Supporting Information

Two New Chemical Constituents from Leaves of *Perilla frutescens* var. *acuta*

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Extraction and Isolation

The dried leaves of *P. frutescens* Britton var. *acuta* Kudo (25 kg) were extracted with petroleum ether, and methanol, successively and evaporated under reduced pressure to give residues (264 g and 2 kg, respectively). The MeOH extracts (1 kg) were suspended in distilled water (2.4 L) and then successively partitioned with *n*-hexane, $CHCl_3$, EtOAc, and hydrated *n*-BuOH, 190 g, 144 g, 60 g, and 95 g, respectively.

The Petroleum ether fraction (120 g) was separated on a silica gel (70-230 mesh, 1 Kg), eluting with a gradient solvent system of Hexane/EtOAc (1:0 to 1:1) to yield three crude fractions (Fr. PA – PC). Fr. PA (4.2 g) was separated on a silica gel, eluting with solvent system of Hexane/EtOAc (40:1) to yield five fractions (PA1 – PA5). Subfraction PA4 (180 mg) was separated over an RP-C_{18} silica gel, eluting with solvent system 90% MeOH and purified by semi-preparative reversed-phase HPLC, using a solvent system of 90% MeOH to obtain **32** (40 mg) and **33** (2 mg). Fr. PB (37 g) was subfractionated with a silica gel column with Hexane-EtOAc (1:0 - 1:1) as the eluent to give seven fractions (PB1 – PB7). Subfraction PB5 fraction (8.7 g) was separated by silica gel column chromatography using a solvent system of Hexane-EtOAc (30:1 - 1:1) as the eluent to yield five fractions (PB51 – PB55). The PB53 fraction (1.0 g) was also subjected to a RP-C_{18} silica gel column with 100% MeCN and purified by preparative normal-phase HPLC with solvent system of Hexane-EtOAc (20:1) to yield **23** (20 mg), **24** (360 mg), **25** (167 mg), **29** (6 mg), **31** (3 mg) and **35** (24 mg). Fr. PC (32 g) was separated on a silica gel, eluting with solvent system of Hexane/EtOAc (40:1) to yield five fractions (PC1 – PC5). Subfraction PC2 (10.4 g) was separated over an RP-C_{18} silica gel, eluting with a gradient solvent system of 80 to 100% MeOH, to afford ten subfractions (PC21 – PC210). Subfraction PC21 (218 mg) was seperated on a silica gel, eluting with gradient solvent system of Hexane/EtOAc (30:1) and purified with silica gel prep. HPLC (Hexane/ EtOAc = 40:1) to obtain **34** (16 mg). Subfraction PC22 (778 mg) was separated on a silica gel, eluting with a gradient solvent system of Hexane/EtOAc (30:1) and purified with silica gel prep. HPLC (Hexane/EtOAc = 40:1) to obtain **26** (5 mg) and **27** (200 mg).

The $CHCl_3$ soluble fraction (25 g) was separated on a silica gel (70-230 mesh, 1 Kg), eluting with a gradient solvent system of $CHCl_3$/MeOH (40:1 to 1:1) to yield seven crude fractions (Fr. CA – CG). Fr. CB (9.0 g) was separated over an RP-C_{18} silica gel (230-400 mesh, 300 g), eluting with a gradient solvent system of 80 to 100% MeOH, to afford four subfractions (CB1 – CB4). Subfraction CB2 (1.4 g) was was separated on a silica gel, eluting with solvent system of $CHCl_3$/MeOH (40:1) and purified with RP-C_{18} silica gel prep. HPLC 50% MeOH to yield compound **28** (13 mg) and **30** (4 mg). Subfraction CB3 (2.5 g) was separated on a silica gel, eluting with solvent system of $CHCl_3$/MeOH (40:1) and purified with RP-C_{18} silica gel prep. HPLC (60% MeOH) to yield **21** (5 mg).

The EtOAc soluble fraction (33 g) was separated on a silica gel (70-230 mesh, 1 Kg), eluting with a gradient solvent system of $CHCl_3$/MeOH (40:1 to 1:1) to yield seven crude fractions (Fr. EA – EG). Fr. EB (2.6 g) was separated over an RP-C_{18} silica gel (230-400 mesh, 300 g), eluting with gradient solvent system of 30 to 100% MeOH, to afford fifteen subfractions (EB1 – EB15). Subfration EB3 (16 mg) and EB7 (100 mg) were purified with RP-C_{18} silica gel prep. HPLC (40% MeOH) to yield compound **8** (3 mg) and **9** (26 mg). Subfraction EB10 (120 mg) was chromatographed on LiChroprep Lobar®-A Silca gel column ($CHCl_3$/MeOH = 40:1) and further purified by semi-preparative reversed-phase HPLC, using a solvent system of 50% MeOH to obtain **16** (10 mg). Fr. EC (2.5 g) was separated over an RP-C_{18} silica gel (230-400 mesh, 300 g), eluting with a gradient solvent system of 30 to 100% MeOH, to afford ten subfractions (EC1 – EC10). Subfraction EC1 (400 mg) was separated over a silica gel column with a solvent system of $CHCl_3$-MeOH (35:1 to 1:1) and further purified by semi-preparative reversed-phase HPLC, using a solvent system of 50% MeOH to obtain **10** (6 mg) and **17** (2 mg). Subfraction EC2 (220 mg) was chromatographed on Sephadex LH-20 (80% MeOH) and purified with RP-C_{18} silica gel prep. HPLC (40% MeOH) to yield **22** (9 mg). Subfraction EC4 (150 mg) was chromatographed on Sephadex LH-20 (80% MeOH) and purified with RP-C_{18} silica gel prep. HPLC (55% MeOH) to yield compound **1** (7 mg) and **2** (25 mg). Fr. ED (4.5 g) was separated over an RP-C_{18} silica gel (230-400

