

Supplementary Material

Combination of pyridinium and isoquinolinium ylides with phenylisocyanate and isothiocyanates: Unexpected formation of a novel subclass of mesoionic monosubstituted 3-oxo-propanamide or thioamide compounds

Mohammad Seifi¹, S. Yousef Ebrahimpour¹, Jim Simpson², Michal Dusek³, Vaclav Eigner³
and Hassan Sheibani*¹

¹*Department of Chemistry, Shahid Bahonar University of Kerman, Kerman 76169, Iran*

²*Department of Chemistry, University of Otago, P.O. Box 56, Dunedin 9054, New Zealand*

³*Institute of Physics of the ASCR, v.v.i., Na Slovance 2, 182 21 Prague 8, Czech Republic*

E-mail: hsheibani@mail.uk.ac.ir

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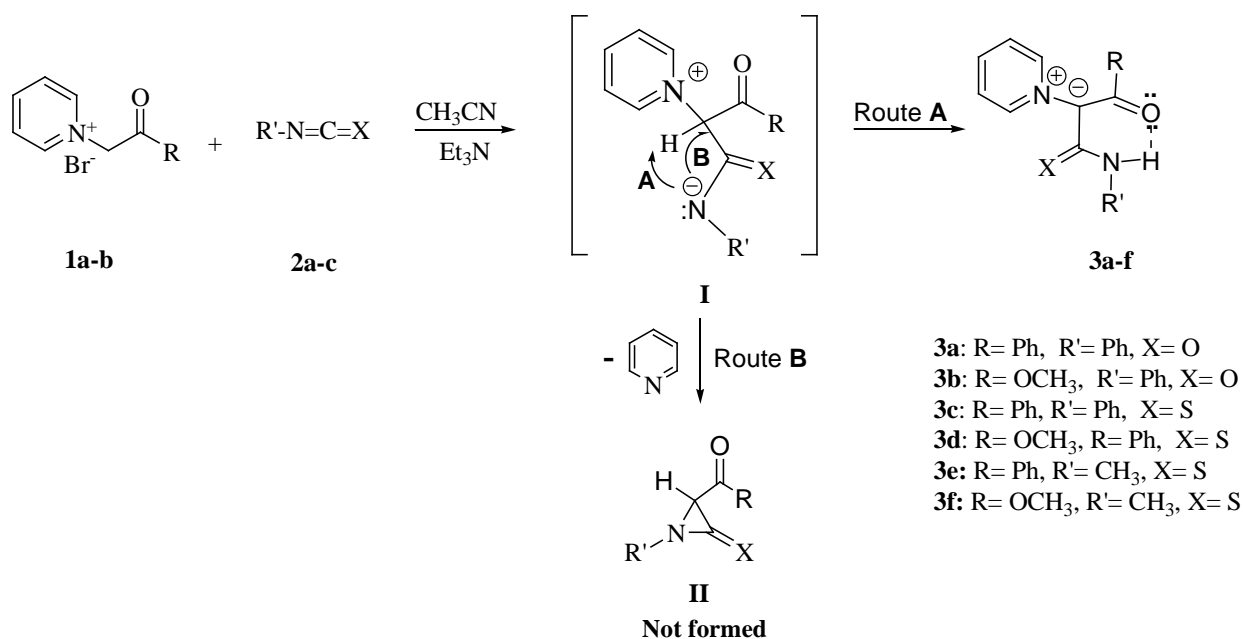
1-(Methylamino)-3-oxo-3-phenyl-2-(pyridin-1-ium-1-yl)-1-thioxopropan-2-ide (3e):

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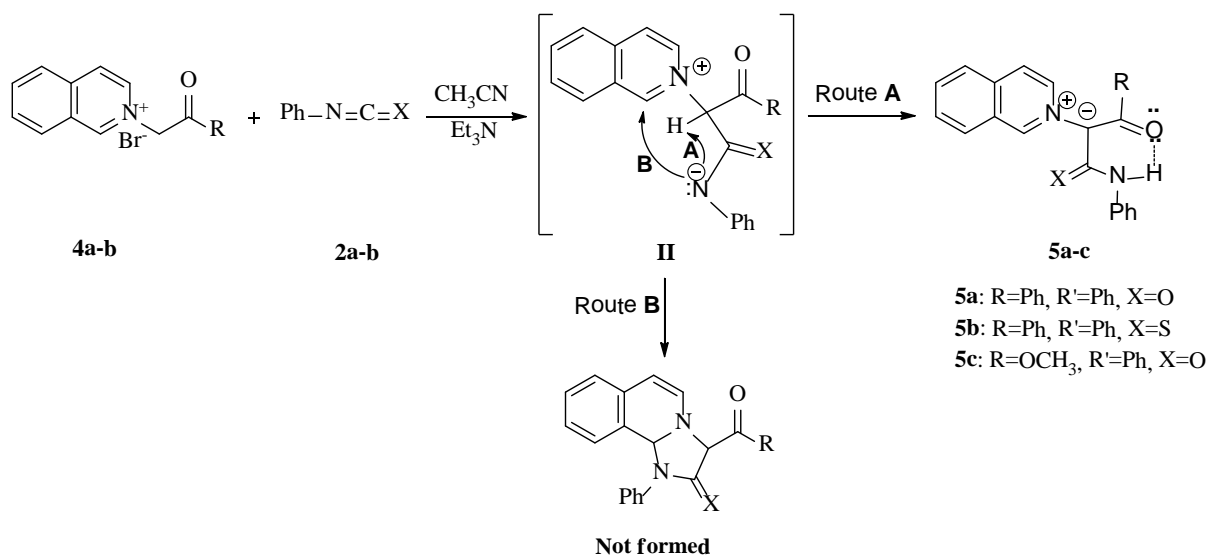
Table 1. Solvent and base effects on the reaction of pyridinium or isoquinolinium bromides with phenylisocyanate

Compd, No	Solvent	Base	Time (min)	Yield (%)
3a	Acetonitrile	Et ₃ N	15	95
3a	Acetonitrile	K ₂ CO ₃	18	92
3a	Toluene	Et ₃ N	30	90
3a	Toluene	K ₂ CO ₃	25	92
3a	CH ₂ Cl ₂	Et ₃ N	20	90
3a	CH ₂ Cl ₂	K ₂ CO ₃	25	88
5a	Acetonitrile	Et ₃ N	12	96
5a	Acetonitrile	K ₂ CO ₃	15	90
5a	Toluene	Et ₃ N	25	88
5a	Toluene	K ₂ CO ₃	22	90
5a	CH ₂ Cl ₂	Et ₃ N	18	87
5a	CH ₂ Cl ₂	K ₂ CO ₃	22	85



Scheme 1

Scheme 1. Reaction of pyridinium salts **1a**, **b** with phenylisocyanate **2a**, phenylisothiocyanate **2b** and methylisothiocyanate in the presence of triethylamane.



Scheme 2

Scheme 2. Synthesis of 2-(Isoquinolin-2-ium-2-yl)-1-oxo-3-(phenylaminopropan-2-ide derivatives **5a-c**.

Experimental part

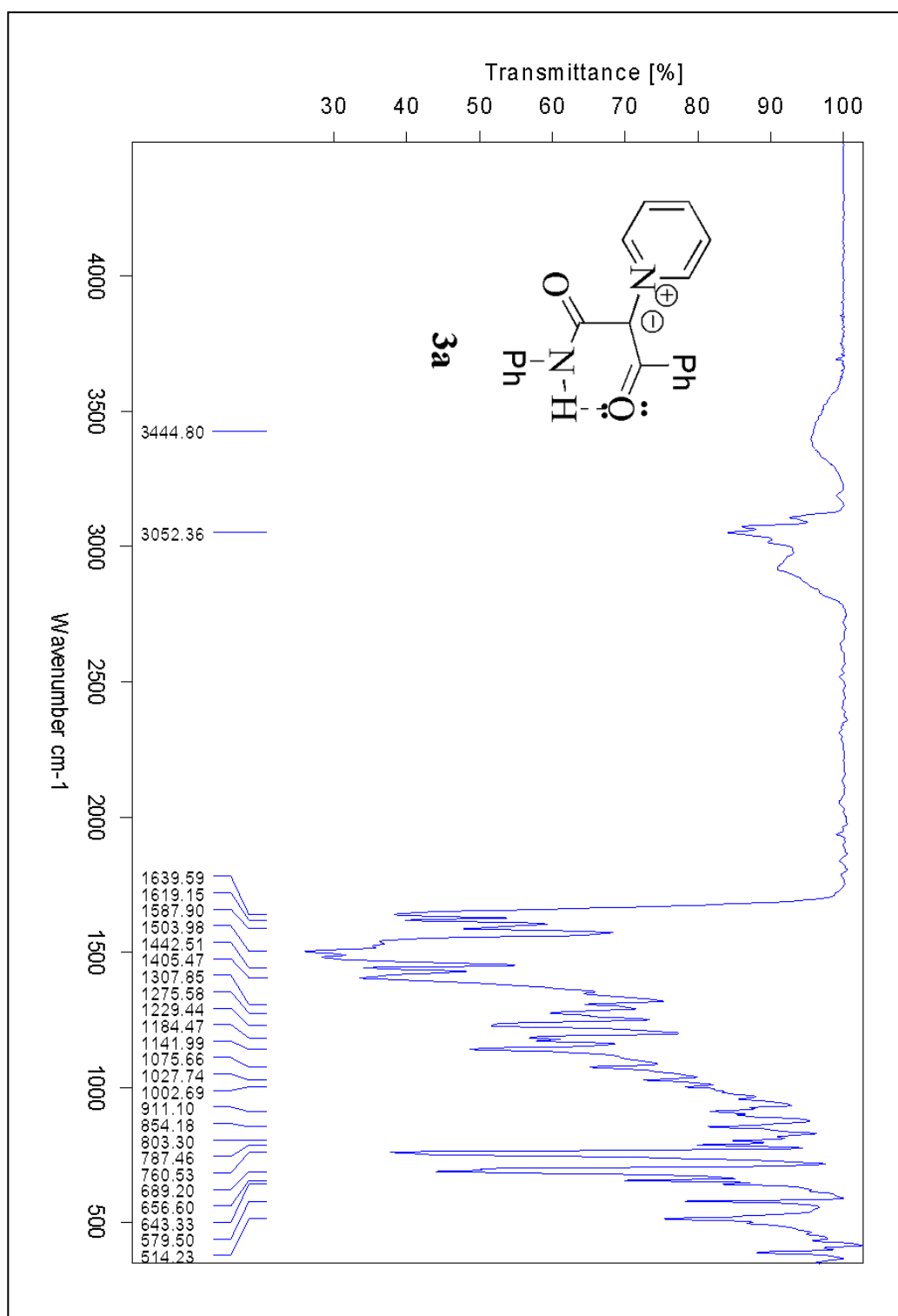
Materials and methods

Melting points were measured on an Electrothermal-9100 apparatus and are uncorrected. IR spectra were recorded on a Bruker FT-IR Tensor 27 infrared spectrophotometer. ¹H NMR and spectra were recorded on a Avance III 400 or 300 MHz Bruker spectrometer. ¹³C NMR spectra were recorded on the same instruments at 100 or 75 MHz using TMS as an internal standard. Mass spectra were measured on a GCMS-QP1000 EX spectrometer at 70 eV. Elemental analyses were performed using a Heracus CHN-O-Rapid analyzer. Pyridinium and isoquinolinium salts were prepared according to a literature procedure.

Typical procedure for the preparation of compounds **3a-f** and **5a-c** in acetonitrile.

A solution of the pyridinium salts (**1a, b**) or the isoquinolinium salts (**4a, b**) (2 mmol), phenylisocyanate or isothiocyanates (2 mmol) and triethylamine (0.2 mL) in acetonitrile (20 mL) was stirred at room temperature for about 15 minute (the progress of the reaction was monitored by TLC, using n-hexane/ethyl acetate as the eluent). The solvent was diluted with 50 mL of water and the resulting precipitate was collected by filtration. The crude product was recrystallized with dichloromethane/n-hexane (60/40) to give the pure solid sample for analysis.

1,3-Dioxo-1-phenyl-3-(phenylamino)-2-(pyridin-1-ium-1-yl)propan-2-ide (3a). Greenish yellow crystals; yield: 95%. mp 219 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3444 (broad, NH), 1639, 1619 (C=O), 1587, 1503 (C=C). ^1H NMR (400 MHz, CDCl_3): 12.4 (s, 1H, NH, amide), 8.52-7.01 (m, 15H, Ar). ^{13}C NMR (100 MHz, CDCl_3): 178.22, 163.58 (C=O), 149.12, 141.66, 140.46, 129.04, 128.82, 128.76, 128.43, 127.01, 119.85. MS (m/z): 316 (M^+) (5), 235(21), 196 (100), 167 (19), 119 (80), 105 (30), 91 (68), 77 (62), 65 (94), 51 (50). Anal. calcd. for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_2$: C, 75.93; H, 5.10; N, 8.86%. Found: C, 75.79; H, 5.01; N, 8.52%.



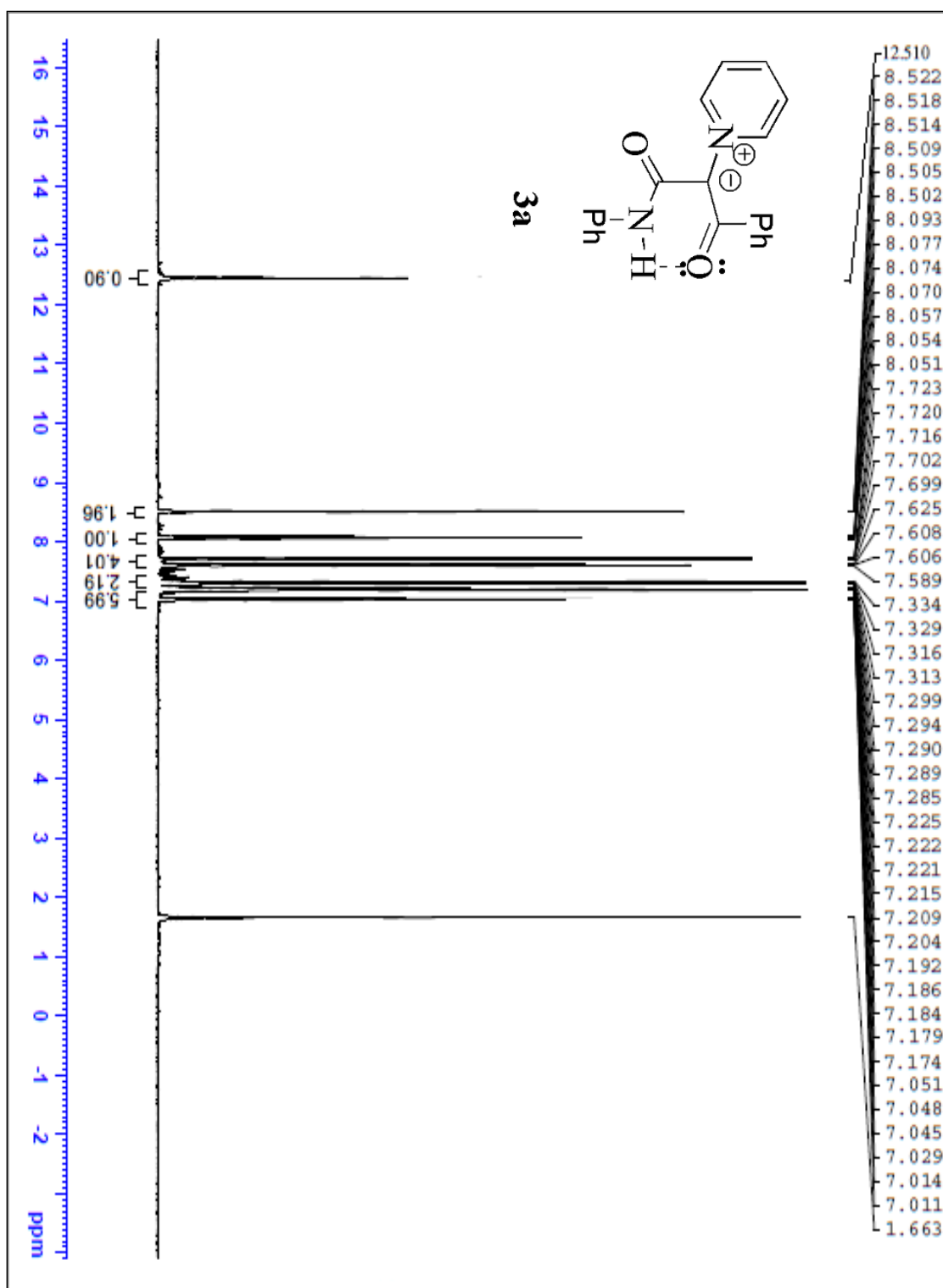


Figure 2. ¹H NMR 3a.

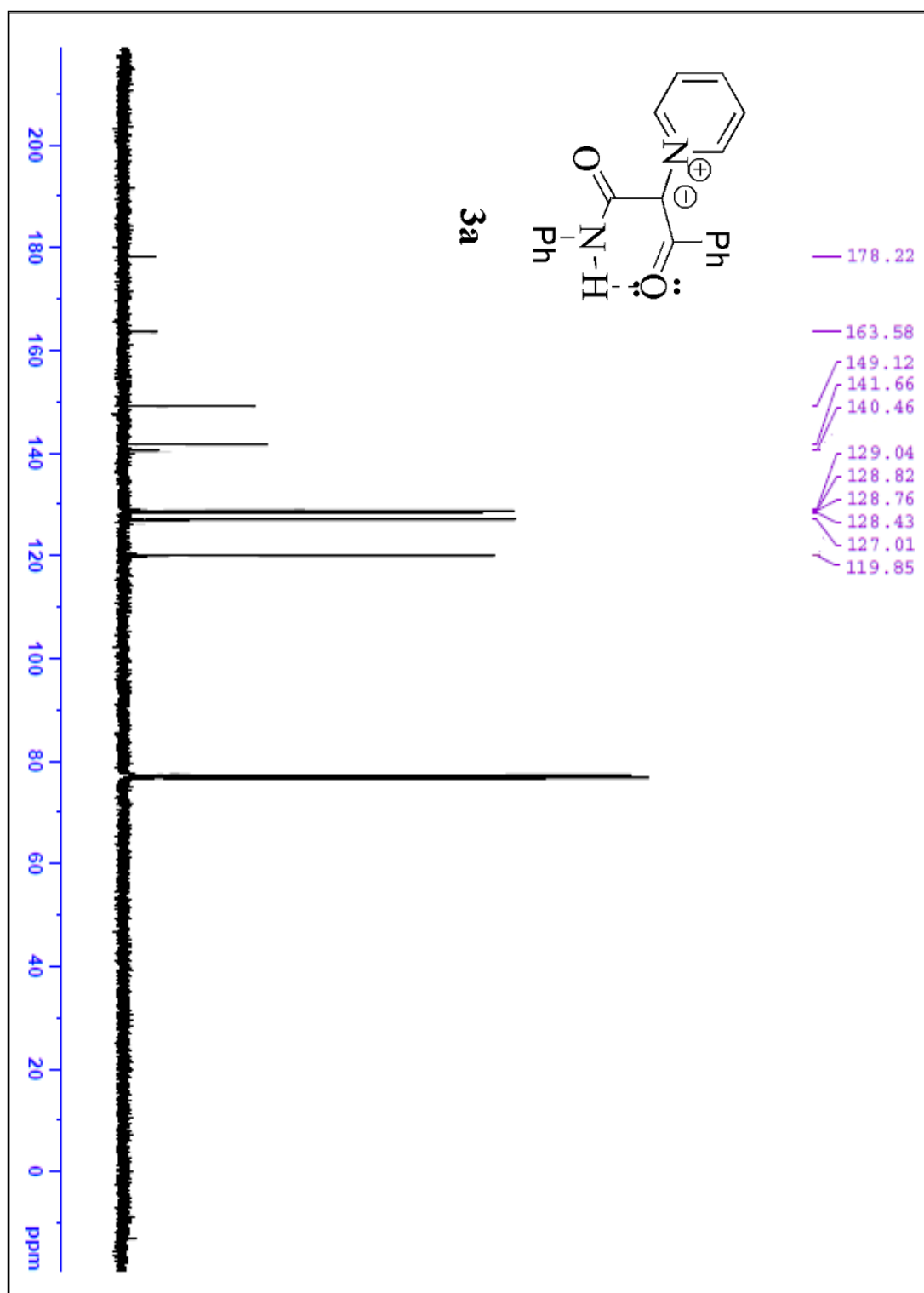


Figure 3. ^{13}C NMR 3a.

