

**An Efficient Route to
Tetrahydroindeno[2,1-*b*]pyrroles via a
Base-Promoted Reaction of
(*E*)-2-Alkynylphenylchalcone with 2-Isocyanoacetate**

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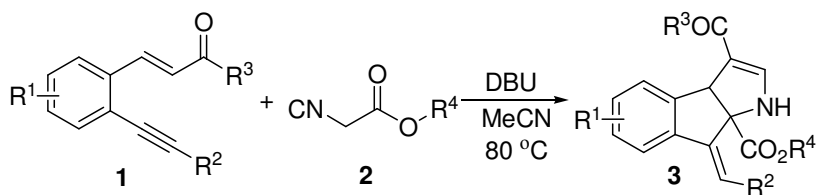
Supporting Information

1. General experimental methods (S2).
2. General experimental procedure and characterization data (S2-S9).
3. ¹H and ¹³C NMR spectra of compound **3** (S10-S39).

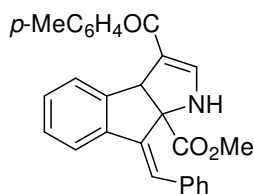
General experimental methods:

All reactions were performed in reaction tubes under air atmosphere. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 μm , standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr (house vacuum) at 25–35°C. Commercial reagents and solvents were used as received. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale.

General procedure for the base-promoted cascade reaction of (E)-2-alkynylphenylchalcone 1 with 2-isocyanoacetate 2.

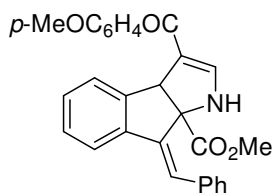


2-Isocyanoacetate **2** (0.24 mmol, 1.2 equiv) and DBU (0.2 mmol, 1.0 equiv) were added to a solution of (E)-2-alkynylphenylchalcone **1** (0.20 mmol) in CH₃CN (1.0 mL). The mixture was stirred at 80 °C for 3~5 hours. After completion of reaction as indicated by TLC, the mixture was purified directly by flash column chromatograph (EtOAc/*n*-hexane, 1:3) to give the desired product **3**.



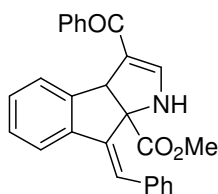
(Z)-Methyl

8-benzylidene-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3a**): White solid, mp: 190.3-191.0 °C. ¹H NMR (400MHz, CDCl₃) δ 7.82-7.84 (m, 1H), 7.61 (dd, *J* = 2.4, 5.6 Hz, 1H), 7.46 (s, 1H), 7.44 (s, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.29-7.32 (m, 3H), 7.22-7.25 (m, 3H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 2.8 Hz, 1H), 5.52 (d, *J* = 2.8 Hz, 1H), 5.18 (s, 1H), 3.47 (s, 3H), 2.34 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 190.1, 173.3, 150.2, 145.5, 144.5, 141.1, 139.3, 138.0, 136.2, 130.1, 129.0, 128.9, 128.4, 128.2, 128.1, 128.0, 127.2, 123.4, 120.6, 116.4, 77.2, 58.5, 53.1, 21.6; HRMS (ESI) calcd for C₂₈H₂₃NO₃: 422.1756 (M + H⁺), found: 422.1771.



(Z)-Methyl

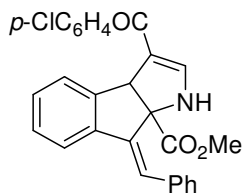
8-benzylidene-3-(4-methoxybenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3b**): White solid, 231.3-232.2 °C. ¹H NMR (400MHz, CDCl₃) δ 7.81 (dd, *J* = 3.6, 5.6 Hz, 1H), 7.61 (dd, *J* = 3.2, 6.4 Hz, 1H), 7.56 (d, *J* = 2.4 Hz, 1H), 7.54 (d, *J* = 2.4 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.29-7.32 (m, 3H), 7.23 (t, *J* = 6.4 Hz, 3H), 7.01 (d, *J* = 3.2 Hz, 1H), 6.84 (dd, *J* = 1.6, 7.2 Hz, 2H), 5.42 (d, *J* = 2.8 Hz, 1H), 5.18 (s, 1H), 3.80 (s, 3H), 3.48 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 189.2, 173.3, 161.7, 149.7, 145.4, 144.5, 139.2, 136.1, 133.3, 132.4, 129.9, 128.7, 128.2, 128.0, 127.9, 126.9, 123.2, 120.5, 116.3, 113.4, 77.06, 58.5, 55.4, 52.9; HRMS (ESI) calcd for C₂₈H₂₃NO₄: 438.1705 (M + H⁺), found: 438.1700.



(Z)-Methyl

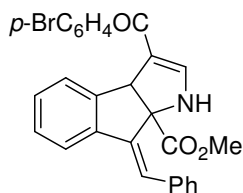
3-benzoyl-8-benzylidene-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate

(3c): White solid, 98.2-98.9 °C. ¹H NMR (400MHz, CDCl₃) δ 7.83-7.85 (m, 1H), 7.60 (d, *J* = 5.2 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.28-7.39 (m, 8H), 7.22-7.25 (m, 3H), 6.99 (d, *J* = 3.2 Hz, 1H), 5.58 (s, 1H), 5.17 (s, 1H), 3.47 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 190.1, 173.1, 154.8, 150.8, 145.3, 144.3, 140.7, 139.2, 136.0, 130.6, 130.0, 128.7, 128.3, 128.2, 127.9, 127.9, 127.0, 123.3, 120.5, 116.2, 77.2, 52.9; HRMS (ESI) calcd for C₂₇H₂₁NO₃: 408.1600 (M + H⁺), found: 408.1591.



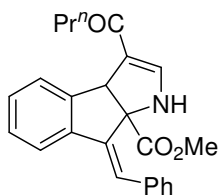
(Z)-Methyl

8-benzylidene-3-(4-chlorobenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate **(3d)**: White solid, 100.0-101.0 °C. ¹H NMR (400MHz, CDCl₃) δ 7.80-7.82 (m, 1H), 7.61 (dd, *J* = 2.4, 6.0 Hz, 1H), 7.45-7.48 (m, 2H), 7.34-7.38 (m, 2H), 7.26-7.32 (m, 5H), 7.21-7.22 (m, 3H), 5.56 (d, *J* = 2.4 Hz, 1H), 5.15 (s, 1H), 3.49 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 188.6, 173.0, 150.8, 144.1, 139.2, 139.0, 136.6, 135.9, 130.0, 129.3, 128.8, 128.5, 128.4, 128.2, 128.0, 126.9, 123.4, 120.5, 118.9, 115.9, 77.2, 57.9, 52.9; HRMS (ESI) calcd for C₂₇H₂₀ClNO₃: 442.1210 (M + H⁺), found: 442.1205.



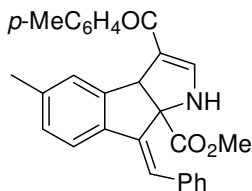
(Z)-Methyl

8-benzylidene-3-(4-bromobenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3e**): White solid, 219.0-220.0 °C. ¹H NMR (400MHz, CDCl₃) δ 7.80-7.82 (m, 1H), 7.60-7.62 (dd, *J* = 2.8, 5.6 Hz, 1H), 7.45-7.49 (m, 2H), 7.38-7.42 (m, 2H), 7.28-7.37 (m, 5H), 7.23 (s, 2H), 7.20 (s, 1H), 6.97 (d, *J* = 3.2 Hz, 1H), 5.58 (s, 1H), 5.15 (s, 1H), 3.49 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 188.7, 173.3, 150.7, 145.1, 144.1, 139.5, 139.1, 135.9, 131.4, 130.0, 129.5, 128.8, 128.2, 128.1, 128.0, 127.0, 125.1, 123.4, 120.5, 116.0, 77.2, 58.1, 52.9; HRMS (ESI) calcd for C₂₇H₂₀BrNO₃: 486.0705 (M + H⁺), found: 486.0710.



(Z)-Methyl

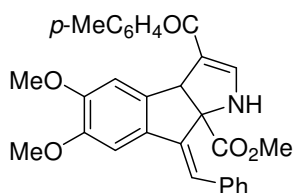
8-benzylidene-3-butyryl-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3f**): White solid, 64.0-65.0 °C. ¹H NMR (400MHz, CDCl₃) δ 7.74-7.76 (m, 1H), 7.57 (t, *J* = 4.4 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.25-7.31 (m, 3H), 7.18-7.21 (m, 3H), 7.15 (d, *J* = 2.8 Hz, 1H), 5.25 (s, 1H), 4.95 (s, 1H), 3.43 (s, 3H), 2.36-2.46 (m, 2H), 1.60-1.65 (m, 2H), 0.88 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 194.9, 173.3, 147.0, 145.3, 144.4, 139.1, 136.1, 129.9, 128.7, 128.2, 127.9, 127.8, 127.0, 123.0, 120.4, 117.4, 76.8, 57.9, 52.9, 40.1, 19.0, 14.0; HRMS (ESI) calcd for C₂₄H₂₃NO₃: 374.1756 (M + H⁺), found: 374.1732.



(Z)-Methyl

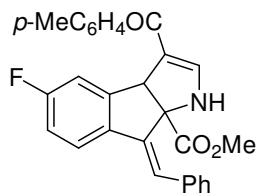
8-benzylidene-5-methyl-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3g**): White solid, 78.0-79.0 °C. ¹H NMR (400MHz, CDCl₃) δ 7.63

(s, 1H), 7.46-7.50 (m, 3H), 7.33-7.37 (m, 2H), 7.27-7.29 (m, 1H), 7.21 (d, $J = 6.8$ Hz, 2H), 7.11-7.15 (m, 4H), 7.01 (d, $J = 2.8$ Hz, 1H), 5.51 (d, $J = 2.4$ Hz, 1H), 5.14 (s, 1H), 3.47 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 189.98, 173.3, 150.4, 145.6, 144.3, 141.0, 137.9, 136.6, 136.2, 129.0, 128.8, 128.7, 128.4, 128.2, 128.1, 127.8, 127.3, 122.1, 120.3, 116.3, 77.3, 58.2, 52.9, 21.6, 21.5; HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{25}\text{NO}_3$: 436.1913 ($\text{M} + \text{H}^+$), found: 436.1907.



(Z)-Methyl

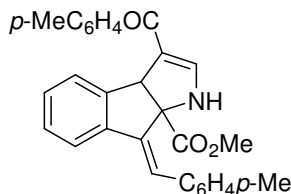
8-benzylidene-5,6-dimethoxy-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3h**): White solid, 97.6-98.5 °C. ^1H NMR (400MHz, CDCl_3) δ 7.44 (d, $J = 8.4$ Hz, 2H), 7.38 (s, 1H), 7.34 (t, $J = 7.2$ Hz, 2H), 7.26 (t, $J = 7.6$ Hz, 1H), 7.21 (d, $J = 7.2$ Hz, 2H), 7.13 (d, $J = 8.0$ Hz, 2H), 7.03 (s, 1H), 7.00-7.01 (m, 2H), 5.53 (d, $J = 2.8$ Hz, 1H), 5.09 (s, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.50 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 190.2, 173.2, 151.4, 150.5, 149.7, 144.5, 140.9, 138.7, 136.3, 131.3, 129.8, 128.9, 128.7, 128.2, 128.0, 127.6, 120.5, 116.1, 108.7, 102.4, 77.3, 58.1, 56.2, 56.1, 52.9, 21.4; HRMS (ESI) calcd for $\text{C}_{30}\text{H}_{27}\text{NO}_5$: 482.1967 ($\text{M} + \text{H}^+$), found: 482.1966.



(Z)-Methyl

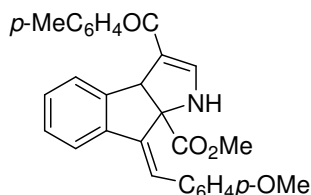
8-benzylidene-5-fluoro-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3i**): White solid, 80.6-81.6 °C. ^1H NMR (400MHz, CDCl_3) δ 7.77-7.80 (m, 1H), 7.45 (s, 1H), 7.43 (s, 1H), 7.34-7.34 (m, 2H), 7.28-7.31 (m, 1H), 7.21-7.25 (m, 3H), 7.16 (s, 1H), 7.14 (s, 1H), 7.12 (s, 1H), 6.95-7.00 (m, 2H), 5.58 (d,

$J = 2.8$ Hz, 1H), 5.10 (s, 1H), 3.47 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 190.0, 172.8, 163.2 (d, $^1J_{\text{CF}} = 244.1$ Hz), 150.4, 143.5, 143.4, 141.1, 140.9, 140.8, 137.8, 135.6, 128.9 (d, $^3J_{\text{CF}} = 6.7$ Hz), 128.5 (d, $^3J_{\text{CF}} = 8.6$ Hz), 128.3, 128.2, 128.0, 124.5, 117.1 (d, $^2J_{\text{CF}} = 22.9$ Hz), 116.1, 106.9 (d, $^2J_{\text{CF}} = 22.9$ Hz), 77.6, 57.8, 53.0, 21.5; HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{22}\text{FNO}_3$: 440.1662 ($\text{M} + \text{H}^+$), found: 440.1669.



