SUPPORTING INFORMATION

FOR

Triclorosilane-mediated stereoselective synthesis of β-amino esters and their conversion to highly enantiomerically enriched β-lactams.

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1.General. All reactions were carried out in oven-dried glassware with magnetic stirring under nitrogen atmosphere, unless otherwise stated. All commercially available reagents including dry solvents were used as received. Organic extracts were dried over sodium sulfate, filtered, and concentrated under vacuum using a rotatory evaporator. Nonvolatile materials were dried under high vacuum. Reactions were monitored by thin-layer chromatography on pre-coated Merck silica gel 60 F254 plates and visualized either by UV or by staining with a solution of cerium sulfate (1g) and ammonium heptamolybdate tetrahydrate (27 g) in water (469 mL) and concentrated sulfuric acid (31 mL). Flash chromatography was performed on Fluka silica gel 60. Proton NMR spectra were recorded on spectrometers operating at 200, 300 or 500 MHz respectively. Proton chemical shifts are reported in ppm (δ) with the solvent reference relative to tetramethylsilane (TMS) employed as the internal standard ($CDCl_3$ δ = 7.26 ppm). Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ = 77.0 ppm). Optical rotations were obtained on a polarimeter at 589 nm using a 5 mL cell with a length of 1 dm. HPLC for e.e. determination was performed under the conditions reported below. Mass spectra (MS) were performed on a hybrid quadrupole time of flight mass spectrometer equipped with an ESI ion source. Microwave-accelerated reactions were performed in CEM Discover class S instrument.

2. Synthesis of ß-keto esters and N-aryl ß-enamino esters

To a dried three-necked flask equipped with a dropping funnel, a condenser, and a magnetic stirrer was added NaH (700 mg, 95%, 28 mmol), dimethyl carbonate (1.8 g, 20 mL), and toluene (10 mL).

The mixture was heated to reflux. A solution of ketone (10 mmol) in toluene (5 mL) was added dropwise from the dropping funnel over 1-2 h. After the addition, the mixture was heated to reflux until the evolution of hydrogen ceased (15-20 min). When the reaction was cooled to room temperature, glacial acetic acid (3 mL) was added dropwise and a heavy, pasty solid appeared.

Ice-water was added until the solid was dissolved completely. The toluene layer was separated, and the water layer was washed with toluene (3×10 mL). The combined toluene solution was washed with water (10 mL) and brine (10 mL), then dried over Na_2SO_4. After evaporation of the solvent, the mixture was distilled under reduced pressure or subjected chromatography to give the desired.[20]

N-aryl ß-enamino esters

A mixture of *β*-keto ester (10 mmol), arylamine (10 mmol) was dissolved in 10 mL of benzene and refluxed overnight with a Dean Stark apparatus in the presence of molecular sieves (3 Å). After the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure. The crude product was purified on silica flash.

(Z)-methyl 3-(benzylamino)-3-phenylacrylate (3):

Yield: 40% This product was purified with a 9:1 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (200MHz, $CDCl_3$): δ 3.69 (s, 3H); δ 4.27 (d, 2H); δ 4.69 (s, 1H); δ 7.15-7.38 (m, 10H); δ 8.91 (br, 1H).

(*R*,Z)-methyl 3-phenyl-3-(1-phenylethylamino)acrylate (5):

Yield: 46% This product was purified with a 98:2 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.51 (d, 3H); δ 3.74 (s, 3H); δ 4.50 (q, 1H); δ 4.70 (s, 1H); δ 7.12-7.40 (m, 10H); δ 9.20 (br, 1H).

(Z)-methyl 3-(benzylamino)-3-(4-(trifluoromethyl)phenyl)acrylate (7):

Yield: 81% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 3.70 (s, 3H); δ 4.23 (d, 2H); δ 4.69 (s, 1H); δ 7.15 (d, 2H); δ 7.21-7.32 (m, 3H); δ 7.44 (d, 2H); δ 7.64 (d, 2H); δ 8.90 (br, 1H).

(*R*,Z)-methyl 3-(1-phenylethylamino)-3-(4-(trifluoromethyl)phenyl)acrylate (9):

Yield: 81% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.45 (d, 3H); 3.70 (s, 3H); δ 4.33 (q, 1H); δ 4.69 (s, 1H); δ 7.15 (d, 2H); δ 7.21-7.32 (m, 5H); δ 7.64 (d, 2H); δ 9.0 (br, 1H).

(Z)-methyl 3-(benzylimino)-3-(4-methoxyphenyl)propanoate (11):

Yield: 35% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 3.68 (s, 3H); δ 3.82 (s, 3H); δ 4.31 (d, 2H); δ 4.68 (s, 1H); δ 6.82 (d, 2H); δ 7.21-7.31 (m, 7H).

(*R*,Z)-methyl 3-(4-methoxyphenyl)-3-(1-phenylethylamino)acrylate (13):

Yield: 35% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.47 (d, 3H); δ 3.71 (s, 3H); δ 3.81 (s, 3H); δ 4.49 (q, 1H); δ 4.63 (s, 1H); δ 6.82 (d, 2H); δ 7.09-7.30 (m, 7H); δ 8.91 (br, 1H).

(Z)-methyl 3-(benzylimino)-3-(naphthalen-2-yl)propanoate (15):

Yield: 45% This product was purified with a 9:1 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 3.7 (s, 3H); δ 4.32 (d, 2H); δ 4.72 (s, 1H); δ 7.2-7.3 (m, 5H); δ 7.45-7.55 (m, 3H); δ 7.8-7.9 (m, 4H); δ 9 (br, 1H).

(*R*,Z)-methyl 3-(naphthalen-1-yl)-3-(1-phenylethylamino)acrylate (17):

Yield: 45% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): **E**: δ 1.40 (d, 3H); δ 3.74 (s, 3H); δ 4.00 (q, 1H); δ 4.68 (s, 1H); δ 6.83-8.15 (m, 12H); δ 9.24 (br, 1H).
Z: δ 1.49 (d, 3H); δ 3.75 (s, 3H); δ 4.50 (q, 1H); δ 4.76 (s, 1H); δ 6.83-8.15 (m, 12H); δ 9 (br, 1H).

(Z)-methyl 3-(benzylamino)pent-2-enoate (23)

Yield: 80% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.11 (t, 3H); δ 2.22 (q, 2H); δ 3.61 (s, 3H); δ 4.43 (d, 2H); δ 4.57 (s, 1H); δ 7.24-7.35 (m, 5H); δ 8.96 (br, 1H).

(Z)-methyl 3-(benzylimino)-4-phenylbutanoate (25)

Yield: 80% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 3.53 (s, 2H); δ 3.66 (s, 3H); δ 4.29 (d, 2H); δ 4.56 (s, 1H); δ 7.19-7.33 (m, 10H); δ 9.0 (br, 1H).

(*R*,Z)-methyl 4-phenyl-3-(1-phenylethylimino)butanoate (27)
Yield: 70% This product was purified with a 99:1hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.40 (d, 3H); δ 3.38 (q, 2H); δ 3.68 (s, 3H); δ 4.48 (m, 2H); δ 7.17-7.40 (m, 10H); δ 9.0 (b, 1H).

(Z)-methyl 3-(benzylamino)-4-methylpent-2-enoate (29)
Yield: 71% The product was purified by fractional distillation at P = 1 mbar the desired product at about 100 °C.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.11 (d, 6H); δ 2.66 (m, 1H); δ 3.63 (s, 3H); δ 4.45 (d, 2H); δ 4.61 (s, 1H); δ 7.26-7.38 (m, 5H); δ 9.05 (br, 1H).

(*R*,Z)-methyl 4-methyl-3-(1-phenylethylamino)pent-2-enoate (31):
Yield: 80% The product was purified by fractional distillation at P = 1 mbar the desired product at about 100 °C.
^{1}H-NMR (300MHz, $CDCl_3$): δ 0.80 (d, 3H); δ 1.12 (d, 3H); δ 1.52 (d, 3H); δ 2.55 (m, 1H); δ 3.66 (s, 3H); δ 4.56 (s, 1H); δ 4.72 (q, 1H); δ 7.23-7.36 (m, 5H); δ 9.15 (br, 1H).

(Z)-tert-butyl 3-(benzylamino)-3-phenylacrylate (33):
Yield: 30% This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.55 (s, 9H); δ 4.30 (d, 2H); δ 4.60 (s, 1H); δ 7.15-7.40 (m, 10H); δ 8.80 (br, 1H).

3. Reduction reaction. *General procedure*: To a stirred solution of catalyst (0.1-0.01% mol/eq mmol) in the chosen solvent (2 mL), the imine (1 mmol/eq) was added. The mixture was then cooled to the chosen temperature and trichlorosilane (3.5 mmol/eq) was added dropwise by means of a syringe. After stirring at the proper temperature, the reaction was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (1 mL). The mixture was allowed to warm up to room temperature and water (2 mL) and dichloromethane (5 mL) were added. The organic phase was separated and the combined organic phases were dried over Na_2SO_4, filtered, and concentrated under vacuum at room temperature to afford the crude product. If necessary, the amine was purified by flash chromatography.

(*R*)-methyl 3-(benzylamino)-3-phenylpropanoate (4)[21]
This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (200MHz, $CDCl_3$): δ 2.65 (dd, 1H); δ 2.80 (dd, 1H); δ 3.53 (d, 1H); δ 3.62 (s, 3H); δ 3.69 (d, 2H); δ 4.12 (m, 1H); δ 7.25-7.36 (m, 10H).
The enantiomeric excess was determined by HPLC on a Chiralcel OD (96:4 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 210 nm): t_R = 13.99 min, t_S = 25.18 min.

(*R*)-methyl 3-phenyl-3-((*R*)-1-phenylethylamino)propanoate (6)
This product was purified with a 95:5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): (*R*,*R*): δ 1.31 (d, 3H); δ 2.00 (br, 1H); δ 2.53-2.80 (m, 2H); δ 3.50 (q, 1H); δ 3.61 (s, 3H); δ 3.84 (m, 1H); δ 7.18-7.37 (m, 10H).
(*R*,*S*): δ 1.35 (d, 3H); δ 2.53-2.80 (m, 2H); δ 3.61 (s, 3H); δ 3.68 (q, 1H); δ 4.21 (m, 1H); δ 7.18-7.37 (m, 10H).

^{13}C NMR (75 MHz,$CDCl_3$): δ 24.56 (1C); 42.49 (1C), 51.54 (1C), 55.25 (1C); 56.70 (1C), 126.95 (2C), 127.36 (2C), 127.71 (2C), 128.49 (2C), 128.64 (2C), 139.49 (1C); 146.4 (1C); 171.75 (1C).
IR: 3691 cm^{-1} (N-H); 1732 cm^{-1} (C=O).
$[\alpha]^{25}_D$ = + 61.4 (*c* = 0.32 g/100 mL, DCM, λ = 589 nm).

(*R*)-methyl 3-(benzylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (8)

^{1}H-NMR (300MHz, $CDCl_3$): δ 2.01 (br, 1H); δ 2.61 (dd, 1H); δ 2.72 (dd, 1H); δ 3.53 (d, 1H); δ 3.64 (s, 3H); δ 3.64 (d, 1H); δ 4.19 (m, 1H); δ 7.22-7.33 (m, 5H); δ 7.50 (d, 2H); δ 7.62 (d, 2H).
^{13}C NMR (75 MHz,$CDCl_3$):δ 42.44 (1C), 51.28 (1C), 51.73 (1C); 58.41 (1C), 125.63 (2C), 127.17 (2C), 127.90 (2C), 128.02 (2C), 128.59 (1C), 128.15 (1C, quartetto); 129.28 (1C, quartetto?), 139.49 (1C); 146.4 (1C); 171.69 (1C).
The enantiomeric excess was determined by HPLC on a Chiralcel OD-H (9:1 hexane/isopropanol; flow rate: 0.5 mL/min; λ = 220 nm): t_R = 12.11 min, t_S = 13.46 min.

$[\alpha]^{25}_D$ = + 38.8 (*c* = 1.08 g/100 mL, DCM, λ = 589 nm).

(*R*)-methyl 3-((*R*)-1-phenylethylamino)-3-(4-(trifluoromethyl)phenyl)propanoate Metil 3-(α-feniletilammino)-3-(4-trifluorometilfenil)propanoato (10)

This product was purified with a 98:2 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (75MHz, $CDCl_3$): δ 1.28 (d, 3H); δ 2.06 (br, 1H); δ 2.51 (dd, 1H); δ 2.64 (dd, 1H); δ 3.46 (q, 1H); δ 3.67 (s, 3H); δ 3.89 (m, 1H); δ 7.19 (d, 2H); δ 7.22-7.37 (m, 5H); δ 7.63 (d, 2H).
^{13}C NMR (75 MHz,$CDCl_3$): δ 24.56 (1C); 42.49 (1C), 51.54 (1C), 55.25 (1C); 56.70 (1C), 126.9 (2C), 127.36 (2C), 127.71 (2C), 127.8 (1C, q); 128.49 (2C), 128.54 (1C), 128.73 (1C, q), 144 (1C); 146.2 (1C); 171.75 (1C).

$[\alpha]^{25}_D$ = + 36.6 (*c* = 0.348 g/100 mL, DCM, λ = 589 nm).

(*R*)-methyl 3-(benzylamino)-3-(4-methoxyphenyl)propanoate (12)

This product was purified with a 97:3 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (75MHz, $CDCl_3$): δ 1.28 (d, 3H); δ 2.06 (br, 1H); δ 2.51 (dd, 1H); δ 2.64 (dd, 1H); δ 3.43-3.63 (q, 2H); δ 3.62 (s, 3H); δ 3.85 (s, 3H); δ 4.01 (m, 1H); δ 6.90 (d, 2H); δ 7.26-7.35 (m, 5H).
^{13}C NMR (75 MHz,$CDCl_3$): δ 29.69 (1C); 42.67 (1C), 51.03 (1C), 55.25 (1C); 58.05 (1C), 114.00 (2C), 127.00 (2C), 128.36 (3C), 128.75 (2C), 133.91 (1C); 140.00 (1C); 155.00 (1C), 172.26 (1C).
The enantiomeric excess was determined by HPLC on a Chiralpak AD (9:1 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 230 nm): t_R = 8.74 min, t_S = 9.28 min.

$[\alpha]^{25}_D$ = + 32.4 (*c* = 0.4 g/100 mL, DCM, λ = 589 nm).

(*R*)-methyl 3-(4-methoxyphenyl)-3-((*R*)-1-phenylethylamino)propanoate (14)

This product was purified with a 9:1 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.30 (d, 3H); δ 2.10 (br, 1H); δ 2.55 (dd, 1H); δ 2.67 (dd, 1H); δ 3.52 (q, 1H); δ 3.65 (s, 3H); δ 3.77 (m, 1H); δ 3.85 (s, 3H); δ 6.89 (d, 2H); δ 7.14-7.38 (m, 7H).
^{13}C NMR (75 MHz,$CDCl_3$): δ 24.91 (1C); 43.01 (1C), 51.46 (1C), 54.89 (1C); 55.09 (1C), 55.93 (1C), 113.93 (2C), 127.17 (2C), 127.93 (3C), 127.99 (2C), 134.25 (1C); 144.83 (1C); 158.93 (1C); 172.07 (1C).

$[\alpha]^{25}_D$ = + 18.8 (*c* = 0.308 g/100 mL, DCM, λ = 589 nm).

(*R*)-methyl 3-(benzylamino)-3-(naphthalen-2-yl)propanoate (16)

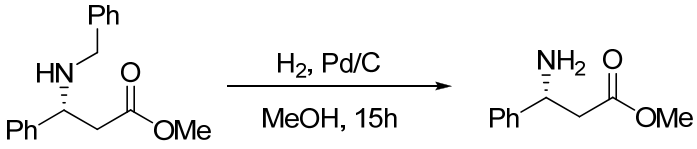
This product was purified with a 9:1 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 2.0 (br, 1H); δ 2.62 (dd, 1H); δ 2.75 (dd, 1H); δ 3.62 (q, 2H); δ 3.62 (s, 3H); δ 4.3 (m, 1H); δ 7.2 (m, 5H); δ 7.5 (m, 3H); δ 7.84 (m, 4H).
The enantiomeric excess was determined by HPLC on a Chiralpak AD (9:1 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 230 nm): t_S = 9 min, t_R = 9.8 min.
^{13}C NMR (75 MHz,$CDCl_3$): δ 42.8 (1C), 51.3 (1C), 51.6 (1C); 60.7 (1C), 126.1 (1C), 126.3 (1C), 126.9 (1C), 127.7 (2C), 127.9 (1C), 128.2 (1C), 128.4 (1C), 128.5 (2C), 129.7 (2C), 133.1 (1C), 133.5 (1C); 139.8 (1C); 140.2 (1C); 172.2 (1C).
$[\alpha]^{25}_D$ = + 30.69 (*c* = 0.216 g/100 mL, EtOH, λ = 589 nm).

(*R*)-methyl 3-(naphthalen-2-yl)-3-((*R*)-1-phenylethylamino)propanoate (18)
This product was purified with a 85:15 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 1.29 (d, 3H); δ 2.10 (br, 1H); δ 2.62 (dd, 1H); δ 2.75 (dd, 1H); δ 3.50 (q, 1H); δ 3.62 (s, 3H); δ 4.00 (m, 1H); δ 7.18-7.70 (m, 9H); δ 7.79-7.85 (m, 3H).
^{13}C NMR (75 MHz,$CDCl_3$): δ 24,6 (1C), 42.4 (1C), 51.6 (1C), 55.1 (1C); 56.7 (1C), 125.9 (1C), 126.1 (1C), 126.5 (1C), 126.9 (1C), 127.2 (1C), 127.4 (1C), 127.8 (1C), 128.1 (2C), 128.2 (2C), 128.5 (1C), 133.0 (1C), 133.3 (1C); 138.8 (1C); 144 (1C); 171.9 (1C).
$[\alpha]^{25}_D$ = +39.0 (*c* = 0.228 g/100 mL, DCM, λ = 589 nm).
(*S*)-methyl 2-((*R*)-1-phenylethylamino)pentanoate (24)
This product was purified with a 95: 5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 0.95 (t, 3H); δ 1.40-1.59 (m, 2H); δ 1.64 (br, 1H); δ 2.45 (d, 2H); δ 2.99 (q, 1H); δ 3.68 (s, 3H); δ 3.78 (s, 2H); δ 7.21-7.33 (m, 5H).
^{13}C NMR (75 MHz,$CDCl_3$): δ 9.91 (1C); 26.76 (1C), 38.62 (1C), 50.92 (1C), 51.5 (1C); 55.49 (1C), 126.9 (1C); 127.33 (1C), 128.81 (2C); 129.05 (1C); 140.44 (1C); 173.07 (1C)
The enantiomeric excess was determined by HPLC on a Chiralcel OD (99:1 hexane/isopropanol; flow rate: 0.5 mL/min; λ = 210 nm): t_S = 12.53 min, t_R= 16.16 min.
$[\alpha]^{25}_D$ = +36.0 (*c* = 1.6 g/100 mL, DCM, λ = 589 nm).
(*S*)-methyl 3-(benzylamino)-4-phenylbutanoate (26)
This product was purified with a 95: 5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 2.45 (d, 2H); δ 2.75 (dd, 1H); δ 2.9 (dd, 1H); δ 3.35 (m, 1H); δ 3.65 (s, 3H); δ 3.88 (s, 2H); δ 7.10-7.33 (m, 10H).
The enantiomeric excess was determined by HPLC on a Chiralpak AD (99:1 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 210 nm): t_S = 13.90 min, t_R= 15.47 min.
(*S*)-methyl 4-phenyl-3-((*R*)-1-phenylethylamino)butanoate (28)
This product was purified with a 95: 5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): (*R*,*S*): δ 1.27 (d, 3H); δ 2.00 (br, 1H); δ 2.23-2.28 (m, 2H); 2.68 (m, 1H); 2.92 (m, 2H); δ 3.59 (s, 3H); δ 4 (q, 1H); δ 7.04-7.33 (m, 10H).
(*R*,*R*): δ 1.32 (d, 3H); δ 2.23-2.28 (m, 2H); 2.68 (m, 1H); 2.92 (m, 2H); δ 3.66 (s, 3H); δ 3.85 (q, 1H); δ 7.04-7.33 (m, 10H).
^{13}C NMR (75 MHz,$CDCl_3$): δ 24.57 (1C), 38.84 (1C), 39.16 (1C), 51.40 (1C), 53.33 (1C); 55.18 (1C), 126.32 (1C); 126.44 (1C), 126.81 (2C); 128.75 (3C); 129.36 (3C); 138.20 (1C); 144.64 (1C); 172.69 (1C).
(*R*)-methyl 3-(benzylamino)-4-methylpentanoate (30)
This product was purified with a 95: 5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): δ 0.95 (t, 6H); δ 1.56 (br, 1H); δ 1.93 (m, 1H); δ 2.39 (dd, 1H); δ 2.49 (dd, 1H); δ 2.94 (m, 1H); δ 3.70 (s, 3H); δ 3.82 (s, 2H); δ 7.26-7.36 (m, 5H).
^{13}C NMR (75 MHz,$CDCl_3$): δ 17.6 (1C), 18.8 (1C), 26.76 (1C), 29.7 (1C), 36 (1C), 51.5 (2C); 59.6 (1C), 125 (1C), 128.3 (2C); 129.0 (2C); 140.1 (1C); 173.6 (1C)
The enantiomeric excess was determined by HPLC on a Chiralcel OD (99:1 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 210 nm): t_R= 9.13 min, t_S= 9.72 min.
$[\alpha]^{25}_D$ = +42.0 (*c* = 0.45 g/100 mL, DCM, λ = 589 nm).
(*R*)-methyl 2-methyl-3-((*R*)-1-phenylethylamino)pentanoate (32)
This product was purified with a 95: 5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (300MHz, $CDCl_3$): (*R*,*R*): δ 0.81 (d, 3H); δ 1.28 (d, 3H) δ 1.92 (m, 1H); δ 2.17 (dd, 1H); δ 2.30 (dd, 1H); δ 2.74 (q, 1H); δ 3.60 (s, 3H); δ 3.85 (m, 1H); δ 7.21-7.32 (m, 5H).
(*R*,*S*): δ 0.81 (d, 3H); δ 1.28 (dd, 6H); δ 1.66 (m, 1H); δ 2.35 (dd, 1H); δ 2.45 (dd, 1H); δ 2.65 (q, 1H); δ 3.68 (s, 3H); δ 3.85 (m, 1H); δ 7.21-7.32 (m, 5H)
^{13}C NMR (75 MHz,$CDCl_3$): δ 16.39 (1C), 18.98 (1C), 24.86 (1C), 29.01 (1C), 29.39 (1C), 35.76 (1C), 54.89 (1C), 56.72 (1C), 126.71 (1C), 126.80 (2C); 129.0 (2C); 145.8 (1C); 173.6 (1C)
$[\alpha]^{25}_D$ = + 26.1 (*c* = 0.322 g/100 mL, DCM, λ = 589 nm).
tert-butyl 3-(benzylamino)-3-phenylpropanoate (34)[23]

This product was purified with a 95: 5 hexane/ethyl acetate mixture as eluent.
^{1}H-NMR (200MHz, $CDCl_3$): δ 1.35 (s, 9H); δ 2.60 (m, 2H); δ 3.55 (dd, 2H); δ 4.10 (m, 1H); δ 7.27 (m, 10H).
The enantiomeric excess was determined by HPLC on a Chiralcel OD-H (96:4 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 220 nm): t_R= 6.69 min, t_S= 7.5 min.

4. Hydrogenolysis procedure and Synthesis of azetidin-2-ones.

Synthesis of (*R*)-methyl 3-amino-3-phenylpropanoate[24] (19)



A suspension of (*R*)-methyl 3-(benzylamino)-3-phenylpropanoate (**4a**) (0.58 mmol) and Pd/C (10%, 36 mg) in methanol (3.5 mL) were stirred in under hydrogen atmosphere at room temperature for 16 h. The catalyst was removed by filtration through a pad of celite, and the filtrate was concentrated and purified by column chromatography (5:5 hexane/ethyl acetate 100 mL, 4:6 hexane/ethyl acetate 100 mL, 3:7 hexane/ethyl acetate 100 mL mixture as eluent).

