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Supporting Information

**Synthesis of 6*H*-Indolo[2,3-*b*][1,6]naphthyridines and Related Compounds as the 5-Aza
Analogues of Ellipticine Alkaloids**

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Methyl 2-[(1-Cyclohexenyl)ethynyl]benzoate (12c). The same procedure was repeated as described for **12a** except that a degassed solution of 2.43 g of 1-ethynylcyclohexene (22.9 mmol) in 10 mL of DMF was added via cannula to a degassed solution of 1.053 g of Pd(PPh₃)₂Cl₂ (1.50 mmol), 0.285 g of CuI (1.50 mmol), 3.931 g of **11** (15.0 mmol), and 7.84 mL of *N,N*-diisopropylethylamine (45.0 mmol) in 30 mL of DMF to afford **12c** (3.27 g, 13.63 mmol, 91%) as a light yellow liquid: IR (neat) 2201, 1731, 1594, 756 cm⁻¹; ¹H δ 7.91 (1 H, dd, *J* = 7.8 and 1.4 Hz), 7.52 (1 H, dd, *J* = 7.7 and 1.5 Hz), 7.42 (1 H, td, *J* = 7.5 and 1.5 Hz), 7.30 (1 H, td, *J* = 7.5 and 1.5 Hz), 6.27 (1 H, tt, *J* = 4.1 and 1.9 Hz), 3.91 (3 H, s), 2.25 (2 H, m), 2.15 (2 H, m), 1.65 (4 H, m); ¹³C δ 166.9, 136.0, 133.8, 131.6, 131.5, 130.3, 127.3, 124.2, 120.9, 96.4, 85.7, 52.1, 29.0, 25.8, 22.3, 21.5; MS *m/z* 240 (M⁺), 225, 210, 197, 179; HRMS calcd for C₁₆H₁₆O₂ 240.1150, found 240.1148.

2-[(1-Cyclohexenyl)ethynyl]benzoic Acid (13c). The same procedure was repeated as described for **13a** except that 2.98 g (12.4 mmol) of **12c** in 100 mL of THF was treated with 46 mL of a 1 N NaOH solution to afford **13c** (2.42 g, 10.7 mmol, 86%) as pale yellow needles: IR 3300–2400 (br), 2201, 1694, 752 cm^{-1} ; ^1H δ 9.8 (1 H, br OH) 8.08 (1 H, dd, $J = 7.7$ and 1.0 Hz), 7.56 (1 H, dd, $J = 7.6$ and 1.4 Hz), 7.49 (1 H, td, $J = 7.3$ and 1.4 Hz), 7.36 (1 H, td, $J = 7.6$ and 1.7 Hz), 6.30 (1 H, tt, $J = 4.1$ and 1.7 Hz), 2.28 (2 H, m), 2.17 (2 H, m), 1.67 (4 H, m); ^{13}C δ 171.0, 136.5, 133.9, 132.4, 131.3, 130.3, 127.5, 124.6, 120.8, 97.7, 85.4, 28.8, 25.9, 22.3, 21.5; MS m/z 226 (M^+), 211, 197, 181, 165; HRMS calcd for $\text{C}_{15}\text{H}_{14}\text{O}_2$ 226.0994, found 226.0992.

2-[(1-Cyclohexenyl)ethynyl]phenyl Isocyanate (6c). The same procedure was repeated as described for **6a** except that 2.14 g (9.46 mmol) of **13c** was treated with 1.32 mL of triethylamine and 2.03 mL (9.46 mmol) of DPPA to afford **6c** (1.614 g, 7.24 mmol, 77%) as a light yellow liquid: IR (neat) 2256, 1593, 1505, 753 cm^{-1} ; ^1H δ 7.41 (1 H, dd, $J = 7.7$ and 1.7 Hz), 7.21 (1 H, td, $J = 7.7$ and 1.7 Hz), 7.12 (1 H, td, $J = 7.5$ and 1.4 Hz), 7.01 (1 H, dd, $J = 7.9$ and 1.2 Hz), 6.34 (1 H, tt, $J = 4.0$ and 1.7 Hz), 2.27 (2 H, m), 2.17 (2 H, m), 1.67 (4 H, m); ^{13}C δ 136.5, 134.5, 132.1, 128.7, 127.2, 125.3, 123.4, 121.5, 120.3, 99.4, 82.2, 28.6, 25.8, 22.2, 21.4; MS m/z 223 (M^+), 194, 180, 167; HRMS calcd for $\text{C}_{15}\text{H}_{13}\text{NO}$ 223.0997, found 223.0988.

11-(1-Cyclohexenyl)-6H-indolo[2,3-*b*][1,6]naphthyridine (5c). The same procedure was repeated as described for **5a** except that 0.361 g (1.02 mmol) of **14** was treated with 0.227 g (1.02 mmol) of **6c**. Purification by flash column chromatography (silica gel/10% ethanol and 20% diethyl ether in hexanes) afforded **5c** (0.253 g, 0.846 mmol, 83%) as yellow crystals: mp 218.5–219 °C; IR 1596, 1404, 726 cm^{-1} ; ^1H δ 11.12 (1 H, br s, NH), 9.50 (1 H, s), 8.73 (1 H, d, $J = 5.9$ Hz), 8.14 (1 H, d, $J = 7.9$ Hz), 7.91 (1 H, d, $J = 5.9$ Hz), 7.54–7.53 (2 H, m), 7.31 (1 H, m),

6.06 (1 H, m), 2.6–2.4 (4 H, m), 2.1–1.9 (4 H, m); ^{13}C δ 155.4, 151.3, 149.2, 146.4, 145.9, 140.9, 132.2, 129.6, 128.4, 123.5, 121.0, 119.8, 119.2, 116.5, 111.1, 29.3, 25.4, 23.0, 22.1; MS m/z 299 (M^+), 284, 270, 256, 244; HRMS calcd for $\text{C}_{20}\text{H}_{17}\text{N}_3$ 299.1422, found 299.1417.

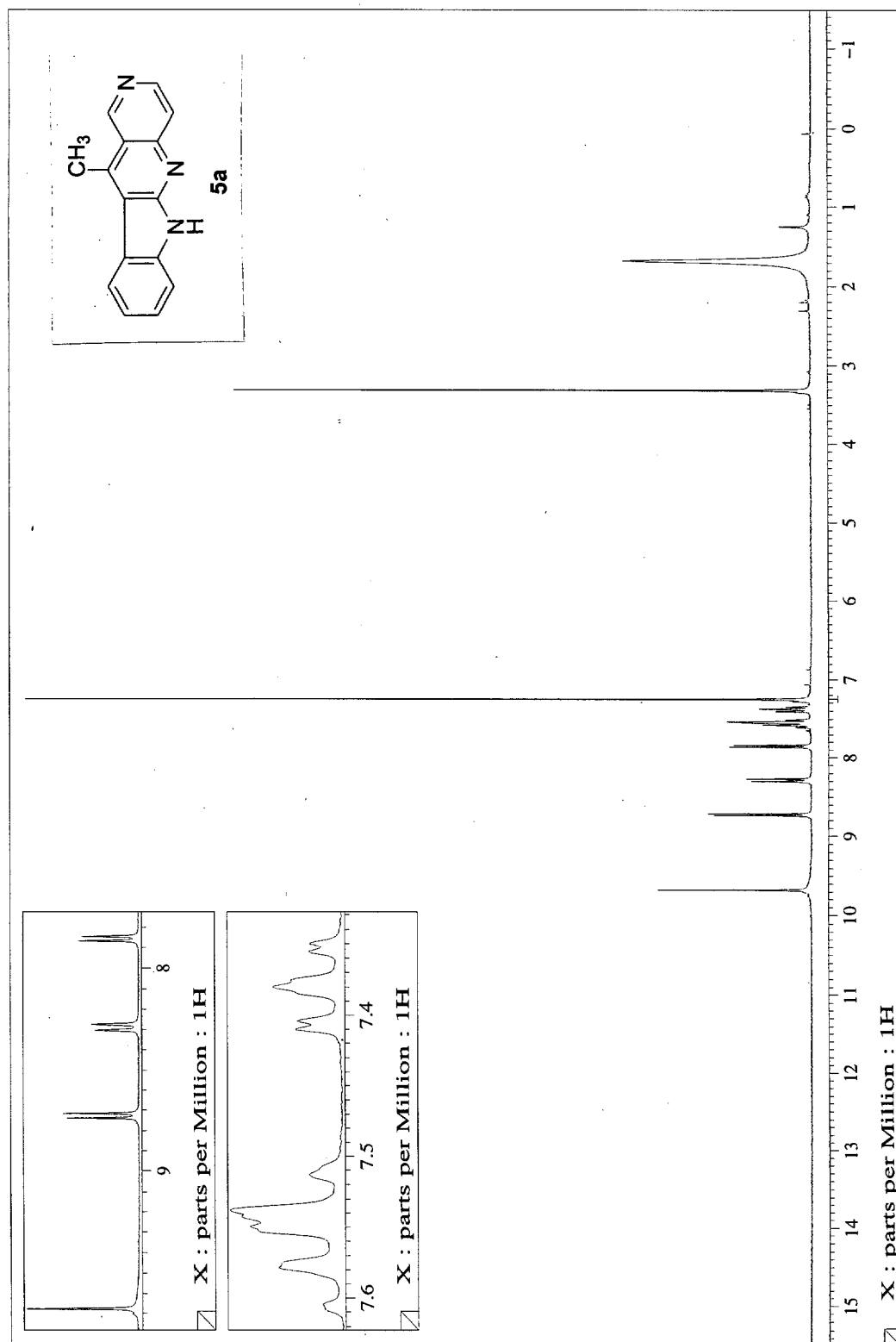
11-Phenyl-6*H*-indolo[2,3-*b*][1,6]naphthyridine (5d). The same procedure was repeated as described for **5a** except that 0.522 g of **14** (1.474 mmol) was treated with 0.323 g of **6d**^{9a} (1.474 mmol). Purification by flash chromatography (silica gel/10% ethanol and 20% diethyl ether in hexanes) afforded **5d** (0.253 g, 0.86 mmol, 58%) as a light yellow solid: mp 244–245 °C; IR 1610, 1594, 731 cm^{-1} ; ^1H δ 13.62 (1 H, br s, NH), 8.94 (1 H, s), 8.56 (1 H, d, $J = 5.9$ Hz), 7.81 (1 H, d, $J = 5.9$ Hz), 7.73–7.62 (3 H, m), 7.45–7.39 (2 H, m), 7.18 (1 H, d, $J = 7.7$ Hz), 7.15–7.02 (2 H, m), 6.91 (1 H, t, $J = 7.6$ Hz); ^{13}C δ 154.7, 151.3, 148.8, 145.5, 143.3, 141.2, 134.1, 129.4, 129.2, 129.0, 128.3, 122.9, 120.32, 120.27, 119.2, 118.9, 117.5, 111.0; MS m/z 295 (M^+), 191; HRMS calcd for $\text{C}_{20}\text{H}_{13}\text{N}_3$ 295.1109, found 295.1124.

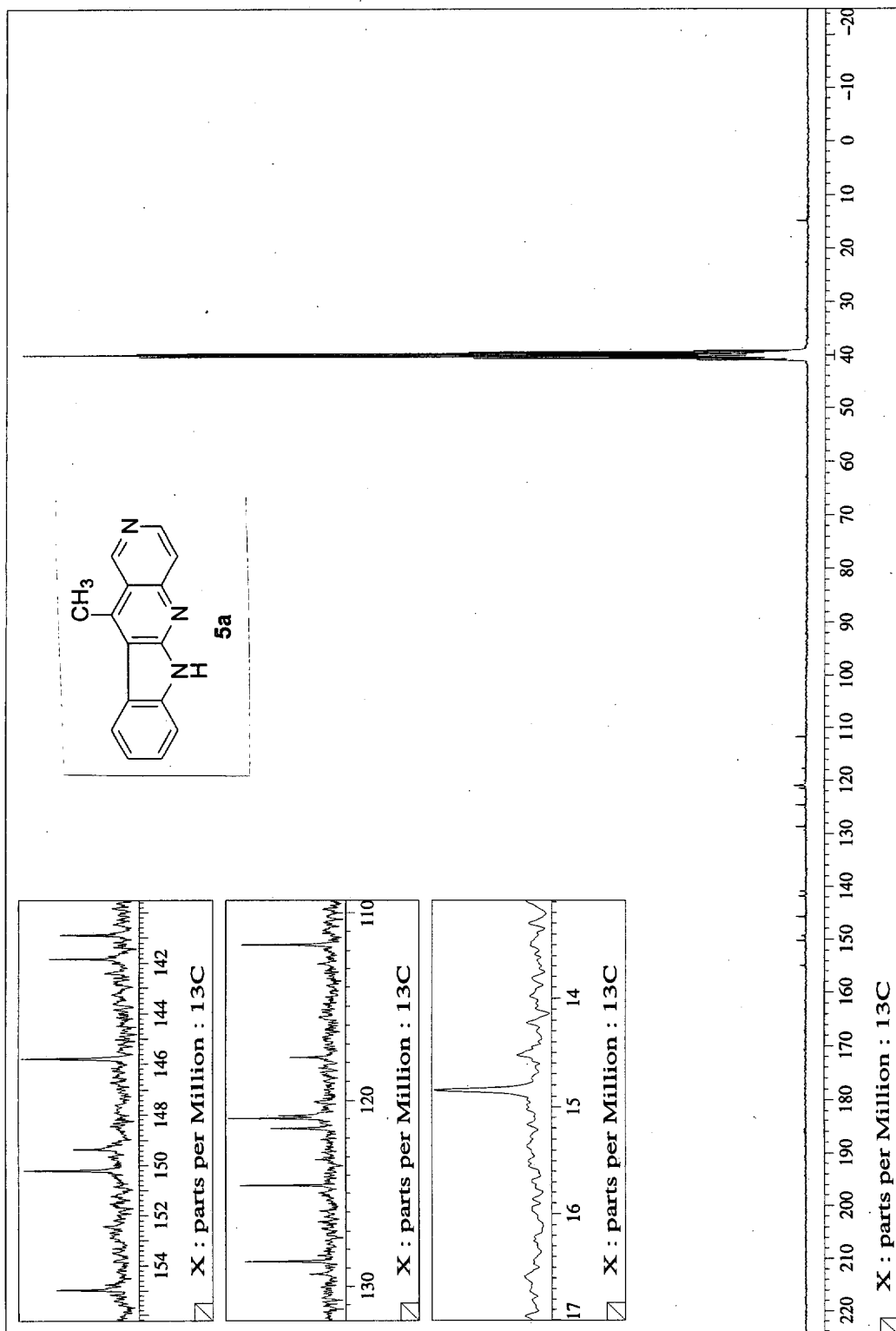
11-(1-Cyclohexenyl)-6*H*-indolo[2,3-*b*][1,5]naphthyridine (25c) and 5-(1-Cyclohexenyl)-10*H*-indolo[2,3-*b*][1,7]naphthyridine (26c). The same procedure was repeated as described for **25b** and **26b** except that 0.223 g of **6c** (1.00 mmol) was treated with 0.354 g (1.00 mmol) of **20**. Purification by flash chromatography (silica gel/10% ethanol and 20% diethyl ether in hexanes) afford **25c** (0.233 g, 0.78 mmol, 78%) and **26c** (0.026 g, 0.086 mmol, 9%) as yellow crystalline needles. **25c**: mp 229–230 °C (dec); IR 1606, 1398 cm^{-1} ; ^1H δ 10.73 (1 H, br s, NH), 8.97 (1 H, dd, $J = 3.9$ and 1.7 Hz), 8.39 (1 H, dd, $J = 8.4$ and 1.7 Hz), 8.33 (1 H, d, $J = 7.9$ Hz), 7.63 (1 H, dd, $J = 8.6$ and 4.1 Hz), 7.57–7.47 (2 H, m), 7.27 (1 H, ddd, $J = 7.8, 6.4,$ and 2.1 Hz), 6.07 (1 H, m), 2.39 (1 H, d, $J = 16$ Hz), 2.46 (2 H, br), 2.35 (1 H, d, $J = 16$ Hz), 2.2–1.8 (4 H, m); ^{13}C δ 153.3, 146.6, 146.5, 141.9, 141.2, 138.9, 134.4, 133.8, 128.1, 127.7, 123.8, 122.9, 121.2, 120.1,

