Electronic Supplementary Material (ESI) for RSC Advances

A Simple and efficient method for mild and selective oxidation of propargylic alcohols using TEMPO and calcium hypochlorite

Sabbasani Rajasekhara Reddy,[a,b] Anju Chadha[b,c*]

[a]School of Advanced Sciences, Organic Chemistry Division, VIT University, VELLORE: 632014, Chennai 600036, India

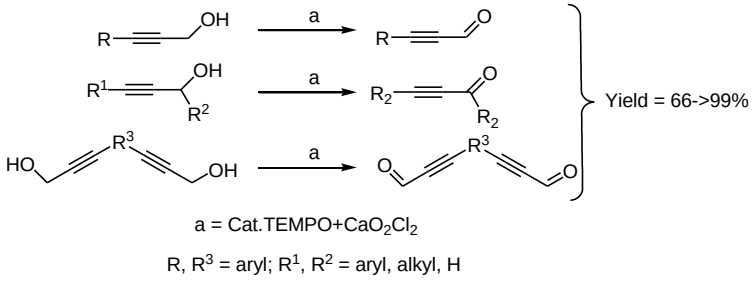
[b]Laboratory of Bioorganic Chemistry, Department of Biotechnology, Indian Institute of Technology Madras, Chennai 600036, India

[c]National Center for Catalysis Research, Indian Institute of Technology Madras, Chennai 600036, India

Fax: 91 44 2257 4102, Tel: 91 44 2257 4106
E-mail: anjuc@iitm.ac.in

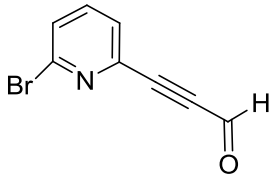
SUPPORTING INFORMATION

Supporting information available: Detailed experimental procedures and characterization data, along with spectra for novel compounds.



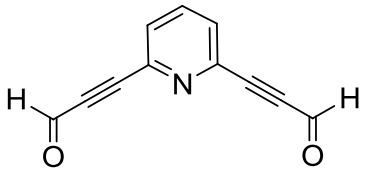
3-phenylpropiolaldehyde (Table 1, 2a) (Maeda *et al*., 2002)
1-Phenylprop-2yn-1-one (Table 1, 2b) (Maeda *et al*., 2002)
4-phenylbut-3-yn-2-one (Table 1. 2c) (Hanson, *et al*., 2011)
1,3-diphenylprop-2-yn-1-ol (Table 1. 2d) (*Liu, J.; Xie, X.; Ma, Synthesis* **2012**, *44*, *1569*)
1-Octyn-3-one (Table 1. 2e) (Maeda *et al*., 2002)

3-(6-bromopyridin-2-yl)propiolaldehyde (Table 1, 2f)



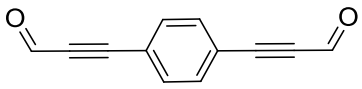
Colorless solid, mp: (97-100 °C)
^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ_H = 9.37 (s, 1H), 7.58-7.50 (m, 3H) (Figure 1**)**
^{13}C NMR (CDC_{l3}, 100 MHz): δ_C = 176.1, 142.5, 140.6, 138.6, 130.0, 127.8, 90.0, 86.4 (Figure 2**)**
IR (neat): ν = 3063, 2933, 2204, 1651, 1566, 1550, 1434 cm^{-1}
HRMS$[M+H]^+$: Calc. for C_8H_5BrNO 209.9554, found: $(M)^+$ 209.9558 **(**Figure 3**)**

3,3′-(Pyridine-2,6diyl)dipropiolaldehyde (Table 1. 2g)



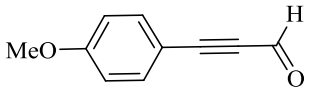
Solid (unstable)
^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ_H = δ 9.38 (s, 2H), 7.80-7.61 (m, 3H) **(**Figure 4**)**
^{13}C NMR (100 MHz, $CDCl_3$,TMS) δ_C = 176.3, 141.5, 137.6, 129.8, 90.1, 86.1 **(**Figure 5**)**
IR (neat), ν = 3421, 3059, 2956, 2207, 1654, 1567, 1445 cm^{-1}

3, 3'-(1,4-phenylene)dipropiolaldehyde (Table 1, 2h) (Ye *et al*., 2004)



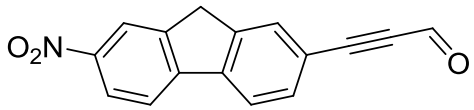
Colourless solid
^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ_H = 9.37(s, 2H), 7.56 (s, 4H) **(**Figure 6**)**
^{13}CNMR (100 MHz, $CDCl_3$,TMS) δ_C = 176.1, 133.1, 122.1, 92.5, 90.0 **(**Figure 7**)**
IR (neat) : 2187, 1650, 1606, 1499 cm^{-1}

3-(4-methoxyphenyl)propiolaldehyde (Table 1, 2i) (Nowa-Krol, *et. al.*, 2012)



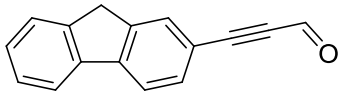
Colourless solid
^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ_H = 9.37(s, 2H), 7.56 (s, 4H)
^{13}CNMR (100 MHz, TMS, $CDCl_3$) δ_C = 176.1, 133.1, 122.1, 92.5, 90.0
IR (neat) : 2187, 1650, 1606, 1499 cm^{-1}

3-(7-nitro-9H-fluoren-2-yl)prop-2-yn-1-al (Table 1, 2j)



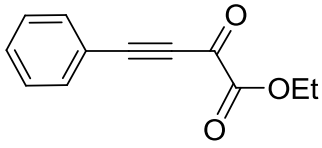
Solid, mp: 145-150 °C
^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ_H = 9.46 (s, 1H), 8.45-7.70 (m, 6H), 4.07 (s, 2H) **(**Figure, 8)
^{13}CNMR (100 MHz, $CDCl_3$,TMS); 176.5, 147.6, 146.4, 144.8, 144.6, 142.3, 132.8, 130.1, 123.4, 121.6, 120.9, 120.7, 119.4, 94.9, 89.2, 36.8 **(**Figure**,** 9**)**
IR (neat): ν = 2855, 1646, 1516, 1415 cm^{-1}

3-(9H-fluoren-2-yl)propiolaldehyde (Table 1, 2k)



Colourless solid, mp: 110-112 °C
^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ_H = 9.45 (s, 1H), 7.38-7.82 (m, 7H), 3.92 (s, 2H) **(**Figure 10)
^{13}C NMR(400 MHz, $CDCl_3$,TMS): δ_C = 177.0, 145.3, 144.3, 143.7, 140.7, 132.8, 130.2, 128.4, 127.5, 125.5, 121.0,120.4, 117.3, 96.9, 89.2, 37.0 **(**Figure 11)
IR (KBr) ν = 700, 888, 1644, 1604, 2179, 2925, 3060 cm^{-1}
HRMS.. Calc for $C_{16}H_{11}O$; 219.0810, Obs. 219.0811 (Figure 12**)**

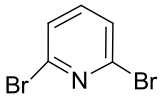
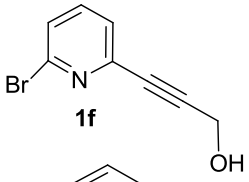
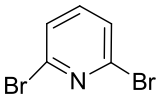
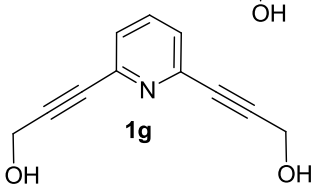
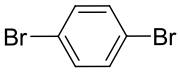
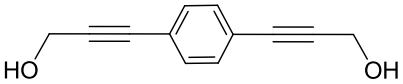
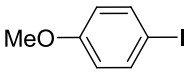
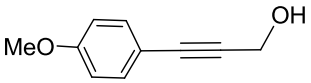
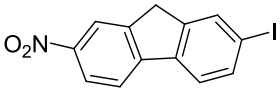
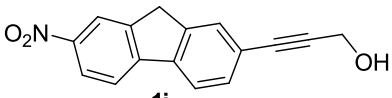
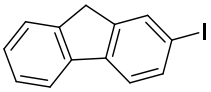
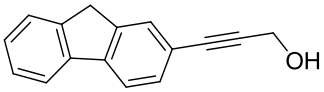
Ethyl 2-oxo-4-phenylbut-3-ynoate (Table 1, 2l) (Guo *et al*., 2003)



^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ_H = 7.68-7.40 (m, 5H), 4.12 (q, *J* = 7.1, 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR(400 MHz, $CDCl_3$,TMS) δ_C = 169.6, 159.2, 133.8, 131.8, 128.8, 119.1, 98.0, 87.2, 63.3, 14.0
IR (neat) ν cm^{-1} = 2179, 1722, 1626
HRMS. Calc for $C_{12}H_{10}O_3Na$; 225.0528, Obs. 225.0531

Table 2 Synthesis of propargylic alcohols using Sonogashira coupling (Sonogashira *et al*., 1975)

Entry	Substrate	Time (h)	Product	Isolated yeild%[a]
1		4	 **1f**	61
2		4	 **1g**	72
3		4	 **1h**	65
4		4	 **1i**	55
5		12	 **1j** N.R	59
6		12	 **1k** N.R	40

[a]All the alcohols were confirmed by their spectral data ^{1}H NMR, ^{13}C NMR, IR and HRMS

N. R = Not Reported

(6-Bromopyridin-2-yl-ol) prop-2-yn-1-ol (Table 1and 2- 1f)

Colorless solid, mp. 68-70 ºC
^{1}H-NMR ($CDCl_3$, TMS, 400 MHz) δ_H = 7.60 (t, *J* = 7.5 Hz, 1H). 7.50 (d, *J* = 8 Hz, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 4.59 (s, 2H), (Figure 13**)**
^{13}C NMR ($CDCl_3$, TMS,100 MHz) δ_C = 143.5. 141.9, 138.8, 128.0, 126.1, 89.9, 83.6, 51.4
IR: 3361, 3102, 3052, 1160, 1123, 901, 801, 771, 604 cm $^{-1}$ **(**Figure 14**)**
HRMS $[M+H]^+$: Cal.209.9554, Obs. 209.9567 (C_8H_5NOBr)

