SUPPORTING INFORMATION

**Silver-Catalyzed Decarboxylative Homo-coupling reaction to Form Symmetrical Difluoromethylated Derivatives**

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1. **General Information:**

1H, 13C and 19F NMR spectra were recorded in CDCl3 on a Bruker AV-500 spectrometer. Chemical shifts for lH NMR spectra are reported in ppm relative to residual CHCl3 as internal reference (δ 7.26 ppm for 1H) downfield from TMS, chemical shifts for 13C NMR spectra are reported in ppm relative to internal CDCl3 (δ 77.16 ppm for 13C), and chemical shifts for 19F NMR spectra are reported in ppmdownfield from internal fluorotrichloromethane (CFCl3). Coupling constants (*J*) are given in Hertz (Hz). The terms m, s, d, t, q refer to multiplet, singlet, doublet, triplet, quartet, respectively; br refers to a broad signal. High resolution mass spectra (HRMS) and Mass spectra (MS) were recorded using an Electron impact (EI) or Electrospray ionization (ESI) techniques. High resolution mass spectra (HRMS) was recorded on Agilent G6500 iFunnel Q-TOF LC/MS.

1. **General Procedure for the Synthesis of difluoromethylated derivatives**

A mixture of Aryldifluoroacetates(0.60 mmol), AgNO3 (0.3 mmol), and (NH4)S2O8 (1.2 mmol) and KHCO3 (0.3 mmol) was added to in 3.0 mL of DMSO under N2 atmosphere. The solution was stirred at 120oC for 2 h. Then the reaction mixture was extracted with ethyl acetate and water. The combined organic layer was dried over Na2SO4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel to give the desired difluoromethylated derivatives (**2a**-**2m**).

1. **Optimization of the Reaction Conditions**



**Table S1**. Optimization varying different oxidant

|  |
| --- |
| Entry Oxidant Yield(%) |

1 K2S2O8  34

2 (NH4)2S2O8  68

3 Na2S2O8 42

4 PhI(OAC)2 31

Determined by 19F NMR spectroscopy using PhCF3 as an internal standard, in the presence of **1a** (0.6mmol), AgNO3 (0.3 mmol), KHCO3 (0.3 mmol), with different oxidant (1.2 mmol), 2h, N2 atmosphere at 120oC temperature.

**Conclusion: initially we carried out the optimization reactions with 1a, giving maximum 19F-NMR from (NH4)2S2O8.**

**Table S2. Optimization varying different base**

|  |
| --- |
| Entry Base Yield(%)  1 K2CO3 40  2 KOH 38  3 Cs2CO3 36  4 KHCO3 68  5 NA 28 |

Determined by 19F NMR spectroscopy using PhCF3 as an internal standard, in the presence of **1a** (0.6mmol), AgNO3 (0.3 mmol), (NH4)2S2O8 (1.2 mmol), with different Base, 2h, N2 atmosphere at 120oC temperature

**Conclusion: initially we found that KHCO3 gave best result.**

**Table S3**. Optimization varying different catalyst

|  |
| --- |
| Entry Catalyst Yield(%)  1 AgNO3 68  2 Ag2CO3 30  3 AgBF4 43  4 AgOAC 34  5 Ag(CF3SO3) 36  6 Cu(I), or Cu(II),or Cu( III) NA |

Determined by 19F NMR spectroscopy using PhCF3 as an internal standard, in the presence of **1a** (0.6mmol), (NH4)2S2O8 (1.2 mmol),KHCO3 (0.3mmol) with different catalyst, 2h, N2 atmosphere at 120oC temperature.

**Conclusion: initially we found that Combination of AgNO3 gave best result.**

**Table S4**. Optimization varying different equivalent of catalyst

|  |
| --- |
| Entry Catalys(eq) Yield(%)  1 AgNO3(0.3eq) 41  2 AgNO3(0.5eq) 68  3 AgNO3(1eq) 26  4 AgNO3(2eq) 23 |

Determined by 19F NMR spectroscopy using PhCF3 as an internal standard, in the presence of **1a** (0.6 mmol), (NH4)2S2O8 (1.2 mmol),KHCO3 (0.3mmol) with different equiv catalyst, 2h, N2 atmosphere at 120oC.

**Conclusion: we found that Combination of 0.5 equiv. of AgNO3 gave best result.**

**Table S5**. Optimization varying different time.

|  |
| --- |
| Entry 1Time(h) Yield(%)  1 12 9  2 6 40  3 4 51  4 2 68  5 1 33  6 1/3 31 |
| Determined by 19F NMR spectroscopy using PhCF3 as an internal standard, in the presence of **1a** (0.6 mmol), (NH4)2S2O8 (1.2 mmol),KHCO3 (0.3mmol) with different time,, N2 atmosphere at 120oC. |

**Conclusion: we found that 2h gave best result.**

1. **Mechanistic Study**
   1. **Primary Mechanistic Study.**



|  |
| --- |
| Entry Additive Yield(%)  1 1.0 equiv 1,4-dinitrobenzene 57  2 1.0 equiv hydroquinone 63  3 1.0 equiv TEMPO 4  4 2.0 equiv TEMPO 0 |
| aReaction condition:1a (0.6 mmol), AgNO3 (0.3mmol), and (NH4)S2O8(1.2mmol), KHCO3 (0.3mmol) under N2 at 120oC for 2h. bYields determined by 19F NMR analysis with PhCF3 as the internal stander. |

A mixture of aryldifluoroacetate(0.60mmol), AgNO3 (0.3mmol), and (NH4)S2O8(1.2mmol), KHCO3 (0.3mmol) and TEMPO (0.6mmol) or (1.2mmol) in 3.0mL of DMSO under N2 atmosphere. The solution was stirred at 120oC for 2 h. When 1.0 equiv TEMPO was added, the reaction yield decreased to 4%. When 2.0 equiv TEMPO was added, no product was observed, The reaction was completely suppressed, but unfortunately we did not capture TEMPO-CF2Ph, probably because this species is unstable at high temperatures.

* 1. **Study on defluoro homocoupling reaction**



1. **Characterization of the products**

**1,2-Bis(4-methoxyphenyl)-1,1,2,2-tetrafluoroethane (2a)**



White solid, m.p. 201-203°C, 65% yield. 1H NMR (CDCl3) δ: 7.34 (d, *J*=8.8 Hz, 4H), 6.90 (d, *J*=8.8 Hz, 4H), 3.86 (s, 6H). 19F NMR (CDCl3) δ: -110.96 (s, CF2). 13C NMR ((CD3)2SO): low solubility, only four kinds of carbons were observed δ: 161.9, 128.6 (m), 114.4, 55.9. IR(KBr, cm-1): *ν*max = 3031, 2969, 1614, 1514, 1251, 1090, 828, 783. HRMS (EI): calcd for C16H14F4O2 (M+) 314.0924; found 314.0926.

**1,2-Bis(4-methylphenyl)-1,1,2,2-tetrafluoroethane (2b)**



White solid, mp 137-140°C, 53% yield. 1H NMR (CDCl3) δ: 7.33 (d, *J*=8.3 Hz, 4H), 7.21 (d, *J*=8.1 Hz, 4H), 2.39 (s, 6H). 19F NMR (CDCl3) δ: -111.36 (s, 2CF2). 13C NMR (CDCl3) δ: 141.0, 128.8, 128.1-128.3 (m), 126.9 (m), 116.8 (tt, *1JCF*=250.7 Hz, *2JCF*=36.4 Hz), 21.4. IR(KBr, cm-1): *ν*max = 3029, 2927, 1612, 1510, 1257, 1088, 866, 768. MS (EI) m/z: 282 (M+, 10%), 141 (100), 101 (7), 91 (14). HRMS (EI): calcd for C16H14F4 (M+) 282.1026; found 282.1029

**1,2-bis(4-fluorophenyl)-1,1,2,2-tetrafluoroethane (2c)**



White solid, mp 163-166 °C, 21% yield. 1H NMR (CDCl3) δ: 7.46 (s, 8H), 1.35 (s, 18H), 19F NMR (CDCl3) δ: -110.5 (s, 4F, CF2). 13C NMR (CDCl3) δ: 154.1, 128.1 (t, *2JCF*=25.0 Hz), 126.8 (m), 125.1, 116.8 (tt, *1JCF*=250.7 Hz, *2JCF*=37.7 Hz), 34.8, 31.2. IR(KBr, cm-1): *ν*max = 3063, 2959, 1614, 1514, 1262, 1084, 862, 820. HRMS (EI) calcd for C22H26F4 (M+) 366.1965; found 366.1967.

**1,2-Bis(4-fluorophenyl)-1,1,2,2-tetrafluoroethane (2d)**



White solid, mp 99-100 °C, 40% yield. 1H NMR (CDCl3) δ: 7.44-7.46 (m, 4H), 7.11 (t, *J*=8.5 Hz, 4H). 19F NMR (CDCl3) δ: -108.9 (s, 2F, Ar–F), -111.09 (s, 4F, CF2). 13C NMR (CDCl3) δ: 164.4 (d, *1JCF*=249.8 Hz), 129.2 (m), 126.7 (t, *2JCF*=27.1 Hz), 116.3 (tt, *1JCF*=251.7 Hz, *2JCF*=36.6 Hz), 115.4 (d, *2JC*F=21.9 Hz). IR(KBr, cm-1): *ν*max = 3076, 1606, 1513, 1243, 1086, 832, 794. MS (EI) m/z: 290 (M+, 5%), 145 (100), 125 (3), 95 (10), 75 (6). HRMS (EI) calcd for C14H8F6 (M+) 290.0525; found 290.0528.

**1,2-Bis(4-chlorophenyl)-1,1,2,2-tetrafluoroethane** **(2e)**



White solid, mp. 93-94 °C, 26% yield. 1H NMR (CDCl3) δ: 7.38-7.43 (m, 8H). 19F NMR (CDCl3) δ: -111.63 (s, CF2). 13C NMR (CDCl3) δ: 137.6, 129.0 (t, *2JCF*=25.5 Hz), 128.6, 128.4 (m), 116.2 (tt, *1JCF*=252.2 Hz, *2JCF*=36.4 Hz). IR(KBr, cm-1): *ν*max = 3097, 1596, 1488, 1253, 1090, 887, 813. HRMS (EI) calcd for C14H8Cl2F4 (M+) 321.9934; found 321.9935.

**1,2-bis(4-bromophenyl)-1,1,2,2-tetrafluoroethane (2g)**



White solid, mp. 98-100 °C, 38% yield. 1H NMR (CDCl3) δ: 7.58 (d, *J*=8.6 Hz, 4H), 7.11 (d, *J*=8.5 Hz, 4H). 19F NMR (CDCl3) δ: -116.77 (s, CF2). 13C NMR (CDCl3) δ: 131.6, 129.5 (t, *2JCF*=25.9 Hz), 128.6 (m), 125.9, 116.2 (tt, *1JCF*=252.3 Hz, *2JCF*=36.5 Hz). IR(KBr, cm-1): *ν*max = 3099, 1587, 1483, 1254, 1082, 881, 803. HRMS (EI) calcd for C14H8Br2F4 (M+) 409.8923; found 409.8924.

**1,1,2,2-Tetrafluoro-1,2-diphenylethane (2h)**



White solid, mp. 125-127 °C, 48% yield. 1H NMR (CDCl3) δ: 7.40-7.51 (m, 10H). 19F NMR (CDCl3) δ: -111.84 (s, 4F, CF2). 13C NMR (CDCl3) δ: 130.9, 130.9 (t, *2JCF*=26.4 Hz), 128.1, 126.9 (m), 116.6 (tt, *1JCF*=254.9 Hz, *2JCF*=36.3 Hz). IR(KBr, cm-1): *ν*max = 3073, 1606, 1494, 1253, 1074, 876, 753. MS (EI) m/z: 254 (M+, 10%), 127 (100), 77 (15), 51 (5). HRMS (EI) calcd for C14H10F4 (M+) 254.0713; found 254.0716.

**1,1,2,2-tetrafluoro-1,2-di-o-tolylethane (2i)**



White solid, mp. 55-58°C, 34% yield. 1H NMR (CDCl3) δ: 7.35-7.37 (m, 4H), 7.19-7.23 (m, 4H), 2.31 (s, 6H), 19F NMR (CDCl3) δ: -106.7 (s, 4F, CF2). 13C NMR (CDCl3) δ: 137.9, 132.1, 130.8, 128.8 (m), 129.0 (t, *2JCF*=22.0 Hz), 125.4, 118.7 (tt, *1JCF*=253.4 Hz, *2JCF*=36.6 Hz), 20.4 (m). IR(KBr, cm-1): *ν*max = 3053, 2925, 1603, 1498, 1252, 1064, 884, 758. HRMS (EI) calcd for C16H14F4 (M+) 282.1026; found 282.1027.

**1,1,2,2-tetrafluoro-1,2-bis(2-methoxyphenyl)ethane (2j)**



Pale yellow solid, mp. 77-80 °C, 30% yield. 1H NMR (CDCl3) δ: 7.37-7.42 (m, 4H), 6.93-6.96 (m, 2H), 6.88 (d, *J*=8.2 Hz, 2H), 3.58 (s, 6H). 19F NMR (CDCl3) δ: -108.8 (s, 4F, CF2). 13C NMR (CDCl3) δ: 158.2, 132.3, 129.4 (m), 119.8, 119.7 (t, *2JCF*=23.3 Hz), 117.3 (tt, *1JCF*=255.2 Hz, *2JCF*=35.4 Hz), 111.8, 55.6. IR(KBr, cm-1): *ν*max = 3044, 2979, 1614, 1508, 1247, 1081, 821, 757. HRMS (EI) calcd for C16H14F4O2 (M+) 314.0924; found 314.0923.

**1,2-bis(3,4-dimethylphenyl)-1,1,2,2-tetrafluoroethane (2k)**



White solid, mp 152-155 °C, 46% yield. 1H NMR (CDCl3) δ: 7.27 (t, *J*=8.6 Hz, 2H), 7.12 (t, *J*=7.7 Hz, 1H), 2.31 (s, 3H), 2.24 (s, 3H). 19F NMR (CDCl3) δ: -103.9 (s, 4F, CF2). 13C NMR (CDCl3) δ: 138.3, 136.6, 132.5, 129.2 (t, *2JCF*=24.6 Hz), 126.7 (m), 118.9 (tt, *1JCF*=253.1 Hz, *2JC*F=37.4 Hz), 20.9, 16.1. IR(KBr, cm-1): *ν*max = 3035, 2979, 1614, 1510, 1253, 1085, 802, 757. HRMS (EI) calcd for C18H18F4 (M+) 310.1339; found 310.1341.

**1,1,2,2-tetrafluoro-1,2-dimesitylethane (2l)**



White solid, mp 103-106 °C, 85% yield. 1H NMR (CDCl3) δ: 6.86 (s, 4H), 2.27-2.30 (m, 18H), 19F NMR (CDCl3) δ: -100.3 (s, 4F, CF2). 13C NMR (CDCl3) δ: 140.1, 139.3 (m), 131.5, 125.1 (t, *2JCF*=21.1 Hz), 121.0 (tt, *1JCF*=255.3 Hz, *2JCF*=38.3 Hz), 22.2, 20.8. IR(KBr, cm-1): *ν*max = 3052, 2969, 1610, 1507, 1232, 1071, 848. HRMS (EI) calcd for C20H22F4 (M+) 338.1652; found 338.1651.

**1,1,2,2-tetrafluoro-1,2-di(naphthalen-2-yl)ethane (2m)**



White solid, mp 153-156 °C, 32% yield). 1H NMR (CDCl3) δ: 8.20 (d, J=8.2 Hz, 1H), 7.95 (d, J=8.2 Hz, 1H), 7.85-7.87 (m, 1H), 7.57-7.59 (m, 1H), 7.43-7.50 (m, 2H), 7.38-7.41 (m, 1H), 19F NMR (CDCl3) δ: -103.9 (s, 4F, CF2). 13C NMR (CDCl3) δ: 133.9, 132.4, 130.6, 128.7, 127.9 (m), 126.9, 126.7 (t, *2JCF*=22.2 Hz), 125.9, 125.3 (m), 124.1, 119.2 (tt, *1JCF*=254.4 Hz, *2JCF*=36.6 Hz). IR(KBr, cm-1): *ν*max = 3050, 2921, 1594, 1511, 1141, 1071, 887, 776. HRMS (EI) calcd for C22H14F4 (M+) 354.1026; found 354.1029.

**thiophene-2-carboxylic acid (3n)**



Yellowish solid, mp. 125-129 °C, 70% yield). 1H NMR (CDCl3) δ: 7.89-7.90 (m, 1H), 7.64-7.65 (m, 1H), 7.14-7.15 (m, 1H). 13C NMR (CDCl3) δ: 167.8, 135.0, 134.0, 133.0, 128.1. IR(KBr, cm-1): *ν*max = 3084, 1652, 1403, 1243, 1114, 1037, 809, 702. MS (EI) m/z: 128 (M+, 74%), 111 (100), 45 (12), 57 (10).

**2,4-dimethoxybenzoic acid (3o)**



Yellowish solid, mp 105-107 °C, 60% yield. 1H NMR (CDCl3) δ: 8.12 (d, *J*=8.8 Hz, 1H), 6.62-6.65 (m, 1H), 6.52 (d, *J*=2.3 Hz, 1H), 4.03 (s, 3H), 3.87 (s, 3H). 13C NMR (CDCl3) δ: 165.5, 165.2, 135.5, 110.4, 106.5, 98.6, 56.6, 55.8. IR (KBr, cm-1): *ν*max = 2978, 2842, 1646, 1615, 1272, 1064, 836, 778. MS (EI) m/z: 182 (M+, 94%), 135 (100),165 (74), 153 (39).

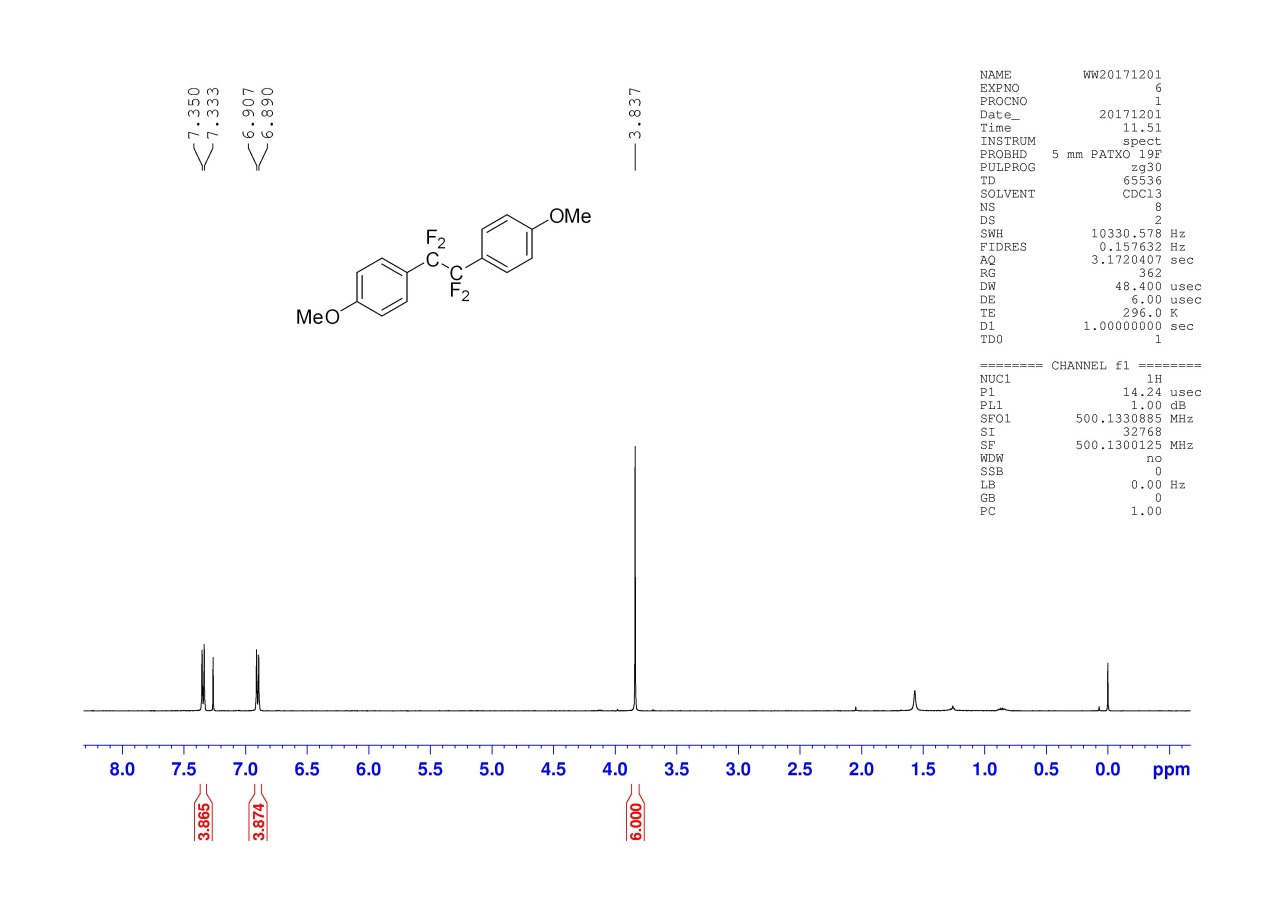
**1,2-bis(2,4-dimethoxyphenyl)ethane-1,2-dione (4o)**



