

Synthesis of Mono- and Bis-Pyrazoles Bearing Flexible *p*-tolyl Ether and Rigid Xanthene Backbones and their Application as Ligands in the *Pd*-Catalysed Suzuki-Miyaura Cross-Coupling Reaction

Zahid Hussain,¹ Cristiane S. Schwalm,^{1,2} Renieidy F. C. Dias,¹ Raoní S. Rambo,¹ Rafael Stieler,¹ Adriano L. Monteiro^{1,*}

¹ Laboratory of Molecular Catalysis, Instituto of Chemistry, Federal University of Rio Grande do Sul (UFRGS), Av. Bento Gonçalves, 9500, Porto Alegre 91501-970, CEP 15003 – Brazil.

² Faculty of Exact Science and Technology, Universidade Federal da Grande Dourados (UFGD), Rodovia Dourados-Itahum, km 12, Dourados, 79804-970 – CP 364, MG, Brazil.

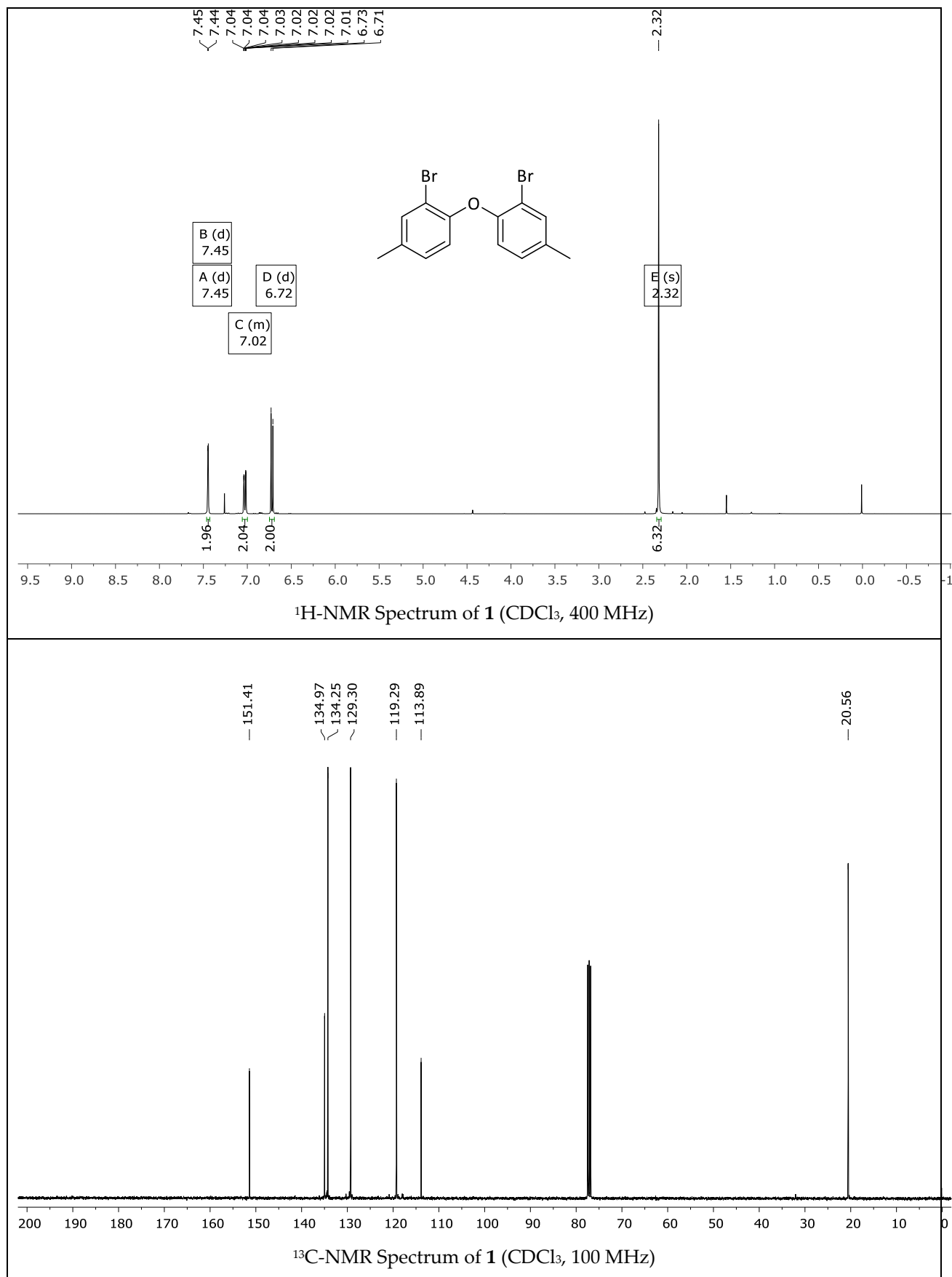
*^a e-mail: adriano.monteiro@ufrgs.br

Table of Contents

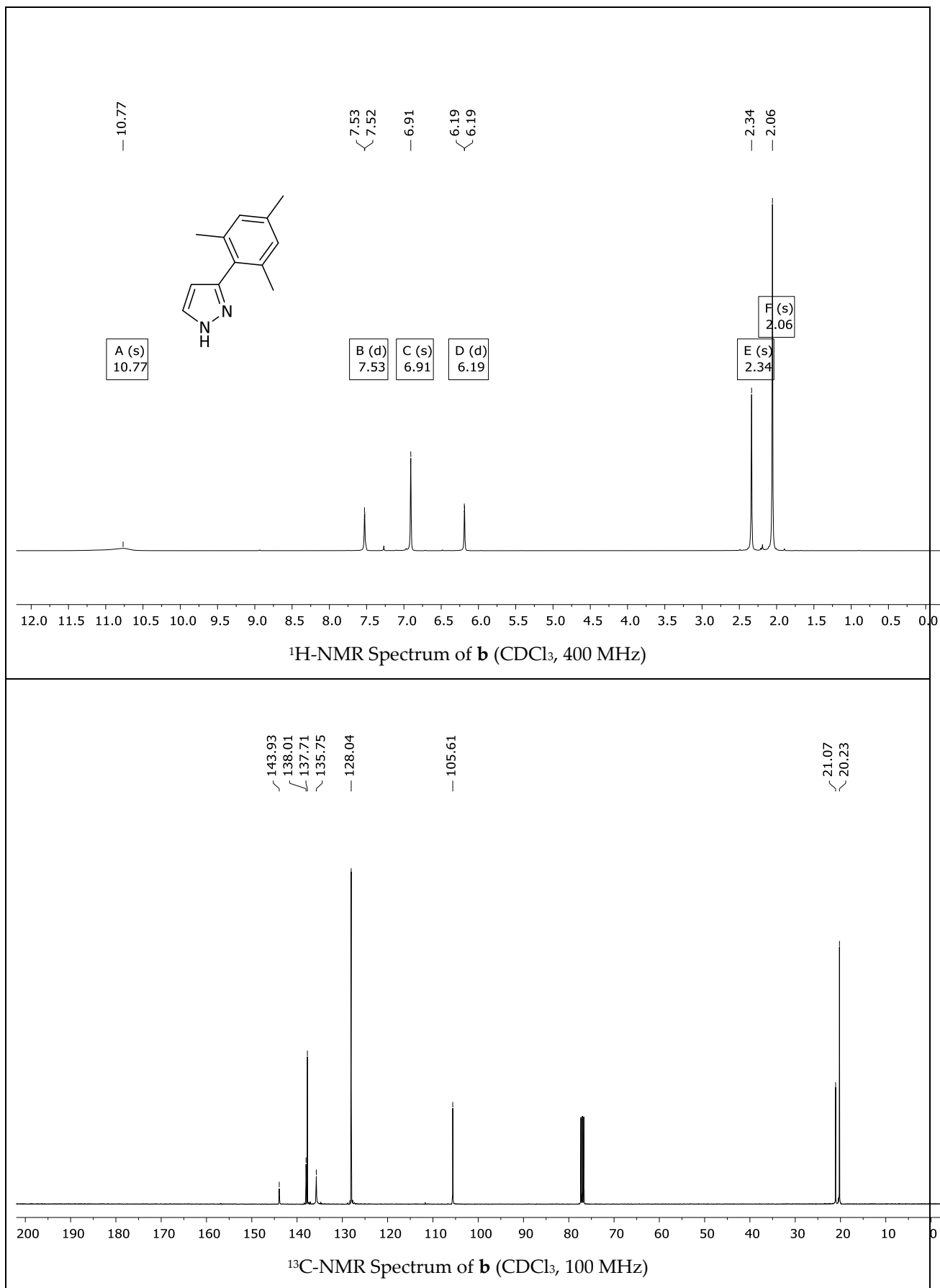
1. ¹ H- and ¹³ C-NMR Spectra for Synthetic Precursors and Pyrazolyl Ligands	S2
2. Table 5. Crystallographic Data and Structure Refinement Parameters for 1 , 1a , 2a , 2b and 2b'	S12
3. Analytical and Spectroscopic Data for <i>SM</i> Cross-coupling Products	S14
4. ¹ H and ¹³ C-NMR Spectra for <i>SM</i> Cross-coupling Products	S16
5. References	S26

1 ^1H - and ^{13}C -NMR Spectra for Synthetic Precursors and Pyrazolyl Ligands

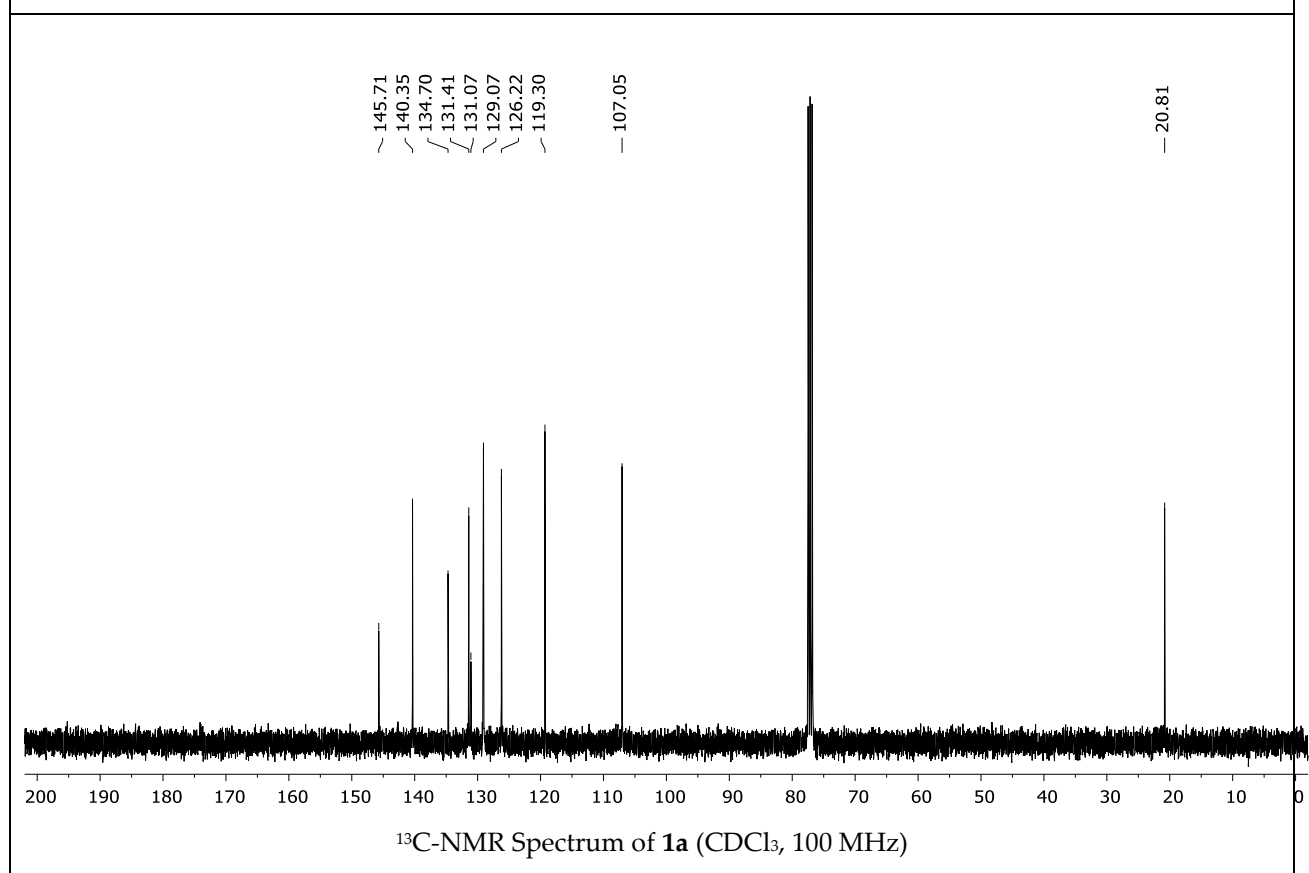
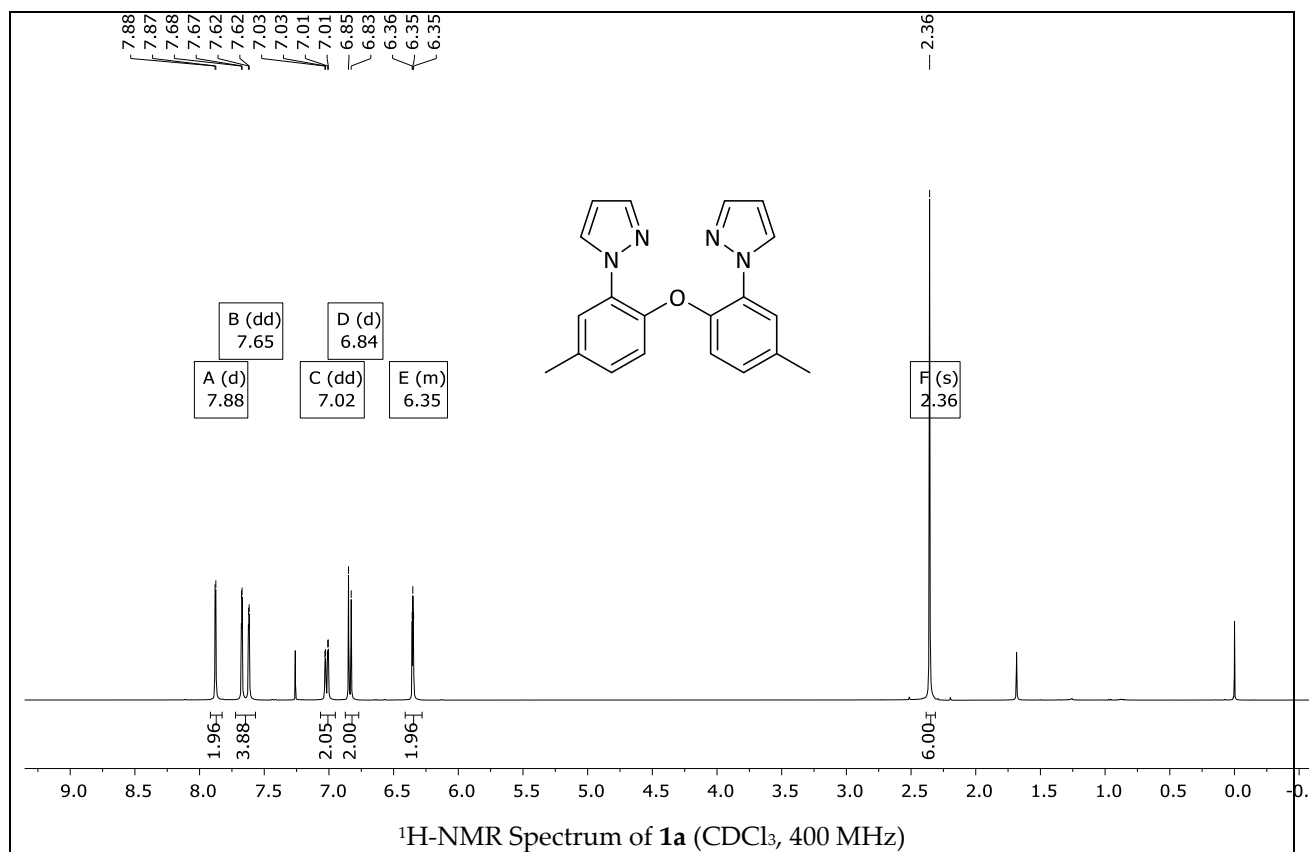
1.1 ^1H - and ^{13}C -NMR Spectra of 1



