Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Cumene promoted tandem radical cyclization of *N*-methacryloyl benzamides: an approach to brominated isoquinolinediones using CBr_4 as bromine source

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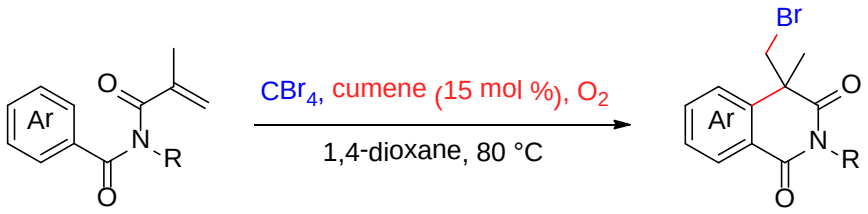

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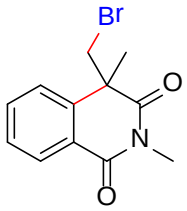
General Information.

The starting materials, reagents and solvents, purchased from commercial suppliers, were used without further purification. Analytical TLC was performed with silica gel GF254 plates, and the products were visualized by UV detection. Flash chromatography was carried out using silica gel 200−300. ^{1}HNMR (600 MHz) and ^{13}CNMR (150 MHz) spectra were measured with $CDCl_3$ as solvent. All chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. High resolution mass spectra (HR-MS) were recorded under electrospray ionization (ESI) conditions.

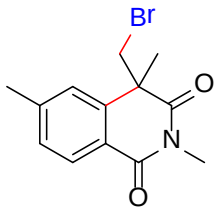
General procedure for cumene promoted tandem radical cyclization of *N*-methacryloyl benzamides to construct brominated isoquinolinediones.

To a stirred solution of *N*-methacryloyl benzamide (**1**, 0.5 mmol) and CBr_4 (0.75 mmol) in dioxane (5 mL), cumene (15 mol %) were added. The reactions were performed at 80 ^{o}C under O_2 atmosphere (ballon) and completed within 2-18 hours as monitored by TLC. The products (**2**) were isolated by flash column chromatographic separation (acetone/PE = 1:50 – 1:20).

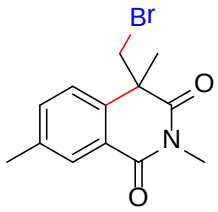
Characterization data for all compounds



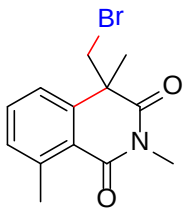
4-(bromomethyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2a) The desired pure product was obtained in 80% yield (112.5 mg) as a white solid, mp 133-134 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.6 Hz, 1H), 7.69 (t, *J* = 8.2 Hz, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 4.16 (d, *J* = 9.9 Hz, 1H), 3.67 (d, *J* = 9.9 Hz, 1H), 3.41 (s, 3H), 1.72 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.2, 163.9, 141.1, 134.2, 129.0, 128.1, 125.3, 124.6, 49.1, 40.2, 28.3, 27.3. HRMS (ESI) exact mass calcd for $C_{12}H_{12}BrNO_2$ [M+H] m/z 282.0124, found 282.0115.



4-(bromomethyl)-2,4,6-trimethylisoquinoline-1,3(2H,4H)-dione (2b) The desired pure product was obtained in 82% yield (120.8 mg) as a white solid, mp 171-173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.17 (s, 1H), 4.16 (d, *J* = 9.8 Hz, 1H), 3.67 (d, *J* = 9.8 Hz, 1H), 3.40 (s, 3H), 2.48 (s, 3H), 1.71 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 164.2, 145.4, 141.3, 129.4, 129.3, 125.2, 123.1, 49.3, 40.6, 28.5, 27.4, 22.3. HRMS (ESI) exact mass calcd for $C_{13}H_{15}BrNO_2$ [M+H] m/z 296.0281, found 296.0277.

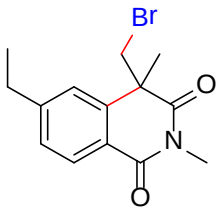


4-(bromomethyl)-2,4,7-trimethylisoquinoline-1,3(2H,4H)-dione (2c) The desired pure product was obtained in 96% yield (141.7 mg) as a white solid, mp 125-127 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.49 (d, *J* = 9.6 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 4.14 (d, *J* = 9.8 Hz, 1H), 3.64 (d, *J* = 9.8 Hz, 1H), 3.39 (s, 3H), 2.44 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.4, 164.1, 138.2, 138.1, 135.2, 129.1, 125.2, 124.5, 48.9, 40.4, 28.2, 27.3, 21.0. HRMS (ESI) exact mass calcd for $C_{13}H_{15}BrNO_2$ [M+H] m/z 296.0281, found 296.0271.

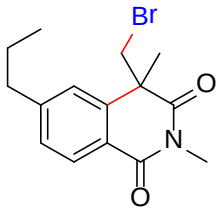


4-(bromomethyl)-2,4,8-trimethylisoquinoline-1,3(2H,4H)-dione (2d) The desired pure product was obtained in 75% yield (109.8 mg) as a white solid, mp 159-161 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 7.9 Hz, 1H), 4.17 (d, *J* = 9.9 Hz, 1H), 3.65 (d, *J* = 9.9 Hz, 1H), 3.37 (s, 3H), 2.79 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (151 MHz,

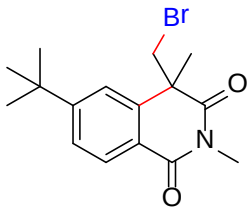
$CDCl_3$) δ 173.9, 164.4, 142.7, 142.3, 133.0, 132.1, 123.7, 122.9, 49.1, 40.7, 28.7, 27.3, 24.0. HRMS (ESI) exact mass calcd for $C_{13}H_{15}BrNO_2$ [M+H] m/z 296.0281, found 296.0286.



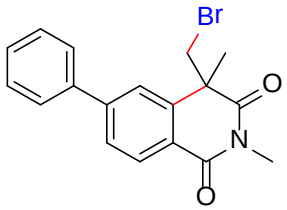
4-(bromomethyl)-6-ethyl-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2e) The desired pure product was obtained in 84% yield (130.2 mg) as a white solid, mp 123-125 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (d, J = 8.1 Hz, 1H), 7.32 (d, J = 9.5 Hz, 1H), 7.17 (s, 1H), 4.15 (d, J = 9.8 Hz, 1H), 3.67 (d, J = 9.8 Hz, 1H), 3.39 (s, 3H), 2.76 (q, J = 7.6 Hz, 2H), 1.71 (s, 3H), 1.29 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.4, 164.0, 151.2, 141.1, 129.1, 127.9, 123.8, 123.0, 49.1, 40.3, 29.2, 28.3, 27.2, 15.1. HRMS (ESI) exact mass calcd for $C_{14}H_{17}BrNO_2$ [M+H] m/z 310.0437, found 310.0433.



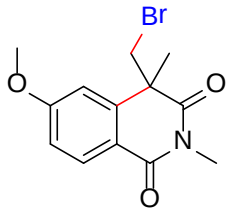
4-(bromomethyl)-2,4-dimethyl-6-propylisoquinoline-1,3(2H,4H)-dione (2f) The desired pure product was obtained in 87% yield (140.5 mg) as a white solid, mp 113-115 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 9.5 Hz, 1H), 7.15 (s, 1H), 4.15 (d, *J* = 9.9 Hz, 1H), 3.66 (d, *J* = 9.8 Hz, 1H), 3.39 (s, 3H), 2.69 (q, *J* = 15.2 Hz, 2H), 1.70 (s, 3H), 1.67(t, *J* = 8.4 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.4, 164.0, 149.8, 141.0, 129.0, 128.5, 124.4, 123.0, 49.1, 40.2, 38.2, 28.3, 27.2, 24.2, 13.7. HRMS (ESI) exact mass calcd for $C_{15}H_{19}BrNO_2$ [M+H] m/z 324.0594, found 324.0602.



4-(bromomethyl)-6-(tert-butyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2g) The desired pure product was obtained in 83% yield (140.3 mg) as a white solid, mp 143-145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 10.2 Hz, 1H), 7.36 (s, 1H), 4.17 (d, *J* = 9.8 Hz, 1H), 3.69 (d, *J* = 9.8 Hz, 1H), 3.40 (s, 3H), 1.73 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 163.9, 158.0, 140.7, 128.8, 125.5, 122.7, 121.1, 49.3, 40.3, 35.4, 31.1, 28.3, 27.2. HRMS (ESI) exact mass calcd for $C_{16}H_{21}BrNO_2$ [M+H] m/z 338.0750, found 338.0747.

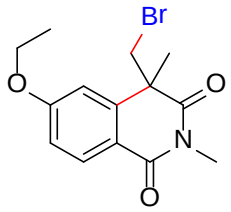


4-(bromomethyl)-2,4-dimethyl-6-phenylisoquinoline-1,3(2H,4H)-dione (2h) The desired pure product was obtained in 81% yield (145.2 mg) as a white solid, mp 231-233 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 9.9 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.55 (s, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 4.20 (d, *J* = 10.0 Hz, 1H), 3.74 (d, *J* = 10.0 Hz, 1H), 3.43 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.3, 163.8, 147.2, 141.6, 139.5, 129.6, 129.1, 128.6, 127.4, 127.0, 124.1, 123.3, 49.3, 40.2, 28.4, 27.3. HRMS (ESI) exact mass calcd for $C_{18}H_{17}BrNO_2$ [M+H] m/z 358.0437, found 358.0426.

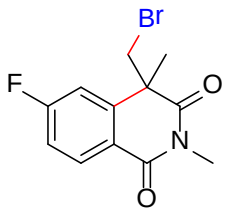


4-(bromomethyl)-6-methoxy-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2i) The desired pure product was obtained in 96% yield (162.0 mg) as a white solid, mp 139-140 °C. ^{1}H NMR (600

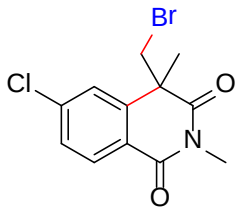
MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.8 Hz, 1H), 7.00 (d, *J* = 11.2 Hz, 1H), 6.82 (d, *J* = 2.4 Hz, 1H), 4.14 (d, *J* = 9.9 Hz, 1H), 3.90 (s, 3H), 3.62 (d, *J* = 9.8 Hz, 1H), 3.38 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.3, 164.3, 163.6, 143.3, 131.4, 118.3, 113.5, 110.2, 55.6, 49.3, 40.2, 28.4, 27.1. HRMS (ESI) exact mass calcd for $C_{13}H_{15}BrNO_3$ [M+H] m/z 312.0230, found 312.0225.



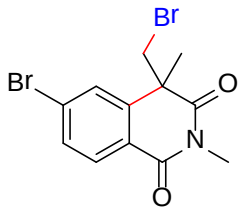
4-(bromomethyl)-6-ethoxy-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2j) The desired pure product was obtained in 85% yield (137.9 mg) as a white solid, mp 166-167 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.8 Hz, 1H), 6.98 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.81 (s, 1H), 4.13 (q, *J* = 9.8 Hz, 2H), 4.11 (d, *J* = 7.0 Hz, 1H), 3.62 (d, *J* = 9.8 Hz, 1H), 3.37 (s, 3H), 1.69 (s, 3H), 1.45 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.4, 163.7, 163.6, 143.2, 131.3, 118.1, 113.9, 110.6, 64.0, 49.3, 40.2, 28.4, 27.1, 14.6. HRMS (ESI) exact mass calcd for $C_{14}H_{17}BrNO_3$ [M+H] m/z 326.0386, found 326.0379.



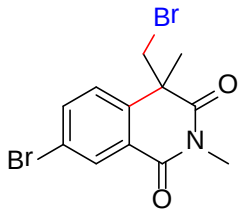
4-(bromomethyl)-6-fluoro-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2k) The desired pure product was obtained in 82% yield (123.1 mg) as a white solid, mp 137-139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (t, 1H), 7.21 (t, *J* = 9.2 Hz, 1H), 7.08 (d, *J* = 11.5 Hz, 1H), 4.16 (d, *J* = 10.0 Hz, 1H), 3.61 (d, *J* = 10.0 Hz, 1H), 3.41 (s, 3H), 1.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 167.7, 165.2, 163.0, 144.1, 144.0, 132.1, 132.0, 121. 8, 116.2, 116.0, 111.8, 111.6, 49.3, 39.8, 28.2, 27.3. HRMS (ESI) exact mass calcd for $C_{12}H_{12}BrFNO_2$ [M+H] m/z 300.0030, found 300.0022.



4-(bromomethyl)-6-chloro-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2l) The desired pure product was obtained in 82% yield (129.8 mg) as a white solid, mp 187-188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.5 Hz, 1H), 7.48 (d, *J* = 10.4 Hz, 1H), 7.38 (s, 1H), 4.16 (d, *J* = 10.0 Hz, 1H), 3.62 (d, *J* = 10.0 Hz, 1H), 3.41 (s, 3H), 1.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 163.1, 142.7, 140.8, 130.6, 128.8, 124.9, 123.8, 49.2, 39.9, 28.1, 27.3. HRMS (ESI) exact mass calcd for $C_{12}H_{12}BrClNO_2$ [M+H] m/z 315.9734, found 315.9743.

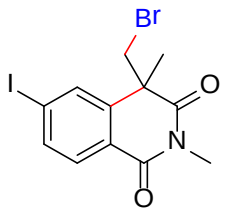


6-bromo-4-(bromomethyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2m) The desired pure product was obtained in 80% yield (143.6 mg) as a white solid, mp 199-200 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.4 Hz, 1H), 7.63 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.53 (d, *J* = 1.8 Hz, 1H), 4.13 (d, *J* = 10.0 Hz, 1H), 3.60 (d, *J* = 10.0 Hz, 1H), 3.39 (s, 3H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.6, 163.2, 142.8, 131.7, 130.6, 129.4, 127.9, 124.3, 49.1, 39.9, 28.1, 27.4. HRMS (ESI) exact mass calcd for $C_{12}H_{12}Br_2NO_2$ [M+H] m/z 359.9229, found 359.9235.

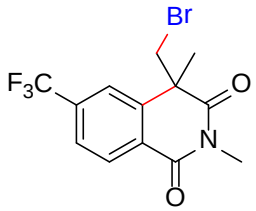


7-bromo-4-(bromomethyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2n) The desired pure product was obtained in 78% yield (140.0 mg) as a white solid, mp 126-128 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.79 (d, *J* = 10.6 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 4.14 (d, *J* = 10.0

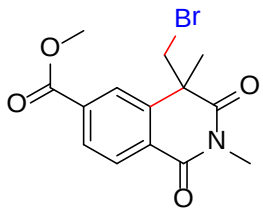
Hz, 1H), 3.61 (d, *J* = 10.0 Hz, 1H), 3.40 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.7, 162.7, 139.9, 137.2, 131.8, 127.0, 126.5, 122.2, 49.0, 39.8, 28.1, 27.5. HRMS (ESI) exact mass calcd for $C_{12}H_{12}Br_2NO_2$ [M+H] m/z 359.9229, found 359.9236.



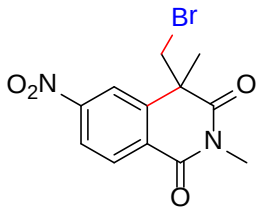
4-(bromomethyl)-6-iodo-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (2o) The desired pure product was obtained in 50% yield (120.1 mg) as a white solid, mp 176-178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 9.9 Hz, 1H), 7.75 (s, 1H), 4.14 (d, *J* = 10.0 Hz, 1H), 3.61 (d, *J* = 9.9 Hz, 1H), 3.40 (s, 3H), 1.72 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 173.5, 163.5, 142.6, 137.6, 133.9, 130.3, 124.8, 102.1, 49.0, 39.9, 28.1, 27.4. HRMS (ESI) exact mass calcd for $C_{12}H_{12}BrINO_2$ [M+H] m/z 407.9091, found 407.9099.



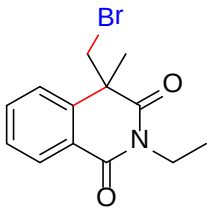
4-(bromomethyl)-2,4-dimethyl-6-(trifluoromethyl)isoquinoline-1,3(2H,4H)-dione (2p) The desired pure product was obtained in 72% yield (125.6mg) as a white solid, mp153-155 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.63 (s, 1H), 4.17 (d, *J* = 10.2 Hz, 1H), 3.66 (d, *J* = 10.1 Hz, 1H), 3.42 (s, 3H), 1.76 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.5, 162.8, 141.9, 135.6, 129.9, 128.2, 124.9, 122.3, 121.8, 49.3, 39.8, 28.0, 27.5. HRMS (ESI) exact mass calcd for $C_{13}H_{11}BrF_3NO_2$ [M+H] m/z 349.9998, found 349.9994.



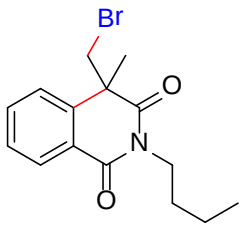
Methyl 4-(bromomethyl)-2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinoline-6-carboxylate (2q) The desired pure product was obtained in 78% yield (132.7 mg) as a white solid, mp 112-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.6 Hz, 1H), 8.14 (dd, *J* = 8.2, 1.5 Hz, 1H), 8.08 (s, 1H), 4.18 (d, *J* = 9.9 Hz, 1H), 3.99 (s, 3H), 3.73 (d, *J* = 9.9 Hz, 1H), 3.43 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.8, 165.7, 163.2, 141.3, 135.2, 129.3, 128.8, 128.6, 126.1, 52.7, 49.3, 40.1, 28.1, 27.4. HRMS (ESI) exact mass calcd for $C_{14}H_{15}BrNO_4$ [M+H] m/z 340.0179, found 340.0187.



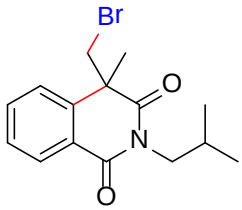
4-(bromomethyl)-2,4-dimethyl-6-nitroisoquinoline-1,3(2H,4H)-dione (2r) The desired pure product was obtained in 77% yield (126.3 mg) as a white solid, mp160-162 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.6 Hz, 1H), 8.32 (dd, *J* = 8.6, 2.1 Hz, 1H), 8.26 (d, *J* = 2.1 Hz, 1H), 4.20 (d, *J* = 10.2 Hz, 1H), 3.69 (d, *J* = 10.2 Hz, 1H), 3.43 (s, 3H), 1.80 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.1, 162.2, 151.3, 142.8, 130.8, 130.0, 122.9, 120.3, 49.5, 39.7, 28.0, 27.6. HRMS (ESI) exact mass calcd for $C_{12}H_{12}BrN_2O_4$ [M+H] m/z 326.9975, found 326.9968.



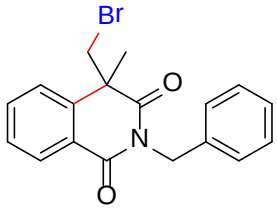
4-(bromomethyl)-2-ethyl-4-methylisoquinoline-1,3(2H,4H)-dione (2s) The desired pure product was obtained in 93% yield (141.8mg) as a colorless oily liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.9 Hz, 1H), 7.67 (t, *J* = 8.3 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 4.15 (d, *J* = 9.9 Hz, 1H), 4.09 (dd, *J* = 7.1, 2.8 Hz, 1H), 4.06 (q, *J* = 7.1, 1H), 3.65 (d, *J* = 9.8 Hz, 1H), 1.70 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.7, 163.4, 141.1, 134.1, 129.0, 128.0, 125.5, 124.6, 48.8, 40.5, 35.9, 28.1, 13.0. HRMS (ESI) exact mass calcd for $C_{13}H_{15}BrNO_2$ [M+H] m/z 296.0281, found 296.0285.



4-(bromomethyl)-2-butyl-4-methylisoquinoline-1,3(2H,4H)-dione (2t) The desired pure product was obtained in 89% yield (142.9mg) as a colorless oily liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.0 Hz, 1H), 7.67 (t, *J* = 8.3 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 4.16 (d, *J* = 9.9 Hz, 1H), 4.07 – 3.98 (m, 2H), 3.66 (d, *J* = 9.9 Hz, 1H), 1.70 (s,3H), 1.66 – 1.58 (m, 2H), 1.42 – 1.34 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.9, 163.6, 141.2, 134.1, 129.0, 128.0, 125.5, 124.6, 48.9, 40.6, 40.34, 29.9, 28.3, 20.3, 13.8. HRMS (ESI) exact mass calcd for $C_{15}H_{19}BrNO_2$ [M+H] m/z 324.0594, found 324.0596.

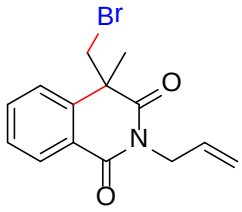


4-(bromomethyl)-2-isobutyl-4-methylisoquinoline-1,3(2H,4H)-dione (2u) The desired pure product was obtained in 84% yield (135.6mg) as a colorless oily liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.9 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 4.17 (d, *J* = 11.2 Hz, 1H), 3.93 – 3.83 (m, 2H), 3.68 (d, *J* = 9.9 Hz, 1H), 2.19 – 2.08 (m, 1H), 1.69 (s, 3H), 0.92(dd, *J* = 6.7, 1.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.2, 163.9, 141.2, 134.1, 129.2, 128.0, 125.4, 124.6, 49.1, 47.5, 40.0, 28.7, 27.2, 20.3, 20.2. HRMS (ESI) exact mass calcd for $C_{15}H_{19}BrNO_2$ [M+H] m/z 324.0594, found 324.0596.

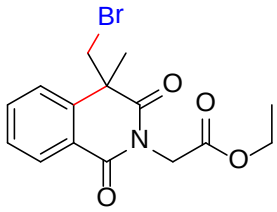


2-benzyl-4-(bromomethyl)-4-methylisoquinoline-1,3(2H,4H)-dione (2v) The desired pure product was obtained in 82% yield (147.6 mg) as a white solid, mp 115-117 °C. ^{1}H NMR (600

MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.9 Hz, 1H), 7.68 (t, *J* = 8.3 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 5.26 (d, *J* = 14.0 Hz, 1H), 5.19 (d, *J* = 14.0 Hz, 1H), 4.19 (d, *J* = 9.9 Hz, 1H), 3.68 (d, *J* = 9.9 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.1, 163.6, 141.2, 136.8, 134.3, 129.2, 128.5, 128.4, 128.1, 127.4, 125.3, 124.6, 49.3, 43.9, 40.0, 28.5. HRMS (ESI) exact mass calcd for $C_{18}H_{17}BrNO_2$ [M+H] m/z 358.0437, found 358.0441.

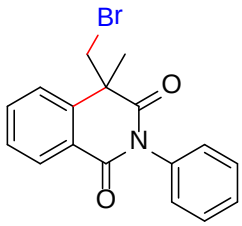


2-allyl-4-(bromomethyl)-4-methylisoquinoline-1,3(2H,4H)-dione (2w) The desired pure product was obtained in 69% yield (105.5 mg) as a white solid, mp 105-106 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 9.2 Hz, 1H), 7.69 (t, *J* = 8.3 Hz, 1H), 7.50 (t, *J* = 8.1 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 5.99 – 5.79 (m, 1H), 5.27 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.17 (dd, *J* = 10.3, 1.3 Hz, 1H), 4.64 (d, *J* = 5.6 Hz, 2H), 4.18 (d, *J* = 9.9 Hz, 1H), 3.68 (d, *J* = 9.9 Hz, 1H), 1.72 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.7, 163.3, 141.2, 134.3, 131.7, 129.1, 128.1, 125.3, 124.6, 117.5, 49.2, 42.7, 40.1, 28.4. HRMS (ESI) exact mass calcd for $C_{14}H_{15}BrNO_2$ [M+H] m/z 308.0281, found 308.0280.

