

Supporting Information

Oxidative rearrangement of indoles to oxindoles

Wesley J. Moran,* Kerry MacRory and Arantxa Rodríguez*

*Department of Chemical & Biological Sciences, University of Huddersfield, Queensgate,
Huddersfield HD1 3DH UK*

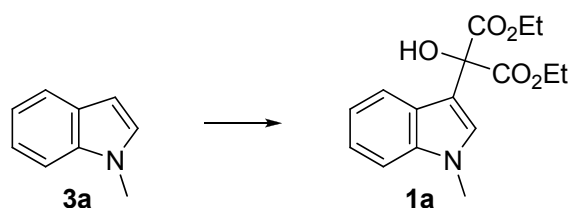
w.j.moran@hud.ac.uk; a.r.menendez@hud.ac.uk

Contents

General	S2
Synthesis of starting materials	S2
Representative procedure for oxidative rearrangement of indoles	S9
Copies of ^1H and ^{13}C NMR spectra	S18

General. ^1H NMR spectra were recorded at 400 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 : 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR were recorded at 100 MHz with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (CDCl_3 : 77.4 ppm). Mass spectrometry (m/z) was performed in ESI mode, with only molecular ions being reported. Infrared (IR) spectra ν_{max} are reported in cm^{-1} . Bands are characterized as broad (br), strong (s), medium (m) and weak (w). All purchased reagents were used as received without further purification. THF was pre-dried with 3Å molecular sieves then distilled from sodium benzophenone ketyl. All reactions were performed in oven dried glassware.

Synthesis of diethyl 2-hydroxy-2-(1-methyl-1*H*-indol-3-yl)malonate, **1a.¹**



1-Methyl-1*H*-indole **3a** (1.07 g, 8.2 mmol) and diethyl ketomalonate (1.26 mL, 8.2 mmol) were refluxed in toluene (67 mL) for 16 hours open to air. The solvent was removed *in vacuo* to furnish the desired product **1a** as a red solid (2.36 g, 95%).

IR (neat): 1754 (w), 1722 (s), 1276 (m), 1217 (s), 1063 (m), 1017 (m), 732 (s) cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 7.74 (1H, d, J = 8.5 Hz), 7.40 (1H, s), 7.34 (1H, d, J = 8.5 Hz), 7.26 (1H, t, J = 7.6 Hz), 7.14 (1H, t, J = 7.6 Hz), 4.27-4.40 (5H, m), 3.80 (3H, s), 1.32 (6H, t, J = 7.6 Hz).

^{13}C NMR (100 MHz, CDCl_3): δ 170.4 (2C), 137.3, 128.5, 125.9, 121.9, 121.0, 119.6, 110.3, 109.4, 77.6, 62.8 (2C), 33.0, 14.0 (2C).

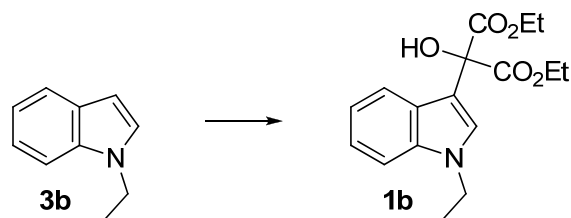
MS: m/z ($M+23$) 328.1

HRMS: m/z calc'd for $\text{C}_{16}\text{H}_{19}\text{NaO}_5$ 328.1155, found 328.1146

¹ Pindur, U.; Kim, M.-H. *Arch. Pharm.* **1992**, 325, 353.

Melting point: 77-79 °C (lit. 78 °C)¹

Synthesis of diethyl 2-(1-ethyl-1*H*-indol-3-yl)-2-hydroxymalonate, **1b**.



1-Ethyl-1*H*-indole **3b** (100 mg, 0.69 mmol) and diethyl ketomalonate (0.11 mL, 0.69 mmol) were refluxed in toluene (5.5 mL) for 16 hours. The solvent was removed *in vacuo* and the mixture was purified by flash chromatography on silica gel (20:1 petroleum ether 40-60 °C/ethyl acetate). The product **1b** was isolated as a brown/red oil (195 mg, 89%).

IR (neat): 1749 (m), 1723 (s), 1463 (m), 1273 (s), 1213 (s), 1189 (s), 1139 (m), 1093 (m), 1055 (m), 1008 (s), 745 (s) cm⁻¹

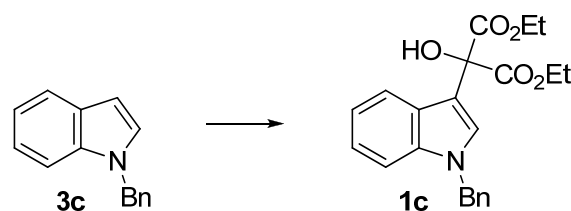
¹H NMR (400 MHz, CDCl₃): δ 7.74 (1H, d, *J* = 8.2 Hz), 7.46 (1H, s), 7.35 (1H, d, *J* = 8.2 Hz), 7.23 (1H, t, *J* = 8.0 Hz), 7.12 (1H, t, *J* = 7.5), 4.26-4.42 (5H, m), 4.15 (2H, q, *J* = 7.0), 1.48 (3H, t, *J* = 7.0), 1.30 (6H, t, *J* = 7.0 Hz).

¹³C NMR (100 MHz, CDCl₃): δ 170.6 (2C), 136.7, 127.1, 126.3, 122.0, 121.5, 119.8, 110.6, 109.8, 78.0, 63.1 (2C), 41.4, 15.6, 14.3 (2C).

MS: *m/z* (M+23) 342.1

HRMS: *m/z* calc'd for C₁₇H₂₁NaO₅ 342.1312, found 342.1312

Synthesis of diethyl 2-(1-benzyl-1*H*-indol-3-yl)-2-hydroxymalonate, **1c**.



1-Benzyl-1*H*-indole **3c** (2.53 g, 12 mmol) and diethyl ketomalonate (1.89 mL, 12 mmol) were refluxed in toluene (100 mL) for 16 hours. The solvent was removed *in vacuo* and the

mixture was purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 °C/ethyl acetate). The product **1c** was isolated as a red solid (2.37 g, 51%).

IR (neat): 1722 (s), 1469 (w), 1238 (s), 1215 (m), 1090 (m), 1028 (m), 749 (m), 734 (s) cm⁻¹

¹H NMR (400 MHz, CDCl₃): δ 7.79 (1H, dd, *J* = 7.2, 1.1 Hz), 7.48 (1H, s), 7.22-7.33 (4H, m), 7.11-7.22 (4H, m), 5.27 (2H, s), 4.43 (1H, s), 4.23-4.41 (4H, m), 1.29 (6H, t, *J* = 7.1 Hz).

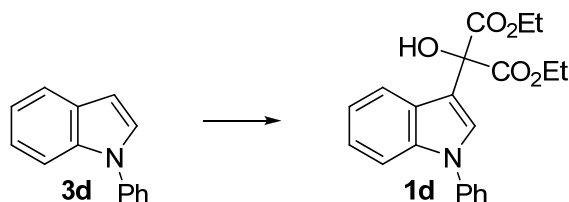
¹³C NMR (100 MHz, CDCl₃): δ 170.4 (2C), 137.2, 137.1, 129.0 (2C), 128.3, 127.9, 127.2 (2C), 126.50, 122.3, 121.5, 120.1, 111.2, 110.2, 78.0, 63.1 (2C), 50.5, 14.3 (2C).

MS: *m/z* (M+23) 404.1

HRMS: *m/z* calc'd for C₂₂H₂₃NaNO₅ 404.1468, found 404.1534

Melting point: 68-71 °C

Synthesis of diethyl 2-hydroxy-2-(1-phenyl-1*H*-indol-3-yl)malonate, **1d**.



1-Phenyl-1*H*-indole **3d** (319 mg, 1.7 mmol) and diethyl ketomalonate (0.26 mL, 1.7 mmol) were refluxed in toluene (14 mL) for 16 hours. The solvent was removed *in vacuo* and the mixture was purified by flash chromatography on silica gel (20:1 petroleum ether 40-60 °C/ethyl acetate). The product **1d** was isolated as a yellow oil (258 mg, 43%).

IR (neat): 1731 (s), 1596 (w), 1500 (s), 1457 (m), 1205 (s), 1019 (m), 741 (s), 697 (s) cm⁻¹

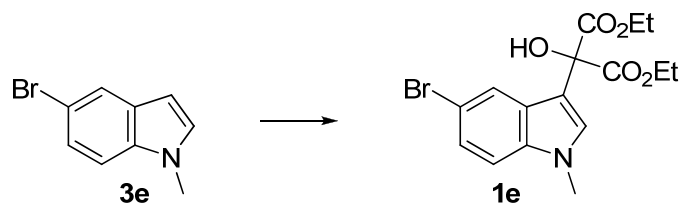
¹H NMR (400 MHz, CDCl₃): δ 7.76-7.81 (1H, d, *J* = 7.5 Hz), 7.65 (1H, s), 7.48-7.55 (5H, m), 7.34-7.40 (1H, m), 7.14-7.25 (2H, m), 4.24-4.44 (5H, m), 1.31 (6H, t, *J* = 7.1 Hz).

¹³C NMR (100 MHz, CDCl₃): δ 170.4 (2C), 139.6, 136.9, 129.9 (2C), 128.0, 127.1, 127.0, 124.9 (2C), 123.0, 121.7, 120.9, 113.2, 111.0, 77.9, 63.3 (2C), 14.4 (2C).

MS: *m/z* (M+23) 390.1

HRMS: m/z calc'd for $C_{21}H_{21}NaNO_5$ 390.1303, found 390.1312

Synthesis of diethyl 2-(5-bromo-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate, 1e.



5-Bromo-1-methyl-1*H*-indole **3e** (200 mg, 0.95 mmol) and diethyl ketomalonate (0.15 mL, 0.95 mmol) were refluxed in toluene (7.8 mL) for 16 hours. The solvent was removed *in vacuo* and the mixture was purified by flash chromatography on silica gel (3:1 petroleum ether 40-60 °C/ethyl acetate). The product **1e** was isolated as an orange/brown solid (174 mg, 53%).

IR (neat): 1749 (m), 1720 (s), 1474 (m), 1274 (m), 1216 (m), 1196 (s), 1136 (s), 1107 (s), 1048 (s), 1016 (s), 781 (s) cm^{-1}

1H NMR (400 MHz, $CDCl_3$): δ 7.88 (1H, d, J = 1.8 Hz), 7.36 (1H, s), 7.26-7.31 (1H, m), 7.14 (1H, d, J = 8.7 Hz), 4.22-4.40 (5H, m), 3.71 (3H, s), 1.30 (6H, t, J = 7.2 Hz).

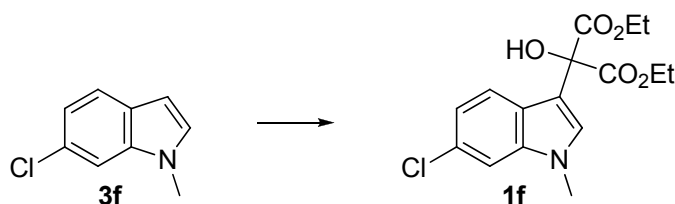
^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3 (2C), 136.3, 129.9, 127.7, 125.0, 124.2, 113.4, 111.2, 110.2, 77.8, 63.3 (2C), 33.4, 14.3 (2C).

MS: m/z ($M+23$) 406.0

HRMS: m/z calc'd for $C_{16}H_{18}BrNaNO_5$ 406.0261, found 406.0262

Melting point: 109-111 °C

Synthesis of diethyl 2-(6-chloro-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate, 1f.



6-Chloro-1-methyl-1*H*-indole **3f** (200 mg, 1.2 mmol) and diethyl ketomalonate (0.19 mL, 1.2 mmol) were refluxed in toluene (9.7 mL) for 16 hours. The solvent was removed *in vacuo* and the mixture was purified by flash chromatography on silica gel (20:1 petroleum ether 40-60 °C/ethyl acetate). The product **1f** was isolated as a brown solid (321 mg, 78%).

IR (neat): 1723 (s), 1217 (m), 1190 (s), 1111 (m), 1063 (s), 1019 (s), 928 (s), 802 (s) cm⁻¹

¹H NMR (400 MHz, CDCl₃): δ 7.63 (1H, d, *J* = 8.6 Hz), 7.35 (1H, s), 7.26-7.29 (1H, m), 7.07 (1H, dd, *J* = 8.6, 1.8 Hz), 4.39 (1H, br), 4.21-4.36 (4H, m), 3.69 (3H, s), 1.27 (6H, t, *J* = 7.1 Hz).

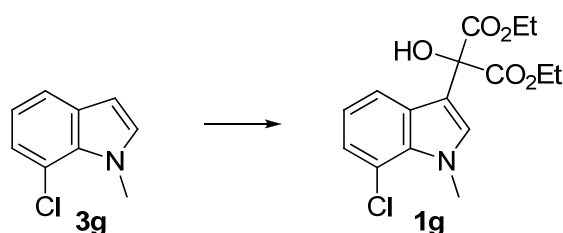
¹³C NMR (100 MHz, CDCl₃): δ 170.4 (2C), 138.1, 129.5, 128.3, 124.8, 122.5, 120.7, 111.0, 109.8, 77.8, 63.3 (2C), 33.4, 14.4 (2C).

MS: *m/z* (*M*+23) 362.1

HRMS: *m/z* calc'd for C₁₆H₁₈ClNaO₅ 362.0733, found 362.0766

Melting point: 86-89 °C

Synthesis of diethyl 2-(7-chloro-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate, **1g**.



7-Chloro-1-methyl-1*H*-indole **3g** (100 mg, 0.60 mmol) and diethyl ketomalonate (0.09 mL, 0.60 mmol) were refluxed in toluene (4.8 mL) for 16 hours. The solvent was removed *in vacuo*, to furnish the desired product **1g** as a yellow oil (201 mg, 98%).

IR (neat): 1726 (s), 1246 (m), 1211 (s), 1193 (s), 1072 (s), 1037 (m), 854 (w), 782 (m), 734 (m) cm⁻¹

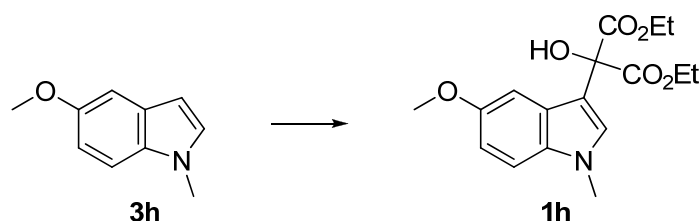
¹H NMR (400 MHz, CDCl₃): δ 7.55-7.60 (1H, m), 7.31 (1H, s), 7.14 (1H, d, *J* = 7.6 Hz), 6.97 (1H, t, *J* = 7.8 Hz), 4.21-4.39 (5H, m), 4.12 (3H, s), 1.27 (6H, t, *J* = 7.1 Hz).

^{13}C NMR (100 MHz, CDCl_3): δ 170.0 (2C), 132.7, 131.3, 129.0, 123.5, 120.5, 119.9, 117.1, 110.4, 63.0 (2C), 37.1, 31.0, 14.1 (2C).

MS: m/z ($M+23$) 362.1

HRMS: m/z calc'd for $\text{C}_{16}\text{H}_{18}\text{NaNO}_5$ 362.0766, found 362.0780

Synthesis of diethyl 2-hydroxy-2-(5-methoxy-1-methyl-1H-indol-3-yl)malonate, **1h**.



5-Methoxy-1-methyl-1*H*-indole **3h** (400 mg, 2.5 mmol), cerium(III) chloride heptahydrate (475 mg, 2.7 mmol) and diethyl ketomalonate (0.42 mL, 2.7 mmol) were dissolved in CH_2Cl_2 (8 mL) and stirred at room temperature for 6 hours. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride solution and extracted with CH_2Cl_2 . The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo*. The mixture was purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 $^\circ\text{C}$ /ethyl acetate). The product **1h** was isolated as a pale yellow oil (0.79 g, 95%).

