Supporting Information

Pd-Catalyzed Direct *ortho*-C–H Arylation of Aromatic Ketones Enabled by a Transient Directing Group

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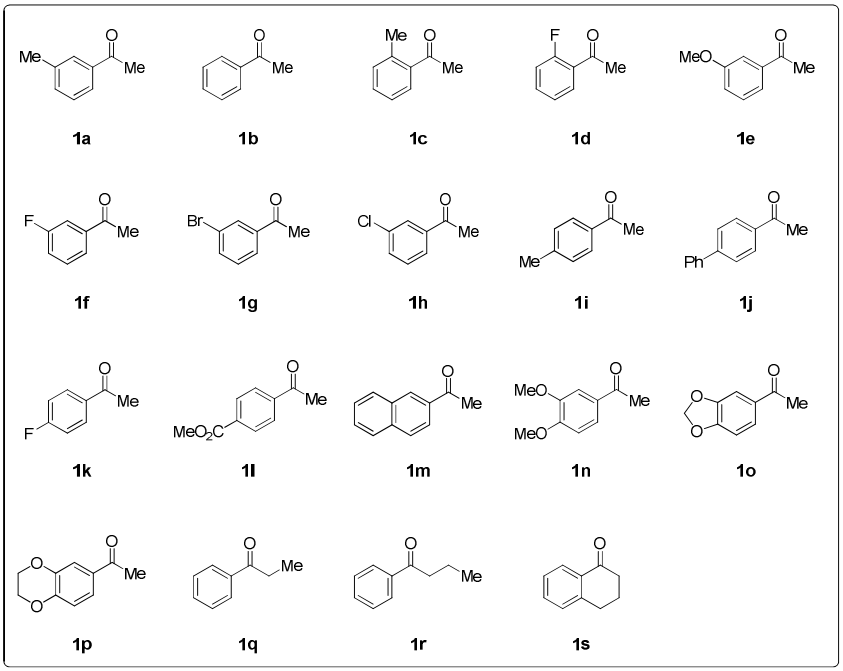
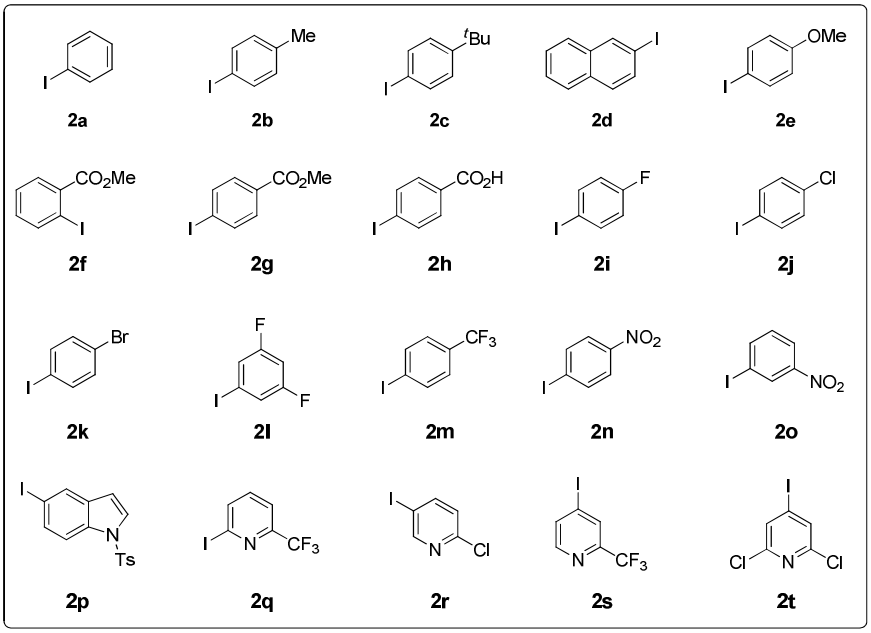
1. General Information

All solvents and chemicals were from Sigma-Aldrich, Acros and Alfa Aesar and used directly without further purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light. Preparative TLC was performed on 1.0 mm silica gel (Analtech). Columns for flash chromatography (FC) contained silica gel (32–63μ, Dynamic Adsorbents, Inc.). ^{1}H NMR spectra were recorded on Bruker AV-400 instrument (400 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to 0.00 ppm for tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker AV-400 instrument (100 MHz), and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet peak at 77.0 ppm of chloroform-*d* and the center line of a septet peak at 40.0 ppm of d_6-DMSO. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

Aromatic ketones used in the C–H arylation (1a–1s)



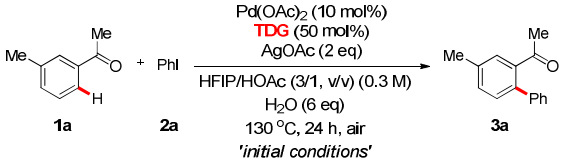
Aryl iodides used in the C–H arylation (2a–2t)

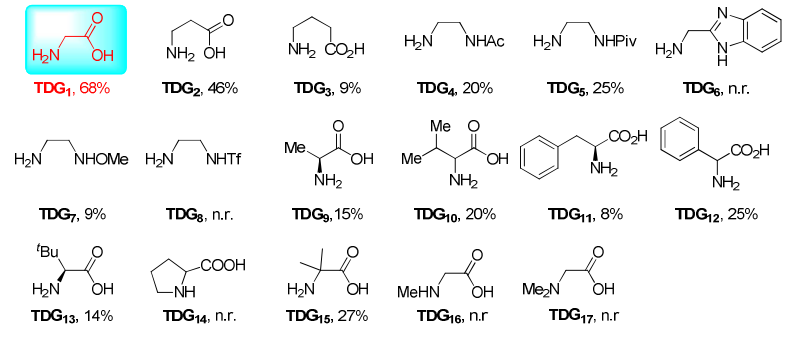


2. Experimental Section

2.1. Optimization for ortho-C(sp^2)–H Arylation of Aromatic Ketones

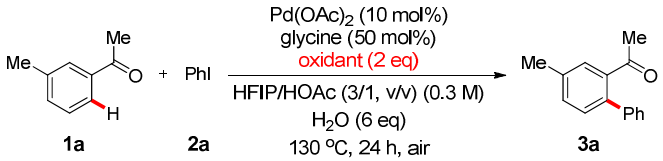
2.1.1. Screening of Directing Group





n.r.: no reaction.

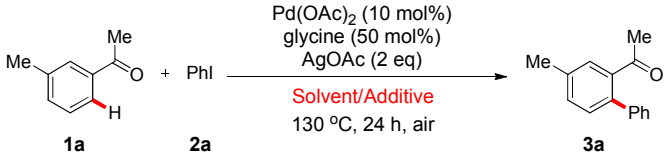
2.1.2 Screening of Oxidant



1a **2a** **3a**

AgOAc, 68%	AgTFA, 40%	AgF_2, 11%
AgOTf, 30%	$AgNO_3$, n.r.	AgO, 17%
Ag_2CO_3, 44%	AgOBz, 63%	Ag_2O, 48%

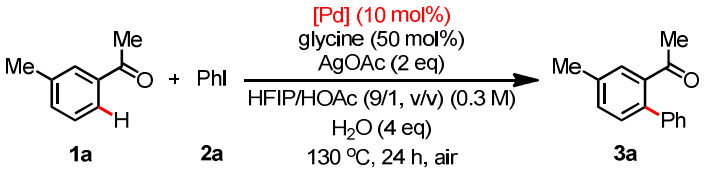
2.1.3 Screening of Solvent and Additive



1a **2a** **3a**

Entry	Solvent	Additive	NMR yield (%)
1	HFIP	-	43
2	HOAc	-	13
3	HFIP/HOAc (1:1,v/v)	-	54
4	HFIP/HOAc (3:1,v/v)	-	64
5	HFIP/HOAc (5:1,v/v)	-	60
6	HFIP/HOAc (7:1,v/v)	-	68
7	HFIP/HOAc (9:1,v/v)	-	73
8	HFIP/HOAc (9:1,v/v)	2eq H_2O	74
9	HFIP/HOAc (9:1,v/v)	4eq H_2O	78
10	HFIP/HOAc (9:1,v/v)	6eq H_2O	71
11	HFIP/HOAc (9:1,v/v)	8eq H_2O	60
12	HFIP/HOAc (9:1,v/v)	10eq H_2O	59
13	HFIP/HOAc (9:1,v/v)	20eq H_2O	55
14	HFIP/HOAc (9:1,v/v)	100eq H_2O	27
15	HFIP/HOAc (9:1,v/v)	1000eq H_2O	20

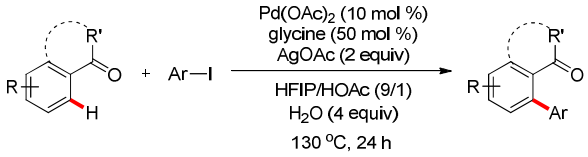
2.1.4 Screening of Palladium Catalyst



1a 2a 3a

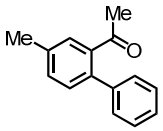
Pd catalyst	Yield(%)	Pd catalyst	Yield(%)
$Pd(OAc)_2$	78	$Pd(PCy_3)_2Cl_2$	25
$PdCl_2$	69	$PdCl_2/P(2\text{-}Fu)_3$	72
$Pd(TFA)_2$	62	$PdCl_2/PPh_3$(2eq)	85
$Pd(acac)_2$	35	$Pd(OAc)_2/PPh_3$(2eq)	81
$Pd(OPiv)_2$	65	$Pd(dppf)Cl_2$	22
$Pd(CH_3CN)_2Cl_2$	60	$Pd(dppp)Cl_2$	25
$Pd(PhCN)_2Cl_2$	65	$Pd(dppe)Cl_2$	20
$Pd(PPh_3)_2Cl_2$	86	$Pd(dppb)Cl_2$	35
$Pd(o\text{-}Tol_3P)_2Cl_2$	85	$Pd(PPh_3)_4$	12

3. General Procedure for ortho-C–H Arylation of Aromatic Ketones Using a Transient Directing Group



Typical procedure for Pd-catalyzed C–H arylation of aromatic ketones:

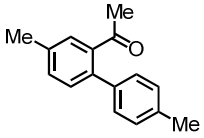
To a 20 mL reaction tube was added $Pd(PPh_3)_2Cl_2$ (72 mg, 0.1 mmol, 0.1 equiv), glycine (37.5 mg, 0.5 mmol, 0.5 equiv), AgOAc (334 mg, 2 mmol, 2 equiv), 3-methyl acetophenone (**1a**, 134 mg, 1 mmol), iodobenzene (**2a**, 612 mg, 3 mmol, 3 equiv), hexafluoroisopropanol (3 mL), acetic acid (350 μL), and H_2O (125 μL). The tube was then sealed and the mixture was stirred at room temperature for 15 min before being heated to 130 °C for 24 h. The reaction mixture was cooled to room temperature, filtrated via celite, washed with ethyl acetate exhaustively and the filtrate concentrated under reduced pressure. The resulting residue was purified by column chromatography (eluent: hexane/ethyl acetate, v/v 20 : 1) to provide the biaryl products **3a**[1] (169 mg, 80 % yield) as a colorless thick oil.



1-(4-methyl-[1,1′-biphenyl]-2-yl)ethanone (3a)[1]

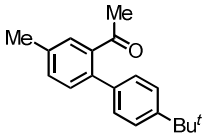
Yield: 80 % (169 mg), colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.36–7.34 (m, 1H), 7.32–7.28 (m, 3H), 7.26–7.24 (m, 3H), 7.22–7.18 (m, 1H), 2.34 (s, 3H), 1.91 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 205.2, 140.7, 140.6, 137.7, 137.3, 131.4, 130.1, 128.8, 128.6, 128.3, 127.6, 30.4, 20.9. HR-MS (ESI) m/z calcd for $C_{15}H_{15}O$ [M+H$^+$] 211.1117, found 211.1115.

Followed by the aforementioned general procedure, compounds **3b–3t and 4a–4r** were synthesized on 0.2 mmol scale using $Pd(PPh_3)_2Cl_2$ or $Pd(OAc)_2$ as a catalyst, respectively, as indicated in the Schemes 2 and 3 (see main text for details). The physical characterization data for these biaryl compounds were outlined in the following section.



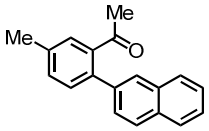
1-(4,4′-dimethyl-[1,1′-biphenyl]-2-yl)ethanone (3b)[1]

Yield: 80% (36 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.35–7.33 (m, 1H), 7.32–7.30 (m, 1H), 7.28–7.26 (m, 1H), 7.23–7.20 (m, 4H), 2.41 (s, 3H), 2.40 (s, 3H), 2.00 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 205.5, 140.7, 137.7, 137.5, 137.0, 131.4, 130.1, 129.3, 128.7, 128.2, 30.4, 21.1, 20.9. HR-MS (ESI) m/z calcd for $C_{16}H_{17}O$ [M+H$^+$] 225.1274, found 225.1272.



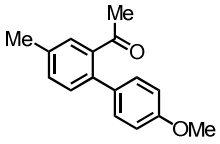
1-(4′-(tert-butyl)-4-methyl-[1,1′-biphenyl]-2-yl)ethanone (3c)

Yield: 70% (37 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.44–7.42 (d, J = 8.0 Hz, 2H), 7.34 (s, 1H), 7.29–7.24 (m, 4H), 2.41 (s, 3H), 1.99 (s, 3H), 1.35 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 205.4, 150.7, 140.8, 137.66, 137.60, 137.0, 131.3, 130.1, 128.5, 128.2, 125.2, 34.5, 31.3, 30.4, 20.9. HR-MS (ESI) m/z calcd for $C_{19}H_{23}O$ [M+H$^+$] 267.1743, found 267.1740.



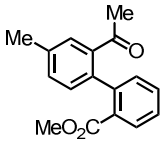
1-(5-methyl-2-(naphthalen-2-yl)phenyl)ethanone (3d)

Yield: 61% (32 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.91–7.85 (m, 3H), 7.79 (s, 1H), 7.55–7.50 (m, 2H), 7.47 (dd, J = 8.4, 1.6 Hz, 1H), 7.42–7.35 (m, 3H), 2.45 (s, 3H), 1.99 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 205.2, 140.9, 138.1, 137.6, 137.4, 133.2, 132.5, 131.5, 130.5, 128.5, 128.3, 128.1, 127.72, 127.70, 127.0, 126.5, 126.2, 30.5, 20.9. HR-MS (ESI) m/z calcd for $C_{19}H_{17}O$ [M+H$^+$] 261.1274, found 261.1269.



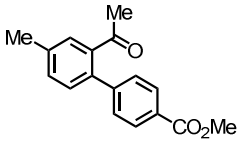
1-(4′-methoxy-4-methyl-[1,1′-biphenyl]-2-yl)ethanone (3e)[2]

Yield: 69% (33 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.34–7.29 (m, 2H), 7.28–7.22 (m, 3H), 7.34–7.29 (m, 2H), 6.97-6.93 (m, 2H), 3.85 (s, 3H), 2.40 (s, 3H), 2.00 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 205.7, 159.3, 140.7, 137.3, 136.9, 132.9, 131.4, 130.1, 129.9, 128.3, 114.1, 55.3, 30.5, 20.9. HR-MS (ESI) m/z calcd for $C_{16}H_{17}O_2$ [M+H$^+$] 241.1223, found 241.1221.



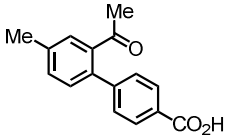
Methyl 2′-acetyl-4′-methyl-[1,1′-biphenyl]-2-carboxylate (3f)

Yield: 60% (32 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.97 (d, J = 8.0 Hz, 1H), 7.55–7.48 (m, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 7.6 Hz, 1H), 7.20 (d, J = 7.6 Hz, 1H), 7.06 (d, J = 7.6 Hz, 1H), 3.67 (s, 3H), 2.44 (s, 3H), 2.16 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.1, 167.5, 142.7, 138.5, 137.9, 137.0, 131.5, 131.4, 131.0, 130.1, 129.9, 129.6, 128.7, 127.3, 51.9, 29.3, 21.1. HR-MS (ESI) m/z calcd for $C_{17}H_{17}O_3$ [M+H$^+$] 269.1172, found 269.1167.



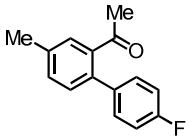
Methyl 2′-acetyl-4′-methyl-[1,1′-biphenyl]-4-carboxylate (3g)

Yield: 83% (45 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.08 (d, J = 8.4 Hz, 2H), 7.43–7.37 (m, 3H), 7.35–7.33 (m, 1H), 7.29–7.26 (m, 1H), 3.94 (s, 3H), 2.43 (s, 3H), 2.05 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 204.1, 166.7, 145.4, 140.5, 138.1, 136.6, 131.5, 130.1, 129.8, 129.3, 128.8, 128.6, 52.1, 30.4, 20.9. HR-MS (ESI) m/z calcd for $C_{17}H_{17}O_3$ [M+H$^+$] 269.1172, found 269.1169.



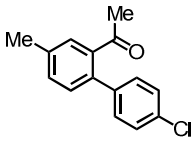
2′-acetyl-4′-methyl-[1,1′-biphenyl]-4-carboxylic acid (3h)

Yield: 80% (41 mg); white solid; mp 185–186 °C. ^{1}H-NMR (400 MHz, DMSO-d_6) δ = 7.99–7.94 (m, 2H), 7.50(s, 1H), 7.43–7.36 (m, 3H),7.32 (d, J = 8.0 Hz, 1H), 2.40 (s, 3H), 2.23 (s, 3H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ = 202.8, 167.1, 145.0, 139.9, 137.6, 136.3, 131.5, 130.3, 129.5, 129.4, 128.8, 128.5, 30.2, 20.5. HR-MS (ESI) m/z calcd for $C_{16}H_{15}O_3$ [M+H$^+$] 255.1016, found 255.1013.



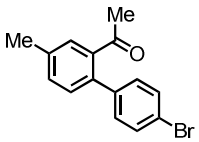
1-(4′-fluoro-4-methyl-[1,1′-biphenyl]-2-yl)ethanone (3i)

Yield: 62% (28 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.49 (s, 1H), 7.46–7.36 (m, 4H), 7.27–7.21 (m, 2H), 2.55 (s, 3H), 2.17 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 204.7, 162.5 (d, $J_{C\text{-}F}$ = 245 Hz), 140.6, 137.5, 136.7 (d, $J_{C\text{-}F}$ = 3 Hz), 136.6, 131.4, 130.4 (d, $J_{C\text{-}F}$ = 8 Hz), 130.2, 128.4, 115.6 (d, $J_{C\text{-}F}$ = 22 Hz), 30.4, 20.9. HR-MS (ESI) m/z calcd for $C_{15}H_{14}FO$ [M+H$^+$] 229.1023, found 229.1019.



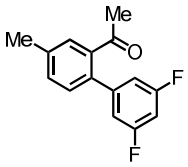
1-(4′-chloro-4-methyl-[1,1′-biphenyl]-2-yl)ethanone (3j)

Yield: 83% (41 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.40–7.33 (m, 3H), 7.31–7.29 (m, 1H), 7.25–7.20 (m, 3H), 2.40 (s, 3H), 2.05 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 204.4, 140.5, 139.2, 137.7, 136.4, 133.8, 131.5, 130.1, 130.0, 128.8, 128.5, 30.4, 20.9. HR-MS (ESI) m/z calcd for $C_{15}H_{14}ClO$ [M+H$^+$] 245.0728, found 245.0722.



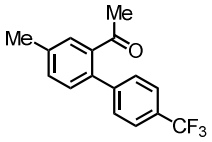
1-(4′-bromo-4-methyl-[1,1′-biphenyl]-2-yl)ethanone (3k)

Yield: 69% (40 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.54 (d, J = 8.4 Hz, 2H), 7.36 (s, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.19 (d, J = 8.4 Hz, 2H), 2.42 (s, 3H), 2.07 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 204.5, 140.4, 139.6, 137.8, 136.4, 131.7, 131.6, 130.4, 130.1, 128.5, 122.0, 30.5, 21.0. HR-MS (ESI) m/z calcd for $C_{15}H_{14}BrO$ [M+H$^+$] 289.0223, found 289.0222.



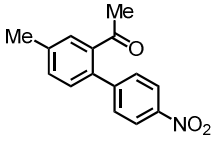
1-(3′,5′-difluoro-4-methyl-[1,1′-biphenyl]-2-yl)ethanone (3l)

Yield: 52% (26 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.28 (s, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.21 (d, J = 7.6 Hz, 1H), 6.87-6.78 (m, 3H), 2.43 (s, 3H), 2.16 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 203.4, 162.9 (d, $J_{C\text{-}F}$ = 248 Hz), 162.8 (d, $J_{C\text{-}F}$ = 248 Hz), 144.2 (t, $J_{C\text{-}F}$ = 10 Hz), 140.2, 138.4, 135.5 (t, $J_{C\text{-}F}$ = 2 Hz), 131.6, 130.0, 128.7, 112.0 (d, $J_{C\text{-}F}$ = 18 Hz), 111.9 (d, $J_{C\text{-}F}$ = 19 Hz), 102.9 (t, $J_{C\text{-}F}$ = 25 Hz), 30.2, 21.0. HR-MS (ESI) m/z calcd for $C_{15}H_{13}F_2O$ [M+H$^+$] 247.0929, found 247.0926.



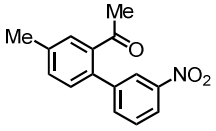
1-(4-methyl-4′-(trifluoromethyl)-[1,1′-biphenyl]-2-yl)ethanone (3m)

Yield: 70% (39 mg); colorless thick oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.66 (d, J = 8.0 Hz, 2H), 7.45–7.39 (m, 3H), 7.35 (d, J = 8.0 Hz, 1H), 7.26–7.23 (m, 1H), 2.43 (s, 3H), 2.11 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 203.9, 144.5, 140.3, 138.2, 136.3, 131.6, 130.3, 129.6 (q, $J_{C\text{-}F}$ = 32 Hz), 129.0, 128.7, 125.4 (q, $J_{C\text{-}F}$ = 4 Hz), 124.1 (q, $J_{C\text{-}F}$ = 270 Hz), 30.4, 21.0. HR-MS (ESI) m/z calcd for $C_{16}H_{14}F_3O$ [M+H$^+$] 279.0991, found 279.0990.



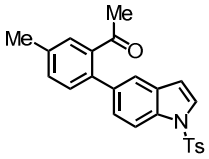
1-(4-methyl-4′-nitro-[1,1′-biphenyl]-2-yl)ethanone (3n)

Yield: 70% (36 mg); yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.30–8.26 (m, 2H), 7.51–7.45 (m, 3H), 7.42–7.38 (m, 1H), 7.29–7.26 (m, 1H), 2.48 (s, 3H), 2.25 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.8, 147.9, 147.0, 139.7, 138.8, 135.7, 131.9, 130.3, 129.5, 129.1, 123.6, 30.1, 21.0. HR-MS (ESI) m/z calcd for $C_{15}H_{14}NO_3$ [M+H$^+$] 256.0968, found 256.0965.



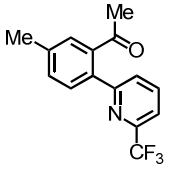
1-(4-methyl-3′-nitro-[1,1′-biphenyl]-2-yl)ethanone (3o)

Yield: 82% (42 mg); yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.22–8.17 (m, 2H), 7.59–7.52 (m, 2H), 7.47(s, 1H), 7.38–7.35 (m, 1H), 7.26–7.23 (m, 1H), 2.44 (s, 3H), 2.24 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.6, 148.2, 142.7, 139.5, 138.5, 135.6, 134.9, 131.9, 130.6, 129.2, 129.1, 123.3, 122.2, 30.1, 21.0. HR-MS (ESI) m/z calcd for $C_{15}H_{14}NO_3$ [M+H$^+$] 256.0968, found 256.0963.



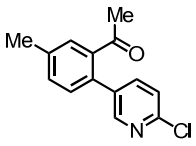
1-(5-methyl-2-(1-tosyl-1H-indol-5-yl)phenyl)ethanone (3p)

Yield: 60% (48 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.01 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 4.0 Hz, 1H), 7.46 (d, J = 1.2 Hz, 1H), 7.34 (s, 1H), 7.32–7.29 (m, 1H), 7.28–7.27 (m, 1H), 7.26–7.24 (m, 2H), 7.24–7.22 (m, 1H), 6.67 (dd, J = 3.6, 0.4 Hz, 1H), 2.41 (s, 3H), 2.35 (s, 3H), 1.89 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 205.3, 145.0, 140.9, 137.5, 137.2, 135.9, 135.1, 134.2, 131.3, 131.0, 130.4, 129.9, 128.3, 127.1, 126.8, 125.5, 121.4, 113.5, 109.0, 30.4, 21.5, 20.9. HR-MS (ESI) m/z calcd for $C_{24}H_{22}NO_3S$ [M+H$^+$] 404.1315, found 404.1313.



1-(5-methyl-2-(6-(trifluoromethyl)pyridin-2-yl)phenyl)ethanone (3q)

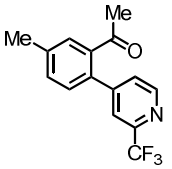
Yield: 72% (40 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.92 (t, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.36–7.29 (m, 2H), 2.43 (s, 3H), 2.42 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 204.3, 157.9, 147.4 (q, $J_{C\text{-}F}$ = 34 Hz), 142.2, 139.5, 138.1, 134.0, 130.6, 129.1, 127.8, 124.5, 121.3 (q, $J_{C\text{-}F}$ = 272 Hz), 118.4 (q, $J_{C\text{-}F}$ = 3 Hz), 30.4, 21.1. HR-MS (ESI) m/z calcd for $C_{15}H_{13}F_3NO$ [M+H$^+$] 280.0944, found 280.0938.



1-(2-(6-chloropyridin-3-yl)-5-methylphenyl)ethanone (3r)

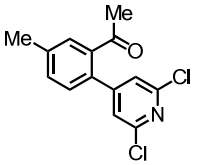
Yield: 41% (20 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.31 (d, J = 2.4 Hz, 1H), 7.57 (dd, J = 8.0, 2.4 Hz, 1H), 7.48 (s, 1H), 7.38–7.34 (m, 2H), 7.21 (d, J = 8.0 Hz, 1H), 2.45 (s, 3H), 2.28 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.3, 150.4, 148.9, 139.6, 138.9, 138.6, 135.6, 132.9, 132.0, 130.8, 129.2, 123.7, 30.1, 21.0. HR-MS (ESI) m/z calcd for $C_{14}H_{13}ClNO$

[M+H$^+$] 246.0680, found 246.0675.



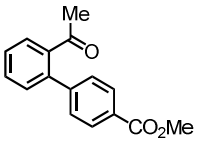
1-(5-methyl-2-(2-(trifluoromethyl)pyridin-4-yl)phenyl)ethanone (3s)

Yield: 50% (28 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.72 (d, J = 5.2 Hz, 1H), 7.60 (s, 1H), 7.54 (s, 1H), 7.42–7.35 (m, 2H), 7.23 (d, J =8.0 Hz, 1H), 2.47 (s, 3H), 2.35 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 201.5, 151.1, 149.7, 148.3 (q, $J_{C\text{-}F}$ = 34 Hz), 139.5, 138.9, 134.4, 132.2, 130.5, 129.5, 126.3, 121.5 (q, $J_{C\text{-}F}$ = 273 Hz), 120.4 (q, $J_{C\text{-}F}$ = 2 Hz), 29.7, 21.1. HR-MS (ESI) m/z calcd for $C_{15}H_{13}F_3NO$ [M+H$^+$] 280.0944, found 280.0943.



1-(2-(2,6-dichloropyridin-4-yl)-5-methylphenyl)ethanone (3t)

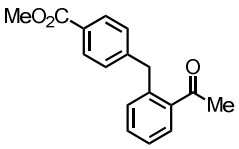
Yield: 90% (50 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.53 (s, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.18–7.13 (m, 3H), 2.46 (s, 3H), 2.41 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 200.9, 155.0. 150.2, 139.7, 138.4. 133.2, 132.3, 130.3, 129.7, 122.7, 29.5, 21.1. HR-MS (ESI) m/z calcd for $C_{14}H_{12}Cl_2NO$ [M+H$^+$] 280.0290, found 280.0283.



Methyl 2′-acetyl-[1,1′-biphenyl]-4-carboxylate (4a)

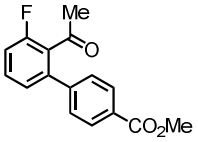
Yield: 75% (38 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.55–7.50 (m, 1H), 7.48–7.36 (m, 4H), 3.94 (s, 3H), 2.08 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 203.8, 166.7, 145.4, 140.5, 139.5, 130.8, 130.2, 129.8, 129.5, 128.8, 128.1, 128.0, 52.1, 30.3. HR-MS (ESI) m/z calcd for $C_{16}H_{15}O_3$ [M+H$^+$] 255.1016, found

255.1010.



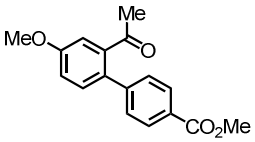
Methyl 4-(2-acetylbenzyl)benzoate (4b′)

Yield: 70% (37 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, J = 8.0 Hz, 2H), 7.70 (dd, J = 7.6, 0.8 Hz, 1H), 7.43 (td, J = 7.6, 1.2 Hz, 1H), 7.33 (td, J = 7.6, 0.8 Hz, 1H), 7.24–7.18 (m, 3H), 4.34 (s, 2H), 3.88 (s, 3H), 2.47 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 201.7, 167.0, 146.4, 139.7, 137.8, 132.0, 131.6, 129.6, 129.4, 128.9, 127.8, 126.5, 51.9, 39.4, 29.5. HR-MS (ESI) m/z calcd for $C_{17}H_{16}O_3$ [M+H$^+$] 268.1099, found 268.1096.



Methyl 2′-acetyl-3′-fluoro-[1,1′-biphenyl]-4-carboxylate (4c)

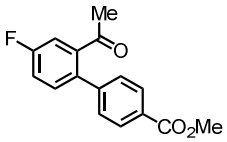
Yield: 50% (27 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.07 (d, J = 8.0 Hz, 2H), 7.48–7.37 (m, 3H), 7.19–7.13 (m, 2H) 4.34 (s, 2H), 3.94 (s, 3H), 2.25 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 200.6, 166.6, 160.1, 157.6, 143.6 (d, $J_{C\text{-}F}$ = 2 Hz), 140.5 (d, $J_{C\text{-}F}$ = 4 Hz), 130.0 (d, $J_{C\text{-}F}$ = 9 Hz), 129.8, 129.7, 129.3 (d, $J_{C\text{-}F}$ = 17 Hz), 128.8, 125.7 (d, $J_{C\text{-}F}$ = 3 Hz), 115.5 (d, $J_{C\text{-}F}$ = 22 Hz), 52.2, 32.4 (d, $J_{C\text{-}F}$ = 1 Hz). HR-MS (ESI) m/z calcd for $C_{16}H_{14}FO_3$ [M+H$^+$] 273.0921, found 273.0918.



