Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Synthesis of Passerini adducts from aldehydes and isocyanides under the auxiliary of water

Ming Li,* Bin Qiu, Xiang-Jing Kong and Li-Rong Wen*

State Key Laboratory Base of Eco-Chemical Engineering, College of Chemistry and Molecular Engineering, Qingdao University of Science and Technology, Qingdao 266042, China
E-mail: wenlirong@qust.edu.cn; liming928@qust.edu.cn

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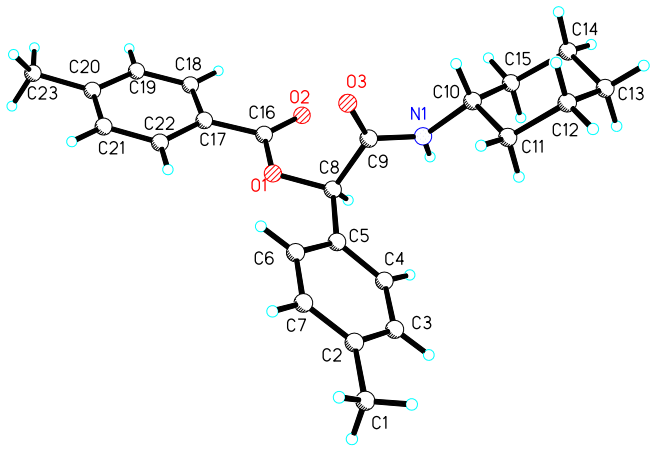


Figure S1. X-Ray crystal structure of **3g** with 50% ellipsoids (CCDC 891438)**.**

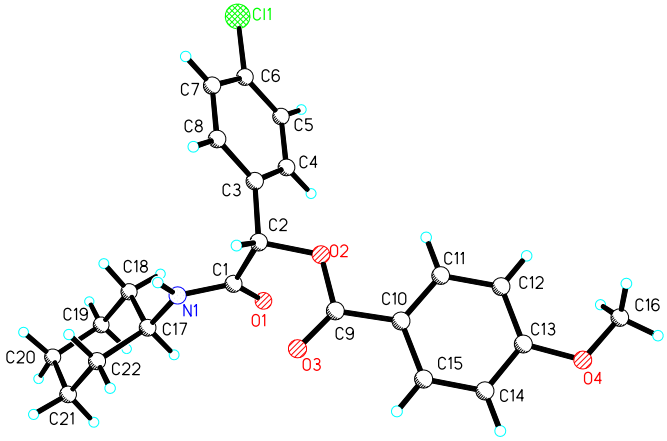
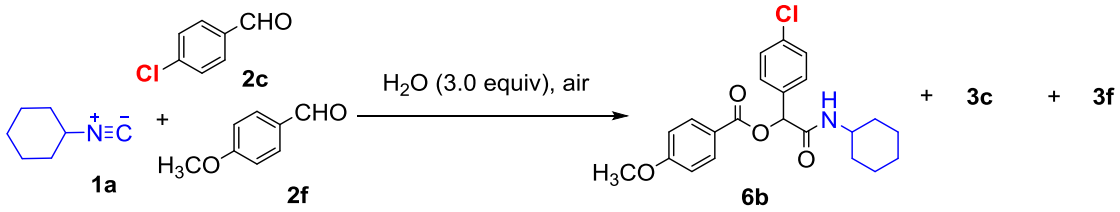


Figure S2. X-Ray crystal structure of **6b** with 50% ellipsoids (CCDC 900082).

Table S1. Study on the crossing reaction of **2c**, **2f** with **1a**[a]



Entry	**2c/2f/1a**	Yield (%)[b]		
		6b	3c	3f
1	1:1:1	18	20	19
2	1.5:1.5:1	30	35	15
3	2:1:1	40	42	trace
4	1:2:1	35	10	38

[a] Reaction conditions: **1a** (0.5 mmol), **2c** and **2f** (equiv. based on **1a**), H_2O (1.5 mmol), 60 °C, 3 h. [b] Isolated yields by silica gel column chromatography.

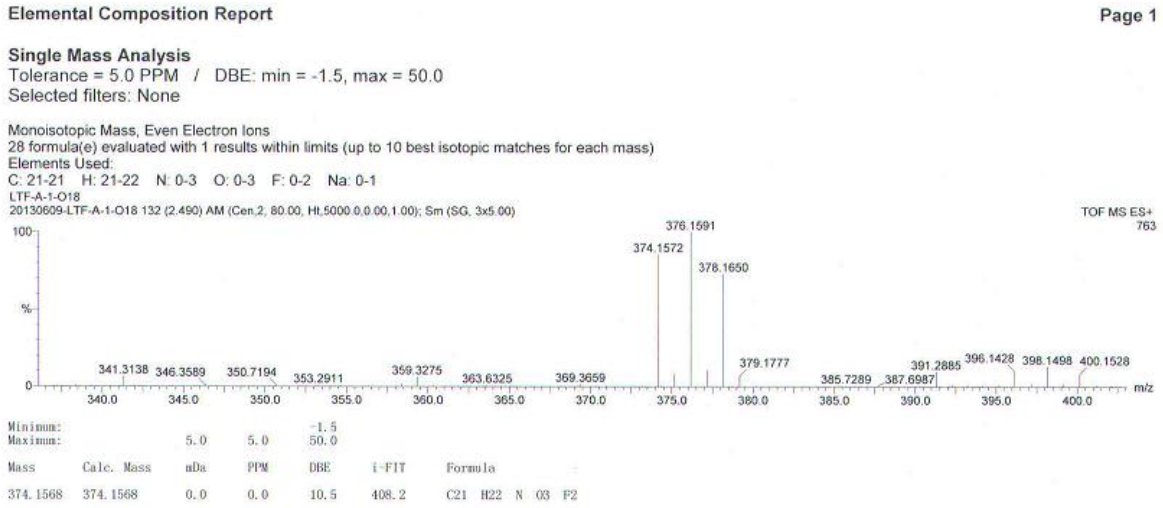
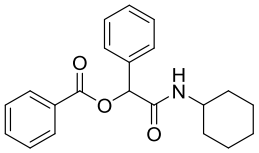


Figure S3. HRMS spectrum of isotope labeled **3b**.

Characterization data of compounds 3/4/5/6

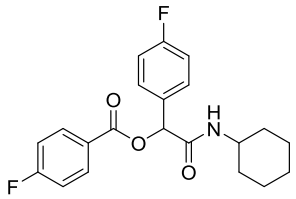
2-(Cyclohexylamino)-2-oxo-1-phenylethyl benzoate (3a)



3a

White powder, m.p.: 144-146 ℃; **IR** (KBr, cm^{-1}) 3305, 3069, 3041, 2935, 2854, 1733, 1659, 1602, 1549, 1498, 1450, 731, 703. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.11-1.25 (m, 3H, CH),1.34-1.37 (m, 2H, CH), 1.62-1.68 (m, 3H, CH), 1.88-1.96 (m, 2H, CH), 3.82-3.84 (m, 1H, CH), 6.04 (d, *J* = 7.0 Hz, 1H, NH), 6.31 (s, H, CH), 7.26-7.63 (m, 8H, ArH), 8.09-8.10 (m, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.5, 25.8, 32.9, 33.0, 48.2, 76.0, 91.6, 127.4, 128.6, 128.8, 128.9, 129.4, 129.8, 133.6, 135.8, 164.9, 167.3. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{24}NO_3$, 338.1756, found 338.1765.

2-(Cyclohexylamino)-1-(4-fluorophenyl)-2-oxoethyl 4-fluorobenzoate (3b)

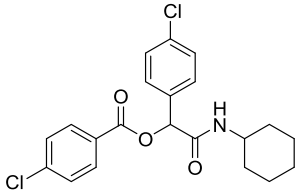


3b

White powder, m.p.: 212-214 ℃; **IR** (KBr, cm^{-1}) 3266, 3099, 2930, 2854, 1719, 1657, 1604, 1569, 1510, 1449, 768. **^{1}H NMR** (500 MHz, DMSO-d_6) 1.06-1.25 (m, 5H, CH),

1.50-1.76 (m, 5H, CH), 3.47-3.50 (m, 1H, CH), 6.04 (s, 1H, CH), 8.27 (d, J = 7.9 Hz, 1H, NH), 7.24-7.64 (m, 6H, ArH), 8.08-8.10 (m, 2H, ArH); **^{13}C NMR** (125 MHz, DMSO-d_6) 24.4, 25.1, 32.0, 32.1, 32.9, 47.7, 74.9, 115.3 (d, $^3J_{C\text{-}F}$ = 7.5 Hz), 115.9 (d, $^2J_{C\text{-}F}$ = 22.1 Hz), 125.8, 129.3 (d, $^3J_{C\text{-}F}$ = 7.3 Hz), 132.2, 132.4 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 141.4, 162.1 (d, $^1J_{C\text{-}F}$ = 245.3 Hz), 164.0, 165.3 (d, $^1J_{C\text{-}F}$ = 251.8 Hz), 166.6. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{22}F_2NO_3$, 374.1568, found 374.1556.

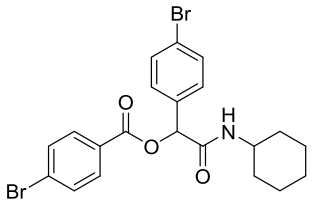
1-(4-Chlorophenyl)-2-(cyclohexylamino)-2-oxoethyl 4-chlorobenzoate (3c)



3c

White powder, m.p.: 210-212 ℃; **IR** (KBr, cm^{-1}) 3271, 3093, 2927, 2853, 1724, 1655, 1595, 1567, 1490, 1447, 854. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.14-1.20 (m, 3H, CH), 1.32-1.41 (m, 2H, CH), 1.58-1.72 (m, 3H, CH), 1.88-1.95 (m, 2H, CH), 3.80-3.84 (m, 1H, CH), 5.93 (d, J = 7.5 Hz, 1H, NH), 6.23 (s, 1H, CH), 7.36-7.48 (m, 6H, ArH), 8.00-8.02 (m, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.4, 32.9, 48.4, 75.4, 127.5, 128.8, 129.0, 131.1, 134.0, 135.1, 140.3, 164.1, 166.7. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{22}Cl_2NO_3$, 406.0977, found 406.0983.

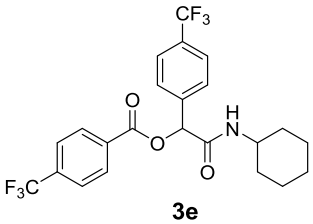
1-(4-Bromophenyl)-2-(cyclohexylamino)-2-oxoethyl 4-bromobenzoate (3d)



3d

White powder, m.p.: 191-193 ℃; **IR** (KBr, cm^{-1}) 3289, 3092, 2932, 2854, 1728, 1658, 1590, 1557, 1488, 1450, 755. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.08-1.20 (m, 3H, CH), 1.34-1.36 (m, 2H, CH), 1.62-1.70 (m, 3H, CH), 1.87-1.94 (m, 2H, CH), 3.79-3.83 (m, 1H, CH), 5.93 (d, J = 7.0 Hz, 1H, NH), 6.20 (s, H, CH), 7.26-7.93 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.4, 32.8, 48.4, 75.4, 123.3, 128.0, 129.1, 131.2, 132.0, 132.1, 134.5, 164.2, 166.6. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{22}Br_2NO_3$, 493.9966, found 493.9959.

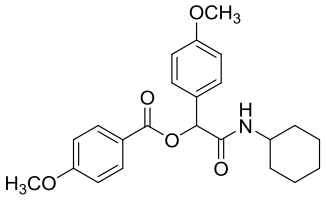
1-(4-Trifluoromethylphenyl)-2-(cyclohexylamino)-2-oxoethyl 4-trifluoromethyl-benzoate (3e)



3e

White powder, m.p.: 178-179 ℃; **IR** (KBr, cm^{-1}) 3288, 2936, 2857, 1736, 1661, 1560, 1413, 1327, 1129, 755. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.10-1.25 (m, 3H, CH), 1.33-1.37 (m, 2H, CH), 1.60-1.72 (m, 3H, CH), 1.89-1.96 (m, 2H, CH), 3.79-3.82 (m, 1H, CH), 6.01 (d, 1H, *J* = 7.8 Hz, NH), 6.32 (s, 1H, CH), 7.67 (s, 4H, ArH), 7.77 (d, *J* = 8.2 Hz, 2H, ArH), 8.21 (d, *J* = 8.1 Hz, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 25.2, 25.9, 33.4, 49.1, 122.8, 123.2, 125.0, 125.4, 126.4, 128.3, 130.8, 131.8 (q, $^{2}J_{C\text{-}F}$ = 32.4 Hz), 132.7, 135.8 (q, $^{2}J_{C\text{-}F}$ = 32.9 Hz), 139.6, 164.3, 166.7. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{23}H_{22}F_6NO_3$, 474.1504, found 474.1515.

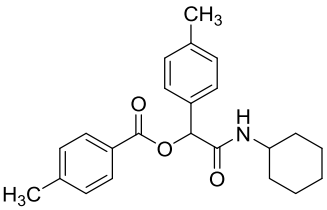
2-(Cyclohexylamino)-1-(4-methoxyphenyl)-2-oxoethyl 4-methoxybenzoate (3f)



3f

White powder, m.p.: 152-154 ℃; **IR** (KBr, cm^{-1}) 3287, 3078, 2932, 2853, 1716, 1657, 1607, 1546, 1514, 848. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.12-1.20 (m, 3H, CH), 1.34-1.39 (m, 2H, CH), 1.60-1.71 (m, 3H, CH), 1.88-1.96 (m, 2H, CH), 3.80-3.88 (m, 6H, CH), 6.02 (d, *J* = 8.0 Hz, 1H, NH), 6.24 (s, 1H, CH), 6.89-7.45 (m, 6H, ArH), 8.02-8.04 (m, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.5, 33.0, 48.1, 55.3, 55.5, 75.4, 113.9, 114.2, 121.8, 128.2, 128.9, 131.8, 160.0, 164.7, 167.8. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{23}H_{29}NO_5$, 398.1967, found 398.1975.

2-(Cyclohexylamino)-2-oxo-1-(*p*-tolyl)ethyl 4-methylbenzoate (3g)

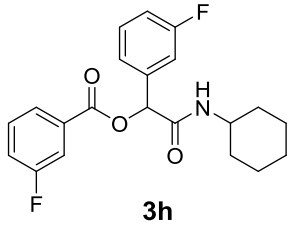


3g

White powder, m.p.: 157-159 ℃; **IR** (KBr, cm^{-1}) 3283, 3093, 2924, 2856, 1732, 1652, 1613, 1564, 1514, 1450. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.12-1.20 (m, 3H, CH), 1.35-1.37 (m, 2H, CH), 1.59-1.70 (m, 3H, CH), 1.88-1.96 (m, 2H, CH), 2.35 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 3.82-3.84 (m, 1H, CH), 6.03 (d, *J* = 7.5 Hz, 1H, NH), 6.26 (s, 1H, CH), 7.18-7.42 (m, 6H, ArH), 7.97-7.98 (m, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 21.2, 21.7, 24.7, 25.4, 32.9, 33.0, 48.1, 75.7, 126.7, 127.4, 129.3, 129.4, 129.8,

133.0, 138.8, 144.4, 165.0, 167.6. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{23}H_{28}NO_3$, 366.2069, found 366.2056.

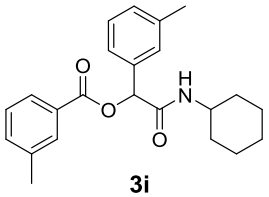
2-(Cyclohexylamino)-1-(3-fluorophenyl)-2-oxoethyl 3-fluorobenzoate (3h)



3h

White powder, m.p.: 155-157 ℃; **IR** (KBr, cm^{-1}) 3318, 3078, 2935, 2857, 1735, 1659, 1593, 1547, 1488, 1449, 760, 680. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.14-1.97 (m, 10H, CH), 3.83-3.84 (m, 1H, CH), 5.98 (d, J = 8.0 Hz, 1H, NH), 6.27 (s, 1H, CH), 7.07-7.92 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.4, 32.9, 48.4, 75.5, 115.1 (d, $^1J_{C\text{-}F}$ = 218.9 Hz), 115.3 (d, $^1J_{C\text{-}F}$ = 217.2 Hz), 116.7 (d, $^2J_{C\text{-}F}$ = 23.1 Hz), 120.9 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 123.1, 125.5, 130.4 (d, $^3J_{C\text{-}F}$ = 6.8 Hz), 131.2, 137.7, 161.8 (d, $^3J_{C\text{-}F}$ = 26.6 Hz), 163.62, 163.8, 166.5. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{22}F_2NO_3$, 374.1568, found 374.1576.

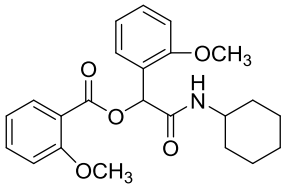
2-(Cyclohexylamino)-2-oxo-1-(m-tolyl)ethyl 3-methylbenzoate (3i)



3i

White powder, m.p.: 148-150 ℃; **IR** (KBr, cm^{-1}) 3271, 3088, 2932, 2855, 1720, 1657, 1611, 1589, 1558, 1491, 1451. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.12-1.20 (m, 3H, CH), 1.34-1.39 (m, 2H, CH), 1.60-1.70 (m, 3H, CH), 1.88-1.96 (m, 2H, CH), 2.36 (s, 1H, CH), 2.42 (s, 1H, CH), 3.82-3.84 (m, 1H, CH), 6.03 (d, J = 7.0 Hz, 1H, NH), 6.26 (s, H, CH), 7.16-7.89 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 21.3, 21.4, 24.7, 25.4, 32.9, 48.2, 75.9, 124.4, 126.9, 128.3, 128.5, 128.6, 129.3, 129.7, 130.3, 134.3, 135.7, 138.4, 165.1, 167.5. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{23}H_{28}NO_3$, 366.2069, found 366.2079.

2-(Cyclohexylamino)-1-(2-methoxyphenyl)-2-oxoethyl 2-methoxybenzoate (3j)

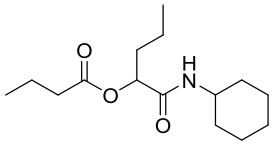


3j

White powder, m.p.: 150-152 ℃; **IR** (KBr, cm^{-1}) 3361, 3074, 2931, 2851, 1701, 1675, 1602, 1536, 1492, 1467, 766. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.12-1.72 (m, 10H, CH), 3.84-3.86 (m. 1H, CH), 3.87 (s, 3H, CH), 3.96 (s, 3H, CH), 6.63 (s, 1H, CH), 6.82 (d,

J = 8.0 Hz, 1H, NH), 6.89-7.87 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.8, 25.6, 33.0, 33.4, 47.9, 55.7, 56.2, 71.2, 111.2, 112.3, 119.9, 120.7, 120.8, 124.9, 129.4, 130.0, 132.4, 133.9, 157.3, 159.0, 165.0, 168.0. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{23}H_{28}NO_5$, 398.1967, found 398.1975.

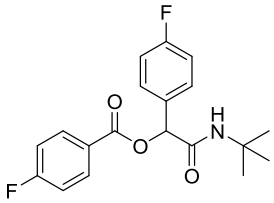
1-(Cyclohexylamino)-1-oxohexan-2-yl pentanoate (3k)



3k

White powder, m.p.: 67-68 ℃; **IR** (KBr, cm^{-1}) 3292, 2961, 2933, 2874, 2856, 1743, 1655, 1558, 1450. **^{1}H NMR** (500 MHz, $CDCl_3$) 0.90-1.00 (m, 6H, CH), 1.09-1.21 (m, 4H, CH), 1.32-1.41 (m, 2H, CH), 1.60-1.92 (m, 10H, CH), 2.36-2.39 (m, 2H, CH), 3.75-3.81 (m, 1H, CH), 5.15-5.17 (m, 1H, CH), 5.87 (d, *J* = 6.7 Hz, 1H, NH); **^{13}C NMR** (125 MHz, $CDCl_3$) 12.7, 17.0, 17.5, 20.8, 23.7, 24.5, 32.0, 33.0, 35.2, 46.8, 72.7, 168.0, 171.2. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{15}H_{28}NO_3$, 270.2069, found 270.2060.

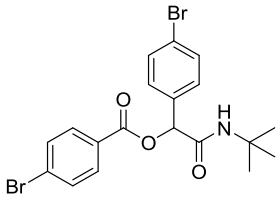
2-(*tert*-Butylamino)-1-(4-fluorophenyl)-2-oxoethyl 4-fluorobenzoate (4a)



4a

White powder, m.p.: 168-170 ℃; **IR** (KBr, cm^{-1}) 3284, 3085, 2976, 2933, 1727, 1656, 1606, 1560, 1511, 1450. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.36 (s, 9H, CH), 5.86 (s, 1H, NH), 6.15 (s, 1H, CH), 7.06-8.10 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 27.8, 28.7, 51.7, 75.4, 115.8, 115.9, 125.5, 129.5, 131.7, 132.3, 162.1, 164.0, 165.1, 167.0. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{19}H_{20}F_2NO_3$, 348.1411, found 348.1419.

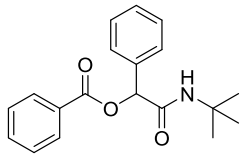
1-(4-Bromophenyl)-2-(*tert*-butylamino)-2-oxoethyl 4-bromobenzoate (4b)



4b

White powder, m.p.: 173-175 ℃; **IR** (KBr, cm^{-1}) 3308, 3087, 2974, 2927, 1727, 1659, 1591, 1557, 1490, 1453. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.36(s, 9H, CH), 5.86 (s, 1H, NH), 6.12 (s, 1H, CH), 7.37-7.93 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 28.4, 28.6, 51.8, 75.6, 123.3, 128.1, 129.0, 129.1, 131.2, 132.0, 132.1, 134.7, 164.2, 166.6. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{19}H_{20}Br_2NO_3$, 467.9810, found 467.9805.

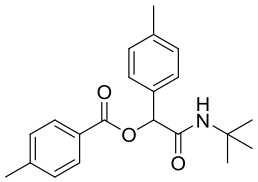
2-(*tert*-Butylamino)-2-oxo-1-phenylethyl benzoate (4c)[1,2,3]



4c

White powder, m.p.: 153-154 ℃ (lit. 148-150 ℃); **IR** (KBr, cm^{-1}) 3308, 3087, 2974, 2927, 1727, 1659, 1591, 1557, 1490, 1453.

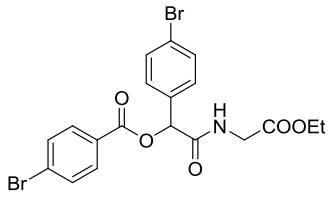
2-(*tert*-Butylamino)-2-oxo-1-(*p*-tolyl)ethyl 4-methylbenzoate (4d)



4d

White powder, m.p.: 170-171 ℃; **IR** (KBr, cm^{-1}) 3296, 2984, 2927, 1743, 1660, 1514, 1542, 1516, 1440. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.36 (s, 9H, CH), 2.34 (s, 3H, CH), 2.42 (s, 3H, CH), 5.99 (s, 1H, NH), 6.17 (s, 1H, CH), 7.18-7.97 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 20.4, 21.3, 21.8, 28.7, 30.8, 51.5, 75.8, 126.7, 127.4, 129.4, 129.5, 129.9, 133.2, 138.7, 144.4, 165.0, 167.7. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{26}NO_3$, 340.1913, found 340.1909.

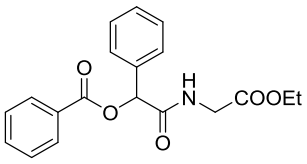
1-(4-Bromophenyl)-2-((2-ethoxy-2-oxoethyl)amino)-2-oxoethyl 4-bromobenzoate (5a)



5a

White powder, m.p.: 134-136 ℃; **IR** (KBr, cm^{-1}) 3299, 3089, 2983, 2939, 1733, 1663, 1591, 1560, 1490, 1446, 745, 709. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.26-1.29 (m, 3H, CH), 4.01-4.25 (m, 4H, CH), 6.30 (s, 1H, CH), 6.75 (s, 1H, NH), 7.26-7.97 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 14.1, 41.3, 61.9, 75.3, 123.6, 127.9, 129.2, 131.3, 132.1, 134.1, 164.2, 167.8, 169.4. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{19}H_{18}Br_2NO_5$, 497.9552, found 497.9549.

