Electronic Supplementary Material (ESI) for Chemical Communications

Lewis Acid-Catalyzed Friedel-CraftsAlkylations of 3-Hydroxy-2-Oxindole: Approach to the core structure ofAzonazine

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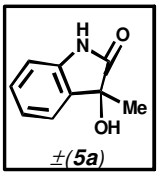
Materials and Methods

Unless otherwise stated, reactions were performed in oven-dried glassware fitted with rubber septa under a nitrogen atmosphere and were stirred with Teflon-coated magnetic stirring bars. Liquid reagents and solvents were transferred via syringe using standard Schlenk techniques. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled over sodium/benzophenoneketyl. Dichloromethane (CH_2Cl_2), toluene, and benzene were distilled over calcium hydride. All other reagents such as isatins, MeMgBr, lewis acids etc. were used as received, unless otherwise noted. Thin layer chromatography was performed using Merck Silicagel 60 F-254 precoated plates (0.25 mm) and visualized by UV irradiation, anisaldehyde stain and other stains. Silicagel from Merck (particle size 100-200 mesh) was used for flash chromatography. Melting points were recorded on a digital melting point apparatus from Jyoti Scientific (AN ISO 9001:2000) and are uncorrected.

^1H and ^{13}C NMR spectra were recorded on Bruker 400, 500 MHz spectrometers with ^{13}C operating frequencies of 100, 125 MHz, respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (δ = 7.26 for ^1H NMR and δ = 77.0 for ^{13}C NMR). Data for ^1H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, number of hydrogens). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). IR spectra were recorded on a FT-IR system (Spectrum BX) from PerkinElmer spectrometer and are reported in frequency of absorption (cm^{-1}). Only selected IR absorbencies are reported. High resolution mass spectral data were obtained from the Central Instrumentation Facility (CIF) at the Indian Institute of Science Education and Research (IISER) Bhopal.

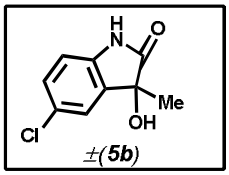
General experimental procedure for the synthesis of 3-hydroxy-2oxindoles (5a-e): A flame-dried round-bottom flask was charged with isatin [5 mmol,1.0 equiv.] in anhydrous 20 mL of THF and the round bottom flask was placed at 0 ºC. To this reaction mixture, Grignard reagent [12.5 mmol,2.5 equiv.] was added dropwise via a syringe and stirring was continued for 4-5 hours. Upon completion of the reaction (TLC showed complete conversion of starting material), the reaction mixture was quenched at 0 ºC with saturated aqueous NH_4Cl (5 mL). The whole mixture was filtered through a celite-bed and washed with diethylether. The organic layer was

evaporated under reduced pressure and the crude mixture was purified by a silica-gel column chromatography to afford 3-hydroxy-2oxindoles (**5a-e**) in good to excellent yields.



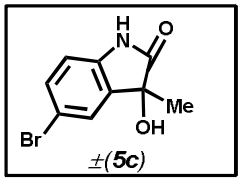
±(5a)

(±) 3-hydroxy-3-methylindolin-2-one ±(5a):92% yield,R_f = 0.42 (50% EtOAc in hexane), yellowish solid. **^{1}H NMR** (400 MHz, 0.1 mL DMSO-d_6, 0.5 mL $CDCl_3$)δ: 9.86 (s, 1H), 7.29 (d, *J*=7.2 Hz, 1H), 7.14 (t, *J*=7.64 Hz, 1H), 6.95 (m, 1H), 6.86 (d, *J*=7.68 Hz, 1H), 5.65 (m, 1H), 1.49 (br, s, 3H); **^{13}C NMR** (100 MHz, 0.1mL DMSO-d_6, 0.5 mL $CDCl_3$)δ: 181.1, 140.9, 133.3, 129.1, 123.5, 122.4, 110.4, 73.6, 24.7;**IR** (film) υ_{max} 3294, 2924, 1716, 1622, 1472, 1195, 1142, 1019 cm^{-1}; **HRMS** (ESI) 186.0528 [$(M+Na)^+$; calculated for [$C_9H_9NO_2$ + Na]$^+$: 186.0525]; **MP** 157–159 ºC.



±(5b)

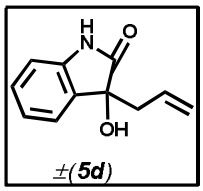
(±) 5-chloro-3-hydroxy-3-methylindolin-2-one ±(5b):66% yield,R_f = 0.45 (50% EtOAc in hexane), yellowish solid. **^{1}H NMR** (400 MHz, 0.1 mL DMSO-d_6, 0.5 mL $CDCl_3$)δ: 10.02 (s, 1H), 7.20 (br, s, 1H), 7.07 (dd, *J*= 8.24, 2.12 Hz, 1H), 6.72 (d, *J*=8.24 Hz, 1H), 5.83 (s, 1H), 1.41 (s, 3H); **^{13}C NMR** (100 MHz, 0.1mL DMSO-d_6, 0.5 mL $CDCl_3$) δ: 180.1, 139.9, 135.5, 128.6, 126.8, 123.9, 111.2, 73.4, 24.7;**IR** (film) υ_{max} 3172, 2920, 2852, 1698, 1456, 1185 cm^{-1};**HRMS** (ESI) m/z 220.0143 [$(M+Na)^+$; calculated for [$C_9H_8NO_2$ + Na]$^+$: 220.0136]; **MP** 230–235 ºC.



±(5c)

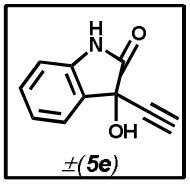
(±) 5-bromo-3-hydroxy-3-methylindolin-2-one ±(5c): 65% yield, R_f = 0.47 (50% EtOAc in hexane), yellowish solid. **^{1}H NMR** (400 MHz, 0.1mL DMSO-d_6, 0.5 mL $CDCl_3$) δ: 10.12 (s,

1H), 7.33 (br, s, 1H), 7.23 (dd, *J*=8.2, 2.04 Hz, 1H), 6.70 (dd, *J*=8.24, 2.8 Hz, 1H), 5.89 (br, s, 1H), 1.40 (s, 3H);**^{13}C NMR** (100 MHz, 0.1mL DMSO-d_6, in 0.5 mL $CDCl_3$) δ: 179.9, 140.6, 136.0, 131.5, 126.6, 114.1, 111.8, 73.3, 24.7; **IR** (film) υ_{max} 3173, 2923, 2853, 1698, 1470, 1185 cm^{-1}; **HRMS** (ESI) m/z 263.9622 $[(M+Na)^+$; calculated for $[C_9H_8BrN_2O_2 + Na]^+$: 263.9636]; **MP** 231–234 ºC.



*±(**5d**)*

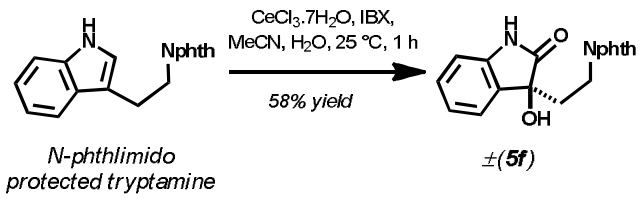
(±) 3-allyl-3-hydroxyindolin-2-one ±(5d): 69% yield, R_f = 0.48 (50% EtOAc in hexane), yellowish solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.89 (s, 1H), 7.36 (d, *J*=7.24 Hz, 1H), 7.07 (t, *J*=7.4 Hz, 1H), 6.89 (d, *J*=7.64 Hz, 1H), 5.65 (m, 1H), 5.65 (m, 1H), 5.10 (m, 2H), 4.02 (s, 1H), 2.75 (m, 1H), 2.63 (m, 1H);**^{13}C NMR** (100 MHz, $CDCl_3$) δ: 180.7, 140.4, 130.4, 130.3, 129.6, 124.4, 123.1, 120.4, 110.5, 76.5, 42.7; **IR** (film) υ_{max} 3321, 1716, 1274, 1187, 1110, 921, 747 cm^{-1};**HRMS** (ESI) m/z 188.0703 $[(M–H)^+$; calculated for $[C_{11}H_{10}NO_2]^+$: 188.706]; **MP** 109–113 ºC.



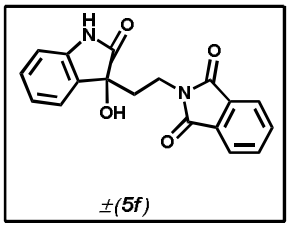
*±(**5e**)*

(±) 3-ethynyl-3-hydroxyindolin-2-one ±(5e): 69% yield, R_f = 0.49 (50% EtOAc in hexane), yellowish solid. **^{1}H NMR** (400 MHz, 0.1mL DMSO-d_6, 0.5mL $CDCl_3$) δ: 9.90 (s, 1H), 7.38 (d, *J*=7.4 Hz,1H), 7.14 (td, *J*=7.72, 1.24 Hz, 1H), 6.94 (td, *J*=7.56, 0.84 Hz, 1H), 6.80 (d, *J*=7.72 Hz, 1H), 6.47 (s, 1H), 2.56 (br, s, 1H);**^{13}C NMR** (100 MHz, 0.1 mL DMSO-d_6, in 0.5 ml $CDCl_3$) δ: 170.6, 136.4, 125.5, 125.2, 119.7, 117.9, 105.8, 76.8, 69.1, 64.2; **IR** (film) υ_{max} 3290, 2925, 2856, 1698, 1622, 1470, 1183, 1019 cm^{-1}; **HRMS** (ESI) m/z 196.0355 $[(M+Na)^+$; calculated for $[C_{10}H_7NO_2 + Na]^+$: 196.0369]; **MP** 185–190 ºC.

Experimental procedure for the preparation of(±) 2-(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)isoindoline-1,3-dione:



A round-bottom flask was charged with *N*-phthalimido protected tryptamine (5 mmol,1.0 equiv.) in MeCN and H_2O (9:1) then it was placed at 0 ºC. IBX (12.5 mmol,2.5 equiv.) was added in one portion followed by the addition of cerious(III)chloride heptahydrate and then stirring was continued for 1 h. Upon completion of the reaction (judged by TLC), the reaction mixture was quenched at 0 ºC with saturated aqueous $NaHCO_3$ (15 mL for 5 mmol). Then the reaction mixture was diluted with 100 mL of CH_2Cl_2. The whole reaction mixture was taken in a separatory funnel and extracted with CH_2Cl_2 (50 mL x 2). The organic filtrate was dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude products were purified by flash chromatography (2:1-1:1 hexanes/EtOAc) to afford compound ±(**5f**) in58% yield.

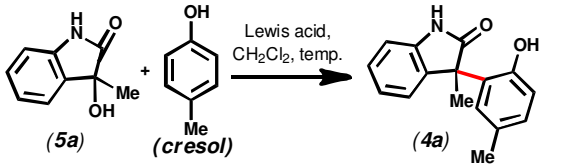


(±) 2-(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)isoindoline-1,3-dione±(5f): 58% yield, R_f = 0.39 (75% EtOAc in hexane), colorless solid. **^{1}H NMR** (400 MHz, 0.1 mL DMSO-d_6, 0.5 mL $CDCl_3$) δ: 10.05 (br,s, 1H), 7.68 (m, 4H), 7.26 (m, 1H), 7.03 (m, 1H), 6.80 (m, 1H), 6.73 (m, 1H), 5.88 (br, s,1H), 3.74 (m, 1H), 3.66 (m, 1H), 2.25 (m, 1H), 2.13 (m, 1H);**^{13}C NMR** (100 MHz, 0.1 mL DMSO-d_6, 0.5 mL $CDCl_3$) δ: 179.2, 167.7, 141.8, 134.0, 132.0, 131.5, 129.1, 124.0, 122.9, 121.9, 110.2, 74.7, 35.7, 33.0; **IR** (film) υ_{max} 3348, 1713, 1678, 1620, 1470, 1404, 1281, 1196, 1115, 1022, 899,710 cm^{-1}; **HRMS** (ESI) m/z 345.0845 [$(M+Na)^+$; calculated for [$C_{18}H_{14}N_2O_4$ + Na]$^+$: 345.0851]; **MP** 165–167 ºC.

General experimental procedure for Friedel-Creaft's alkylations using 3-hydroxy-2-oxindoles in presence of Lewis acids:

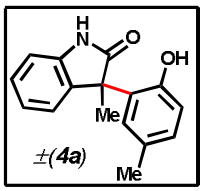
A flame-dried round-bottom flask was charged with 3-alkyl-3-hydroxy-2-oxindole (0.5 mmol, 1.0 equiv.) in dichloromethane. To this Lewis acid (10-50 mol%) was added and stirred at rt for 5 minutes. Then 4-substituted phenol (1.5 mmol, 3.0 equiv.) was added to the reaction mixture.The reaction mixture wasthen stirred at rt for 5 minutes and then it was heated under refluxed at 45 ºC for indicated time. Upon completion of the reaction (TLC showed complete consumption of starting material), the reaction mixture was cooled to room temperature. Most of the volatile components were evaporated under reduced pressure and the crude materials were purified by flash chromatography using EtOAc and petroleum ether as eluents to afford Friedel-Craft's alkylated products (**4**).

Table 1: Optimization with Lewis acids as catalyst.



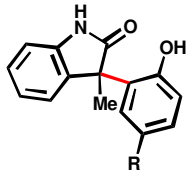
entry	Lewis acid	eqiuv.[a]	temp.	time	yield[b,c]
1.	$Sc(OTf)_3$	50 mol%	25 ºC	24 h	10%
2.	$In(OTf)_3$	50 mol%	25 ºC	24 h	46%
3.	$Zn(OTf)_2$	50 mol%	25 ºC	24 h	*traces*
4.	$Zn(OTf)_2$	25 mol%	45 ºC	12 h	*traces*
5.	$Cu(OTf)_2$	50 mol%	25 ºC	24 h	24%
6.	$Sn(OTf)_2$	50 mol%	25 ºC	18 h	42%
7.	$FeCl_3$	50 mol%	25 ºC	24 h	40%
8.	$In(OTf)_3$	50 mol%	45 ºC	4 h	95%
9.	$In(OTf)_3$	25 mol%	45 ºC	5 h	92%
10.	**$In(OTf)_3$**	**10 mol%**	**45 ºC**	**7 h**	**92%**
11.	$FeCl_3$	50 mol%	45 ºC	18 h	56%
13.	$Ce(OTf)_3$	50 mol%	45 ºC	12 h	90%
14.	$Ce(OTf)_3$	25 mol%	45 ºC	12 h	82%
14.	$Ce(OTf)_3$	10 mol%	45 ºC	16 h	53%
15.	$Cu(OTf)_2$	50 mol%	45 ºC	12 h	92%
16.	$Cu(OTf)_2$	25 mol%	45 ºC	14 h	91%
17.	**$Cu(OTf)_2$**	**10 mol%**	**45 ºC**	**12 h**	**91%**
18.	$Bi(OTf)_3$	50 mol%	25 ºC	12 h	94%
19.	$Bi(OTf)_3$	25 mol%	45 ºC	12 h	93%
20.	**$Bi(OTf)_3$**	**10 mol%**	**45 ºC**	**10 h**	**94%**
21.	$Sn(OTf)_2$	50 mol%	45 ºC	14 h	86%
22.	$Sn(OTf)_2$	25 mol%	45 ºC	14 h	79%
22.	$Sn(OTf)_2$	10 mol%	45 ºC	15 h	65%

[a]Reactions were carried out on a 0.50mmol of **4** with 1.50 mmol of cresol in 6 mL of dichloromethane at rt or 45 °C, unless noted otherwise. [b]Isolated yields after column chromatography.

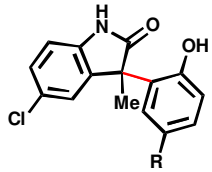


(±) 3-(2-hydroxy-5-methylphenyl)-3-methylindolin-2-one ±(4a): Colorless solid, R_f= 0.64 (50% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 9.09 (s, 1H), 8.80 (s, 1H), 7.28 (m, 2H), 7.17 (m, 1H), 6.98 (m, 2H), 6.93 (m, 1H), 6.85 (d, *J*=8.08 Hz, 1H), 2.22 (s, 3H), 1.89 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 184.9, 153.6, 139.8, 133.7, 129.8, 129.4, 128.4, 128.3, 125.4, 125.2, 123.1, 119.1, 110.7, 52.9, 22.7, 20.7; **IR** (film) υ_{max} 3290, 2970, 2924, 1685, 1682, 1620, 1512, 1454, 1419, 1373, 1334, 1269, 1196, 1130, 818, 752 cm^{-1}; **HRMS** (ESI) m/z 254.1172 [$(M+H)^+$; calculated for $[C_{16}H_{16}NO_2]^+$: 254.1176]; **MP** 108−112 ºC.

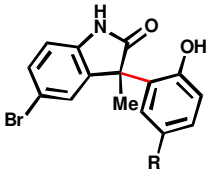
Figure 2: Substrates Scope.



*R = Me (**4a**), 94%, 7h (**A**: 10 mol% cat.)*
*R = Me (**4a**), 92%, 12h (**B**: 10 mol% cat.)*
*R = Me (**4a**), 91%, 10h (**C**: 10 mol% cat.)*
*R = Me (**4a**), 90%, 6h (**D**: 50 mol% cat.)*
*R = ^{t}Bu (**4b**), 63%, 16h (**A**: 10 mol% cat.)*
*R = ^{t}Bu (**4b**), 52%, 18h (**B**: 10 mol% cat.)*
*R = ^{t}Bu (**4b**), 85%, 15h (**C**: 10 mol% cat.)*
*R = ^{t}Bu (**4b**), 89%, 12h (**D**: 50 mol% cat.)*



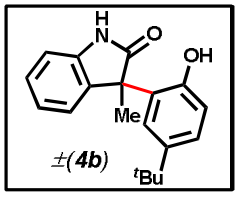
*R = Me (**4c**), 86%, 18h (**A**: 25 mol% cat.)*
*R = Me (**4c**), 87%, 18h (**B**: 25 mol% cat.)*
*R = Me (**4c**), 82%, 16h (**C**: 25 mol% cat.)*
*R = Me (**4c**), 75%, 12h (**D**: 50 mol% cat.)*
*R = ^{t}Bu (**4d**), 61%, 17h (**A**: 25 mol% cat.)*
*R = ^{t}Bu (**4d**), 85%, 18h (**B**: 50 mol% cat.)*
*R = ^{t}Bu (**4d**), 63%, 18h (**C**: 25 mol% cat.)*
*R = ^{t}Bu (**4d**), 84%, 12h (**D**: 50 mol% cat.)*



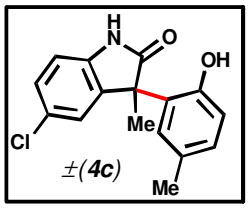
*R = Me (**4e**), 60%, 15h (**A**: 25 mol% cat.)*
*R = Me (**4e**), 63%, 15h (**B**: 25 mol% cat.)*
*R = Me (**4e**), 88%, 15h (**C**: 25 mol% cat.)*
*R = Me (**4e**), 72%, 12h (**D**: 50 mol% cat.)*
*R = ^{t}Bu (**4f**), 56%, 15h (**A**: 25 mol% cat.)*
*R = ^{t}Bu (**4f**), 84%, 16h (**B**: 25 mol% cat.)*
*R = ^{t}Bu (**4f**), 90%, 15h (**C**: 25 mol% cat.)*
*R = ^{t}Bu (**4f**), 70%, 12h (**D**: 50 mol% cat.)*

***Condition A**: $In(OTf)_3$*
***Condition B**: $Cu(OTf)_2$*
***Condition C**: $Bi(OTf)_3$*
***Condition D**: $BF_3.OEt_2$*

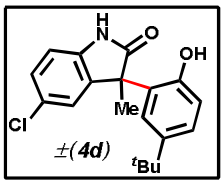
[a]Reactions were carried out on a 0.50mmol of 3-alkyl-3-hydroxy-2-oxindole derivatives with 1.50mmol of cresol or 4-*tert*-butylphenol in 6 mL of dichloromethane at 45 °C, unless noted otherwise. [b]Isolated yields after column chromatography.



(±) 3-(5-(tert-butyl)-2-hydroxyphenyl)-3-methylindolin-2-one ±(4b): Colorless gel, R_f= 0.52 (30% EtOAc in hexane). **^{1}H NMR** (400 MHz, 0.1 mL of DMSO-d_6, 0.5 mL of $CDCl_3$) δ: 9.88 (s, 1H), 9.47 (s, 1H), 7.15 (d, *J*= 2.12 Hz, 1H), 7.09 (t, *J*=7.64 Hz, 1H), 7.03 (m, 2H), 6.93 (t, *J*=7.44 Hz, 1H), 6.84 (d, *J* = 7.72 Hz, 1H), 6.67 (d, *J*=8.36 Hz, 1H), 1.7 (s, 3H), 1.13 (s, 9H); **^{13}C NMR** (100 MHz, 0.1 mL of DMSO-d_6, 0.5 mL of $CDCl_3$) δ: 184.2, 153.4, 141.9, 141.0, 134.7, 127.6, 125.5, 125.1, 124.6, 124.3, 122.0, 117.4, 110.2, 52.4, 34.1, 31.5, 23.0; **IR** (film) υ_{max} 3460, 3348, 2256, 1647, 1010, 999, 825, 764 cm^{-1}; **HRMS** (ESI) m/z 318.1462 $[(M+H)^+$; calculated for $[C_{19}H_{21}NO_2]^+$: 318.1465]; **MP** 215–218 ºC.

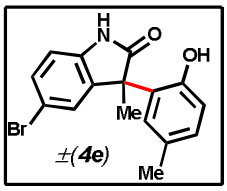


(±) 5-chloro-3-(2-hydroxy-5-methylphenyl)-3-methylindolin-2-one±(4c): Colorless gel, R_f= 0.52 (30% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.80 (s, 1H), 8.15 (s, 1H), 7.09-7.12 (m, 2H), 7.03 (d, *J*=1.64 Hz, 1H), 6.95 (dd, *J*=8.08, 1.52 Hz, 1H), 6.73 (d, *J* = 8.16 Hz, 1H), 6.68 (d, *J*=8.08 Hz, 1H), 2.29 (s, 3H), 1.82 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 184.7, 152.5,138.4, 136.2, 129.9, 129.7, 128.3, 128.1, 128.0, 125.0, 124.8, 118.1, 111.4, 52.4, 22.9, 20.8; **IR** (film) υ_{max} 3283, 2924, 2854, 2357, 1693, 1620, 1477, 1192, 995, 814, 737 cm^{-1}; **HRMS** (ESI) m/z 310.0601 $[(M+Na)^+$; calculated for $[C_{16}H_{14}ClNO_2 + Na]^+$: 310.0605].

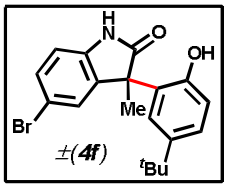


(±)3-(5-(tert-butyl)-2-hydroxyphenyl)-5-chloro-3-methylindolin-2-one ±(4d): Colorless gel, R_f= 0.50 (30% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ:8.61 (s, 1H), 8.42 (s, 1H), 7.20 (s, 2H), 7.17 (m, 2H), 6.82 (d, *J* = 8.24 Hz, 1H), 6.79 (d, *J* = 7.68 Hz, 1H), 1.87 (s, 3H), 1.28 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 184.6, 152.8, 143.1, 138.3, 135.9, 128.3, 128.2, 126.4,

125.3, 124.5, 124.1, 118.2, 111.5, 53.0, 34.3, 31.5, 22.9; **IR** (film) υ_{max}3314, 2924, 2858, 2322, 1697, 1612, 1473, 1273, 1199, 1123, 903, 818, 748 cm^{-1}; **HRMS** (ESI) m/z 352.1071 $[(M+Na)^+$; calculated for $[C_{10}H_{20}ClNO_2 + Na]^+$: 352.1075].

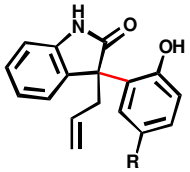


(±)5-bromo-3-(2-hydroxy-5-methylphenyl)-3-methylindolin-2-one±(4e): Colorless gel, R_f= 0.55 (40% EtOAc in hexane). **^{1}H NMR** (400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) δ:10.45 (s, 1H), 9.10 (s, 1H), 2.27-7.30 (m, 2H), 6.91-6.94 (m, 2H), 6.80 (d, *J* = 8.20 Hz, 1H), 6.54 (d, *J* = 8.04 Hz, 1H), 2.29 (s, 3H), 1.56 (s, 3H), [3.37 (br, DMSO)]; **^{13}C NMR** (100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) δ:181.6, 152.9, 142.0, 139.4, 130.0, 129.1, 128.8, 127.5, 127.0, 125.5, 115.4, 113.1, 111.2, 50.4, 23.7, 20.9; **IR** (film) υ_{max}3525, 2897, 2360, 2252, 1647, 1001, 995, 825, 763 cm^{-1}; **HRMS** (ESI) m/z 354.0088 $[(M+Na)^+$; calculated for $[C_{16}H_{14}BrNO_2 + Na]^+$: 354.0100].

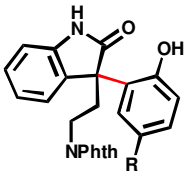


(±) 5-bromo-3-(5-(tert-butyl)-2-hydroxyphenyl)-3-methylindolin-2-one ±(4f): Colorless gel, R_f= 0.56 (40% EtOAc in hexane). **^{1}H NMR** (400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) δ: 9.87 (s, 1H), 8.84 (s, 1H), 7.22 (m, 1H), 7.12-7.15 (m, 1H), 7.00-7.04 (m, 1H), 6.94 (m, 1H), 6.66-6.70 (m, 1H), 6.56-6.58 (m, 1H), 1.63 (s, 3H), 1.18 (s, 9H); **^{13}C NMR** (100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) δ: 183.1, 152.7, 141.7, 140.6, 138.1, 130.0, 126.4, 125.6, 125.0, 124.3, 116.2, 114.1, 111.2, 51.6, 34.1, 31.6, 23.2; **IR** (film) υ_{max} 3426, 2126, 1643, 1269, 1010, 991, 891, 756 cm^{-1}; **HRMS** (ESI) m/z 396.0589 $[(M+Na)^+$; calculated for $[C_{19}H_{20}BrNO_2 + Na]^+$: 396.0570].

Figure 3: Substrates Scope.

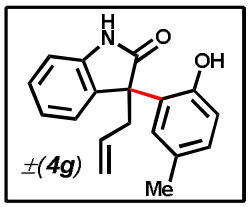


*R = Me (**4g**), 60%, 18h (**A**: 25 mol% cat.)*
*R = Me (**4g**), 93%, 18h (**B**: 25 mol% cat.)*
*R = Me (**4g**), 82%, 18h (**C**: 25 mol% cat.)*
*R = Me (**4g**), 90%, 12h (**D**: 50 mol% cat.)*
*R = ^{t}Bu (**4h**), 50%, 16h (**A**: 40 mol% cat.)*
*R = ^{t}Bu (**4h**), 84%, 16h (**B**: 40 mol% cat.)*
*R = ^{t}Bu (**4h**), 92%, 16h (**C**: 40 mol% cat.)*
*R = ^{t}Bu (**4h**), 94%, 12h (**D**: 50 mol% cat.)*

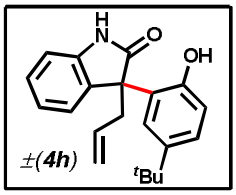


*R = Me (**4i**), 62%, 16h (**A**: 25 mol% cat.)*
*R = Me (**4i**), 71%, 16h (**B**: 25 mol% cat.)*
*R = Me (**4i**), 80%, 16h (**C**: 25 mol% cat.)*
*R = Me (**4i**), 75%, 12h (**D**: 50 mol% cat.)*
*R = ^{t}Bu (**4j**), 82%, 18h (**A**: 25 mol% cat.)*
*R = ^{t}Bu (**4j**), 78%, 18h (**B**: 25 mol% cat.)*
*R = ^{t}Bu (**4j**), 84%, 18h (**C**: 25 mol% cat.)*
*R = ^{t}Bu (**4j**), 76%, 12h (**D**: 50 mol% cat.)*

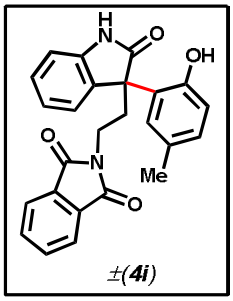
[a]Reactions were carried out on a 0.50mmol of **5** with 1.50 mmol of cresol in 6 mL of dichloromethane at 45 °C, unless noted otherwise. [b]Isolated yields after column chromatography.



(±) 3-allyl-3-(2-hydroxy-5-methylphenyl)indolin-2-one ±(4g): Colorless gel, R_f= 0.48 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 9.86 (s, 1H), 8.83 (s, 1H), 7.38 (d, *J* = 7.44 Hz, 1H), 7.35 (td, *J* = 7.72, 1.02 Hz, 1H), 7.24 (td, *J* = 7. 6, 0.96 Hz, 1H), 7.02 (m, 2H), 6.94 (m, 1H), 6.87 (d, *J*=1.76 Hz, 1H), 5.33-5.42 (m, 1H), 5.06 (dd, *J* = 16.92, 1.24 Hz, 1H), 4.95 (m, 1H), 3.43 (dd, *J* = 13.76, 8.2 Hz, 1H), 2.99 (dd, *J* = 13.72, 6.32 Hz, 1H), 2.20 (s, 3H) [EtOAc: 4.16 (q, *J* = 7.16 Hz, 2H), 2.08 (s, 3H), 1.29 (t, *J* = 13.72, 6.28 Hz, 1H), 2.19 (s, 3H) ; **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 183.6, 154.2, 140.2, 131.8, 130.7, 130.1, 129.4, 128.9, 128.6, 126.6, 123.5, 123.0, 119.9, 119.7, 110.8, 58.1, 39.4, 20.7; **IR** (film) υ_{max} 3260, 2959, 2666, 2360, 2334, 1681, 1620, 1473, 1342, 1269, 1238, 1192, 1130, 918 cm^{-1}; **HRMS** (ESI) m/z 302.1154 $[(M+Na)^+$; calculated for $[C_{18}H_{17}NO_2 + Na]^+$: 302.1151].

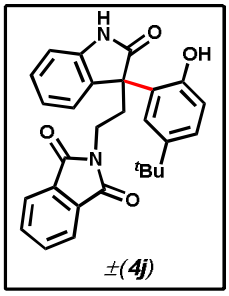


(±) 3-allyl-3-(5-(tert-butyl)-2-hydroxyphenyl)indolin-2-one ±(4h): Colorless gel, R_f= 0.60 (25% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ:10.00 (s, 1H), 9.08 (s, 1H), 7.39 (d, *J* = 7.44 Hz, 1H), 7.34 (dt, *J* = 7.72, 1.16 Hz, 1H), 7.22-7.26 (m, 2H), 7.14 (br, 1H), 7.03 (d, *J* = 7.60 Hz, 1H), 6.99 (d, *J* = 8.36 Hz, 1H), 5.34-5.41 (m, 1H), 5.06 (dd, *J* = 16.96, 1.24 Hz, 1H), 4.95 (dd, *J* = 10.12, 1.76 Hz, 1H), 3.48 (dd, *J* = 13.80, 8.16 Hz, 1H), 2.97 (dd, *J* = 13.76, 6.28 Hz, 1H), 1.20 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 183.7, 154.0, 142.8, 140.3, 131.9, 130.7, 128.6, 126.5, 126.4, 125.5, 122.84, 122.83, 119.7, 119.5, 110.9, 58.6, 39.5, 34.3, 31.5; **IR** (film) υ_{max}3267, 3210, 2959, 2866, 1678, 1620, 1485, 1469, 1269, 1188, 1103, 910, 822, 737 cm^{-1}; **HRMS** (ESI) m/z 344.1622 [$(M+Na)^+$; calculated for $[C_{21}H_{23}NO_2 + Na]^+$: 344.1621].



±(4i)

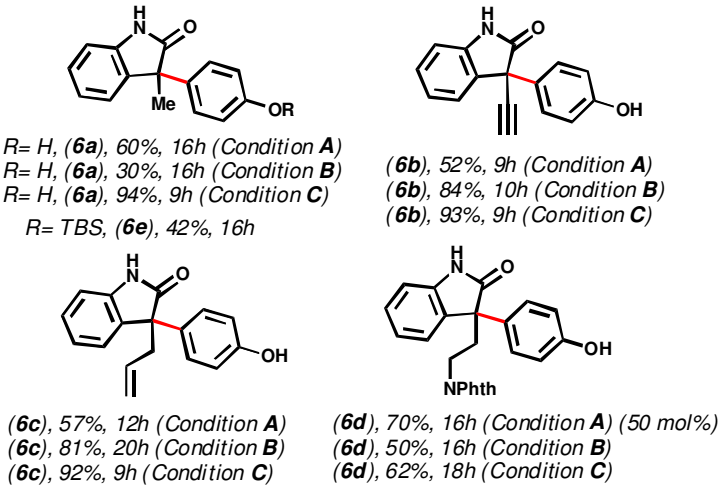
(±) 2-(2-(3-(2-hydroxy-5-methylphenyl)-2-oxoindolin-3-yl)ethyl)isoindoline-1,3-dione ±(4i): Colorless gel, R_f= 0.62 (25% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 9.69 (s, 1H), 9.05 (s, 1H), 7.70 (m, 2H), 7.59 (m, 2H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.14 (td, *J* = 7.68, 1.12 Hz, 1H), 7.05 (td, *J* = 7.56, 0.92 Hz, 1H), 6.94-6.98 (m, 2H), 6.87 (m, 1H), 6.80 (d, *J* = 1.64 Hz, 1H), 3.60-3.73 (m, 2H), 3.24 (dt, *J* = 14.32, 5.72 Hz, 1H), 2.74 (m, 1H), 2.16 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 183.3, 168.0, 154.1, 140.5, 133.8, 131.8, 130.2, 130.0, 129.4, 128.6, 128.5, 126.0, 123.6, 123.1, 123.0, 119.8, 111.3, 60.5, 56.4 (CH_2Cl_2), 34.5, 32.2, 20.6; **IR** (film) υ_{max} 3560, 3271, 2924, 1767, 1713, 1612, 1470, 1400, 1261, 1029, 752, 717 cm^{-1}; **HRMS** (ESI) m/z 435.1316 [$(M+Na)^+$; calculated for $[C_{25}H_{20}N_2O_4 + Na]^+$: 435.1315].



±(4j)

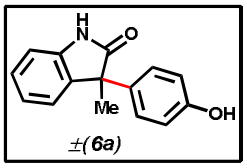
(±) 2-(2-(3-(5-(tert-butyl)-2-hydroxyphenyl)-2-oxoindolin-3-yl)ethyl)isoindoline-1,3-dione ±(4j): Colorless gel, R_f= 0.41 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 9.82 (s, 1H), 9.19 (s, 1H), 7.69 (dd, *J*=5.48, 3.04 Hz, 2H), 7.53 (dd, *J*=5.44, 3.04 Hz, 2H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.4-7.19 (m, 2H), 7.07 (dd, *J* = 7.56, 1.08 Hz, 1H), 7.05(d, *J*=2.4 Hz, 1H), 6.98 (m, 1H), 6.91 (d, *J* = 8.40 Hz, 1H), 3.61-3.75 (m, 2H), 3.25-3.32 (dt, *J* = 14.44, 5.88 Hz, 1H), 2.70 (m, 1H), 1.18 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 183.3, 167.9, 154.1, 142.8, 140.5, 133.8, 131.8, 130.1, 128.7, 126.4, 126.1, 125.1, 123.0, 122.9, 122.8, 119.5, 111.5, 56.9, 34.5, 34.3, 32.3, 31.4; **IR** (film) υ_{max} 3284, 2959, 1770, 1708, 1616, 1400, 1369, 1269, 1192, 1030, 910, 752 cm^{-1}; **HRMS** (ESI) m/z 477.1786 [$(M+Na)^+$; calculated for $[C_{28}H_{26}N_2O_4 + Na]^+$: 477.1785].

Figure 4: Substrates scope of F-C alkylations with phenol.



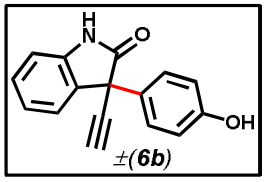
General experimental procedure for Friedel-Creaft'salkylations using 3-hydroxy-2-oxindoles in presence of Lewis acids:

A flame-dried round-bottom flask was charged with 3-alkyl-3-hydroxy-2-oxindole (0.5 mmol, 1.0 equiv.) and phenol (1.50 mmol, 3.0 equiv.) in dichloromethane. To this reaction mixture was 25 mol% of catalyst and then it was heated under refluxed at 45 ºC for 12-16 h. Upon completion of the reaction (TLC showed complete consumption of starting material), the reaction mixture was cooled to room temperature. Most of the volatile components were evaporated under reduced pressure and the crude materials were purified by flash chromatography using EtOAc and petroleum ether as eluents to afford compound (**6**).



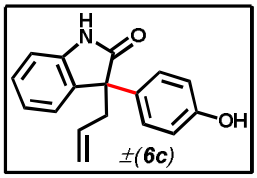
±(6a)

(±) 3-(4-hydroxyphenyl)-3-methylindolin-2-one±(6a): Colorless gel, R_f= 0.50 (40% EtOAc in hexane). **^{1}H NMR** (400 MHz, 1:1 $CDCl_3$and DMSO-d_6) δ 7.26 (m, 1H), 7.16-7.19 (m, 3H), 7.08 (m, 1H), 6.95 (d, *J* = 7.76 Hz, 1H), 6.78 (m, 2H), 1.79 (s, 3H);**IR** (film) υ_{max}3410, 3367, 1709, 1512, 1050, 1002, 825, 764cm^{-1}; **HRMS** (ESI) m/z 262.0839 [(M+Na)$^+$; calculated for [$C_{15}H_{13}NO_2$ + Na]$^+$: 262.0838].



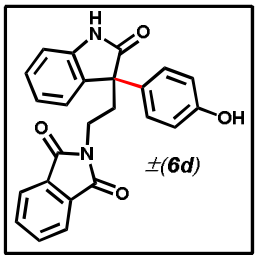
±(6b)

(±) 3-ethynyl-3-(4-hydroxyphenyl)indolin-2-one ±(6b): Colorless gel, R_f= 0.51 (40% EtOAc in hexane). **^{1}H NMR** (400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) δ:10.25 (s, 1H), 8.95 (br, 1H), 7.11-7.20 (m, 4H), 6.88-7.00 (m, 2H), 6.68-6.73 (m, 2H), 2.56 (br, s, 1H); **^{13}C NMR** (100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) δ:176.0, 157.2, 141.6, 132.5, 128.9, 128.5, 127.8, 124.8, 122.8, 115.6, 110.4, 81.9, 72.7, 51.9; **IR** (film) υ_{max} 3537, 2349, 2252, 1720, 1632, 1258, 1010, 1007, 829, 759 cm^{-1}; **HRMS** (ESI) m/z 272.0744 [(M+Na)$^+$; calculated for [$C_{16}H_{11}NO_2$ + Na]$^+$: 272.0744].



±(6c)

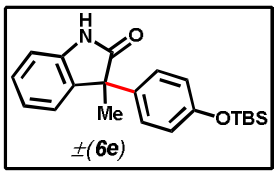
(±) 3-allyl-3-(4-hydroxyphenyl)indolin-2-one ±(6c): Colorless gel, R_f= 0.50 (40% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ:9.91 (s, 1H), 8.88 (s, 1H), 7.16-7.23 (m, 4H), 7.02 (m, 1H), 6.93 (d, *J* = 7.48 Hz, 1H), 6.76 (d, *J* = 8.64 Hz, 2H), 5.41-5.51 (m, 1H), 5.03 (d, *J* = 17.04 Hz, 1H), 4.91 (d, *J* = 10.12 Hz, 1H), 2.96 (d, *J* = 6.88 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ:180.3, 156.5, 142.0, 132.9, 132.8, 130.4, 128.0, 127.8, 125.1, 121.7, 118.7, 115.4, 109.9, 56.0, 41.7; **IR** (film) υ_{max} 3580, 3495, 3414, 2252, 2129, 1647, 1516, 1473, 999, 825, 771, 706 cm^{-1}; **HRMS** (ESI) m/z 288.0964 [(M+Na)$^+$; calculated for [$C_{17}H_{15}NO_2$ + Na]$^+$: 288.0995].