Methyl 2′-acetyl-4′-methoxy-[1,1′-biphenyl]-4-carboxylate (4d)

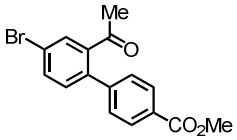
Yield: 80% (46 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.07 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.4 Hz, 1H), 7.09–7.04 (m, 2H), 3.94 (s, 3H), 3.87 (s, 3H), 2.04 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 204.1, 166.8, 159.3, 145.1, 141.7, 131.8, 131.5, 129.8, 129.1, 128.8, 116.8, 112.8, 55.5, 52.1, 30.4. HR-MS (ESI) m/z calcd for $C_{17}H_{17}O_4$ [M+H$^+$]

285.1121, found 285.1116.



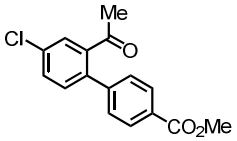
Methyl 2′-acetyl-4′-fluoro-[1,1′-biphenyl]-4-carboxylate (4e)

Yield: 50% (27 mg); pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.4 Hz, 2H), 7.40–7.34 (m, 3H), 7.29 (dd, J = 8.8, 2.4 Hz, 1H), 7.25–7.20 (m, 1H), 3.95 (s, 3H), 2.05 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.3, 166.6, 163.4, 160.9, 144.3, 142.1 (d, $J_{C\text{-}F}$ = 7 Hz), 135.5 (d, $J_{C\text{-}F}$ = 4 Hz), 132.1 (d, $J_{C\text{-}F}$ = 18 Hz), 123.0, 129.9 (d, $J_{C\text{-}F}$ = 27 Hz), 128.9, 117.8 (d, $J_{C\text{-}F}$ = 21 Hz), 115.1 (d, $J_{C\text{-}F}$ = 23 Hz), 52.2, 30.2. HR-MS (ESI) m/z calcd for $C_{16}H_{14}FO_3$ [M+H$^+$] 273.0921, found 273.0917.



Methyl 2′-acetyl-4′-bromo-[1,1′-biphenyl]-4-carboxylate (4f)

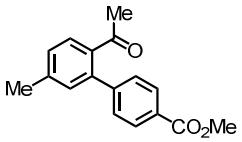
Yield: 66% (44 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.03 (d, J = 8.0 Hz, 2H), 7.65–7.58 (m, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.21–7.19 (m, 1H), 3.88 (s, 3H), 1.99 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.2, 166.5, 144.1, 141.9, 138.2, 133.7, 131.7, 130.9, 130.0, 129.8, 128.7, 122.3, 52.2, 30.2. HR-MS (ESI) m/z calcd for $C_{16}H_{14}BrO_3$ [M+H$^+$] 333.0121, found 333.0120.



Methyl 2′-acetyl-4′-chloro-[1,1′-biphenyl]-4-carboxylate (4g)

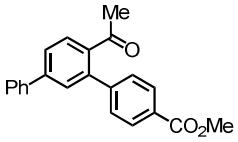
Yield: 72% (42 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 2.0 Hz, 1H), 7.51–7.48 (m, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 1H), 3.94 (s, 3H), 2.05 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.3, 166.5, 144.1, 141.7, 137.7, 134.3, 131.5, 130.7, 129.9, 129.8, 128.7, 128.0, 52.2, 30.2. HR-MS (ESI) m/z calcd for

$C_{16}H_{14}ClO_3$ [M+H$^+$] 289.0626, found 289.0620.



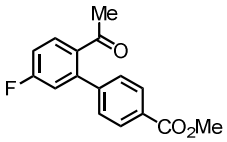
Methyl 2′-acetyl-5′-methyl-[1,1′-biphenyl]-4-carboxylate (4h)

Yield: 78% (42 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.30–7.26 (m, 2H), 7.20 (s, 1H), 3.97 (s, 3H), 5.46 (s, 3H), 2.09 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 203.2, 166.7, 145.8, 141.4, 139.8, 137.6, 131.0, 129.7, 129.3, 128.8, 128.6, 128.5, 52.1, 30.2, 21.3. HR-MS (ESI) m/z calcd for $C_{17}H_{17}O_3$ [M+H$^+$] 269.1172, found 269.1170.



Methyl 6′-acetyl-[1,1′:3′,1″-terphenyl]-4-carboxylate (4i)

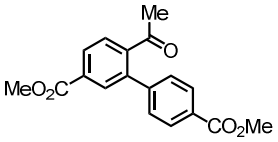
Yield: 71% (47 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.12 (d, J = 8.0 Hz, 2H), 7.74–7.68 (m, 2H), 7.66–7.62 (m, 2H), 7.60–7.58 (m, 1H), 7.50–7.44 (m, 4H), 7.42–7.38 (m, 1H), 3.95 (s, 3H), 2.13 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 203.1, 166.7, 145.6, 143.8, 140.3, 139.5, 138.9, 129.8, 129.5, 129.0, 128.9, 128.8, 128.2, 127.2, 126.5, 52.2, 30.3. HR-MS (ESI) m/z calcd for $C_{22}H_{19}O_3$ [M+H$^+$] 331.1329, found 331.1326.



Methyl 2′-acetyl-5′-fluoro-[1,1′-biphenyl]-4-carboxylate (4j)

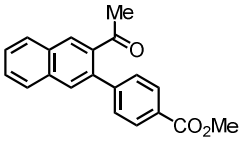
Yield: 52% (28 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, J = 8.0 Hz, 2H), 7.66–7.62 (m, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.16–7.12 (m, 1H), 7.10–7.07 (m, 1H), 3.95 (s, 3H), 2.06 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.0, 166.5, 164.9, 162.4, 144.3 (d, $J_{C\text{-}F}$ = 1 Hz), 142.5 (d, $J_{C\text{-}F}$ = 9 Hz), 136.5 (d, $J_{C\text{-}F}$ = 3 Hz), 130.9 (d, $J_{C\text{-}F}$ = 9 Hz), 129.9, 128.6, 117.2 (d, $J_{C\text{-}F}$ = 23 Hz), 115.0 (d, $J_{C\text{-}F}$ = 21 Hz), 52.2, 30.2. HR-MS (ESI) m/z calcd for $C_{16}H_{14}FO_3$ [M+H$^+$]

273.0921, found 273.0913.



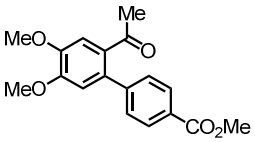
Dimethyl 6-acetyl-[1,1′-biphenyl]-3,4′-dicarboxylate (4k)

Yield: 70% (44 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.12–8.07 (m, 4H), 7.61 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 2H), 3.95 (s, 6H), 2.07 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 203.5, 166.5, 165.9, 144.24, 144.23, 139.3, 132.0, 131.3, 130.0, 129.9, 129.1, 128.8, 128.0, 52.5, 52.2, 30.3. HR-MS (ESI) m/z calcd for $C_{18}H_{17}O_5$ [M+H$^+$] 313.1071, found 313.1066.



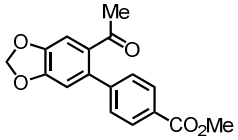
Methyl 4-(3-acetylnaphthalen-2-yl)benzoate (4l)

Yield: 88% (54 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.14–8.12 (m, 3H), 7.95 (d, J = 7.6 Hz, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.84 (s, 1H), 7.63–7.55 (m, 2H), 7.50 (d, J = 8.0 Hz, 2H), 3.96 (s, 6H), 2.22 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 203.0, 166.8, 145.7, 138.4, 136.4, 133.9, 131.9. 129.8, 129.7, 129.2, 129.0, 128.8, 128.7, 128.3, 127.8, 127.2, 52.1, 30.2. HR-MS (ESI) m/z calcd for $C_{20}H_{17}O_3$ [M+H$^+$] 305.1172, found 305.1170.



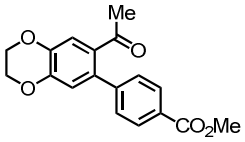
Methyl 2′-acetyl-4′,5′-dimethoxy-[1,1′-biphenyl]-4-carboxylate (4m)

Yield: 51% (31 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.21 (s, 1H), 6.80 (s, 1H), 3.96 (s, 3H), 3.95 (s, 3H), 1.97 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 202.4, 166.7, 150.9, 148.4, 145.8, 134.1, 132.5, 129.8, 129.4, 129.0, 112.7, 111.5, 56.15, 56.13, 52.2, 30.4. HR-MS (ESI) m/z calcd for $C_{18}H_{19}O_5$ [M+H$^+$] 315.1227, found 315.1223.



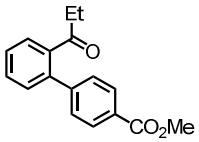
Methyl 4-(6-acetylbenzo[d][1,3]dioxol-5-yl)benzoate (4n)

Yield: 50% (30 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.04 (s, 2H), 3.94 (s, 3H), 2.12 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 200.6, 166.7, 149.9, 145.8, 139.4, 134.1, 129.7, 129.4, 124.3, 121.8, 107.5, 101.8, 52.2, 29.9, 29.6. HR-MS (ESI) m/z calcd for $C_{17}H_{15}O_5$ [M+H$^+$] 299.0914, found 299.0911.



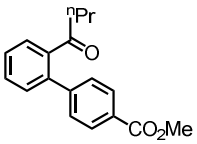
Methyl 4-(7-acetyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)benzoate (4o)

Yield: 53% (33 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.05 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H),7.21 (s, 1H), 6.84 (s, 1H), 4.32 (s, 2H), 3.93 (s, 3H), 2.06 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 201.4, 166.8, 145.6, 145.4, 143.0, 134.2, 133.3, 130.0, 129.7, 129.3, 129.1, 128.7, 119.1, 118.2, 64.6, 64.3, 52.1, 30.0. HR-MS (ESI) m/z calcd for $C_{18}H_{17}O_5$ [M+H$^+$] 313.1071, found 313.1068.



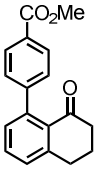
Methyl 2′-propionyl-[1,1′-biphenyl]-4-carboxylate (4p)

Yield: 49% (26 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.0 Hz, 2H), 7.54–7.50 (m, 2H), 7.46–7.43 (m, 1H), 7.42–7.37 (m, 3H), 3.93 (s, 3H), 2.33 (q, J = 7.2 Hz, 2H), 0.93 (t, J = 7.2 Hz, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 207.7, 166.7, 145.4, 140.8, 138.9, 130.5, 130.1, 129.8, 129.4, 128.7, 128.0, 127.7, 52.2, 36.1, 8.5. HR-MS (ESI) m/z calcd for $C_{17}H_{17}O_3$ [M+H$^+$] 269.1172, found 269.1166.



Methyl 2′-butyryl-[1,1′-biphenyl]-4-carboxylate (4q)

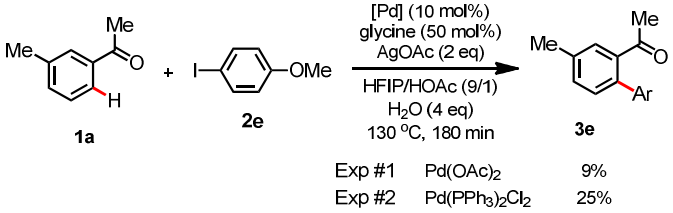
Yield: 60% (34 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.09 (d, J = 8.4 Hz, 2H), 7.55–7.49 (m, 2H), 7.47–7.43 (m, 1H), 7.43–7.36 (m, 3H), 3.94 (s, 3H), 2.30 (t, J = 7.2 Hz, 2H), 1.52–1.42 (m, 2H), 0.73 (t, J = 7.6 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 207.0, 166.7, 145.4, 140.9, 139.0, 130.4, 130.1, 129.8, 129.4, 128.8, 128.0, 127.7, 52.1, 44.7, 17.8, 13.5. HR-MS (ESI) m/z calcd for $C_{18}H_{19}O_3$ [M+H$^+$] 283.1329, found 283.1325.

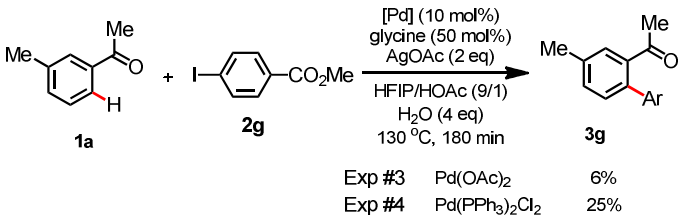


Methyl 4-(8-oxo-5,6,7,8-tetrahydronaphthalen-1-yl)benzoate (4r)

Yield: 59% (33 mg); pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.04 (d, J = 8.4 Hz, 2H), 7.45 (t, J = 7.6 Hz, 1H), 7.31–7.26 (m, 4H), 7.10 (d, J = 7.2 Hz, 1H), 3.93 (s, 3H), 3.03 (t, J = 6.0 Hz, 2H), 2.62 (t, J = 6.8 Hz, 2H), 2.19–2.12 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 198.1, 167.1, 148.0, 145.7, 142.9, 131.9, 131.0, 129.8, 129.1, 128.7, 128.3, 128.1, 51.9, 40.3, 30.6, 23.0. HR-MS (ESI) m/z calcd for $C_{18}H_{17}O_3$ [M+H$^+$] 281.1172, found 281.1169.

4. Parallel Experiments on Palladium Catalysts

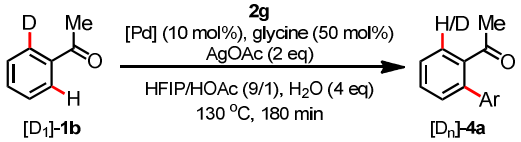




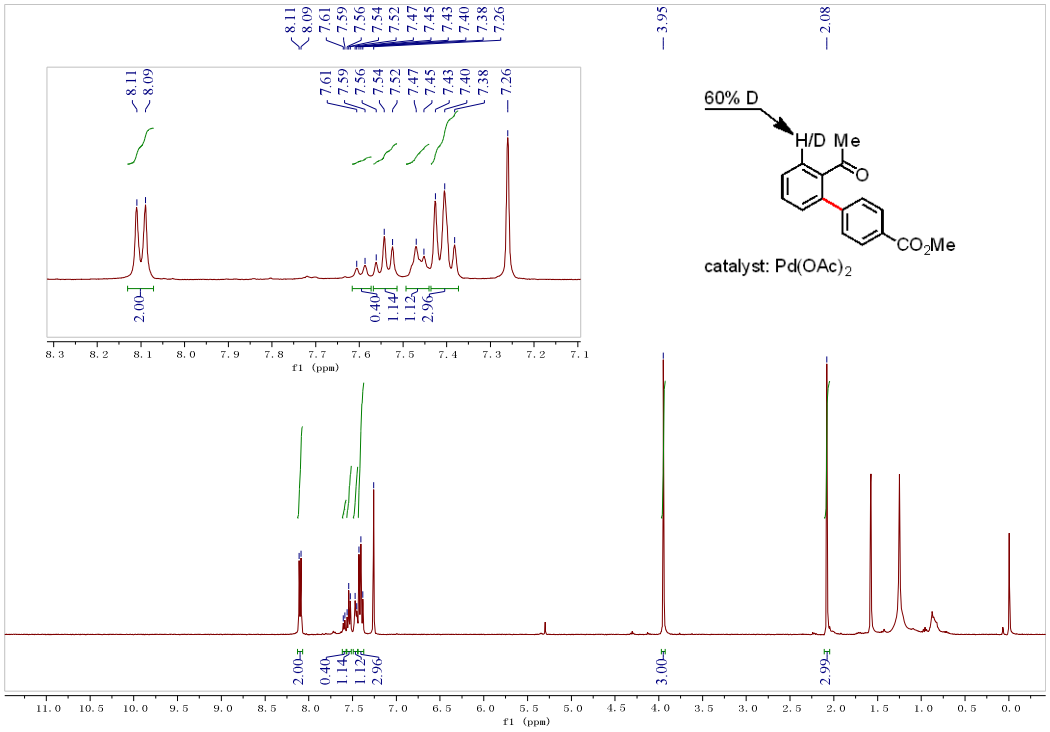
To a 20 mL reaction tube was added $Pd(OAc)_2$ or $Pd(PPh_3)_2Cl_2$ (0.02 mmol), glycine (7.5 mg, 0.1 mmol), AgOAc (67 mg, 0.4 mmol), 3-methyl acetophenone **1a** (0.2 mmol), Aryl iodide **2e** or **2g** (0.6 mmol), hexafluoroisopropanol (0.6 mL), acetic acid (70 μL), and H_2O (15 μL). The tube was then sealed and the mixture was stirred at room temperature for 15 min before being heated to 130 °C for 180 min. The reaction mixture was then cooled to room temperature, filtrated via celite, and concentrated under reduced pressure. The resulting residue was analyzed by ^1H NMR spectra with 1,1,2,2-tetrachloroethane as an internal standard.

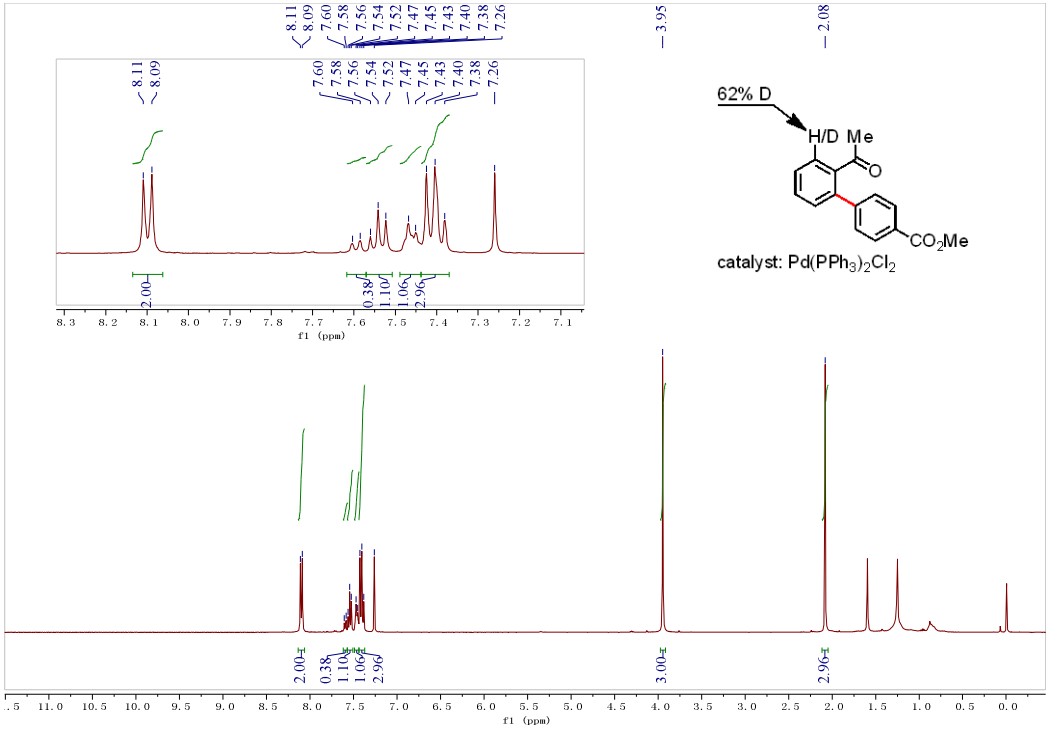
5. Deuteration Experiments

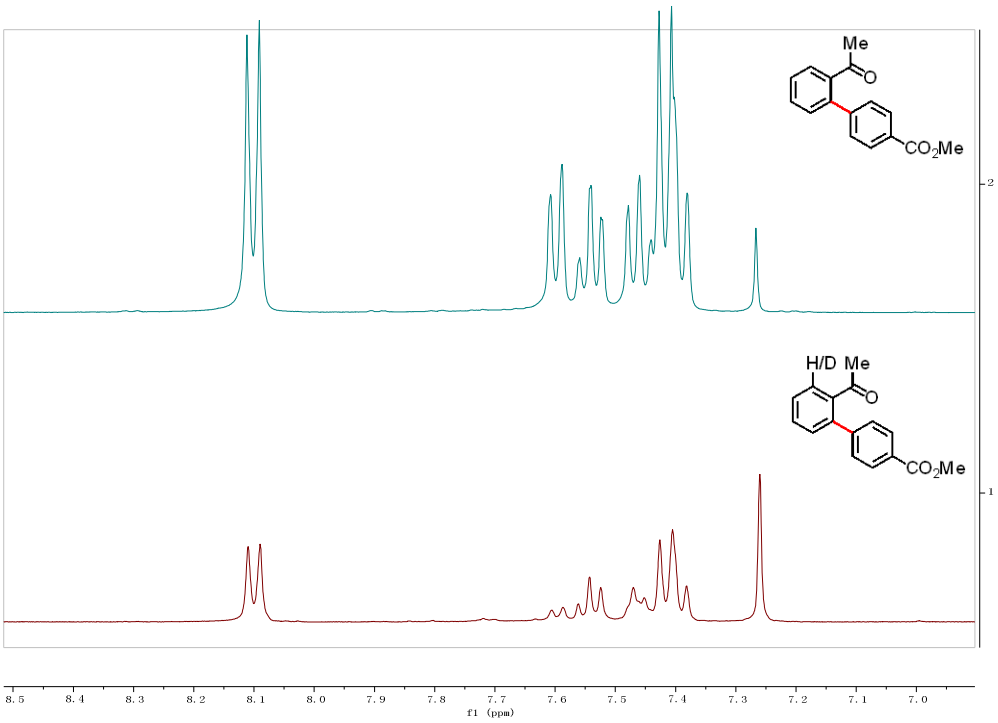
Intramolecular KIE experiments



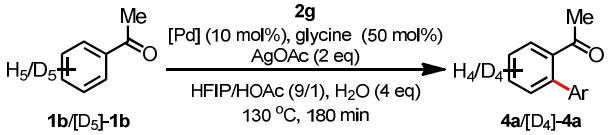
To a 20 mL reaction tube was added $Pd(OAc)_2$ or $Pd(PPh_3)_2Cl_2$ (0.02 mmol), glycine (7.5 mg, 0.1 mmol), AgOAc (67 mg, 0.4 mmol), [D_1]-acetophenone[3] **[D_1]-1b** (0.2 mmol), Aryl iodide **2g** (0.6 mmol), hexafluoroisopropanol (0.6 mL), acetic acid (70 μL), and H_2O (15 μL). The tube was then sealed and the mixture was stirred at room temperature for 15 min before being heated to 130 °C for 180 min. The reaction mixture was then cooled to room temperature, filtrated via celite, and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel and analyzed for its isotopic distribution by ^1H NMR spectra.


60% D
H/D Me
O
CO2Me
catalyst: Pd(OAc)2
f1 (ppm)


62% D
H/D Me
O
CO2Me
catalyst: Pd(PPh3)2Cl2
f1 (ppm)

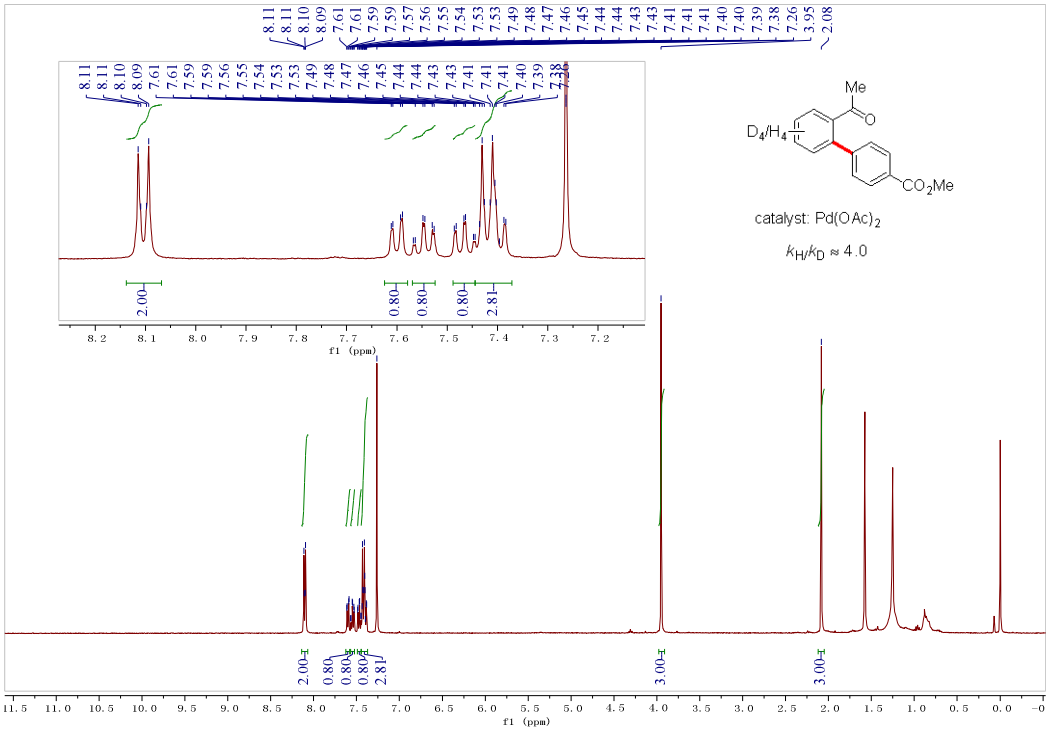


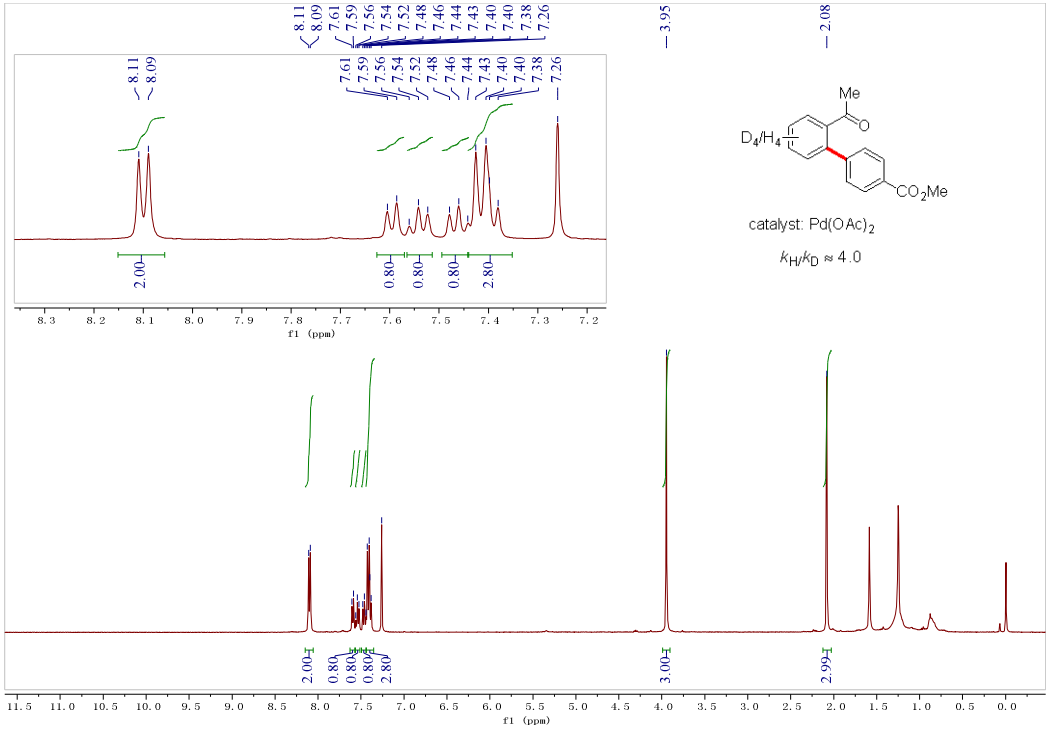
Intermolecular KIE experiments



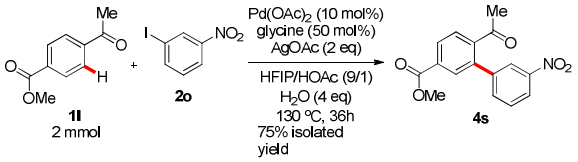
1b/[D_5]-**1b** **4a**/[D_4]-**4a**

To a 20 mL reaction tube was added $Pd(OAc)_2$ or $Pd(PPh_3)_2Cl_2$ (0.02 mmol), glycine (7.5 mg, 0.1 mmol), AgOAc (67 mg, 0.4 mmol), acetophenone **1b** (0.1 mmol), [D_5]-acetophenone[3] **[D_5]-1b** (0.1 mmol), Aryl iodide **2g** (0.6 mmol), hexafluoroisopropanol (0.6 mL), acetic acid (70 μL), and H_2O (15 μL). The tube was then sealed and the mixture was stirred at room temperature for 15 min before being heated to 130 ^oC for 180 min. The reaction mixture was then cooled to room temperature, filtrated via celite, and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel and analyzed for its isotopic distribution. The KIE value for this reaction was estimated to be $k_H/k_D \approx 4.0$ by ^1H NMR spectra.

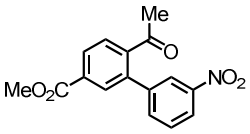

Me
O
D4/H4
CO2Me
catalyst: Pd(OAc)2
kH/kD ≈ 4.0
f1 (ppm)


Me
O
D4/H4
CO2Me
catalyst: Pd(OAc)2
kH/kD ≈ 4.0
f1 (ppm)

6. Scale up Reaction



To a 20 mL reaction tube was added $Pd(OAc)_2$ (45 mg, 0.2 mmol), glycine (75 mg, 1 mmol), AgOAc (670 mg, 4 mmol), ketone **1l** (356 mg, 2 mmol), 3-iodo nitrobenzene **2o** (1.5g, mmol), hexafluoroisopropanol (6 mL), acetic acid (0.7 mL), and H_2O (150 μL). The tube was then sealed and the mixture was stirred at room temperature for 15 min before being heated to 130 ^oC for 24 h. The reaction mixture was cooled to room temperature, filtrated via celite, and concentrated under reduced pressure. The resulting residue was purified by column chromatography (eluent: Hexane/Ethyl Acetate) to provide the target biaryl **4s** (450 mg, 75% yield).



Methyl 6-acetyl-3′-nitro-[1,1′-biphenyl]-3-carboxylate (4s)

^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.30–8.22 (m, 2H), 8.16 (d, J = 8.0 Hz, 1H), 8.06 (s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.66–7.59 (m, 2H), 3.97 (s, 3H), 2.28(s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 201.9, 165.7, 148.3, 143.3, 141.6, 138.3, 134.8, 132.4, 131.7, 129.57, 129.56, 128.4, 123.4, 122.8. HR-MS (ESI) m/z calcd for $C_{16}H_{14}NO_5$ [M+H$^+$] 300.0866, found 300.0861.

