Supporting Information

Copper Mediated Selective C-H Activation and Cross Dehydrogenative C-N Coupling of 2-Aminoacetophenones

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General Information:

All the reagents were purchased commercially and used without further purification. ^{1}H NMR and ^{13}C NMR were recorded with Bruker 400MHz. ^{1}H NMR (400MHz) and ^{13}C NMR (100MHz) spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard. Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad resonance. All the NMR spectra were acquired at ambient temperature. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 Å F254 pre-coated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and staining with I_2 on silica gel. The elemental analysis was done with vario MICRO V1.3.2 Elemental Analyser system, GmbH instruments.

General method A: Typical experimental procedure for Copper catalyzed synthesis of N-alkyl/arylisatin

To a solution of 1-(2-(alkyl/arylamino)phenyl)ethanone (**1**, 1 equiv) in DMSO, $Cu(OAc)_2.H_2O$ (0.5 equiv) and sodium acetate (1.5 equiv) was added at ambient temperature and heated at 80 °C under the atmosphere of air. Progress of the reaction was monitored by TLC. Upon on completion of the reaction it was allowed to cool to ambient temperature and diluted with ethyl acetate and water. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel column chromatography using hexane / ethyl acetate as eluent.

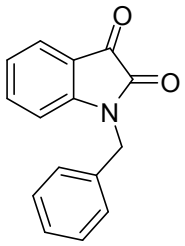
General method B: Typical experimental procedure for copper catalyzed synthesis of N-methylisatins from 1-(2-(dialkylamino)phenyl)ethanone

To a solution of 1-(2-(dialkylamino)phenyl)ethanone (**3**, 1 equiv) in DMSO, $Cu(OAc)_2.H_2O$ (0.5 equiv.) and sodium acetate (1.5 equiv) was added at ambient temperature and heated at 80 °C under the atmosphere of air. Progress of the reaction was monitored by TLC. Upon on completion of the reaction it was allowed to cool to ambient temperature and diluted with ethyl acetate and water. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel column chromatography using hexane / ethyl acetate as eluent.

General method C: Typical procedure for copper catalyzed oxidation of benzyl amines to benzamides:

To a solution of 1-(2-(benzylamino)phenyl)ethanone (**1,** 1 equiv) in CH_3CN, CuBr was added at ambient temperature and heated at 80 °C under the atmosphere of air. Progress of the reaction was monitored by TLC. Upon on completion of the reaction it was allowed to cool to ambient temperature and diluted with ethyl acetate and water. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel column chromatography using hexane / ethyl acetate as eluent.

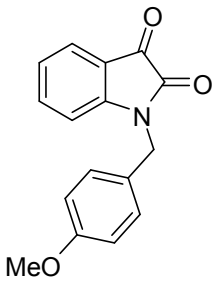
Preparation of 1-Benzyl-1H-indole-2,3-dione (3a):



The reaction was carried out according to **general method A** using 1-(2-(benzylamino)phenyl)ethanone (**1a**) (100 mg, 0.443 mmol), $Cu(OAc)_2.H_2O$ (44.3 mg, 0.221 mmol), NaOAc (54.6 mg, 0.665 mmol) and DMSO (2 mL). Conditions: 80 °C, 4h. The title compound **3a** (86.3 mg, 82% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 126-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.62 (d, J = 7.2 Hz, 1H), 7.46-7.49 (t, J = 7.8 Hz, 1H), 7.29-7.37 (m, 5H), 7.07-7.11 (t, J = 7.6 Hz, 1H), 6.76-6.78 (d, J = 8 Hz, 1H), 4.93 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.26, 158.29, 150.74, 138.35, 134.53, 129.07, 128.18, 127.45, 125.41, 123.88, 117.69, 111.03, 44.06. The spectral data of the compound **3a** was in agreement with the values reported in the literature.[1]

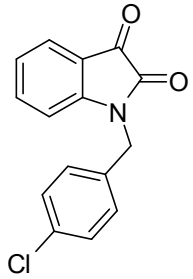
Preparation of 1-(4-Methoxy-benzyl)-1H-indole-2,3-dione (3b):



The reaction was carried out according to **general method A** using 1-(2-(4-methoxybenzylamino)phenyl)ethanone (**1b**,100 mg, 0.391 mmol), $Cu(OAc)_2.H_2O$ (39 mg, 0.195 mmol), NaOAc (48.2 mg, 0.587 mmol) and DMSO (2 mL). Conditions: 80 °C, 4h. The title compound **3b** (87.9 mg, 84% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 120-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.61 (dd, J = 7.2 Hz, 1H), 7.46-7.50 (m, 1H), 7.28 (s, 2H), 7.06-7.10 (m, 1H), 6.86-6.88 (dd, J = 6.8 Hz, 2H), 6.79-6.81 (d, J = 8 Hz, 1H), 4.86 (s, J = Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.37, 159.48, 158.24, 150.80, 138.23, 128.92, 126.50, 125.39, 123.78, 117.72, 114.43, 111.00, 55.30, 43.56. The spectral data of the compound **3b** was in agreement with the values reported in the literature.[2]

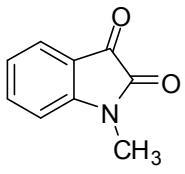
Preparation of 1-(4-Chloro-benzyl)-1H-indole-2,3-dione (3c):



The reaction was carried out according to **general method A** using 1-(2-(4-chlorobenzylamino)phenyl)ethanone (**1c**, 100 mg, 0.385 mmol), $Cu(OAc)_2.H_2O$ (38.4 mg, 0.192 mmol), NaOAc (47.3 mg, 0.577 mmol) and DMSO (2 mL). Conditions: 80 °C, 4.5h. The title compound **3c** (80.5 mg, 77% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp:127-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.63 (d, J = 7.6 Hz, 1H), 7.47-7.51 (m,1H), 7.26-7.33 (m, 5H), 7.09-7.13 (t, J = 7.6 Hz, 1H), 6.73-6.75 (d, J = 8 Hz, 1H), 4.90 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.95, 158.24, 150.41, 138.35, 134.14, 133.07, 129.28, 128.83, 125.56, 124.05, 117.73, 110.81, 43.43. The spectral data of the compound **3c** was in agreement with the values reported in the literature.[3]

Preparation of 1-Methyl-1H-indole-2,3-dione (3d):



The reaction was carried out according to **general method A** using 1-(2-(methylamino)phenyl)ethanone (**1d**, 100 mg, 0.67 mmol), $Cu(OAc)_2.H_2O$ (66.9 mg, 0.335 mmol), NaOAc (82.5 mg, 1.00 mmol) and DMSO (2 mL). Conditions: 80 °C, 10h. The title compound **3d** (81 mg, 75% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

Or

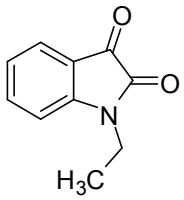
The reaction was carried out according to **general method B** using 1-(2-(dimethylamino)phenyl)ethanone (**2d**, 100 mg, 0.61 mmol), $Cu(OAc)_2.H_2O$ (61.1 mg, 0.306 mmol), NaOAc (75.4 mg, 0.92 mmol) and DMSO (2 mL). Conditions: 80 °C, 12h. The title compound **3d** (69.1 mg, 70% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

Or

The reaction was carried out according to **general method B** using 1-(2-(benzyl(methyl)amino)phenyl)ethanone (**2x**, 100 mg, 0.41 mmol), $Cu(OAc)_2.H_2O$ (41.7 mg, 0.208 mmol), NaOAc (51.4 mg, 0.62 mmol) and DMSO (2 mL). Conditions: 80 °C, 6h. The title compound **3d** (45.8 mg, 68% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 121-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.63 (t, J = 7.4 Hz, 2H), 7.11-7.15 (t, J = 7.4 Hz, 1H), 6.88-6.91 (d, J = 8.4 Hz, 1H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.33, 158.27, 151.51, 138.37, 125.30, 123.84, 117.53, 109.90, and 26.23. The spectral data of the compound **3d** was in agreement with the values reported in the literature.[1]

Preparation of 1-Ethyl-1H-indole-2,3-dione (3e):

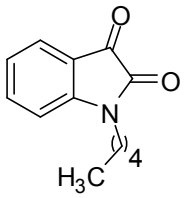


The reaction was carried out according to **general method A** using 1-(2-(ethylamino)phenyl)ethanone (**1e,** 100 mg, 0.612 mmol), $Cu(OAc)_2.H_2O$ (61.1 mg, 0.306

mmol), NaOAc (75.4 mg, 0.919 mmol) and DMSO (2 mL). Conditions: 80 °C, 9h. The title compound **3e** (79.4 mg, 74% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 87-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.61 (t, J = 8.4 Hz, 2H), 7.09-7.12 (t, J = 7.6 Hz, 1H), 6.89-6.91 (d, J = 7.6 Hz, 1H), 3.76-3.81 (q, J = 7.2 Hz, 2H), 1.29-1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.68, 156.86, 149.66, 137.31, 124.48, 122.62, 116.62, 109.00, 33.94, 11.50. The spectral data of the compound **3e** was in agreement with the values reported in the literature.[4]

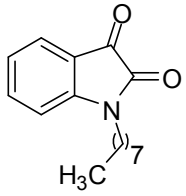
Preparation of 1-Pentyl-1H-indole-2,3-dione (3f):



The reaction was carried out according to **general method A** using 1-(2-(pentylamino)phenyl)ethanone (**1f**, 100 mg, 0.487 mmol), $Cu(OAc)_2.H_2O$ (48.6 mg, 0.243 mmol), NaOAc (60 mg, 0.730 mmol) and DMSO (2 mL). Conditions: 80 °C, 7h. The title compound **3f** (78.3 mg, 74% yield) was obtained as red semi solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.61 (m, 2H), 7.09-7.13 (t, J = 7.2 Hz, 1H), 6.89-6.91 (d, J = 8 Hz, 1H), 3.70-3.73 (t, J = 7.2 Hz, 2H), 1.68-1.72 (m, 2H), 1.34-1.38 (m, 4H), 0.89-0.92 (t, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.70, 158.15, 151.09, 138.34, 125.44, 123.60, 117.59, 110.18, 40.25, 28.98, 26.94, 22.30, 13.92. The spectral data of the compound **3f** was in agreement with the values reported in the literature.[5]

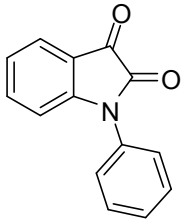
Preparation of 1-Octyl-1H-indole-2,3-dione (3g):



The reaction was carried out according to **general method A** using 1-(2-(octylamino)phenyl)ethanone (**1g**, 100 mg, 0.404 mmol), $Cu(OAc)_2.H_2O$ (40.3 mg, 0.202 mmol), NaOAc (49.7 mg, 0.606 mmol) and DMSO (2 mL). Conditions: 80 °C, 7h. The title compound **3g** (75.4 mg, 72% yield) was obtained as red semi solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.61 (m, 2H), 7.10-7.12 (t, J = 7.6 Hz, 1H), 6.88-6.90 (d, J = 8 Hz, 1H), 3.69-3.73 (t, J = 7.4 Hz, 2H), 1.66-1.73 (m, 2H), 1.24-1.31 (m, 11H), 0.87-0.89 (t, J = 3.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.67, 158.15, 151.13, 138.26, 125.44, 123.57, 117.66, 110.15, 40.31, 31.74, 29.19, 29.13, 27.27, 26.91, 22.60, 14.05. The spectral data of the compound **3g** was in agreement with the values reported in the literature.[5]

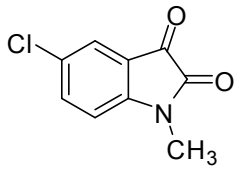
Preparation of 1-Phenyl-1H-indole-2,3-dione (3h):



The reaction was carried out according to **general method A** using 1-(2-(phenylamino)phenyl)ethanone (**1h,** 100 mg, 0.473 mmol), $Cu(OAc)_2.H_2O$ (47.2 mg, 0.236 mmol), NaOAc (58.2 mg, 0.71 mmol) and DMSO (2 mL). Conditions: 80 °C, 3h. The title compound **3h** (98.2 mg, 93% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 127-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 7.2 Hz, 1H), 7.51-7.58 (m, 3H), 7.41-7.47 (m, 3H), 7.15-7.19 (m, 1H), 6.88-6.91 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.87, 157.32, 151.72, 138.27, 132.97, 129.96, 128.82, 126.04, 125.60, 124.27, 117.57, 111.27. The spectral data of the compound **3h** was in agreement with the values reported in the literature.[6]

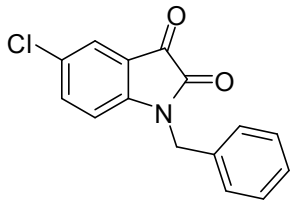
Preparation of 5-Chloro-1-methyl-1H-indole-2,3-dione (3j):



The reaction was carried out according to **general method A** using 1-(5-chloro-2-(methylamino)phenyl)ethanone (**1j**, 100 mg, 0.544 mmol), $Cu(OAc)_2.H_2O$ (54.3 mg, 0.272 mmol), NaOAc (67.0 mg, 0.816 mmol) and DMSO (2 mL). Conditions: 80 °C, 4.5h. The title compound **3j** (72.4 mg, 68% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 157-159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.59 (m, 2H), 6.85-6.87 (m, 1H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.31, 157.70, 149.71, 137.74, 129.72, 125.27, 118.28, 111.18, 26.39. The spectral data of the compound **3j** was in agreement with the values reported in the literature.[7]

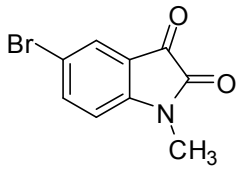
Preparation of 5-Bromo-1-benzyl-1H-indole-2,3-dione (3k):



The reaction was carried out according to **general method A** using 1-(5-chloro-2-(benzylamino)phenyl)ethanone (**1k**, 100 mg, 0.385 mmol), $Cu(OAc)_2.H_2O$ (38.4 mg, 0.192 mmol), NaOAc (47.3 mg, 0.577 mmol) and DMSO (2 mL). Conditions: 80 °C, 4h. The title compound **3k** (76.36 mg, 73% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 135-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.51 (d, J = 4.0 Hz, 1H), 7.35-7.37 (dd, J = 8.0 Hz, 1H), 7.23-7.30 (m, 5H), 6.64-6.66 (d, J = 8.0 Hz, 1H), 4.86 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.26, 157.74, 148.95, 137.68, 134.04, 129.79, 129.18, 128.38, 127.41, 125.35, 118.52, 112.31, 44.21. The spectral data of the compound **3k** was in agreement with the values reported in the literature.[9]

Preparation of 5-Bromo-1-methyl-1H-indole-2,3-dione (3l):



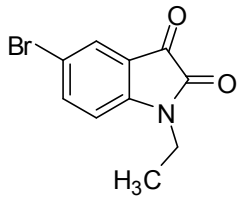
The reaction was carried out according to **general method A** using 1-(5-bromo-2-(methylamino)phenyl)ethanone (**1l**, 100 mg, 0.438 mmol), $Cu(OAc)_2.H_2O$ (43.7 mg, 0.219 mmol), NaOAc (53.9 mg, 0.657 mmol) and DMSO (2 mL). Conditions: 80 °C, 4.5h. The title compound **3l** (70.5 mg, 67% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

Or

The reaction was carried out according to **general method B** using 1-(5-bromo-2-(dimethylamino)phenyl)ethanone (**2l**, 100 mg, 0.41 mmol), $Cu(OAc)_2.H_2O$ (41.2 mg, 0.206 mmol), NaOAc (50.8 mg, 0.61 mmol) and DMSO (2 mL). Conditions: 80 °C, 6h. The title compound **3l** (60.48 mg, 61% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 173-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 1.6 Hz, 1H), 7.71 (s, 1H), 6.79-6.81 (d, J = 8.4 Hz, 1H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.13, 157.50, 150.15, 140.59, 128.06, 118.62, 116.66, 111.63, 26.35. The spectral data of the compound **3l** was in agreement with the values reported in the literature.[7]

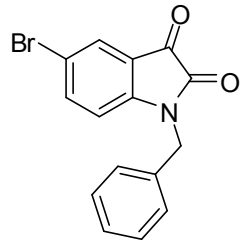
Preparation of 5-Bromo-1-ethyl-1H-indole-2,3-dione (3m):



The reaction was carried out according to **general method A** using 1-(5-bromo-2-(ethylamino)phenyl)ethanone (**1m**, 100 mg, 0.413 mmol), $Cu(OAc)_2.H_2O$ (41.2 mg, 0.206 mmol), NaOAc (50.8 mg, 0.619 mmol) and DMSO (2 mL). Conditions: 80 °C, 4h. The title compound **3m** (71.3 mg, 68% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 147-149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.72 (d, J = 2 Hz, 1H), 7.70 (s, 1H), 6.82-6.84 (d, J = 8.8 Hz, 1H), 3.75-3.81 (q, J = 7.2 Hz, 2H), 1.29-1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.50, 157.15, 149.38, 140.53, 128.26, 118.82, 116.44, 111.72, 35.14, 12.43. The spectral data of the compound **3m** was in agreement with the values reported in the literature.[8]

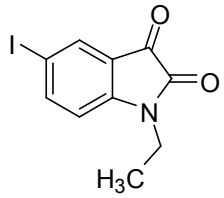
Preparation of 5-Bromo-1-benzyl-1H-indole-2,3-dione (3n):



The reaction was carried out according to **general method A** using 1-(5-bromo-2-(benzylamino)phenyl)ethanone (**1n**, 100 mg, 0.328 mmol), $Cu(OAc)_2.H_2O$ (32.8 mg, 0.164 mmol), NaOAc (40.4 mg, 0.493 mmol) and DMSO (2 mL). Conditions: 80 °C, 4h. The title compound **3n** (76.9 mg, 74% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 149-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 2 Hz, 1H), 7.56-7.59 (dd, J = 2 Hz, 1H), 7.29-7.37 (m, 5H), 6.66-6.68 (d, J = 8.4 Hz, 1H), 4.92 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.05, 157.54, 149.40, 140.49, 134.03, 129.17, 128.36, 128.18, 127.39, 118.88, 116.78, 112.70, 44.20. The spectral data of the compound **3n** was in agreement with the values reported in the literature.[9]

Preparation of 5-Iodo-1-ethyl-1H-indole-2,3-dione (3o):

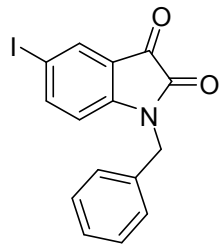


The reaction was carried out according to **general method A** using 1-(5-iodo-2-(ethylamino)phenyl)ethanone (**1o**, 100 mg, 0.345 mmol), $Cu(OAc)_2.H_2O$ (34.5 mg, 0.172 mmol), NaOAc (42.5 mg, 0.518 mmol) and DMSO (2 mL). Conditions: 80 °C, 4h. The title compound **3o** (71.8 mg, 69% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 141-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.90 (m, 2H), 6.71-6.73 (d, J = 8.8 Hz, 1H), 3.74-3.80 (q, J = 7.2 Hz, 2H), 1.28-1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.29, 156.87, 149.98, 146.34, 133.98, 119.22, 112.11, 85.78, 35.10,

12.44. The spectral data of the compound **3o** was in agreement with the values reported in the literature.[10]

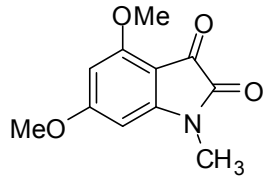
Preparation of 5-Iodo-1-benzyl-1H-indole-2,3-dione (3p):



The reaction was carried out according to **general method A** using 1-(5-bromo-2-(benzylamino)phenyl)ethanone (**1p,** 100 mg, 0.284 mmol), $Cu(OAc)_2.H_2O$ (28.4 mg, 0.142 mmol), NaOAc (35 mg, 0.427 mmol) and DMSO (2 mL). Conditions: 80 °C, 4h. The title compound **3p** (78.5 mg, 76% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 151-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.89 (d, J = 1.6 Hz, 1H), 7.75-7.77 (dd, J = 8.4 Hz, 1H), 7.29-7.37 (m, 5H), 6.56-6.58 (d, J = 8 Hz, 1H), 4.91 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.87, 157.25, 150.00, 146.33, 134.04, 133.86, 129.17, 128.36, 127.40, 119.23, 113.14, 86.21, 44.15. The spectral data of the compound **3p** was in agreement with the values reported in the literature.[10]

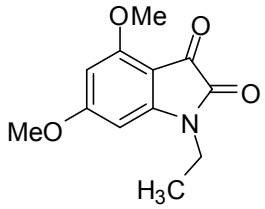
Preparation of 4,6-Dimethoxy-1-methyl-1H-indole-2,3-dione (3q):



The reaction was carried out according to **general method B** using 1-(2-(dimethylamino)-4,6-dimethoxyphenyl)ethanone (**2q,** 100 mg, 0.477 mmol), $Cu(OAc)_2.H_2O$ (47.7 mg, 0.238 mmol), NaOAc (58.8 mg, 0.716 mmol) and DMSO (2 mL). Conditions: 80 °C, 5h. The title compound **3q** (76.1 mg, 72% yield) was obtained as yellow solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 141-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.00-6.02 (dd, J = 8.6 Hz, 2H), 3.93 (s, 3H), 3.95 (s, 3H), 3.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.32, 170.13, 161.15, 160.13, 154.32, 100.63, 92.00, 90.27, 56.34, 56.5, 26.31; MS (ESI): 222.1 (M+1) for $C_{11}H_{11}NO_4$; Anal. calcd. for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33; O, 28.93; Found: C, 59.71; H, 5.04.

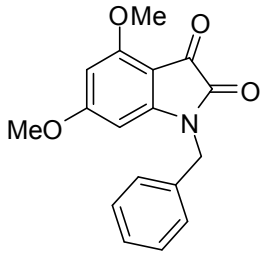
Preparation of 1-Ethyl-4,6-dimethoxy-1H-indole-2,3-dione (3r):



The reaction was carried out according to **general method A** using 1-(2-(ethylamino)-4,6-dimethoxyphenyl)ethanone (**1r**, 100 mg, 0.447 mmol), $Cu(OAc)_2.H_2O$ (44.7 mg, 0.223 mmol), NaOAc (55.1 mg, 0.671 mmol) and DMSO (2 mL). Conditions: 80 °C, 3.2h. The title compound **3r** (83.2 mg, 79% yield) was obtained as yellow solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp:143-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.01 (s, 2H), 3.93 (s, 3H), 3.95 (s, 3H), 3.69-3.74 (q, J = 7.2 Hz, 2H), 1.25-1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.58, 170.11, 161.31, 159.77, 153.30, 100.68, 91.61, 90.48, 56.29, 56.17, 34.98, 12.97; MS (ESI): 236.15 (M+1) for $C_{12}H_{13}NO_4$; Anal. calcd. for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95; O, 27.21; Found: C, 61.24; H, 5.59.

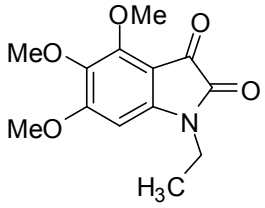
Preparation of 1-Benzyl-4,6-dimethoxy-1H-indole-2,3-dione (3s):



The reaction was carried out according to **general method A** using 1-(2-(benzylamino)-4,6-dimethoxyphenyl)ethanone (**1s**, 100 mg, 0.35 mmol), $Cu(OAc)_2.H_2O$ (35 mg, 0.175 mmol), NaOAc (43.1 mg, 0.525 mmol) and DMSO (2 mL). Conditions: 80 °C, 3h. The title compound **3s** (88.5 mg, 85% yield) was obtained as yellow solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp:181-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.36 (m, 5H), 5.97-5.98 (d, J = 2 Hz, 1H), 5.88-5.89 (d, J = 2 Hz, 1H), 4.86 (s, 2H), 3.94 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.10, 169.96, 161.23, 160.16, 153.33, 135.06, 128.98, 128.01, 127.29, 100.82, 91.86, 91.48, 56.31, 56.05, 44.03; MS (ESI): 298.13 (M+1) for $C_{17}H_{15}NO_4$; Anal. calcd. for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71; O, 21.53; Found: C, 68.66; H, 5.12.

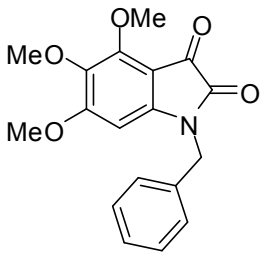
Preparation of 1-Ethyl-4,5,6-trimethoxy-1H-indole-2,3-dione (3t):



The reaction was carried out according to **general method A** using 1-(2-(ethylamino)-2,3,4-trimethoxyphenyl)ethanone (**1t,** 100 mg, 0.394 mmol), $Cu(OAc)_2.H_2O$ (39.4 mg, 0.197 mmol), NaOAc (48.5 mg, 0.592 mmol) and DMSO (2 mL). Conditions: 80 °C, 3h. The title compound **3t** (79.5 mg, 76% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 115-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.11 (s, 1H), 4.21 (s, 3H), 4.00 (s, 3H), 3.77 (s, 3H), 3.72-3.77 (q, J = 7.2 Hz, 2H), 1.28-1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.03, 162.37, 158.93, 154.33, 148.66, 136.28, 102.54, 89.37, 62.22, 61.53, 56.81, 34.76, 12.97; MS (ESI): 266.12 (M+1) for $C_{13}H_{15}NO_5$; Anal. calcd. for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28; O, 30.16; Found: C, 58.83; H, 5.73.

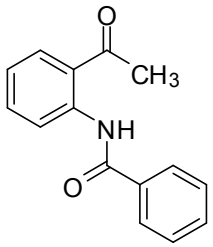
Preparation of 1-Benzyl-4,5,6-trimethoxy-1H-indole-2,3-dione (3u):



The reaction was carried out according to **general method A** using 1-(2-(benzylamino)-2,3,4-trimethoxyphenyl)ethanone (**1u**, 100 mg, 0.317 mmol), $Cu(OAc)_2.H_2O$ (31.6 mg, 0.158 mmol), NaOAc (39 mg, 0.475 mmol) and DMSO (2 mL). Conditions: 80 °C, 3h. The title compound **3u** (92.3 mg, 89% yield) was obtained as red solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9:1).

mp: 151-152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.38 (m, 5H), 5.99 (s, 1H), 4.89 (s, 2H), 4.20 (s, 3H), 3.81 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.56, 162.24, 159.37, 154.20, 148.68, 136.39, 134.95, 129.08, 128.16, 127.29, 102.62, 90.54, 62.25, 61.48, 56.60, 43.95; MS (ESI): 328.12 (M+1) for $C_{18}H_{17}NO_5$; Anal. calcd. for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28; O, 24.44; Found: C, 66.02; H, 5.25.

