# Supplementary Information

## Secondary Metabolites Produced by the Citrus Phytopathogen *Phyllosticta citricarpa*

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## 1. **METHODS**

### *1.1 General Experimental Procedures*

Optical rotation measurements were recorded on a Jasco DIP-370 digital polarimeter (Jasco, Easton, MD, USA). All NMR data were recorded using a Varian (Palo Alto, CA) Vnmr 400 ($^{1}$H, 400 MHz; $^{13}$C, 100 MHz) spectrometer, $\delta$-values were referenced to the respective solvent signals ($CD_3OD$, $\delta_H$ 3.31 ppm, $\delta_C$ 49.15 ppm; DMSO-$d_6$, $\delta_H$ 2.50 ppm, $\delta_C$ 39.51 ppm; $CDCl_3$, $\delta_H$ 7.24 ppm, $\delta_C$ 77.23 ppm). HPLC-MS analyses were accomplished using a Waters (Milford, MA) 2695 LC module (Waters Symmetry Anal $C_{18}$, 4.6 × 250 mm, 5 μm; solvent A: $H_2O$/0.1% formic acid, solvent B: $CH_3CN$/0.1% formic acid; flow rate: 0.5 mL min$^{-1}$; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-30 min, 10 % B). HPLC analyses were performed on an Agilent 1260 system equipped with a photodiode array detector (PDA) and a Phenomenex $C_{18}$ column (4.6 × 250 mm, 5 μm; Phenomenex, Torrance, CA), and a gradient elution profile (solvent A: $H_2O$/0.1% TFA; solvent B: $CH_3CN$; flow rate: 1.0 mL min$^{-1}$; 0-30 min, 5%-100% B; 30-35 min, 100% B; 35-36 min, 100%-5% B; 36-40 min, 5 % B). *Semi*-preparative HPLC was accomplished using Phenomenex (Torrance, CA) $C_{18}$ column (10 × 250 mm, 5 μm) on a Varian (Palo Alto, CA) ProStar Model 210 equipped with a photodiode array detector and a gradient elution profile (solvent A: $H_2O$, solvent B: $CH_3CN$; flow rate: 5.0 mL min$^{-1}$; 0-2 min, 25% B; 2-15 min, 25-100% B; 15-17 min, 100% B; 17-18 min, 100%-25% B; 18-19 min, 25% B). Size exclusion chromatography was performed on Sephadex LH-20 (25-100 μm; GE Healthcare, Piscataway, NJ). All solvents used were of ACS grade and purchased from the Pharmco-AAPER (Brookfield, CT).

### *1.2 Biological Material*

*Phyllostica citricarpa* LGMF06 was isolated from CBS disease in *Citrus sinensis* (Rutaceae) fruits, the strain identification was based on multilocus sequence analysis [1]. Potato Dextrose agar (IBI Scientific) were used to *Phyllostica citricarpa* LGMF06

maintenance, and liquid medium for fermentation was Malt Extract Broth (20 g of malt extract, 1 g of peptone and 20 g of glucose per litter).

*1.3 Microbial Cultivation and Secondary Metabolites Isolation*

The fungus *P. citricarpa* LGMF06 was cultivated in potato dextrose agar at 28 ºC for 10 days. The agar was cut into 8 mm plugs and 10 plugs were used to inoculate five Erlenmeyer flasks (2 L) containing 1 L of MEB medium. After incubation at 28 ºC for 14 days on rotary shaker (120 rpm), the culture was filtered-off on Whatman n. 4, and the supernatant was extracted with ethyl acetate (3 × V/V) and then recovered organics were evaporated *in vacuo* at 40 °C to yield 752 mg of brown extract. The crude extract was subjected to a Reverse Phase $C_{18}$ column chromatography (20 × 8 cm, 250 g) eluted with a gradient of $H_2O$-$CH_3CN$ (100:0-0:100) to produce eight fractions, which were finally subjected to HPLC purification to yield compounds **1a** (6.3 mg), **1b** (15.0 mg), **2a** (3.2 mg), **3** (2.6 mg) and **4** (8.2 mg) in pure forms (Figures 1 and S1).

*Phenguignardic acid butyl ester (**1a**):* brown oil, UV absorbing (254 nm); HPLC $R_t$ 29.52 min (Figure S5); $[\alpha]_D^{25}$ + 261.0 (*c* = 1.0, MeOH); UV/VIS $\lambda_{max}$ 220, 230, 298 nm; $^1$H NMR ($CD_3OD$, 400 MHz) and $^{13}$C NMR ($CD_3OD$, 100 MHz), see Table 1; $^1$H NMR ($CDCl_3$, 400 MHz) and $^{13}$C NMR ($CDCl_3$,100 MHz), see Table 1; (+)-APCI-MS: *m/z* 367 $[M + H]^+$; (+)-HR-ESI-MS: *m/z* 384.1809 $[M + NH_4]^+$ (calcd for $C_{22}H_{26}N_1O_5$, 384.1805).

*Phenguignardic acid methyl ester (**1b**):* brown oil, UV absorbing (254 nm); HPLC $R_t$ 26.12 min (Figure S22); $[\alpha]_D^{25}$ + 223 (*c* = 1.0, MeOH); $[\alpha]_D^{25}$ + 31.5 (*c* = 0.10, Acetone), Literature [11]; UV/VIS $\lambda_{max}$ 225, 300 nm; $^1$H NMR ($CDCl_3$, 400 MHz) and $^{13}$C NMR ($CDCl_3$, 100 MHz), see Table 1; (+)-APCI-MS: *m/z* 325 $[M + H]^+$, *m/z* 347 $[M + Na]^+$; (–)-APCI-MS: *m/z* 309 $[M – CH_3]^–$; (+)-HR-ESI-MS: *m/z* 325.1073 $[M + H]^+$ (calcd for $C_{19}H_{17}O_5$, 325.1071); (–)-HR-ESI-MS: *m/z* 309.0756 $[M – CH_3]^–$ (calcd for $C_{18}H_{13}O_5$, 309.0768).

*Peniisocoumarin G (**2a**):* pale-yellow solid, UV absorbing (254 nm); HPLC $R_t$ 12.46 min (Figure S34); UV/VIS $\lambda_{max}$ 230, 265, 350 nm; $^1$H NMR (DMSO-$d_6$, 400 MHz) and $^{13}$C NMR (DMSO-$d_6$, 100 MHz), see Table S1; (+)-APCI-MS: *m/z* 253 $[M + H]^+$; (–)-APCI-MS: *m/z* 251 $[M – H]^–$, 503 $[2M – H]^–$; (–)-HR-ESI-MS: *m/z* 251.0553 $[M – H]^–$ (calcd for $C_{12}H_{11}O_6$, 251.0561), 503.1187 $[2M – H]^–$ (calcd for $C_{24}H_{23}O_{12}$, 503.1195).

*Protocatechuic acid (3,4-Dihydroxy-benzoic acid; **3**):* pale-yellow solid, UV absorbing (254 nm); HPLC $R_t$ 18.41 min (Figure S44); UV/VIS $\lambda_{max}$ 200, 210, 320 nm; $^1$H NMR ($CD_3OD$, 400 MHz), $\delta$ 7.43 (brs, 1H, 2-H), 7.42 (d, $J$ = 7.9 Hz, 1H, 6-H), 6.79 (d, $J$ = 7.9 Hz, 1H, 5-H); $^{13}$C NMR ($CD_3OD$, 100 MHz), $\delta$ 170.6 (Cq-7), 151.6 (Cq-4), 146.2 (Cq-3), 124.0 (CH-6), 123.6 (Cq-1), 117.8 (CH-2), 115.9 (CH-5); (+)-APCI-MS: *m/z* 155 $[M + H]^+$; (–)-APCI-MS: *m/z* 153 $[M – H]^–$.

*1.4 Chemical Synthesis of Compounds **1a** and **1b***

Phenguignardic acid (**1c**) was synthesized following the procedure previously described by Stoye et al. [2]. To a stirred solution of **1c** (1 mmol) in dry DMF (6 mL) were added potassium carbonate (2 mmol) and alkyl halide (2 mmol). The reaction mixture was stirred at rt for 24 h, filtered, washed with acetone and concentrated under reduced pressure. It was diluted with water (10 mL) and extracted with ethyl acetate (15 mL × 3). The combine organic fraction was washed with brine, dried using sodiun sulfate and concentrated under reduced pressure. Column chromatography with silica gel using 20% ethyl acetate in hexane as eluent to afford the correspond ester. Phenguignardic acid methyl ester (**1b**, 7.7 mg, 65%) was prepared as a yellow semisolid from **1c** (12 mg, 0.04 mmol) with methyl iodide (0.005 ml, 0.08 mmol) using $K_2CO_3$ (12 mg, 0.08 mmol) as base, following the general procedure described above. Phenguignardic acid butyl ester (**1a**, 6.0 mg, 55%) was prepared as a yellow semisolid from **1c** (9 mg, 0.03 mmol) with *n*-butyl bromide (0.007 ml, 0.06 mmol) using $K_2CO_3$ (9 mg, 0.06 mmol) as base, following the general procedure described above.

*1.5 Phytotoxicity of Dioxolanones (**1a**, **1b**) and peniisocoumarin G (**2a**) in Citrus Leaves and Fruits*

For phytotoxicity analysis, the leaf disks were collected from intact mature leaves of *Citrus sinensis* and placed on $H_2O$ agar (15 grams of agar per 1 L of deionized $H_2O$), and mature citrus fruits were deposited in plastic boxes. The pure compounds, phenguignardic acid methyl ester (**1b**), phenguignardic acid butyl ester (**1a**) and peniisocoumarin G (**2a**) were dissolved in methanol at 1 mg/mL and applied onto the leaf disks and fruits to give amounts ranging from 5 to 100 µg. A 30 µL sample of 10% lactic acid was used as the positive control, and 30 µL of methanol was used as the negative control. Incubation was carried out at 24 °C for approximately 48 h.

*1.6 Antibacterial activity - Minimum Inhibitory Concentration*

The antibacterial activity of the extract produced by the fungus *P. citricarpa* LGMF06 and purified compounds were evaluated by minimum inhibitory concentration determination (MIC). The MIC was performed as described by Ostrosky et al. Ostrosky *et al*. [3] and CLSI [4, 5]. Bacteria used in our study were *Staphylococcus aureus* (ATCC 25923) and methicillin-resistant *Staphylococcus aureus* (BACHC-MRSA).

*1.7 Cytotoxicity Assay*

The cell cytotoxicity assays using human cancer cell lines A549 (lung non-small cell carcinoma, ATCC, Manassas, VA, USA) and PC3 (prostate adenocarcinoma, ATCC, Manassas, VA, USA), and human normal cell line HEL 299 (lung fibroblast embryonic, ATCC, Manassas, VA, USA) were accomplished in triplicate following our previous reports [6-10] and 10 µg/ml actinomycin D and 1.5 mM hydrogen peroxide were used as positive controls. Cells were plated in 96-well plates (Corning 3610, VWR, Radnor, PA, USA) and incubated with vehicle (DMSO) or compounds for 72 h.

## 2. SUPPLEMENTRY REFRENCES


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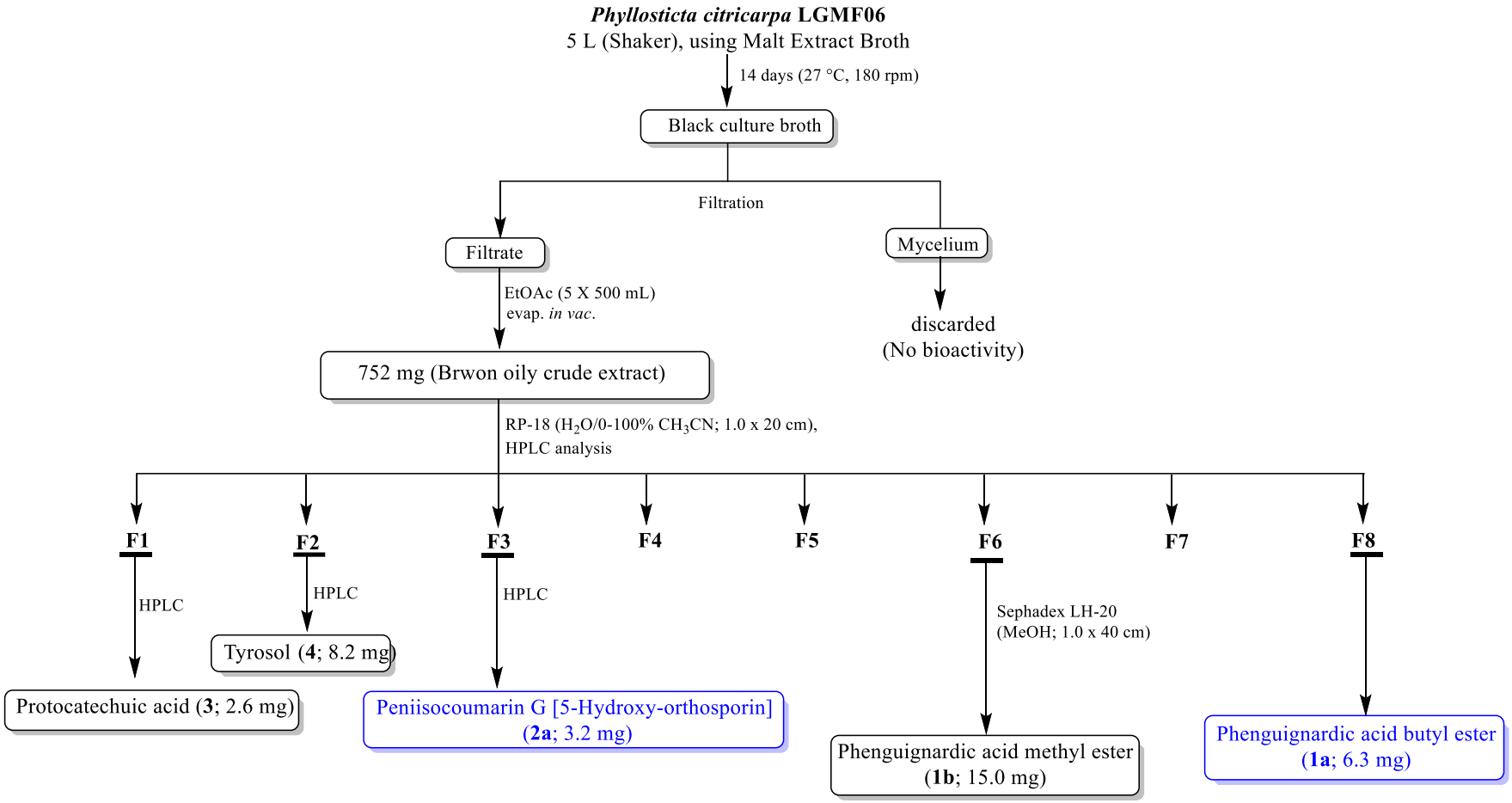



**Figure S1.** Work-up scheme of the metabolites produced by *Phyllosticta citricarpa* LGMF06.

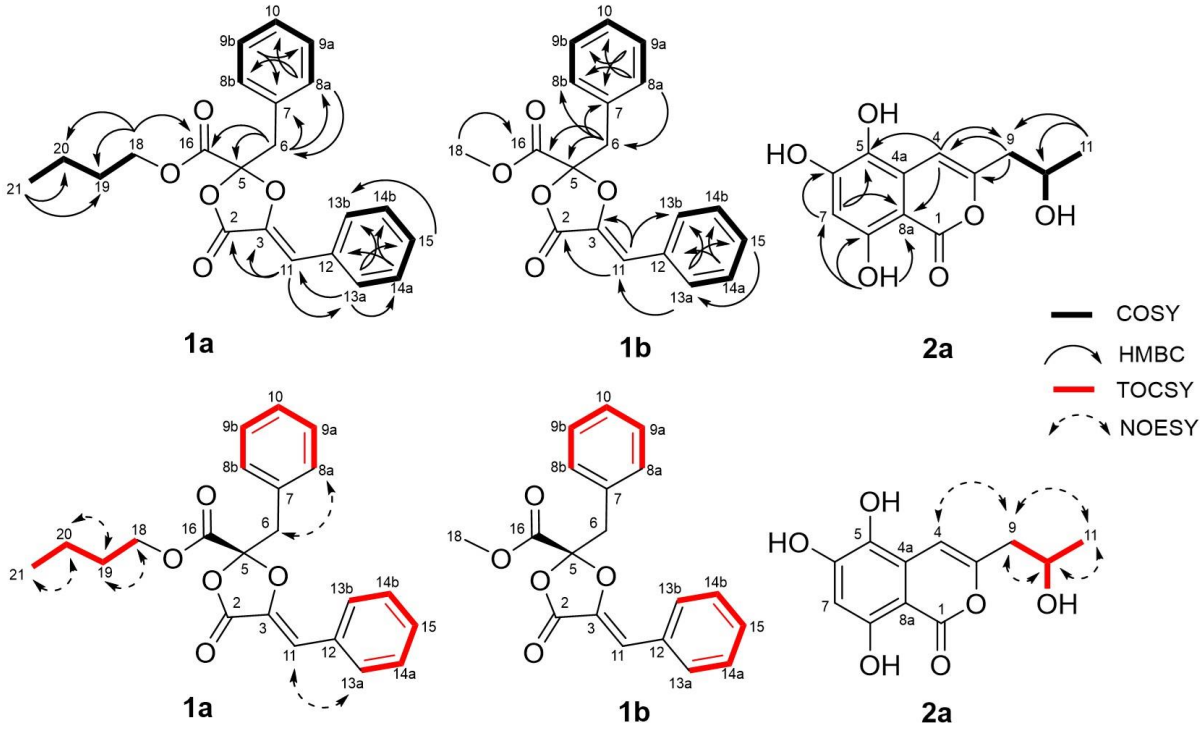



**Figure S2.** $^{1}$H,$^{1}$H-COSY (—), TOCSY (—), selected HMBC (→) and NOESY (⤳) correlations of compounds **1a/1b** and **2a**.

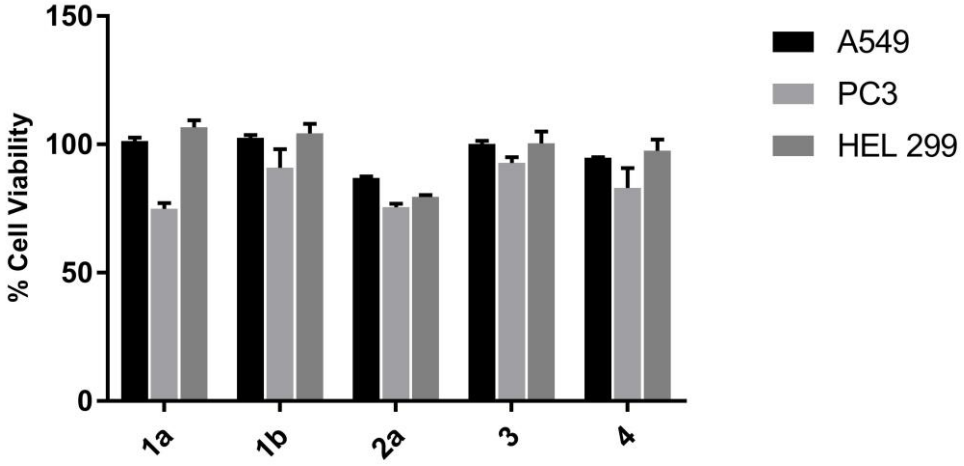



**Figure S3.** Viability of A549 (non-small cell lung cancer), PC3 (prostate cancer) and HEL 299 normal (epithelial lung) human cell lines at 80 μM treatment with compounds **1a**, **1b**, **2a**, **3** and **4** after 48 h.

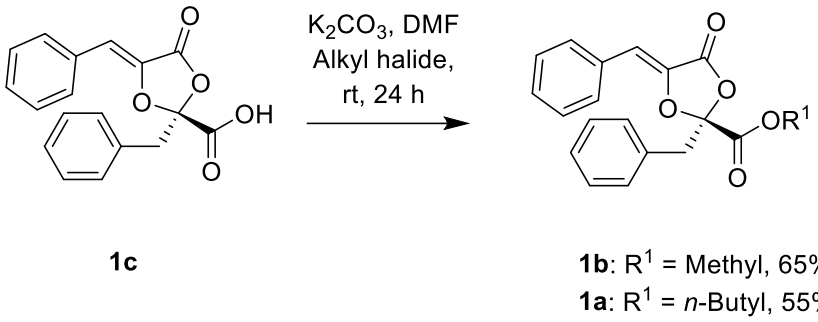



**Figure S4.** Chemical synthesis of phenguignardic acid butyl ester (**1a**) and phenguignardic acid methyl ester (**1b**).

**Table S1.** $^{13}C$ (100 MHz) and $^{1}H$ (400 MHz) NMR Spectroscopic Data for Compound **2a** ($\delta$ in ppm).

| Position | Compound **2a** (DMSO-$d_6$) | | Compound **2a** (Acetone-$d_6$) [12] | |
|---|---|---|---|---|
| | $\delta_C$, type | $\delta_H$ (mult, *J* in [Hz]) | $\delta_C$, type | $\delta_H$ (mult, *J* in [Hz]) |
| 1 | 166.0, C | | 167.3, C | |
| 3 | 153.5, C | | 154.9, C | |
| 4 | 100.4, CH | 6.61 (s) | 101.1, CH | 6.69 (s) |
| 4a | 125.1, C | | 126.0, C | |
| 5 | 131.3 C | | 132.1 C | |
| 5-OH | | 10.78 (brs)* | | |
| 6 | 154.2, C | | 154.2, C | |
| 6-OH | | 8.65 (brs)* | | |
| 7 | 101.4, CH | 6.40 (s) | 102.1, CH | 6.45 (s) |
| 8 | 155.6, C | | 157.7, C | |
| 8-OH | | 10.61 (s) | | |
| 8a | 96.8, C | | 98.6, C | |
| 9 | 42.8, $CH_2$ | 2.53 (brm),<br>2.55-2.50 (m) | 44.1, $CH_2$ | 2.64 (dd, 5.1, 14.2),<br>2.60 (dd, 7.4, 14.2) |
| 10 | 64.0, CH | 3.96 (m) | 65.6, CH | 4.17 (m) |
| 10-OH | | 4.78 (brd, 4.9) | | |
| 11 | 23.3, $CH_3$ | 1.13 (d, 6.2) | 23.6, $CH_3$ | 1.25 (d, 6.2) |

See Supplementary Information for NMR spectra. Assignments supported by 2D HSQC and HMBC experiments. *May be exchangeable

**Table S2.** Minimum inhibitory concentration of compounds isolated from *Phyllosticta citricarpa* LGMF06 against methicillin sensitive and resistant *Staphylococcus aureus*.

| Compound | Microorganism | |
|---|---|---|
| | **Methicillin-sensitive *Staphylococcus aureus*** | **Methicillin-resistant *Staphylococcus aureus*** |
| Phenguignardic acid butyl ester (**1a**) | 111 µg/mL | 111 µg/mL |
| Phenguignardic acid methyl ester (**1b**) | 333 µg/mL | 333 µg/mL |
| Peniisocoumarin G(**2a**) | 333 µg/mL | 1.5 mg/mL |
| Protocatechuic acid (**3**) | > 1.5 mg/mL | > 1.5 mg/mL |
| Tyrosol (**4**) | > 1.5 mg/mL | > 1.5 mg/mL |

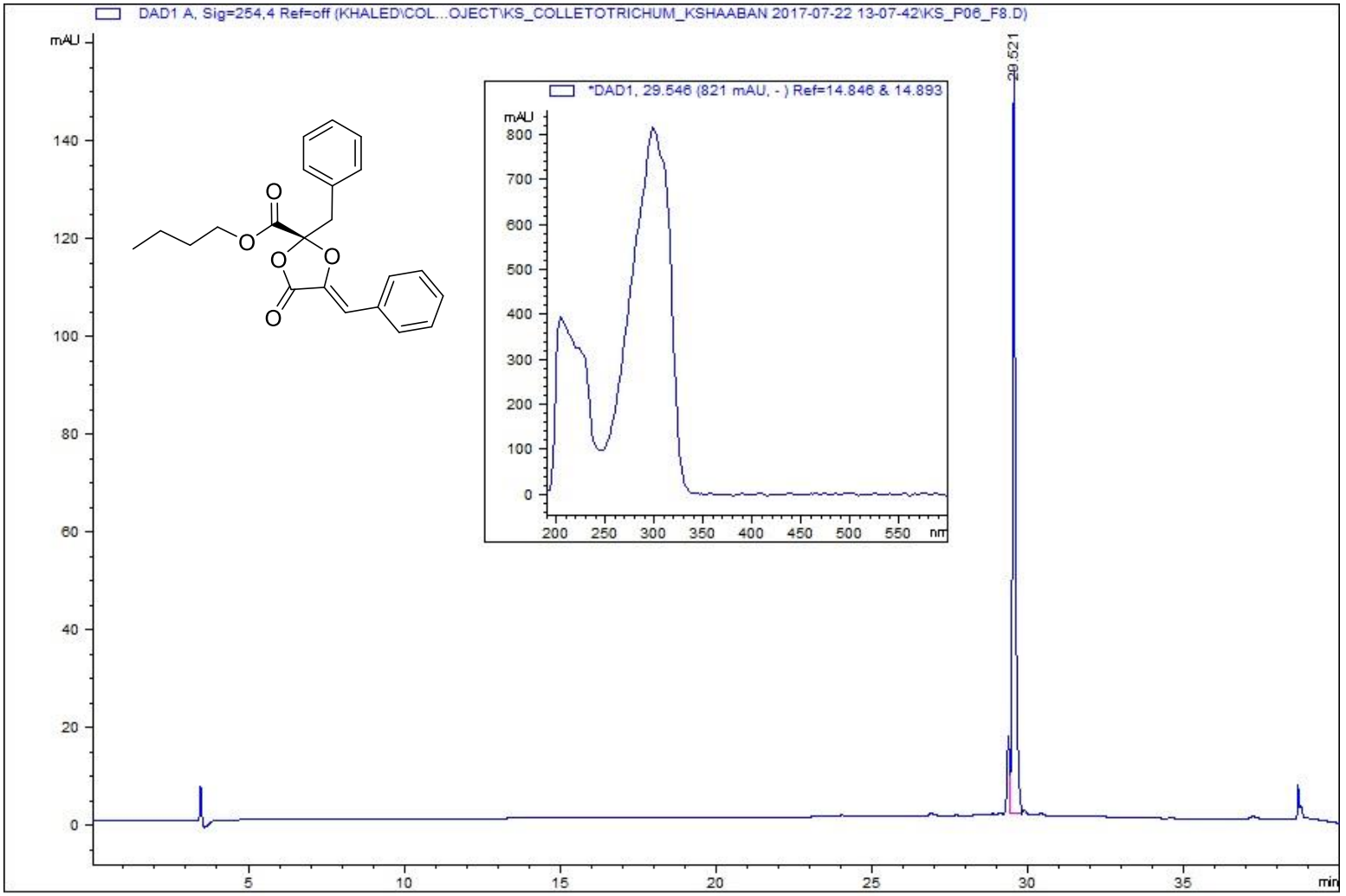



**Figure S5.** HPLC analysis of phenguignardic acid butyl ester (**1a**). HPLC-conditions: solvent A: $H_2O$/0.1% TFA; solvent B: $CH_3CN$; flow rate: 1.0 mL $min^{-1}$; 0-30 min, 5%-100% B; 30-35 min, 100% B; 35-36 min, 100%-5% B; 36-40 min, 5 % B; Phenomenex C18 column (250 × 4.6 mm, 5 $\mu$m); 254 nm. UV-VIS inset of full wavelength scan (190-600 nm).

