A domino synthetic approach for some new, angular pyrazol– and isoxazol–heterocycles using [DBU][Ac] as an effective reaction medium

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Supporting Information

1.1 General method:

All solvents and reagents were used as supplied from commercial sources. The recorded melting points are uncorrected. IR spectra were recorded in KBr on Shimadzu FT-IR 8401 spectrometer and are reported in wave numbers (cm-1). 1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer operating at 400 MHz for ^{1}H NMR and 100 MHz for 13C NMR as solutions in $CDCl_3$, unless otherwise indicated. Chemical shifts are reported as parts per million (ppm) and referenced to the residual protic solvent. Coupling constants are reported in Hertz (Hz). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; br, broad; m, multiplet. The degree of substitution (C, CH, CH_2, and CH_3) was determined by the DEPT-135 method. UV spectra were record on Shimadzu Type 160-A spectrometer. The ESI mass spectra were measured on Shimadzu LCMS-2010 spectrometer. TLC was performed on Merck 60 F254 Precoated silica plates, spots were detected either by UV (254 nm, 366 nm) or dipping into a permanganate [$KMnO_4$ (3 g), K_2CO_3 (20 g), NaOH (5 mL, 5% in H2O), H_2O (300 mL)] or an anisaldehyde solution [3% p- methoxybenzaldehyde and 1% H_2SO_4 in MeOH] or 2,4 Dinitro phenyl hydrazine solution [2,4-DNP (12 g), Conc. H_2SO_4 (6 mL), Water (8 mL), EtOH (20 mL)] followed by heating.

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- **General procedure for Synthesis of o-alkenylated/alkynylated acetophenones:**

A 2.0 mL solution of respective alkenyl/alkynyl halide (0.013 mol) in DMF was added drop-wise to a stirred solution of corresponding *O*-hydroxyacetophenone **1a**–**c** (0.01 mol) with the anhydrous K_2CO_3 (0.015 mol) suspended in DMF (10 mL). It was stirred further at room temperature until the completion of reaction as confirmed by TLC (10–12 h). It was then poured into ice (100 g) with constant stirring. All solid products **2**,**5, 6b and 8b** were filtered, washed with cold water (3×10 mL), and then dried at room temperature. In case of oily products **3**, **4**, **6a**, **7** and **8a**, the emulsified content was extracted with three 25 mL diethyl ether portions, and combined ether extracts collected were dried using anhydrous sodium sulfate. They gave pure oily products in the 94–98% range on removal of ether

- **General Procedure for Preparation of Ionic Liquid [DBU][Ac].**

A 50 mL three-necked flask was loaded with 6mmol of DBU and after that acetic acid (6 mmol) was then added drop-wise at the temperature ≤5 °C cooled by an ice bar. After drop-wise addition, the ice bar was removed and the reaction mixture was stirred at room temperature for 24 h. The oil residue was vacuum-dried at 60 °C for 24 h to afford [DBU][Ac] as a light yellow, viscous liquid.

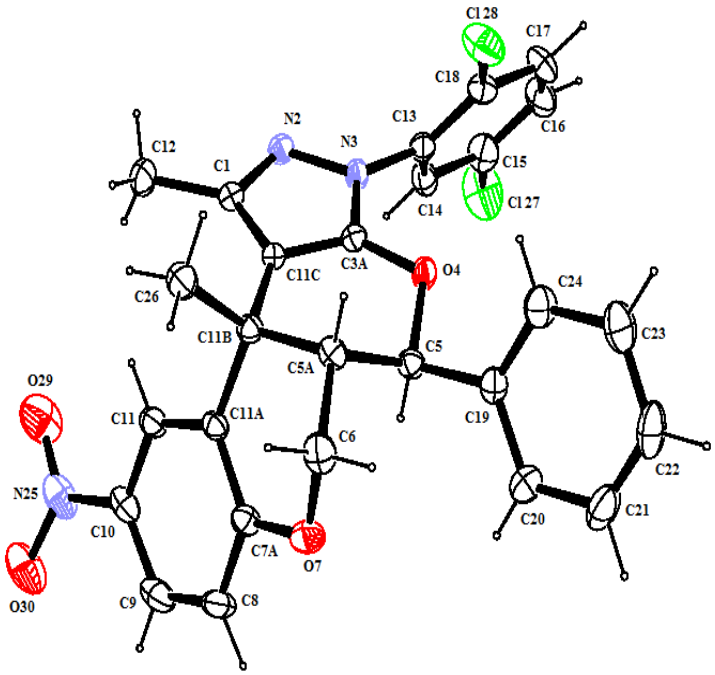
- **General Procedure for Preparation of chromeno-fused pyrano[2,3-c]pyrazoles{10-13(a-f)}**

In a 50ml round-bottom flask, a mixture of o-alkenylated acetophenone(1 equiv) and pyrazolones (1 equiv) was taken in ionic liquid [DBU][Ac](25 mol%) heated at 130˚C. The reaction continuously monitoring by TLC, after completion of reaction, reaction mixture was extracted with ethyl acetate (3×10 ml) to separate the IL from the product. The combined solution of ethyl acetate was dried with Na_2SO_4 and then concentrated through vacuum evaporation of ethyl acetate to give the crude product, which was further purified by column chromatography by using n-hexane/ethyl acetate(10%v/v) as mobile phase. The overall yields were in the 70-92 % range. The recovered IL [DBU][Ac] was vacuum-dried at 60 °C for 8 h and it reused in the next reaction as the catalyst. It was noticed that ionic liquid can be recycled at least four-time with its unaltered efficiency.

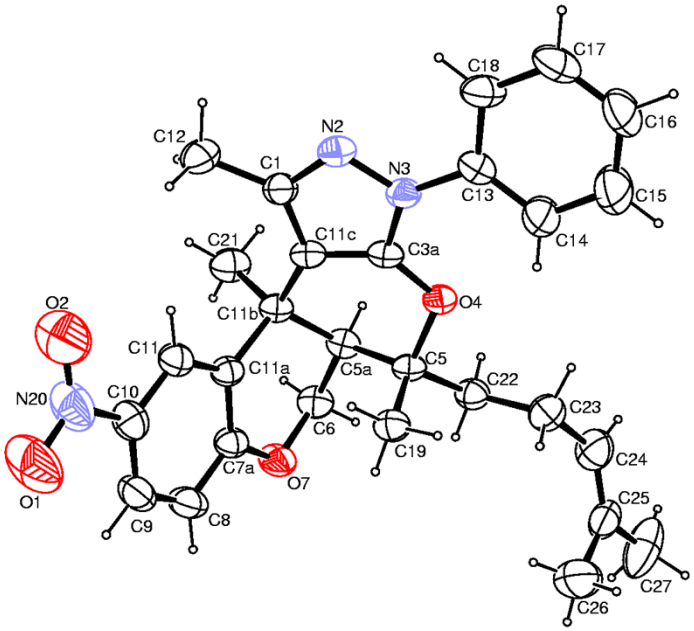
- **General Procedure for Preparation of chromeno-fused pyrano[2,3-c]isoxazoles{15-17(a-b)}**

In a 50ml round-bottom flask, a mixture of *o*- alkenylated/alkynylated acetophenone (1 equiv.) and isoxazolone (1 equiv.) was taken in ionic liquid [DBU][Ac](25 mol%) for substract(6-7) and for substract 8 add ZnO(25 mol%) to activate inactive dienophile along with[DBU][Ac](25 mol%) and heated at 130˚C. The reaction continuously monitoring by TLC, after completion of reaction, reaction mixture was extracted with ethyl acetate three times to separate the IL from the product. The combined solution of ethyl acetate was dried with Na_2SO_4 and then concentrated through vacuum evaporation to give the crude product, which was further purified by crystallization in ethanol. The overall yields were in the 78-86 % range. The recovered IL was vacuum-dried at 60 °C for 8 h and reused in the next reaction as the catalyst.

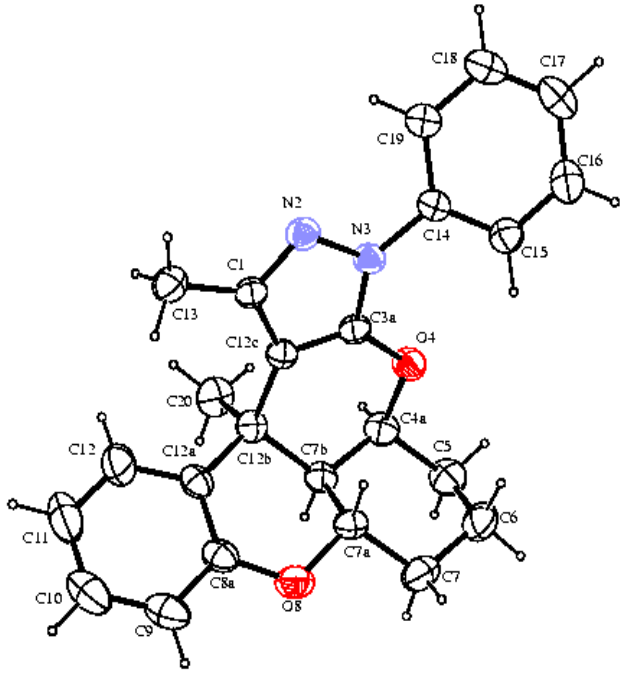
- **Single crystal X-Ray data of 10f (CCDC No. 978637)**



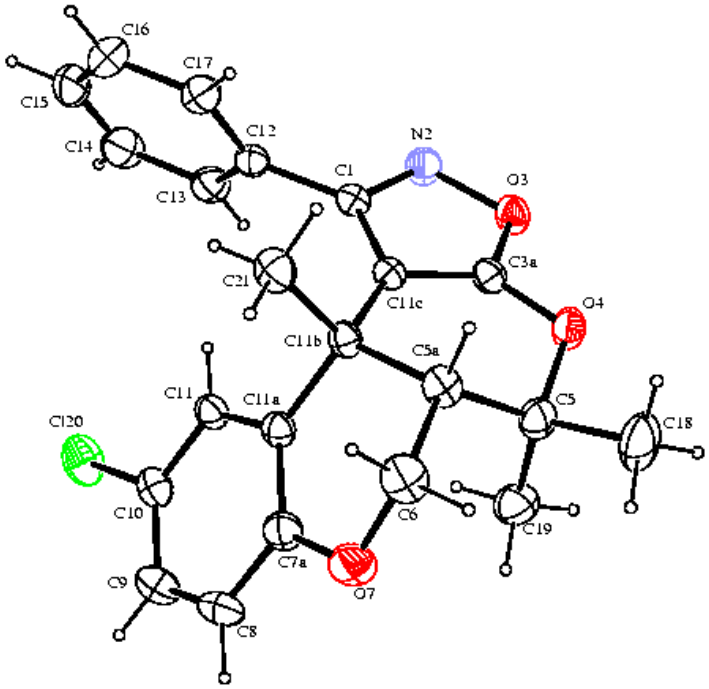
- **Single crystal X-Ray data of 11e (CCDC No. 989312)**



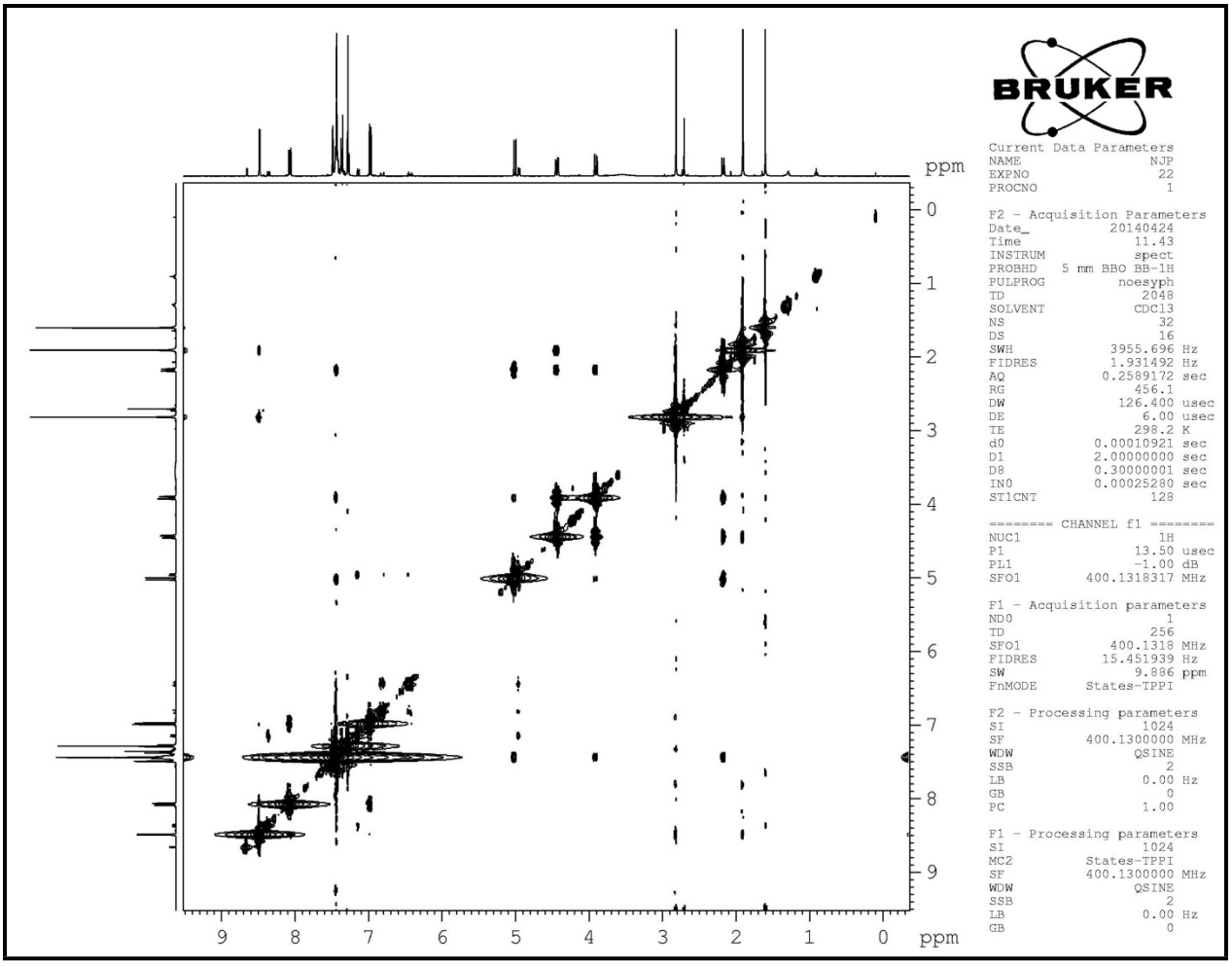
- **Single crystal X-Ray data of 12a (CCDC No. 1025475)**



- **Single crystal X-Ray data of 15b (CCDC No. 1024805)**

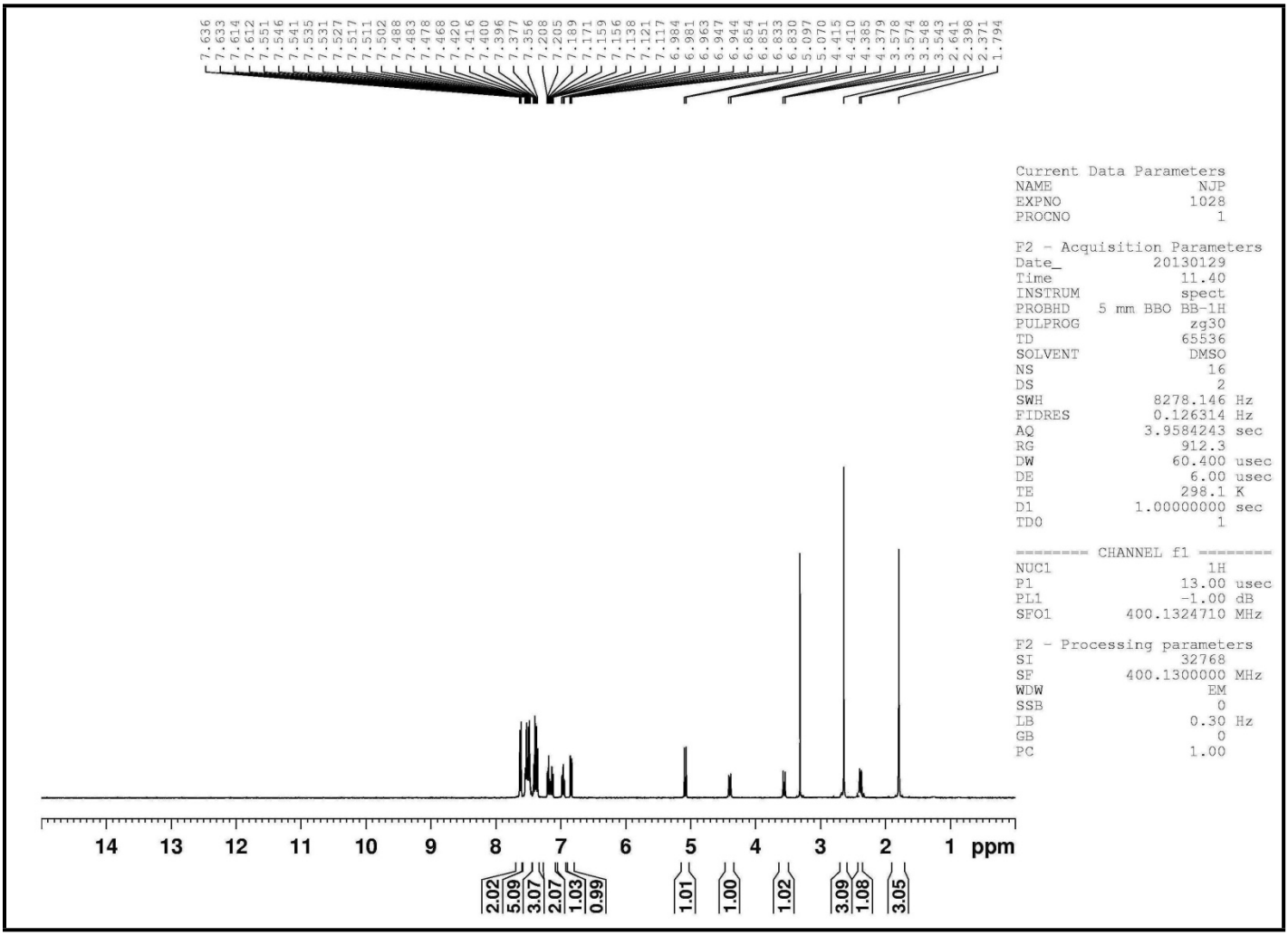


- **2D NMR experiments: NOESY of 10f**

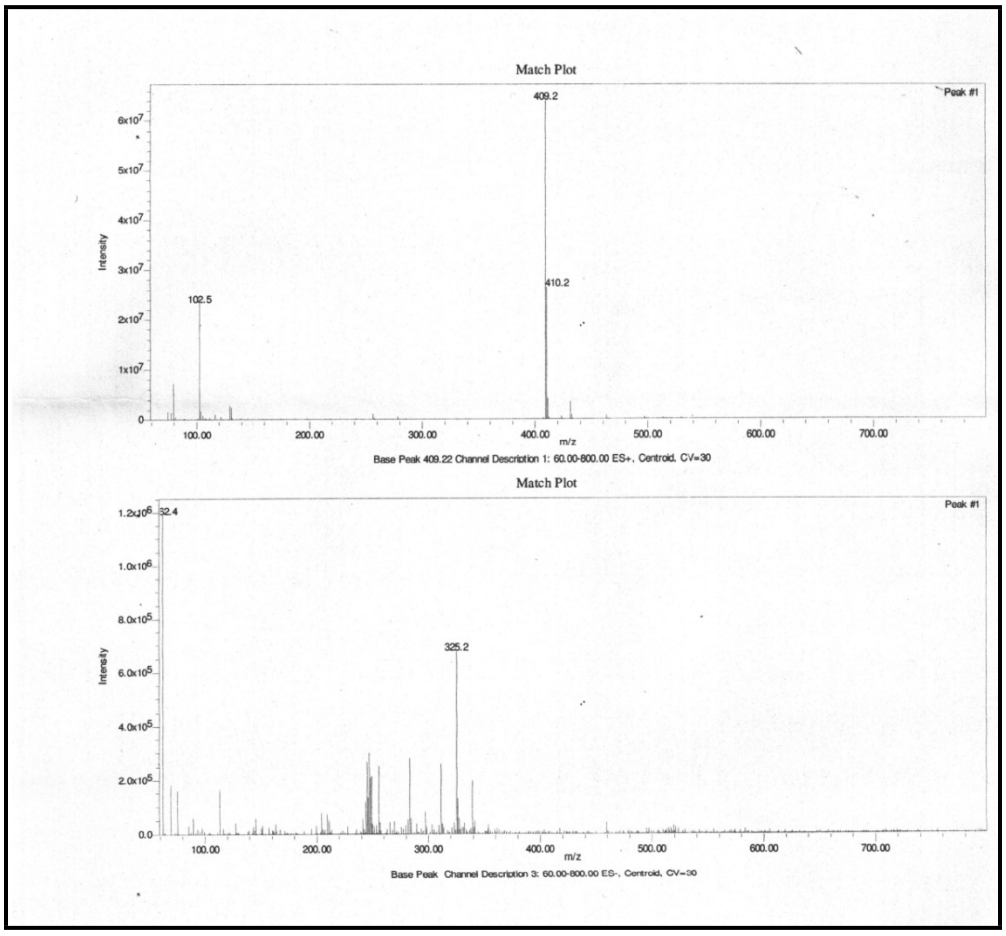


➢ ^{1}H NMR, ^{13}C NMR, IR and Mass Spectral Data

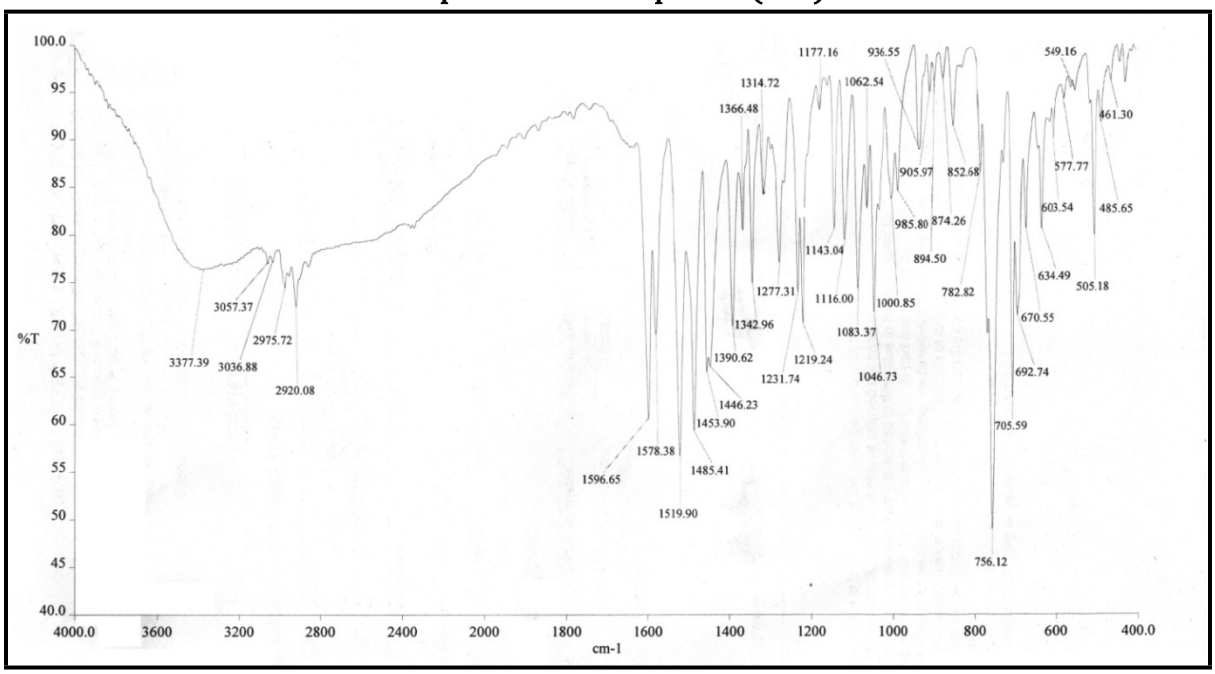
^{1}H NMR spectrum of compound (10a)



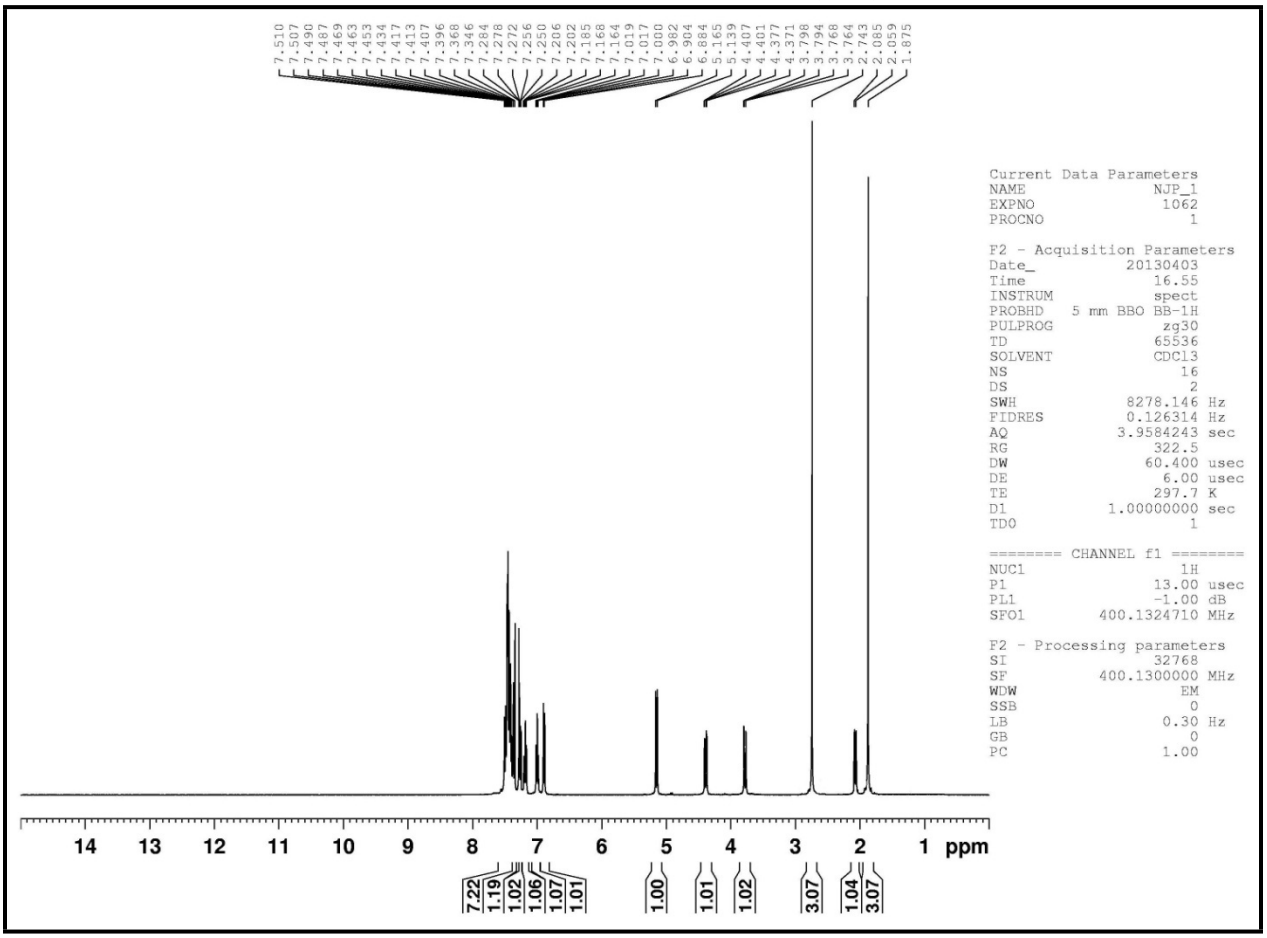
MS spectrum of compound (10a)



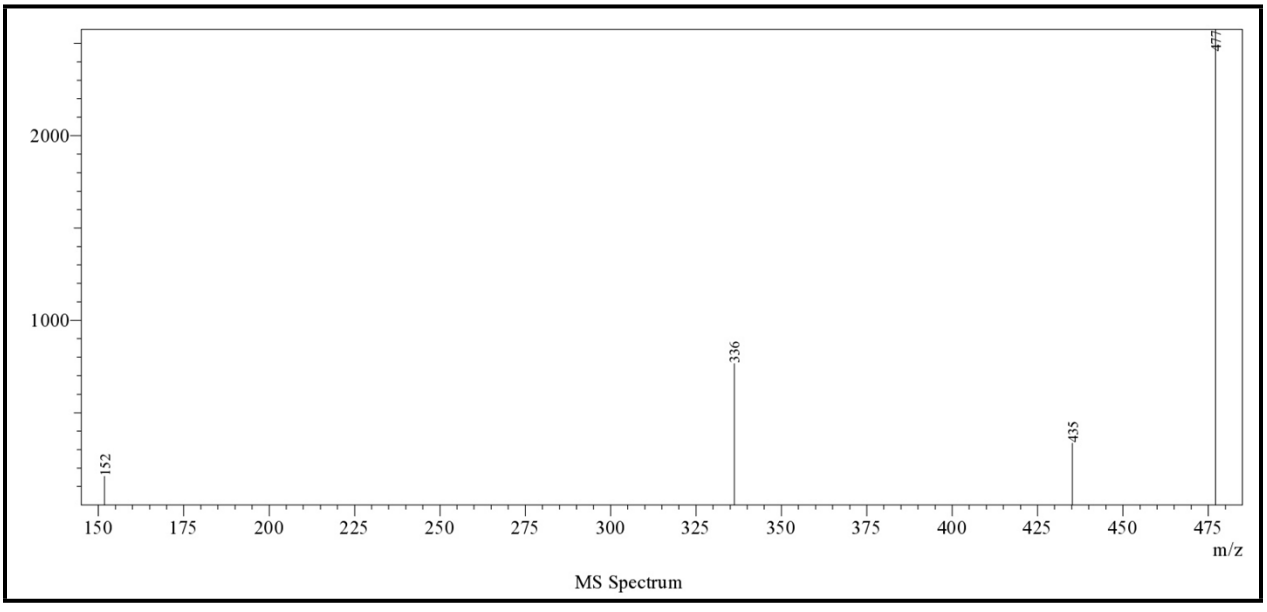
IR spectrum of compound (10a)