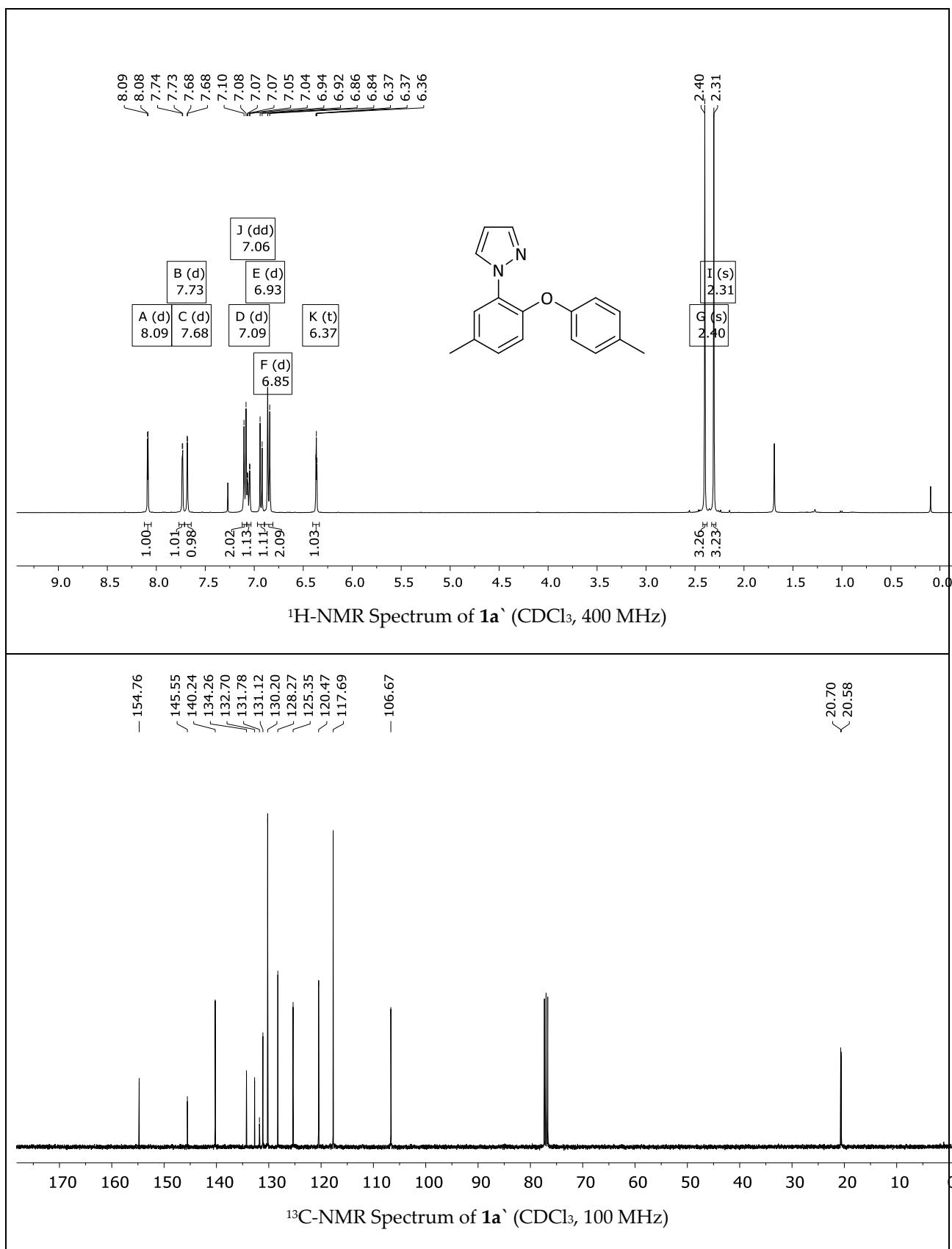
1.2 ^1H - and ^{13}C -NMR Spectra of 3-Mesityl-1H-pyrazole (**b**)



1.3 ^1H - and ^{13}C -NMR Spectra of **1a**

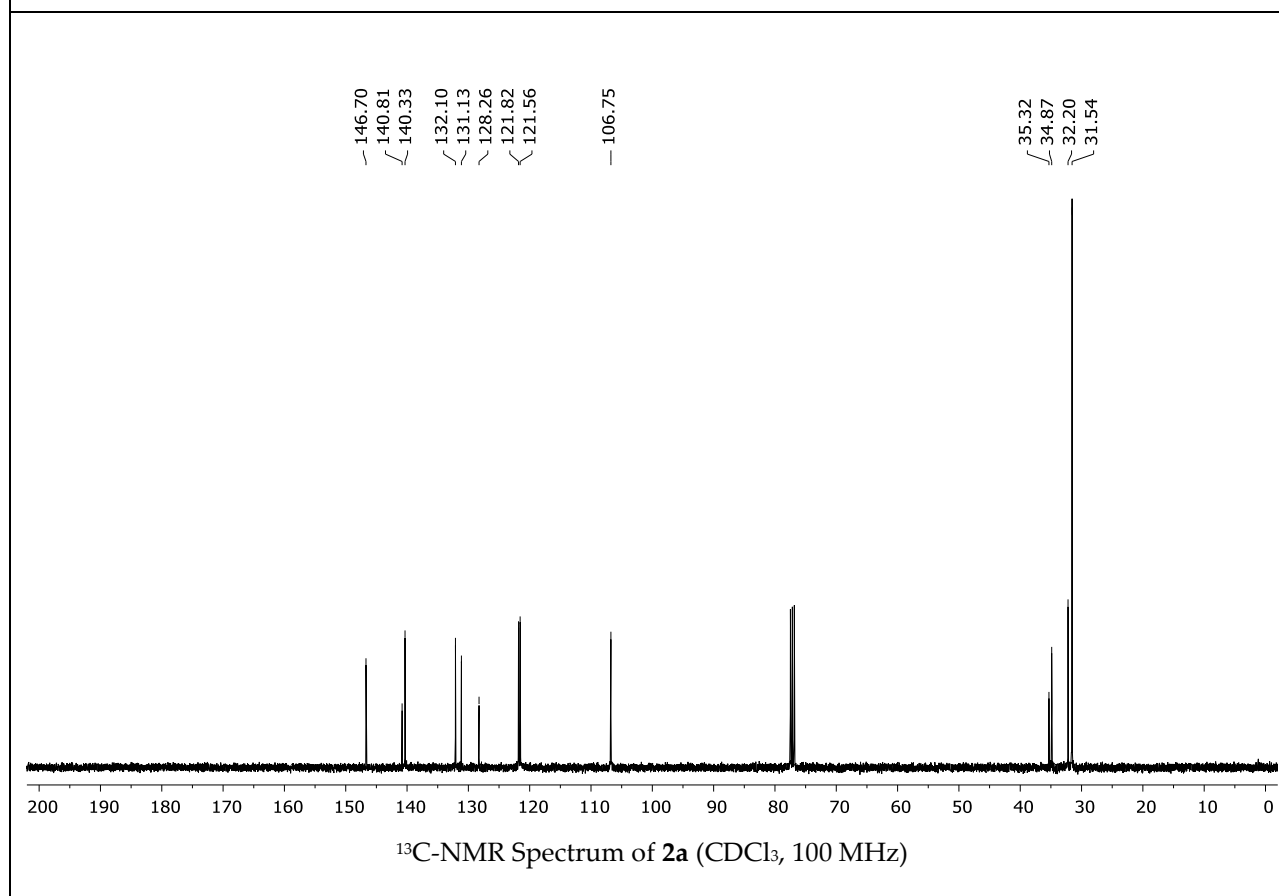
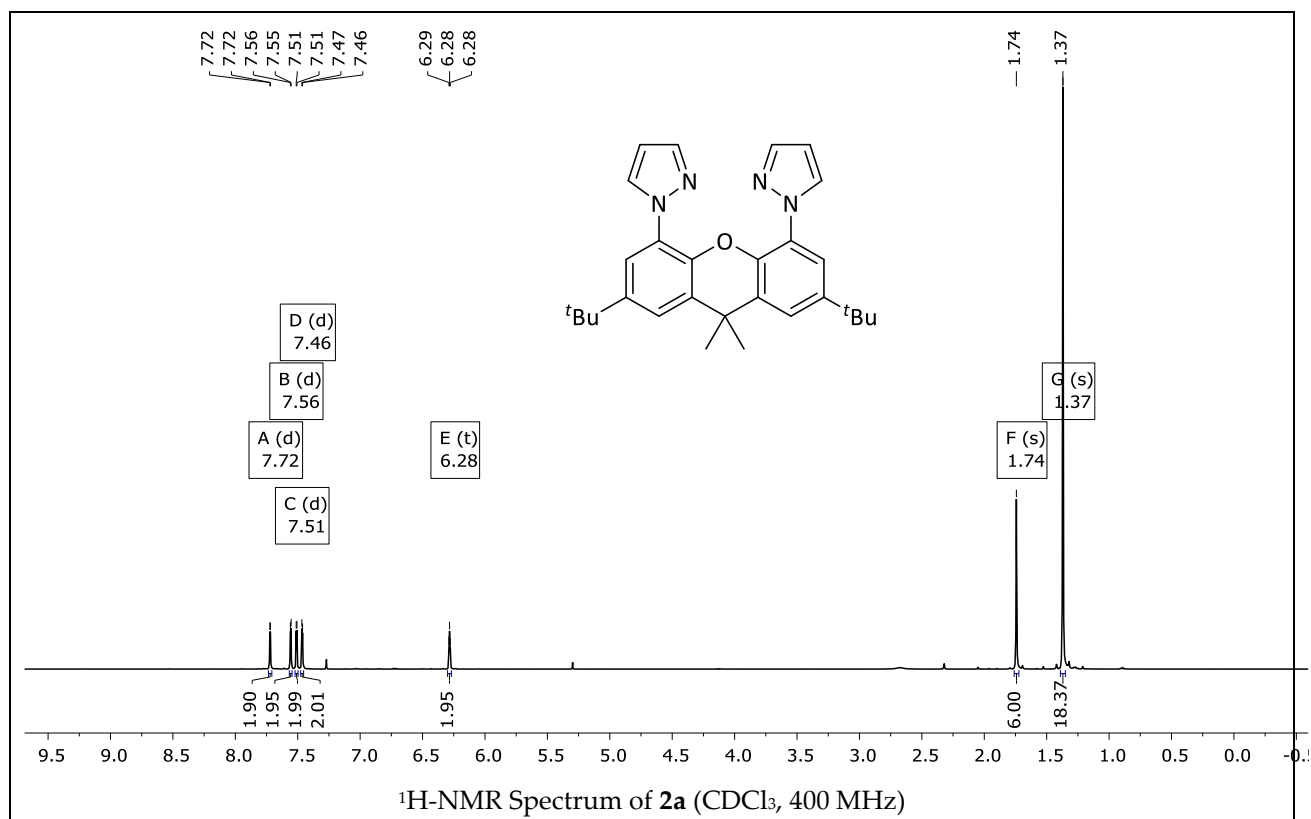


1.4 ^1H - and ^{13}C -NMR Spectra of **1a'**

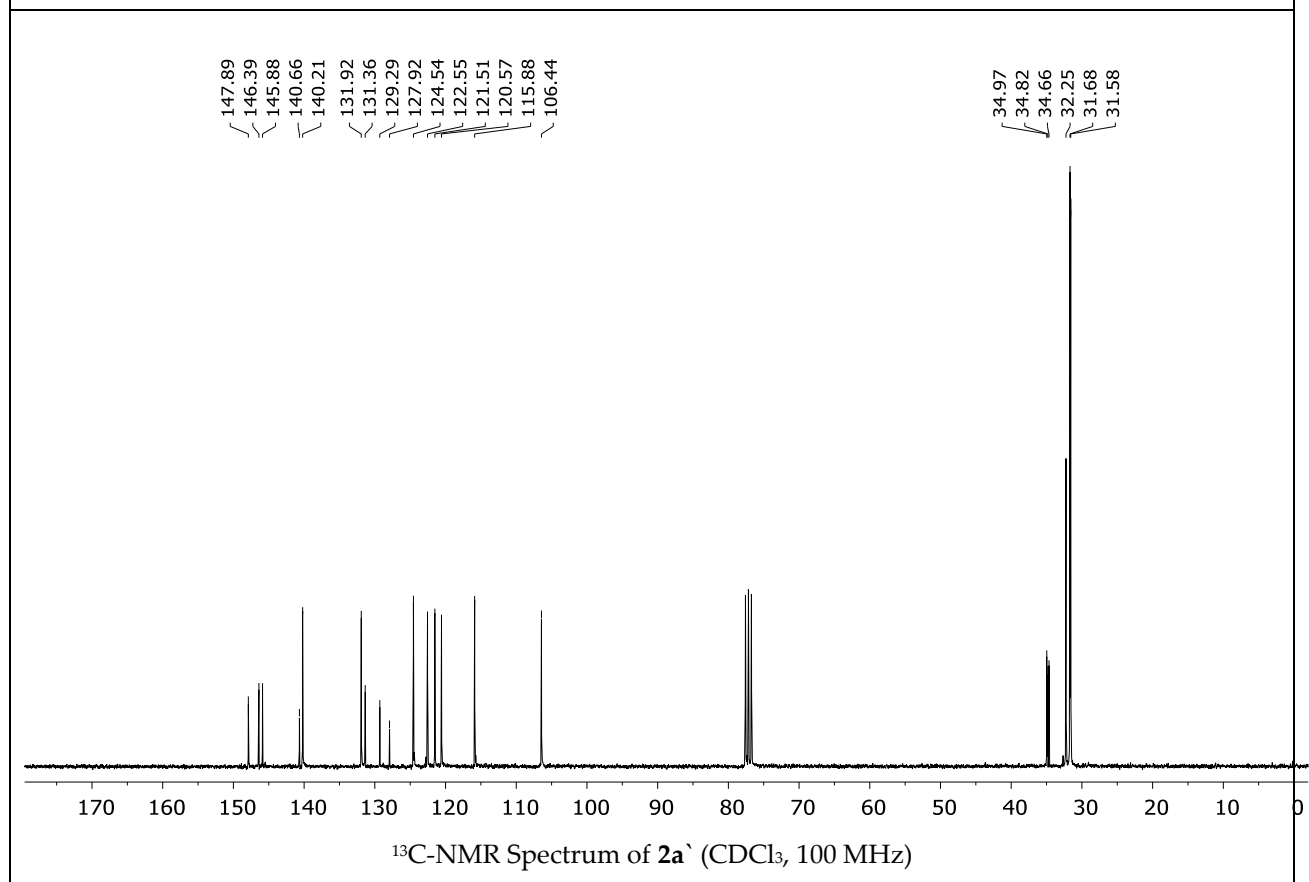
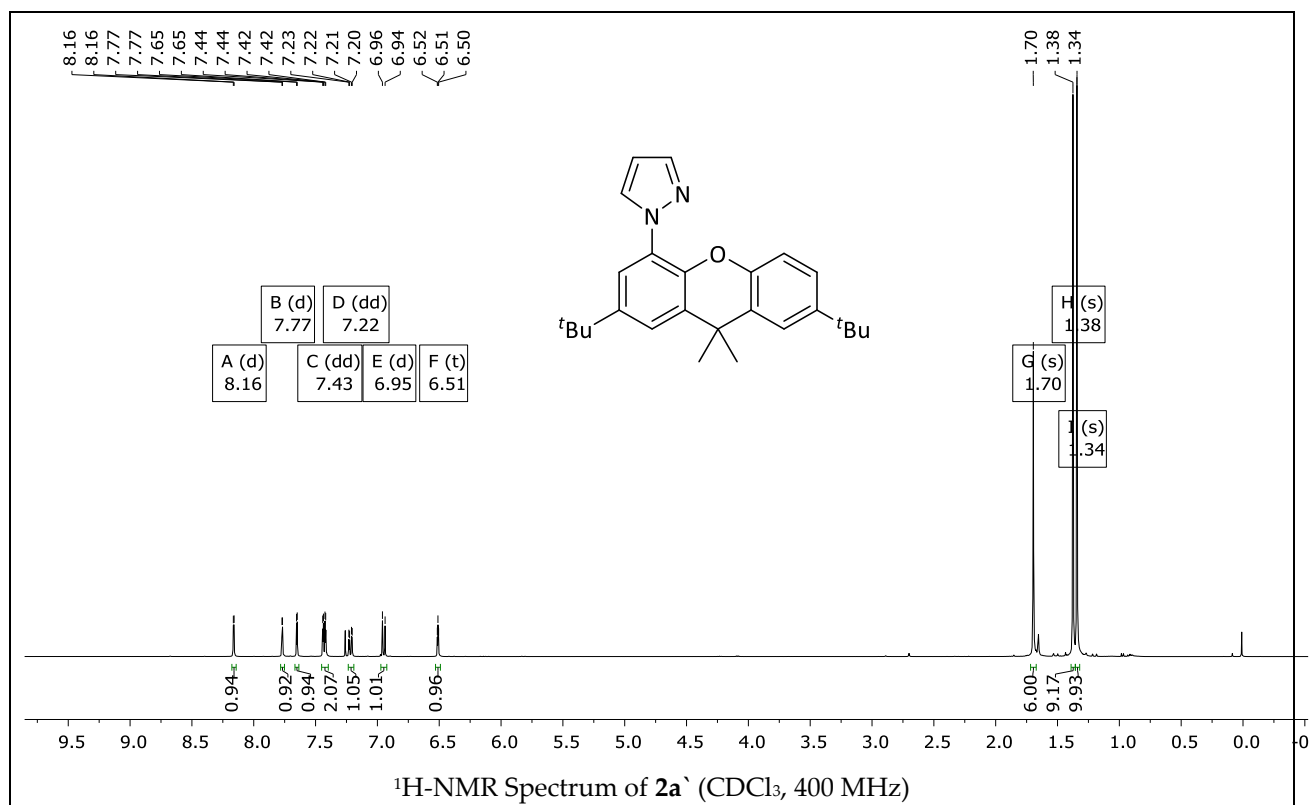


