Total synthesis of siphonazole and its *O*-methyl derivative, structurally unusual bis-oxazole natural products

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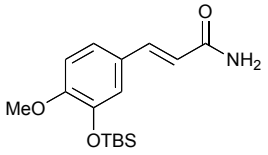
ELECTRONIC SUPPLEMENTARY INFORMATION

Methyl 2-diazo-3-oxobutanoate

Prepared by the literature method.[1]

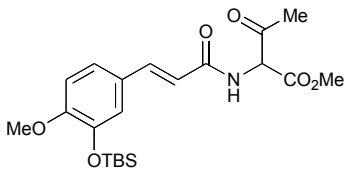
***(E)*-3-(3-*tert*-Butyldimethylsiloxy-4-methoxyphenyl)acrylamide 4a**



3-Hydroxy-4-methoxycinnamic acid **3a** (5.0 g, 25.7 mmol) was dissolved in DMF (30 mL), *tert*-butyldimethylchlorosilane (8.92 g, 59.2 mmol) and imidazole (7.30 g, 111 mmol) were added and the mixture stirred at room temperature for 20 h. The mixture was poured into water (50 mL), extracted with ether (2 × 100 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was dissolved in dichloromethane (80 mL), cooled to 0 °C and treated with oxalyl chloride (2.6 mL, 30.8 mmol) and DMF (2 drops). The mixture was stirred for 1 h at this temperature before ammonia (gas) was bubbled through for 45 min. Saturated aqueous sodium hydrogen carbonate (40 mL) was added, the layers separated and the aqueous layer extracted with dichloromethane (2 × 50 mL), the combined organic layers dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification by chromatography (light petroleum: ethyl acetate 1:1 + 0.5% triethylamine) gave the *title compound* **4a** as a colourless solid (6.5 g, 82%); R_f = 0.22 (light petroleum: ethyl acetate 1:1); mp 161-163 °C; (Found: C, 62.4; H, 8.1; N, 4.5. $C_{16}H_{25}NO_3Si$ requires C, 62.5; H, 8.2; N, 4.6%); (Found: MH^+, 308.1683. $C_{16}H_{26}NO_3Si$ requires 308.1676); ν_{max} ($CHCl_3$)/cm^{-1} 3528, 3412 2931, 1676, 1628, 1587, 1376, 1275, 1139, 983; δ_H (400 MHz; $CDCl_3$) 7.51 (1H, d, *J* 15.6, ArC<u>H</u>=CH), 7.06 (1H, dd, *J* 8.3, 2.1, ArH-6), 7.02 (1H, d, *J* 2.1, ArH-2), 6.80 (1H, d, *J* 8.3, ArH-5), 6.29 (1H, d, *J* 15.6, ArCH=C<u>H</u>), 6.11 (1H, s, NH_2), 5.86 (1H, s, NH_2), 3.81 (3H, s, OMe), 0.99

(9H, s, CMe_3), 0.14 (6H, s, SiMe); δ_C (100 MHz; $CDCl_3$) 168.5 (C), 152.7 (C), 145.1 (C), 142.1 (CH), 127.5 (C), 122.8 (CH), 119.6 (CH), 117.3 (CH), 111.7 (CH), 55.4 (Me), 25.6 (Me), 18.4 (C), -4.7 (Me); *m/z* (ESI^+) 308 (MH^+, 100%).

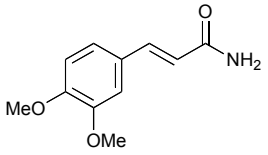
(*E*)-3-Methyl 2-((3-*tert*-butyldimethylsiloxy 4-methoxyphenyl)acrylamido)-3-oxobutanoate 5a



A solution of *(E)*-3-(3-*tert*-butyldimethylsiloxy-4-methoxyphenyl)acrylamide **4a** (2.0 g, 6.40 mmol) and dirhodium tetraacetate (71.0 mg, 0.20 mmol, 2.50 mol%) in dry dichloromethane (25 mL) was heated to reflux. A solution of methyl 2-diazo-3-oxobutanoate (1.50 g, 10.3 mmol) in dichloromethane (5 mL) was then added *via* syringe pump over a 16 h period. After the addition was complete the reaction mixture was heated under reflux for a further 4 h. After removal of the solvent under reduced pressure, and purification by chromatography (eluting ethyl acetate/light petroleum 2/3), the *title compound* **5a** was obtained as a colourless oil (2.40 g, 90%); R_f = 0.68 (light petroleum: ethyl acetate 2:3); (Found: MH^+, 422.1993. $C_{21}H_{32}NO_6Si$ requires 422.1998); ν_{max} ($CHCl_3$)/cm^{-1} 3416, 2939, 1756, 1729, 1668, 1626, 1491, 1361, 1275, 1137, 1031; δ_H (400 MHz; $CDCl_3$) 7.53 (1H, d, *J* 15.6, ArC<u>H</u>=CH), 7.08 (1H, dd, *J* 8.3, 2.1, ArH-6), 7.04 (1H, d, *J* 2.1, ArH-2), 6.82 (1H, d, *J* 8.3, ArH-5), 6.72 (1H, d, *J* 6.4, NH), 6.33 (1H, d, *J* 15.6, ArCH=C<u>H</u>), 5.40 (1H, d, *J* 6.4, CH), 3.84 (3H, s, OMe), 3.83 (3H, s, OMe), 2.43 (3H, s, Me), 1.01 (9H, s, CMe_3), 0.17 (6H, s, $SiMe_2$); δ_C (100 MHz; $CDCl_3$) 198.7 (C), 166.7 (C), 165.7 (C), 152.9 (C), 145.1 (CH), 142.4 (C), 127.4 (C), 123.0

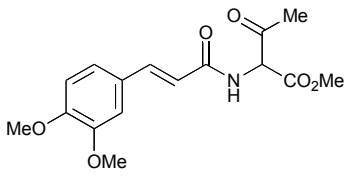
(CH), 119.6 (CH), 116.6 (CH), 111.7 (CH), 63.1 (C), 55.4 (Me), 53.4 (Me), 28.1 (Me), 25.7 (Me), 18.4 (C), -4.6 (Me); *m/z* (ESI^+) 444 (MNa^+, 100%), 422 (MH^+, 31%), 291 (100%).

***(E)*-3-(3,4-Dimethoxyphenyl)acrylamide 4b**



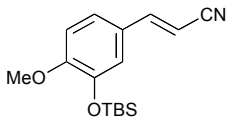
To a solution of 3,4-dimethoxycinnamic acid **3b** (10.0 g, 48.0 mmol) in THF (150 mL) was added triethylamine (14.7 mL, 111 mmol) and the solution cooled to 0 °C. A solution of ethyl chloroformate (10.6 mL, 111 mmol) in THF (25 mL) was added and the mixture stirred for 15 min. Aqueous ammonium hydroxide (30% in water; 40 mL) in THF (25 mL) was then added dropwise over 5 min. After 15 min, the reaction mixture was warmed to room temperature and stirred for a further 18 h. The solvent was evaporated to give a pale yellow solid. The crude product was dissolved in dichloromethane and washed with water and brine, dried ($MgSO_4$) and the solvent was evaporated under reduced pressure to give the *title compound* as a colourless solid (3.60 g, 36%); mp 162-164 °C (lit.,[2] mp 166.5 °C); (Found: C, 63.5; H, 6.3; N, 6.8. $C_{11}H_{13}NO_3$ requires C, 63.8; H, 6.3; N, 6.8%); (Found: MH^+, 208.0978. $C_{11}H_{14}NO_3$ requires 208.0968); ν_{max} ($CHCl_3$)/cm^{-1} 3528, 3412, 2953, 1678, 1620, 1464, 1378, 1268, 1139, 1025; δ_H (400 MHz; DMSO-d_6) 7.45 (1H, br s), 7.37 (1H, d, *J* 15.8), 7.16 (1H, d, *J* 1.9), 7.10 (1H, dd, *J* 8.3, 1.9), 7.04 (1H, br s), 6.96 (1H, d, *J* 8.3), 6.51 (1H, d, *J* 15.8), 3.79 (3H, s), 3.77 (3H, s); δ_C (100 MHz; DMSO-d_6) 167.0 (C), 150.0 (C), 148.8 (C), 139.3 (CH), 127.6 (C), 121.4 (CH), 119.9 (CH), 111.6 (CH), 109.9 (CH), 55.4 (Me), 55.4 (Me); *m/z* (ESI^+) 208 (MH^+, 100 %).

_(E)_-Methyl 2-(-3-(3,4-dimethoxyphenyl)acrylamido)-3-oxobutanoate 5b



A solution of *(E)*-3-(3,4-dimethoxyphenyl)acrylamide **4b** (6.30 g, 30.4 mmol) and dirhodium tetraacetate (336 mg, 0.76 mmol, 2.50 mol%) in dry dichloromethane (60 mL) was heated to reflux. A solution of methyl 2-diazo-3-oxobutanoate (6.90 g, 48.6 mmol) in dichloromethane (15 mL) was then added *via* syringe pump over a 16 h period. After the addition was complete the reaction mixture was heated under reflux for a further 4 h. After removal of the solvent under reduced pressure, and purification by chromatography (eluting with ethyl acetate/light petroleum 3/2), the *title compound* **5b** was obtained as a light yellow solid (9.30 g, 95%); R_f = 0.28 (light petroleum: ethyl acetate 2:3); mp 46-48 °C; (Found: MH^+, 322.1270. $C_{16}H_{20}NO_6$ requires 322.1285); ν_{max} ($CHCl_3$)/cm^{-1} 3418, 2957, 1757, 1728, 1688, 1626, 1464, 1359, 1140, 1025; δ_H (400 MHz; $CDCl_3$) 7.58 (1H, d, *J* 15.6, ArC<u>H</u>=CH), 7.08 (1H, dd, *J* 8.3, 1.8, ArH-6), 7.03 (1H, d, *J* 1.8, ArH-2), 6.85 (1H, d, *J* 8.3, ArH-5), 6.78 (1H, d, *J* 6.4, NH), 6.39 (1H, d, *J* 15.6, ArCH=C<u>H</u>), 5.40 (1H, d, *J* 6.4, CH), 3.91 (3H, s, OMe), 3.90 (3H, s, OMe), 3.84 (3H, s, OMe), 2.43 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 198.7 (C), 166.7 (C), 165.6 (C), 150.8 (C), 149.0 (C), 142.3 (CH), 127.3 (C), 122.3 (CH), 116.9 (CH), 110.9 (CH), 109.5 (CH), 63.1 (CH), 55.9 (Me), 55.8 (Me), 53.3 (Me), 28.0 (Me); *m/z* (ESI^+) 344 (MNa^+, 83%), 322 (MH^+, 25%), 191 (100%).

_(E)_-(3-_tert_-Butyldimethylsilane-4-methoxyphenyl) acrylonitrile 9a



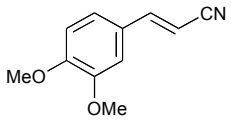
1,8-Diazabicyclo[5.4.0]undec-7-ene (3.70 mL, 24.5 mmol) and amide **4a** were dissolved in dichloromethane (25 mL) and stirred for 10 min at room temperature. Ethyl dichlorophosphate (1.70 mL, 14.6 mmol) was added and the mixture heated to reflux for 1 h. A solution of saturated aqueous ammonium chloride (10 mL) was added and the mixture stirred for further 10 min. The layers were separated, and the aqueous layer extracted with dichloromethane (20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure. Chromatography (light petroleum/ethyl acetate 4/1) gave the *title compound* **9a** (1.10 g, 75%) as a colourless solid, R_f = 0.72 (light petroleum: ethyl acetate 1:1); mp 64-66 °C; (Found: MH^+, 290.1577. $C_{16}H_{24}NO_2Si$ requires 290.1571); ν_{max} ($CHCl_3$)/cm^{-1} 3011, 2934, 2218, 1598, 1512, 1431, 1274, 1139, 853; δ_H (400 MHz; $CDCl_3$) 7.27 (1H, d, *J* 16.6, ArC<u>H</u>=CH), 7.02 (1H, dd, *J* 8.3, 1.9, ArH-6), 6.95 (1H, d, *J* 1.9, ArH-2), 6.84 (1H, d, *J* 8.3, ArH-5), 5.30 (1H, d, *J* 16.6, ArCH=C<u>H</u>), 3.85 (3H, s, Me), 1.00 (9H, s, CMe_3), 0.12 (6H, s, $SiMe_2$); δ_C (100 MHz; $CDCl_3$) 153.7 (C), 150.1 (CH), 145.4 (C), 126.6 (C), 122.5 (CH), 118.8 (CH), 118.6 (C), 111.7 (CH), 93.4 (CH), 55.4 (Me), 25.6 (Me), 18.6 (C), -5.0 (Me); *m/z* (ESI^+) 312 (MNa^+, 100%), 290 (MH^+, 48 %).

Methyl 2-*(3-tert*-butyldimethylsiloxy-4-methoxystyryl)-5-methyloxazole-4-carboxylate 6a

To a solution of nitrile **9a** (250 mg, 0.86 mmol) and dirhodium tetraacetate (9.50 mg, 0.02 mmol, 2.50 mol%) in dichloromethane (4 mL) heated to reflux was added dropwise a solution of methyl 2-diazo-3-oxobutanoate (246 mg, 1.73 mmol) in dichloromethane (1 mL)

over a period of 16 h. After removal of the solvent under reduced pressure, purification by chromatography (eluting with ethyl acetate/light petroleum 1/5) gave the *title compound* **6a** as a light yellow solid (143 mg, 41%); data identical to previous sample.

***(E)*-3-(3,4-Dimethoxyphenyl)acrylonitrile 9b**

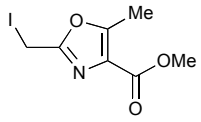


1,8-Diazabicyclo[5.4.0]undec-7-ene (3.60 mL, 24.2 mmol) and amide **4b** (1.0 g, 4.83 mmol) were dissolved in dichloromethane (20 mL) and stirred for 10 min at room temperature. Ethyl dichlorophosphate (1.72 mL, 14.5 mmol) was added and the mixture heated to reflux for 1 h. A solution of saturated aqueous ammonium chloride (10 mL) was added and the mixture stirred for further 10 min. The layers were separated, the aqueous extracted with dichloromethane (20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure. Chromatography (light petroleum/ethyl acetate 3/1) gave the *title compound* **9b** as a colourless solid (500 mg, 55%), R_f = 0.57 (light petroleum: ethyl acetate 1:1); mp 97-99 °C; (Found: C, 69.7; H, 5.8; N, 7.3. $C_{11}H_{11}NO_2$ requires C, 69.8; H, 5.9; N, 7.4%); (Found: MH^+, 190.0862. $C_{11}H_{12}NO_2$ requires 190.0863); ν_{max} ($CHCl_3$)/cm^{-1} 3011, 2218, 1619, 1514, 1465, 1272, 1142, 1024; δ_H (400 MHz; $CDCl_3$) 7.30 (1H, d, *J* 16.6, ArC<u>H</u>=C<u>H</u>), 7.02 (1H, dd, *J* 8.3, 2.0, ArH-6), 6.93 (1H, d, *J* 2.0, ArH-5), 6.86 (1H, d, *J* 8.3, ArH-5), 5.71 (1H, d, *J* 16.6, ArCH=C<u>H</u>), 3.90 (6H, s, OMe); δ_C (100 MHz; $CDCl_3$) 157.8 (C), 150.2 (CH), 149.3 (C), 126.5 (C), 122.0 (CH), 118.5 (CH), 111.0 (CH), 108.8 (CH), 93.5 (CH), 56.0 (Me), 55.9 (Me); *m/z* (ESI^+) 212 (MNa^+, 100%), 190 (MH^+, 43%).

***(E)*-Methyl 2-(3,4-dimethoxystyryl)-5-methyloxazole-4-carboxylate 6b**

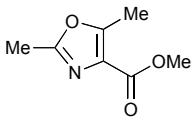
To a solution of nitrile **9b** (100 mg, 0.53 mmol) and dirhodium tetraacetate (5.80 mg, 0.01 mmol, 2.50 mol%) in dichloromethane (2 mL) heated to reflux was added dropwise a solution of methyl 2-diazo-3-oxobutanoate (151 mg, 1.06 mmol) in dichloromethane (0.8 mL) over a period of 16 h. After removal of the solvent under reduced pressure, purification by chromatography (eluting with ethyl acetate/light petroleum 1/2) gave the *title compound* **6b** as a light yellow solid (37 mg, 23%); data identical to previous sample.

Methyl 2-(iodomethyl)-5-methyloxazole-4-carboxylate 10



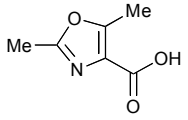
To a solution of iodoacetonitrile (9.40 g, 56.2 mmol) and dirhodium tetraacetate (310 mg, 0.70 mmol, 2.50 mol%) in dichloromethane (30 mL) heated to reflux was added dropwise a solution of methyl 2-diazo-3-oxobutanoate (4.0 g, 28.1 mmol) in dichloromethane (10 mL) over a period of 16 h. After the addition was complete the reaction mixture was heated to reflux for a further 2 h. After removal of the solvent under reduced pressure, purification by chromatography (eluting with ethyl acetate/light petroleum 1/4) gave the *title compound* **10** as a yellow solid (6.0 g, 76%); R_f = 0.56 (light petroleum: ethyl acetate 1:1); mp 81-83 °C; (Found: MH^+, 281.9616. $C_7H_9INO_3$ requires 281.9627); ν_{max} ($CHCl_3$)/cm^{-1} 2954, 1727, 1618, 1424, 1353, 1103; δ_H (400 MHz; $CDCl_3$) 4.31 (2H, s, CH_2), 3.88 (3H, s, OMe), 2.59 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 162.2 (C), 158.4 (C), 157.2 (C), 128.2 (C), 52.0 (Me), 12.0 (Me), -11.9 (CH_2); *m/z* (ESI^+) 304 (MNa^+, 100%), 282 (MH^+, 23%).

Methyl 2,5-dimethyloxazole-4-carboxylate 11



To a solution of dirhodium tetraacetate (310 mg, 0.7 mmol, 2.50 mol%) in acetonitrile (12 mL) heated to reflux was added dropwise a solution of methyl 2-diazo-3-oxobutanoate (4.0 g, 28.2 mmol) in acetonitrile (3 mL) over a period of 16 h. After the addition was complete the reaction mixture was heated to reflux for a further 4 h. After removal of the solvent under reduced pressure, purification by chromatography (eluting with ethyl acetate/ light petroleum 1/3 to 1:1) gave the *title compound* **11** as a colourless solid (3.2 g, 73%); $R_f = 0.27$ (light petroleum: ethyl acetate 1:1); mp 42-44 °C (lit.,[3] mp not given); (Found: M^+, 156.0655. $C_7H_{10}NO_3$ requires 156.0655); ν_{max} ($CHCl_3$)/cm^{-1} 3005, 1715, 1627, 1442, 1353, 1193, 1102; δ_H (400 MHz; $CDCl_3$) 3.85 (3H, s, OMe), 2.54 (3H, s, Me), 2.40 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 162.7 (C), 159.4 (C), 156.1 (C), 127.0 (C), 51.7 (Me), 13.5 (Me), 11.7 (Me); *m/z* (ESI^+) 178 (MNa^+, 100%), 156 (M^+, 38%).

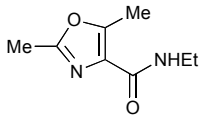
2,5-Dimethyloxazole-4-carboxylic acid 12



Ester **11** (0.80 g, 5.2 mmol) was dissolved in THF (20 mL). A solution of lithium hydroxide (0.62 g, 26 mmol) in water (5 mL) was added and the reaction mixture was stirred for 18 h at room temperature. The reaction mixture was diluted with aqueous citric acid (10%; 20 mL) and stirred for 10 min. The THF was removed *in vacuo*, ethyl acetate (90 mL) added, and the organic layer was separated, washed with water (30 mL) and brine (30 mL), dried ($MgSO_4$)

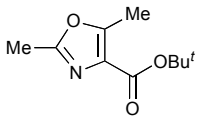
and the solvent evaporated under reduced pressure to give the *title compound* **12** as a colourless solid (0.53 g, 72%); mp 191-194 °C (lit.,[4] mp 182.5-184.5); (Found: M^-, 140.0355 $C_6H_6NO_3$ requires 140.0353); ν_{max} (solid)/cm^{-1} 1703, 1634, 1328, 1223, 1099, 958; δ_H (400 MHz; $CDCl_3$) 2.50 (3H, s, Me), 2.36 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.3 (C), 158.8 (C), 155.3 (C), 127.4 (C), 13.3 (Me), 11.7 (Me); *m/z* (ESI^-) 140 (M^-, 29%).

_N_-Ethyl-2,5-dimethyloxazole-4-carboxamide 13



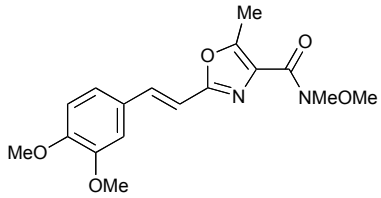
Carboxylic acid **12** (300 mg, 2.13 mmol) was dissolved in DMF (8 mL), diisopropylethylamine (1.77 mL, 10.7 mmol) and PyBOP (1.33 g, 2.55 mmol) were added and the mixture stirred at room temperature for 15 min. Ethylamine hydrochloride (208 mg, 2.55 mmol) was added and stirring continued at room temperature for 12 h. The mixture was diluted with diethyl ether (40 mL) and subsequently washed with water (2 × 10 mL) and brine (15 mL). After drying ($MgSO_4$) and removal of the solvent under reduced pressure, purification by chromatography (eluent: ethyl acetate/light petroleum 1/1) gave the *title compound* **13** as colourless solid (310 mg, 87%); R_f = 0.44 (light petroleum: ethyl acetate 1:3); mp 32-33 °C; (Found: MH^+, 169.0960. $C_8H_{13}N_2O_2$ requires 169.0972); ν_{max} ($CHCl_3$)/cm^{-1} 3419, 3009, 1656, 1526, 1442, 1332, 1138; δ_H (400 MHz; $CDCl_3$) 6.87 (1H, br, NH), 3.42-3.35 (2H, m, C<u>H</u>$_2$CH$_3$), 2.56 (3H, s, Me), 2.37 (3H, s, Me), 1.18 (3H, t, *J* 7.3, CH$_2$C<u>H</u>$_3$); δ_C (100 MHz; $CDCl_3$) 161.7 (C), 158.3 (C), 152.5 (C), 128.8 (C), 33.6 (CH_2), 14.8 (Me), 13.6 (Me), 11.4 (Me); *m/z* (ESI^+) 191 (MNa^+, 100%), 169 (MH^+, 38%).

tert-Butyl 2,5-dimethyloxazole-4-carboxylate 14



Di-*tert*-butyl dicarbonate (5.70 g, 25.5 mmol) and 4-dimethylaminopyridine (0.60 g, 5.10 mmol) were sequentially added to a solution of carboxylic acid **12** (2.40 g, 17.0 mmol) in *tert*-butanol (60 mL) at 35 °C and stirred for 48 h. The solvent was removed under reduced pressure, followed by chromatography (light petroleum/ethyl acetate 1/1) to give the *title compound* **14** (3.0 g, 90%) as a yellow solid (3.0 g, 90%); $R_f = 0.75$ (light petroleum: ethyl acetate 1:3); mp 30-31 °C (lit.,[4] mp 33-35 °C); (Found: MNa^+, 220.0964. $C_{10}H_{15}NO_3$ requires 220.0944); ν_{max} ($CHCl_3$)/cm^{-1} 2984, 1716, 1623, 1392, 1358, 1166, 1100; δ_H (400 MHz; $CDCl_3$) 2.49 (3H, s, Me), 2.39 (3H, s, Me), 1.53 (9H, s, CMe_3); δ_C (100 MHz; $CDCl_3$) 161.5 (C), 159.0 (C), 155.0 (C), 128.3 (C), 81.4 (C), 28.1 (Me), 13.6 (Me), 11.8 (Me); *m/z* (ESI^+) 220 (MNa^+, 100%).

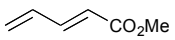
***N*-Methoxy-*N*-methyl-2-(3,4-dimethoxystyryl)-5-methyloxazole-4-carboxamide**



A solution of dimethylaluminum chloride (1 M; 8.25 mL, 8.25 mmol) in hexane was added over a 5 min period to a stirred suspension of *N,O*-dimethylhydroxylamine hydrochloride (805 mg, 8.25 mmol) in dichloromethane (20 mL) at 0 °C and the mixture stirred for 1 h at room temperature. A solution of ester **6b** (500 mg, 1.65 mmol) in dichloromethane (4 mL) was added dropwise over a period of 2 min and stirring continued. After completion of the

reaction, it was quenched with saturated aqueous sodium hydrogen carbonate (25 mL), diluted with dichloromethane (25 mL) and filtered through a short pad of Celite. The aqueous layer was extracted with dichloromethane (15 mL), the combined organic layers washed with brine (40 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure. Purification by chromatography using ethyl acetate/ light petroleum (2/1) gave the *title compound* as a light yellow solid (350 mg, 64%); R_f = 0.25 (light petroleum: ethyl acetate 1:1); mp 85-87 °C; (Found: C, 61.4; H, 6.0; N, 8.3. $C_{17}H_{20}N_2O_5$ requires C, 61.4; H, 6.1; N, 8.4%); (Found: MH^+, 333.1458 $C_{17}H_{21}N_2O_5$ requires 333.1445); ν_{max} ($CHCl_3$)/cm^{-1} 3011, 1730, 1640, 1512, 1465, 1266, 1140, 1025; δ_H (400 MHz; $CDCl_3$) 7.40 (1H, d, *J* 16.4, ArC<u>H</u>=CH), 7.08 (1H, dd, *J* 8.3, 1.9, ArH-6), 7.05 (1H, d, *J* 1.9, ArH-2), 6.87 (1H, d, *J* 8.3, ArH-5), 6.76 (1H, d, *J* 16.4, ArCH=C<u>H</u>), 3.92 (3H, s, OMe), 3.91 (3H, s, OMe), 3.83 (3H, s, OMe), 3.44 (3H, s, NMe), 2.59 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.3 (C), 158.5 (C), 154.1 (C), 150.2 (C), 149.2 (C), 136.0 (CH), 130.1 (C), 128.4 (C), 121.2 (CH), 111.5 (CH), 111.2 (CH), 108.9 (CH), 67.9 (Me), 61.6 (Me), 55.9 (Me), 55.8 (Me), 12.0 (Me)*; m/z* (ESI^+) 355 (MNa^+, 100%), 333 (MH^+, 50 %).

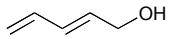
Methyl (*E*)-penta-2,4-dienoate



Acrolein (17.5 g, 310 mmol) and 4-dimethylaminopyridine (2.80 g, 23.0 mmol) were rapidly added to a solution of monomethyl malonate (37.0 g, 310 mmol) in pyridine (50 mL). The solution was warmed to 50 °C and stirred for 3 days at this temperature. The mixture was poured into water (250 mL) and extracted with ether (3 × 100 mL). The ether extract was washed with hydrochloric acid (2 M; 3 × 40 mL) and brine (80 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure to yield a light yellow oil (17.5 g, 50%). Further

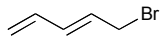
purification was done by distillation to obtain a colourless liquid (8.50 g, 25%); bp 45 °C at 15 mmHg; (lit.,[5] bp 54 °C at 27 mmHg); ν_{max} ($CHCl_3$)/cm^{-1} 2953, 1711, 1646, 1601, 1363, 1312, 1149, 905; δ_H (400 MHz; $CDCl_3$) 7.13 (1H, dd, *J* 11.0, 15.4, CH_2=CH=C<u>H</u>), 6.32 (1H, dt, *J* 17.0, 10.5, CH_2=C<u>H</u>), 5.77 (1H, d, *J* 15.4, $CHCO_2Me$), 5.46 (1H, d, *J* 17.0,C<u>H</u>H *E*), 5.34 (1H, d, *J* 10.0, CH<u>H</u>*Z*), 3.60 (3H, s, OMe); δ_C (100 MHz; $CDCl_3$) 166.7 (C), 144.4 (CH), 134.4 (CH), 125.2 (CH_2), 121.5 (CH), 51.1 (Me).

(*E*)-2,4-Pentadienol



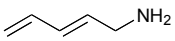
Lithium aluminum hydride (2.88 g, 76.0 mmol) was suspended in ether (50 mL) and cooled down to 0 °C. The above ester (8.50 g, 76.0 mmol) was dissolved in ether (10 mL) and added dropwise over a period of 1 h (*via* syringe pump) to the reaction mixture. The reaction was quenched by adding water (2.88 mL), aqueous sodium hydroxide (2 M; 2.88 mL), water (8.6 mL) and stirring continued for further 30 min. The mixture was poured through a short pad of Celite and diluted with ether (50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed under reduced pressure to give the title compound as a colourless liquid (5.20 g, 81%) used without any further purification for the next step; the spectroscopic data corresponded to literature values,[6] ν_{max} ($CHCl_3$)/cm^{-1} 3616, 3444, 2873, 2254, 1824, 1731, 1606, 1455, 1377, 1083, 994, 902; δ_H (400 MHz; $CDCl_3$) 6.25 (2H, m, CH_2=C<u>H</u>=C<u>H</u>), 5.74 (1H, dt, *J* 14.7, 5.7, C<u>H</u>=CH_2OH), 5.13 (1H, d, *J* 16.4, C<u>H</u>H *E*), 5.01 (1H, d, *J* 9.6, CH<u>H</u>*Z*), 4.07 (2H, m, C<u>H</u>$_2$OH); δ_C (100 MHz; $CDCl_3$) 136.2 (CH), 132.5 (CH), 131.2 (CH), 116.9 (CH_2), 62.3 (CH_2).

(*E*)-5-Bromo-1,3-pentadiene



The above alcohol (7.10 g, 84.0 mmol) was dissolved in ether (60 mL) and cooled to 0 °C. Phosphorus tribromide (27.3 g, 101 mmol) was added dropwise over 30 min (*via* syringe pump) and stirring continued at this temperature for further 30 min. The mixture was poured into ice–water (100 mL) and the aqueous layer extracted with ether (3 × 50 mL). The combined organic layers were washed with water (80 mL), saturated aqueous sodium hydrogen carbonate (80 mL), brine (80 mL) and dried ($MgSO_4$). The solvent was removed in *vacuo* and further purification by distillation gave a colourless liquid (7.20 g, 58%); bp 35 °C at 5.2 mmHg, (lit.,[6] bp 54-55 °C at 34 mmHg); ν_{max} ($CHCl_3$)/cm^{-1} 2971, 1831, 1600, 1292, 1114, 1002, 949, 913; δ_H (400 MHz; $CDCl_3$) 6.30 (2H, m, CH_2=C<u>H</u>=C<u>H</u>), 5.90 (1H, m, C<u>H</u>=CH_2Br), 5.25 (1H, d, *J* 13.7, C<u>H</u>H *E*), 5.14 (1H, d, *J* 10.0, CH<u>H</u> *Z*), 4.00 (2H, d, *J* 7.9, CH_2Br); δ_C (100 MHz; $CDCl_3$) 135.3 (CH), 135.0 (CH), 129.0 (CH), 119.2 (CH_2), 32.7 (CH_2).

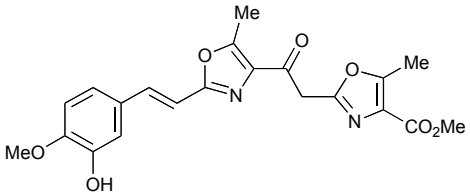
(*E*)-2,4-Pentadienylamine



The above bromide (6.80 g, 46.0 mmol) was dissolved in DMSO (80 mL) and sodium azide (4.50 g, 69.0 mmol) added in one portion at room temperature and the mixture stirred for 1.5 h. The reaction was diluted with water (100 mL) and extracted with ether (3 × 100 mL). The combined organic layers were washed with water (80 mL) and brine (80 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure. The azide (4.80 g, 96%) was obtained as a yellow liquid and used without further purification.

Lithium aluminum hydride (1.20 g, 32.0 mmol) was suspended in ether (70 mL) and cooled down to 0 °C. The azide (4.60 g, 42.0 mmol) was dissolved in ether (10 mL) and added dropwise over a period of 30 min (*via* syringe pump) to the reaction mixture. Stirring was continued for further 30 min at 0 °C. The reaction was then quenched by adding water (1.20 mL), aqueous sodium hydroxide (2 M; 1.20 mL), water (3.60 mL) and stirred for 20 min. The mixture was poured through a short pad of Celite and diluted with ether (30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed under reduced pressure to give a yellow liquid (2.80 g, 80%). After distillation (*E*)-2,4-pentadienylamine was obtained as colourless oil (1.50 g, 43%); bp 30-33 °C at 8 mmHg; (lit.,[7] bp 43-45 °C at 40 mmHg); ν_{max} ($CHCl_3$)/cm^{-1} 3616, 3444, 2873, 2253, 1824, 1731, 1606, 1455, 1377, 1083, 994, 902; δ_H (400 MHz; $CDCl_3$) 6.30 (1H, dt, *J* 16.9, 10.3, CH_2=C<u>H</u>), 6.09 (1H, dd, *J* 15.2, 10.5, CH_2=CHC<u>H</u>), 5.77 (1H, dt, *J* 15.2, 5.6, C<u>H</u>=CH_2NH_2), 5.08 (1H, d, *J* 16.9, C<u>H</u>H *E*), 4.95 (1H, d, *J* 10.0, CH<u>H</u> *Z*), 3.15 (2H, d, *J* 5.6, C<u>H</u>$_2$$NH_2$), 2.0 (2H, br, NH_2); δ_C (100 MHz; $CDCl_3$) 137.0 (CH), 136.9 (CH), 129.0 (CH), 115.4 (CH_2), 43.1 (CH_2).