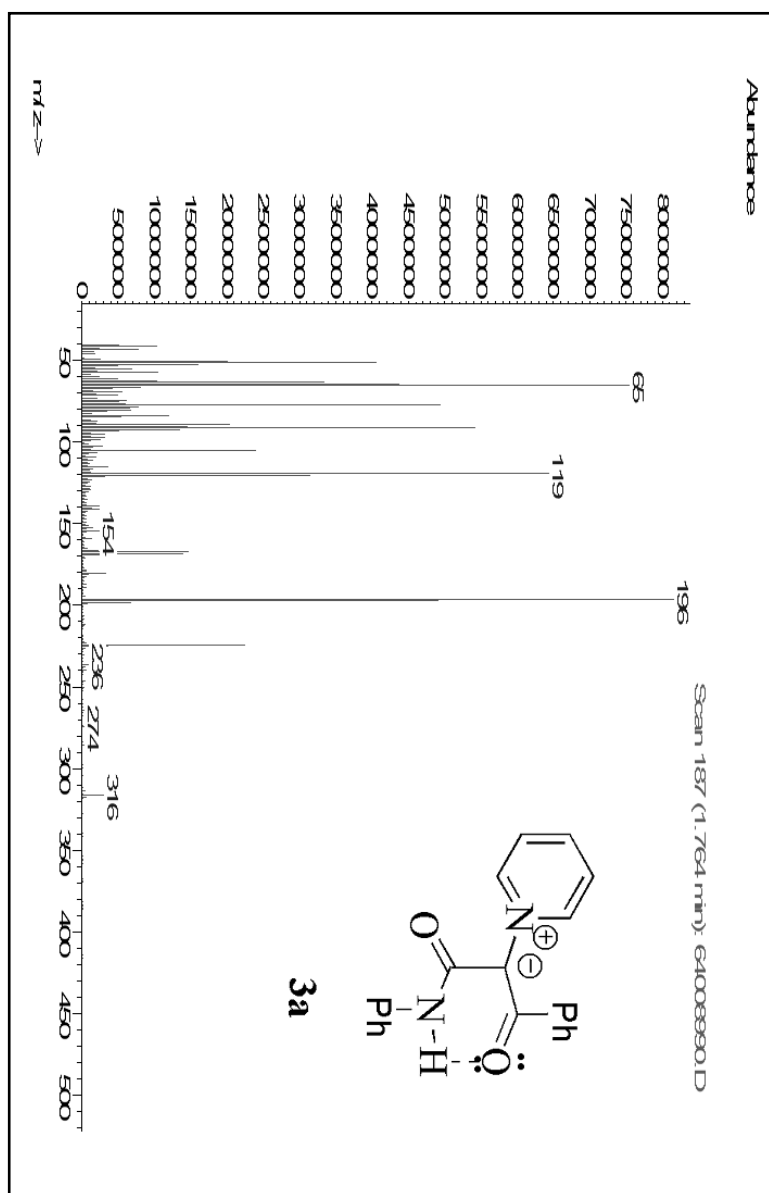


Figure 4. Mass 3a.

1-Methoxy-1,3-dioxo-3-(phenylamino)-2-(pyridin-1-ium-1-yl)propan-2-ide (3b). Yellow crystals; yield: 93%. mp 178-181 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3411 (broad, NH), 1627 (C=O), 1580, 1520, 1482 (C=C). ^1H NMR (300 MHz, CDCl_3): 10.62 (s, 1H, NH, amide), 8.57-6.95 (m, 10H, Ar), 3.62 (s, 3H, CH_3). ^{13}C NMR (75 MHz, CDCl_3): 174.87, 164.14 (C=O), 149.69, 141.21, 128.71, 125.69, 119.34, 50.14 (OCH_3). MS (m/z): 270 (M^+) (6), 213(9), 178 (13), 152 (68), 119 (100), 101 (14), 91 (94), 86 (24), 79 (24), 64 (53), 52 (30). Anal. calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_3$: C, 66.66; H, 5.22; N, 10.36%. Found: C, 66.57; H, 5.19; N, 10.15%.

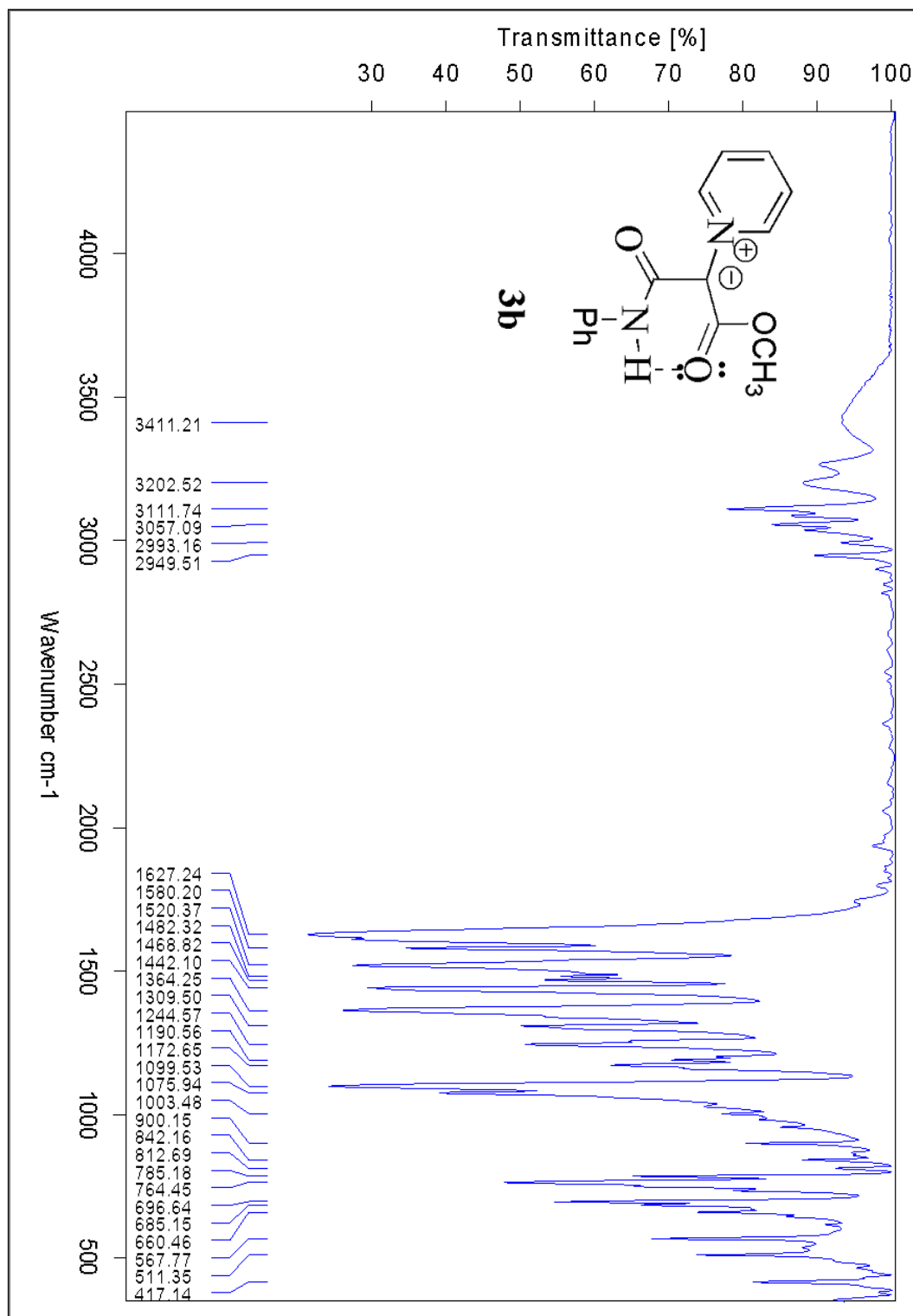


Figure 5. IR 3b.

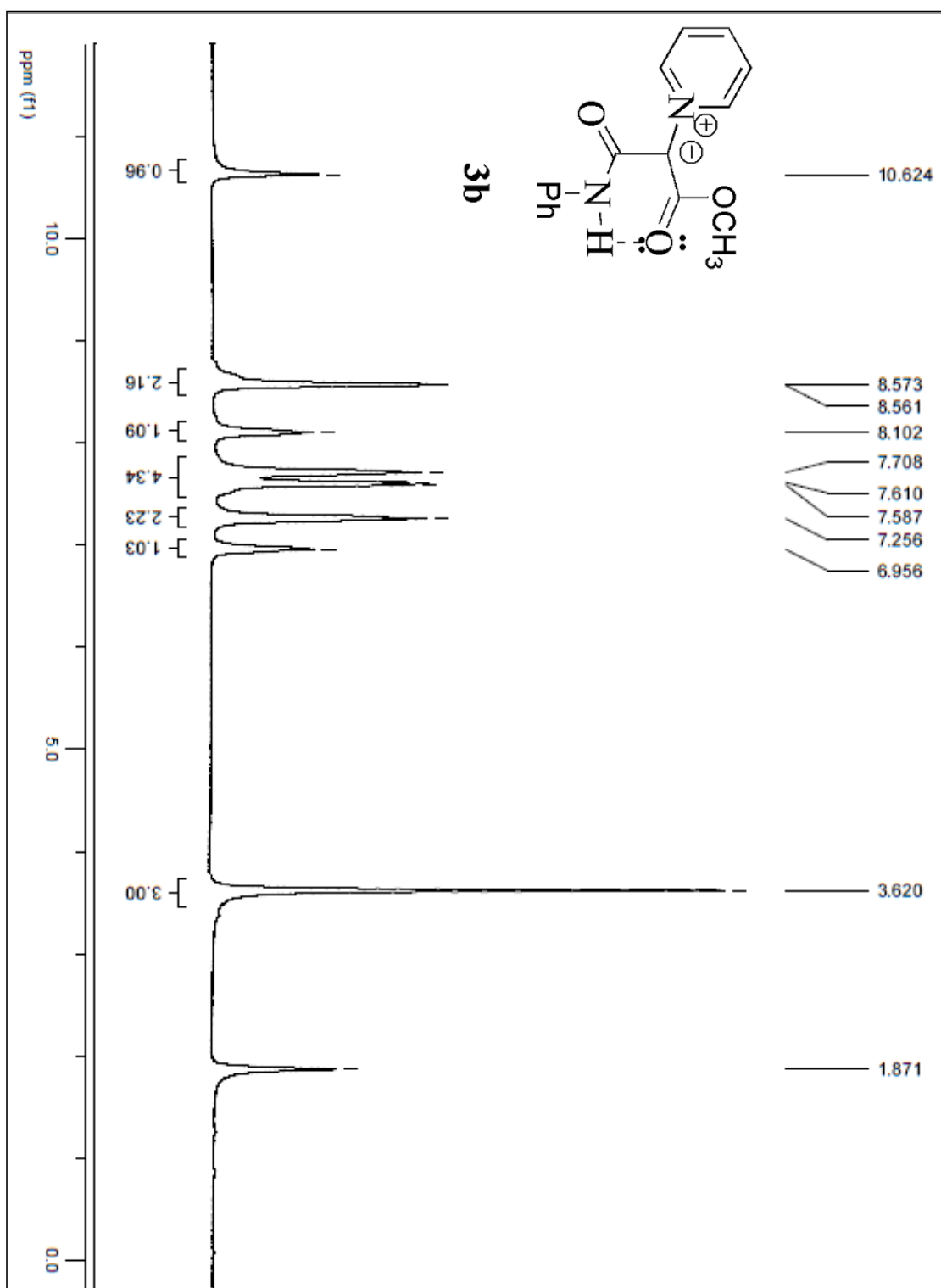


Figure 6. ¹H NMR 3b.

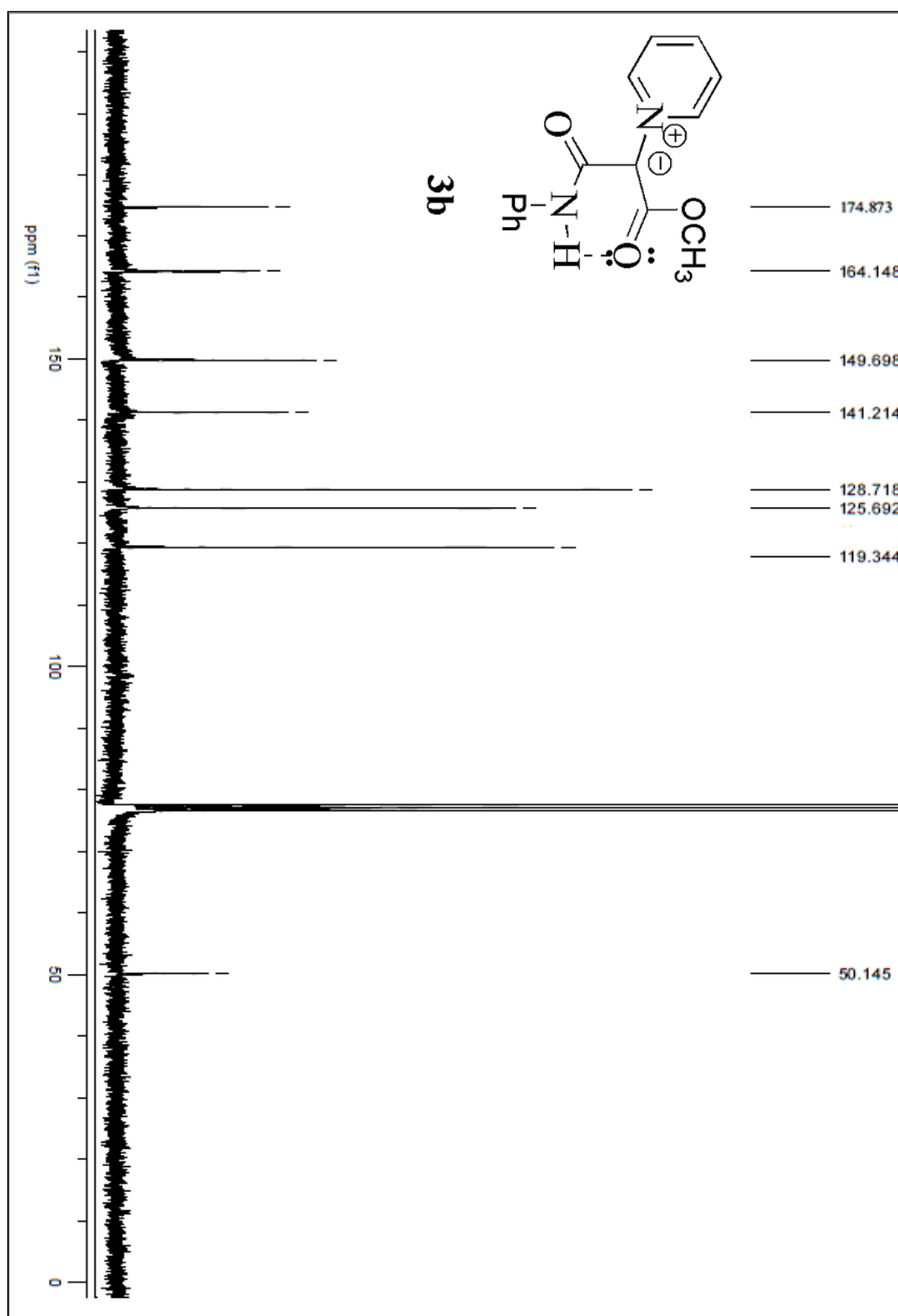


Figure 7. ¹³C NMR 3b.

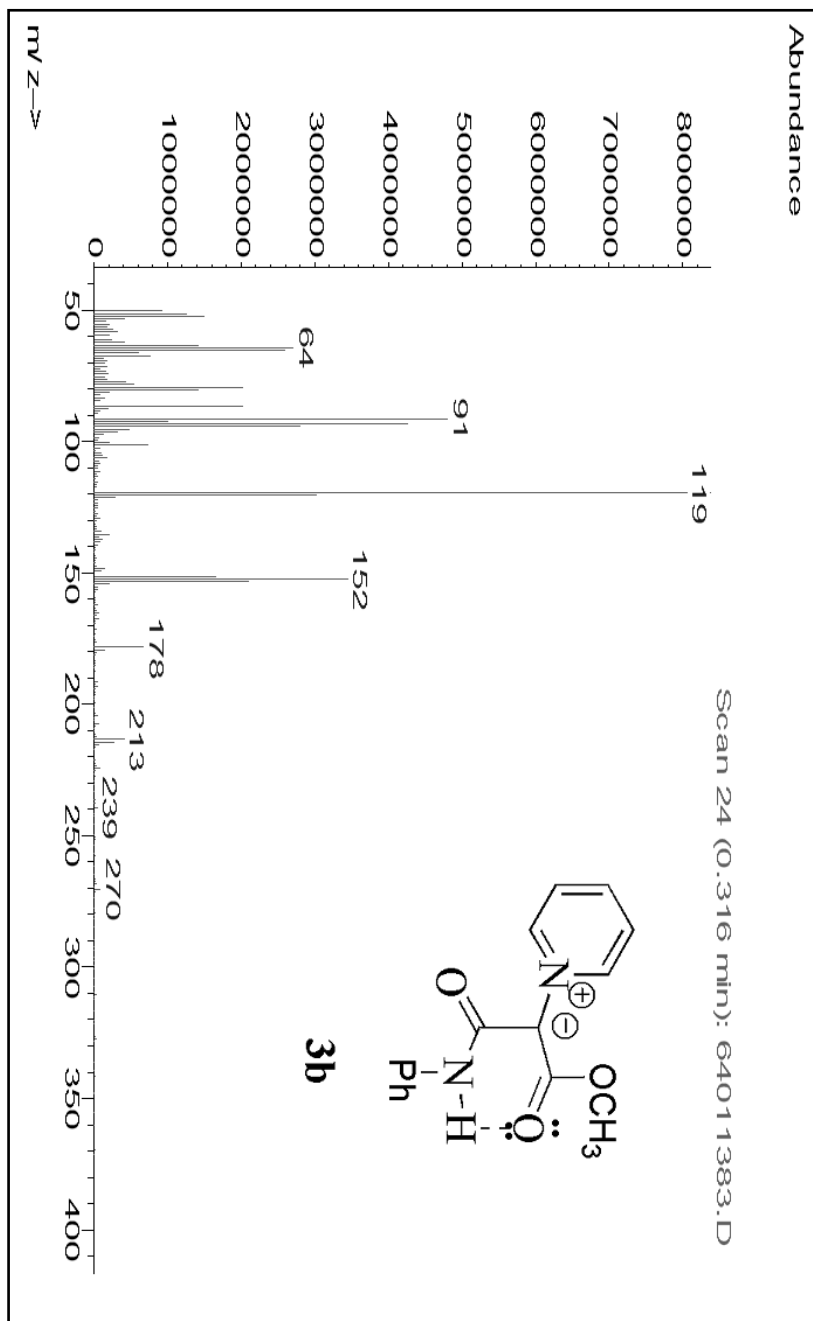


Figure 8. Mass 3b.