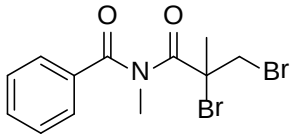


Ethyl 2-(4-(bromomethyl)-4-methyl-1,3-dioxo-3,4-dihydroisoquinolin-2(1H)-yl)acetate (2x) The desired pure product was obtained in 71% yield (125.0 mg) as a white solid, mp 108-110 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.2 Hz, 1H), 7.71 (t, *J* = 8.3 Hz, 1H), 7.50 (t, *J* = 8.1 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 4.77 (q, *J* = 45.2 Hz, 2H), 4.24 – 4.16 (m, 3H), 3.72 (d, *J* = 10.1 Hz, 1H), 1.74 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.8, 167.6, 163.2, 141.2, 134.6, 129.3, 128.2, 124.8, 124.7, 61.6, 49.5, 41.5, 39.1, 28.8, 14.1. HRMS

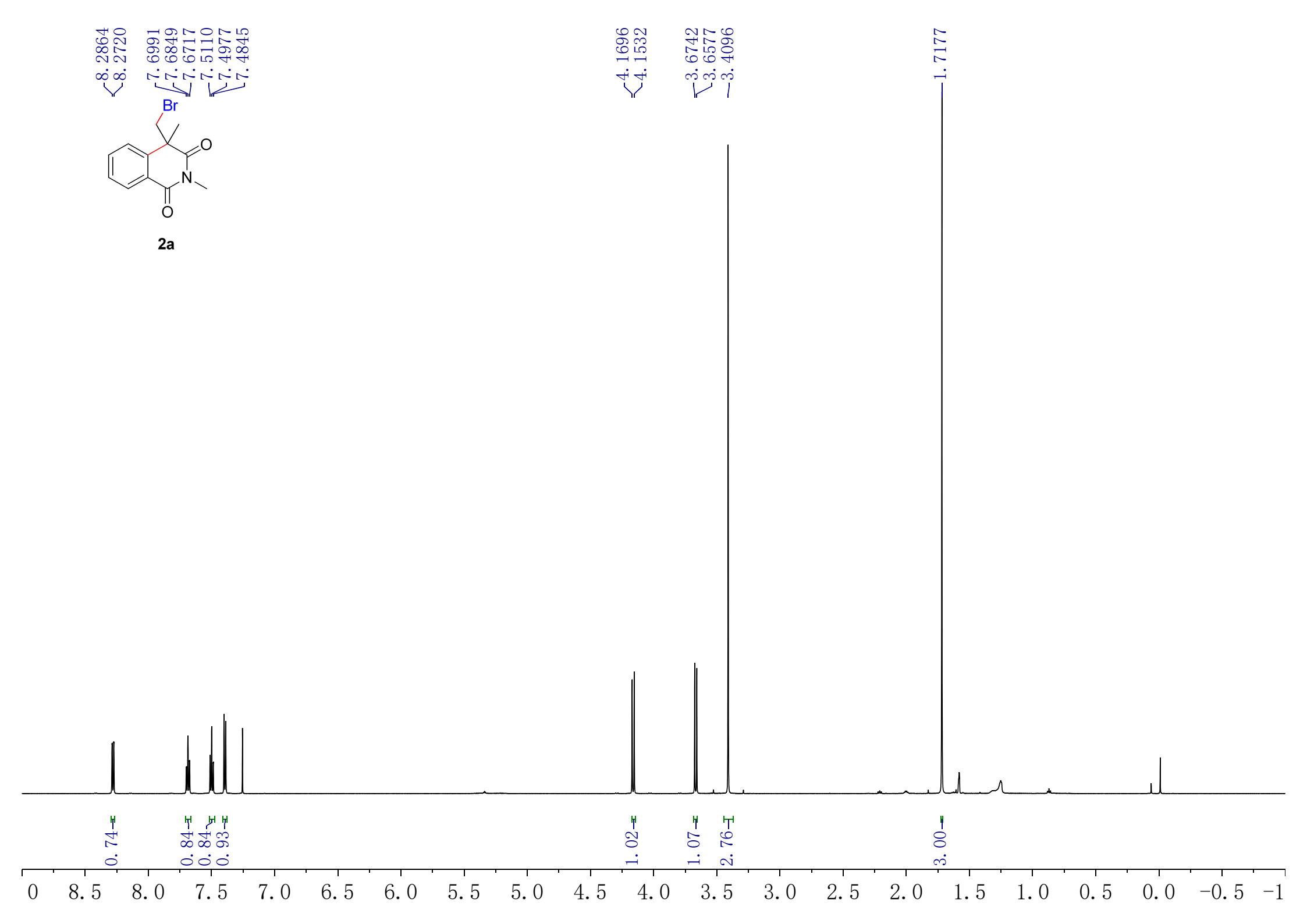
(ESI) exact mass calcd for $C_{15}H_{17}BrNO_4$ [M+H] m/z 354.0335, found 354.0330.



4-(bromomethyl)-4-methyl-2-phenylisoquinoline-1,3(2H,4H)-dione (2y) The desired pure product was obtained in 86% yield (148.1 mg) as a white solid, mp 213-215 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.7 Hz, 1H), 7.74 (t, *J* = 8.3 Hz, 1H), 7.56 – 7.43 (m, 5H), 7.24 (d, *J* = 7.4 Hz, 2H), 4.19 (d, *J* = 9.9 Hz, 1H), 3.72 (d, *J* = 9.8 Hz, 1H), 1.84 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.2, 163.9, 141.2, 135.3, 134.6, 129.3, 129.3, 128.7, 128.3, 128.3, 125.6, 124.8, 49.5, 41.2, 27.8. HRMS (ESI) exact mass calcd for $C_{17}H_{15}BrNO_2$ [M+H] m/z 344.0281, found 344.0277.



N-(2,3-dibromo-2-methylpropanoyl)-N-methylbenzamide The desired pure product was obtained in 11% yield (19.8 mg) as a yellow oily liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 4.38 (d, *J* = 10.0 Hz, 1H), 3.92 (d, *J* = 10.1 Hz, 1H), 3.26 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.5, 173.5, 133.4, 133.0, 129.4, 128.8, 60.7, 41.5, 36.0, 29.7. HRMS (ESI) exact mass calcd for $C_{12}H_{13}Br_2NO_2$ [M+Na] m/z 383.9205, found 383.9200.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1.7177
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N
O
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0.84
0.84
0.93
1.02
1.07
2.76
3.00
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7.5
7.0
6.5
6.0
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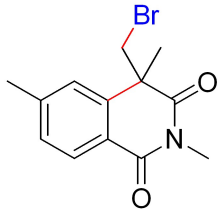
-1



2b

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3.4030
2.4784
1.7105

0.82
0.91
0.93
0.99
1.00
2.94
3.01
3.00

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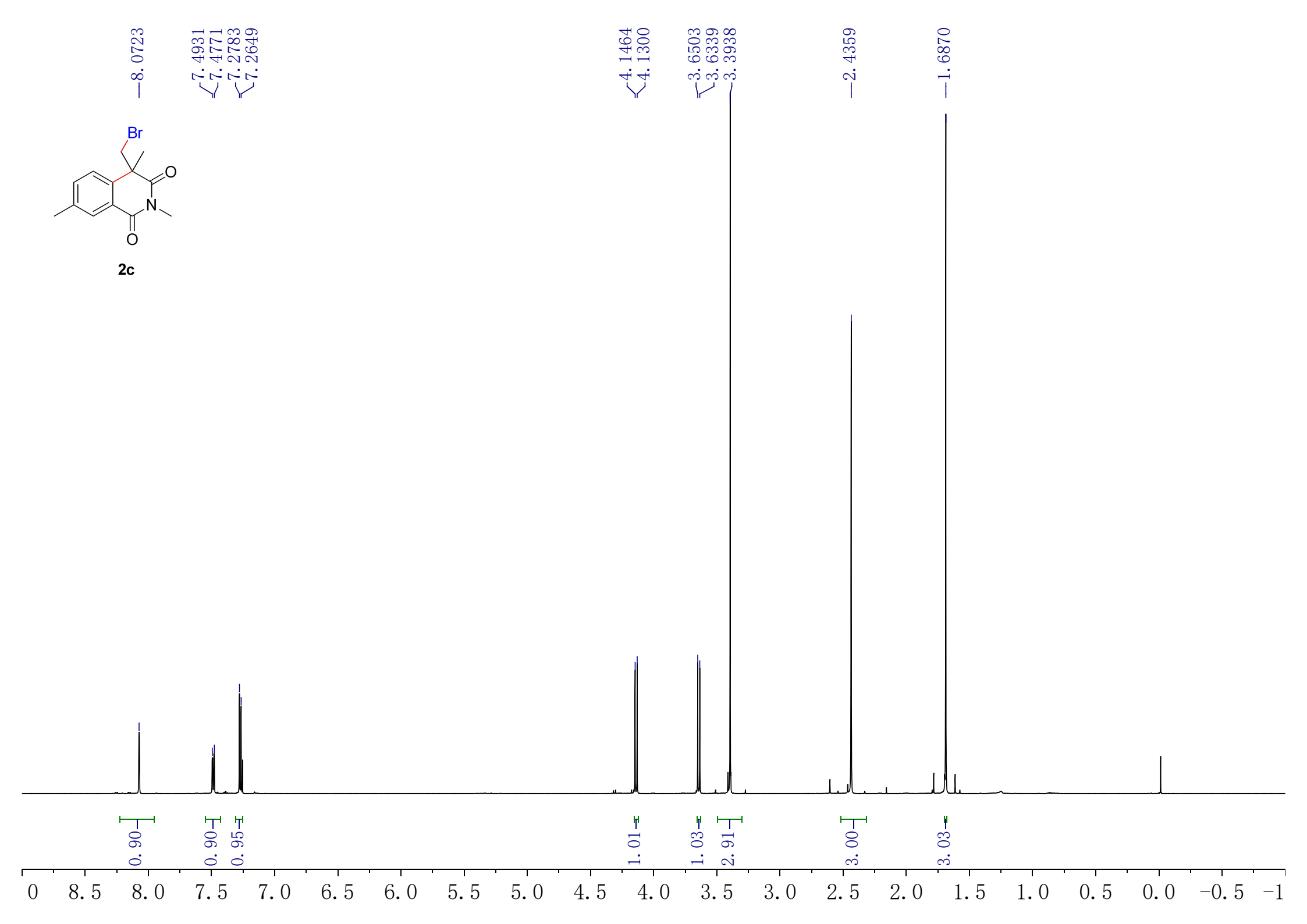
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3.6339
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2.4359
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N
O
2c
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0.90
0.95
1.01
1.03
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3.00
3.03
0
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8.0
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7.0
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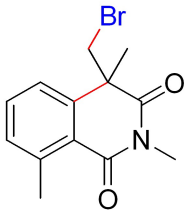

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2.7933
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0.93
0.90
0.96
1.05
1.07
2.90
3.00
2.99

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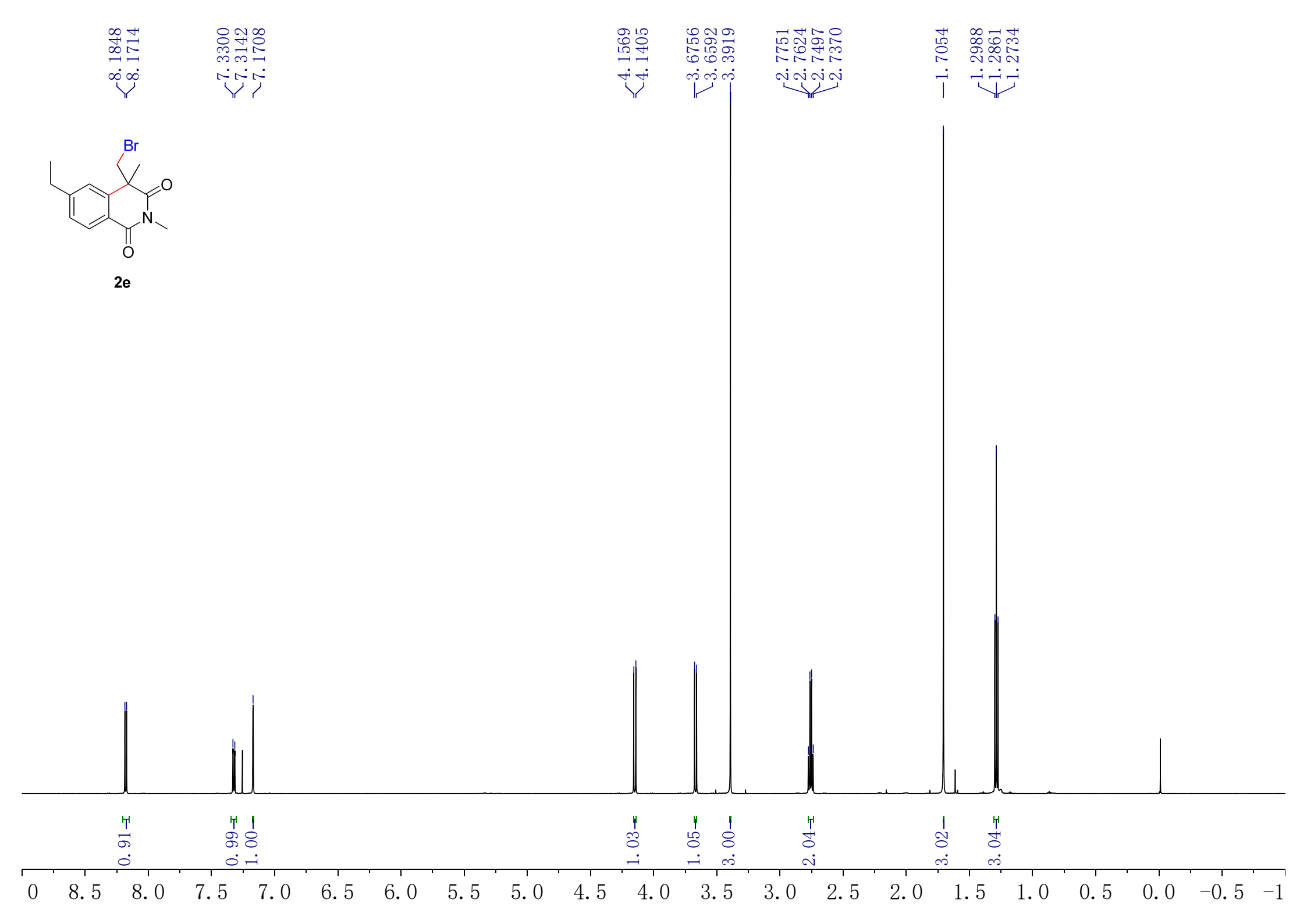
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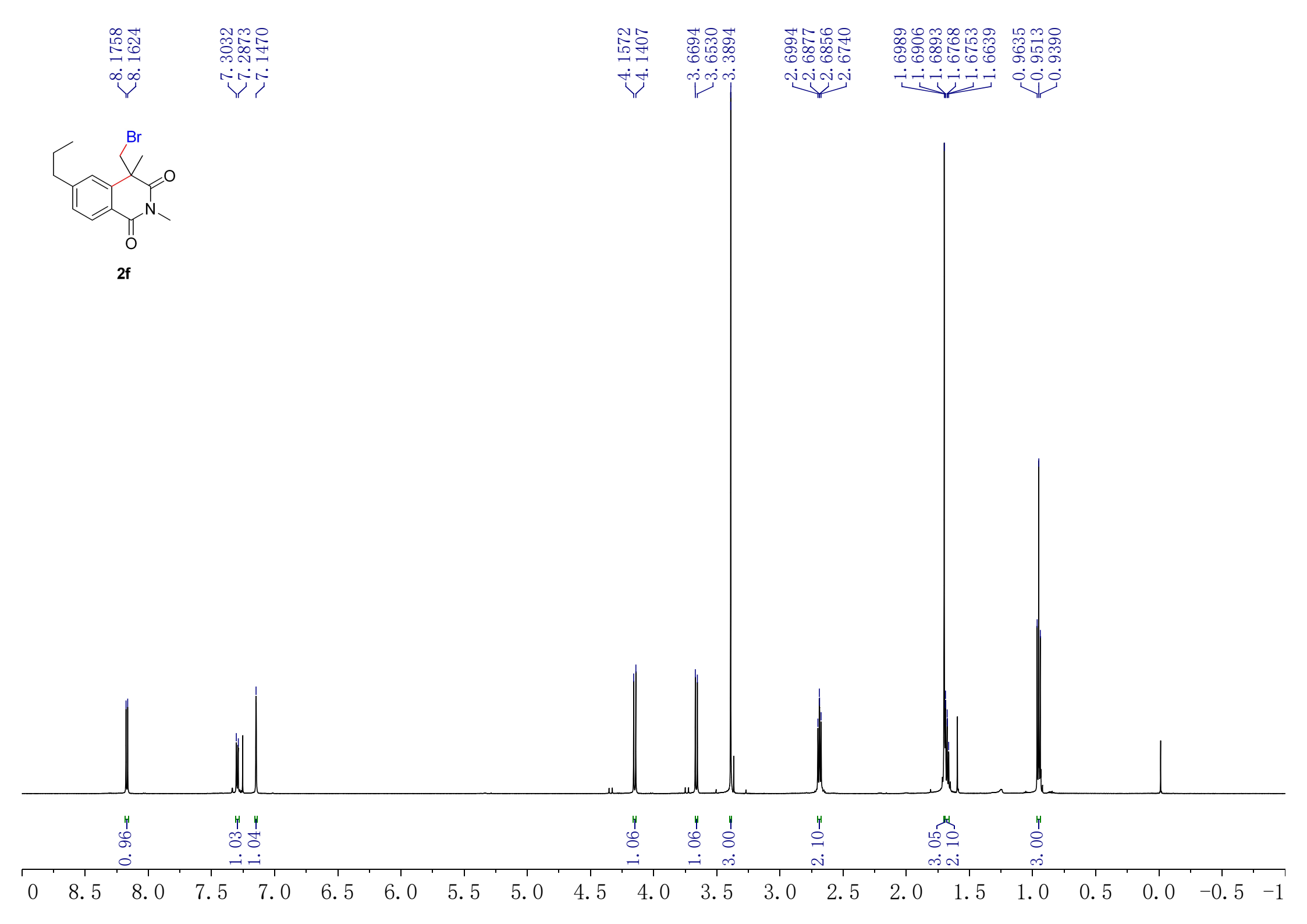
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2.6877
2.6856
2.6740
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1.6906
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1.6768
1.6753
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0.9635
0.9513
0.9390
Br
O
N
O
2f
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1.03
1.04
1.06
1.06
3.00
2.10
3.05
2.10
3.00
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6.5
6.0
5.5
5.0
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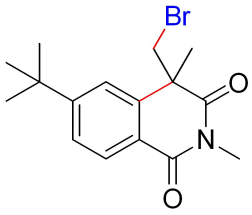

2g

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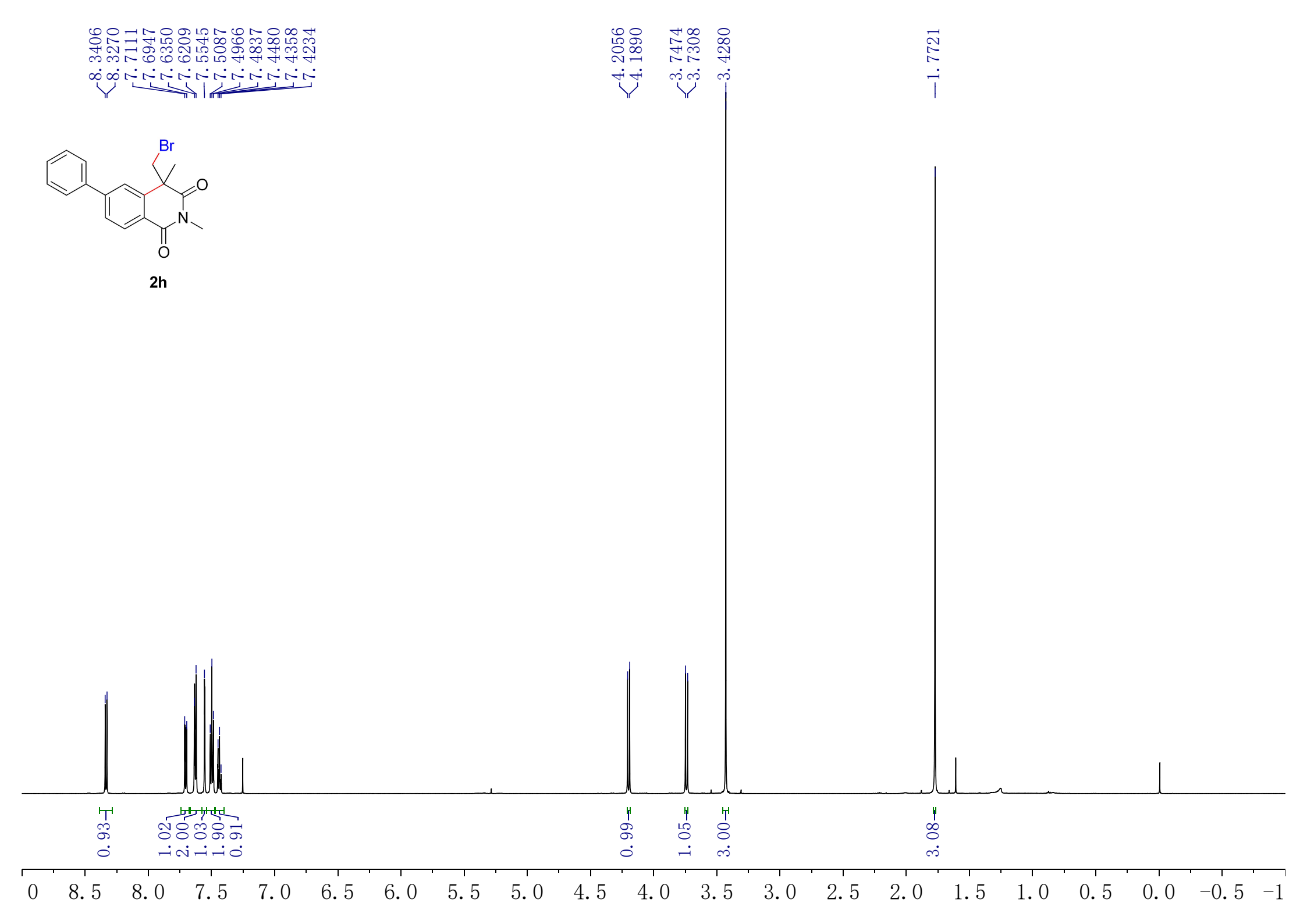
4.1538
3.7072
3.6827
3.4029
1.7252
1.3738