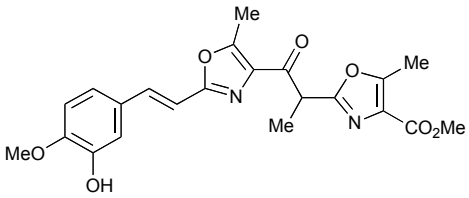
Methyl 2-(2-(2-(3-hydroxy-4-methoxystyryl)-5-methyloxazol-4-yl)-2-oxoethyl)-5-methyloxazole-4-carboxylate 20



Ester **15** (300 mg, 0.57 mmol) was dissolved in THF (5 mL), cooled to 0 °C and triethylamine trihydrofluoride (276 μL, 1.71 mmol) was added dropwise over a period of 5 min. The mixture was stirred at 0 °C for 3 h before an aqueous solution of saturated ammonium chloride (5 mL) was added and the mixture warmed to room temperature. The

THF was removed under reduced pressure and the aqueous extracted with ethyl acetate (2 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$) and evaporated to give the *title compound* **20** as a light yellow solid (157 mg, 65%) used without further purification; mp 71-73 °C; (Found: MH^+, 413.1346. $C_{21}H_{21}N_2O_7$ requires 413.1343); ν_{max} ($CHCl_3$)/cm^{-1} 3544, 3011, 1719, 1588, 1511, 1442, 1353, 1281, 1106; δ_H (400 MHz; $CDCl_3$) 7.38 (1H, d, *J* 16.3, ArCH=CH), 7.12 (1H, d, *J* 2.0, ArH-2), 7.00 (1H, dd, *J* 8.3, 2.0, ArH-6), 6.84 (1H, d, *J* 8.3, ArH-5), 6.69 (1H, d, *J* 16.3, ArCH=CH), 5.9 (1H, br, OH), 4.47 (2H, s, CH_2), 3.90 (3H, s, OMe), 3.88 (3H, s, OMe), 2.63 (3H, s, Me), 2.62 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 189.3 (C), 162.7 (C), 159.1 (C), 157.2 (C), 156.5 (C), 155.4 (C), 148.0 (C), 145.9 (C), 137.1 (CH), 134.3 (C), 128.7 (C), 127.6 (C), 120.6 (CH), 112.4 (CH), 111.0 (CH), 110.6 (CH), 56.0 (Me), 51.8 (Me), 39.5 (CH_2), 12.3 (Me), 11.9 (Me); *m/z* (ESI^+) 435 (MNa^+, 100%), 413 (MH^+, 42%).

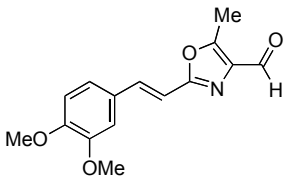
Methyl 2-(2-(2-(3-hydroxy-4-methoxystyryl)-5-methyloxazol-4-yl)-2-oxo-1-methylethyl)-5-methyloxazole-4-carboxylate 21

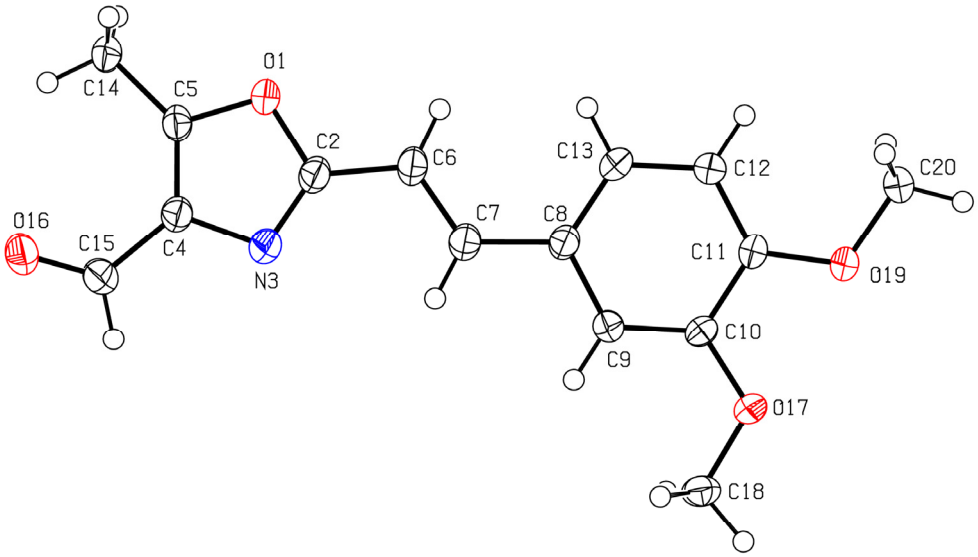


Phenol **20** (15.0 mg, 35.0 μmol) was dissolved in DMF (0.5 mL) and cooled to 0 °C. Subsequently potassium carbonate (15.0 mg, 110 μmol) and iodomethane (6.60 μL, 180 μmol) were added and the mixture stirred at this temperature for 30 min. Saturated aqueous ammonium chloride (5 mL) and ethyl acetate (20 mL) were added and the layers separated. The aqueous layer was extracted with ethyl acetate (10 mL) and the combined organic layers

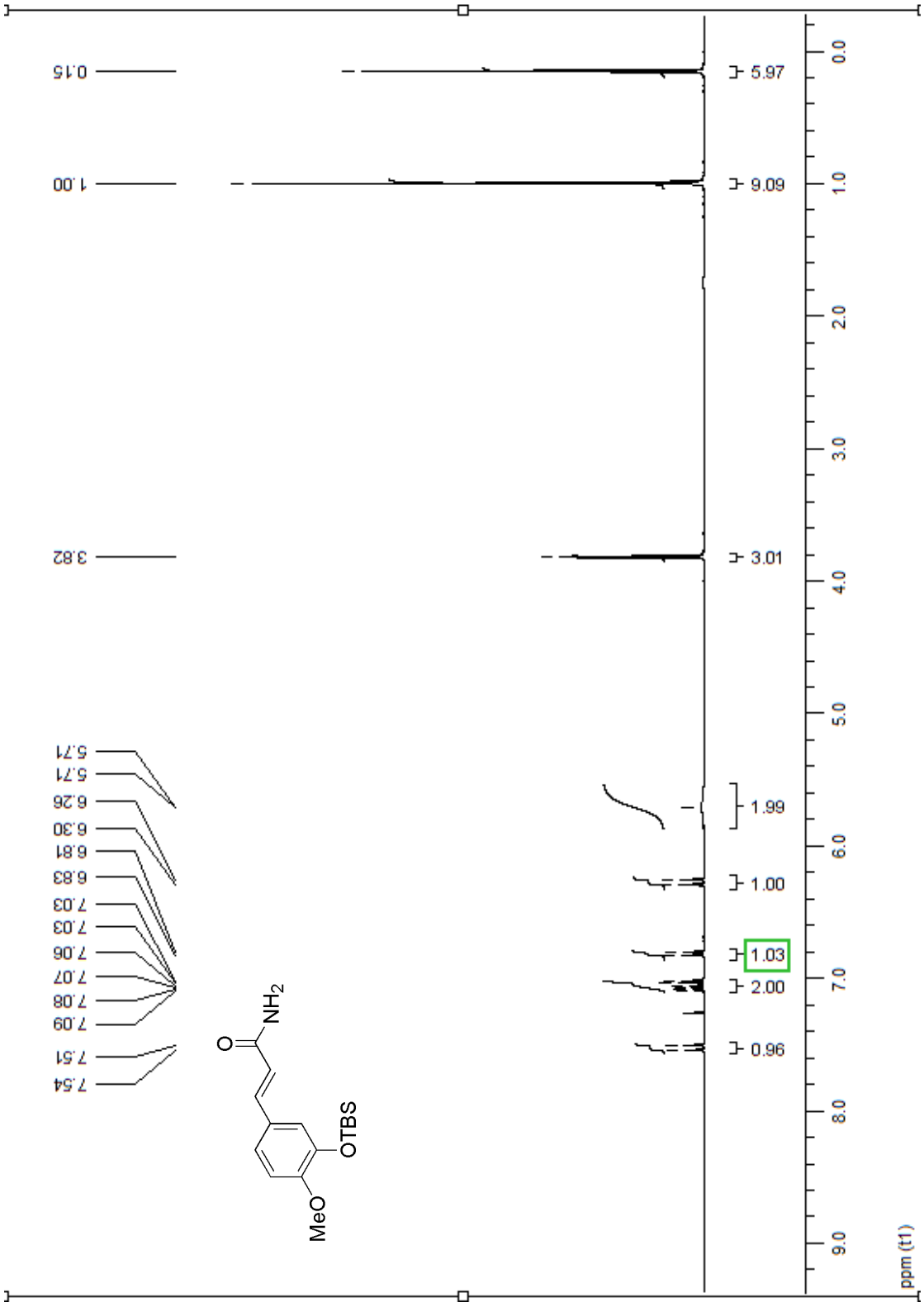
washed with brine (15 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure. Purification by chromatography (eluent light petroleum/ethyl acetate 1/1 + 0.5% triethylamine) gave the *title compound* **21** as a colourless solid (6.5 mg, 42%); R_f = 0.22 (light petroleum: ethyl acetate 1:1); mp 57-58 °C; (Found: MH^+, 427.1501. $C_{22}H_{23}N_2O_7$ requires 427.1500; ν_{max} ($CHCl_3$)/cm^{-1} 3543, 3012, 1724, 1601, 1511, 1442, 1267, 1103; δ_H (400 MHz; $CDCl_3$) 7.38 (1H, d, *J* 16.3, ArC<u>H</u>=CH), 7.14 (1H, d, *J* 2.0, ArH-2), 7.03 (1H, dd, *J* 8.3, 2.0, ArH-6), 6.86 (1H, d, *J* 8.3, ArH-5), 6.71 (1H, d, *J* 16.3, ArCH=C<u>H</u>), 5.0 (1H, q, *J* 7.3, C<u>H</u>Me), 3.93 (3H, s, OMe), 3.89 (3H, s, OMe), 2.70 (3H, s, Me), 2.62 (3H, s, Me), 1.69 (3H, d, *J* 7.3, CH<u>Me</u>); OH not observed; δ_C (100 MHz; $CDCl_3$) 193.1 (C), 162.8 (C), 160.8 (C), 158.9 (C), 156.9 (C), 156.1 (C), 147.9 (C), 145.9 (C), 137.0 (CH), 134.0 (C), 128.8 (C), 127.4 (C), 120.6 (CH), 112.4 (CH), 111.3 (CH), 110.7 (CH), 56.0 (Me), 51.8 (Me), 43.1 (CH), 14.7 (Me), 12.8 (Me), 12.0 (Me); *m/z* (ESI^+) 449 (MNa^+, 87%), 427 (MH^+, 65%).

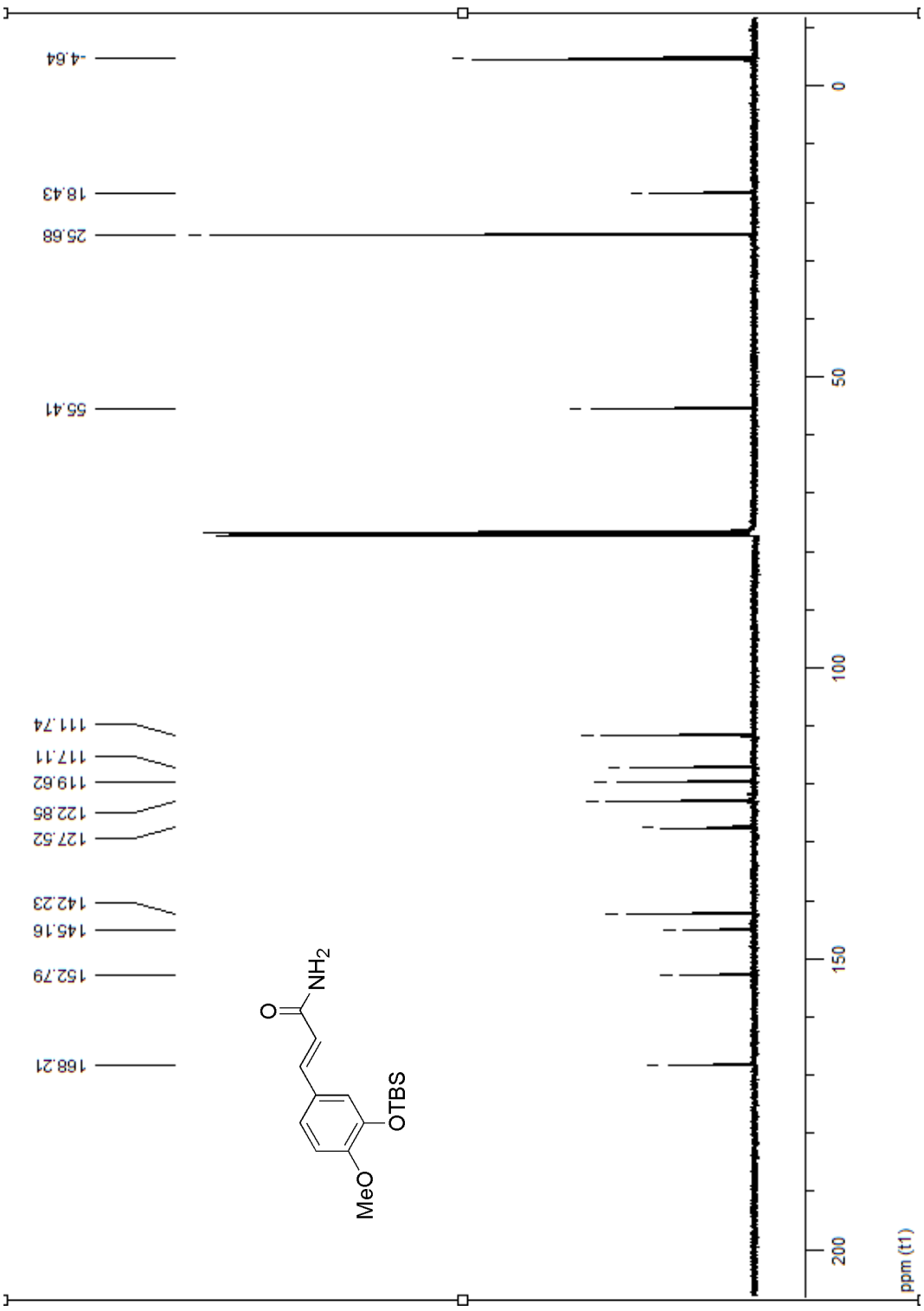
X-Ray crystal structure of 2-(3,4-dimethoxystyryl)-5-methyloxazole-4-carbaldehyde 8b





(*E*)-3-(3-*tert*-Butyldimethylsiloxy-4-methoxyphenyl)acrylamide 4a

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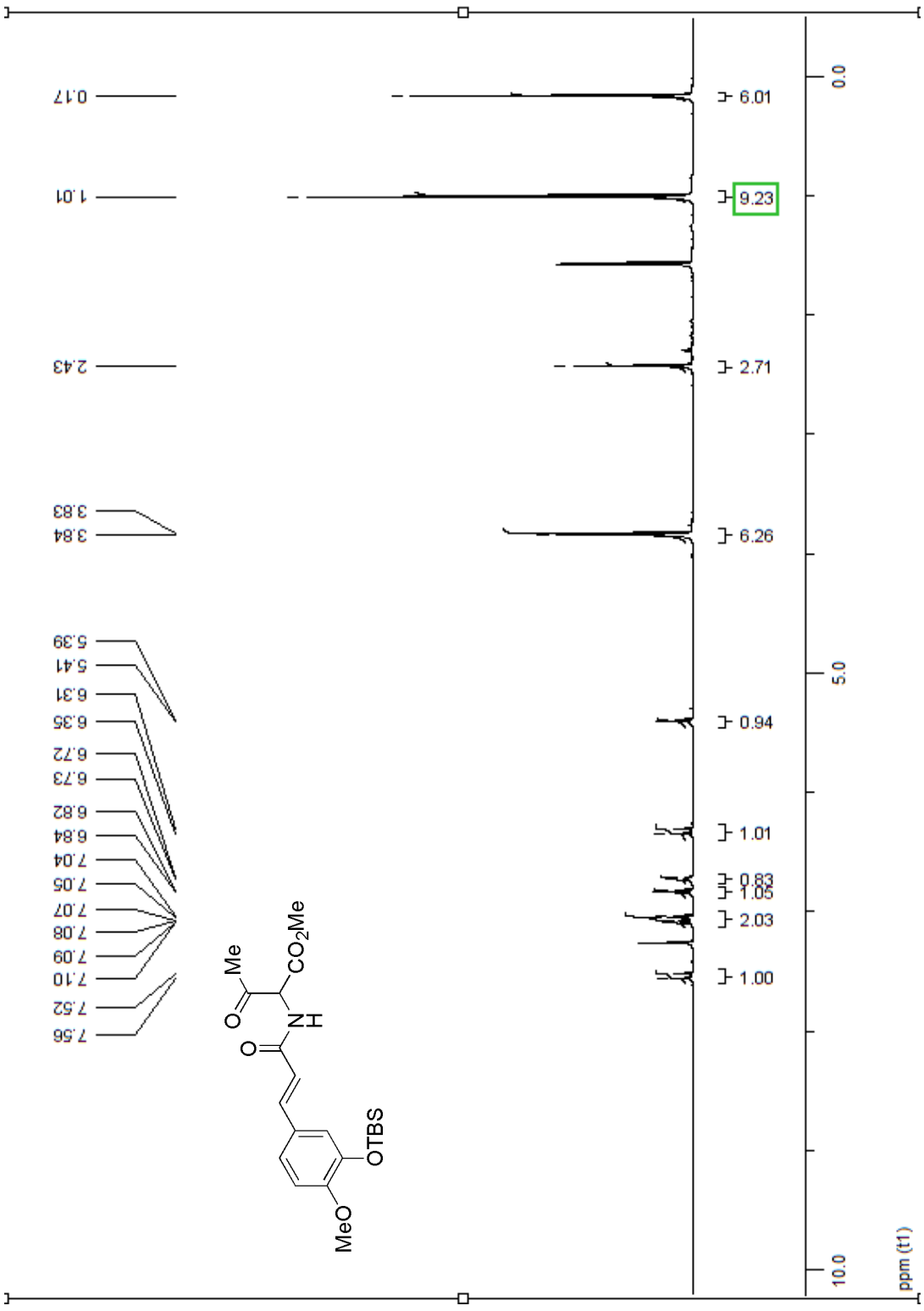
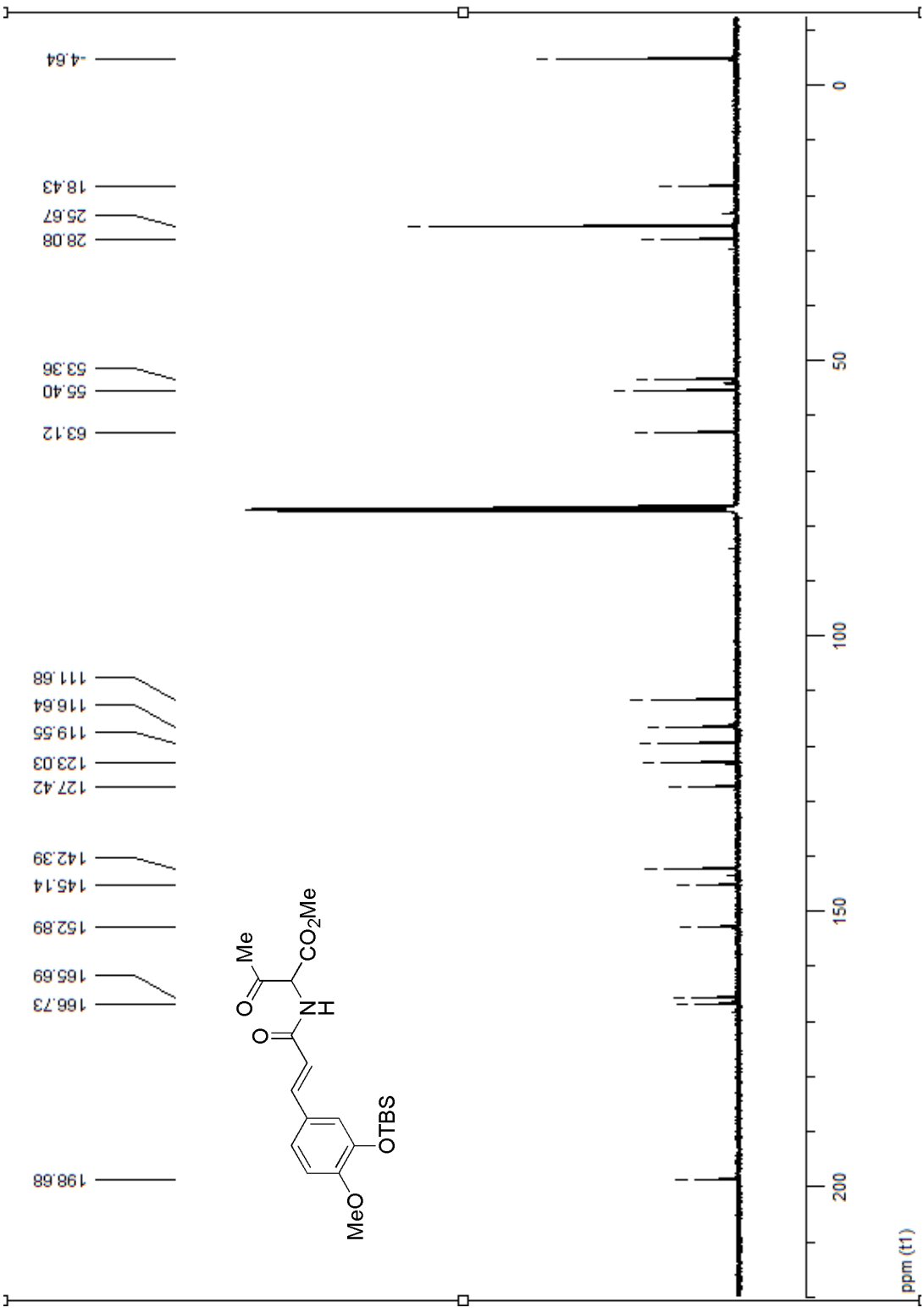
55.41
111.74
117.11
119.62
122.85
127.52
142.23
145.16
152.79
168.21
0
50
100
150
200
ppm (t1)
NH2
O
OTBS
MeO

(*E*)-3-Methyl 2-((3-*tert*-butyldimethylsiloxy 4-methoxyphenyl)acrylamido)-3-oxobutanoate 5a

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116.64
119.55
123.03
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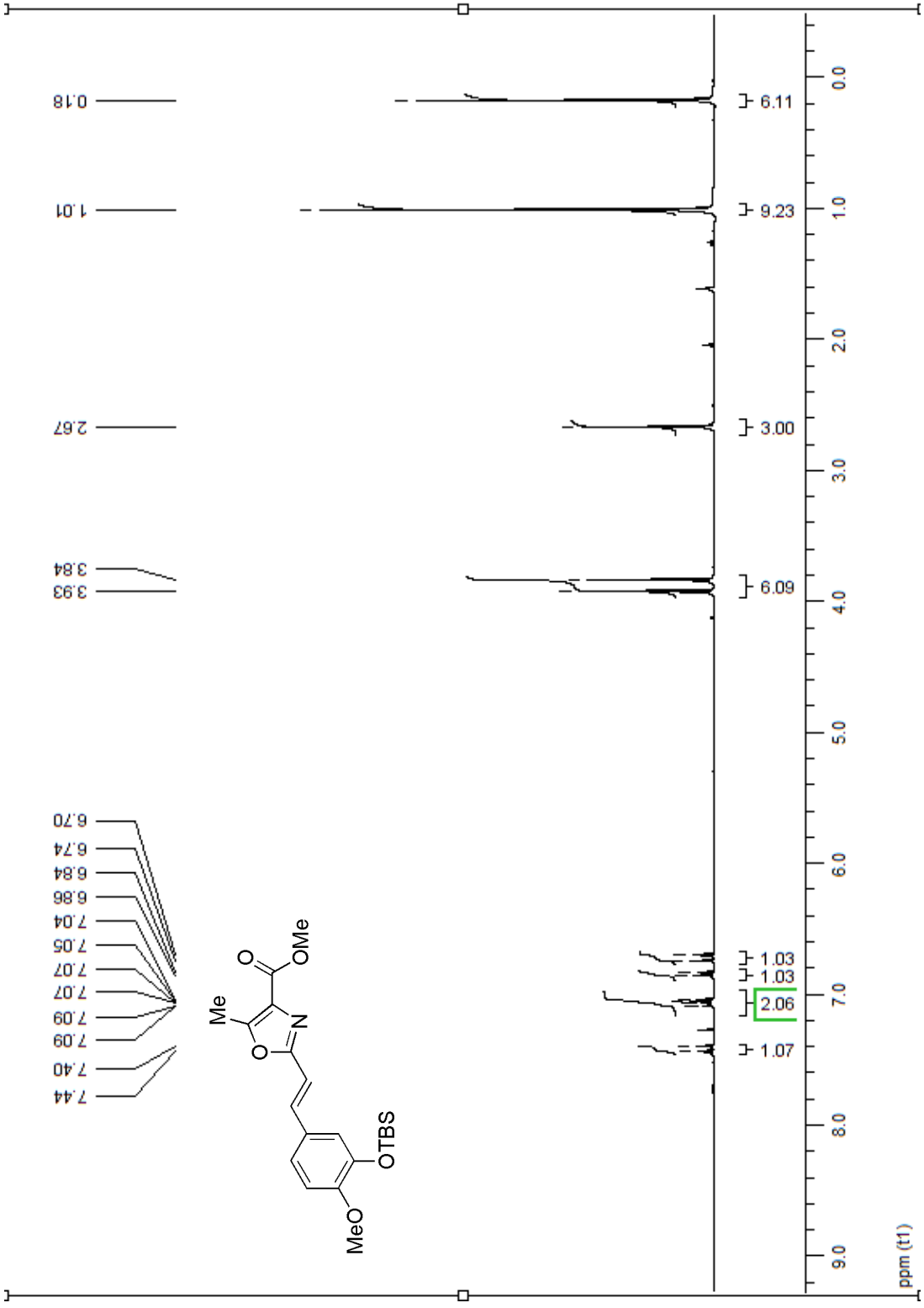
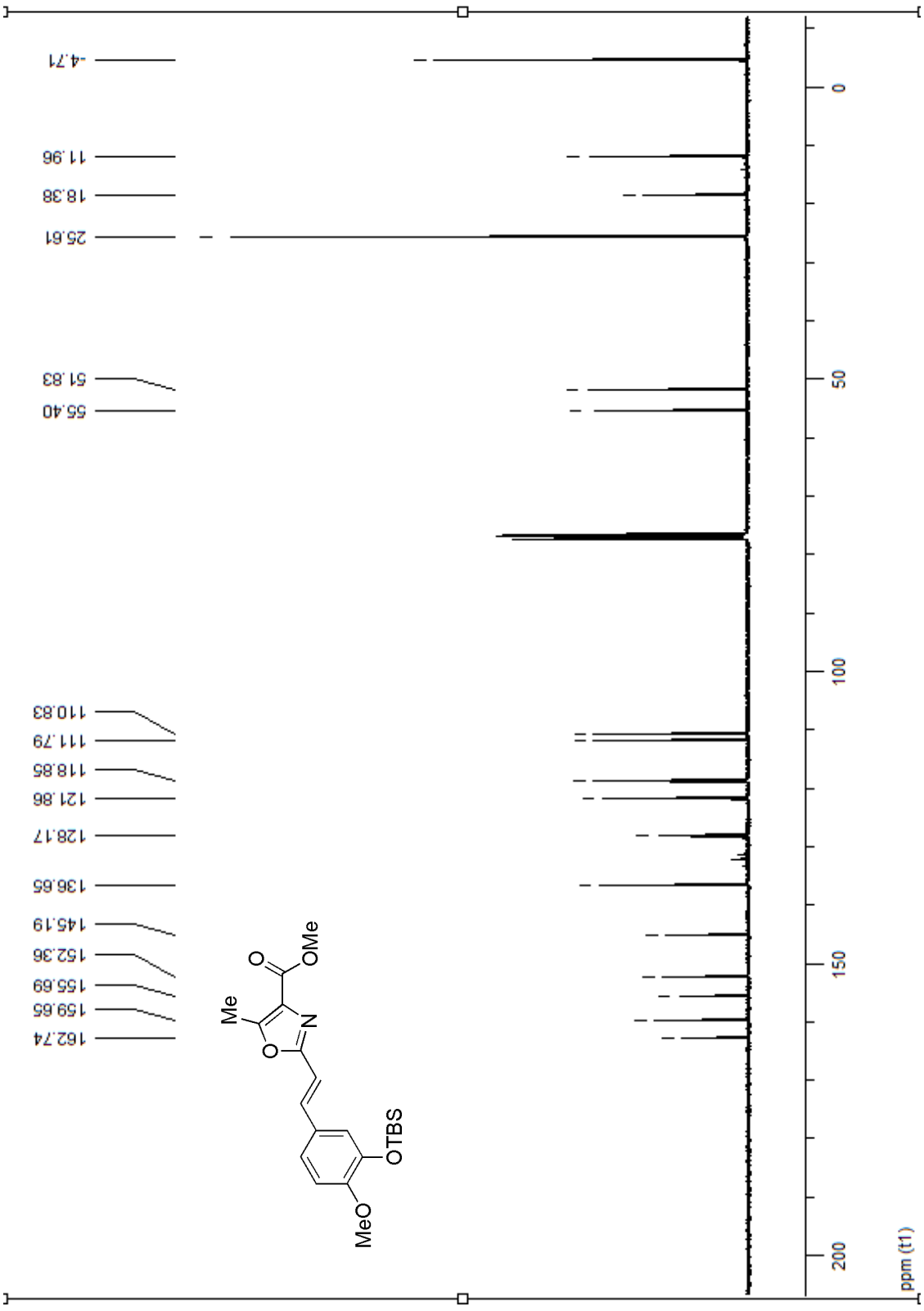
145.14
152.89
165.69
166.73
198.68
0
50
100
150
200
ppm (t1)
Me
CO2Me
O
N
H
O
OTBS
MeO

Methyl 2-*(3-tert*-butyldimethylsiloxy-4-methoxystyryl)-5-methyloxazole-4-carboxylate 6a