(Z)-Methyl

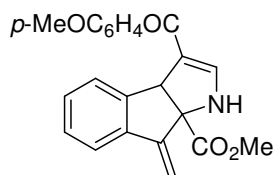
3-(4-methylbenzoyl)-8-(4-methylbenzylidene)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3j**): White solid, 222.8-223.4 °C. ^1H NMR (400MHz, CDCl_3) δ 7.79-7.84 (m, 1H), 7.58 (t, $J = 5.6$ Hz, 1H), 7.45 (d, $J = 8.0$ Hz, 2H), 7.29 (t, $J = 3.6$ Hz, 2H), 7.07-7.17 (m, 7H), 7.00 (d, $J = 2.8$ Hz, 1H), 5.46 (s, 1H), 5.17 (s, 1H), 3.50 (s, 3H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 192.7, 173.3, 150.2, 145.2, 143.7, 140.9, 139.4, 137.8, 133.1, 129.7, 129.5, 129.1, 128.8, 128.2, 128.1, 127.8, 127.0, 123.2, 120.4, 116.2, 77.3, 58.4, 52.9, 21.4, 21.3; HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{25}\text{NO}_3$: 436.1913 ($\text{M} + \text{H}^+$), found: 436.1907.



(Z)-Methyl

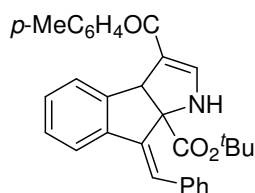
8-(4-methoxybenzylidene)-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3k**): White solid, 106.0-107.0 °C. ^1H NMR (400MHz, CDCl_3) δ 7.81-7.83 (m, 1H), 7.58 (d, $J = 6.4$ Hz, 1H), 7.45 (d, $J = 8.0$ Hz, 2H), 7.28 (t, $J = 4.0$ Hz, 2H), 7.12-7.18 (m, 5H), 7.01 (d, $J = 2.8$ Hz, 1H), 6.89 (d, $J = 8.0$ Hz, 2H), 5.48 (s, 1H), 5.17 (s, 1H), 3.80 (s, 3H), 3.52 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz,

CDCl₃) δ 192.0, 176.4, 159.8, 150.2, 145.1, 143.0, 140.9, 139.6, 133.1, 129.7, 129.6, 128.8, 128.4, 128.1, 128.1, 127.8, 123.0, 120.2, 116.3, 114.2, 77.1, 58.5, 57.7, 52.9, 21.4; HRMS (ESI) calcd for C₂₉H₂₅NO₄: 452.1862 (M + H⁺), found: 452.1849.



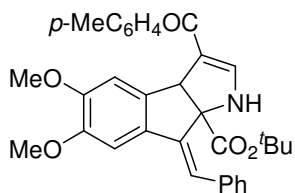
Methyl

3-(4-methylbenzoyl)-8-methylene-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3l**): Yellow solid, 151.0-152.0 °C. ¹H NMR (400MHz, CDCl₃) δ 7.83 (d, *J* = 7.2 Hz, 1H), 7.51-7.56 (m, 3H), 7.25-7.31 (m, 2H), 7.01 (d, *J* = 2.8 Hz, 1H), 6.86 (s, 1H), 6.84 (s, 1H), 5.73 (d, *J* = 1.6 Hz, 1H), 5.67 (s, 1H), 5.35 (s, 1H), 5.20 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 189.4, 173.5, 161.8, 151.8, 149.2, 147.2, 137.0, 133.5, 130.6, 130.0, 127.9, 127.3, 121.3, 116.4, 113.6, 105.8, 78.1, 55.6, 55.2, 53.3; HRMS (ESI) calcd for C₂₂H₁₉NO₄: 362.1392 (M + H⁺), found: 362.1390.



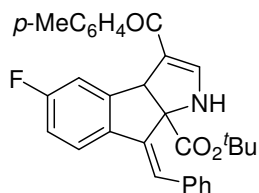
(Z)-tert-Butyl

8-benzylidene-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3m**): Yellow solid, 89.2-90.2 °C. ¹H NMR (400MHz, CDCl₃) δ 7.87 (t, *J* = 5.2 Hz, 1H), 7.59 (t, *J* = 2.8 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.25-7.37 (m, 7H), 7.11-7.14 (m, 3H), 7.00 (d, *J* = 2.8 Hz, 1H), 5.61 (s, 1H), 5.13 (s, 1H), 2.33 (s, 3H), 1.20 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 190.0, 171.5, 150.7, 145.4, 143.9, 140.8, 140.0, 138.0, 136.1, 129.6, 128.9, 128.8, 128.3, 128.1, 127.8, 127.7, 127.0, 122.7, 120.3, 116.2, 82.8, 77.7, 58.9, 27.6, 21.4; HRMS (ESI) calcd for C₃₁H₂₉NO₃: 464.2226 (M + H⁺), found: 464.2230.



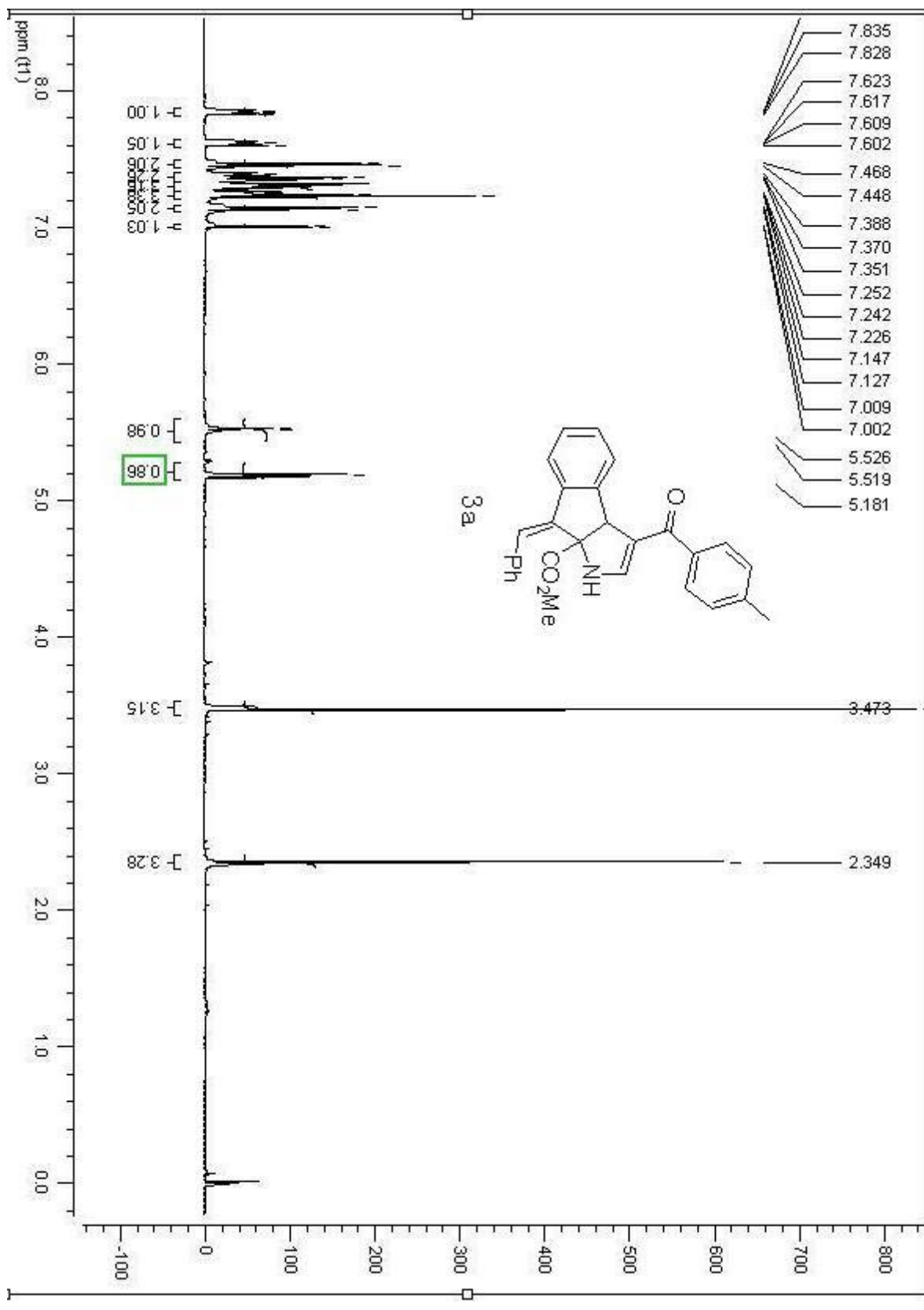
(*Z*)-*tert*-Butyl

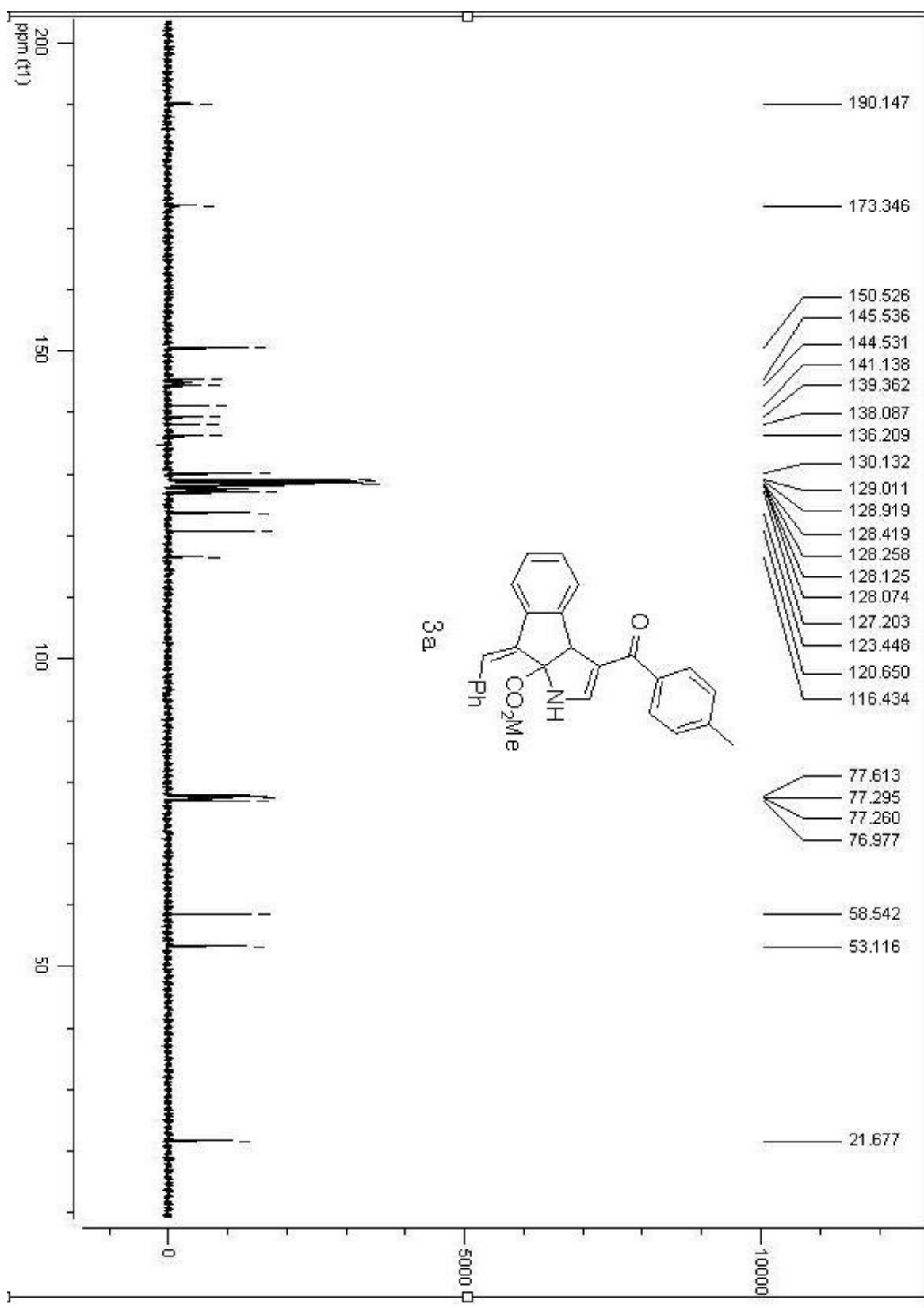
8-benzylidene-5,6-dimethoxy-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3n**): Yellow solid, 101.5-102.5 °C. ¹H NMR (400MHz, CDCl₃) δ 7.43 (t, *J* = 8.0 Hz, 3H), 7.27-7.35 (m, 4H), 7.24 (d, *J* = 4.8 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.01 (t, *J* = 4.0 Hz, 2H), 6.91 (s, 1H), 5.58 (s, 1H), 5.04 (s, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 2.33 (s, 3H), 1.22 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 190.3, 171.6, 151.1, 150.8, 149.5, 144.1, 140.8, 138.7, 138.1, 136.3, 132.1, 128.8, 128.1, 128.0, 127.4, 120.1, 116.1, 108.8, 102.3, 102.3, 82.8, 78.1, 58.6, 56.1, 56.0, 27.6, 21.4; HRMS (ESI) calcd for C₃₃H₃₃NO₅: 542.2437 (M + H⁺), found: 524.2422.