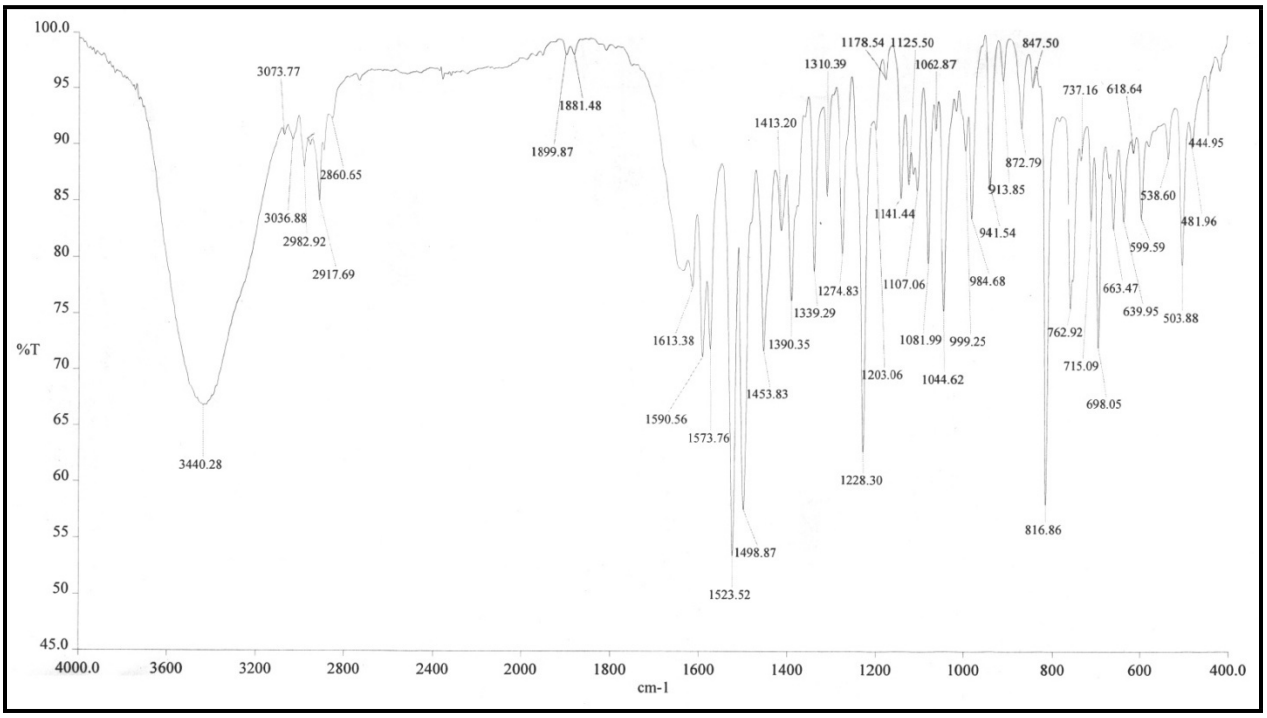
^{1}H NMR spectrum of compound (10b)



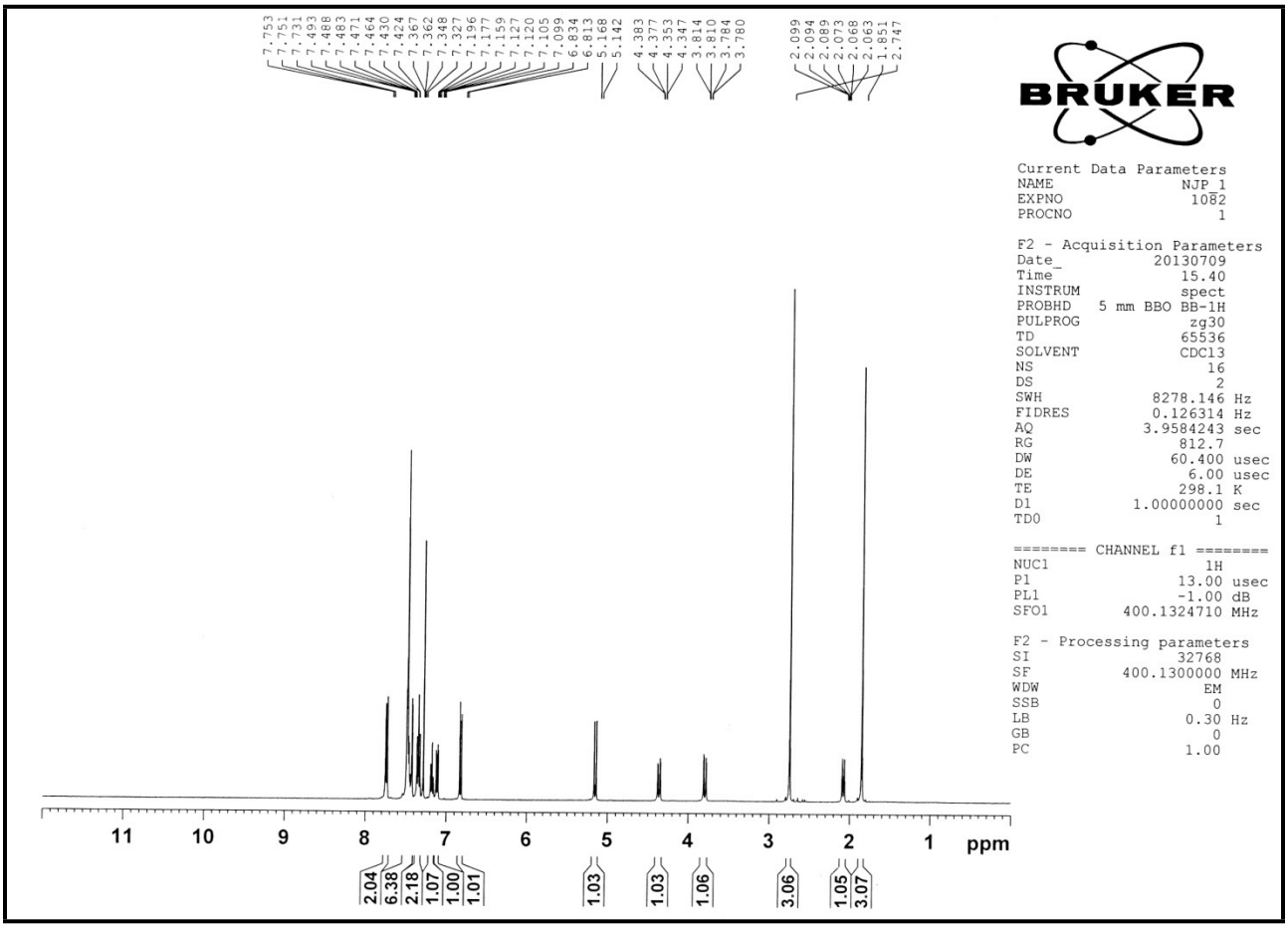
IR spectrum of compound (10b)



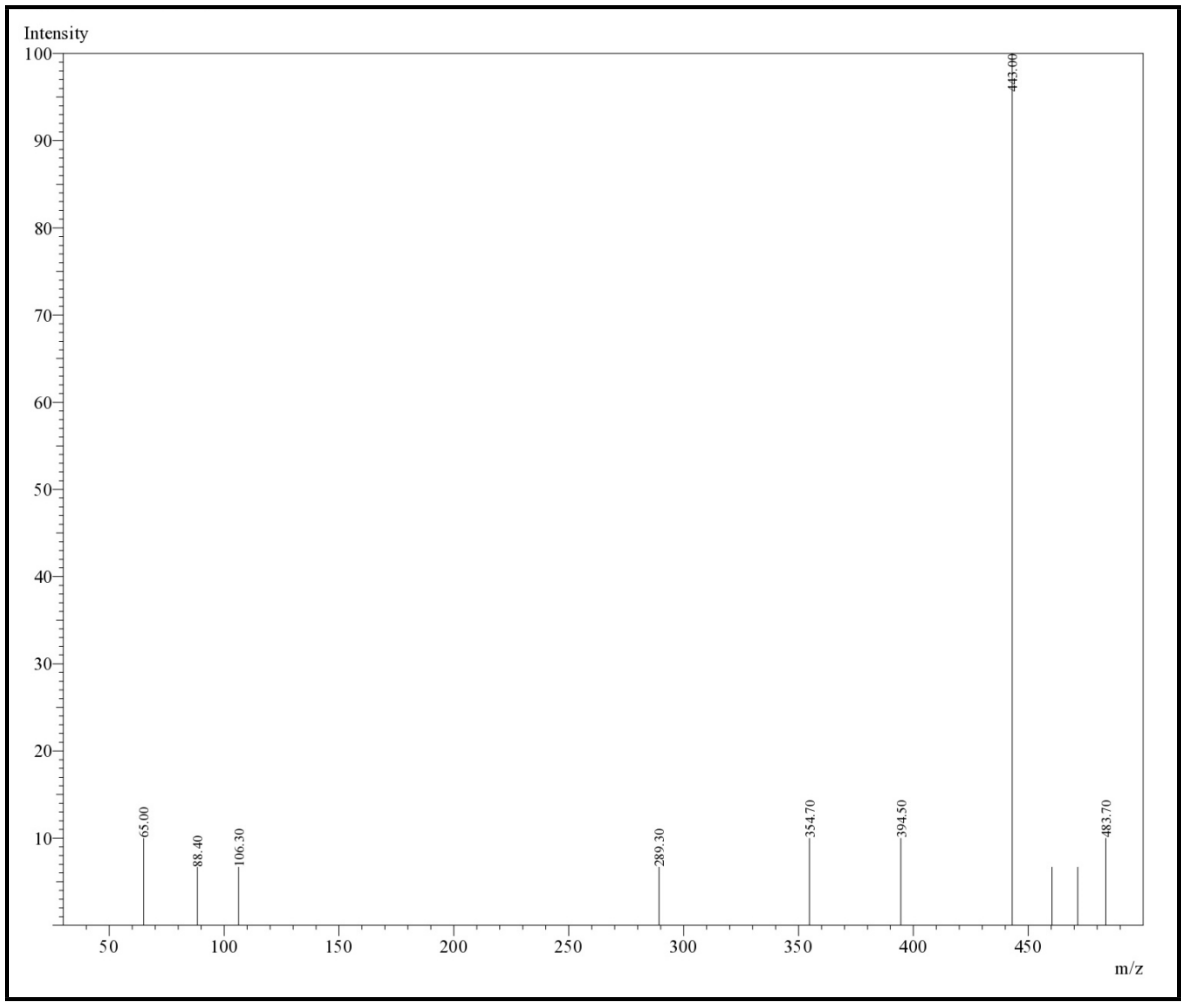
ESI–MS spectrum of compound (10b)



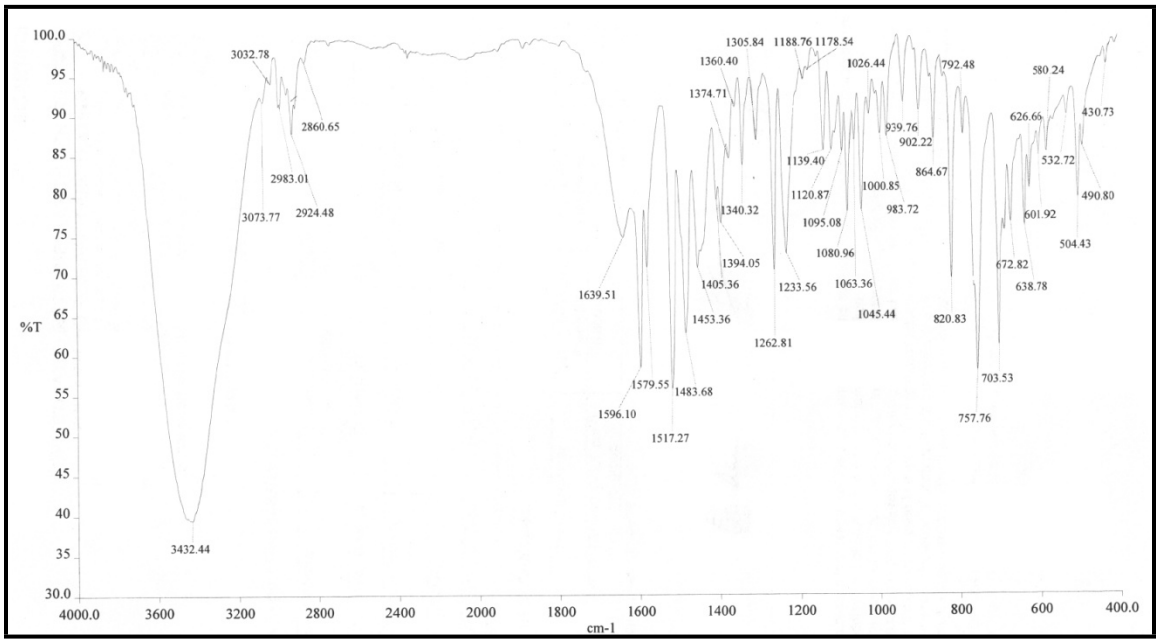
^{1}H NMR spectrum of compound (10c)



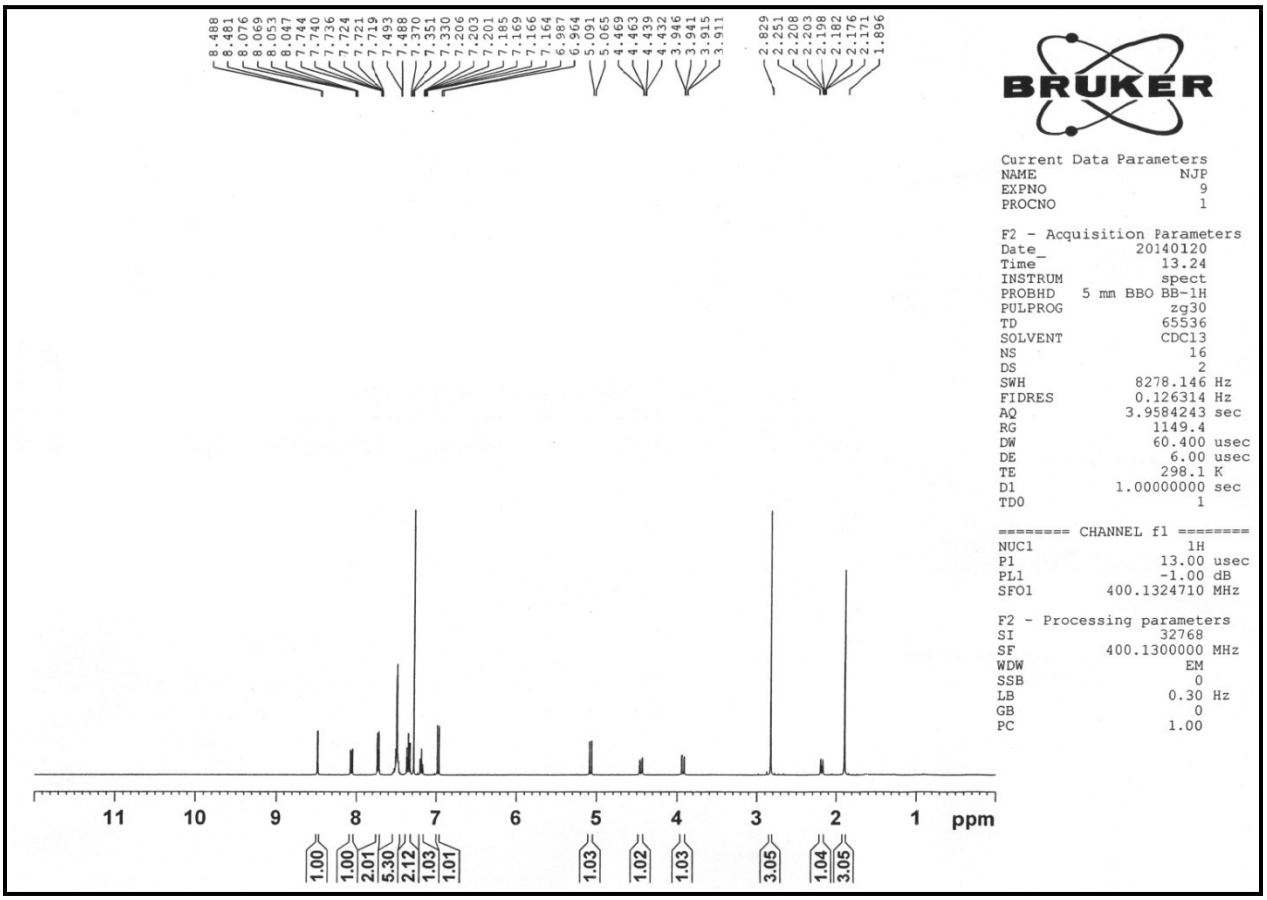
ESI-MS spectrum of compound (10c)



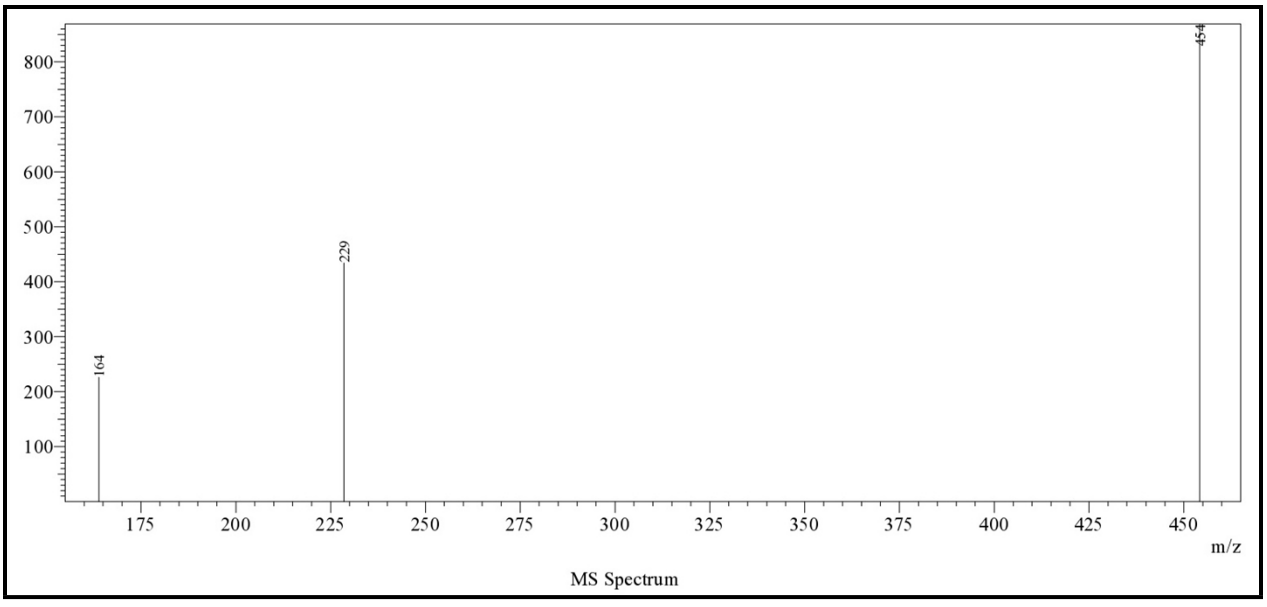
IR spectrum of compound (10c)



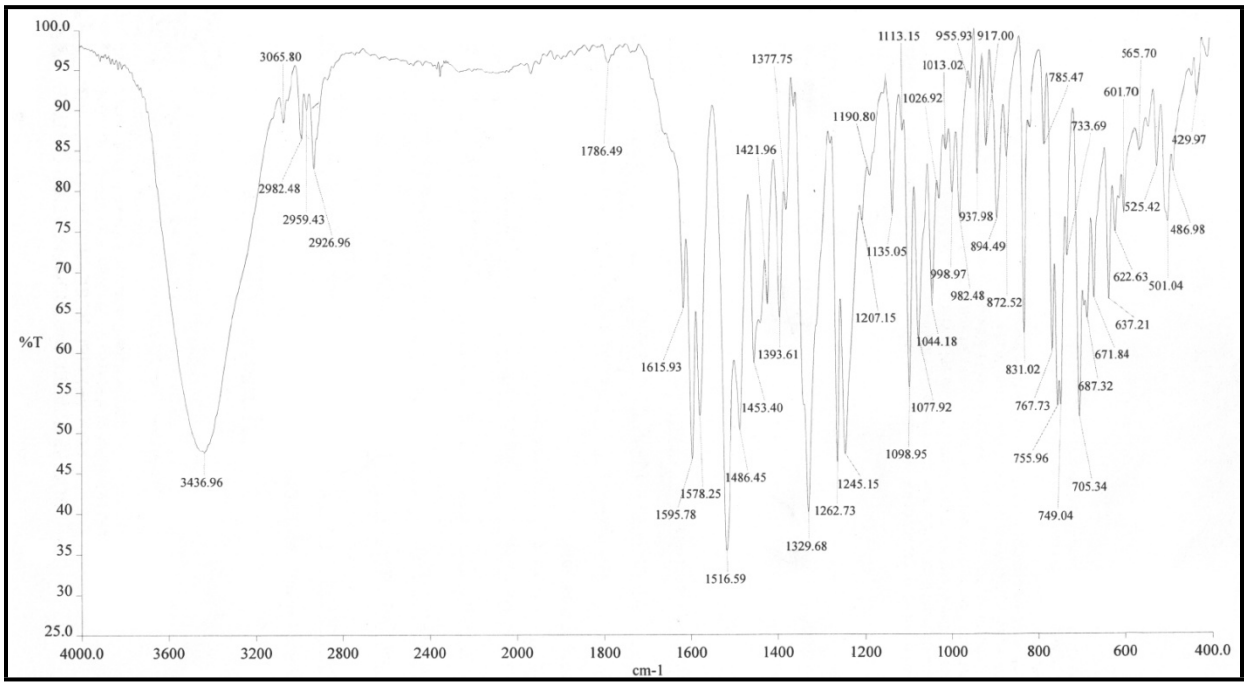
^{1}H NMR spectrum of compound (10e)



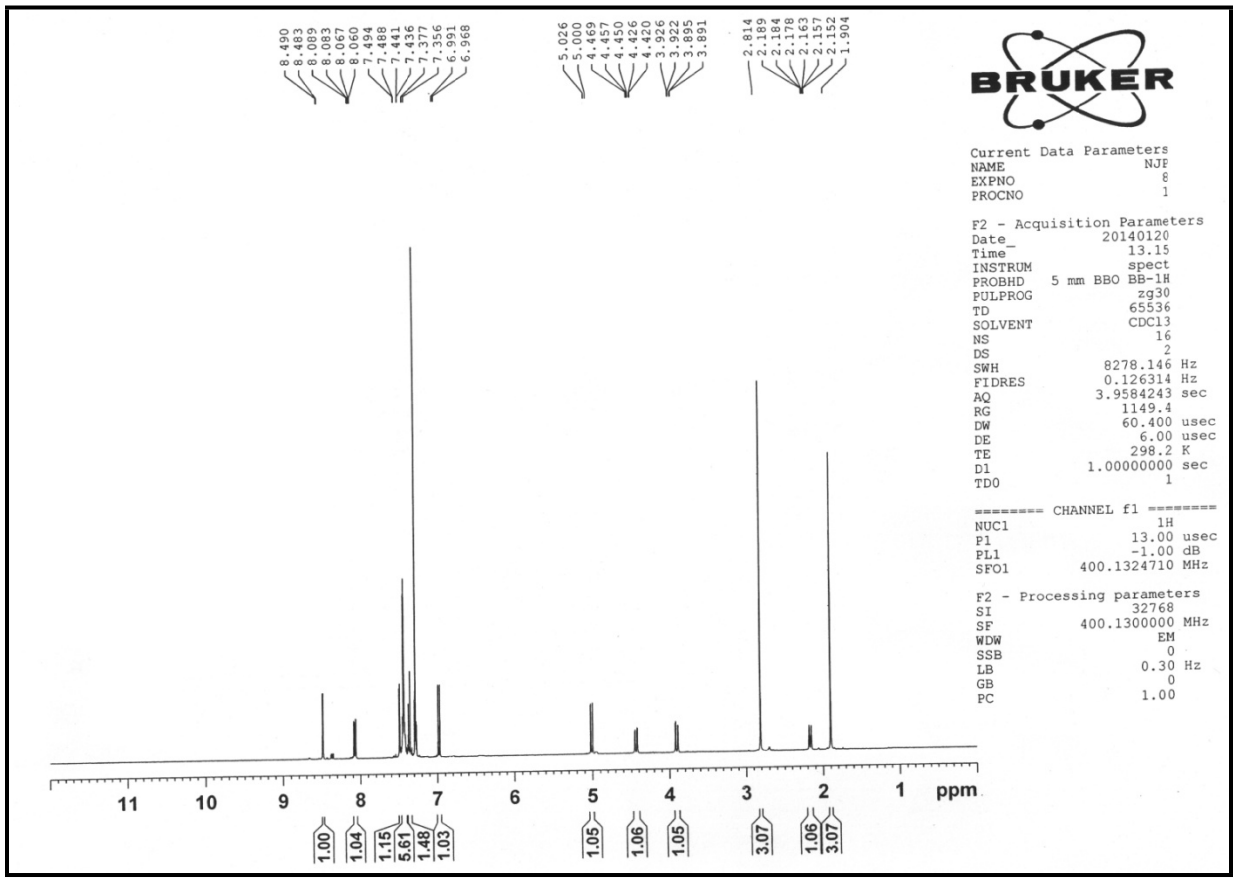
ESI-MS spectrum of compound (10e)



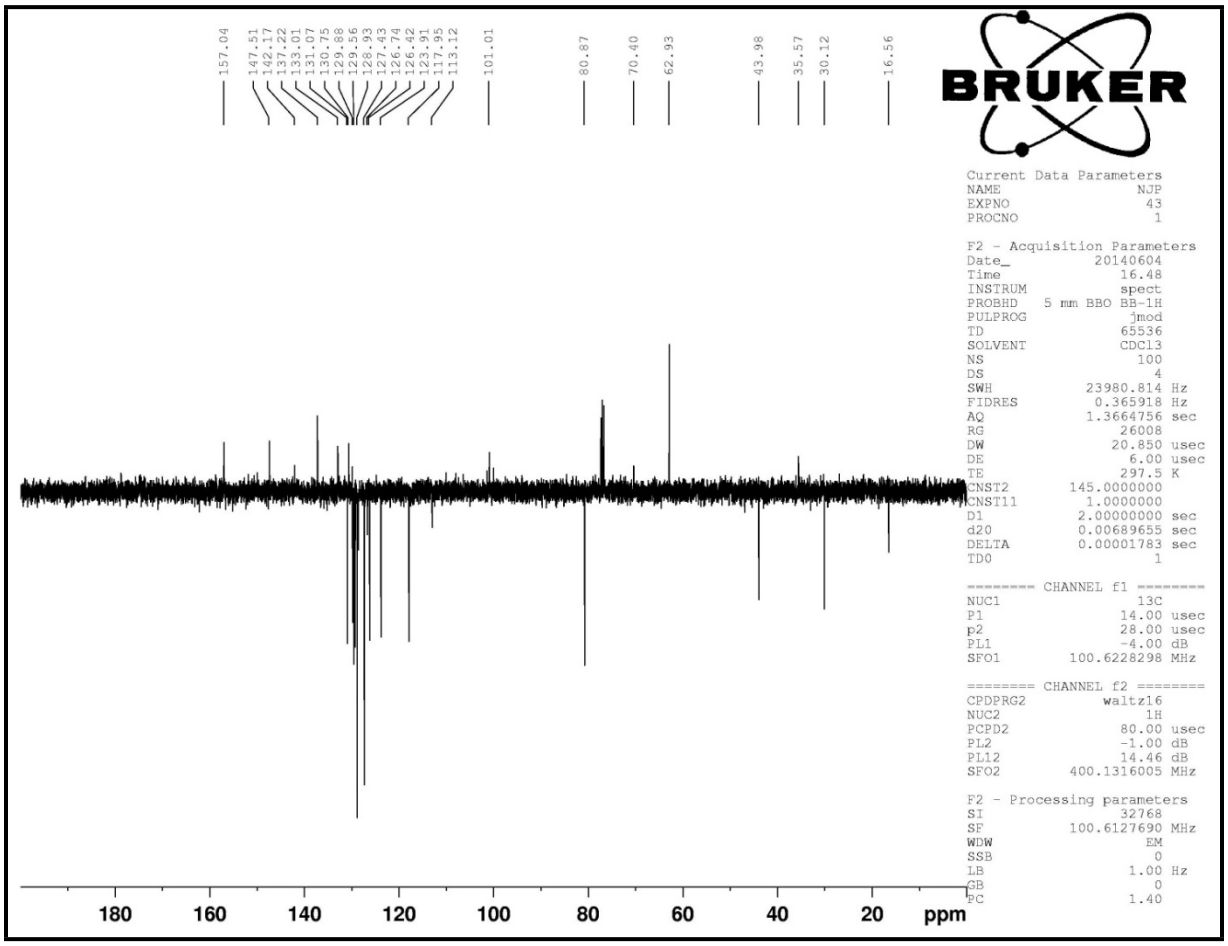
IR spectrum of compound (10e)



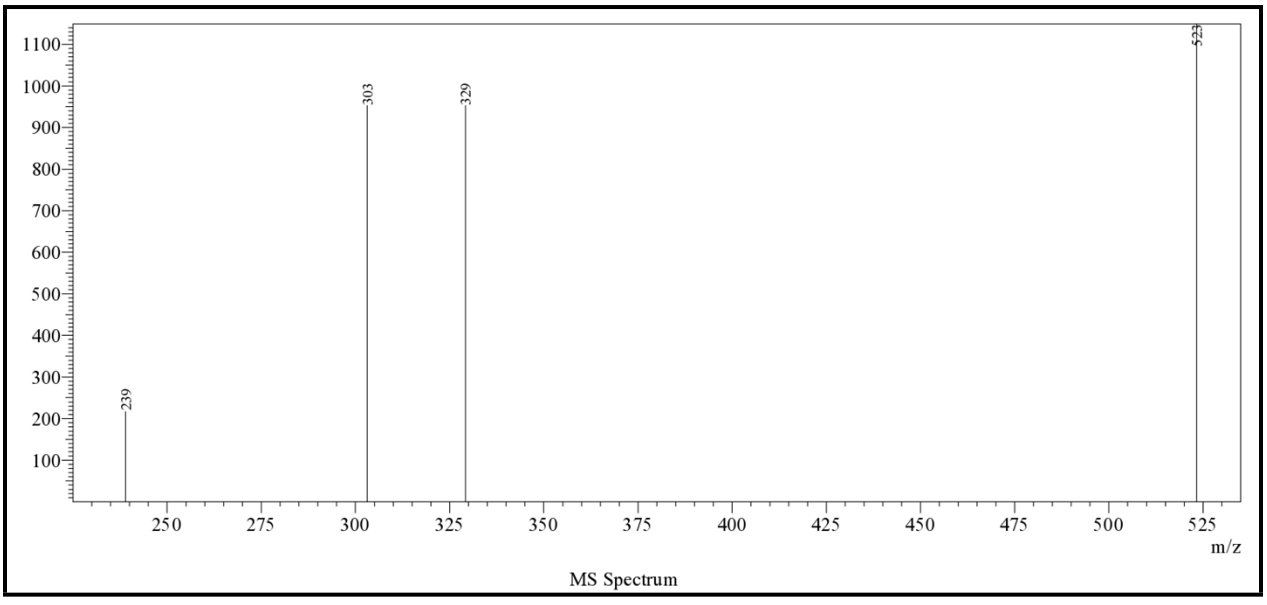
^{1}H NMR spectrum of compound (10f)