2-((2-Ethoxy-2-oxoethyl)amino)-2-oxo-1-phenylethyl benzoate (5b)

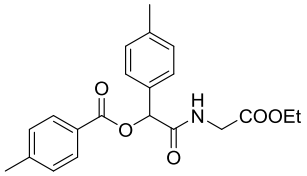


5b

White powder, m.p.: 110-112 ℃; **IR** (KBr, cm^{-1}) 3296, 3068, 2983, 2936, 1728, 1662,

1602, 1559, 1498, 1451, 745, 709. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.25-1.28 (m, 3H, CH), 3.98-4.24 (m, 4H, CH), 6.40 (s, 1H, CH), 6.81 (s, 1H, NH), 7.37-8.14 (m, 10H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 14.0, 41.3, 61.7, 75.8, 127.5, 128.6, 128.8, 129.1, 129.2, 129.9, 133.7, 135.3, 164.8, 168.5, 169.5. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{19}H_{20}NO_5$, 342.1341, found 342.1346.

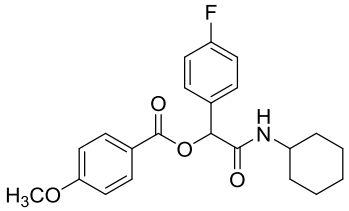
2-((2-Ethoxy-2-oxoethyl)amino)-2-oxo-1-(*p*-tolyl)ethyl 4-methylbenzoate (5c)



5c

White powder, m.p.: 109-111 ℃; **IR** (KBr, cm^{-1}) 3355, 3037, 2974, 2931, 2871, 1735, 1686, 1665, 1613, 1543, 1515, 1457, 745, 709. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.24-1.28 (m, 3H, CH), 2.34 (s, 3H, CH), 2.42 (s, 3H, CH), 4.00-4.23 (m, 4H, CH), 6.34 (s, 1H, CH), 6.80 (s, 1H, NH), 7.18-8.00 (m, 8H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 14.1, 21.2, 21.7, 41.3, 61.6, 75.5, 126.5, 127.5, 129.3, 129.5, 129.9, 132.6, 139.0, 144.4, 164.9, 168.8, 169.5. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{24}NO_5$, 370.1654, found 370.1665.

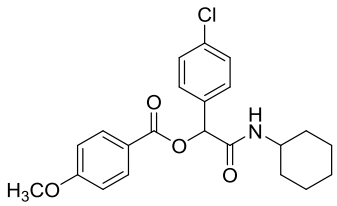
2-(Cyclohexylamino)-1-(4-fluorophenyl)-2-oxoethyl 4-methoxybenzoate (6a)



6a

White powder, m.p.: 205-207 ℃; **IR** (KBr, cm^{-1}) 3276, 3088, 2934, 2853, 1709, 1653, 1608, 1413, 1452, 1266, 770. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.12-1.23 (m, 3H, CH), 1.35-1.50 (m, 2H, CH), 1.61-1.68 (m, 3H, CH), 1.89-1.95 (m, 2H, CH), 3.73-3.81 (m, 1H, CH), 3.89 (s, 3H, CH), 6.09 (d, J = 7.5 Hz, 1H, NH), 6.26 (s, 1H, CH), 6.91-7.51 (m, 6H, ArH), 8.02-8.04 (m, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.4, 32.9, 33.0, 48.2, 55.5, 74.8, 114.0, 114.2, 115.7 (d, $^{2}J_{C\text{-}F}$ = 21.6 Hz), 121.4, 129.3 (d, $^{3}J_{C\text{-}F}$ = 7.4 Hz), 131.8, 132.3, 161.9, 164.0, 164.5, 167.3. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{22}H_{25}FNO_4$, 386.1768, found 386.1772.

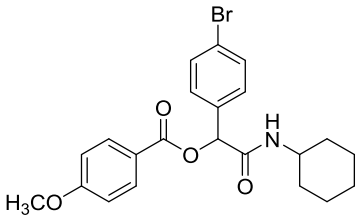
1-(4-Chlorophenyl)-2-(cyclohexylamino)-2-oxoethyl 4-methoxybenzoate (6b)[1,2]



6b

White powder, m.p.: 195-197 ℃ (lit. 184-186 ℃) ; **IR** (KBr, cm^{-1}) 3283, 3087, 2929, 2852, 1713, 1654, 1607, 1595, 1494, 1448, 1265, 772. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.14-1.21 (m, 3H, CH), 1.36-1.39 (m, 2H, CH), 1.58-1.74 (m, 3H, CH), 1.87-1.97 (m, 2H, CH), 3.80-3.84 (m, 1H, CH), 3.89 (s, 3H, CH), 6.07 (d, *J* = 7.5 Hz, 1H, NH), 6.26 (s, 1H, CH), 7.36-7.47 (m, 6H, ArH), 8.02-8.05 (m, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.4, 32.9, 33.0, 48.2, 55.5, 74.8, 114.0, 121.4, 128.7, 128.9, 131.8, 134.5, 134.8, 164.0, 164.4, 167.1. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{22}H_{25}ClNO_4$, 402.1472, found 402.1481.

1-(4-Bromophenyl)-2-(cyclohexylamino)-2-oxoethyl 4-methoxybenzoate (6c)



6c

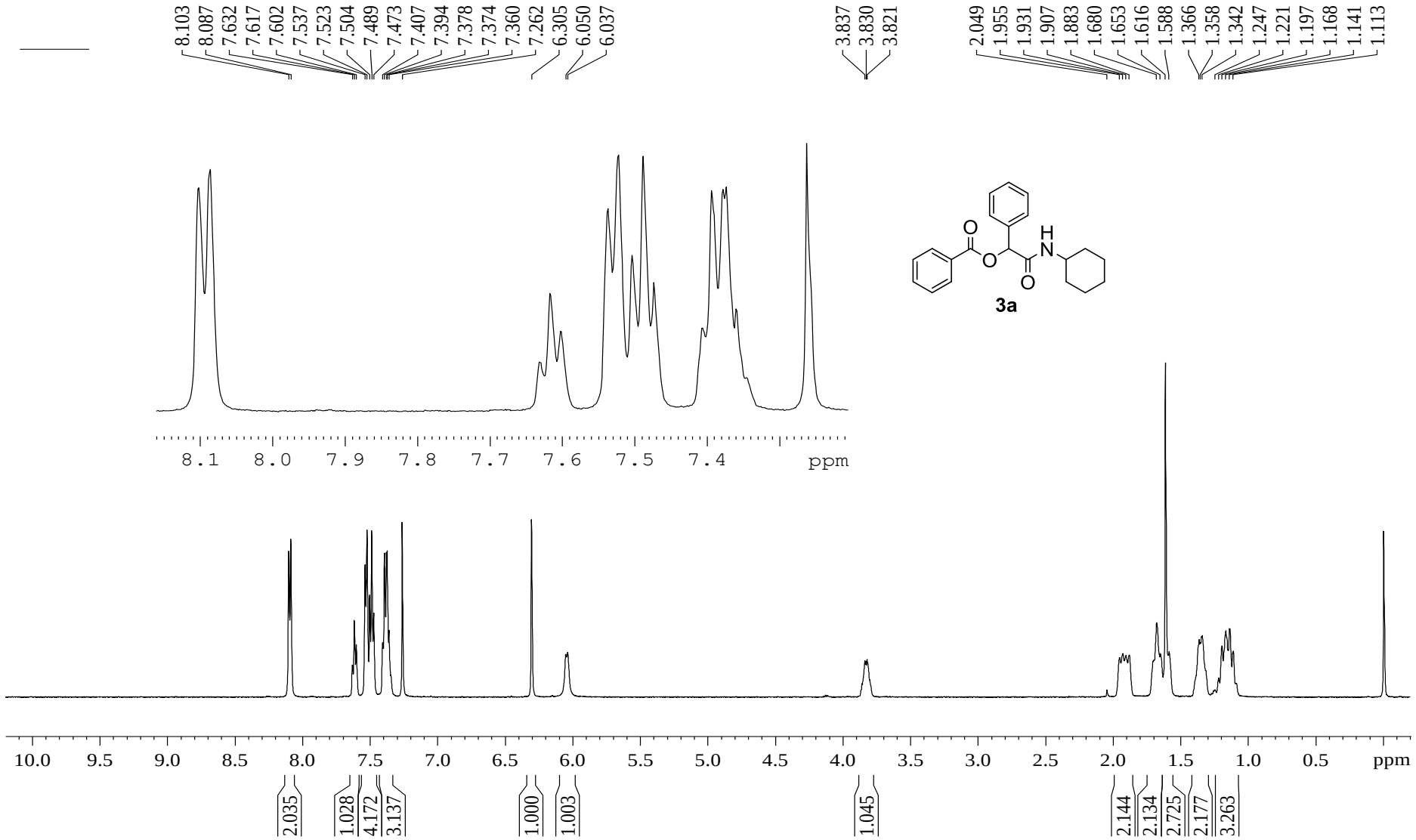
White powder, m.p.: 185-186 ℃; **IR** (KBr, cm^{-1}) 3288, 3082, 2934, 2854, 1715, 1655, 1607, 1580, 1511, 1452, 1262, 770. **^{1}H NMR** (500 MHz, $CDCl_3$) 1.10-1.26 (m, 3H, CH), 1.32-1.40 (m, 2H, CH), 1.59-1.68 (m, 3H, CH), 1.89-1.94 (m, 2H, CH), 3.78-3.84 (m, 1H, CH), 3.89 (s, 3H, CH), 6.06 (d, *J* = 7.5 Hz, 1H, NH), 6.23 (s, H, CH), 6.90-7.61 (m, 6H, ArH), 8.02-8.04 (m, 2H, ArH); **^{13}C NMR** (125 MHz, $CDCl_3$) 24.7, 25.5, 33.0, 33.7, 48.3, 55.6, 75.0, 114.1, 121.4, 123.0, 129.0, 131.0, 131.3, 131.9, 135.1, 164.1, 164.4, 167.0. **HRMS** (ESI-TOF, $[M+H]^+$): calcd for $C_{22}H_{25}BrNO_4$, 446.0967, found 446.0973.

