Supporting Information (SI)

Crocrassins A and B, two novel sesquiterpenoids with an unprecedented carbon skeleton from *Croton crassifolius*

Zhan-Xin Zhang,*[a] Hui-Hong Li,[a] Feng-Ming Qi,[b] Le-Le Dong,[a] Yang Hai,[a] Gai-Xia Fan[a] and Dong-Qing Fei*[a]

[a]*School of Pharmacy, Lanzhou University, Lanzhou 730000, People's Republic of China. E-mail: zhangzhx@lzu.edu.cn (Z.X. Zhang); feidq@lzu.edu.cn (D.Q. Fei); Fax: +86 931 8915686; Tel: +86 931 8915686*

[b]*State Key Laborratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, People's Republic of China*

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1. Detailed experimental procedures

1.1 General Experimental Procedures

Melting points were determined on an X-4 digital display micromelting point apparatus, and are uncorrected. Optical rotations were measured on a Perkin Elmer 341 polarimeter. IR spectra were taken on a Nicolet NEXUS 670 FT-IR spectrometer. NMR spectra were recorded on a Varian INOVA-600 NMR spectrometer with TMS as internal standard. HRESIMS data were recorded on a Thermo LTQ Orbitrap Elite mass spectrometer. Sephadex LH-20 was supplied by Amersham Pharmacia Biotech. Silica gel (200-300 mesh) used for column chromatography and silica gel GF_{254} (10-40 μM) used for TLC were supplied by the Qingdao Marine Chemical Factory, Qingdao, China. Spots were detected on TLC under UV light or by heating after spraying with 5% H_2SO_4 in C_2H_5OH (v/v).

1.2 Plant Material

The roots of *C. crassifolius* were purchased from Hebei Anguo Medicine Market, and were originally collected from Fujian province of China in September 2012. The plant was identified by Dr. Jian-Yin Li (School of Pharmacy, Lanzhou University, Lanzhou, China). A voucher specimen (No. 201209CC) was deposited at the School of Pharmacy, Lanzhou University.

1.3 Extraction and isolation

The air-dried and powdered roots of *C. crassifolius* (9.5 kg) were extracted four times in 95% EtOH at room temperature. The filtrate was combined and concentrated under reduced pressure to afford a residue (962 g). The residue was suspended in H_2O and extracted with EtOAc, and n-BuOH, successively. The EtOAc extract (731 g) was subjected to CC over silica gel eluting with a petroleum ether-acetone step gradient system (40:1 to 0:1) to give fractions A-F. Fraction C was chromatographed over silica gel column, eluted with a gradient solvent system of increasing polarity (petroleum ether-acetone, 30:1 to 3:1), yielding four subfractions C1-C4. Subfraction C1 was subjected to repeated chromatography over silica gel (petroleum ether-EtOAc, 40:1 to 3:1) to give subfractions C1A-C1C. Subfraction C1B was purified by silica gel CC ($CHCl_3$-EtOAC, 80:1 to 20:1) followed by gel permeation chromatography (GPC) on Sephadex LH-20 in $CHCl_3$-MeOH (1:1) to furnish compound **2** (2 mg). Subfrcation C2 was separated over silica gel CC eluting with petroleum ether-EtOAc (40:1 to 2:1) to yield subfractions C2A-C2C. Subfarction C2C was further purified by silica gel CC ($CHCl_3$-acetone, 10:1 to 2:1) and Sephadex LH-20 ($CHCl_3$-MeOH, 1:1) to afford compound **1** (4 mg).

1.4 Chemical transformations

1.4.1 Preparation of methyl ester derivative 2 of compound 1

To a solution of **1** (2 mg) in diethyl ether (0.5 mL), an ethereal solution of diazomethane was added dropwise until persistence of yellow color. The solution was set aside for 10 min, the excess of diazomethane was destroyed by slowly adding dropwise a 5% ethereal solution of acetic acid (yellow color disappearance) and the solvent evaporated to yield **2** (2 mg).