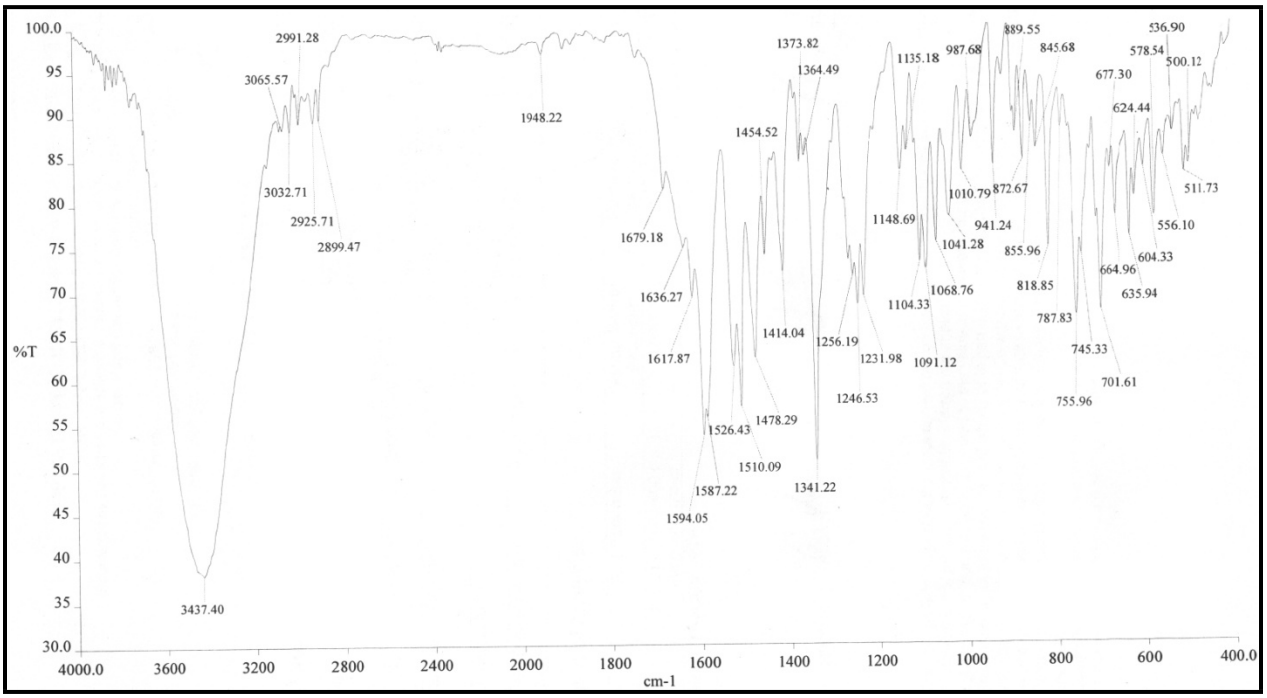
APT spectrum of compound (10f)



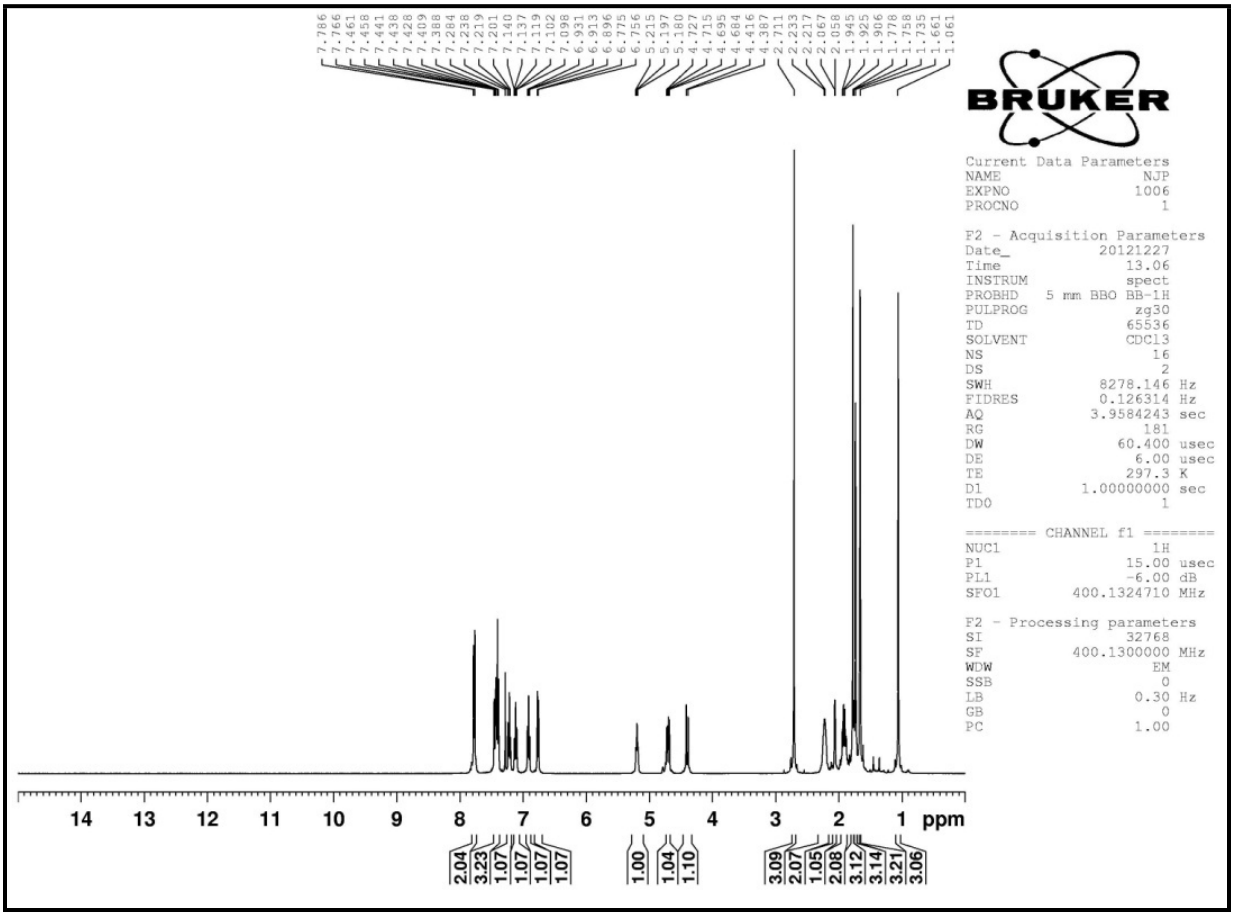
ESI-MS spectrum of compound (10f)



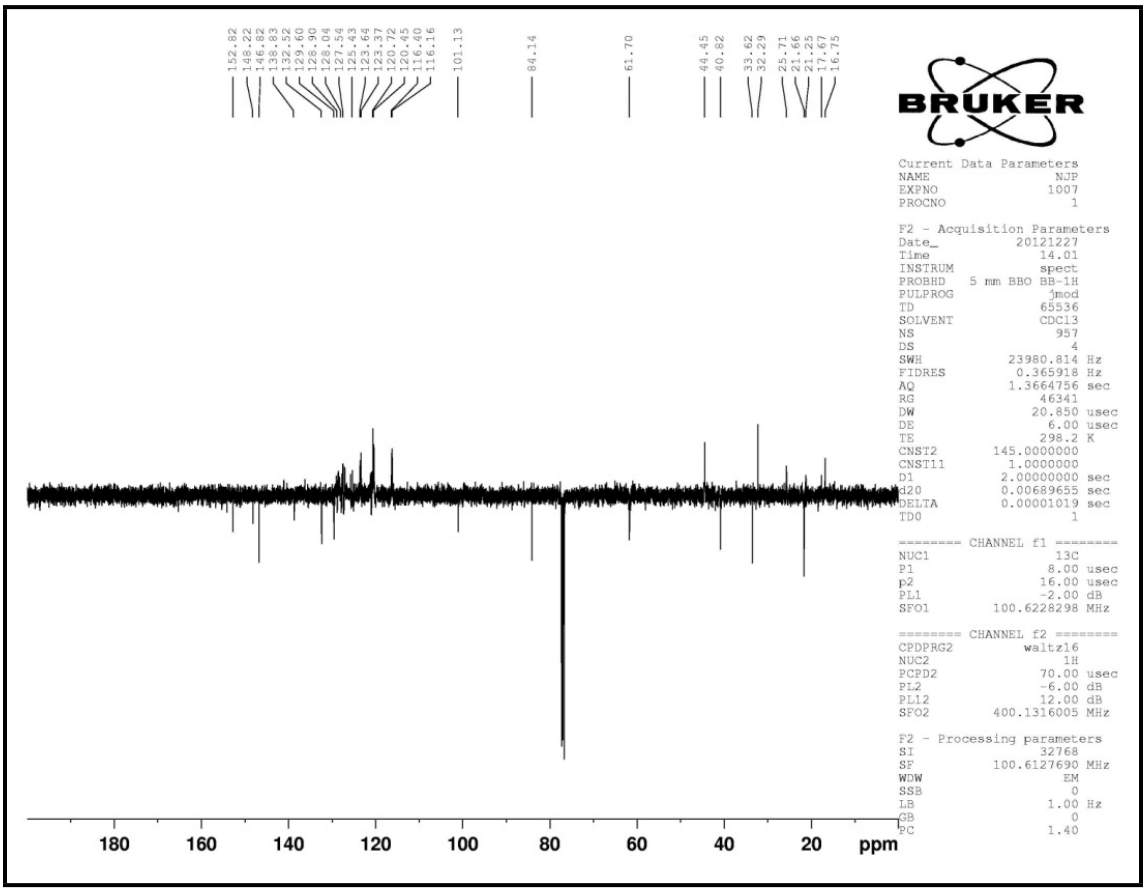
ESI-MS spectrum of compound (10f)



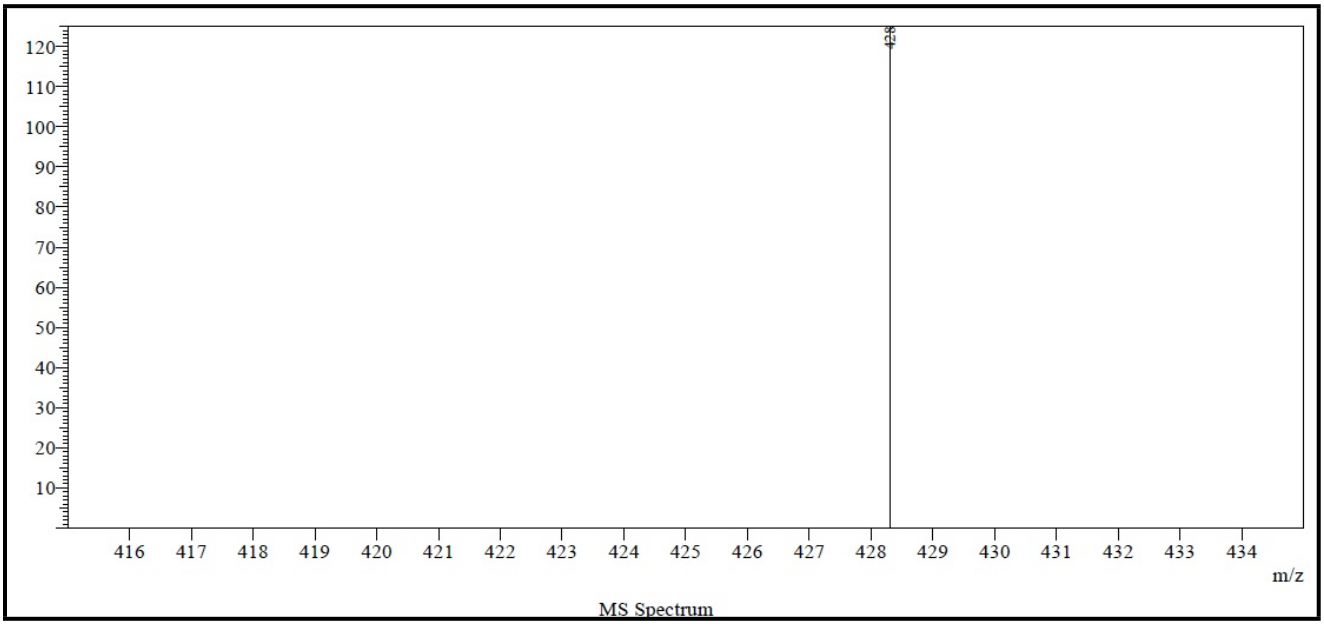
^{1}H NMR spectrum of compound (11a)



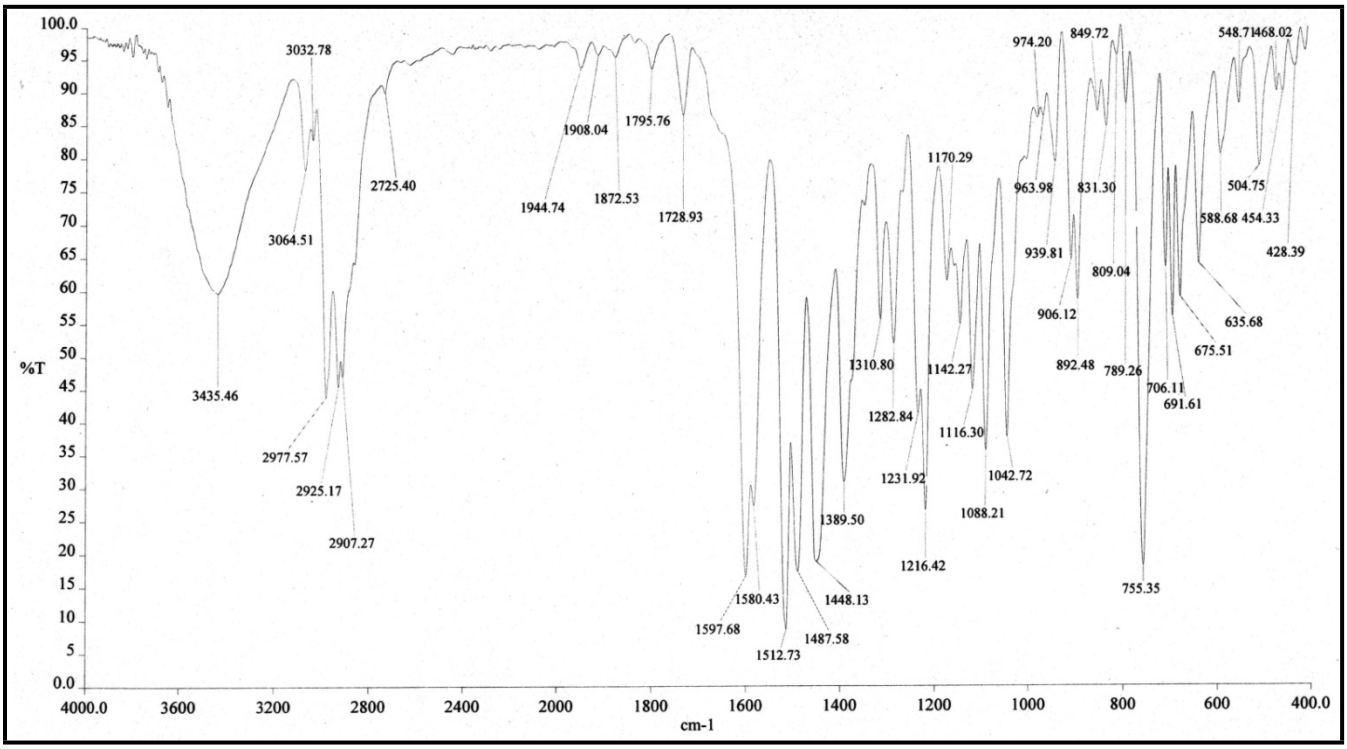
APT spectrum of compound (11a)



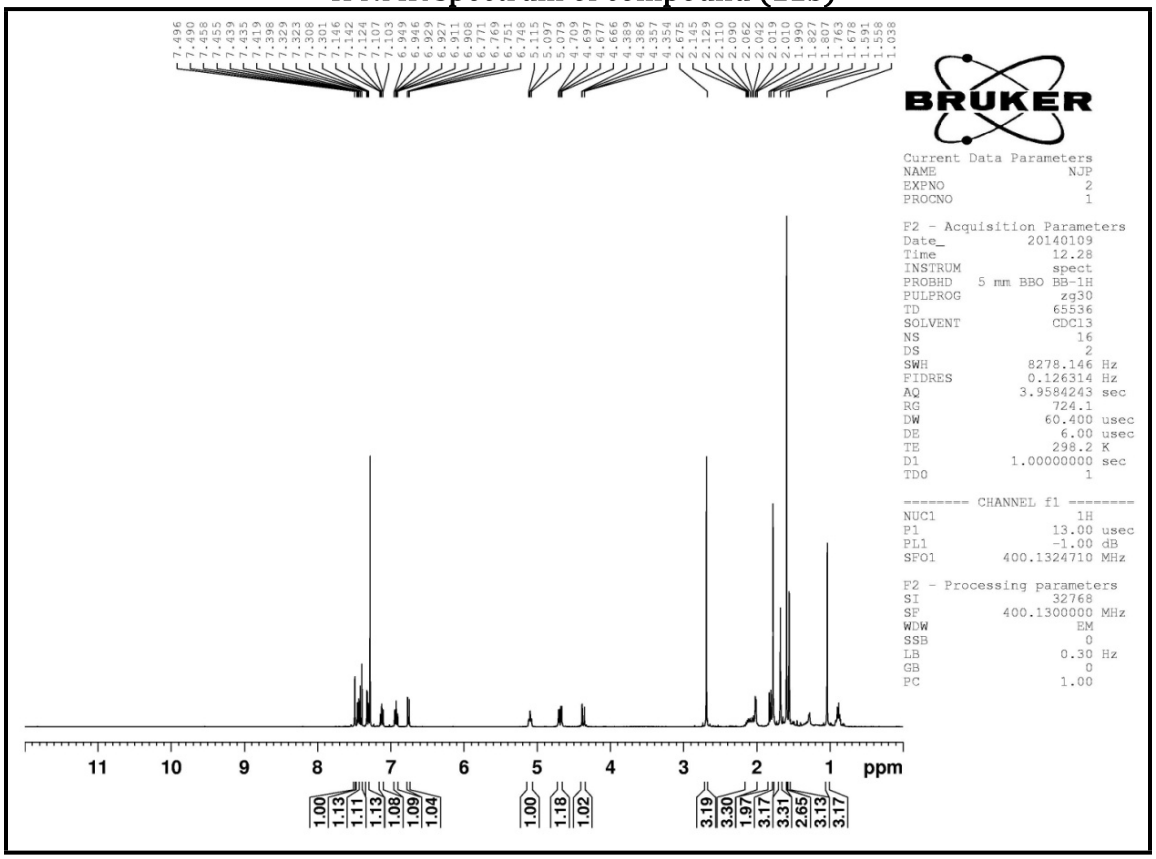
ESI–MS of compound (11a)



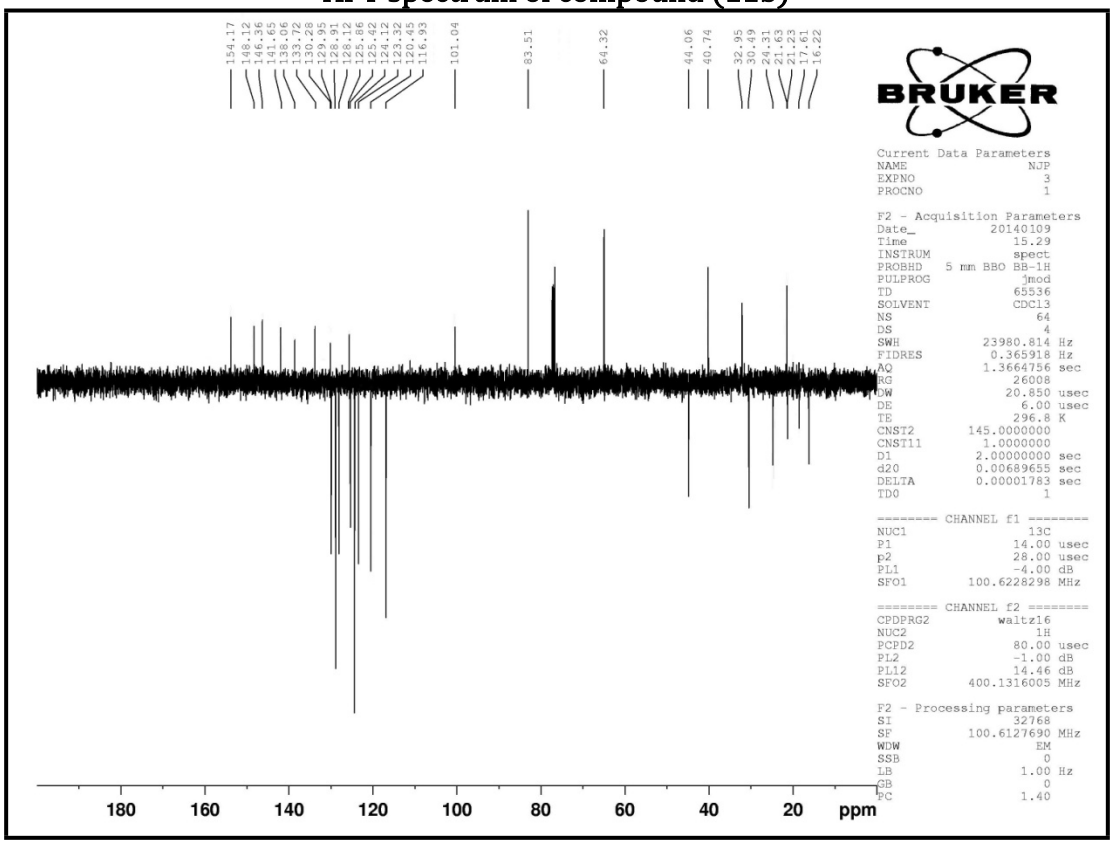
IR of compound (11a)



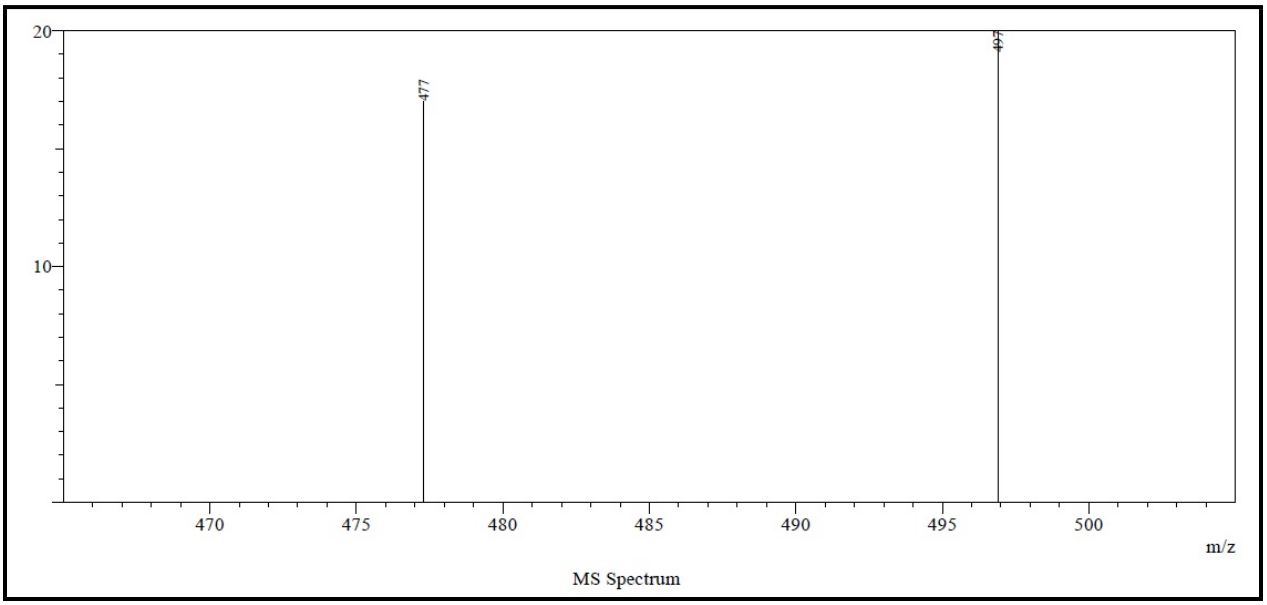
^{1}H NMR spectrum of compound (11b)



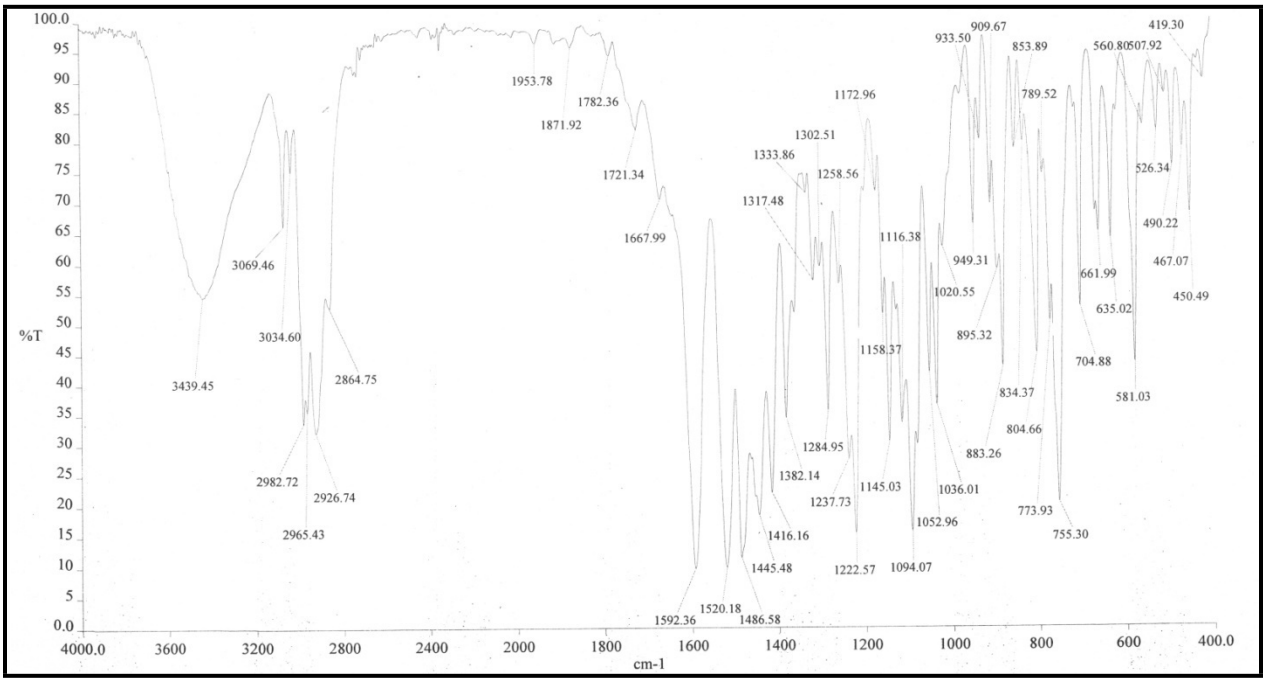
APT spectrum of compound (11b)



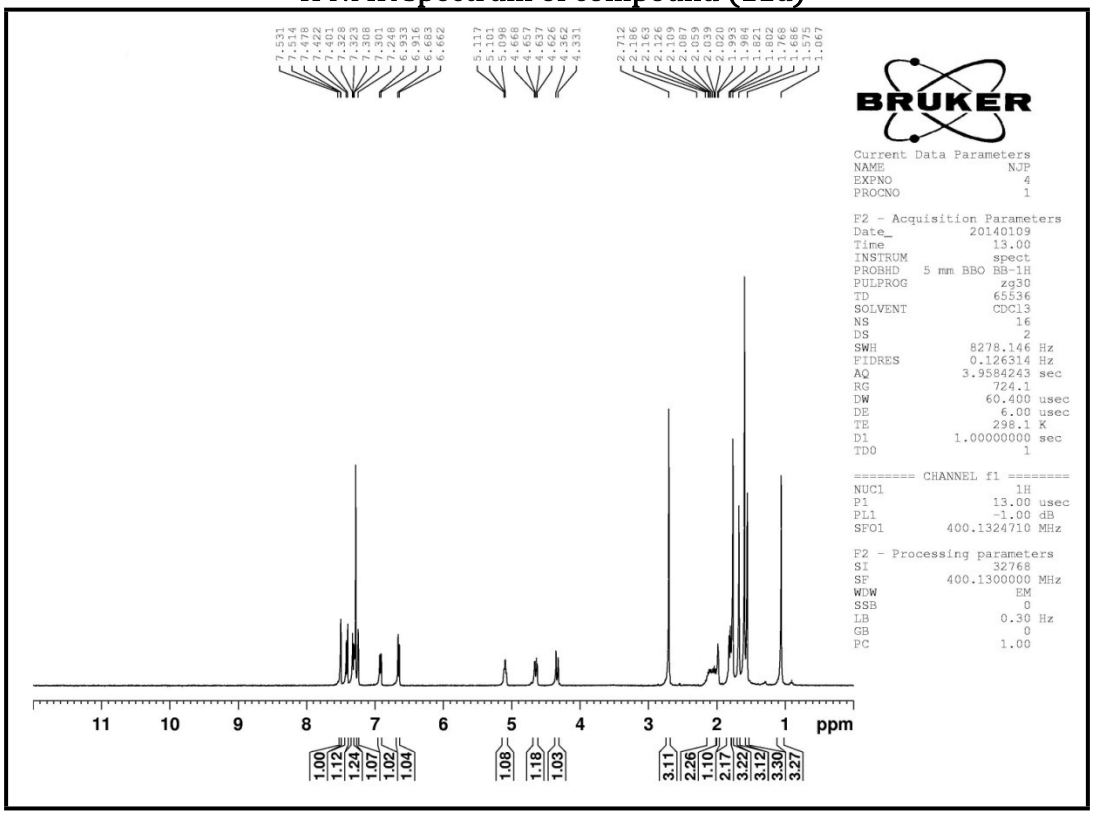
ESI–MS of compound (11b)



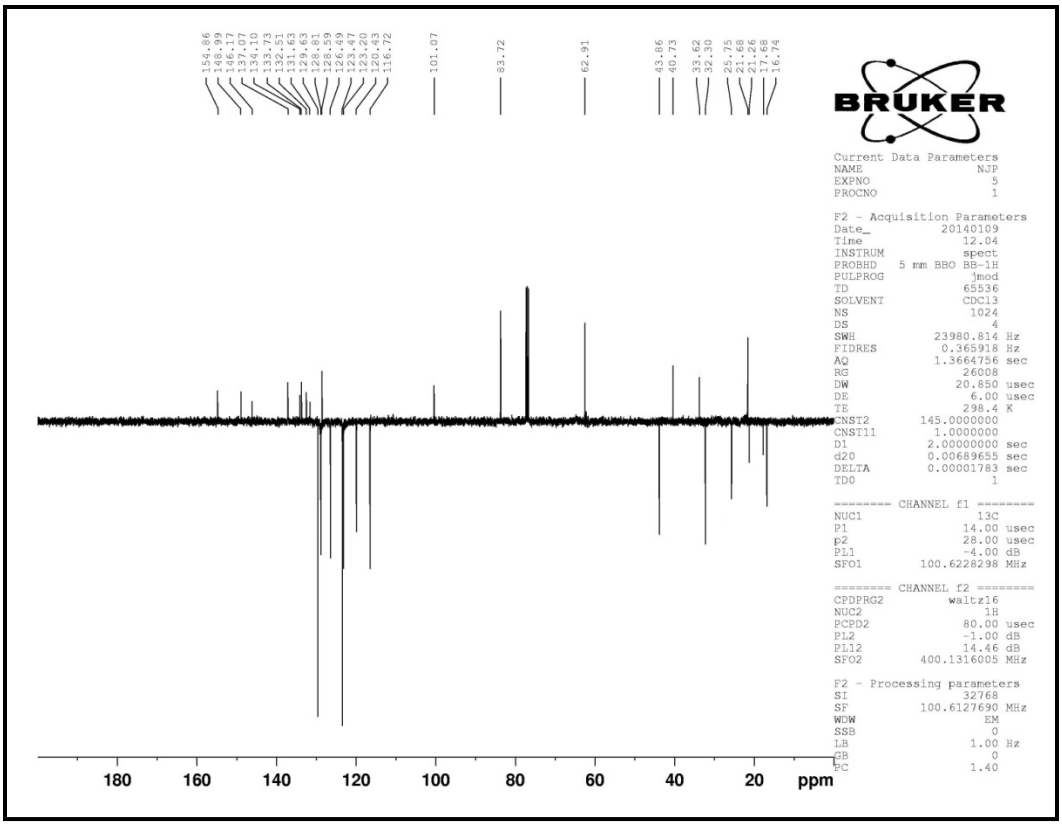
IR of compound (11b)