IR (neat): 1732 (s), 1490 (m), 1219 (s) cm^{-1}

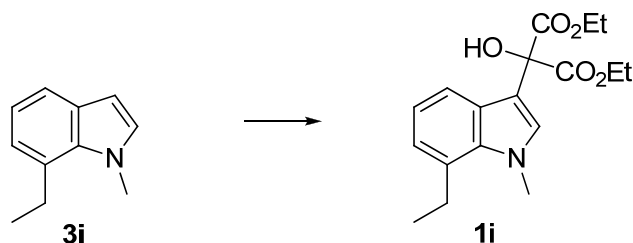
^1H NMR (400 MHz, CDCl_3): δ 7.32 (1H, s), 7.17 (1H, d, J = 9.2 Hz), 7.16 (1H, d, J = 2.0 Hz), 6.88 (1H, dd, J = 8.8, 2.5 Hz), 4.22-4.39 (5H, m), 3.83 (3H, s), 3.72 (3H, s), 1.29 (6H, t, J = 7.1 Hz).

^{13}C NMR (100 MHz, CDCl_3): δ 170.6 (2C), 154.3, 133.0, 129.2, 126.5, 112.6, 110.5, 110.0, 103.0, 78.0, 63.1 (2C), 56.0, 33.4, 14.4 (2C).

MS: m/z ($M+23$) 358.1

HRMS: m/z calc'd for $\text{C}_{17}\text{H}_{21}\text{NaNO}_6$ 358.1261, found 358.1261

Synthesis of diethyl 2-(7-ethyl-1-methyl-1H-indol-3-yl)-2-hydroxymalonate **1i**



7-Ethyl-1-methyl-1*H*-indole **3i** (100 mg, 0.63 mmol), cerium(III) chloride heptahydrate (234 mg, 0.63 mmol) and diethyl ketomalonate (0.11 mL, 0.69 mmol) were dissolved in CH₂Cl₂ (2 mL) and stirred at room temperature for 6 hours. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride solution and extracted with CH₂Cl₂. The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo*. The mixture was purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 °C/ethyl acetate). The product **1i** was isolated as a dark red solid (0.16 g, 74%).

IR (neat): 3485 (br), 1754 (s), 1728 (s) cm⁻¹

¹H NMR (400 MHz, CDCl₃): δ 7.52 (1H, dd, *J* = 7.7, 1.2 Hz), 7.26 (1H, s), 7.06-6.95 (2H, m), 4.42-4.20 (5H, m), 4.01 (3H, s), 3.10 (2H, q, *J* = 7.5 Hz), 1.40-1.23 (9H, m).

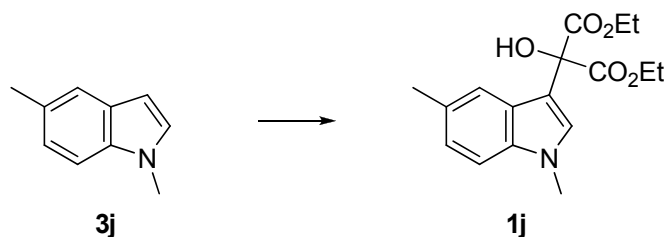
¹³C NMR (100 MHz, CDCl₃): δ 170.6 (2C), 135.6, 130.7, 128.2, 127.6, 123.2, 120.3, 119.2, 110.4, 77.9, 63.1 (2C), 37.4, 25.7, 17.0, 14.4 (2C).

MS: *m/z* (*M*+23) 356.1

HRMS: *m/z* calc'd for C₁₈H₂₃NaO₅ 356.1468, found 356.1452

Melting point: 65-68 °C

Synthesis of diethyl 2-(1,5-dimethyl-1H-indol-3-yl)-2-hydroxymalonate **1j**



5-Methyl-1-methyl-1*H*-indole **3j** (400 mg, 2.75 mmol), cerium(III) chloride heptahydrate (1.0 g, 2.75 mmol) and diethyl ketomalonate (0.46 mL, 3.0 mmol) were dissolved in CH₂Cl₂

(6 mL) and stirred at room temperature for 6 hours. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride solution and extracted with CH₂Cl₂. The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo*. The mixture was purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 °C/ethyl acetate). The product **1j** was isolated as a red solid (0.60 g, 69%).

IR (neat): 3467 (br), 1753 (s), 1720 (s), 1190 (s) cm⁻¹

¹H NMR (400 MHz, CDCl₃): δ 7.48 (1H, br), 7.31 (1H, s), 7.18 (1H, d, *J* = 8.4 Hz), 7.05 (1H, dd, *J* = 8.4, 1.3 Hz), 4.41-4.22 (5H, m), 3.74 (3H, s), 2.44 (3H, s), 1.30 (6H, t, *J* = 7.1 Hz).

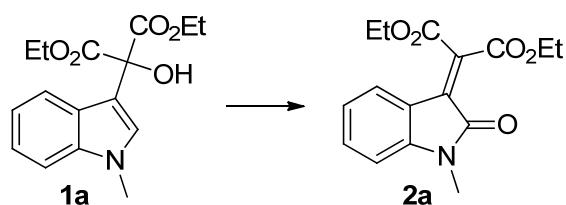
¹³C NMR (100 MHz, CDCl₃): δ 170.6 (2C), 136.1, 129.2, 128.8, 126.4, 123.9, 120.9, 110.0, 109.4, 78.0, 63.1 (2C), 33.3, 21.9, 14.3 (2C).

MS: *m/z* (*M*+23) 342.1

HRMS: *m/z* calc'd for C₁₇H₂₁NaNO₅ 342.1312, found 342.1311

Melting point: 83-85 °C

Representative procedure for the oxidative rearrangement: Preparation of diethyl 2-(1-methyl-2-oxoindolin-3-ylidene)malonate, 2a.



Iodine (83 mg, 0.33 mmol) in dry THF (0.9 mL) was added *via* cannula to a mixture of silver trifluoroacetate (87 mg, 0.39 mmol) and diethyl 2-hydroxy-2-(1-methyl-1*H*-indol-3-yl)malonate **1a** (100 mg, 0.33 mmol) in dry THF (1.8 mL) at room temperature under nitrogen. The reaction mixture was stirred for 16 hours, then quenched with saturated sodium thiosulfate solution and extracted with EtOAc. The combined organic fractions were dried over magnesium sulfate, filtered and concentrated. The resulting mixture was purified by flash chromatography on silica gel (9:1 petroleum ether 40-60 °C/ethyl acetate). The product **2a** was isolated as a red solid (60 mg, 61%).

IR (neat): 1730 (s), 1709 (s), 1599 (m), 1469 (m), 1375 (m), 1238 (s), 1079 (s), 1013 (s) cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 8.40 (1H, d, $J = 7.8$ Hz), 7.38 (1H, t, $J = 7.8$ Hz), 7.04 (1H, t, $J = 7.8$ Hz), 6.80 (1H, d, $J = 7.8$ Hz), 4.44 (2H, q, $J = 7.1$ Hz), 4.37 (2H, q, $J = 7.1$ Hz), 3.19 (3H, s), 1.38 (3H, t, $J = 7.1$ Hz), 1.36 (3H, t, $J = 7.1$ Hz).

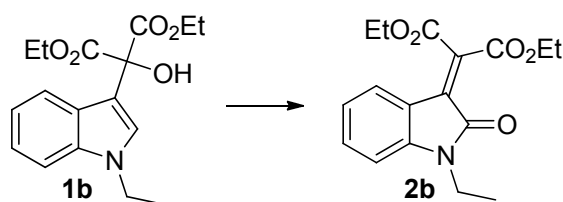
^{13}C NMR (100 MHz, CDCl_3): δ 166.5, 165.9, 163.3, 146.4, 134.8, 133.5, 129.9, 129.3, 123.3, 119.5, 108.7, 62.7, 62.6, 26.5, 14.3, 14.2.

MS: m/z ($M+23$) 326.1

HRMS: m/z calc'd for $\text{C}_{16}\text{H}_{17}\text{NaNO}_5$ 326.0999, found 326.0996

Melting point: 112-115 $^\circ\text{C}$

Diethyl 2-(1-ethyl-2-oxoindolin-3-ylidene)malonate, **2b**.



Prepared according to the representative procedure using iodine (40 mg, 0.16 mmol), THF (0.42 mL), silver trifluoroacetate (42 mg, 0.19 mmol) and diethyl 2-(1-ethyl-1*H*-indol-3-yl)-2-hydroxymalonate **1b** (50 mg, 0.16 mmol) in THF (0.84 mL). Purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 $^\circ\text{C}$ /ethyl acetate). The product **2b** was isolated as an orange solid (21 mg, 42%).

IR (neat): 1707 (s), 1602 (m), 1470 (m), 1362 (m), 1242 (s), 1224 (s), 1183 (s), 1091 (m), 1077 (s), 753 (s) cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 8.37 (1H, d, $J = 7.8$ Hz), 7.36 (1H, td, $J = 7.8, 1.2$ Hz), 7.01 (1H, td, $J = 7.8, 1.0$ Hz), 6.78 (1H, d, $J = 7.8$ Hz), 4.43 (2H, q, $J = 7.2$ Hz), 4.36 (2H, q, $J = 7.1$ Hz), 3.73 (2H, q, $J = 7.2$ Hz), 1.37 (3H, t, $J = 7.1$ Hz), 1.35 (3H, t, $J = 7.2$ Hz), 1.24 (3H, t, $J = 7.2$ Hz).

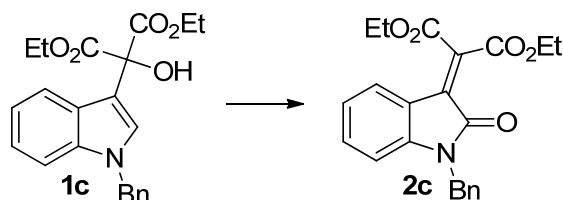
^{13}C NMR (100 MHz, CDCl_3): δ 166.0, 165.9, 163.3, 145.5, 134.9, 133.3, 129.7, 129.3, 123.0, 119.7, 108.8, 62.6, 62.5, 35.0, 14.3, 14.2, 12.9.

MS: m/z (M+23) 340.1

HRMS: m/z calc'd for $C_{17}H_{19}NaNO_5$ 340.1155, found 340.1154

Melting point: 78-80 °C

Diethyl 2-(1-benzyl-2-oxoindolin-3-ylidene)malonate, 2c.



Prepared according to the representative procedure using iodine (33 mg, 0.13 mmol), THF (0.38 mL), silver trifluoroacetate (35 mg, 0.16 mmol) and diethyl 2-(1-benzyl-1*H*-indol-3-yl)-2-hydroxymalonate **1c** (50 mg, 0.13 mmol) in THF (0.76 mL). Purified by flash chromatography on silica gel (9:1 petroleum ether 40-60 °C/ethyl acetate). The product **2c** was isolated as an orange solid (31 mg, 62%).

IR (neat): 1716 (s), 1604 (m), 1469 (m), 1245 (s), 1182 (m), 1093 (m) cm^{-1}

1H NMR (400 MHz, $CDCl_3$): δ 8.41 (1H, d, J = 7.6 Hz), 7.25-7.38 (6H, m), 7.03 (1H, td, J = 7.8, 0.8 Hz), 6.69 (1H, d, J = 7.8 Hz), 4.92 (2H, s), 4.49 (2H, q, J = 7.2 Hz), 4.41 (2H, q, J = 7.1 Hz), 1.42 (3H, t, J = 7.2 Hz), 1.40 (3H, t, J = 7.1 Hz).

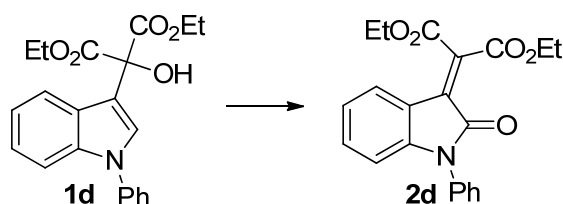
^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 165.8, 163.3, 145.5, 135.5, 134.6, 133.3, 130.1, 129.2 (2C), 129.1, 128.1, 127.6 (2C), 123.3, 119.6, 109.7, 62.7, 62.6, 44.1, 14.4, 14.3.

MS: m/z (M+23) 402.1

HRMS: m/z calc'd for $C_{22}H_{21}NO_5Na$ 402.1312, found 402.1322

Melting point: 93-96 °C

Diethyl 2-(2-oxo-1-phenylindolin-3-ylidene)malonate, 2d.



Prepared according to the representative procedure using iodine (35 mg, 0.14 mmol), THF (0.37 mL), silver trifluoroacetate (36 mg, 0.16 mmol) and diethyl 2-hydroxy-2-(1-phenyl-1*H*-indol-3-yl)malonate **1d** (50 mg, 0.14 mmol) in THF (0.74 mL). Purified by flash chromatography on silica gel (9:1 petroleum ether 40-60 °C/ethyl acetate). The product **2d** was isolated as a yellow solid (17 mg, 34%).

IR (neat): 1731 (m), 1710 (s), 1601 (m), 1462 (m), 1375 (m), 1243 (s), 1188 (m), 1084 (s), 759 (s), 751 (s) cm⁻¹

¹H NMR (400 MHz, CDCl₃): δ 8.45 (1H, dd, *J* = 7.9, 0.7 Hz), 7.51 (2H, t, *J* = 7.9 Hz), 7.36-7.44 (3H, m), 7.30 (1H, td, *J* = 7.7, 1.2 Hz), 7.08 (1H, td, *J* = 7.9, 1.0 Hz), 6.75 (1H, d, *J* = 7.9 Hz), 4.36-4.44 (4H, m), 1.38 (3H, t, *J* = 7.1), 1.35 (3H, t, *J* = 7.1).

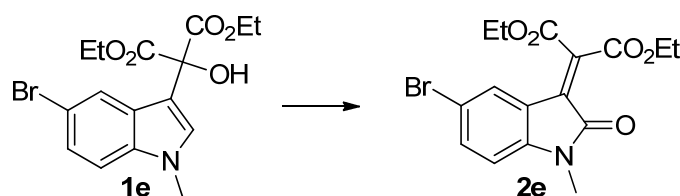
¹³C NMR (100 MHz, CDCl₃): δ 165.8, 165.7, 163.3, 146.4, 134.5, 133.8, 133.3, 130.3, 130.1 (2C), 129.3, 128.8, 127.0 (2C), 123.7, 119.5, 110.0, 62.7, 62.6, 14.4, 14.3.

MS: *m/z* (*M*+23) 388.1

HRMS: *m/z* calc'd for C₂₁H₁₉NaNO₅ 388.1155, found 388.1145

Melting point: 98-101 °C

Diethyl 2-(5-bromo-1-methyl-2-oxoindolin-3-ylidene)malonate, **2e**.



Prepared according to the representative procedure using iodine (31 mg, 0.12 mmol), THF (0.30 mL), silver trifluoroacetate (32 mg, 0.15 mmol) and diethyl 2-(5-bromo-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate **1e** (47 mg, 0.12 mmol) in THF (0.60 mL). Purified by flash chromatography on silica gel (3:1 petroleum ether 40-60 °C/ethyl acetate). The product **2e** was isolated as a red solid (24 mg, 51%).

IR (neat): 1738 (m), 1723 (m), 1706 (s), 1598 (m), 1472 (m), 1364 (m), 1240 (s), 1175 (s), 1080 (s), 1020 (s), 838 (s) cm⁻¹

^1H NMR (400MHz, CDCl_3): δ 8.59 (1H, s), 7.50 (1H, dd, J = 7.8, 1.7 Hz), 6.67 (1H, d, J = 8.8 Hz), 4.48 (2H, q, J = 8.2 Hz), 4.40 (2H, q, J = 7.8 Hz), 3.18 (3H, s), 1.39 (6H, m).

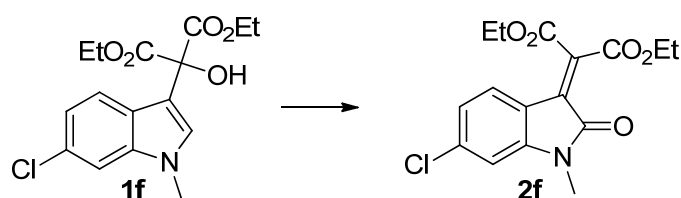
^{13}C NMR (100 MHz, CDCl_3): δ 165.6, 165.0, 162.7, 144.9, 135.6, 133.3, 131.8, 130.8, 120.7, 115.6, 109.7, 62.6, 62.4, 26.2, 14.0, 13.9.