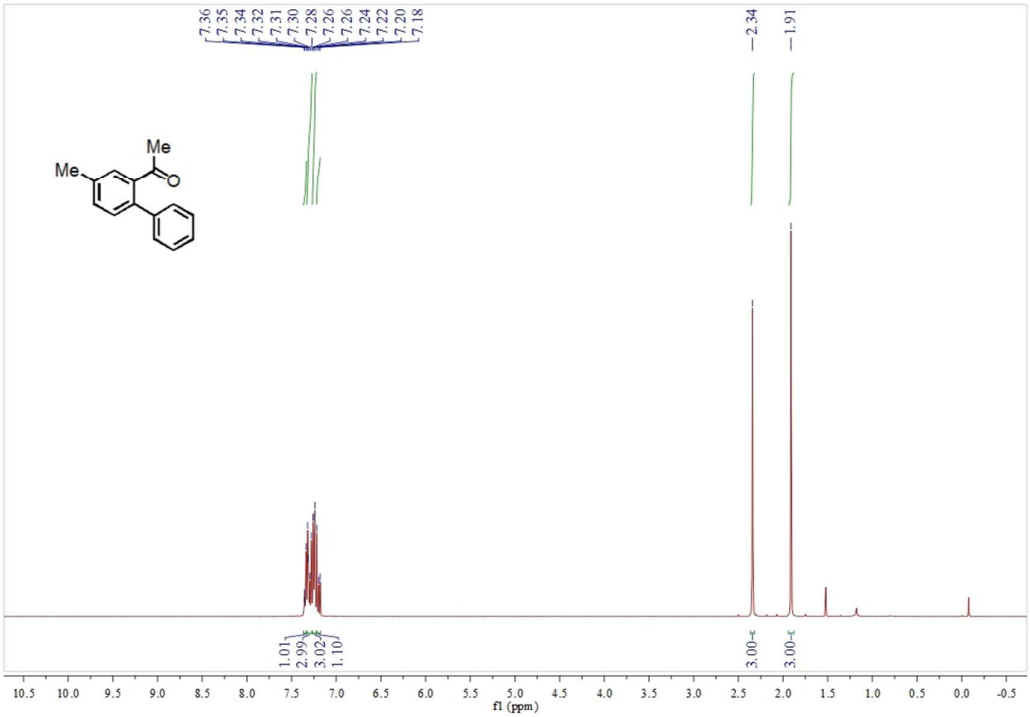
7. References

(1) Wiemann, J. et al. *Bull. Soc. Chim. Fr.* **1967**, 2935.

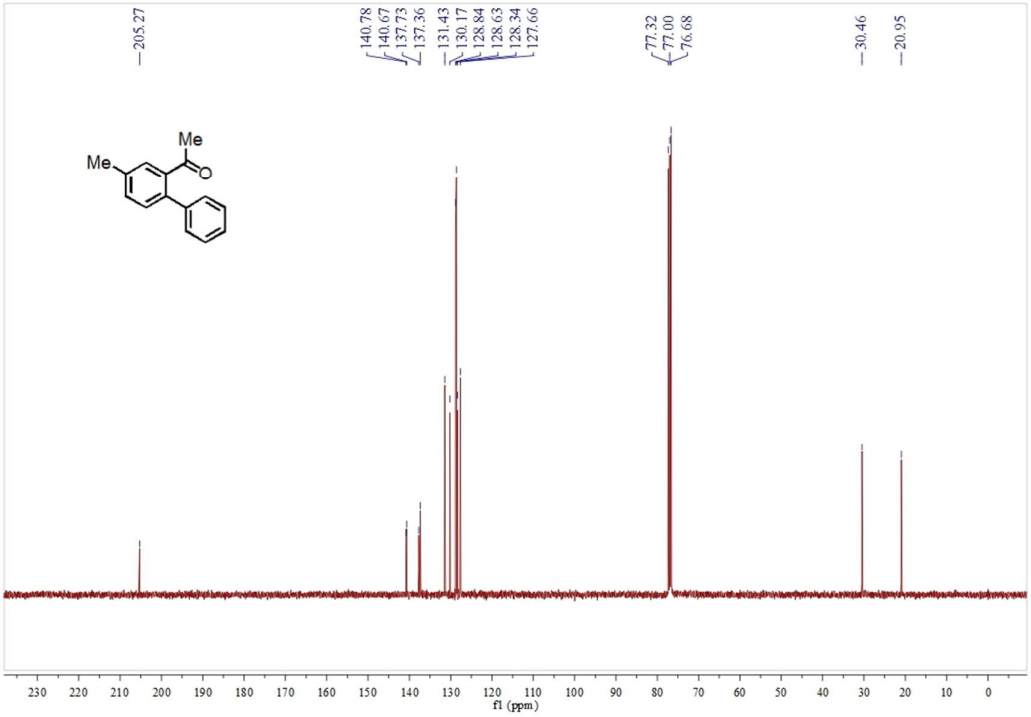
(2) Gao, K.; Lee, P.-S.; Long, C.; Yoshikai, N. *Org. Lett.* **2012**, *14*, 4234.

(3) Liu, W.; Zell, D.; John, M.; Ackermann, L. *Angew. Chem. Int. Ed.* **2015**, *54*, 4092.

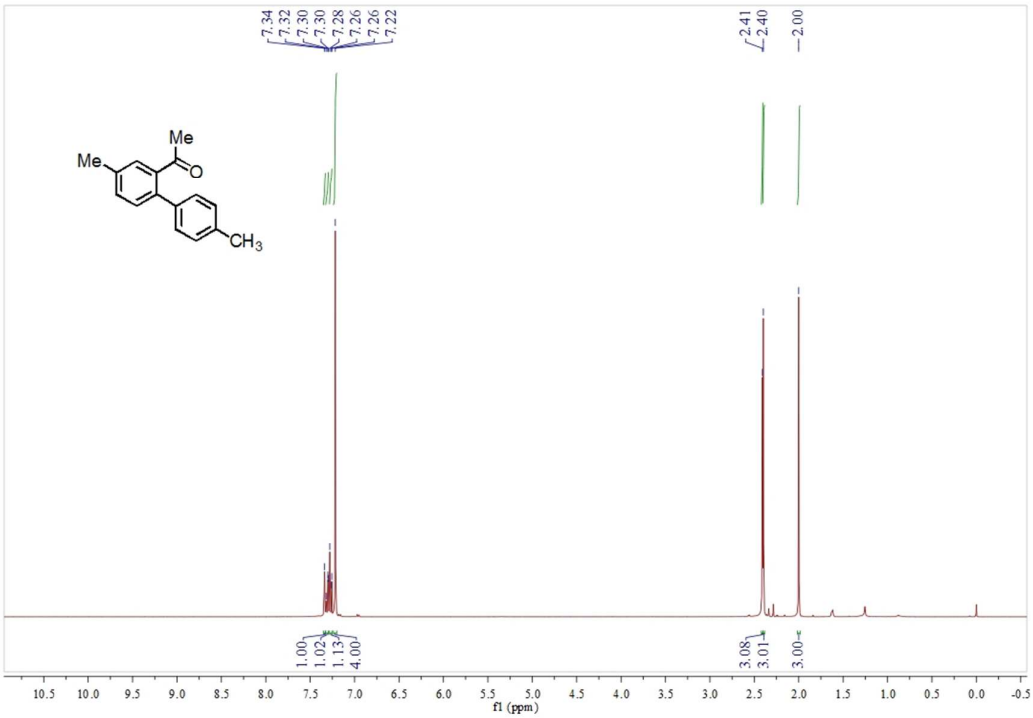
NMR Spectra Data



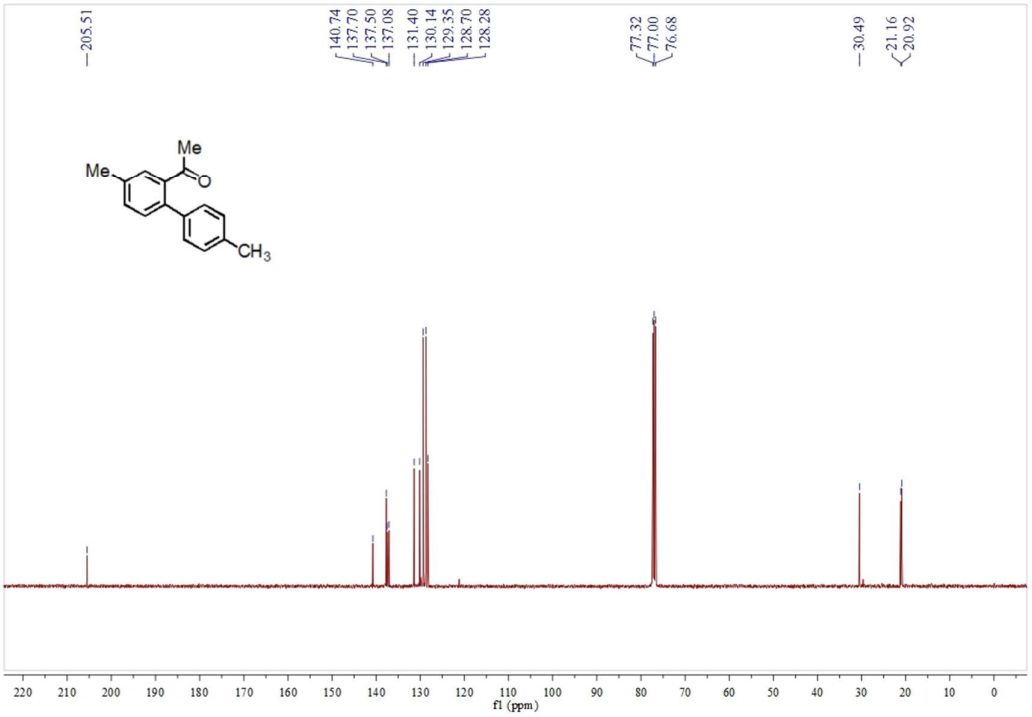
^{1}H NMR Spectra of Compound **3a**



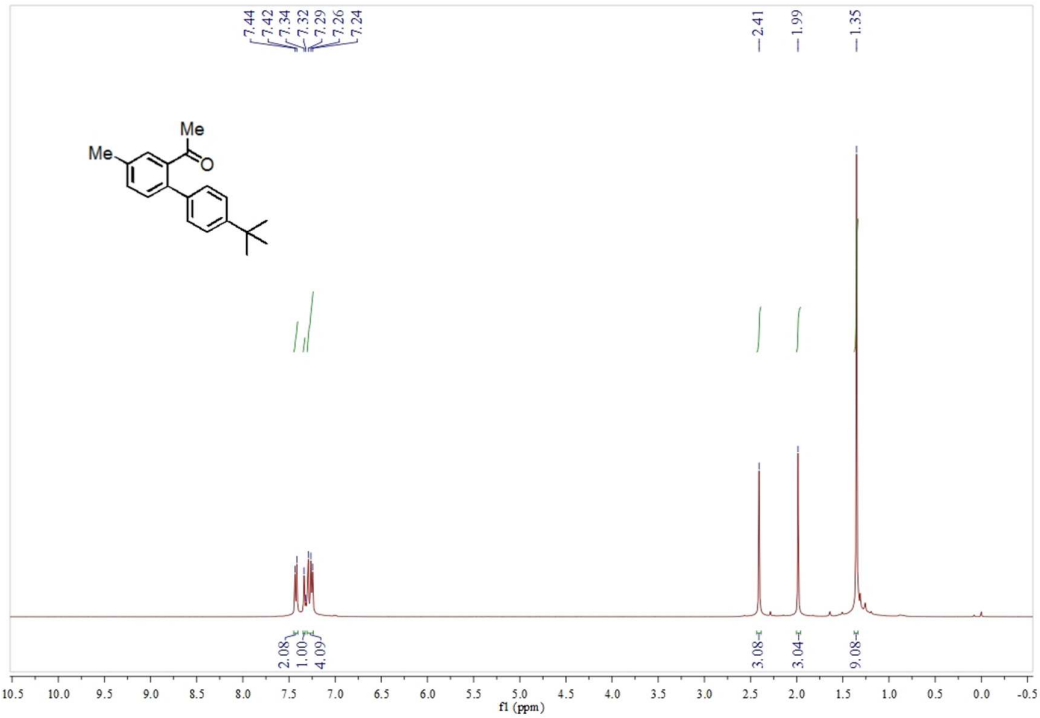
^{13}C NMR Spectra of Compound **3a**



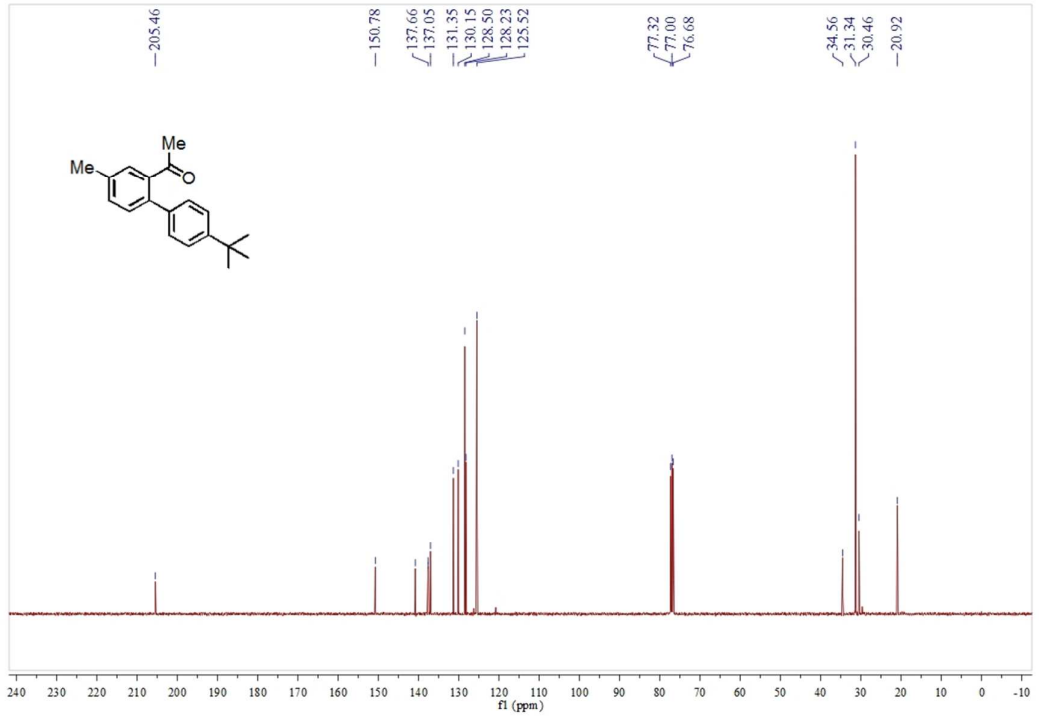
^{1}H NMR Spectra of Compound **3b**



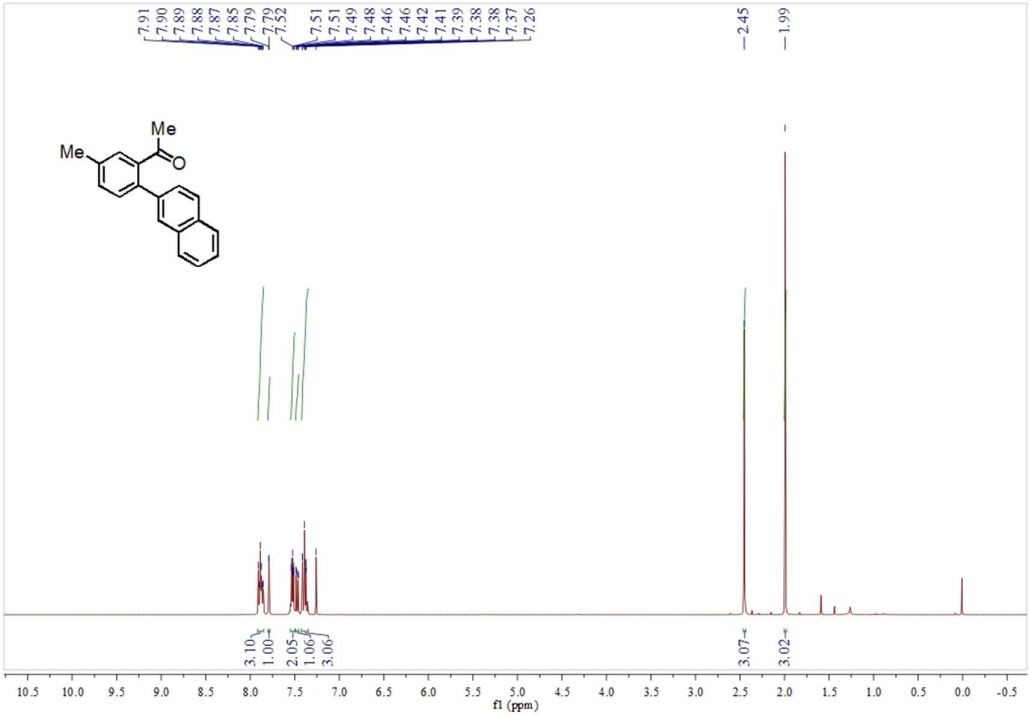
^{13}C NMR Spectra of Compound **3b**



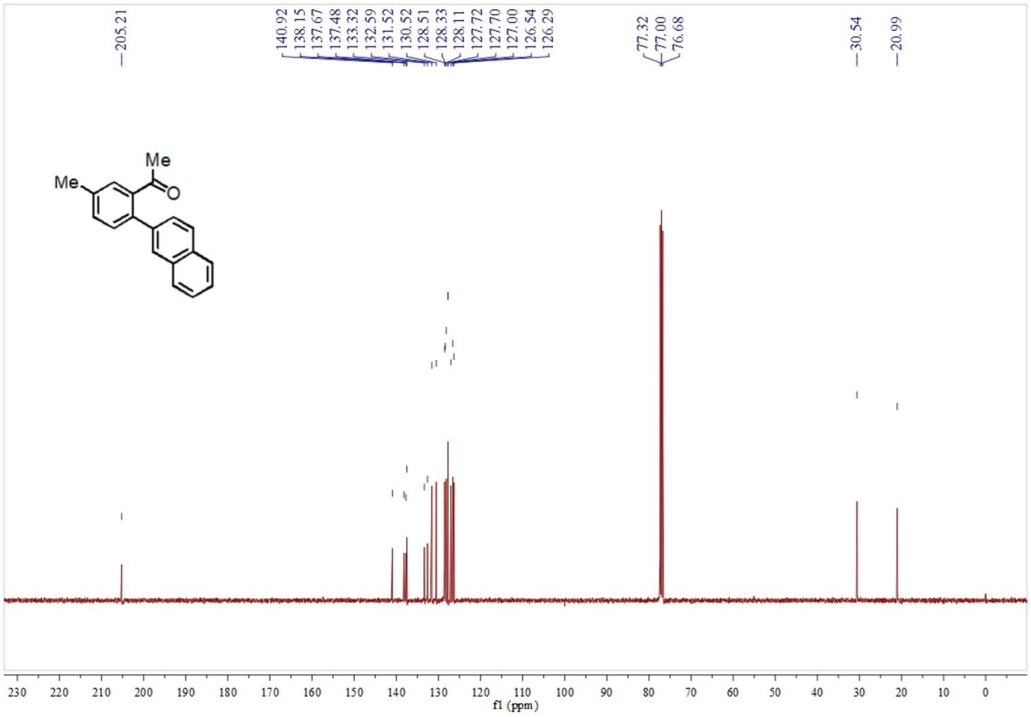
^{1}H NMR Spectra of Compound **3c**



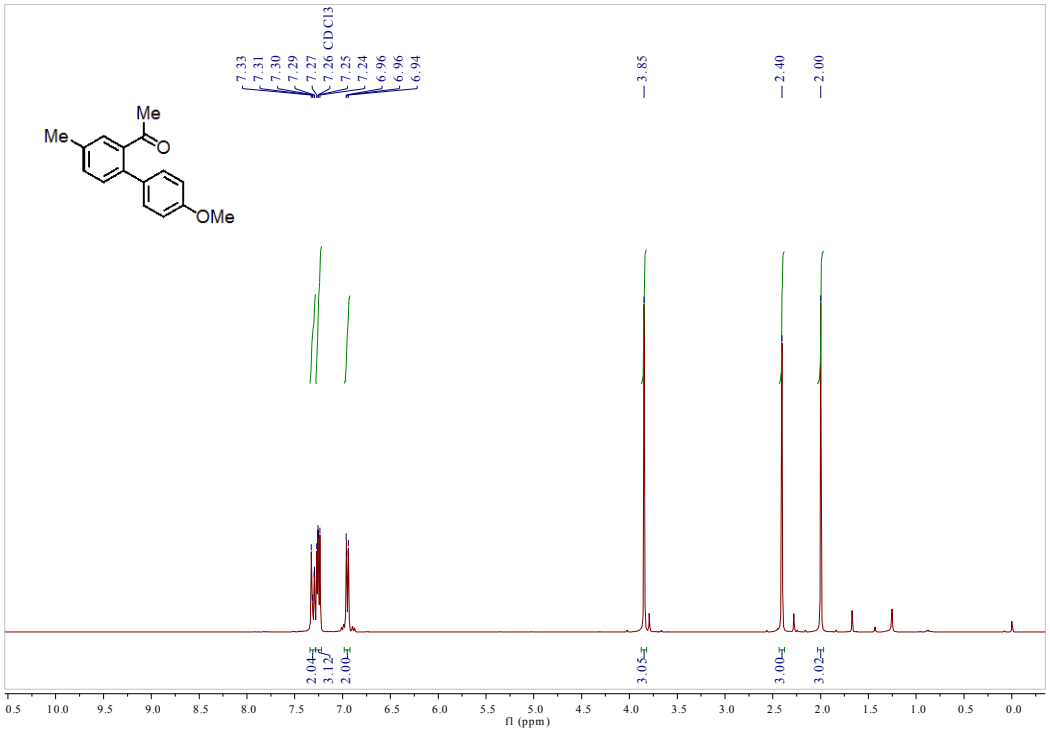
^{13}C NMR Spectra of Compound **3c**



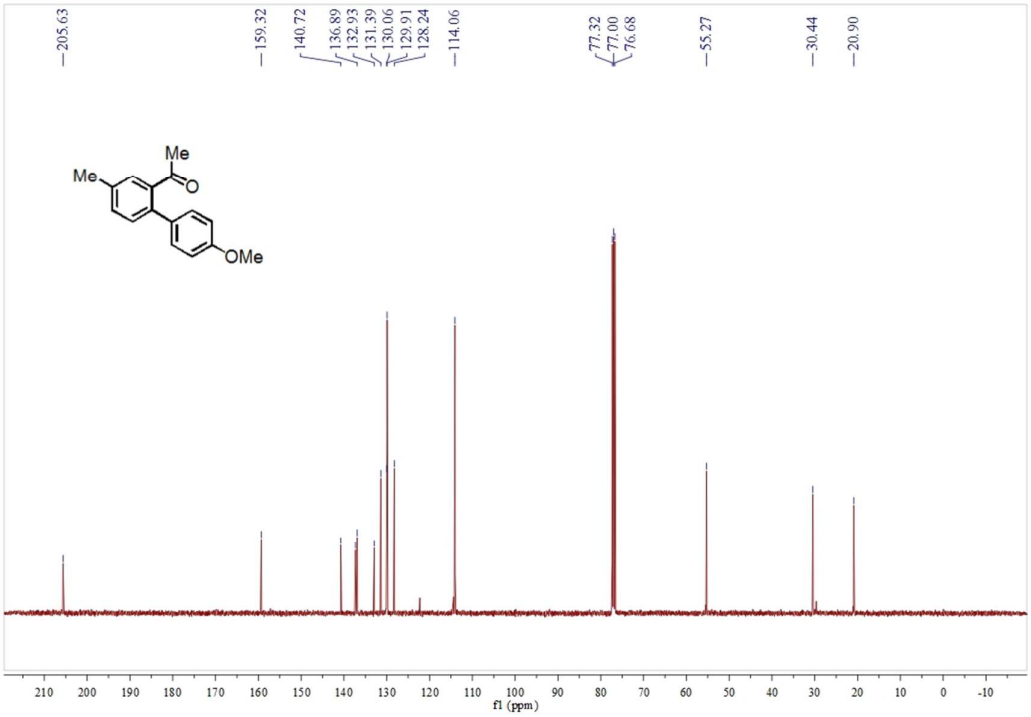
^{1}H NMR Spectra of Compound **3d**



^{13}C NMR Spectra of Compound **3d**



^{1}H NMR Spectra of Compound **3e**



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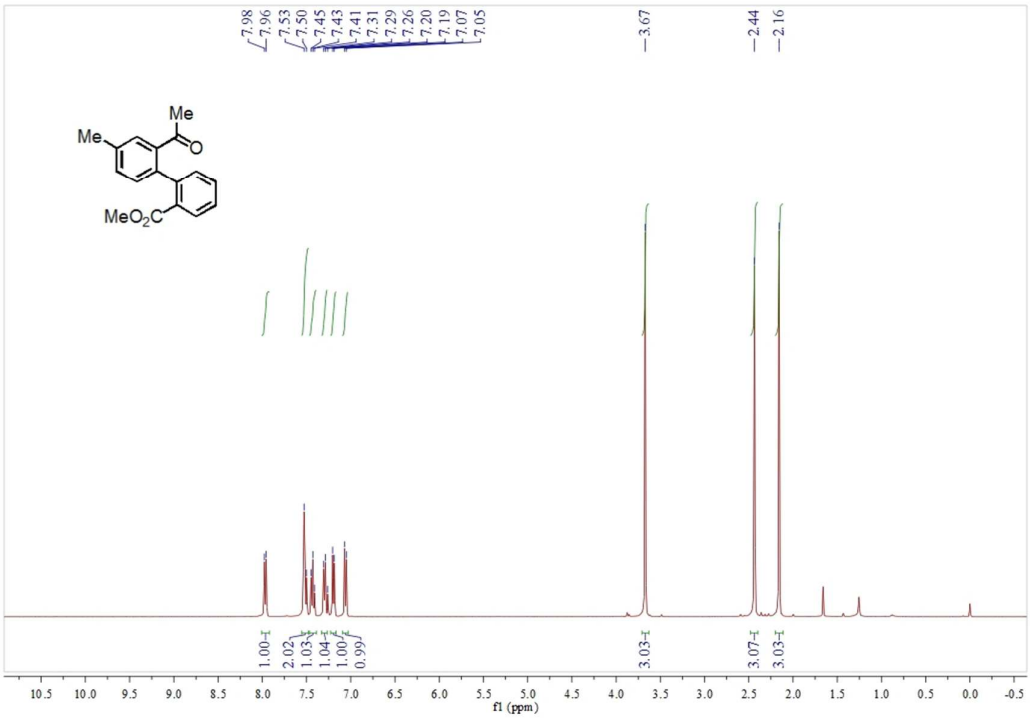
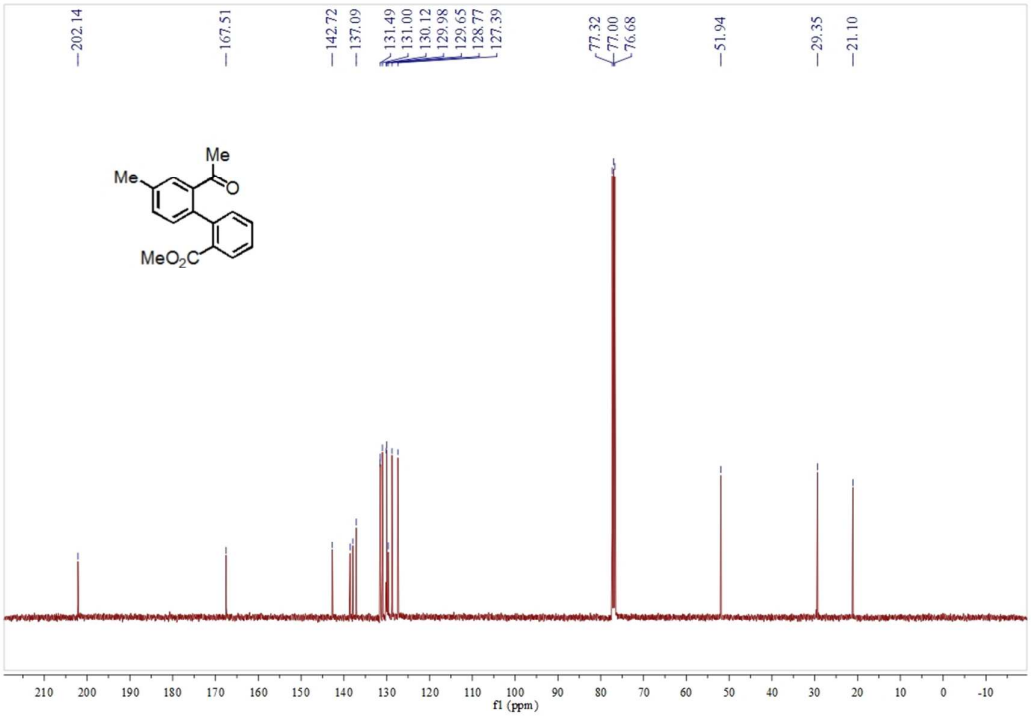


^{1}H NMR Spectra of Compound **3f**



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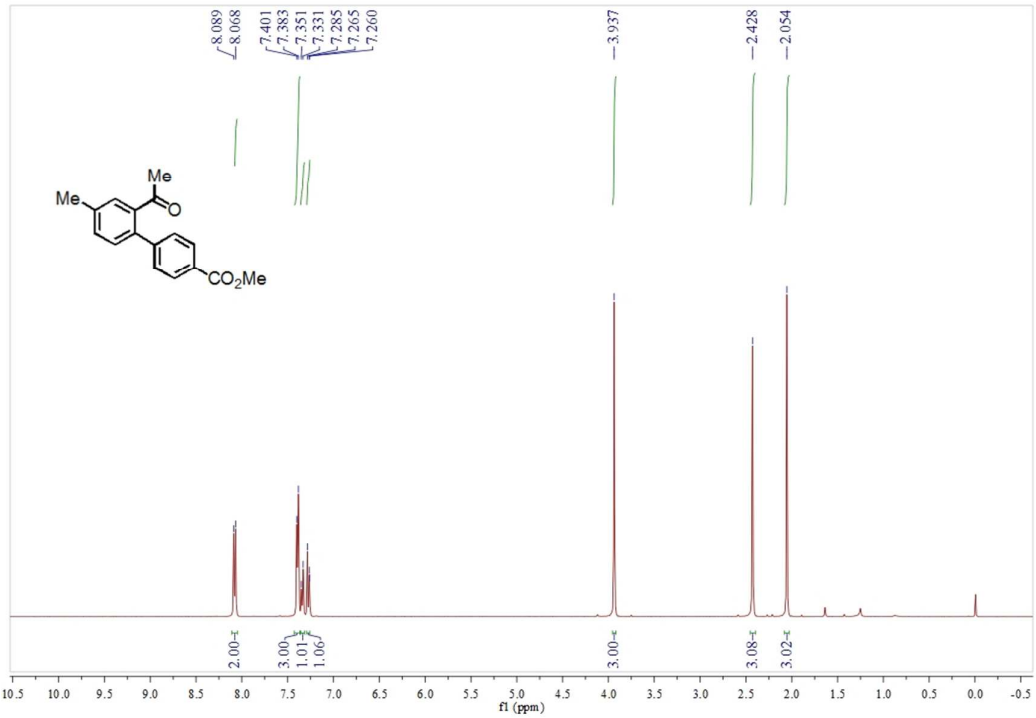
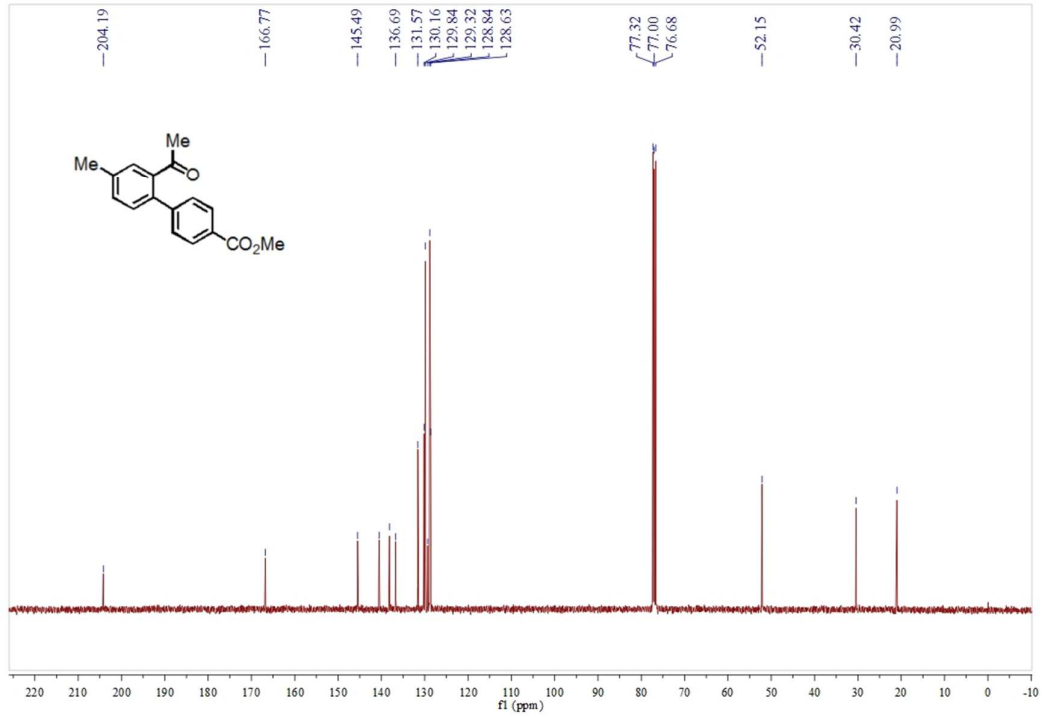