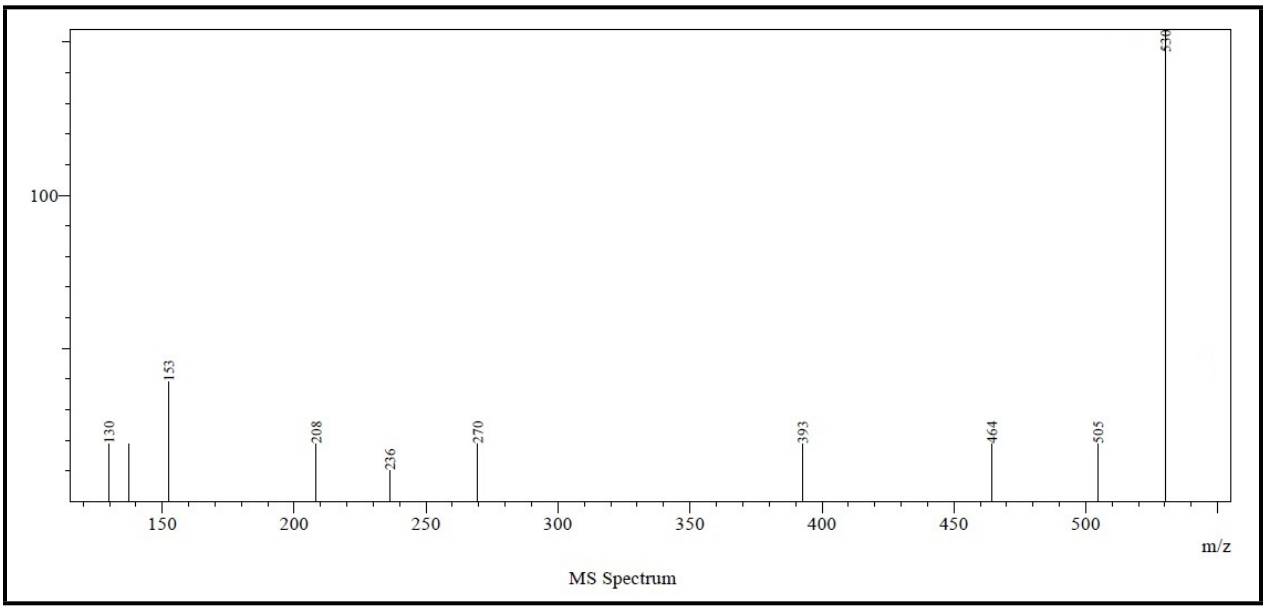
^{1}H NMR spectrum of compound (11d)



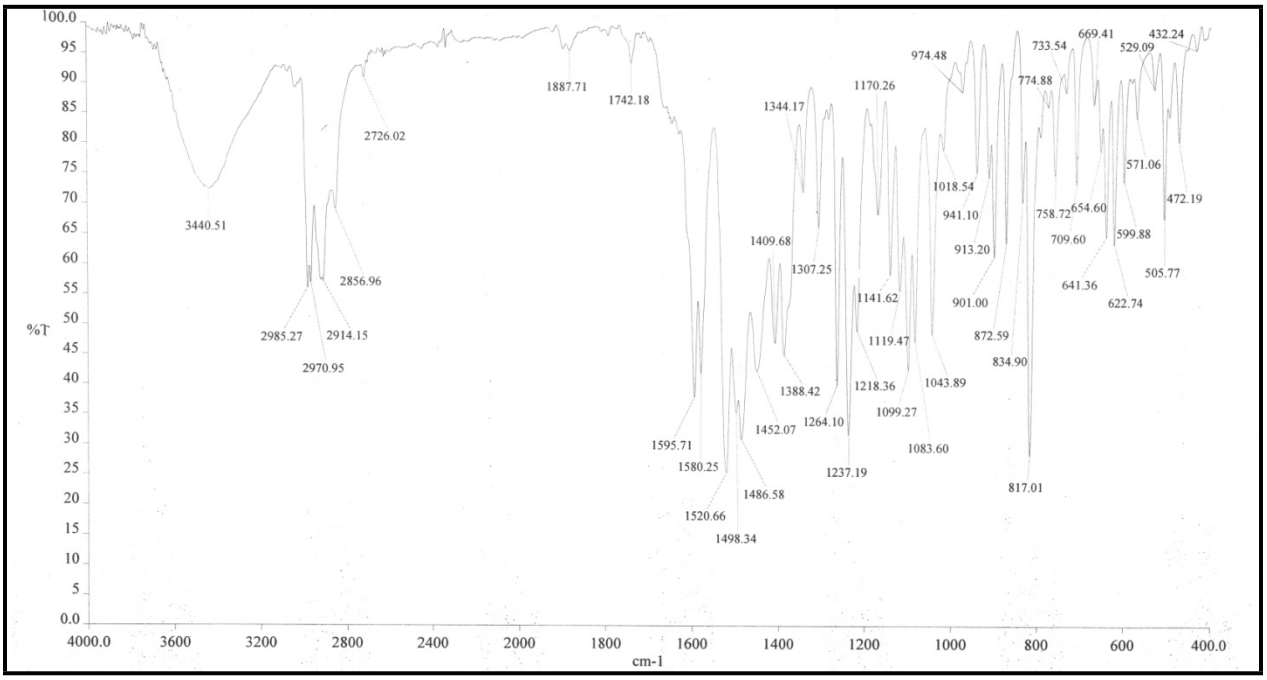
APT spectrum of compound (11d)



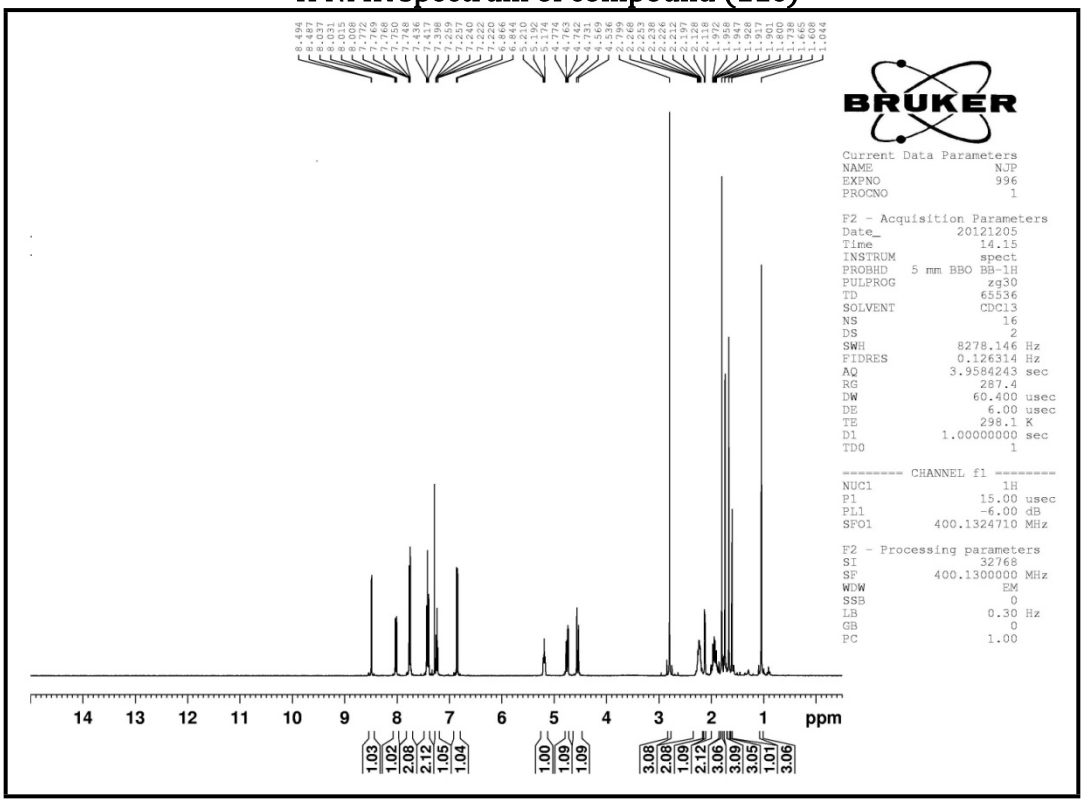
ESI–MS of compound (11d)



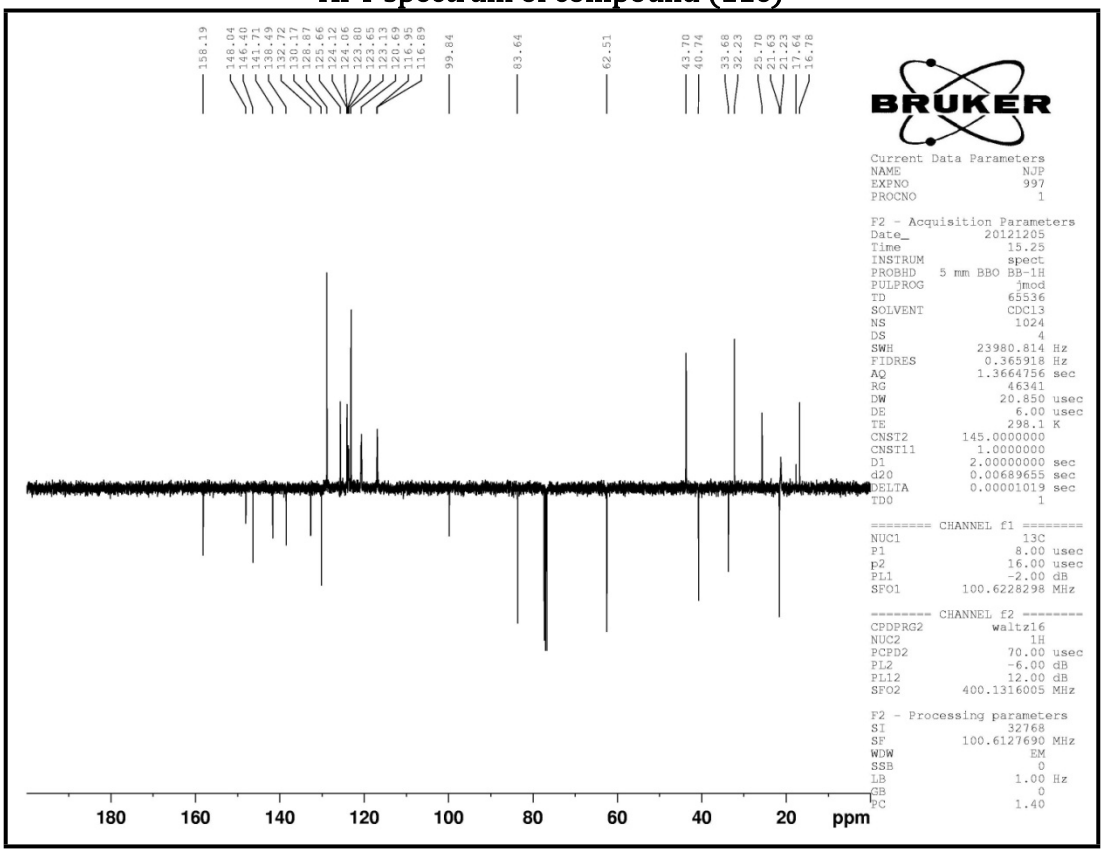
IR of compound (11d)



^{1}H NMR spectrum of compound (11e)



APT spectrum of compound (11e)



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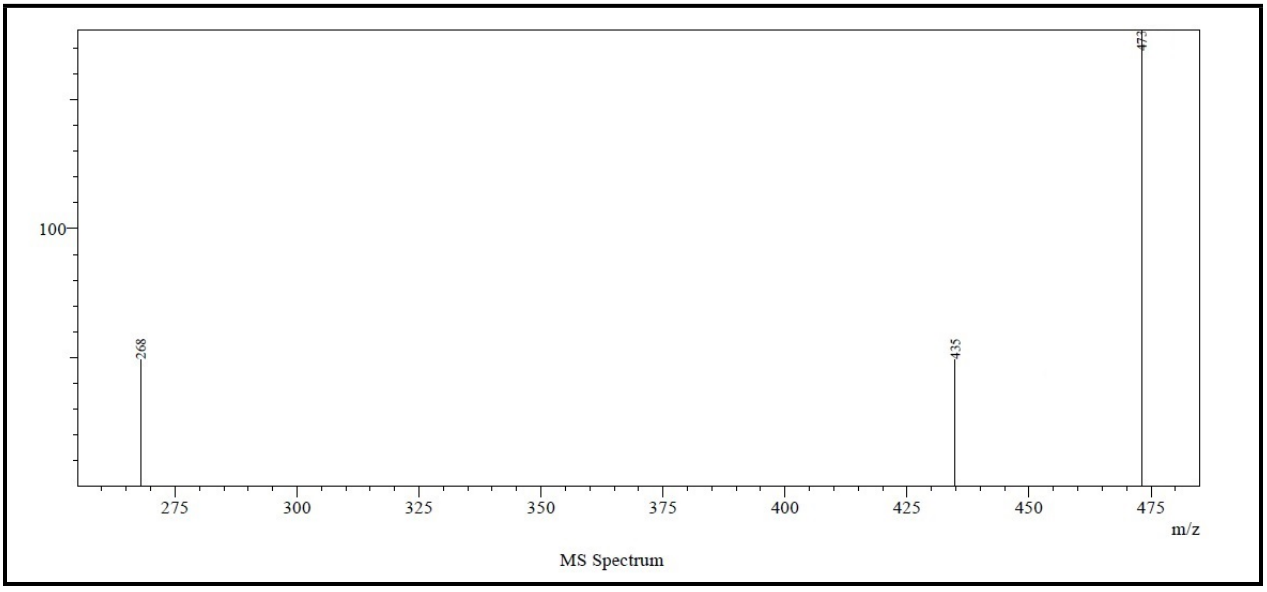
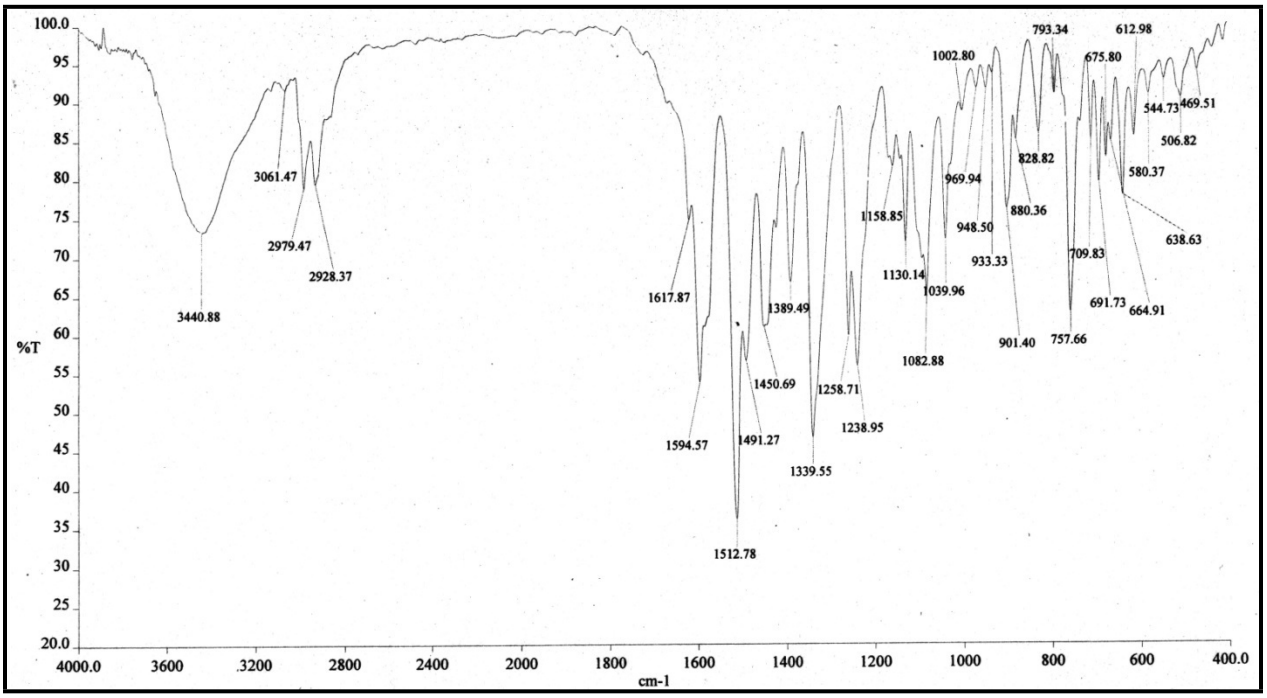
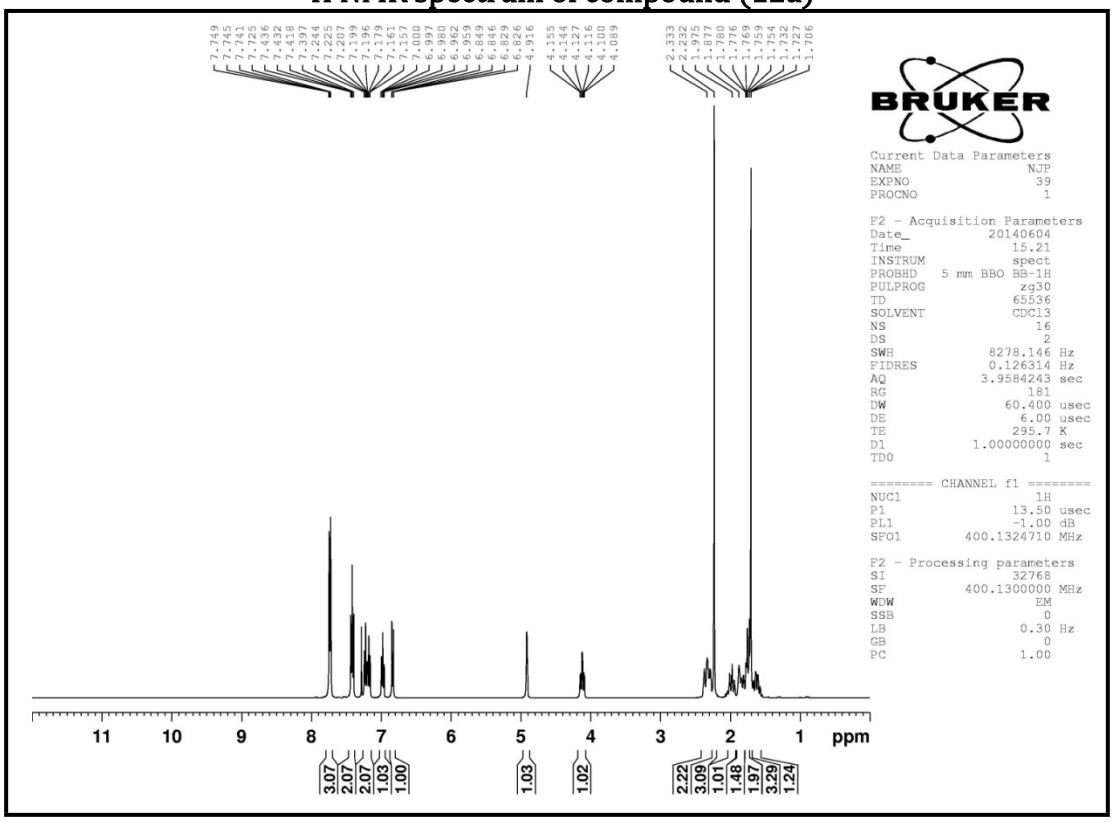


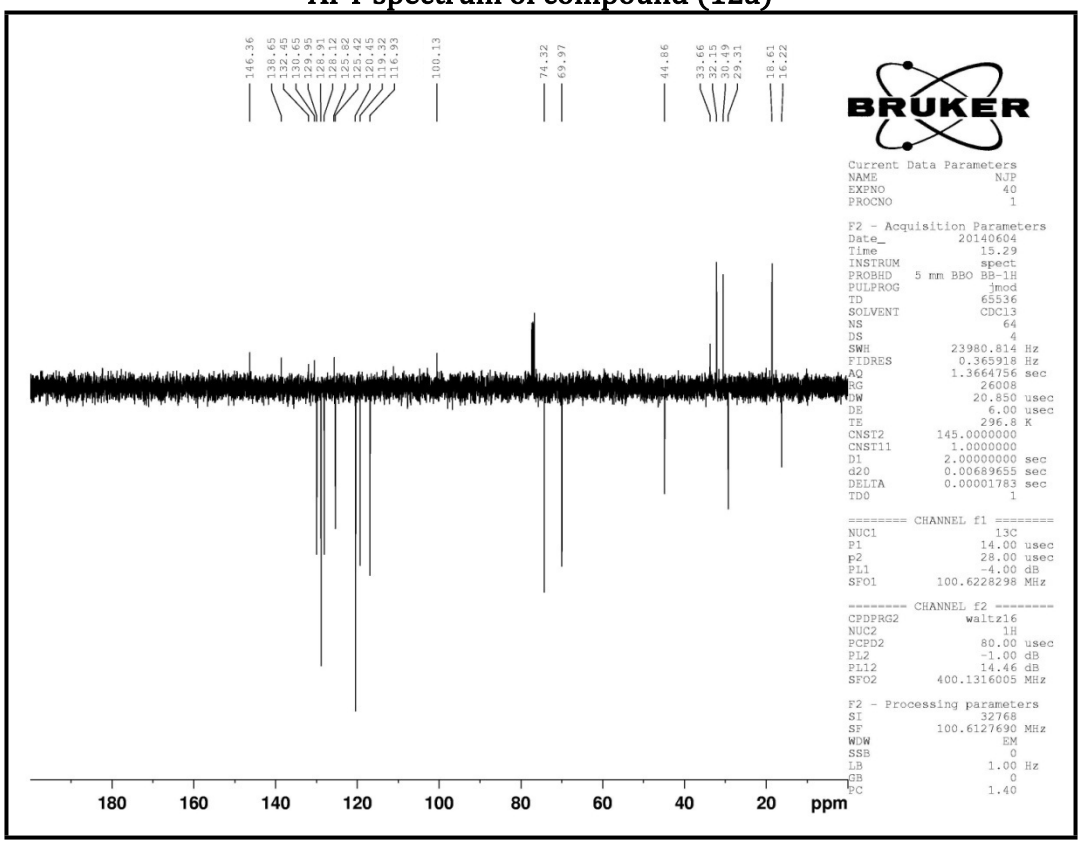
IR of compound (11e)



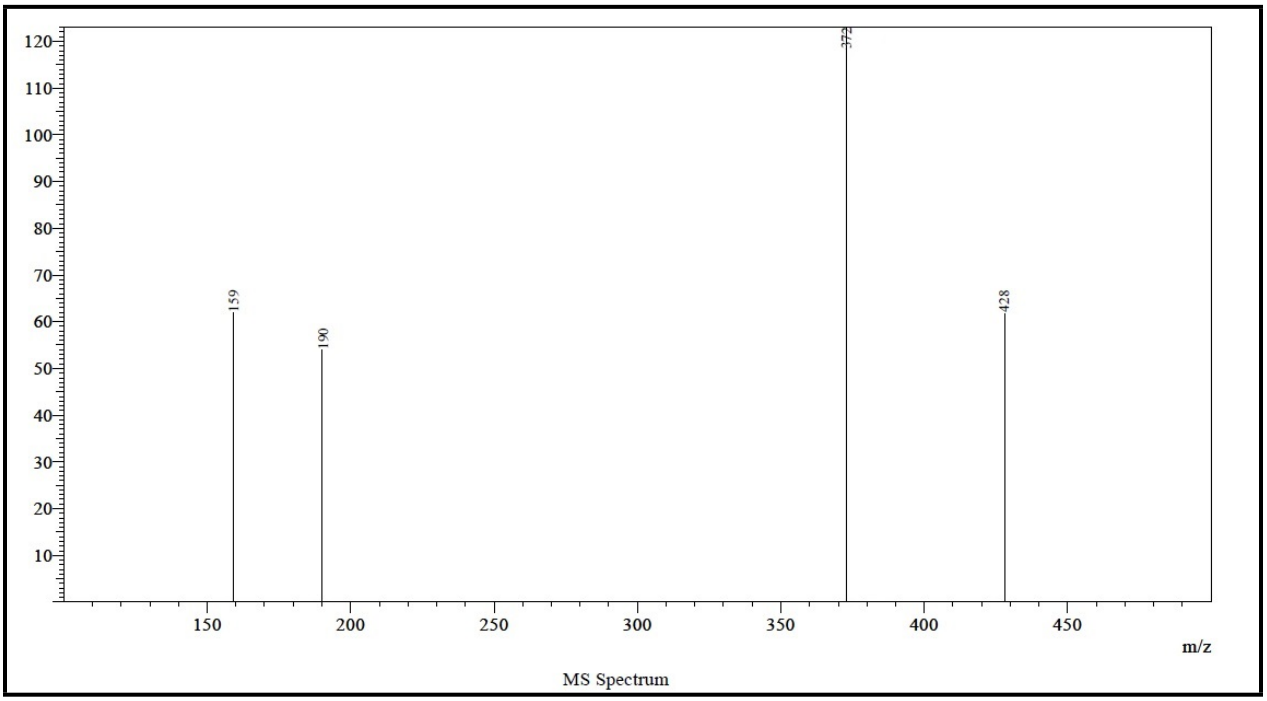
^{1}H NMR spectrum of compound (12a)



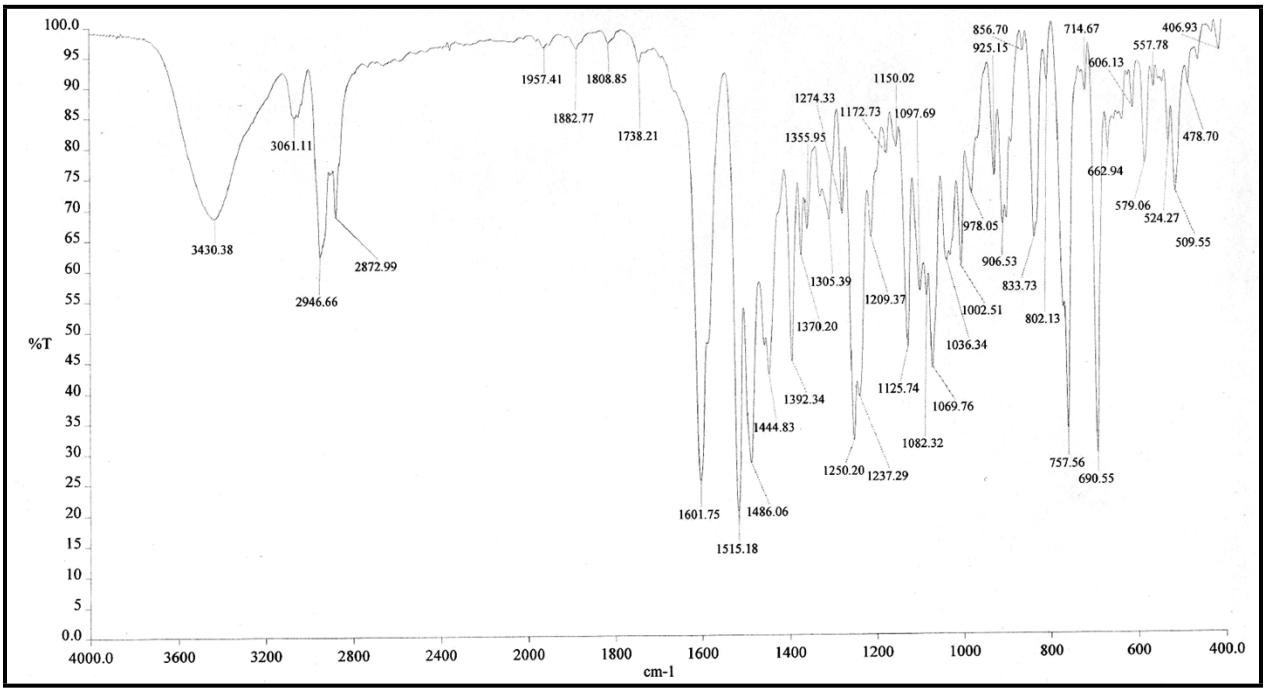
APT spectrum of compound (12a)



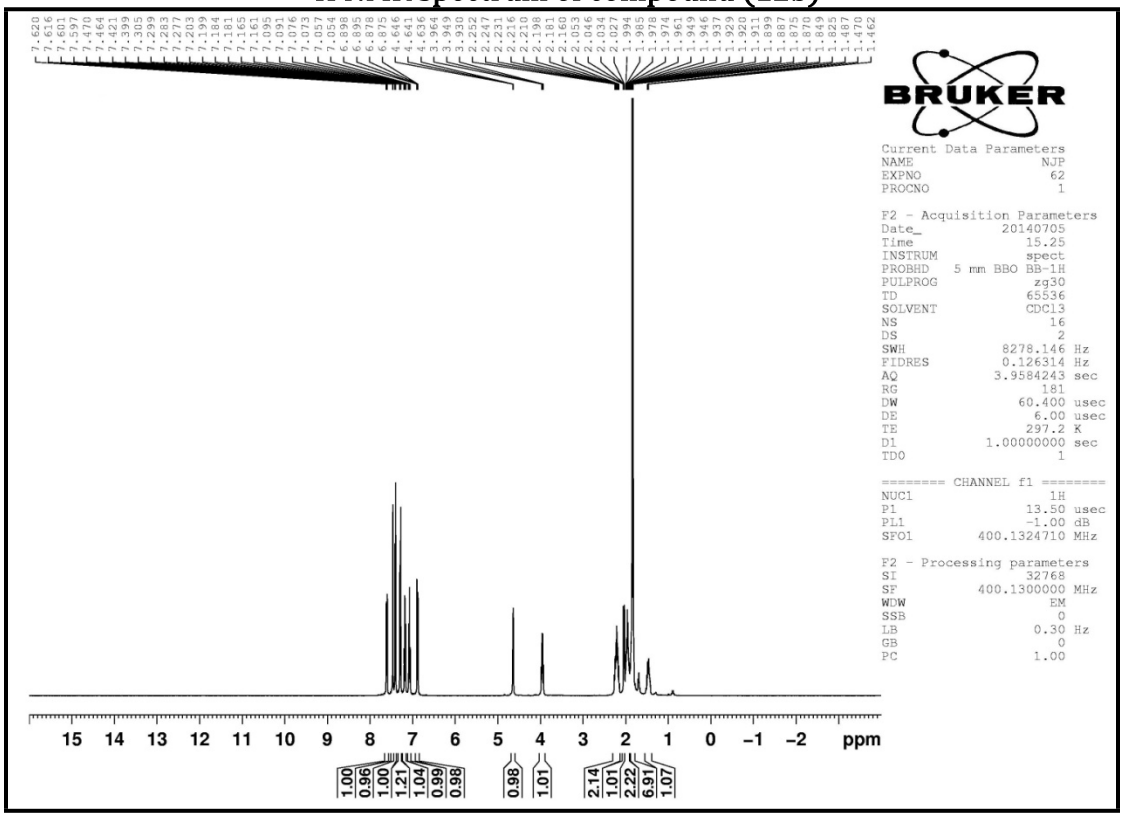
ESI–MS of compound (12a)