MS: m/z ($M+23$) 406.0

HRMS: m/z calc'd for $\text{C}_{16}\text{H}_{16}\text{BrNaNO}_5$ 406.0084, found 406.0020

Melting point: 117-121 $^\circ\text{C}$

Diethyl 2-(6-chloro-1-methyl-2-oxoindolin-3-ylidene)malonate, 2f.



Prepared according to the representative procedure using iodine (37 mg, 0.15 mmol), THF (0.39 mL), silver trifluoroacetate (39 mg, 0.18 mmol) and diethyl 2-(6-chloro-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate **1f** (50 mg, 0.15 mmol) in THF (0.78 mL). Purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 $^\circ\text{C}$ /ethyl acetate). The product **2f** was isolated as a yellow solid (23 mg, 45%).

IR (neat): 1728 (s), 1709 (s), 1597 (s), 1375 (w), 1254 (s), 1233 (s), 1179 (s), 1065 (s), 1019 (m) cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 8.39 (1H, d, J = 8.4 Hz), 7.00 (1H, dd, J = 8.4, 2.0 Hz), 6.78 (1H, d, J = 1.9 Hz), 4.43 (2H, q, J = 7.1), 4.35 (2H, q, J = 7.1 Hz), 3.18 (3H, s), 1.38 (3H, t, J = 7.2 Hz), 1.35 (3H, t, J = 7.2 Hz).

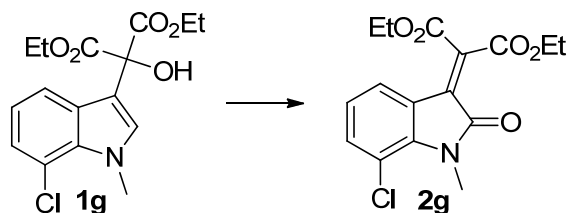
^{13}C NMR (100 MHz, CDCl_3): δ 166.4, 165.6, 163.2, 147.4, 139.4, 133.8, 130.5, 130.1, 123.2, 117.9, 109.4, 62.8, 62.6, 26.6, 14.3, 14.2.

MS: m/z ($M+23$) 360.1

HRMS: m/z calc'd for $\text{C}_{16}\text{H}_{18}\text{ClNaNO}_5$ 360.0609, found 360.0590

Melting point: 138-140 $^\circ\text{C}$

Diethyl 2-(7-chloro-1-methyl-2-oxoindolin-3-ylidene)malonate, **2g**.



Prepared according to the representative procedure using iodine (37 mg, 0.15 mmol), THF (0.39 mL), silver trifluoroacetate (39 mg, 0.18 mmol) and diethyl 2-(7-chloro-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate **1g** (50 mg, 0.15 mmol) in THF (0.78 mL). Purified by flash chromatography on silica gel (9:1 petroleum ether 40-60 °C/ethyl acetate). The product **2g** was isolated as an orange solid (17 mg, 34%).

IR (neat): 1734 (m), 1712 (s), 1596 (m), 1454 (m), 1368 (m), 1247 (s), 1209 (s), 1181 (s), 1135 (s), 1077 (s), 1054 (s), 1018 (m), 724 (s) cm⁻¹

¹H NMR (400 MHz, CDCl₃): δ 8.31 (1H, dd, *J* = 7.8, 1.1 Hz), 7.30 (1H, dd, *J* = 8.2, 1.1 Hz), 6.95 (1H, t, *J* = 8.0 Hz), 4.44 (2H, q, *J* = 7.1 Hz), 4.37 (2H, q, *J* = 7.1 Hz), 3.58 (3H, s), 1.38 (3H, t, *J* = 7.2 Hz), 1.36 (3H, t, *J* = 7.2 Hz).

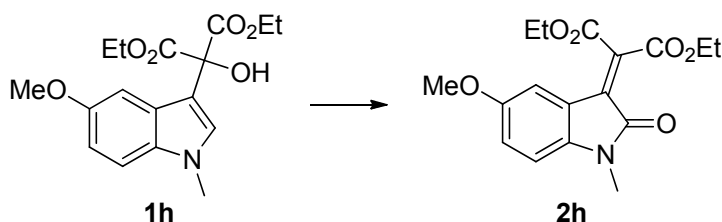
¹³C NMR (100 MHz, CDCl₃): δ 166.7, 165.5, 163.1, 142.0, 135.4, 133.1, 131.0, 127.5, 123.8, 122.2, 116.2, 62.9, 62.7, 30.2, 14.3, 14.2.

MS: *m/z* (M+23) 360.1

HRMS: *m/z* calc'd for C₁₆H₁₆ClNaNO₅ 360.0609, found 360.0625

Melting point: 93-95 °C

Diethyl 2-(5-methoxy-1-methyl-2-oxoindolin-3-ylidene)malonate, **2h**



Iodine (76 mg, 0.30 mmol) in dry THF (0.9 mL) was added *via* cannula to a mixture of silver trifluoroacetate (87 mg, 0.39 mmol) and diethyl 2-hydroxy-2-(5-methoxy-1-methyl-

1H-indol-3-yl)malonate **1h** (100 mg, 0.30 mmol) in dry THF (1.8 mL) at 0 °C under nitrogen. The reaction mixture was stirred for 16 hours, then quenched with saturated sodium thiosulfate solution and extracted with EtOAc. The combined organic fractions were dried over magnesium sulfate, filtered and concentrated. The resulting mixture was purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 °C/ethyl acetate). The product **2h** was isolated as a dark red solid (66 mg, 68%).

IR (neat): 1728 (s), 1707 (s), 1481 (m), 1215 (s) cm⁻¹

¹H NMR (400 MHz, CDCl₃): δ 8.11 (1H, d, *J* = 2.7 Hz), 6.93 (1H, dd, *J* = 8.5, 2.5 Hz), 6.67 (1H, d, *J* = 8.7 Hz), 4.43 (2H, q, *J* = 7.2 Hz), 4.36 (2H, q, *J* = 7.0 Hz), 3.81 (3H, s), 3.15 (3H, s), 1.38 (3H, t, *J* = 7.0 Hz), 1.35 (3H, t, *J* = 7.2 Hz).

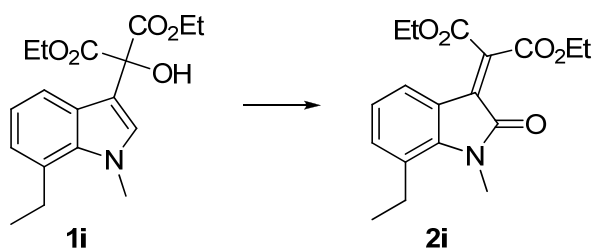
¹³C NMR (100 MHz, CDCl₃): δ 166.3, 165.8, 163.2, 156.1, 140.3, 135.3, 130.1, 120.2, 118.9, 115.5, 109.0, 62.7, 62.5, 56.3, 26.5, 14.3 (2C).

MS: *m/z* (M+23) 356.1

HRMS: *m/z* calc'd for C₁₇H₁₉NaNO₆ 356.1105, found 356.1105

Melting point: 85-88 °C

Diethyl 2-(7-ethyl-1-methyl-2-oxoindolin-3-ylidene)malonate, **2i**



Iodine (76 mg, 0.30 mmol) in dry THF (0.9 mL) was added *via* cannula to a mixture of silver trifluoroacetate (87 mg, 0.39 mmol) and diethyl 2-(7-ethyl-1-methyl-1H-indol-3-yl)-2-hydroxymalonate **1i** (100 mg, 0.30 mmol) in dry THF (1.8 mL) at 0 °C under nitrogen. The reaction mixture was stirred for 16 hours, then quenched with saturated sodium thiosulfate solution and extracted with EtOAc. The combined organic fractions were dried over magnesium sulfate, filtered and concentrated. The resulting mixture was purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 °C/ethyl acetate). The product **2i** was isolated as a red solid (58 mg, 58%).

IR (neat): 1732 (s), 1709 (s), 1446 (m), 1252 (s) cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 8.20 (1H, dd, J = 7.8, 1.0 Hz), 7.16 (1H, d, J = 7.7 Hz), 6.95 (1H, t, J = 7.8 Hz), 4.44 (2H, q, J = 7.2 Hz), 4.36 (2H, q, J = 7.1 Hz), 3.47 (3H, s), 2.86 (2H, q, J = 7.5 Hz), 1.38 (3H, t, J = 7.1 Hz), 1.35 (3H, t, J = 7.2 Hz), 1.25 (3H, t, J = 7.6 Hz).

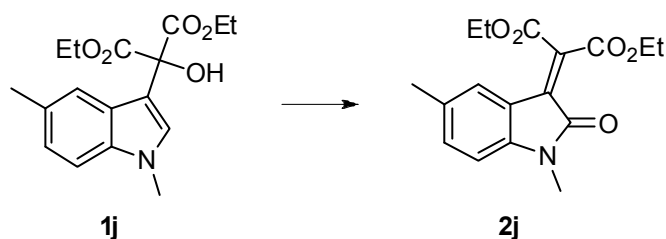
^{13}C NMR (100 MHz, CDCl_3): δ 167.4, 165.9, 163.4, 143.4, 135.9, 134.1, 129.4, 126.9, 126.6, 123.2, 120.4, 62.6, 62.5, 29.9, 25.2, 17.0, 14.3 (2C).

MS: m/z ($M+23$) 354.1

HRMS: m/z calc'd for $\text{C}_{18}\text{H}_{21}\text{NaNO}_5$ 354.1312, found 354.1304

Melting point: 61-63 $^{\circ}\text{C}$

Diethyl 2-(1,5-dimethyl-2-oxoindolin-3-ylidene)malonate, **2j**



Iodine (76 mg, 0.30 mmol) in dry THF (0.9 mL) was added *via* cannula to a mixture of silver trifluoroacetate (87 mg, 0.39 mmol) and diethyl 2-(1,5-dimethyl-1H-indol-3-yl)-2-hydroxymalonate **1j** (96 mg, 0.30 mmol) in dry THF (1.8 mL) at 0 $^{\circ}\text{C}$ under nitrogen. The reaction mixture was stirred for 16 hours, then quenched with saturated sodium thiosulfate solution and extracted with EtOAc. The combined organic fractions were dried over magnesium sulfate, filtered and concentrated. The resulting mixture was purified by flash chromatography on silica gel (5:1 petroleum ether 40-60 $^{\circ}\text{C}$ /ethyl acetate). The product **2j** was isolated as a red solid (50 mg, 53%).

IR (neat): 1738 (m), 1716 (s), 1245 (s), 1066 (s) cm^{-1}

^1H NMR (400 MHz, CDCl_3): δ 8.20 (1H, s), 7.17 (1H, d, J = 7.9 Hz), 6.65 (1H, t, J = 8.0 Hz), 4.43 (2H, q, J = 7.2 Hz), 4.36 (2H, q, J = 7.1 Hz), 3.15 (3H, s), 2.32 (3H, s), 1.38 (3H, t, J = 7.1 Hz), 1.36 (3H, t, J = 7.2 Hz).

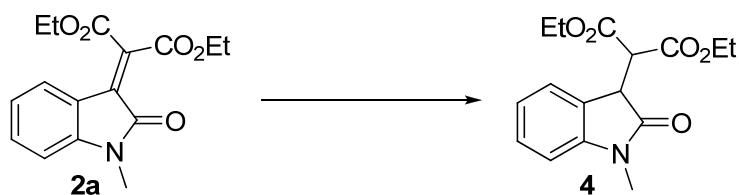
^{13}C NMR (100 MHz, CDCl_3): δ 166.4, 165.9, 163.4, 144.2, 135.1, 133.8, 132.6, 129.8, 129.5, 119.4, 108.4, 62.6, 62.4, 26.4, 21.5, 14.3 (2C).

MS: m/z ($M+23$) 340.1

HRMS: m/z calc'd for $\text{C}_{17}\text{H}_{19}\text{NaNO}_5$ 340.1155, found 340.1143

Melting point: 142-144 $^\circ\text{C}$

Synthesis of diethyl 2-(1-methyl-2-oxoindolin-3-yl)malonate, **4**



Sodium borohydride (7.2 mg, 0.19 mmol) was added to ethyl 3-(2-ethoxy-2-oxoacetyl) 1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine-2-carboxylate **2a** (29 mg, 0.096 mmol) in MeOH (2 mL) and stirred at room temperature. The reaction was stirred until completion was indicated by TLC analysis. Then it was quenched with saturated ammonium chloride solution and extracted with ethyl acetate. After drying over MgSO_4 , filtration and concentration, the product **4** was isolated as a red liquid (21 mg, 71%).

IR (neat): 1720 (s), 1612 (s), 1353 (s), 752 (s) cm^{-1}

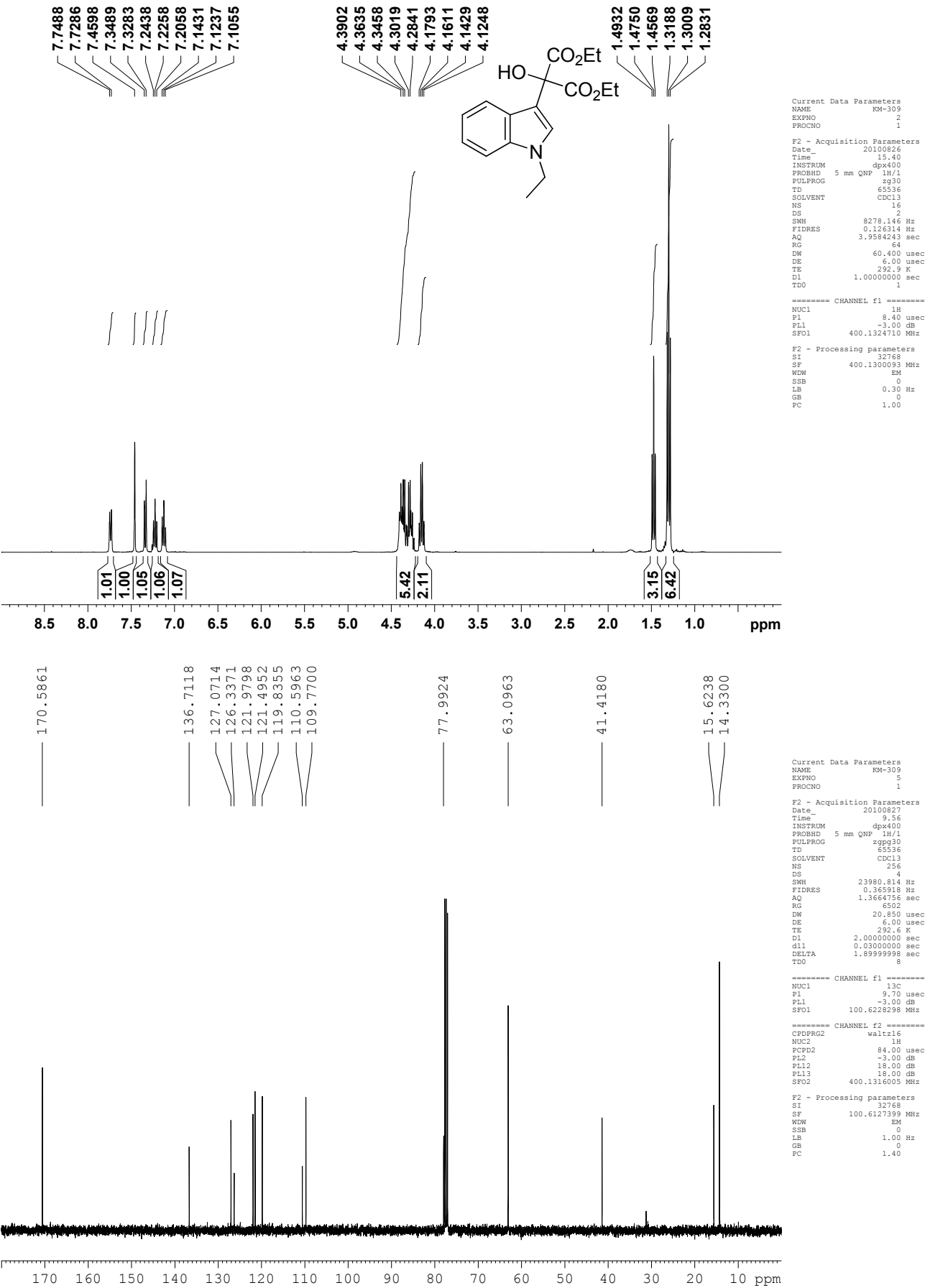
^1H NMR (400 MHz, CDCl_3): δ 7.39 (1H, d, J = 7.4 Hz), 7.25-7.32 (1H, m), 7.02 (1H, td, J = 7.6, 0.76 Hz), 6.82 (1H, J = 7.8 Hz), 4.22-4.32 (2H, m), 4.21 (1H, d, J = 3.6 Hz), 3.92-4.03 (3H, m), 3.23 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 0.98 (3H, t, J = 7.2 Hz).