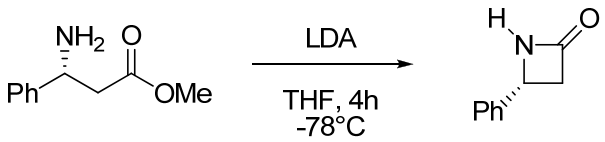
Yield = 98%

^{1}H-NMR (300MHz, $CDCl_3$): δ 2.31 (br, 2H); δ 2.67 (d, 2H); δ 3.66 (s, 3H); δ 4.42 (t, 1H); δ 7.21-7.38 (m, 5H).

The enantiomeric excess was determined by HPLC on a Chiralcel OD-H (98:2 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 210 nm): t_R= 26.04 min, t_S= 32.44 min

$[\alpha]^{25}_D$ = + 10.5 (*c* = 0.258 g/100 mL, DCM, λ = 589 nm).

Synthesis of (*R*)-4-phenylazetidin-2-one[25] (35)



To a solution of LDA (0.676 mmol) in THF (3 mL) at -78°C was added a THF (1 mL) solution of (*R*)-methyl 3-amino-3-phenylpropanoate (**19**). Stirring was continued at -78°C for 16 h after which the reaction was quenched with $NaHCO_3$ aq, and then extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and

concentrated. The residue was purified by column chromatography (7:3 hexane/ethyl acetate 100 mL, 5:5 hexane/ethyl acetate 100 mL mixture as eluent).

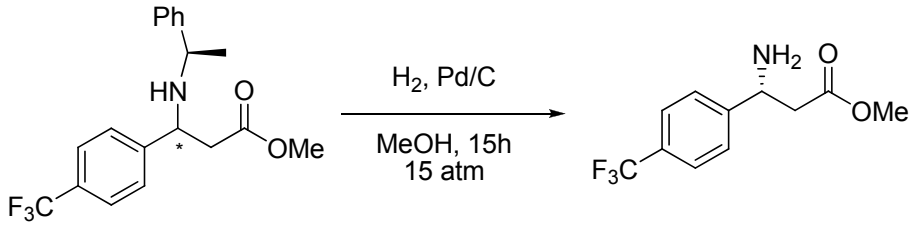
Yield = 84%

$[\alpha]^{25}_{D}$ = + 106 (*c* = 0.02 g/100 mL, EtOH, λ = 589 nm).

^{1}H-NMR (300MHz, $CDCl_3$): δ 2.87 (dd, 1H); δ 3.44 (dd, 1H); δ 4.71 (dd, 1H); δ 6.30 (br, 1H); δ 7.30-7.43 (m, 5H).

GLC (β–cyclodextrin column, Isotherm 150°C): t_R = 66.0 min,t_S= 74.0 min

Synthesis of (*R*)-methyl 3-amino-3-(4-(trifluoromethyl)phenyl)propanoate (20)



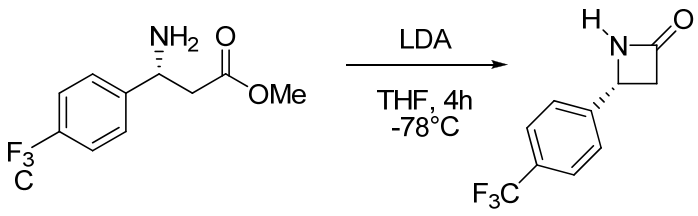
The deprotection of *N*-α-methyl benzyl amine **10a** required more drastic conditions and it was successfully performed by hydrogenating the starting material for 16 hours in methanol with Pd/C at 15 atm.

Yield = 98%

^{1}H-NMR (200MHz, $CDCl_3$): δ 2.43 (br, 2H); δ 2.72 (d, 2H); δ 3.68 (s, 3H); δ 4.52 (t, 1H); δ 7.51 (d, 2H) ; δ 7.60 (d, 2H).

The enantiomeric excess was determined by HPLC on a Chiralpak AD (9:1 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 210 nm): t_S= 9.7 min, t_R= 10.5 min

Synthesis of (*R*)-4-(4-(trifluoromethyl)phenyl)azetidin-2-one (35)



The synthesis of **36** was identical to that reported for compound **35**.

Yield = 80%

^{1}H-NMR (125 MHz, $CDCl_3$): δ 2.87 (dd, 1H); δ 3.44 (dd, 1H); δ 4.81 (dd, 1H); δ 6.50 (br, 1H); δ 7.5 (d, 1H); δ 7.55 (d, 1H).

^{13}C NMR (125 MHz, $CDCl_3$):δ 47.46 (1C); 49.91 (1C); 125.00 (q, 1C); 126.00 (2C); 126.55 (2C); 130.44 (q, 1C); 144.27 (1C); 167.62 (1C).

^{19}F-NMR (75 MHz, $CDCl_3$): δ –63.46 (1 F).

The enantiomeric excess was determined by HPLC on a Chiralpak IB (9:1 hexane/isopropanol; flow rate: 0.8 mL/min; λ = 225 nm): t_R= 16.13 min, t_S= 20.8.

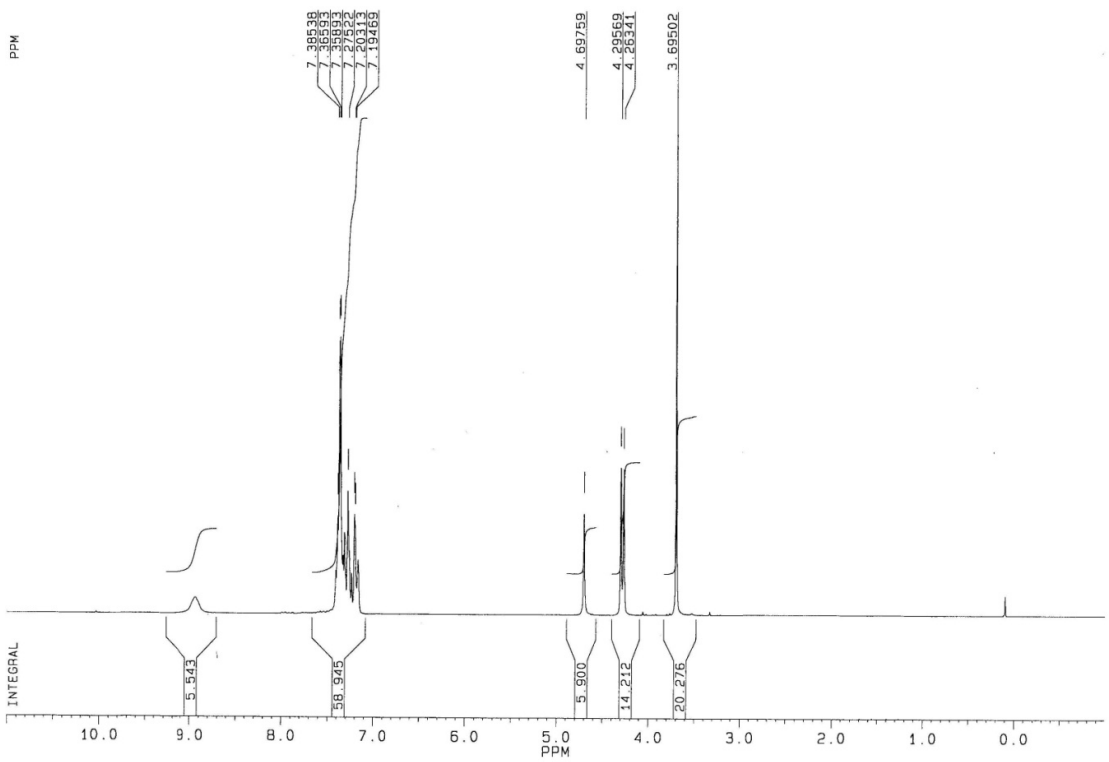
$[\alpha]^{25}_D$ = + 61 (*c* = 0.2 g/100 mL, DCM, λ = 589 nm).

Finally, by following the same synthetic procedure β–amino ester **21**[26] and **22**[27] were reduced by hydrogenation and the corresponding amines were isolated in quantitative yield.

References

20. For the synthesis of ketoesters see ref.13 in the text.
21. Murahashi, S.I.; Imada, Y.; Kawakami, T.; Harada, K.; Yonemushi, Y.; Tomita, N., *J. Am. Chem. Soc.* **2002**, *124*, 2888.
22. Gmeiner, P.; Hummel, E., *Synthesis* **1994**, *10*, 1026.
23. Doi, H.; Sakai, T.; Iguchi, M.; Yamada, K.; Tomioka, K., *J. Am. Chem. Soc.* **2003**, *125*, 2886.
24. Hata, S.; Iguchi, M.; Iwasawa, T.; Yamada, K.; Tomioka, K., *Org. Lett.* **2004**, *11*, 1721.
25. Stephen G. Davies, S. G.; Walters, I. A. S. *J. Chem. Soc., Perkin Trans. 1*, **1994**, 1129.
26. Hsiao, Y.; Rivera, N. R.; Rosner, T., Krska, S. W., Njolito, E.; Wang, F.; Sun, Y.; Armstrong, J. D. III; Grabowski, E. J. J.; Tillyer, R. D. *J.;* Spindler, F.; Malan, C. *J. Am. Chem. Soc.* **2004**, *126*, 9918.
27. Ikemoto, N.; Tellers, D. M.; Dreher, S. D.; Liu, J.; Huang, A.; Rivera N. R., Njolito E; Hsiao, Y; McWilliams, J. C.; Williams J. M.; Armstrong, J. D. III; Sun, Y.; Mathre, D. J.; Grabowski, E. J. J., Tillyer, R. D., *J. Am. Chem. Soc.* **2004**, *10*, 3048.

3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4.26341
3.69502
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5.543
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5.900
14.212
20.276
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7.0
6.0
5.0
4.0
3.0
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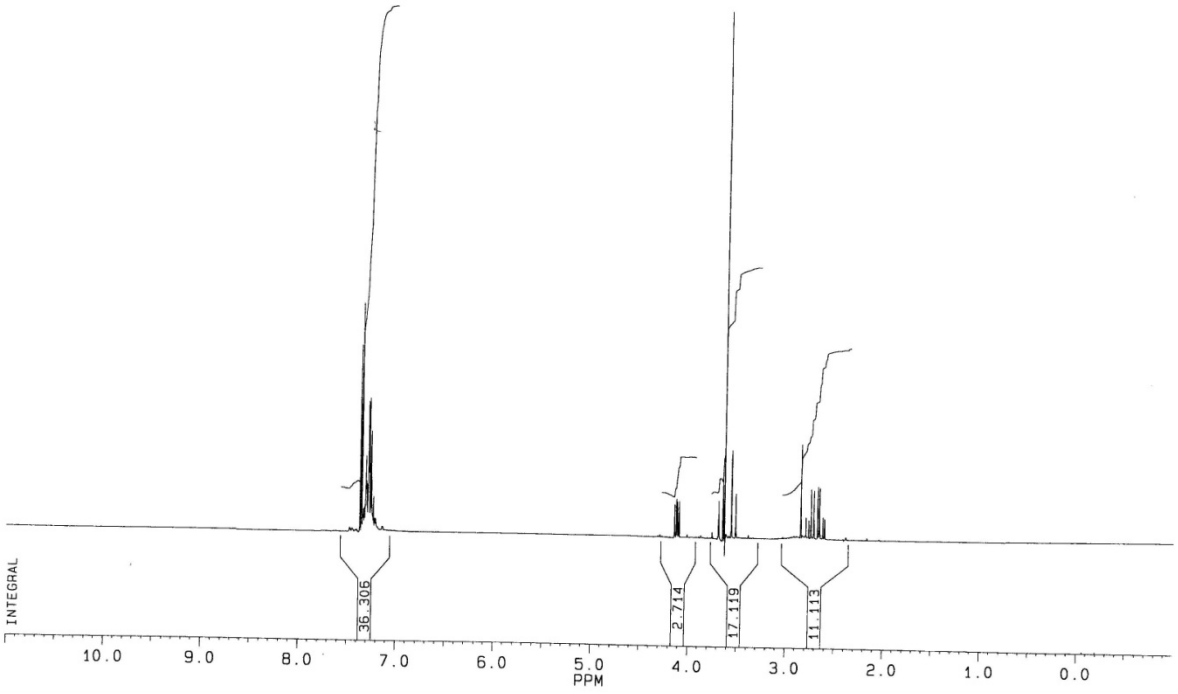
0.0
PPM

4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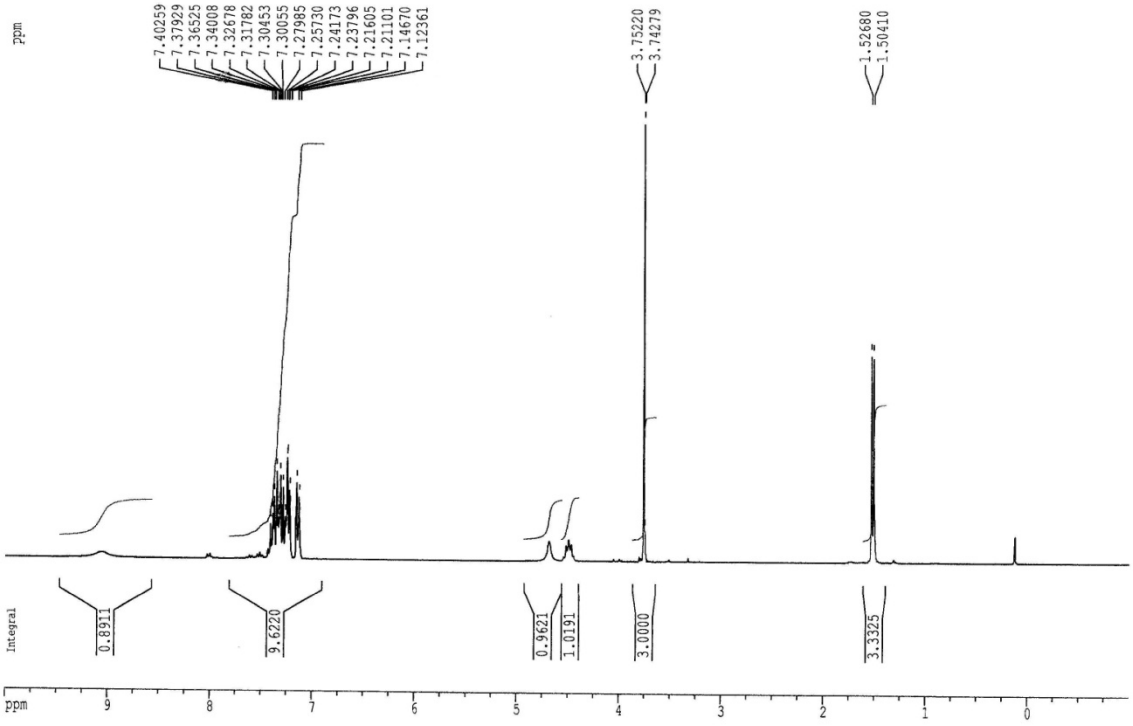
2.0
1.0
0.0
PPM

5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7.21605
7.21101
7.14670
7.12361
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3.0000
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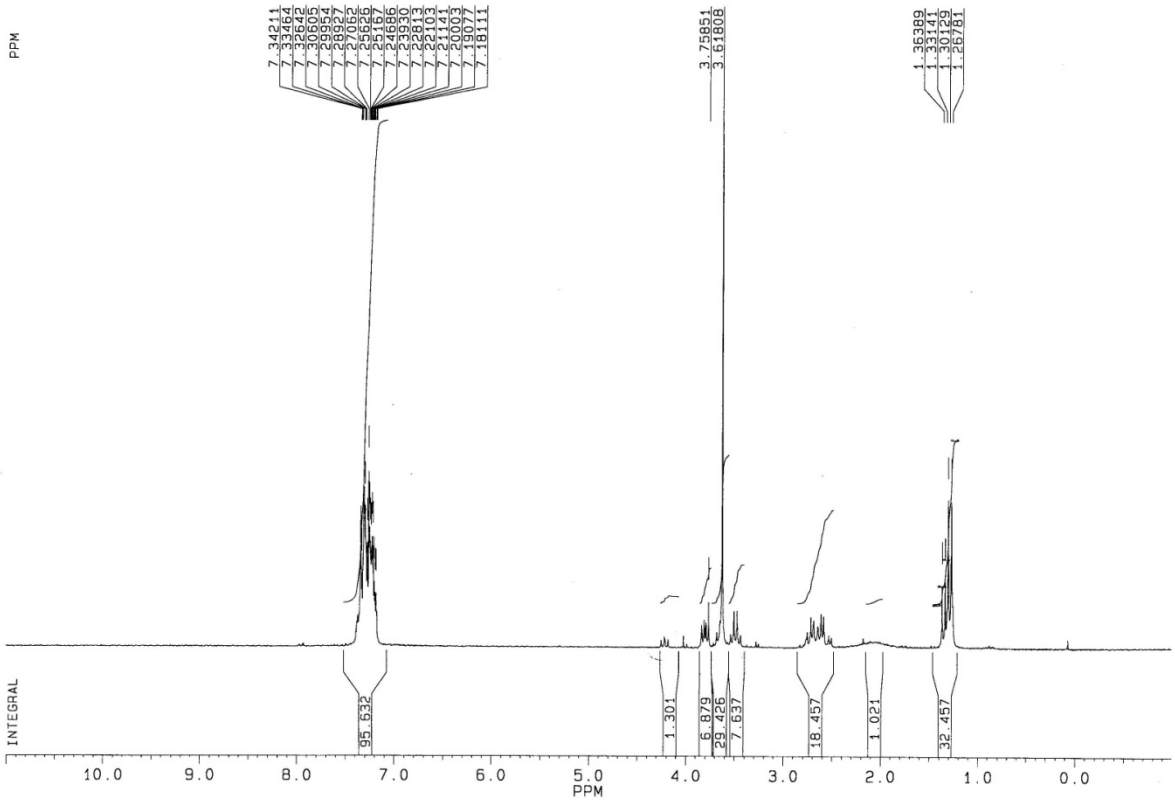
ppm

6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7.23930
7.22813
7.22103
7.21141
7.20003
7.19077
7.18111
3.75851
3.74808
3.61808
1.36389
1.33141
1.30129
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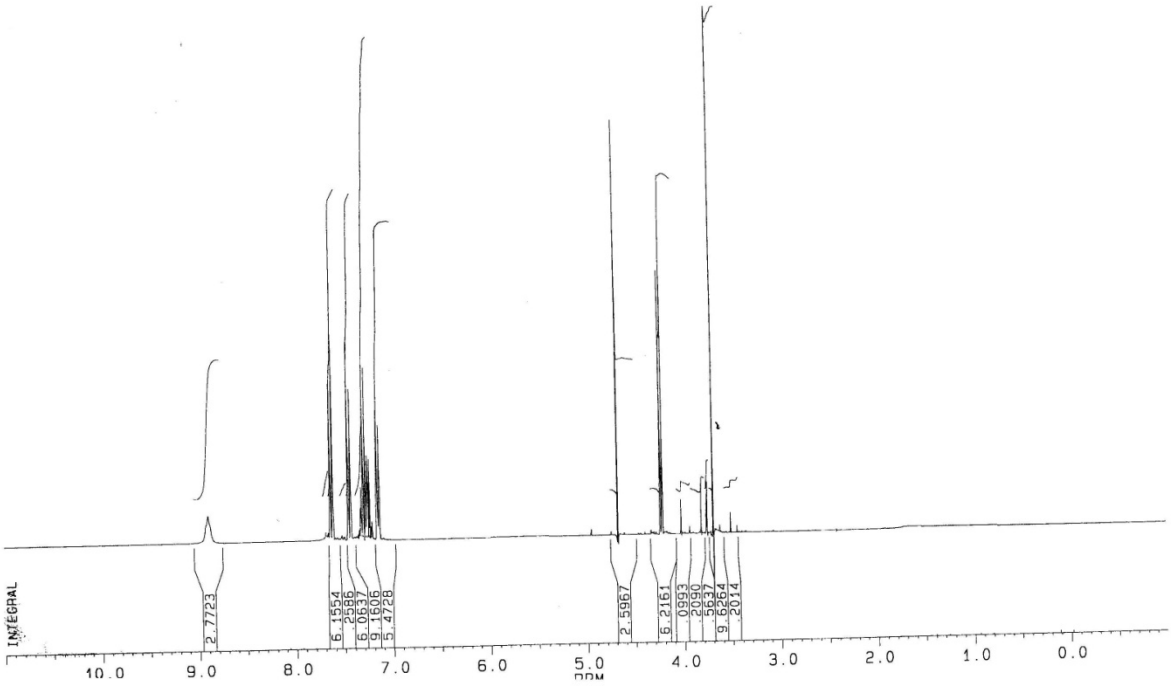
6.879
29.426
7.637
18.457
1.021
32.457
PPM

7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2.014
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5.0
4.0
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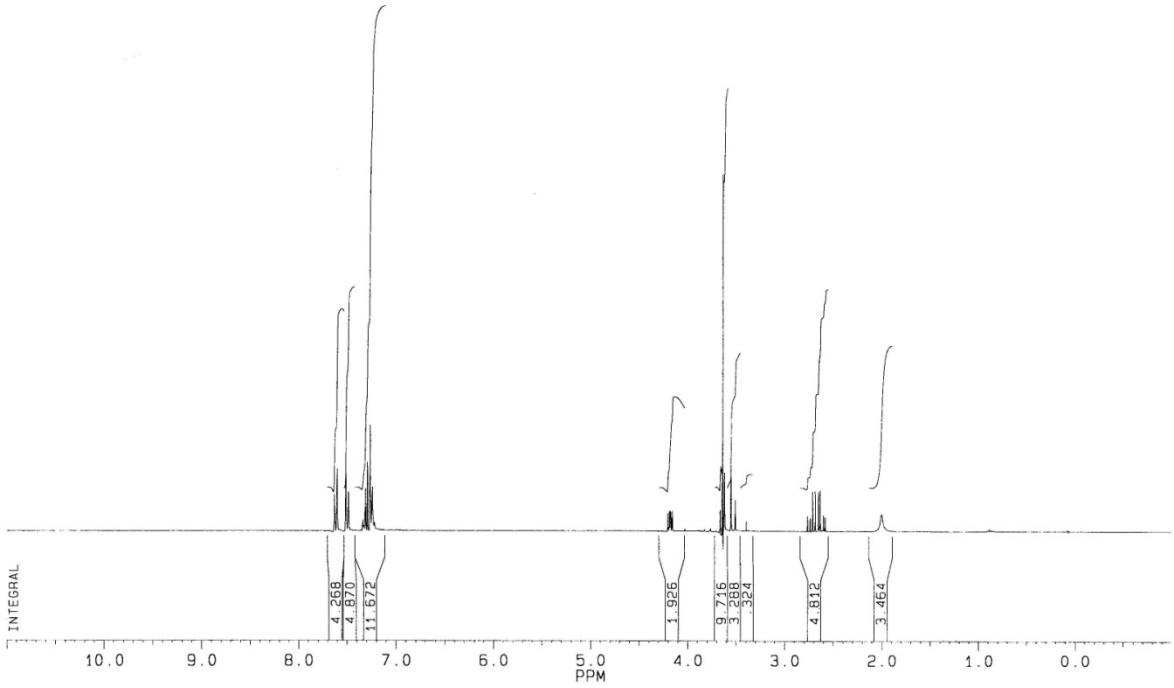
2.0
1.0
0.0
PPM

