Supporting Information

Copper-Mediated C-H Trifluoromethylation of Quinones

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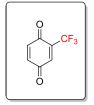
All manipulations were performed under air without using inert conditions and without degassing the solvents. Trifluoromethylating agent **1a** was prepared by a literature procedure from 2-iodobenzoic acid¹ and quinone **2j** was synthesized according to a literature procedure from 1,2,3-trimethoxybenzene.² All other chemicals were obtained from commercial sources and used as received. ¹H NMR, ¹³C NMR and ¹⁹F NMR spectra were recorded in CDCl₃ (internal standard: 7.26 ppm, ¹H; 77.16 ppm, ¹³C) or acetone-*d*6 (internal standard: 2.05 ppm, ¹H; 29.84 ppm, ¹³C), using 400 MHz spectrometers. High resolution mass data (HRMS) were obtained using ESI technique except for quinones **3i-k** for which APCI technique was used. For column chromatography, silica gel (35-70 microns) was used.

Warning! The new quinone-CF₃ compounds should be handled with care because of their unknown biological effects. Menadione (2b) itself has banned from the US market of food supplements by the FDA (US Food and Drug Administration) because of its potential toxicity in human use. Large doses of 2b may cause neonatal brain or liver damages in some rare cases.

Experimental Procedures and Spectral Data

General procedure for trifluoromethylation of quinones: To a 3 ml screwtop vial was added copper cyanide 4 (9.0 mg, 0.1 mmol, 1 equiv.), bis(pinacolato)diboron 5 (1.3 mg, 0,005 mmol, 5 mol%), reagent 1a (47.4 mg, 0.15 mmol, 1.5 equiv.) and the corresponding quinone 2 (0.1 mmol, 1 equiv.) in CDCl₃ (0.5 mL). The vial was equipped with a stirring bar, screwed shut and stirred at room temperature for 18 h. The products were isolated by column chromatography using pentane: dichloromethane systems as eluents.

2-(Trifluoromethyl)benzoquinone (3a)

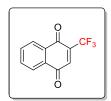


This compound was prepared according to the general procedure. The product was isolated as fine yellow crystals using pentane:dichloromethane, 1:3 as eluent system (16 mg, 89 %). The reaction was also performed at larger scale (ten times scale) than

described in the general procedure. In this case the reaction was performed according to the general procedure except 4 (90 mg, 1 mmol, 1 equiv.), 5 (13 mg,

0,05 mmol, 5 mol%), **1a** (474 mg, 1.5 mmol, 1.5 equiv.) and **2a** (109 mg, 1 mmol, 1 equiv.) in CDCl₃ (5 mL) were used in a 6 mL screwtop vial. The product was isolated as yellow crystals (128 mg, 72 %). N.B. This compound can easily sublimate, and therefore the drying in high vacuum should be avoided. **1H-NMR** (400 MHz, CDCl₃) δ 7.11 (br s, 1H), 6.89 (m, 2H); **19F-NMR** (376 MHz, CDCl₃) δ -65.89 (s); **13C-NMR** (100 MHz, CDCl₃) δ 185.6, 181.4, 137.1 (q, J_{CF} = 1.5 Hz), 136.5, 135.1 (q, J_{CF} = 31.5 Hz), 134.6 (q, J_{CF} = 4.9 Hz), 120.6 (q, J_{CF} = 274.5 Hz); **HRMS** (ESI): m/z calcd. for [C₇H₃F₃O₂+Na]⁺ 198.9977, found: 198.9982.

2-(Trifluoromethyl)-1,4-naphthoquinone (3b)



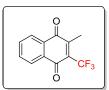
This compound was prepared according to the general procedure. The product was isolated as yellow crystals using pentane:dichloromethane, 1:1 as eluent system (17 mg, 76 %). The NMR data obtained for **3b** is in agreement with literature values.³

¹**H-NMR** (400 MHz, CDCl₃) δ 8.18 (m, 1H), 8.12 (m, 1H), 7.84 (m, 2H), 7.31(q, J_{HF} = 0.9 Hz, 1H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -65.51 (d, J_{HF} = 0.9 Hz); ¹³**C-NMR** (100 MHz, CDCl₃) δ 183.5, 179.6, 136.9, (q, J_{CF} = 4.9 Hz), 136.6 (q, J_{CF} = 30.7 Hz), 134.9, 134.7, 131.6 (q, J_{CF} = 1.4 Hz), 131.5, 127.1, 126.6, 120.9 (q, J_{CF} = 275.3 Hz); **HRMS** (ESI): m/z calcd. for $[C_{11}H_5F_3O_2+Na]^+$ 249.0134, found: 249.0130.