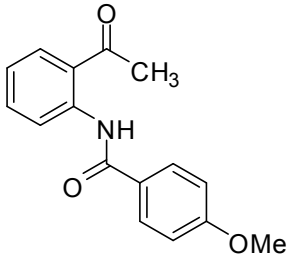
Preparation of N-(2-Acetyl-phenyl)-benzamide (4a):



The reaction was carried out according to **general method C** using 1-(2-(benzylamino)phenyl)ethanone (**1a**, 100 mg, 0.443 mmol), CuBr (12.7 mg, 0.088 mmol), and CH_3CN (2 mL). Conditions: 80 °C, 16h. The title compound **4a** (55 mg, 52% yield) was obtained as yellow solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9.5:0.5).

mp: 100-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.70 (s, 1H), 8.97-9.00 (d, J = 8.8 Hz, 1H), 8.06-8.08 (dd, J = 7.9 Hz, 2H), 7.95-7.97 (dd, J = 8 Hz, 1H), 7.60-7.64 (m, 1H), 7.50-7.56 (m, 3H), 7.14-7.18 (t, J = 7.6 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.27, 166.16, 141.46, 135.42, 134.86, 132.00, 131.83, 128.82, 127.51, 122.51, 122.03, 120.88, 28.60. The spectral data of the compound **4a** was in agreement with the values reported in the literature.[11]

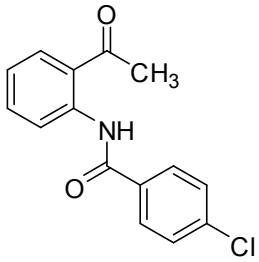
Preparation of N-(2-Acetyl-phenyl)-4-methoxy-benzamide (4b):



The reaction was carried out according to **general method C** using 1-(2-(4-methoxybenzylamino)phenyl)ethanone (**1b**, 100 mg, 0.391 mmol), CuBr (11.2 mg, 0.078 mmol), and CH_3CN (2 mL). Conditions: 80 °C, 13h. The title compound **4b** (61.1 mg, 58% yield) was obtained as light pink solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9.5:0.5).

mp: 119-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.62 (s, 1H), 8.95-8.97 (dd, J = 8.6 Hz, 1H), 8.02-8.05 (dd, J = 6.8 Hz, 2H), 7.92-7.94 (dd, J = Hz, 1H), 7.57-7.61 (m, J = Hz, 1H), 7.10-7.14 (m, J = Hz, 1H), 6.98-7.01 (m, J = 8 Hz 2H), 3.87(s, 3H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.26, 165.69, 162.65, 141.73, 135.37, 132.82, 131.83, 129.43, 127.16, 122.19, 121.84, 120.74, 114.02, 55.45, 28.60. The spectral data of the compound **4b** was in agreement with the values reported in the literature.[12]

Preparation of N-(2-Acetyl-phenyl)-4-chloro-benzamide (4c):

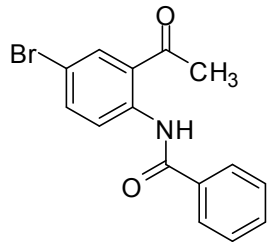


The reaction was carried out according to **general method C** using 1-(2-(4-chlorobenzylamino)phenyl)ethanone (**1c**, 100 mg, 0.385 mmol), CuBr (11 mg, 0.077 mmol), and CH_3CN (2 mL). Conditions: 80 °C, 15h. The title compound **4c** (54.7 mg, 52% yield) was obtained as white solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9.5:0.5).

mp: 114-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.72 (s, 1H), 8.93-8.96 (dd, J = 8.6 Hz, 1H), 7.99-8.03 (m, 2H), 7.95-7.98 (dd, J = 7.8 Hz, 1H), 7.61-7.65 (m, 1H), 7.47-7.51 (m, 2H), 7.16-7.20 (m, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.44, 165.02, 141.29, 138.35, 135.50, 133.25, 131.88, 129.09, 128.94, 122.72, 121.99, 120.84, 28.60.

The spectral data of the compound **4c** was in agreement with the values reported in the literature.[12]

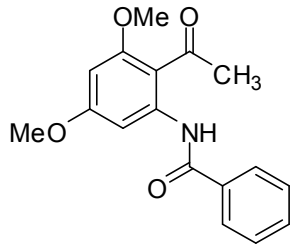
Preparation of N-(2-Acetyl-4-bromo-phenyl)-benzamide (4n):



The reaction was carried out according to **general method C** using 1-(2-(benzylamino)-5-bromophenyl)ethanone (**1n,** 100 mg, 0.328 mmol), CuBr (9.4 mg, 0.065 mmol), and CH_3CN (2 mL). Conditions: 80 °C, 15h. The title compound **4n** (46 mg, 44% yield) was obtained as light yellow solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9.5:0.5).

mp: 105-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.58 (s, 1H), 8.91-8.94 (d, J = 9.2 Hz, 1H), 8.03-8.06 (m, 3H), 7.69-7.72 (m, 1H), 7.50-7.57 (m, 3H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.10, 166.08, 140.44, 137.99, 134.52, 134.24, 132.20, 128.87, 127.50, 123.49, 122.69, 114.76, 28.58. The spectral data of the compound **4n** was in agreement with the values reported in the literature.[13]

Preparation of N-(2-Acetyl-3,5-dimethoxy-phenyl)-benzamide (4s):

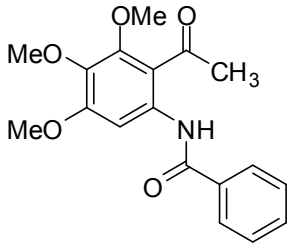


The reaction was carried out according to **general method C** using 1-(2-(benzylamino)-4,6-dimethoxyphenyl)ethanone (**1s,** 100 mg, 0.35 mmol), CuBr (10 mg, 0.07 mmol), and CH_3CN (2 mL). Conditions: 80 °C, 17h. The title compound **4s** (56.6 mg, 54% yield) was obtained as white solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9.5:0.5).

mp: 116-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.87 (s, 1H), 8.26 (d, J = 2.4 Hz, 1H), 8.03-8.06 (m, 2H), 7.50-7.55 (m, 3H), 6.24-6.25 (d, J = 2.4 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.95, 166.31, 164.83, 162.73, 143.97, 134.94, 131.95, 128.80, 127.47, 108.65, 96.82, 94.43, 55.68, 55.58, 34.19.

The spectral data of the compound **4s** was in agreement with the values reported in the literature.[14]

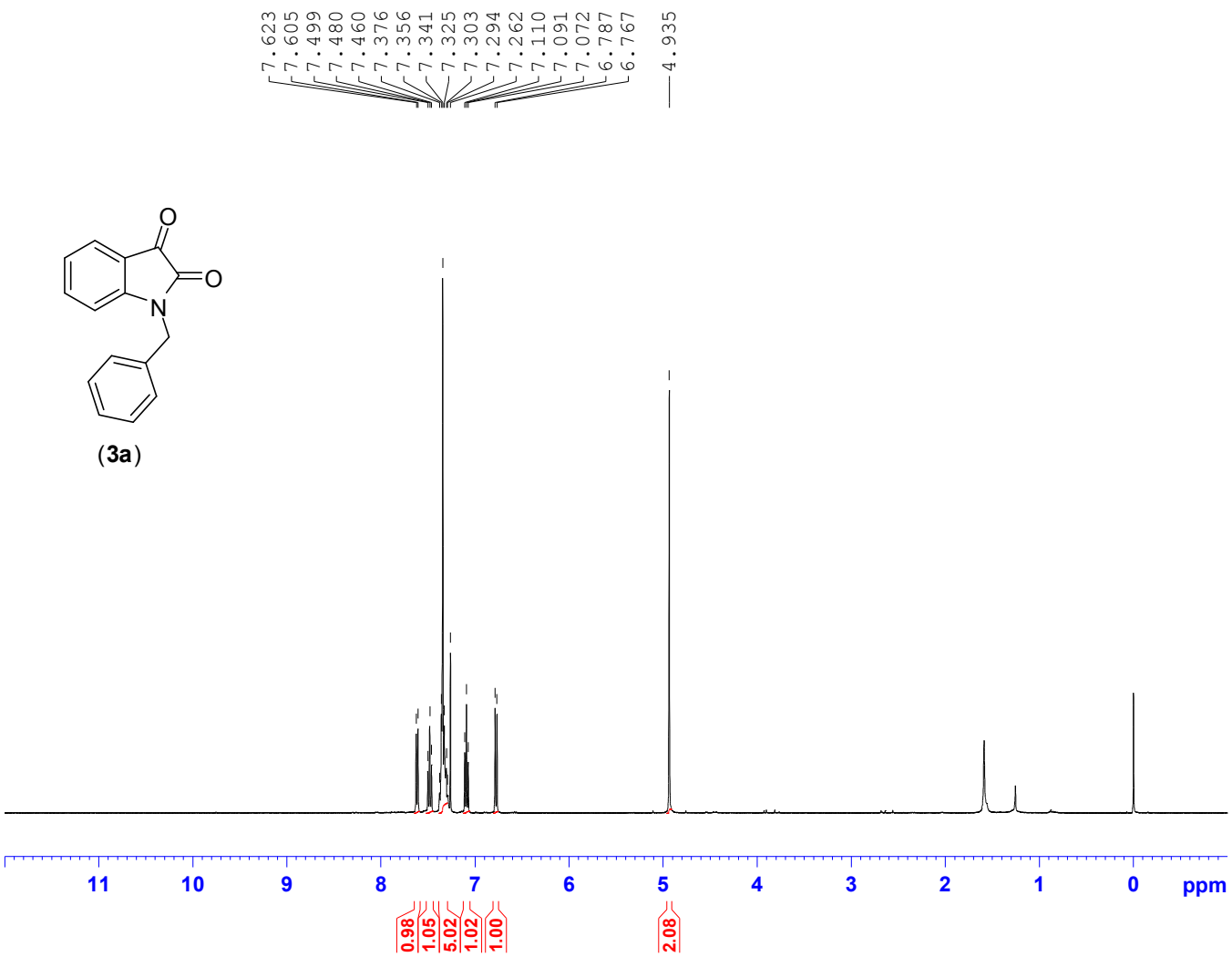
Preparation of N-(2-Acetyl-3,4,5-trimethoxy-phenyl)-benzamide (4u):



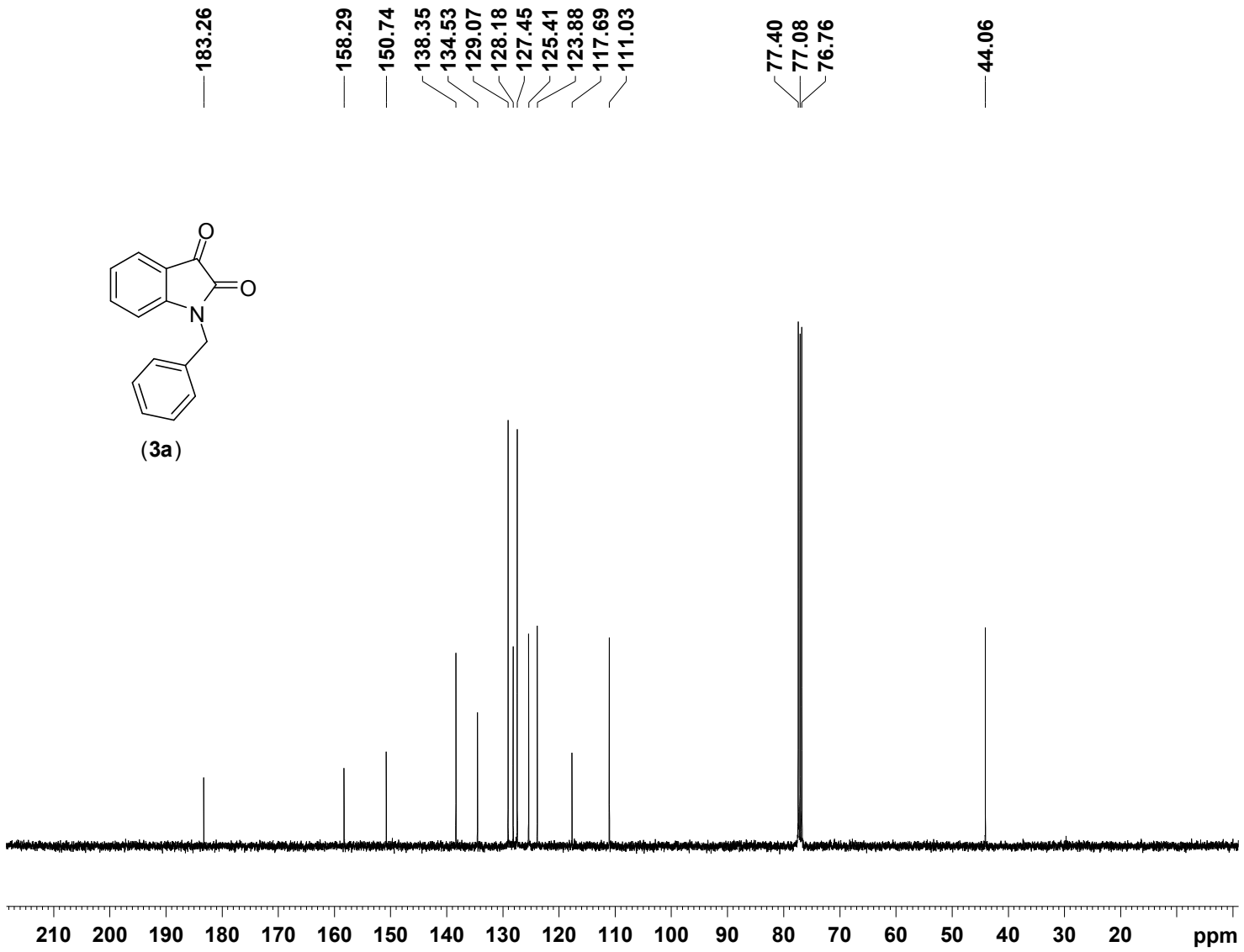
The reaction was carried out according to **general method C** using 1-(6-(benzylamino)-2,3,4-trimethoxyphenyl)ethanone (**1u,** 100 mg, 0.317 mmol), CuBr (9mg, 0.063 mmol), and CH_3CN (2 mL). Conditions: 80 °C, 17h. The title compound **4u** (57.4 mg, 55% yield) was obtained as yellow solid after passing through a short silica gel column chromatography (hexane/ethyl acetate, 9.5:0.5).

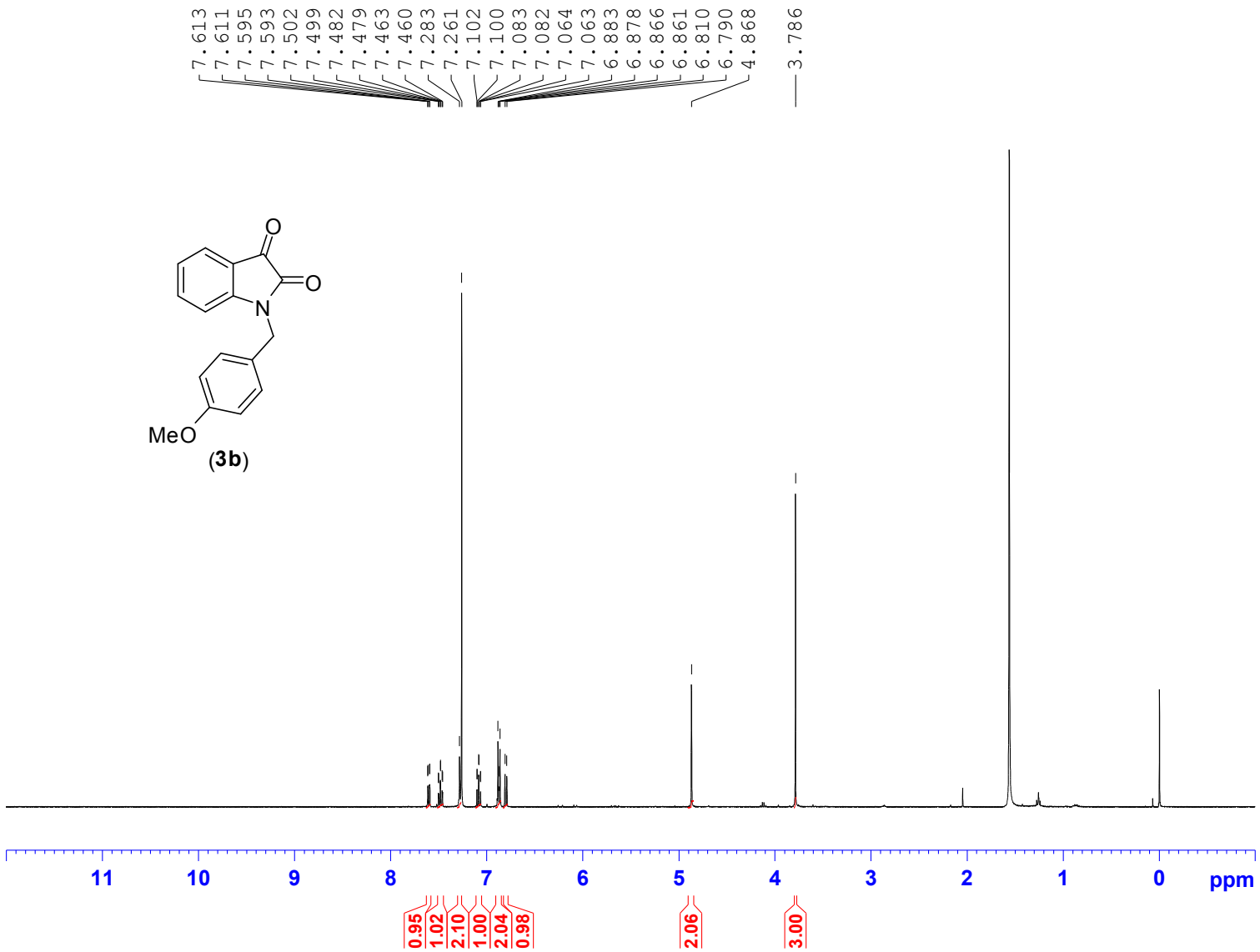
mp: 86-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.35 (s, 1H), 8.42 (s, 1H), 8.00-8.03 (m, 2H), 7.49-7.57 (m, 3H), 4.00 (s, 3H), 3.99(s, 3H), 3.85 (s, 3H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.10, 166.12, 157.97, 155.53, 137.73, 137.64, 134.79, 132.00, 128.84, 127.35, 112.96, 100.06, 61.54, 60.99, 56.20, 33.39.

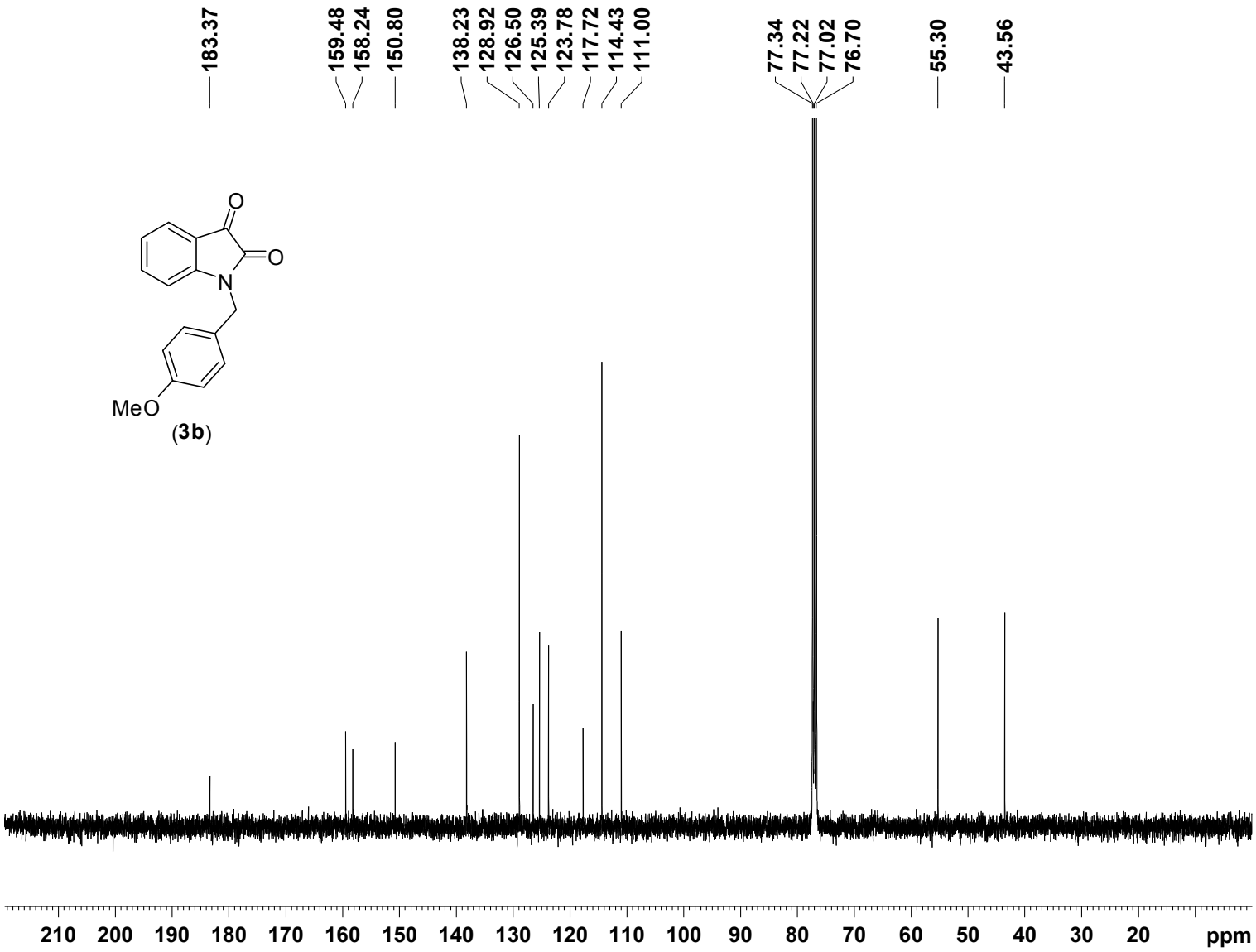
The spectral data of the compound **4u** was in agreement with the values reported in the literature.[14]

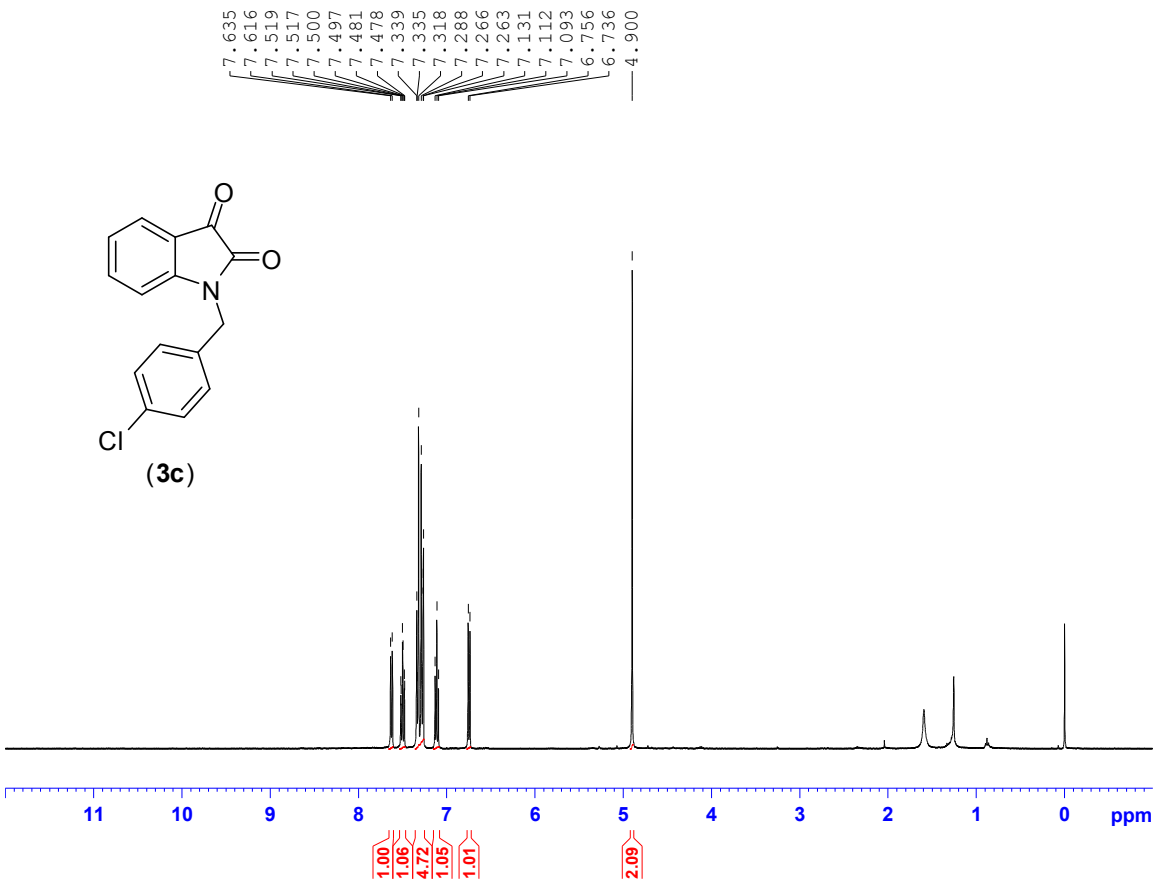

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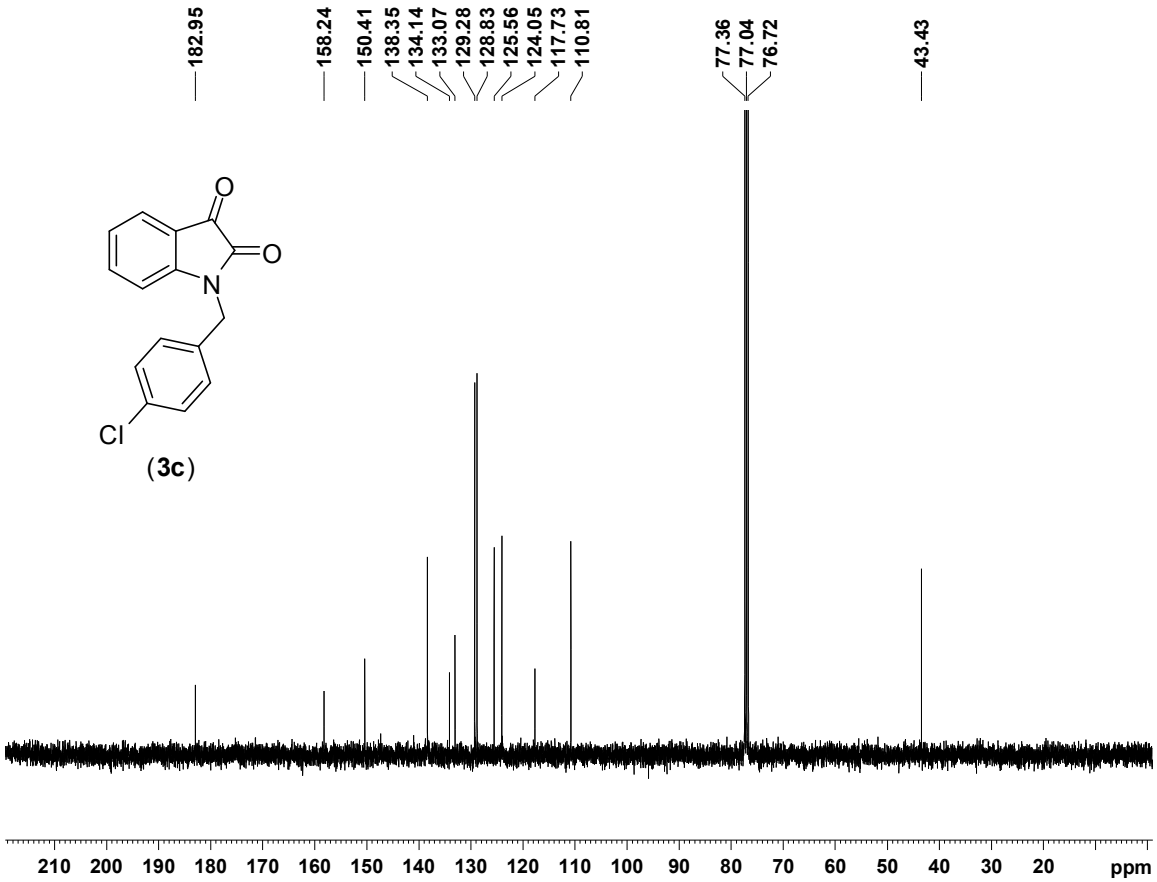
(**3a**)

