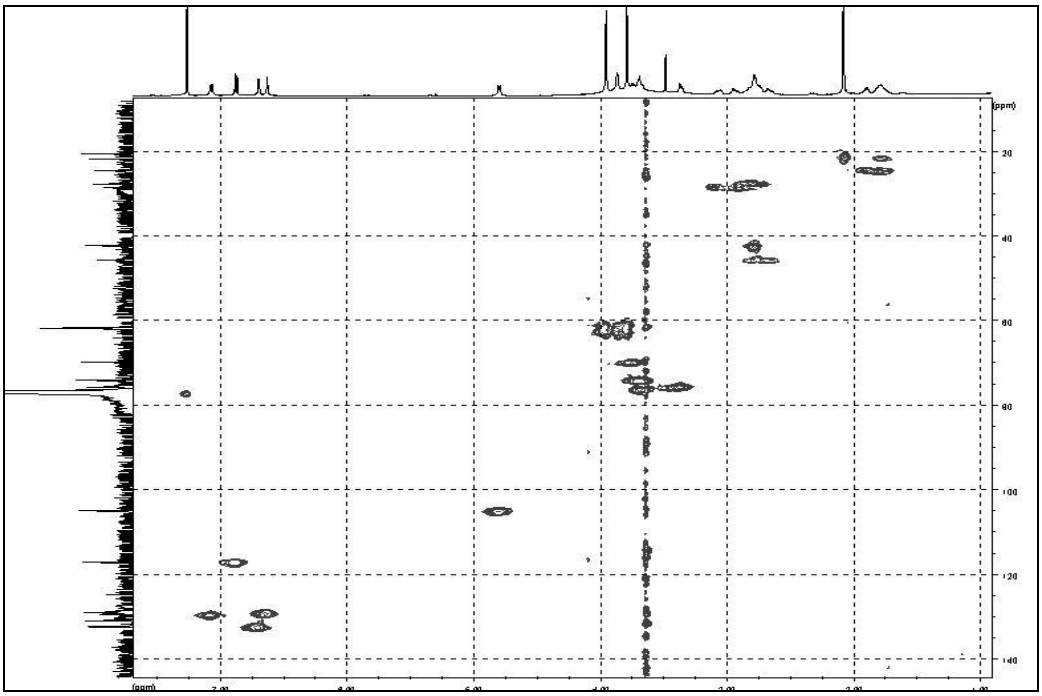
S4: ^{13}C NMR spectrum of compound **3** (100 MHz, $CDCl_3$).



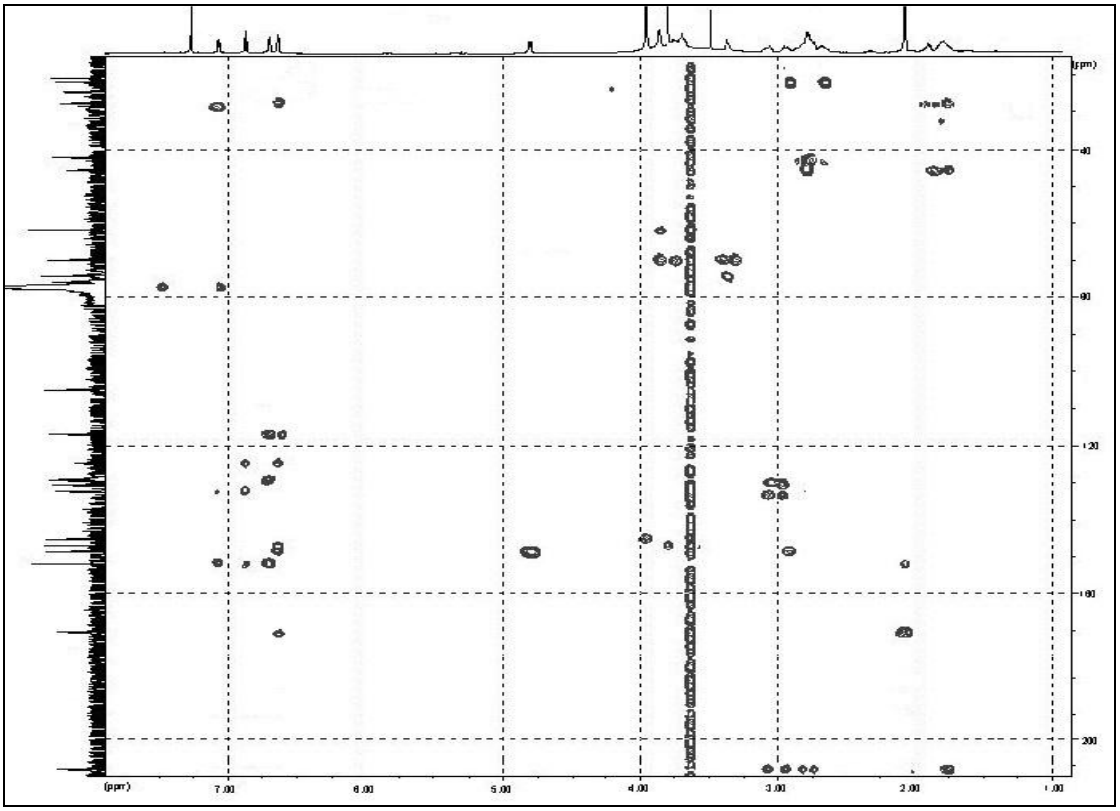
S5: DEPT ^{13}C NMR spectrum of compound **3** (100 MHz, $CDCl_3$).



S6: ^{1}H-^{1}H COSY spectrum of compound **3.**



S7: HMQC spectrum of compound **3**.



S8: HMBC spectrum of compound **3**.