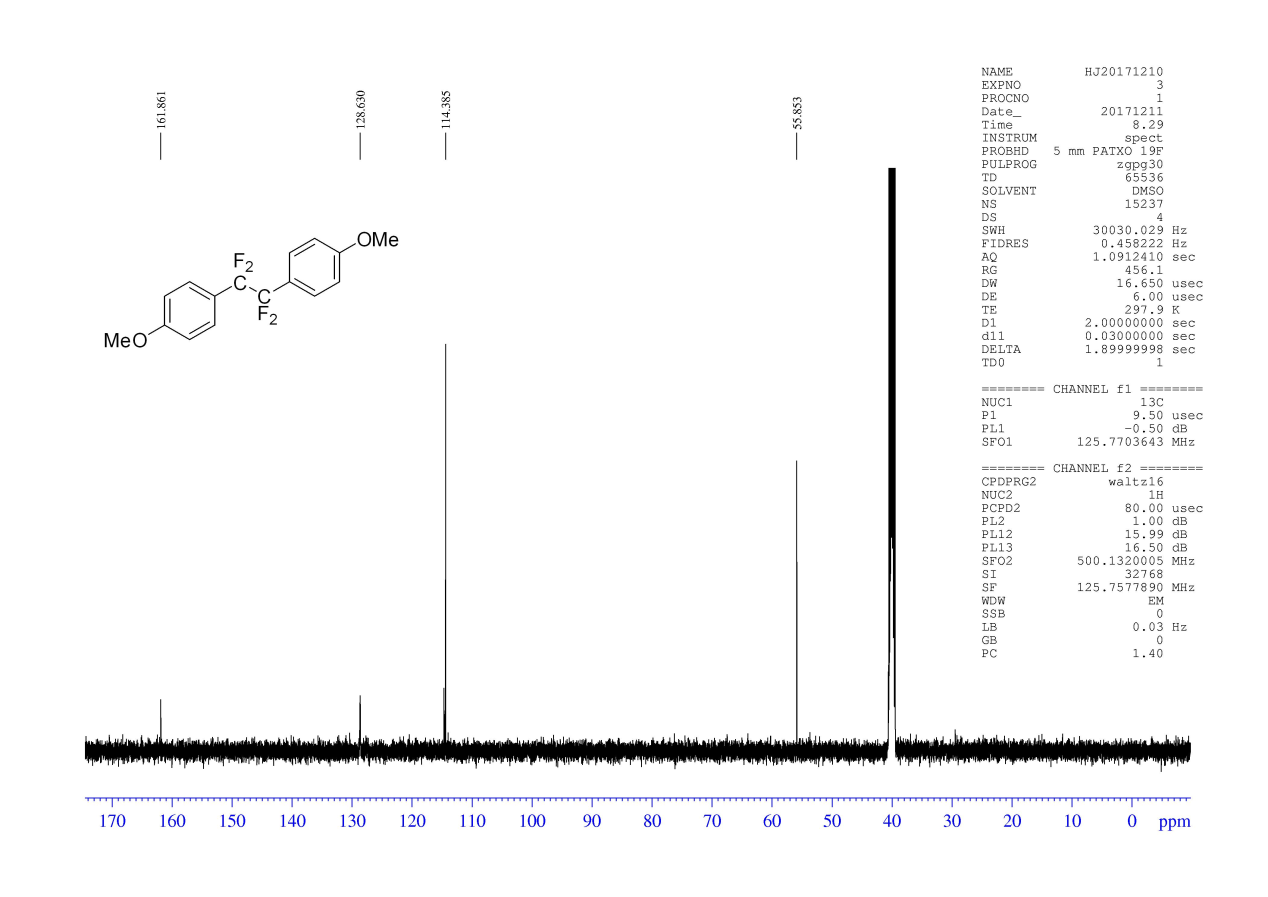
Pale yellow solid, mp 195-197 °C, 31% yield. 1H NMR (CDCl3) δ: 8.04 (d, *J*=8.8 Hz, 1H), 6.62-6.64 (m, 1H), 6.40 (d, *J*=2.3 Hz, 1H), 3.87 (s, 3H), 3.58 (s, 3H). 13C NMR (CDCl3) δ: 192.0, 165.9, 162.1, 117.0, 106.5, 98.5, 55.8, 55.6. IR(KBr, cm-1): *ν*max = 3075, 2971, 1679, 1618, 1478, 736. MS (ESI) m/z: 330 (M+,2%), 165 (100), 166 (10), 122 (6).

1. **Copies of 1H NMR, 19F NMR, 13C NMR spectra of 2a-2m**

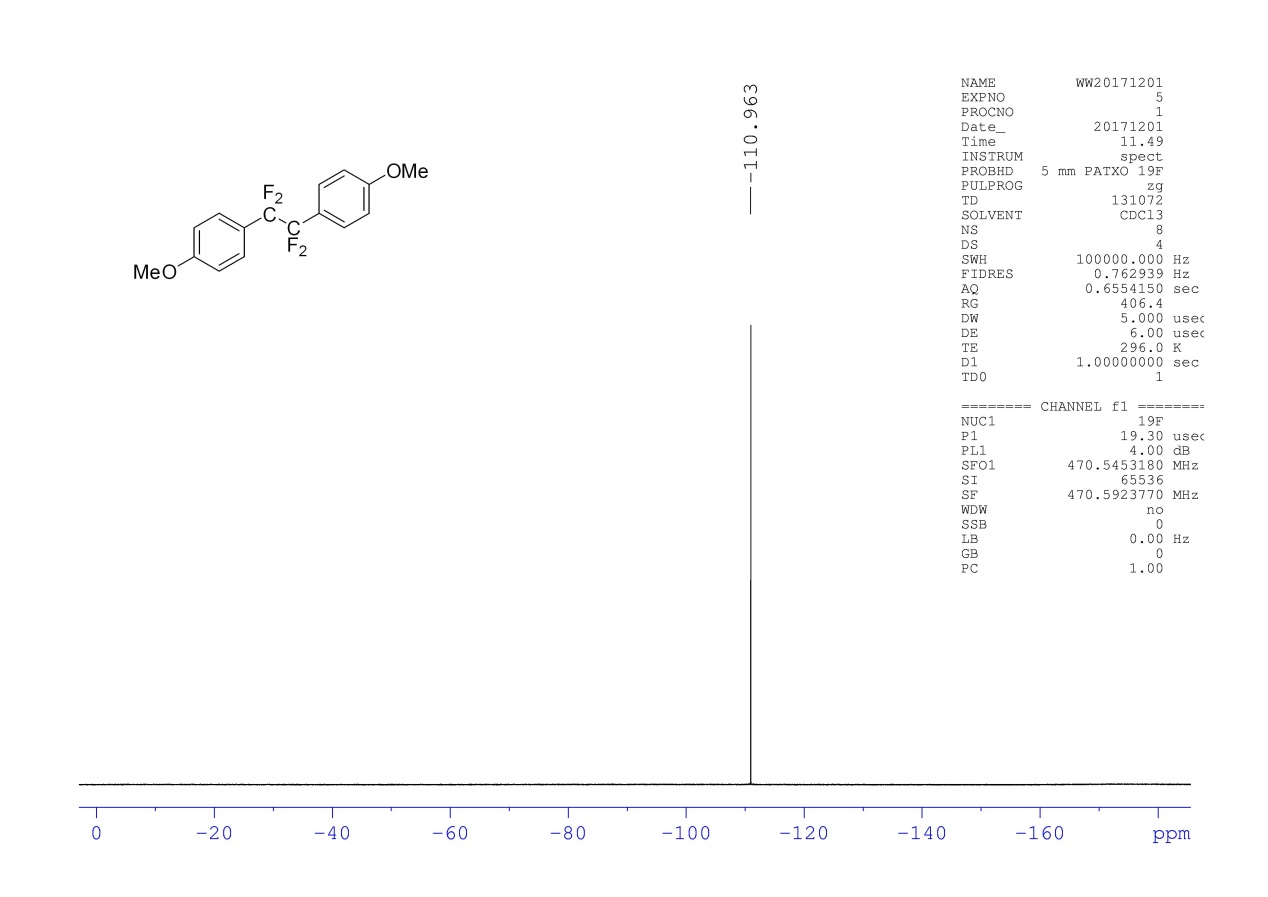
**1H NMR Spectra of 2a**

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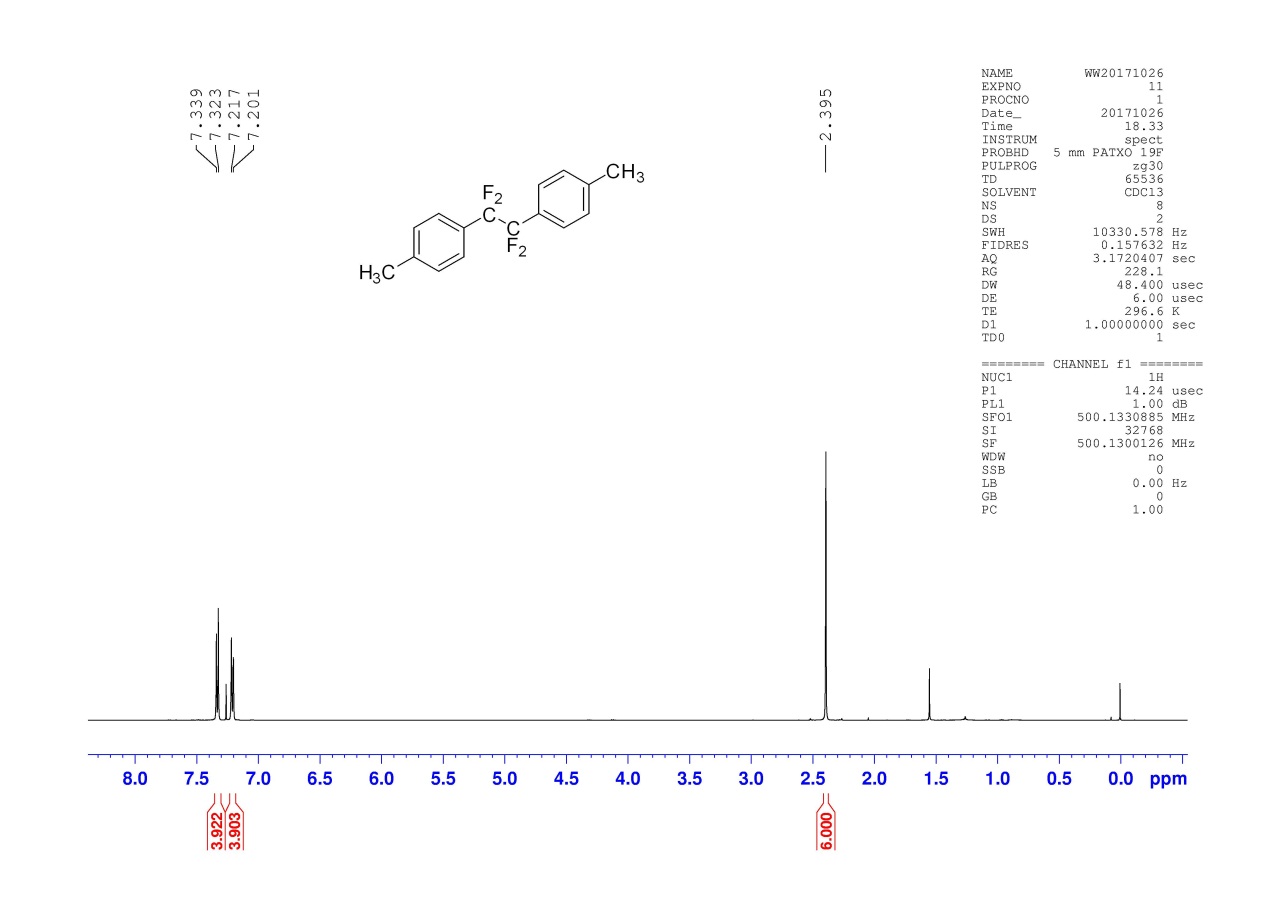
**13C NMR Spectra of 2a**

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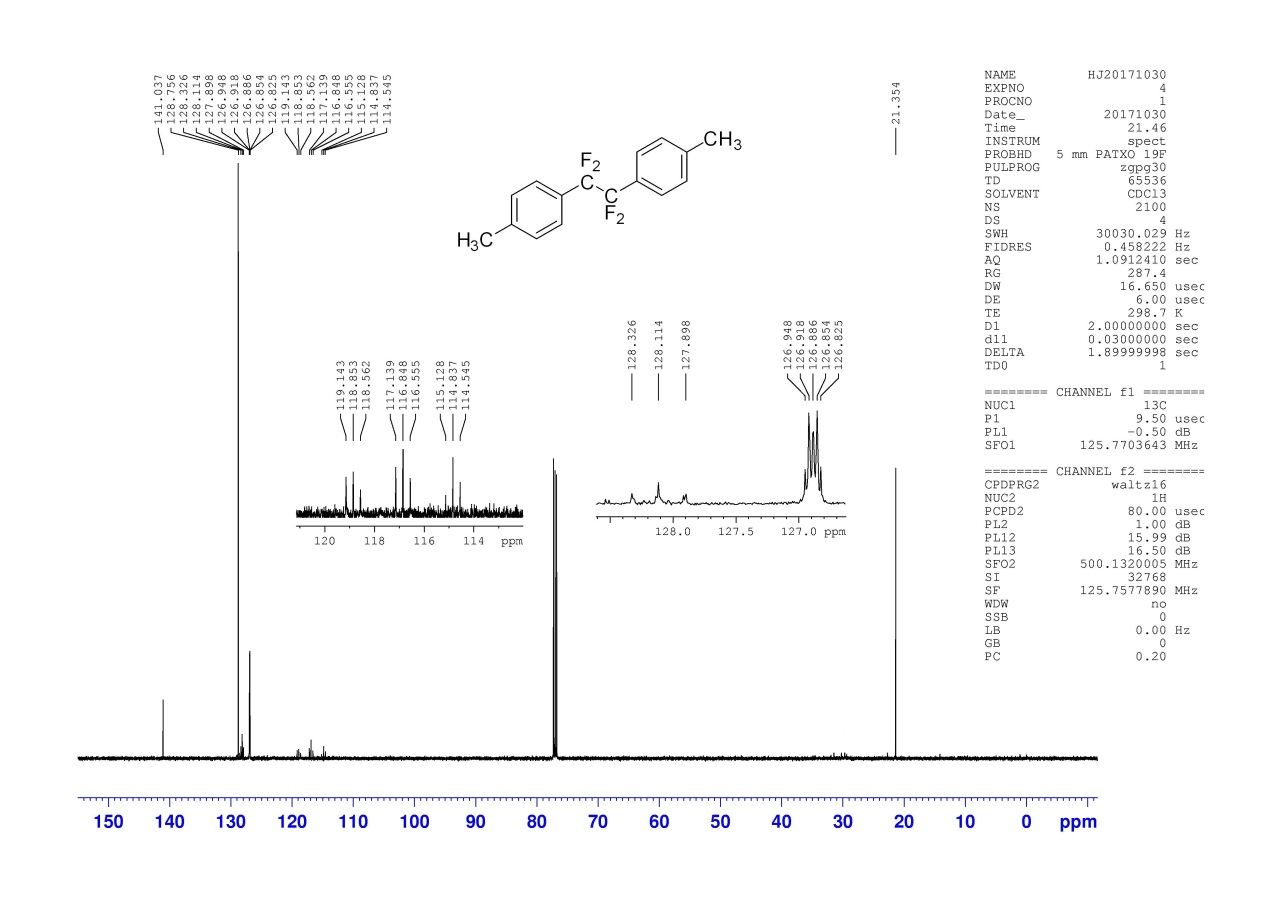
**19F NMR Spectra of 2a**

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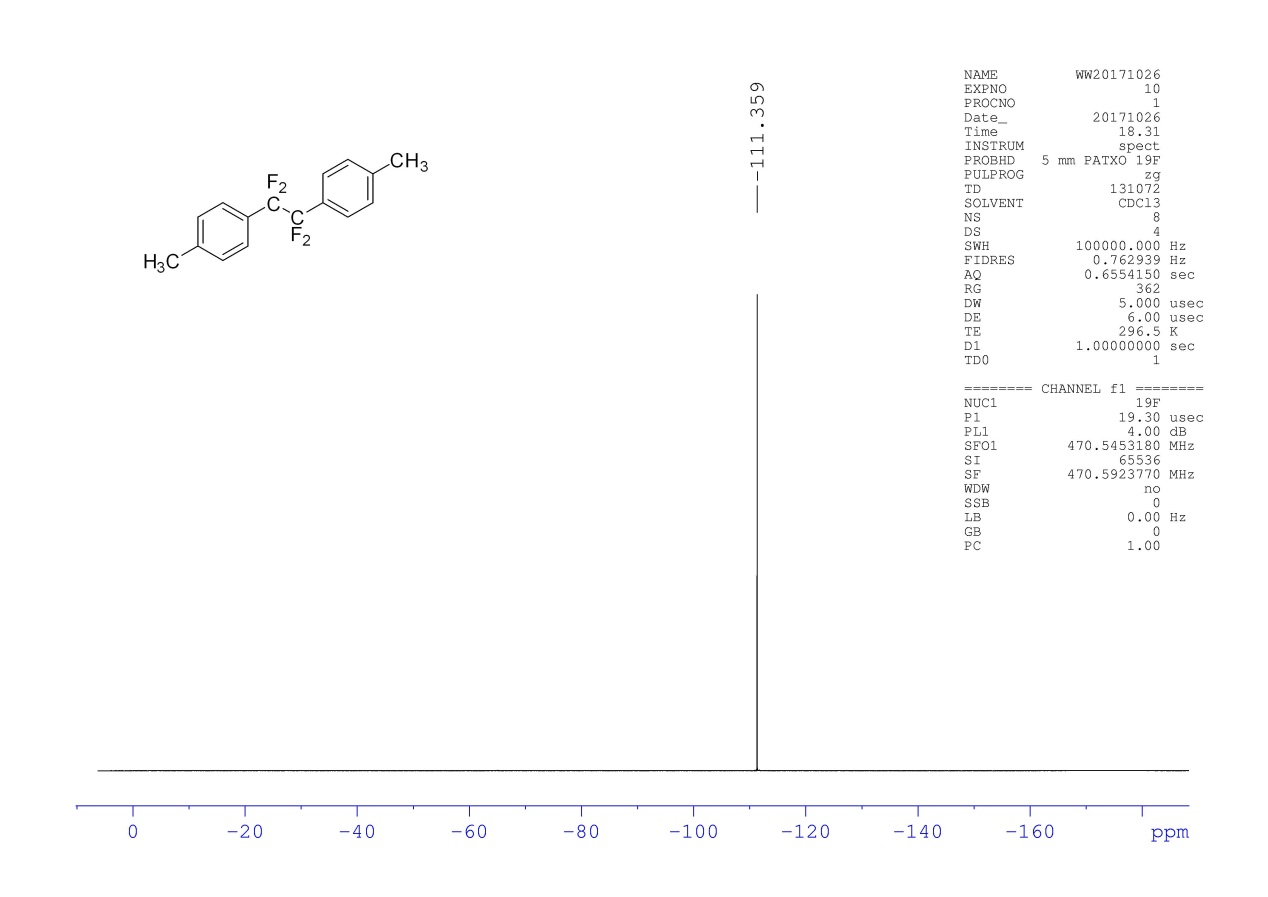
**1H NMR Spectra of 2b**