The previously reported synthesis of **3b** from **2b** was performed in four steps³:

(a) SnCl₂ (2.5 eq.), HCl (37%), EtOH, 10 min, RT; then (CH₃O)₂SO₂ (3.0 eq.), KOH (5.0 eq.) in MeOH, acetone, 2.5 h, 60 °C; (b) Br₂ (1.0 eq.), CHCl₃, 45 min, 0 °C, (c) CF₃COONa (3.0 eq.), CuI (2.0 eq.), DMA–toluene, 18 h, 145 °C. CAN (3.0 eq.), CH₃CN–H₂O, 15 min, r.t.

2-methyl-3-(Trifluoromethyl)-1,4-naphthoquinone (3c)

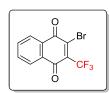


This compound was prepared according to the general procedure. The product was isolated as yellow crystals using pentane:dichloromethane, 1:1 as eluent system (17 mg, 71 %).

1H-NMR (400 MHz, CDCl₃) δ 8.07 (m, 2H), 7.76 (m, 2H), 2.40

 $(q, J_{HF} = 3.0 \text{ Hz}, 3\text{H}); ^{19}\text{F-NMR} (376 \text{ MHz}, \text{CDCl}_3) \delta -57.88 (q, J_{HF} = 3.0 \text{ Hz}); ^{13}\text{C-NMR} (100 \text{ MHz}, \text{CDCl}_3) \delta 183.8, 180.1, 148.8 (q, J_{CF} = 1.6 \text{ Hz}), 134.6, 134.1, 133.2 (q, J_{CF} = 28.0 \text{ Hz}), 131.7 (q, J_{CF} = 1.5 \text{ Hz}), 131.1, 126.8, 126.6, 122.7 (q, J_{CF} = 277.4 \text{ Hz}), 12.9 (q, J_{CF} = 3.6 \text{ Hz});$ **HRMS**(ESI): <math>m/z calcd. for $[C_{12}H_7F_3O_2+Na]^+$ 263.0290, found: 263.0281.

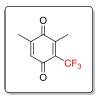
2-Bromo-3-(trifluoromethyl)-1,4-naphthoquinone (3d)



This compound was prepared according to the general procedure. The product was isolated as yellow crystals using pentane:dichloromethane, 1:1 as eluent system (20 mg, 67 %). 1 H-NMR (400 MHz, CDCl₃) δ 8.15 (m, 2H), 7.83 (m, 2H); 19 F-NMR

 $(376 \text{ MHz}, \text{CDCl}_3) \delta$ -59.34 (s); ¹³C-NMR (100 MHz, CDCl₃) δ 177.9, 176.6, 142.3 (q, J_{CF} = 1.7 Hz), 136.9 (q, J_{CF} = 29.4 Hz), 135.3, 134.6, 131.4 (q, J_{CF} = 1.2 Hz), 129.9, 128.0, 127.4, 121.1 (q, J_{CF} = 278.6 Hz); **HRMS** (ESI): m/z calcd. for $[C_{11}H_4BrF_3O_2+Na]^+$ 326.9239, found:326.9234.

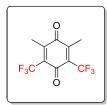
3,5-Dimethyl-2-(trifluoromethyl)-1,4-benzoquinone (3e)



This compound was prepared according to the general procedure except that 1 mL of CDCl₃ was used. The product was isolated as yellow crystals using pentane:dichloromethane, 1:1 as eluent system (14 mg, 72 %). ¹**H-NMR** (400 MHz, CDCl₃) δ 6.63 (q, J_{HH} = 1.5

Hz, 1H), 2.29 (q, J_{HF} = 3.2 Hz, 3H), 2.09 (d, J_{HH} =1.5 Hz, 3H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -57.74 (q, J_{HF} = 3.2 Hz); ¹³**C-NMR** (100 MHz, CDCl₃) δ 186.6, 181.9, 146.5 (q, J_{CF} = 1.8 Hz), 145.6, 133.8 (q, J_{CF} = 1.5 Hz), 130.9 (q, J_{CF} = 28.5 Hz), 122.1 (q, J_{CF} = 277.5 Hz), 15.9, 12.64 (q, J_{CF} = 3.4 Hz); **HRMS** (ESI): m/z calcd. for $[C_9H_7F_3O_2+Na]^+$ 227.0296, found: 227.0290.

2,6-Dimethyl-3,5-bis(trifluoromethyl)-1,4-benzoquinone (3f)



This compound was prepared according to the general procedure except that the amounts of the reactants were changed; 95 mg (0.3

mmol, 3 equiv.) of **1a**, 18 mg (0.2 mmol) of CuCN **4** and 2.5 mg (0.010 mmol, 10 mol%) of B₂pin₂ **5** was used. The product was isolated as yellow crystals using pentane:dichloromethane, 1:1 as eluent system (13 mg, 50 %). ¹**H-NMR** (400 MHz, CDCl₃) δ 2.33 (q, J_{HF} = 3.0 Hz, 6H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -57.90 (q, J_{HF} = 3.0 Hz); ¹³**C-NMR** (100 MHz, CDCl₃) δ 185.4, 177.1, 146.4, 131.7 (q, J_{CF} = 29.7 Hz), 121.6 (q, J_{CF} = 278.2 Hz), 12.9 (q, J_{CF} = 3.3 Hz); **HRMS** (ESI): m/z calcd. for [C₁₀H₆F₆O₂+Na]⁺ 295.0164, found: 295.0163.