3,3'-(pyridine-2,6-diyl)diprop- yn-1-ol (Table 1 and 2, 1g)

Colorless crystalline solid, mp, 120-124 ºC
^{1}H-NMR ($CDCl_3$, TMS, 400 MHz) δ_H = 7.64 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 2H), 4.96 (t, *J* = 5.9 Hz, 2H), 4.35 (d, *J* =6.3 Hz, 4H) **(**Figure 15**)**
^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ_C = 142.5, 136.1, 125.5, 88.8, 82.7, 49.7 (Figure 16)
IR : 3341, 3138, 2858, 2234, 1578, 1562, 1445, 1346, 1251, 1223, 1163, 1085,1057, 1030, 1011, 996, 978, 947, 805, 732 cm $^{-1}$
HRMS $[M+H]^+$: Cal.188.0712, Obs. 188.0712 ($C_{11}H_{10}NO_2$) **(**Figure 17**)**

3,3'-(1,4-Phenylene)diprop-2-yn-1-ol (Table 1 and 2, 1h) (Ye, *et. al*., 2004)

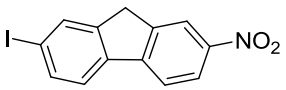
Yellow colour solid, mp, 125-129 ºC
^{1}H-NMR ($CDCl_3$, TMS, 400 MHz) δ_H = 7.37-7.30 (m, 4H), 4.42-4.29 (m, 4H), 4.00 (bs, 2H)
^{13}C NMR($CDCl_3$, TMS, 100 MHz) δ_C = 131.5, 122.1, 90.8, 83.8, 50.0
IR: 3268, 2903, 2241, 1495, 1421, 1406, 1355, 1312, 1268, 1257, 1222, 1104, 1024, 994, 947, 837, 637 cm $^{-1}$
HRMS $[M+H]^+$: Calc. 209.0578, Obs. 209.0584 ($C_{12}H_{10}O_2Na$)

3-(4-methoxyphenyl)prop-2-yn-1-ol (Table 1 and 2, entry 1i) (Nowak-Krol *et. al.*, 2011)

Synthesis of 3-(7-nitro-9H-fluoren-2-yl)prop-2-yn-1-ol (Table 1, entry 1j)

(i) 2-iodo-7-nitro-9H-fluorene (Marhevka *et al.*, 1985) (Table 2, Entry 5)

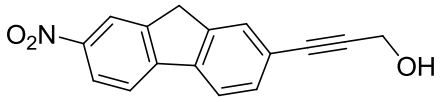
A mixture of 2-nitro fluorene 1.6 g (7.5 mmol), glacial acetic acid (50 mL) and iodine 0.93 g (3.5 mmol) were stirred at room temperature for 10 minutes. To the reaction mixture was added conc. H_2SO_4 (5 mL), sodium nitrate 0.55g (7.5 mmol) and refluxed for 30 min. The crude reaction mixture was poured into 100 g of ice, and the yellow solid was collected by filtration. The crude reaction mixture was recrystalized from glacial acetic acid to afford light yellow color solid in 45% (1.12 g) yield.



Solid, mp. 240-245 °C (reported 240-245 °C)
^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ_H = 8.38-7.43 (m, 6H), 4.03 (s, 2H)

(ii) 3-(7-nitro-9H-fluoren-2-yl)prop-2-yn-1-ol (Table 1, entry 1j) (Sonogashira *et al*., 1975)

A mixture of bis(triphenylphosphine)-palladium(II)chloride (35 mg, 0.05 mmol), 2-iodo-7-nitro-9H-fluorene (505.5 mg, 1.5 mmol), copper iodide (20 mg, 0.1 mmol), dry triethylamine (20 mL), dry THF (20 mL) and propargylic alcohol (140 µL, 2.5 mmol) was stirred under an argon atmosphere. The mixture was stirred for 12 h and then filtered through celite pad, solvent was distilled under reduced pressure. The residue was purified by column chromatography using $CHCl_3$ to give yellow color crystalline solid **1j** in 59% yield.

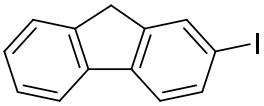


Yellow color solid, mp: 200-205 °C.
^{1}H NMR (400 MHz, TMS, DMSO-D_6,) δ_H = 8.39-7.46 (m, 6H), 4.38 (s, 2H), 4.02 (s, 2H), 3.39 (bs, 1H) (Figure 18)
^{13}C NMR (400 MHz, TMS, $CDCl_3$) δ_C = 145.3, 144.9, 143.2, 142.6, 137.4, 129.0, 126.5, 121.4, 121.3, 119.8, 118.9, 118.6, 89.0, 82.3, 48.3, 34.9 (Figure 19**)**
IR (KBr) ν = 3485, 2927, 2856, 2216, 2241, 1619, 1587, 1508 cm^{-1}
HRMS $[M+H]^+$: Calc. 266.0817, Obs. 266.0812 ($C_{16}H_{11}NO_3$) (Figure 20**)**

Synthesis of 3-(9H-fluoren-2-yl)prop-2-yn-1-ol (Table 1, entry 1k)

(i) 2-iodo-9H-fluorene (Lee *et al.*, 2001)

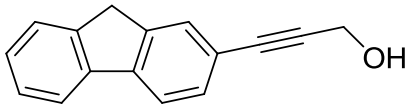
Fluorene 2g (12 mmol) was dissolved in 20 mL of boiling solvent (CH_3COOH : H_2O : H_2SO_4 = 16 : 3 : 0.1) (50 mL) with mechanical stirrer, followed by cooling to 60-65 °C, added periodic acid dihydrate (0.46 g, 2 mmol) and iodine 1.02 g (4 mmol). After 4 h the elemental iodine was almost disappeared and precipitate was formed. Upon cooling, the pale yellow solid was collected by filtration and washed with 2N aqueous Na_2CO_3 and water. The crude product was recrystallized from hexane to give a white crystalline solid in 2.14 g, 61%.



2-iodo-9H-fluorene

Solid, mp : 122-127 ºC, reported 120-121 °C (Lee *et al.*, 2001)
^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ_H = 7.88-7.31 (m, 7H), 3.88 (s, 2H)

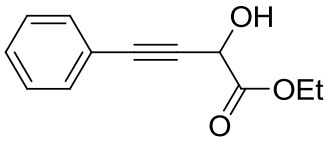
(9H-fluoren-2-yl)prop-2-yn-1-ol 1k (Sonogashira *et al*., 1975)



Solid, mp: 148-150 °C
^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ_H = 7.78-7.30 (m, 7H), 4.53 (s, 2H), 3.88 (s, 2H) **(**Figure 21)
^{13}C NMR (400 MHz, TMS,$CDCl_3$) δ_C = 143.5, 143.1, 142.1, 141.0, 130.5, 127.2, 128.2, 126.9, 125.07, 120.5, 120.2, 119.7, 87.1, 86.4, 51.8, 29.7 **(**Figure 22**)**
IR (neat) ν = 3335, 3045, 2903, 2219, 1485, 1450, 1419, 1393, 1340, 1220, 1194, 1176, 1150, 1020, 996 cm $^{-1}$
HRMS $[M+Na]^+$: Calc. 243.0786, Obs. 243.0787 ($C_{16}H_{12}O$ Na) (Figure 23)

Synthesis of 1-ethoxy-1-hydroxy-4-phenylbut-3-yn-2-one (Table 1, entry 12, 1i) (Tanaka *et al*., 2007)

An oven-dried 50 mL two neck round bottom flask equipped with a magnetic stirrer bar and a teflon stopcock was evacuated while hot and allowed to cool under argon. The round bottom flask was charged in order with CuI (10.1 mg, 0.05 mmol), triethylamine (0.28 mL, 2 mmol), and THF (5 mL). Once a colorless clear solution formed, the alkyne (1 mmol) and monooxalyl chloride (2 mmol) were added and the reaction was allowed to proceed at room temperature. When the reaction was complete, saturated aqueous $NaHCO_3$ (5 mL) and diethyl ether (20 mL) were added. The reaction system was allowed to partition, and the organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give in 85% yield.



Pale yellow liquid
^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ_H = 7.46 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.34-7.31 (m, 3H), 5.06 (s, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.2, 3H)
^{13}CNMR (100 MHz, TMS, CDCl3) δ_C = 170.3, 131.8, 128.8, 128.2, 121.8, 85.3, 84.2, 62.8, 61.9, 14.0

