Electronic supporting information

Highly efficient regio and diastereoselective synthesis of functionalized bis-spirooxindoles and their antibacterial properties

Pambala Ramesh,[a] Kadiyala Srinivasa Rao,[a] Rajiv Trivedi,[a,]* B. Sudheer Kumar,[b] R. S. Prakasham[b] and B. Sreedhar,[c]

[a.] *Inorganic and Physical Chemistry Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500007, India*
[b.] *Bio Engineering and Environmental Centre, CSIR-Indian Institute of Chemical Technology, Hyderabad 500007, India*
[c.] *Laboratory of X-ray Crystallography.*
CSIR-Indian Institute of Chemical Technology, Hyderabad-500007 (India)
Fax: ++91-40-27193275, E-mail: rtrajiv401@gmail.com.

Contents

Experimental Section:

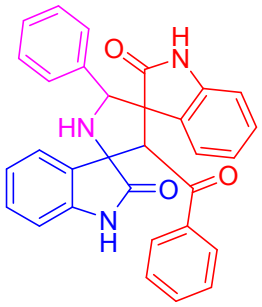
General information: Benzylamine, Isatins, Acetophenone, Ceric ammonium nitrate and all solvents were purchased from Sigma Aldrich and Alfa Aesar company and used without further purification as received. All ^{1}H and ^{13}C NMR spectra were recorded in deuterated chloroform ($CDCl_3$) or $CDCl_3$+DMSO-d_6 (deuterated dimethyl sulfoxide) (6:4) on Avance 300 or Avance 400 or Avance 500 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual $CHCl_3$ (^{1}H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm) as an internal reference. Coupling constants (J) are reported in Hertz (Hz). Peak multiplicity is indicated as follows: s-singlet, d-doublet, t-triplet, q-quartet, m-multiplet and dd-doublet of doublet. Melting points were measured on a BUCHI melting point machine. IR spectra were recorded on Thermo Nicolet FT/IR-5700 spectrometer. Mass spectra were recorded using Waters mass spectrometer. High resolution mass spectrums (HRMS) were recorded using Applied Bio-Sciences HRMS spectrometer at national center for mass spectroscopy-IICT.

General Procedure for preparation for synthesis of (3a-31):

A 5 ml RB flask containing Isatin (**1**) (1.0 mmol), Benzylamine (**2**) (1.0 mmol), Isatin chalcone (**3**) (1.0 mmol), Ceric ammonium nitrate (0.5 mol%) and water (2 mL) was placed in oil bath and refluxed for the appropriate time, at 100 ^{o}C (temperature monitored by a thermometer). The progress of reaction was monitored by TLC. After the reaction was completed, the aqueous mixture was extracted with ethyl acetate and dried over Na_2SO_4, and the solvent was removed under reduced pressure. The reaction mixture was purified by (silica gel) column chromatography (hexane/AcOEt, 80:20 as eluent) to give pure products.

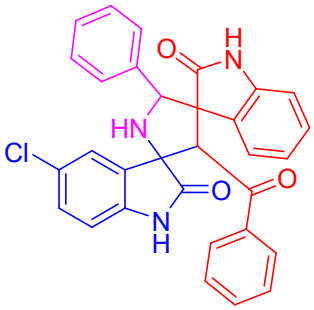
Spectral data of all compounds:

Compound **4a:-**



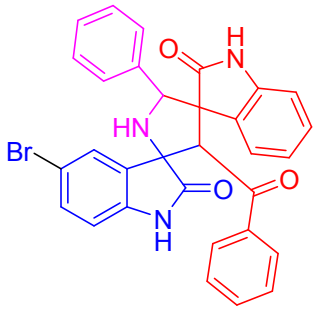
Colorless solid; Mp 248-250 ^{o}C; IR: ν_{max} 3655, 3374, 3295, 3163, 3033, 2897, 2855, 1706, 1620, 1473, 1448, 1345, 1294, 1191, 1106, 1023, 970, 759, 696 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.02 (s, 1H), 9.70 (s, 1H), 7.74 - 7.81 (m, 1H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.56 (s, 1H), 7.17 - 7.34 (m, 4H), 7.00 - 7.17 (m, 6H), 6.84 - 7.00 (m, 5H), 6.31 - 6.39 (m, 1H), 5,81 (d, *J* = 9.1 Hz, 1H), 5.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.3, 179.7, 179.6, 142.2, 140.7, 136.3, 136.1, 128.8, 128.7, 128.5, 127.3, 127.2, 127.0, 126.8, 126.4, 125.8, 125.0, 122.7, 121.6, 121.1, 109.2, 108.3, 70.5, 67.6, 66.2, 61.3; m/z (ESI): 486 $[M+H]^{+}$; HRMS calcd for $C_{31}H_{24}O_3N_3$: 486.18122, found: 486.18159.

Compound **4b:-**



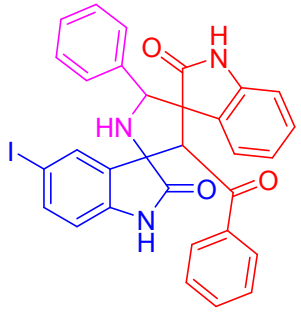
White solid; Mp 273-275 ^{o}C; IR: ν_{max} 3384, 3319, 1719, 1675, 1618, 1476, 1443, 1342, 1292, 1255, 1186, 1122, 1063, 819, 755, 695, 566 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.01 (s, 1H), 9.54 (s, 1H), 7.76 (d, *J* = 5.84 Hz, 1H), 7.68 (s, 1H), 7.46 (s, 1H), 7.18 - 7.36 (m, 4H), 7.03-7.18 (m, 5H), 6.82 - 7.03 (m, 5H), 6.35 (d, *J* = 6.23 Hz, 1H), 5.81 (d, *J* = 6.98 Hz, 1H), 5.01(s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.4, 179.9, 179.6, 141.0, 140.8, 136.4, 136.2, 131.9, 130.7, 129.0, 128.5, 127.7, 127.4, 127.2, 127.1, 126.7, 126.4, 126.1, 125.2, 123.6, 121.9, 110.6, 108.5, 70.5, 67.7, 66.4, 61.2, 57.0; m/z (ESI): 520 $[M+H]^{+}$; HRMS calcd for $C_{31}H_{23}O_3N_3Cl$: 520.14225, found: 520.14330.

Compound **4c:-**



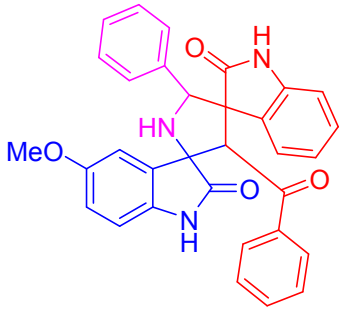
White solid; Mp 228-230 ^{o}C; IR: ν_{max} 3655, 3392, 3323, 2960, 2890, 1713, 1679, 1616, 1475, 1442, 1345, 1295, 1256, 1220, 1189, 1157, 1127, 1080, 836, 755, 690, 560 cm^{-1}; ^{1}H NMR (300 MHz $CDCl_3$+DMSO-d_6,): δ 10.01 (s, 1H), 9.62 (s, 1H), 7.68 - 7.87 (m, 2H), 7.48 (s, 1H), 7.19 - 7.38 (m, 4H), 7.04 - 719 (m, 5H), 6.95 - 7.04 (m, 2H), 6.81 - 6.95 (m, 3H), 6.30 - 6.39 (m, 1H), 5.80 (d, *J* = 6.98 Hz, 1H), 5.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.7, 179.0, 178.8, 141.2, 140.4, 135.8, 135.7, 131.2, 131.0, 130.7, 128.0, 127.0, 126.8, 126.5, 126.0, 125.5, 124.4, 121.0, 112.5, 110.3, 107.8, 69.8, 66.9, 65.6, 60.4, 55.9; m/z (ESI): 564 $[M+H]^{+}$; HRMS calcd for $C_{31}H_{25}O_3N_3Br$: 566.0925, found: 566.09163.

Compound 4d:-



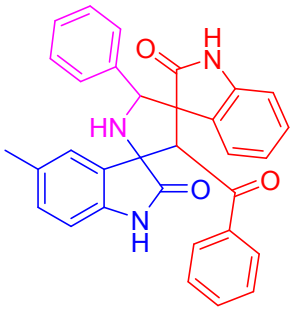
White solid; Mp 248-250 ^{o}C; IR: ν_{max} 3357, 3316, 3060, 2891, 1719, 1675, 1615, 1473, 1390, 1340, 1301, 1252, 1185, 1126, 995, 809, 752, 692, 593, 529 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.19 (s, 1H), 9.72 (s, 1H), 7.93 (d, *J* = 7.51 Hz, 1H), 7.71 - 7.78 (m, 1H), 7.50 - 7.60 (m, 2H), 7.19 - 7.34 (m, 3H), 7.03 - 7.19 (m, 5H), 6.83 - 7.03 (m, 4H), 6.72 - 6.78 (m, 1H), 6.31 - 6.37 (m, 1H), 5.79 (d, *J* = 8.12 Hz, 1H), 4.98 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.8, 178.9, 178.8, 141.9, 140.4, 137.1, 135.9, 135.8, 131.3, 131.1, 128.0, 127.0, 126.8, 126.6, 126.1, 125.6, 124.5, 121.1, 111.0, 107.9, 82.5, 69.8, 66.8, 65.7, 60.5; m/z (ESI): 612 $[M+H]^+$; HRMS calcd for $C_{31}H_{23}O_3N_3I$: 612.07786, found: 612.08023.

Compound **4e:-**



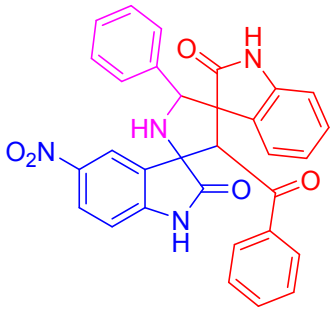
White solid; Mp 219-220 ^{o}C; IR: ν_{max} 3405, 3296, 3276, 3060, 2999, 2970, 2913, 2833, 1720, 1697, 1619, 1489, 1451, 1410, 1356, 1301, 1261, 1188, 1130, 1066, 1032, 989, 868, 817, 775, 747, 695, 678, 658, 616, 574, 533, 509 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 9.82 (s, 1H), 9,67 (s, 1H), 7.71 - 7.86 (m, 1H), 7.71 - 7.64 (m, 5H), 7.02 - 7.17 (m, 5H), 6.94 - 7.03 (m, 2H), 6.81 - 6.94 (m, 3H), 6.74 - 6.82 (m, 1H), 6.30 - 6.39 (m, 1H), 5.83 (d, *J* = 3.7 Hz, 1H), 5.01 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.2, 179.7, 179.5, 154.7, 140.6, 136.3, 136.1, 135.5, 131.5, 129.9, 128.5, 127.3, 127.1, 126.9, 126.7, 126.4, 125.8, 125.0, 121.5, 113.5, 109.9, 109.6, 108.2, 70.4, 67.9, 66.2, 61.1, 55.2; m/z (ESI): 517 $[M+H]^+$.

Compound **4f:-**



White solid; Mp 238-240 ^{o}C; IR: ν_{max} 3510, 3388, 3324, 3058, 2890, 1713, 1674, 1618, 1494, 1471, 1448, 1388, 1342, 1301, 1249, 1192, 1160, 1119, 1029, 993, 821, 795, 755, 686, 595, 587 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 9.93 (s, 1H), 9.77 (s, 1H), 7.73 - 7.81 (m, 1H), 7.60 (s, 1H), 7.47 (s, 1H), 7.26 - 7.32 (m, 2H), 7.18 - 7.32 (m, 1H), 7.01 - 7.17 (m, 6H), 6.79 - 7.00 (m, 5H), 6.31 - 6.37 (m 1H), 5.80 (s, 1H), 5.02 (s, 1H), 2.36 (s, 3H); ^{3}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.2, 179.6, 140.6, 139.6,136.3, 136.1, 131.4, 130.4, 129.1, 128.6, 128.5, 127.2, 127.1, 126.9, 126.7, 126.4, 125.7, 124.9, 123.2, 121.4, 108.8, 108.2, 70.4, 67.6, 66.1, 61.2, 20.2; m/z (ESI): 500 $[M+H]^{+}$; HRMS calcd for $C_{32}H_{26}O_3N_3$: 500.1952, found: 500.19732.

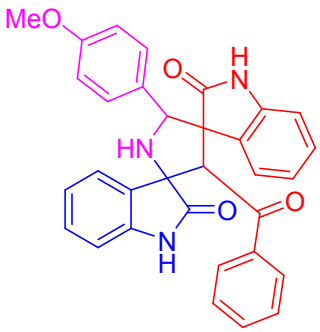
Compound **4g:-**



White solid; Mp 194-196 ^{o}C; IR: ν_{max} 3646, 3337, 1731, 1675, 1624, 1521, 1478, 1451, 1403, 1341, 1243, 1182, 1103, 1025, 980, 906, 831, 755, 696, 598, 562, 458 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.8 (s, 1H), 9.71(s, 1H), 8.55 (d, J = 2.07 Hz, 1H), 8.19 - 8.24 (m, 1H), 7.70 - 7.76 (m, 1H), 7.52 (s, 1H), 7.20 - 7.34 (m, 3H), 6.97 - 7.20 (s, 8H), 6.83 - 6.97 (m, 2H), 6.32 - 6.39 (m, 1H), 5.79 (d, J = 6.23 Hz, 1H), 5.09(s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.3, 180.1, 179.1, 148.9, 142.0, 140.8, 135.9, 136.0, 131.9, 129.7, 128.2, 127.6, 127.3,

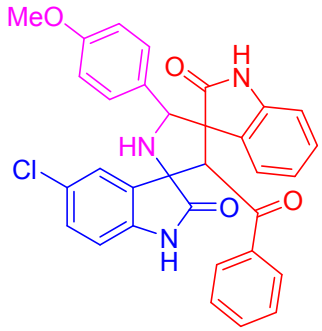
127.0, 126.6, 126.0, 124.8, 121.6, 119.3, 109.0, 108.4, 70.3, 67.1, 66.4, 60.8; m/z (ESI): 531, $[M+H]^+$; HRMS calcd for $C_{31}H_{23}O_5N_4$: 531.16630, found: 531.16778.

Compound **4h:-**



White solid; Mp 224-226 ^oC; IR: ν_{max} 3318, 3181, 3083, 2952, 2839, 1707, 1617, 1511, 1472, 1349, 1293, 1248, 1190, 1112, 1024, 978, 835, 784, 751, 692, 568, 501 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.01 (s, 1H), 9.65 (s, 1H), 7.72 - 7.77 (m, 1H), 7.66 (d, J = 7.76 Hz, 1H), 7.57 (s, 1H), 7.17 - 7.32 (m, 4H), 7.00 - 7.12 (m, 3H), 6.82 - 6.96 (m, 5H), 6.65(d, J = 8.68 Hz, 2H), 6.32 - 6.37 (m, 1H), 5,74 (d, J = 9.06 Hz, 1H), 5.04 (s, 1H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.2, 179.7, 179.6, 158.1, 142.2, 140.6, 136.3, 131.5, 128.7, 128.5, 128.0, 127.2, 127.1, 126.9, 126.4, 124.8, 122.6, 121.4, 120.9, 112.2, 109.1, 108.1, 70.2, 67.5, 66.0, 61.3, 54.2; m/z (ESI): 516 $[M+H]^+$; HRMS calcd for $C_{32}H_{26}O_4N_3$: 516.19178, found: 516.19232.

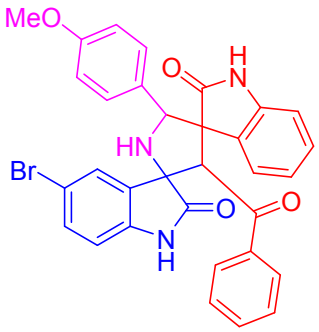
Compound **4i:-**



White solid; Mp 194-196 ^oC; IR: ν_{max} 3650, 3177, 3066, 2840, 1727, 1697, 1618, 1516, 1477, 1449, 1351, 1292, 1253, 1185, 1129, 1062, 1021, 961, 877, 826, 751, 693, 627, 598, 567, 501 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.2 (s, 1H), 9.68 (s, 1H), 7.69 - 7.75 (m, 1H),

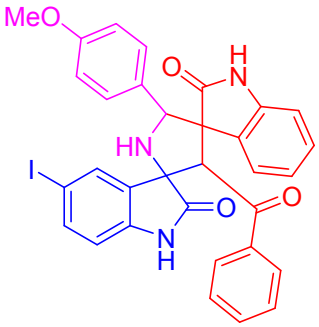
7.65 (d, J = 1.88 Hz, 1H), 7.57 (s, 1H), 7.18 - 7.32 (m, 4H), 7.05 - 7.13 (m, 2H), 6.82 - 6.96 (m, 5H), 6.66 (d, J = 8.87 Hz, 2H), 6.32 - 6.37 (m, 1H), 5,73 (d, J = 7.93 Hz, 1H), 4.99 (s, 1H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.5, 178.8, 178.5, 157.5, 135.5, 140.5, 140.2, 130.9, 127.8, 126.5, 125.7, 124.9, 124.1, 122.6, 120.6, 111.5, 109.5, 107.4, 69.4, 66.6, 65.2, 60.2, 53.6; m/z (ESI): 550 $[M+H]^+$; HRMS calcd for $C_{32}H_{25}O_4N_3Cl$: 550.15281, found: 550.15428.