2. NMR, HRESIMS, and IR spectra of compounds 1–2

Figure S1. ^{1}H NMR spectrum of crocrassin A (**1**) in $CDCl_3$

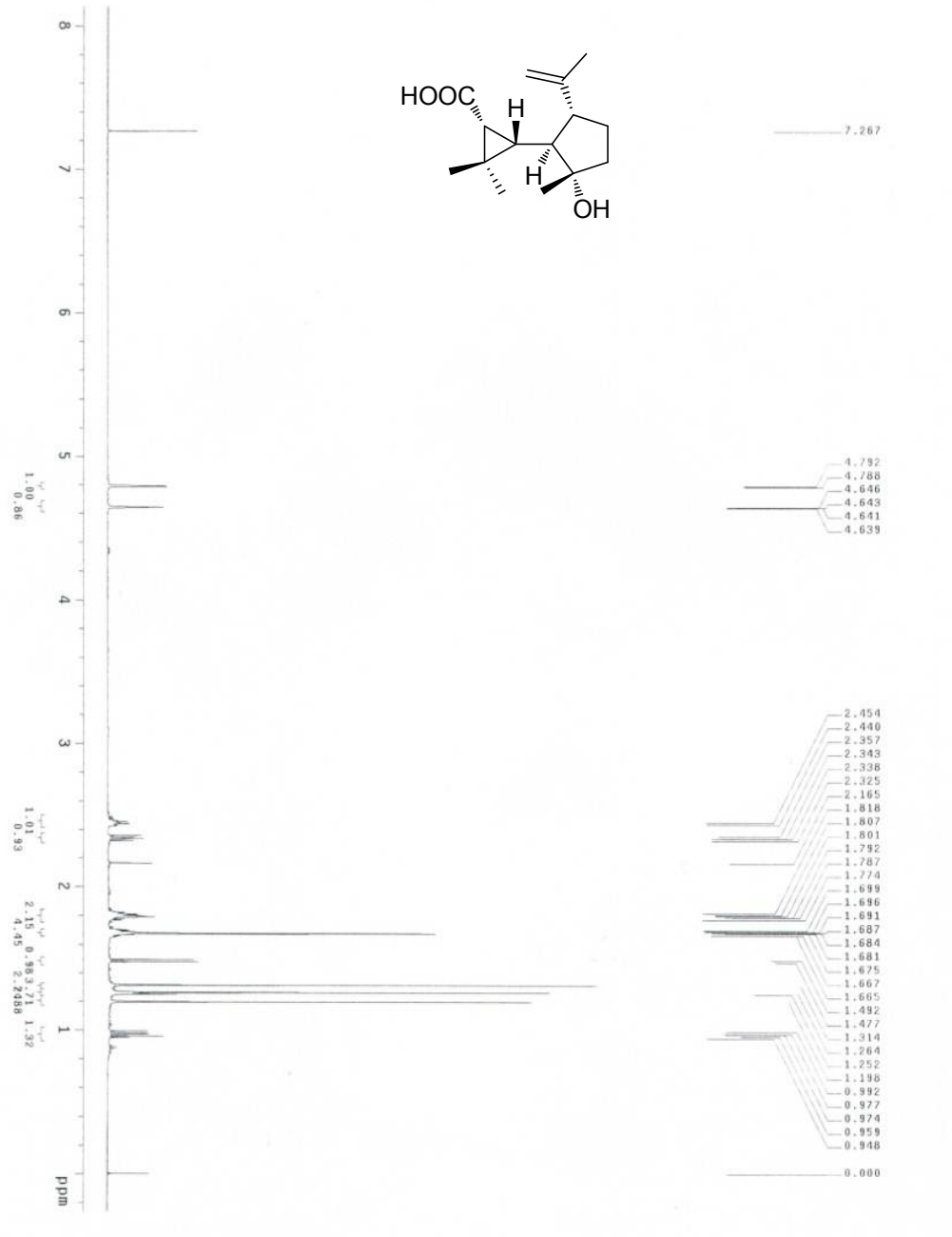

Figure S2. ^{13}C NMR spectrum of crocrassin A (**1**) in $CDCl_3$

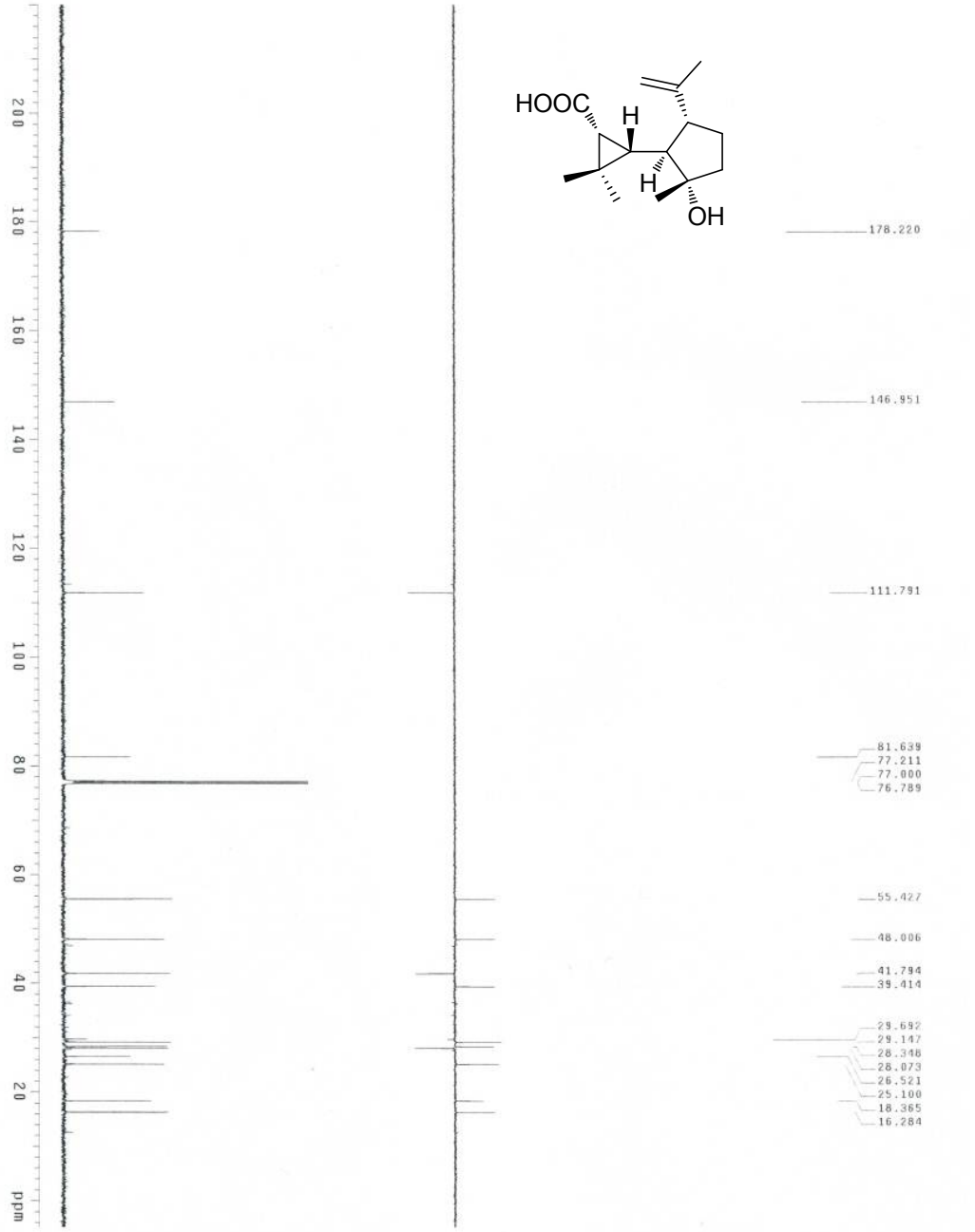