1-Oxo-1-phenyl-3-(phenylamino)-2-(pyridin-1-ium-1-yl)-3-thioxopropan-2-ide (3c). Greenish yellow crystals; yield: 90%. mp 179-180 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3424 (broad, NH), 1618 (C=O), 1595 (C=S), 1570 (C=C). ^1H NMR (300 MHz, DMSO): 14.54 (s, 1H, NH, thioamide), 8.95-7.10 (m, 15H, Ar). ^{13}C NMR (75 MHz, DMSO): 184.59 (C=S), 177.81 (C=O), 151.85, 145.61, 141.42, 141.29, 128.81, 128.61, 128.28, 126.88, 123.27. MS (m/z): 332 (M^+) (6), 253 (7), 251 (10), 236 (5), 196 (12), 162 (57), 135 (100), 105 (61), 91 (12), 77 (98), 51 (44). Anal. calcd. for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{OS}$: C, 72.26; H, 4.85; N, 8.43%. Found: C, 72.01; H, 4.75; N, 8.22%.

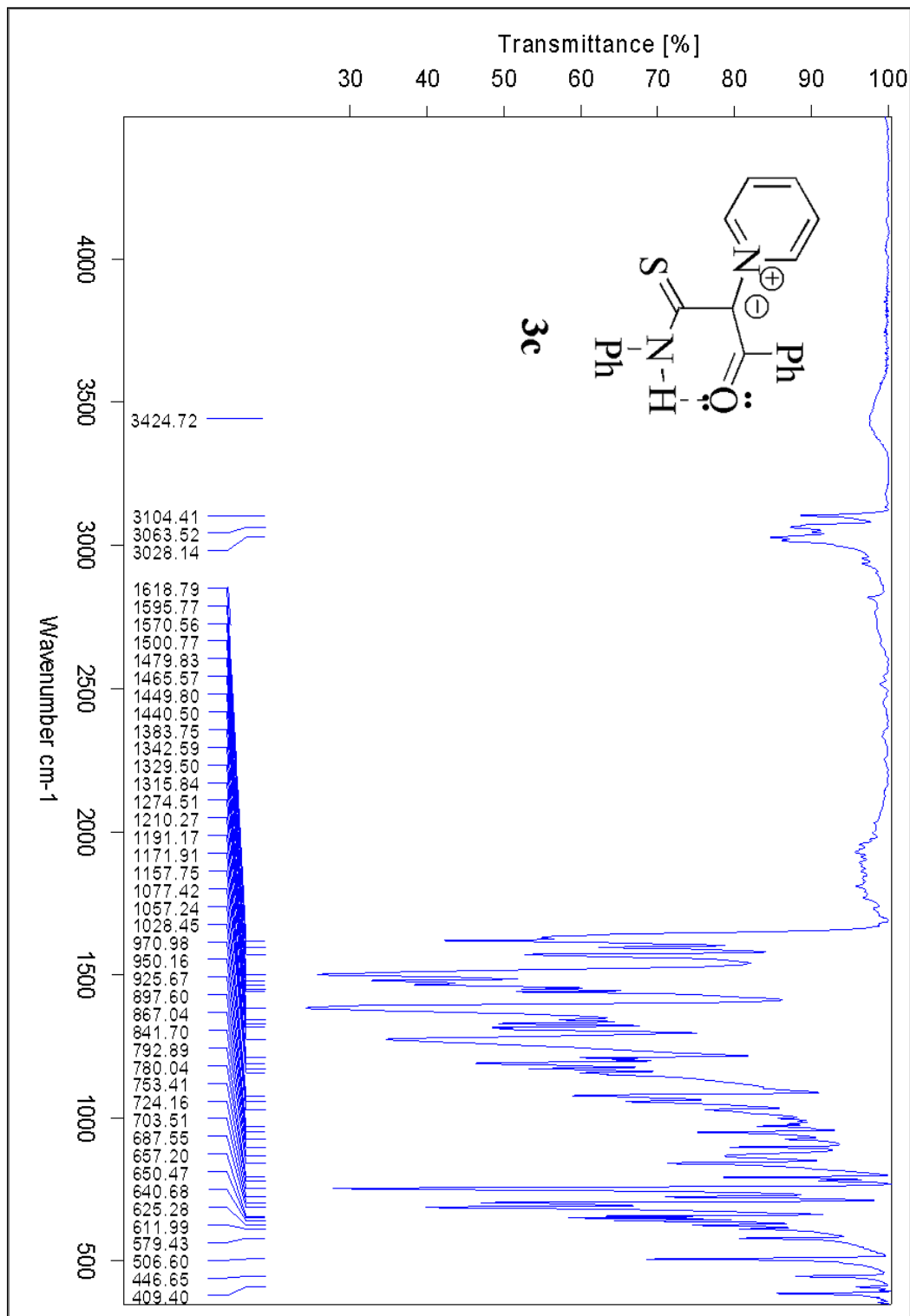


Figure 9. IR 3c.

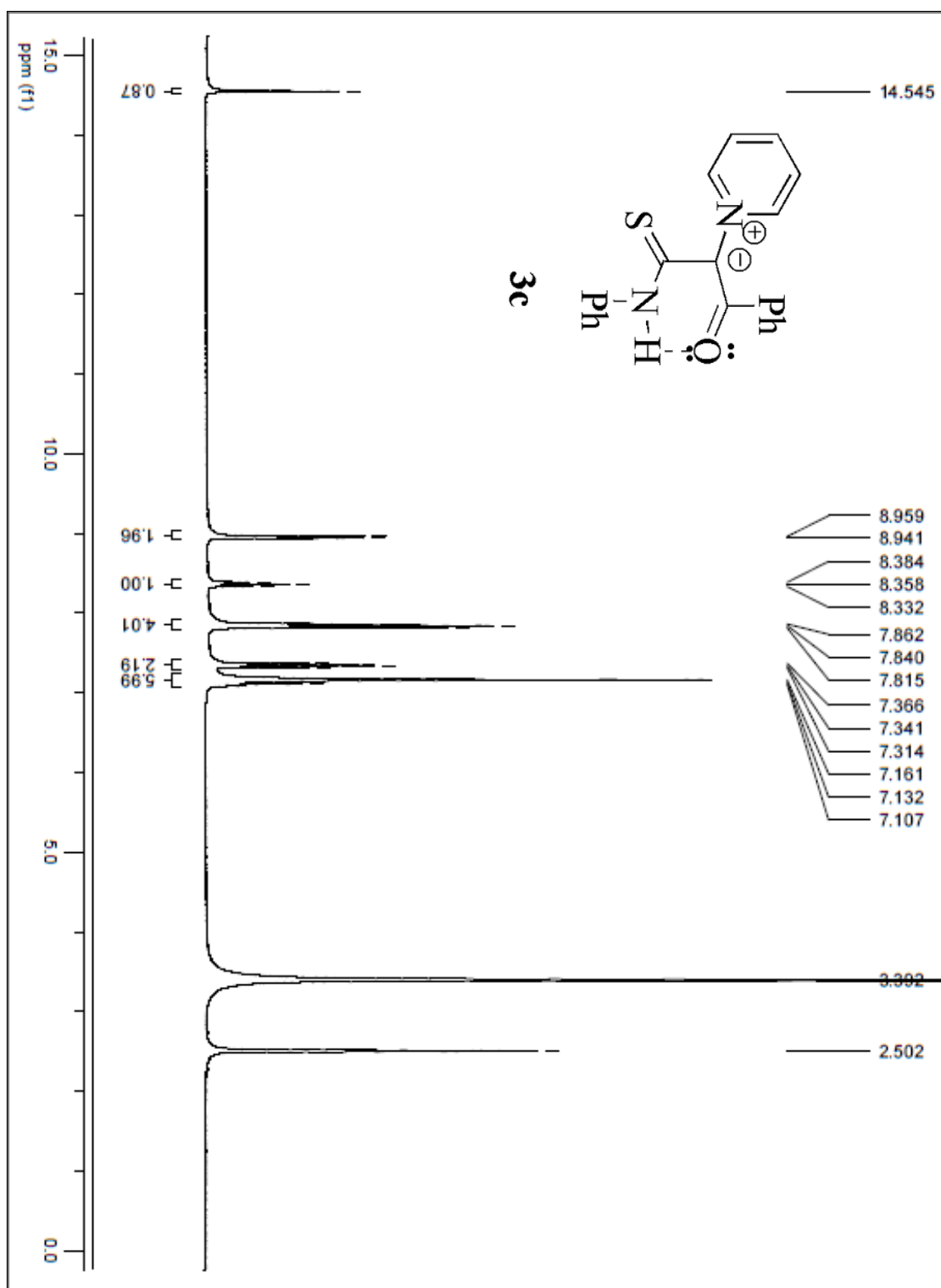


Figure 10. ^1H NMR **3c**.

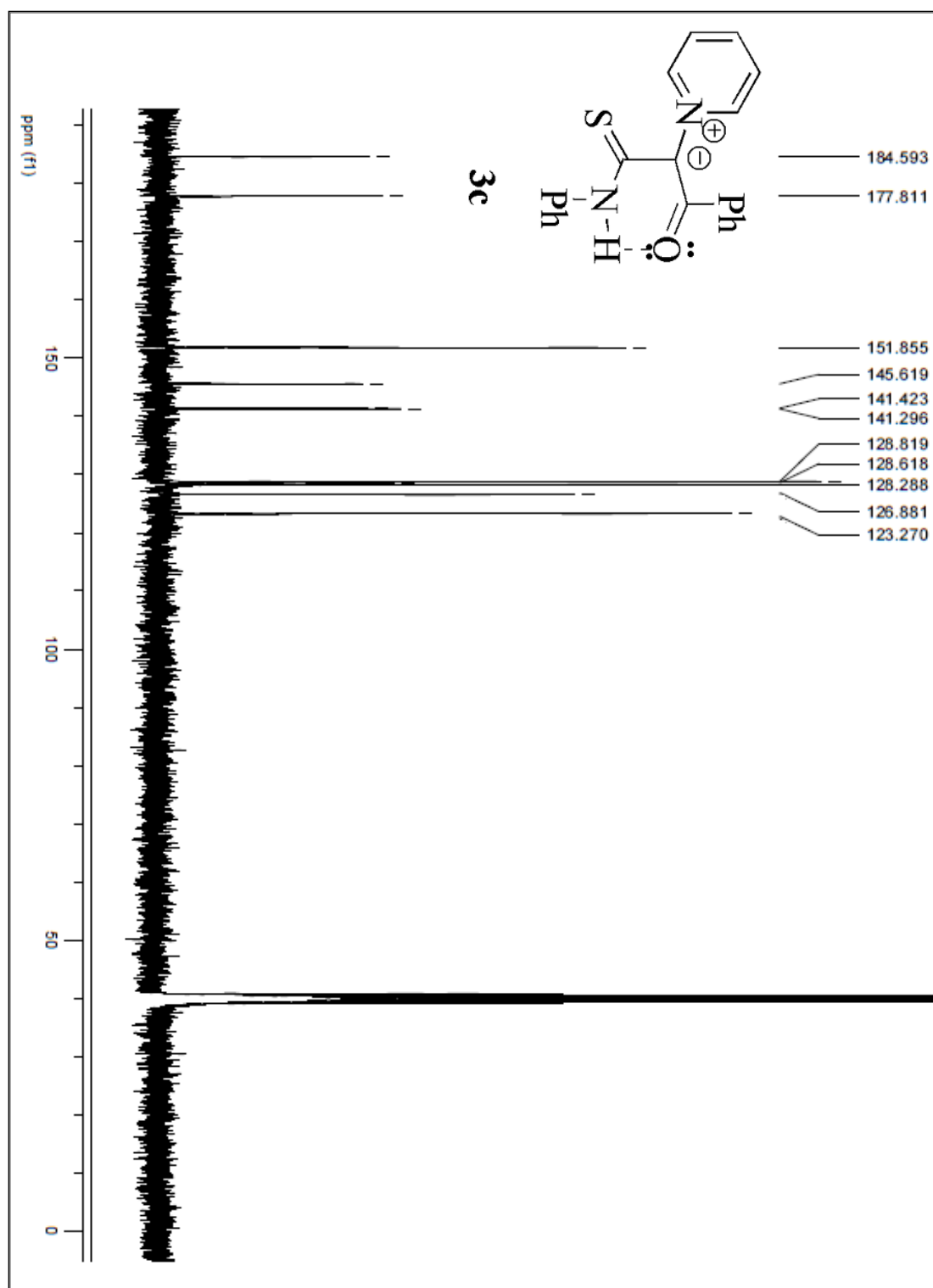


Figure 11. ^{13}C NMR **3c**.

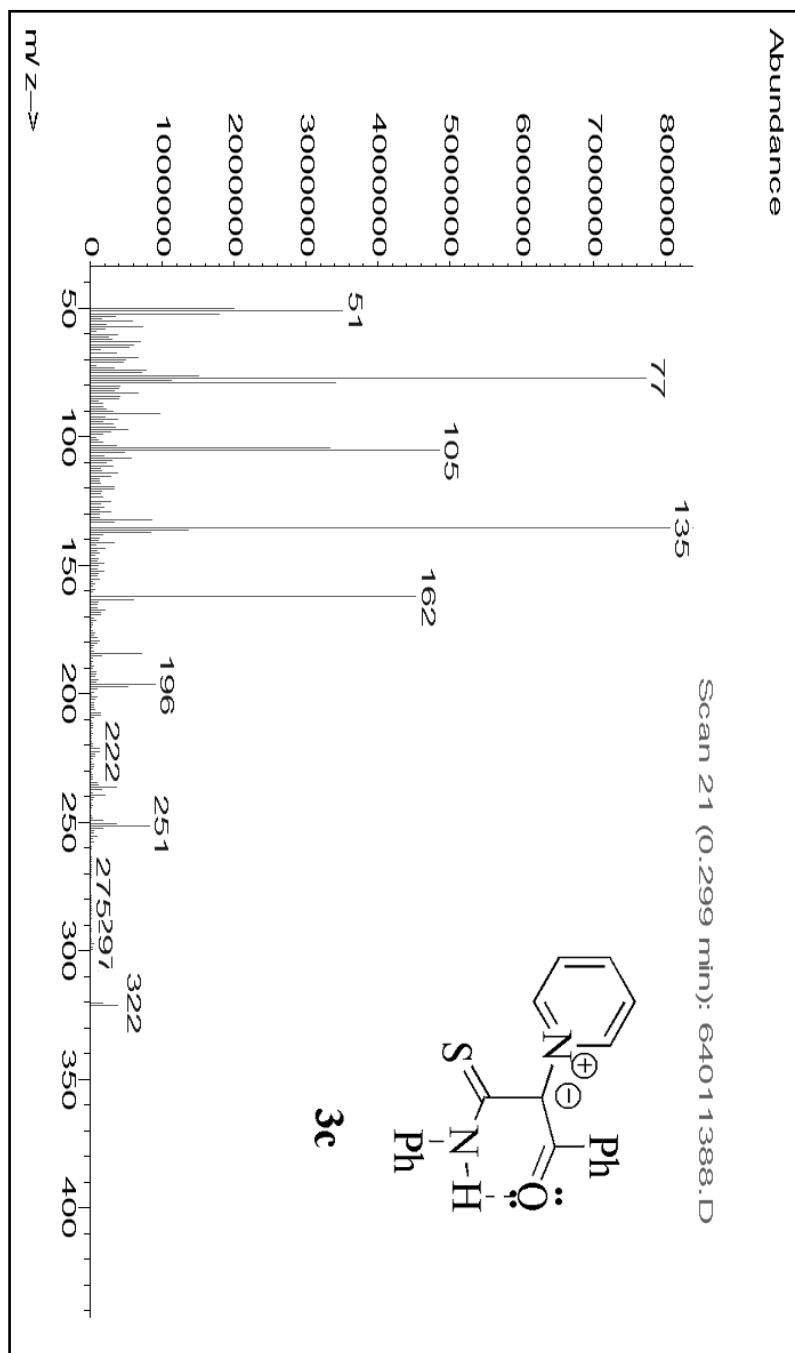


Figure 12. Mass 3c.

1-Methoxy-1-oxo-3-(phenylamino)-2-(pyridin-1-ium-1-yl)-3-thioxopropan-2-ide (3d). Yellow crystals; yield: 93%. mp 170 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3444 (broad, NH), 1640 (C=O), 1592 (C=S), 1564 (C=C). ^1H NMR (300 MHz, CDCl_3): 11.83 (s, 1H, NH, thioamide), 8.61-7.09 (m, 10H, Ar), 3.59 (s, 3H, CH_3). ^{13}C NMR (75 MHz, CDCl_3): 182.87 (C=S), 162.79 (C=O), 151.30, 143.47, 128.26, 126.23, 109.67, 50.49 (OCH_3). MS (m/z): 286 (M^+) (4), 260 (6), 234 (12), 207 (7), 205 (13), 191 (12), 176 (13), 135 (100), 119 (32), 104 (11), 91 (28), 77 (87), 64 (18), 51 (58). Anal. calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$: C, 62.92; H, 4.93; N, 9.78%. Found: C, 62.75; H, 4.85; N, 9.67%.

