Electronic Supplementary Material (ESI) for Chemical Science
This journal is © The Royal Society of Chemistry 2012

Rhodium(III)-Catalyzed Synthesis of Phthalides by Cascade Addition and Cyclization of Benzimidates with Aldehydes

Yajing Lian, Robert G. Bergman,* Jonathan A. Ellman*

Supporting Information

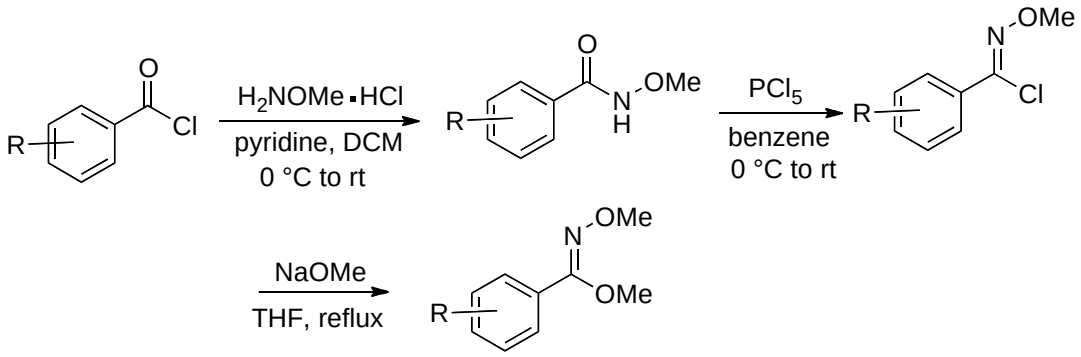
This journal is © The Royal Society of Chemistry 2012

I. General Information

Unless noted, all catalytic reactions were set up inside an inert atmosphere (N_2) glovebox utilizing glassware that was oven-dried (150 ^oC) and evacuated while hot prior to use, whereas the work-up and isolation of the products from the catalytic reactions were conducted on the bench-top using standard techniques. Dichloroethane and other solvents were passed through a column of activated alumina under nitrogen and were stored in a glovebox over activated 4 Å molecular sieves prior to use. Chloroform-d_1 (Cambridge Isotopes) was used as received. All aldehydes were freshly distilled or purified by flash column chromatography before use. Unless otherwise noted, all other reagents and materials were obtained from commercial suppliers and used without further purification. $[Cp^*RhCl_2]_2$[1] and *N*-methoxybenzimidates[2] were synthesized according to published procedures. Chromatography was performed on Merck 60 230-240 mesh silica gel. ^1H and $^{13}C\{1H\}$ NMR characterization data were collected at 300K on a Bruker AV-500 spectrometer operating at 500.1 and 125.8 MHz (respectively) with chemical shifts reported in parts per million relative to $CHCl_3$ (^1H NMR; 7.26 ppm, $^{13}C\{1H\}$ NMR; 77.00 ppm). IR spectra were recorded on a Nicolet 6700 FTIR spectrometer and only partial data are provided. Melting points were determined on a Mel-Temp apparatus and are reported uncorrected. Mass spectra (HRMS) were obtained by the Keck Center of Yale University using a Bruker 9.4 TAPEXQe FT-ICR mass spectrometer.

This journal is © The Royal Society of Chemistry 2012

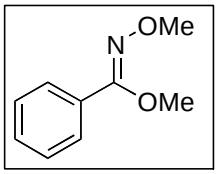
II. Preparation of starting materials



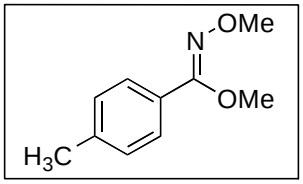
General Procedure for Preparation *N*-Methoxybenzimidates: To a 250 mL round-bottom flask was added O-methylhydroxylamine hydrochloride (2.00 g, 24.0 mmol, 1.2 equiv) and a stir bar, and the flask was then fitted with a rubber septum. The flask was purged with nitrogen followed by the addition of anhydrous CH_2Cl_2 (100 mL) and the aroyl chloride (20.0 mmol, 1.0 equiv). The mixture was cooled to 0 °C in an ice-water bath. Pyridine (4.83 mL, 60 mmol, 3.0 equiv) was added slowly with stirring, and the solution was allowed to warm to rt overnight. The reaction was quenched with water (300 mL), and the resulting mixture was extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined and dried over $MgSO_4$ followed by removal of the solvent under reduced pressure and then at high vacuum for 2 h to remove any residual pyridine. The white solid or viscous oil was transferred to a 100 mL oven-dried round-bottom flask with a stir bar, and dried benzene (60 mL) was added. The solution was cooled to 5 °C, and PCl_5 (6.25 g, 30.0 mmol, 1.5 equiv) was added in one portion. The heterogeneous mixture was stirred at 5 °C for 2 h and then allowed to warm to rt. The solution was poured into a separatory funnel containing hexane (150 mL) and water (150 mL). The organic layer was washed with additional water (150 mL) and brine (150 mL) and then dried over $MgSO_4$ followed by removal of solvent under reduced pressure. The pale yellow residue was then dissolved in dry THF (150 mL) in a round-bottom flask with a stir bar, and sodium methoxide (5.40 g, 100 mmol, 5.0 equiv) was added in one portion. The heterogeneous solution was heated to reflux with stirring overnight. The mixture was cooled to rt and poured into a separatory funnel containing ether (150 mL) and water (150 mL). The organic layer was washed with additional water (150 mL) and brine (150

This journal is © The Royal Society of Chemistry 2012

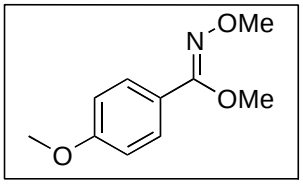
mL) and then dried over $MgSO_4$ followed by removal of solvent under reduced pressure. The residue was purified by flash column chromatography with hexane/EtOAc on silica gel to afford the benzimidates as colorless oils.



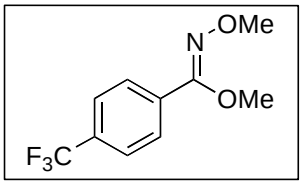
(*Z*)-methyl *N*-methoxybenzimidate (3a): Derived from benzoyl chloride (2.81 g, 20.0 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1) as eluent afforded the product (2.51 g, 76% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[3]



(*Z*)-methyl *N*-methoxy-4-methylbenzimidate (3b): Derived from 4-methylbenzoyl chloride (3.09 g, 20.0 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1) as eluent afforded the product (3.04 g, 85% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[3]



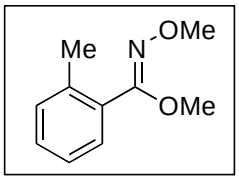
(*Z*)-methyl *N*,4-dimethoxybenzimidate (3c): Derived from 4-methoxybenzoyl chloride (3.41 g, 20.0 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1) as eluent afforded the product (2.89 g, 74% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[4]



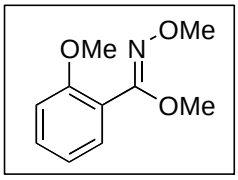
(*Z*)-methyl *N*-methoxy-4-(trifluoromethyl)benzimidate (3d): Derived from 4-(trifluoromethyl)benzoyl chloride (2.09 g, 10.0 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1) as eluent afforded the product (1.66 g, 72% yield) as a colorless oil. IR (film): 2944, 1613, 1315, 1165, 1122, 1105, 1049, 1015, 981, 845 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 4.02 (s, 3H), 3.94 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 153.4,

This journal is © The Royal Society of Chemistry 2012

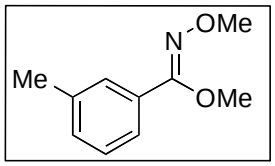
134.5, 131.7 (q, J = 32.6 Hz), 127.2, 125.3 (q, J = 3.8 Hz), 123.9 (q, J = 272.3 Hz), 62.6, 59.9; HRMS (ESI/$[M+H]^+$) calcd. for $C_{10}H_{11}F_3NO_2$: 234.0736. Found: 234.0734.



(*Z*)-methyl *N*-methoxy-2-methylbenzimidate (3e): Derived from 2-methylbenzoyl chloride (3.09 g, 20.0 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1) as eluent afforded the product (2.81 g, 78% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[3]



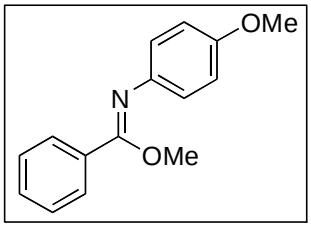
(*Z*)-methyl *N*,2-dimethoxybenzimidate (3f): Derived from 4-methoxybenzoyl chloride (3.41 g, 20.0 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (15/1) as eluent afforded the product (3.03 g, 78% yield) as a colorless oil. IR (film): 2947, 1628, 1600, 1459, 1326, 1244, 1097, 1055, 1044, 882, 753 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.44 (t, J = 7.4 Hz, 1H), 7.42 (d, J = 7.4 Hz, 1H), 6.99 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 7.4 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.63 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 157.7, 155.3, 131.9, 131.6, 120.8, 118.2, 110.7, 62.2, 56.7, 55.5; HRMS (ESI/$[M+H]^+$) calcd. for $C_{10}H_{14}NO_3$: 196.0968. Found: 196.0967.



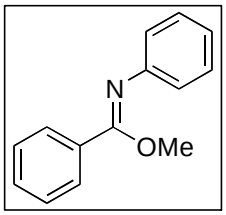
(*Z*)-methyl *N*-methoxy-3-methylbenzimidate (3g): Derived from 3-methylbenzoyl chloride (3.09 g, 20.0 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (15/1) as eluent afforded the product (2.93 g, 82% yield) as a colorless oil. IR (film): 2941, 1604, 1442, 1317, 1204, 1051, 1006, 981, 789 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.46 (s, 1H), 7.43 (d, J = 7.4 Hz, 1H), 7.28 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 7.4 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 155.7, 138.2, 130.8, 130.1, 128.3, 127.9, 124.5, 62.4, 59.2, 21.3; HRMS (ESI/$[M+H]^+$) calcd. for $C_{10}H_{14}NO_2$: 180.1019. Found: 180.1017.

This journal is © The Royal Society of Chemistry 2012

General Procedure of making *N*-arylbenzimidates: To a 100 mL round-bottom flask with the aid of Dean-Stark apparatus was added anilines (22.0 mmol, 1.1 equiv), trimethyl orthobenzoate (3.64 g, 20.0 mmol, 1.0 equiv) and *p*-toluenesulfonic acid (150 mg, 0.0100 mmol, 0.05 equiv) in toluene (75 mL) with a stir bar. After being heated with stirring under reflux overnight, the reaction mixture was cooled to rt and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography using hexane/EtOAc containing 0.5% of Et_3N as eluent to afford the desired arylbenzimidates.

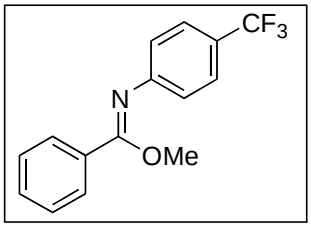


(*Z*)-methyl *N*-(4-methoxyphenyl)benzimidate (7a): Derived from 4-methoxyaniline (1.86 g, 22.0 mmol, 1.1 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1 with 0.5% Et_3N) as eluent afforded the product (3.91 g, 81% yield) as a pale yellowish oil. IR (film): 1653, 1503, 1432, 1269, 1234, 1175, 1113, 1028, 830 cm^{-1}; ^1H NMR (CD_2Cl_2): δ 7.24-7.37 (m, 5H), 6.72-6.76 (m, 2H), 6.59-6.64 (m, 2H), 3.90 (s, 3H), 3.70 (s, 3H), 3; $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ 184.2, 180.5, 166.8, 156.9, 154.7, 154.2, 152.9, 147.4, 139.0, 79.7, 78.1; HRMS (ESI/$[M+H]_+$) calcd. for $C_{15}H_{15}NO_2$: 242.1176 Found: 242.1170.



(*Z*)-methyl *N*-phenylbenzimidate (8a): Derived from aniline (1.86 g, 22.0 mmol, 1.1 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1 with 0.5% Et_3N) as eluent afforded the product (3.30 g, 78% yield) as a pale yellowish oil. The analytical data for this compound are consistent with previously reported data.[5]

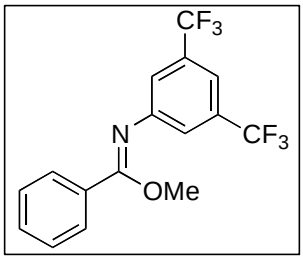
dd



(*Z*)-methyl *N*-(4-trifluoromethylphenyl)benzimidate (9a): Derived from 4-trifluoromethylaniline (3.55 g, 22.0 mmol, 1.1 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1 with 0.5% Et_3N) as eluent afforded the product (3.85 g, 69% yield) as a white powder (mp: 47-49 °C). IR (film): 1661, 1610, 1600, 1324, 1297, 1275, 1158, 1101, 1062, 844, 694 cm^{-1}; ^1H NMR (CD_2Cl_2): δ 7.47 (d, J = 7.8 Hz, 2H), 7.22-7.37 (m, 5H), 6.86 (d, J = 7.8 Hz, 2H),

This journal is © The Royal Society of Chemistry 2012

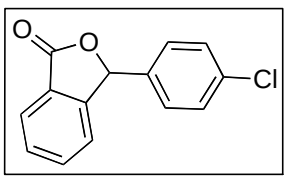
3.92 (s, 3H); $^{13}C\{^{1}H\}$ NMR (CD_2Cl_2): δ 185.1, 177.6, 156.1, 155.3, 154.2, 153.1, 151.0 (q, *J* = 3.8 Hz), 149.8 (q, *J* = 268.9 Hz), 148.8 (q, *J* = 31.9 Hz), 147.0, 78.7; HRMS (ESI/$[M+H]^+$) calcd. for $C_{15}H_{12}F_3NO$: 280.0944 Found: 280.0934.



(*Z*)-methyl *N*-(3,5-bis(trifluoromethyl)phenyl)benzimidate (10a): Derived from 3,5-bis(trifluoromethyl)aniline (3.55 g, 22.0 mmol, 1.1 equiv). Purification by silica gel column chromatography using hexane/EtOAc (20/1 with 0.5% Et_3N) as eluent afforded the product (5.81 g, 76% yield) as a white powder (mp: 40-41 °C). IR (film): 1648, 1376, 1273, 1239, 1167, 1118, 962, 883, 775 cm^{-1}; ^{1}H NMR (CD_2Cl_2): δ 7.48 (s, 1H), 7.35-7.40 (m, 1H), 7.24-7.30 (m, 4H), 7.16 (s, 2H), 4.00 (s, 3H); $^{13}C\{^{1}H\}$ NMR (CD_2Cl_2): δ 162.2, 150.9, 132.5 (q, *J* = 32.9 Hz), 131.2, 130.8, 129.7, 128.9, 124.0 (q, *J* = 272.5 Hz), 122.7 (m), 116.5 (hept, *J* = 4.0 Hz), 55.1; HRMS (ESI/$[M+H]^+$) calcd. for $C_{16}H_{11}F_6NO$: 348.0818 Found: 348.0804.

III. Rh(III)-catalyzed C-H activation and addition to aromatic aldehydes

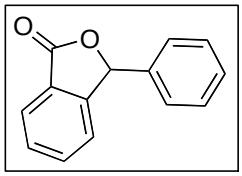
General procedure: In a N_2-filled glovebox, $[Cp^*RhCl_2]_2$ (6.2 mg, 0.010 mmol, 0.05 equiv), $AgSbF_6$ (13.7 mg, 0.0400 mmol, 0.2 equiv), the benzimidates (0.200 mmol, 1.0 equiv) and the corresponding aldehydes (0.40 mmol, 2.0 equiv) were added to a screw-capped conical vial with a stir bar followed by addition of DCE (1.0 mL, [benzimidate] = 0.2 M). The vial was sealed with a cap containing a PTFE septum and was removed from the glovebox. The reaction vial was then placed in a temperature-controlled oil bath at 110 °C. After 20 h of stirring, the vial was removed from the oil bath and was cooled to ambient temperature. The mixture was directly loaded onto a silica gel column for chromatographic purification.