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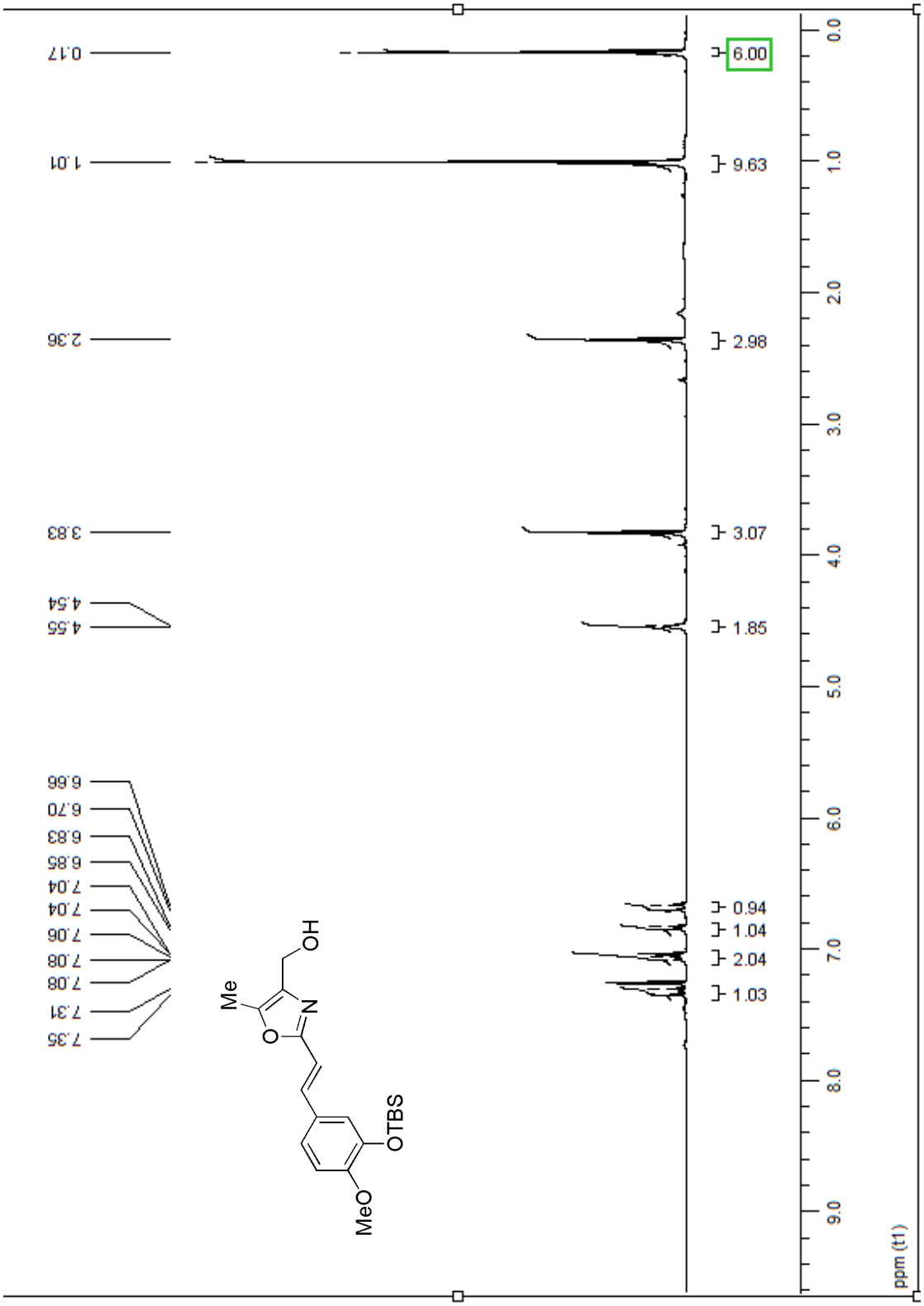
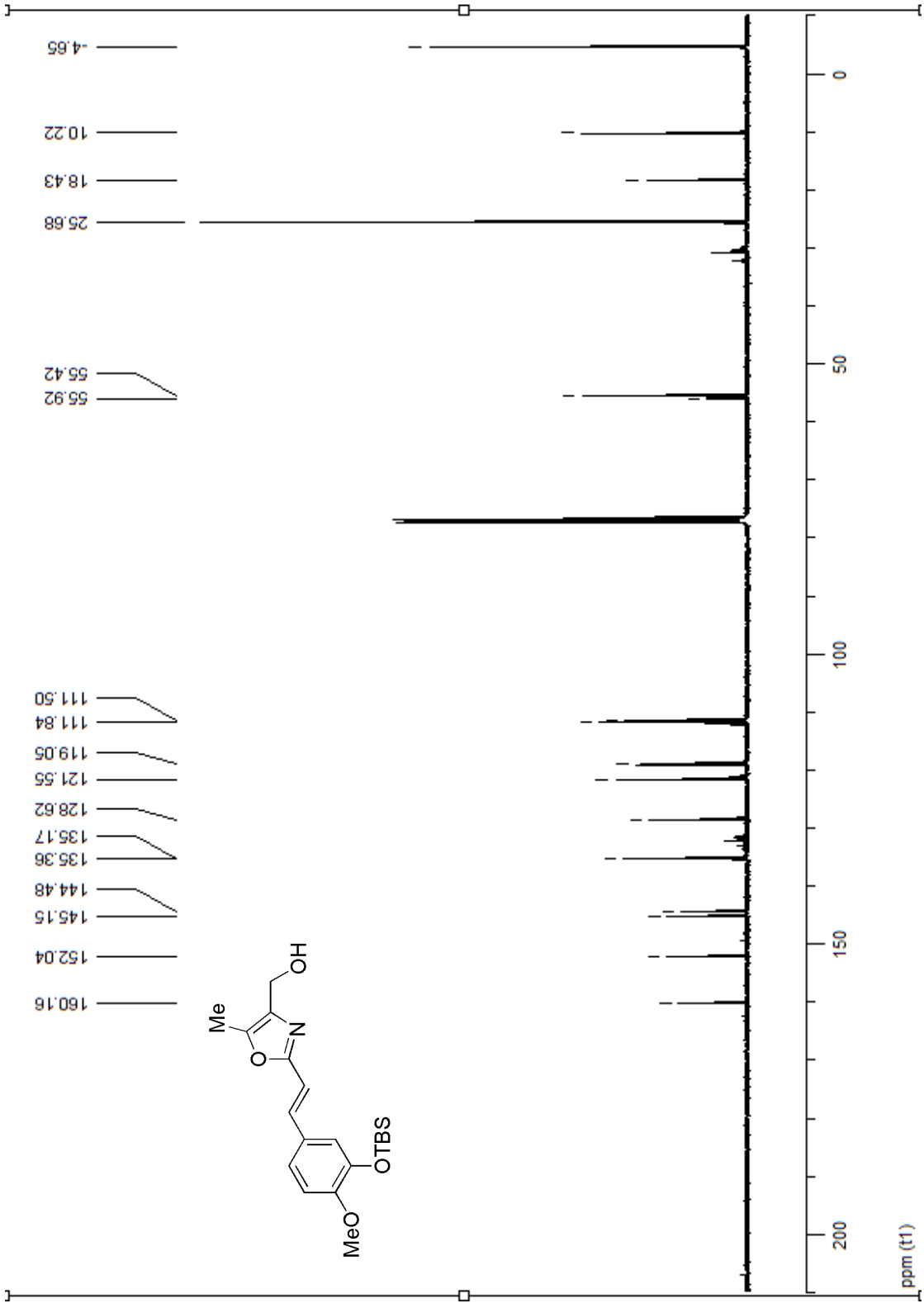
152.36
155.69
159.65
162.74
0
50
100
150
200
ppm (t1)
Me
O
OMe
N
O
OTBS
MeO

[2-(3-*tert*-Butyldimethylsiloxy-4-methoxystyryl)-5-methyloxazol-4-yl)]methanol 7a

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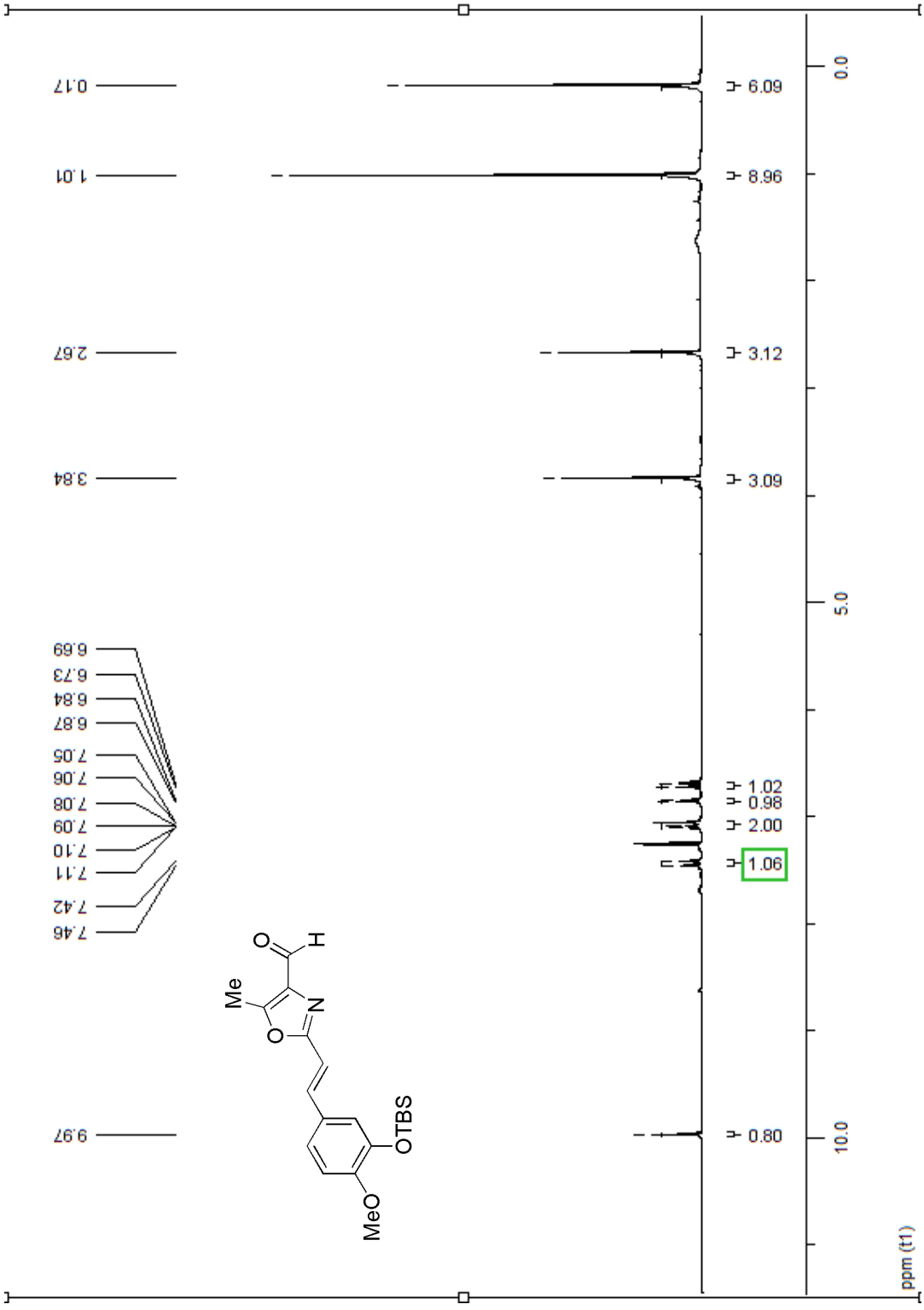
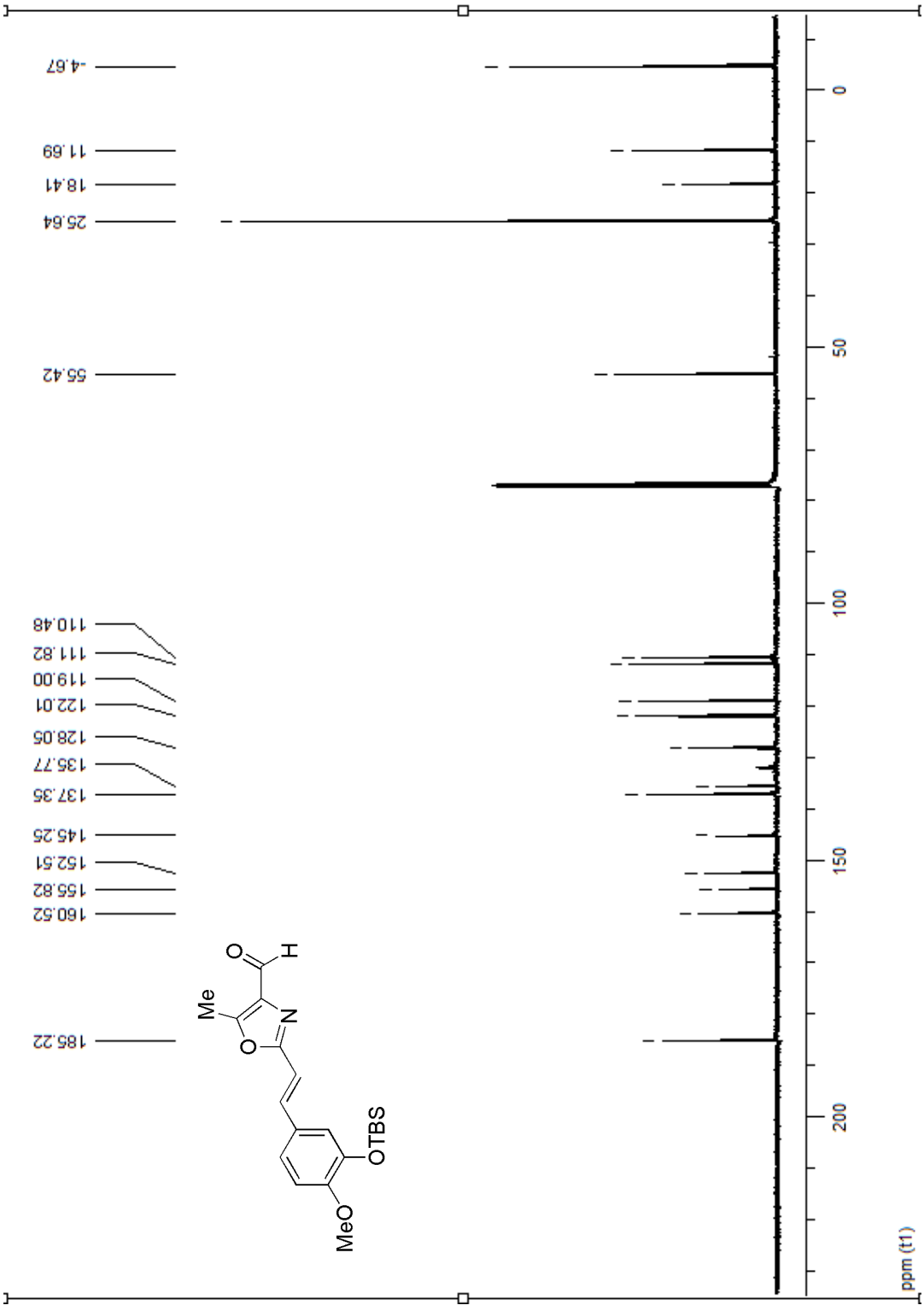
144.48
145.15
152.04
160.16
Me
O
N
OH
OTBS
MeO
0
50
100
150
200
ppm (t1)

2-(3-*tert*-Butyldimethylsiloxy-4-methoxystyryl)-5-methyloxazole-4-carbaldehyde 8a

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55.42
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119.00
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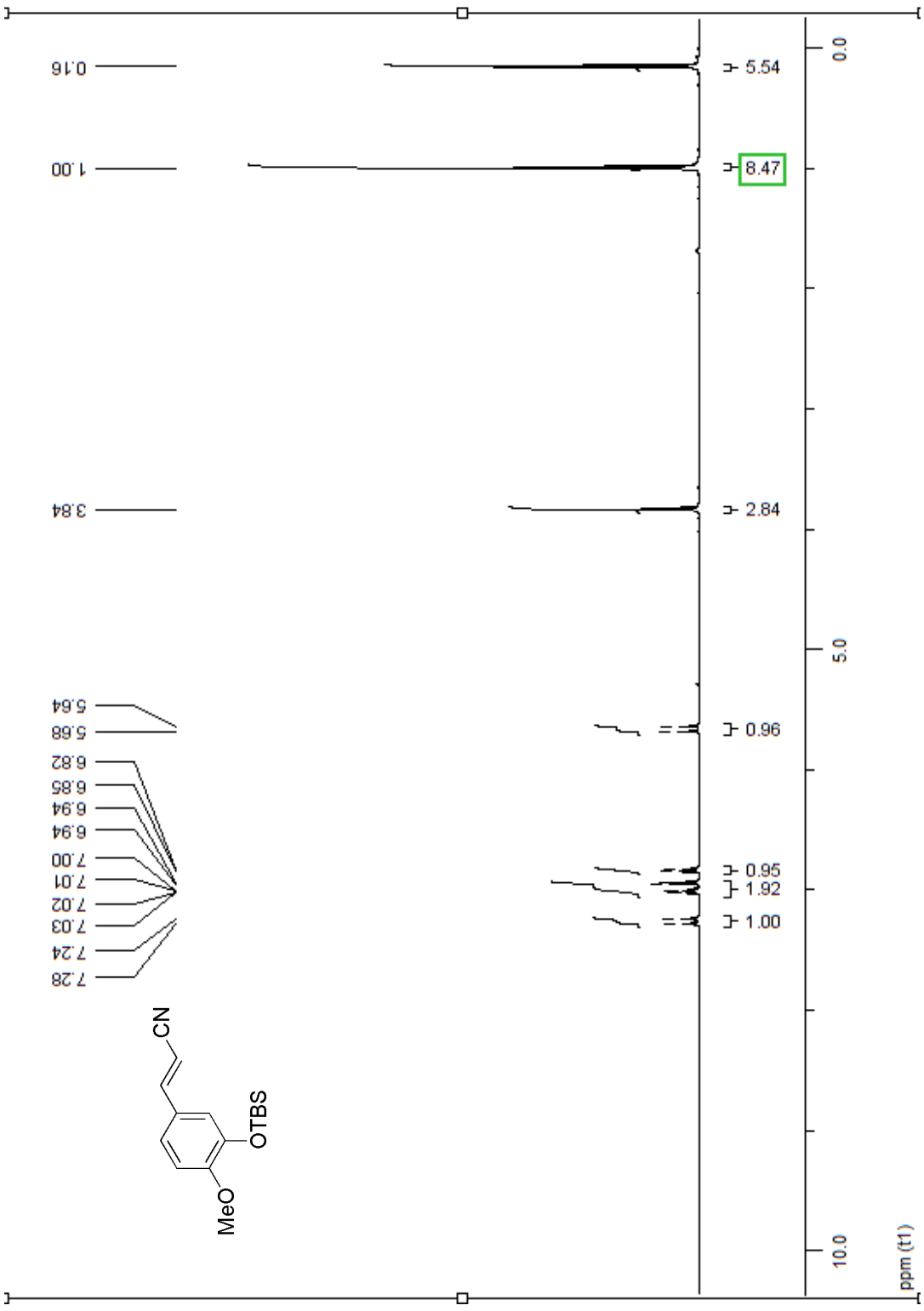
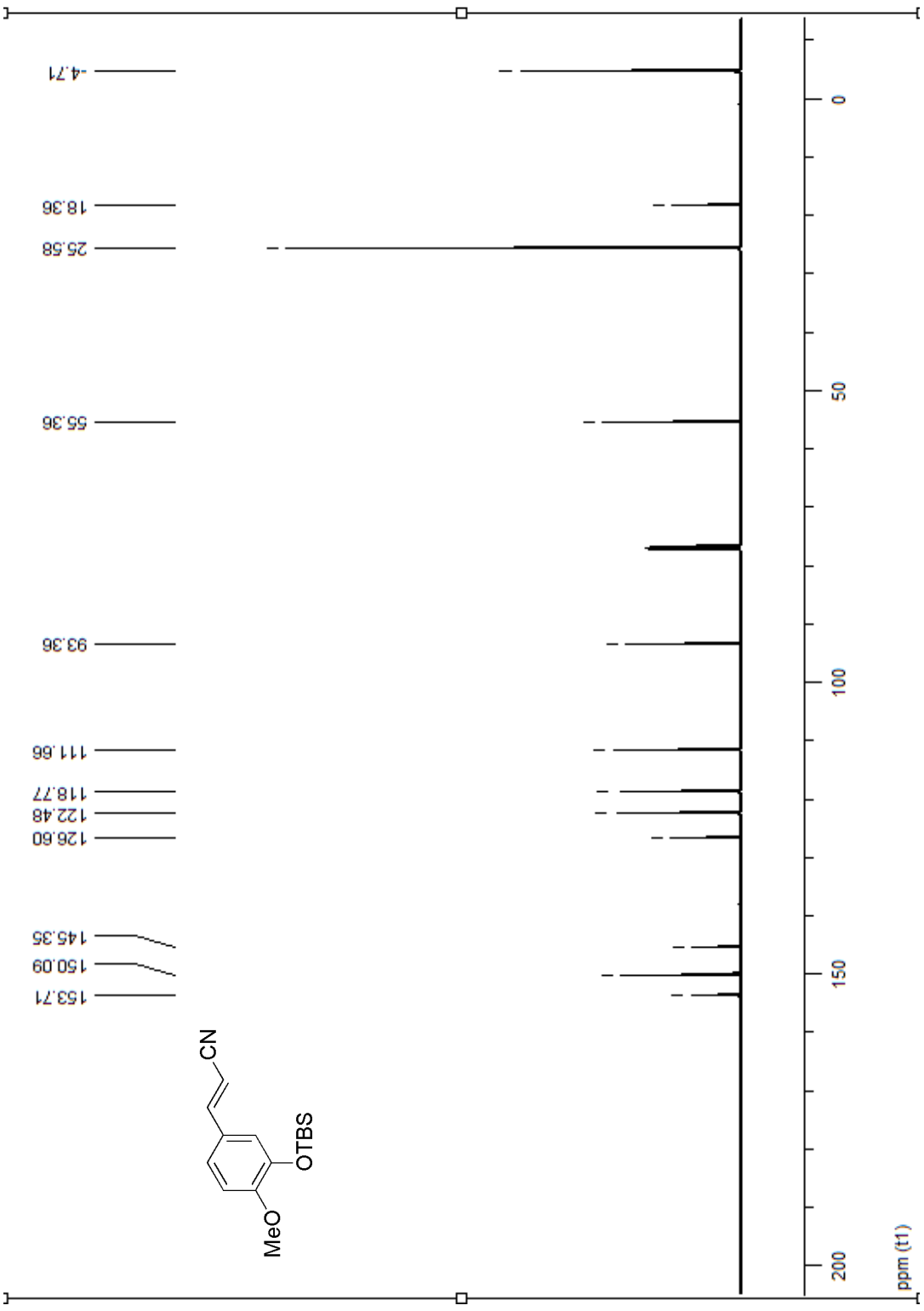
152.51
155.82
160.52
185.22
0
50
100
150
200
ppm (t1)
O
H
Me
O
N
OTBS
MeO

(*E*)-(3-*tert*-Butyldimethylsilane-4-methoxyphenyl) acrylonitrile 9a

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18.36
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55.36
93.36
111.66
118.77
122.48
126.60
145.35
150.09
153.71
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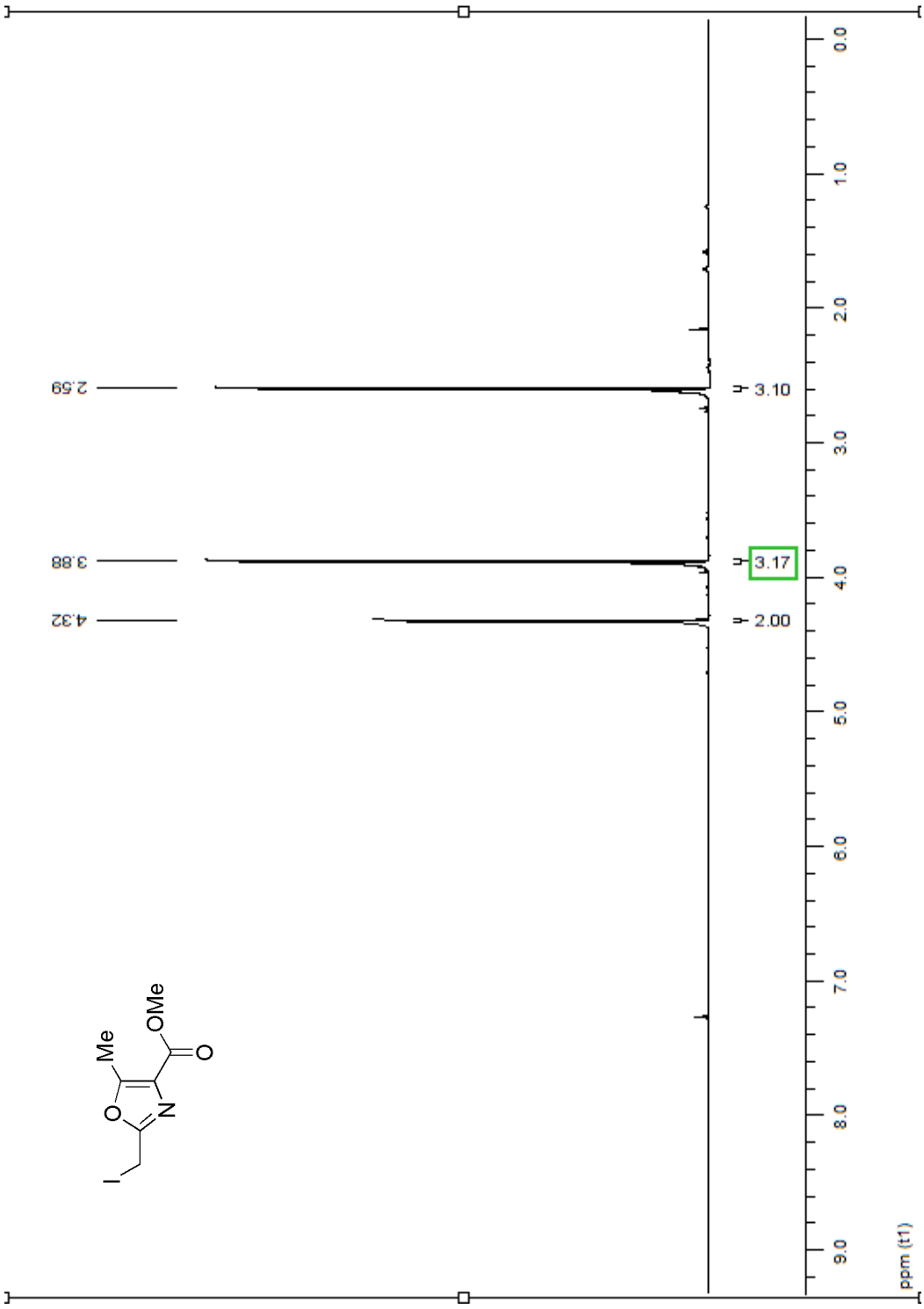
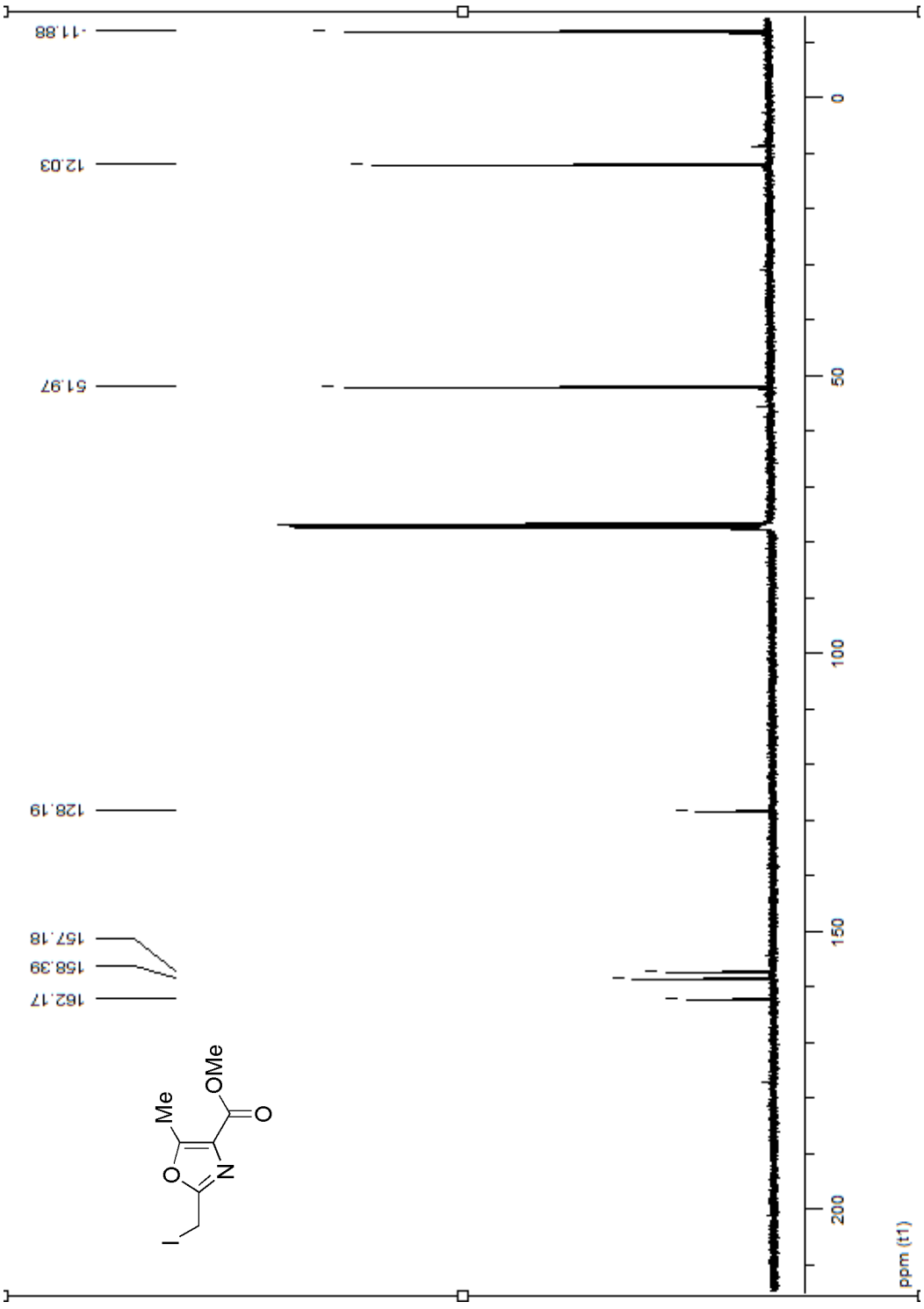
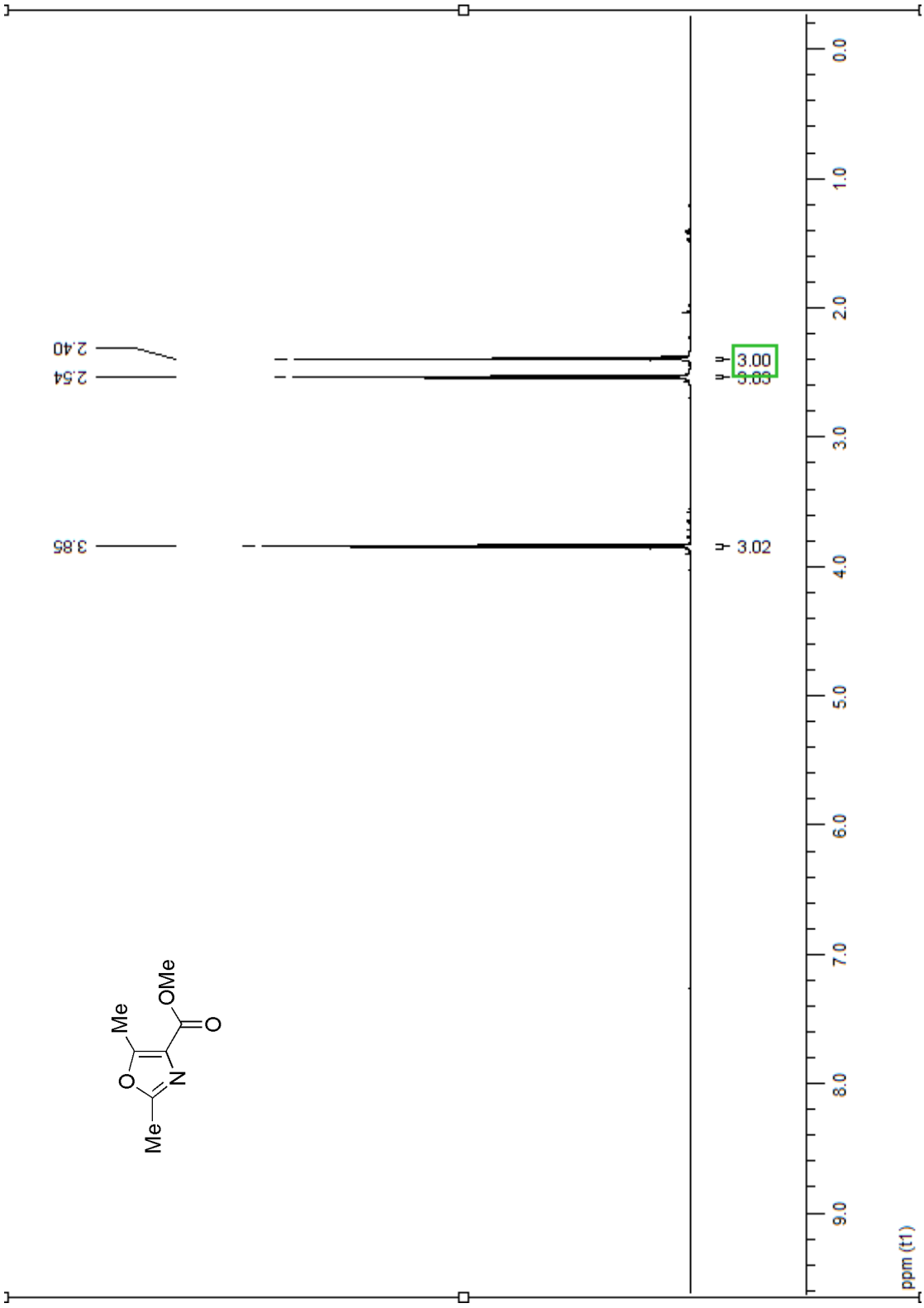
50
100
150
200
ppm (t1)
CN
OTBS
MeO