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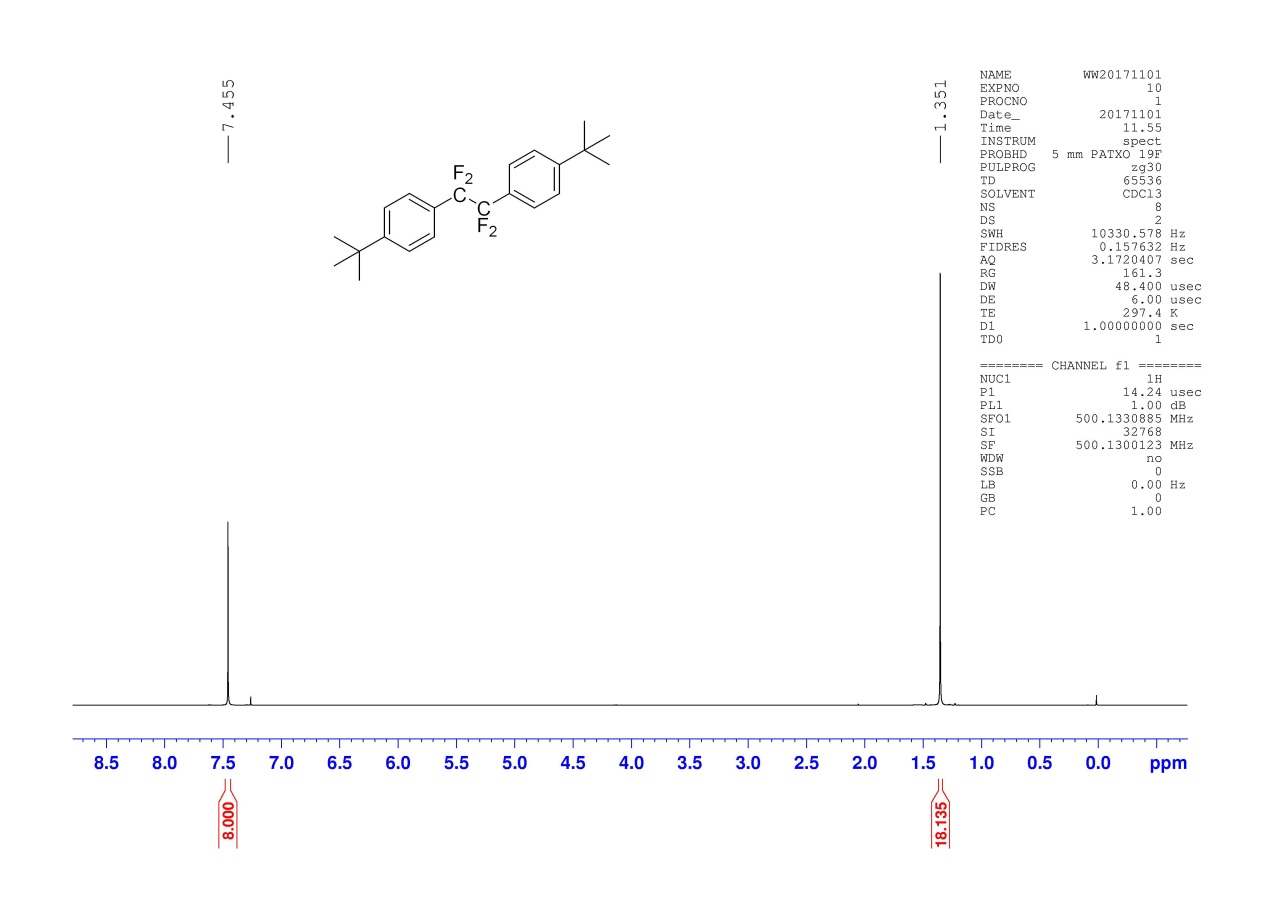
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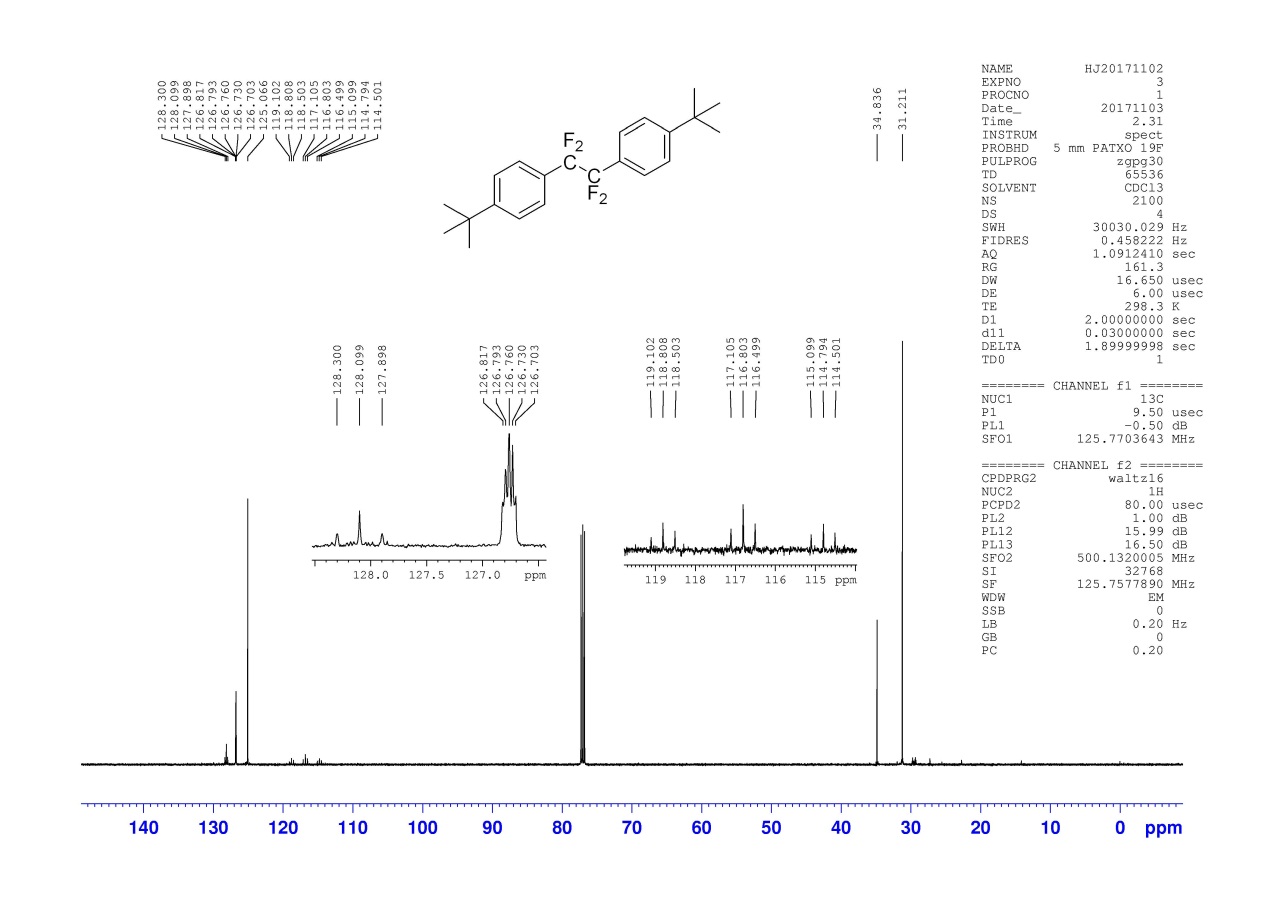
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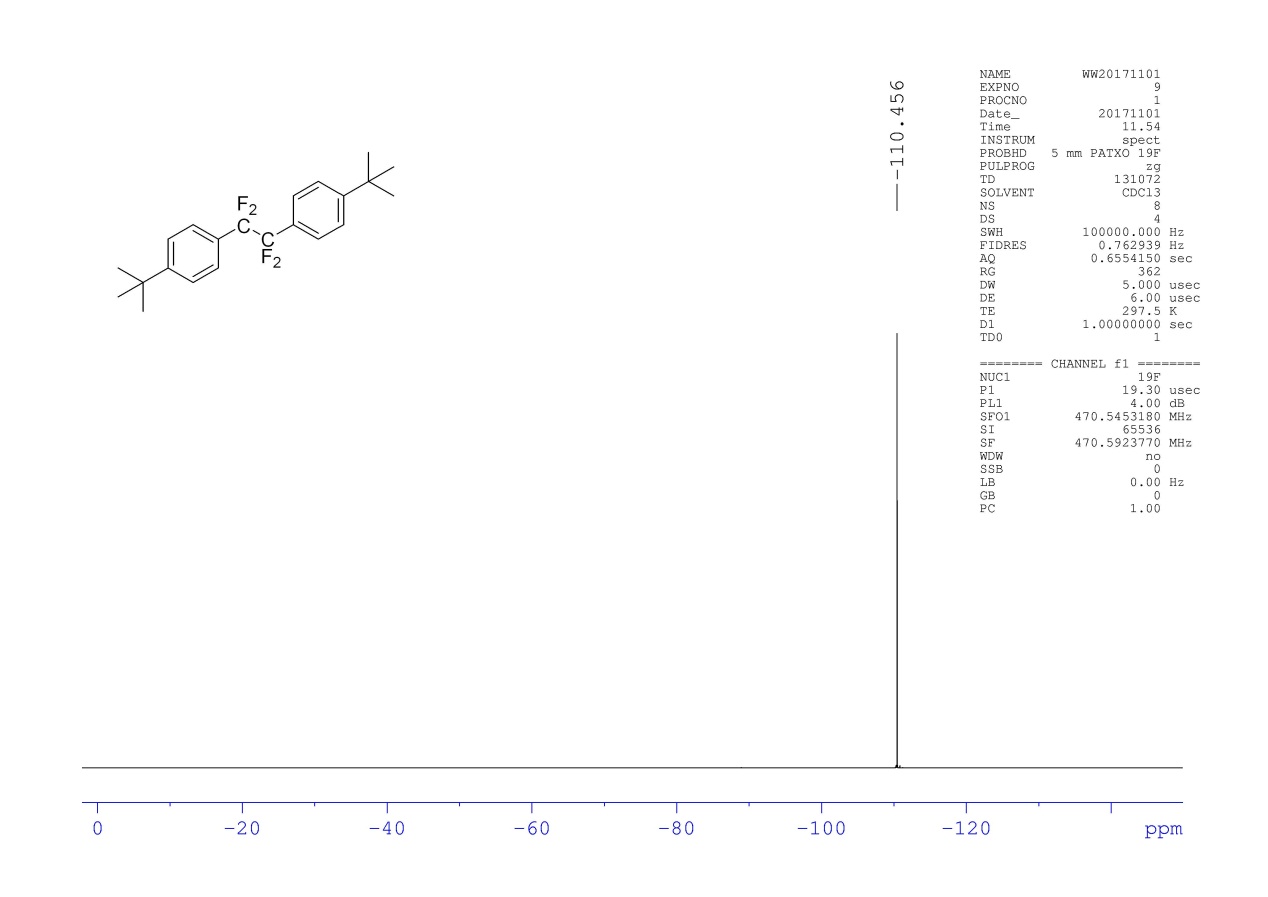
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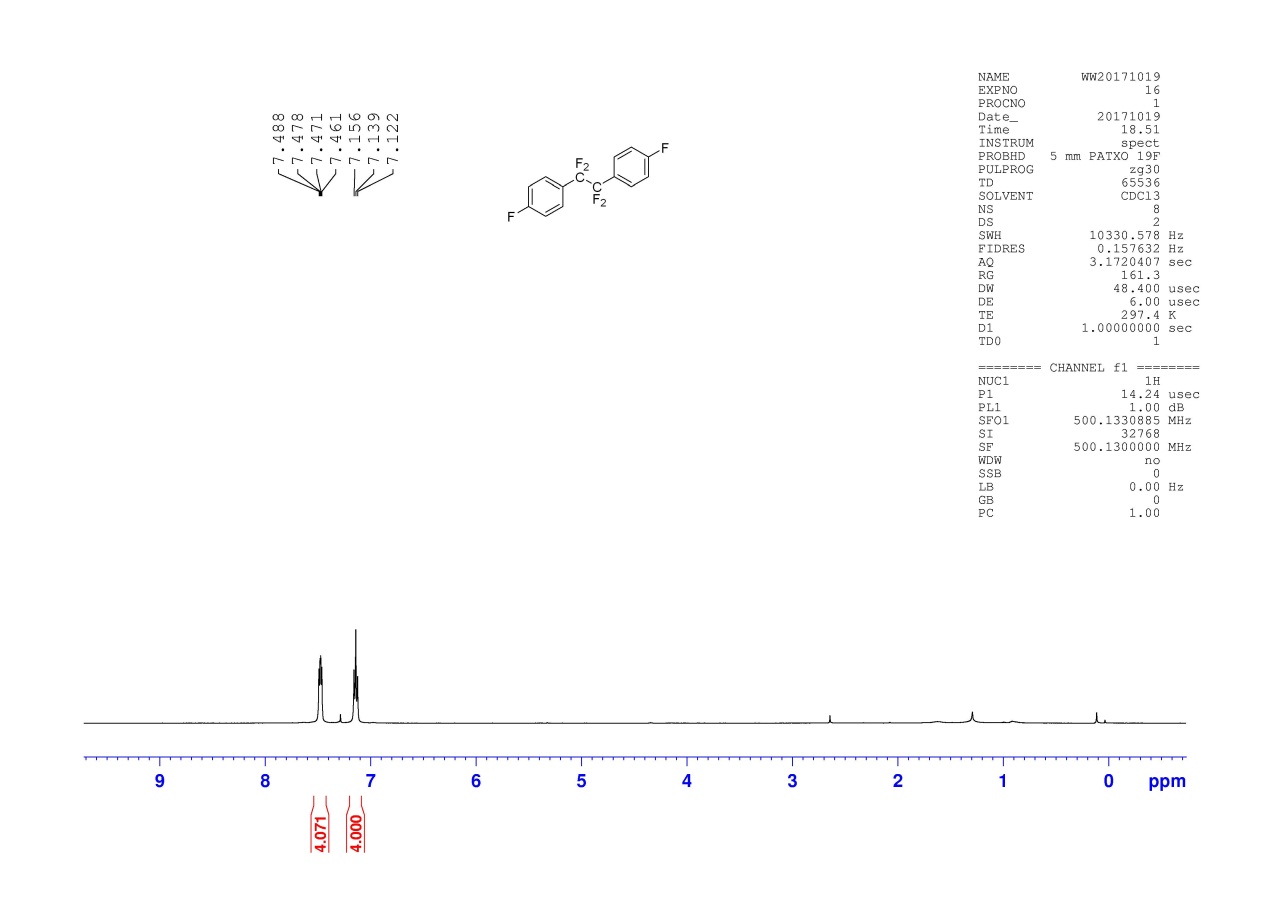
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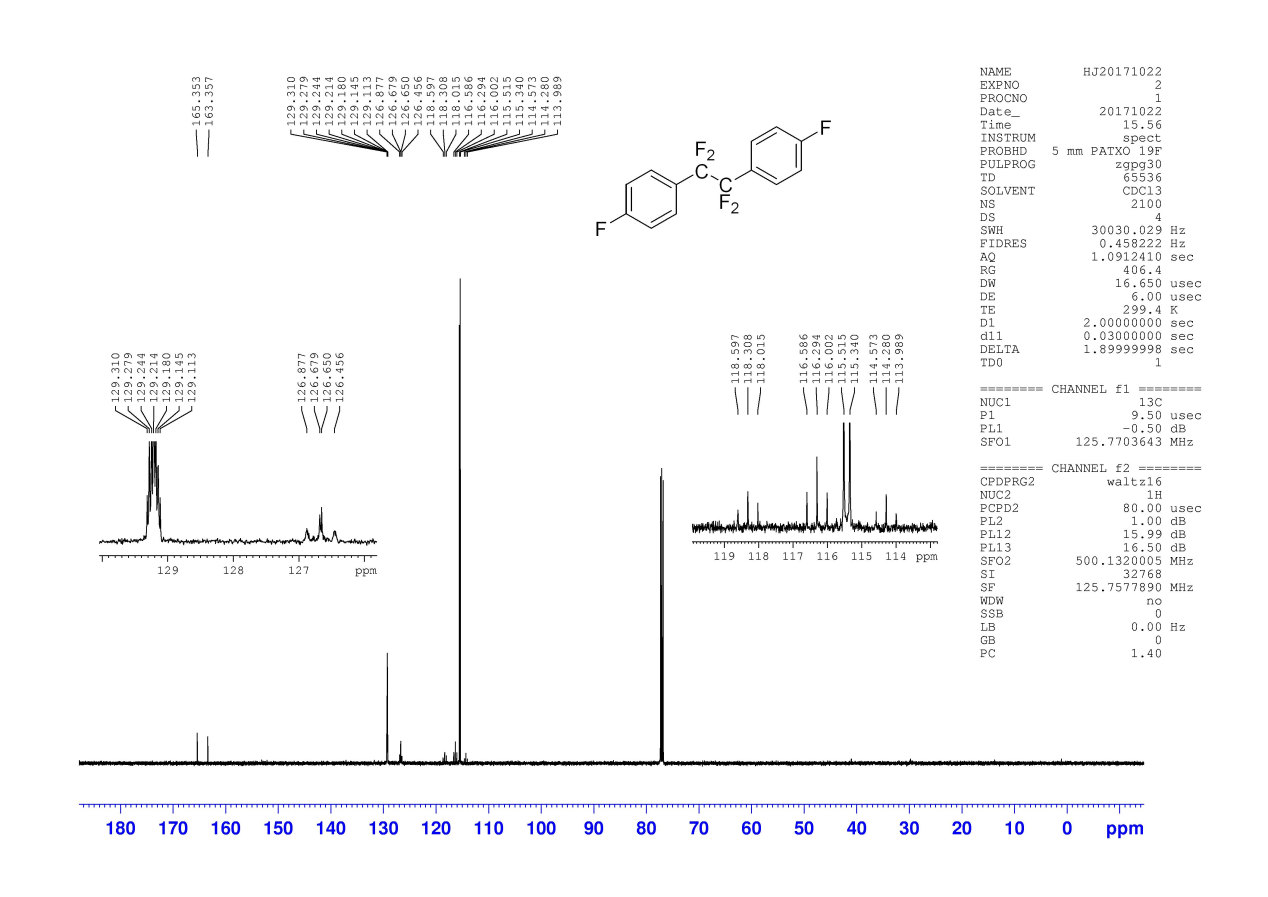
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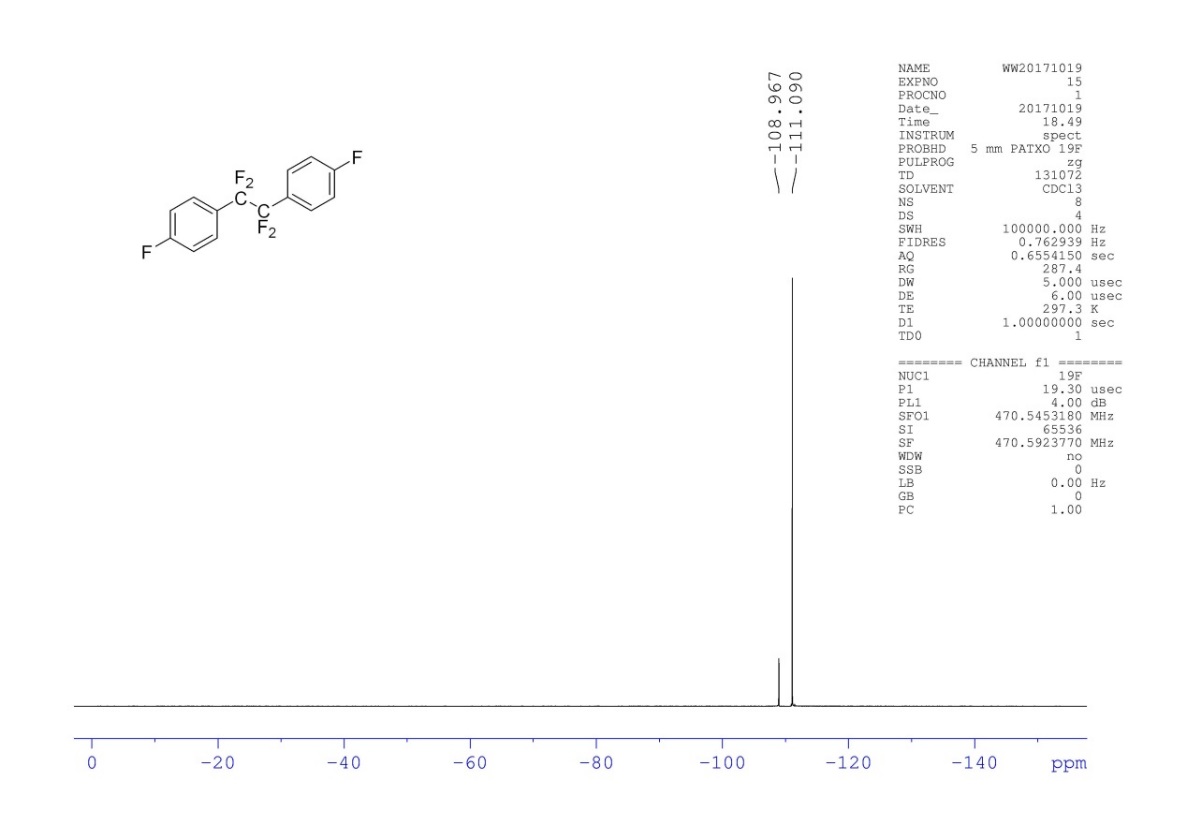
**1H NMR Spectra of 2d**