Figure S3. HMQC spectrum ofcrocrassin A (**1**) in $CDCl_3$

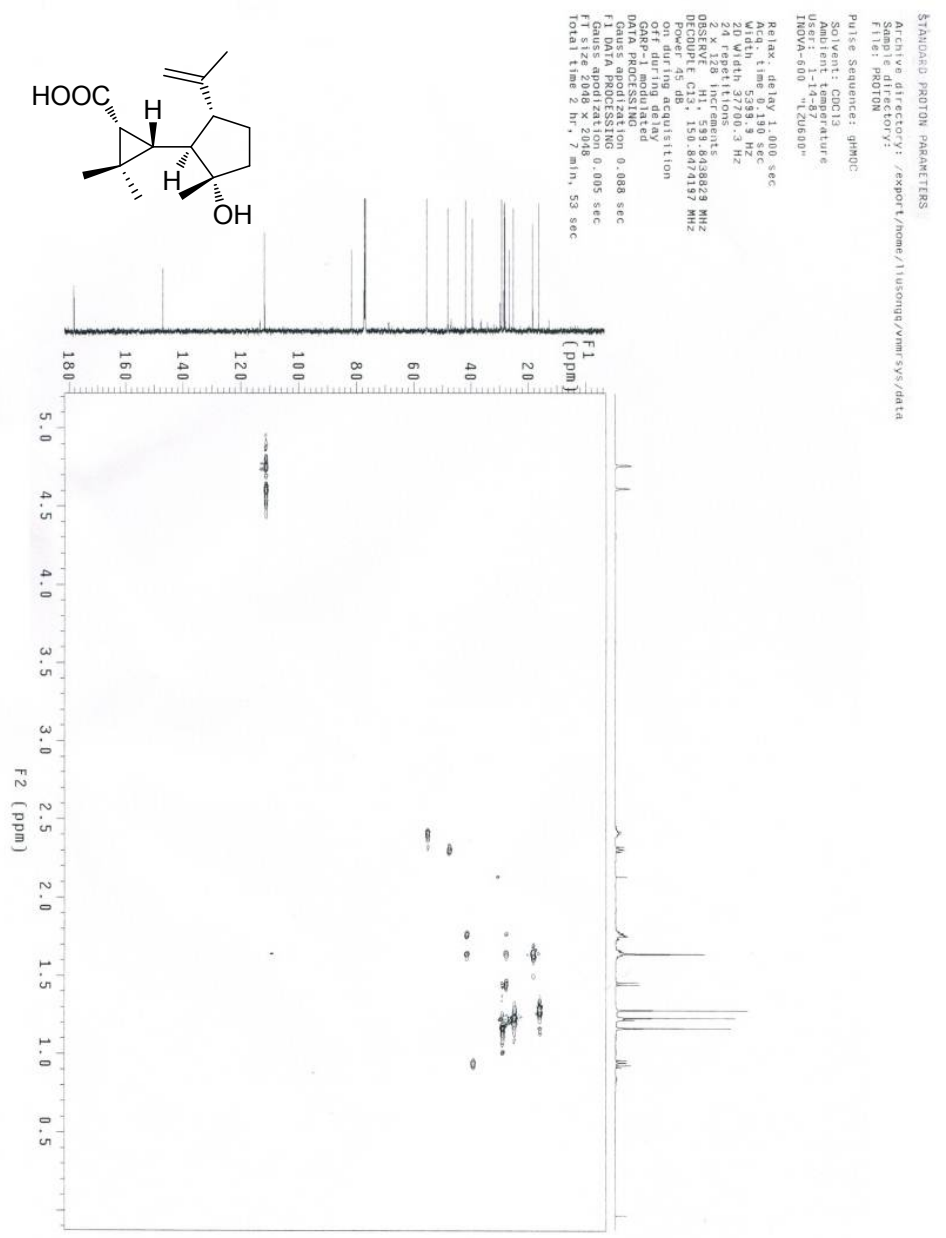

Figure S4. HMBC spectrum of crocrassin A (**1**) in $CDCl_3$

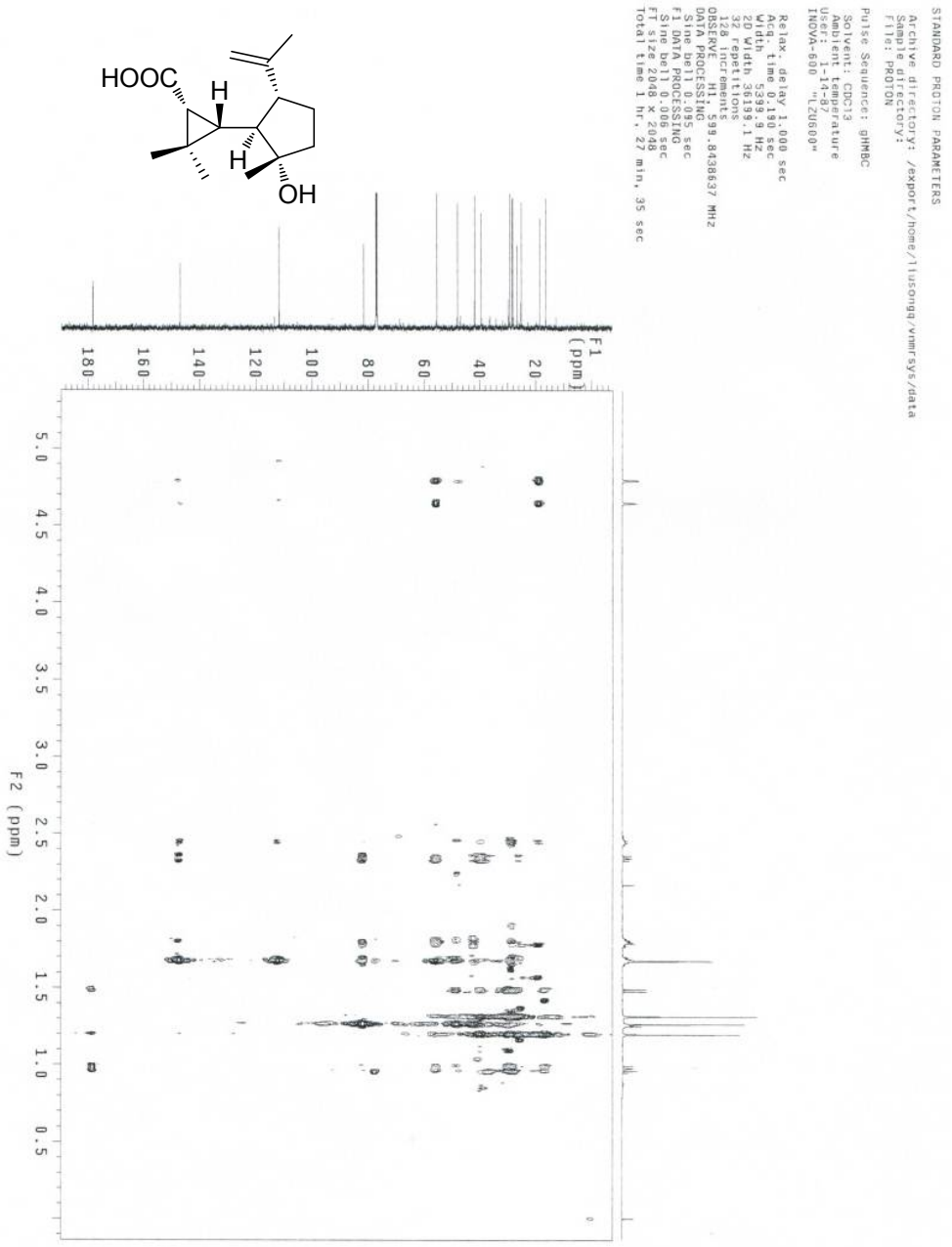

Figure S5. ^{1}H-^{1}H COSY spectrum of crocrassin A (**1**) in $CDCl_3$