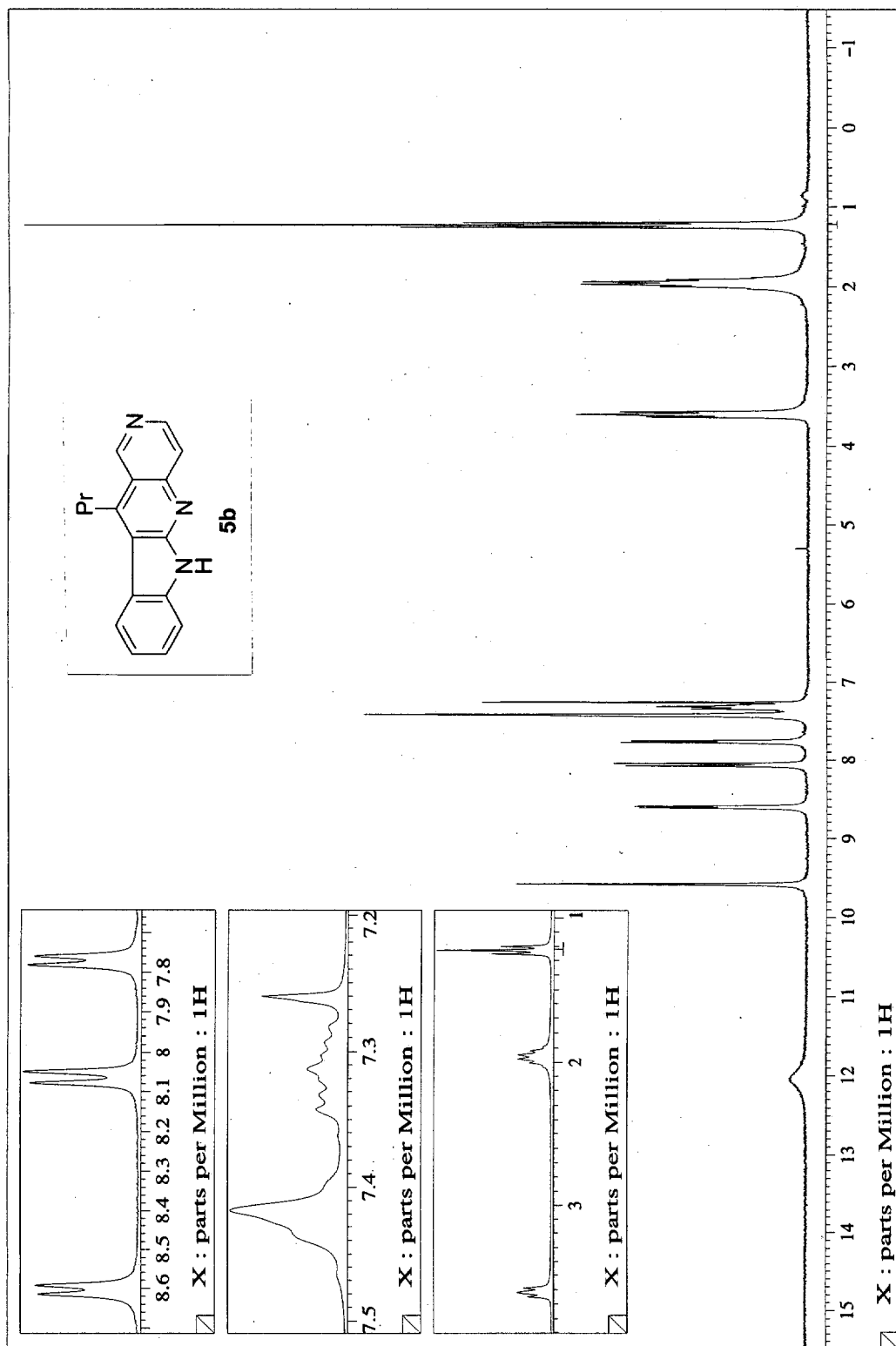
118.5, 110.8, 29.2, 25.4, 23.0, 22.1; MS m/z 299 (M^+), 270, 257, 244, 226; HRMS calcd for $C_{20}H_{17}N_3$ 299.1422, found 299.1425; Anal. Calcd for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72; N, 14.04. Found: C, 80.11; H, 5.71; N, 13.91. **26c**: mp 235–236 °C; IR 1607, 1375 cm^{-1} ; 1H δ 9.51 (1 H, d, $J = 1$ Hz), 9.34 (1 H, br s, NH), 8.56 (1 H, d, $J = 5.9$ Hz), 8.18 (1 H, d, $J = 7.9$ Hz), 7.92 (1 H, dd, $J = 5.9$ and 1 Hz), 7.62–7.52 (2 H, m), 7.31 (1 H, ddd, $J = 8.1, 6.6,$ and 1.5 Hz), 6.02 (1 H, m), 2.58–2.32 (4 H, m), 2.12–1.93 (4 H, m); ^{13}C δ 153.9, 151.0, 144.0, 141.9, 141.2, 140.0, 132.6, 129.3, 129.1, 126.4, 124.0, 120.7, 120.5, 118.9, 118.4, 111.2, 28.8, 25.4, 23.0, 22.1; MS m/z 299 (M^+), 270, 257, 244; HRMS calcd for $C_{20}H_{17}N_3$ 299.1422, found 299.1418.

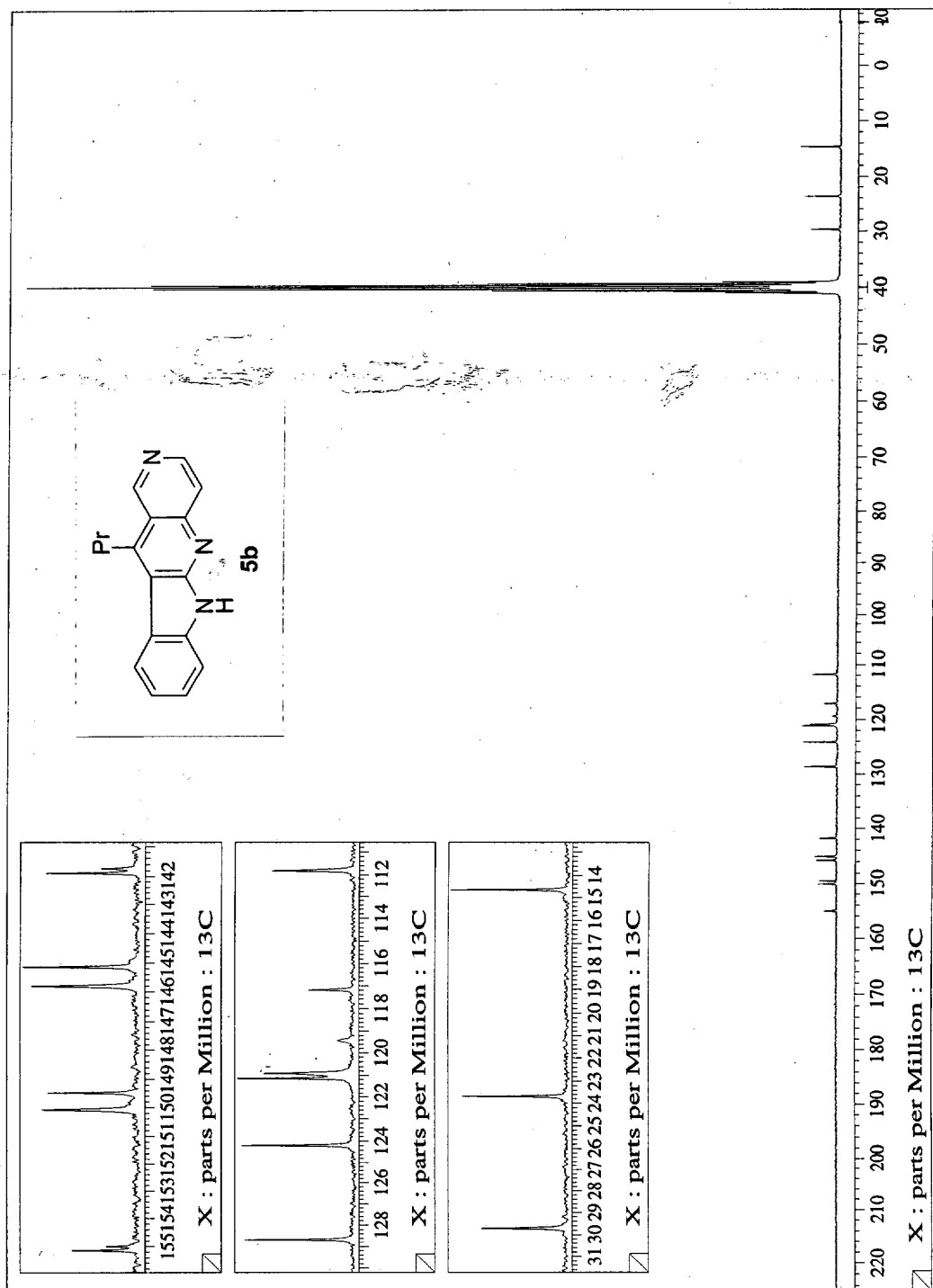
11-Phenyl-6H-indolo[2,3-*b*][1,5]naphthyridine (25d) and 5-Phenyl-10H-indolo[2,3-*b*][1,7]naphthyridine (26d). The same procedure was repeated as described for **25b** and **26b** except that 0.219 g (1.00 mmol) of **6d**^{9a} was treated with 0.354 g (1.00 mmol) of **20**. Purification by flash chromatography (silica gel/10% ethanol and 20% diethyl ether in hexanes) afforded **25d** (0.220 g, 0.75 mmol, 75%) and **26d** (0.050 g, 0.17 mmol, 17%) as yellow solids. **25d**: mp 273–274 °C; IR 1611, 1402, 730, 699 cm^{-1} ; 1H δ 9.55 (1 H, br s, NH), 8.93 (1 H, dd, $J = 4.1$ and 1.5 Hz), 8.43 (1 H, dd, $J = 8.4$ and 1.7 Hz), 7.7–7.6 (6 H, m), 7.48 (2 H, d, $J = 3.6$ Hz), 7.24 (1 H, d, $J = 8.1$ Hz), 7.04 (1 H, m); ^{13}C δ 152.7, 147.6, 143.6, 141.61, 141.55, 139.2, 135.5, 134.3, 129.7, 128.7, 128.6, 123.9, 123.3, 121.0, 120.4, 119.5, 110.8; MS m/z 295 (M^+), 294, 281; HRMS calcd for $C_{20}H_{12}N_3$ ($M-H$)⁺ 294.1031, found 294.1034. Anal. Calcd for $C_{20}H_{13}N_3$: C, 81.34; H, 4.44; N, 14.23. Found: C, 80.58; H, 4.39; N, 14.14. **26d**: mp 242–243 °C; IR 1611, 1377 cm^{-1} ; 1H δ 10.05 (1 H, br s, NH), 9.62 (1 H, s), 8.50 (1 H, d, $J = 5.9$ Hz), 7.73–7.66 (3 H, m), 7.62–7.48 (5 H, m), 7.20 (1 H, d, $J = 8.1$ Hz), 7.05 (1 H, ddd $J = 8.0, 6.5,$ and 1.5 Hz); ^{13}C δ 153.6, 151.1, 142.0, 141.3, 141.1, 140.5, 134.8, 129.4, 129.3, 129.2, 129.1, 126.8, 123.9, 120.5,

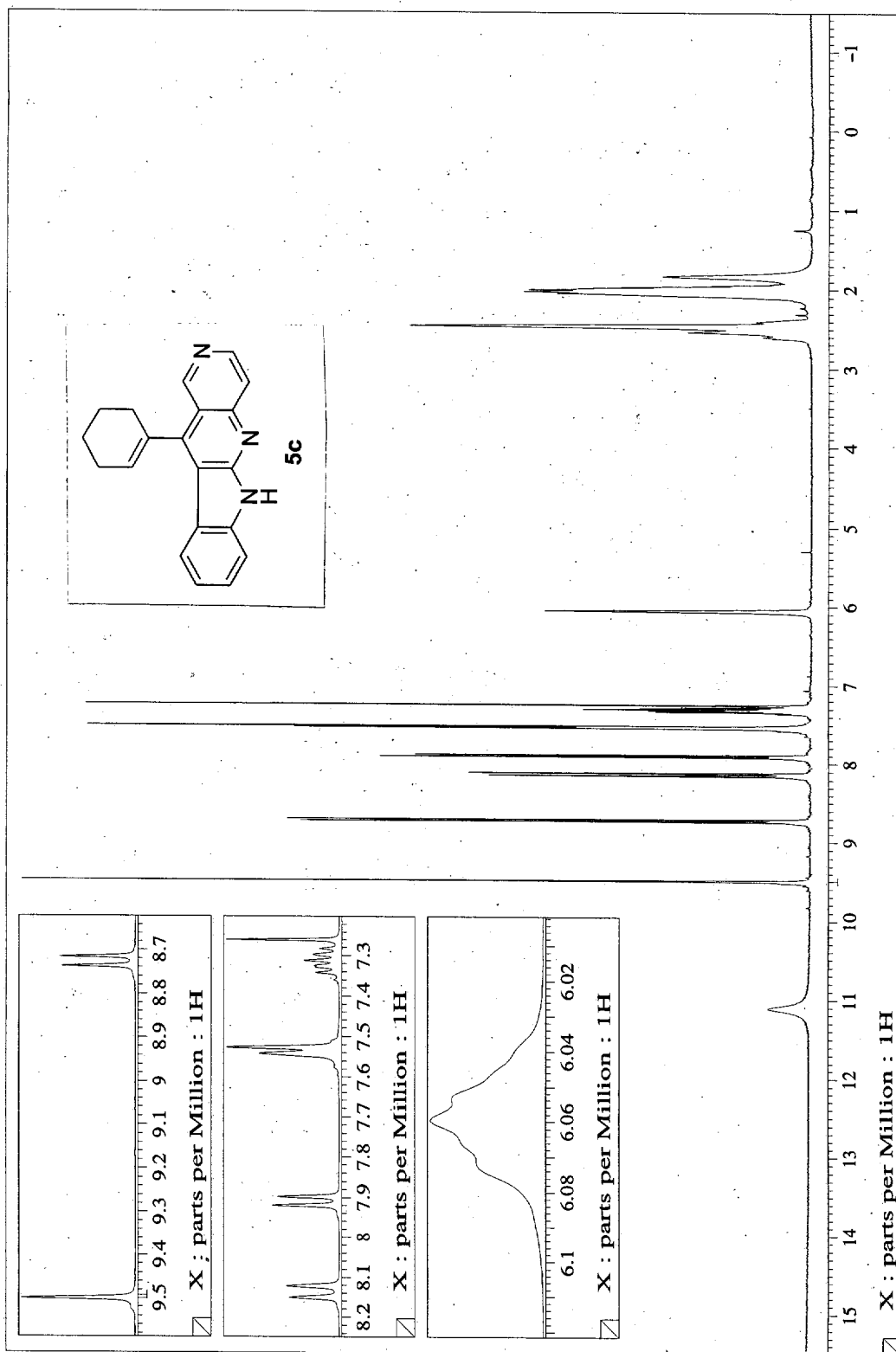
120.3, 119.9, 118.6, 111.1; MS m/z 295 (M^+), 268, 242; HRMS calcd for $C_{20}H_{13}N_3$ 295.1109, found 295.1107.