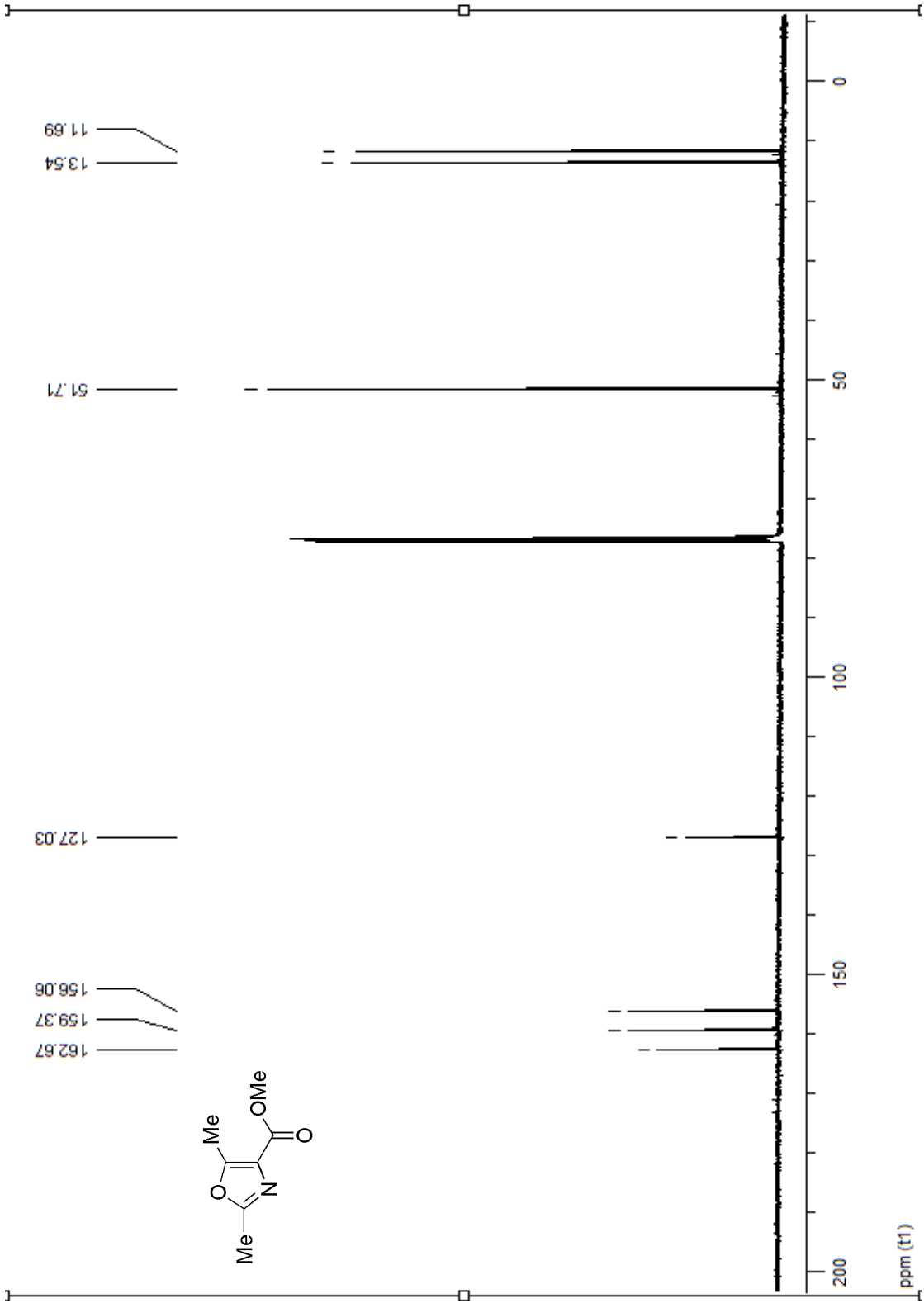
Methyl 2-(iodomethyl)-5-methyloxazole-4-carboxylate 10



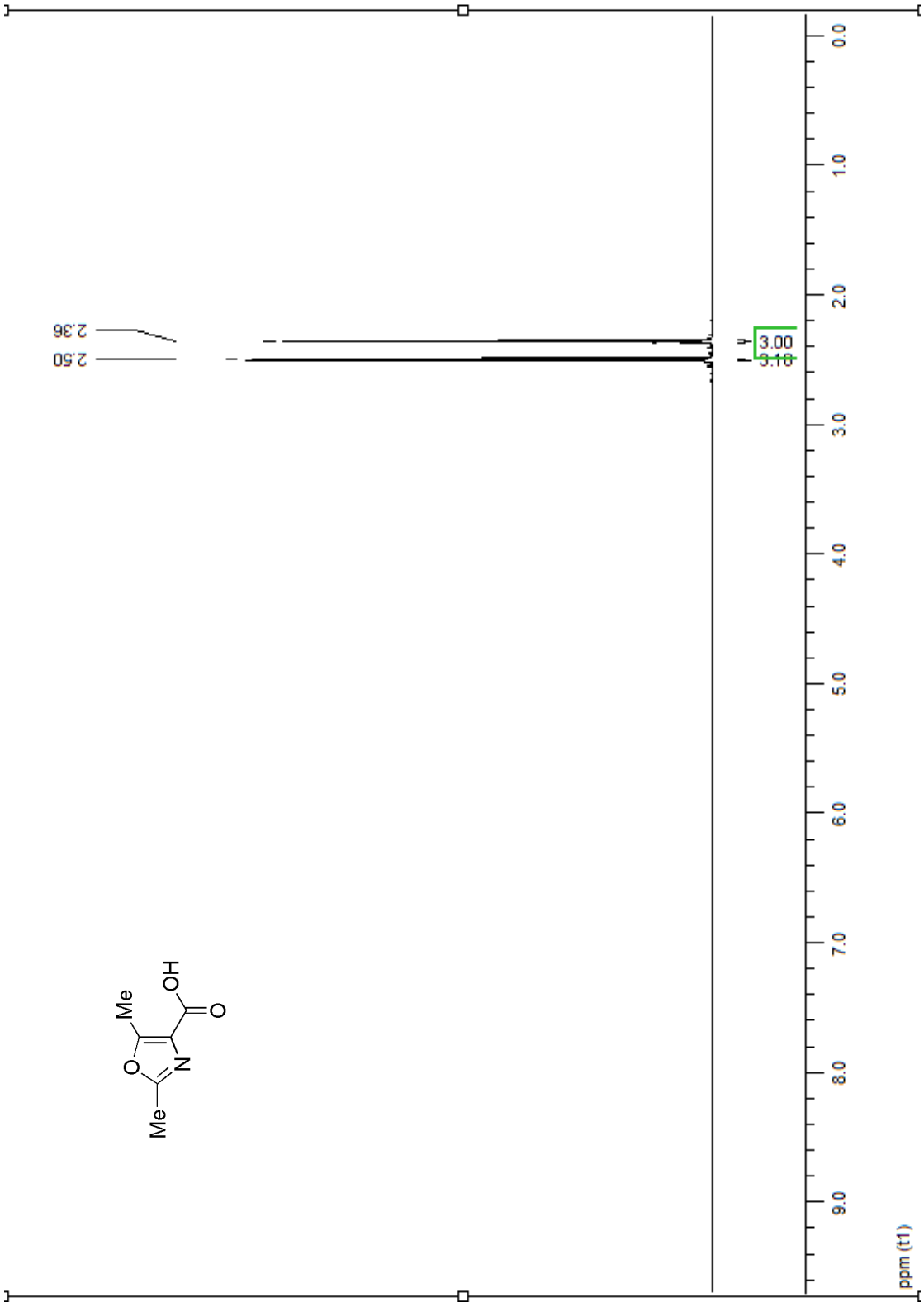

11.88
12.03
51.97
128.19
157.18
158.39
162.17
Me
OMe
O
O
N
0
50
100
150
200
ppm (t1)

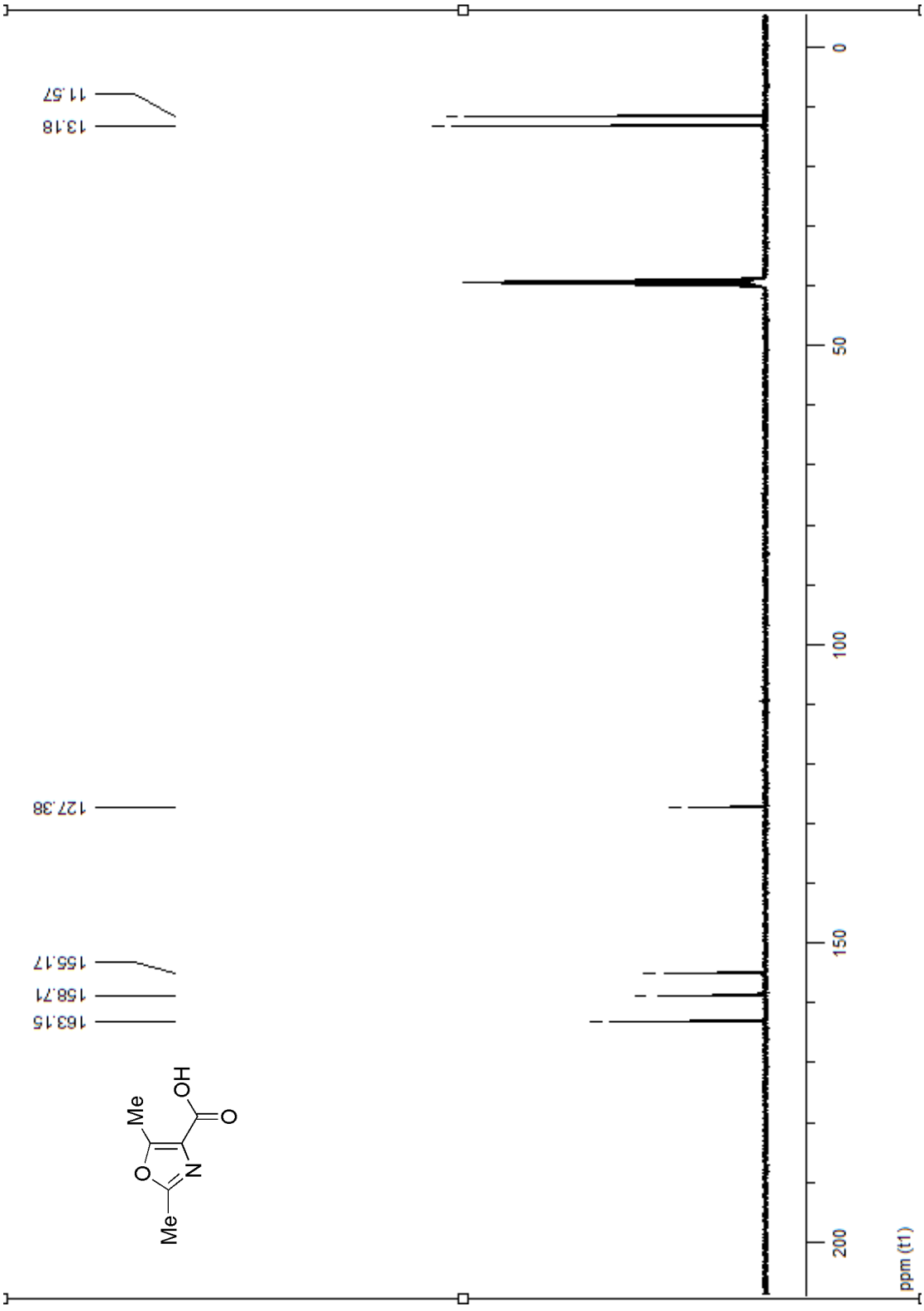
Methyl 2,5-dimethyloxazole-4-carboxylate 11



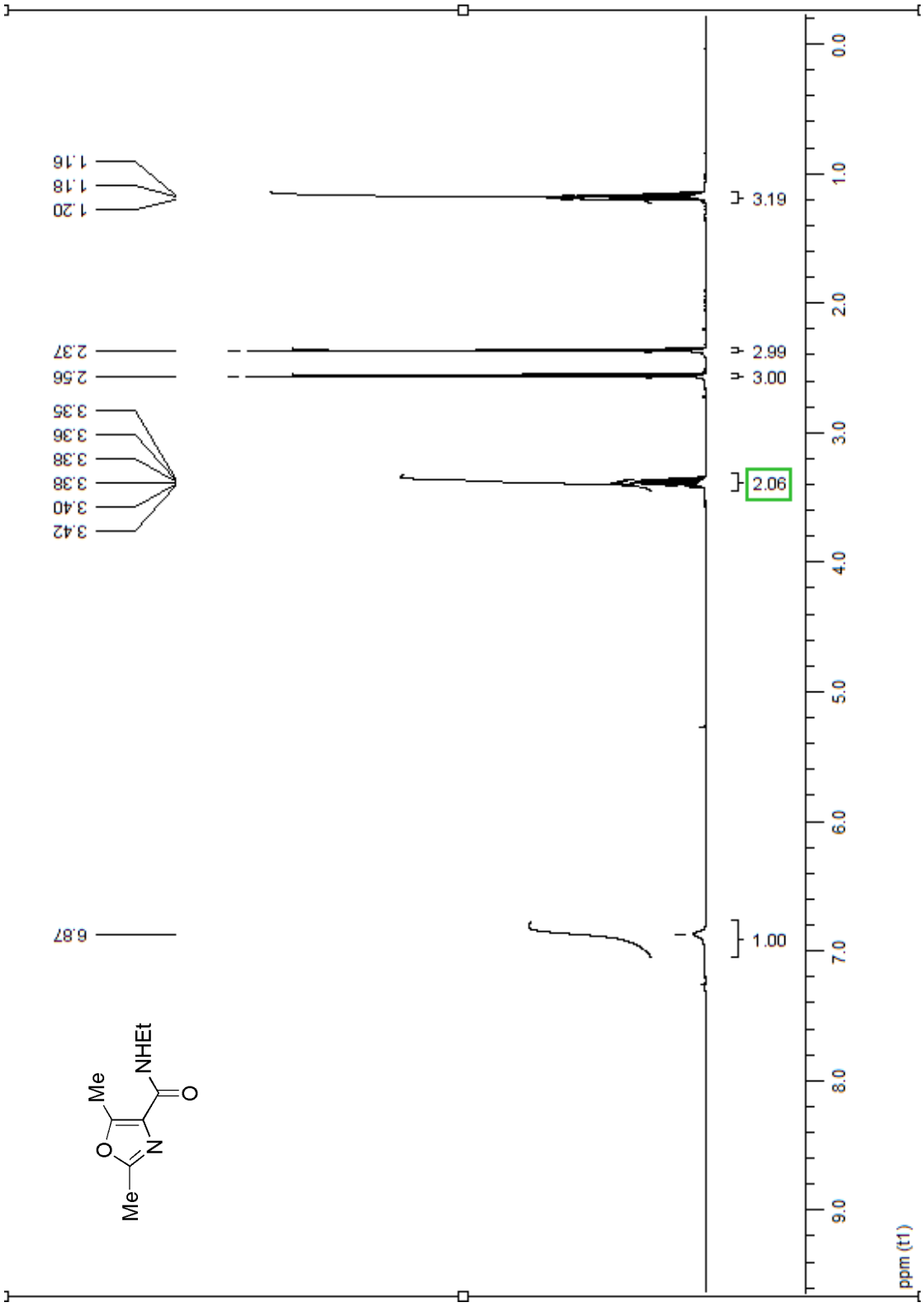

11.69
13.54
51.71
127.03
156.06
159.37
162.67
Me
OMe
O
O
N
Me
0
50
100
150
200
ppm (t1)

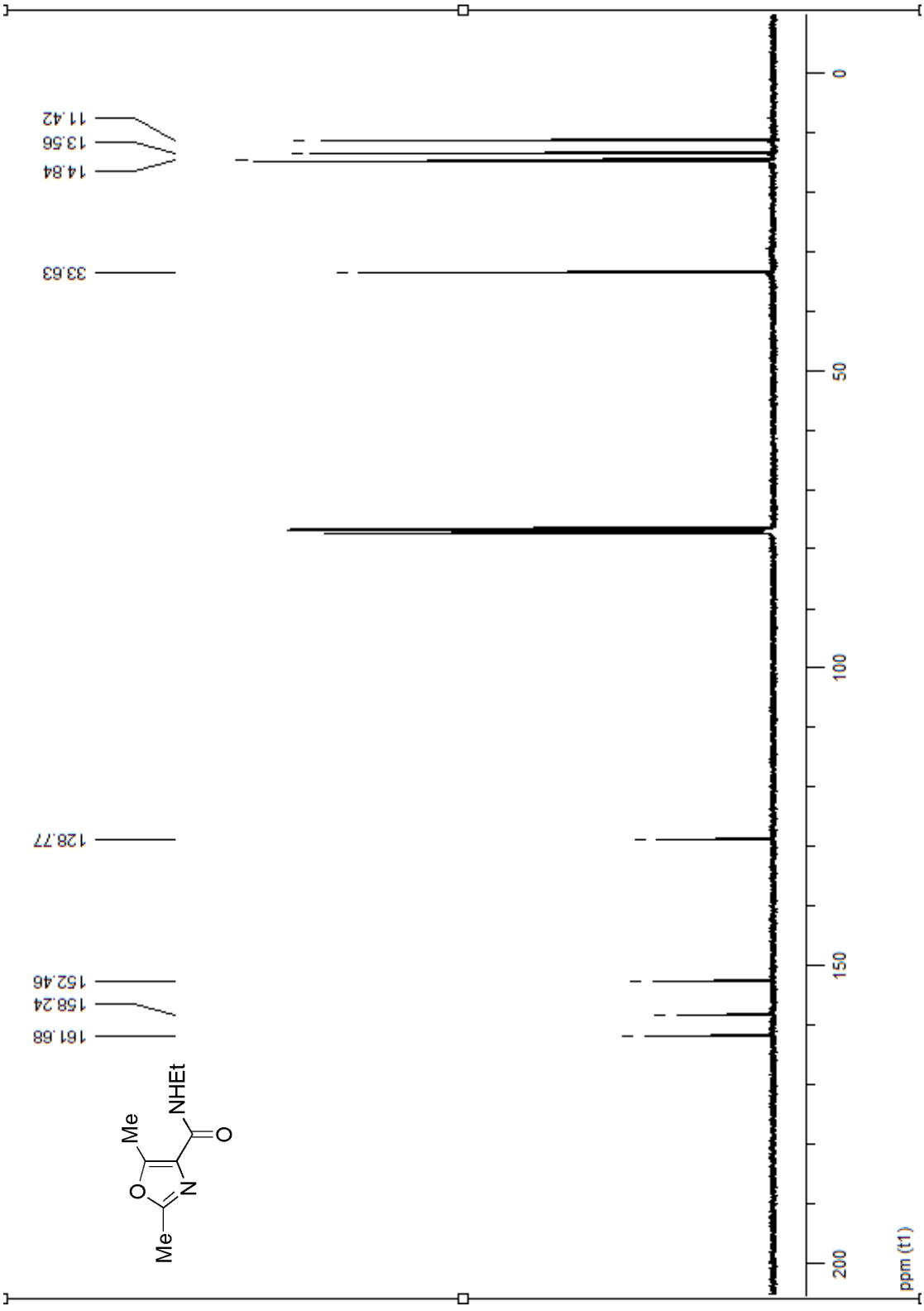
2,5-Dimethyloxazole-4-carboxylic acid 12



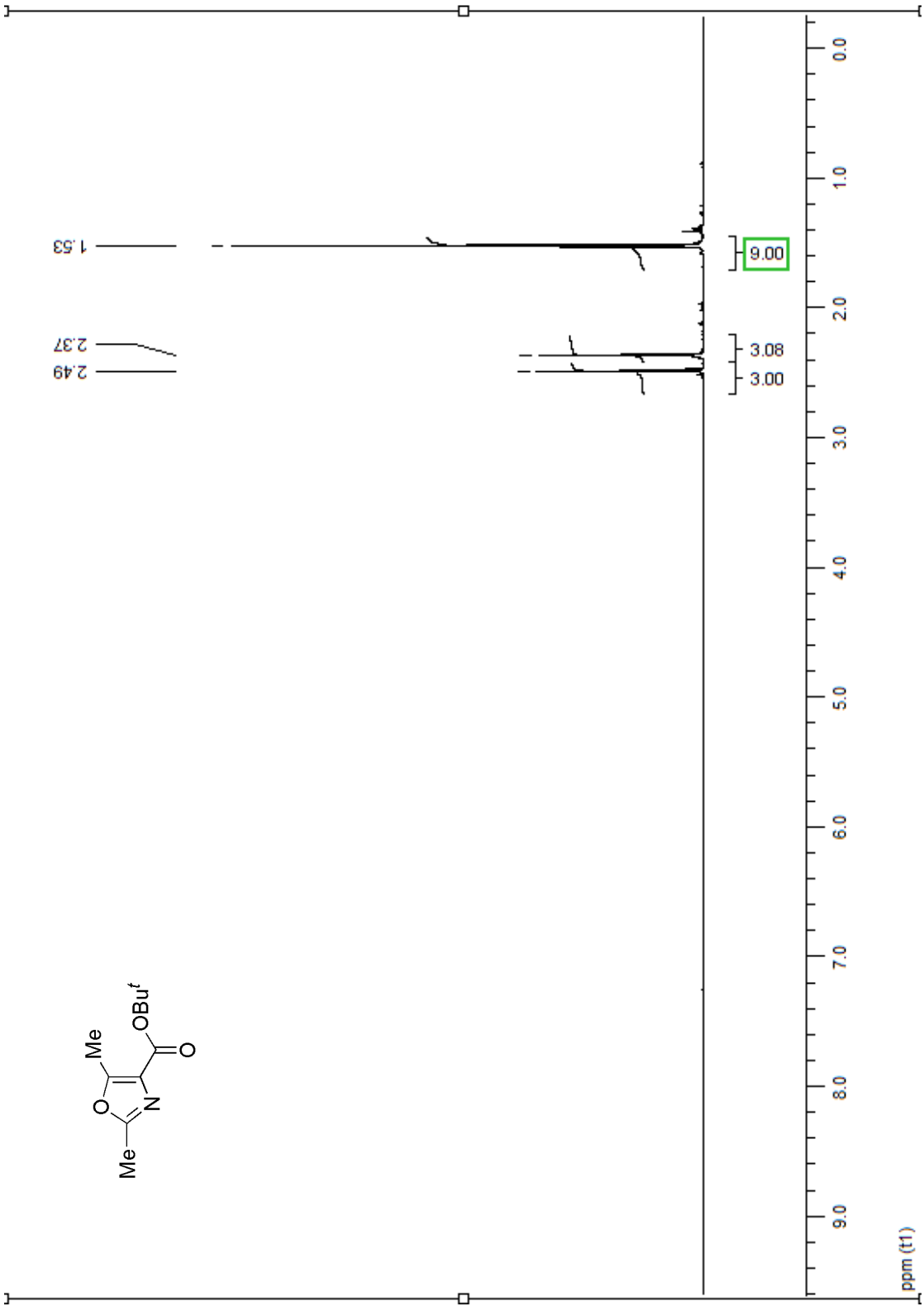

11.57
13.18
127.38
155.17
158.71
163.15
Me
OH
O
O
N
Me
0
50
100
150
200
ppm (t1)

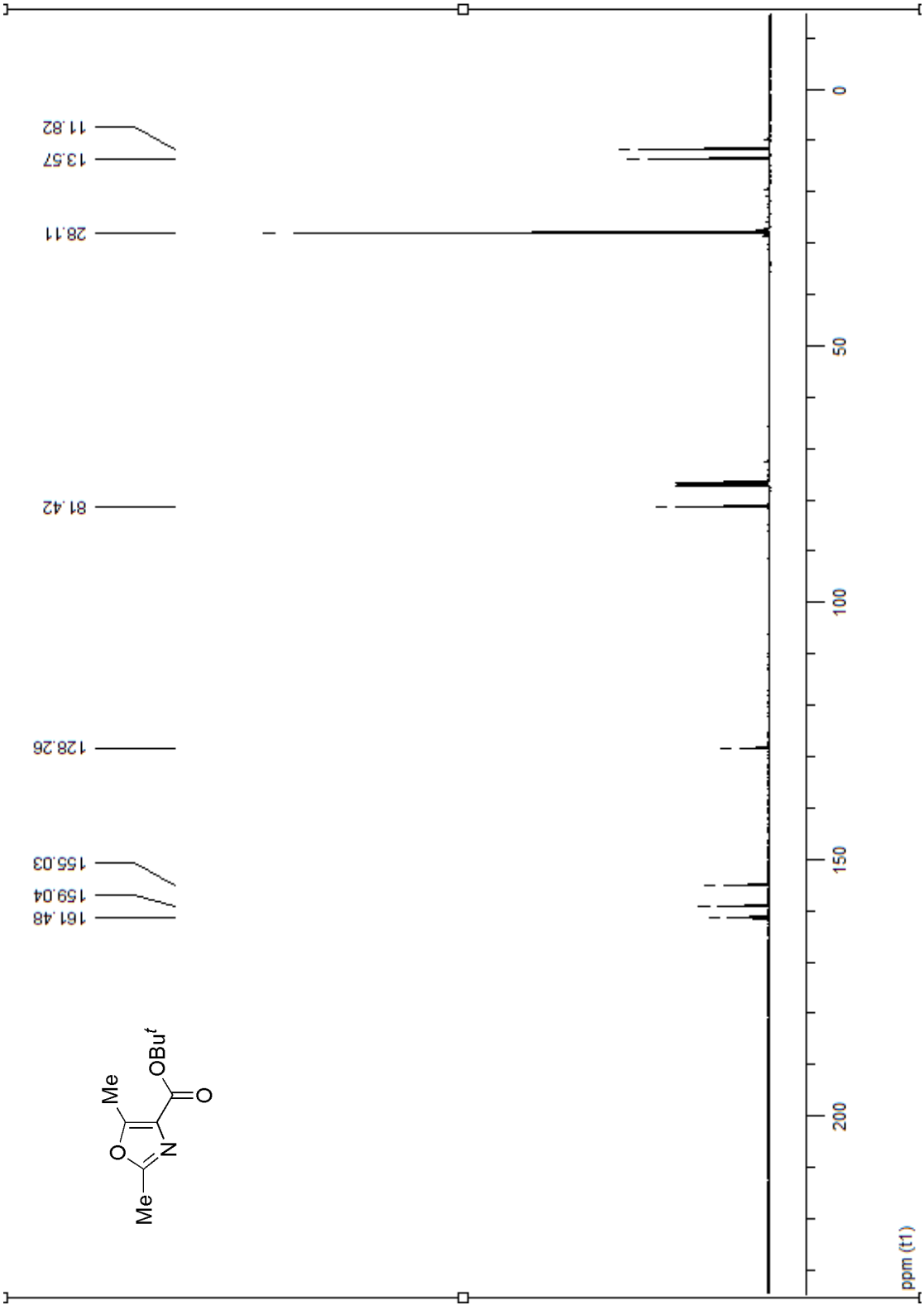
N-Ethyl-2,5-dimethyloxazole-4-carboxamide 13



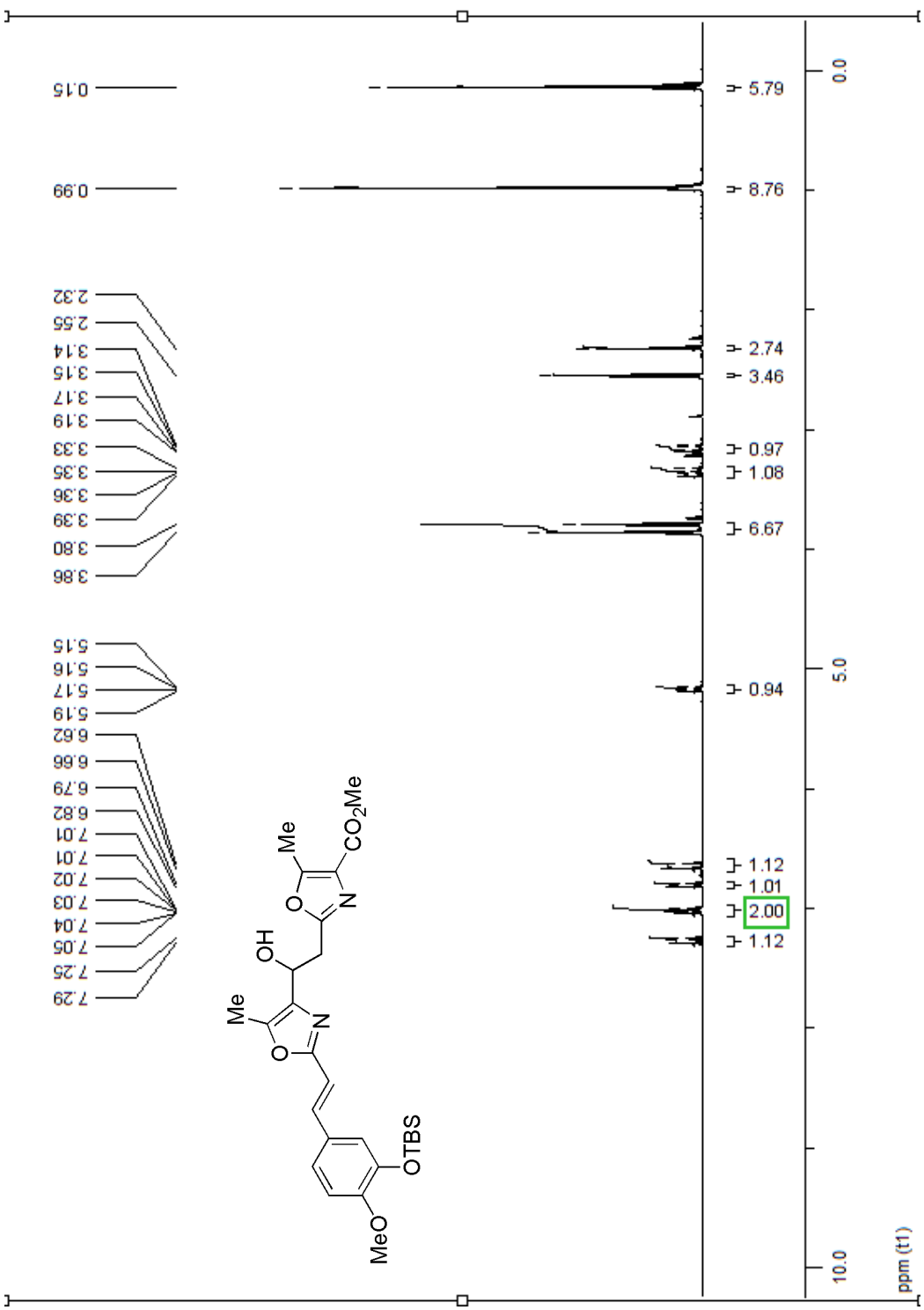

11.42
13.56
14.84
33.63
128.77
152.46
158.24
161.68
Me
NHEt
O
O
N
Me
0
50
100
150
200
ppm (t1)