0.95
0.97
0.97
1.01
1.01
2.99
3.00
9.03

0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1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3.00
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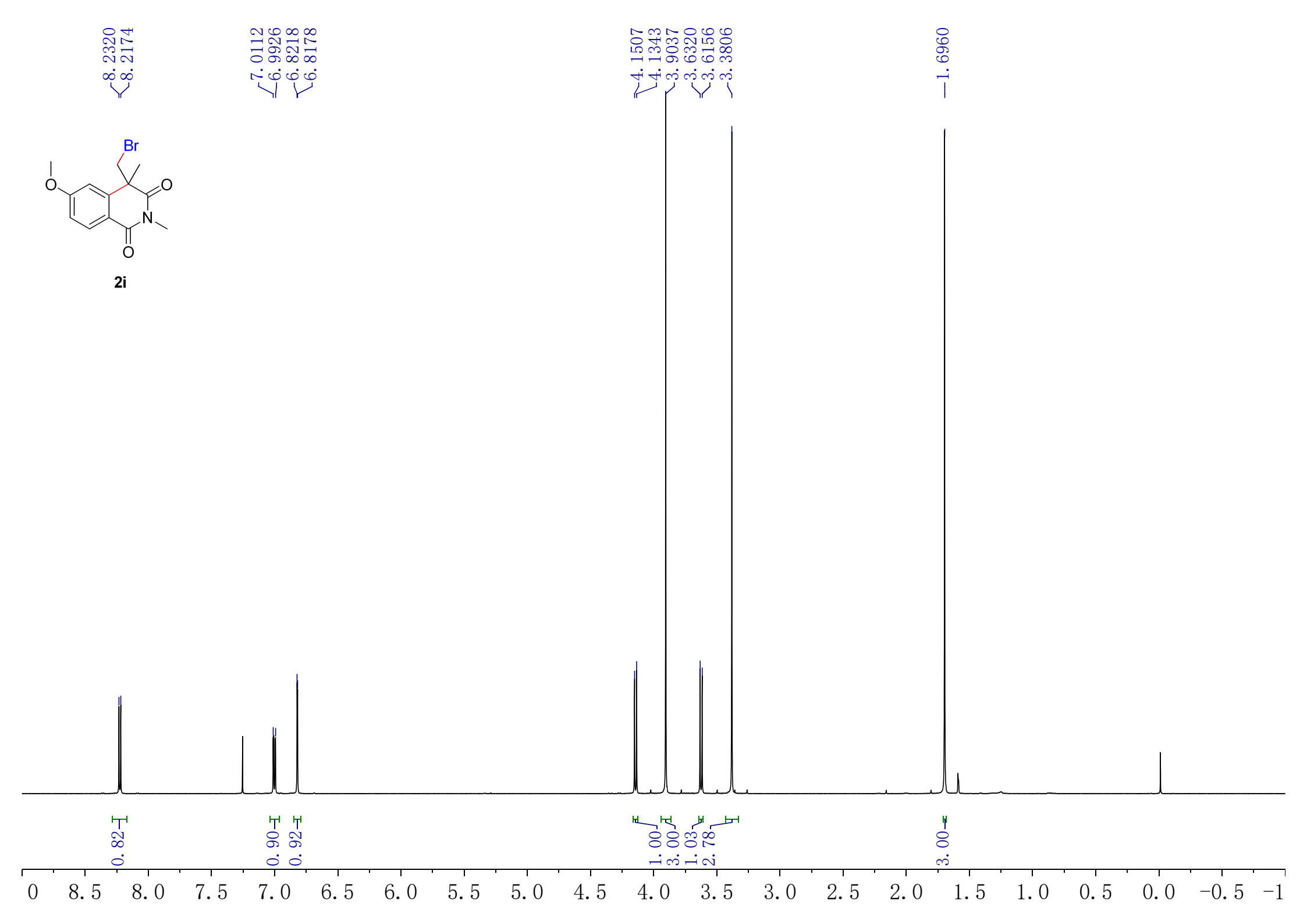
2h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O
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O
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0.90
0.92
1.00
3.00
1.03
2.78
3.00
0
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
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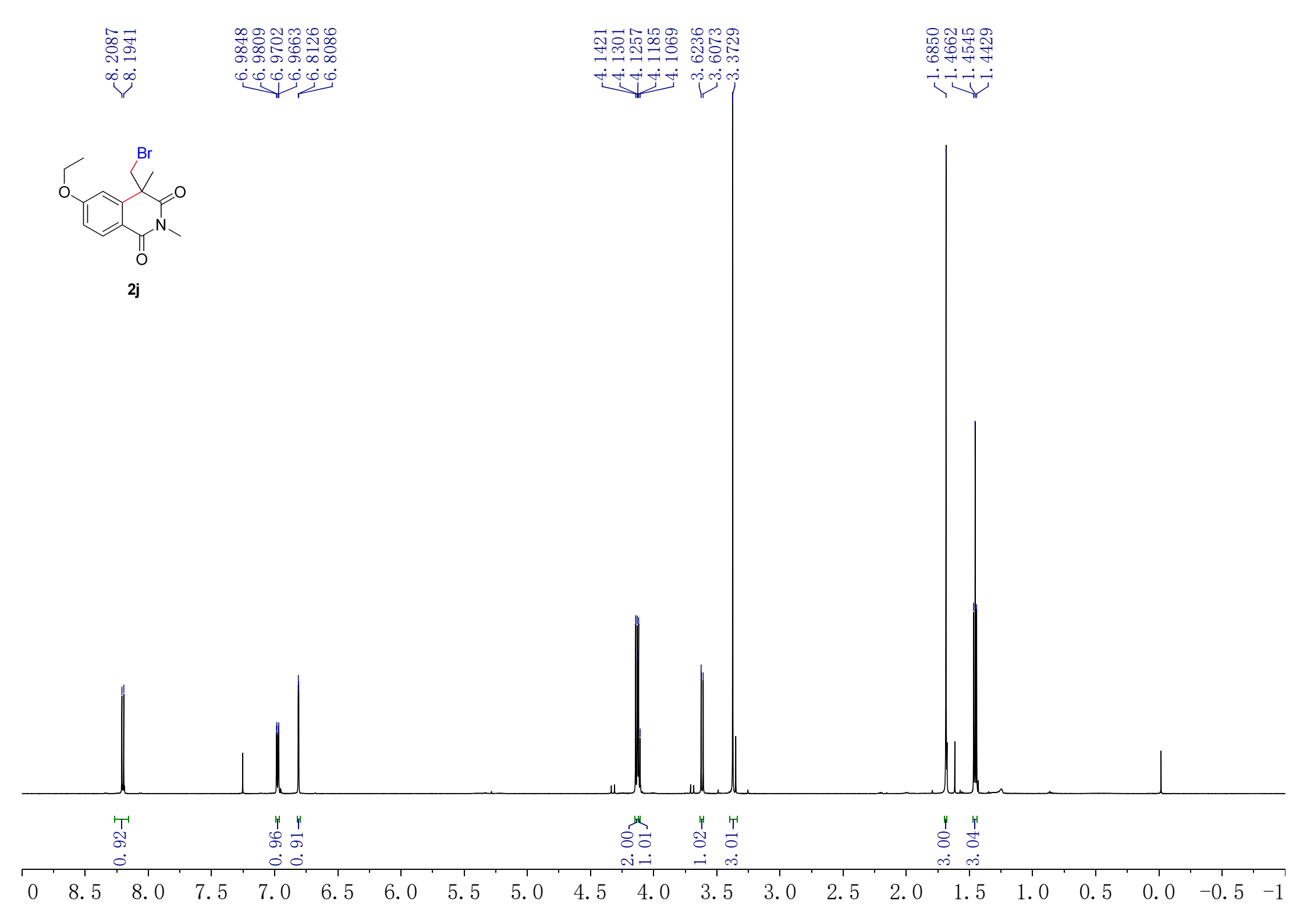
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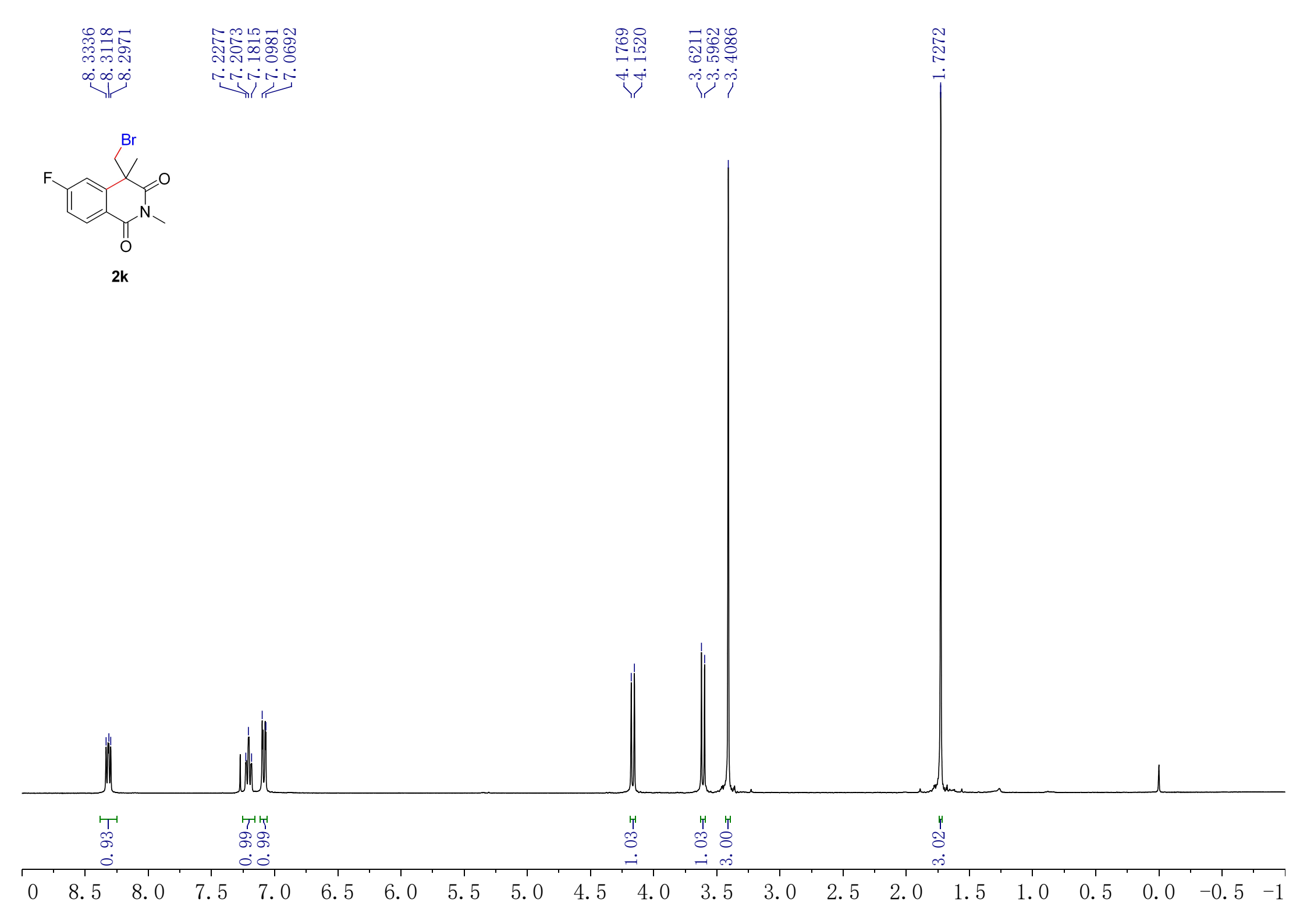
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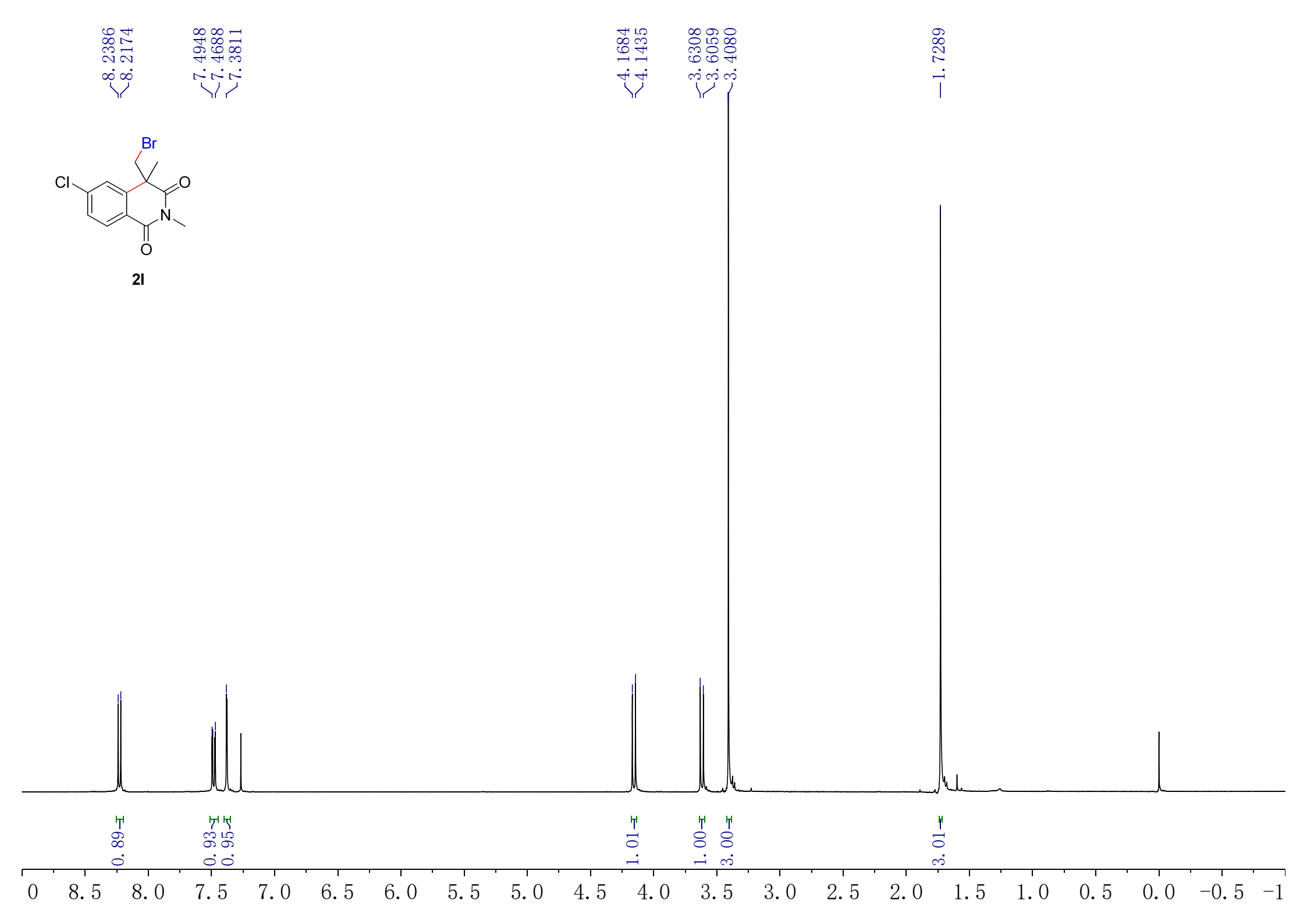
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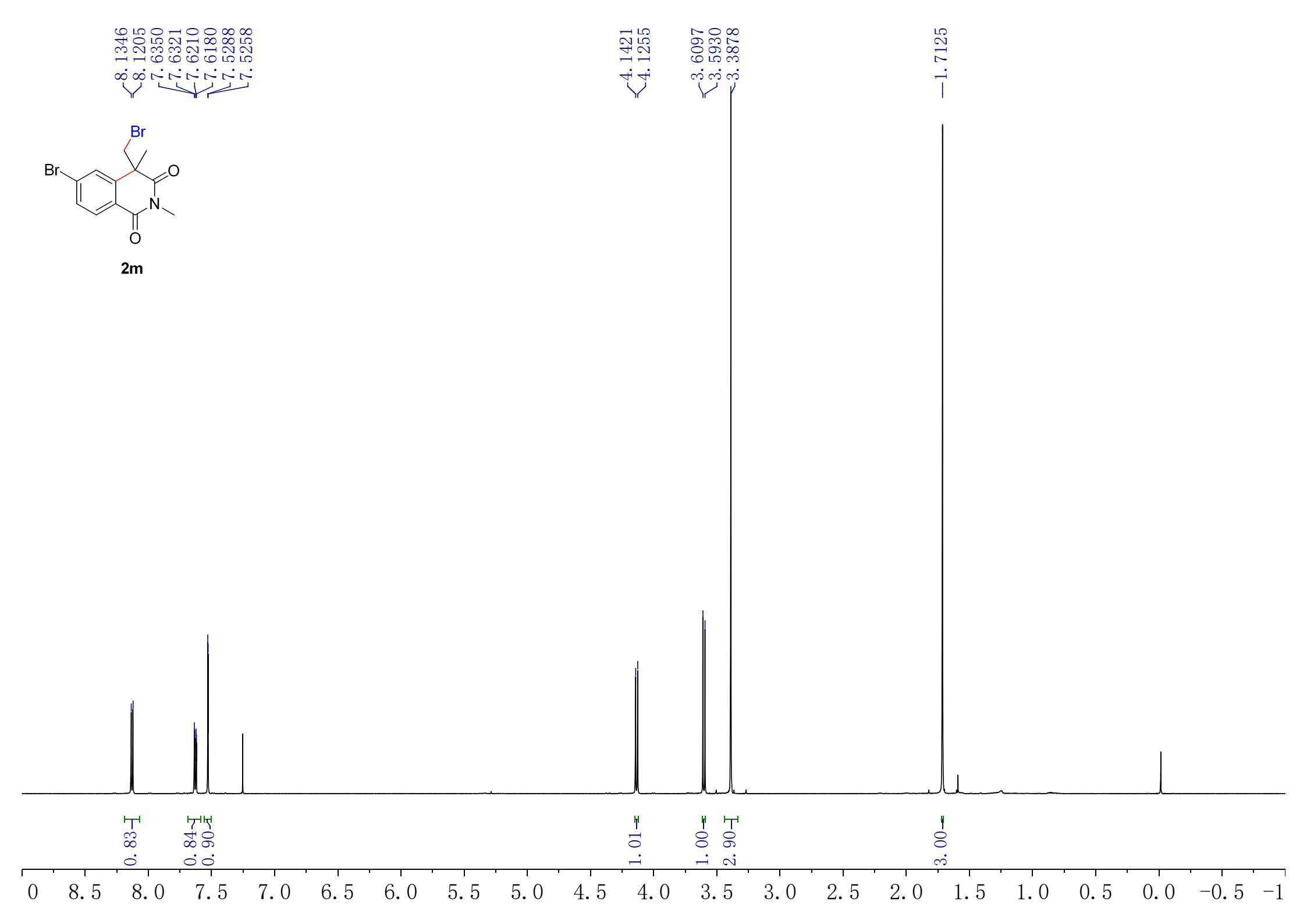
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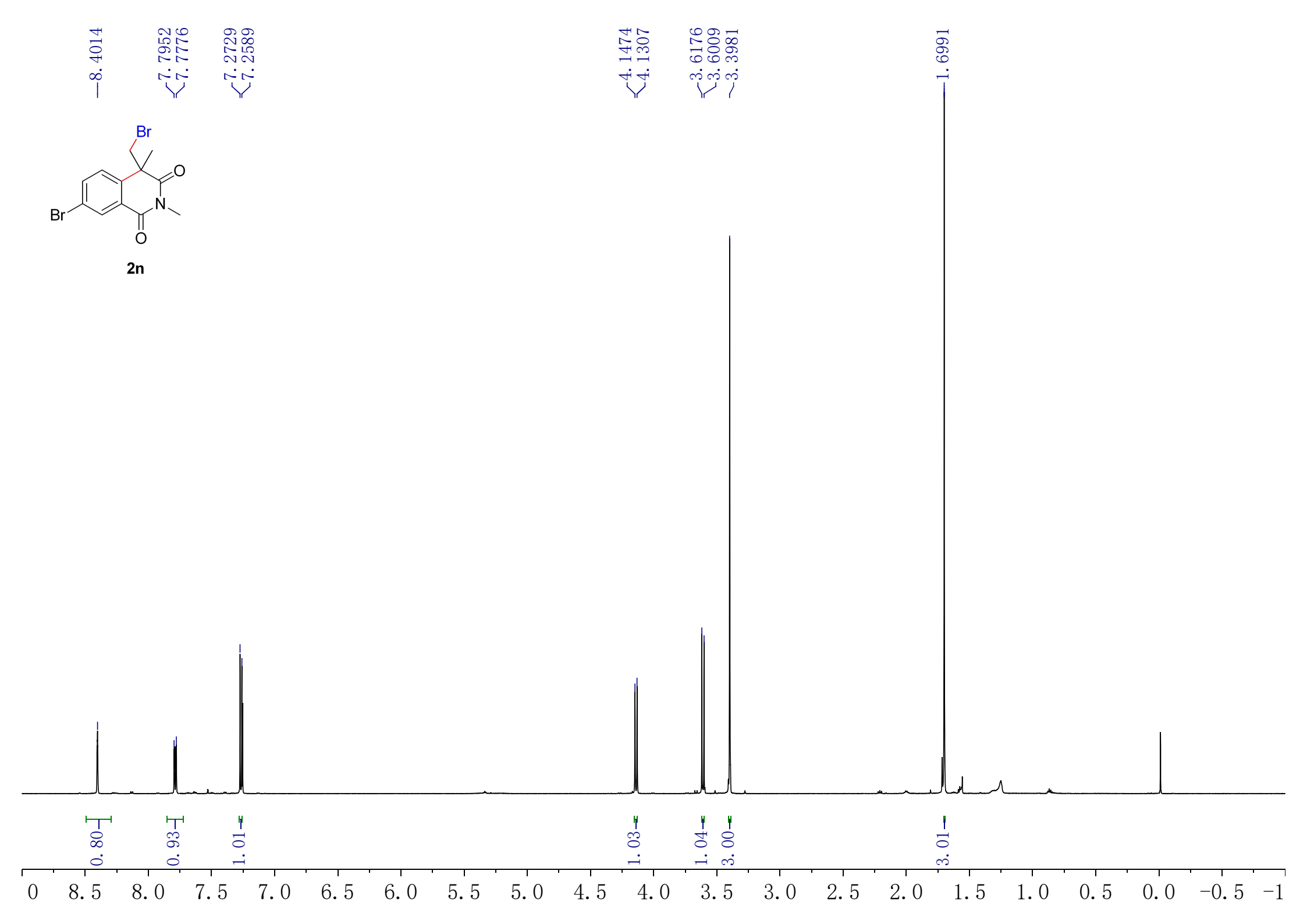
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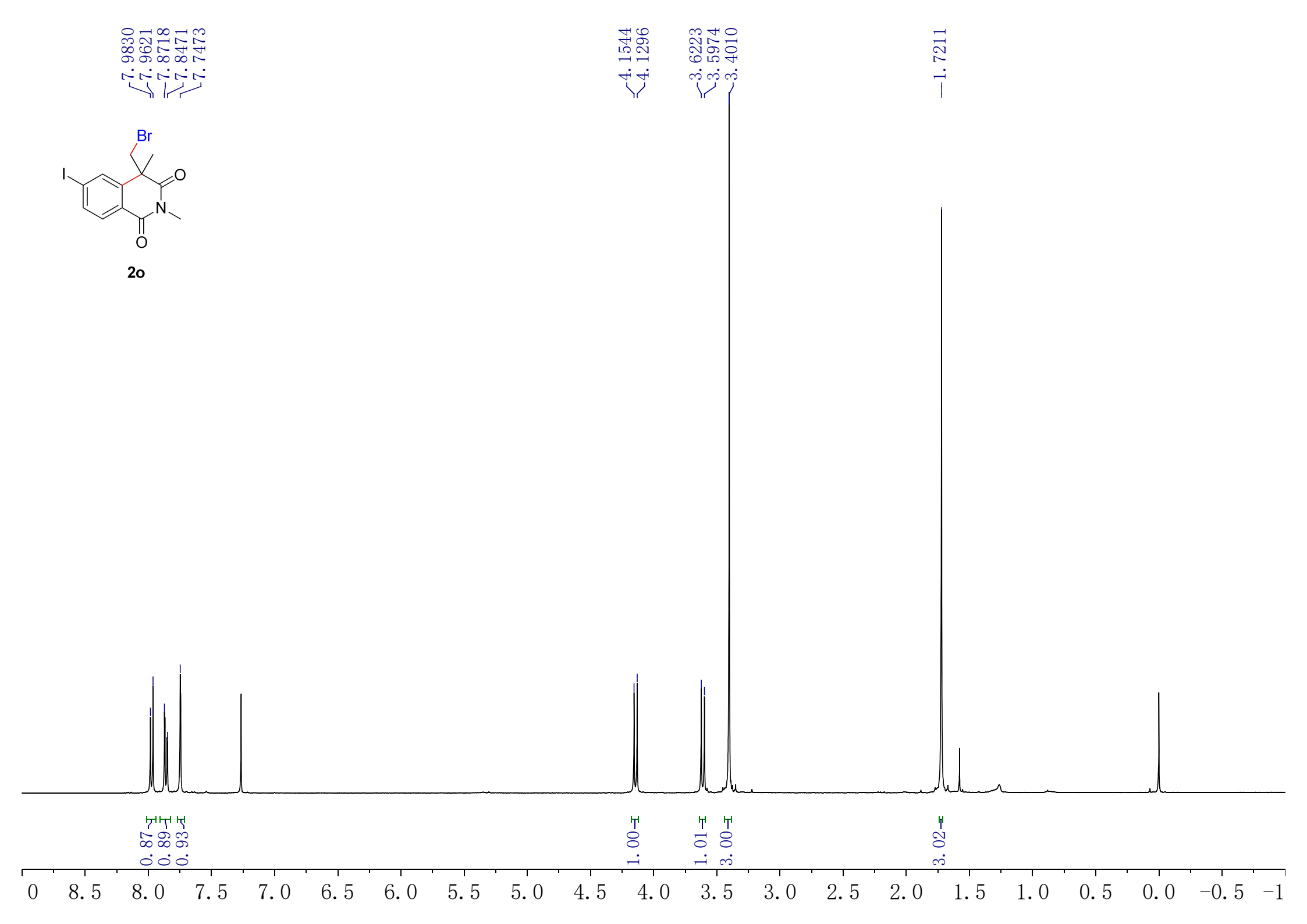
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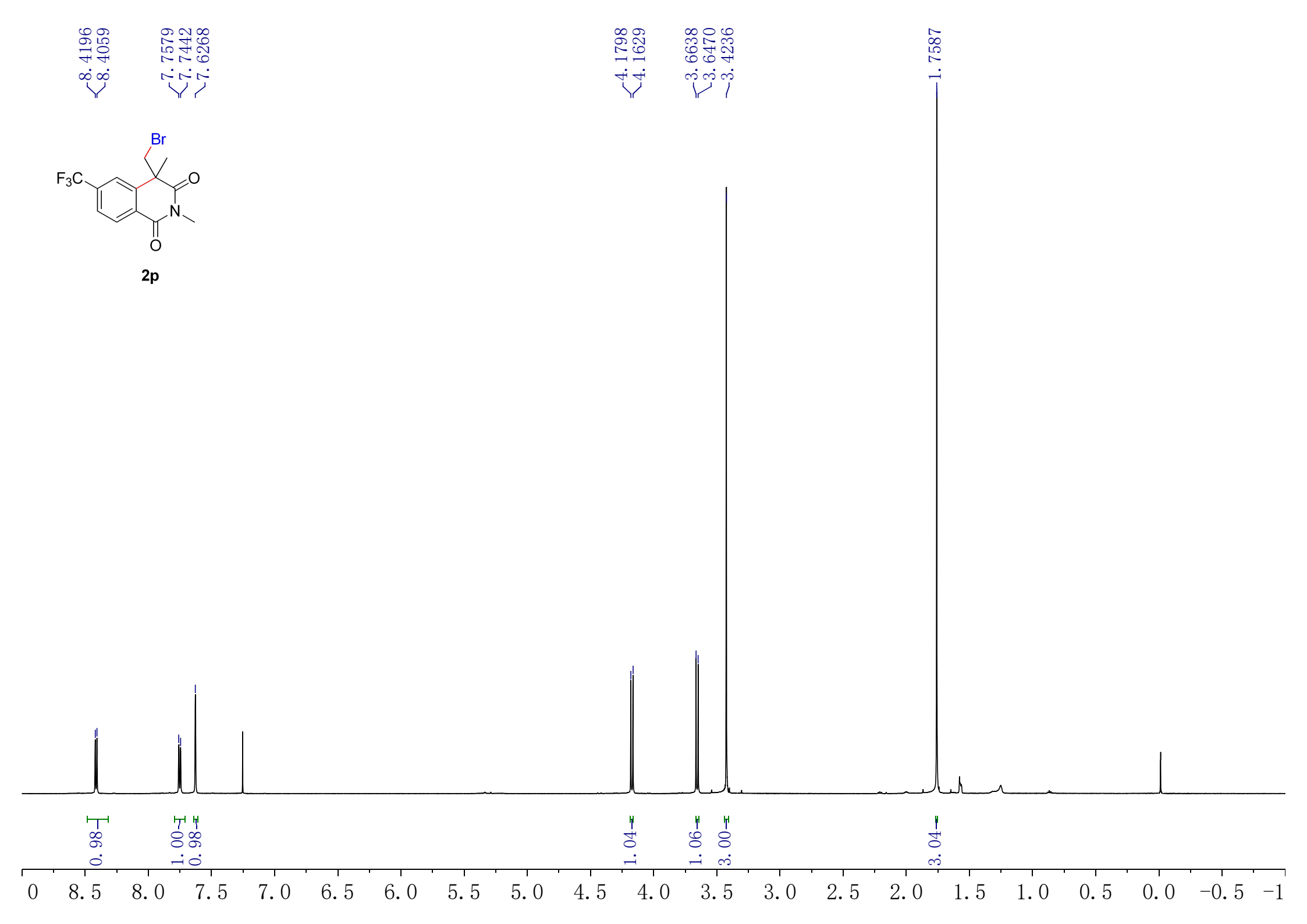
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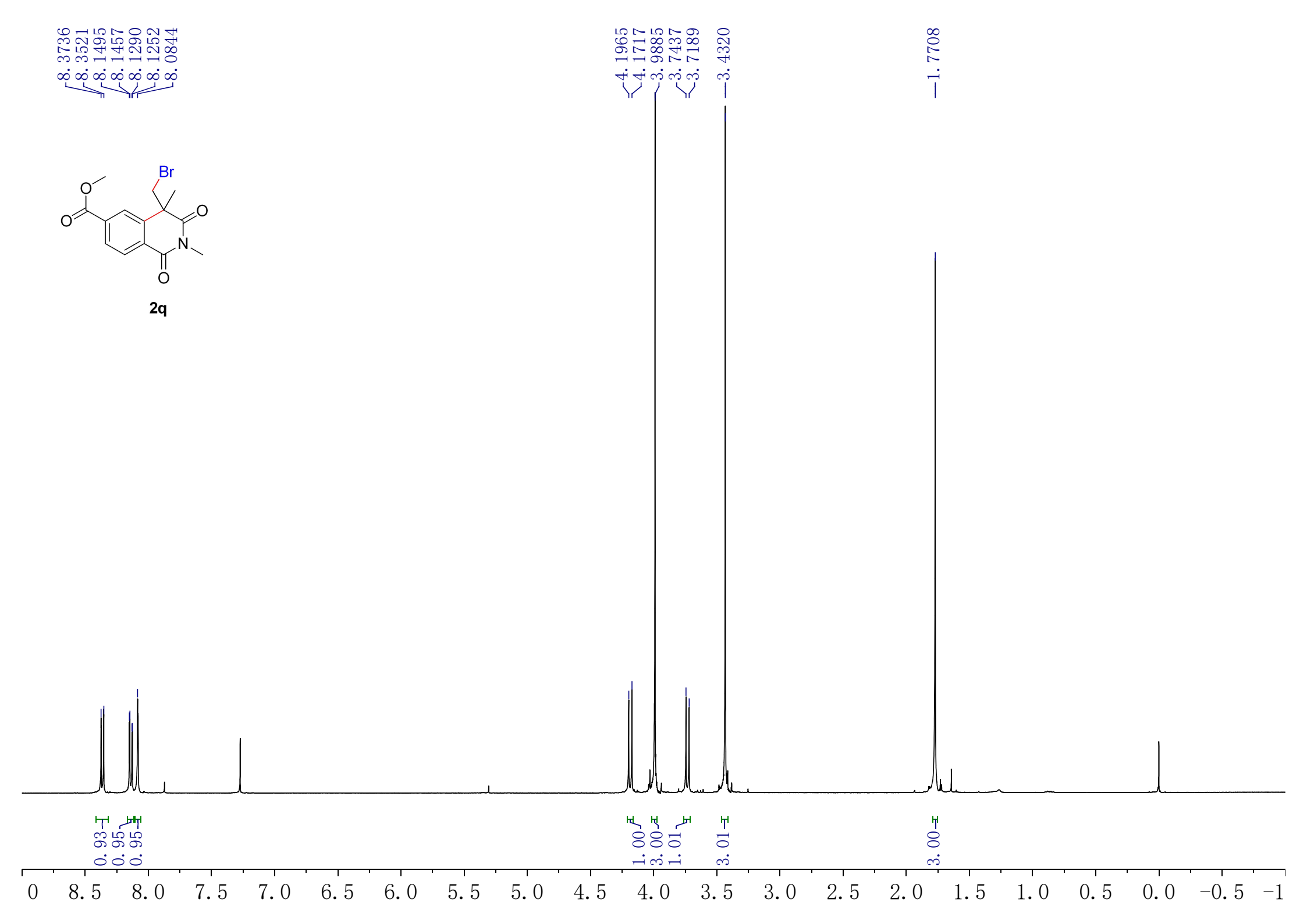
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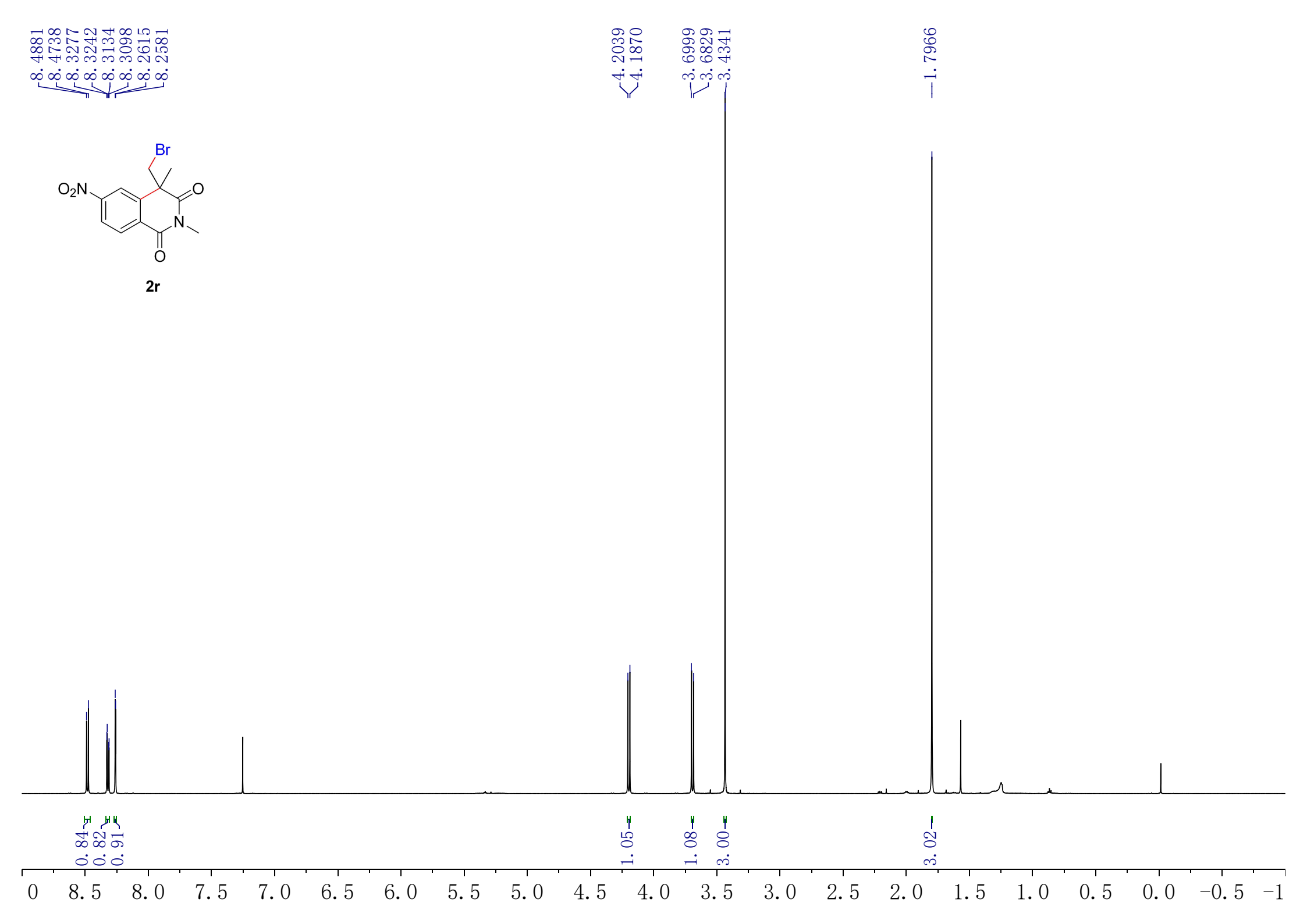
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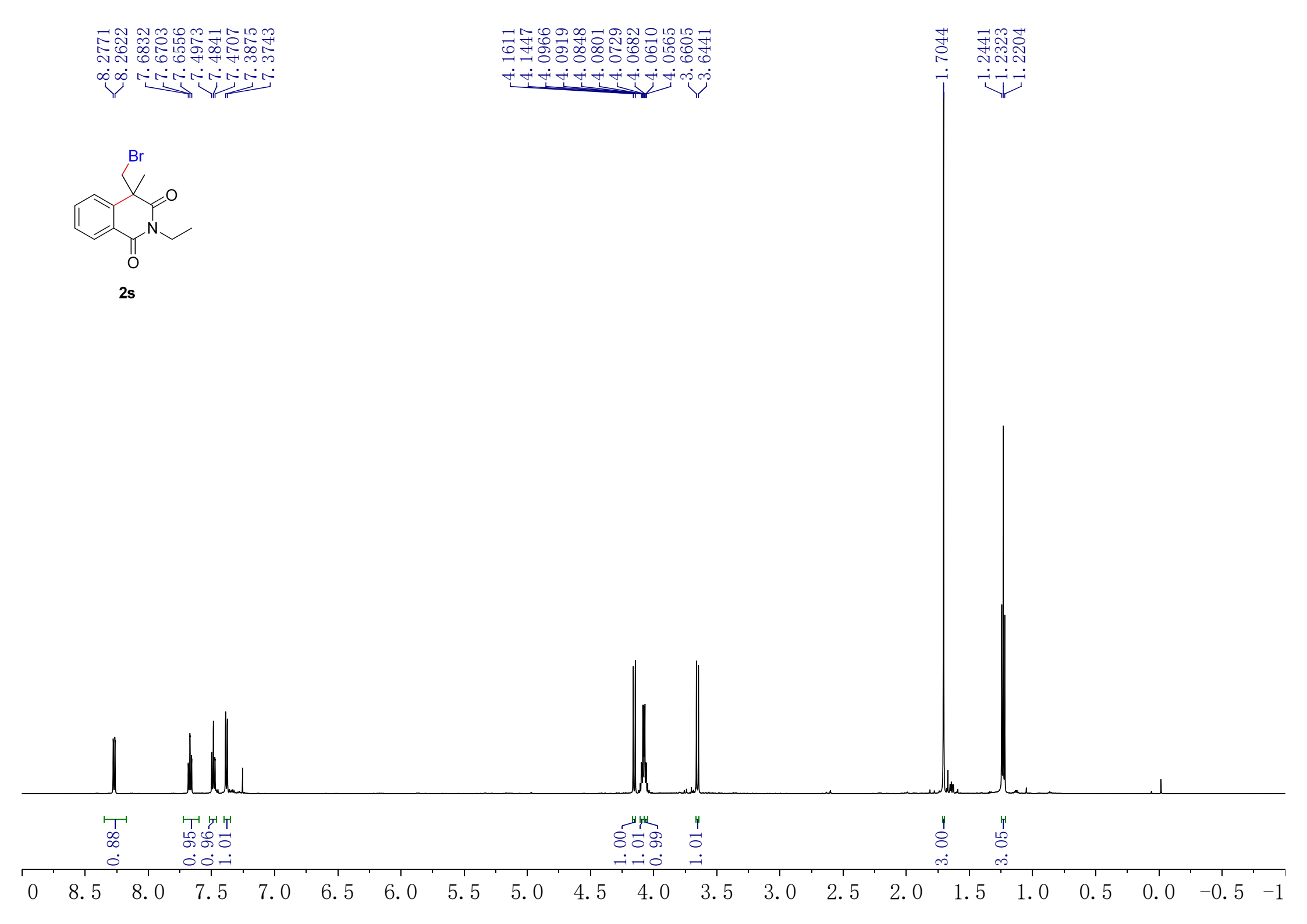
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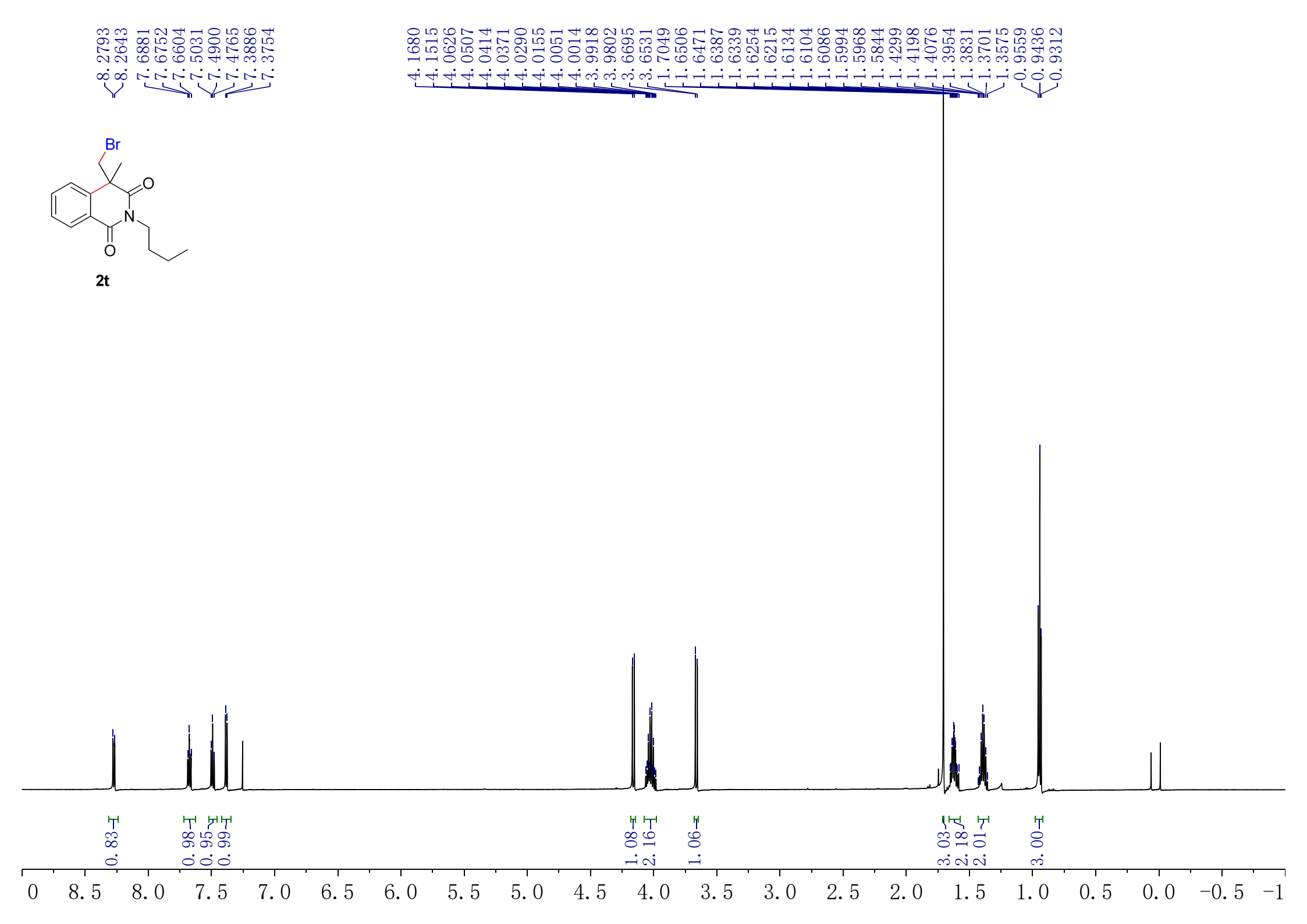
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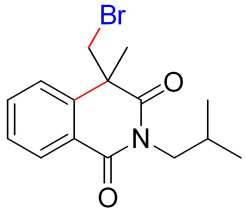