1.5

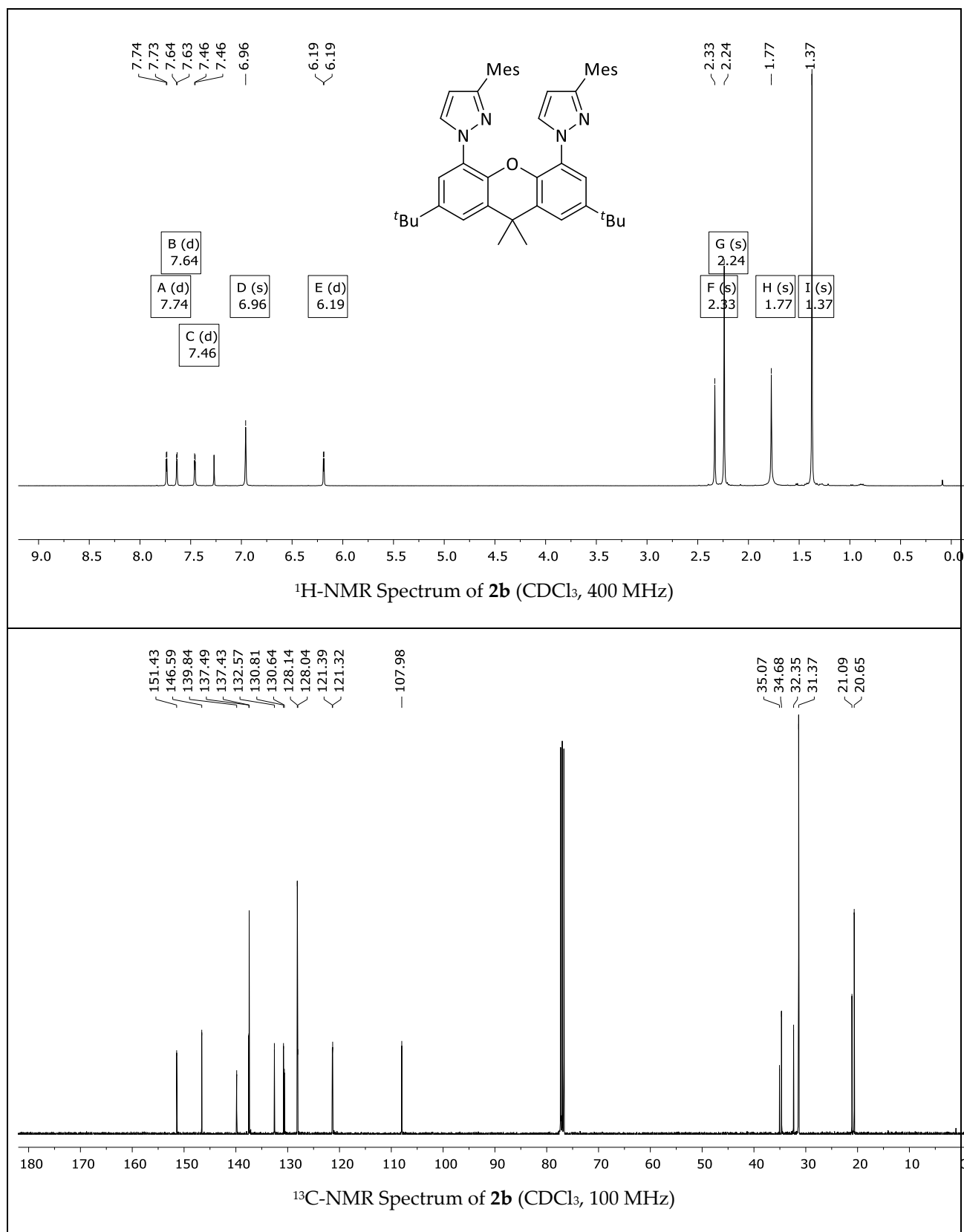
¹H- and ¹³C-NMR Spectra of **2a**



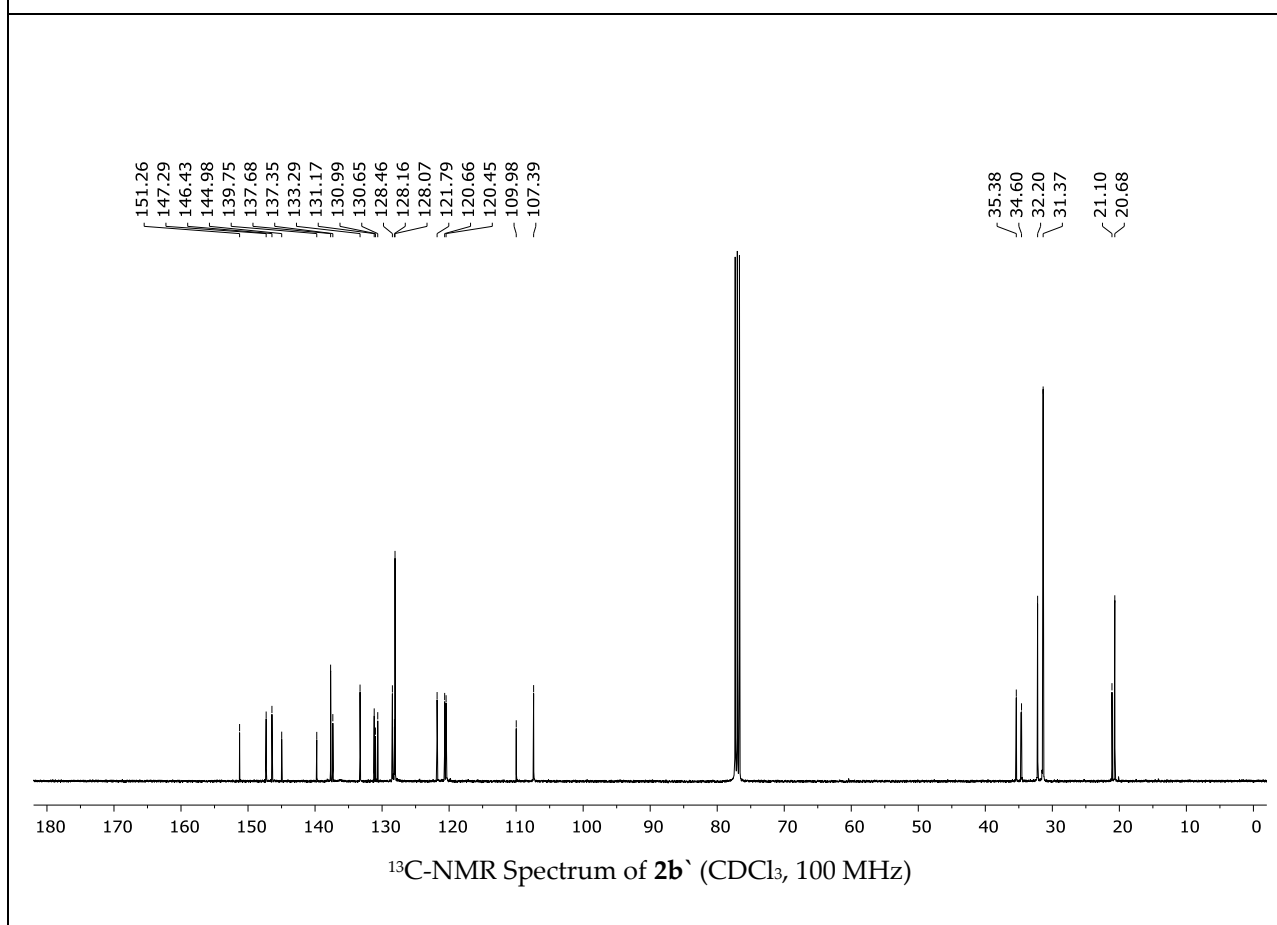
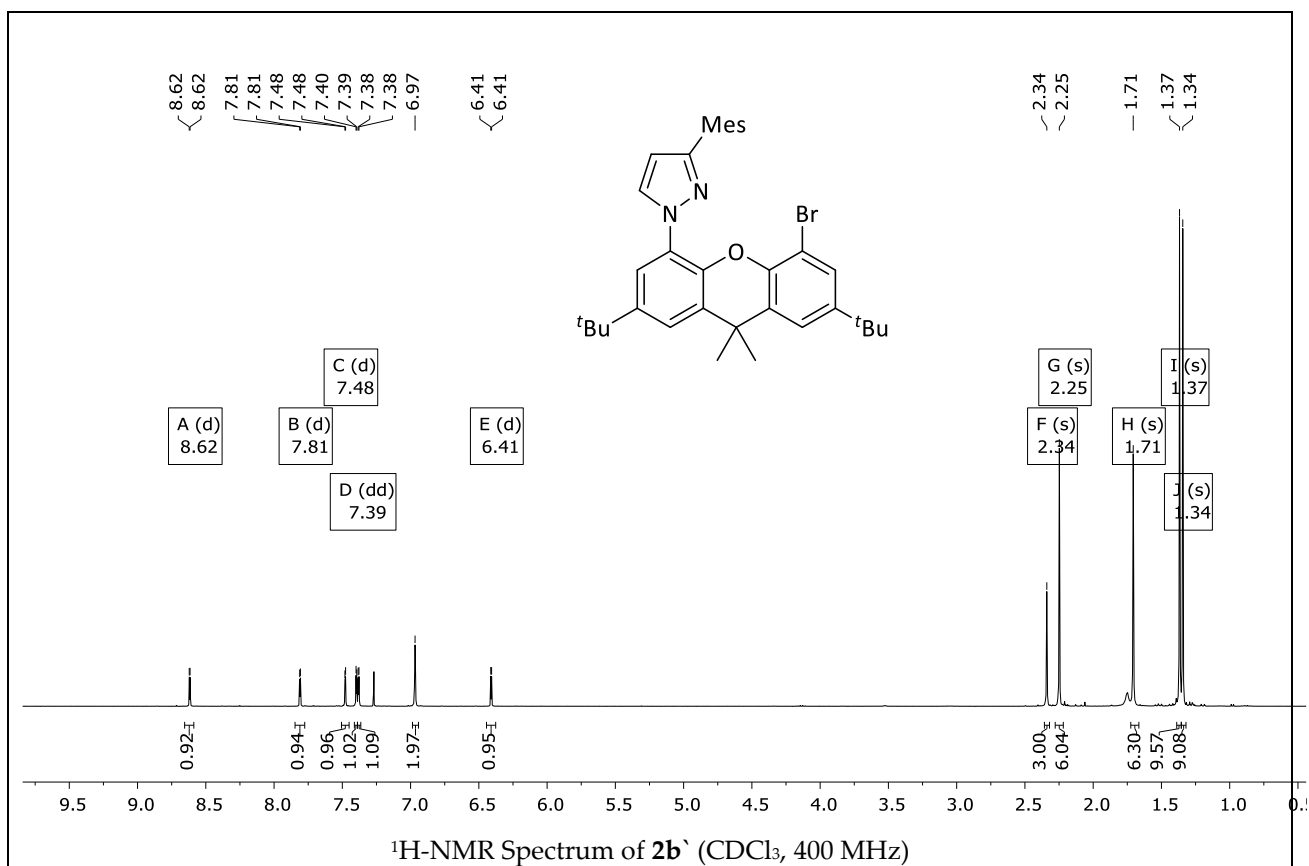
1.6 ^1H - and ^{13}C -NMR Spectra of **2a**



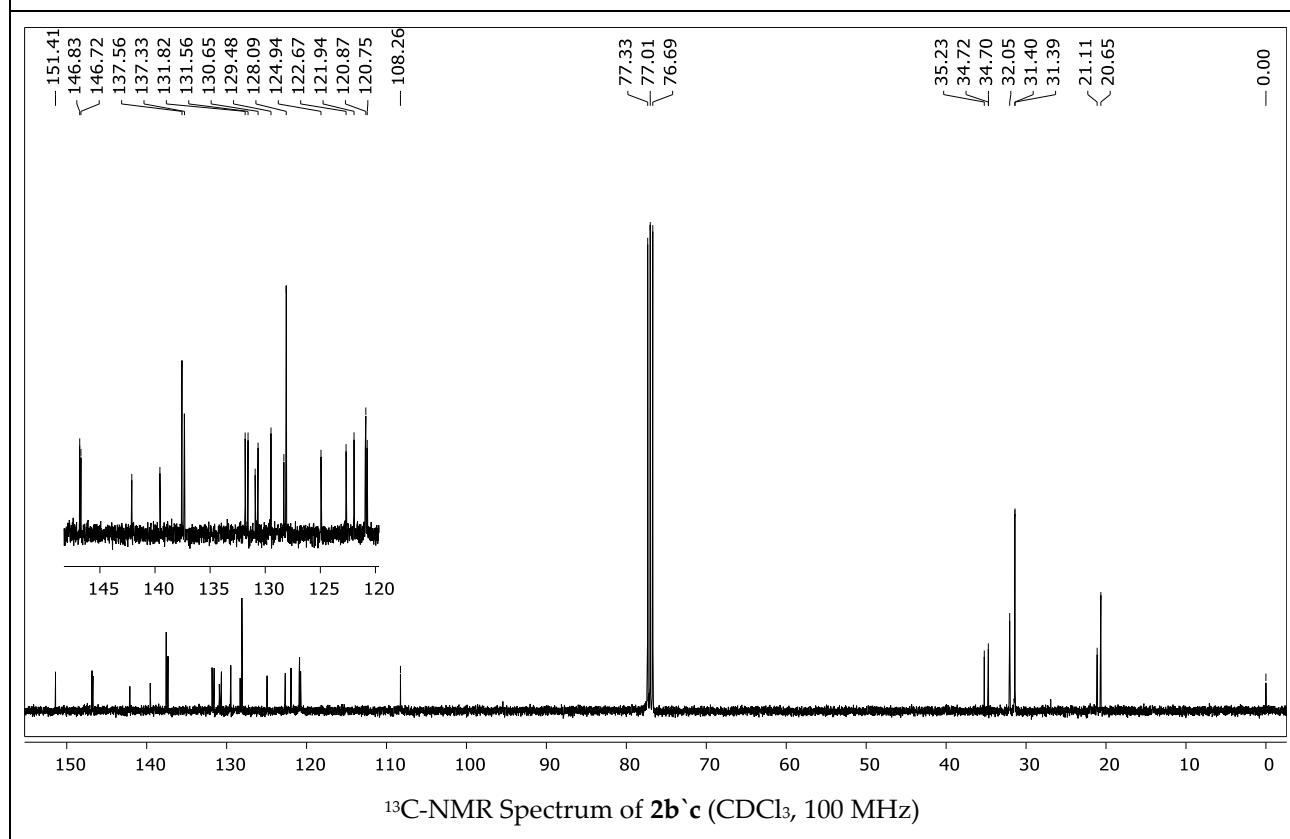
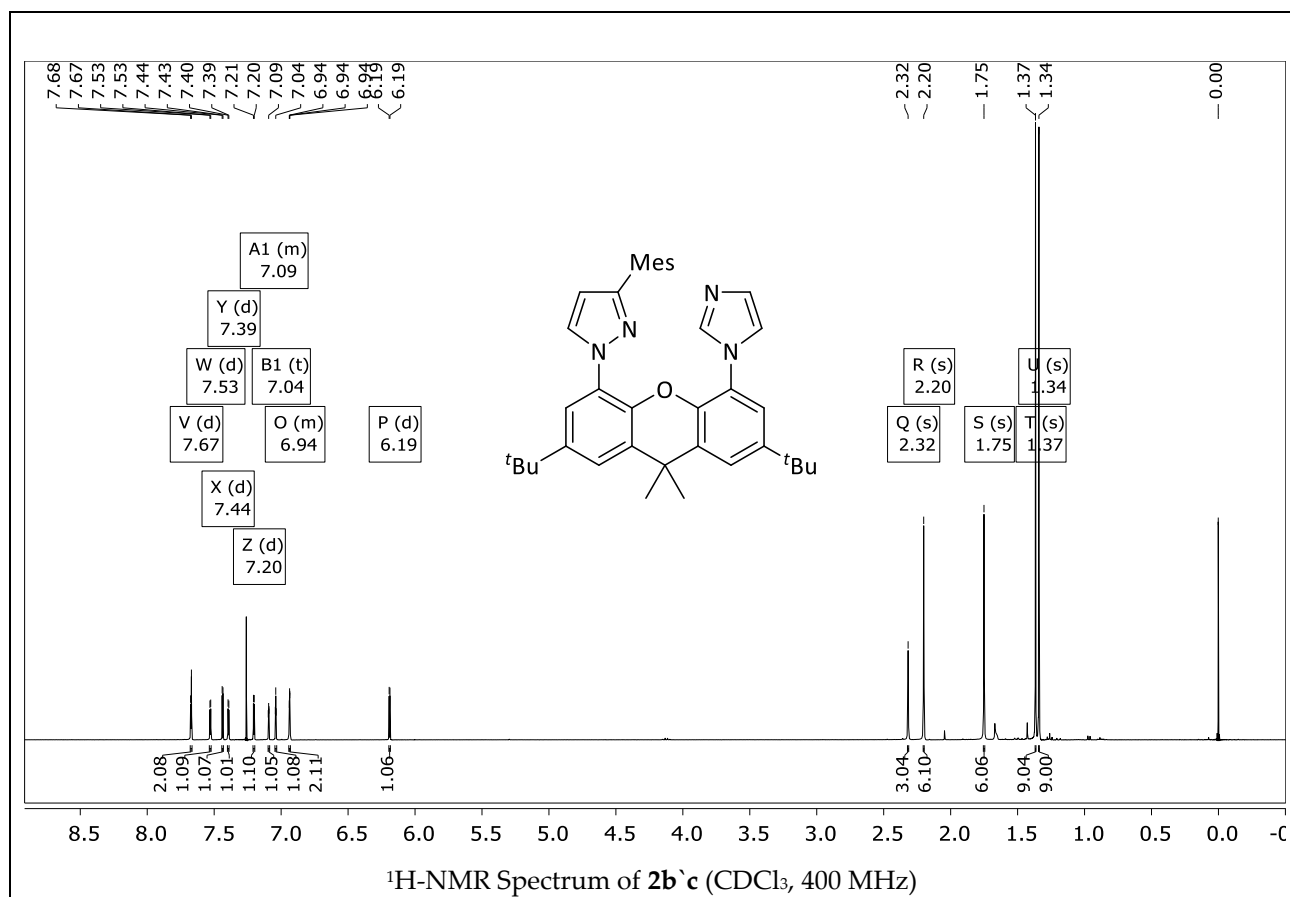
1.7 ^1H - and ^{13}C -NMR Spectra of Ligand **2b**