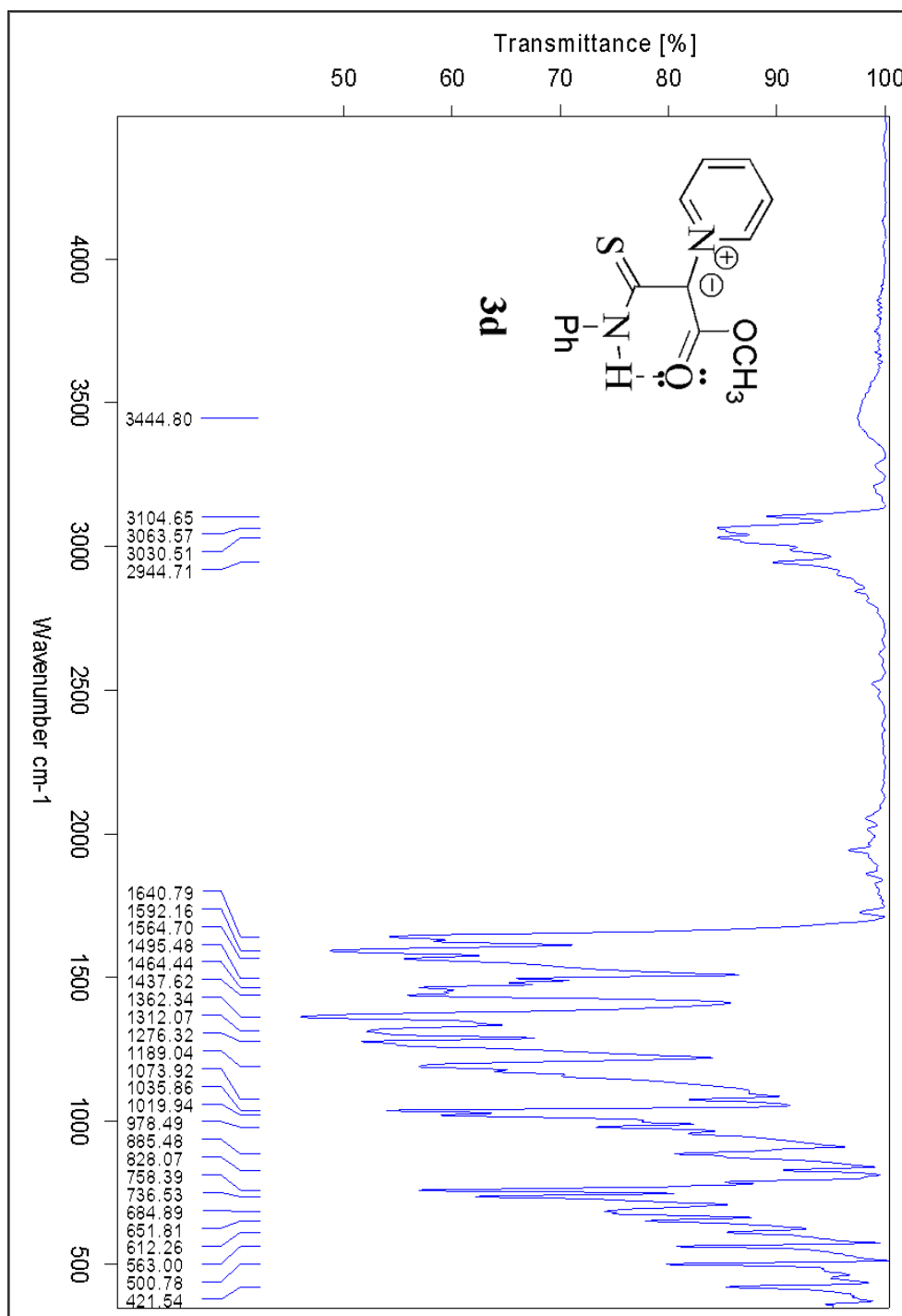


Figure 13. IR 3d.

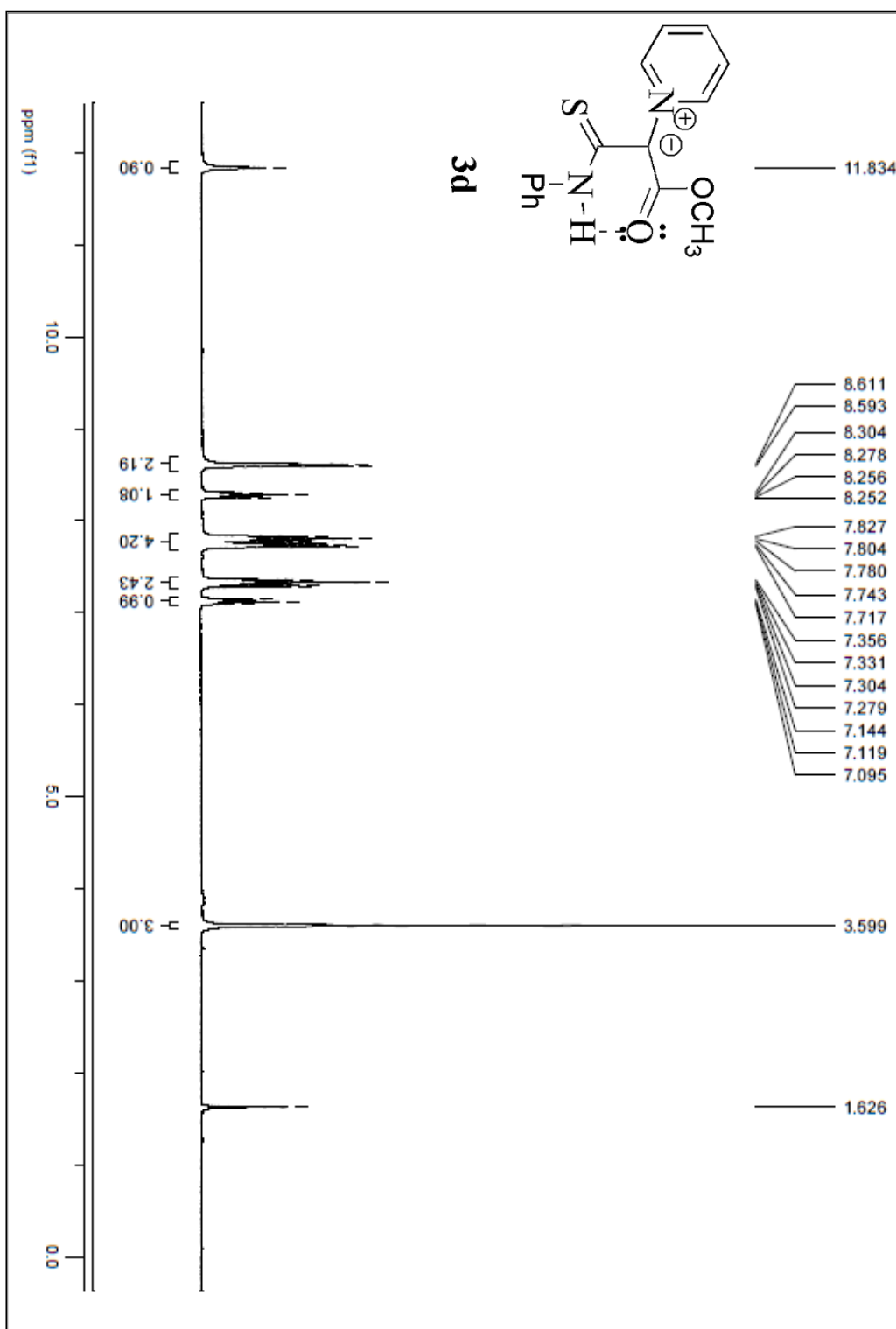


Figure 14. ^1H NMR **3d**.

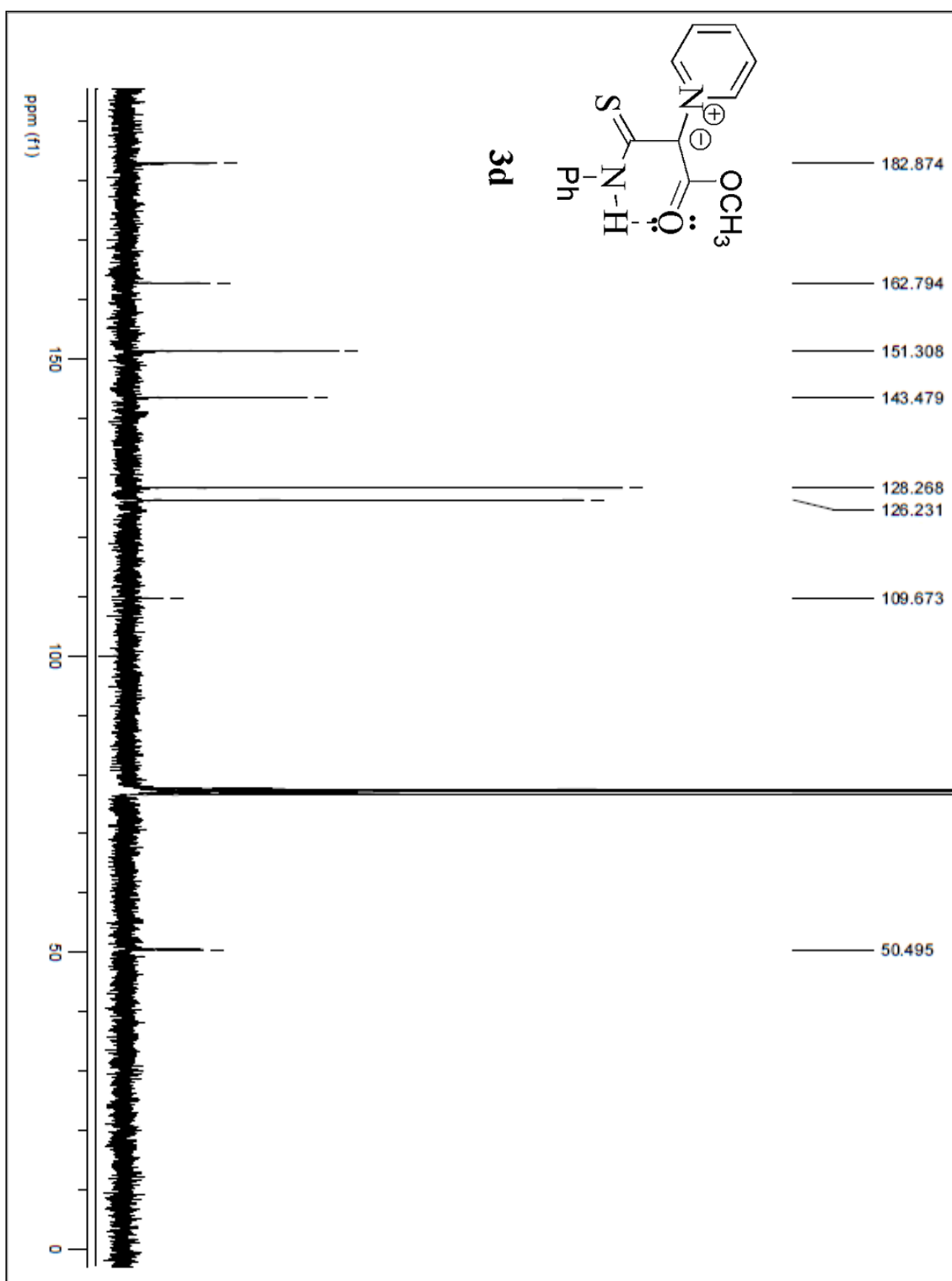


Figure 15. ¹³C NMR 3d.

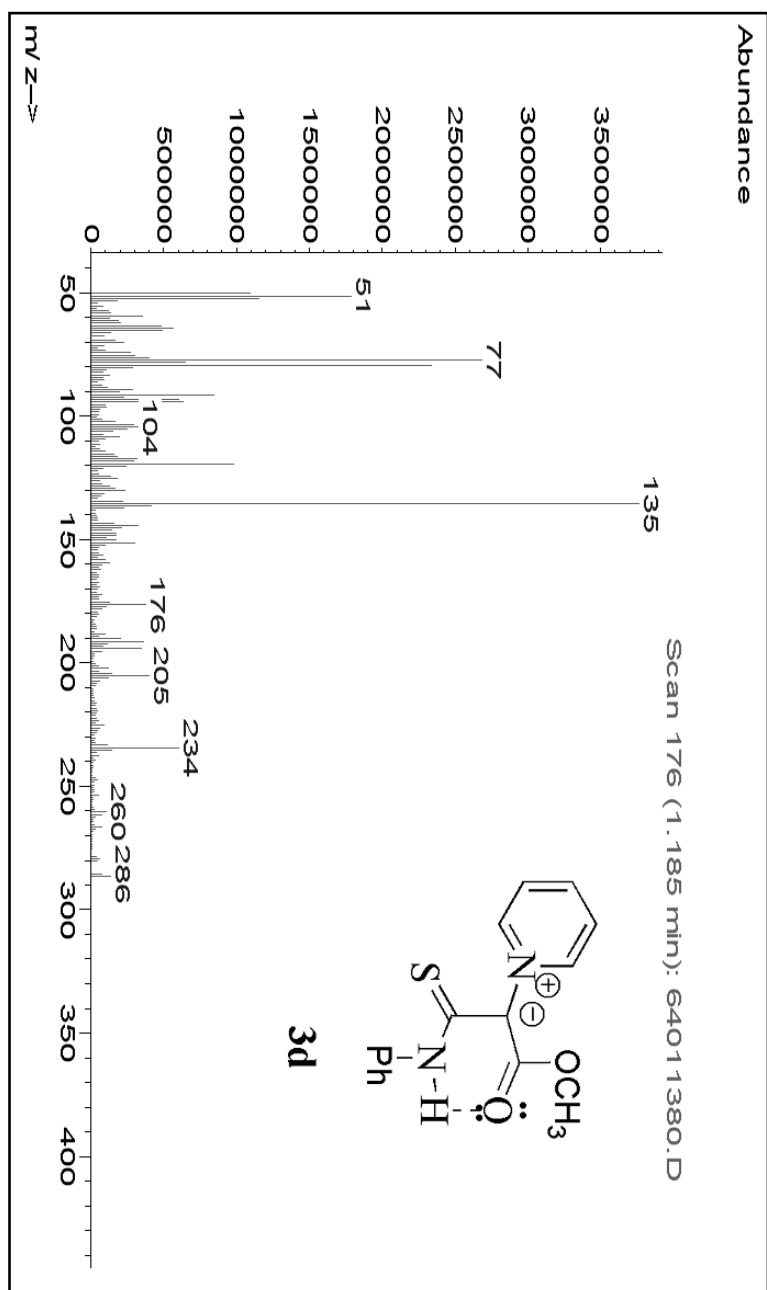


Figure 16. Mass 3d.

1-(Methylamino)-3-oxo-3-phenyl-2-(pyridin-1-ium-1-yl)-1-thioxopropan-2-ide (3e). Russet brown crystals; yield: 90%. mp 95 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3493 (NH), 1639 (C=O), 1619 (C=N). ^1H NMR (400 MHz, DMSO- d_6): 12.16 (q, 1H, NH, $^3J_{\text{H-H}}=4$ Hz), 8.83 (d, 2H, $\text{H}_{\alpha\text{-py}}$, $^3J_{\text{H-H}}=8$ Hz), 8.32 (t, 1H, $\text{H}_{\gamma\text{-py}}$, $^3J_{\text{H-H}}=8$ Hz), 7.79 (t, 2H, $\text{H}_{\beta\text{-py}}$, $^3J_{\text{H-H}}=8$ Hz), 7.12-7.08 (m, 5H, Ar), 3.10 (d, 3H, CH_3 , $^3J_{\text{H-H}}=4$ Hz). ^{13}C NMR (100 MHz, DMSO- d_6): 183.34 (C=S), 163.83 (C=O), 151.29 (C=N), 144.67, 141.49, 127.75, 127.68, 126.15, 126.06, 112.02 (C), 31.16 (N- CH_3). MS (m/z): 270 (M^+) (35), 269 (14), 237 (16), 191 (21), 163 (8), 118 (15), 105 (100), 77 (85), 51 (43). Anal. calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{OS}$: C, 66.64; H, 5.22; N, 10.36%. Found: C, 66.48; H, 5.04; N, 10.09%.

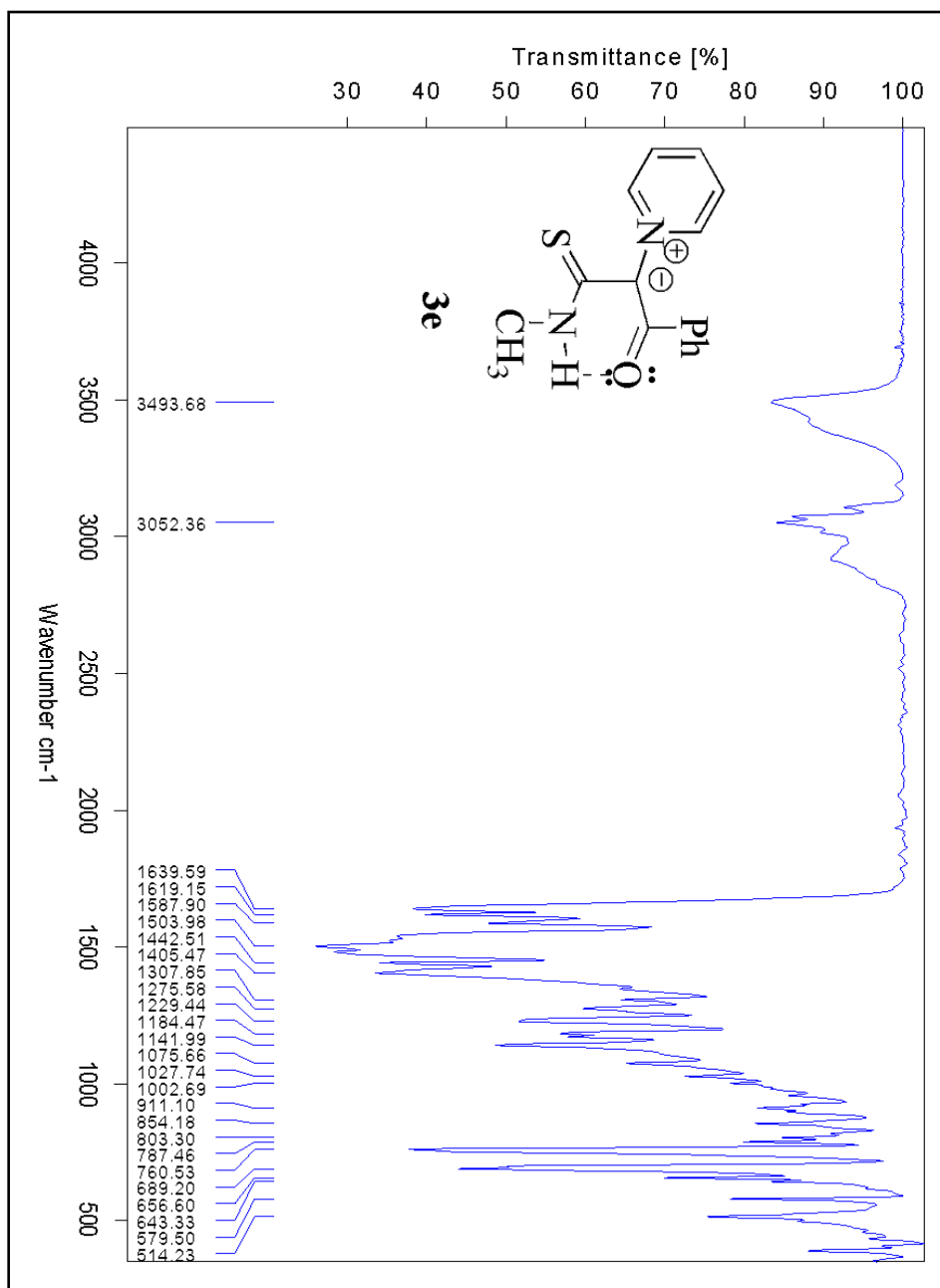


Figure 13. IR 3d.