2,5-Dimethyl-3-(trifluoromethyl)-1,4-benzoquinone (3g)



This compound was prepared according to general procedure except 0.2 mmol of quinone **2f**, 0.2 mmol of CuCN **4**, 0.01 mmol of B₂Pin₂ **5** and 0.15 mmol **1a** was used. The yield is based on the amount of **1a** used in this reaction. Product was isolated as yellow crystals using

pentane:dichloromethane, 1:1 as eluent system (24 mg, 77 %). ¹**H-NMR** (400 MHz, CDCl₃) δ 6.73 (q, J_{HH} = 1.6 Hz, 1H), 2.26 (q, J_{HF} = 3.3 Hz, 3H), 2.09 (d, J_{HH} = 1.6 Hz, 3H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -58.29 (q, J_{HF} = 3.3 Hz); ¹³**C-NMR** (100 MHz, CDCl₃) δ 185.7, 183.0, 146.7 (q, J_{CF} = 1.5 Hz), 146.5 (q, J_{CF} = 1.8 Hz), 133.1, 131.6 (q, J_{CF} = 28.5 Hz), 122.4 (q, J_{CF} = 277.6 Hz), 15.9, 12.4 (q, J_{CF} = 3.5 Hz); **HRMS** (ESI): m/z calcd. for $[C_9H_7F_3O_2+Na]^+$ 227.0290, found: 227.0288.

2,5-Dimethyl-3,6-bis(trifluoromethyl)-1,4-benzoquinone (3h)



This compound was prepared according to the general procedure except 95 mg (0.3 mmol, 3 equiv.) of $\bf{1a}$, 18 mg (0.2 mmol) of CuCN $\bf{4}$ and 2.5 mg (0.010 mmol, 10 mol%) of B_2pin_2 $\bf{5}$ was used. The

product was isolated as yellow crystals using pentane:dichloromethane, 1:1 as eluent system (14 mg, 49 %). ¹**H-NMR** (400 MHz, CDCl₃) δ 2.33 (q, J_{HF} = 3.1 Hz, 6H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -58.82 (q, J_{HF} = 2.8 Hz); ¹³**C-NMR** (100 MHz, CDCl₃) δ 181.1, 147.3 (app. pent., J_{CF} = 1.6 Hz), 131.8 (q, J_{CF} = 29.6 Hz), 121.9 (q, J_{CF} = 277.6 Hz), 12.7 (q, J_{CF} = 3.5 Hz); **HRMS** (ESI): m/z calcd. for [C₁₀H₆F₆O₂+Na]⁺ 295.0164, found: 295.0154.

2-Chloro-3-(trifluoromethyl)-1,4-benzoquinone (3i)

This compound was prepared according to general procedure. The product was isolated as yellow crystals using pentane:dichloromethane, 2:1 as eluent system (17 mg, 63 %). 1 H-NMR (400 MHz, CDCl₃) δ 7.03 (d, J_{HH} = 10.1 Hz, 1H), 6.91 (d, J_{HH}

= 10.1 Hz, 1H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -58.87 (s); ¹³**C-NMR** (100 MHz, CDCl₃) δ 179.7, 177.5, 145.2 (q, J_{CF} = 1.8 Hz), 137.5 (q, J_{CF} = 1.2 Hz), 135.3, 131.4 (q, J_{CF} = 30.1 Hz), 120.6 (q, J_{CF} = 278.0 Hz); **HRMS** (APCI): m/z calcd. for [C₇H₂ClF₃O₂] 217.9701, found: 217.9700.

3,5-Dichloro-2-(trifluoromethyl)-1,4-benzoquinone (3j)

This compound was prepared according to general procedure except 0.2 mmol of quinone **2h**, 0.2 mmol of CuCN, 0.01 mmol of B₂Pin₂ **5** and 0.1 mmol **1a** was used. Yield was calculated based on reagent **1a**. Product was isolated as yellow crystals using

pentane:dichloromethane, 1:1 as eluent system (15 mg, 58 %). ¹**H-NMR** (400 MHz, CDCl₃) δ 7.11 (s, 1H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -58.84 (s); ¹³**C-NMR** (100 MHz, CDCl₃) δ 177.5, 171.9, 144.9 (q, J_{CF} = 1.7 Hz), 142.9, 134.3 (q, J_{CF} = 1.3 Hz), 131.4 (q, J_{CF} = 30.5 Hz), 120.4 (q, J_{CF} = 278.1 Hz); **HRMS** (APCI): m/z calcd. for [C₇HCl₂F₃O₂]⁻ 243.9311, found: 243.9320.