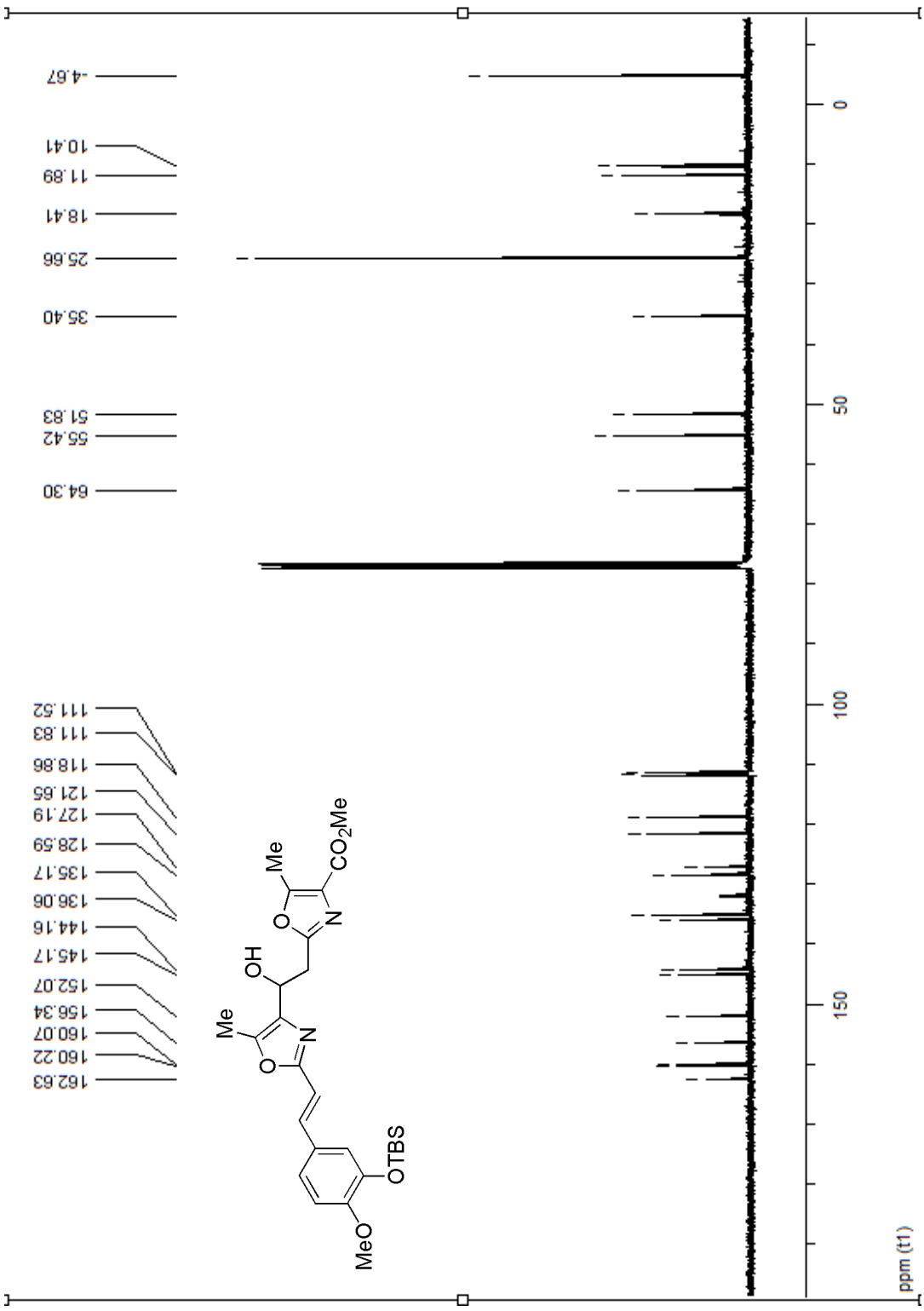
tert-Butyl 2,5-dimethyloxazole-4-carboxylate 14




11.82
13.57
28.11
81.42
128.26
155.03
159.04
161.48
Me
OBu^t
O
O
N
Me
0
50
100
150
200
ppm (t1)

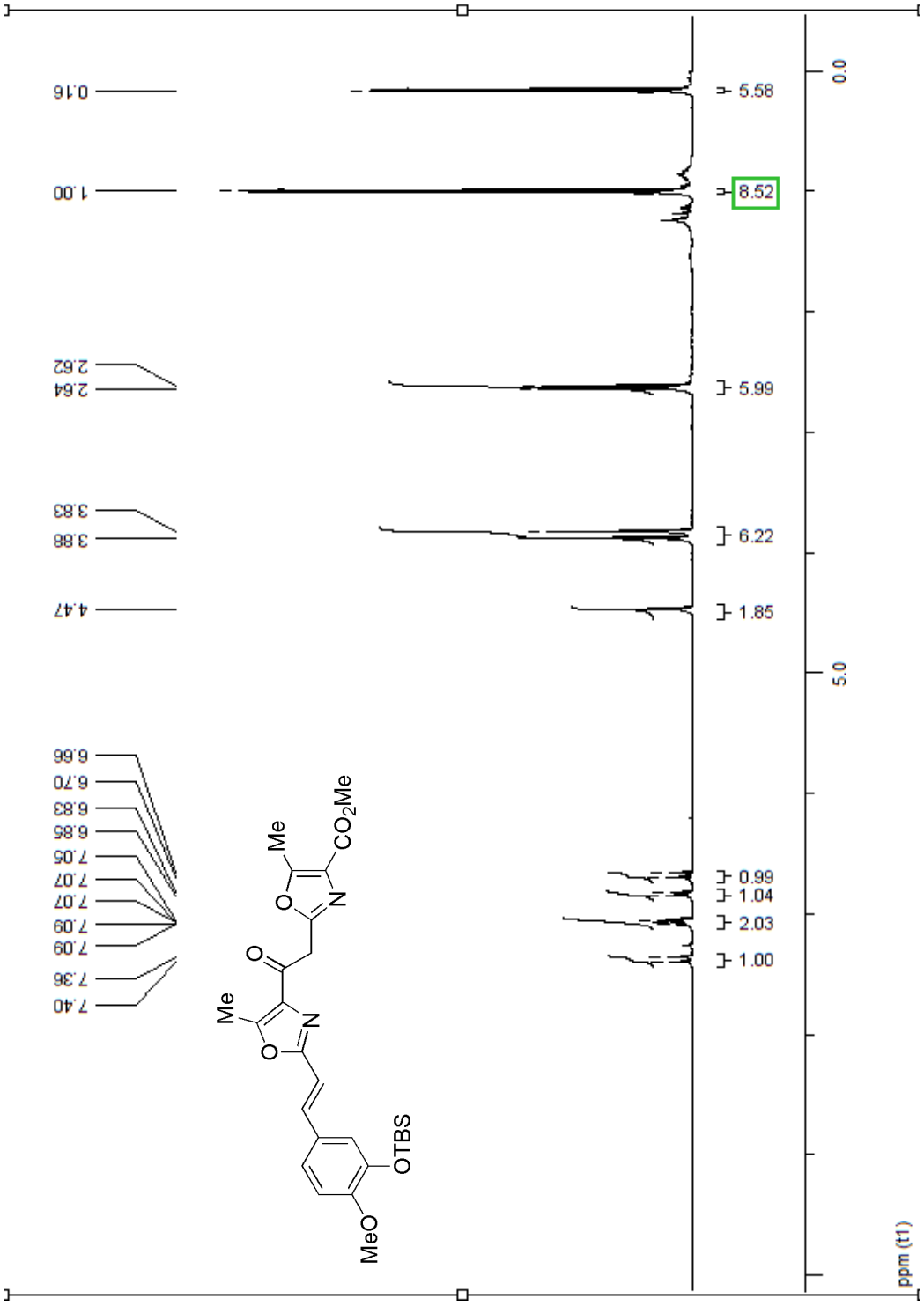
Methyl 2-(2-(2-(3-*tert*-butyldimethylsiloxy-4-methoxystyryl)-5-methyloxazol-4-yl)-2-hydroxyethyl)-5-methyloxazole-4-carboxylate 17a

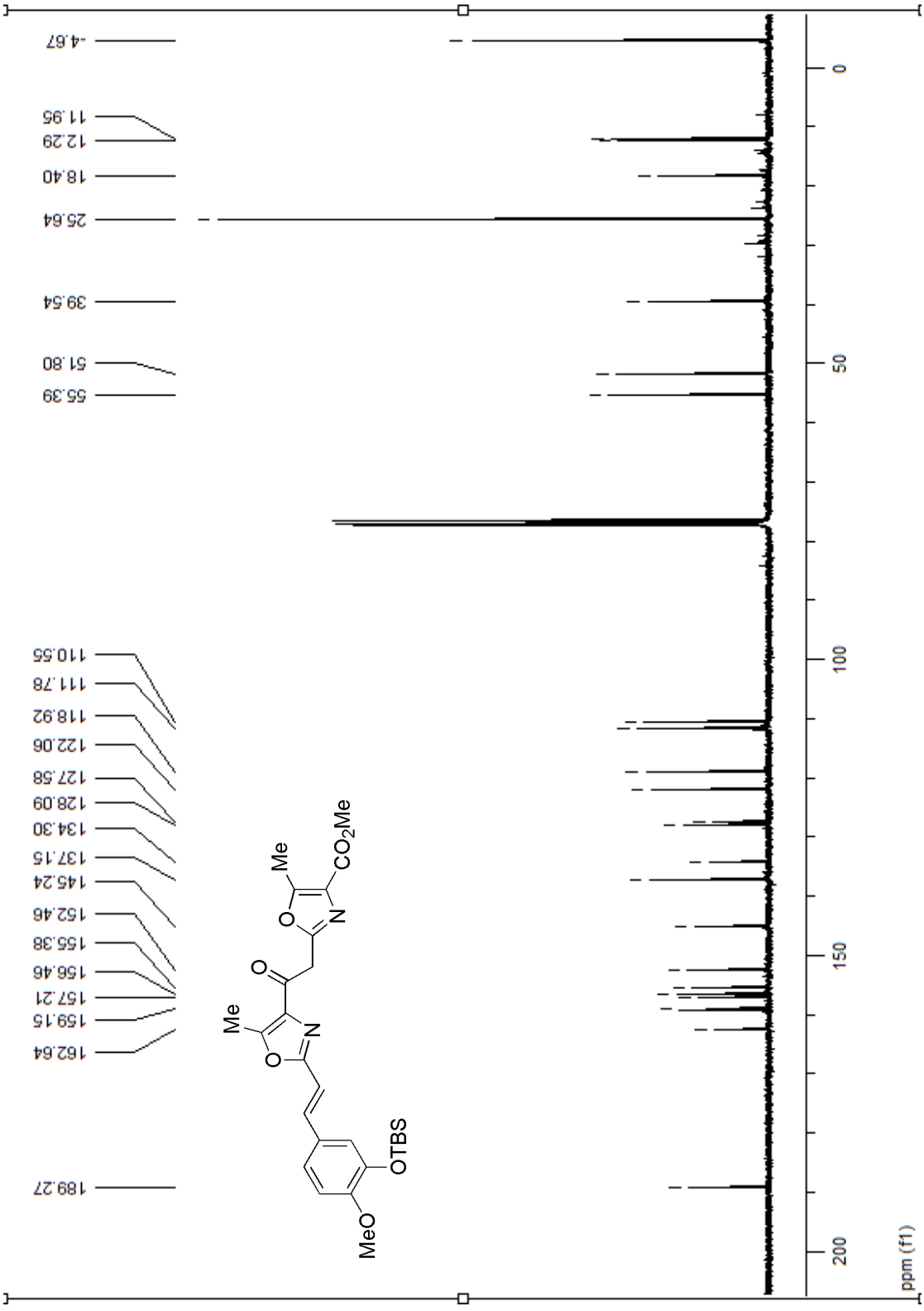



-4.67
10.41
11.89
18.41
25.66
35.40
51.83
55.42
64.30
111.52
111.83
118.86
121.65
127.19
128.59
135.17
136.06
144.16
145.17
152.07
156.34
160.07
160.22
162.63
Me
CO2Me
OH
Me
OTBS
MeO
0
50
100
150
ppm (t1)

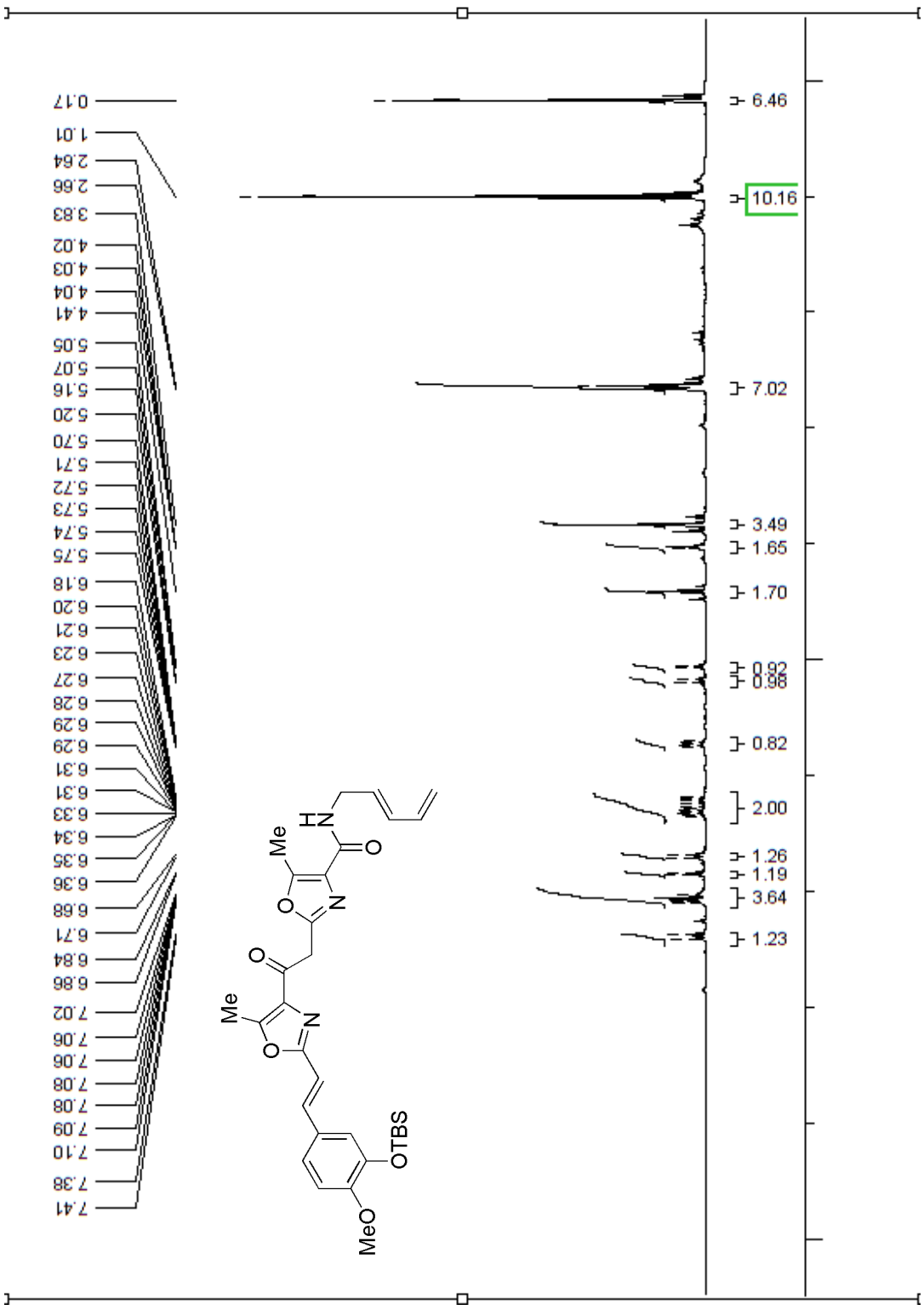
Methyl 2-(2-(2-(3-*tert*-butyldimethylsiloxy-4-methoxystyryl)-5-methyloxazol-4-yl)-2-oxoethyl)-5-methyloxazole-4-carboxylate

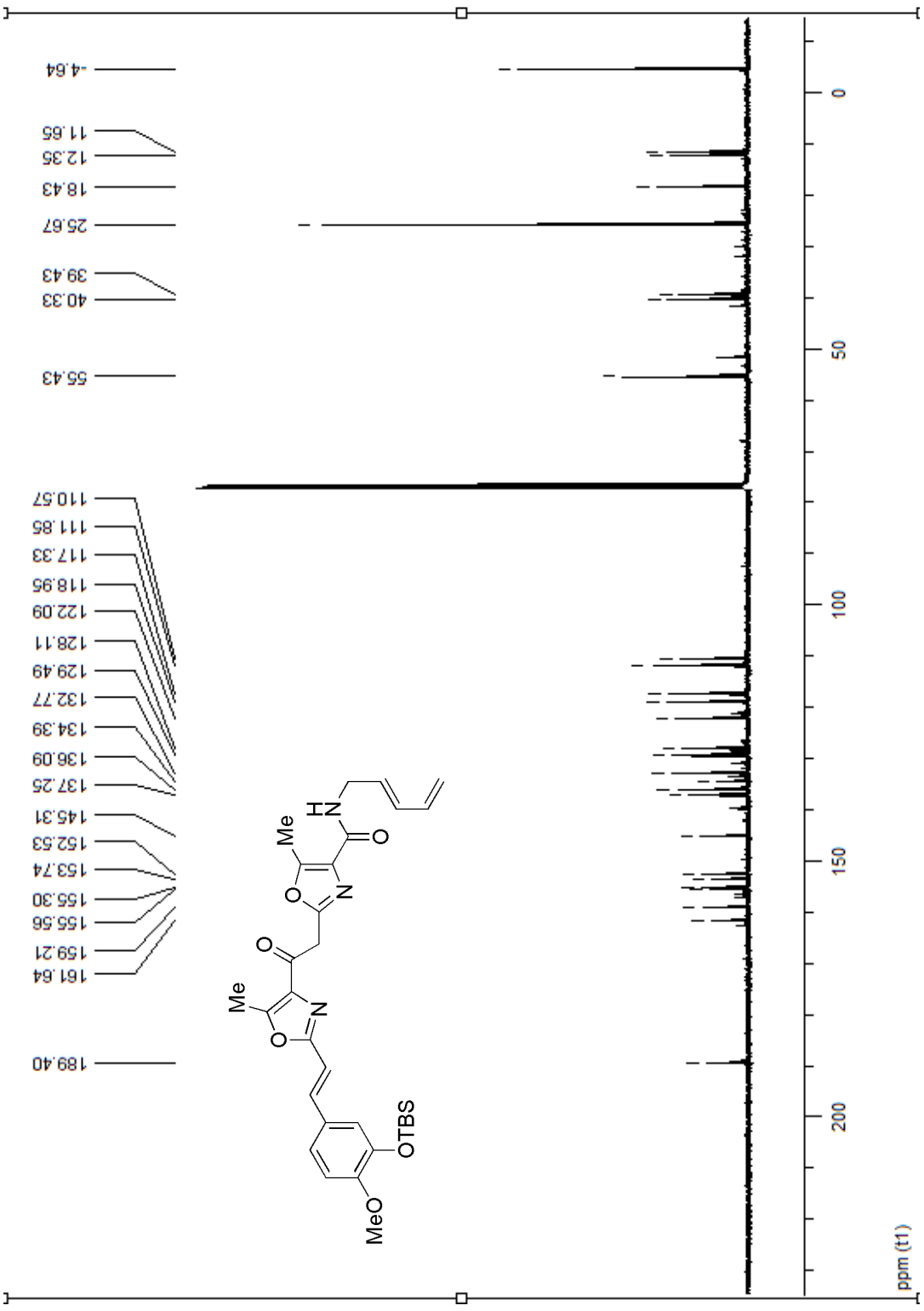
15



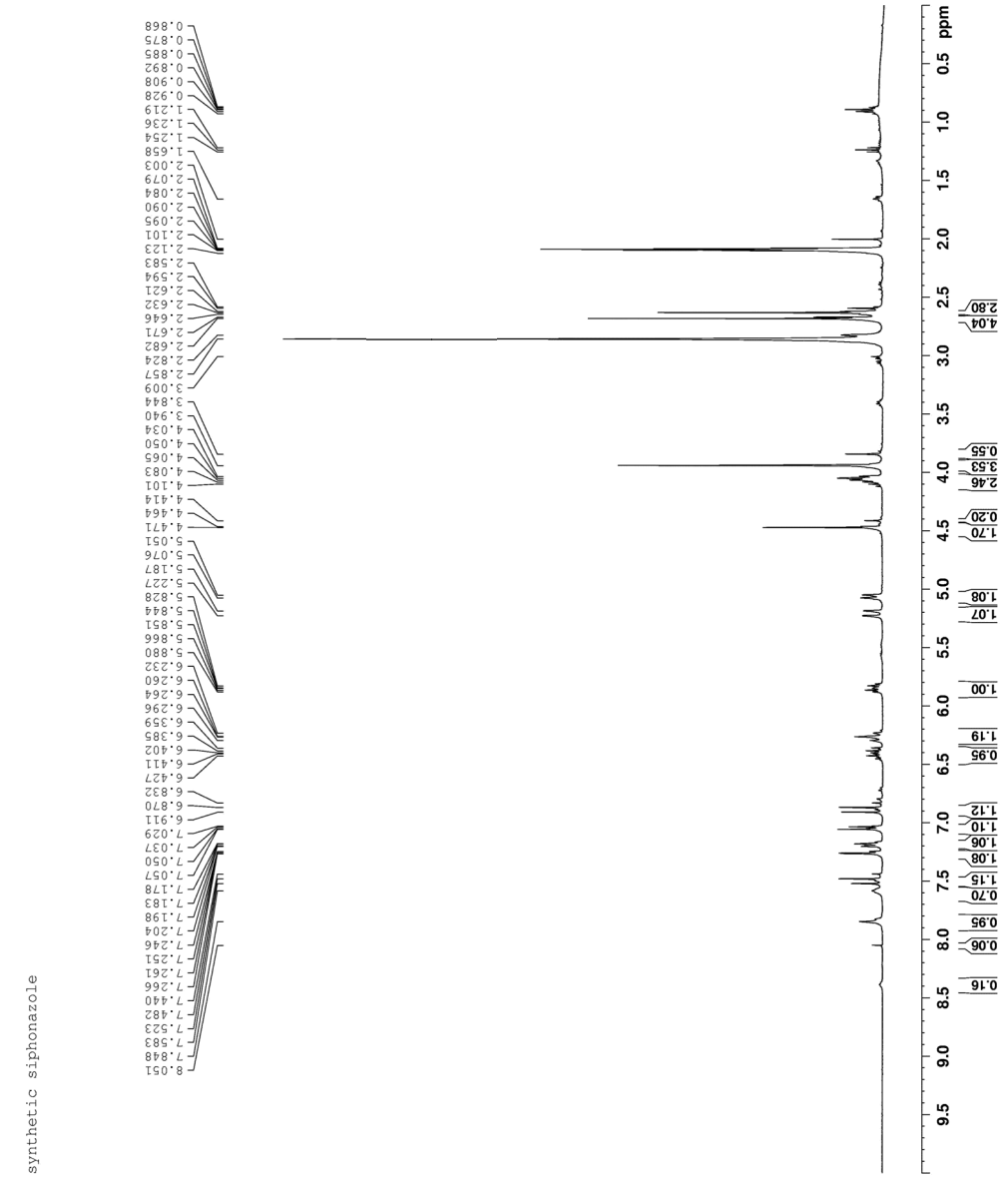

-4.67
11.95
12.29
18.40
25.64
39.54
51.80
55.39
110.55
111.78
118.92
122.06
127.58
128.09
134.30
137.15
145.24
152.46
155.38
156.46
157.21
159.15
162.64
189.27
Me
CO2Me
O
N
O
Me
O
N
OTBS
MeO
0
50
100
150
200
ppm (f1)

TBDMS-protected siphonazole 19

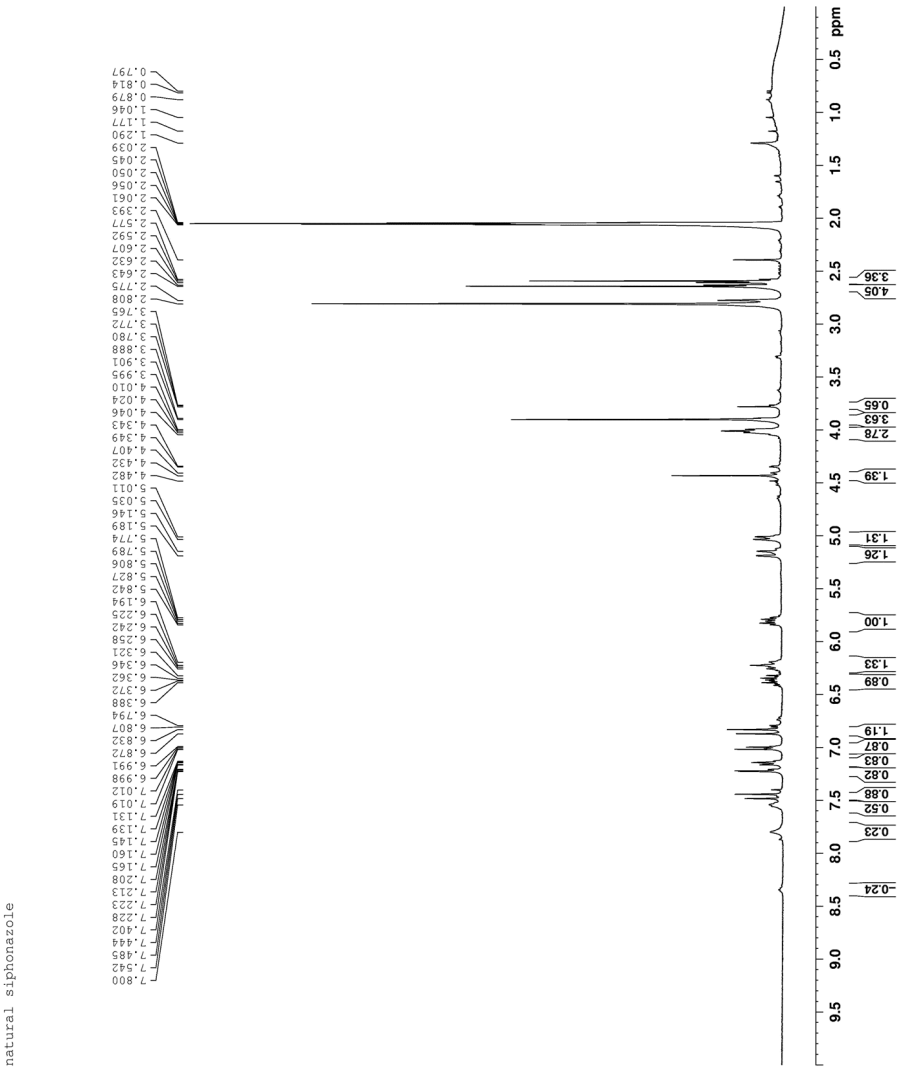



-4.64
11.65
12.35
18.43
25.67
39.43
40.33
55.43
110.57
111.85
117.33
118.95
122.09
128.11
129.49
132.77
134.39
136.09
137.25
145.31
152.53
153.74
155.30
155.56
159.21
161.64
189.40
0
50
100
150
200
ppm (t1)
Me
O
N
O
N
H
O
Me
O
N
O
OTBS
MeO

Synthetic siphonazole 1.