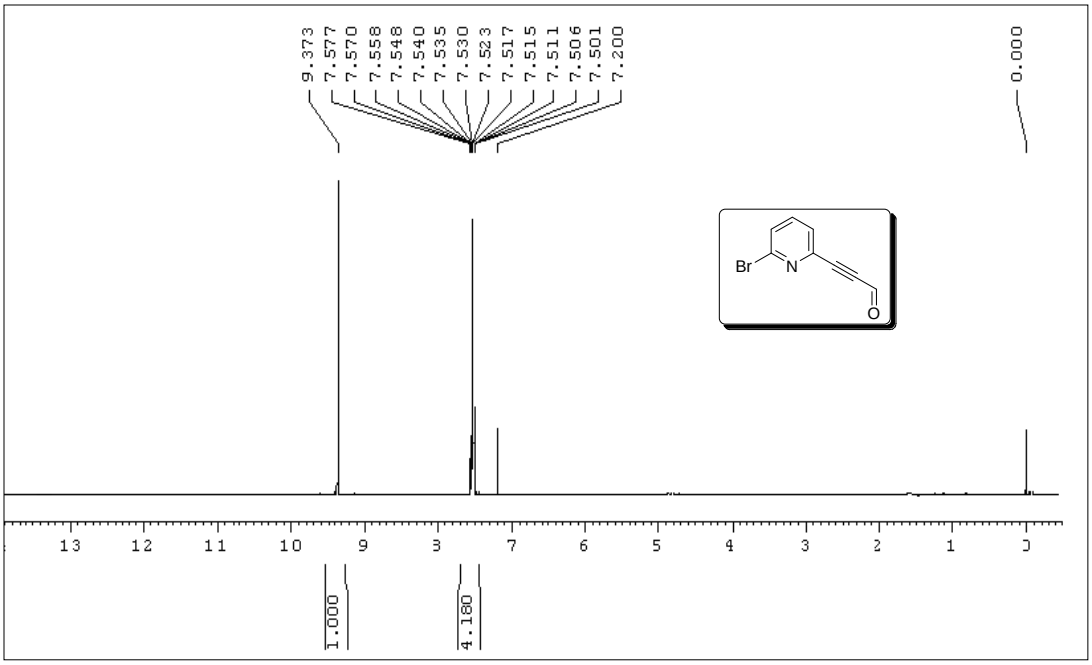


Figure 1: ^{1}H NMR spectrum of compound **2f** in $CDCl_3$

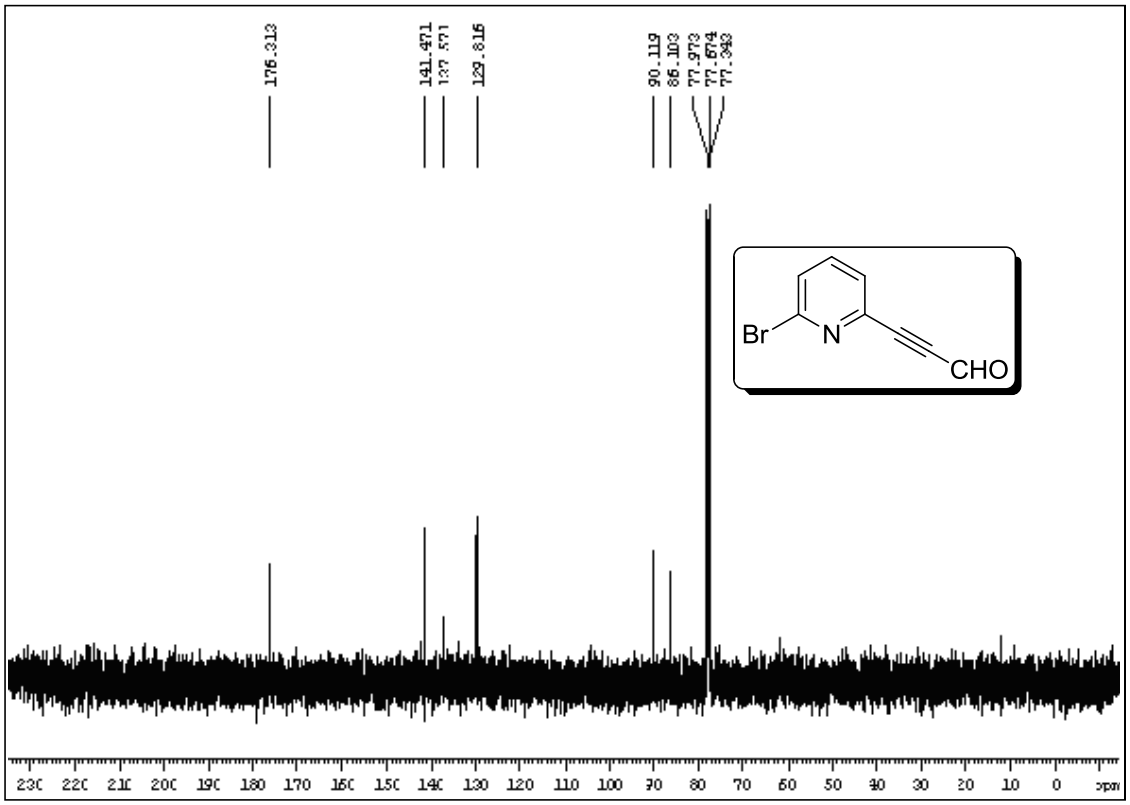


Figure 2: ^{13}CNMR spectrum of compound **2f** in $CDCl_3$

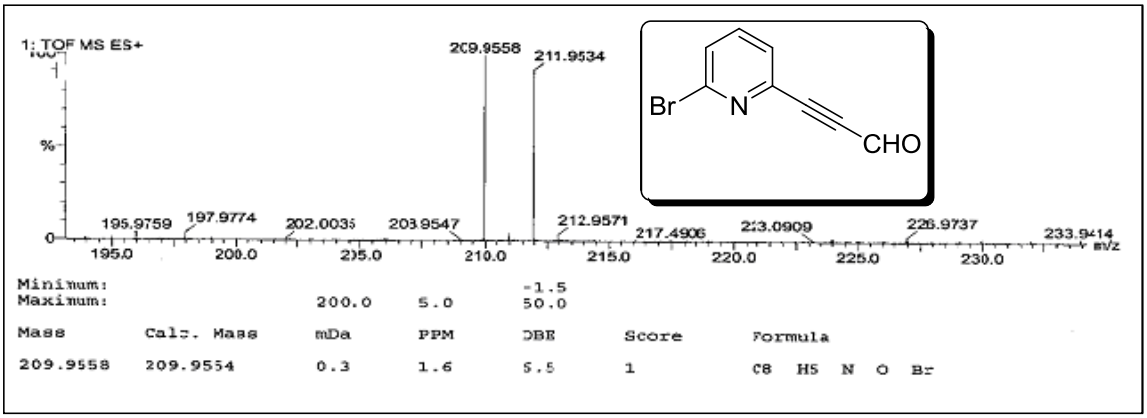


Figure 3 HRMS spectrum of compound **2f**

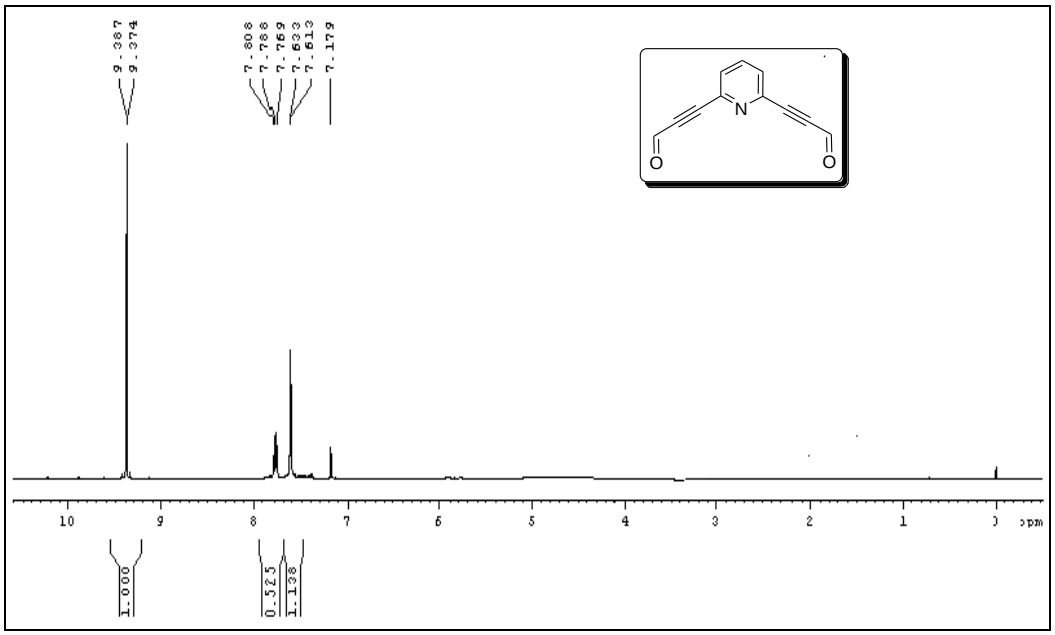


Figure 4: ^{1}H NMR spectrum of compound **2g** in $CDCl_3$

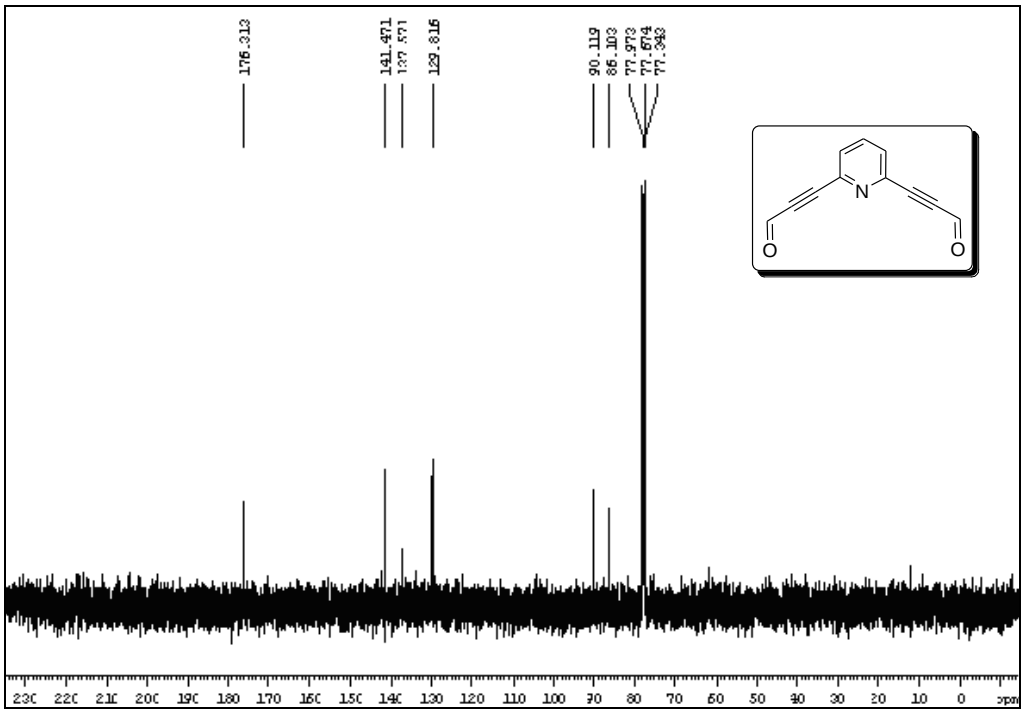


Figure 5: ^{13}C NMR spectrum of compound **2g** in $CDCl_3$

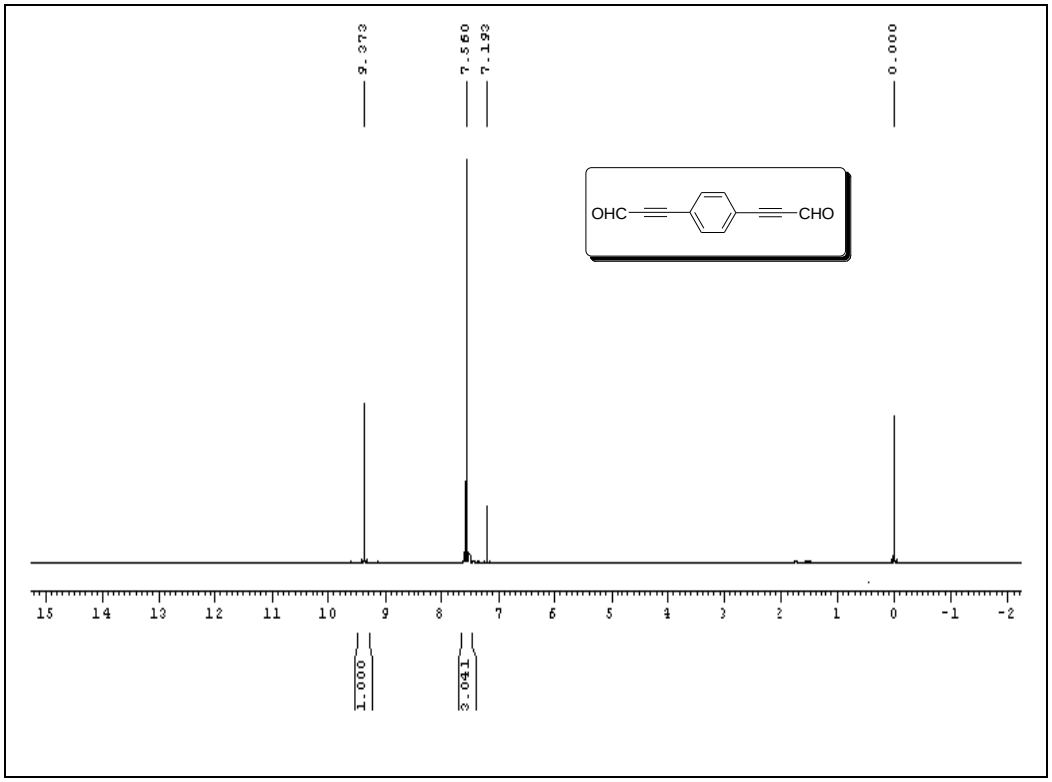