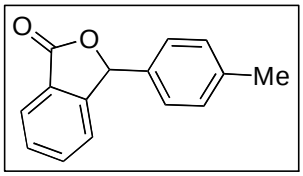
3-(4-chlorophenyl)isobenzofuran-1(3*H*)-one (6a): Derived

This journal is © The Royal Society of Chemistry 2012

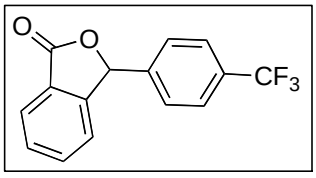
from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and 4-chlorobenzaldehyde (56.2 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6a** (37.2 mg, 76% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[6]



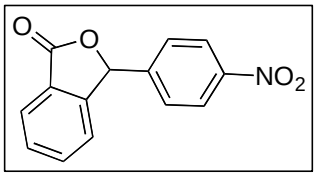
3-phenylisobenzofuran-1(3*H*)-one (6b): Derived from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and benzaldehyde (42.5 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6b** (29.0 mg, 69% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[6]



3-(*p*-tolyl)isobenzofuran-1(3*H*)-one (6c): Derived from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and *p*-tolualdehyde (48.1 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6c** (28.7 mg, 64% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[6]



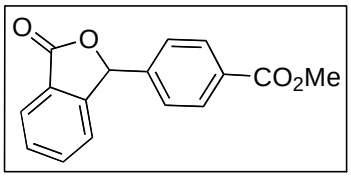
3-(4-(trifluoromethyl)phenyl)isobenzofuran-1(3*H*)-one (6d): Derived from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and 4-trifluoromethylbenzaldehyde (69.7 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6d** (46.7 mg, 84% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[7]



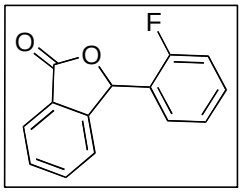
3-(4-nitrophenyl)isobenzofuran-1(3*H*)-one (6e): Derived

This journal is © The Royal Society of Chemistry 2012

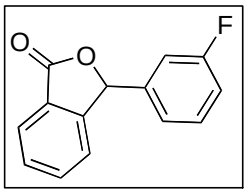
from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and 4-nitrobenzaldehyde (60.4 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (7/3) as eluent afforded product **6e** (41.4 mg, 84% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[8]



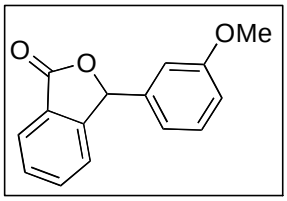
methyl 4-(3-oxo-1,3-dihydroisobenzofuran-1-yl)benzoate (6f): Derived from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and methyl 4-formylbenzoate (65.7 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (7/3) as eluent afforded product **6f** (41.9 mg, 78% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[9]



3-(2-fluorophenyl)isobenzofuran-1(3*H*)-one (6g): Derived from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and 2-fluorobenzaldehyde (49.6 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6g** (32.4 mg, 71% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[10]

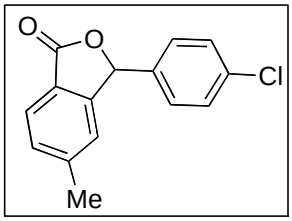


3-(3-fluorophenyl)isobenzofuran-1(3*H*)-one (6h): Derived from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and 3-fluorobenzaldehyde (49.6 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6h** (33.3 mg, 73% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[11]

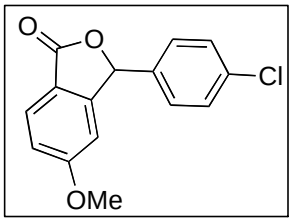


3-(3-methoxyphenyl)isobenzofuran-1(3*H*)-one (6i): Derived from $[Cp^*RhCl_2]_2$ (12.4 mg, 0.0200 mmol, 0.10 equiv), $AgSbF_6$

(27.4 mg, 0.0800 mmol, 0.4 equiv), (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and 3-anisaldehyde (54.5 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (4/1) as eluent afforded product **6i** (25.5 mg, 53% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[7]

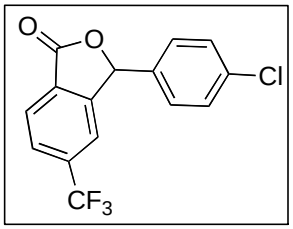


3-(4-chlorophenyl)-5-methylisobenzofuran-1(3*H*)-one (6j): Derived from (*Z*)-methyl *N*-methoxy-4-methylbenzimidate (**3b**) (35.8 mg, 0.200 mmol, 1.0 equiv) and 4-chlorobenzaldehyde (56.2 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6j** (40.4 mg, 78% yield) as a white powder (mp: 134-135 °C). IR (film): 1764, 1615, 1296, 1279, 1087, 1065, 983, 837, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.32-7.37 (m, 3H), 7.19-7.23 (m, 2H), 7.08 (m, 1H), 6.31 (s, 1H), 2.43 (s, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 170.2, 149.8, 145.8, 135.2, 135.1, 130.7, 129.1, 128.3, 125.4, 122.6, 122.8, 81.5, 22.0; HRMS (ESI/$[M+H]^+$) calcd. for $C_{15}H_{12}ClO_2$: 259.0520. Found: 259.0518.

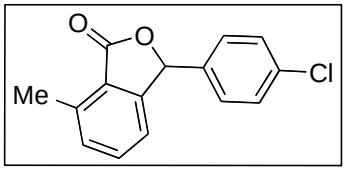


3-(4-chlorophenyl)-5-methoxyisobenzofuran-1(3*H*)-one (6k): Derived from (*Z*)-methyl *N*,4-dimethoxybenzimidate (**3c**) (39.1 mg, 0.200 mmol, 1.0 equiv) and 4-chlorobenzaldehyde (56.2 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (4/1) as eluent afforded product **6k** (43.4 mg, 79% yield) as a colorless powder (mp: 116-117 °C). IR (film): 1764, 1615, 1296, 1279, 1087, 1065, 983, 837, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.85 (d, *J* = 8.6 Hz, 1H), 7.33-7.37 (m, 2H), 7.19-7.23 (m, 2H), 7.05 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.69 (d, *J* = 2.2 Hz, 1H), 6.27 (s, 1H), 3.83 (s, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 169.9, 165.0, 152.0, 135.2, 135.1, 129.2, 128.4, 127.2, 117.7, 117.0, 106.5, 81.2, 55.8; HRMS (ESI/$[M+H]^+$) calcd. for $C_{15}H_{12}ClO_3$: 275.0469. Found: 275.0465.

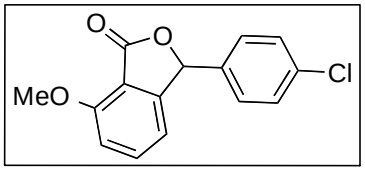
This journal is © The Royal Society of Chemistry 2012



3-(4-chlorophenyl)-5-(trifluoromethyl)isobenzofuran-1(3*H*)-one (6l): Derived from $[Cp^*RhCl_2]_2$ (12.4 mg, 0.0200 mmol, 0.10 equiv), $AgSbF_6$ (27.4 mg, 0.0800 mmol, 0.4 equiv), (*Z*)-methyl *N*-methoxy-4-(trifluoromethyl)benzimidate (**3d**) (46.6 mg, 0.200 mmol, 1.0 equiv) and 4-chlorobenzaldehyde (56.2 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6l** (16.9 mg, 27% yield) as a white powder (mp: 109-111 °C). IR (film): 1763, 1493, 1331, 1285, 1163, 1132, 1115, 1066, 982, 844, 774 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 1.3 Hz, 1H), 7.38-7.42 (m, 2H), 7.20-7.24 (m, 2H), 6.44 (s, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 168.7, 149.6, 136.6 (q, *J* = 33.1 Hz), 135.9, 133.8, 129.5, 128.7, 128.3, 127.0 (q, *J* = 3.5 Hz), 126.6, 123.1 (q, *J* = 273.3 Hz), 120.2 (q, *J* = 3.8 Hz), 81.9; HRMS (ESI/[M+H]+) calcd. for $C_{15}H_9ClF_2O_2$: 313.0238. Found: 313.0235.



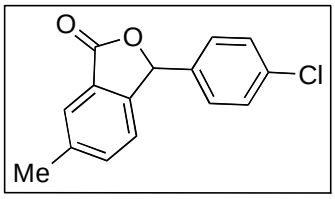
3-(4-chlorophenyl)-7-methylisobenzofuran-1(3*H*)-one (6m): Derived from $[Cp^*RhCl_2]_2$ (12.4 mg, 0.0200 mmol, 0.10 equiv), $AgSbF_6$ (27.4 mg, 0.0800 mmol, 0.4 equiv), (*Z*)-methyl *N*-methoxy-2-methylbenzimidate (**3e**) (35.8 mg, 0.200 mmol, 1.0 equiv) and 4-chlorobenzaldehyde (56.2 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6m** (31.5 mg, 61% yield) as a white powder (mp: 116-118 °C). IR (film): 1751, 1600, 1491, 1480, 1287, 1206, 1088, 1005, 758 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.50 (t, *J* = 7.6 Hz, 1H), 7.33-7.36 (m, 2H), 7.30 (dm, *J* = 7.6 Hz, 1H), 7.20-7.23 (m, 2H), 7.09 (dm, *J* = 7.6 Hz, 1H), 6.29 (s, 1H), 2.74 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 170.4, 149.7, 139.8, 135.4, 135.1, 134.1, 131.1, 129.1, 128.3, 122.9, 120.1, 80.9, 17.4; HRMS (ESI/[M+H]+) calcd. for $C_{15}H_{12}ClO_2$: 259.0520. Found: 259.0517.



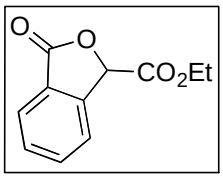
3-(4-chlorophenyl)-7-methoxyisobenzofuran-1(3*H*)-one (6n): Derived from $[Cp^*RhCl_2]_2$ (12.4 mg, 0.0200 mmol,

This journal is © The Royal Society of Chemistry 2012

0.10 equiv), $AgSbF_6$ (27.4 mg, 0.0800 mmol, 0.4 equiv), (*Z*)-methyl *N*,2-dimethoxybenzimidate (**3f**) (39.1 mg, 0.200 mmol, 1.0 equiv) and 4-chlorobenzaldehyde (56.2 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (4/1) as eluent afforded product **6n** (36.8 mg, 67% yield) as a white powder (mp: 147-149 °C). IR (film): 1772, 1758, 1601, 1413, 1290, 1234, 1196, 1064, 1026, 985 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.58 (t, *J* = 7.6 Hz, 1H), 7.32-7.35 (m, 2H), 7.19-7.23 (m, 2H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.27 (s, 1H), 4.01 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 168.2, 158.5, 151.9, 136.6, 135.2, 135.1, 129.1, 128.2, 114.3, 112.8, 111.0, 80.7, 56.1; HRMS (ESI/$[M+H]^+$) calcd. for $C_{15}H_{12}ClO_3$: 275.0469. Found: 275.0466.



3-(4-chlorophenyl)-6-methylisobenzofuran-1(3*H*)-one (6o): Derived from (*Z*)-methyl *N*-methoxy-3-methylbenzimidate (**3g**) (35.8 mg, 0.200 mmol, 1.0 equiv) and 4-chlorobenzaldehyde (56.2 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6o** (37.7 mg, 73% yield) as a white powder (mp: 121-122 °C). IR (film): 1758, 1490, 1287, 1157, 1056, 1001, 769 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.74 (s, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.31-7.36 (m, 2H), 7.16-7.22 (m, 3H), 6.33 (s, 1H), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 170.3, 146.6, 139.9, 135.6, 135.2, 135.1, 129.1, 128.3, 125.6 (2C), 122.4, 81.7, 21.2; HRMS (ESI/$[M+H]^+$) calcd. for $C_{15}H_{12}ClO_2$: 259.0520. Found: 259.0517.



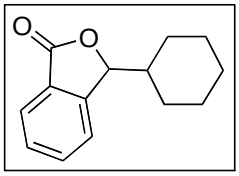
ethyl 3-oxo-1,3-dihydroisobenzofuran-1-carboxylate (6p): Derived from (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv) and ethyl glyoxalate (50% solution in toluene) (81.7 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (4/1) as eluent afforded product **6p** (30.5 mg, 74% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[11]

This journal is © The Royal Society of Chemistry 2012

IV. Rh(III)-catalyzed C-H activation and addition to aliphatic aldehydes

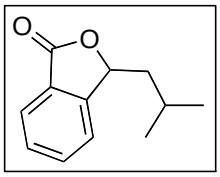
General procedure A: In a N_2-filled glovebox, $[Cp^*RhCl_2]_2$ (12.4 mg, 0.0200 mmol, 0.10 equiv), $AgSbF_6$ (27.4 mg, 0.0800 mmol, 0.4 equiv), K_2CO_3 (13.8 mg, 0.100 mmol, 0.5 equiv), the (*Z*)-methyl *N*-methoxybenzimidate (33.4 mg, 0.200 mmol, 1.0 equiv) and the corresponding aldehyde (0.400 mmol, 2.0 equiv) were added to a screw-capped conical vial with a stir bar followed by addition of DCE (1.0 mL, [benzimidate] = 0.2 M). The vial was sealed with a cap containing a PTFE septum and was removed from the glovebox. The reaction vial was then placed in a temperature-controlled oil bath at 110 °C. After 20 h of stirring, the vial was removed from the oil bath and was cooled to ambient temperature. The mixture was directly loaded onto a silica gel column for chromatographic purification.

General procedure B: In a N_2-filled glovebox, $[Cp^*RhCl_2]_2$ (12.4 mg, 0.0200 mmol, 0.10 equiv), $AgSbF_6$ (27.4 mg, 0.0800 mmol, 0.4 equiv), the (*Z*)-methyl *N*-(3,5-bis(trifluoromethyl)phenyl)benzimidate (**10a**)(69.5 mg, 0.200 mmol, 1.0 equiv) and the corresponding aldehyde (0.400 mmol, 2.0 equiv) were added to a screw-capped conical vial with a stir bar followed by addition of DCE (1.00 mL, [benzimidate] = 0.20 M). The vial was sealed with a cap containing a PTFE septum and was removed from the glovebox. The reaction vial was then placed in a temperature-controlled oil bath at 110 °C. After 20 h of stirring, the vial was removed from the oil bath and was cooled to ambient temperature. The mixture was directly loaded onto a silica gel column for chromatographic purification.

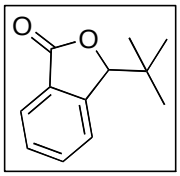


3-cyclohexylisobenzofuran-1(3*H*)-one (6q): General procedure **B** was followed using cyclohexanecarboxaldehyde (**2c**) (44.9 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6q** (28.1 mg, 65% yield) as a white powder. The analytical data for this compound are consistent with previously reported data.[9]

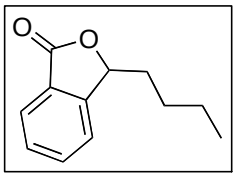
This journal is © The Royal Society of Chemistry 2012



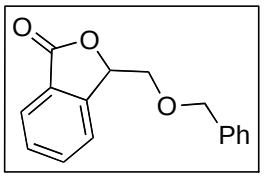
3-isobutylisobenzofuran-1(3*H*)-one (6r): General procedure **B** was followed using 3-methylbutanal (34.5 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6r** (30.1 mg, 79% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[9]



3-(*tert*-butyl)isobenzofuran-1(3*H*)-one (6s): General procedure **B** was followed using pivalaldehyde (34.5 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6s** (27.4 mg, 72% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[12]

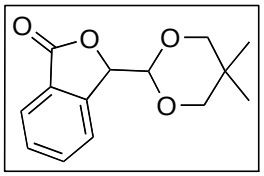


3-butylisobenzofuran-1(3*H*)-one (6t): General procedure **B** was followed using pentanal (34.5 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (10/1) as eluent afforded product **6t** (25.5 mg, 67% yield) as a colorless oil. The analytical data for this compound are consistent with previously reported data.[8]



3-((benzyloxy)methyl)isobenzofuran-1(3*H*)-one (6u): General procedure **A** was followed using 2-(benzyloxy)acetaldehyde (60.1 mg, 0.400 mmol, 2.0 equiv) and (*Z*)-methyl *N*-methoxybenzimidate (**3a**) (33.4 mg, 0.200 mmol, 1.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (4/1) afforded product **6u** (31.0 mg, 61% yield) as a colorless oil. IR (film): 1754, 1466, 1348, 1284, 1209, 1067, 1037, 921 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.91 (d, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.50–7.58 (m, 2H), 7.32–7.37 (m, 2H), 7.27–7.32 (m, 3H), 5.60 (t, *J* = 5.3 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 3.84 (d, *J* = 5.4 Hz, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 170.2, 147.3, 137.4, 133.9, 129.4, 128.4, 127.8, 127.6, 126.3,

125.7, 122.4, 79.8, 73.7, 70.8; HRMS (ESI/[M+H]+) calcd. for $C_{16}H_{15}O_3$: 255.1016. Found: 255.1012.



3-(5,5-dimethyl-1,3-dioxan-2-yl)isobenzofuran-1(3*H*)-one (6v): General procedure **B** was followed using 5,5-dimethyl-1,3-dioxane-2-carbaldehyde (57.7 mg, 0.400 mmol, 2.0 equiv). Purification by silica gel column chromatography using hexane/EtOAc (4/1) as eluent afforded product **6v** (41.7 mg, 84% yield) as a colorless oil. IR (film): 1763, 1467, 1393, 1285, 1129, 1077, 1036, 975, 718 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.89 (d, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 5.40 (d, *J* = 3.9 Hz, 1H), 4.79 (d, *J* = 3.9 Hz, 1H), 3.72 (dd, *J* = 11.2, 2.7 Hz, 1H), 3.54 (dd, *J* = 11.2, 2.7 Hz, 1H), 3.50 (d, *J* = 11.2 Hz, 1H), 3.38 (d, *J* = 11.2 Hz, 1H), 1.09 (s, 3H), 0.72 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 170.2, 145.8, 133.6, 129.4, 126.5, 125.3, 124.1, 99.5, 79.8, 77.3, 76.7, 30.4, 22.9, 21.6; HRMS (ESI/[M+H]+) calcd. for $C_{14}H_{17}O_3$: 249.1121. Found: 249.1117.

Reference:

1. White, C.; Thompson S. J.; Maitlis P. M. J. Chem. Soc., *Dalton Trans.* **1977**, 1654.
2. Miyata, O.; Koizumi, T.; Asai, H.; Iba, R.; Naito, T. *Tetrahedron*, **2004**, *60*, 3893.
3. Johnson, J. E.; Nalley, E. A.; Kunz, Y. K.; Springfield, J, R. *J. Org. Chem.* **1976**, *41*, 252.
4. Johnson, J. E.; Dolliver, D. D.; Yu, L.; Canseco, D. C.; McAllister, M. A.; Rowe, J. E. *J. Org. Chem.* **2004**, *69*, 2741.
5. Roychowdhury, A.; Kumar, V. V.; Bhaduri, A. P. *Synth. Commun.* **2006**, *36*, 715.
6. Ye, Z.; Qian, P.; Lv, G.; Luo, F.; Cheng, J. *J. Org. Chem.* **2010**, *75*, 6043.
7. Chang, H.; Jeganmohan, M.; Cheng, C. *Chem. Eur. J.* **2007**, *13*, 4356.
8. Phan, D. H. T.; Kim, B.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 15608.
9. Ogawa, Y.; Saiga, A.; Mori, M.; Shibata, T.; Takagi, K. *J. Org. Chem.* **2000**, *65*,

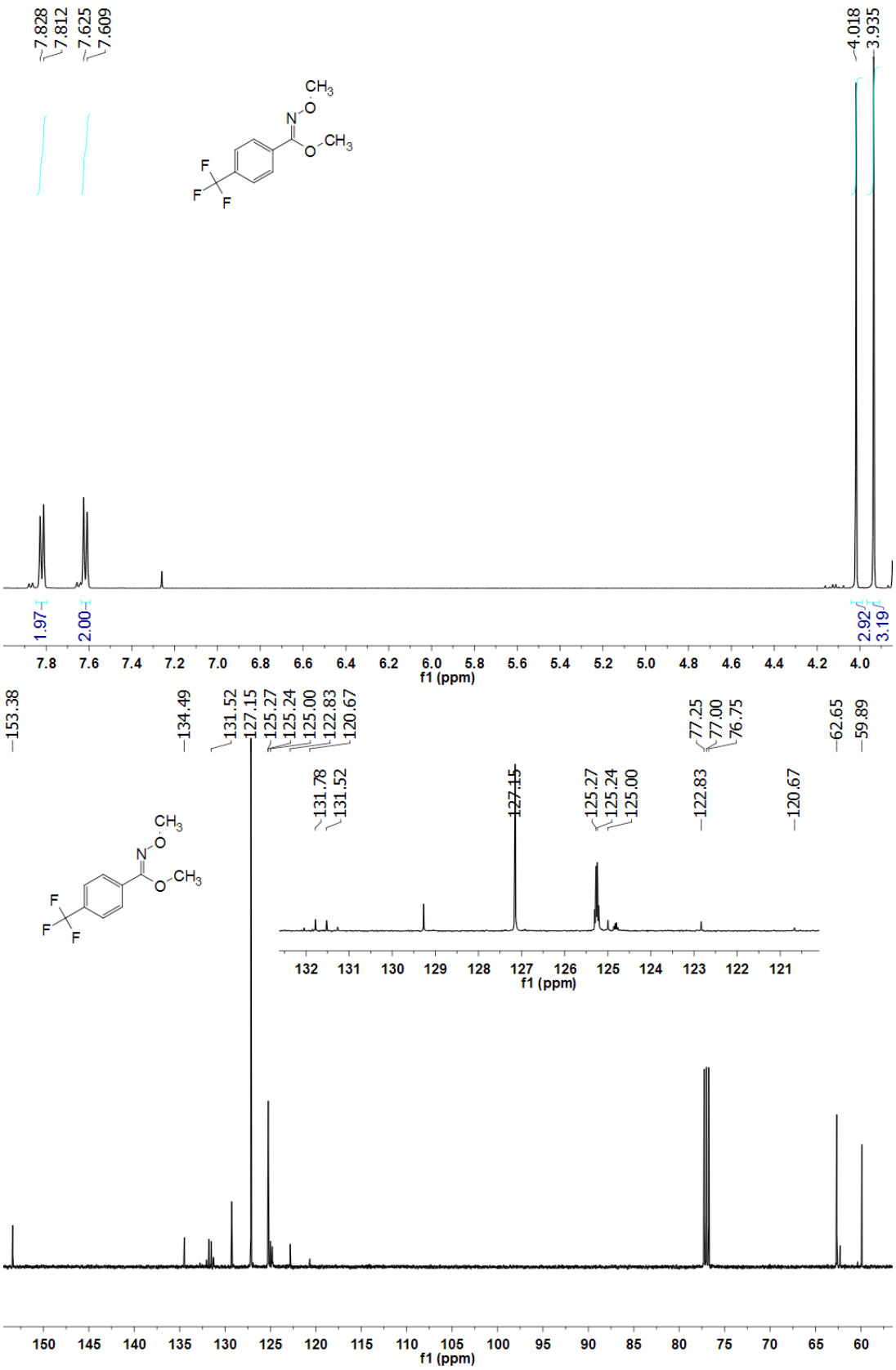
This journal is © The Royal Society of Chemistry 2012

1031.

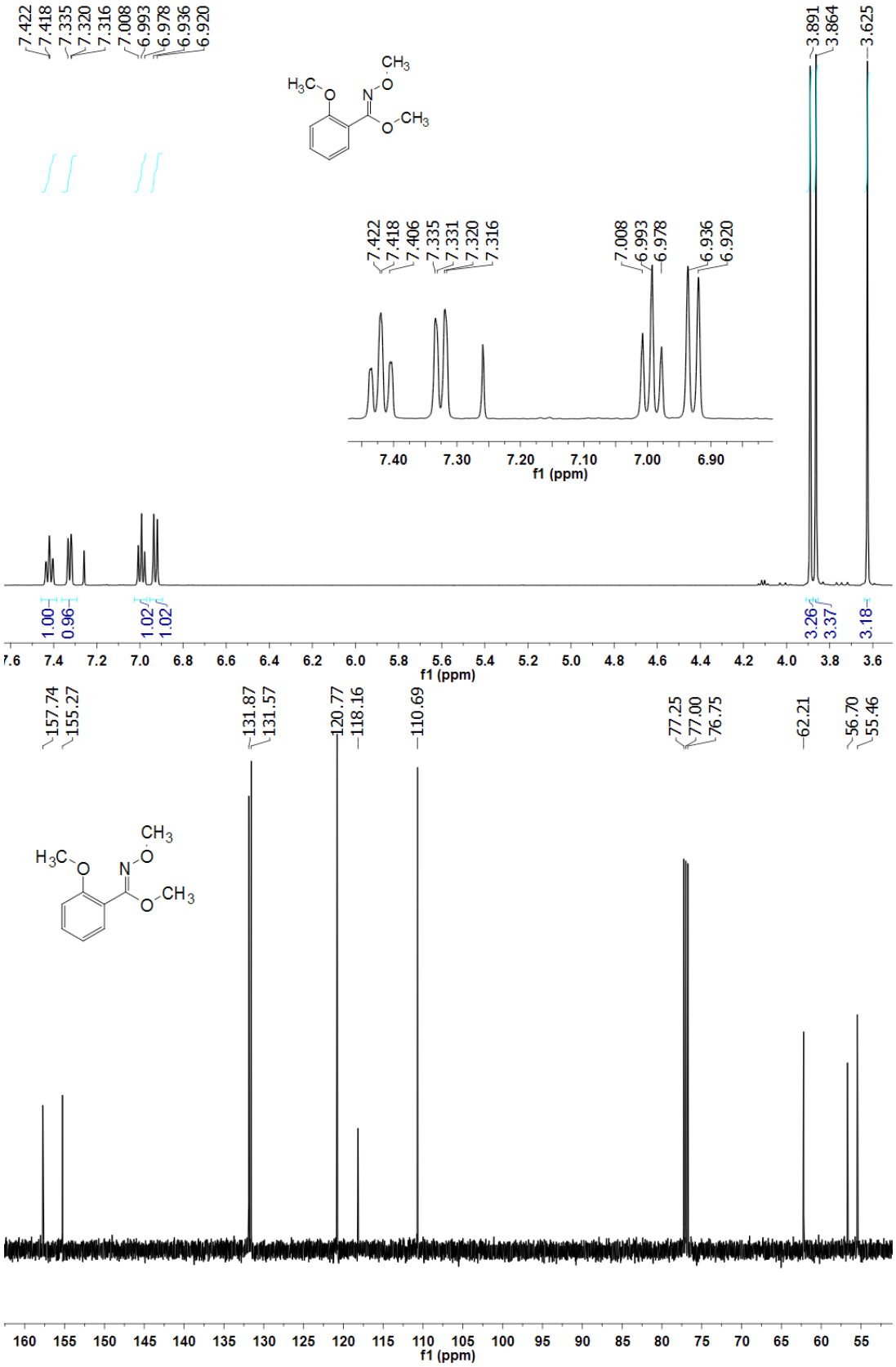
10. Kuriyama, M.; Ishiyama, N.; Shimazawa, R.; Shirai, R.; Onomura, O. *J. Org. Chem.* **2009**, *74*, 9210.
11. Karthikeyan, J.; Parthasarathy, K.; Cheng, C. *Chem. Commun.* **2011**, *47*, 10461.
12. Tatsugi, J.; Hara, T.; Izawa, Y. *Chem. Lett.* **1997**, *2*, 177.

^{1}H NMR and ^{13}C NMR of compound **3d**

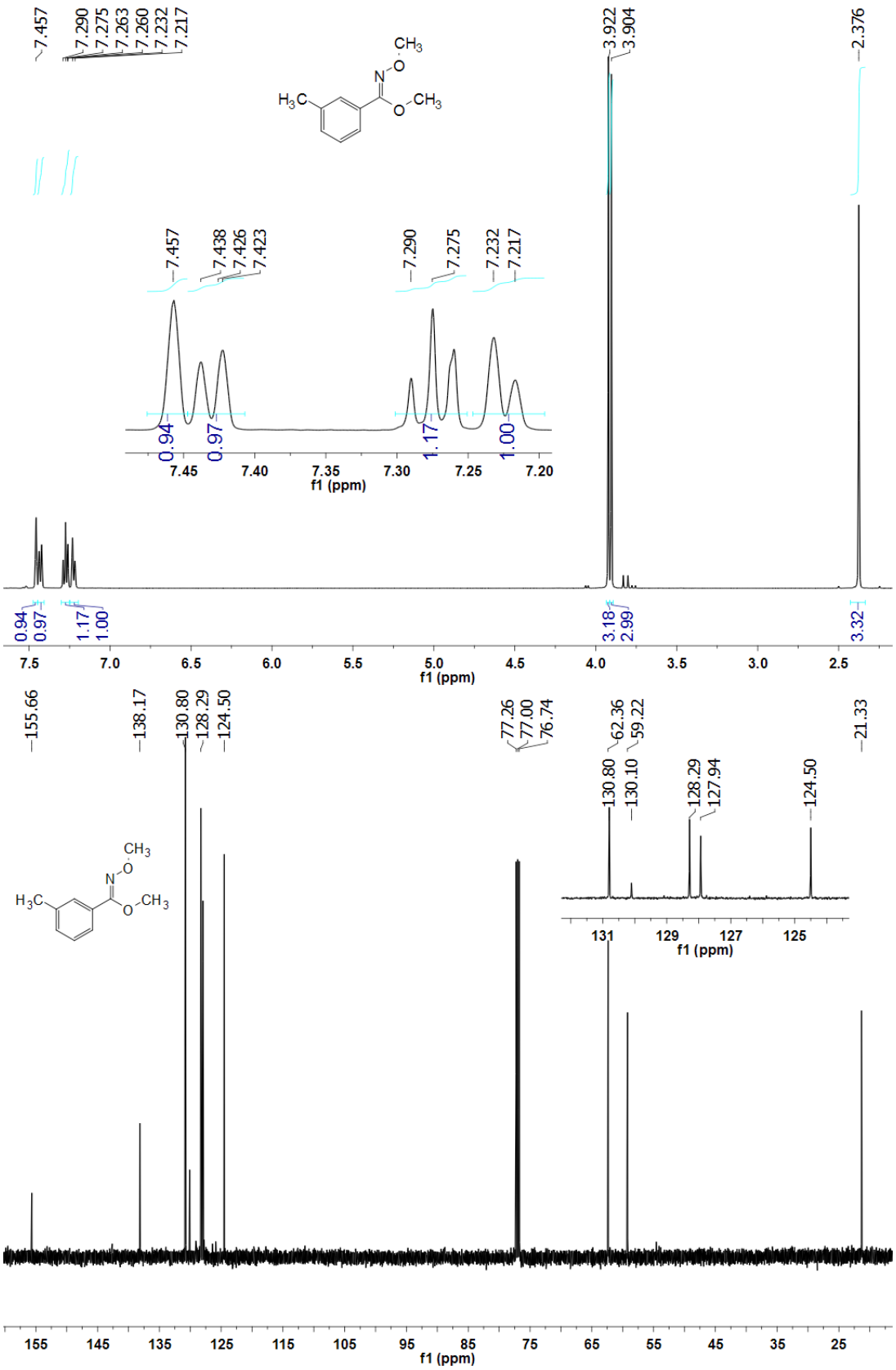
This journal is © The Royal Society of Chemistry 2012



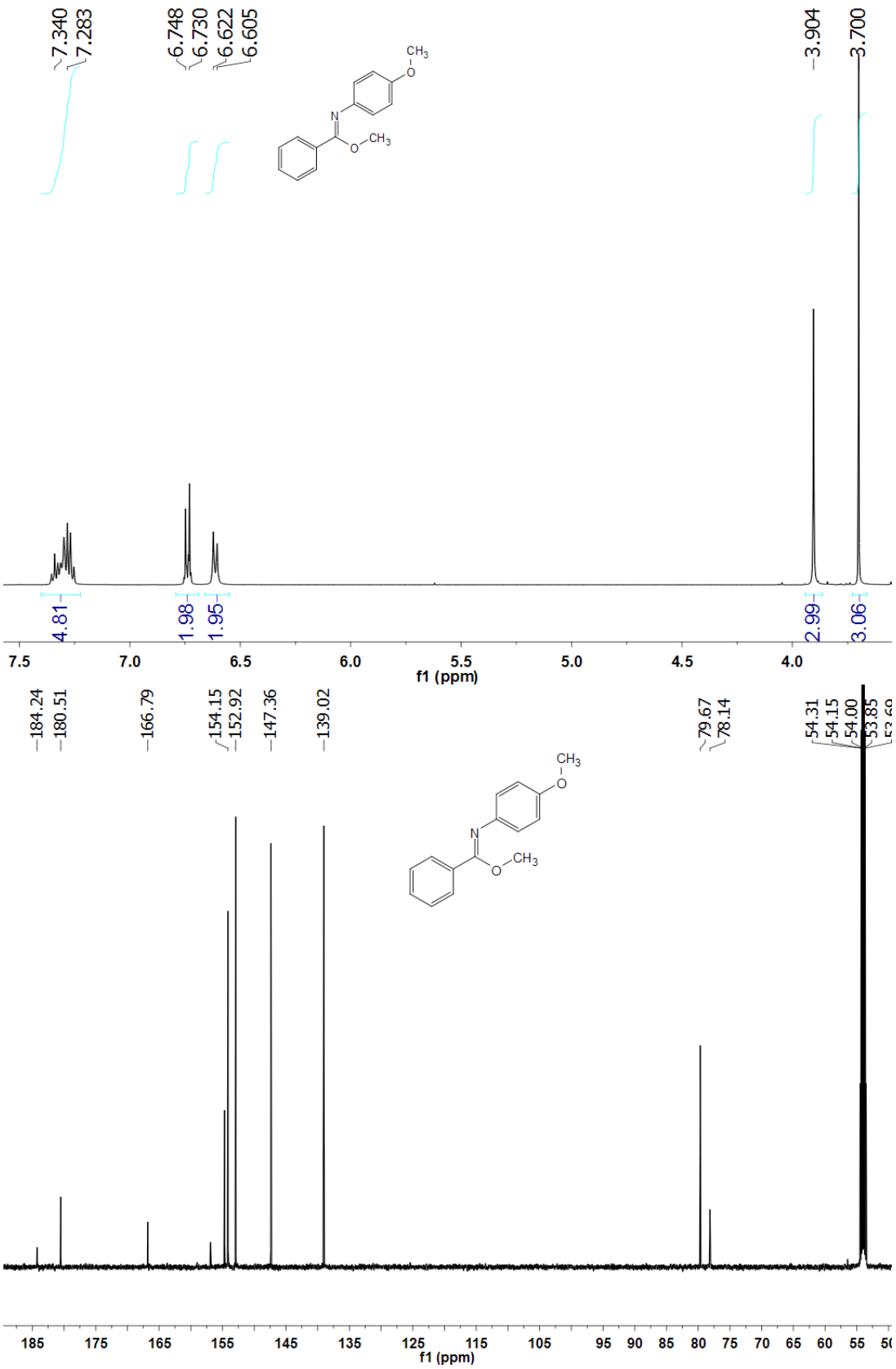
^{1}H NMR and ^{13}C NMR of compound **3f**



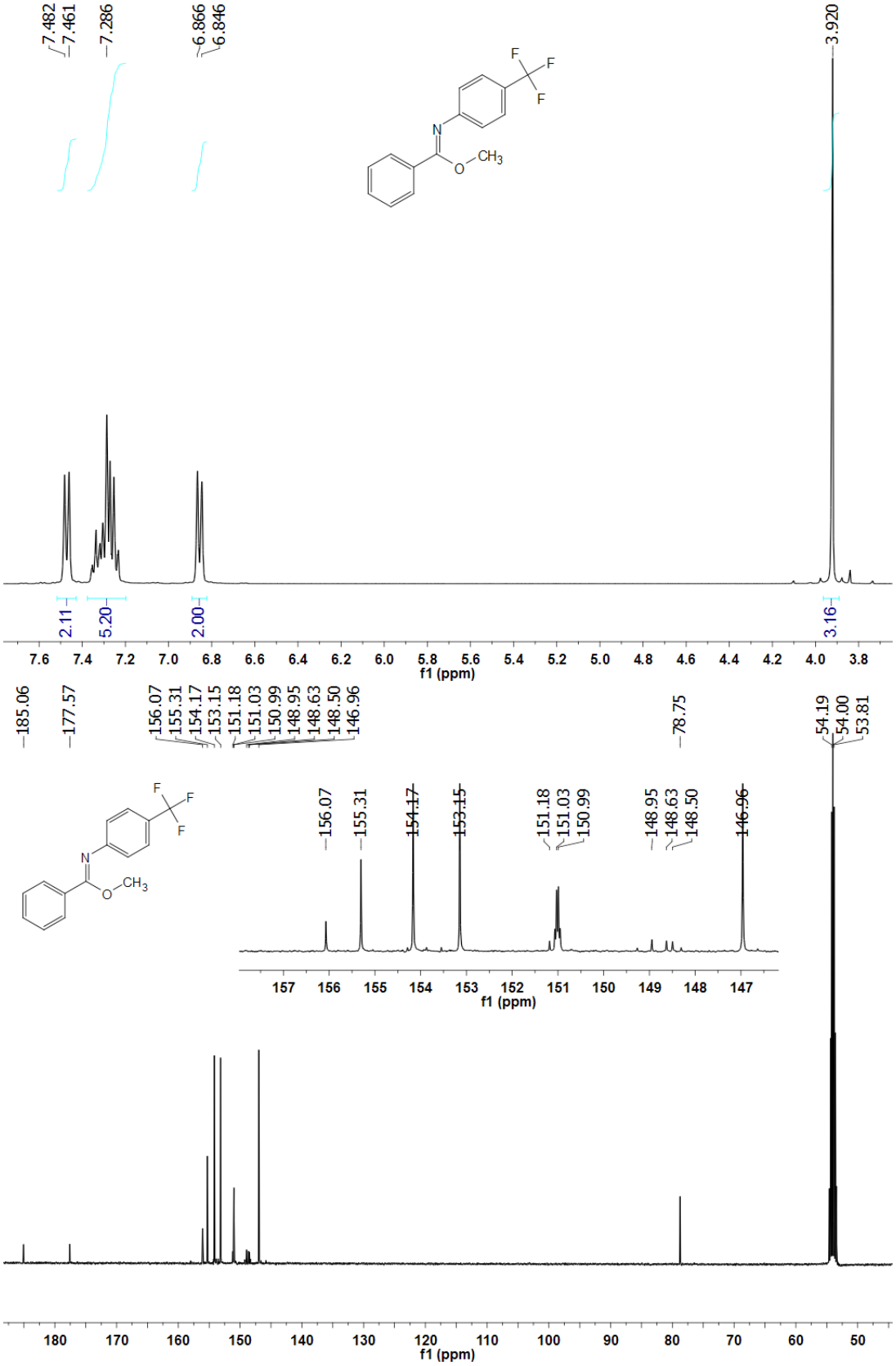
^{1}H NMR and ^{13}C NMR of compound **3g**



^{1}H NMR and ^{13}C NMR of compound **7a**

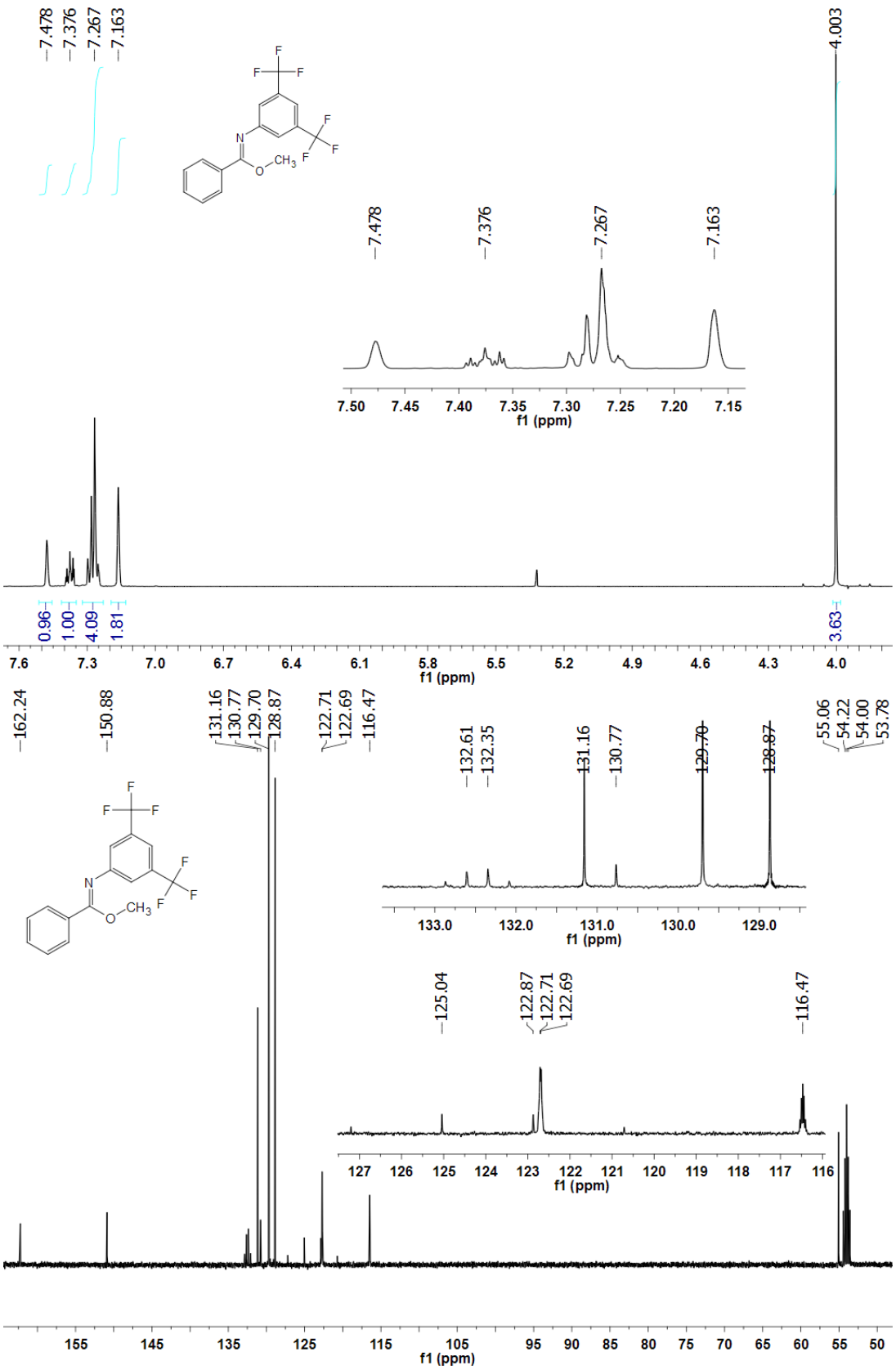


^{1}H NMR and ^{13}C NMR of compound **9a**



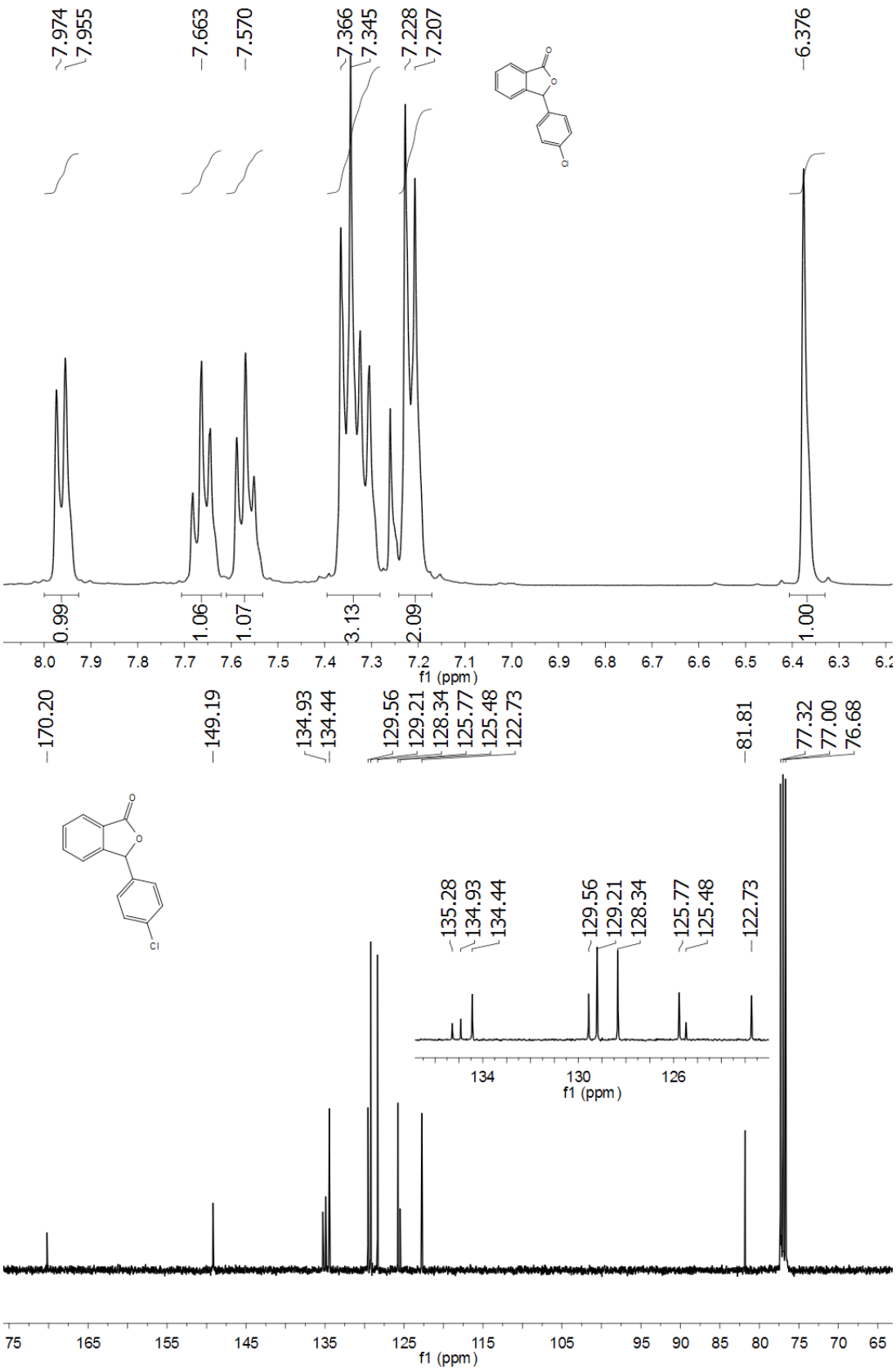
^{1}H NMR and ^{13}C NMR of compound **10a**

This journal is © The Royal Society of Chemistry 2012

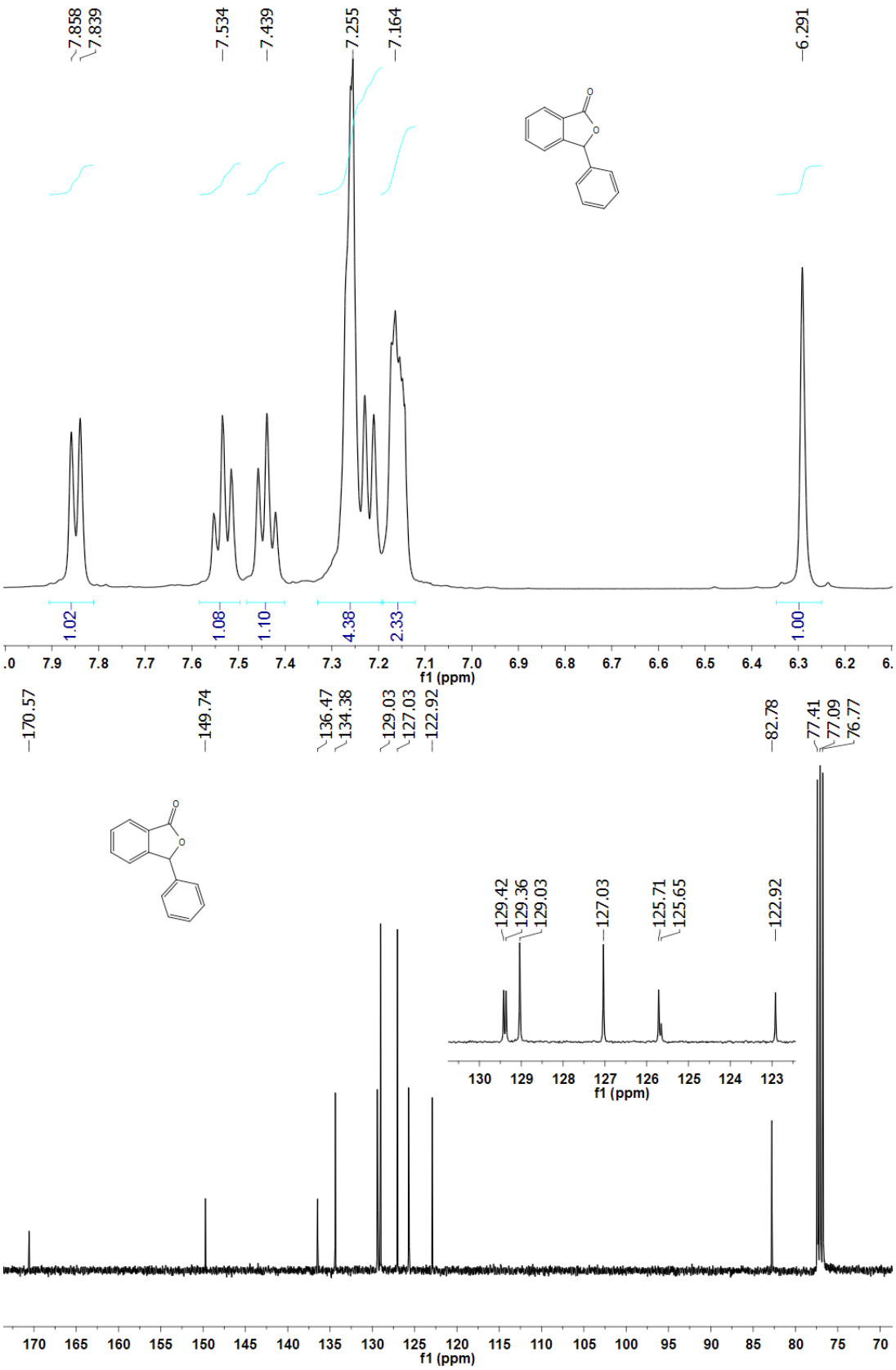


^{1}H NMR and ^{13}C NMR of compound **6a**

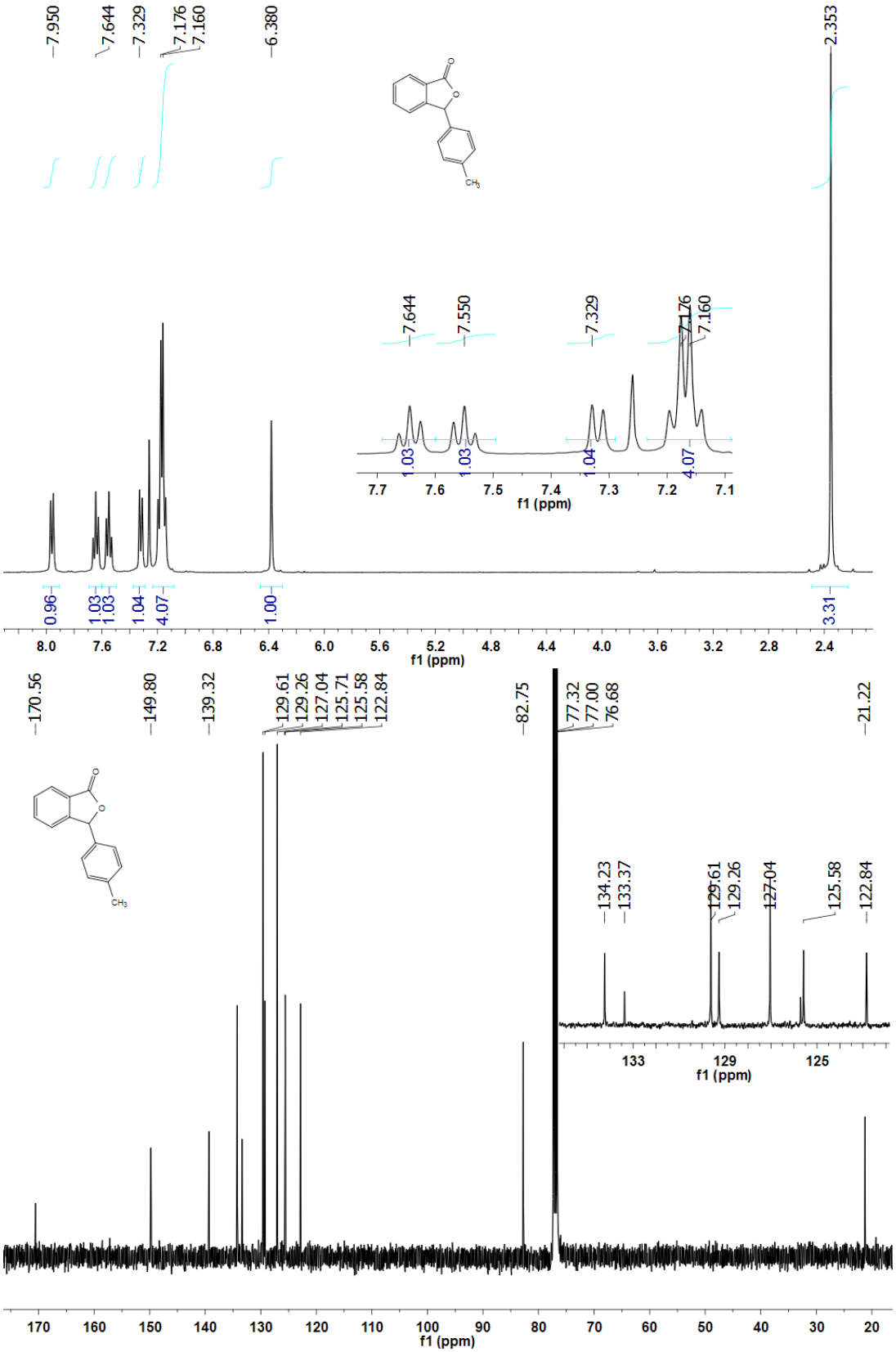
This journal is © The Royal Society of Chemistry 2012



^{1}H NMR and ^{13}C NMR of compound **6b**

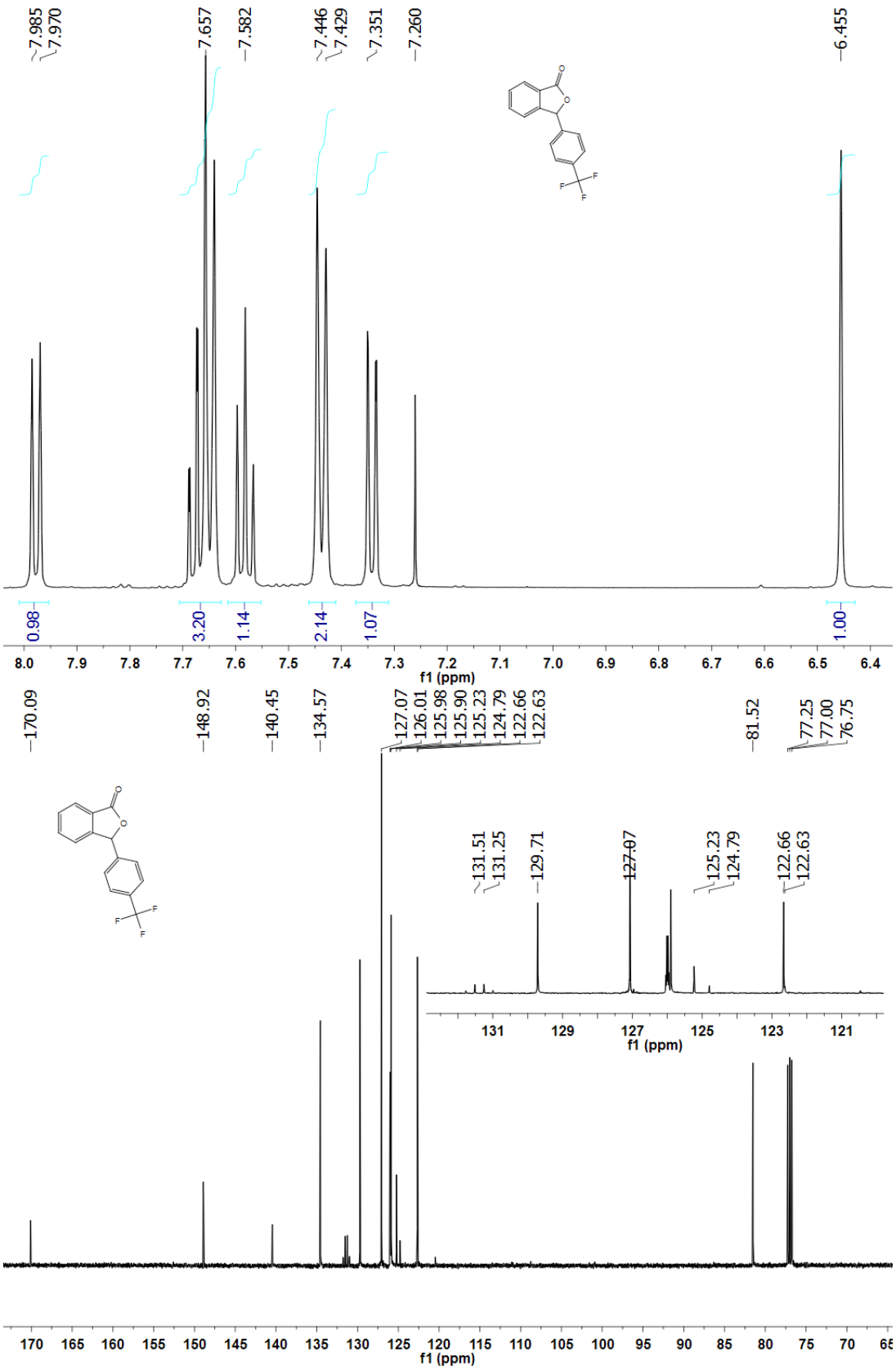


^{1}H NMR and ^{13}C NMR of compound **6c**

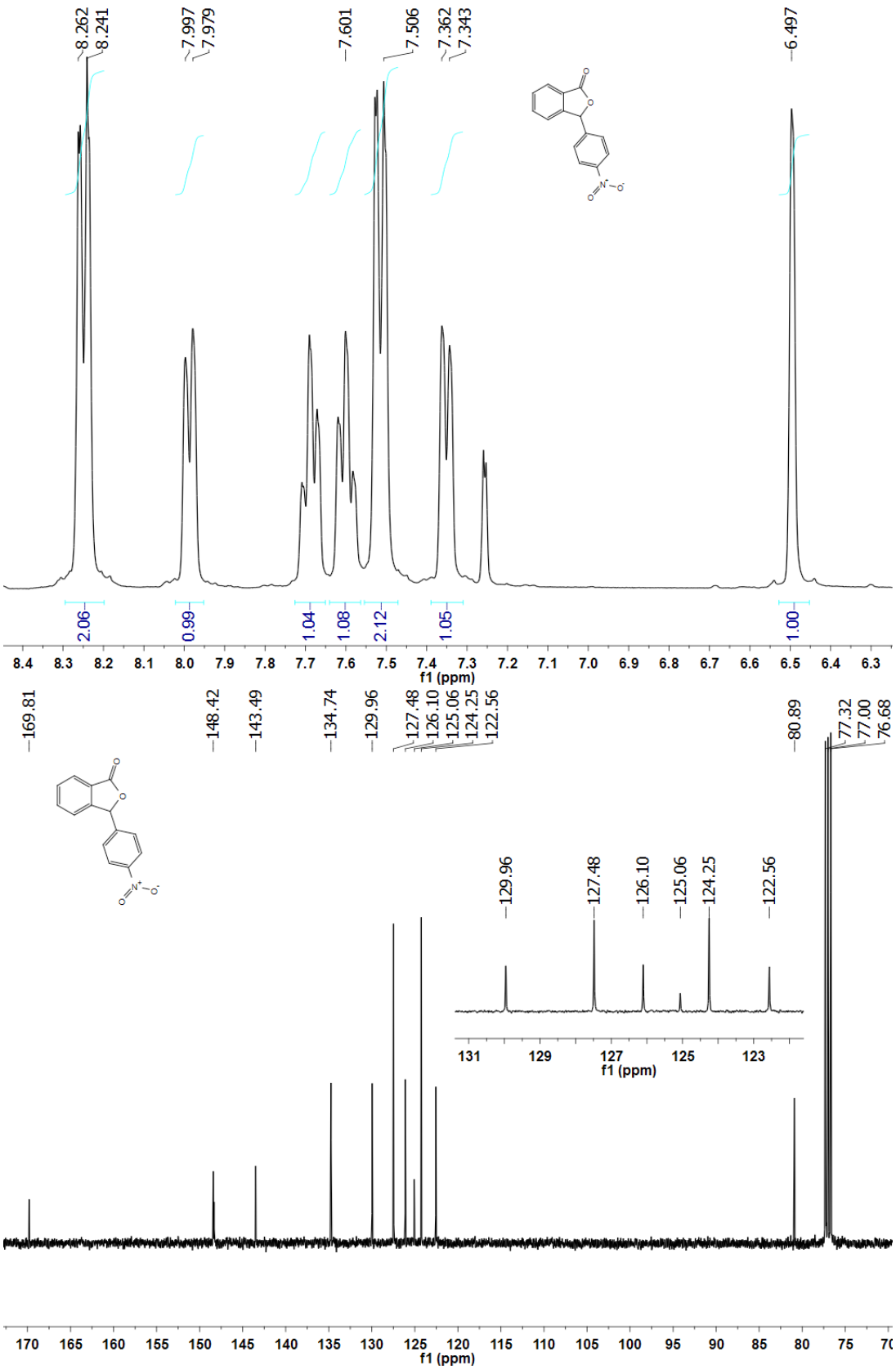


^{1}H NMR and ^{13}C NMR of compound **6d**

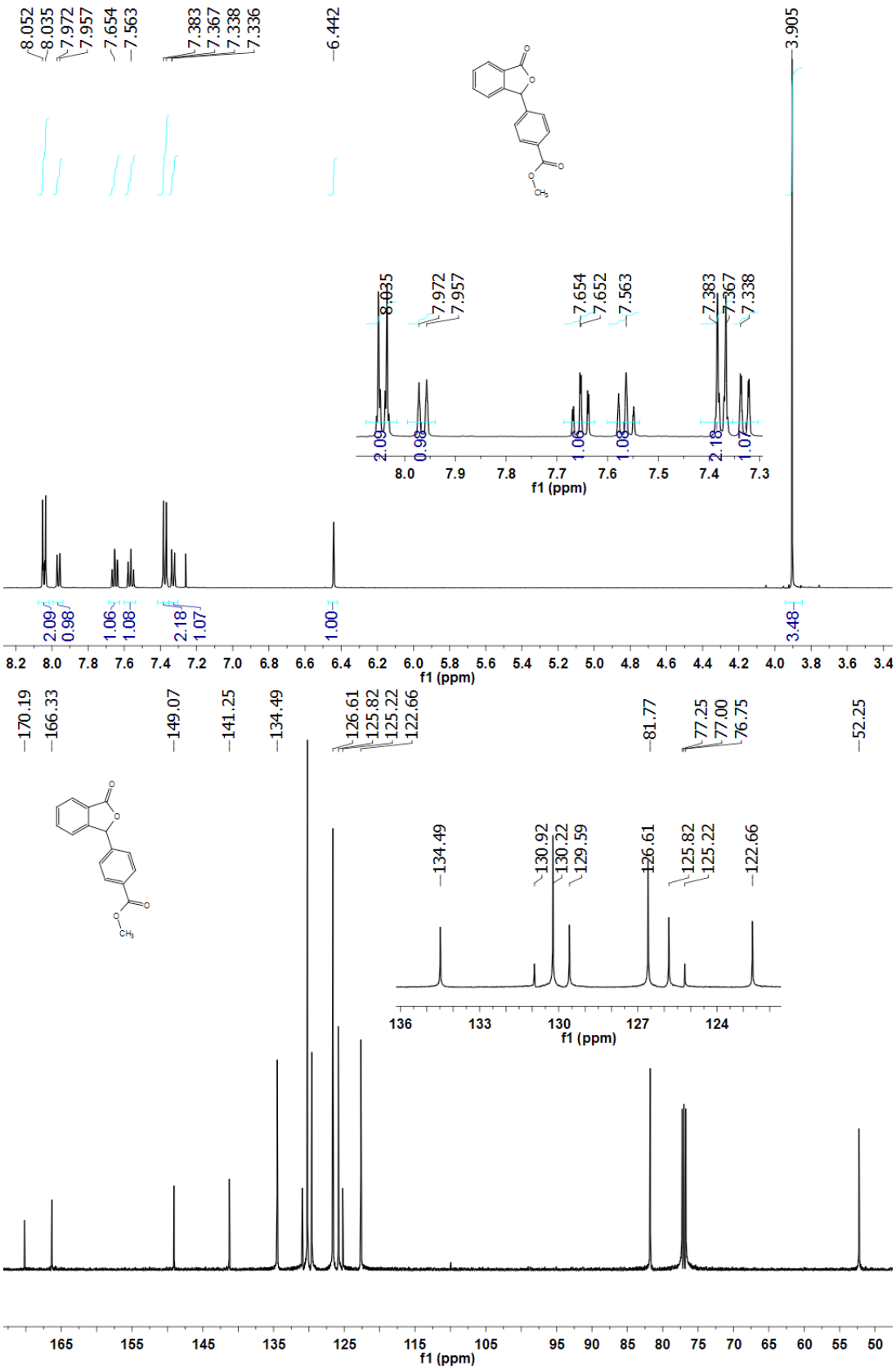
This journal is © The Royal Society of Chemistry 2012



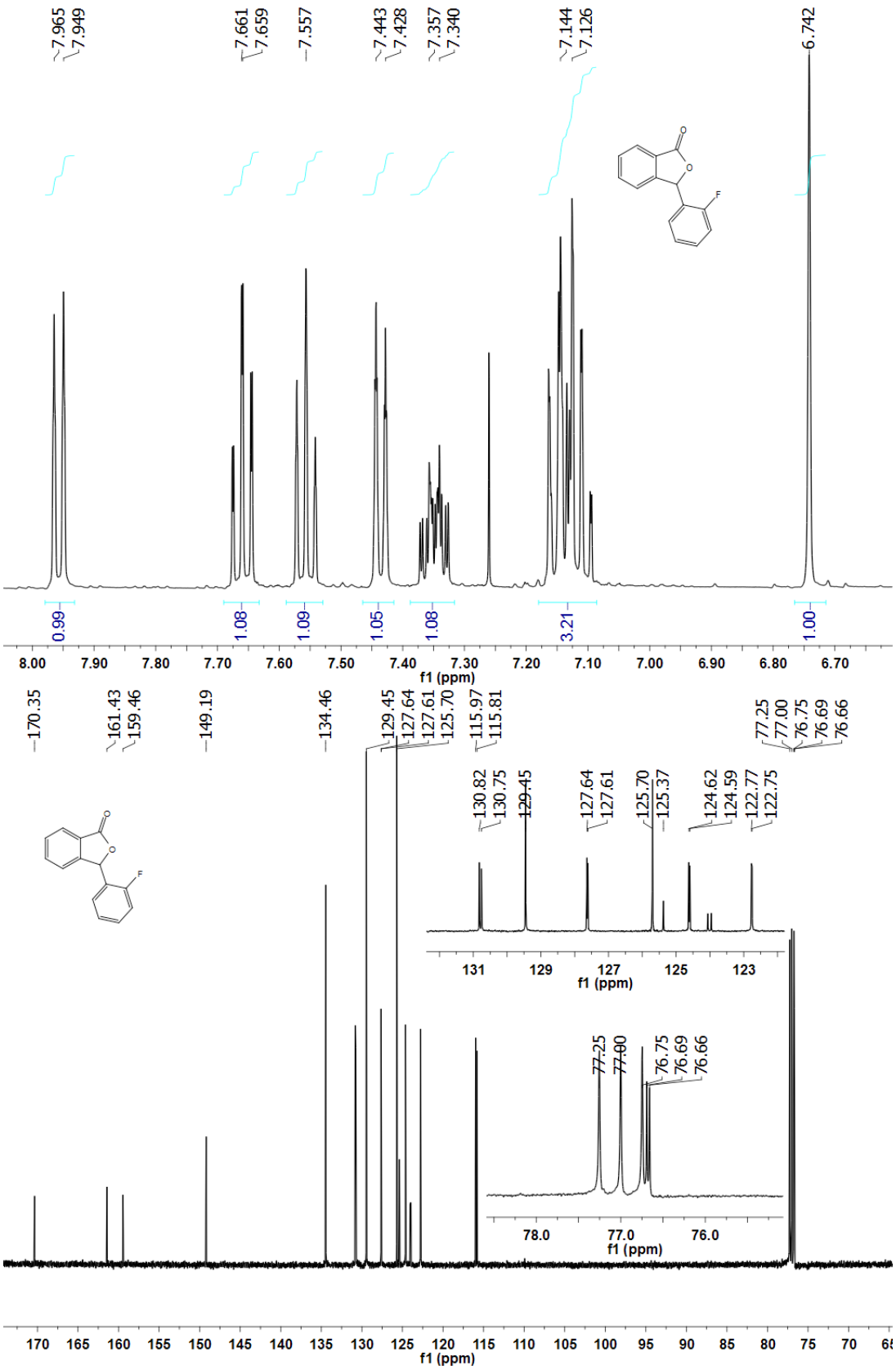
^{1}H NMR and ^{13}C NMR of compound **6e**



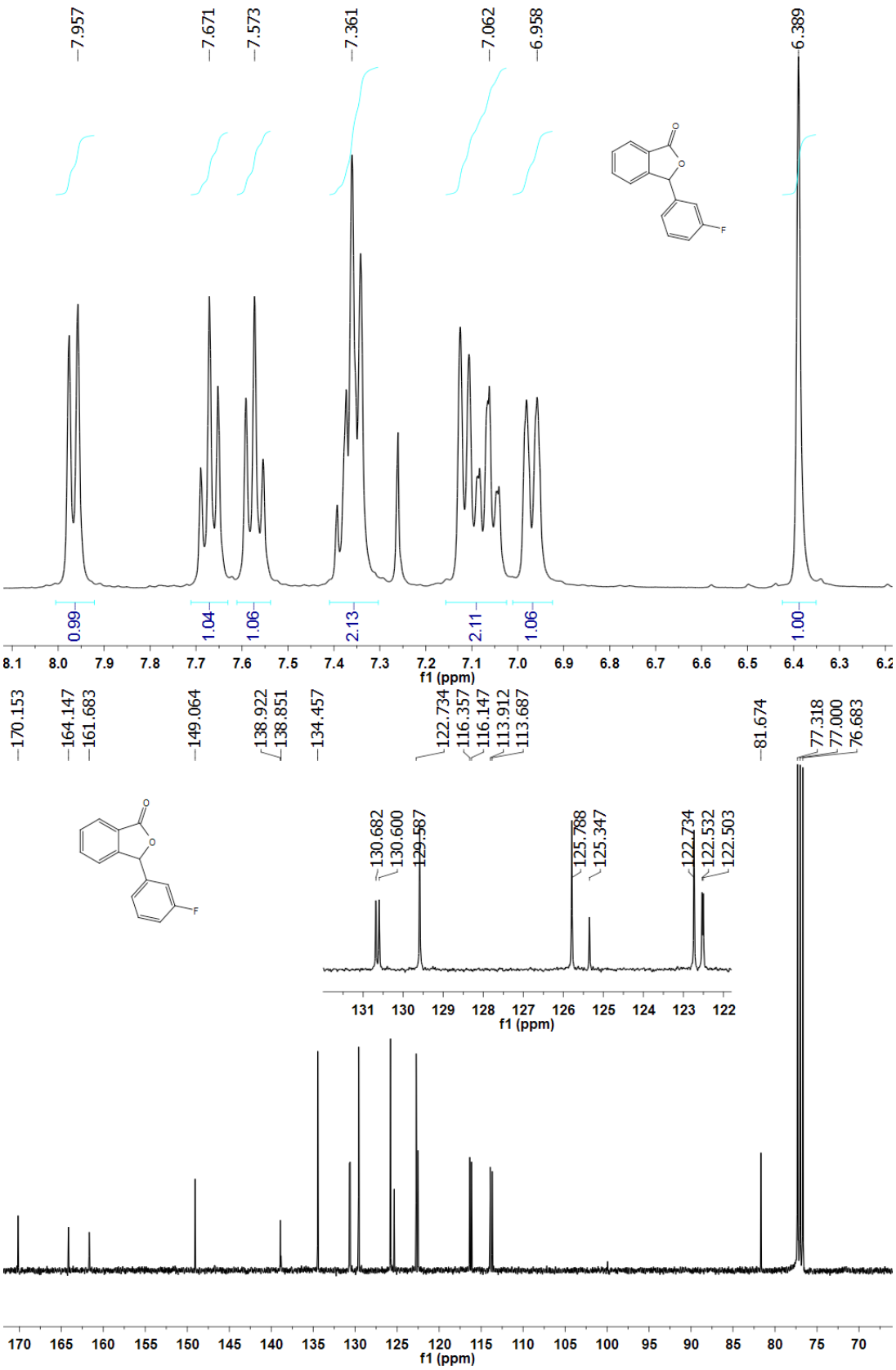
^{1}H NMR and ^{13}C NMR of compound **6f**



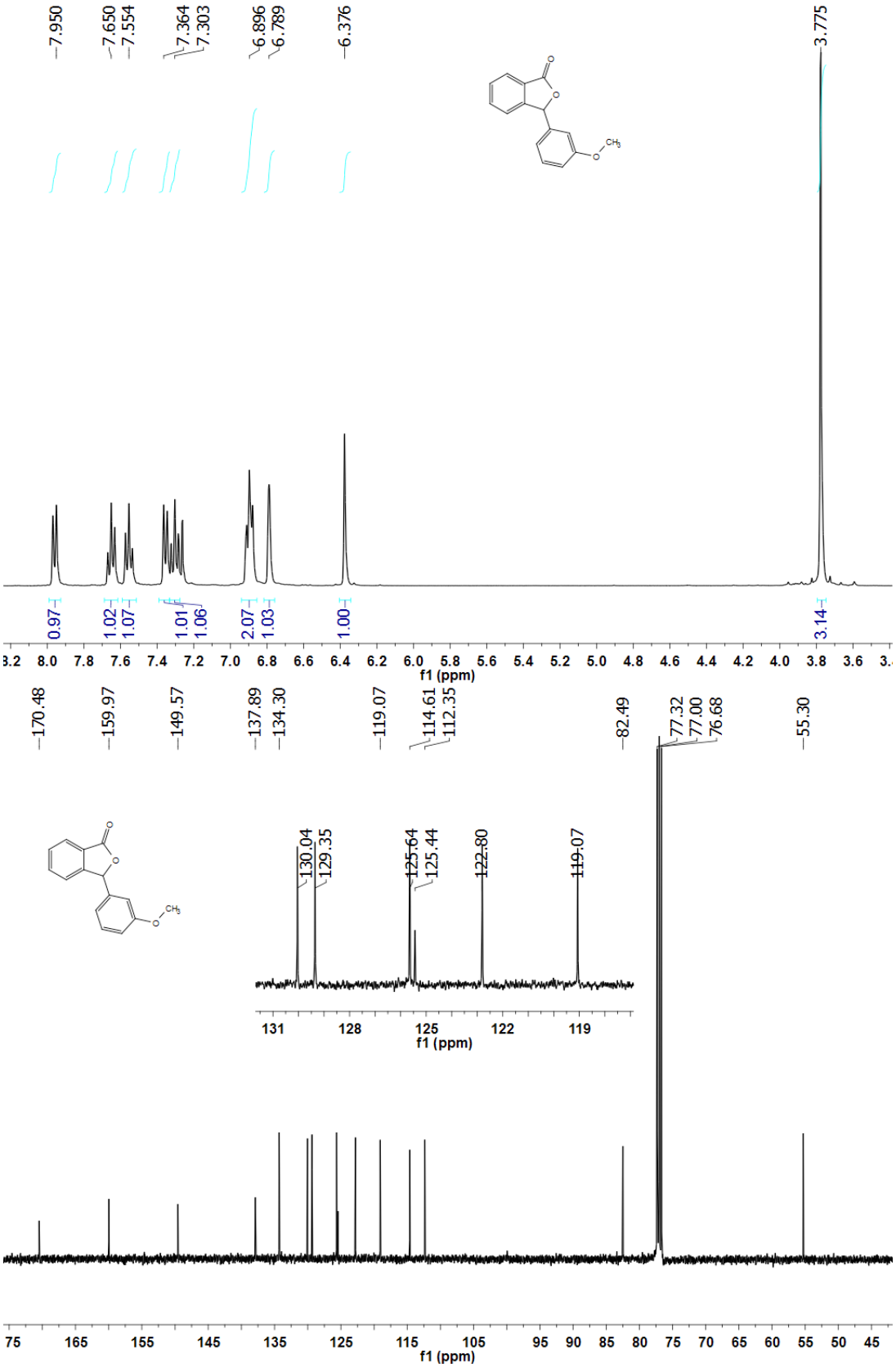
^{1}H NMR and ^{13}C NMR of compound **6g**



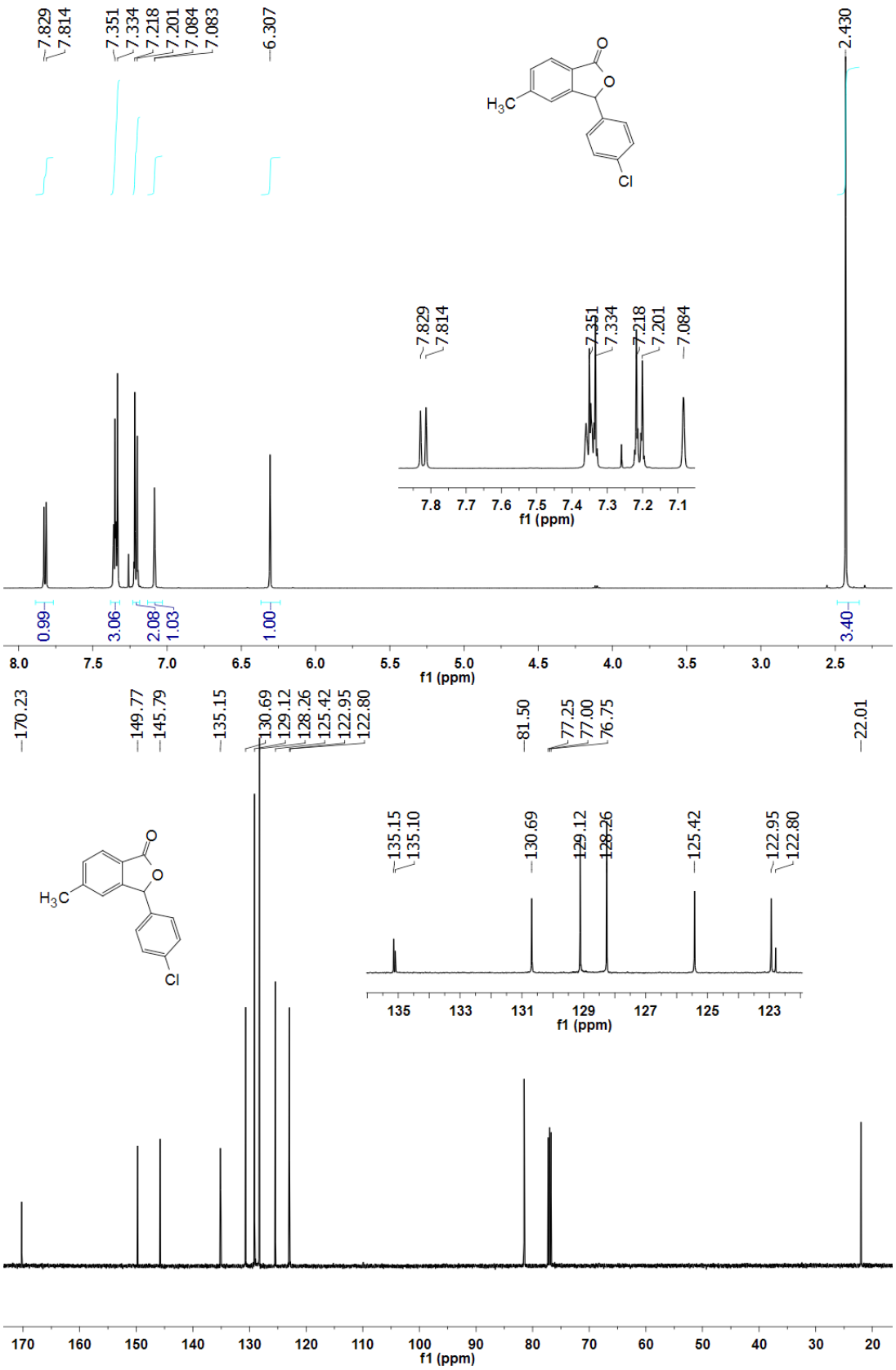
^{1}H NMR and ^{13}C NMR of compound **6h**



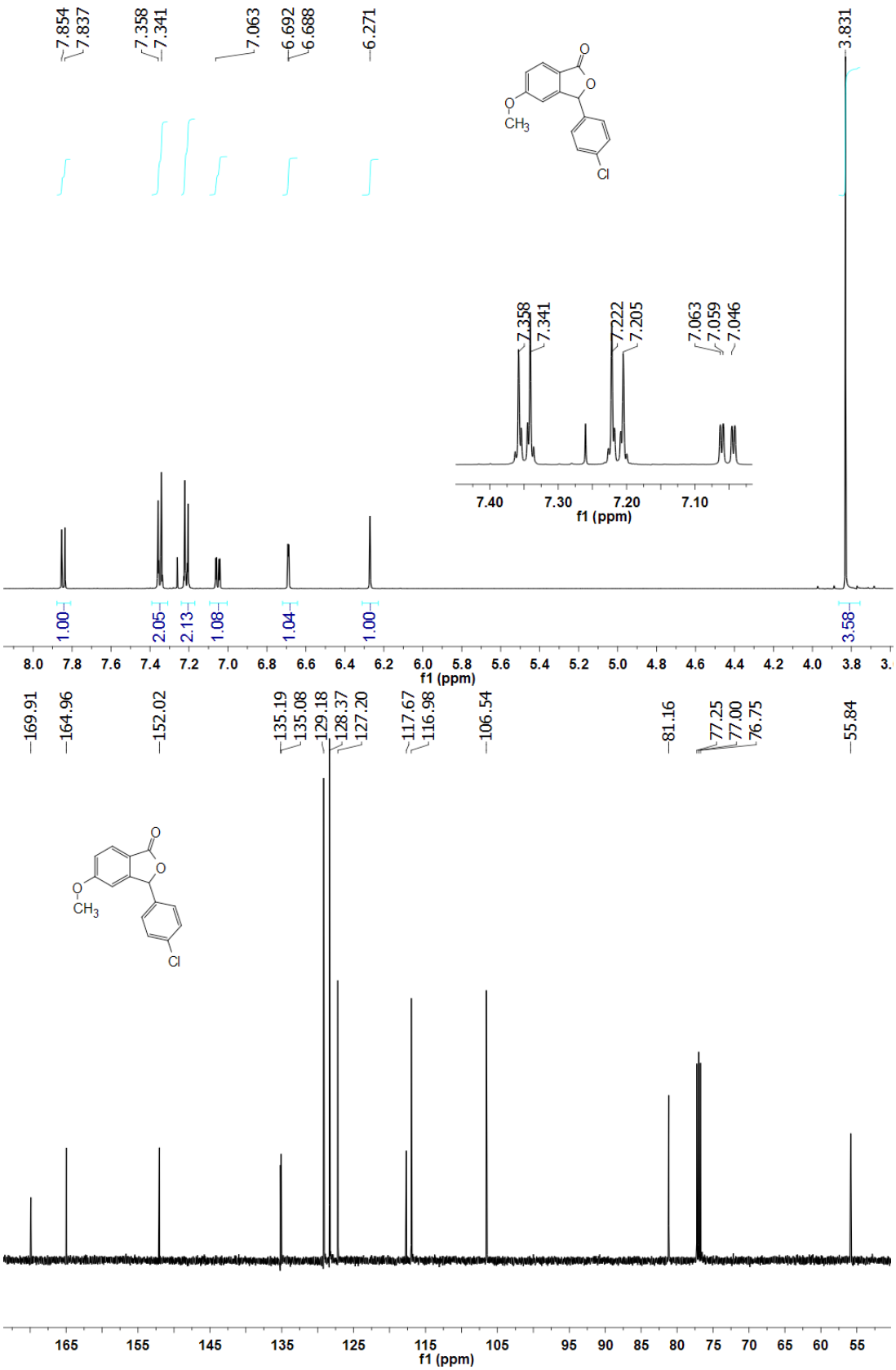
^{1}H NMR and ^{13}C NMR of compound **6i**



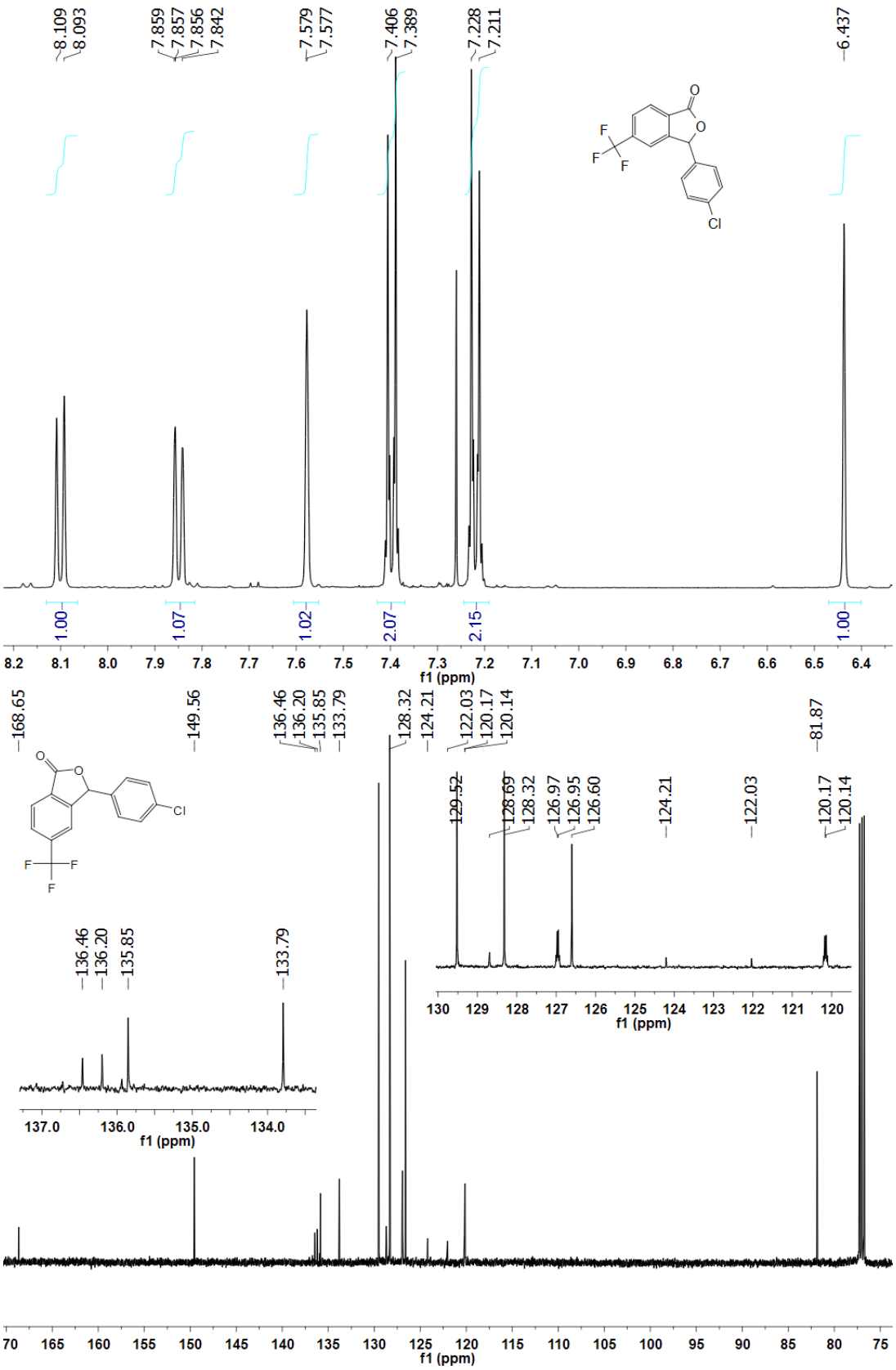
^{1}H NMR and ^{13}C NMR of compound **6j**



^{1}H NMR and ^{13}C NMR of compound **6k**

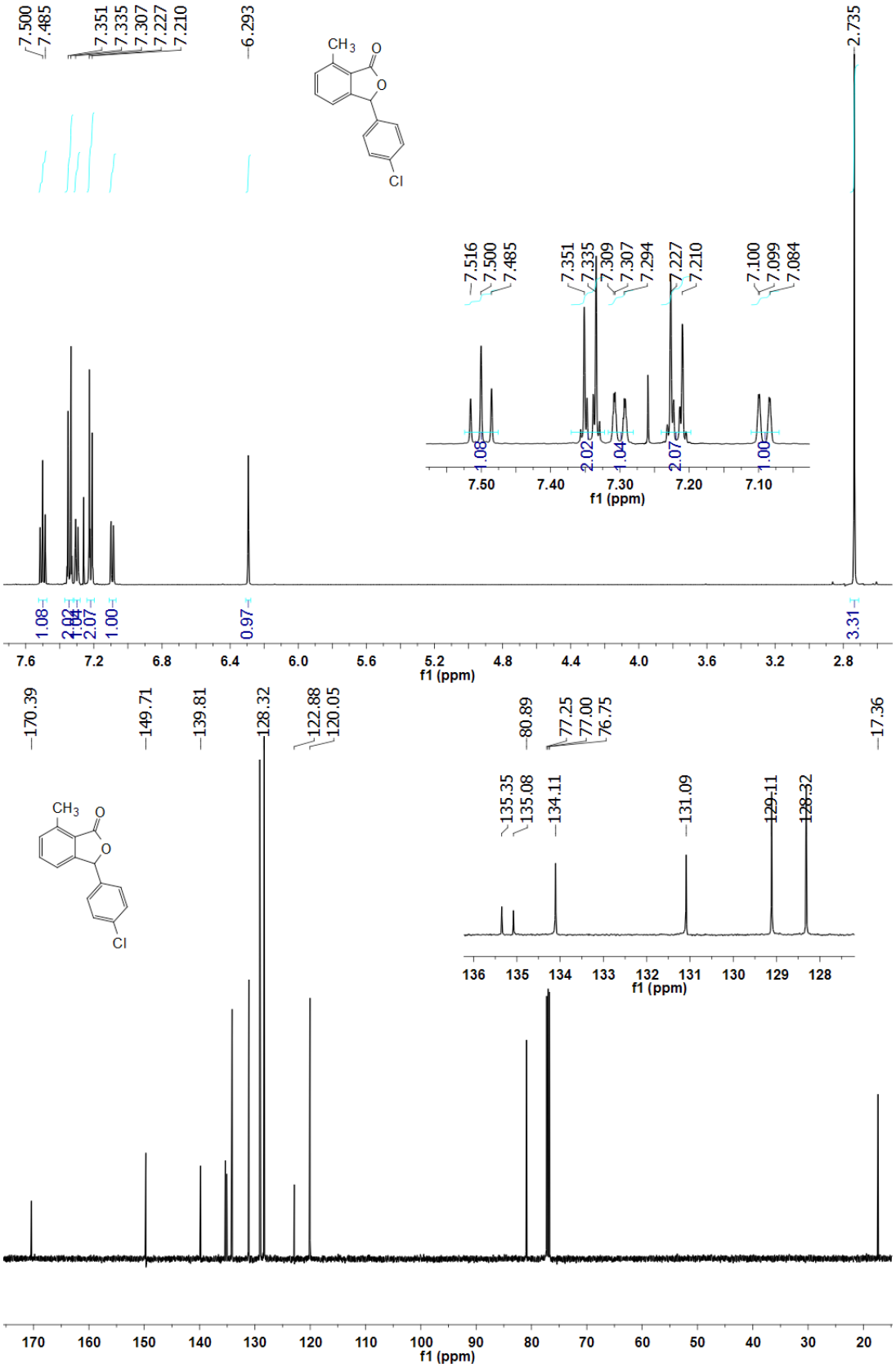


^{1}H NMR and ^{13}C NMR of compound **6l**



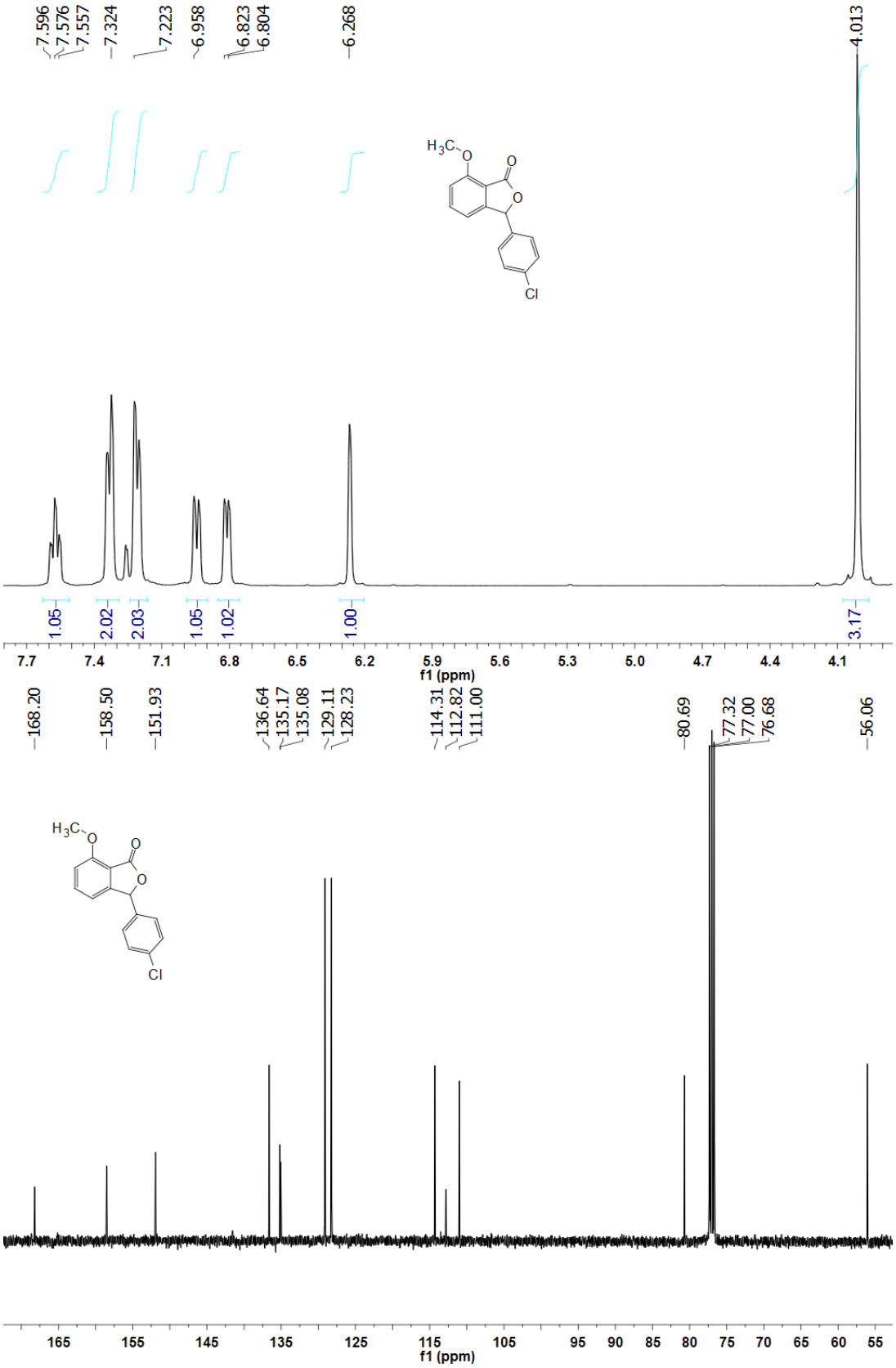
^{1}H NMR and ^{13}C NMR of compound **6m**

This journal is © The Royal Society of Chemistry 2012



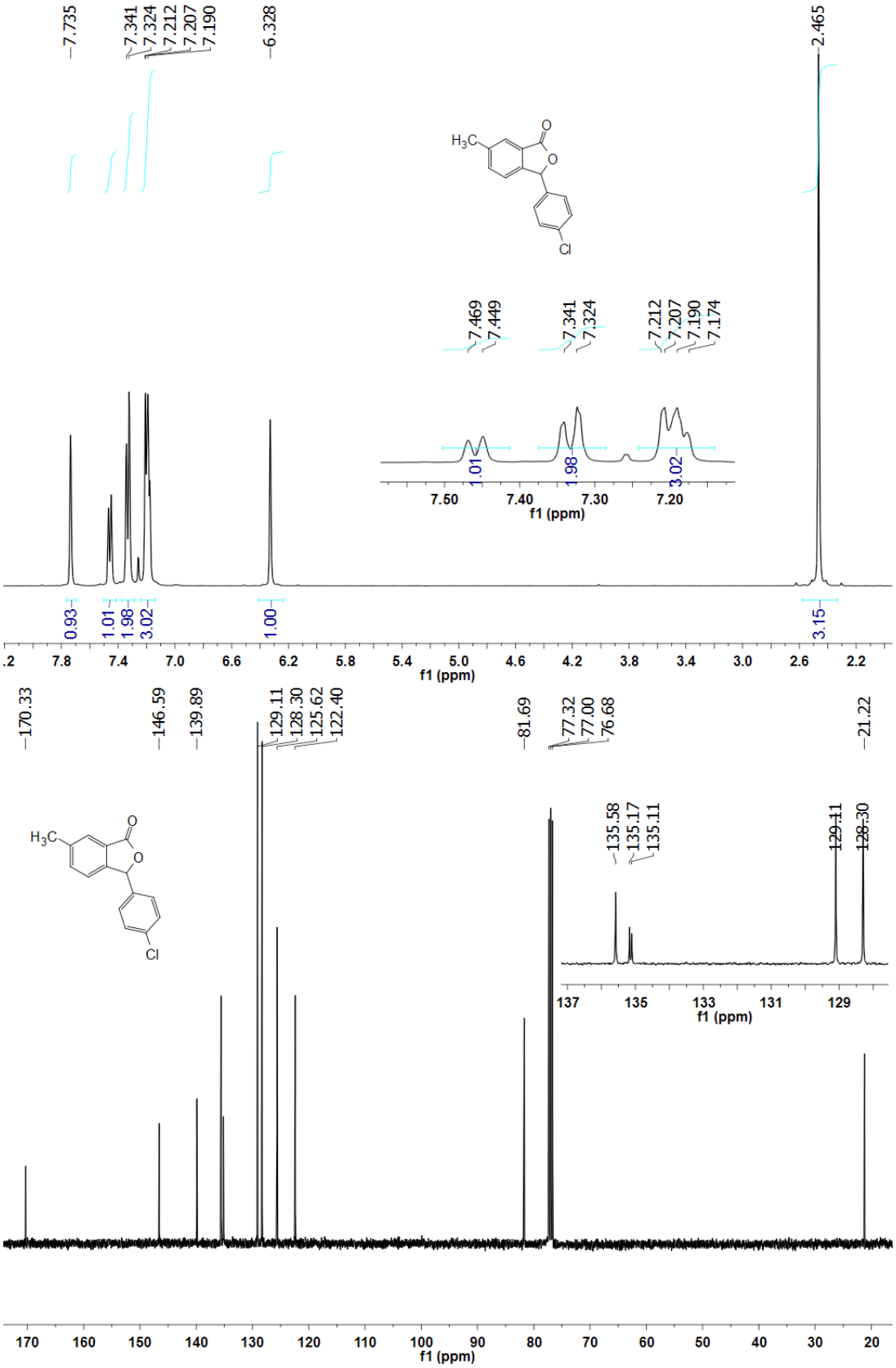
^{1}H NMR and ^{13}C NMR of compound **6n**

This journal is © The Royal Society of Chemistry 2012

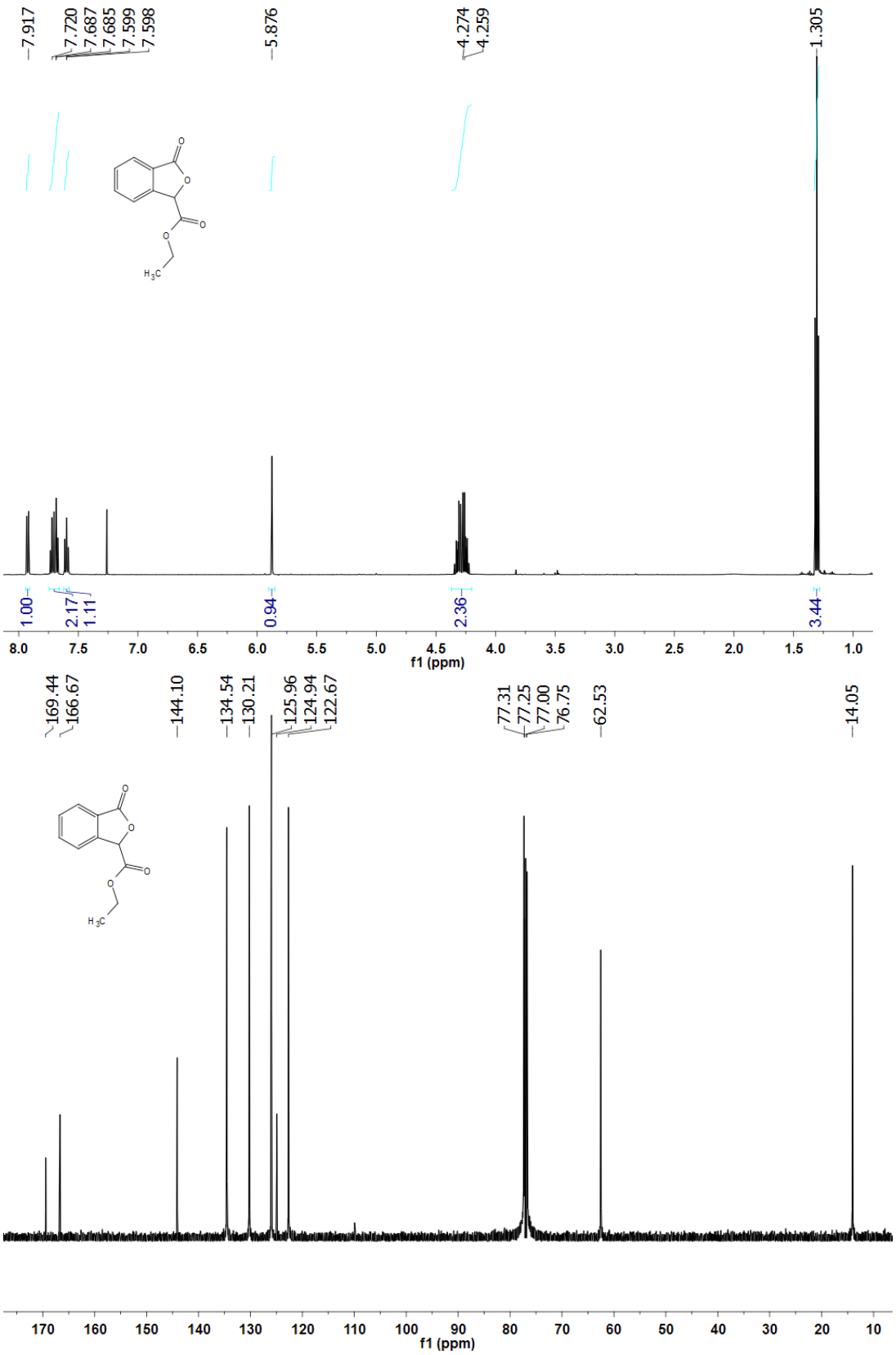


^{1}H NMR and ^{13}C NMR of compound **6o**

This journal is © The Royal Society of Chemistry 2012

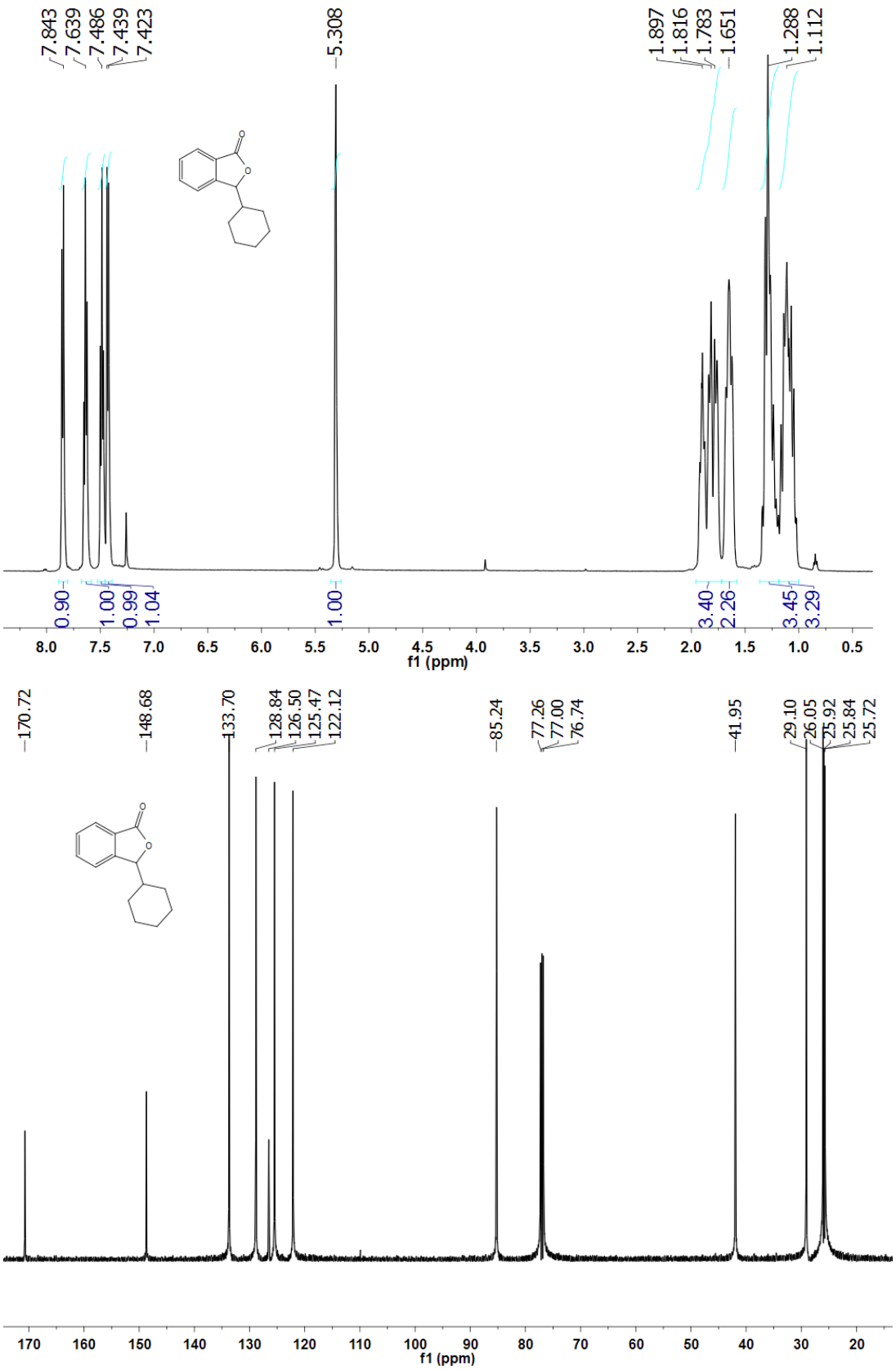


^{1}H NMR and ^{13}C NMR of compound **6p**

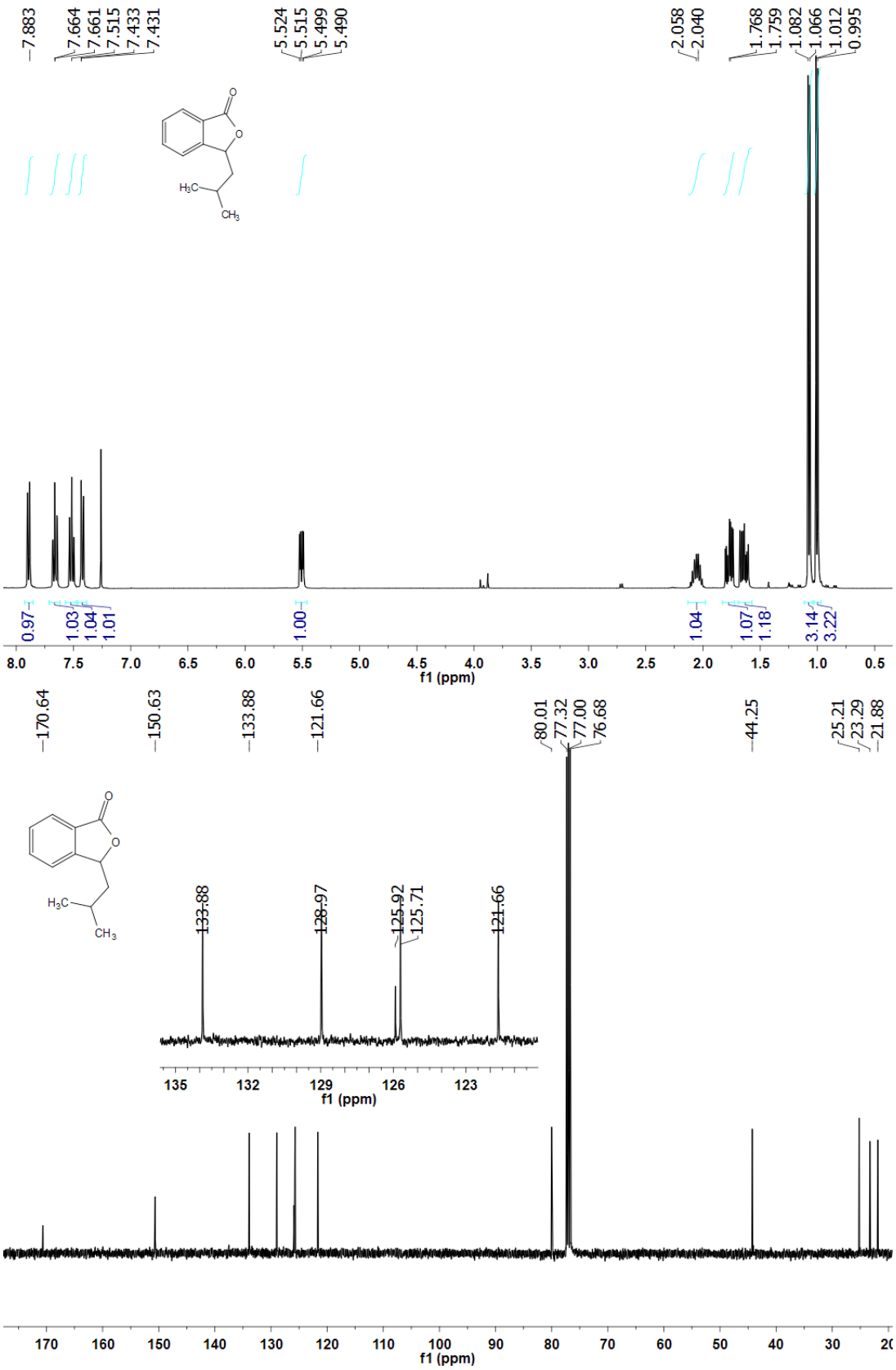


^{1}H NMR and ^{13}C NMR of compound **6q**

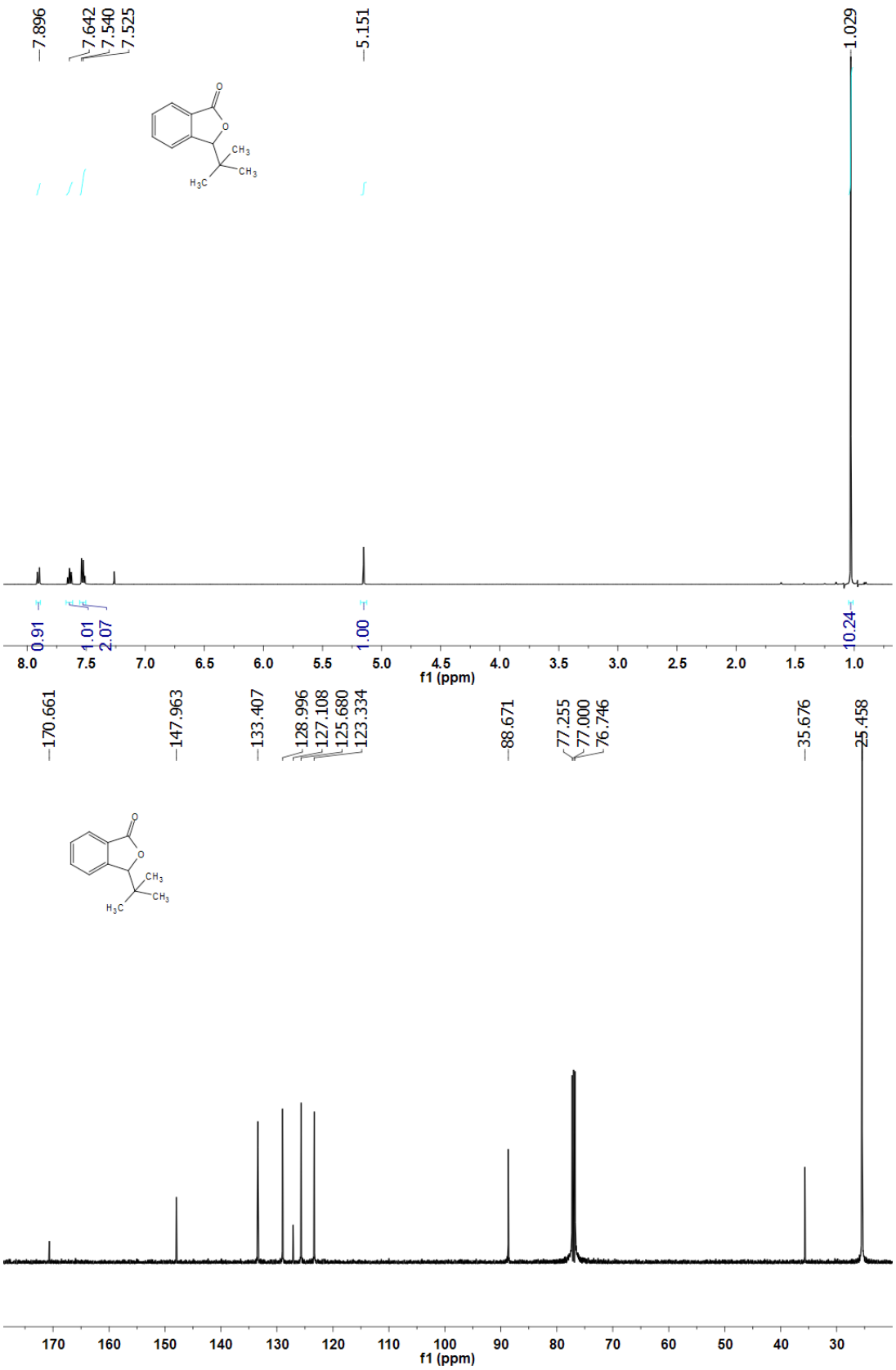
This journal is © The Royal Society of Chemistry 2012



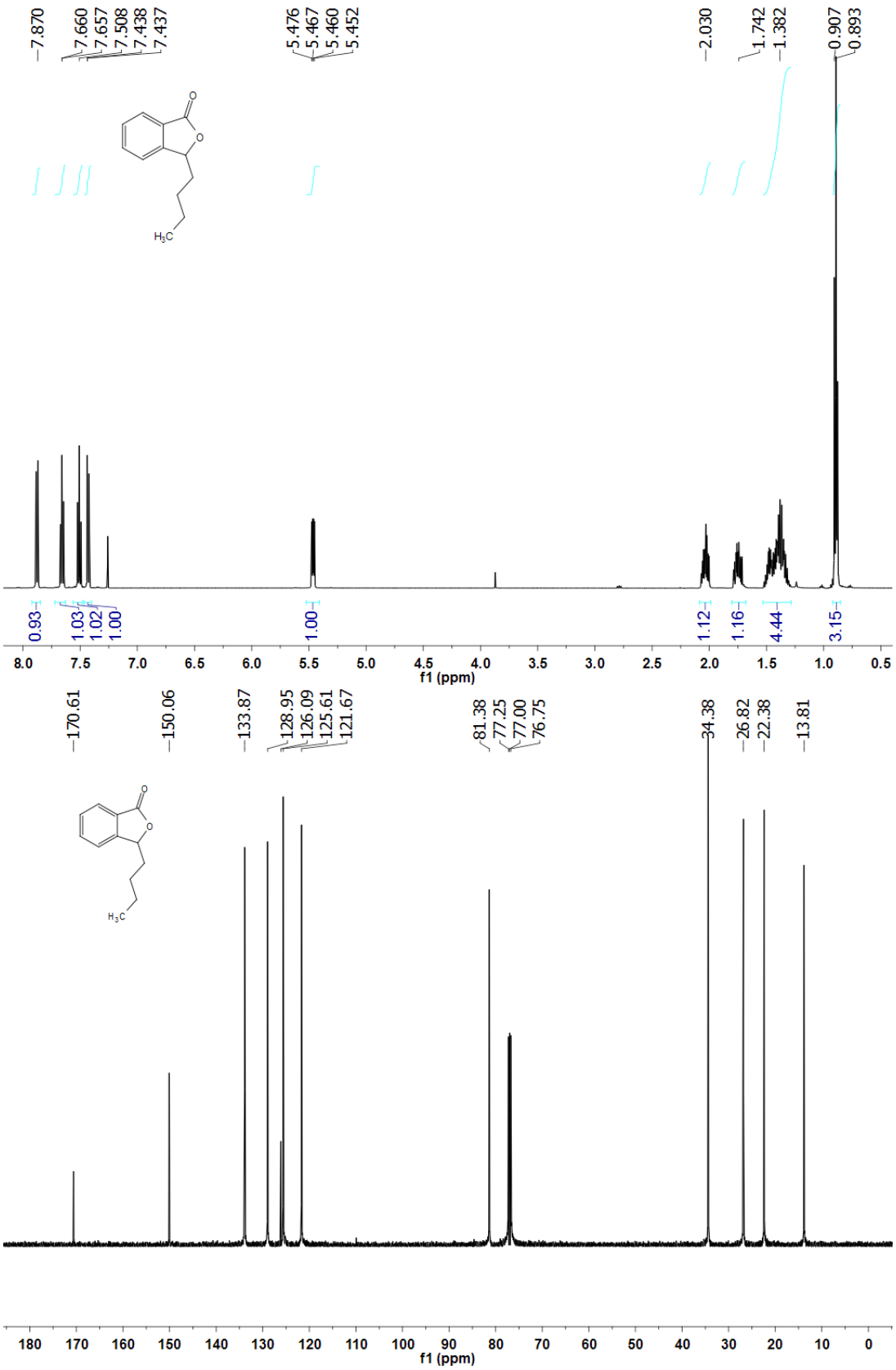
^{1}H NMR and ^{13}C NMR of compound **6r**



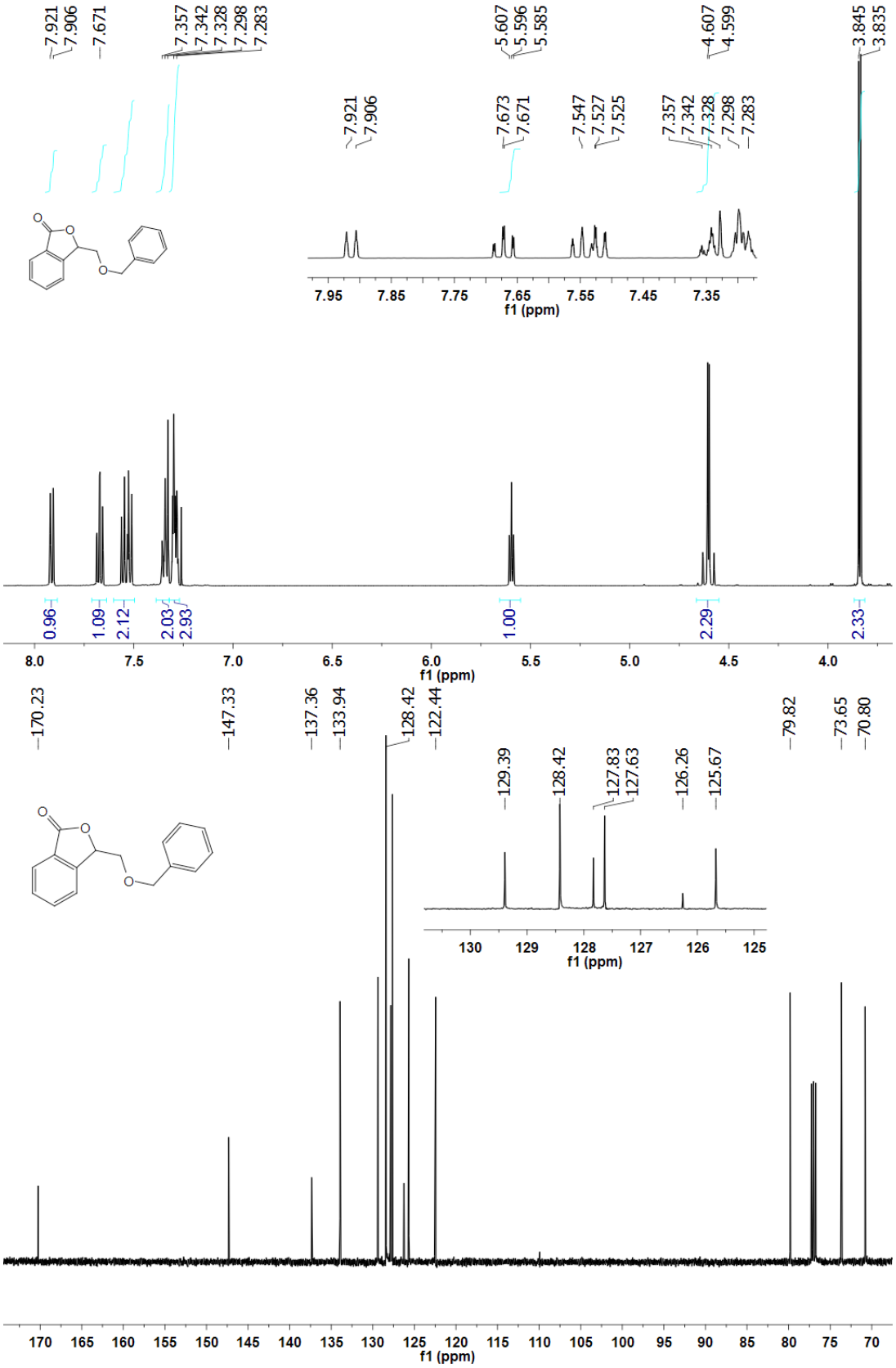
^{1}H NMR and ^{13}C NMR of compound **6s**



^{1}H NMR and ^{13}C NMR of compound **6t**



^{1}H NMR and ^{13}C NMR of compound **6u**



^{1}H NMR and ^{13}C NMR of compound **6v**

This journal is © The Royal Society of Chemistry 2012