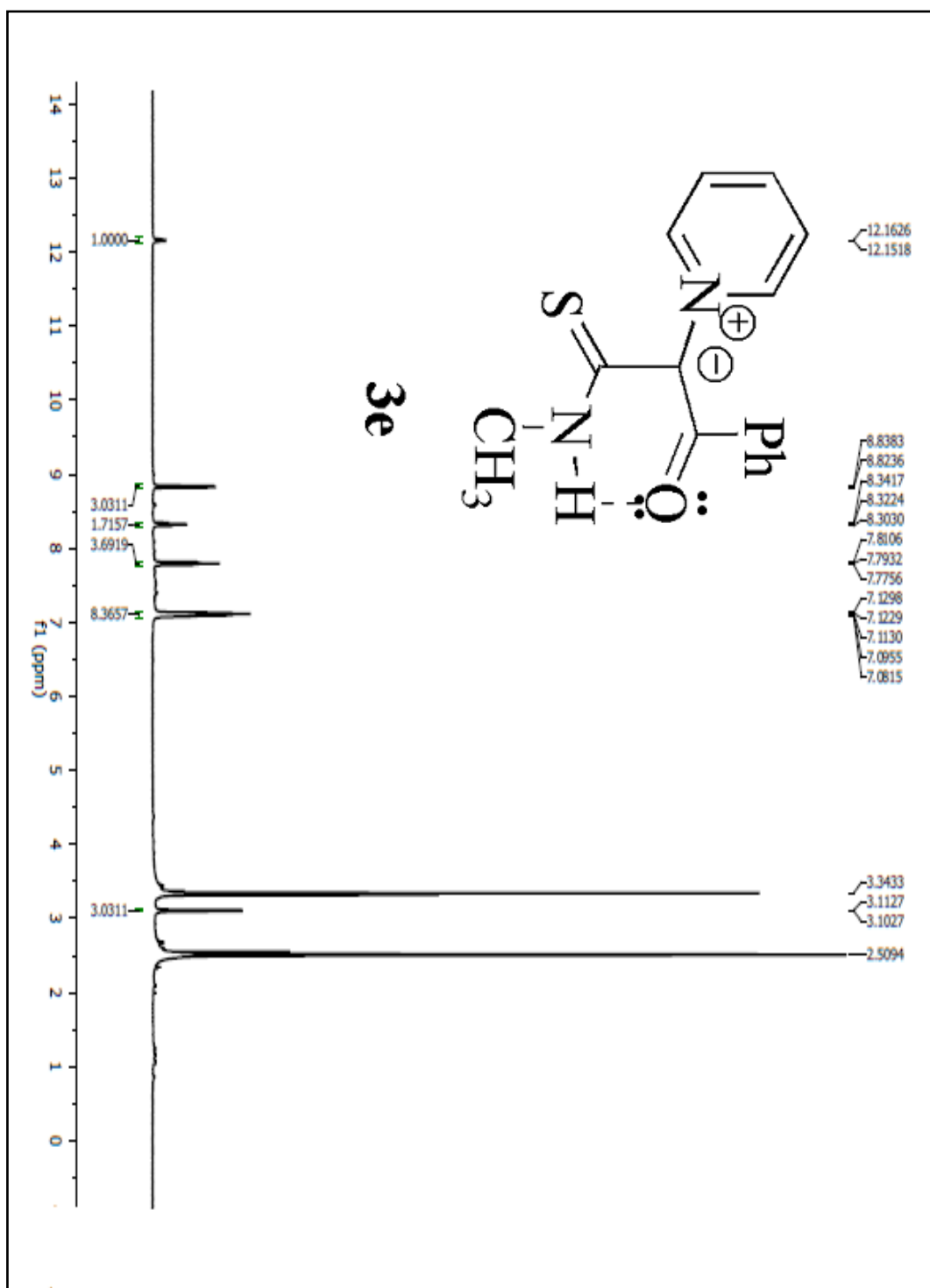


Figure 18. ¹H NMR **3e**.

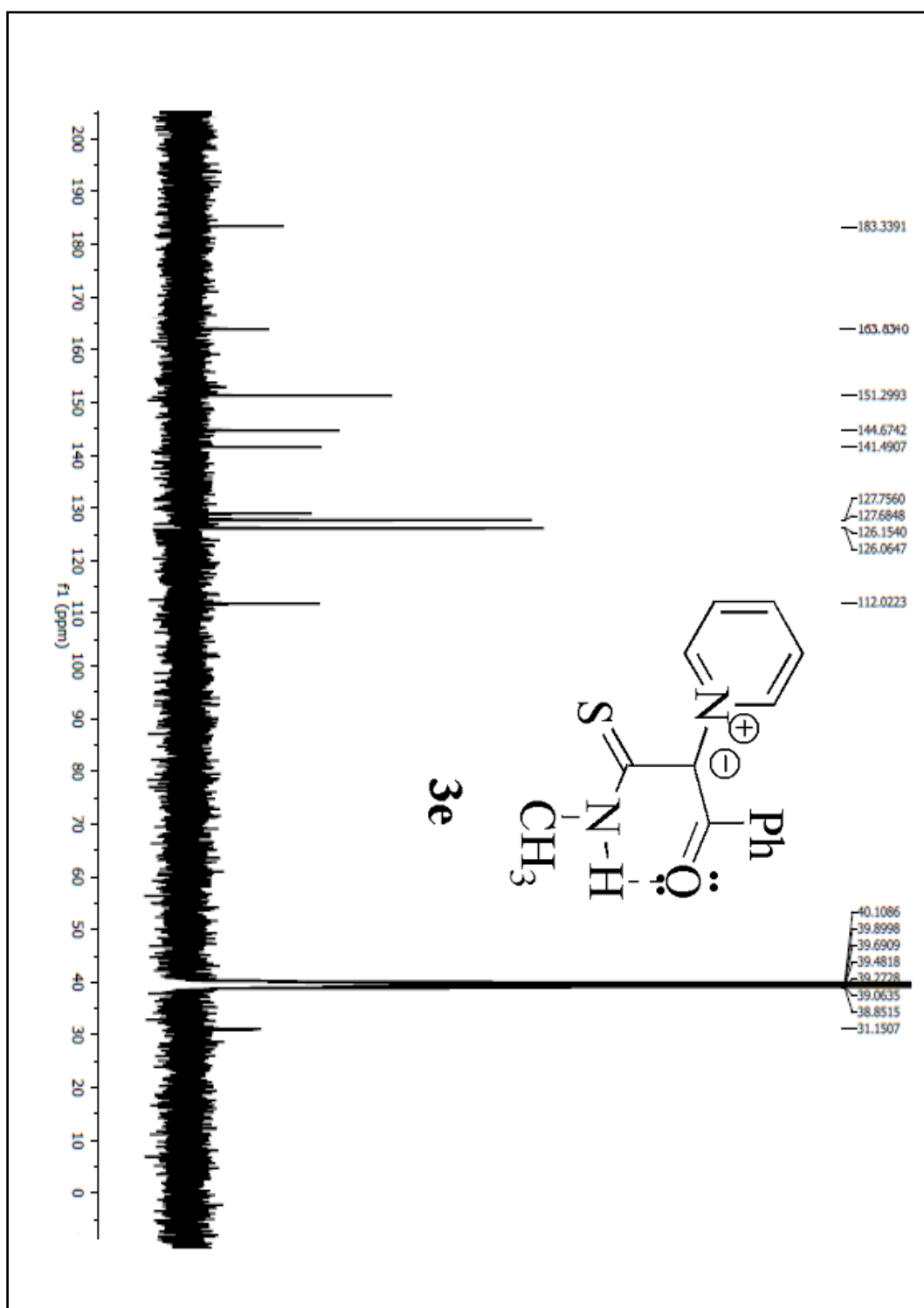


Figure 19. ¹³C NMR **3e**.

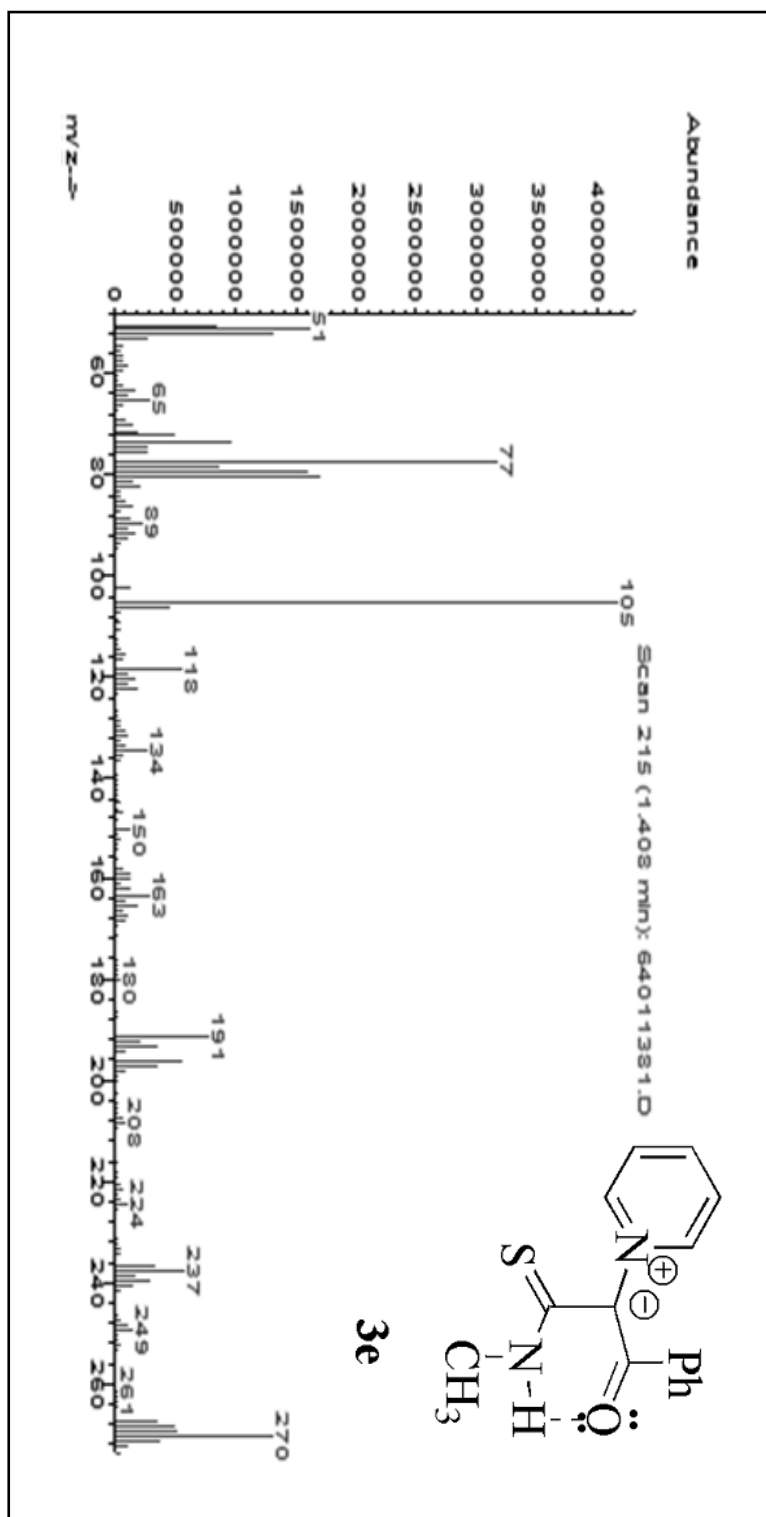


Figure 20. Mass 3e.

1-Methoxy-3-(methylamino)-1-oxo-2-(pyridin-1-ium-1-yl)-3-thioxopropan-2-ide (3f). Yellow crystals; yield: 90%. mp 174-175 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3493 (NH), 1695 (C=O), 1632 (C=N). ^1H NMR (300 MHz, DMSO- d_6): 9.70 (q, 1H, NH, $^3J_{\text{H-H}}=6$ Hz), 8.74 (d, 2H, $\text{H}_{\alpha\text{-py}}$, $^3J_{\text{H-H}}=6$ Hz), 8.47 (t, 1H, $\text{H}_{\gamma\text{-py}}$, $^3J_{\text{H-H}}=6$ Hz), 7.96 (t, 2H, $\text{H}_{\beta\text{-py}}$, $^3J_{\text{H-H}}=6$ Hz), 3.39 (s, 3H, OCH₃), 3.02 (d, 3H, N-CH₃, $^3J_{\text{H-H}}=6$ Hz). ^{13}C NMR (75 MHz, DMSO- d_6): 185.71 (C=S), 164.14 (C=O), 151.91 (C=N), 144.96, 127.15, 107.45 (C), 50.11 (OCH₃), 31.51 (N-CH₃). MS (m/z): 224 (M^+) (100), 223 (66), 191 (49), 164 (13), 113 (11), 93 (10), 80 (93), 52 (34). Anal. calcd. for C₁₀H₁₂N₂O₂S: C, 53.55; H, 5.39; N, 12.49%. Found: C, 51.08; H, 5.19; N, 12.22%.

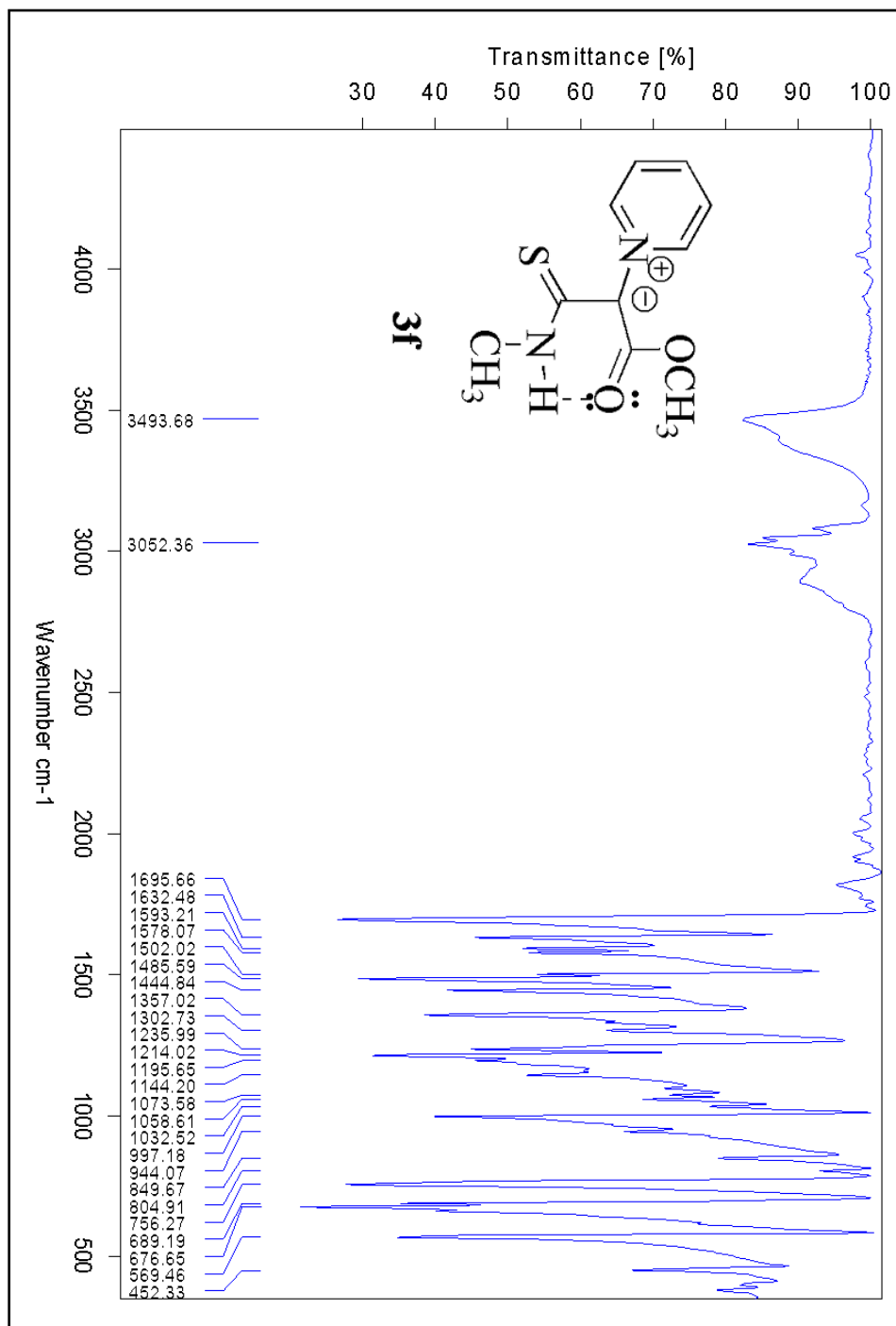


Figure 21. IR 3f.

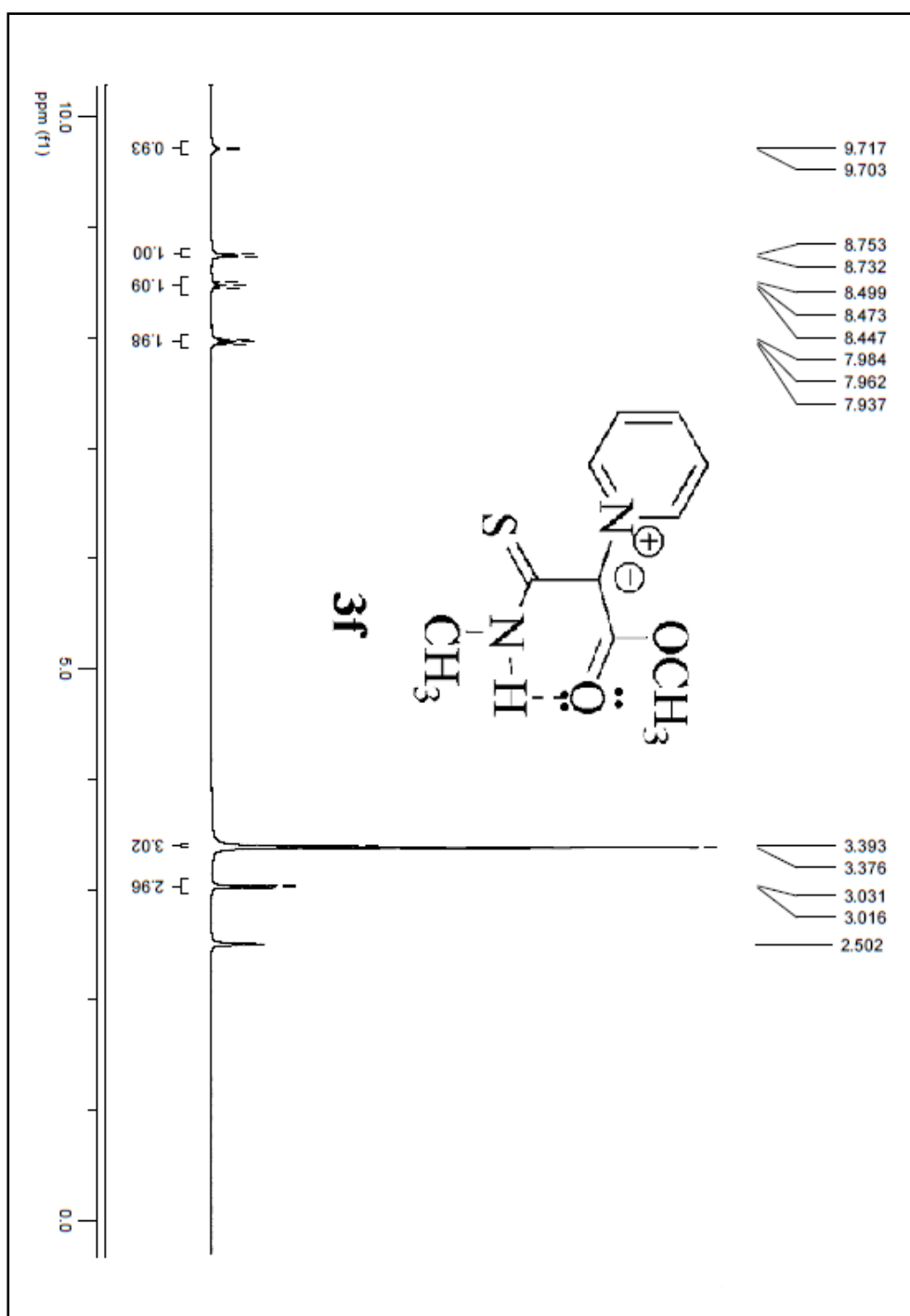


Figure 22. ^1H NMR **3f**.