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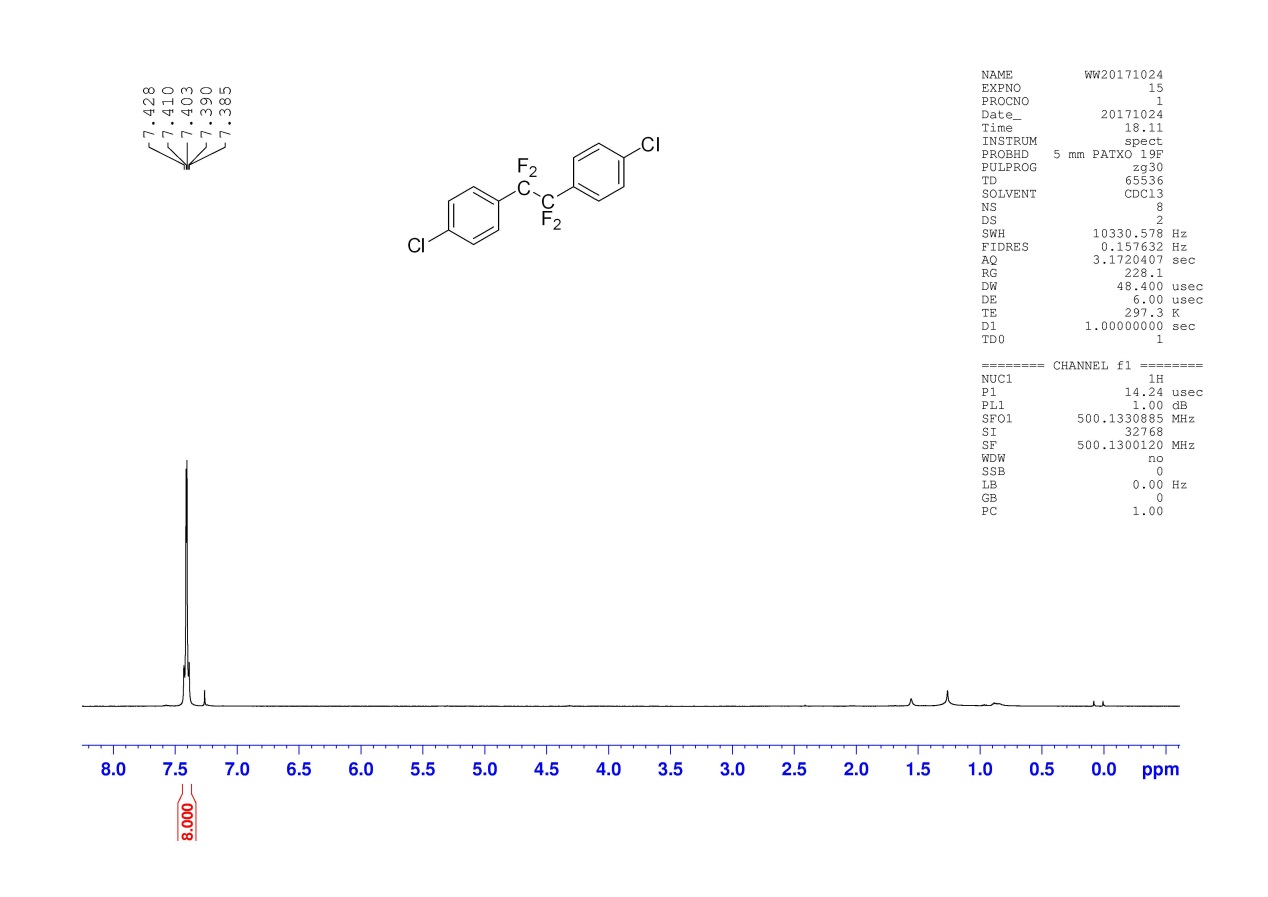
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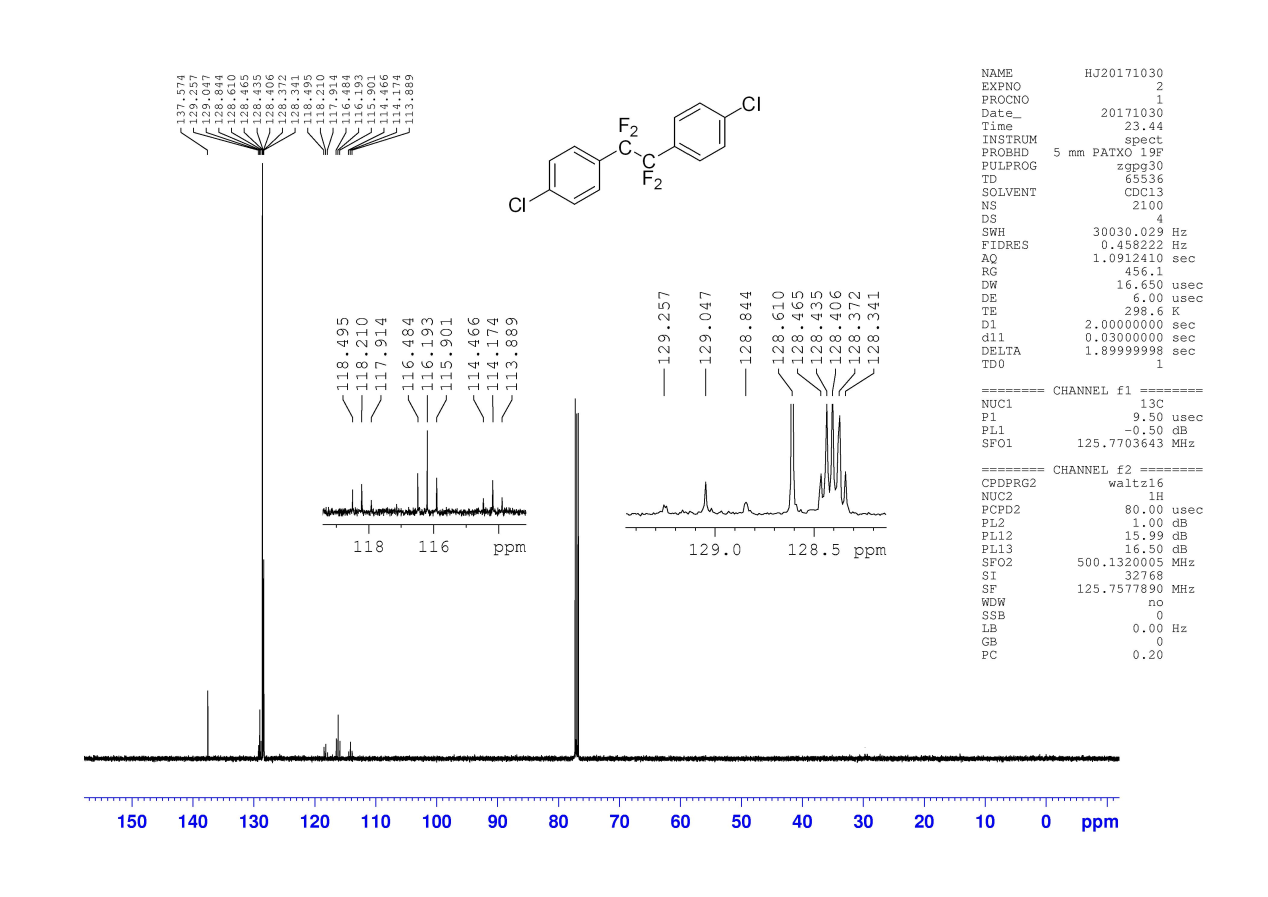
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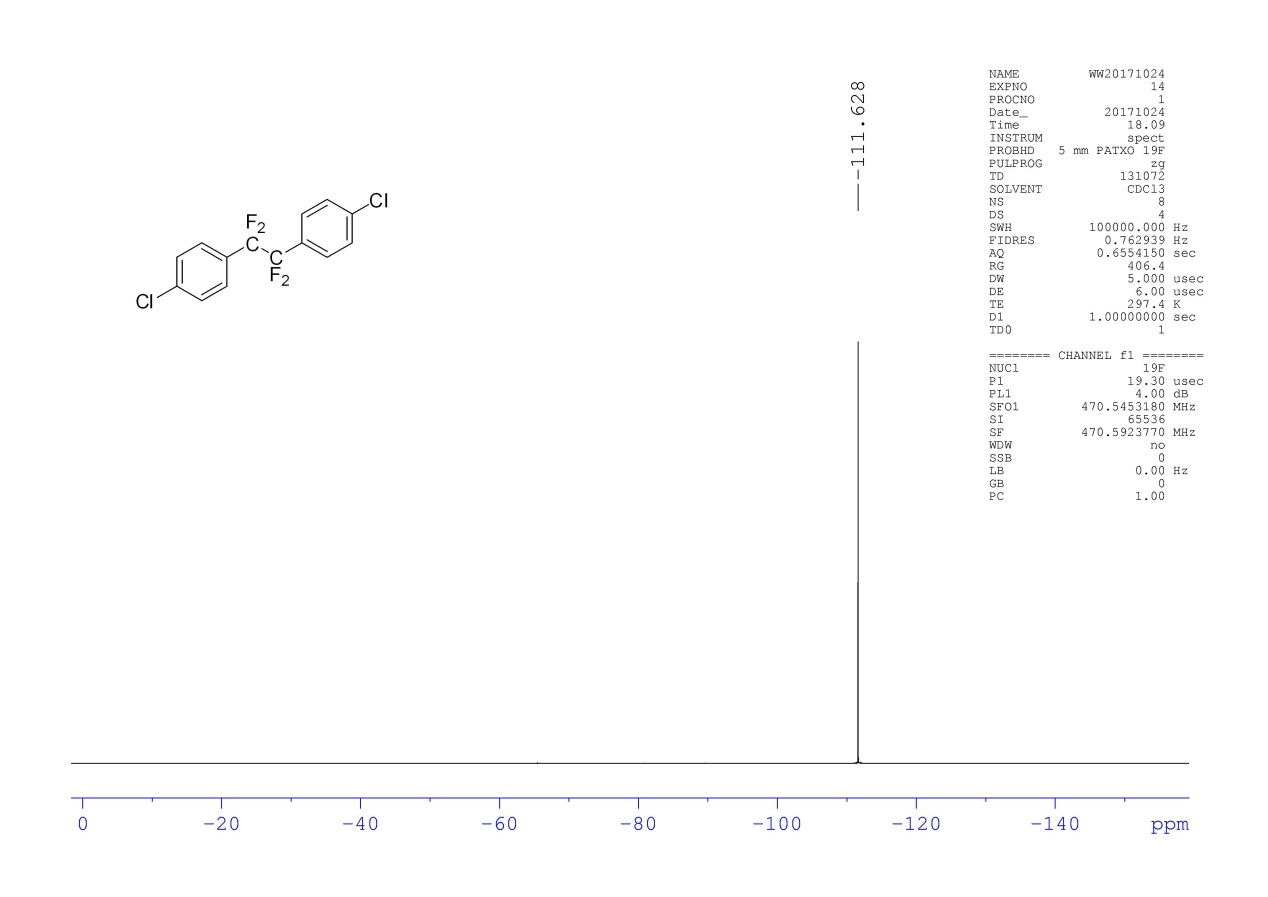
**1H NMR Spectra of 2e**

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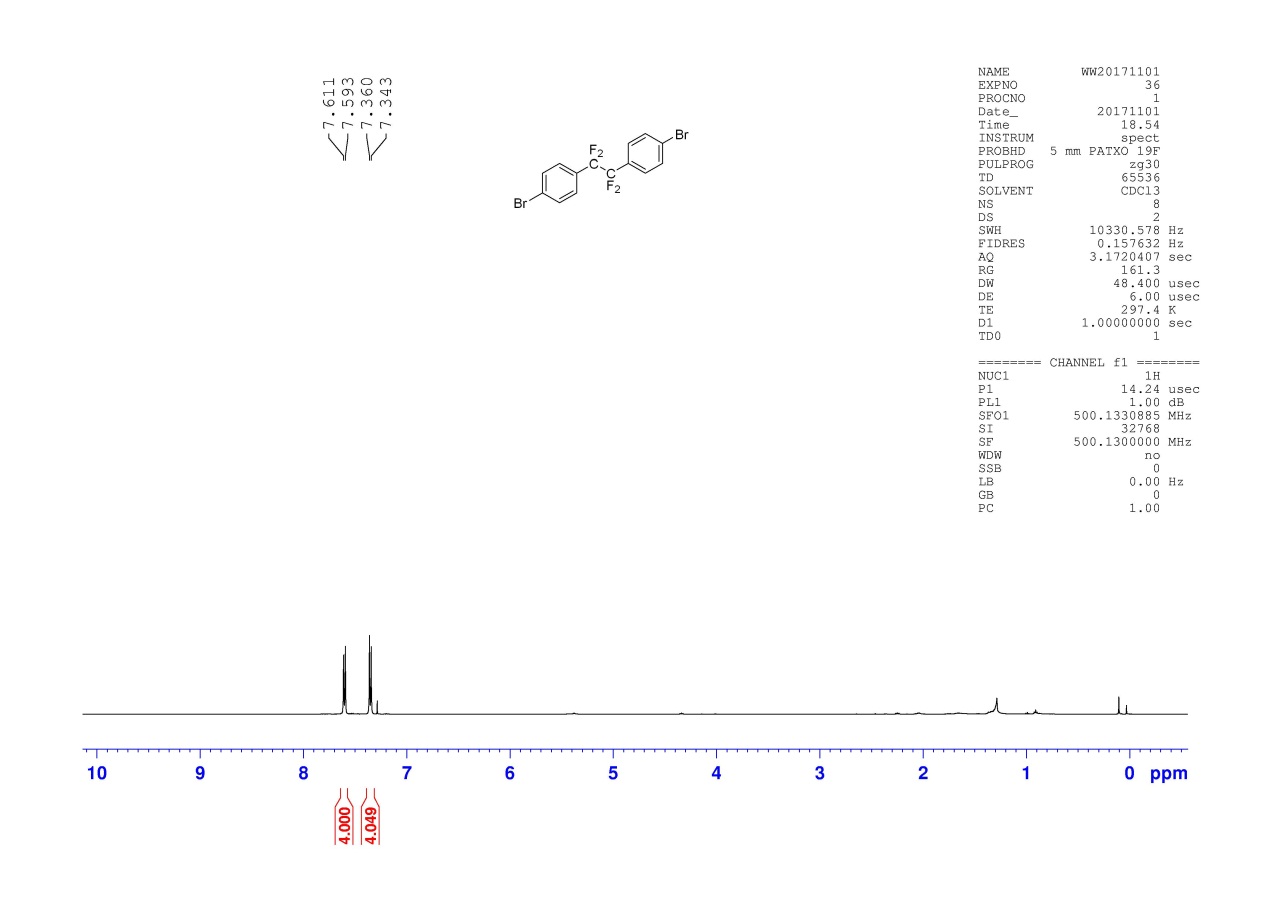
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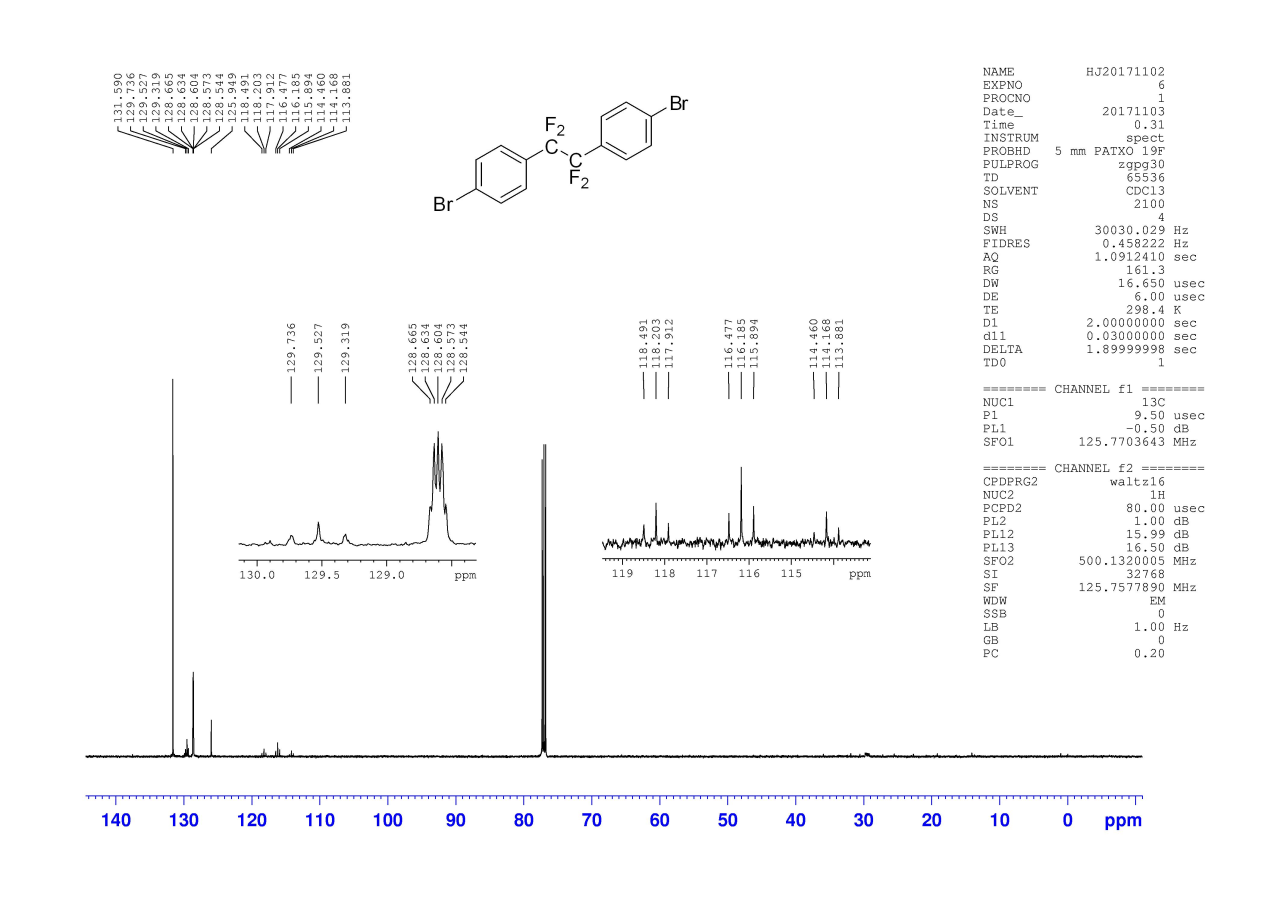
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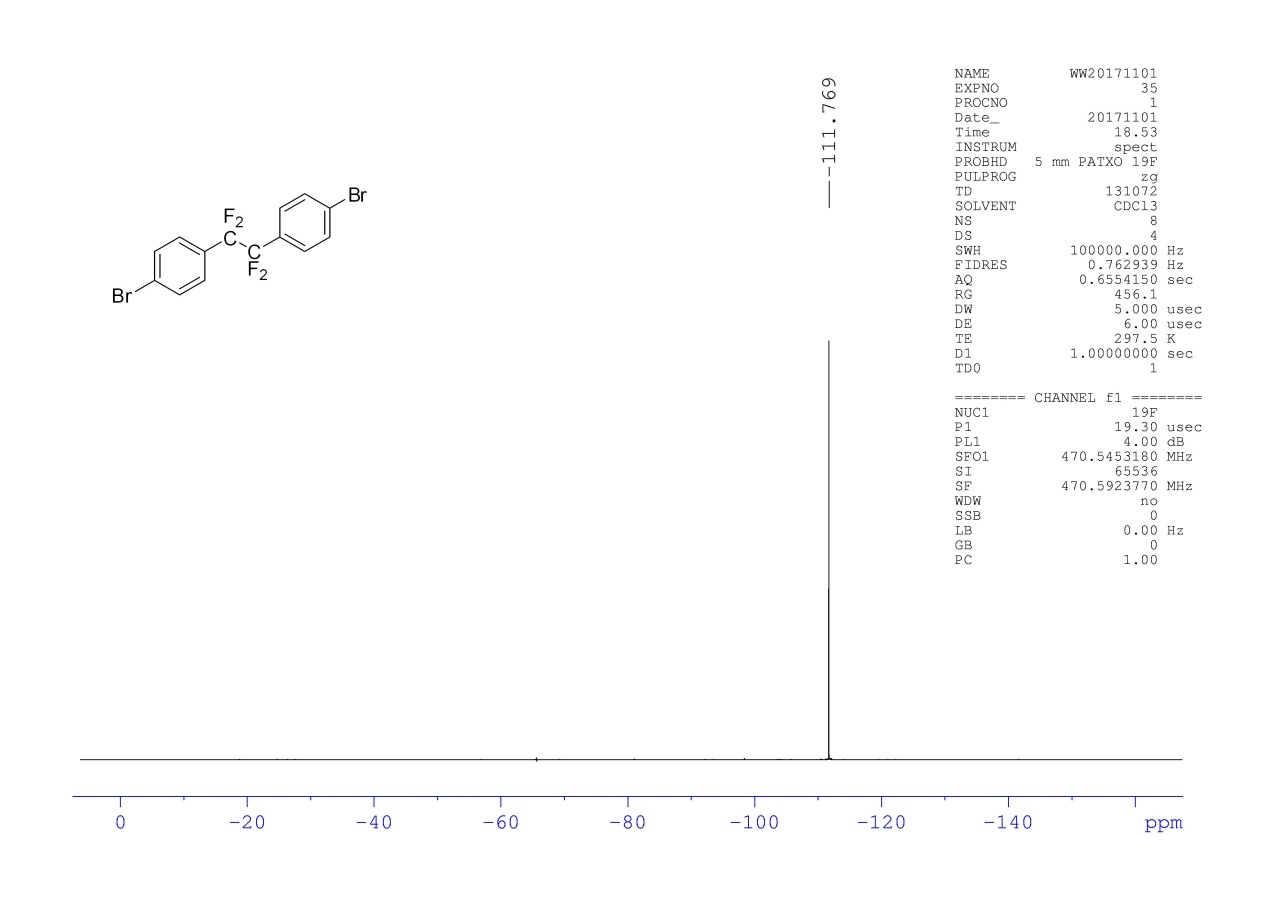
**1H NMR Spectra of 2f**