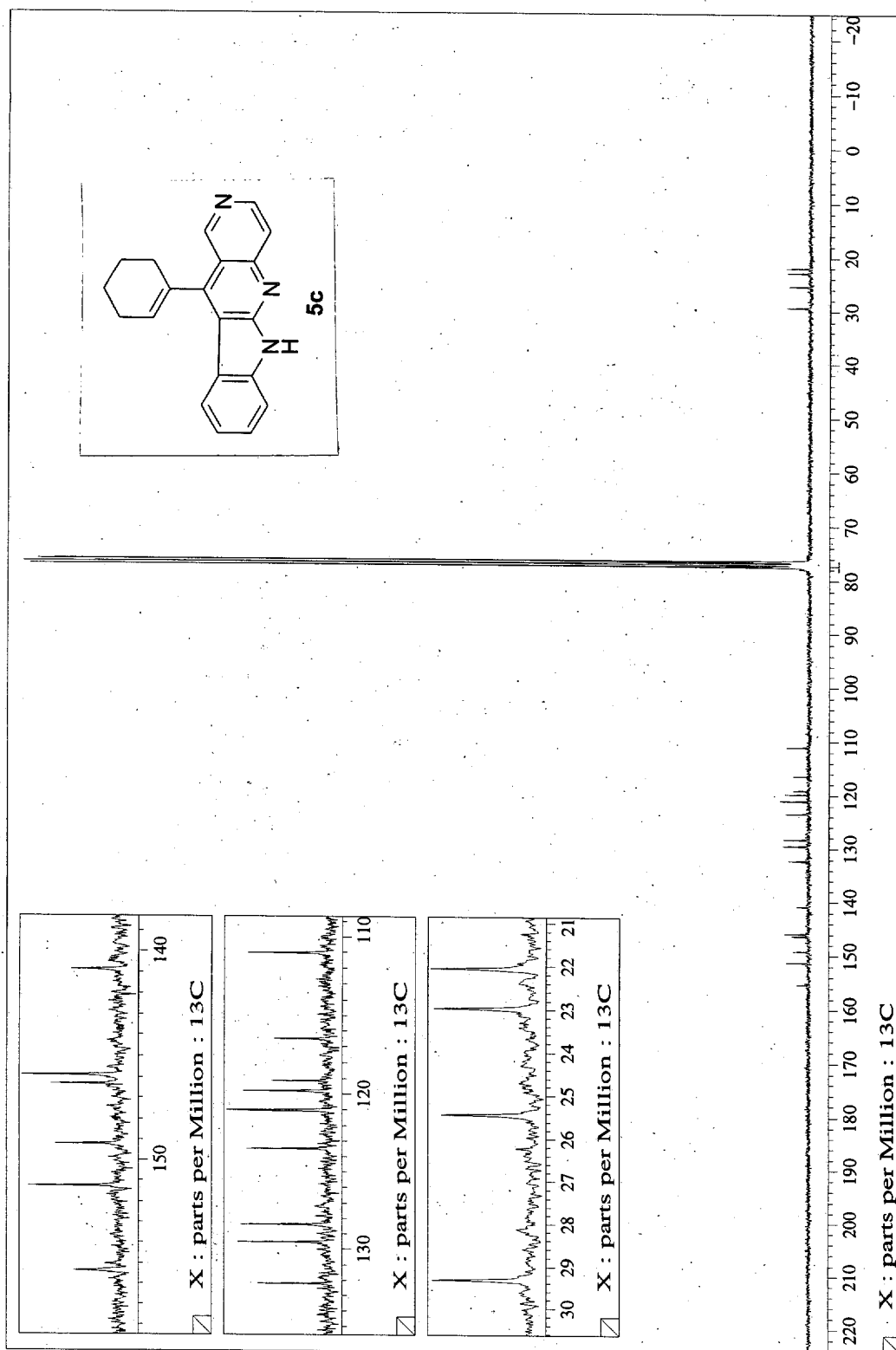


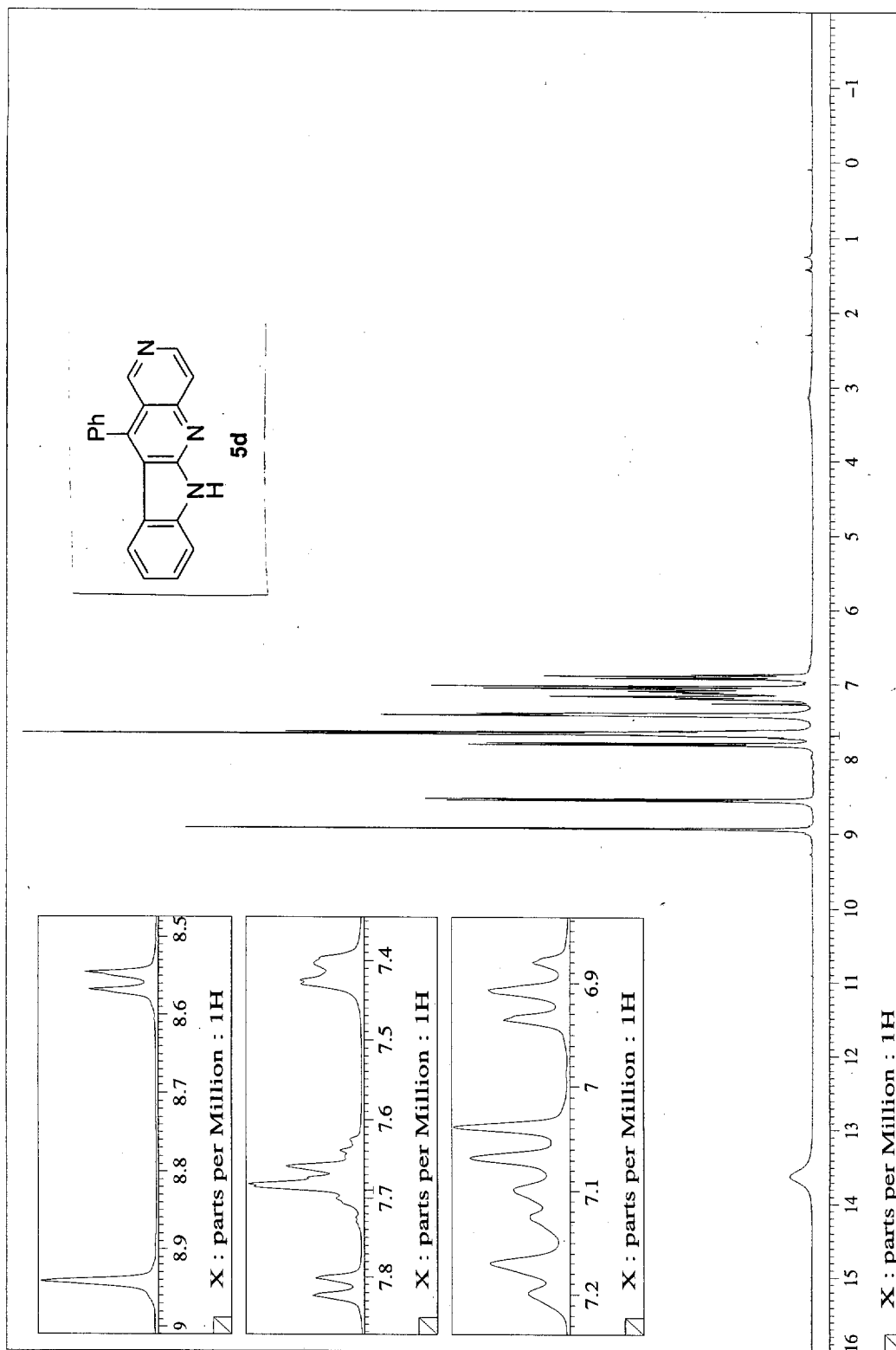


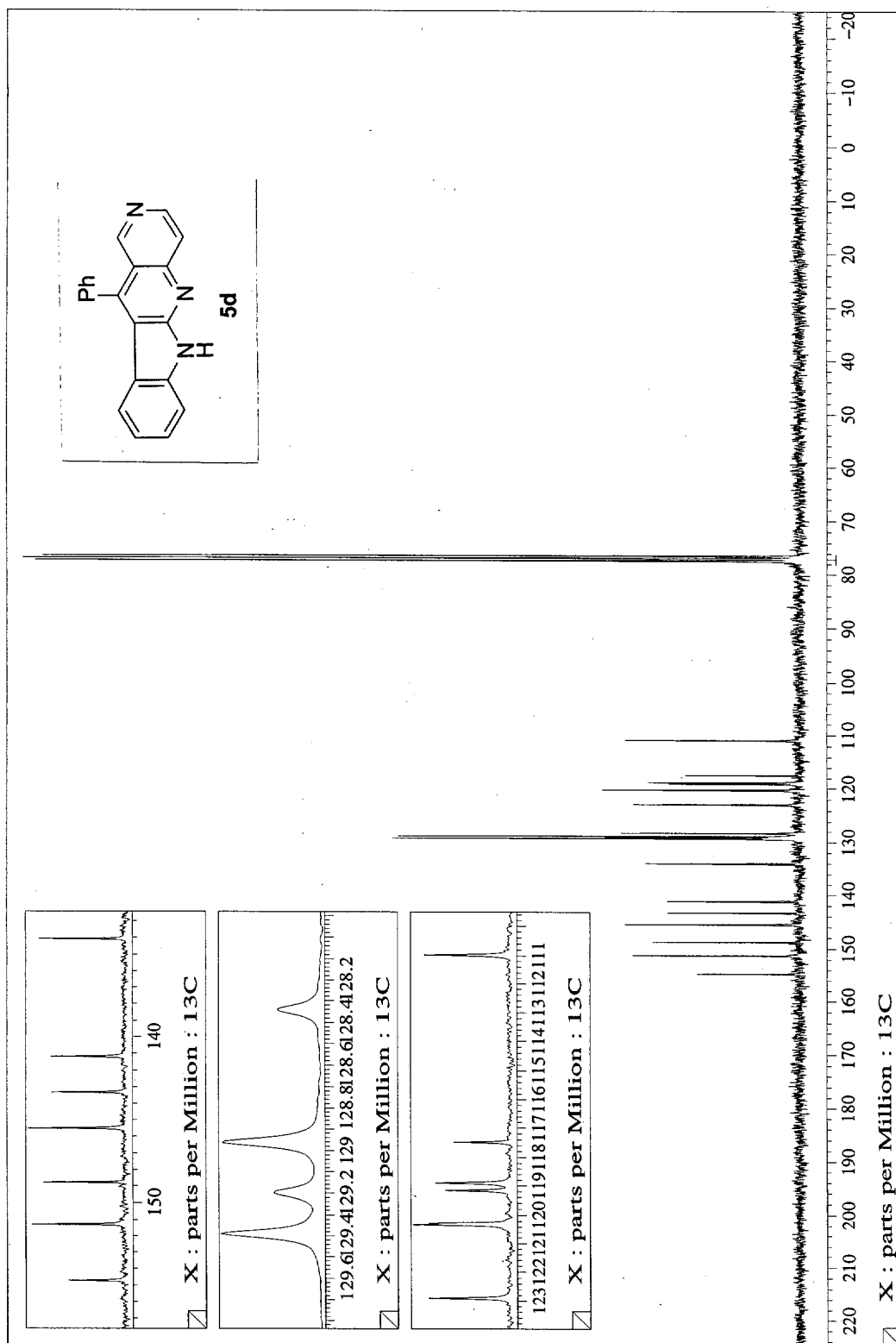


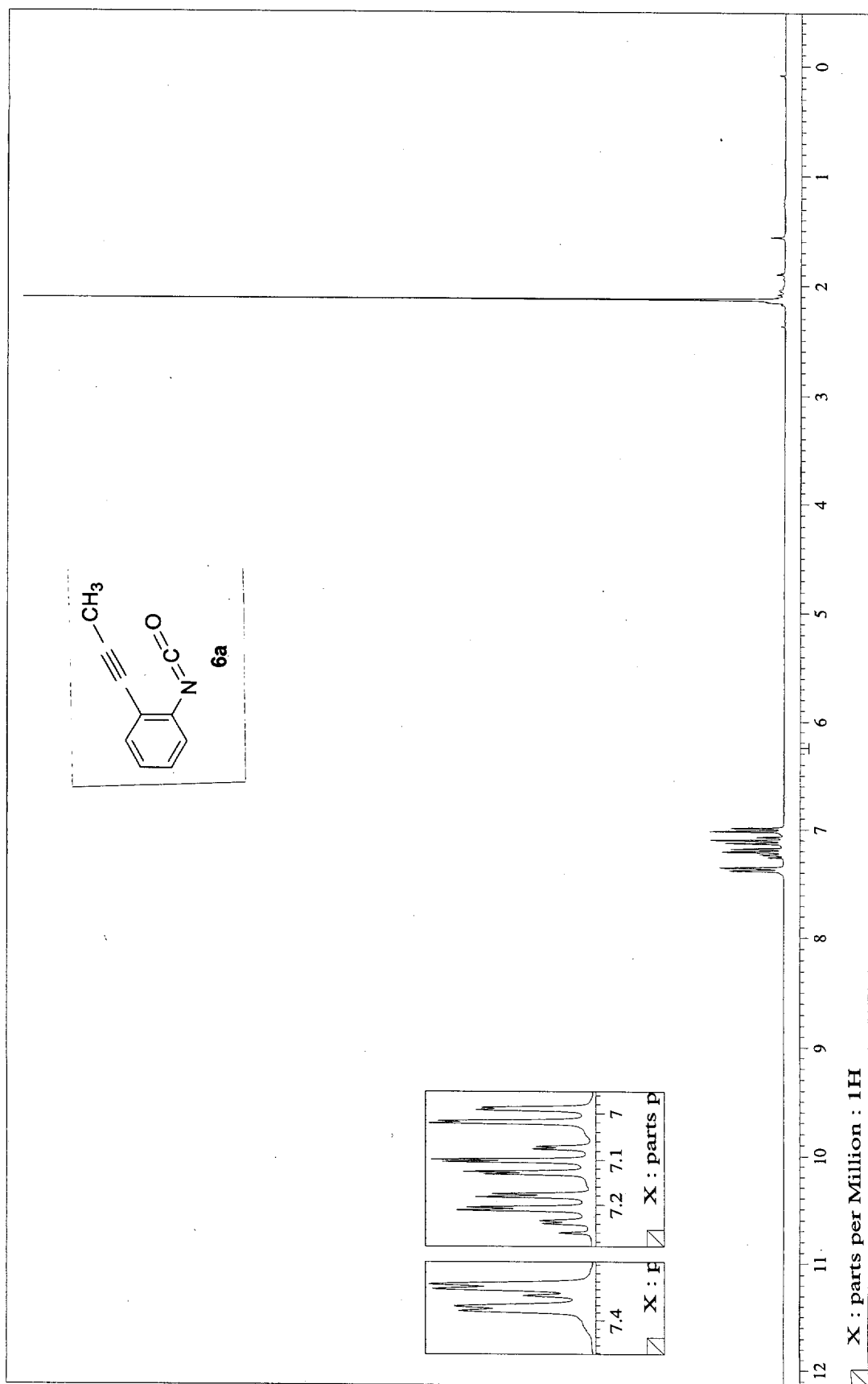


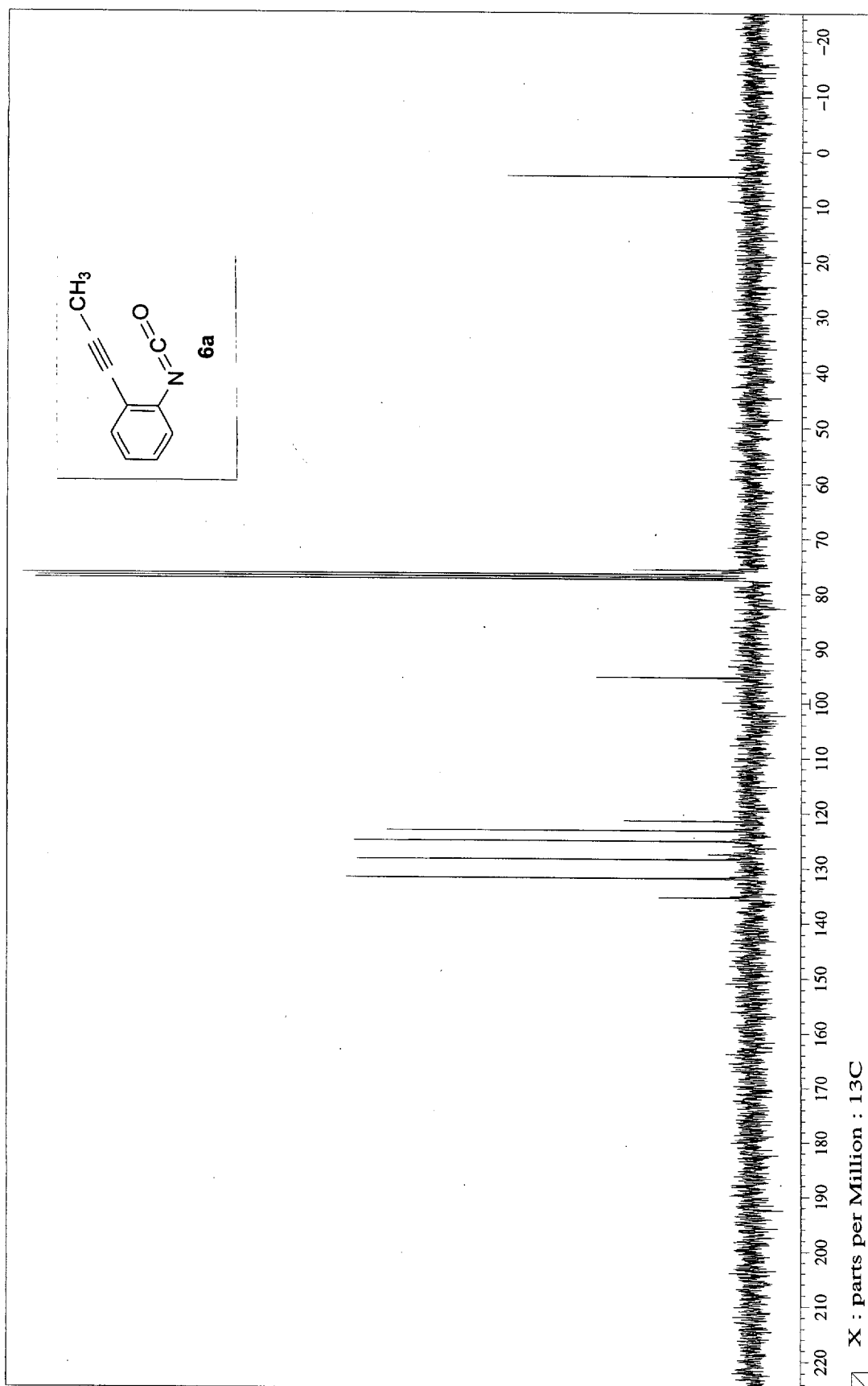


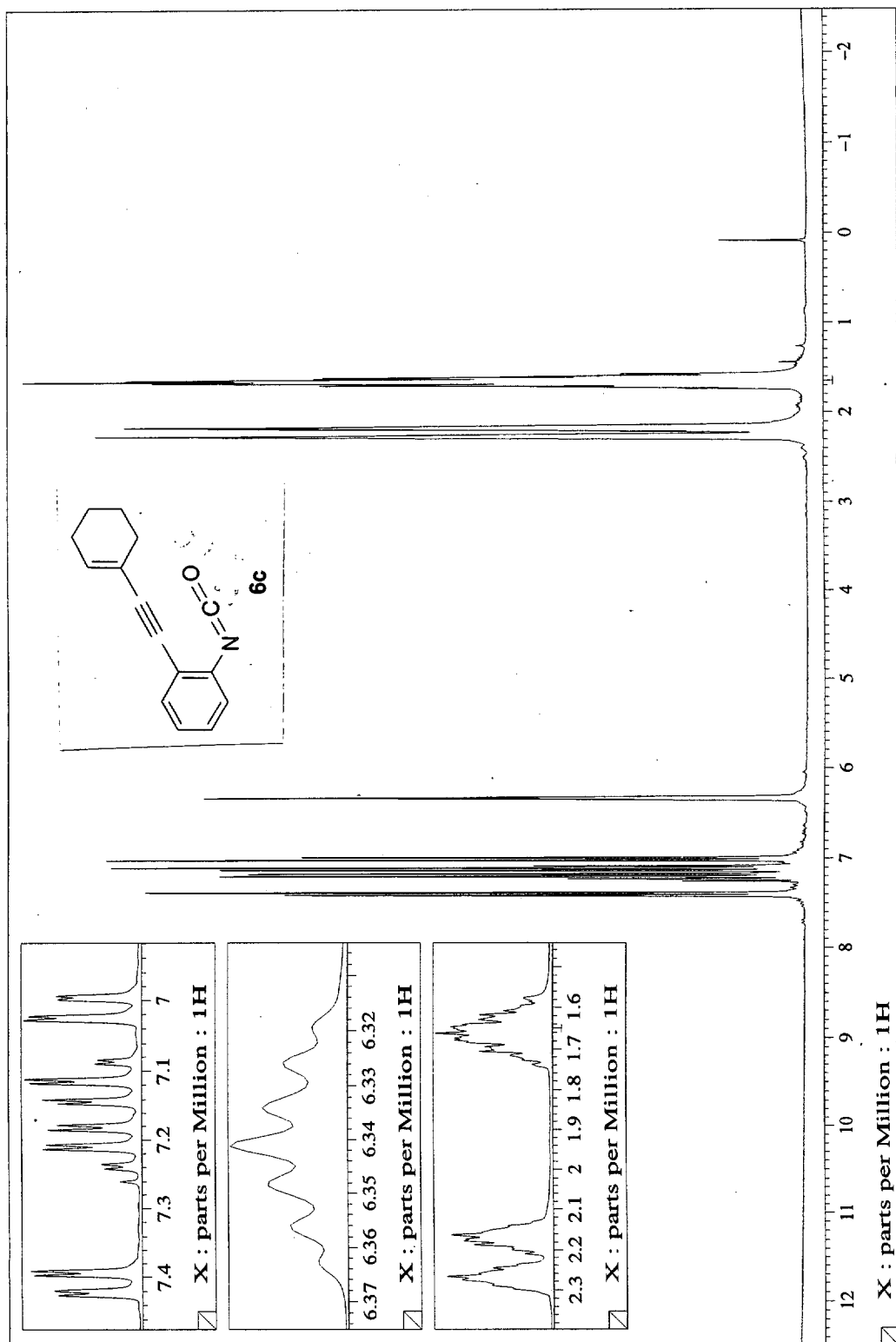