^{13}C NMR (100 MHz, CDCl_3): δ 175.7, 168.5, 167.3, 145.1, 129.0, 125.9, 125.3, 122.9, 108.3, 62.3, 62.0, 52.7, 45.0, 26.8, 14.4, 14.1.

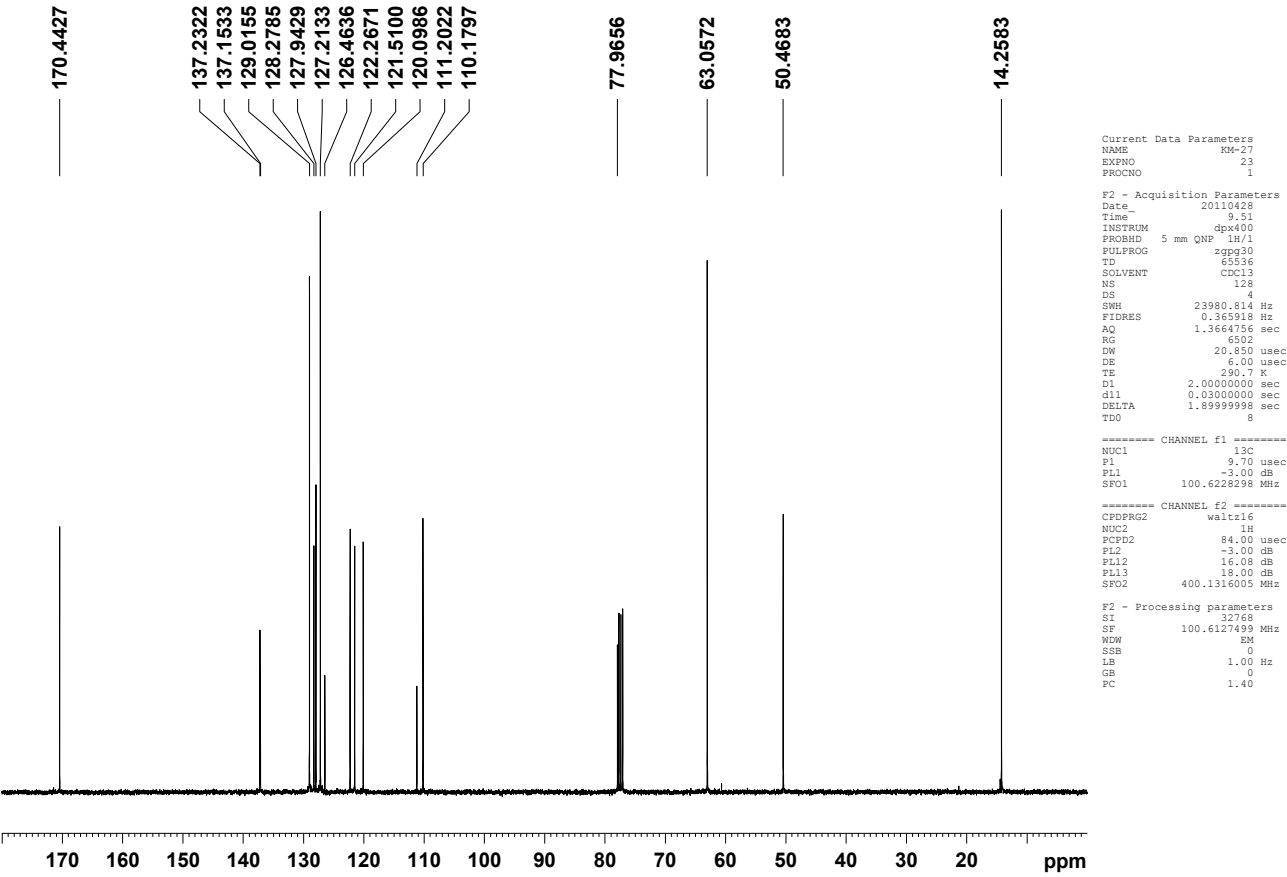
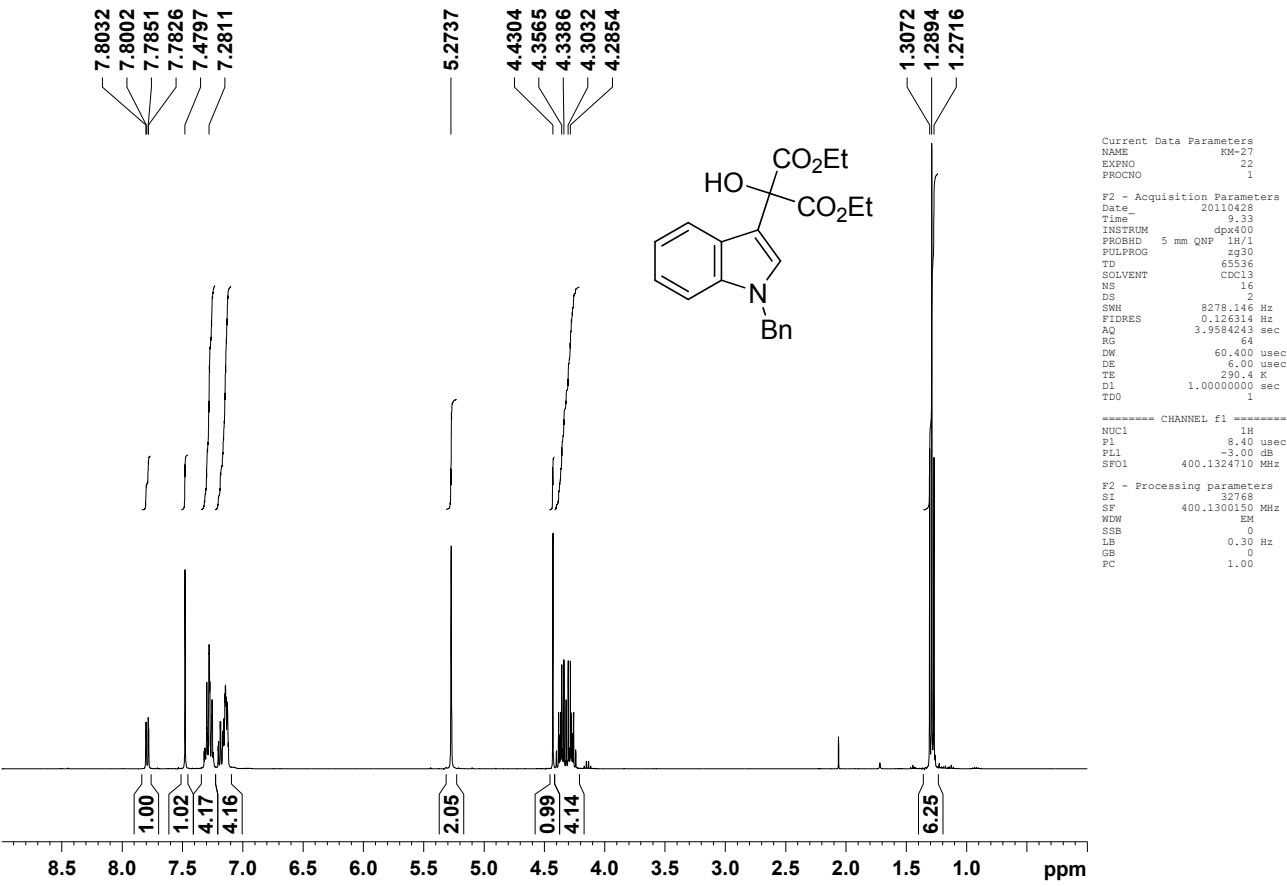
MS: m/z ($M+23$) 328.1

HRMS: m/z calc'd for $\text{C}_{16}\text{H}_{19}\text{NaNO}_5$ 328.3155, found 328.1156

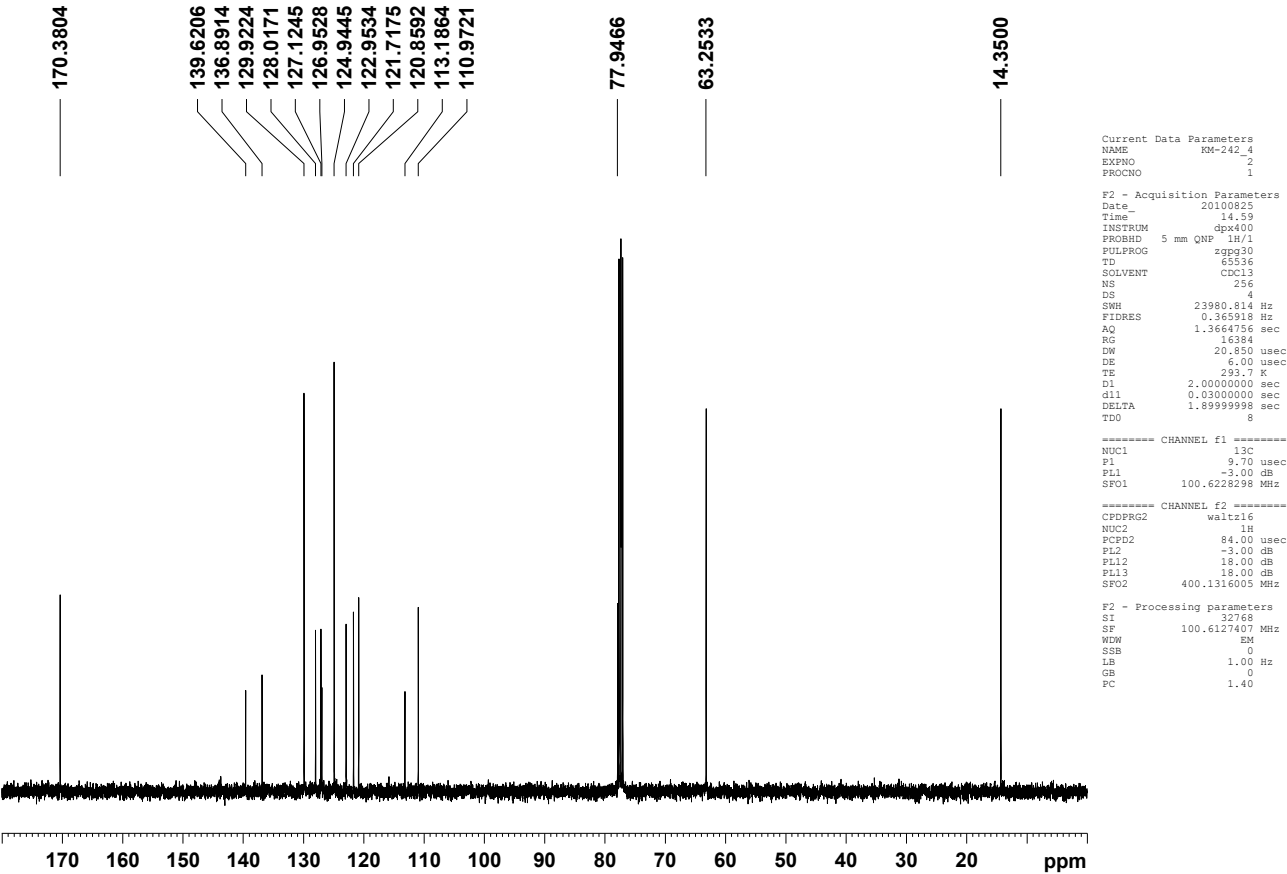
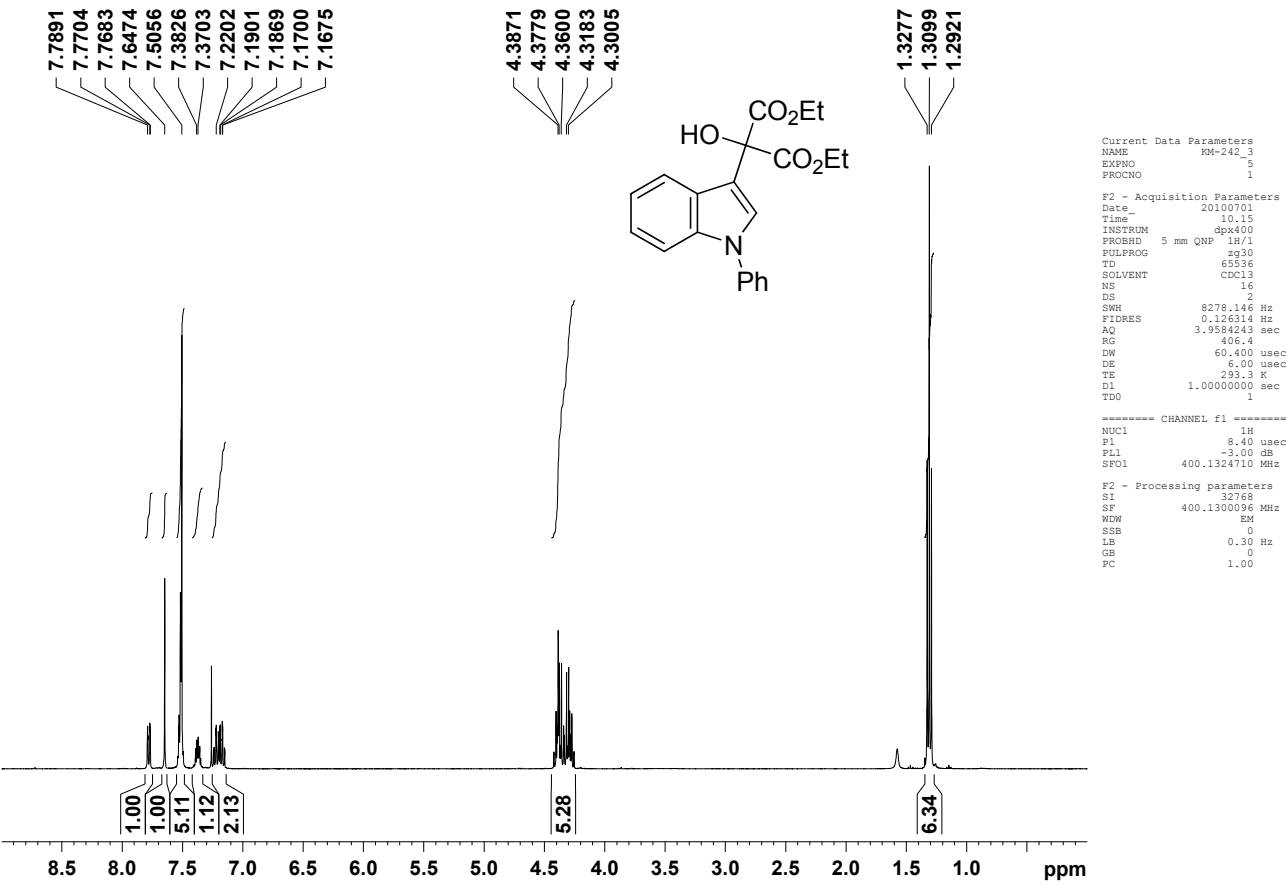
NMR spectra for diethyl 2-(1-ethyl-1*H*-indol-3-yl)-2-hydroxymalonate **1b**