(±) 2-(2-(3-(4-hydroxyphenyl)-2-oxoindolin-3-yl)ethyl)isoindoline-1,3-dione±(6d): Colorless gel, R_f= 0.53 (40% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ:10.08 (s, 1H), 8.88 (s, 1H), 7.70-7.76 (m, 4H), 7.16-7.22 (m, 3H), 7.11 (m, 1H), 6.89-6.92 (m, 2H), 6.72-6.74 (m, 2H), 3.59-3.62 (m, 2H), 2.58-2.65 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ:179.9, 167.7, 156.6, 142.0, 133.9, 132.2, 131.9, 130.2, 128.0, 127.7, 124.7, 122.9, 121.9, 115.5, 110.3, 54.6, 34.8, 34.4; **IR** (film) υ_{max} 3348, 2924, 2357, 2337, 1766, 1708, 1616, 1400, 1184, 1030, 752, 718 cm^{-1}; **HRMS** (ESI) m/z 421.1182 [$(M+Na)^+$; calculated for $[C_{24}H_{18}N_2O_4 + Na]^+$: 421.1159].

Procedure for TBS protection of phenol:

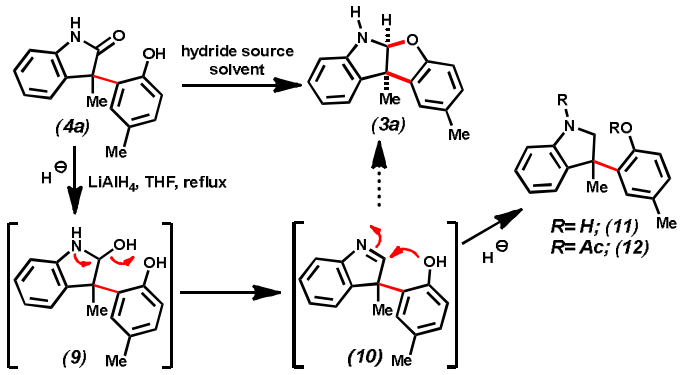
A flame-dried round-bottom flask was charged with phenol derivative **6a**(0.2 mmol, 1.0 equiv.) in DMF (1.5 mL) and 3 equiv. of imidazole (0.6 mmol, 3.0 equiv.). To this reaction mixture was added TBSCl (0.26 mmol, 1.3 equiv.) at room temperature and the reaction mixture was stirred at room temperature for 12 h. Upon completion of the reaction (TLC showed complete formation of product), the reaction mixture was diluted with diethylether (5 mL) and water (5 mL). The whole reaction mixture was taken in a separatory funnel and extracted with ether (5 mL x 2). The organic filtrate was dried over Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude products were purified by flash chromatography (10:1 hexanes/EtOAc) to afford compound ±(**6e**).



(±) 3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-3-methylindolin-2-one ±(6e): Colorless gel, R_f= 0.70 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.63 (s, 1H), 7.25 (dt, *J* = 7.64, 1.32 Hz, 1H), 7.18-7.21 (m, 2H), 7.15 (m, 1H), 7.07 (dt, *J* = 7.52, 1.00 Hz, 1H), 6.98 (d, *J* = 7.68 Hz,

1H), 6.76-6.80 (m, 2H), 1.80 (s, 3H), 0.99 (s, 9H), 0.20 (s, 3H), 0.19 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ:182.3, 154.9, 140.3, 135.8, 133.1, 128.0, 127.7, 124.4, 122.7, 120.0, 110.1, 52.1, 29.7, 25.7, 23.7, 18.2, -04.4; **IR**(film) υ_{max} 3217, 2928, 2856, 2357, 2333, 1717, 1612, 1508, 1469, 1323, 918, 837, 748 cm^{-1}; **HRMS** (ESI) m/z 354.1896 $[(M+H)^+$; calculated for $[C_{21}H_{27}NO_2Si + H]^+$: 354.1884].

Scheme 3: Unsuccessful reductive approach to tetracyclic core.

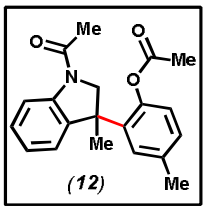


Reaction of (4a)with $LiAlH_4$ followed by acetylation:

Compound **4a** (0.5 mmol, 1.0 equiv.) was taken in anhydrous THF (5 mL) and cooled the reaction mixture at 0 ºC. To this reaction mixture was added $LiAlH_4$ (1.5 mmol, 3.0 equiv.) portion wise and the reaction mixture was placed in a pre-heated oil-bath maintaining the temperature at 75 ºC for 5 h. Upon completion of the reaction (TLC showed complete consumption of starting material), the reaction mixture was cooled to room temperature and then placed on an ice-bath. The reaction mixture was quenched with EtOAc (1 mL), water (1 mL), followed by 2(*N*) NaOH (1 mL), successively. The whole mixture was filtered through a celite-bed and washed with EtOAc (5 mL). The organic layer was evaporated under reduced pressure and the crude product (**11**) was directly used for acylation reaction.

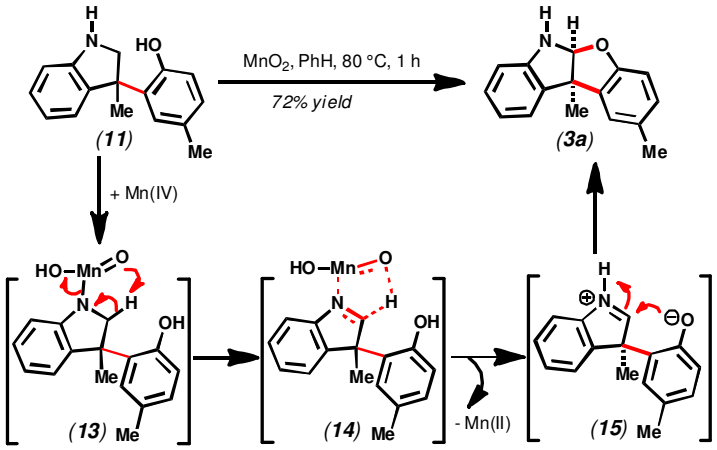
Compound **11** (0.5 mmol, 1.0 equiv.) was taken in anhydrous dichloromethane (3 mL) and triethylamine (3.0 mmol, 6.0 equiv.) was added to this mixture. Ac_2O (2.5 mmol, 5.0 equiv.) was added to this reaction mixture and it was stirred at rt for overnight.Upon completion of the reaction (TLC showed complete consumption of starting material), the reaction mixture was

evaporated under reduced pressure and the crude materials were purified by flash chromatography using EtOAc and petroleum ether to afford bis-acetylated compound (**12**) in 79% overall yield.



(±) 2-(1-acetyl-3-methylindolin-3-yl)-4-methylphenyl acetate±(12): Colorless gel, R_f= 0.38 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ:8.28 (d, *J* = 8.00 Hz, 1H), 7.35 (d, *J* = 1.52 Hz, 1H), 7.23 (dt, *J* = 8.08, 1.28 Hz, 1H), 7.15 (dd, *J* = 8.16, 1.48 Hz, 1H), 6.99 (dt, *J* = 7.48, 1.04 Hz, 1H),6.91 (d, *J* = 8.12 Hz, 1H), 6.82 (dd, *J*= 7.52, 0.76 Hz, 1H), 5.31 (s, 1H, CH_2Cl_2),4.33 (d, *J* = 10.32 Hz, 1H), 3.91 (d, *J* = 10.32 Hz, 1H), 2.41 (s, 3H), 2.24 (s, 3H), 1.73 (s, 3H), 1.69 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ:168.78, 168.71, 146.55, 141.56, 139.39, 136.21, 135.20, 128.95, 128.26, 127.74, 124.24, 124.09, 123.13, 116.78, 64.09, 53.45 (CH_2Cl_2), 45.81, 28.91, 24.25, 21.21, 20.16;**HRMS** (ESI) m/z 346.1416 [(M+ Na)$^+$; calculated for [$C_{20}H_{21}NO_3$ + Na]$^+$: 346.1414].

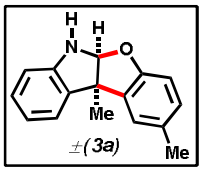
Scheme 4: Crafting the tetracyclic core *via* oxidative coupling.



Synthesis of tetracyclic core by reduction of (4a)with $LiAlH_4$ followed by MnO_2 treatment:

Compound **4a** (0.5 mmol, 1.0 equiv.) was taken in anhydrous THF (5 mL) and cooled the reaction mixture at 0 ºC. To this reaction mixture was added $LiAlH_4$ (1.5 mmol, 3.0 equiv.) portion wise and the reaction mixture was placed in a pre-heated oil-bath maintaining the temperature at 75 ºC for 5 h. Upon completion of the reaction (TLC showed complete consumption of starting material), the reaction mixture was cooled to room temperature and then placed on an ice-bath. The reaction mixture was quenched with EtOAc (1 mL), water (1 mL), followed by 2(*N*) NaOH (1 mL), successively. The whole mixture was filtered through a celite-bed and washed with EtOAc (5 mL). The organic layer was evaporated under reduced pressure and the crude product (**11**) was directly used for MnO_2-oxidation.

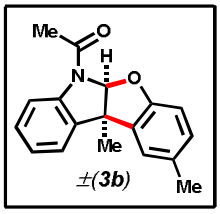
In a flame-dried round-bottom flask, compound **11** (0.5 mmol, 1.0 equiv.) was taken in anhydrous benzene (3 mL). To this solution was added MnO_2 (5.0 mmol, 10.0 equiv.) and the reaction mixture was heated under reflux (80 ºC) for an hour. Upon completion of the reaction (TLC showed complete consumption of starting material), the reaction mixture was filtered through celite-bed and washed with 30% EtOAc in hexane. Most of the organic volatiles was evaporated under reduced pressure and the crude materials were purified by flash chromatography using EtOAc and petroleum ether to afford tetracyclic core (**3a**) in 70% overall yield.



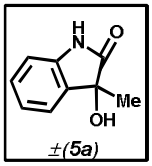
(±)-2,10b-dimethyl-6,10b-dihydro-5aH-benzofuro[2,3-b]indole±(3a): 70% yield,Colorless gel, R_f**=** 0.40 (20% EtOAc in hexane). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.28 (dd, *J* = 7.56, 0.76 Hz, 1H), 7.17 (m, 1H), 7.07 (dt, *J* = 7.60, 1.20 Hz, 1H), 6.90-6.92 (m, 1H), 6.81 (dt, *J* = 7.44, 0.96 Hz, 1H), 6.69 (t, *J* = 8.24 Hz, 1H), 6.08 (d, *J* = 2.20 Hz, 1H), 5.01 (br, s, 1H), 2.32 (s, 3H), 1.72 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ:156.3, 147.0, 133.6, 132.9, 130.4, 128.6, 128.0, 123.3, 122.6, 119.7, 109.3, 109.2, 104.4, 56.1, 24.3, 20.9; **IR**(film) υ_{max} 3402, 2927, 2854, 1724, 1612, 1481, 1261, 1196, 1064, 810, 736 cm^{-1}; **HRMS** (ESI) m/z 260.1038 $[(M+ Na)^+$; calculated for $[C_{16}H_{15}NO + Na]^+$: 260.1046].

Synthesis of acetylated tetracyclic core (3b):

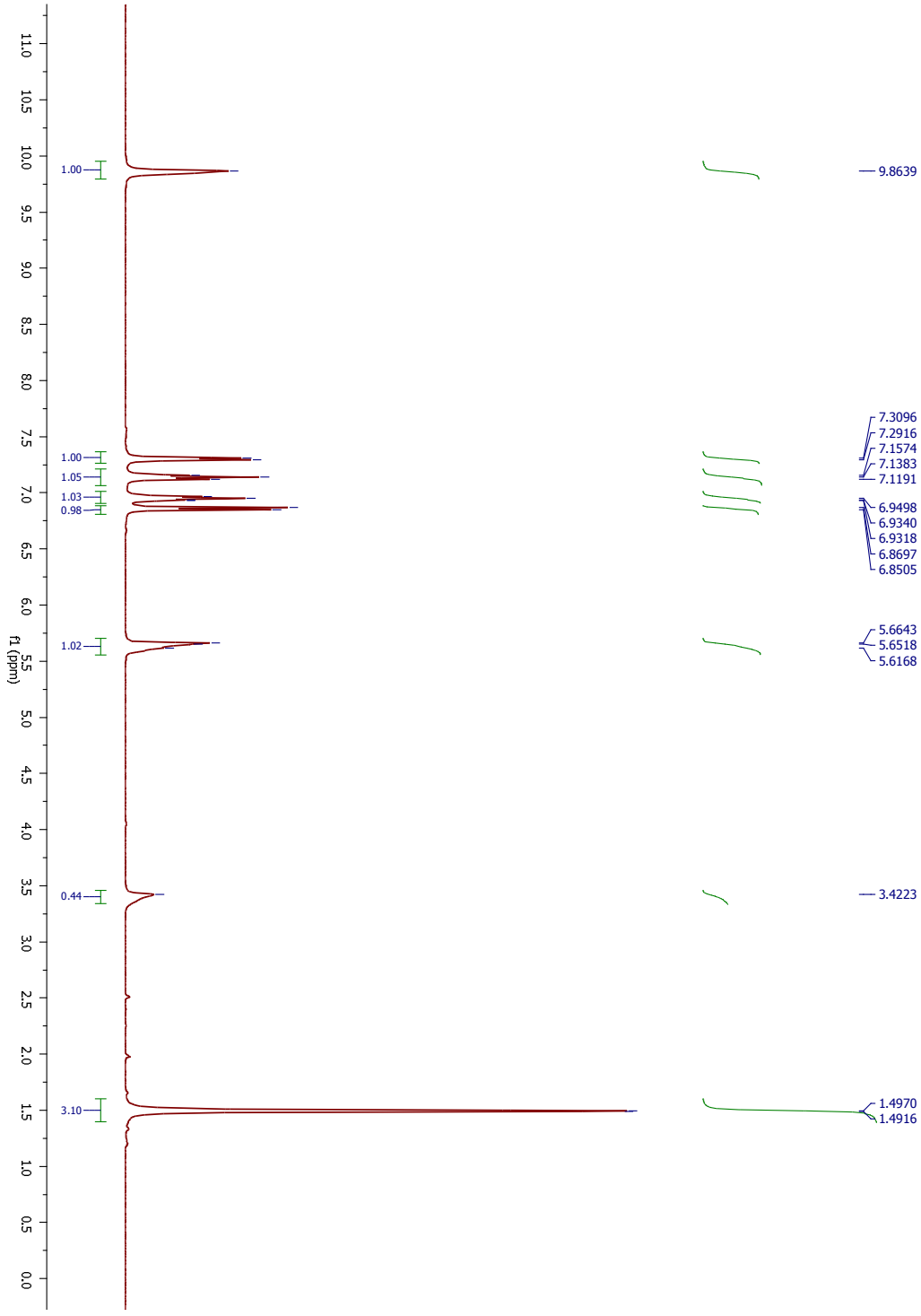
Compound **3a** (0.3mmol, 1.0 equiv.) was taken in anhydrous dichloromethane (2 mL) and triethylamine (0.9mmol, 3.0 equiv.) was added to this mixture. Ac_2O (0.9mmol, 3.0 equiv.) was added to this reaction mixture and it was stirred at rt for overnight.After 12 h (TLC showed product formation), the reaction mixture was evaporated under reduced pressure and the crude materials were purified by flash chromatography using EtOAc and petroleum ether to afford acetylated tetracyclic compound (**3b**) in 72% yield.



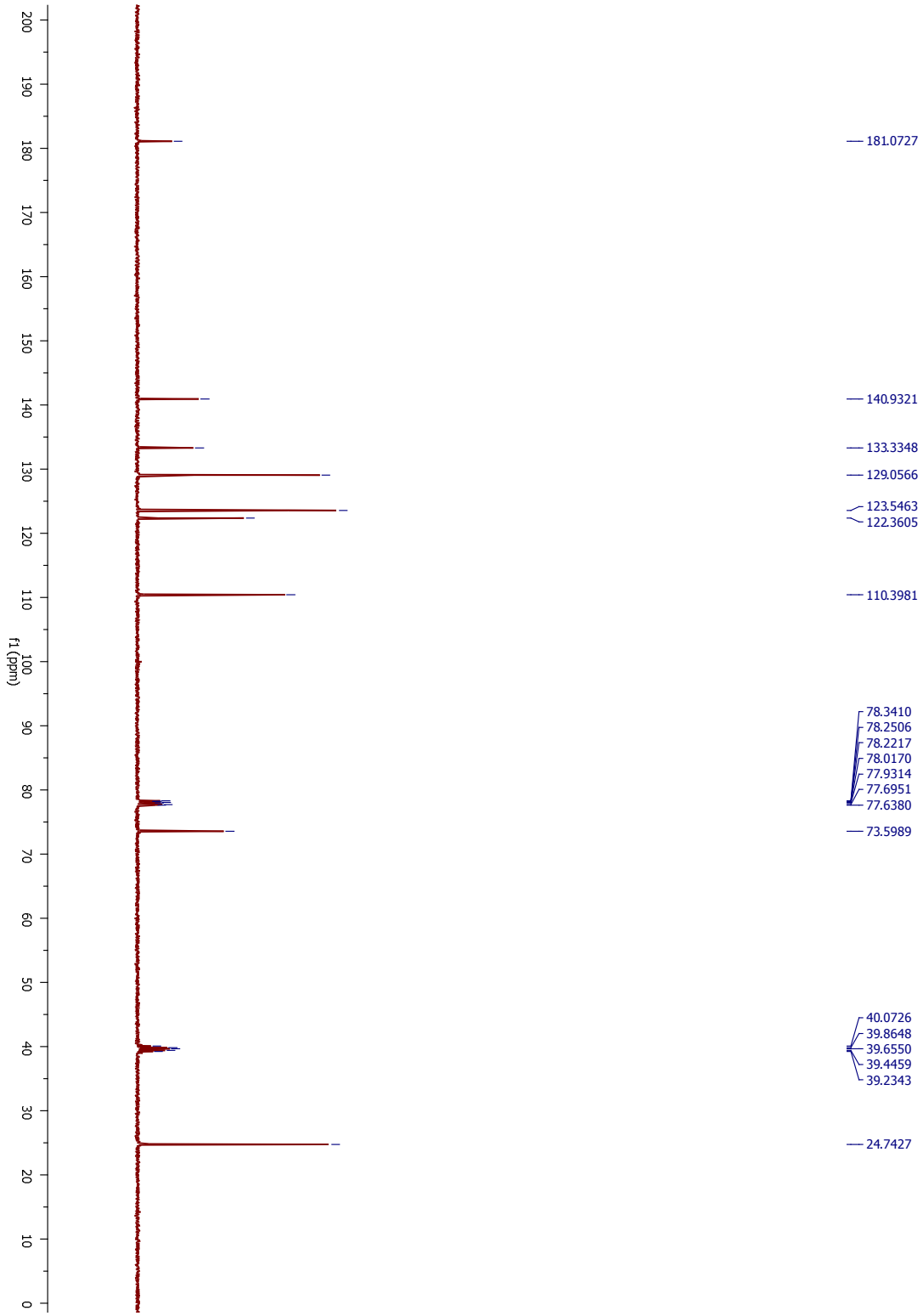
1-((±)-2,10b-dimethyl-5aH-benzofuro[2,3-b]indol-6(10bH)-yl)ethanone (3b): 72% yield, R_f= 0.50 (30% EtOAc in hexane).**^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.20 (d, *J* = 8.04 Hz, 1H),7.36 (d, *J* = 7.56 Hz, 1H), 7.23 (dt, *J* = 8.12, 1.32 Hz, 1H), 7.18 (m, 1H), 7.10 (dt, *J* = 7.44, 1.04 Hz, 1H),6.94 (m, 1H), 6.71 (d, *J* = 8.12 Hz, 1H), 6.34 (s, 1H), 2.54 (s, 3H), 2.33 (s, 3H), 1.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ:170.2, 155.5, 141.0, 135.6, 131.9, 131.3, 129.2, 128.4, 124.5, 123.2, 122.2, 117.0, 109.5, 103.0, 55.0, 24.9, 23.9, 20.9; **IR** (film) υ_{max} 2963, 2924, 2858, 2384, 1681, 1605, 1485, 1392, 1288, 1192, 968, 810, 752 cm^{-1}; **HRMS** (ESI) m/z 302.1160 $[(M+ Na)^+$; calculated for $[C_{18}H_{17}NO_2 + Na]^+$: 302.1151].



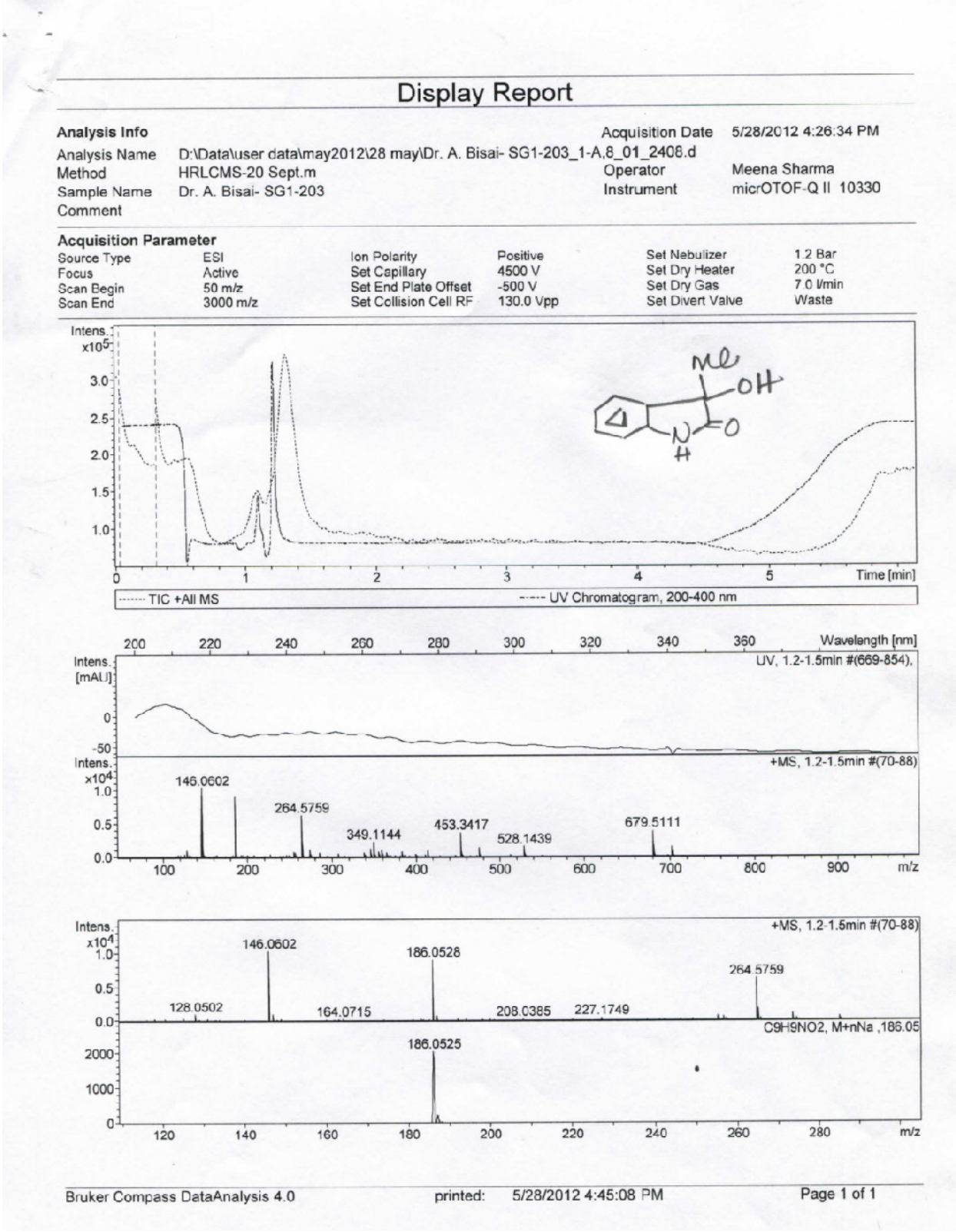
±(5a)



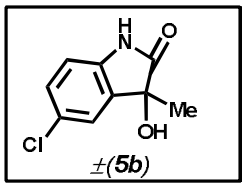
^{1}H NMR(400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5a**)



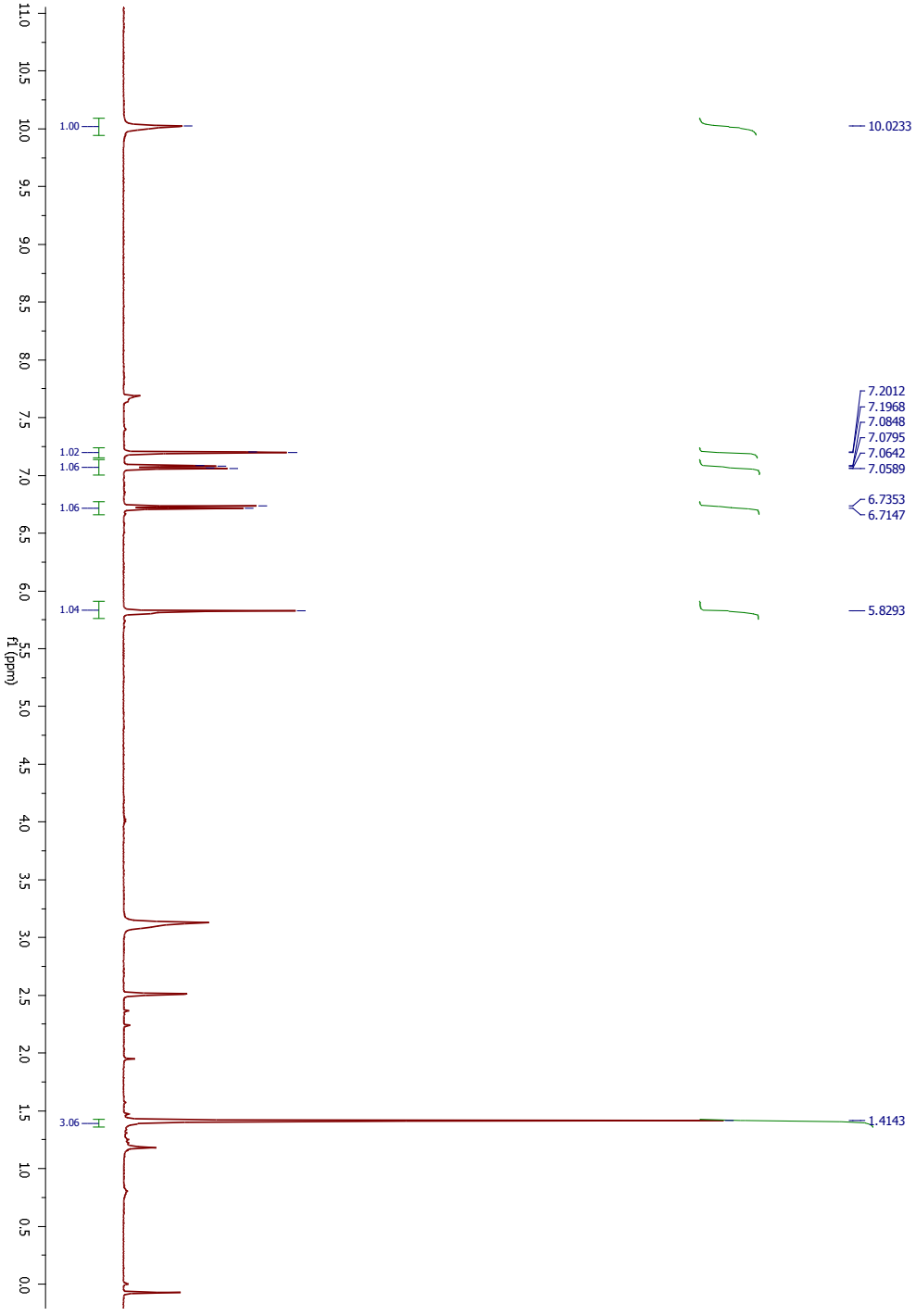
^{13}CNMR (100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5a**)



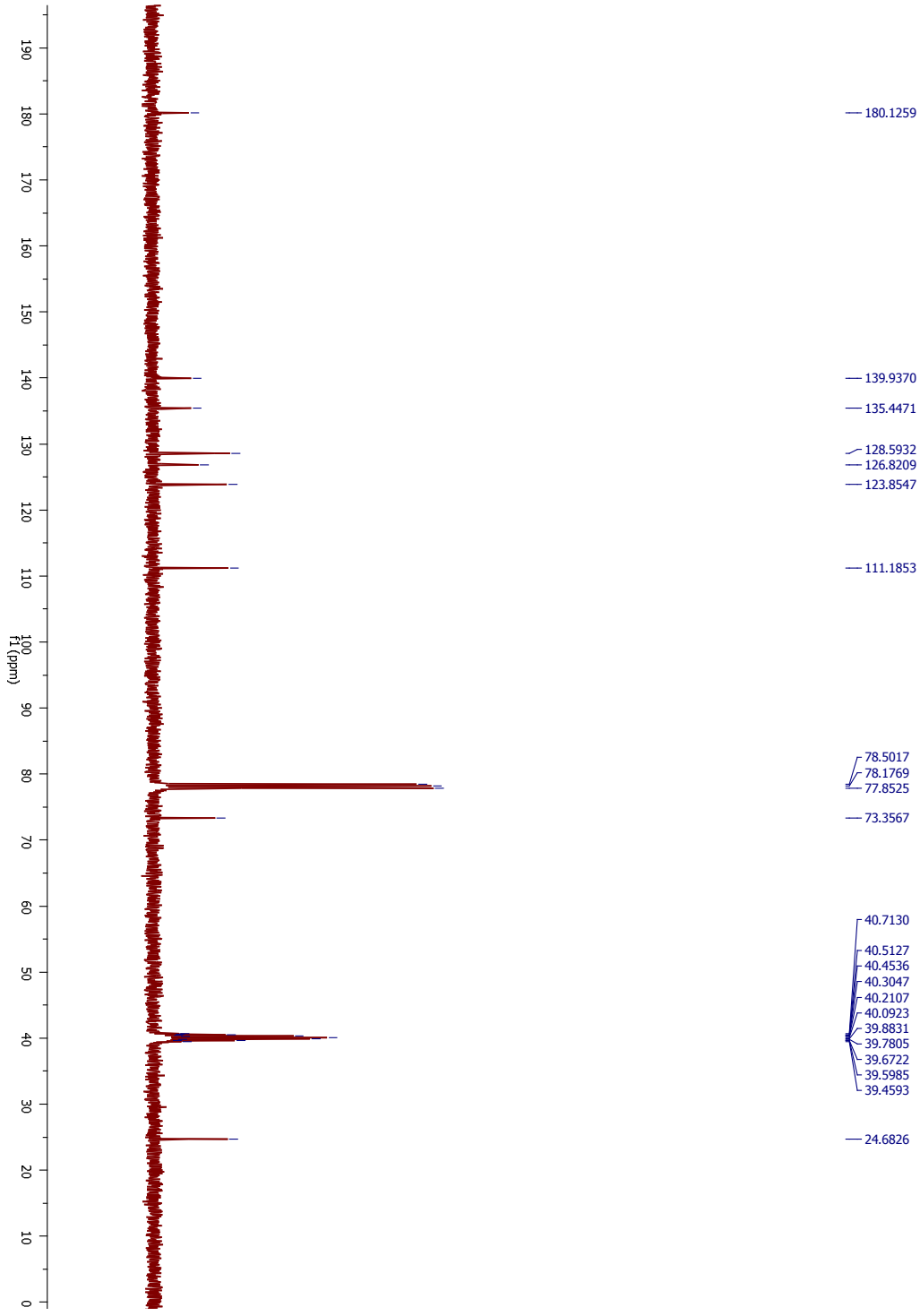
Scanned copy of mass spectrum of compound±(**5a**)



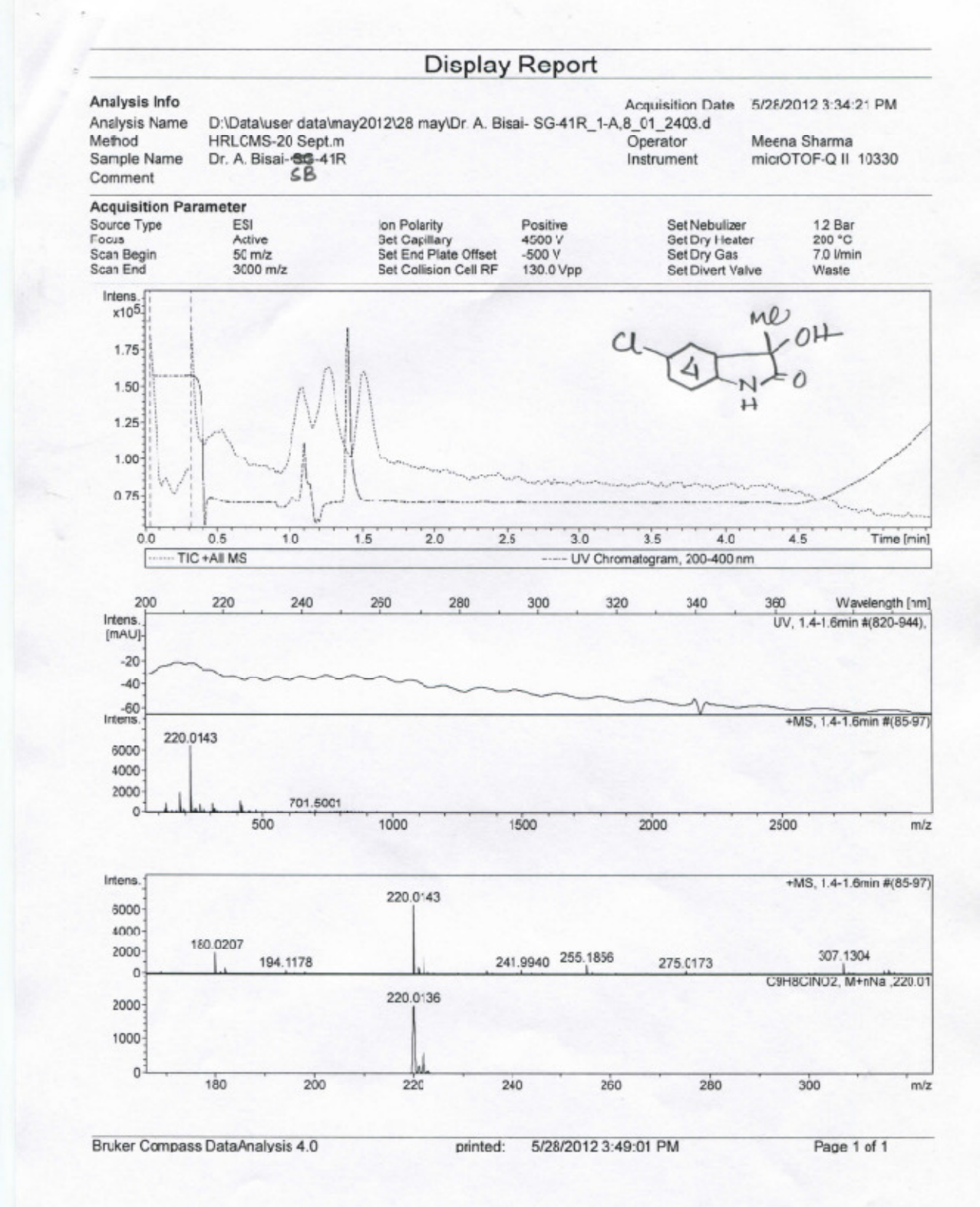
±(**5b**)



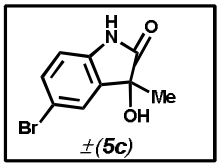
^{1}H NMR(400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5b**)



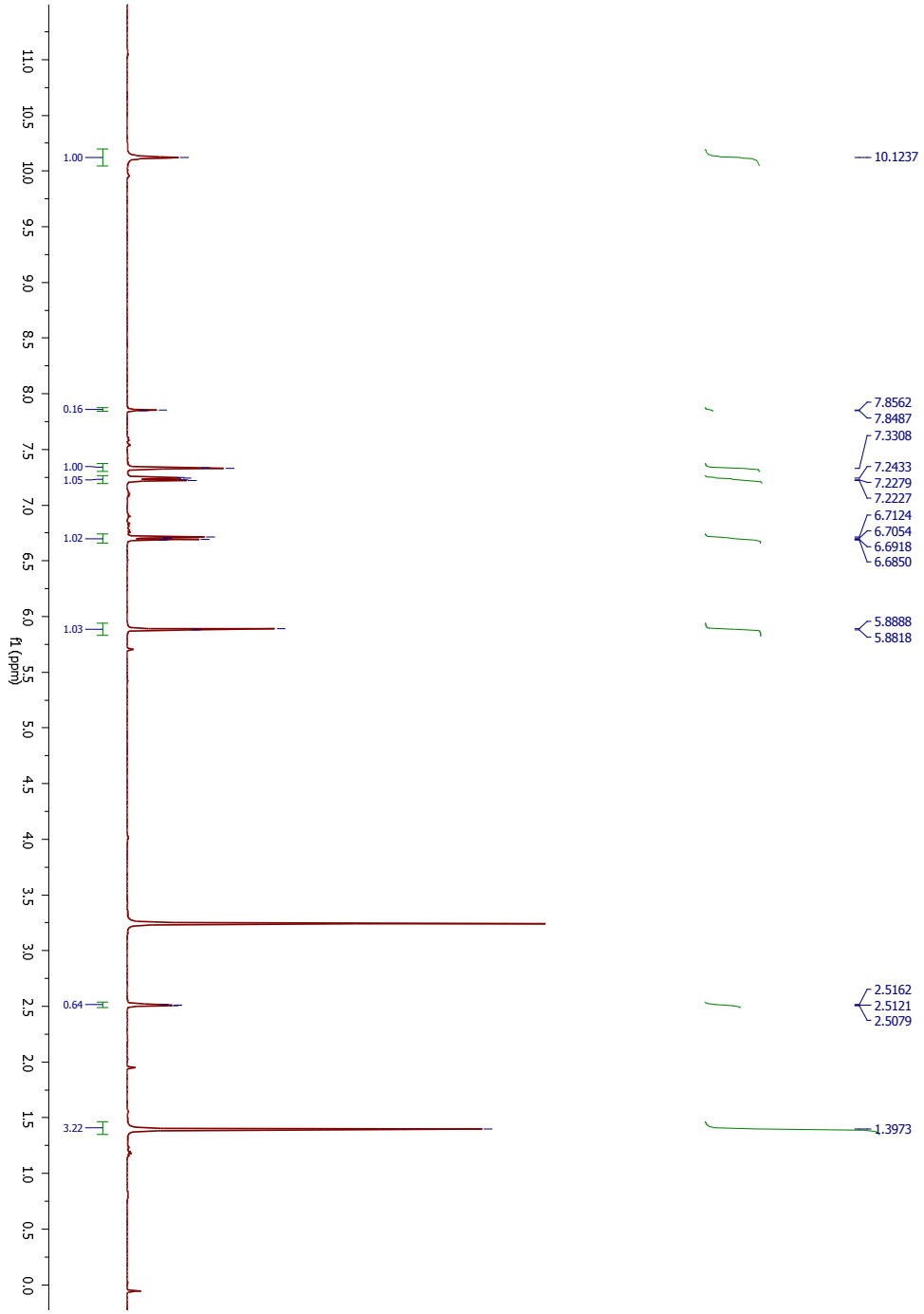
^{13}CNMR(100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5b**)