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mesh, 300 g), eluting with a gradient solvent system of 40 to 100% MeOH, to afford nine subfractions (ED1 – ED9). Subfration ED8 (30 mg) was purified with RP-C_{18} silica gel prep. HPLC (70% MeOH) to yield compound **20** (5 mg). Fr. EE (14.7 g) was separated over an RP-C_{18} silica gel (230-400 mesh, 400 g), eluting with a gradient solvent system of 50 to 100% MeOH, to afford ten fractions (EE1 – EE10). Fraction EE1 (7.9 g) was separated over a silica gel column with a solvent system of $CHCl_3$-MeOH (30:1 to 1:1) to yield eight subfractions (EE11 – EE18). Subfraction EE14 (27 mg) was purified with RP-C_{18} silica gel prep. HPLC (30% MeOH) to yield compound **18** (4 mg). Subfraction EE15 (750 mg) was separated over an RP-C_{18} silica gel (50 to 100% MeOH) to yield two subfractions (EE151 – EE152). Subfraction EE151 (320 mg) was chromatographed on Sephadex LH-20 (80% MeOH) and further purified with RP-C_{18} silica gel prep. HPLC (25% MeOH) to yield compound **5** (25 mg), **13** (1.5 mg), and **15** (80 mg). Subfraction EE155 (400 mg) was purified with RP-C_{18} silica gel prep. HPLC (60% MeOH) to yield compound **4** (245 mg). Subfraction EE18 (4.2 g) was chromatographed on Sephadex LH-20 (80% MeOH) four subfractions (EE181 – EE184). Subfraction EE181 (390 mg) was separated over an RP-C_{18} silica gel (230-400 mesh, 150 g), eluting with a gradient solvent system of 30 to 100% MeOH, and purified with silica gel prep. HPLC ($CHCl_3$/MeOH = 15:1) to obtain **6** (4 mg), **12** (25 mg), and **19** (5 mg). Subfraction EE182 (250 mg) was separated over an RP-C_{18} silica gel (230-400 mesh, 100 g), eluting with gradient solvent system of 30% MeOH, and purified with RP-C_{18} silica gel prep. HPLC (50% MeOH) to afford **11** (3 mg). Subfraction EE184 (3.2 g) was separated over an RP-C_{18} silica gel (230-400 mesh, 100 g), eluting with a gradient solvent system of 30% MeOH, to yield three subfractions (EE1841 – EE1843). Subfraction EE1842 (2.9 g) was purified with RP-C_{18} silica gel prep. HPLC (30% MeCN) to afford **3** (1.2 g).

The BuOH soluble fraction (21 g) was separated over an RP-C_{18} silica gel (230-400 mesh, 500 g), eluting with a gradient solvent system of 50 to 100% MeOH, to yield four crude fractions (Fr. BA – BD). Fr. BA (16.0 g) was subfractionated with a silica gel column with $CHCl_3$-MeOH-H_2O (5:1:0 to 1:1:0.3) as the eluent to give five fractions (BA1 – BA5). Subfraction BA4 (3 g) was separated over an RP-C_{18} silica gel (230-400 mesh, 100 g), eluting with a gradient solvent system of 30 to 100 % MeOH and purified with RP-C_{18} silica gel prep. HPLC (45% MeOH) to afford **7** (25 mg), **14** (12 mg), and **36** (13 mg).