Reference

1. X.-Y. Zhang, Y.-Z. Li，X.-S. Fan，G.-R. Qu，J.-J. Wang, X.-Y. Hu, *Chinese Chem. Lett.*, 2006, **17**, 578-580.

2. X.-S. Fan, Y.-Z. Li, X.-Y. Zhang, G.-R. Qu, J.-J. Wang, *Can. J. Chem.*, 2006, **84**, 794–799.

3. H. R. Lagiakos, M.-I. Aguilar, P. Perlmutter, *J. Org. Chem.*, 2009, **74**, 8001-8003.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6.050
6.037
3.837
3.830
3.821
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7.8
7.7
7.6
7.5
7.4
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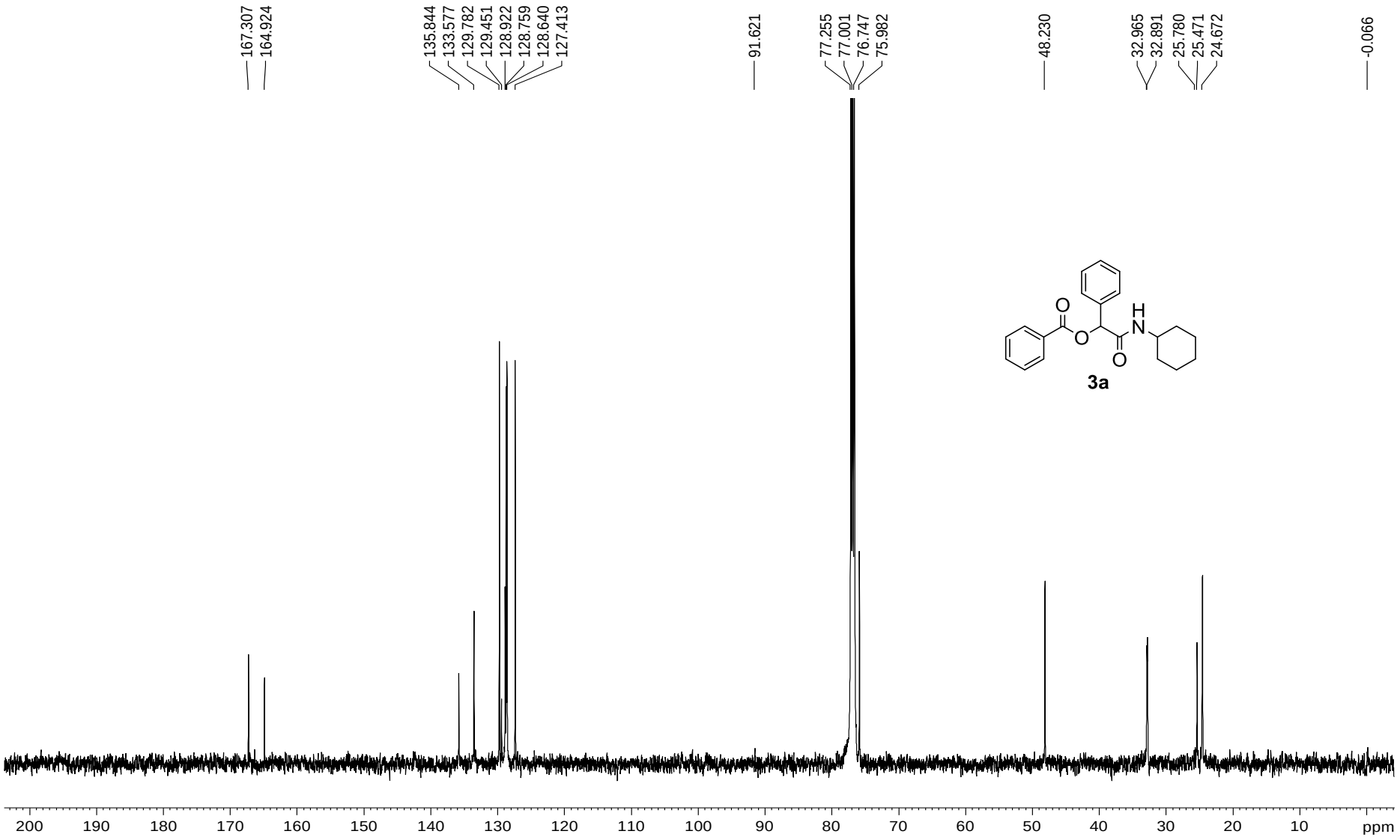
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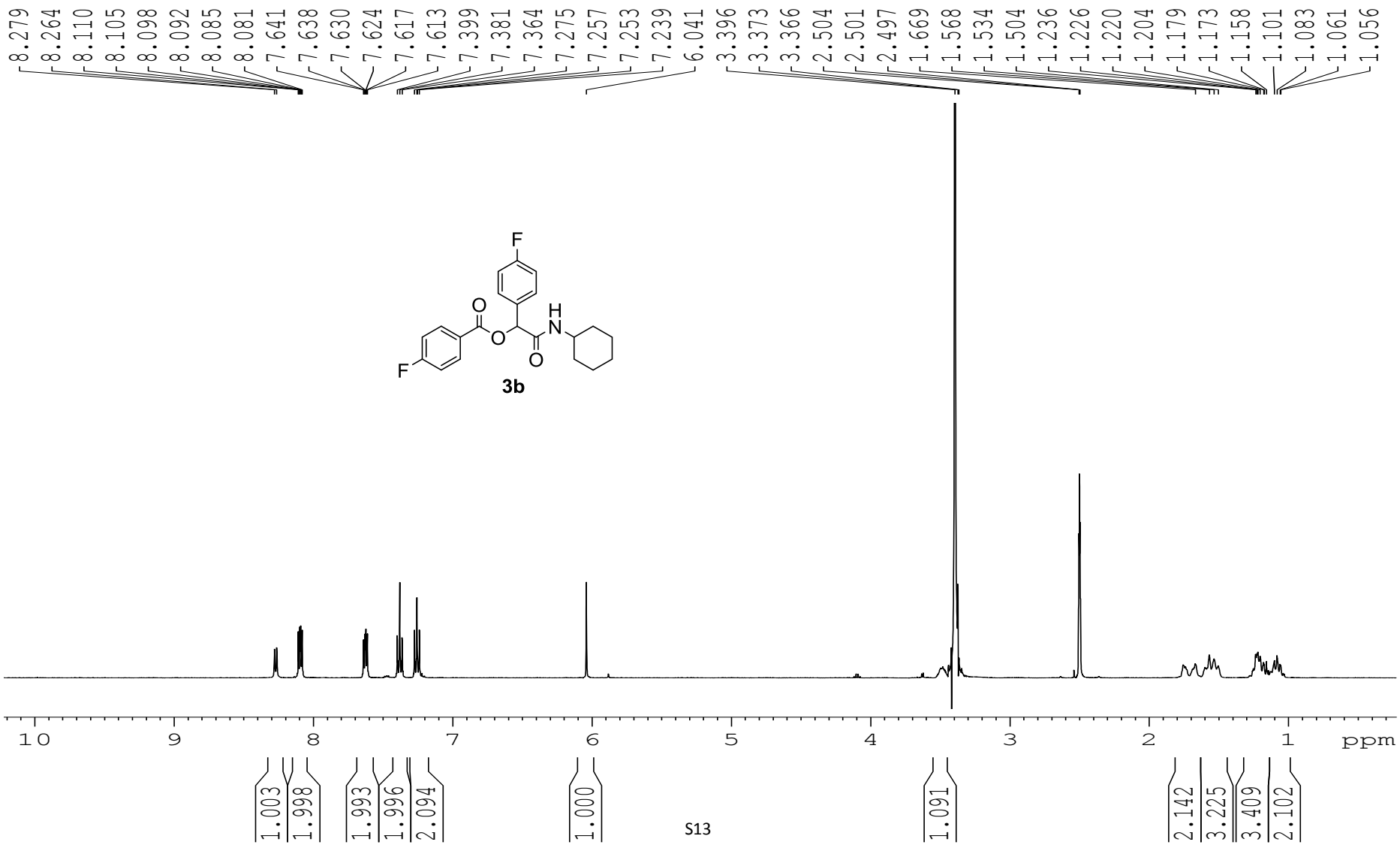
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7.253
7.239
6.041
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3.373
3.366
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1.534
1.504
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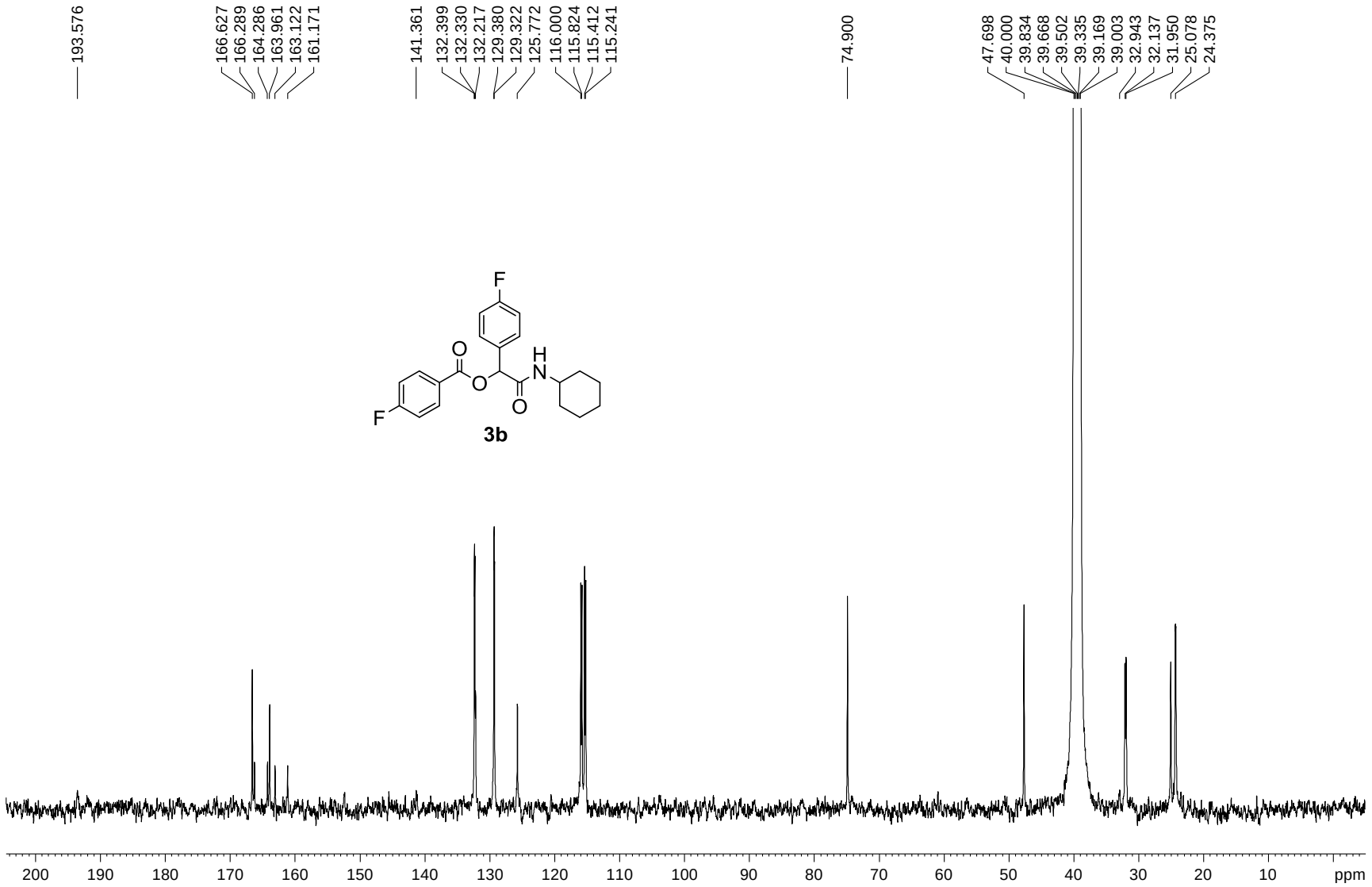
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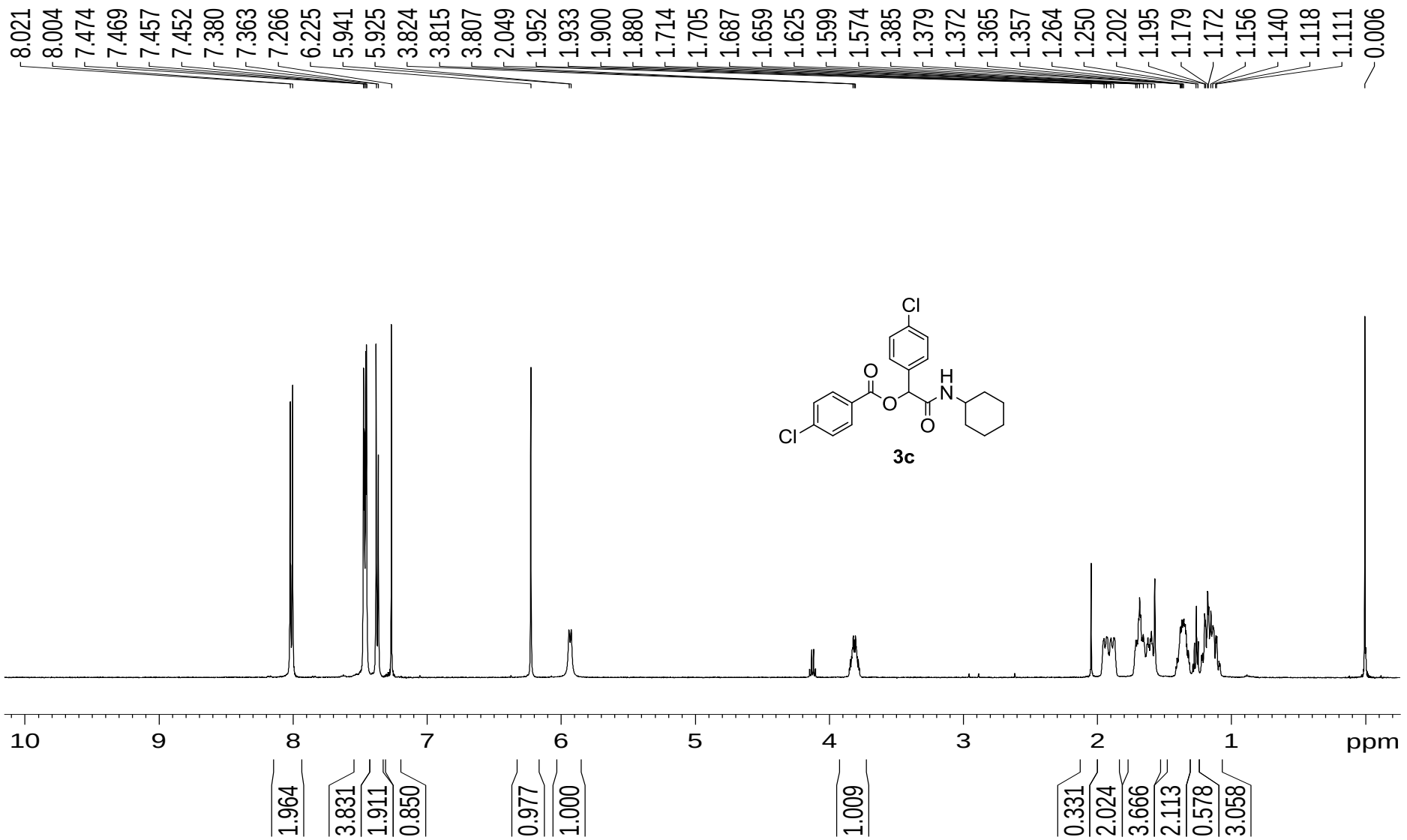
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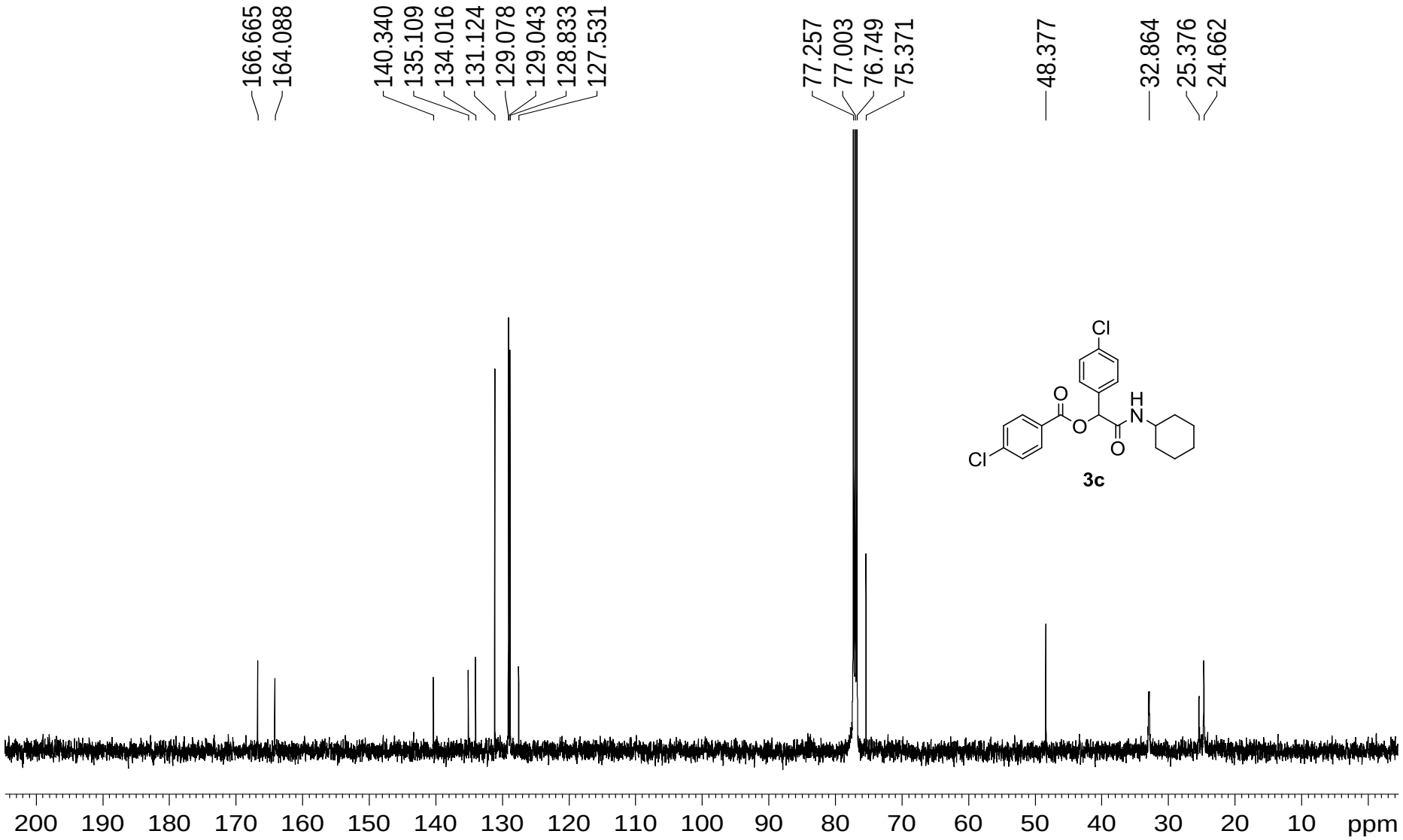
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Cl
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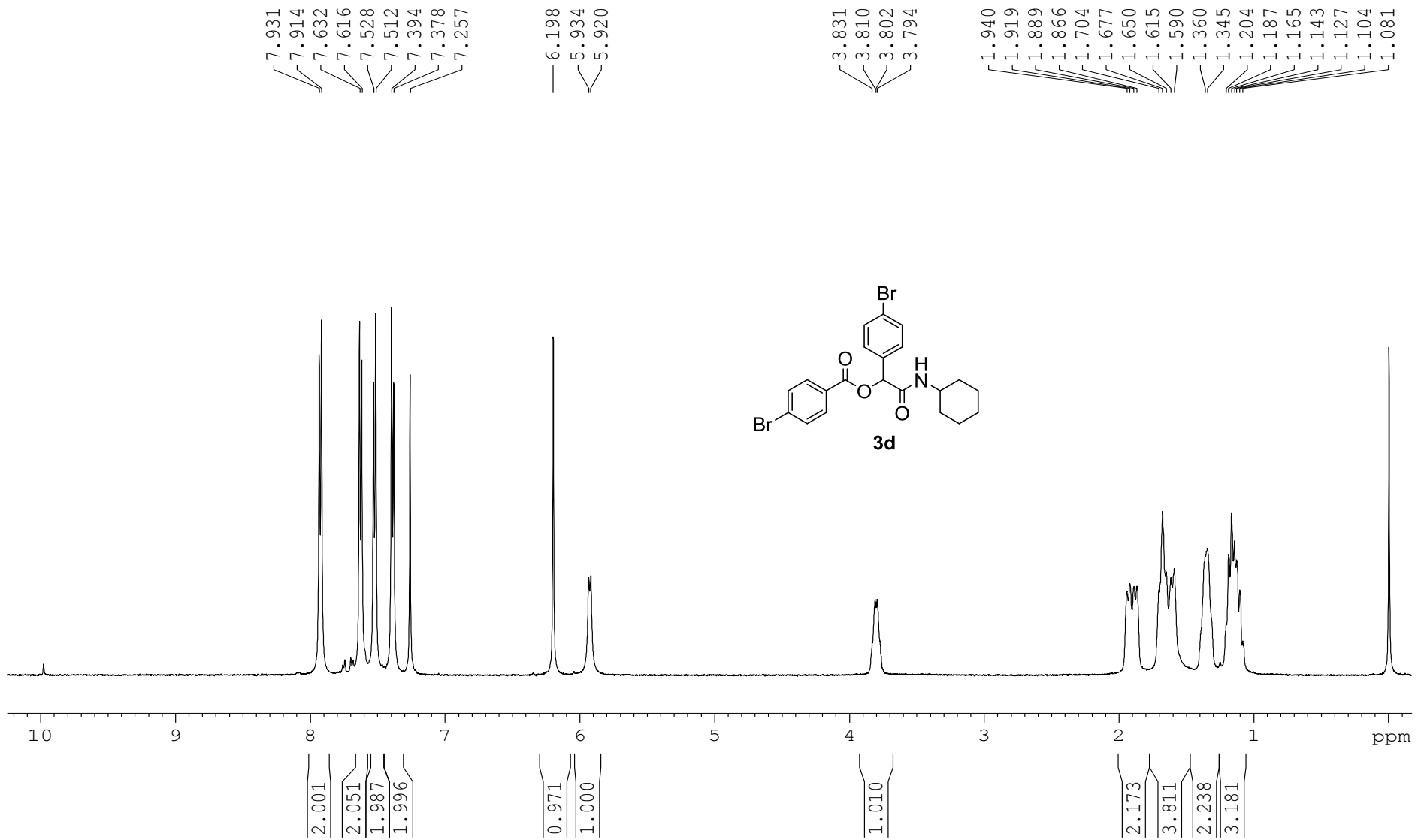
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Br
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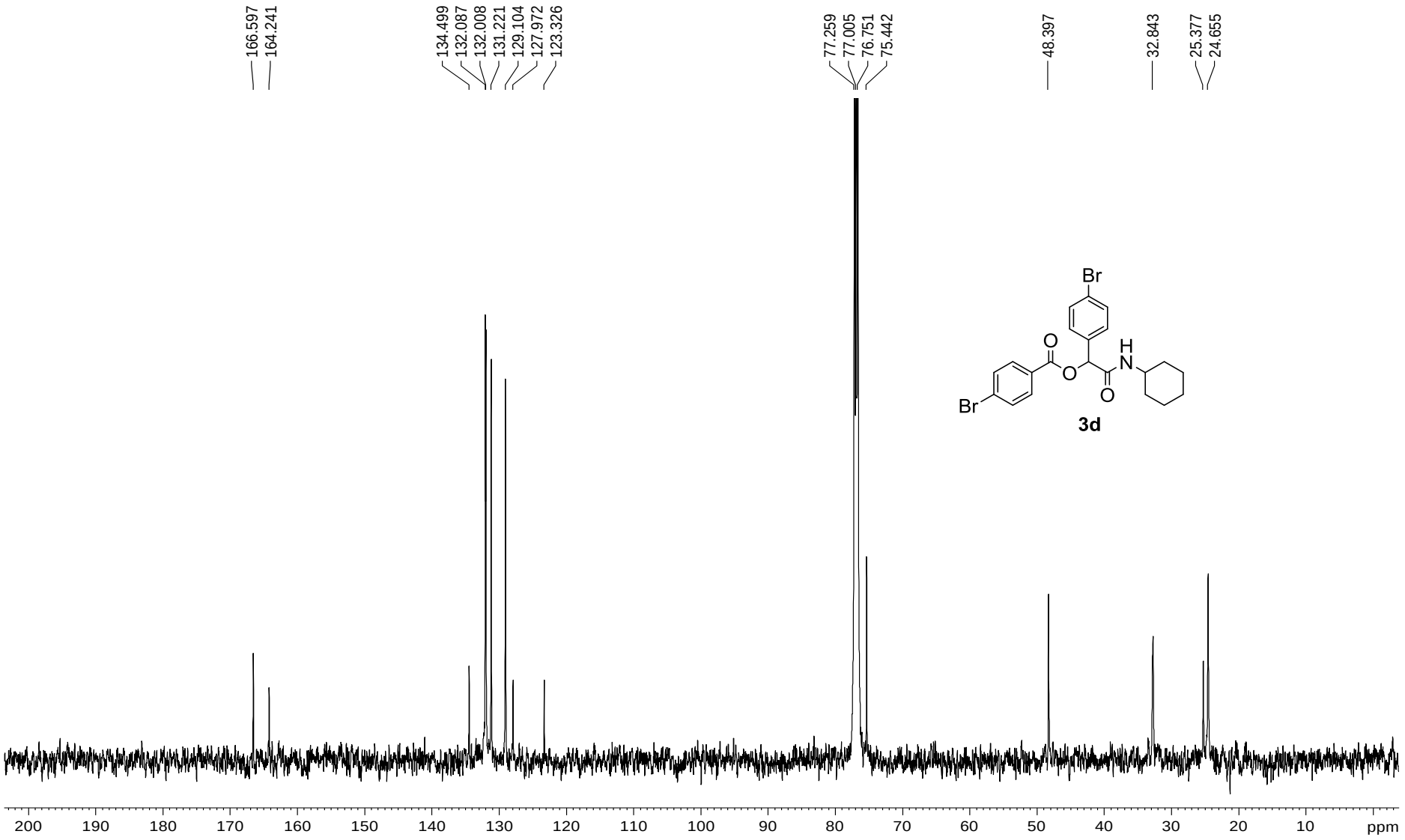
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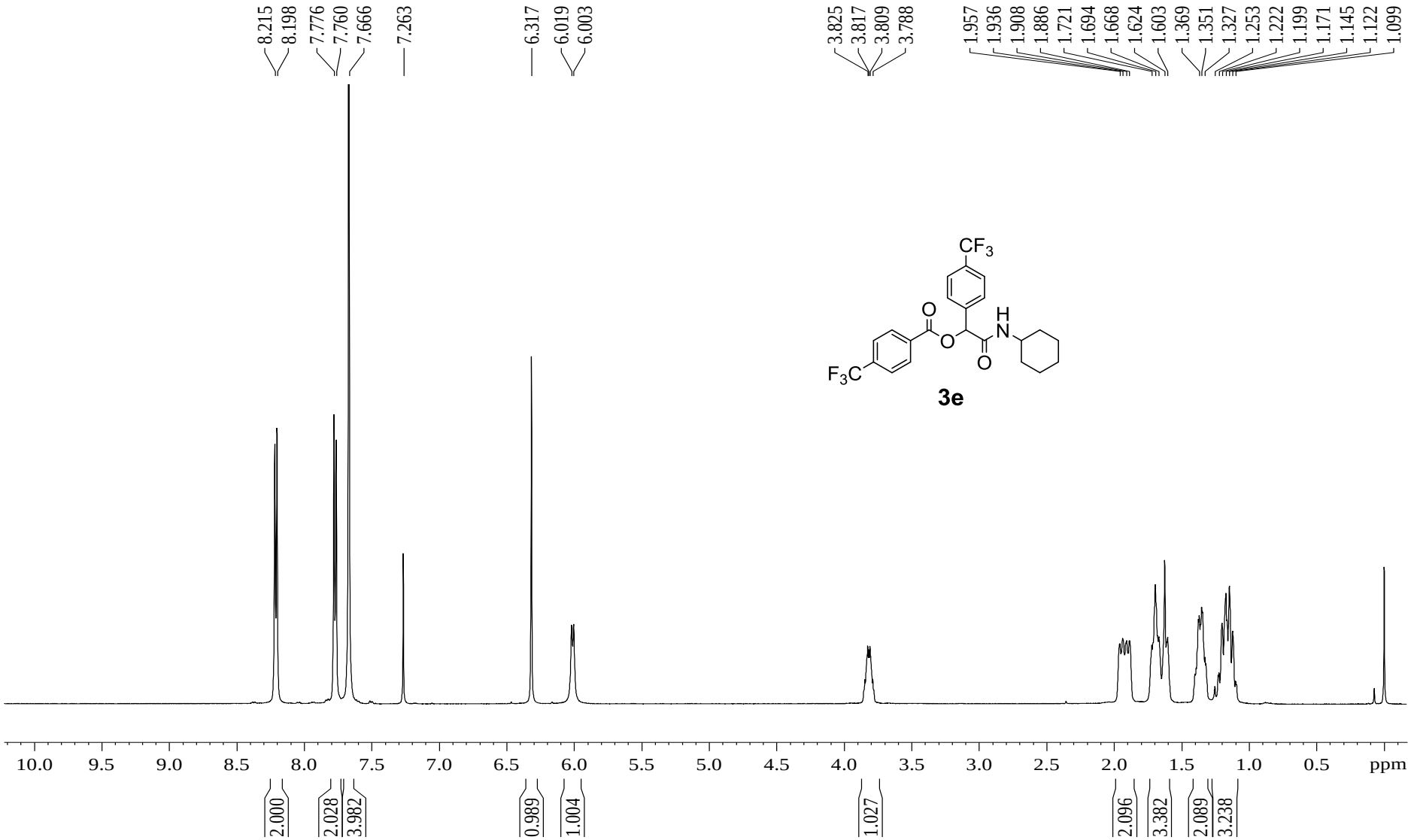
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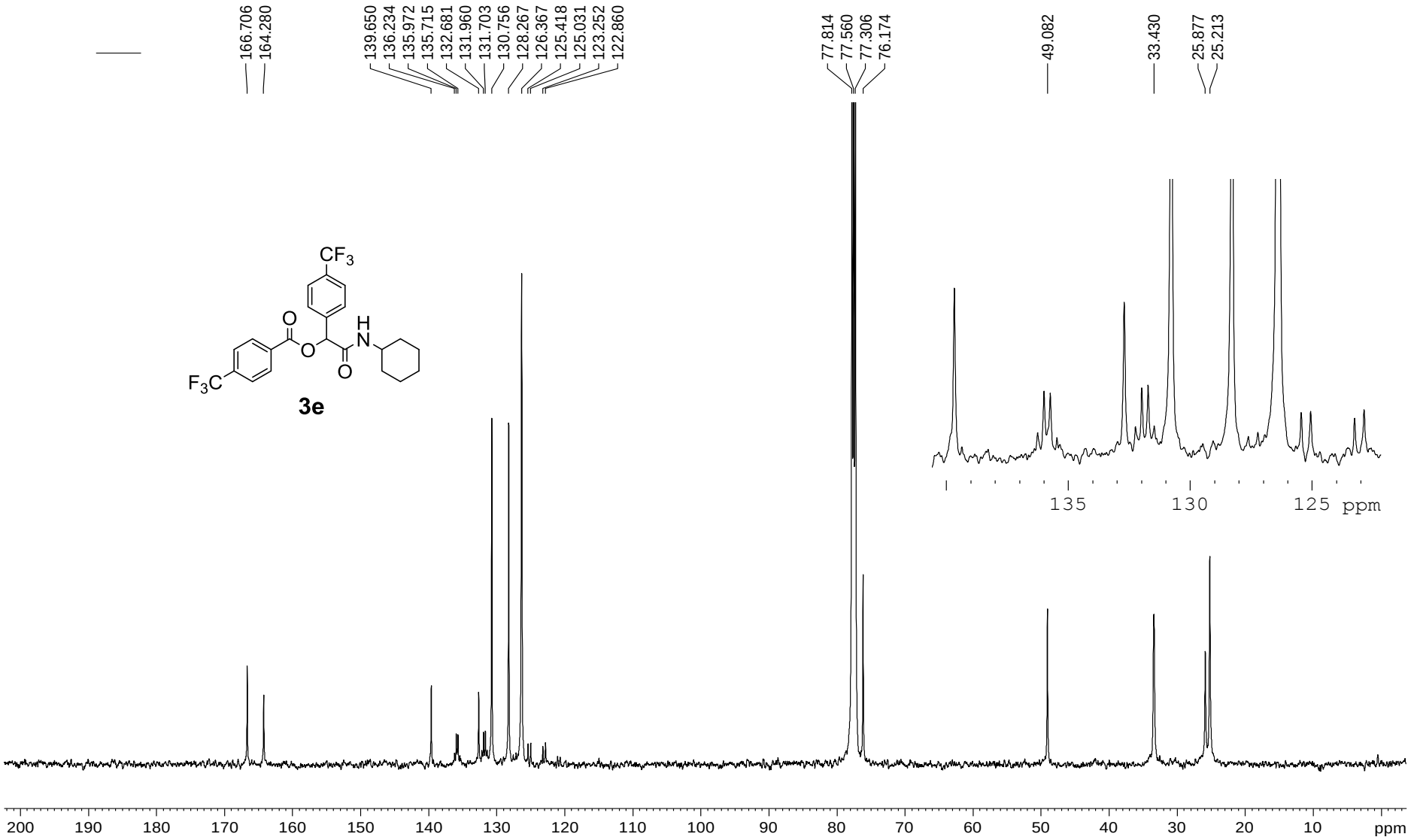
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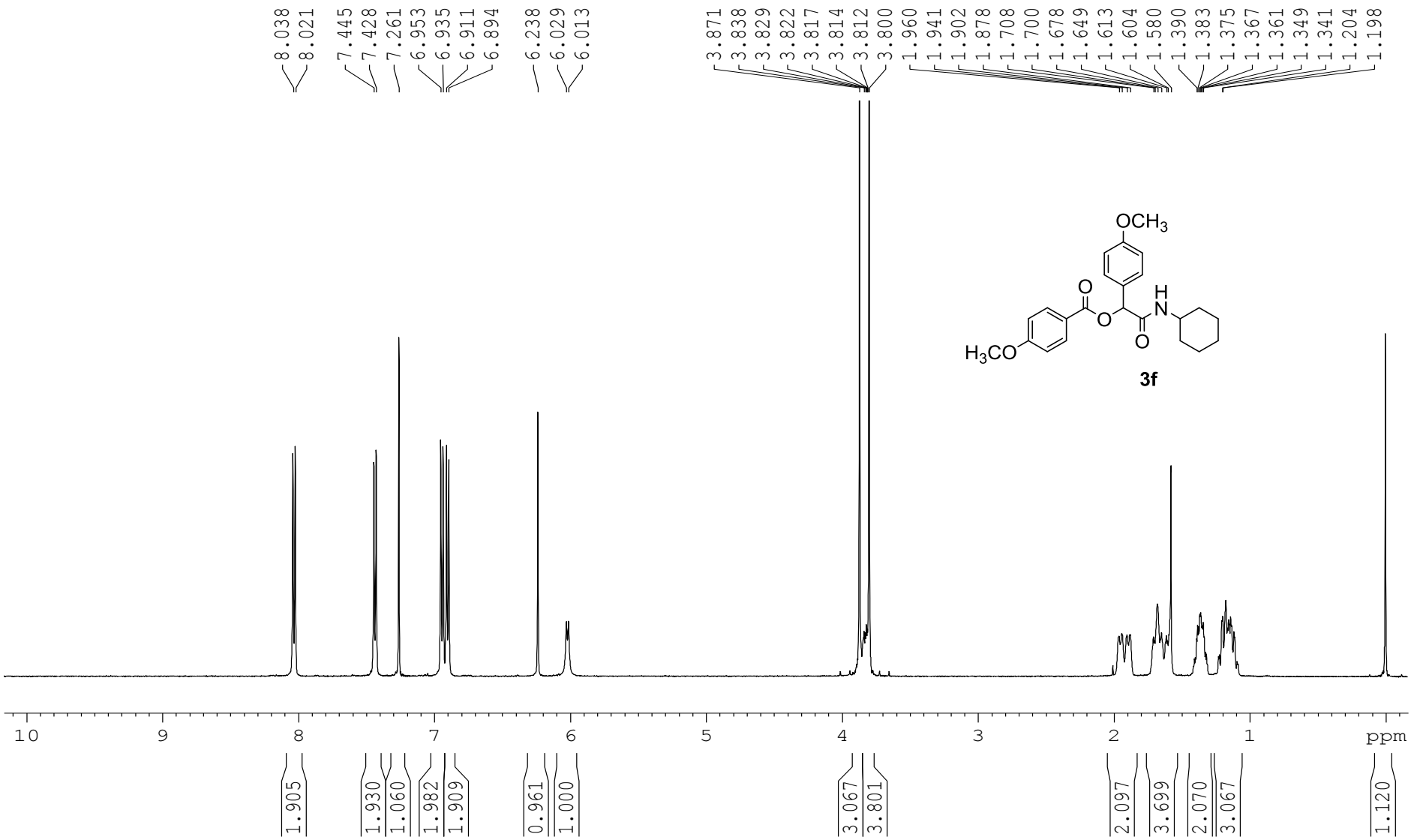
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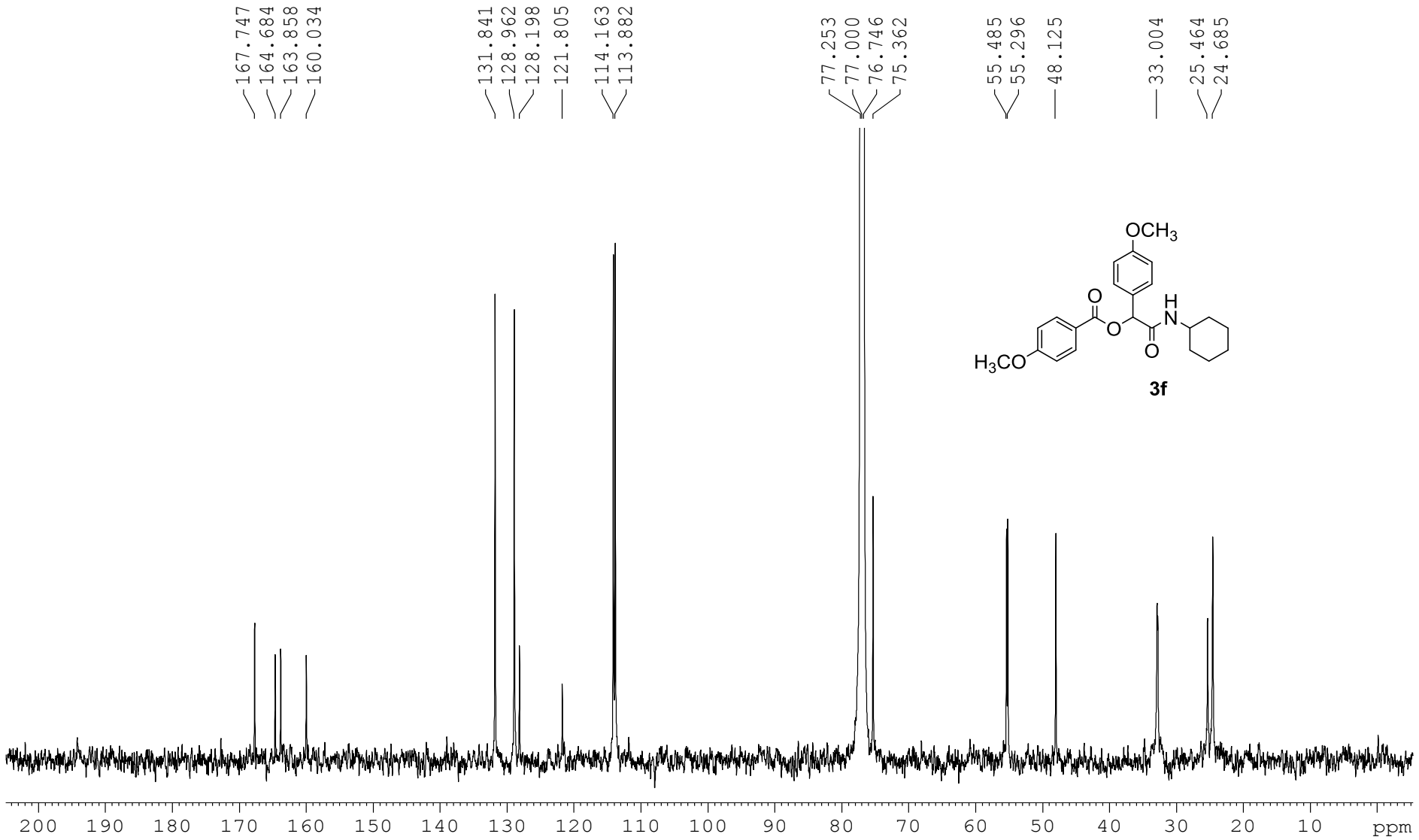
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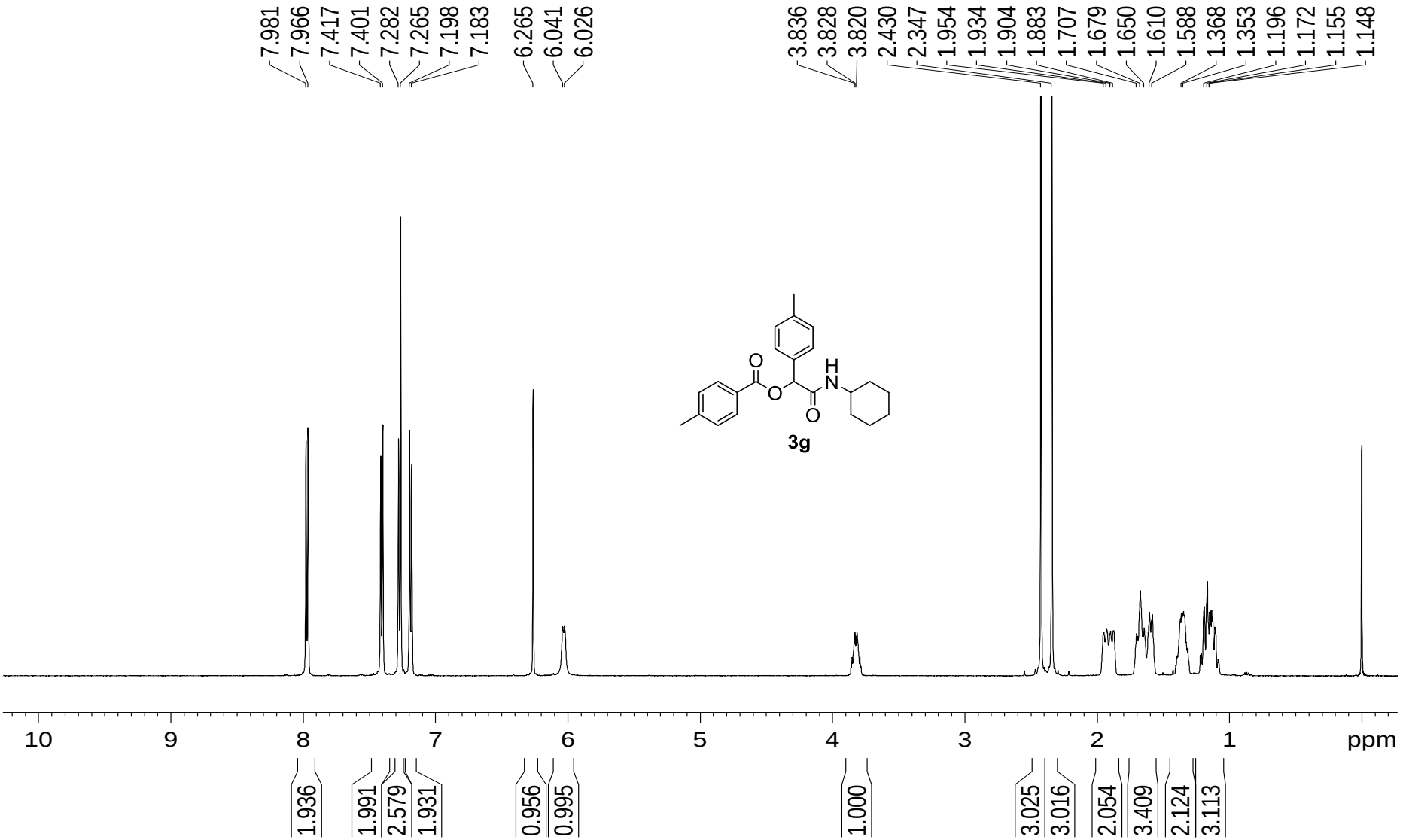
164.684
163.858
160.034
131.841
128.962
128.198
121.805
114.163
113.882
77.253
77.000
76.746
75.362
55.485
55.296
48.125
33.004
25.464
24.685
OCH3
H3CO
O
O
O
H
N
3f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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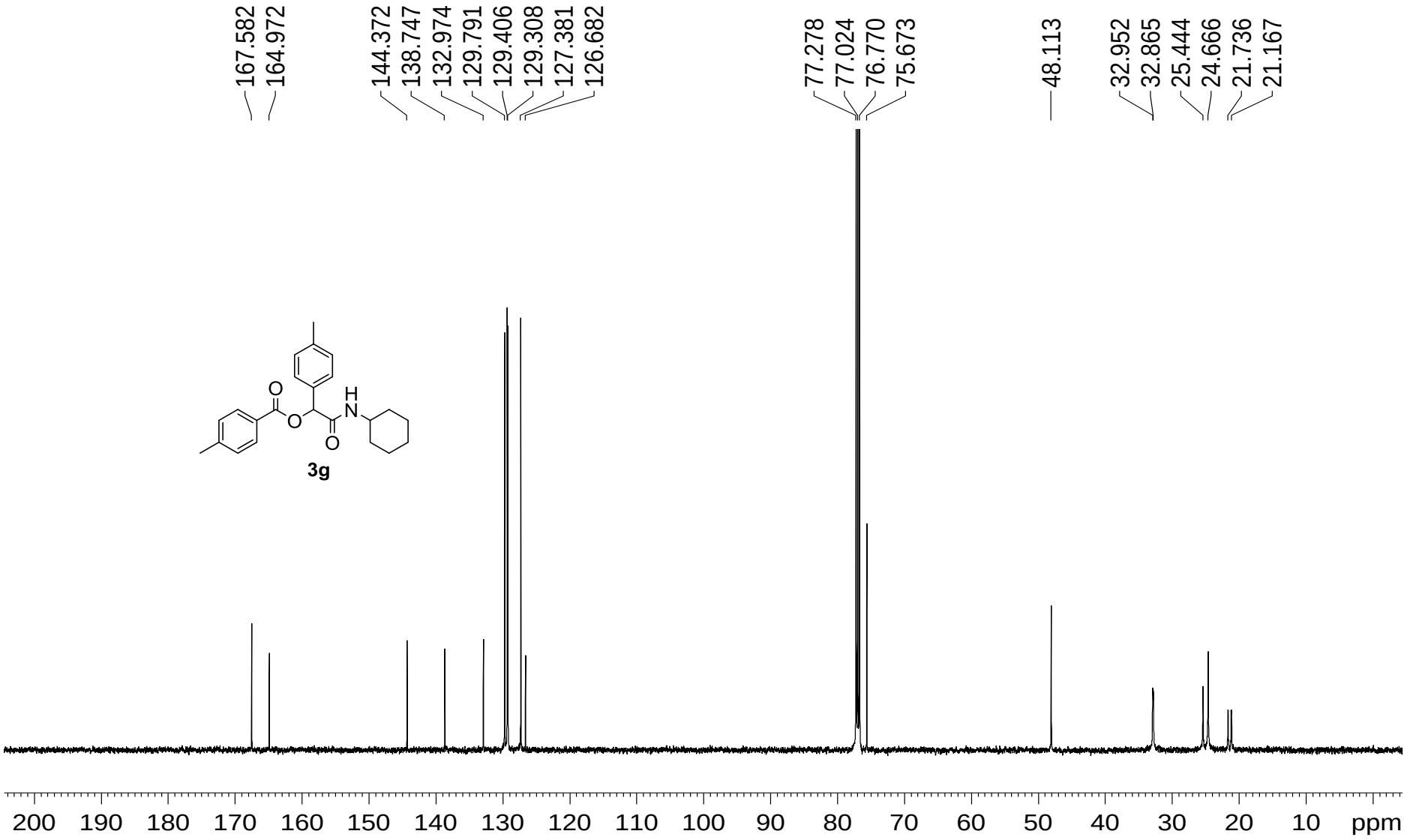
7.966
7.417
7.401
7.282
7.265
7.198
7.183
6.265
6.041
6.026
3.836
3.828
3.820
2.430
2.347
1.954
1.934
1.904
1.883
1.707
1.679
1.650
1.610
1.588
1.368
1.353
1.196
1.172
1.155
1.148
3g
10
9
8
7
6
5
4
3
2
1
ppm
1.936
1.991
2.579
1.931
0.956
0.995
1.000
3.025
3.016
2.054
3.409
2.124
3.113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138.747
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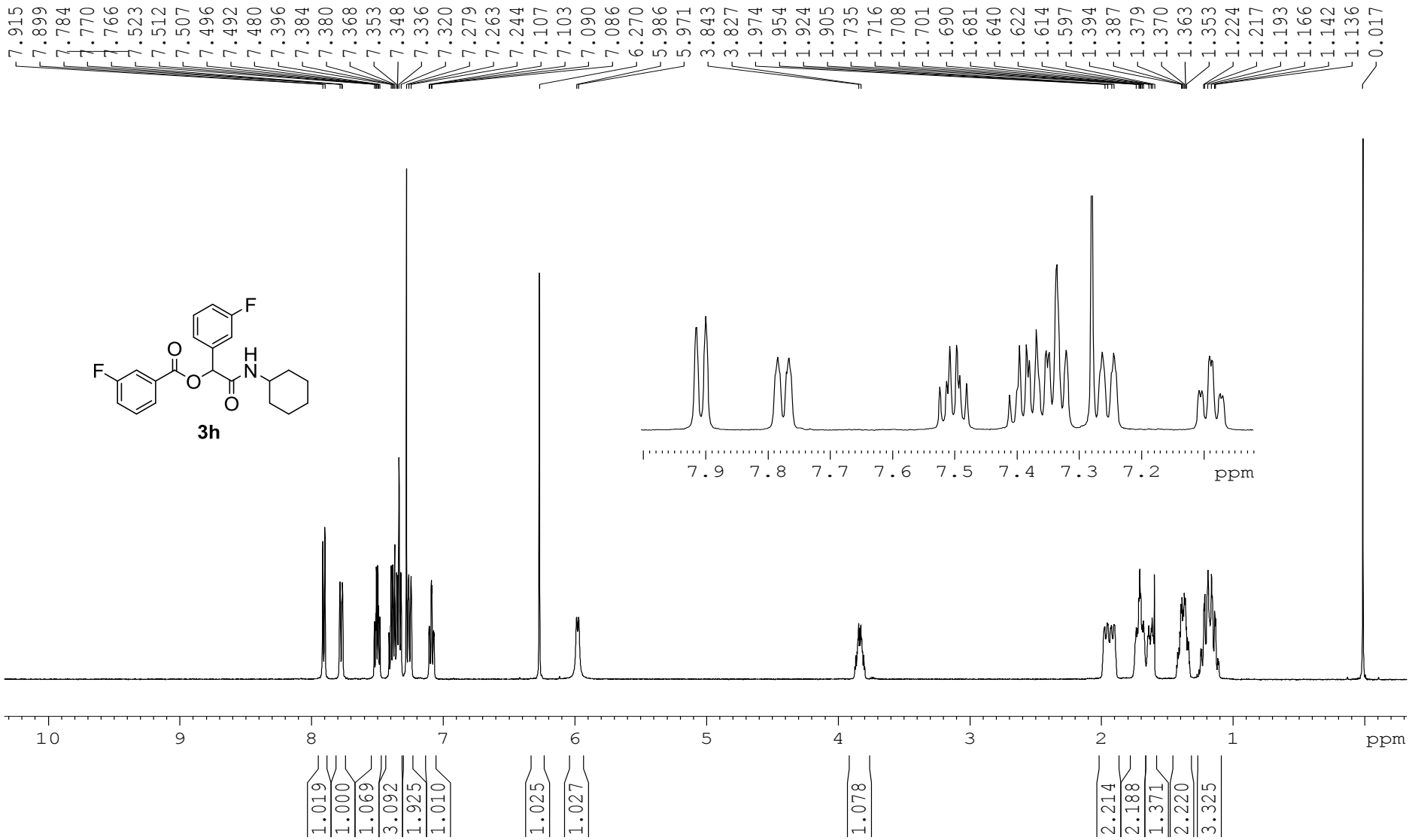