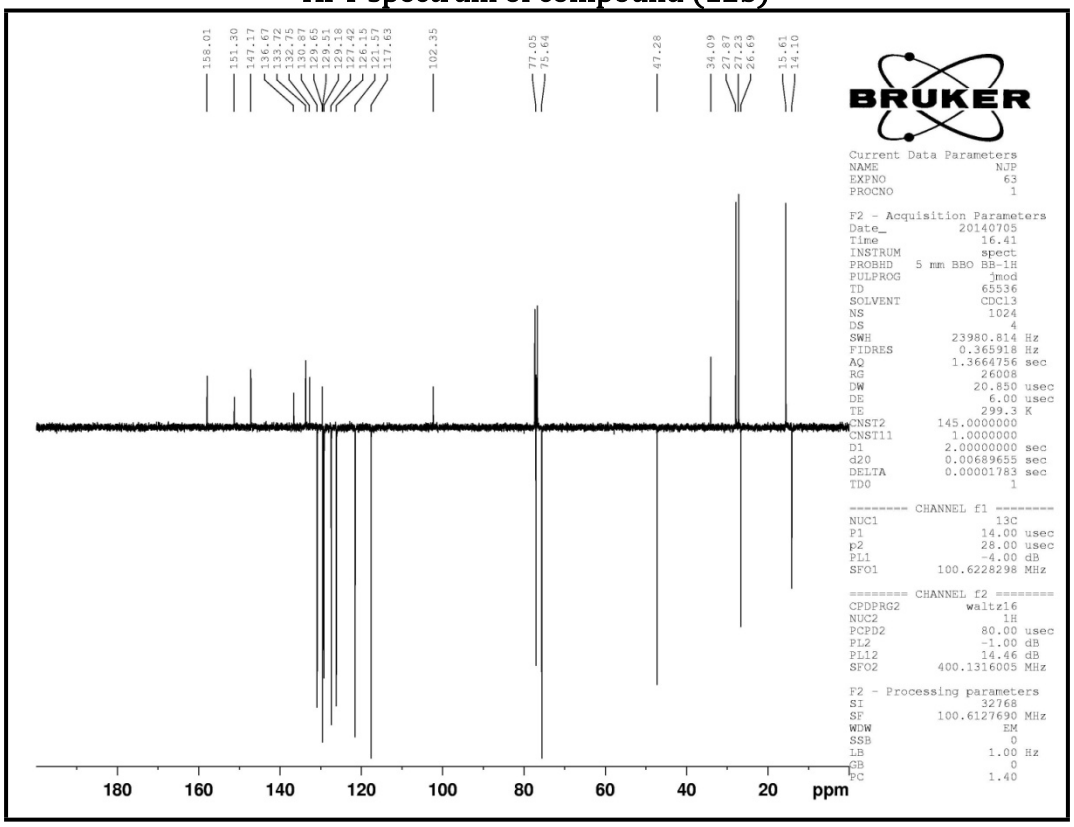
IR of compound (12a)



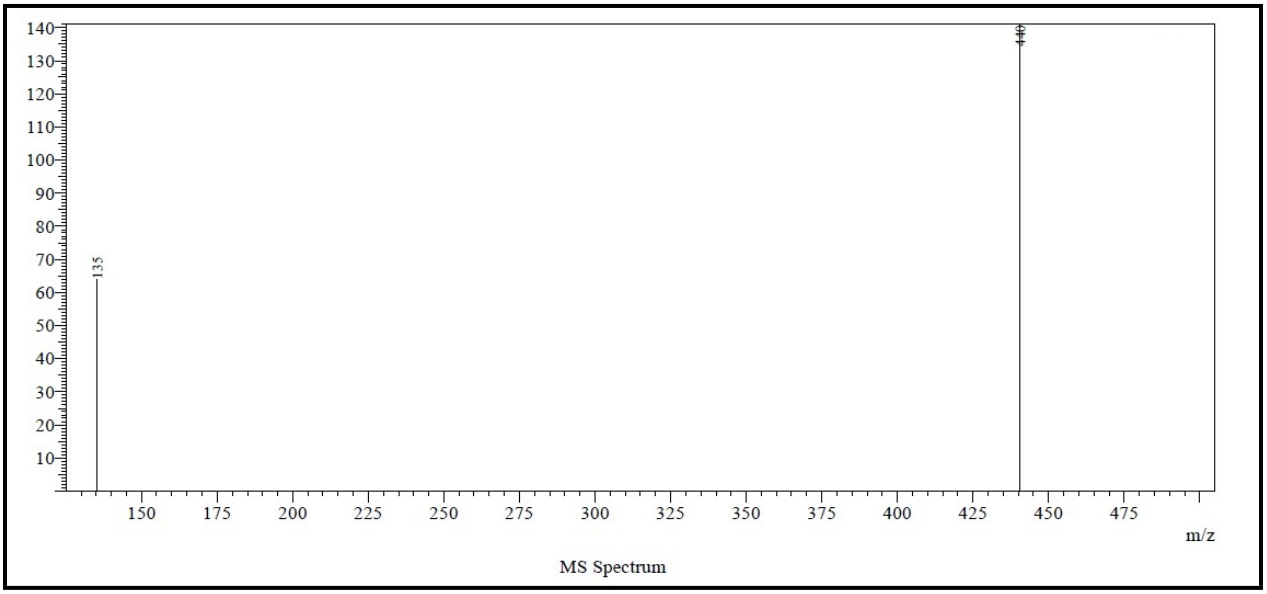
^{1}H NMR spectrum of compound (12b)



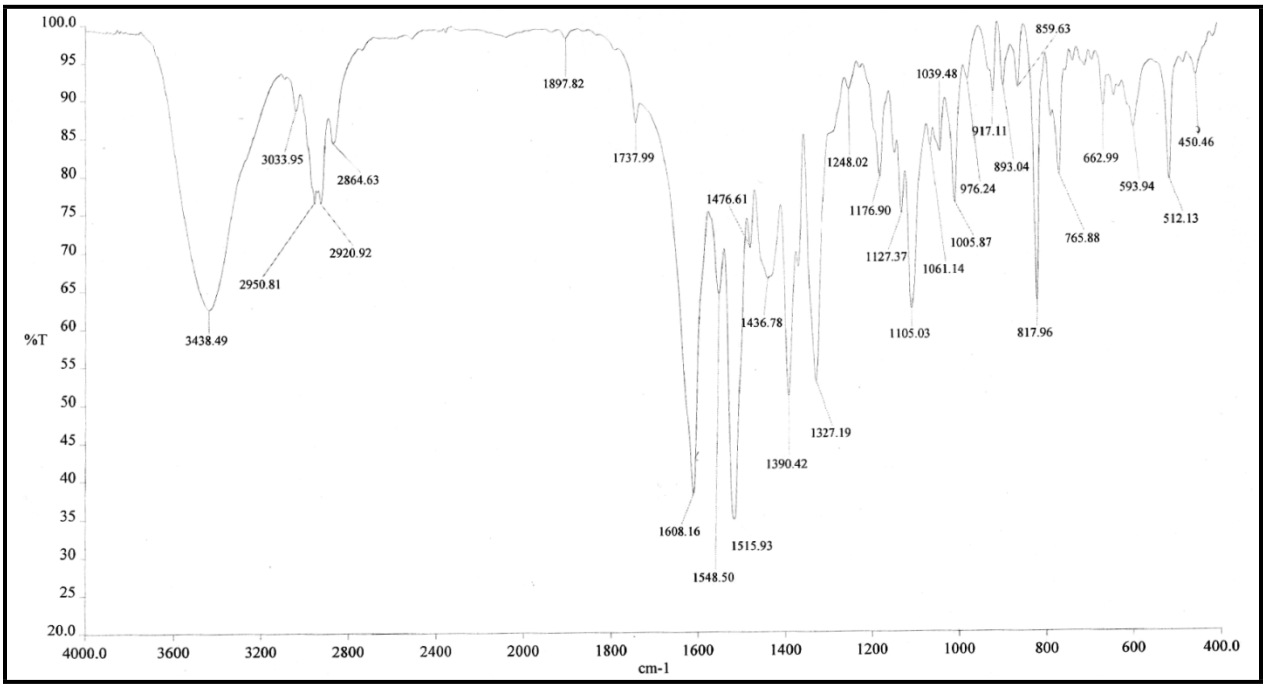
APT spectrum of compound (12b)



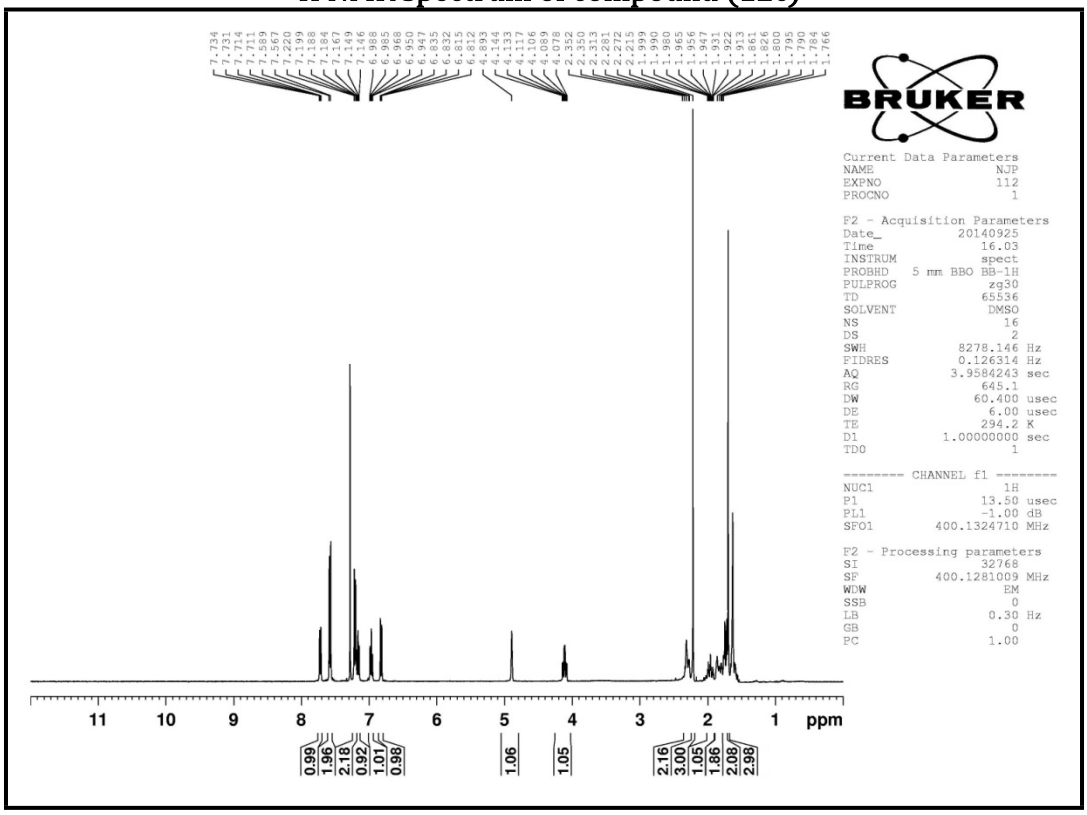
ESI–MS of compound (12b)



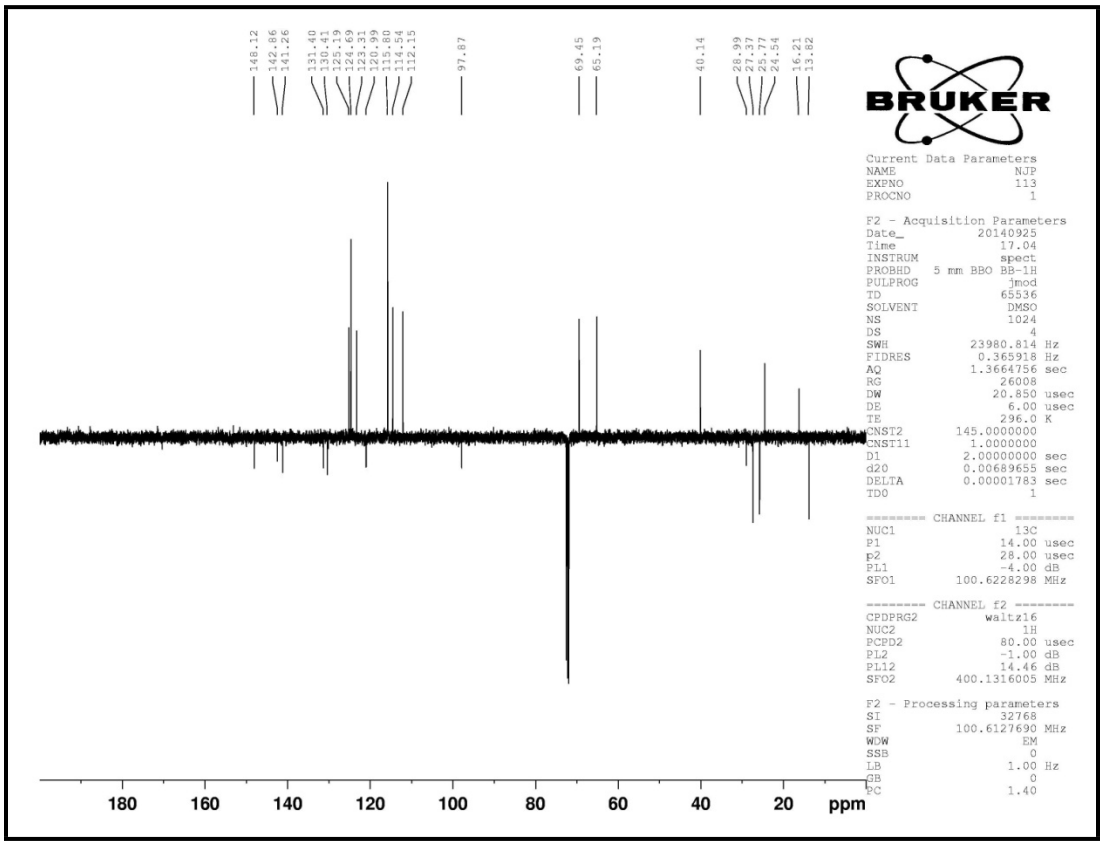
IR of compound (12b)



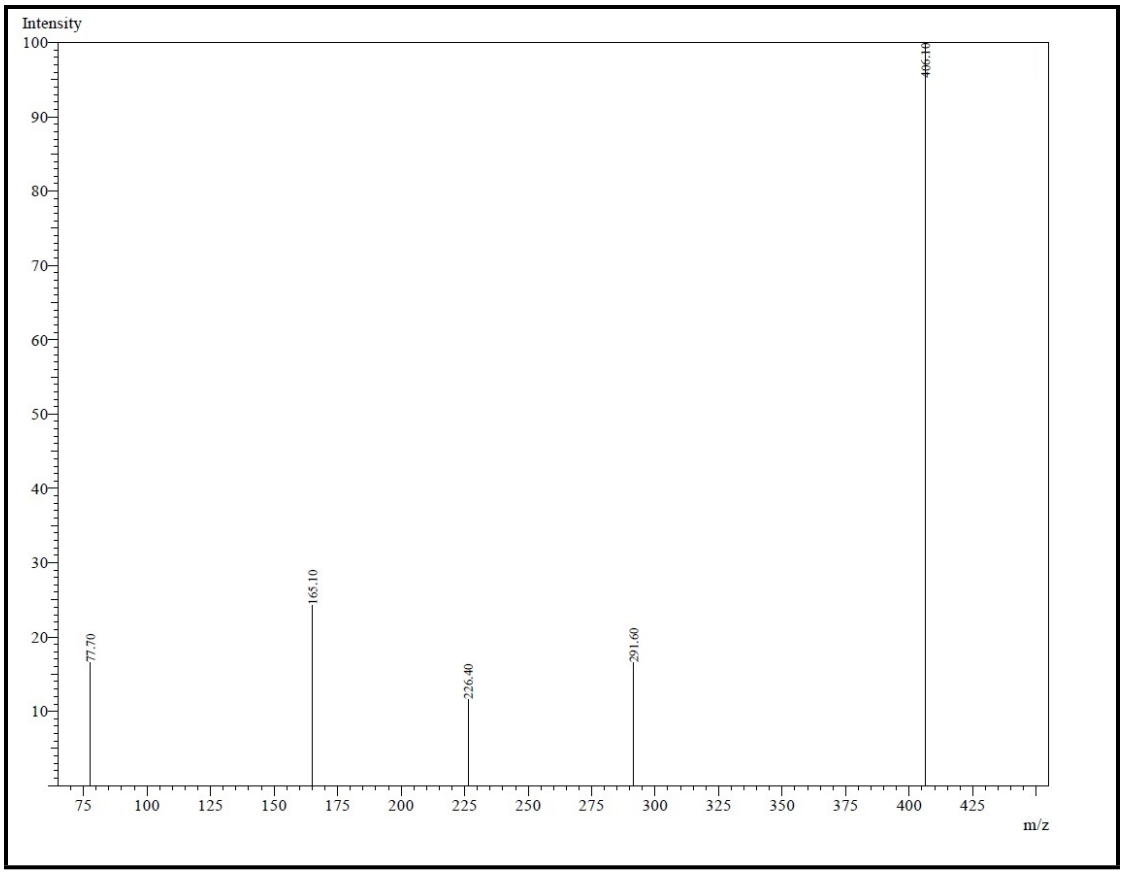
^{1}H NMR spectrum of compound (12c)



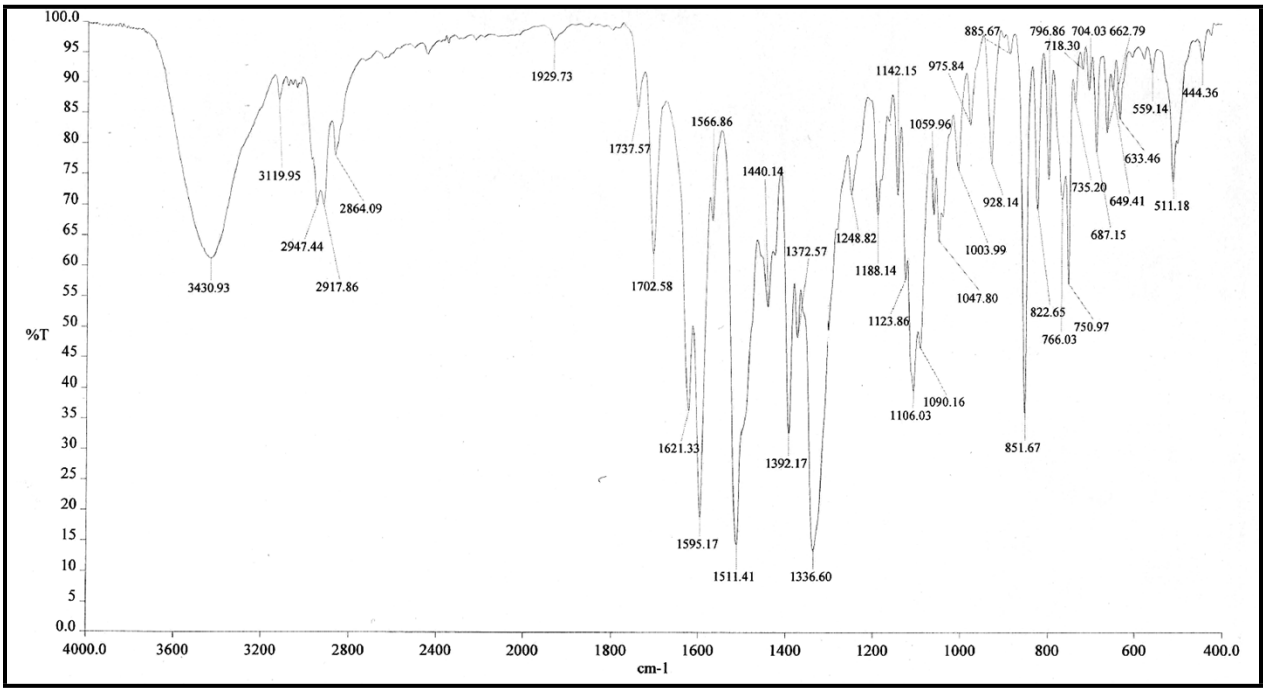
APT spectrum of compound (12c)



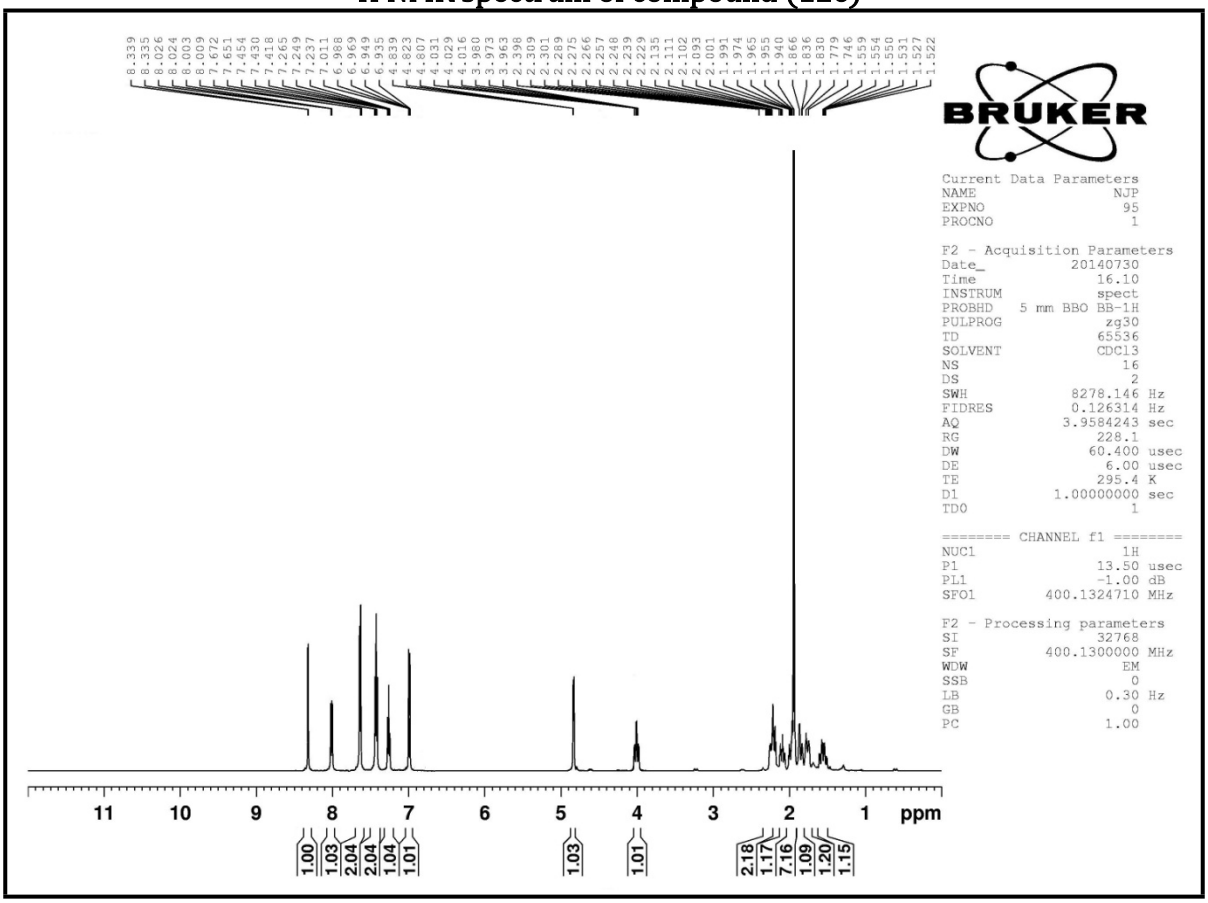
ESI–MS of compound (12c)



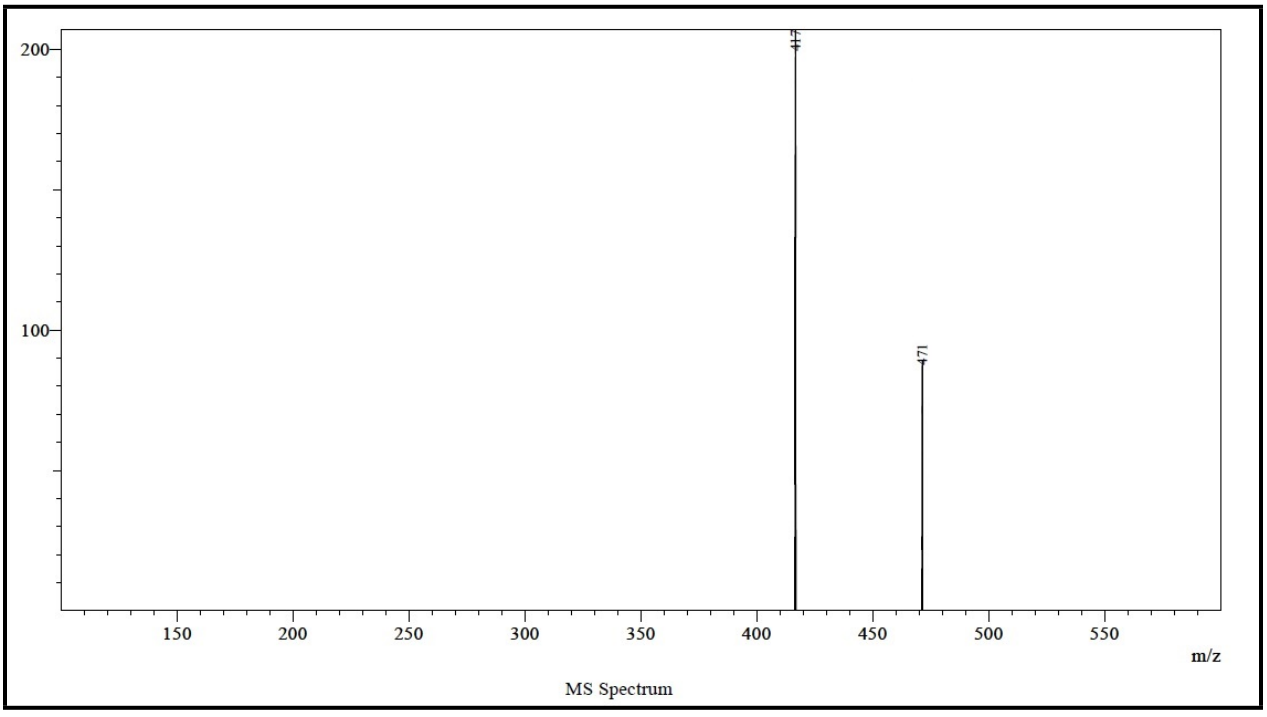
IR of compound (12c)



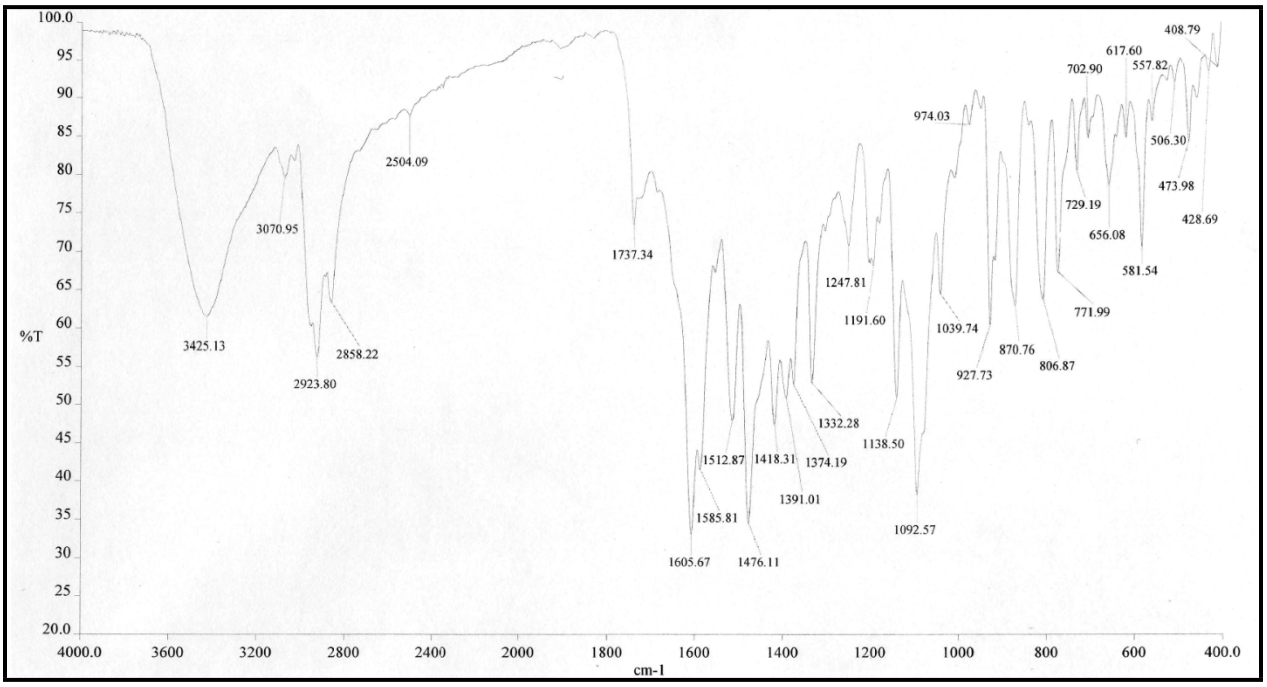
^{1}H NMR spectrum of compound (12e)