8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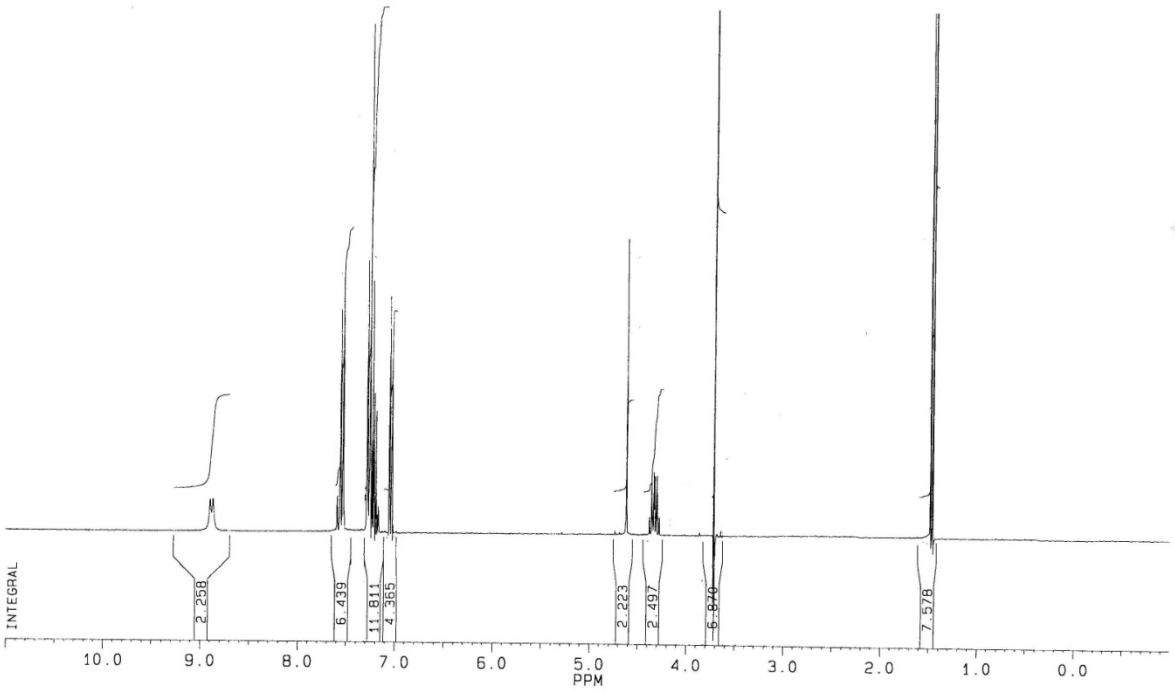
PPM

9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1.0
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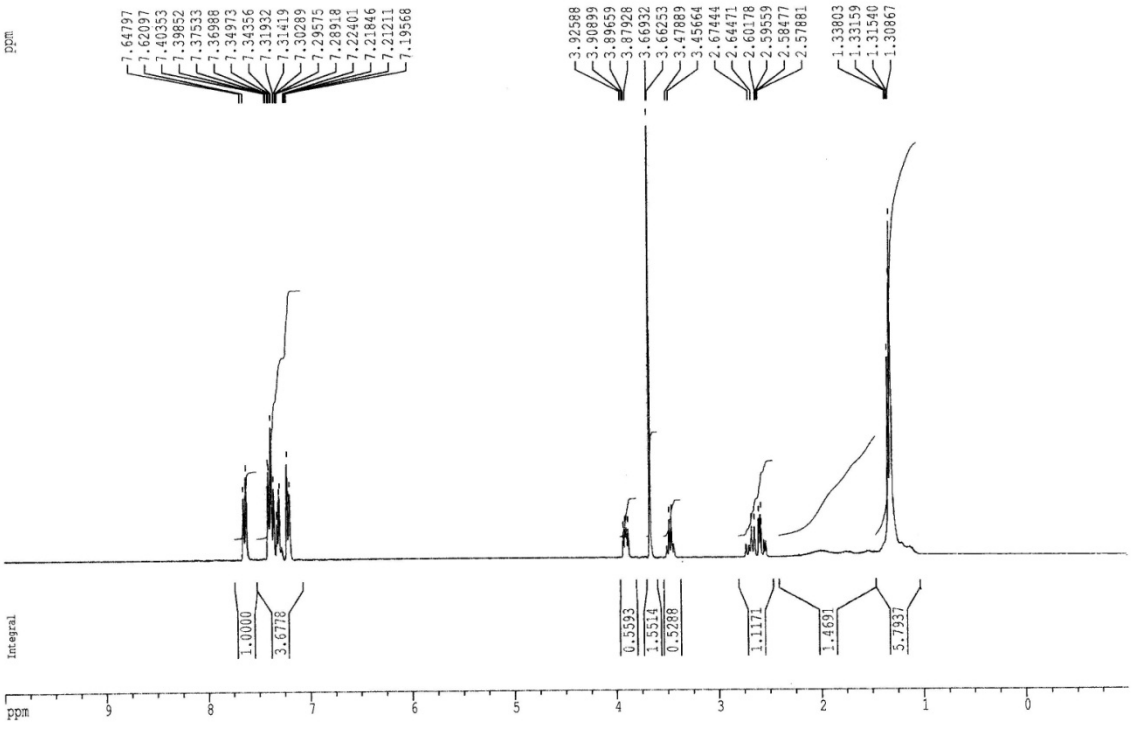
PPM

10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2
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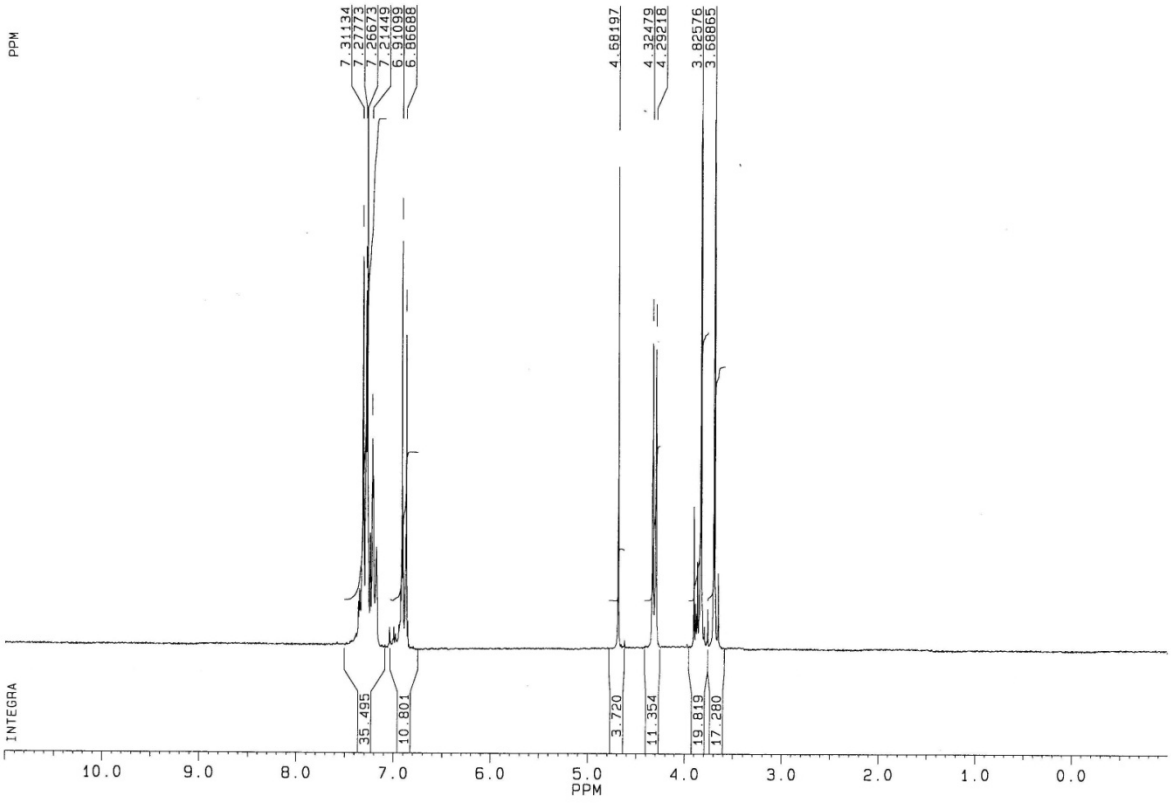
11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3.68865
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11.354
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17.280
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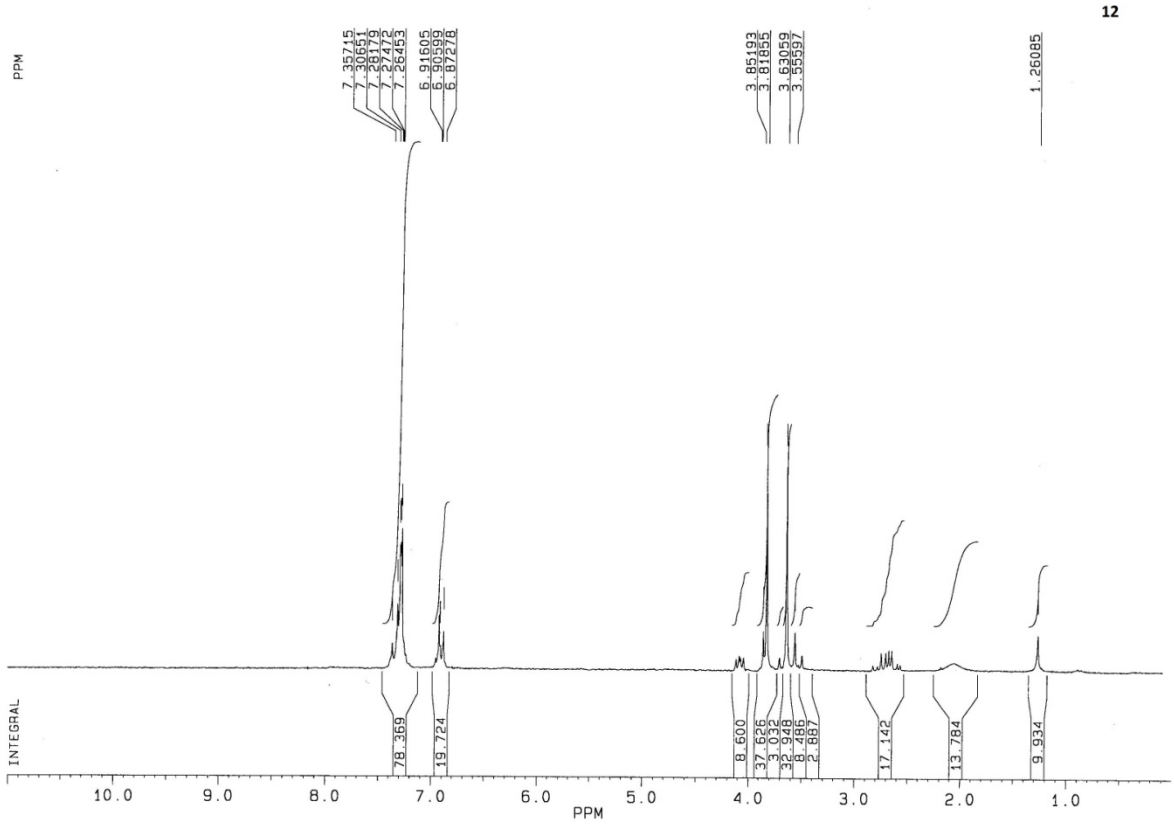
PPM

12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1.26085
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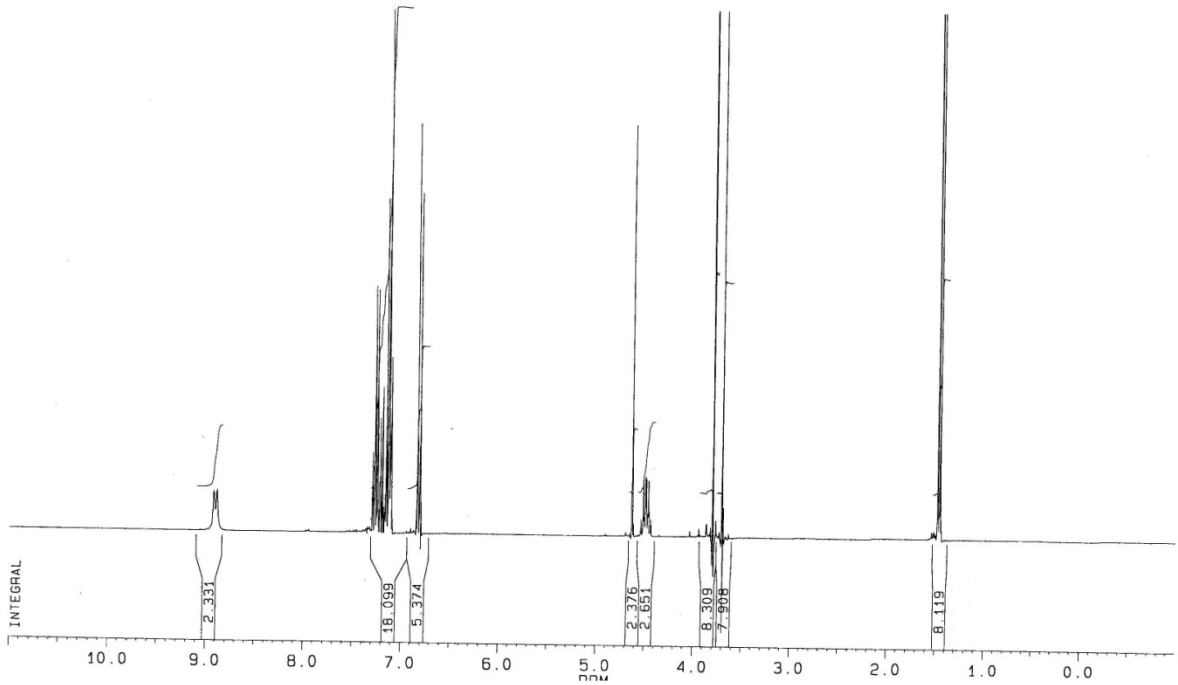
13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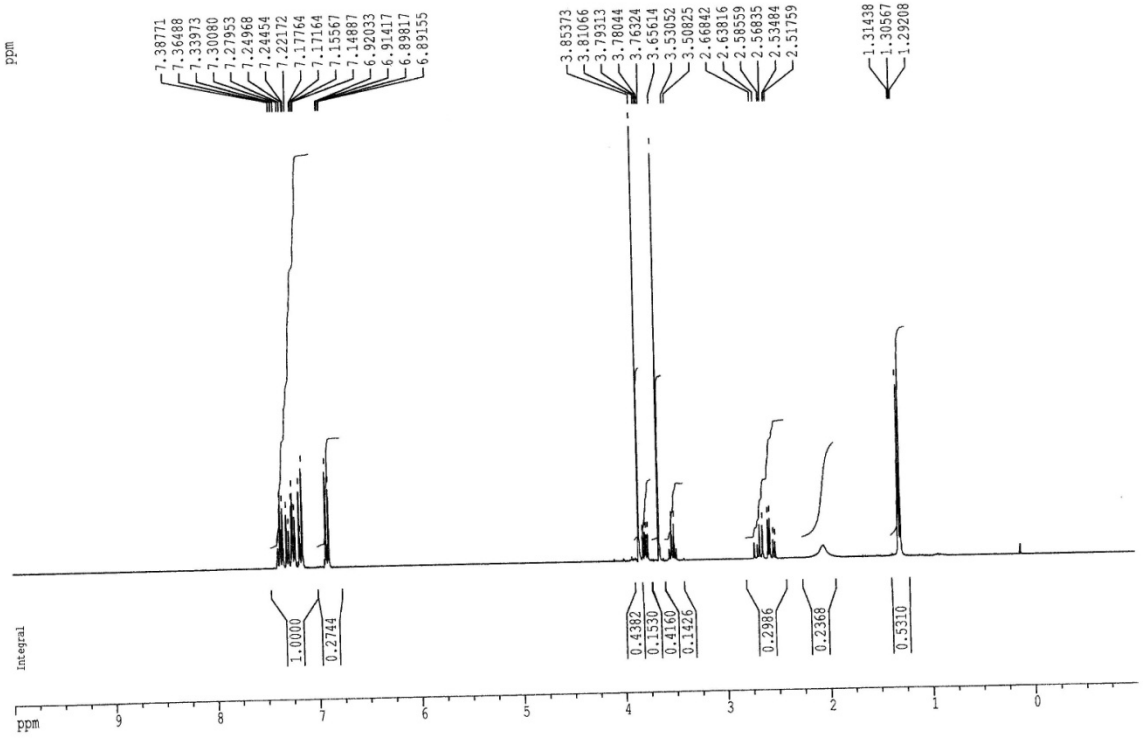
14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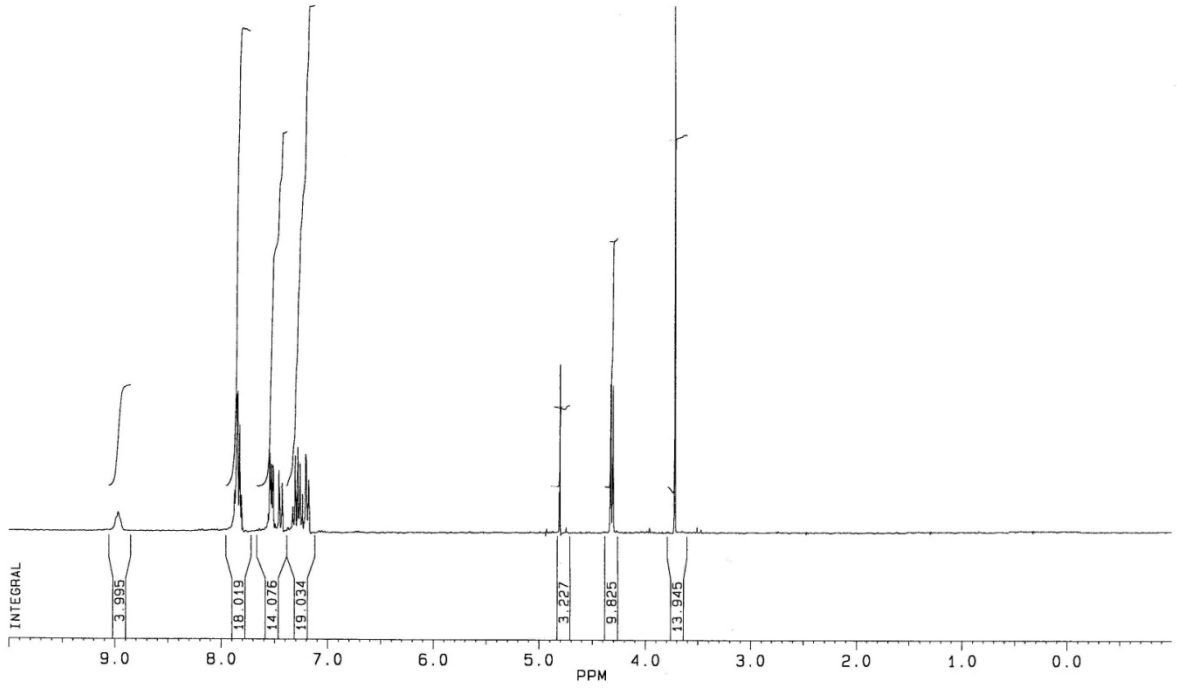
15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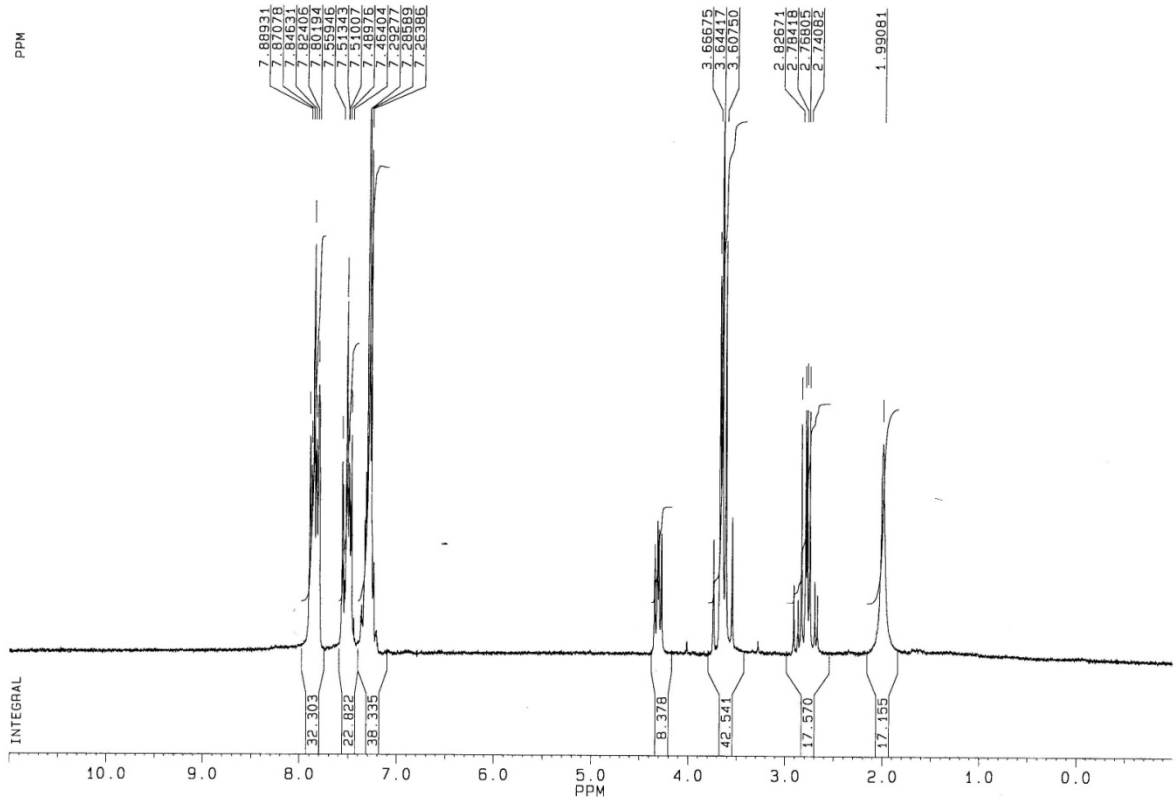
PPM

16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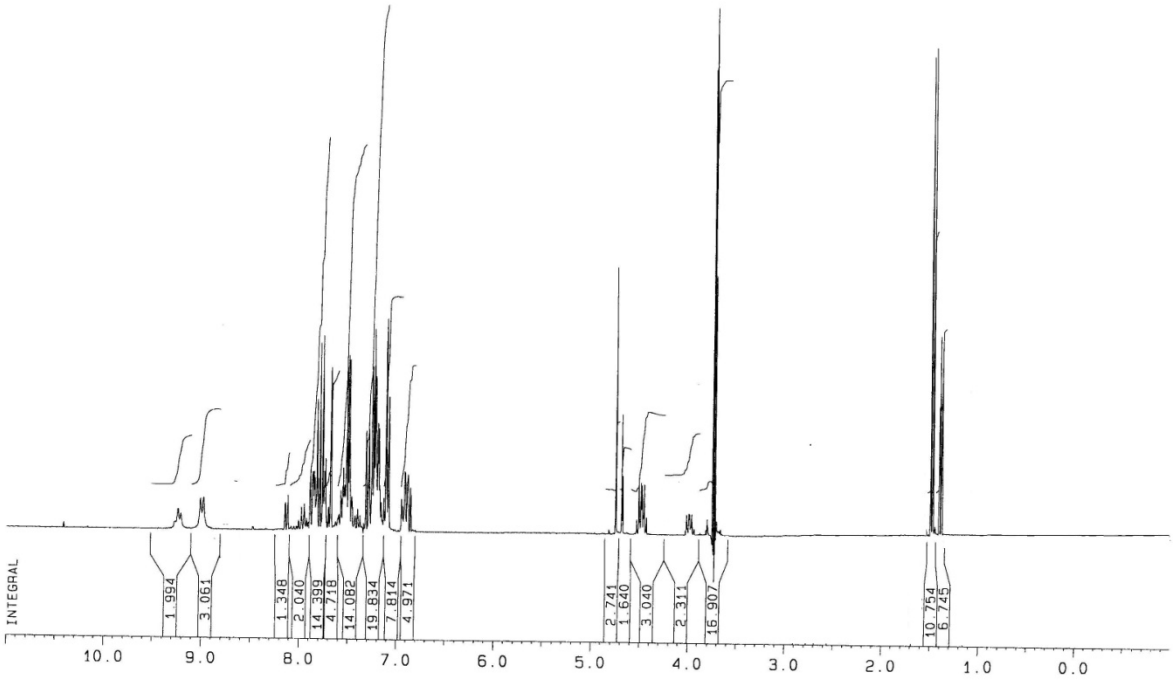
PPM