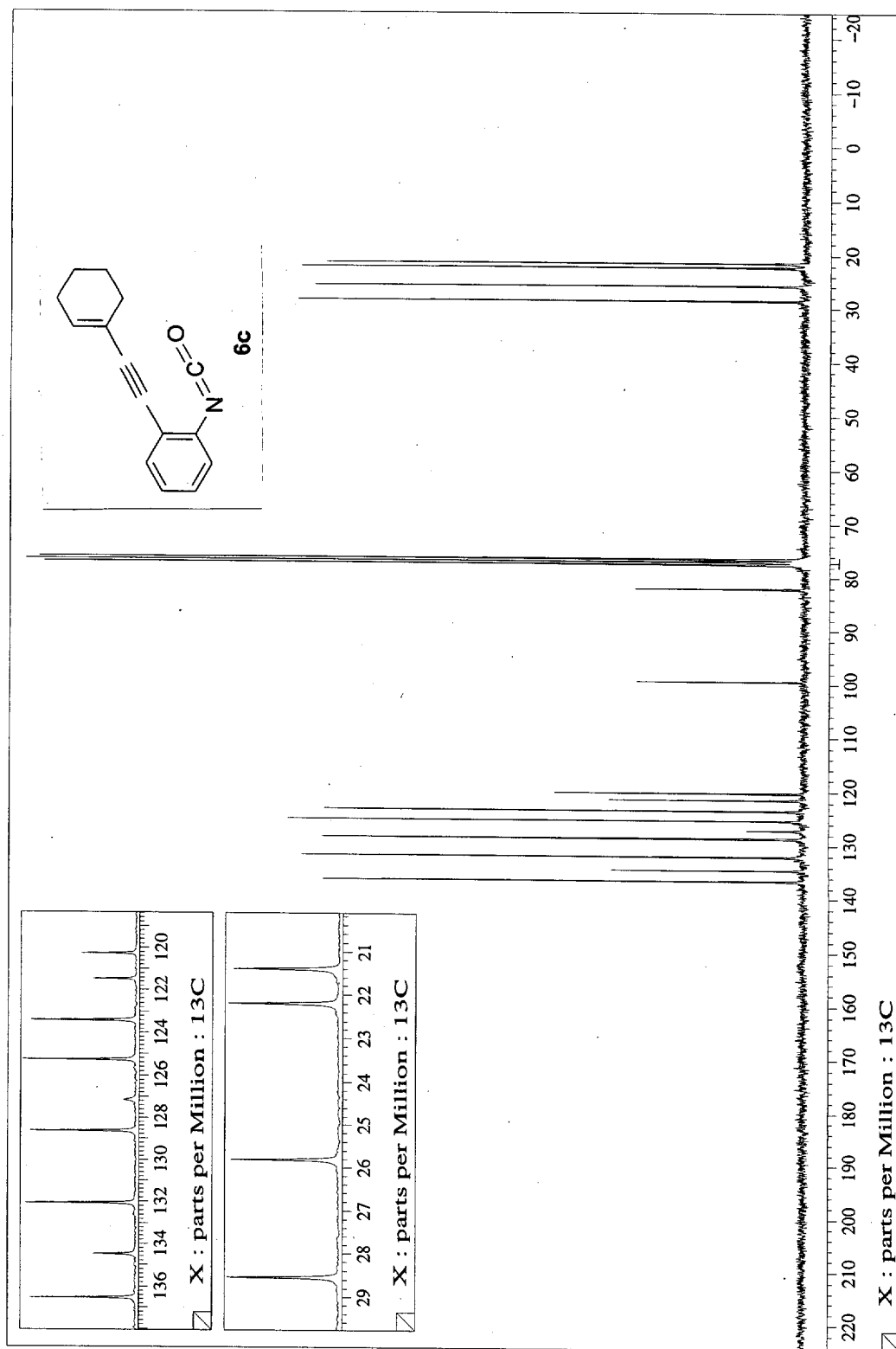


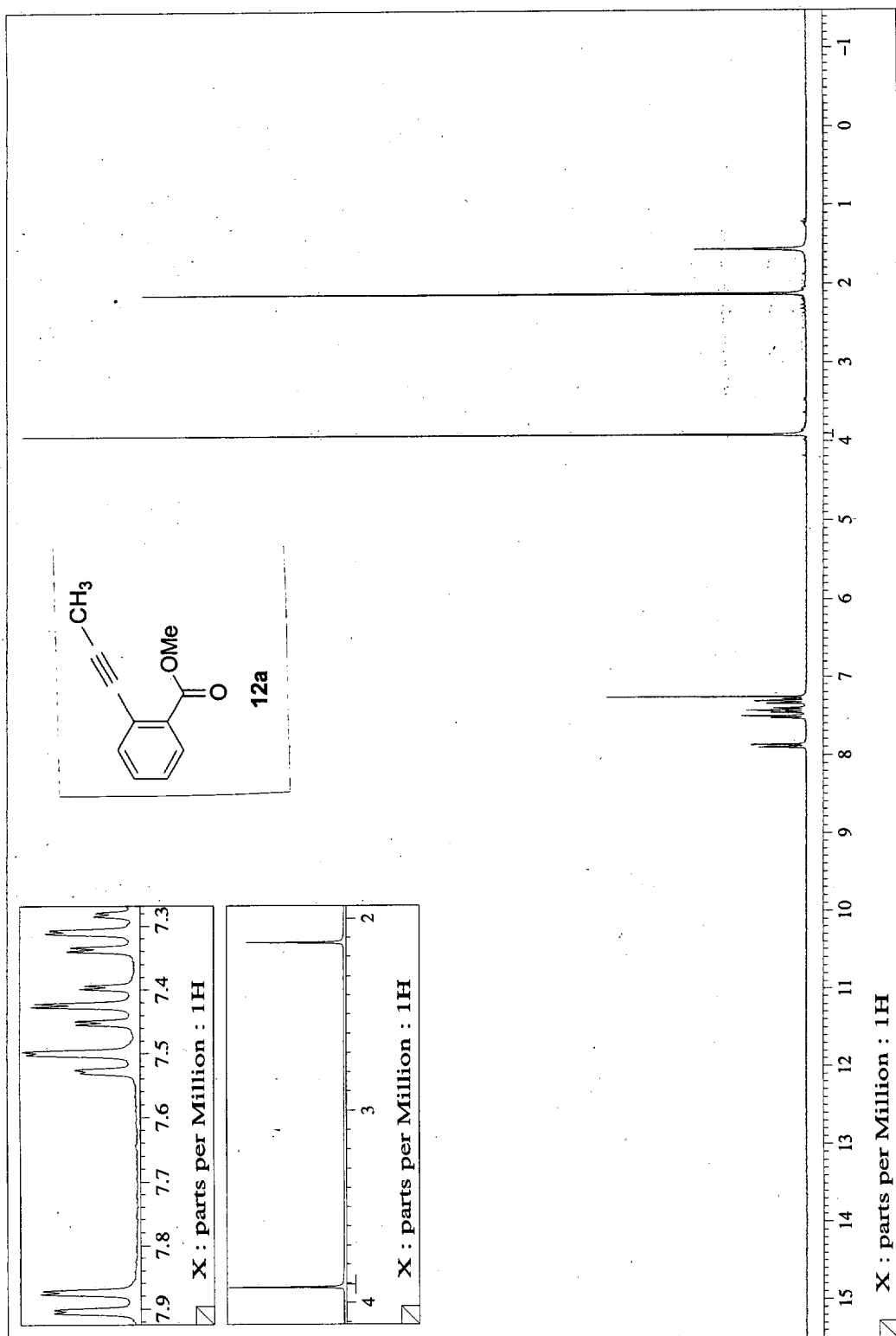


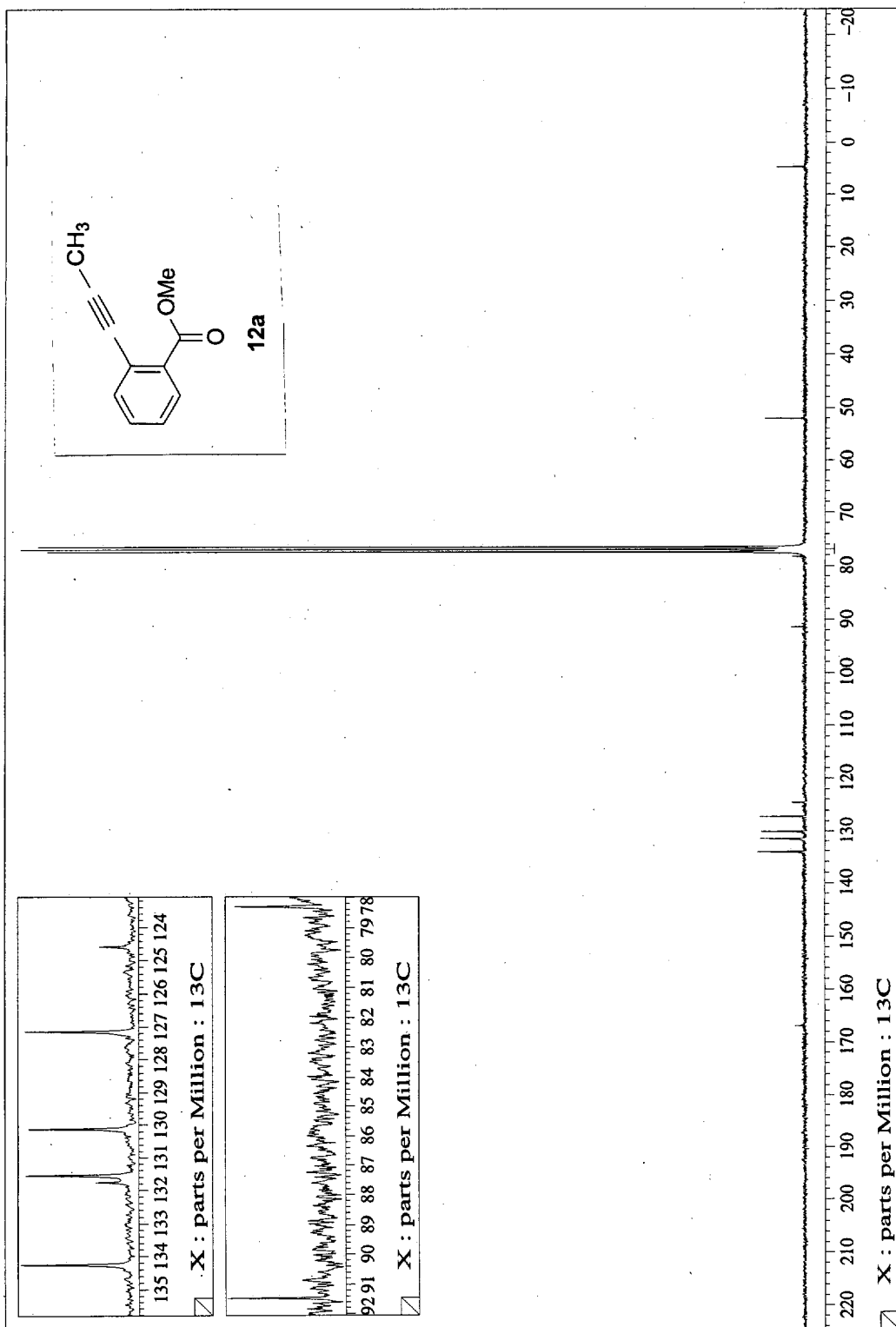


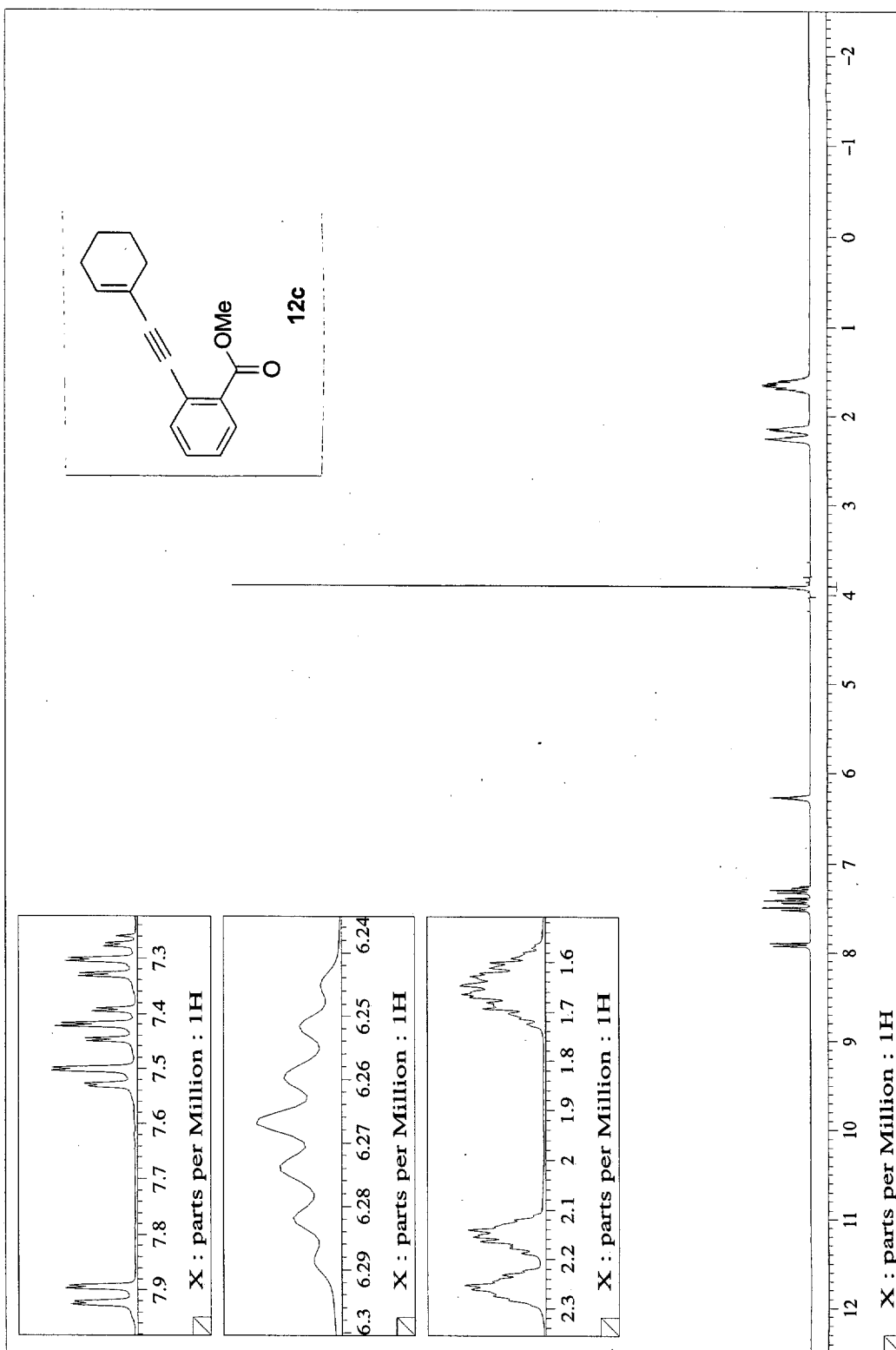


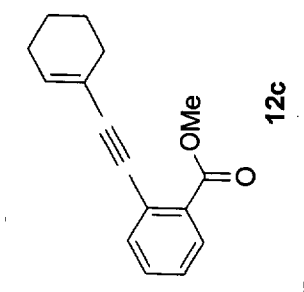












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