Compound **4j:-**



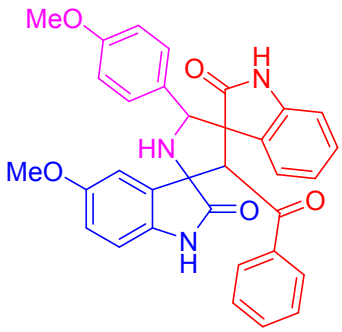
White solid; Mp 222-224 ^{o}C; IR: ν_{max} 3653, 3182, 2921, 1727, 1695, 1617, 1517, 1476, 1448, 1351, 1292, 1253, 1185, 1130, 1022, 959, 877, 826, 751, 687, 627, 570, 502 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.18(s,1 H), 9.65 (s, 1H), 7.63 - 7.89 (m, 2H), 7.46 - 7.62 (m, 1H), 7.16 - 7.46 (m, 4H), 7.01 - 7.16 (m, 2H), 6.75 - 7.00 (m, 5H), 6.56 - 6.75 (m, 2H), 6.28 - 6.46 (m, 1H), 5.73 (d, J = 4.9 Hz, 1H), 4.99 (s, 1H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.1, 179.5, 179.4, 158.2, 141.4, 140.6, 136.1, 131.6, 131.5, 131.0, 128.3, 128.0, 127.3, 127.2, 127.1, 126.4, 125.9, 124.8, 121.4, 113.1, 112.2, 110.8, 108.2, 70.0, 67.3, 65.9, 60.9, 56.6, 54.2; m/z (ESI): 594 $[M+H]^+$; HRMS calcd for $C_{32}H_{25}O_4N_3Br$: 594.10230, found: 594.10464.

Compound **4k:-**



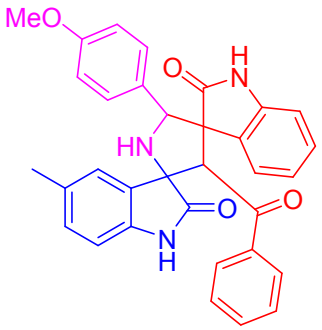
White solid; Mp 212-214 ^{o}C; IR: ν_{max} 3655, 3438, 3192, 3064, 2839, 1726, 1693, 1615, 1516, 1475, 1449, 1350, 1291, 1250, 1185, 1131, 1022, 955, 880, 826, 751, 687, 628, 594, 531, 500, 457 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.49 (s, 1H), 9.98 (s, 1H), 8.03 (s, 1H), 7.87 (s, 1H), 7.71 (d, J=6.98 Hz, 1H), 7.50 - 7.57 (m, 1H), 7.20 - 7.31 (m, 3H), 7.05 - 7.18 (m, 2H), 6.79 - 6.97 (m, 4H), 6.70 - 6.78 (m, 1H), 6.61 - 6.70 (m, 2H), 6.31 (d, *J* = 7.17 Hz, 1H), 5.62 (d, *J* = 6.60 Hz, 1H), 4.93 (s, 1H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.5, 179.8, 179.7, 158.6, 142.1, 140.7, 137.9, 136.4, 132.0, 131.9, 131.6, 128.7, 128.3, 127.7, 127.5, 127.4, 126.8, 125.2, 122.0, 112.6, 111.7, 108.5, 83.5, 70.3, 67.5, 66.3, 61.3, 57.2, 54.6; m/z (ESI): 642 $[M+H]^+$; HRMS calcd for $C_{32}H_{25}O_4N_3I$: 642.08843, found: 642.09099.

Compound **4l:-**



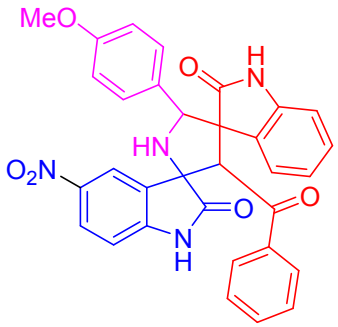
White solid; Mp 190-192 ^{o}C; IR: ν_{max} 3393, 3265, 3062, 2933, 2837, 1701, 1614, 1492, 1444, 1347, 1296, 1251, 1186, 1131, 1072, 1027, 832, 750, 692, 621, 571, 501 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.1 (s, 1H), 9.86 (s, 1H), 7.63 - 7.95 (m, 2H), 7.17 - 7.34 (m, 4H), 7.00 - 7.17 (m, 2H), 6.73 - 7.00 (m, 6H), 6.58 - 6.72 (m, 2H), 6.27 - 6.38 (m, 1H), 5.62 - 5.75 (m, 1H), 4.96 (s, 1H), 3.82 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.2, 179.7, 179.6, 158.2, 154.8, 140.6, 136.4, 135.5, 131.5, 130.0, 128.6, 128.1, 127.3, 127.2, 127.1, 126.5, 125.0, 121.5, 113.6, 112.3, 109.9, 109.6, 108.2, 70.3, 67.9, 66.1, 61.3, 55.3, 54.3; m/z (ESI): 546 $[M+H]^+$; HRMS calcd for $C_{33}H_{28}O_5N_3$: 546.20235, found: 546.20339.

Compound **4m:-**



White solid; Mp 194-196 ^{o}C; IR: ν_{max} 3307, 3200, 2964, 1710, 1683, 1617, 1509, 1476, 1344, 1298, 1247, 1196, 1169, 1111, 1028, 814, 781, 751, 672, 627, 600, 563, 501, 451 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 9.84 (s, 1H), 9.65 (s, 1H), 7.75 (d, *J* = 6.23 Hz, 1H), 7.55 (s, 1H), 7.48 (s, 1H), 7.15 - 7.34 (m, 3H), 6.98 - 7.15 (m, 3H), 6.77 - 6.96 (m, 5H), 6.58 - 6.72 (m, 2H), 6.28 - 6.40 (m, 1H), 5.75 (d, *J* = 8.12 Hz, 1H), 5.02 (s, 1H), 3.70 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.3, 179.8, 158.2, 140.6, 140.5, 139.7, 139.6, 136.4, 131.5, 130.5, 129.2, 128.7, 128.6, 128.1, 127.3, 127.2, 127.0, 126.5, 125.0, 123.4, 121.6, 112.3, 109.0, 108.2, 70.3, 67.6, 66.0, 61.4, 54.4, 20.3: m/z (ESI): 530 $[M+H]^{+}$; HRMS calcd for $C_{33}H_{28}O_4N_3$: 530.20743, found: 530.20830.

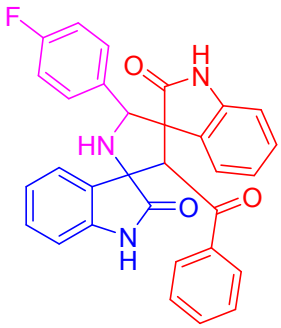
Compound **4n:-**



White solid; Mp 222-224 ^{o}C; IR: ν_{max} 3650, 3423, 3199, 3071, 2845, 1735, 1698, 1620, 1518, 1468, 1410, 1337, 1298, 1249, 1183, 1098, 1022, 965, 905, 832, 751, 689, 627, 565, 507, 459 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 11.05 (s, 1H), 9.92 (s, 1H), 8.50 (d, *J* = 1.88 Hz, 1H), 8.15-8.24 (m, 1H), 7.85 (s, 1H), 7.70 (d, *J* = 6.98 Hz, 1H), 7.19-7.33 (m, 3H), 7.00-7.18 (m, 3H), 6.78-7.00 (m, 4H), 6.62-6.74 (m, 2H), 6.29-6.37 (m, 1H), 5.67 (d, *J* = 6.60 Hz, 1H), 5.06 (s, 1H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.4, 180.2, 179.2, 158.4, 148.9, 142.1, 140.7, 136.0, 131.9, 129.8, 128.3, 128.0, 127.5, 127.3, 126.6, 126.1, 124.8, 121.6, 119.3,

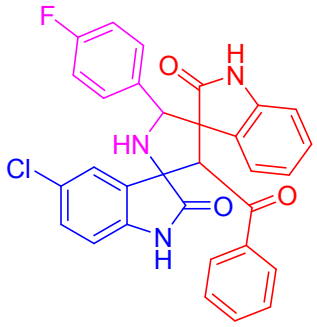
112.4, 109.0, 108.4, 70.2, 67.1, 66.3, 60.9, 56.8, 54.4, 49.2; m/z (ESI): 561 $[M+H]^+$; HRMS calcd for $C_{32}H_{25}O_6N_4$: 561.17686, found: 561.17833.

Compound **4o:-**



White solid; Mp 260-262 ^oC; IR: v_{max} 3527, 3368, 3327, 2891, 2825, 1715, 1675, 1618, 1509, 1476, 1448, 1396, 1335, 1290, 1224, 1187, 1108, 1023, 994, 960, 834, 798, 759, 680, 641, 594, 569, 545, 497 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 9.99 (s, 1H), 9.65 (s, 1H),7.73 - 7.81 (m, 1H), 7.68 (d, J = 7.36 Hz, 1H), 7.51 - 7.61 (m, 1H), 7.18 - 7.33 (m, 4H), 6.75 - 7.15 (m, 10H), 6.31 - 6.39 (m, 1H), 5.79 (s, 1H), 5,05 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 196.1, 179.8, 179.3, 142.2, 140.6, 136.2, 132.1, 131.5, 128.8, 128.6, 128.2, 127.7, 127.6, 127.4, 127.1, 126.4, 124.9, 122.8, 121.5, 121.0, 113.8, 113.5, 109.1, 108.2, 69.7, 67.3, 65.7, 61.0; m/z (ESI): 504 $[M+H]^+$; HRMS calcd for $C_{31}H_{23}O_3N_3F$: 504.17180, found: 504.17214.

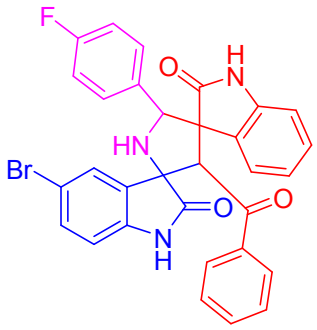
Compound **4p:-**



White solid; Mp 256-258 ^oC; IR: v_{max} 3657, 3388, 3324, 2891, 1717, 1679, 1619, 1507, 1477, 1442, 1392, 1344, 1296, 1255, 1221, 1188, 1158, 1122, 837, 757, 674, 594, 562 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.1 (s, 1H), 9.61 (s, 1H), 7.71 - 7.81 (m, 1H), 7.66 (d, J = 1.88 Hz, 1H), 7.49 (s, 1H), 7.16 - 7.33 (m, 4H), 6.96 - 7.15 (m, 4H), 6.76 - 6.96 (m, 5H), 6.28 - 6.40

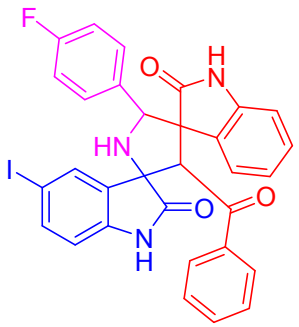
(m, 1H), 5.78 (d, *J* = 7.17 Hz, 1H), 5.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.7, 179.3, 178.7, 159.4, 140.7, 140.3, 135.8, 131.9, 131.3, 130.4, 128.2, 127.8, 127.5, 127.4, 127.1, 126.8, 126.1, 125.4, 124.5, 123.0, 121.1, 113.4, 131.1, 109.9, 107.9, 69.2, 66.9, 65.3, 60.3, 56.0; m/z (ESI): 538 $[M+H]^+$; HRMS calcd for $C_{31}H_{22}O_3N_3ClF$: 538.13282, found: 538.13416.

Compound **4q:-**



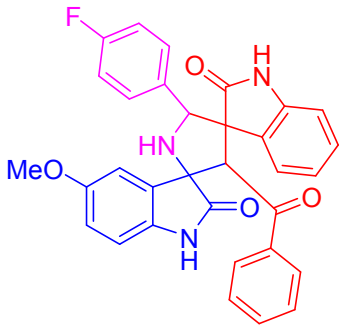
White solid; Mp 234-236 ^{o}C; IR: ν_{max} 3655, 3392, 3326, 2968, 2890, 1718, 1679, 1617, 1506, 1475, 1442, 1391, 1345, 1295, 1256, 1220, 1189, 1157, 1127, 1080, 1048, 1020, 971, 880, 836, 755, 729, 693, 623, 593, 563, 536, 454 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.43 (s, 1H), 9.92 (s, 1H), 7.69 - 7.84 (m, 2H), 7.18 - 7.55 (m, 5H), 6.95 - 7.18 (m, 4H), 6.77 - 6.95 (m, 5H), 6.29 - 6.39 (m, 1H), 5.71 (d, *J* = 6.60 Hz, 1H), 4.96 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.5, 179.0, 178.4, 141.1, 140.1, 135.5, 131.8, 131.1, 130.8, 130.6, 127.7, 127.3, 127.2, 126.9, 126.6, 125.8, 125.6, 124.3, 120.8, 113.1, 112.9, 112.3, 110.1, 107.6, 68.9, 66.6, 65.1, 60.1, 55.6; m/z (ESI): 582 $[M+H]^+$; HRMS calcd for $C_{31}H_{22}O_3N_3BrF$: 582.08231, found: 582.08426.

Compound **4r:-**



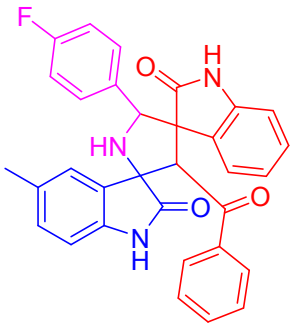
White solid; Mp 189-190 ^{o}C IR: ν_{max} 3358, 2895, 1718, 1677, 1614, 1508, 1473, 1386, 1340, 1299, 1219, 1187, 1159, 1128, 1080, 1019, 995, 967, 835, 813, 751, 684, 595, 530, 491, 452 cm^{-1}; ^{1}H NMR (300 MHz $CDCl_3$+DMSO-d_6,): δ 10.17 (s, 1H), 9.68 (s, 1H), 7.93 (d, *J* = 1.13 Hz, 1H), 7.71 - 7.79 (m, 1H), 7.49 - 7.59 (m, 2H), 7.17 - 7.33 (m, 3H), 6.96 - 7.17 (m, 4H), 6.79 - 6.96 (m, 4H), 6.71 - 6.79 (m, 1H), 6.28 - 6.39 (m, 1H), 5.77 (d, *J* = 6.79 Hz, 1H), 5.00 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.5, 178.6, 178.3, 141.6, 140.1, 136.6, 135.5, 131.8, 131.0, 127.6, 127.2, 127.1, 126.8, 126.5, 125.7, 124.2, 120.7, 113.1, 112.8, 110.6, 107.5, 82.2, 68.8, 66.3, 65.0, 60.0; m/z (ESI): 630 $[M+H]^+$; HRMS calcd for $C_{31}H_{22}O_3N_3IF$: 630.0742, found: 630.07121.