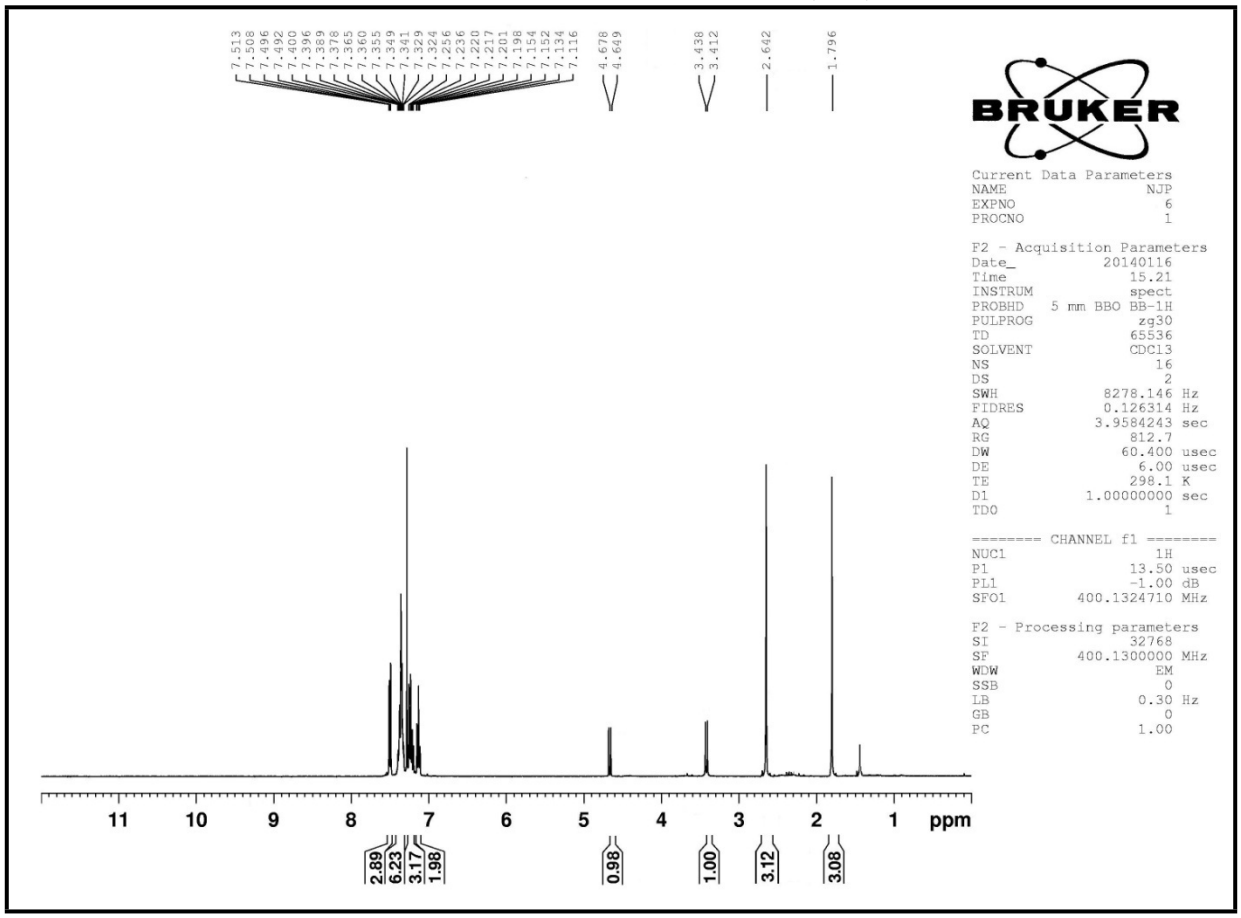
ESI–MS of compound (12e)



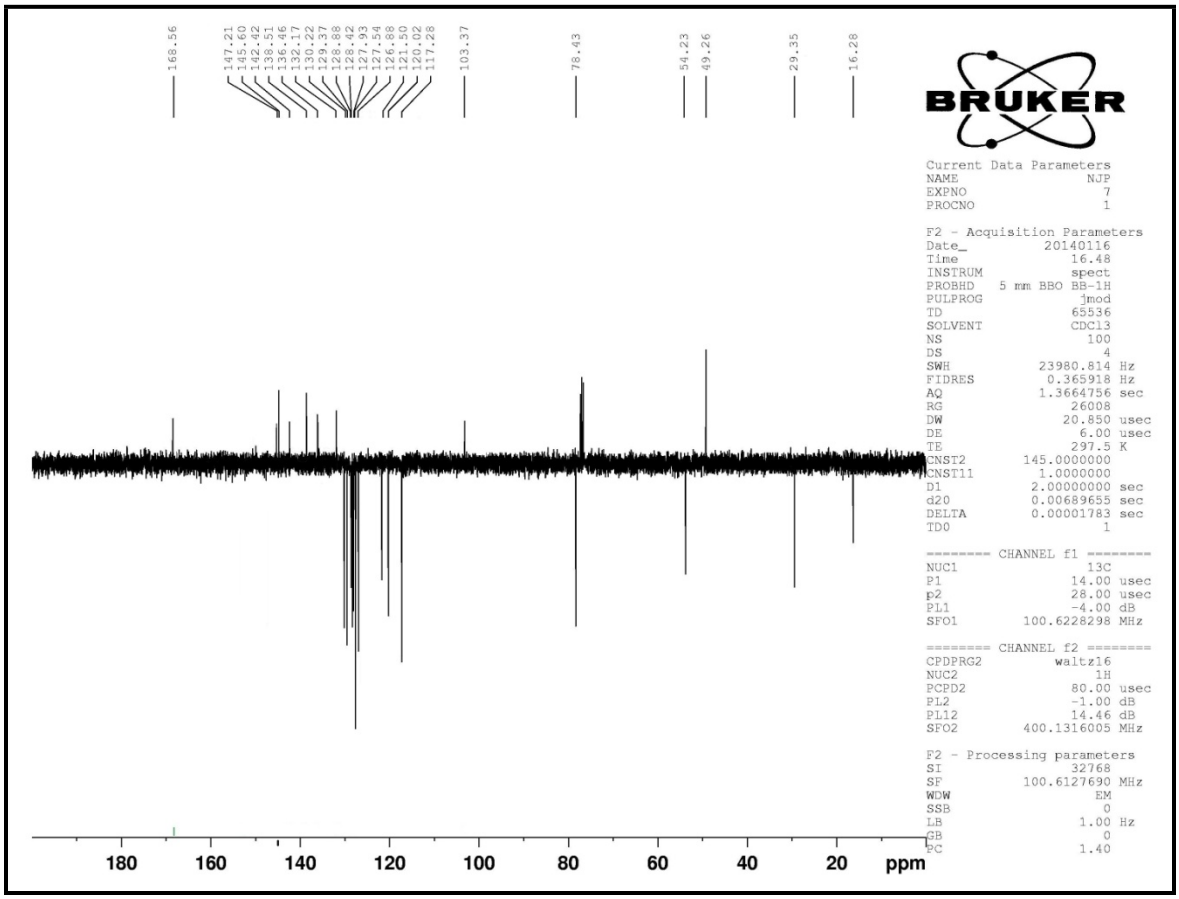
IR of compound (12e)



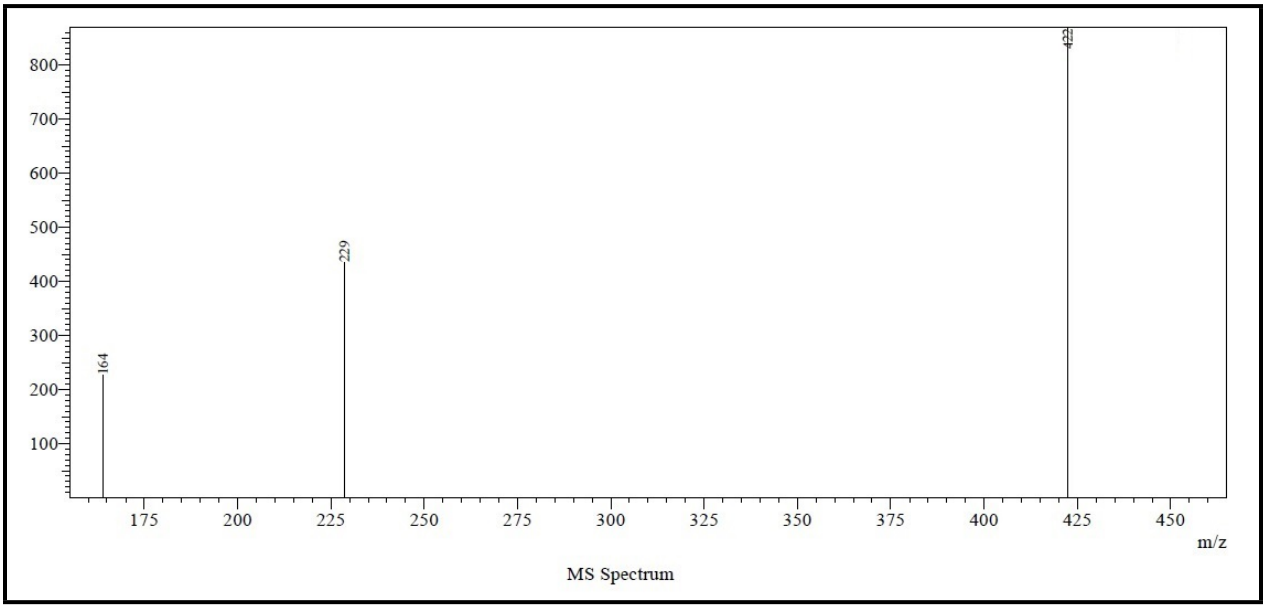
^{1}H NMR spectrum of compound (13a)



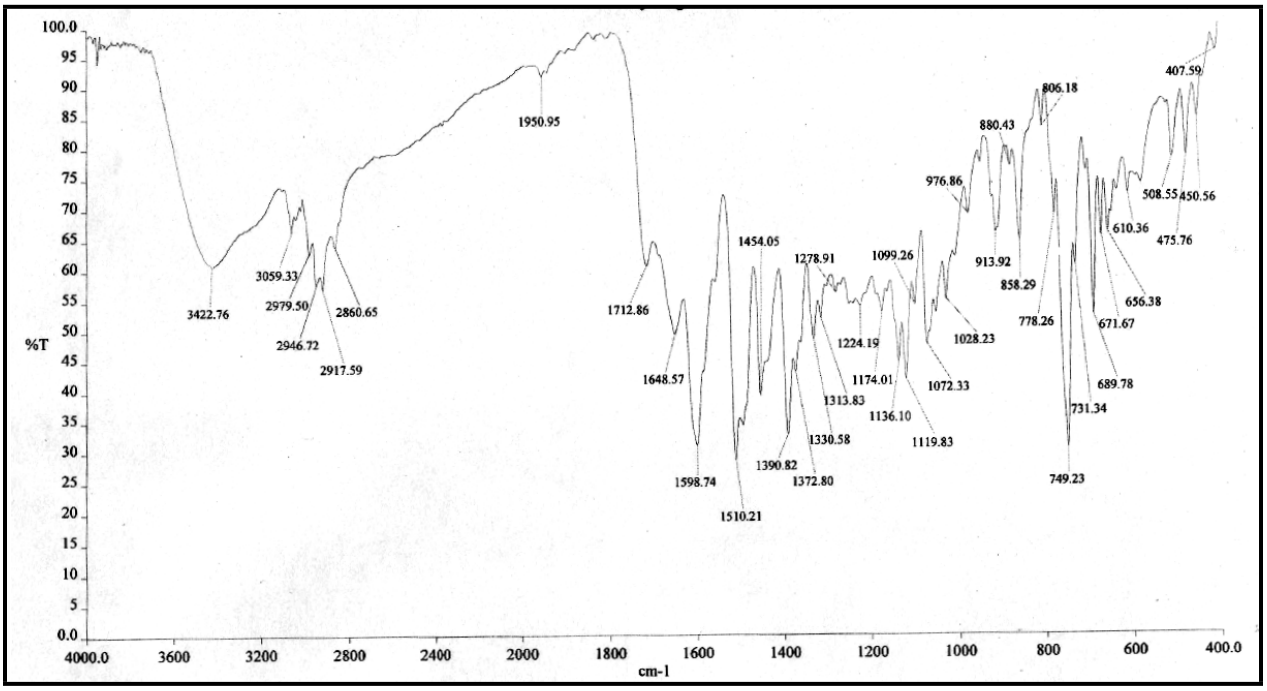
APT spectrum of compound (13a)



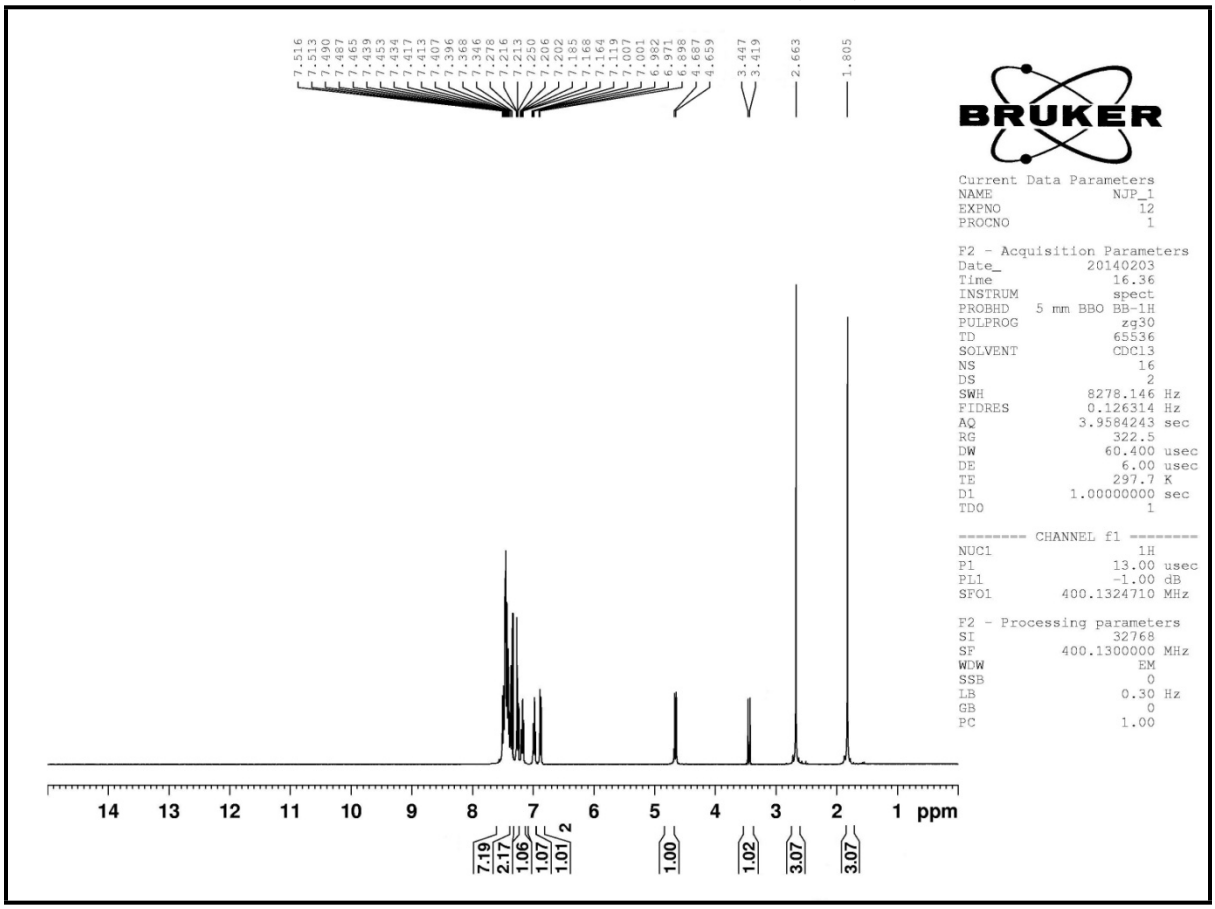
ESI–MS of compound (13a)



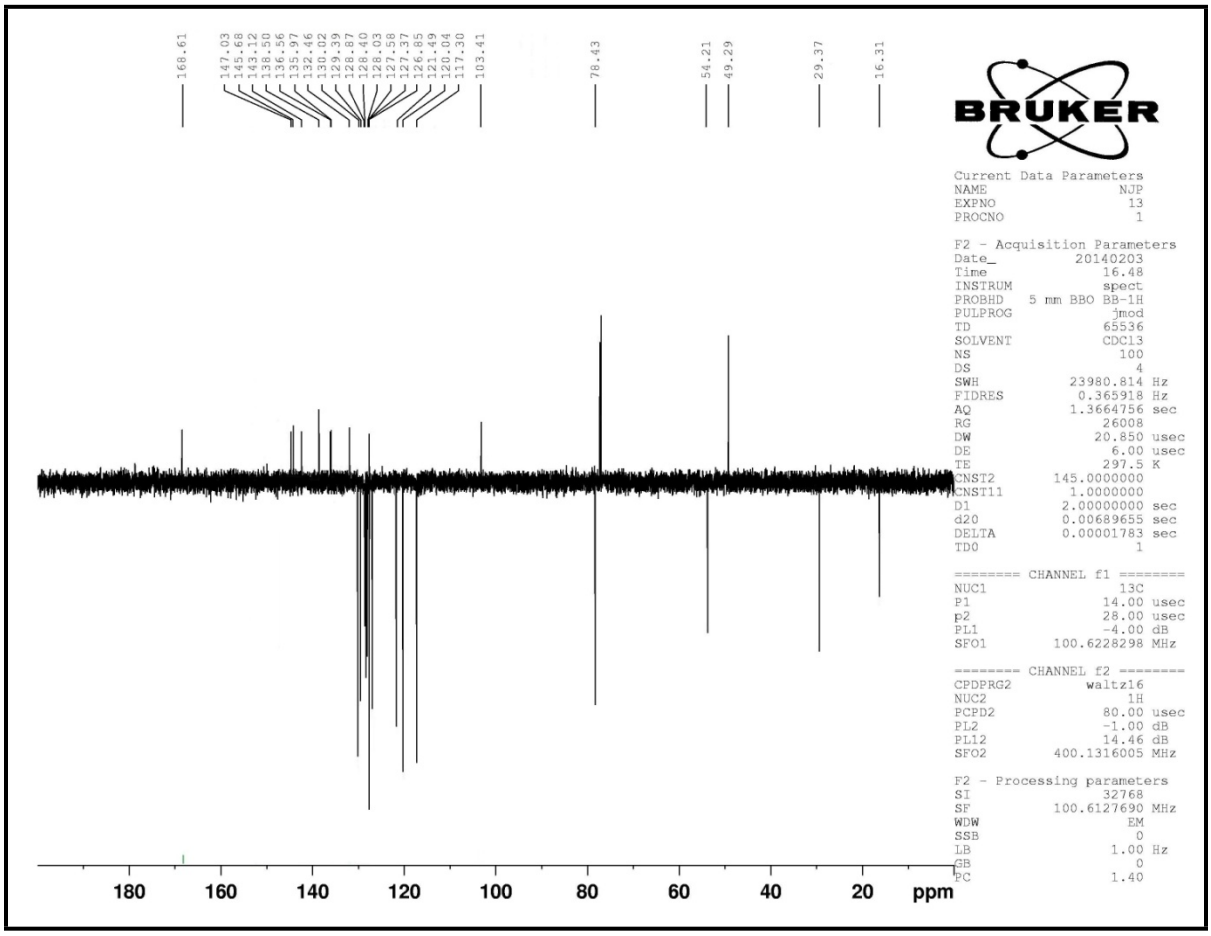
IR of compound (13a)



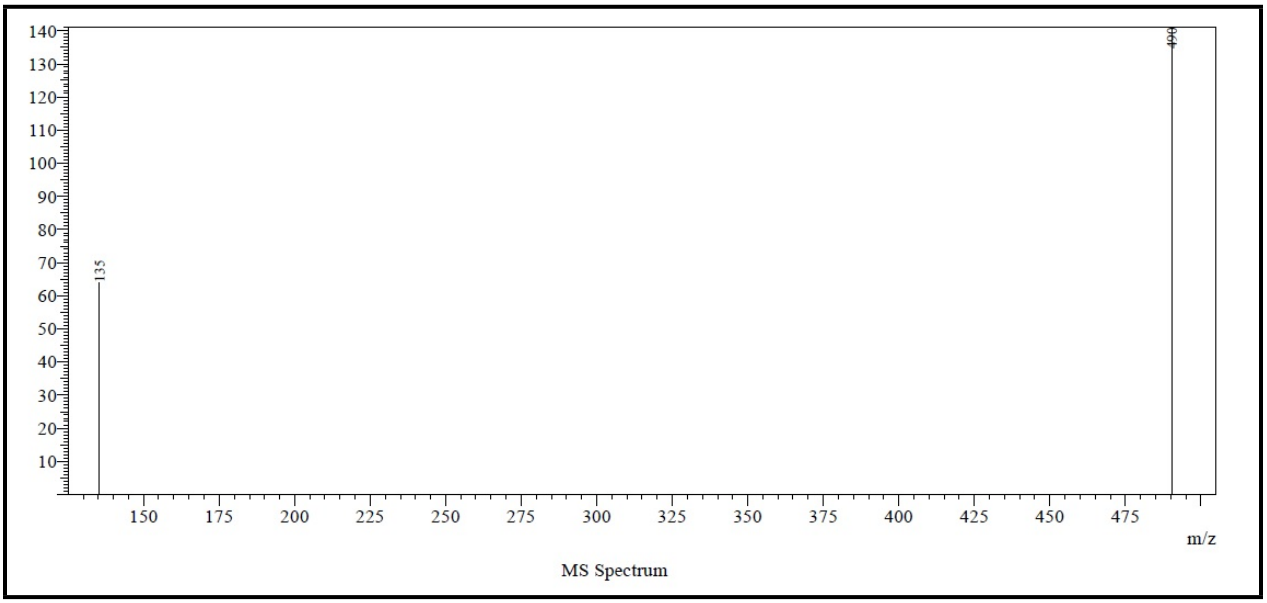
^{1}H NMR spectrum of compound (13b)



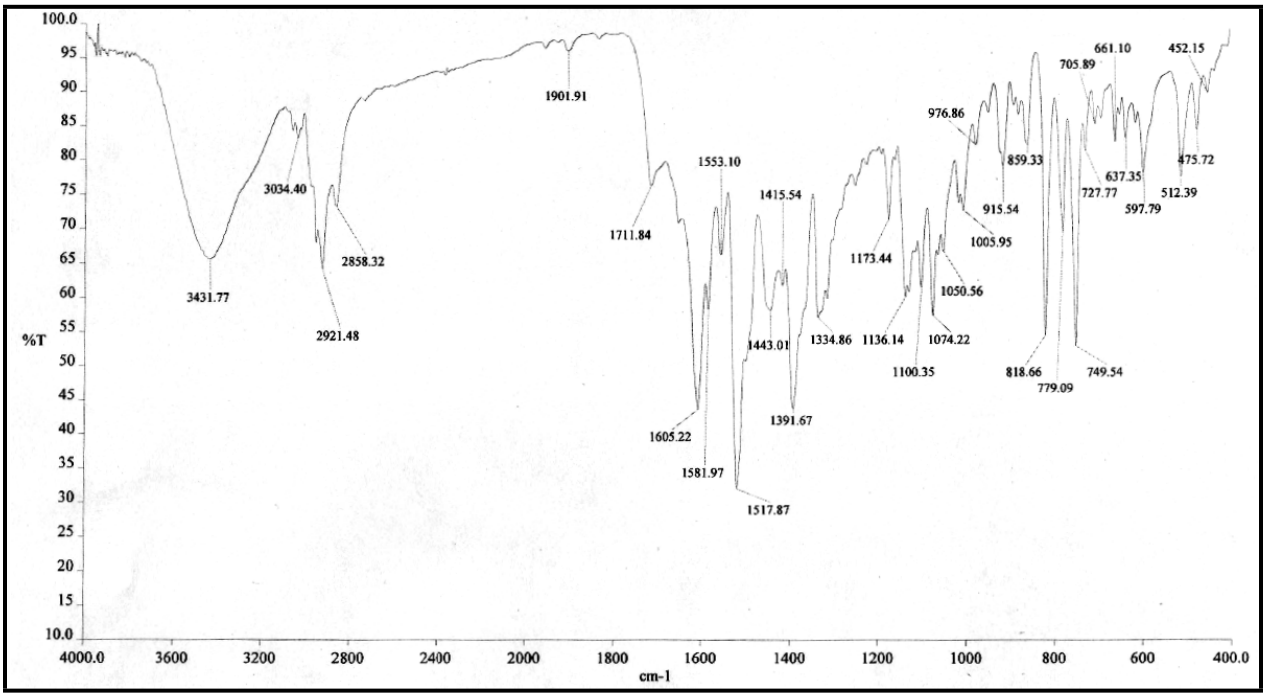
APT spectrum of compound (13b)



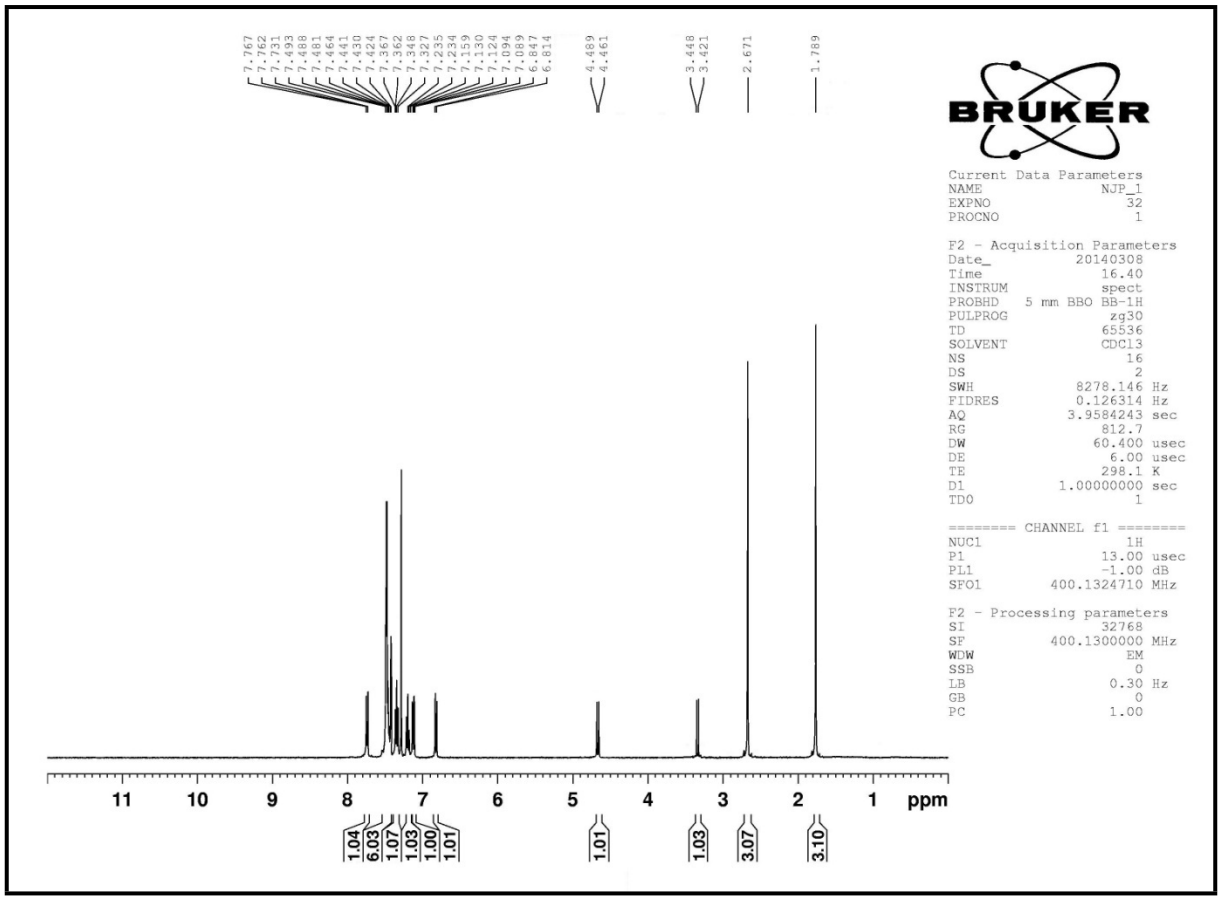
ESI–MS of compound (13b)



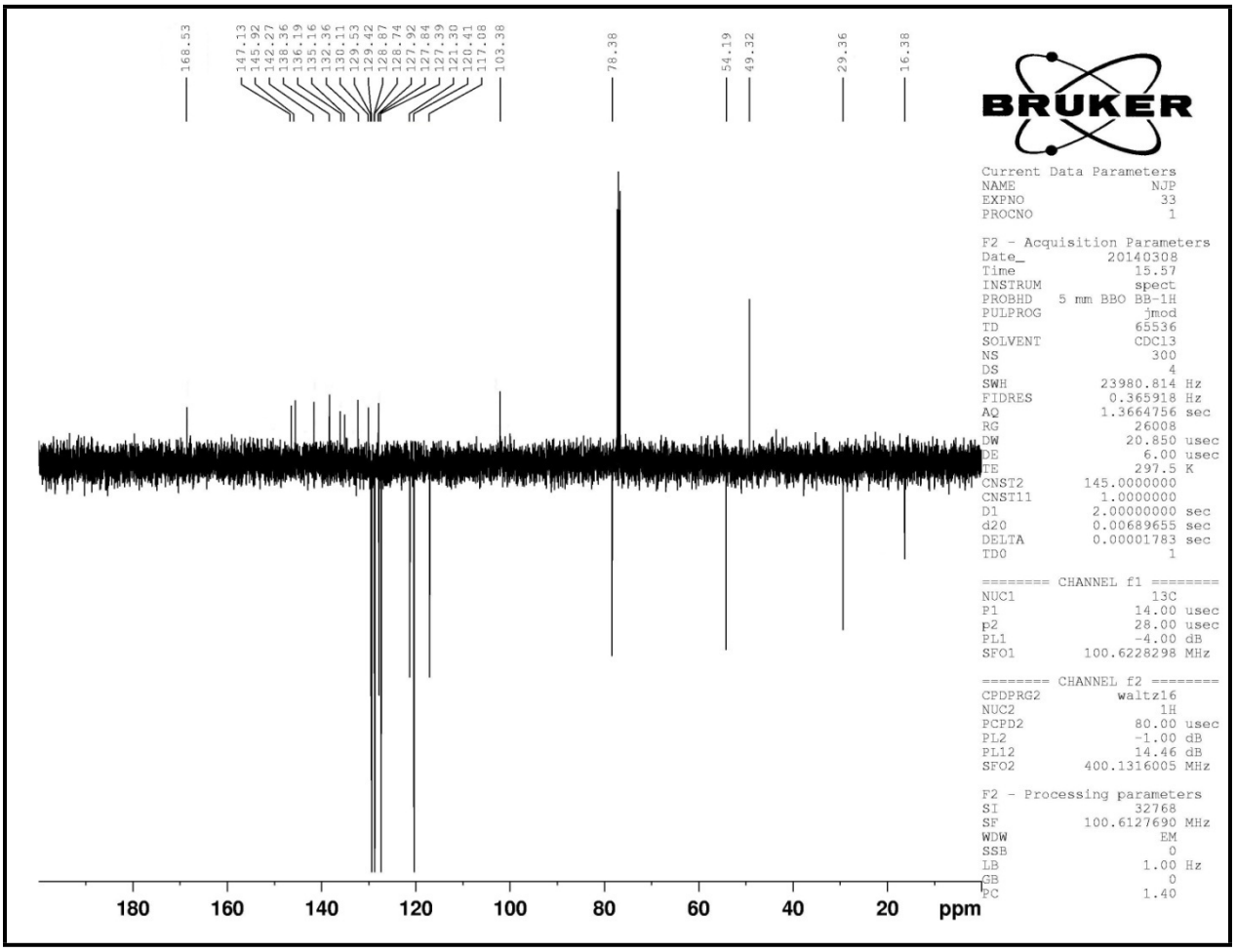
IR of compound (13b)