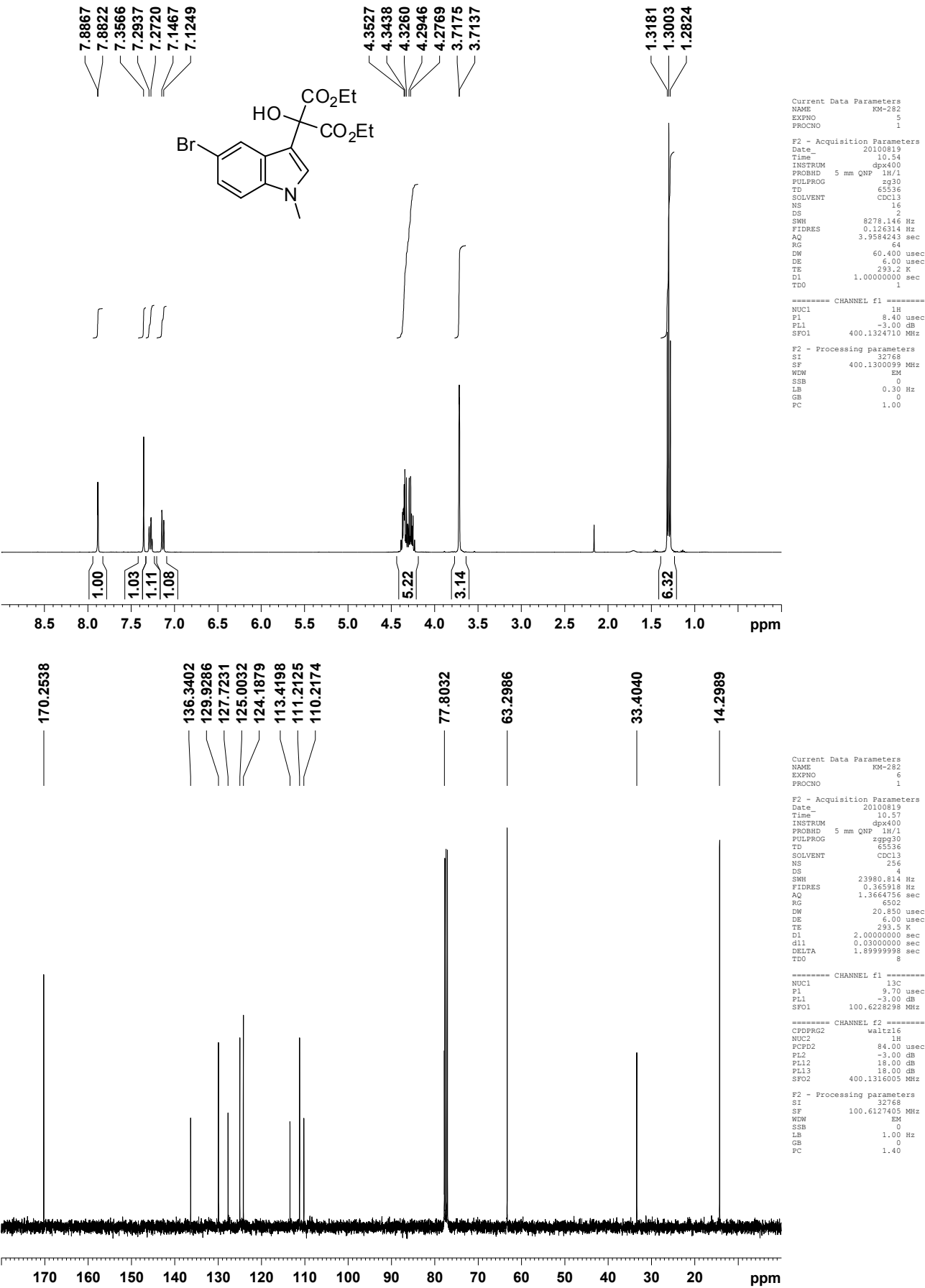
NMR spectra for diethyl 2-(1-benzyl-1H-indol-3-yl)-2-hydroxymalonate 1c



NMR spectra for diethyl 2-hydroxy-2-(1-phenyl-1*H*-indol-3-yl)malonate **1d**

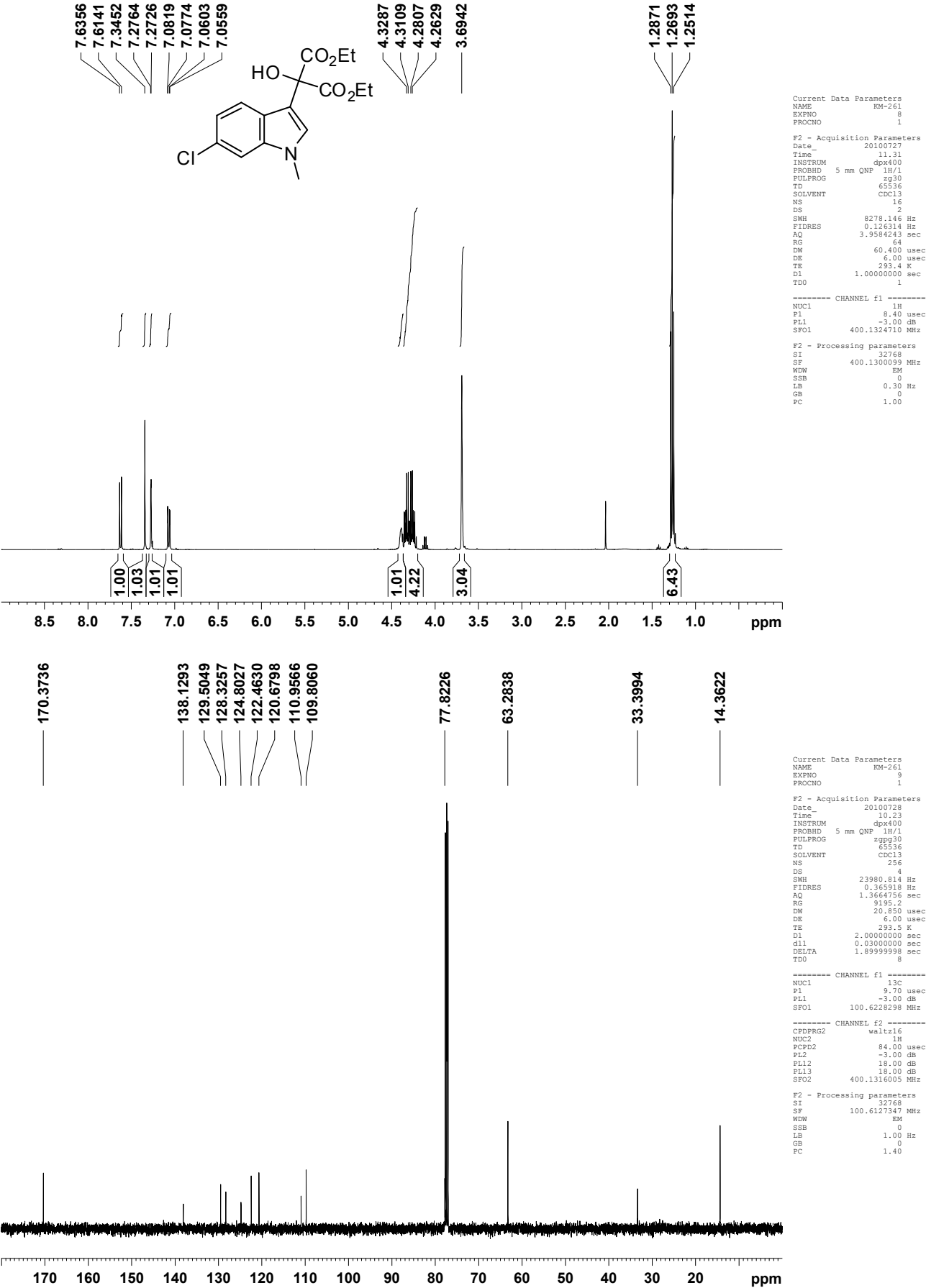


NMR spectra for diethyl 2-(5-bromo-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate **1e**