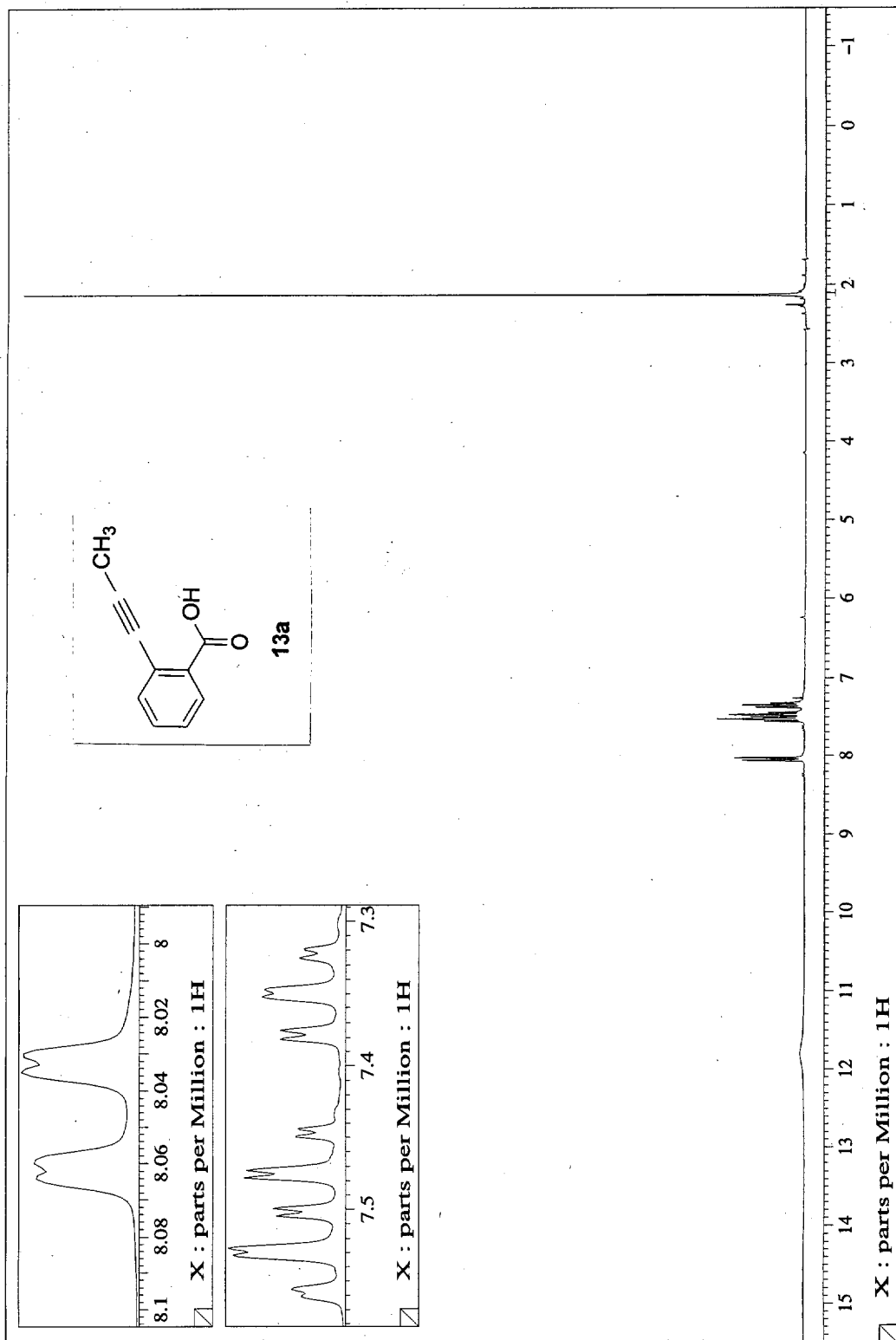
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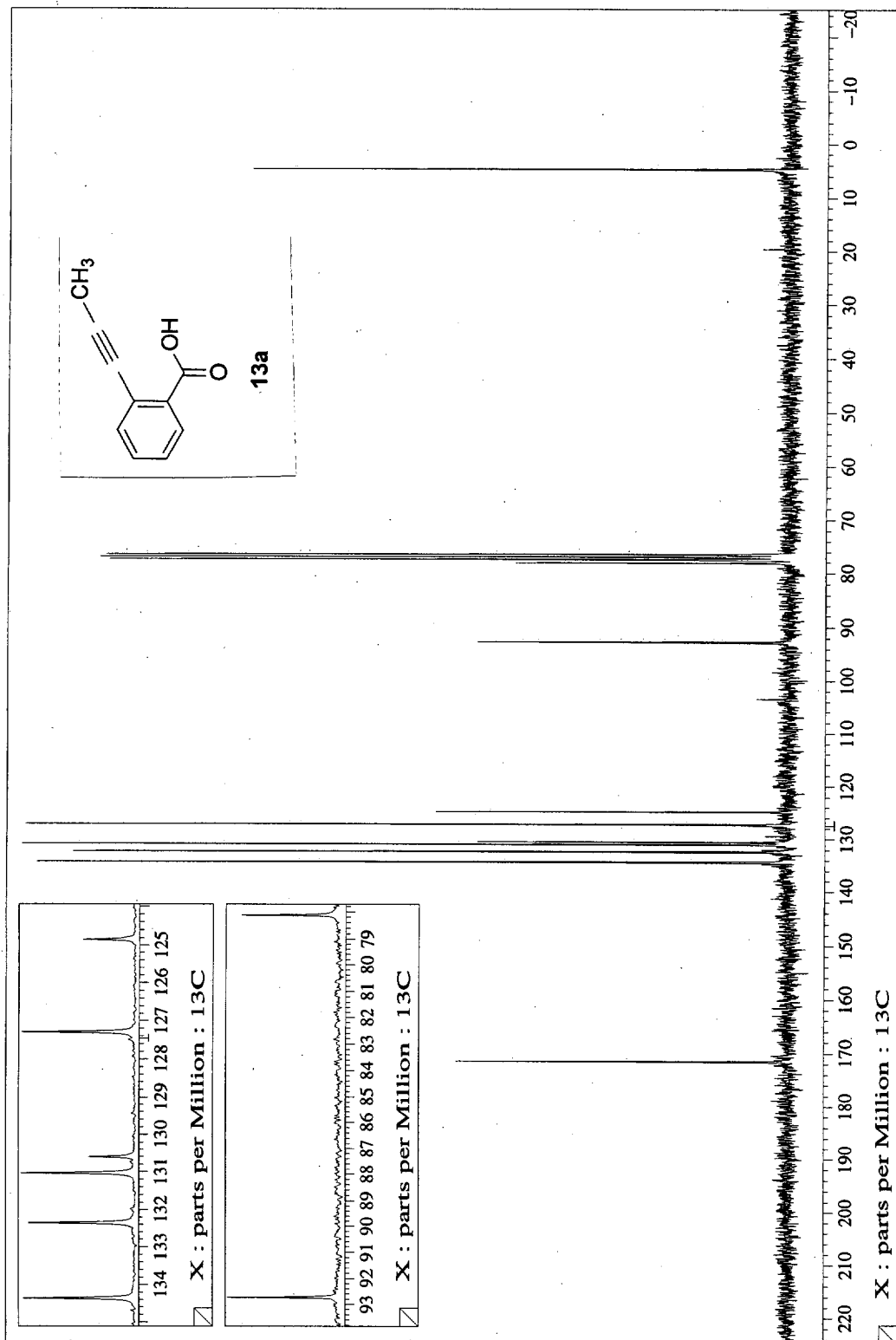
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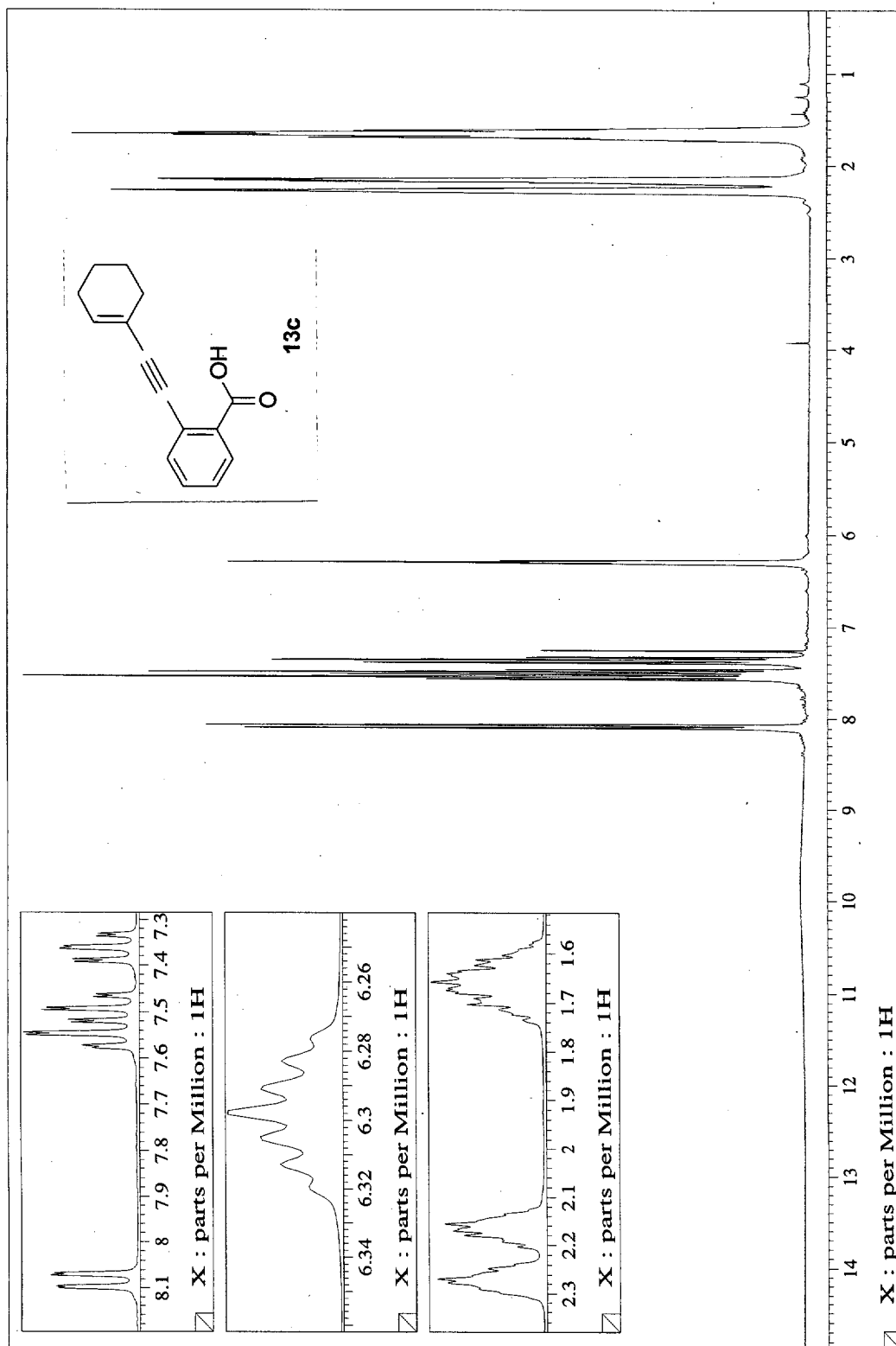