126.682
77.278
77.024
76.770
75.673
48.113
32.952
32.865
25.444
24.666
21.736
21.167
O
O
H
N
O
3g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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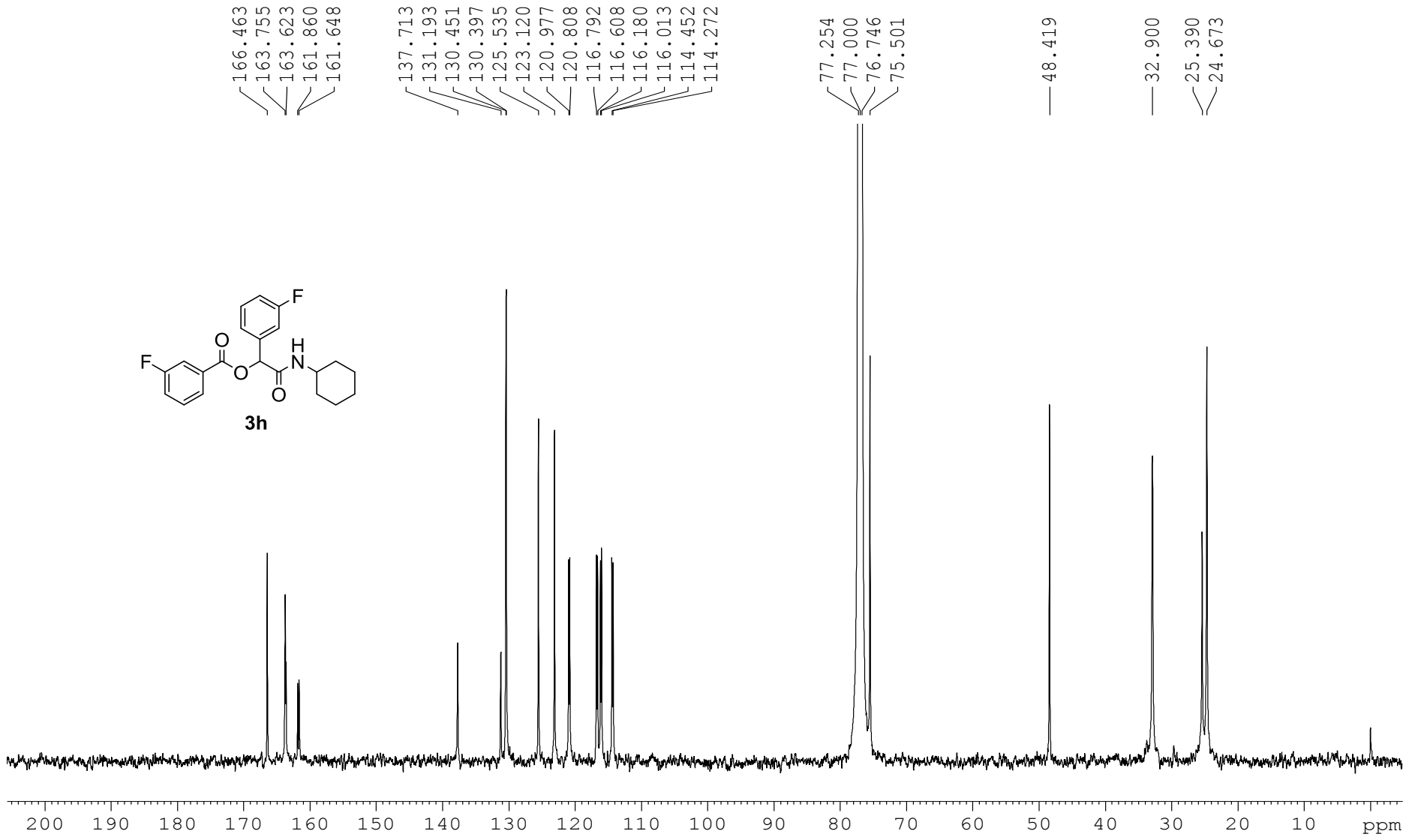
7.899
7.784
7.770
7.766
7.523
7.512
7.507
7.496
7.492
7.480
7.396
7.384
7.380
7.368
7.353
7.348
7.336
7.320
7.279
7.263
7.244
7.107
7.103
7.090
7.086
6.270
5.986
5.971
3.843
3.827
1.974
1.954
1.924
1.905
1.735
1.716
1.708
1.701
1.690
1.681
1.640
1.622
1.614
1.597
1.394
1.387
1.379
1.370
1.363
1.353
1.224
1.217
1.193
1.166
1.142
1.136
0.017
F
O
O
H
N
F
O
3h
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 ppm
10 9 8 7 6 5 4 3 2 1 ppm
1.019
1.000
1.069
3.092
1.925
1.010
1.025
1.027
1.078
2.214
2.188
1.371
2.220
3.325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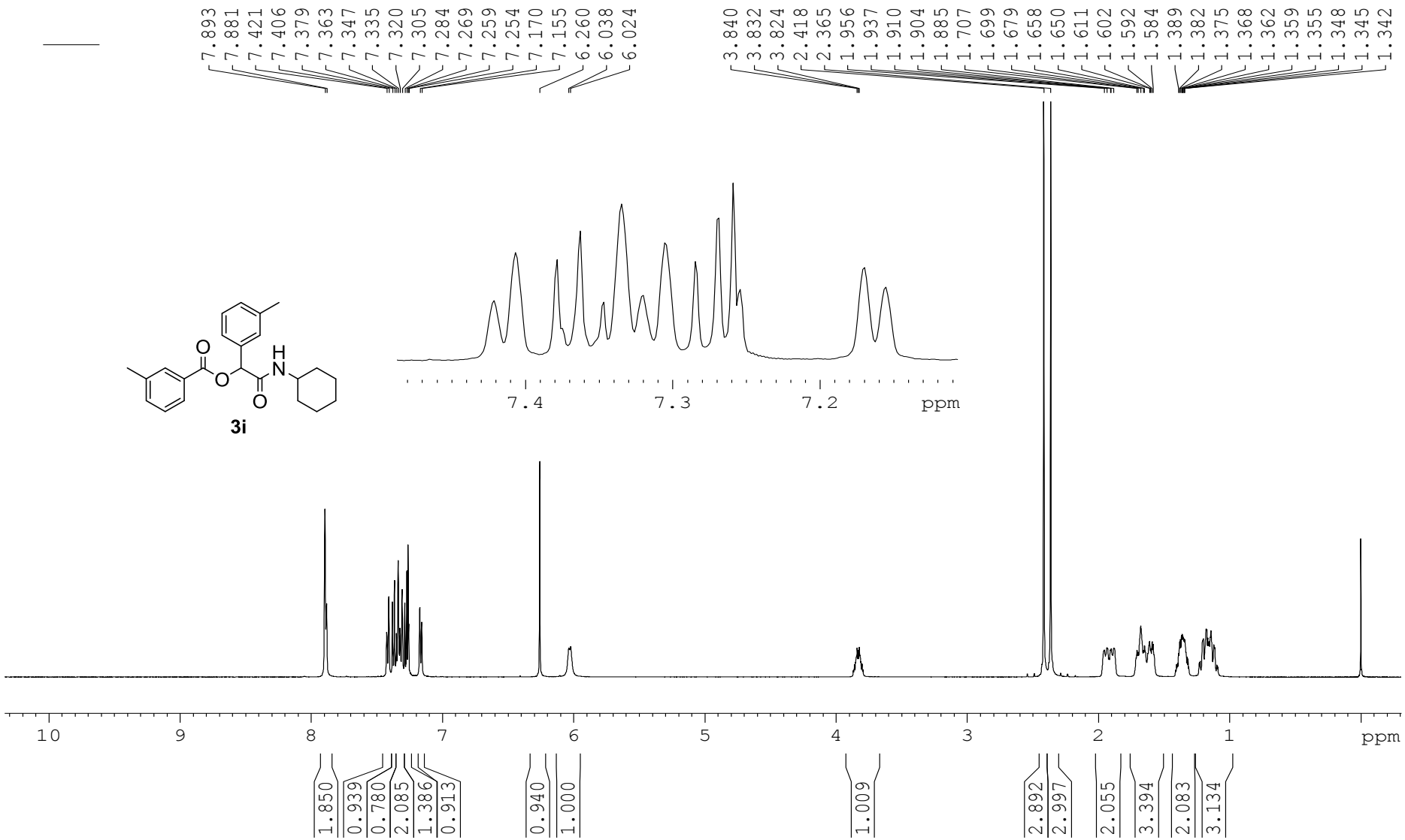
163.755
163.623
161.860
161.648
137.713
131.193
130.451
130.397
125.535
123.120
120.977
120.808
116.792
116.608
116.180
116.013
114.452
114.272
77.254
77.000
76.746
75.501
48.419
32.900
25.390
24.673
F
O
H
N
F
O
O
3h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.421
7.406
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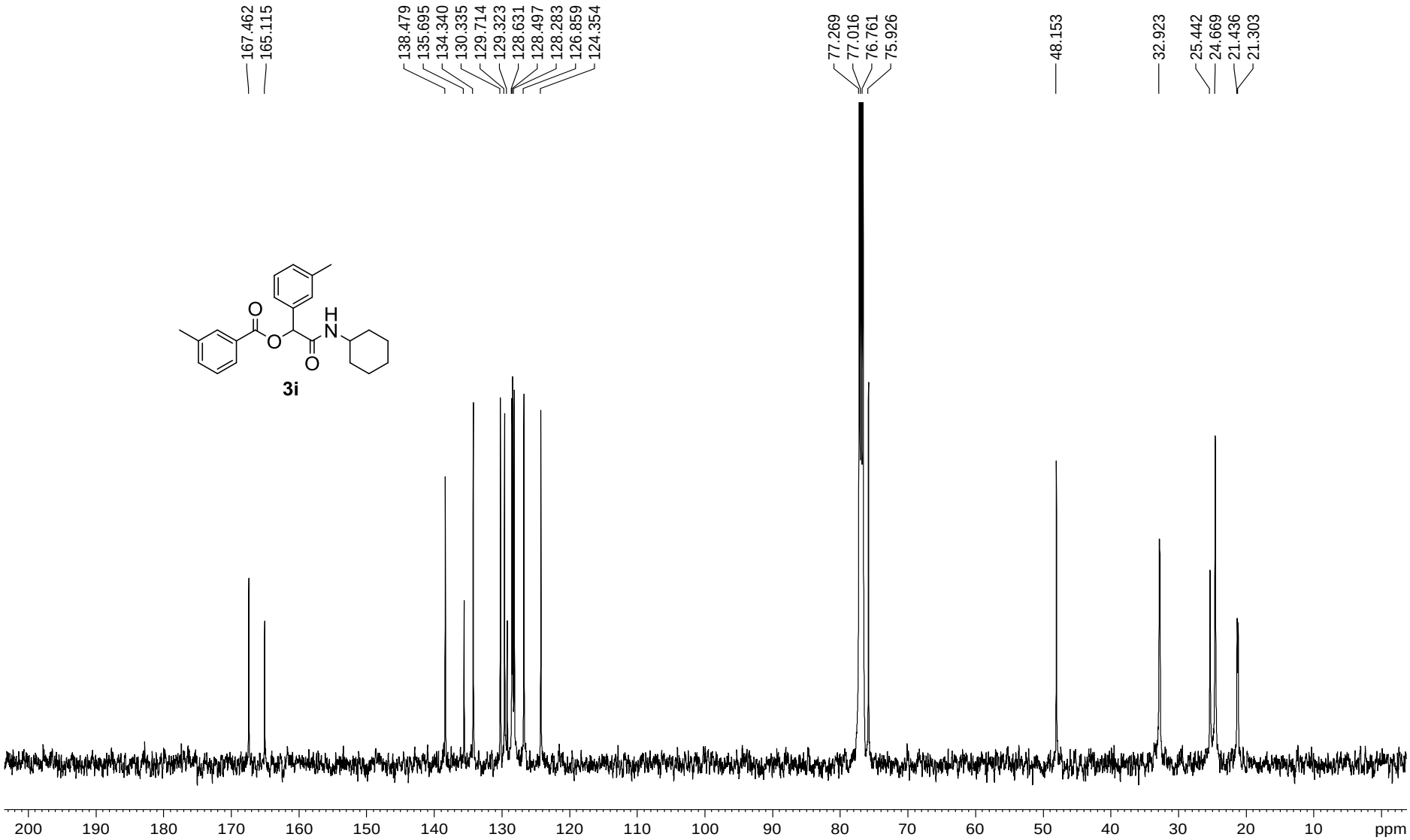
7.347
7.335
7.320
7.305
7.284
7.269
7.259
7.254
7.170
7.155
6.260
6.038
6.024
3.840
3.832
3.824
2.418
2.365
1.956
1.937
1.910
1.904
1.885
1.707
1.699
1.679
1.658
1.650
1.611
1.602
1.592
1.584
1.389
1.382
1.375
1.368
1.362
1.359
1.355
1.348
1.345
1.342
7.4
7.3
7.2
ppm
3i
10
9
8
7
6
5
4
3
2
1
ppm
1.850
0.939
0.780
2.085
1.386
0.913
0.940
1.000
1.009
2.892
2.997
2.055
3.394
2.083
3.134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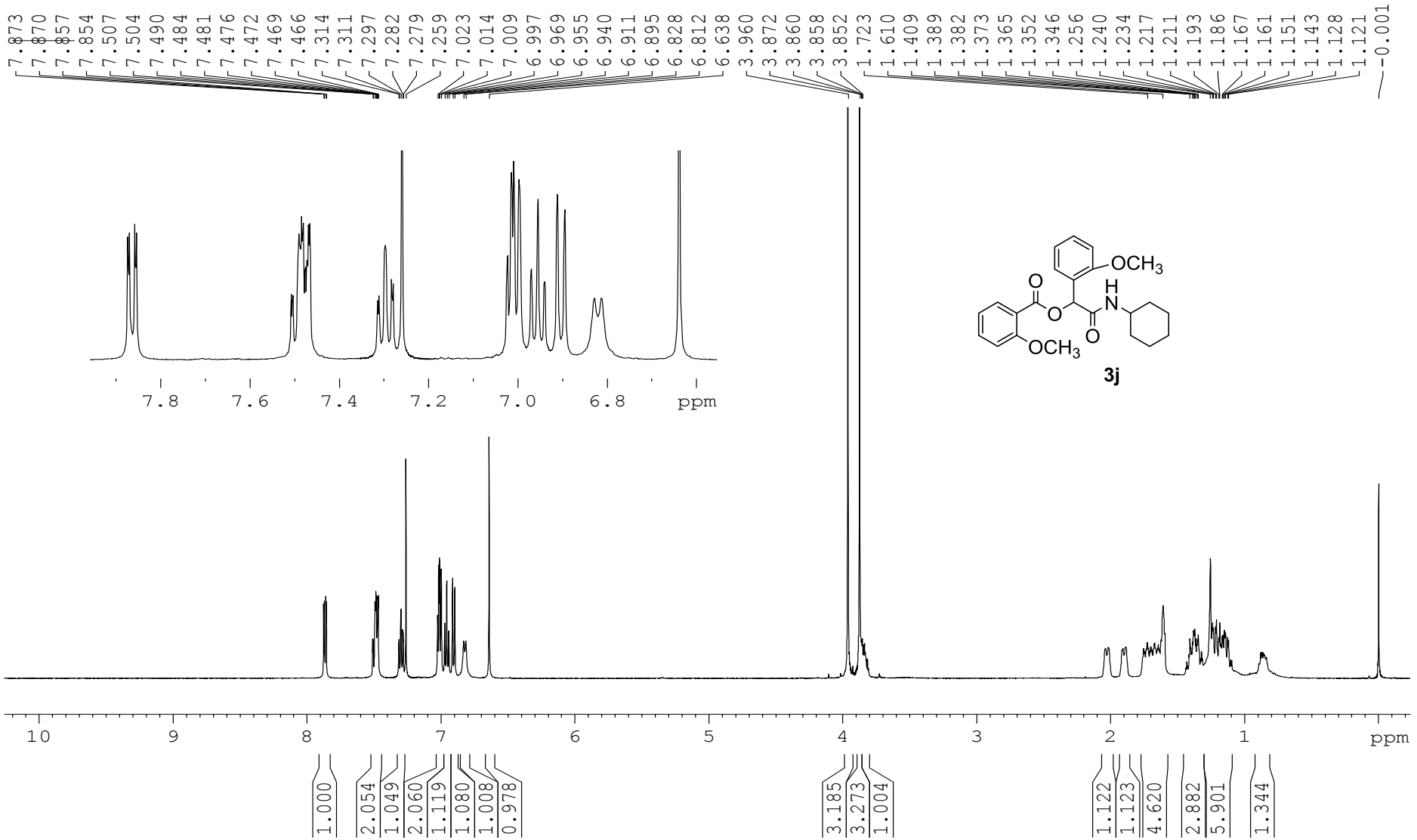
138.479
135.695
134.340
130.335
129.714
129.323
128.631
128.497
128.283
126.859
124.354
77.269
77.016
76.761
75.926
48.153
32.923
25.442
24.669
21.436
21.303
O
O
O
H
N
3i
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.854
7.507
7.504
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7.484
7.481
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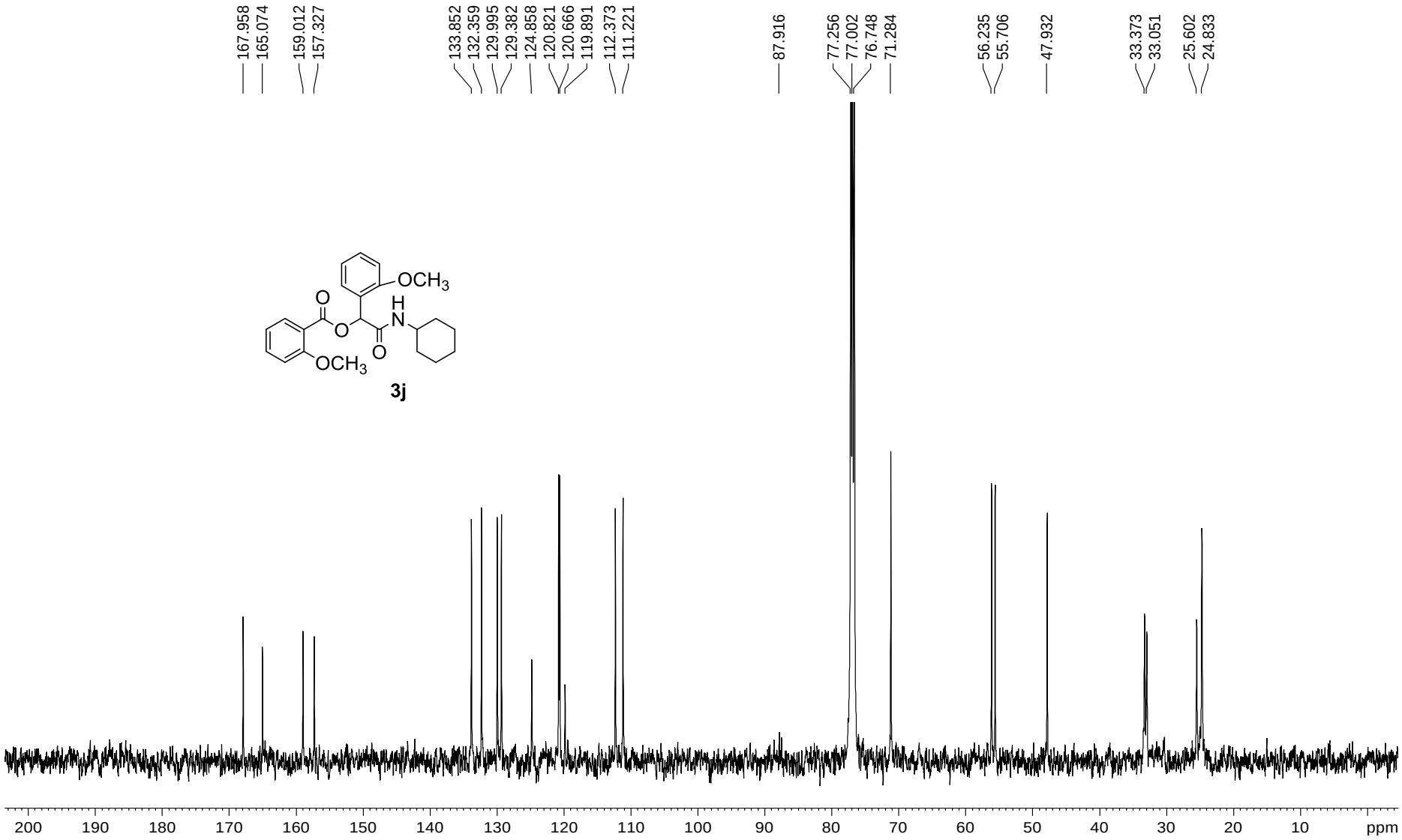
7.472
7.469
7.466
7.314
7.311
7.297
7.282
7.279
7.259
7.023
7.014
7.009
6.997
6.969
6.955
6.940
6.911
6.895
6.828
6.812
6.638
3.960
3.872
3.860
3.858
3.852
1.723
1.610
1.409
1.389
1.382
1.373
1.365
1.352
1.346
1.256
1.240
1.234
1.217
1.211
1.193
1.186
1.167
1.161
1.151
1.143
1.128
1.121
-0.001
7.8
7.6
7.4
7.2
7.0
6.8
ppm
OCH3
OCH3
O
O
O
H
N
10
9
8
7
6
5
4
3
2
1
ppm
1.000
2.054
1.049
2.060
1.119
1.080
1.008
0.978
3.185
3.273
1.004
1.122
1.123
4.620
2.882
5.901
1.344