^{1}H NMR Spectra of Compound **3g**



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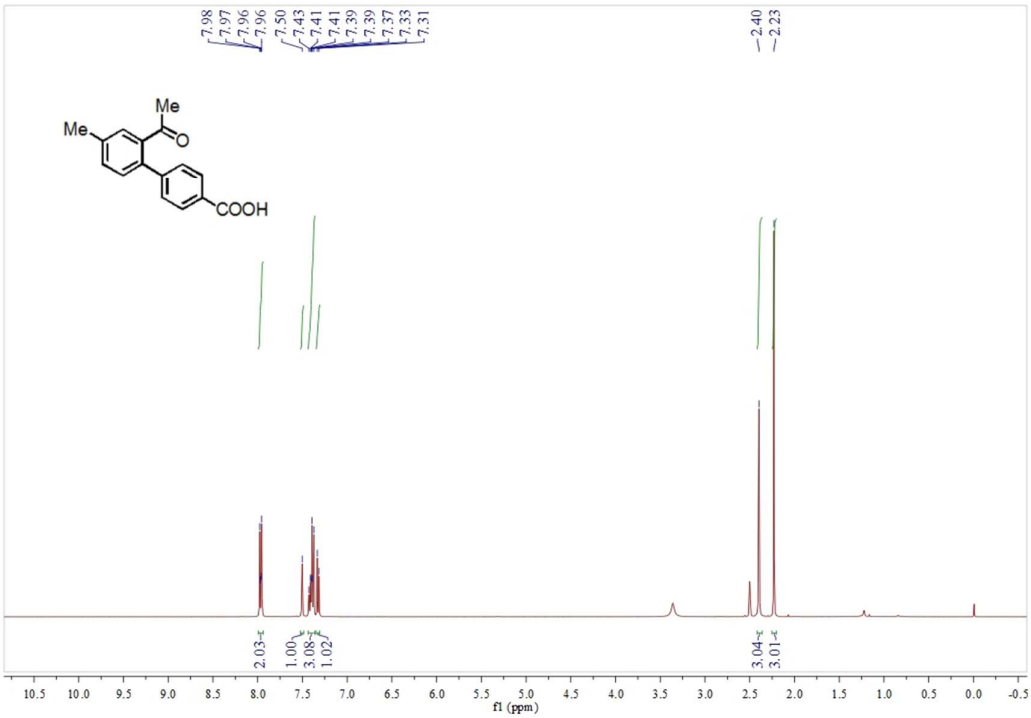
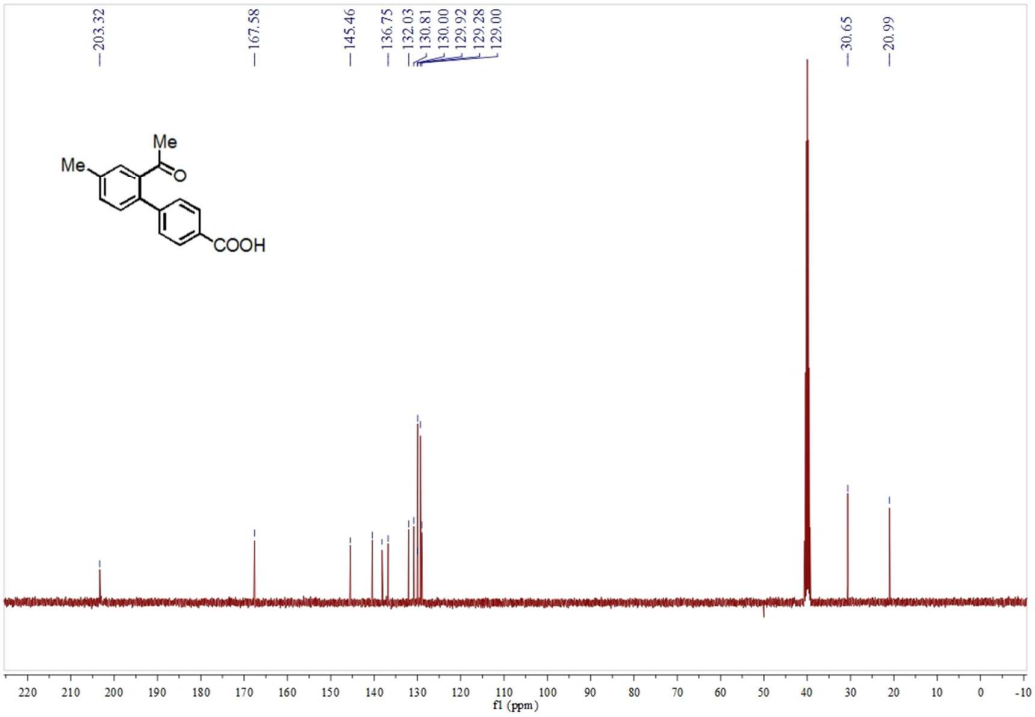
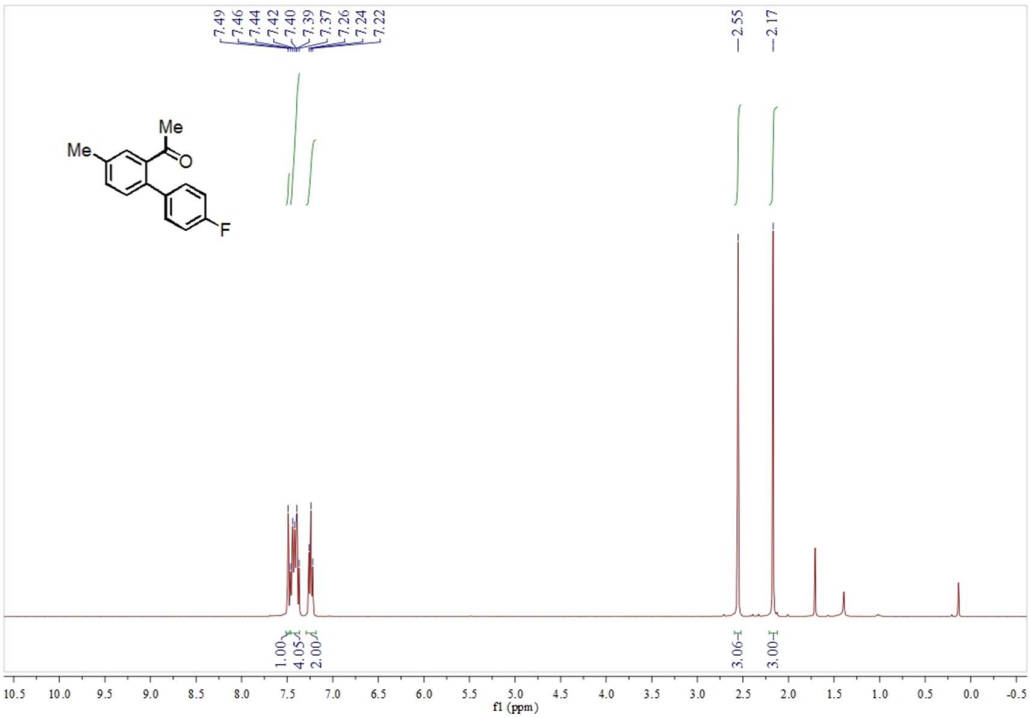