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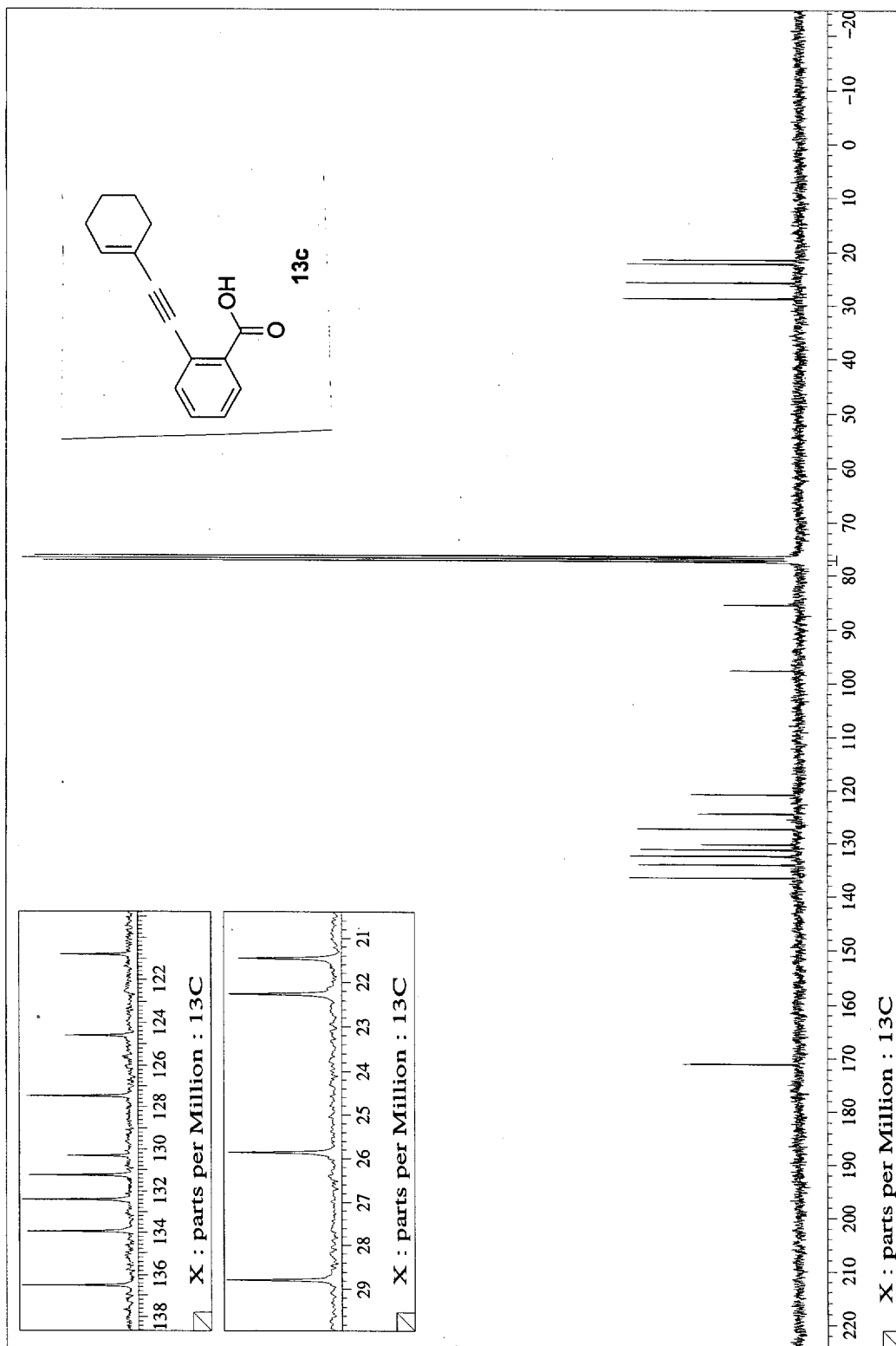
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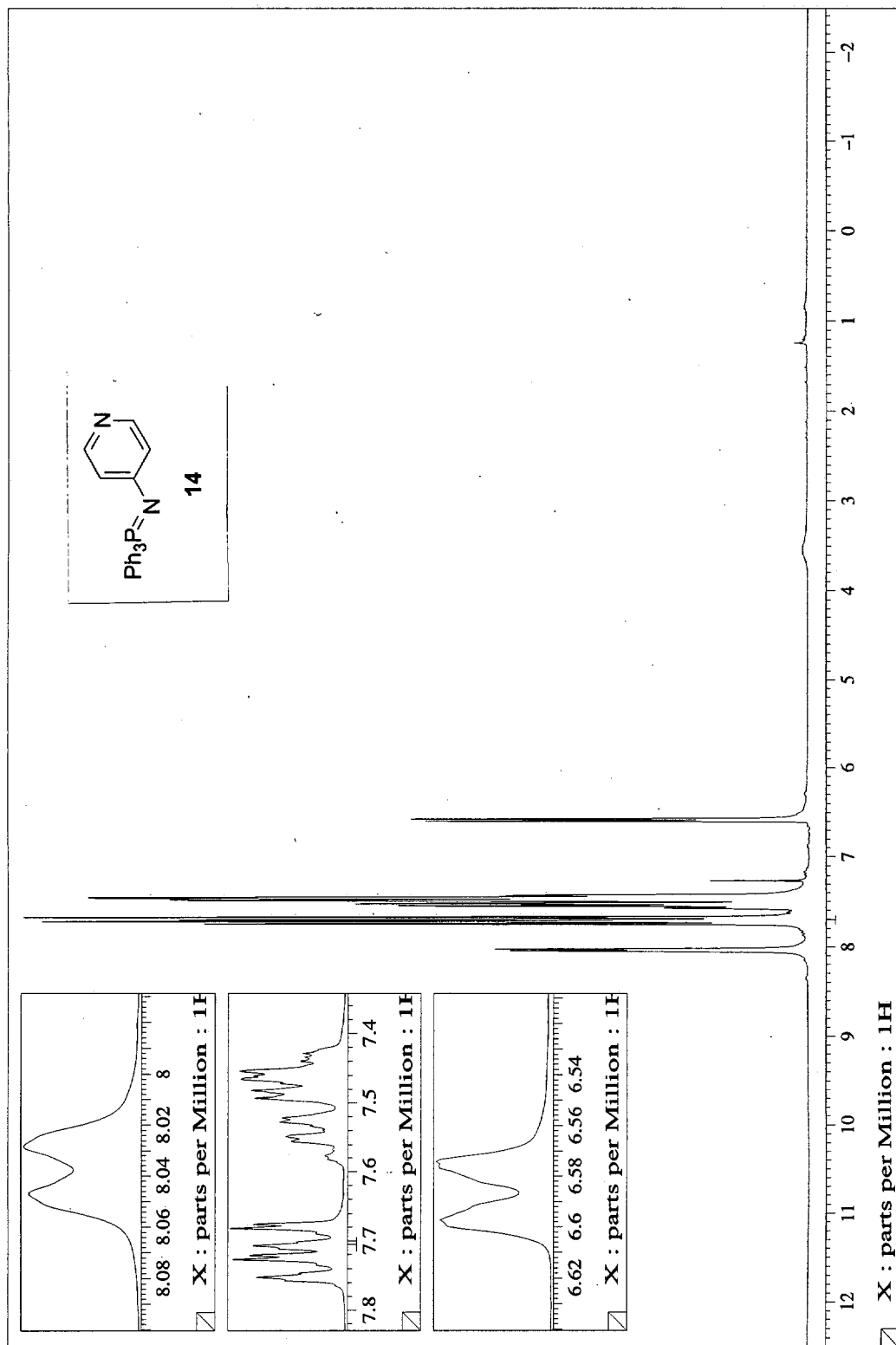
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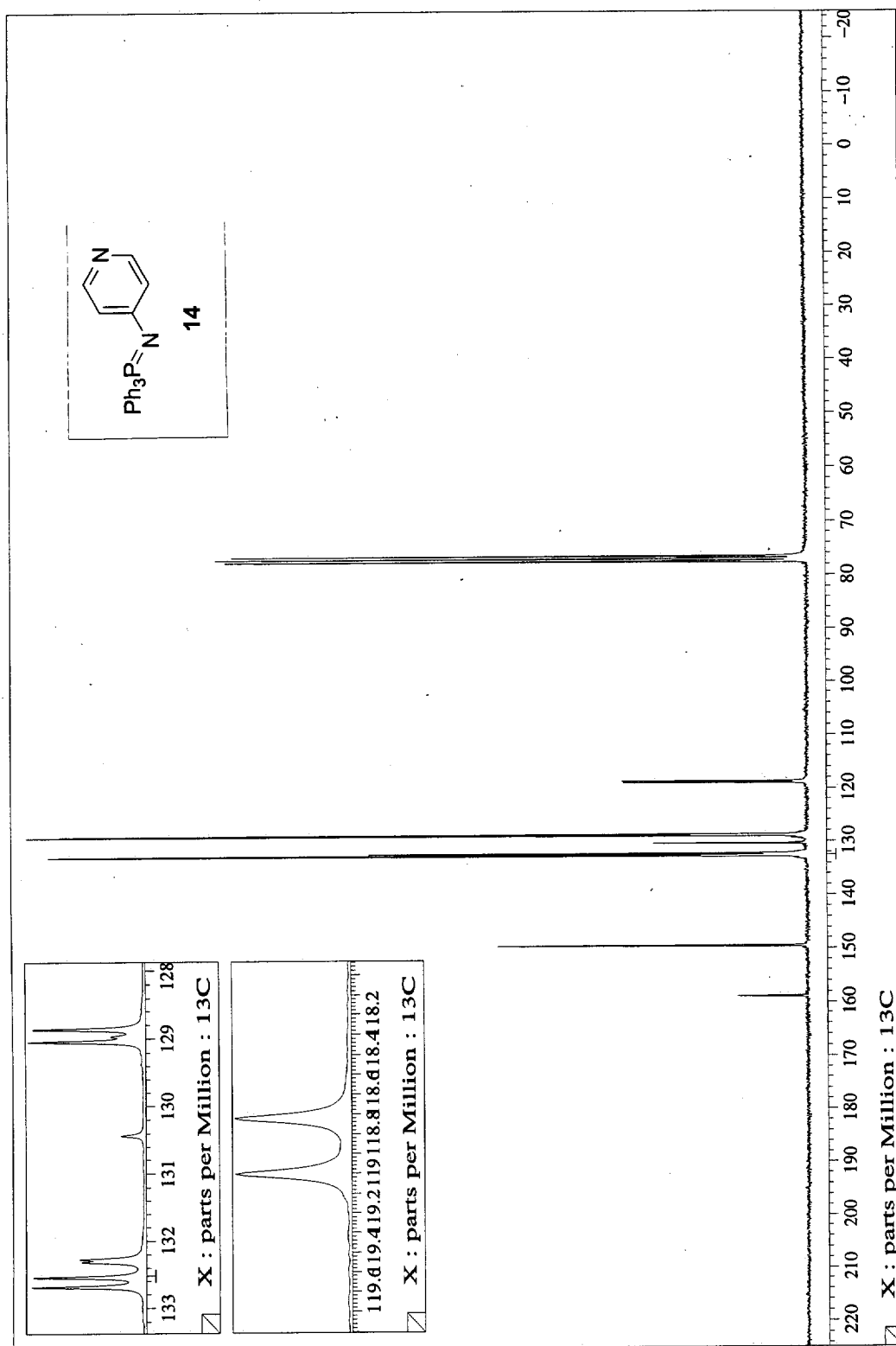