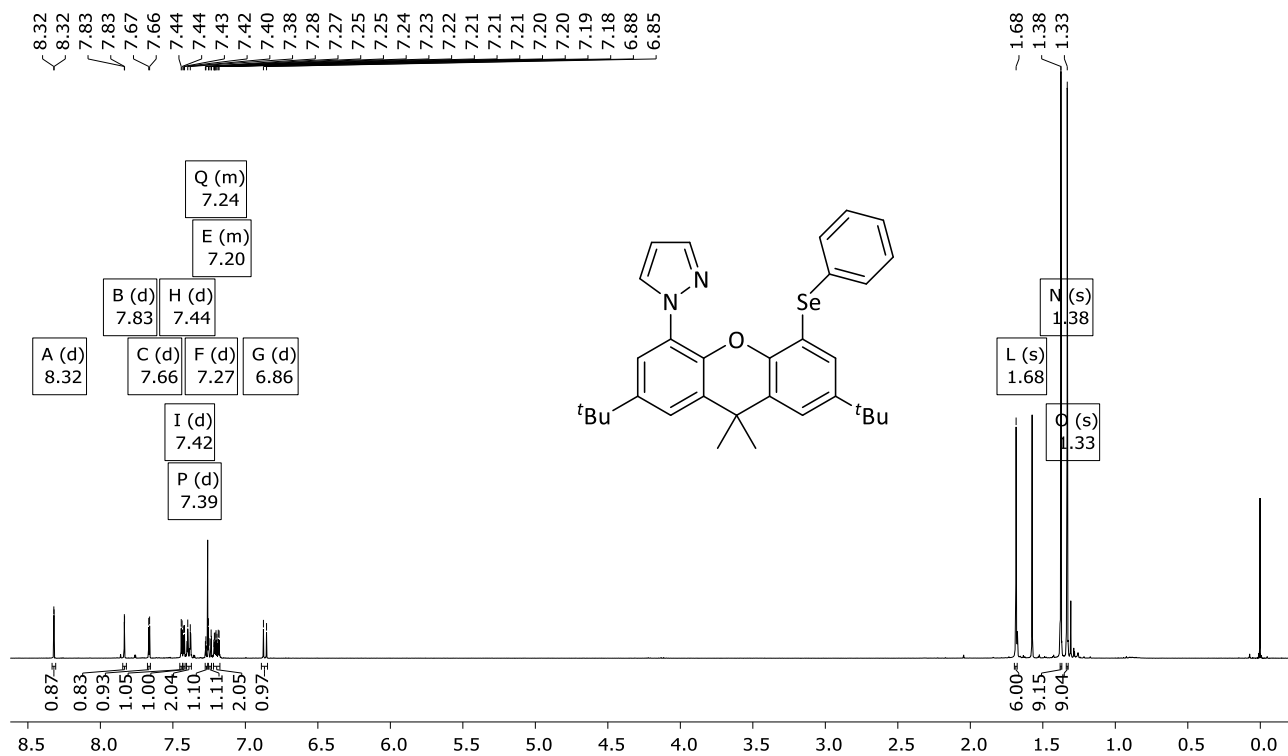
1.8 ^1H - and ^{13}C -NMR Spectra of **2b**



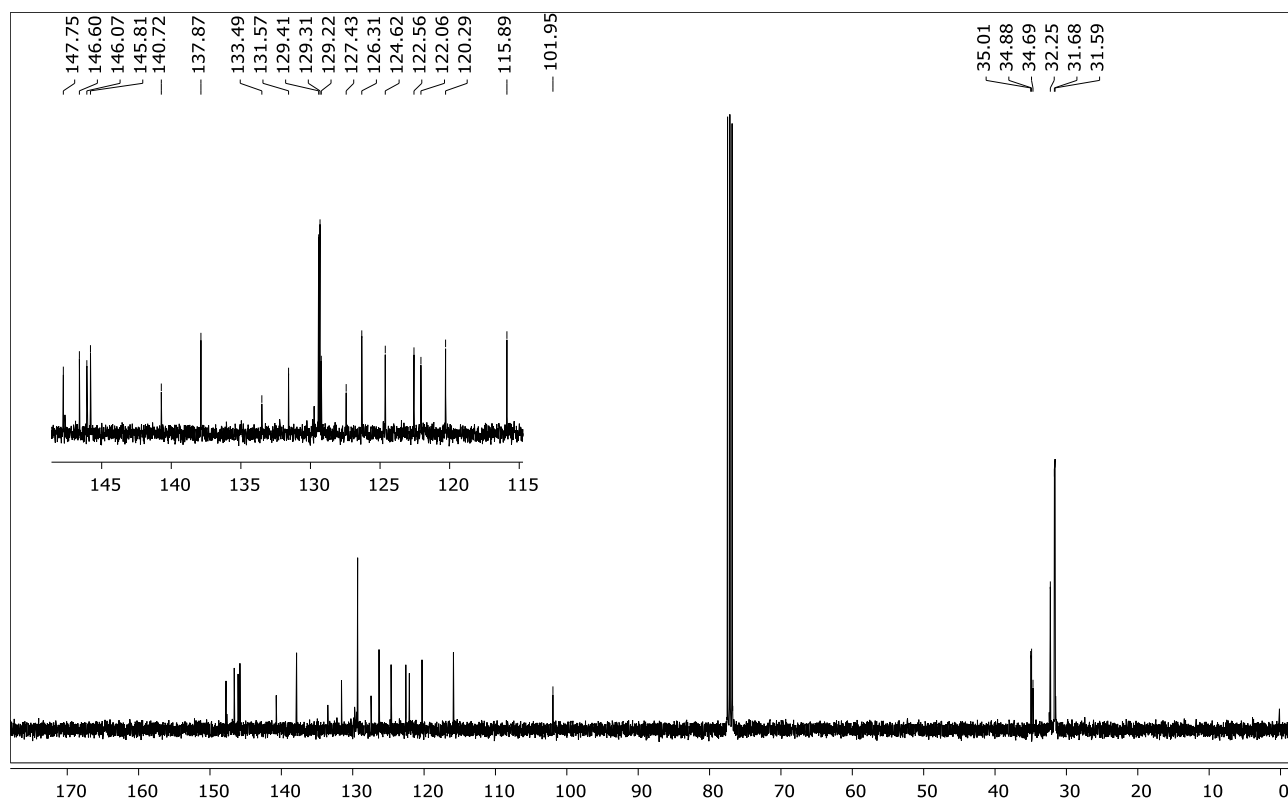
1.9 ^1H - and ^{13}C -NMR Spectra **2b`c**



1.10 ^1H - and ^{13}C -NMR Spectra of **2a**'d



^1H -NMR Spectrum of **2a**'d (CDCl_3 , 400 MHz)



^{13}C -NMR Spectrum of **2a**'d (CDCl_3 , 100 MHz)

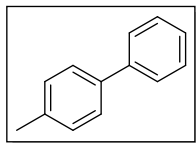
2 *Table S5. Crystallographic data and structure refinement parameters for 1, 1a, 2a, 2b and 2b`.*

	1	1a	2a	2b	2b`
Molecular formula	C ₁₄ H ₁₂ Br ₂ O	C ₂₀ H ₁₈ N ₄ O	C ₂₉ H ₃₄ N ₄ O	C ₄₇ H ₅₄ N ₄ O	C ₃₅ H ₄₁ BrN ₂ O
Formula weight (g mol ⁻¹)	356.06	330.38	454.60	690.94	585.61
<i>T</i> (K)	293(2)	293(2)	292(2)	100(2)	100(2)
Wavelength (Å)	0.71073	1.54178	0.71073	1.54178	0.71073
Crystal system	Triclinic	Monoclinic	Triclinic	Triclinic	Triclinic
Space group	<i>P</i> (-1)	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> (-1)	<i>P</i> (-1)	<i>P</i> (-1)
<i>a</i> (Å)	7.439(5)	13.5819(2)	12.8681(16)	12.1744(3)	12.3909(4)
<i>b</i> (Å)	7.977(5)	8.27900(10)	14.6221(18)	12.8278(3)	15.3171(5)
<i>c</i> (Å)	12.439(5)	15.9832(3)	14.7167(17)	14.9523(4)	17.5440(6)
α (°)	98.873(5)	90	75.649(4)	100.7726(14)	70.7230(10)
β (°)	100.877(5)	106.8260(10)	72.959(4)	103.3895(13)	79.9150(10)
γ (°)	108.201(5)	90	89.887(4)	114.1532(12)	76.2150(10)
<i>V</i> (Å ³)	670.4(7)	1720.28(5)	2557.4(5)	1965.65(9)	3035.57(18)
<i>Z</i> '	2	4	4	2	4
ρ_{calcd} (g cm ⁻³)	1.764	1.276	1.181	1.167	1.281
μ (mm ⁻¹)	6.027	0.652	0.073	0.535	1.384
<i>F</i> (000)	348	696	976	744	1232
Crystal size (mm)	0.26 x 0.19 x 0.14	0.28 x 0.21 x 0.14	0.394 x 0.175 x 0.126	0.14 x 0.14 x 0.12	0.23 x 0.15 x 0.10
θ range (°)	2.979 – 27.545	3.399 – 78.912	2.956 to 27.266	3.204 – 62.381	2.656–26.372
Limiting indices (<i>h</i> , <i>k</i> , <i>l</i>)	-9 ≤ <i>h</i> ≤ 9 -10 ≤ <i>k</i> ≤ 10 -16 ≤ <i>l</i> ≤ 16	-17 ≤ <i>h</i> ≤ 17 -10 ≤ <i>k</i> ≤ 10 -20 ≤ <i>l</i> ≤ 18	-16 ≤ <i>h</i> ≤ 16, -18 ≤ <i>k</i> ≤ 18, -18 ≤ <i>l</i> ≤ 18	- 13 ≤ <i>h</i> ≤ 13 -14 ≤ <i>k</i> ≤ 14 -17 ≤ <i>l</i> ≤ 17	- 15 ≤ <i>h</i> ≤ 15 -19 ≤ <i>k</i> ≤ 19 -21 ≤ <i>l</i> ≤ 21
Reflections collected	28840	30475	118038	18591	106878
Reflections unique (<i>R</i> _{int})	3091 (0.0412)	3688 (0.0463)	11384 (0.1467)	6210 (0.0416)	12409 (0.0618)
Completeness to θ_{max} (%)	99.8	100.0	99.8	99.0	99.9
Data/restraints/param.	3091 / 0 / 154	3688 / 0 / 226	11384 / 0 / 613	6210 / 0 / 469	12409 / 0 / 725
Absorption correction	Gaussian	Gaussian	Semi-empirical from eq.	Gaussian	Gaussian
Min. and max. trans.	0.5529 and 0.7456	0.8612 and 0.9389	0.7455 and 0.6524	0.8412 and 0.9402	0.6987 and 0.8279
<i>R</i> ₁ [<i>I</i> > 2σ(<i>I</i>)]	0.0363	0.0450	0.0991	0.0595	0.0455
w <i>R</i> ₂ [<i>I</i> > 2σ(<i>I</i>)]	0.0943	0.1246	0.2433	0.1497	0.1168

R_1 (all data)	0.0519	0.0585	0.1825	0.0819	0.0598
wR_2 (all data)	0.1036	0.1365	0.3028	0.1643	0.1256
S on F^2	1.055	1.044	n/a	1.044	1.022
Largest diff. peak and hole ($e \text{ \AA}^{-3}$)	0.693 and - 0.683	0.257 and - 0.209	0.721 and - 0.368	0.577 and - 0.576	5.650 and - 1,896

3. Analytical and Spectroscopic Data for SM Cross-coupling Products

3.1 4-methyl-1,1'-biphenyl

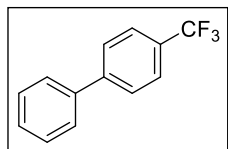


White powder: m.p. = 48-50°C (Literature^[1] 49-50).

¹H-NMR (400 MHz, CDCl₃): δ 7.57 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.39 – 7.42 (m, 2H), 7.25 – 7.33 (m, 1H), 7.24 (d, *J* = 7.9 Hz, 2H), 2.39 (s, 3H).

¹³C-NMR (100 MHz, CDCl₃): δ 141.15, 138.35, 136.99, 129.46, 128.69, 126.98, 126.95, 21.09.

3.2 4-(trifluoromethyl)-1,1'-biphenyl

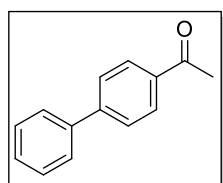


White powder: m.p. = 59-60 °C^[5]

¹H-NMR (400 MHz, CDCl₃): δ 7.69 (m, 4H), δ 7.62 – 7.58 (m, 2H), 7.50 – 7.44 (m, 2H), 7.43 – 7.38 (m, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ 144.74, 139.76, 128.97, 128.17, 127.41, 127.27, 125.71, 125.68.

3.3 1-([1,1'-biphenyl]-4-yl)ethan-1-one

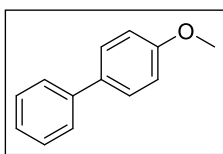


White powder: m.p. = 113-114°C (Literature^[1] 110-111).