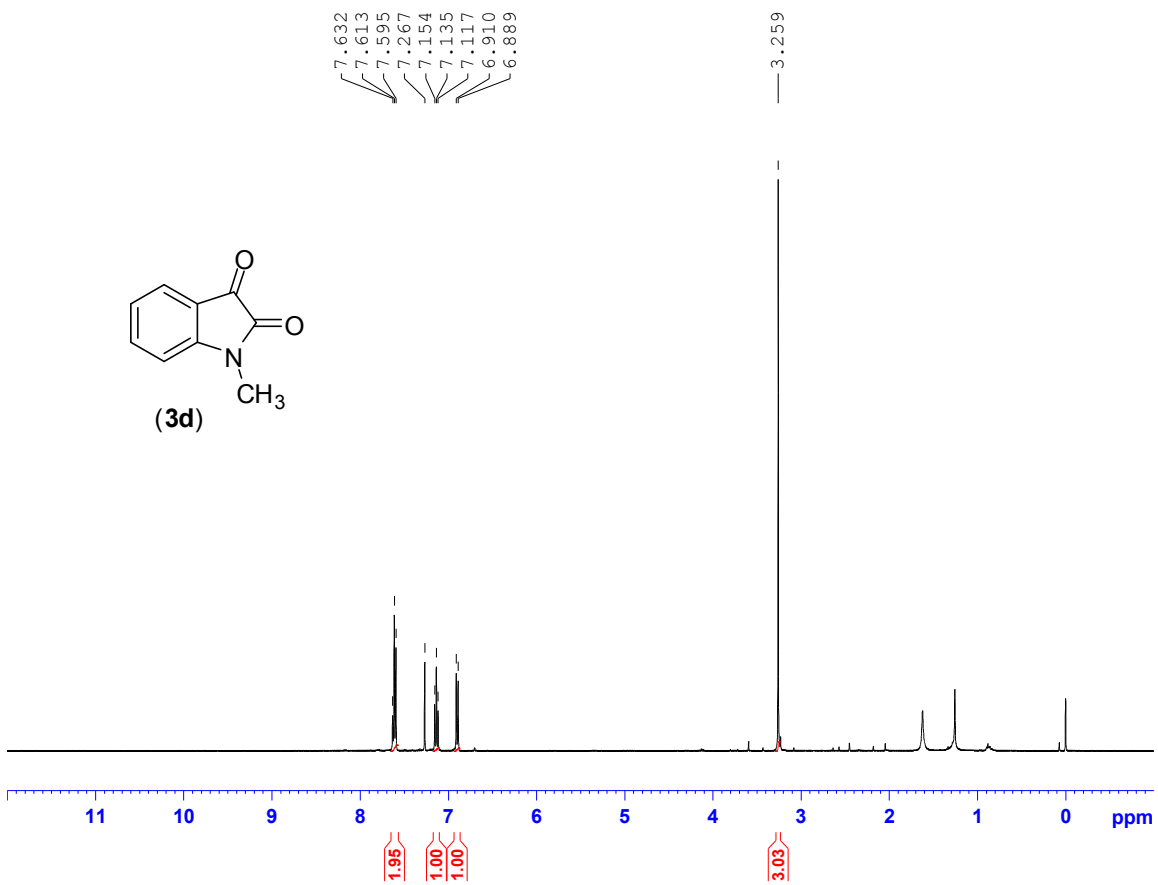

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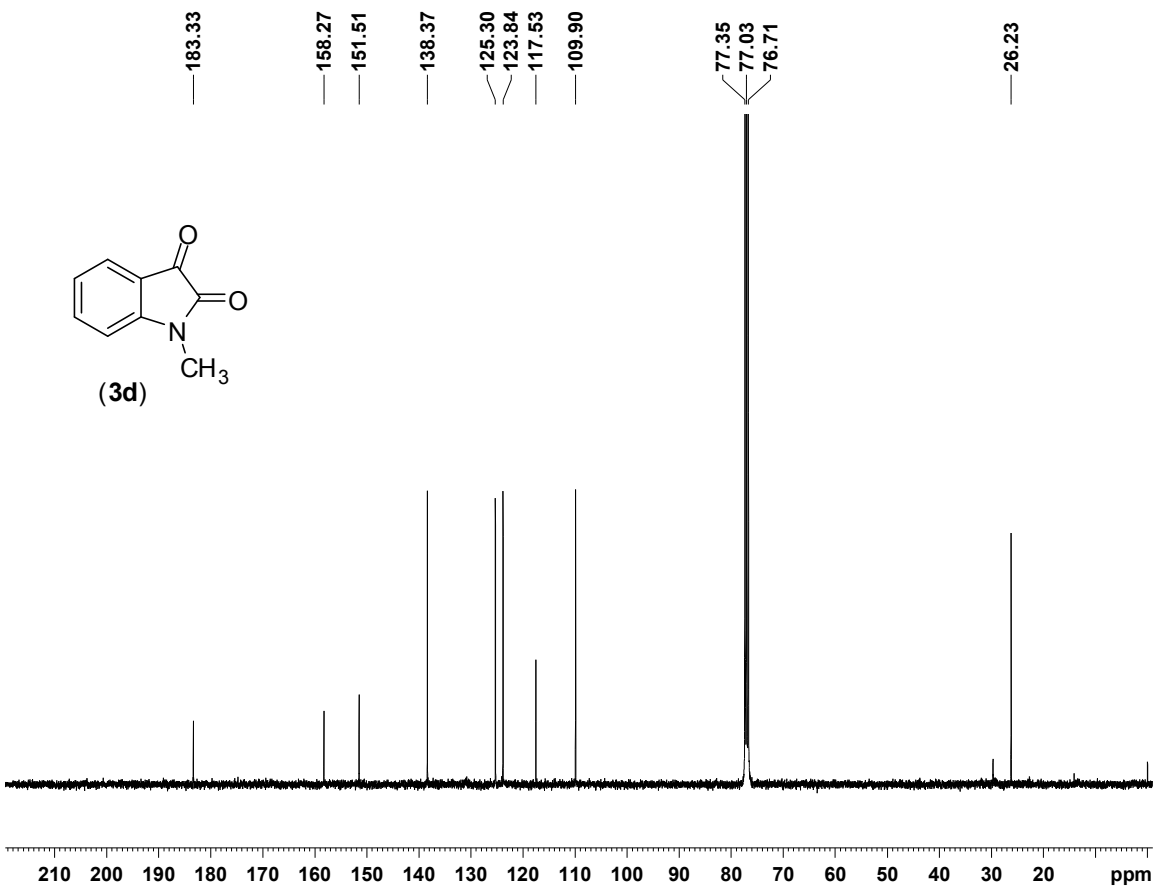

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111.00
77.34
77.22
77.02
76.70
55.30
43.56
O
O
N
MeO
(3b)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

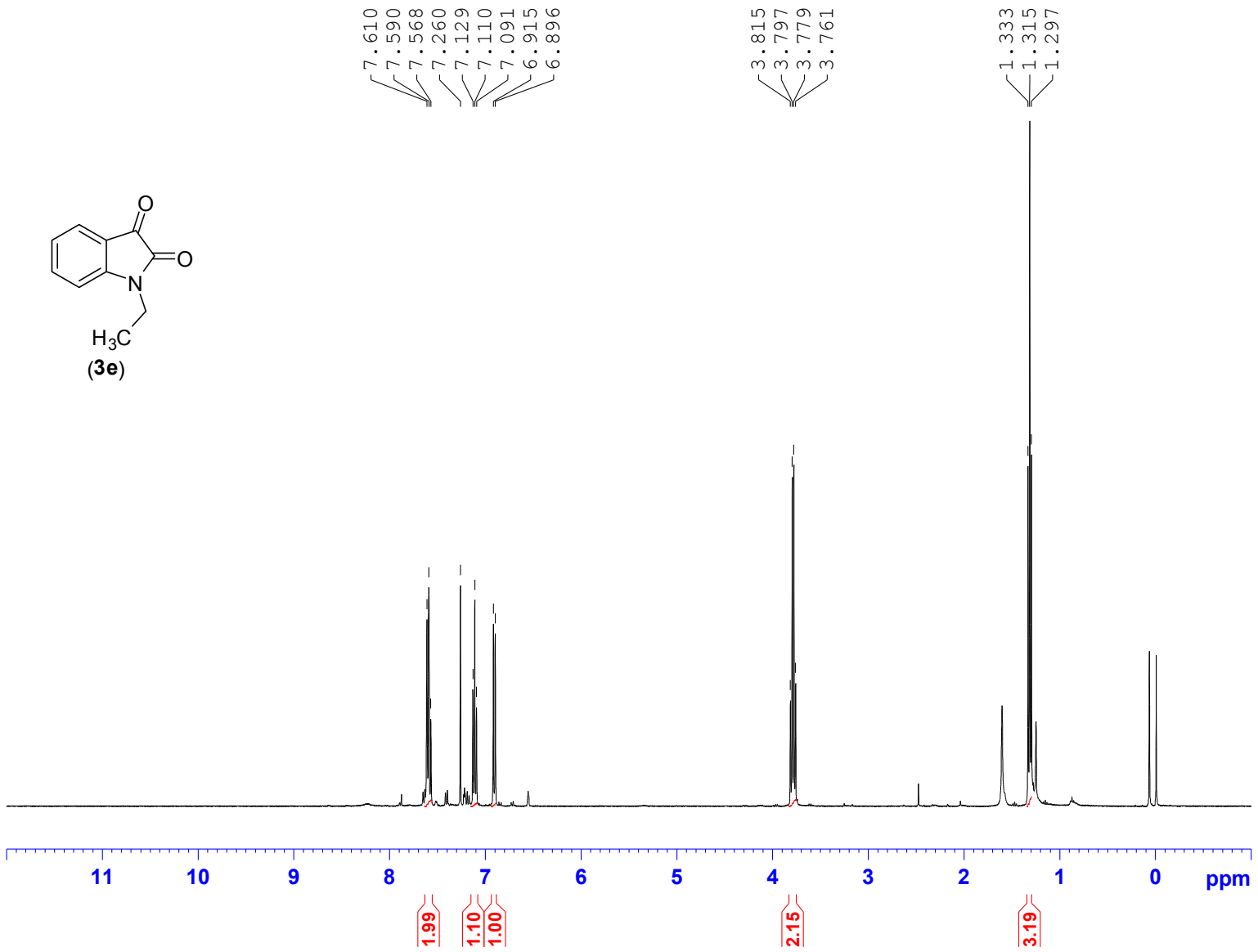

7.635
7.616
7.519
7.517
7.500
7.497
7.481
7.478
7.339
7.335
7.318
7.288
7.266
7.263
7.131
7.112
7.093
6.756
6.736
4.900
O
O
N
Cl
(3c)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.06
4.72
1.05
1.01
2.09

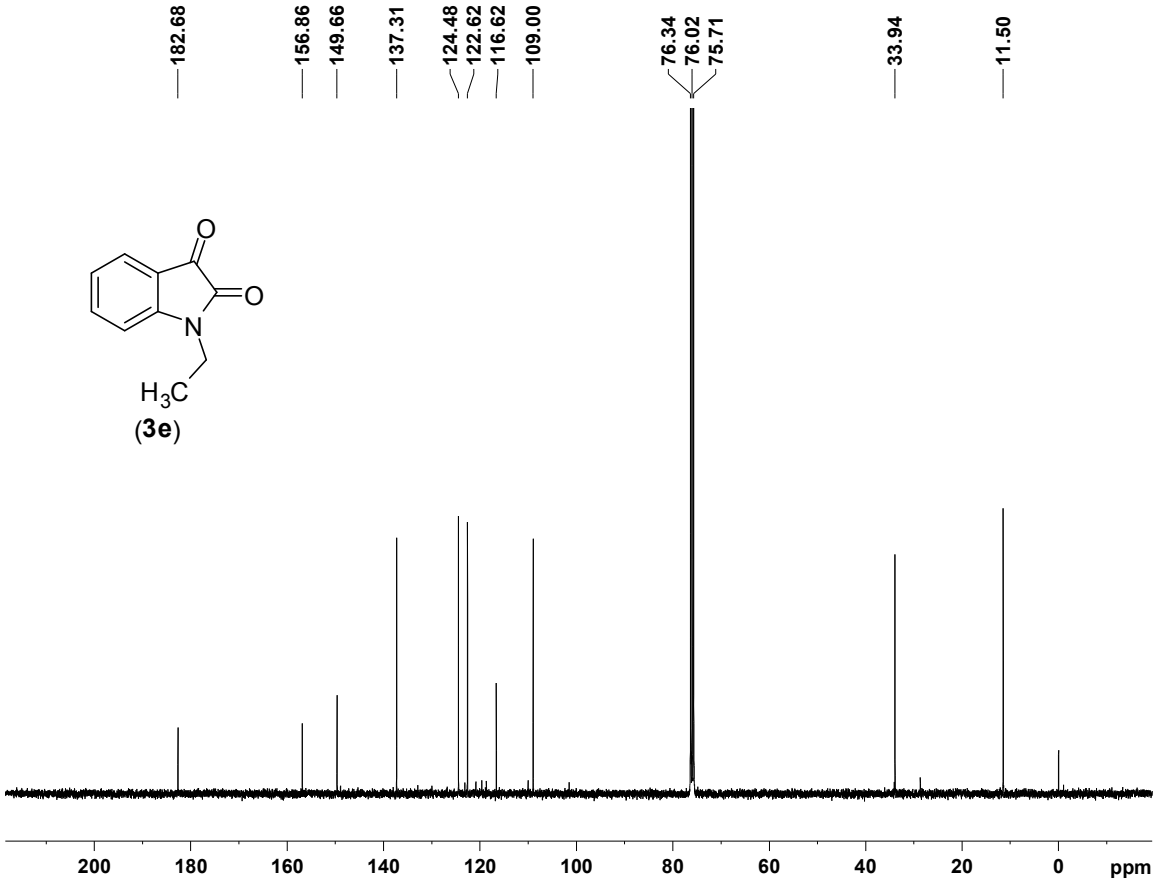

182.95
158.24
150.41
138.35
134.14
133.07
129.28
128.83
125.56
124.05
117.73
110.81
77.36
77.04
76.72
43.43
O
O
N
Cl
(3c)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.632
7.613
7.595
7.267
7.154
7.135
7.117
6.910
6.889
3.259
O
O
N
CH3
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.95
1.00
1.00
3.03

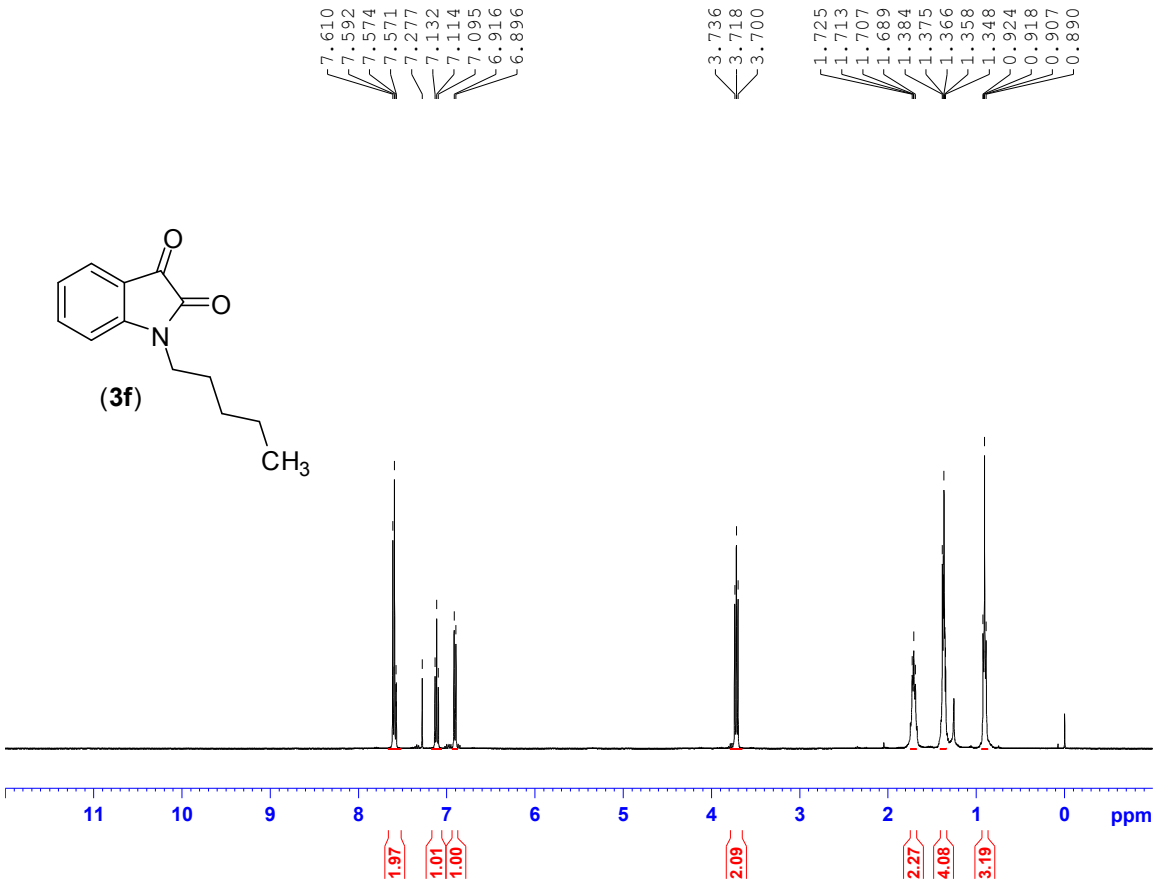
(**3d**)

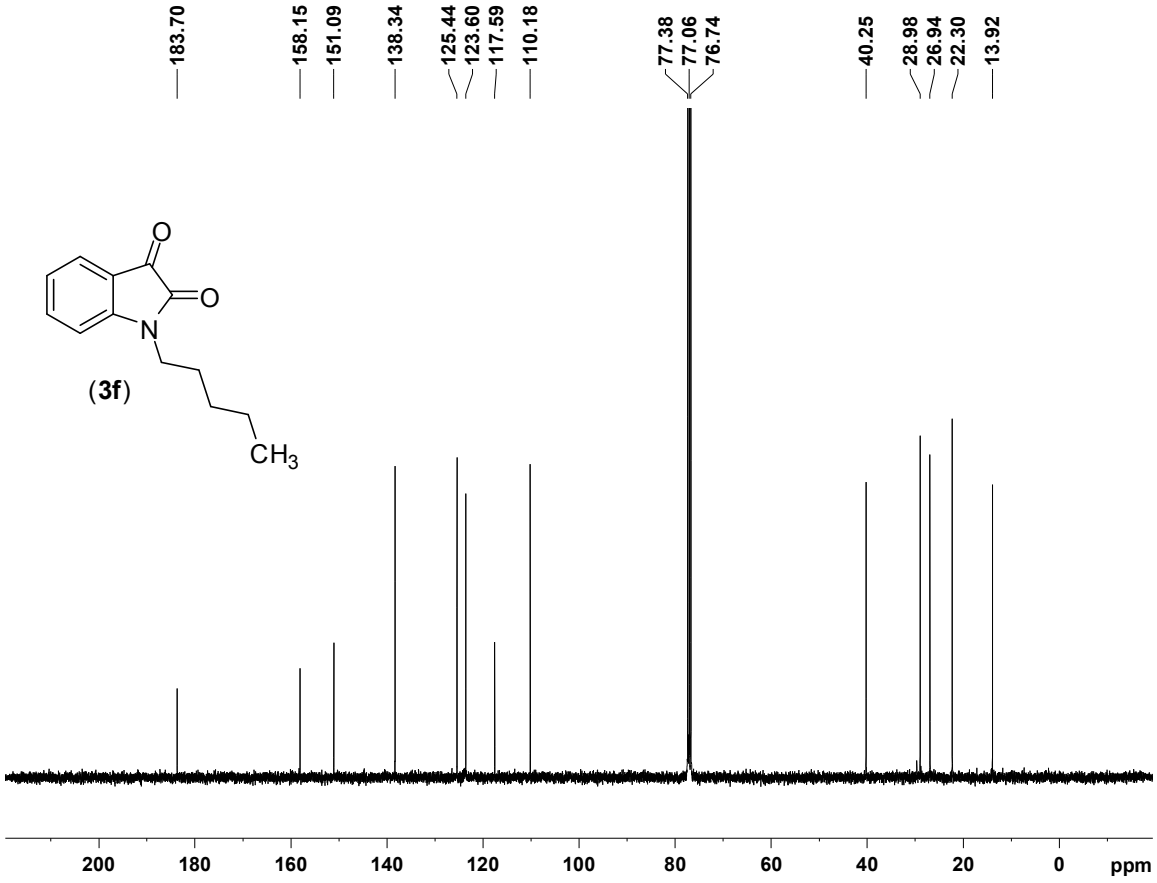

183.33
158.27
151.51
138.37
125.30
123.84
117.53
109.90
77.35
77.03
76.71
26.23
O
O
N
CH3
(3d)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

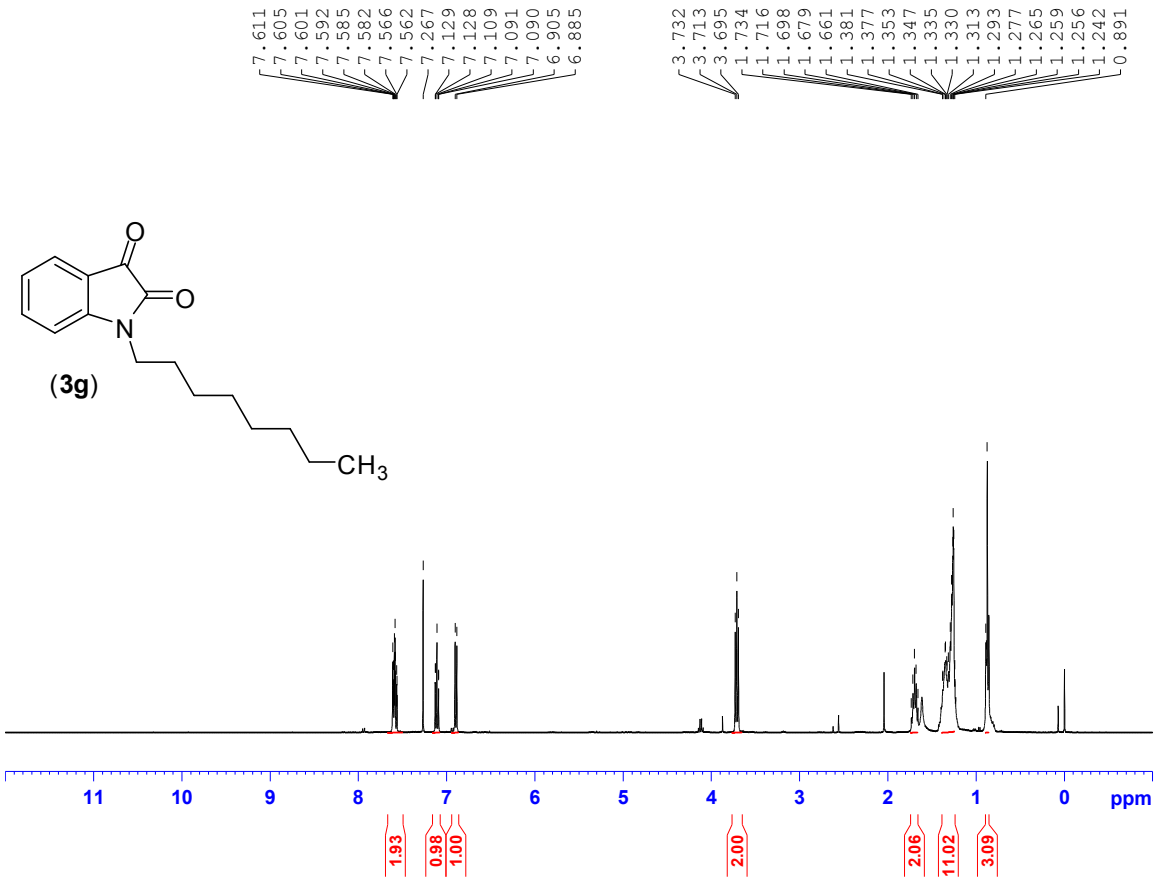

7.610
7.590
7.568
7.260
7.129
7.110
7.091
6.915
6.896
3.815
3.797
3.779
3.761
1.333
1.315
1.297
O
O
N
H3C
(3e)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.99
1.10
1.00
2.15
3.19

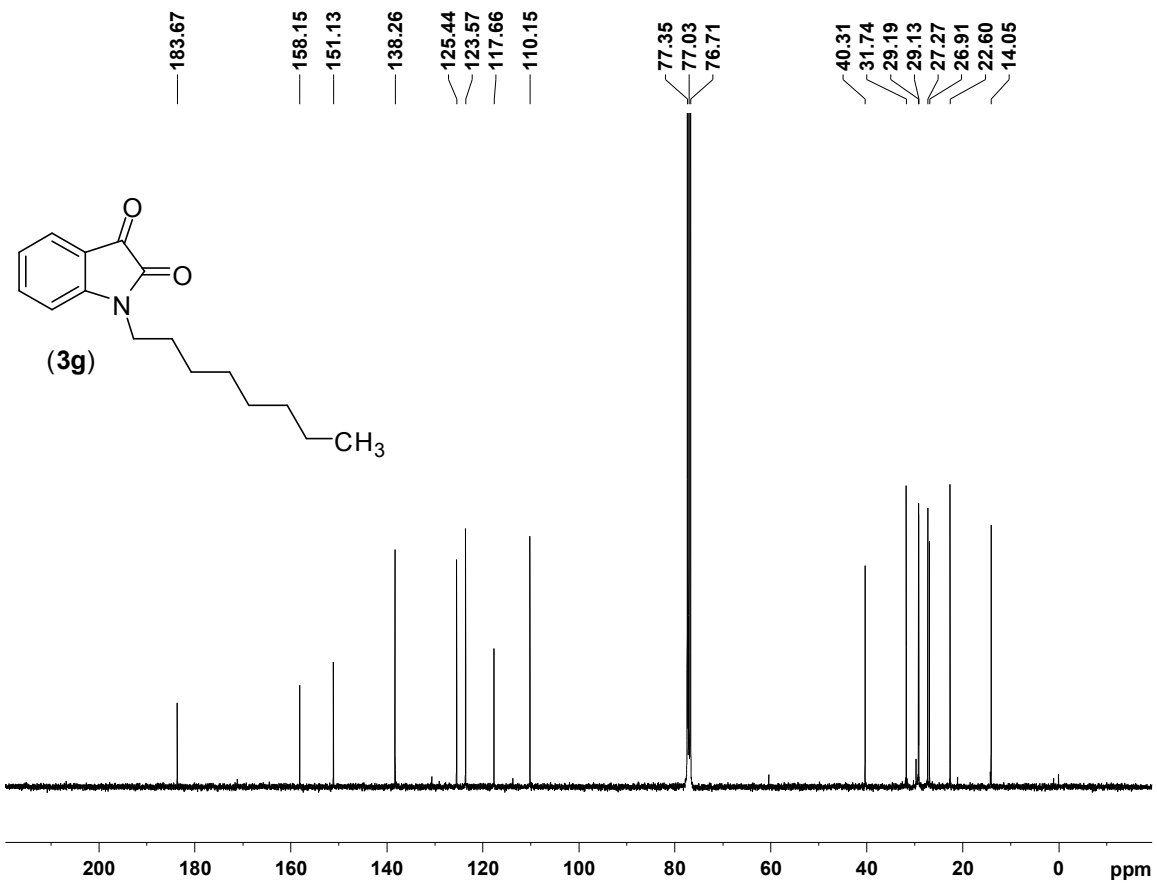

182.68
156.86
149.66
137.31
124.48
122.62
116.62
109.00
76.34
76.02
75.71
33.94
11.50
O
O
N
H3C
200
180
160
140
120
100
80
60
40
20
0
ppm