Compound 4s:-



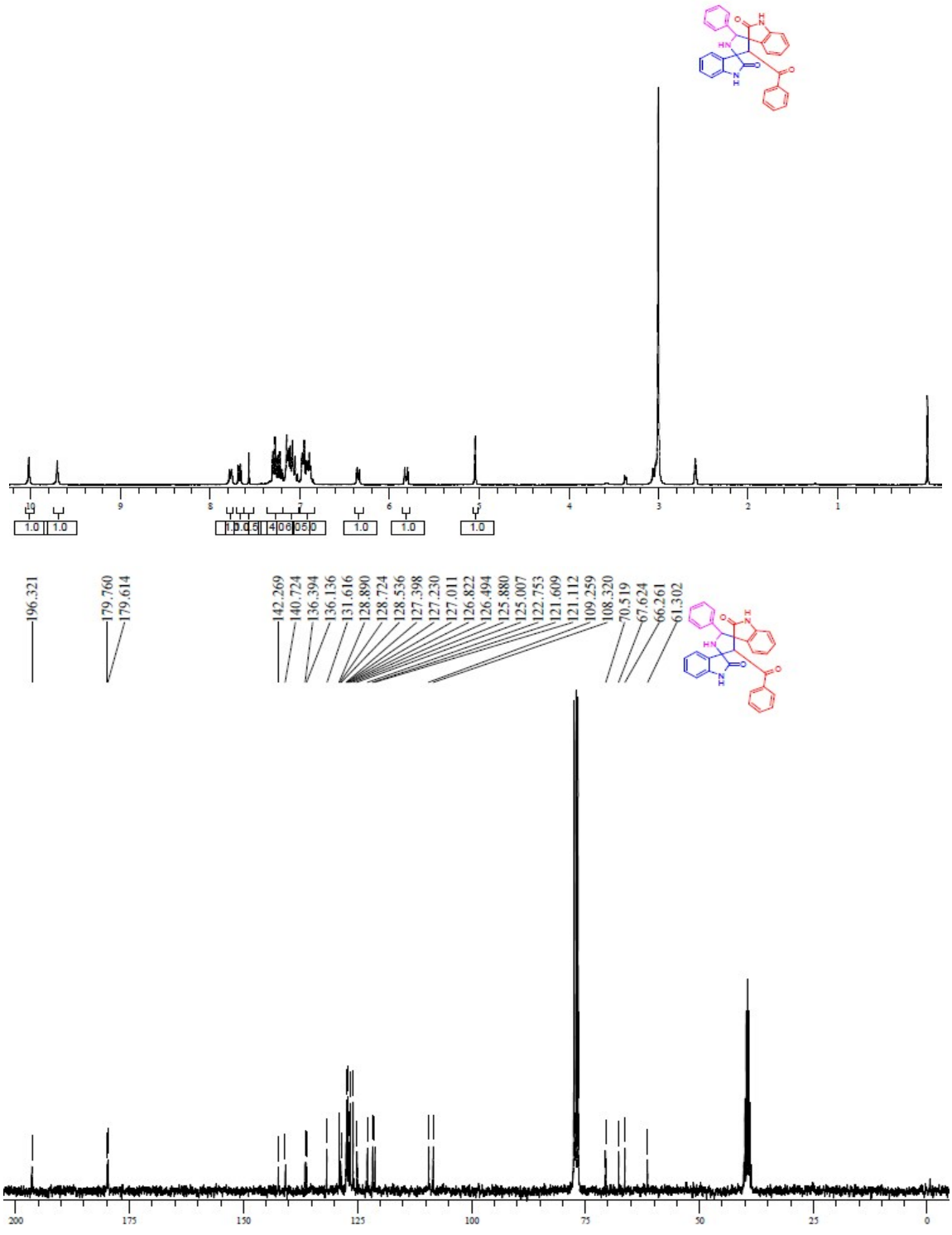
White solid; Mp 236-238 ^{o}C; IR: ν_{max} 3297, 3176, 3052, 1721, 1709, 1683, 1603, 1489, 1471, 1443, 1386, 1359, 1307, 1265, 1239, 1212, 1162, 1107, 1068, 1027, 992, 934, 905, 845, 807, 748, 680, 662, 613, 584, 546, 499, 453 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.1 (s, 1H), 9.87 (s, 1H), 7.77 - 7.81 (m, 1 H), 7.74 - 7.77 (d, *J* = 1.32 Hz, 1H), 7.20 - 7.32 (m, 4H), 7.05 - 7.14 (m, 2H), 6.96 - 7.04 (m, 2H), 6.73 - 6.94 (m, 6H), 6.29 - 6.37 (m, 1H), 5.75 (d, *J* = 7.36 Hz, 1H), 4.97 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.6, 179.3, 178.7, 154.1, 140.2, 135.8, 135.1, 131.8, 131.1, 129.5, 127.9, 127.3, 127.2, 126.9, 126.7, 125.9, 124.5, 120.9, 113.2, 113.0, 109.6, 109.0, 107.7, 69.2, 67.2, 65.2, 60.4, 54.6; m/z (ESI): 534 $[M+H]^+$; HRMS calcd for $C_{32}H_{25}O_4N_3F$: 534.18236, found: 534.18342.

Compound **4t:-**

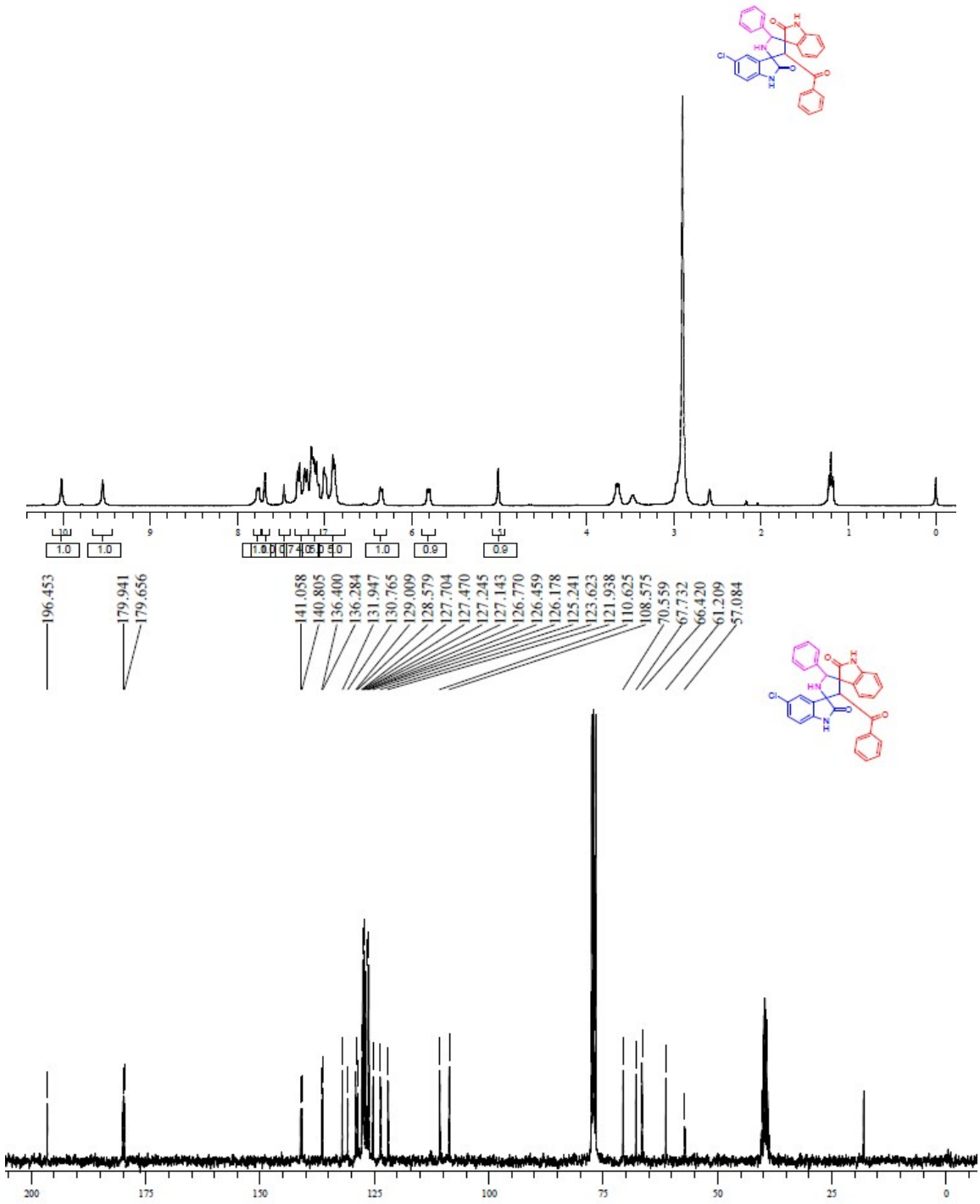


White solid; Mp 242-243 ^{o}C; IR: ν_{max} 3382, 3325, 3214, 2893, 1713, 1678, 1620, 1502, 1387, 1342, 1300, 1222, 1195, 1160, 1114, 1022, 832, 757, 686, 598, 563 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 9.79 (s, 1H), 9.64 (s, 1H), 7.73 - 7.84 (m, 1H), 7.43 - 7.58 (m, 2H), 7.17 - 7.35 (m, 3H), 6.95 - 7.15 (m, 5H), 6.76 - 6.95 (m, 5H), 6.29 - 6.41 (m, 1H), 5.80 (d, J = 7.93 Hz, 1H), 5.03 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 195.6, 179.3, 178.8, 140.2, 139.3, 135.8, 131.8, 131.0, 129.7, 128.5, 128.3, 127.9, 127.2, 127.1, 126.9, 126.6, 125.9, 124.4, 123.0, 120.9, 113.2, 112.9, 108.3, 107.7, 69.1, 66.9, 65.2, 60.5, 19.8; m/z (ESI): 518 $[M+H]^+$; HRMS calcd for $C_{32}H_{25}O_3N_3F$: 518.18745, found: 518.18833.

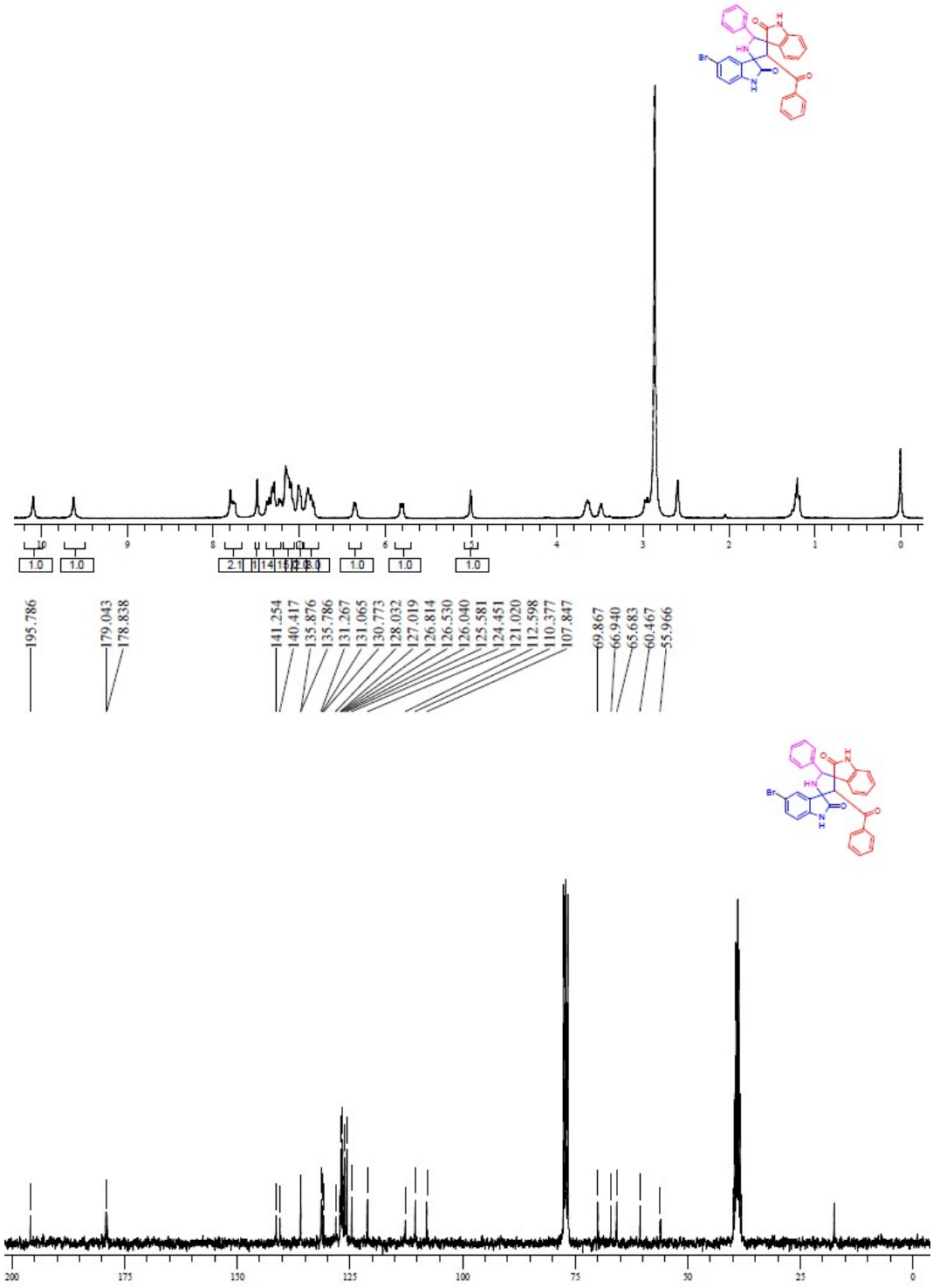
^{1}H and ^{13}C NMR Spectra of compound 4a



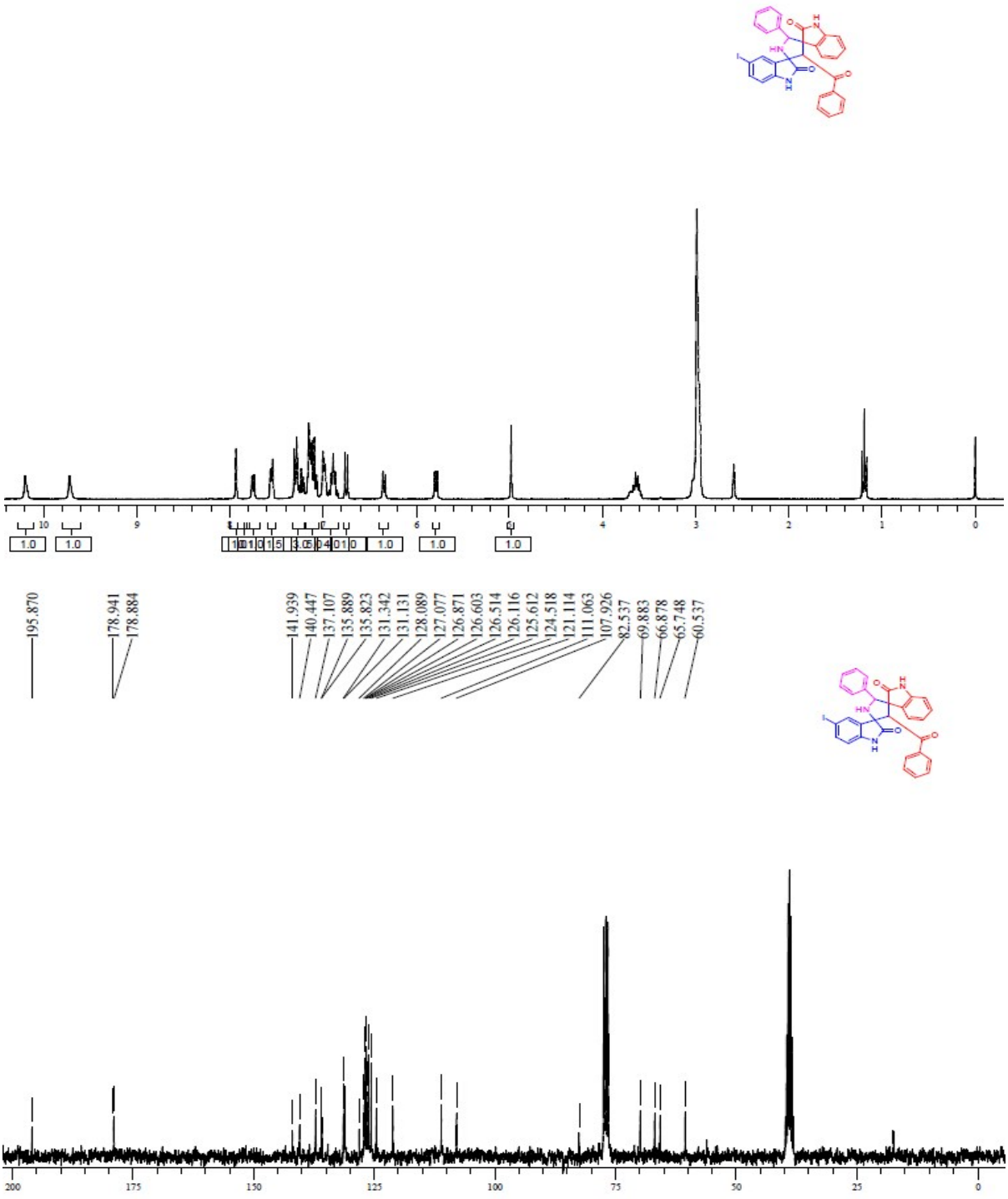
^{1}H and ^{13}C NMR Spectra of compound 4b