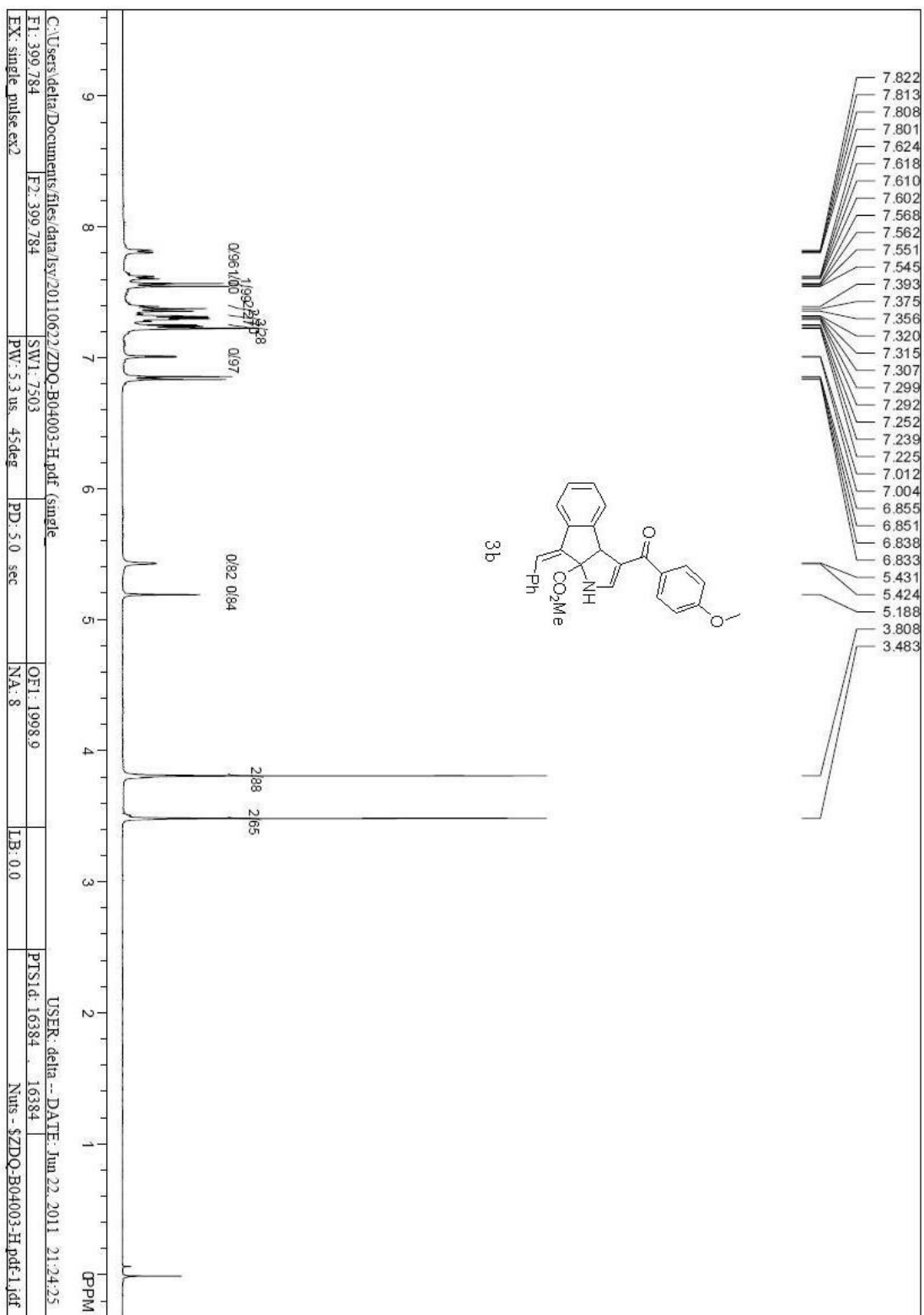


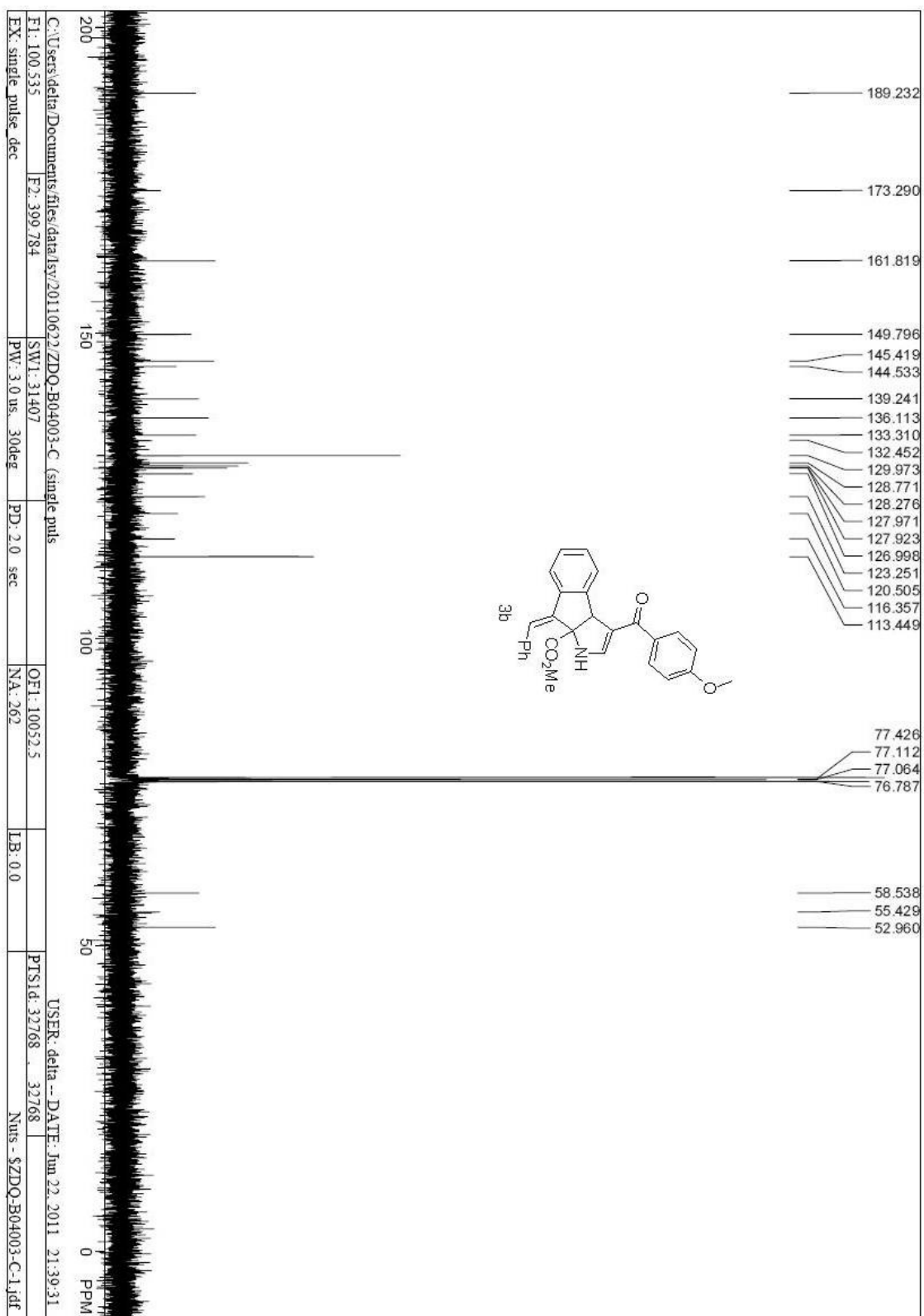
(*Z*)-*tert*-Butyl

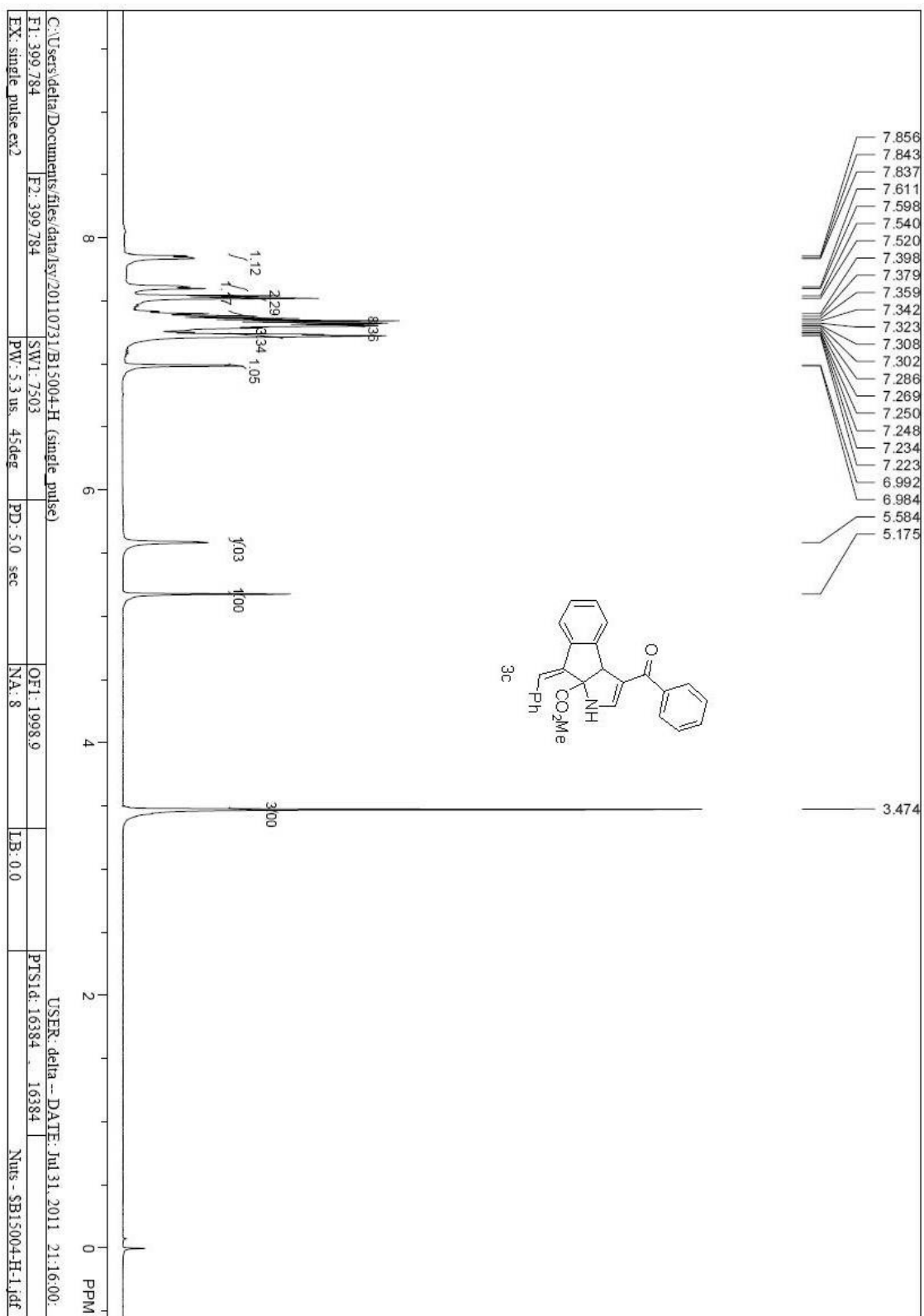
8-benzylidene-5-fluoro-3-(4-methylbenzoyl)-1,3a,8,8a-tetrahydroindeno[2,1-*b*]pyrrole-8a-carboxylate (**3o**): Yellow solid, 88.5-89.5 °C. ¹H NMR (400MHz, CDCl₃) δ 7.81-7.85 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.20-7.39 (m, 7H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.07 (s, 1H), 6.97-6.99 (m, 1H), 5.70 (d, *J* = 7.6 Hz, 1H), 5.07 (s, 1H), 2.22 (s, 3H), 1.20 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 190.1, 171.2, 163.1 (d, ¹*J*_{CF} = 243.1 Hz), 150.8, 143.1, 142.3 (d, ³*J*_{CF} = 8.6 Hz), 141.0 (d, ⁴*J*_{CF} = 1.9 Hz), 140.9, 137.9, 135.6, 128.9 (d, ³*J*_{CF} = 8.6 Hz), 128.6, 128.5, 128.4, 128.3, 128.1, 123.9, 116.8 (d, ²*J*_{CF} = 22.9 Hz), 116.0, 106.7 (d, ²*J*_{CF} = 23.8 Hz), 83.0, 78.2, 58.3, 27.5, 21.4; HRMS (ESI) calcd for C₃₁H₂₈FNO₃: 482.2131 (M + H⁺), found: 482.2129.