17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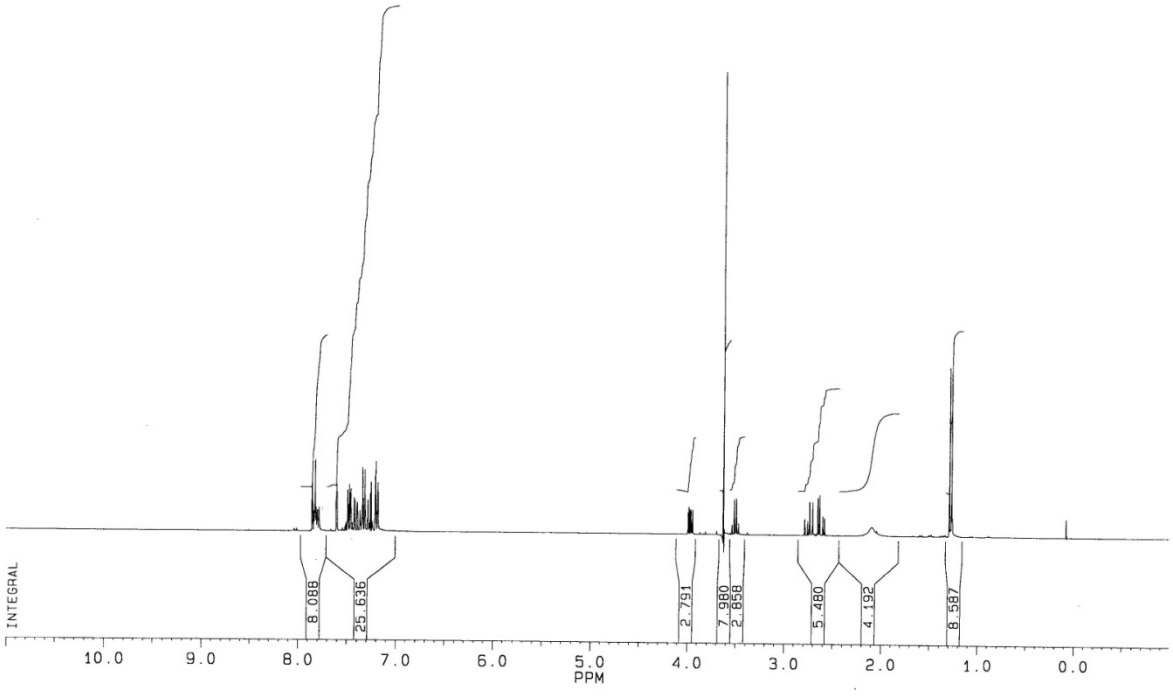
18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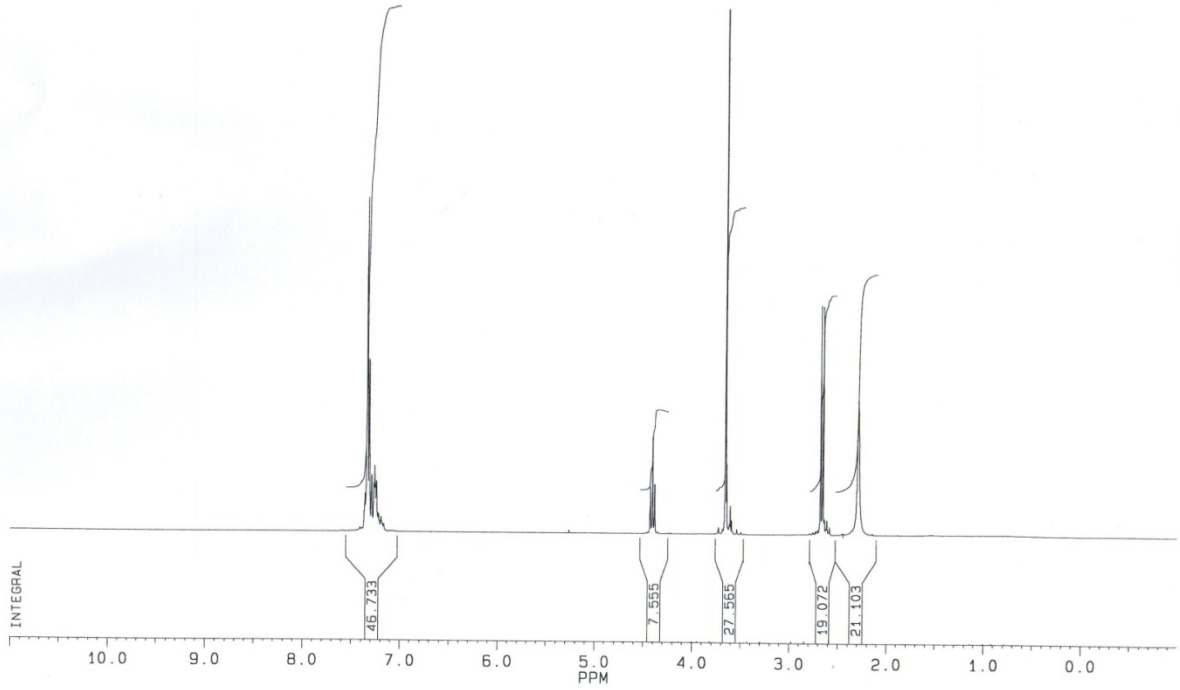
19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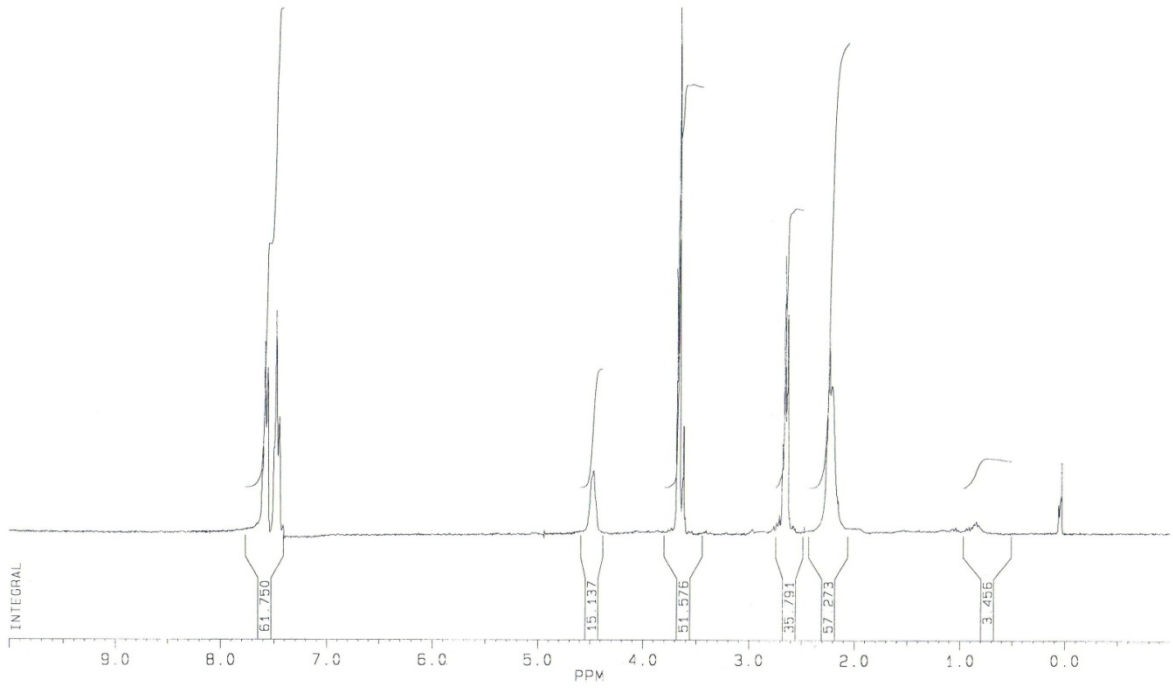
20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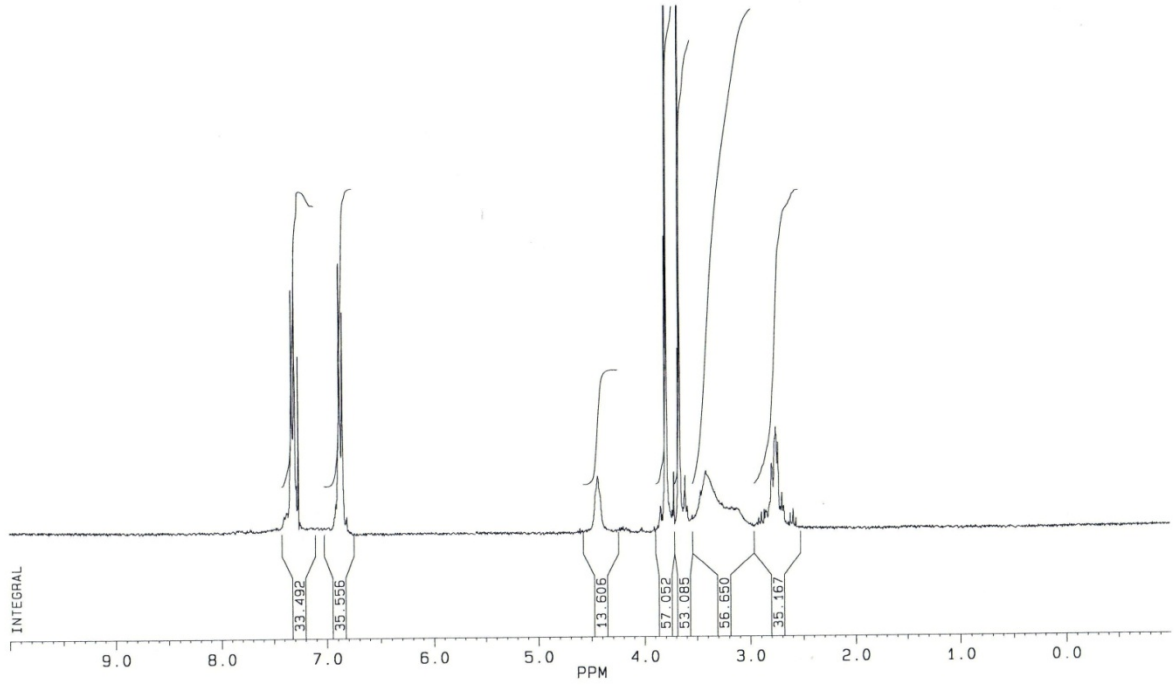
21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PPM

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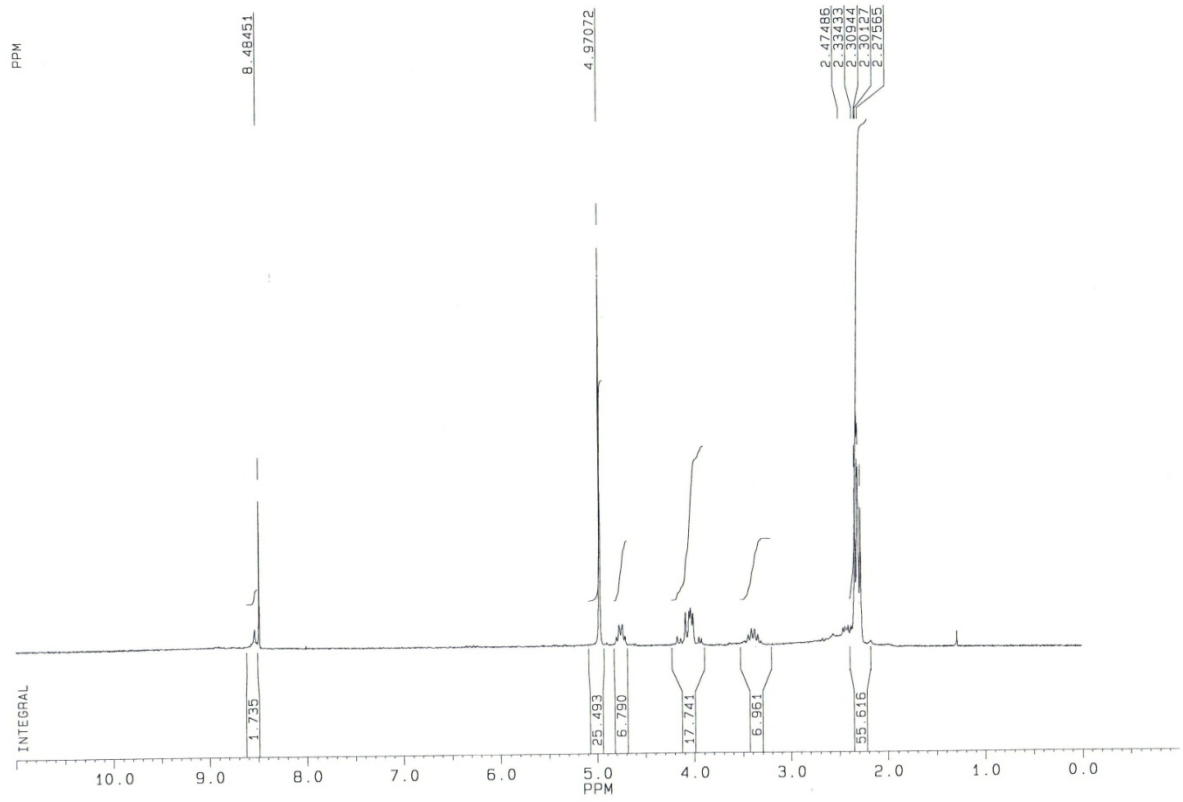
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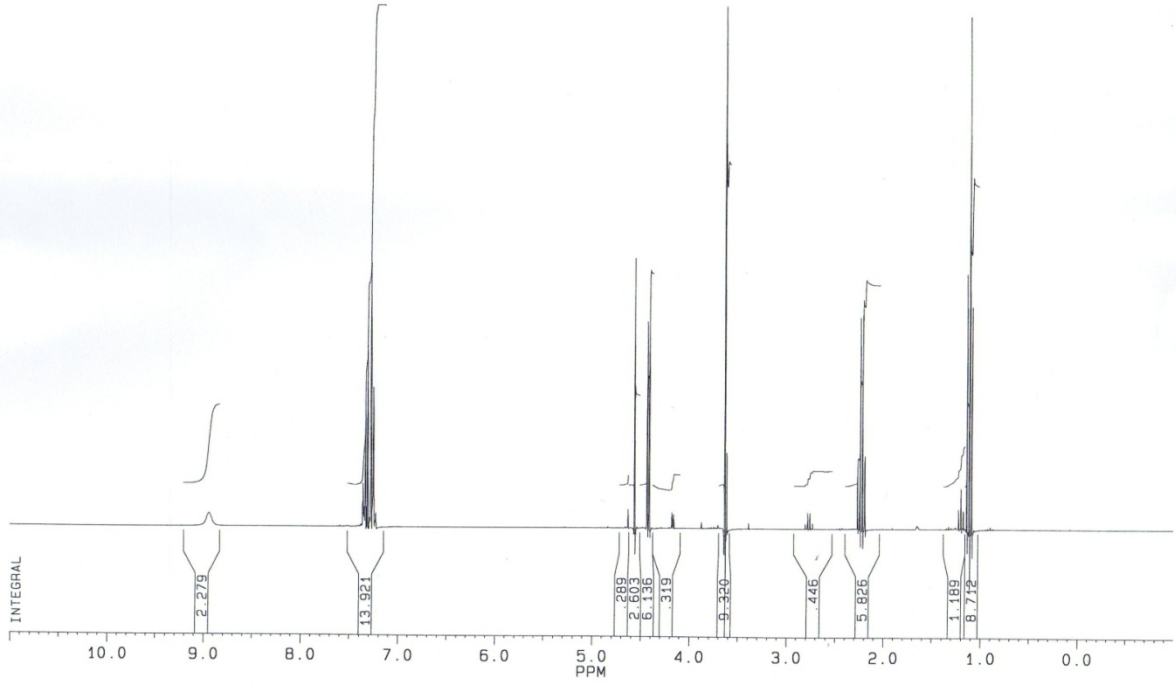
PPM

23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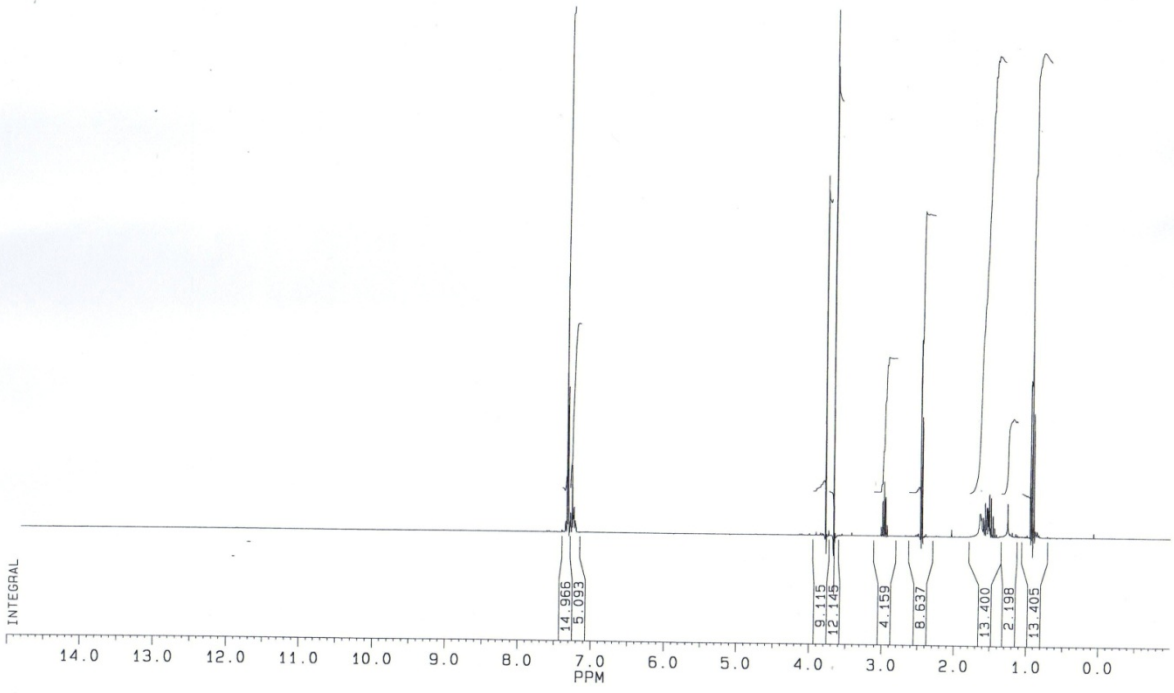
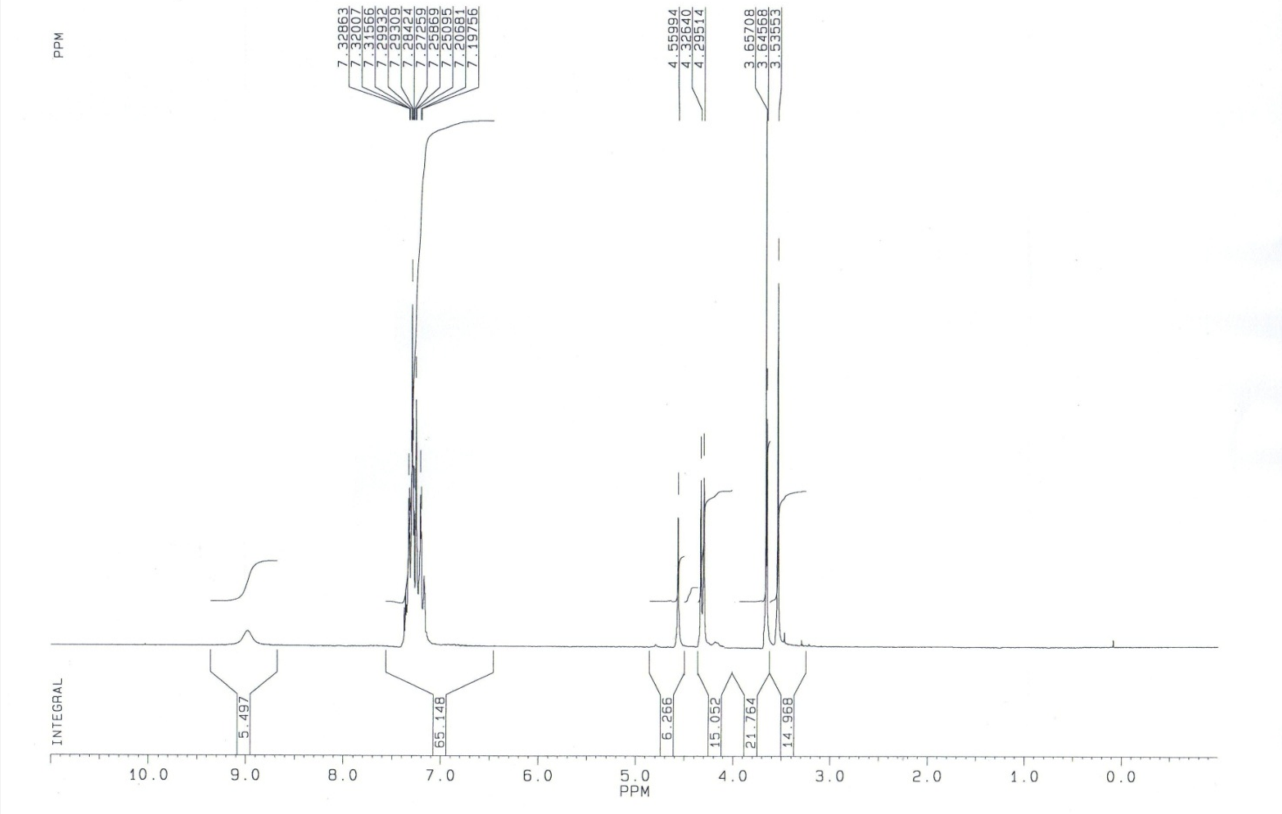
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

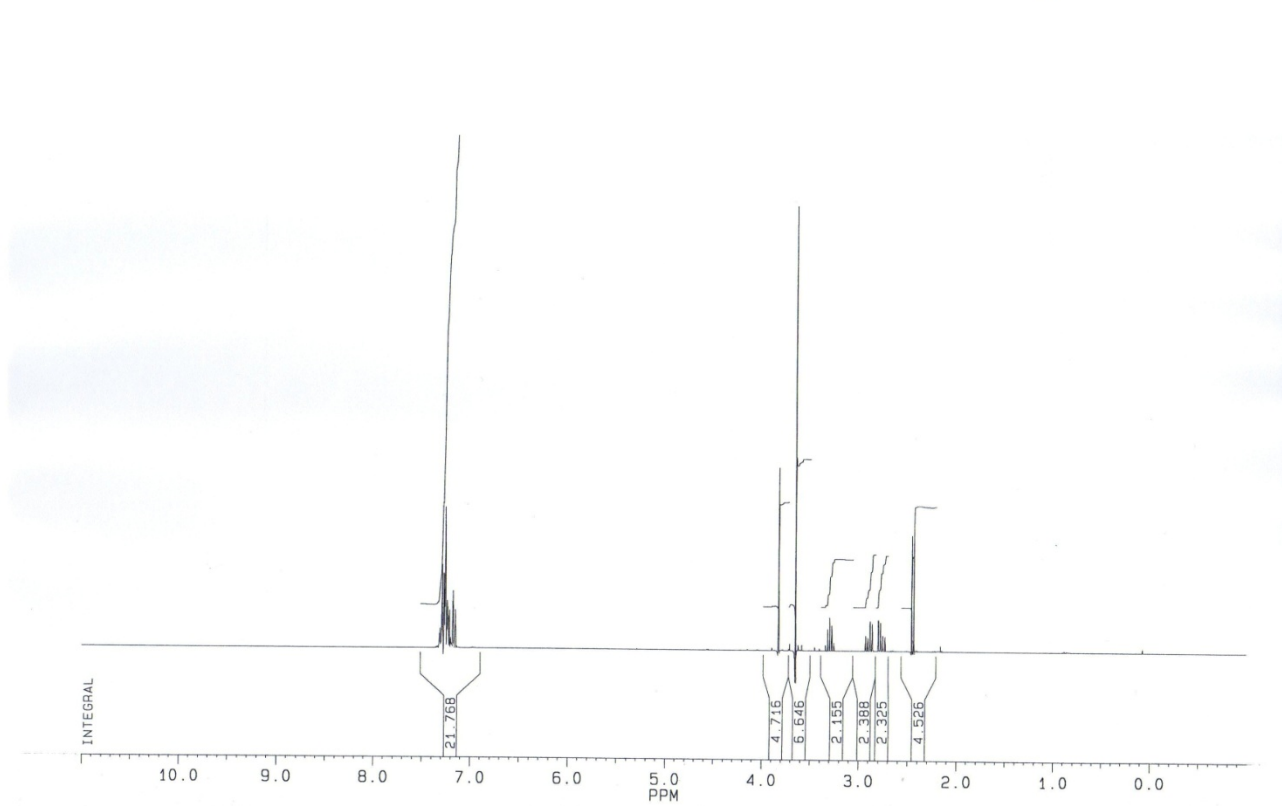
24


INTEGRAL
14.966
5.093
9.115
12.145
4.159
8.637
13.400
2.198
13.405
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