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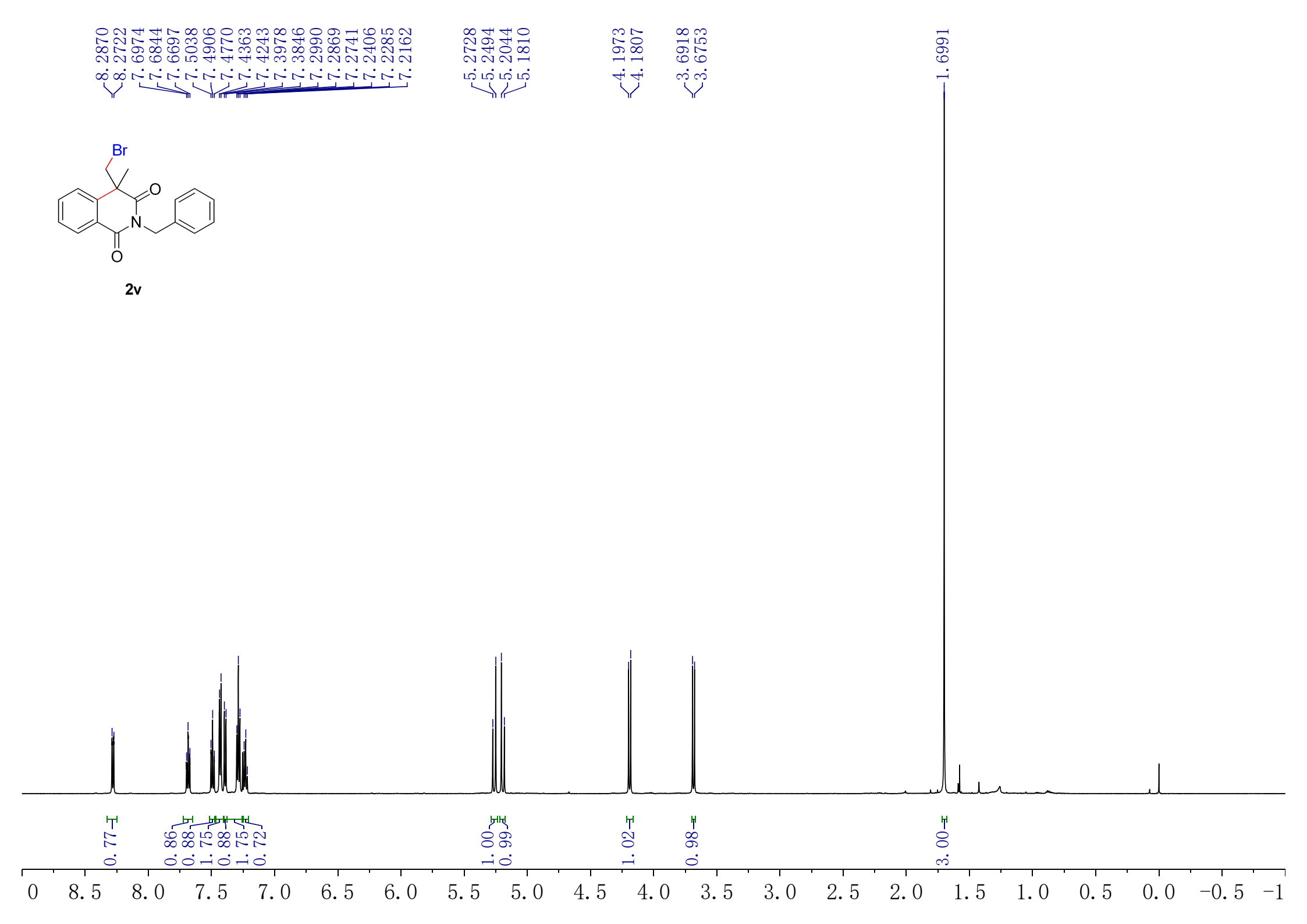
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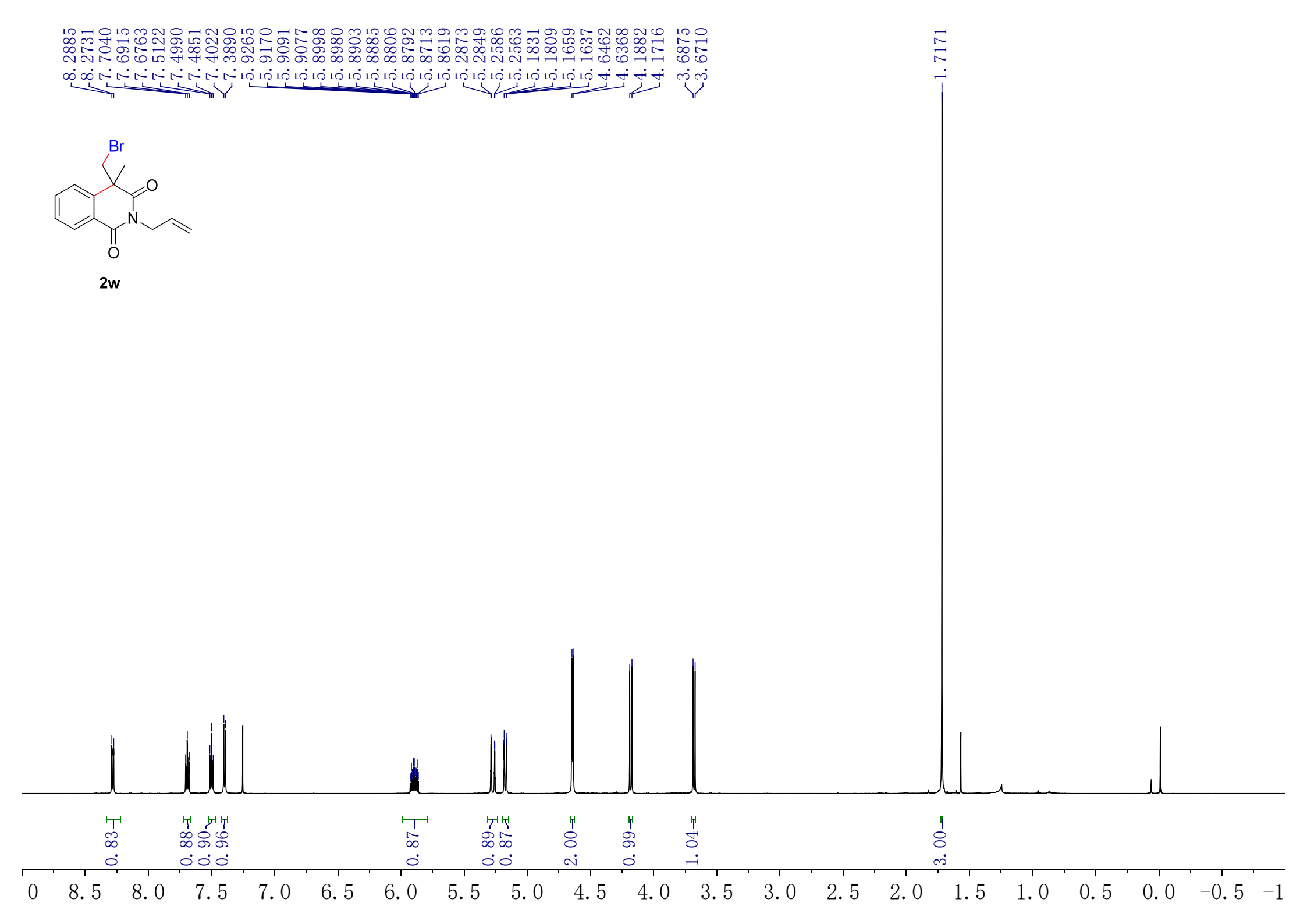
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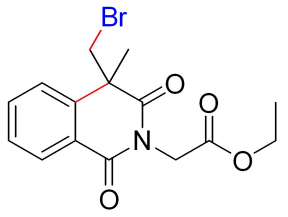