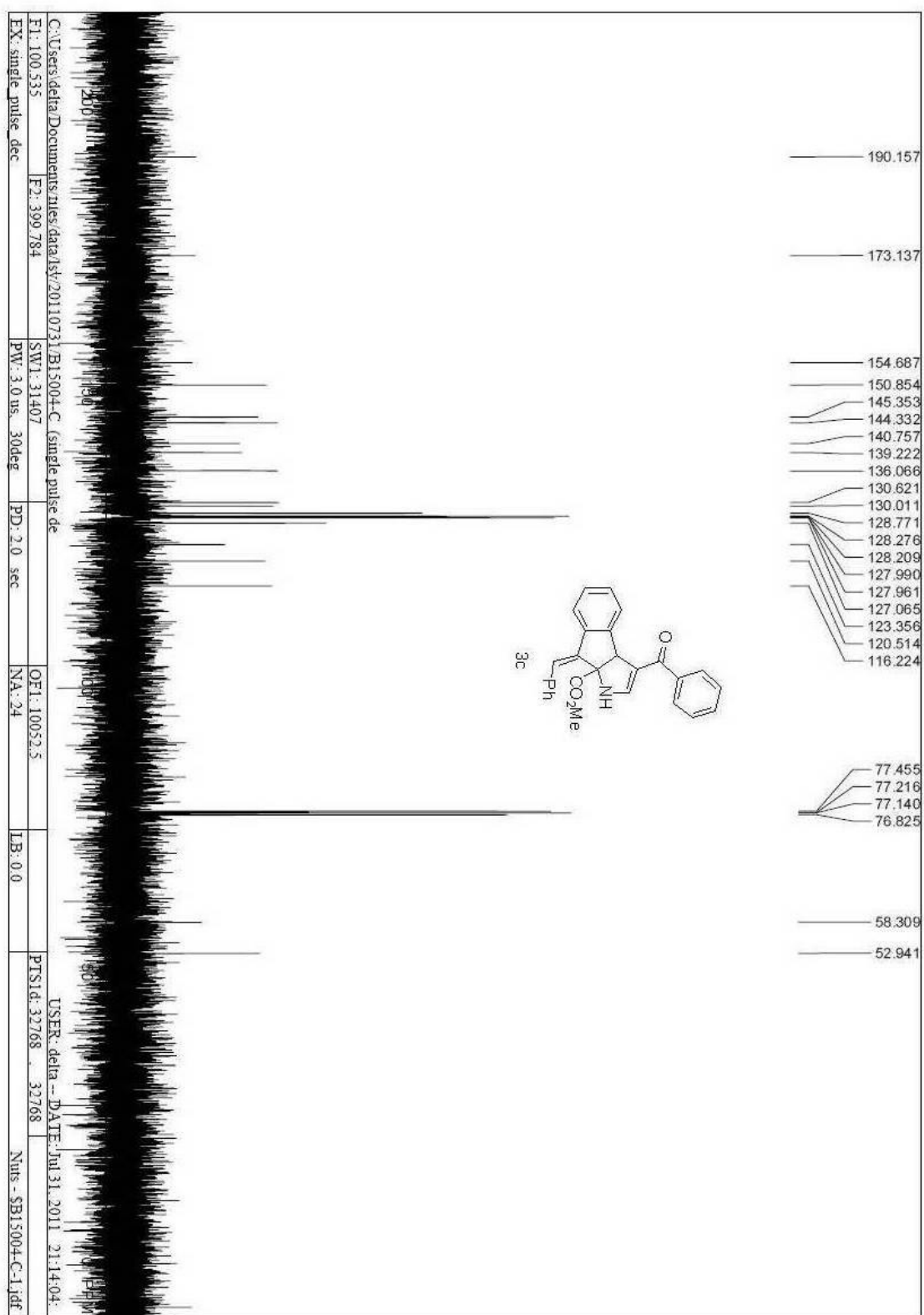


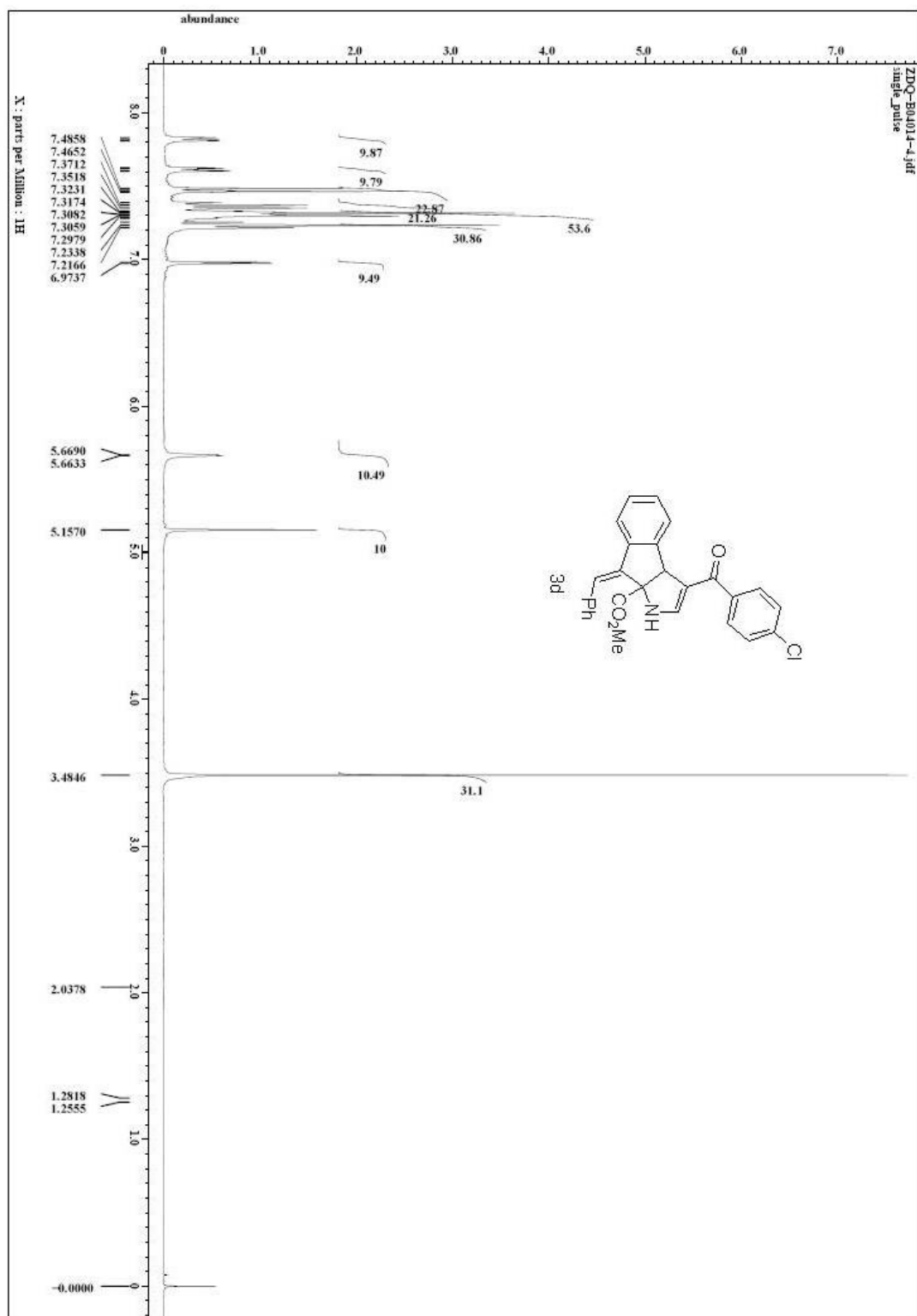


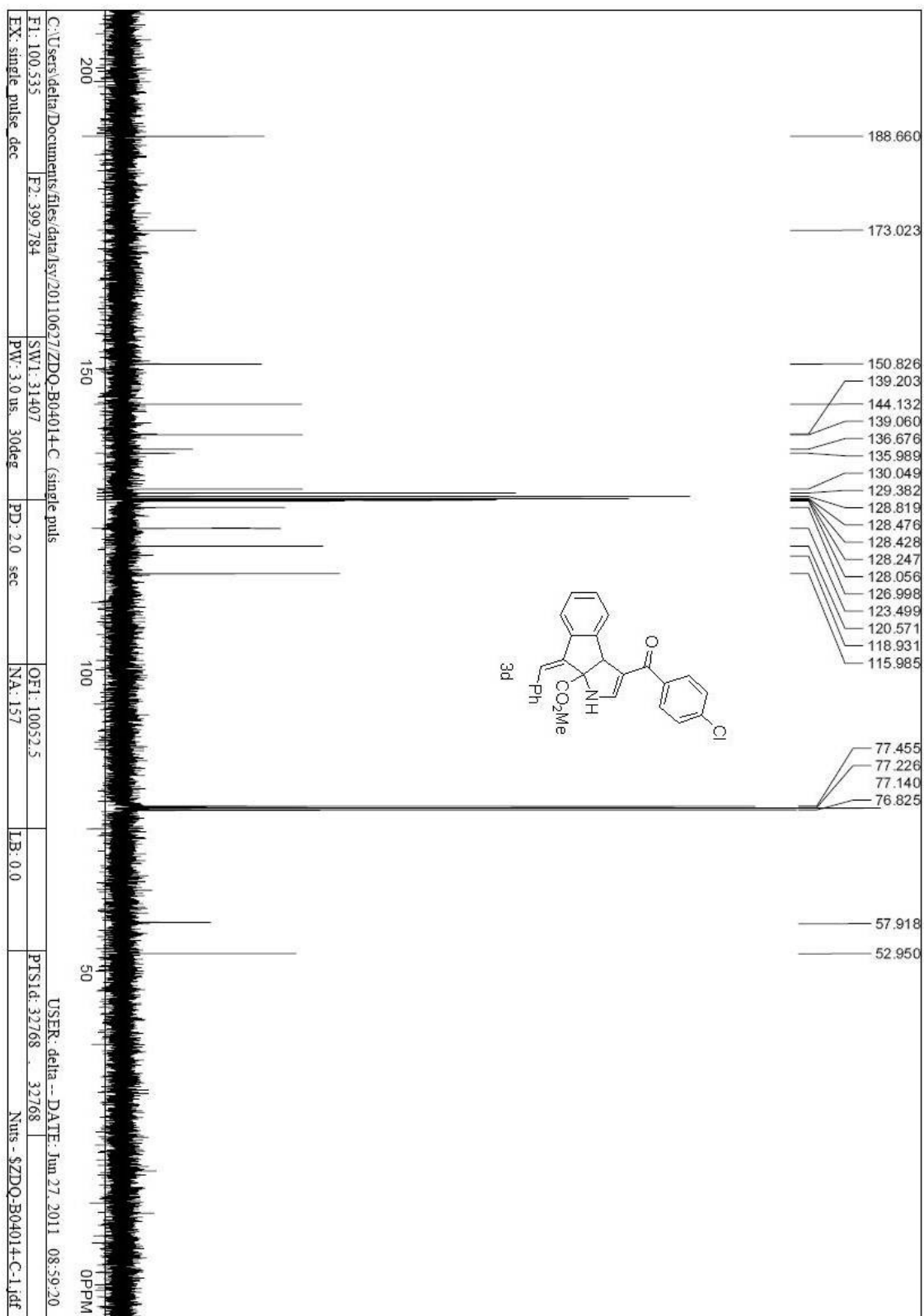


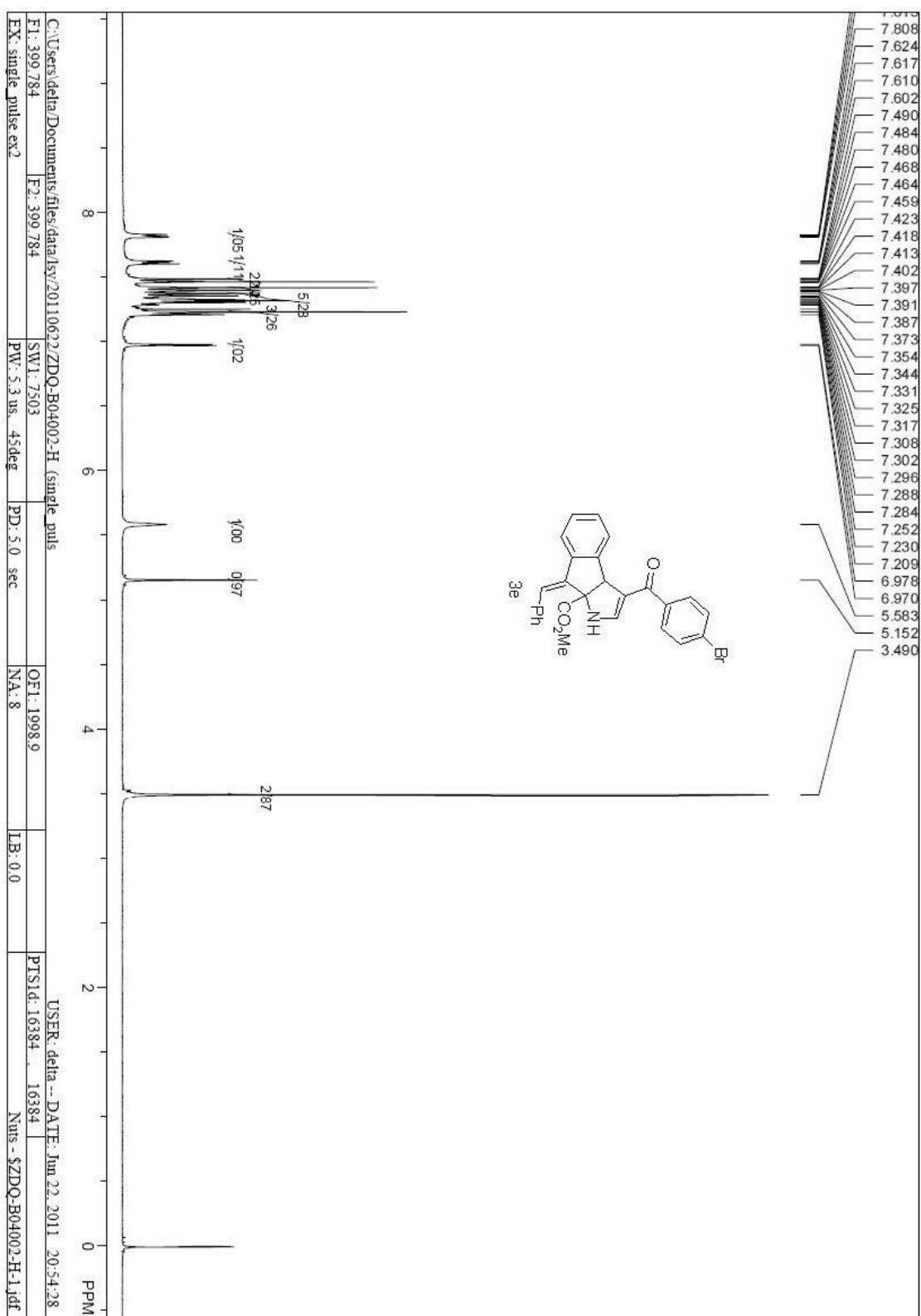