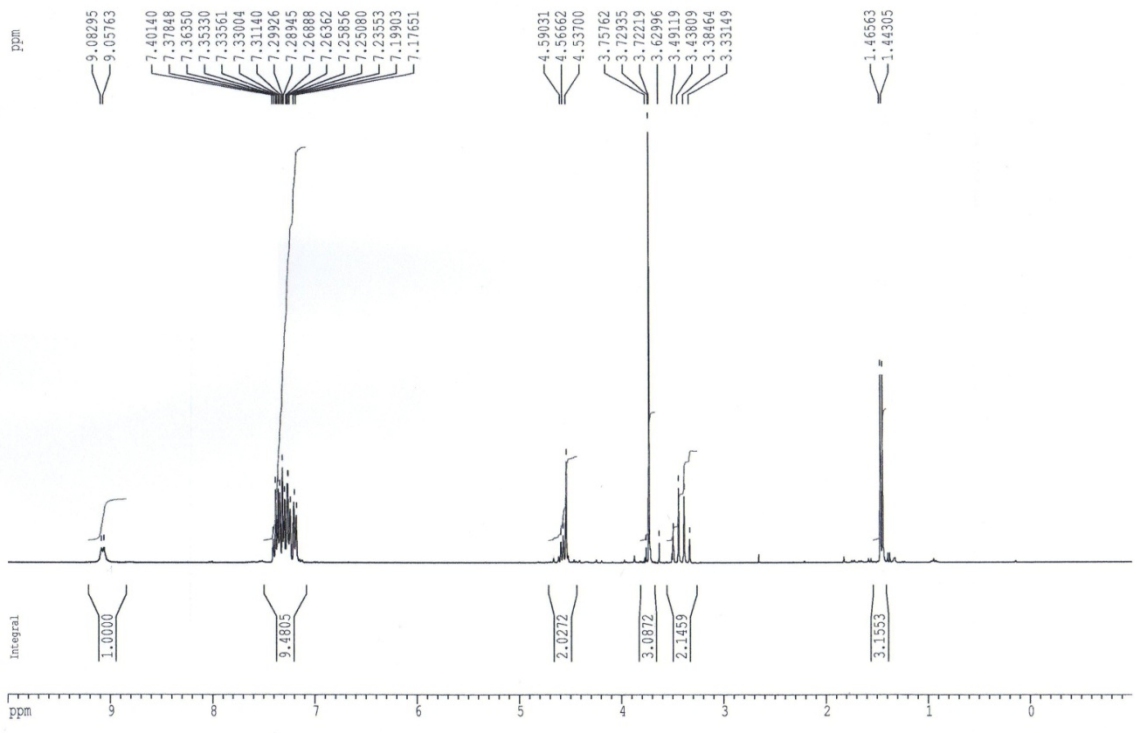
25


PPM
7.32863
7.32007
7.31566
7.29932
7.29309
7.28424
7.27259
7.25869
7.25095
7.20681
7.19756
4.55994
4.36540
4.29514
3.65708
3.64568
3.53553
INTEGRAL
5.497
65.148
6.266
15.052
21.764
14.968
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM

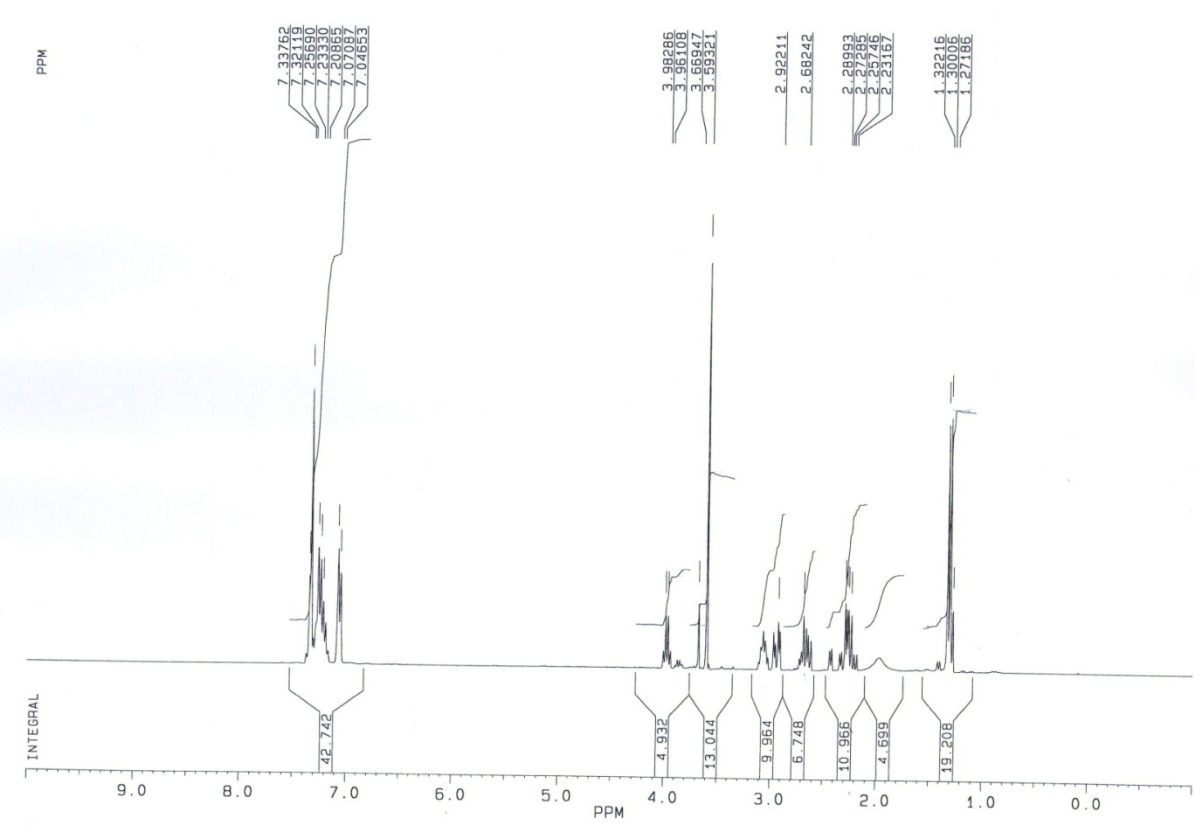
26


INTEGRAL
21.768
4.716
6.646
2.155
2.388
2.325
4.526
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
PPM

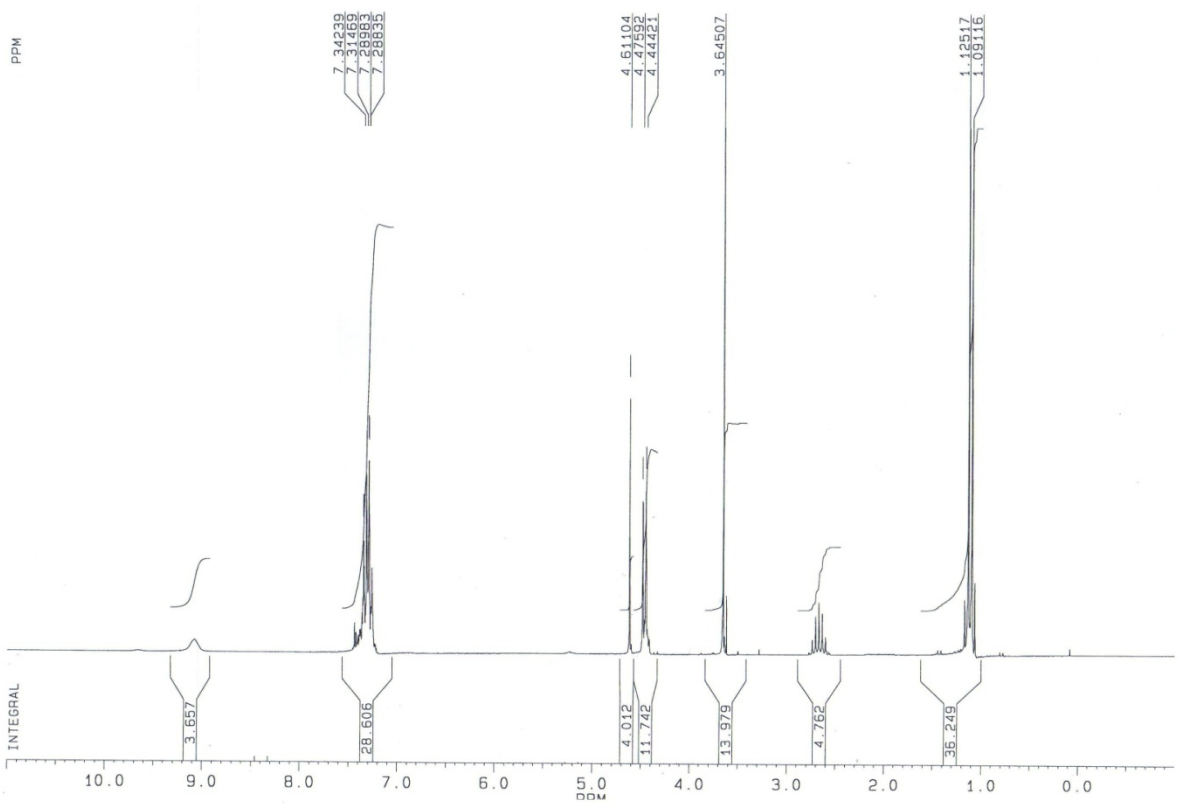
27


ppm
9.08295
9.05763
7.40140
7.37848
7.36350
7.35330
7.33561
7.33004
7.31140
7.29926
7.28945
7.26888
7.26362
7.25856
7.25080
7.23553
7.19903
7.17651
4.59031
4.56662
4.53700
3.75762
3.72935
3.72219
3.62996
3.49119
3.43809
3.38464
3.33149
1.46563
1.44305
Integral
1.0000
9.4805
2.0272
3.0872
2.1459
3.1553
ppm

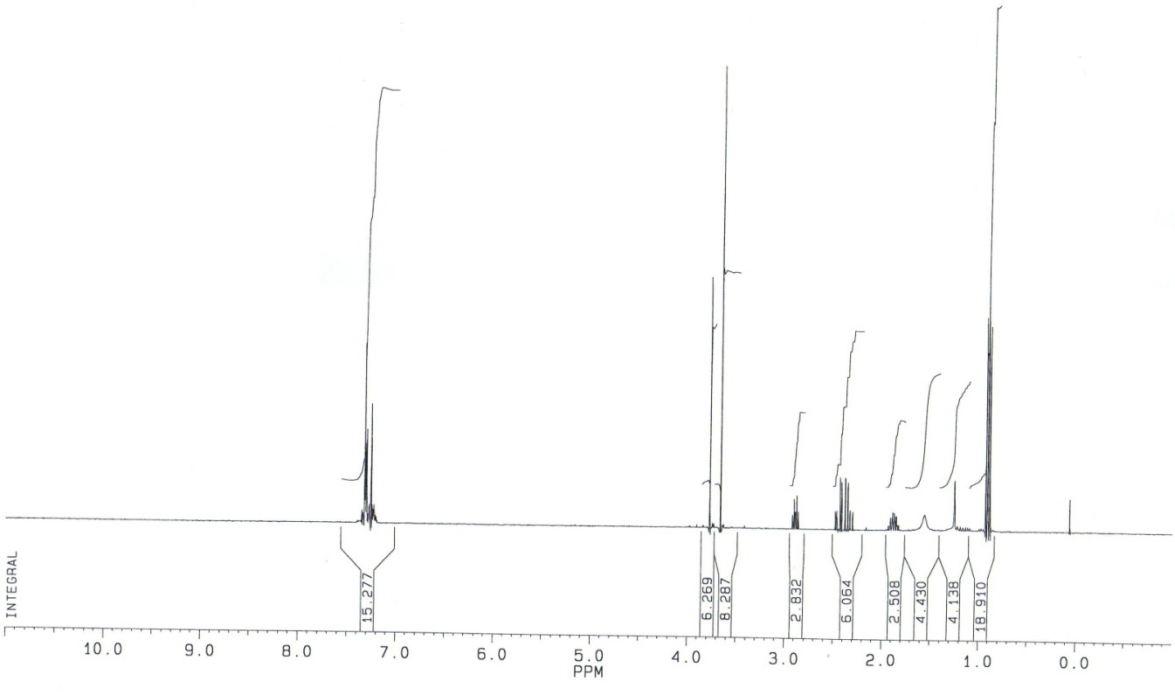
28


PPM
7.33762
7.32119
7.25690
7.23330
7.20865
7.07087
7.04653
3.98286
3.96108
3.69947
3.59321
2.92211
2.68242
2.28993
2.27246
2.25746
2.23167
1.32216
1.30006
1.27186
INTEGRAL
42.742
4.932
13.044
9.964
6.748
10.966
4.699
19.208
PPM

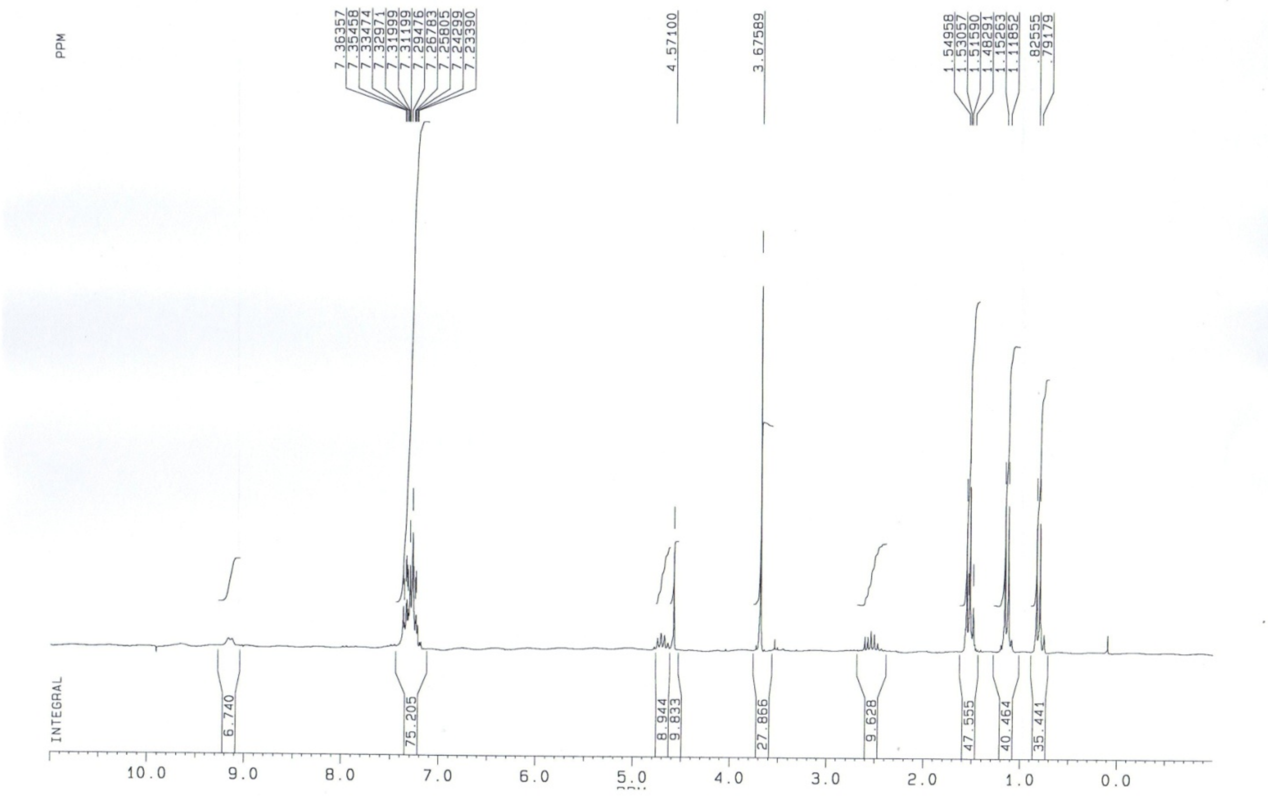
29


PPM
7.34239
7.30063
7.28835
4.61104
4.47592
4.44421
3.64507
1.12517
1.09116
INTEGRAL
3.657
28.606
4.012
11.742
13.979
4.762
36.249
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

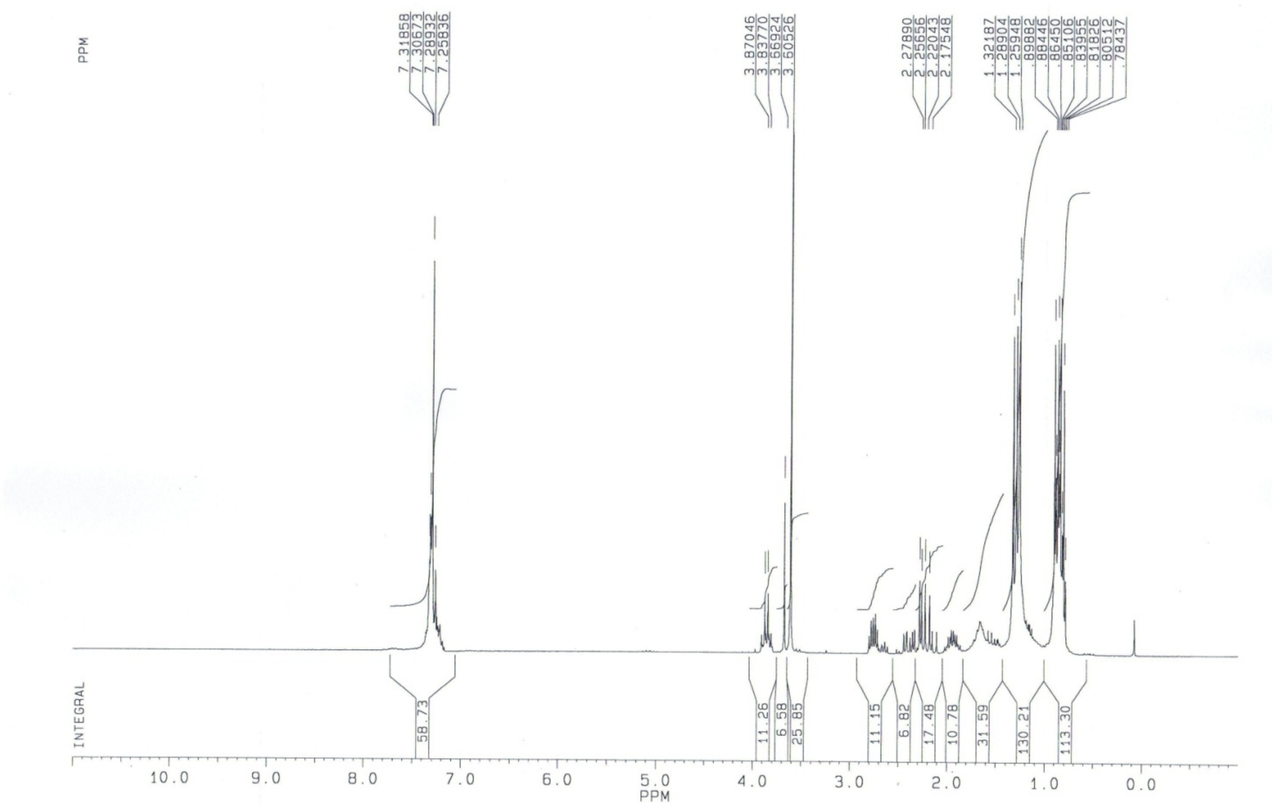
30


INTEGRAL
15.277
6.269
8.287
2.832
6.064
2.508
4.430
4.138
18.910
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