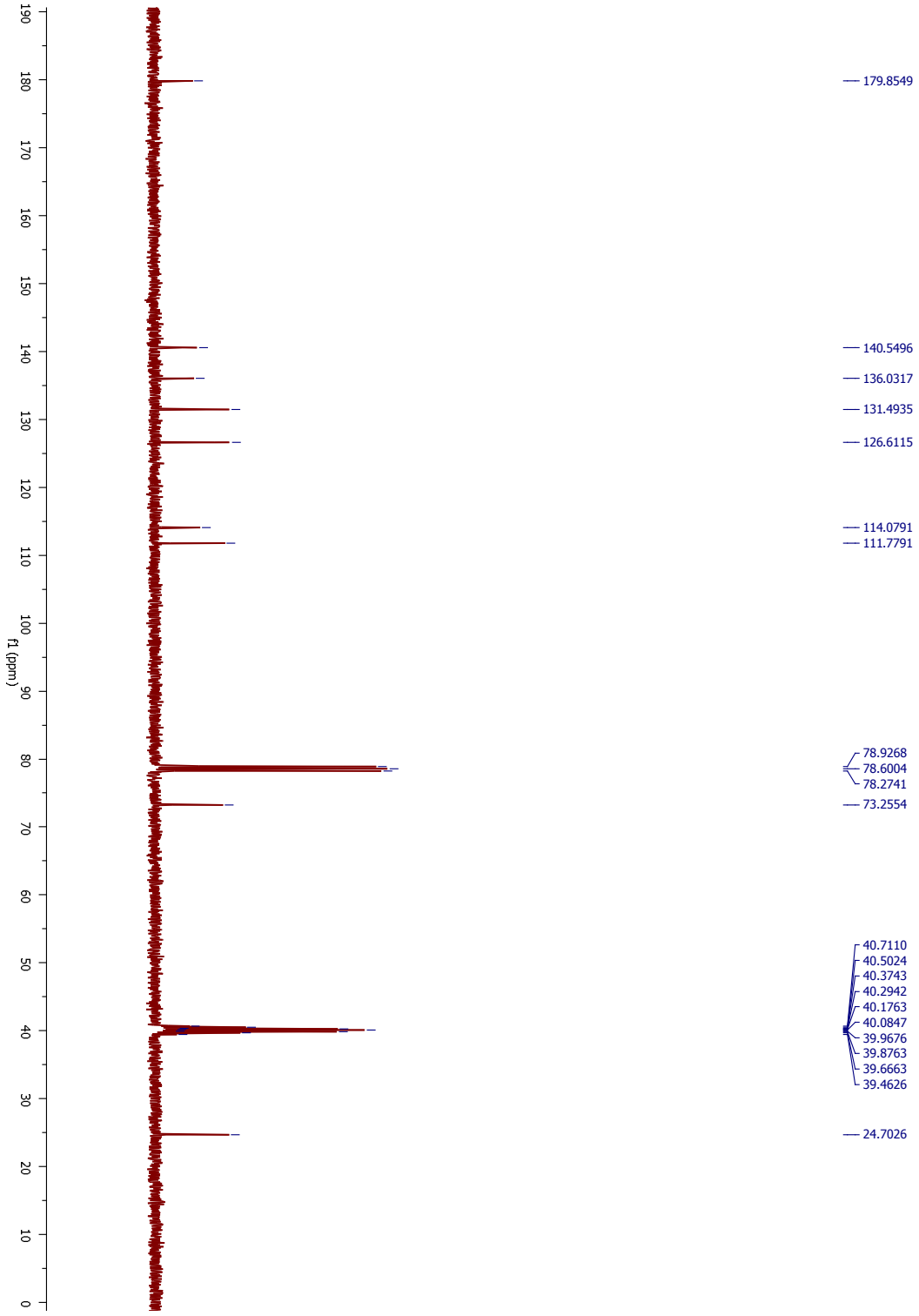
Scanned copy of mass spectrum of compound±(**5b**)



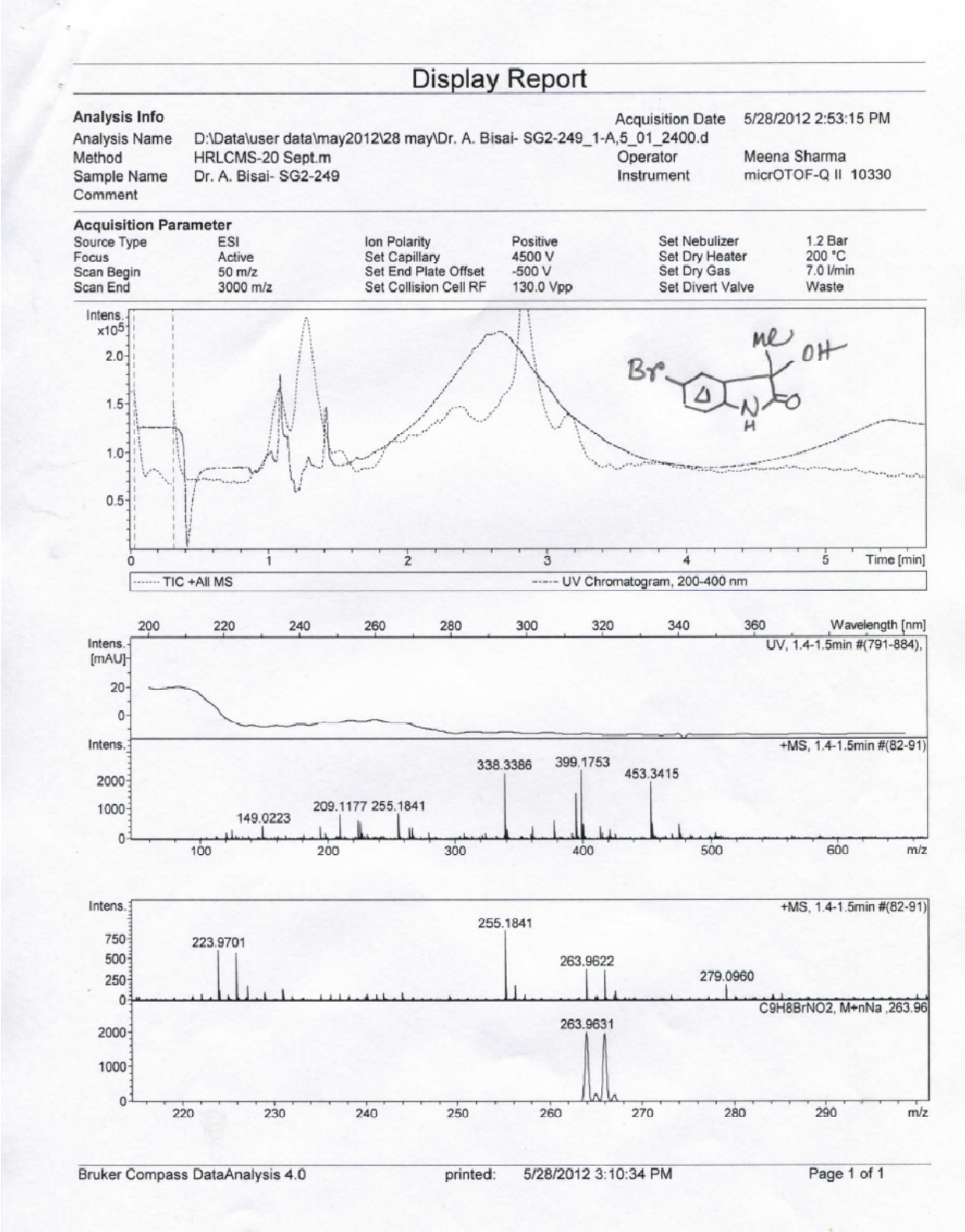
±(**5c**)



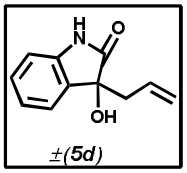
^{1}H NMR(400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5c**)

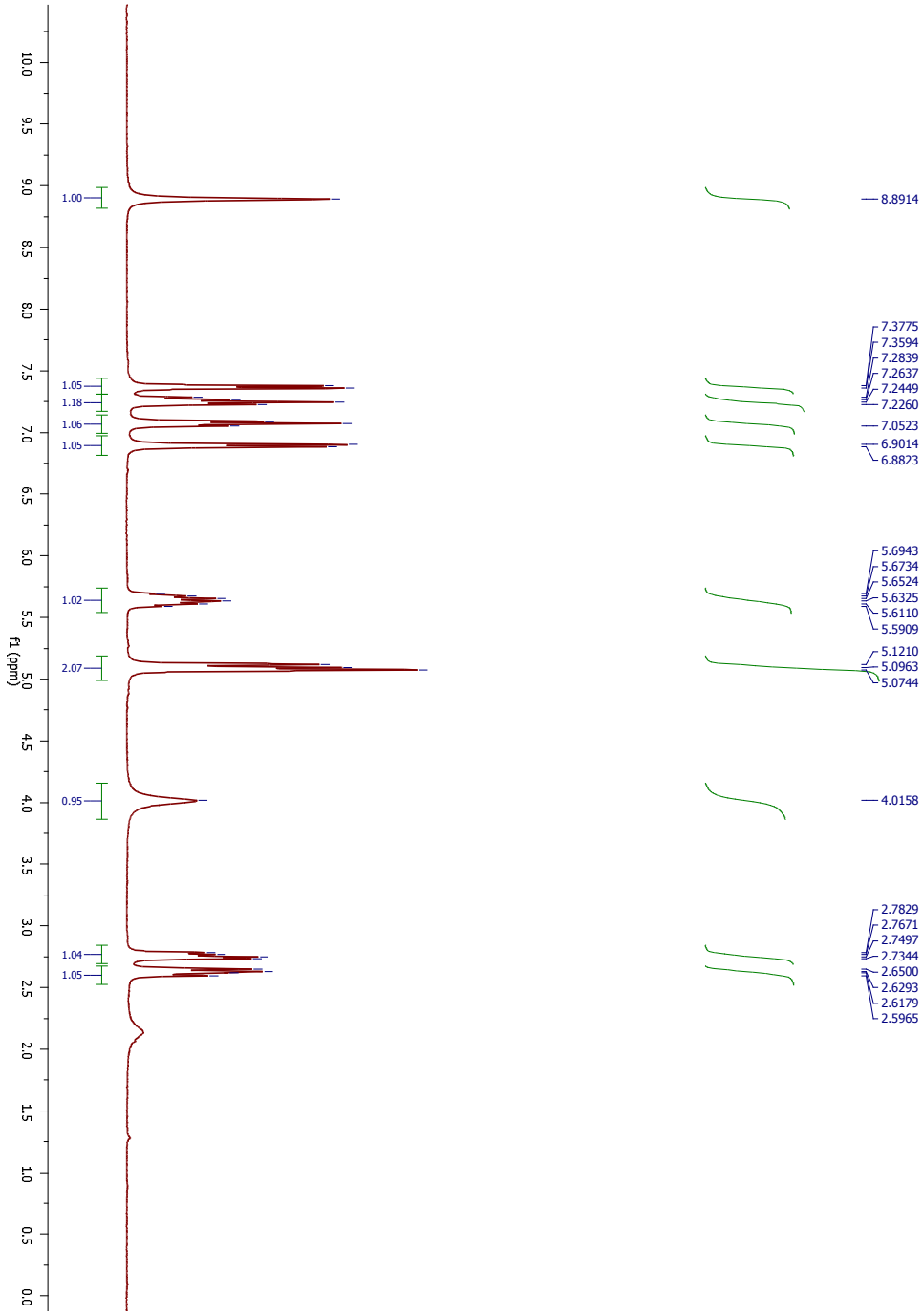


^{13}CNMR(100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5c**)

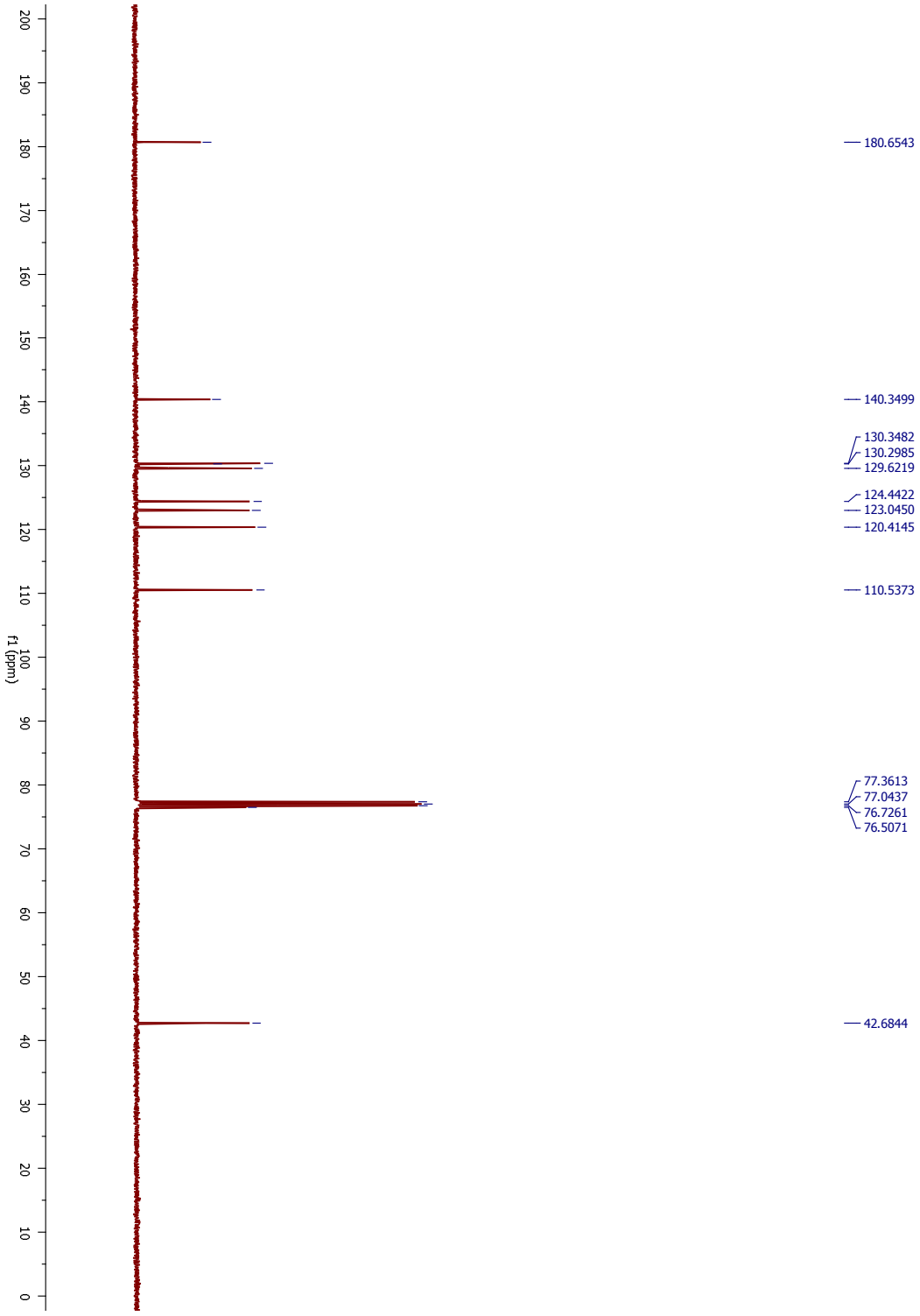


Scanned copy of mass spectrum of compound±(**5c**)

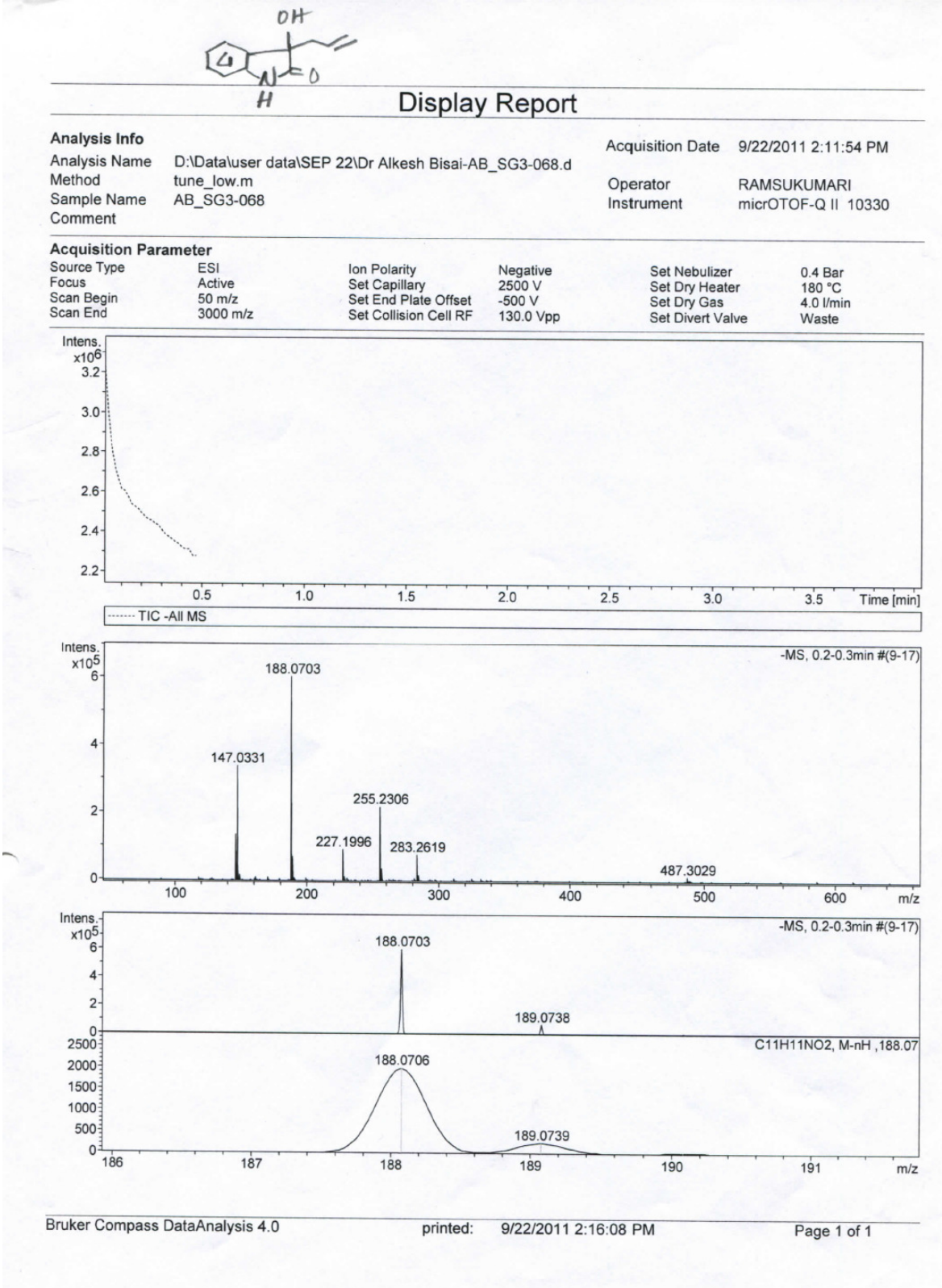




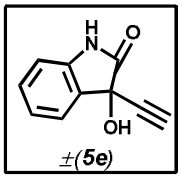
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**5d**)



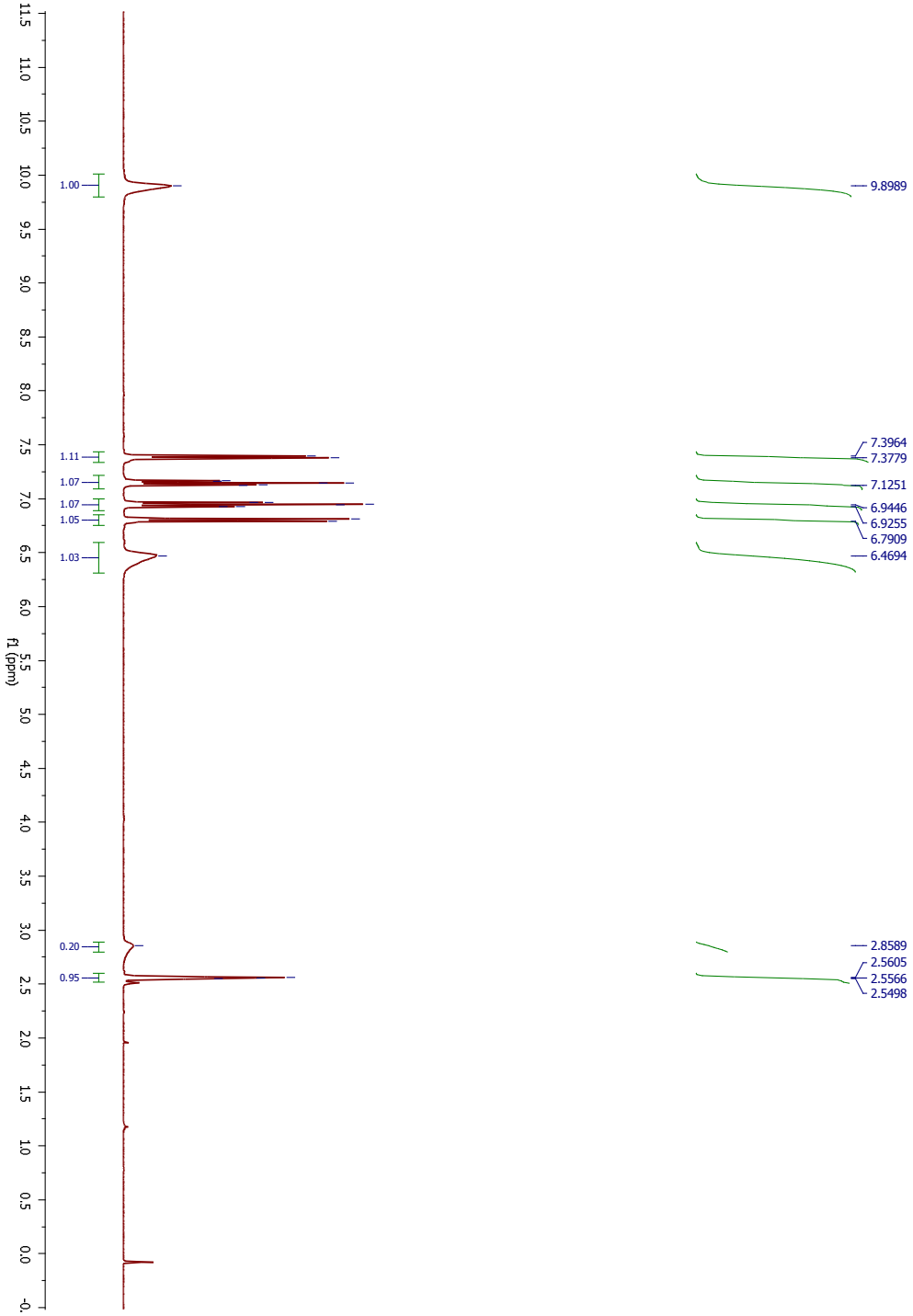
^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**5d**)



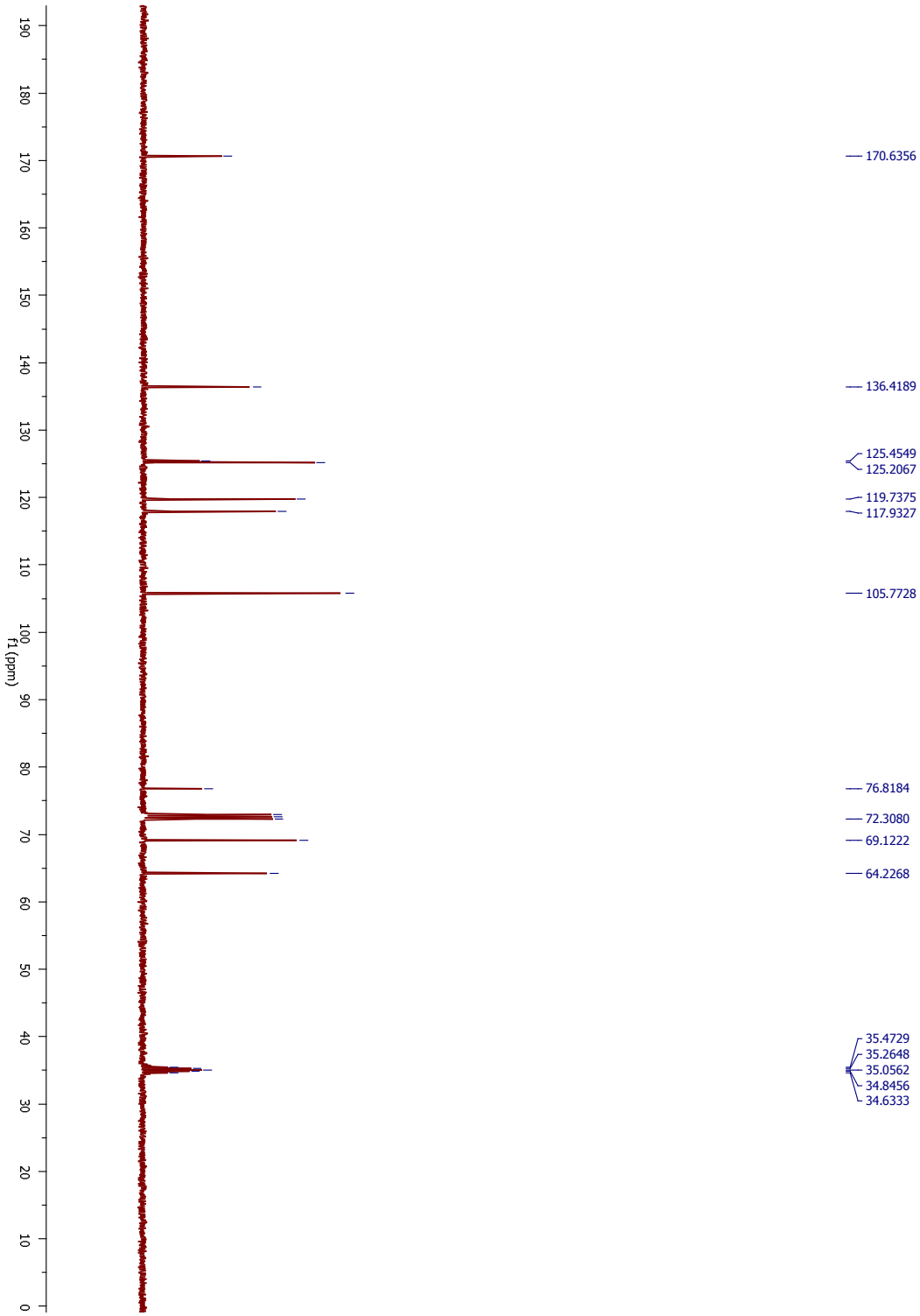
Scanned copy of mass spectrum of compound±(**5d**)



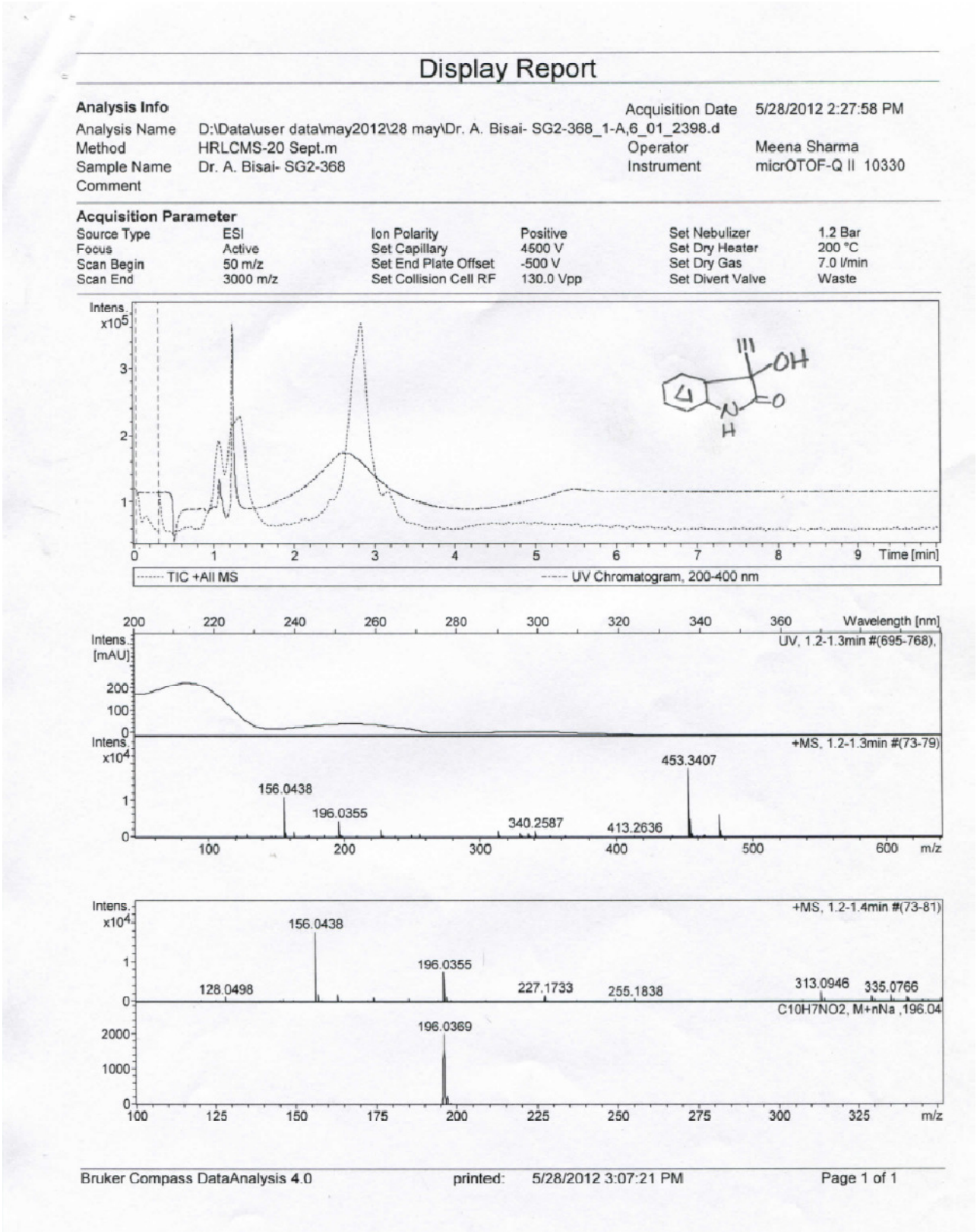
±(**5e**)



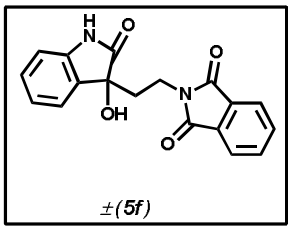
^{1}H NMR(400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5e**)



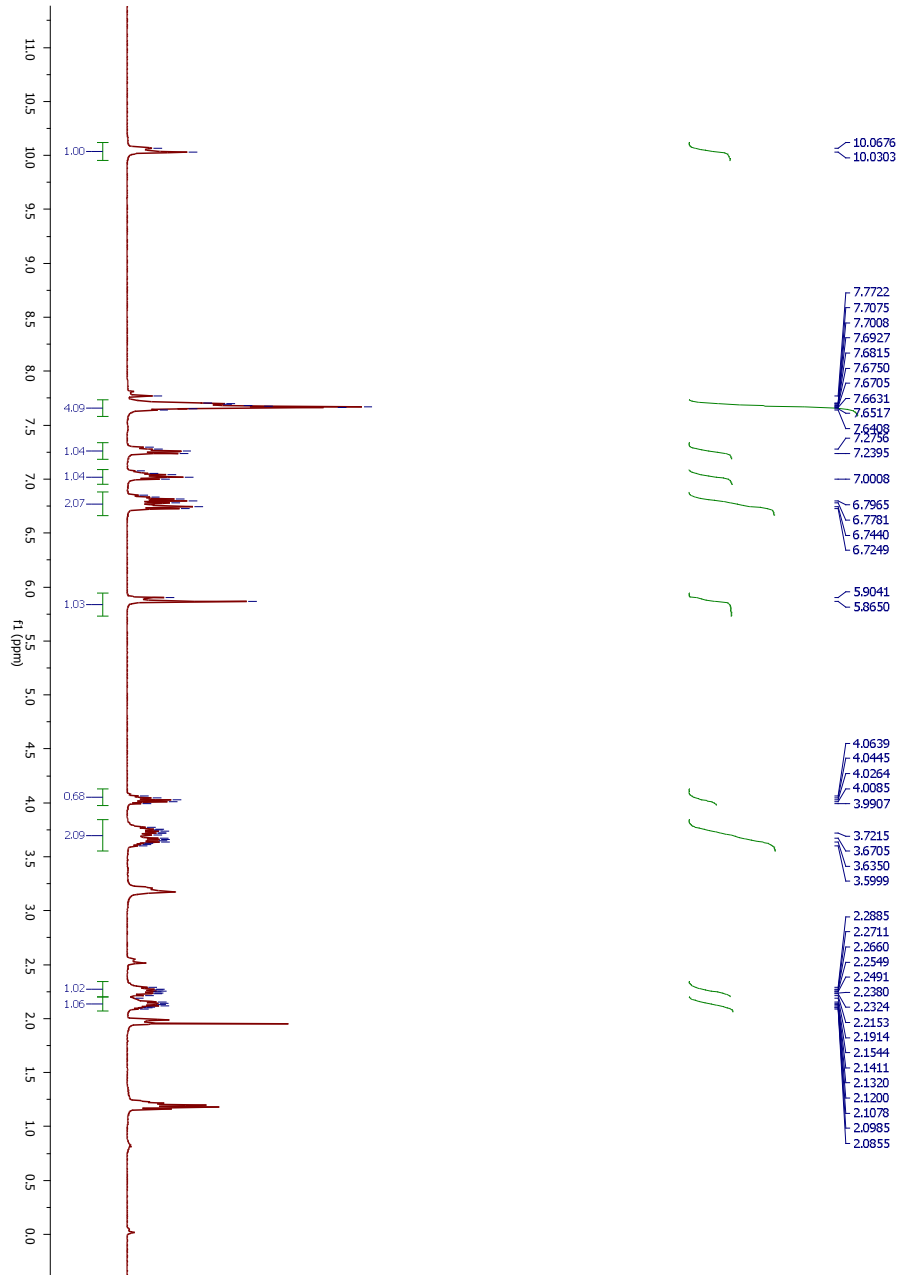
^{13}CNMR(100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5e**)



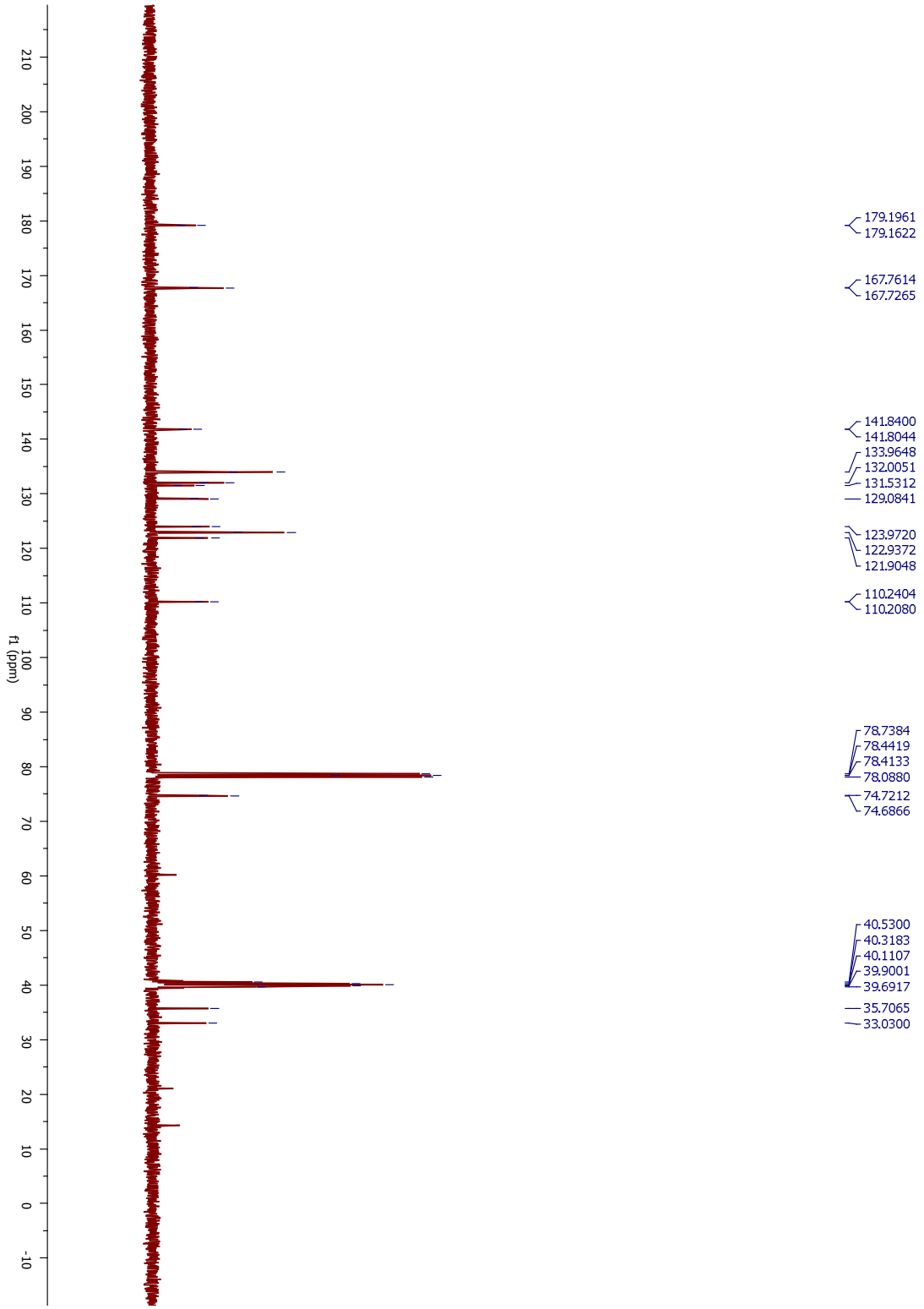
Scanned copy of mass spectrum of compound±(**5e**)



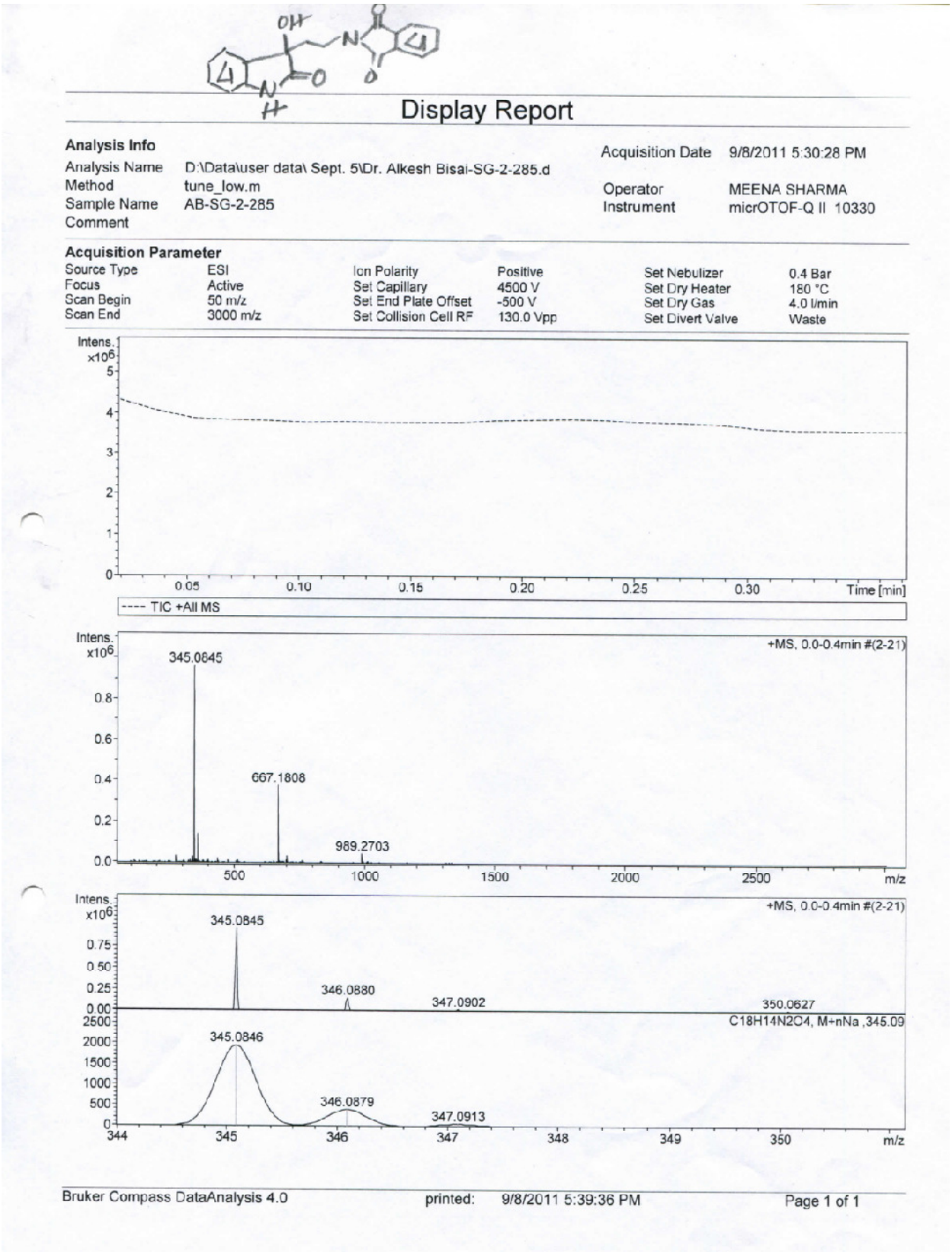
±(**5f**)



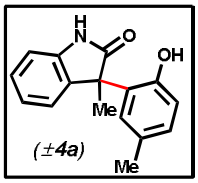
^{1}H NMR(400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5f**)