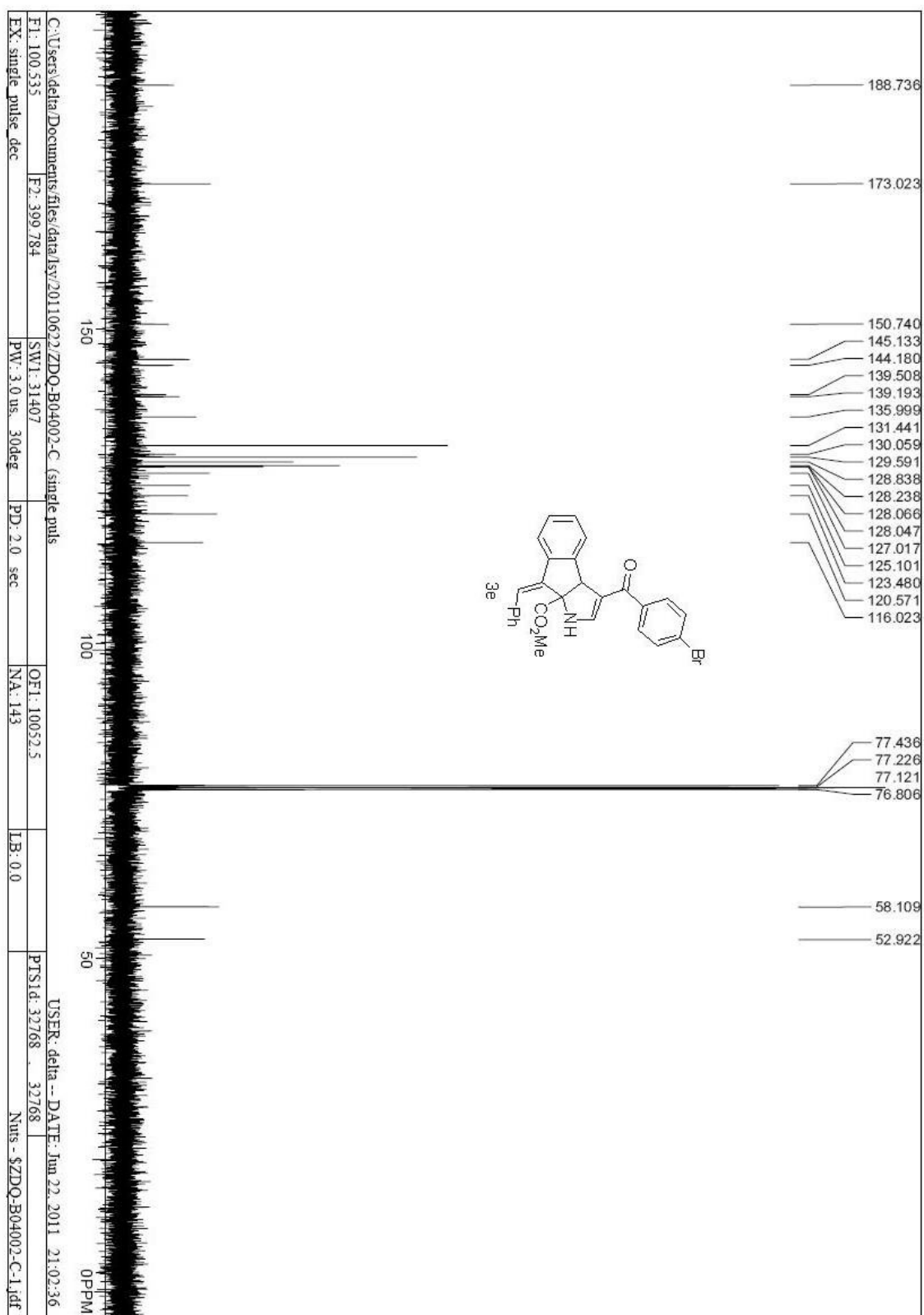


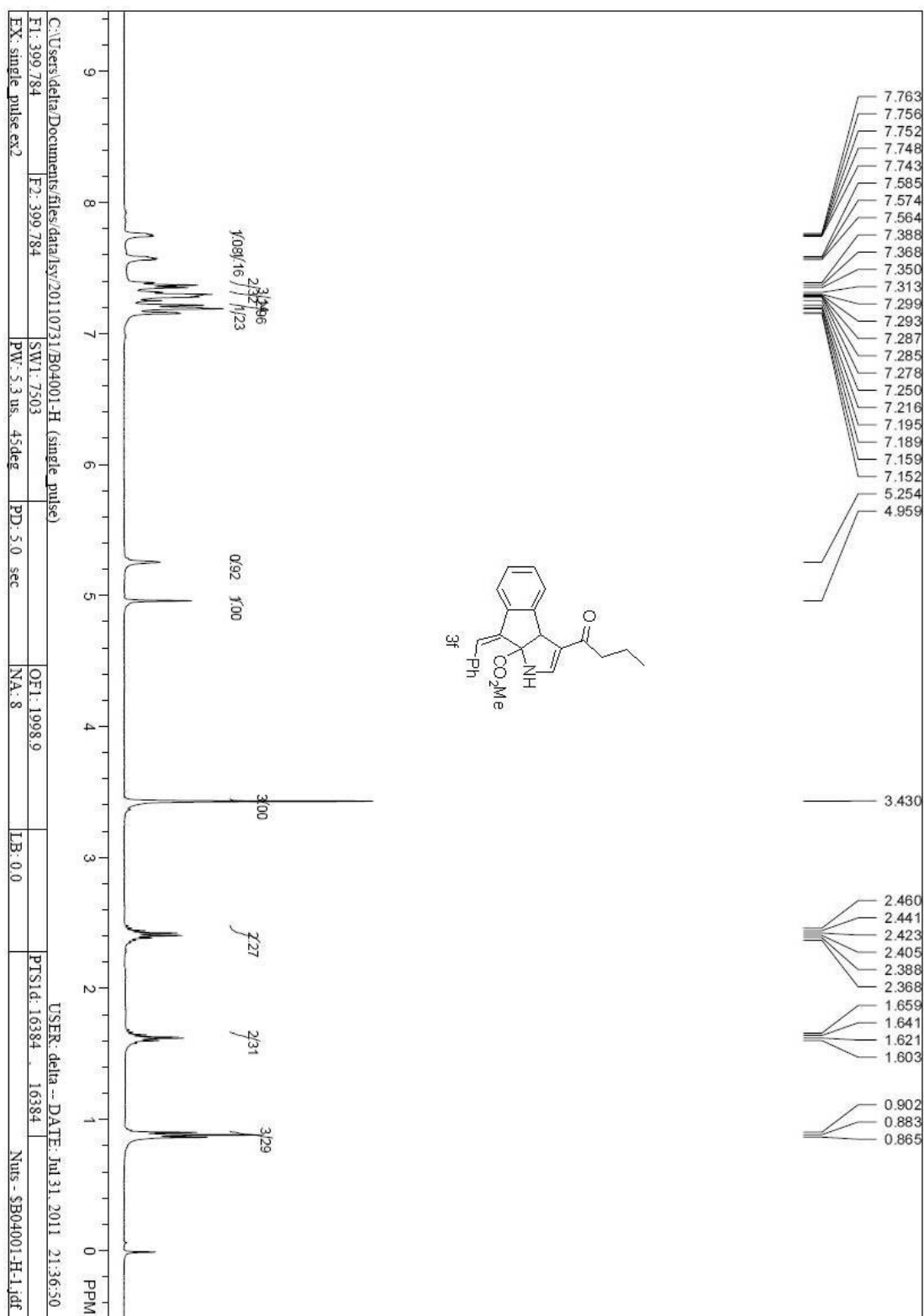


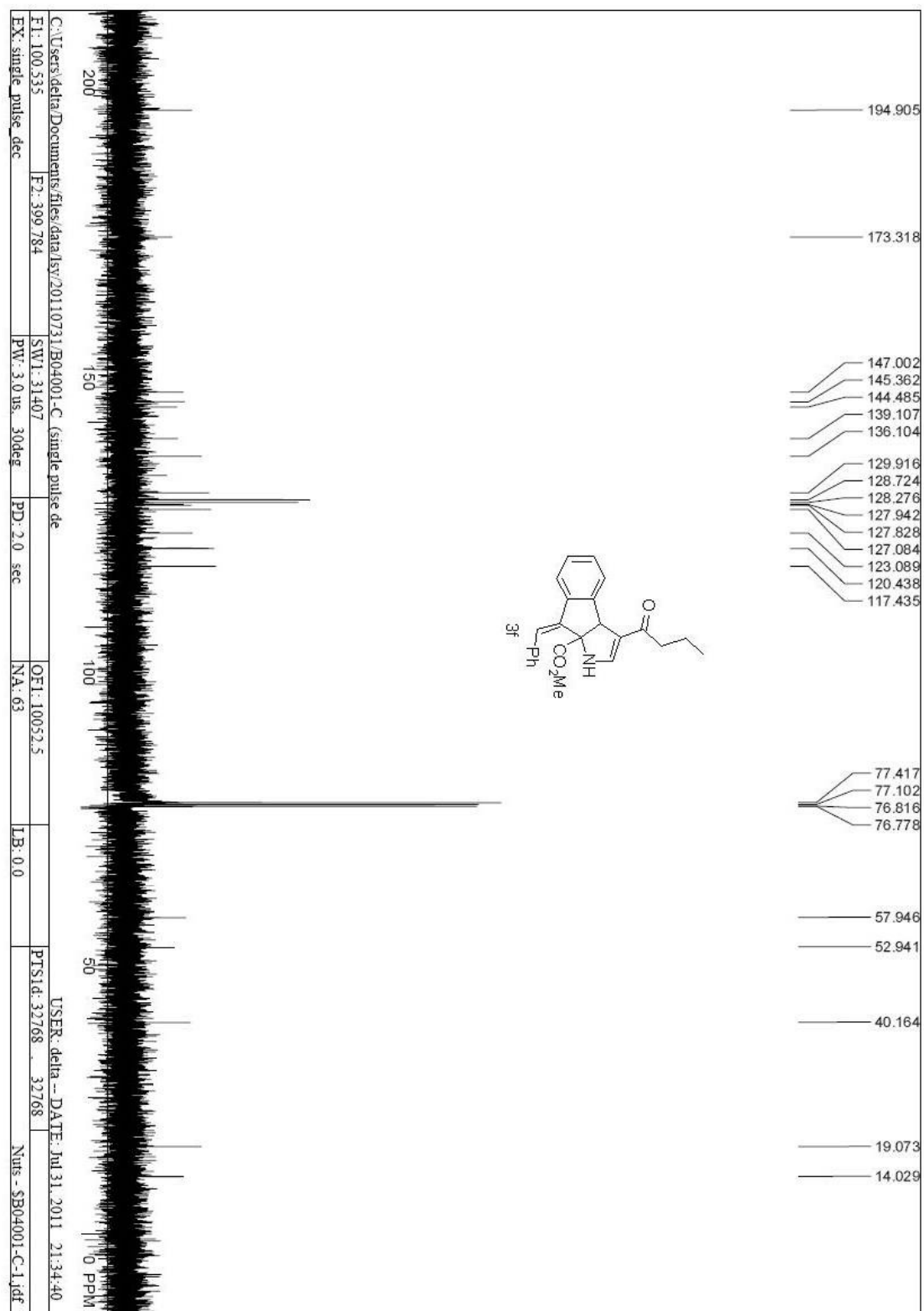


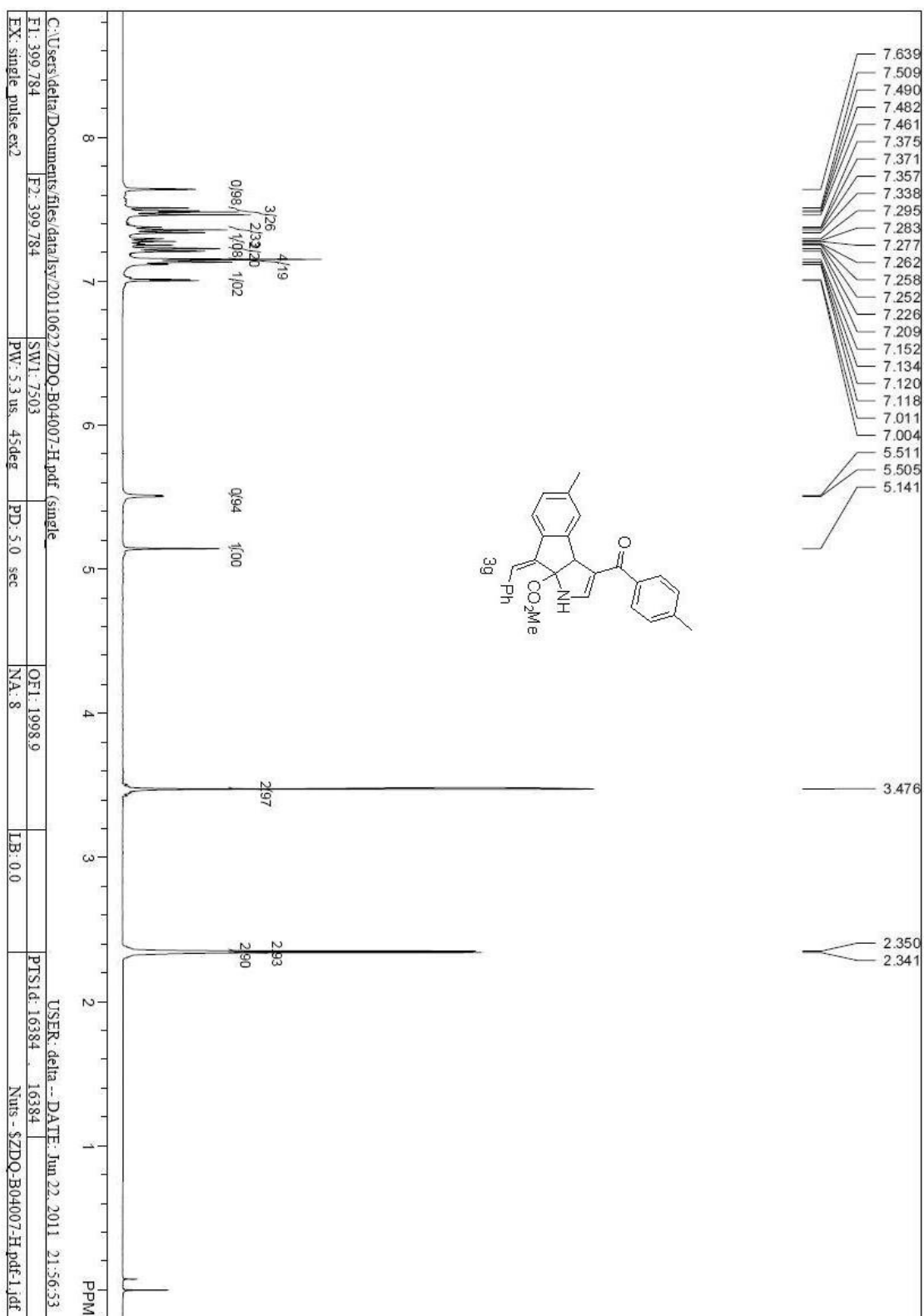