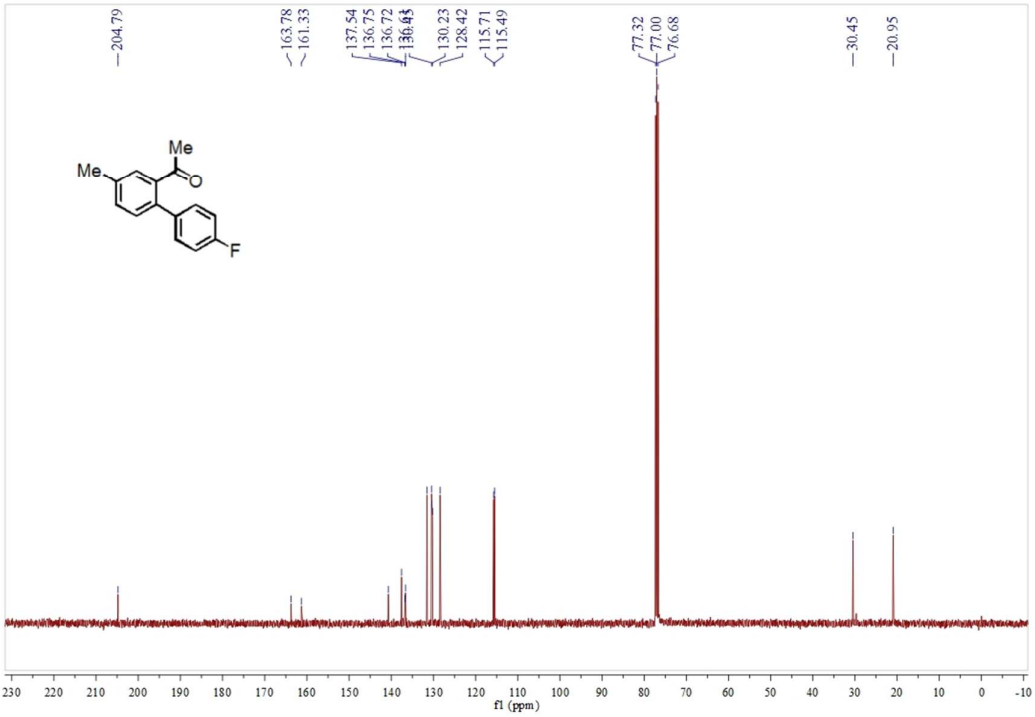
^{1}H NMR Spectra of Compound **3h**



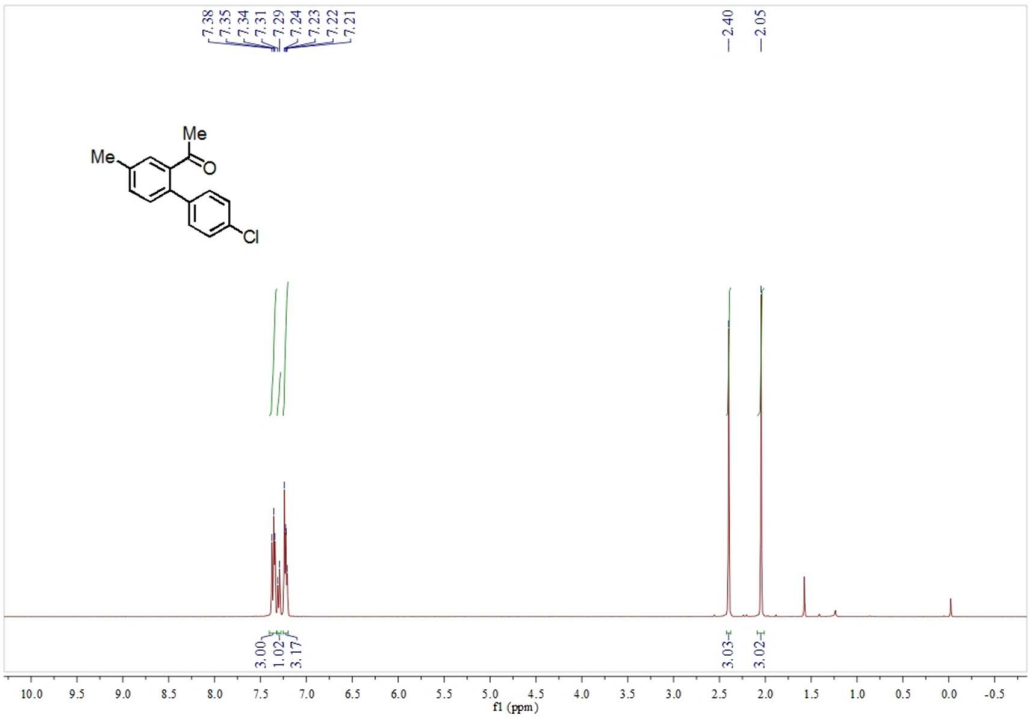
^{13}C NMR Spectra of Compound **3h**



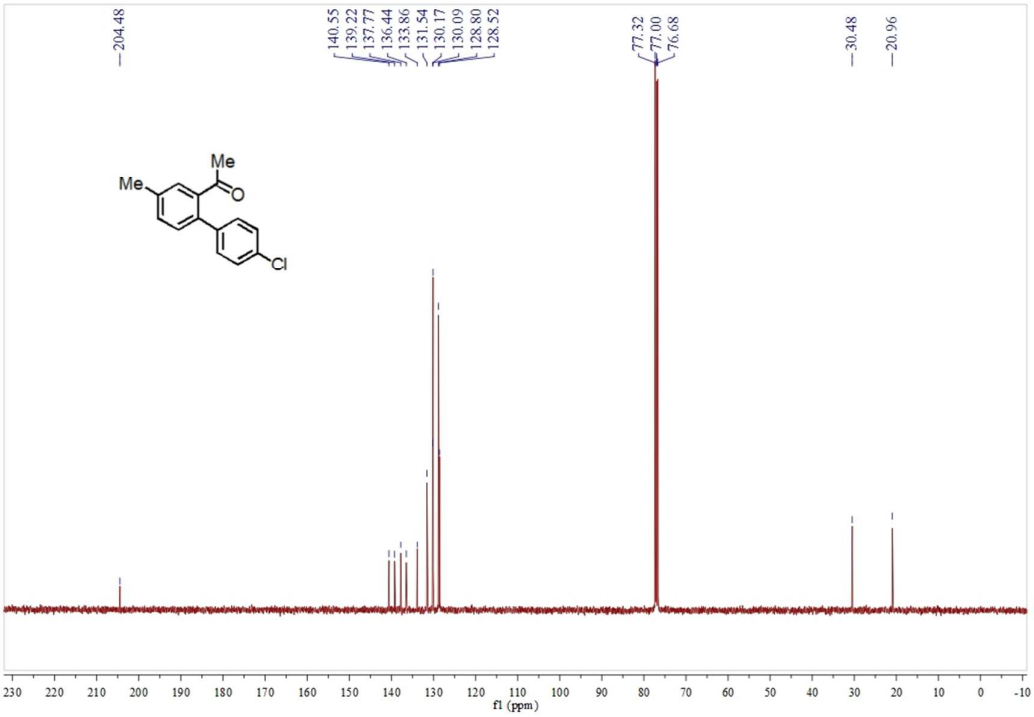
^{1}H NMR Spectra of Compound **3i**



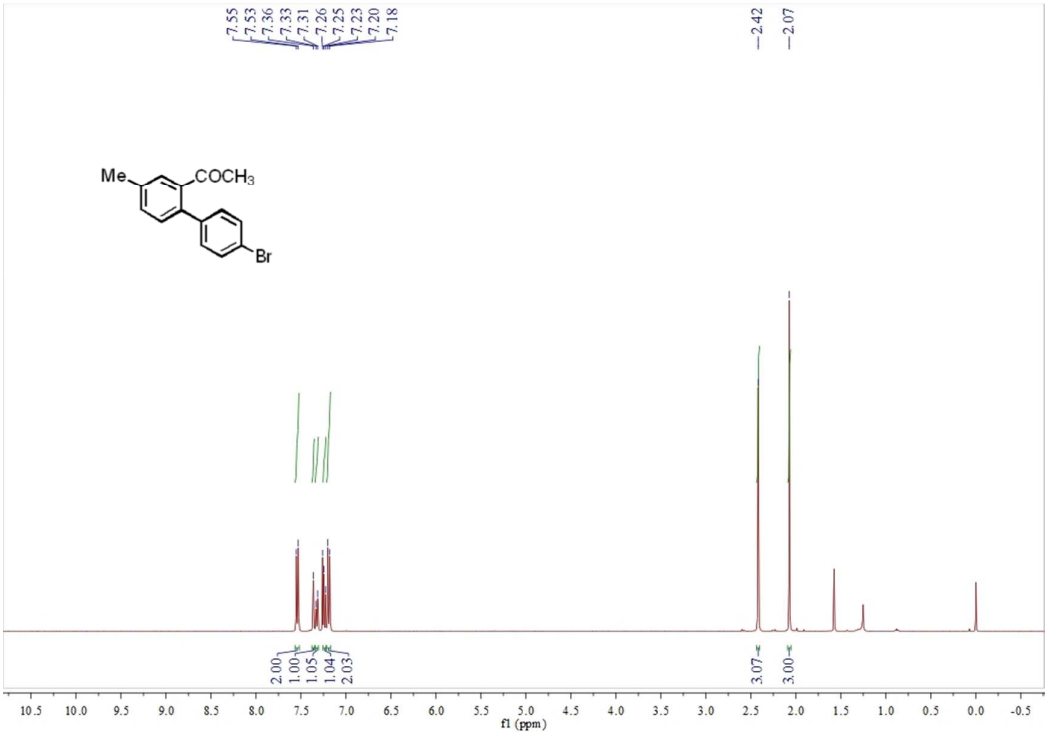
^{13}C NMR Spectra of Compound **3i**



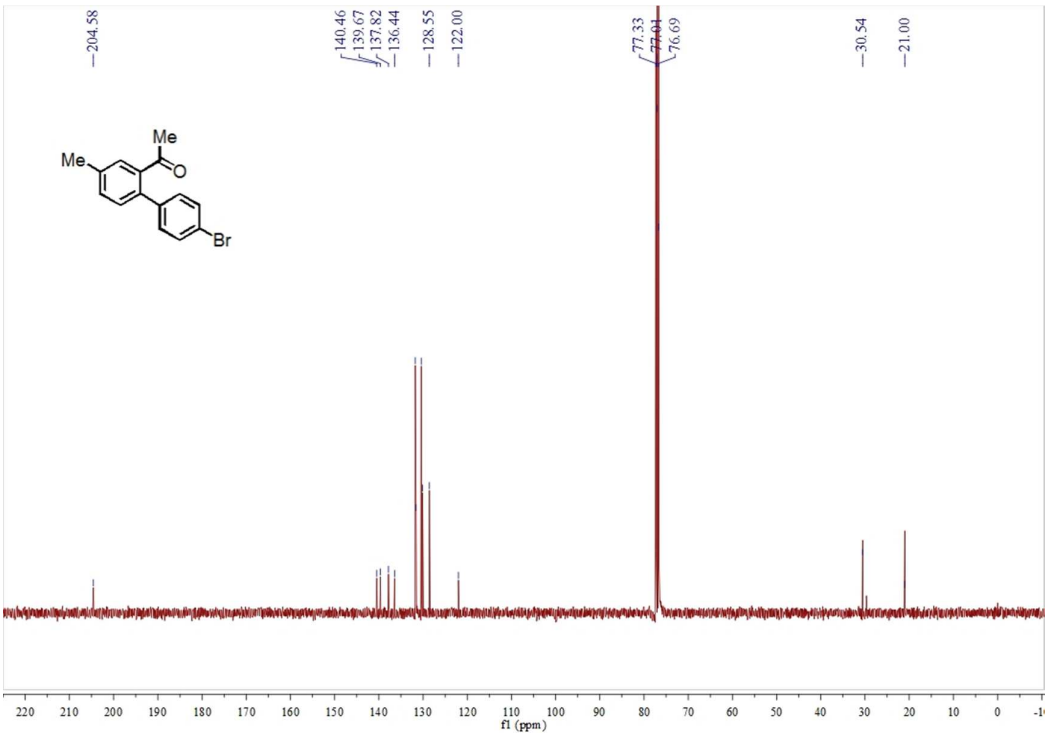
^{1}H NMR Spectra of Compound **3j**



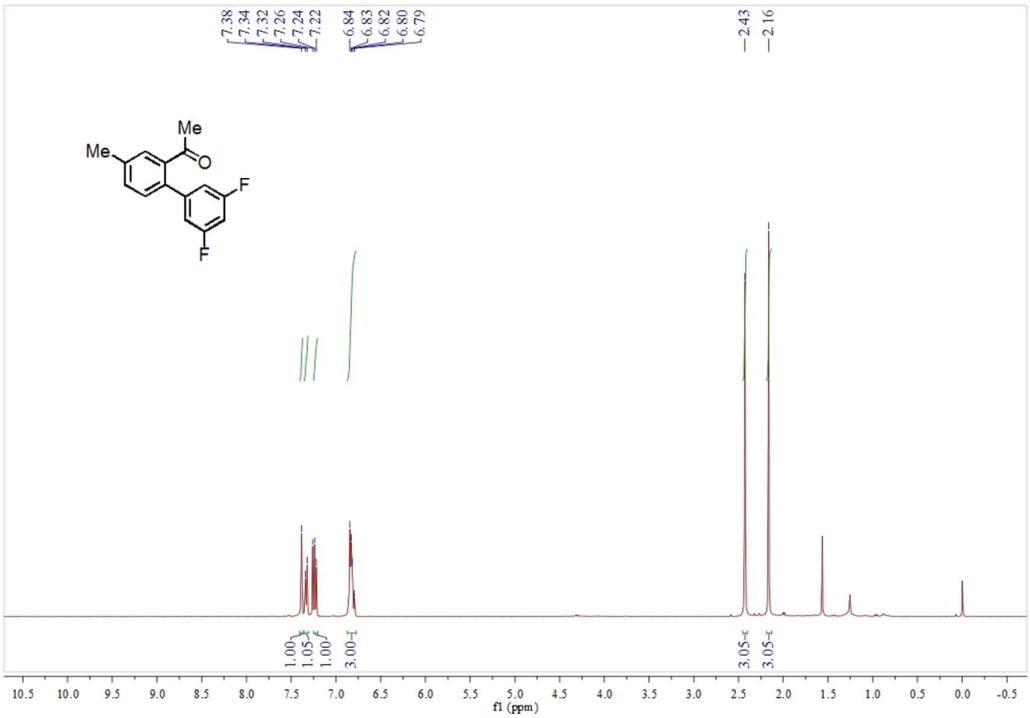
^{13}C NMR Spectra of Compound **3j**



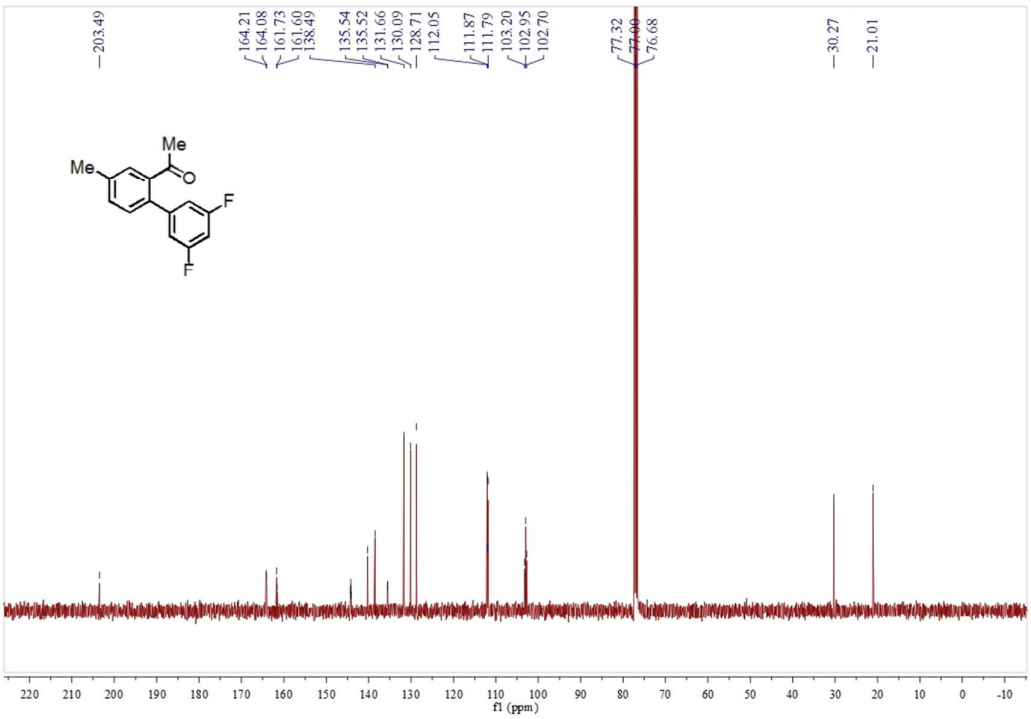
^{1}H NMR Spectra of Compound **3k**



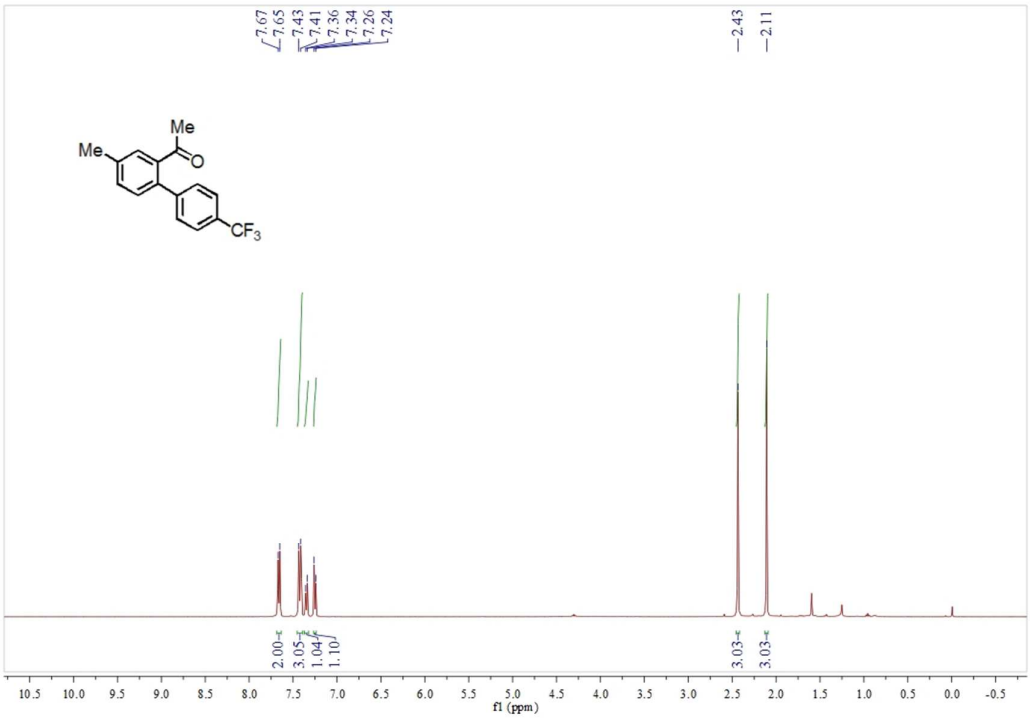
^{13}C NMR Spectra of Compound **3k**



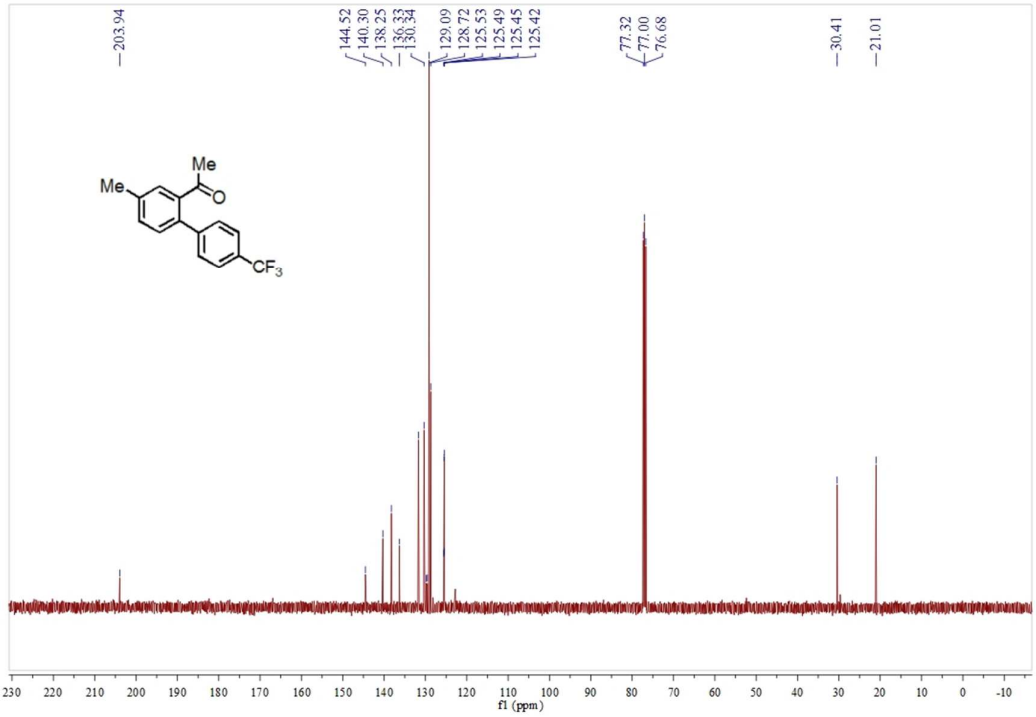
^{1}H NMR Spectra of Compound **3l**



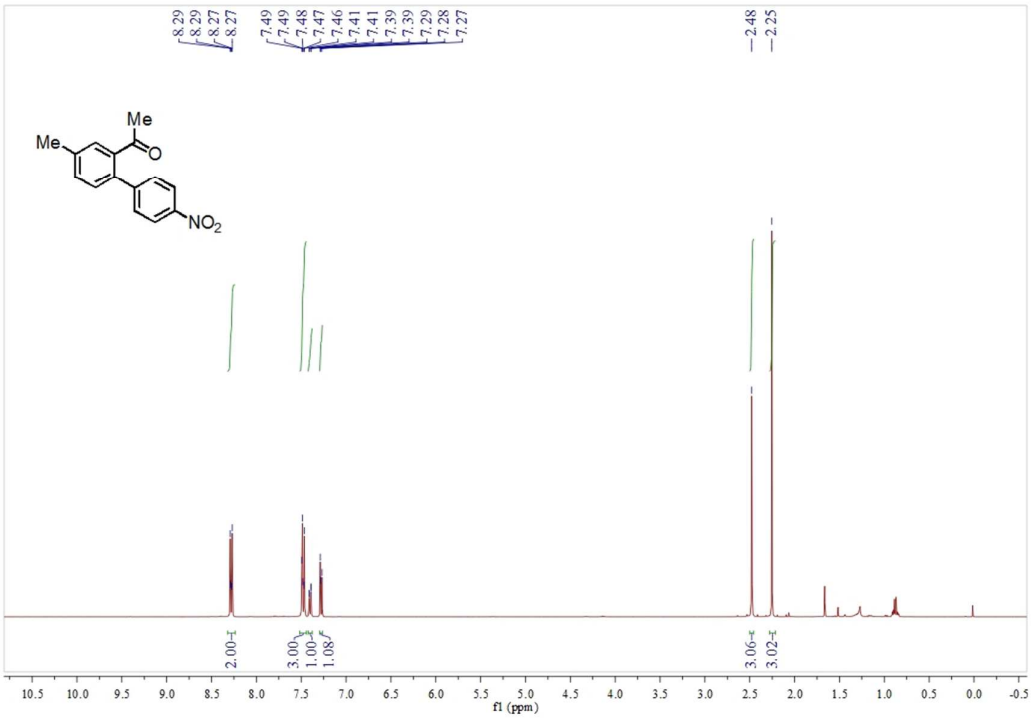
^{13}C NMR Spectra of Compound **3l**



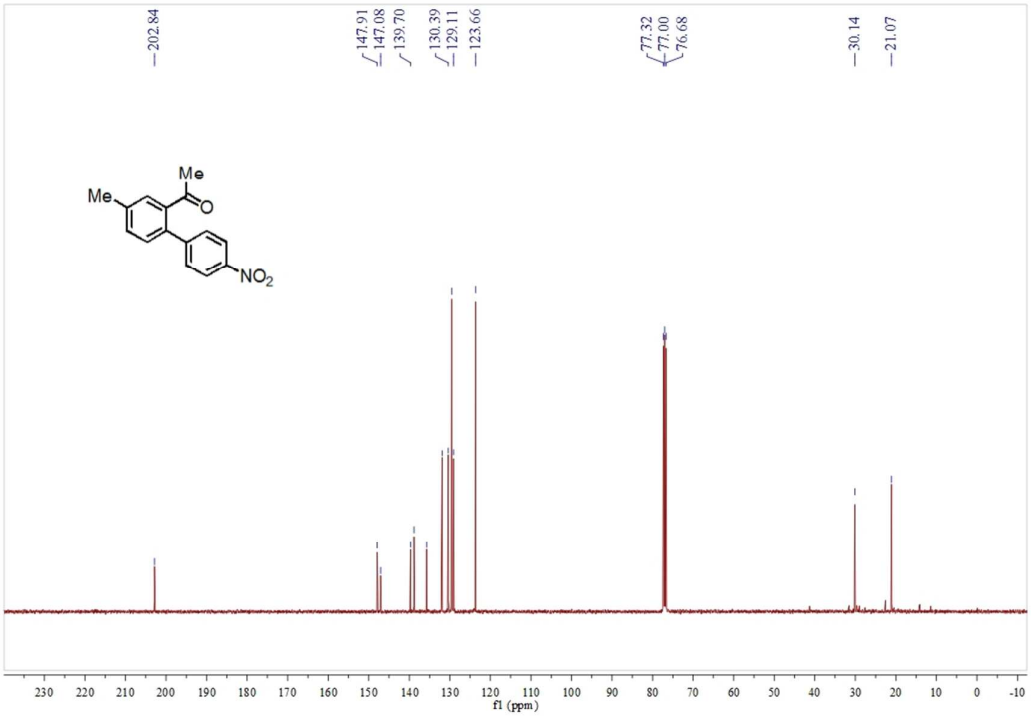
[1]H NMR Spectra of Compound **3m**



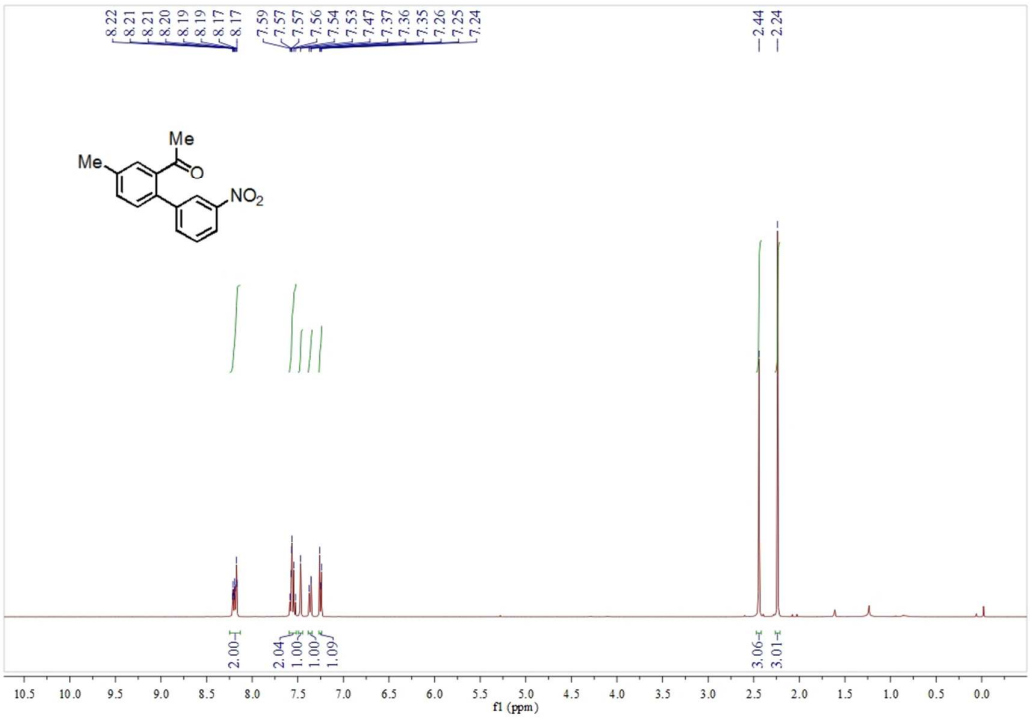
[13]C NMR Spectra of Compound **3m**



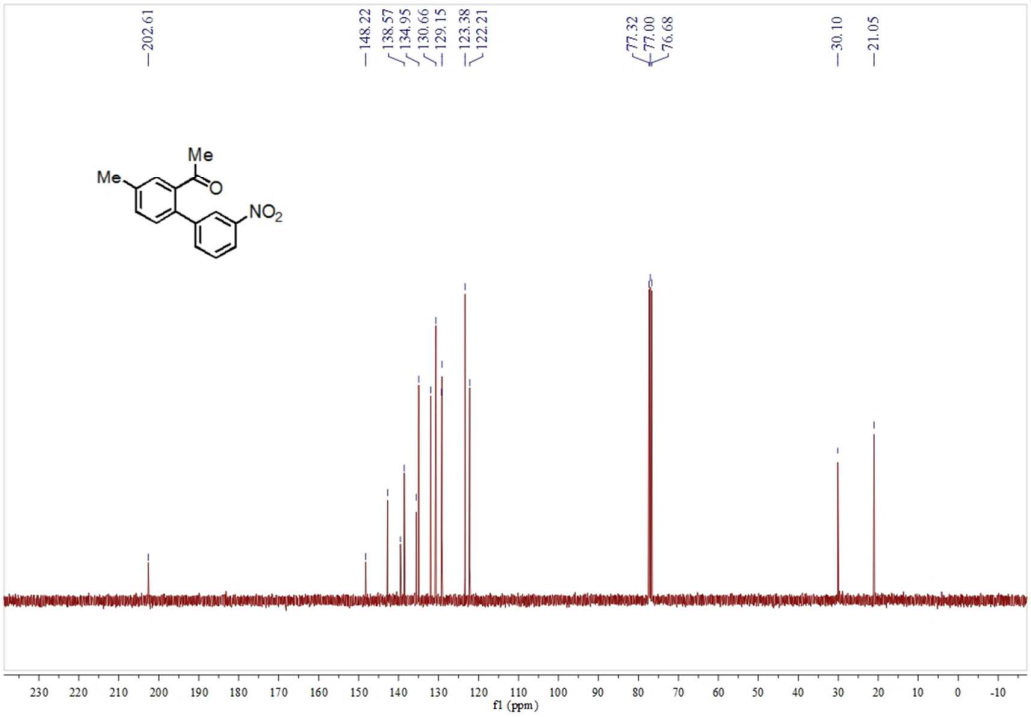
^{1}H NMR Spectra of Compound **3n**



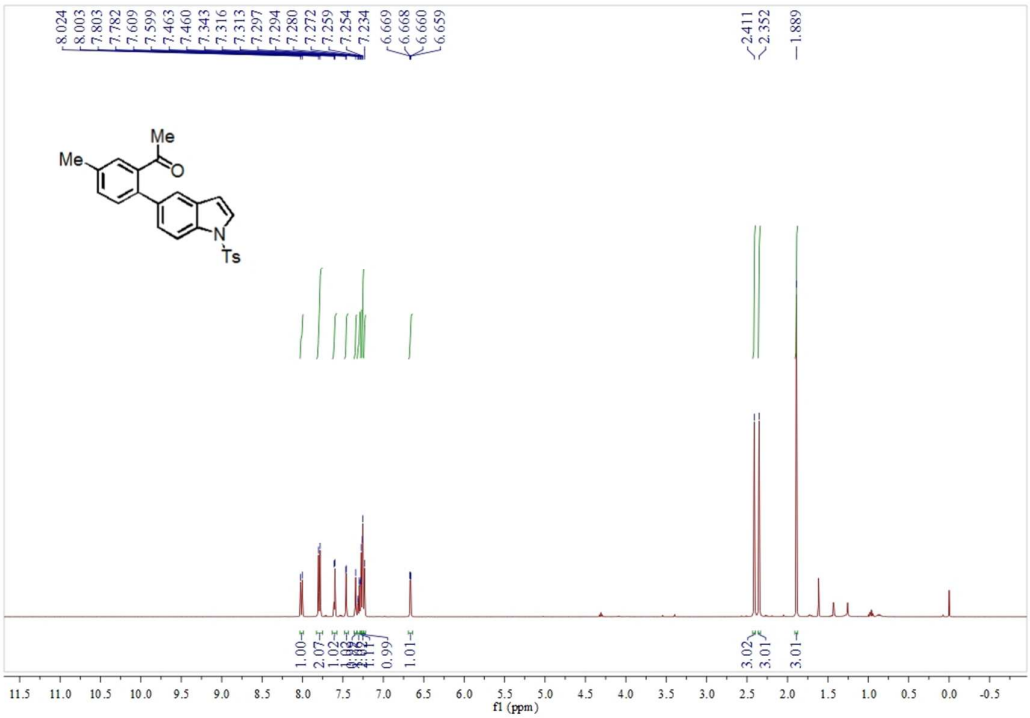
^{13}C NMR Spectra of Compound **3n**



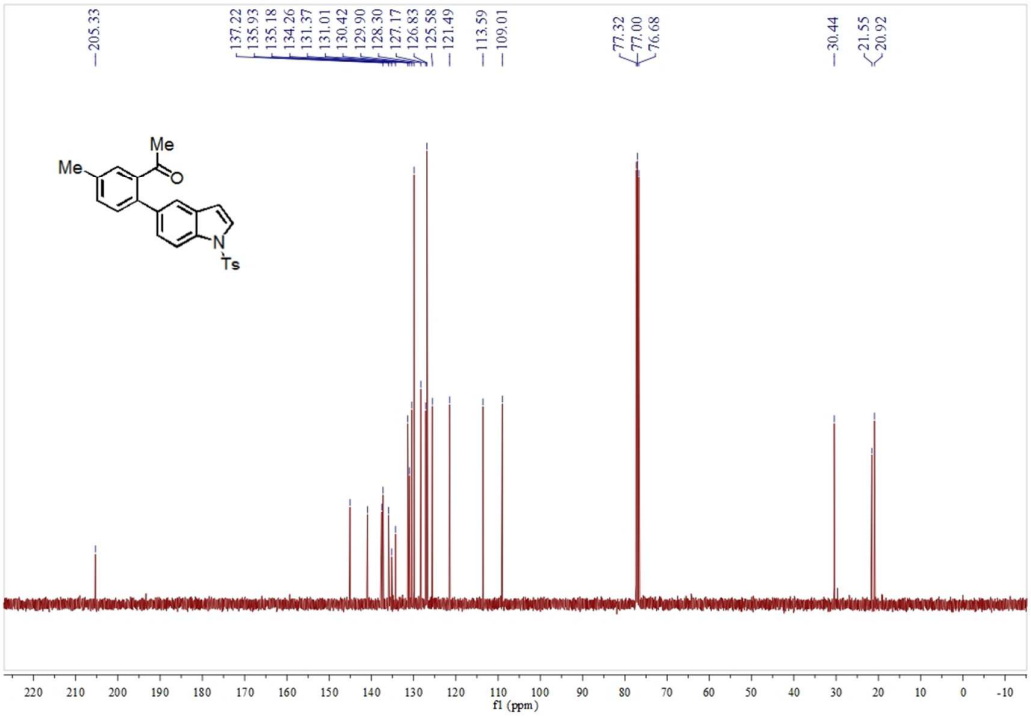
^{1}H NMR Spectra of Compound **3o**



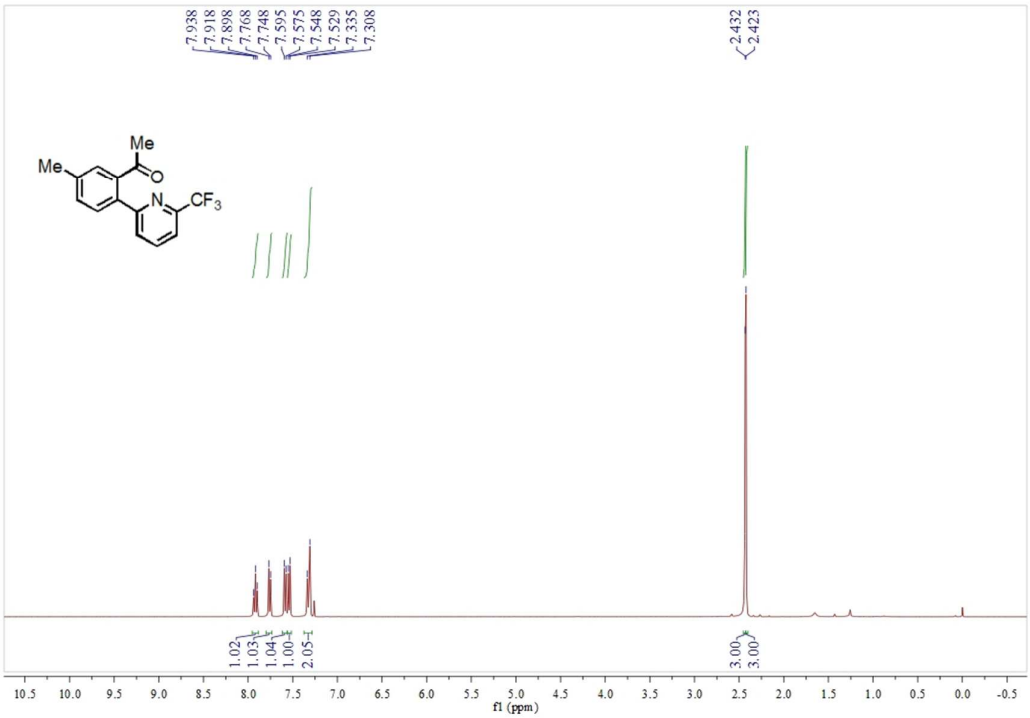