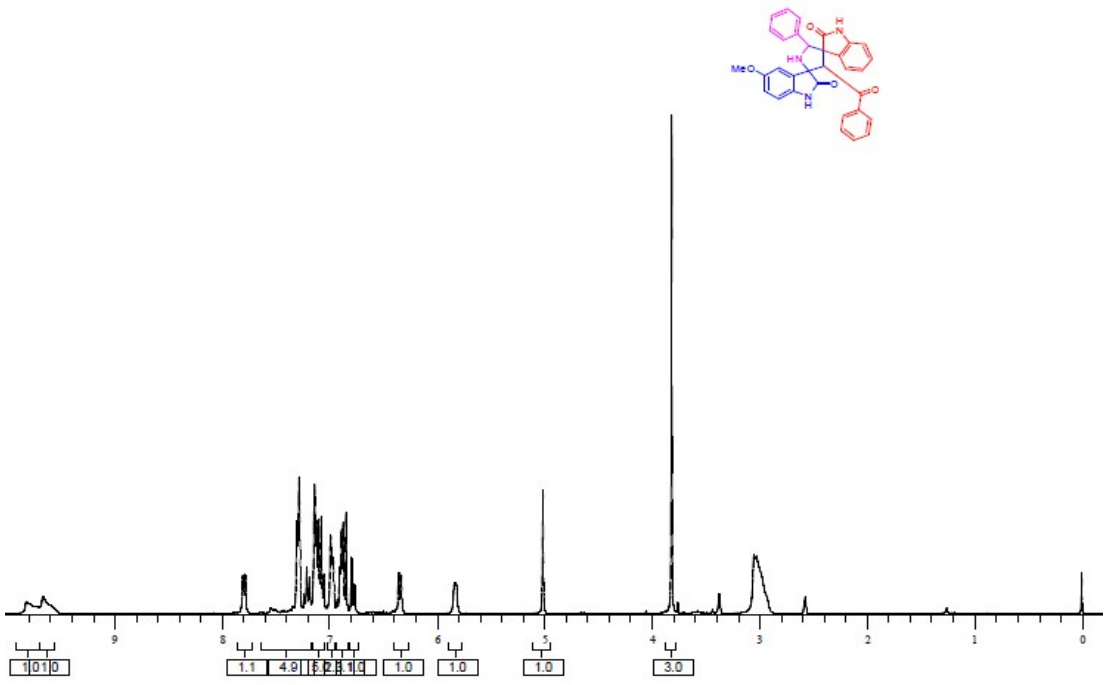
^{1}H and ^{13}C NMR Spectra of compound 4c

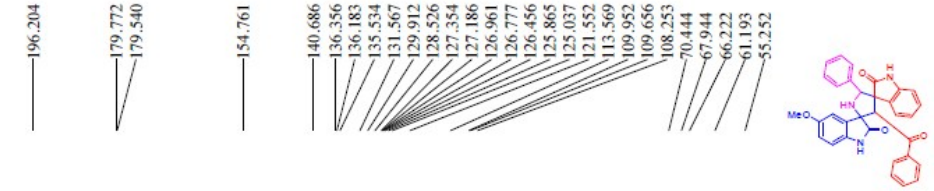


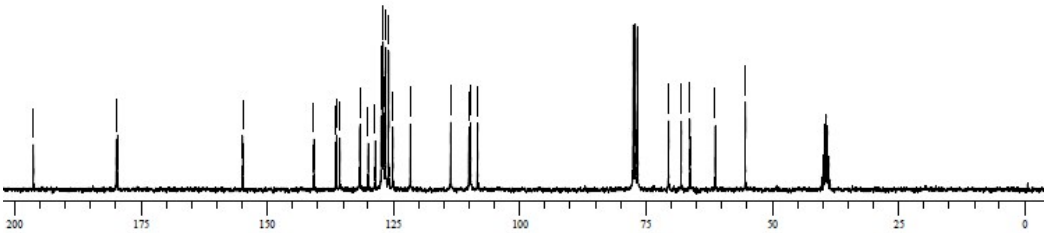
^{1}H and ^{13}C NMR Spectra of compound 4d



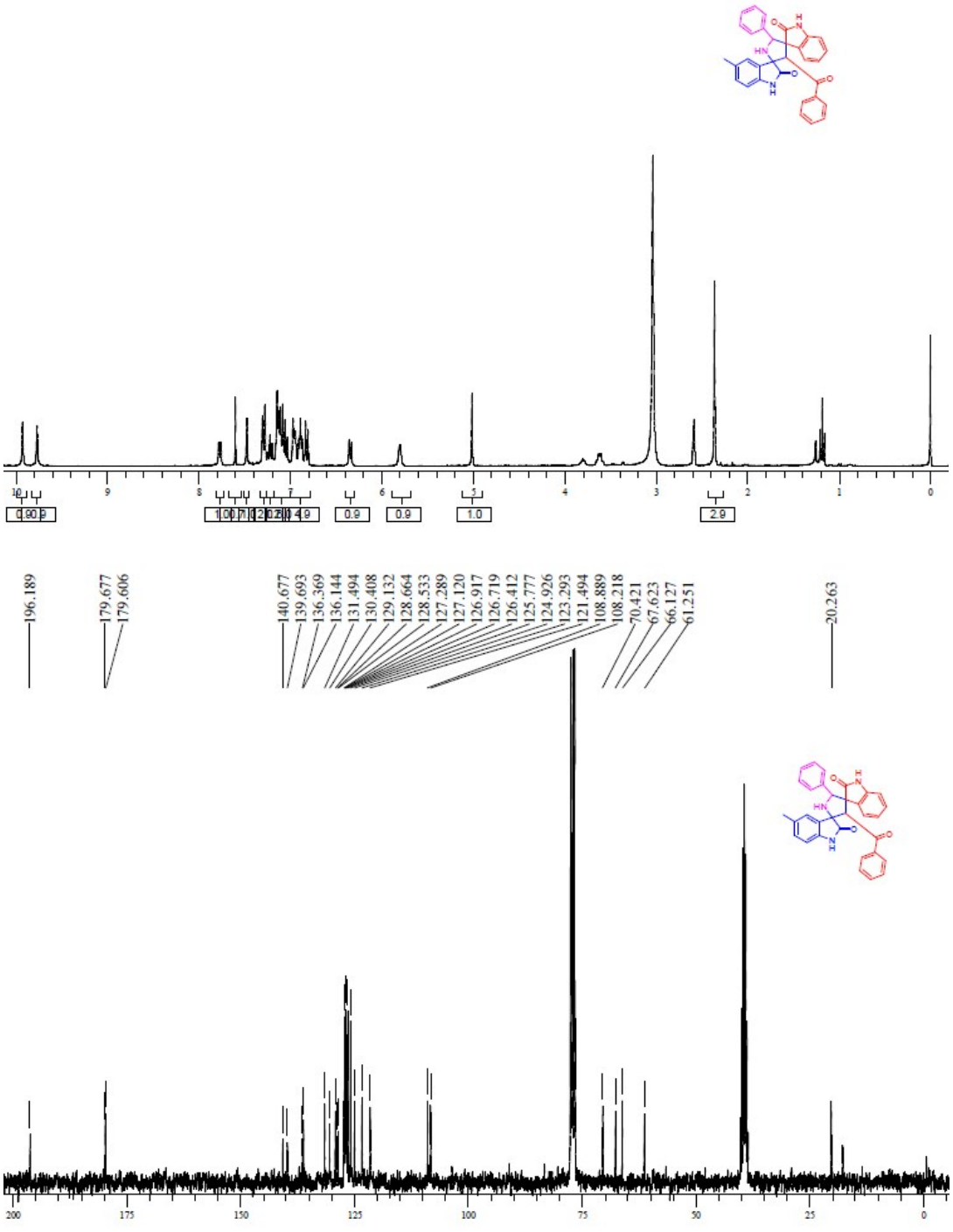
^{1}H and ^{13}C NMR Spectra of compound 4e



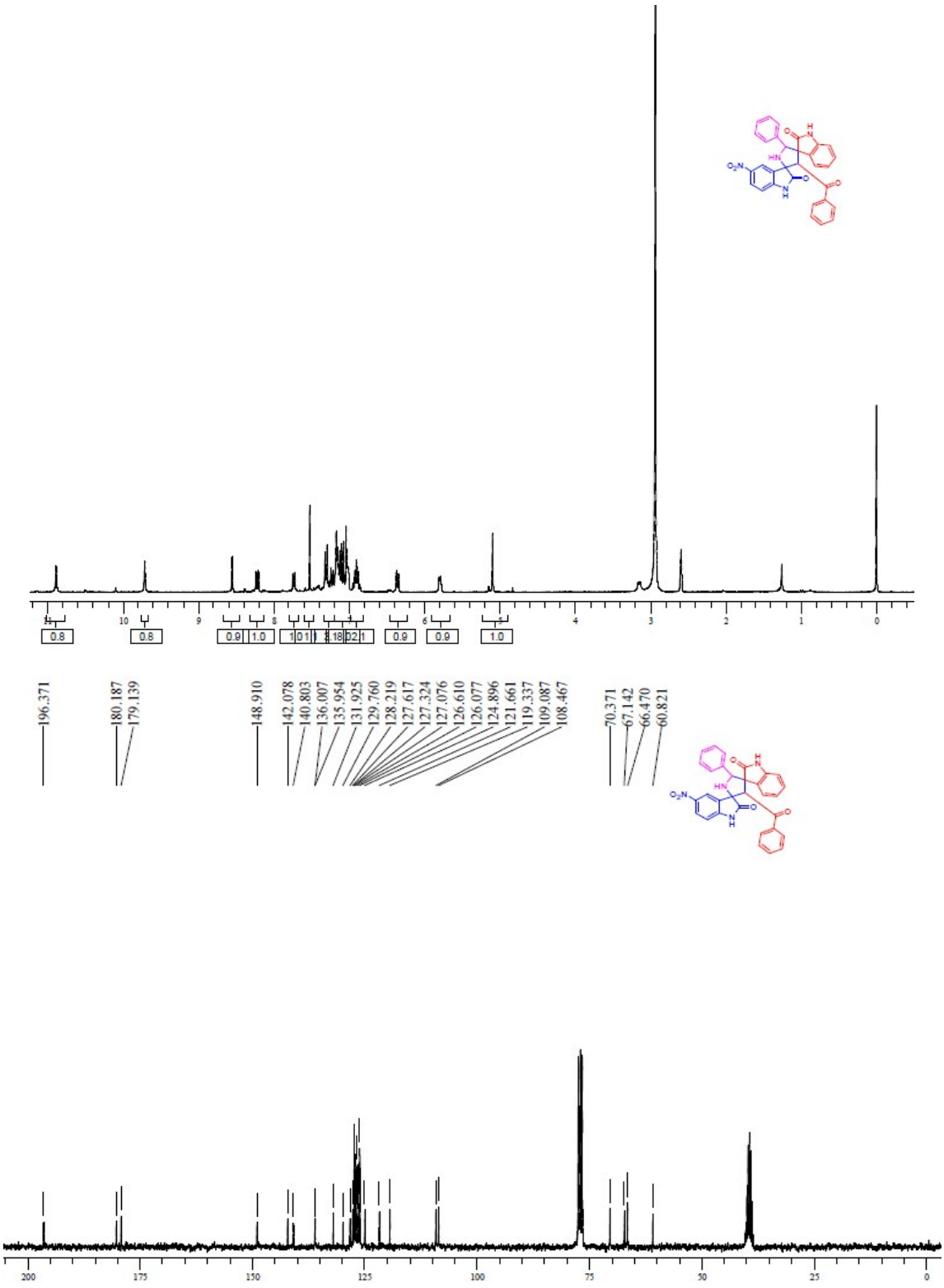




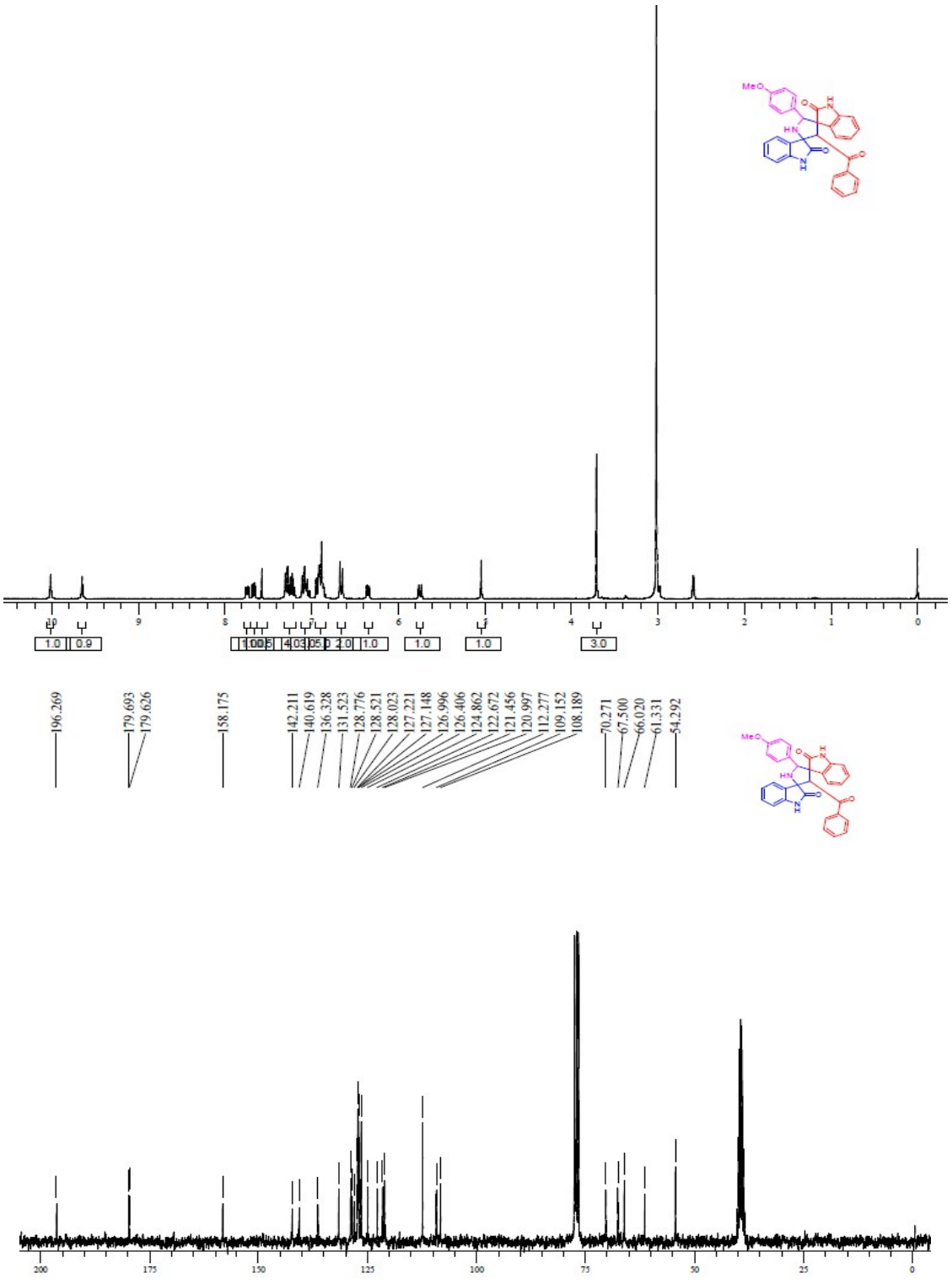
^{1}H and ^{13}C NMR Spectra of compound 4f