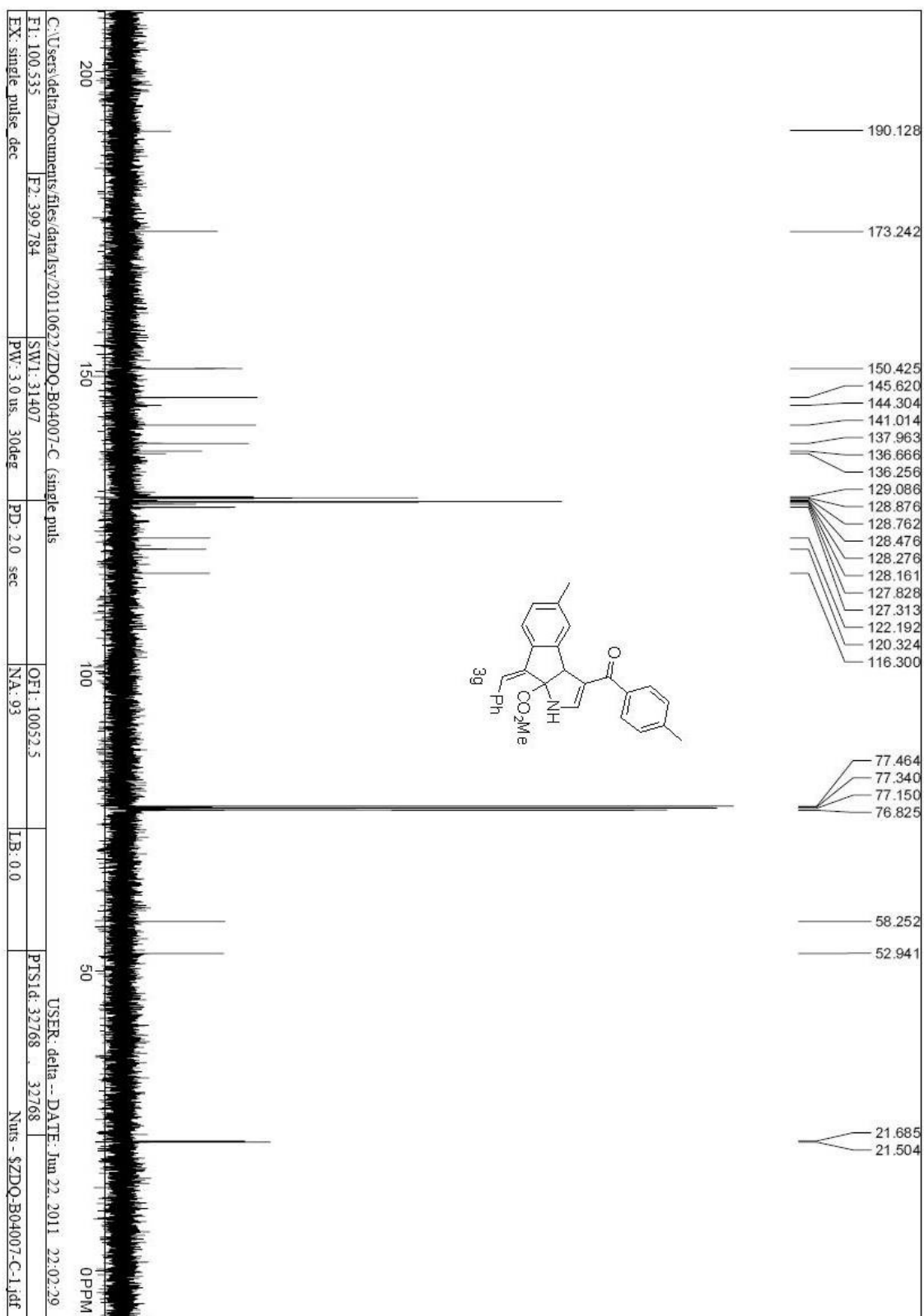


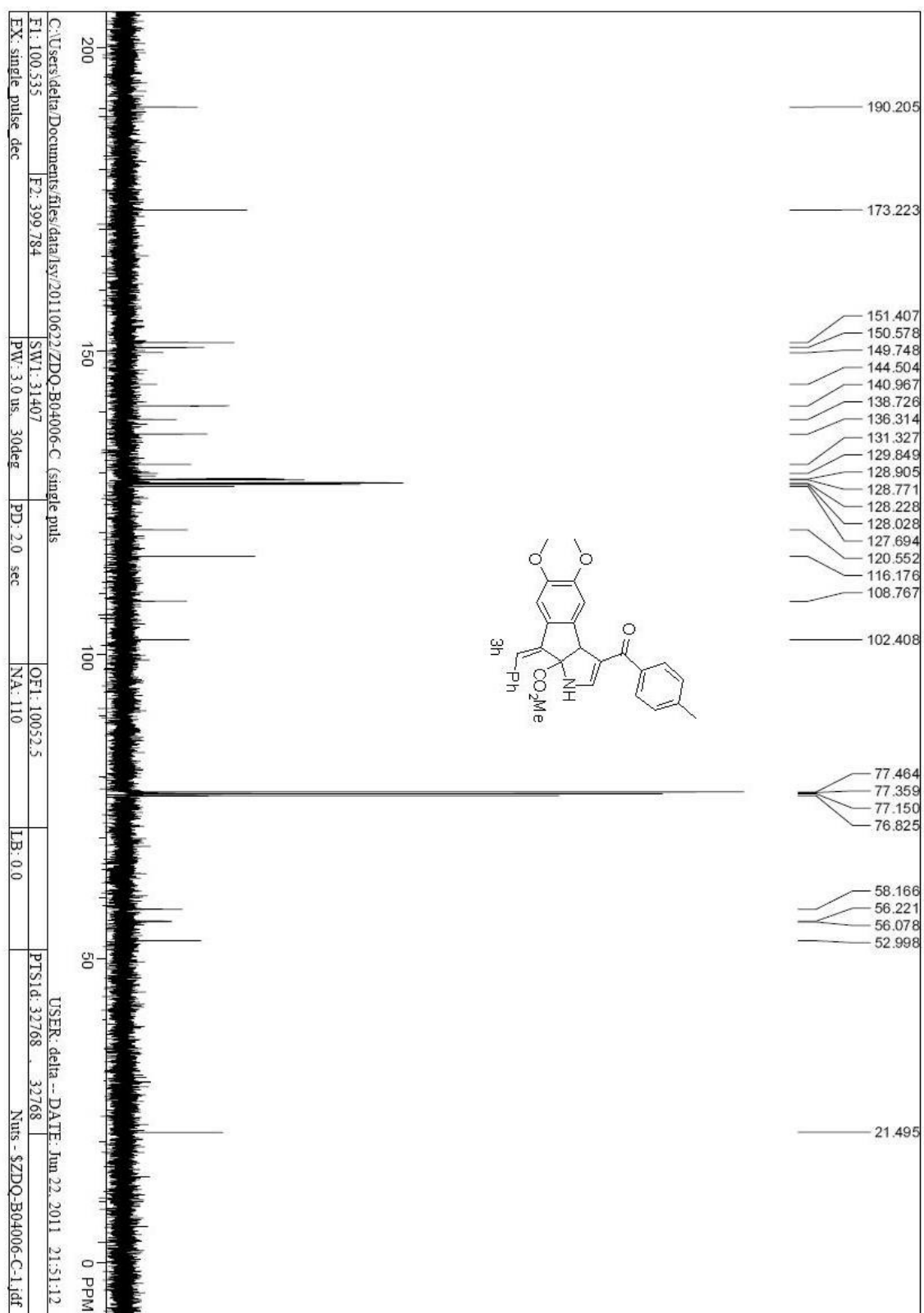


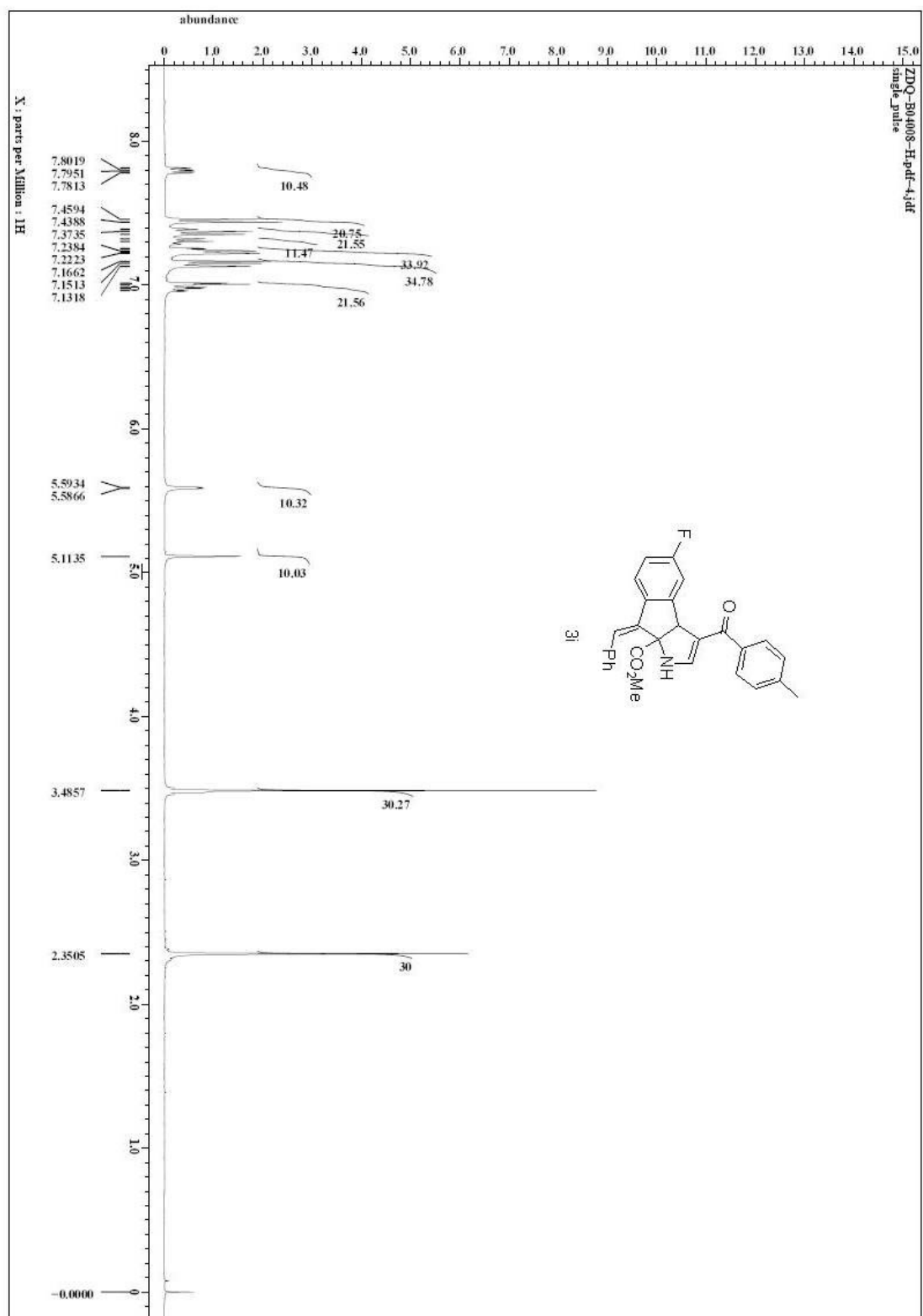


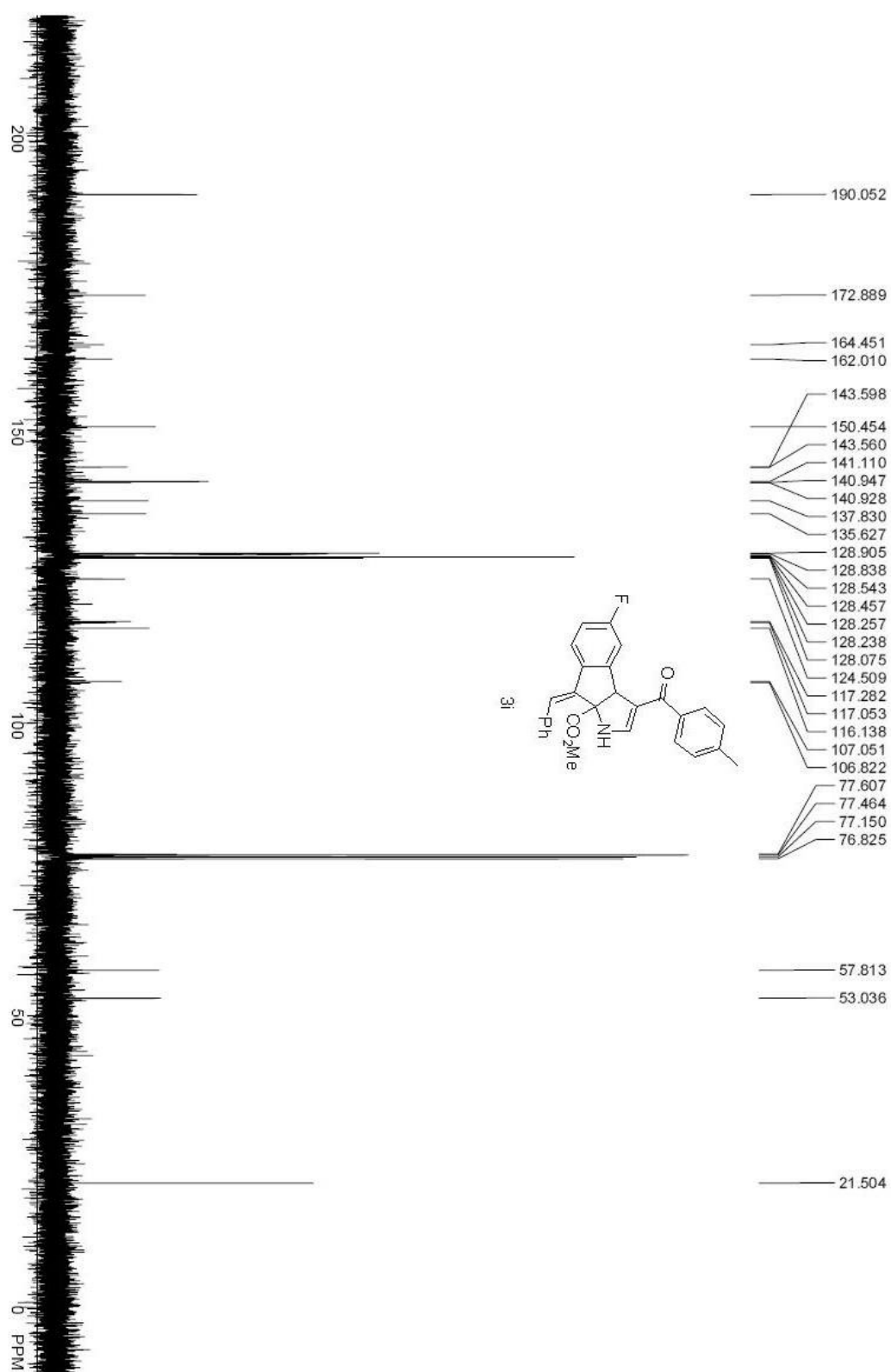