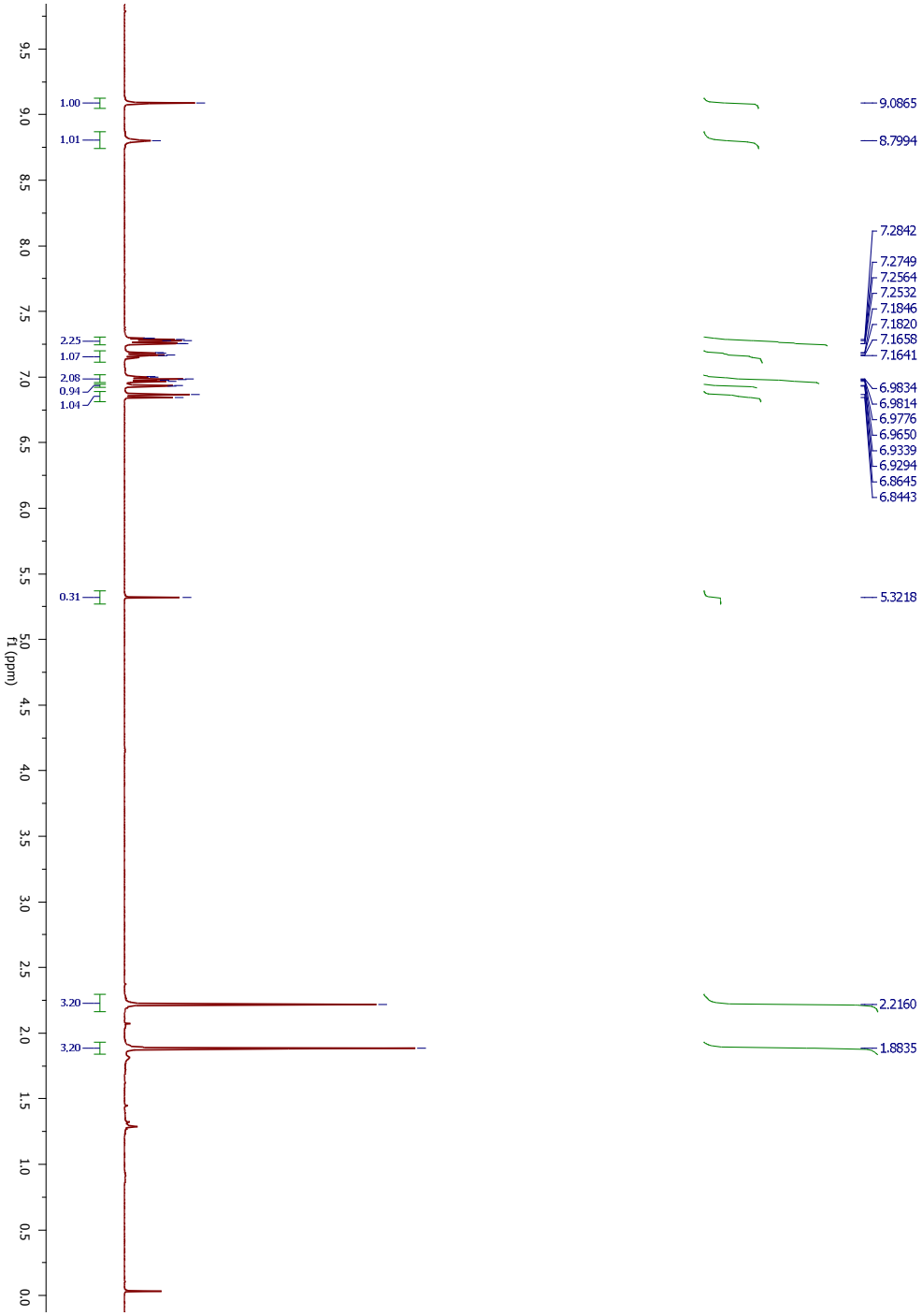


^{13}CNMR(100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**5f**)

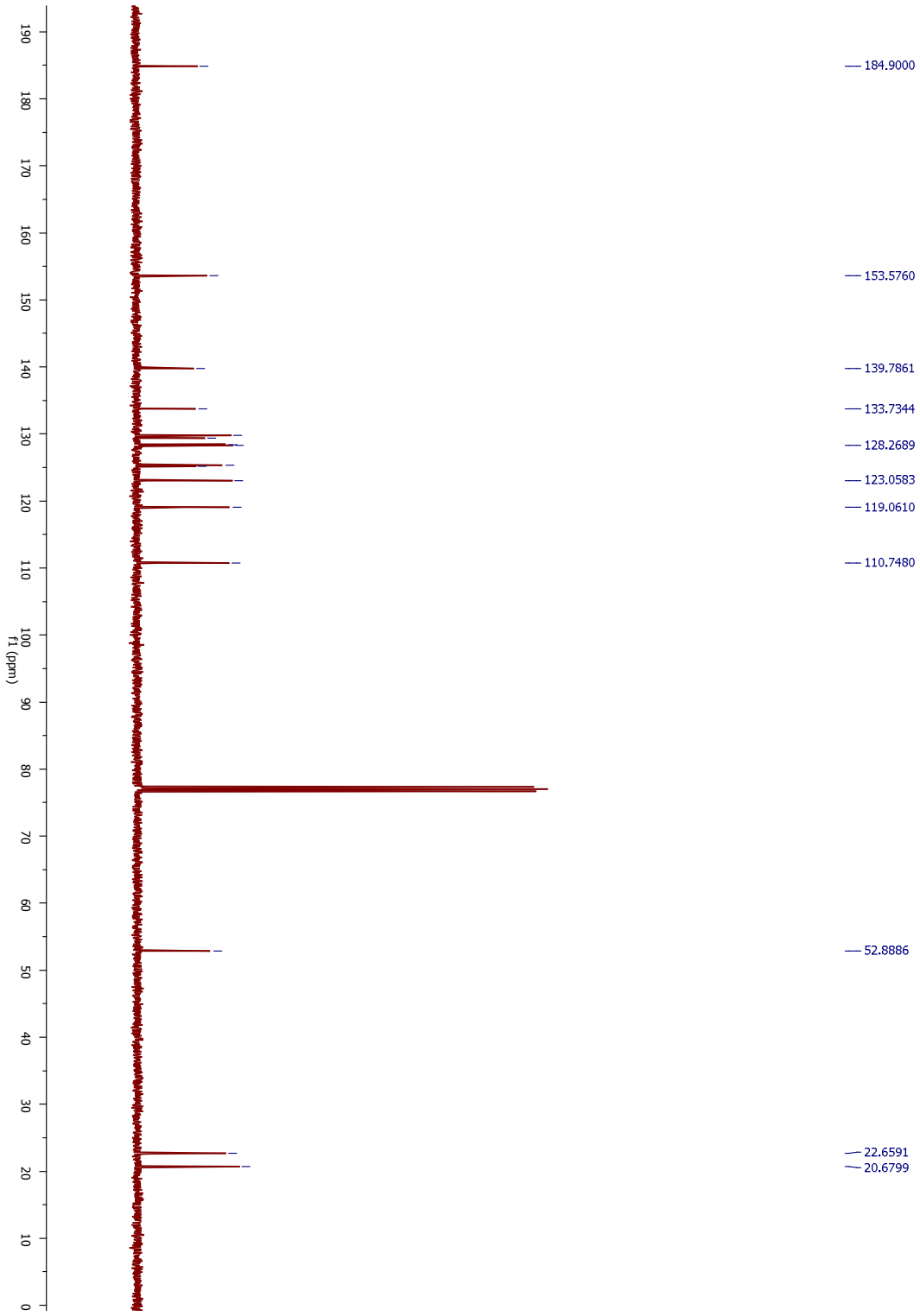


Scanned copy of mass spectrum of compound±(**5f**)

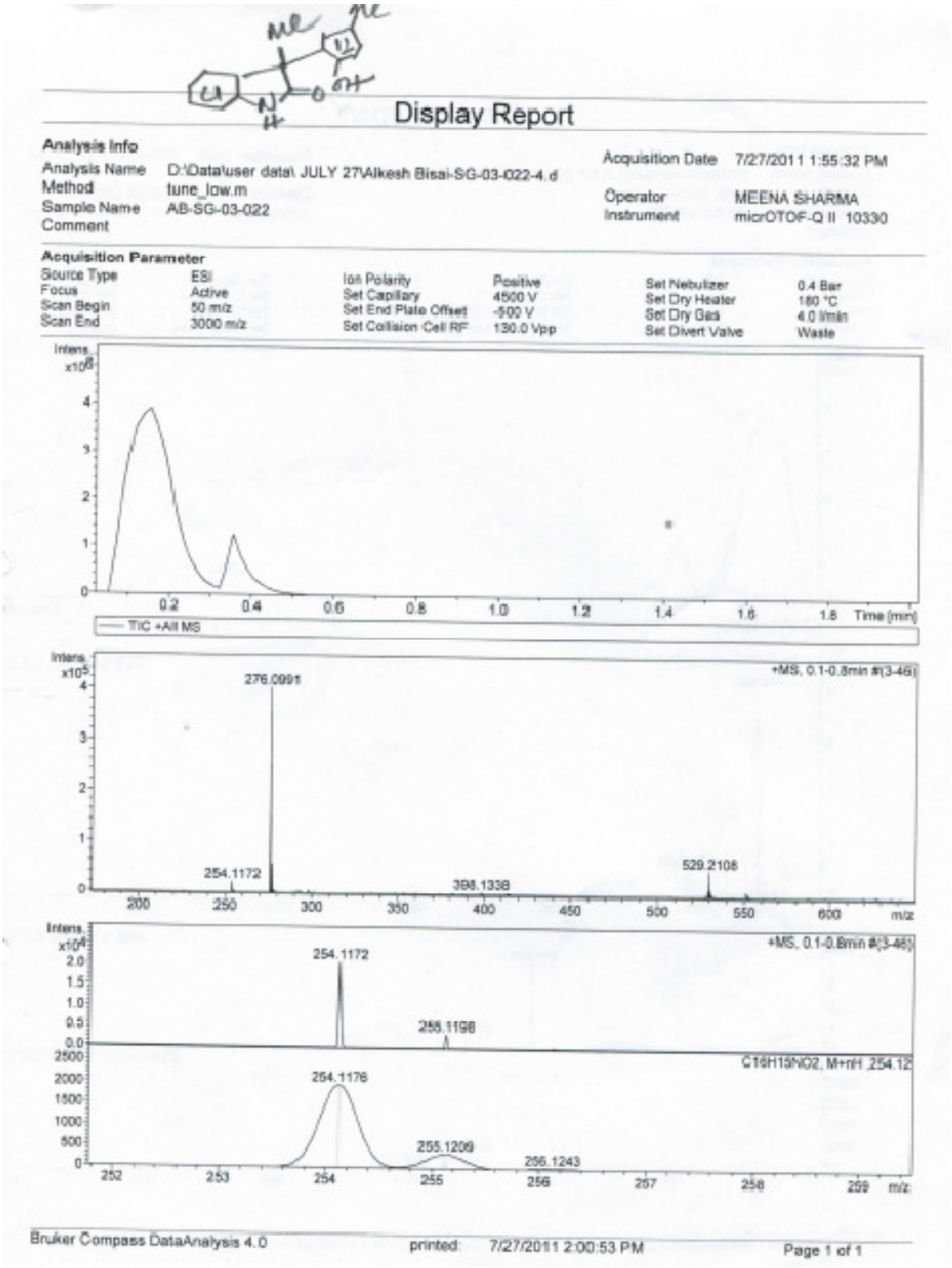




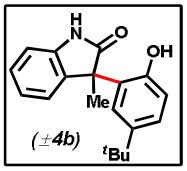
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**4a**)

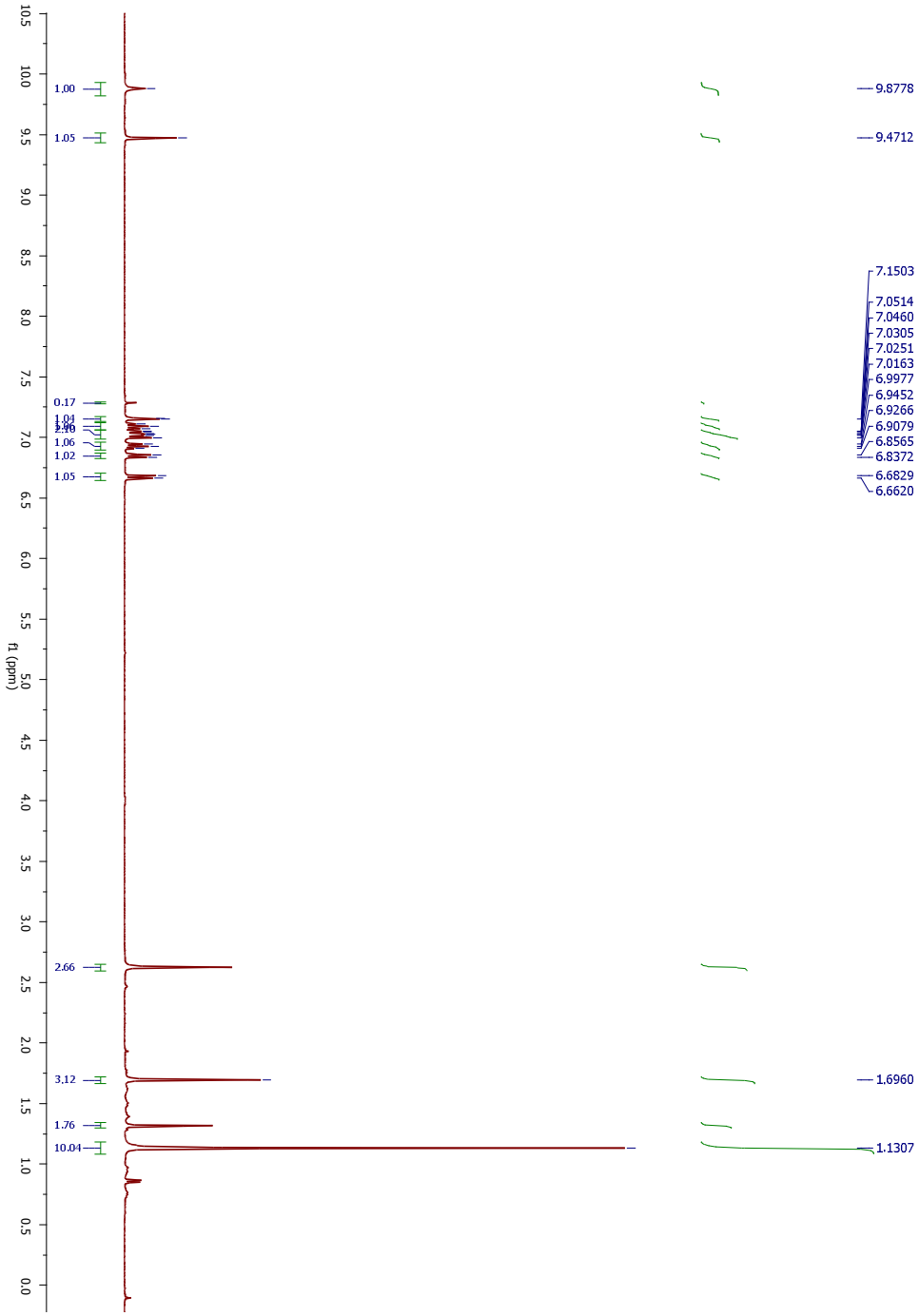


^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**4a**)

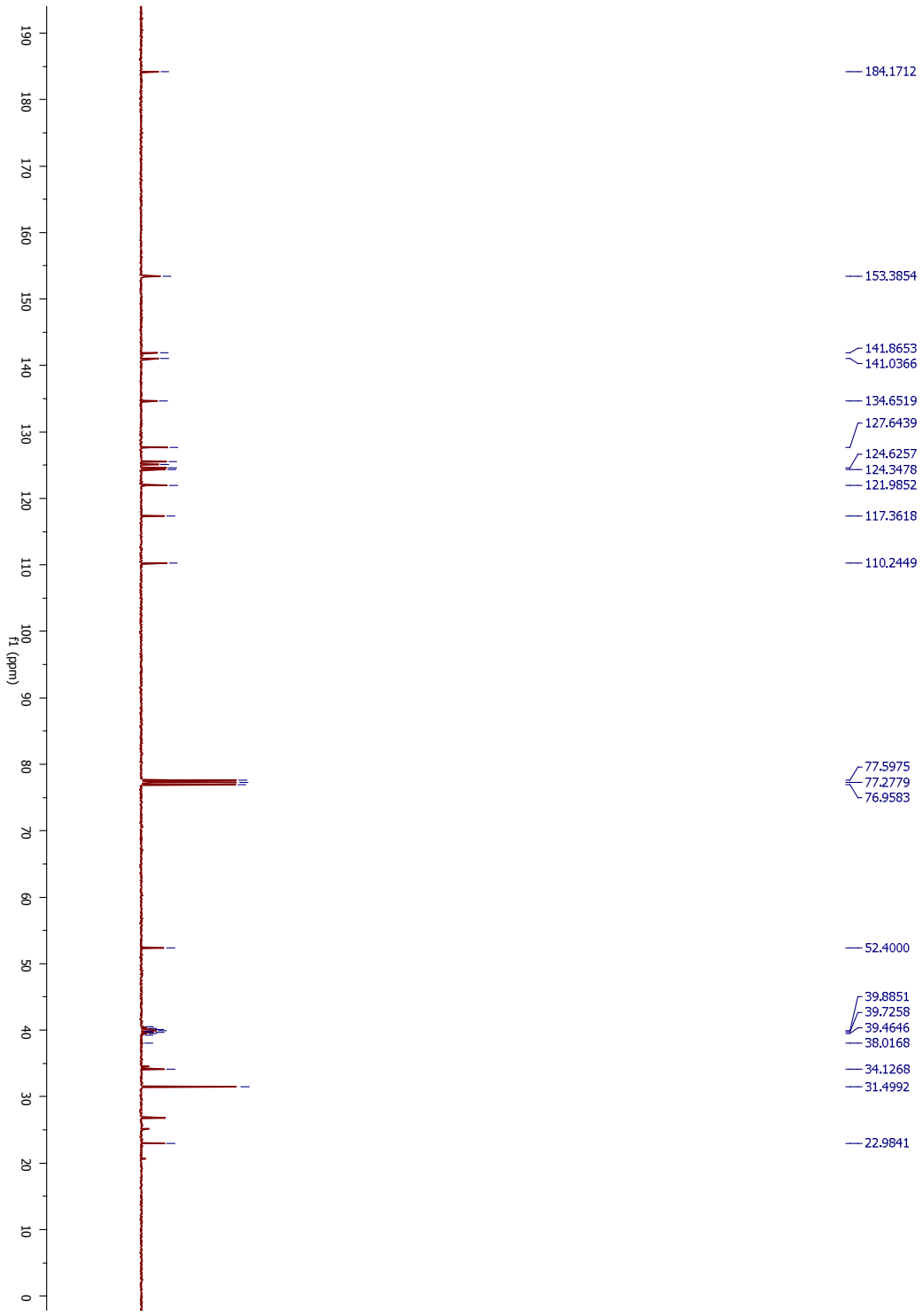


Scanned copy of mass spectrum of compound±(**4a**)

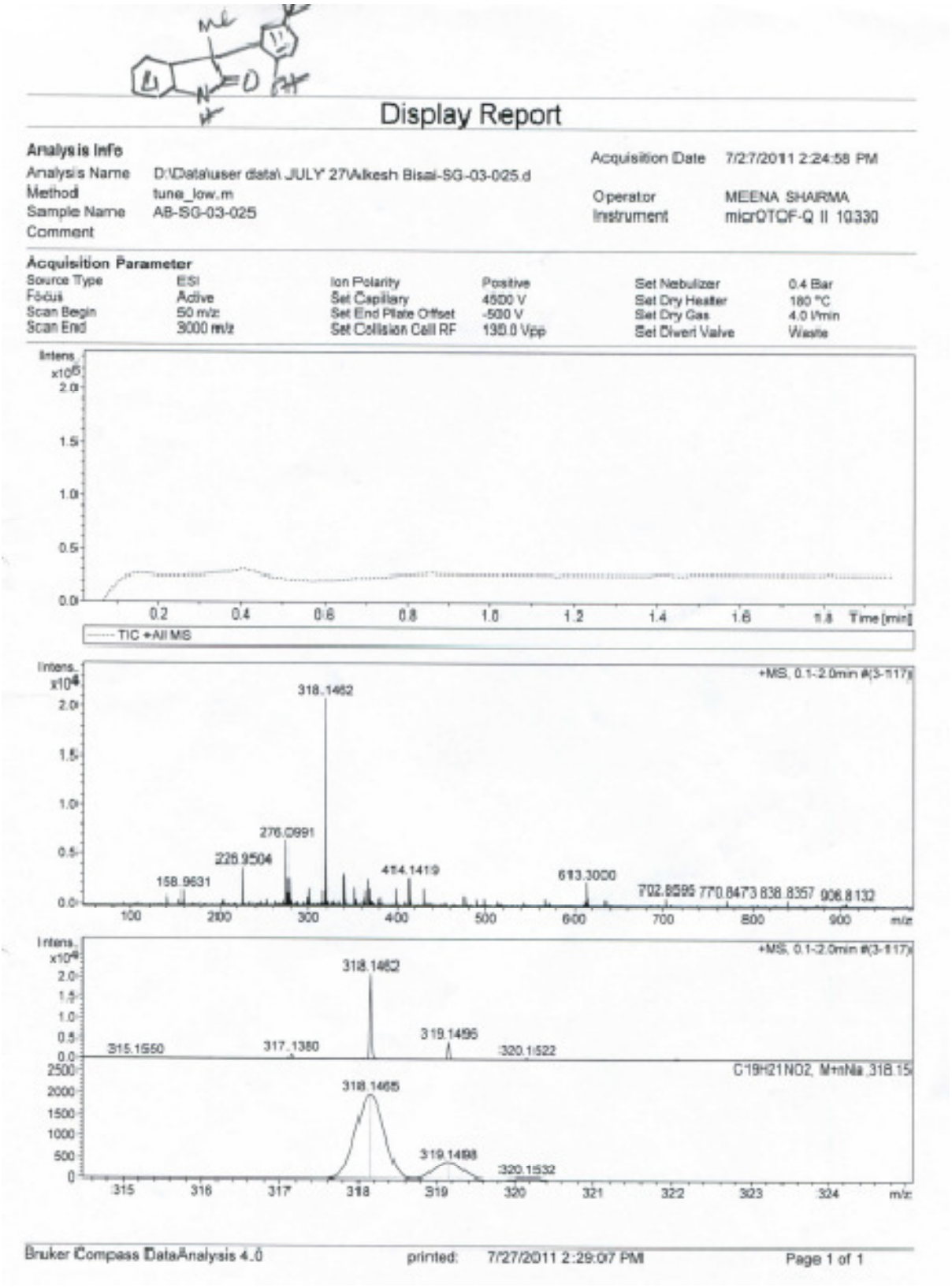




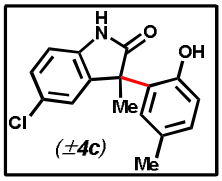
^{1}H NMR(400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**4b**)



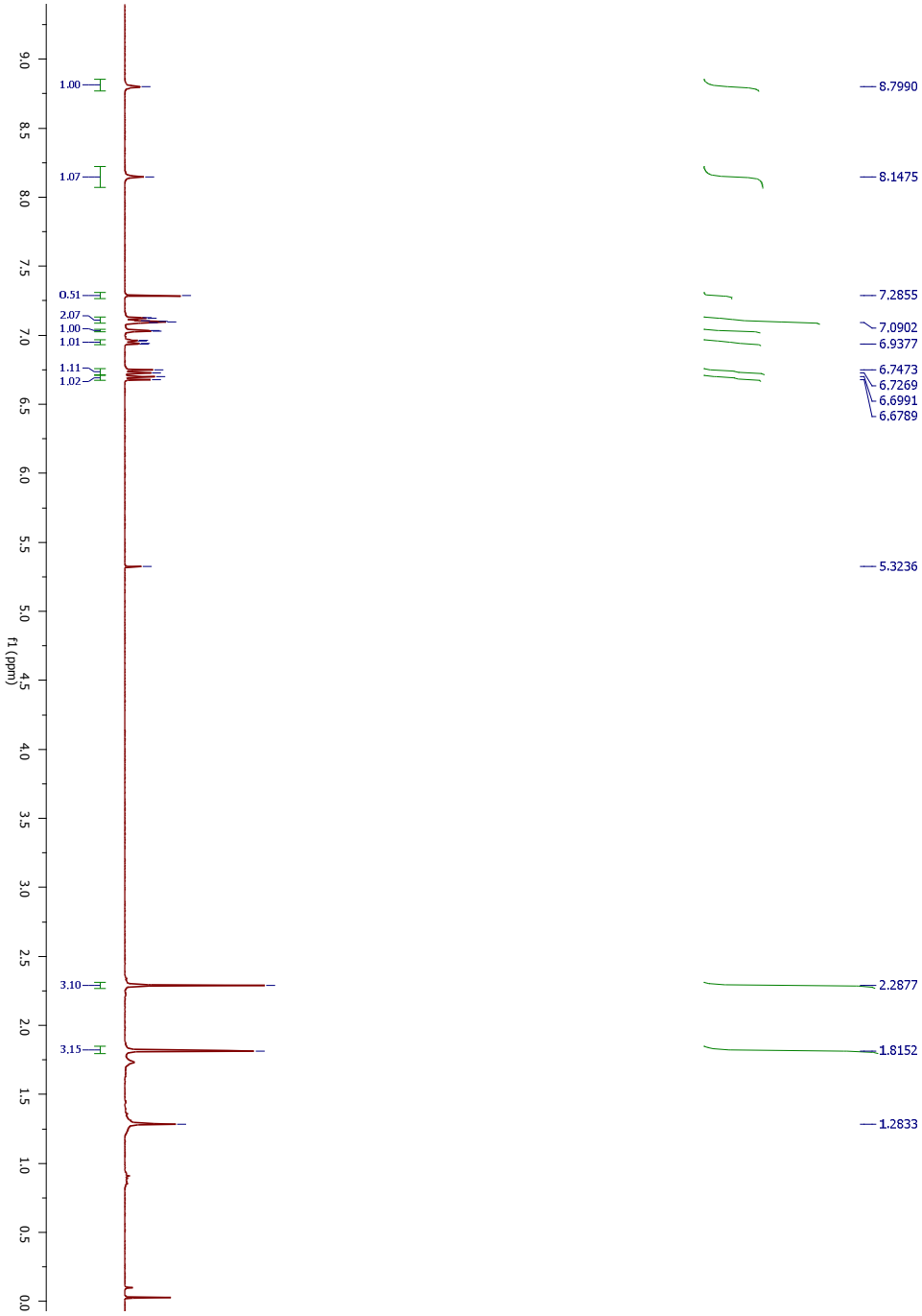
^{13}CNMR(100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**4b**)



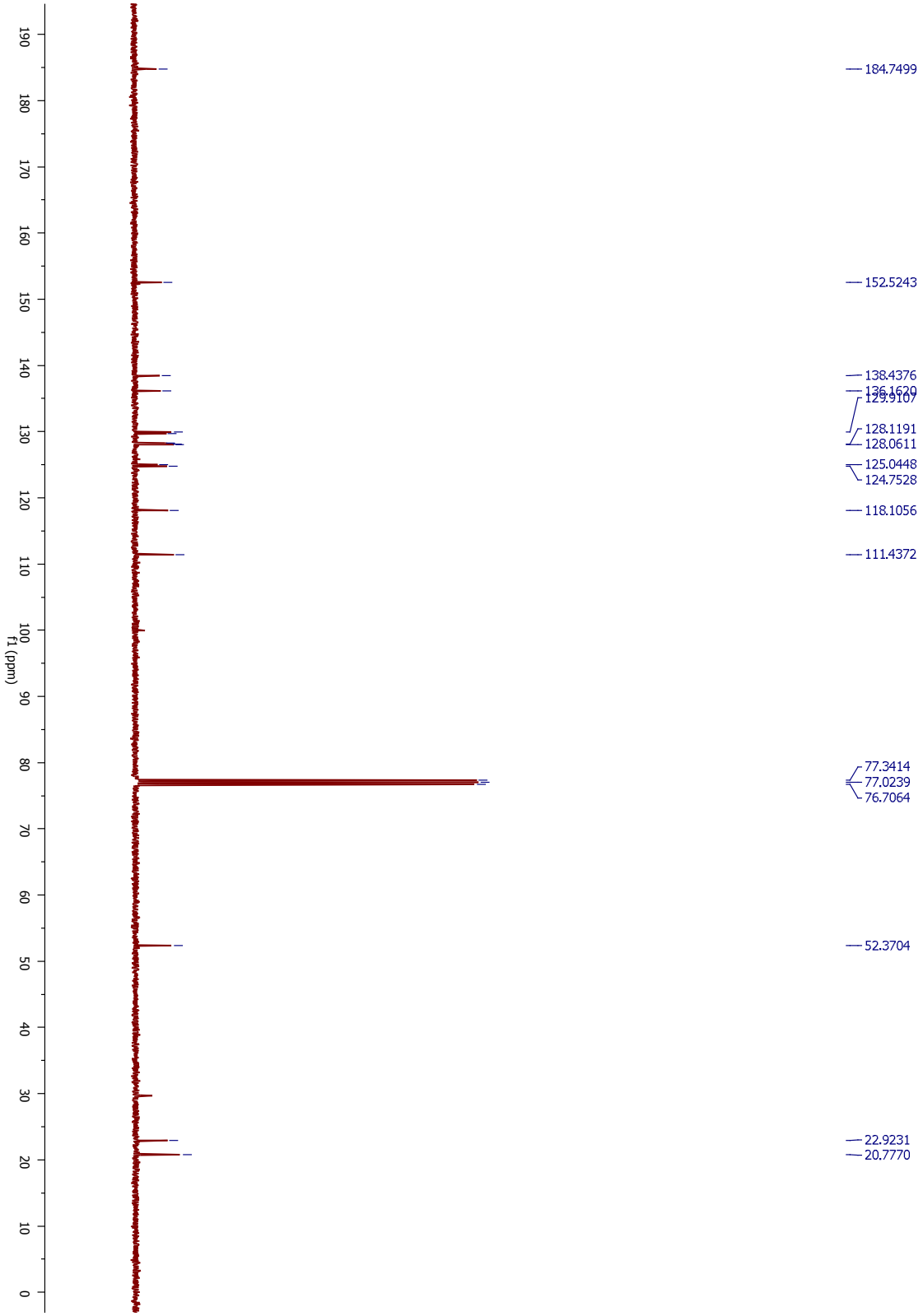
Scanned copy of mass spectrum of compound±(**4b**)



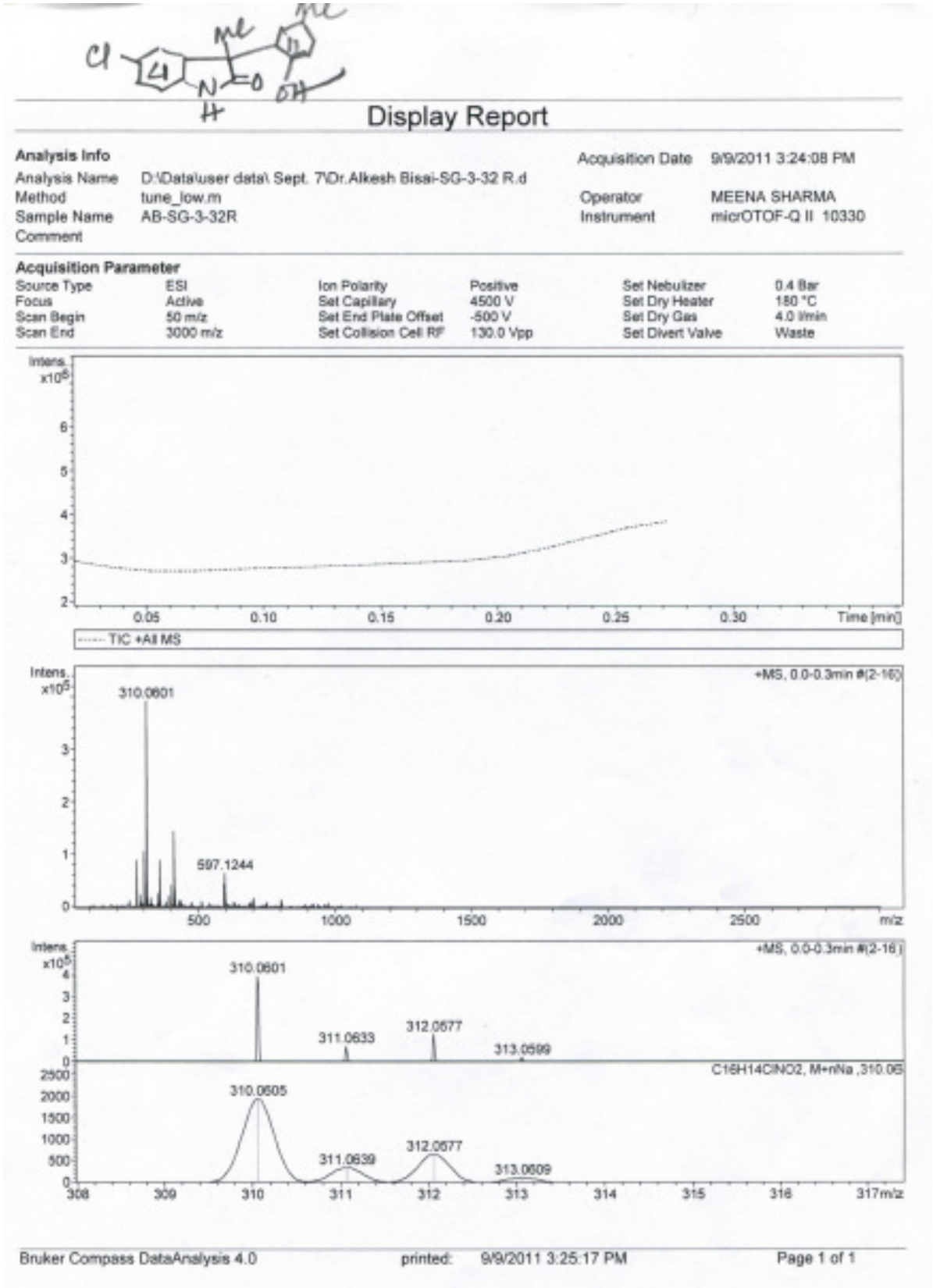
(±**4c**)



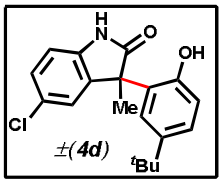
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**4c**)

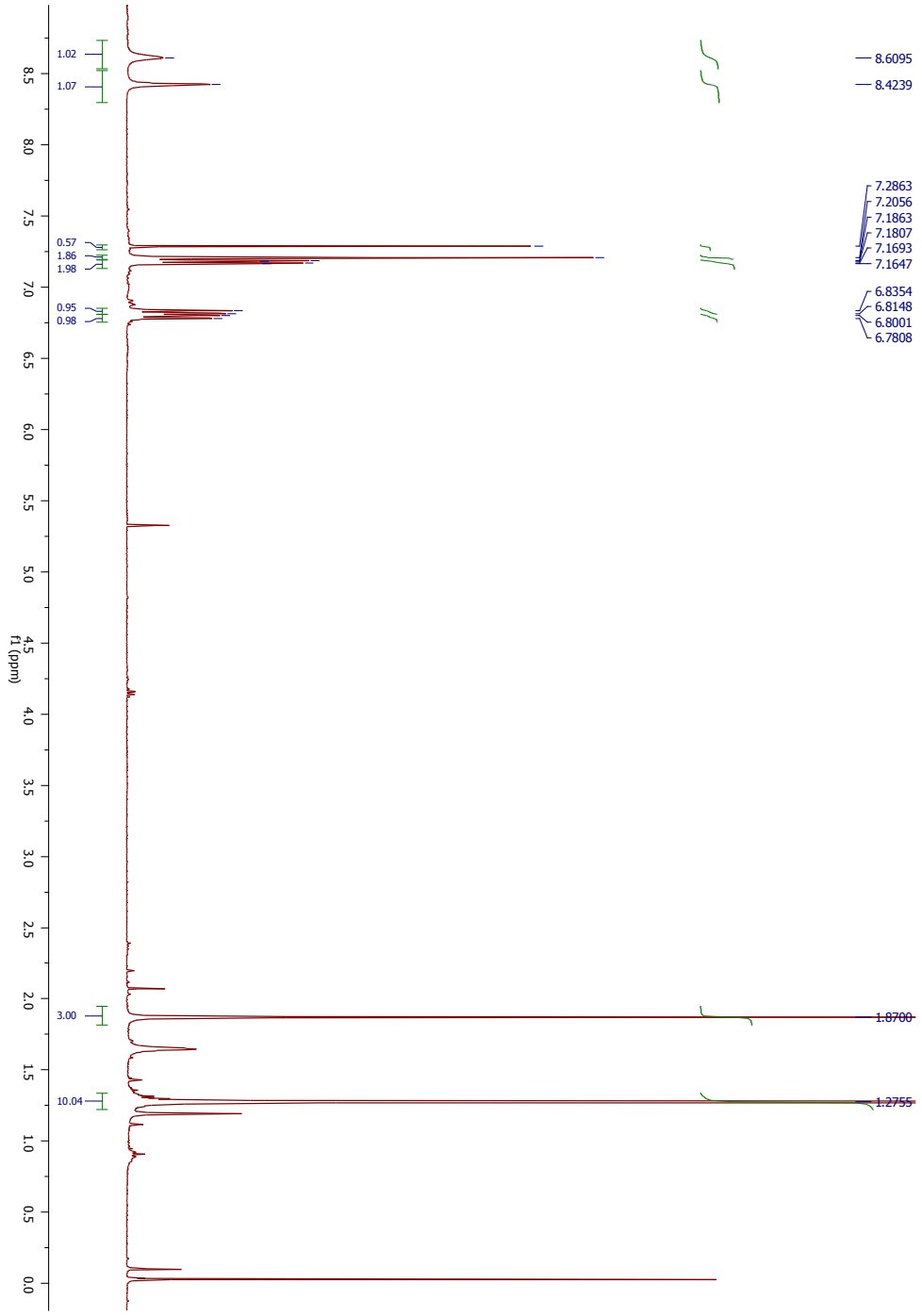


^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**4c**)

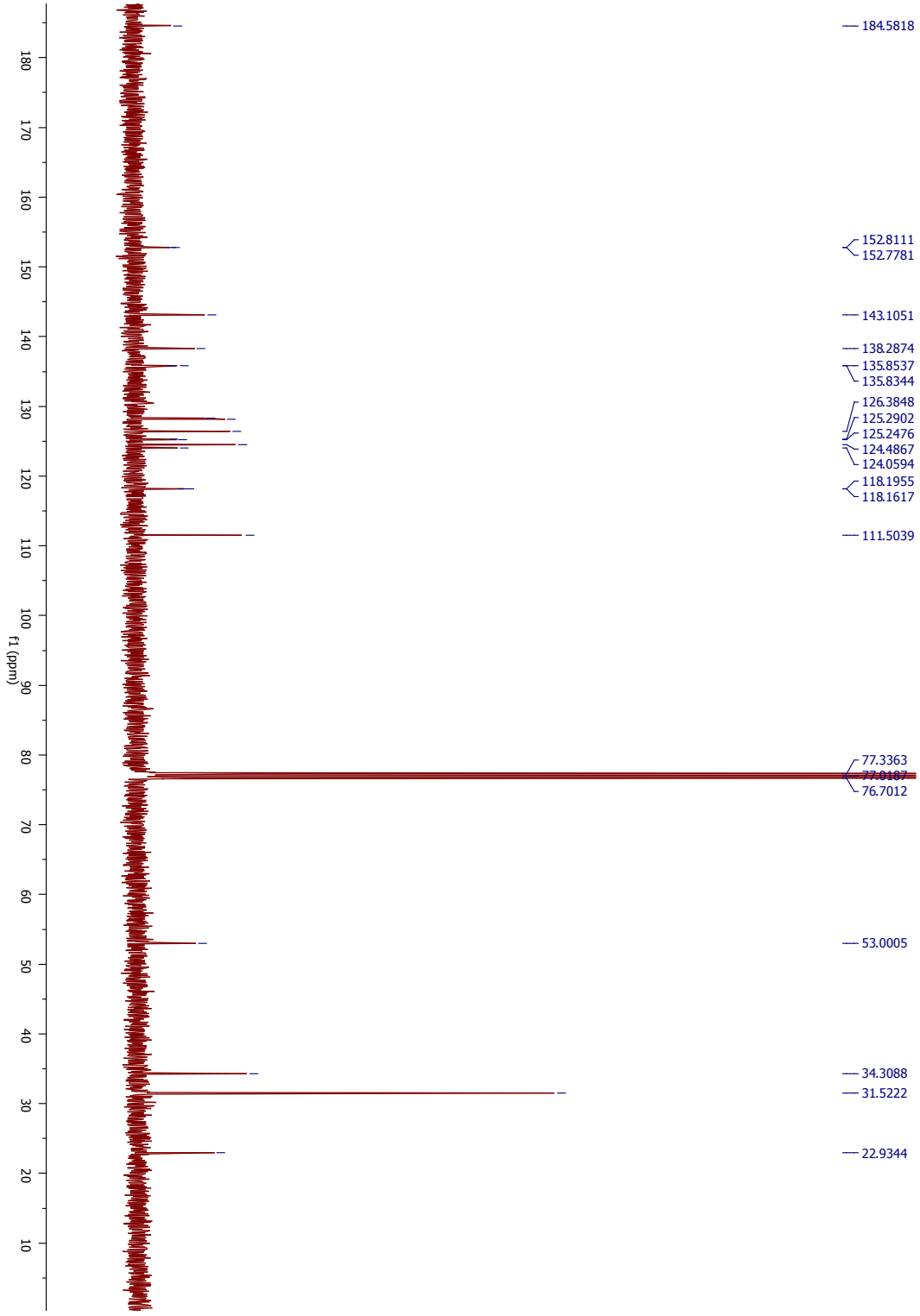


Scanned copy of mass spectrum of compound±(**4c**)