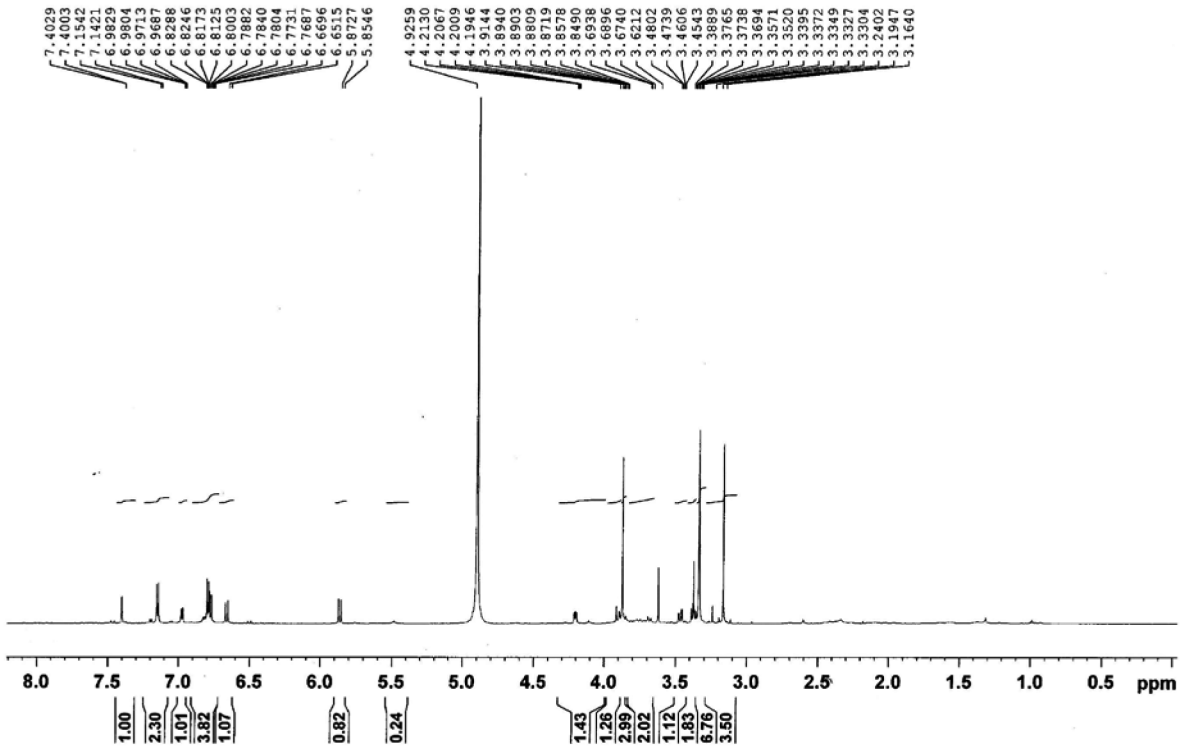

Fig. S1 ^{1}H NMR spectrum of **1** (700 MHz, CD_3OD).

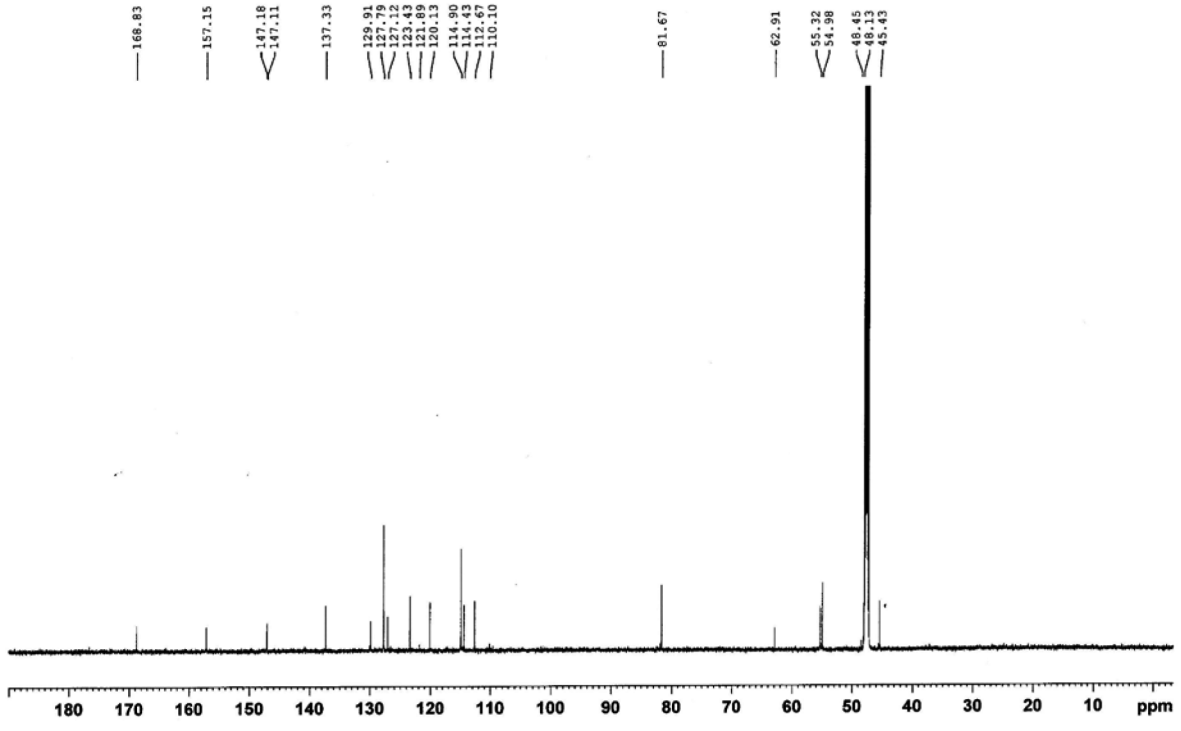

Fig. S2 ^{13}C NMR spectrum of **1** (175 MHz, CD_3OD).