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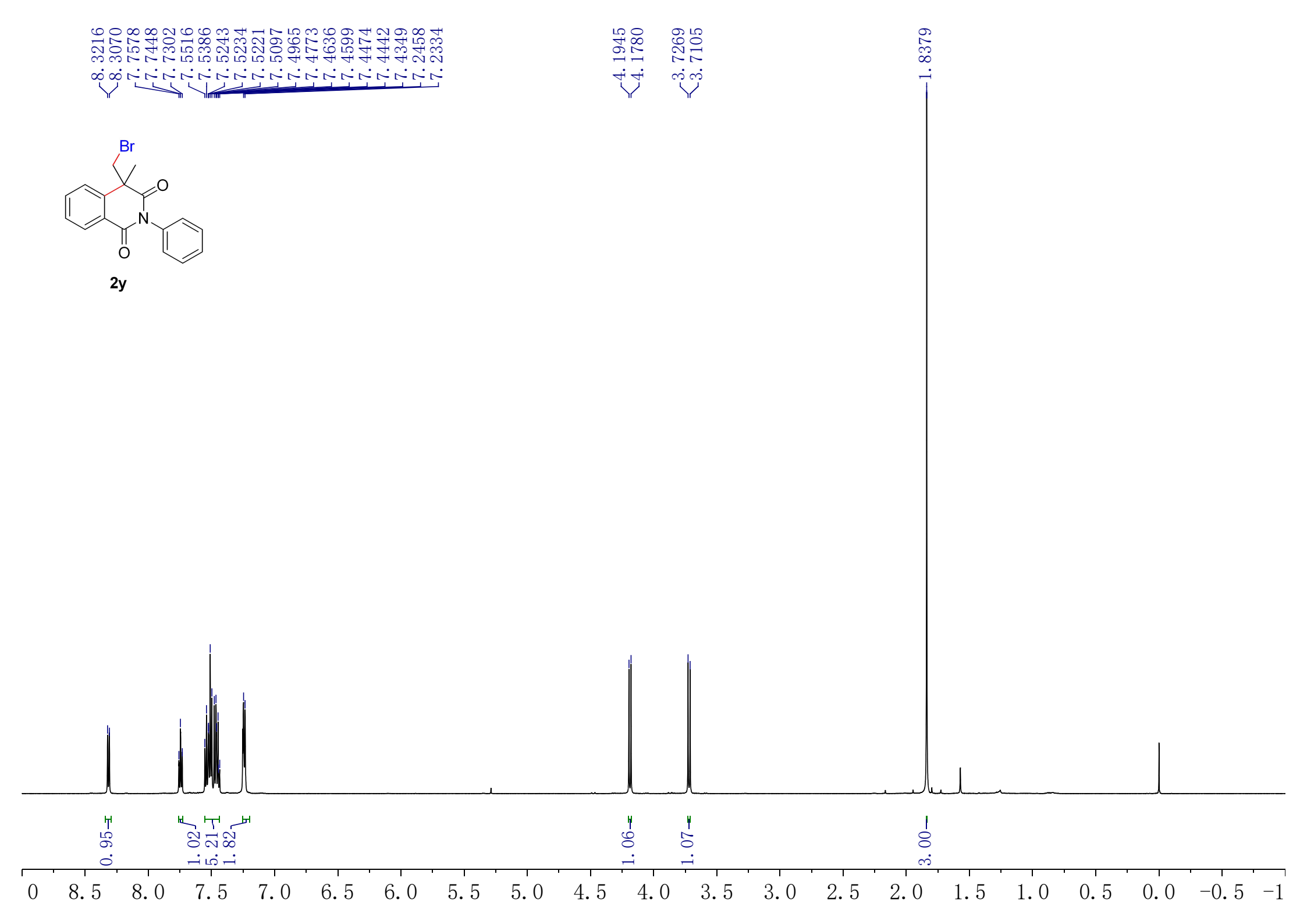
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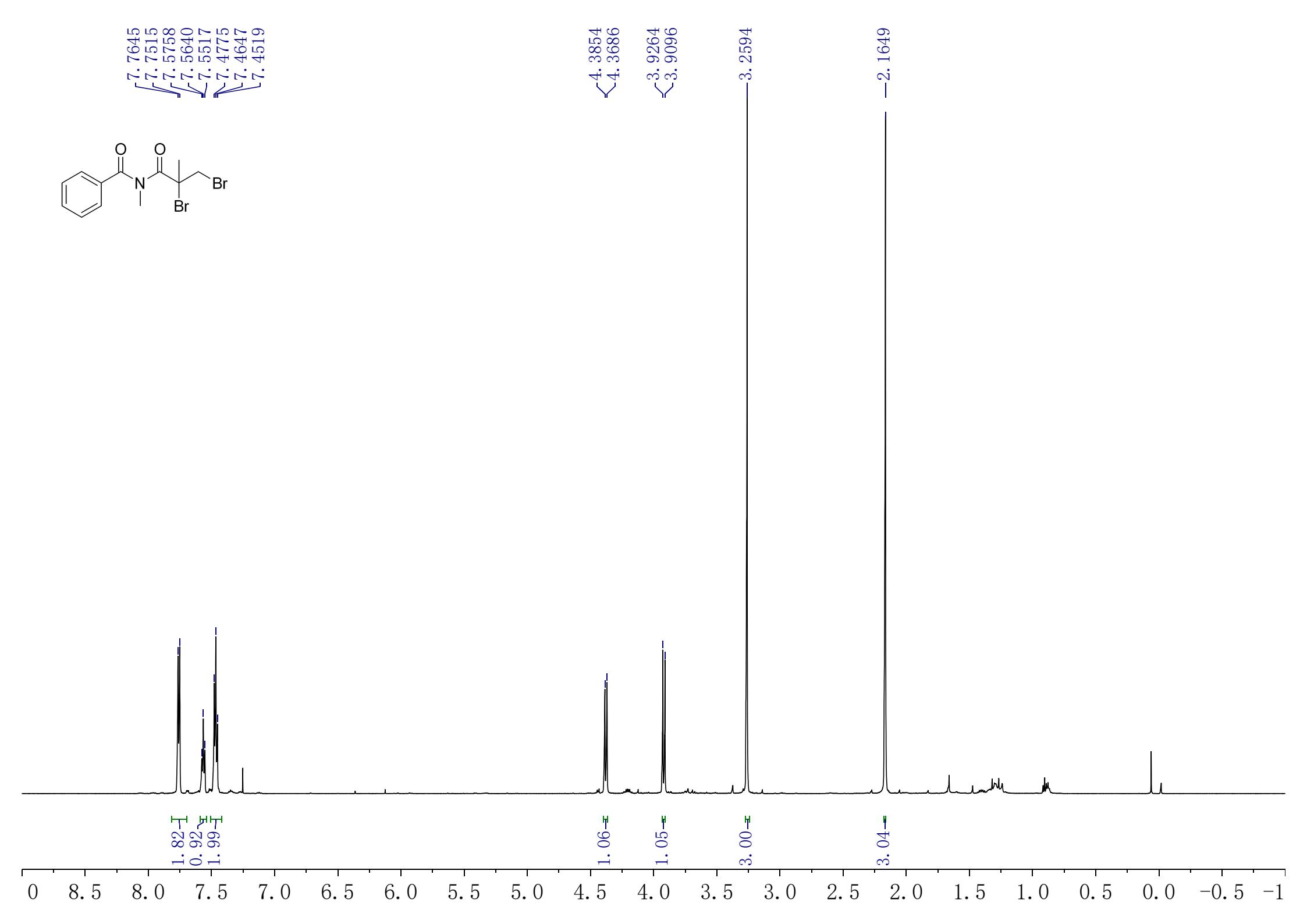
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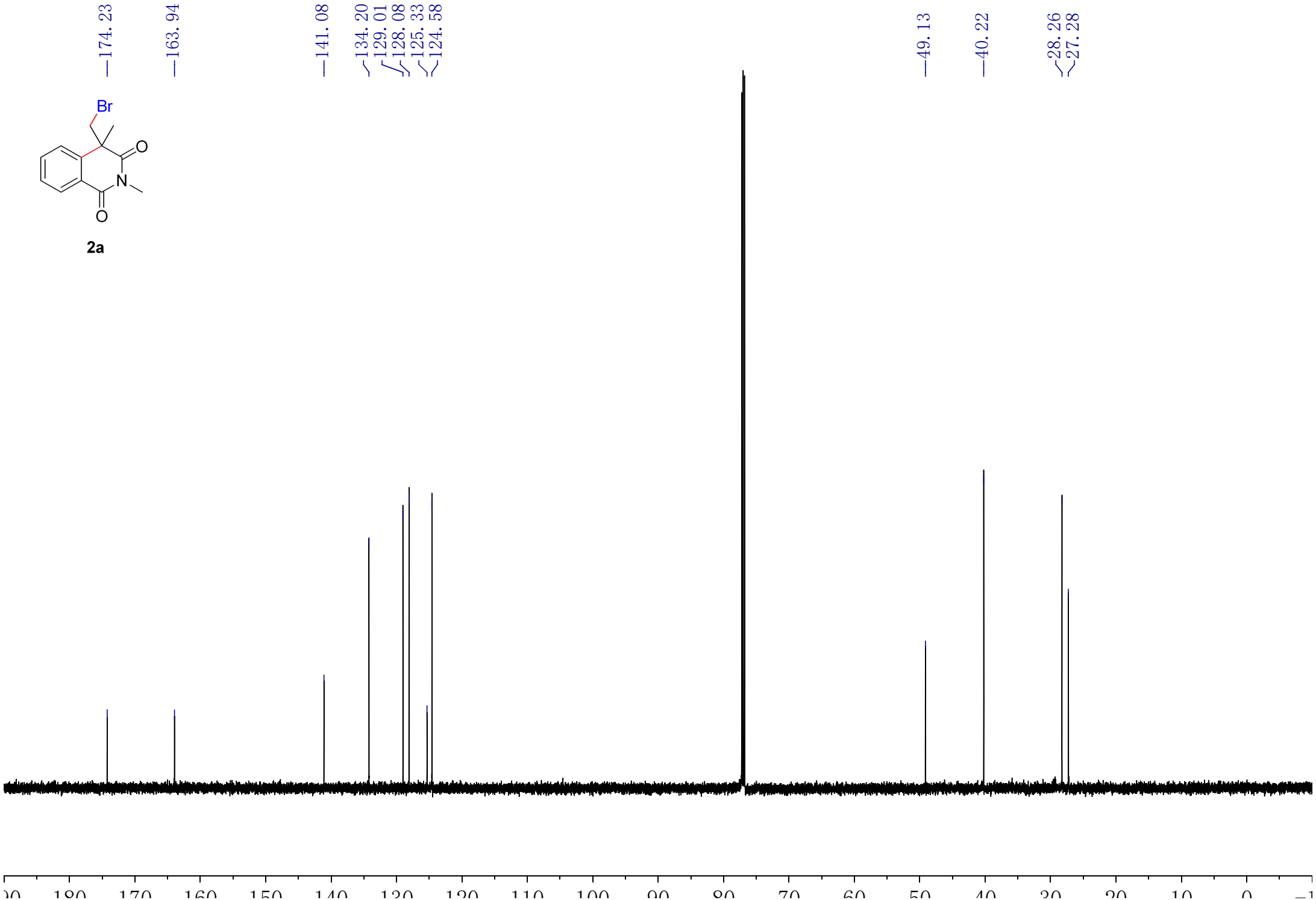
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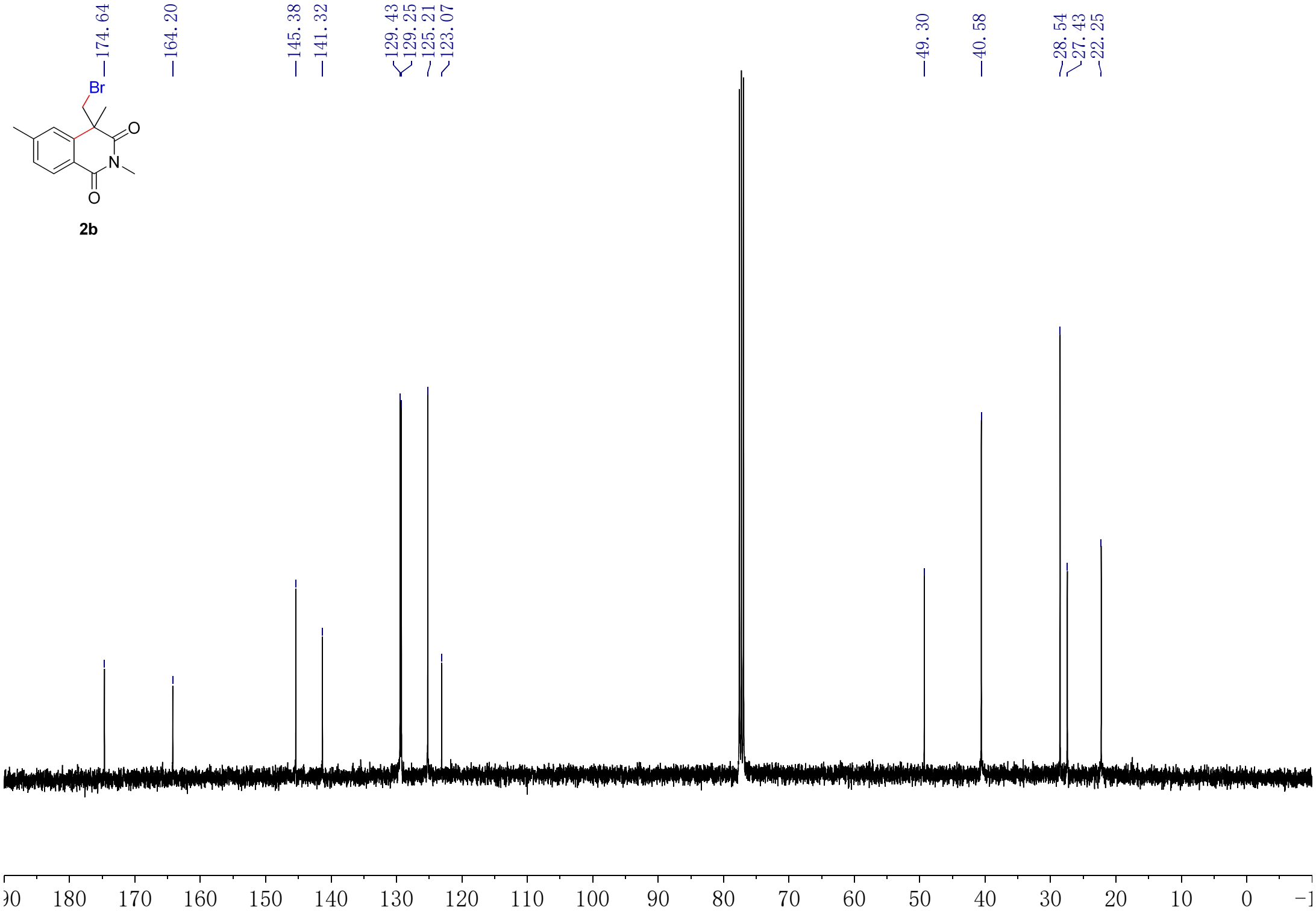
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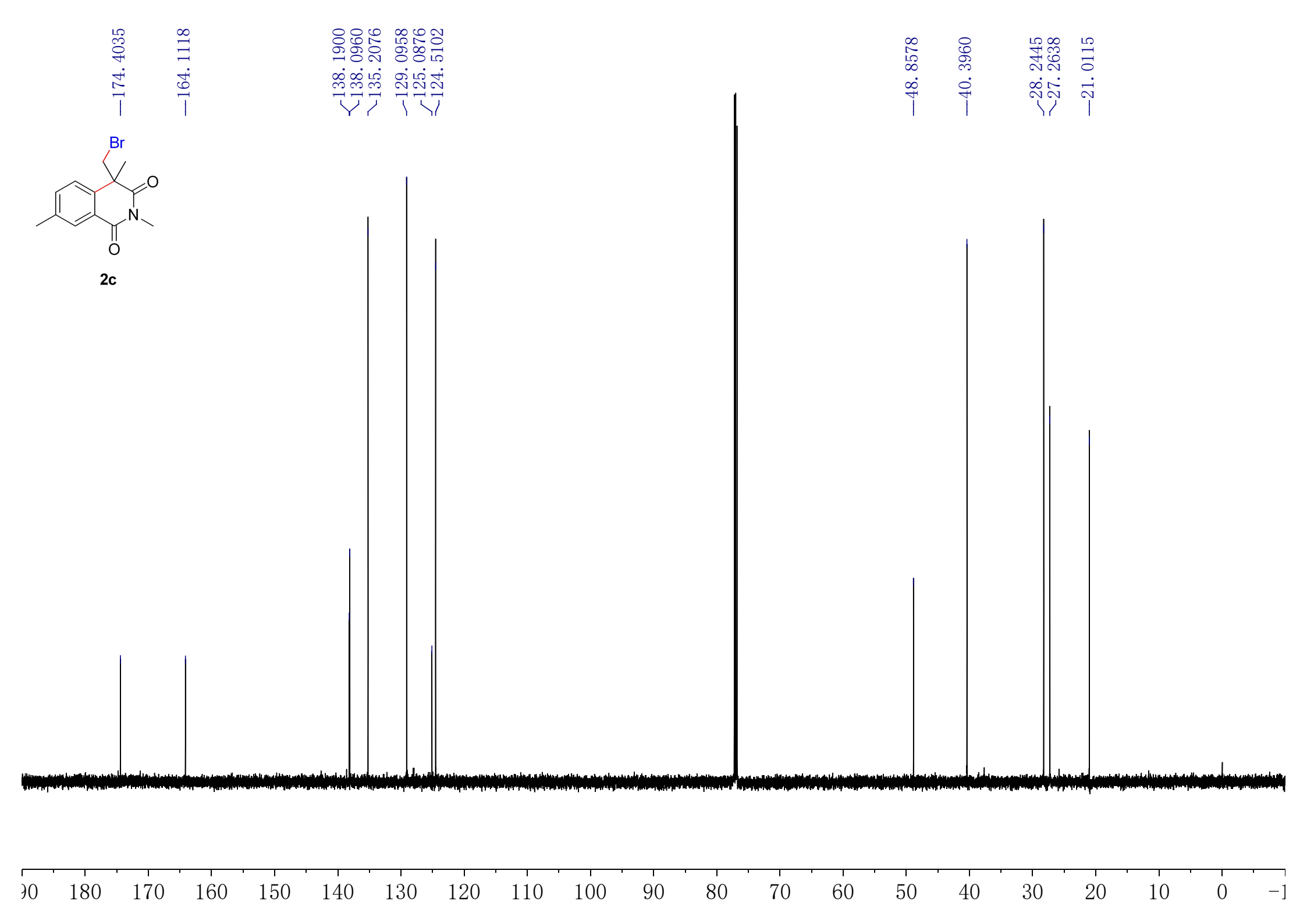
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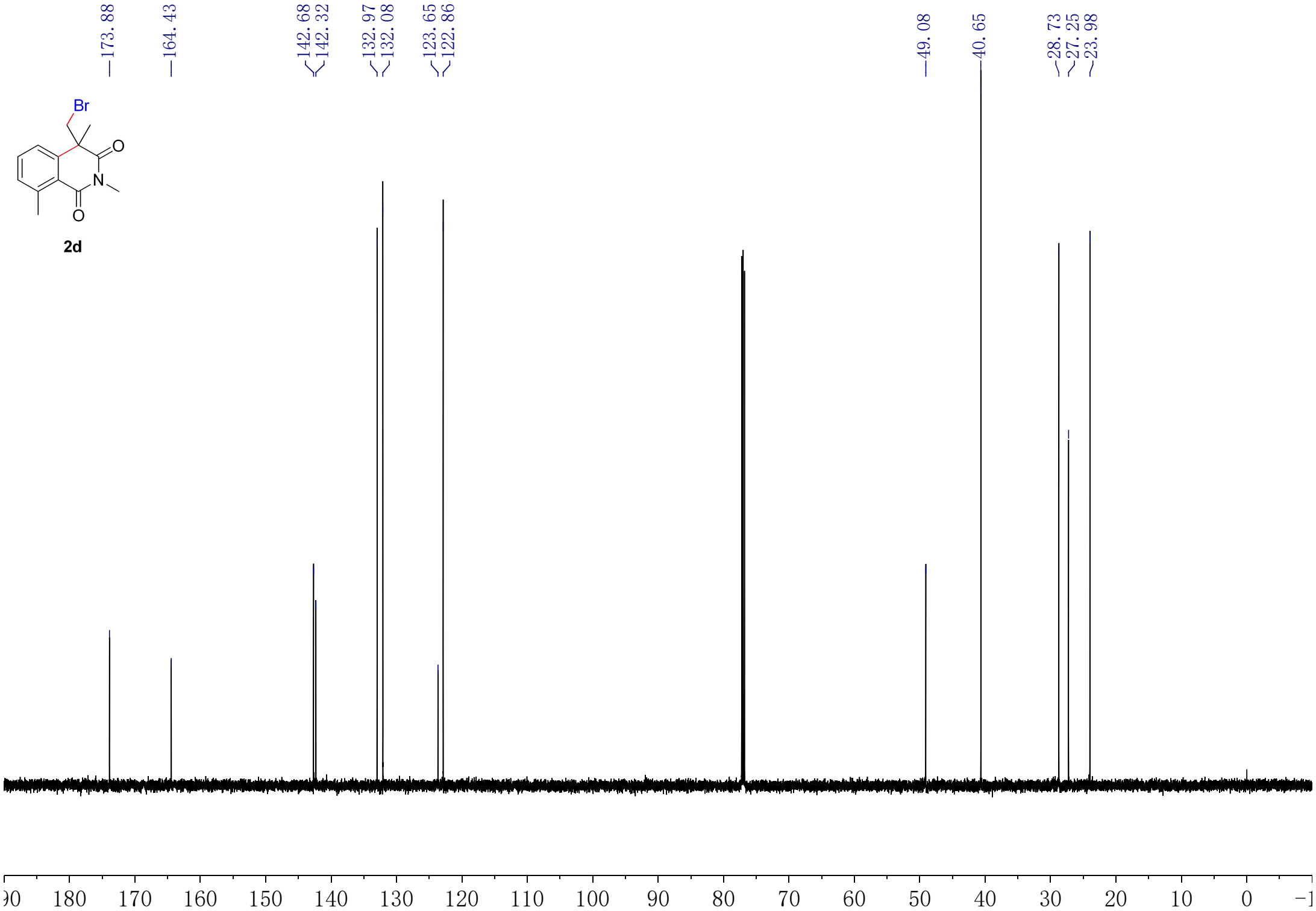
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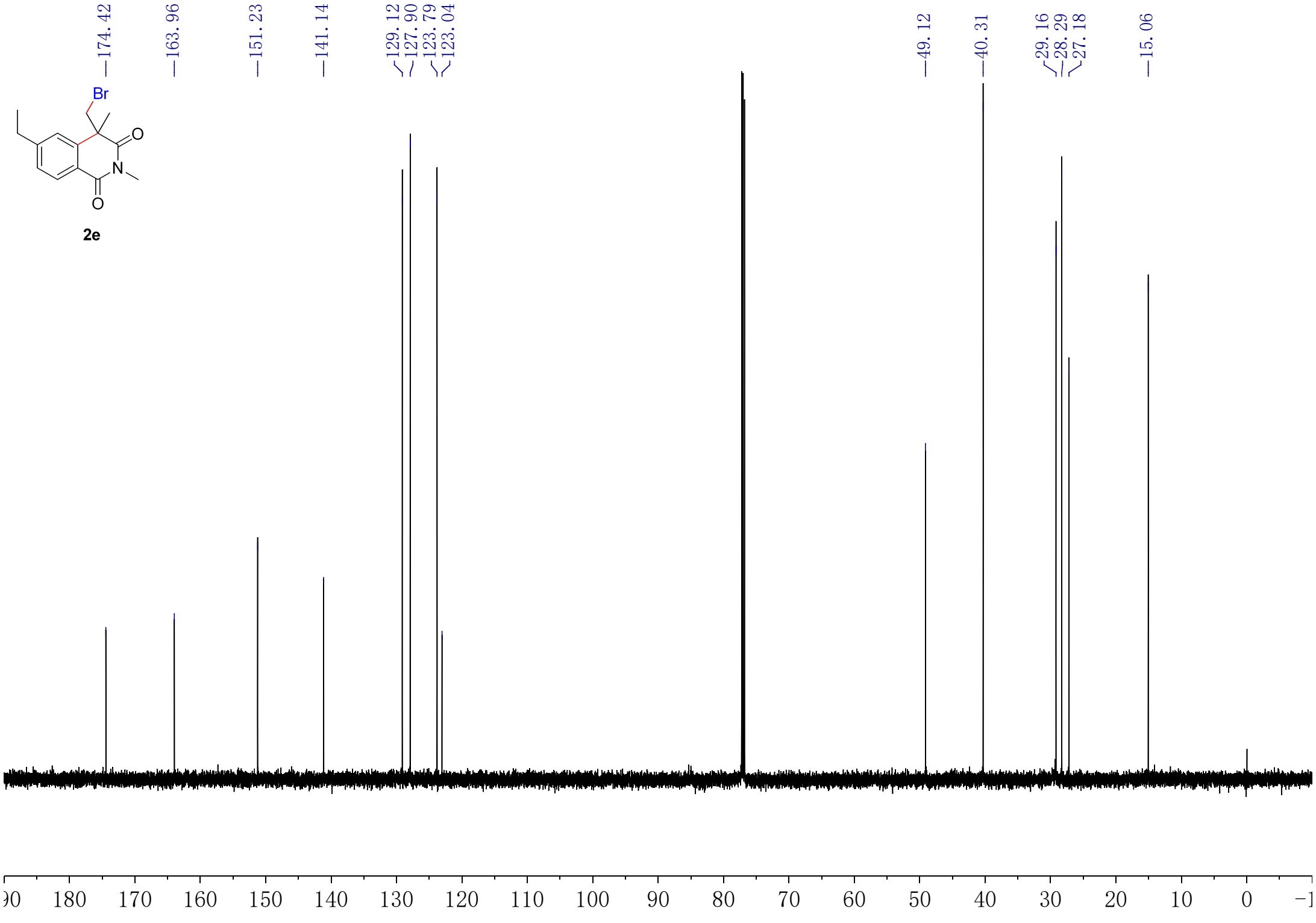