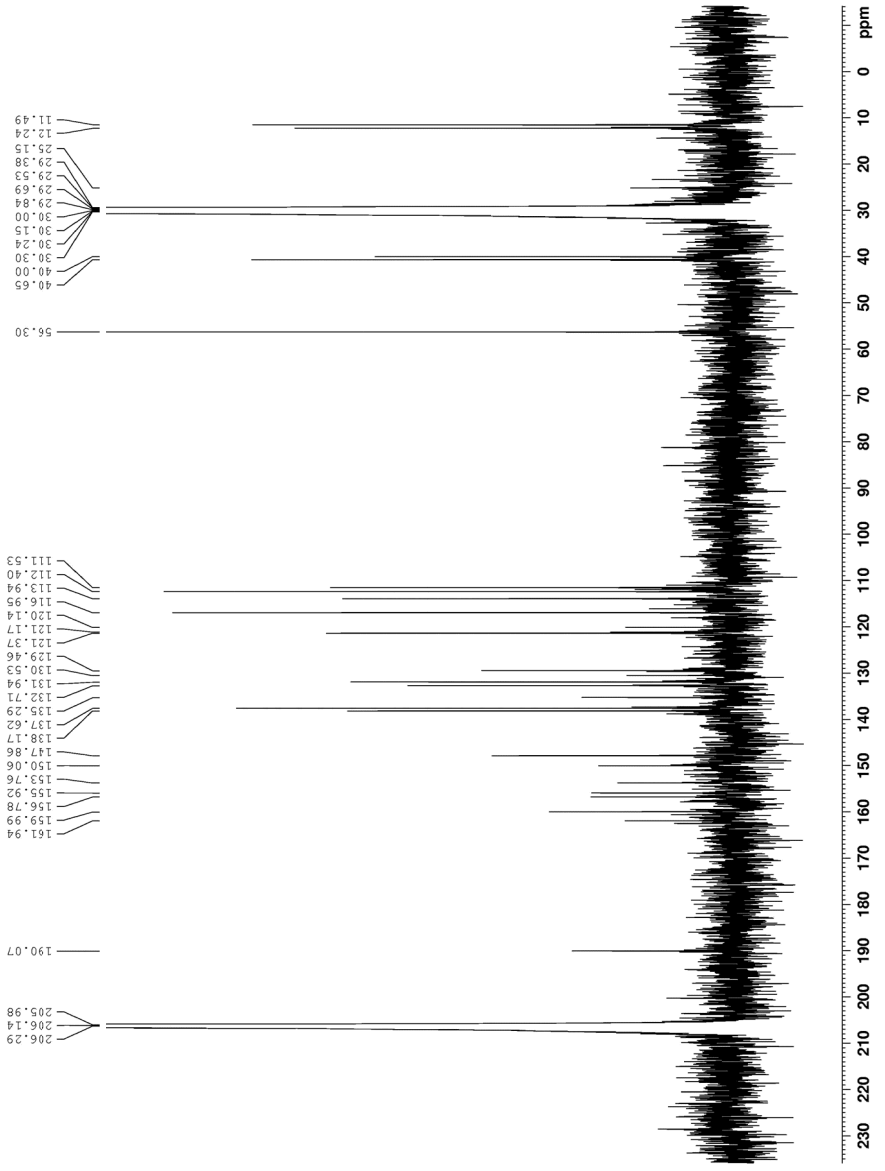


Natural siphonazole 1

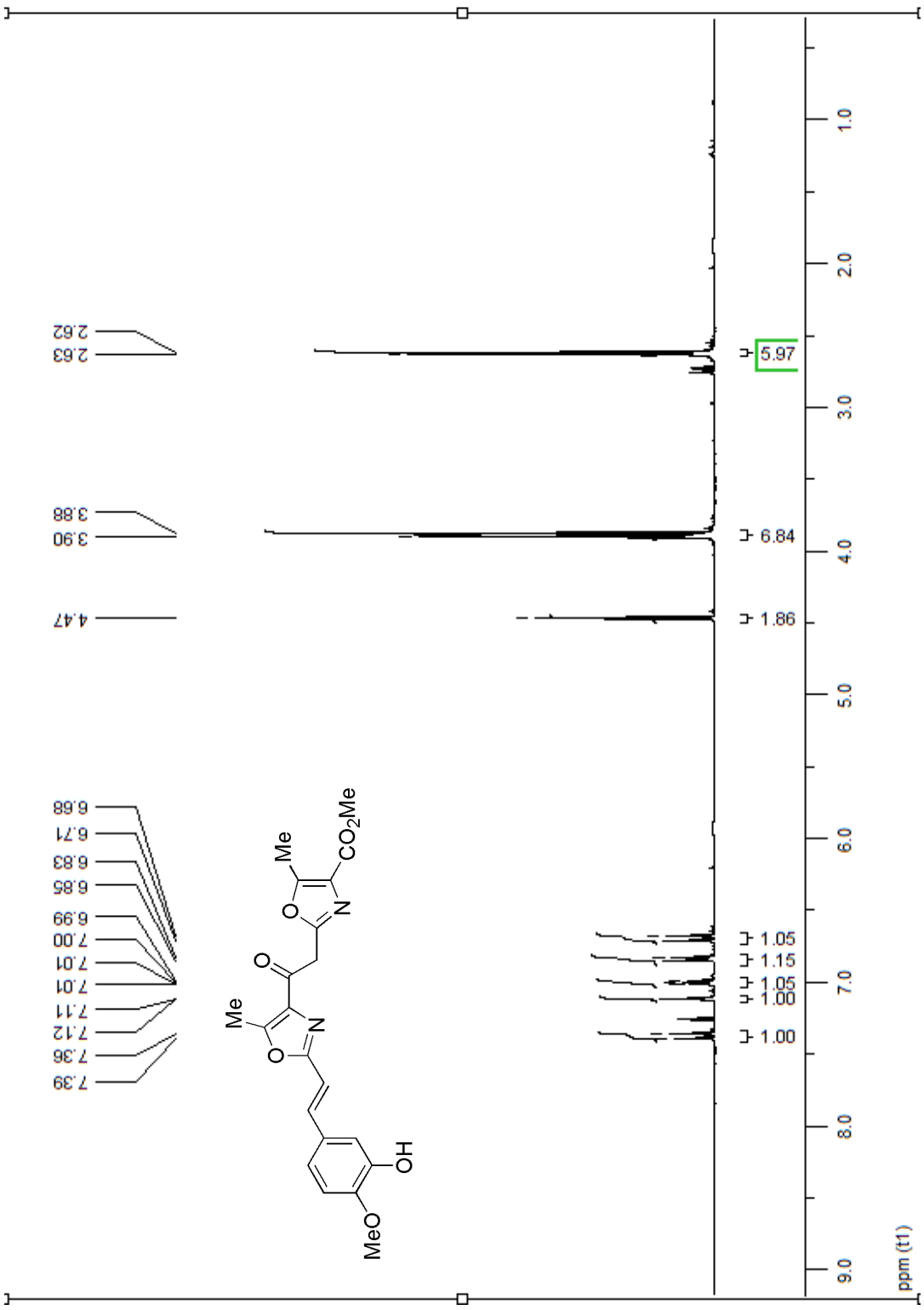


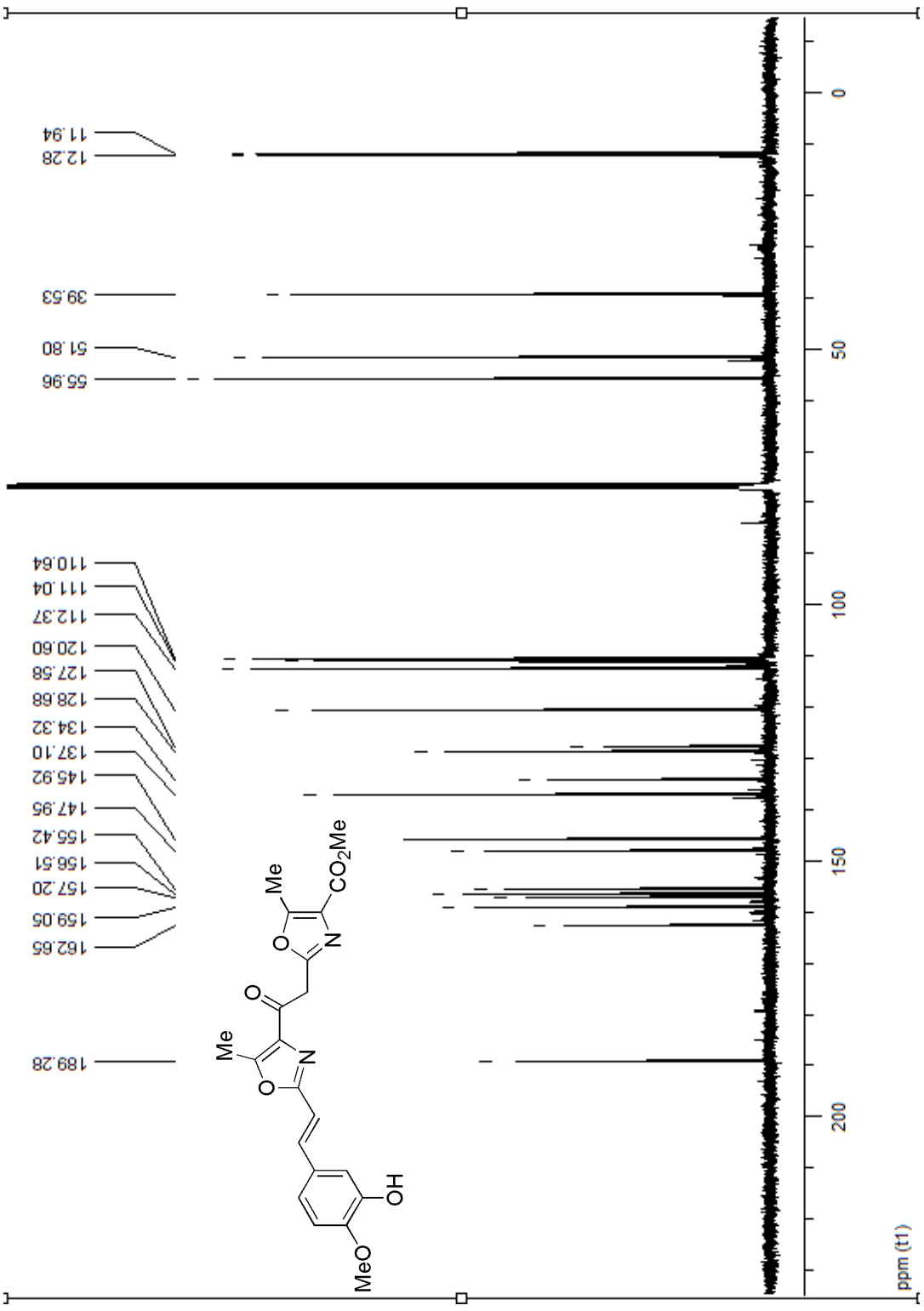
Synthetic siphonazole 1

synthetic siphonazole carbon spectrum, 125 MHz

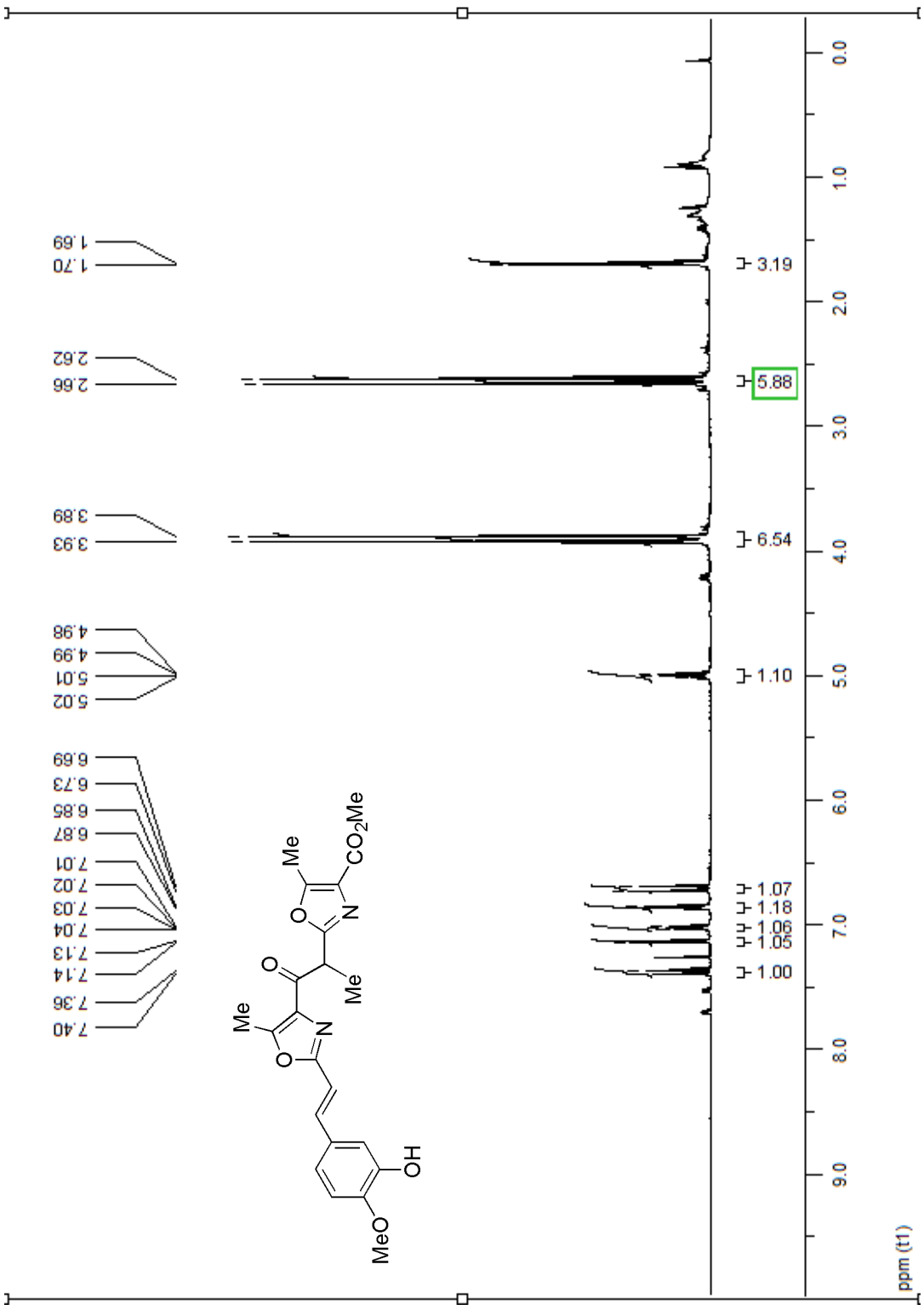


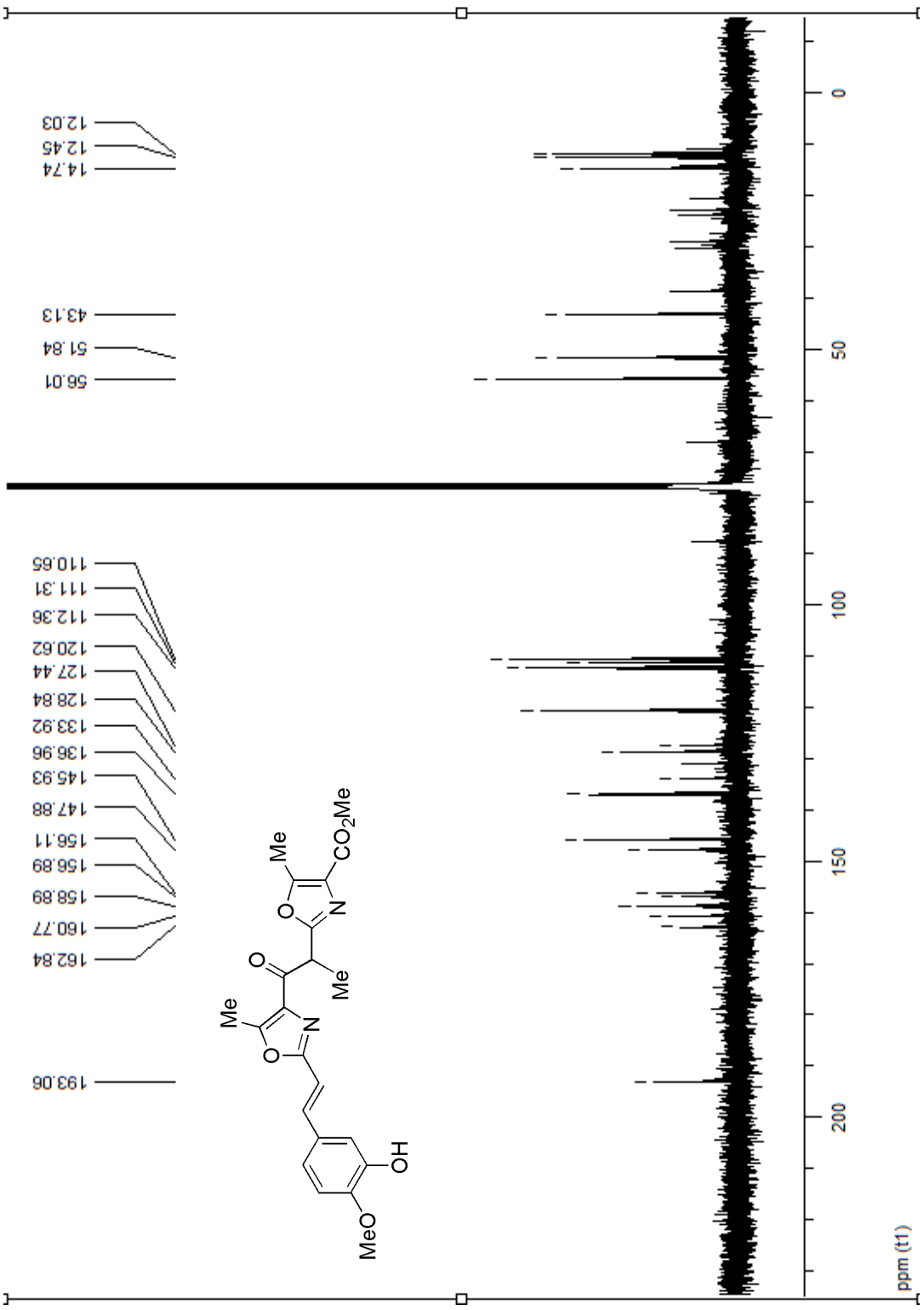
Methyl 2-(2-(2-(3-hydroxy-4-methoxystyryl)-5-methyloxazol-4-yl)-2-oxoethyl)-5-methyloxazole-4-carboxylate 20



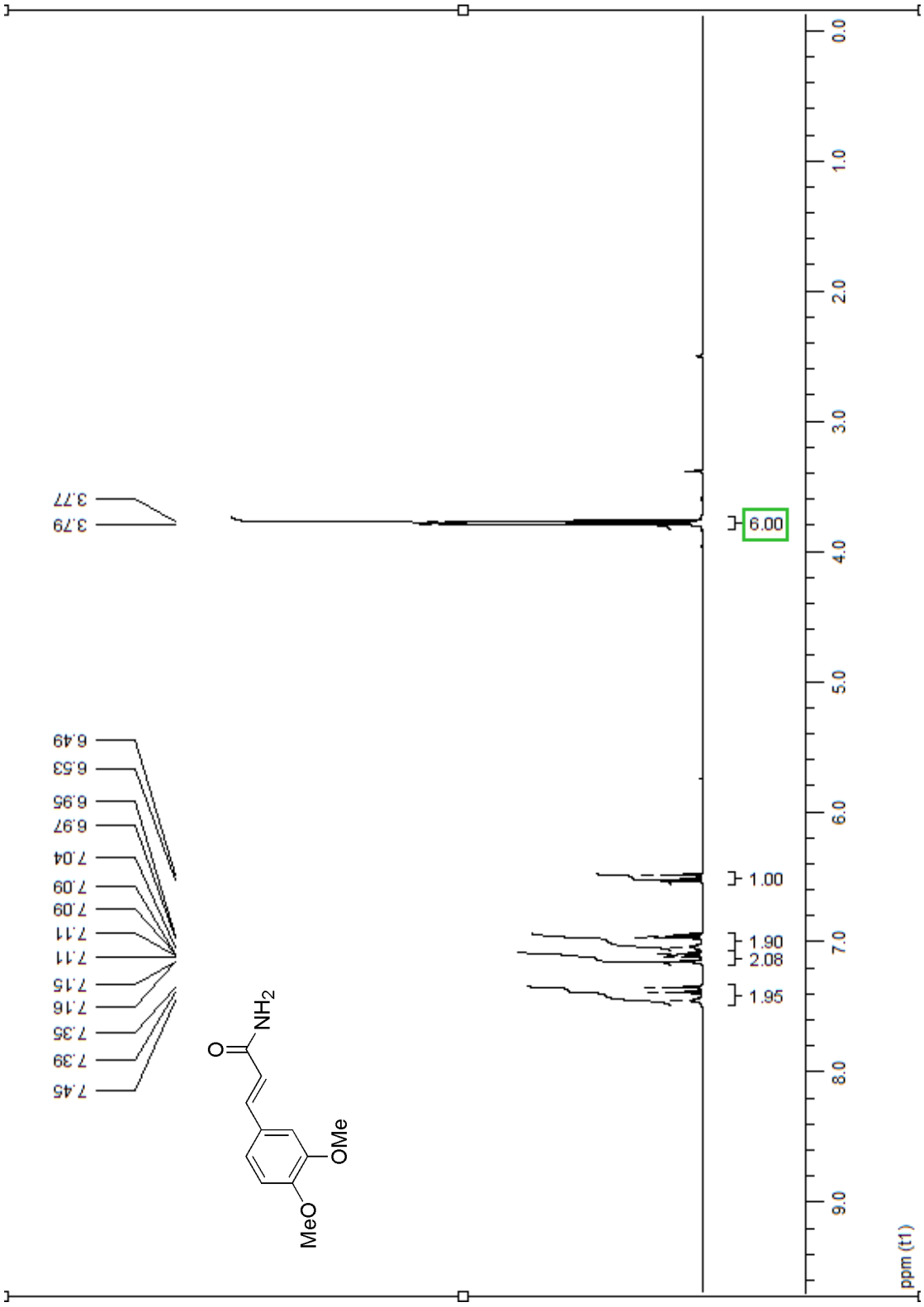

11.94
12.28
39.53
51.80
55.96
110.64
111.04
112.37
120.60
127.58
128.68
134.32
137.10
145.92
147.95
155.42
156.51
157.20
159.05
162.65
189.28
Me
CO2Me
O
N
O
Me
N
O
OH
MeO
0
50
100
150
200
ppm (t1)

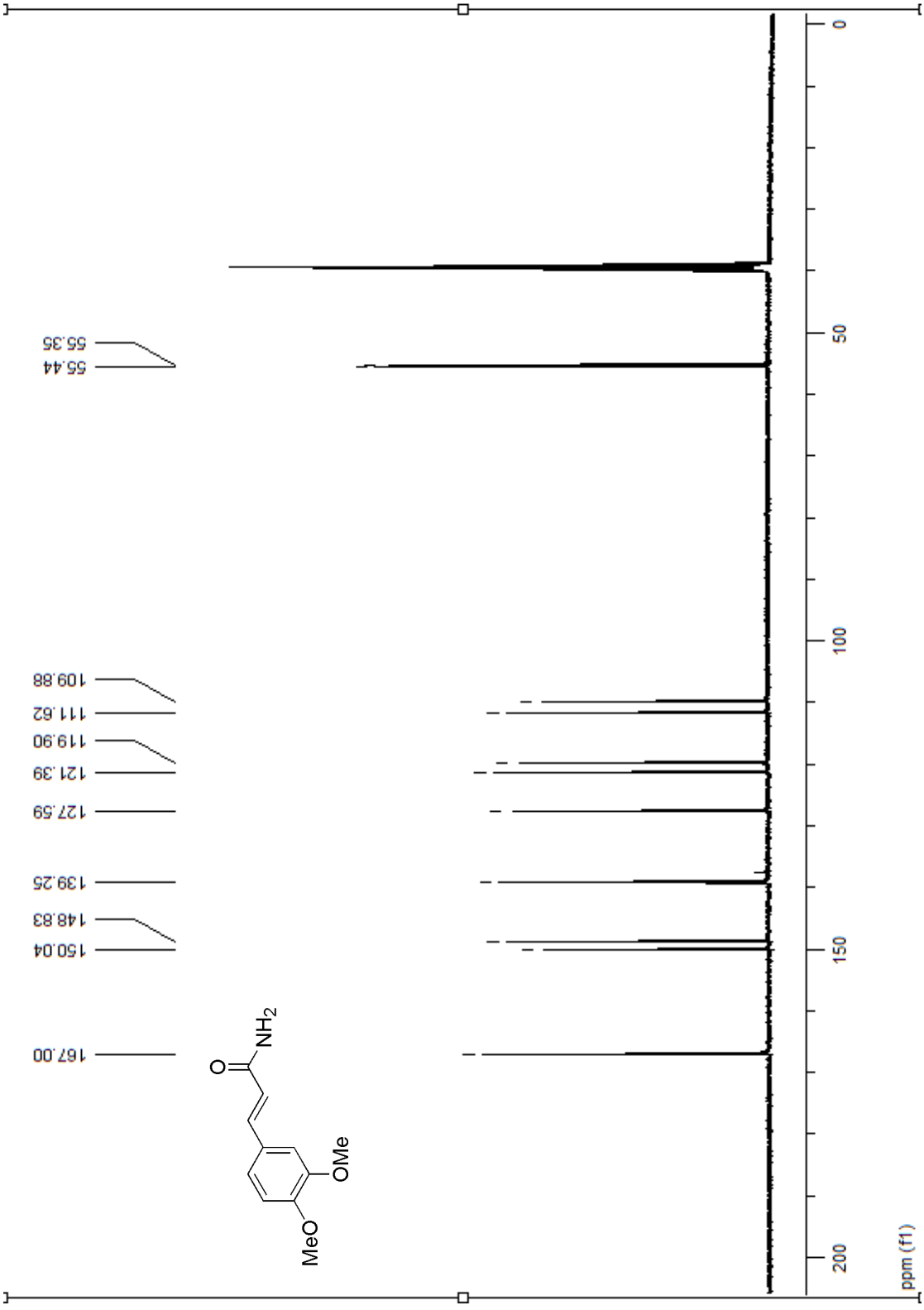
Methyl 2-(2-(2-(3-hydroxy-4-methoxystyryl)-5-methyloxazol-4-yl)-2-oxo-1-methylethyl)-5-methyloxazole-4-carboxylate 21



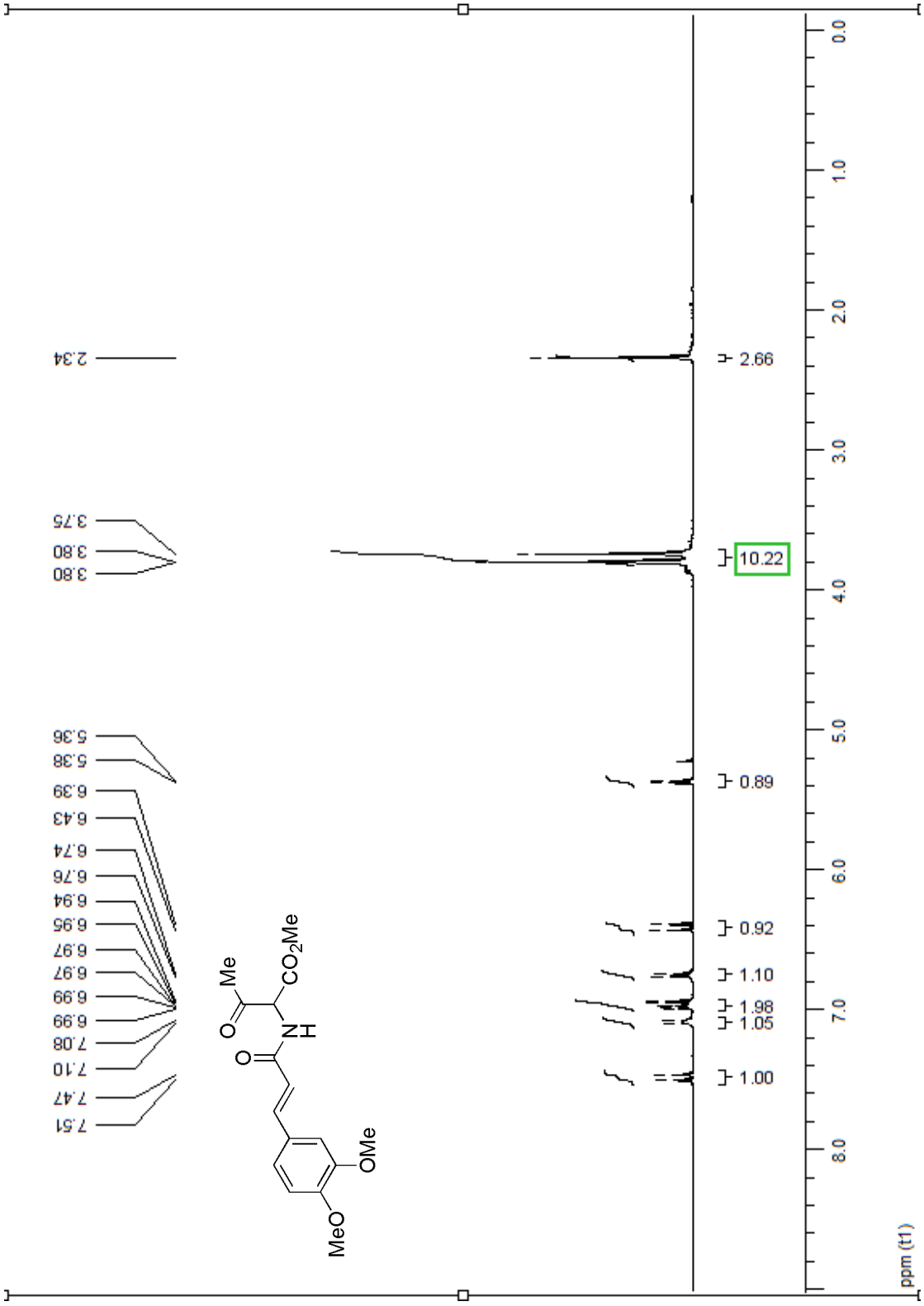

12.03
12.45
14.74
43.13
51.84
56.01
110.65
111.31
112.36
120.62
127.44
128.84
133.92
136.96
145.93
147.88
156.11
156.89
158.89
160.77
162.84
193.06
Me
CO2Me
O
N
Me
O
Me
N
O
OH
MeO
0
50
100
150
200
ppm (t1)

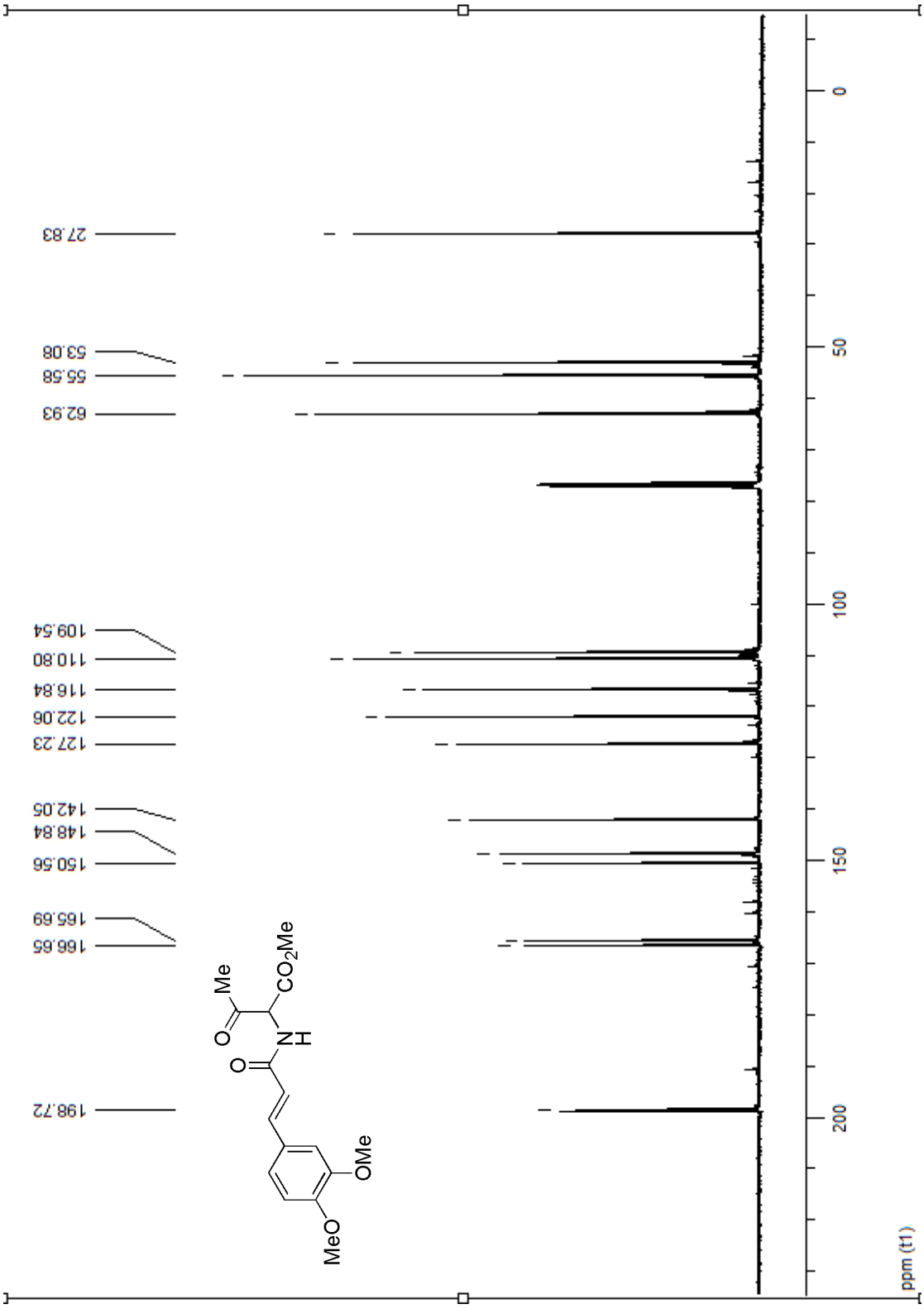
(*E*)-3-(3,4-Dimethoxyphenyl)acrylamide 4b



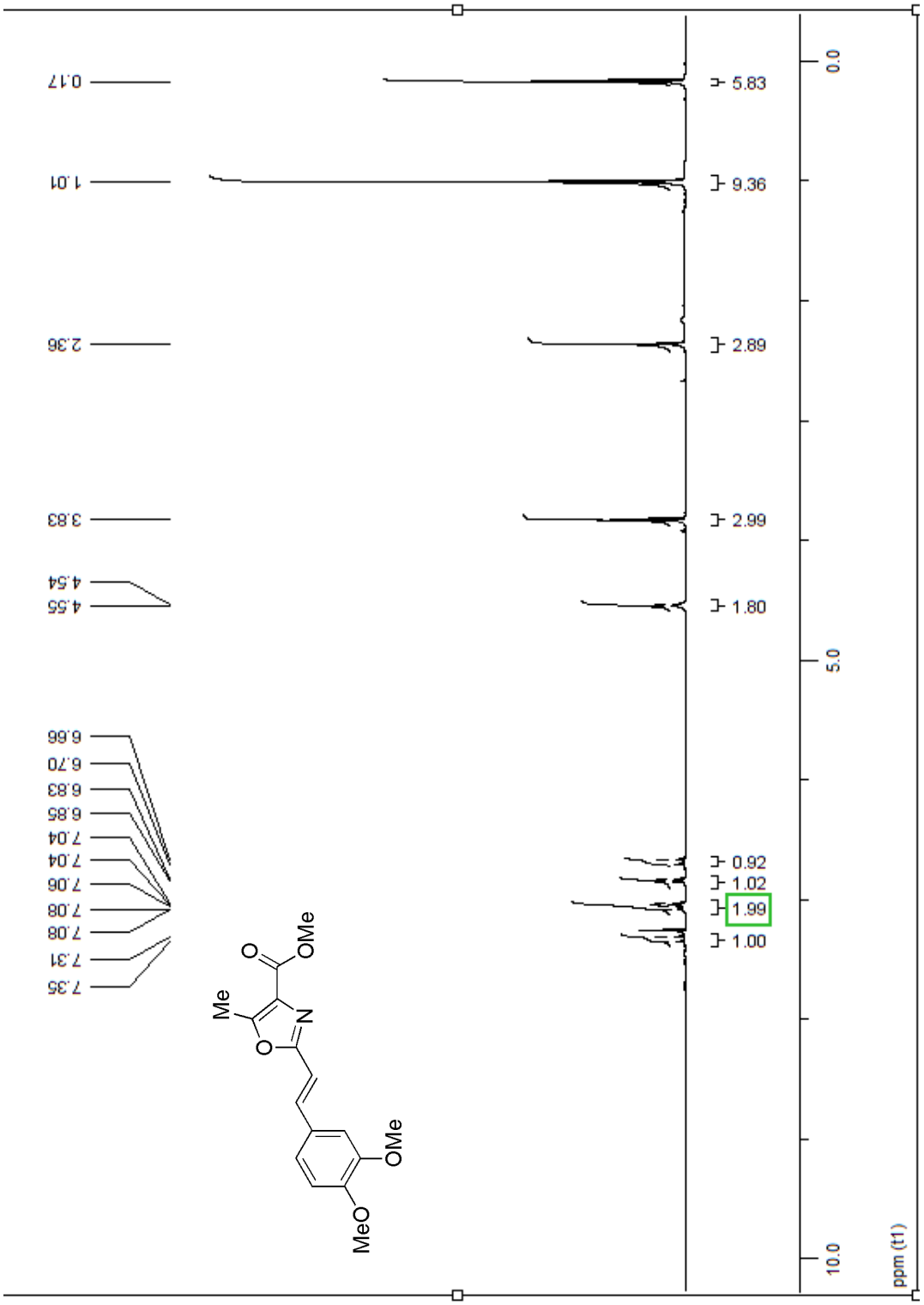

55.35
55.44
109.88
111.62
119.90
121.39
127.59
139.25
148.83
150.04
167.00
O
NH2
OMe
MeO
0
50
100
150
200
ppm (f1)