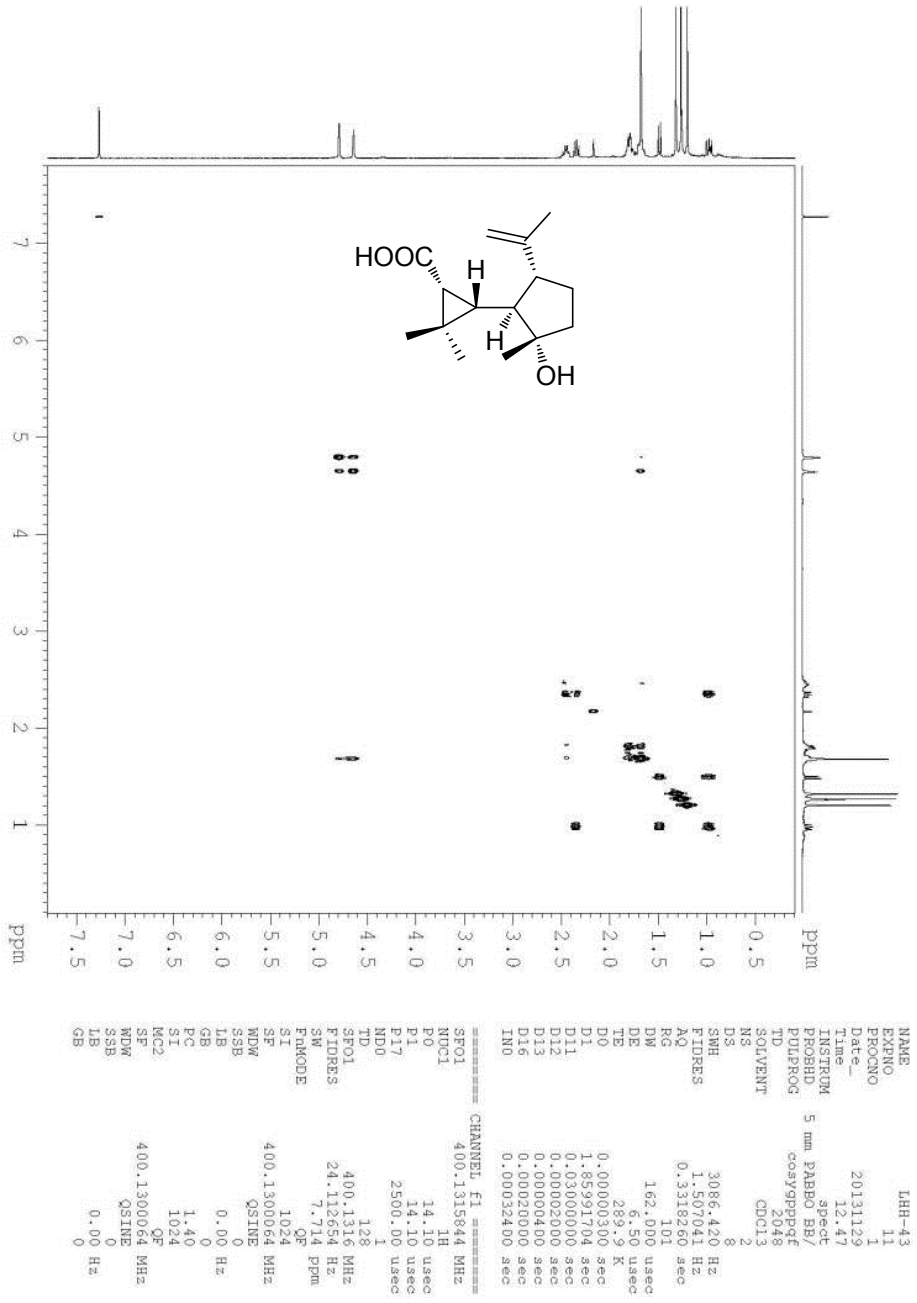

Figure S6. NOESY spectrum of crocrassin A (**1**) in $CDCl_3$

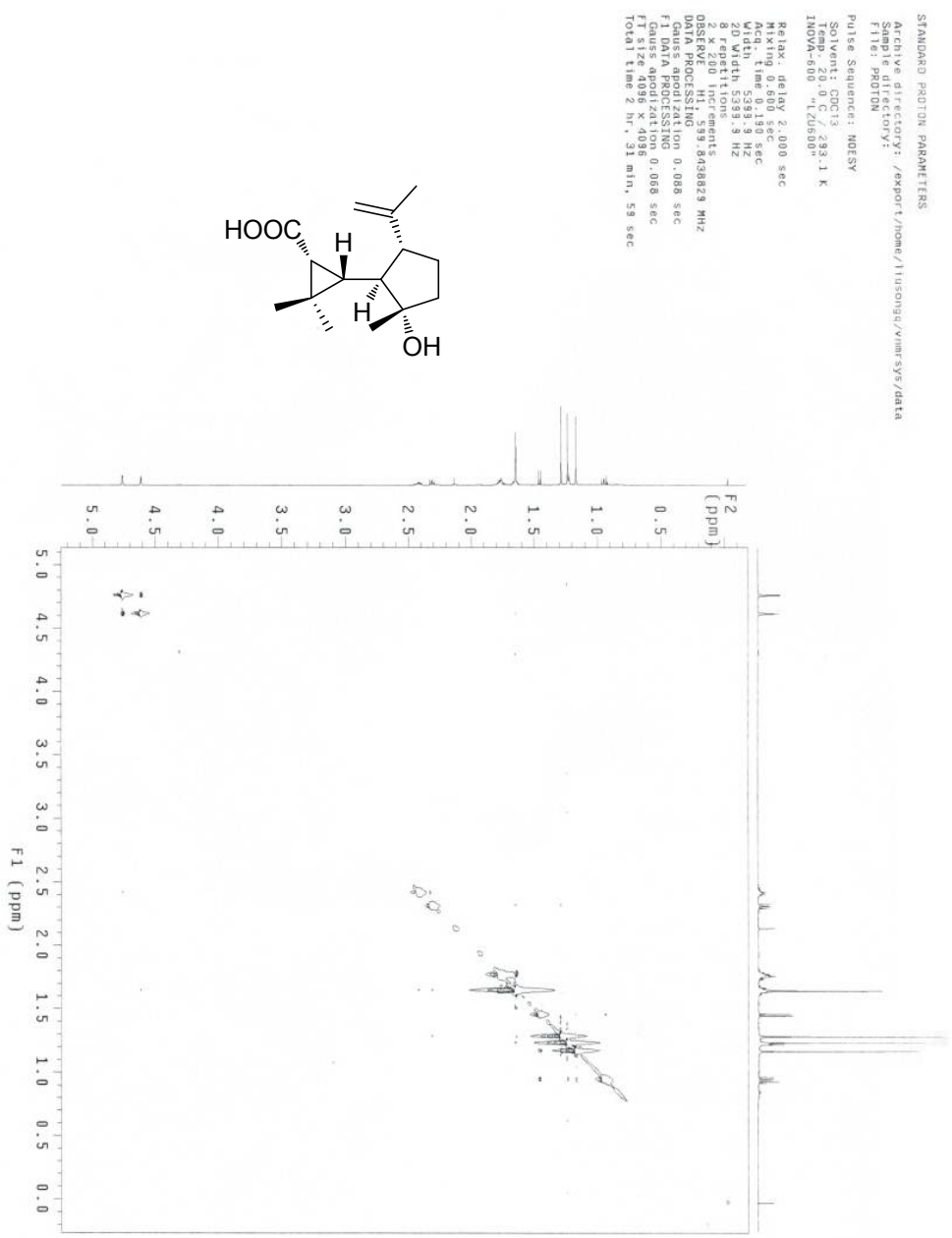

Figure S7. HRESIMS spectrum of crocrassin A (**1**)

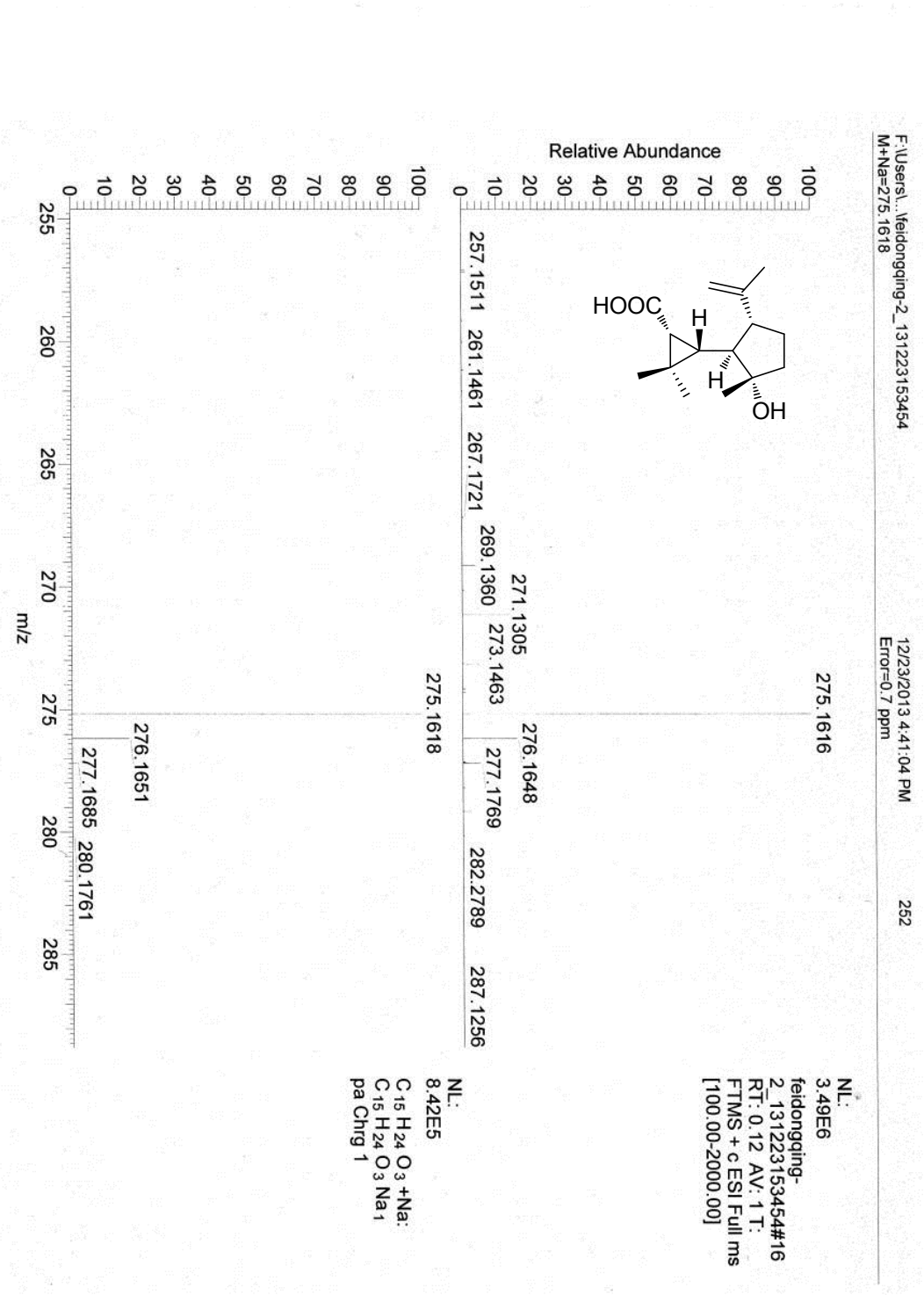

Figure S8. IR spectrum of crocrassin A (**1**)