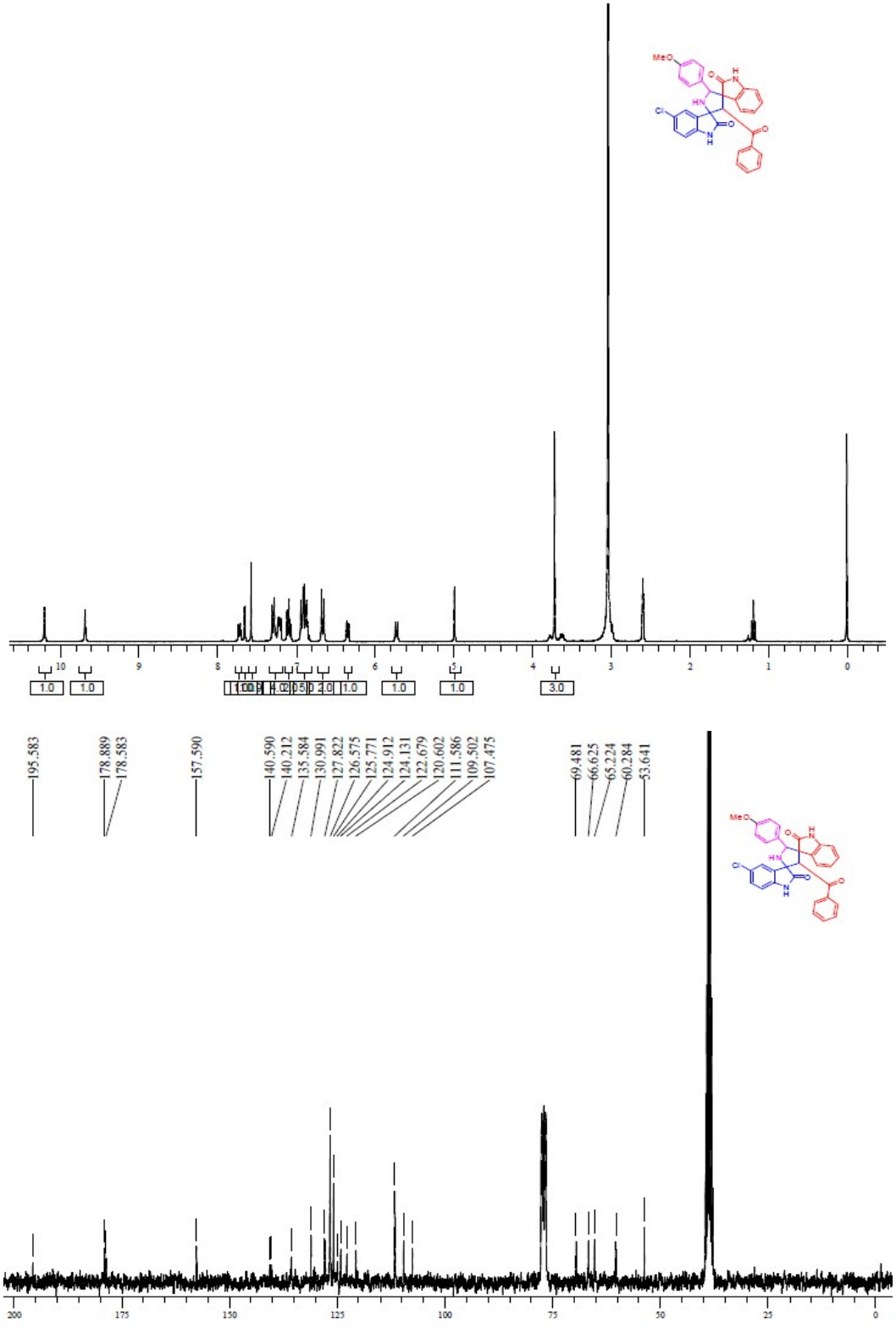
^{1}H and ^{13}C NMR Spectra of compound 4g



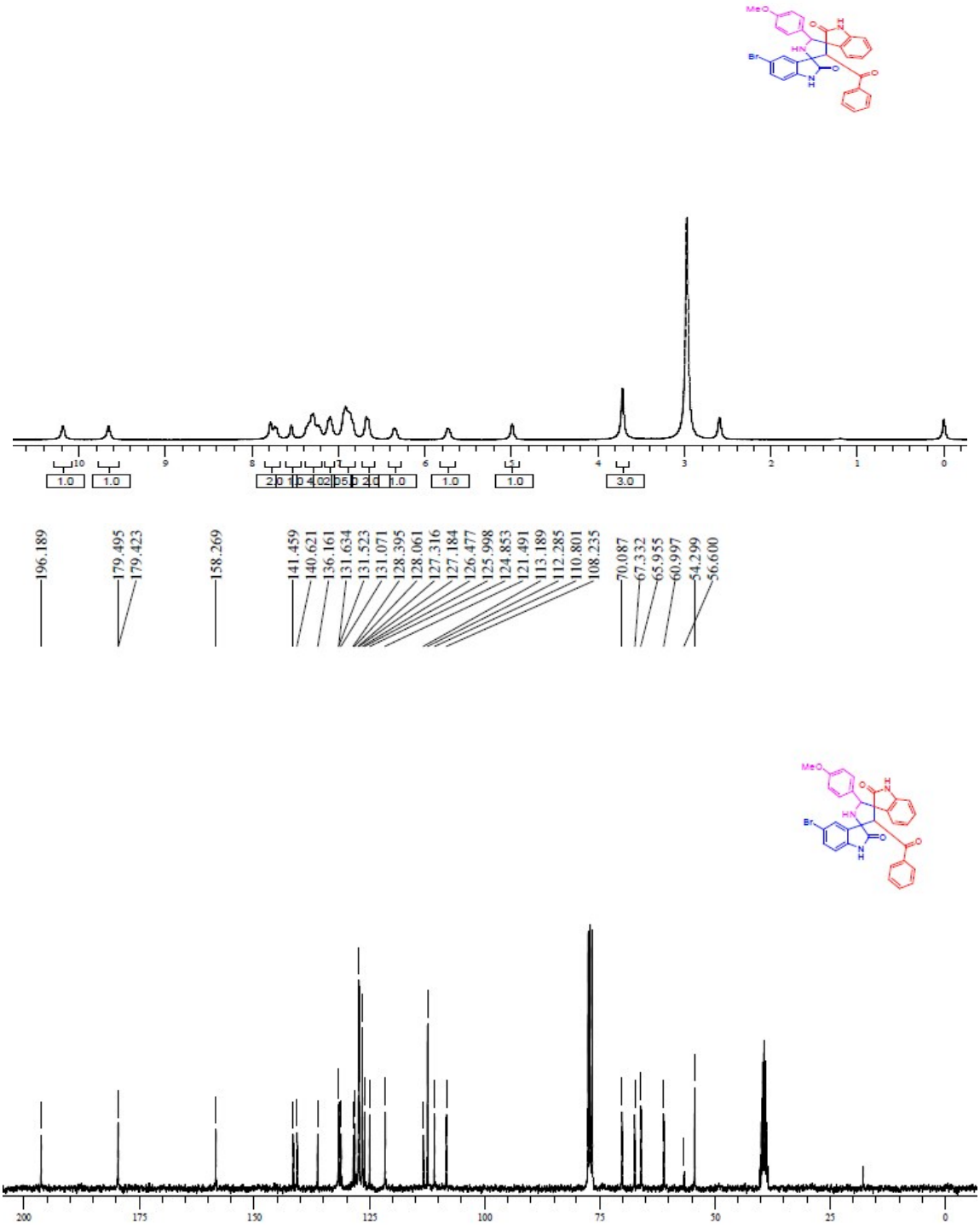
^{1}H and ^{13}C NMR Spectra of compound 4h



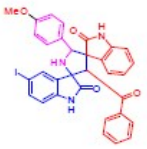
^{1}H and ^{13}C NMR S^{1}pectra of compound 4i

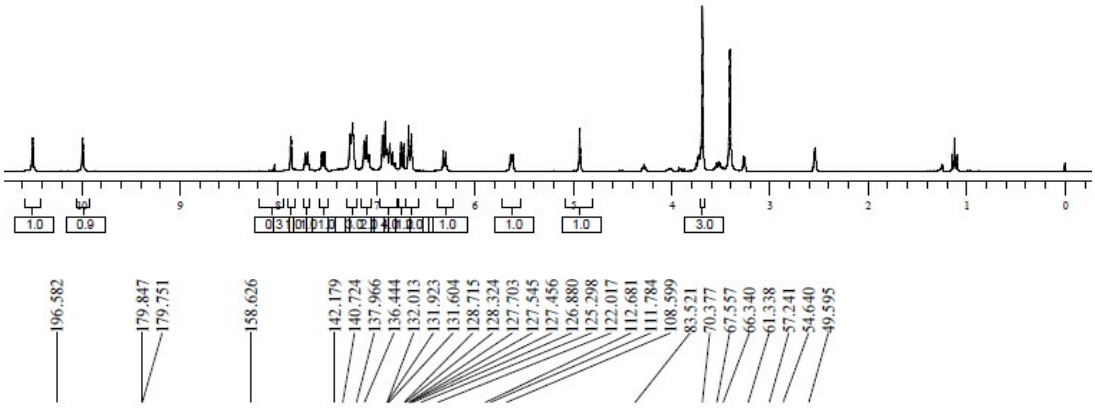


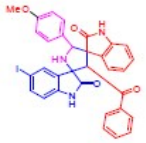
^{1}H and ^{13}C NMR S^{1}pectra of compound 4j

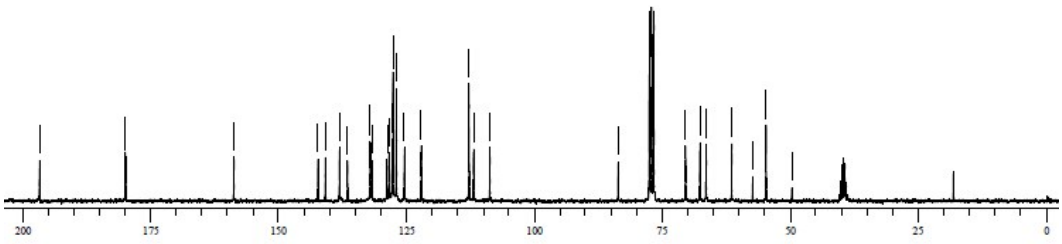


^{1}H and ^{13}C NMR Spectra of compound 4k

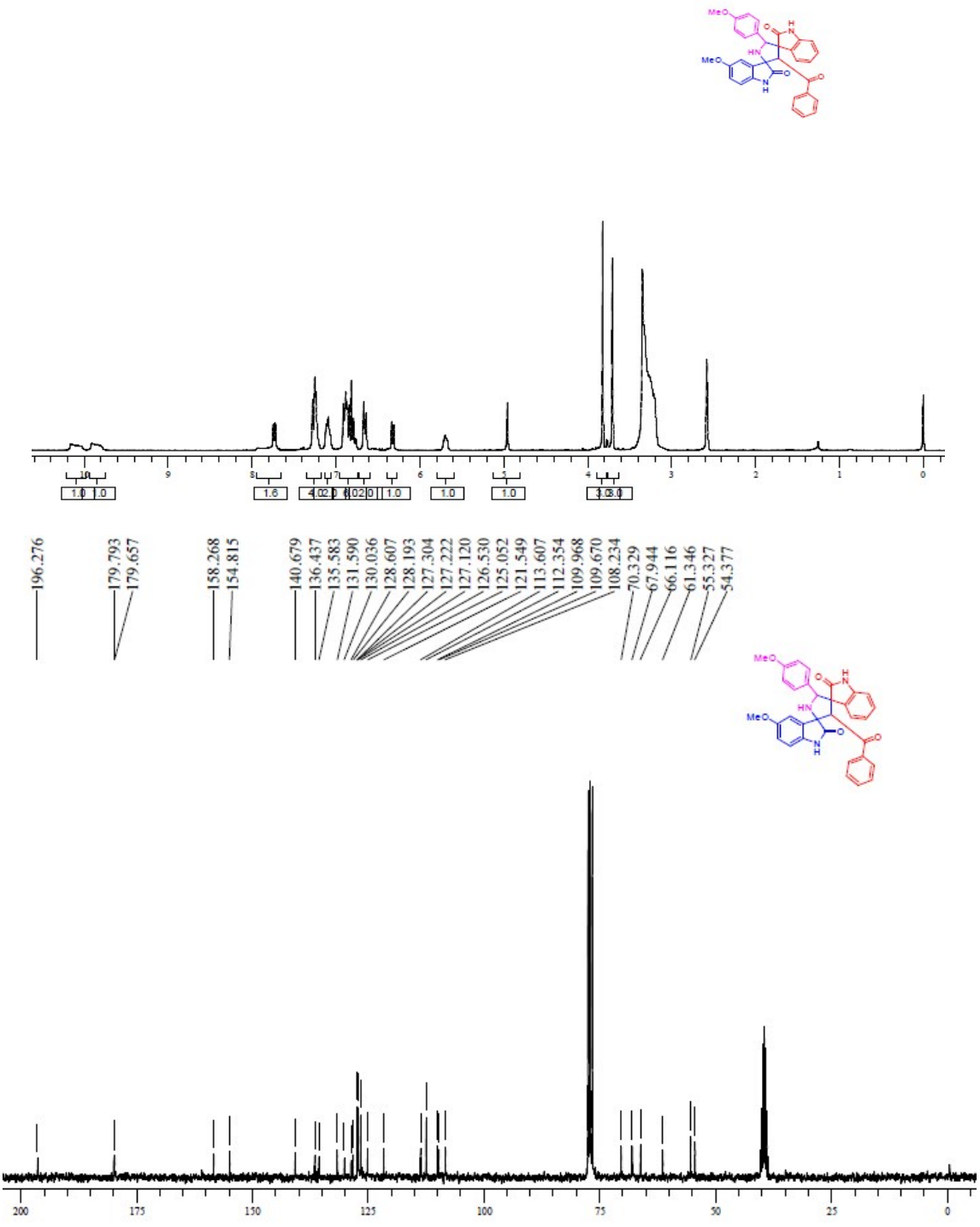




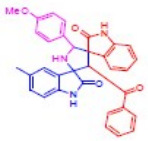


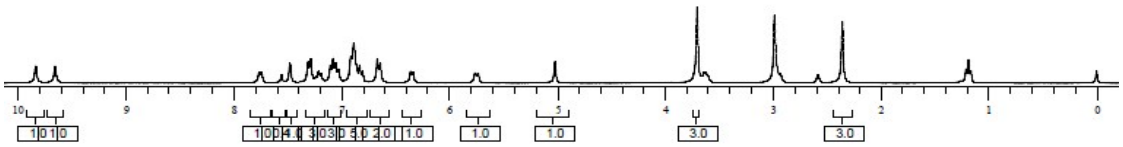


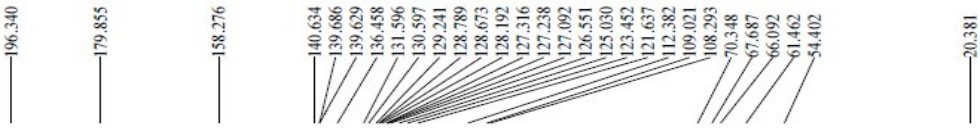
^{1}H and ^{13}C NMR Spectra of compound 4l

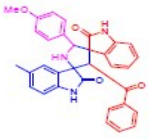


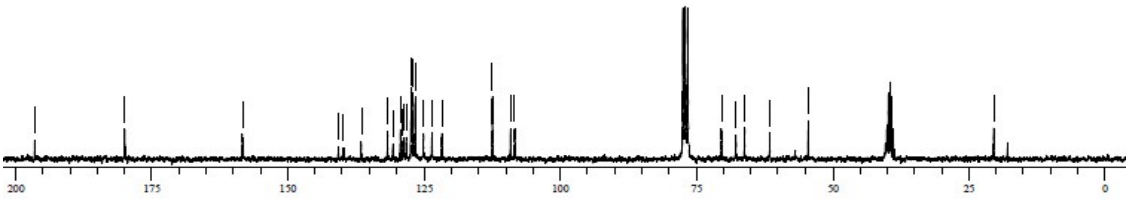
^{1}H and ^{13}C NMR Spectra of compound 4m