Figure 6: ^{1}H NMR spectrum of compound **2h** in $CDCl_3$

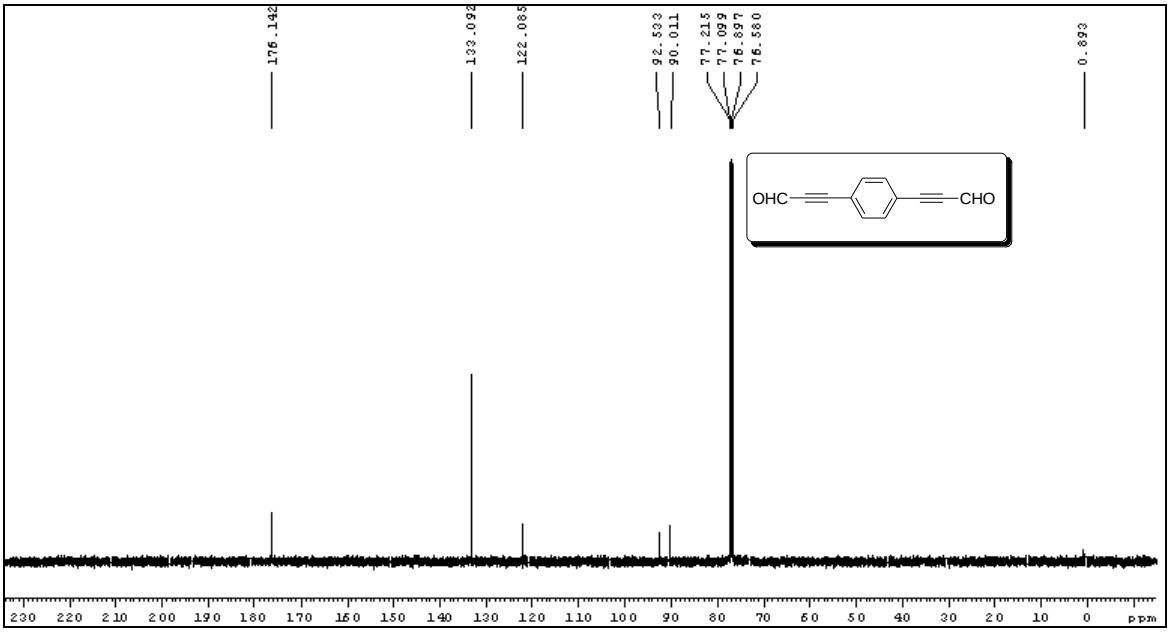


Figure 7: ^{13}C NMR spectrum of compound **2h** in $CDCl_3$

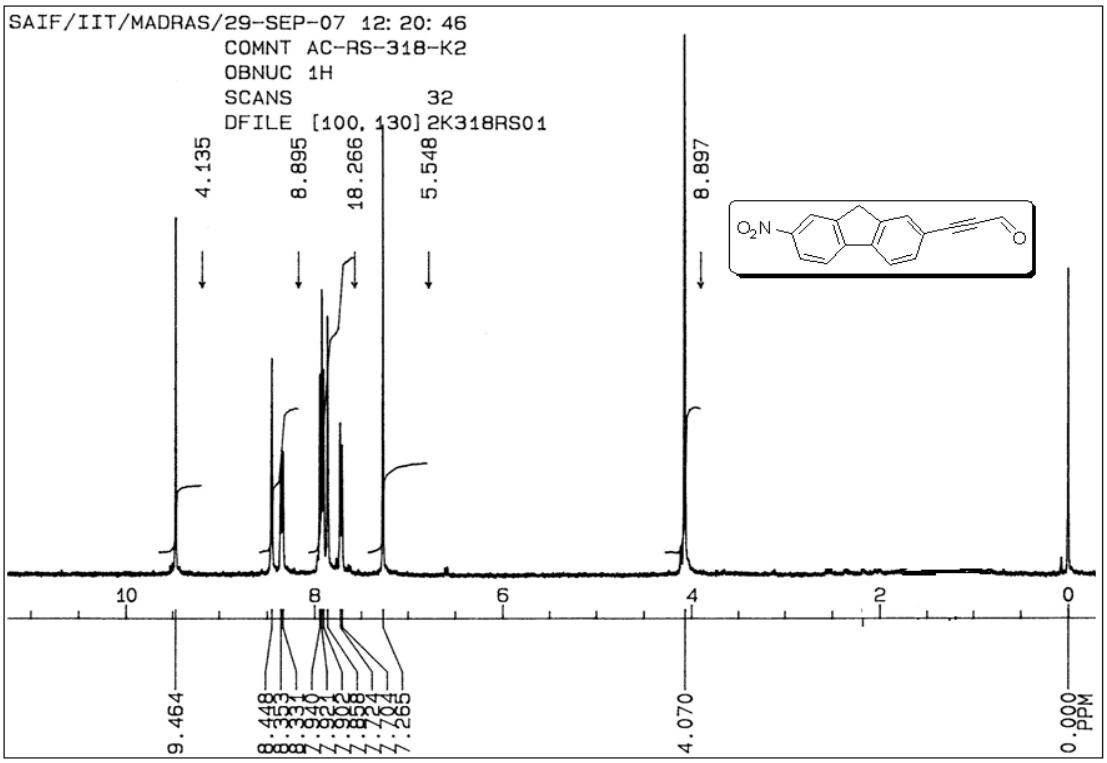


Figure 8: ^{1}H NMR spectrum of compound **2j** in $CDCl_3$

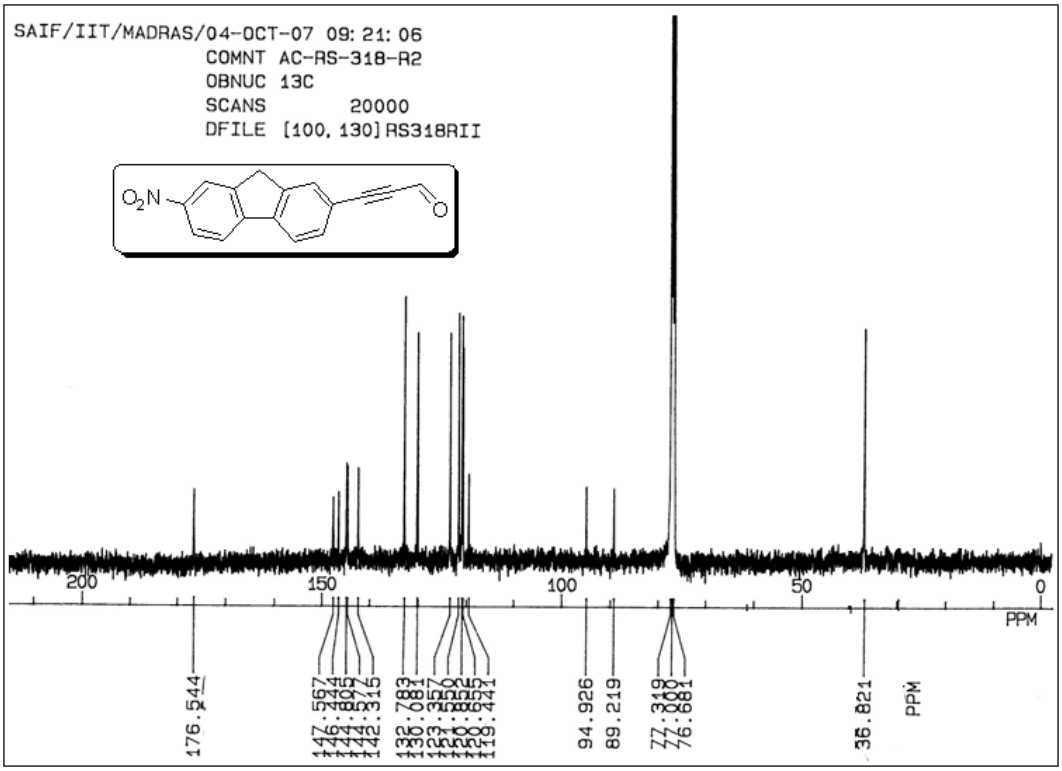


Figure 9: ^{13}C NMR spectrum of compound **2j** in $CDCl_3$

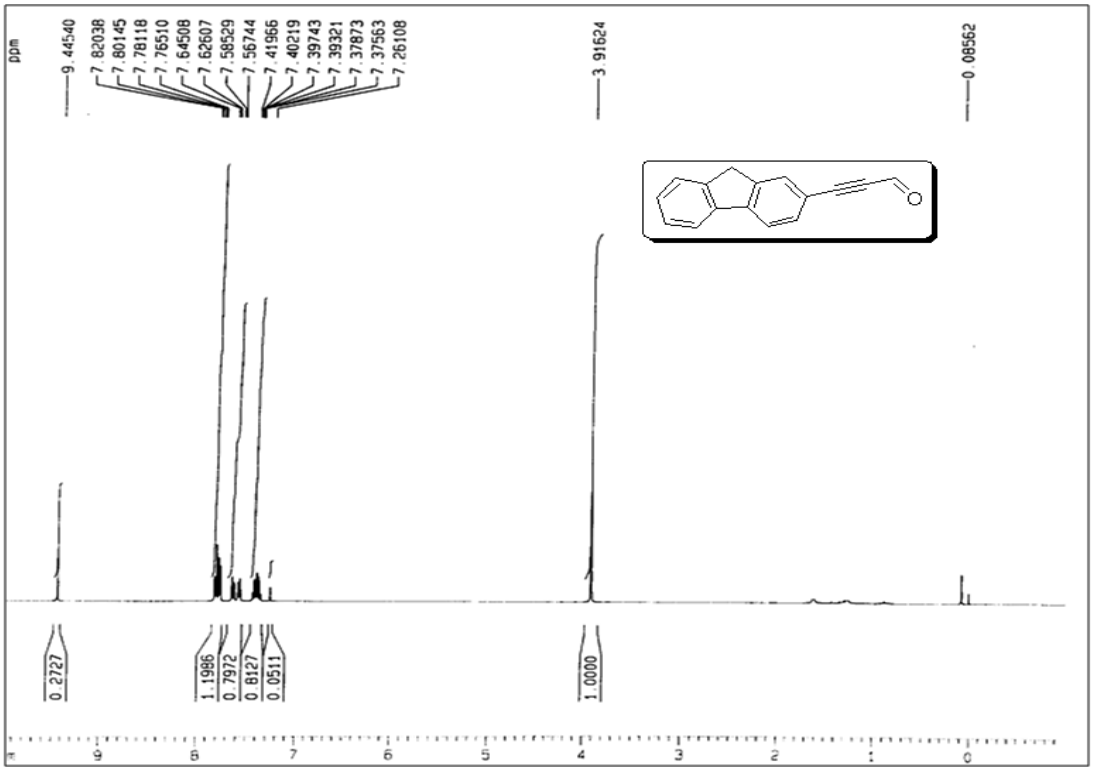


Figure 10: ^{1}H NMR spectrum of compound **2k** in $CDCl_3$

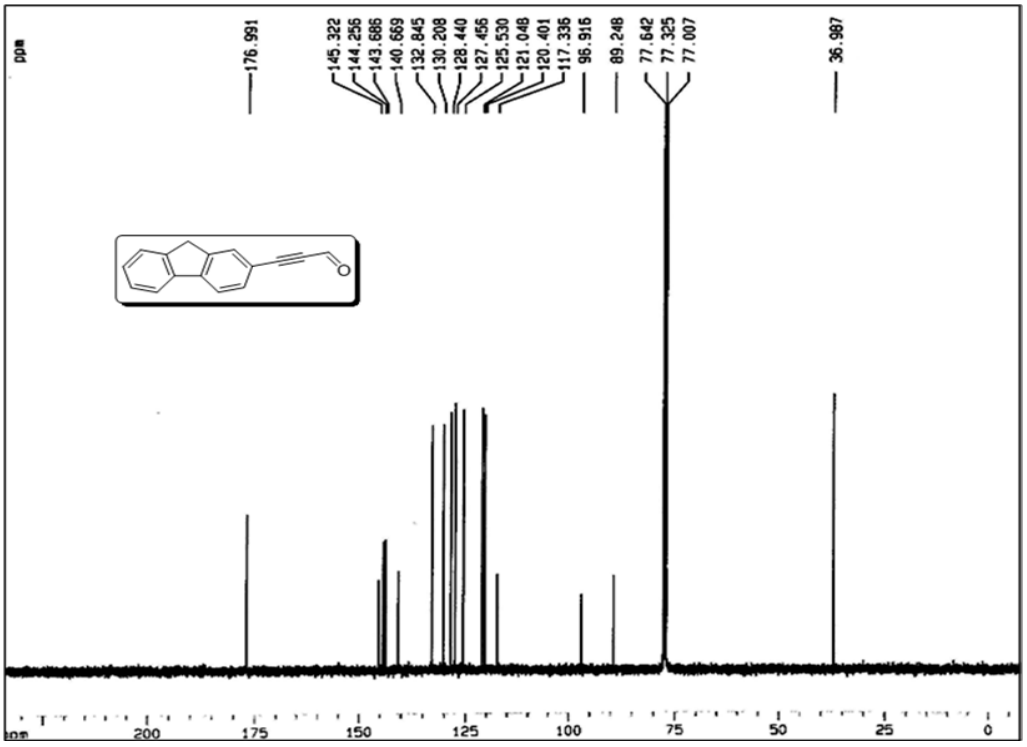


Figure 11 ^{13}C NMR spectrum of compound **2k** in $CDCl_3$