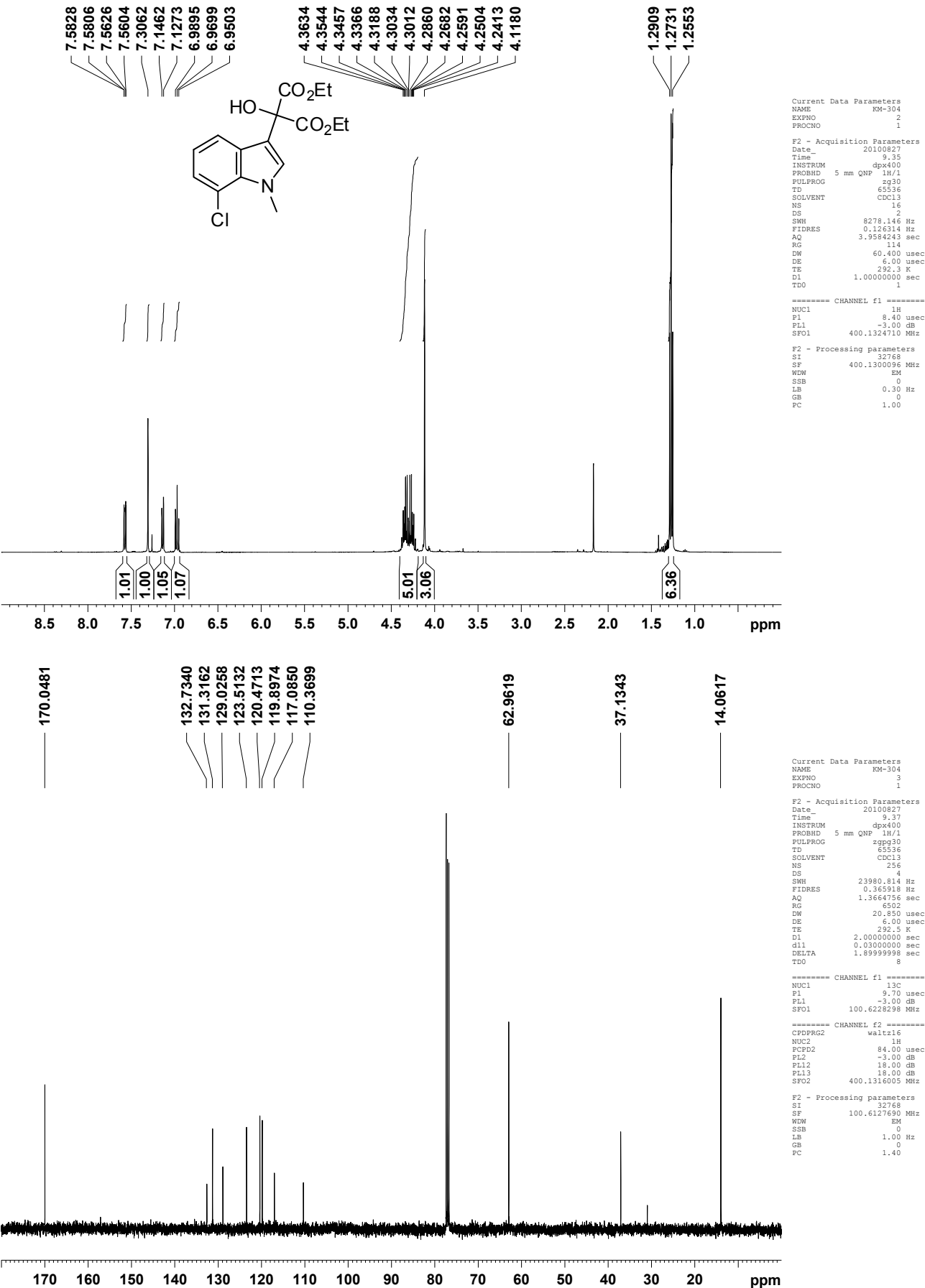


NMR spectra for diethyl 2-(6-chloro-1-methyl-1*H*-indol-3-yl)-2-hydroxymalonate

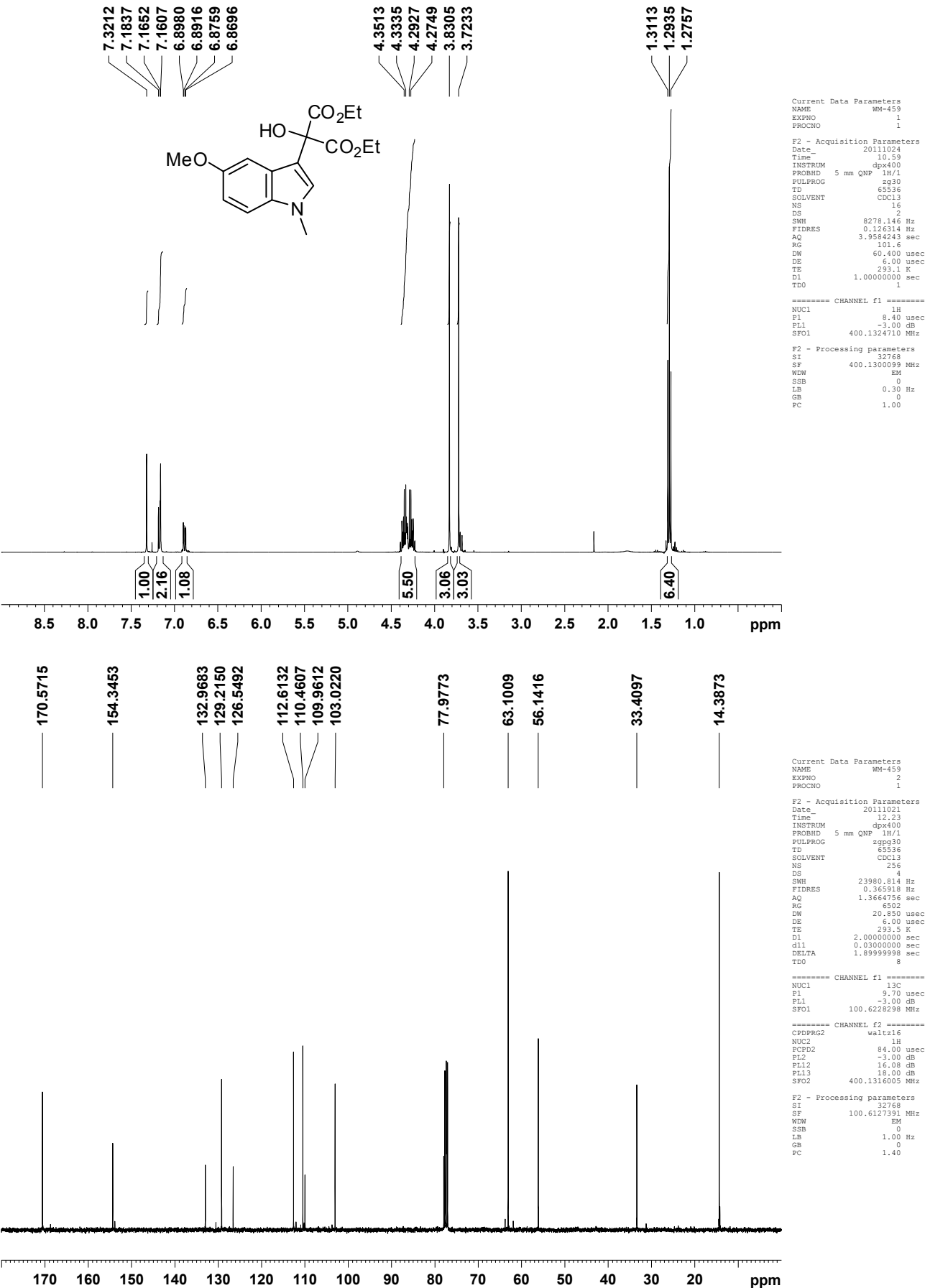
1f



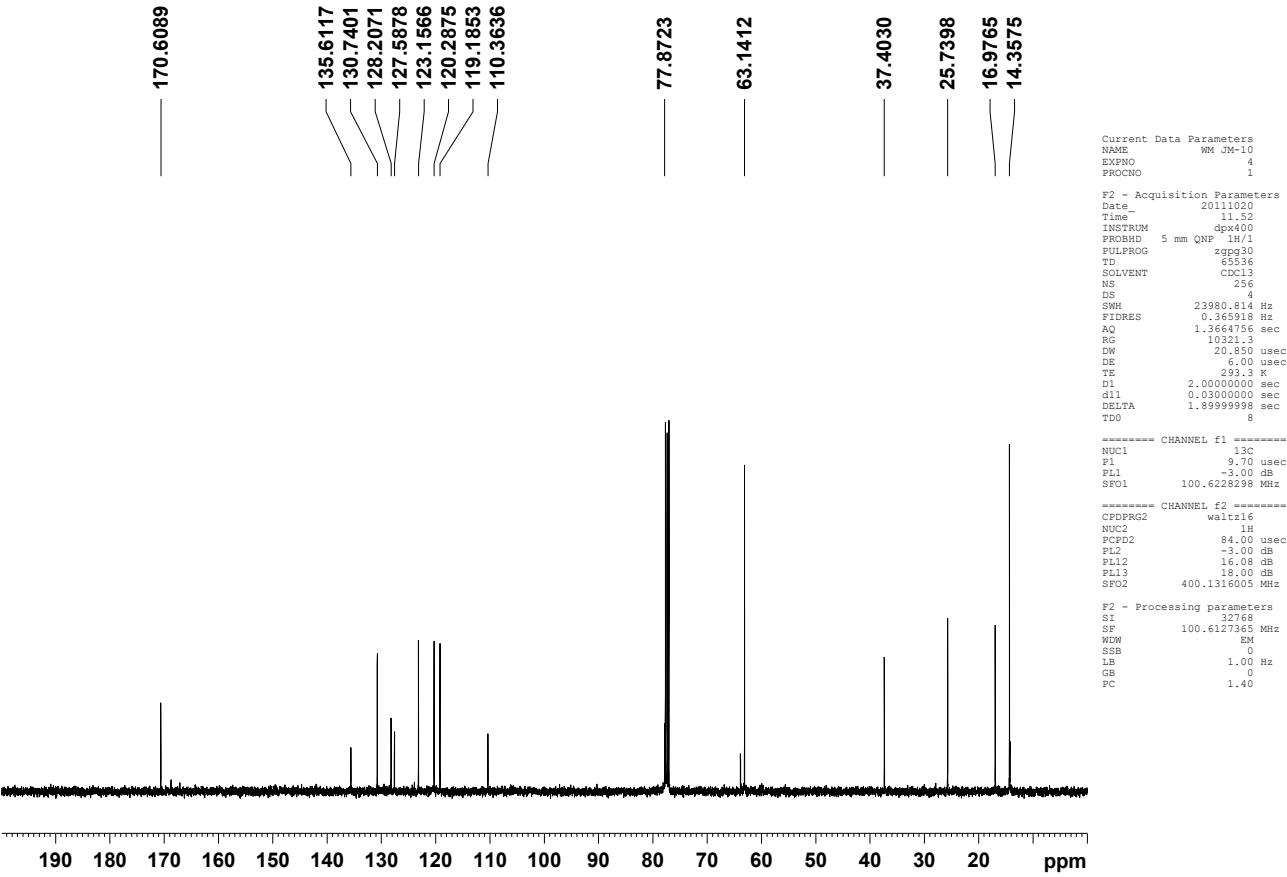
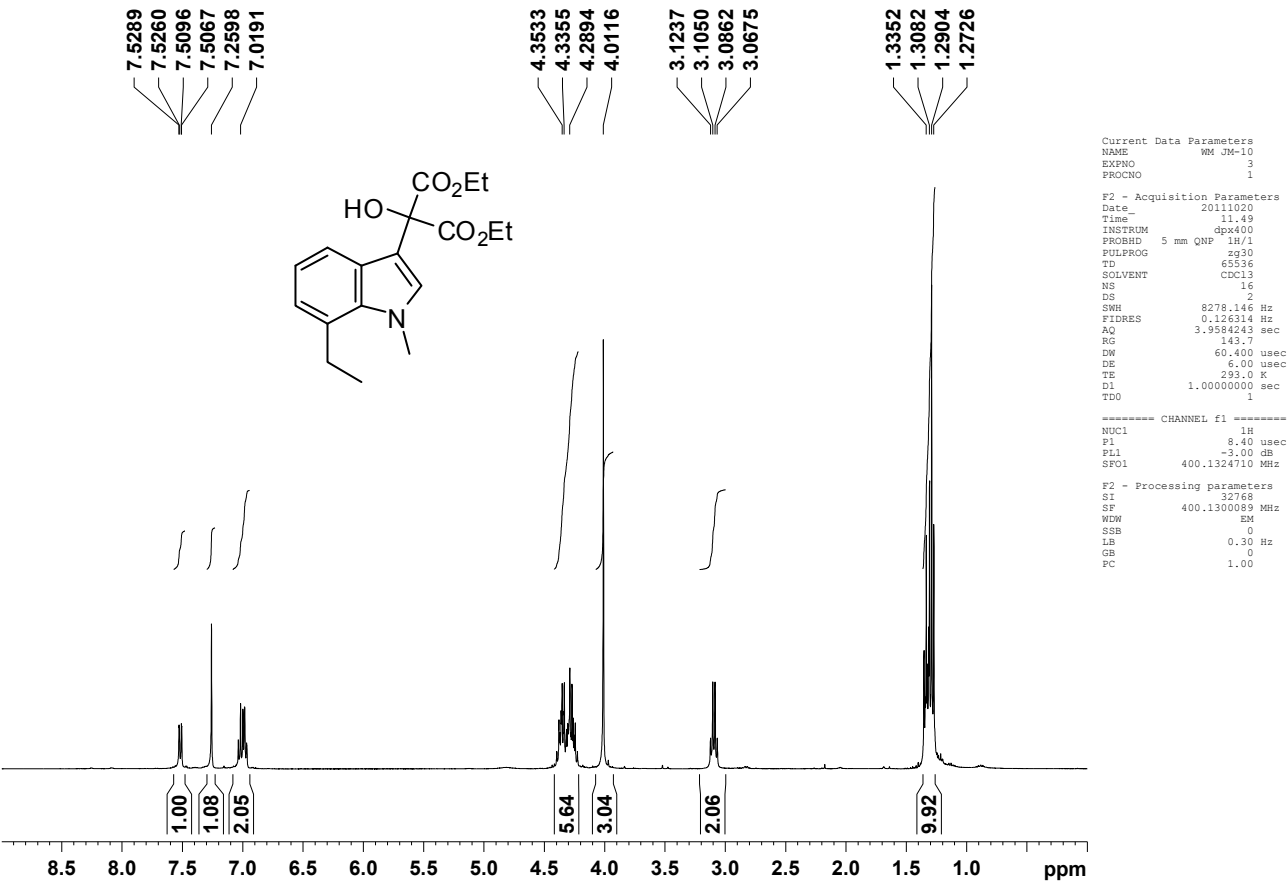
NMR spectra for diethyl 2-(7-chloro-1-methyl-1H-indol-3-yl)-2-hydroxymalonate **1g**



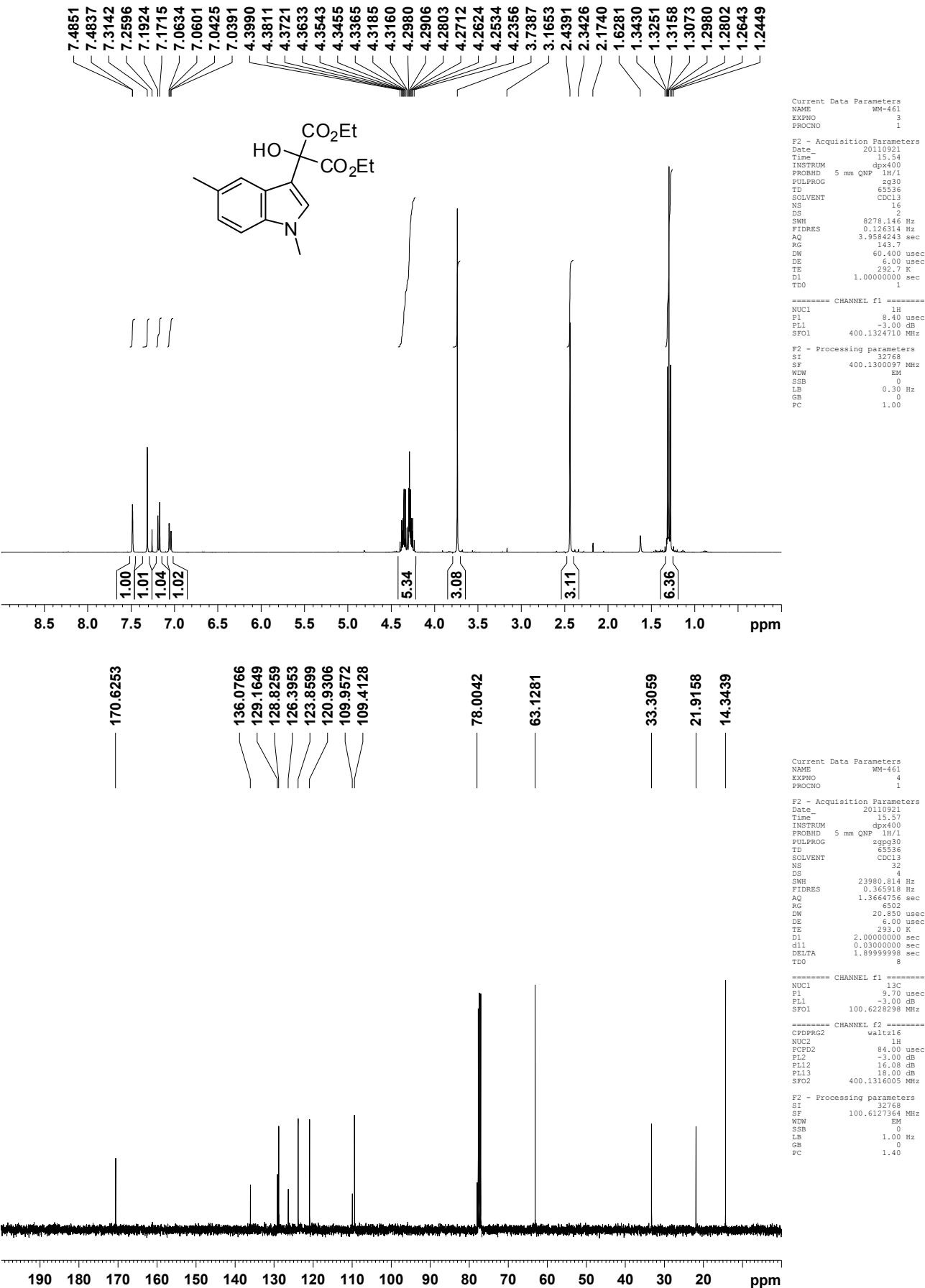
NMR spectra for diethyl 2-hydroxy-2-(5-methoxy-1-methyl-1H-indol-3-yl)malonate 1h



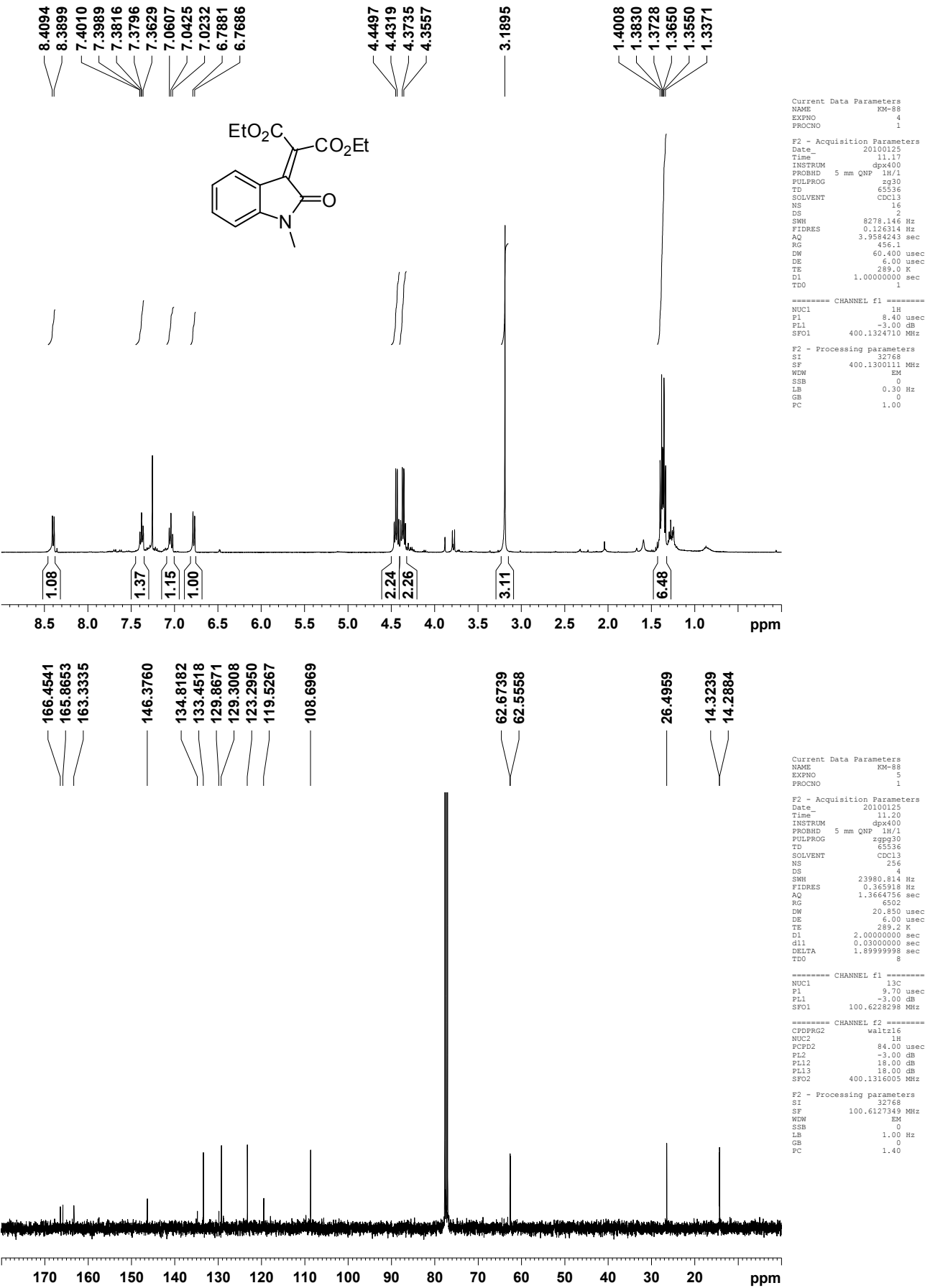
NMR spectra for diethyl 2-(7-ethyl-1-methyl-1H-indol-3-yl)-2-hydroxymalonate 1i



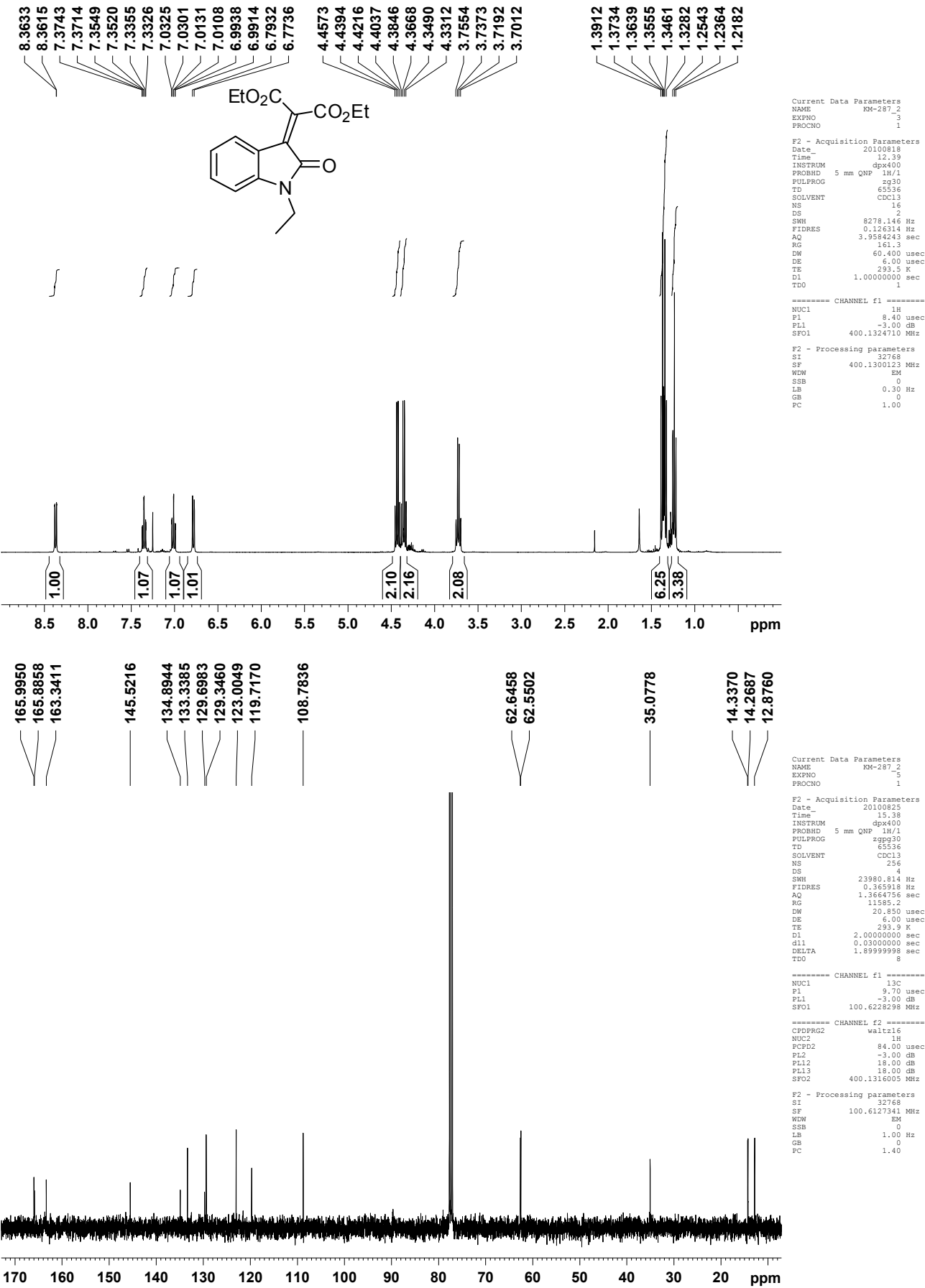
NMR spectra for diethyl 2-(1,5-dimethyl-1H-indol-3-yl)-2-hydroxymalonate 1j