^{13}C NMR Spectra of Compound **3o**



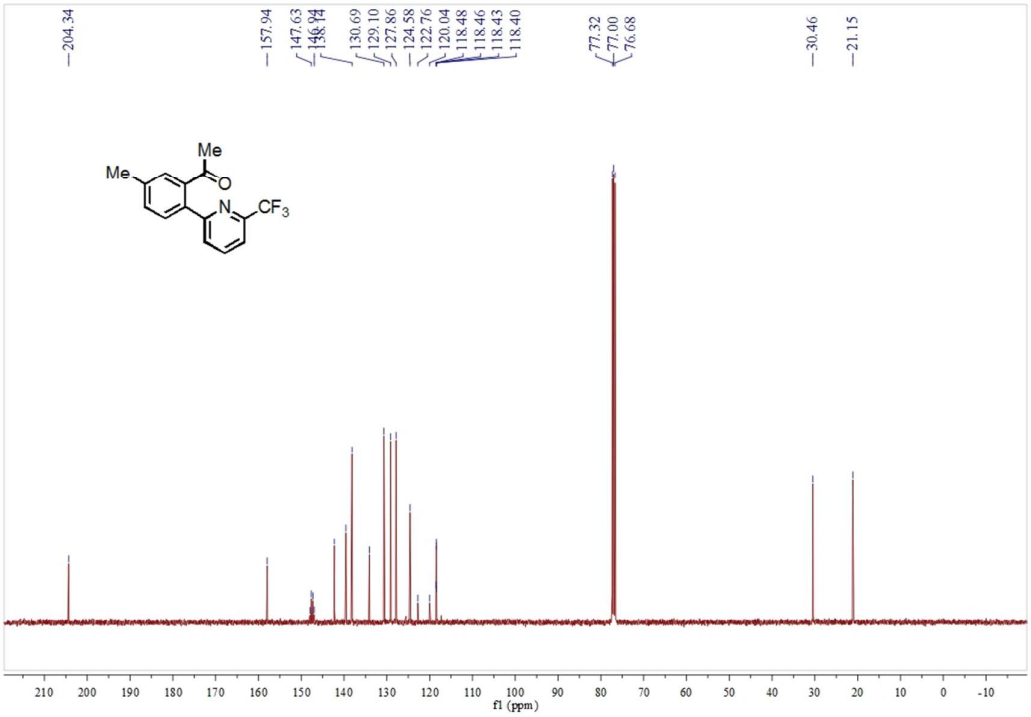
^{1}H NMR Spectra of Compound **3p**



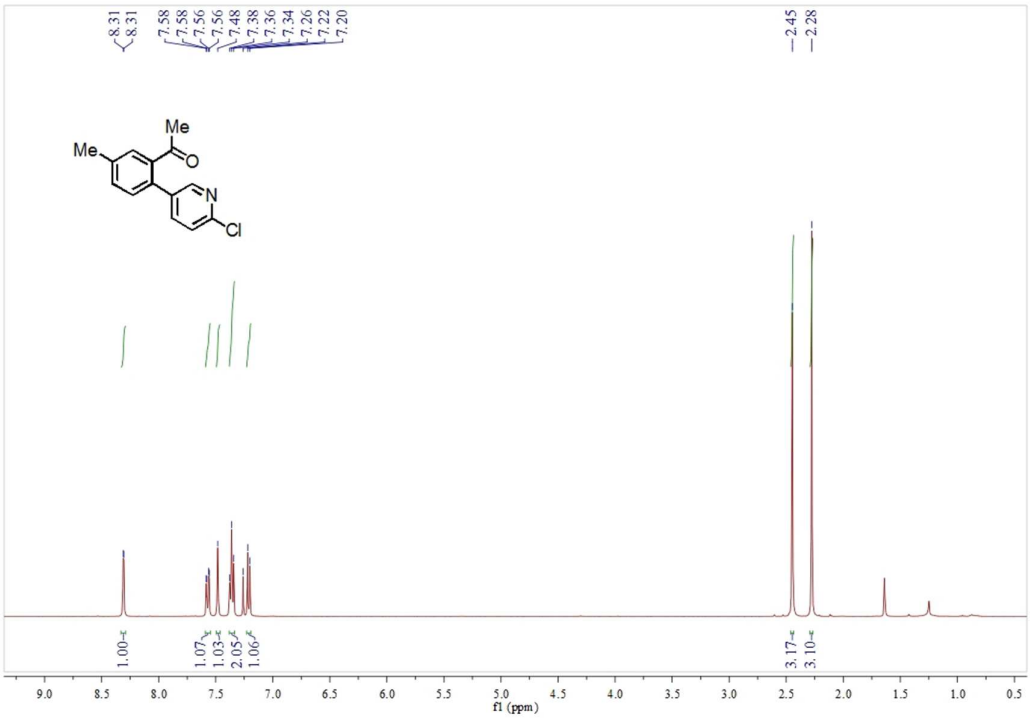
^{13}C NMR Spectra of Compound **3p**



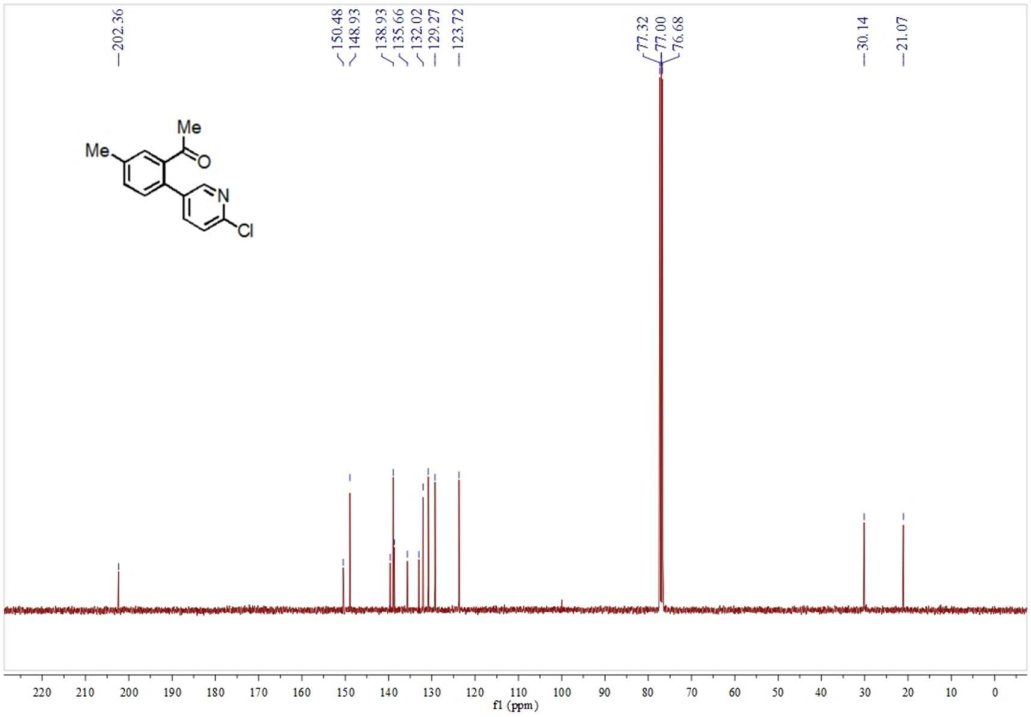
^{1}H NMR Spectra of Compound **3q**



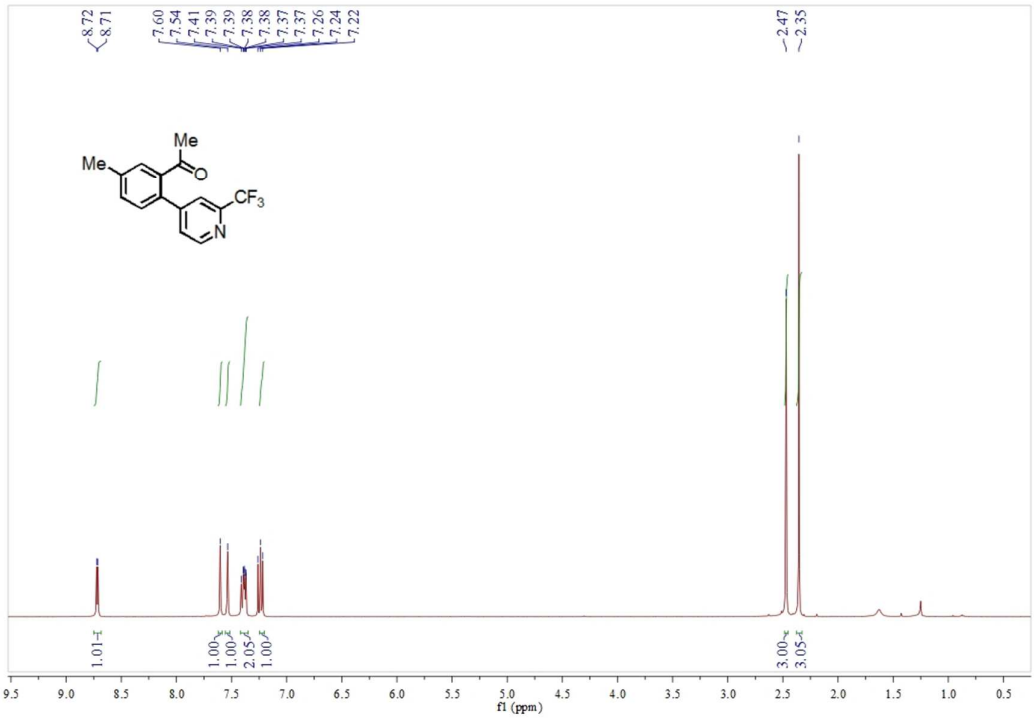
^{13}C NMR Spectra of Compound **3q**



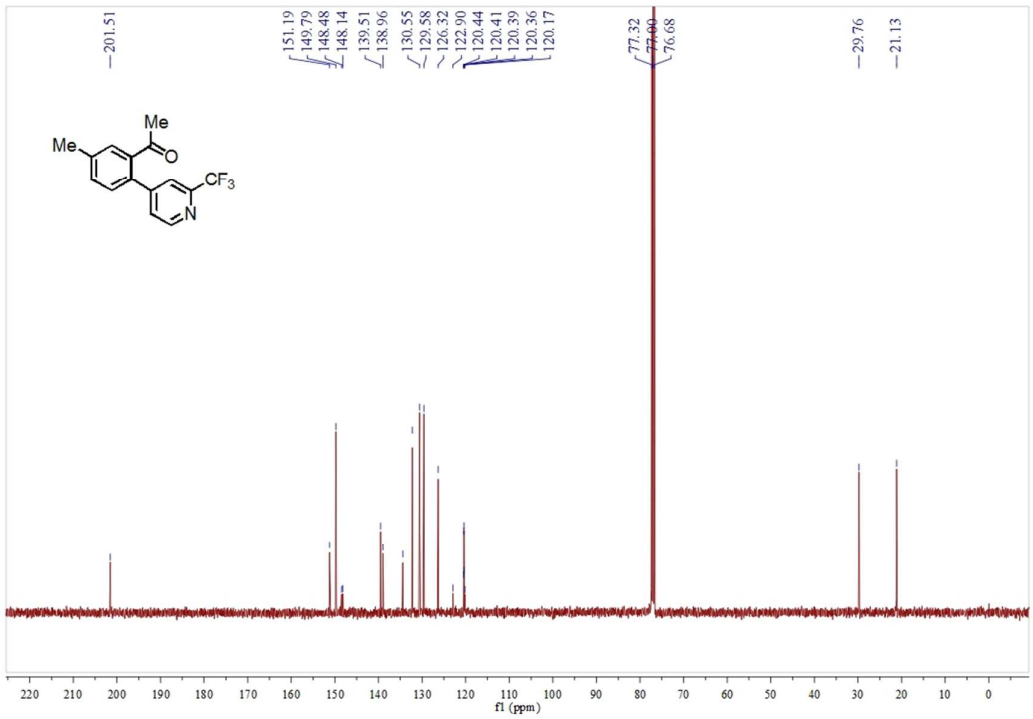
^{1}H NMR Spectra of Compound **3r**



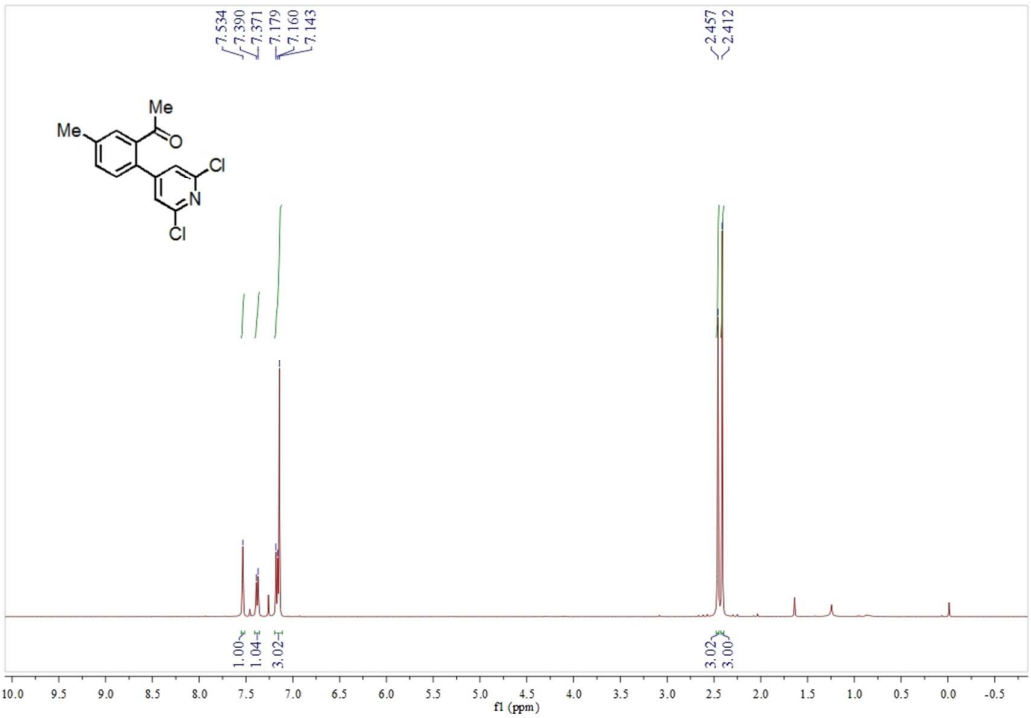
^{13}C NMR Spectra of Compound **3r**



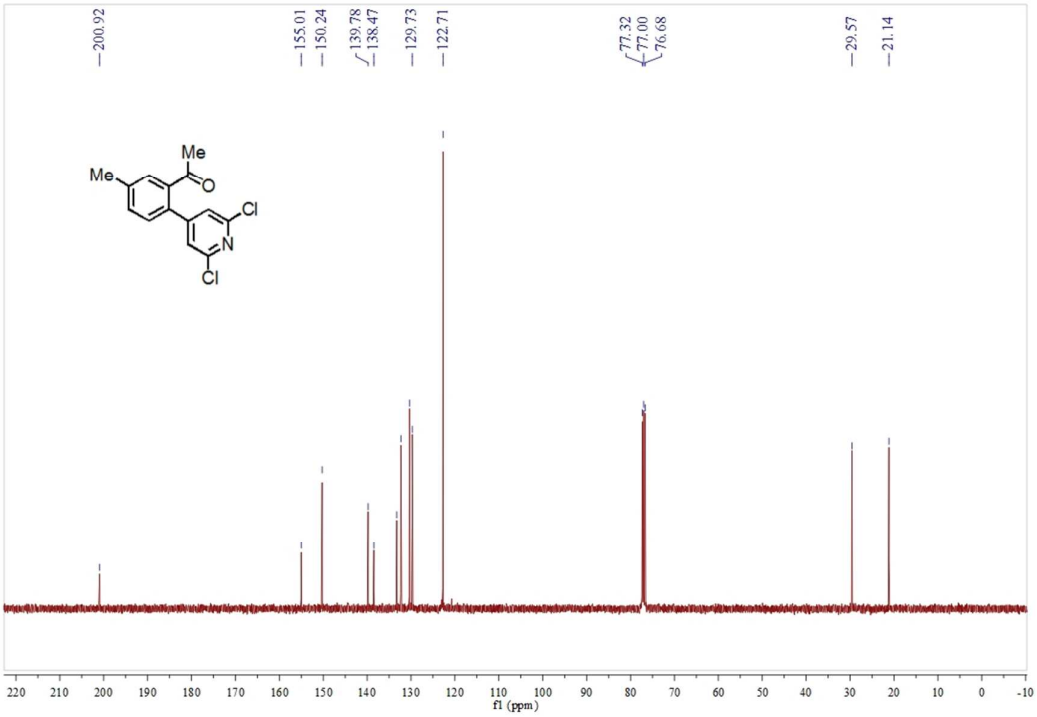
^{1}H NMR Spectra of Compound **3s**



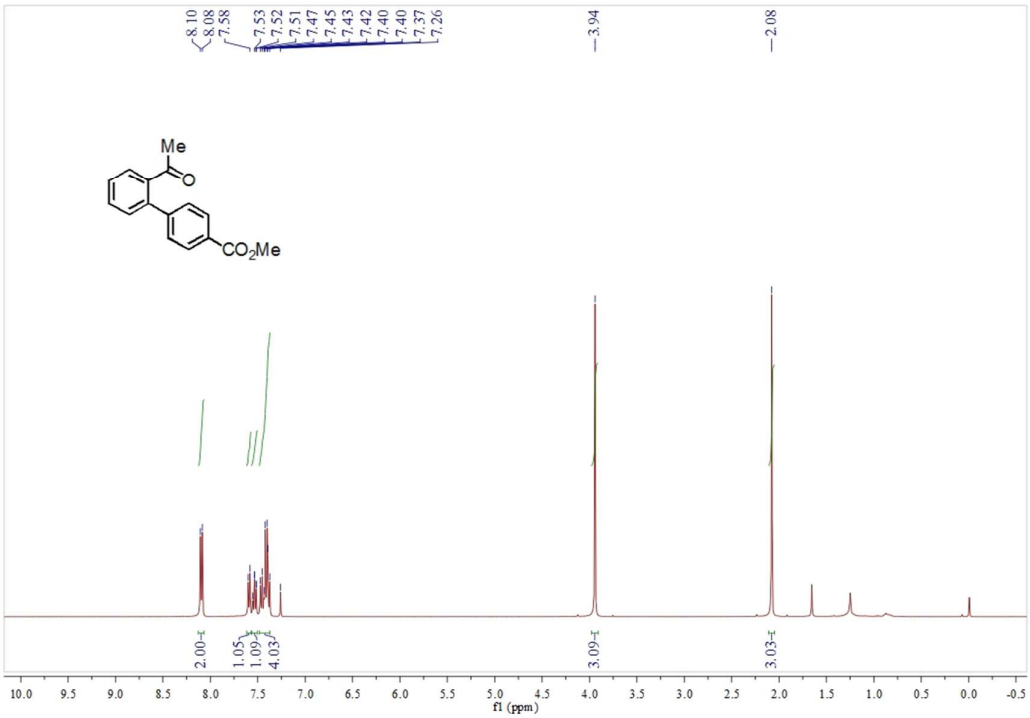
^{13}C NMR Spectra of Compound **3s**



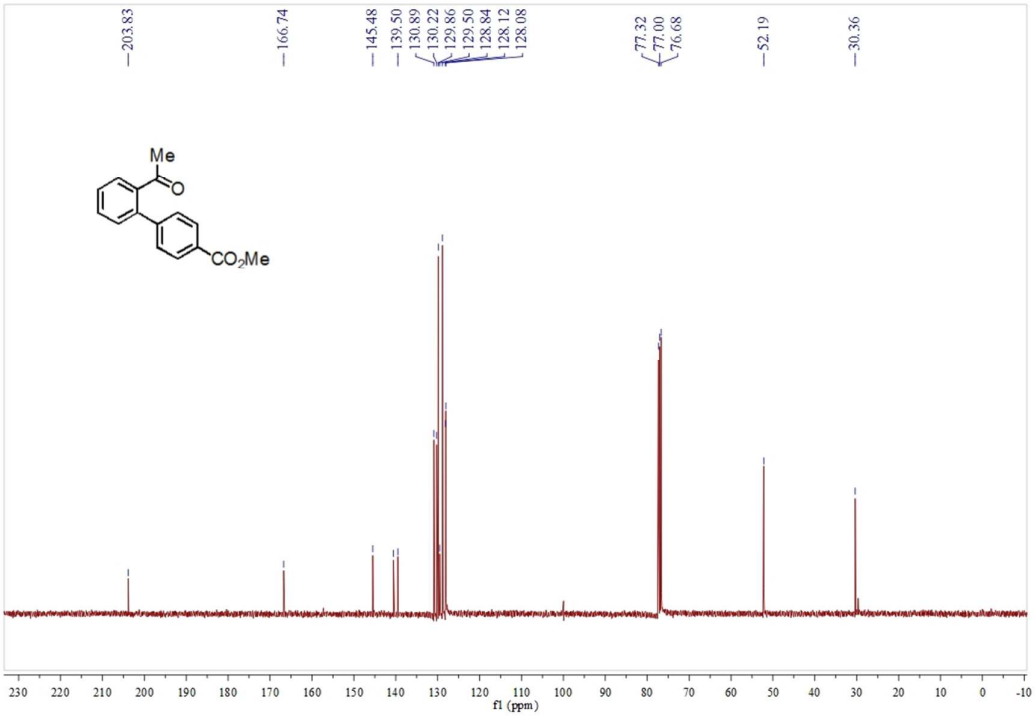
^{1}H NMR Spectra of Compound **3t**



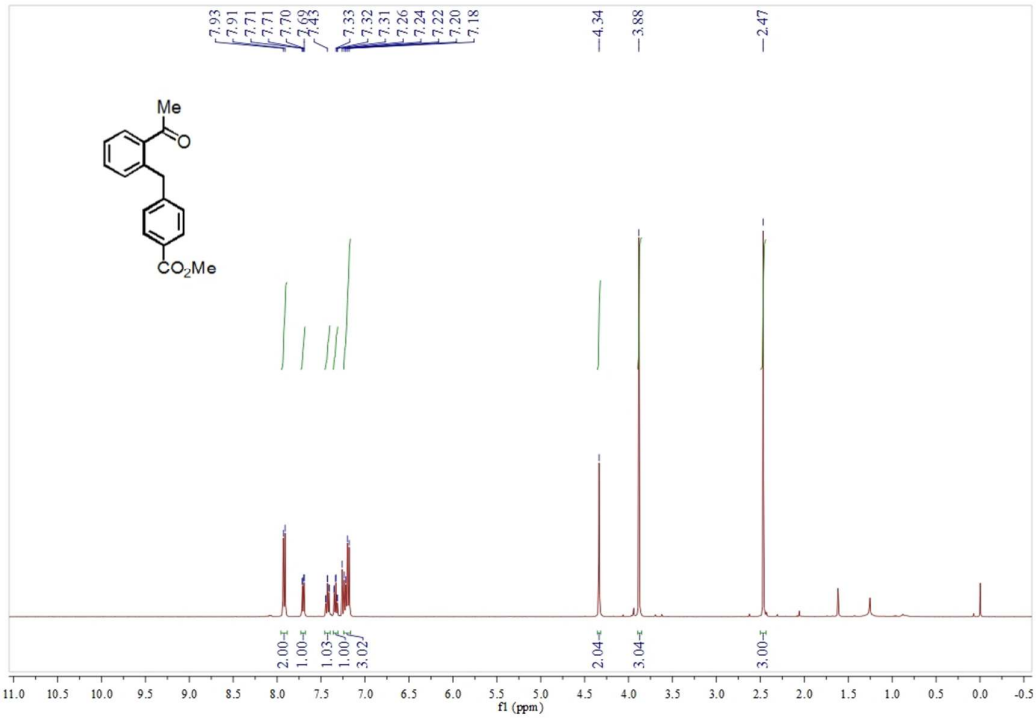
^{13}C NMR Spectra of Compound **3t**



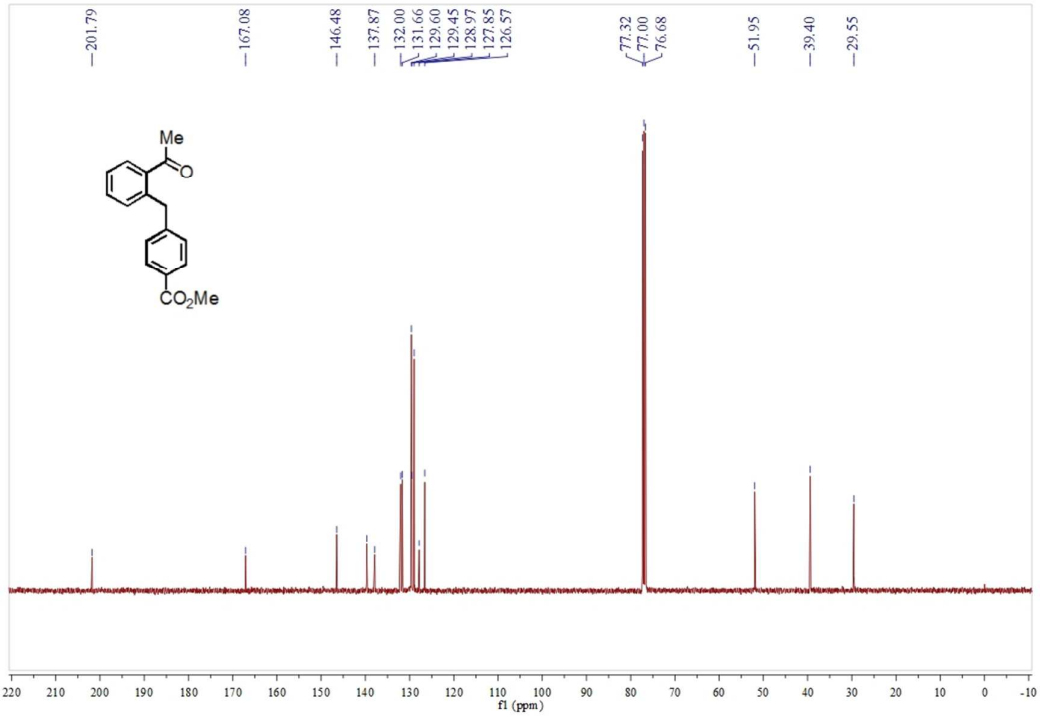
^{1}H NMR Spectra of Compound **4a**



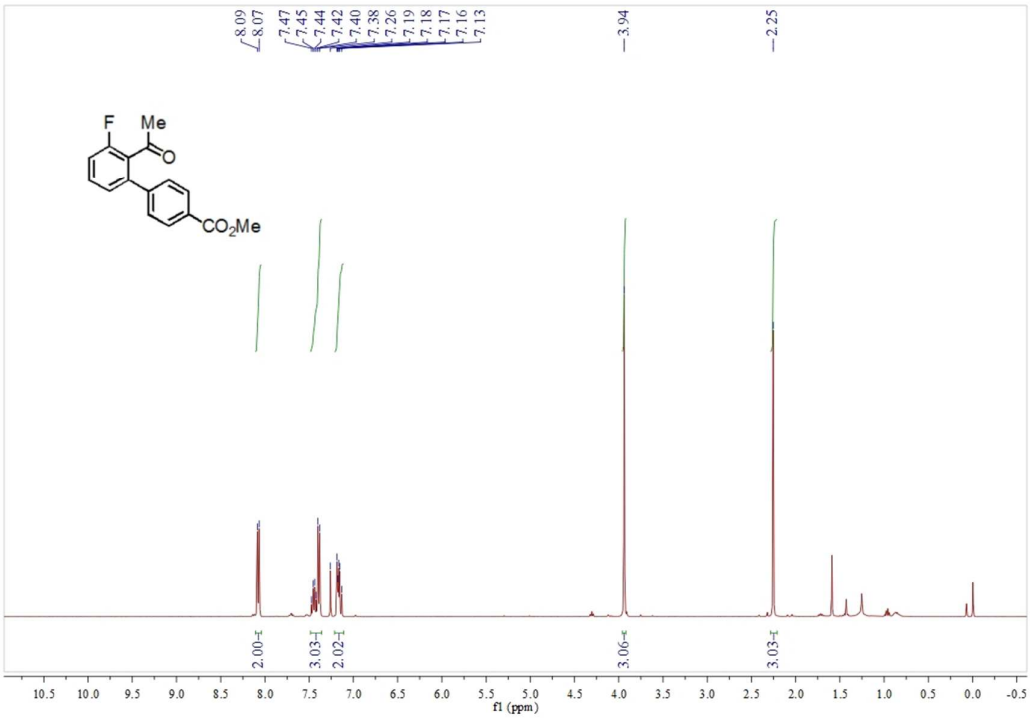
^{13}C NMR Spectra of Compound **4a**



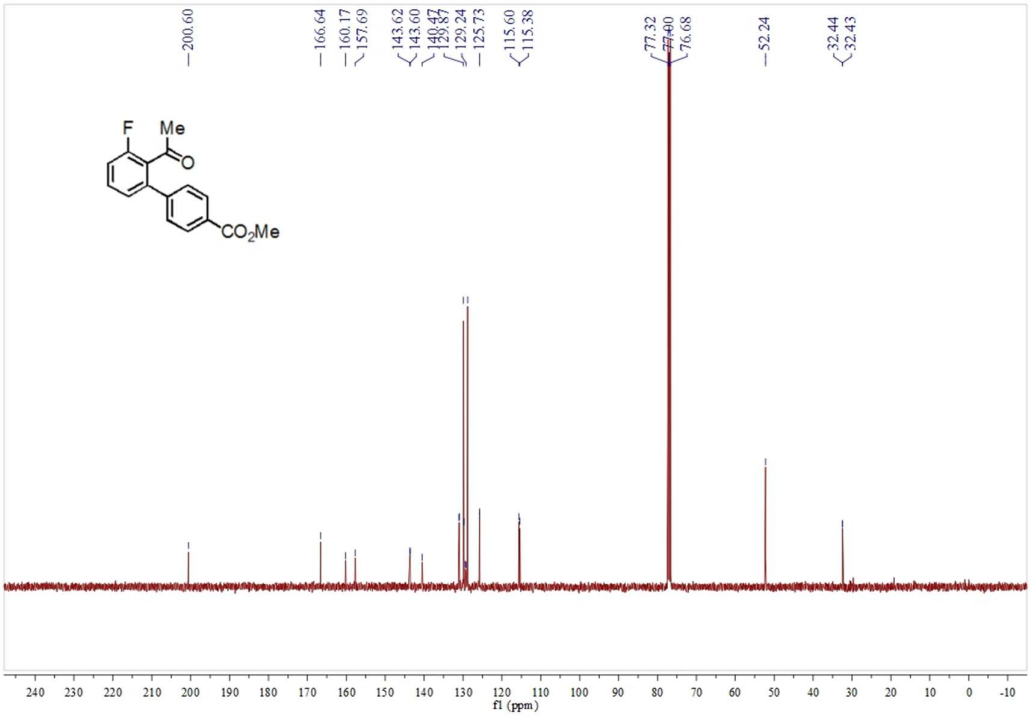
^{1}H NMR Spectra of Compound **4b**



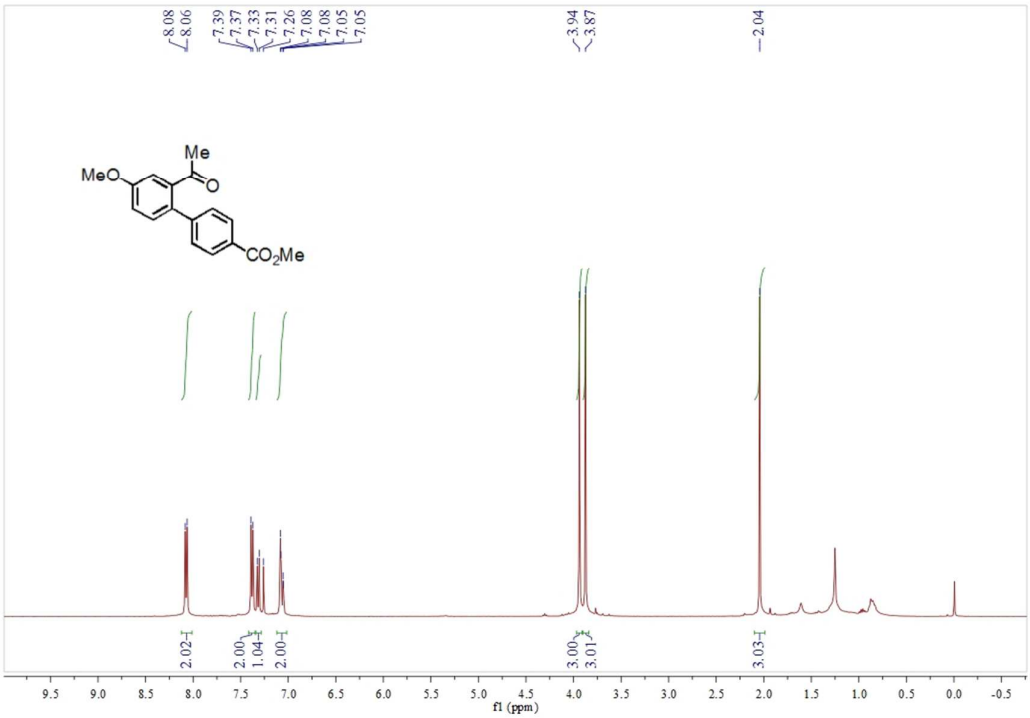
^{13}C NMR Spectra of Compound **4b**



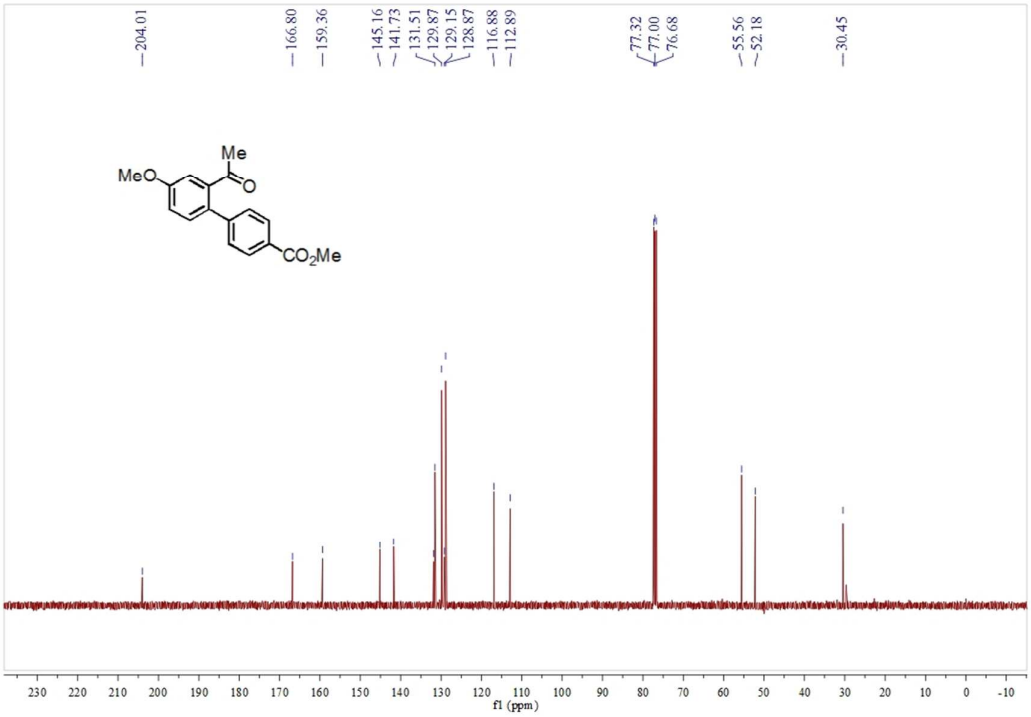
^{1}H NMR Spectra of Compound **4c**