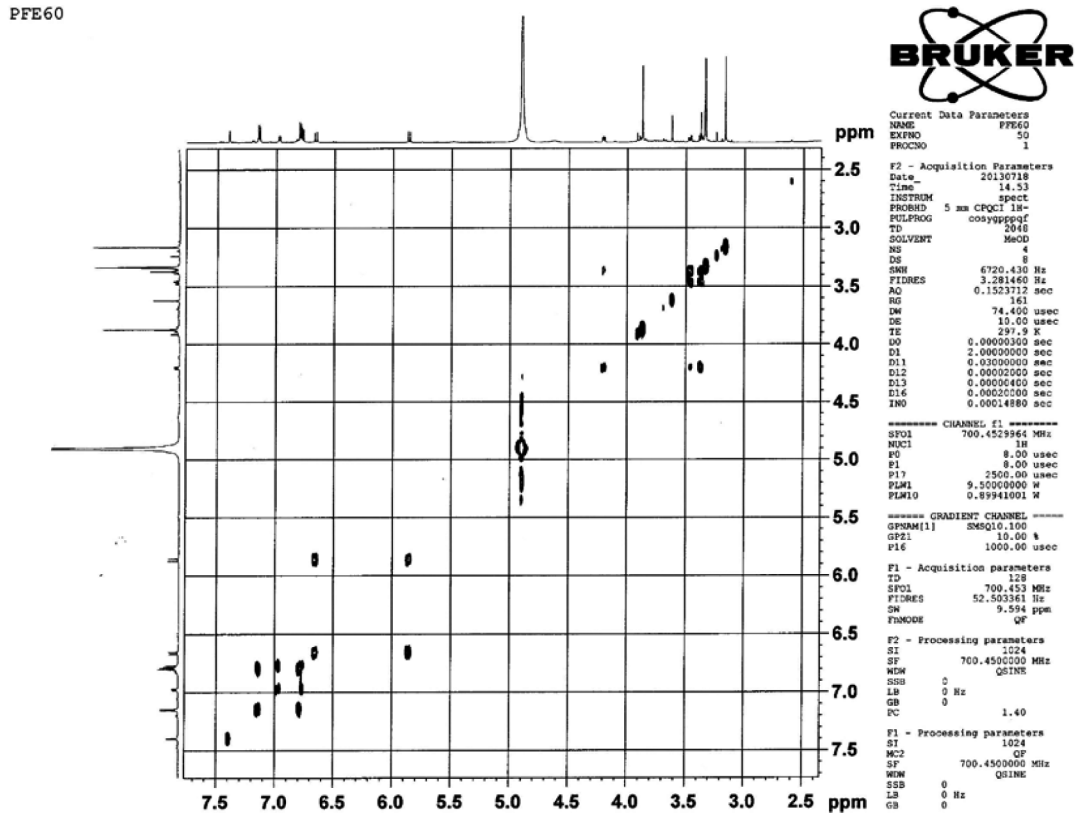

Fig. S3 ^{1}H-^{1}H COSY spectrum of **1**.

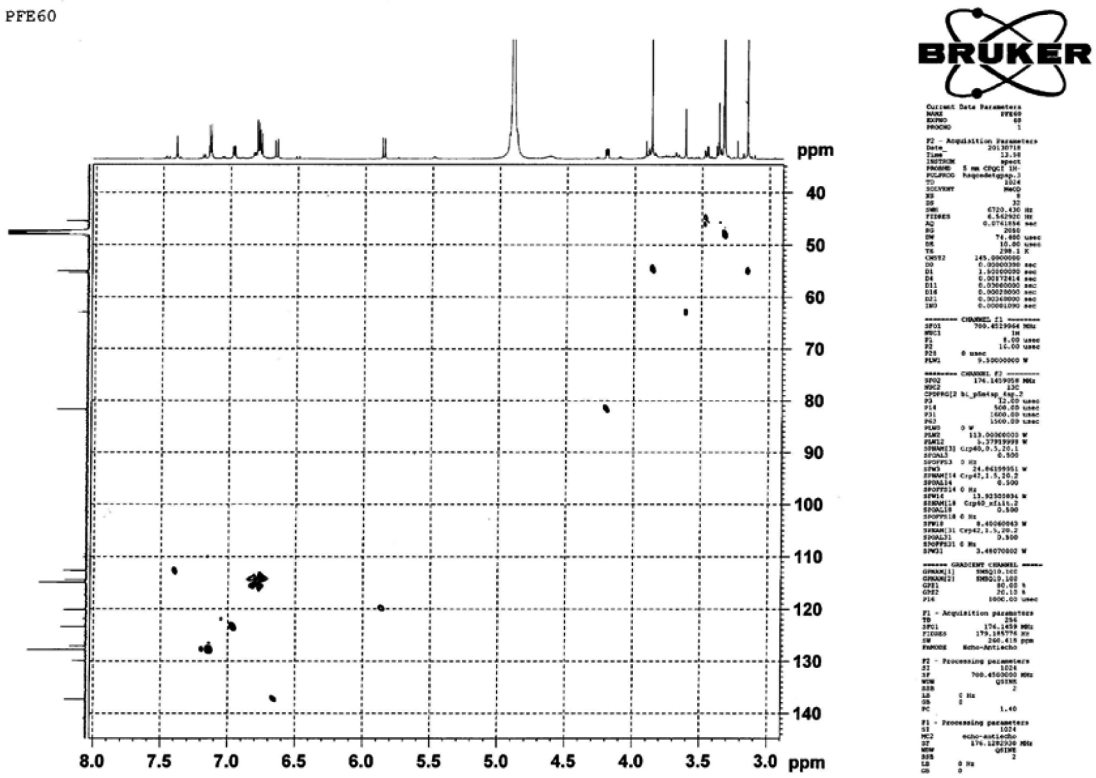

Fig. S4 HSQC spectrum of **1**.