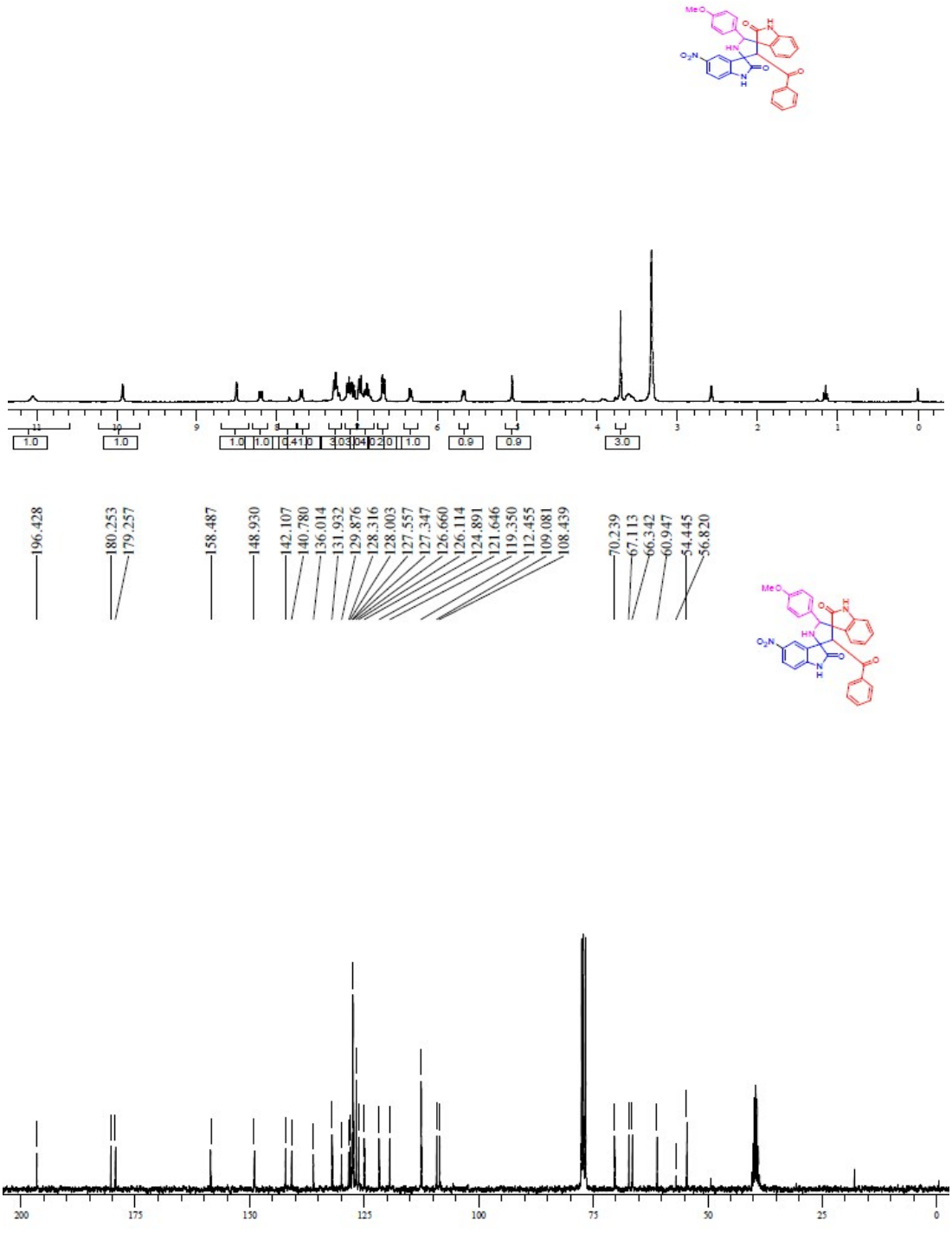




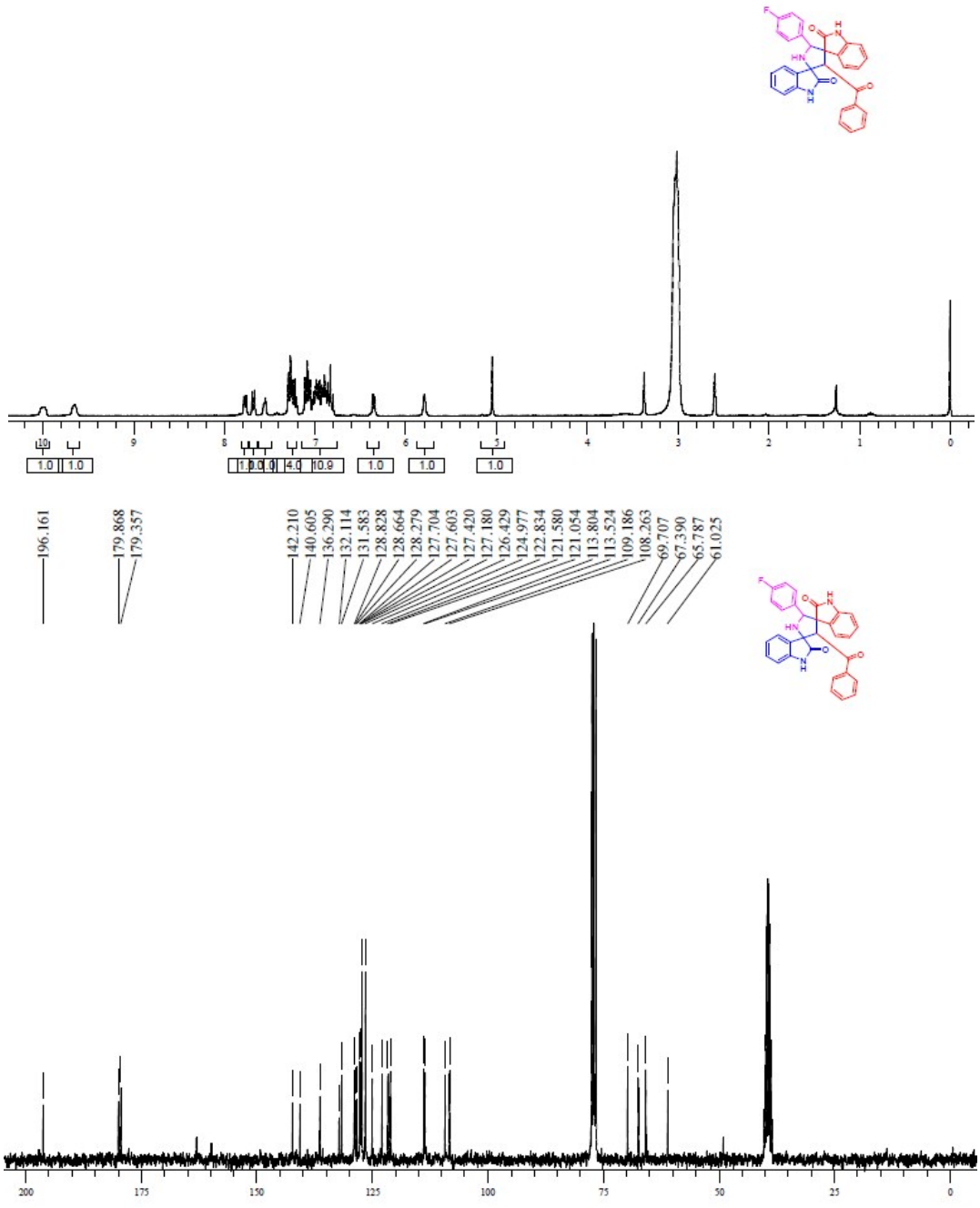




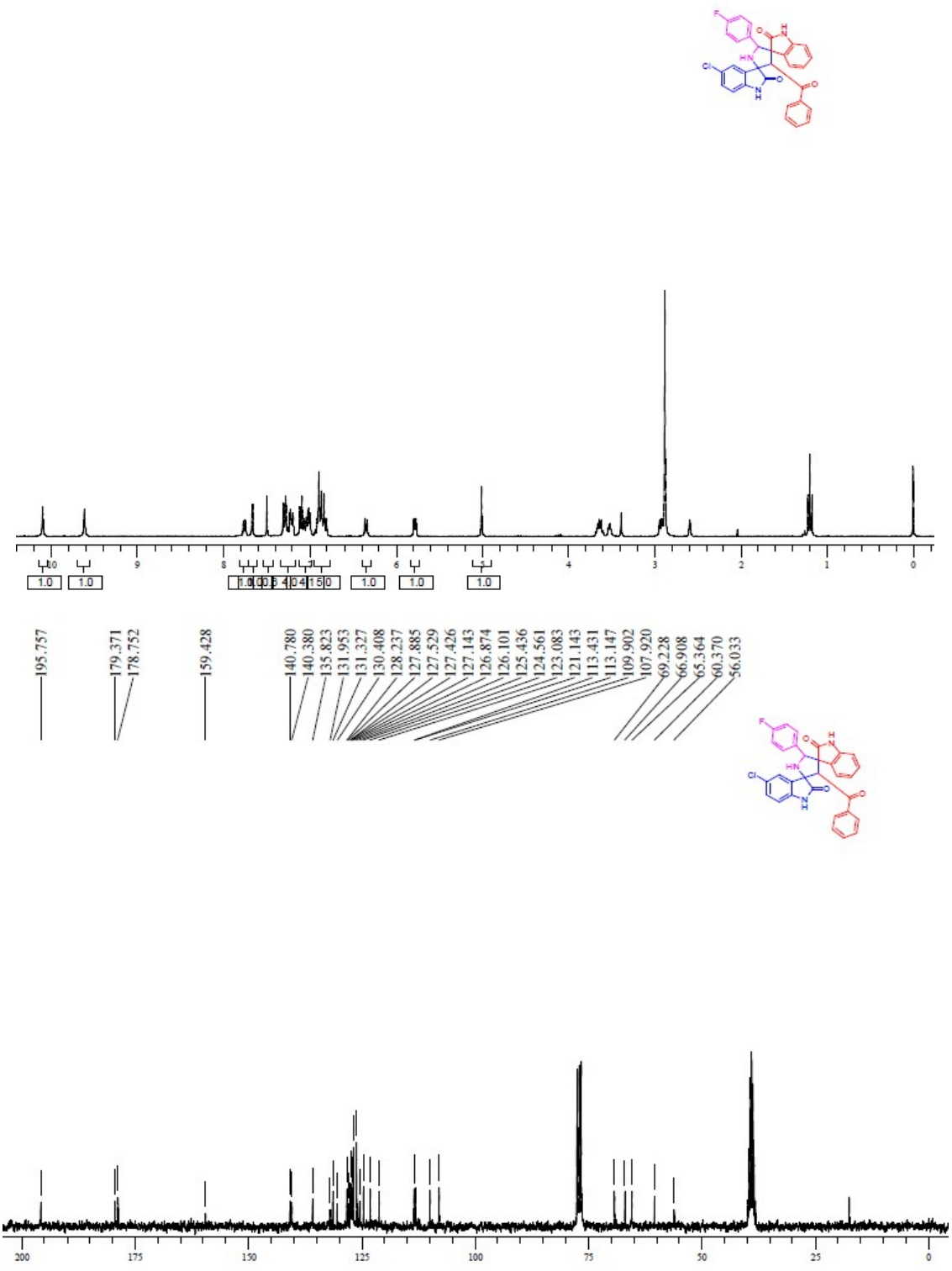
^{1}H and ^{13}C NMR Spectra of compound 4n



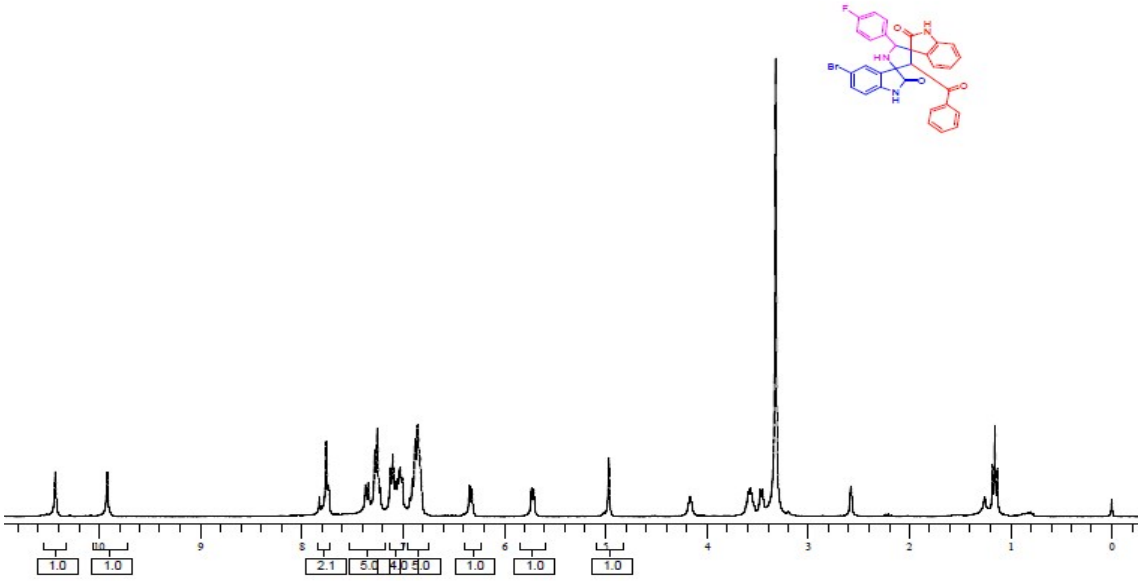
^{1}H and ^{13}C NMR Spectra of compound 4o

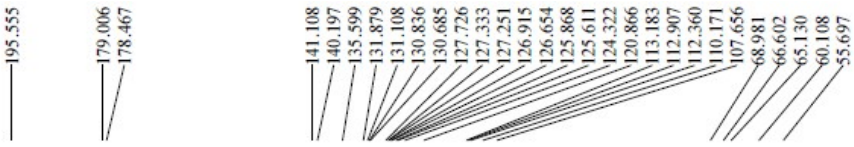


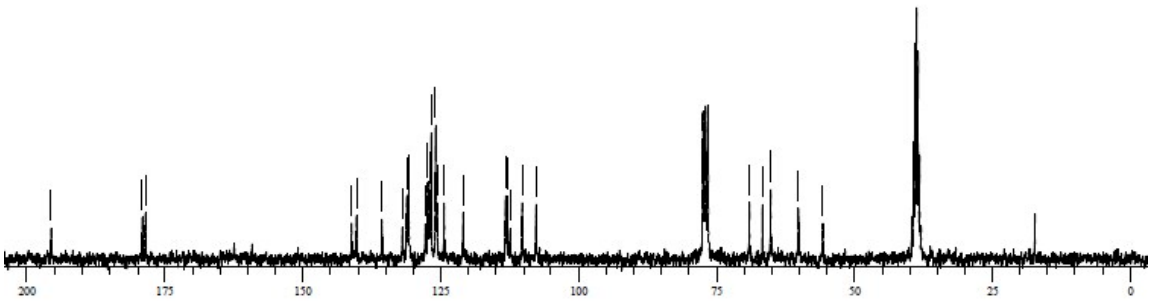
^{1}H and ^{13}C NMR Spectra of compound 4p



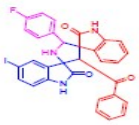
^{1}H and ^{13}C NMR Spectra of compound 4q

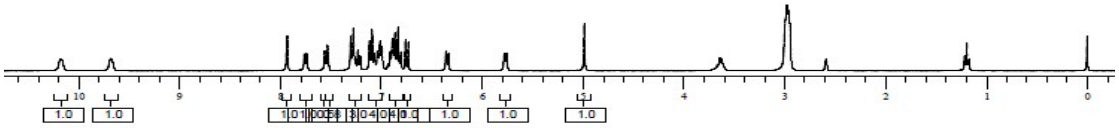


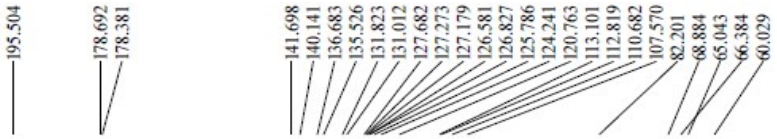


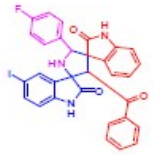


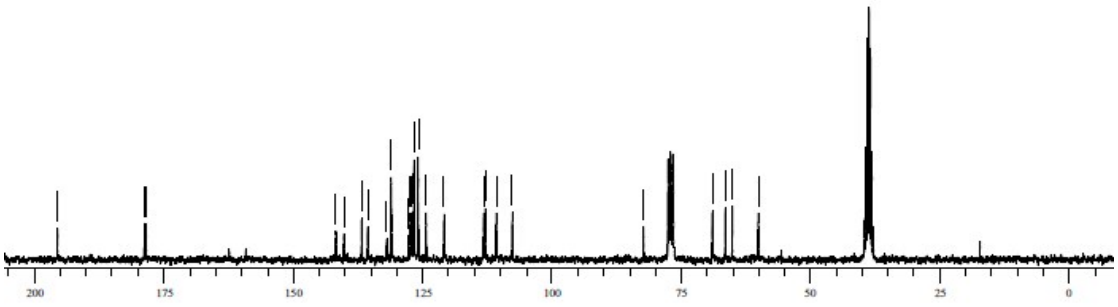
^{1}H and ^{13}C NMR Spectra of compound 4r