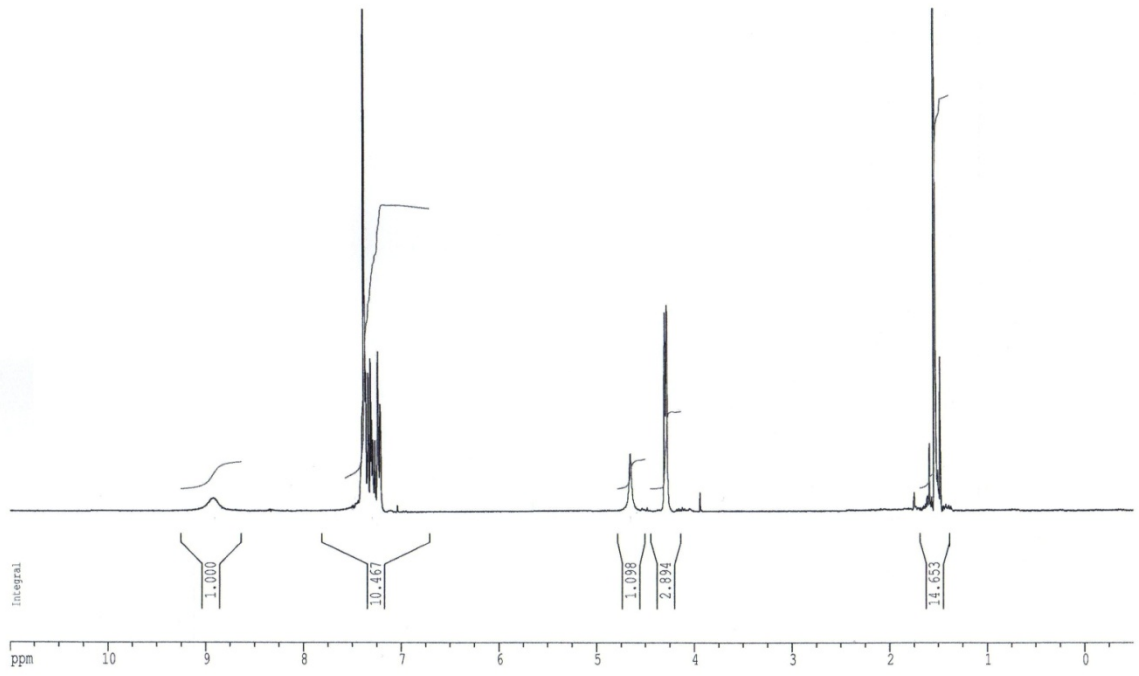
31



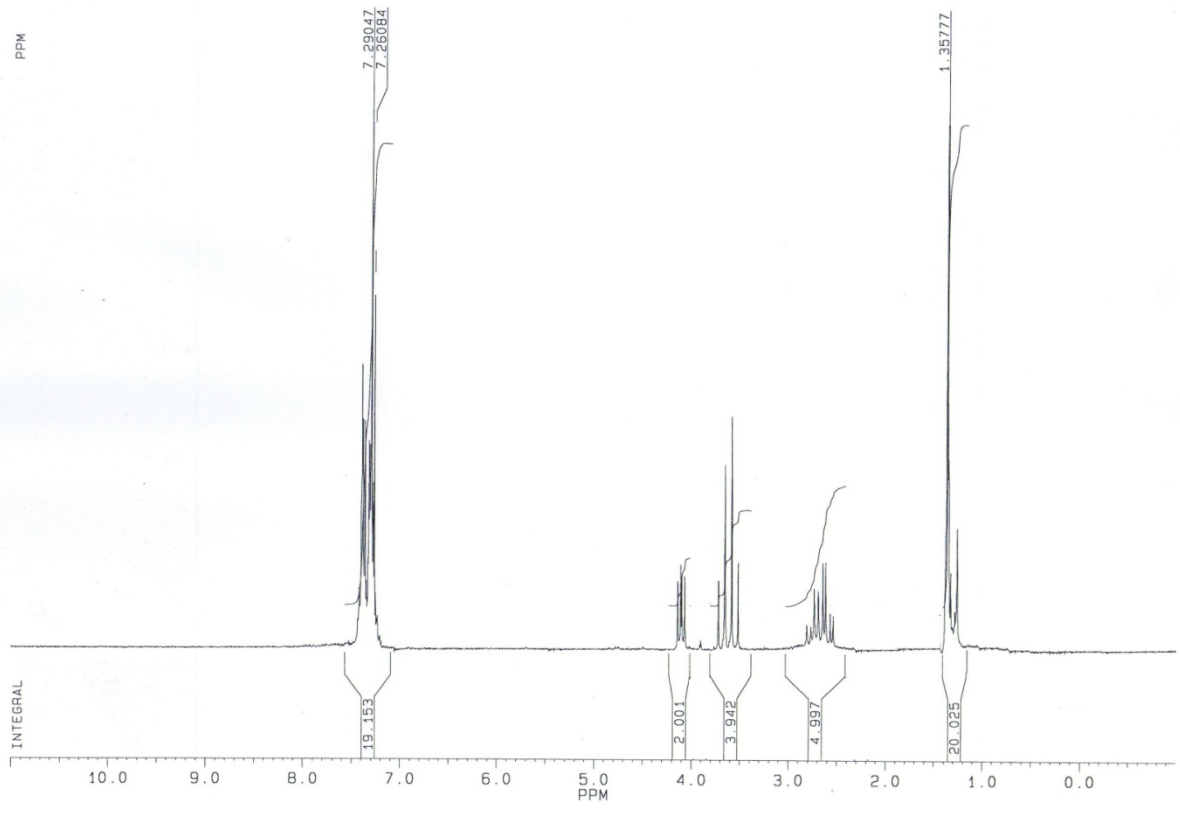
32



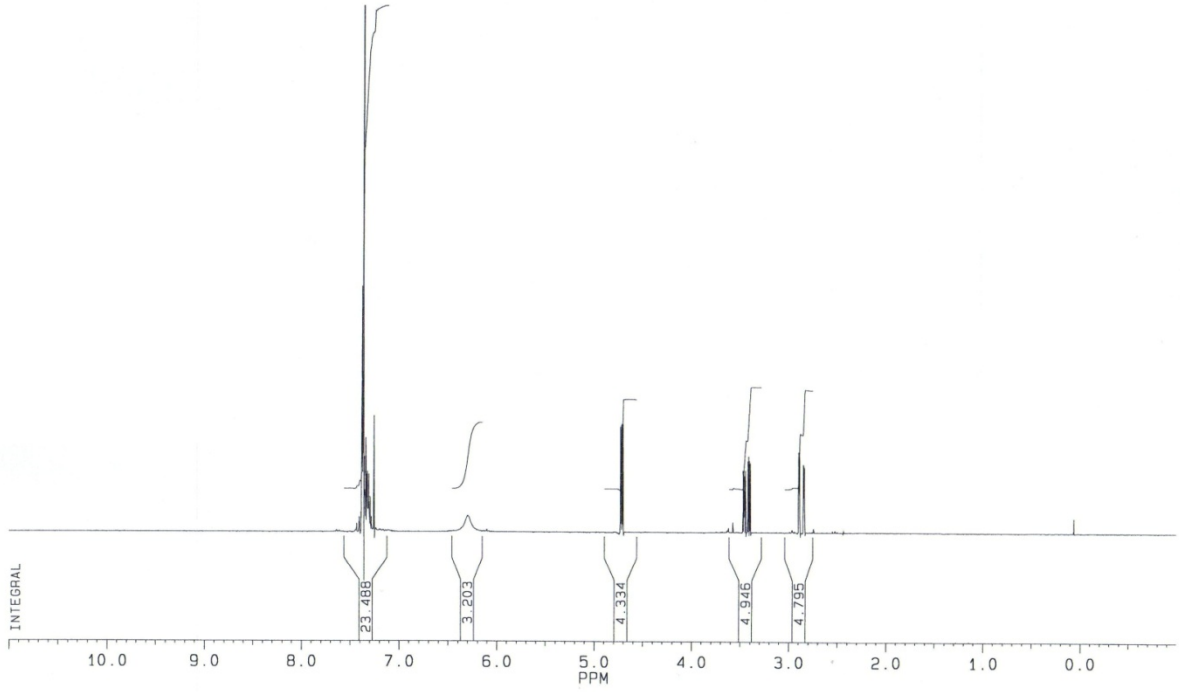
33


Integral
1.000
10.467
1.098
2.894
14.653
ppm
10
9
8
7
6
5
4
3
2
1
0

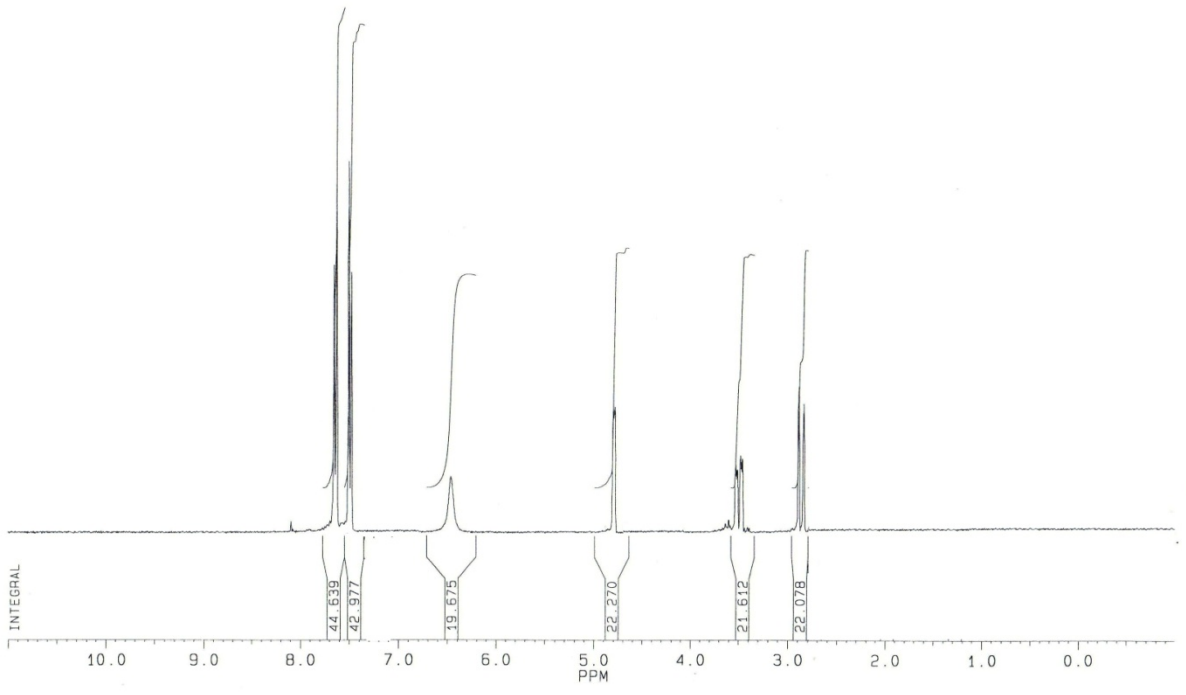
34

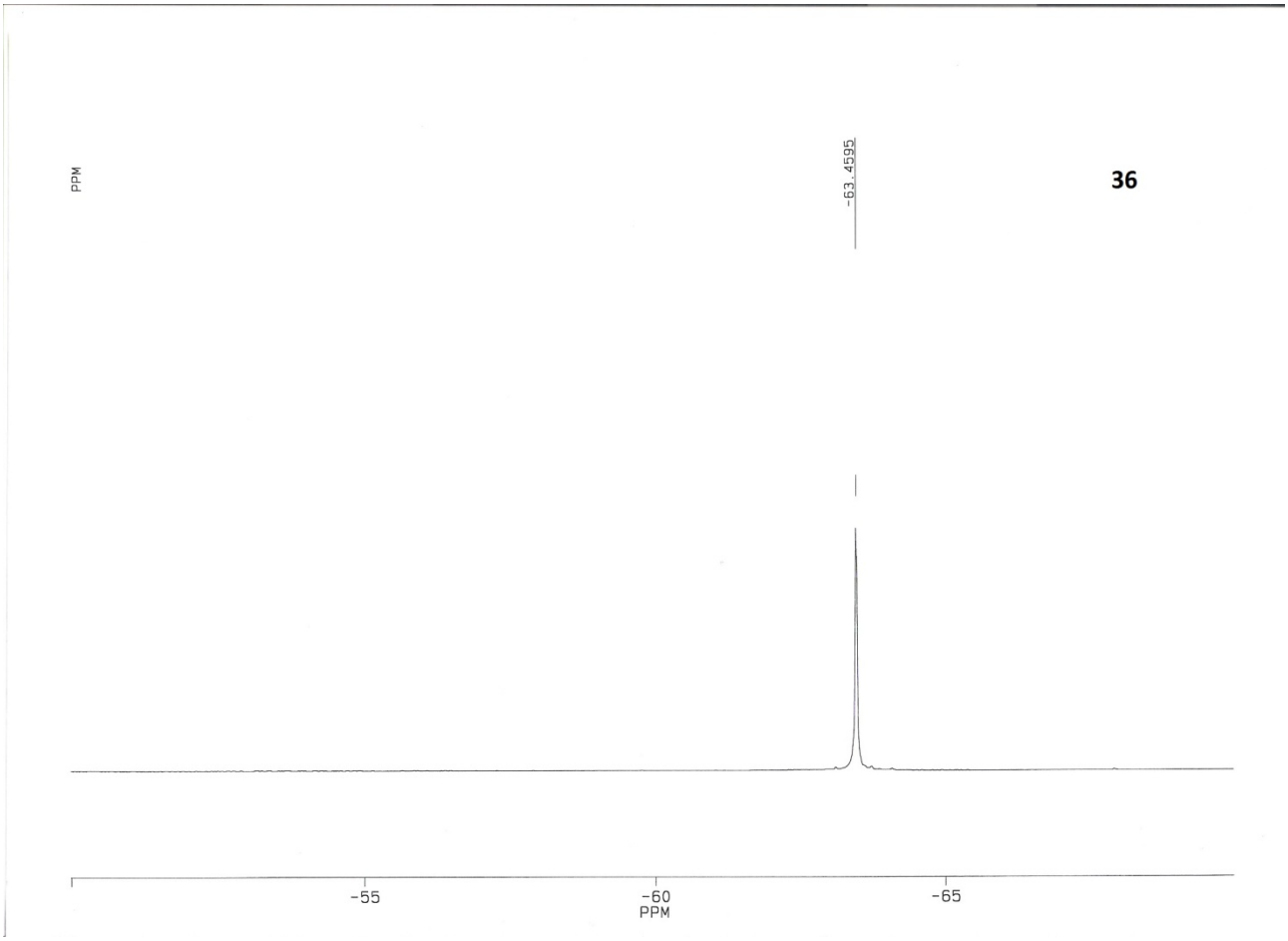

PPM
7.29047
7.26084
1.35777
INTEGRAL
19.153
2.001
3.942
4.997
20.025
10.0
9.0
8.0
7.0
6.0
5.0
PPM
4.0
3.0
2.0
1.0
0.0

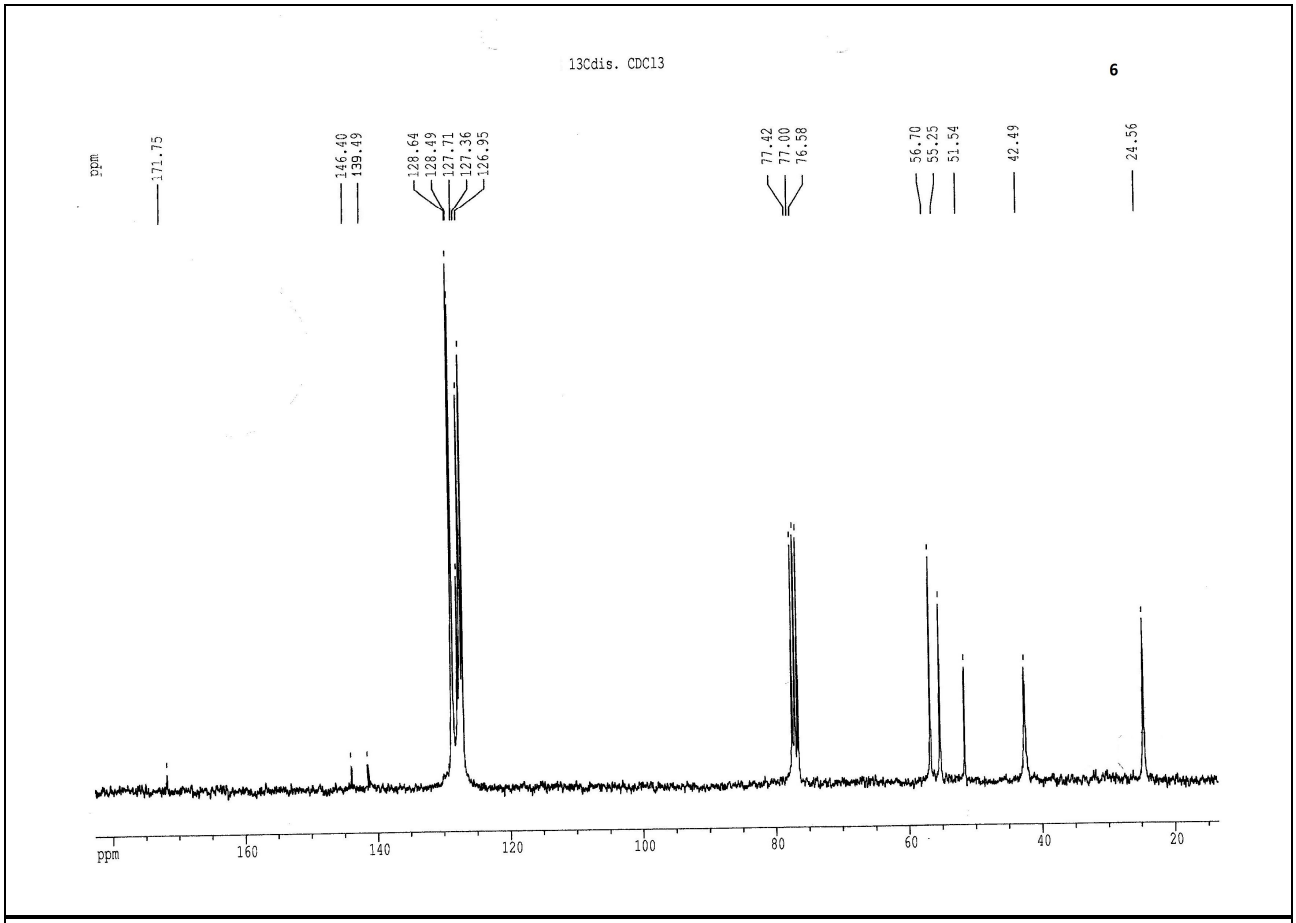
35

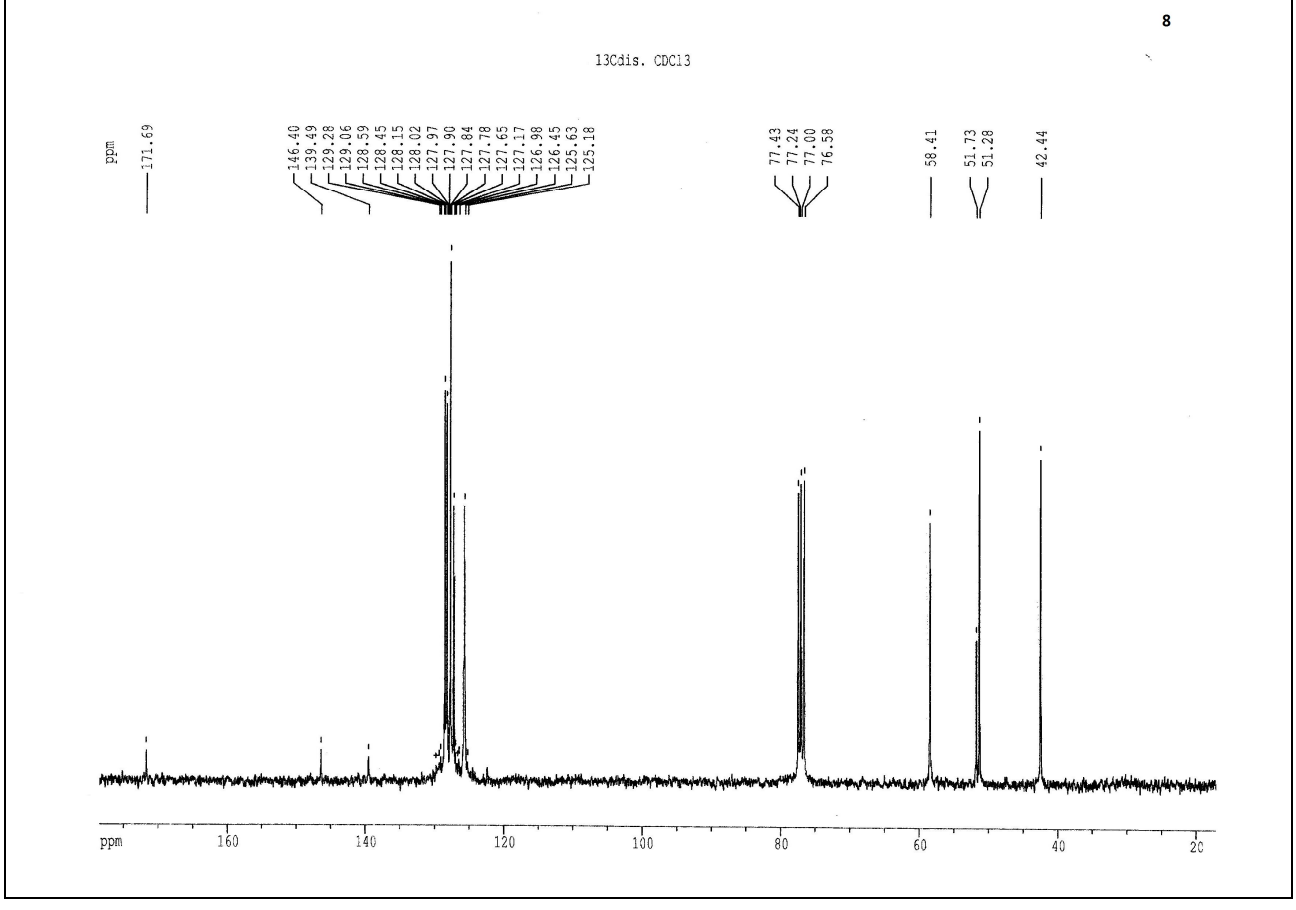

INTEGRAL
23.488
3.203
4.334
4.946
4.795
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM

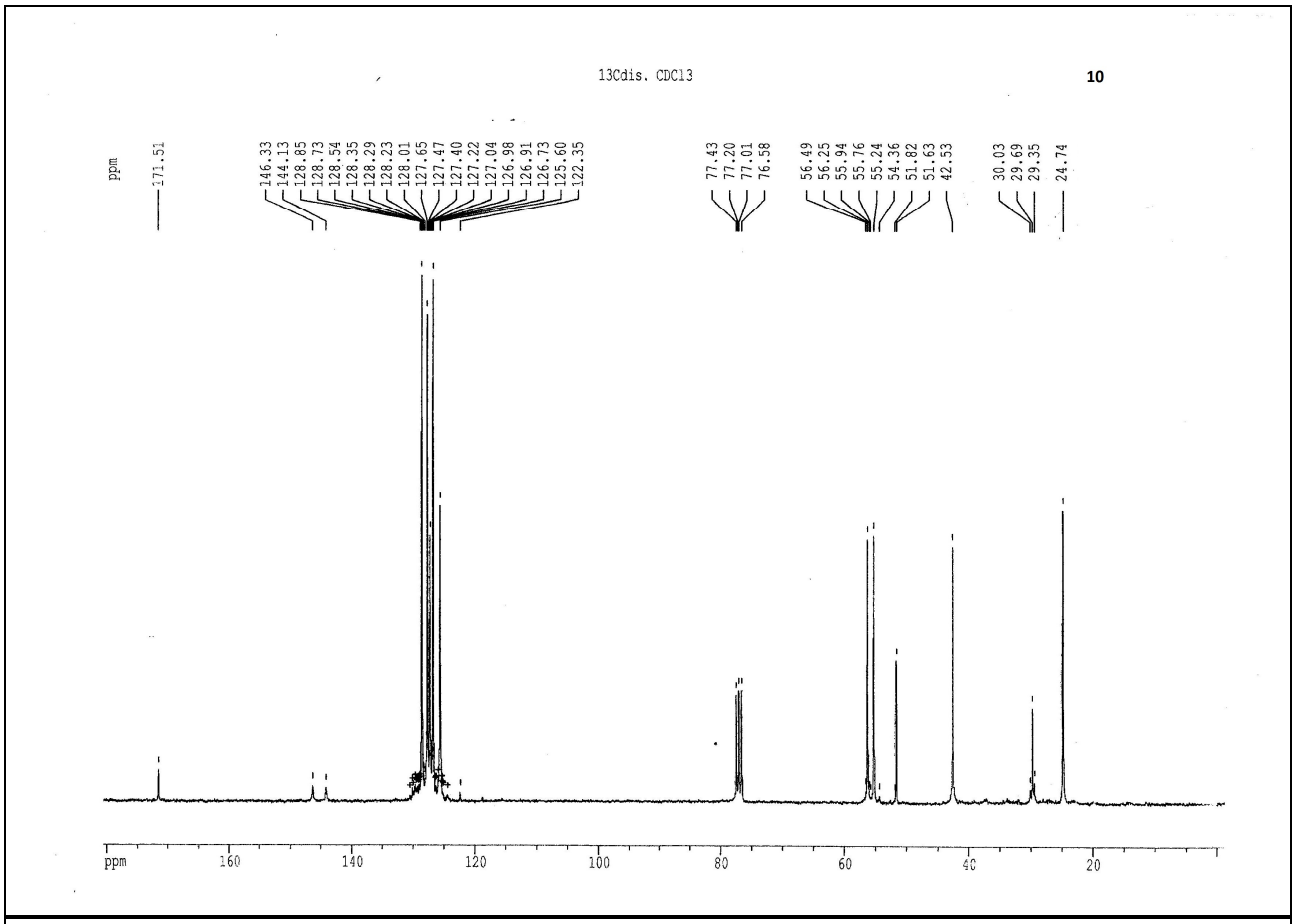
36

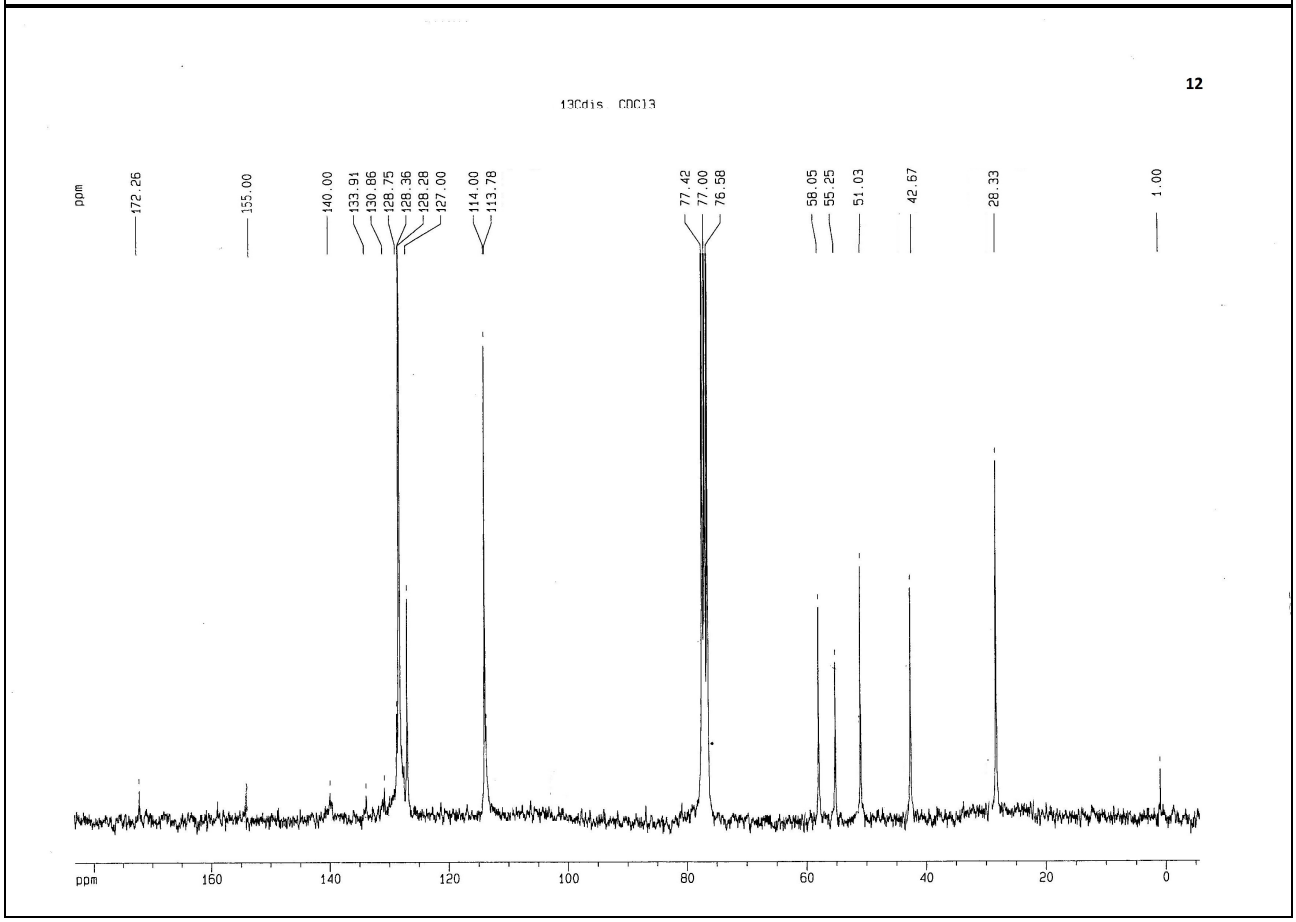

INTEGRAL
44.639
42.977
19.675
22.270
21.612
22.078
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