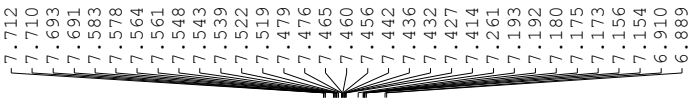
(**3e**)

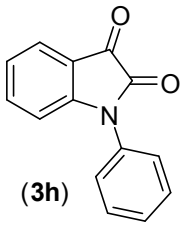

7.610
7.592
7.574
7.571
7.277
7.132
7.114
7.095
6.916
6.896
3.736
3.718
3.700
1.725
1.713
1.707
1.689
1.384
1.375
1.366
1.358
1.348
0.924
0.918
0.907
0.890
O
O
N
CH3
(3f)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.97
1.01
1.00
2.09
2.27
4.08
3.19


183.70
158.15
151.09
138.34
125.44
123.60
117.59
110.18
77.38
77.06
76.74
40.25
28.98
26.94
22.30
13.92
O
O
N
CH3
(3f)
200
180
160
140
120
100
80
60
40
20
0
ppm

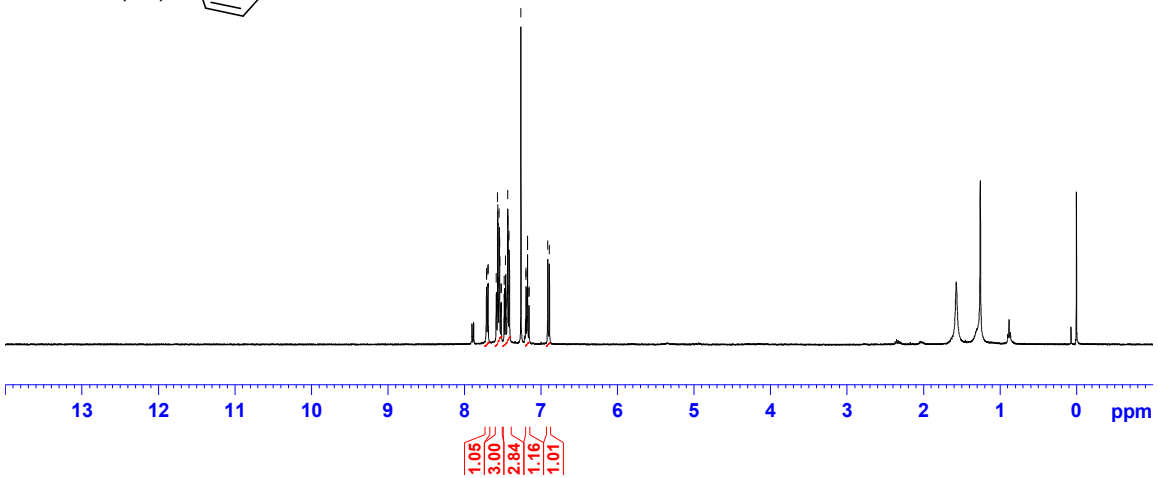

7.611
7.605
7.601
7.592
7.585
7.582
7.566
7.562
7.267
7.129
7.128
7.109
7.091
7.090
6.905
6.885
3.732
3.713
3.695
1.734
1.716
1.698
1.679
1.661
1.381
1.377
1.353
1.347
1.335
1.330
1.313
1.293
1.277
1.265
1.259
1.256
1.242
0.891
O
O
N
(3g)
CH3
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.93
0.98
1.00
2.00
2.06
11.02
3.09

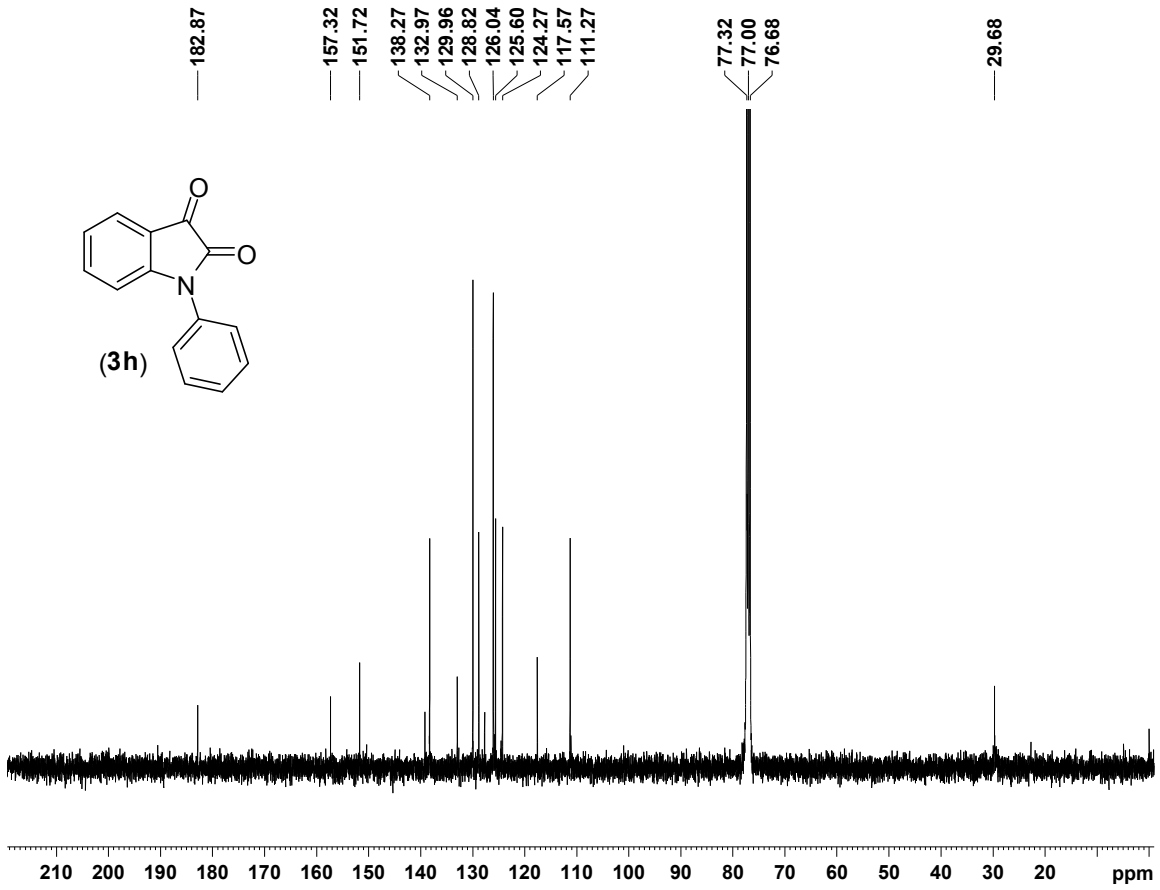

183.67
158.15
151.13
138.26
125.44
123.57
117.66
110.15
77.35
77.03
76.71
40.31
31.74
29.19
29.13
27.27
26.91
22.60
14.05
O
O
N
CH3
(3g)
200
180
160
140
120
100
80
60
40
20
0
ppm

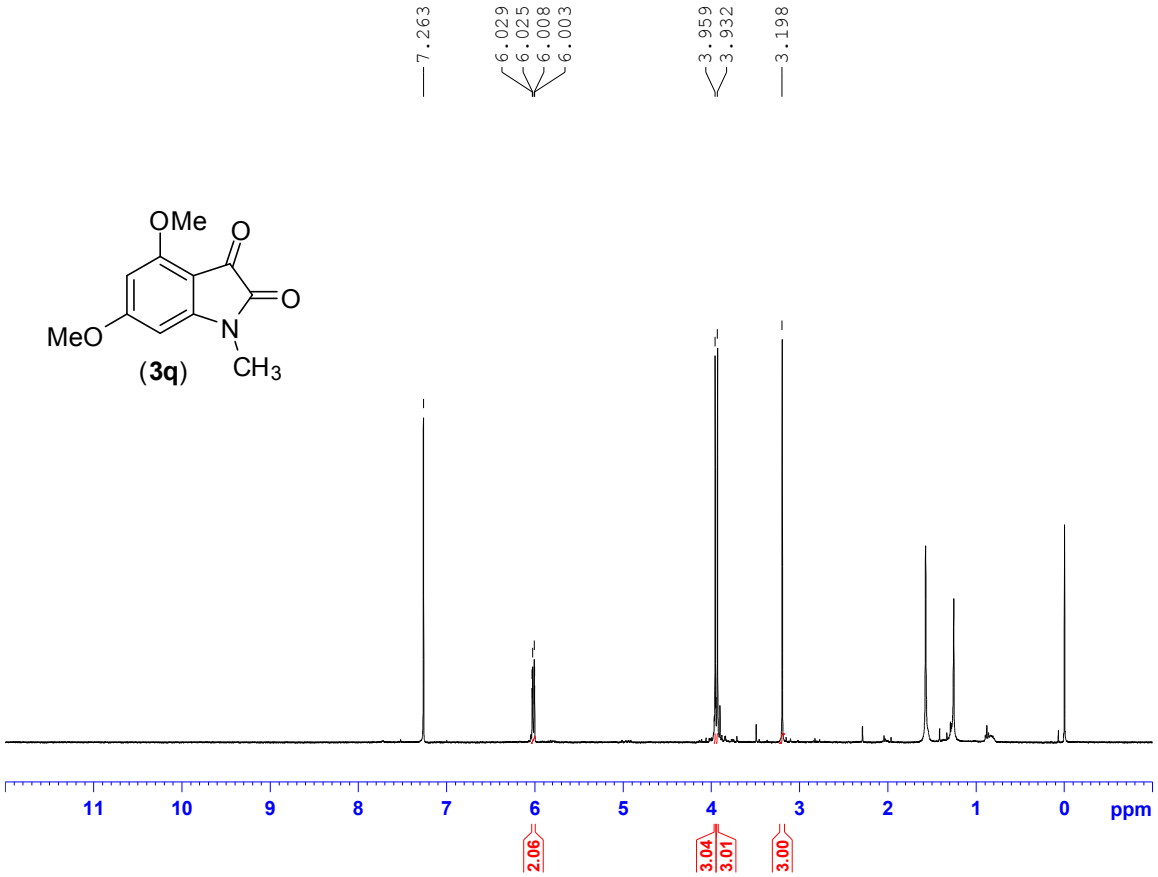

7.712
7.710
7.693
7.691
7.583
7.578
7.564
7.561
7.548
7.543
7.539
7.522
7.519
7.479
7.476
7.465
7.460
7.456
7.442
7.436
7.432
7.427
7.414
7.261
7.193
7.192
7.180
7.175
7.173
7.156
7.154
6.910
6.889

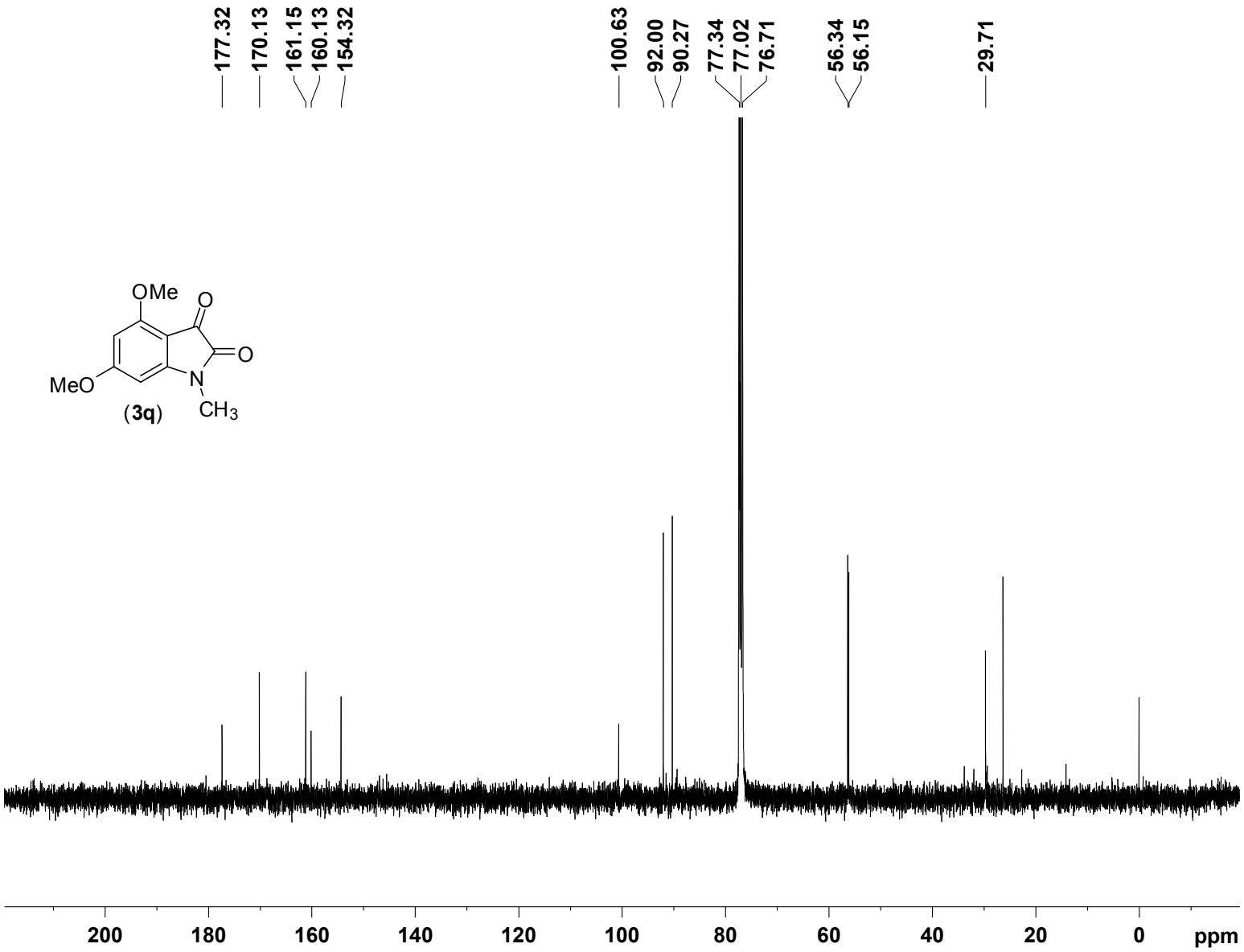

O
O
N

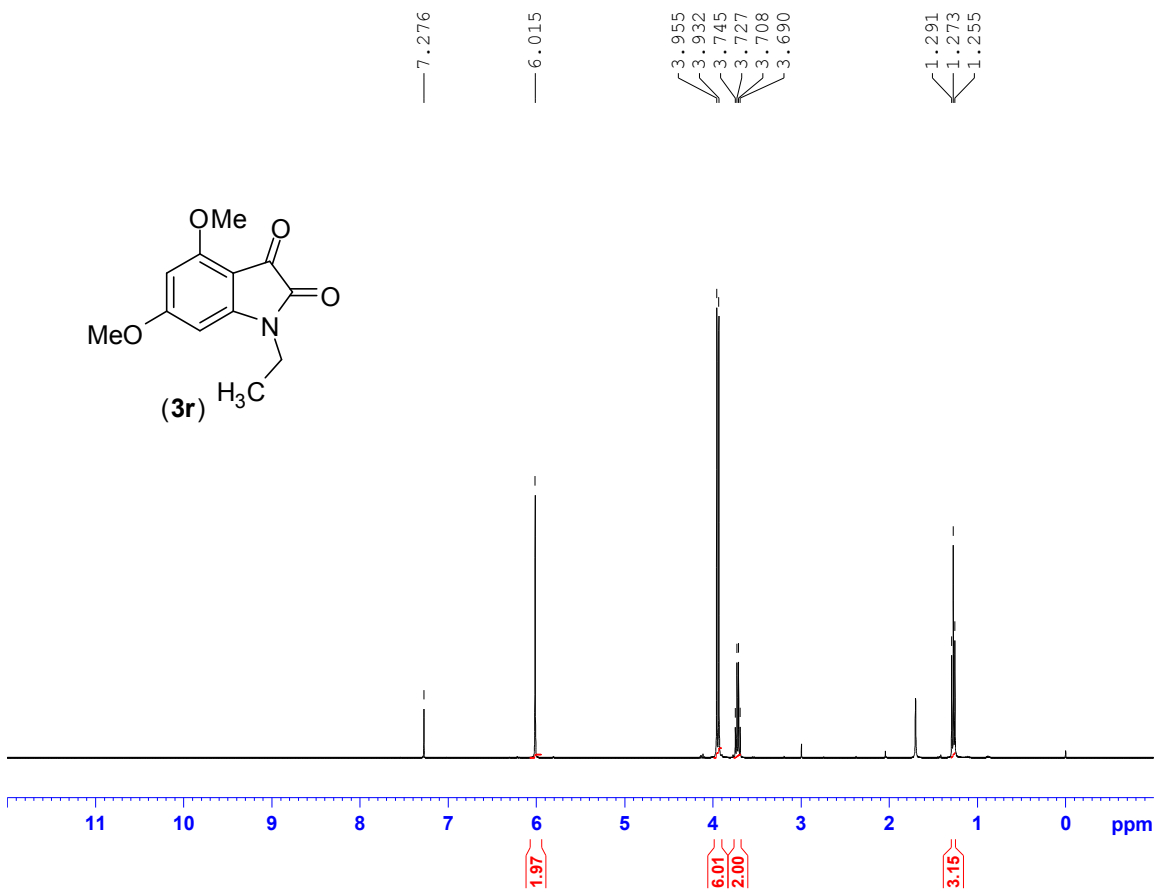
(**3h**)

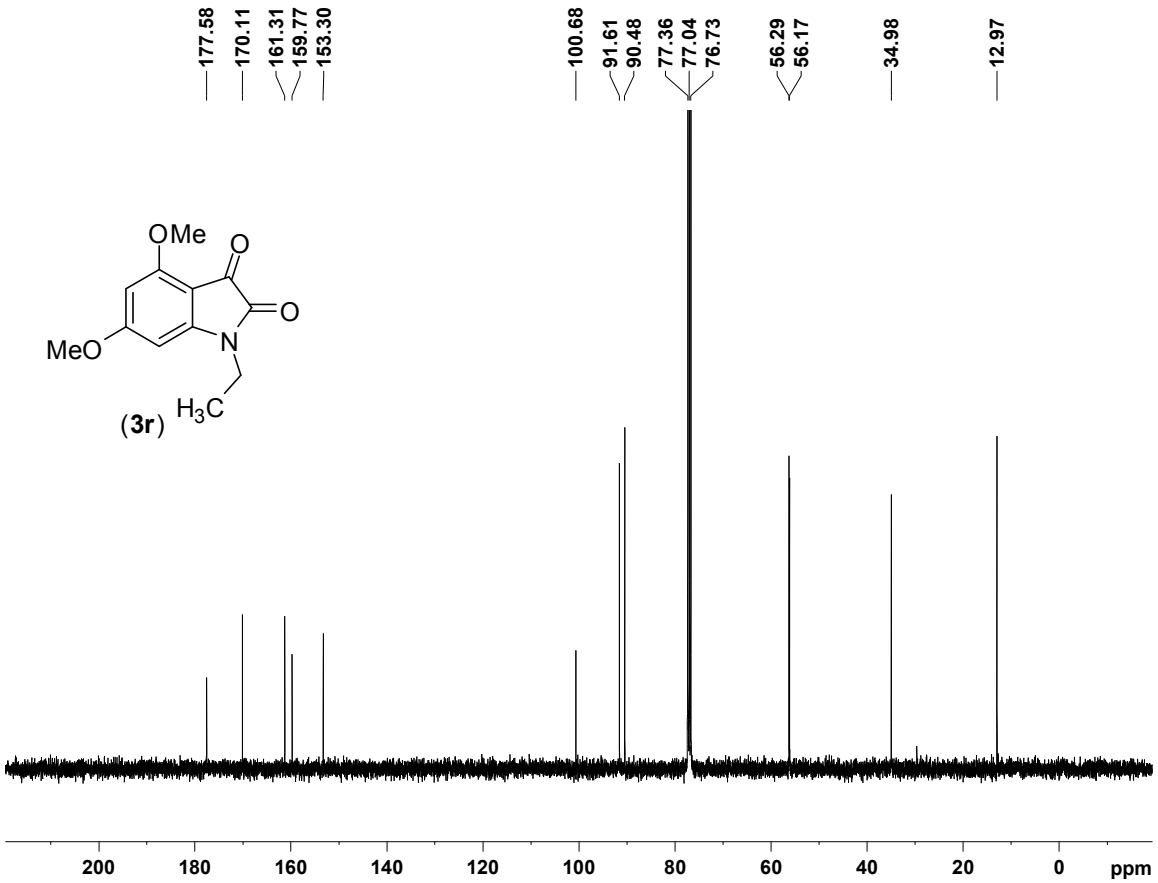

13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.05
3.00
2.84
1.16
1.01

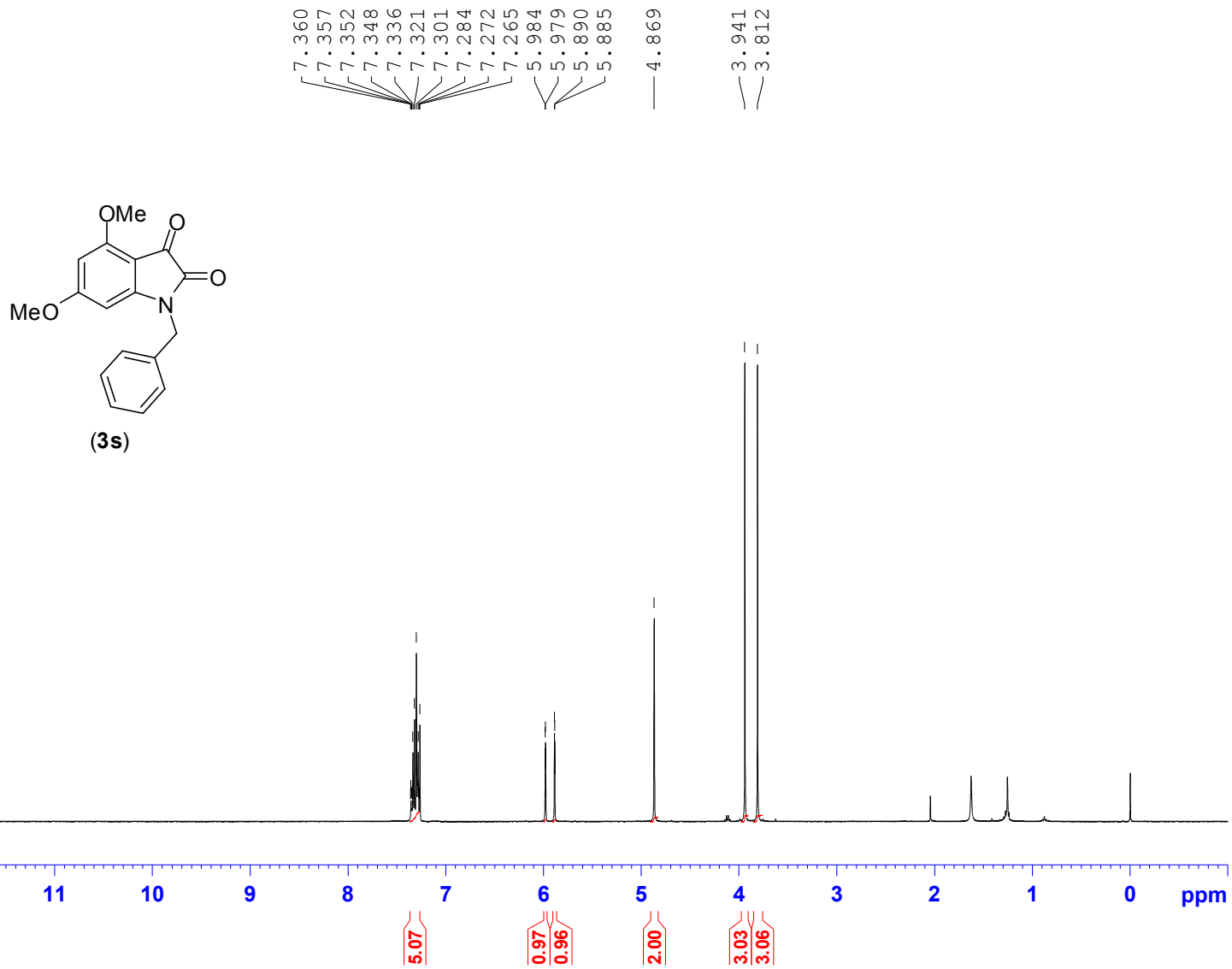

182.87
157.32
151.72
138.27
132.97
129.96
128.82
126.04
125.60
124.27
117.57
111.27
77.32
77.00
76.68
29.68
O
O
N
(3h)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.263
6.029
6.025
6.008
6.003
3.959
3.932
3.198
OMe
O
O
MeO
N
CH3
(3q)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
2.06
3.04
3.01
3.00

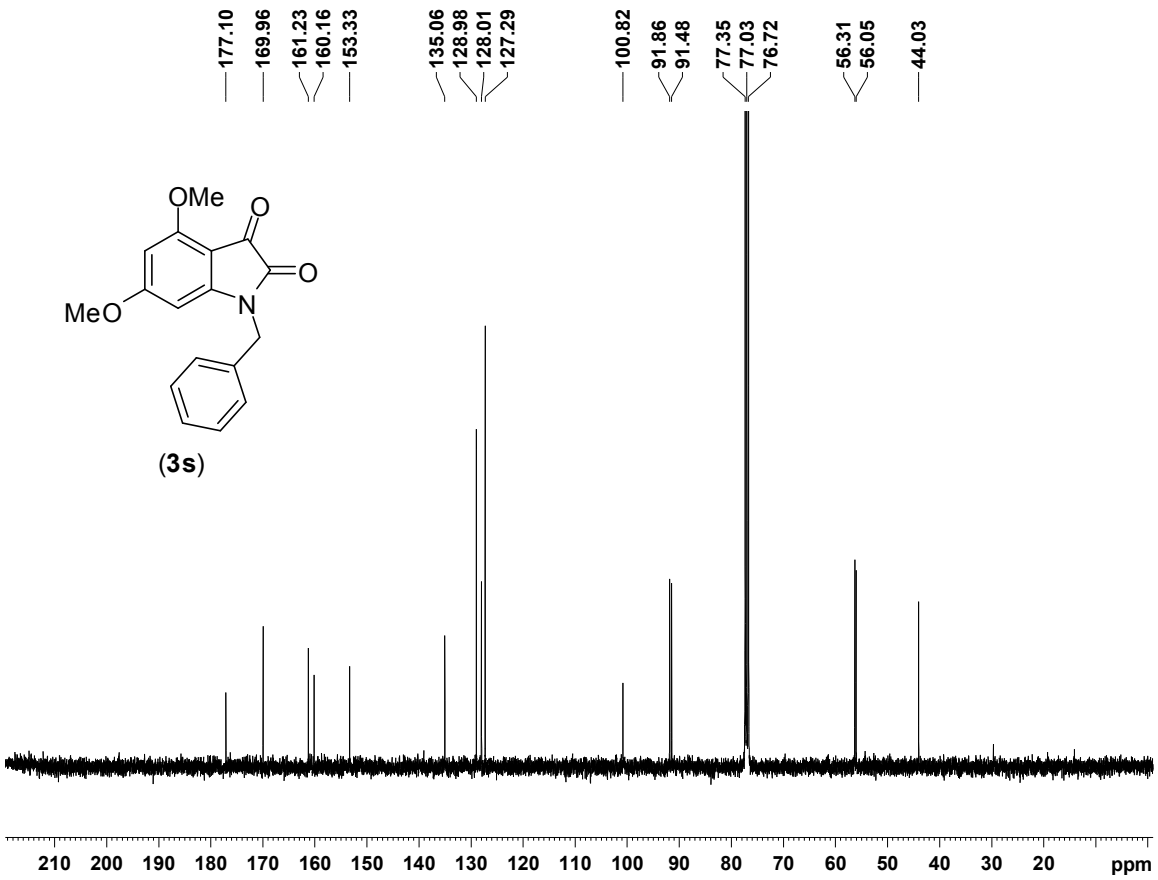

177.32
170.13
161.15
160.13
154.32
100.63
92.00
90.27
77.34
77.02
76.71
56.34
56.15
29.71
OMe
O
O
MeO
N
CH3
(3q)
200
180
160
140
120
100
80
60
40
20
0
ppm