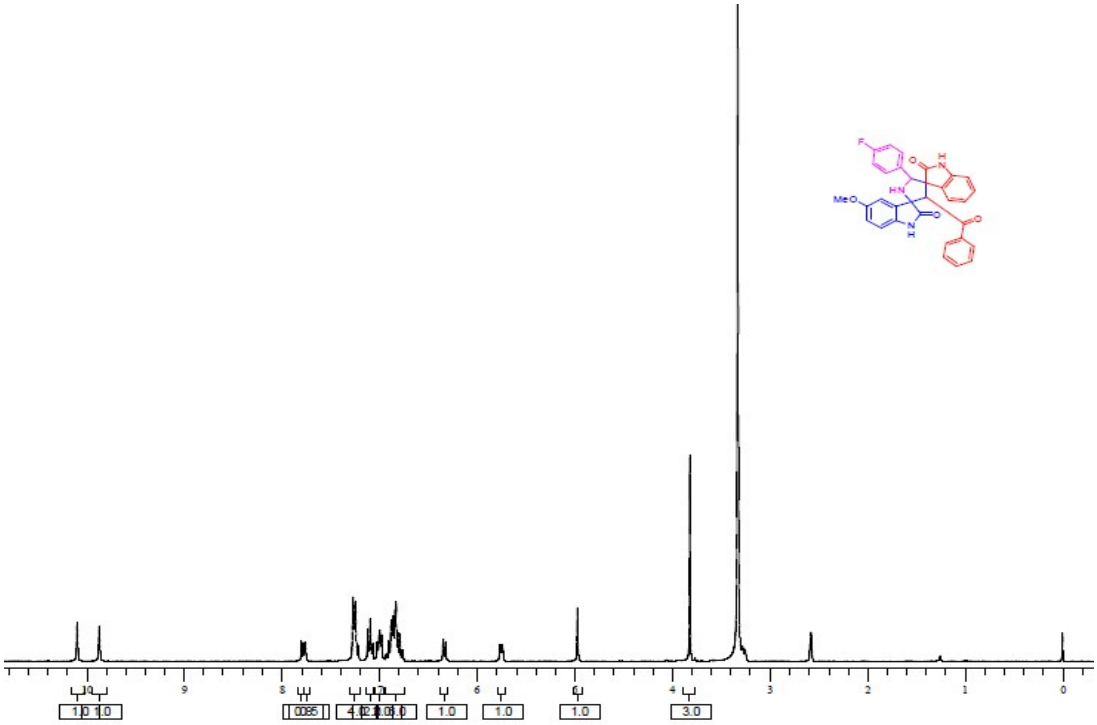


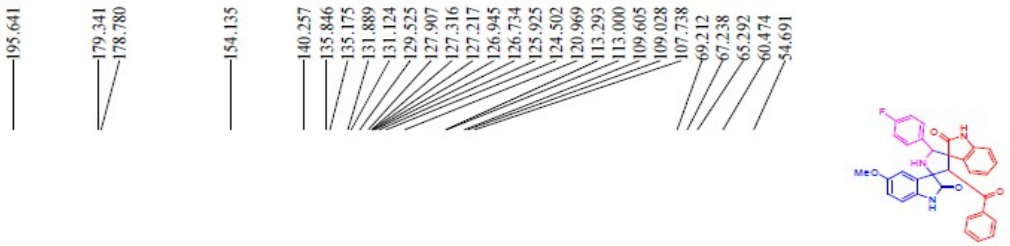


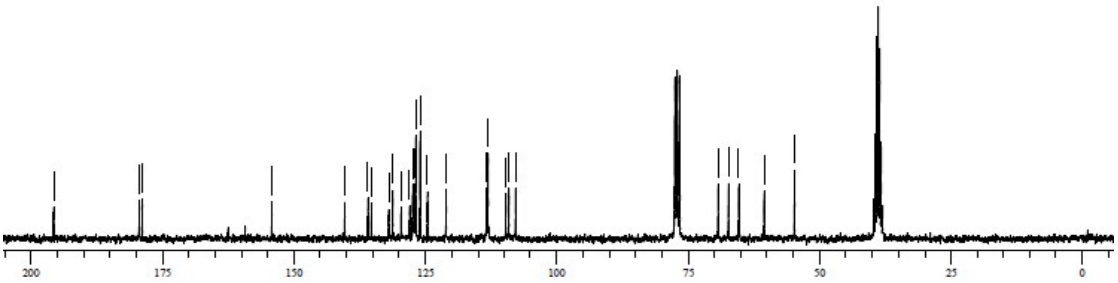




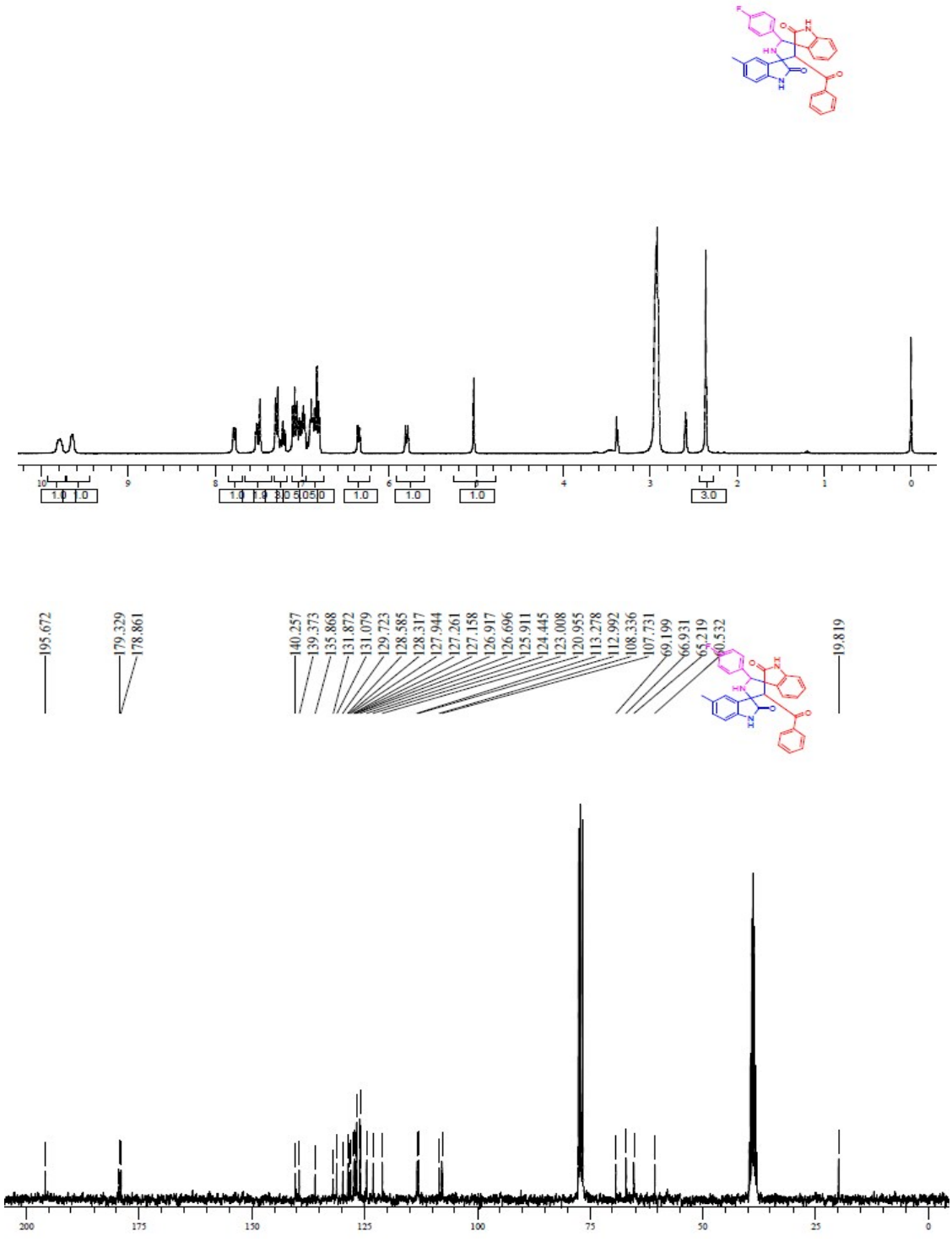
^{1}H and ^{13}C NMR Spectra of compound 4s







^{1}H and ^{13}C NMR Spectra of compound 4t



Crystal data and tables for 4s.

Table 1. Crystal data and structure refinement for **4s**

Identification code	4s	
Empirical formula	$C_{32}H_{24}F\ N_3O_4$	
Formula weight	533.54	
Temperature	294(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 10.7757(13) Å	α= 84.249(2)°.
	b = 11.2641(13) Å	β= 66.118(2)°.
	c = 12.0018(14) Å	γ = 82.085(2)°.
Volume	1317.8(3) $Å^3$	
Z	2	
Density (calculated)	1.345 Mg/m^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	556	
Crystal size	0.180 x 0.160 x 0.070 mm^3	
θ range for data collection	1.827 to 28.135°.	
Index ranges	-14<=h<=14, -14<=k<=14, -15<=l<=15	
Reflections collected	15464	
Independent reflections	6152 [R(int) = 0.0188]	
Completeness to θ = 25.242°	99.7 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6152 / 0 / 374	
Goodness-of-fit on F^2	1.043	
Final R indices [I>2σ(I)]	R1 = 0.0437, wR2 = 0.1187	
R indices (all data)	R1 = 0.0506, wR2 = 0.1251	
Largest diff. peak and hole	0.262 and -0.208 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **4s**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	7282(1)	1907(1)	-289(1)	35(1)
C(2)	8342(1)	932(1)	-69(1)	40(1)
C(3)	9313(1)	1598(1)	-2055(1)	38(1)
C(4)	10229(1)	1754(1)	-3239(1)	45(1)
C(5)	9839(2)	2581(1)	-4007(1)	49(1)
C(6)	8559(2)	3225(1)	-3585(1)	47(1)
C(7)	7633(1)	3061(1)	-2379(1)	43(1)
C(8)	8025(1)	2244(1)	-1624(1)	36(1)
C(9)	5292(1)	1435(1)	1371(1)	38(1)
C(10)	5612(1)	2645(1)	1708(1)	36(1)
C(11)	6861(1)	2988(1)	534(1)	34(1)
C(12)	8013(1)	3402(1)	776(1)	40(1)
C(13)	7861(1)	4638(1)	1181(1)	44(1)
C(14)	6804(2)	5502(1)	1197(1)	52(1)
C(15)	6756(2)	6647(2)	1553(2)	65(1)
C(16)	7770(2)	6930(2)	1873(2)	74(1)
C(17)	8825(2)	6076(2)	1855(2)	70(1)
C(18)	8877(2)	4937(2)	1515(1)	56(1)
C(19)	6643(1)	1808(2)	3318(1)	56(1)
C(20)	4416(1)	3648(1)	1933(1)	40(1)
C(21)	4701(2)	3273(2)	3727(1)	53(1)
C(22)	4549(2)	3343(2)	4915(2)	82(1)
C(23)	5471(2)	2630(2)	5293(2)	92(1)
C(24)	6493(2)	1877(2)	4517(2)	78(1)
C(25)	5741(1)	2524(1)	2922(1)	42(1)
C(26)	3798(1)	1260(1)	1863(1)	40(1)
C(27)	2973(1)	1735(1)	1256(1)	50(1)
C(28)	1584(1)	1630(1)	1765(2)	55(1)
C(29)	1053(1)	1046(1)	2878(2)	52(1)
C(30)	1824(2)	542(2)	3498(2)	58(1)

C(31)	3213(1)	651(1)	2978(1)	51(1)
C(33)	8846(2)	4111(2)	-5563(2)	83(1)
F(1)	-317(1)	963(1)	3393(1)	76(1)
N(1)	9458(1)	819(1)	-1119(1)	42(1)
N(2)	3910(1)	3898(1)	3133(1)	55(1)
N(3)	5951(1)	1474(1)	34(1)	39(1)
O(1)	8157(1)	316(1)	872(1)	52(1)
O(2)	9041(1)	2732(1)	631(1)	59(1)
O(3)	4016(1)	4147(1)	1182(1)	49(1)
O(4)	8112(1)	4077(1)	-4282(1)	68(1)

Table 3. Bond lengths [Å] and angles [°] for **4s**.

C(1)-N(3)	1.4664(15)
C(1)-C(8)	1.5079(16)
C(1)-C(11)	1.5458(16)
C(1)-C(2)	1.5570(16)
C(2)-O(1)	1.2226(15)
C(2)-N(1)	1.3472(16)
C(3)-C(4)	1.3736(17)
C(3)-C(8)	1.3926(16)
C(3)-N(1)	1.4004(16)
C(4)-C(5)	1.3881(19)
C(4)-H(4)	0.9300
C(5)-C(6)	1.385(2)
C(5)-H(5)	0.9300
C(6)-O(4)	1.3750(16)
C(6)-C(7)	1.3976(18)
C(7)-C(8)	1.3722(17)
C(7)-H(7)	0.9300
C(9)-N(3)	1.4667(16)
C(9)-C(26)	1.5079(16)
C(9)-C(10)	1.5790(17)
C(9)-H(9)	0.9800
C(10)-C(25)	1.5096(16)
C(10)-C(20)	1.5451(16)
C(10)-C(11)	1.5631(16)
C(11)-C(12)	1.5231(16)
C(11)-H(11)	0.9800
C(12)-O(2)	1.2112(16)
C(12)-C(13)	1.4867(19)
C(13)-C(14)	1.388(2)
C(13)-C(18)	1.399(2)
C(14)-C(15)	1.387(2)
C(14)-H(14)	0.9300
C(15)-C(16)	1.379(3)

C(15)-H(15)	0.9300
C(16)-C(17)	1.380(3)
C(16)-H(16)	0.9300
C(17)-C(18)	1.372(2)
C(17)-H(17)	0.9300
C(18)-H(18)	0.9300
C(19)-C(25)	1.3797(18)
C(19)-C(24)	1.390(2)
C(19)-H(19)	0.9300
C(20)-O(3)	1.2093(15)
C(20)-N(2)	1.3611(17)
C(21)-C(22)	1.377(2)
C(21)-C(25)	1.3882(19)
C(21)-N(2)	1.3998(18)
C(22)-C(23)	1.381(3)
C(22)-H(22)	0.9300
C(23)-C(24)	1.368(3)
C(23)-H(23)	0.9300
C(24)-H(24)	0.9300
C(26)-C(31)	1.3818(18)
C(26)-C(27)	1.3869(18)
C(27)-C(28)	1.3863(19)
C(27)-H(27)	0.9300
C(28)-C(29)	1.361(2)
C(28)-H(28)	0.9300
C(29)-C(30)	1.361(2)
C(29)-F(1)	1.3626(15)
C(30)-C(31)	1.387(2)
C(30)-H(30)	0.9300
C(31)-H(31)	0.9300
C(33)-O(4)	1.4147(19)
C(33)-H(33A)	0.9600
C(33)-H(33B)	0.9600
C(33)-H(33C)	0.9600
N(1)-H(1N)	0.879(17)

N(2)-H(2N)	0.88(2)
N(3)-H(3N)	0.923(18)

N(3)-C(1)-C(8)	114.99(10)
N(3)-C(1)-C(11)	100.57(9)
C(8)-C(1)-C(11)	113.19(9)
N(3)-C(1)-C(2)	112.91(10)
C(8)-C(1)-C(2)	101.19(9)
C(11)-C(1)-C(2)	114.64(9)
O(1)-C(2)-N(1)	125.77(11)
O(1)-C(2)-C(1)	125.77(11)
N(1)-C(2)-C(1)	108.29(10)
C(4)-C(3)-C(8)	121.55(12)
C(4)-C(3)-N(1)	128.89(11)
C(8)-C(3)-N(1)	109.56(10)
C(3)-C(4)-C(5)	118.20(12)
C(3)-C(4)-H(4)	120.9
C(5)-C(4)-H(4)	120.9
C(6)-C(5)-C(4)	120.56(12)
C(6)-C(5)-H(5)	119.7
C(4)-C(5)-H(5)	119.7
O(4)-C(6)-C(5)	123.91(12)
O(4)-C(6)-C(7)	115.17(12)
C(5)-C(6)-C(7)	120.90(12)
C(8)-C(7)-C(6)	118.25(12)
C(8)-C(7)-H(7)	120.9
C(6)-C(7)-H(7)	120.9
C(7)-C(8)-C(3)	120.54(11)
C(7)-C(8)-C(1)	130.35(10)
C(3)-C(8)-C(1)	109.07(10)
N(3)-C(9)-C(26)	113.42(10)
N(3)-C(9)-C(10)	103.32(9)
C(26)-C(9)-C(10)	114.96(10)
N(3)-C(9)-H(9)	108.3
C(26)-C(9)-H(9)	108.3