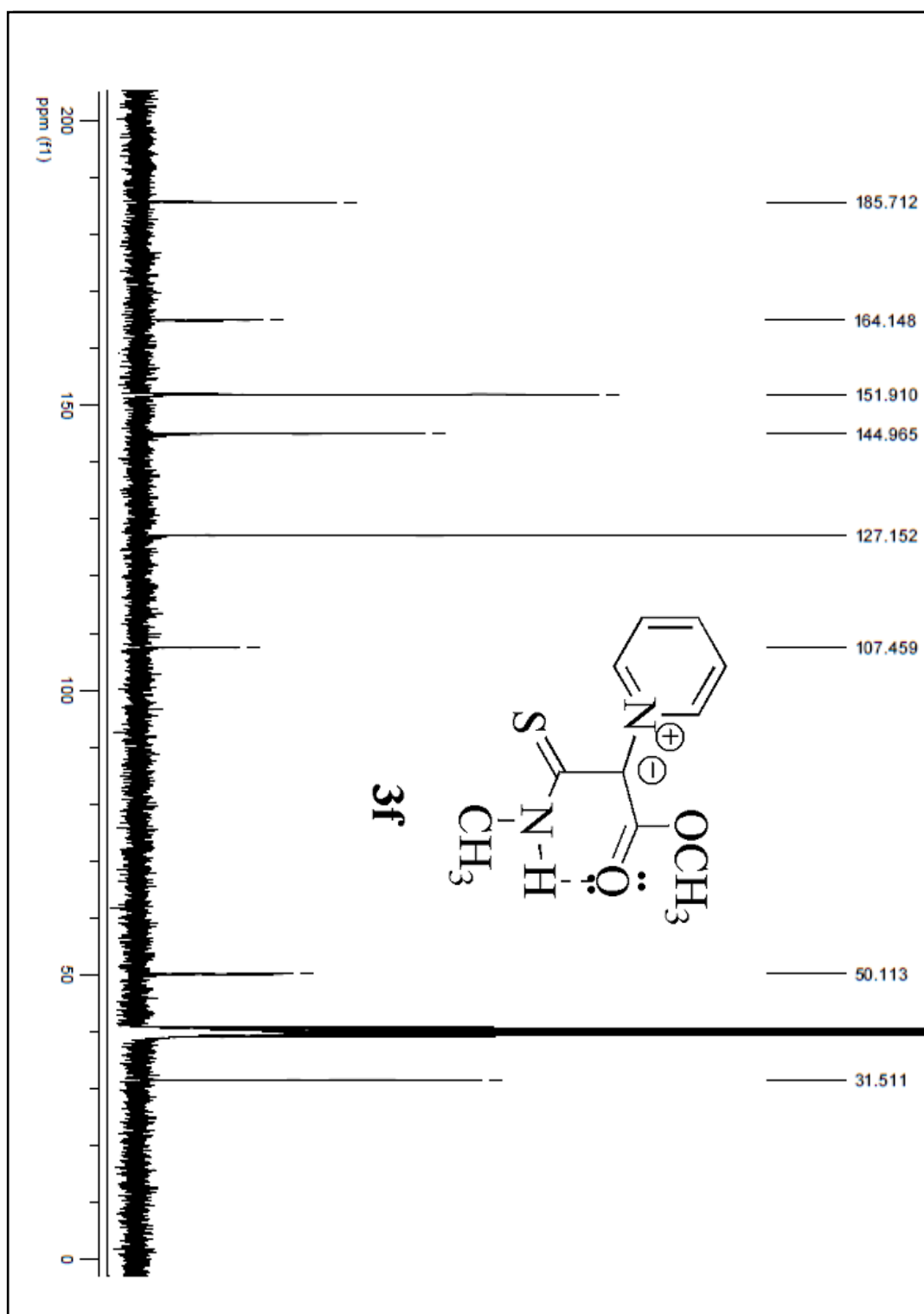


Figure 23. ¹³C NMR 3f.

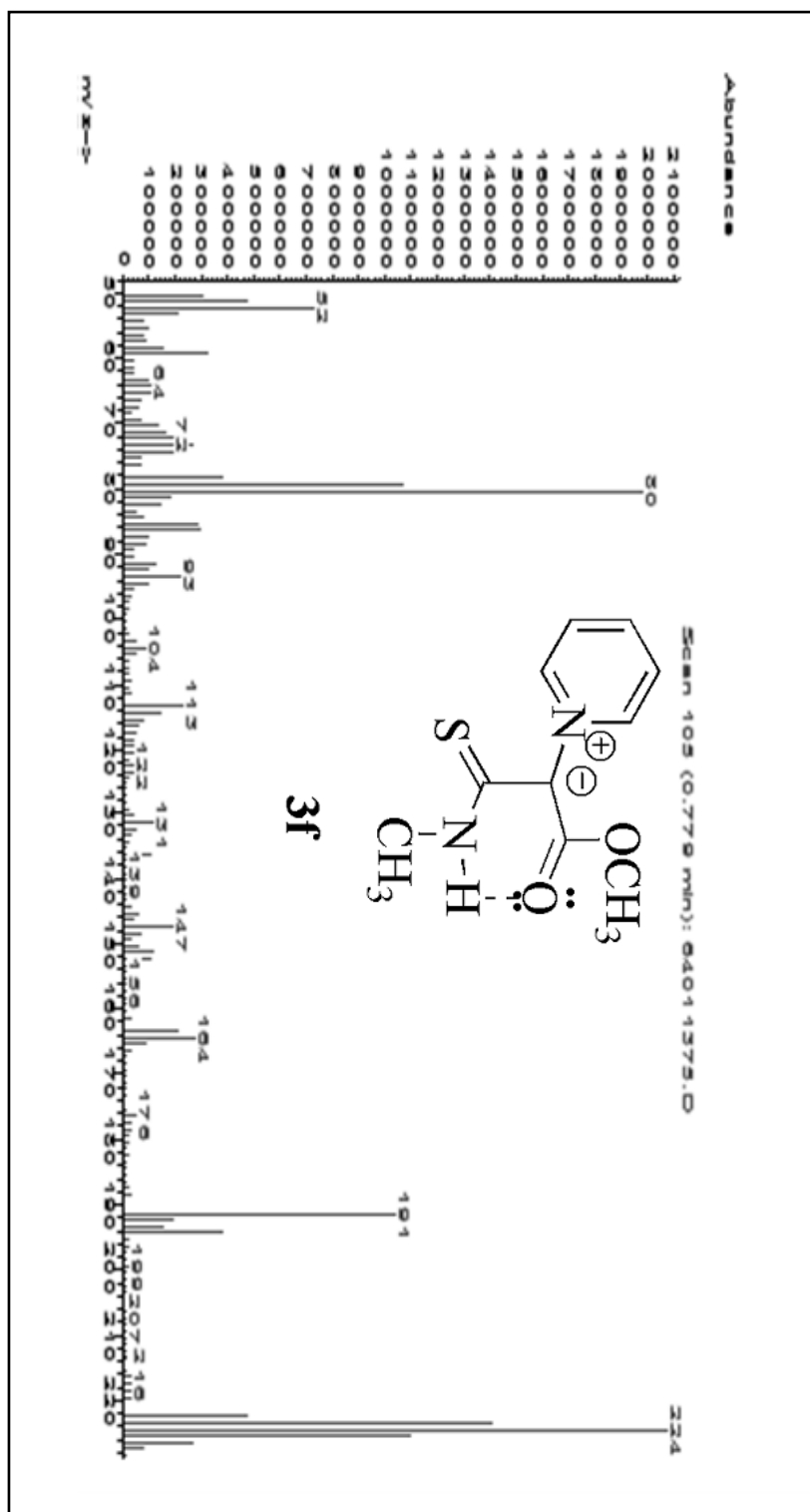


Figure 24. Mass **3f**.

2-(Isoquinolin-2-ium-2-yl)-1,3-dioxo-1-phenyl-3-(phenylamino)propan-2-ide (5a). Orange crystals; yield: 96%. mp 191-193 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3411 (broad, NH), 1632, 1590 (C=O), 1536, 1501 (C=C). ^1H NMR (300 MHz, CDCl_3): 12.57 (s, 1H, NH), 9.20 (s, 1H, H-C $_{\alpha}$ =N), 8.19-6.99 (m, 16H, Ar). ^{13}C NMR (75 MHz, CDCl_3): 178.52, 164.03 (C=O), 152.21, 140.65, 140.47, 140.03, 136.01, 130.55, 129.65, 128.78, 128.73, 128.37, 127.16, 127.02, 126.82, 123.37, 122.43, 120.07, 119.06, 116.06. MS (m/z): 366 (M^+) (2), 363 (59), 347 (8), 247 (41), 204 (12), 144 (10), 129 (60), 105 (100), 91 (10), 77 (93), 51 (35). Anal. calcd. for $\text{C}_{24}\text{H}_{18}\text{N}_2\text{O}_2$: C, 78.67; H, 4.95; N, 7.65%. Found: C, 78.49; H, 4.80; N, 7.37%.

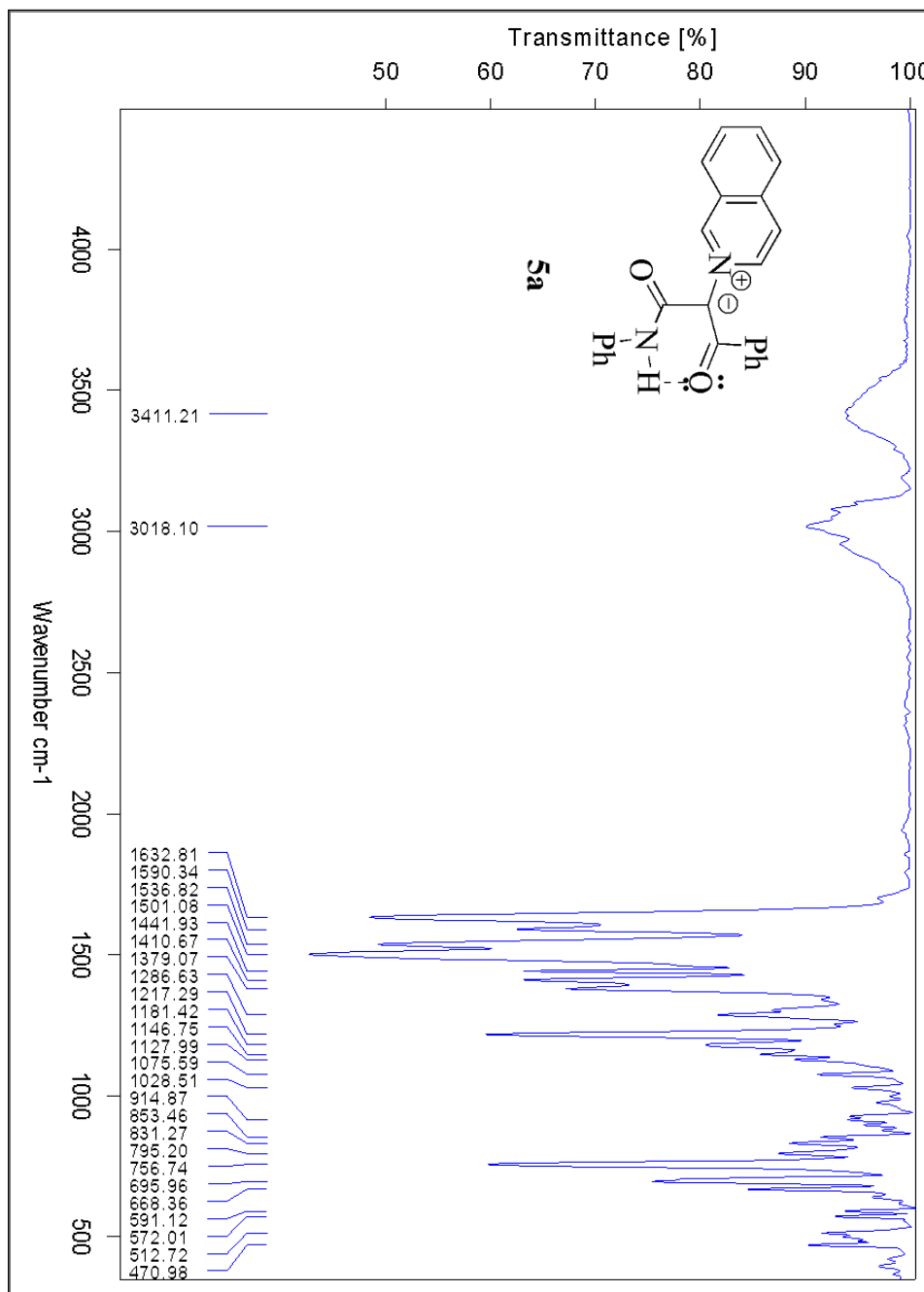


Figure 25. IR 5a.

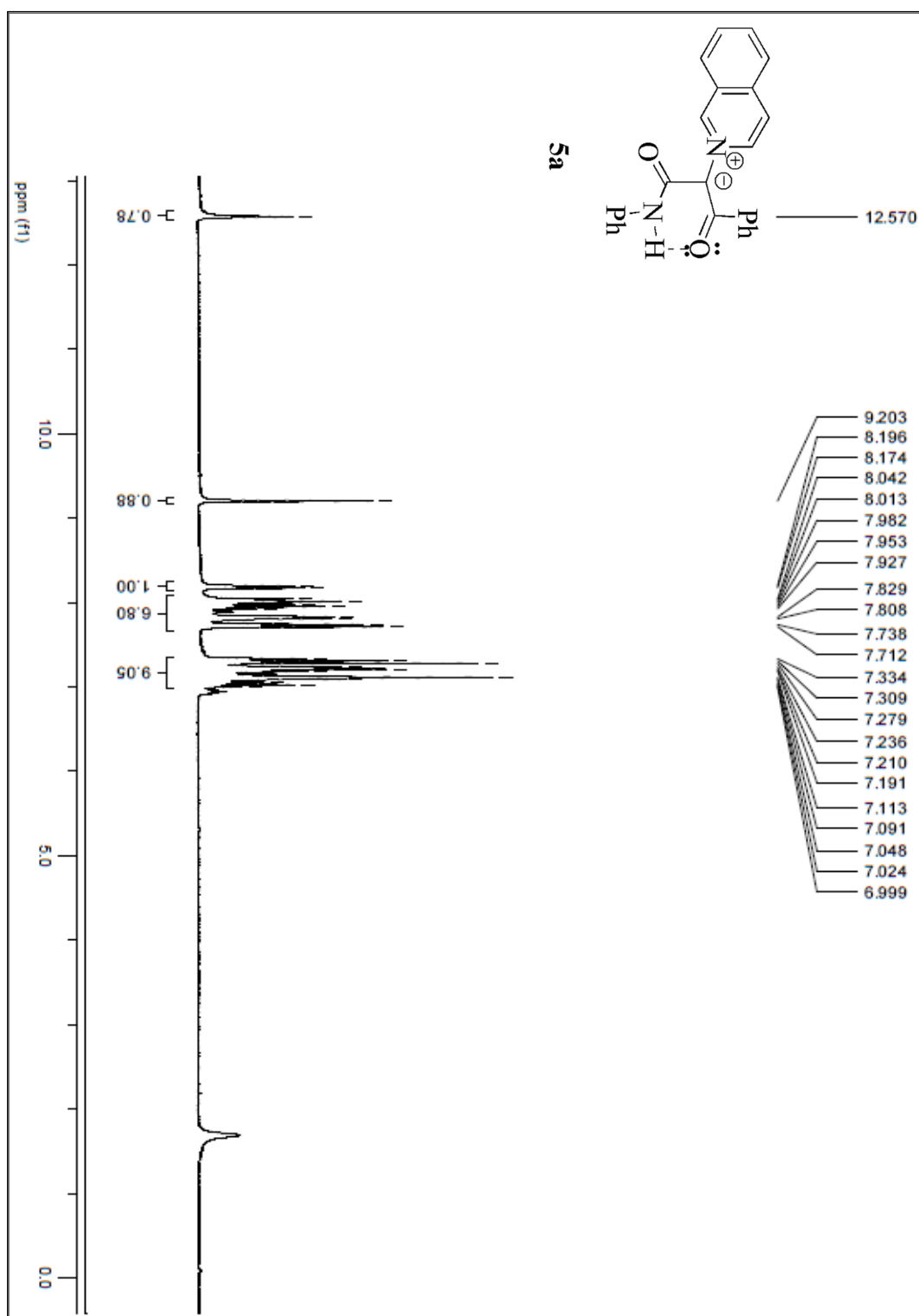


Figure 26. $^1\text{H NMR}$ 5a.