7.276
6.015
3.955
3.932
3.745
3.727
3.708
3.690
1.291
1.273
1.255
OMe
O
O
MeO
N
H3C
(3r)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.97
6.01
2.00
3.15

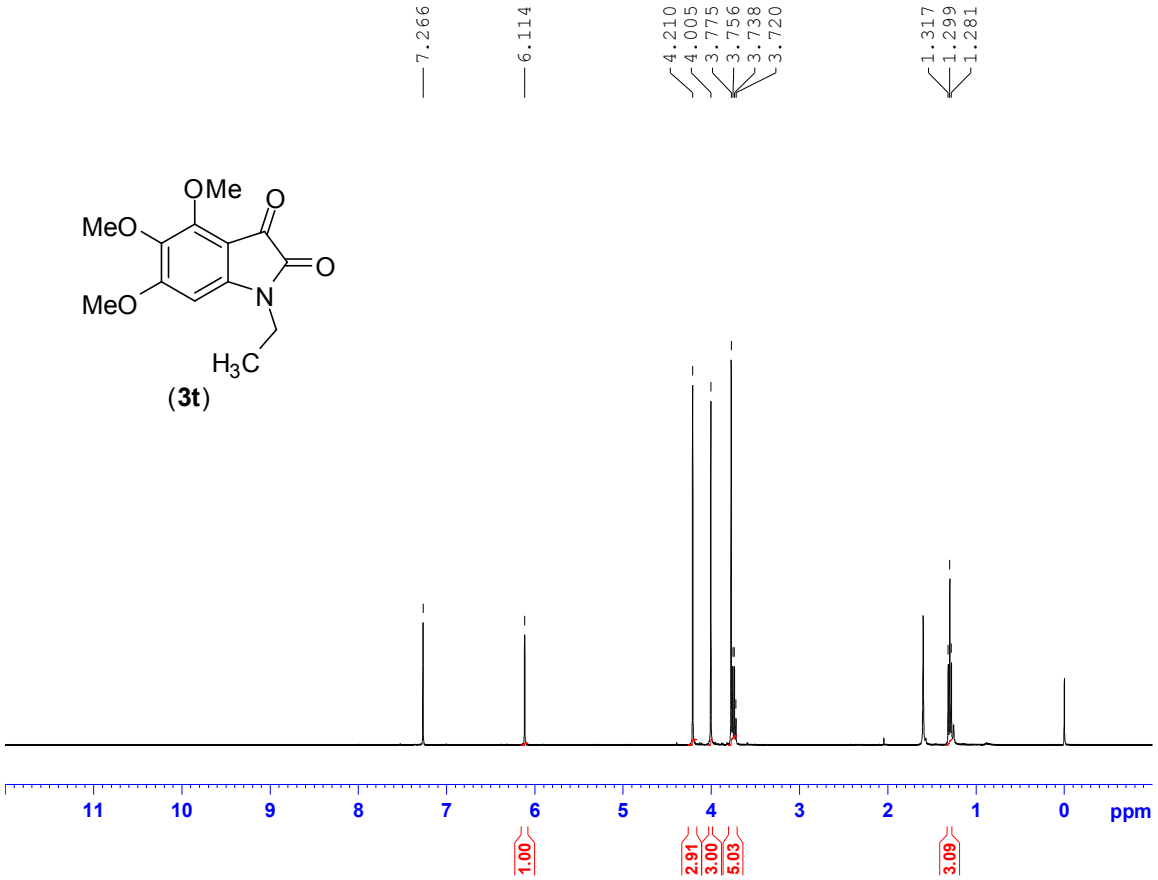

177.58
170.11
161.31
159.77
153.30
100.68
91.61
90.48
77.36
77.04
76.73
56.29
56.17
34.98
12.97
OMe
O
O
MeO
N
H3C
(3r)
200
180
160
140
120
100
80
60
40
20
0
ppm

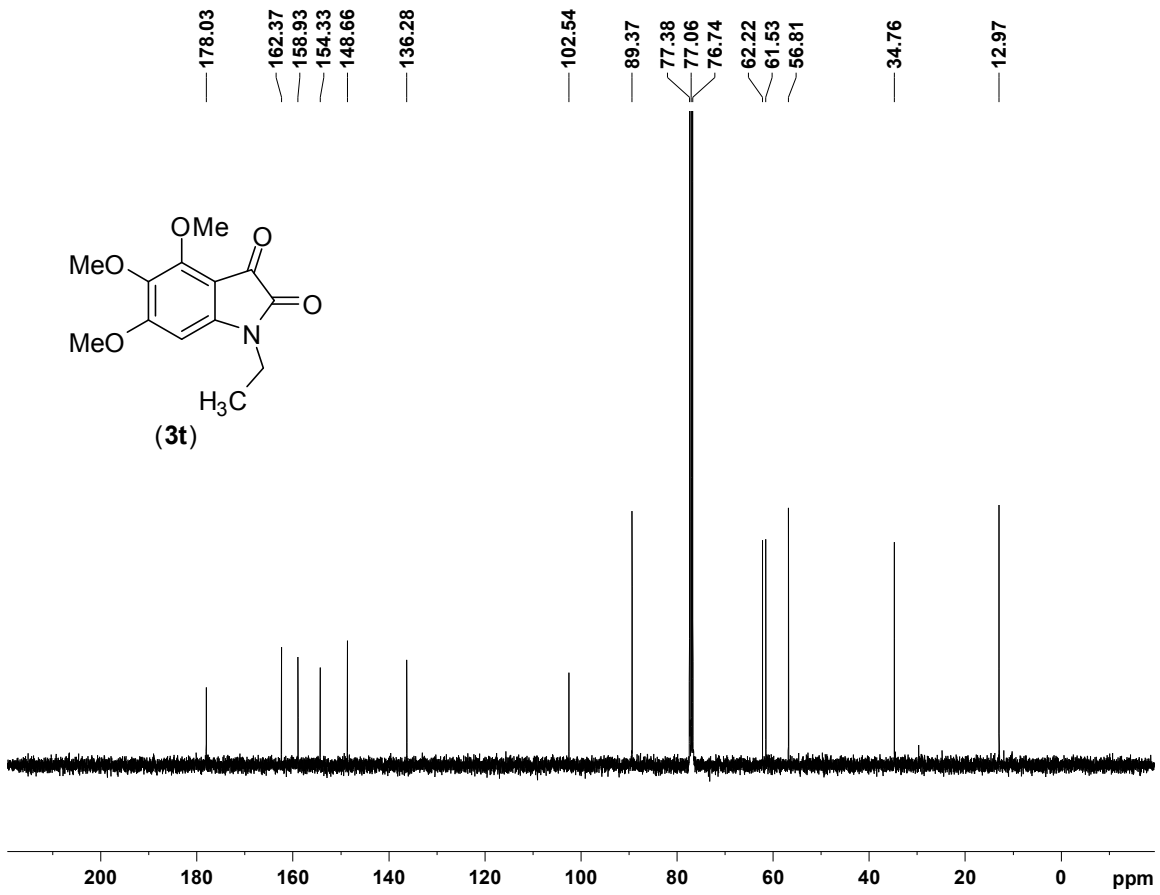

7.360
7.357
7.352
7.348
7.336
7.321
7.301
7.284
7.272
7.265
5.984
5.979
5.890
5.885
4.869
3.941
3.812
OMe
O
O
MeO
N
11
10
9
8
7
6
5
4
3
2
1
0
ppm
5.07
0.97
0.96
2.00
3.03
3.06

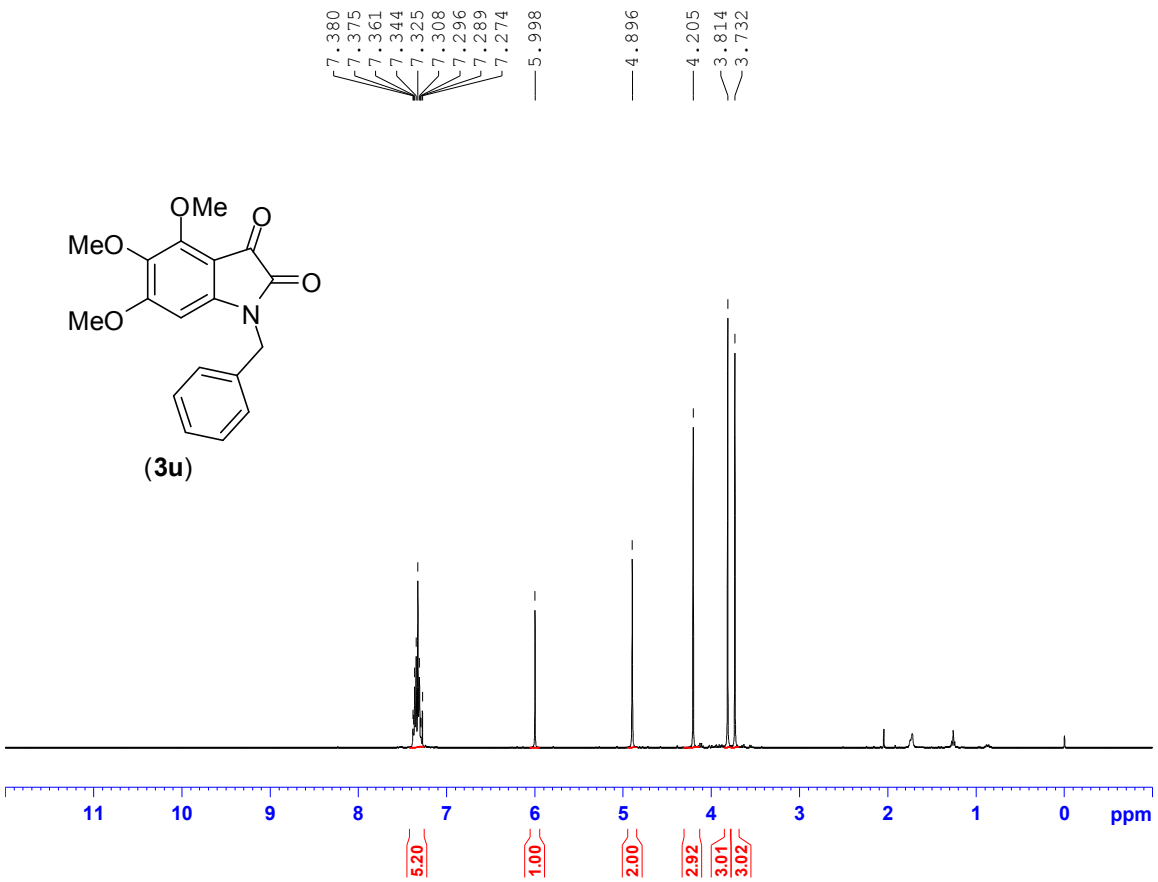
(**3s**)


177.10
169.96
161.23
160.16
153.33
135.06
128.98
128.01
127.29
100.82
91.86
91.48
77.35
77.03
76.72
56.31
56.05
44.03
OMe
O
O
MeO
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

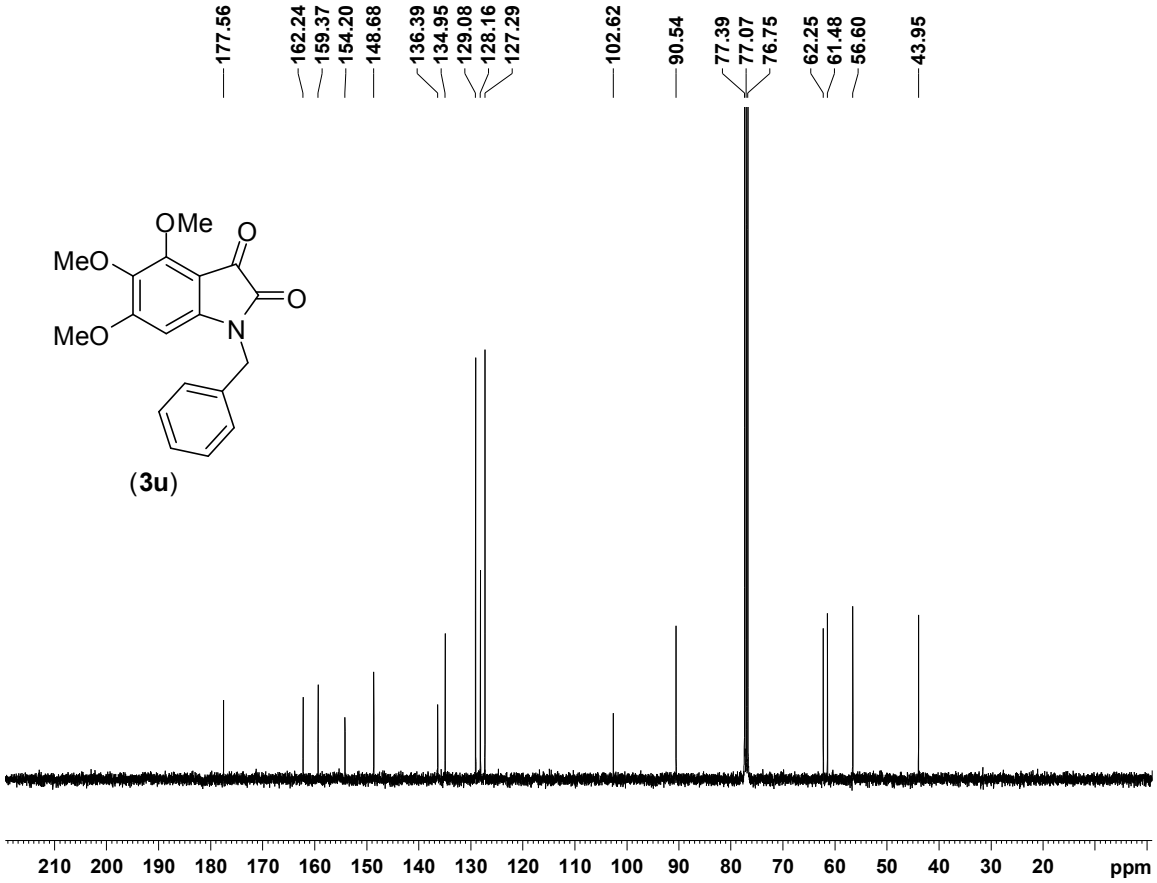
(**3s**)


7.266
6.114
4.210
4.005
3.775
3.756
3.738
3.720
1.317
1.299
1.281
OMe
MeO
MeO
O
O
N
H3C
(3t)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.91
3.00
5.03
3.09

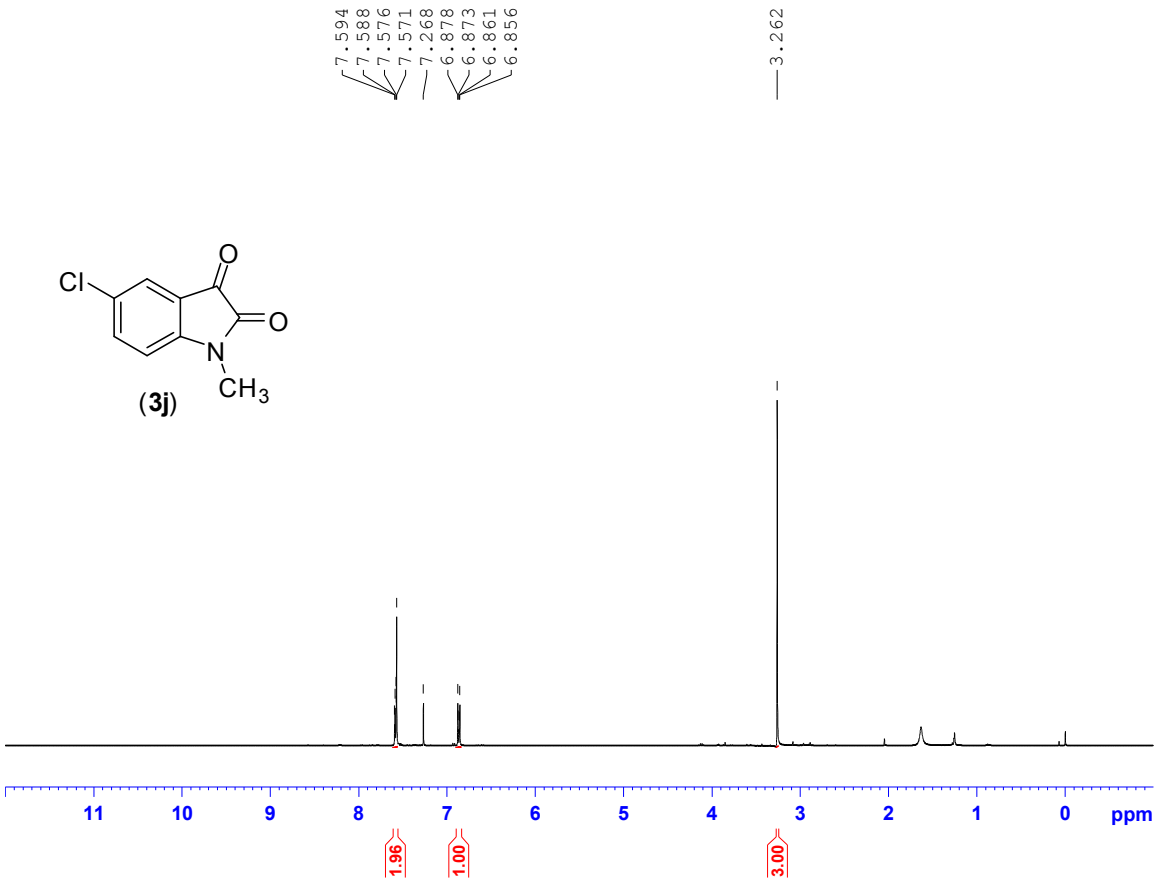

178.03
162.37
158.93
154.33
148.66
136.28
102.54
89.37
77.38
77.06
76.74
62.22
61.53
56.81
34.76
12.97
OMe
O
MeO
O
MeO
N
H3C
(3t)
200
180
160
140
120
100
80
60
40
20
0
ppm

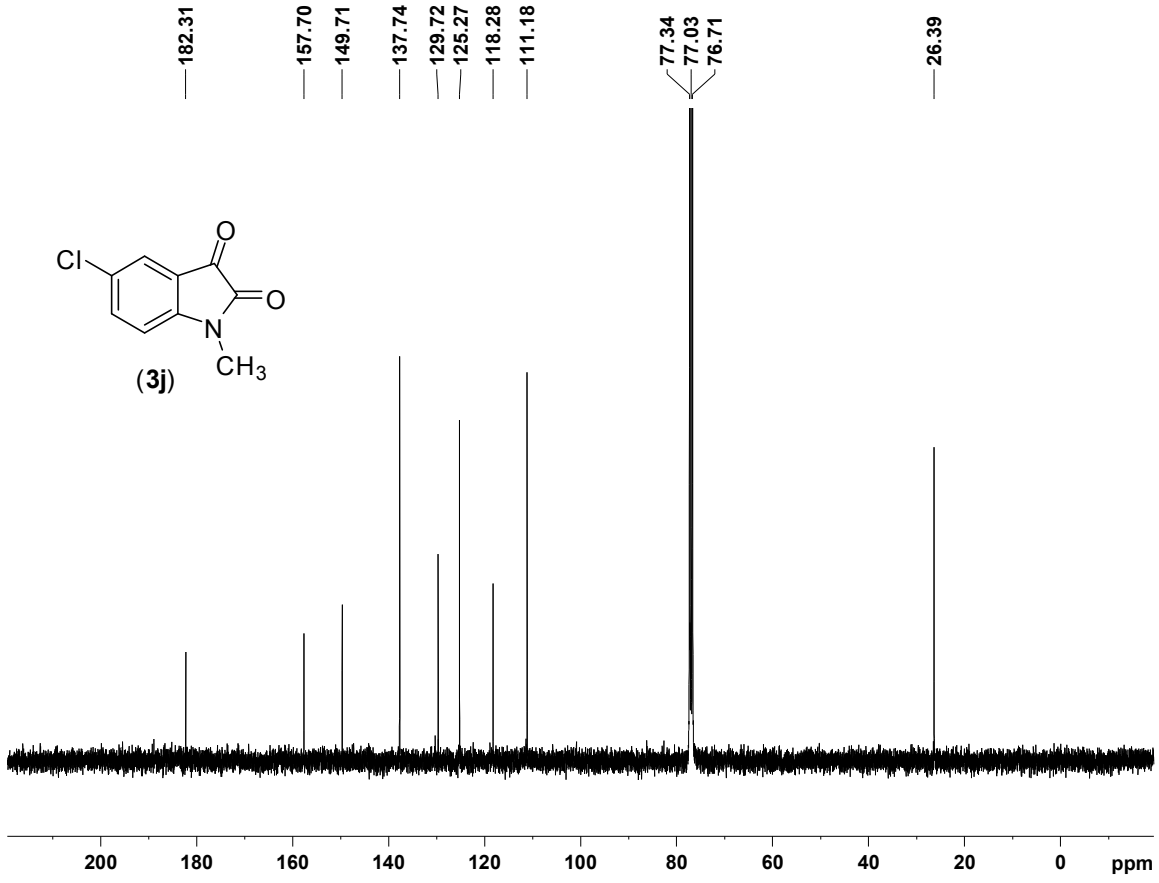

7.380
7.375
7.361
7.344
7.325
7.308
7.296
7.289
7.274
5.998
4.896
4.205
3.814
3.732
OMe
O
MeO
O
MeO
N
11
10
9
8
7
6
5
4
3
2
1
0
ppm
5.20
1.00
2.00
2.92
3.01
3.02

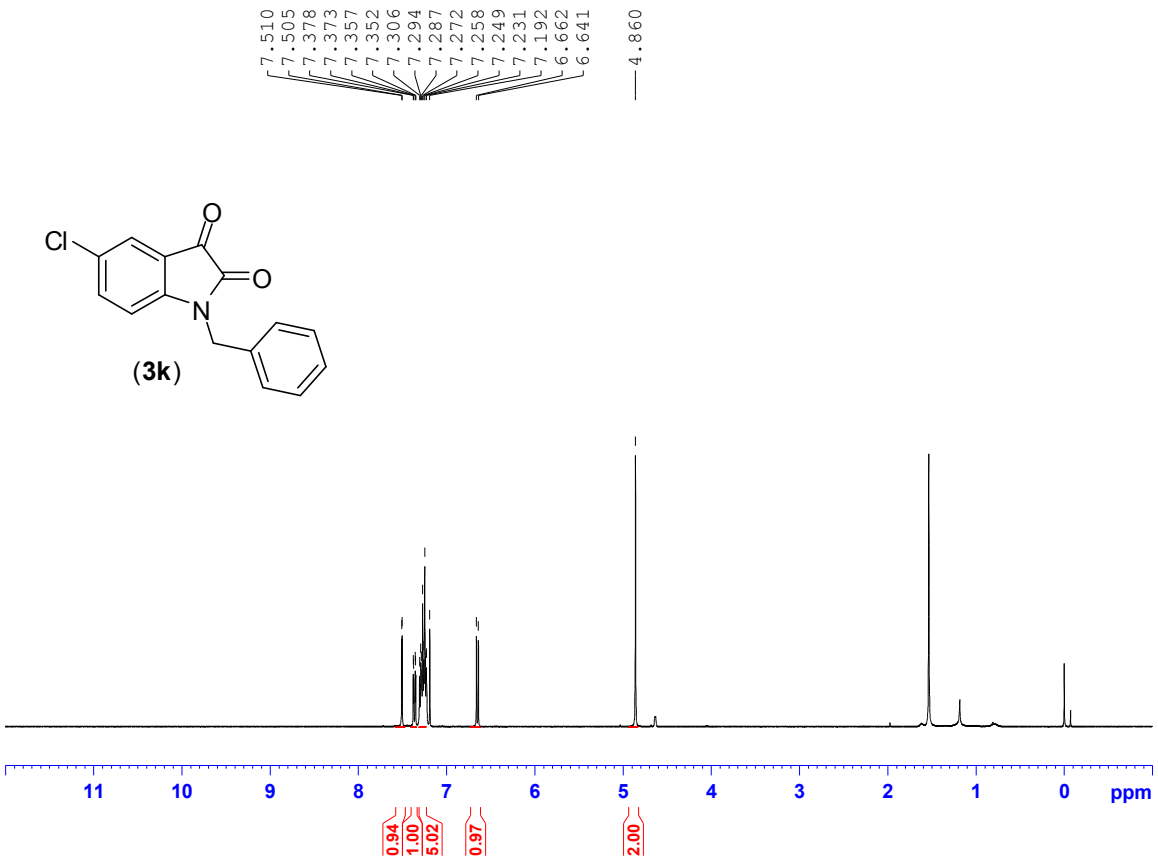
(**3u**)

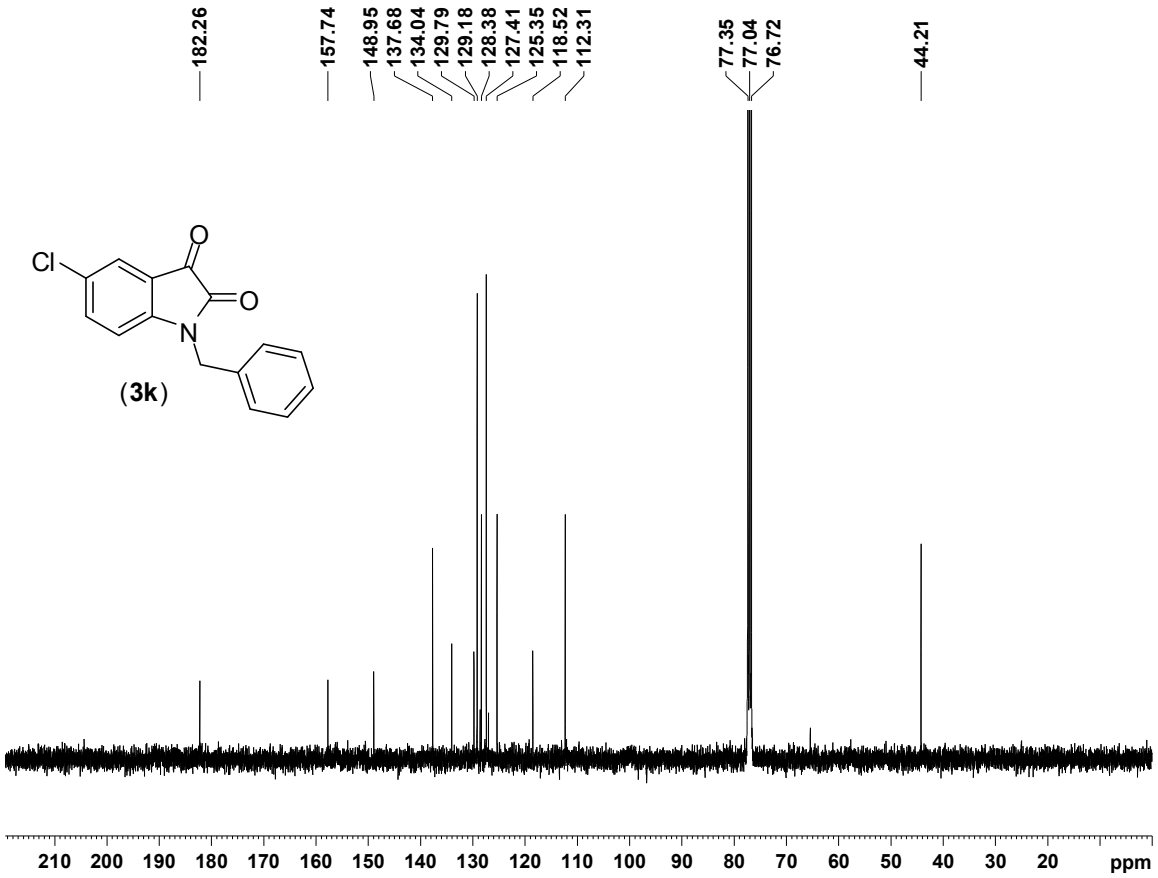

177.56
162.24
159.37
154.20
148.68
136.39
134.95
129.08
128.16
127.29
102.62
90.54
77.39
77.07
76.75
62.25
61.48
56.60
43.95
OMe
O
MeO
O
MeO
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