2,6-Dichloro-3,5-bis(trifluoromethyl)-1,4-benzoquinone (3k)



This compound was prepared according to the general procedure except 95 mg (0.3 mmol, 3 equiv.) of 1a, 18 mg (0.2 mmol) CuCN 4 and 2.5 mg (0.010 mmol, 10 mol%) of B_2pin_2 5 was added. The

product was isolated as off-white crystals using pentane:dichloromethane, 1:1 as eluent system (25 mg, 77 %). ¹⁹**F-NMR** (376 MHz, acetone- d_6) δ -60.00 (s); ¹³**C-NMR** (100 MHz, acetone- d_6) δ 175.16, 172.39, 145.2 (q, J_{CF} = 1.9 Hz), 132.2 (qq, J_{CF} = 30.3, 1.6 Hz), 121.6 (q J_{CF} = 276.8 Hz); **HRMS** (APCI): m/z calcd. for [C₈Cl₂F₆O₂] 311.9185, found: 311.9199.

2,5-Dichloro-3-(trifluoromethyl)-1,4-benzoquinone (3l)

This compound was prepared according to the general procedure. The product was isolated as yellow crystals using pentane:dichloromethane, 1:1 as eluent system (22 mg, 91 %). ¹**H-NMR** (400 MHz, acetone- d_6) δ 7.55 (s, 1H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -59.25 (s); ¹³**C-NMR** (100 MHz, CDCl₃) δ 175.3, 172.9, 145.8 (q, J_{CF} = 1.5 Hz), 145.2 (q, J_{CF} = 1.7 Hz), 132.5, 131.5 (q, J_{CF} = 30.7 Hz), 120.5 (q, J_{CF} = 278.3 Hz); **HRMS** (APCI): m/z calcd. for [C₇HCl₂F₃O₂] 243.9311, found: 243.9311.

3,5-Dimethoxy-2-(trifluoromethyl)-1,4-benzoquinone (3m)

This compound was prepared according to the general procedure. The product was isolated as yellow crystals using pentane:dichloromethane, 1:4 as eluent system (12 mg, 51 %).

¹H-NMR (400 MHz, CDCl₃) δ 5.90 (s, 1H), 4.18 (s, 3H), 3.82 (s,

3H). ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -57.8 (s). ¹³**C-NMR** (100 MHz, CDCl₃) δ 181.8, 177.7, 156.9 (q, J_{CF} = 1.4 Hz), 156.8, 121.4 (q, J_{CF} = 274.0 Hz), 116.9 (q, J_{CF} = 28.5 Hz), 62.7, 56.7. **HRMS** (ESI): m/z calcd. for [C₉H₇F₃O₄+Na]⁺ 259.0189, found: 259.0195.

2,3-Dimethoxy-5-(trifluoromethyl)-1,4-benzoquinone (3n)

This compound was prepared according to the general procedure except that 0.02 mmol (20 mol%) of B_2Pin_2 5 and 0.5 mL of chloroform was used. The reaction was conducted in a microwave

reactor at 100 °C for 60 min. The product was isolated as a deep red oil using pentane:dichloromethane, 1:9 as eluent system (12 mg, 51 %). ¹**H-NMR** (400 MHz, CDCl₃) δ 6.94 (q, J_{HF} = 1.1 Hz, 1H), 4.06 (s, 3H), 4.05 (s, 3H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -65.13 (d, J_{HF} = 1.2 Hz); ¹³**C-NMR** (100 MHz, CDCl₃) δ 182.2, 178.5, 145.6, 145.4 (q, J_{CF} = 1.7 Hz), 133.6 (q, J_{CF} = 4.8 Hz), 133.2 (q, J_{CF} = 31.6 Hz), 120.5 (q, J_{CF} = 274.7 Hz), 61.8, 61.5; **HRMS** (ESI): m/z calcd. for [C₉H₇F₃O₄+Na]⁺ 259.0189, found: 259.0188.

2,3-Dimethoxy-5-methyl-6-(trifluoromethyl)-1,4-benzoquinone (30)



This compound was prepared according to the general procedure.

The product was isolated as a deep red oil using

pentane:dichloromethane, 1:4 as eluent system (17 mg, 64 %). ¹**H-NMR** (400 MHz, CDCl₃) δ 4.03 (s, 3H), 4.00 (s, 3H), 2.26 (q, J_{HF} = 3.3 Hz, 3H); ¹⁹**F-NMR** (376 MHz, CDCl₃) δ -57.46 (q, J_{HF} = 3.2 Hz); ¹³**C-NMR** (100 MHz, CDCl₃) δ 182.6, 179.2, 145.3 (q, J_{CF} = 1.8 Hz), 144.7, 144.6 (q, J_{CF} = 1.8 Hz), 129.4 (q, J_{CF} = 28.9 Hz), 122.2 (q, J_{CF} = 277.2 Hz), 61.6, 61.4, 122.2 (q, J_{CF} = 3.5 Hz); **HRMS** (ESI): m/z calcd. for $[C_{10}H_9F_3O_4+Na]^+$ 273.0345, found: 273.0354.