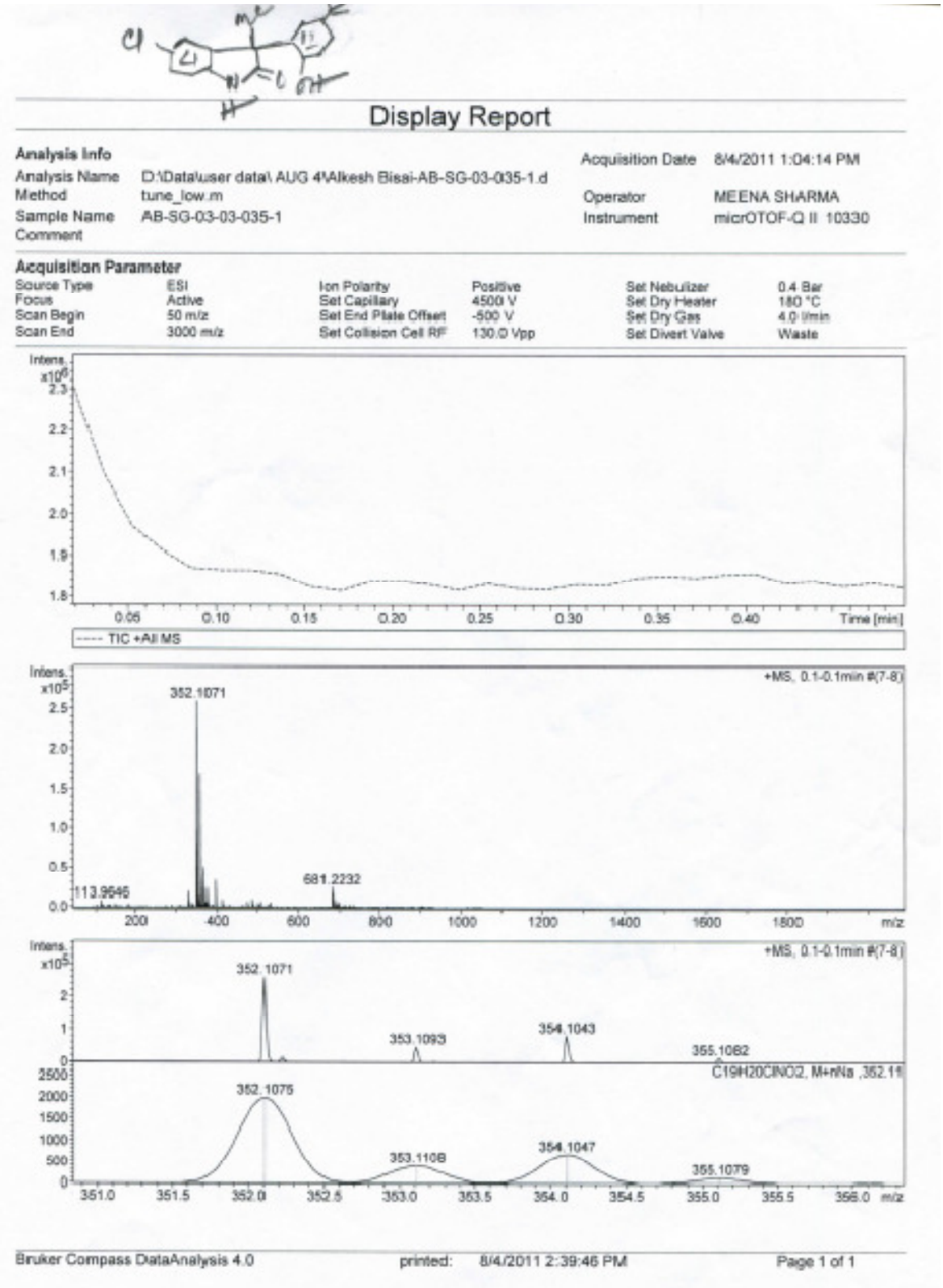




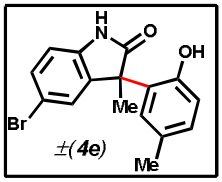
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**4d**)

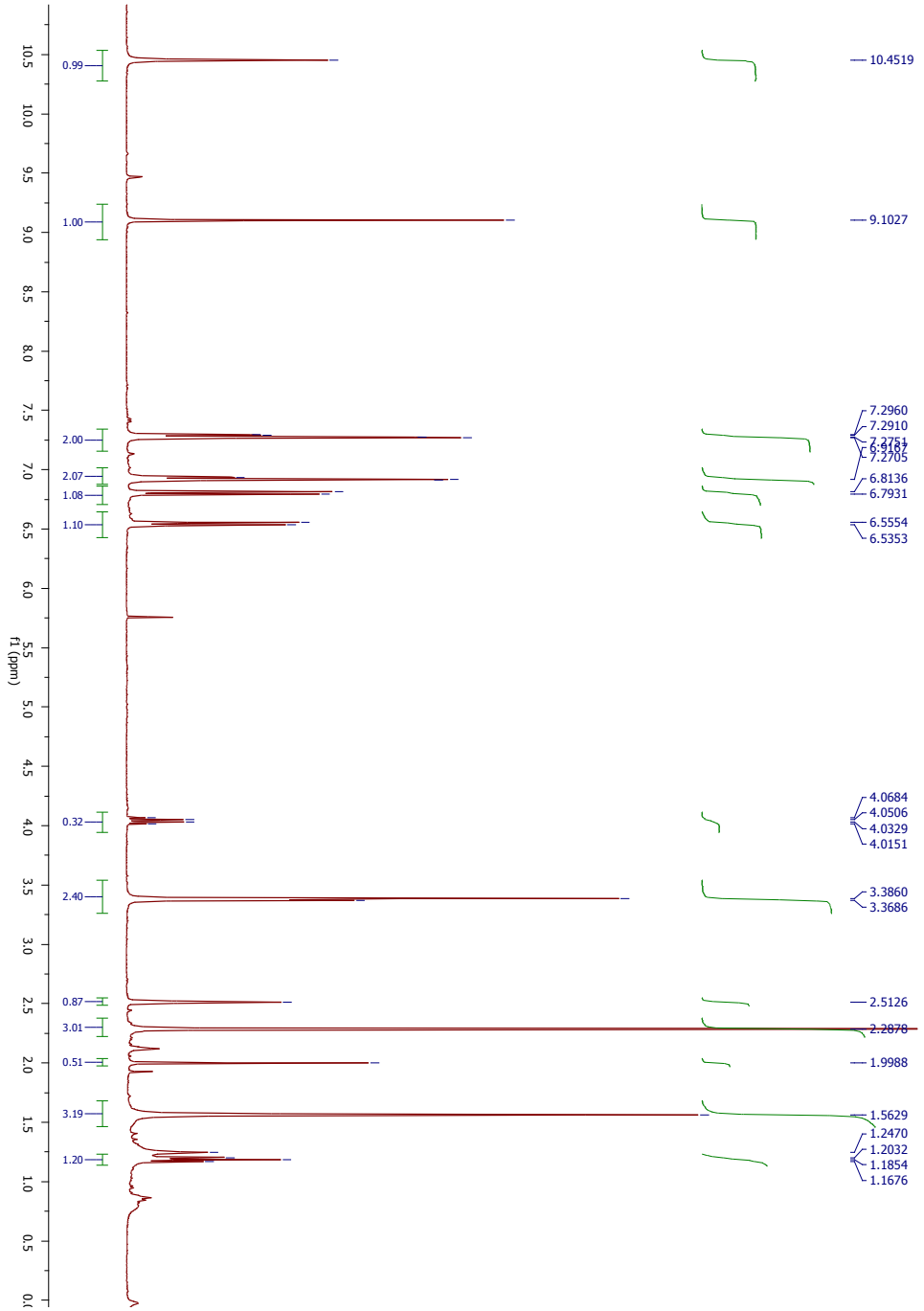


^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**4d**)

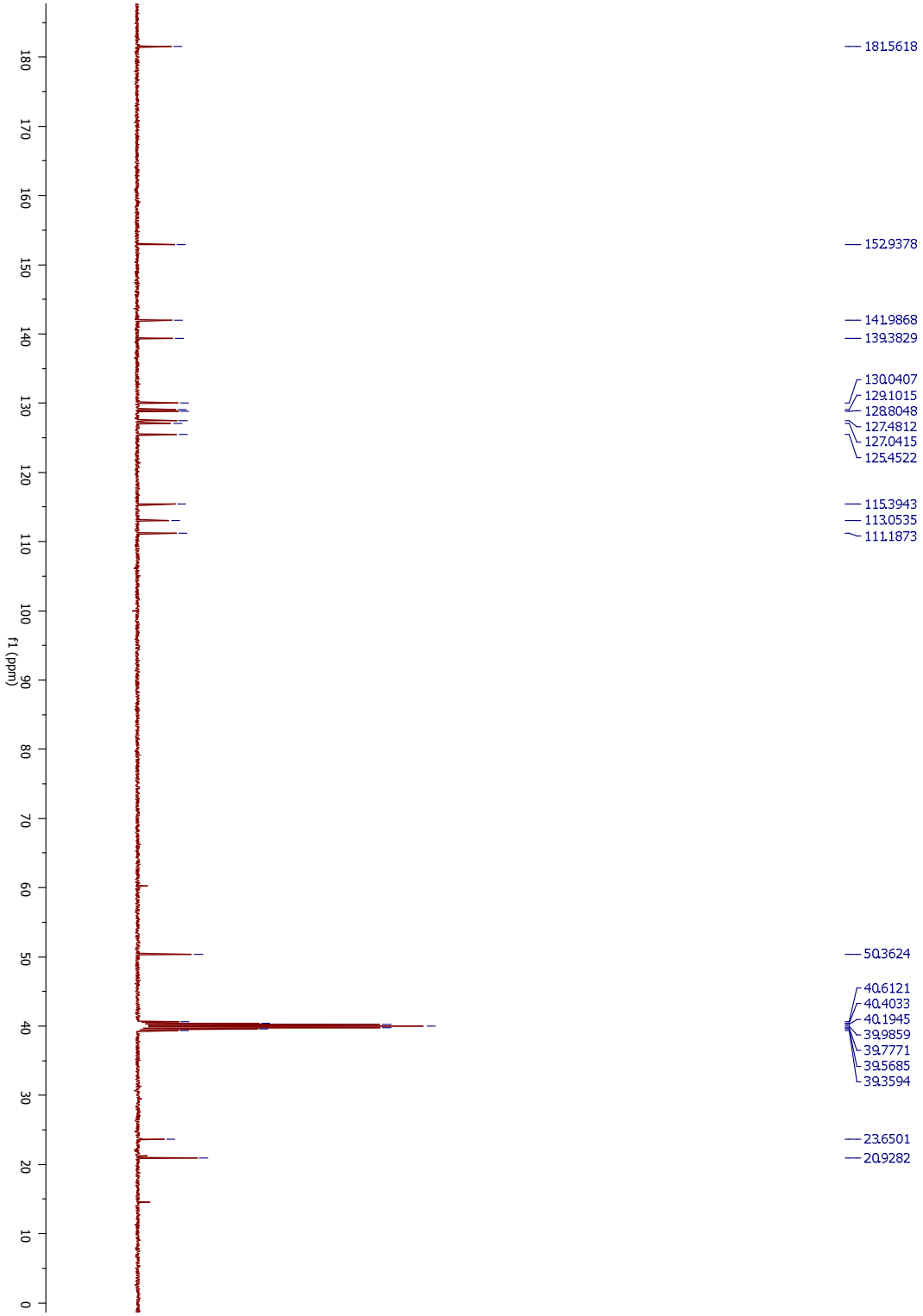


Scanned copy of mass spectrum of compound±(**4d**)

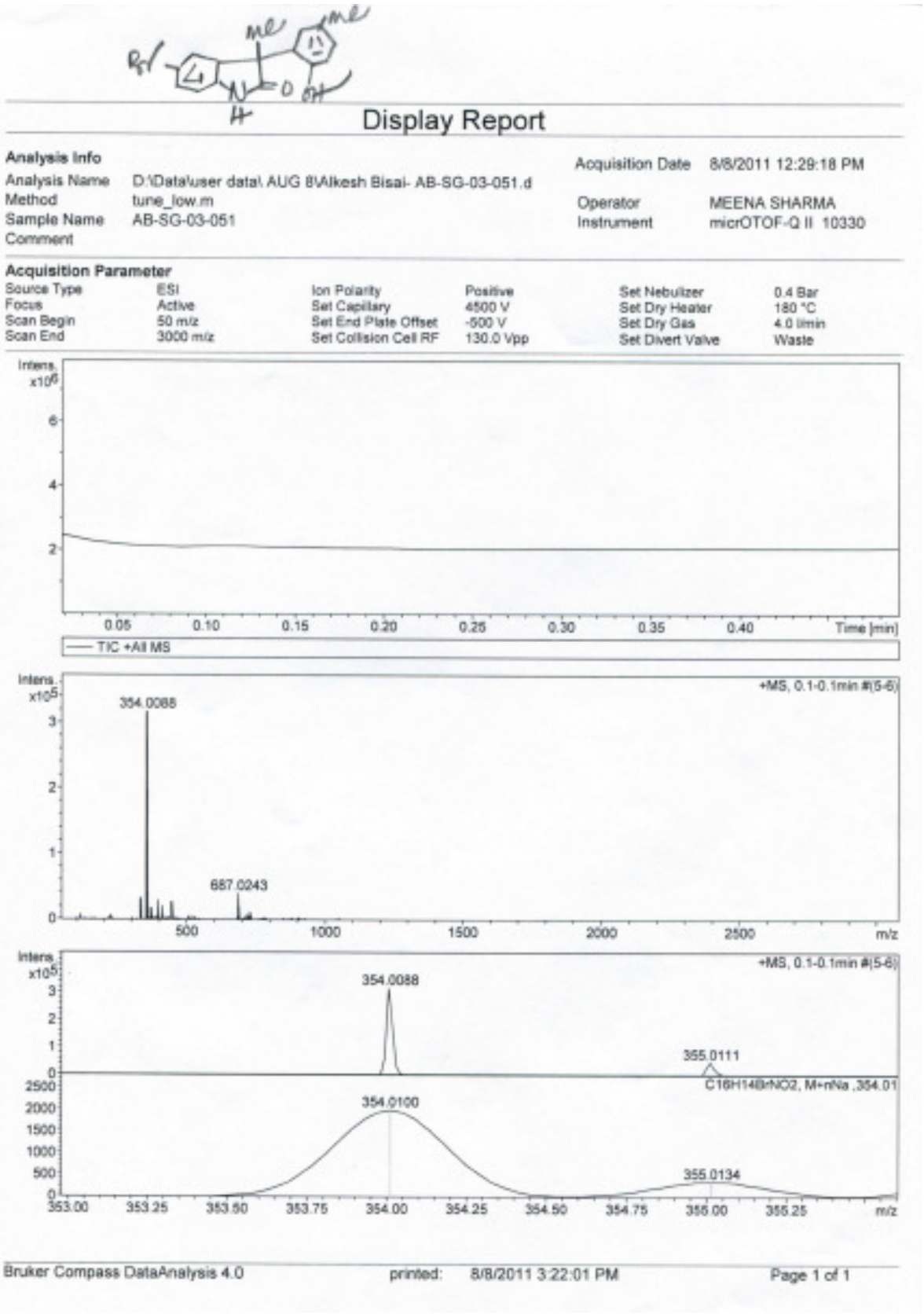




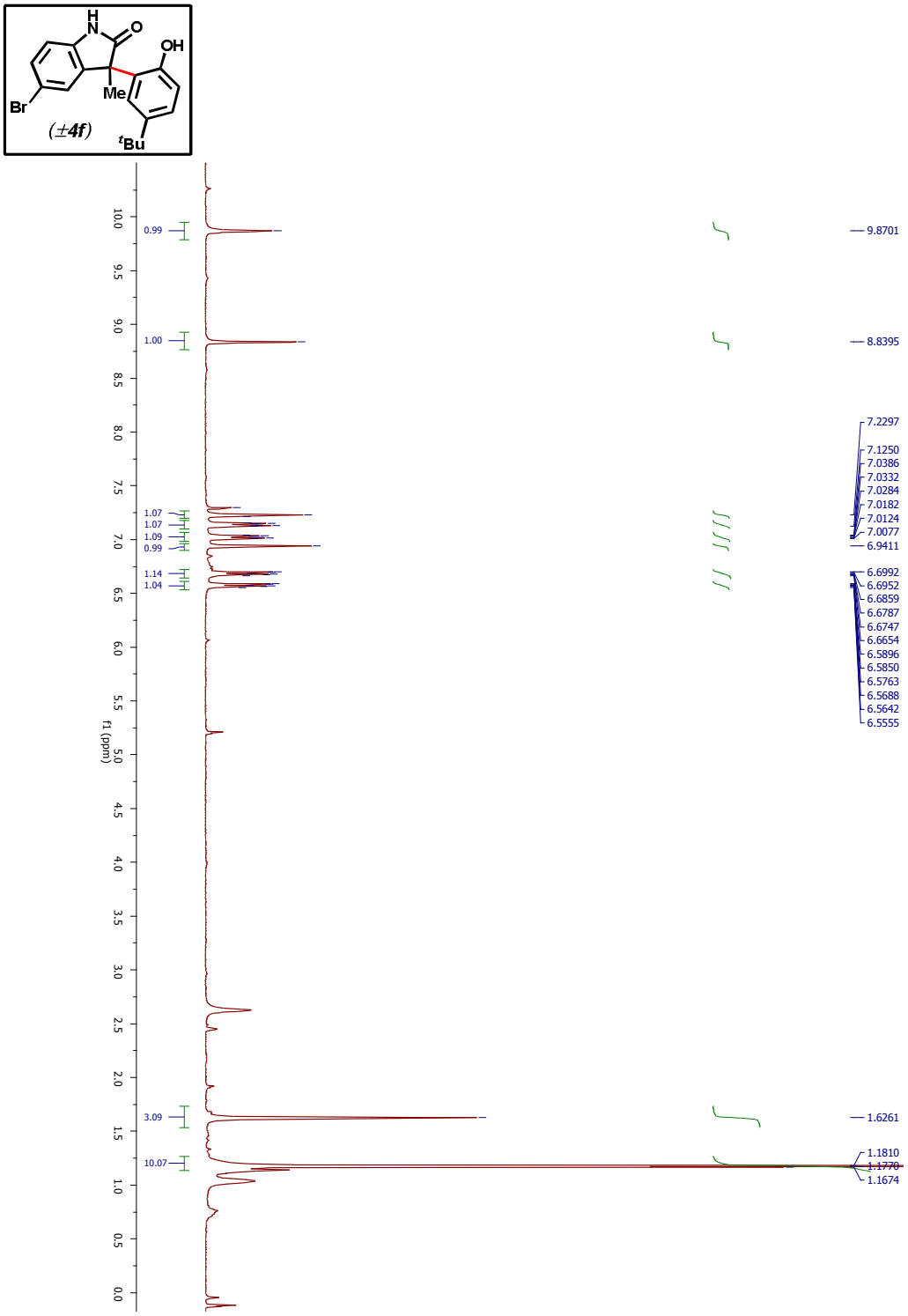
^{1}H NMR(400 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**4e**)



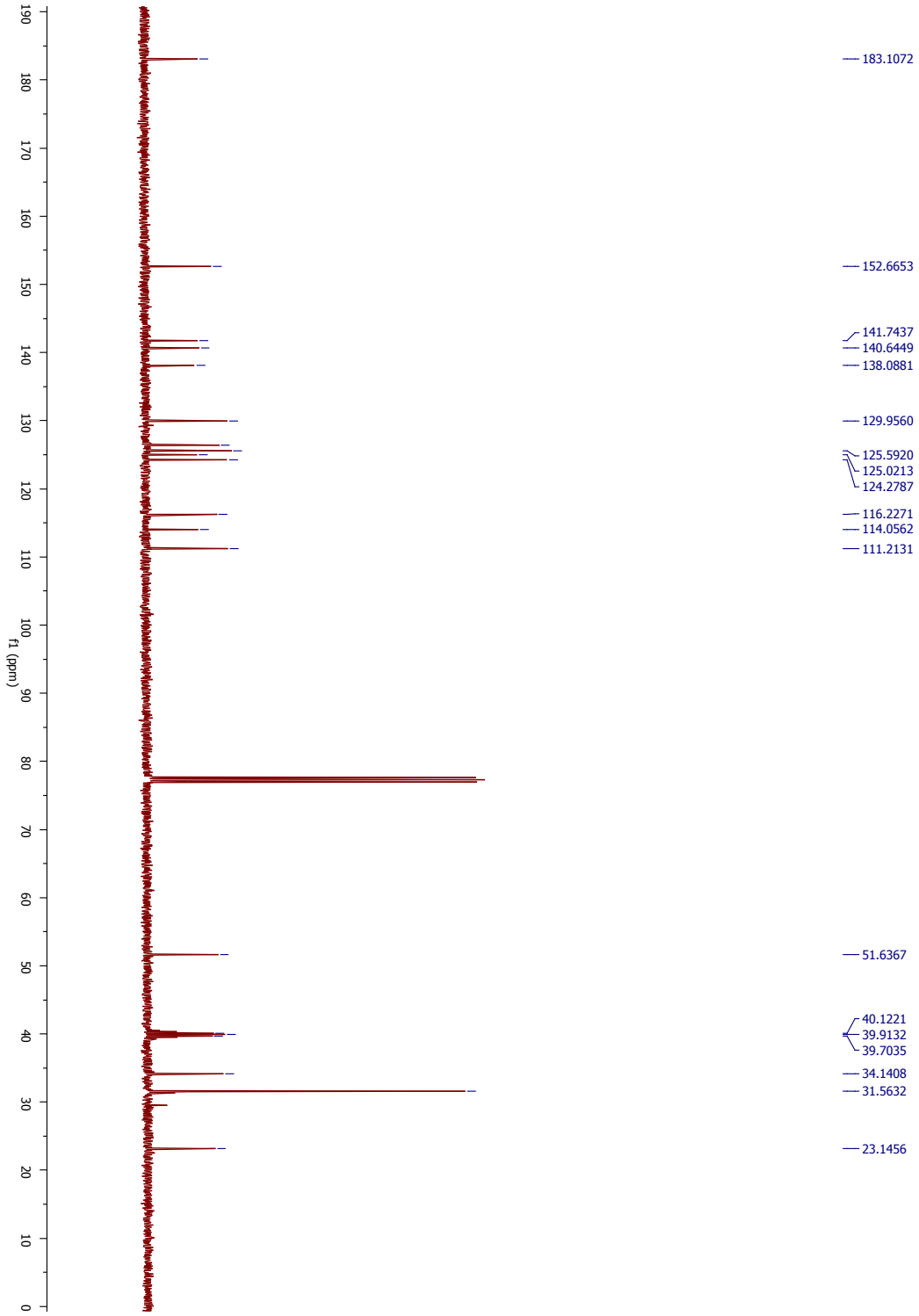
^{13}CNMR(100 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**4e**)



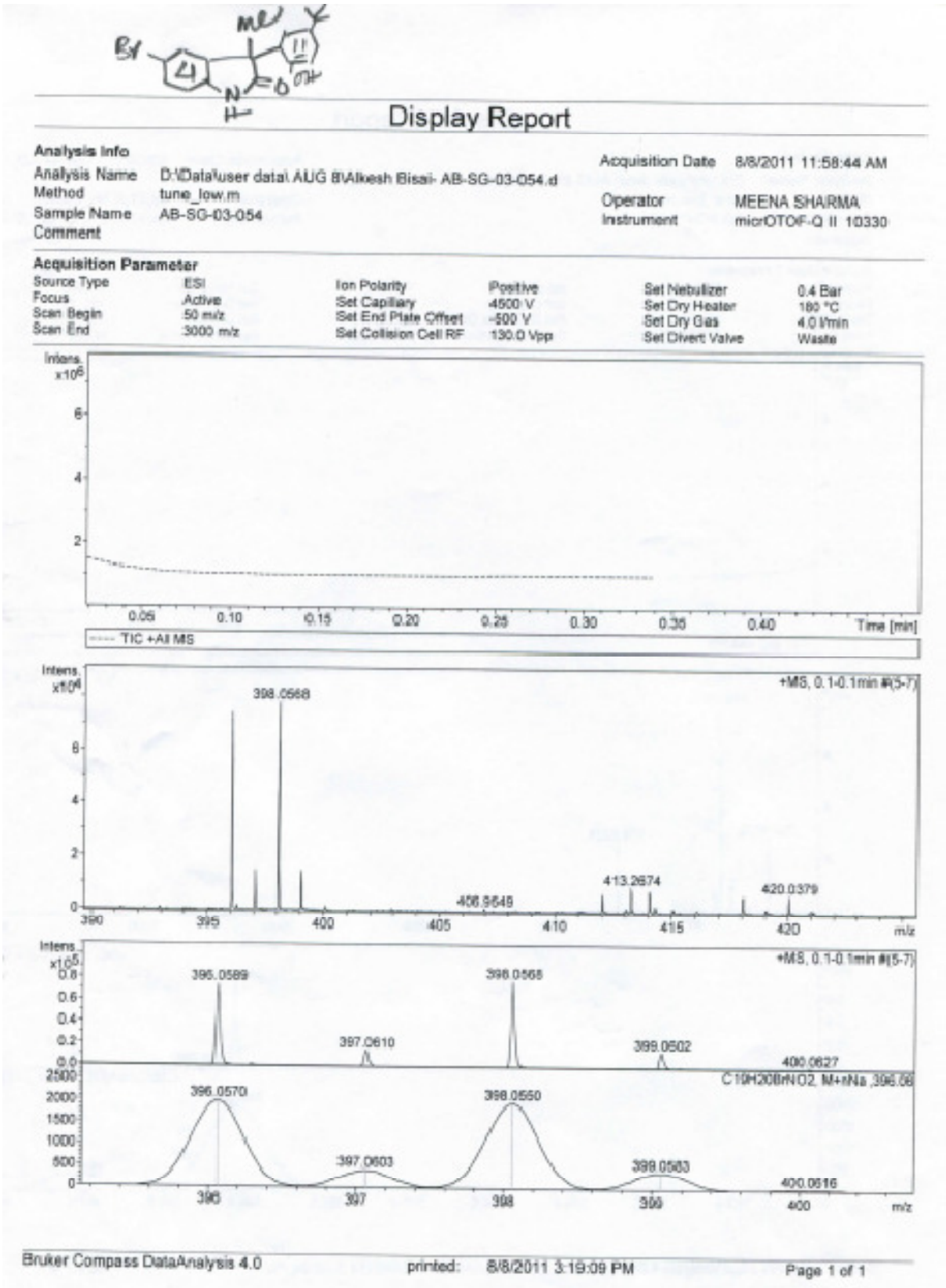
Scanned copy of mass spectrum of compound±(**4e**)



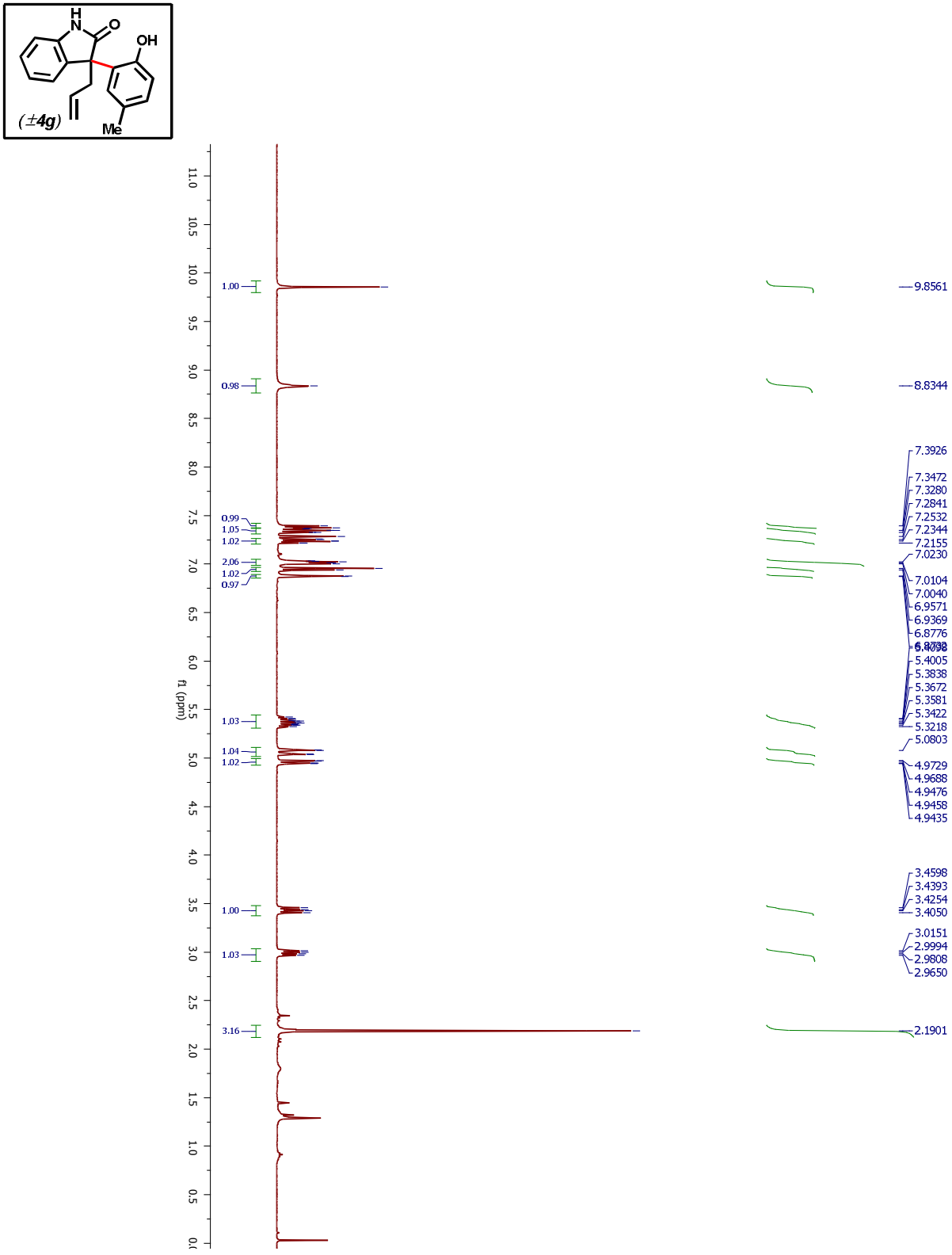
^{1}H NMR(400 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**4f**)



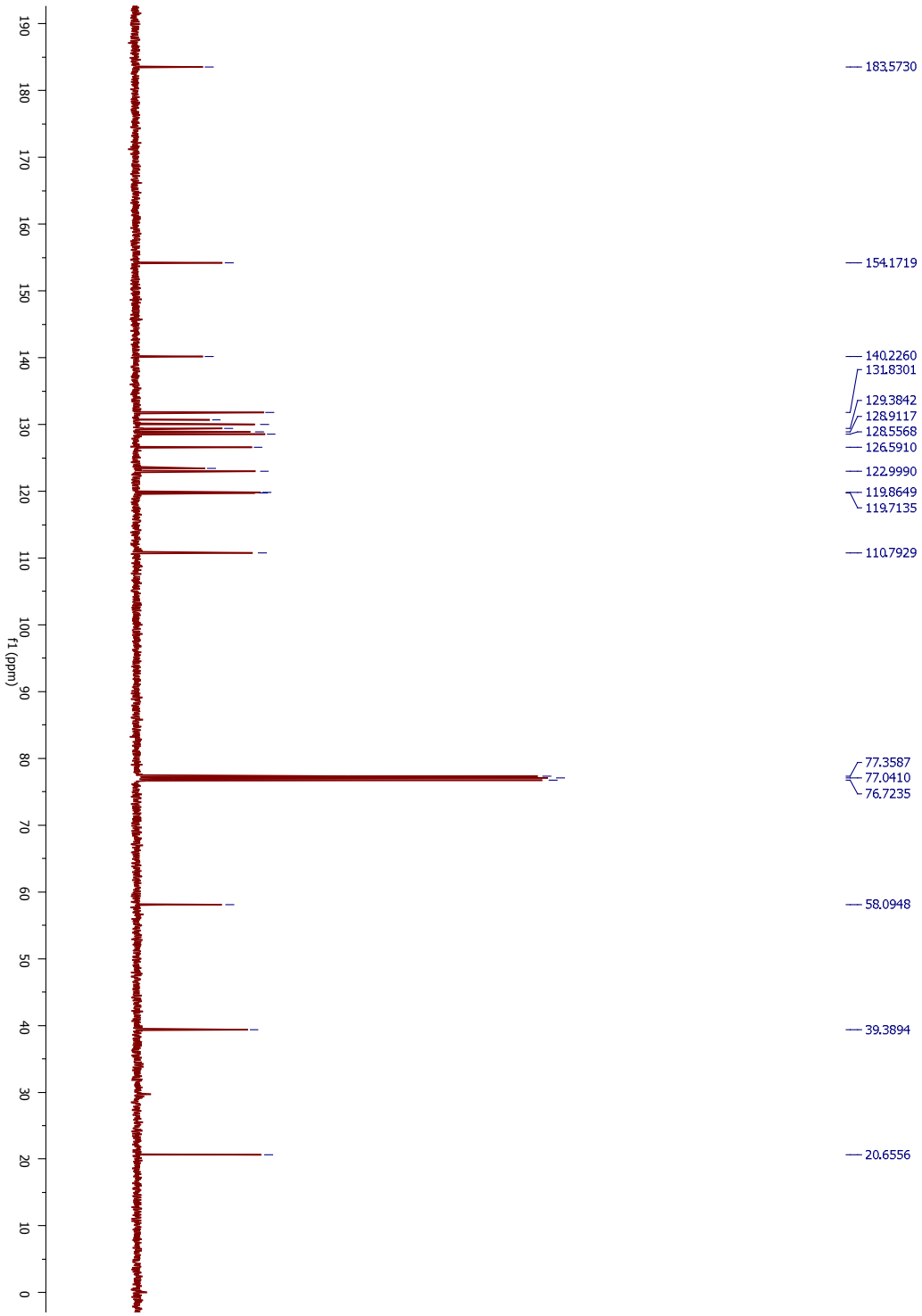
^{13}CNMR(100 MHz, 0.5 mL $CDCl_3$, 0.1 mL DMSO-d_6) of compound ±(**4f**)



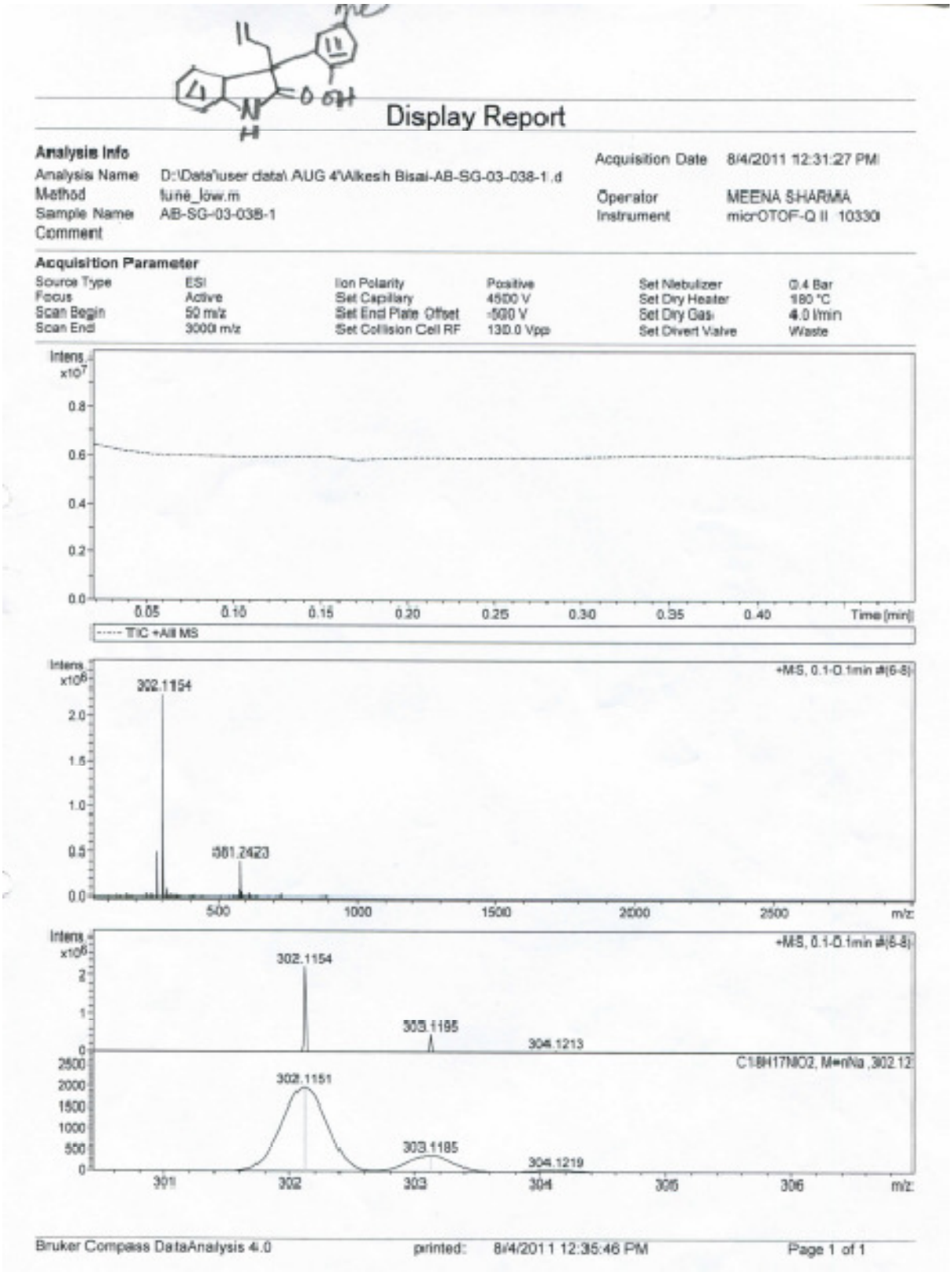
Scanned copy of mass spectrum of compound±(**4f**)



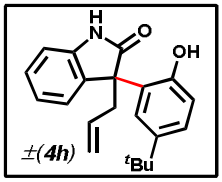
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**4g**)