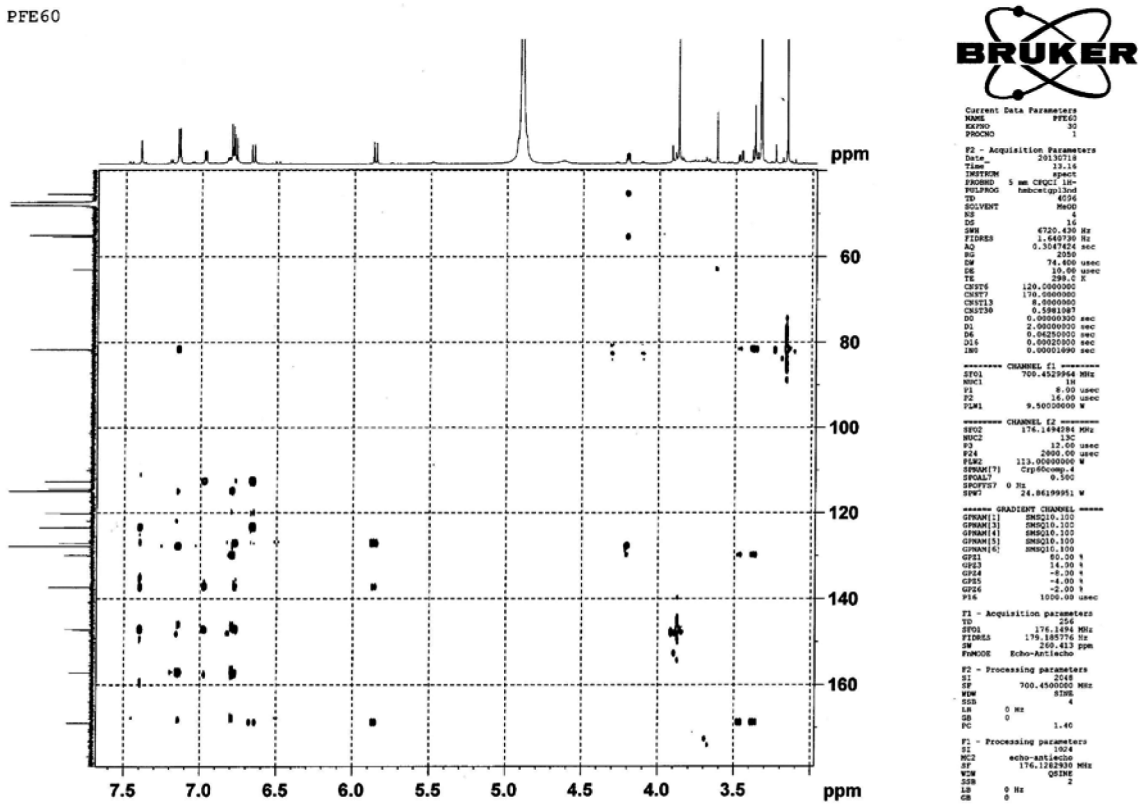

Fig. S5 HMBC spectrum of **1**.

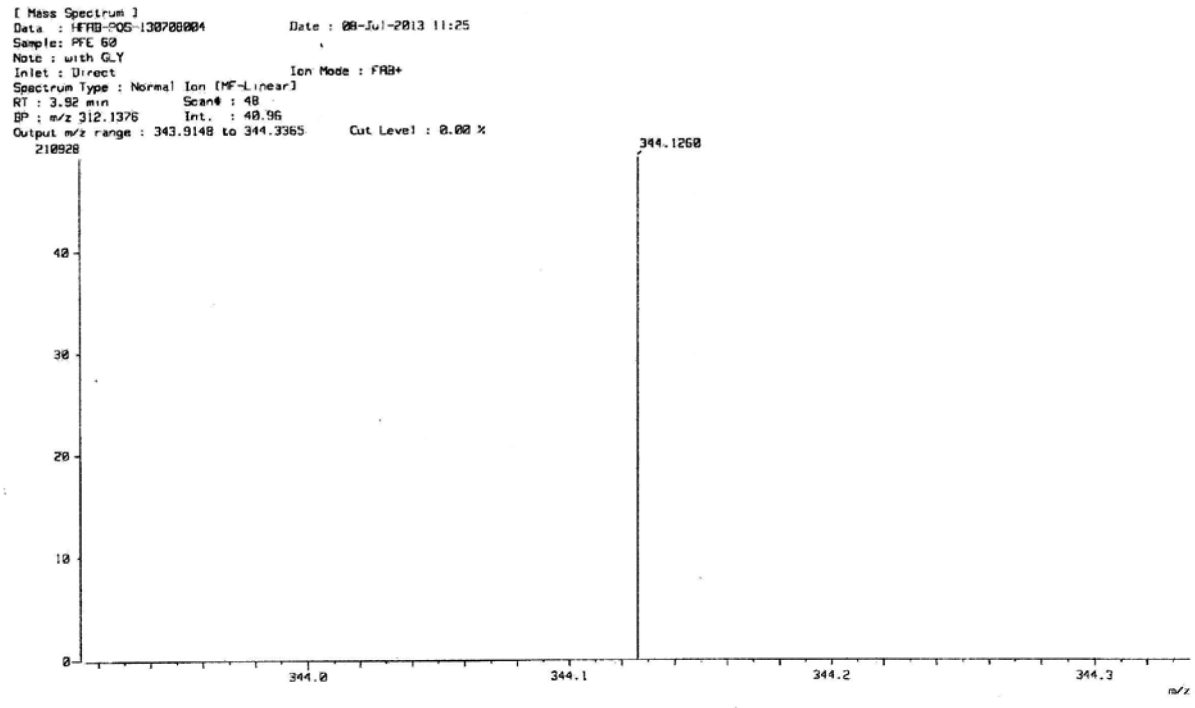

Fig. S6 HR FAB MS spectra of **1**.