C(10)-C(9)-H(9)	108.3
C(25)-C(10)-C(20)	101.79(10)
C(25)-C(10)-C(11)	119.05(10)
C(20)-C(10)-C(11)	109.47(9)
C(25)-C(10)-C(9)	111.93(10)
C(20)-C(10)-C(9)	112.28(9)
C(11)-C(10)-C(9)	102.61(9)
C(12)-C(11)-C(1)	114.96(9)
C(12)-C(11)-C(10)	114.56(9)
C(1)-C(11)-C(10)	106.03(9)
C(12)-C(11)-H(11)	106.9
C(1)-C(11)-H(11)	106.9
C(10)-C(11)-H(11)	106.9
O(2)-C(12)-C(13)	120.68(12)
O(2)-C(12)-C(11)	120.22(12)
C(13)-C(12)-C(11)	119.11(11)
C(14)-C(13)-C(18)	119.41(14)
C(14)-C(13)-C(12)	123.41(12)
C(18)-C(13)-C(12)	117.14(13)
C(15)-C(14)-C(13)	119.90(15)
C(15)-C(14)-H(14)	120.1
C(13)-C(14)-H(14)	120.1
C(16)-C(15)-C(14)	120.01(18)
C(16)-C(15)-H(15)	120.0
C(14)-C(15)-H(15)	120.0
C(15)-C(16)-C(17)	120.36(16)
C(15)-C(16)-H(16)	119.8
C(17)-C(16)-H(16)	119.8
C(18)-C(17)-C(16)	120.18(16)
C(18)-C(17)-H(17)	119.9
C(16)-C(17)-H(17)	119.9
C(17)-C(18)-C(13)	120.15(17)
C(17)-C(18)-H(18)	119.9
C(13)-C(18)-H(18)	119.9
C(25)-C(19)-C(24)	118.54(14)

C(25)-C(19)-H(19)	120.7
C(24)-C(19)-H(19)	120.7
O(3)-C(20)-N(2)	125.68(12)
O(3)-C(20)-C(10)	126.71(11)
N(2)-C(20)-C(10)	107.58(10)
C(22)-C(21)-C(25)	122.09(14)
C(22)-C(21)-N(2)	128.41(14)
C(25)-C(21)-N(2)	109.49(12)
C(21)-C(22)-C(23)	117.58(16)
C(21)-C(22)-H(22)	121.2
C(23)-C(22)-H(22)	121.2
C(24)-C(23)-C(22)	121.22(16)
C(24)-C(23)-H(23)	119.4
C(22)-C(23)-H(23)	119.4
C(23)-C(24)-C(19)	121.02(16)
C(23)-C(24)-H(24)	119.5
C(19)-C(24)-H(24)	119.5
C(19)-C(25)-C(21)	119.54(12)
C(19)-C(25)-C(10)	131.51(12)
C(21)-C(25)-C(10)	108.92(11)
C(31)-C(26)-C(27)	118.61(12)
C(31)-C(26)-C(9)	119.32(11)
C(27)-C(26)-C(9)	122.01(11)
C(28)-C(27)-C(26)	120.96(13)
C(28)-C(27)-H(27)	119.5
C(26)-C(27)-H(27)	119.5
C(29)-C(28)-C(27)	118.09(13)
C(29)-C(28)-H(28)	121.0
C(27)-C(28)-H(28)	121.0
C(30)-C(29)-C(28)	123.18(13)
C(30)-C(29)-F(1)	118.55(14)
C(28)-C(29)-F(1)	118.27(14)
C(29)-C(30)-C(31)	118.16(14)
C(29)-C(30)-H(30)	120.9
C(31)-C(30)-H(30)	120.9

C(26)-C(31)-C(30)	120.98(13)
C(26)-C(31)-H(31)	119.5
C(30)-C(31)-H(31)	119.5
O(4)-C(33)-H(33A)	109.5
O(4)-C(33)-H(33B)	109.5
H(33A)-C(33)-H(33B)	109.5
O(4)-C(33)-H(33C)	109.5
H(33A)-C(33)-H(33C)	109.5
H(33B)-C(33)-H(33C)	109.5
C(2)-N(1)-C(3)	111.82(10)
C(2)-N(1)-H(1N)	121.4(11)
C(3)-N(1)-H(1N)	125.9(11)
C(20)-N(2)-C(21)	111.82(11)
C(20)-N(2)-H(2N)	124.6(12)
C(21)-N(2)-H(2N)	122.3(12)
C(1)-N(3)-C(9)	106.07(9)
C(1)-N(3)-H(3N)	111.0(11)
C(9)-N(3)-H(3N)	110.4(11)
C(6)-O(4)-C(33)	118.41(12)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **4s**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	30(1)	38(1)	36(1)	-1(1)	-13(1)	1(1)
C(2)	33(1)	42(1)	43(1)	-2(1)	-14(1)	2(1)
C(3)	35(1)	39(1)	39(1)	-7(1)	-13(1)	-1(1)
C(4)	38(1)	47(1)	42(1)	-10(1)	-8(1)	1(1)
C(5)	52(1)	50(1)	35(1)	-7(1)	-5(1)	-2(1)
C(6)	57(1)	43(1)	35(1)	-4(1)	-15(1)	4(1)
C(7)	44(1)	44(1)	36(1)	-6(1)	-13(1)	6(1)
C(8)	34(1)	38(1)	34(1)	-6(1)	-11(1)	-1(1)
C(9)	31(1)	39(1)	40(1)	2(1)	-13(1)	-1(1)
C(10)	29(1)	43(1)	33(1)	1(1)	-11(1)	0(1)
C(11)	31(1)	39(1)	31(1)	-1(1)	-11(1)	-1(1)
C(12)	36(1)	52(1)	32(1)	0(1)	-11(1)	-8(1)
C(13)	50(1)	52(1)	30(1)	2(1)	-13(1)	-17(1)
C(14)	64(1)	51(1)	42(1)	0(1)	-22(1)	-12(1)
C(15)	93(1)	50(1)	48(1)	0(1)	-24(1)	-12(1)
C(16)	112(2)	60(1)	51(1)	-3(1)	-25(1)	-37(1)
C(17)	87(1)	79(1)	54(1)	-2(1)	-28(1)	-41(1)
C(18)	60(1)	71(1)	43(1)	0(1)	-20(1)	-25(1)
C(19)	39(1)	83(1)	39(1)	4(1)	-14(1)	7(1)
C(20)	34(1)	41(1)	40(1)	-1(1)	-11(1)	0(1)
C(21)	47(1)	68(1)	36(1)	-3(1)	-12(1)	5(1)
C(22)	75(1)	119(2)	39(1)	-17(1)	-16(1)	24(1)
C(23)	76(1)	157(2)	37(1)	-11(1)	-24(1)	21(1)
C(24)	55(1)	132(2)	41(1)	7(1)	-22(1)	13(1)
C(25)	34(1)	55(1)	33(1)	2(1)	-10(1)	-3(1)
C(26)	32(1)	39(1)	45(1)	0(1)	-13(1)	-3(1)
C(27)	41(1)	57(1)	53(1)	9(1)	-21(1)	-9(1)
C(28)	41(1)	56(1)	74(1)	-1(1)	-29(1)	-3(1)
C(29)	31(1)	49(1)	68(1)	-12(1)	-9(1)	-4(1)
C(30)	44(1)	64(1)	54(1)	7(1)	-7(1)	-13(1)

C(31)	41(1)	57(1)	51(1)	9(1)	-16(1)	-7(1)
C(33)	106(2)	84(1)	36(1)	4(1)	-16(1)	17(1)
F(1)	31(1)	77(1)	103(1)	-13(1)	-8(1)	-8(1)
N(1)	32(1)	47(1)	42(1)	-4(1)	-11(1)	7(1)
N(2)	49(1)	63(1)	40(1)	-8(1)	-12(1)	18(1)
N(3)	32(1)	42(1)	41(1)	-6(1)	-11(1)	-3(1)
O(1)	39(1)	56(1)	49(1)	11(1)	-13(1)	6(1)
O(2)	38(1)	72(1)	69(1)	-16(1)	-24(1)	1(1)
O(3)	47(1)	50(1)	48(1)	0(1)	-22(1)	7(1)
O(4)	85(1)	65(1)	34(1)	0(1)	-14(1)	22(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **4s**..

	x	y	z	U(eq)
H(4)	11086	1317	-3519	54
H(5)	10443	2703	-4813	59
H(7)	6774	3495	-2095	51
H(9)	5760	765	1687	46
H(11)	6525	3662	111	41
H(14)	6128	5313	969	62
H(15)	6041	7223	1576	78
H(16)	7741	7702	2102	88
H(17)	9503	6273	2075	84
H(18)	9589	4363	1506	68
H(19)	7336	1291	2795	67
H(22)	3852	3852	5444	99
H(23)	5395	2663	6089	111
H(24)	7096	1403	4796	94
H(27)	3358	2130	496	60
H(28)	1031	1949	1358	66
H(30)	1430	135	4250	70
H(31)	3758	309	3385	61
H(33A)	9743	4332	-5760	124
H(33B)	8374	4692	-5937	124
H(33C)	8918	3334	-5860	124
H(1N)	10217(18)	396(14)	-1144(15)	54(4)
H(2N)	3280(20)	4488(17)	3464(17)	70(5)
H(3N)	6053(17)	720(16)	-250(16)	60(5)

Table 6. Torsion angles [°] for **4s**..

N(3)-C(1)-C(2)-O(1)	-50.53(17)
C(8)-C(1)-C(2)-O(1)	-173.98(13)
C(11)-C(1)-C(2)-O(1)	63.87(17)
N(3)-C(1)-C(2)-N(1)	124.93(11)
C(8)-C(1)-C(2)-N(1)	1.48(13)
C(11)-C(1)-C(2)-N(1)	-120.68(11)
C(8)-C(3)-C(4)-C(5)	0.14(19)
N(1)-C(3)-C(4)-C(5)	179.28(13)
C(3)-C(4)-C(5)-C(6)	-0.2(2)
C(4)-C(5)-C(6)-O(4)	178.49(13)
C(4)-C(5)-C(6)-C(7)	0.1(2)
O(4)-C(6)-C(7)-C(8)	-178.57(12)
C(5)-C(6)-C(7)-C(8)	-0.1(2)
C(6)-C(7)-C(8)-C(3)	0.06(19)
C(6)-C(7)-C(8)-C(1)	177.60(12)
C(4)-C(3)-C(8)-C(7)	-0.09(19)
N(1)-C(3)-C(8)-C(7)	-179.38(11)
C(4)-C(3)-C(8)-C(1)	-178.11(11)
N(1)-C(3)-C(8)-C(1)	2.60(14)
N(3)-C(1)-C(8)-C(7)	57.79(17)
C(11)-C(1)-C(8)-C(7)	-57.03(16)
C(2)-C(1)-C(8)-C(7)	179.81(13)
N(3)-C(1)-C(8)-C(3)	-124.45(11)
C(11)-C(1)-C(8)-C(3)	120.73(10)
C(2)-C(1)-C(8)-C(3)	-2.43(12)
N(3)-C(9)-C(10)-C(25)	-148.79(9)
C(26)-C(9)-C(10)-C(25)	87.11(12)
N(3)-C(9)-C(10)-C(20)	97.44(10)
C(26)-C(9)-C(10)-C(20)	-26.66(14)
N(3)-C(9)-C(10)-C(11)	-20.00(10)
C(26)-C(9)-C(10)-C(11)	-144.10(10)
N(3)-C(1)-C(11)-C(12)	159.74(9)
C(8)-C(1)-C(11)-C(12)	-77.07(12)

C(2)-C(1)-C(11)-C(12)	38.31(14)
N(3)-C(1)-C(11)-C(10)	32.10(11)
C(8)-C(1)-C(11)-C(10)	155.29(9)
C(2)-C(1)-C(11)-C(10)	-89.32(11)
C(25)-C(10)-C(11)-C(12)	-11.17(15)
C(20)-C(10)-C(11)-C(12)	105.21(11)
C(9)-C(10)-C(11)-C(12)	-135.37(10)
C(25)-C(10)-C(11)-C(1)	116.71(11)
C(20)-C(10)-C(11)-C(1)	-126.91(10)
C(9)-C(10)-C(11)-C(1)	-7.49(11)
C(1)-C(11)-C(12)-O(2)	-19.97(16)
C(10)-C(11)-C(12)-O(2)	103.23(14)
C(1)-C(11)-C(12)-C(13)	159.54(10)
C(10)-C(11)-C(12)-C(13)	-77.26(13)
O(2)-C(12)-C(13)-C(14)	170.52(13)
C(11)-C(12)-C(13)-C(14)	-8.99(18)
O(2)-C(12)-C(13)-C(18)	-7.03(18)
C(11)-C(12)-C(13)-C(18)	173.47(11)
C(18)-C(13)-C(14)-C(15)	-0.6(2)
C(12)-C(13)-C(14)-C(15)	-178.07(13)
C(13)-C(14)-C(15)-C(16)	1.0(2)
C(14)-C(15)-C(16)-C(17)	-0.8(3)
C(15)-C(16)-C(17)-C(18)	0.2(3)
C(16)-C(17)-C(18)-C(13)	0.2(2)
C(14)-C(13)-C(18)-C(17)	0.0(2)
C(12)-C(13)-C(18)-C(17)	177.66(13)
C(25)-C(10)-C(20)-O(3)	172.12(13)
C(11)-C(10)-C(20)-O(3)	45.26(17)
C(9)-C(10)-C(20)-O(3)	-68.01(16)
C(25)-C(10)-C(20)-N(2)	-6.12(13)
C(11)-C(10)-C(20)-N(2)	-132.99(11)
C(9)-C(10)-C(20)-N(2)	113.74(12)
C(25)-C(21)-C(22)-C(23)	-0.4(3)
N(2)-C(21)-C(22)-C(23)	-179.9(2)
C(21)-C(22)-C(23)-C(24)	-0.3(4)

C(22)-C(23)-C(24)-C(19)	0.4(4)
C(25)-C(19)-C(24)-C(23)	0.4(3)
C(24)-C(19)-C(25)-C(21)	-1.1(2)
C(24)-C(19)-C(25)-C(10)	-178.74(16)
C(22)-C(21)-C(25)-C(19)	1.1(3)
N(2)-C(21)-C(25)-C(19)	-179.29(14)
C(22)-C(21)-C(25)-C(10)	179.28(17)
N(2)-C(21)-C(25)-C(10)	-1.15(17)
C(20)-C(10)-C(25)-C(19)	-177.84(15)
C(11)-C(10)-C(25)-C(19)	-57.5(2)
C(9)-C(10)-C(25)-C(19)	62.06(18)
C(20)-C(10)-C(25)-C(21)	4.33(14)
C(11)-C(10)-C(25)-C(21)	124.69(13)
C(9)-C(10)-C(25)-C(21)	-115.78(12)
N(3)-C(9)-C(26)-C(31)	148.97(12)
C(10)-C(9)-C(26)-C(31)	-92.44(14)
N(3)-C(9)-C(26)-C(27)	-33.75(17)
C(10)-C(9)-C(26)-C(27)	84.84(15)
C(31)-C(26)-C(27)-C(28)	1.6(2)
C(9)-C(26)-C(27)-C(28)	-175.72(13)
C(26)-C(27)-C(28)-C(29)	-0.1(2)
C(27)-C(28)-C(29)-C(30)	-1.5(2)
C(27)-C(28)-C(29)-F(1)	178.66(13)
C(28)-C(29)-C(30)-C(31)	1.3(2)
F(1)-C(29)-C(30)-C(31)	-178.78(14)
C(27)-C(26)-C(31)-C(30)	-1.7(2)
C(9)-C(26)-C(31)-C(30)	175.67(13)
C(29)-C(30)-C(31)-C(26)	0.3(2)
O(1)-C(2)-N(1)-C(3)	175.43(13)
C(1)-C(2)-N(1)-C(3)	-0.02(14)
C(4)-C(3)-N(1)-C(2)	179.15(13)
C(8)-C(3)-N(1)-C(2)	-1.63(15)
O(3)-C(20)-N(2)-C(21)	-172.33(14)
C(10)-C(20)-N(2)-C(21)	5.94(16)
C(22)-C(21)-N(2)-C(20)	176.38(19)

C(25)-C(21)-N(2)-C(20)	-3.15(19)
C(8)-C(1)-N(3)-C(9)	-168.78(9)
C(11)-C(1)-N(3)-C(9)	-46.85(11)
C(2)-C(1)-N(3)-C(9)	75.78(12)
C(26)-C(9)-N(3)-C(1)	167.83(10)
C(10)-C(9)-N(3)-C(1)	42.72(11)
C(5)-C(6)-O(4)-C(33)	15.4(2)
C(7)-C(6)-O(4)-C(33)	-166.14(17)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for **4s** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2N)...O(4)#1	0.88(2)	2.07(2)	2.9467(16)	176.4(18)
N(1)-H(1N)...O(1)#2	0.879(17)	1.960(17)	2.8215(14)	166.2(15)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z #2 -x+2,-y,-z