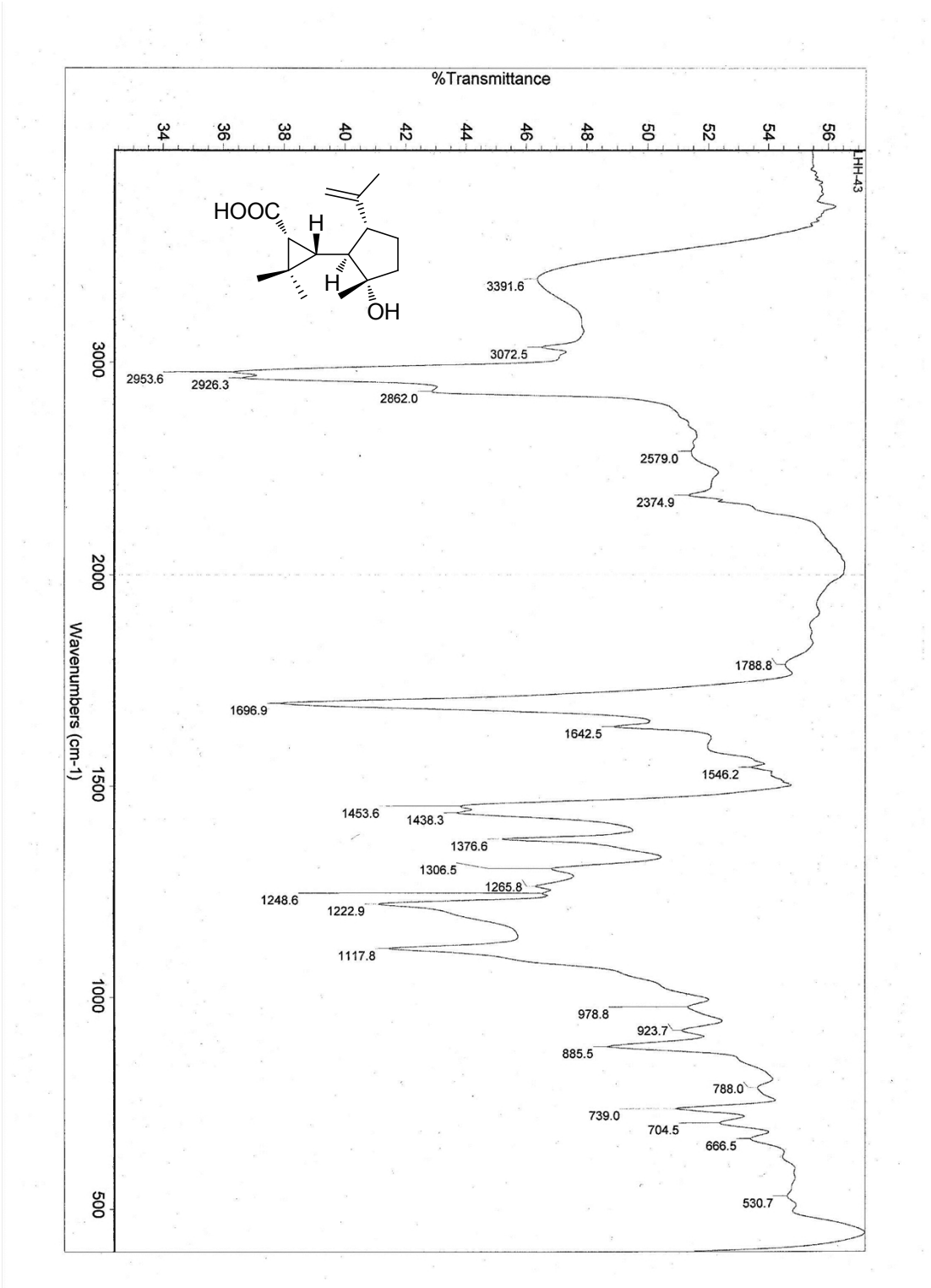

Figure S9. ^{1}H NMR spectrum of crocrassin B (**2**) in $CDCl_3$

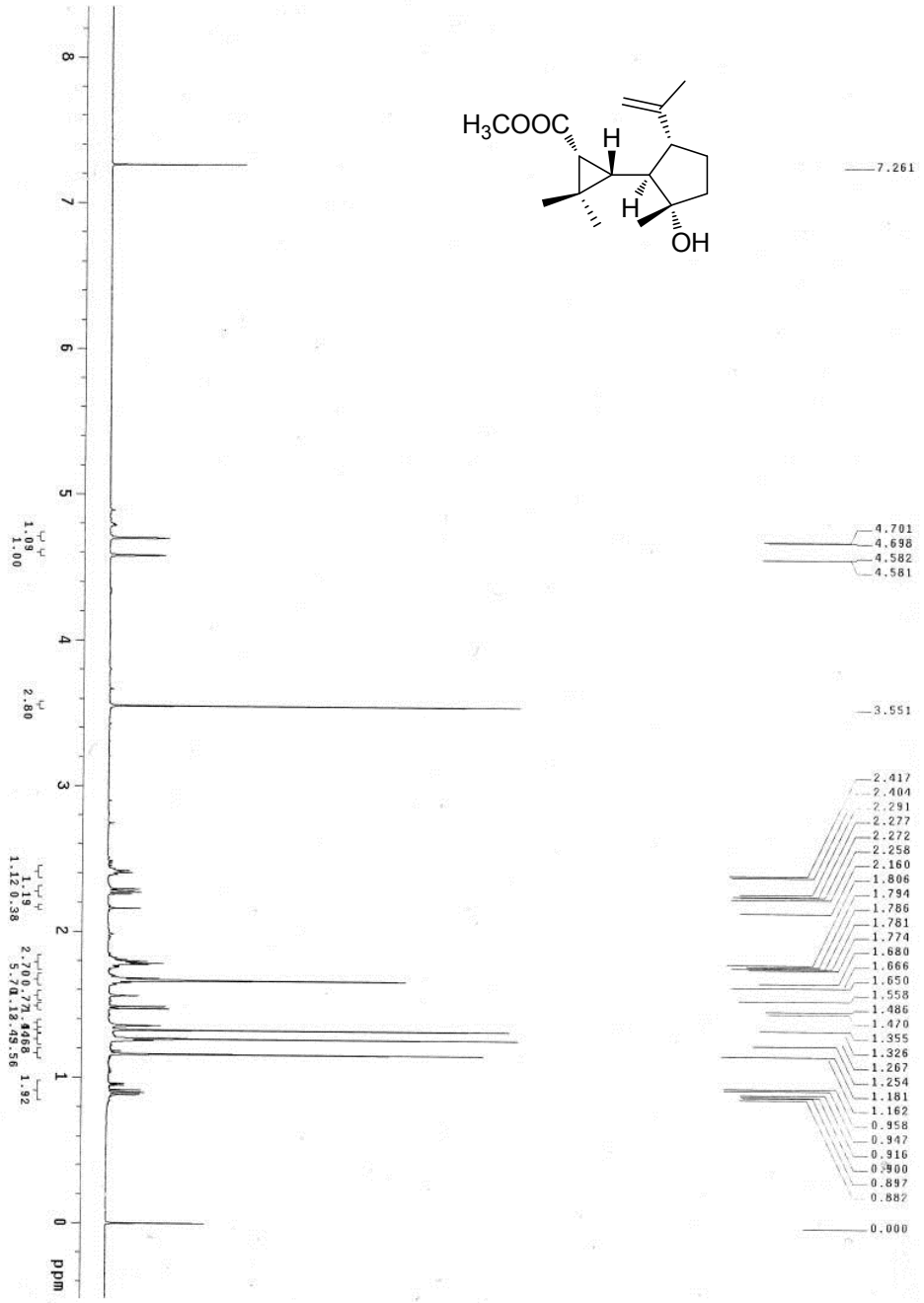

Figure S10. ^{13}C NMR spectrum of crocrassin B (**2**) in $CDCl_3$