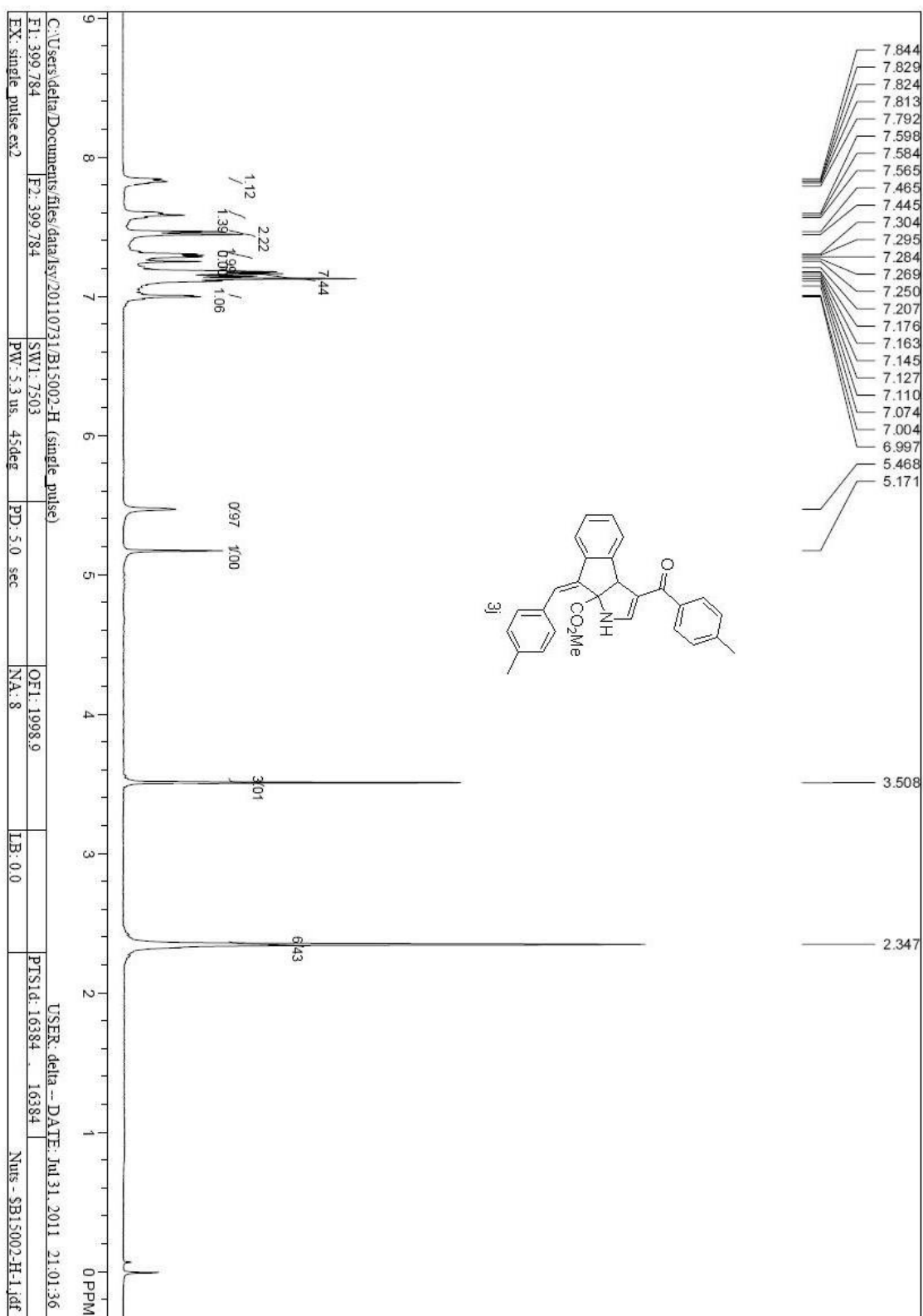


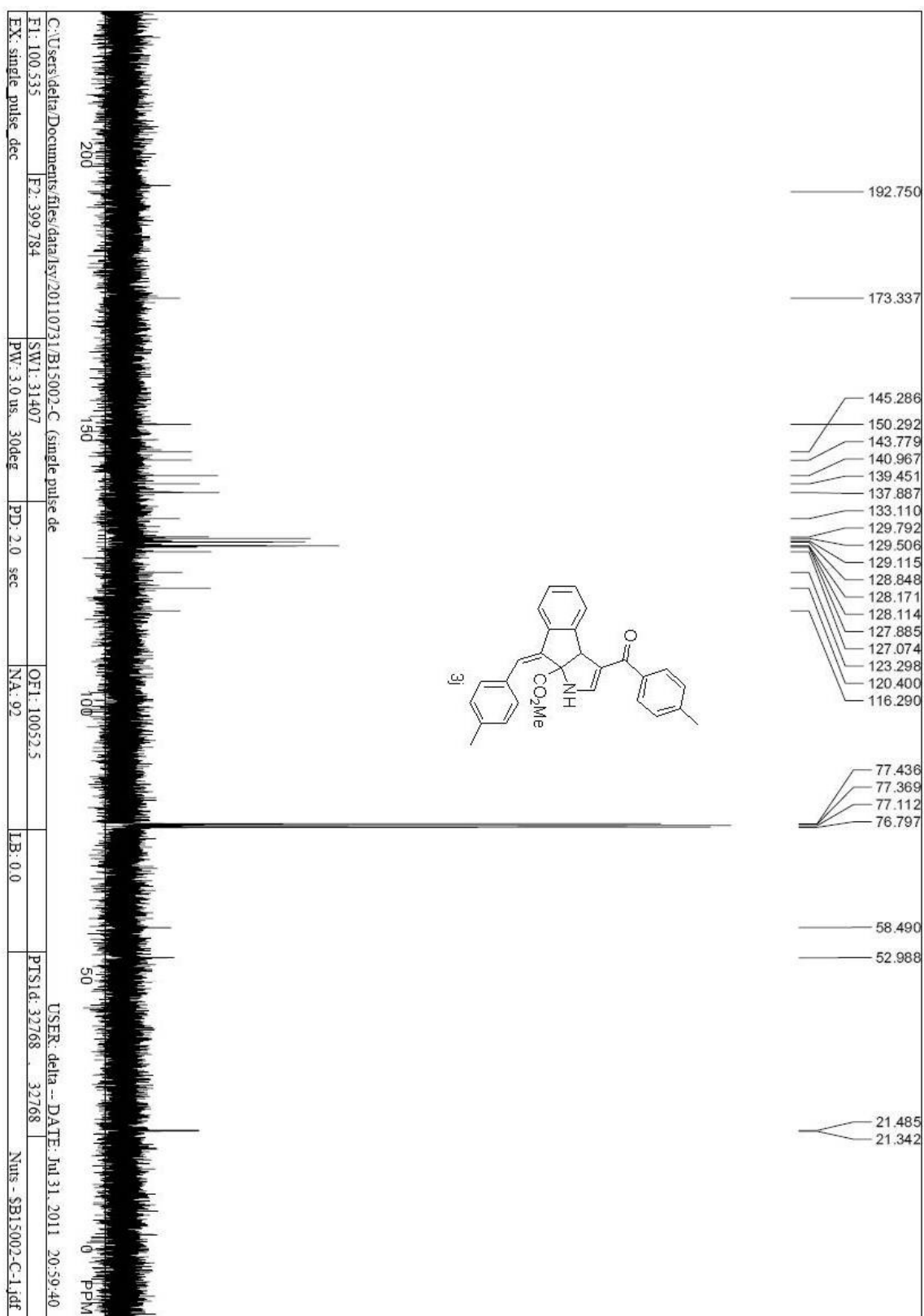


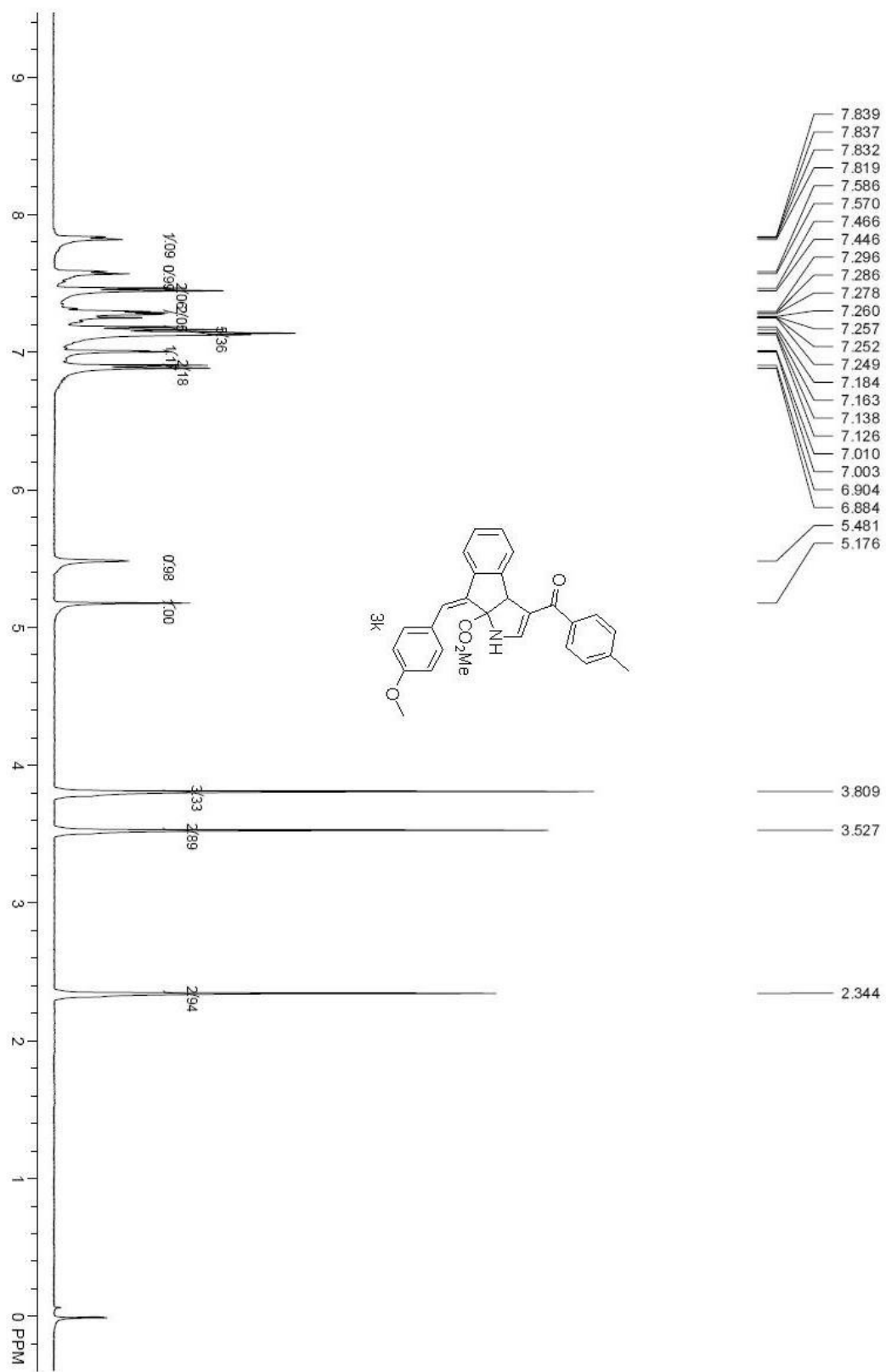


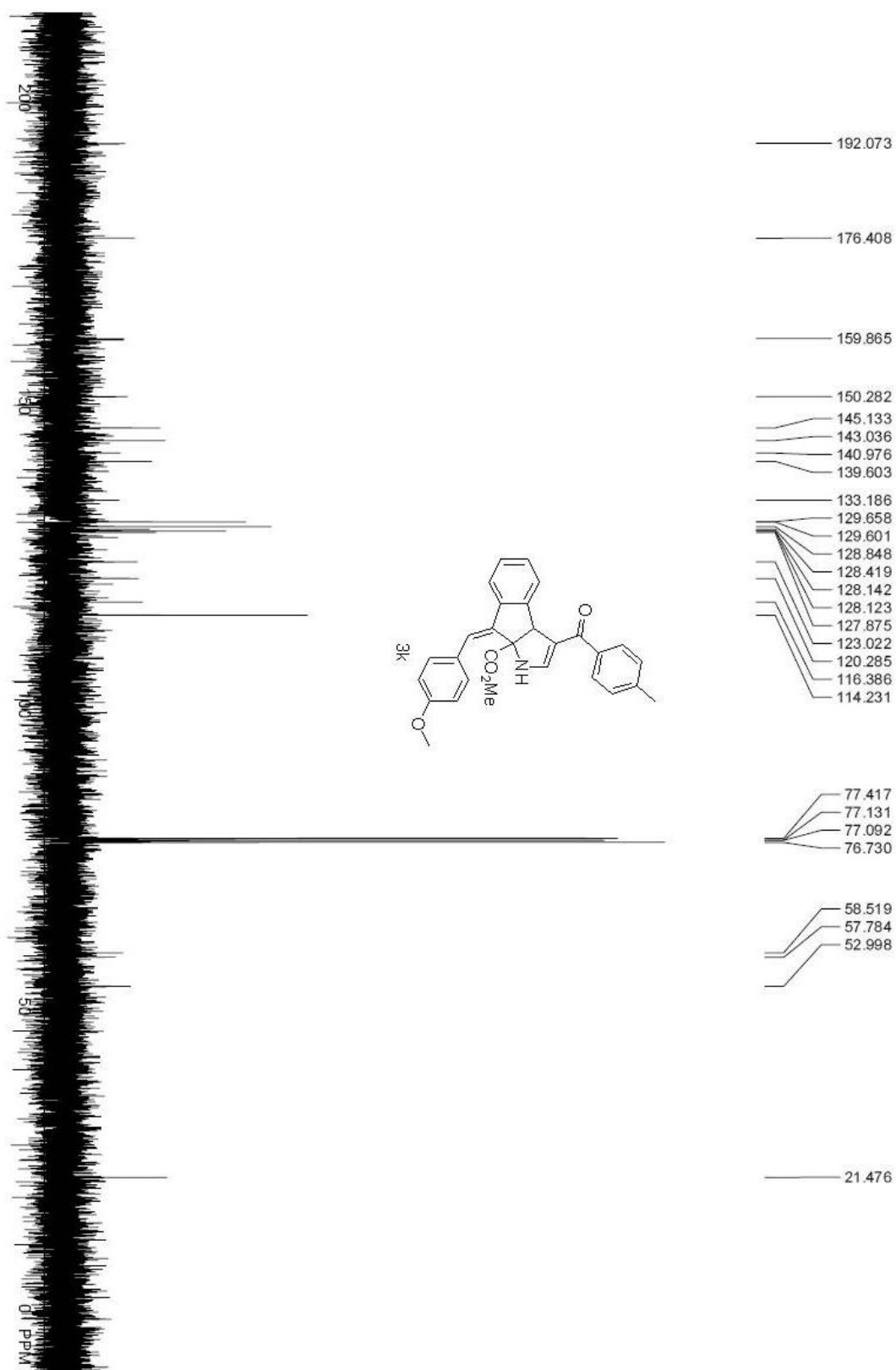