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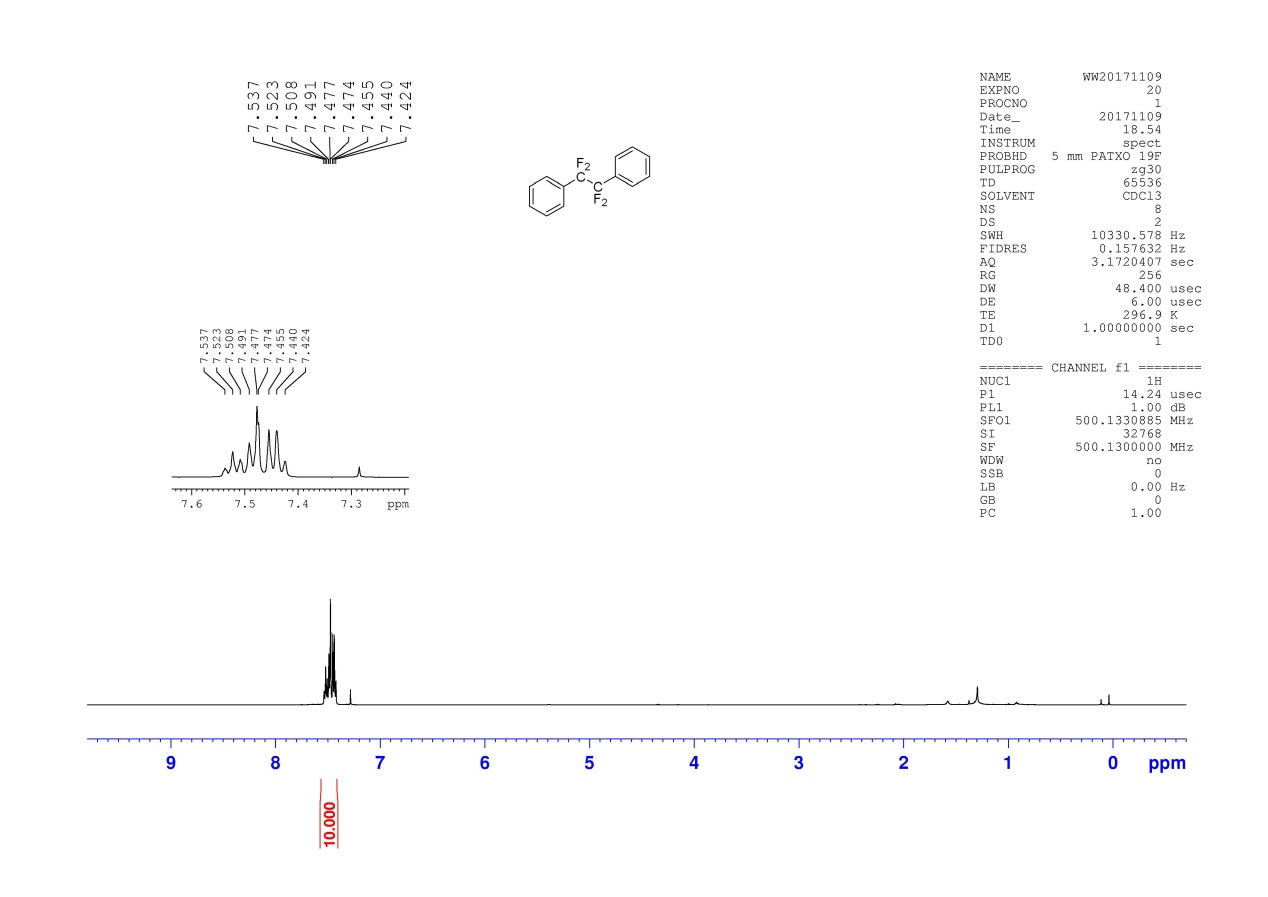
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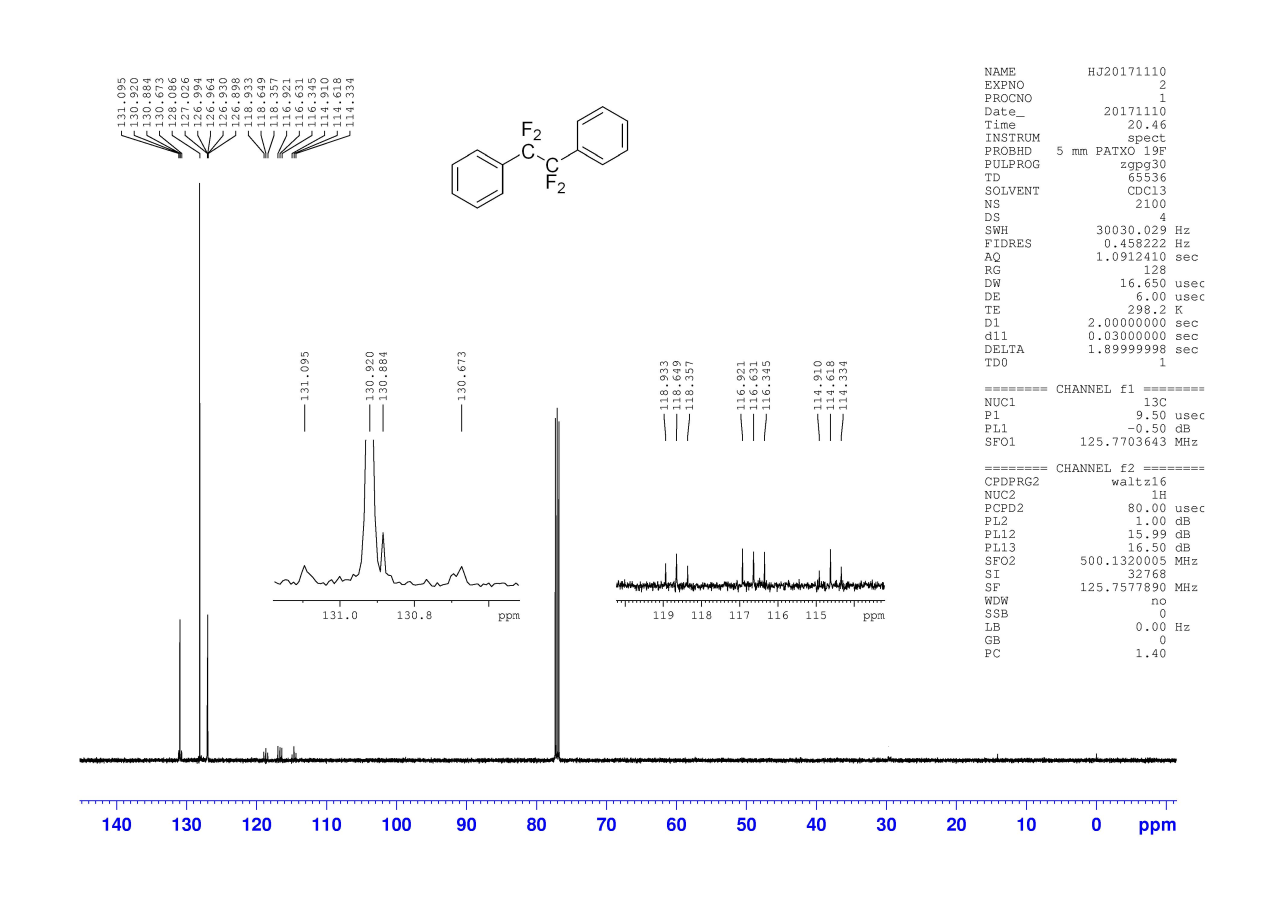
**19F NMR Spectra of 2f**

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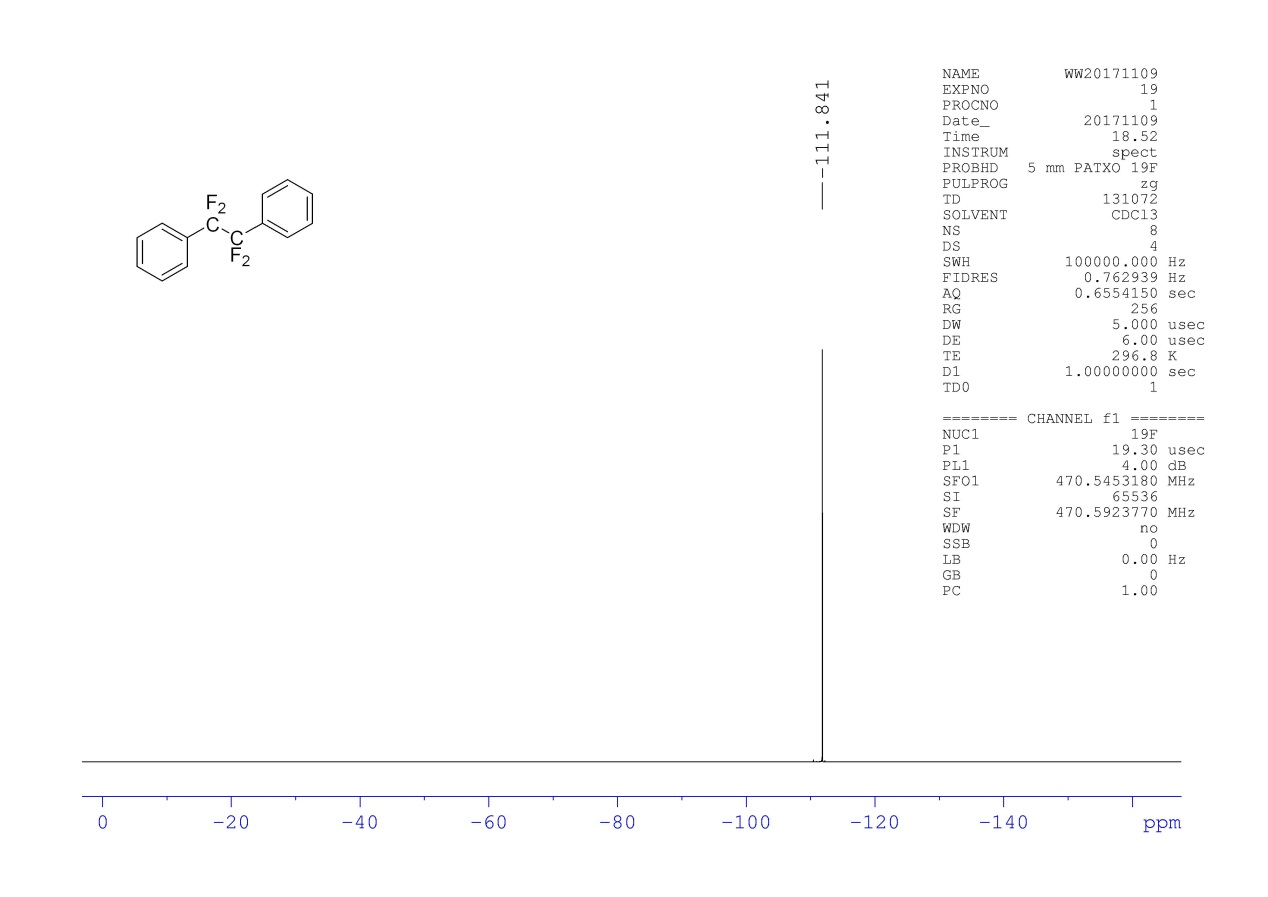
**1H NMR Spectra of 2h**

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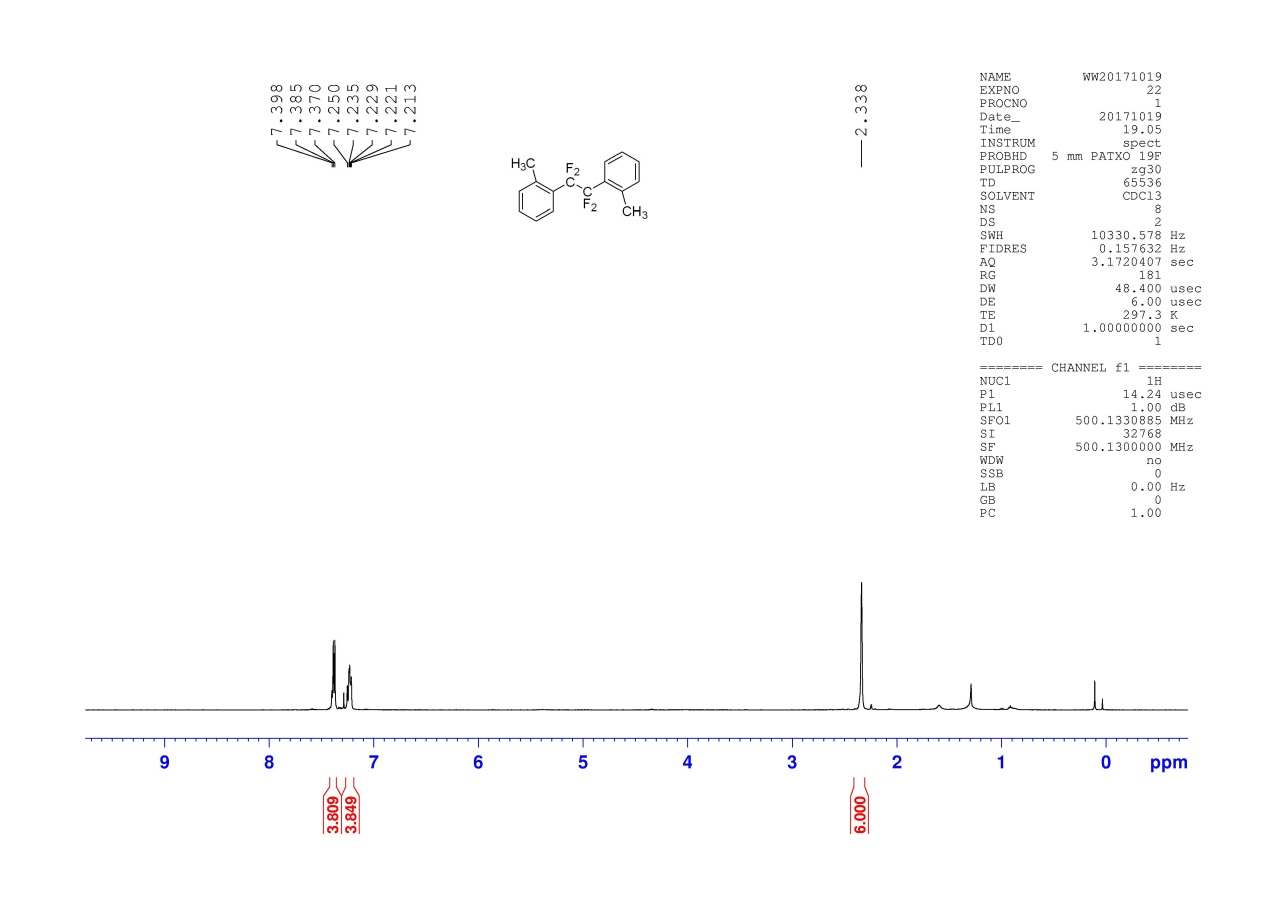
**13C NMR Spectra of 2h**

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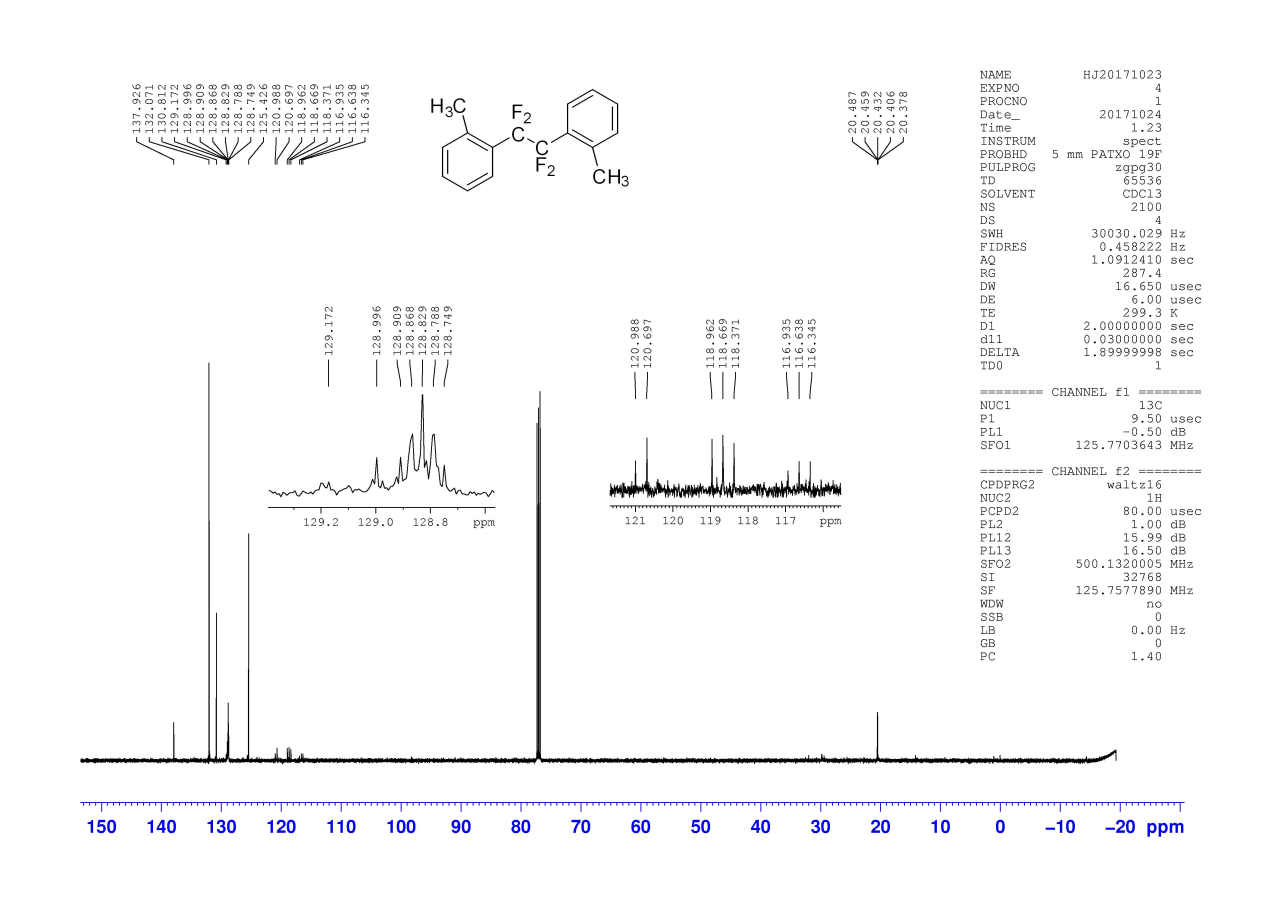
**19F NMR Spectra of 2h**

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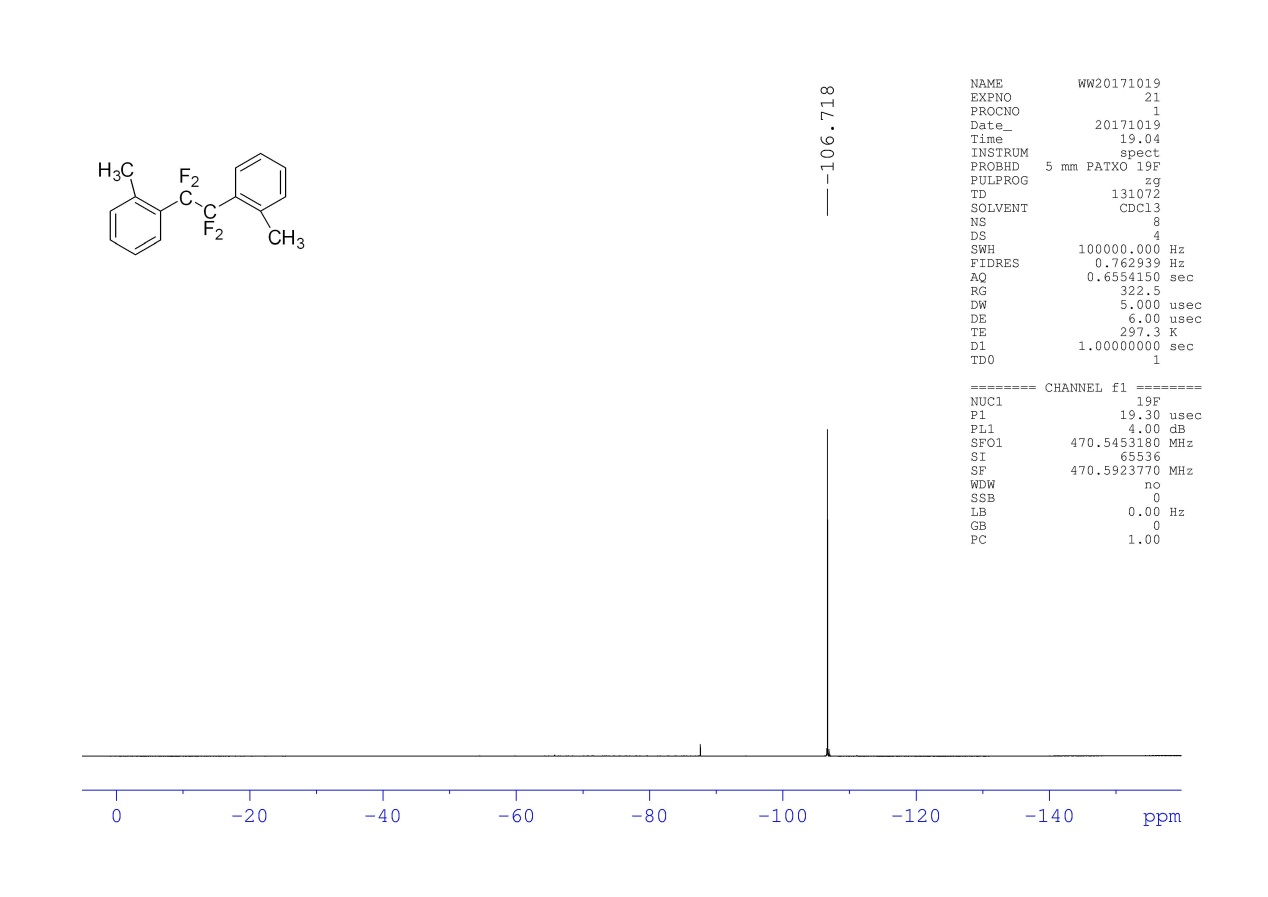
**1H NMR Spectra of 2i**

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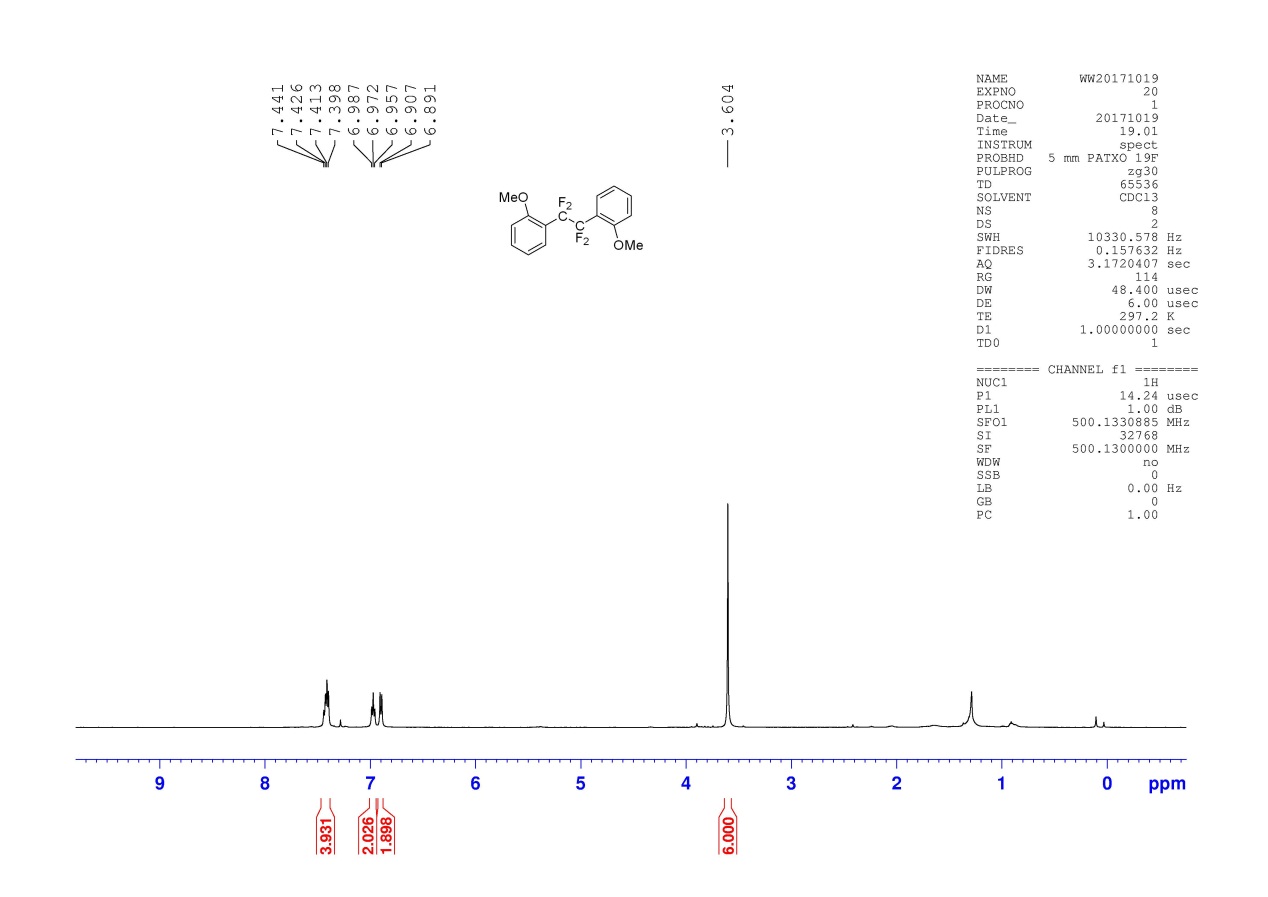
**13C NMR Spectra of 2i**