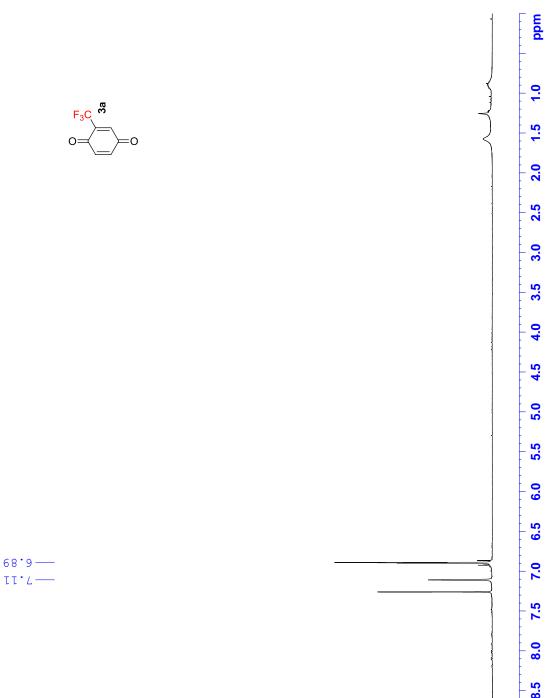
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- 1. K. Stanek, R. Koller and A. Togni, *J. Org. Chem.* 2008, **73**, 7678.
- 2. M. Matsumoto and H. Kobayashi, J. Org. Chem., 1985, 50, 1766.
- 3. D. A. Lanfranchi, D. Belorgey, T. Muller, H. Vezin, M. Lanzer and E. Davioud-Charvet, *Org. Biomol. Chem.*, 2012, **10**, 4795.

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NMR spectra of products 3a-o