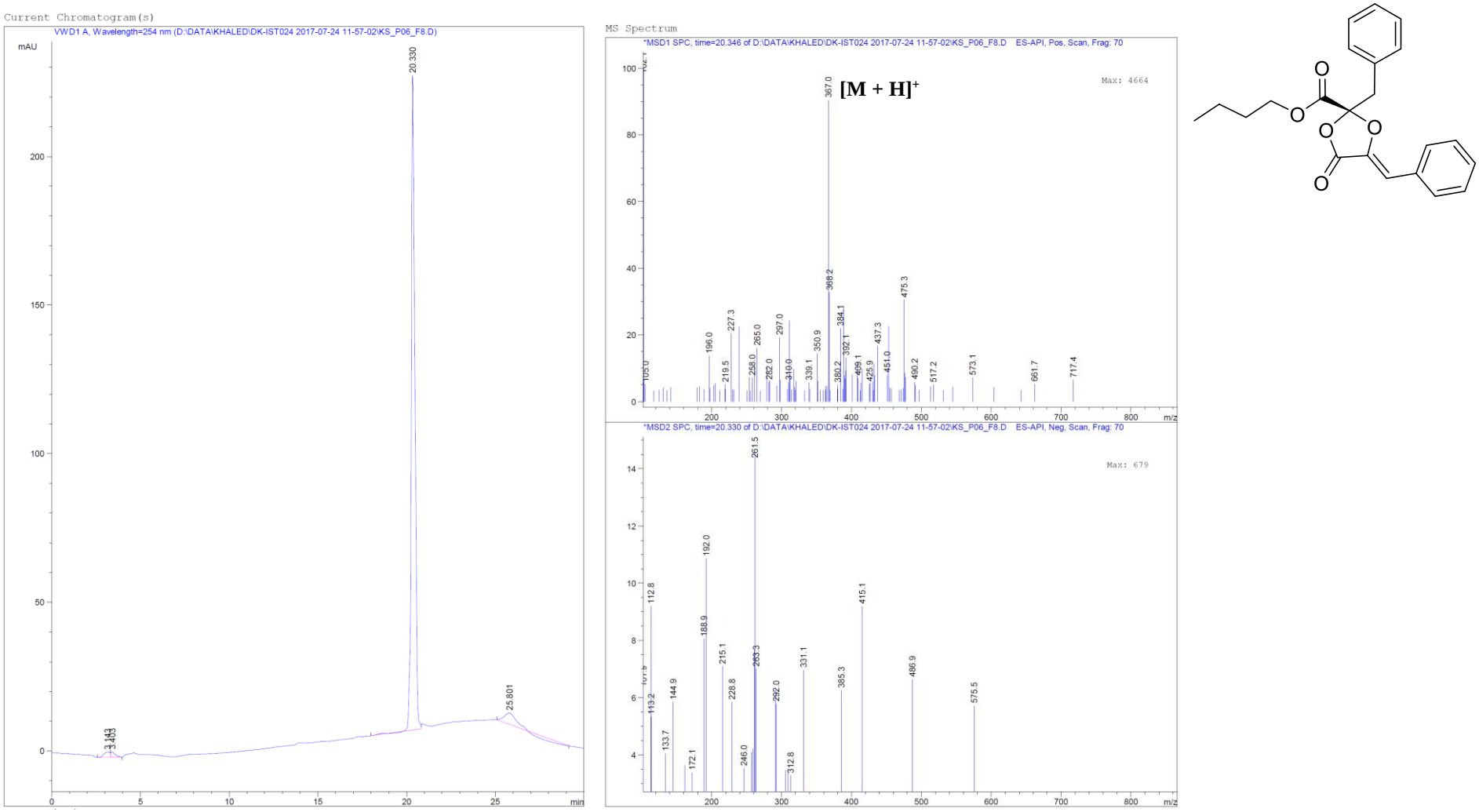



**Figure S6.** HPLC/MS analysis of phenguignardic acid butyl ester (**1a**). HPLC-conditions: solvent A: $H_2O$/0.1% formic acid, solvent B: $CH_3CN$/0.1% formic acid; flow rate: 0.5 mL $min^{-1}$; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-30 min, 10 % B; 254 nm.

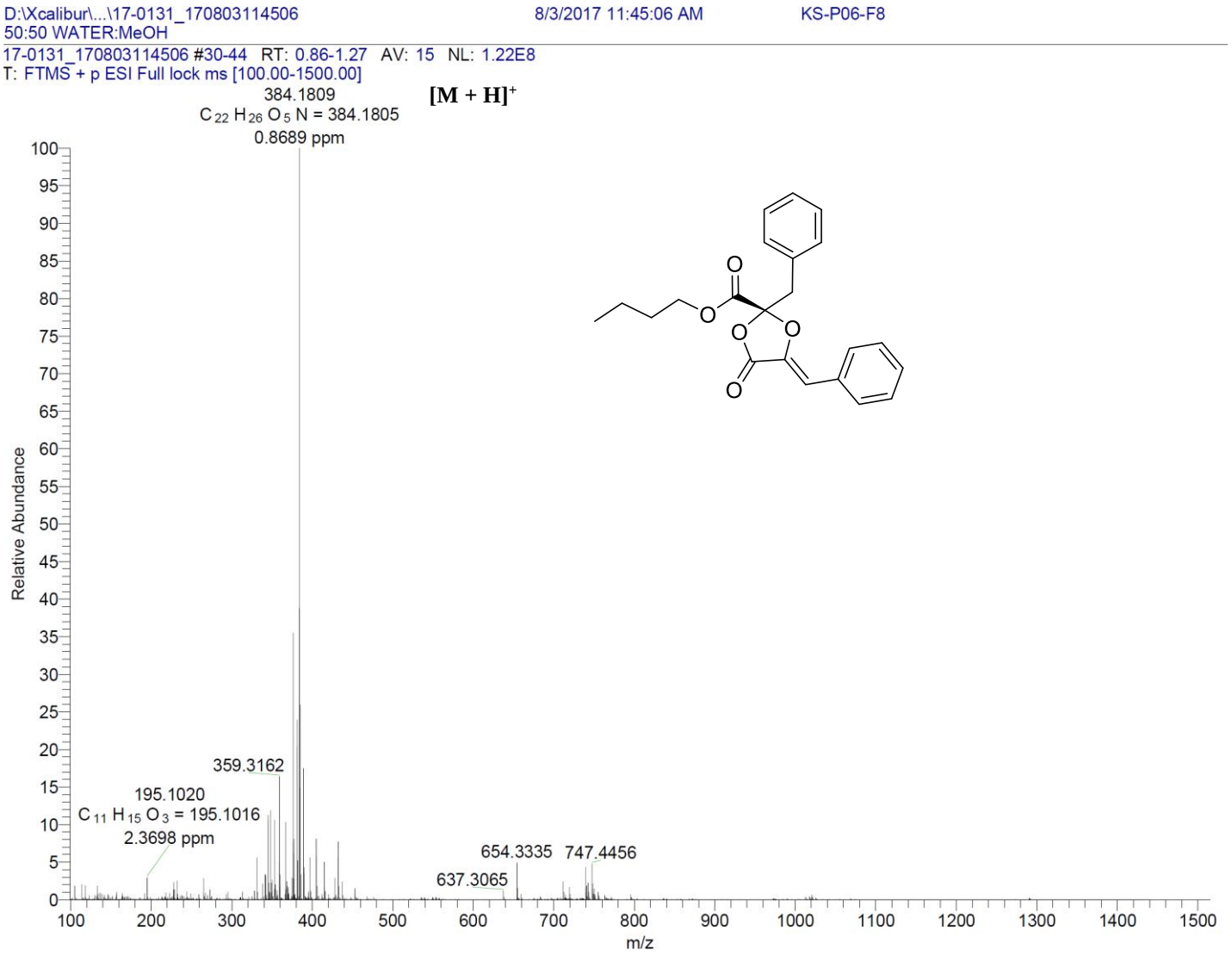



**Figure S7.** (+)-HRESI-MS spectrum of phenguignardic acid butyl ester (**1a**).

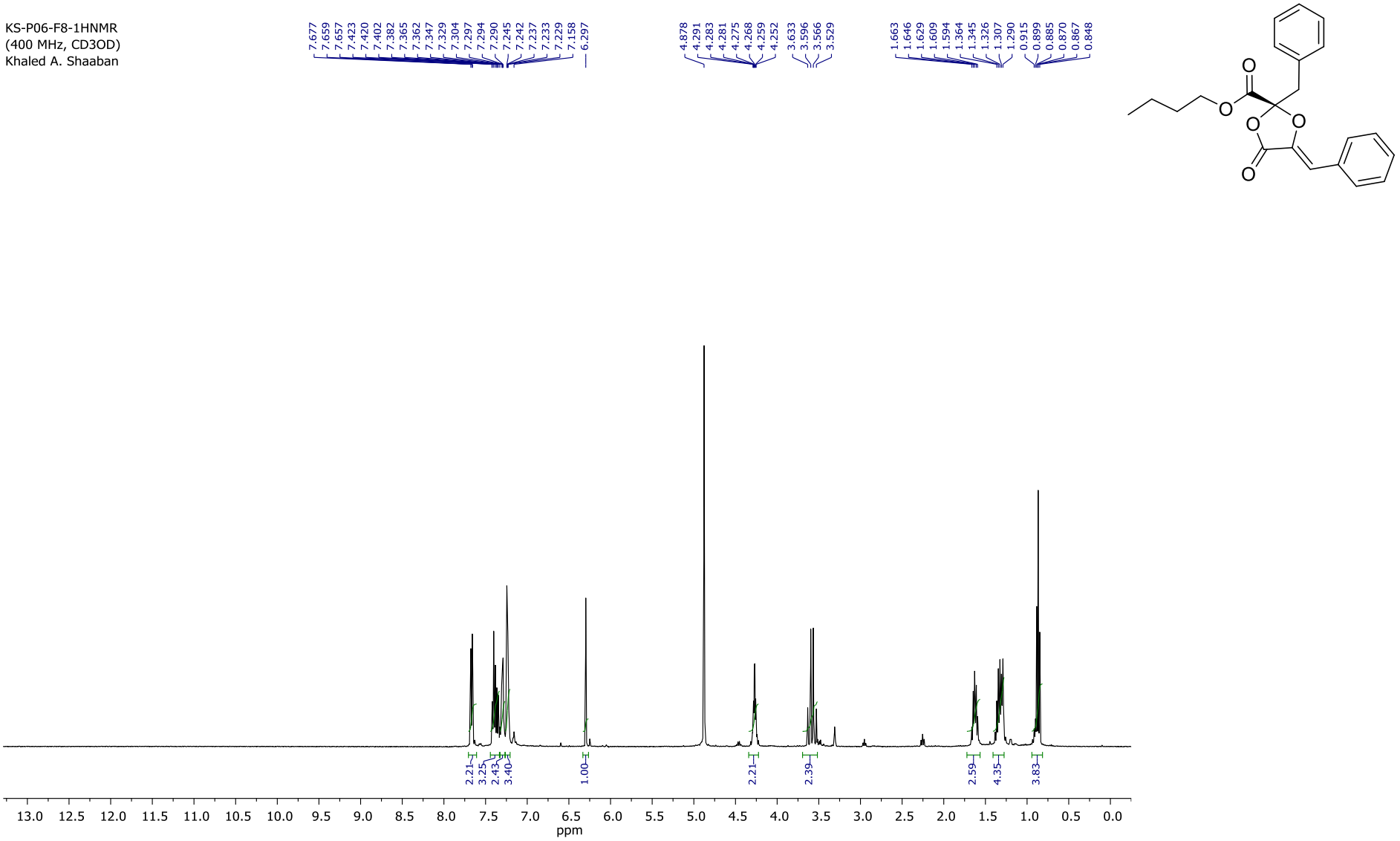



**Figure S8.** $^{1}H$ NMR spectrum ($CD_3OD$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

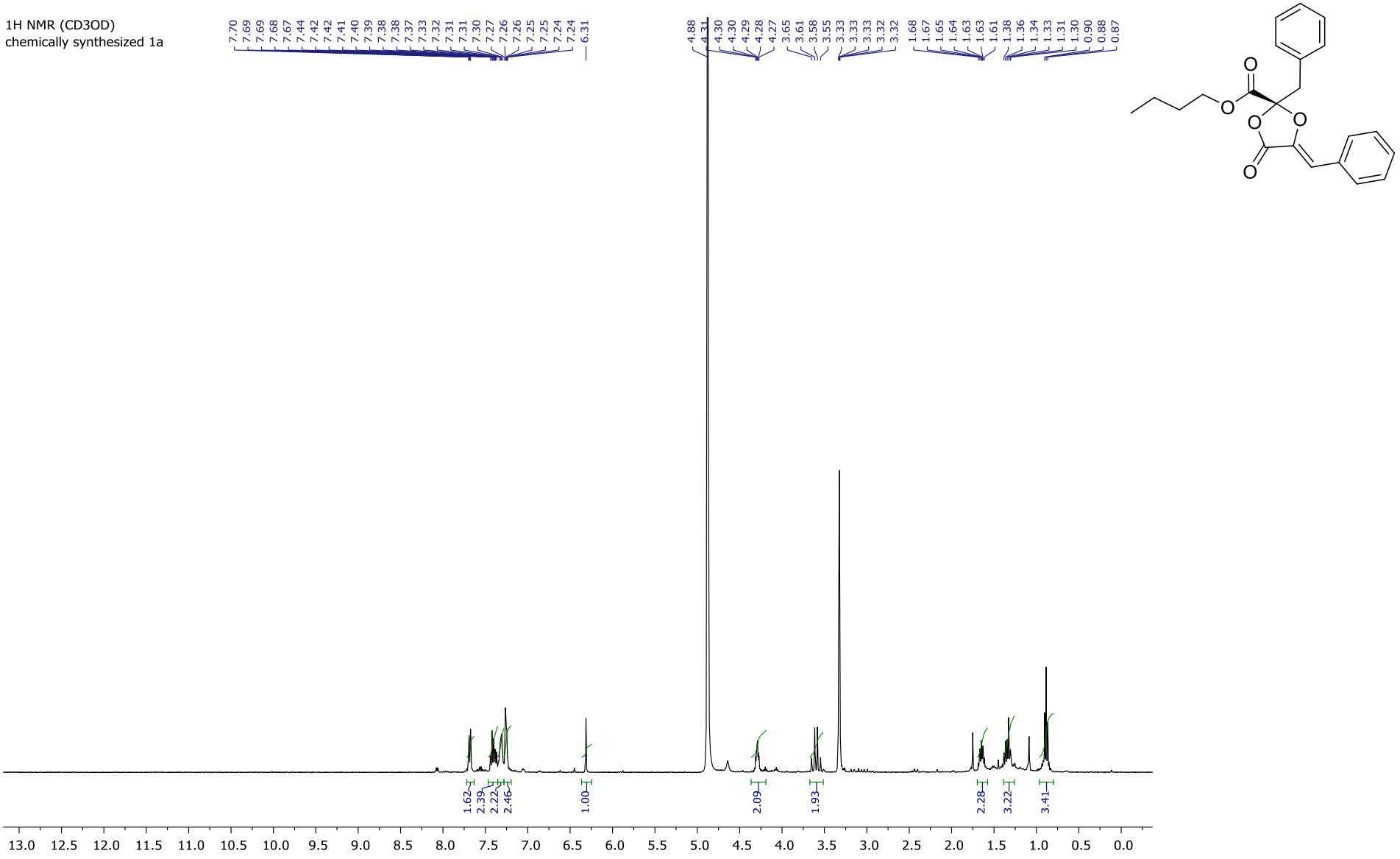



**Figure S9.** $^{1}$H NMR spectrum ($CD_3OD$, 400 MHz) of chemically synthesized phenguignardic acid butyl ester (**1a**).