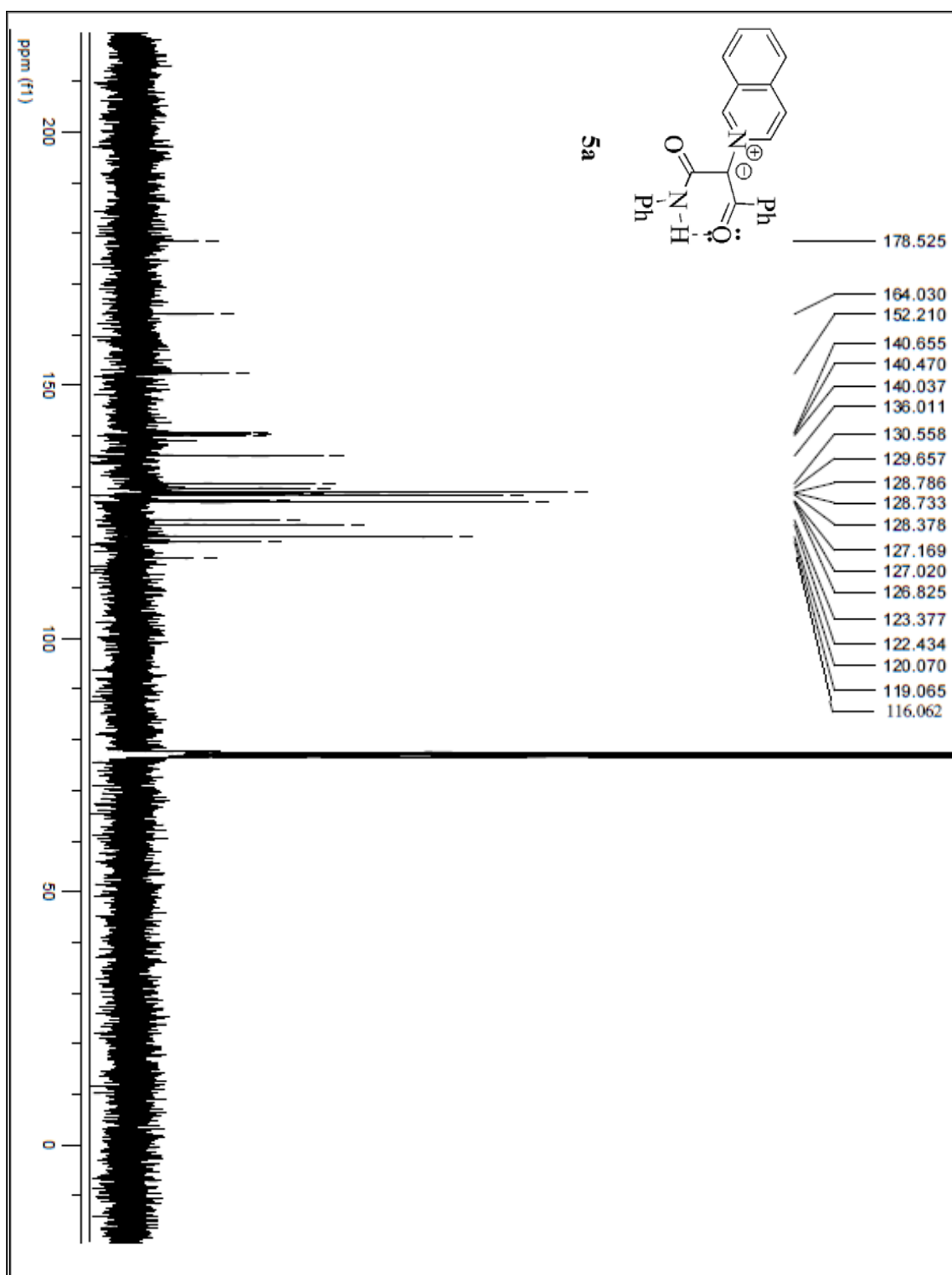


Figure 27. ^{13}C NMR 5a.

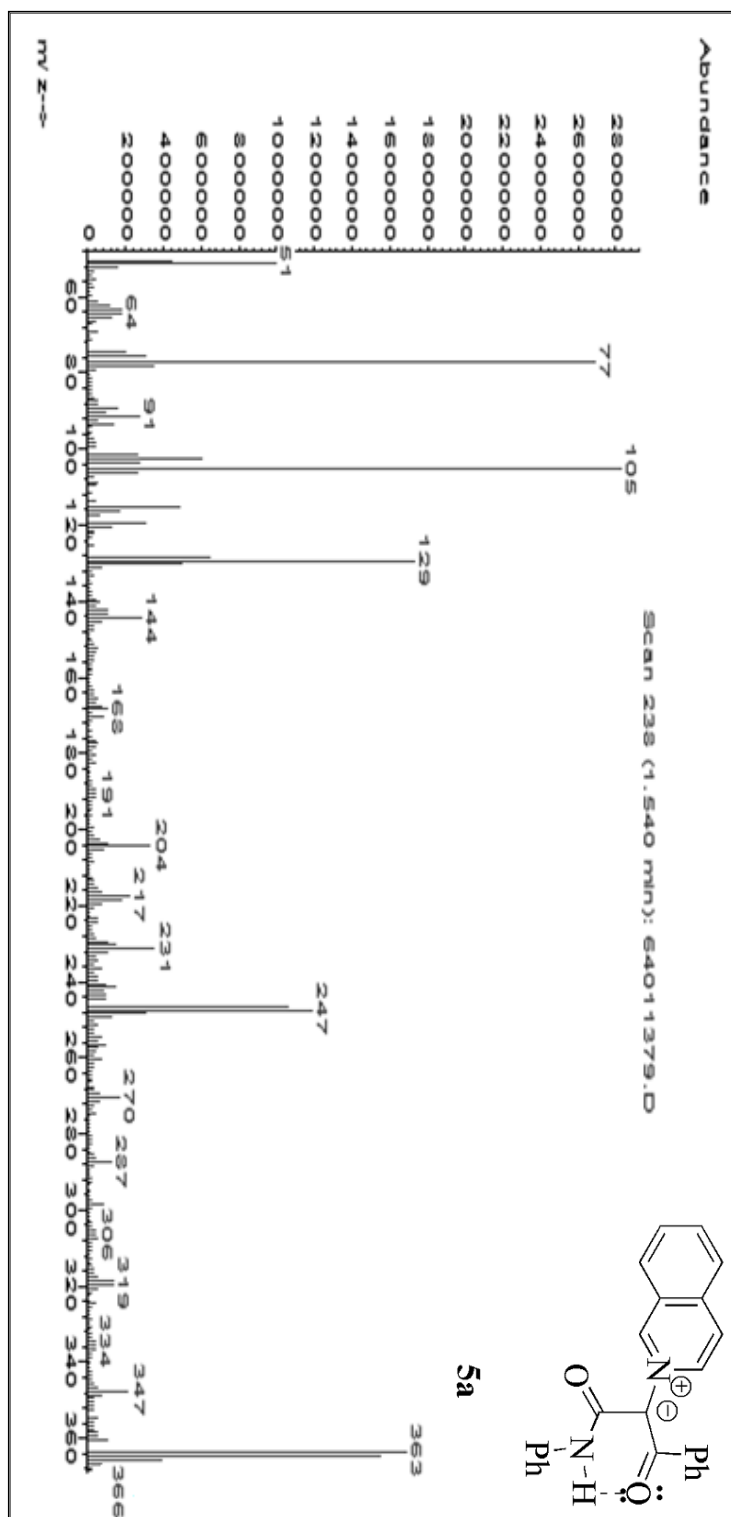
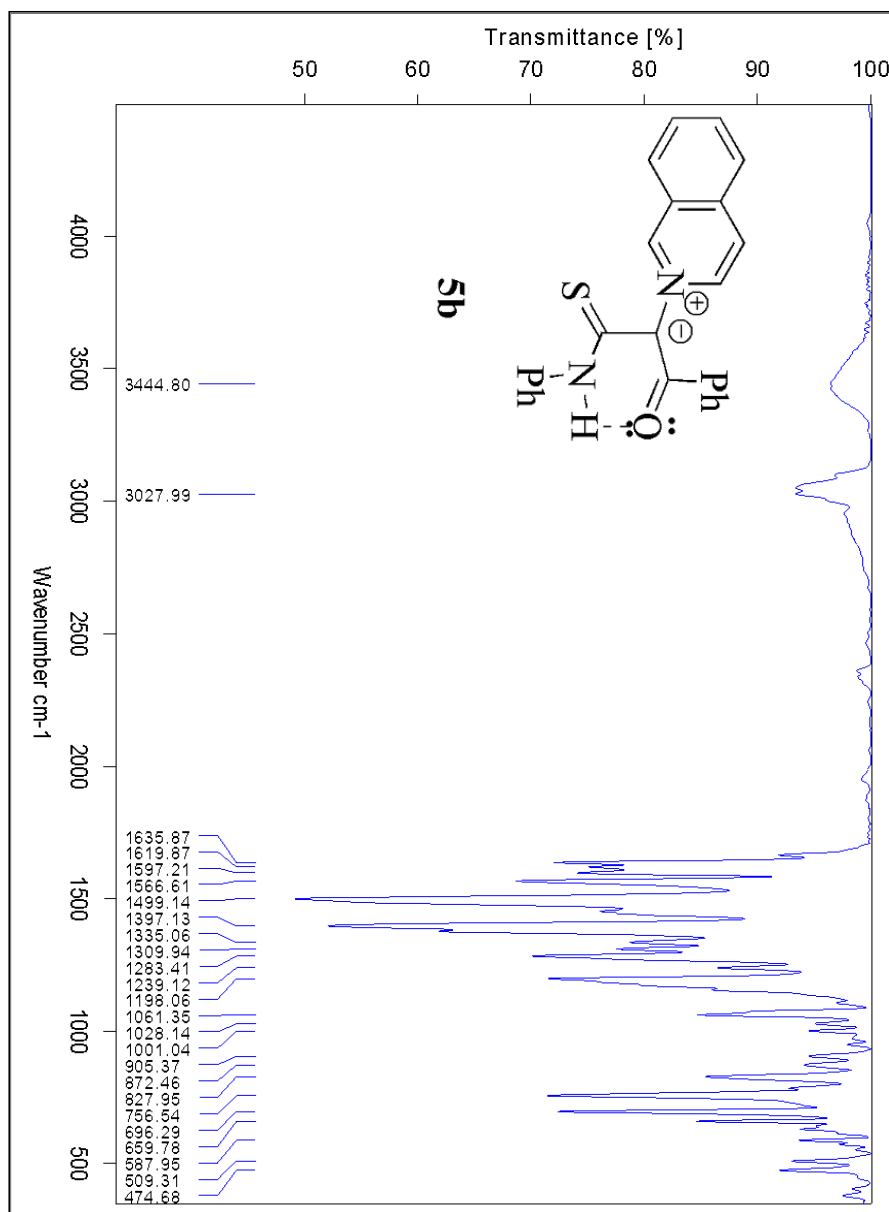


Figure 28. Mass 5a.

2-(Isoquinolin-2-ium-2-yl)-1-oxo-1-phenyl-3-(phenylamino)-3-thioxopropan-2-ide (5b). Brown crystals; yield: 95%. mp 149-151 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3444 (broad, NH), 1635 (C=O), 1619, 1597 (C=C). ^1H NMR (300 MHz, DMSO- d_6): 14.61 (s, 1H, NH), 10.09 (s, 1H, H-C $_{\alpha}$ =N), 8.58-6.80 (m, 16H, Ar). ^{13}C NMR (75 MHz, DMSO- d_6): 184.80 (C=S), 178.14 (C=O), 156.64, 142.14, 141.53, 141.36, 137.28, 137.02, 130.93, 130.66, 129.94, 129.31, 128.83, 128.61, 128.24, 127.37, 127.24, 126.62, 124.05, 123.33. MS (m/z): 382 (M^+) (5), 380 (18), 362 (12), 351 (17), 298 (13), 241 (9), 129 (15), 105 (100), 77 (94), 51 (23). Anal. calcd. for $\text{C}_{24}\text{H}_{18}\text{N}_2\text{OS}$: C, 75.37; H, 4.74; N, 7.32%. Found: C, 75.14; H, 4.55; N, 7.01%.



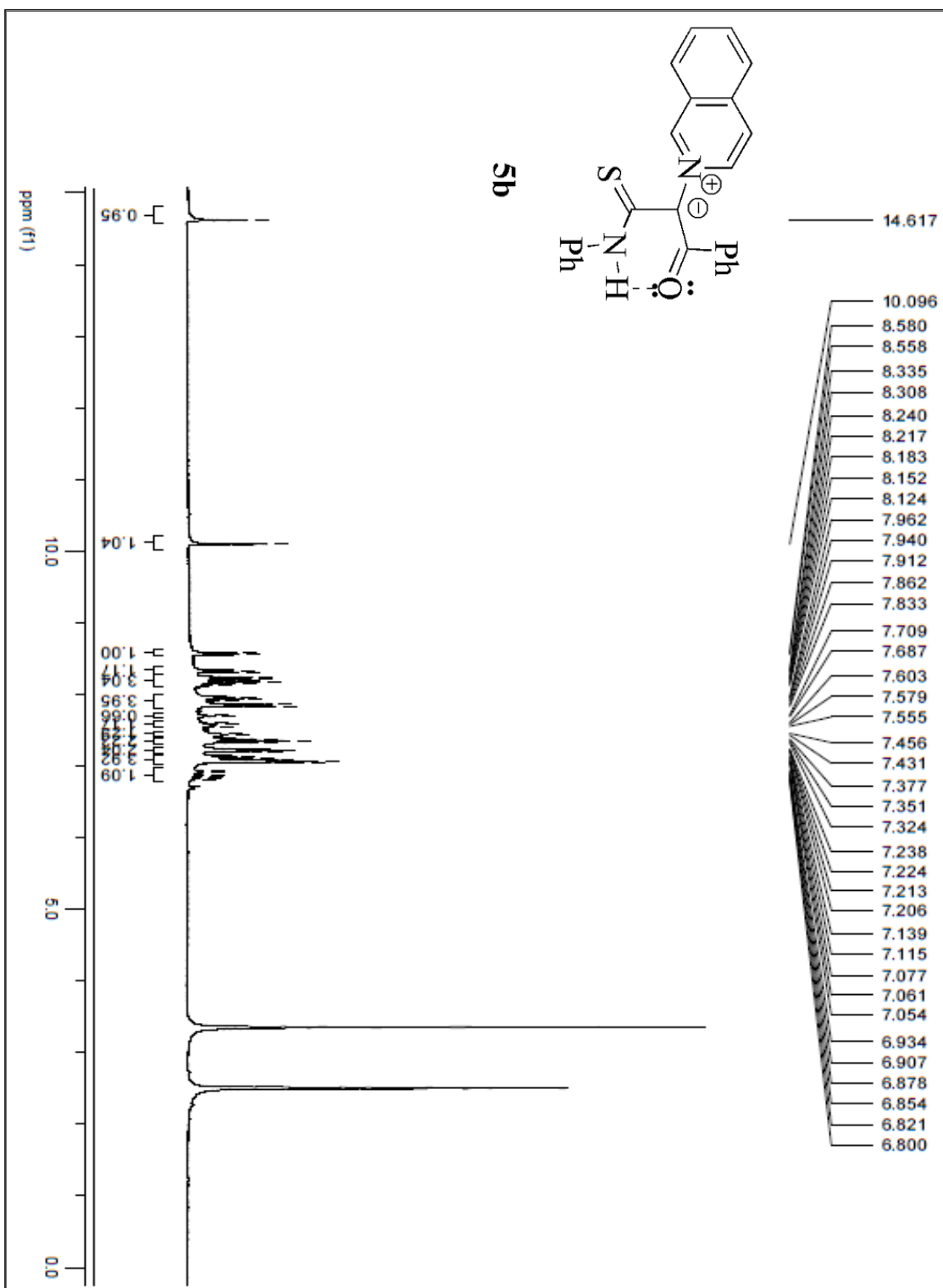


Figure 30. $^1\text{H NMR}$ 5b.

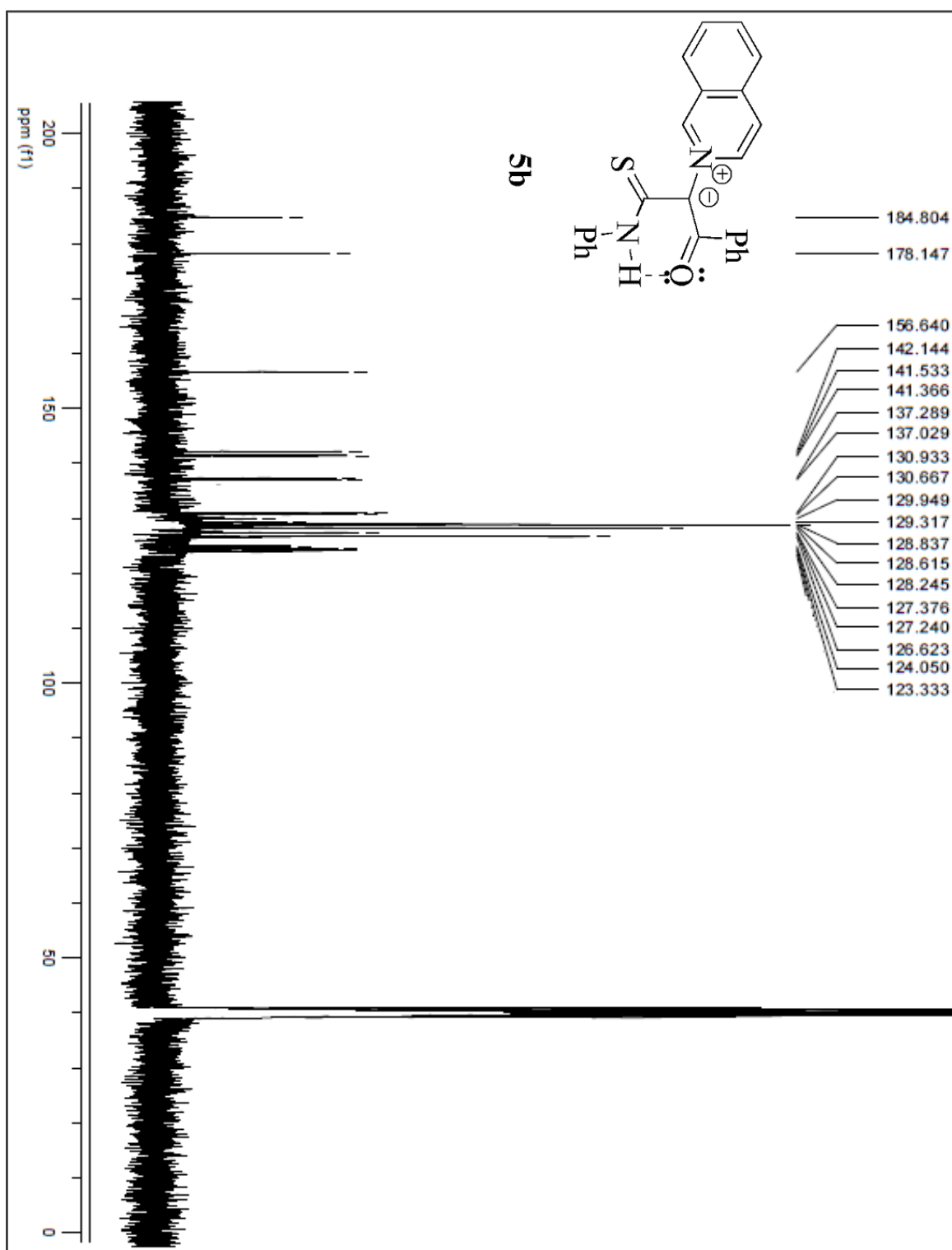


Figure 31. ^{13}C NMR **5b**.