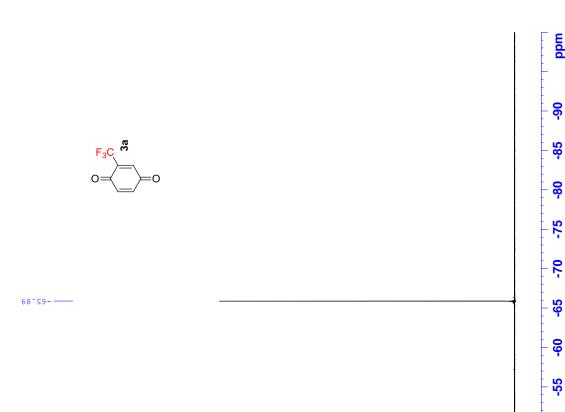


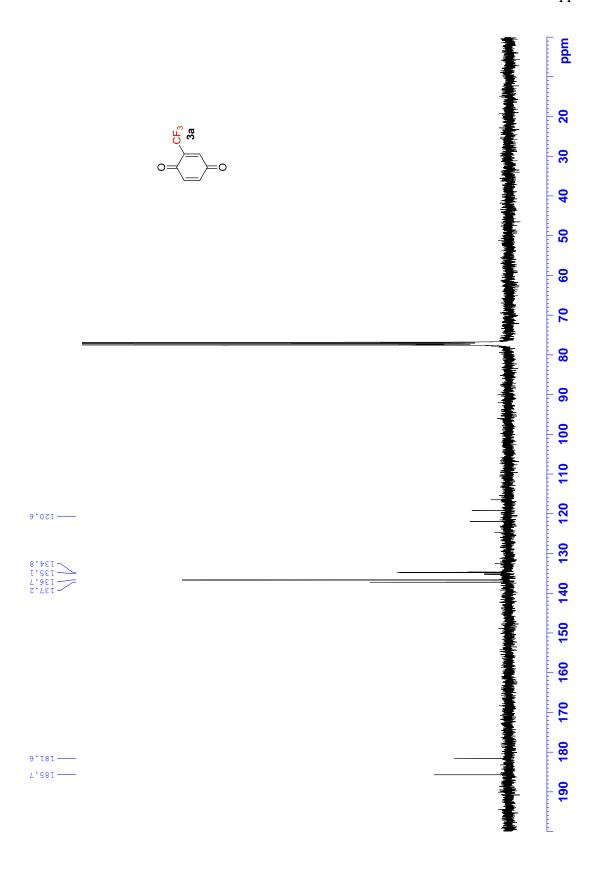
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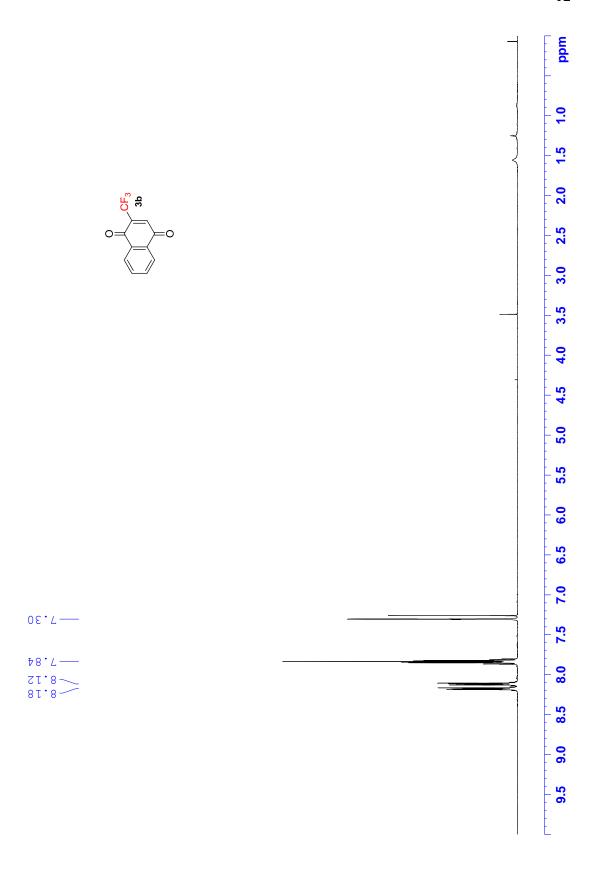
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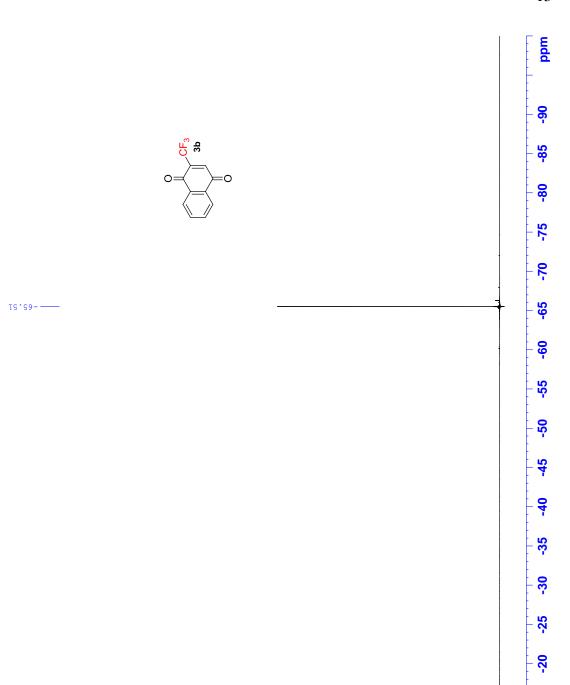