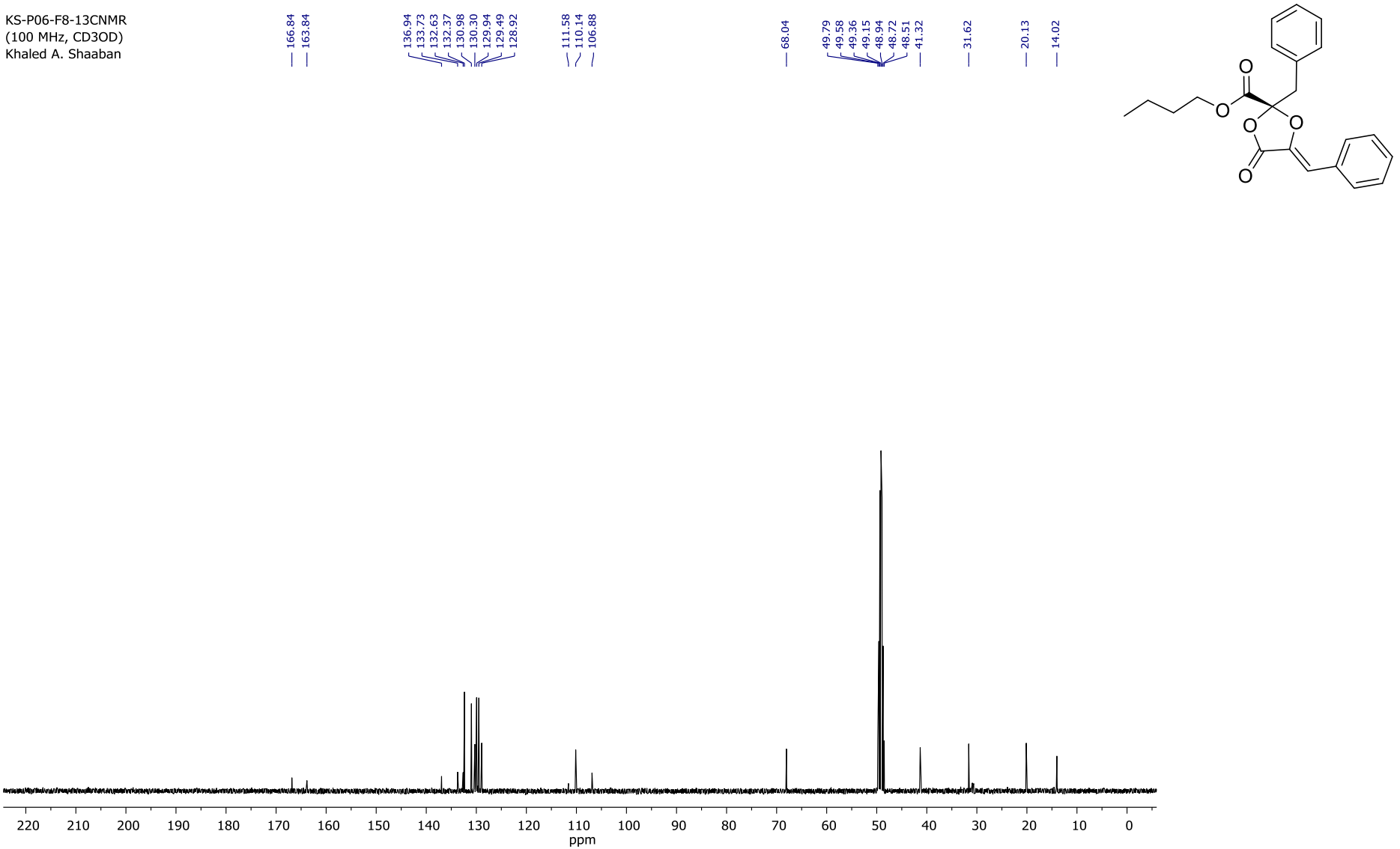



**Figure S10.** $^{13}C$ NMR spectrum ($CD_3OD$, 100 MHz) of phenguignardic acid butyl ester (**1a**).

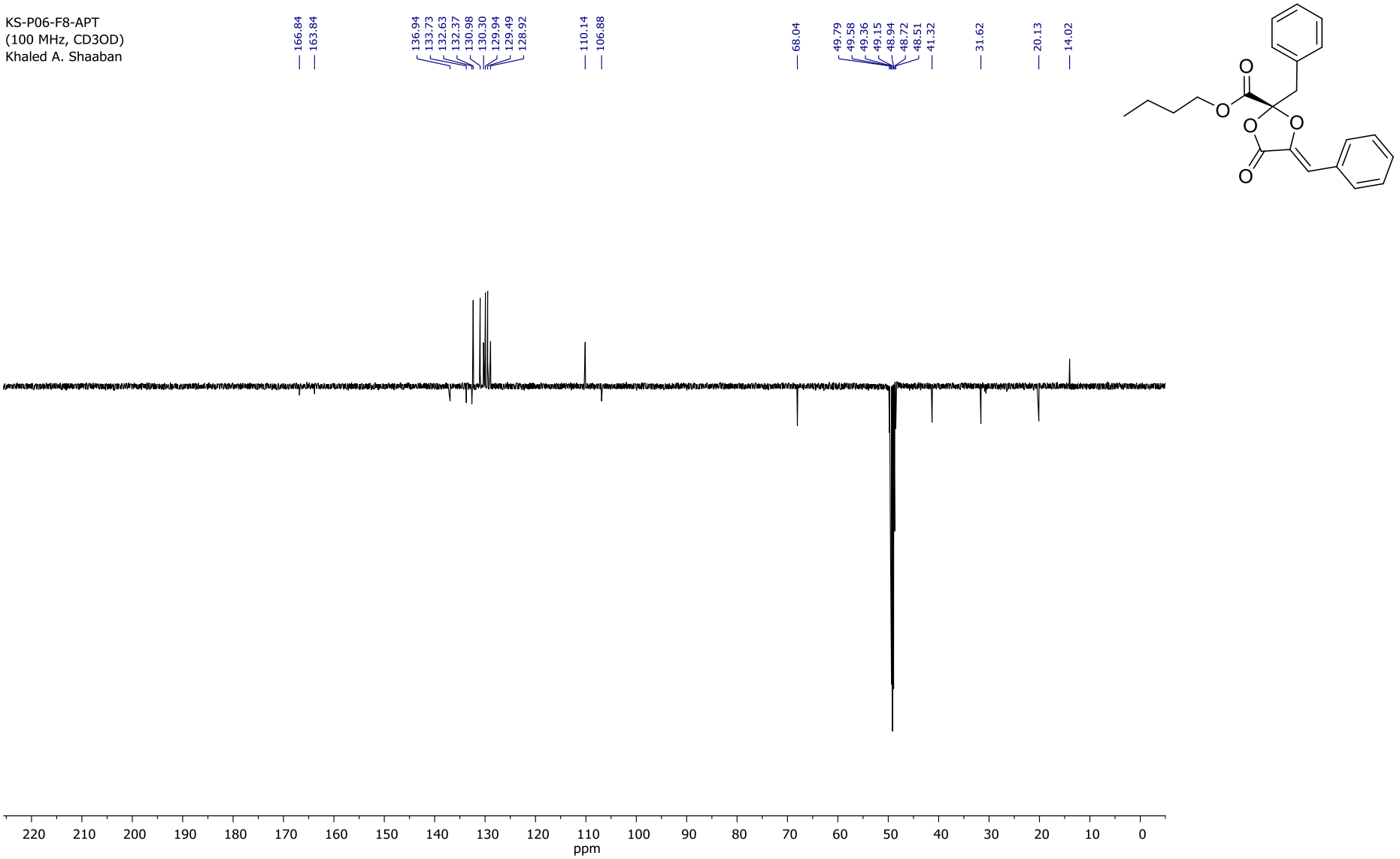



**Figure S11.** APT NMR spectrum ($CD_3OD$, 100 MHz) of phenguignardic acid butyl ester (**1a**).

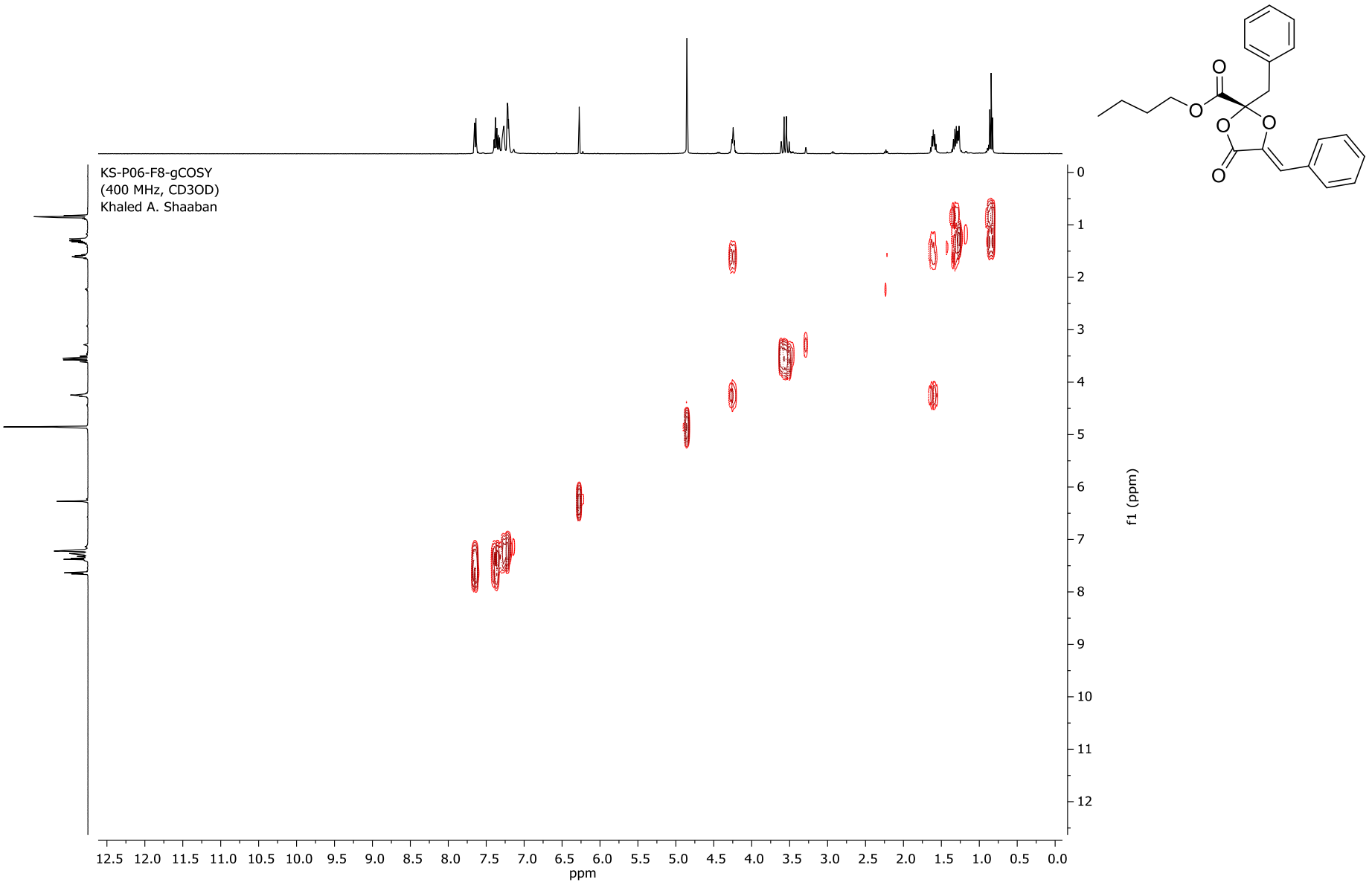



**Figure S12.** $^{1}H,^{1}H$-COSY spectrum ($CD_3OD$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

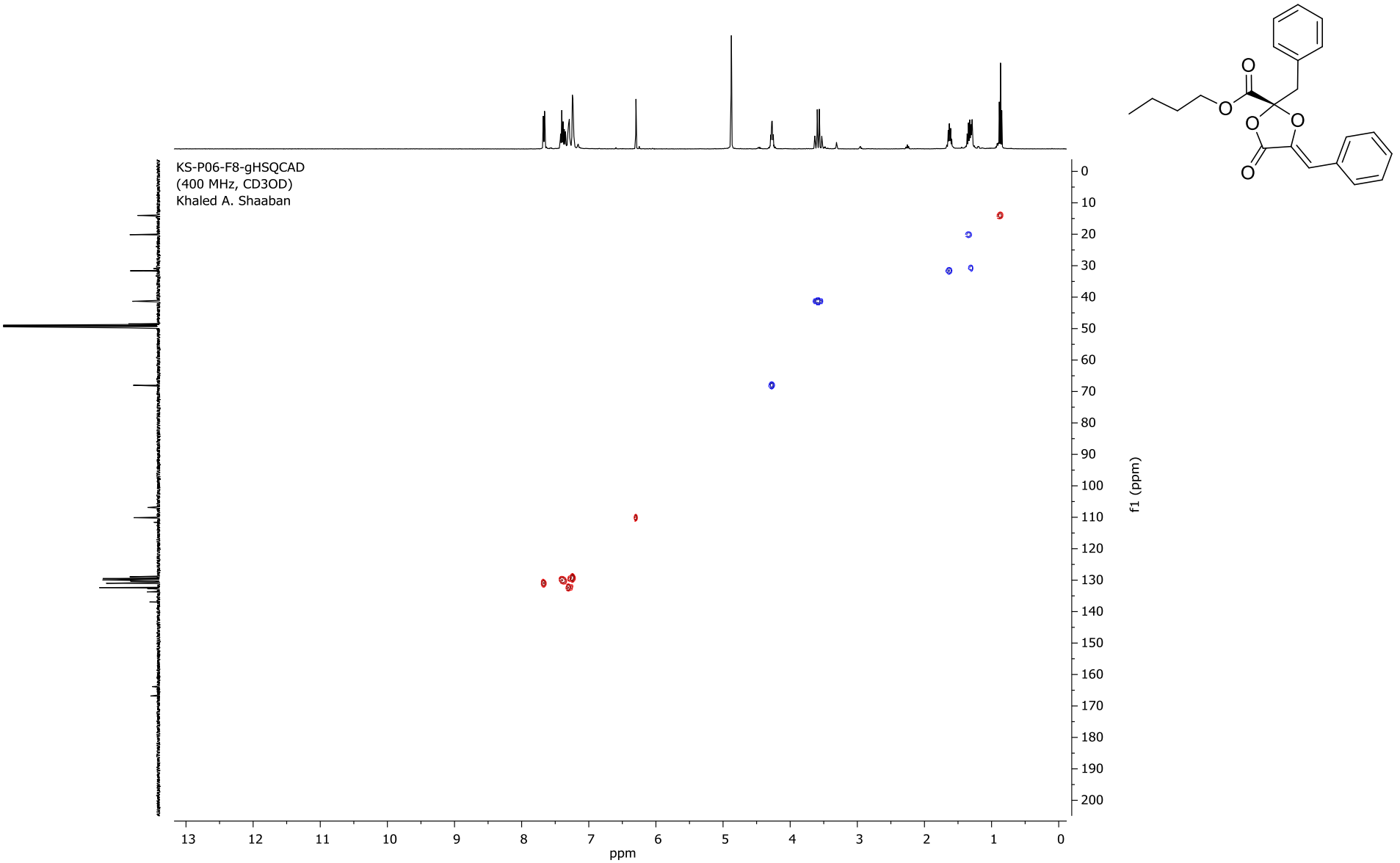



**Figure S13.** HSQC spectrum ($CD_3OD$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

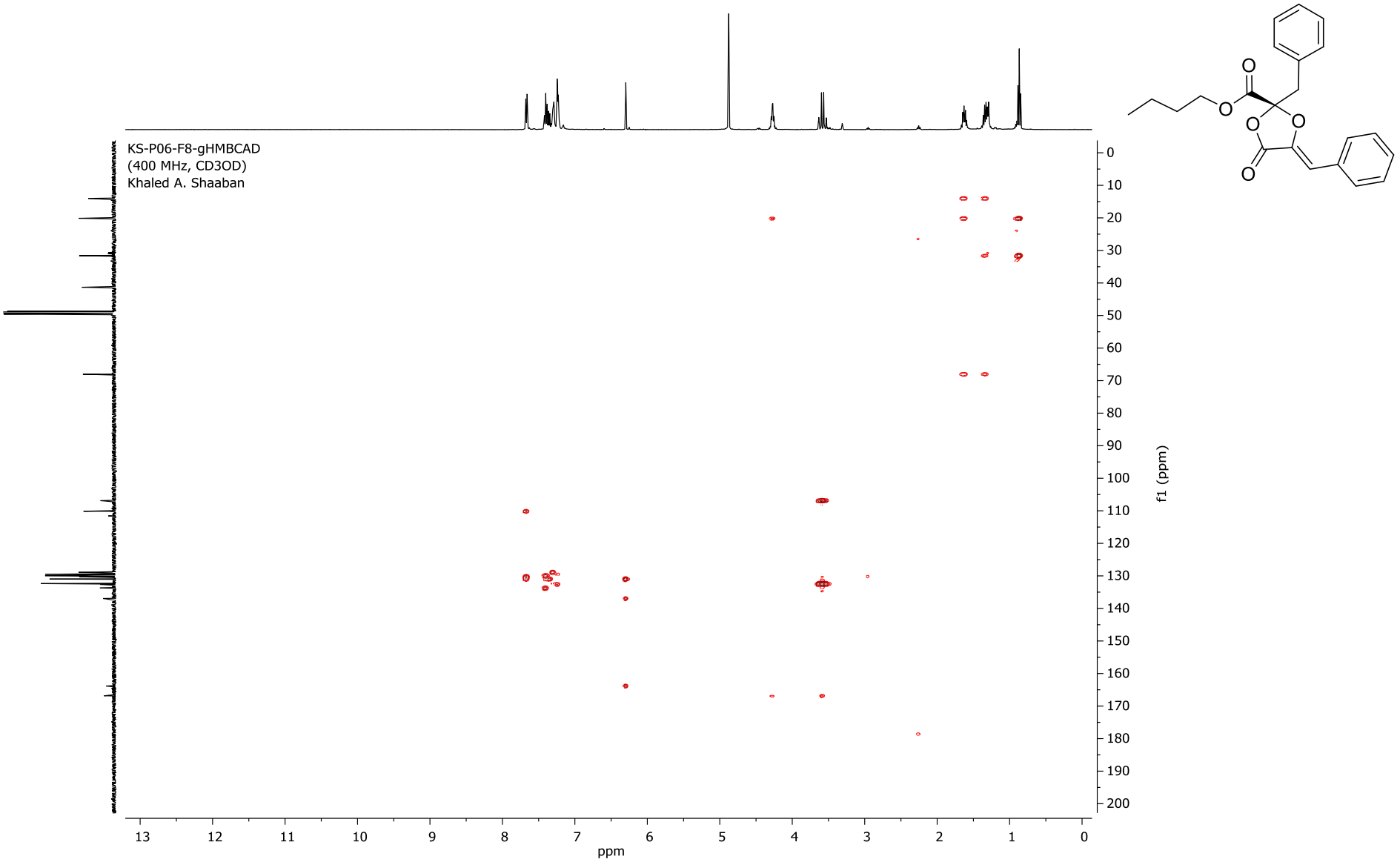



**Figure S14.** HMBC spectrum ($CD_3OD$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

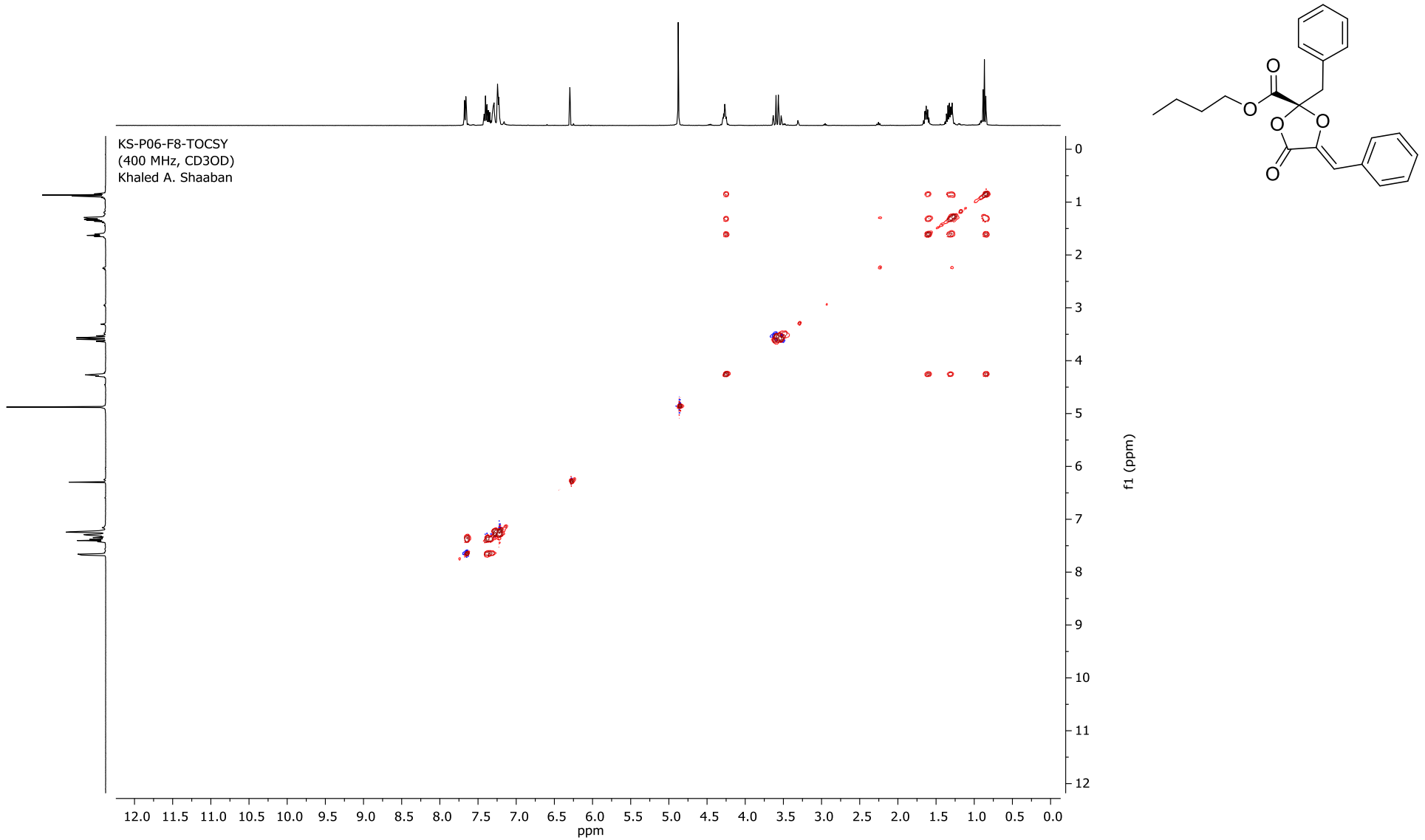



**Figure S15.** TOCSY spectrum ($CD_3OD$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

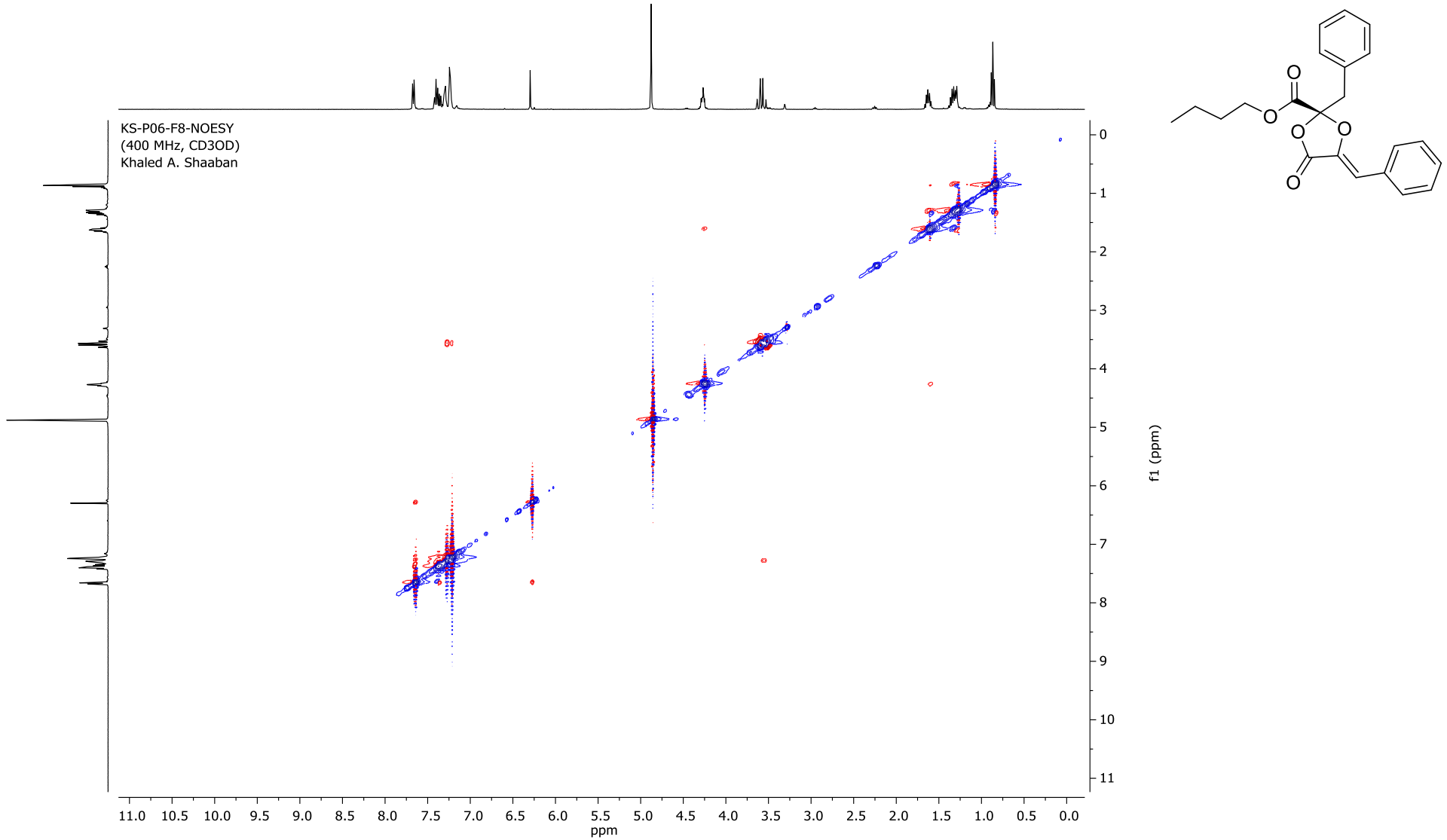
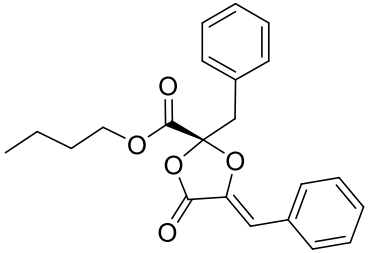



**Figure S16.** NOESY spectrum ($CD_3OD$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

KS-P06-F8-1HNMR
(400 MHz, CDCl3)
Khaled A. Shaaban



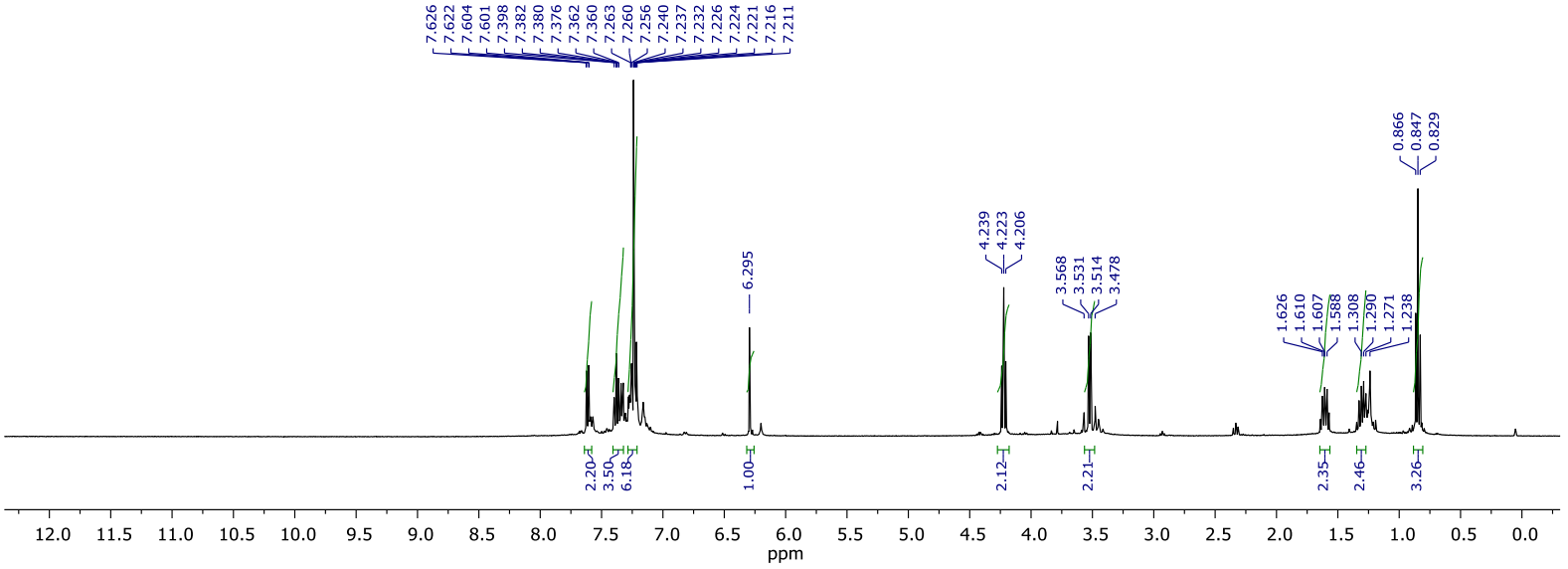
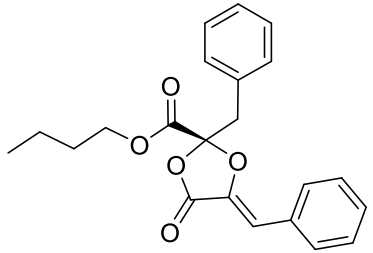