¹H-NMR (400 MHz, CDCl₃): δ 8.04 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.66 – 7.71, (m, 4H), 7.53 – 7.35 (m, 3H), 2.64 (s, 3H).

¹³C-NMR (100 MHz, CDCl₃): δ 197.89, 145.92, 140.01, 135.99, 129.09, 129.05, 128.37, 127.41, 127.36, 26.81.

3.4 4-methoxy-1,1'-biphenyl

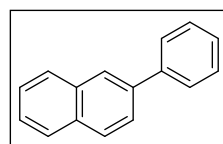


Yellow powder: m.p. = 79-81 (Literature^[1] = 77-78)

¹H-NMR (400 MHz, CDCl₃): δ 7.57 – 7.50 (m, 4H), 7.44 – 7.35 (m, 2H), 7.34 – 7.27 (m, 1H), 7.01 – 6.94 (m, 2H), 3.84 (s, 3H).

¹³C-NMR (100 MHz, CDCl₃): δ 159.13, 140.81, 133.77, 128.70, 128.14, 126.72, 126.64, 114.19, 55.33.

3.5 2-phenylnaphthalene

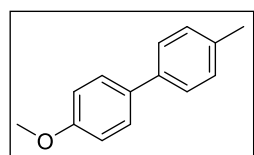


White powder: m.p. = 88-90 °C^[5]

¹H-NMR (400 MHz, CDCl₃): δ 8.04 (d, *J* = 1.8 Hz, 1H), 7.94 – 7.83 (m, 3H), 7.78 – 7.69 (m, 3H), 7.54 – 7.45 (m, 4H), 7.38 (t, *J* = 7.4 Hz, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ 141.12, 138.55, 133.67, 132.61, 128.84, 128.40, 128.18, 127.63, 127.42, 127.33, 126.27, 125.91, 125.79, 125.58.

3.6 4-methoxy-4'-methyl-1,1'-biphenyl

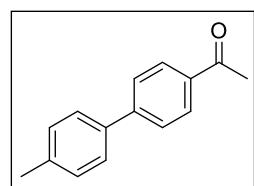


White powder: m.p. 106-108 (Literature^[1] 107-108)

¹H-NMR (400 MHz, CDCl₃): δ 7.54 – 7.48 (m, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 6.98 – 6.93 (m, 2H), 3.84 (s, 3H), 2.38 (s, 3H).

¹³C-NMR (100 MHz, CDCl₃): δ 158.92, 137.96, 136.33, 133.74, 129.42, 127.94, 126.57, 114.15, 55.34, 21.05.

3.7 1-(4'-methyl-[1,1'-biphenyl]-4-yl)ethan-1-one

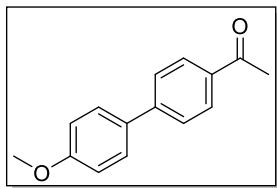


White powder: m.p. 122-123 (Literature^[2] 118-120)

¹H-NMR (300 MHz, CDCl₃): δ 8.02 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 2.63 (s, 3H), 2.41 (s, 3H).

¹³C-NMR (75 MHz, CDCl₃): δ 197.78, 145.71, 138.23, 136.93, 135.56, 129.67, 128.90, 127.09, 126.94, 26.66, 21.17.

3.8 1-(4'-methoxy-[1,1'-biphenyl]-4-yl)ethan-1-one

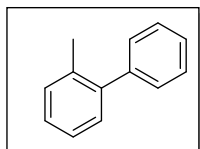


Yellow powder: m.p. = 146-148^[3]

¹H-NMR (400 MHz, CDCl₃): δ 8.04 – 7.97 (m, 2H), 7.67 – 7.53 (m, 4H), 7.03 – 6.96 (m, 2H), 3.86 (s, 3H), 2.62 (s, 3H).

¹³C-NMR (100 MHz, CDCl₃): δ 197.70, 159.92, 145.36, 135.29, 132.25, 128.94, 128.36, 126.61, 114.41, 55.39, 26.62.

3.9 2-methyl-1,1'-biphenyl

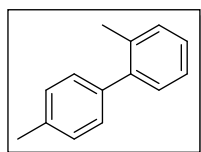


Pale yellow oil:^[5]

¹H-NMR (400 MHz, CDCl₃): δ 7.40 – 7.34 (m, 2H), 7.32 – 7.27 (m, 3H), 7.23 – 7.19 (m, 4H), 2.25 (s, 3H).

¹³C-NMR (100 MHz, CDCl₃): δ 142.09, 142.05, 135.41, 130.41, 129.91, 129.30, 128.17, 127.36, 126.87, 125.88, 20.59.

3.10 2,4'-dimethyl-1,1'-biphenyl

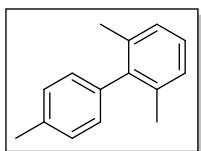


Pale yellow oil:^[4]

¹H-NMR (300 MHz, CDCl₃): δ 7.22 - 7.25 (m, Hz, 8H), 2.40 (s, 3H), 2.28 (s, 3H).

¹³C-NMR (75 MHz, CDCl₃): δ 141.84, 138.99, 136.36, 135.38, 130.26, 129.83, 129.05, 128.75, 127.04, 125.72, 21.17, 20.51.

3.11 2,4',6-trimethyl-1,1'-biphenyl



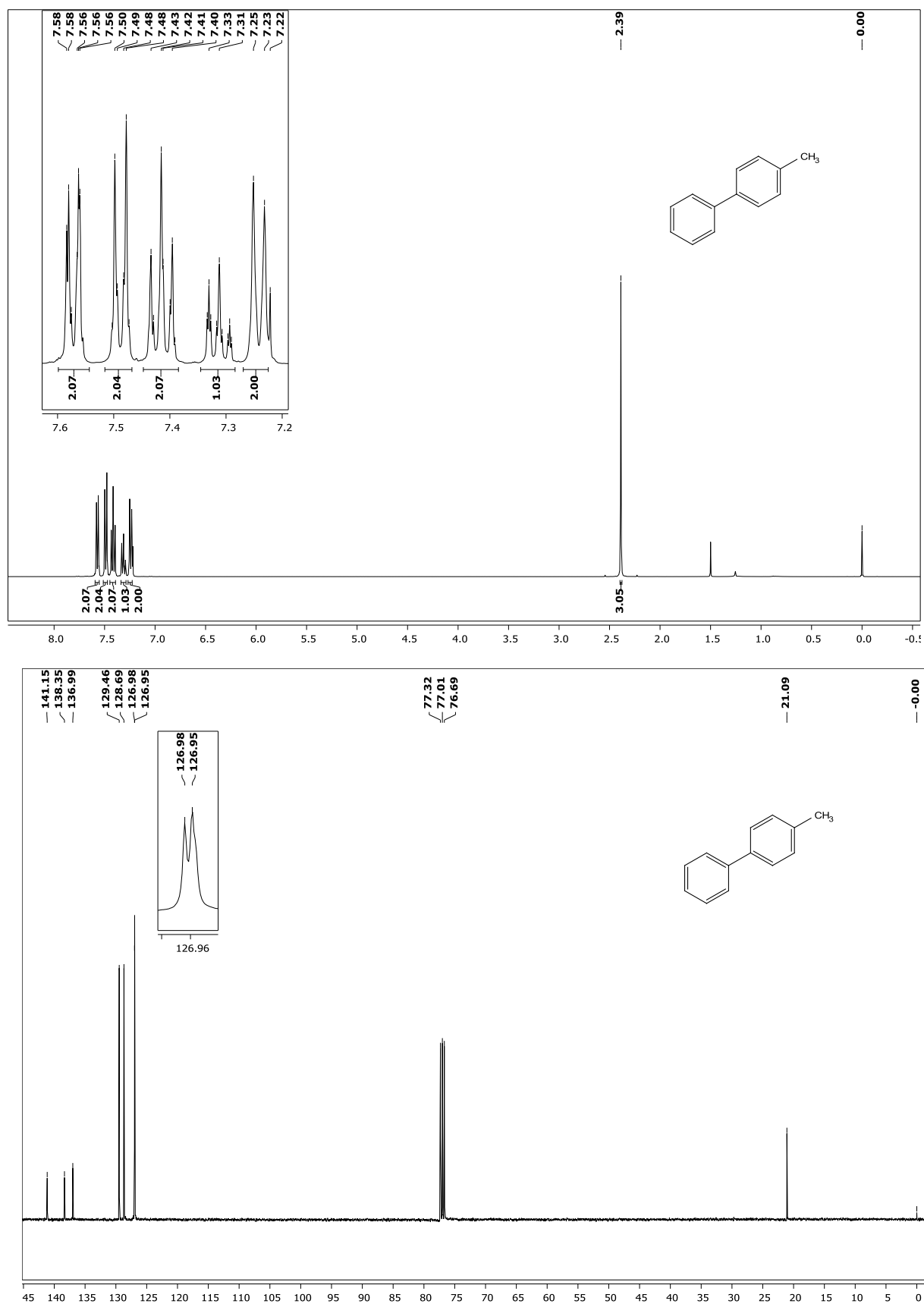
Yellowish oil:^[5]

¹H-NMR (400 MHz, CDCl₃): δ 7.22 (d, *J* = 7.5 Hz, 2H), 7.08 – 7.16 (m, 3H), 7.02 (d, *J* = 7.9 Hz, 2H), 2.40 (s, 3H), 2.03 (s, 6H).

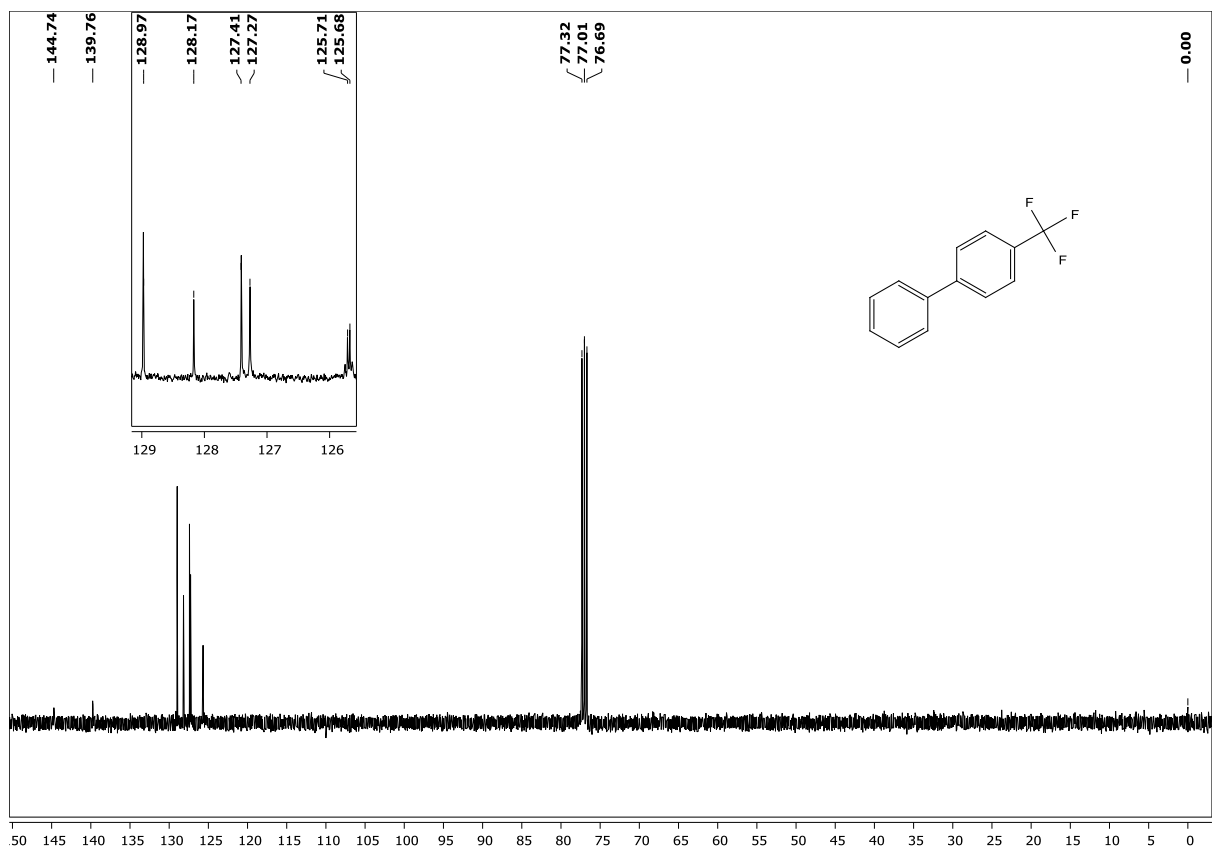
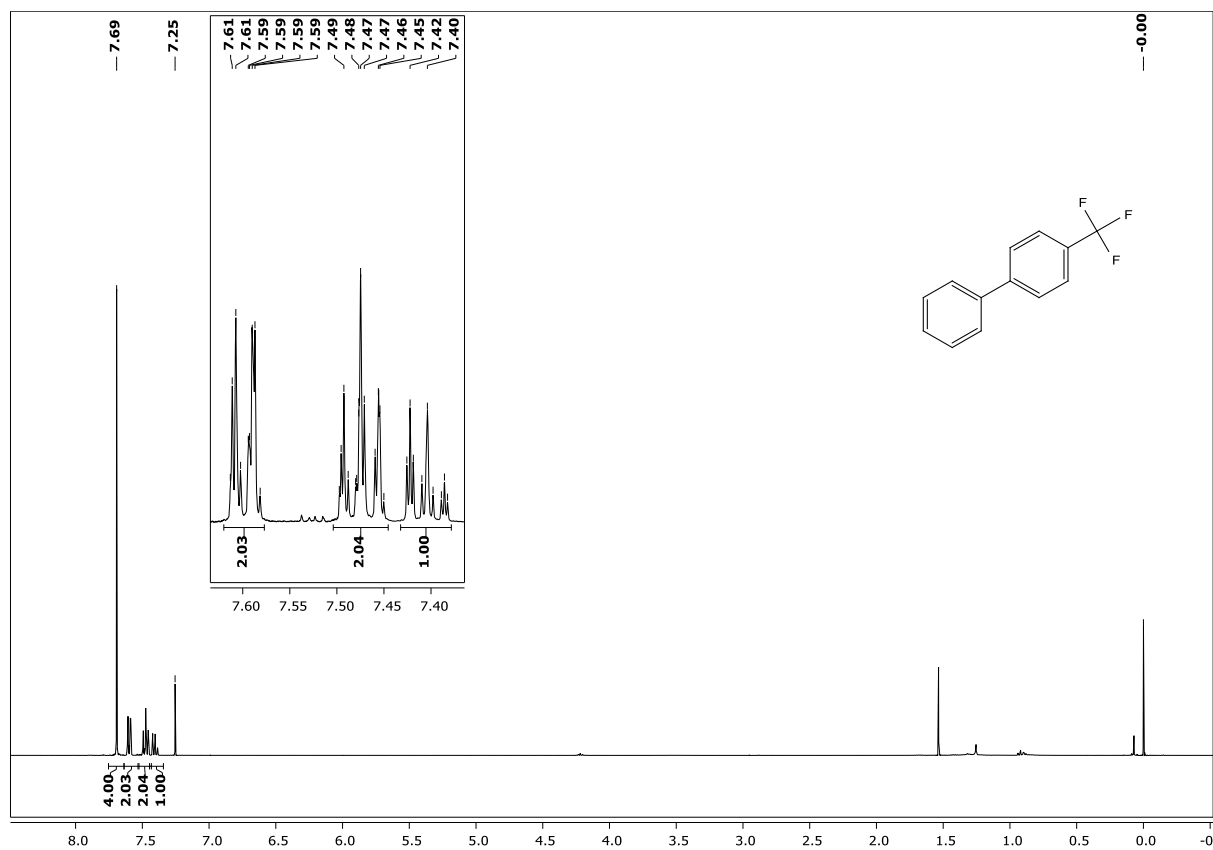
¹³C-NMR (100 MHz, CDCl₃): δ 141.82, 138.00, 136.20, 136.04, 129.09, 128.86, 127.21, 126.85, 21.23, 20.88.