PPM
-63.4595
36
-55
-60
PPM
-65

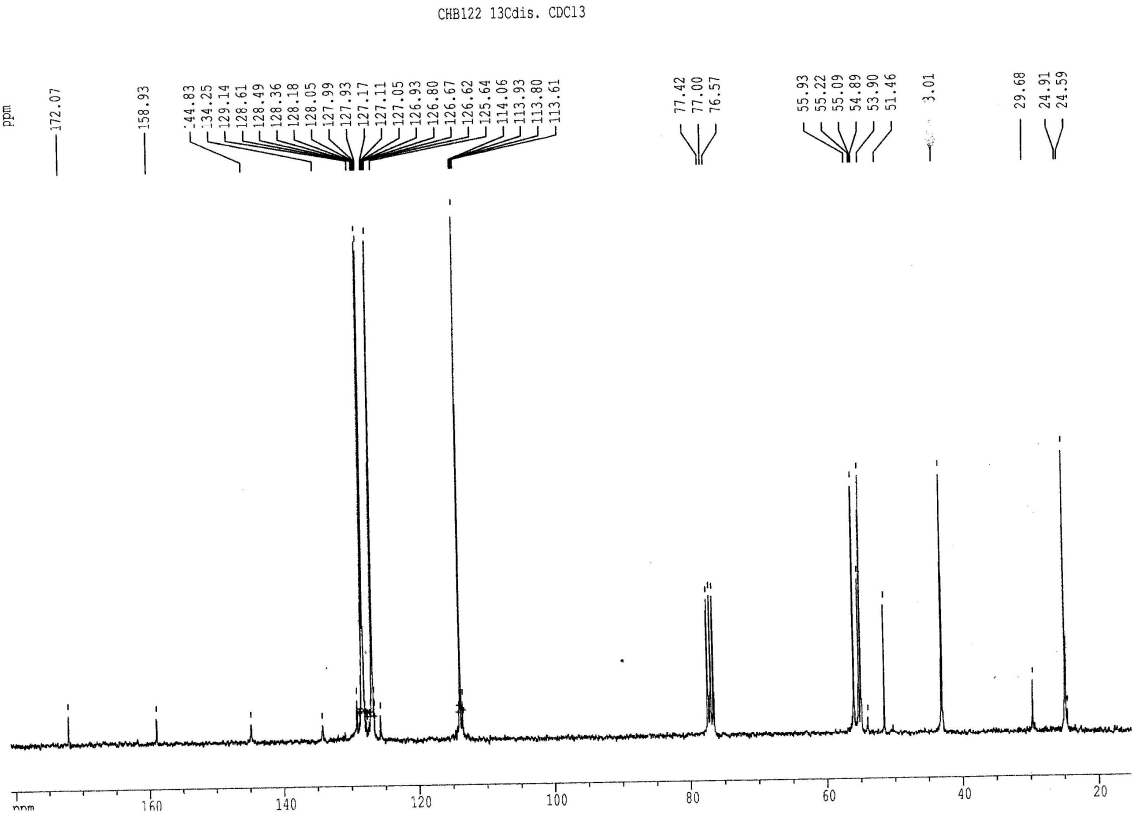

13Cdis. CDCl3
6
ppm
171.75
146.40
139.49
128.64
128.49
127.71
127.36
126.95
77.42
77.00
76.58
56.70
55.25
51.54
42.49
24.56
ppm
160
140
120
100
80
60
40
20


8
13Cdis. CDCl3
ppm
171.69
146.40
139.49
129.28
129.06
128.59
128.45
128.15
128.02
127.97
127.90
127.84
127.78
127.65
127.17
126.98
126.45
125.63
125.18
77.43
77.24
77.00
76.58
58.41
51.73
51.28
42.44
ppm
160
140
120
100
80
60
40
20

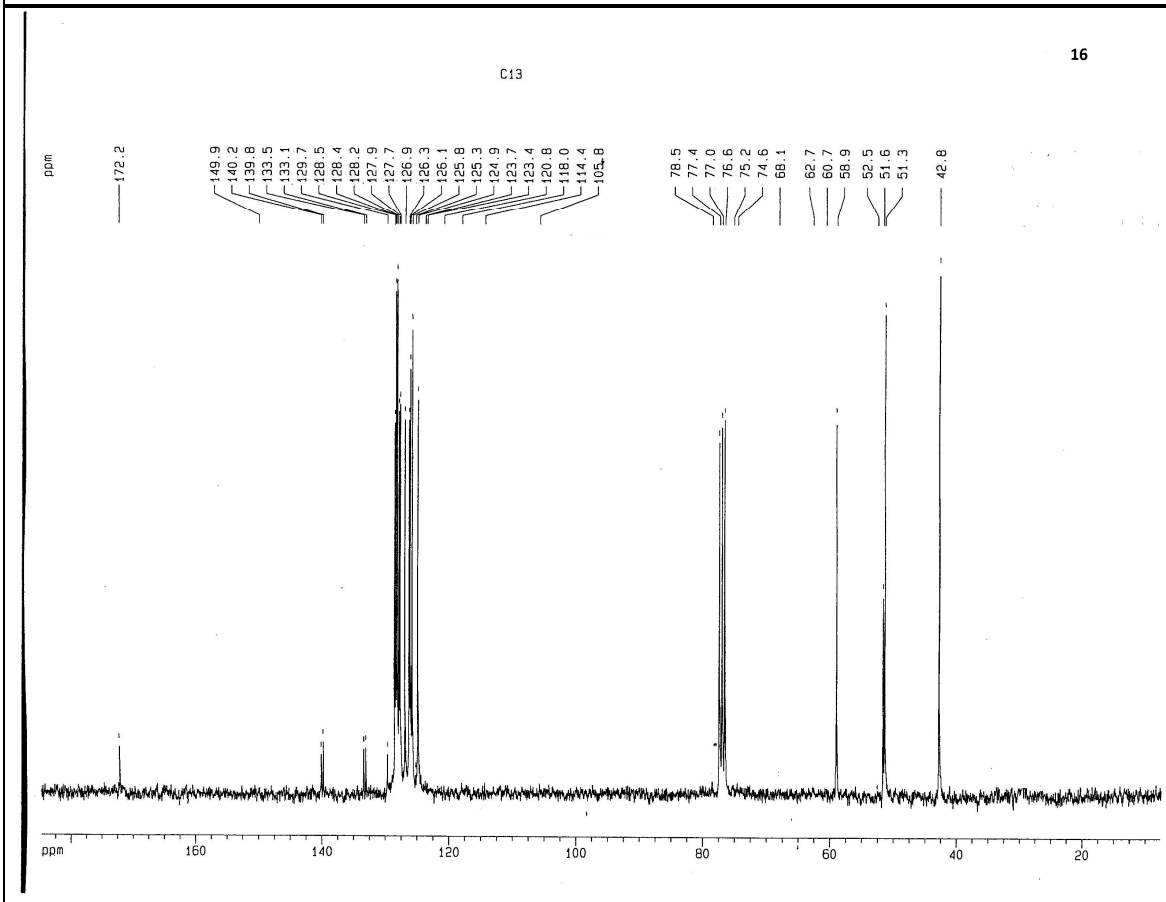

13Cdis. CDCl3
10
ppm
171.51
146.33
144.13
128.85
128.73
128.54
128.35
128.29
128.23
128.01
127.65
127.47
127.40
127.22
127.04
126.98
126.91
126.73
125.60
122.35
77.43
77.20
77.01
76.58
56.49
56.25
55.94
55.76
55.24
54.36
51.82
51.63
42.53
30.03
29.69
29.35
24.74
ppm
160
140
120
100
80
60
40
20


12
13Cdis. CDCl3
ppm
172.26
155.00
140.00
133.91
130.86
128.75
128.36
128.28
127.00
114.00
113.78
77.42
77.00
76.58
58.05
55.25
51.03
42.67
28.33
1.00
ppm
160
140
120
100
80
60
40
20
0

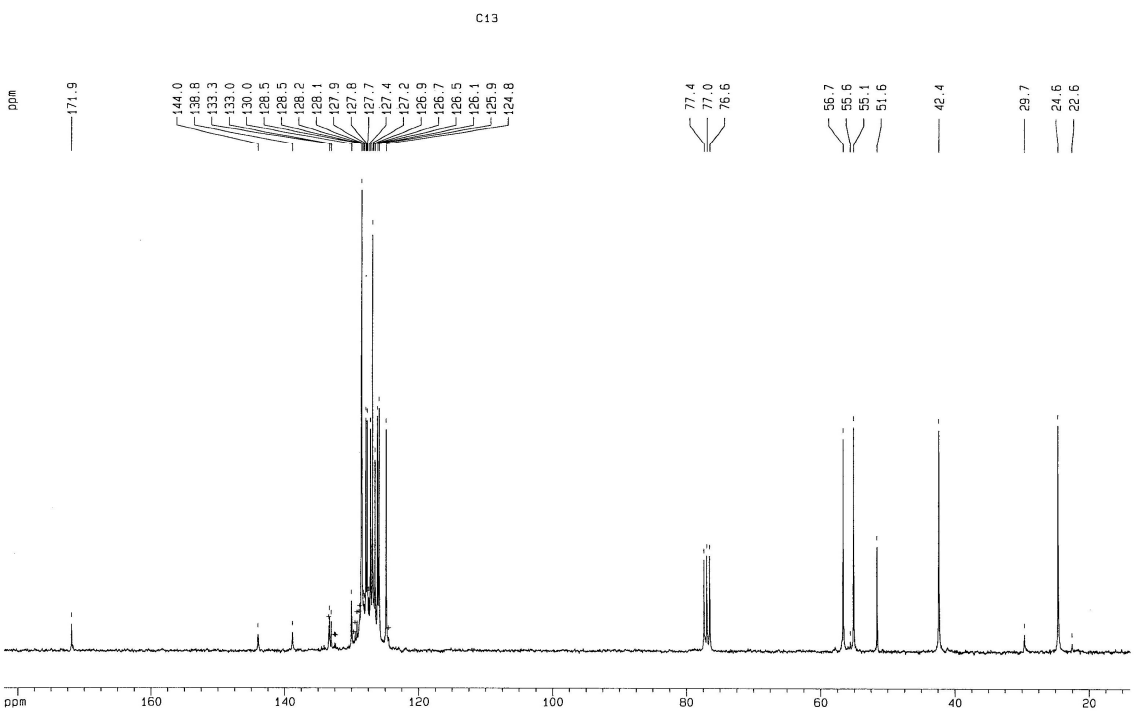
14


CHB122 13Cdis. CDCl3
ppm
172.07
158.93
144.83
134.25
129.14
128.61
128.49
128.36
128.18
128.05
127.99
127.93
127.17
127.11
127.05
126.93
126.80
126.67
126.62
125.64
114.06
113.93
113.80
113.61
77.42
77.00
76.57
55.93
55.22
55.09
54.89
53.90
51.46
3.01
29.68
24.91
24.59
ppm
160
140
120
100
80
60
40
20

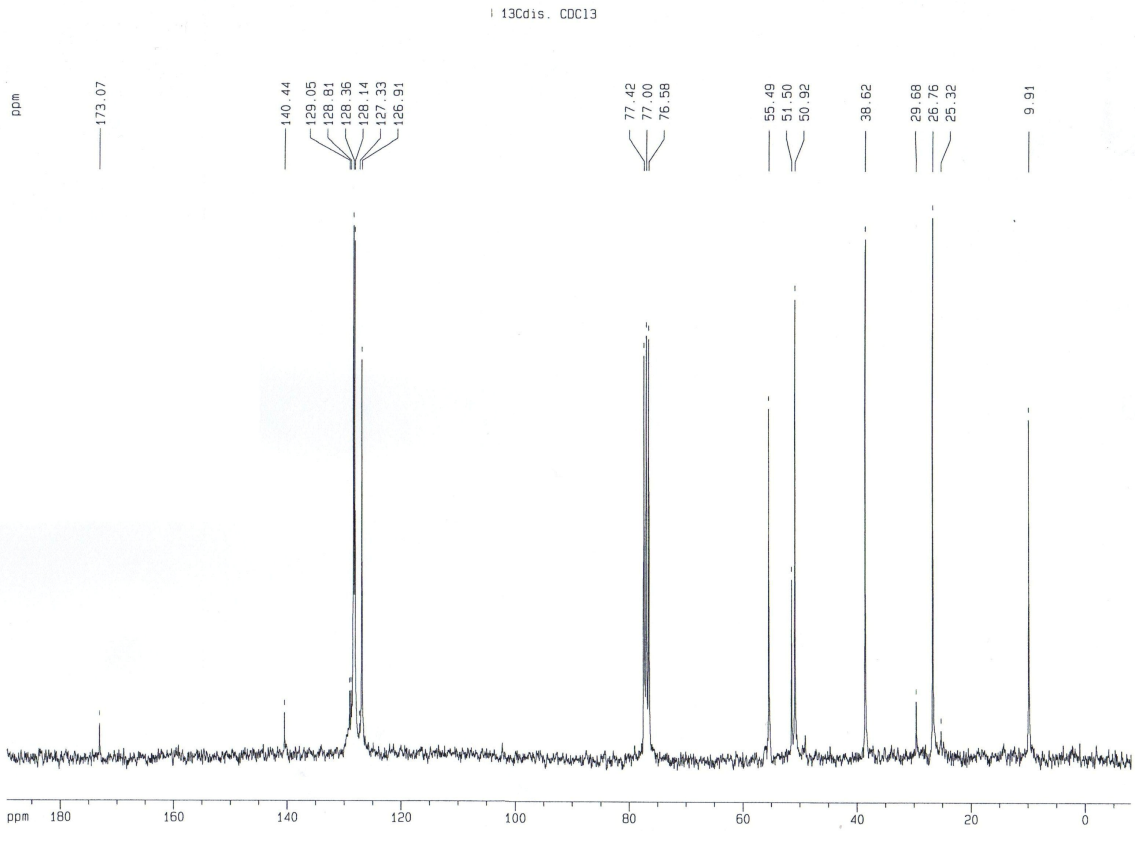
16


C13
ppm
172.2
149.9
140.2
139.8
133.5
133.1
129.7
128.5
128.4
128.2
127.9
127.7
126.9
126.3
126.1
125.8
125.3
124.9
123.7
123.4
120.8
118.0
114.4
105.8
78.5
77.4
77.0
76.6
75.2
74.6
68.1
62.7
60.7
58.9
52.5
51.6
51.3
42.8
ppm
160
140
120
100
80
60
40
20

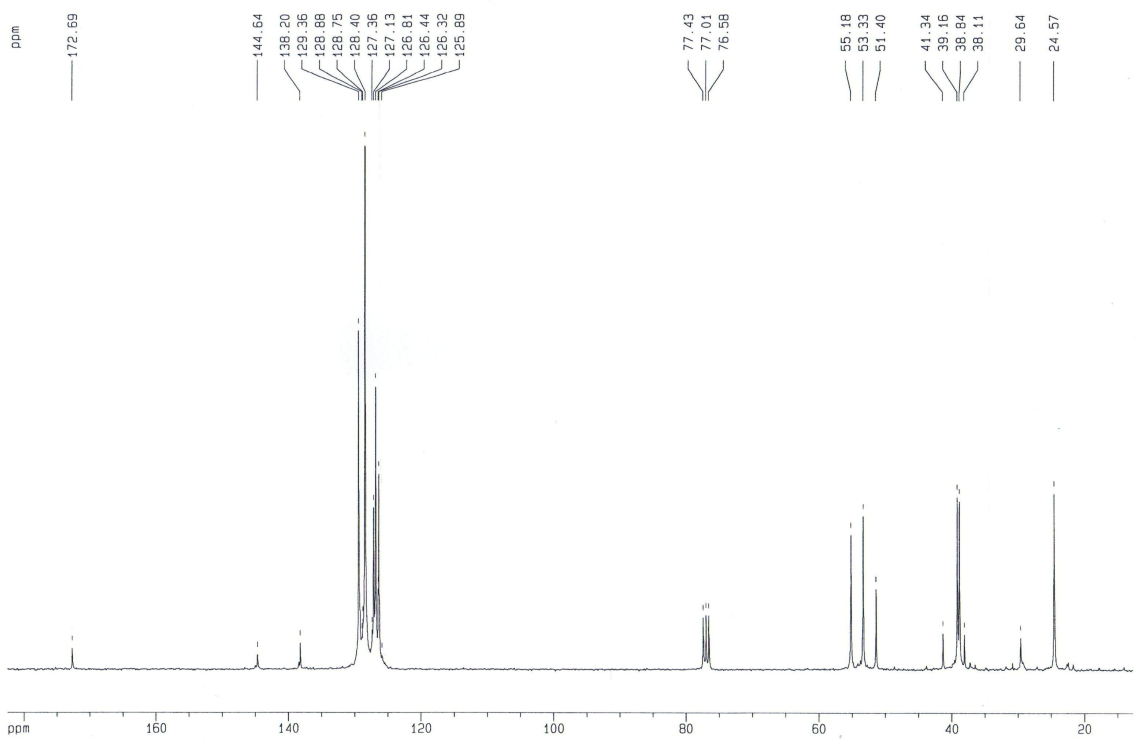
18


C13
ppm
171.9
144.0
138.8
133.3
133.0
130.0
128.5
128.5
128.2
128.1
127.9
127.8
127.7
127.4
127.2
126.9
126.7
126.5
126.1
125.9
124.8
77.4
77.0
76.6
56.7
55.6
55.1
51.6
42.4
29.7
24.6
22.6
ppm
160
140
120
100
80
60
40
20

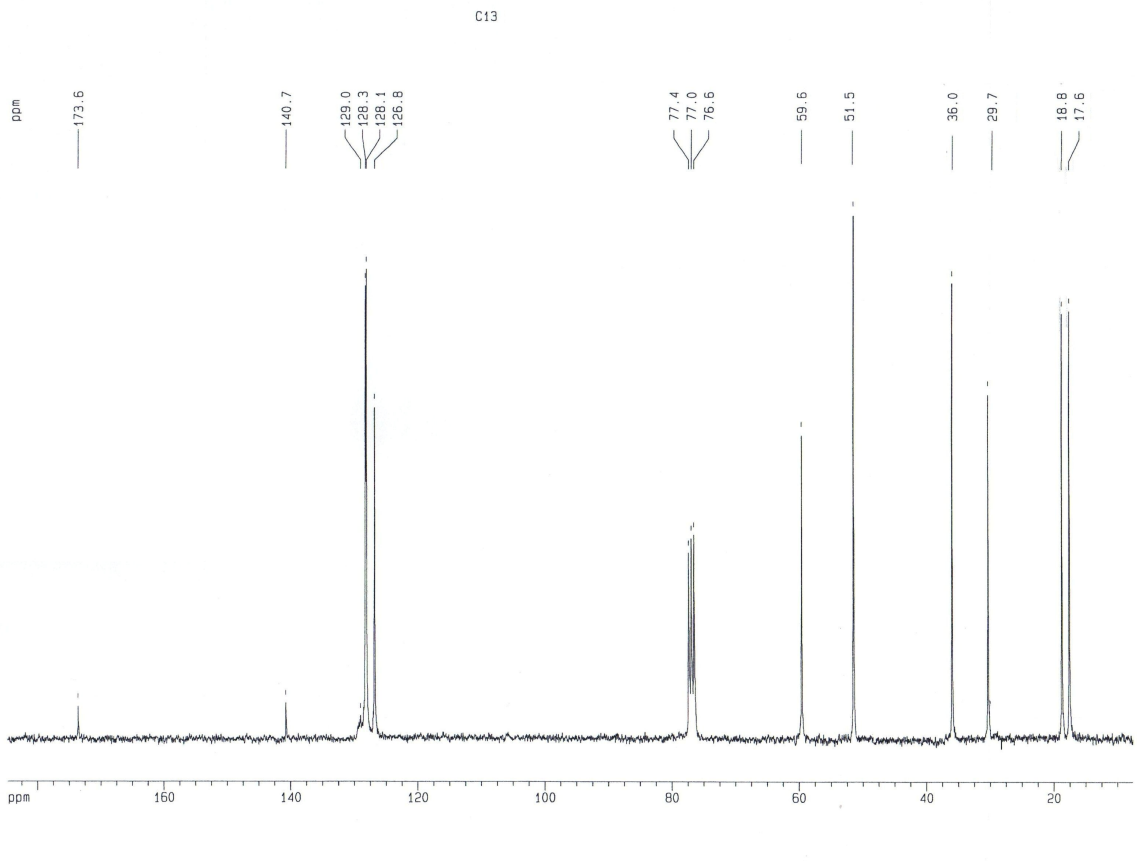
24

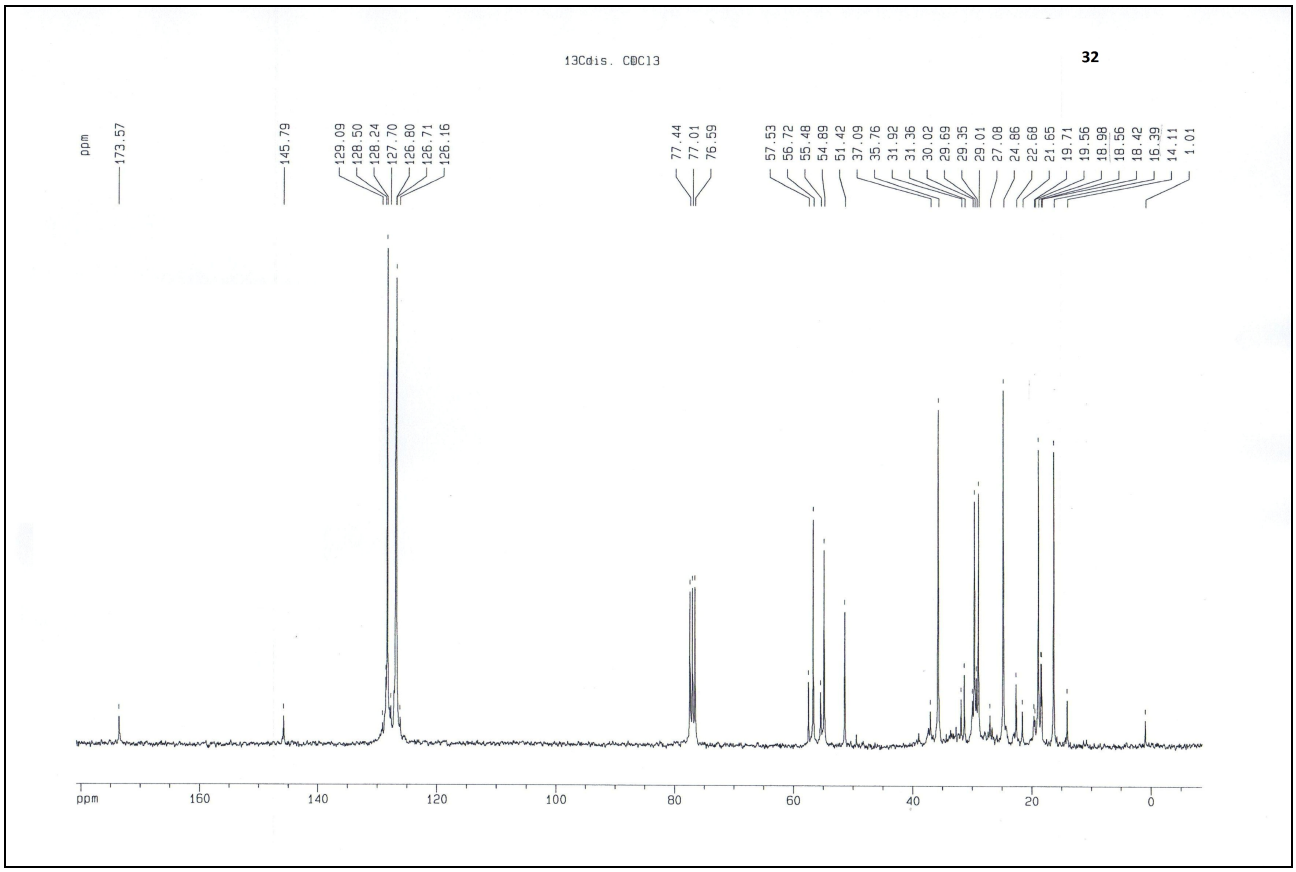

13Cdis. CDCl3
ppm
173.07
140.44
129.05
128.81
128.36
128.14
127.33
126.91
77.42
77.00
76.58
55.49
51.50
50.92
38.62
29.68
26.76
25.32
9.91
ppm
180
160
140
120
100
80
60
40
20
0