**Figure S17.** $^{1}H$ NMR spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

KS-P06-F8-13CNMR
(100 MHz, CDCl3)
Khaled A. Shaaban



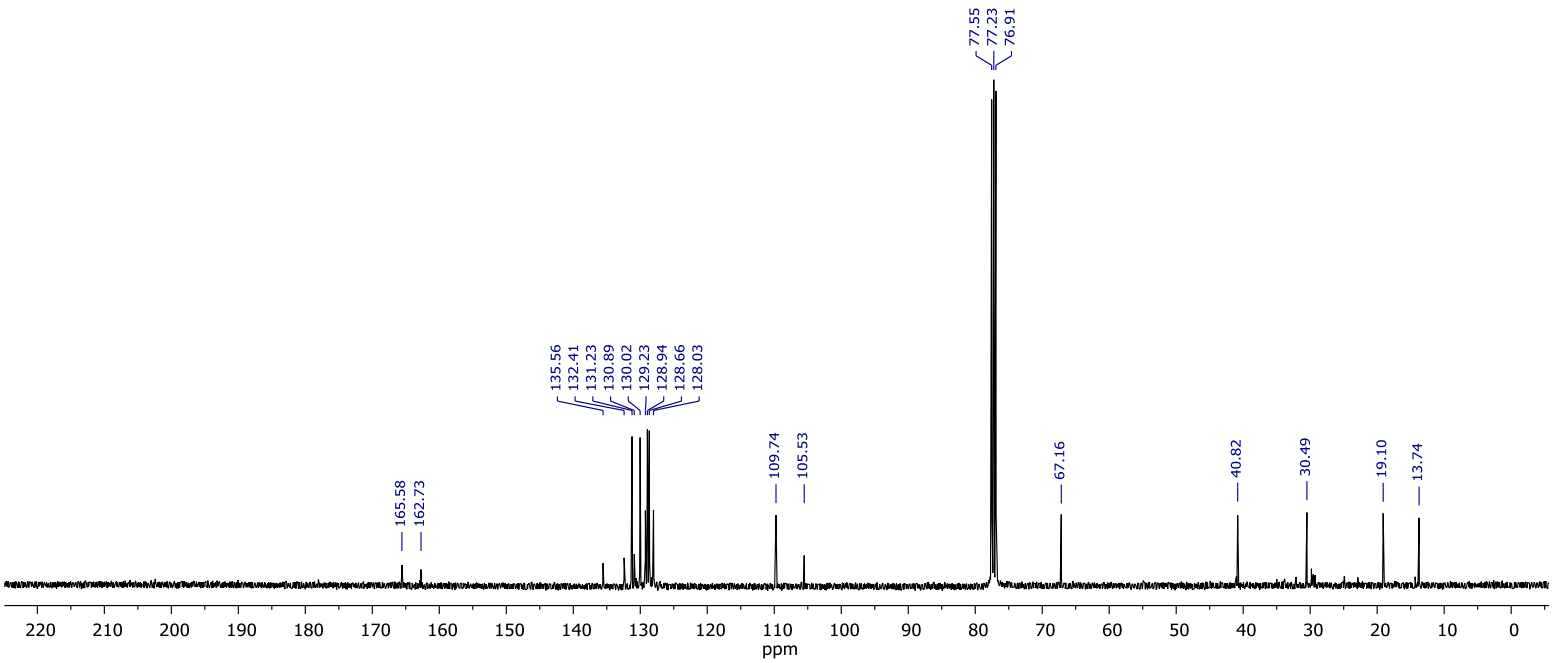



**Figure S18.** $^{13}C$ NMR spectrum ($CDCl_3$, 100 MHz) of phenguignardic acid butyl ester (**1a**).

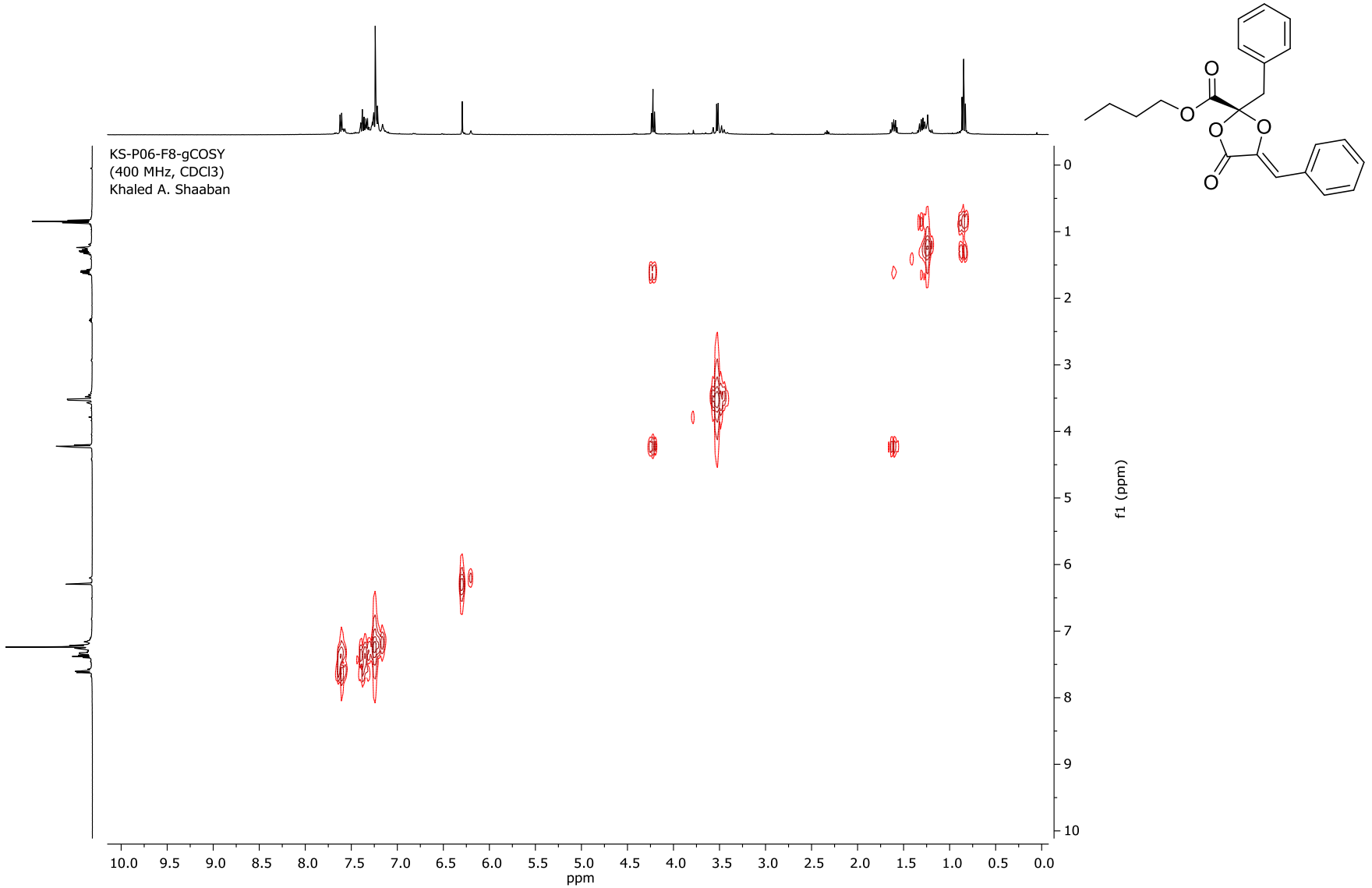



**Figure S19.** $^{1}H,^{1}H$-COSY spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

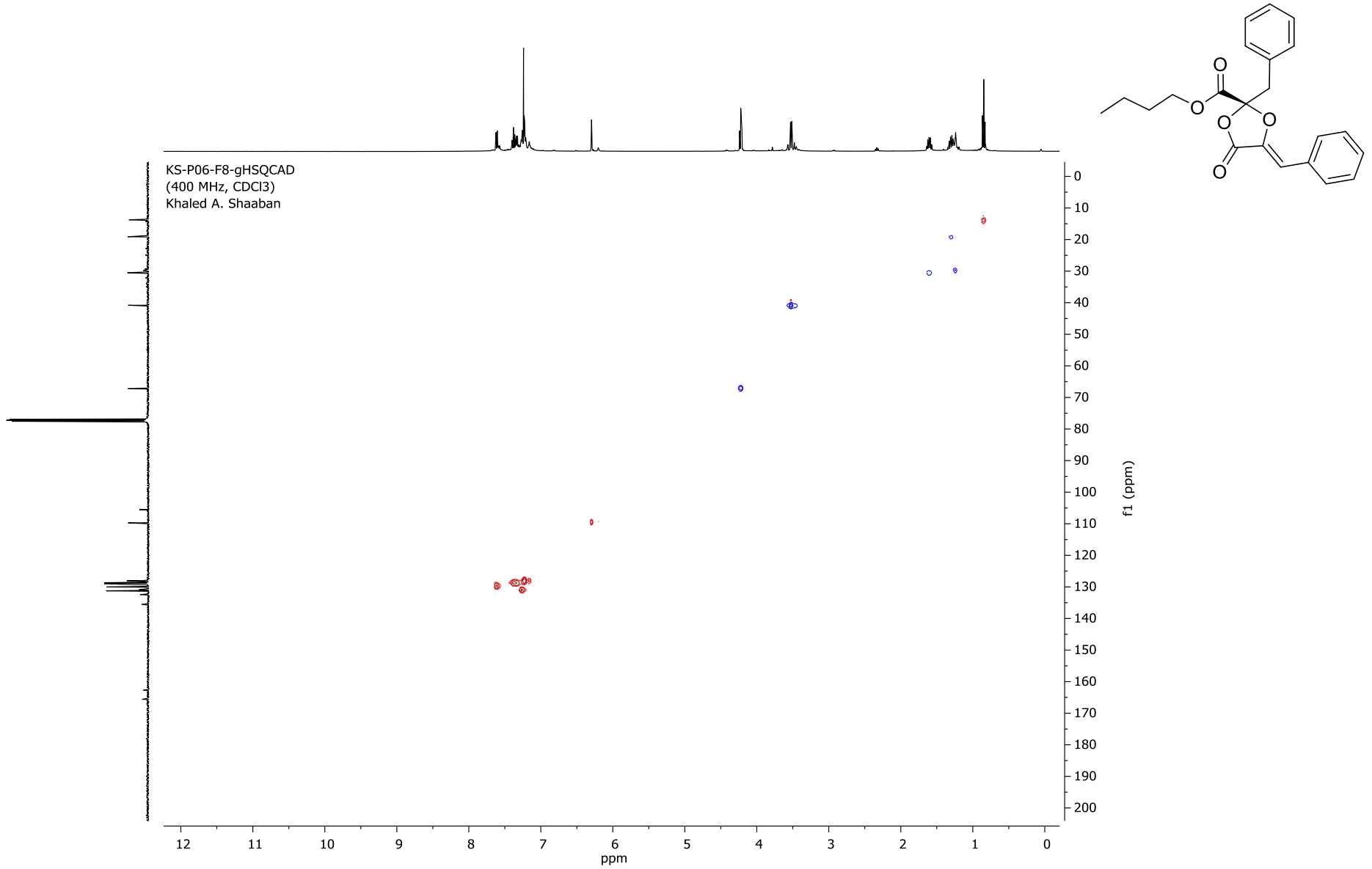



**Figure S20.** HSQC spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

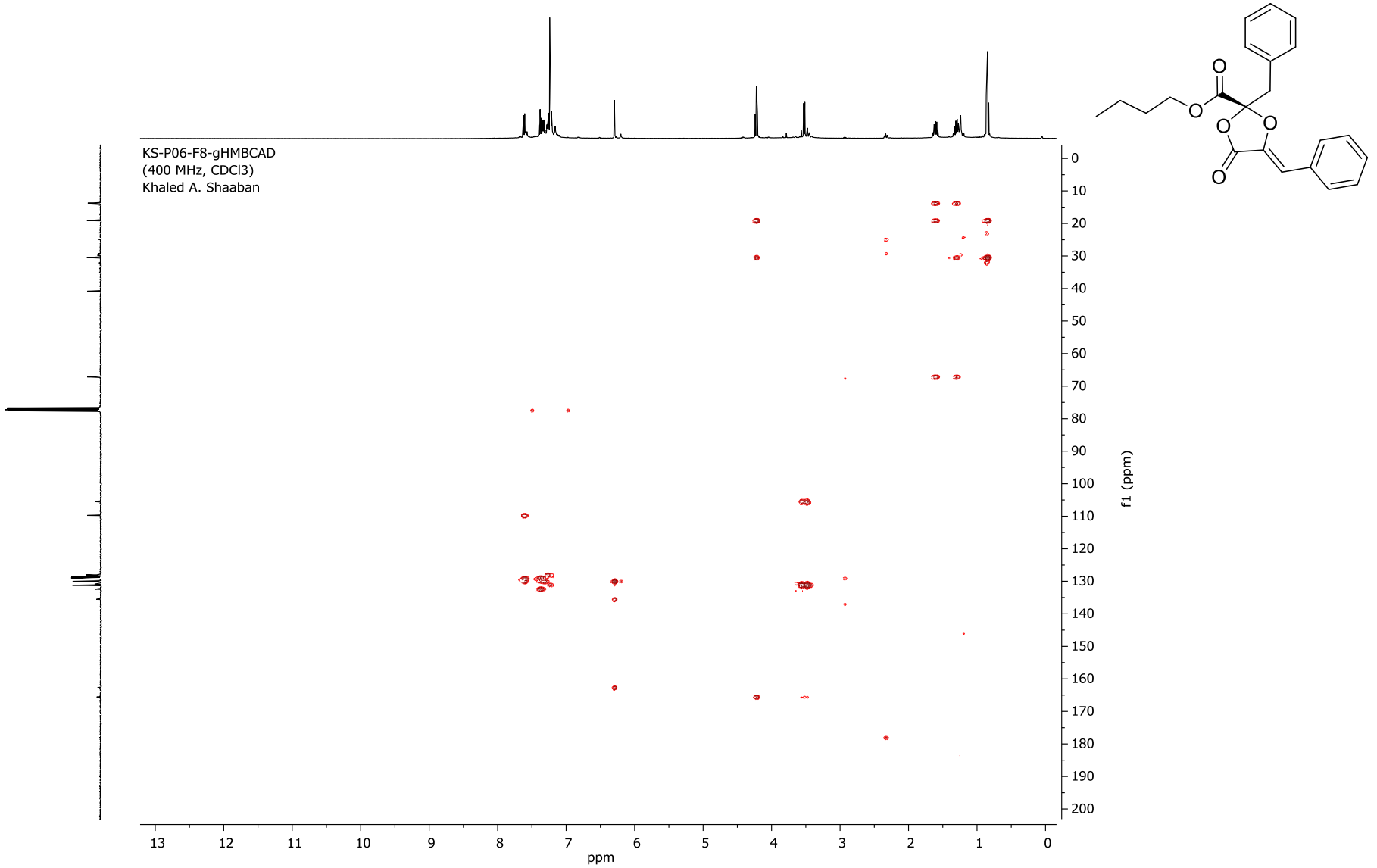



**Figure S21.** HMBC spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid butyl ester (**1a**).

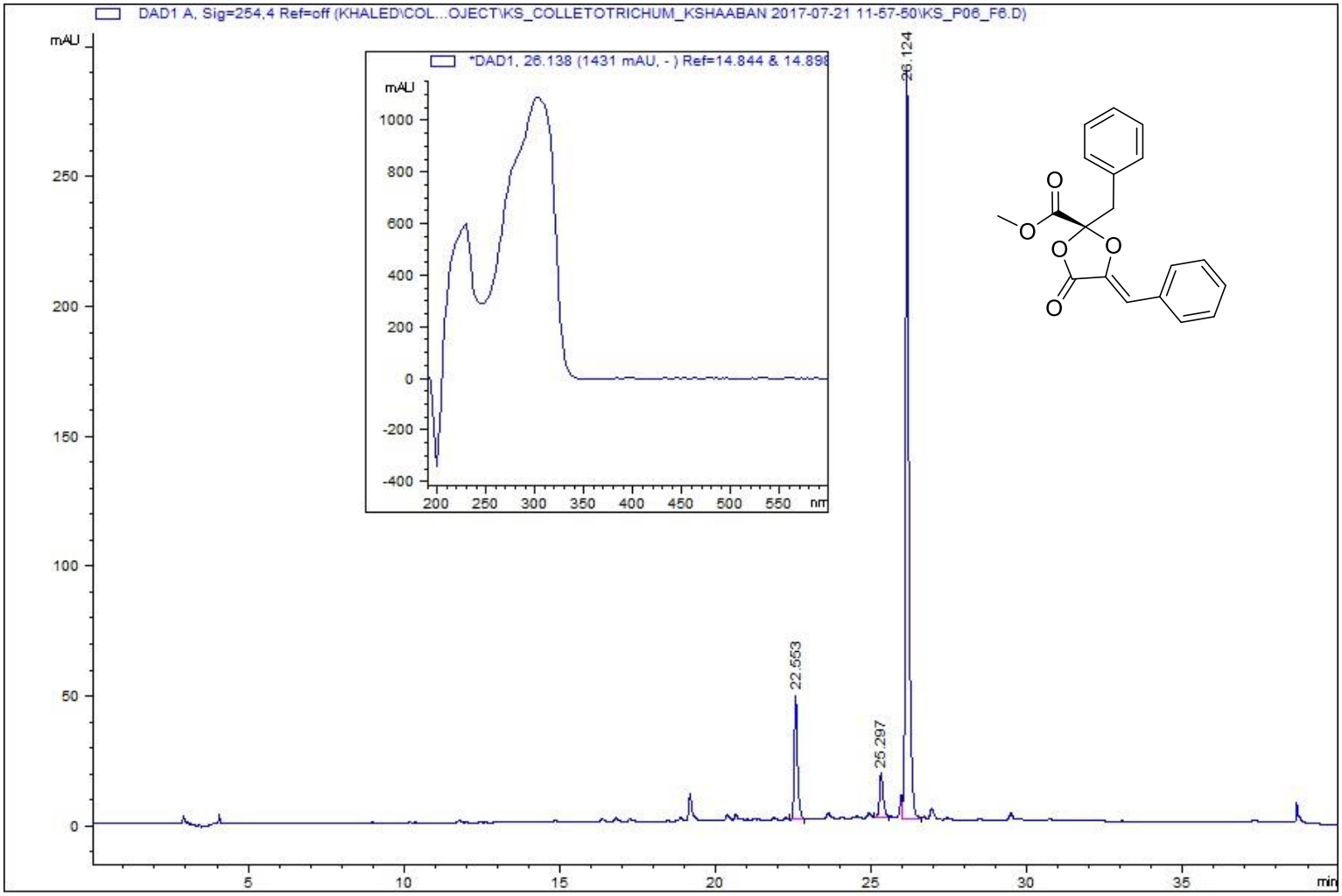



**Figure S22.** HPLC analysis of phenguignardic acid methyl ester (**1b**). HPLC-conditions: solvent A: $H_2O$/0.1% TFA; solvent B: $CH_3CN$; flow rate: 1.0 mL $min^{-1}$; 0-30 min, 5%-100% B; 30-35 min, 100% B; 35-36 min, 100%-5% B; 36-40 min, 5 % B; Phenomenex C18 column (250 × 4.6 mm, 5 $\mu$m); 254 nm. UV-VIS inset of full wavelength scan (190-600 nm).

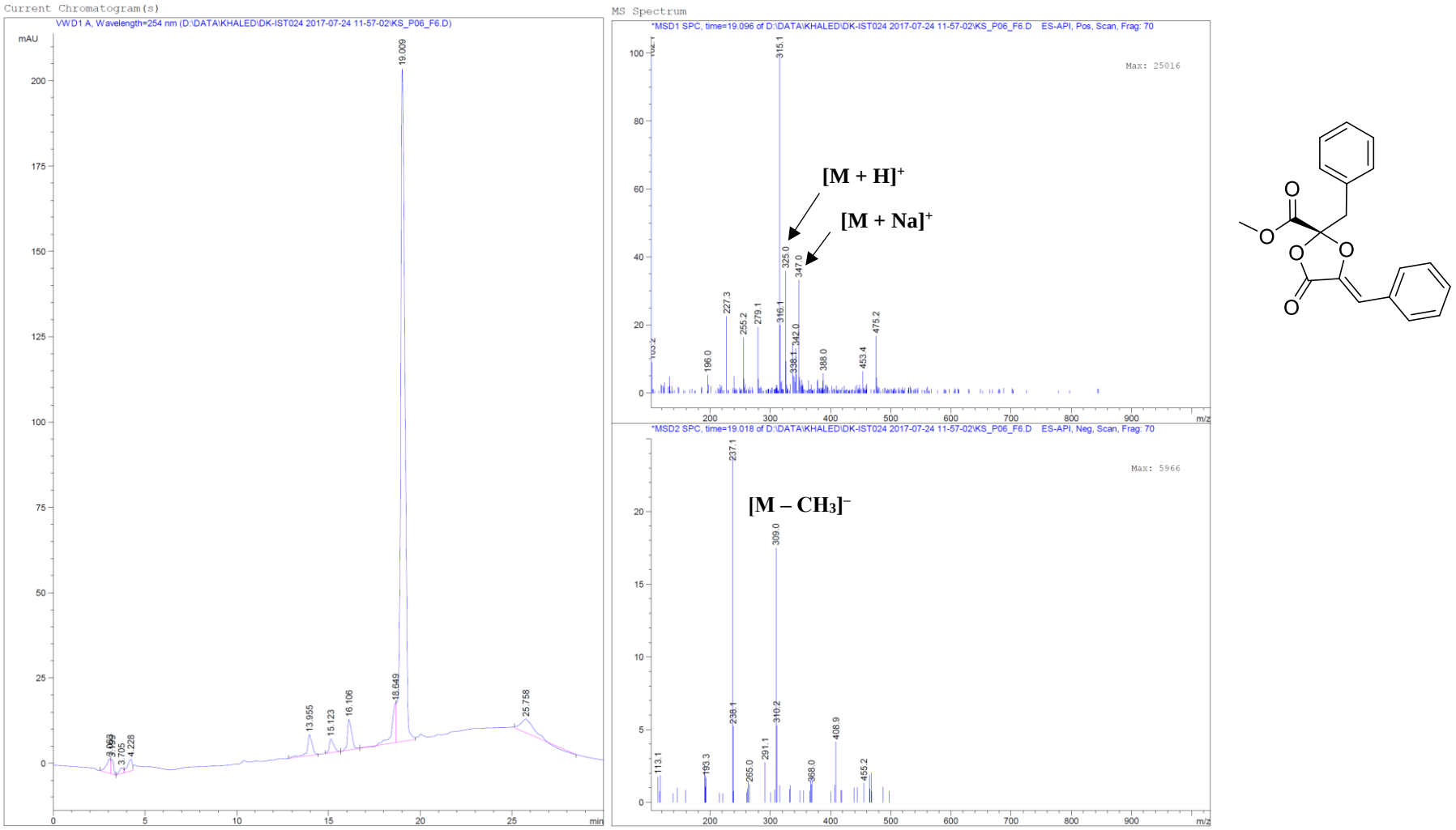



**Figure S23.** HPLC/MS analysis of phenguignardic acid methyl ester (**1b**). HPLC-conditions: solvent A: $H_2O$/0.1% formic acid, solvent B: $CH_3CN$/0.1% formic acid; flow rate: 0.5 mL $min^{-1}$; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-30 min, 10 % B; 254 nm.