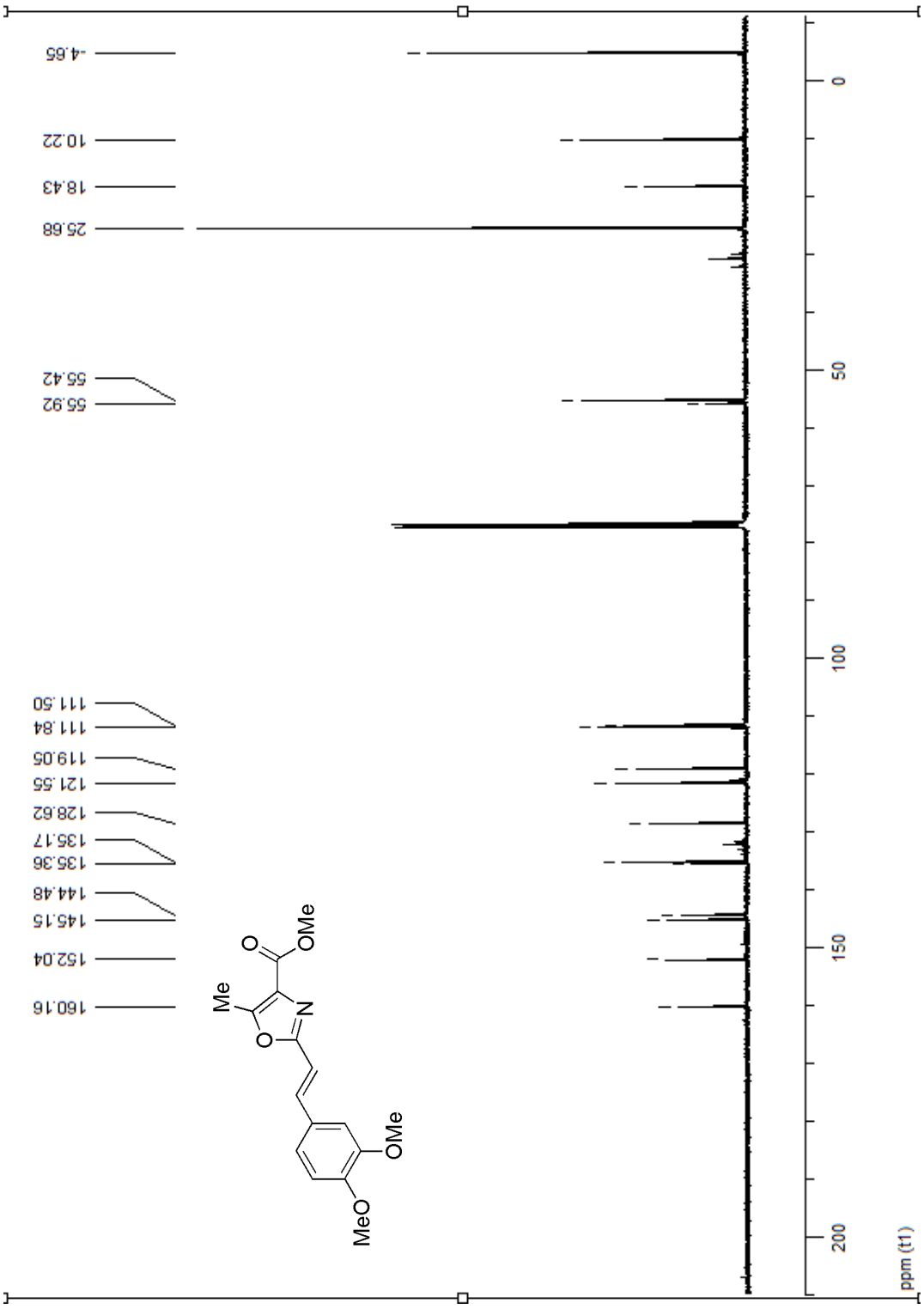
(*E*)-Methyl 2-(-3-(3,4-dimethoxyphenyl)acrylamido)-3-oxobutanoate 5b



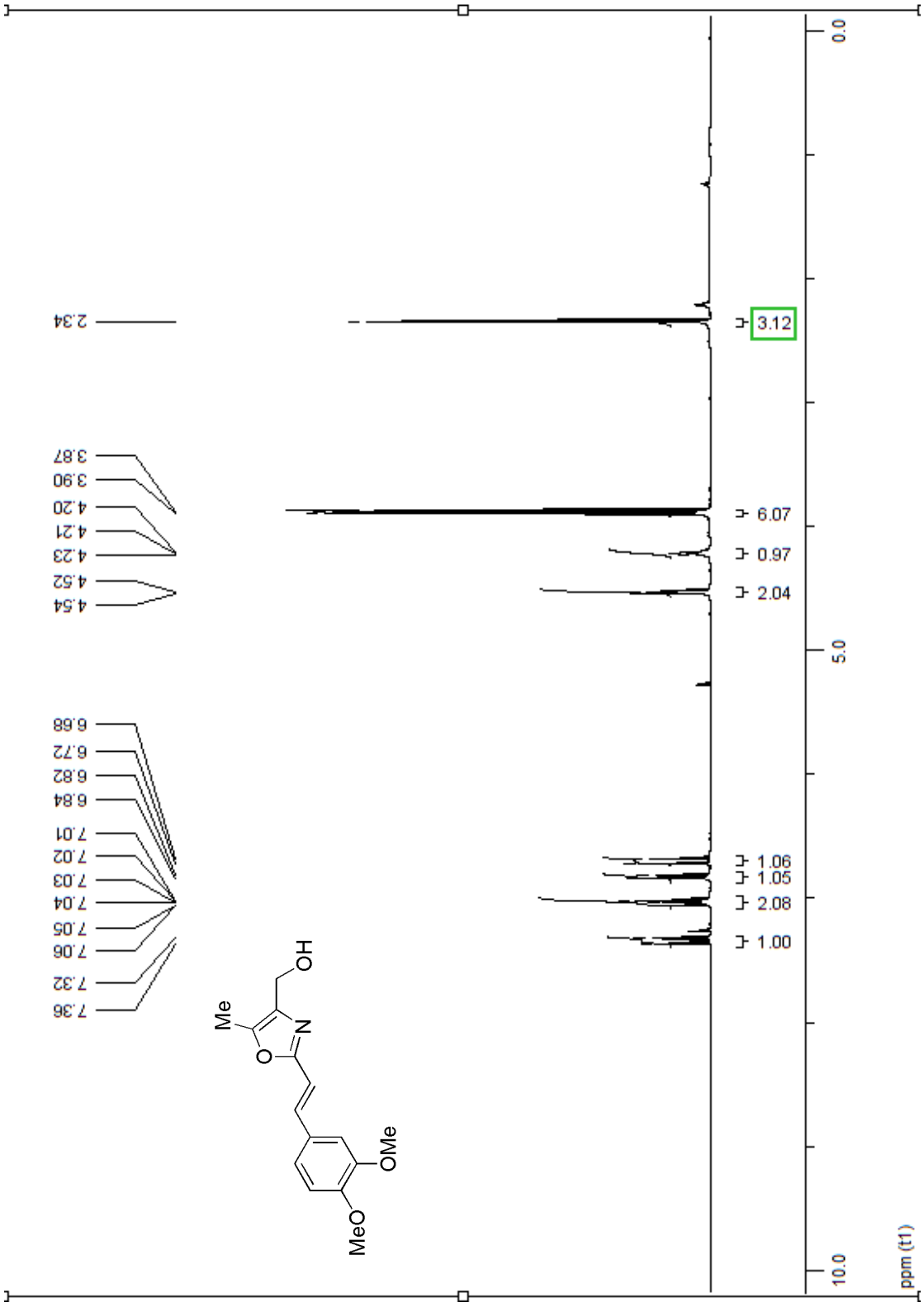

27.83
53.08
55.58
62.93
109.54
110.80
116.84
122.06
127.23
142.05
148.84
150.56
165.69
166.65
198.72
Me
CO2Me
O
N
H
O
OMe
MeO
0
50
100
150
200
ppm (t1)

(*E*)-Methyl 2-(3,4-dimethoxystyryl)-5-methyloxazole-4-carboxylate 6b

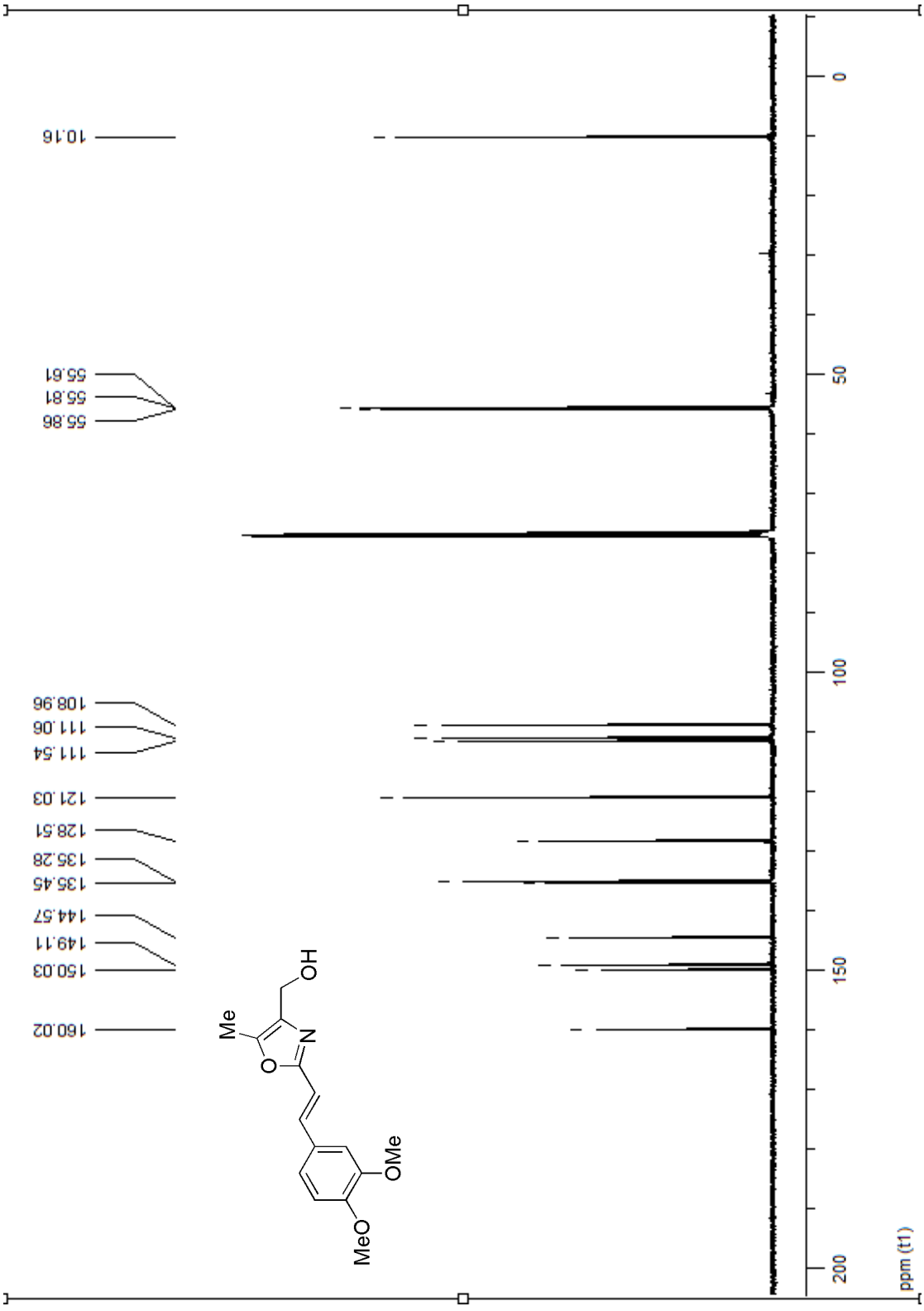



-4.65
10.22
18.43
25.68
55.42
55.92
111.50
111.84
119.05
121.55
128.62
135.17
135.36
144.48
145.15
152.04
160.16
0
50
100
150
200
ppm (t1)
Me
O
OMe
N
O
OMe
MeO

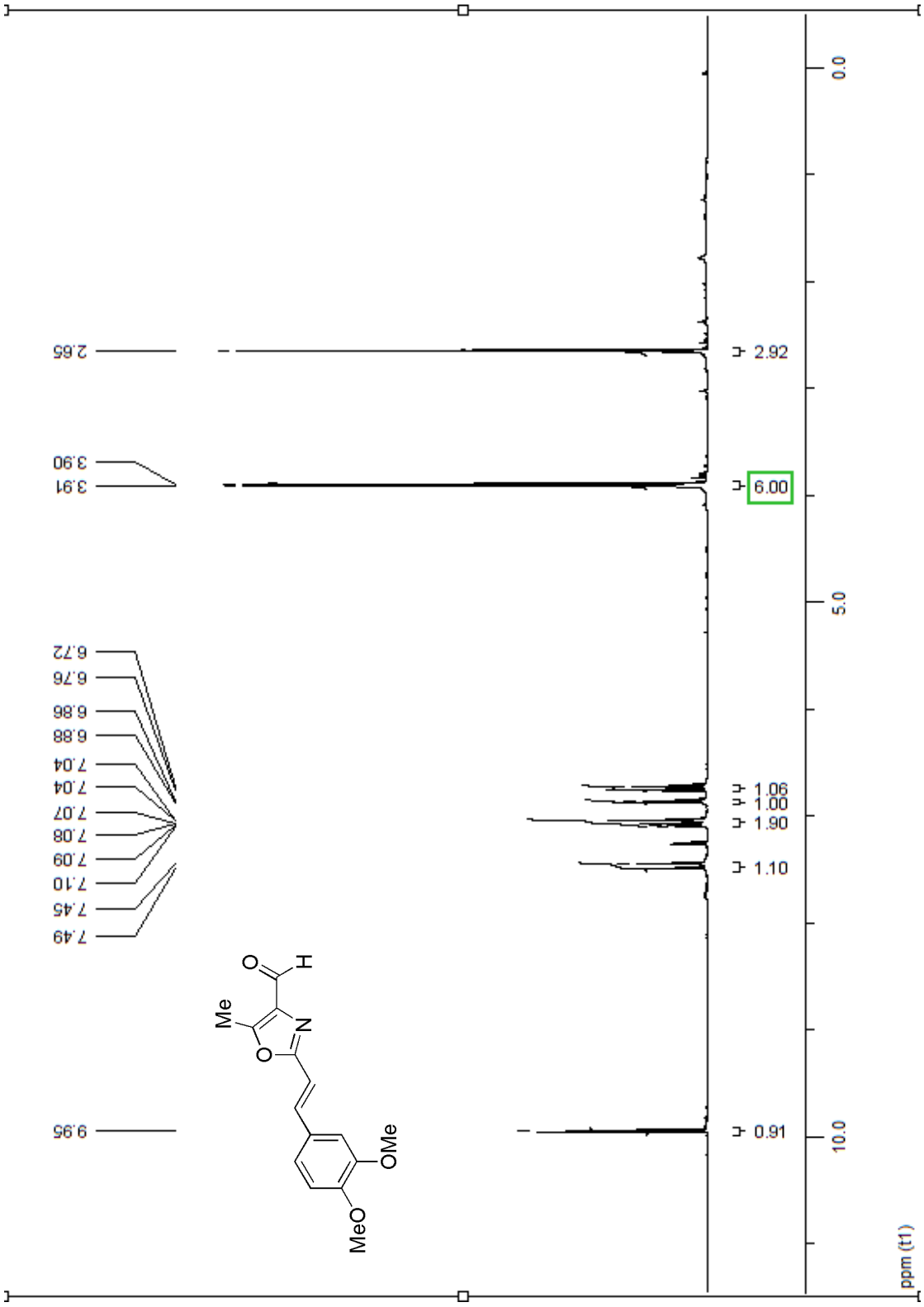
2-(3,4-Dimethoxystyryl)-5-methyloxazol-4-yl)methanol 7b

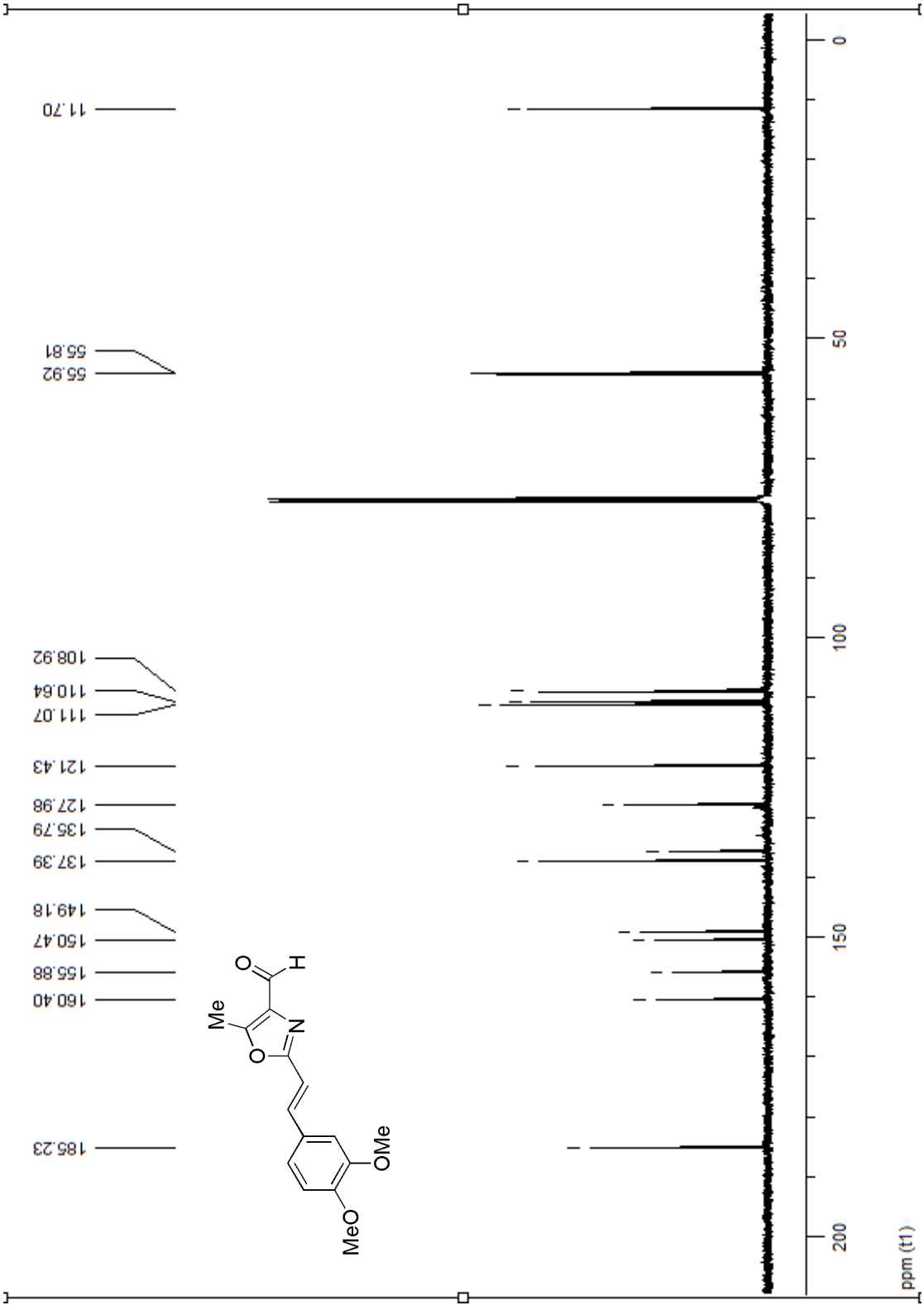


ESI61

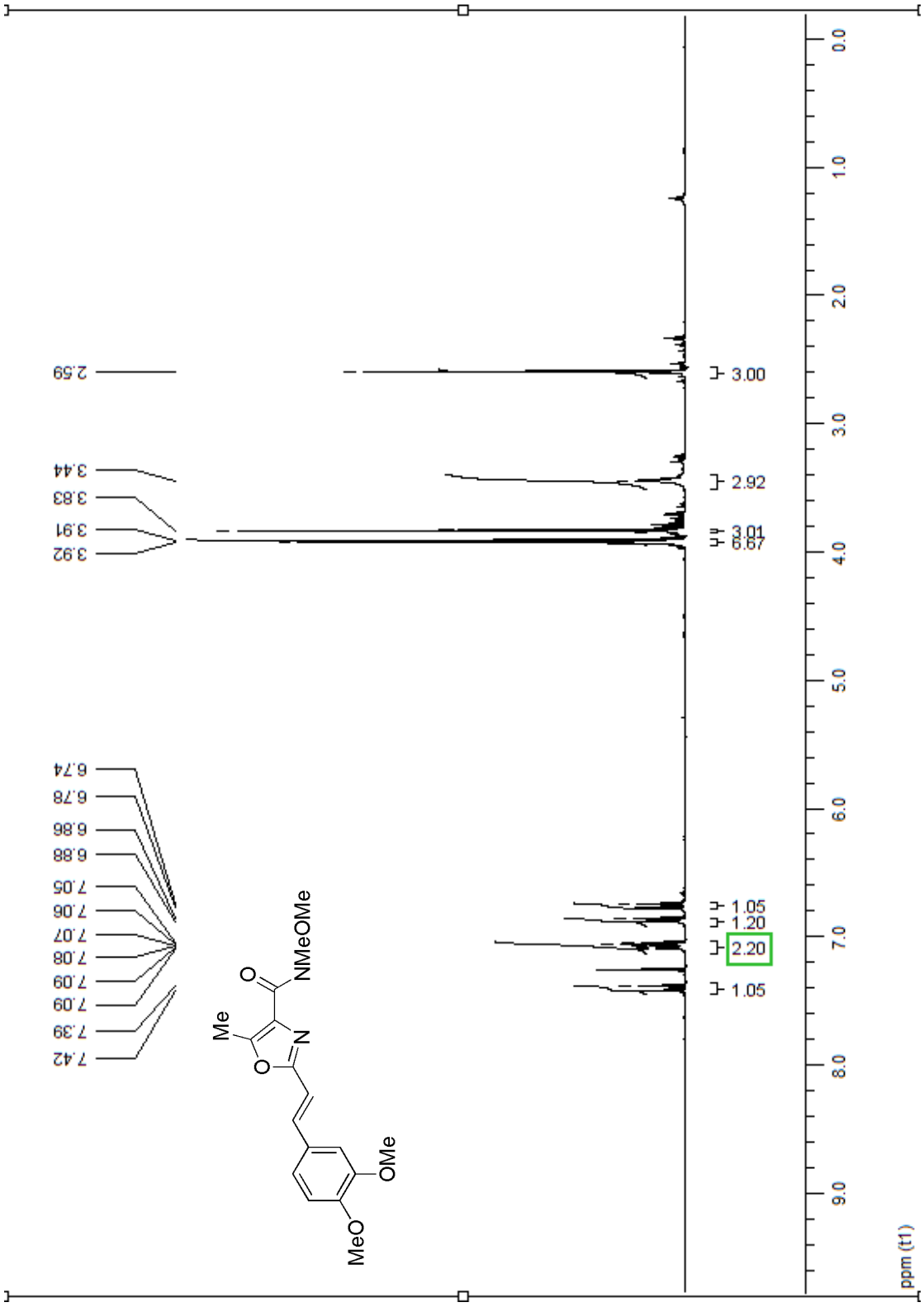

10.16
55.61
55.81
55.86
108.96
111.06
111.54
121.03
128.51
135.28
135.45
144.57
149.11
150.03
160.02
0
50
100
150
200
ppm (t1)
Me
N
O
OH
OMe
MeO

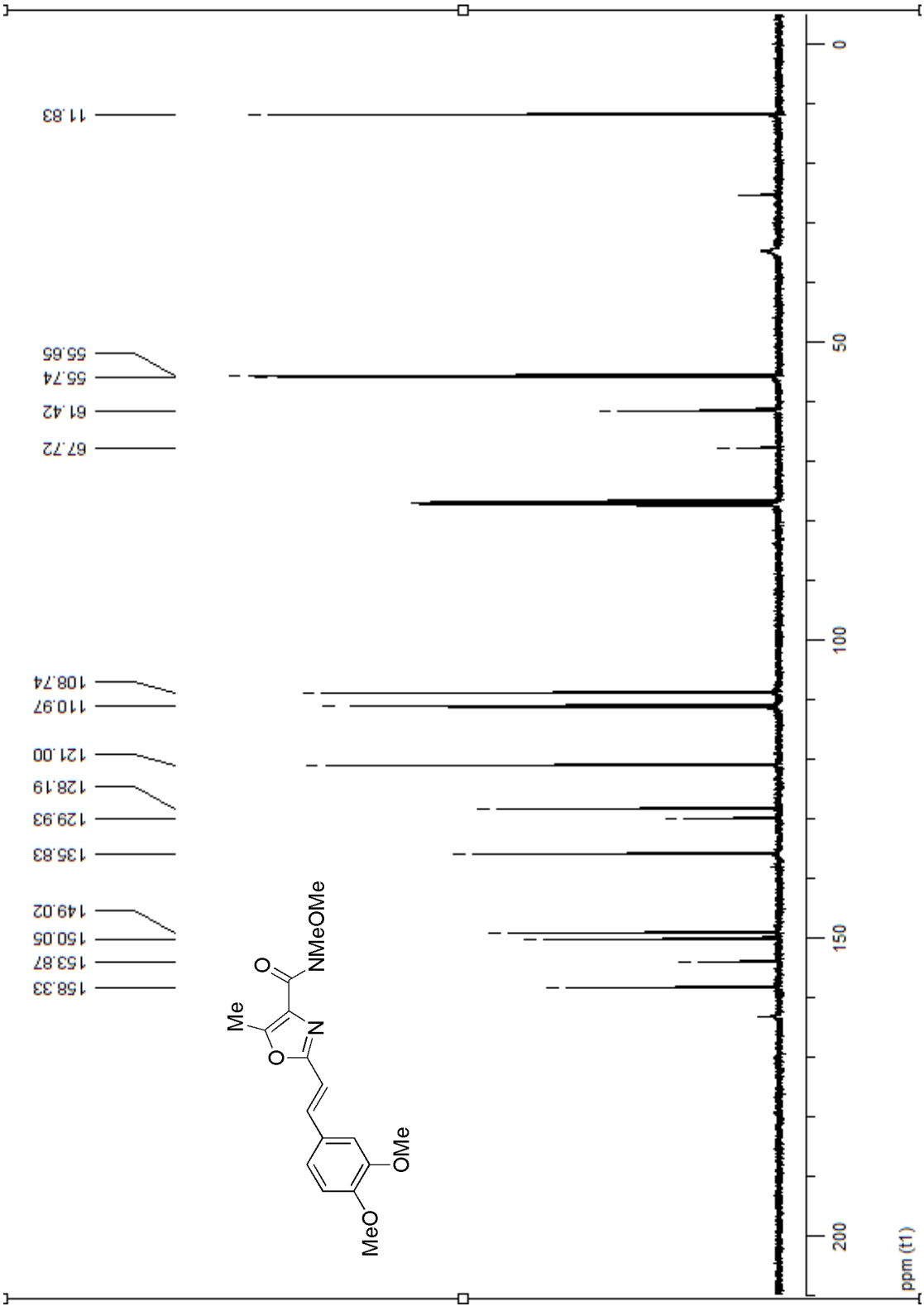
2-(3,4-Dimethoxystyryl)-5-methyloxazole-4-carbaldehyde 8b



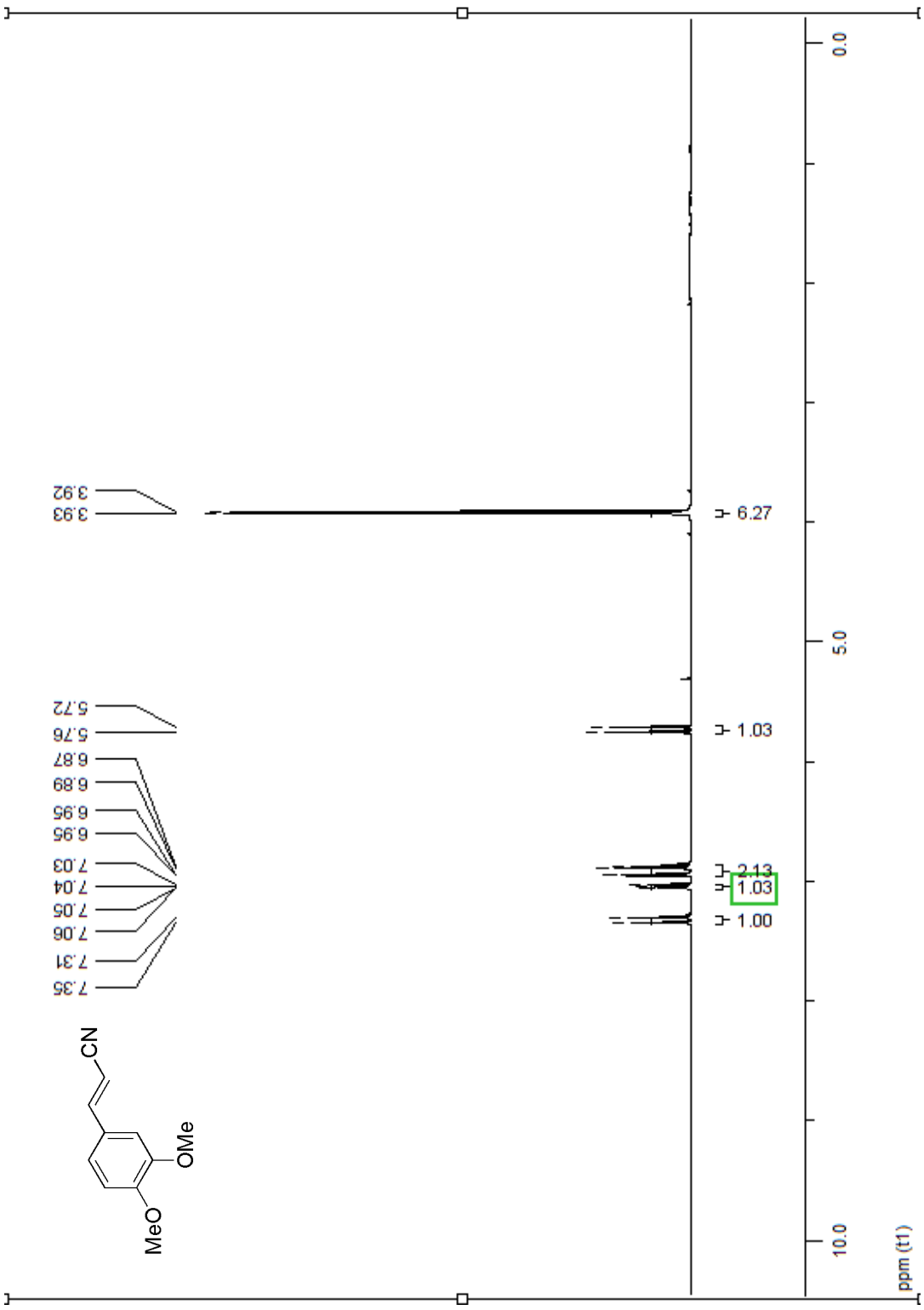

11.70
55.81
55.92
108.92
110.64
111.07
121.43
127.98
135.79
137.39
149.18
150.47
155.88
160.40
185.23
O
H
Me
N
O
OMe
MeO
0
50
100
150
200
ppm (t1)

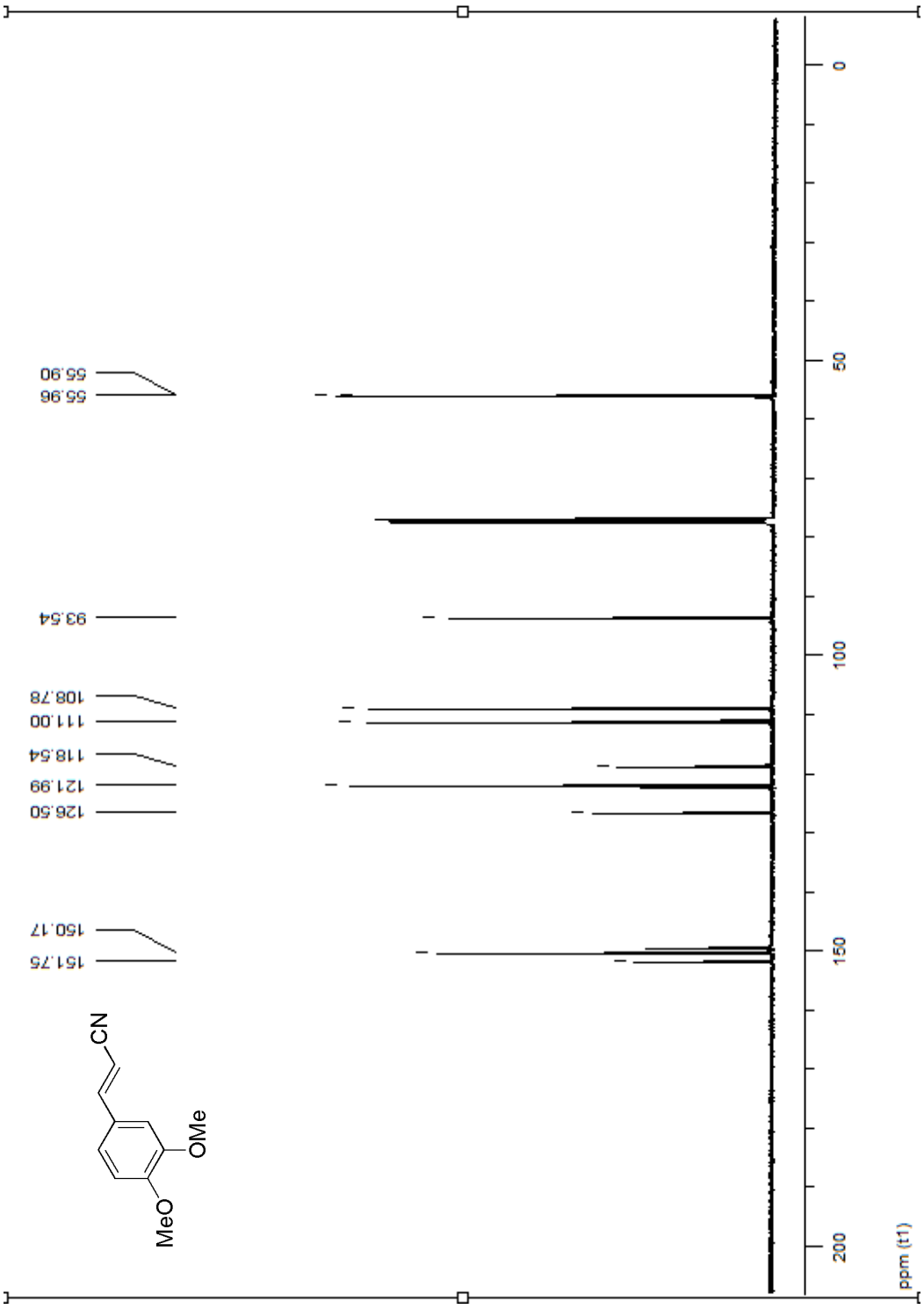
***N*-Methoxy-*N*-methyl-2-(3,4-dimethoxystyryl)-5-methyloxazole-4-carboxamide**