4 ^1H - and ^{13}C -NMR Spectra for SM Cross-coupling Products

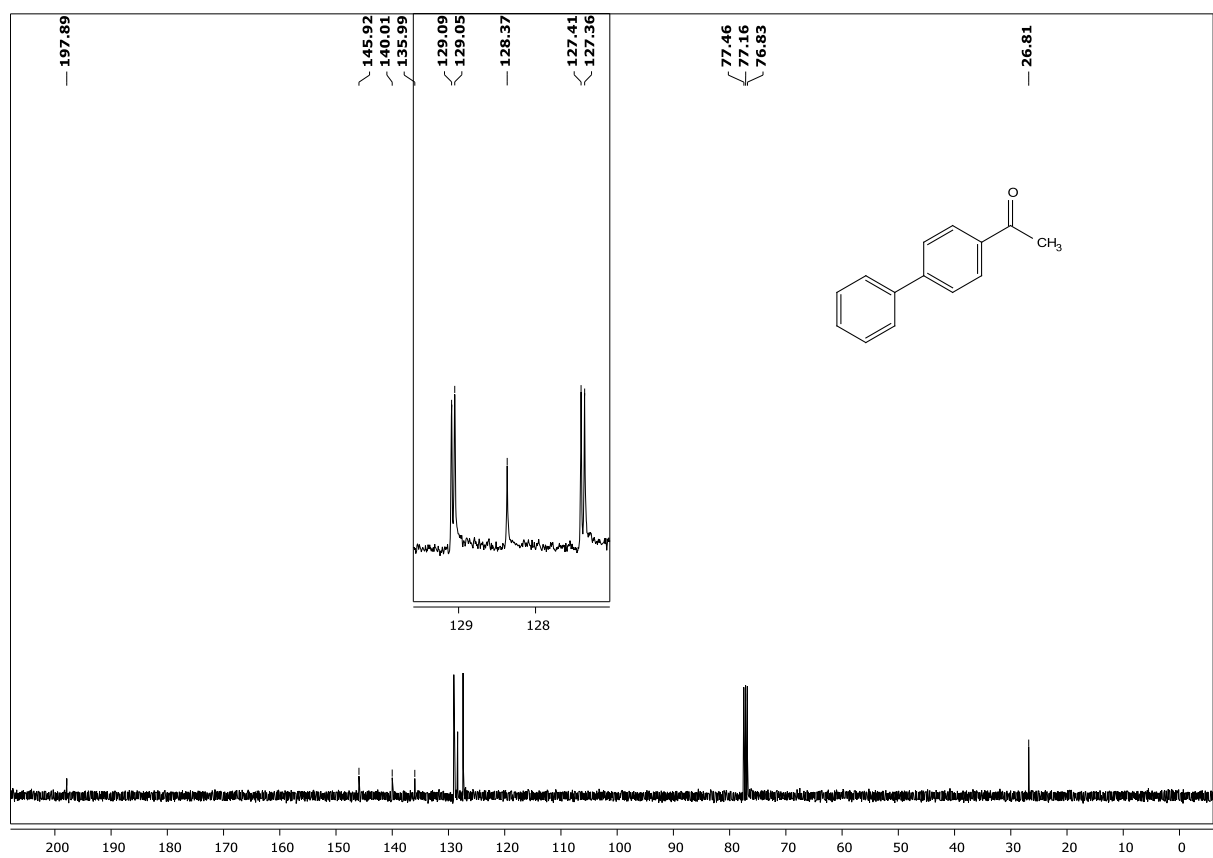
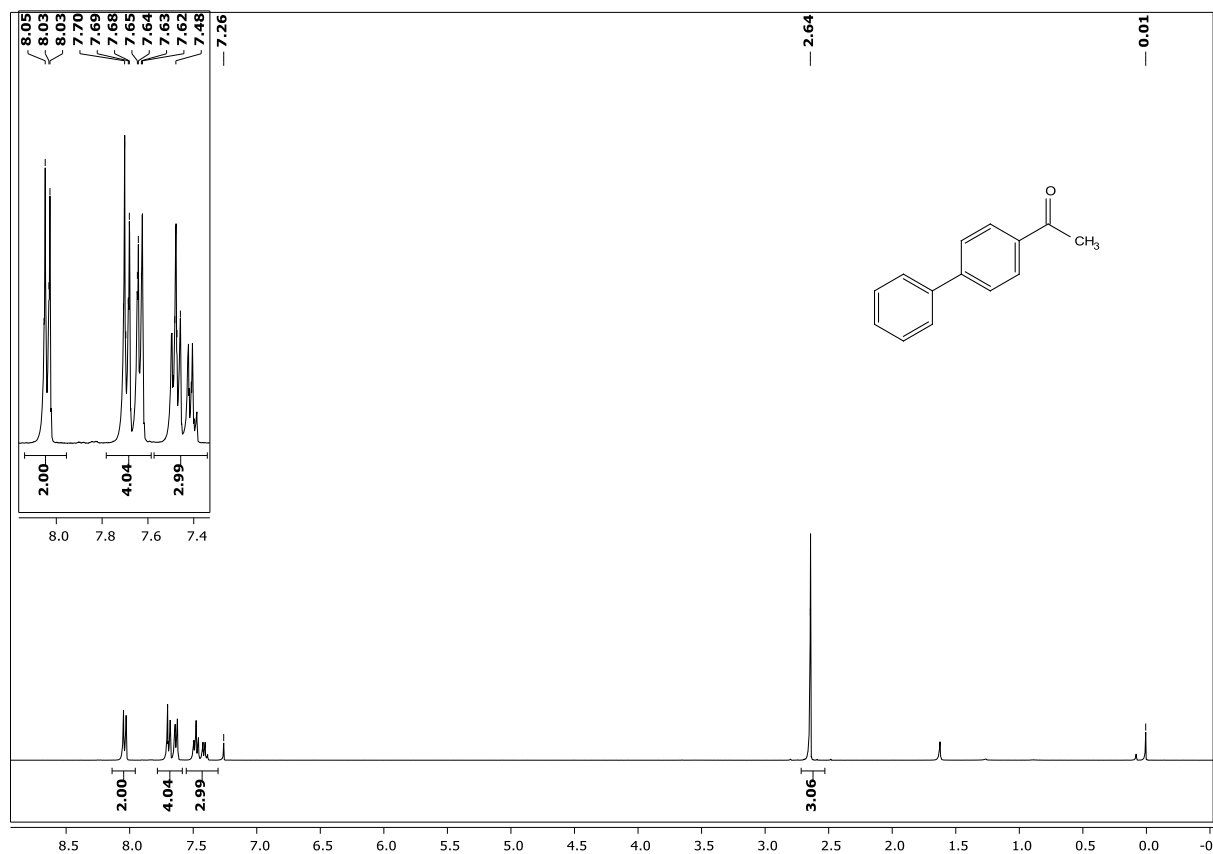
4.1 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 4-methyl-1,1'-biphenyl:



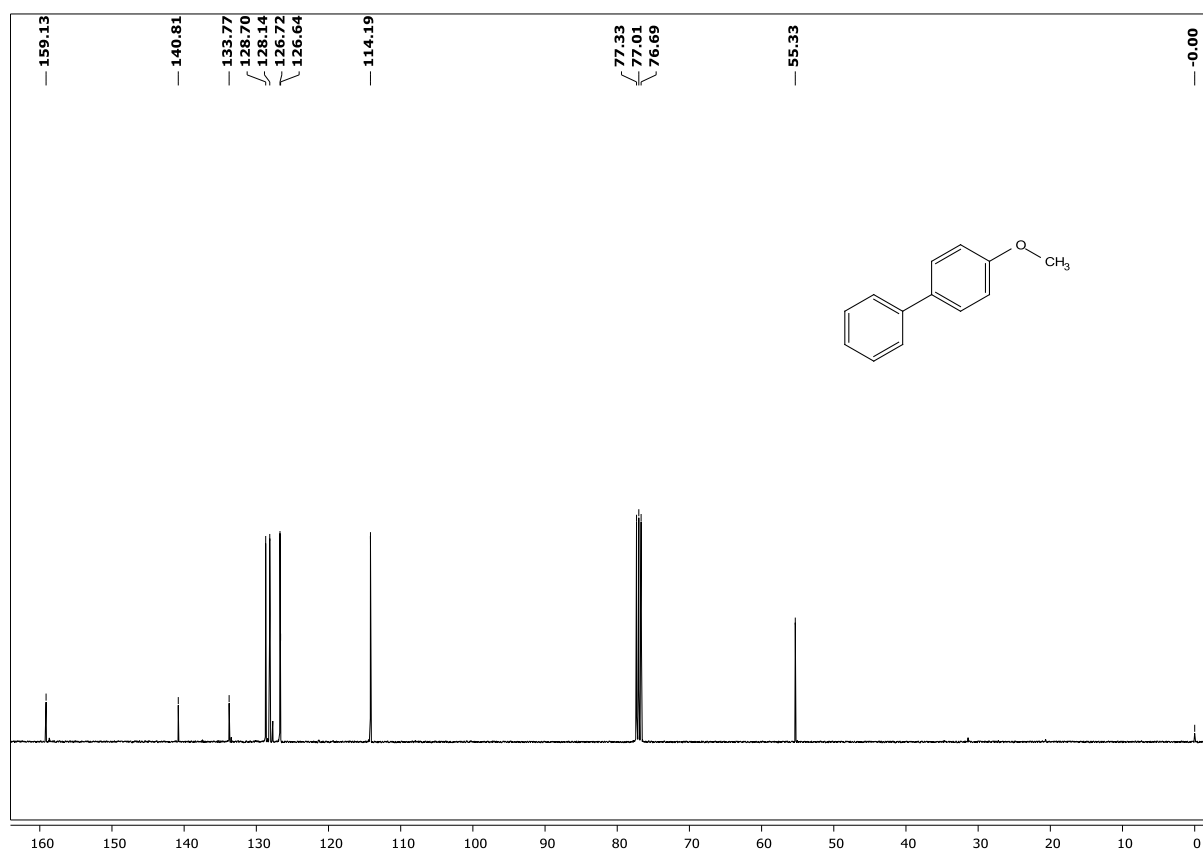
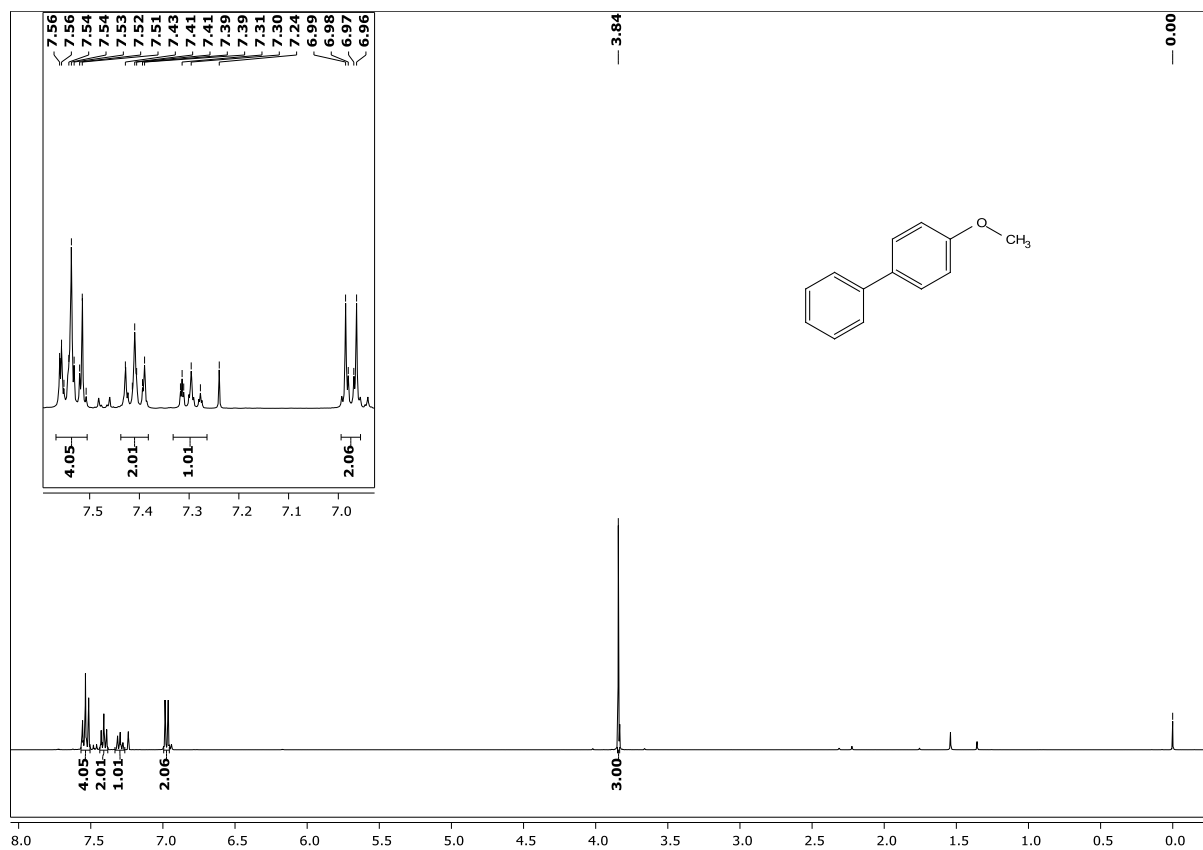
4.2 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 4-(trifluoromethyl)-1,1'-biphenyl.



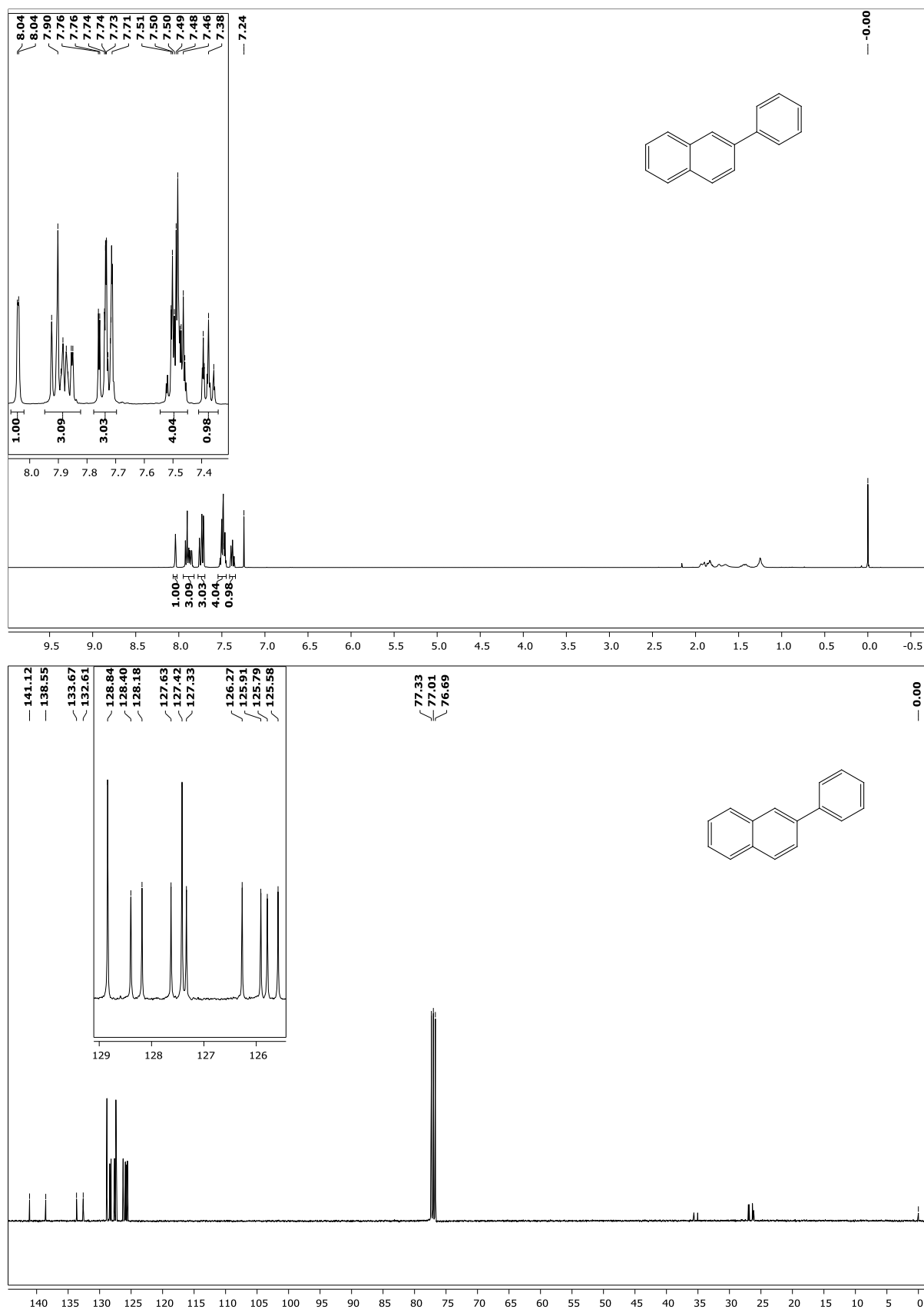
4.3 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 1-([1,1'-biphenyl]-4-yl)ethan-1-one.