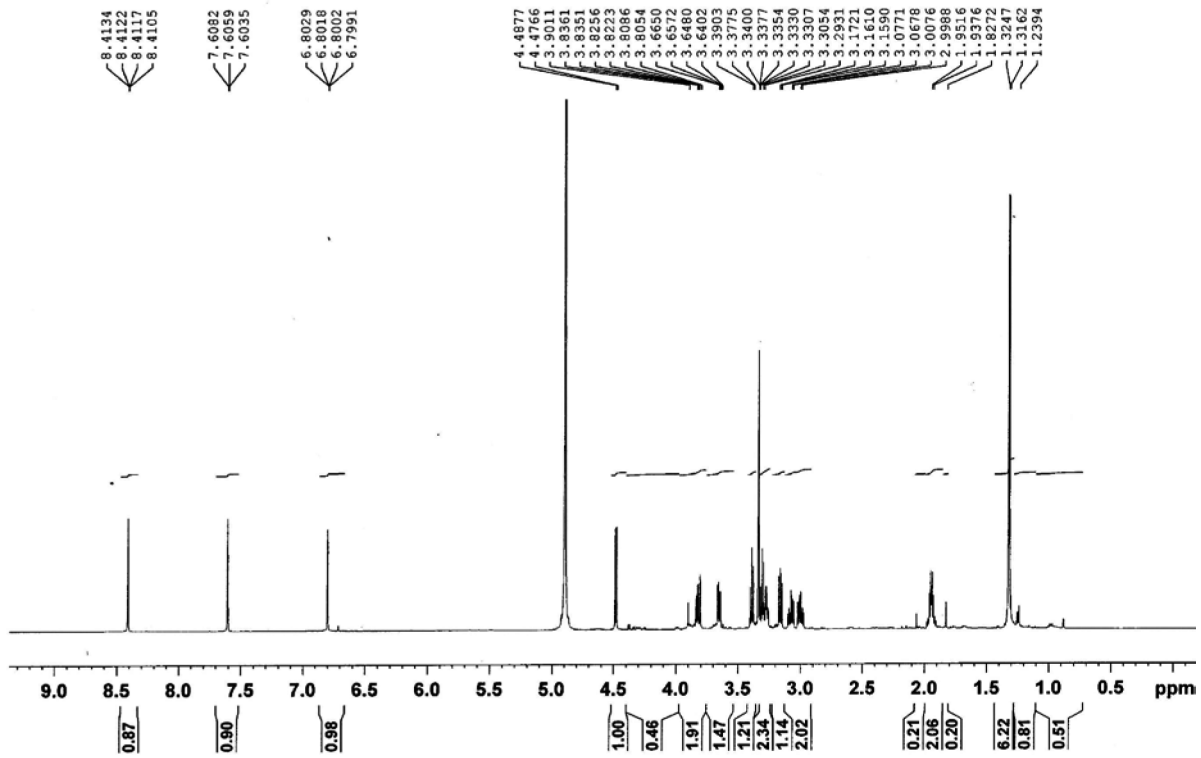

Fig. S7 ^{1}H NMR spectrum of **36** (700 MHz, CD_3OD).

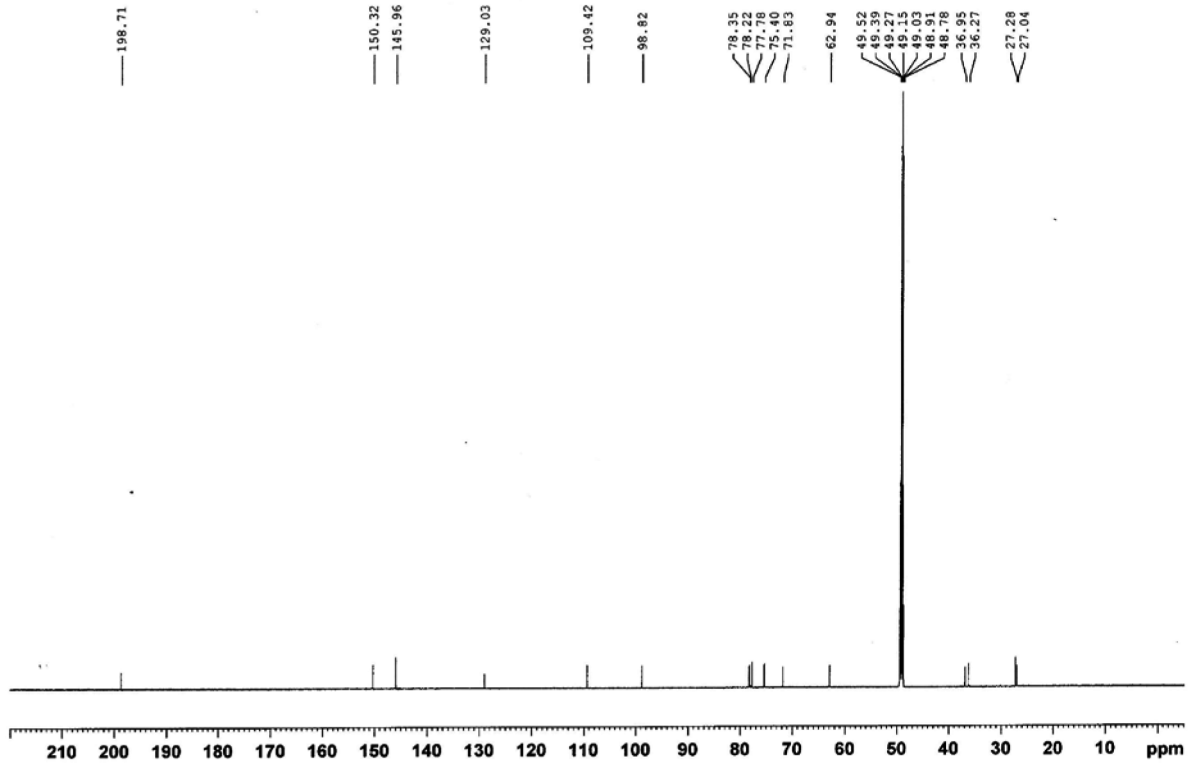

Fig. S8 ^{13}C NMR spectrum of **36** (175 MHz, CD_3OD).