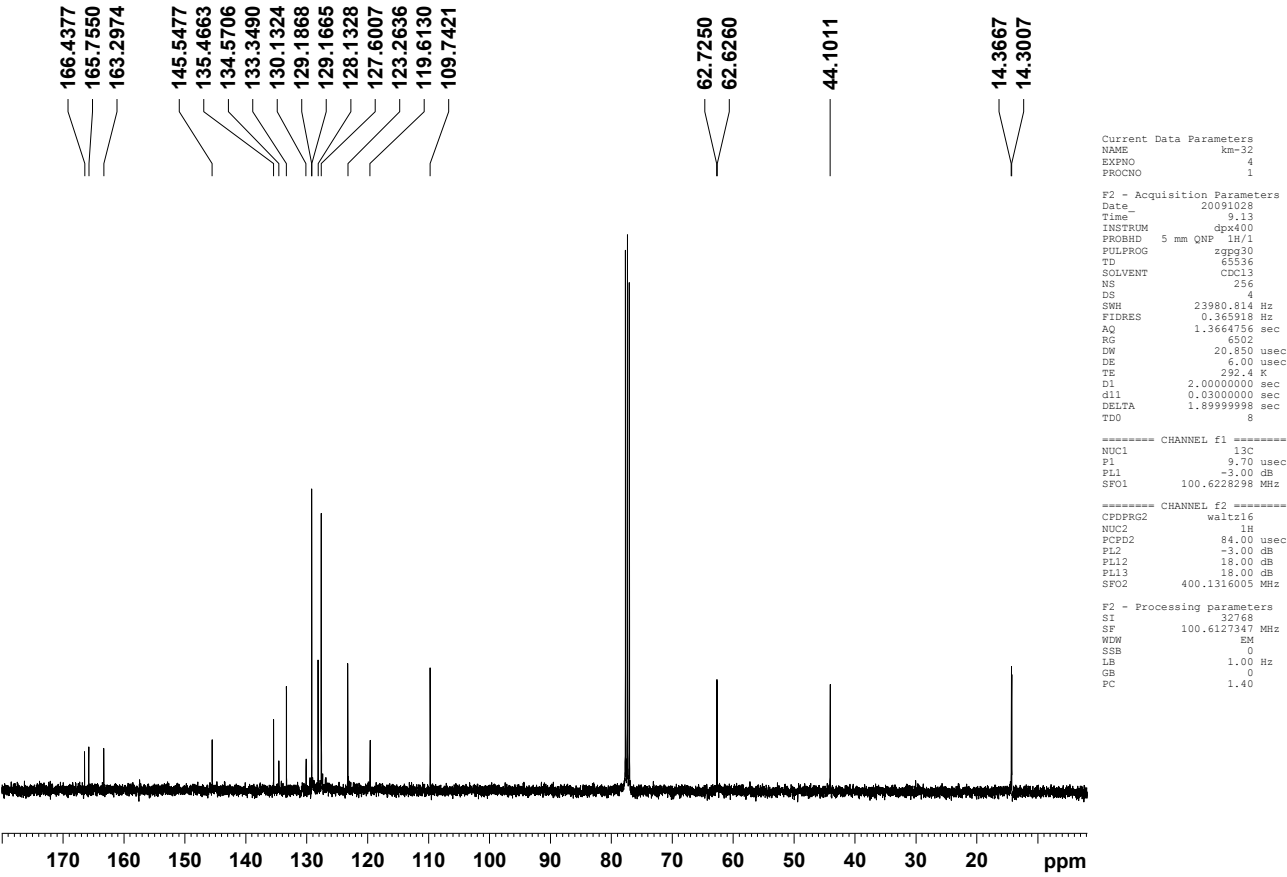
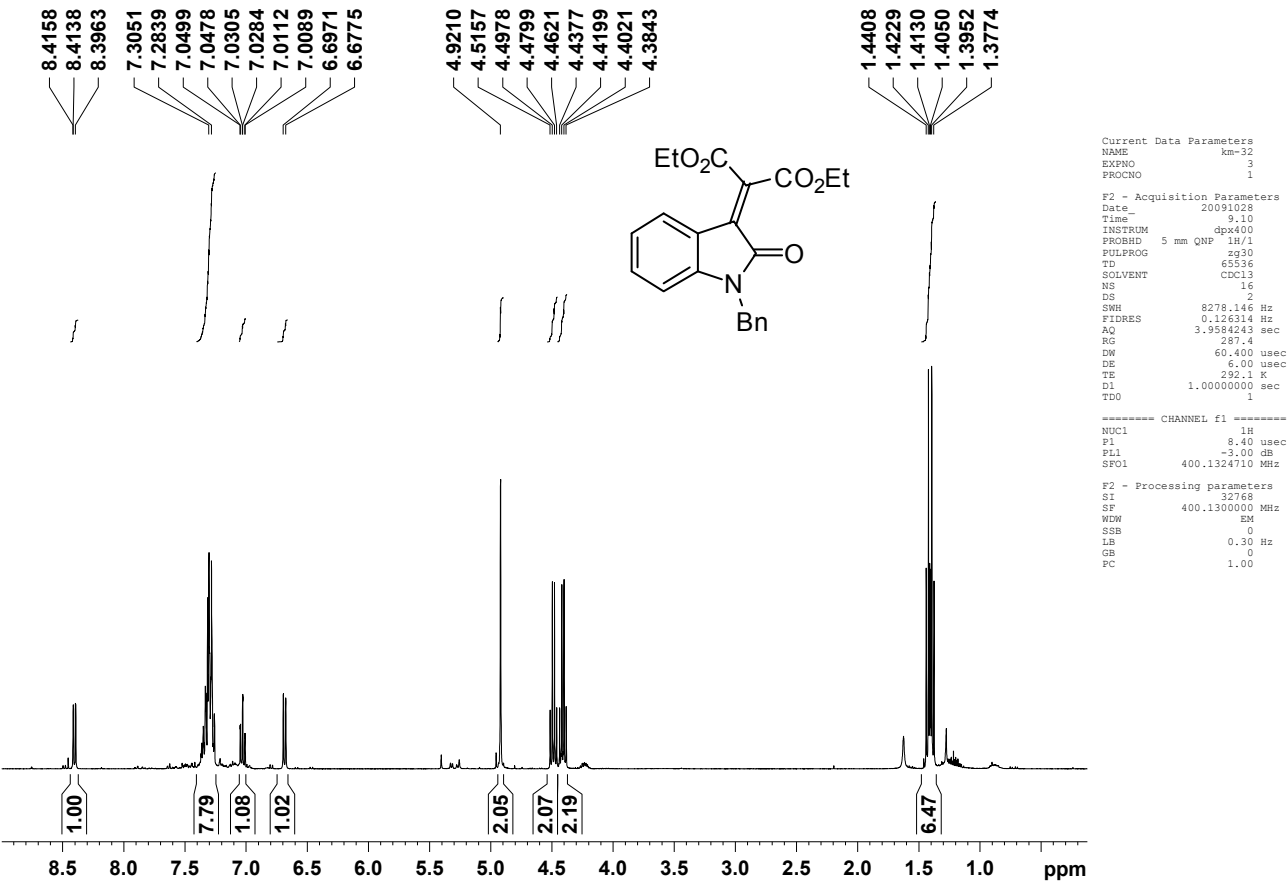
NMR spectra for diethyl 2-(1-methyl-2-oxoindolin-3-ylidene)malonate 2a



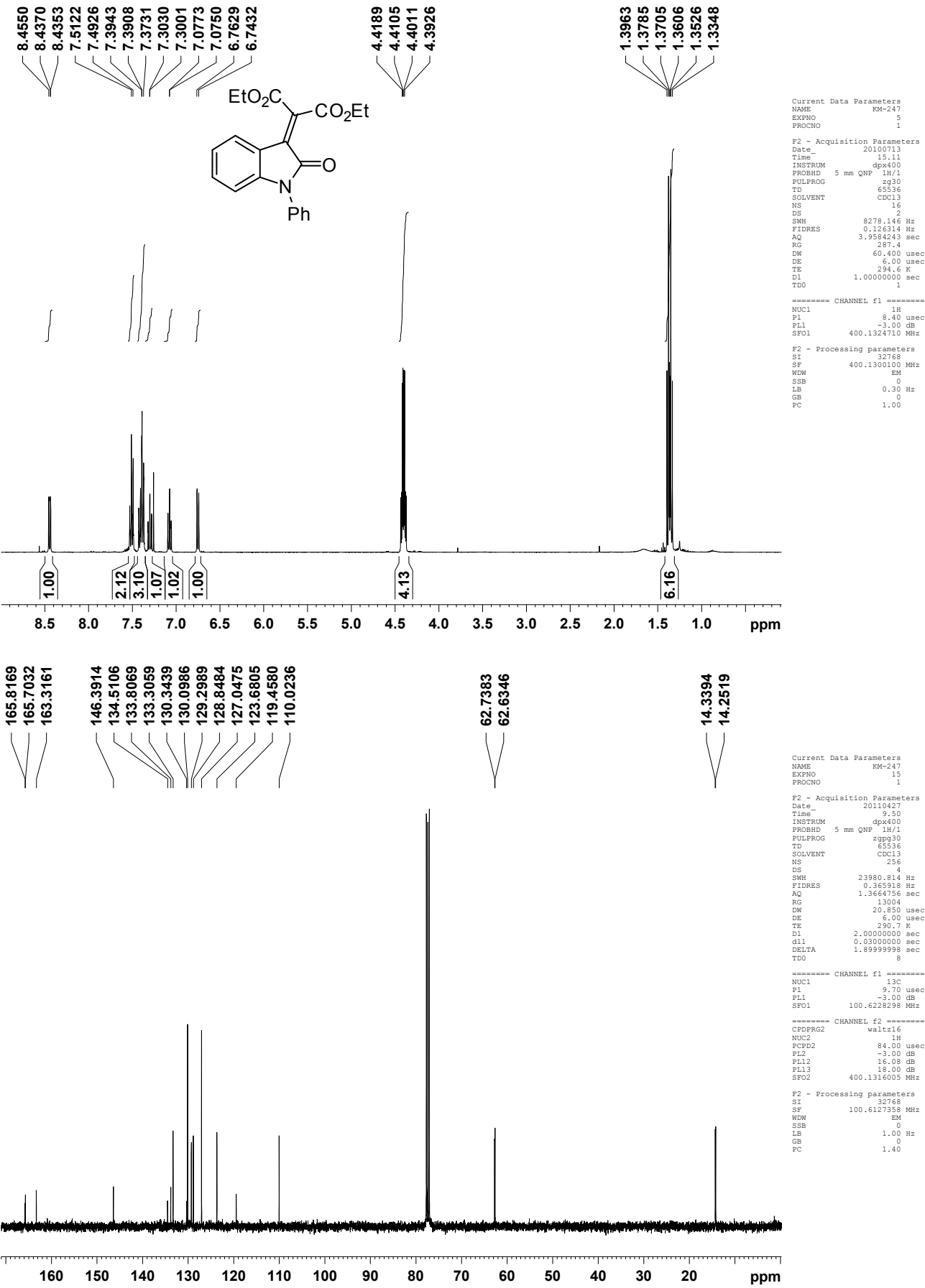
NMR spectra for diethyl 2-(1-ethyl-2-oxoindolin-3-ylidene)malonate 2b



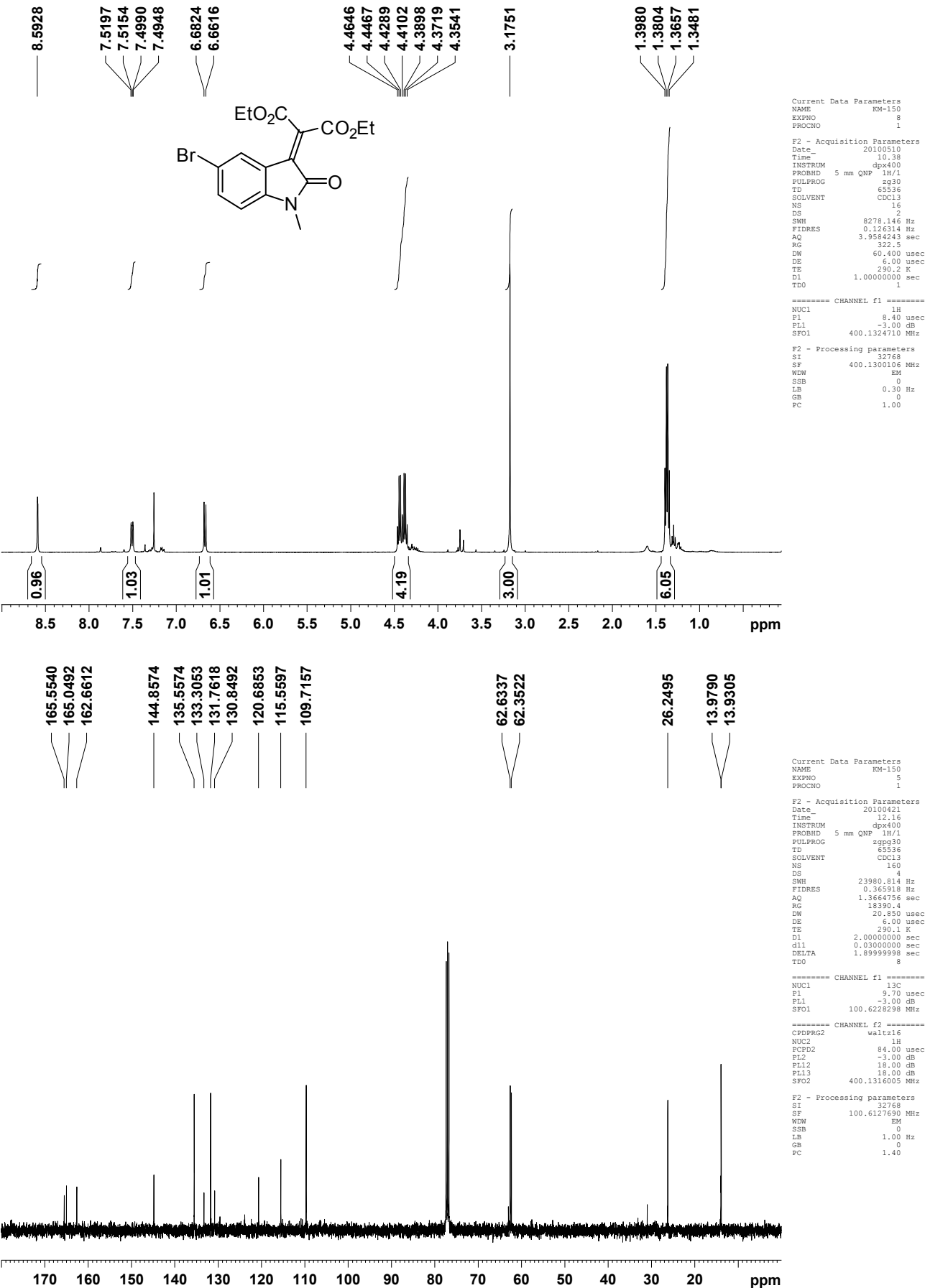
NMR spectra for diethyl 2-(1-benzyl-2-oxoindolin-3-ylidene)malonate 2c