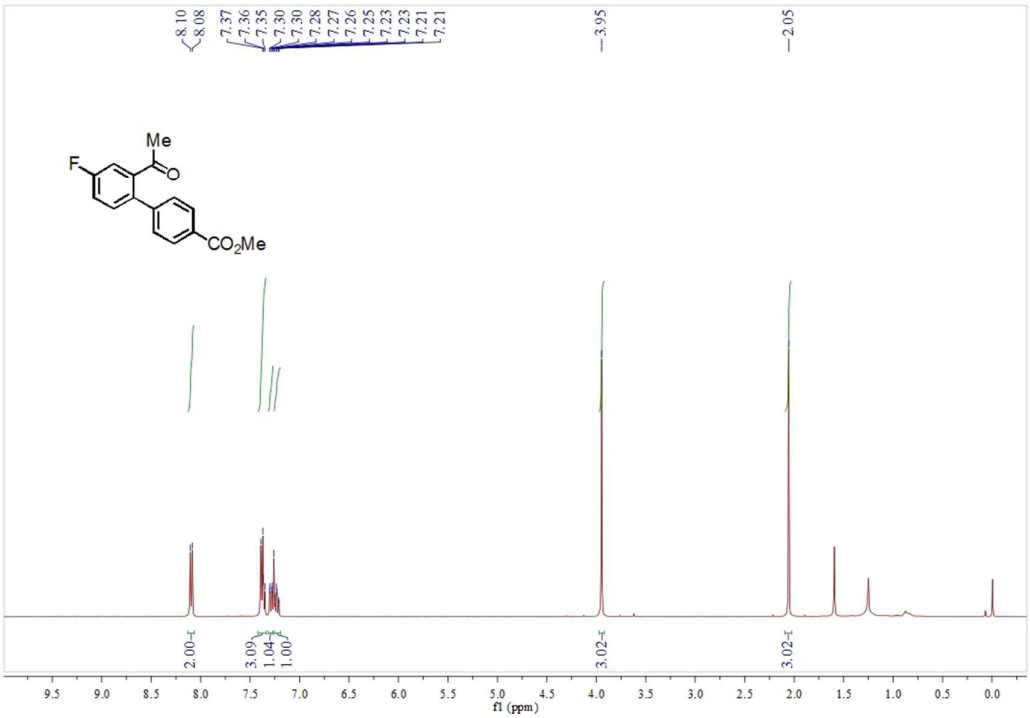
^{13}C NMR Spectra of Compound **4c**



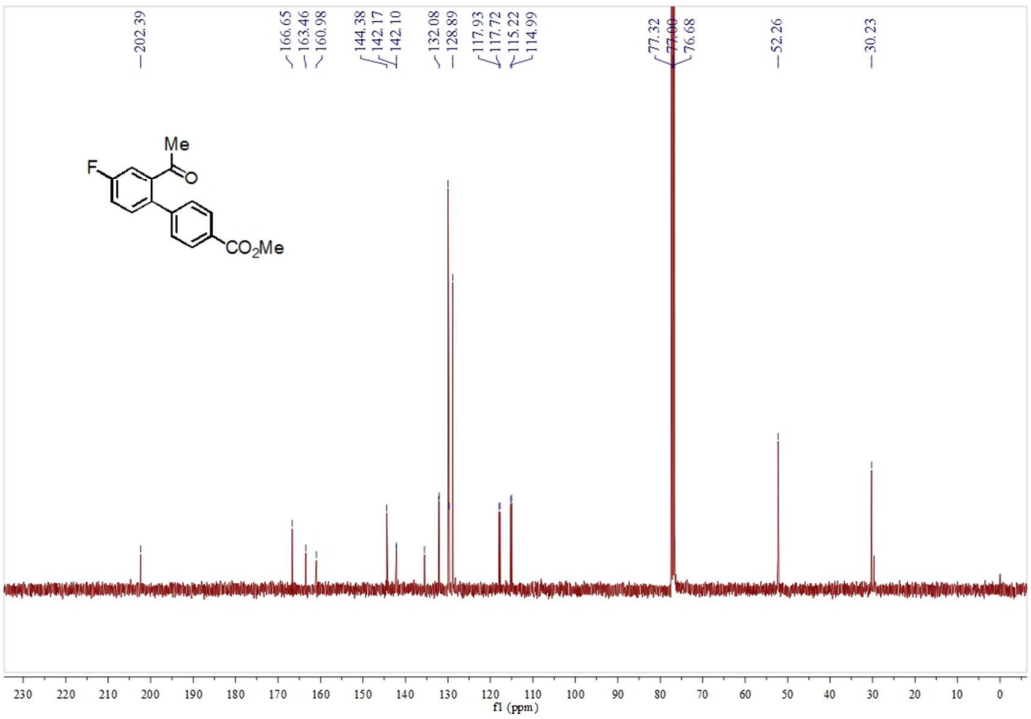
^{1}H NMR Spectra of Compound **4d**



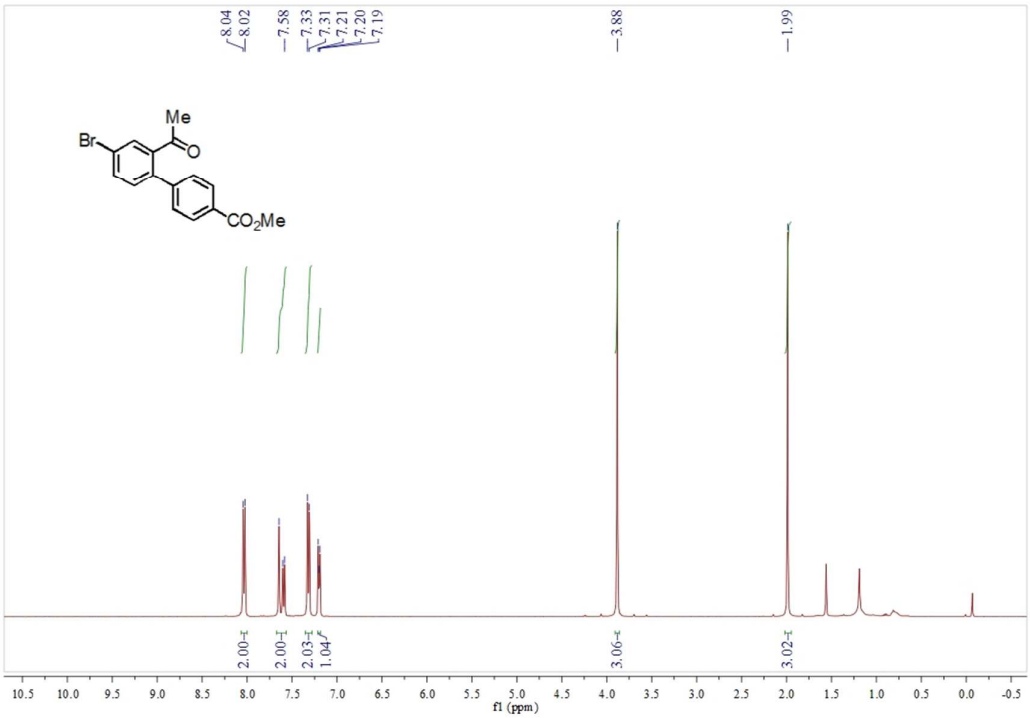
^{13}C NMR Spectra of Compound **4d**



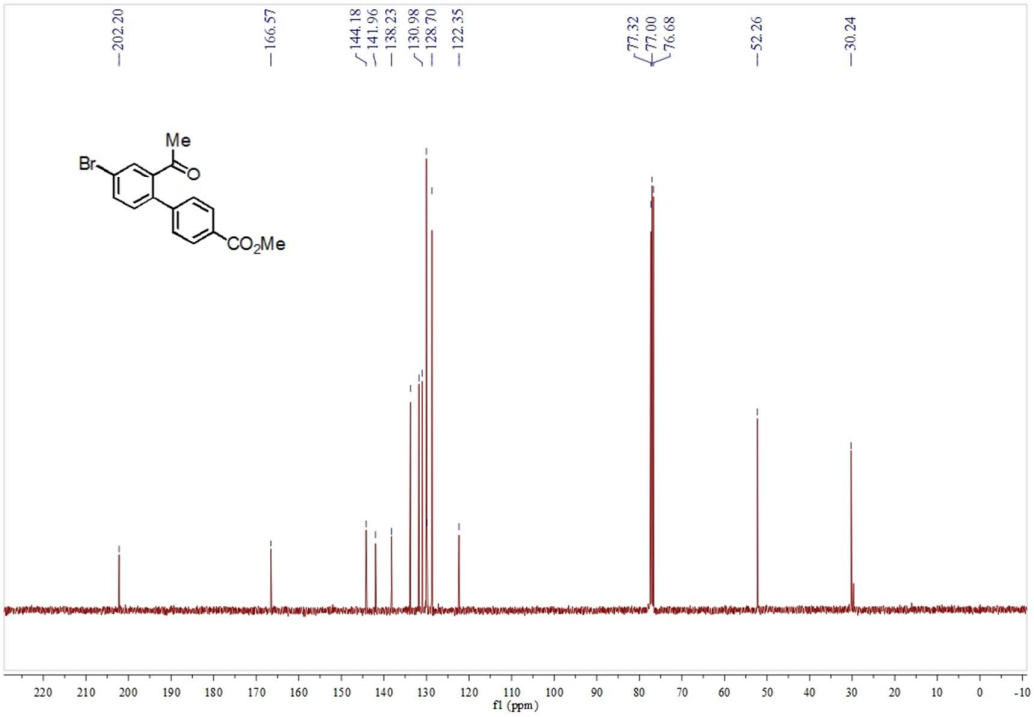
^{1}H NMR Spectra of Compound **4e**



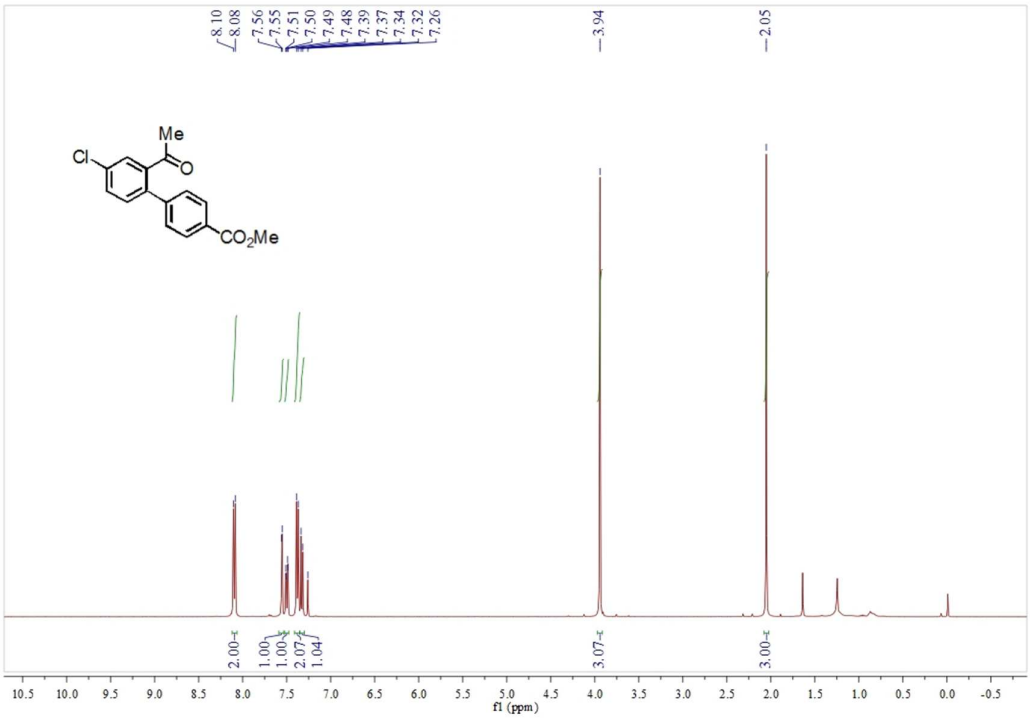
^{13}C NMR Spectra of Compound **4e**



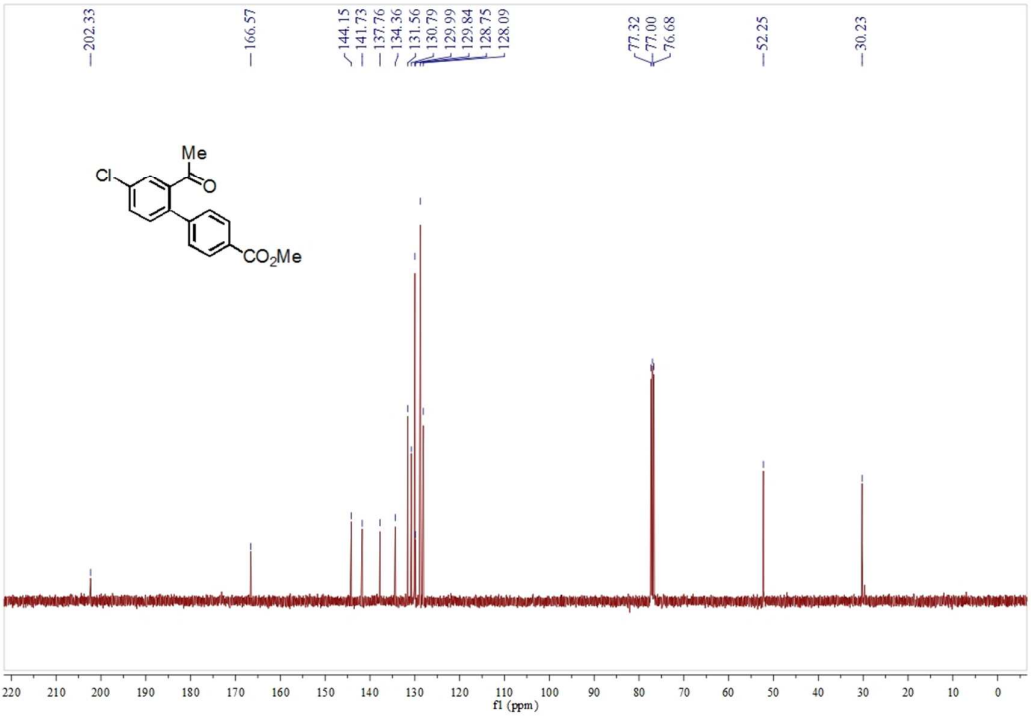
^{1}H NMR Spectra of Compound **4f**



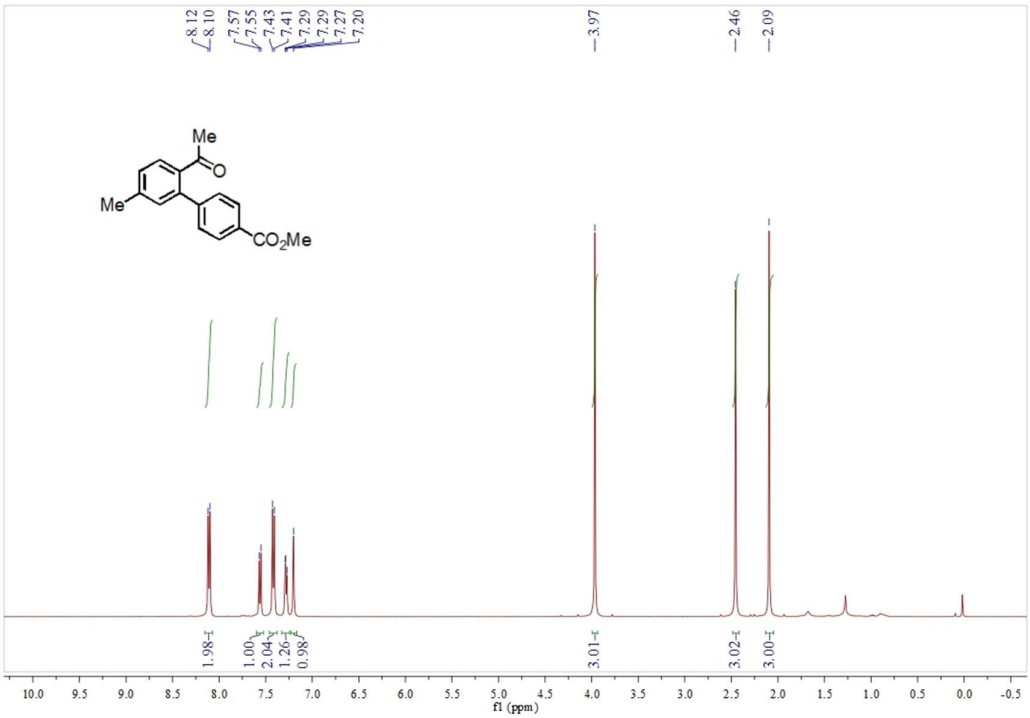
^{13}C NMR Spectra of Compound **4f**



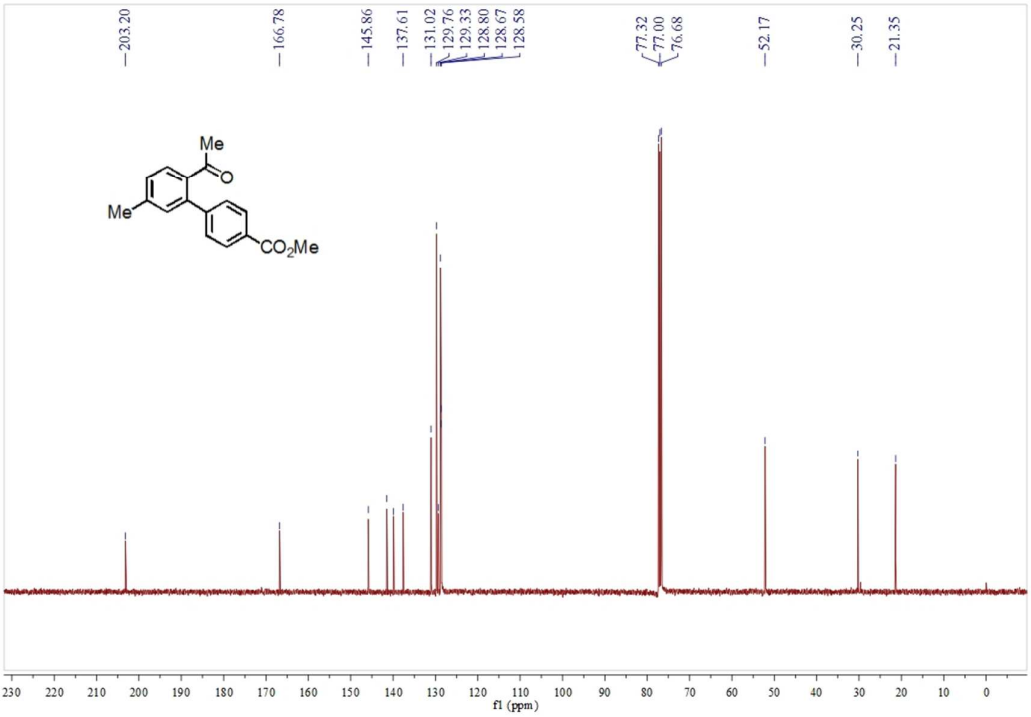
^{1}H NMR Spectra of Compound **4g**



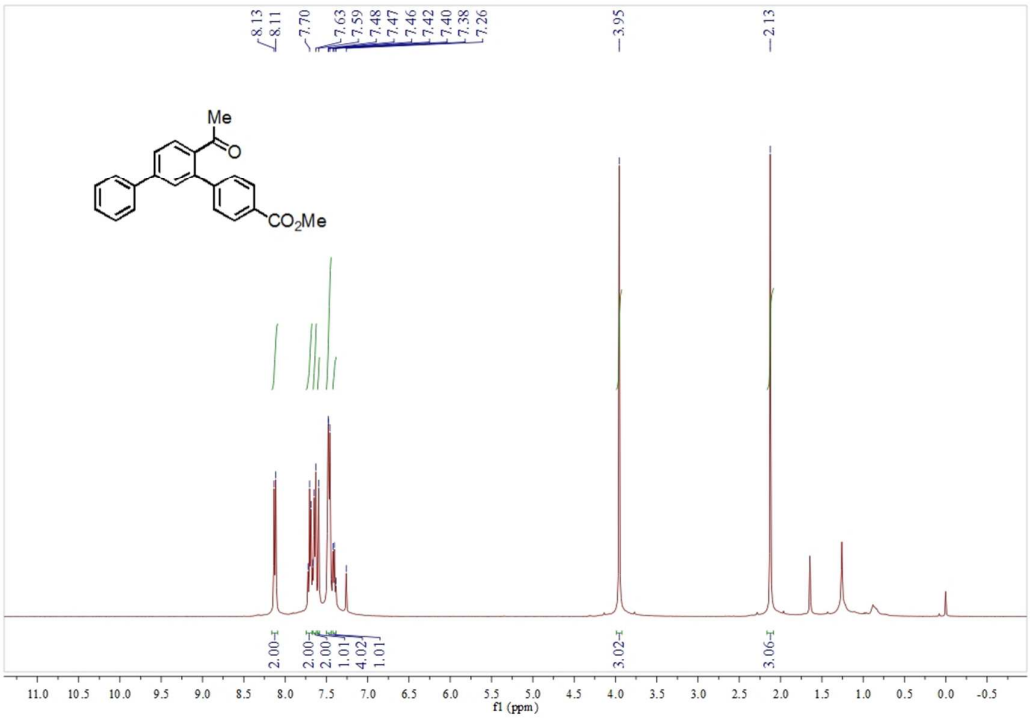
^{13}C NMR Spectra of Compound **4g**



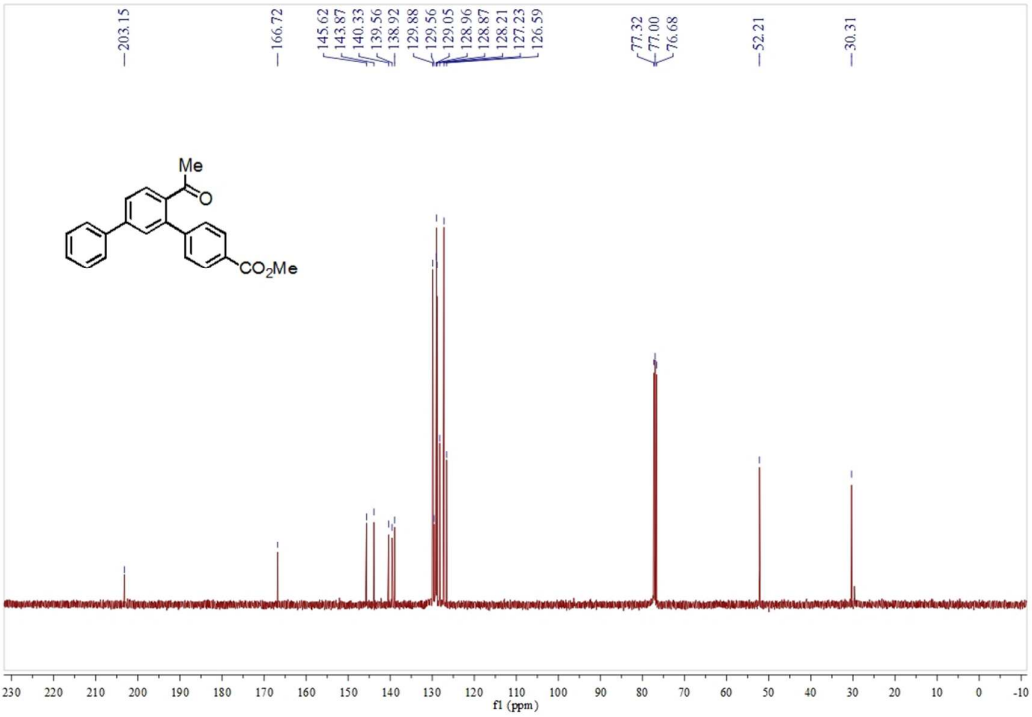
^{1}H NMR Spectra of Compound **4h**



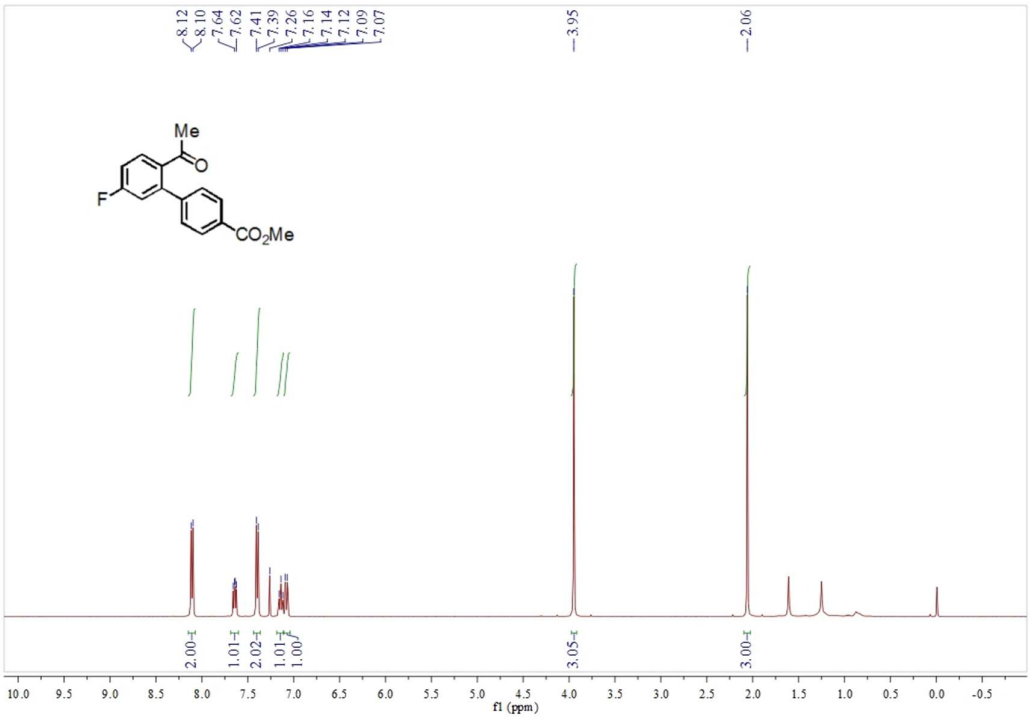
^{13}C NMR Spectra of Compound **4h**



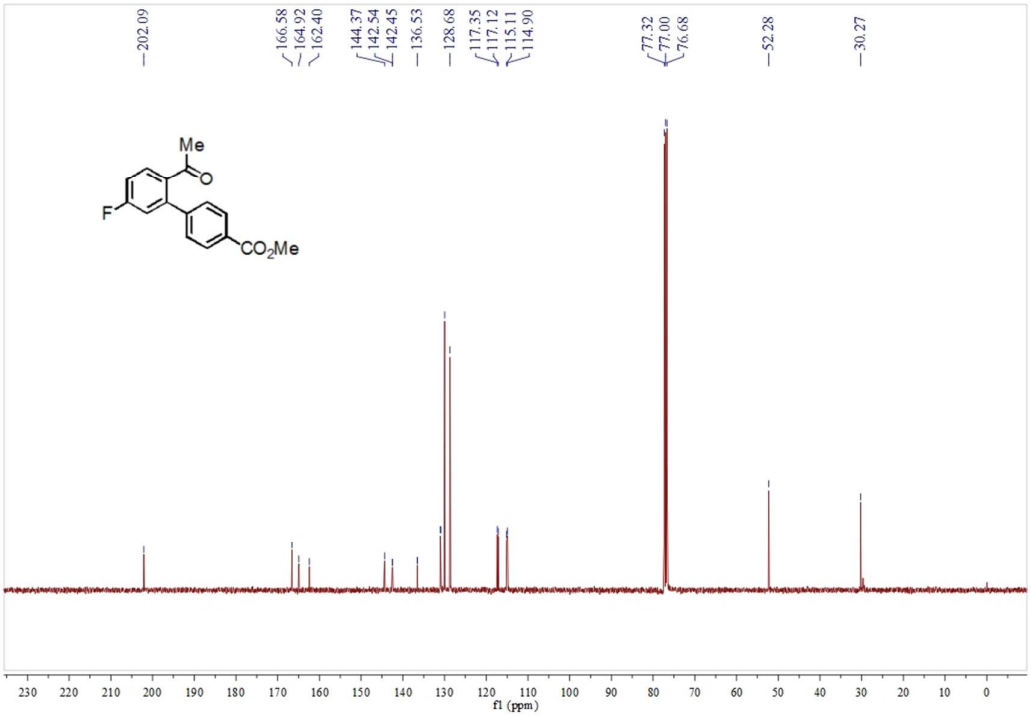
^{1}H NMR Spectra of Compound **4i**



^{13}C NMR Spectra of Compound **4i**



^{1}H NMR Spectra of Compound **4j**



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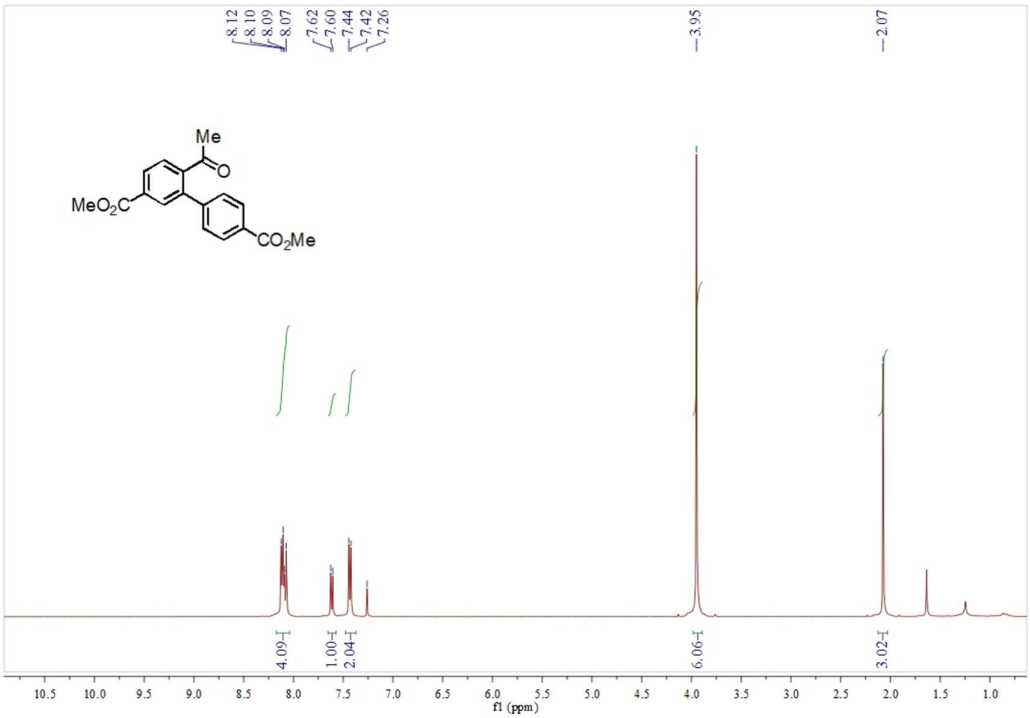
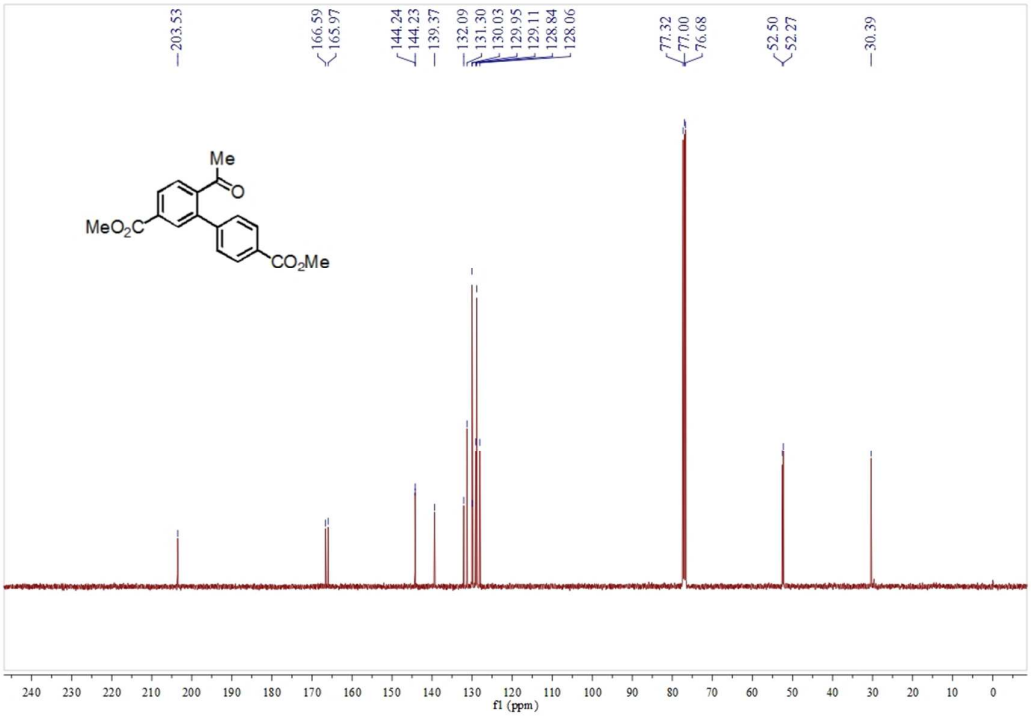
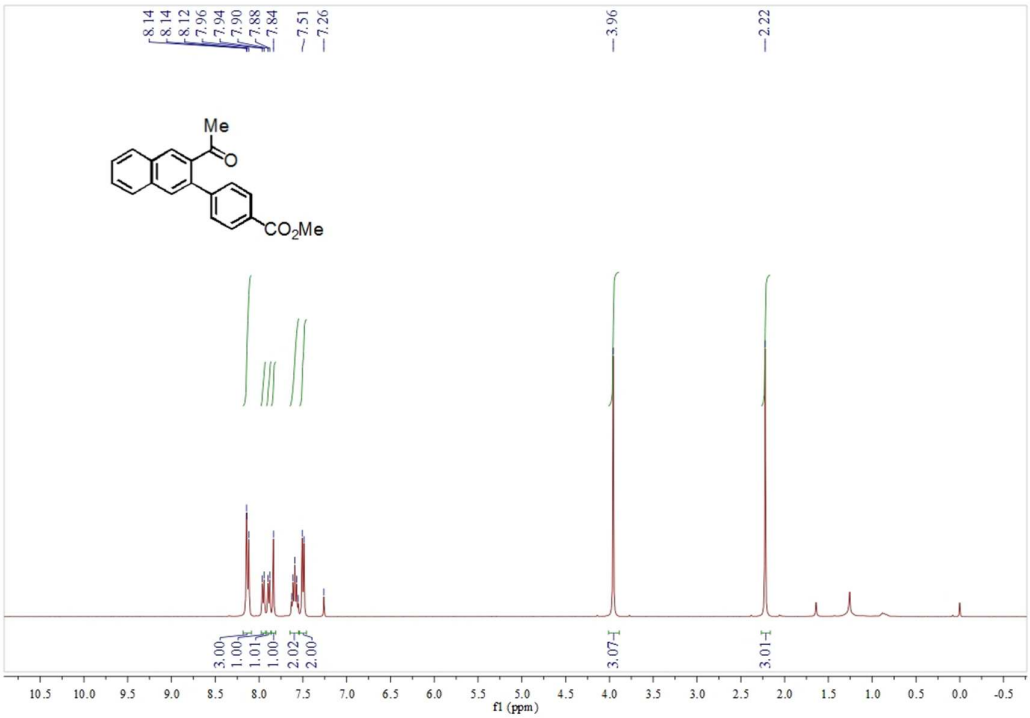