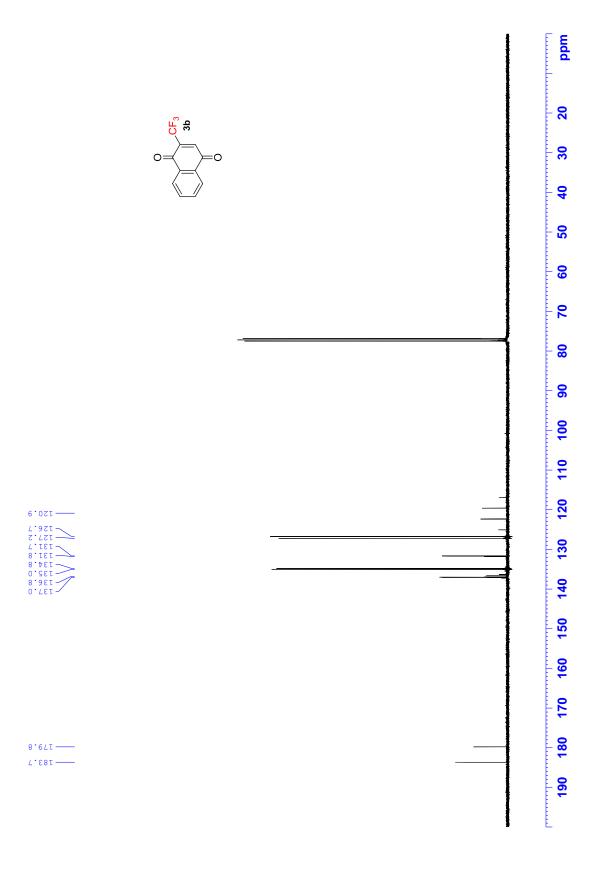


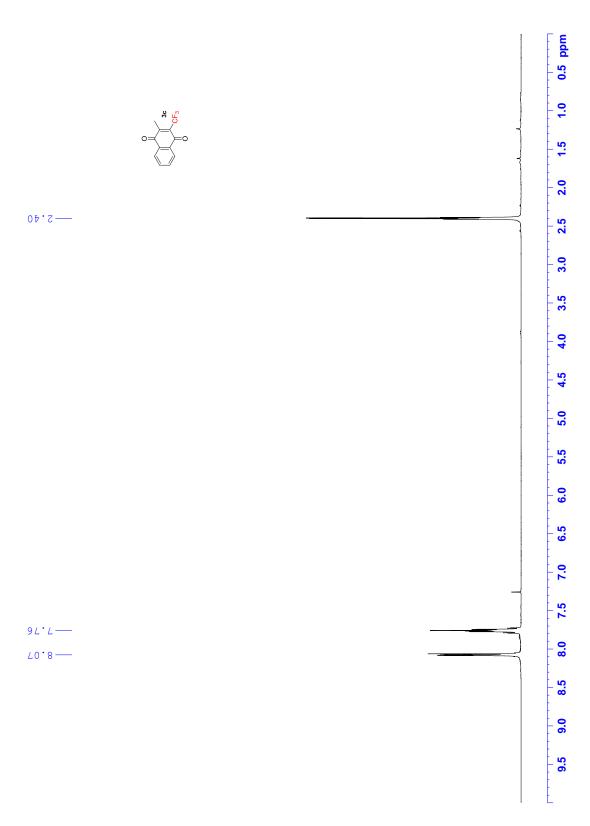




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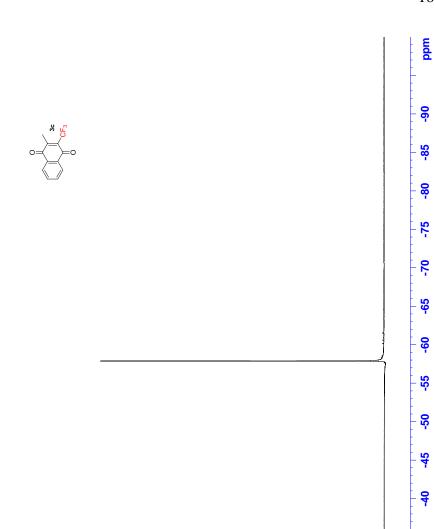


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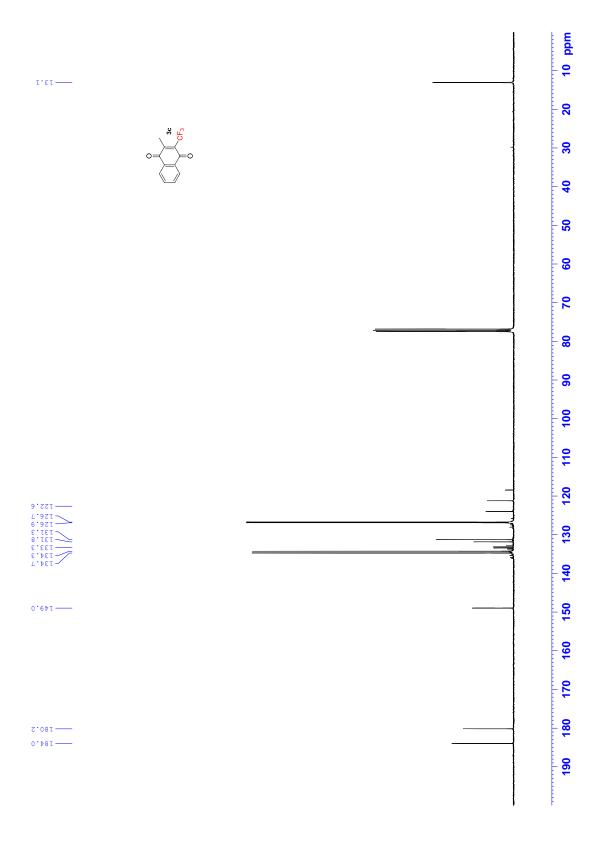


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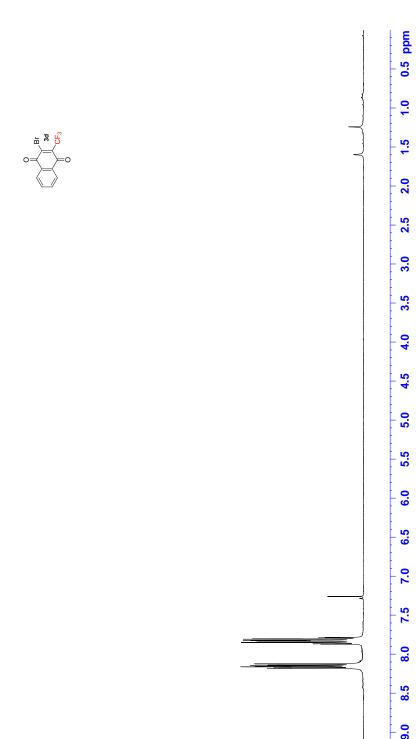