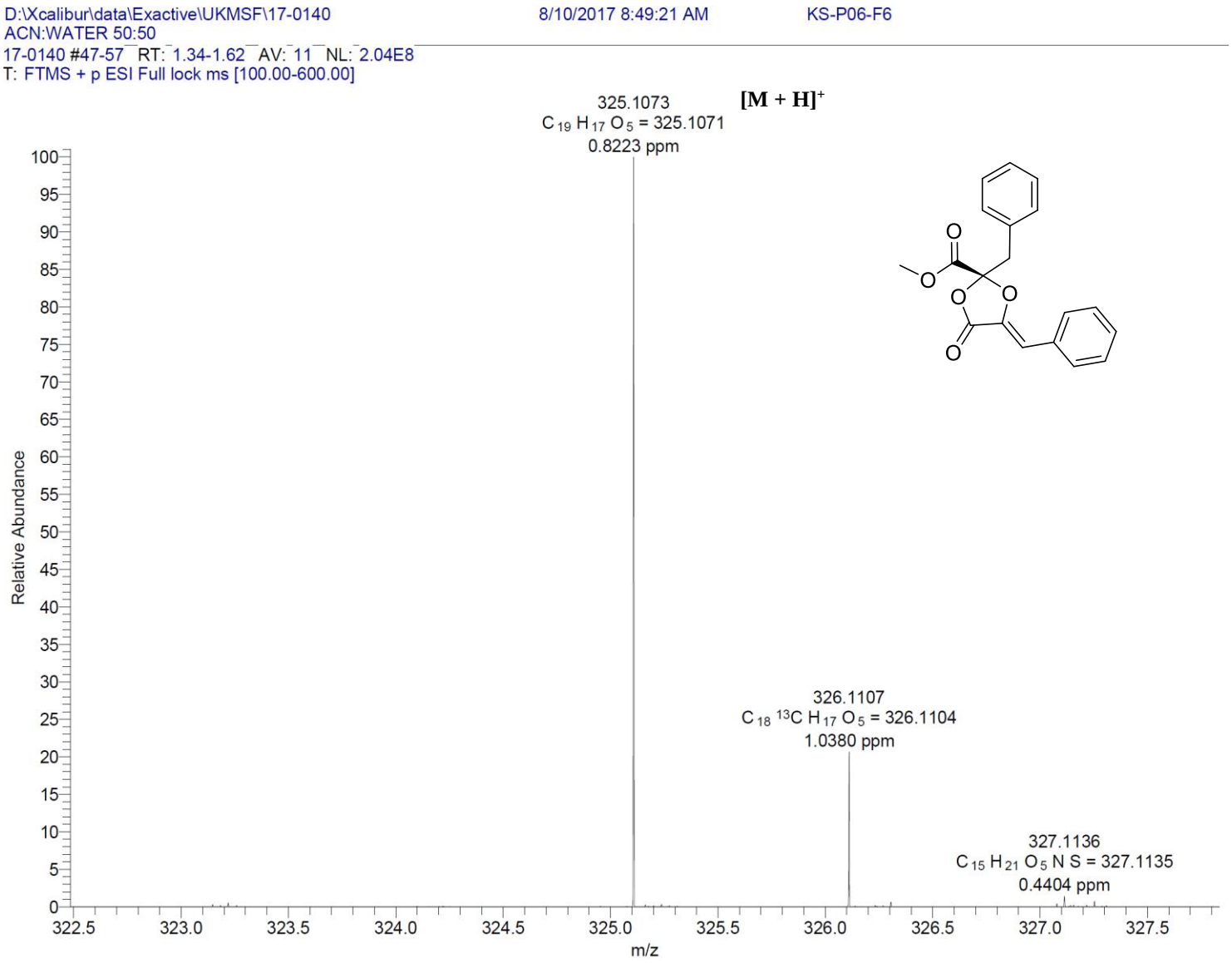



**Figure S24.** (+)-HRESI-MS spectrum of phenguignardic acid methyl ester (**1b**).

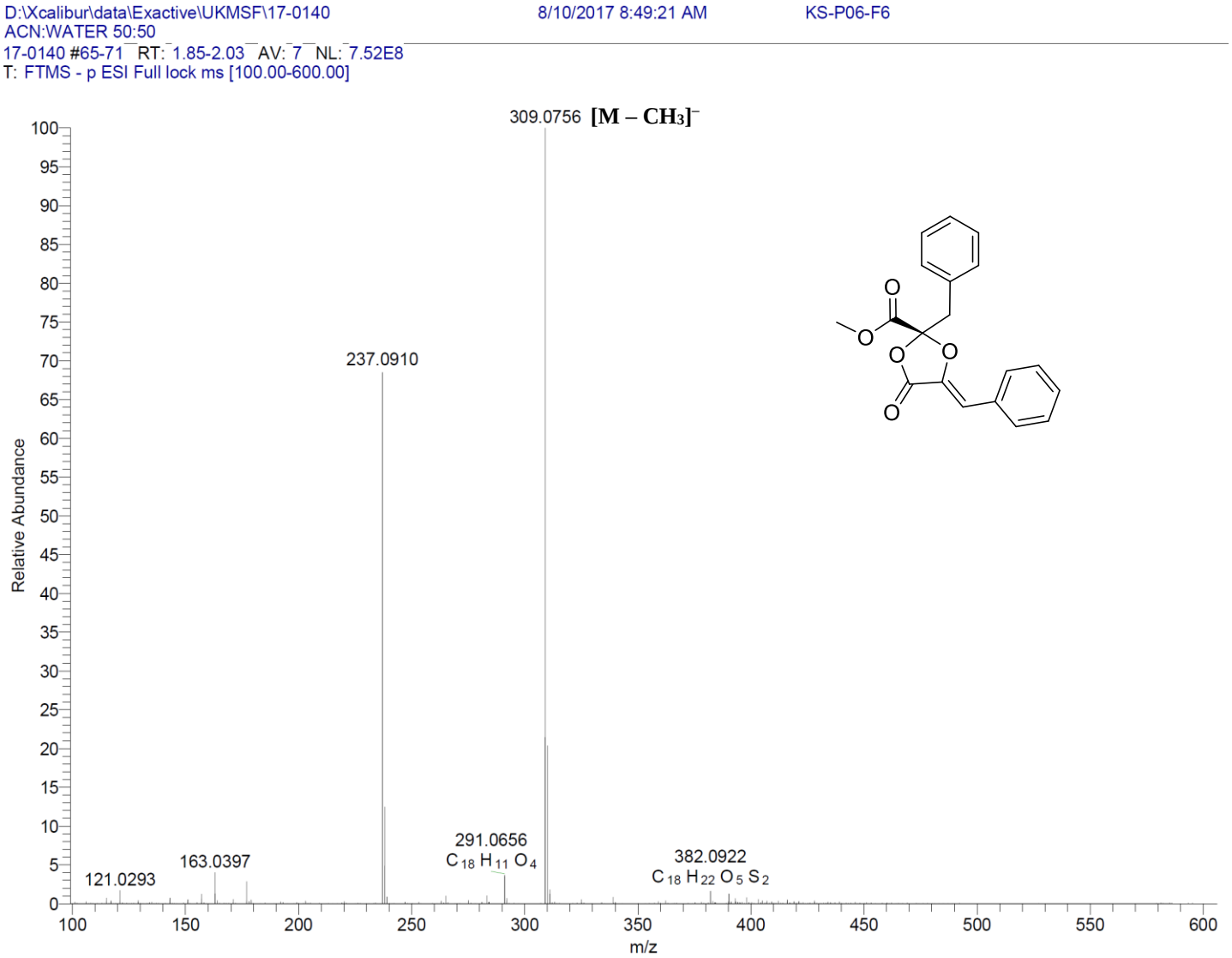



**Figure S25.** (–)-HRESI-MS spectrum of phenguignardic acid methyl ester (**1b**).

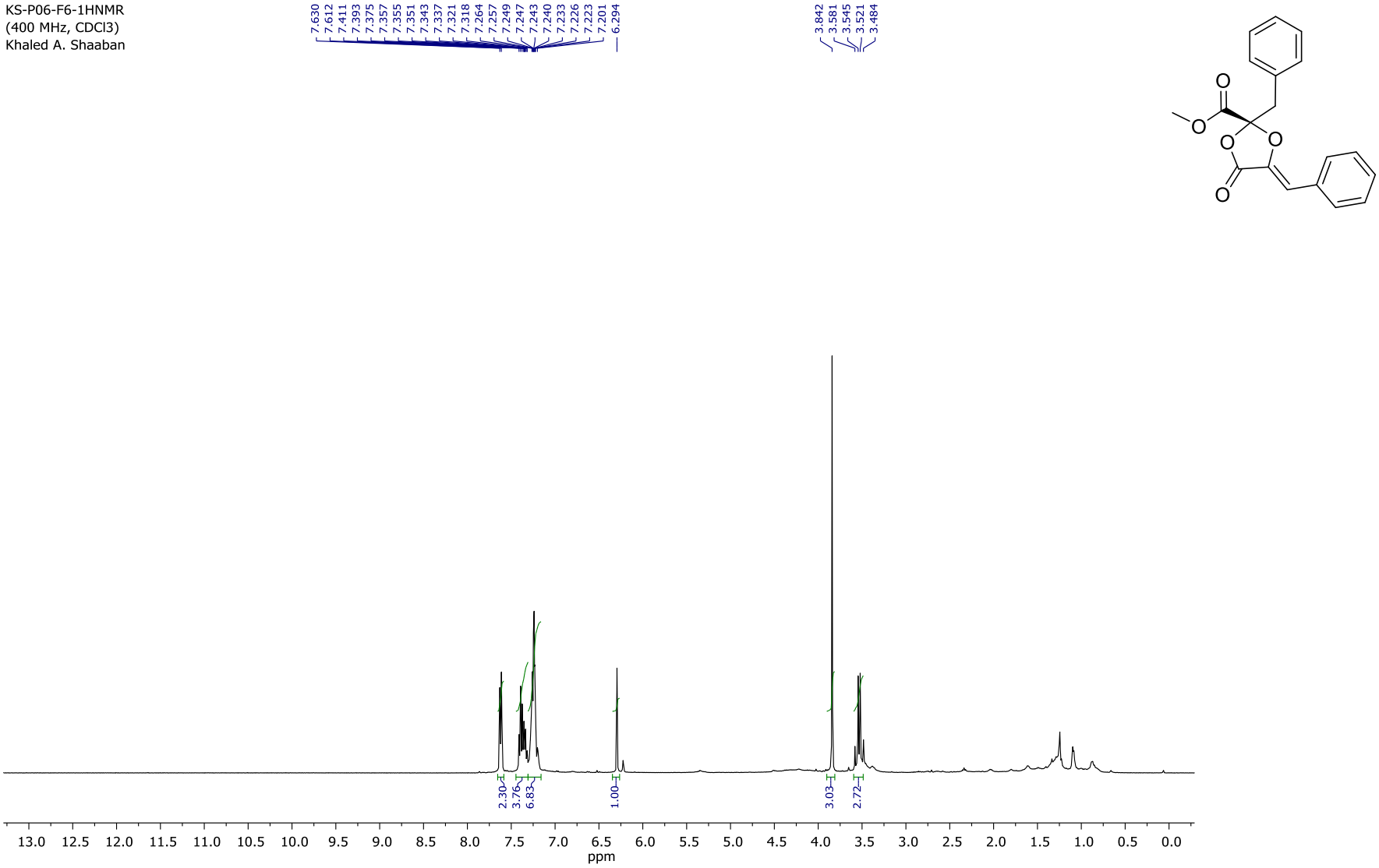



**Figure S26.** $^{1}$H NMR spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid methyl ester (**1b**).

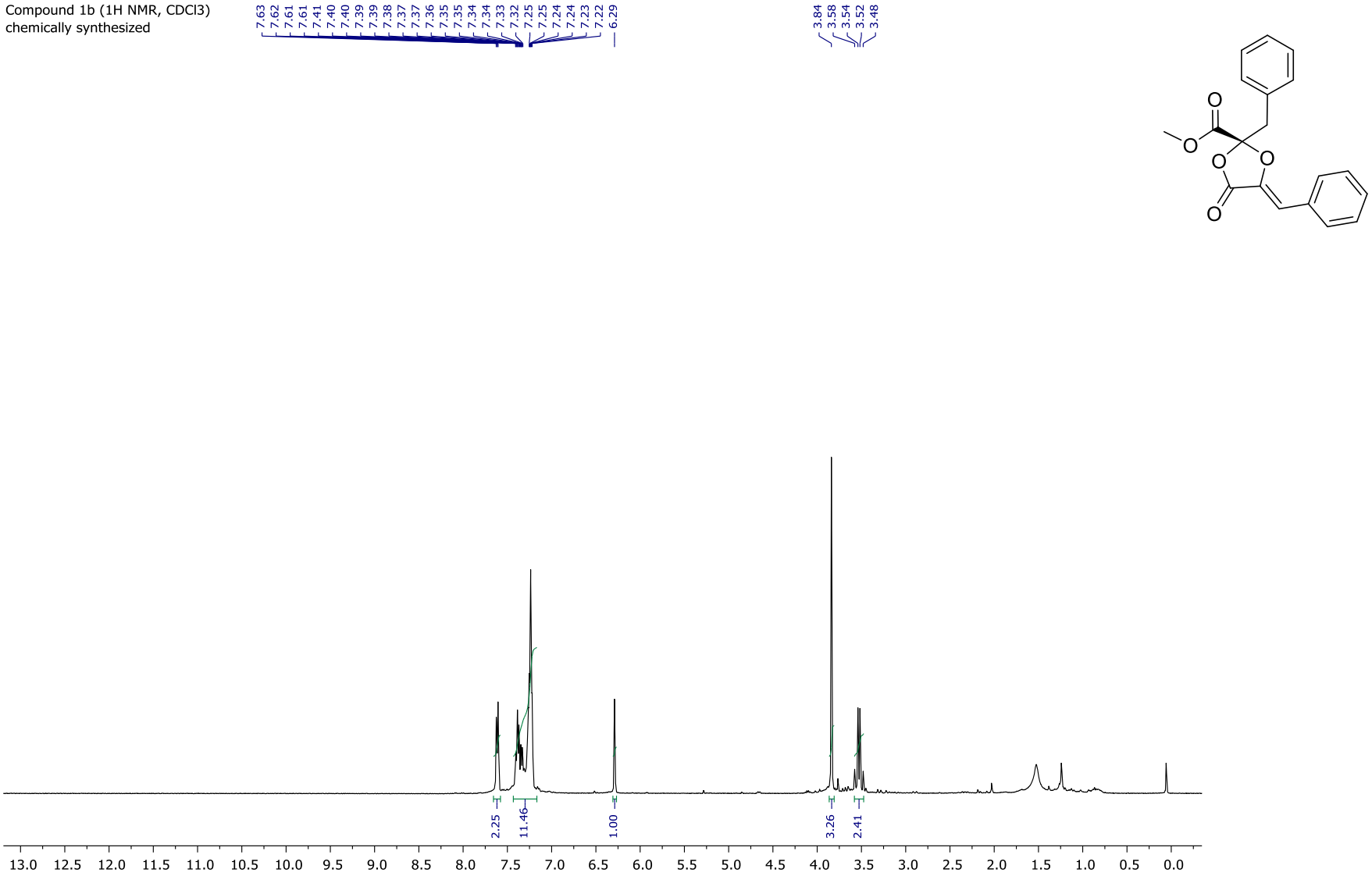



**Figure S27.** $^{1}$H NMR spectrum ($CDCl_3$, 400 MHz) of chemically synthesized phenguignardic acid methyl ester (**1b**).