3j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157.327
133.852
132.359
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129.382
124.858
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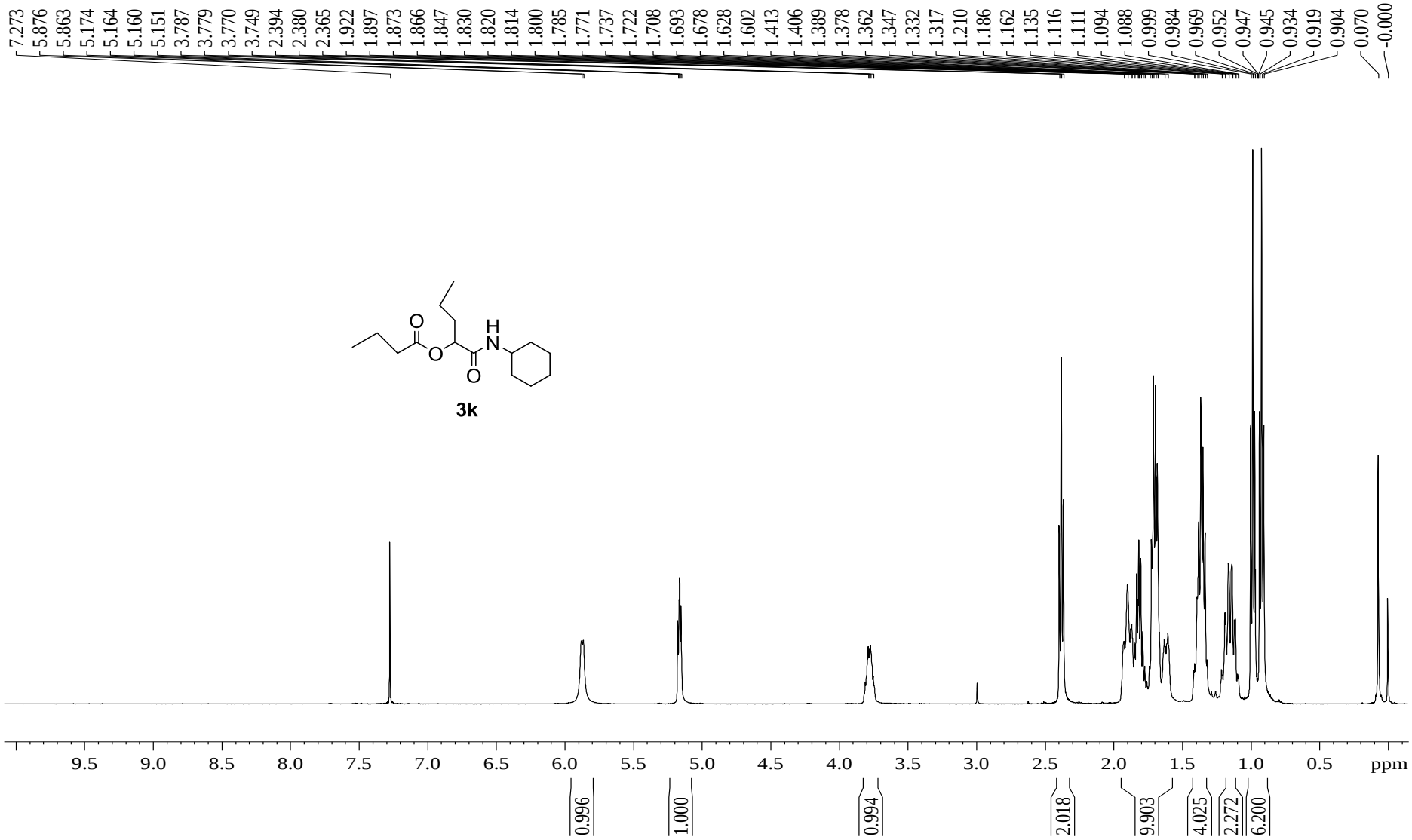
120.666
119.891
112.373
111.221
87.916
77.256
77.002
76.748
71.284
56.235
55.706
47.932
33.373
33.051
25.602
24.833
OCH3
O
H
N
O
O
OCH3
3j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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5.863
5.174
5.164
5.160
5.151
3.787
3.779
3.770
3.749
2.394
2.380
2.365
1.922
1.897
1.873
1.866
1.847
1.830
1.820
1.814
1.800
1.785
1.771
1.737
1.722
1.708
1.693
1.678
1.628
1.602
1.413
1.406
1.389
1.378
1.362
1.347
1.332
1.317
1.210
1.186
1.162
1.135
1.116
1.111
1.094
1.088
0.999
0.984
0.969
0.952
0.947
0.945
0.934
0.919
0.904
0.070
-0.000
O
O
O
H
N
3k
9.5
9.0
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
ppm
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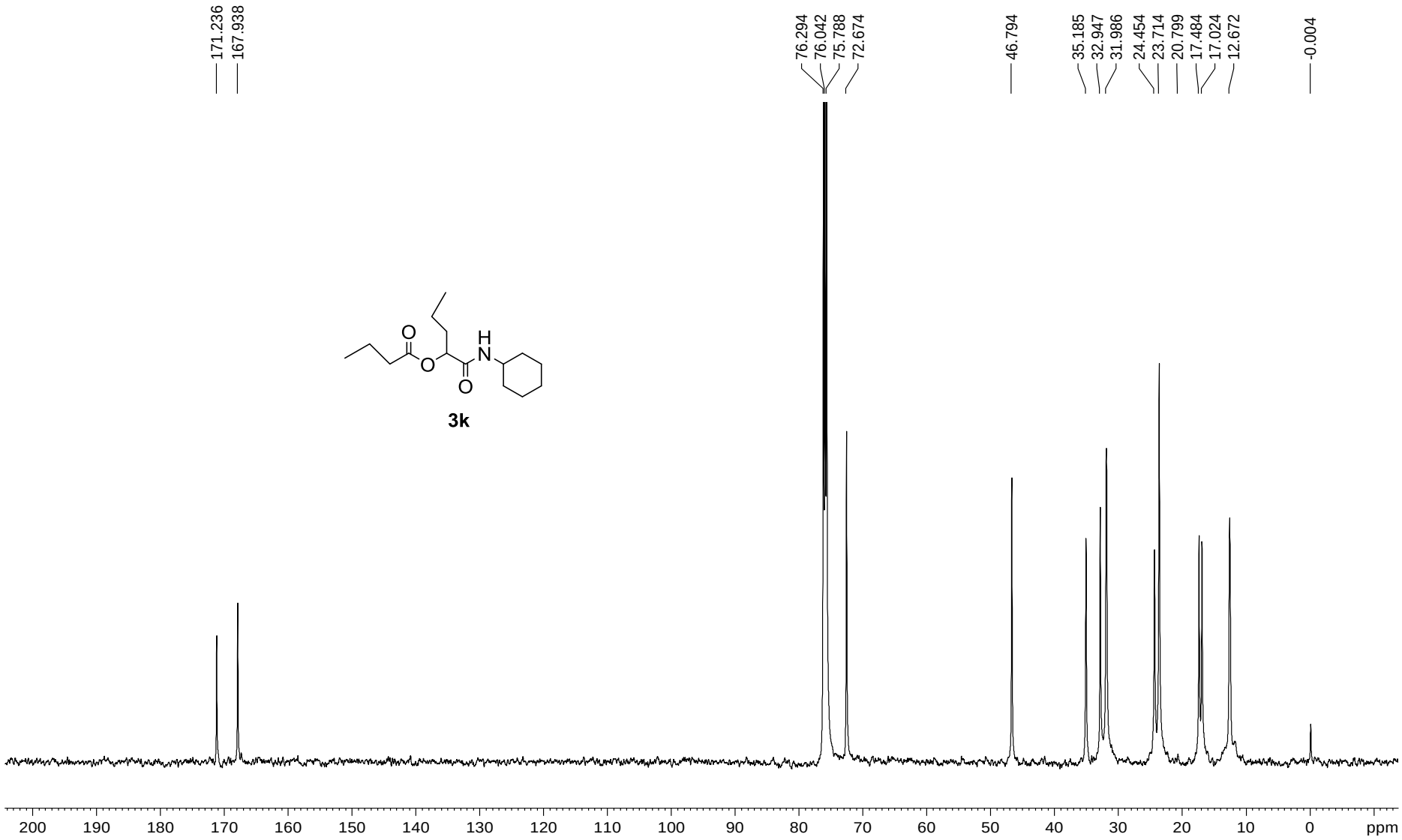
2.272
6.200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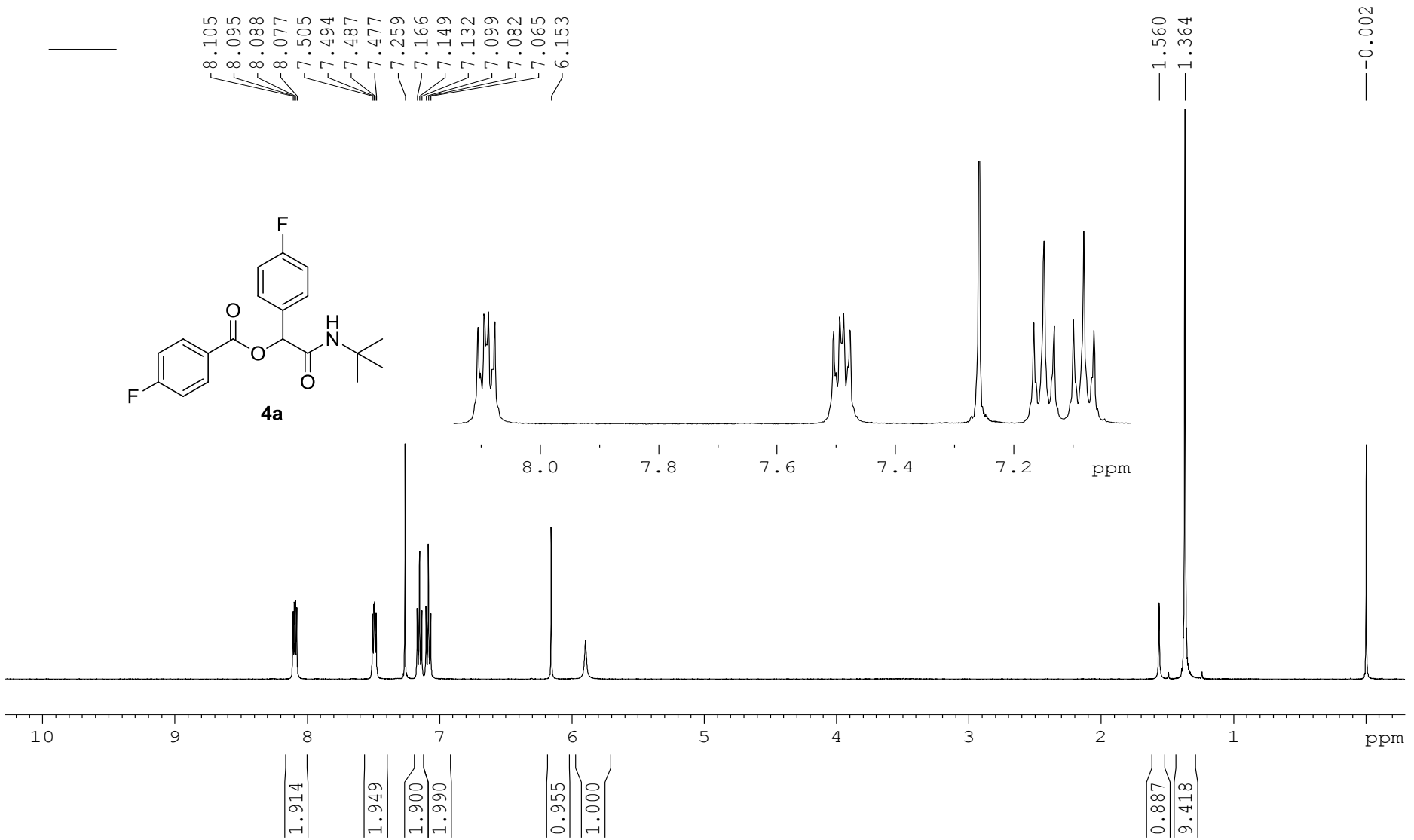
167.938
76.294
76.042
75.788
72.674
46.794
35.185
32.947
31.986
24.454
23.714
20.799
17.484
17.024
12.672
-0.004
O
O
H
N
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