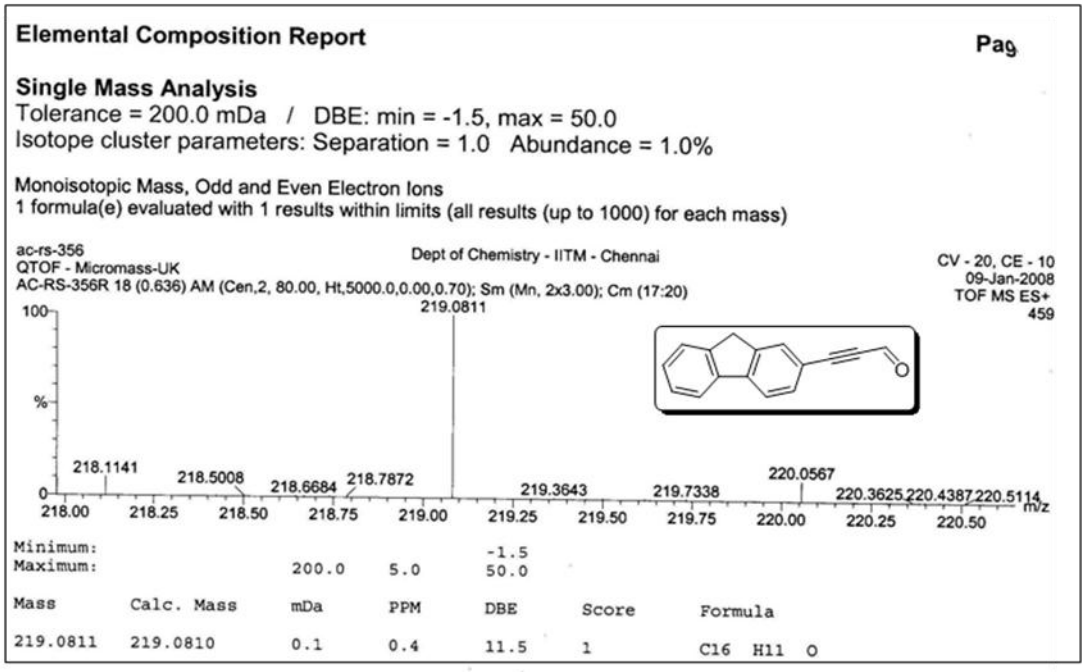


Figure 12 HRMS spectrum of compound **2k**

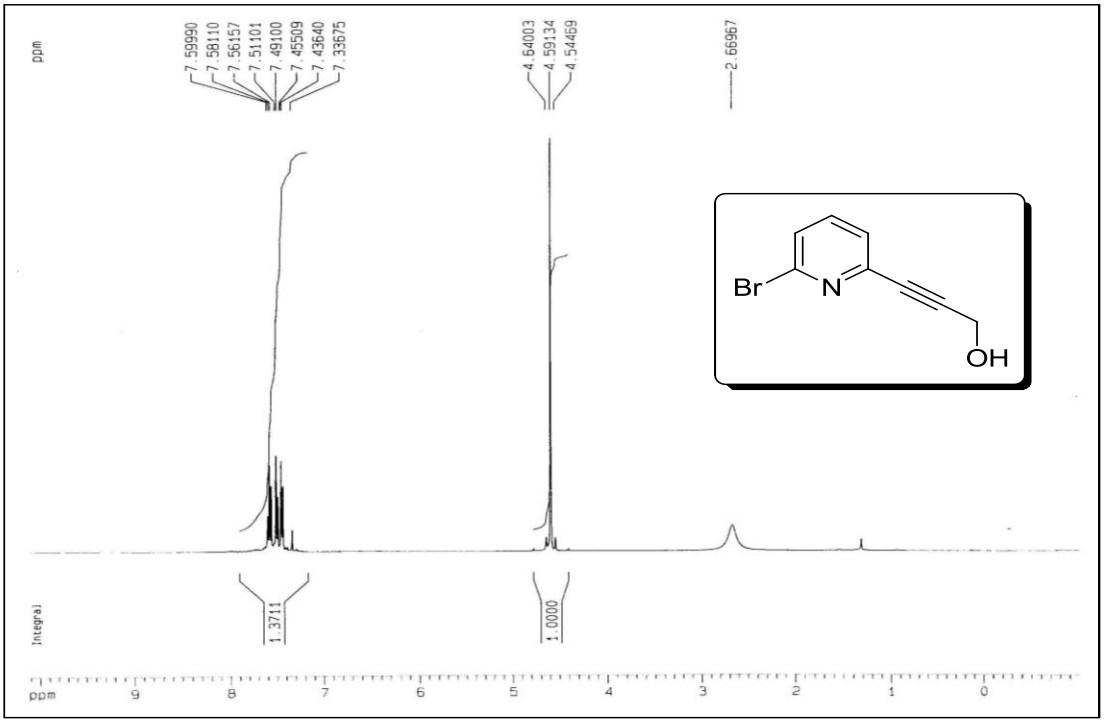


Figure 13 ^{1}H NMR spectrum of compound **1f** in $CDCl_3$

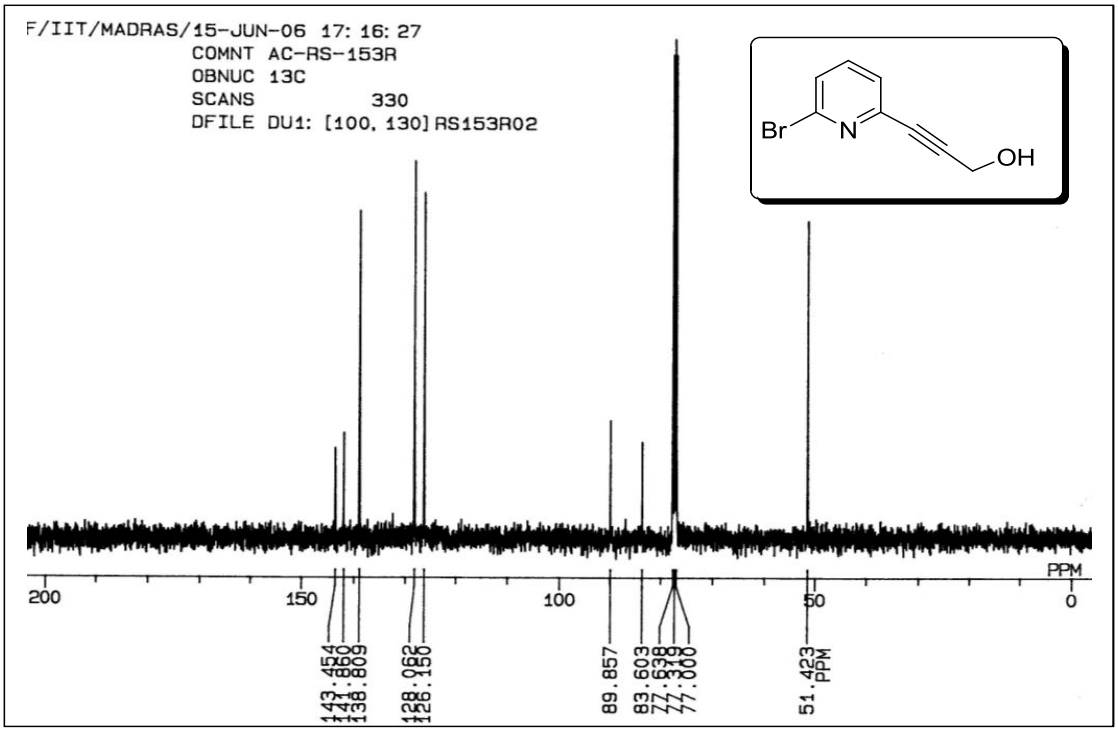


Figure 14 ^{13}C NMR spectrums of compound **7d** in $CDCl_3$

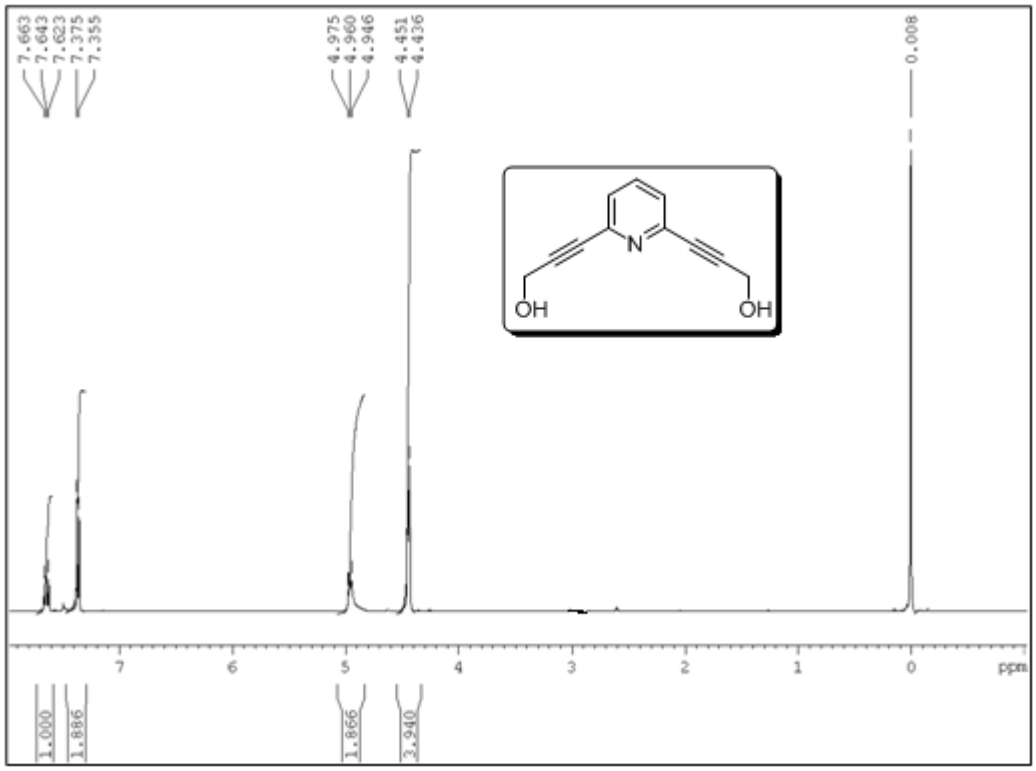


Figure 15 ^{1}H NMR spectrum of compound **1g** in $CDCl_3$

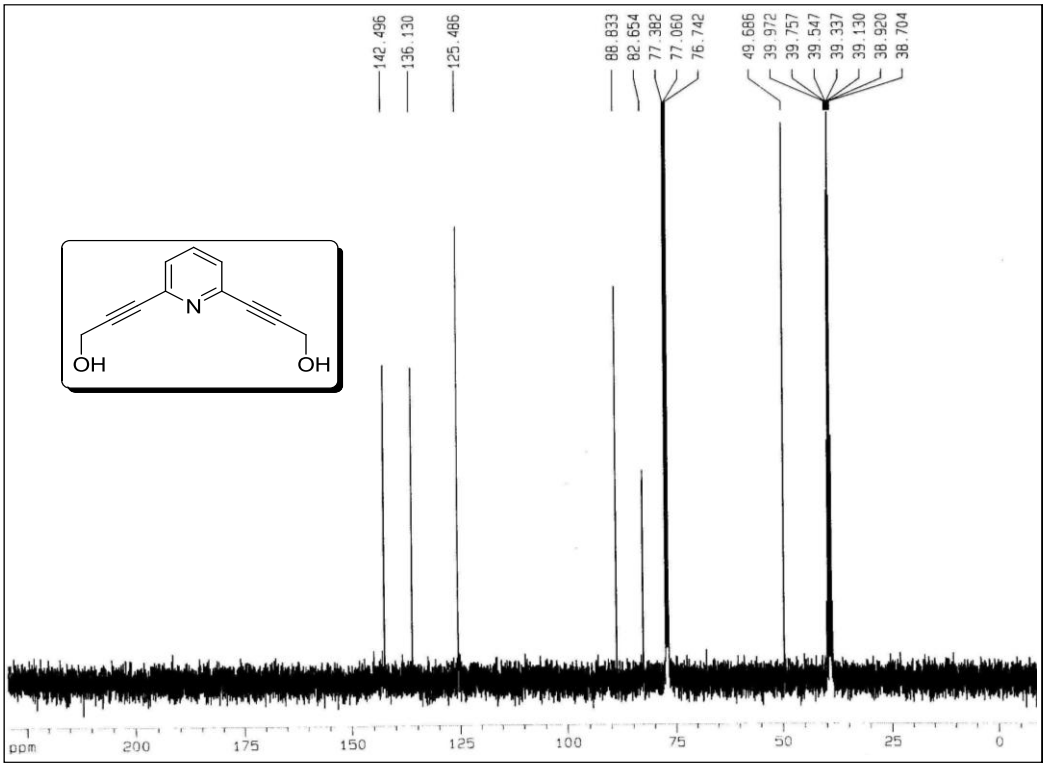


Figure 16 ^{13}C NMR of compound **1g** in $CDCl_3$

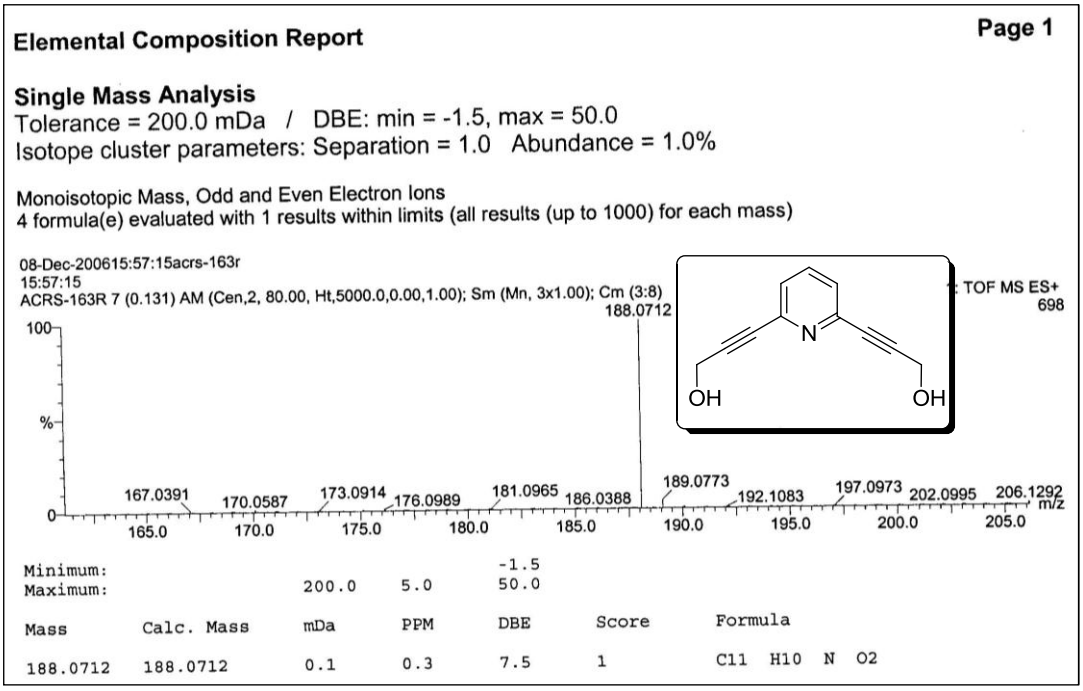