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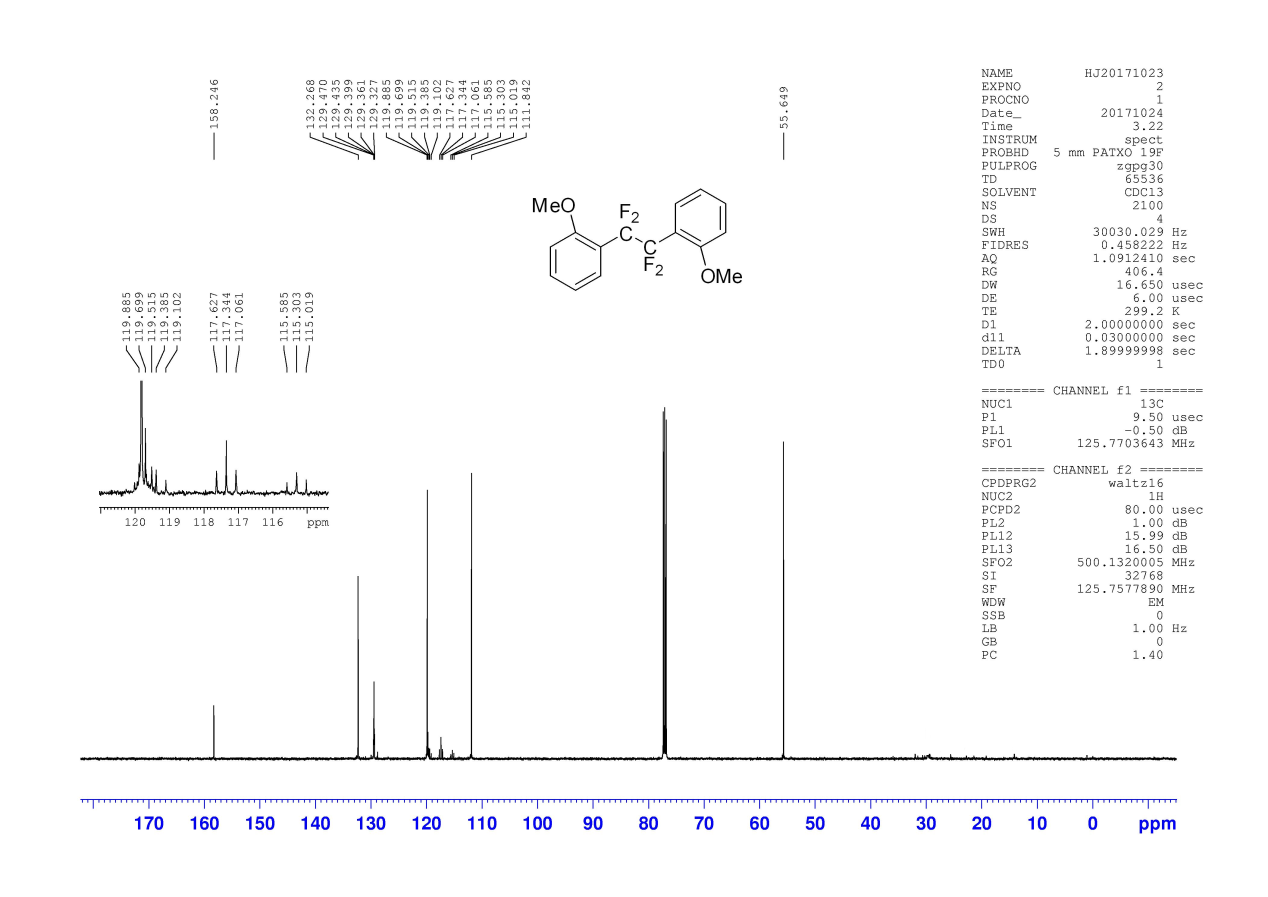
**19F NMR Spectra of 2i**

****

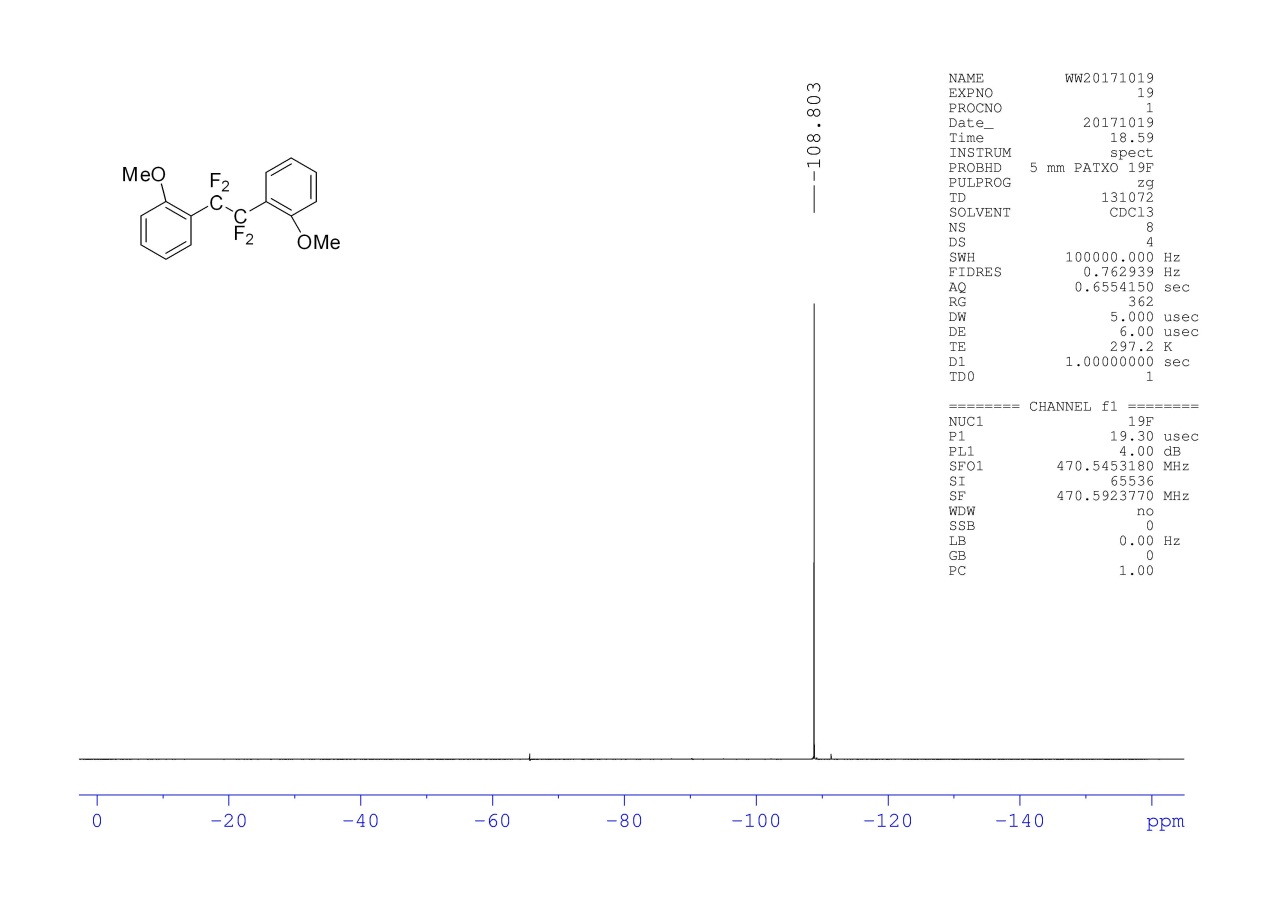
**1H NMR Spectra of 2j**

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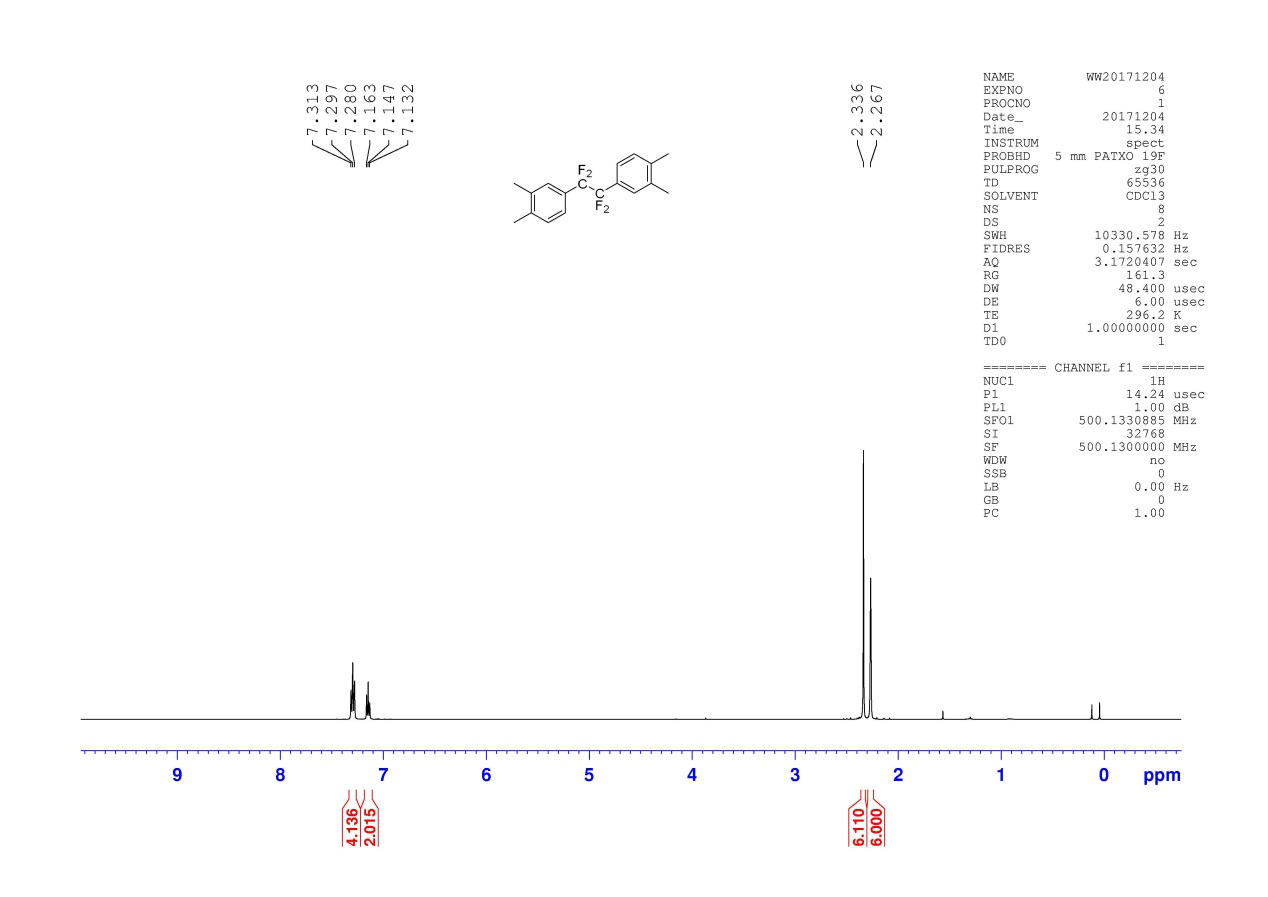
**13C NMR Spectra of 2j**

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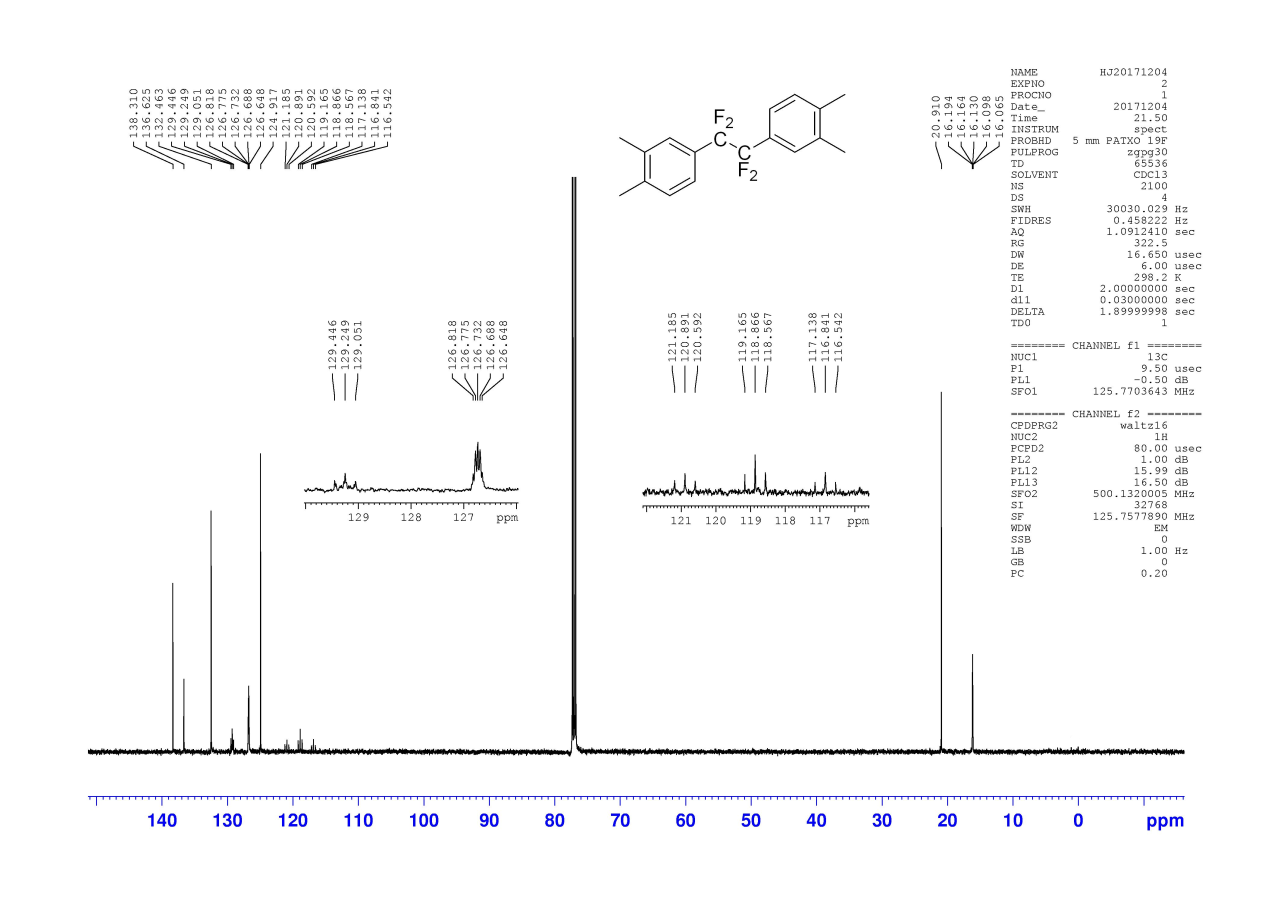
**19F NMR Spectra of 2j**

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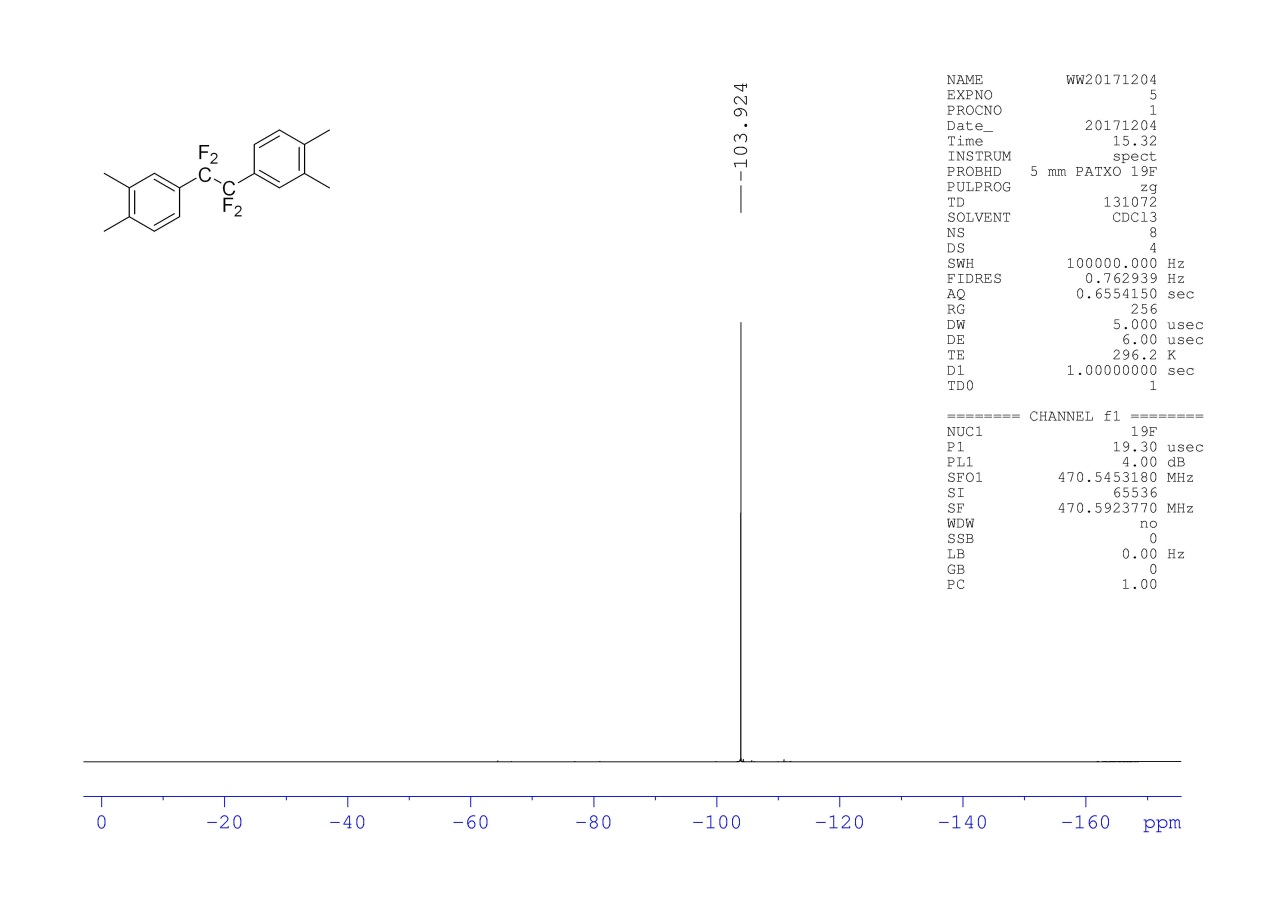
**1H NMR Spectra of 2k**

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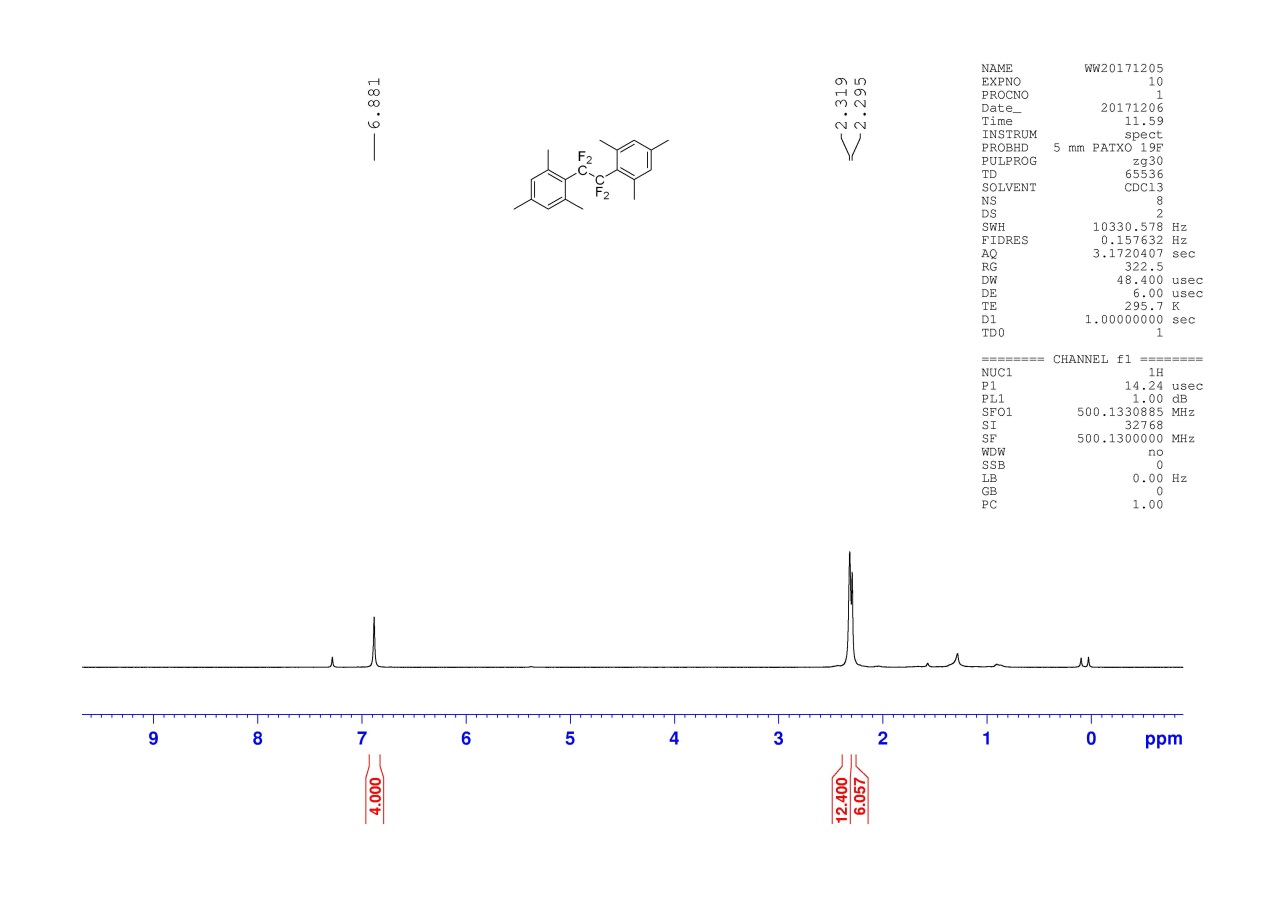
**13C NMR Spectra of 2k**