3k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8.088
8.077
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7.494
7.487
7.477
7.259
7.166
7.149
7.132
7.099
7.082
7.065
6.153
1.560
1.364
-0.002
F
O
O
H
N
O
F
4a
8.0
7.8
7.6
7.4
7.2
ppm
10
9
8
7
6
5
4
3
2
1
ppm
1.914
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1.990
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1.000
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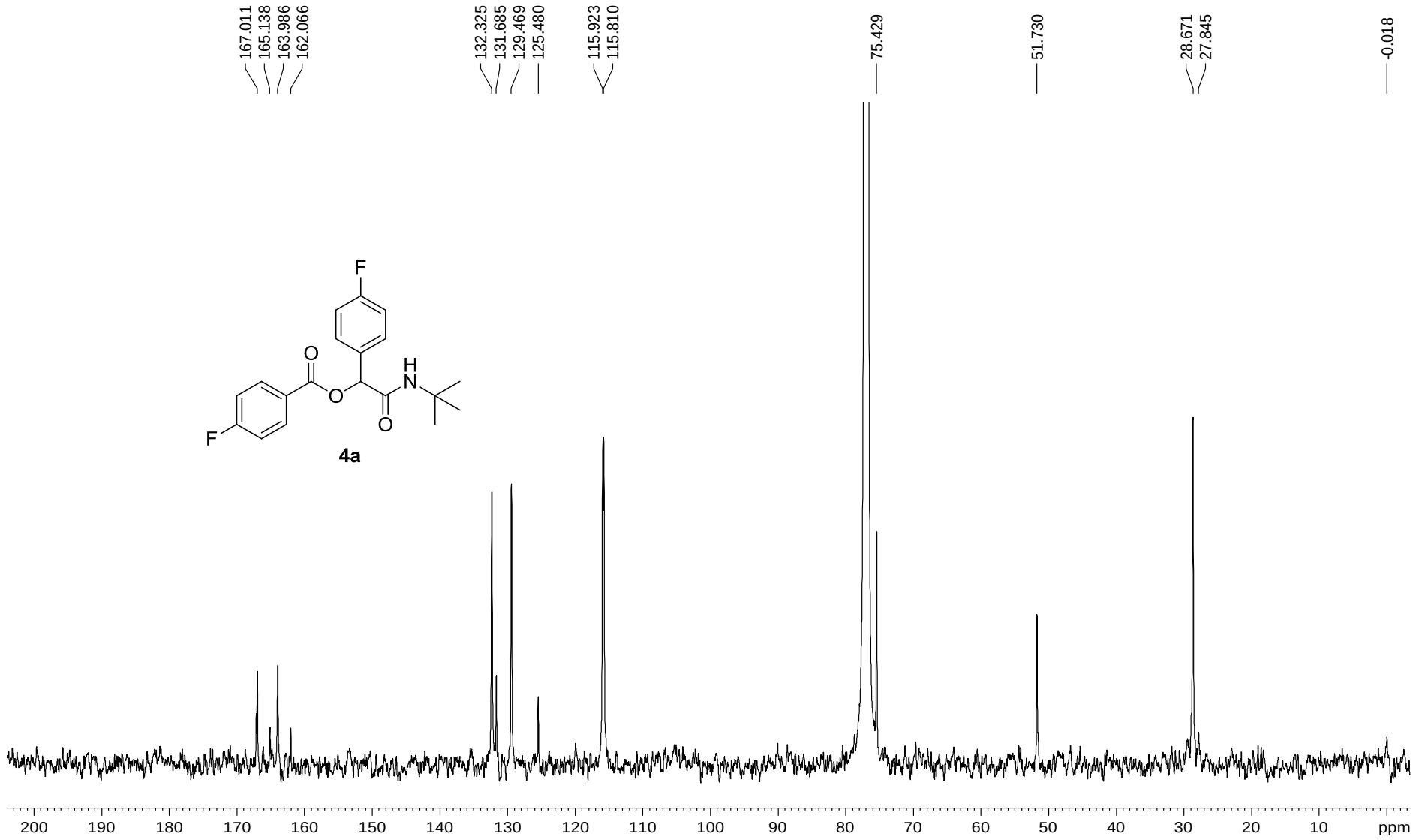
9.418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115.810
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51.730
28.671
27.845
-0.018
F
O
O
H
N
O
F
4a
200
190
180
170
160
150
140
130
120
110
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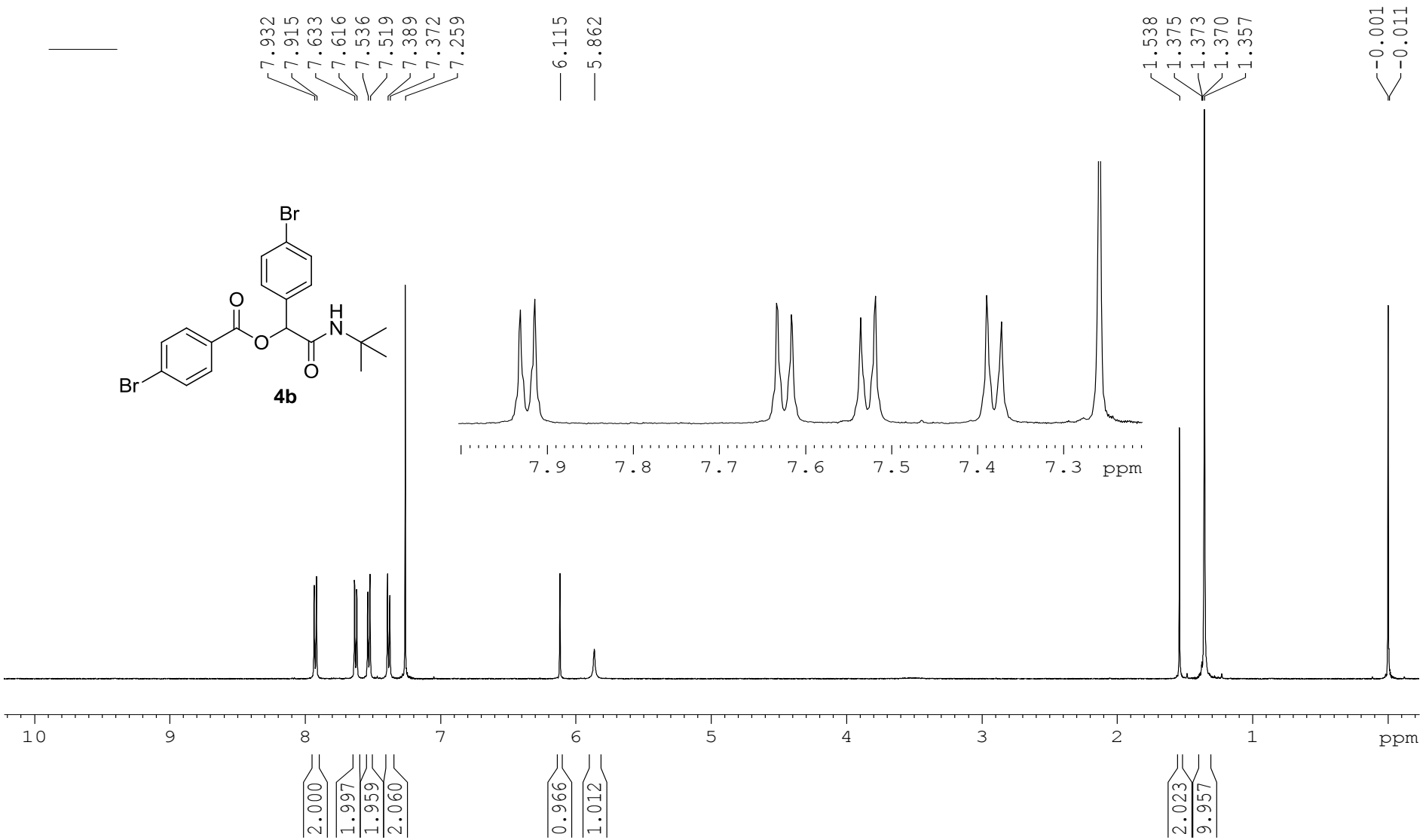
90
80
70
60
50
40
30
20
10
ppm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7.389
7.372
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1.538
1.375
1.373
1.370
1.357
-0.001
-0.011
Br
O
O
H
N
O
Br
4b
7.9
7.8
7.7
7.6
7.5
7.4
7.3
ppm
10
9
8
7
6
5
4
3
2
1
ppm
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0.966
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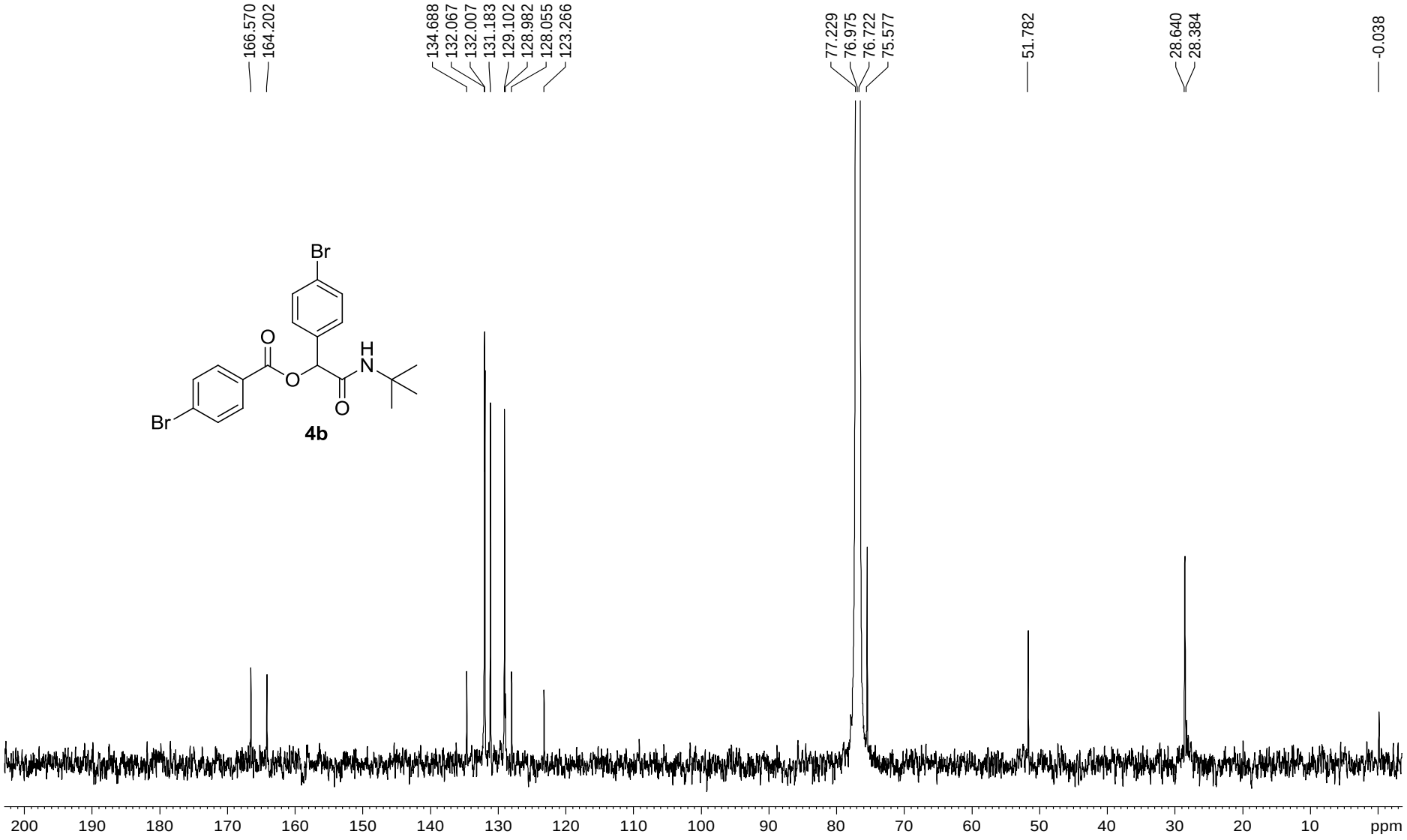
9.957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132.007
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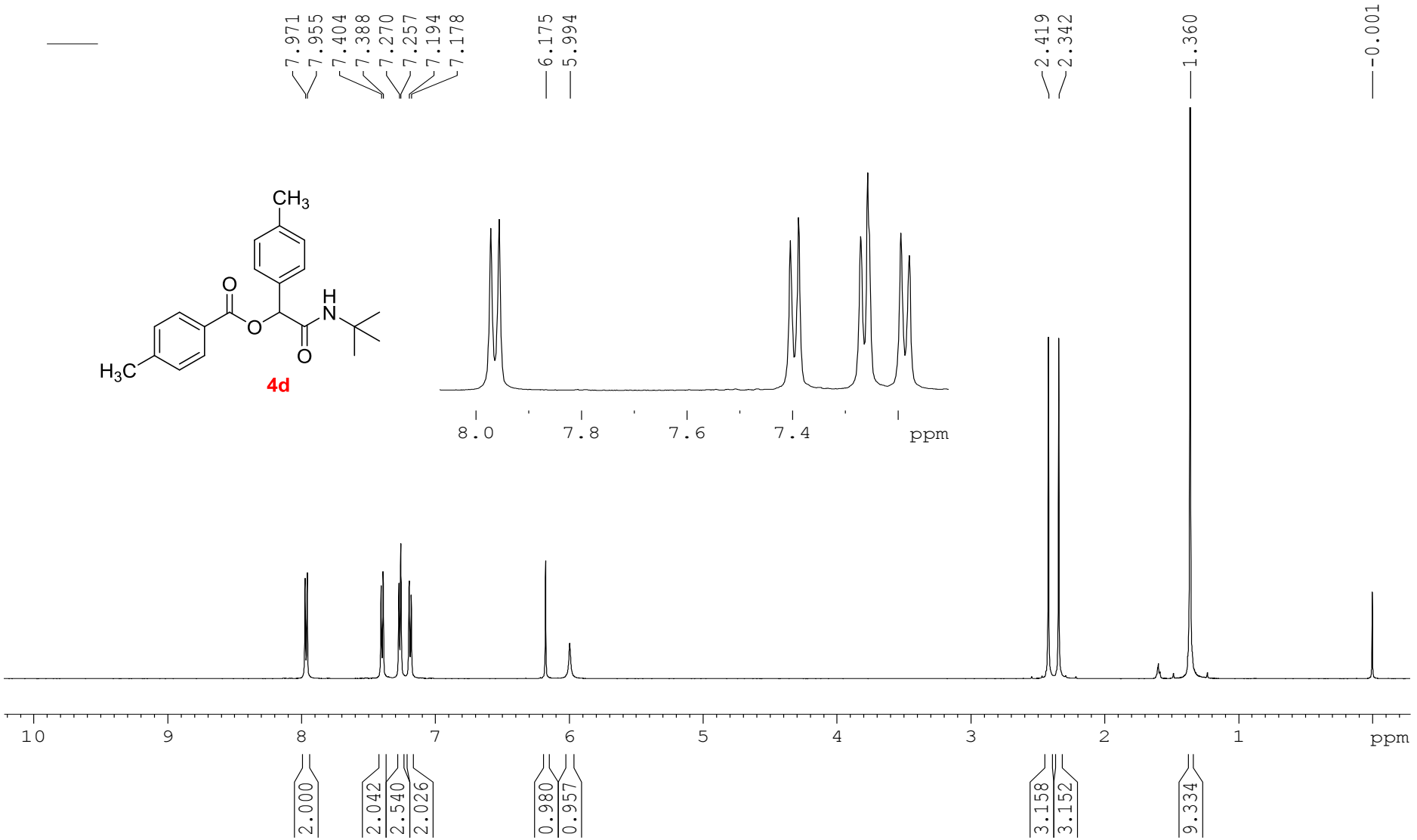
129.102
128.982
128.055
123.266
77.229
76.975
76.722
75.577
51.782
28.640
28.384
-0.038
Br
O
O
H
N
O
Br
4b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.194
7.178
6.175
5.994
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2.342
1.360
0.001
CH3
O
O
H
N
O
H3C
4d
8.0
7.8
7.6
7.4
ppm
10
9
8
7
6
5
4
3
2
1
ppm
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0.957
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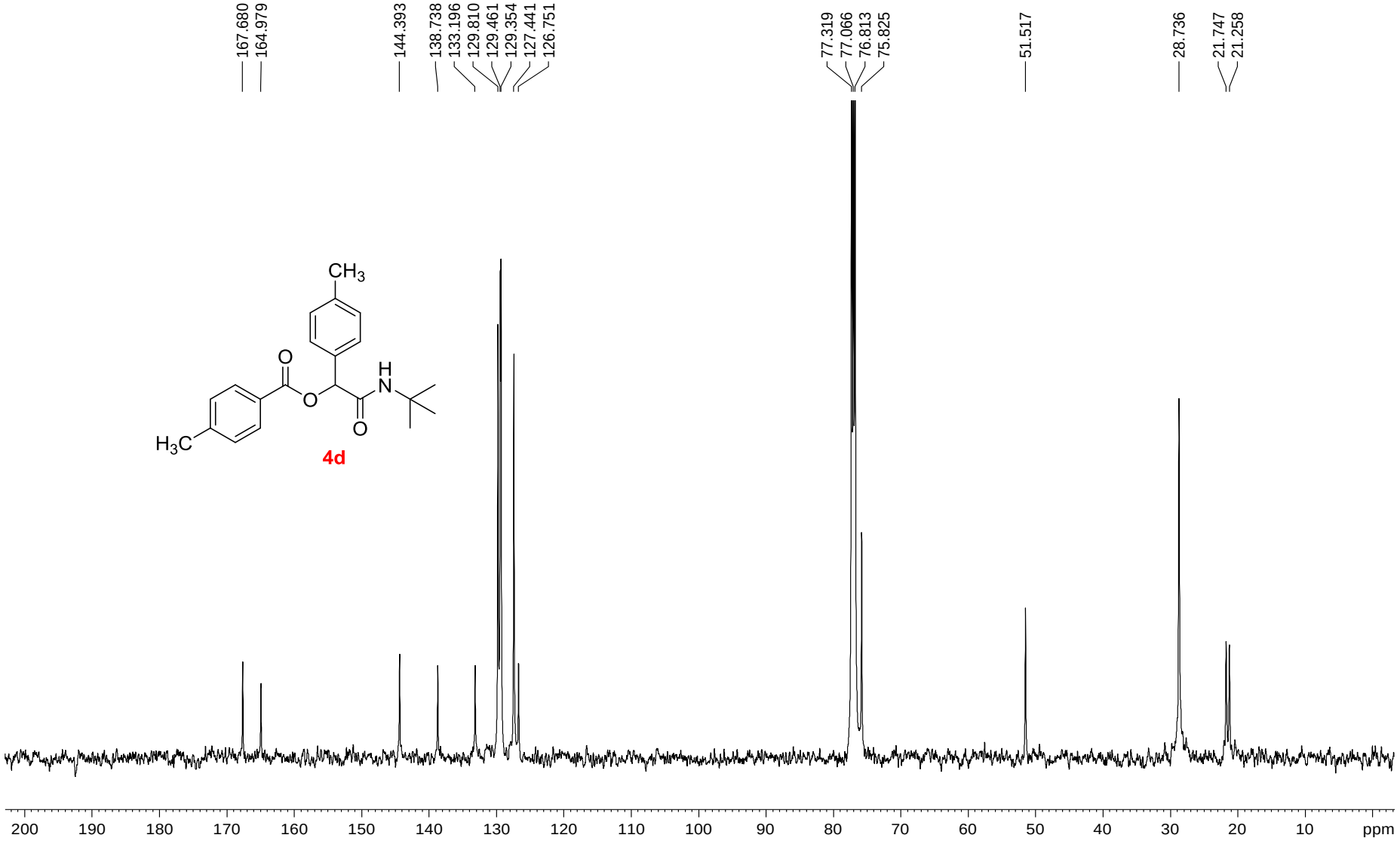
9.334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129.354
127.441
126.751
77.319
77.066
76.813
75.825
51.517
28.736
21.747
21.258
CH3
O
O
H
N
O
H3C
4d
200
190
180
170
160
150
140
130
120
110
100
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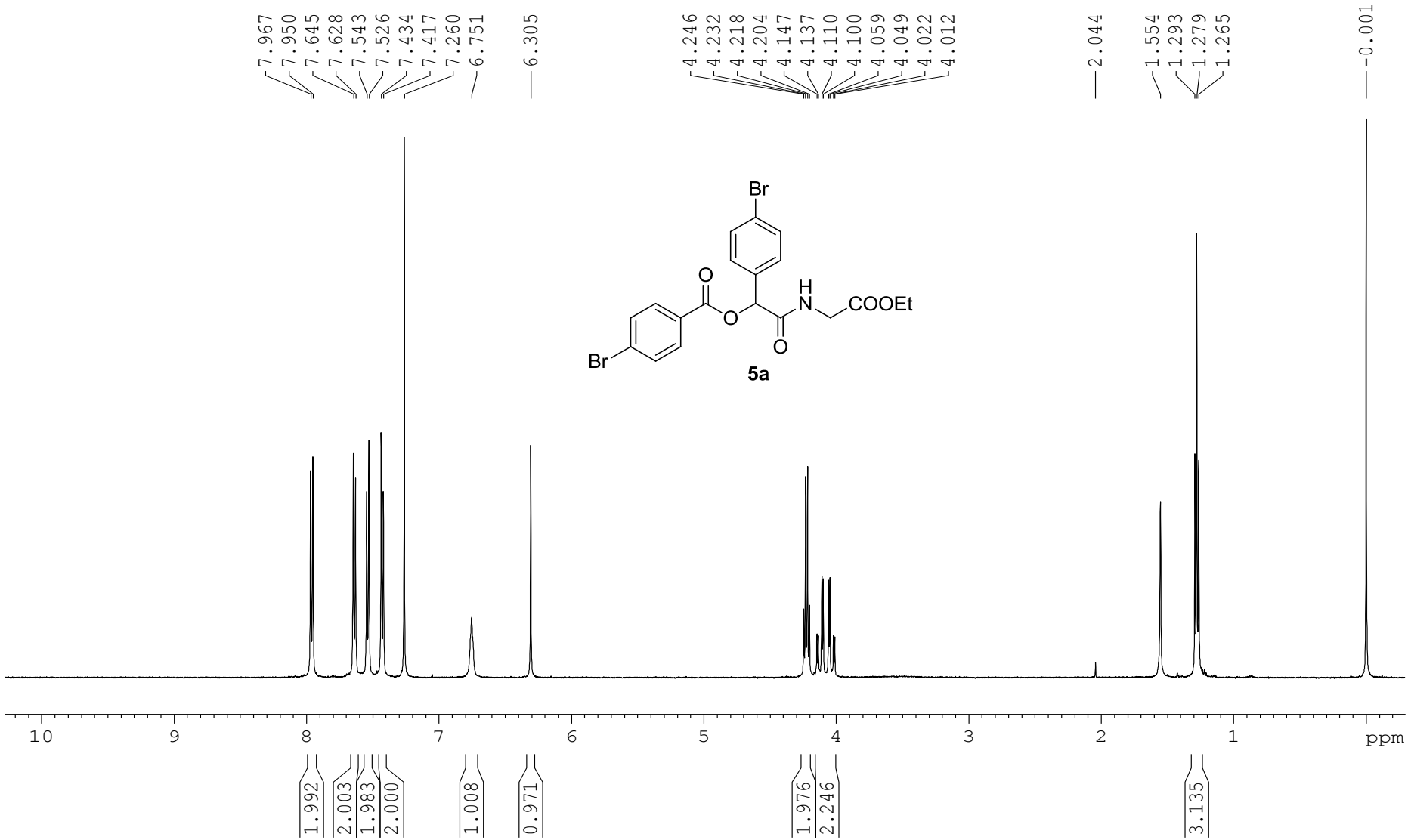
80
70
60
50
40
30
20
10
ppm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7.628
7.543
7.526
7.434
7.417
7.260
6.751
6.305
4.246
4.232
4.218
4.204
4.147
4.137
4.110
4.100
4.059
4.049
4.022
4.012
2.044
1.554
1.293
1.279
1.265
0.001
Br
O
O
H
N
COOEt
O
Br
5a
10
9
8
7
6
5
4
3
2
1
ppm
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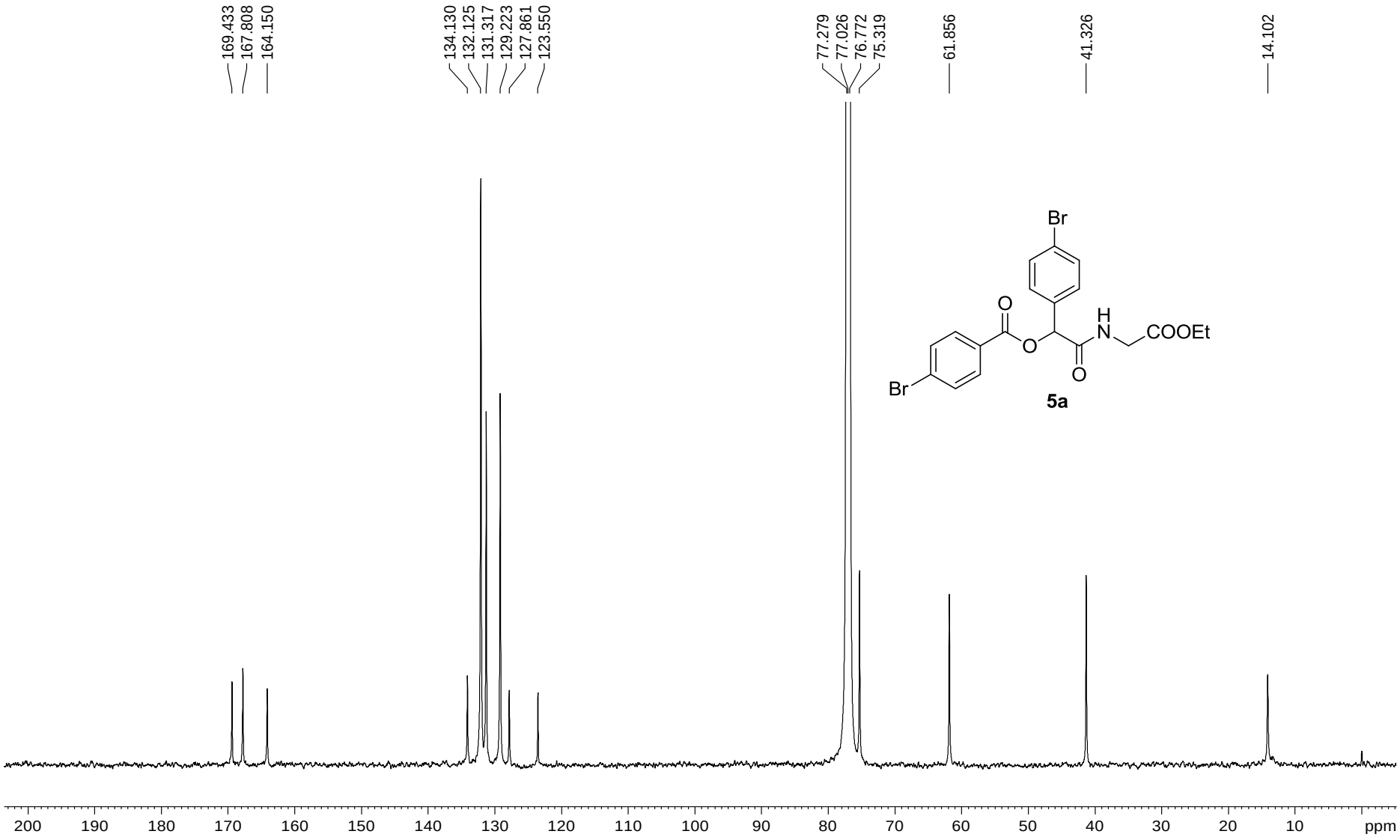
3.135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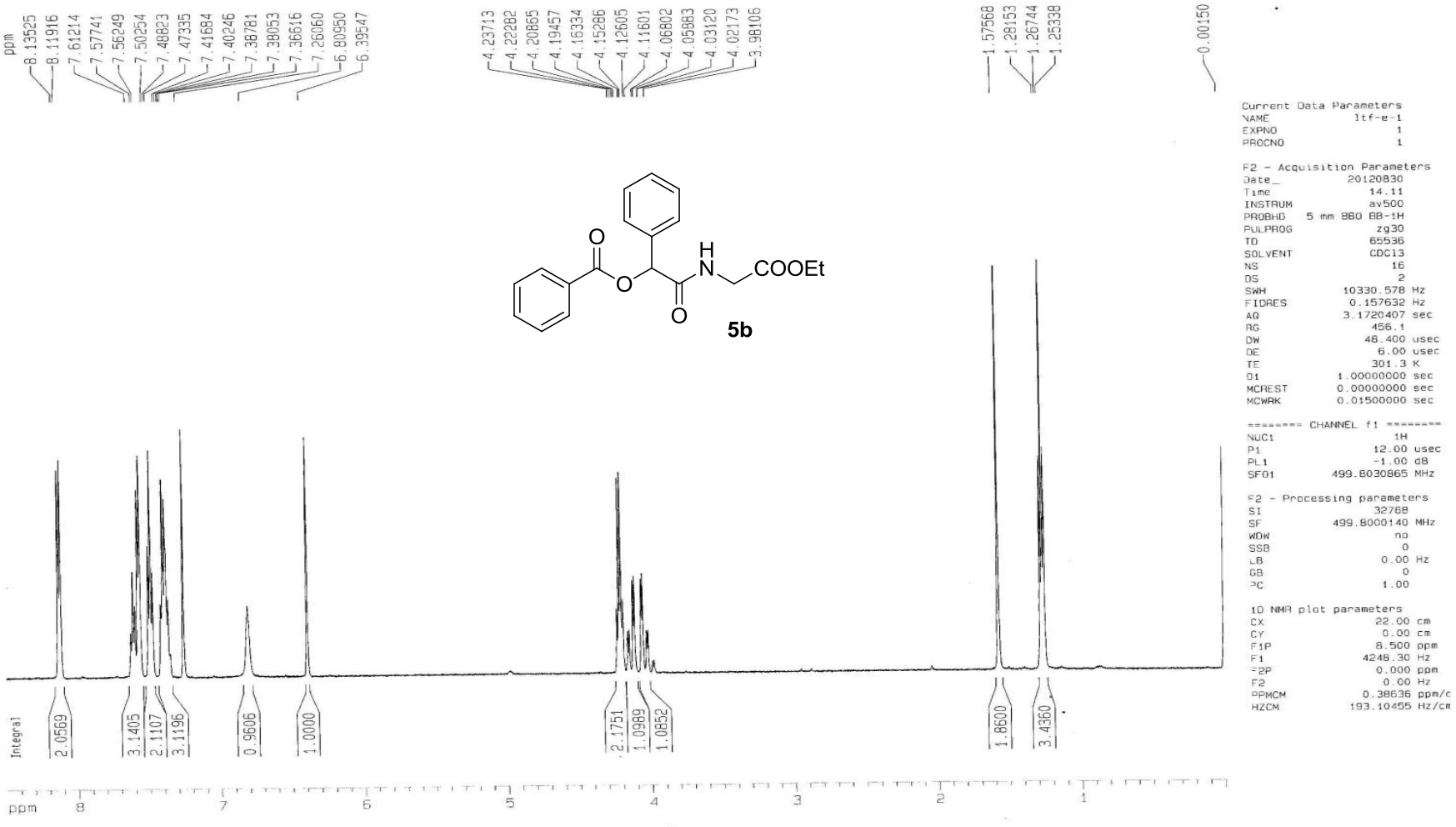
131.317
129.223
127.861
123.550
77.279
77.026
76.772
75.319
61.856
41.326
14.102
Br
O
O
H
N
COOEt
O
Br
5a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