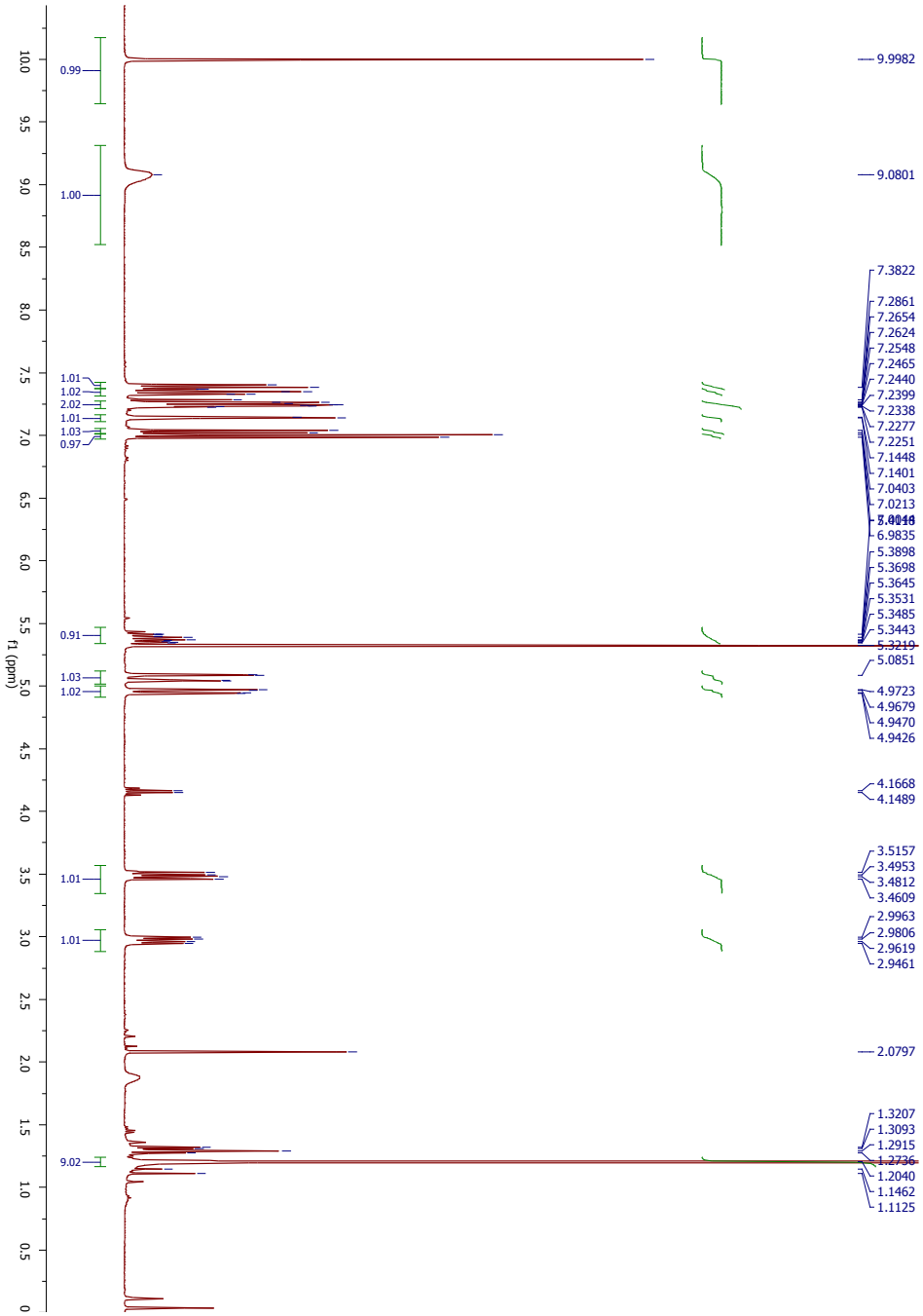


^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**4g**)

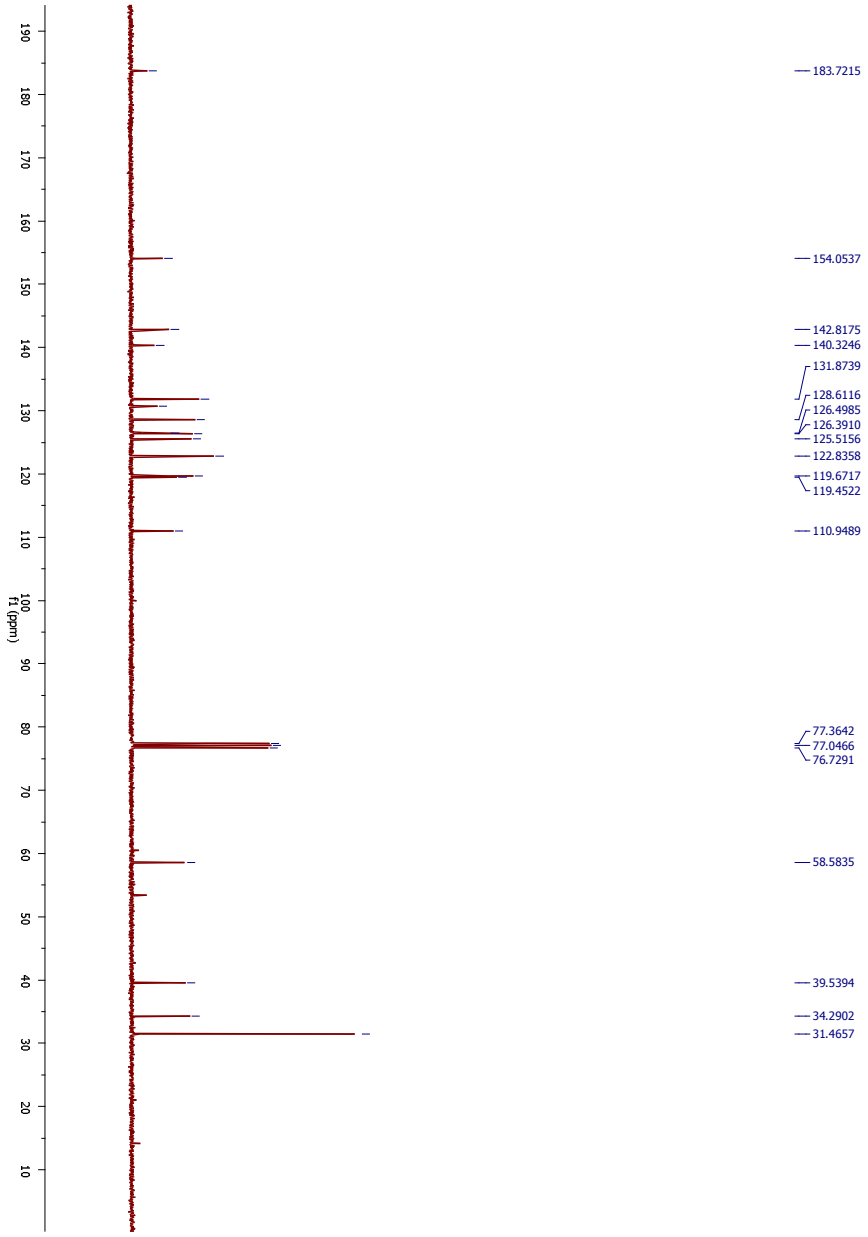


Scanned copy of mass spectrum of compound±(**4g**)

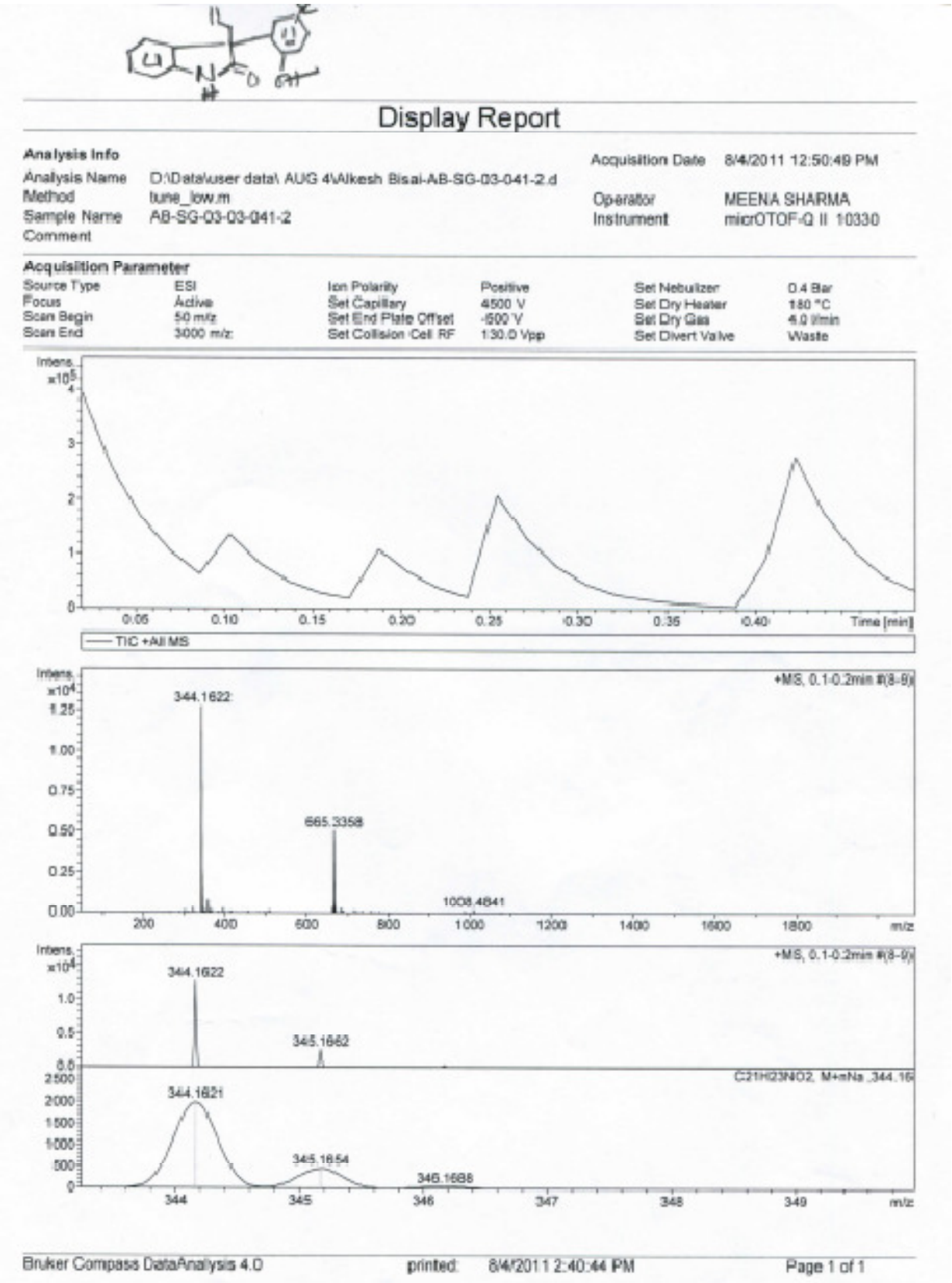




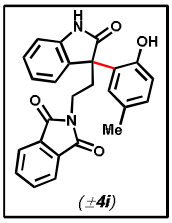
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**4h**)

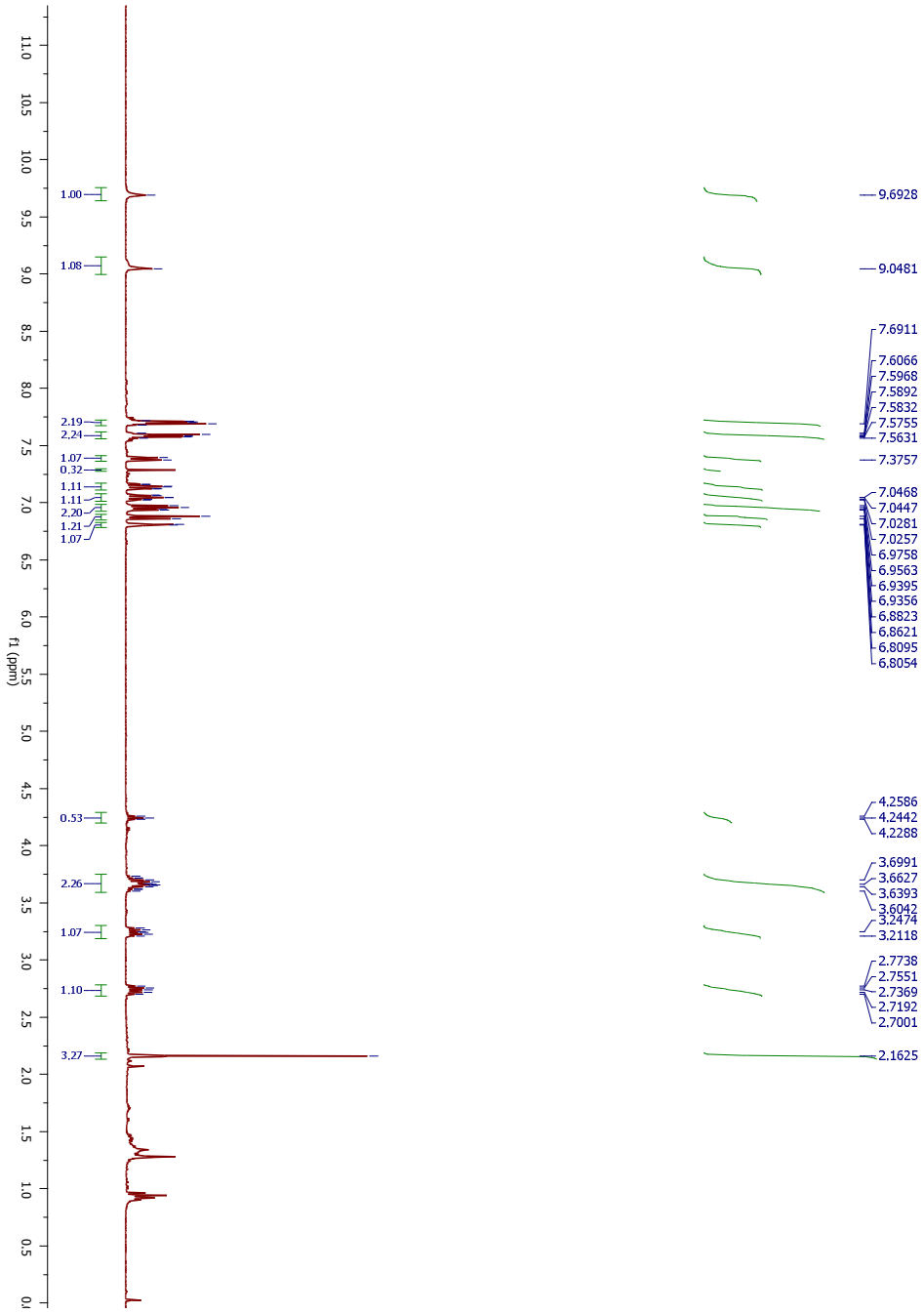


^{13}C NMR(100 MHz, $CDCl_3$) of compound ±(**4h**)

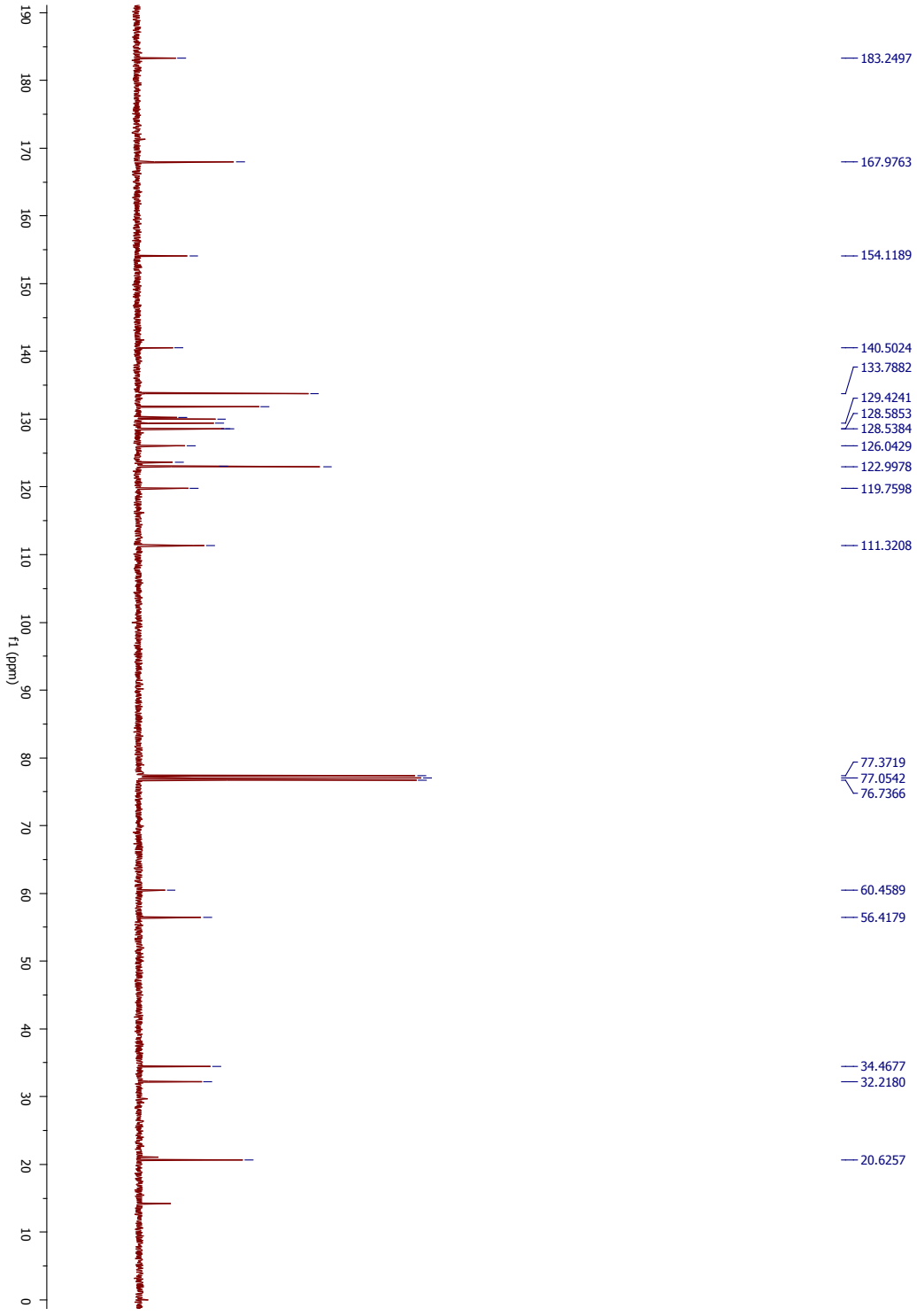


Scanned copy of mass spectrum of compound±(**4h**)

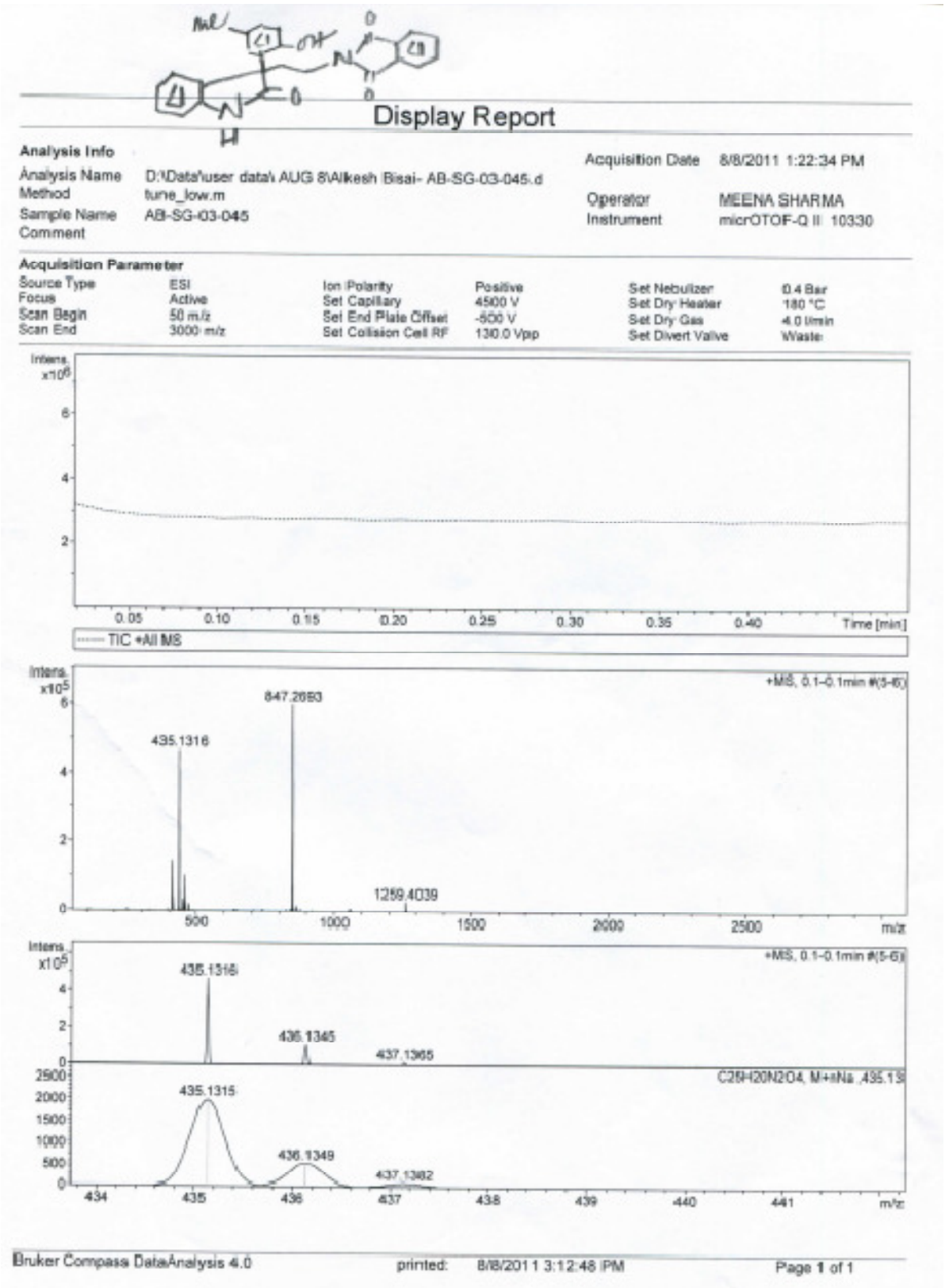




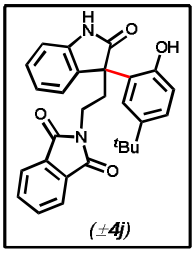
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**4i**)



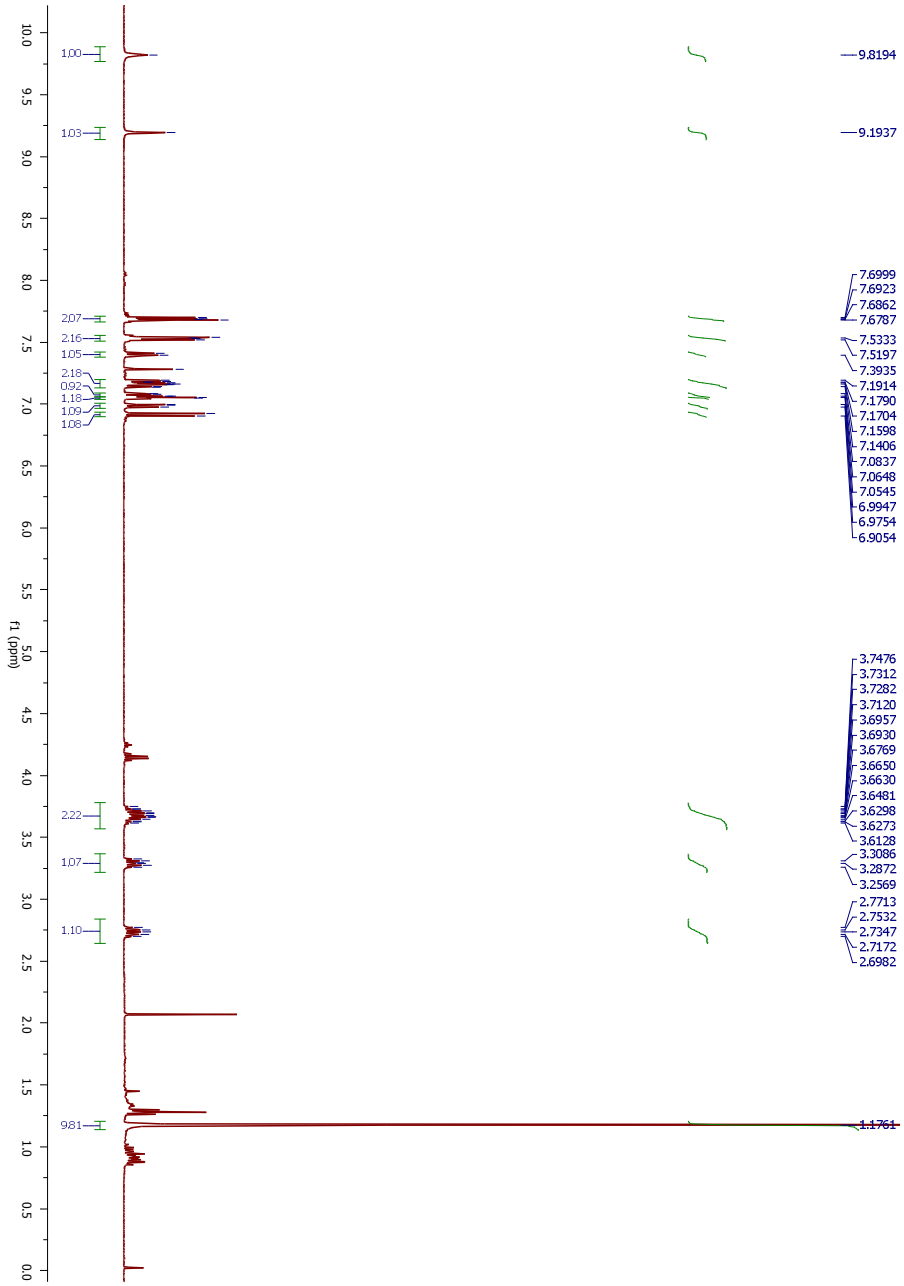
^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**4i**)



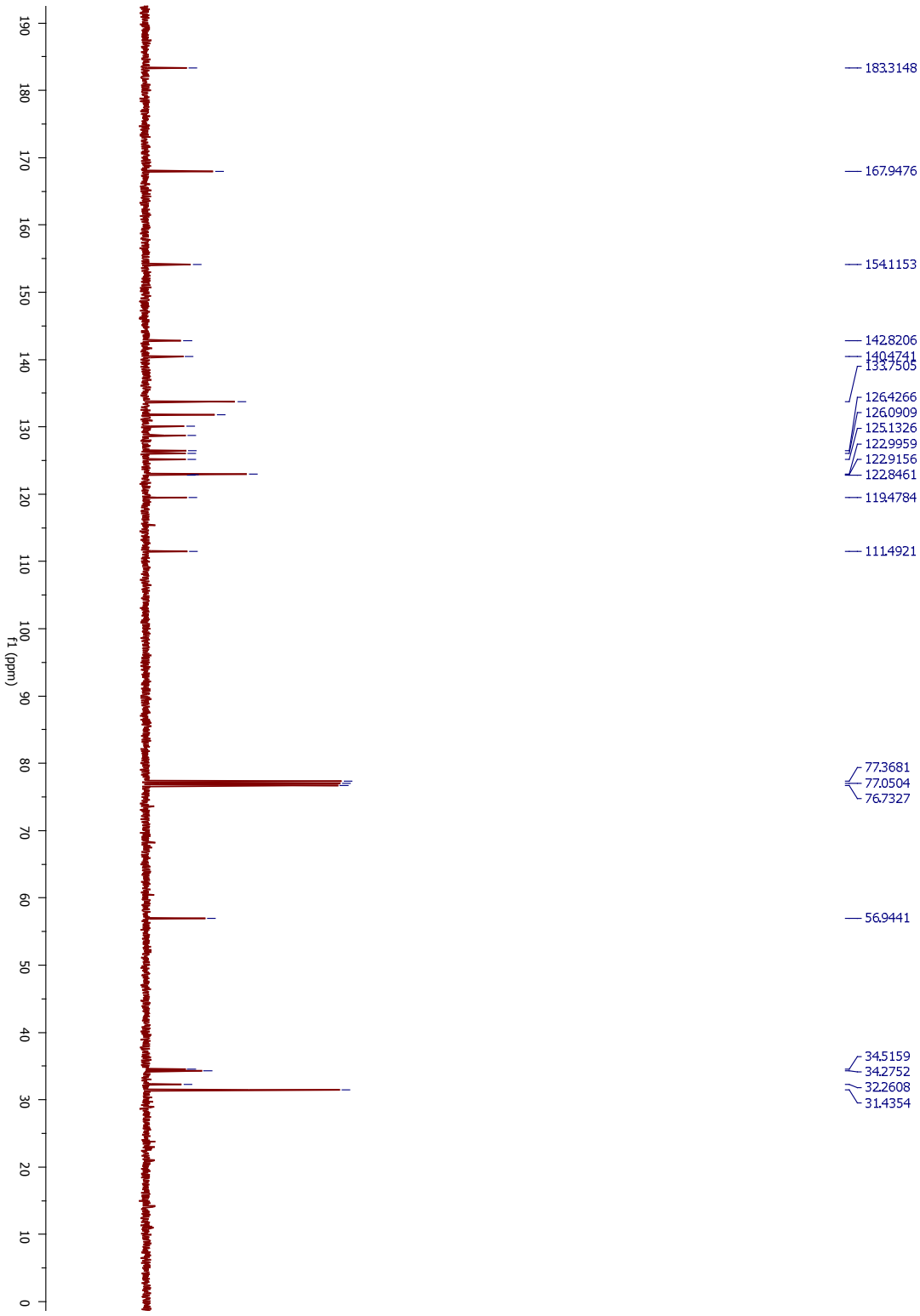
Scanned copy of mass spectrum of compound±(**4i**)



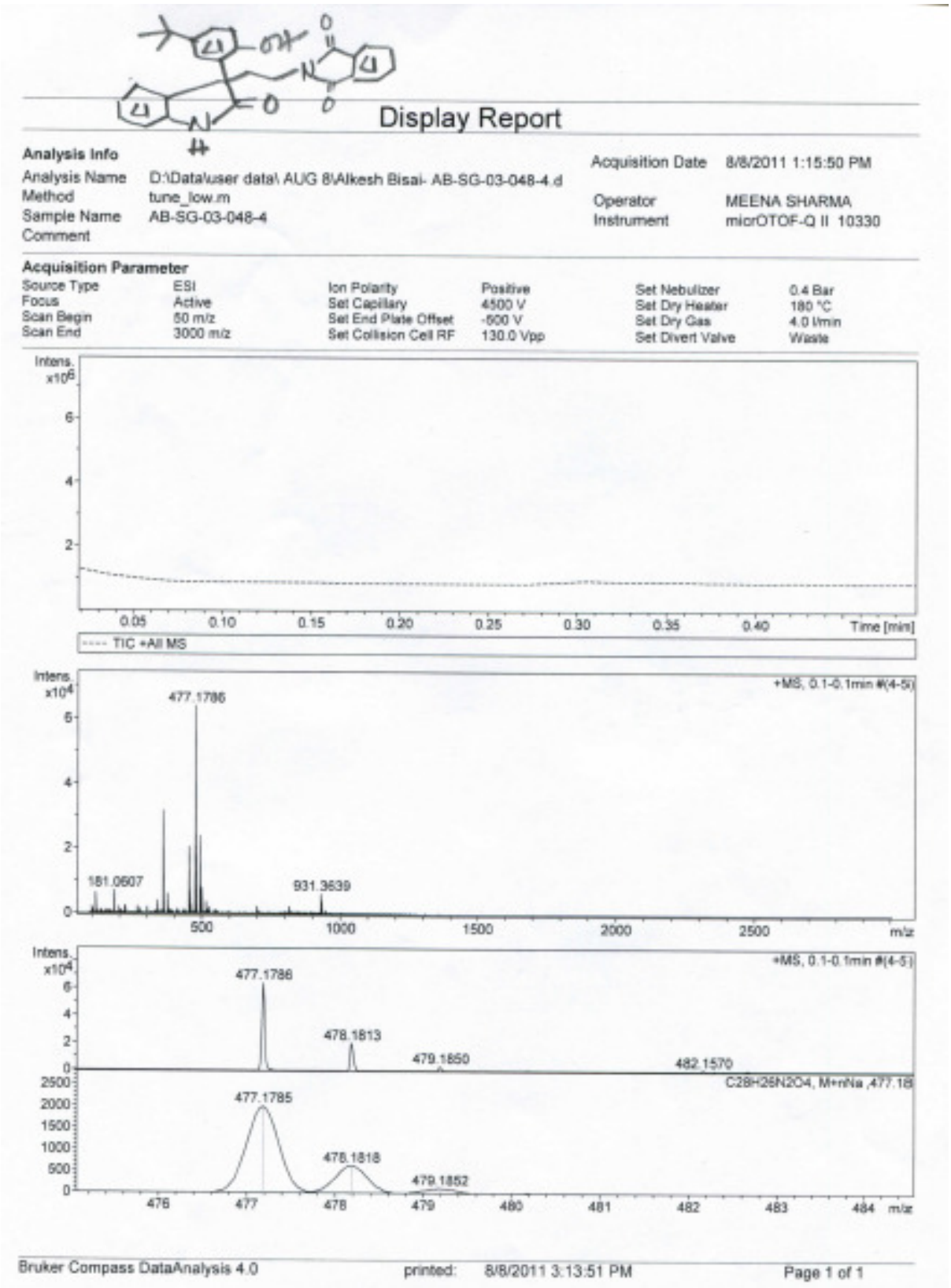
(±**4j**)



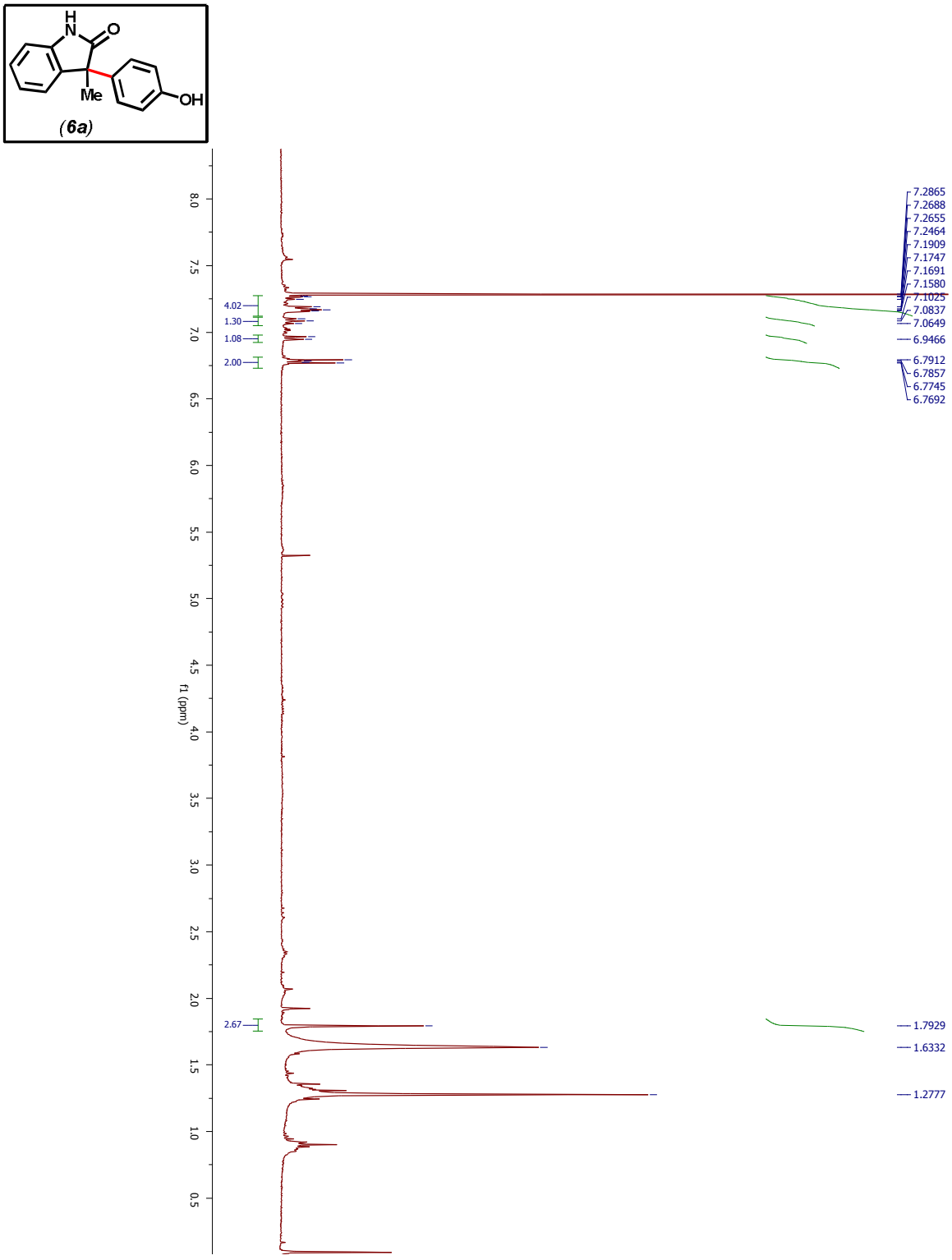
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**4j**)



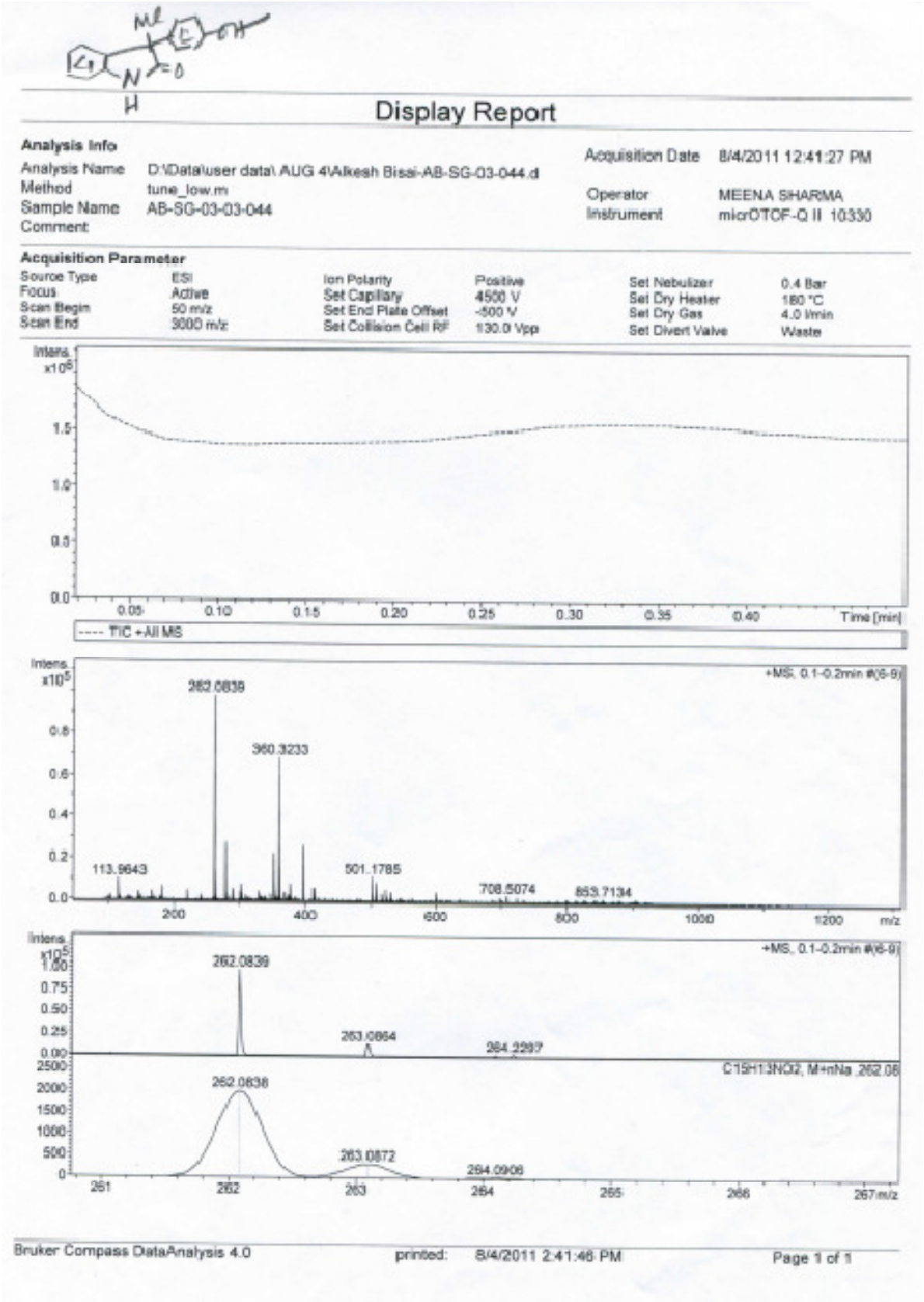
^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**4j**)