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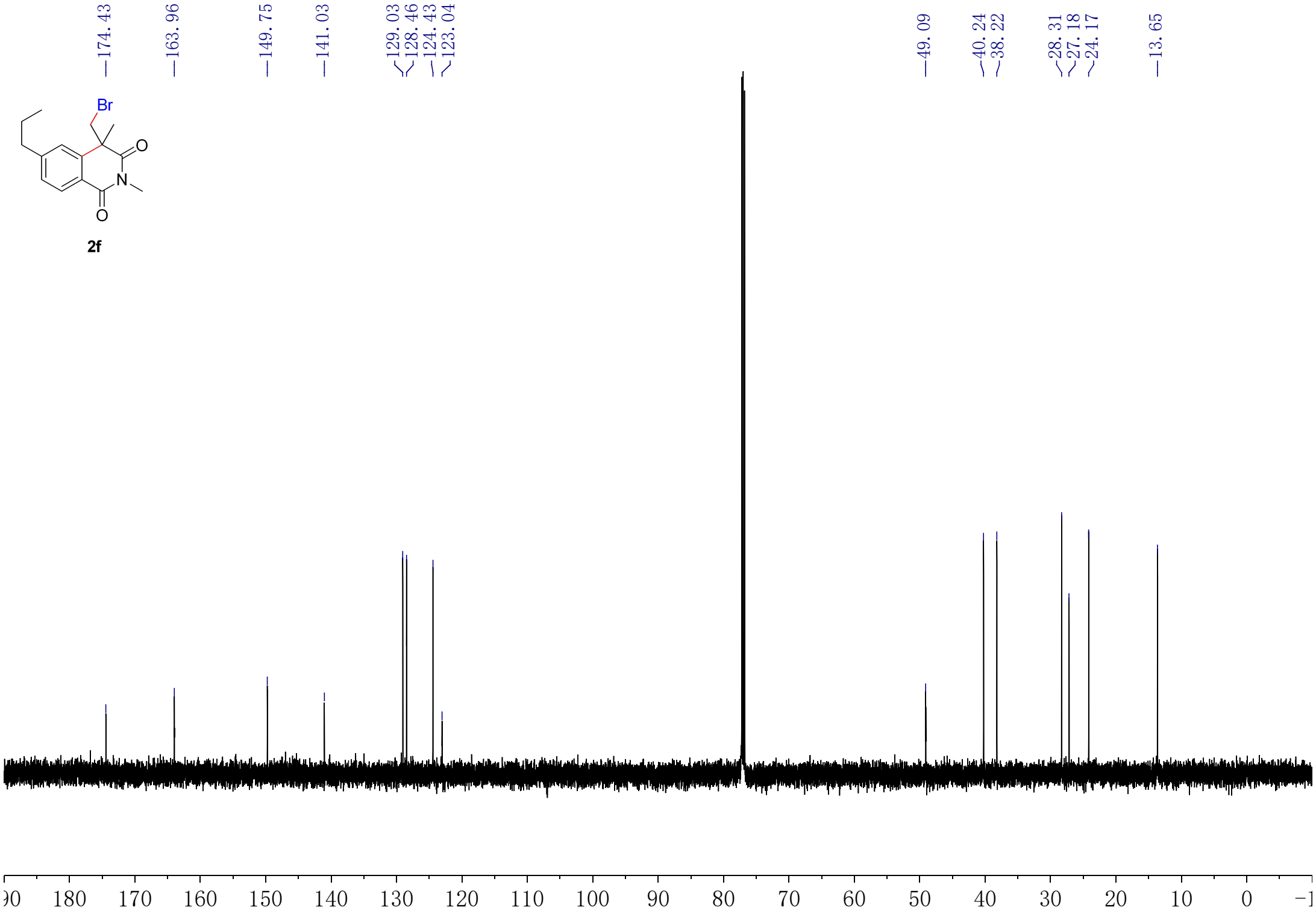
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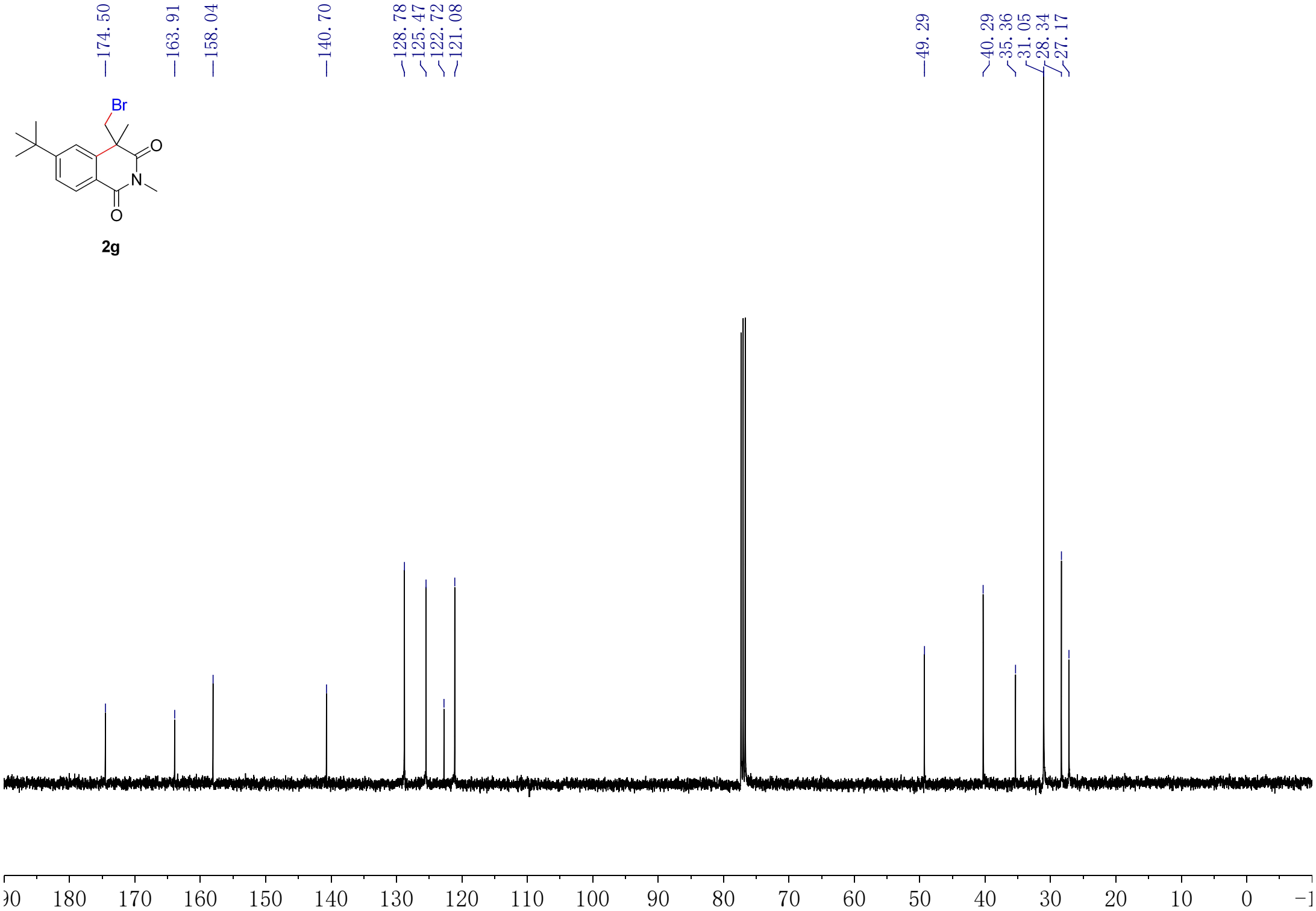
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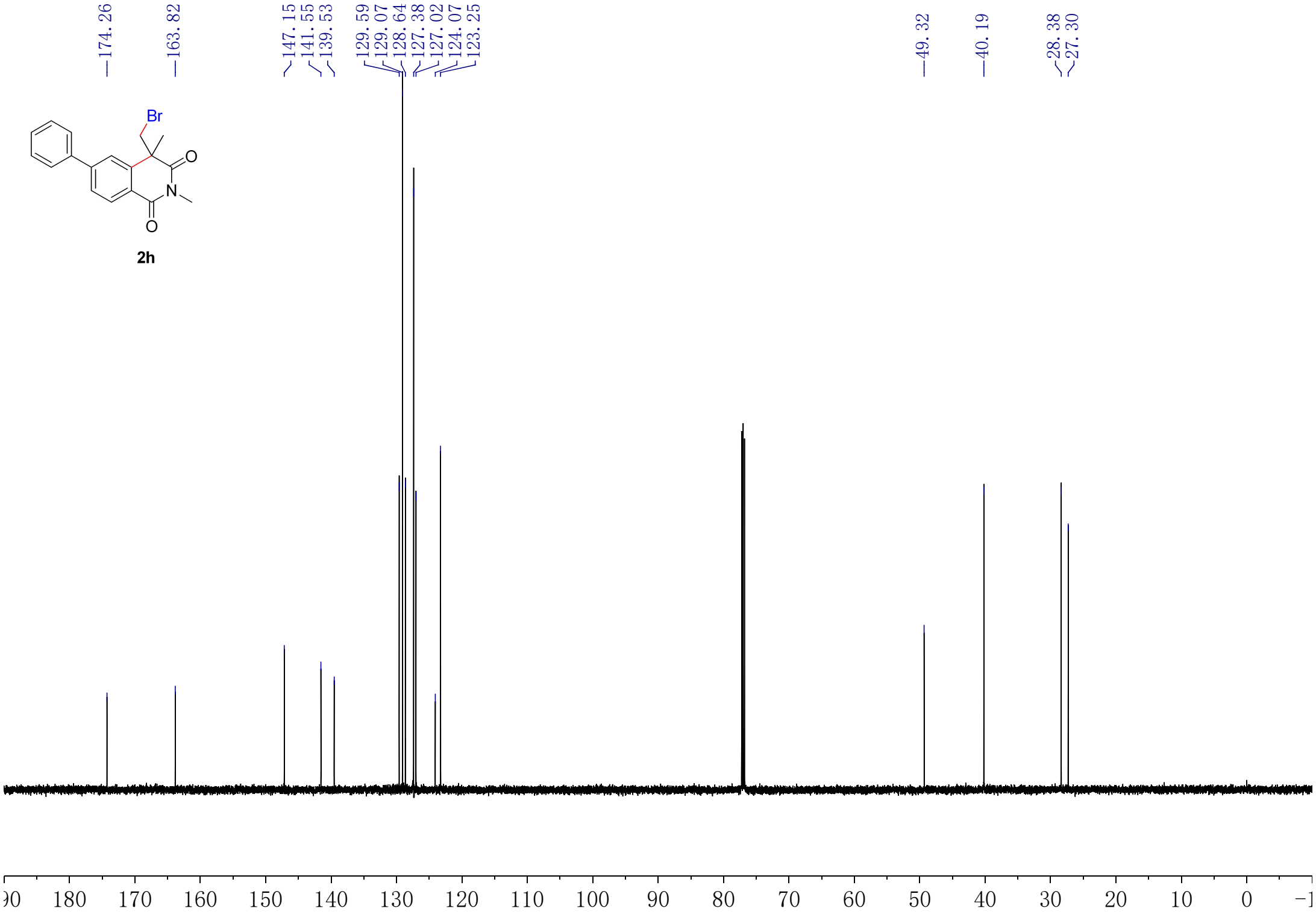
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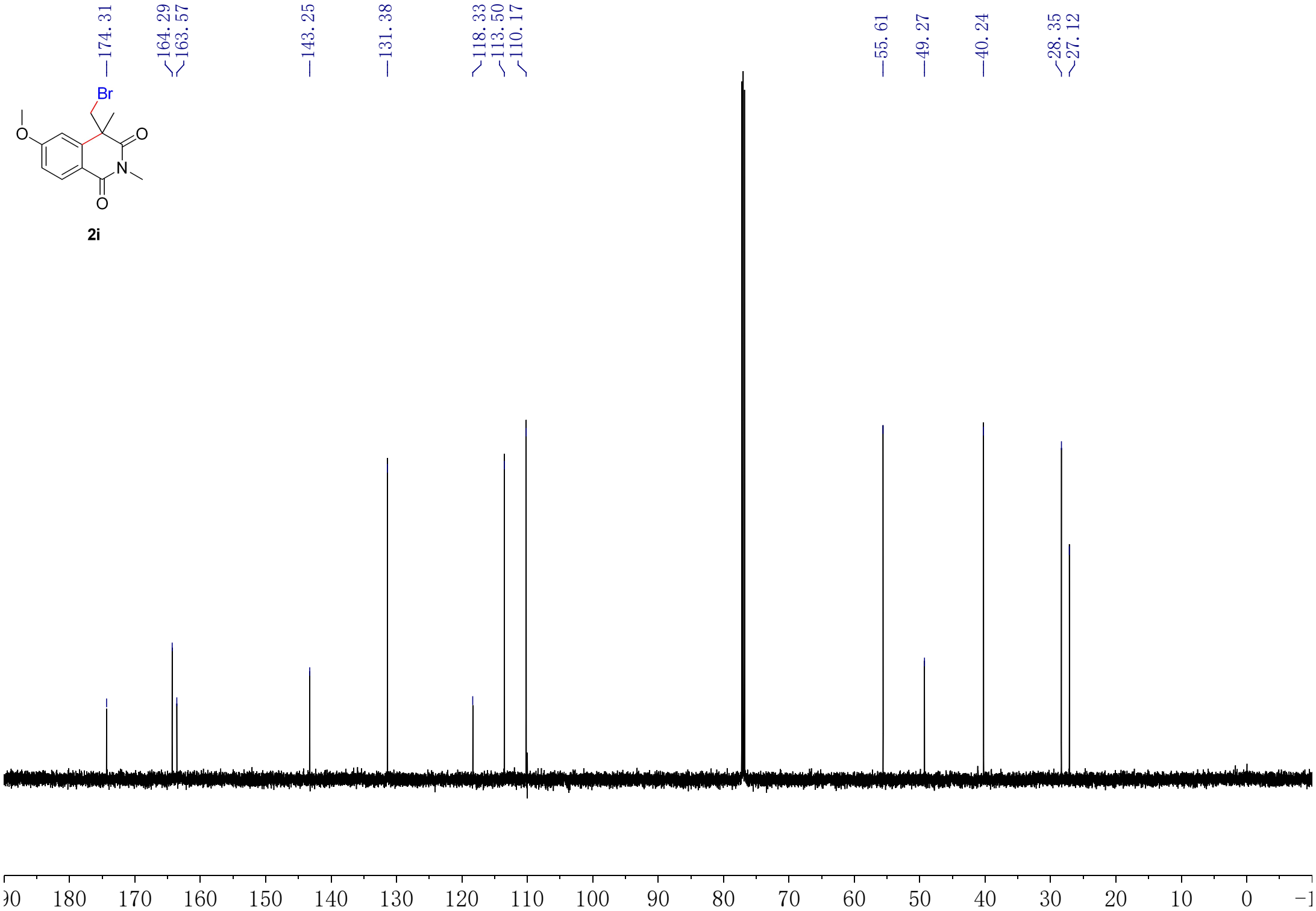
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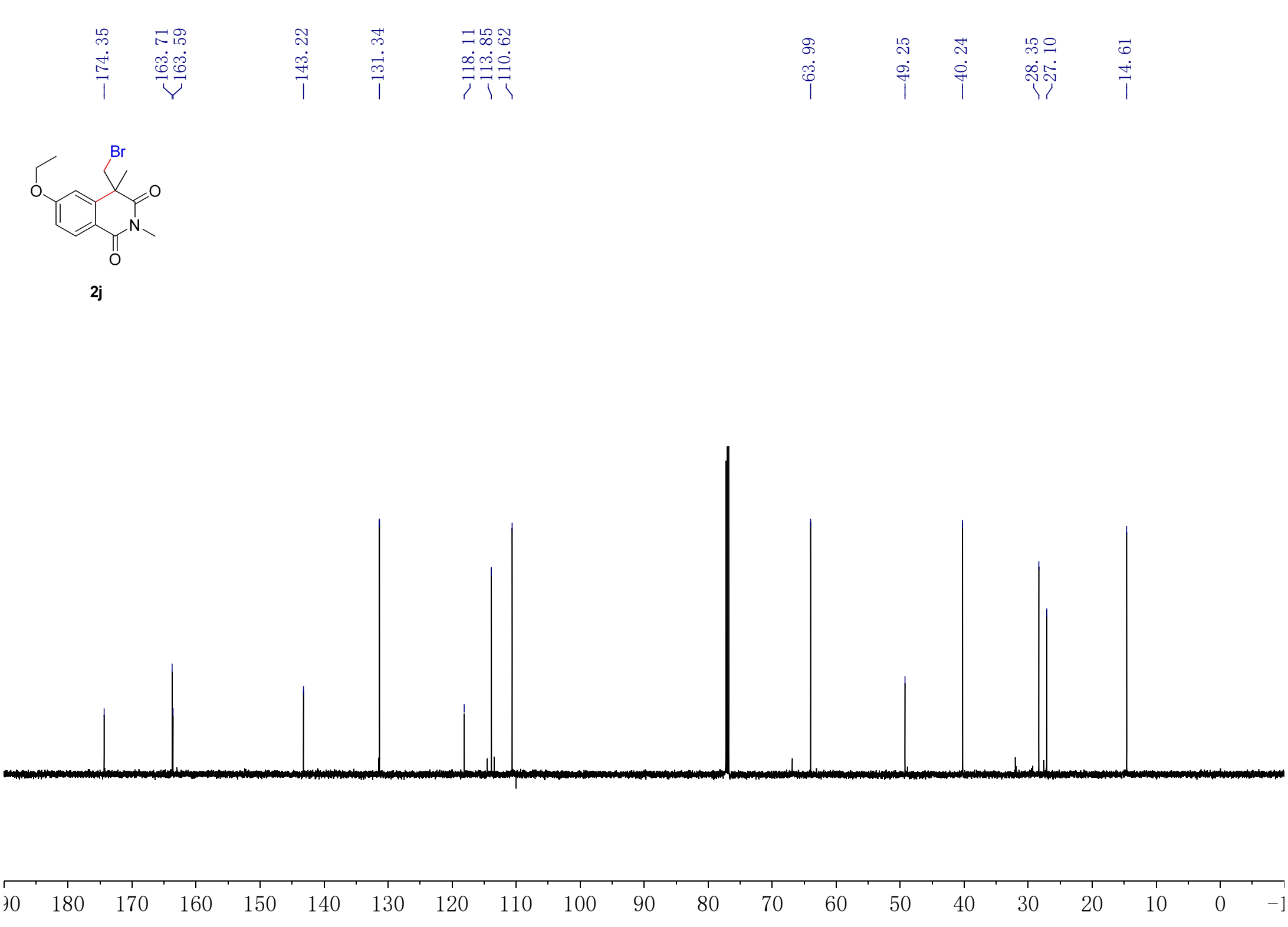
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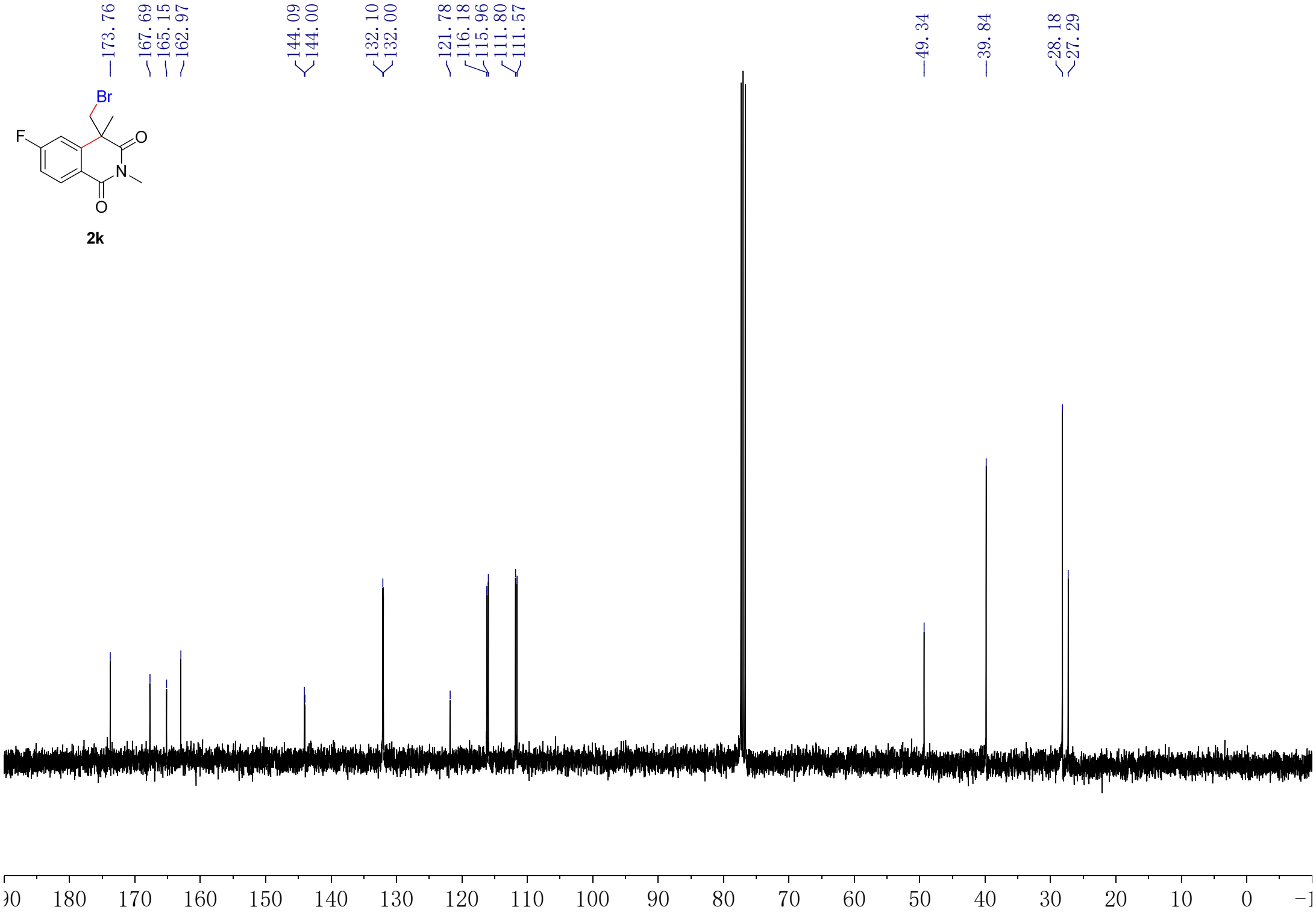
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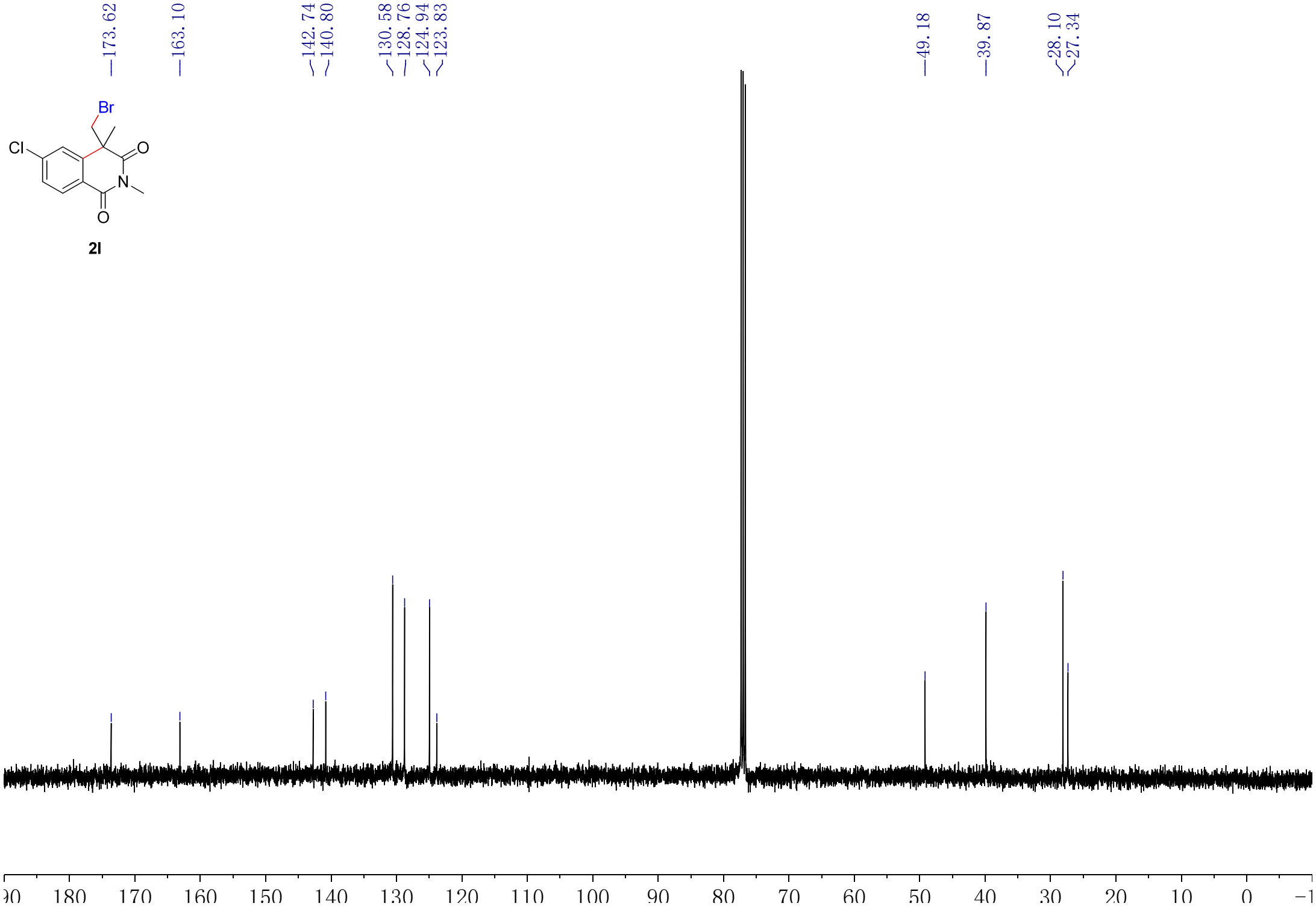