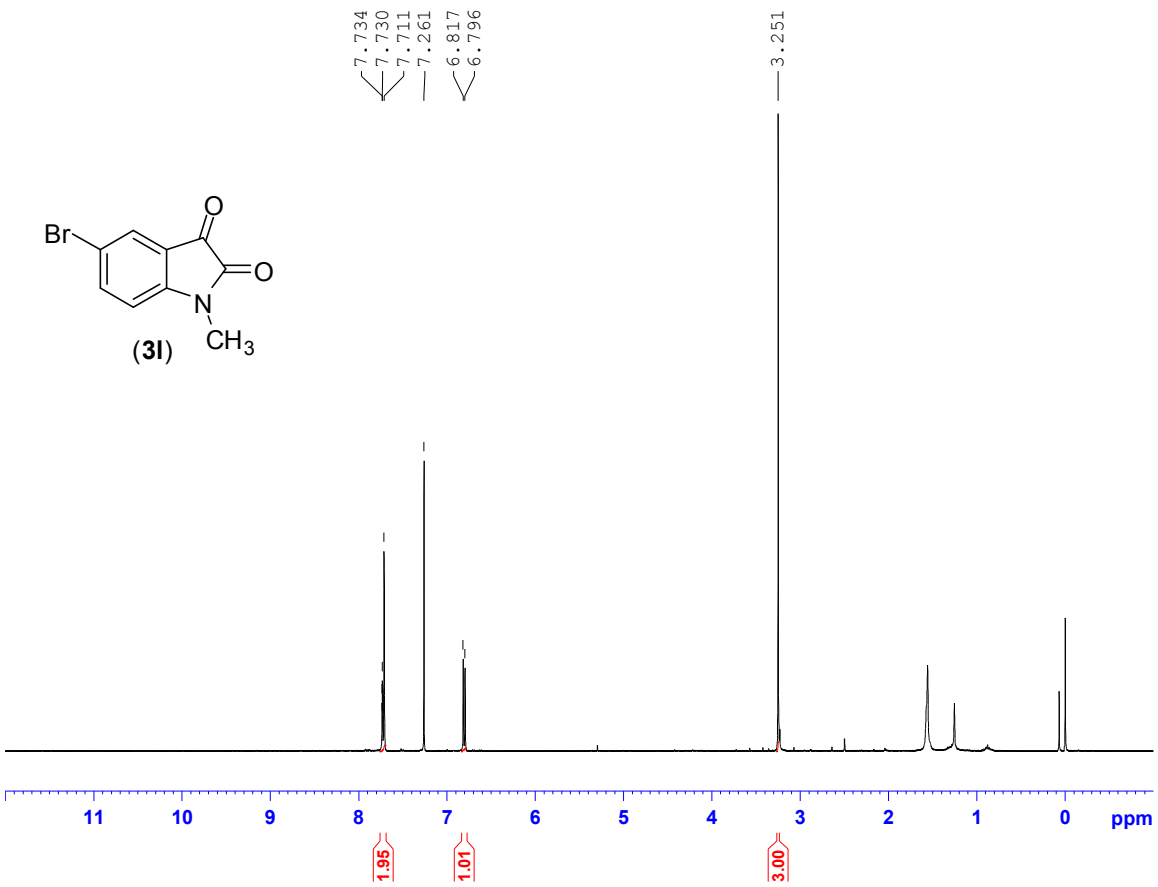
(**3u**)

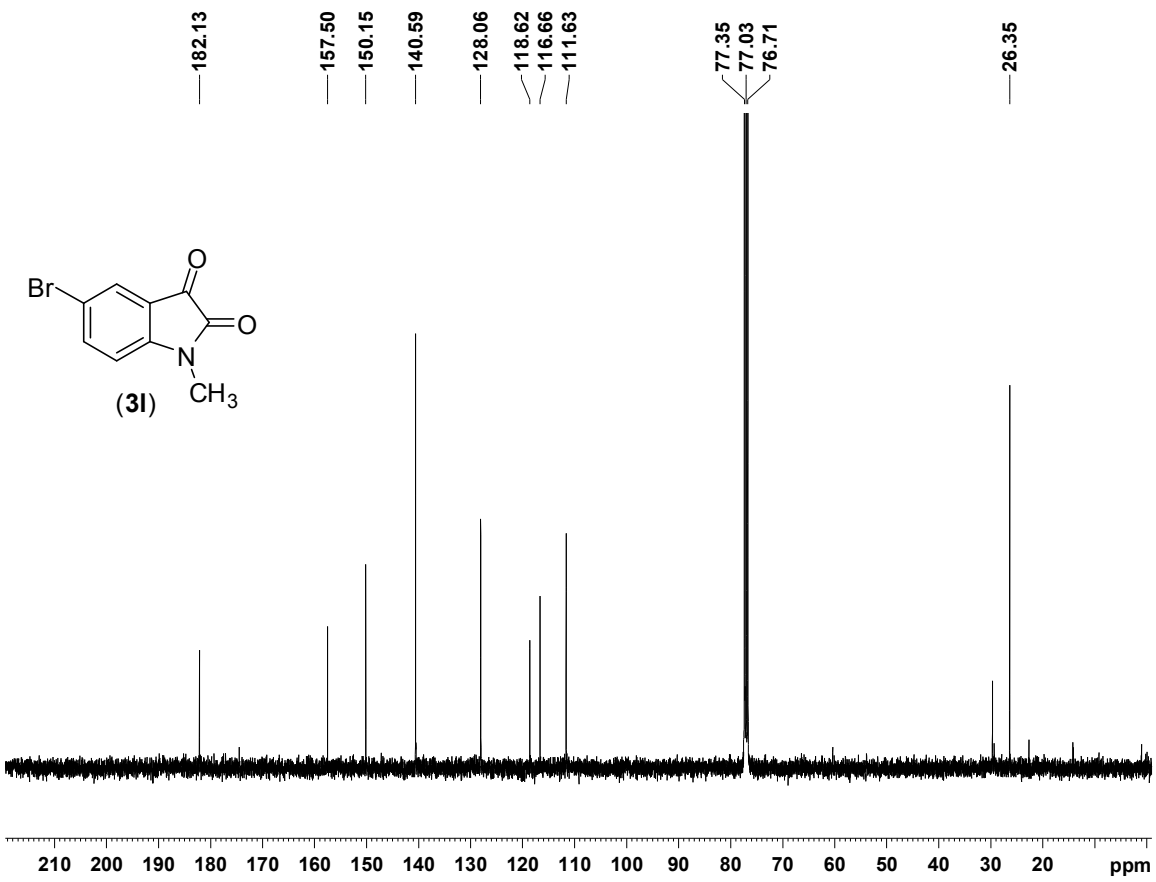

7.594
7.588
7.576
7.571
7.268
6.878
6.873
6.861
6.856
3.262
Cl
O
O
N
CH3
(3j)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.96
1.00
3.00

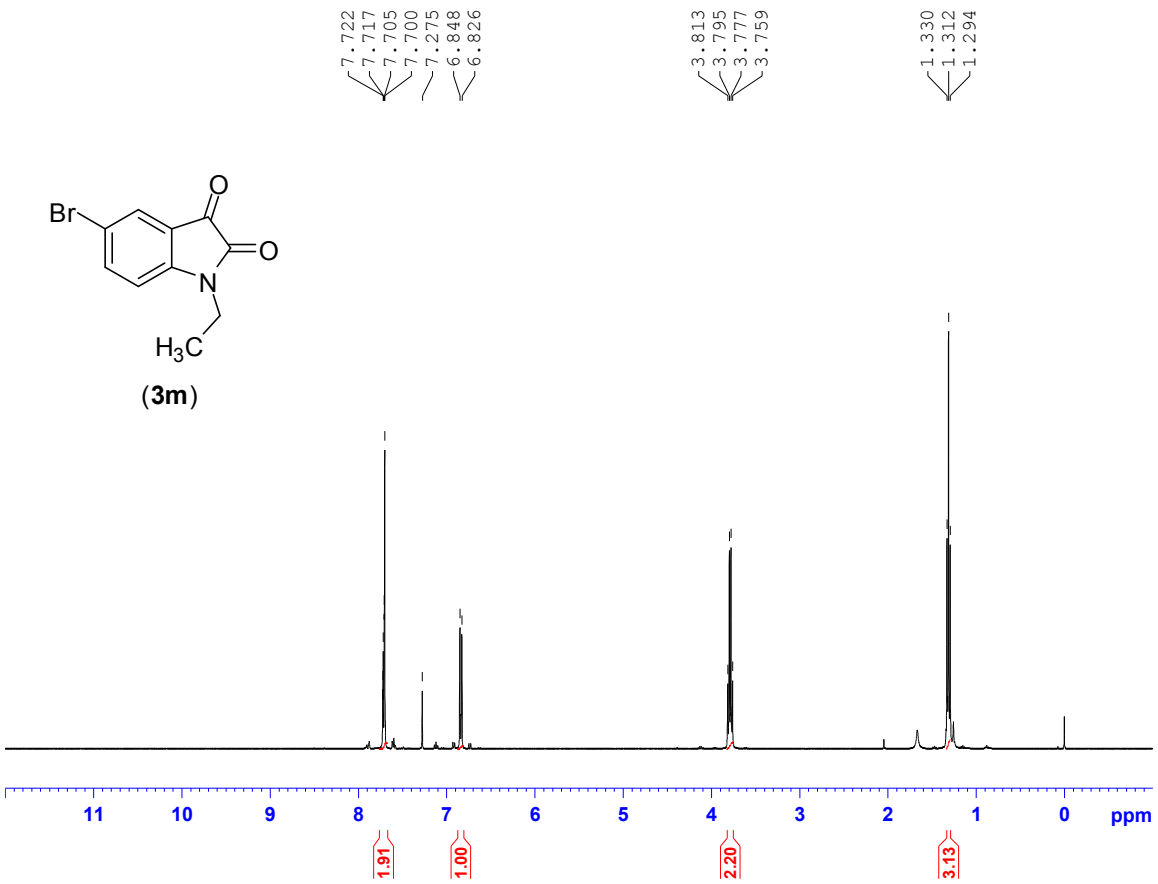

182.31
157.70
149.71
137.74
129.72
125.27
118.28
111.18
77.34
77.03
76.71
26.39
Cl
O
O
N
CH3
(3j)
200
180
160
140
120
100
80
60
40
20
0
ppm


7.510
7.505
7.378
7.373
7.357
7.352
7.306
7.294
7.287
7.272
7.258
7.249
7.231
7.192
6.662
6.641
4.860
Cl
O
O
N
(3k)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.94
1.00
5.02
0.97
2.00

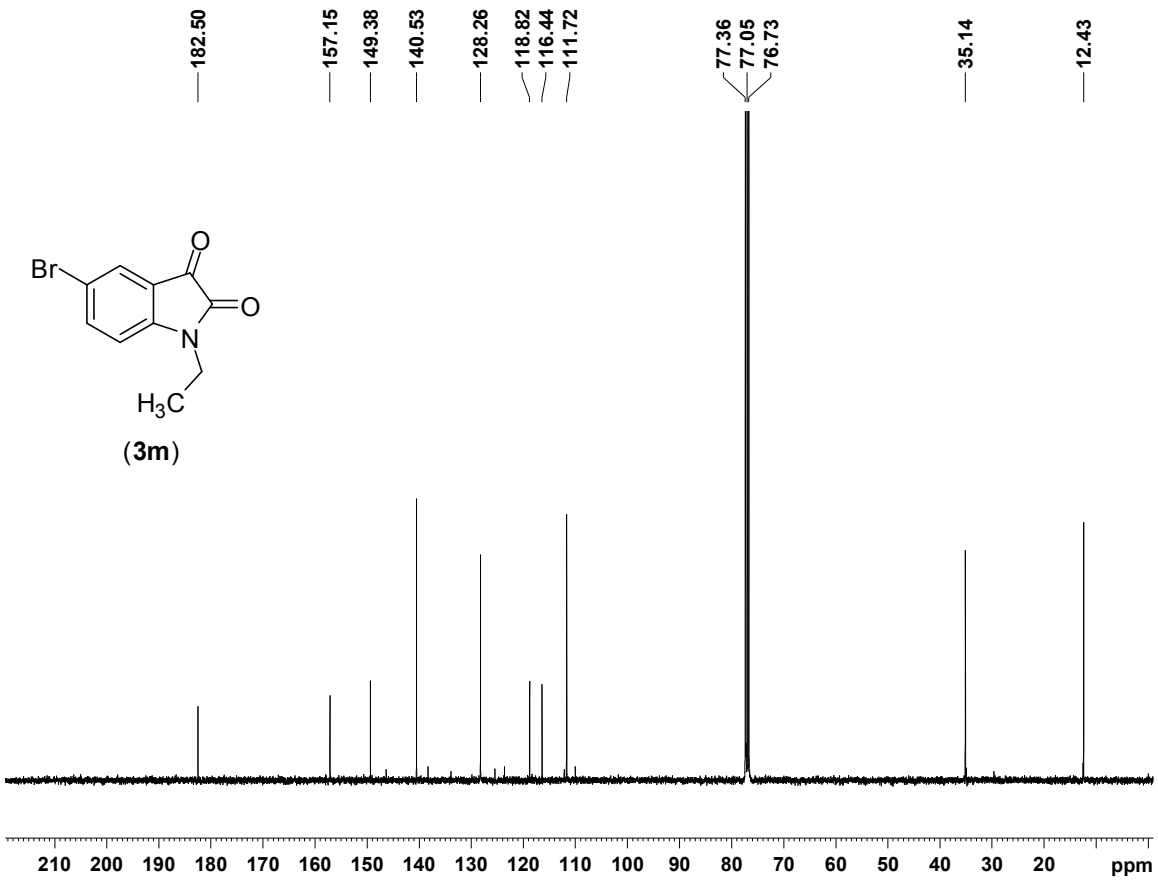

182.26
157.74
148.95
137.68
134.04
129.79
129.18
128.38
127.41
125.35
118.52
112.31
77.35
77.04
76.72
44.21
Cl
O
O
N
(3k)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

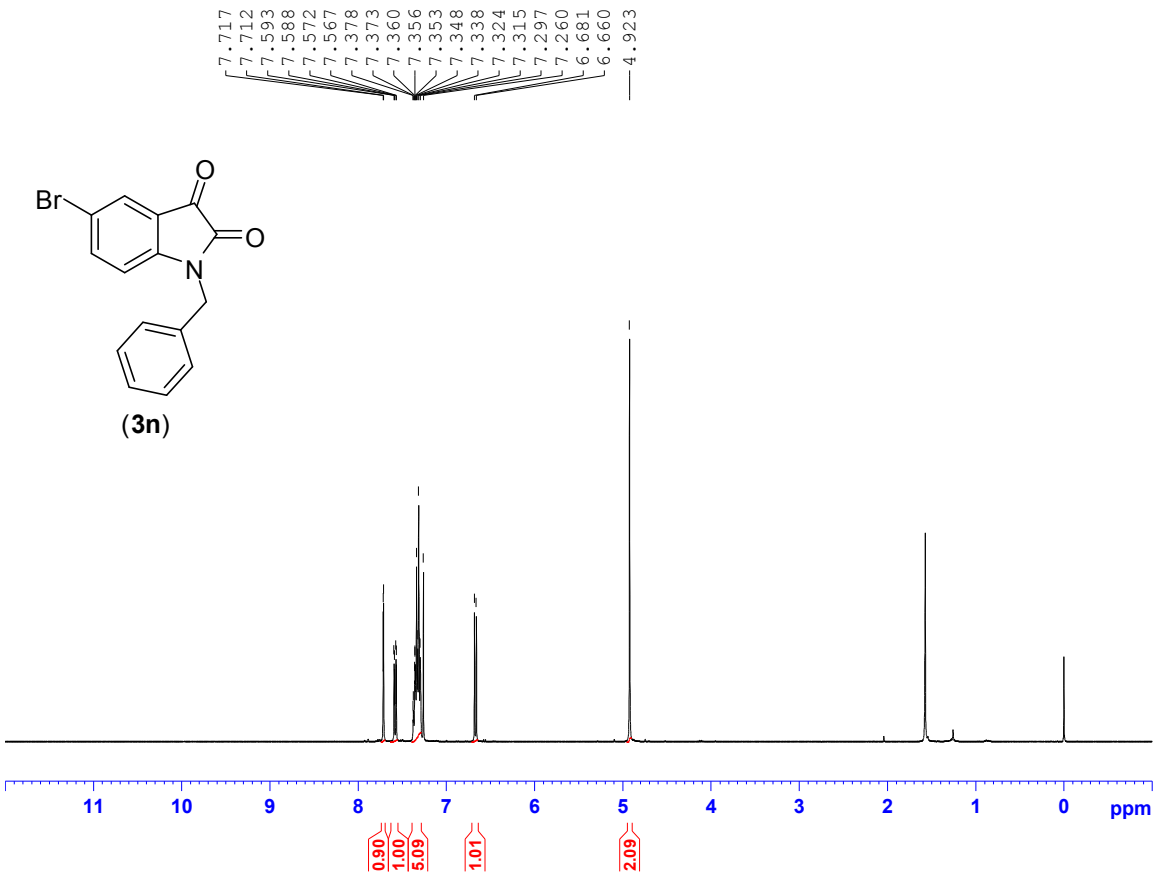

7.734
7.730
7.711
7.261
6.817
6.796
3.251
Br
O
O
N
CH3
(3l)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.95
1.01
3.00


182.13
157.50
150.15
140.59
128.06
118.62
116.66
111.63
77.35
77.03
76.71
26.35
Br
O
O
N
CH3
(3l)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

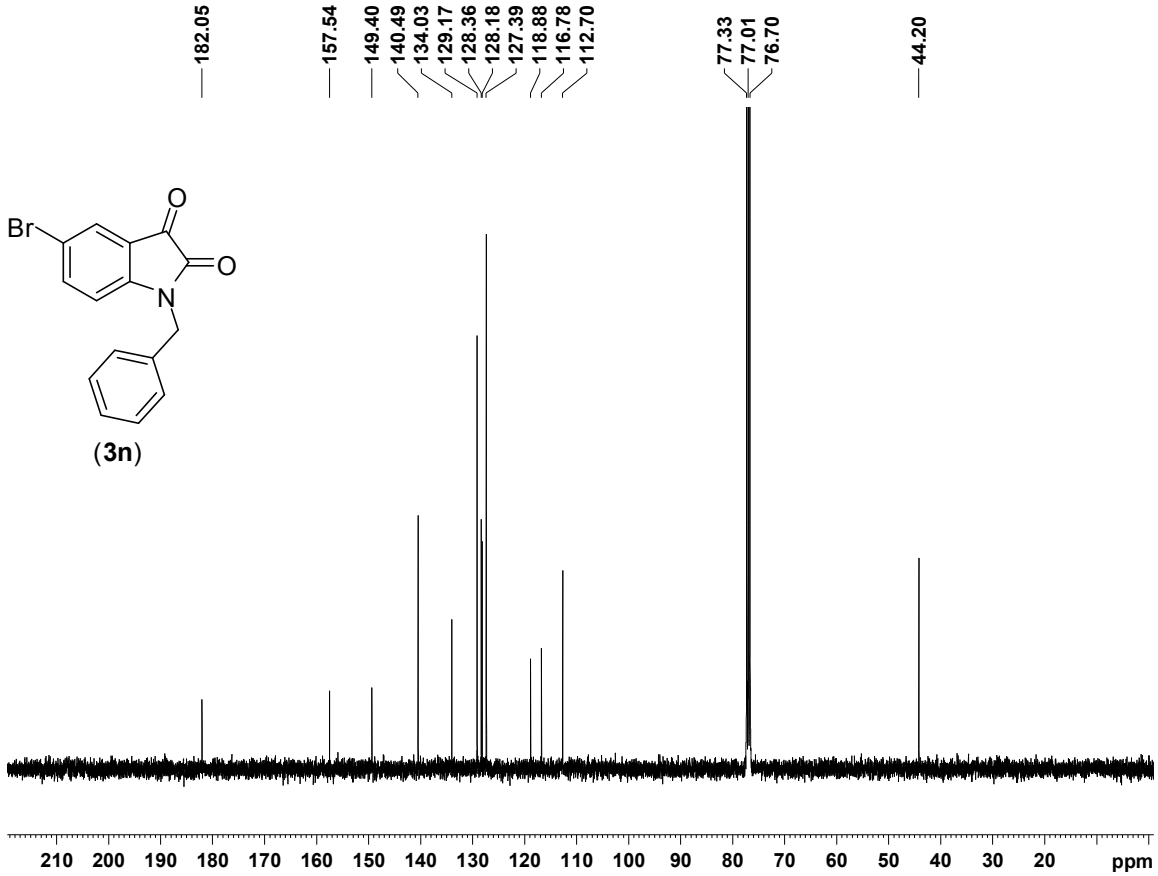

7.722
7.717
7.705
7.700
7.275
6.848
6.826
3.813
3.795
3.777
3.759
1.330
1.312
1.294
Br
O
O
N
H3C
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.91
1.00
2.20
3.13

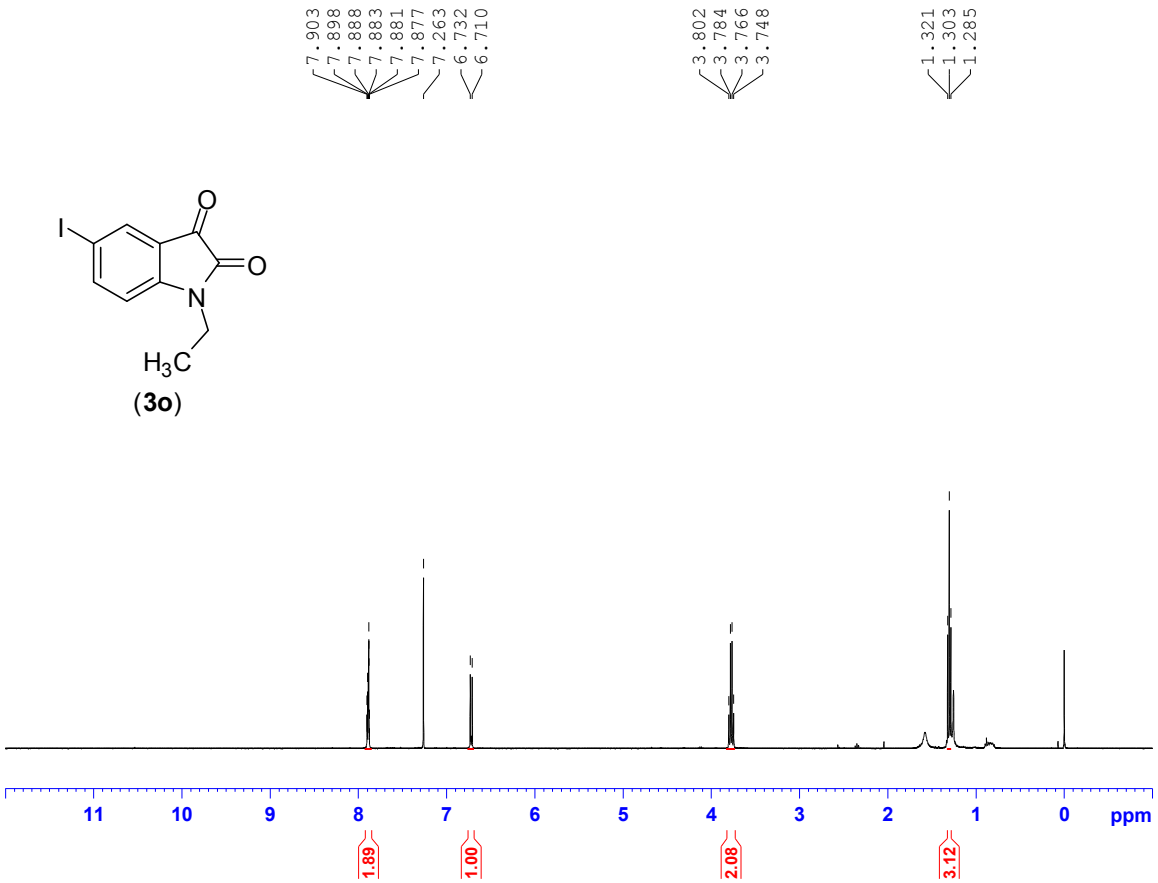
(**3m**)


182.50
157.15
149.38
140.53
128.26
118.82
116.44
111.72
77.36
77.05
76.73
35.14
12.43
Br
O
O
N
H3C
(3m)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

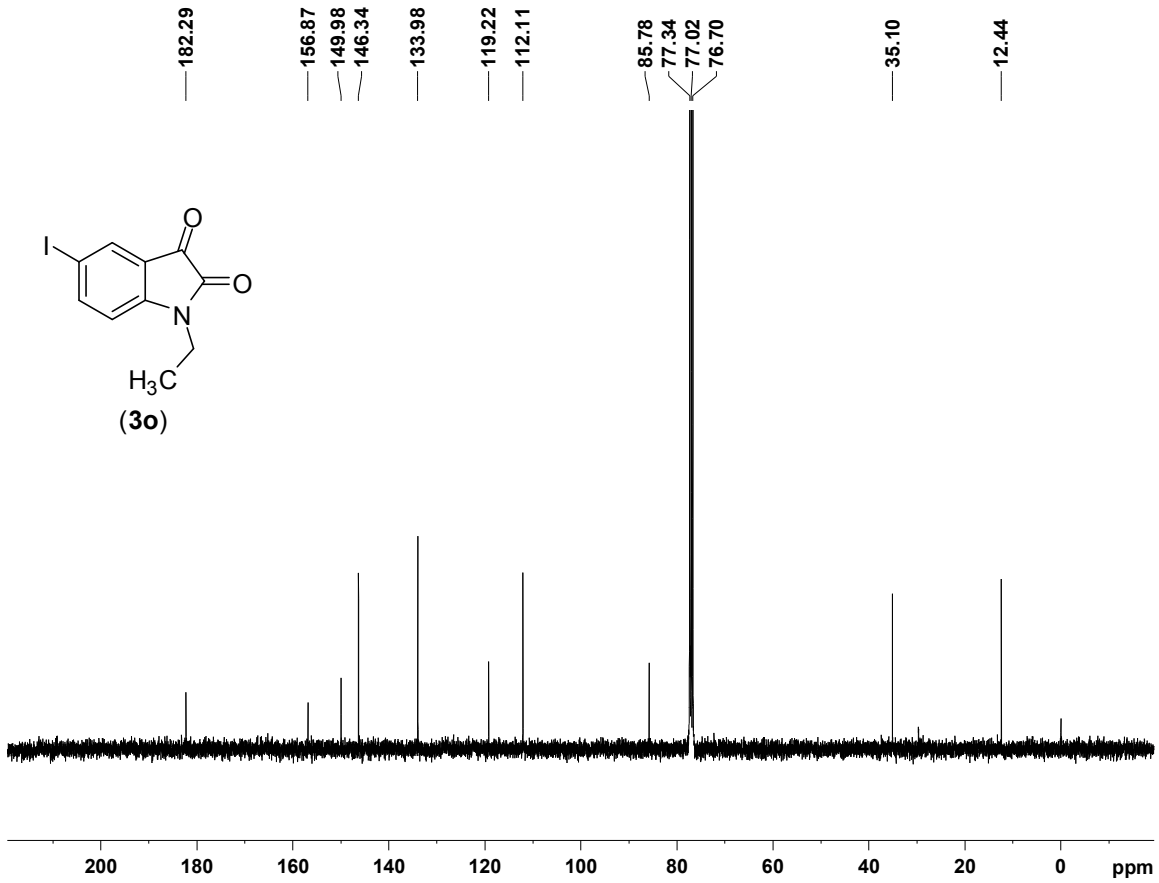

7.717
7.712
7.593
7.588
7.572
7.567
7.378
7.373
7.360
7.356
7.353
7.348
7.338
7.324
7.315
7.297
7.260
6.681
6.660
4.923
Br
O
O
N
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.90
1.00
5.09
1.01
2.09