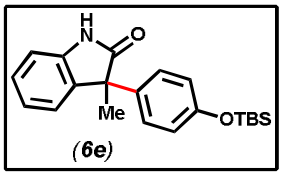
Scanned copy of mass spectrum of compound±(**4j**)

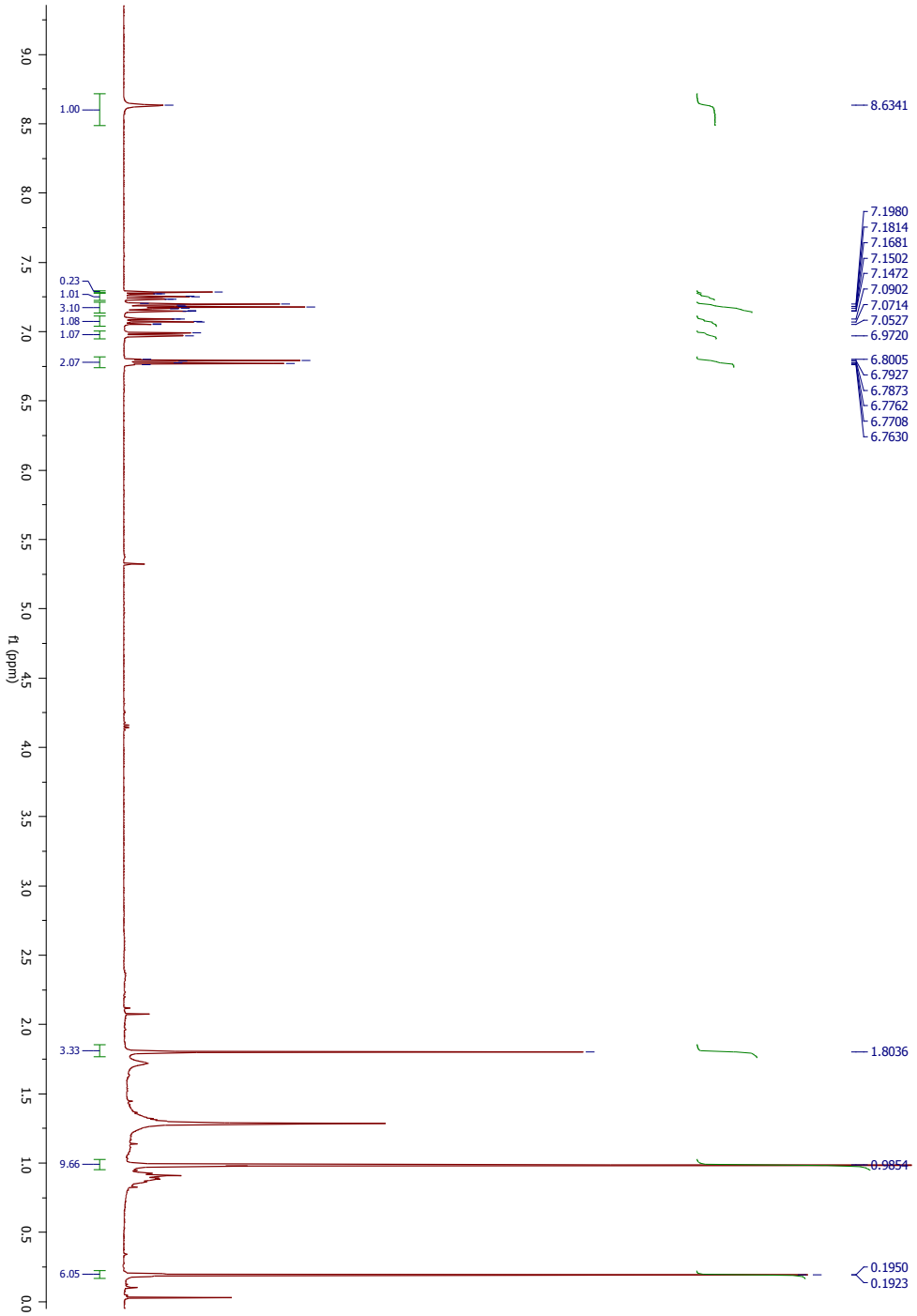


^{1}H NMR(400 MHz, 1:1 $CDCl_3$and DMSO-d_6) of compound ±(**6a**)

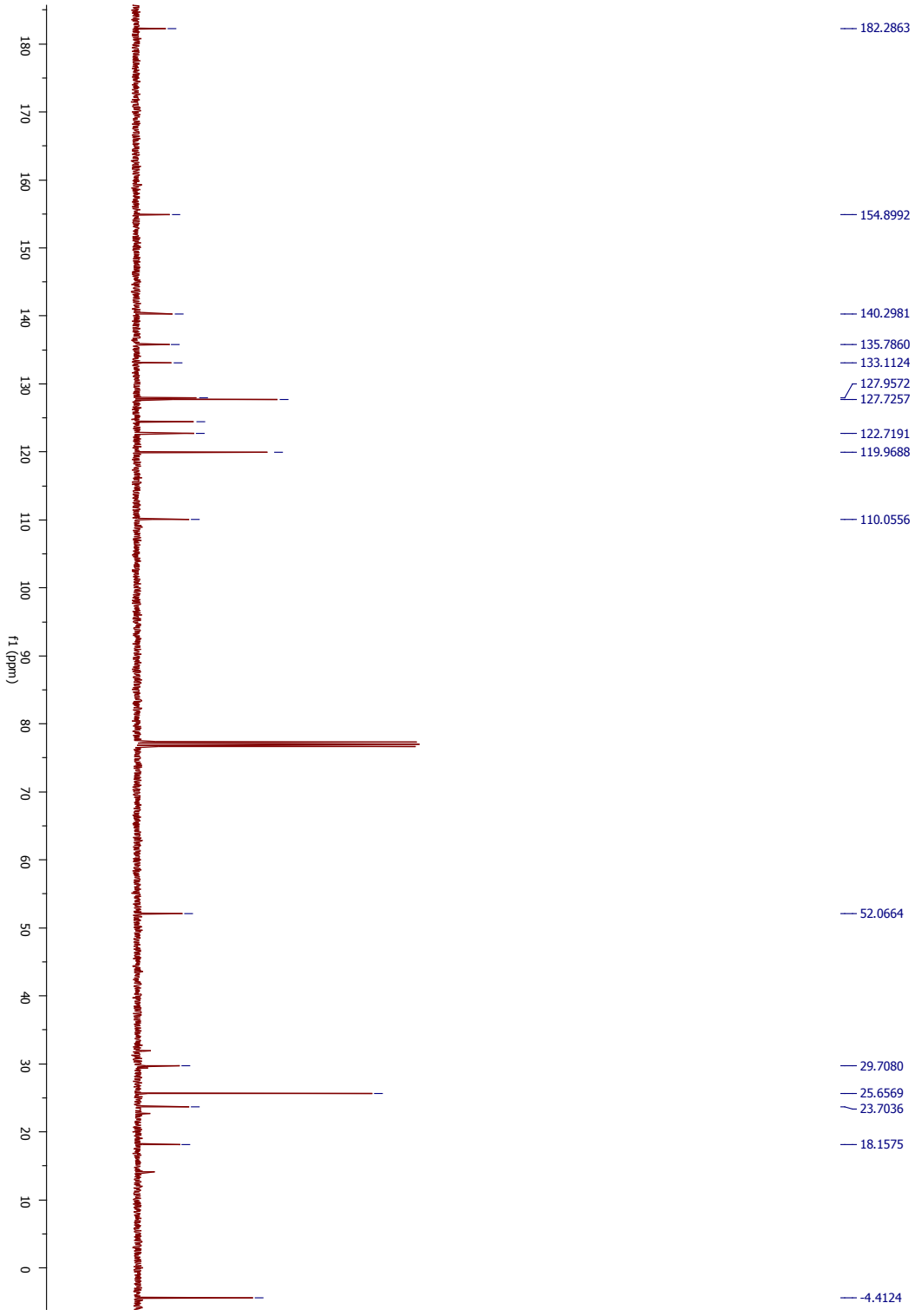


Scanned copy of mass spectrum of compound±(**6a**)

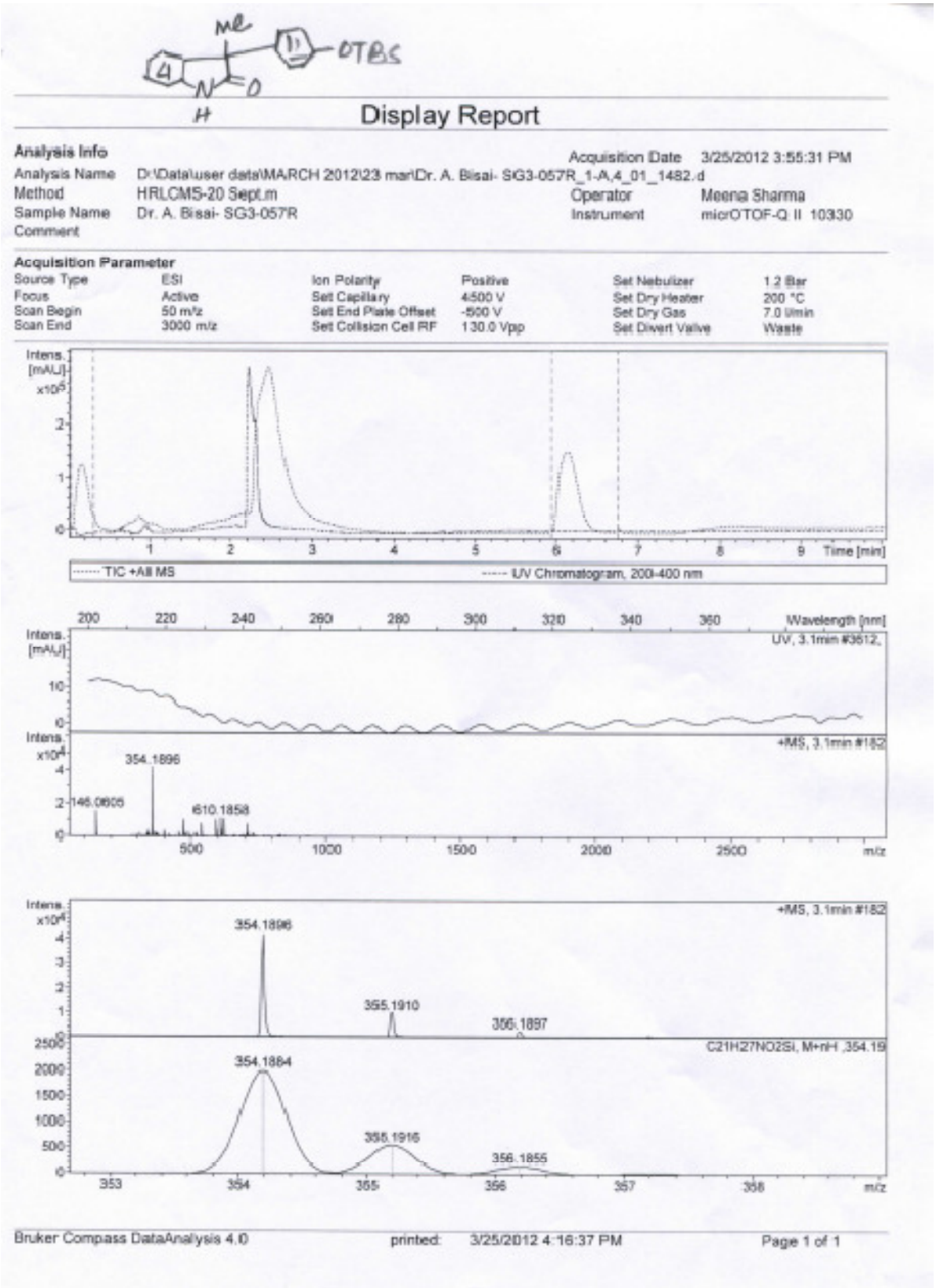




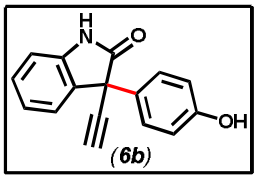
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**6e**)

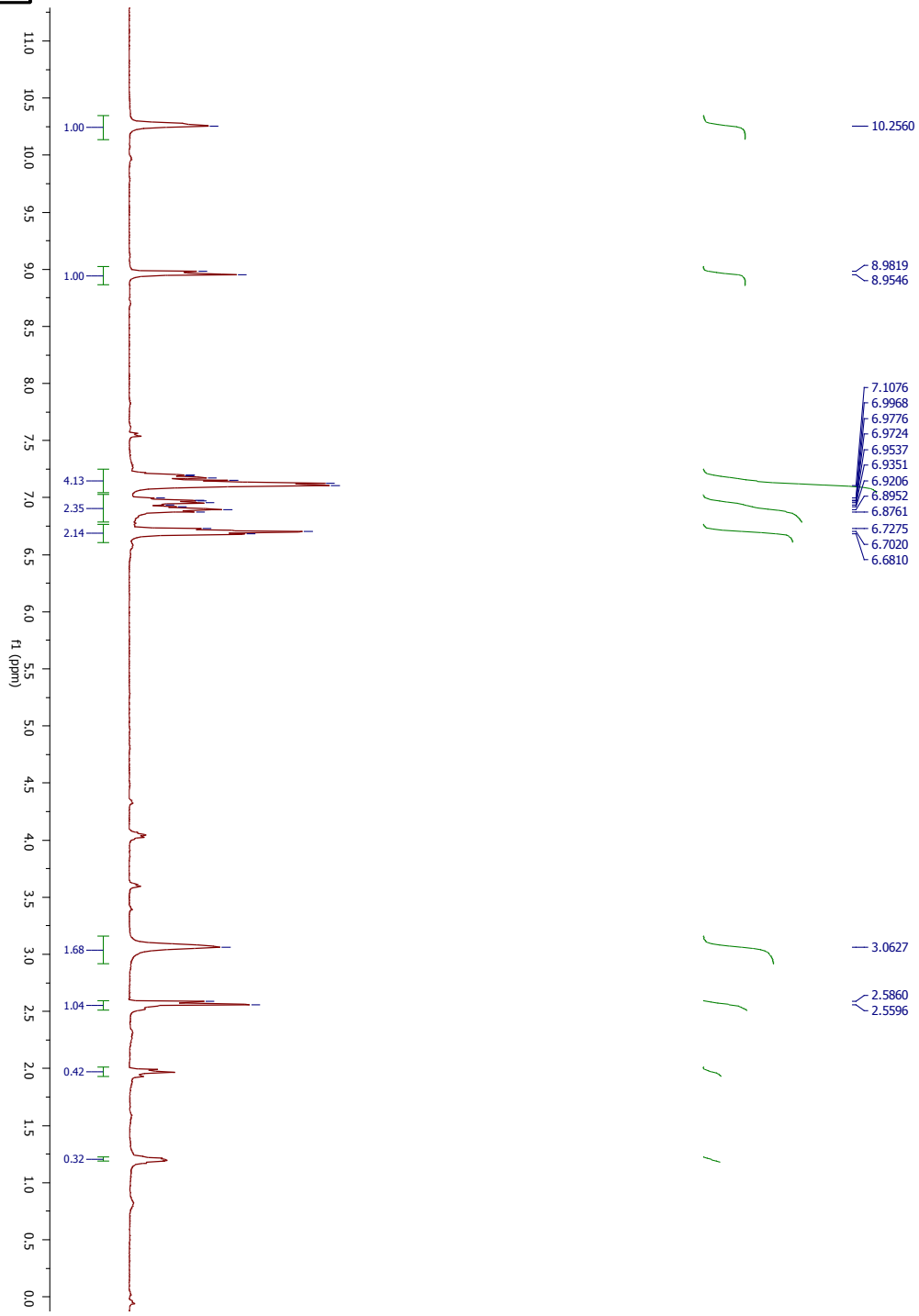


^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**6e**)

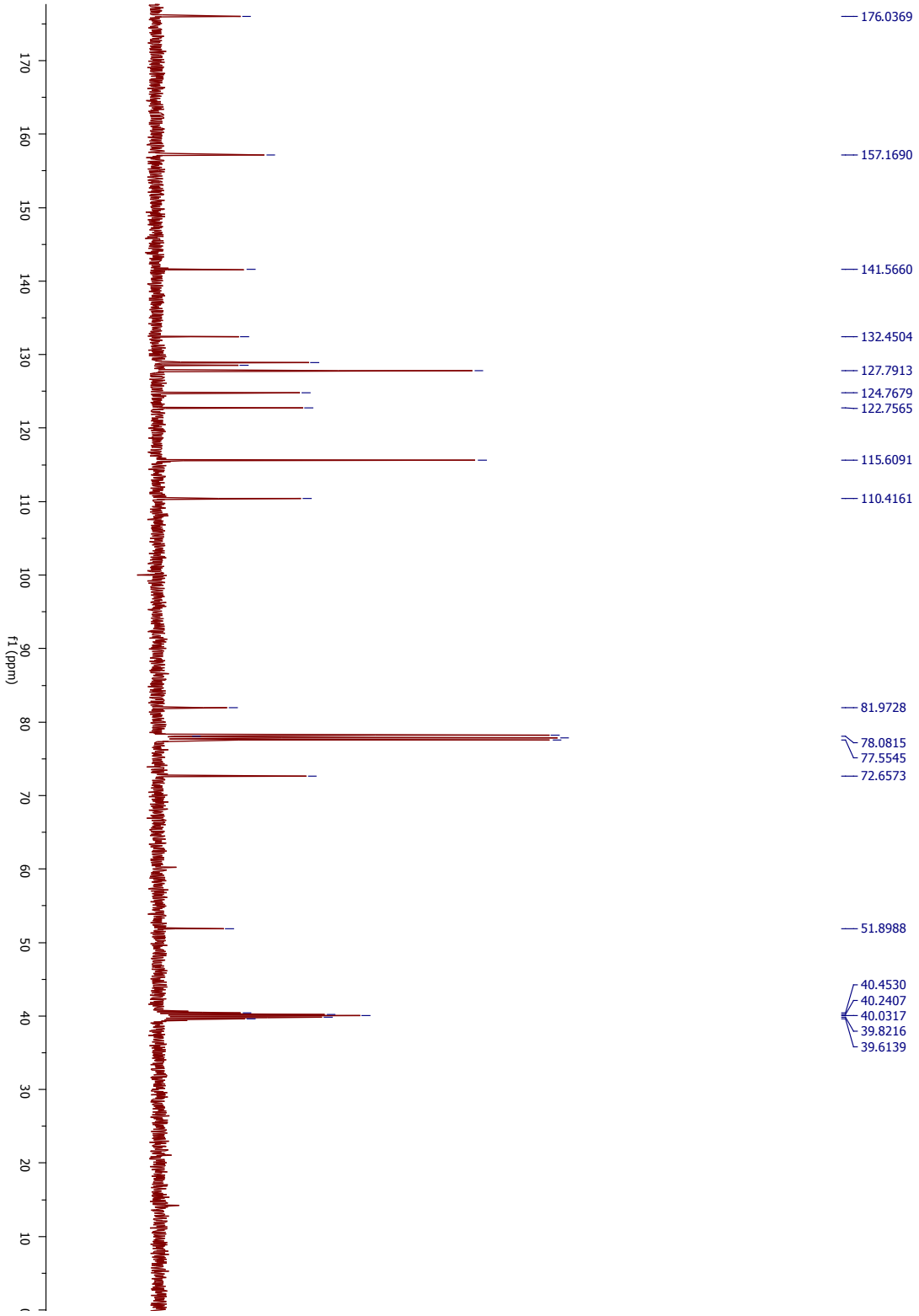


Scanned copy of mass spectrum of compound±(**6e**)

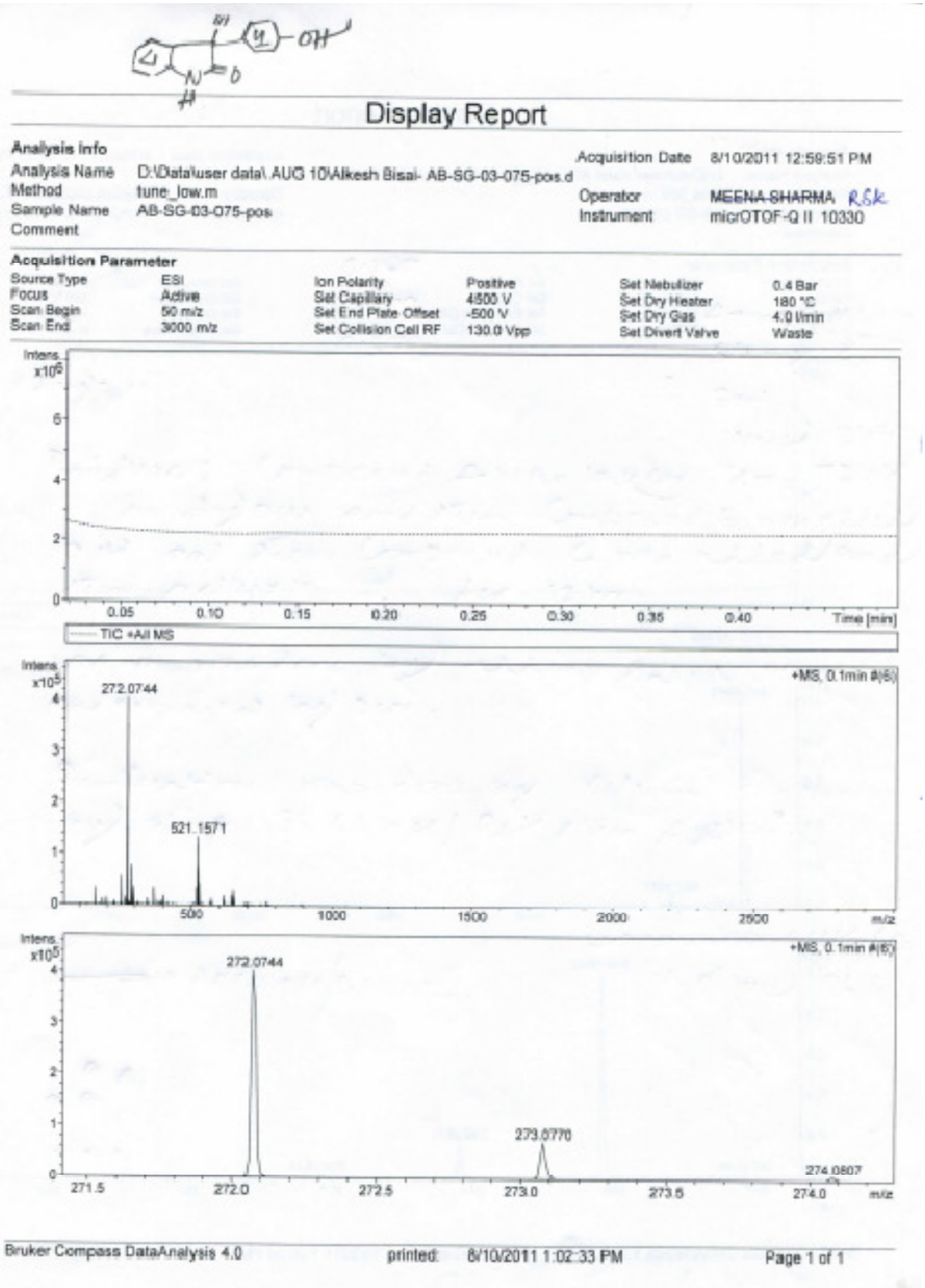




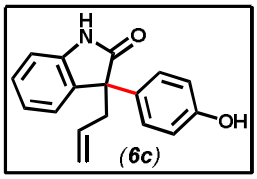
^{1}H NMR(400 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**6b**)

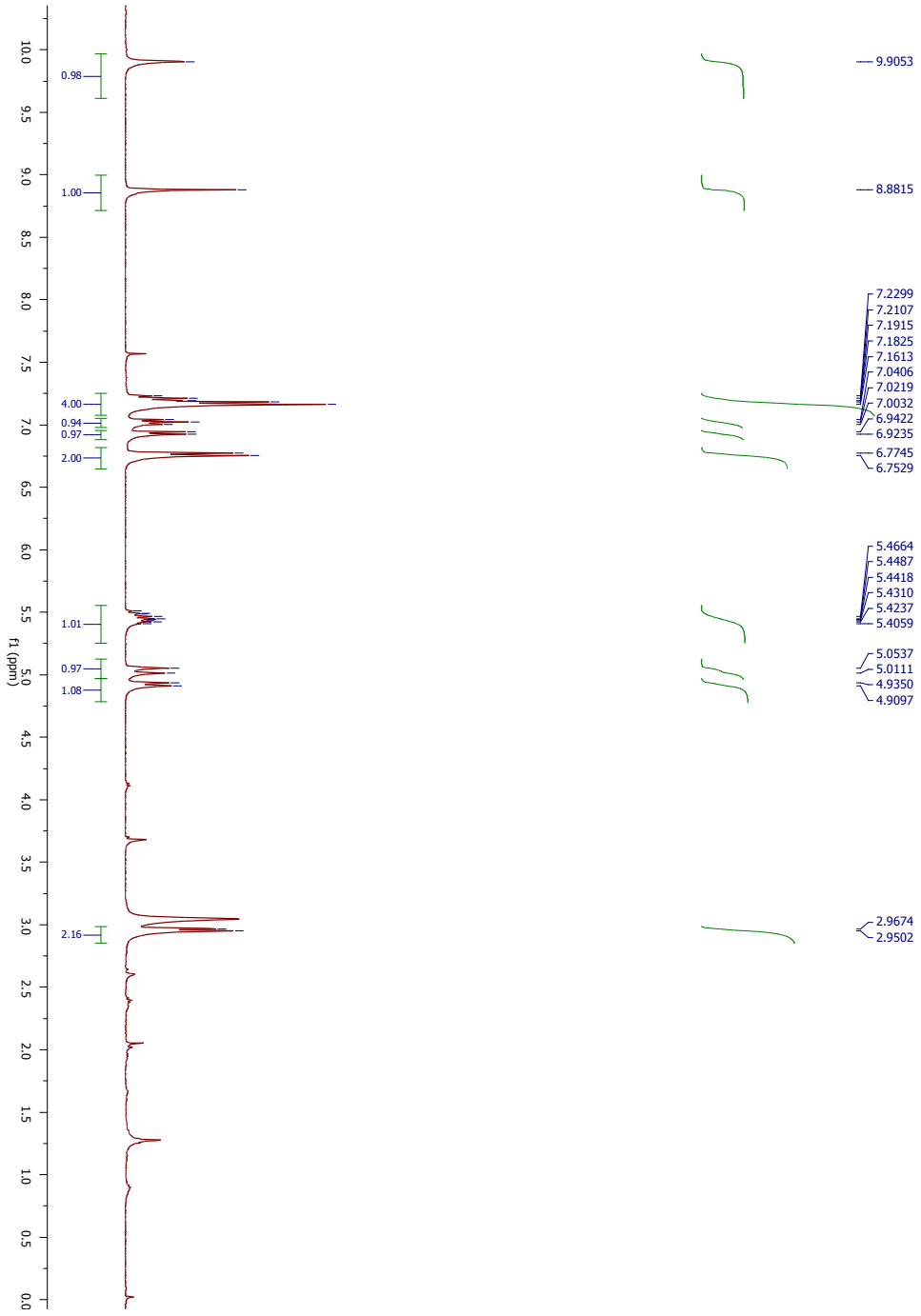


^{13}CNMR(100 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**6b**)

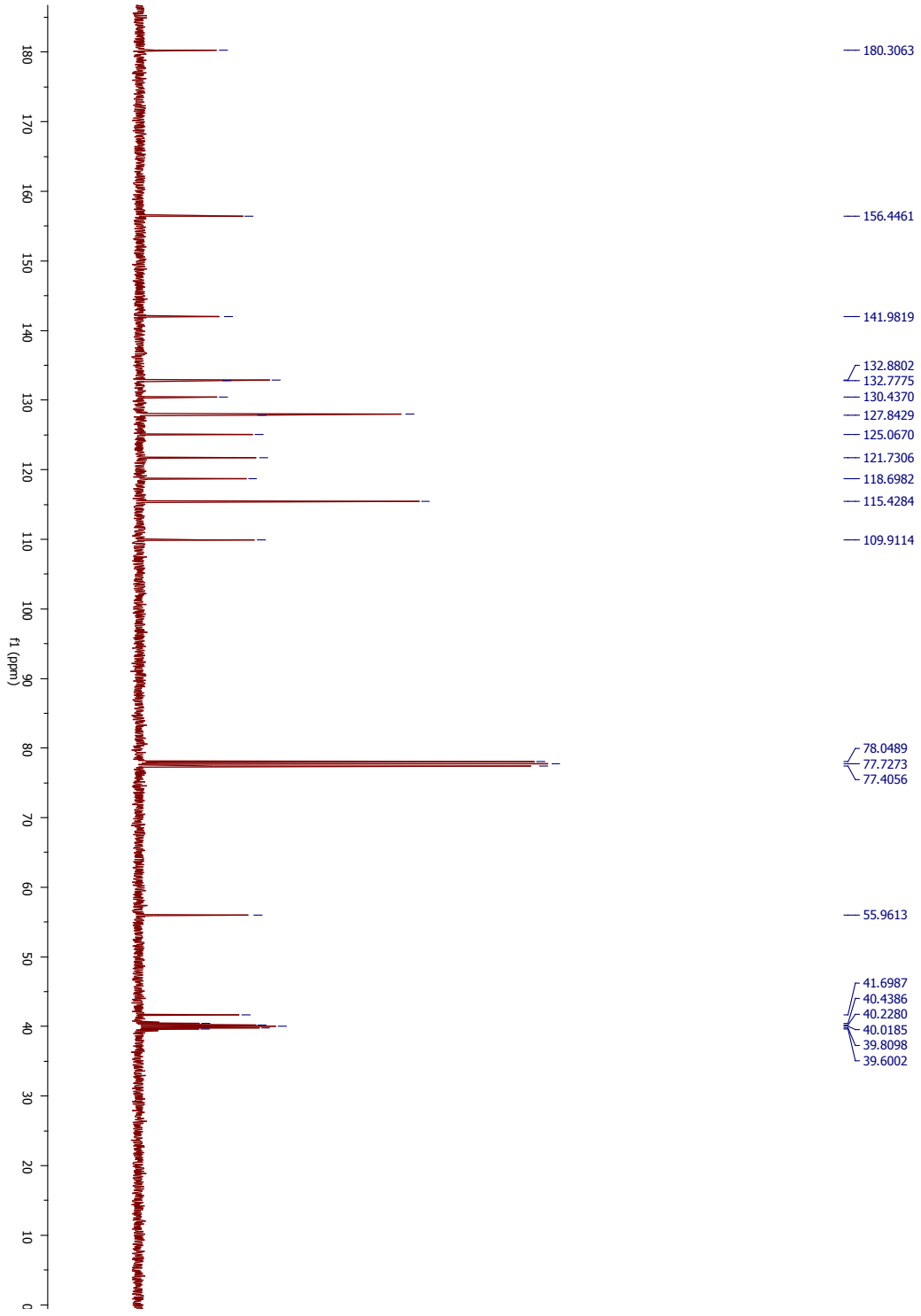


Scanned copy of mass spectrum of compound±(**6b**)

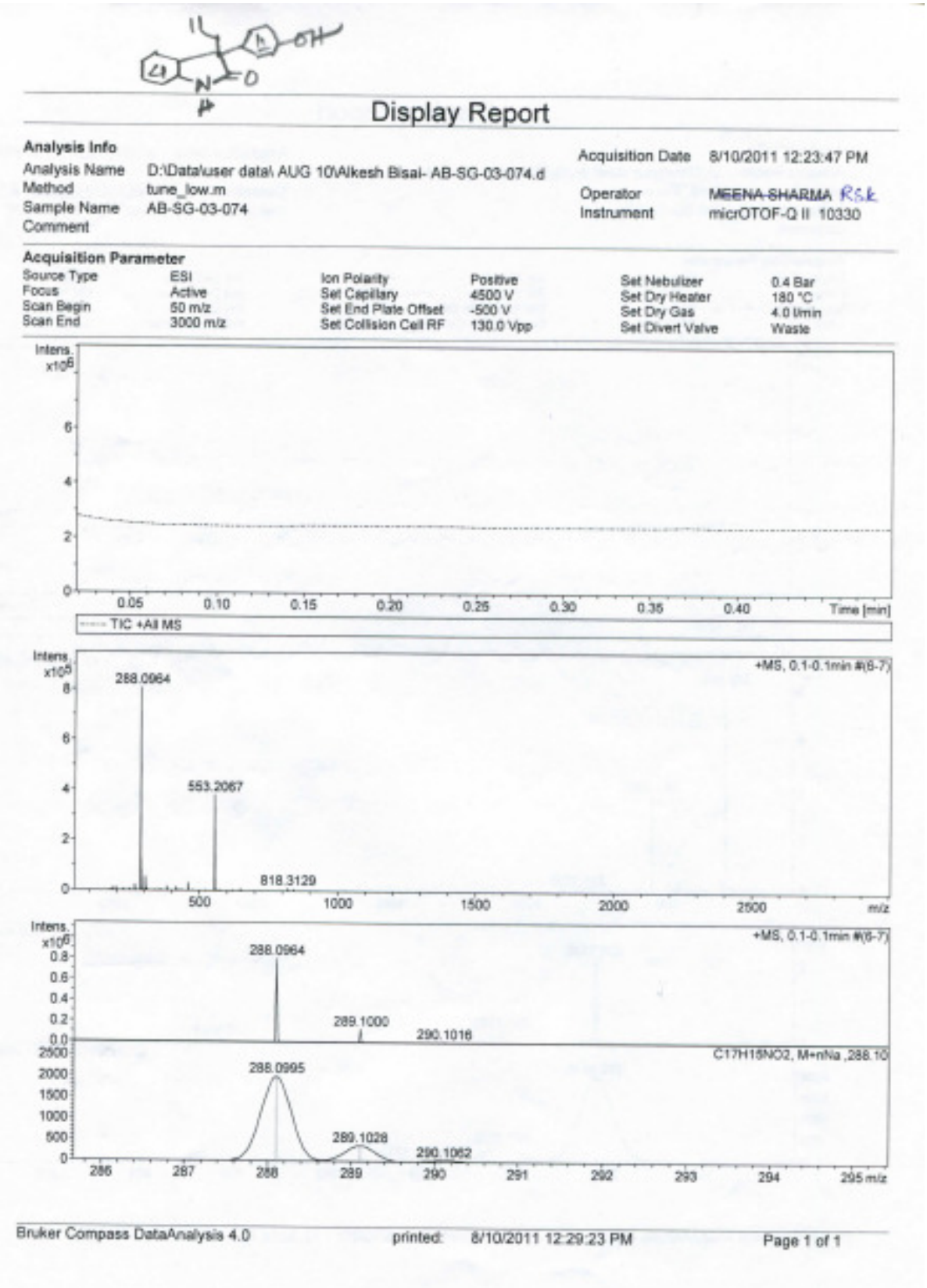




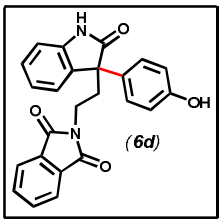
^{1}H NMR(400 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**6c**)

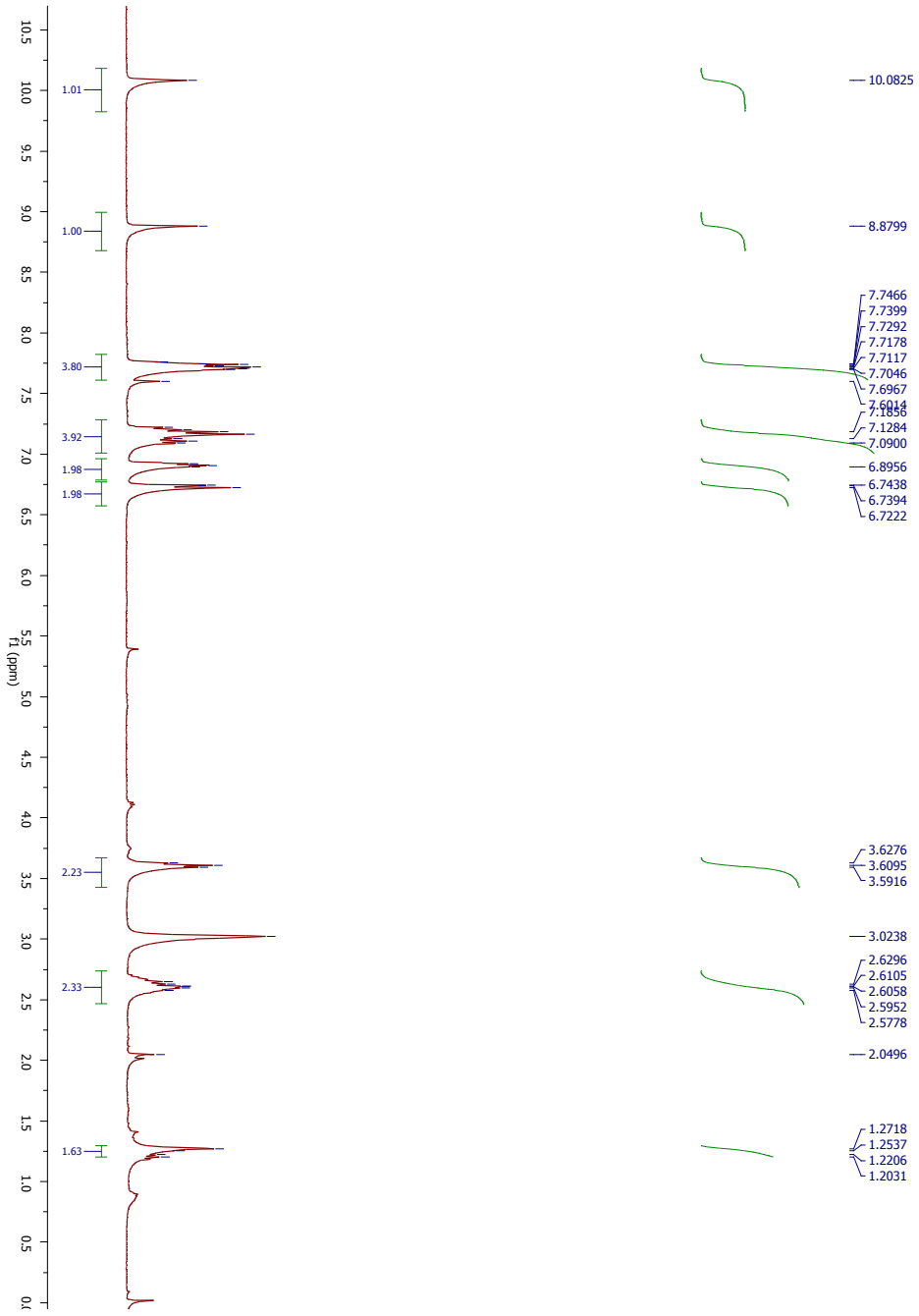


^{13}CNMR(100 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**6c**)