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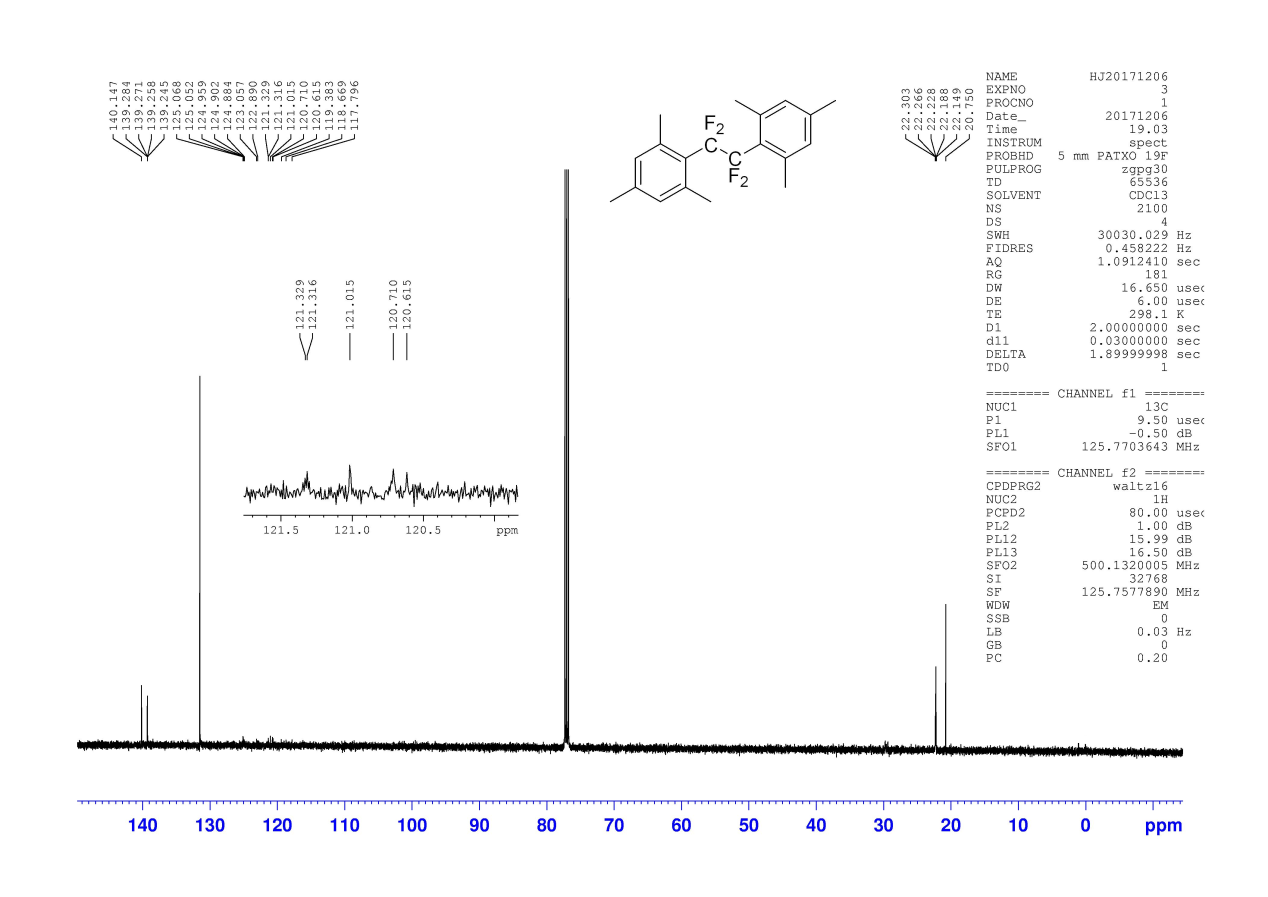
**19F NMR Spectra of 2k**

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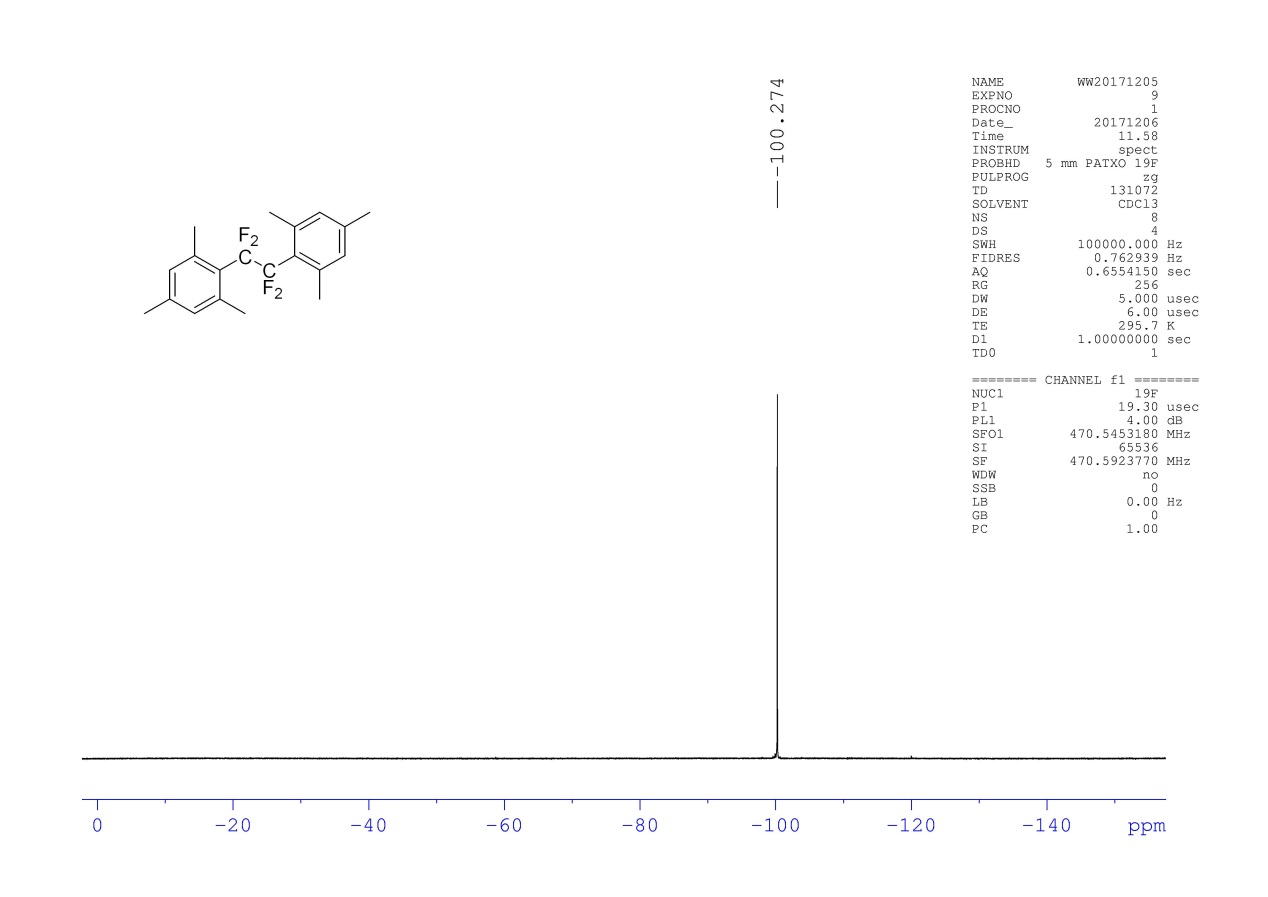
**1H NMR Spectra of 2l**

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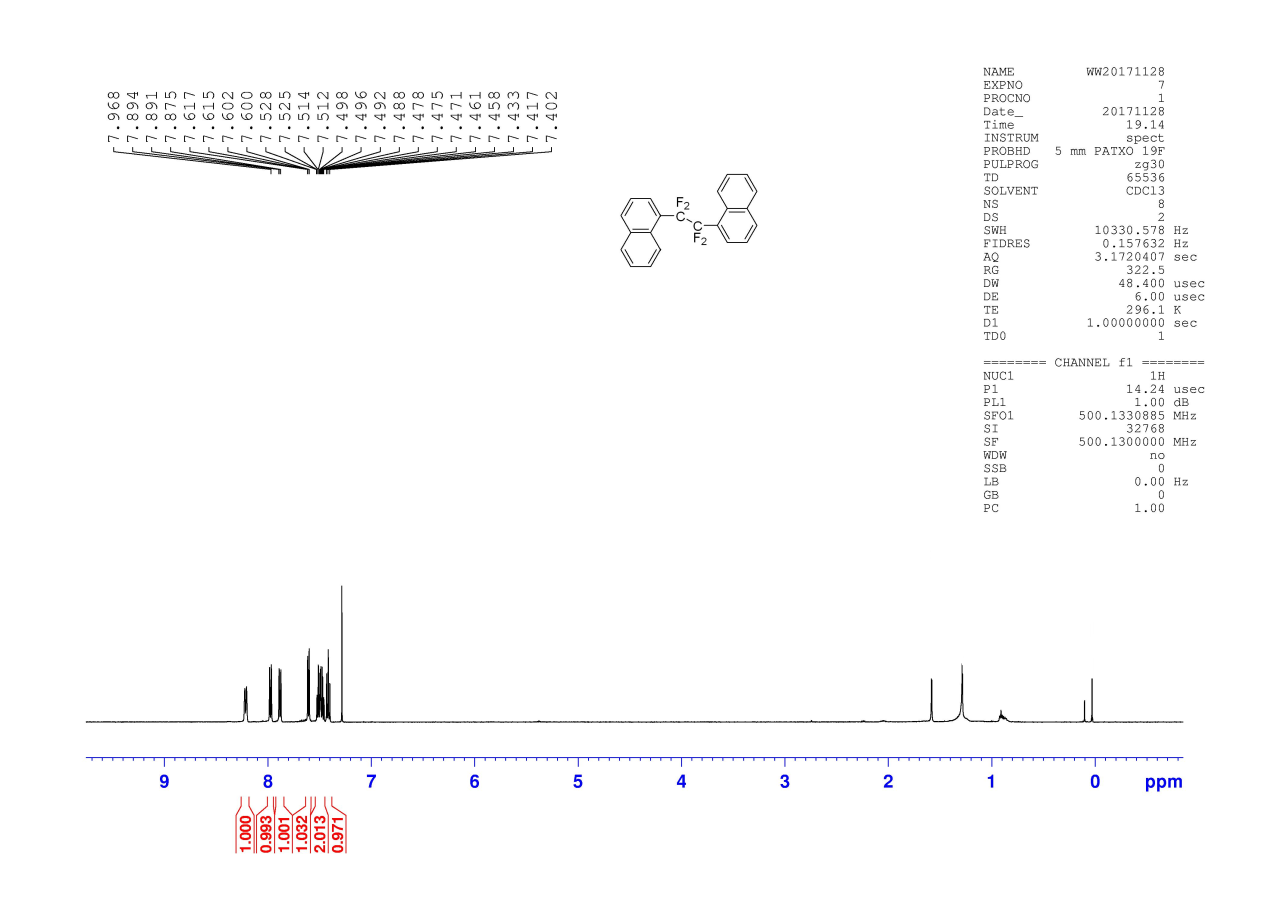
**13C NMR Spectra of 2l**

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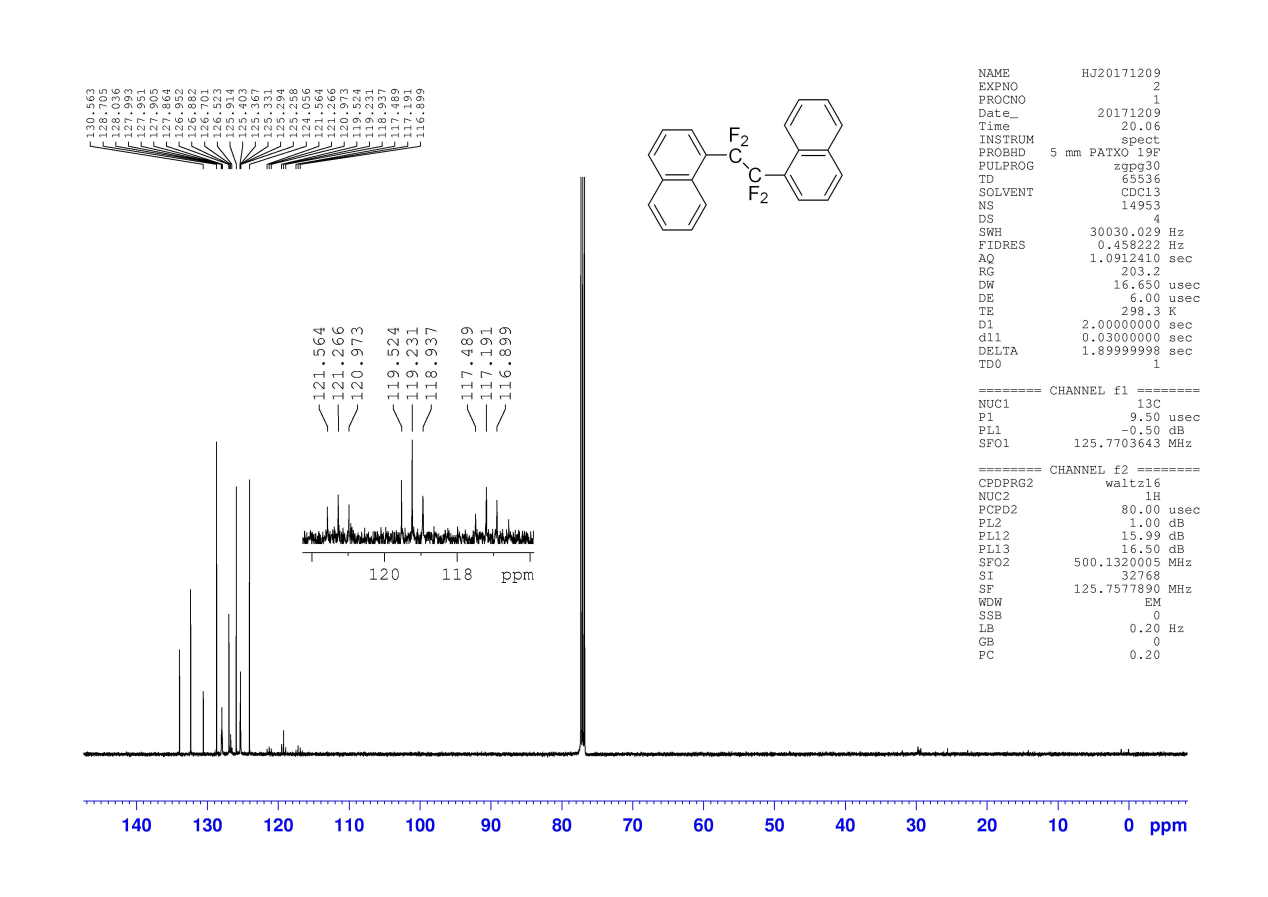
**19F NMR Spectra of 2l**

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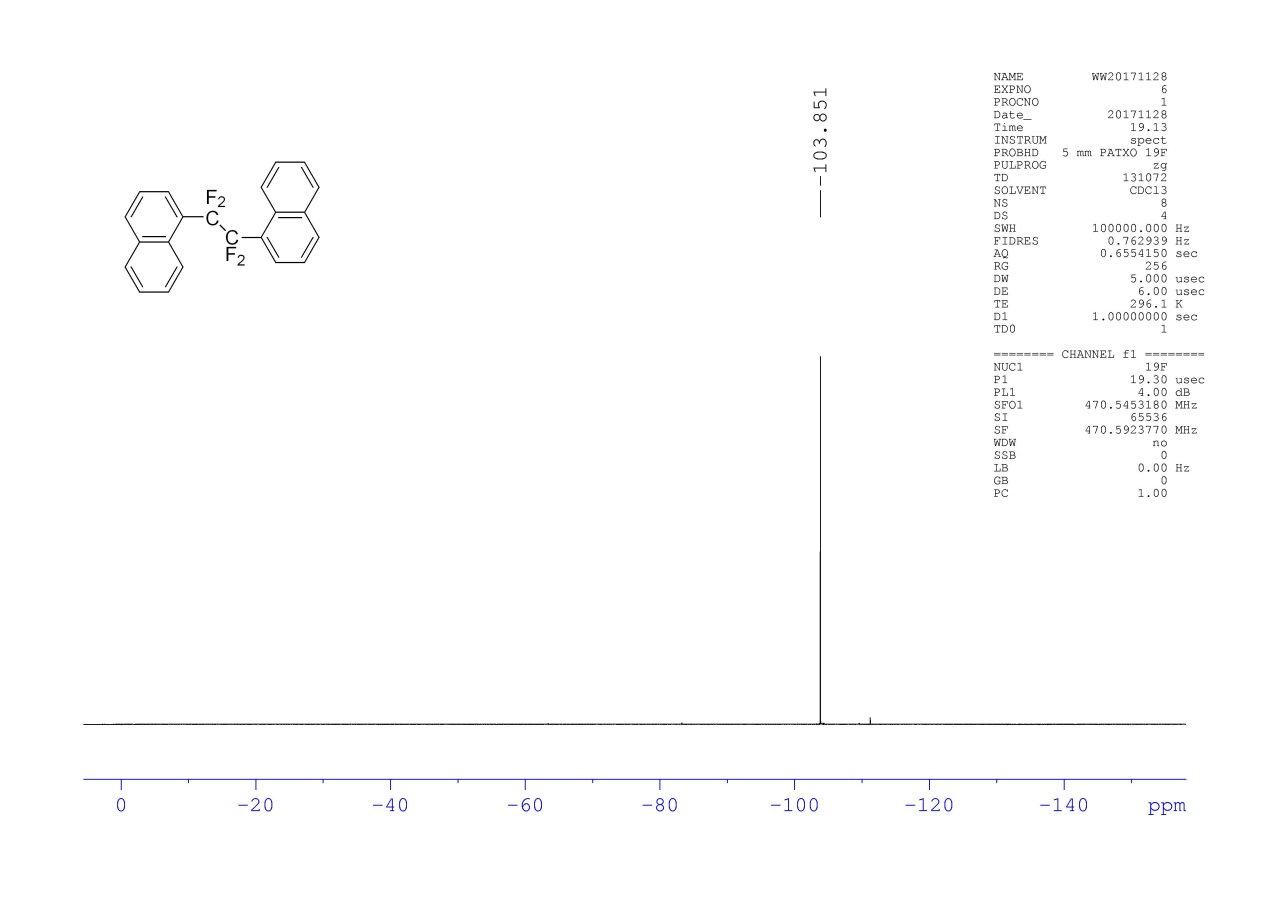
**1H NMR Spectra of 2m**