Current Data Parameters

NAME	ltf-e-1
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20120830
Time	14.11
INSTRUM	av500
PROBHD	5 mm BBO BB-1H
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1720407 sec
RG	456.1
DW	48.400 usec
DE	6.00 usec
TE	301.3 K
D1	1.00000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

======== CHANNEL f1 ========

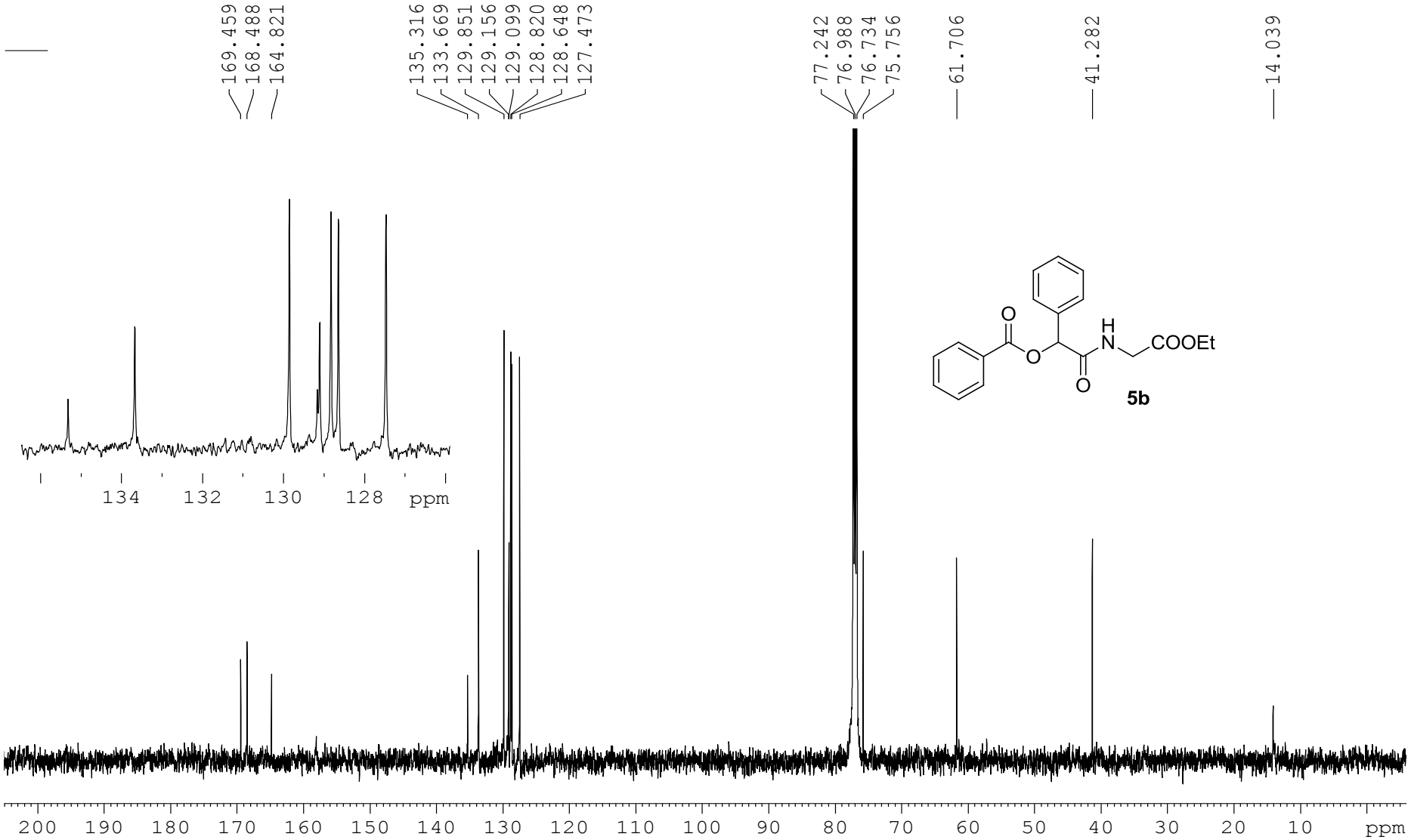
NUC1	1H
P1	12.00 usec
PL1	-1.00 dB
SFO1	499.8030865 MHz