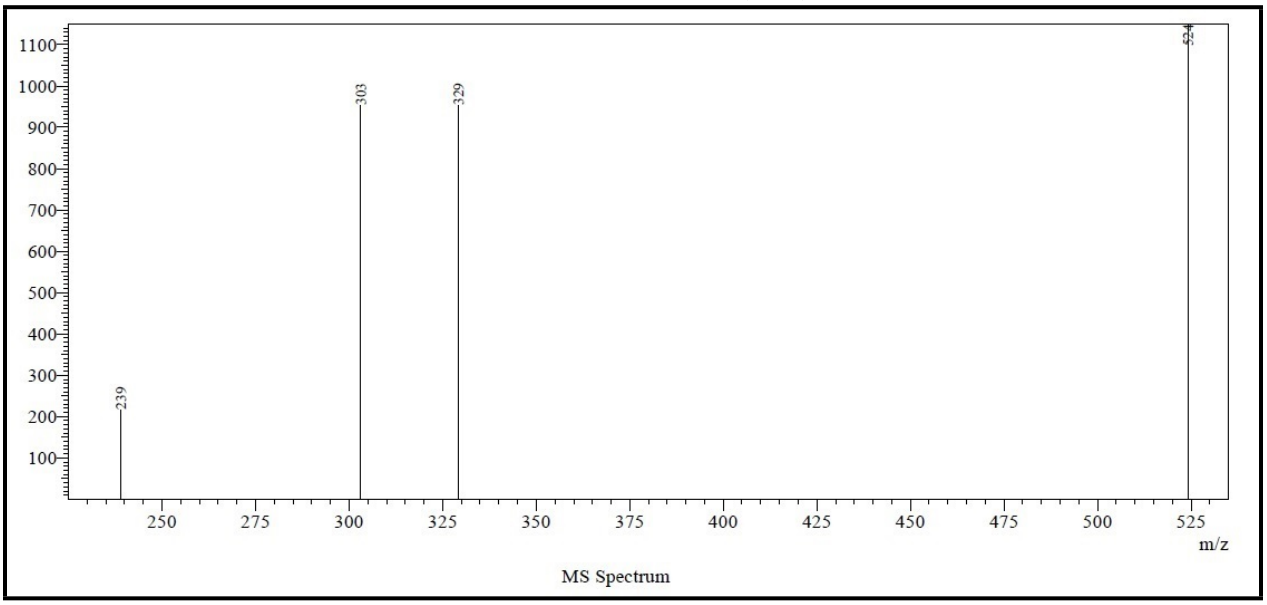
^{1}H NMR spectrum of compound (13d)



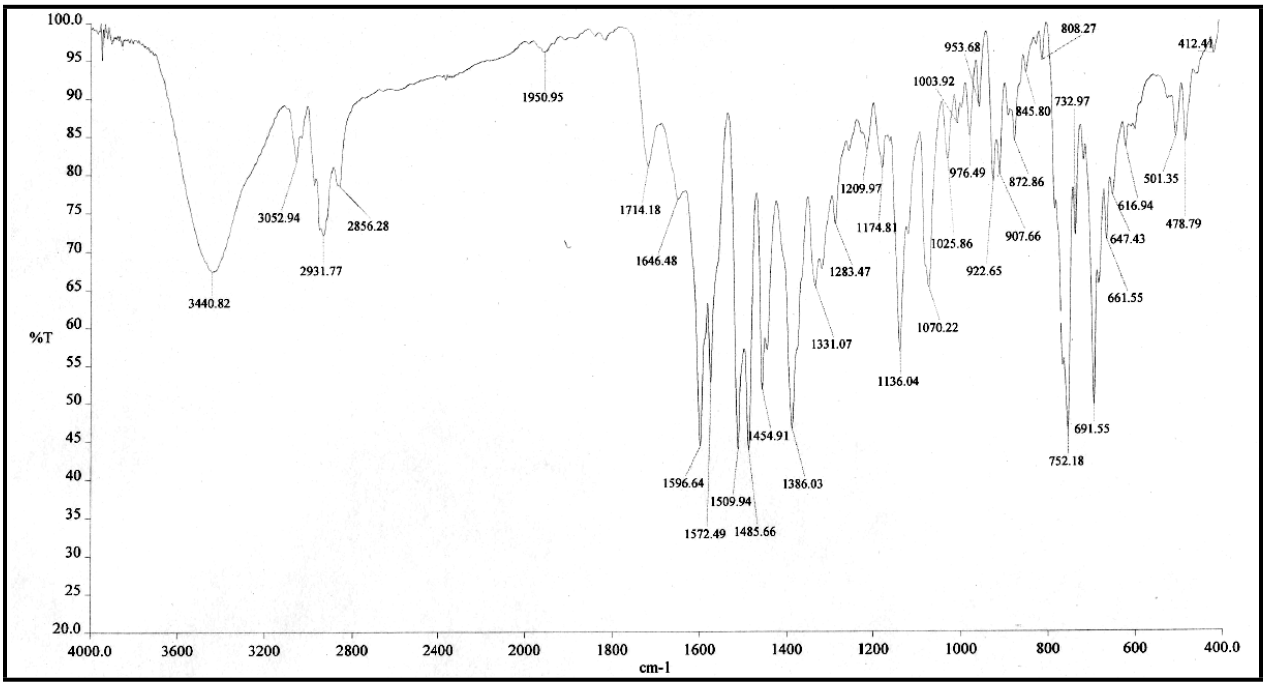
APT spectrum of compound (13d)



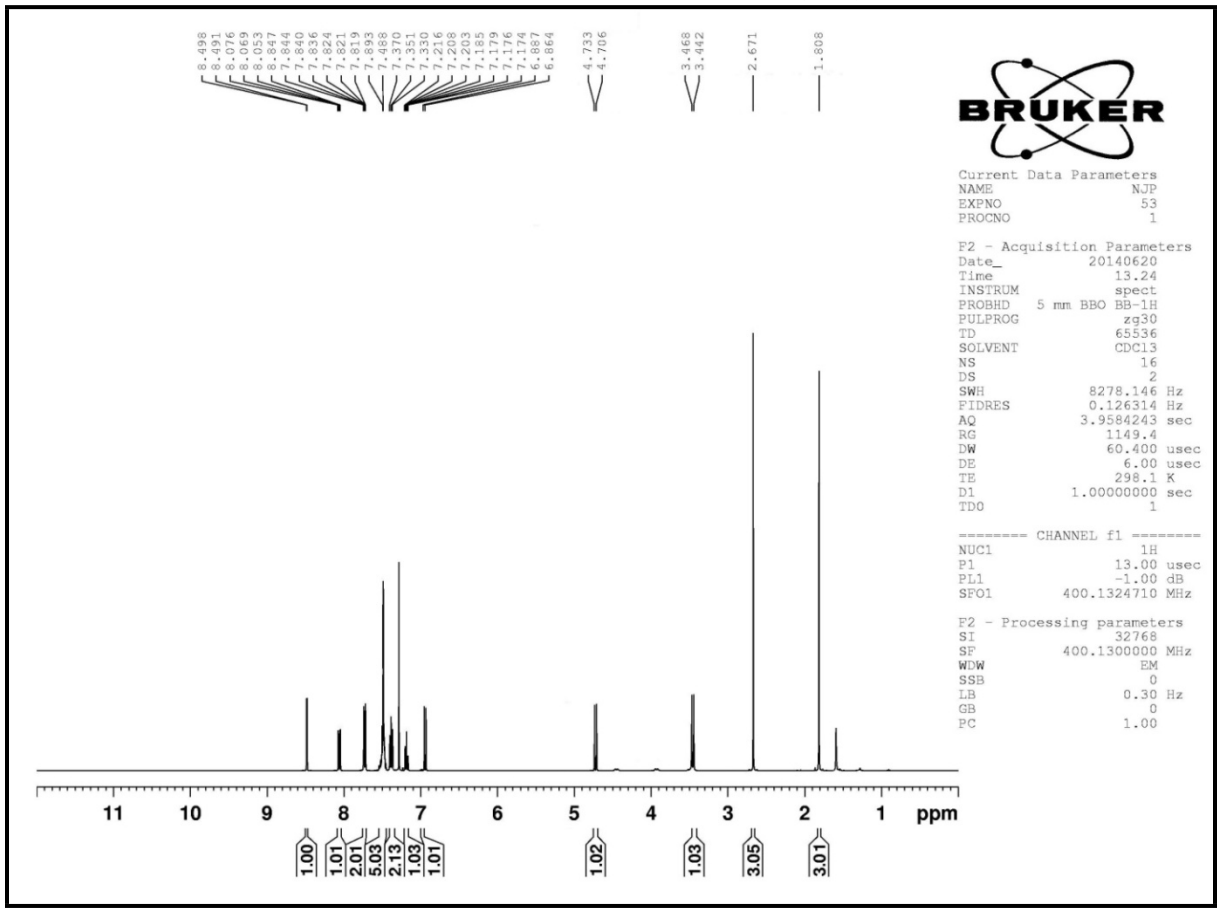
ESI–MS of compound (13d)



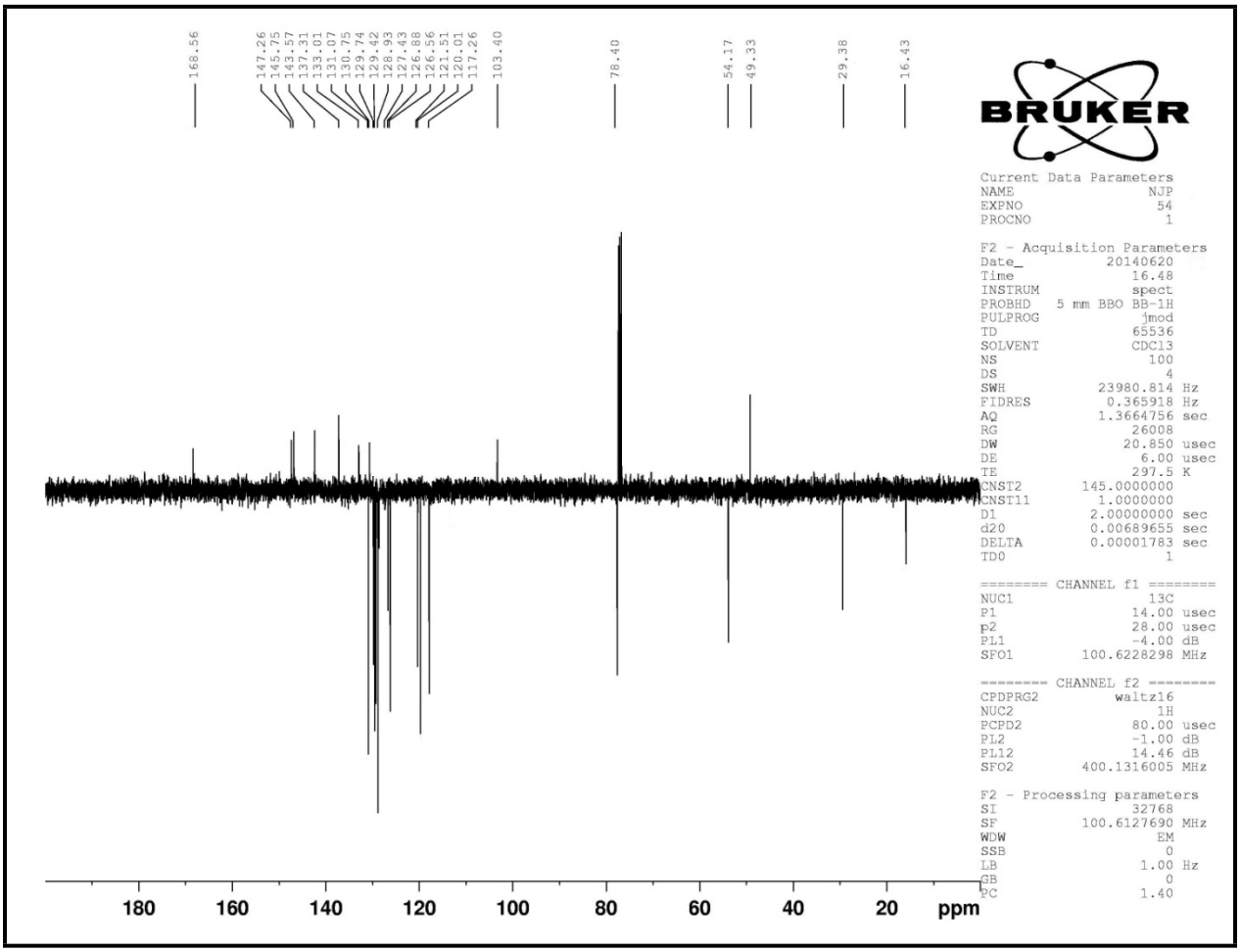
IR of compound (13d)



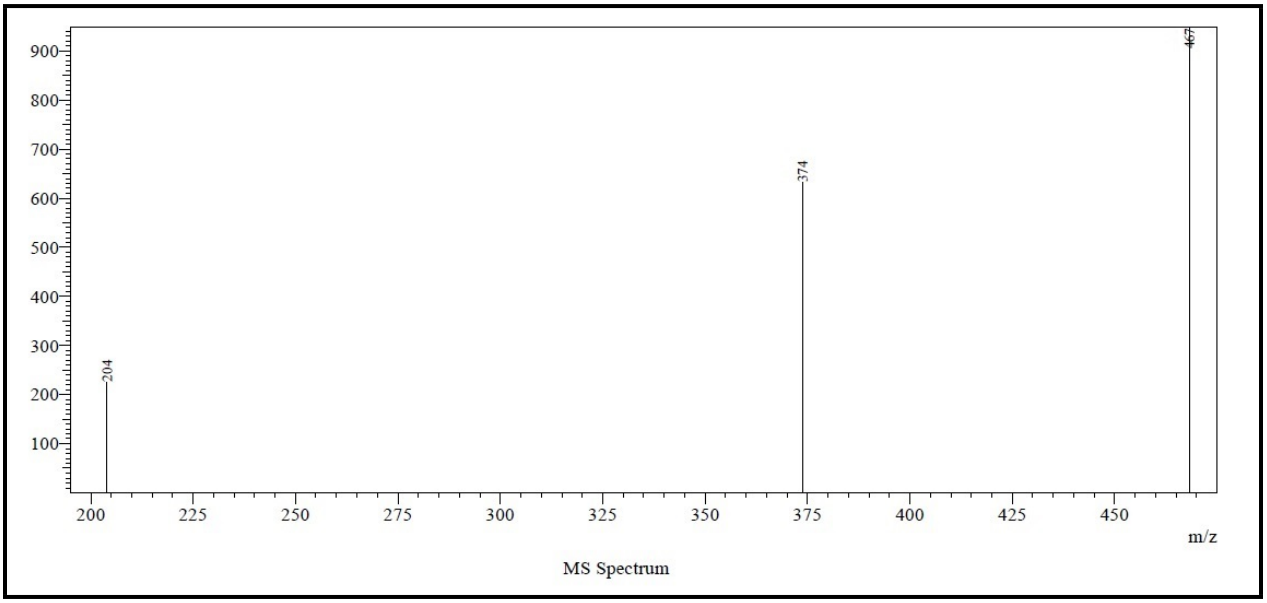
^{1}H NMR spectrum of compound (13e)



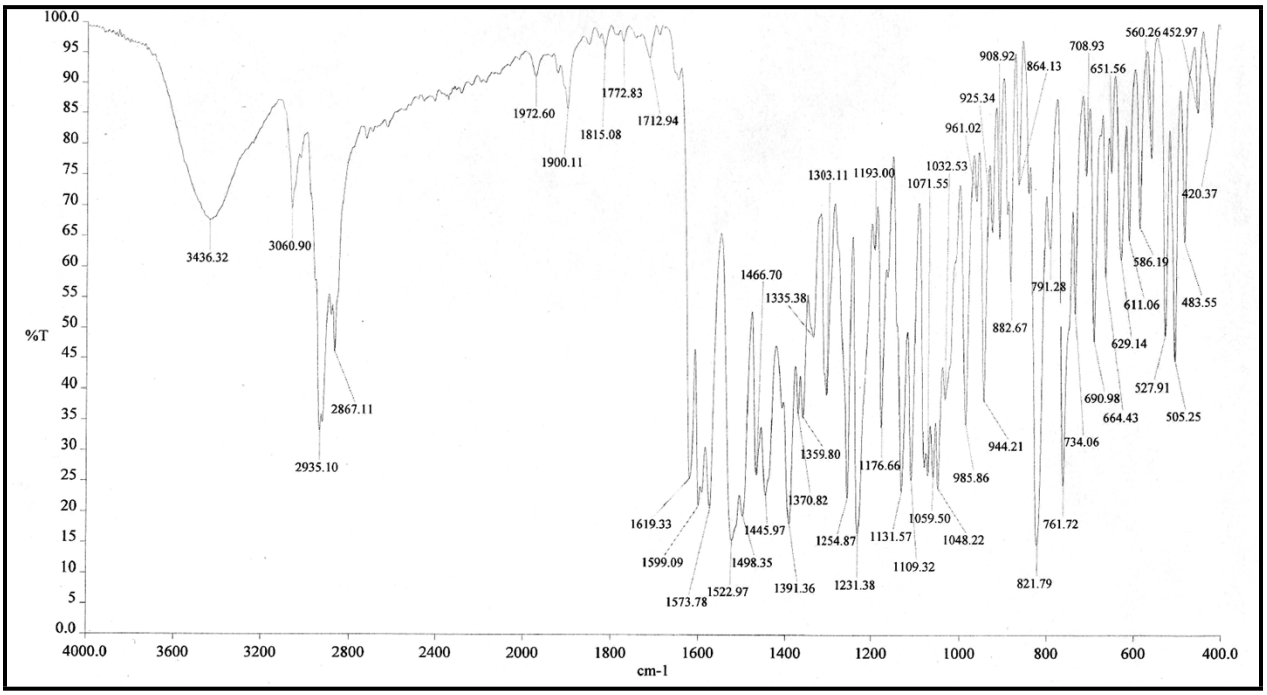
APT spectrum of compound (13e)



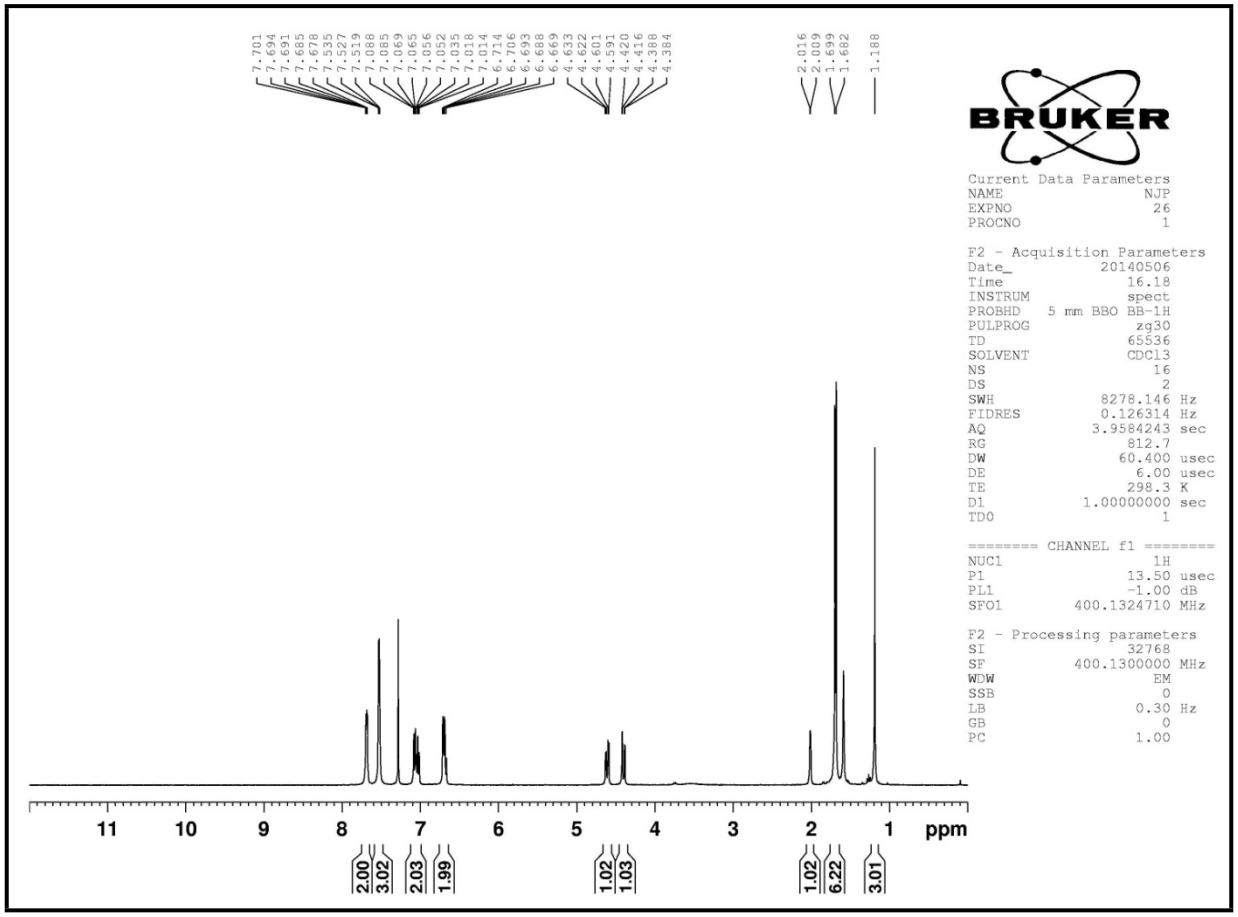
ESI–MS of compound (13e)



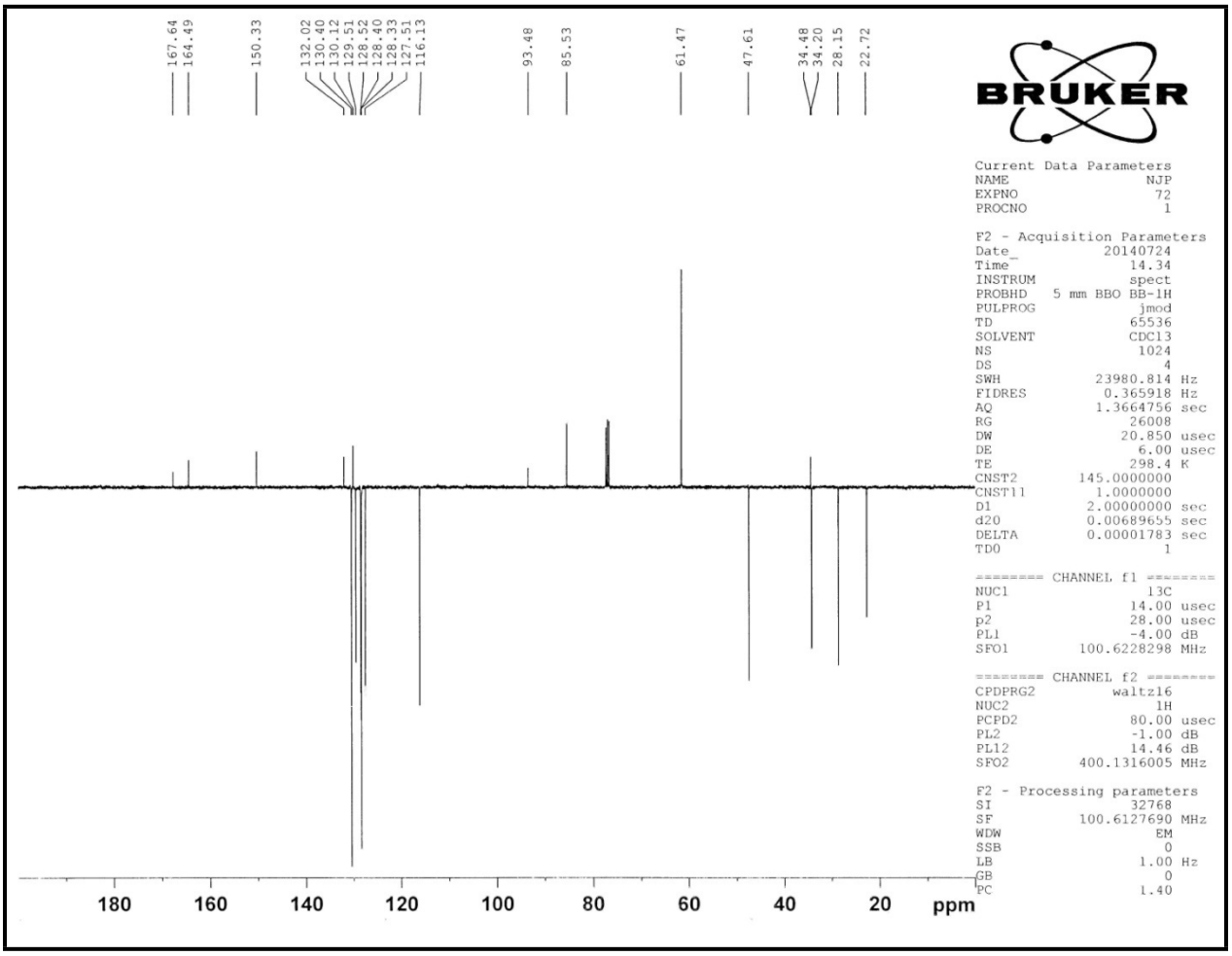
IR of compound (13e)



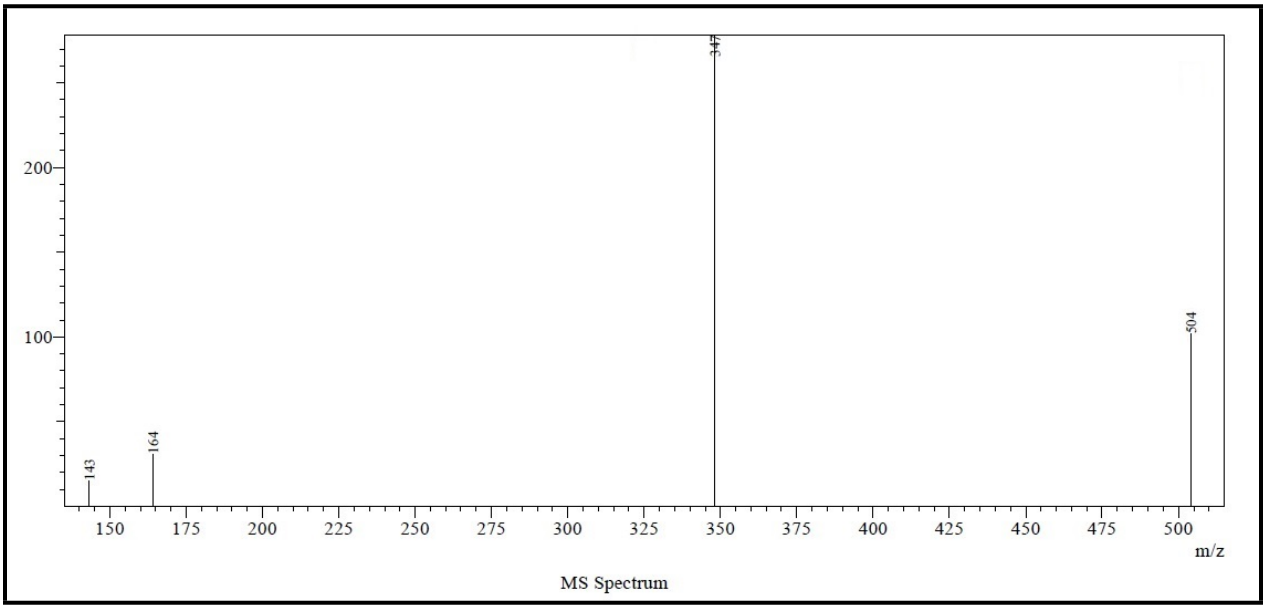
^{1}H NMR spectrum of compound (15a)



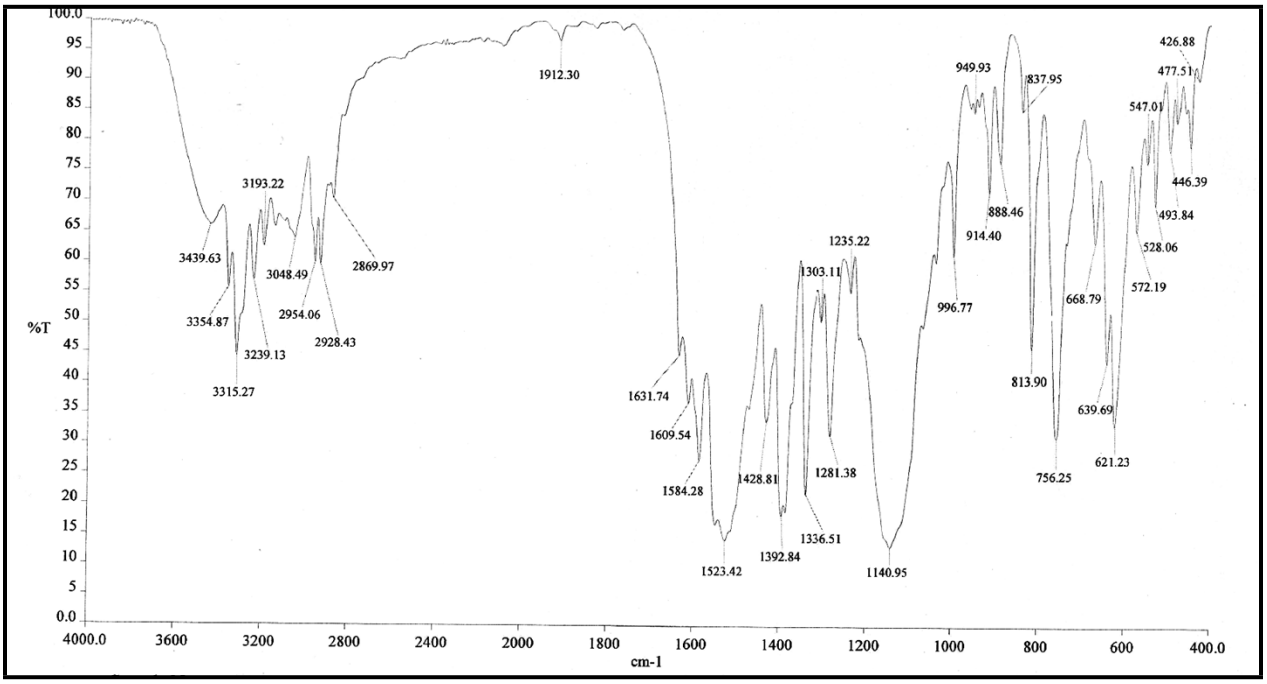
APT spectrum of compound (15a)