NMR spectra for diethyl 2-(2-oxo-1-phenylindolin-3-ylidene)malonate 2d



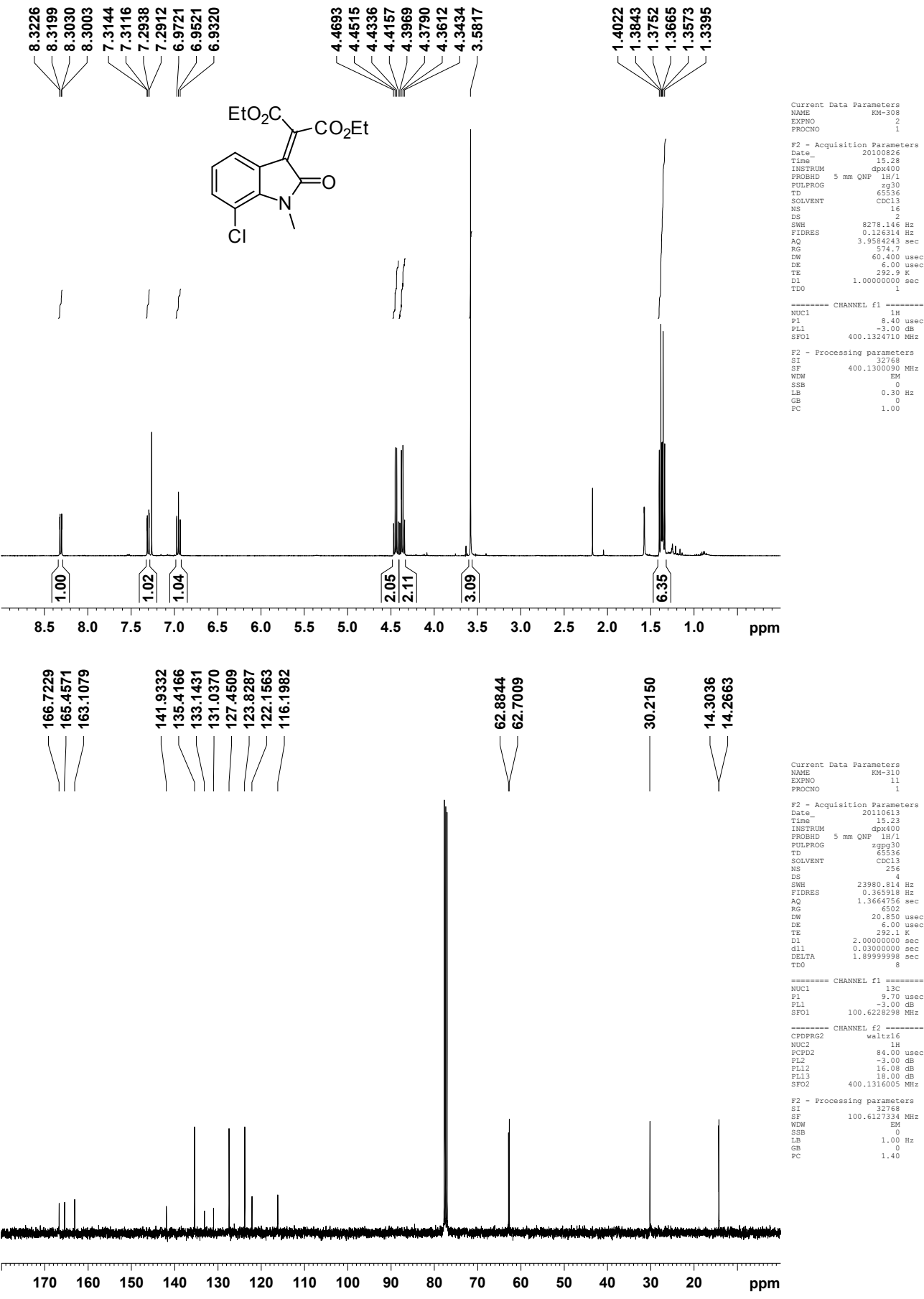
NMR spectra for diethyl 2-(5-bromo-1-methyl-2-oxoindolin-3-ylidene)malonate **2e**



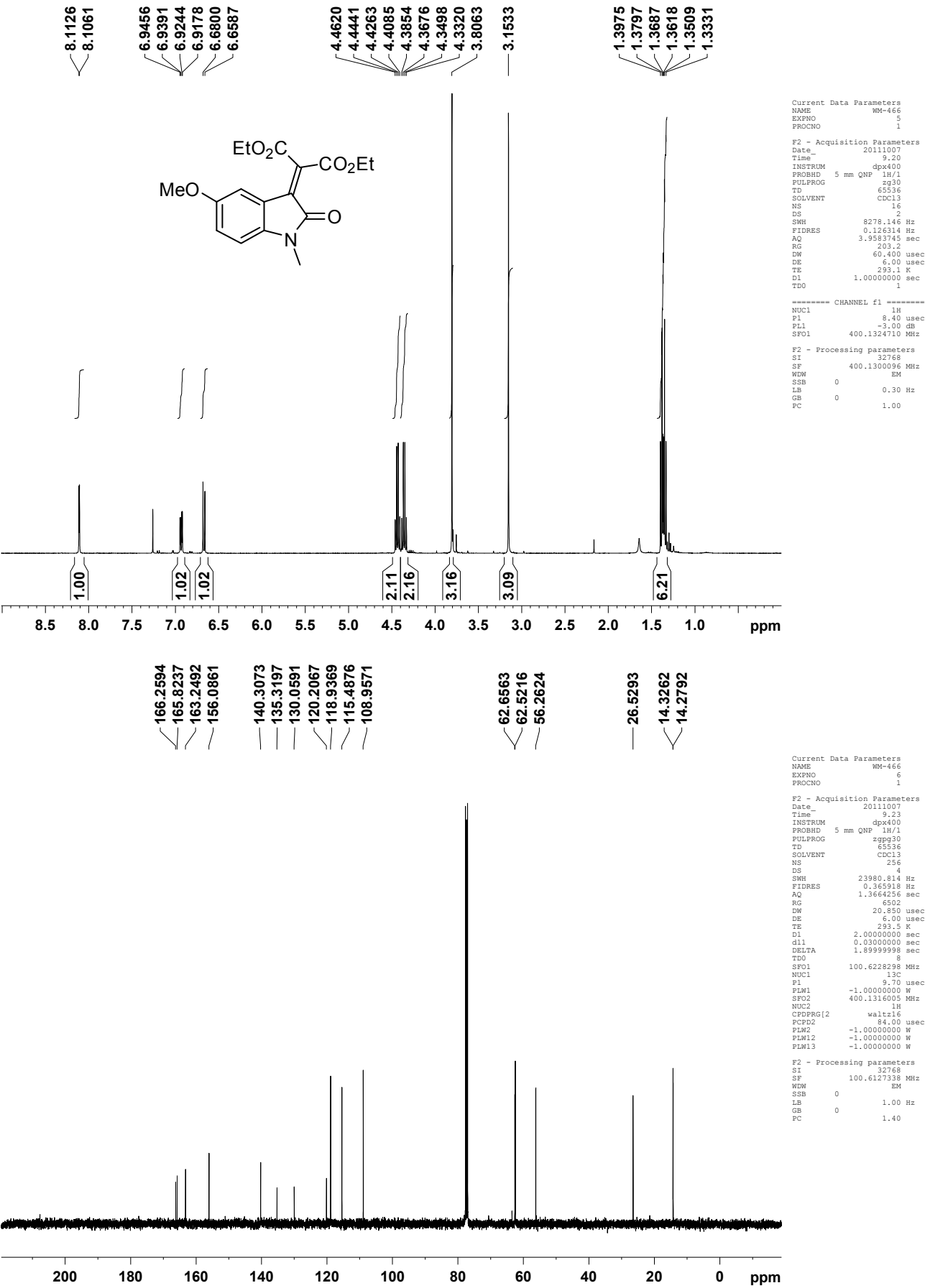
NMR spectra for diethyl 2-(6-chloro-1-methyl-2-oxoindolin-3-ylidene)malonate **2f**



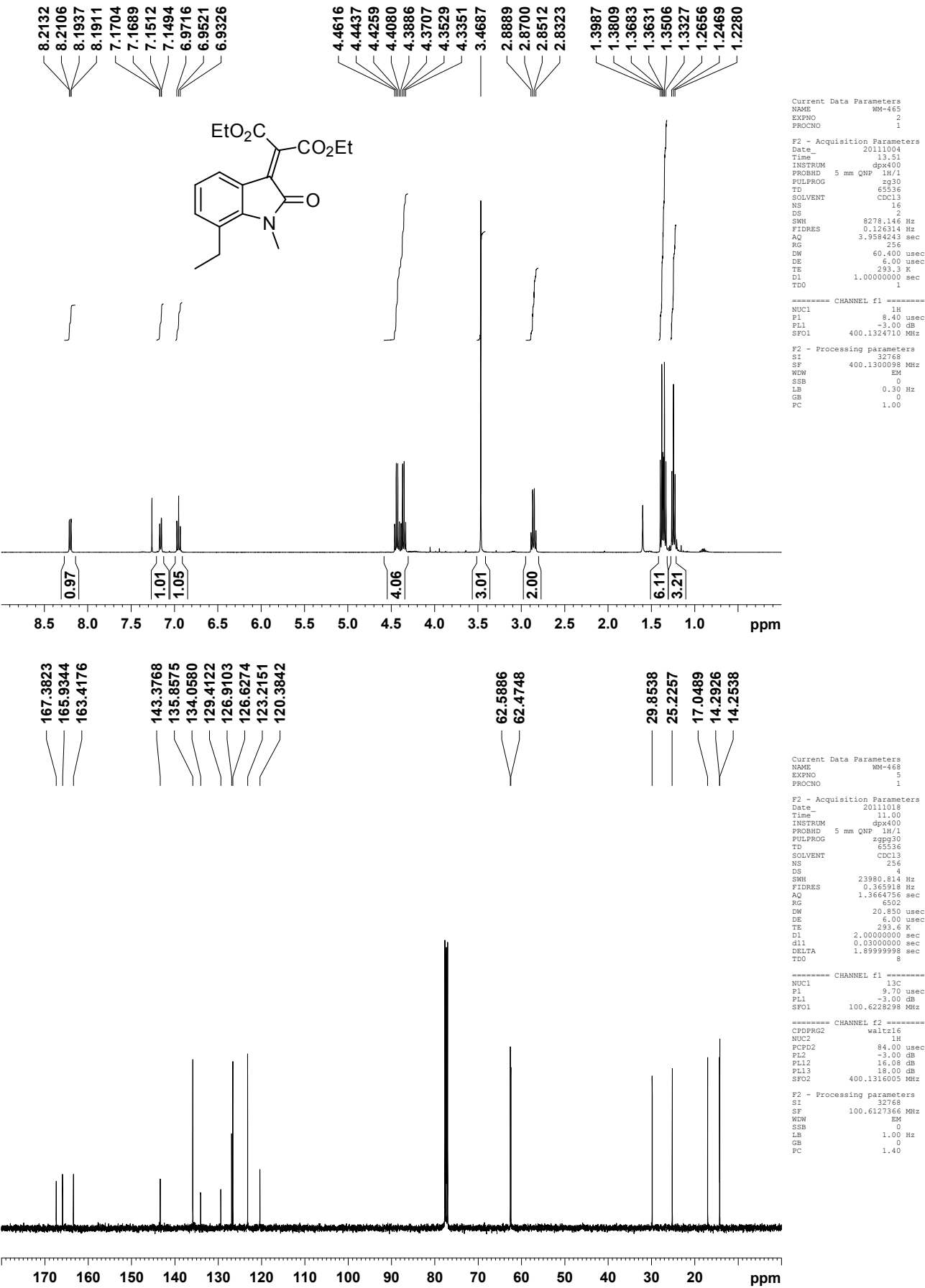
NMR spectra for diethyl 2-(7-chloro-1-methyl-2-oxoindolin-3-ylidene)malonate **2g**



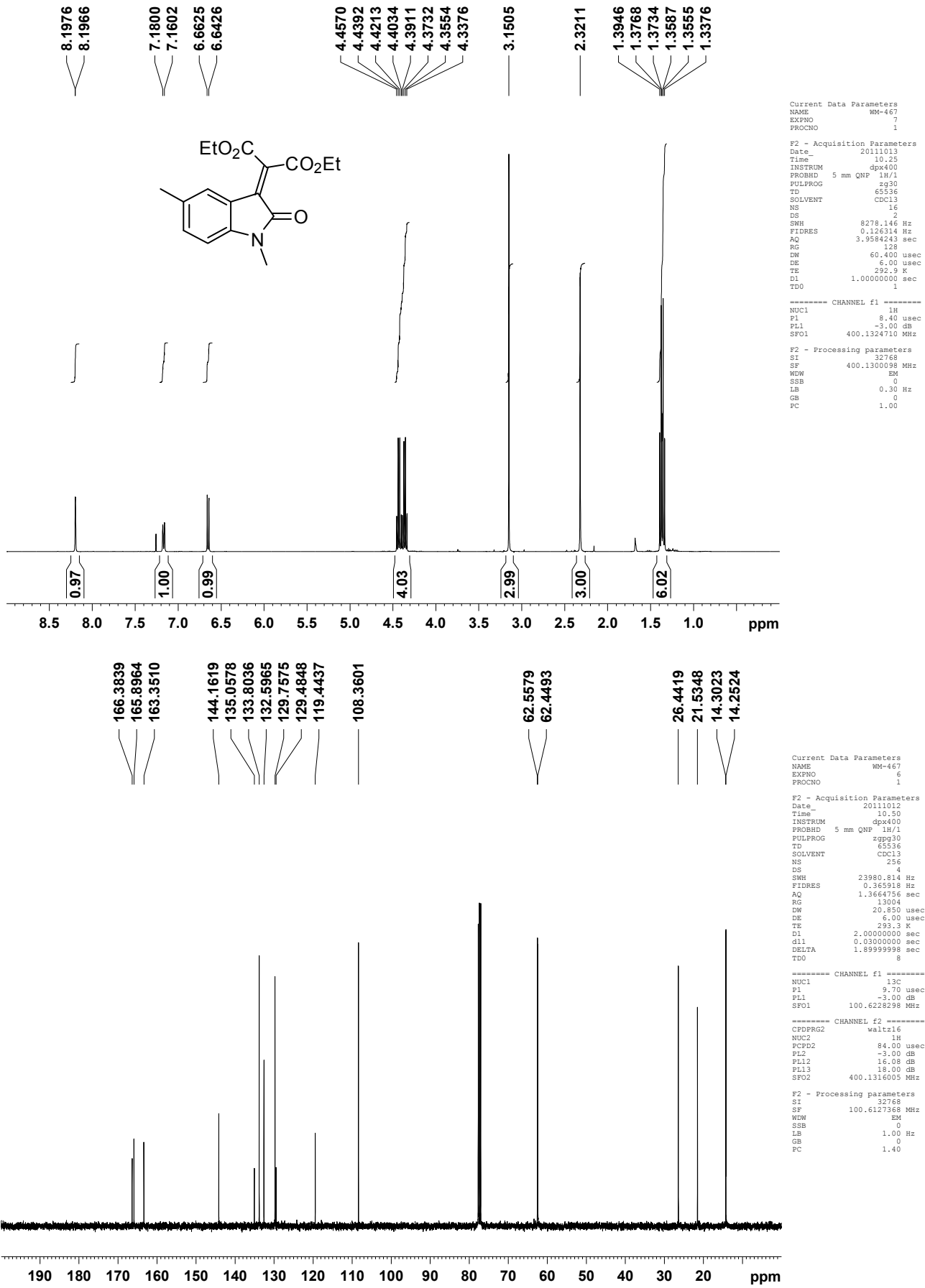
NMR spectra for diethyl 2-(5-methoxy-1-methyl-2-oxoindolin-3-ylidene)malonate 2h



NMR spectra for diethyl 2-(7-ethyl-1-methyl-2-oxoindolin-3-ylidene)malonate 2i



NMR spectra for diethyl 2-(1,5-dimethyl-2-oxoindolin-3-ylidene)malonate 2j



NMR spectra for diethyl 2-(1-methyl-2-oxoindolin-3-yl)malonate 4