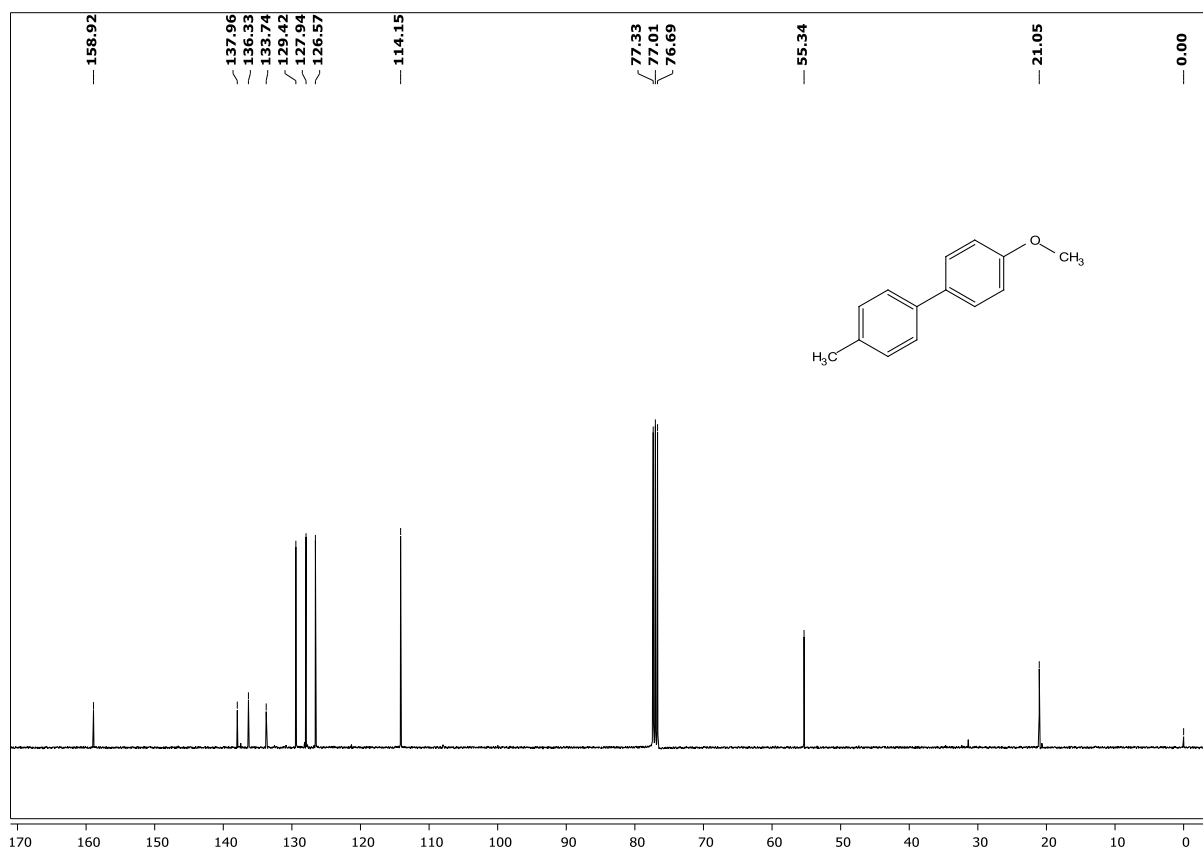
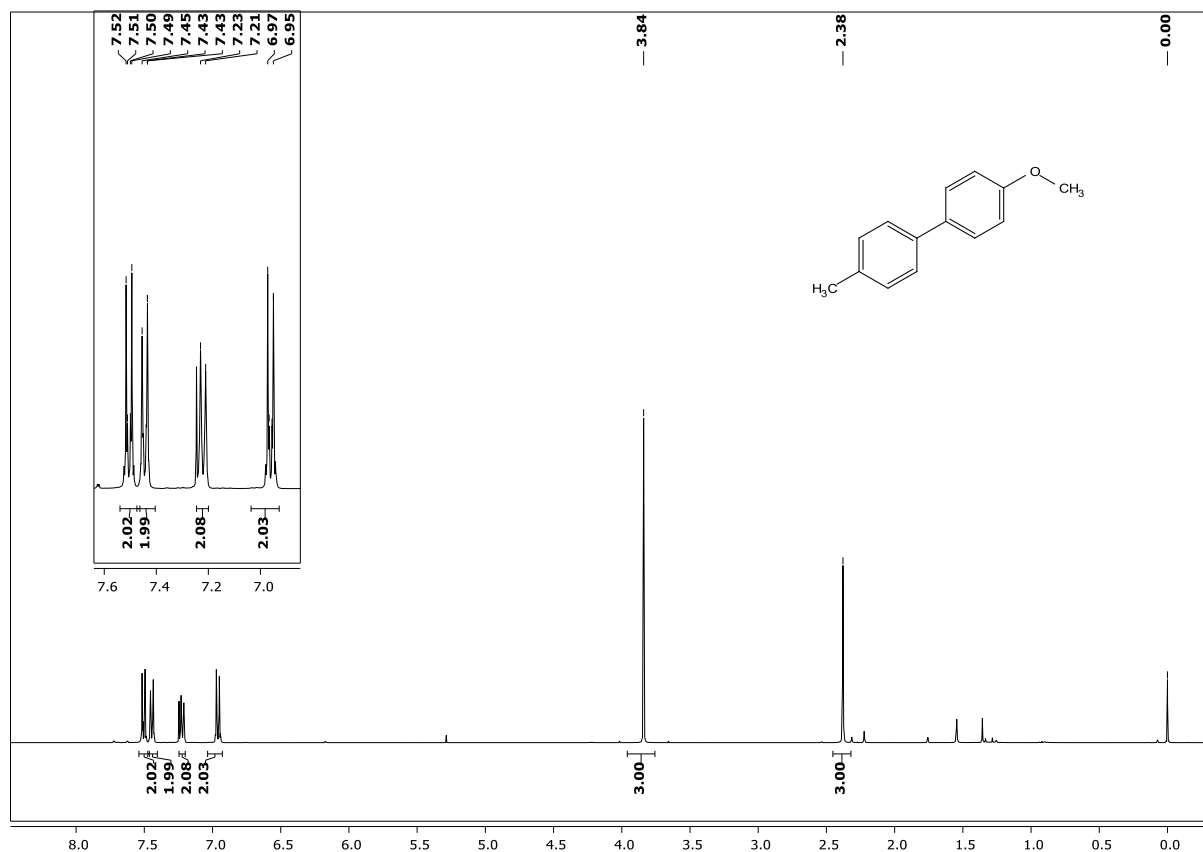
4.4 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 4-methoxy-1,1'-biphenyl.



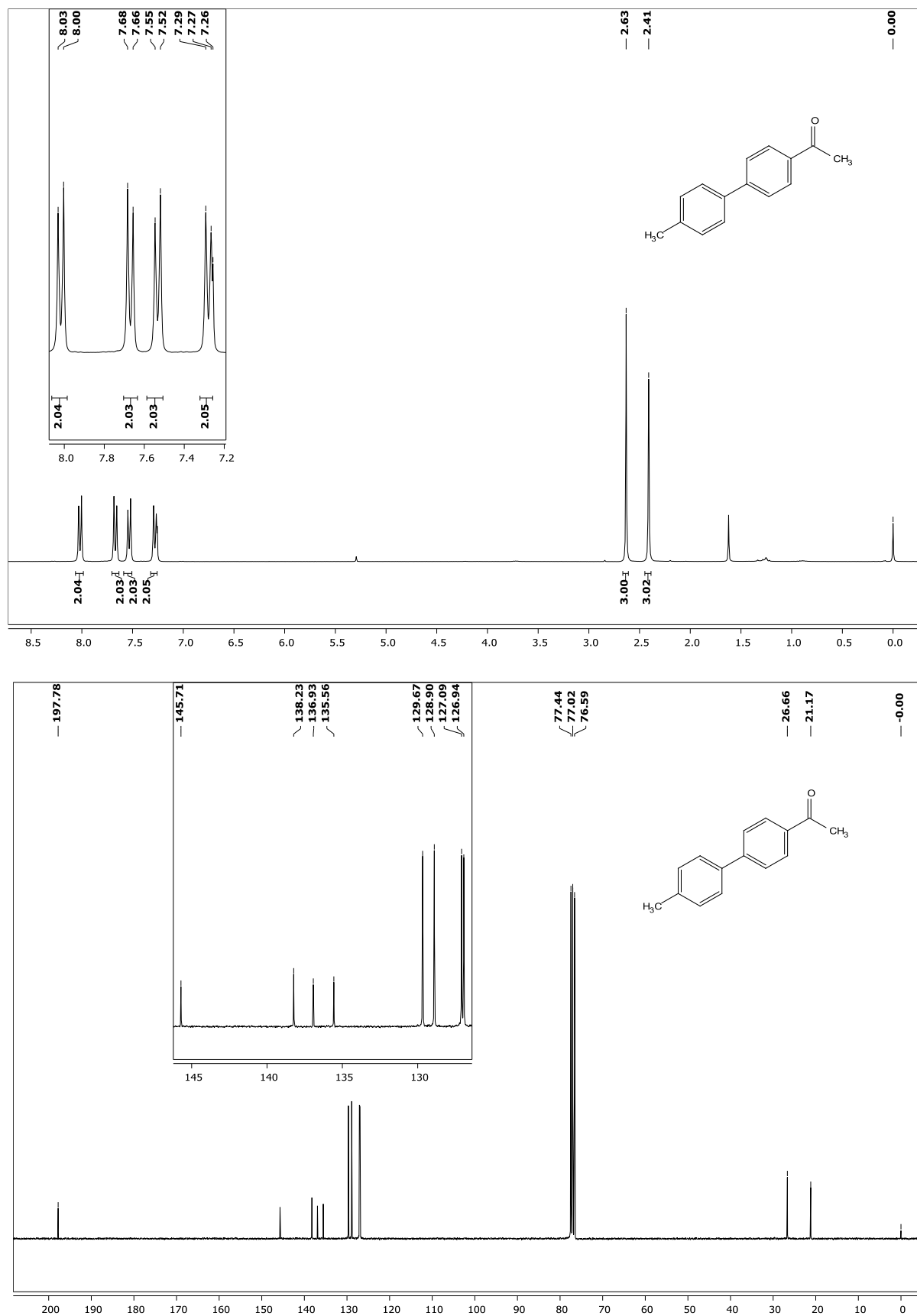
4.5 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 2-phenylnaphthalene.



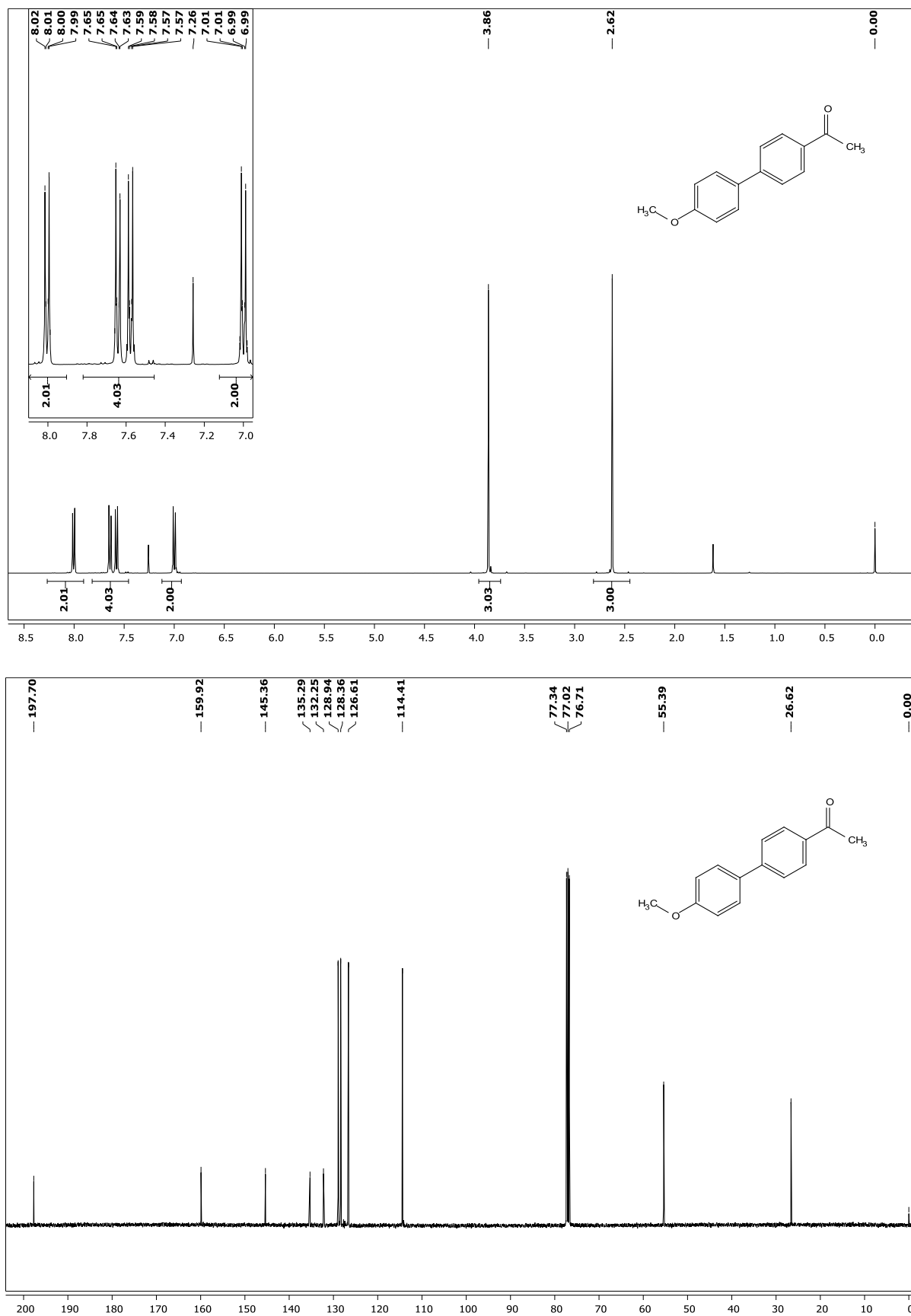
4.6 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 4-methoxy-4'-methyl-1,1'-biphenyl.