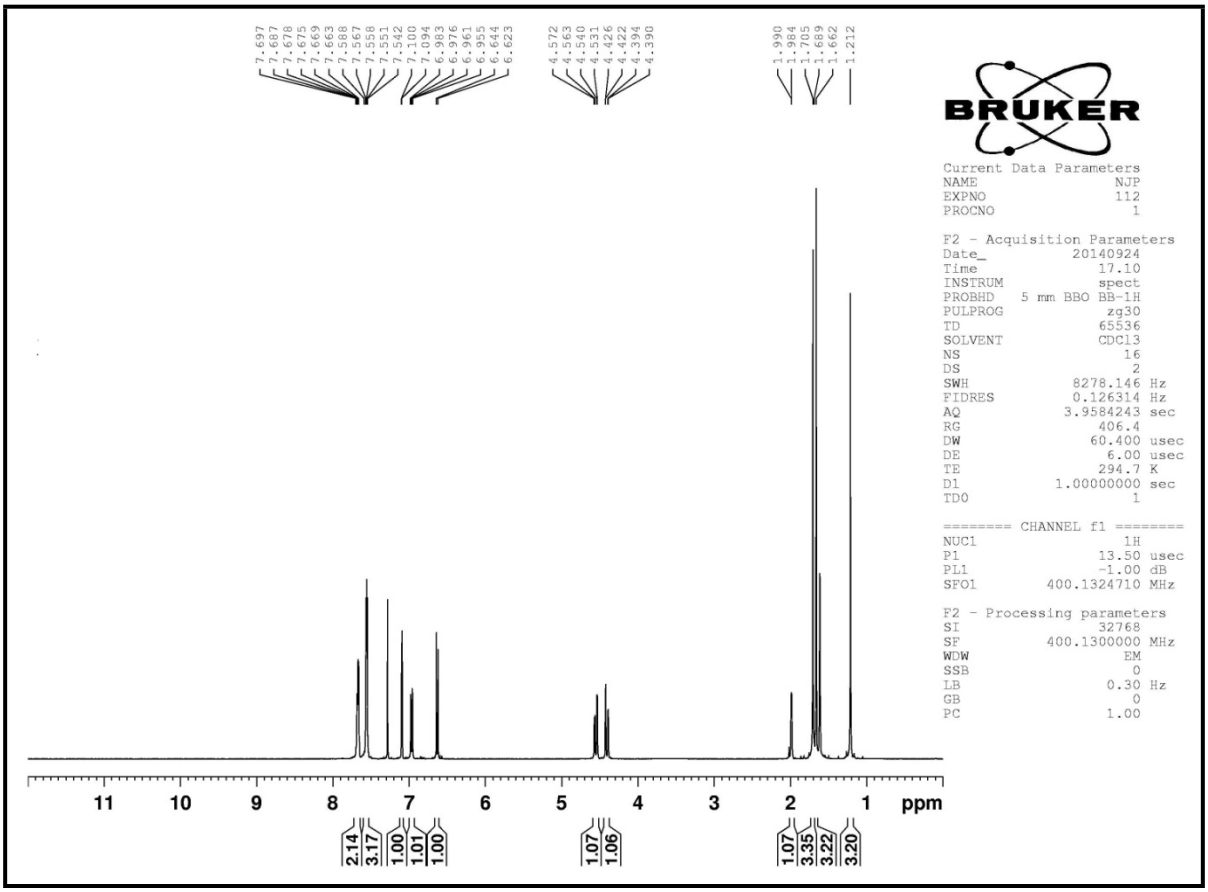
ESI–MS of compound (15a)



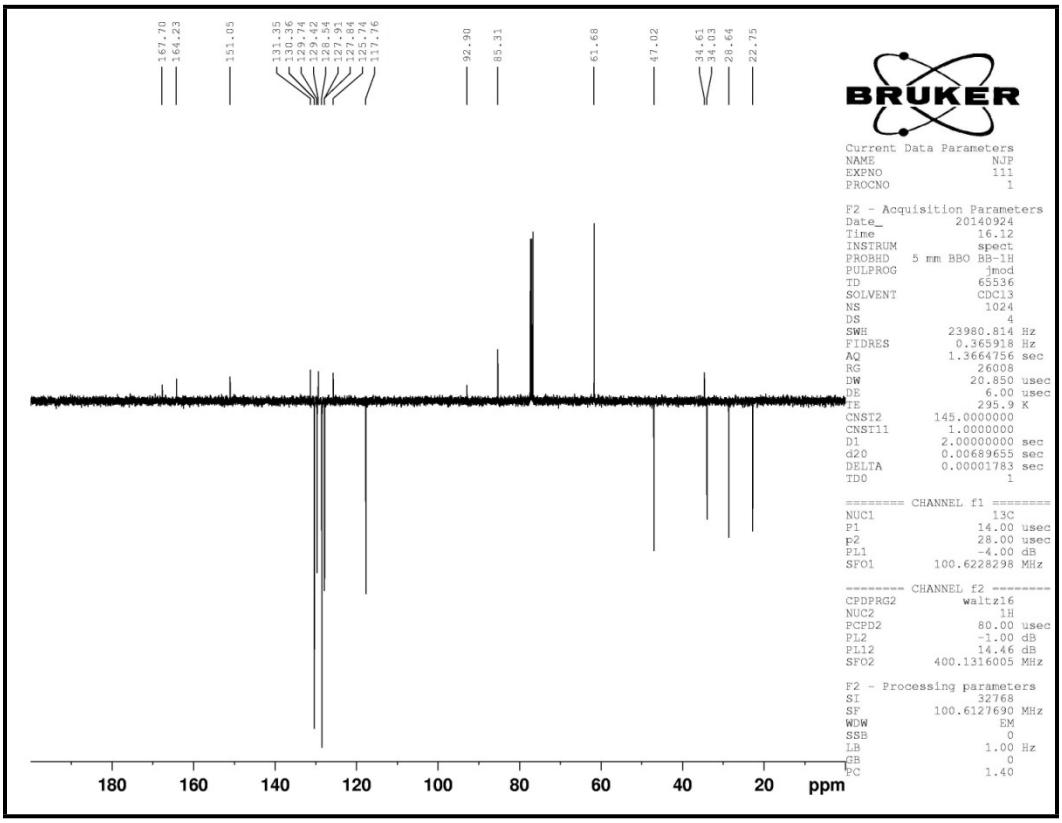
IR of compound (15a)



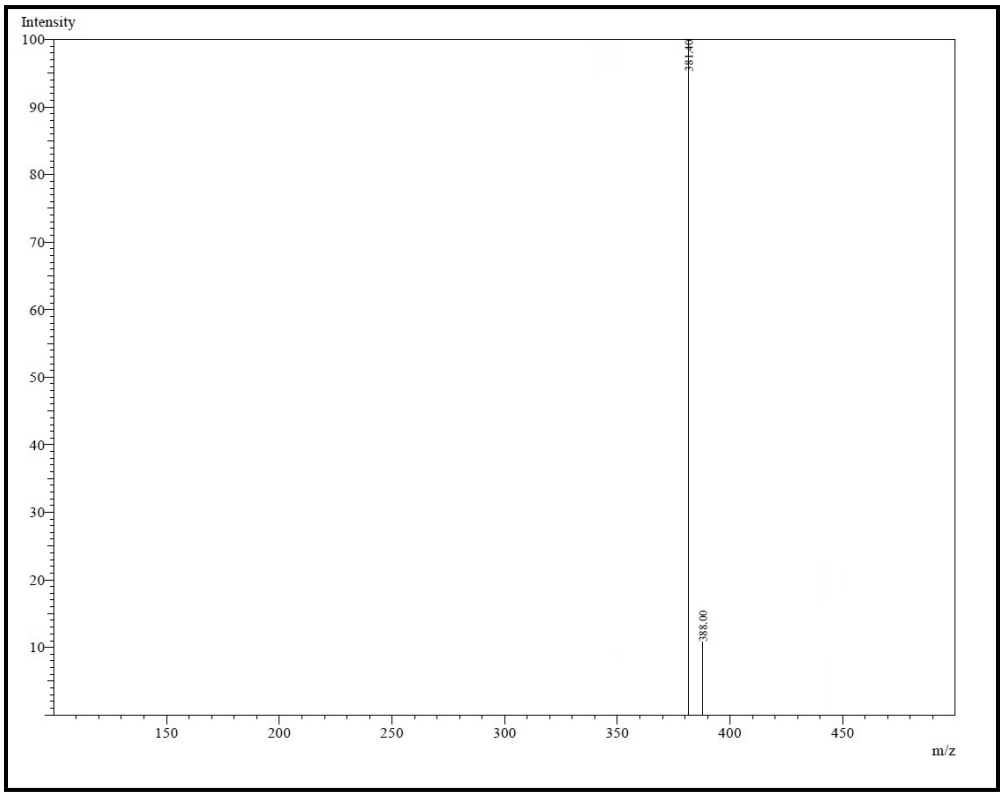
^{1}H NMR spectrum of compound (15b)



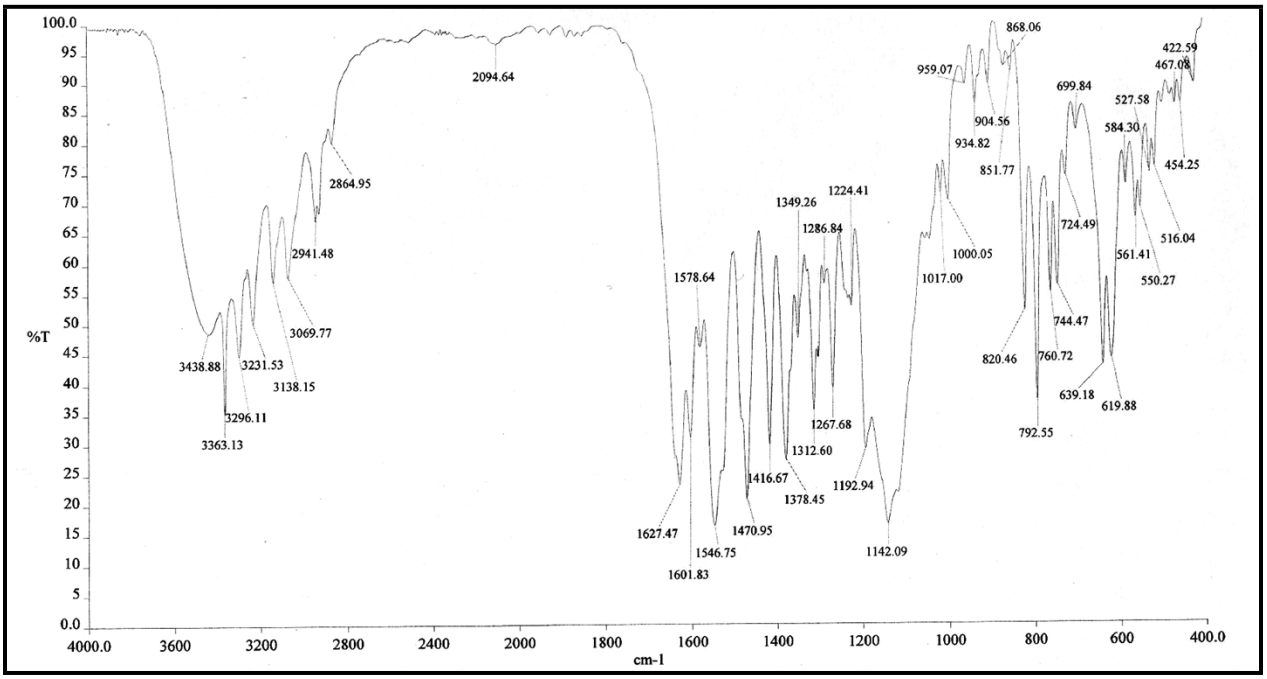
APT spectrum of compound (15b)



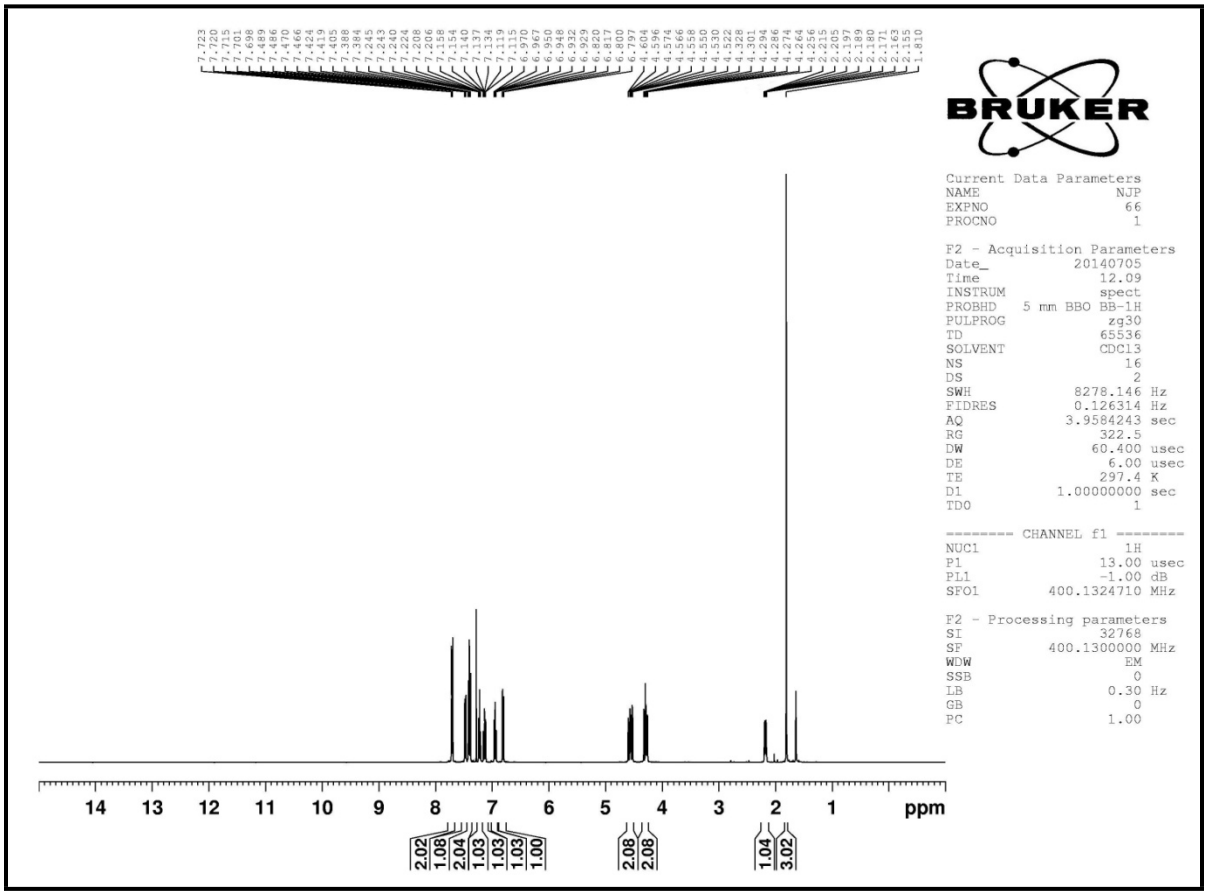
ESI–MS of compound (15b)



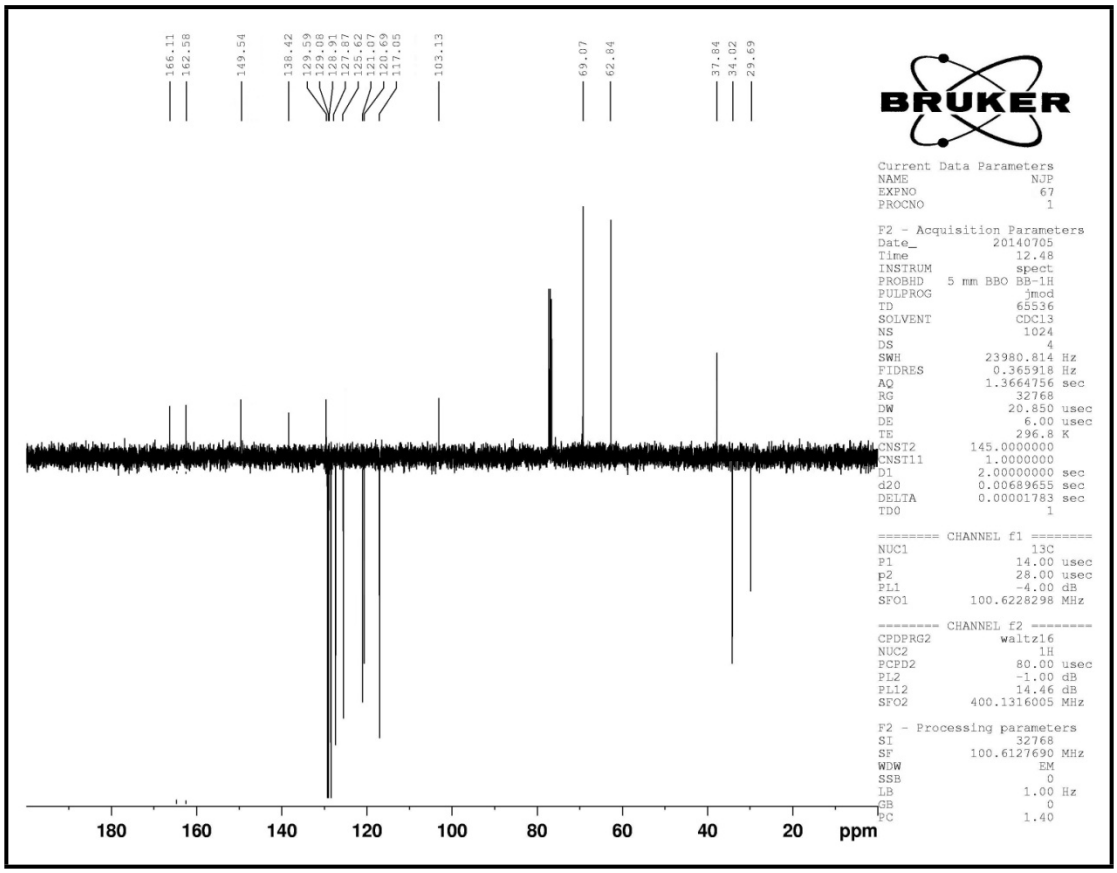
IR of compound (15b)



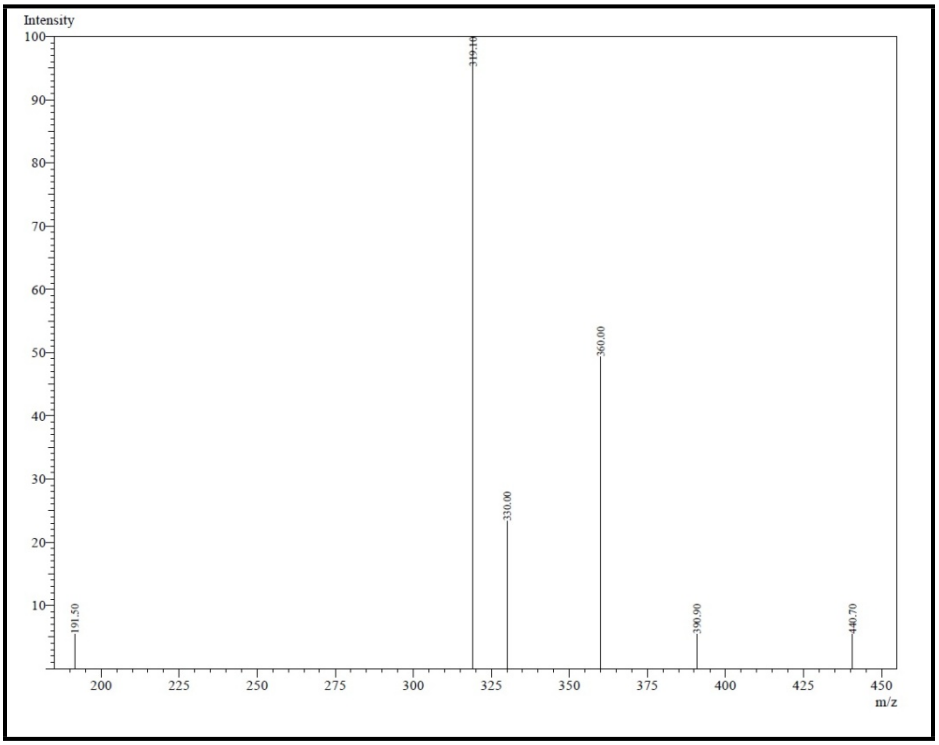
^{1}H NMR spectrum of compound (16a)



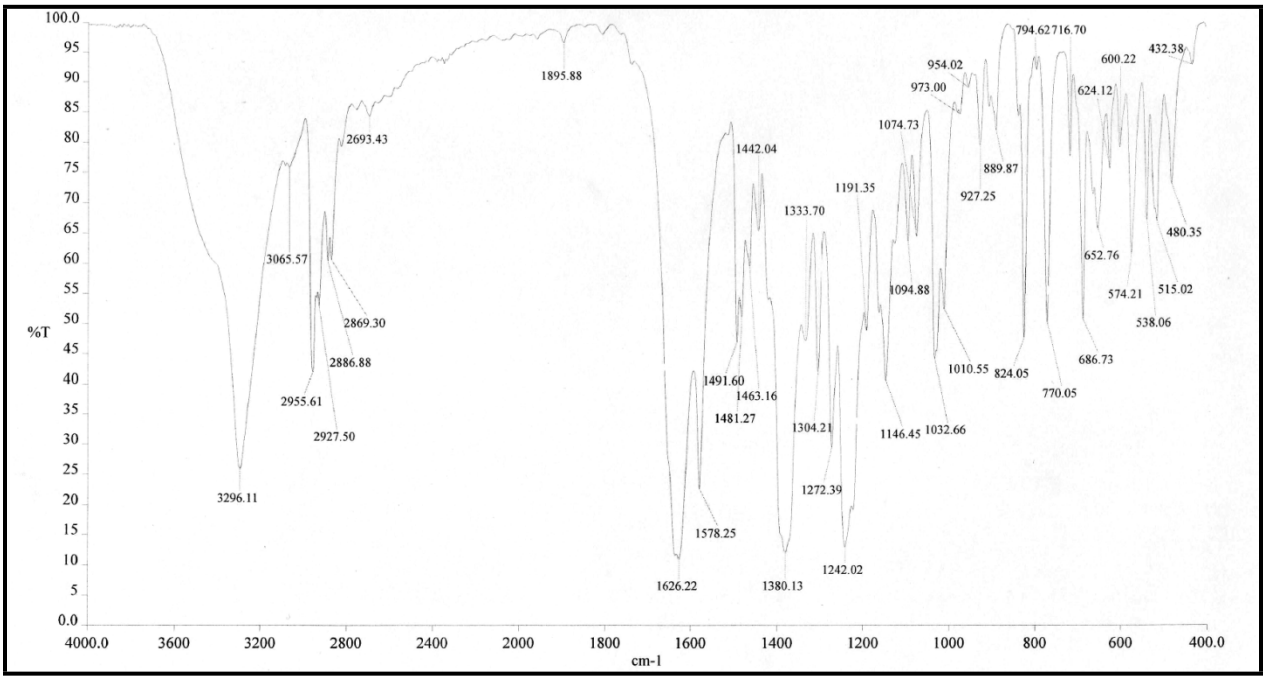
APT spectrum of compound (16a)



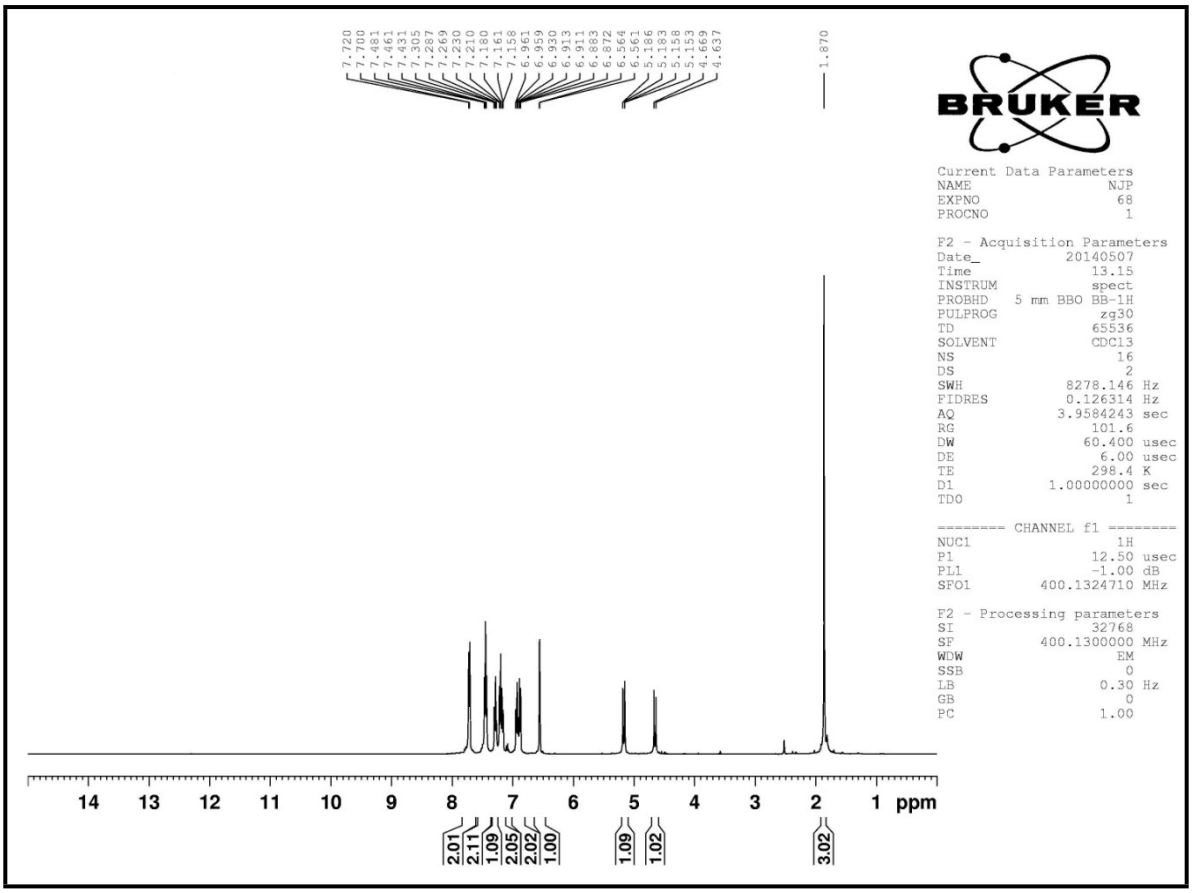
ESI–MS of compound (16a)



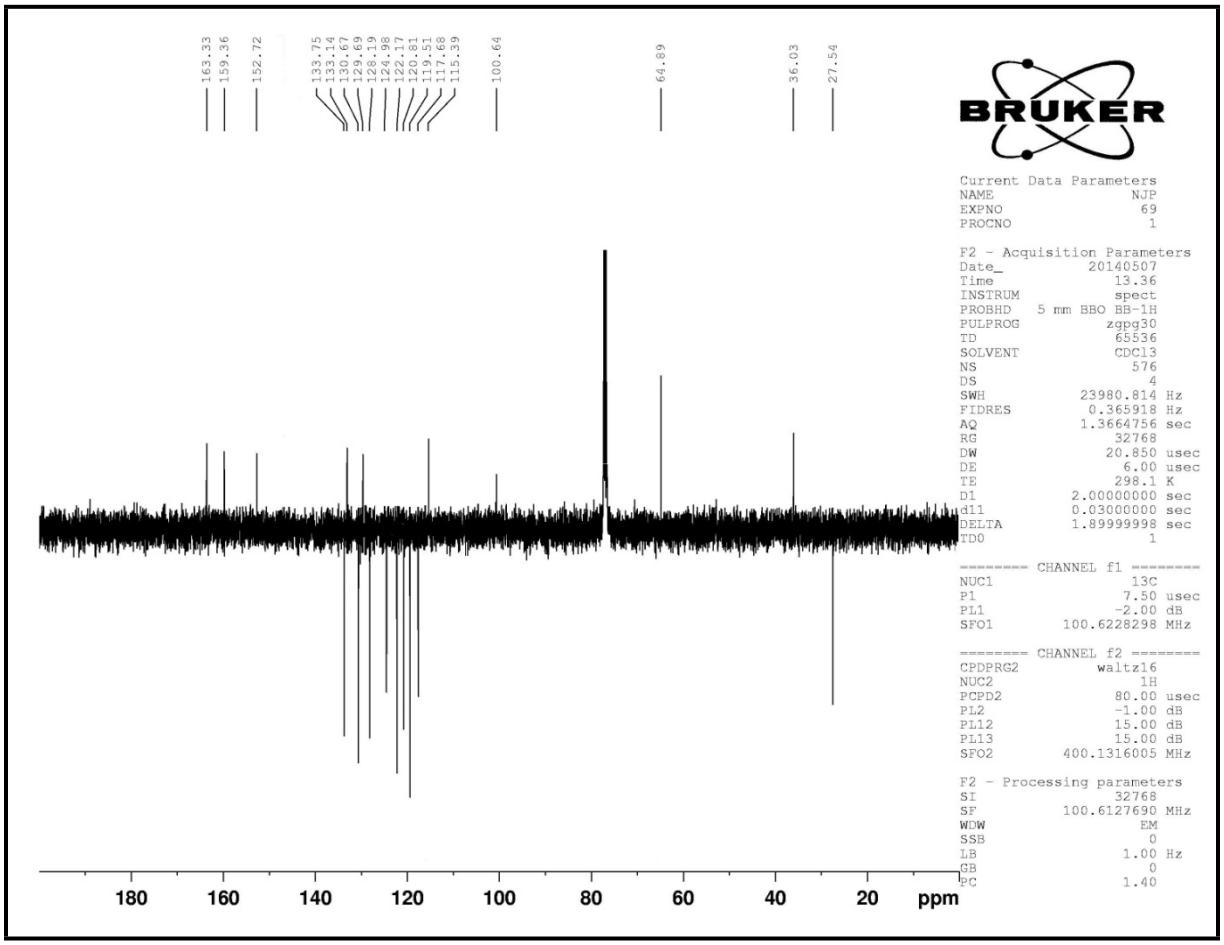
IR of compound (16a)



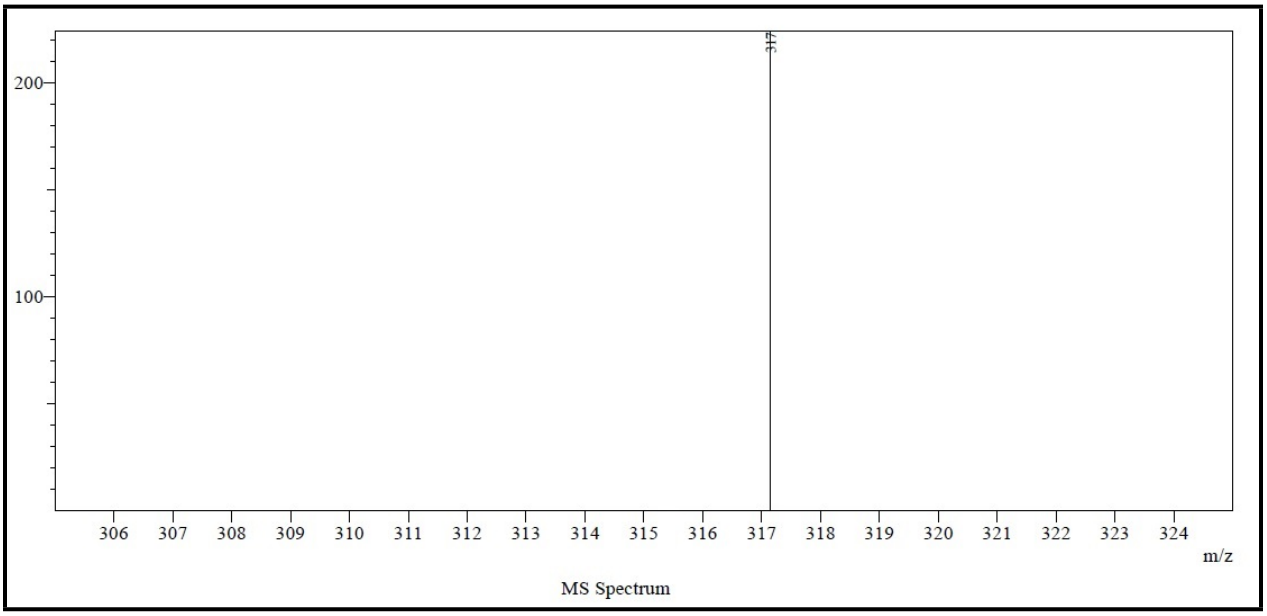
^{1}H NMR spectrum of compound (17a)



APT spectrum of compound (17a)



ESI–MS of compound (17a)



IR of compound (17a)