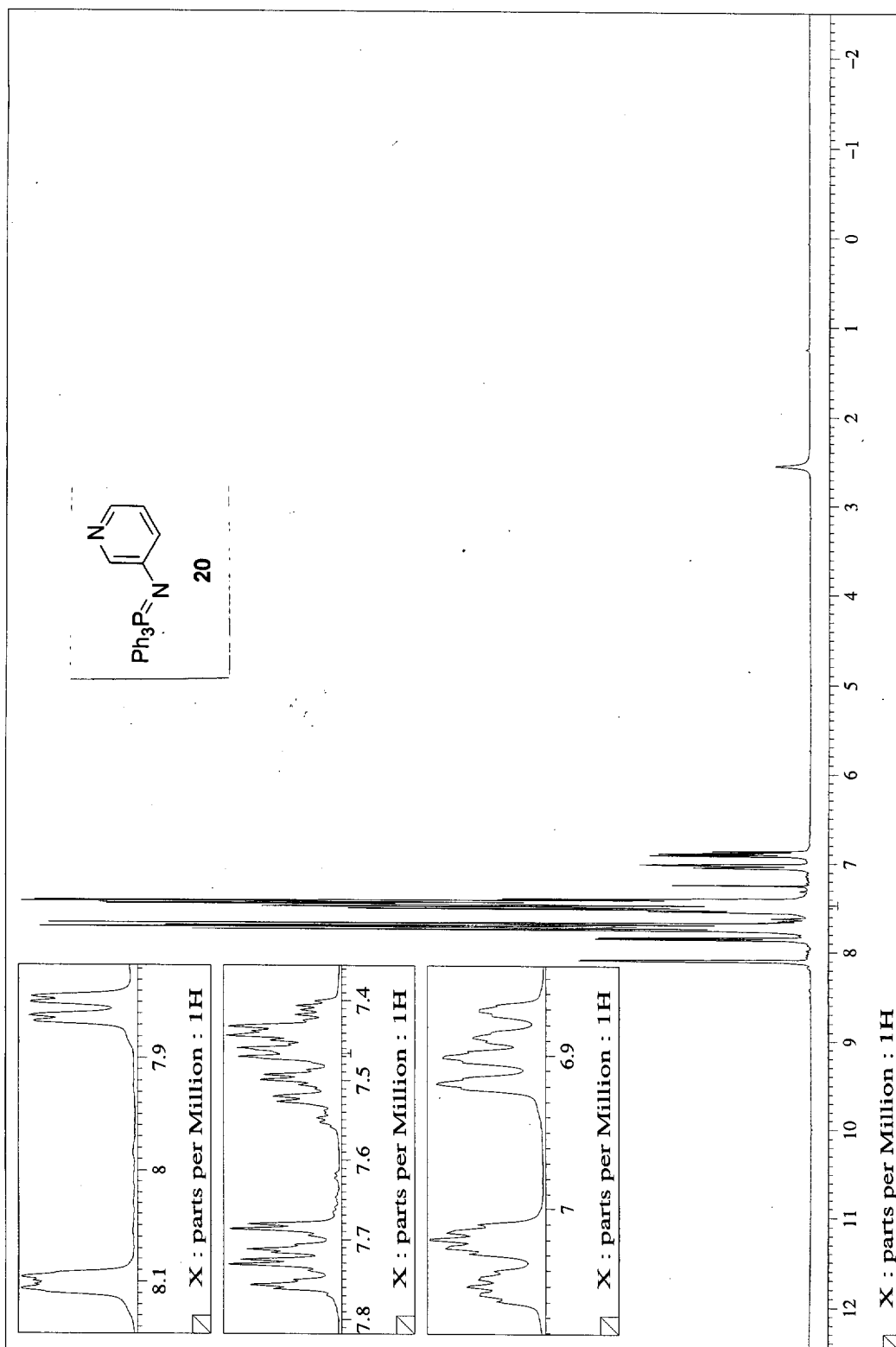


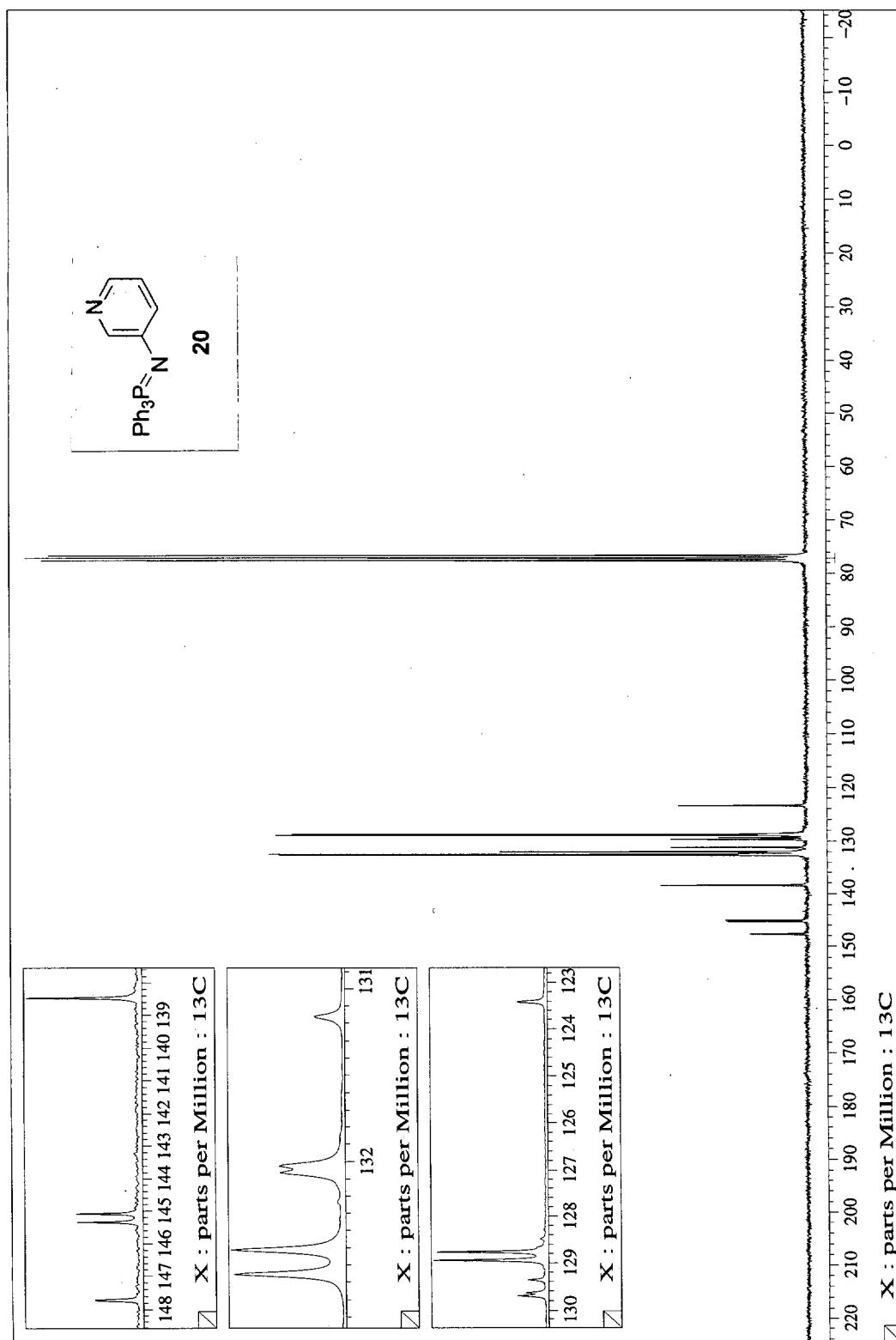


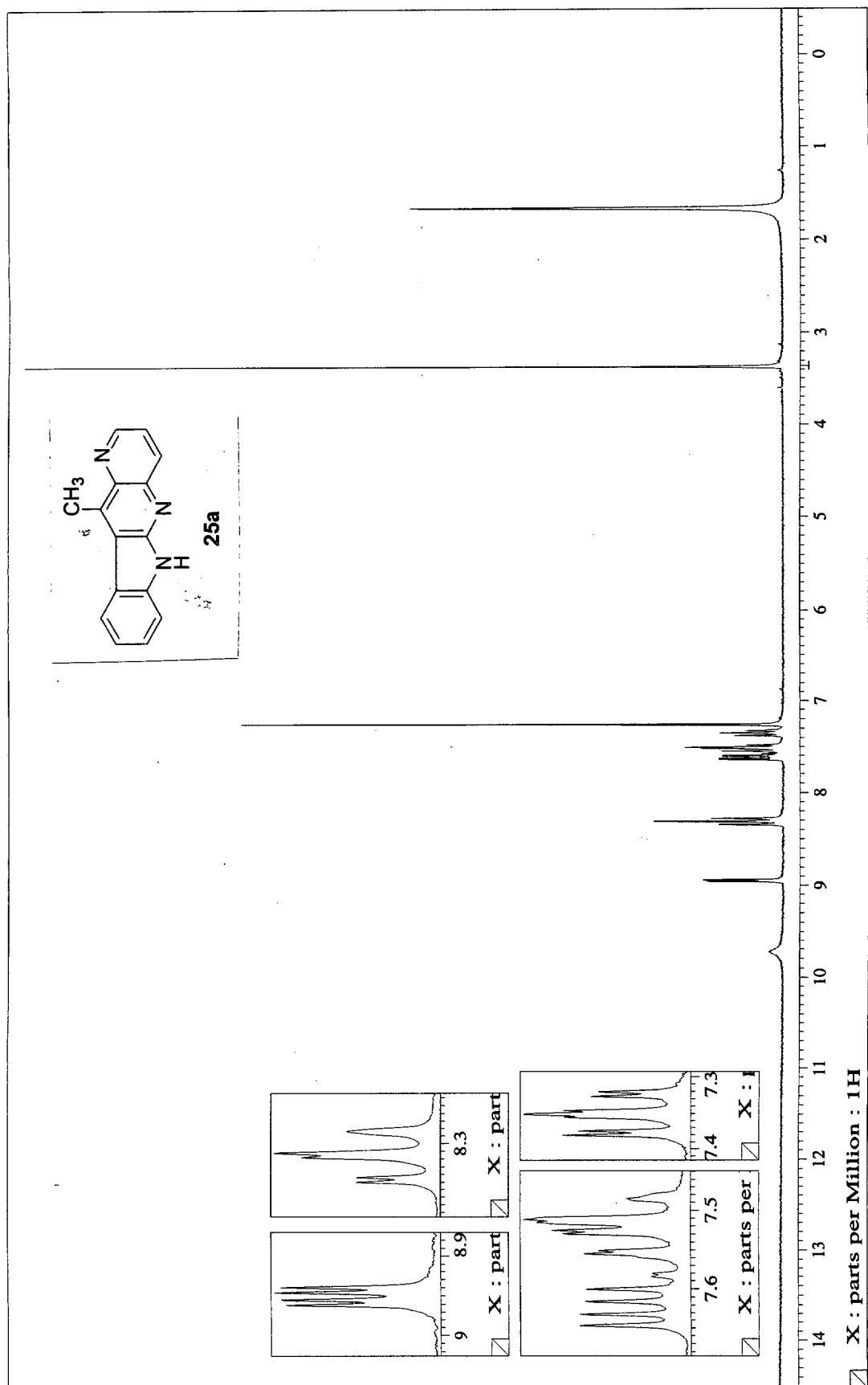


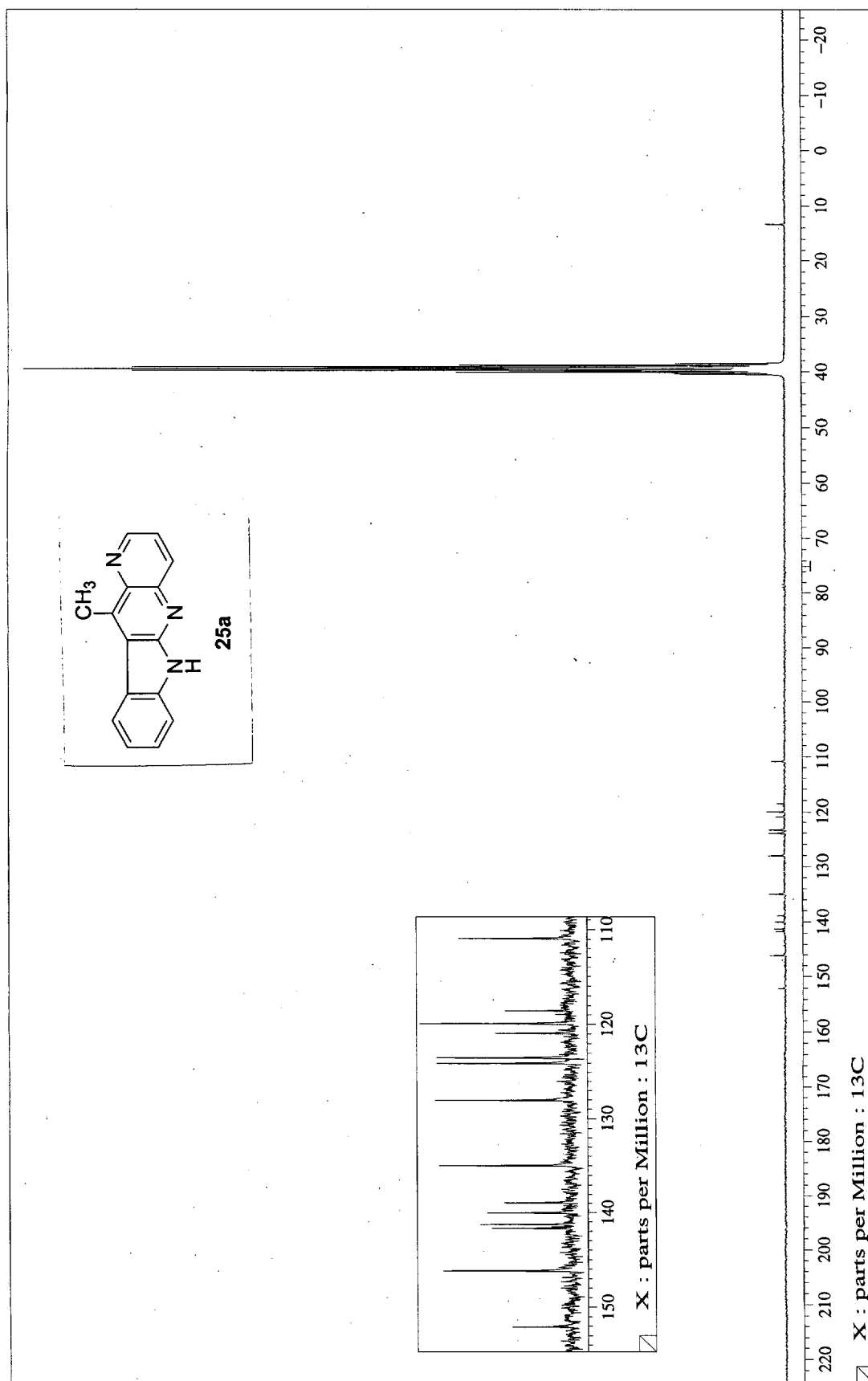


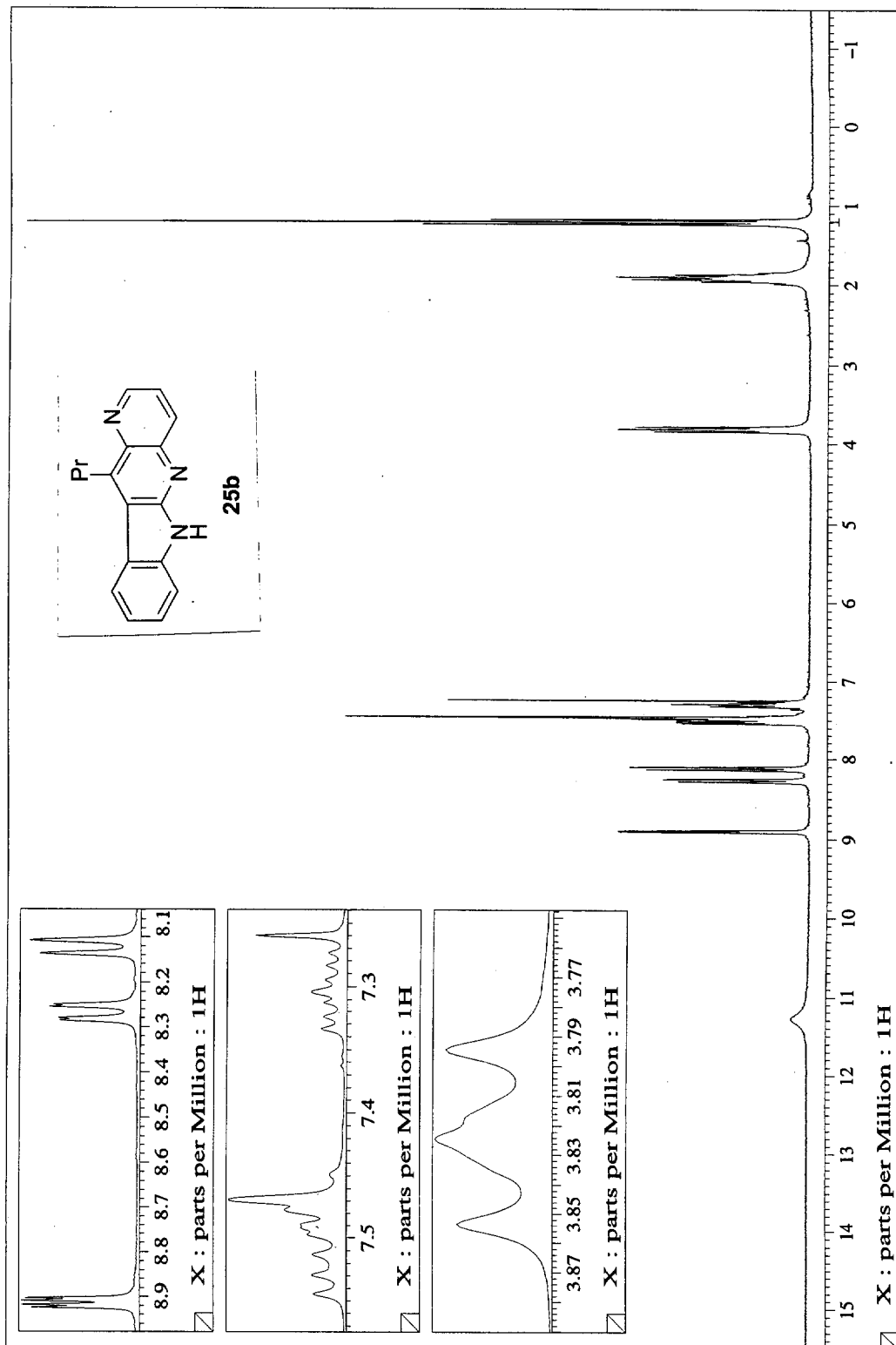


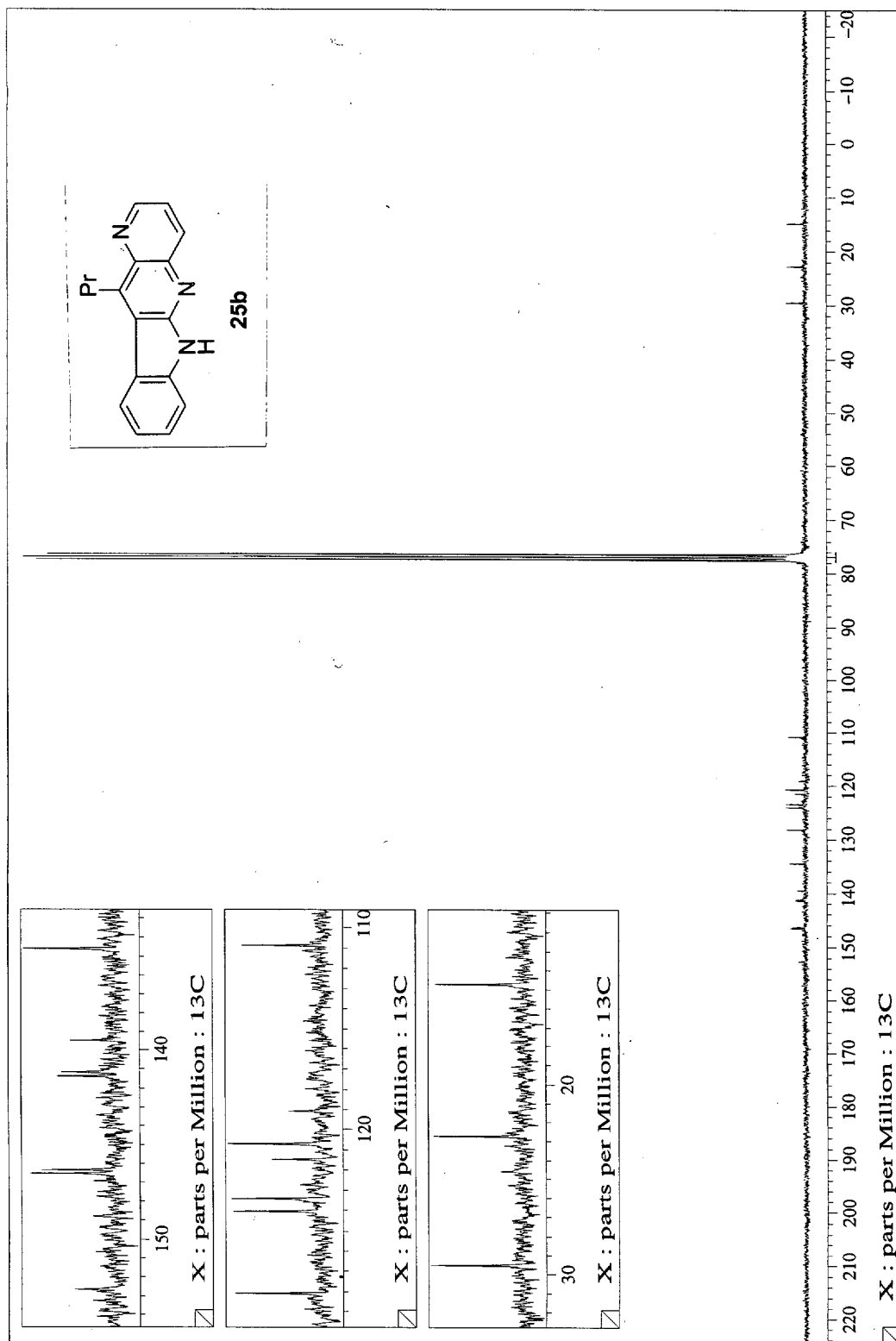


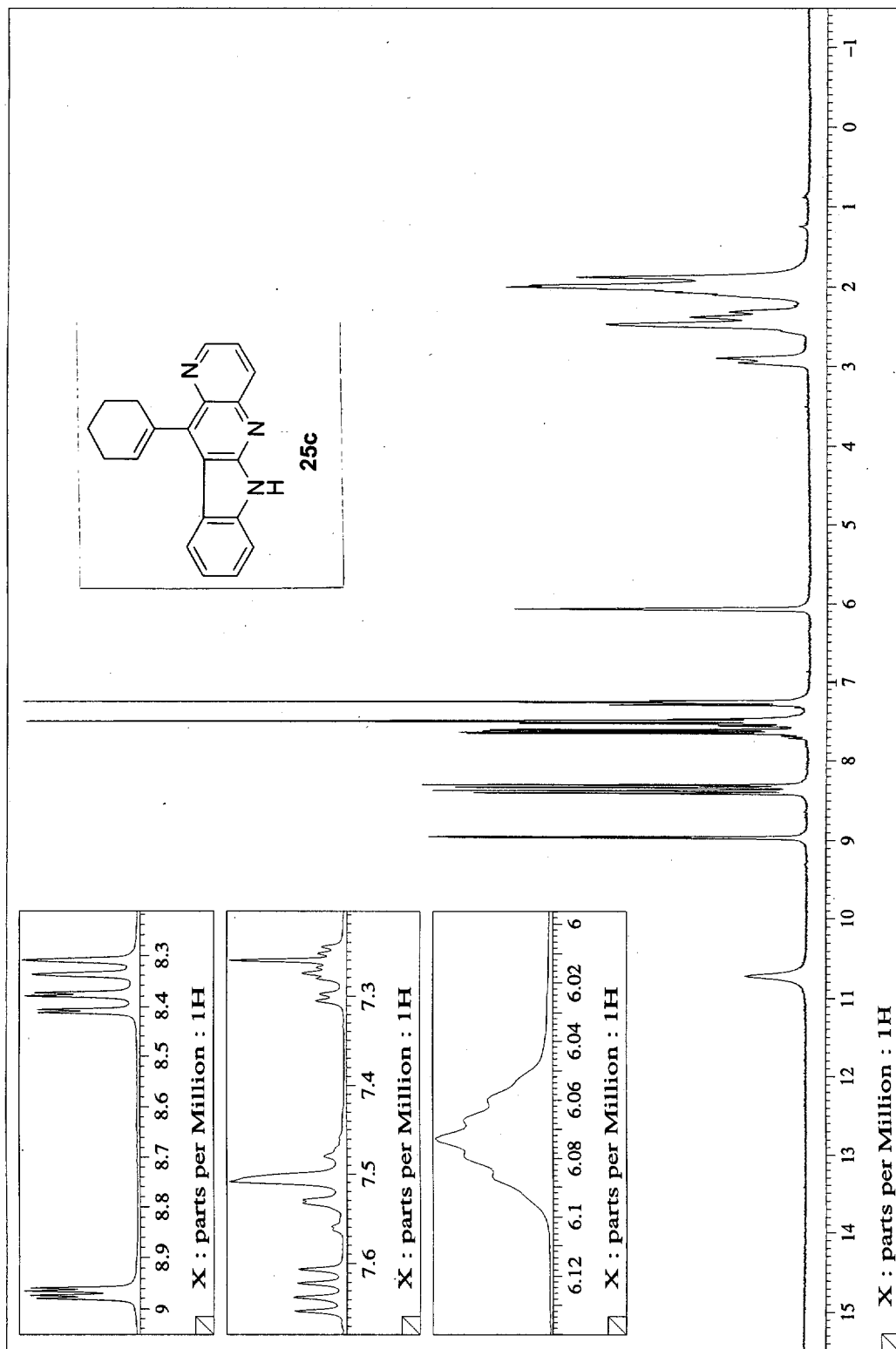