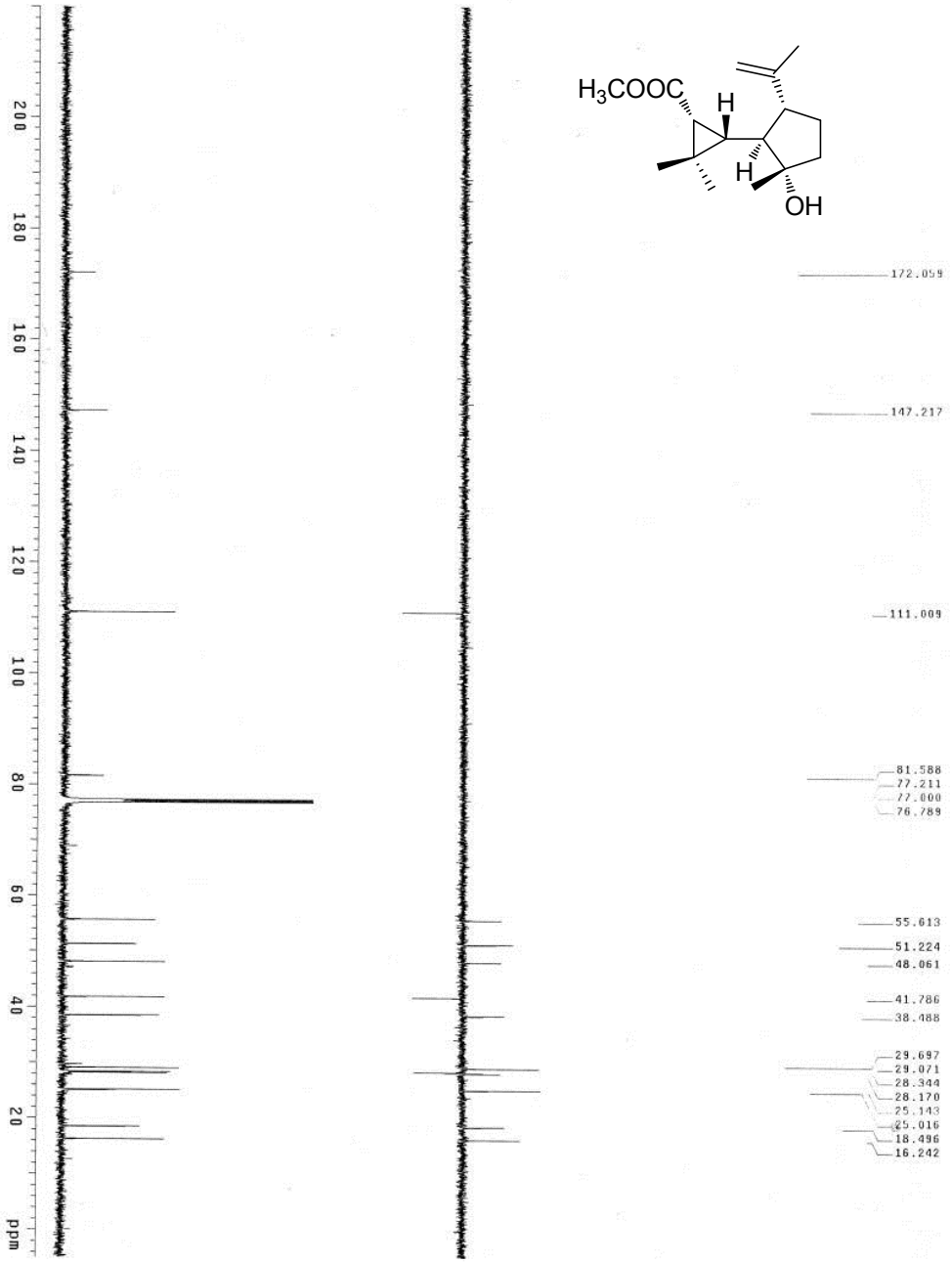

Figure S11. HSQC spectrum of crocrassin B (**2**) in $CDCl_3$

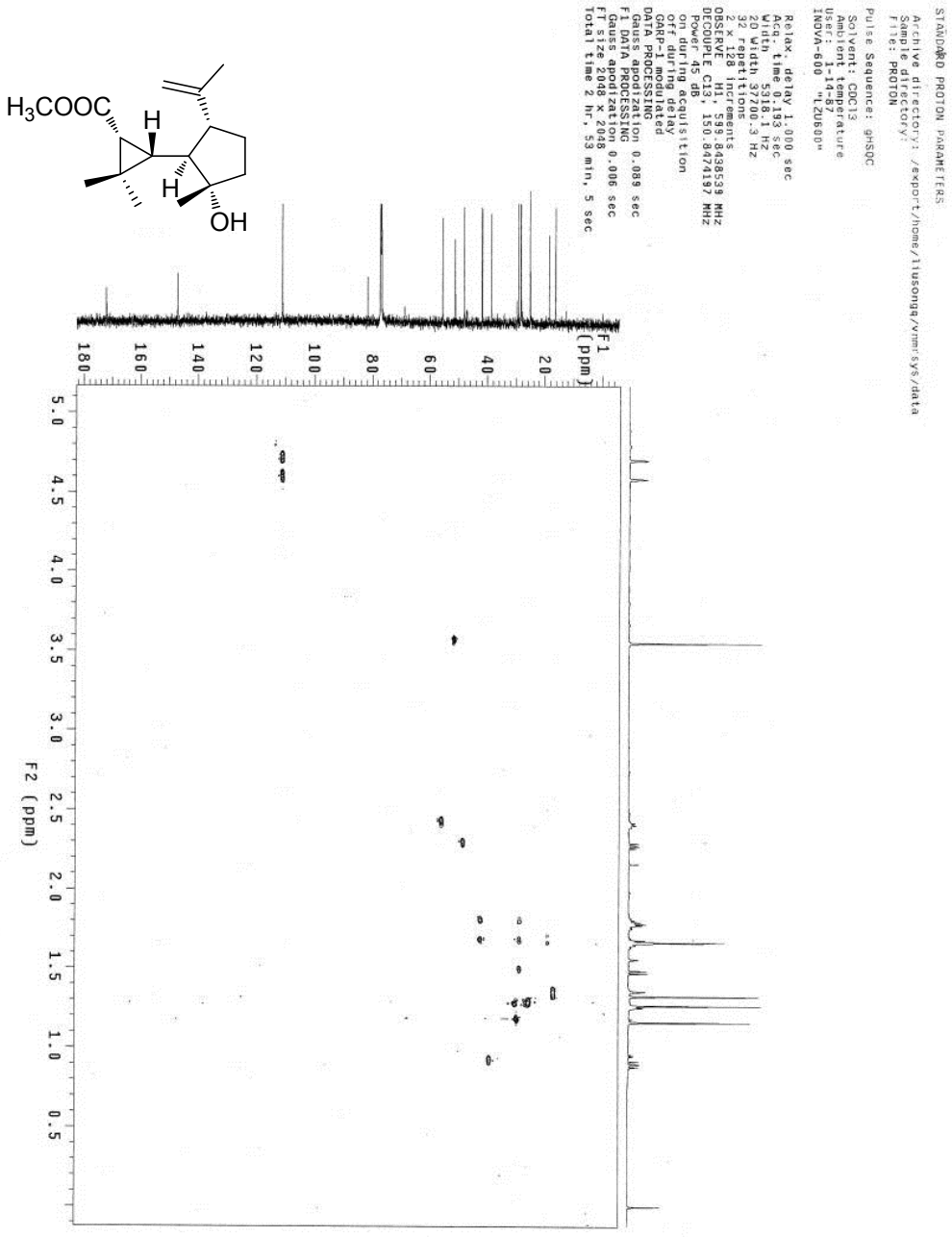

Figure S12. HMBC spectrum of crocrassin B (**2**) in $CDCl_3$