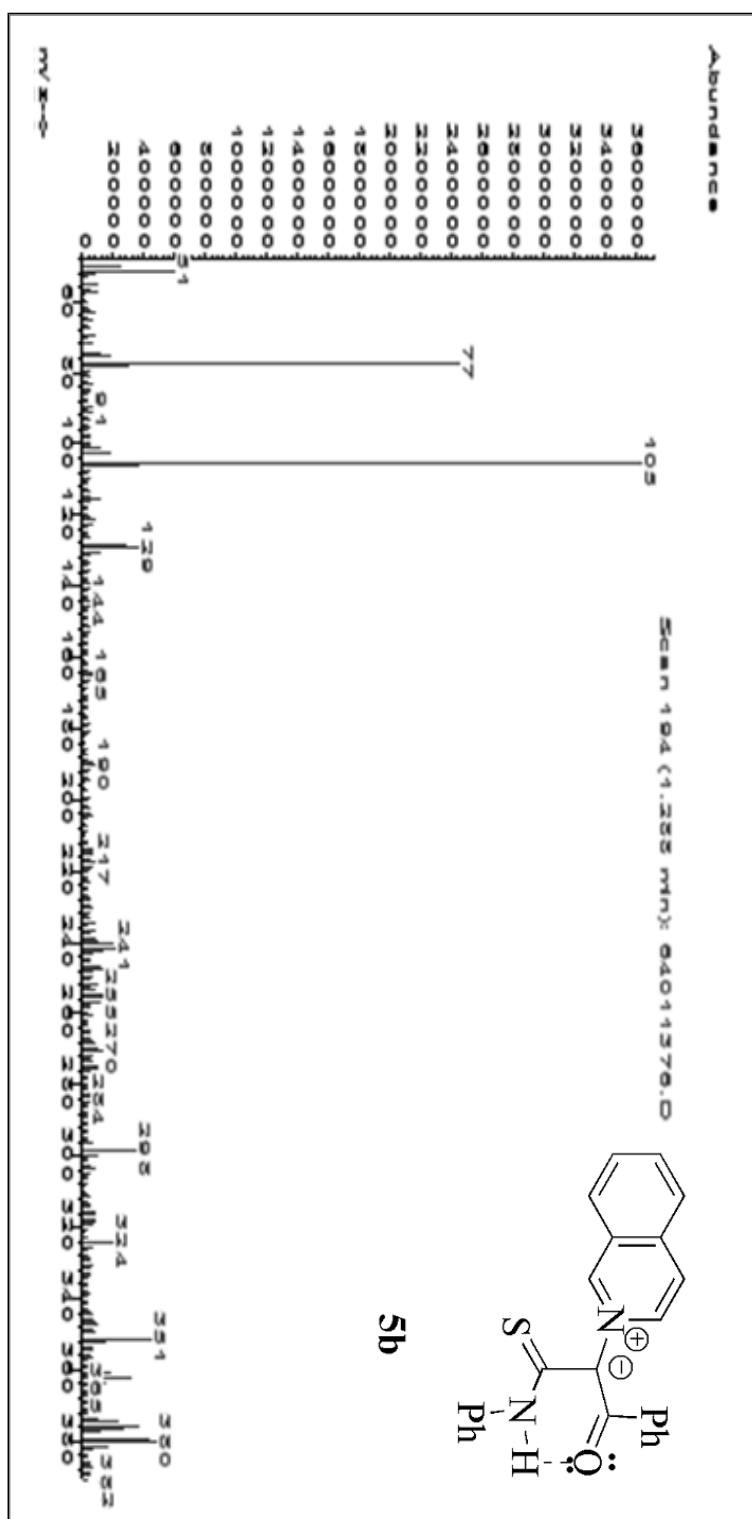


Figure 32. Mass 5b.

2-(Isoquinolin-2-ium-2-yl)-1-methoxy-1,3-dioxo-3-(phenylamino)propan-2-ide (5c). Orange crystals; yield: 93%. mp 135 °C; IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 3443 (broad, NH), 1638, 1617 (C=O), 1581, 1526 (C=C). ^1H NMR (300MHz, CDCl_3): 10.72 (s, 1H, NH), 9.28 (s, 1H, H-C $_{\alpha}$ =N), 8.30-6.94 (m, 11H, Ar), 3.65 (s, 3H, OCH $_3$). ^{13}C NMR (75MHz, CDCl_3): 177.53, 164.46 (C=O), 152.88, 141.04, 140.47, 136.13, 135.53, 130.16, 129.75, 128.72, 127.48, 126.74, 123.31, 121.72, 119.39, 98.20, 50.19 (OCH $_3$). MS (m/z): 320 (M^+) (9), 260 (8), 228 (19), 201 (87), 170 (17), 143 (100), 130 (59), 119 (86), 102 (18), 91 (64), 77 (26), 64 (40), 51 (26). Anal. calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_3$: C, 71.24; H, 5.03; N, 8.74 %. Found: C, 70.94; H, 4.88; N, 8.46%.

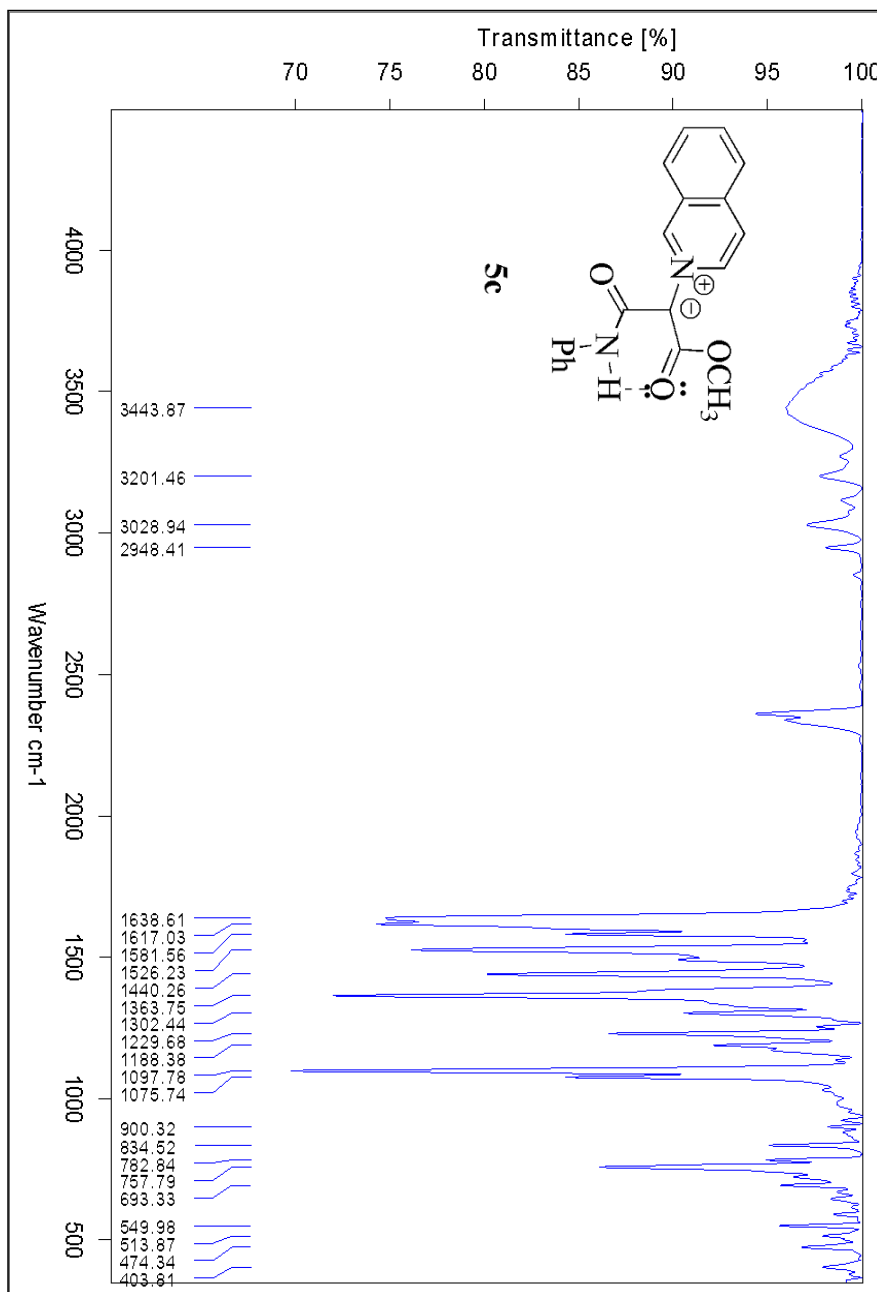
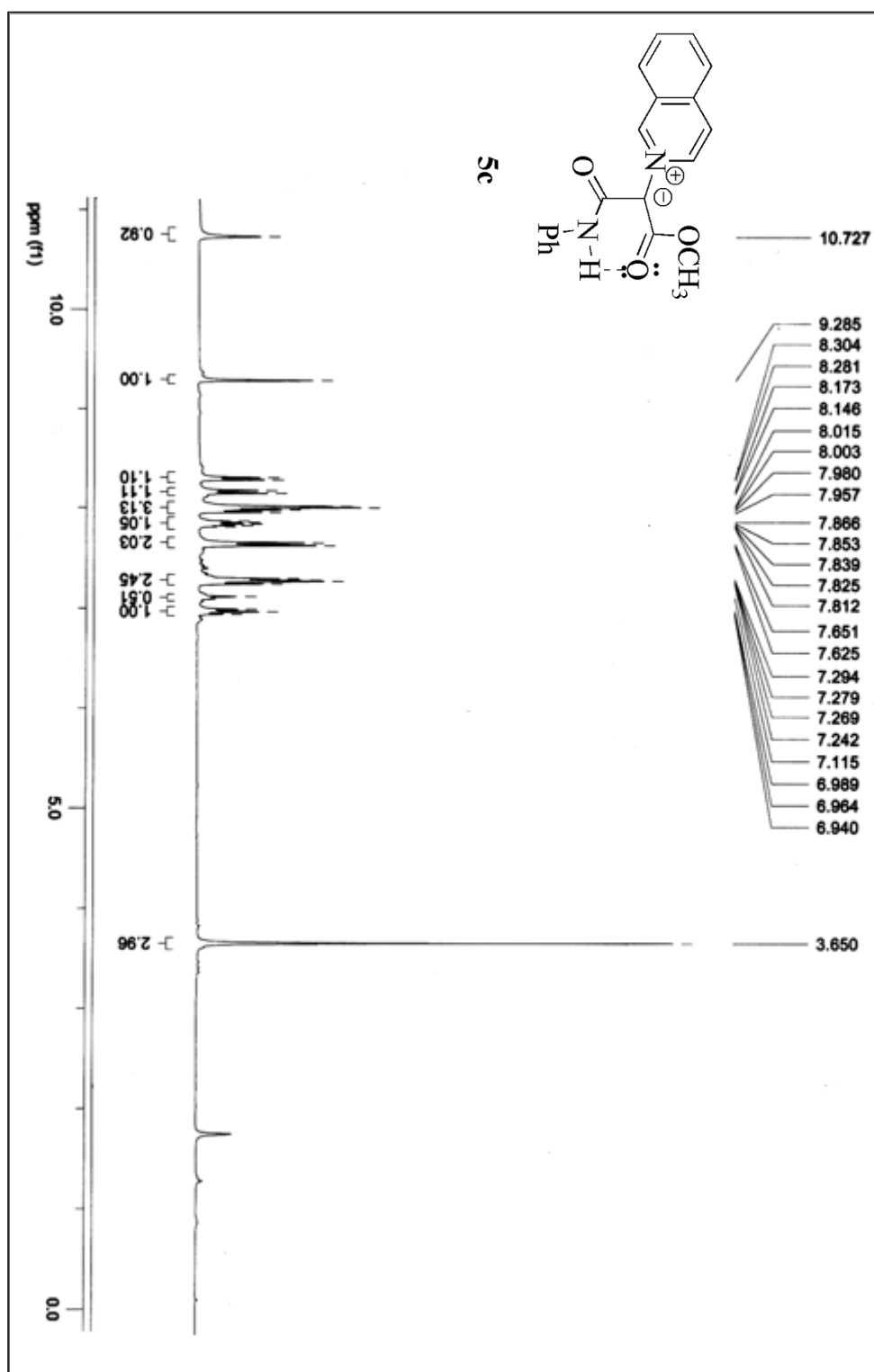


Figure 33. IR 5c.



Figure

NMR 5c.

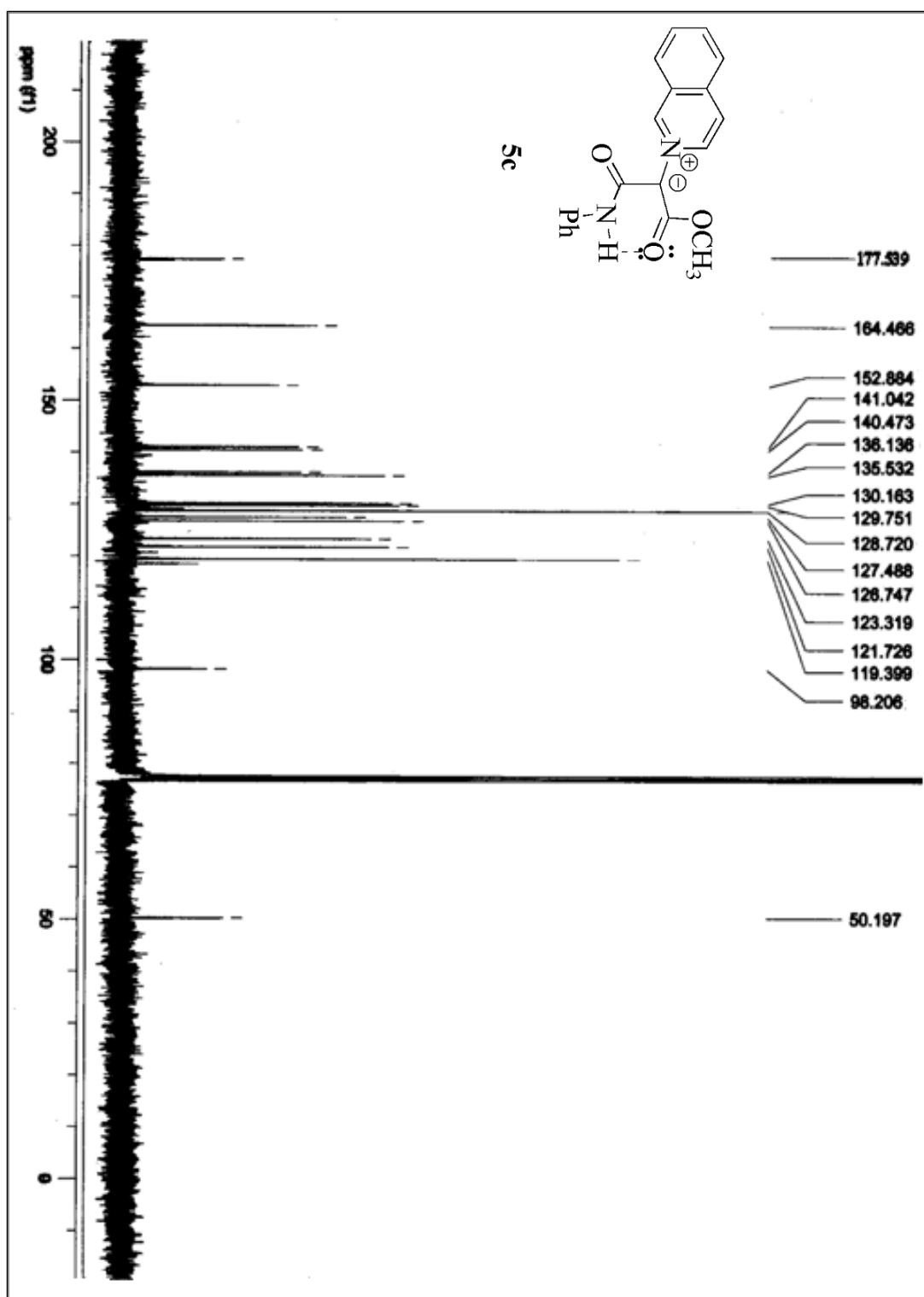


Figure 35. ^{13}C NMR 5c.

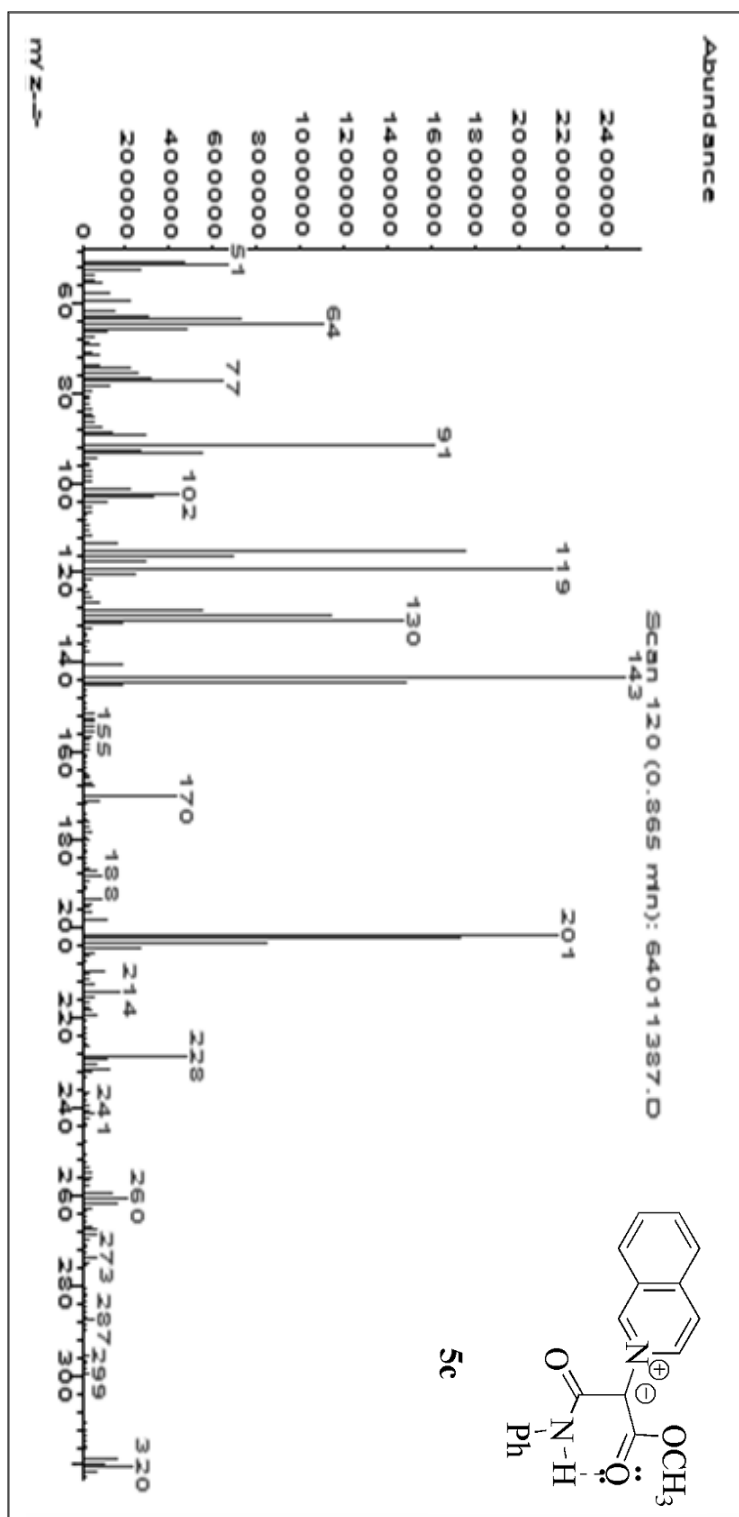


Figure 36. Mass 5c.