F2 - Processing parameters

SI	32768
SF	499.8000140 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	22.00 cm
CY	0.00 cm
F1P	8.500 ppm
F1	4248.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.38636 ppm/c
HZCM	193.10455 Hz/cm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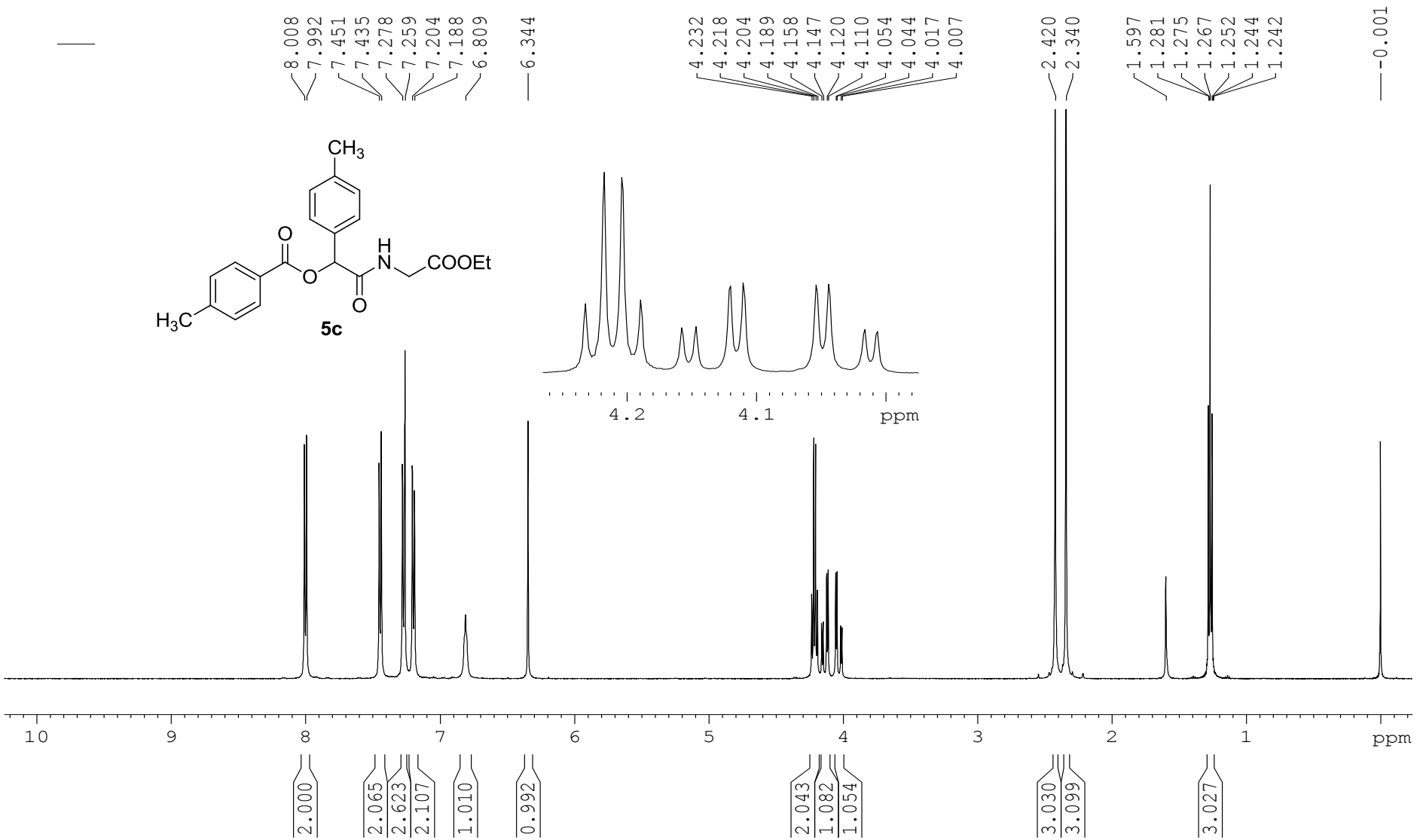
168.488
164.821
135.316
133.669
129.851
129.156
129.099
128.820
128.648
127.473
77.242
76.988
76.734
75.756
61.706
41.282
14.039
134
132
130
128
ppm
O
O
H
N
COOEt
O
5b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.451
7.435
7.278
7.259
7.204
7.188
6.809
6.344
4.232
4.218
4.204
4.189
4.158
4.147
4.120
4.110
4.054
4.044
4.017
4.007
2.420
2.340
1.597
1.281
1.275
1.267
1.252
1.244
1.242
0.001
CH3
O
O
H
N
COOEt
O
H3C
5c
4.2
4.1
ppm
10
9
8
7
6
5
4
3
2
1
ppm
2.000
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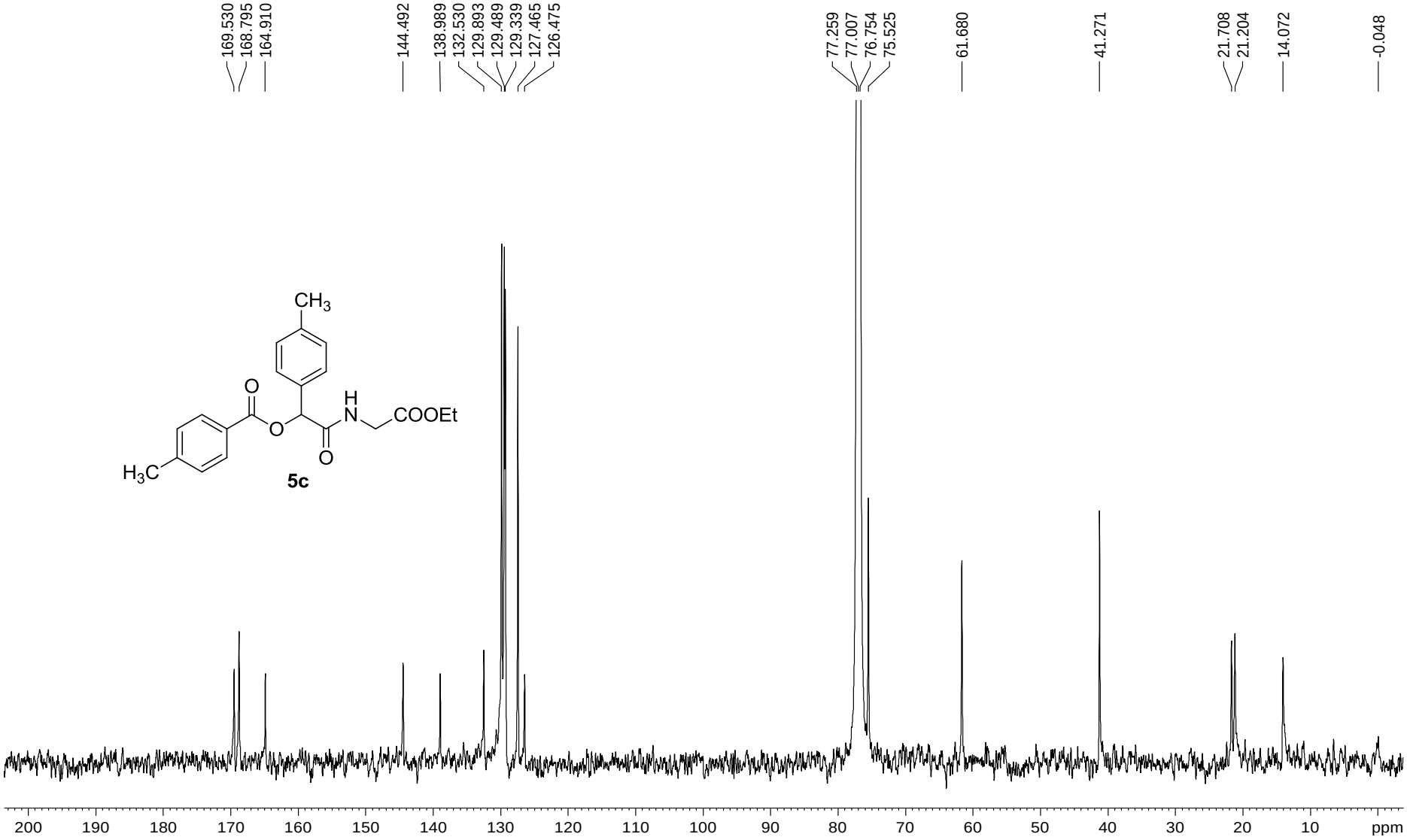
2.623
2.107
1.010
0.992
2.043
1.082
1.054
3.030
3.099
3.027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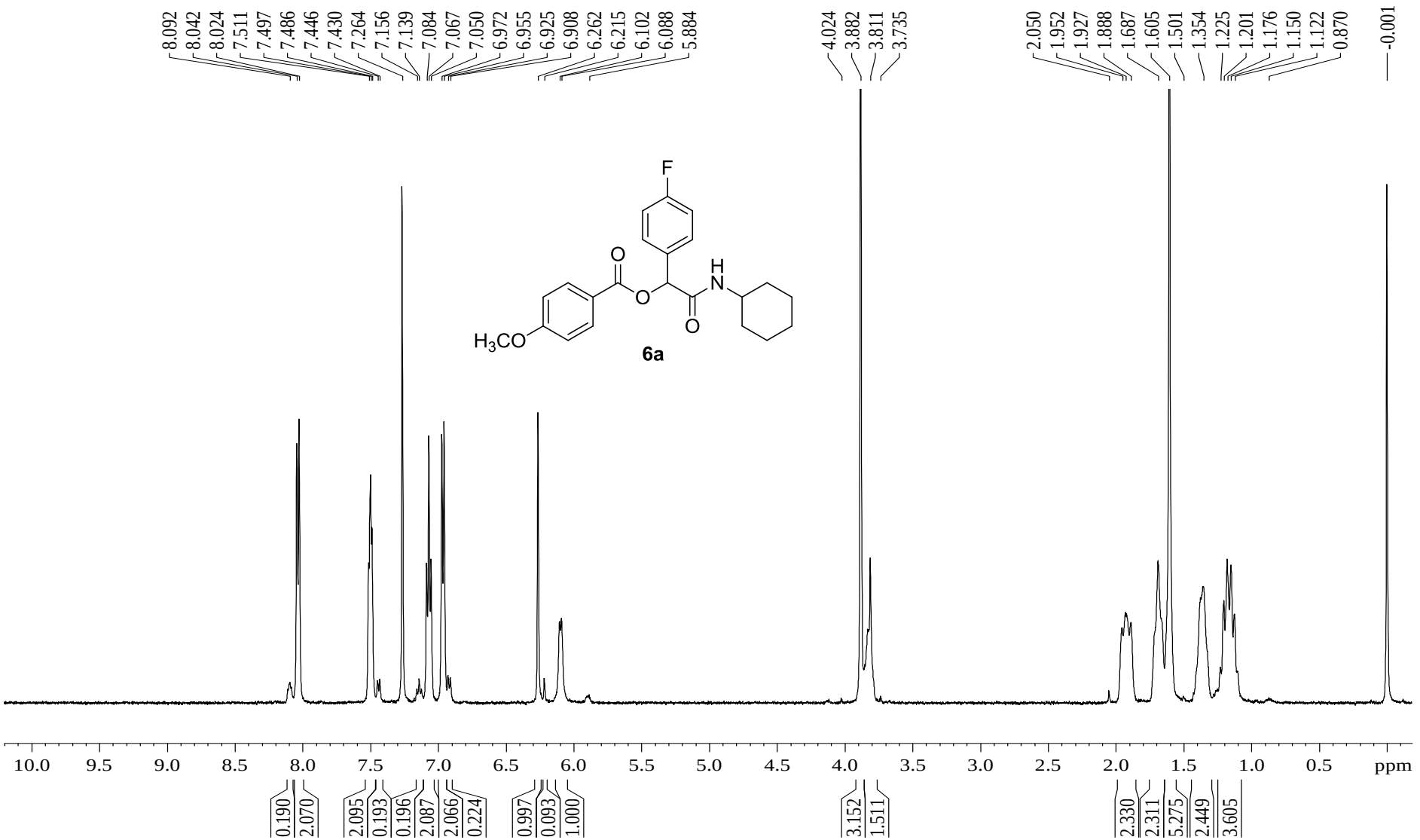
168.795
164.910
144.492
138.989
132.530
129.893
129.489
129.339
127.465
126.475
77.259
77.007
76.754
75.525
61.680
41.271
21.708
21.204
14.072
-0.048
CH3
O
O
H
N
COOEt
O
H3C
5c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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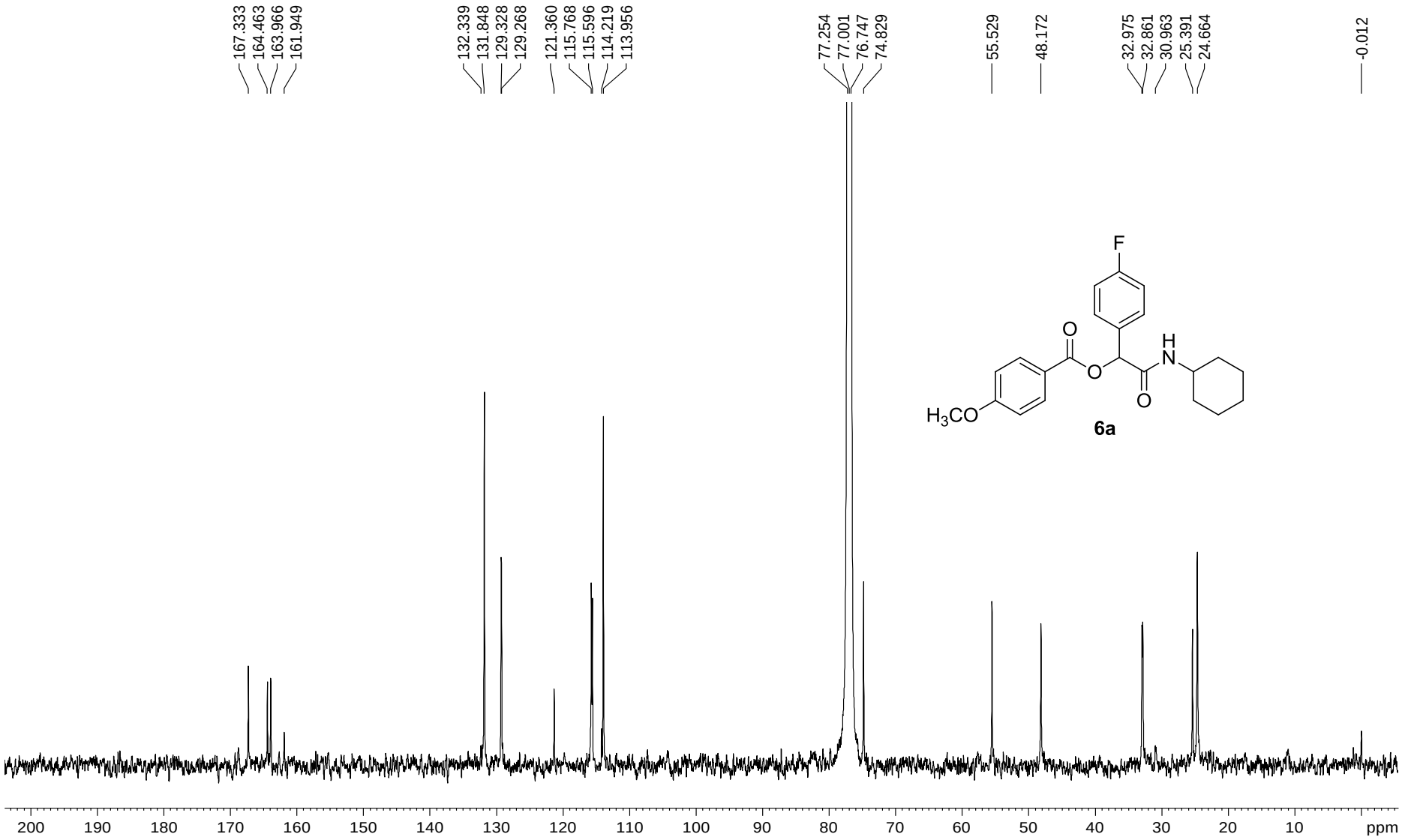
8.042
8.024
7.511
7.497
7.486
7.446
7.430
7.264
7.156
7.139
7.084
7.067
7.050
6.972
6.955
6.925
6.908
6.262
6.215
6.102
6.088
5.884
4.024
3.882
3.811
3.735
2.050
1.952
1.927
1.888
1.687
1.605
1.501
1.354
1.225
1.201
1.176
1.150
1.122
0.870
-0.001
F
O
O
O
H
N
H3CO
6a
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.190
2.070
2.095
0.193
0.196
2.087
2.066
0.224
0.997
0.093
1.000
3.152
1.511
2.330
2.311
5.275
2.449
3.605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163.966
161.949
132.339
131.848
129.328
129.268
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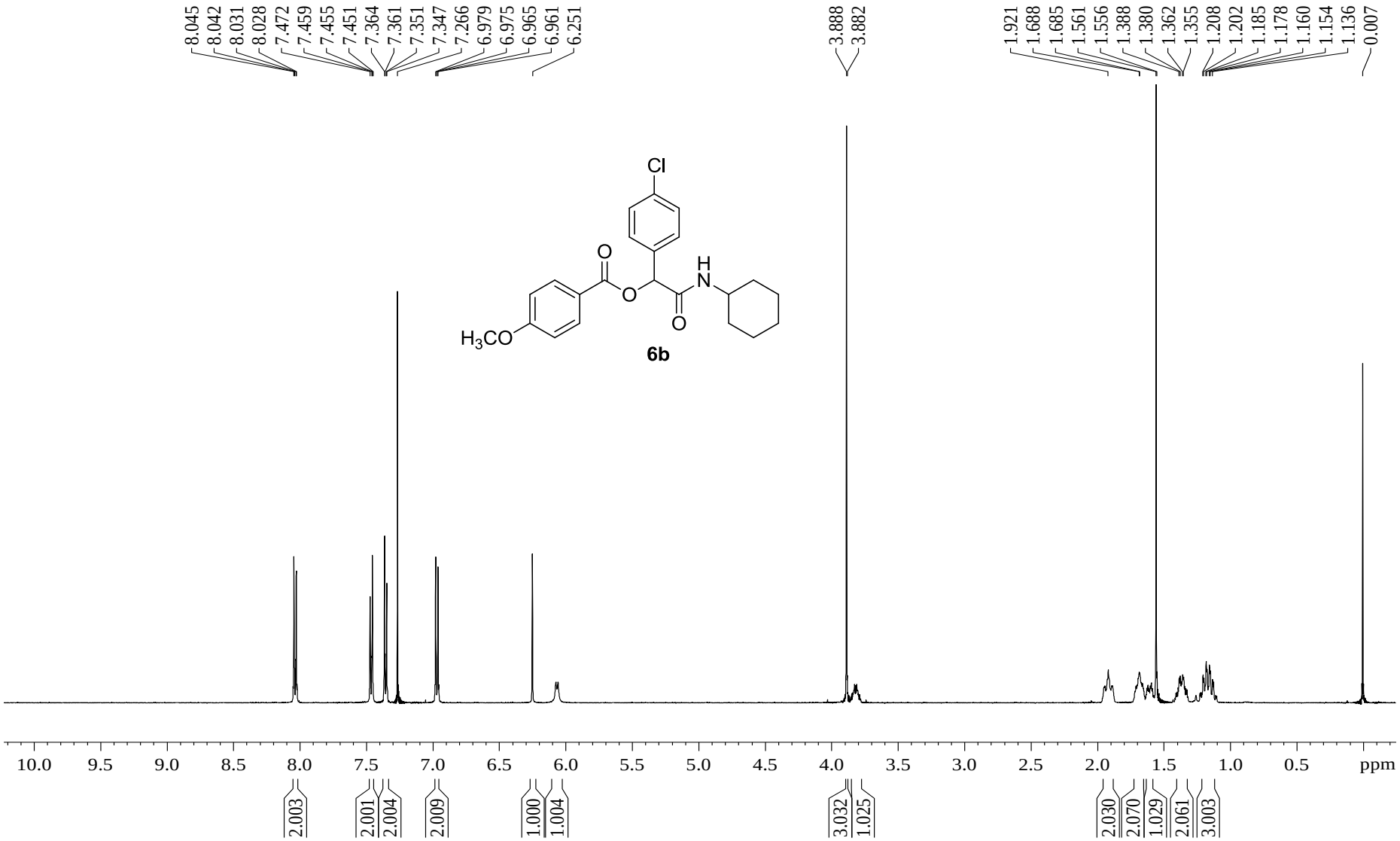
115.768
115.596
114.219
113.956
77.254
77.001
76.747
74.829
55.529
48.172
32.975
32.861
30.963
25.391
24.664
-0.012
F
O
O
H
N
O
H3CO
6a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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8.031
8.028
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7.459
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7.451
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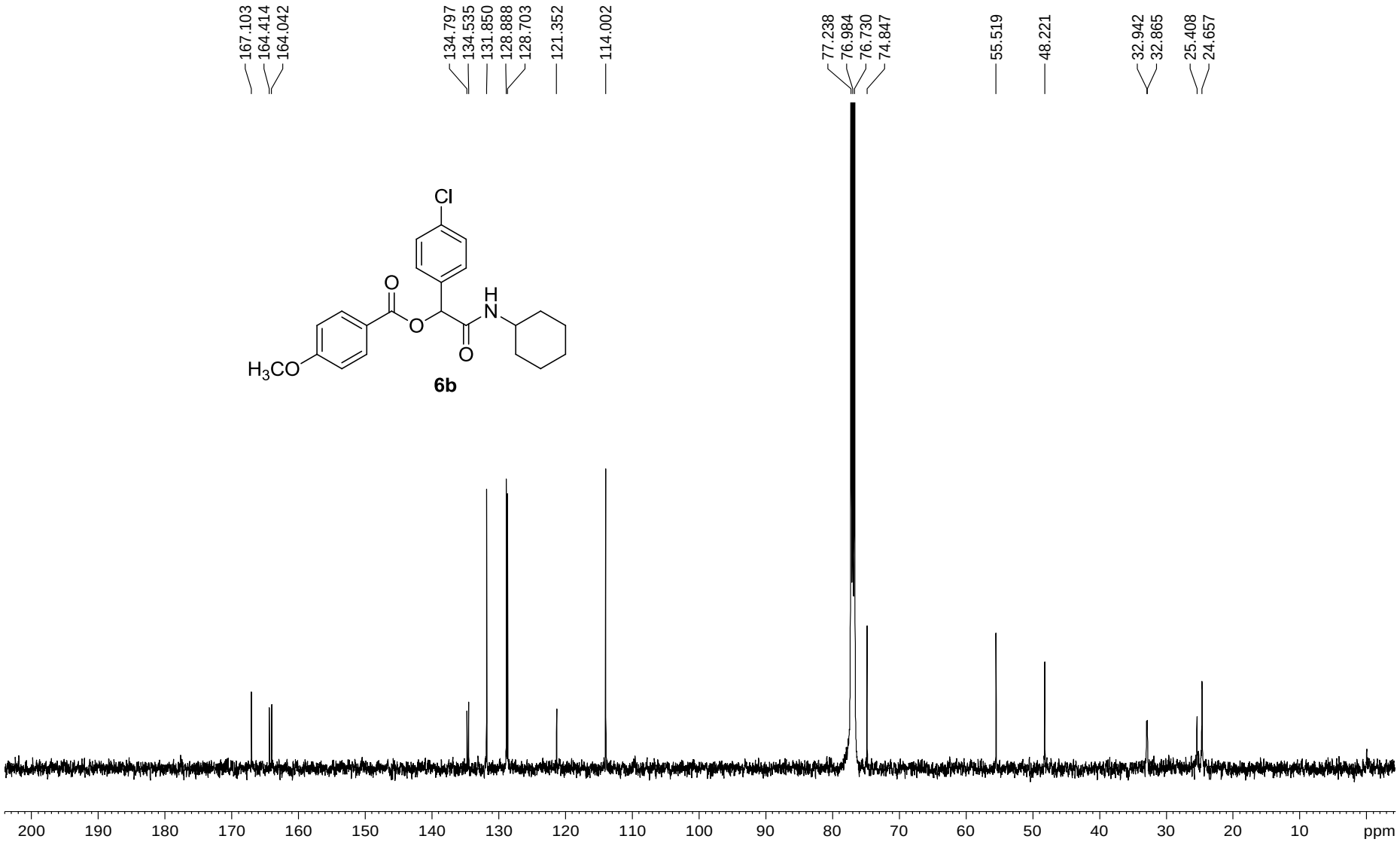
7.361
7.351
7.347
7.266
6.979
6.975
6.965
6.961
6.251
3.888
3.882
1.921
1.688
1.685
1.561
1.556
1.388
1.380
1.362
1.355
1.208
1.202
1.185
1.178
1.160
1.154
1.136
0.007
Cl
O
O
O
H
N
H3CO
6b
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.003
2.001
2.004
2.009
1.000
1.004
3.032
1.025
2.030
2.070
1.029
2.061
3.003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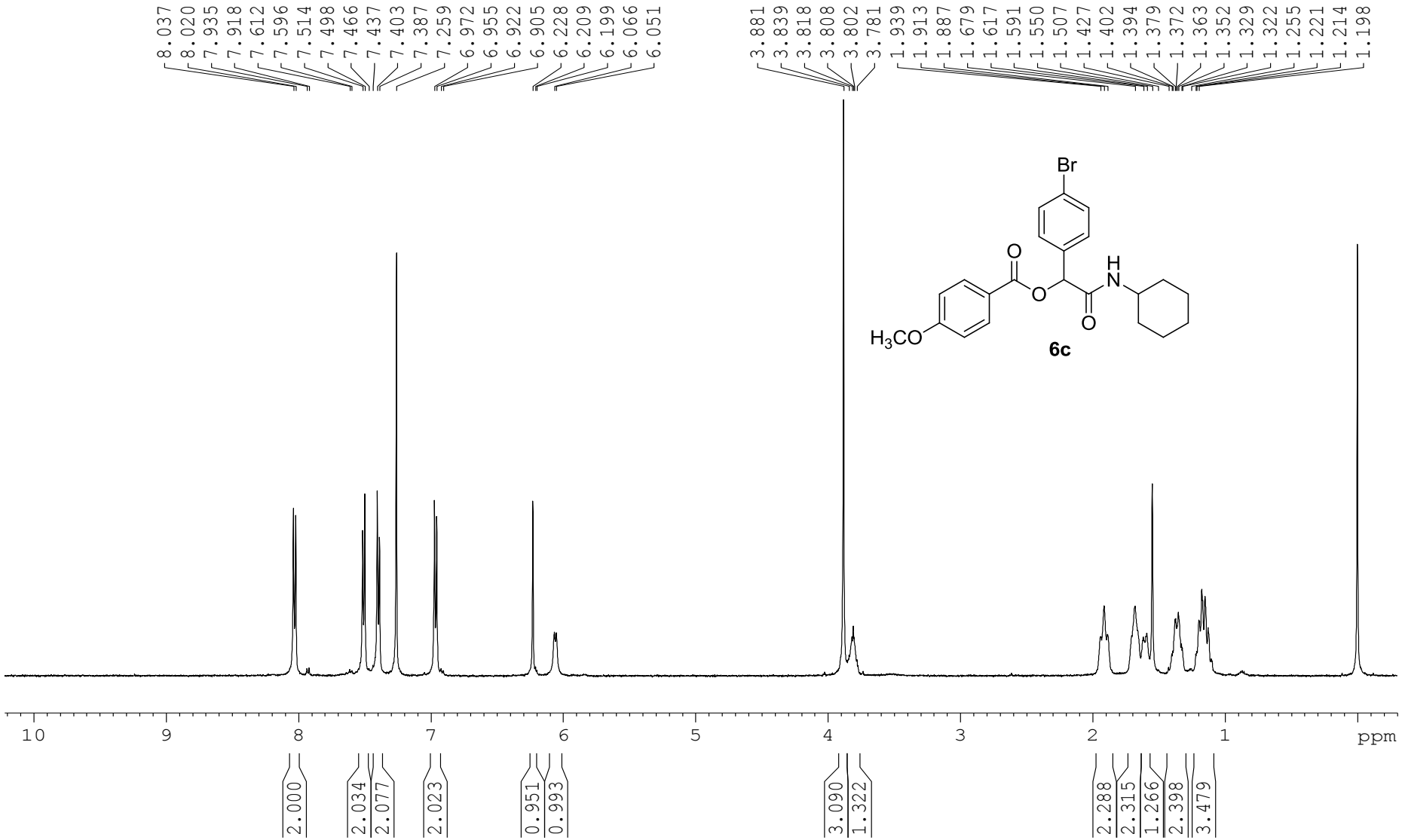
164.414
164.042
134.797
134.535
131.850
128.888
128.703
121.352
114.002
77.238
76.984
76.730
74.847
55.519
48.221
32.942
32.865
25.408
24.657
Cl
O
O
H
N
O
H_3CO
6b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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8.020
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7.918
7.612
7.596
7.514
7.498
7.466
7.437
7.403
7.387
7.259
6.972
6.955
6.922
6.905
6.228
6.209
6.199
6.066
6.051
3.881
3.839
3.818
3.808
3.802
3.781
1.939
1.913
1.887
1.679
1.617
1.591
1.550
1.507
1.427
1.402
1.394
1.379
1.372
1.363
1.352
1.329
1.322
1.255
1.221
1.214
1.198
Br
O
O
H
N
O
H3CO
6c
10
9
8
7
6
5
4
3
2
1
ppm
2.000
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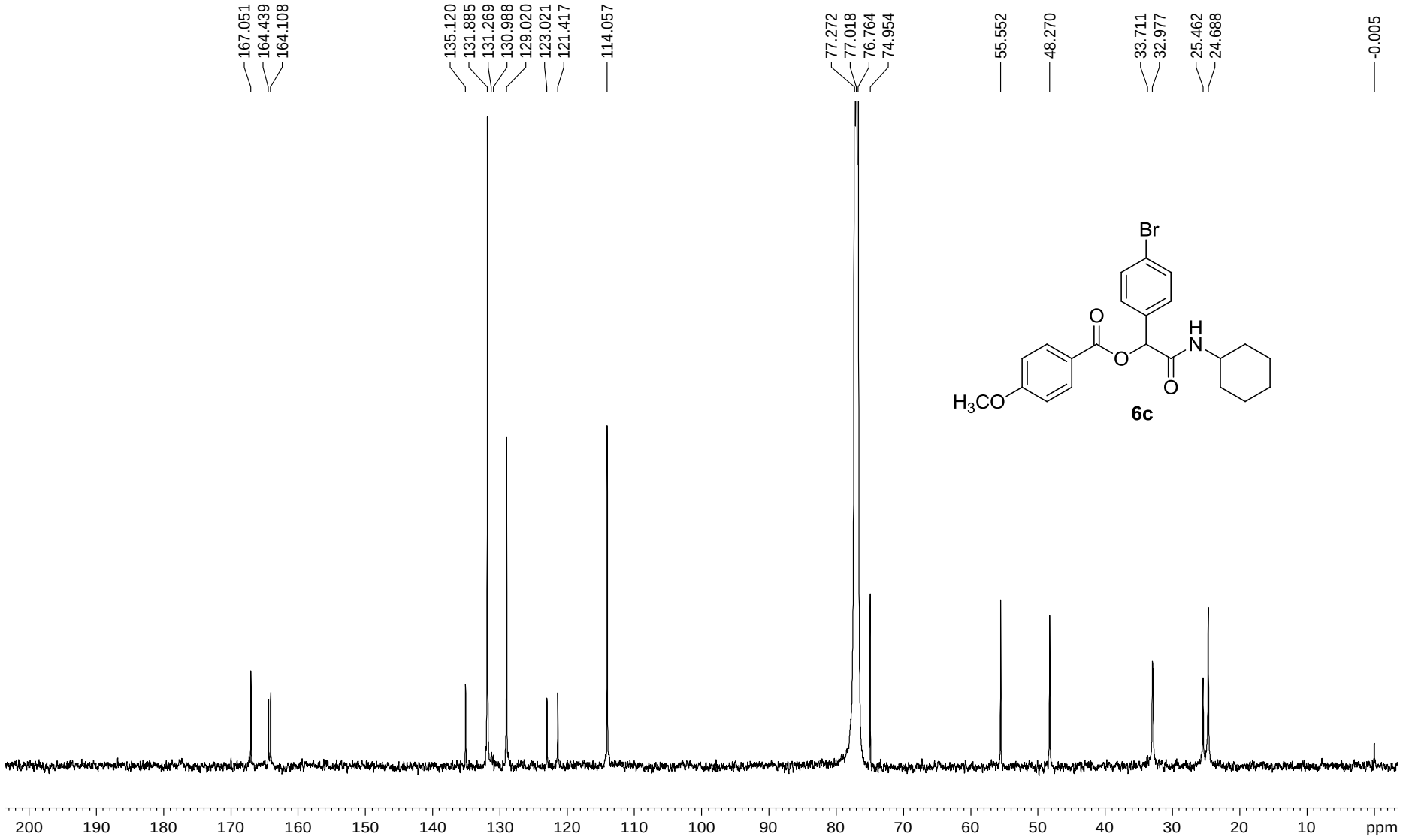
0.951
0.993
3.090
1.322
2.288
2.315
1.266
2.398
3.479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135.120
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131.269
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123.021
121.417
114.057
77.272
77.018
76.764
74.954
55.552
48.270
33.711
32.977
25.462
24.688
-0.005
Br
O
O
O
H
N
H3CO
6c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm