Supporting Information

Pd-catalyzed Thiophene-Aryl Coupling Reaction *via* C-H bond Activation in Deep Eutectic Solvents

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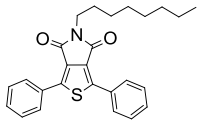
CONTENTS

1. General remarks

Reagents and solvents were purchased at the highest commercial quality and used without further purification. 5-Octylthieno[3,4-*c*]pyrrole-4,6-dione (TPD) **1** was purchased from TCI Europe. Preparative column chromatography was carried out using Macherey-Nagel silica gel (60, particle size 0.063-0.2 mm). Macherey-Nagel aluminum sheets with silica gel 60 F254 were used for TLC analyses. All new compounds were characterized by ^{1}H-NMR, ^{13}C-NMR, IR spectroscopy and LC-MS analysis. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker or on a Varian at 500 and at 126 MHz and on a Varian at 300 and at 75 MHz, respectively, by using the residual proton peak of $CDCl_3$ at δ = 7.26 ppm as internal standard for ^{1}H spectra and the signals of $CDCl_3$ at δ = 77.16 ppm as internal standard for ^{13}C spectra. IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum Bx. High-resolution mass spectra were acquired on an Agilent high performance liquid chromatography mass spectrometer (6530 ACCURATE MASS Q-TOF) via direct infusion of the samples using methanol as the elution solvent. Melting points were determined on a Stuart Scientific Melting point apparatus SMP3.

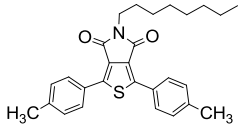
2. Typical procedure (without additive) for the synthesis of compounds 3a-f:

5-octyl-1,3-diphenyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3a).[1]



A schlenk tube (ø = 1.8 cm) with a screw cap was charged with 5-octylthieno[3,4-*c*]pyrrole-4,6-dione (TPD) **1** (100 mg, 0.38 mmol), Cs_2CO_3 (0.25 g, 0.76 mmol), pivalic acid (12 mg, 0.12 mmol), $Pd_2(dba)_3$ (18 mg, 0.02 mmol), P(*o*-MeOPh)$_3$ (13 mg, 0.04 mmol), iodobenzene (384 mg, 1.88 mmol) and, finally, a preformed mixture of choline chloride (2.15 g, 15.4 mmol) and urea (1.85 g, 30.1 mmol). The resulting heterogeneous reaction mixture was reacted at 110 °C under mechanical or magnetic stirring. After 48 h, the mixture was cooled to room temperature and, after water addition, extracted with CH_2Cl_2 (3x40 mL).[2] The organic extracts were dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography (hexane:ethyl acetate = 9:1) afforded 129 mg of compound **3a** (82% yield). After crystallization from hexane, compound **3a** was obtained as a pale yellow solid, m.p. = 85.4-86.1°C ; HRMS *m/z* calculated for $C_{26}H_{27}NO_2S$ $[M+Na]^+$: 440.1660, found: 440.1556; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.12 (d, *J* = 7.0 Hz, 4H), 7.51-7.39 (m, 6H), 3.65 (t, *J* = 7.2 Hz, 2H), 1.73-1.63 (m 2H), 1.40-1.20 (m, 10H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 163.0, 145.0, 130.7, 130.5, 130.2, 129.0, 128.2, 38.7, 31.9, 29.3, 29.3, 28.6, 27.1, 22.7, 14.2; IR (KBr, cm^{-1}) ν: 3063, 2924, 2851, 1743, 1698, 1541, 1491, 1389, 1365, 1072, 753, 688.

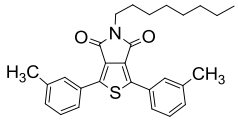
5-octyl-1,3-di-*p*-tolyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3b).



Compound **3b** was synthesized from **1** (100 mg, 0.38 mmol) and 4-iodotoluene (411 mg, 1.88 mmol) in accordance with the typical procedure. Purification by column chromatography (hexane:ethyl acetate = 9:1) afforded 125 mg of compound **3b** (74% yield). After crystallization from hexane, compound **3b** was obtained as a yellow solid, m.p. = 103.6-104.3°C; HRMS *m/z* calculated for $C_{28}H_{31}NO_2S$ $[M+Na]^+$: 468.1973, found: 468.1968; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.01 (d, *J* = 8.2 Hz,

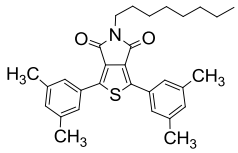
4H), 7.26 (d, *J* = 8.2 Hz, 4H), 3.65 (t, *J* = 7.5 Hz, 2H), 2.40 (s, 6H), 1.17-1.63 (m, 2H), 1.39-1.21 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 163.2, 144.9, 140.6, 129.9, 129.7, 128.1, 128.0, 38.7, 31.9, 29.4, 29.3, 28.6, 27.1, 22.8, 21.6, 14.2; IR (KBr, cm^{-1}) ν: 3059, 3022, 2918, 2853, 1739, 1693, 1537, 1505, 1386, 1361, 1332, 1084, 755.

5-octyl-1,3-di-*m*-tolyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3c).



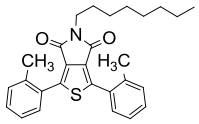
Compound **3c** was synthesized from **1** (100 mg, 0.38 mmol) and 3-iodotoluene (411 mg, 1.88 mmol) in accordance with the typical procedure. Purification by column chromatography (hexane:ethyl acetate = 9:1) afforded 107 mg of compound **3c** (63% yield). After crystallization from hexane, compound **3c** was obtained as a pale yellow solid, m.p. = 66.7-67.2°C; HRMS *m/z* calculated for $C_{28}H_{31}NO_2S$ $[M+Na]^+$: 468.1973, found: 468.1973; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.95-7.91 (m, 4H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 2H), 3.65 (t, *J* = 7.5 Hz, 2H), 2.40 (s, 6H), 1.72-1.64 (m, 2H), 1.40-1.23 (m, 10H), 0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 163.1, 145.2, 138.8, 131.0, 130.6, 130.3, 128.9, 128.7, 125.4, 38.7, 31.9, 29.4, 29.3, 28.6, 27.1, 22.8, 21.6, 14.2; IR (KBr, cm^{-1}) ν: 3059, 2918, 2852, 1739, 1693, 1537, 1386, 1361, 1333, 1084, 755.

1,3-bis(3,5-dimethylphenyl)-5-octyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3d).



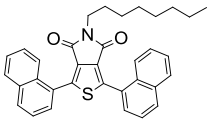
Compound **3d** was synthesized from **1** (100 mg, 0.38 mmol) and 1-iodo-3,5-dimethylbenzene (437 mg, 1.88 mmol) in accordance with the typical procedure. Purification by column chromatography (hexane:ethyl acetate = 9:1) afforded 152 mg of compound **3d** (85% yield). After crystallization from hexane, compound **3d** was obtained as a pale yellow solid, m.p. = 112.1-112.8°C; HRMS *m/z* calculated for $C_{30}H_{35}NO_2S$ $[M+Na]^+$: 496.2286, found: 496.2287. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.76 (s, 4H), 7.08 (s, 2H), 3.66 (t, *J* = 7.3 Hz, 2H), 2.40 (s, 12H), 1.75-1.61 (m, 2H), 1.41-1.21 (m, 10H), 0.87 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 163.2, 145.4, 138.7, 132.0, 130.6, 130.2, 126.0, 38.8, 31.9, 29.4, 29.3, 28.7, 27.2, 22.8, 21.5, 14.2; IR (KBr, cm^{-1}) ν: 3052, 2953, 2917, 2856, 1740, 1687, 1505, 1386, 1360, 1091, 815, 809, 756 .

5-octyl-1,3-di-*o*-tolyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3e).[1]



Compound **3e** was synthesized from **1** (100 mg, 0.38 mmol) and 2-iodotoluene (411 mg, 1.88 mmol) in accordance with the typical procedure. After purification by column chromatography (hexane:ethyl acetate = 9:1), compound **3e** was isolated as a pale yellow viscous liquid (126 mg, 74% yield); HRMS *m/z* calculated for $C_{28}H_{31}NO_2S$ $[M+Na]^+$: 468.1973, found: 468.1971; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.57 (d, *J* = 7.5 Hz, 2H), 7.46-7.29 (m, 6H), 3.63 (t, *J* = 7.4 Hz, 2H), 2.53 (s, 6H), 1.75-1.61 (m, 2H), 1.42-1.24 (m, 10H), 0.91 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 162.8, 144.5, 137.3, 131.6, 131.0, 130.9, 129.9, 129.5, 126.0, 38.5, 31.9, 29.2, 28.6, 27.0, 22.7, 20.6, 14.2 (one coincident signal not observed); IR (neat, cm^{-1}) ν: 3061, 3017, 2918, 2854, 1754, 1712, 1556, 1453, 1385, 1362, 1329, 1084, 1018, 747.

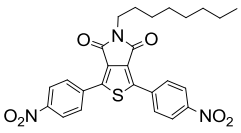
1,3-di(naphthalen-1-yl)-5-octyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3f).



Compound **3f** was synthesized from **1** (100 mg, 0.38 mmol) and 1-iodonaphthalene (479 mg, 1.88 mmol) in accordance with the typical procedure. After purification by column chromatography (hexane:CH_2Cl_2 = 1:1) 83 mg of compound **3f** (42% yield) was isolated as a pale yellow viscous liquid. HRMS *m/z* calculated for $C_{34}H_{31}NO_2S$ $[M+Na]^+$: 540.1973, found: 540.1974; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.25-8.20 (m, 2H), 8.00 (d, *J* = 6.0 Hz, 2H), 7.95-7.93 (m, 2H), 7.83 (dd, *J* = 7.0, 0.5 Hz, 2H), 7.62-7.56 (m, 6H), 3.59 (t, *J* = 7.3 Hz, 2H), 1.66-1.58 (m, 2H), 1.32-1.18 (m, 10H), 0.85 (t, *J* =7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 162.7, 143.6, 133.9, 132.6, 131.2, 130.8, 129.4, 128.8, 127.5, 127.2, 126.7, 125.5, 125.3, 38.6, 31.9, 29.3, 29.3, 28.6, 27.1, 22.8, 14.2; IR (neat, cm^{-1}) ν: 3058, 2925, 2855, 1755, 1705, 1549, 1385, 1363, 1340, 1081, 1043, 797, 771.

3. Typical procedure (with CPME as additive) for the synthesis of compounds 3g-k:

1,3-bis(4-nitrophenyl)-5-octyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3g).[3]

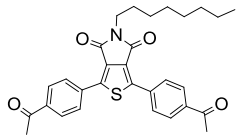


A schlenk tube (ø = 2.5 cm) with a screw cap was charged with 5-octylthieno[3,4-*c*]pyrrole-4,6-dione (TPD) **1** (100 mg, 0.38 mmol), Cs_2CO_3 (0.25 g, 0.76 mmol), pivalic acid (12 mg, 0.12 mmol), $Pd_2(dba)_3$ (18 mg, 0.02 mmol), P(*o*-MeOPh)$_3$ (13 mg, 0.04 mmol), 1-iodo-4-nitrobenzene (284 mg, 1.14 mmol), CPME (0.3 mL) and, finally, a preformed mixture of choline chloride (2.15 g, 15.4 mmol) and urea (1.85 g, 30.1 mmol). The resulting heterogeneous reaction mixture was reacted at 110 °C under magnetic stirring. After 48 h, the mixture was cooled to room temperature and, after water addition, extracted with CH_2Cl_2 (3x40 mL).[2] The organic extracts were dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography (hexane:ethyl acetate = 8:2), afforded compound **3g** (135 mg, 70% yield). After crystallization from hexane, compound **3g** was obtained as a yellow solid, m.p. = 165.6-168.8°C; HRMS *m/z* calculated for $C_{26}H_{25}N_3O_6S$ $[M-H]^-$: 506.1386, found: 506.1374; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.35 (br s, 8H), 3.71 (t, *J* = 7.2 Hz, 2H), 1.75-1.65 (m, 2H), 1.41-1.21 (m, 10H), 0.86 (t, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 162.4, 148.5, 143.0, 135.9, 133.4, 129.2, 124.5, 39.2, 31.9, 29.3, 29.3, 28.5, 27.1, 22.8, 14.2; IR (KBr, cm^{-1}) ν: 3102, 3059, 2926, 2846, 1748, 1699, 1596, 1514, 1342, 1090, 854, 747.

1 mmol scale procedure: Following tipycal procedure, 5-octylthieno[3,4-*c*]pyrrole-4,6-dione (TPD) **1** (265 mg, 1 mmol), Cs_2CO_3 (652 mg, 2 mmol), pivalic acid (31 mg, 0.3 mmol), $Pd_2(dba)_3$ (46 mg, 0.05 mmol), P(*o*-MeOPh)$_3$ (33 mg, 0.1 mmol), 1-iodo-4-nitrobenzene (747 mg, 3 mmol), CPME (0.8 mL) and, finally, a preformed mixture of choline chloride (5.70 g, 40.8 mmol) and urea (4.94 g, 82.3 mmol) were introduced in a schlenk tube (ø = 2.5 cm) with a screw cap. The resulting heterogeneous reaction mixture was reacted at 110 °C, using a sand bath, under magnetic stirring. After 48 h, the mixture was cooled to room temperature and, after water addition (80 mL), extracted with CH_2Cl_2 (3x50 mL). The organic extracts were dried over Na_2SO_4 and concentrated

under vacuum. Purification by column chromatography (hexane:ethyl acetate = 8:2), afforded compound **3g** (381 mg, 75% yield).

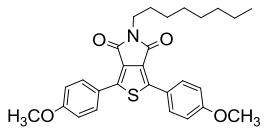
1,3-bis(4-acetylphenyl)-5-octyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3h).



Compound **3h** was synthesized from **1** (100 mg, 0.38 mmol) and 1-(4-iodophenyl)ethanone (280 mg, 1.14 mmol) in accordance with the typical procedure. Purification by column chromatography (hexane:ethyl acetate = 7:3), afforded compound **3h** (132 mg, 69% yield). After crystallization from CH_2Cl_2/hexane, compound **3h** was obtained as a yellow solid, m.p. = 171.1-172.3°C; HRMS *m/z* calculated for $C_{30}H_{31}NO_4S$ $[M+Na]^+$: 524.1871, found: 524.1866; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.26-8.22 (m, 4H), 8.07-8.03 (m, 4H), 3.69 (t, *J* = 7.3 Hz, 2H), 2.64 (s, 6H), 1.73-1.65 (m, 2H), 1.40-1.21 (m, 10H), 0.86 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 197.2, 162.8, 144.1, 138.0, 134.5, 132.3, 129.1, 128.5, 39.0, 31.9, 29.3, 29.3, 28.6, 27.1, 26.9, 22.8, 14.2; IR (KBr, cm^{-1}) ν: 3055, 2916, 2858, 1735, 1686, 1602, 1410, 1385, 1359, 1267, 1089, 957, 844, 756, 694.

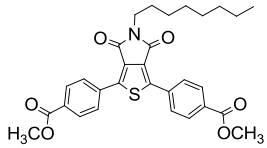
<u>1 mmol scale procedure:</u> Following tipycal procedure, 5-octylthieno[3,4-*c*]pyrrole-4,6-dione (TPD) **1** (265 mg, 1 mmol), Cs_2CO_3 (652 mg, 2 mmol), pivalic acid (31 mg, 0.3 mmol), $Pd_2(dba)_3$ (46 mg, 0.05 mmol), P(*o*-MeOPh)$_3$ (33 mg, 0.1 mmol), 1-(4-iodophenyl)ethanone (738 mg, 3 mmol), CPME (0.8 mL) and, finally, a preformed mixture of choline chloride (5.70 g, 40.8 mmol) and urea (4.94 g, 82.3 mmol) were introduced in a schlenk tube (ø = 2.5 cm) with a screw cap. The resulting heterogeneous reaction mixture was reacted at 110 °C, using a sand bath, under magnetic stirring. After 48 h, the mixture was cooled to room temperature and, after water addition (80 mL), extracted with CH_2Cl_2 (3x50 mL). The organic extracts were dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography (hexane:ethyl acetate = 7:3), afforded compound **3h** (371 mg, 74% yield).

1,3-bis(4-methoxyphenyl)-5-octyl-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3i).



Compound **3i** was synthesized from **1** (100 mg, 0.38 mmol) and 1-iodo-4-methoxybenzene (267 mg, 1.14 mmol) in accordance with the typical procedure. Purification by column chromatography (CH_2Cl_2:hexane = 6:4), afforded compound **3i** (100 mg, 55% yield). After crystallization from CH_2Cl_2/hexane, compound **3i** was obtained as a pale yellow solid, m.p. = 123.6-124.9°C; HRMS *m/z* calculated for $C_{28}H_{31}NO_4S$ $[M+Na]^+$: 500.1871, found: 500.1856; ^1H NMR ($CDCl_3$, 500 MHz) δ: 8.12-8.07 (m, 4H), 6.99-6.95 (m, 4H), 3.86 (s, 6H), 3.65 (t, *J* = 7.5 Hz, 2H), 1.71-1.63 (m, 2H), 1.39-1.20 (m, 10H), 0.86 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 163.4, 161.1, 144.4, 129.8, 129.0, 123.7, 114.4, 55.6, 38.7, 31.9, 29.4, 29.3, 28.6, 27.1, 22.8, 14.2; IR (KBr, cm^{-1}) ν: 3064, 2916, 2846, 1735, 1686, 1605, 1504, 1253, 1186, 1089, 1065, 826.

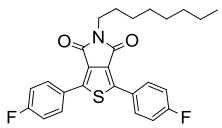
dimethyl 4,4'-(5-octyl-4,6-dioxo-5,6-dihydro-4*H*-thieno[3,4-*c*]pyrrole-1,3-diyl)dibenzoate (3j).



Compound **3j** was synthesized from **1** (100 mg, 0.38 mmol) and methyl 4-iodobenzoate (298 mg, 1.14 mmol) in accordance with the typical procedure. Purification by column chromatography (hexane:ethyl acetate = 8:2), afforded compound **3j** (144 mg, 71% yield). After crystallization from CH_2Cl_2/hexane, compound **3j** was obtained as a yellow solid, m.p. = 150.0-151.5°C; HRMS *m/z*

calculated for $C_{30}H_{31}NO_6S$ [M+Na]$^+$: 556.1770, found: 556.1761; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.23-8.20 (m, 4H), 8.15-8.11 (m, 4H), 3.95 (s, 6H), 3.68 (t, *J* = 8.0 Hz, 2H), 1.73-1.64 (m, 2H), 1.40-1.21 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 166.4, 162.8, 144.2, 134.5, 132.1, 131.5, 130.4, 128.2, 52.5, 39.0, 31.9, 29.3, 29.3, 28.6, 27.1, 22.8, 14.2; IR (KBr, cm^{-1}) ν: 3059, 2947, 2923, 2857, 1729, 1695, 1607, 1433, 1383, 1280, 1201, 1112, 1094, 772, 753, 695.

5-octyl-1,3-bis(4-fluorophenyl)-4*H*-thieno[3,4-*c*]pyrrole-4,6(5*H*)-dione (3k).[1]



Compound **3k** was synthesized from **1** (100 mg, 0.38 mmol) and 1-fluoro-4-iodobenzene (253 mg, 1.14 mmol) in accordance with the typical procedure. Purification by column chromatography (hexane:ethyl acetate = 9:1), afforded compound **3k** (160 mg, 93% yield). After crystallization from hexane, compound **3k** was obtained as a yellow solid, m.p. = 95.4-96.0°C; HRMS *m/z* calculated for $C_{26}H_{25}F_2NO_2S$ [M+Na]$^+$: 476.1472, found: 476.1466; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8-16-8.11 (m, 4H), 7.19-7.13 (m, 4H), 3.66 (t, *J* = 7.2 Hz, 2H), 1.71-1.62 (m, 2H), 1.39-1.19 (m, 10H), 0.86 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 163.9 (d, ^1J = 252.0 Hz), 163.1, 148.8, 130.4 (d, ^3J = 8.8 Hz), 130.3 (d, ^5J = 1.3 Hz), 126.9 (d, ^4J = 3.8 Hz), 116.3 (d, ^2J = 21.4 Hz), 39.8, 31.9, 29.3, 29.3, 28.6, 27.1, 22.8, 14.2; IR (KBr, cm^{-1}) ν: 3059, 2920, 2846, 1741, 1690, 1601, 1507, 1384, 1230, 1167, 1087, 837, 756.

NMR Spectra

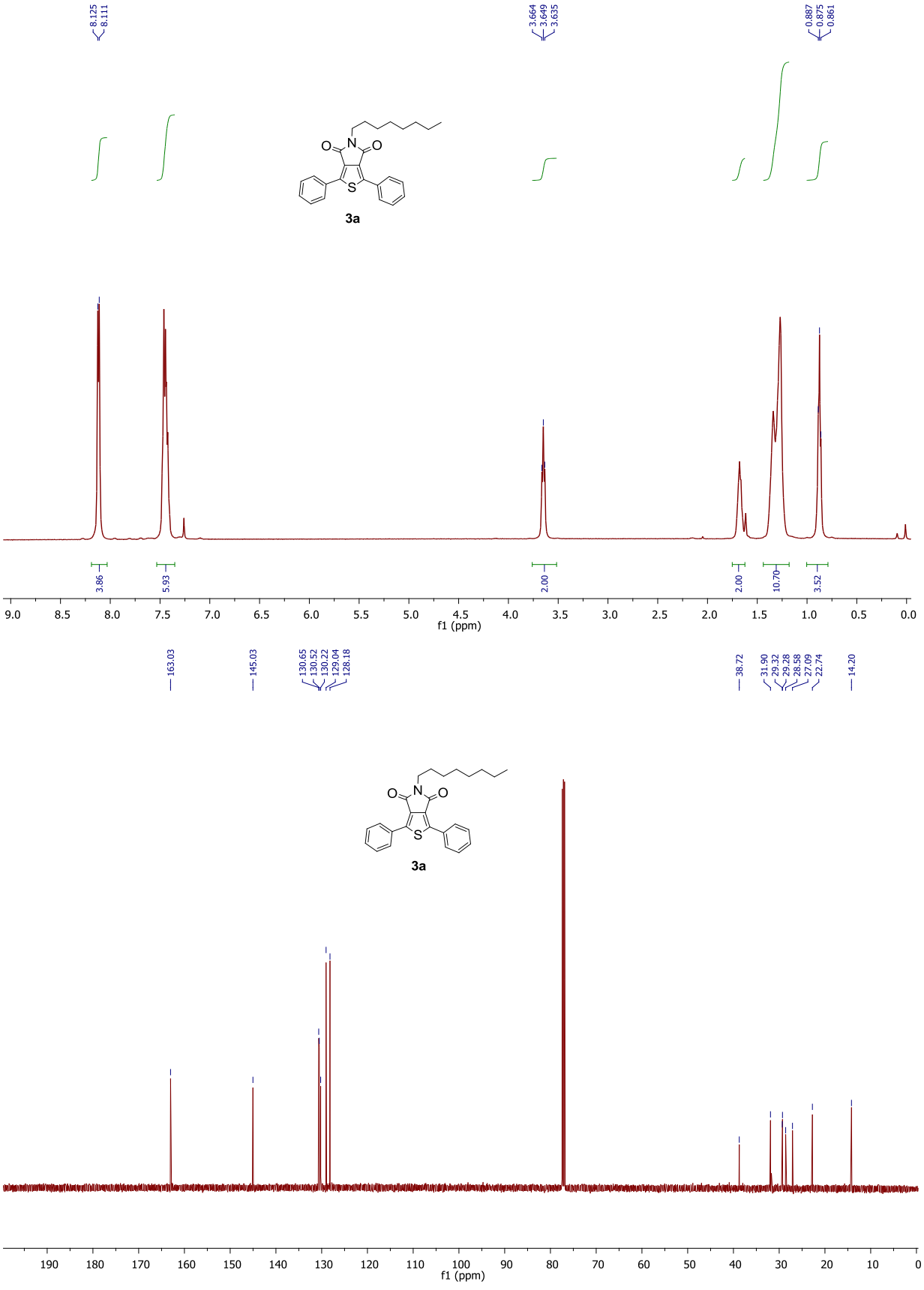


Figure S1. ^{1}H NMR and ^{13}C NMR spectra of compound **3a** (500 and 126 MHz, $CDCl_3$).

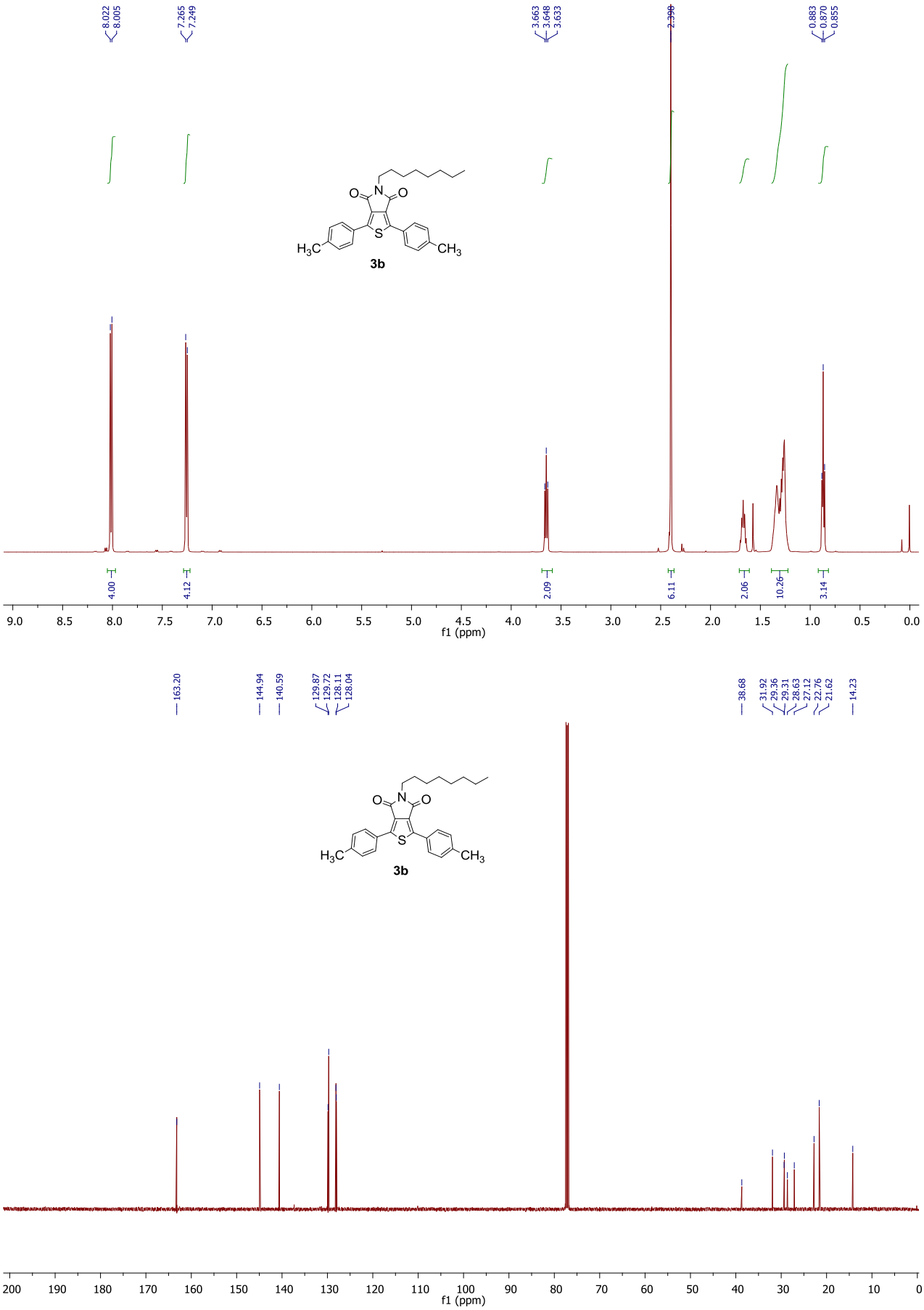


Figure S2. ^{1}H NMR and ^{13}C NMR spectra of compound **3b** (500 and 126 MHz, $CDCl_3$).

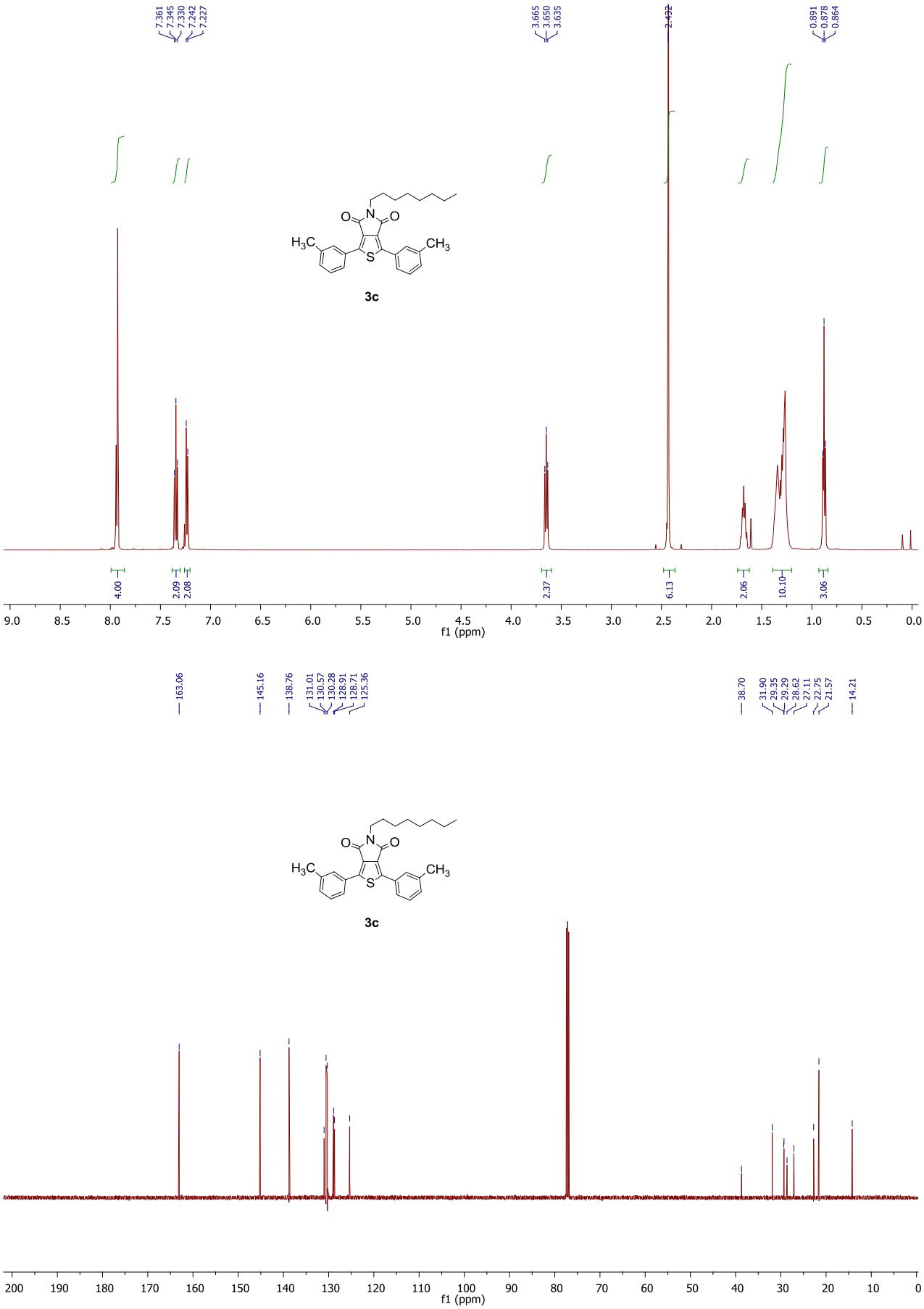


Figure S3. ^{1}H NMR and ^{13}C NMR spectra of compound **3c** (500 and 126 MHz, $CDCl_3$).

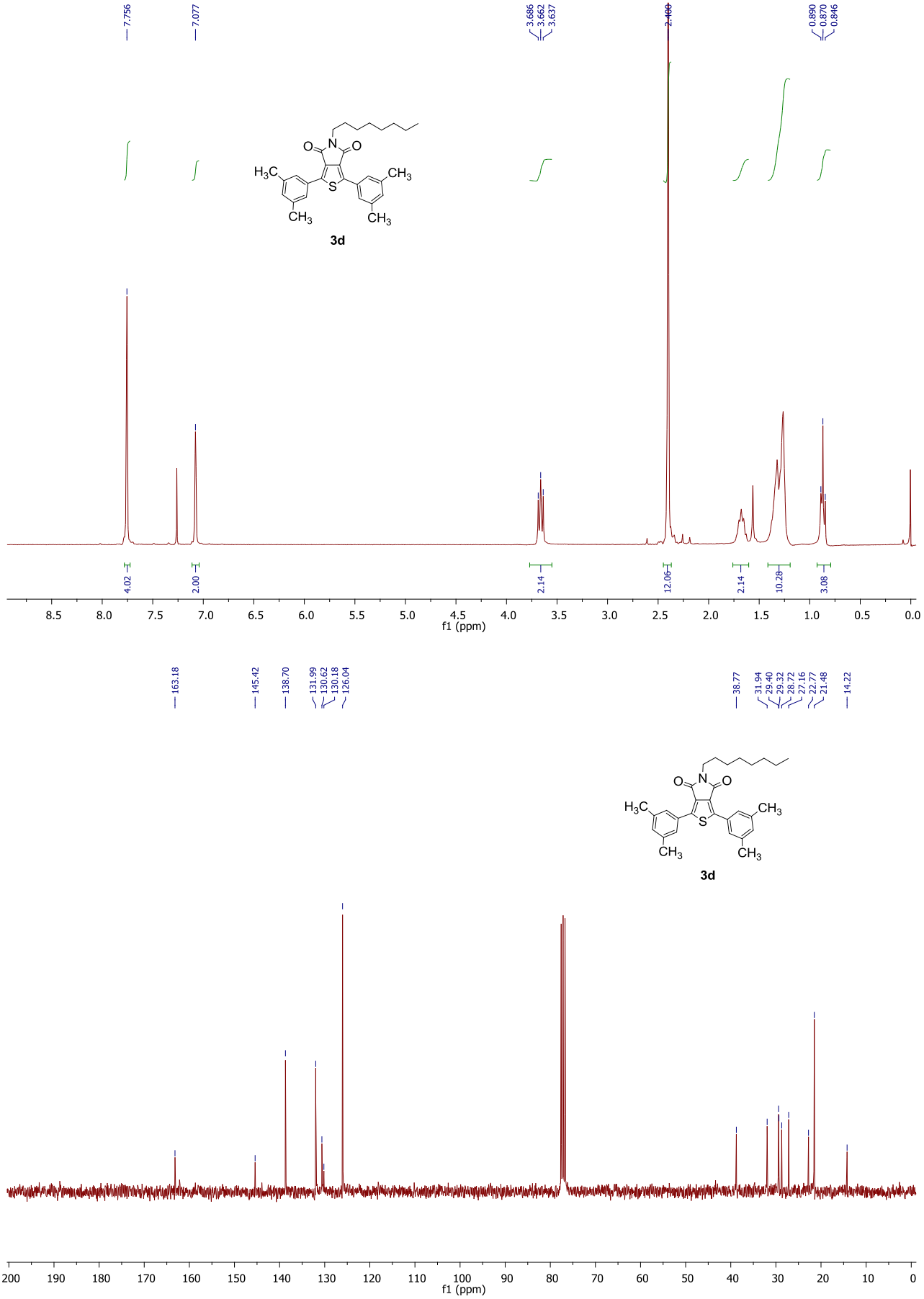


Figure S4. ^{1}H NMR and ^{13}C NMR spectra of compound **3d** (300 and 75 MHz, $CDCl_3$).

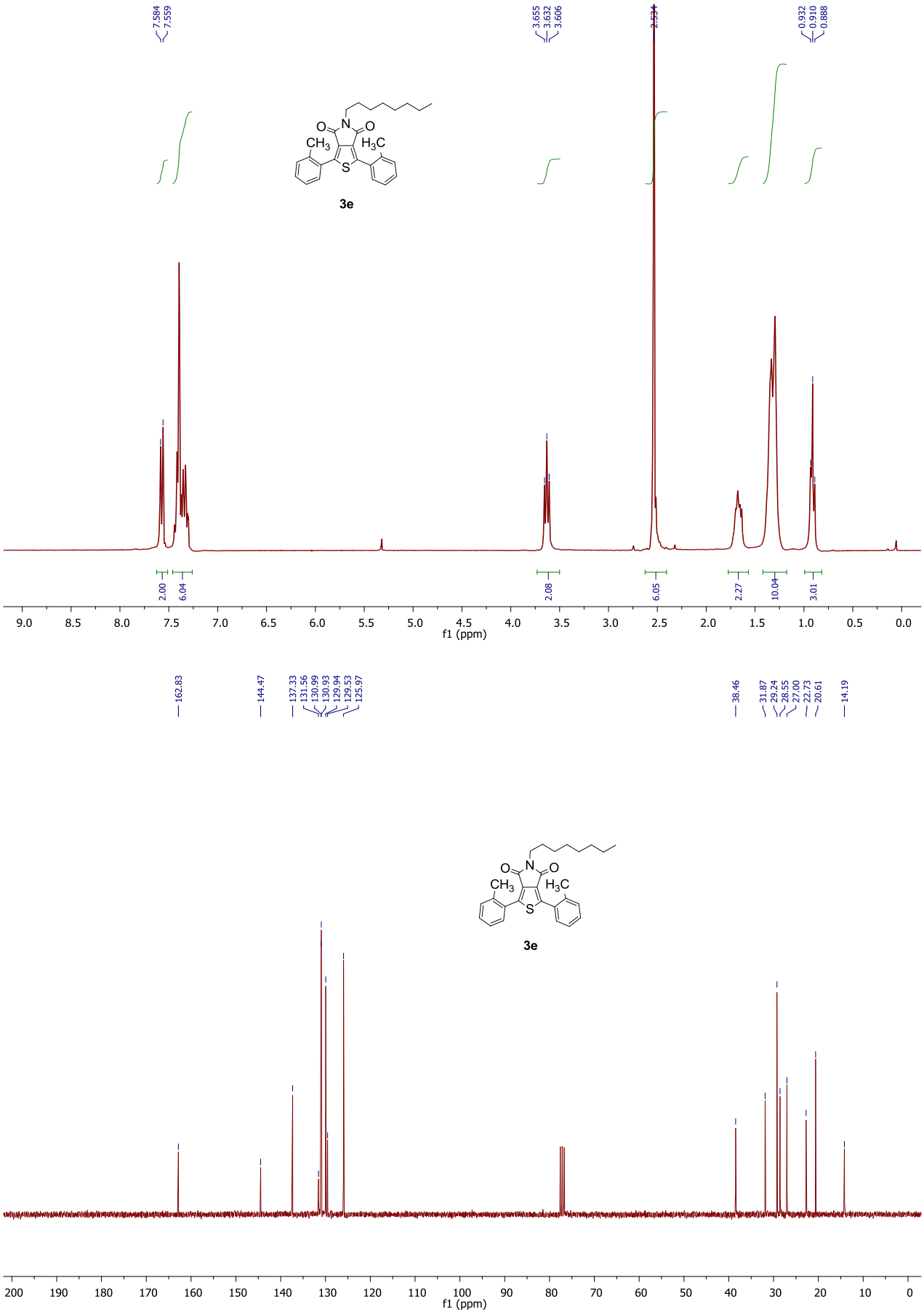


Figure S5. ^{1}H NMR and ^{13}C NMR spectra of compound **3e** (300 and 75 MHz, $CDCl_3$).

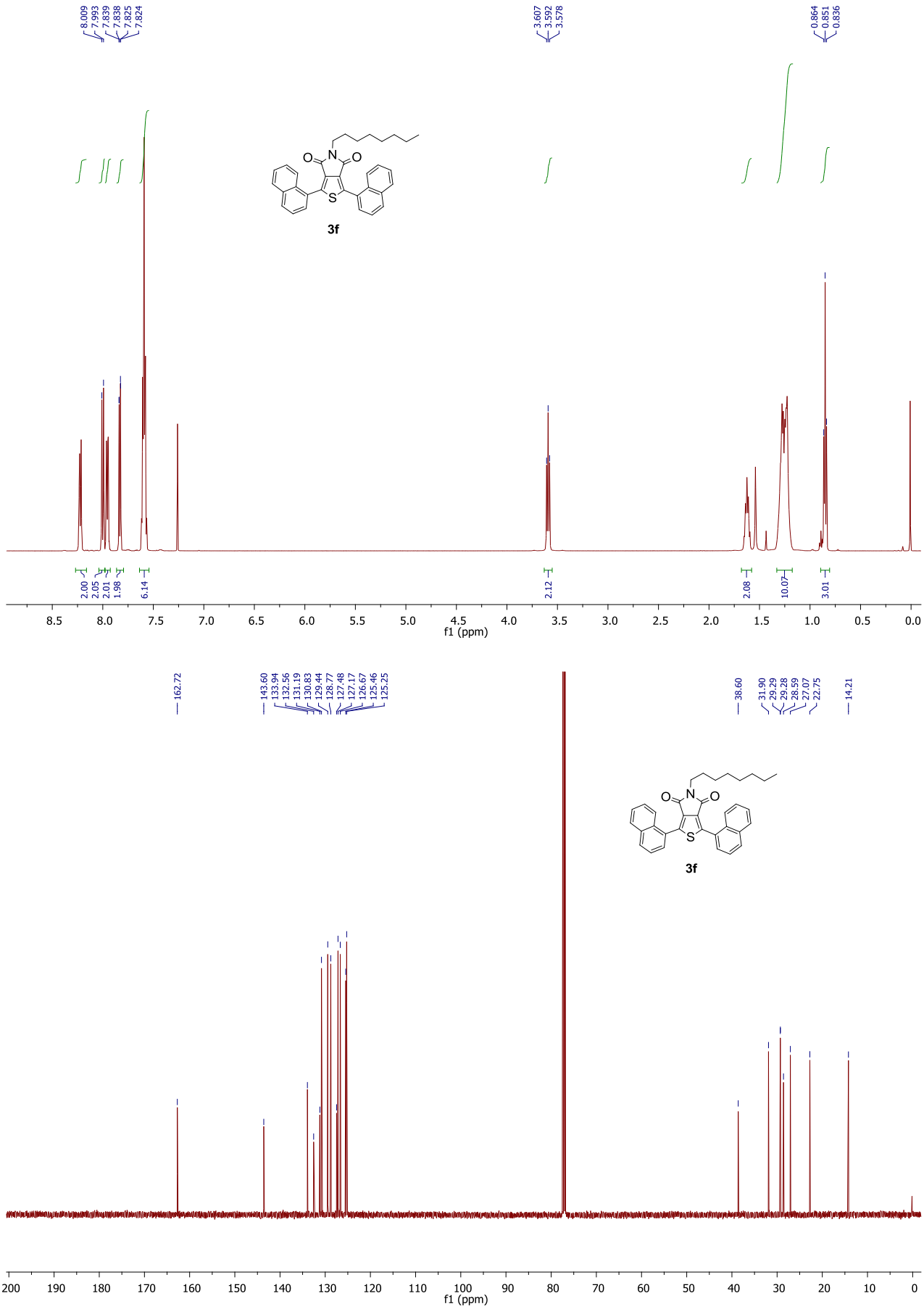


Figure S6. ^{1}H NMR and ^{13}C NMR spectra of compound **3f** (500 and 126 MHz, $CDCl_3$).

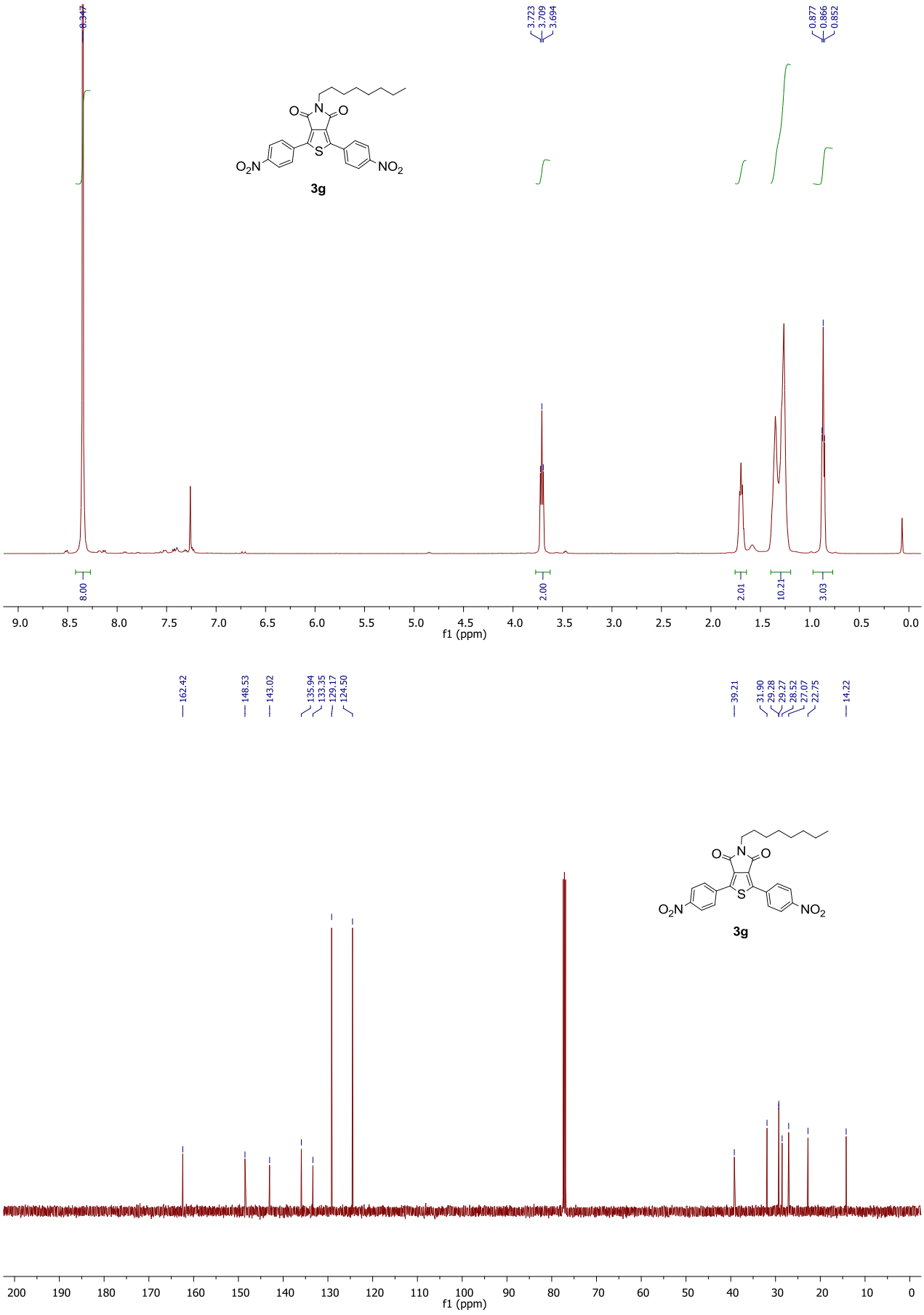


Figure S7. ^{1}H NMR and ^{13}C NMR spectra of compound **3g** (500 and 126 MHz, $CDCl_3$).

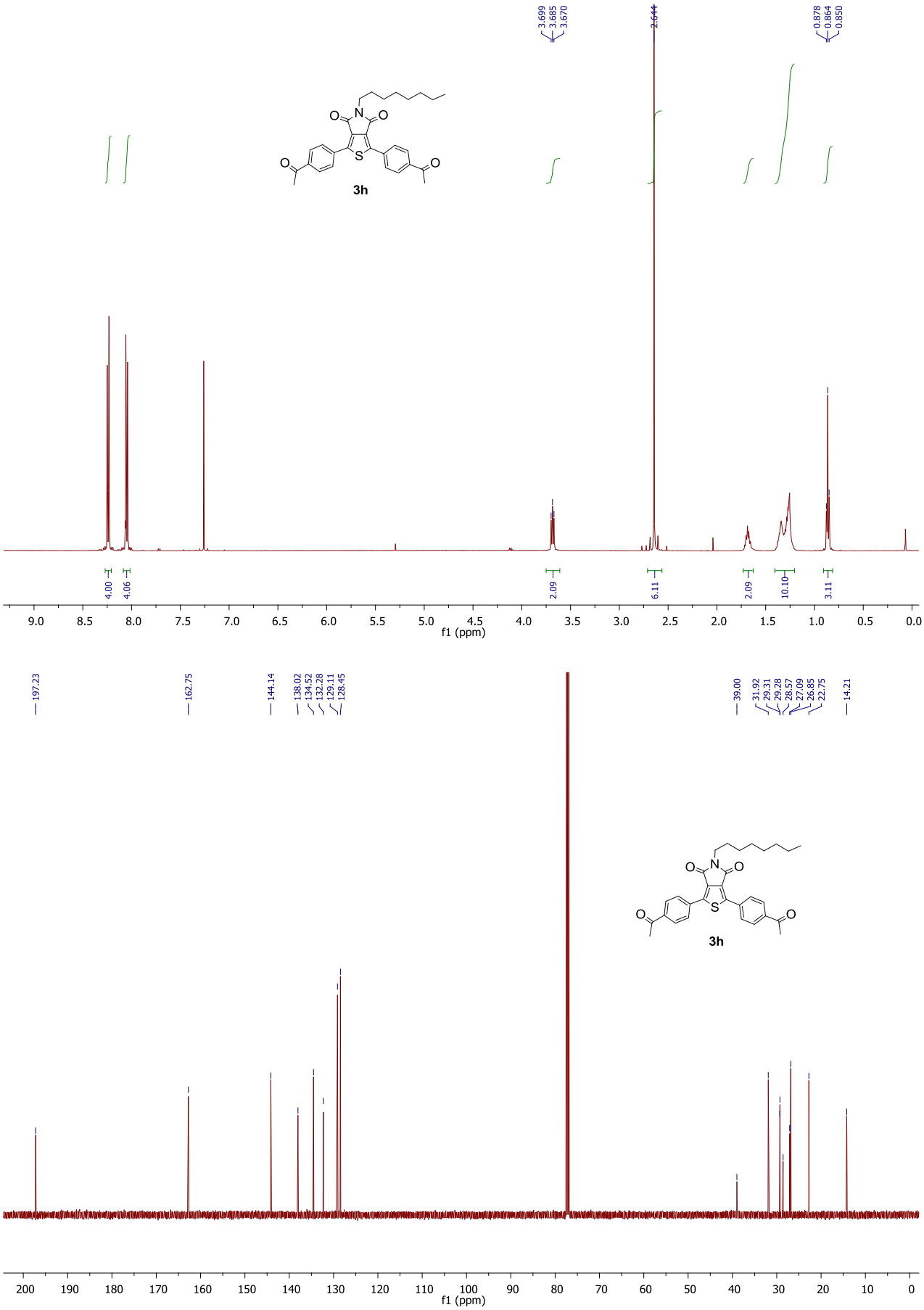


Figure S8. ^{1}H NMR and ^{13}C NMR spectra of compound **3h** (500 and 126 MHz, $CDCl_3$).

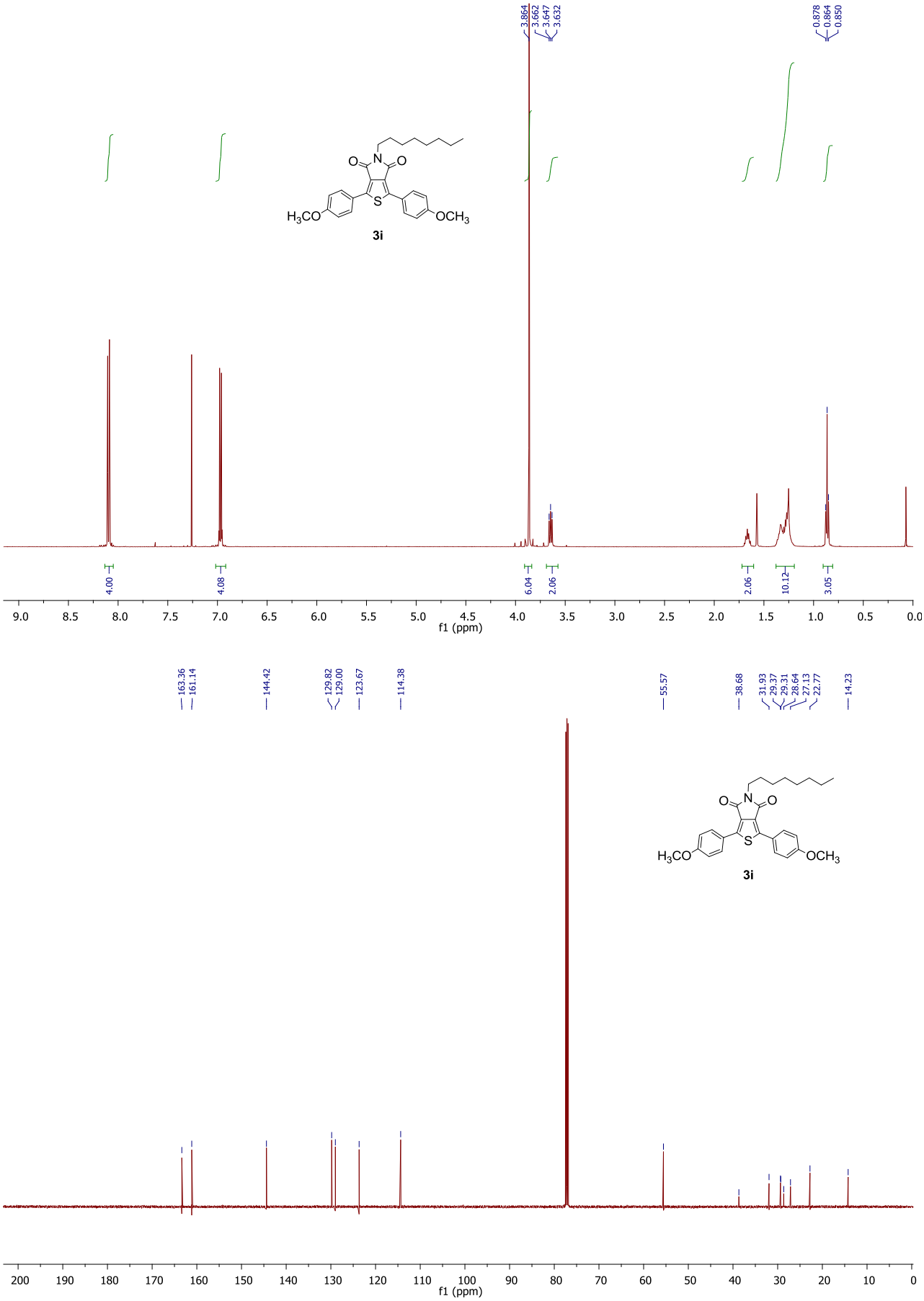


Figure S9. ^{1}H NMR and ^{13}C NMR spectra of compound **3i** (500 and 126 MHz, $CDCl_3$).

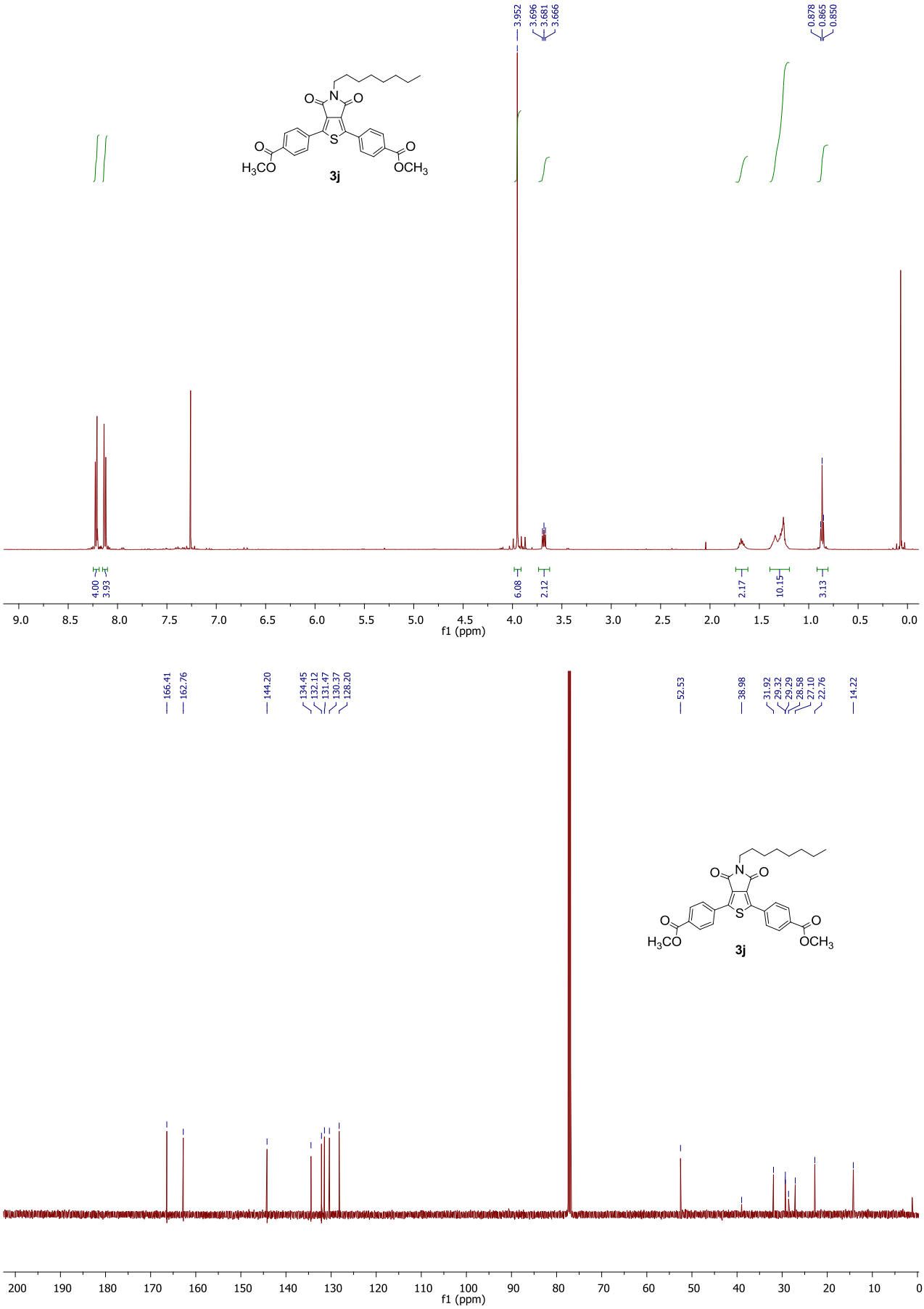


Figure S10. ^{1}H NMR and ^{13}C NMR spectra of compound **3j** (500 and 126 MHz, $CDCl_3$).

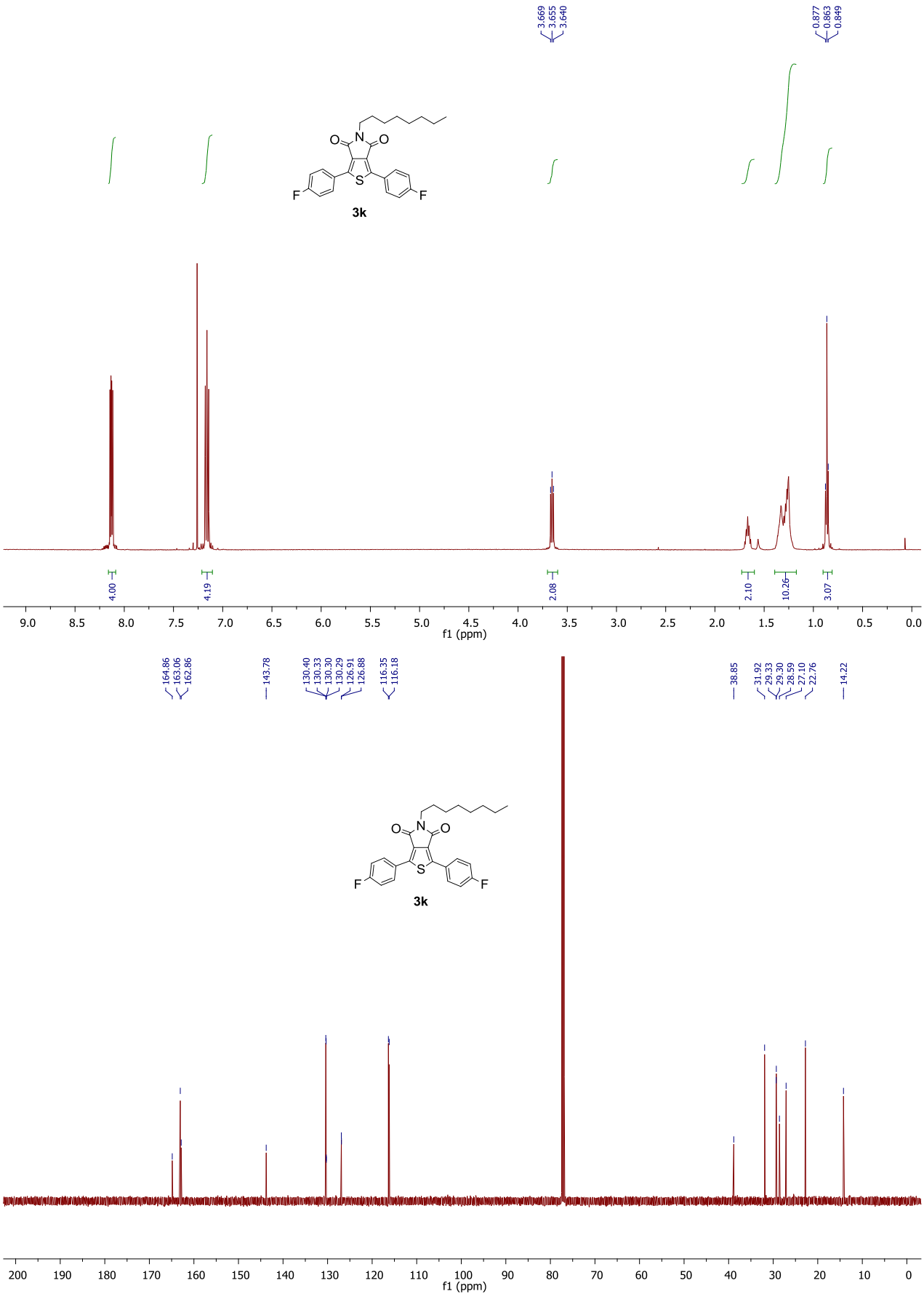


Figure S11. ^{1}H NMR and ^{13}C NMR spectra of compound **3k** (500 and 126 MHz, $CDCl_3$).

4. Notes and references

(1) Song, Y.-T.; Lin, P.-H.; Liu, C.-Y. *Adv. Synth. Catal.* **2014**, 356, 3761-3768.

(2) All synthesized compounds exhibit a fair to good solubility in ethyl acetate, a less toxic solvent than CH_2Cl_2. Consequently, ethyl acetate could be used as extracting solvent instead of CH_2Cl_2.

(3) By using pure CPME (3 mL) as the solvent, the coupling of **1** (100 mg, 0.38 mmol) with 1-iodo-4-nitrobenzene (284 mg, 1.14 mmol), in the presence of Cs_2CO_3 (0.25 g, 0.76 mmol), pivalic acid (12 mg, 0.12 mmol), $Pd_2(dba)_3$ (18 mg, 0.02 mmol) and P(*o*-MeOPh)$_3$ (13 mg, 0.04 mmol), performed in a schlenk tube (ø = 2.5 cm) equipped with a reflux condenser, provides the expected product **3g** in 68% yield. However, CPME should be anyway considered as a conventional flammable solvent, whose use should be restricted. In our protocol only 10% v/v of CPME is used with respect to hydrophilic choline chloride-urea mixture; a larger volume of CPME is required if it is employed as the solvent instead of as an additive.