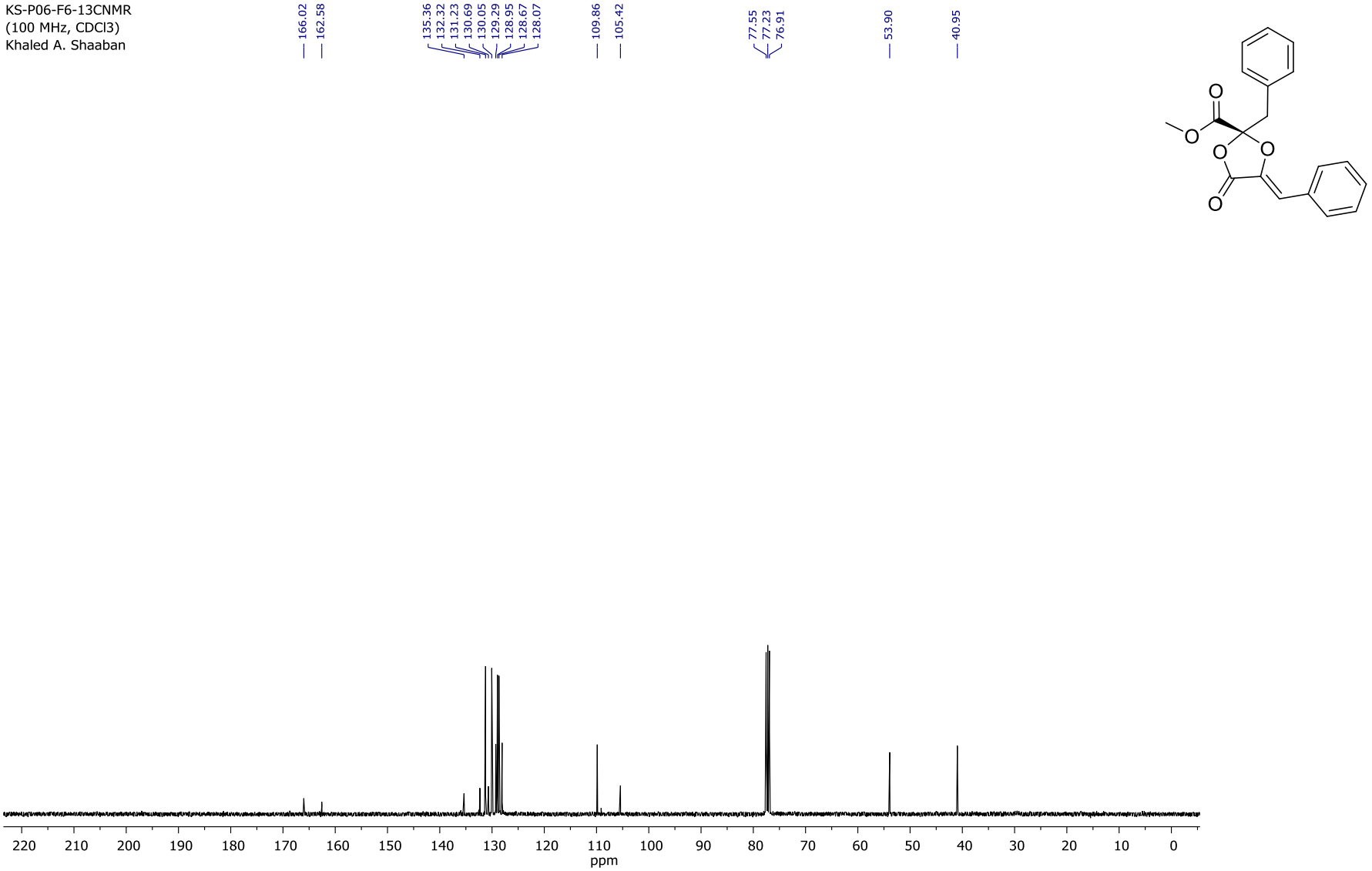



**Figure S28.** $^{13}C$ NMR spectrum ($CDCl_3$, 100 MHz) of phenguignardic acid methyl ester (**1b**).

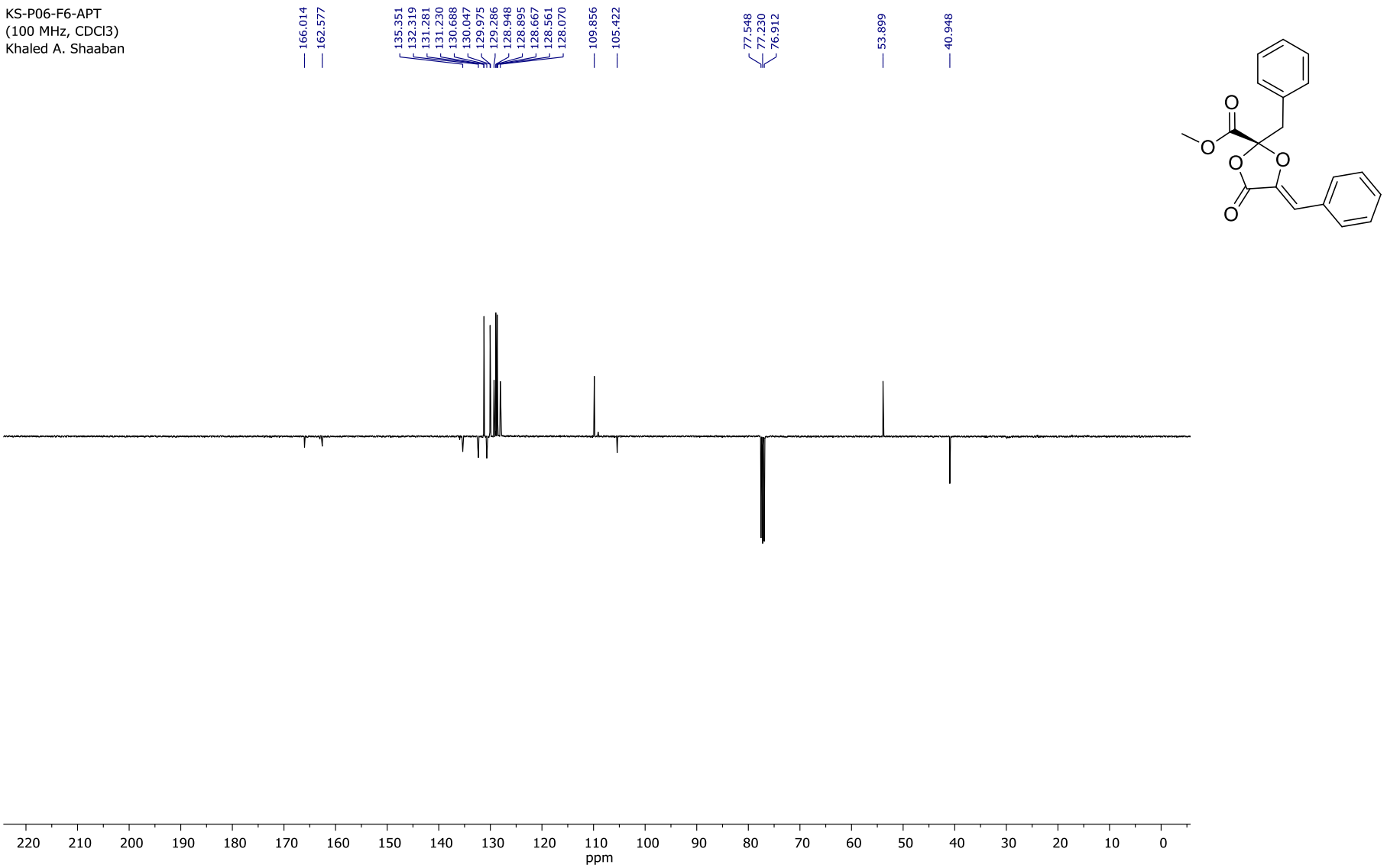



**Figure S29.** APT NMR spectrum ($CDCl_3$, 100 MHz) of phenguignardic acid methyl ester (**1b**).

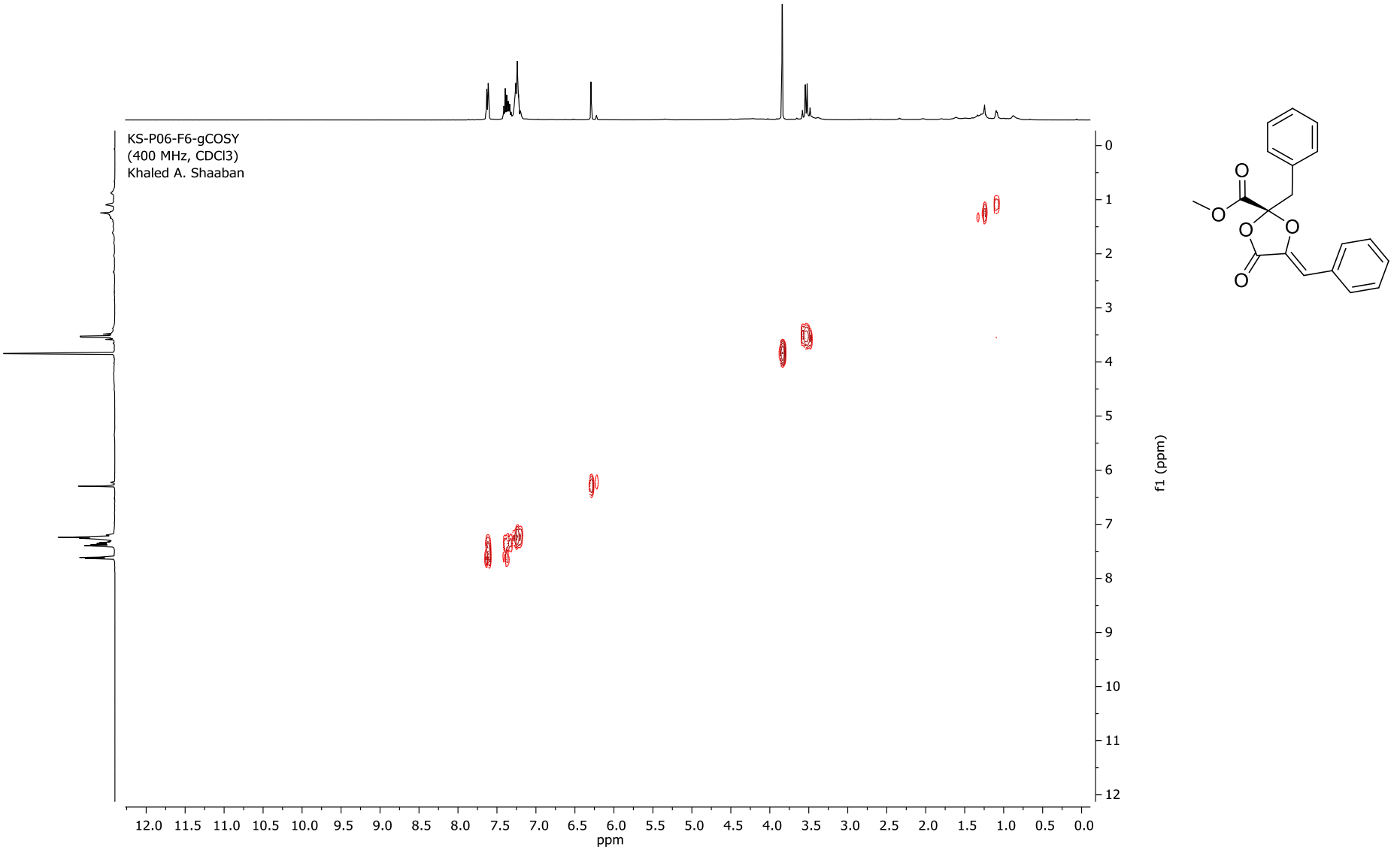



**Figure S30.** $^{1}H,^{1}H$-COSY spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid methyl ester (**1b**).

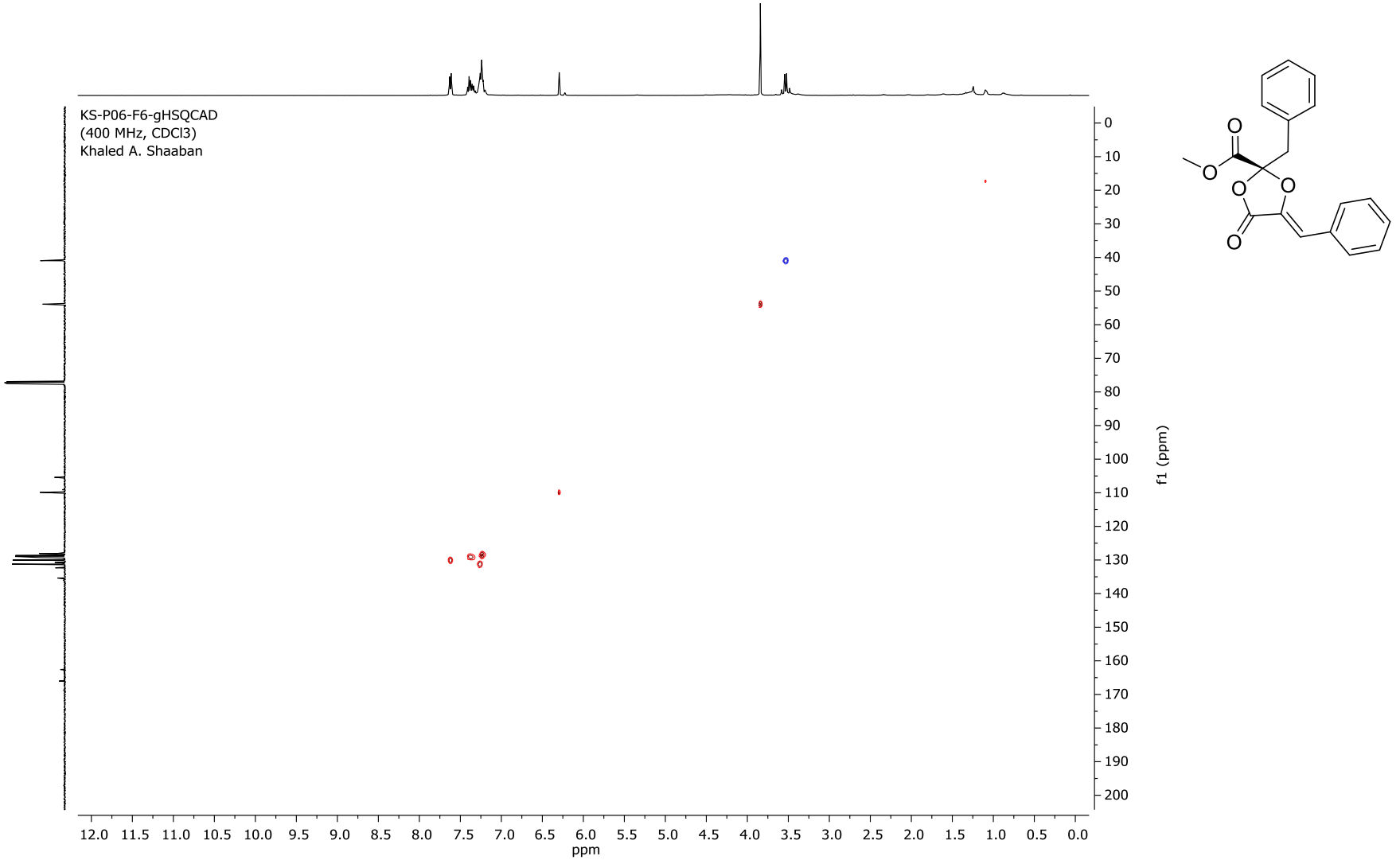



**Figure S31.** HSQC spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid methyl ester (**1b**).

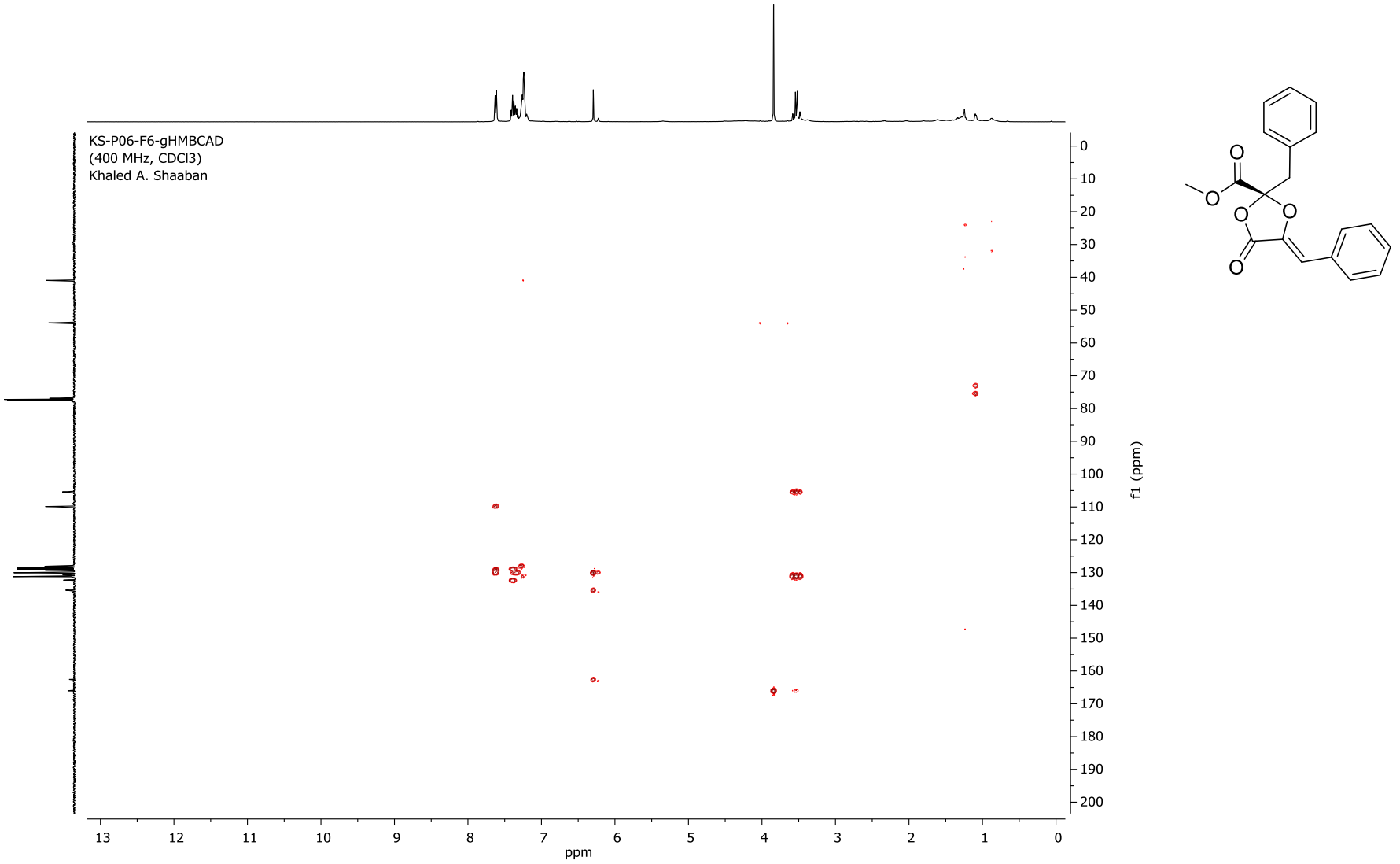



**Figure S32.** HMBC spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid methyl ester (**1b**).

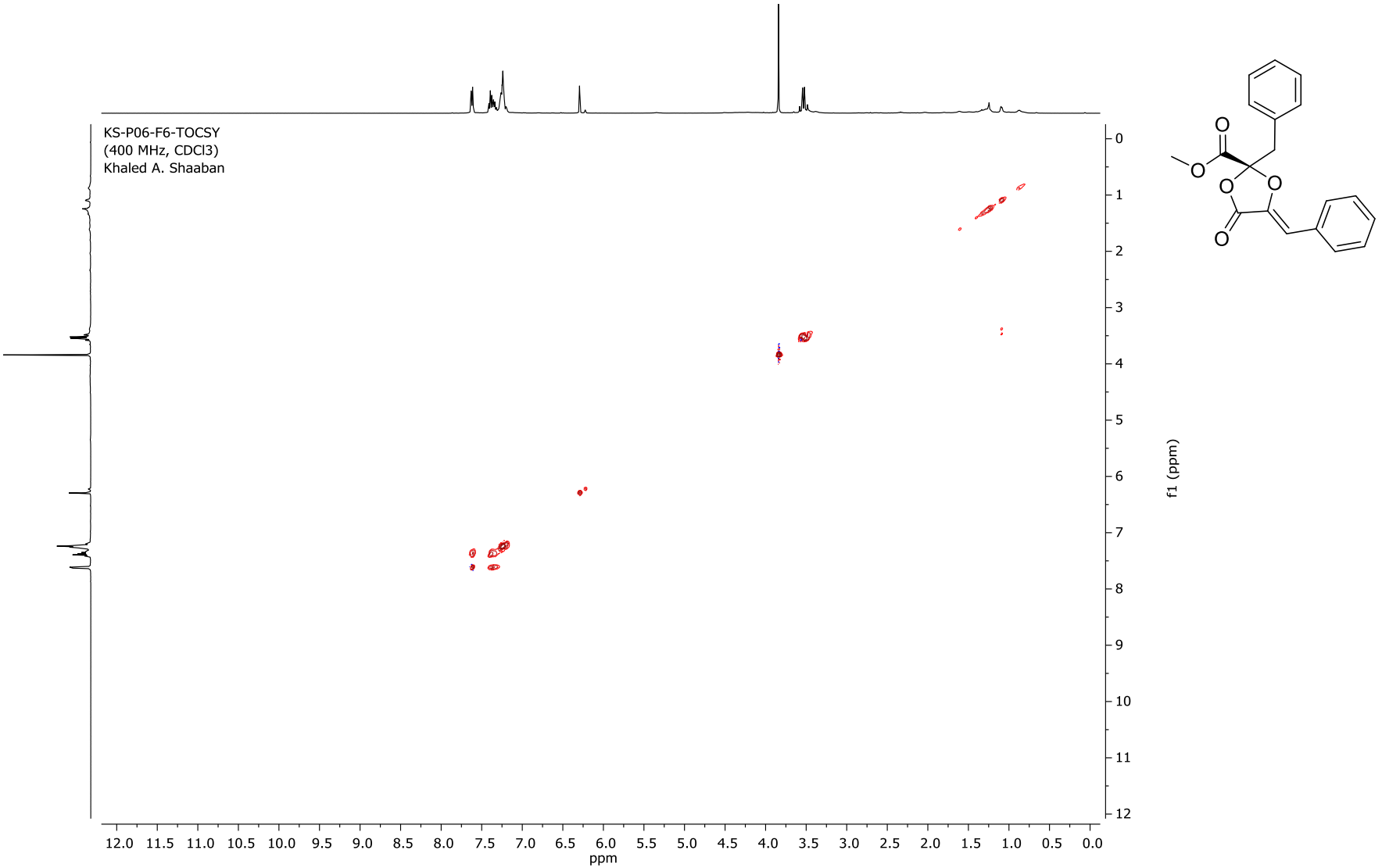



**Figure S33.** TOCSY spectrum ($CDCl_3$, 400 MHz) of phenguignardic acid methyl ester (**1b**).

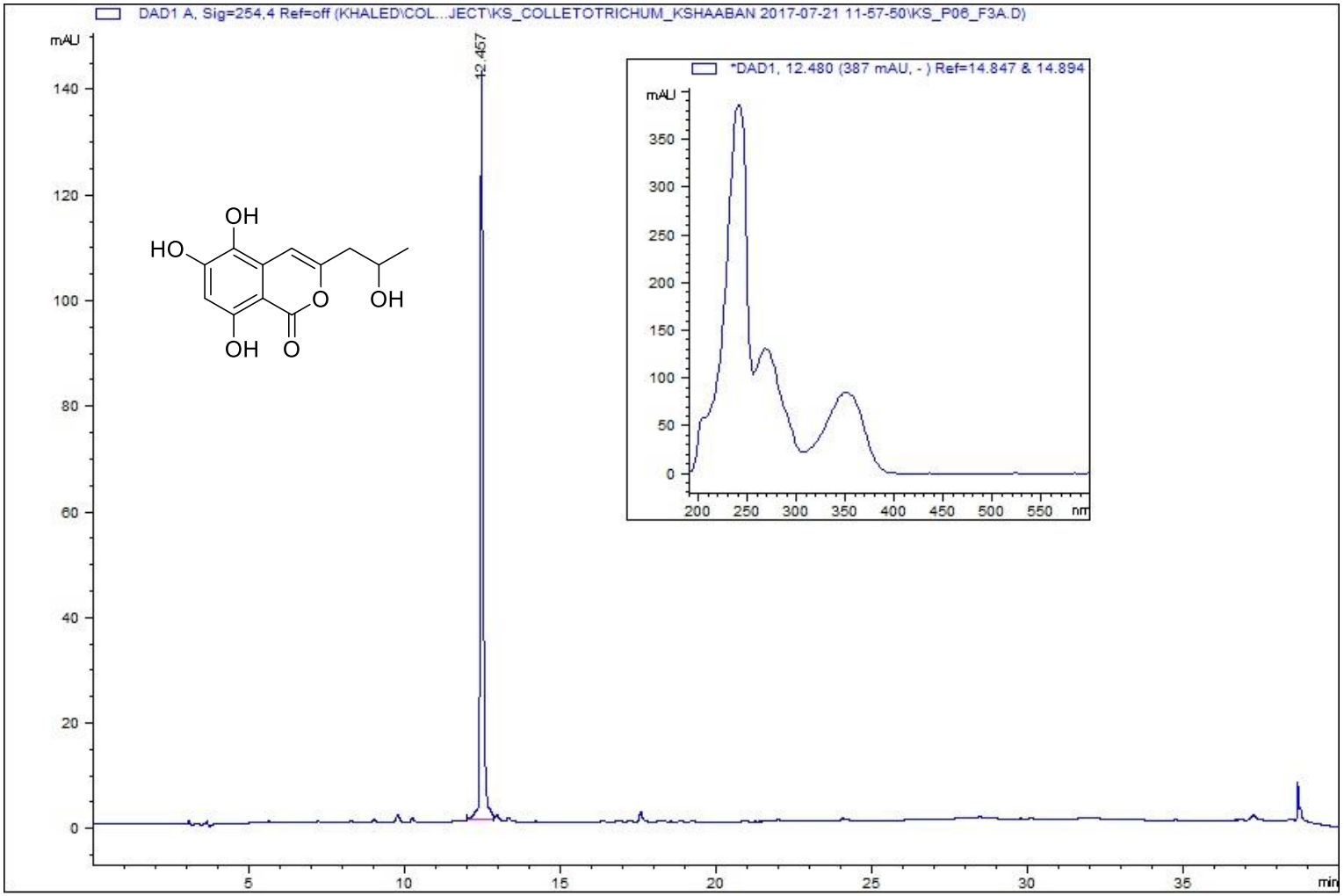



**Figure S34.** HPLC analysis of peniisocoumarin G (**2a**).HPLC-conditions: solvent A: $H_2O$/0.1% TFA; solvent B: $CH_3CN$; flow rate: 1.0 mL $min^{-1}$; 0-30 min, 5%-100% B; 30-35 min, 100% B; 35-36 min, 100%-5% B; 36-40 min, 5 % B; Phenomenex C18 column (250 × 4.6 mm, 5 $\mu$m); 254 nm. UV-VIS inset of full wavelength scan (190-600 nm).

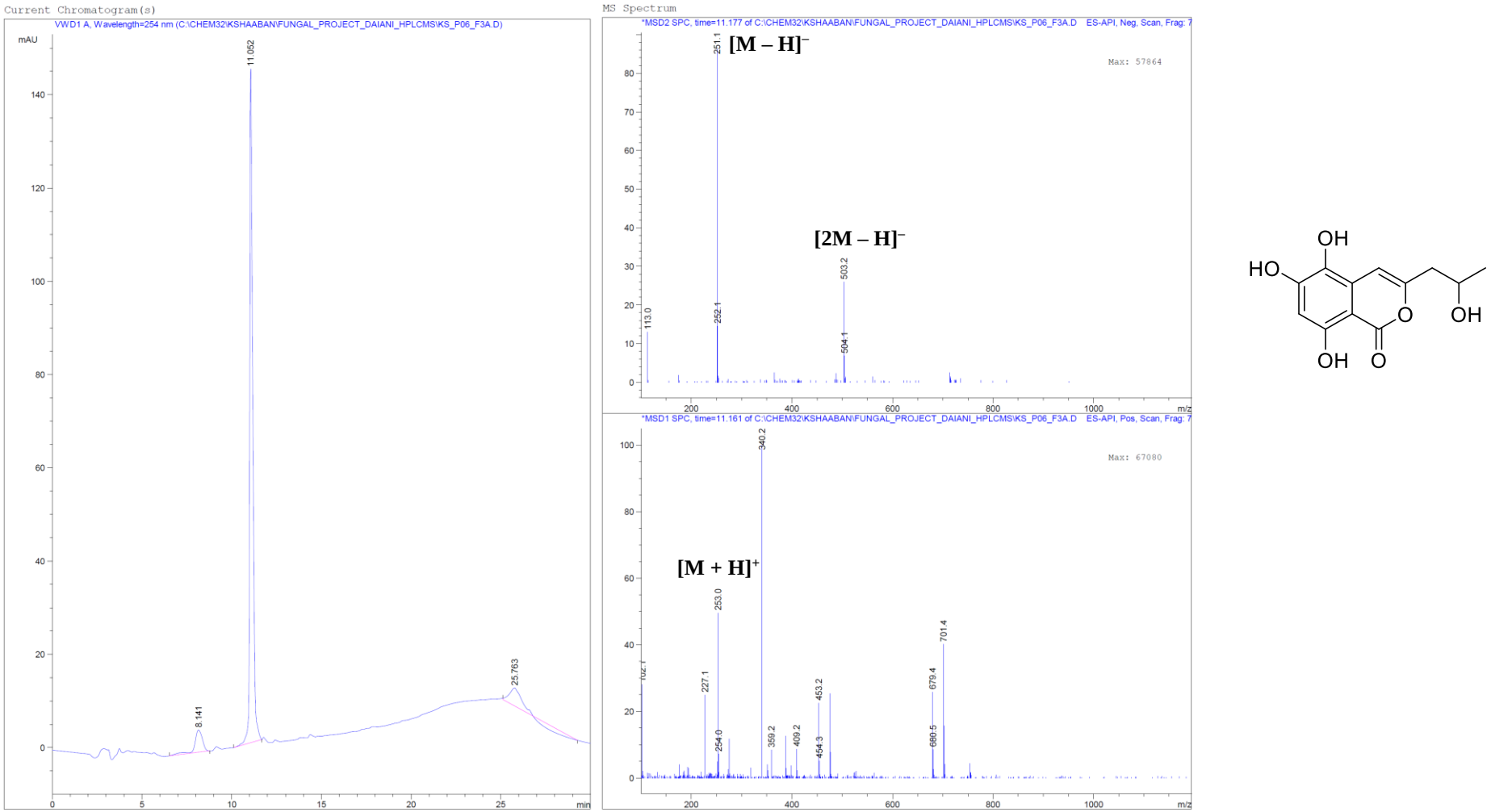



**Figure S35.** HPLC/MS analysis of peniisocoumarin G (**2a**). HPLC-conditions: solvent A: $H_2O$/0.1% formic acid, solvent B: $CH_3CN$/0.1% formic acid; flow rate: 0.5 mL $min^{-1}$; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-30 min, 10 % B; 254 nm.