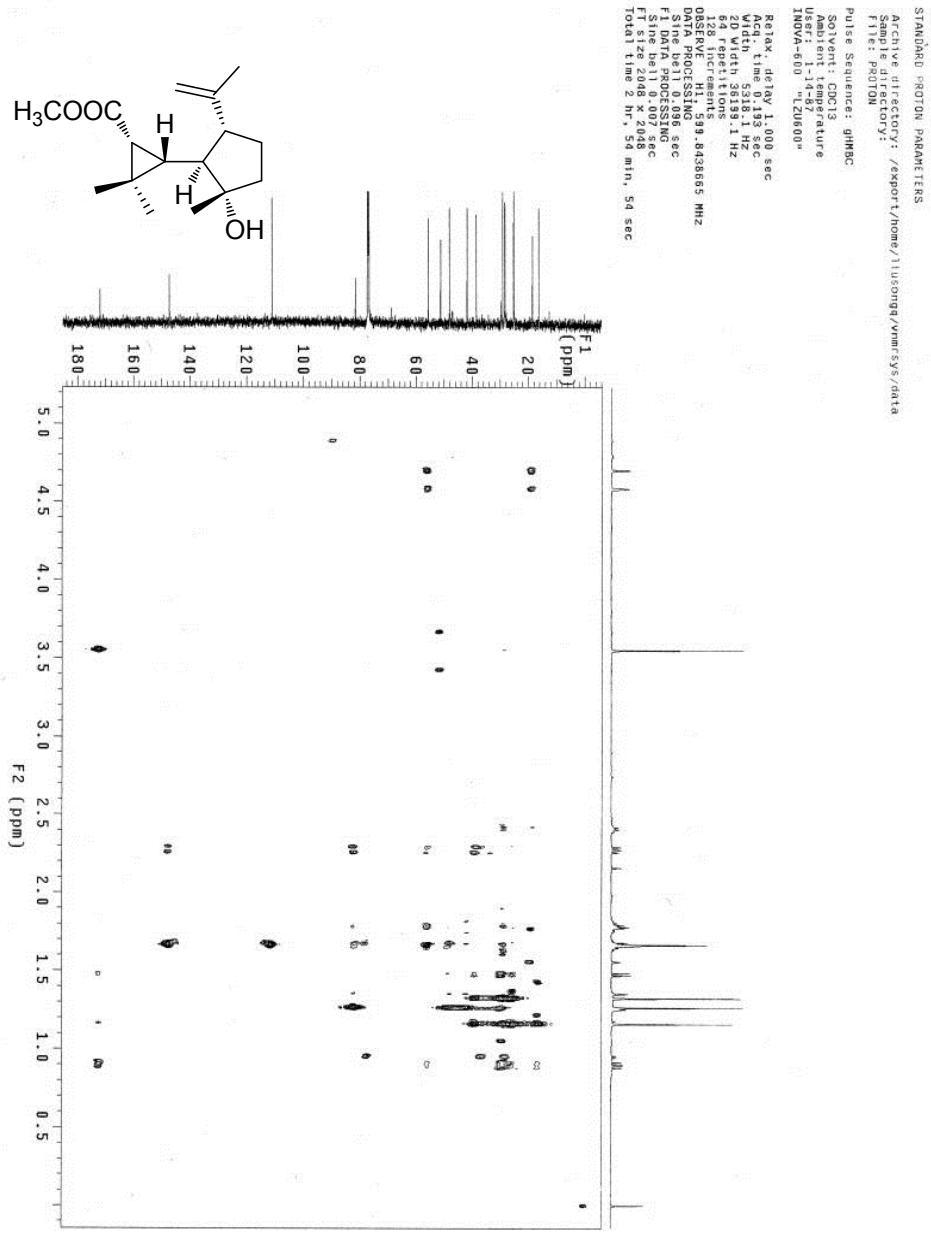

Figure S13. ^{1}H-^{1}H COSY spectrum of crocrassin B (**2**) in $CDCl_3$

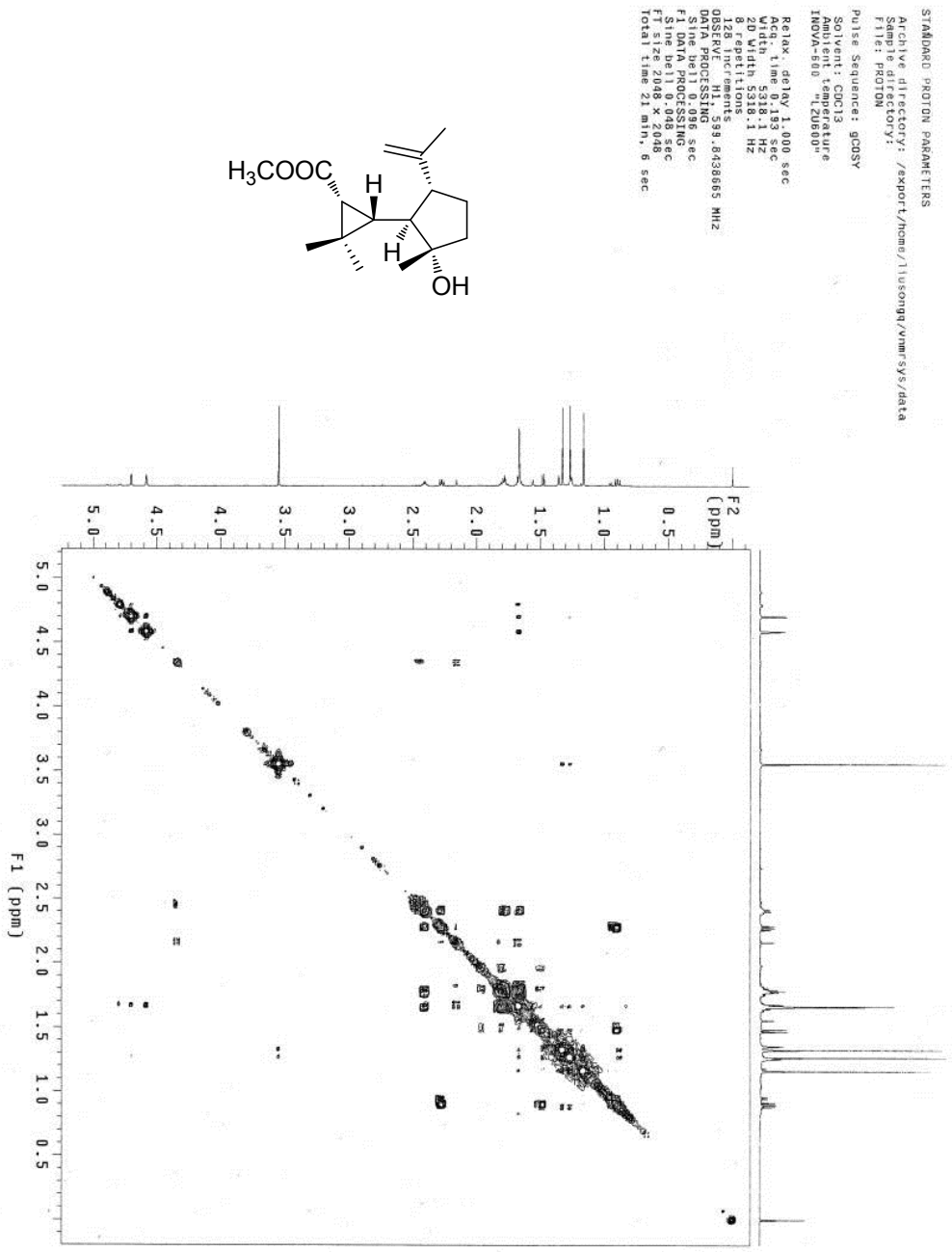

Figure S14. NOESY spectrum of crocrassin B (**2**) in $CDCl_3$