Figure 17 HRMS spectrum of compound **1g**

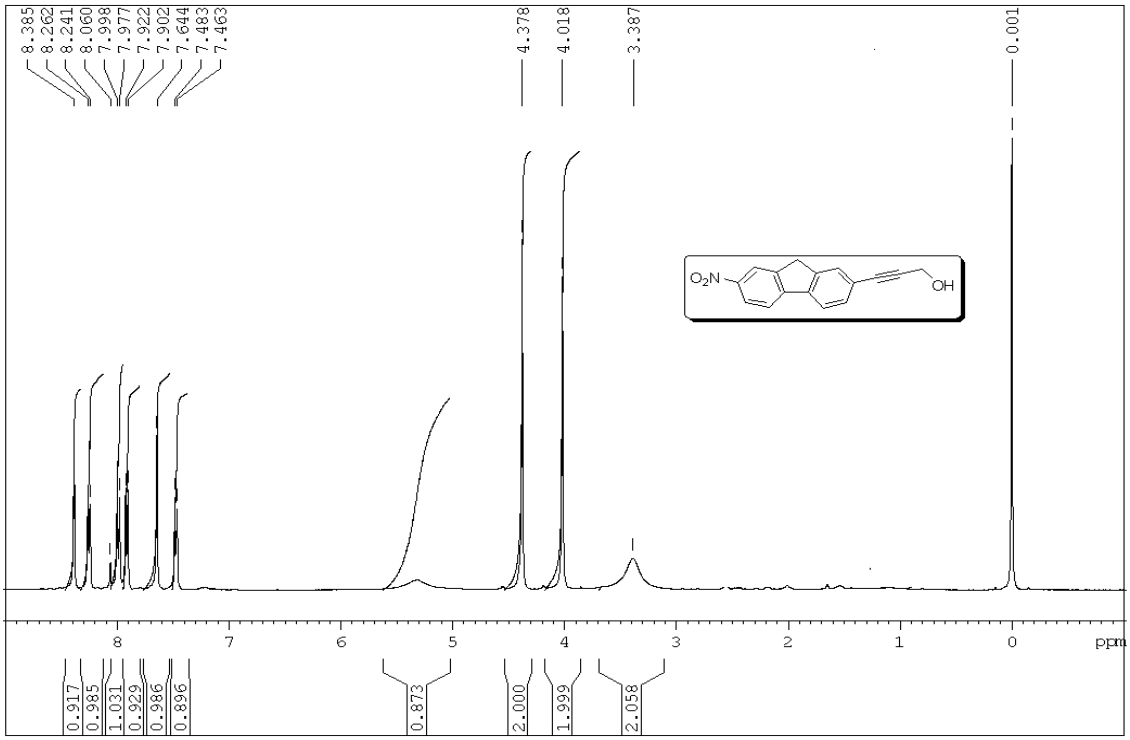


Figure 18 ^{1}H NMR spectrums of **1j** in $CDCl_3$

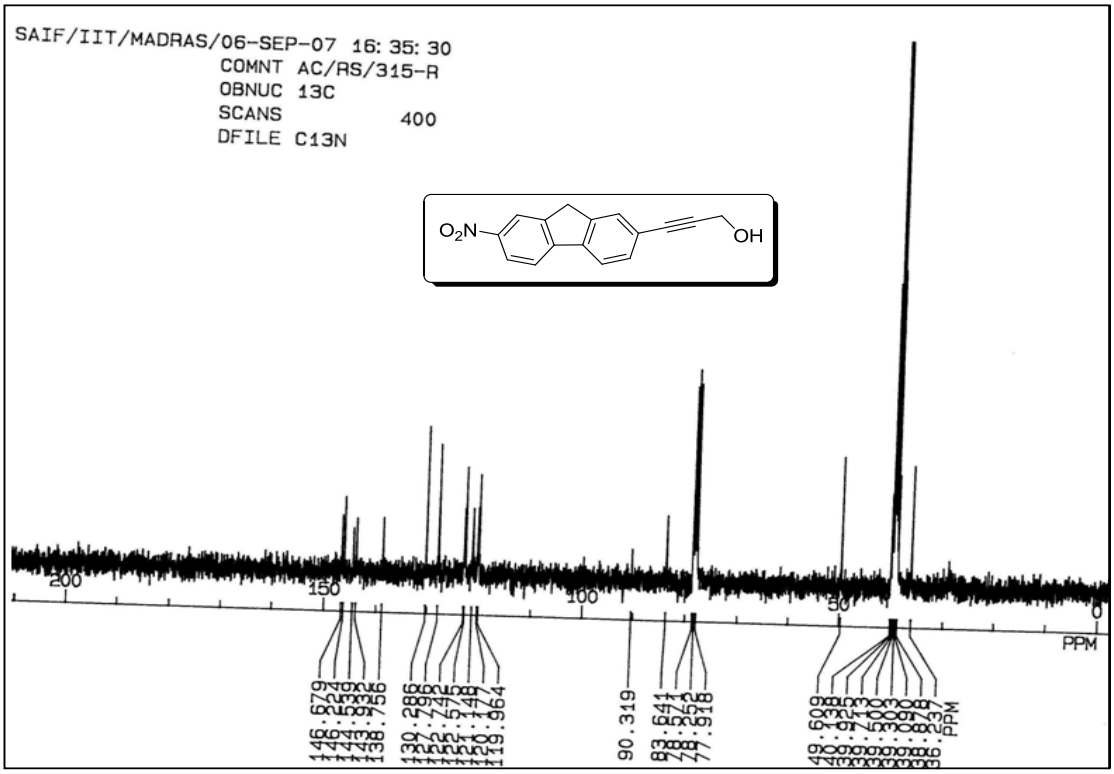


Figure 19 ^{13}C NMR spectrum of compound **1j** in $CDCl_3$

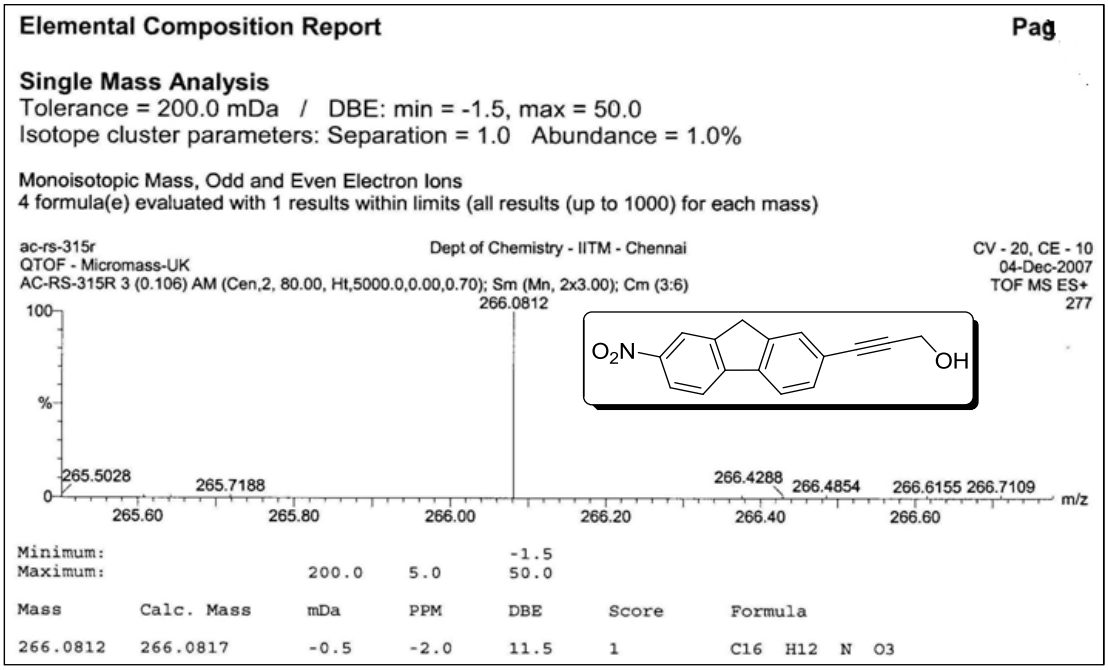


Figure 20 ^{13}C NMR spectrum of compound **1j** in $CDCl_3$

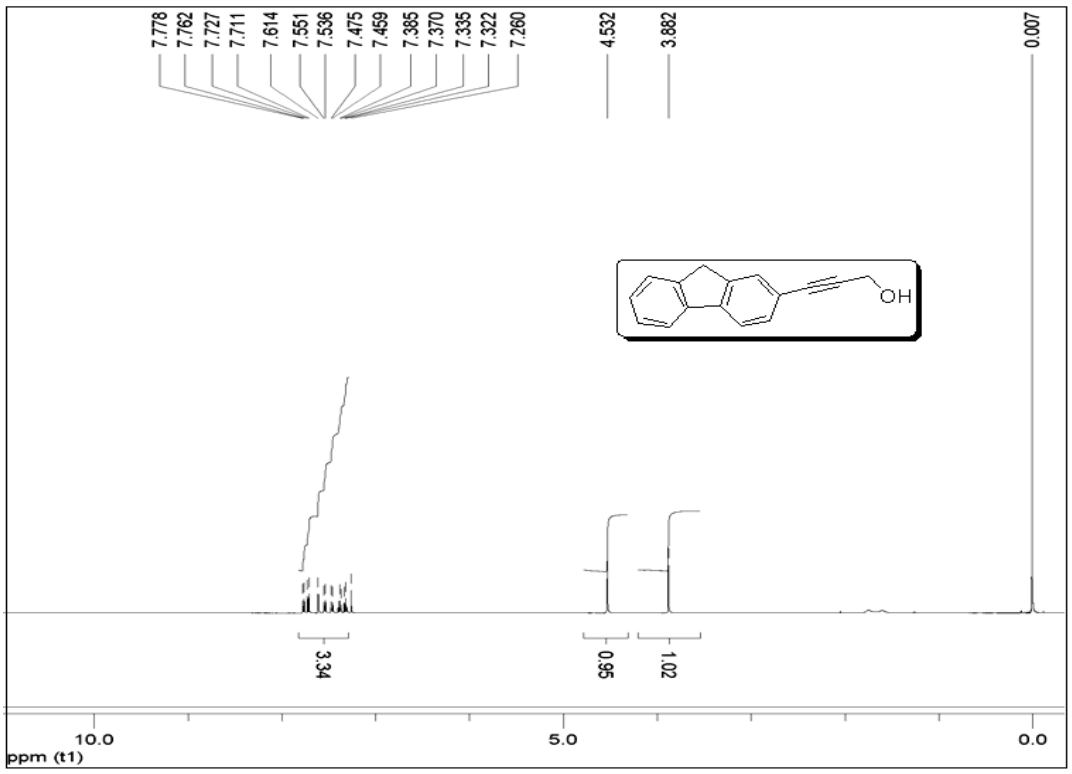


Figure 21 ^{1}H NMR spectrum of compound **1k** in $CDCl_3$

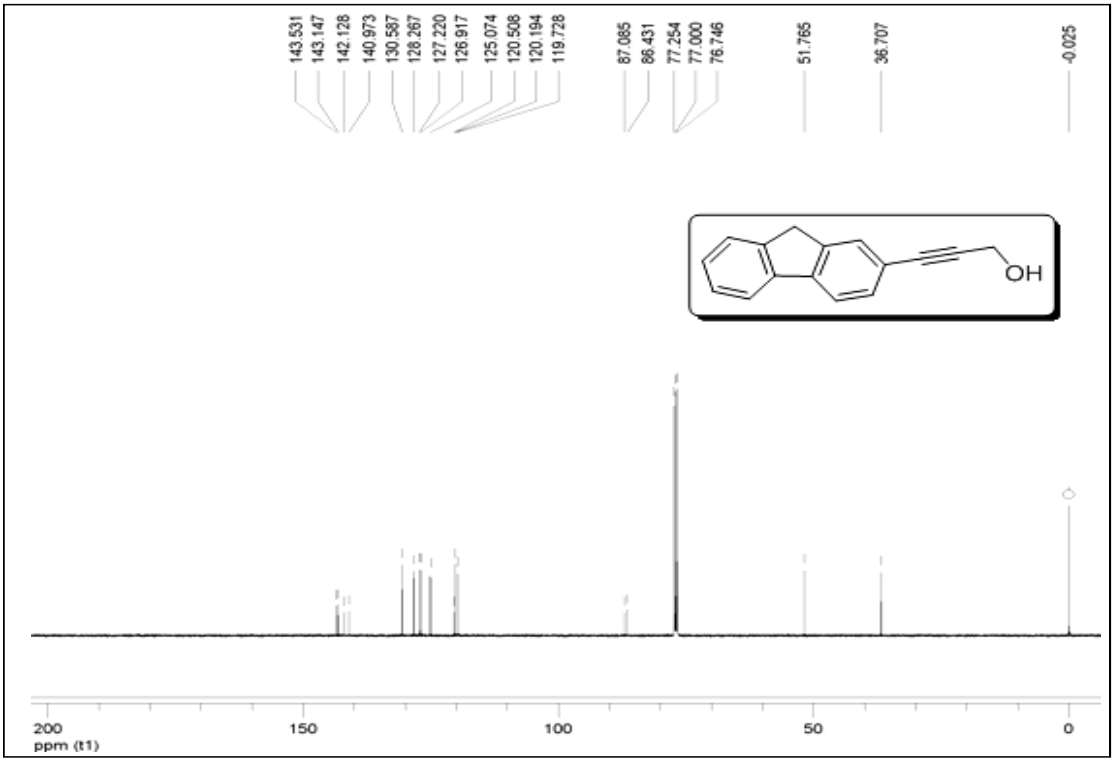


Figure 22 ^{13}C NMR spectrum of compound **1k** in $CDCl_3$