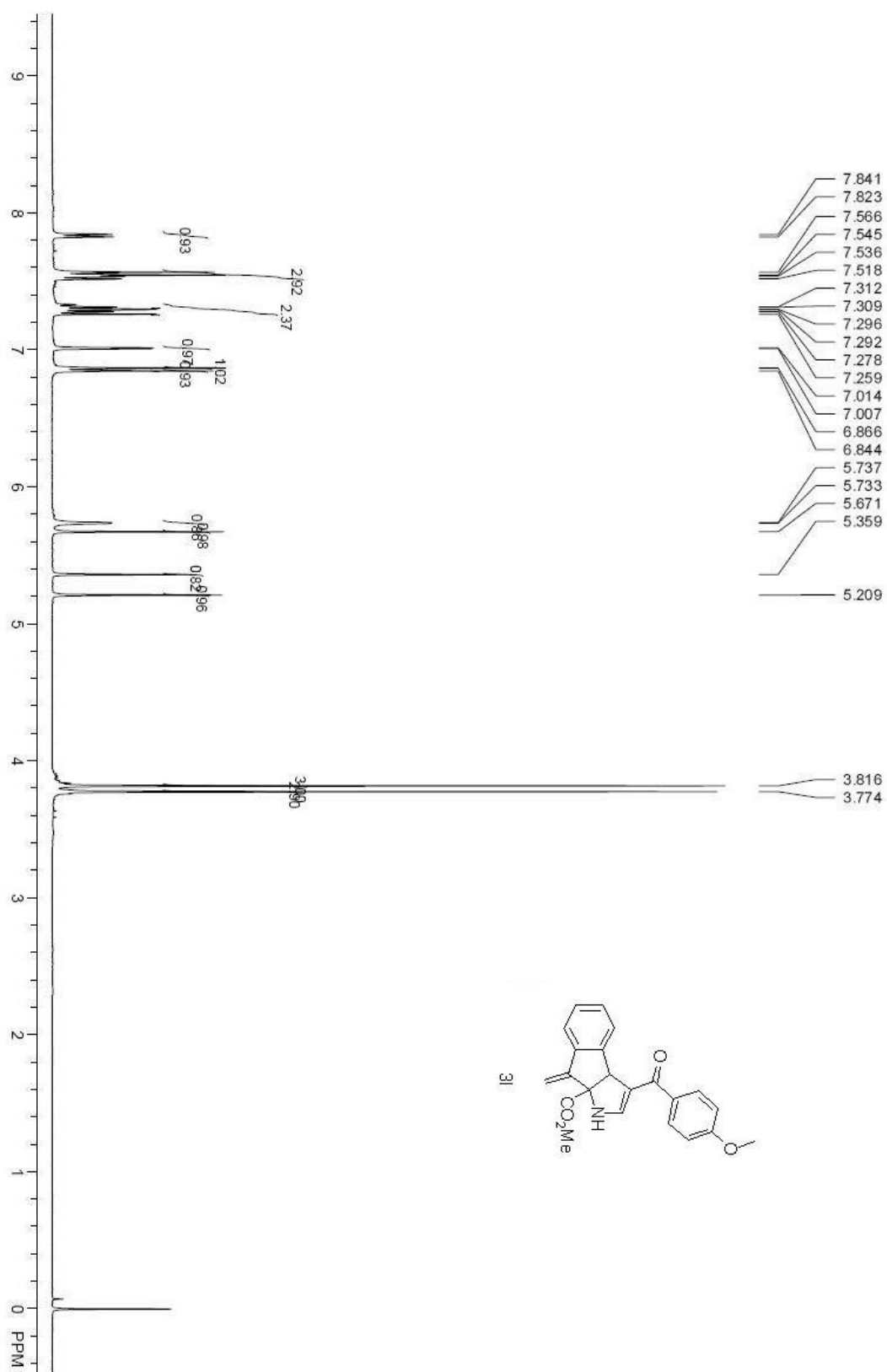


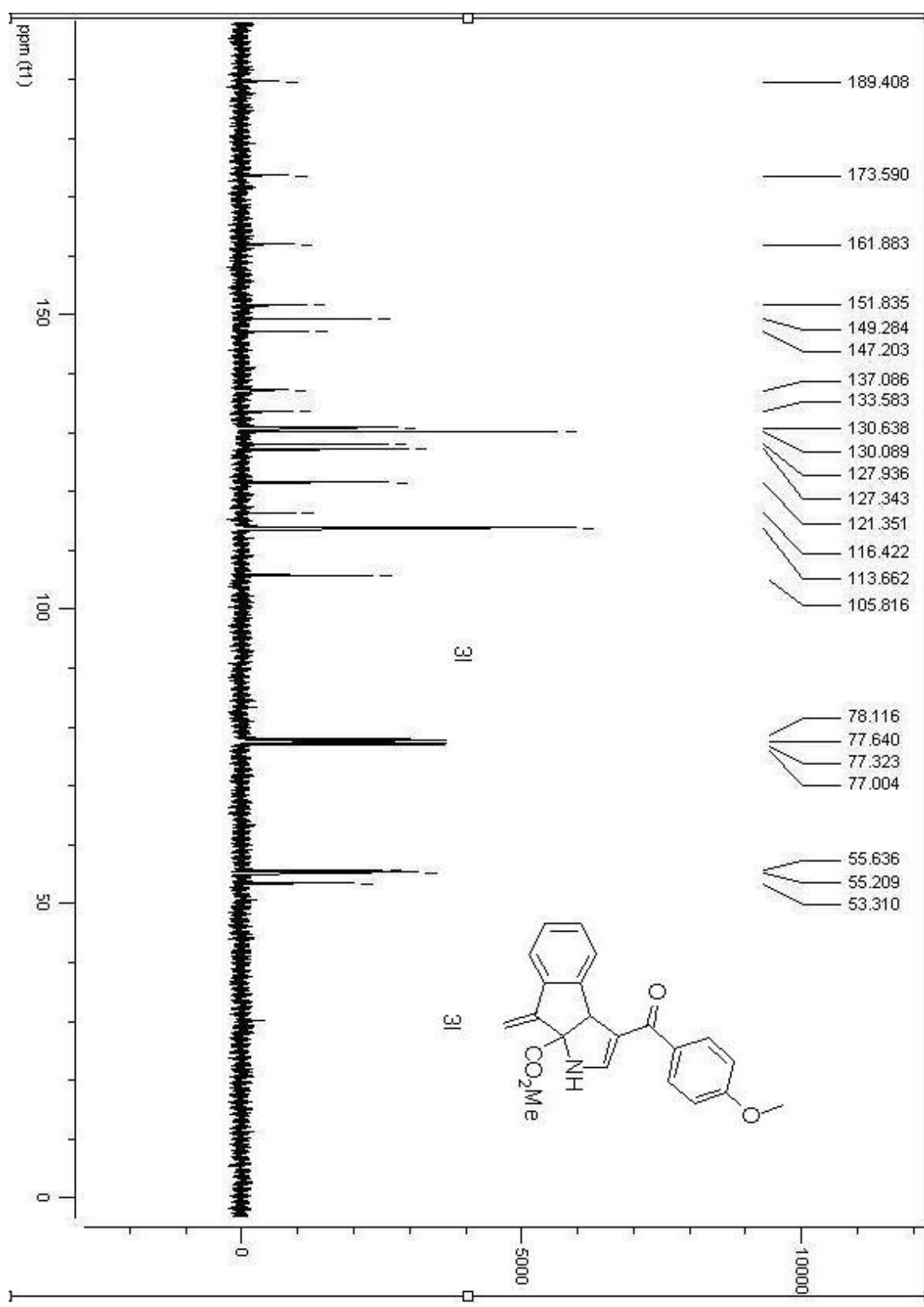


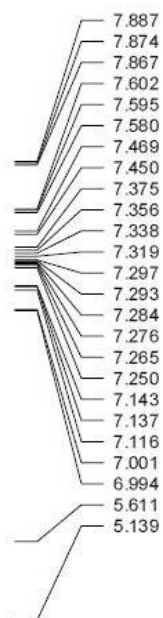












2.338

1.200