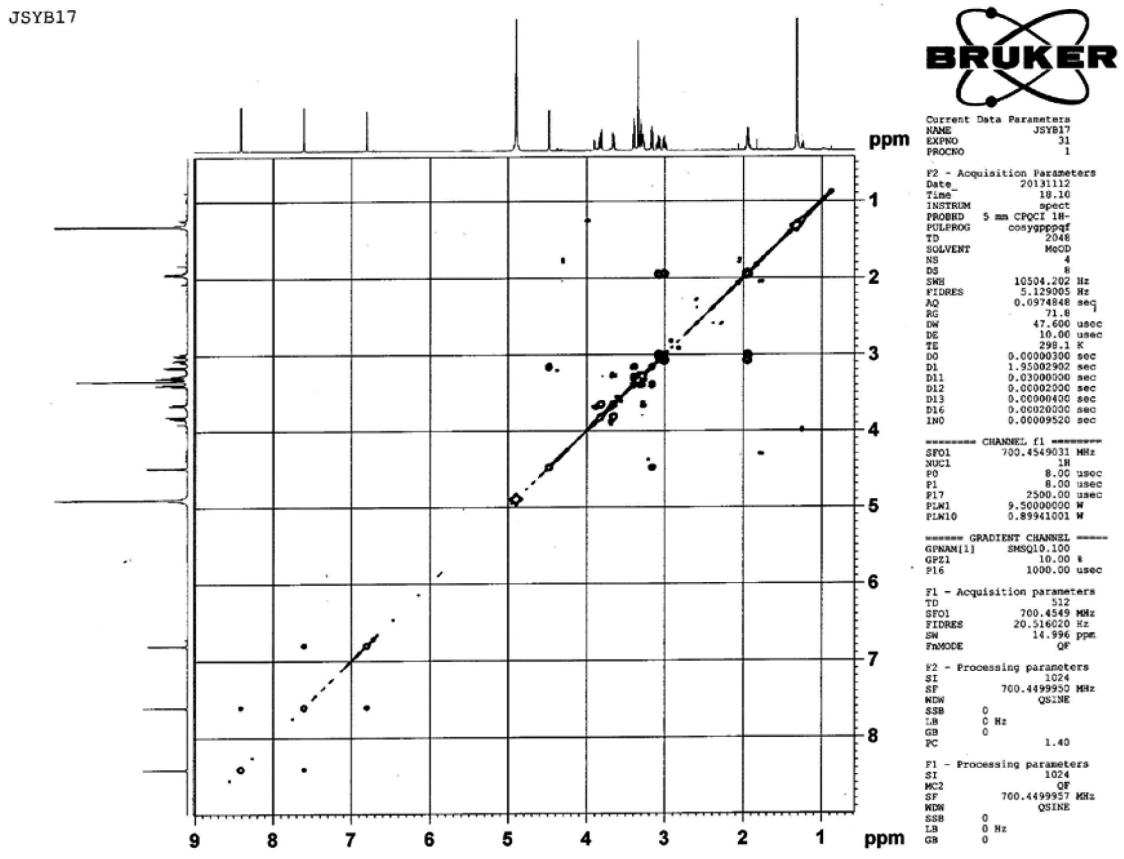

Fig. S9 ^{1}H-^{1}H COSY spectrum of **36**.

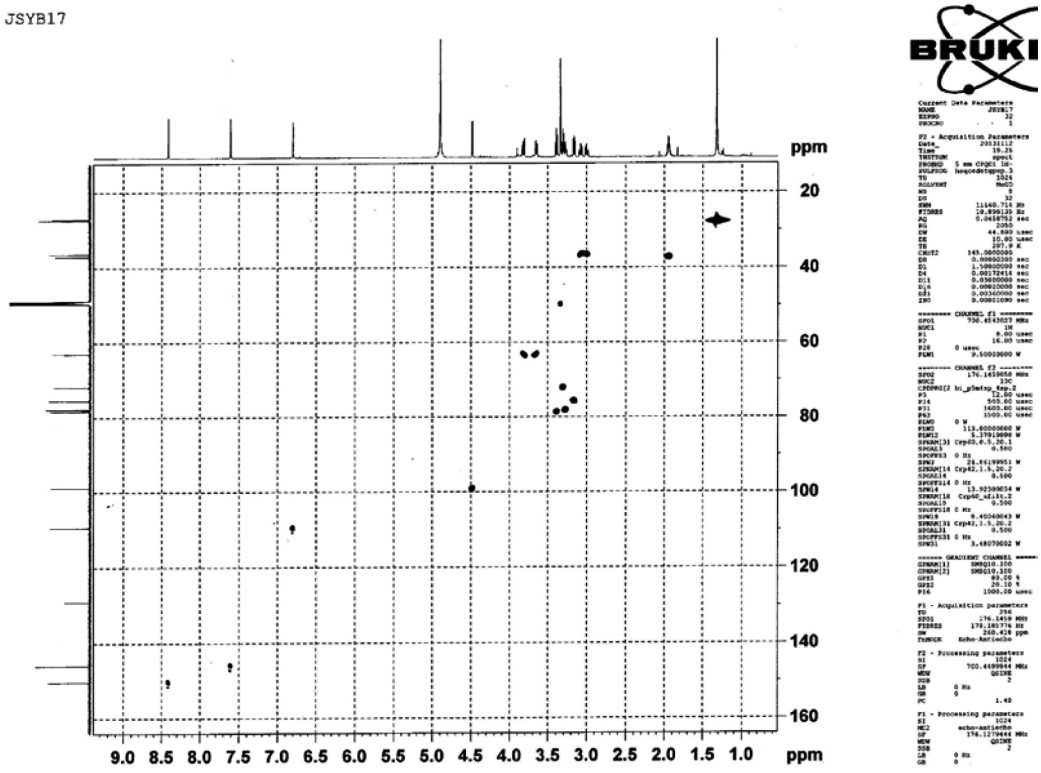

Fig. S10 HSQC spectrum of **36**.