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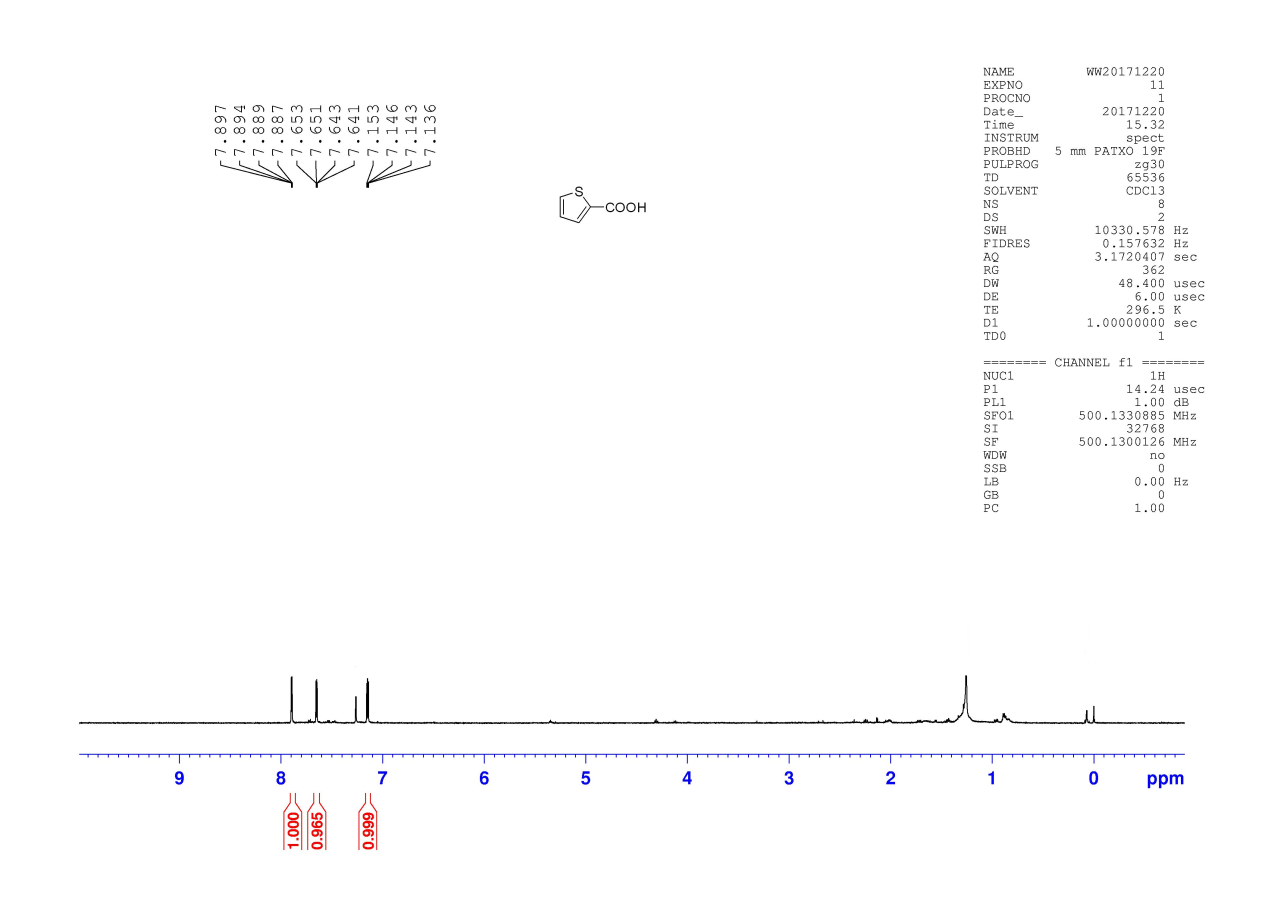
**13C NMR Spectra of 2m**

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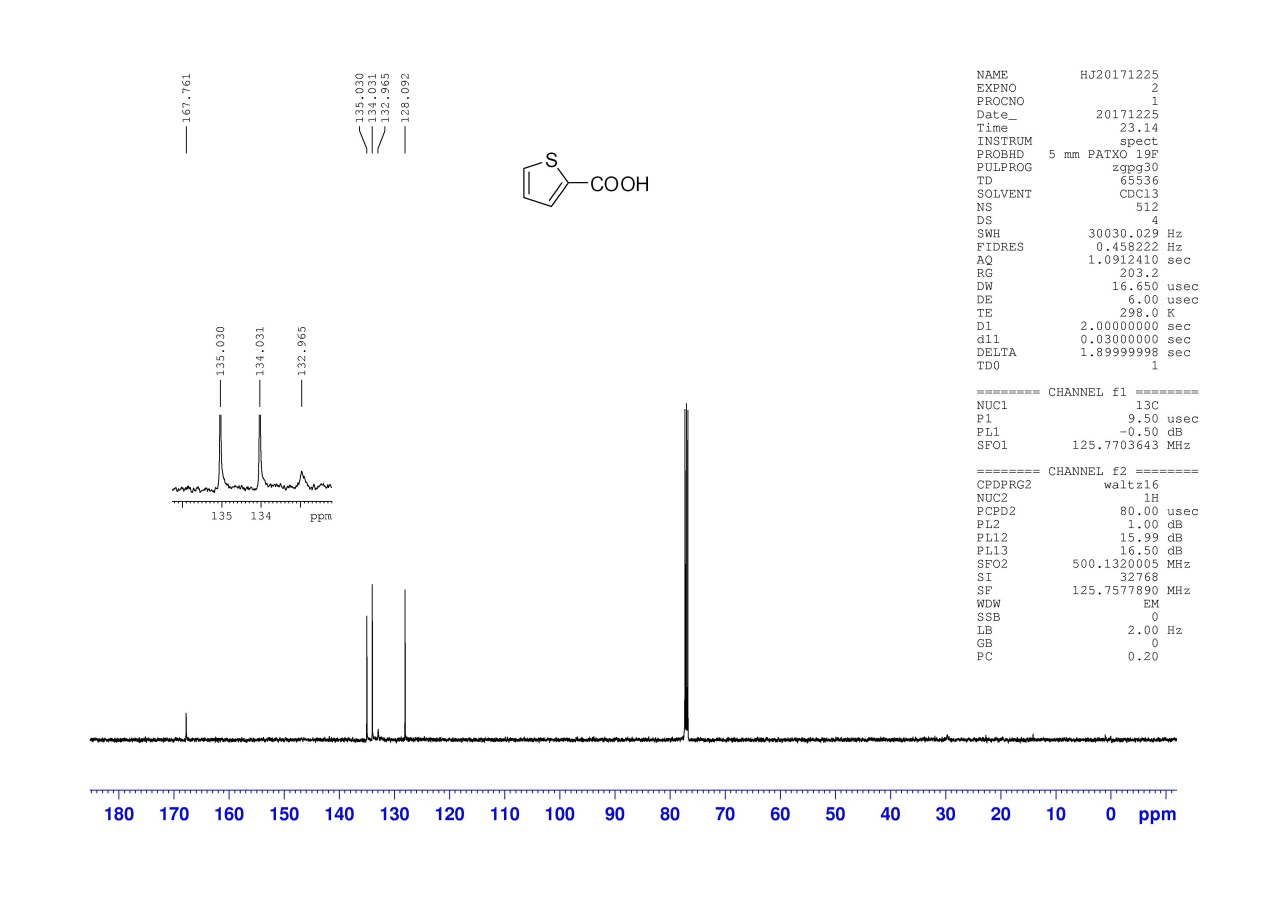
**19F NMR Spectra of 2m**

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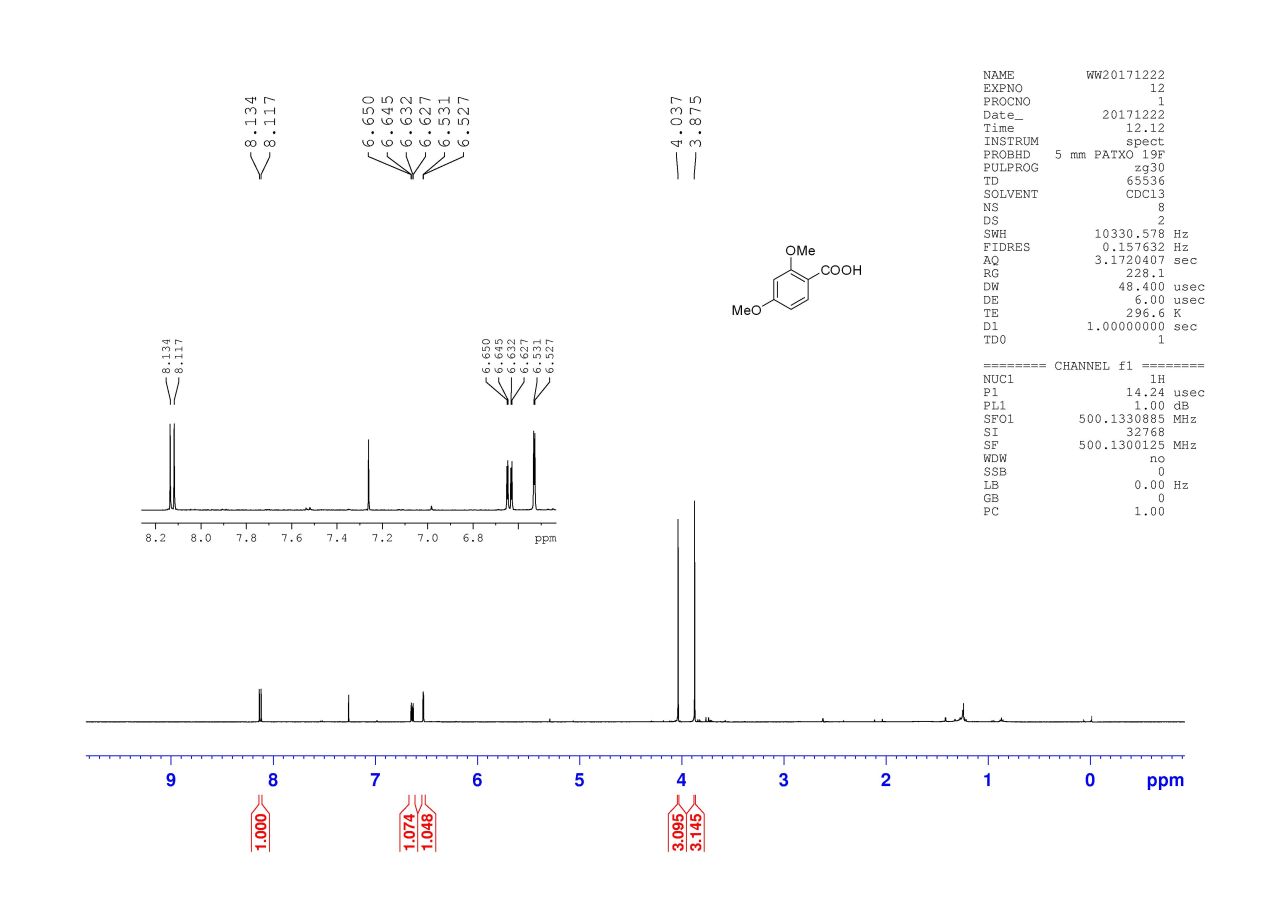
**1H NMR Spectra of 3n**

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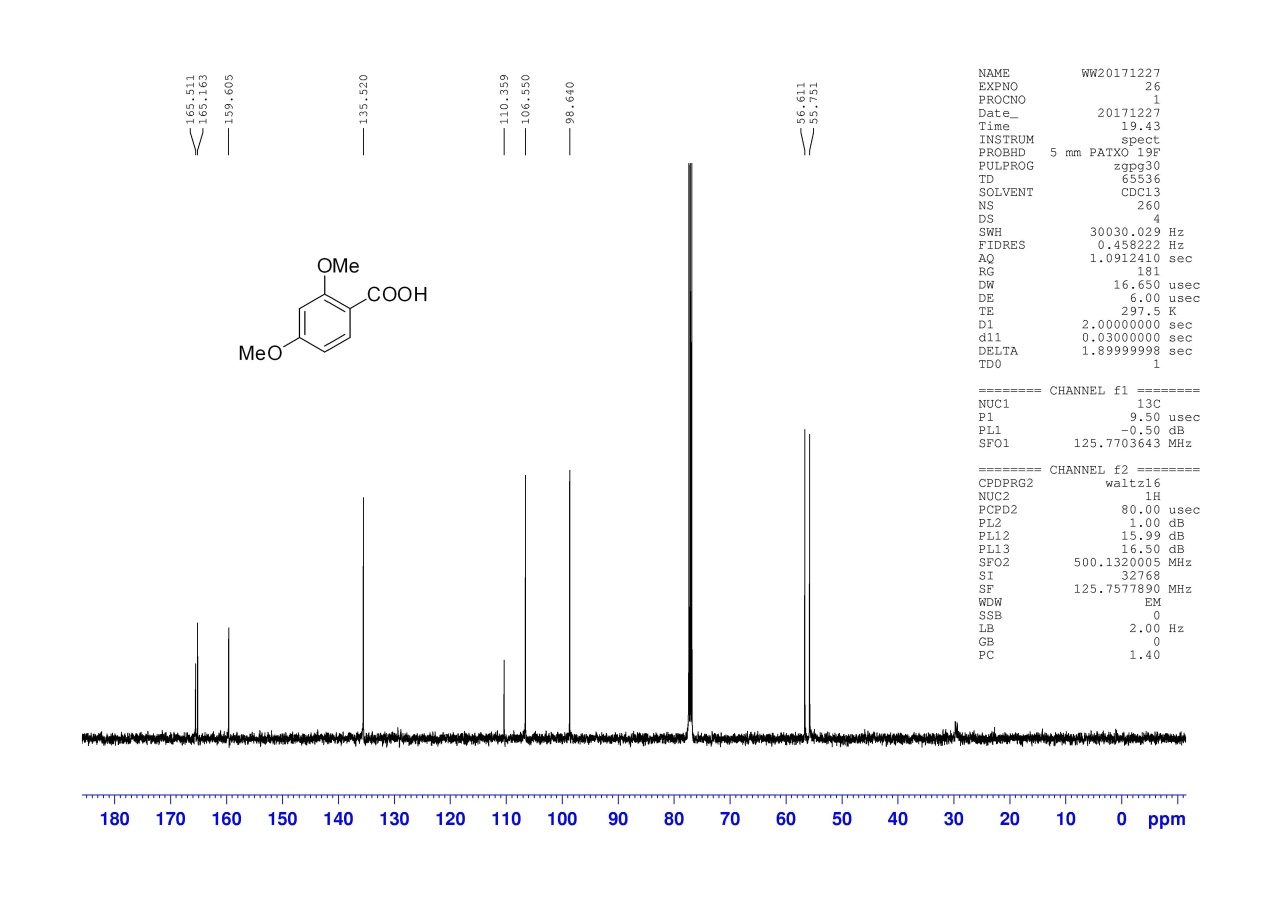
**13C NMR Spectra of 3n**

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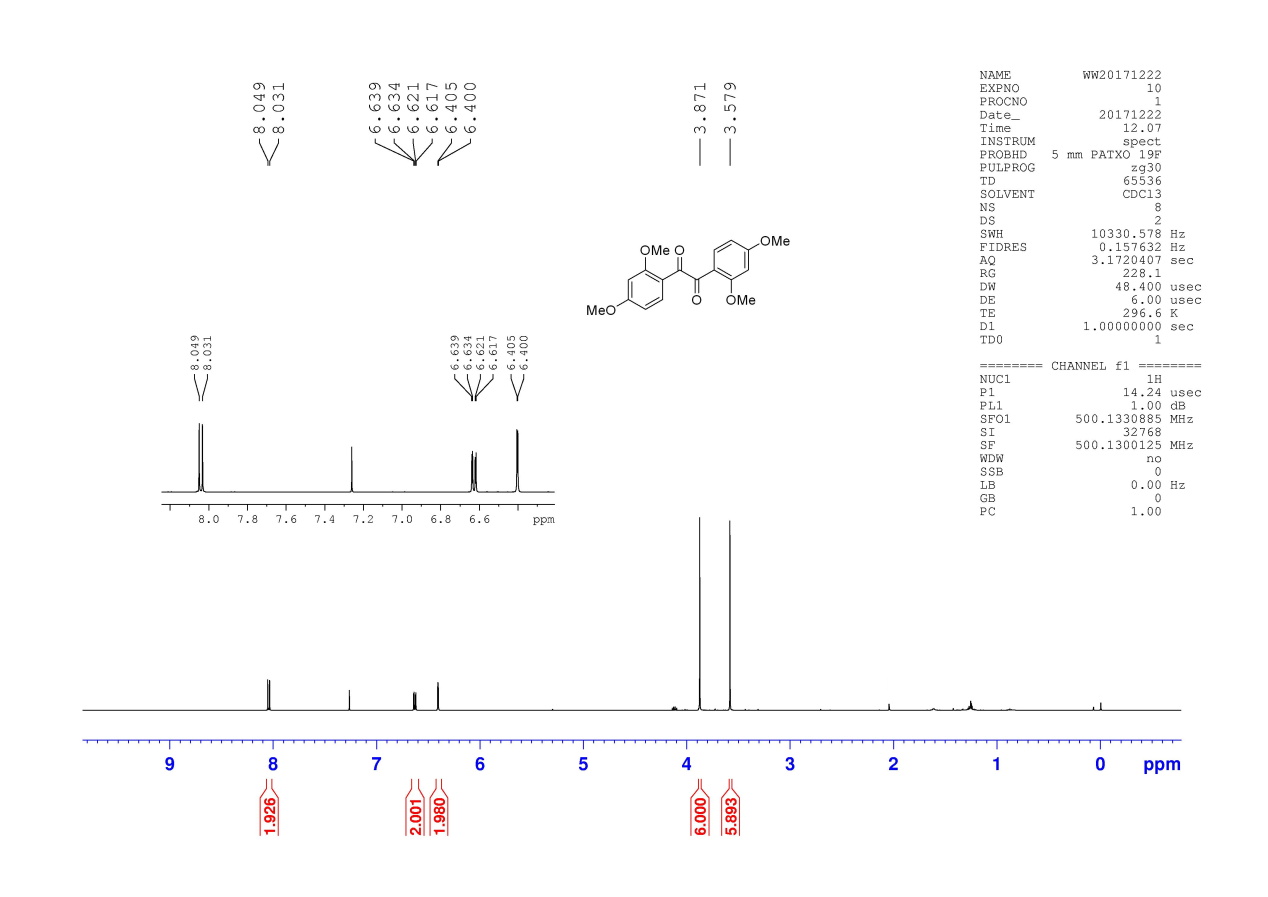
**1H NMR Spectra of 3o**

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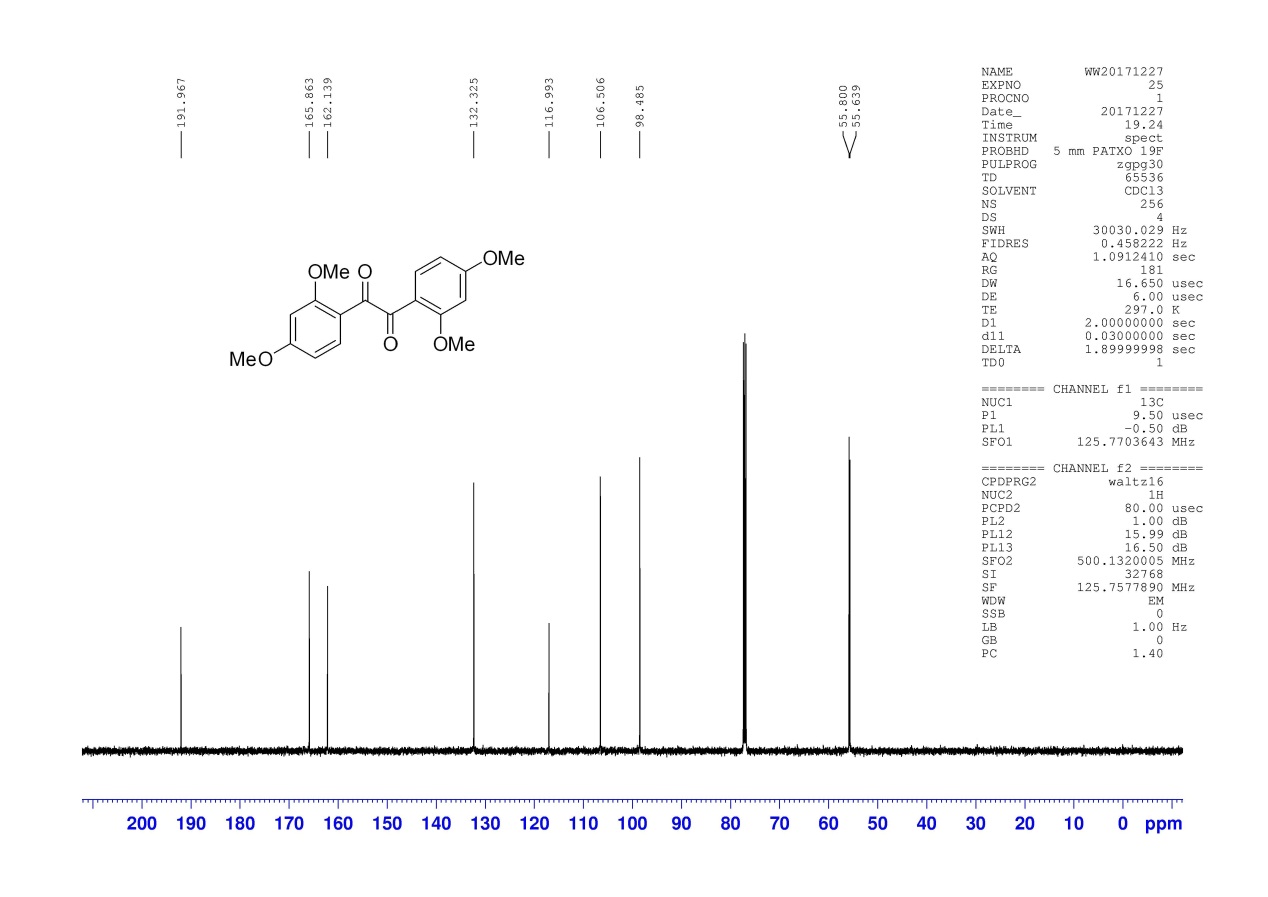
**13C NMR Spectra of 3o**

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**1H NMR Spectra of 4o**

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**13C NMR Spectra of 4o**

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**Reference**

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2. [M. E. Christy](https://pubs.acs.org/author/Christy%2C+Marcia+E.), [C. D. Colton](https://pubs.acs.org/author/Colton%2C+C.+Dylion), [M. Mackay](https://pubs.acs.org/author/Mackay%2C+Mary), [W. H. Staas](https://pubs.acs.org/author/Staas%2C+William+H.), [J. B. Wong](https://pubs.acs.org/author/Wong%2C+Julia+B.), [E. L. Engelhardt](https://pubs.acs.org/author/Engelhardt%2C+Edward+L.), [M. L. Torchiana](https://pubs.acs.org/author/Torchiana%2C+Mary+L.), [C. A. Stone](https://pubs.acs.org/author/Stone%2C+Clement+A.), J. Med. Chem. 1977, 20, 421- 430