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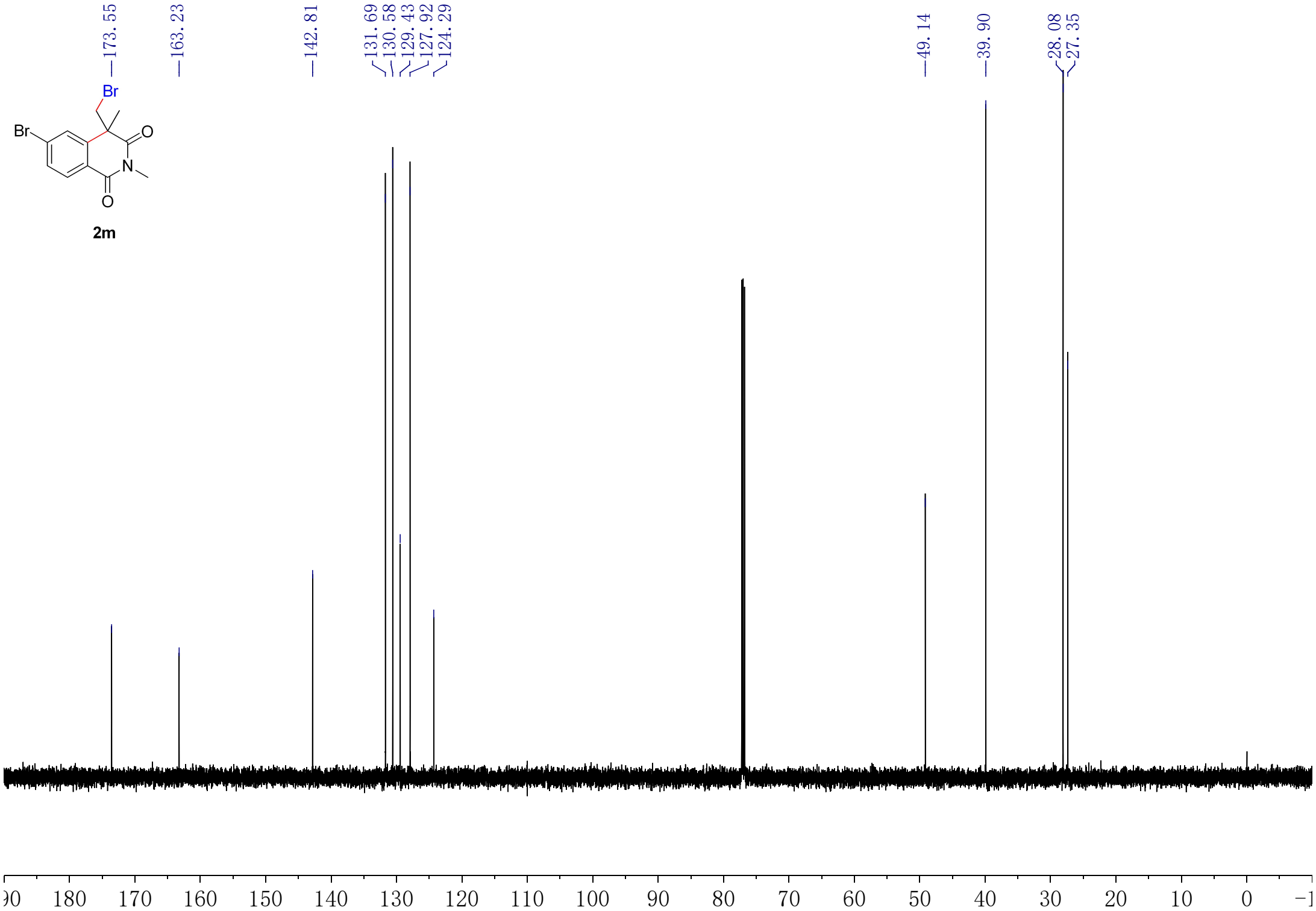
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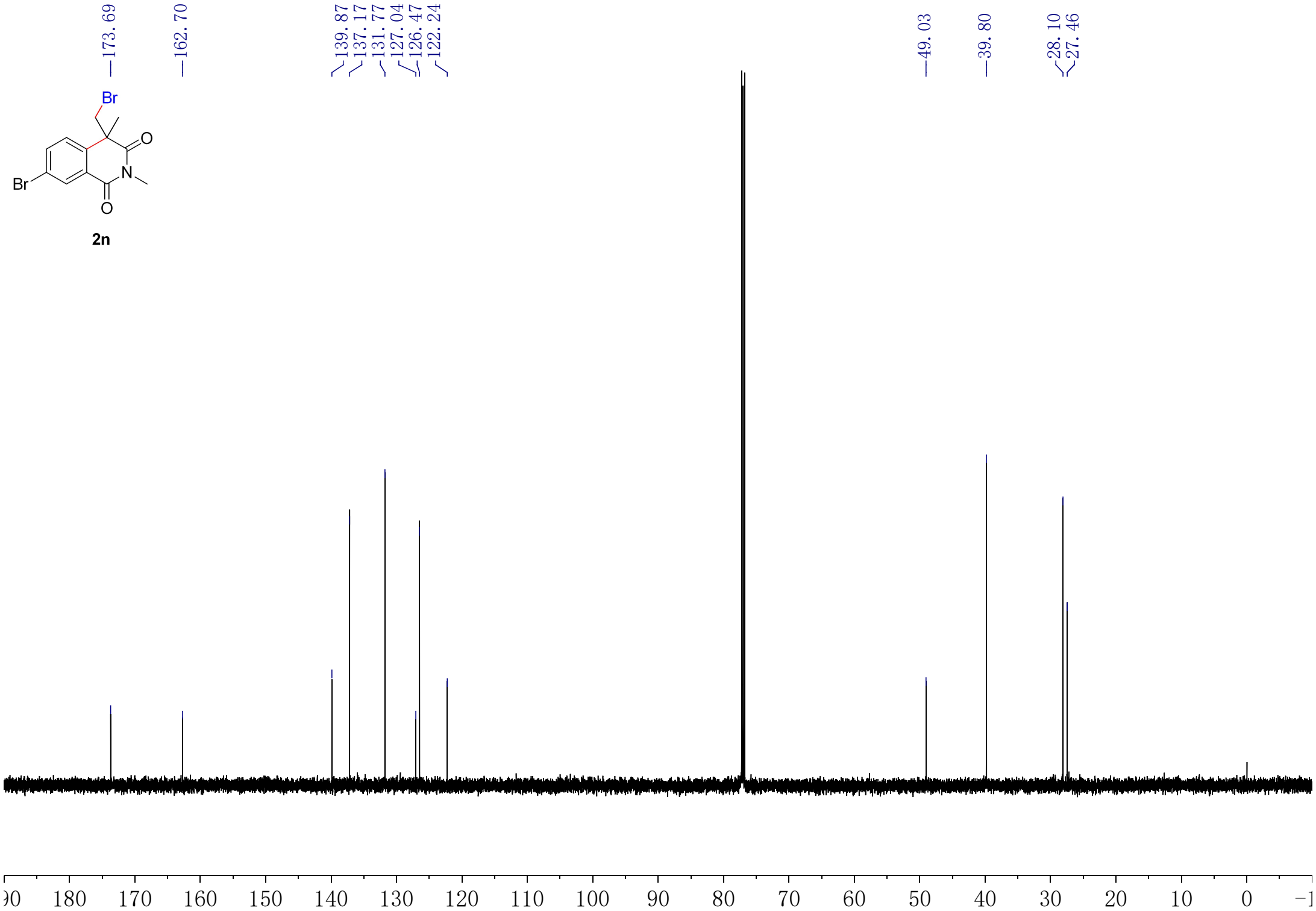
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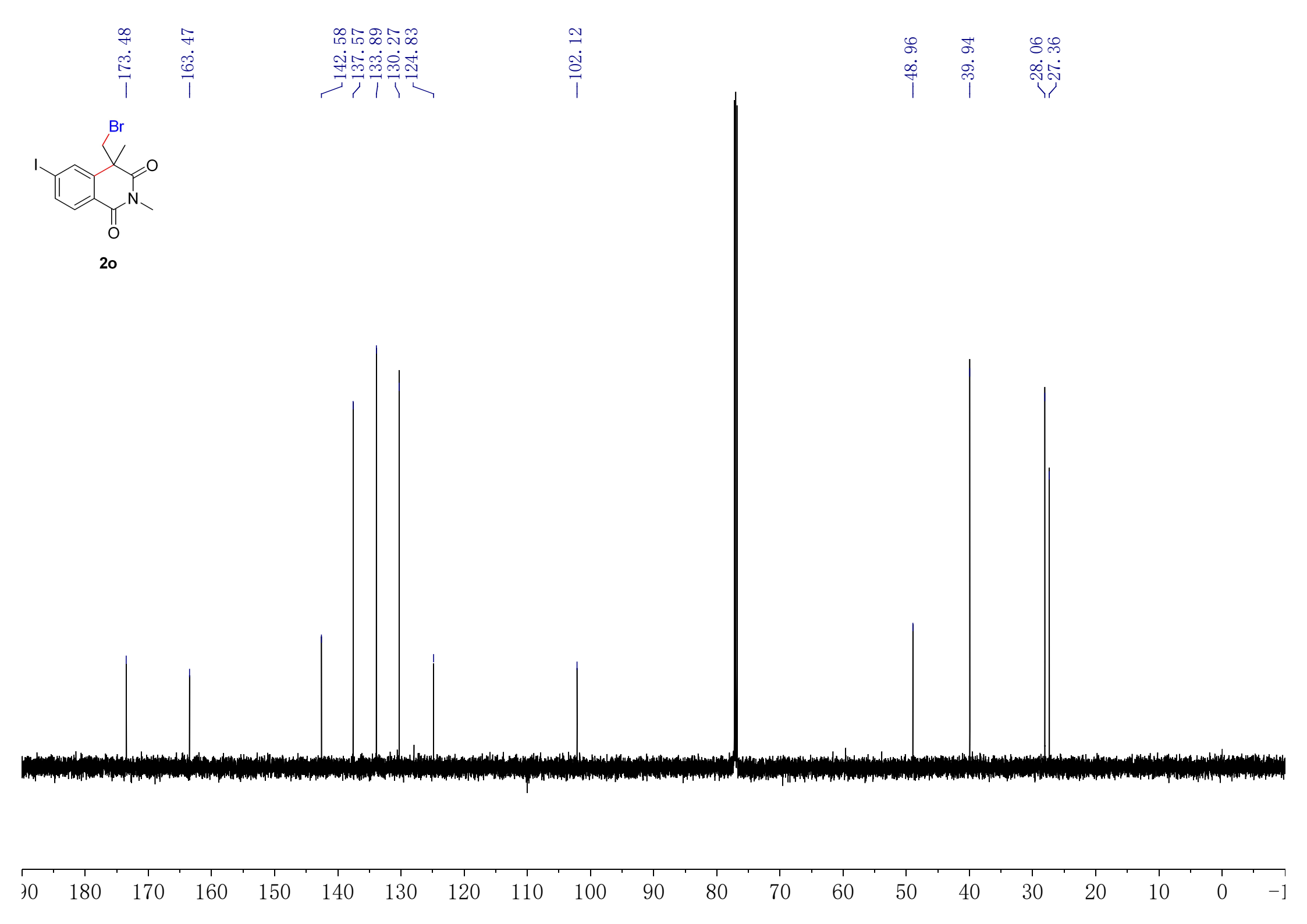
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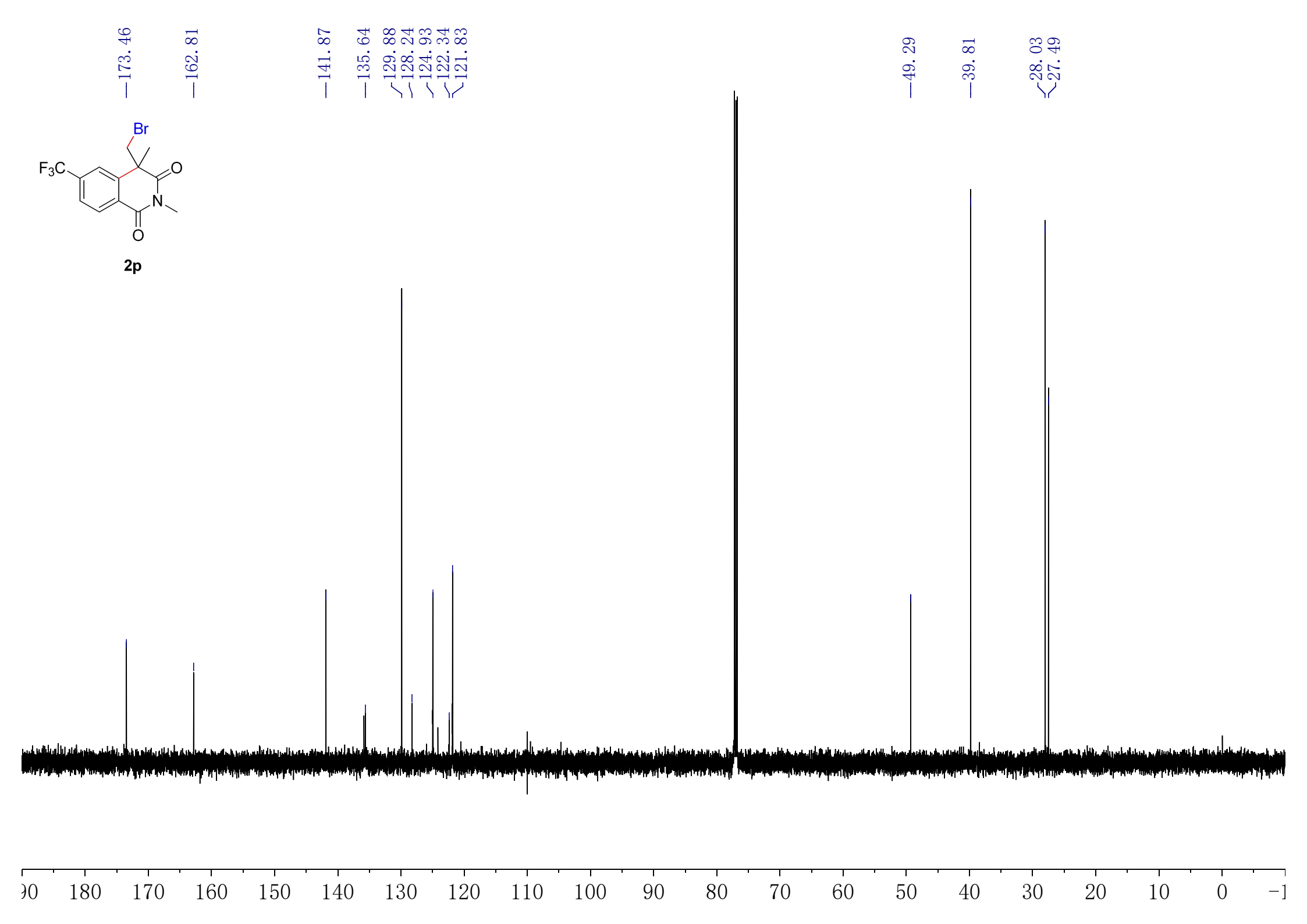
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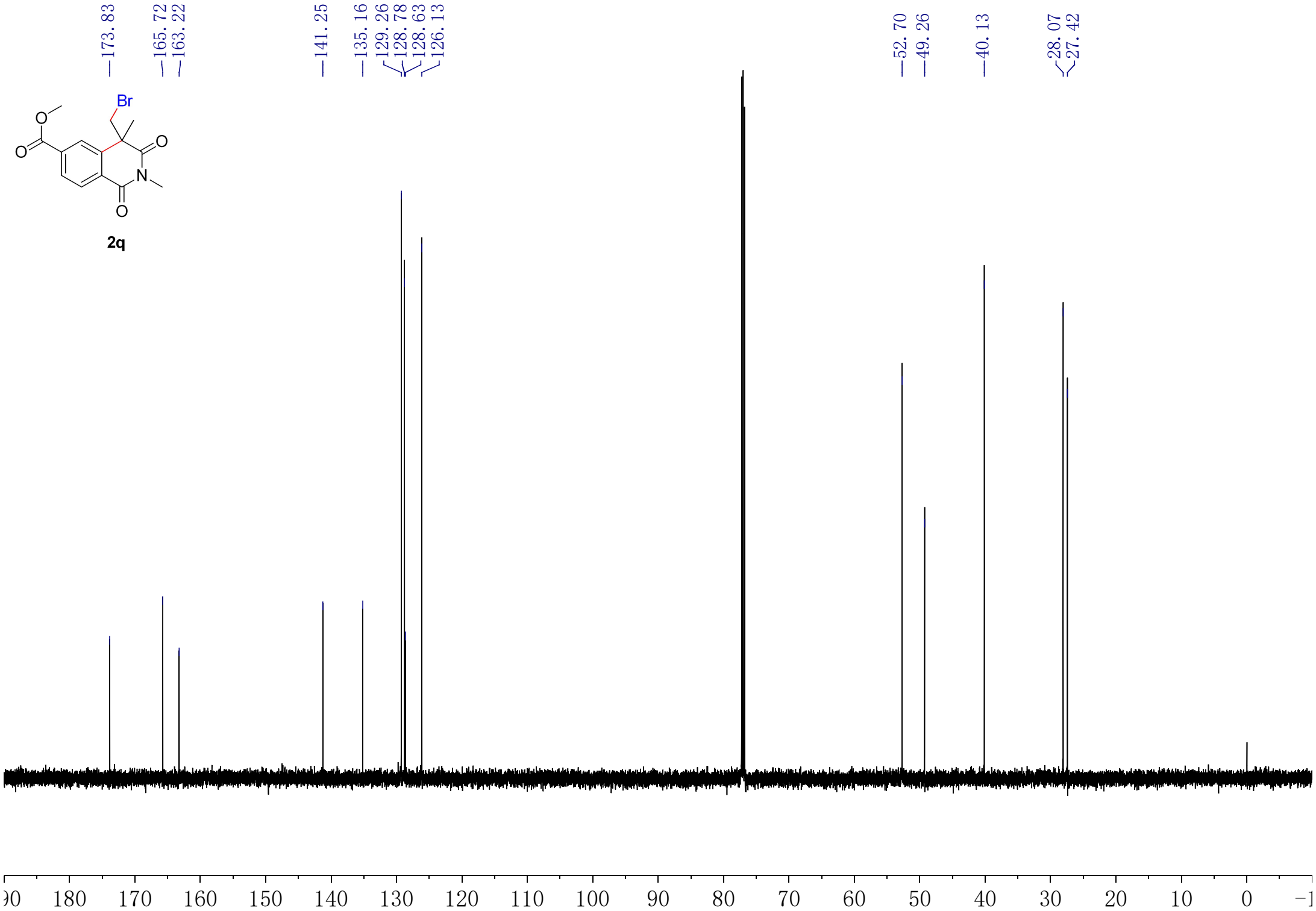
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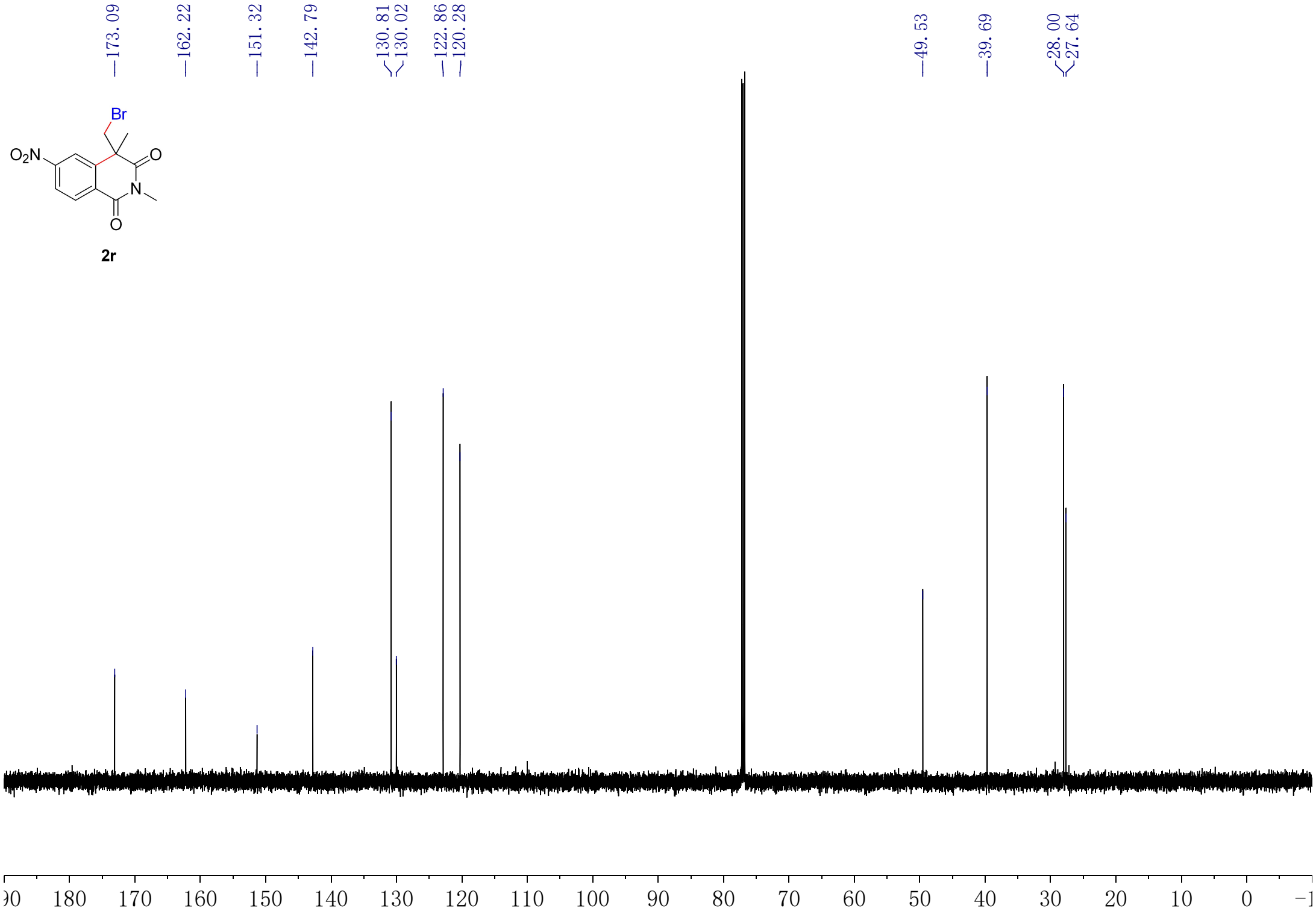
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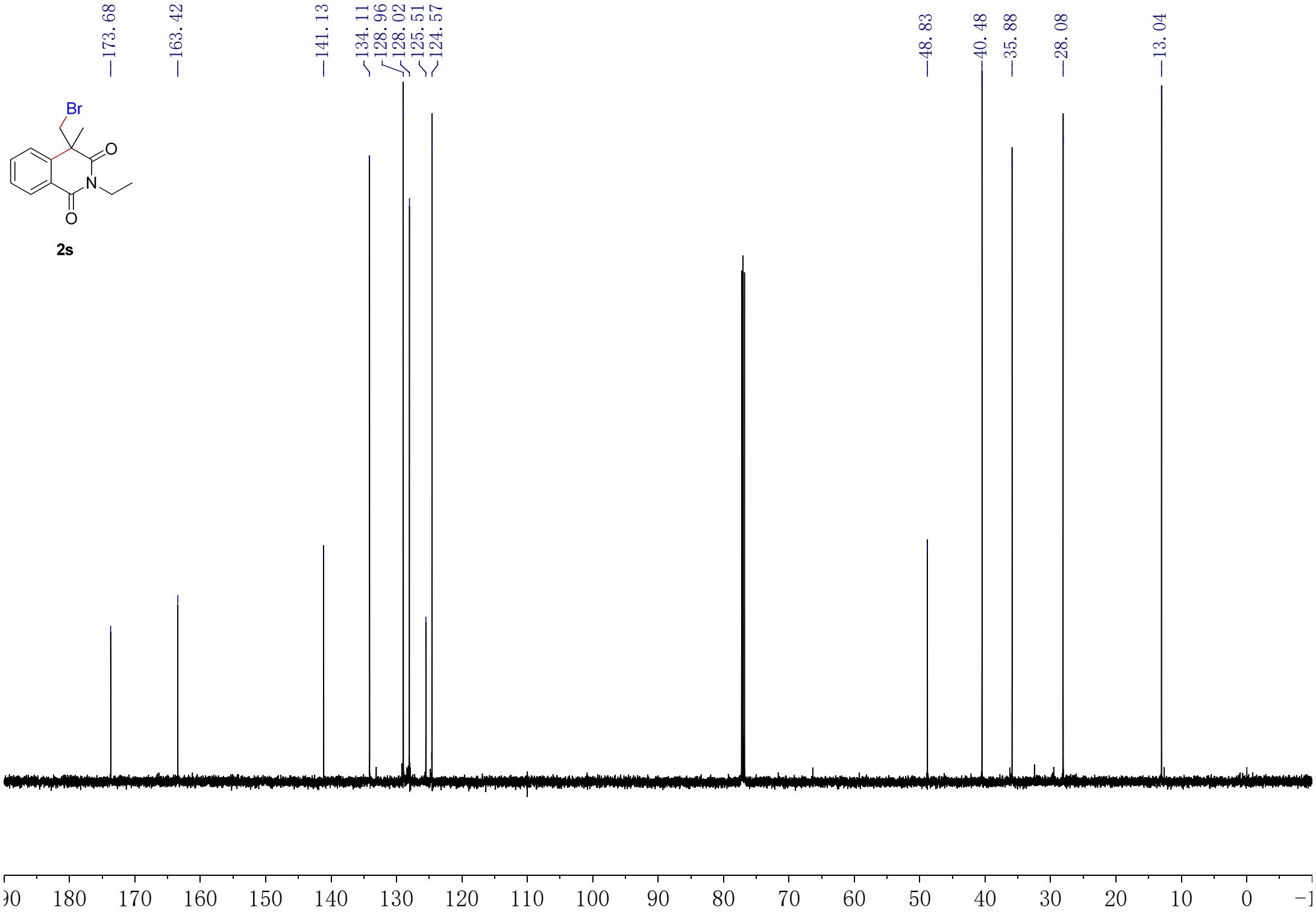