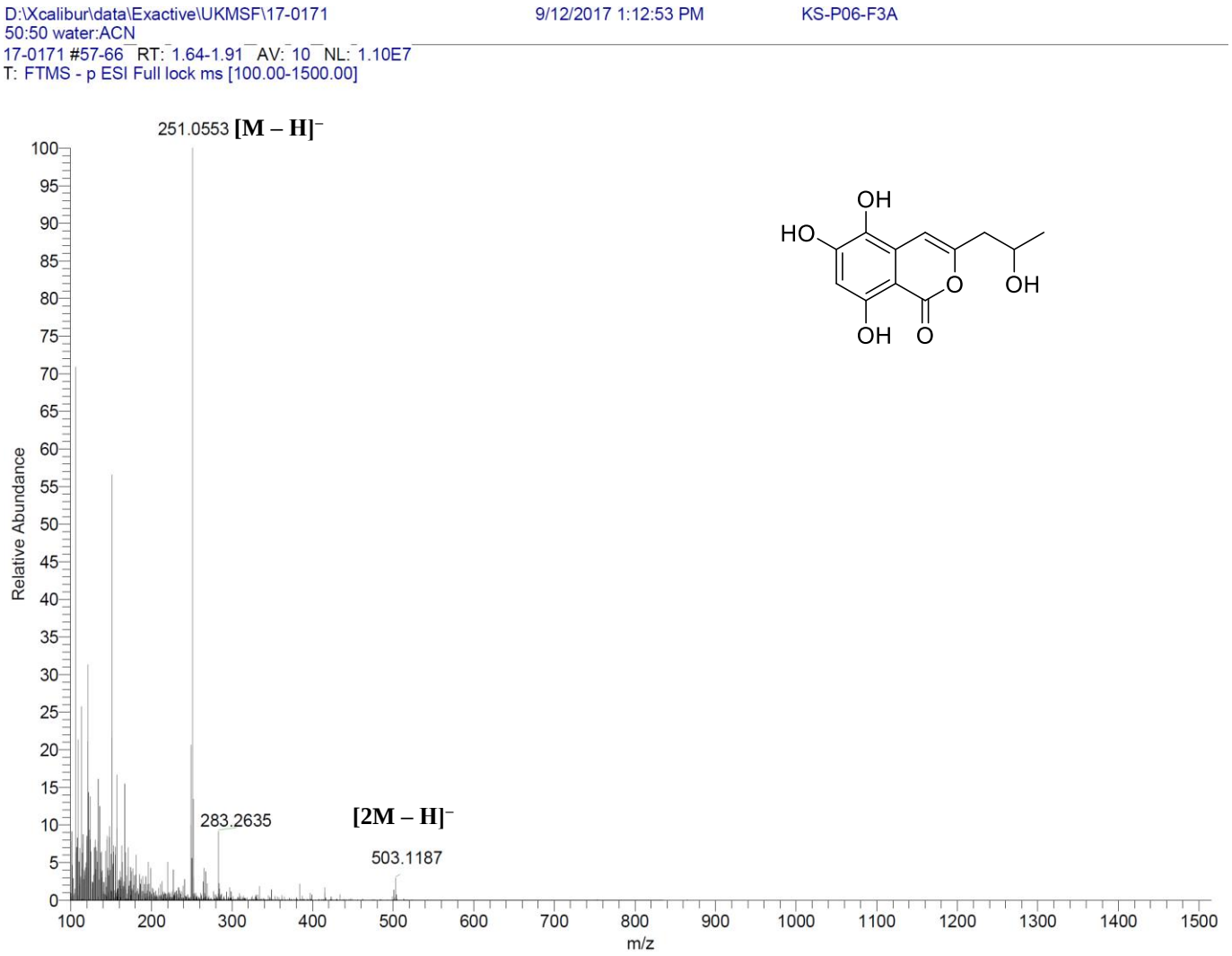



**Figure S36.** (–)-HRESI-MS spectrum of peniisocoumarin G (**2a**).

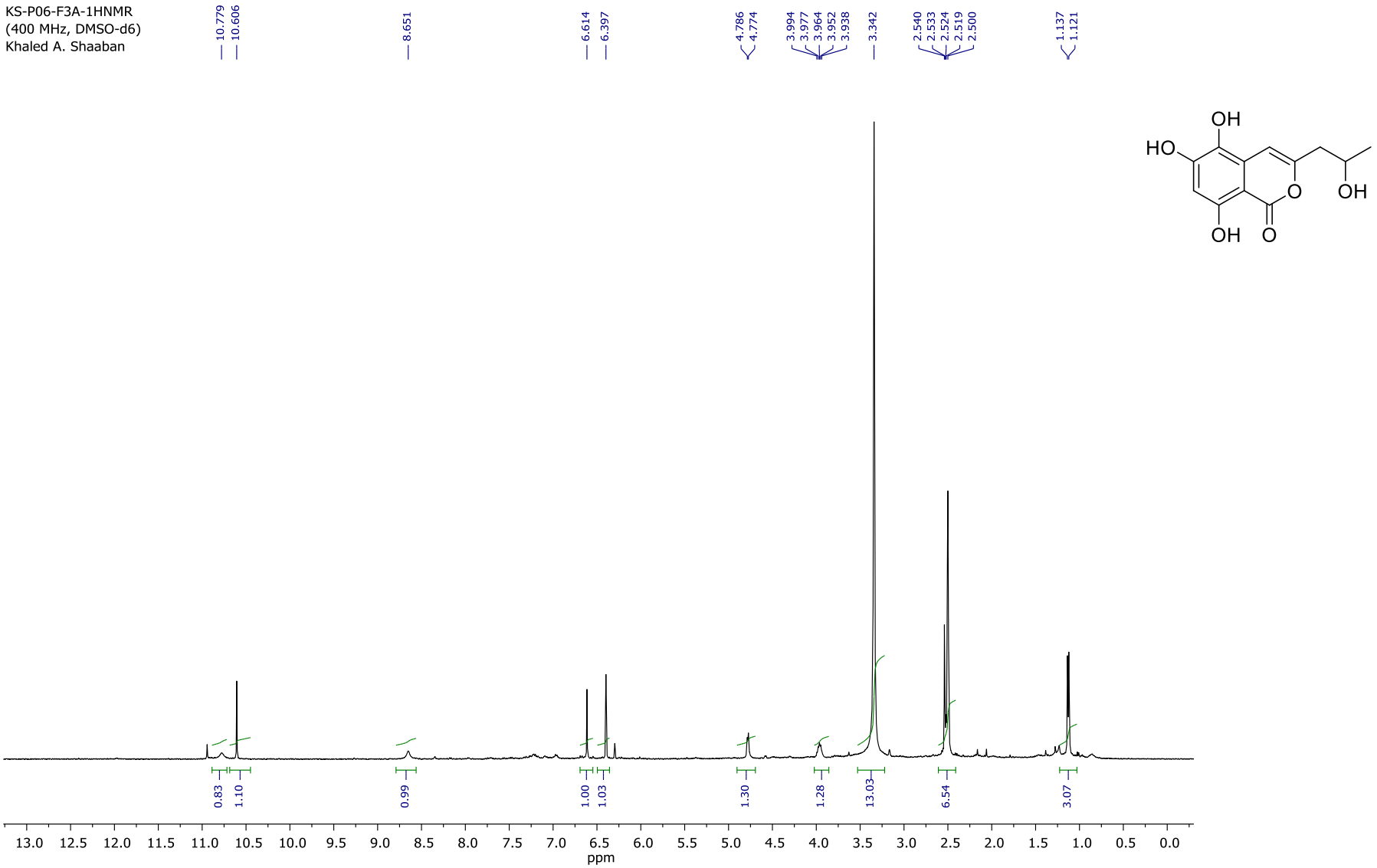



**Figure S37.** $^{1}$H NMR spectrum (DMSO-$d_6$, 400 MHz) of peniisocoumarin G (**2a**).

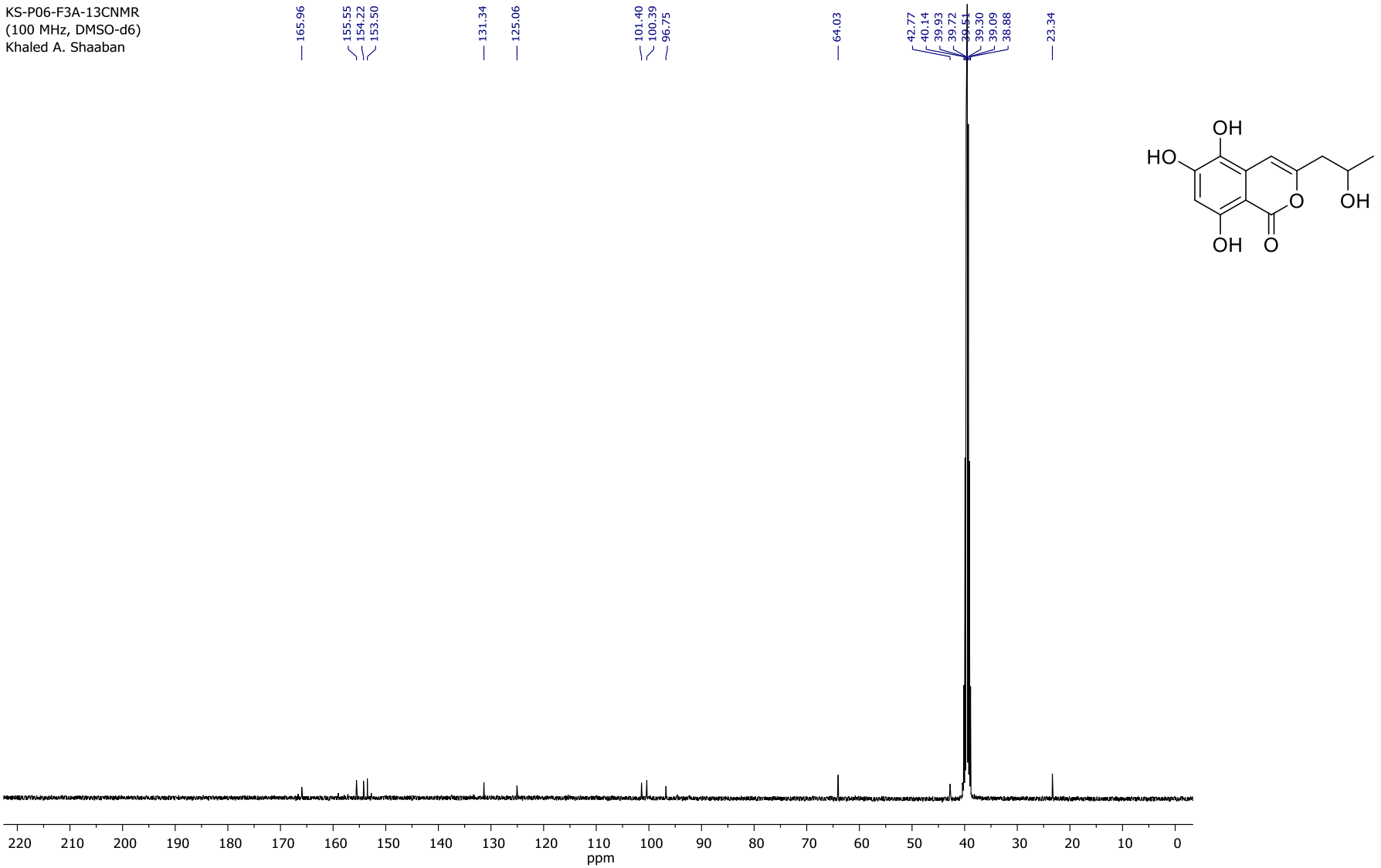



**Figure S38.** $^{13}$C NMR spectrum (DMSO-$d_6$, 100 MHz) of peniisocoumarin G (**2a**).

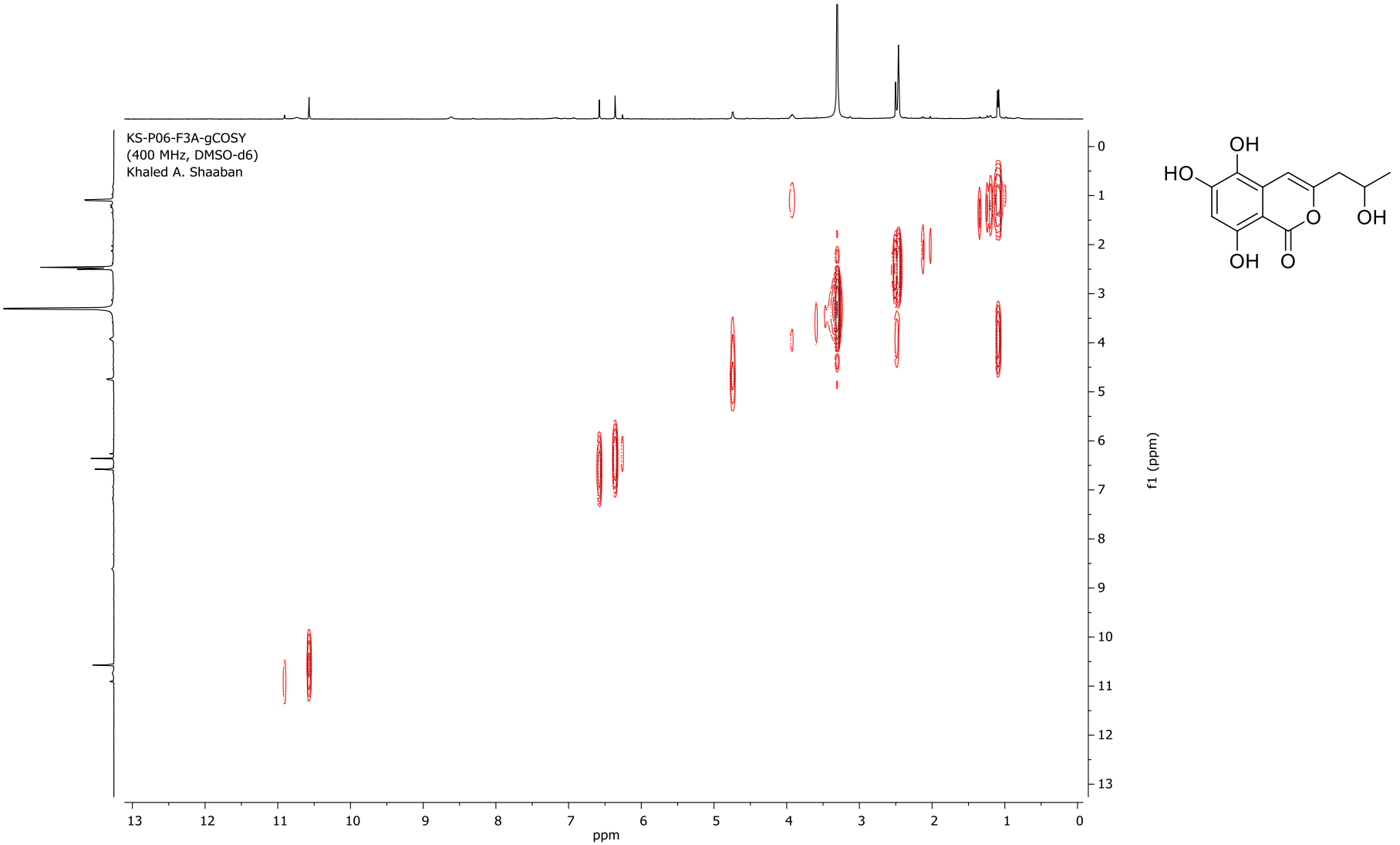



**Figure S39.** $^{1}$H,$^{1}$H-COSY spectrum (DMSO-$d_6$, 400 MHz) of peniisocoumarin G (**2a**).

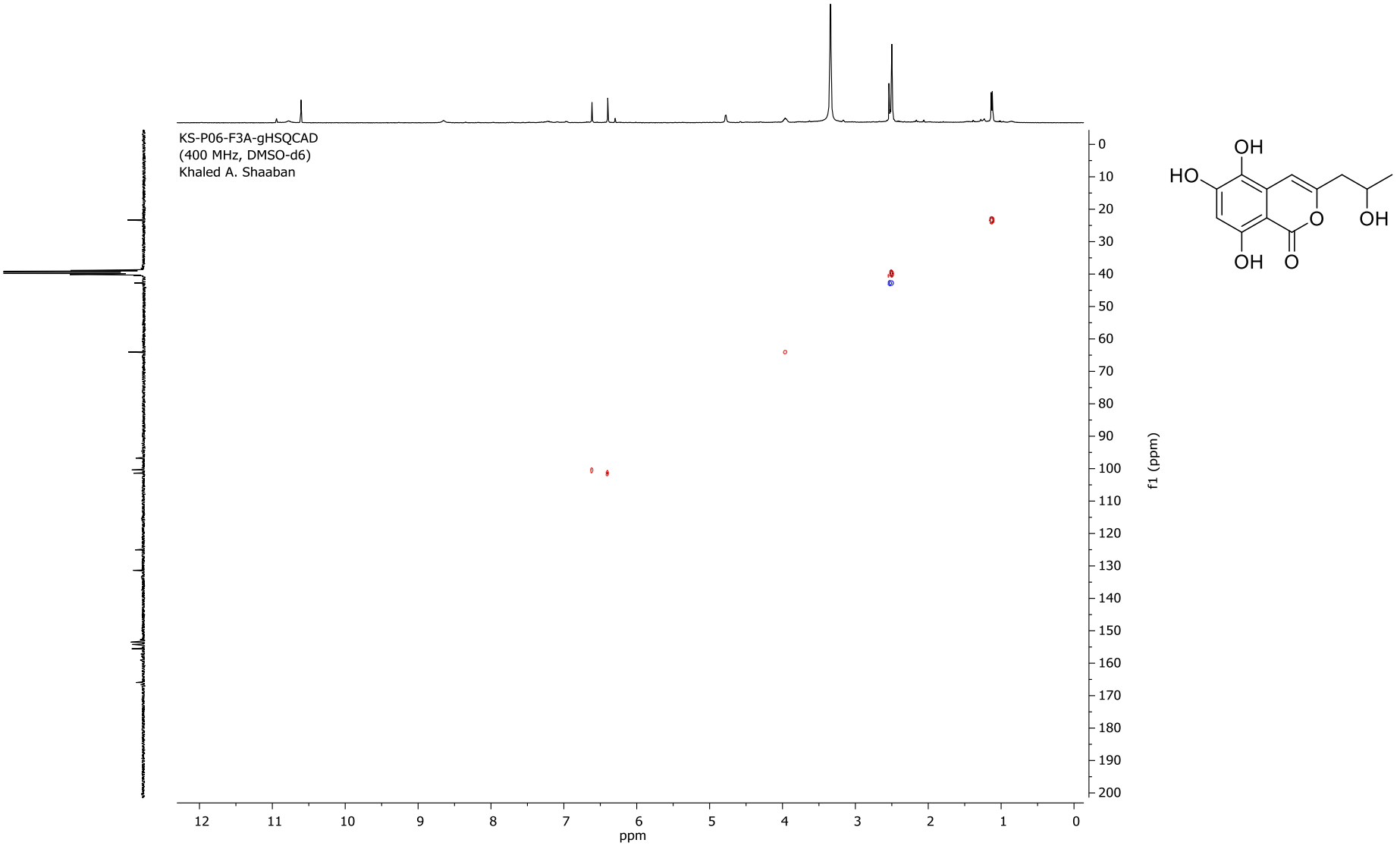



**Figure S40.** HSQC spectrum (DMSO-$d_6$, 400 MHz) of peniisocoumarin G (**2a**).

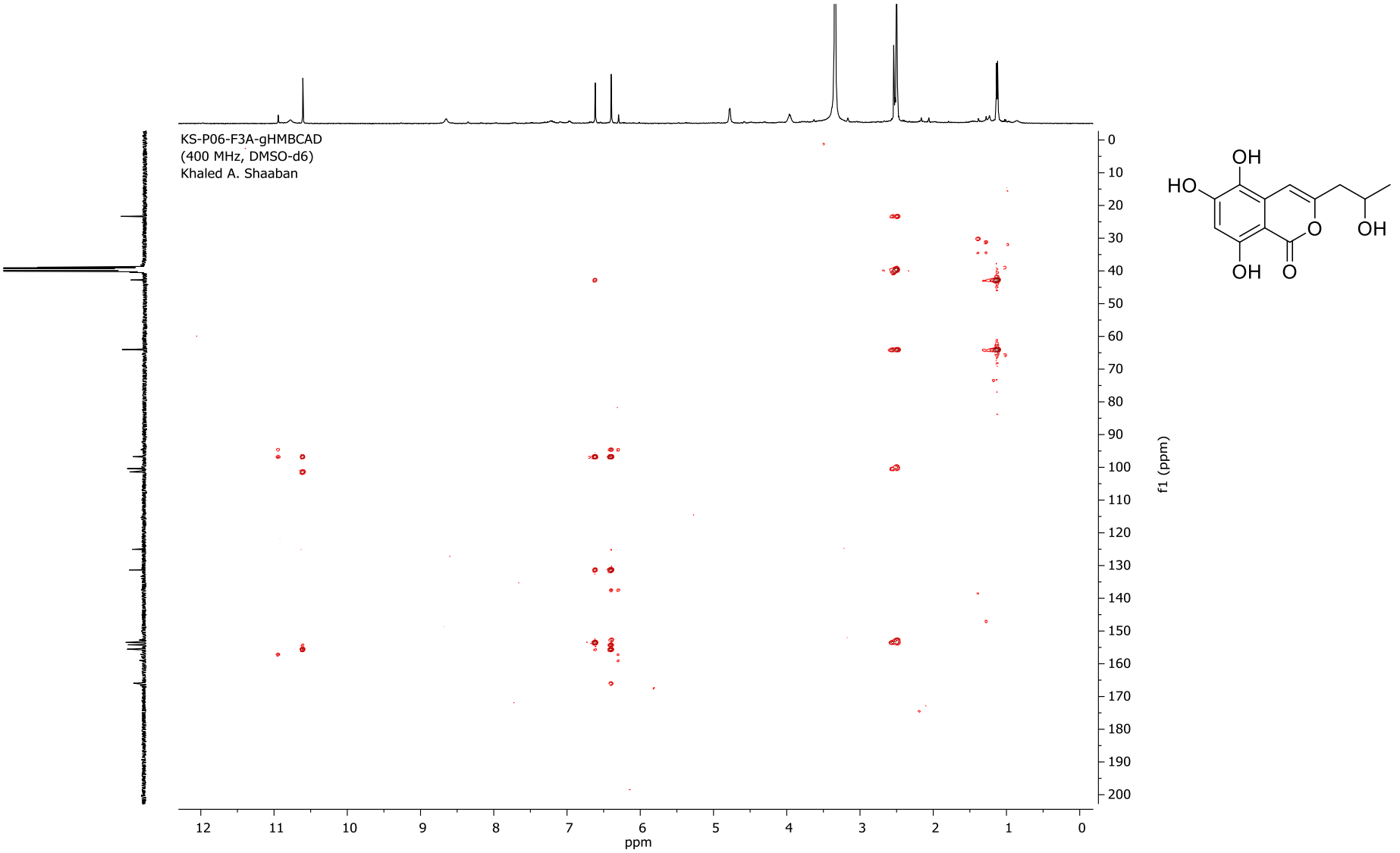



**Figure S41.** HMBC spectrum (DMSO-$d_6$, 400 MHz) of peniisocoumarin G (**2a**).

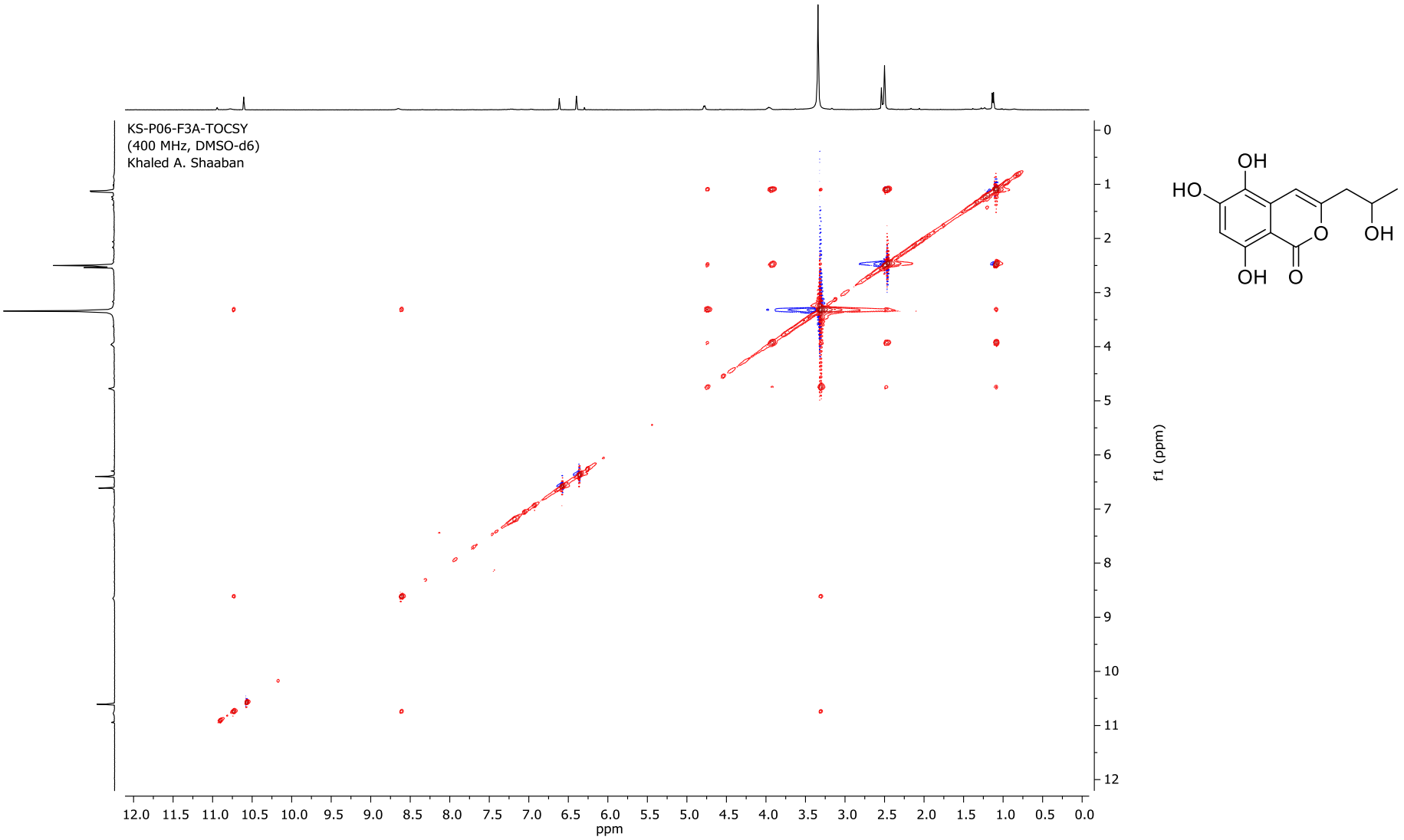



**Figure S42.** TOCSY spectrum (DMSO-$d_6$, 400 MHz) of peniisocoumarin G (**2a**).

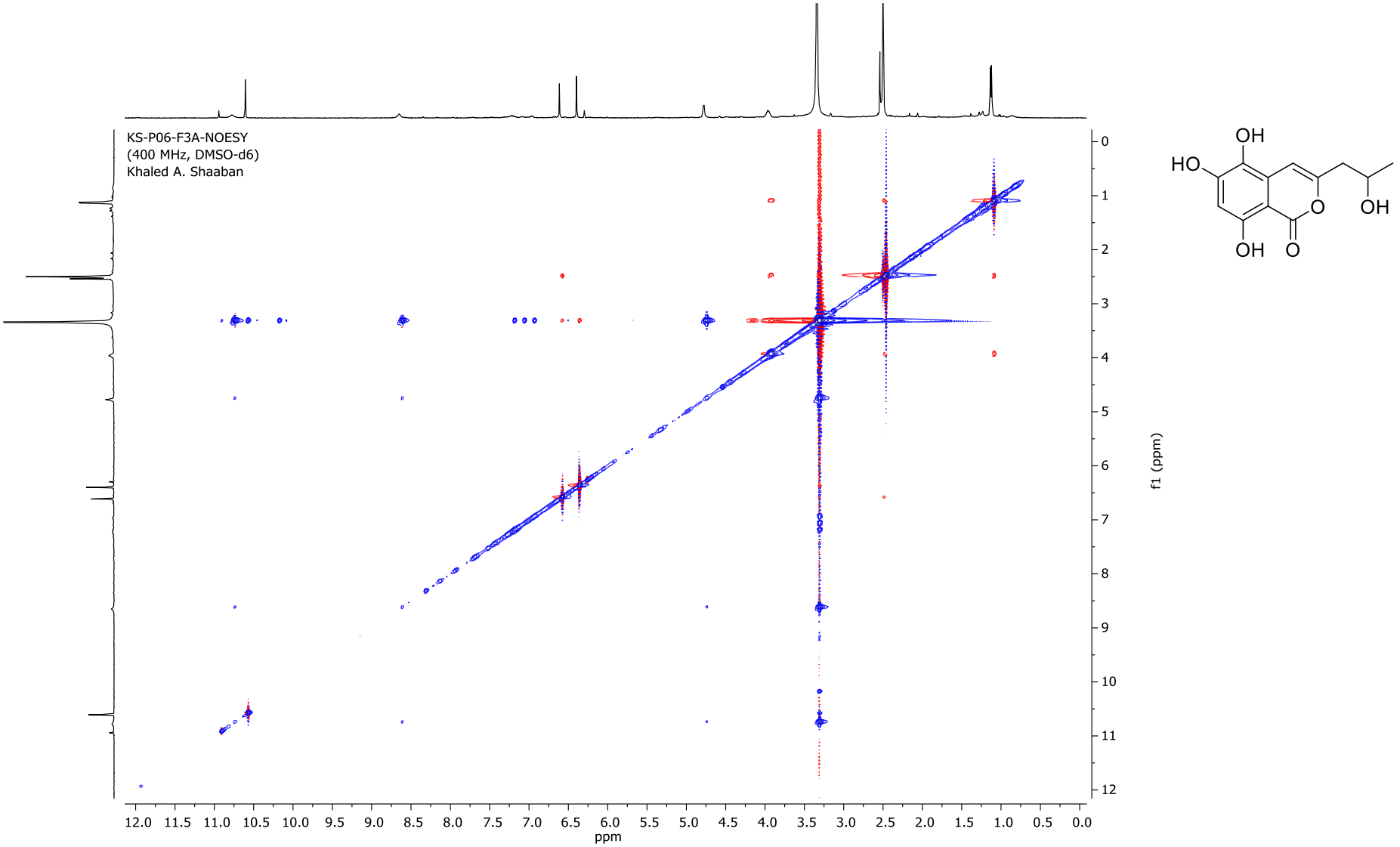



**Figure S43.** NOESY spectrum (DMSO-$d_6$, 400 MHz) of peniisocoumarin G (**2a**).

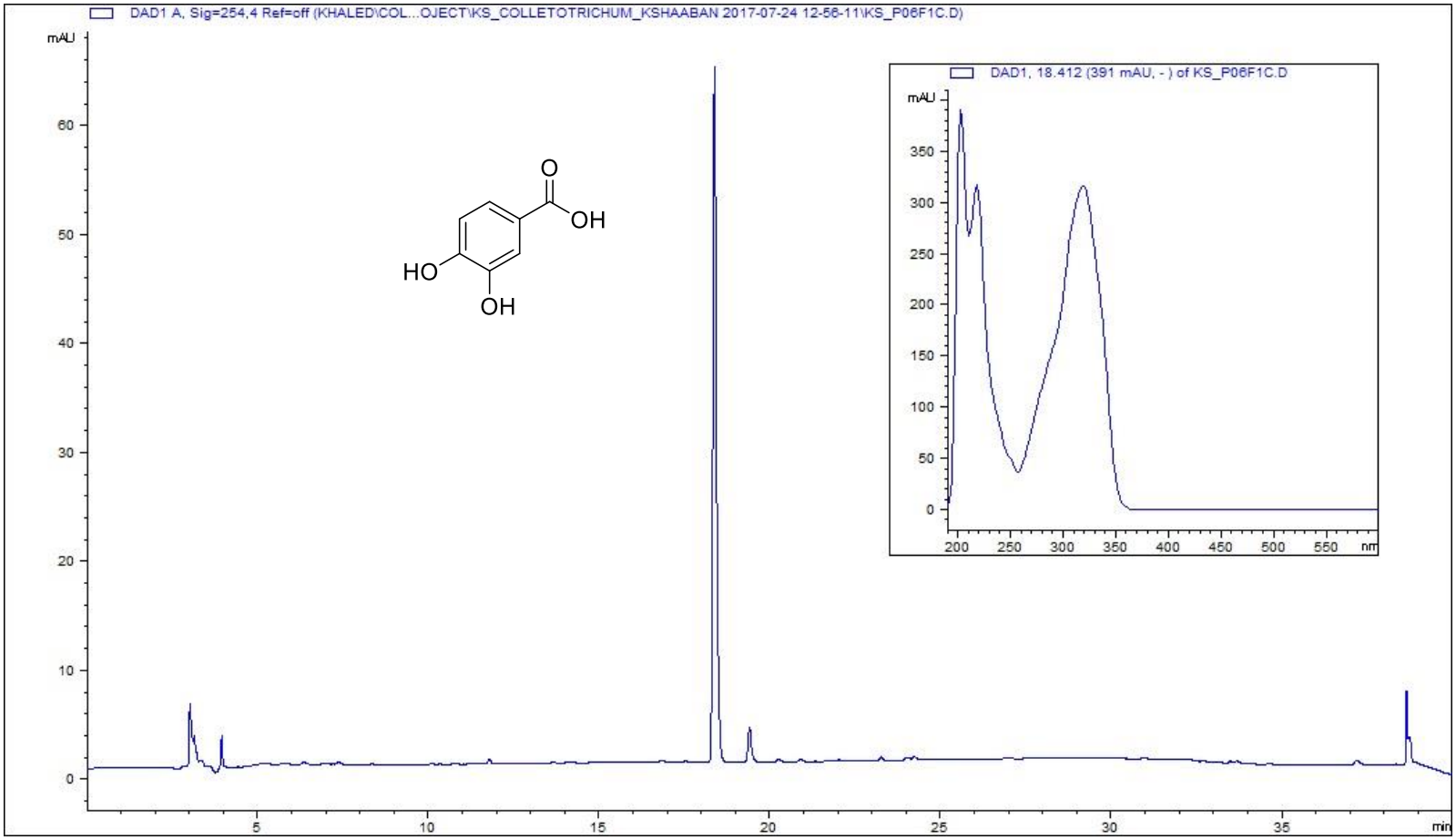



**Figure S44.** HPLC analysis of protocatechuic acid (**3**). HPLC-conditions: solvent A: $H_2O$/0.1% TFA; solvent B: $CH_3CN$; flow rate: 1.0 mL $min^{-1}$; 0-30 min, 5%-100% B; 30-35 min, 100% B; 35-36 min, 100%-5% B; 36-40 min, 5 % B; Phenomenex C18 column (250 × 4.6 mm, 5 $\mu$m); 254 nm. UV-vis inset of full wavelength scan (190-600 nm).

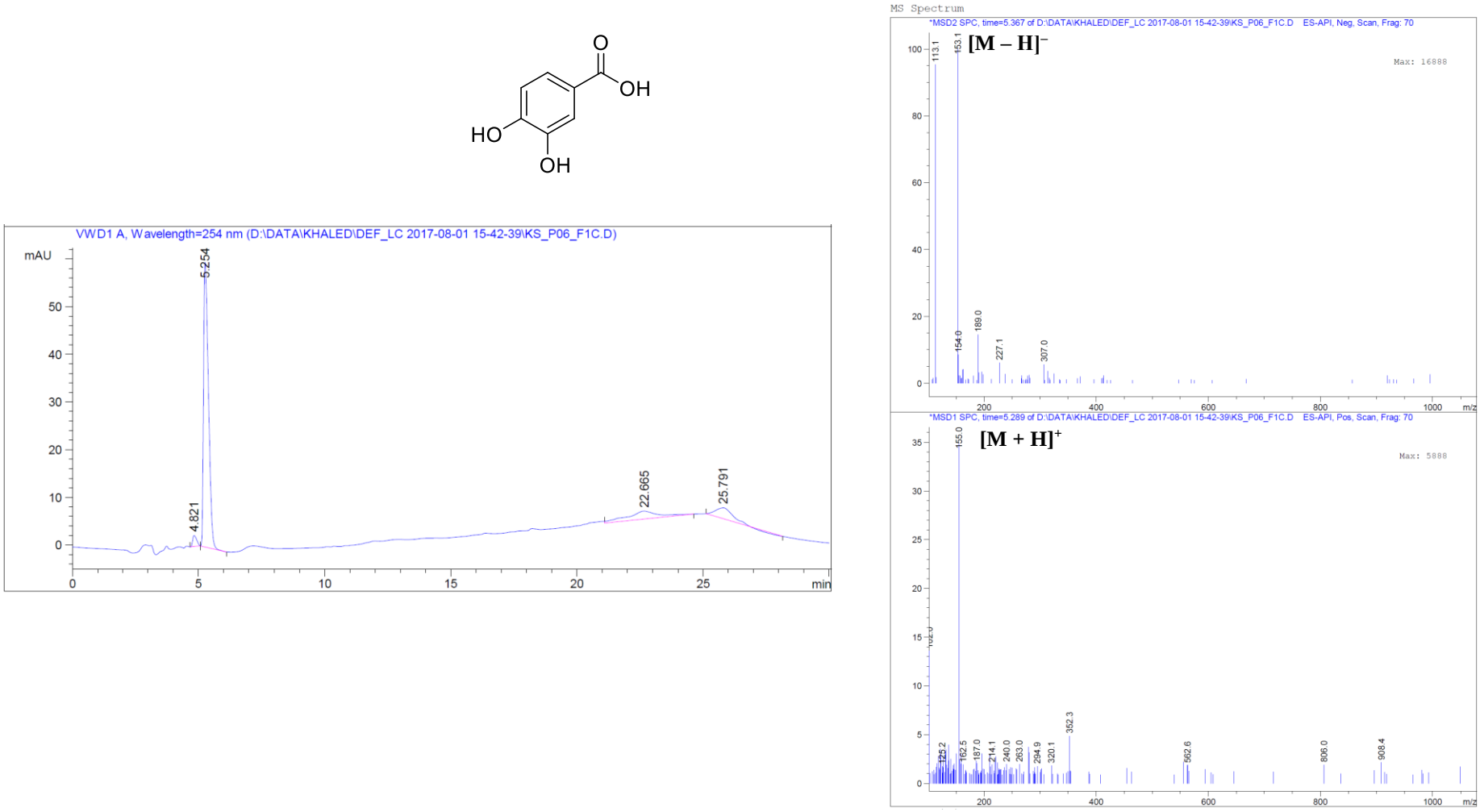



**Figure S45.** HPLC/MS analysis of protocatechuic acid (**3**). HPLC-conditions: solvent A: $H_2O$/0.1% formic acid, solvent B: $CH_3CN$/0.1% formic acid; flow rate: 0.5 mL $min^{-1}$; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-30 min, 10 % B; 254 nm.