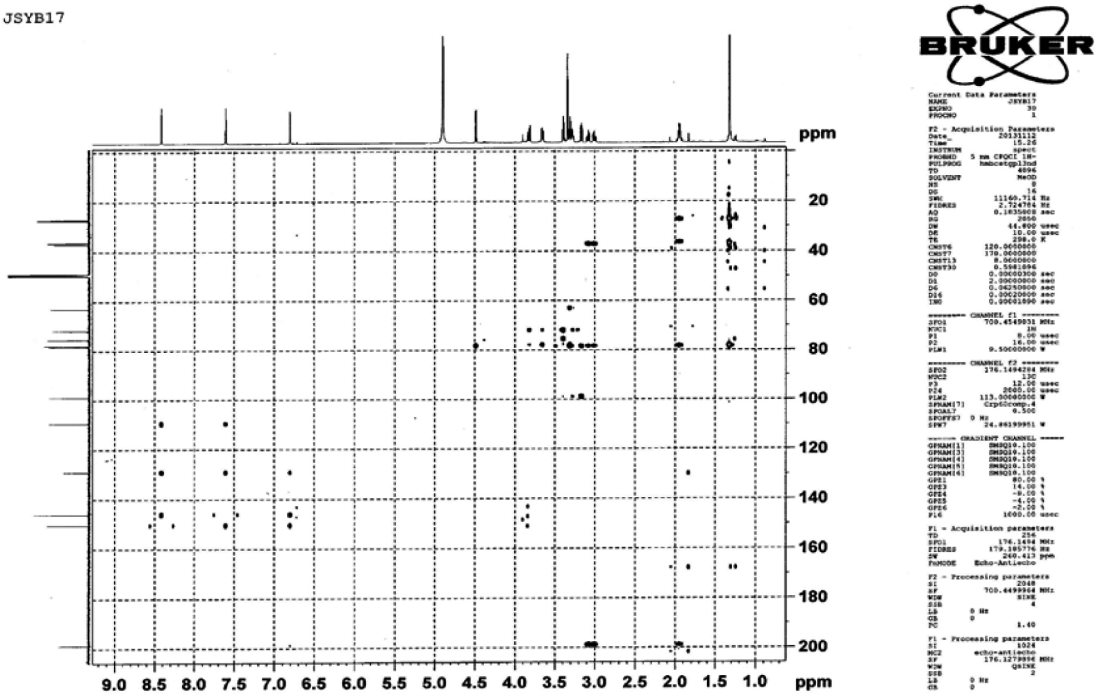

Fig. S11 HMBC spectrum of **36**.

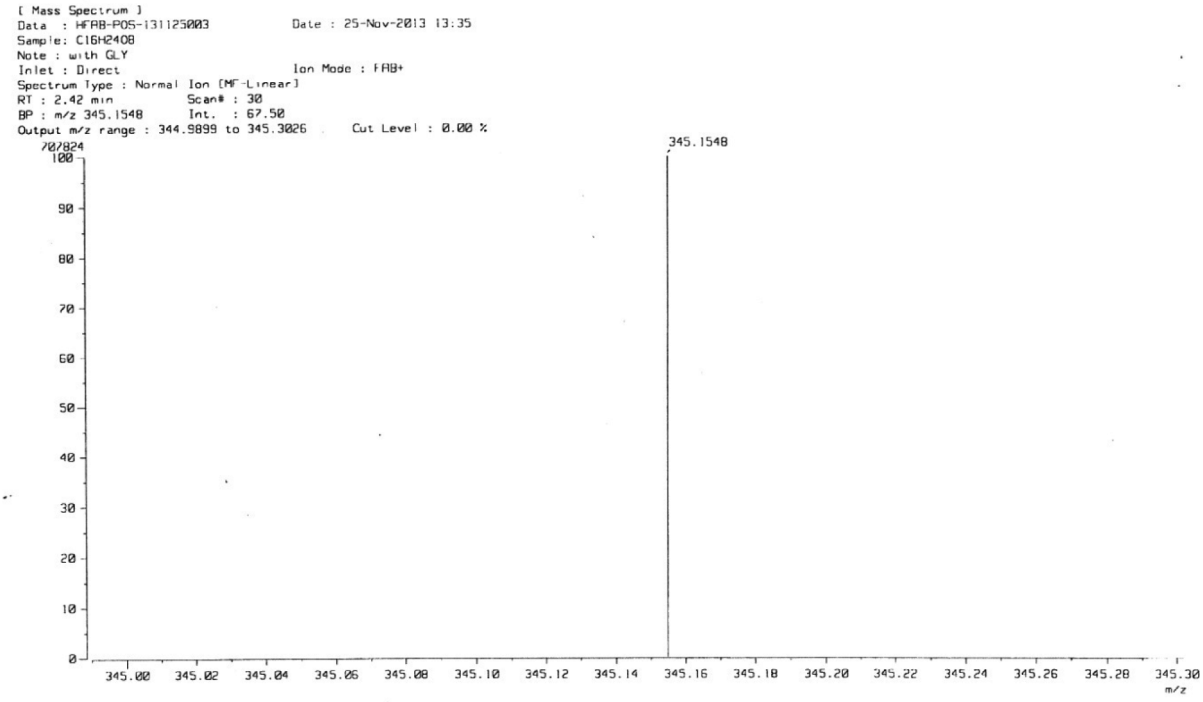

Fig. S12 HR FAB MS spectra of **36**.