(**3n**)

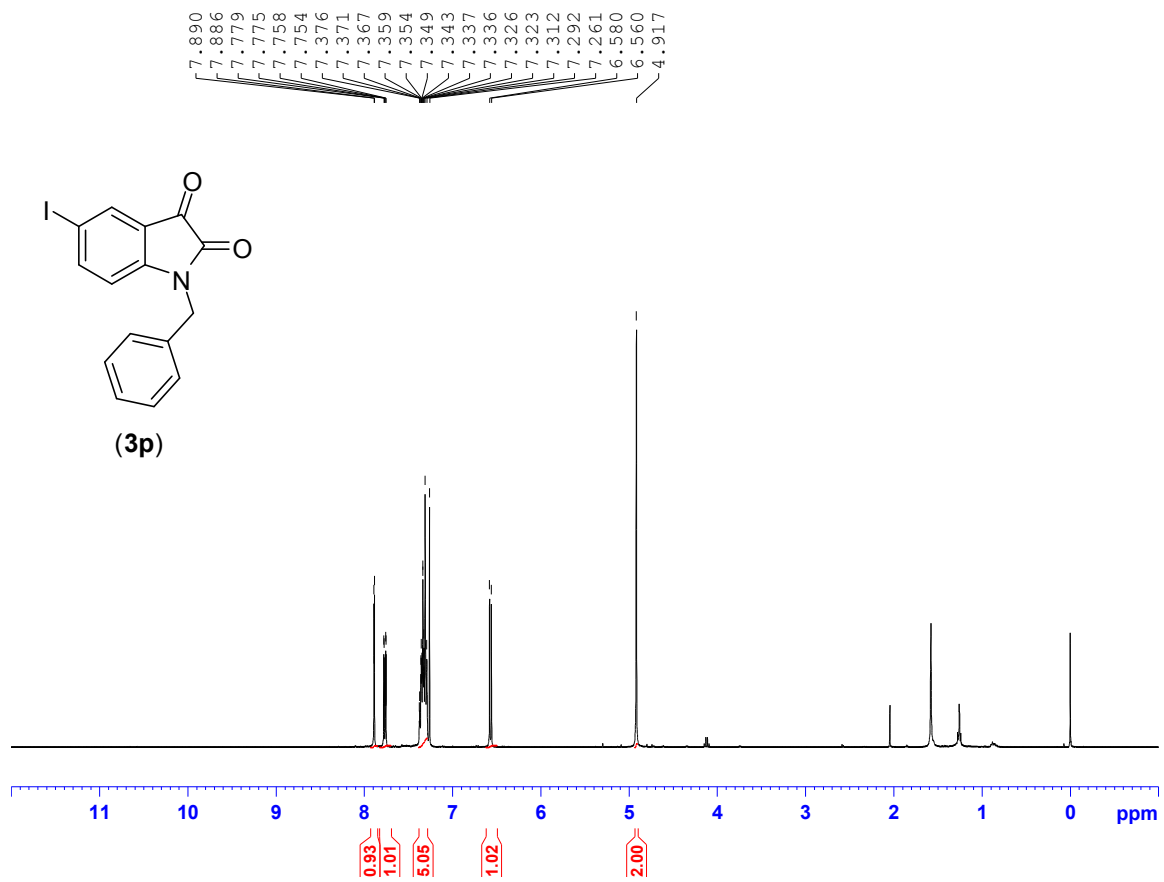

182.05
157.54
149.40
140.49
134.03
129.17
128.36
128.18
127.39
118.88
116.78
112.70
77.33
77.01
76.70
44.20
Br
O
O
N
(3n)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


7.903
7.898
7.888
7.883
7.881
7.877
7.263
6.732
6.710
3.802
3.784
3.766
3.748
1.321
1.303
1.285
O
I
O
N
H3C
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.89
1.00
2.08
3.12

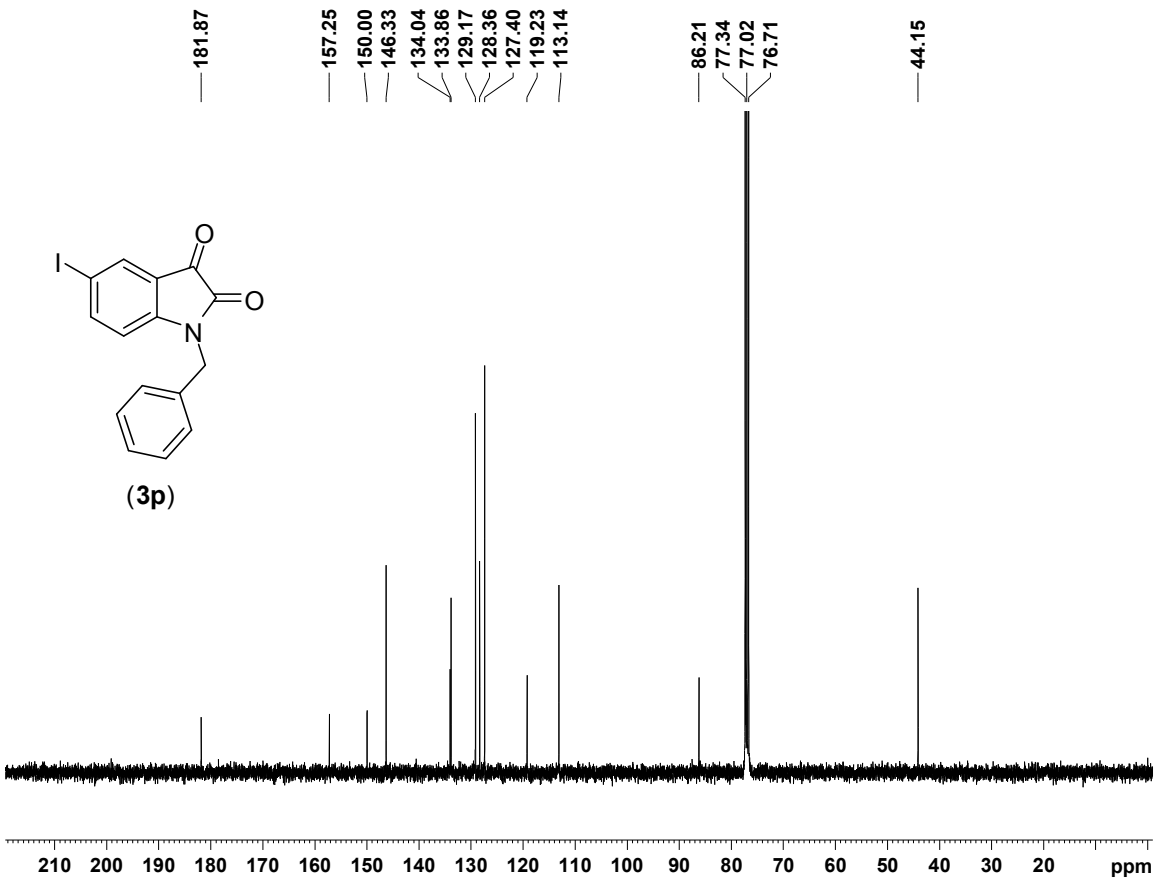
(**3o**)

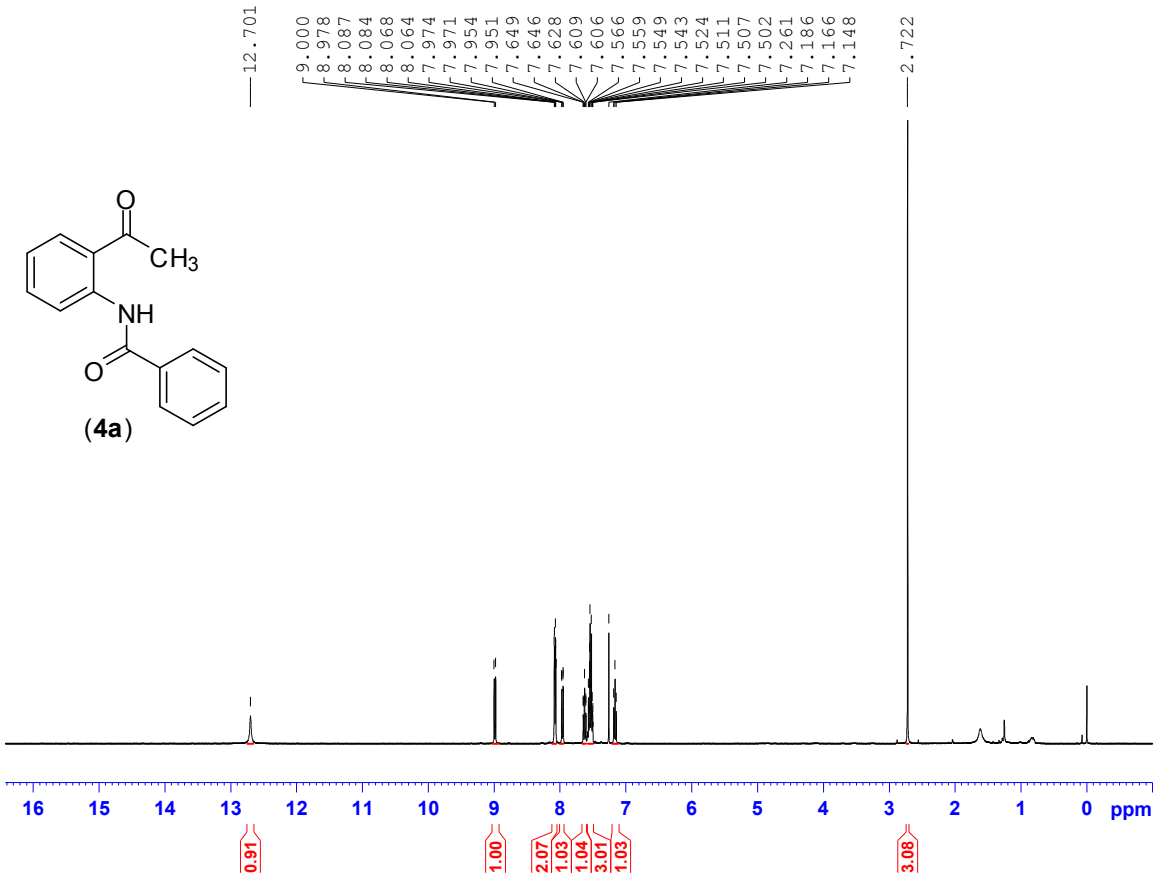

182.29
156.87
149.98
146.34
133.98
119.22
112.11
85.78
77.34
77.02
76.70
35.10
12.44
O
I
O
N
H3C
200
180
160
140
120
100
80
60
40
20
0
ppm

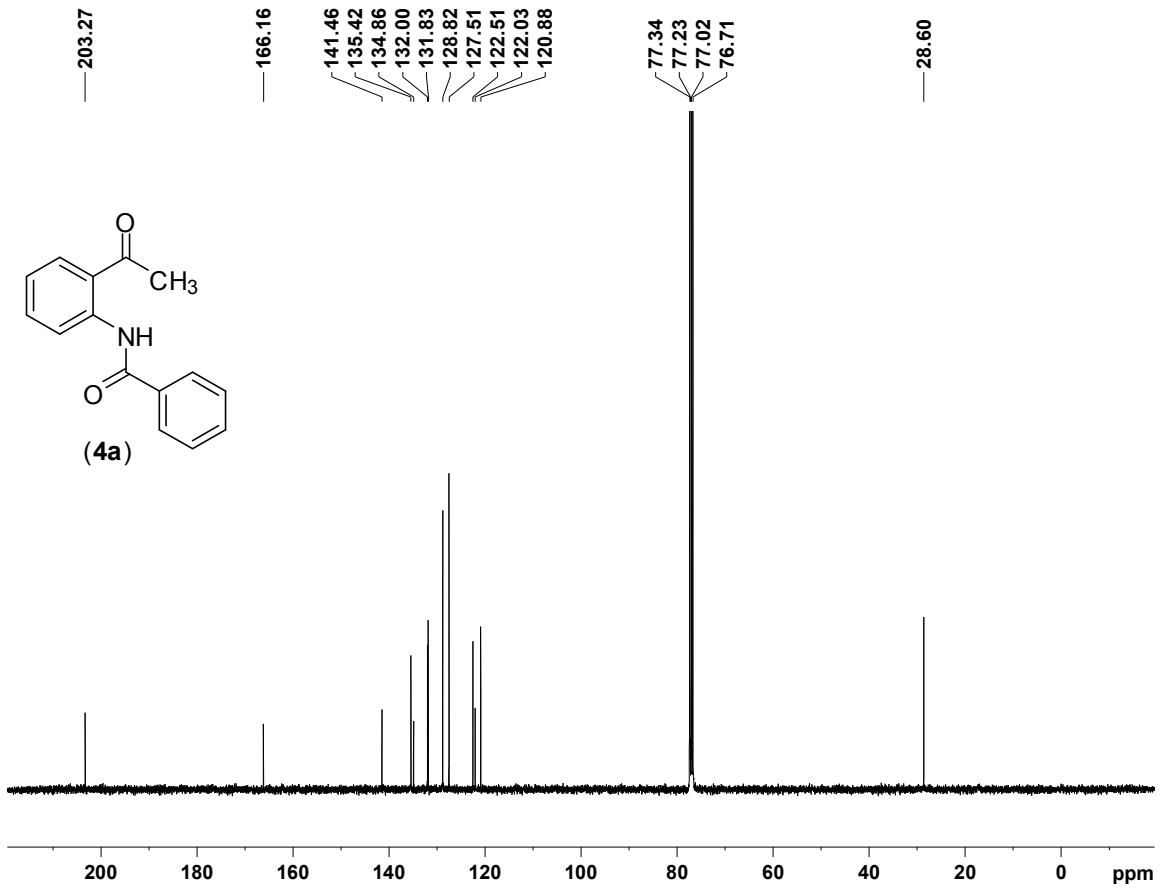
(**3o**)

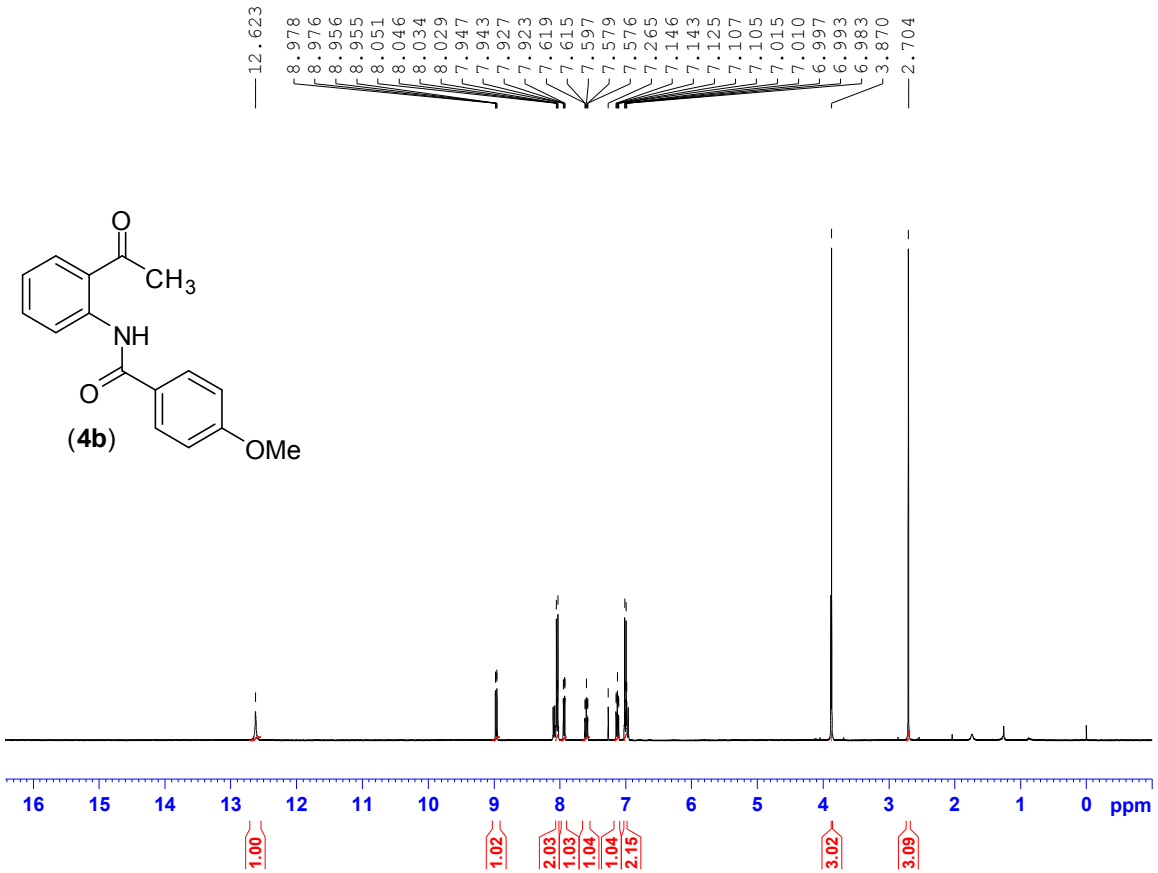

7.890
7.886
7.779
7.775
7.758
7.754
7.376
7.371
7.367
7.359
7.354
7.349
7.343
7.337
7.336
7.326
7.323
7.312
7.292
7.261
6.580
6.560
4.917
O
I
O
N
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.93
1.01
5.05
1.02
2.00

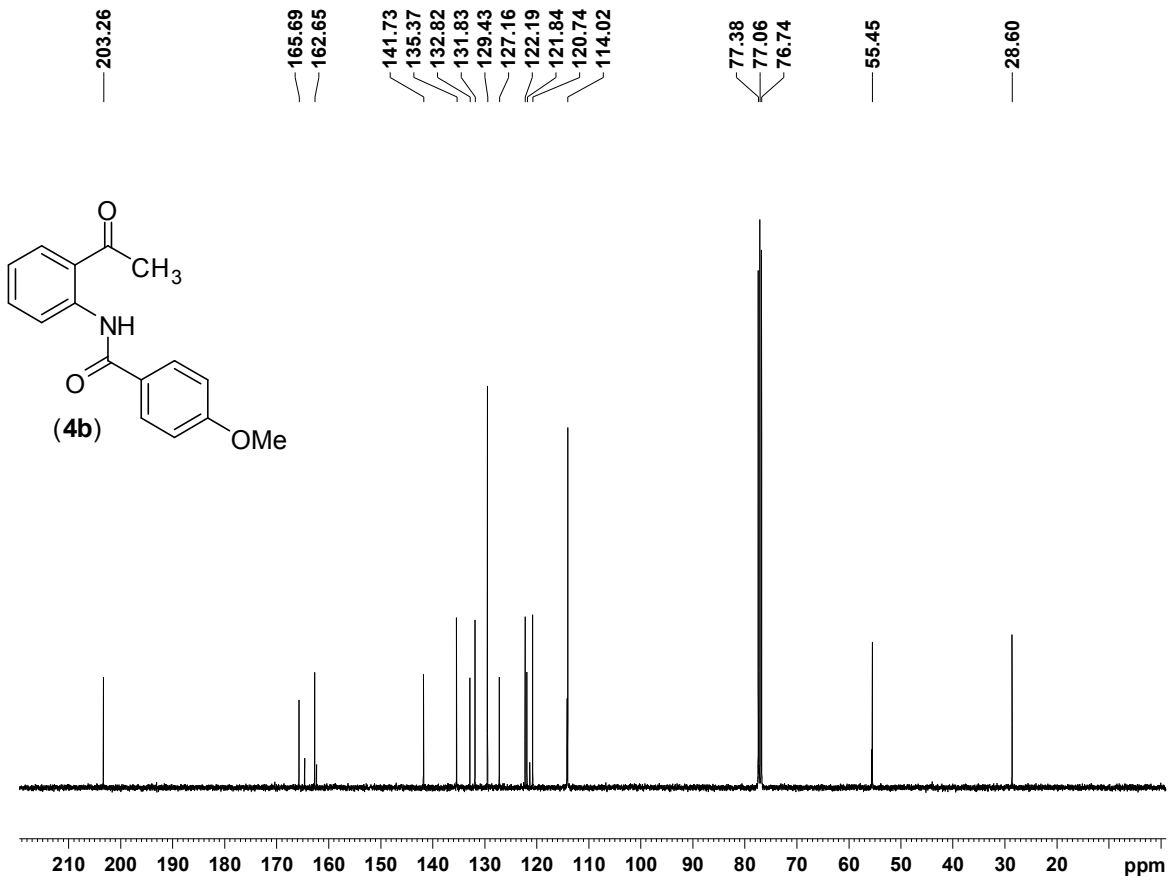
(**3p**)

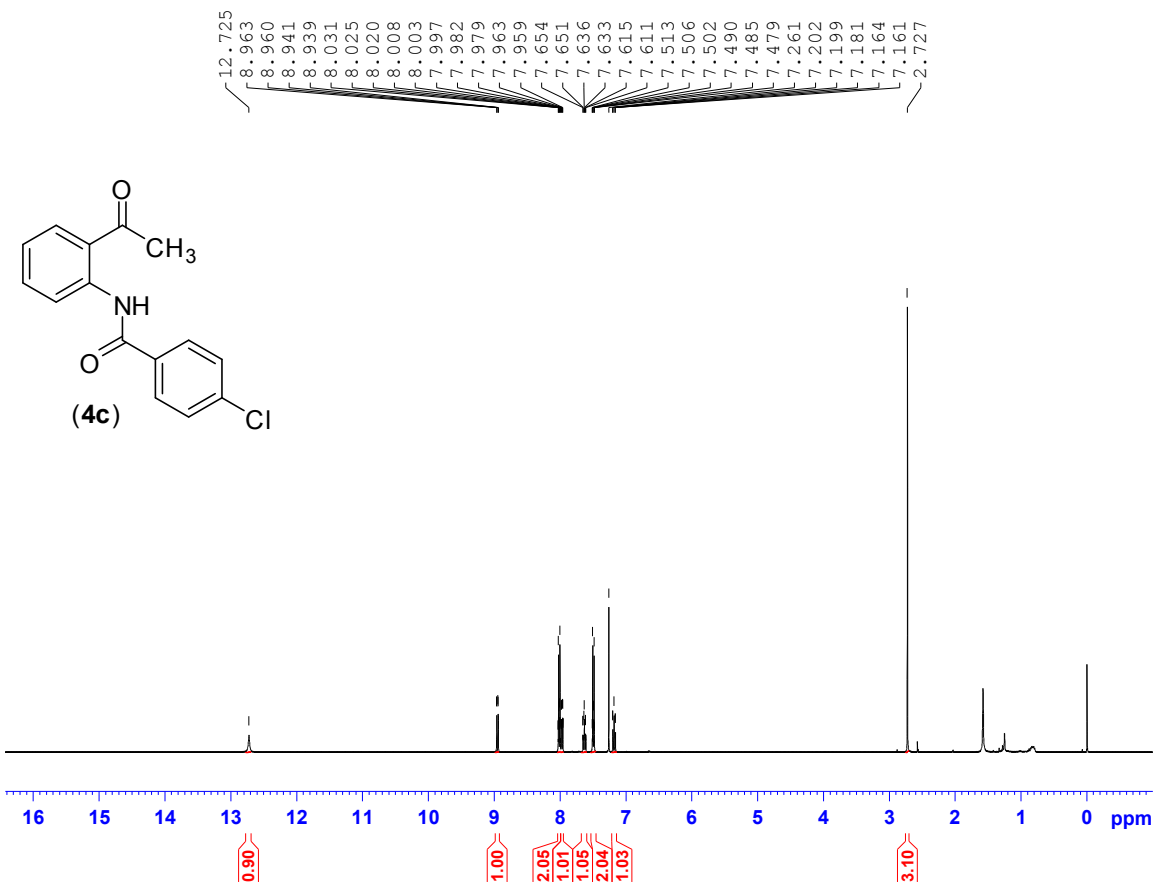

181.87
157.25
150.00
146.33
134.04
133.86
129.17
128.36
127.40
119.23
113.14
86.21
77.34
77.02
76.71
44.15
O
I
O
N
(3p)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

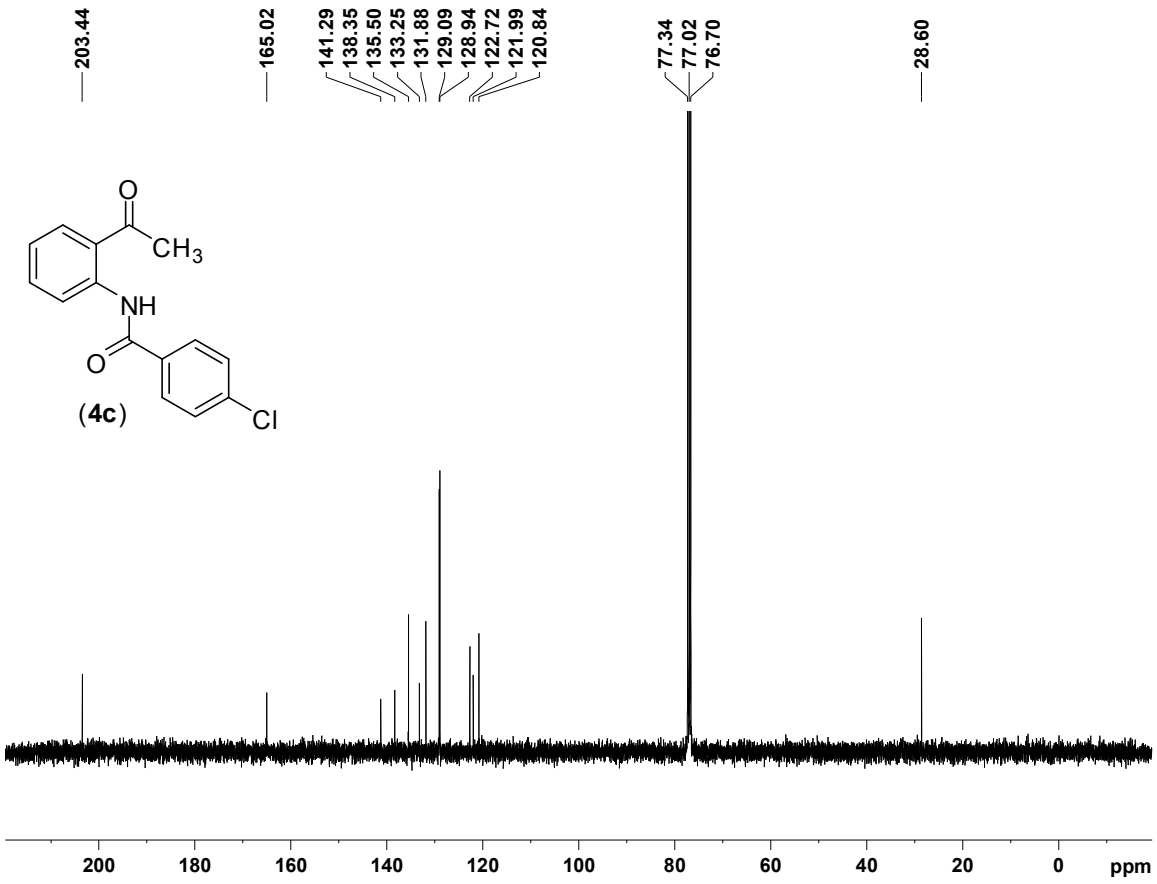

12.701
9.000
8.978
8.087
8.084
8.068
8.064
7.974
7.971
7.954
7.951
7.649
7.646
7.628
7.609
7.606
7.566
7.559
7.549
7.543
7.524
7.511
7.507
7.502
7.261
7.186
7.166
7.148
2.722
O
CH3
NH
O
(4a)
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.91
1.00
2.07
1.03
1.04
3.01
1.03
3.08