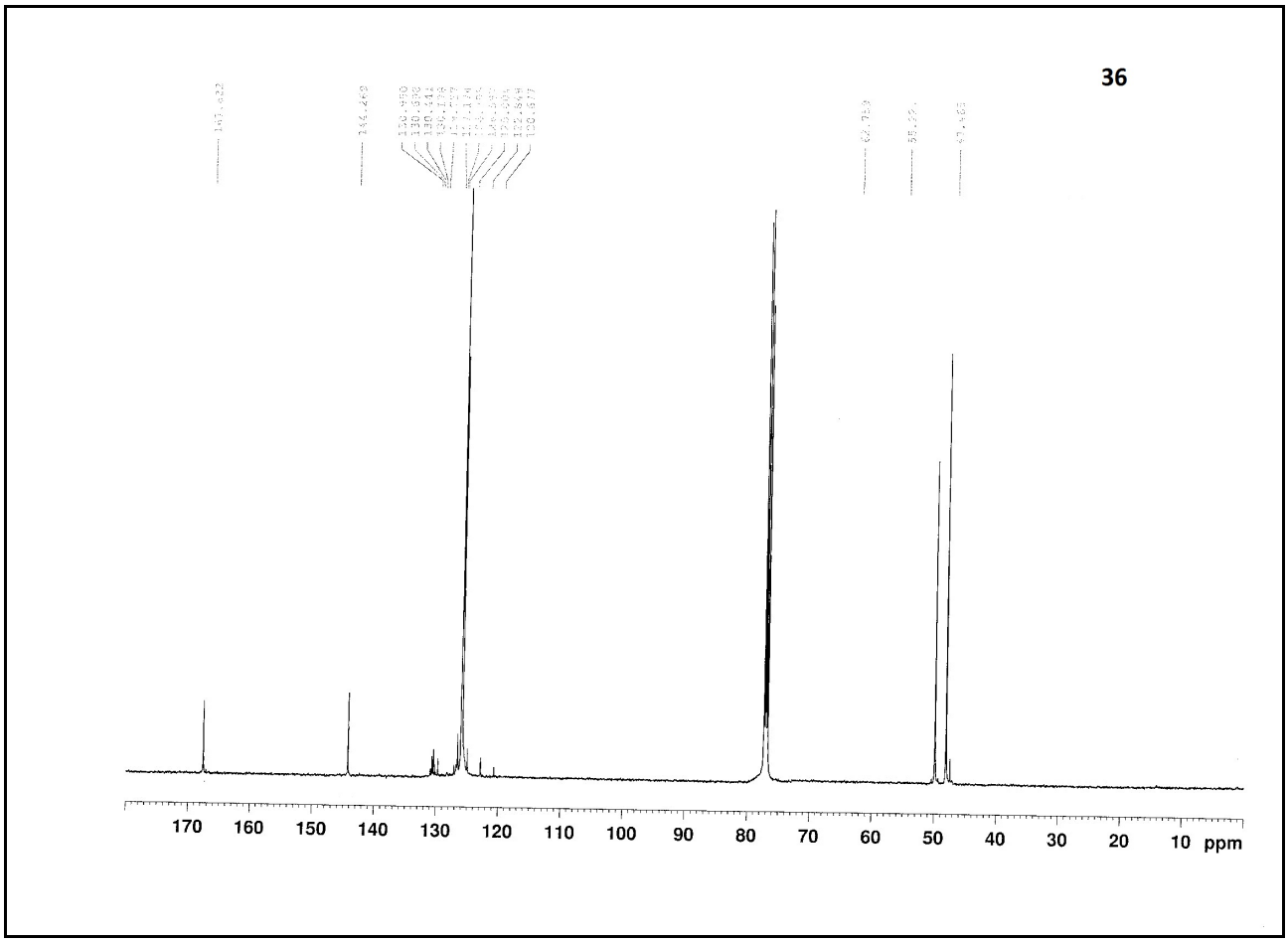
28


13Cdis. CDCl3
ppm
172.69
144.64
138.20
129.36
128.88
128.75
128.40
127.36
127.13
126.81
126.44
126.32
125.89
77.43
77.01
76.58
55.18
53.33
51.40
41.34
39.16
38.84
38.11
29.64
24.57
ppm
160
140
120
100
80
60
40
20

30


C13
ppm
173.6
140.7
129.0
128.3
128.1
126.8
77.4
77.0
76.6
59.6
51.5
36.0
29.7
18.8
17.6
ppm
160
140
120
100
80
60
40
20


13Cdis. CDCl3
32
ppm
173.57
145.79
129.09
128.50
128.24
127.70
126.80
126.71
126.16
77.44
77.01
76.59
57.53
56.72
55.48
54.89
51.42
37.09
35.76
31.92
31.36
30.02
29.69
29.35
29.01
27.08
24.86
22.68
21.65
19.71
19.56
18.98
18.56
18.42
16.39
14.11
1.01
ppm
160
140
120
100
80
60
40
20
0


36
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

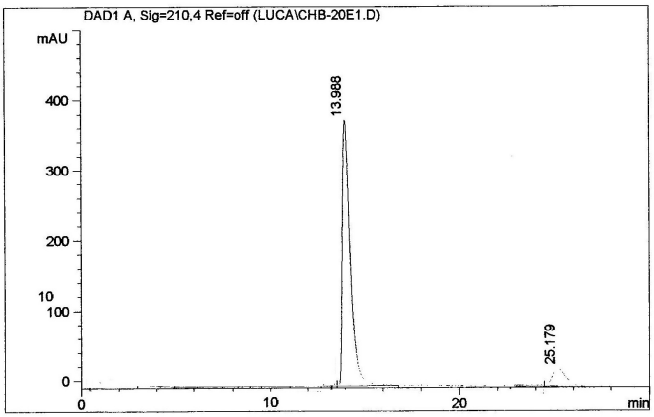
Example of a simple Report Layout

Data File name: C:\HPCHEM\1\METHODS\LUCA.M
Method name:
C:\HPCHEM\1\DATA\LUCA\CHB-20E1.D

4

data acquired by: LUCA
on: 30/03/2009
Sample Info CHB -20 efe

chiralcel OD, Hex/IPA 96:4 0.8 ml/min P=8 bar

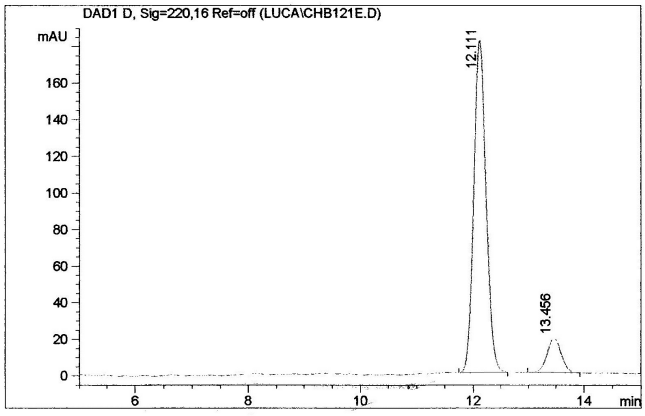


Example of a simple Report Layout

8

Data File name: C:\HPCHEM\1\METHODS\LUCA.M
Method name:
C:\HPCHEM\1\DATA\LUCA\CHB121E.D

data acquired by: FRA
on: 02/07/2009
Sample Info CHB 121 EFE
CHIRALCELL OD-H Hex/IPA 9:1 0.5 ml/min 18 bar

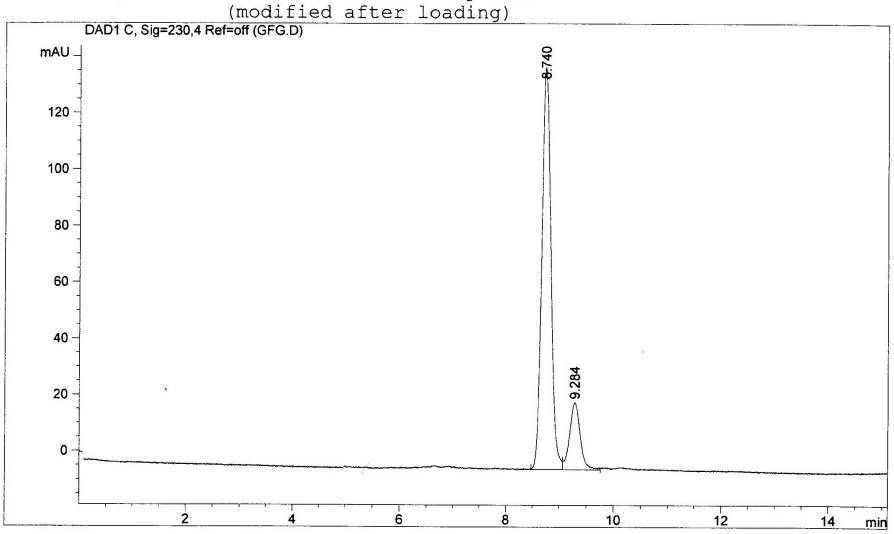


Data File C:\HPCHEM\1\DATA\GFG.D Sample Name: gfg ad10ipa

==========

Injection Date : 17/06/10 15.39.31
Sample Name : gfg adlipa Vial : 1
Acq. Operator : cece
Acq. Method : C:\HPCHEM\1\METHODS\CECE.M
Last changed : 17/06/10 15.12.36 by cece
(modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\CECE.M
Last changed : 17/06/10 15.55.27 by cece
(modified after loading)

12

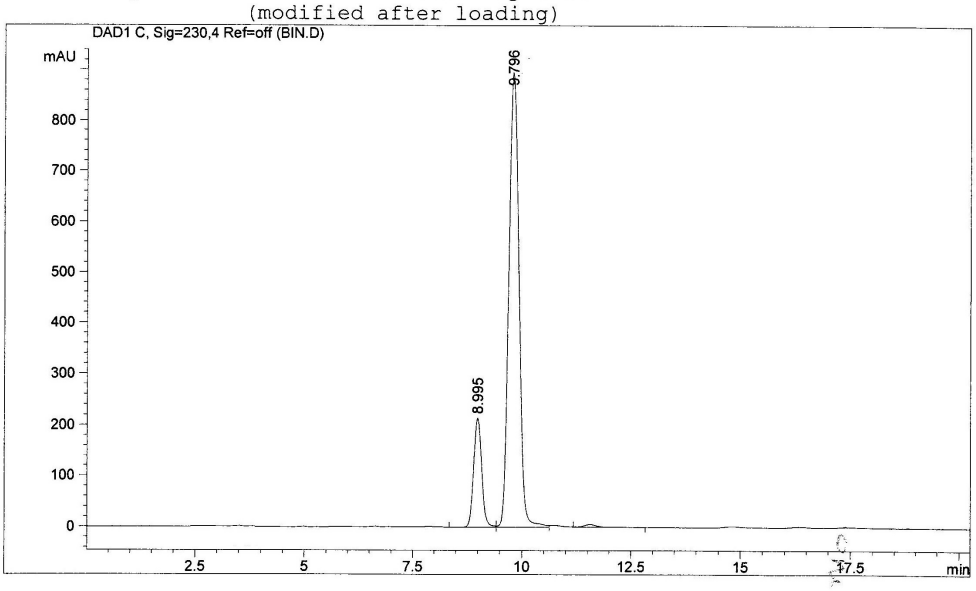


Data File C:\HPCHEM\1\DATA\BIN.D Sample Name: bin ad10ipa

==========

Injection Date : 17/06/10 16.01.15
Sample Name : bin ad10ipa Vial : 1
Acq. Operator : cece
Method : C:\HPCHEM\1\METHODS\CECE.M
Last changed : 17/06/10 15.55.27 by cece
(modified after loading)

16

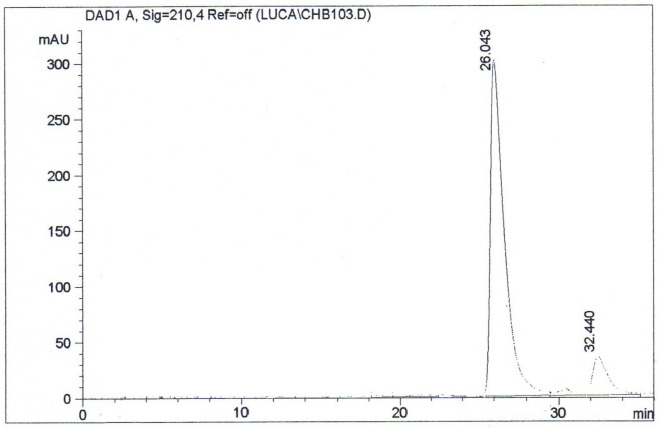


Example of a simple Report Layout

Data File name: C:\HPCHEM\1\METHODS\LUCA.M
Method name:
C:\HPCHEM\1\DATA\LUCA\CHB103.D

19

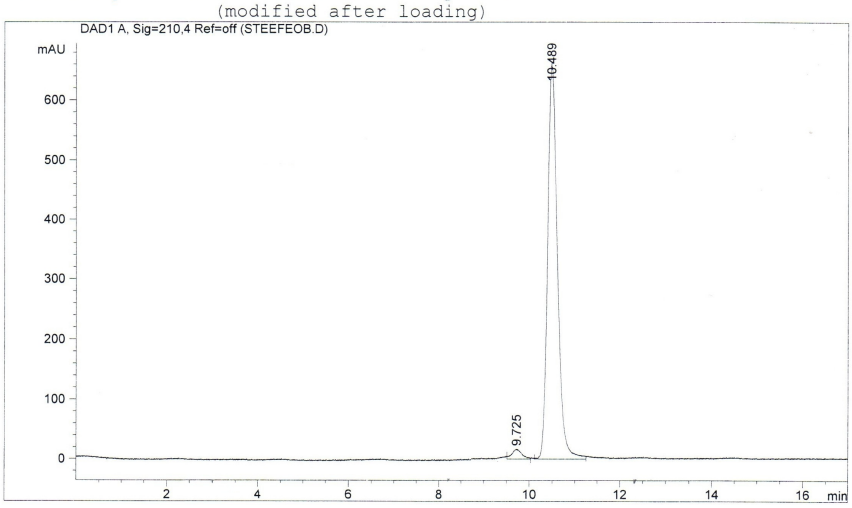
data acquired by: LUCA
on: 12/06/2009
Sample Info CHB 103
CHIRALPAK OD-H Hex/EtOH 98:2 0.8 ml/min P=28 bar



Data File C:\HPCHEM\1\DATA\STEEFEOB.D Sample Name: efeoa ad10ipa

Injection Date : 20/05/10 10.38.58
Sample Name : efeoa ad10ipa Vial : 1
Acq. Operator : cece
Acq. Method : C:\HPCHEM\1\METHODS\CECE.M
Last changed : 20/05/10 10.37.44 by cece
(modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\CECE.M
Last changed : 20/05/10 11.09.51 by cece
(modified after loading)

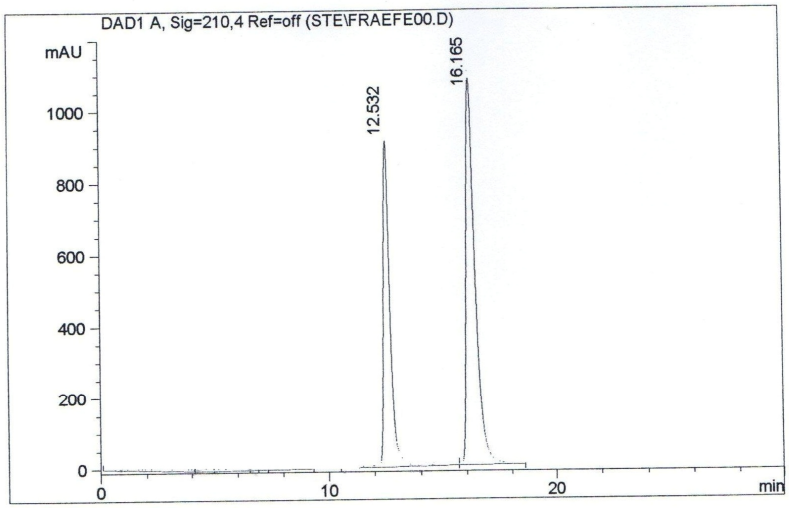
20



ıta File name: C:\HPCHEM\1\METHODS\LUCA.M
ethod name:
C:\HPCHEM\1\DATA\STE\FRAEFE00.D

24

data acquired by: Ste
on: 22/05/2009
Sample Info frabinefealcel OD Hex/IPA 99:1 0.8 ml/min P=13 bar



Data File C:\HPCHEM\1\DATA\TUBENBIN.D Sample Name: tubenzbi ad 1ipa

c

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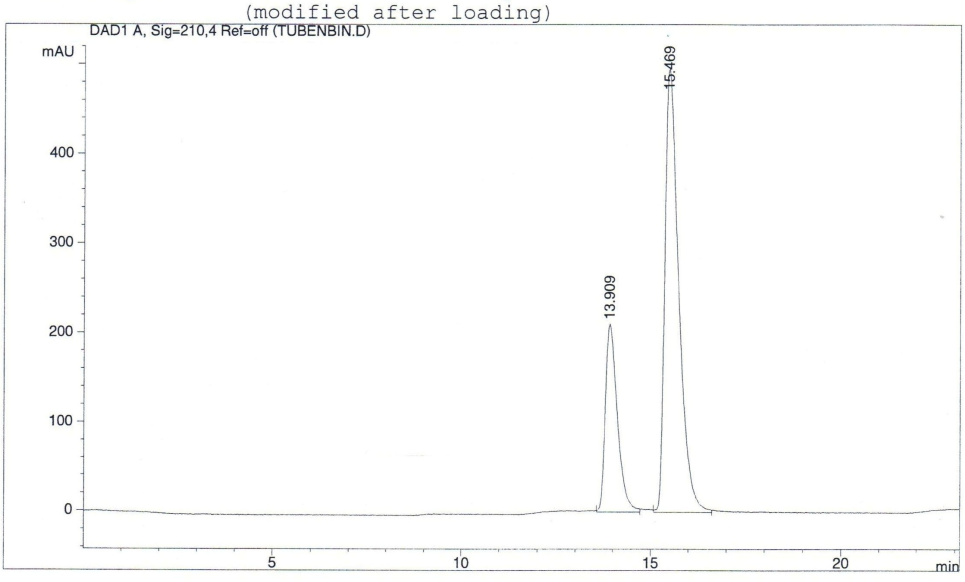
Injection Date : 05/03/09 13.51.00
Sample Name : tubenzbi ad 1ipa Vial : 1
Acq. Operator : cece
Method : C:\HPCHEM\1\METHODS\CECE.M
Last changed : 05/03/09 12.15.36 by cece
(modified after loading)

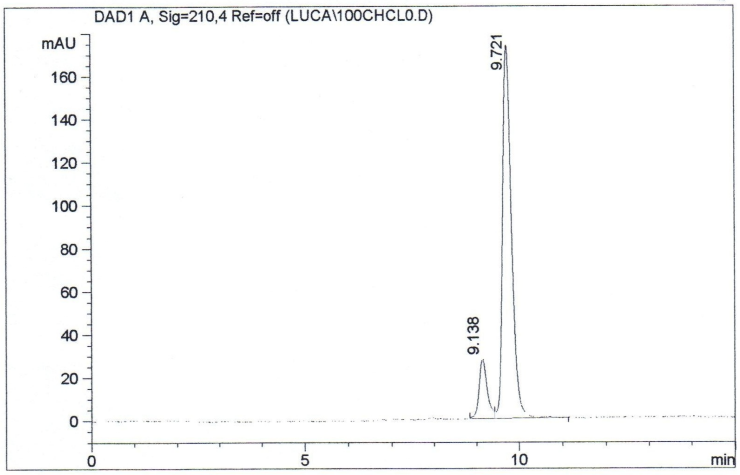
26



Example of a simple Report Layout

Data File name: C:\HPCHEM\1\METHODS\LUCA.M
Method name: **30**
C:\HPCHEM\1\DATA\LUCA\100CHCL0.D

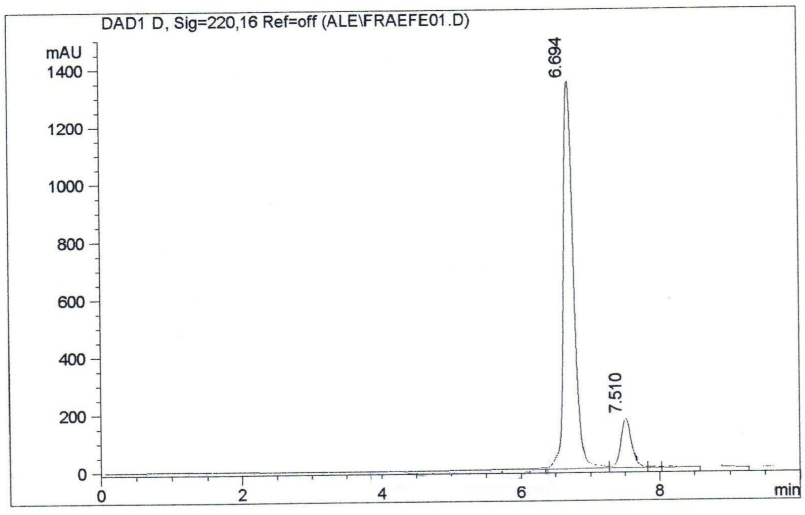
data acquired by: LUCA
on: 28/05/2009
Sample Info CHB 100 CHCl3
HIRALPAK OD-H Hex/IPA 99:1 0.8 ml/min P=27 bar



ta File name: C:\HPCHEM\1\METHODS\LUCA.M
thod name: **34**
C:\HPCHEM\1\DATA\ALE\FRAEFE01.D

ata acquired by: LUCA
n: 09/04/2009
ample Info Fraefe

chiralpack OD-H, Hex/IPA 96:4 0.8 ml/min P=25bar



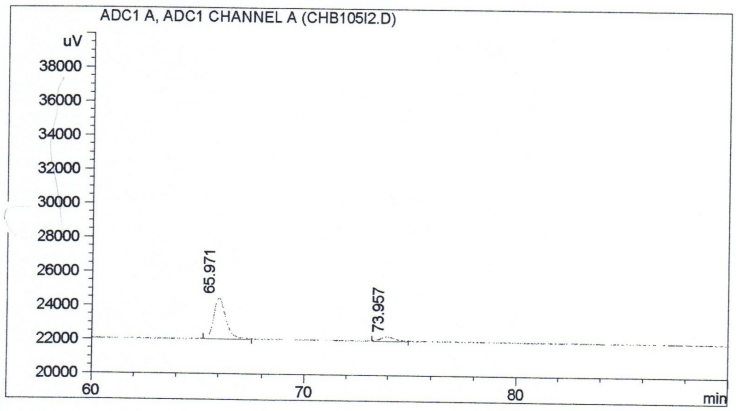
Example of a simple Report Layout

Data File name:
Method name: C:\HPCHEM\3\METHODS\DEF_GC.M

C:\HPCHEM\3\DATA\CHB105I2.D

35

data acquired by: fra
on: 09/06/2009
Sample Info chb 105 isoterma
isoterma 150



Example of a simple Report Layout

36

Data File name:
Method name: C:\HPCHEM\1\METHODS\ALE.M

C:\HPCHEM\1\DATA\ALE\BL3.D

data acquired by: Martina
on: 19/05/2010
Sample Info bl3
CHIRALCELIB 9:1 HEX/IPA 0.8 ml/min 27 bar