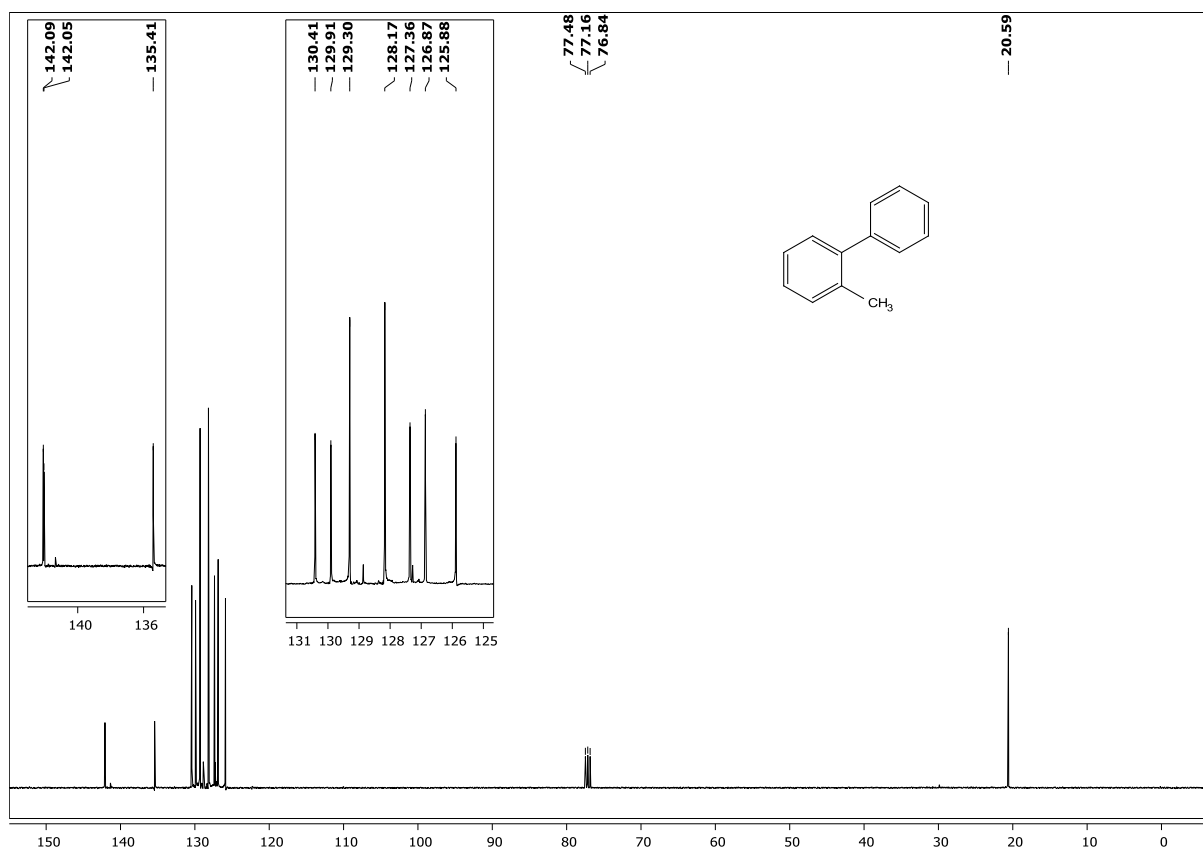
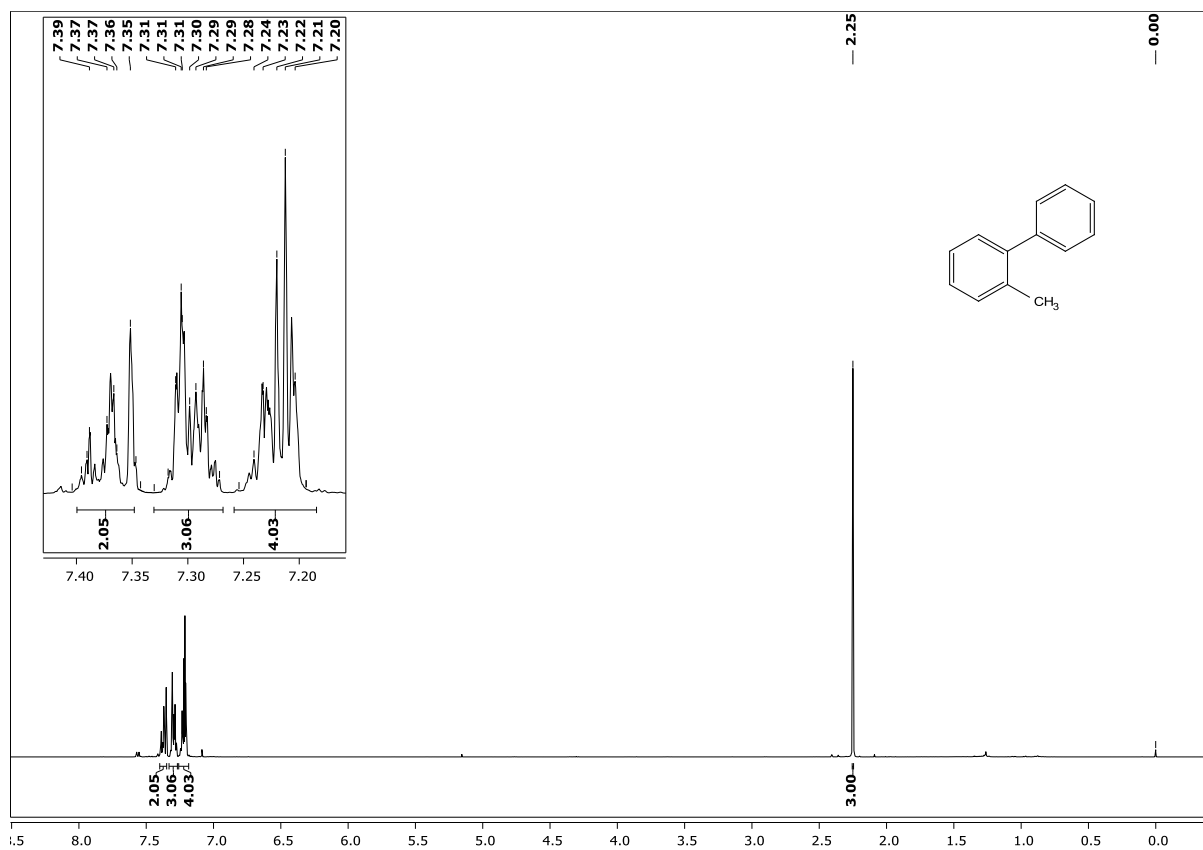
4.7 ^1H -NMR (300 MHz, CDCl_3) and ^{13}C -NMR (75 MHz, CDCl_3) of 1-(4'-methyl-[1,1'-biphenyl]-4-yl)ethan-1-one



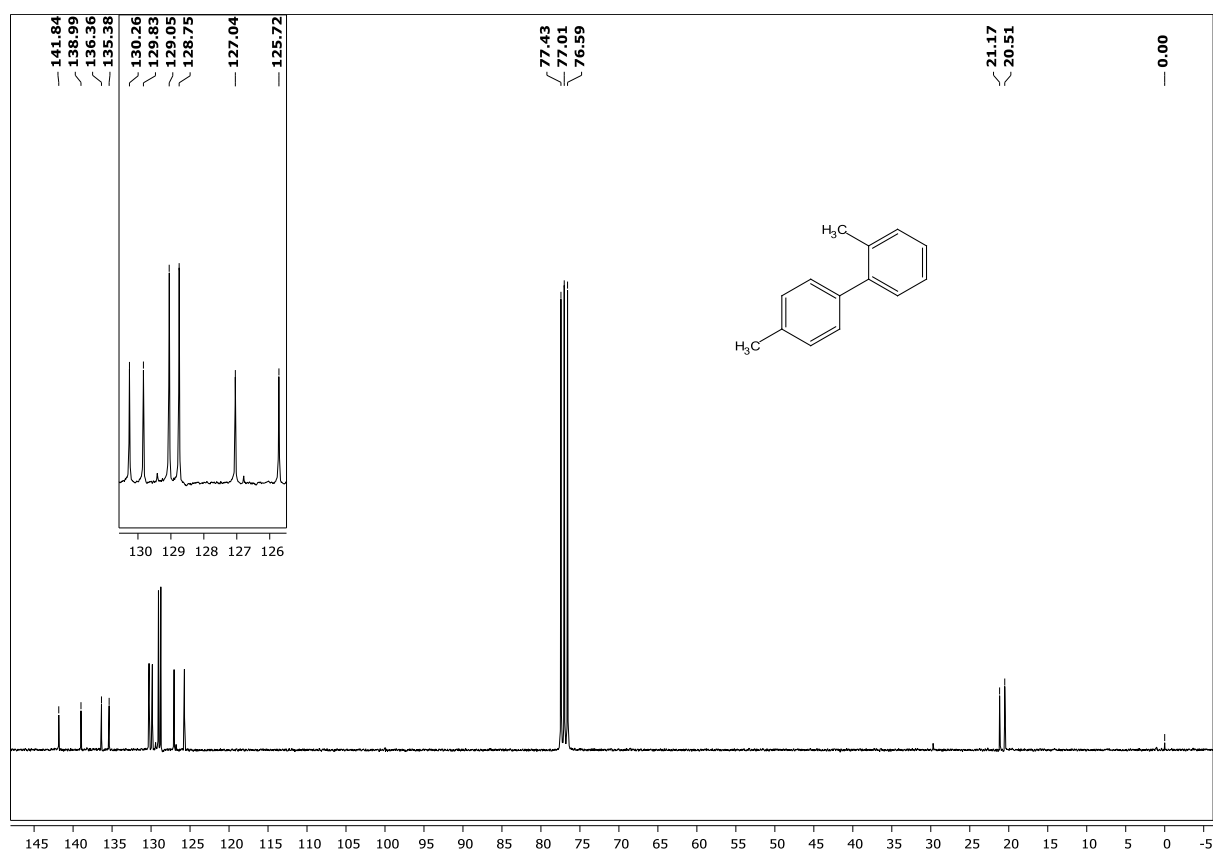
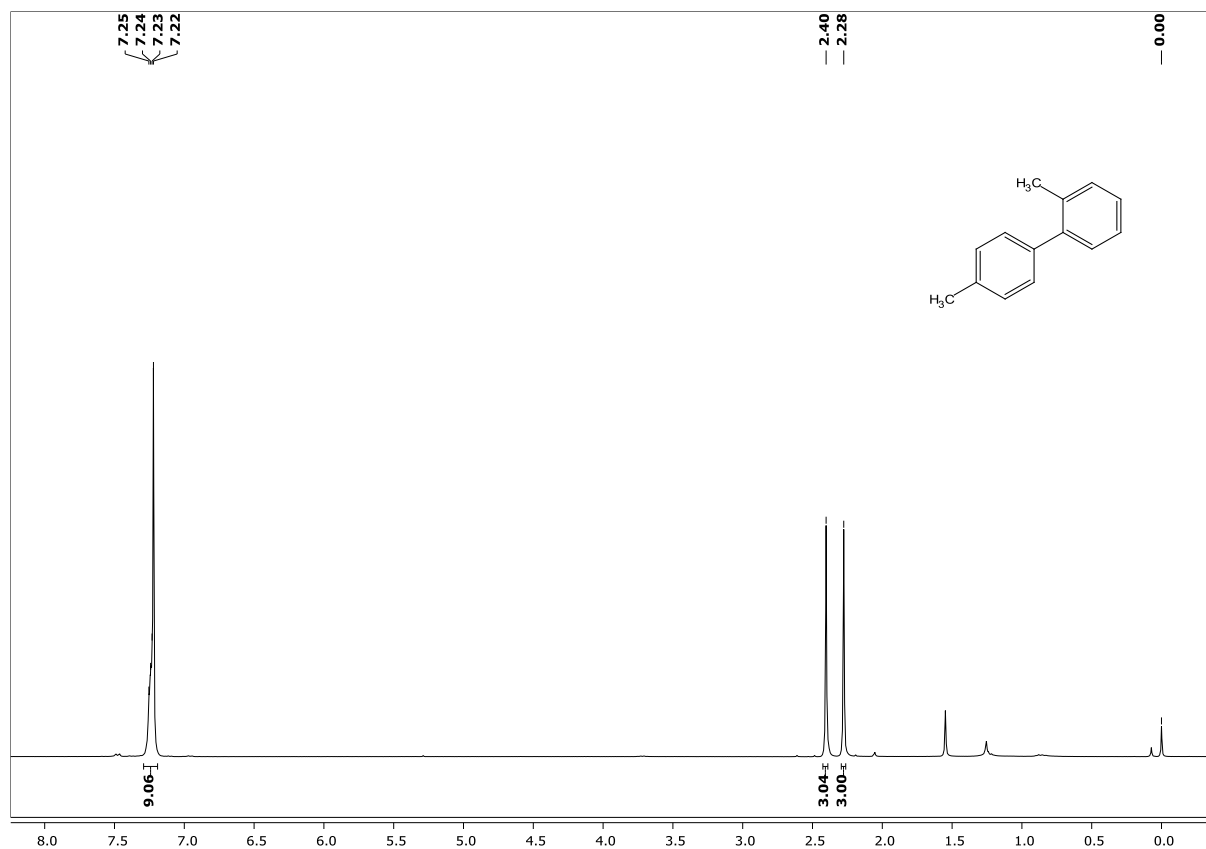
4.8 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 1-(4'-methoxy-[1,1'-biphenyl]-4-yl)ethan-1-one



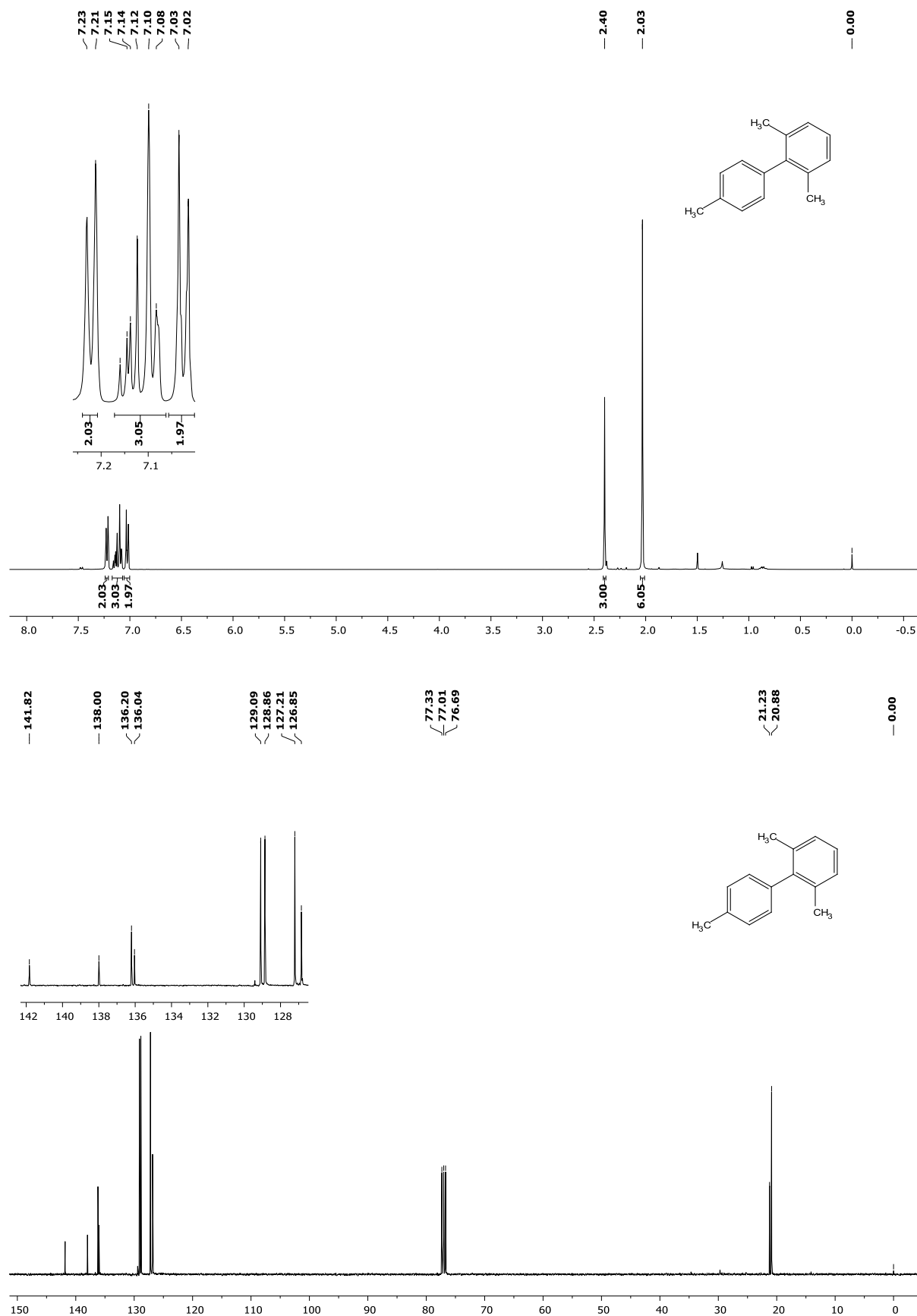
4.9 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 2-methyl-1,1'-biphenyl.



4.10 ^1H -NMR (300 MHz, CDCl_3) and ^{13}C -NMR (75 MHz, CDCl_3) of 2,4'-dimethyl-1,1'-biphenyl.



4.11 ^1H -NMR (400 MHz, CDCl_3) and ^{13}C -NMR (100 MHz, CDCl_3) of 4,2',6'-trimethyl-1,1'-biphenyl.



5 **References:**

- [1]. I. J. S. Fairlamb, A. R. Kapdi, A. F. Lee, *Org. Lett.* 2004, **6**, 4435-4438.
- [2]. D. Badone, M. Baroni, R. Cardamone, A. Ielmini, U. Guzzi, *J. Org. Chem.* 1997, **62**, 7170-7173
- [3]. V. Farina, B. Krishnan, D. R. Marshall, G. P. Roth, *J. Org. Chem.* 1993, **58**, 5434-5444.
- [4]. C. J. Mathews, P. J. Smith, T. Welton, *Chem. Commun.* 2000, **0**, 1249-1250
- [5]. L. Zhang, T. Meng, J. Wu, *J. Org. Chem.* 2007, **72**, 9346-9349.