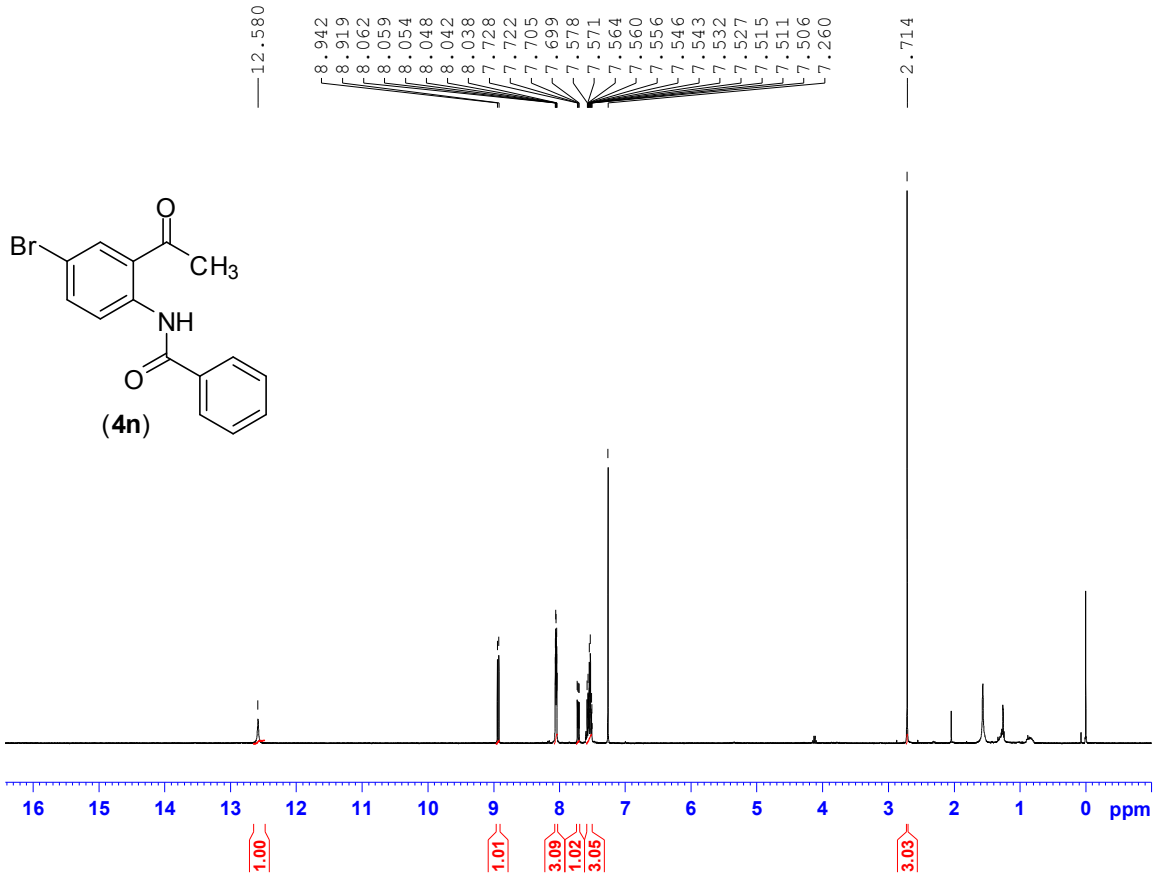

203.27
166.16
141.46
135.42
134.86
132.00
131.83
128.82
127.51
122.51
122.03
120.88
77.34
77.23
77.02
76.71
28.60
O
CH3
NH
O
(4a)
200
180
160
140
120
100
80
60
40
20
0
ppm

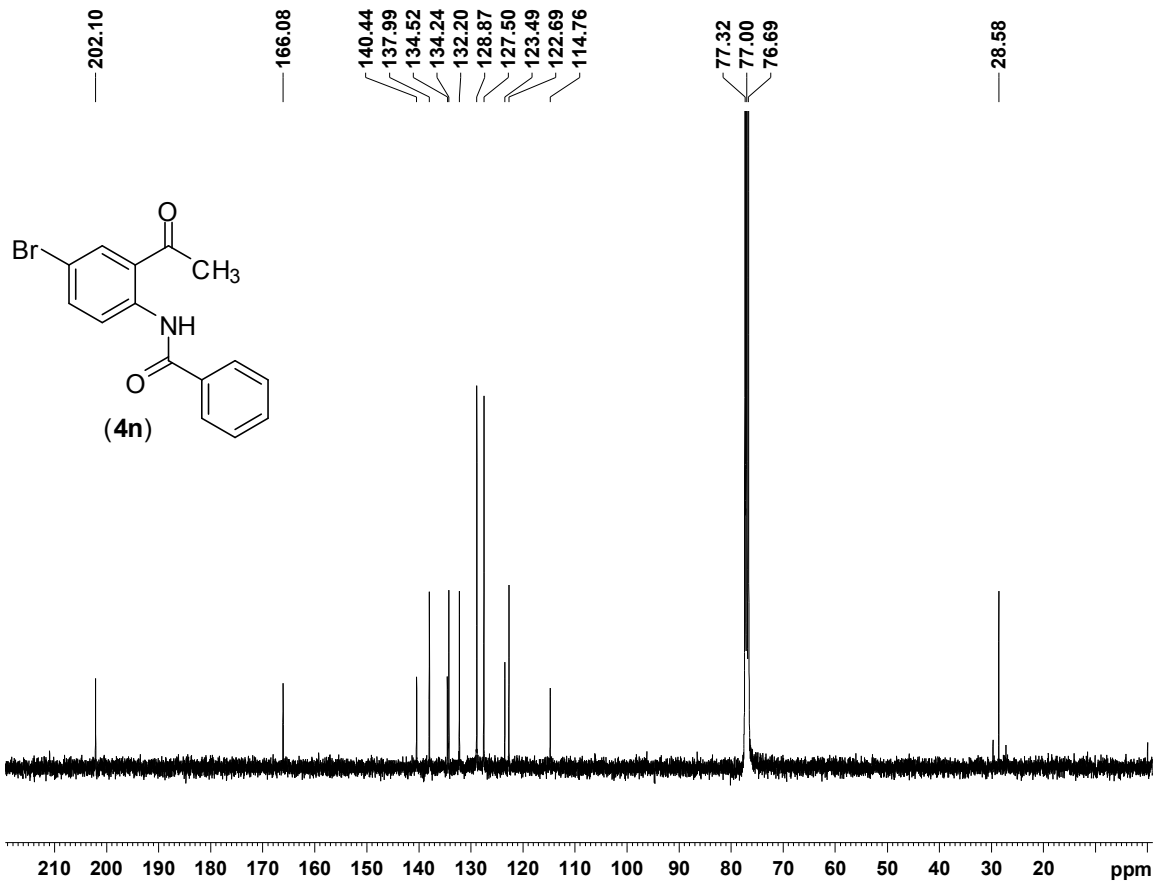

12.623
8.978
8.976
8.956
8.955
8.051
8.046
8.034
8.029
7.947
7.943
7.927
7.923
7.619
7.615
7.597
7.579
7.576
7.265
7.146
7.143
7.125
7.107
7.105
7.015
7.010
6.997
6.993
6.983
3.870
2.704
O
CH3
NH
O
(4b)
OMe
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.02
2.03
1.03
1.04
1.04
2.15
3.02
3.09

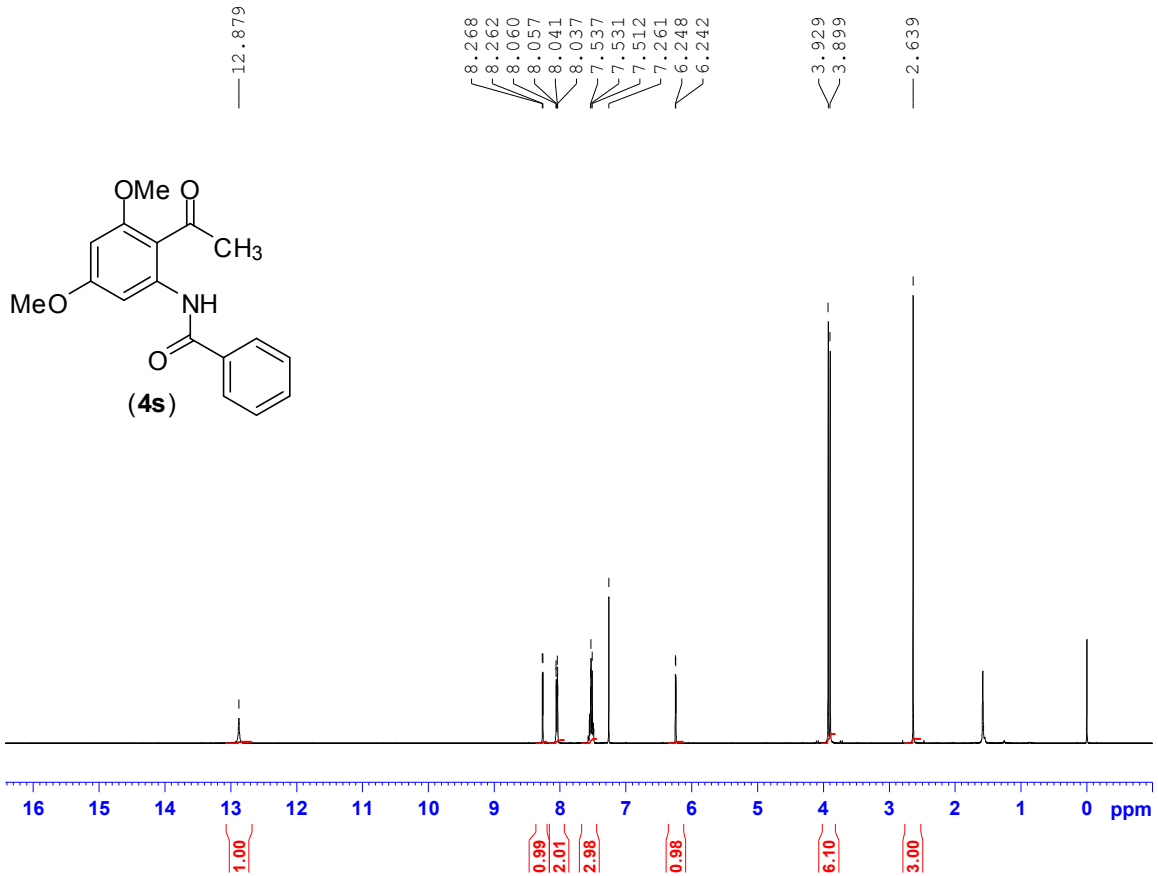

203.26
165.69
162.65
141.73
135.37
132.82
131.83
129.43
127.16
122.19
121.84
120.74
114.02
77.38
77.06
76.74
55.45
28.60
O
CH3
NH
O
(4b)
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

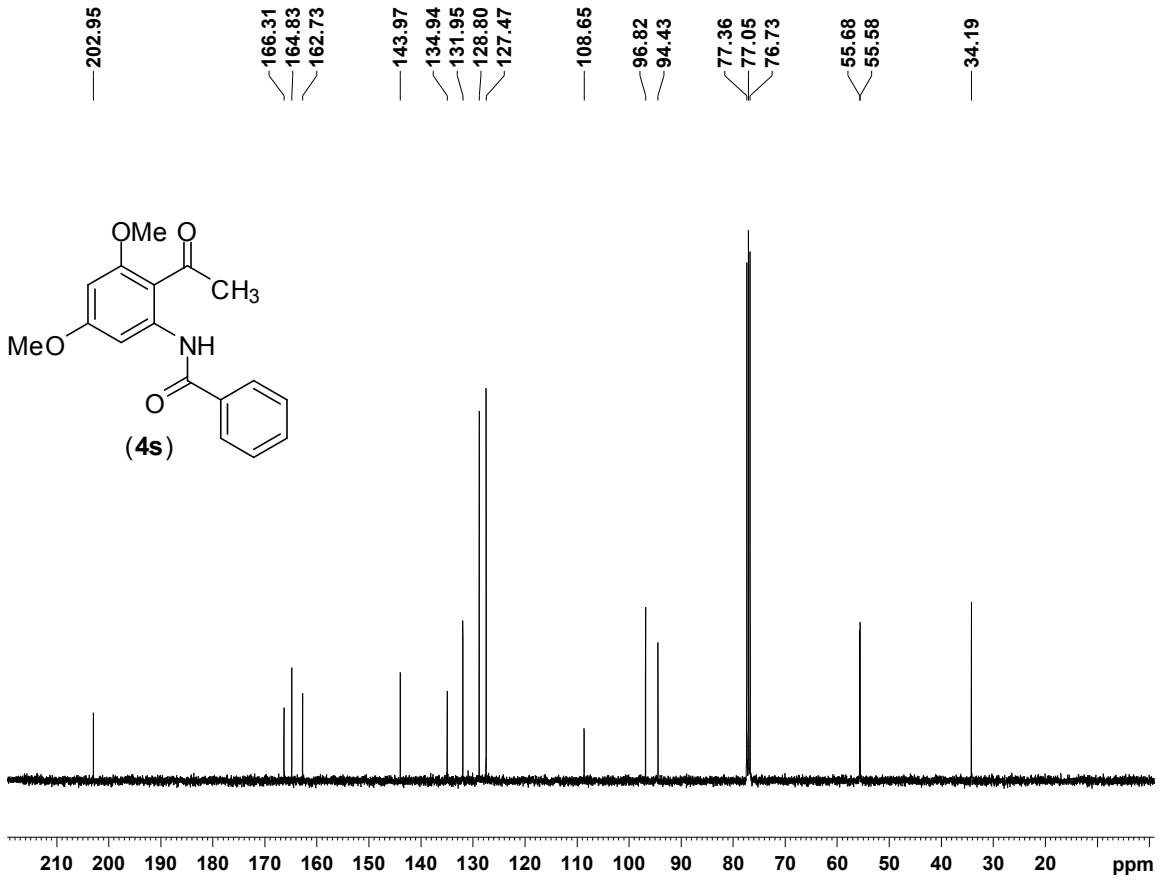

12.725
8.963
8.960
8.941
8.939
8.031
8.025
8.020
8.008
8.003
7.997
7.982
7.979
7.963
7.959
7.654
7.651
7.636
7.633
7.615
7.611
7.513
7.506
7.502
7.490
7.485
7.479
7.261
7.202
7.199
7.181
7.164
7.161
2.727
O
CH3
NH
O
Cl
(4c)
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.90
1.00
2.05
1.01
1.05
2.04
1.03
3.10

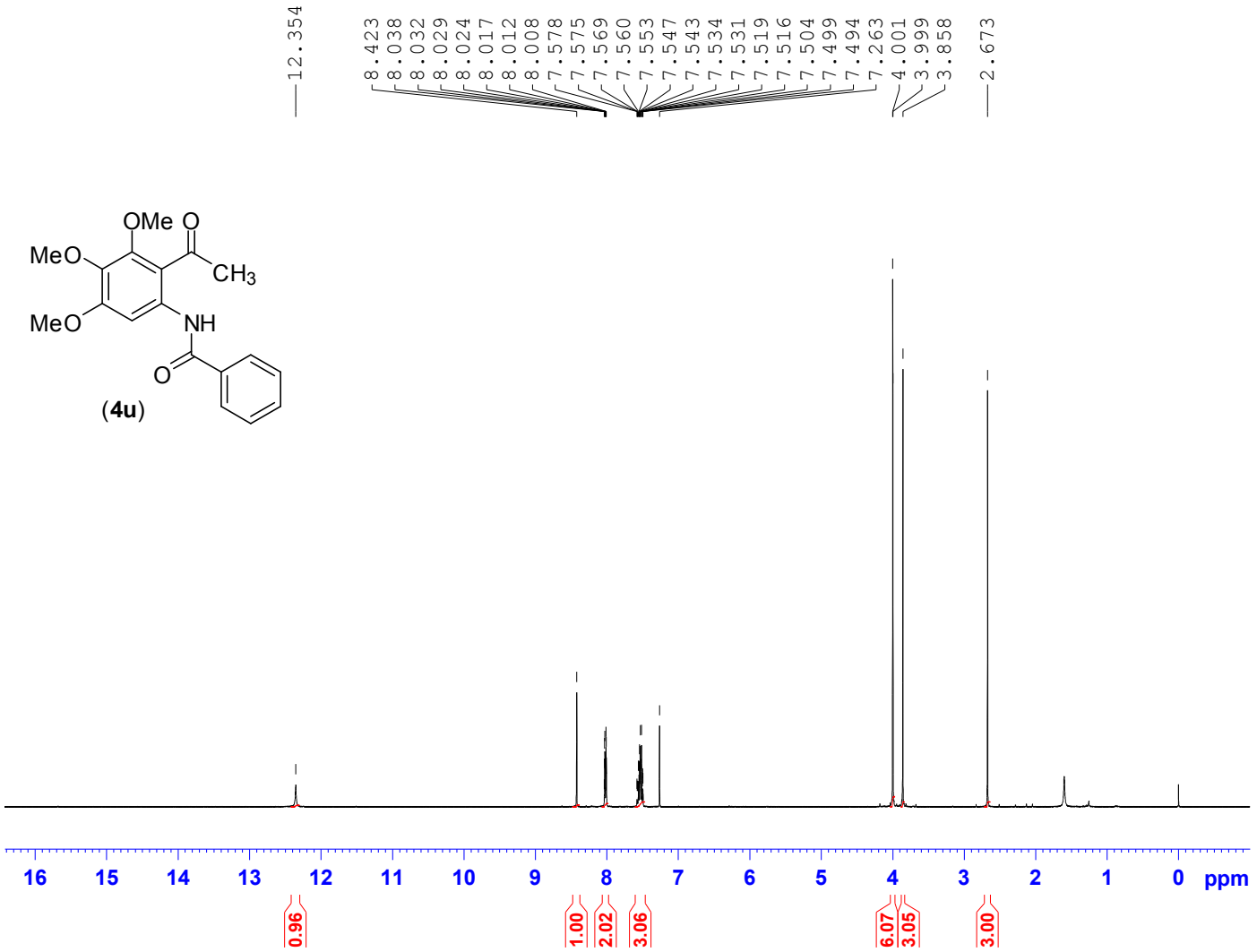

203.44
165.02
141.29
138.35
135.50
133.25
131.88
129.09
128.94
122.72
121.99
120.84
77.34
77.02
76.70
28.60
O
CH3
NH
O
Cl
(4c)
200
180
160
140
120
100
80
60
40
20
0
ppm

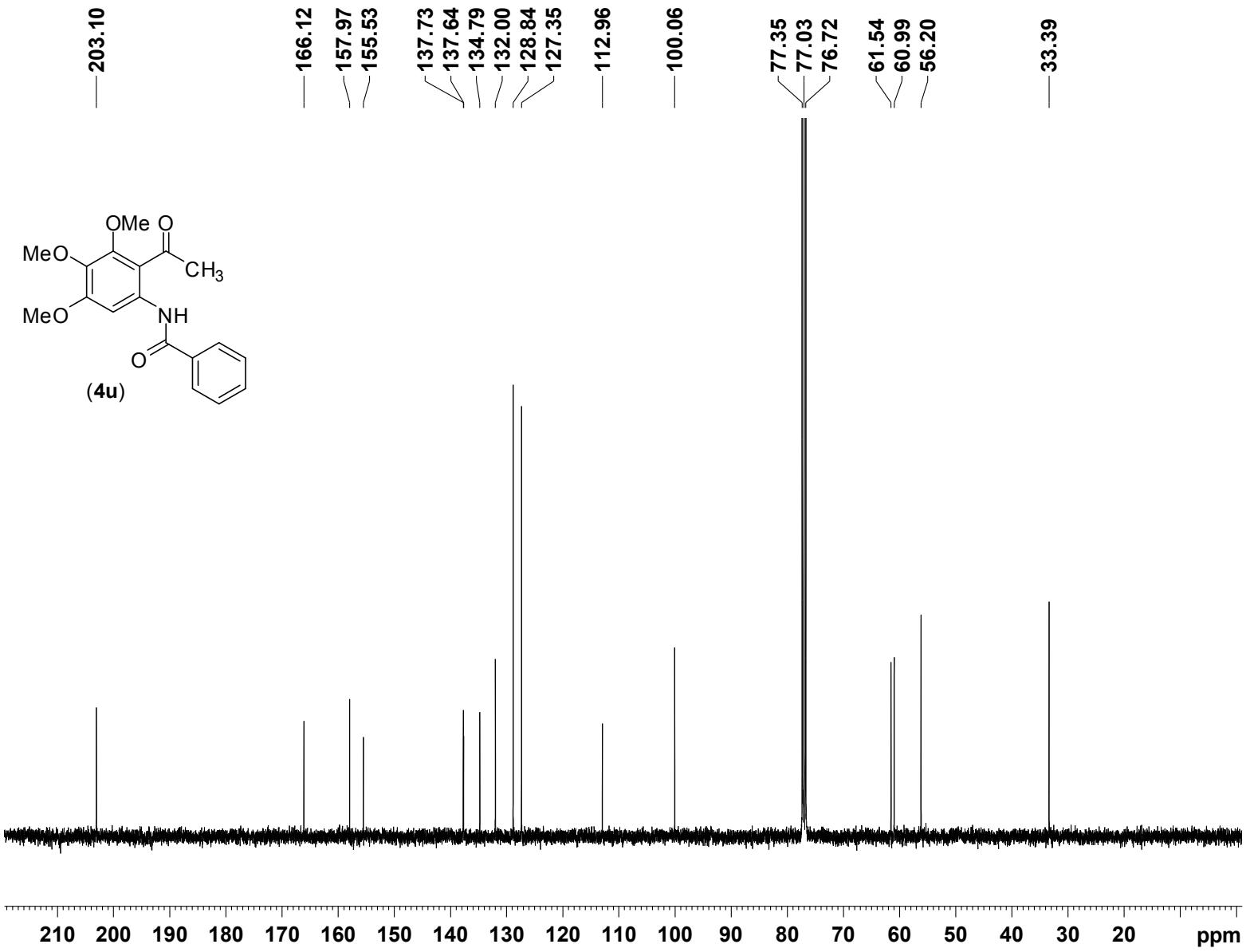

12.580
8.942
8.919
8.062
8.059
8.054
8.048
8.042
8.038
7.728
7.722
7.705
7.699
7.578
7.571
7.564
7.560
7.556
7.546
7.543
7.532
7.527
7.515
7.511
7.506
7.260
2.714
Br
O
CH3
NH
O
(4n)
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.01
3.09
1.02
3.05
3.03


202.10
166.08
140.44
137.99
134.52
134.24
132.20
128.87
127.50
123.49
122.69
114.76
77.32
77.00
76.69
28.58
Br
O
CH3
NH
O
(4n)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


12.879
8.268
8.262
8.060
8.057
8.041
8.037
7.537
7.531
7.512
7.261
6.248
6.242
3.929
3.899
2.639
OMe O
CH3
MeO
NH
O
(4s)
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.00
0.99
2.01
2.98
0.98
6.10
3.00


202.95
166.31
164.83
162.73
143.97
134.94
131.95
128.80
127.47
108.65
96.82
94.43
77.36
77.05
76.73
55.68
55.58
34.19
OMe O
CH3
MeO
NH
O
(4s)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


12.354
8.423
8.038
8.032
8.029
8.024
8.017
8.012
8.008
7.578
7.575
7.569
7.560
7.553
7.547
7.543
7.534
7.531
7.519
7.516
7.504
7.499
7.494
7.263
4.001
3.999
3.858
2.673
OMe O
MeO
CH3
MeO
NH
O
(4u)
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.96
1.00
2.02
3.06
6.07
3.05
3.00


203.10
166.12
157.97
155.53
137.73
137.64
134.79
132.00
128.84
127.35
112.96
100.06
77.35
77.03
76.72
61.54
60.99
56.20
33.39
OMe O
MeO
CH3
MeO
NH
O
(4u)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

References:

(1) Tang, B. X.; Song, R. J.; Wu, C. Y.; Liu, Y.; Zhou, M. B.; Wei, W. T.; Deng, G. B.; Yin, D. L.; Li, J. H. *J. Am. Chem. Soc*. **2010**, *132*, 8900.

(2) Itoh, t.; Ishikawa, H.; Hayashi, Y. *Org. Lett*. **2009**, *11*, 3854.

(3) Chowdhury, S.; Chafeev, M.; Liu, S.; Sun, J.; Raina, V.; Chui, R.; Young, W.; Kwan, R.; Fu, J.; Cadieux, J. A. *Bioorg. Med. Chem. Lett*. **2011**, *21*, 3676.

(4) Schmidt, M. S.; Perillo, I. A.; Gonzalez, M.; Blanco, M. M. *Tetrahedron Lett*. **2012**, *53*, 2514.

(5) Shimazawa, R.; Kuriyama, S.; Shirai, R. *Bioorg. Med. Chem. Lett*. **2008**, *18*, 3350.

(6) Huang, P. C.; Gandeepan, P.; Cheng, C. H. *Chem. Commun*. DOI: 10.1039/c3cc44435J.

(7) Beauchard, A.; Ferandin, Y.; Frere, S.; Lozach, O.; Blairvacq, M.; Meijer, L.; Thiery, V.; Besson, T. *Bioorg. Med. Chem.* **2006**, *14*, 6434.

(8) Aboul-Fadl, T.; Bin-Jubair, F. A. S.; Aboul-wafa, O. *Eur. J. Med. Chem*. **2010**, *45*, 4578.

(9) Vyas, D. J.; Frohlich, R.; Oestreich, M. *J. Org. Chem*. **2010**, *75*, 6720.

(10) Zhou, L.; Liu, Y.; Zhang, W.; Wei, P.; Huang, C.; Pei, J.; Yuan, Y.; Lai, L. *J. Med. Chem*. **2006**, *49*, 3440.

(11) Marques, E. F.; Bueno, M. A.; Duarte, P. D.; Silva, L. R. S. P.; Martinelli, A. M.; Dos Santos, C. Y.; Severino, R. P.; Bromme, D.; Vieira, P. C.; Correa, A. G. *Eur. J. Med. Chem*. **2012**, *54*, 10.

(12) Mphahlele, M. J.; El-Nahas, A. M. *J. Mol. Str*. **2004**, *688*, 129.

(13) Takemoto, M.; Iwakiri, Y.; Tanaka, K. *Heterocycles*, **2007**, *72*, 373.

(14) Hadjeri, M.; Mariotte, A. M.; Boumendjel, A. *Chem. Pharm. Bull*. **2011**, *49*, 1352.