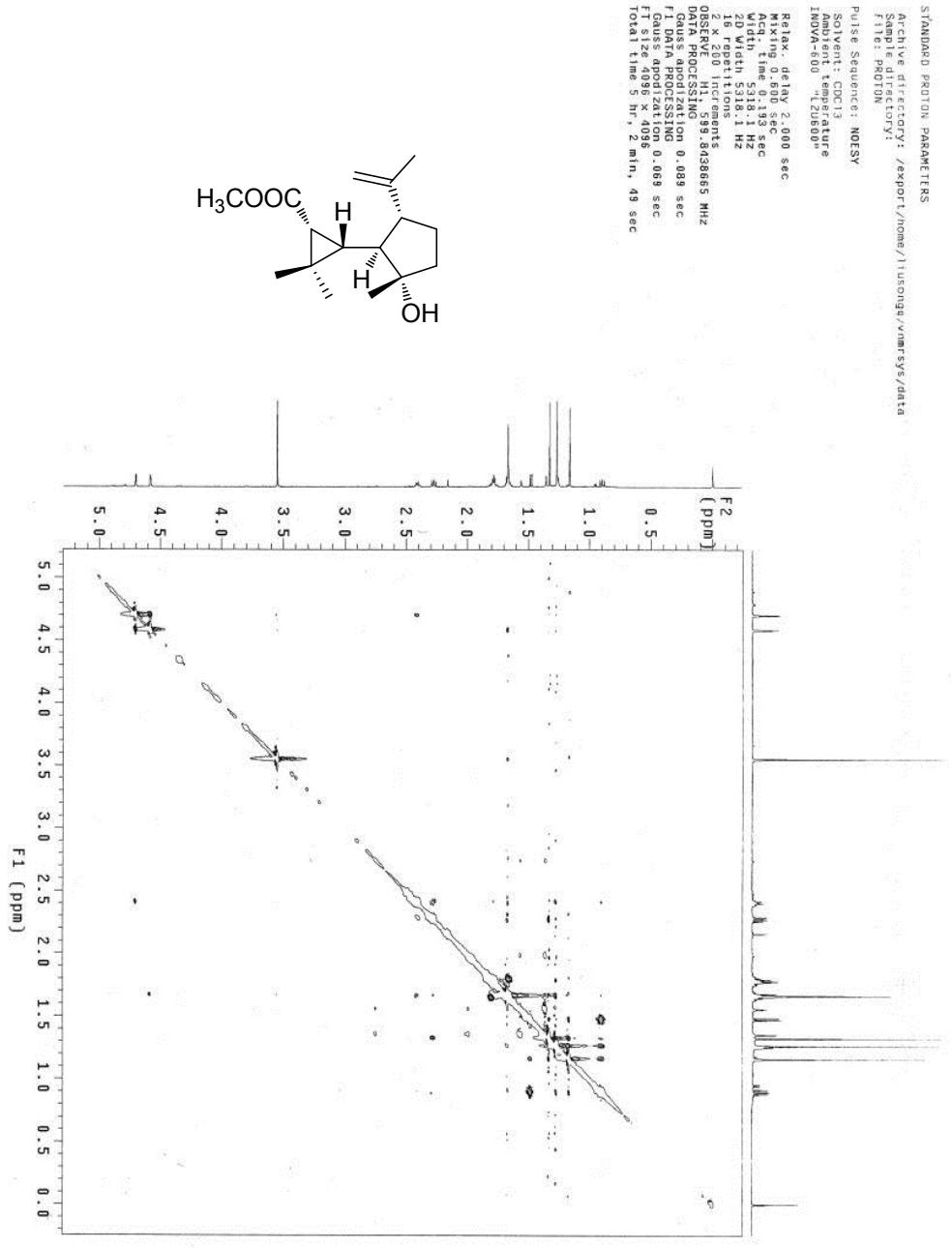

Figure S15. HRESIMS spectrum of crocrassin B (**2**)

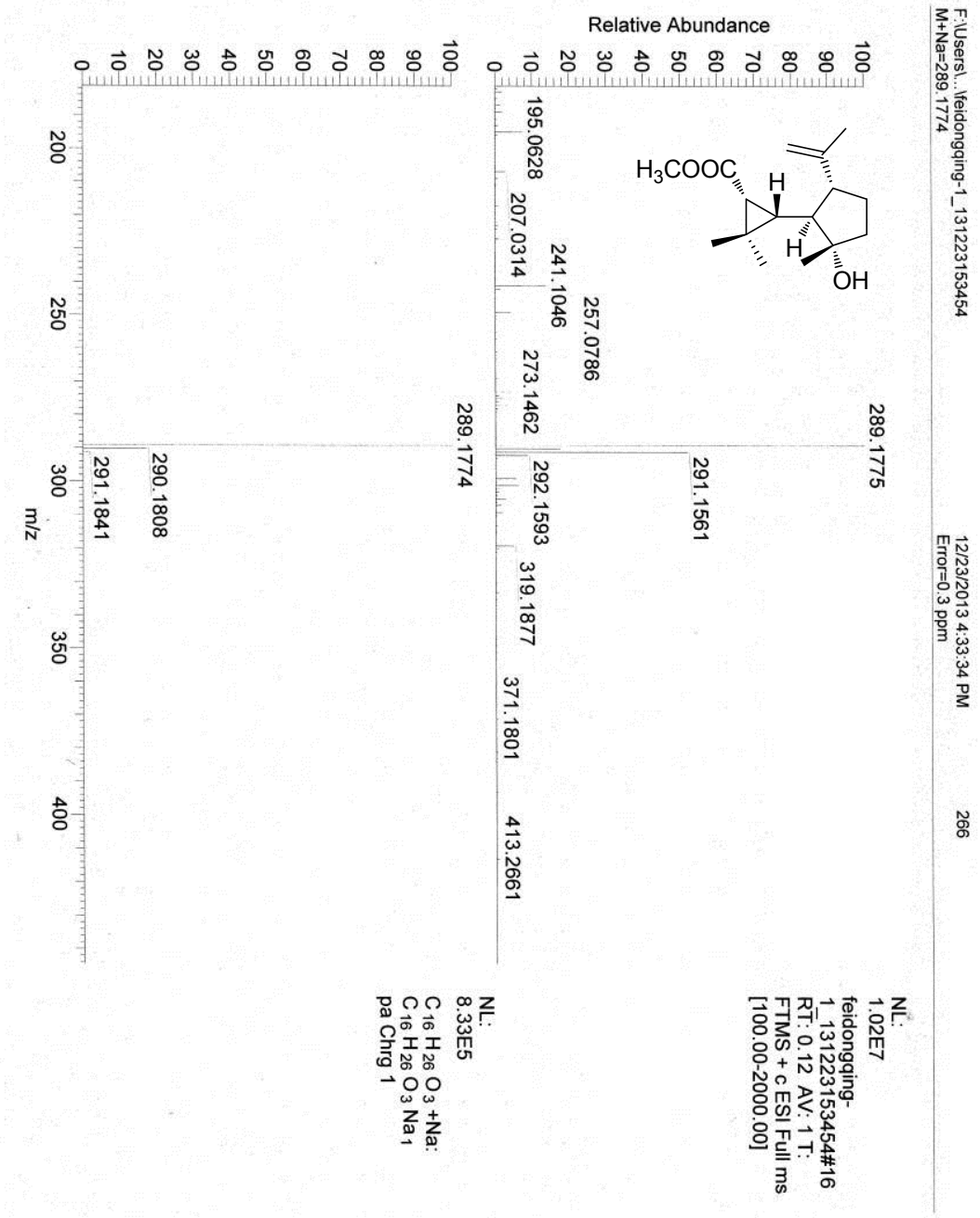

Figure S16. IR spectrum of crocrassin B (**2**)