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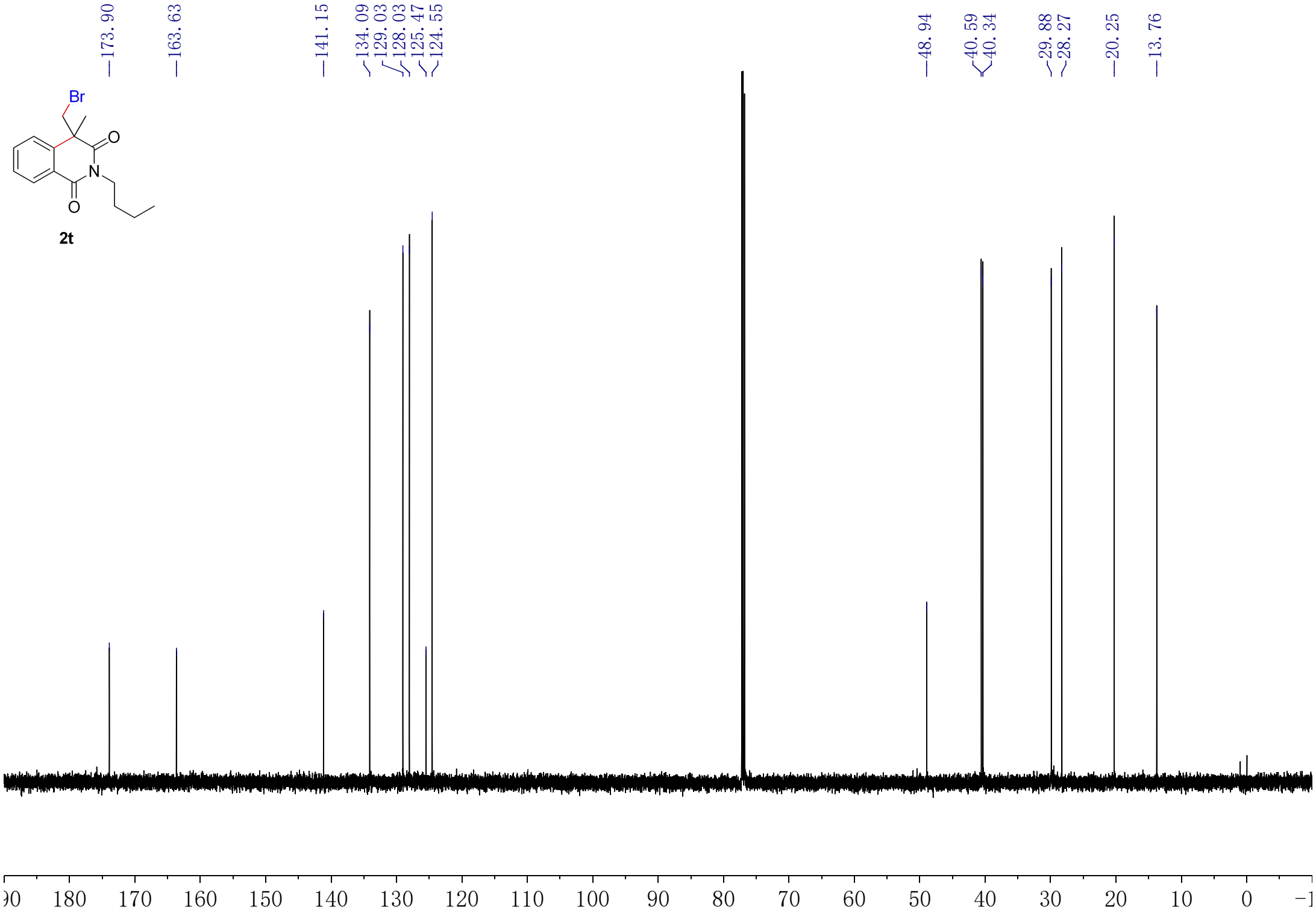
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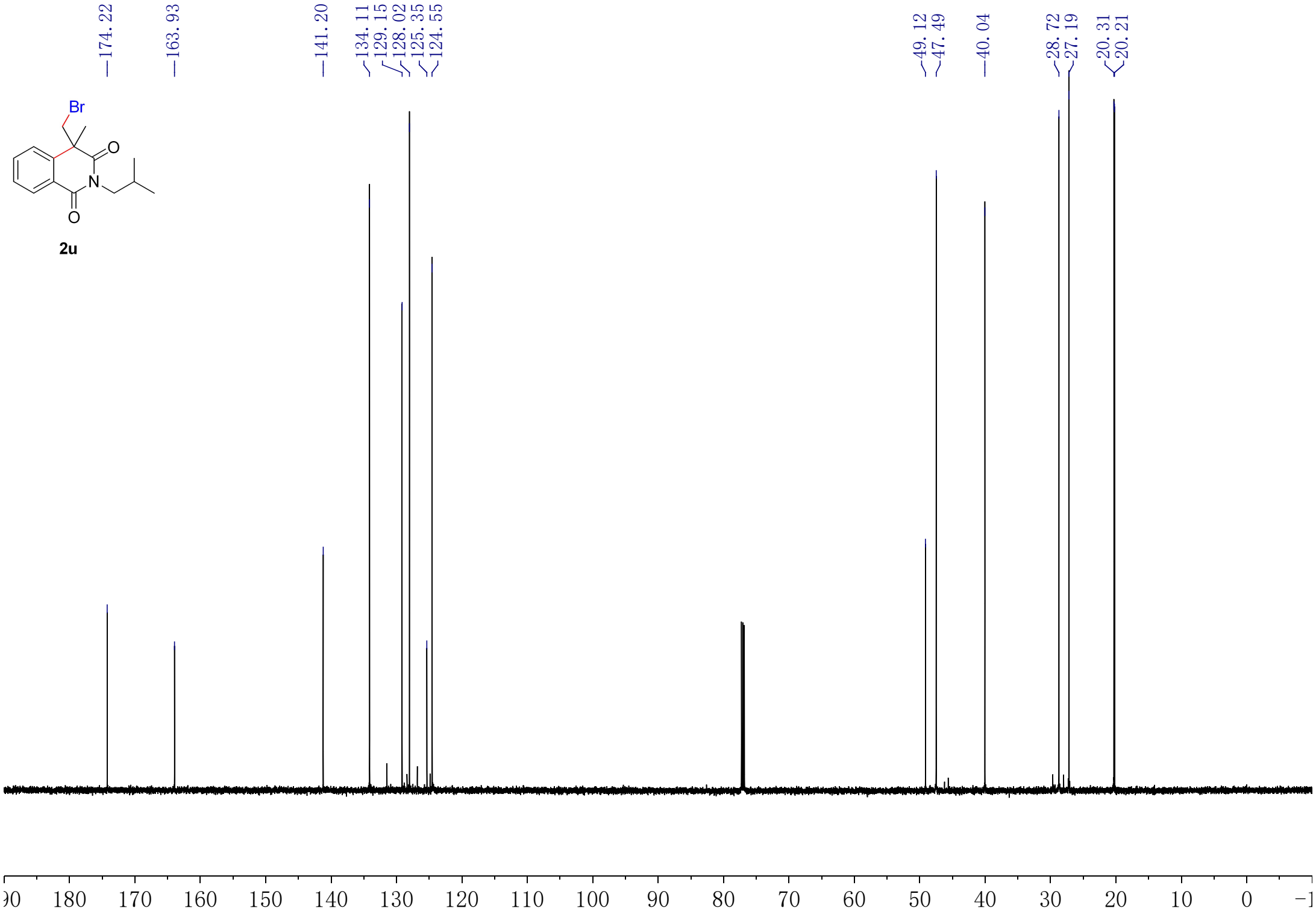
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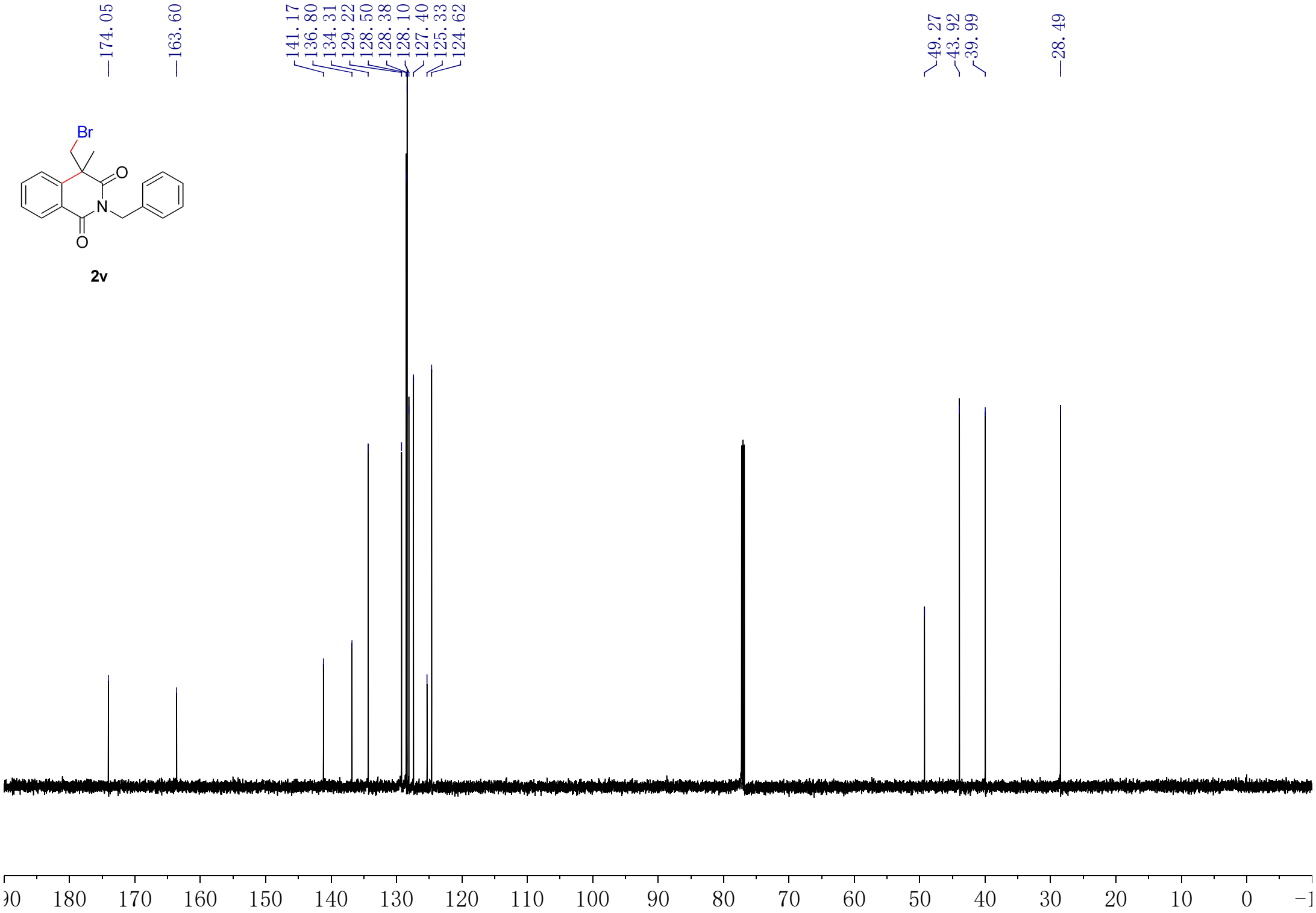
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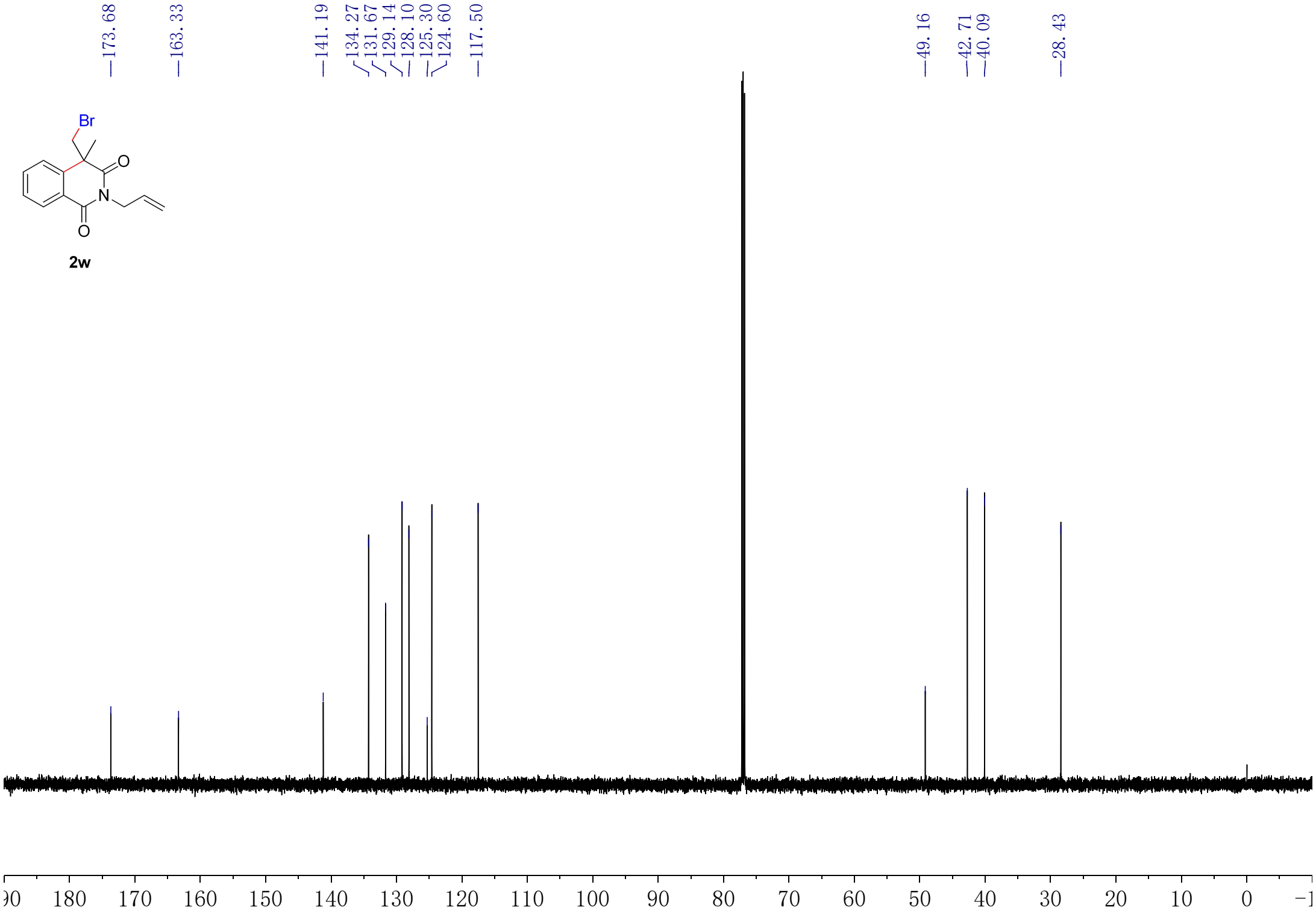
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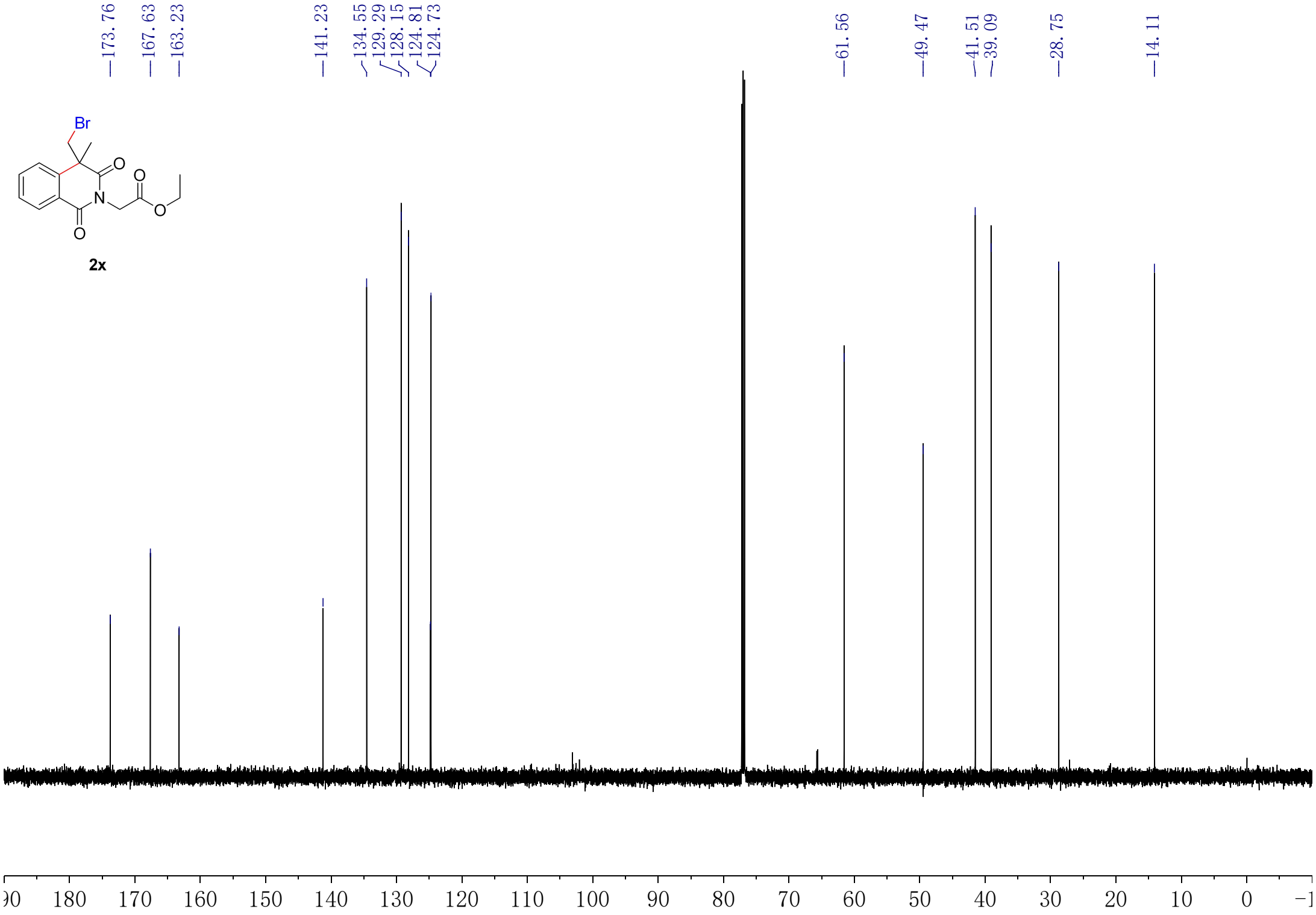
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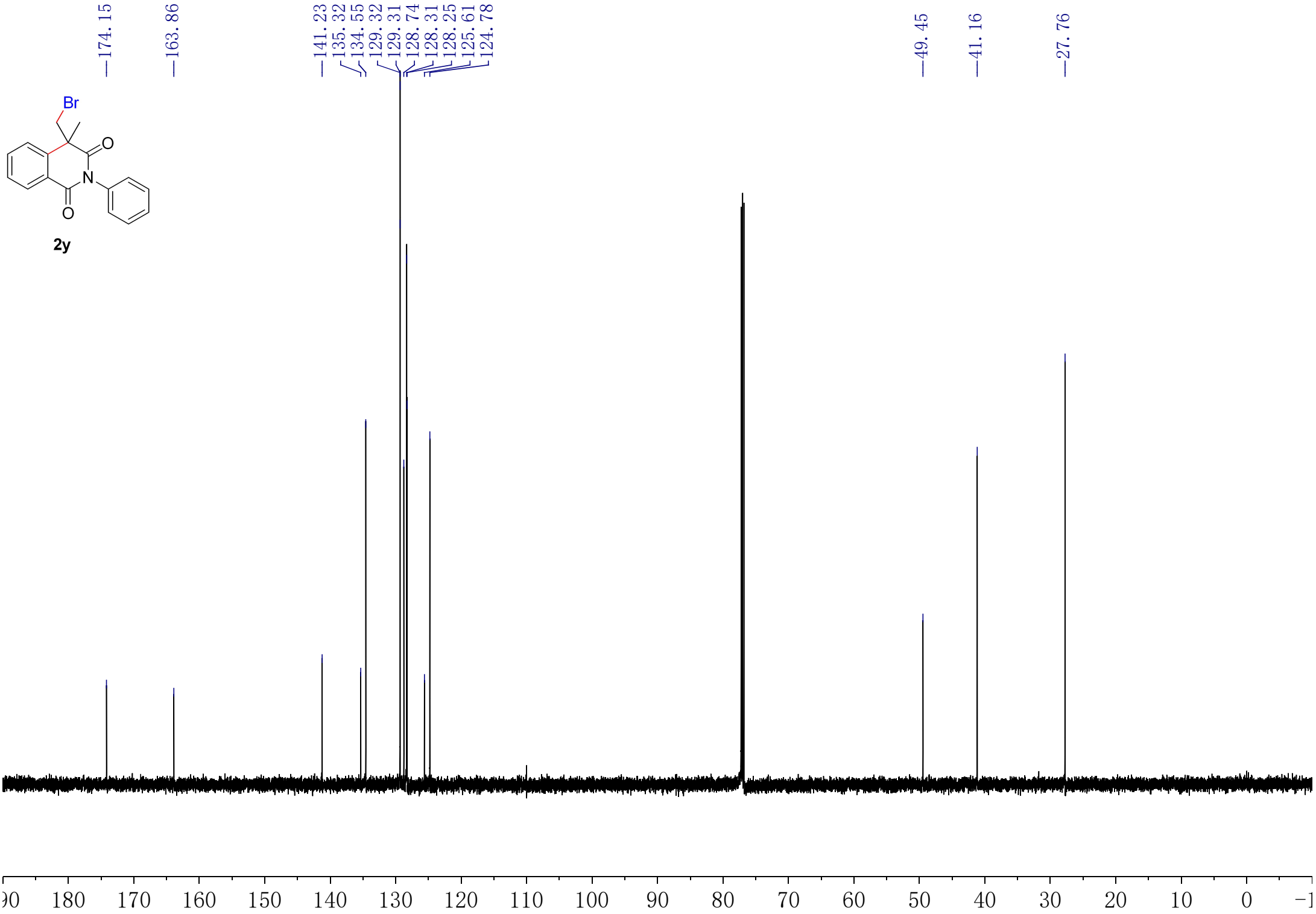
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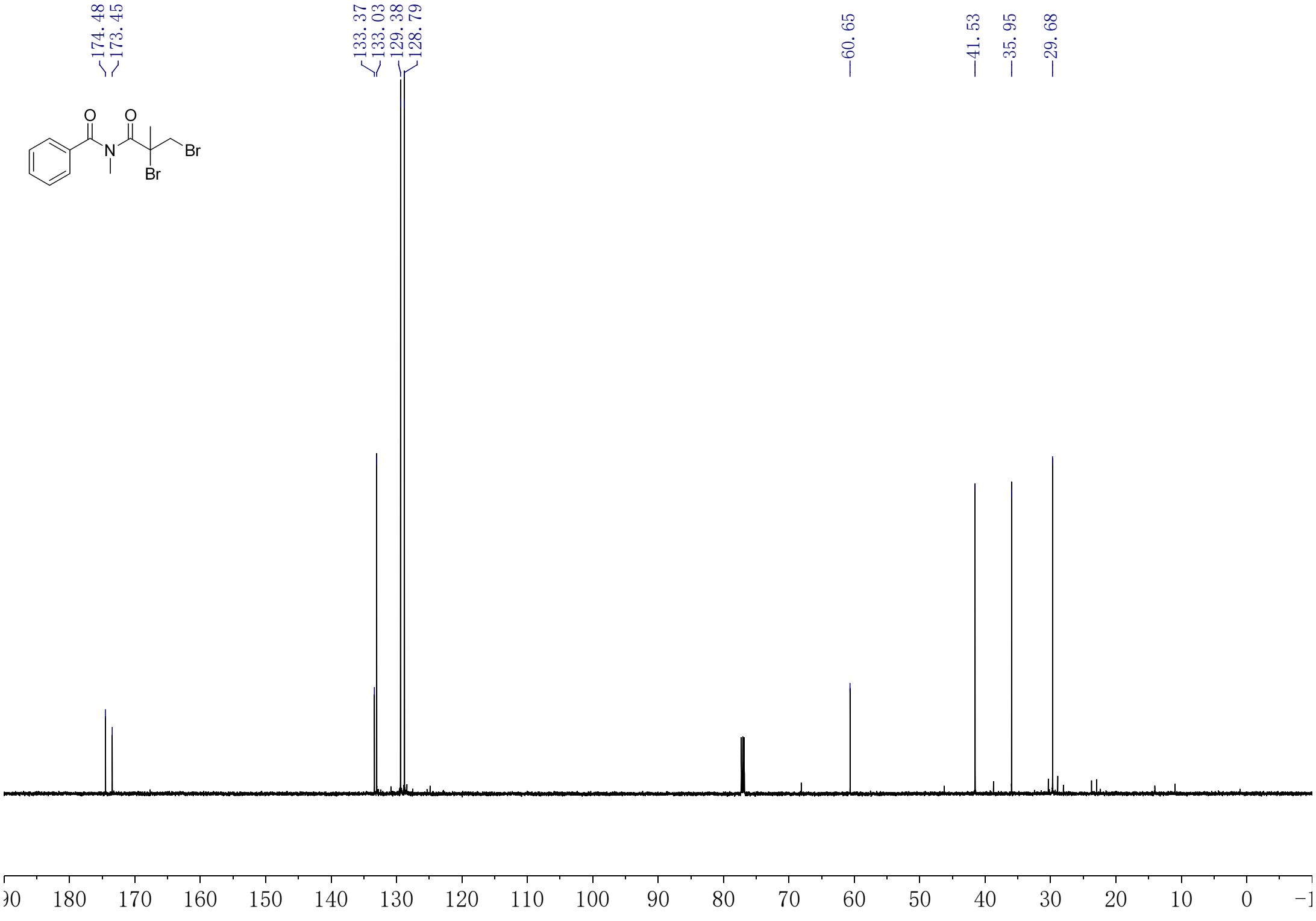
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