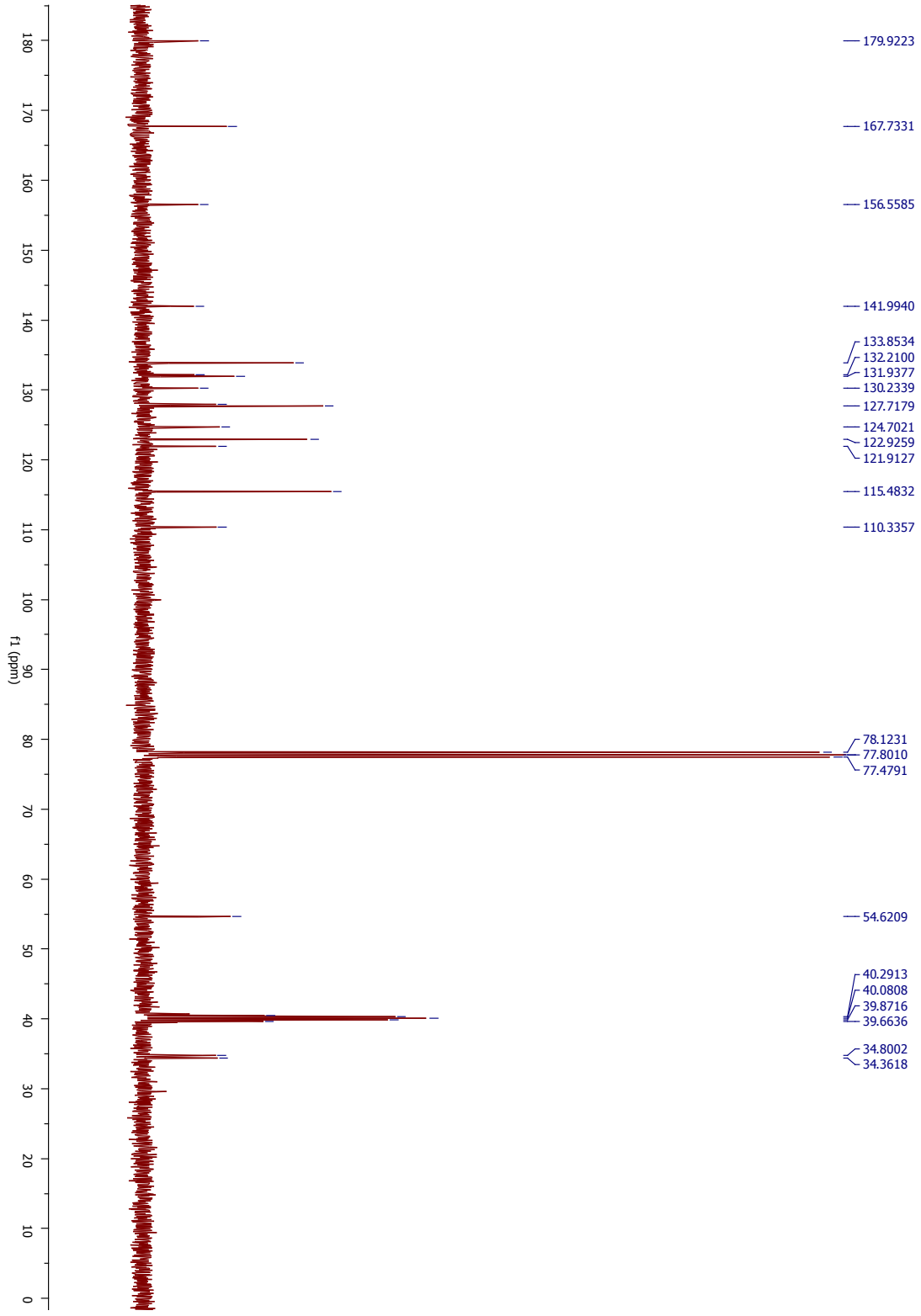


Scanned copy of mass spectrum of compound±(**6c**)

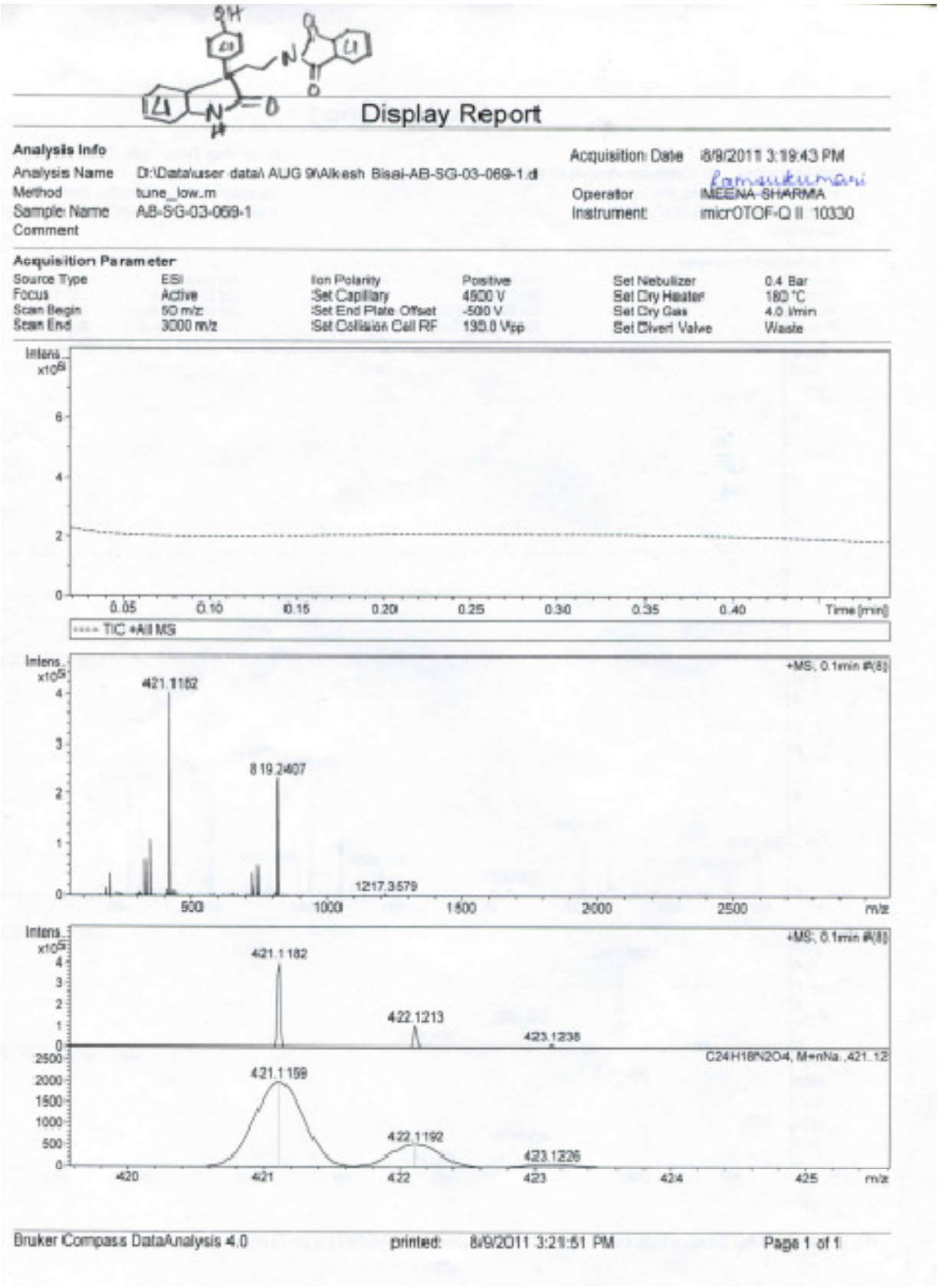




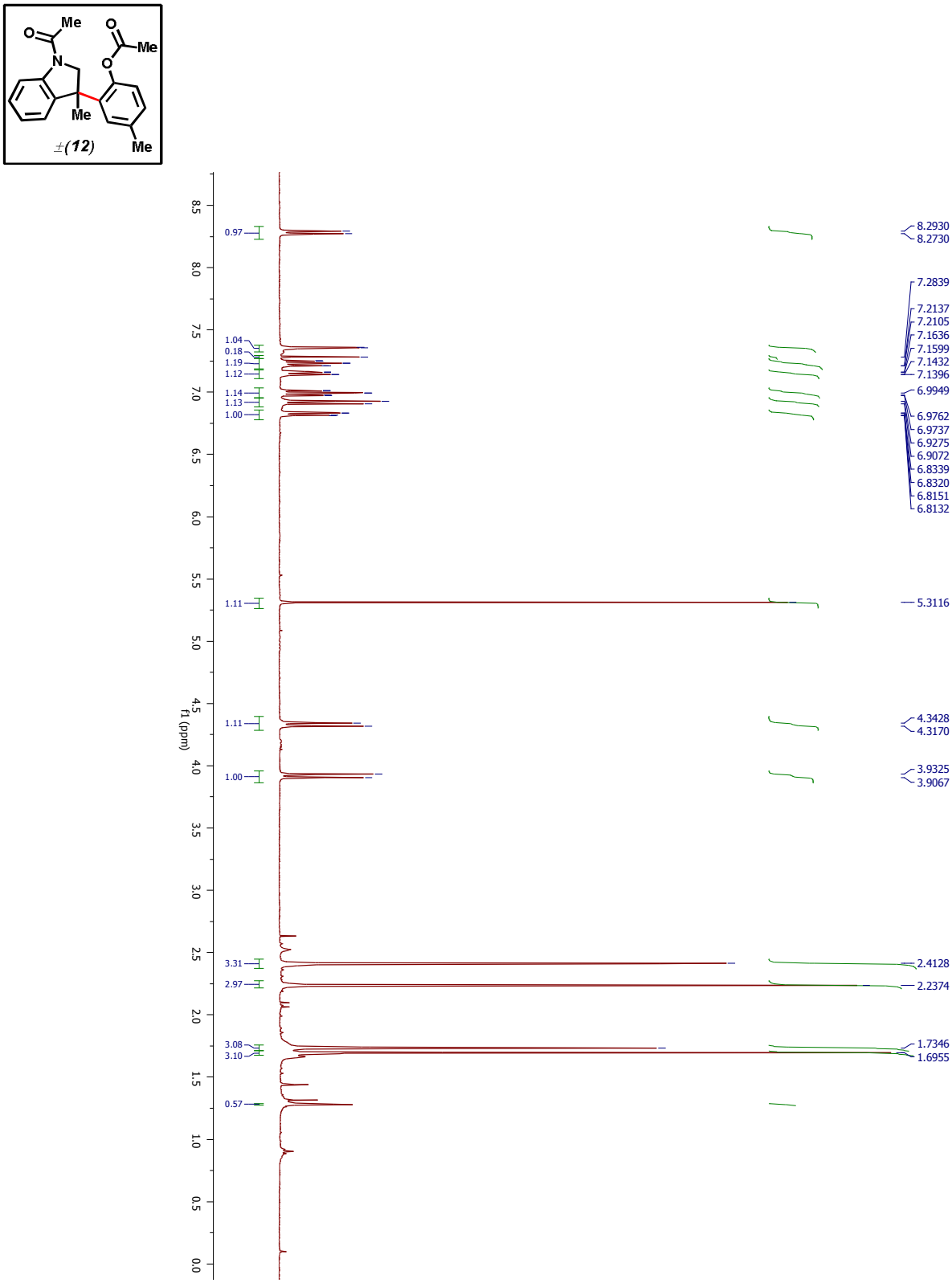
^{1}H NMR(400 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**6d**)



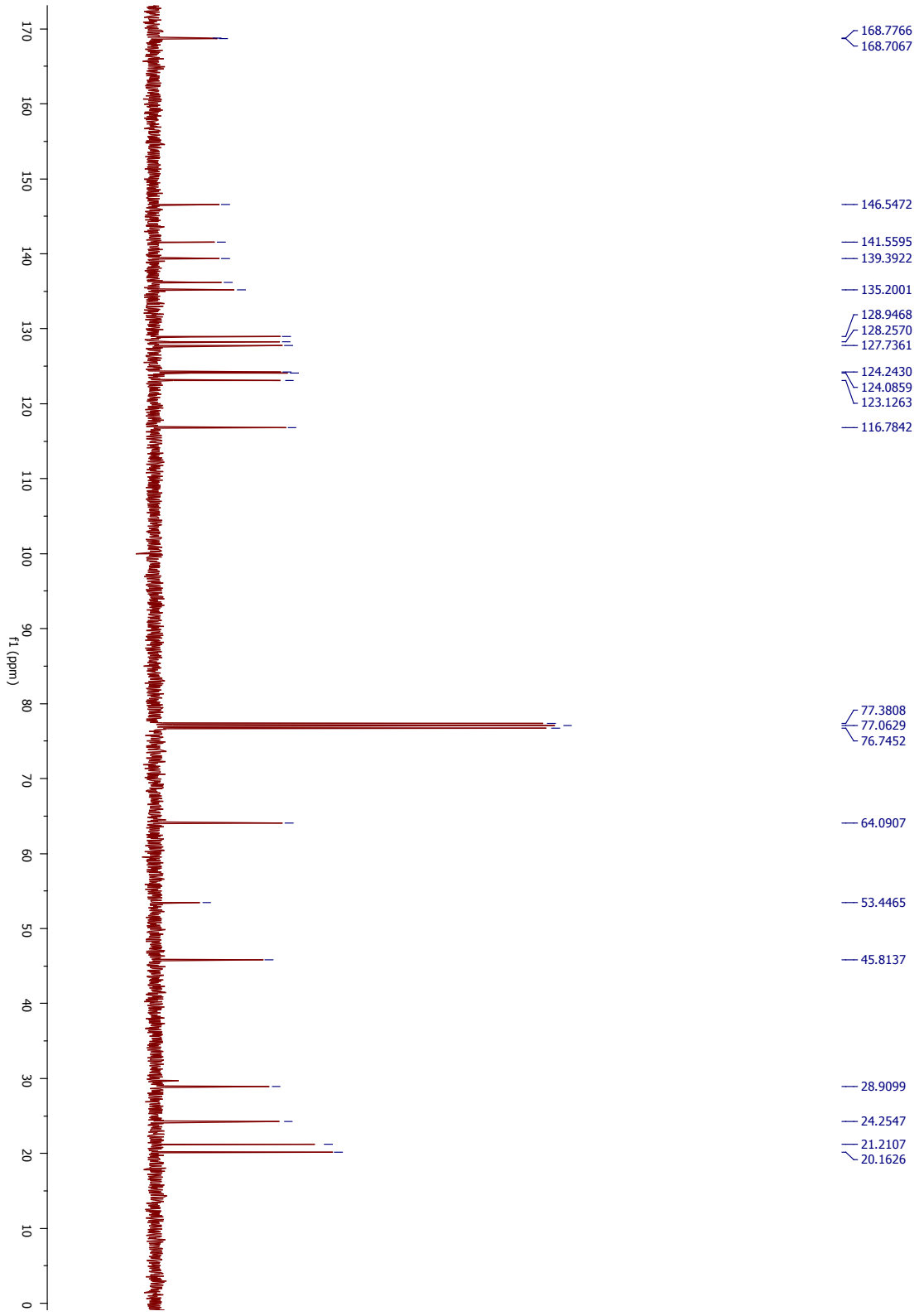
^{13}CNMR(100 MHz, $CDCl_3$ and DMSO-d_6) of compound ±(**6d**)



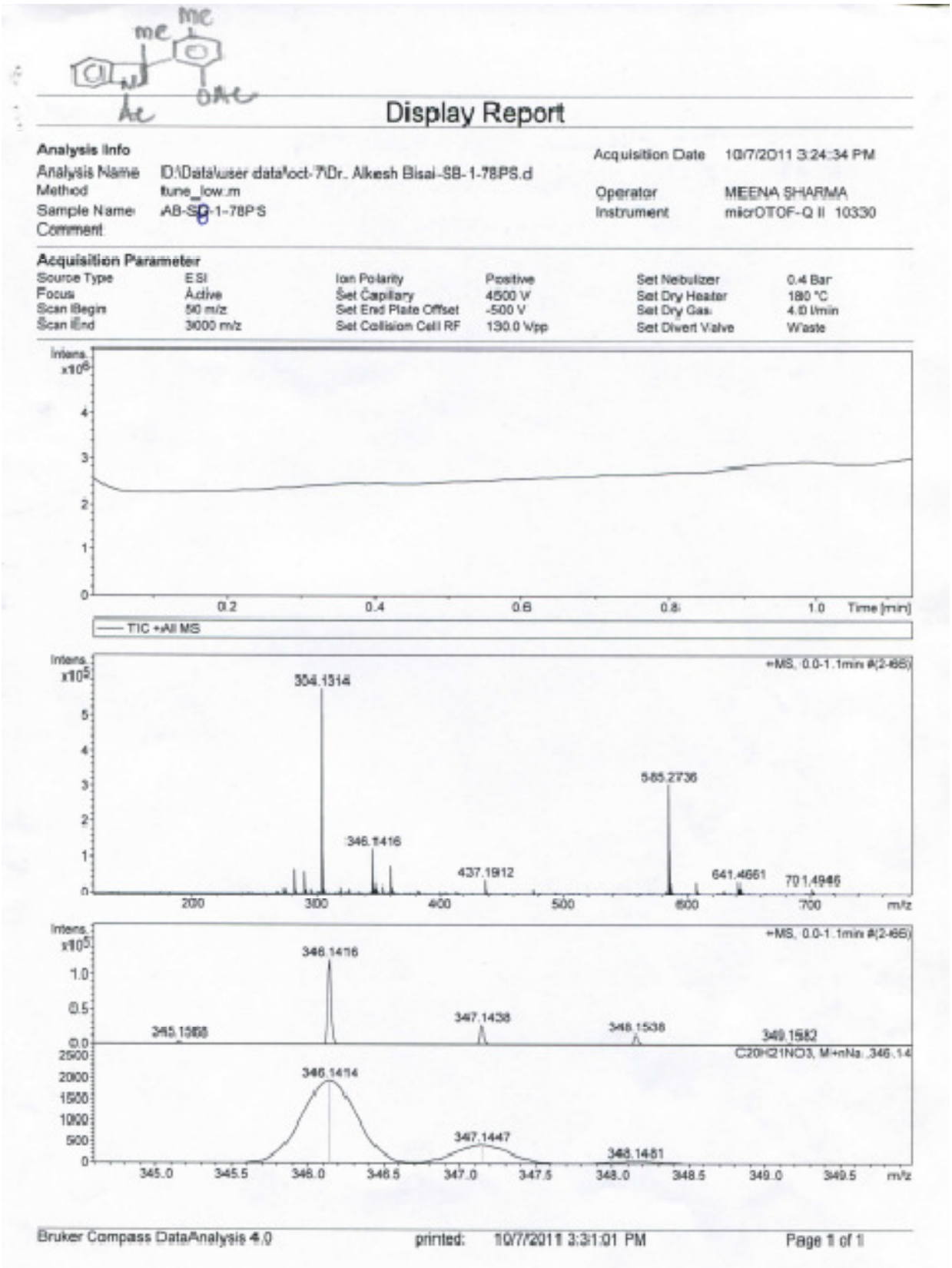
Scanned copy of mass spectrum of compound±(**6d**)



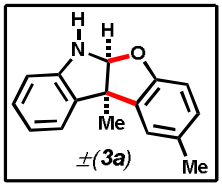
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**12**)

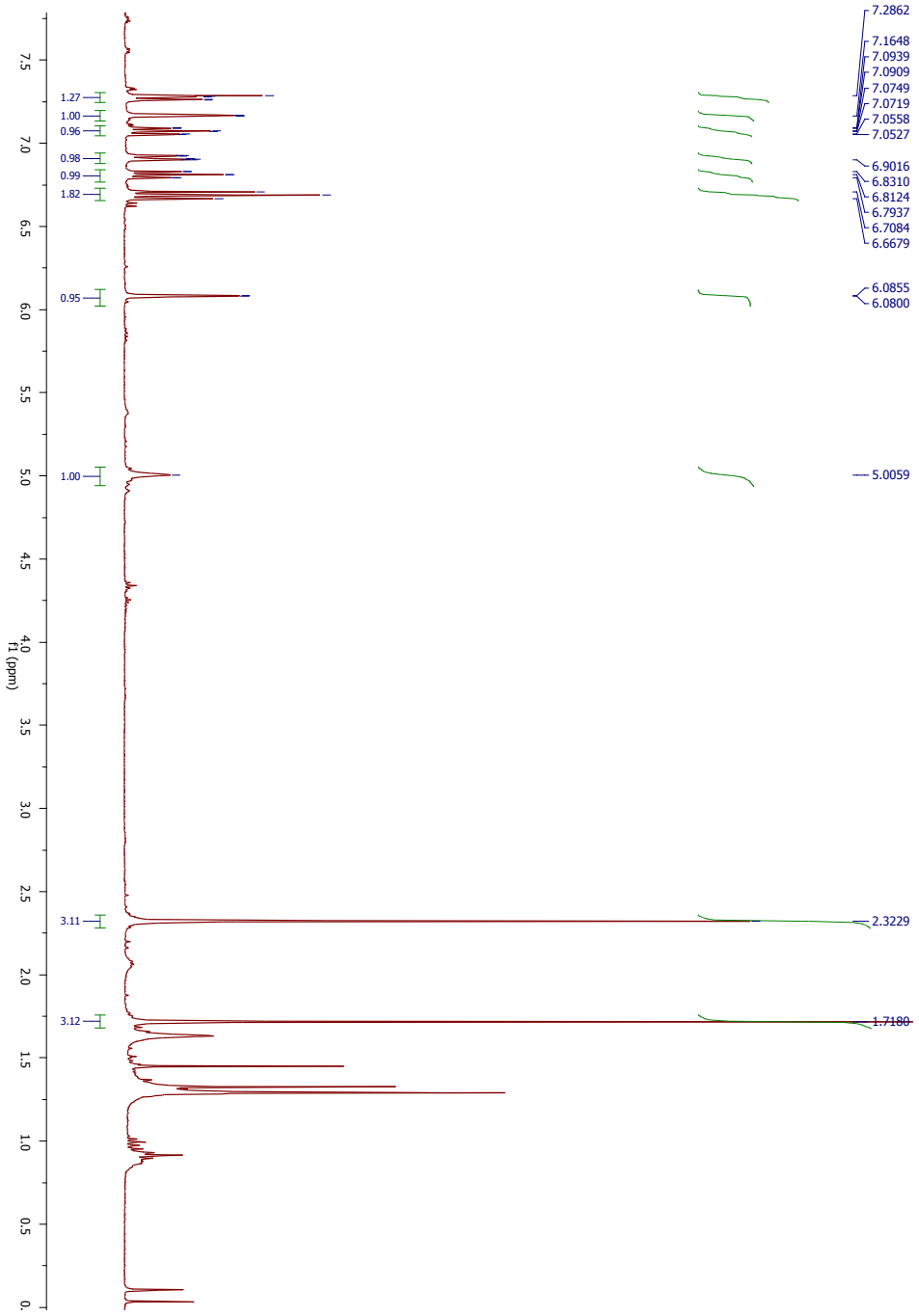


^{13}C NMR(100 MHz, $CDCl_3$) of compound ±(**12**)

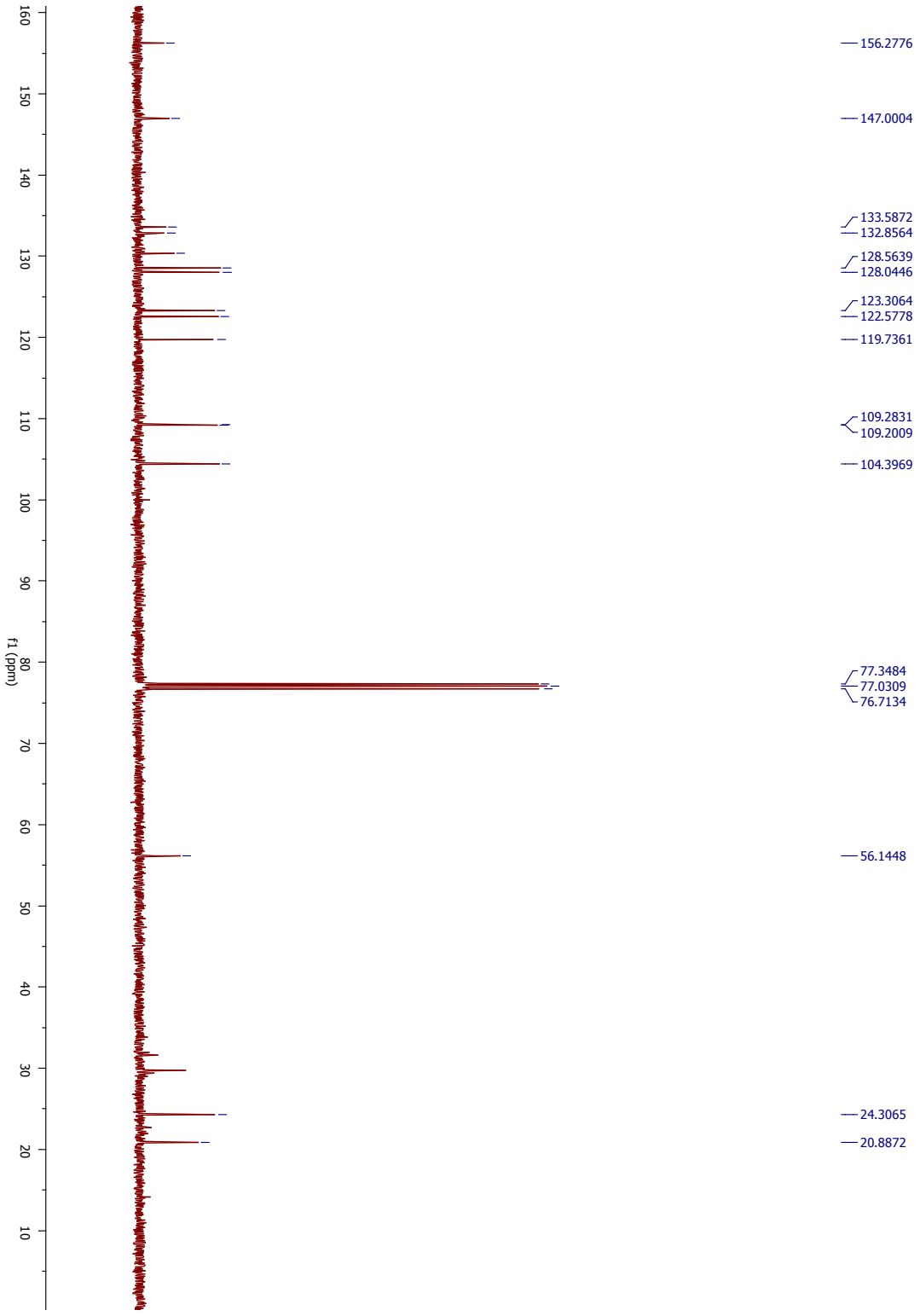


Scanned copy of mass spectrum of compound±(**12)**

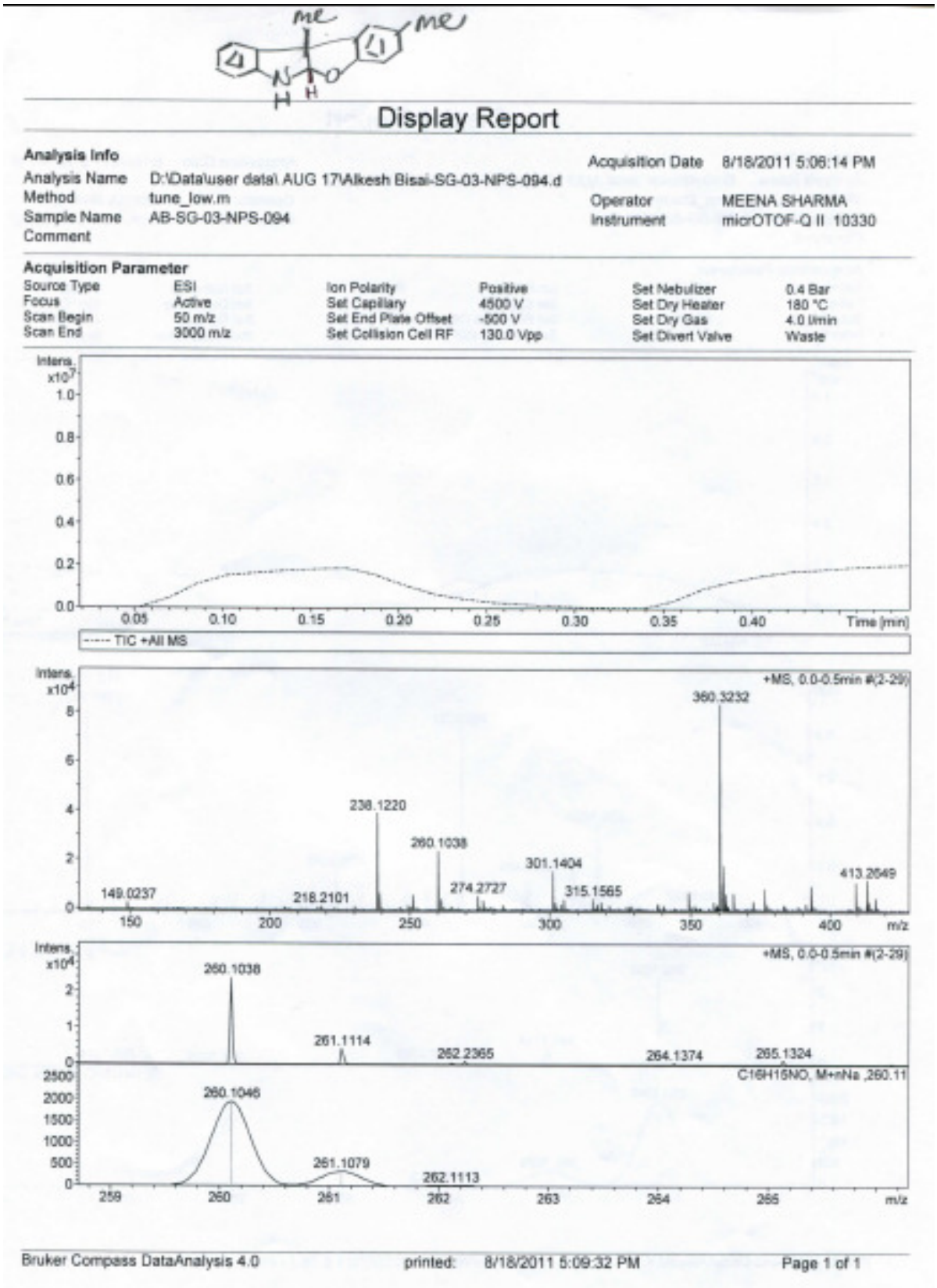




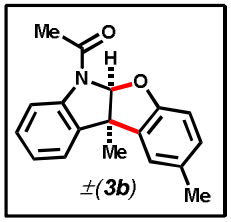
^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**3a**)

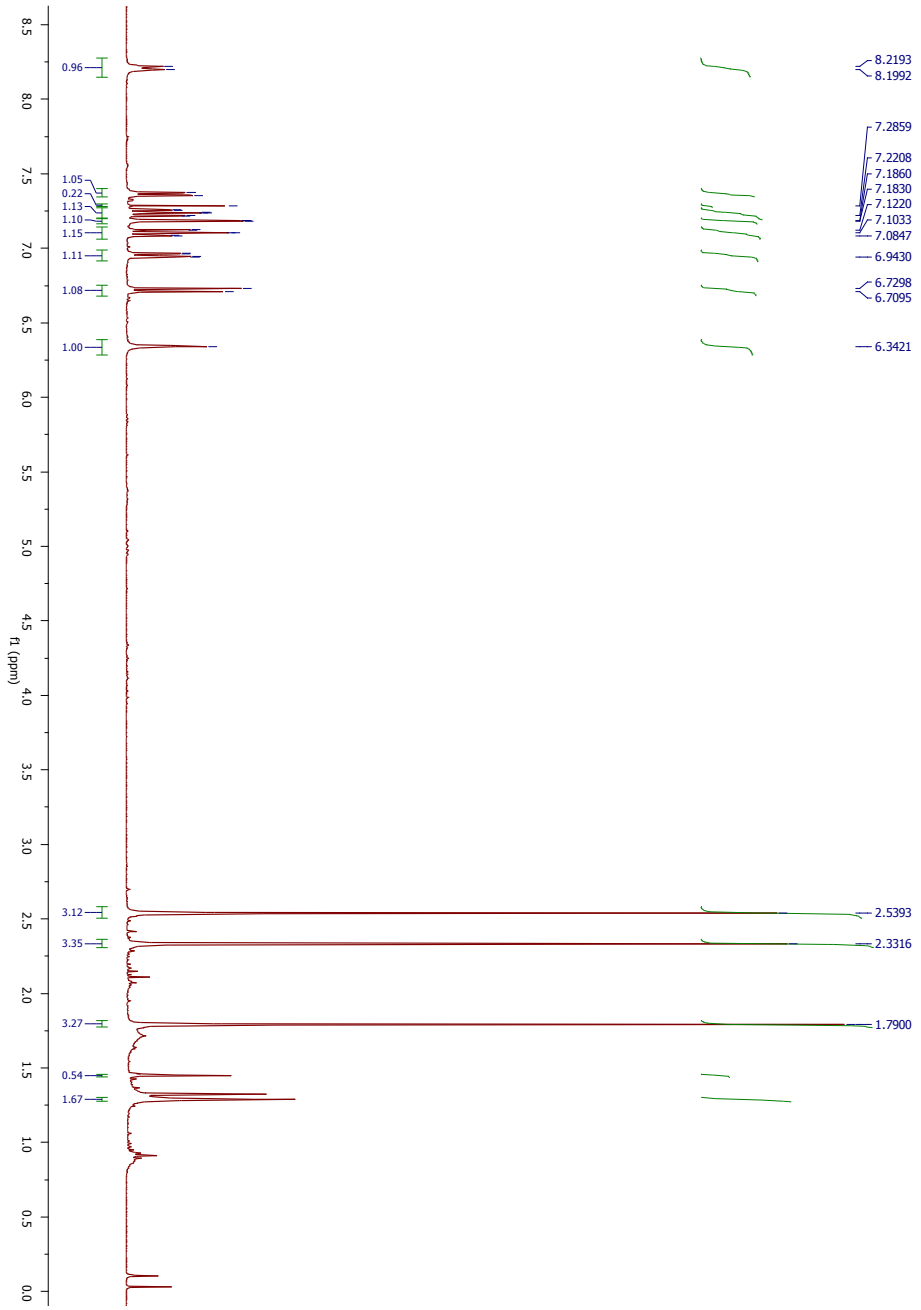


^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**3a**)

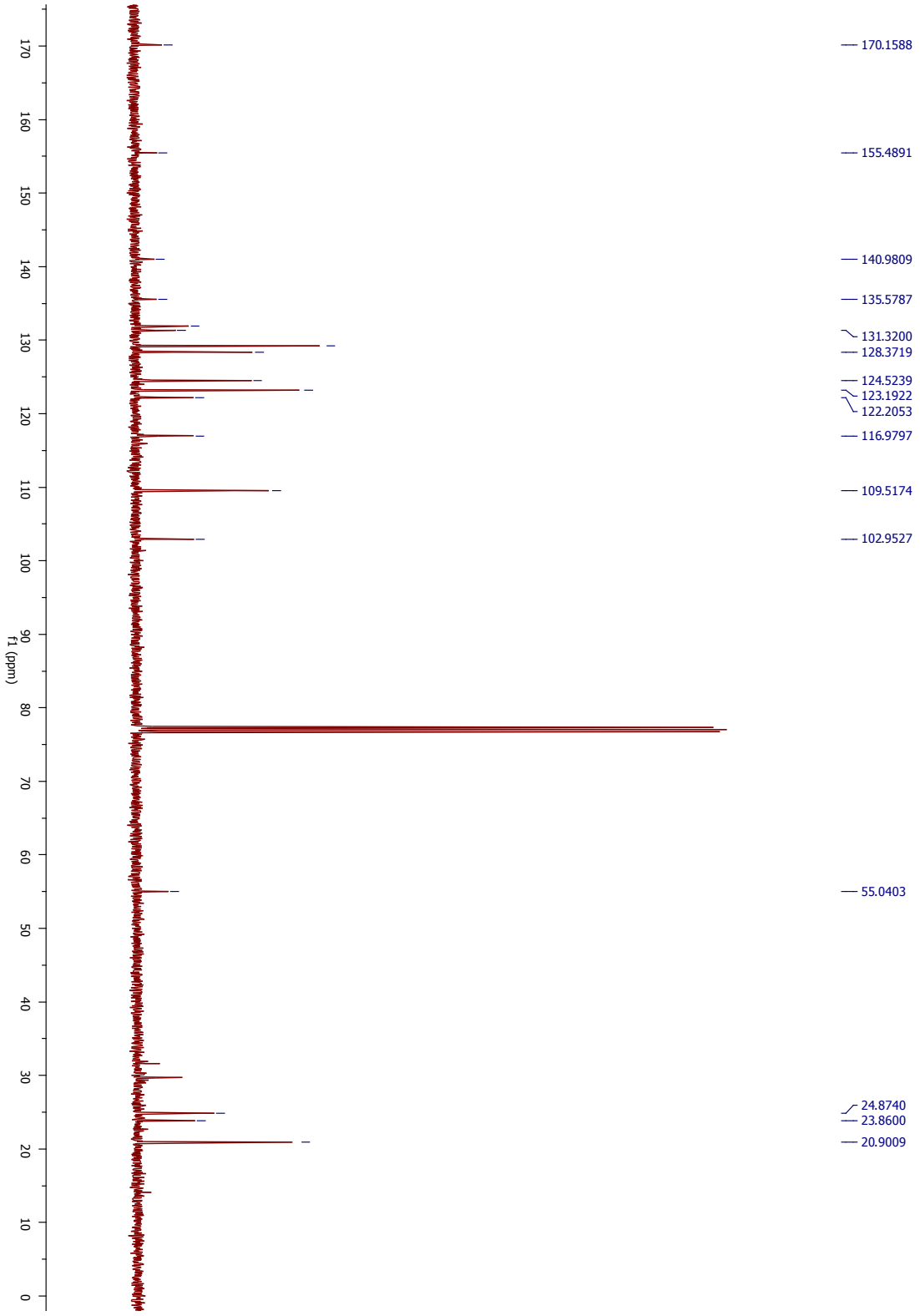


Scanned copy of mass spectrum of compound±(**3a**)

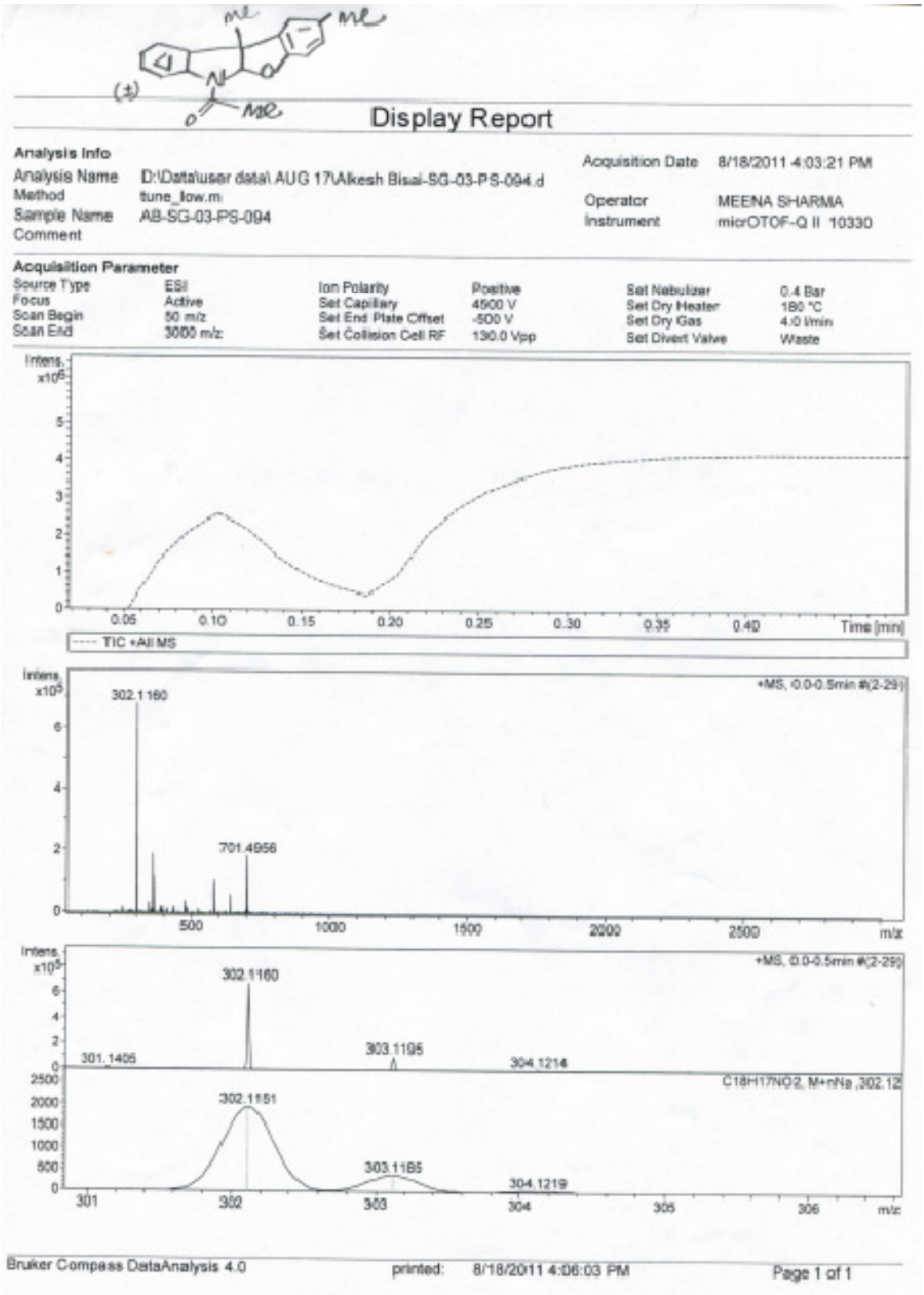




^{1}H NMR(400 MHz, $CDCl_3$) of compound ±(**3b**)



^{13}CNMR(100 MHz, $CDCl_3$) of compound ±(**3b**)



Scanned copy of mass spectrum of compound±(**3b**)