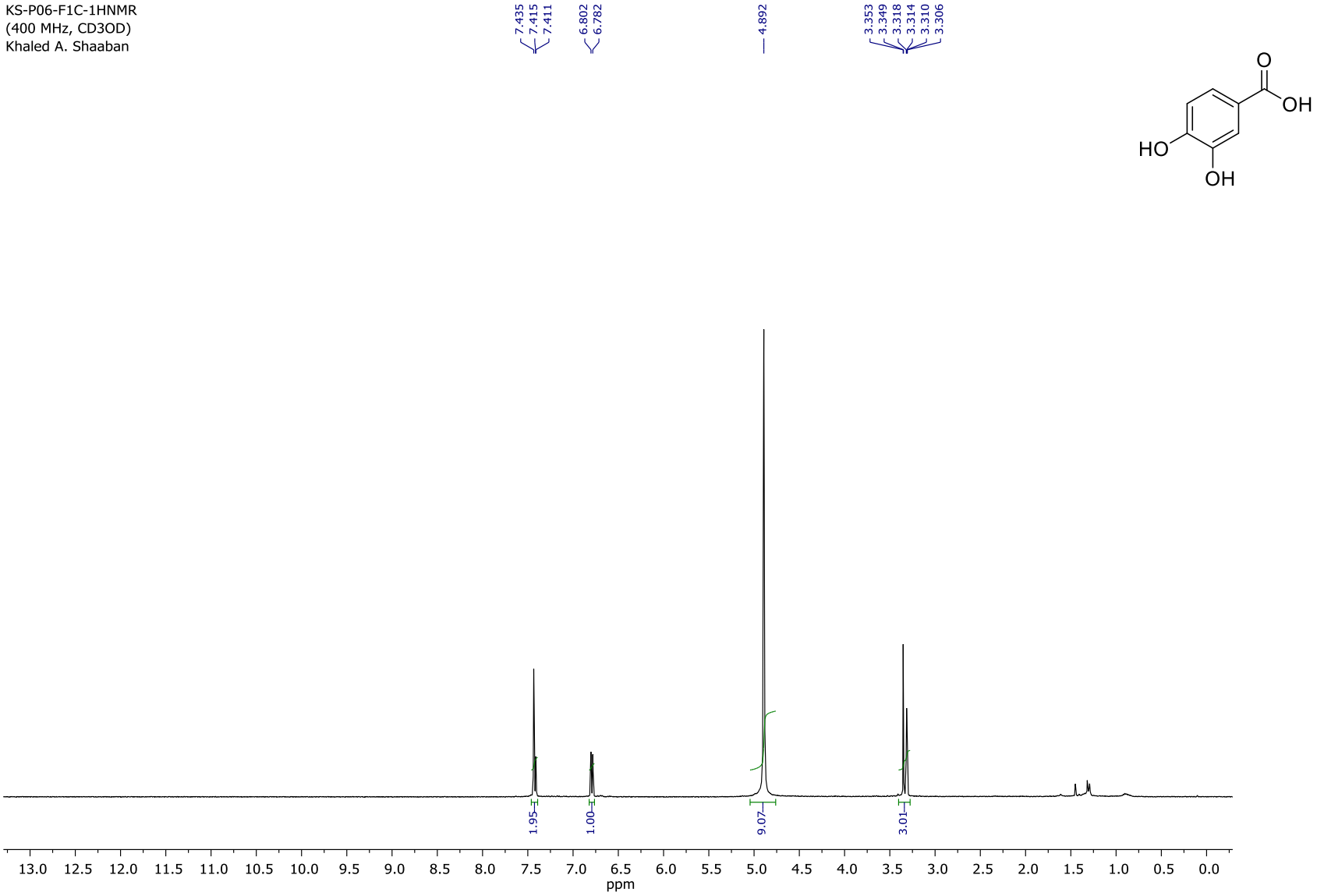



**Figure S46.** $^{1}$H NMR spectrum ($CD_3OD$, 400 MHz) of protocatechuic acid (**3**).

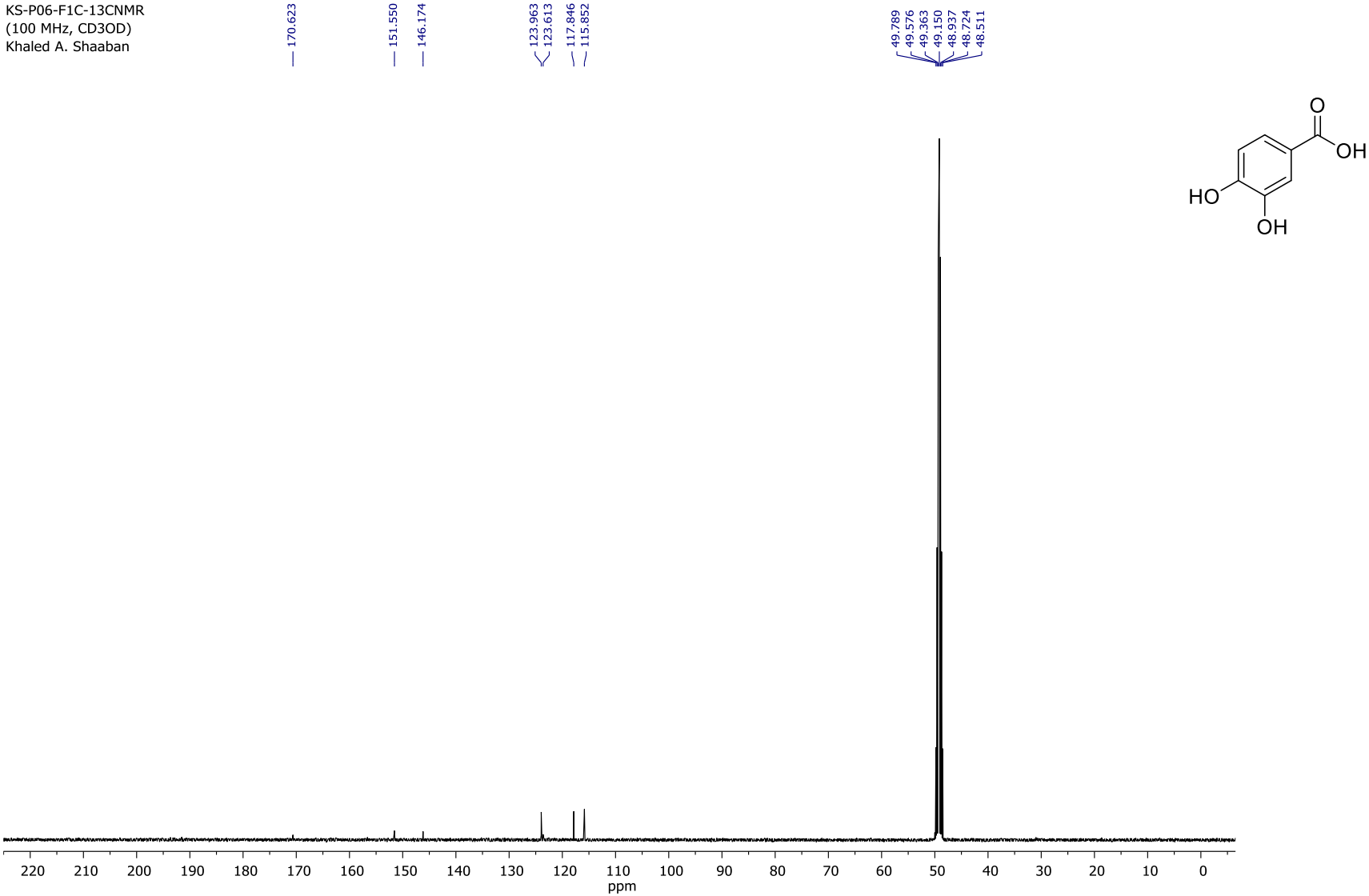



**Figure S47.** $^{13}C$ NMR spectrum ($CD_3OD$, 100 MHz) of protocatechuic acid (**3**).

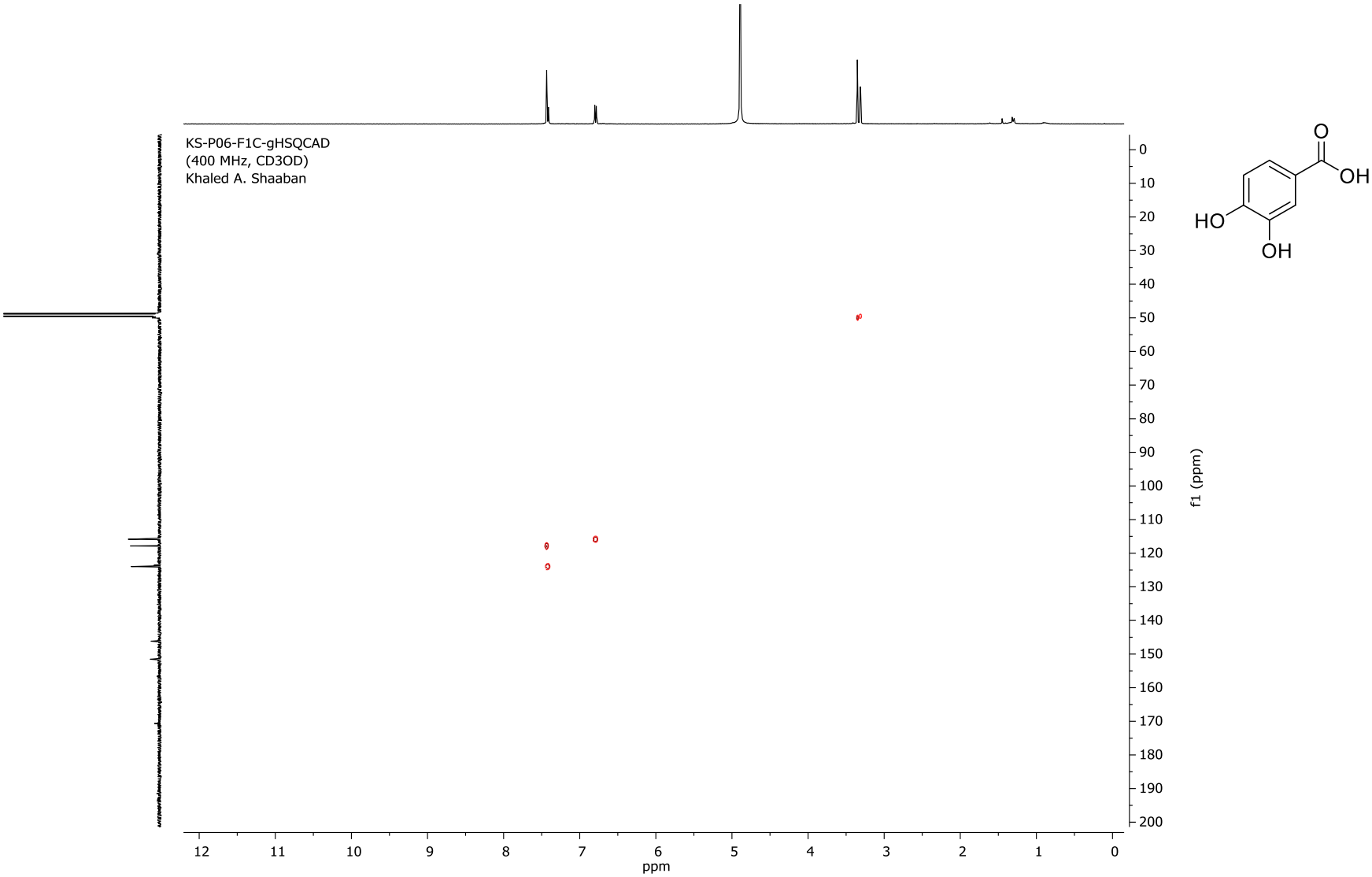



**Figure S48.** HSQC spectrum ($CD_3OD$, 400 MHz) of protocatechuic acid (**3**).

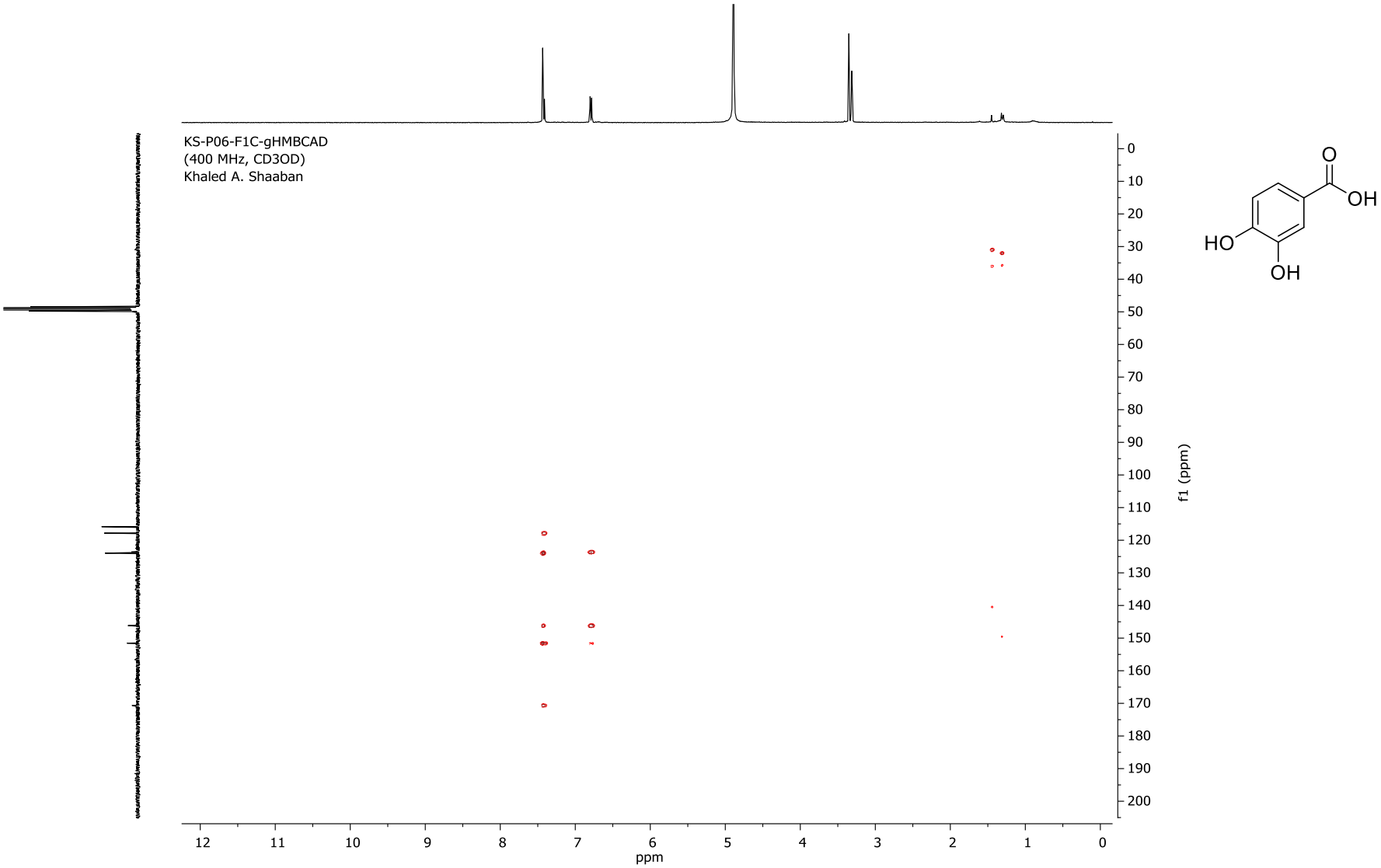



**Figure S49.** HMBC spectrum ($CD_3OD$, 400 MHz) of protocatechuic acid (**3**).

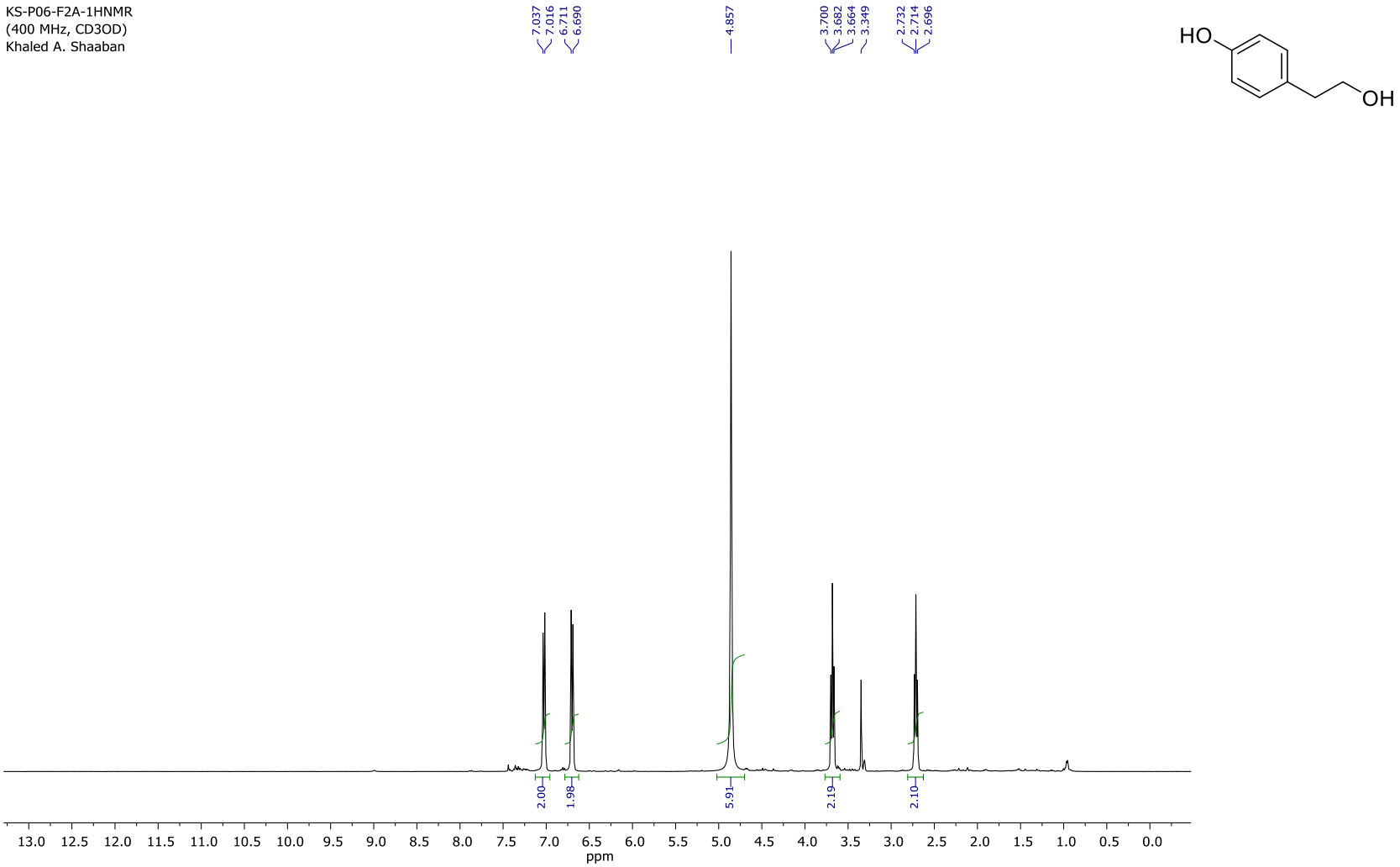



**Figure S50.** $^{1}$H NMR spectrum ($CD_3OD$, 400 MHz) of tyrosol (**4**).

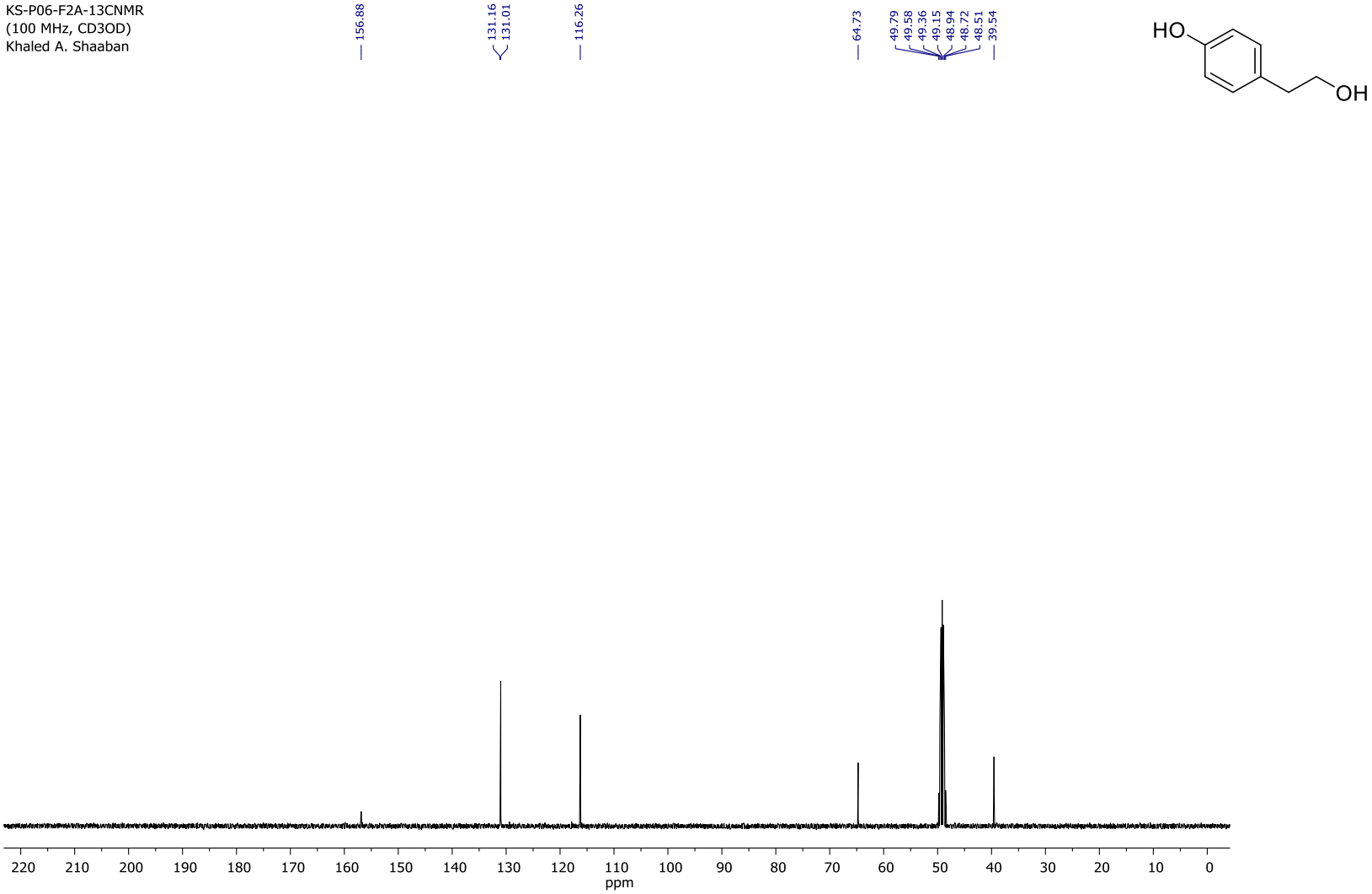



**Figure S51.** $^{13}C$ NMR spectrum ($CD_3OD$, 400 MHz) of tyrosol (**4**).

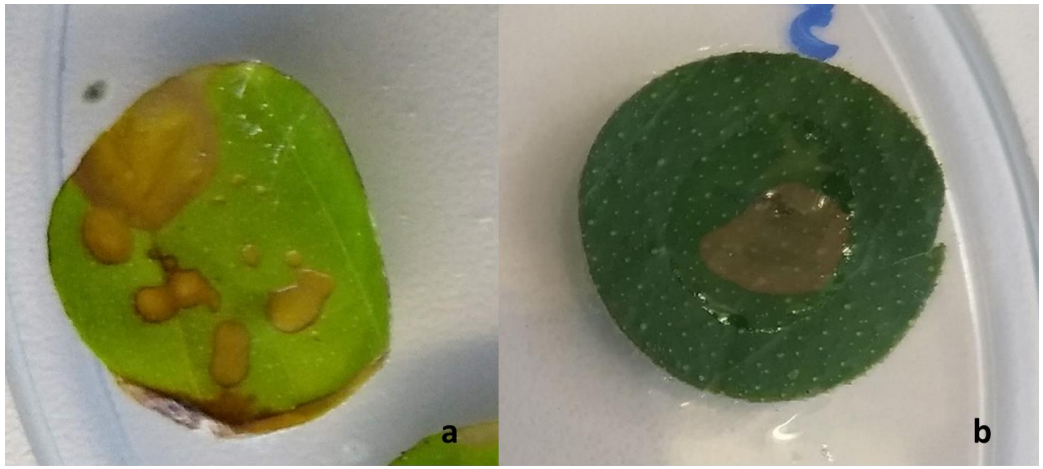



**Figure S52.** Phytotoxicity of phenguignardic acid butyl ester (**1a**) in *Citrus reticulate* (**a**) and *Citrus limon* at 100 µg.