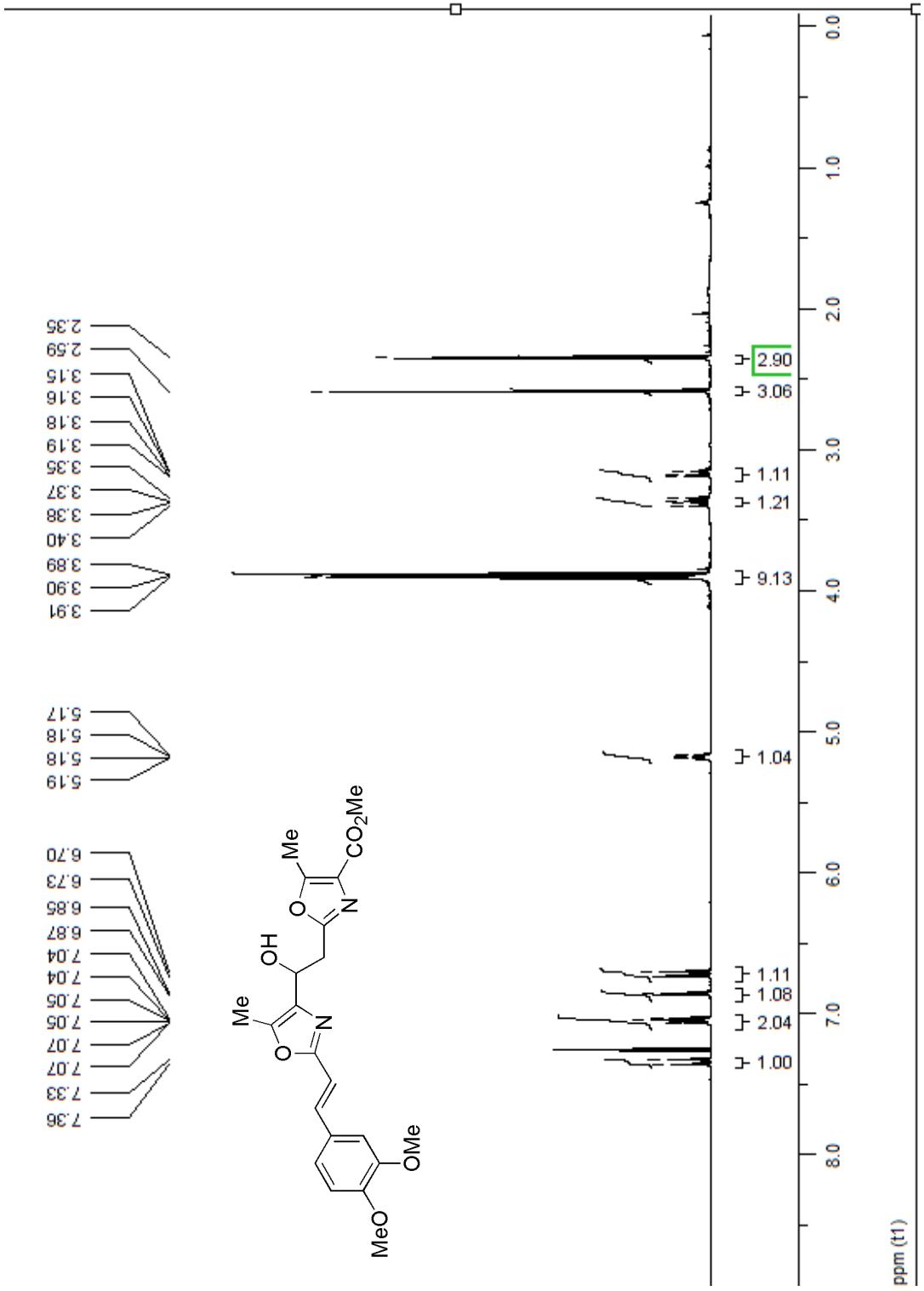

11.83
55.65
55.74
61.42
67.72
108.74
110.97
121.00
128.19
129.93
135.83
149.02
150.05
153.87
158.33
0
50
100
150
200
ppm (t1)
Me
O
NMeOMe
N
O
OMe
MeO

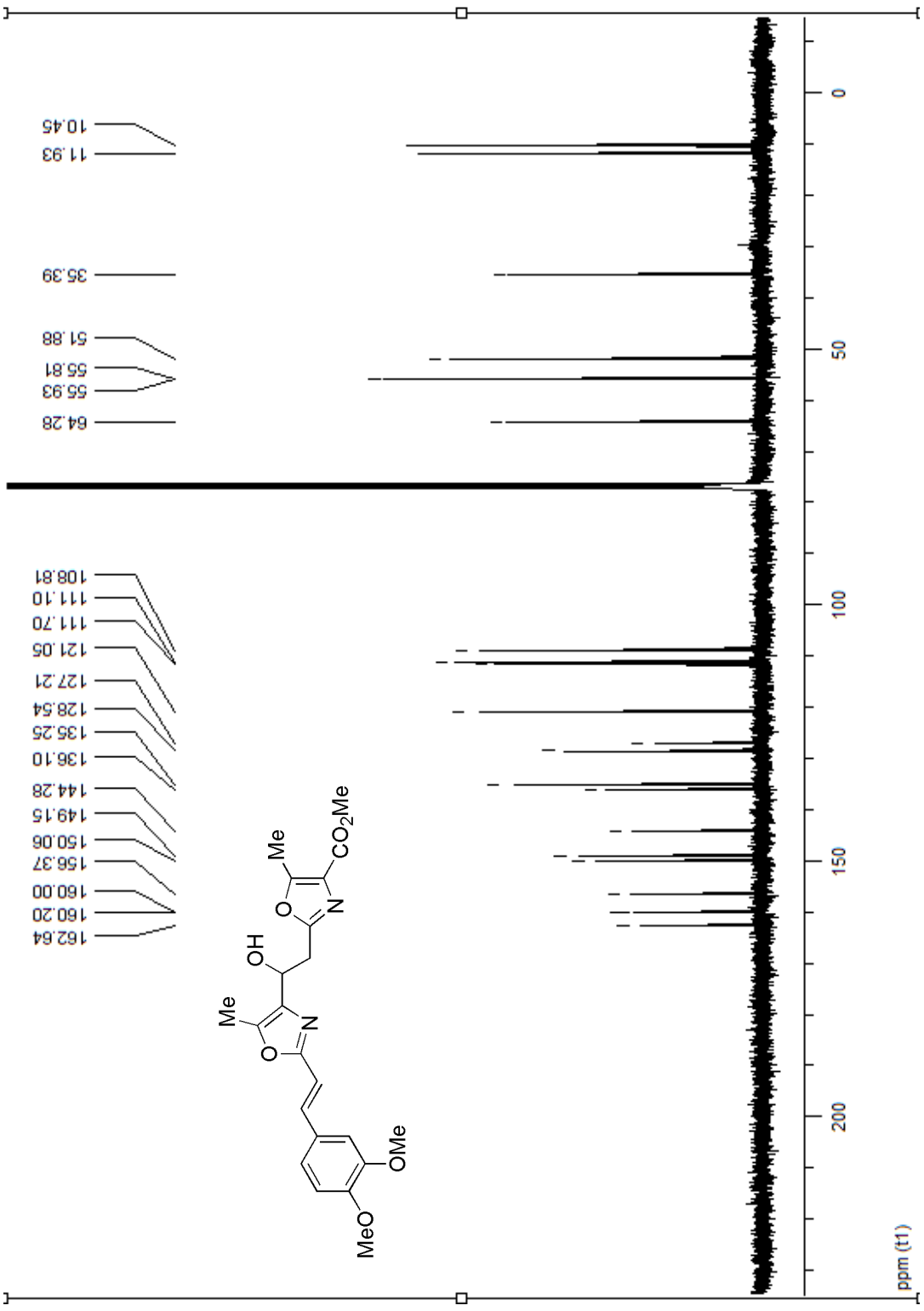
(*E*)-3-(3,4-Dimethoxyphenyl)acrylonitrile 9b



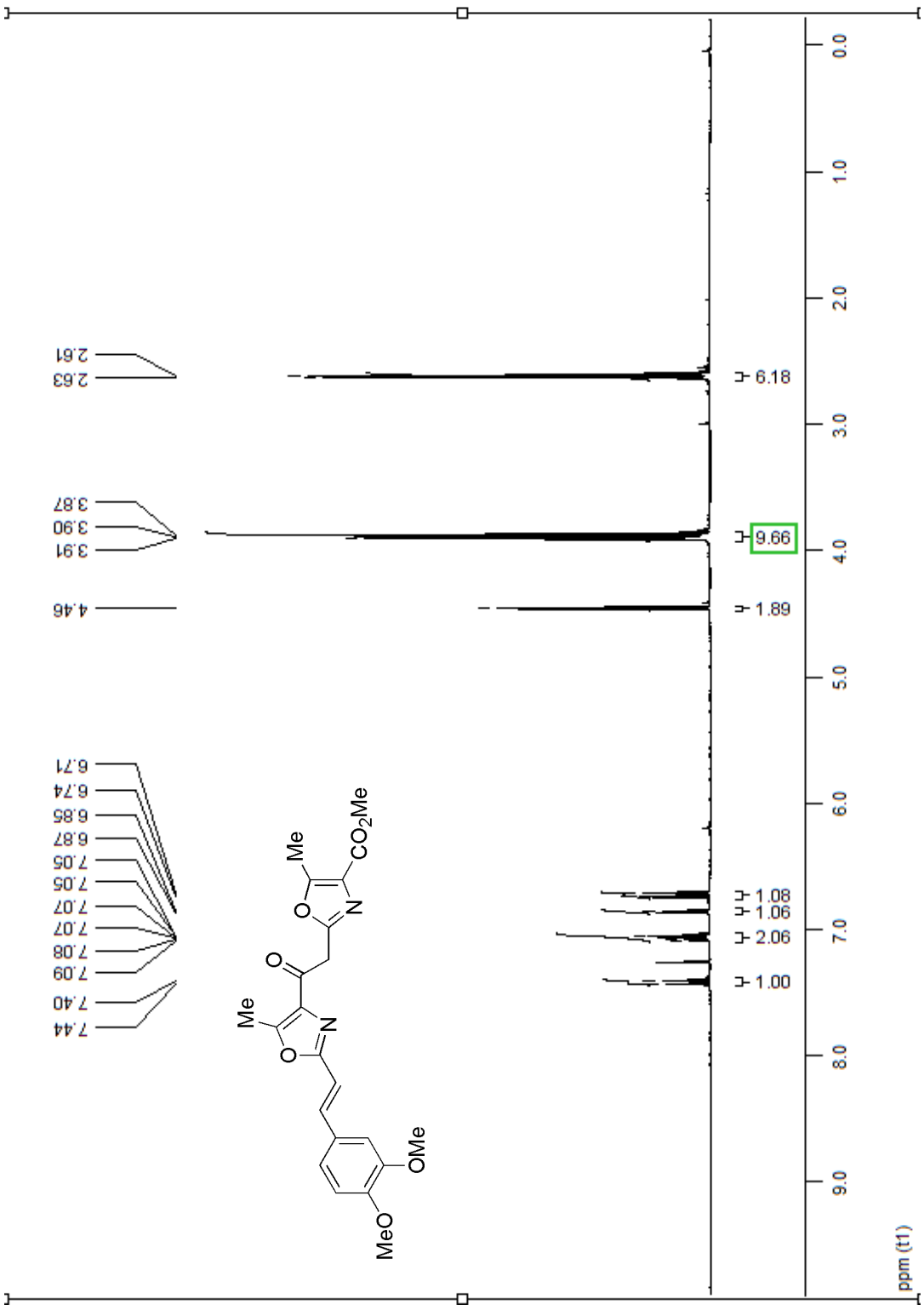

55.90
55.96
93.54
108.78
111.00
118.54
121.99
126.50
150.17
151.75
CN
OMe
MeO
0
50
100
150
200
ppm (t1)

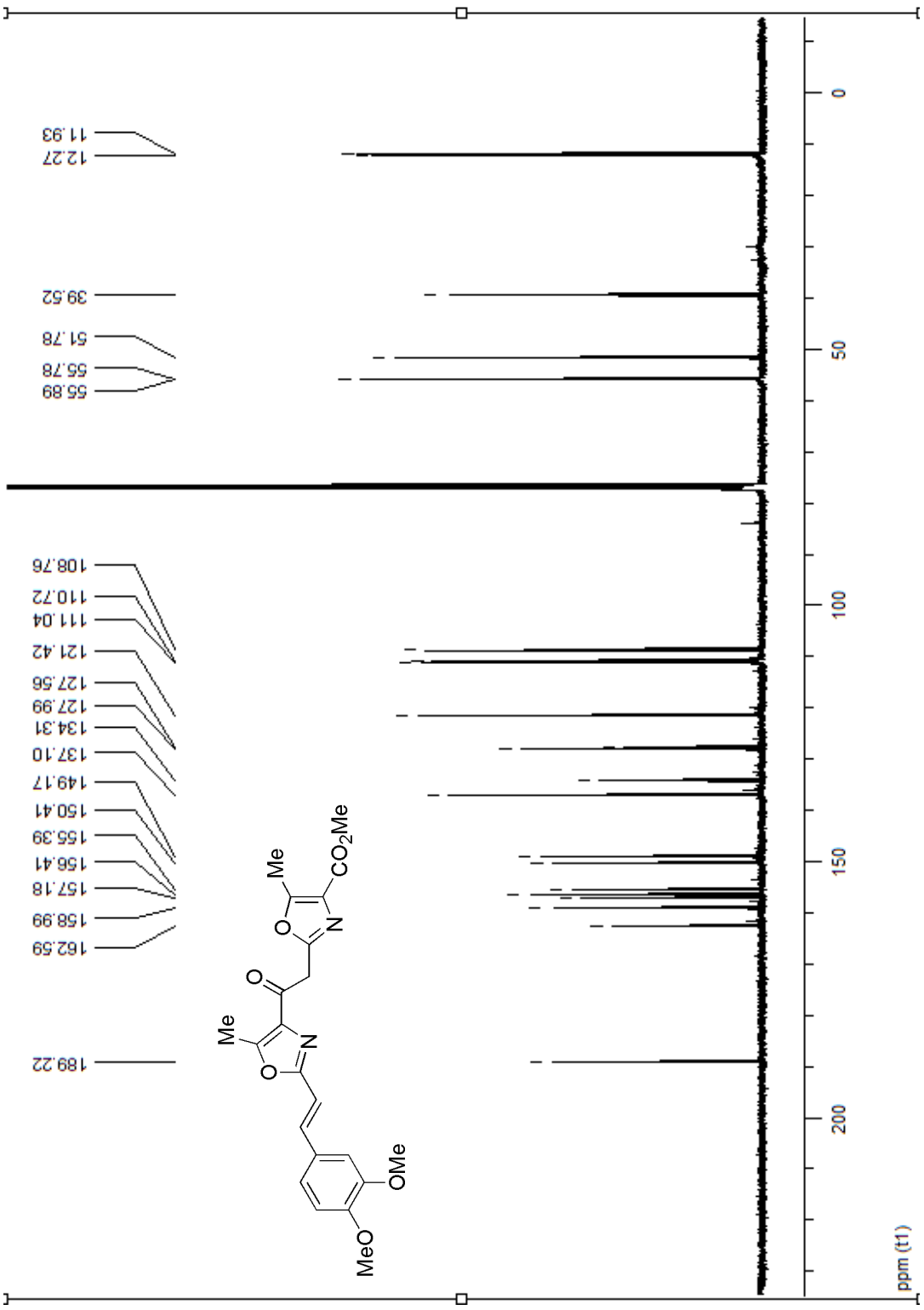
Methyl 2-(2-(2-(3,4-dimethoxystyryl)-5-methyloxazol-4-yl)-2-hydroxyethyl)-5-methyloxazole-4-carboxylate 17b



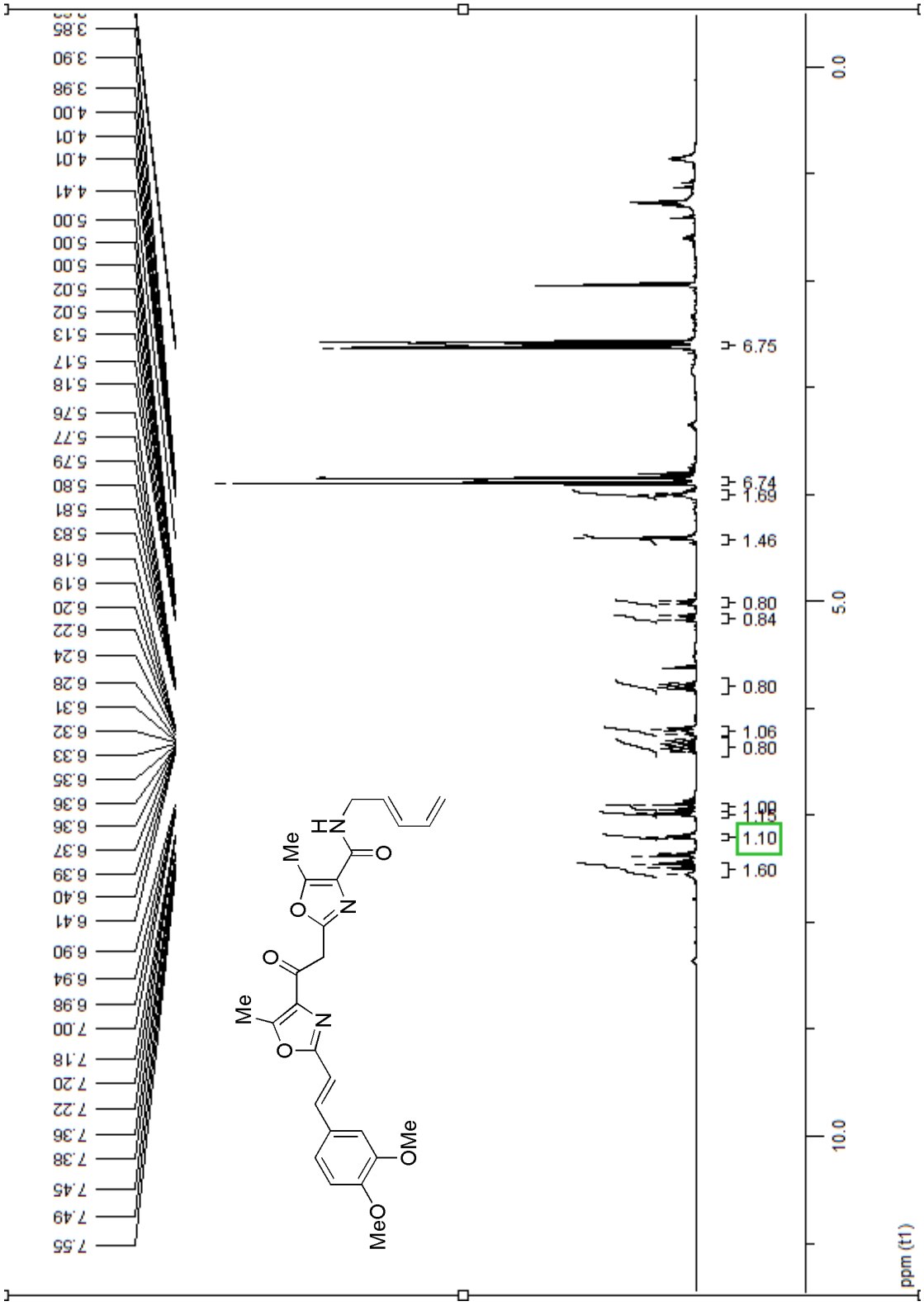

10.45
11.93
35.39
51.88
55.81
55.93
64.28
108.81
111.10
111.70
121.05
127.21
128.54
135.25
136.10
144.28
149.15
150.06
156.37
160.00
160.20
162.64
Me
CO2Me
OH
Me
OMe
MeO
0
50
100
150
200
ppm (t1)

Methyl 2-(2-(2-(3,4-dimethoxystyryl)-5-methyloxazol-4-yl)-2-oxoethyl)-5-methyloxazole-4-carboxylate 18

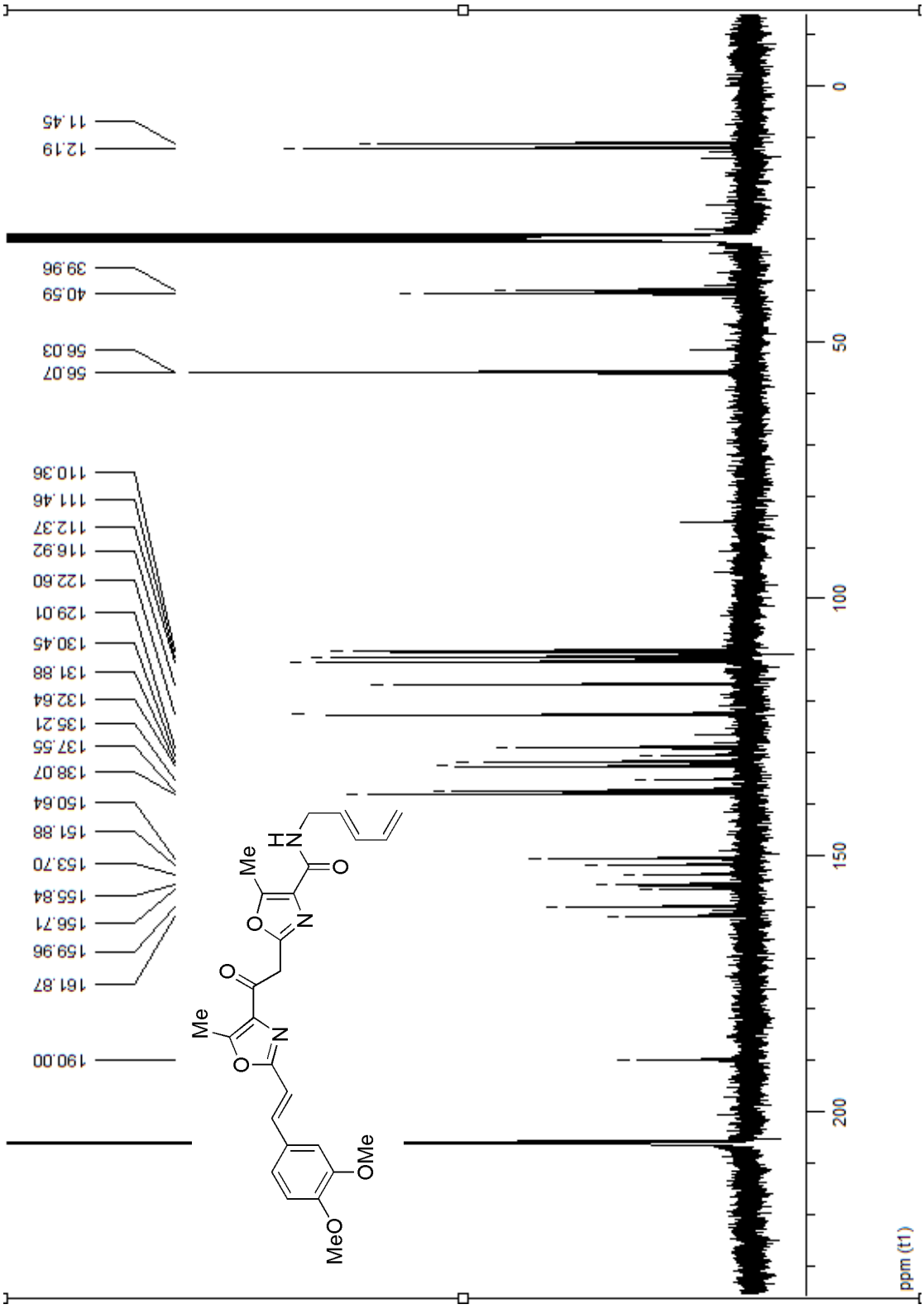



11.93
12.27
39.52
51.78
55.78
55.89
108.76
110.72
111.04
121.42
127.56
127.99
134.31
137.10
149.17
150.41
155.39
156.41
157.18
158.99
162.59
189.22
Me
CO2Me
O
N
O
Me
O
N
OMe
MeO
0
50
100
150
200
ppm (t1)

***O*-Methyl siphonazole 2**

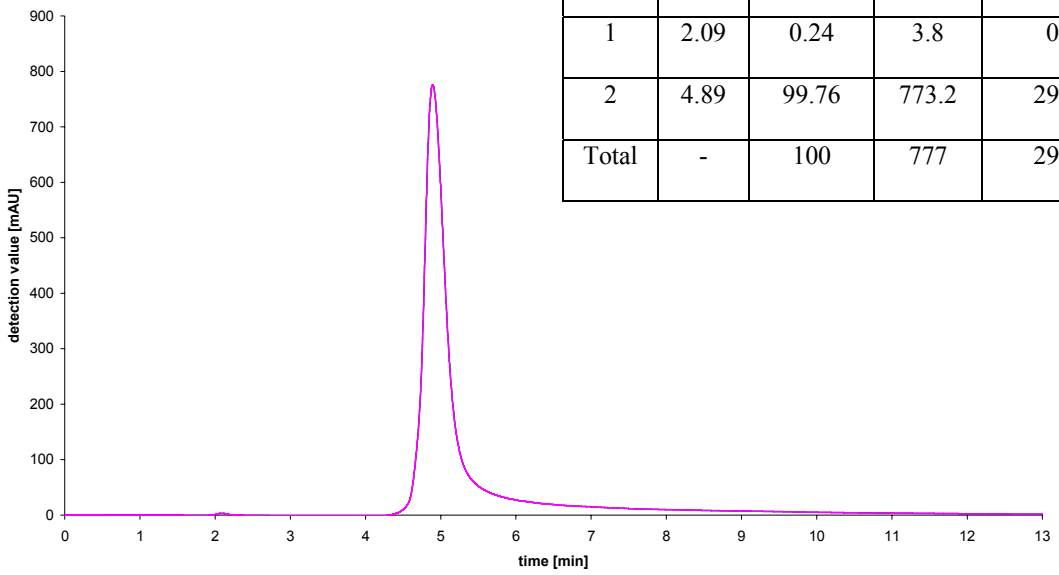


ESI73

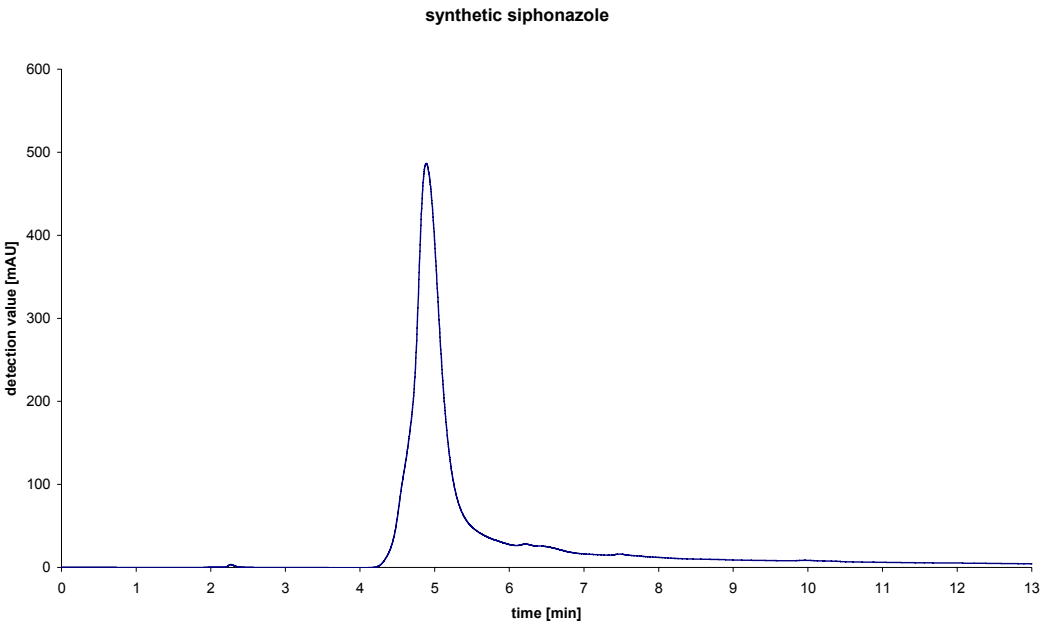

11.45
12.19
39.96
40.59
56.03
56.07
110.36
111.46
112.37
116.92
122.60
129.01
130.45
131.88
132.64
135.21
137.55
138.07
150.64
151.88
153.70
155.84
156.71
159.96
161.87
190.00
Me
O
N
O
HN
O
Me
N
O
OMe
MeO
0
50
100
150
200
ppm (t1)

Comparison of HPLC-retention times of natural, synthetic and a mixture of natural and synthetic siphonazole

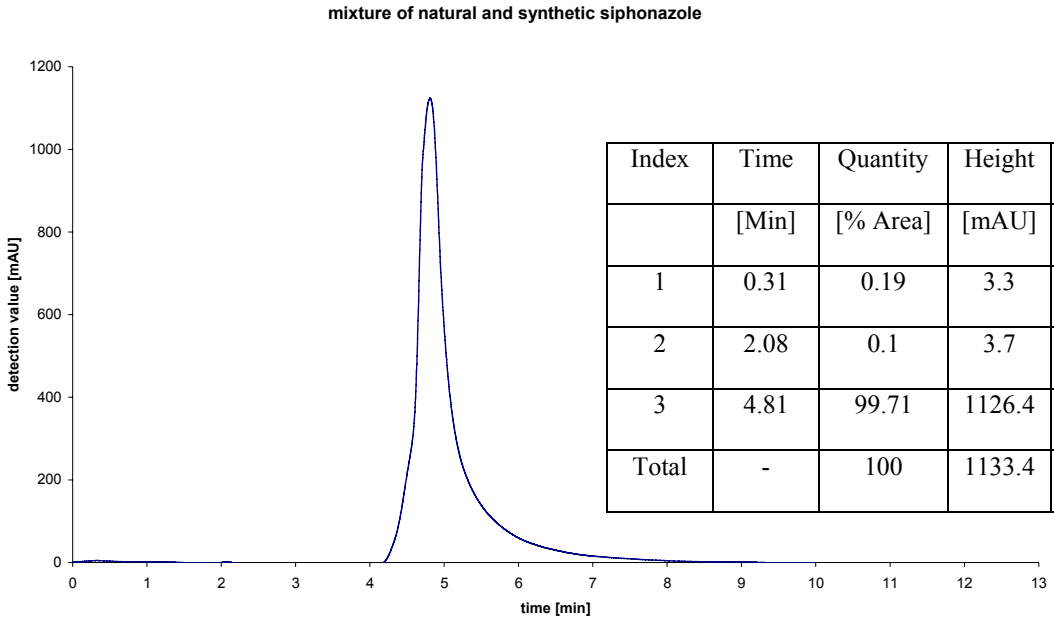
Column: Varian Polaris C_{18}, 5 mm, 250 x 4.6 mm, eluent: acetonitrile/water 75:25; flow rate: 1 $mLmin^{-1}$



Index	Time	Quantity	Height	Area	Area %
	[Min]	[% Area]	[mAU]	[mAU.Min]	[%]
1	2.09	0.24	3.8	0.7	0.242
2	4.89	99.76	773.2	291.1	99.758
Total	-	100	777	291.8	100



Index	Time	Quantity	Height	Area	Area %
	[Min]	[% Area]	[mAU]	[mAU.Min]	[%]
1	2.27	0.21	3.5	0.5	0.205
2	4.88	99.14	478.4	217.6	99.144
3	6.2	0.34	4.2	0.8	0.344
4	7.49	0.24	1.8	0.5	0.237
5	9.97	0.07	0.7	0.2	0.069
Total	-	100	488.6	219.5	100



Index	Time	Quantity	Height	Area	Area %
	[Min]	[% Area]	[mAU]	[mAU.Min]	[%]
1	0.31	0.19	3.3	1.2	0.188
2	2.08	0.1	3.7	0.6	0.104
3	4.81	99.71	1126.4	618.7	99.708
Total	-	100	1133.4	620.5	100

References

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