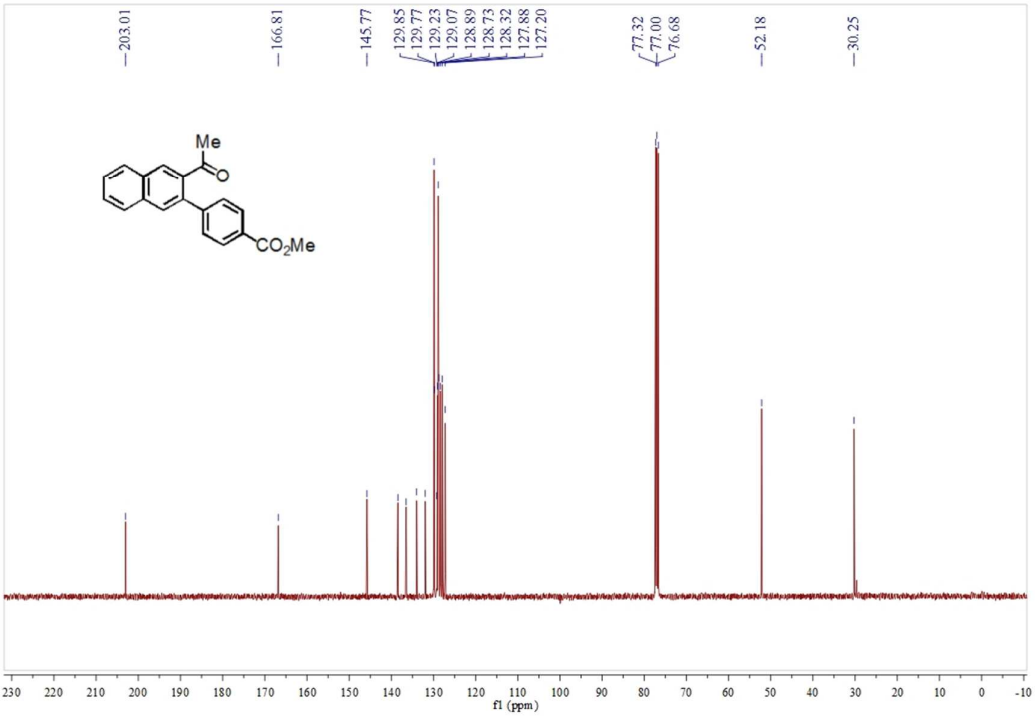
^{1}H NMR Spectra of Compound **4k**



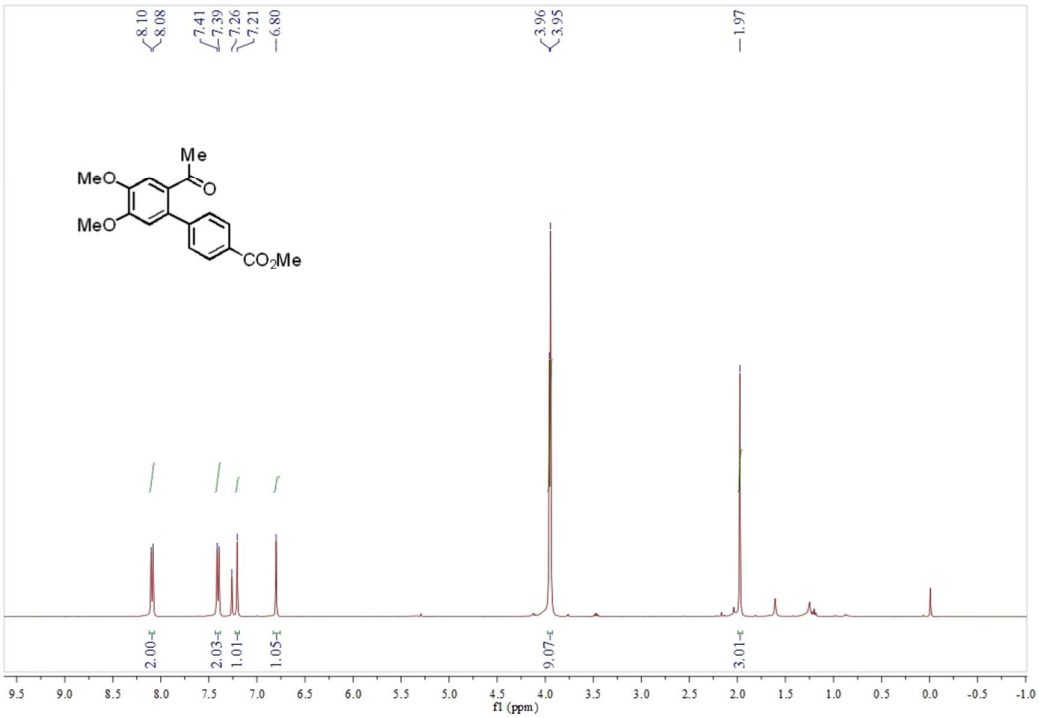
^{13}C NMR Spectra of Compound **4k**



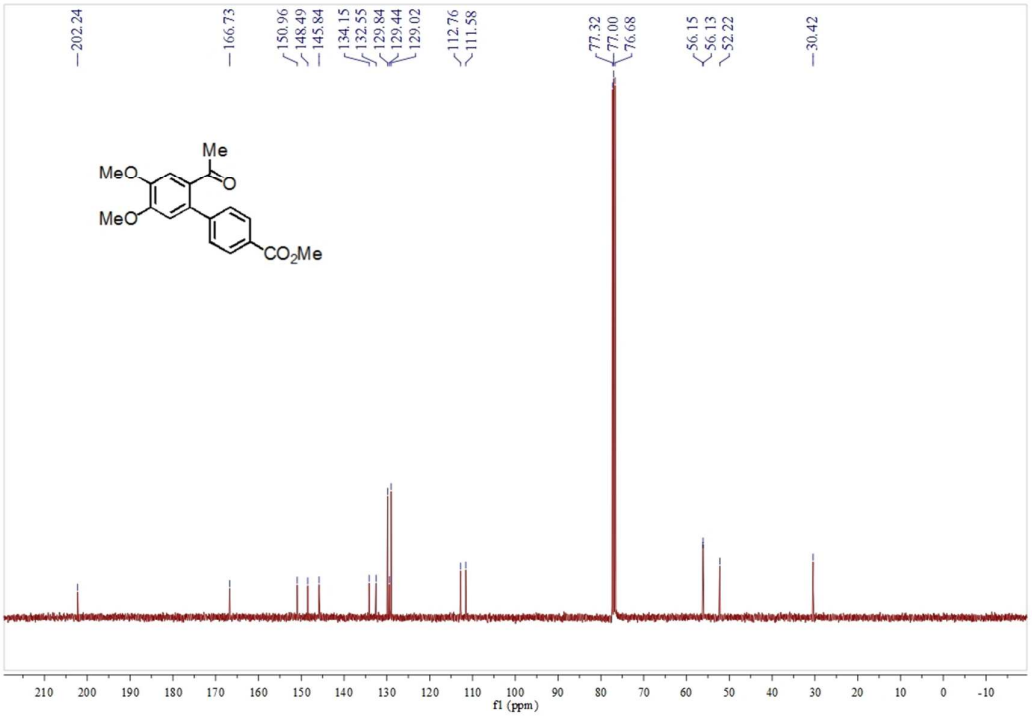
^{1}H NMR Spectra of Compound **4l**



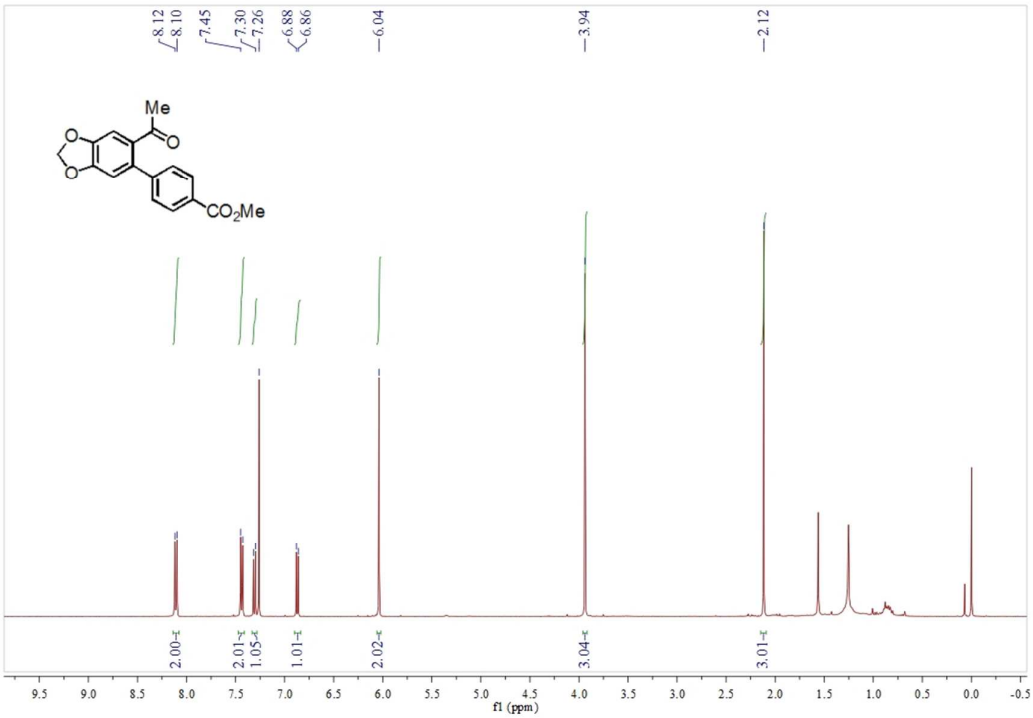
^{13}C NMR Spectra of Compound **4l**



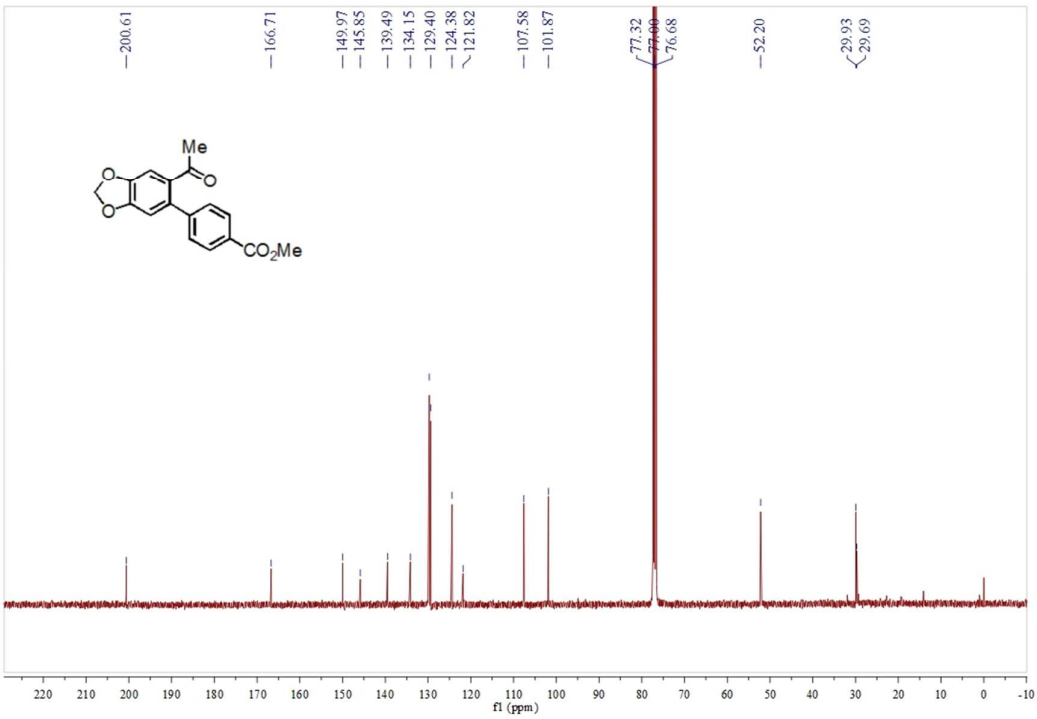
^{1}H NMR Spectra of Compound **4m**



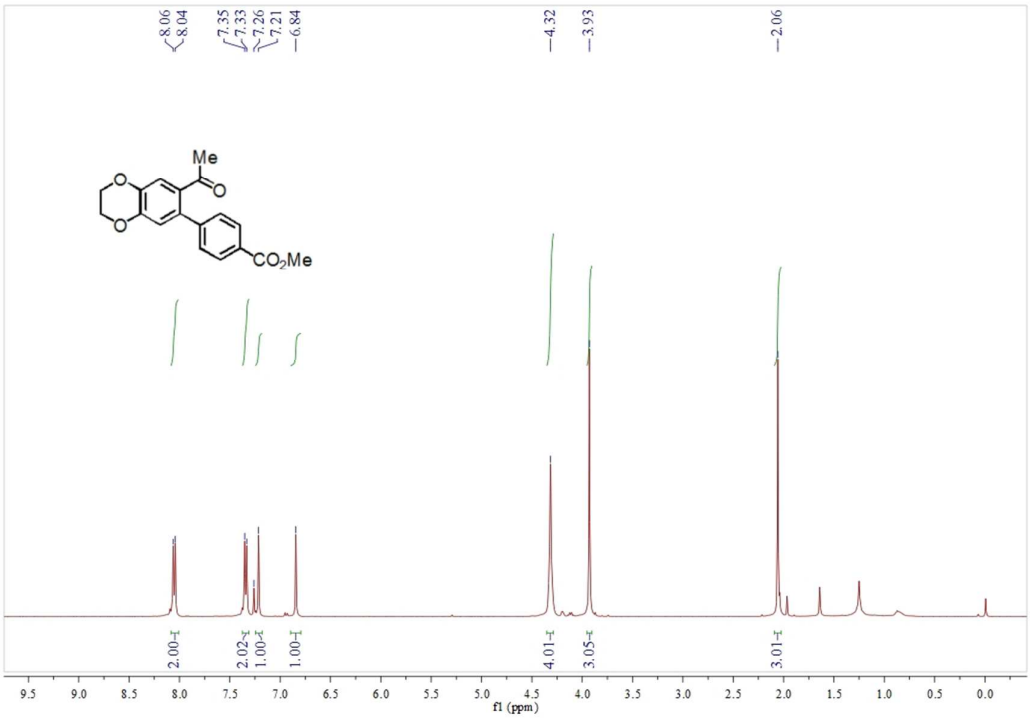
^{13}C NMR Spectra of Compound **4m**



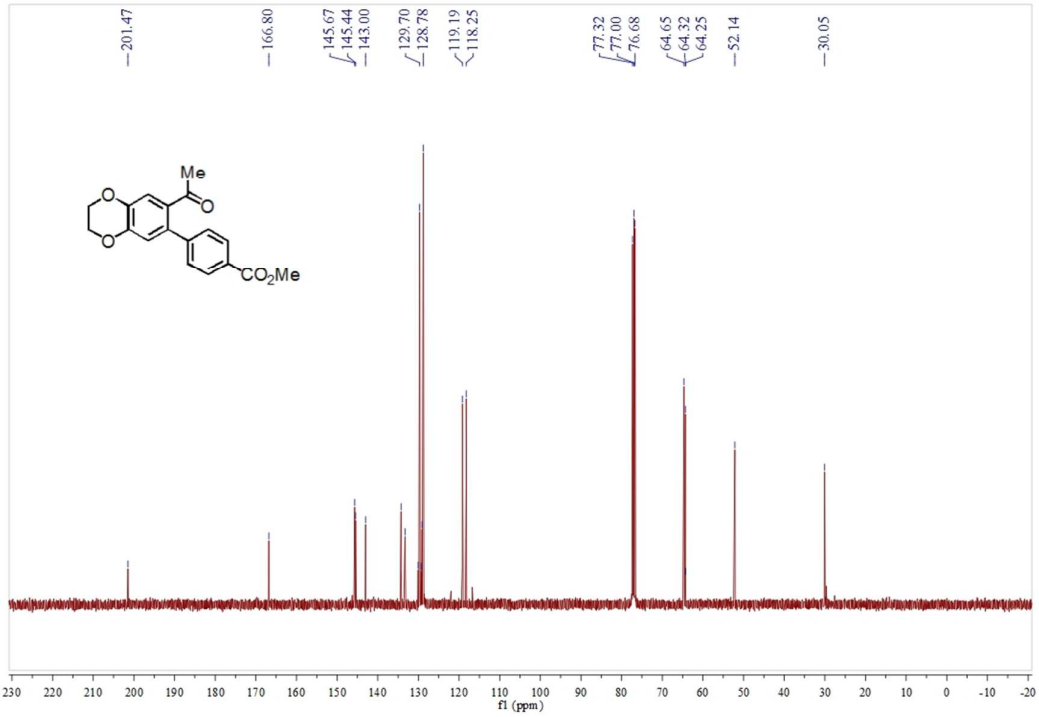
^{1}H NMR Spectra of Compound **4n**



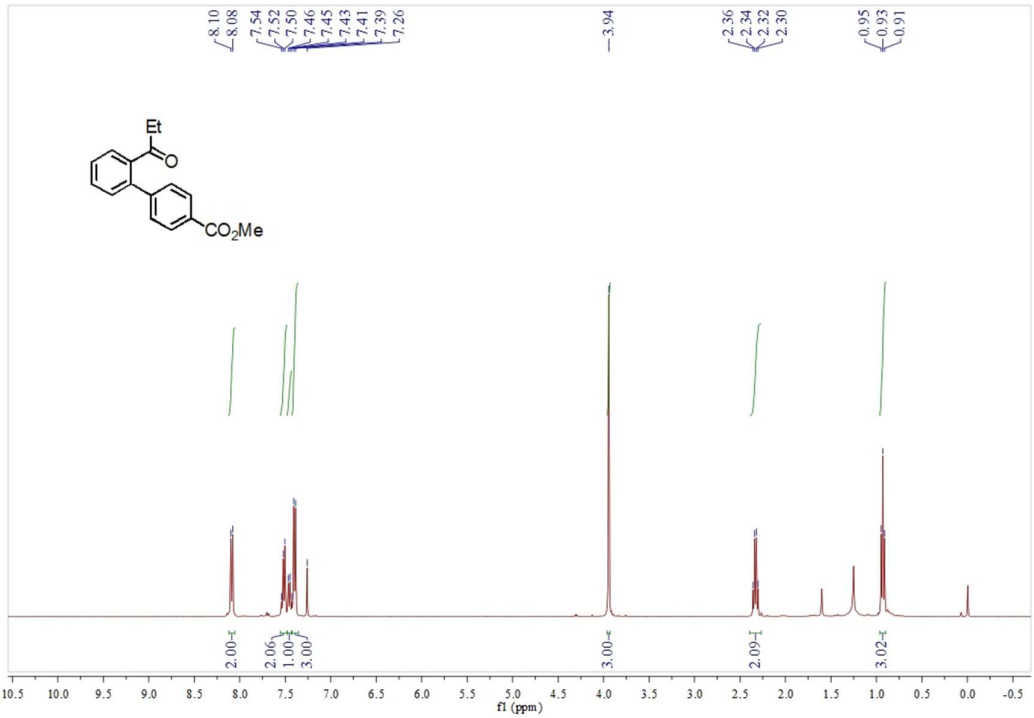
^{13}C NMR Spectra of Compound **4n**



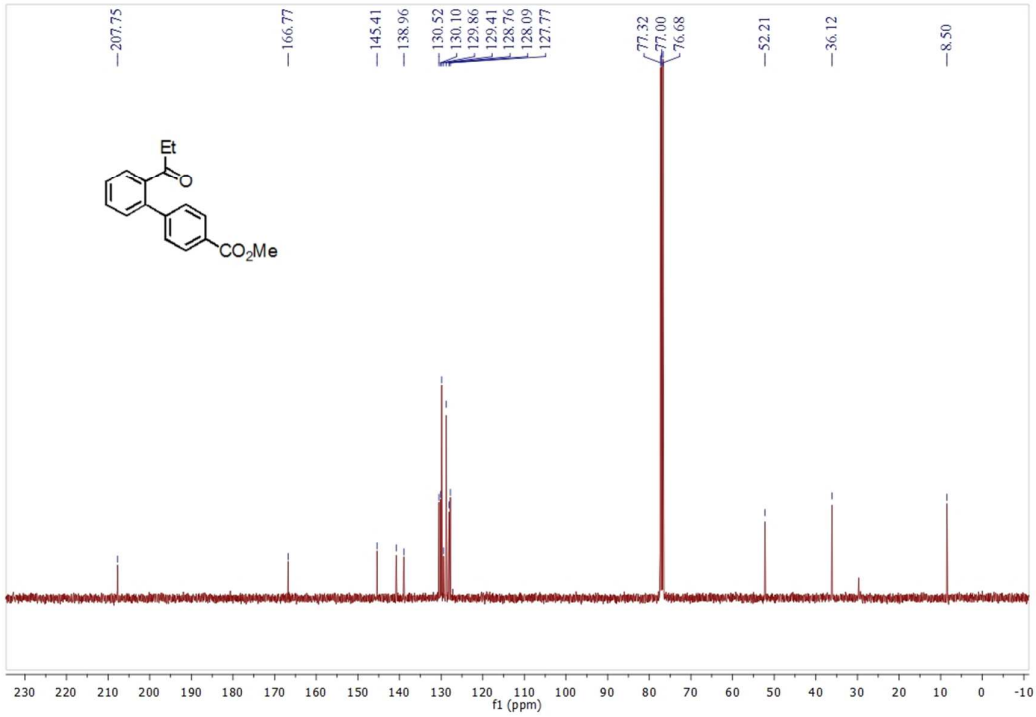
^{1}H NMR Spectra of Compound **4o**



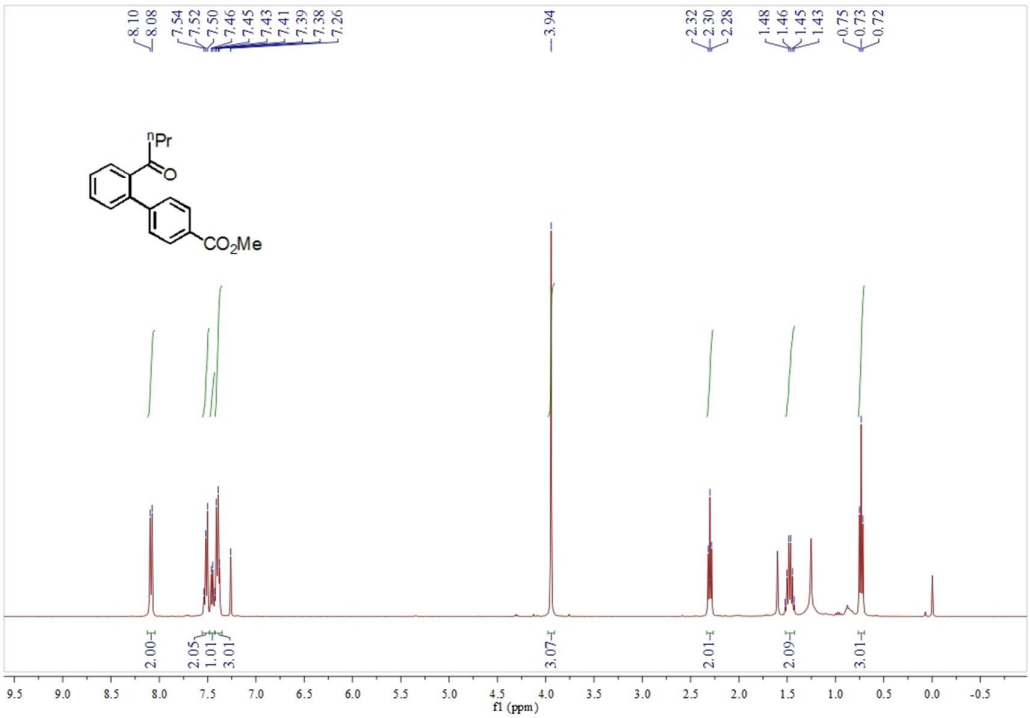
^{13}C NMR Spectra of Compound **4o**



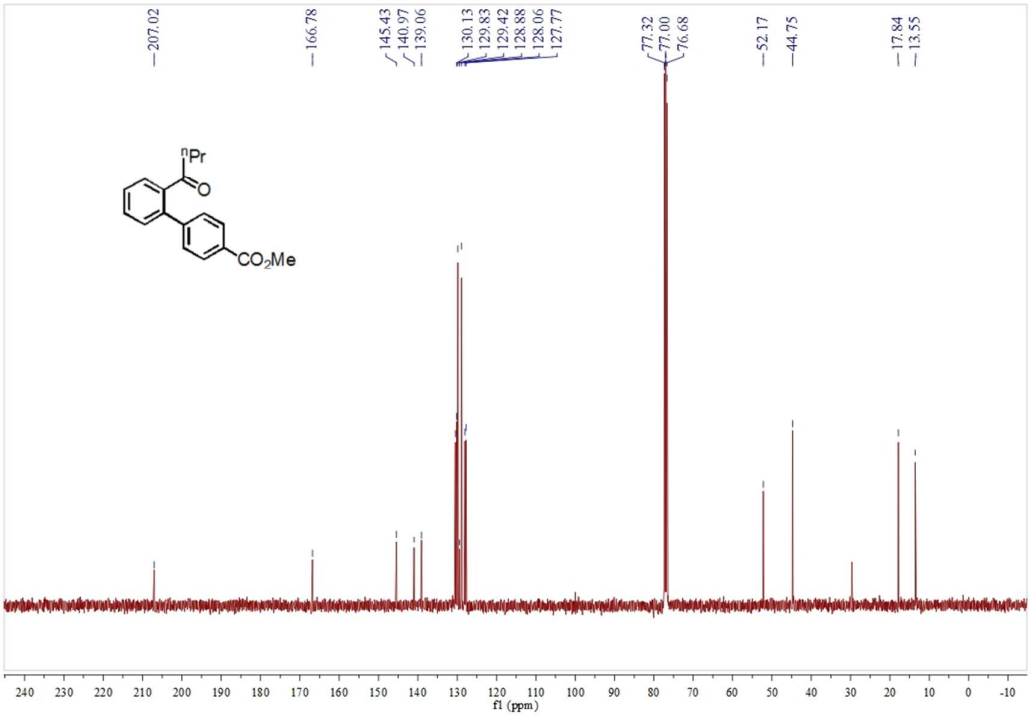
^{1}H NMR Spectra of Compound **4p**



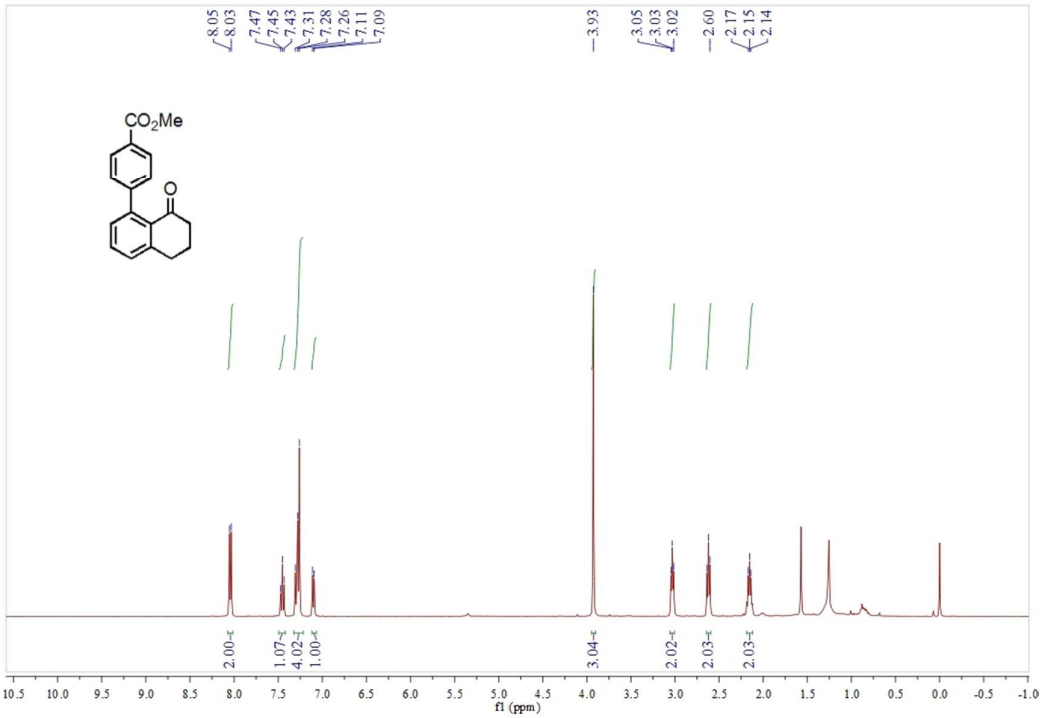
^{13}C NMR Spectra of Compound **4p**



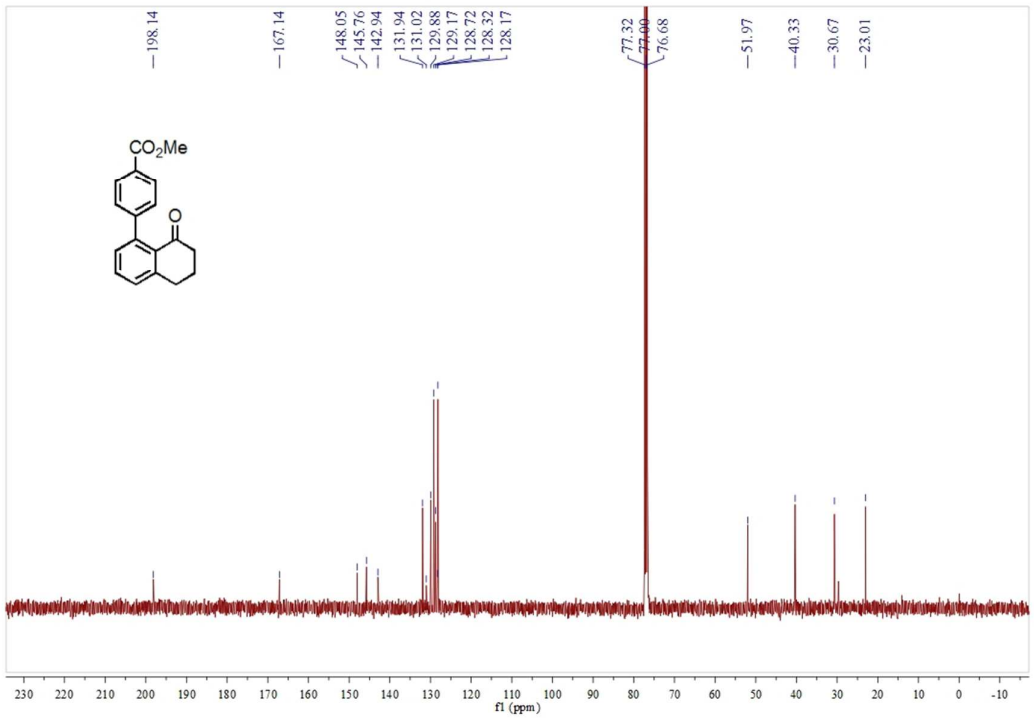
^{1}H NMR Spectra of Compound **4q**



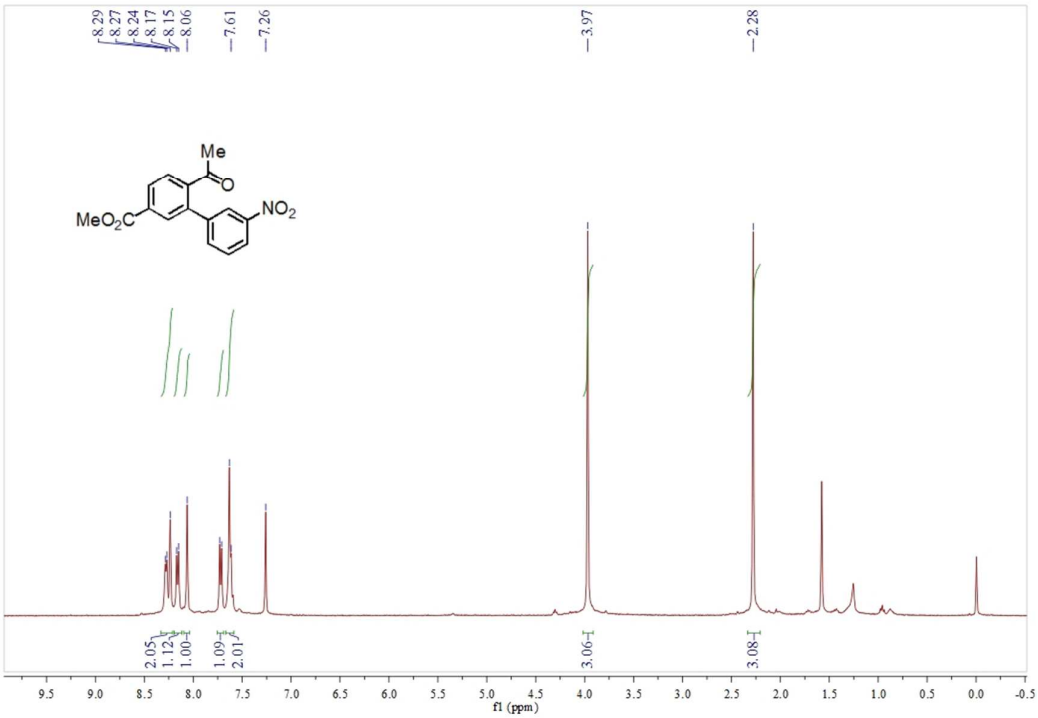
^{13}C NMR Spectra of Compound **4q**



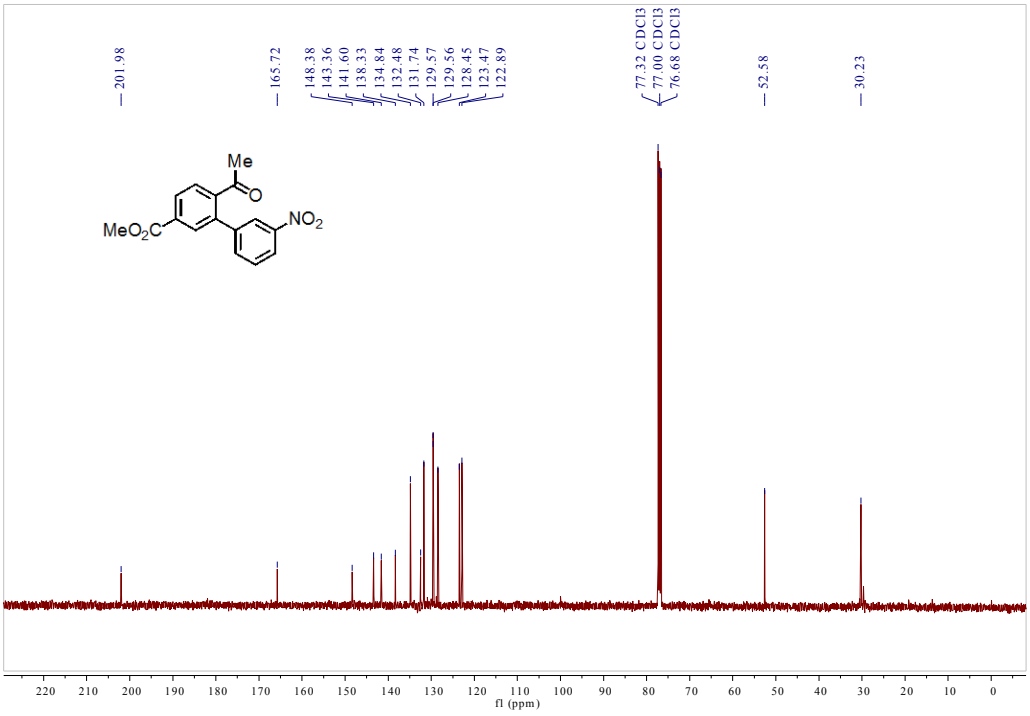
^{1}H NMR Spectra of Compound **4r**



^{13}C NMR Spectra of Compound **4r**



^{1}H NMR Spectra of Compound **4s**



^{13}C NMR Spectra of Compound **4s**