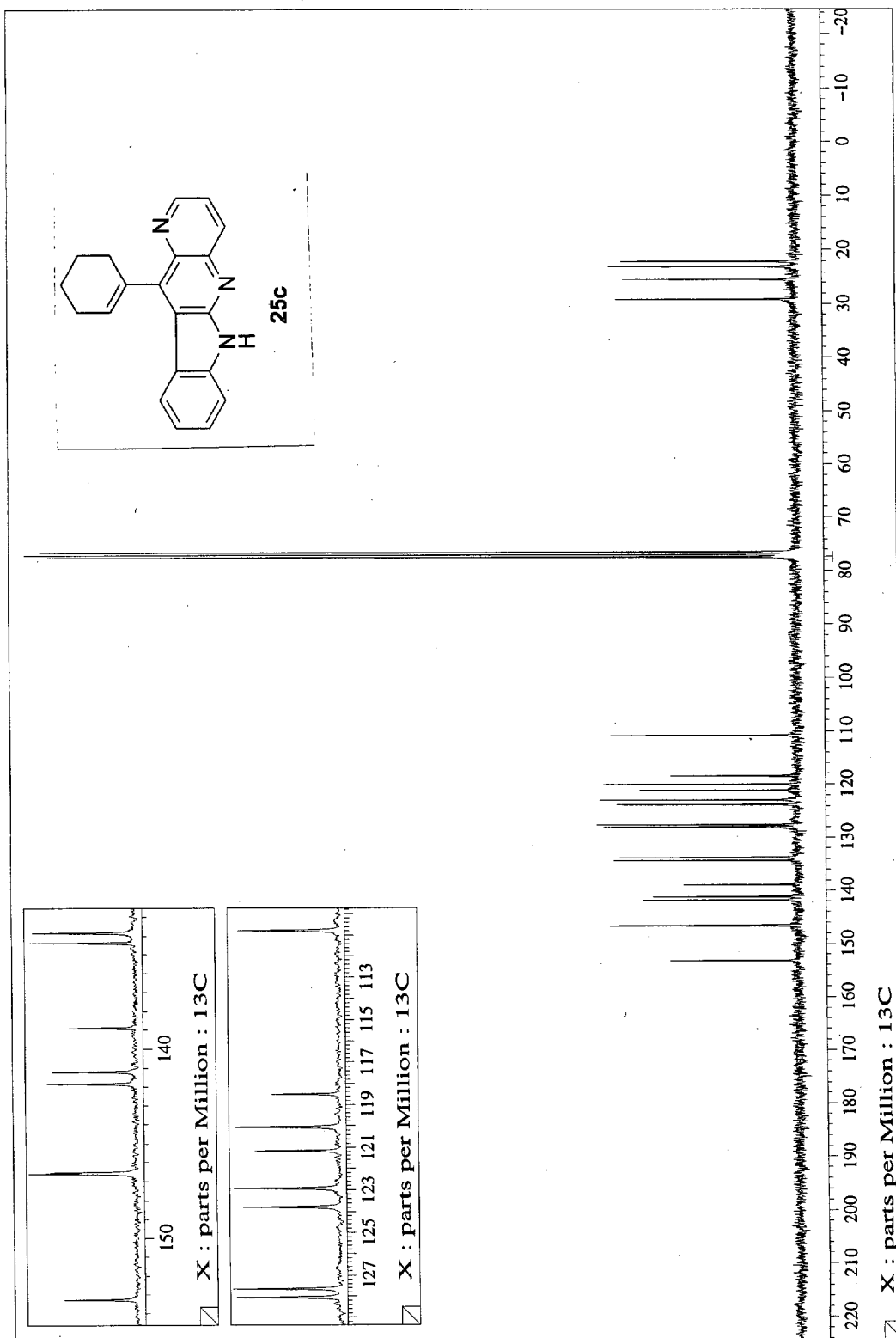


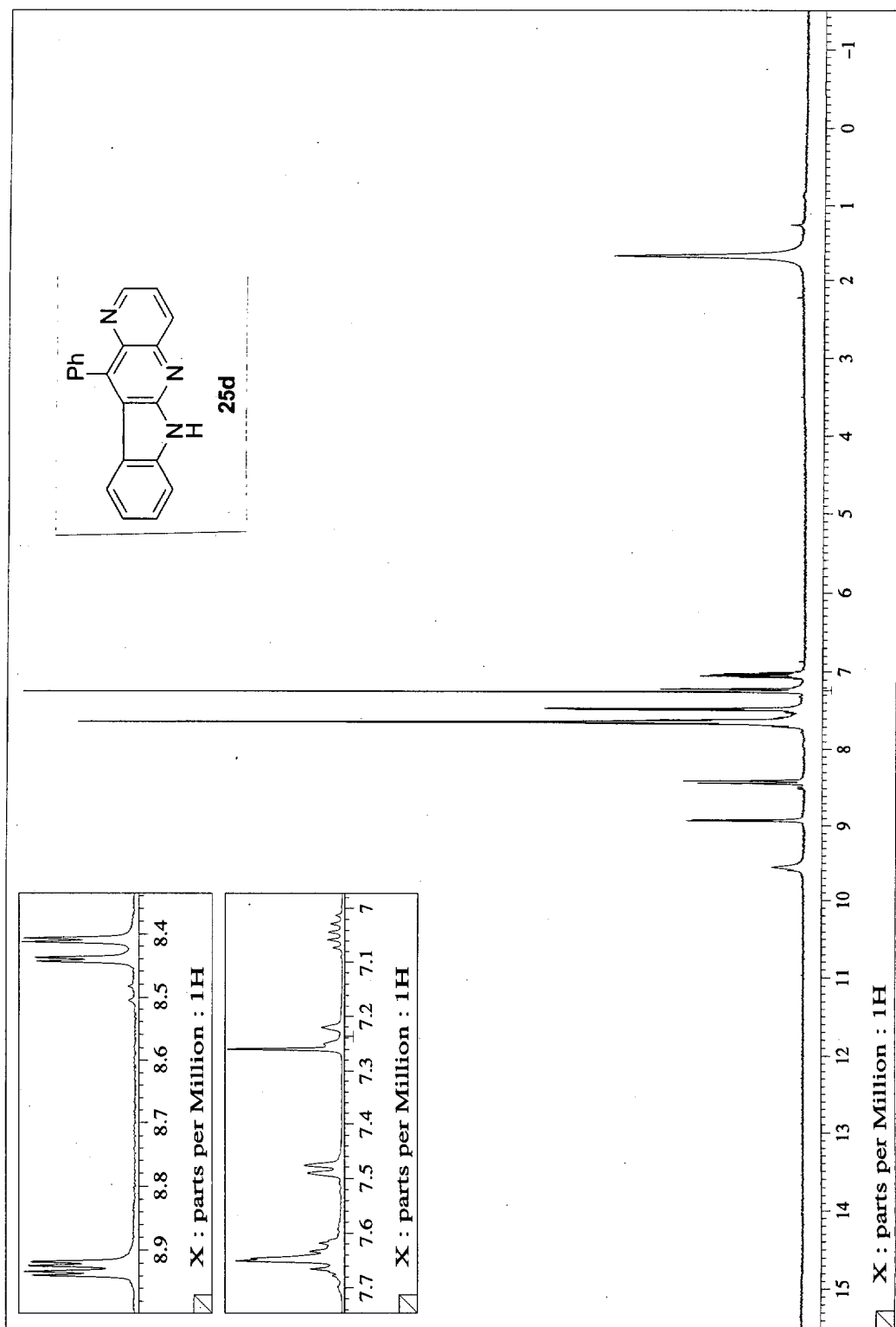


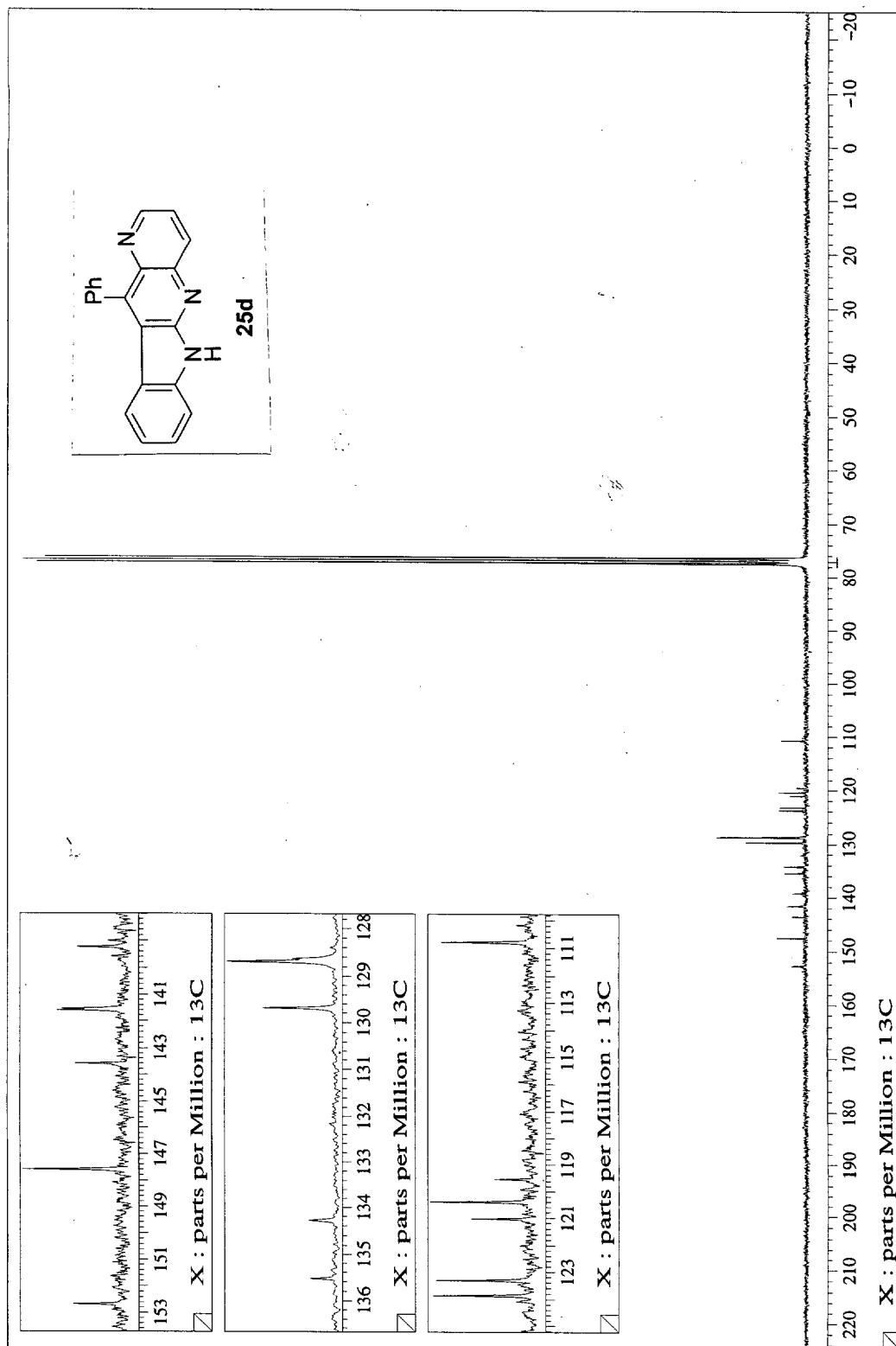


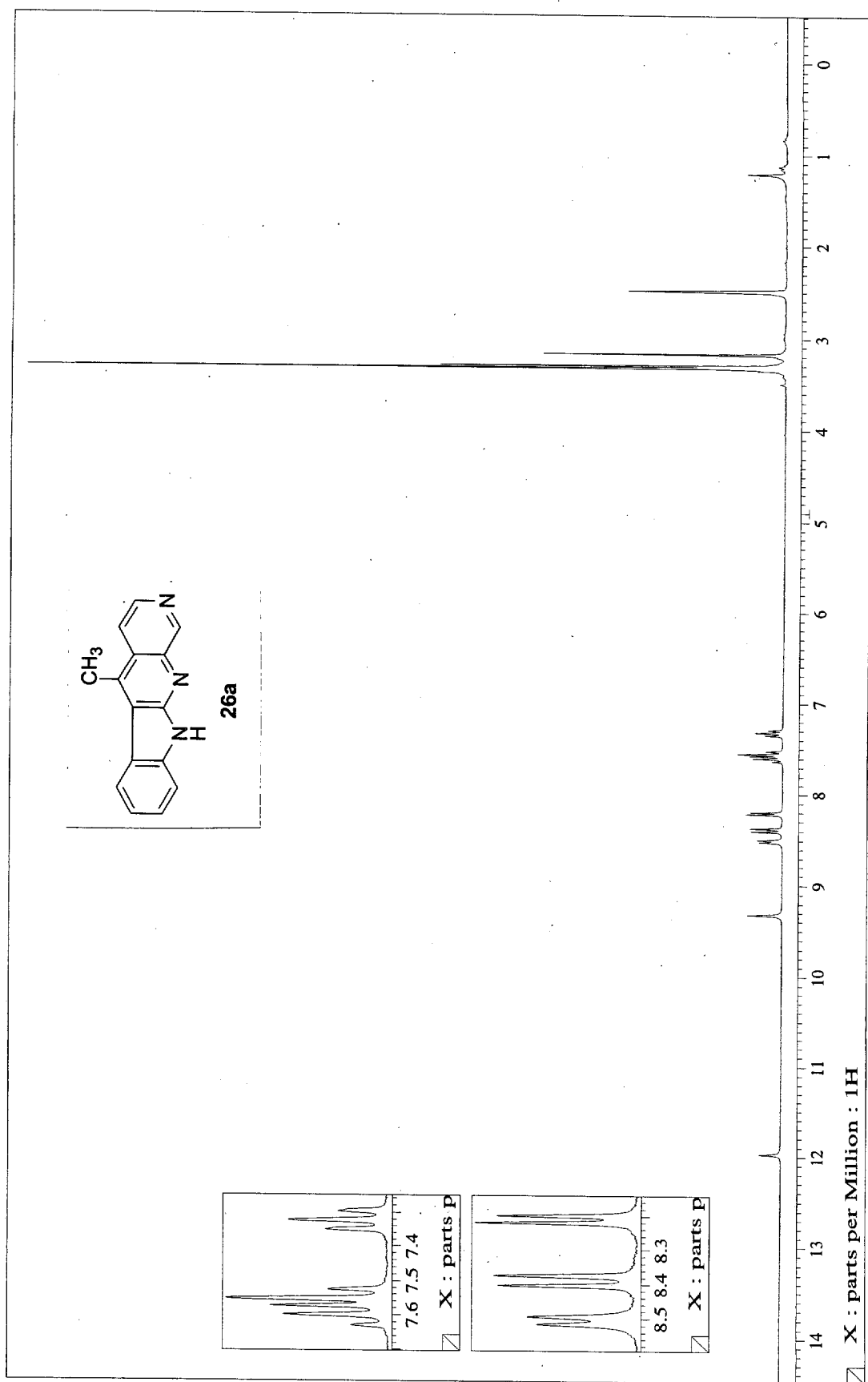


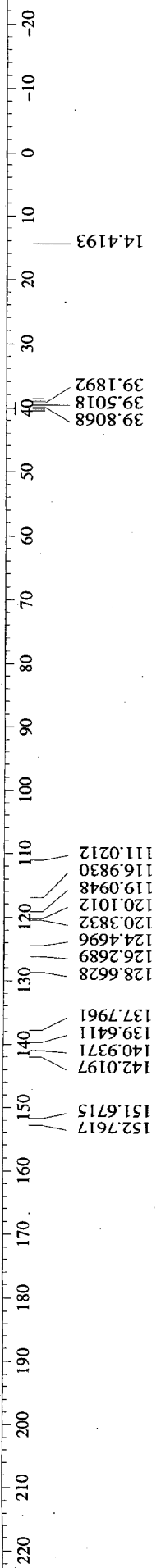
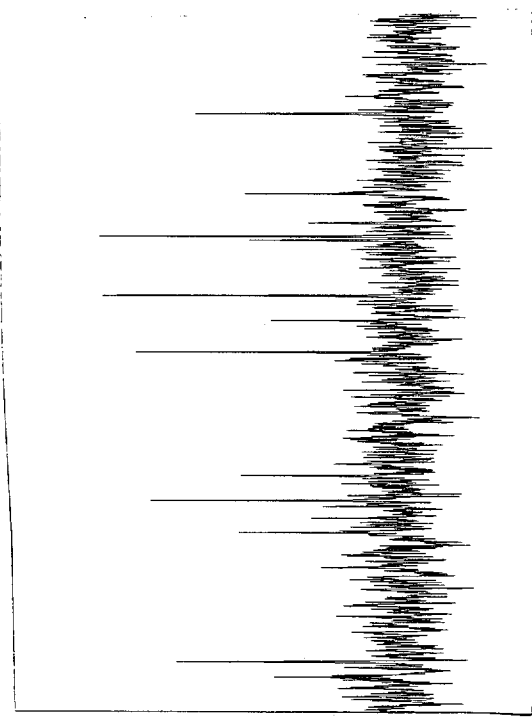
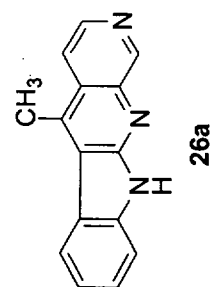












X : parts per Million : 13C