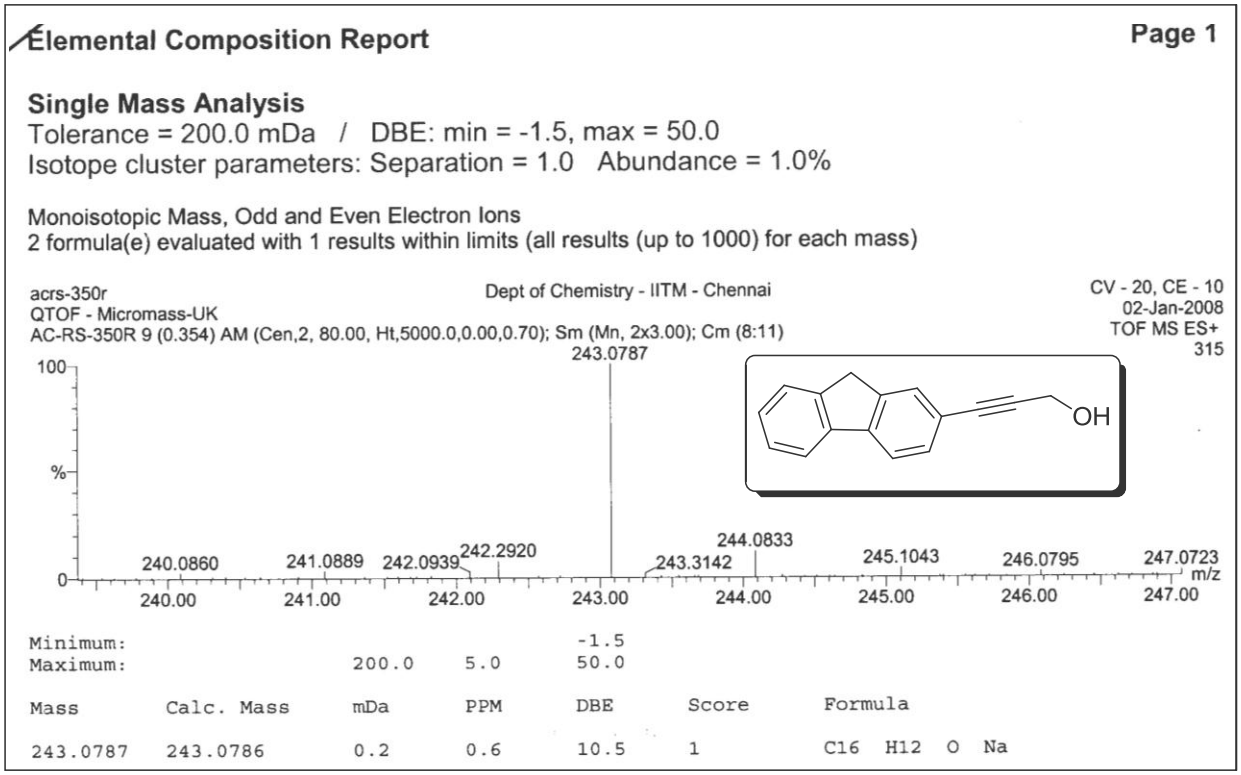


Figure 23 HRMS spectrum of compound **1k**

References

1. Liu, J.; Xie, X.; Ma, *Synthesis* **2012**, *44*, *1569*
2. Y. Maeda, N. Kakiuchi, S. Matsumura, T. Nishimura, T.Ka-wamura, S. Uemura, *J. Org. Chem.* 2002, 67, 6718.
3. F. Ye, A. Orita, J. Yaruva, T. Hamada, J. Otera, *Chem. Lett.***2004,** 528.
4. A. Nowak-Król, B. Koszarna, S. Y. Yoo, J. Chromiński, M. K. Węcławski, C-H. Lee, D. T. Gryko, *J. Org. Chem.* **2011,** *76*, 2627.
5. M. Guo, D. Li, Z. Zhang, *J. Org. Chem.* **2000,** *55*, 462.
6. K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett.* **1975,** *16*, 4467.
7. V. C. Marhevka, N. A. Ebner, R. D. Sehon, P. E. Hanna, *J. Med. Chem.*, **1985**, *28***,** 24.
8. D. Lee, S. A. Long, J. H. Murray, J. L. Adams, M. E. Nuttall, D. P. Nadeau, K. Kikly, J. D. Winkler, C. M. Sung, M. D. Ryan, M. A. Levy, P. M. Keller and W. E. DeWolf, *J. Med. Chem*, **2001,** 44, 2015.
9. K. Tanaka, T. Shoji, M. Hirano, *Eur. J. Org. Chem.* **2007,** 2687.
10. S. K. Hanson, R. Wu, L. A. P. Silks, *Org. Lett.* **2011,** *13*, 1908.