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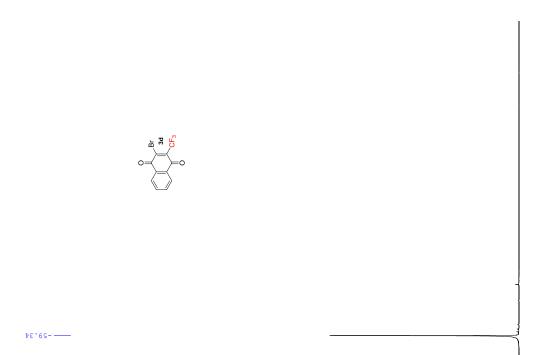
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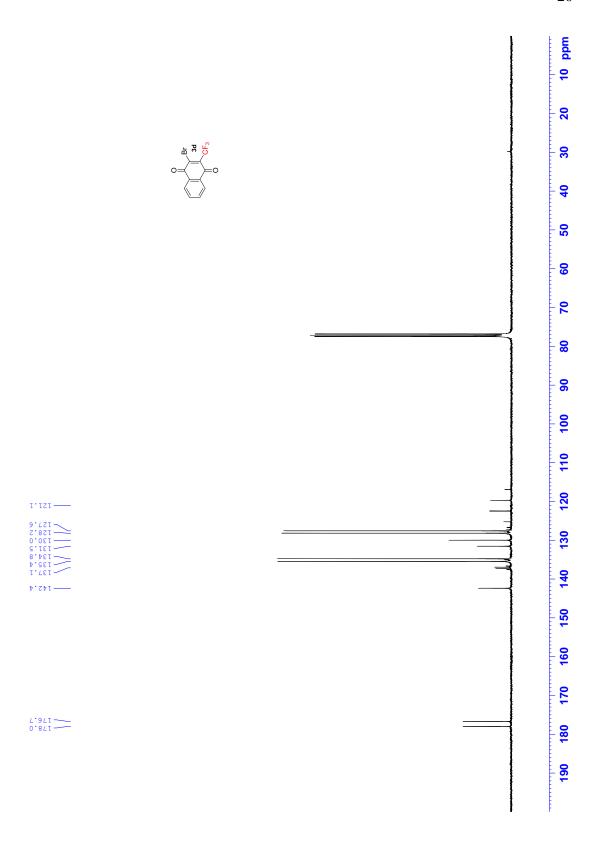
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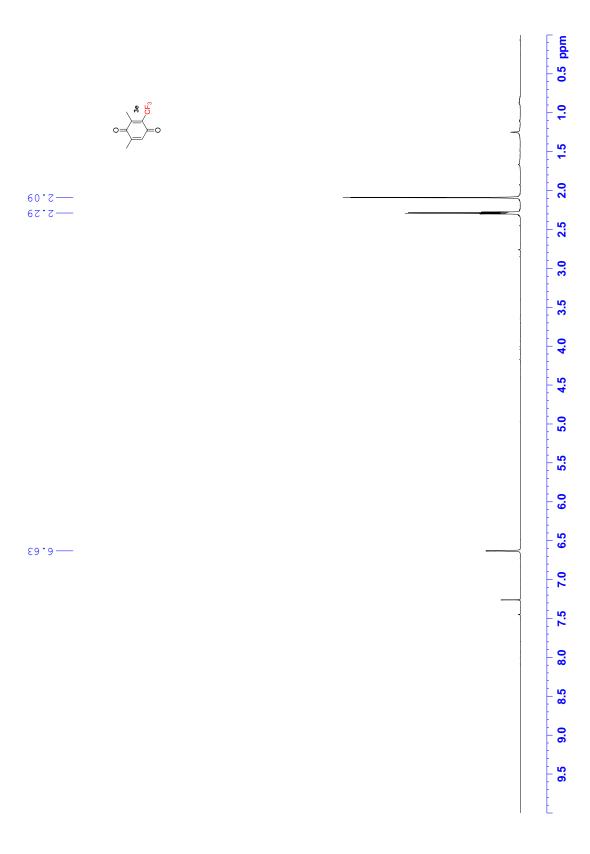
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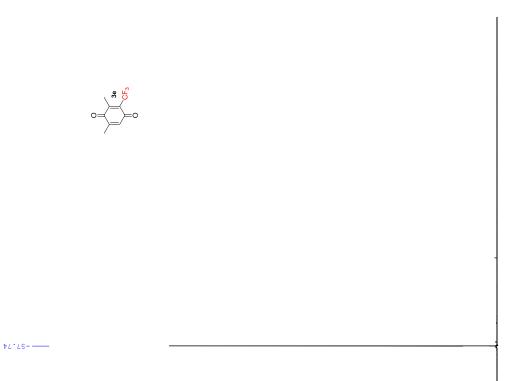
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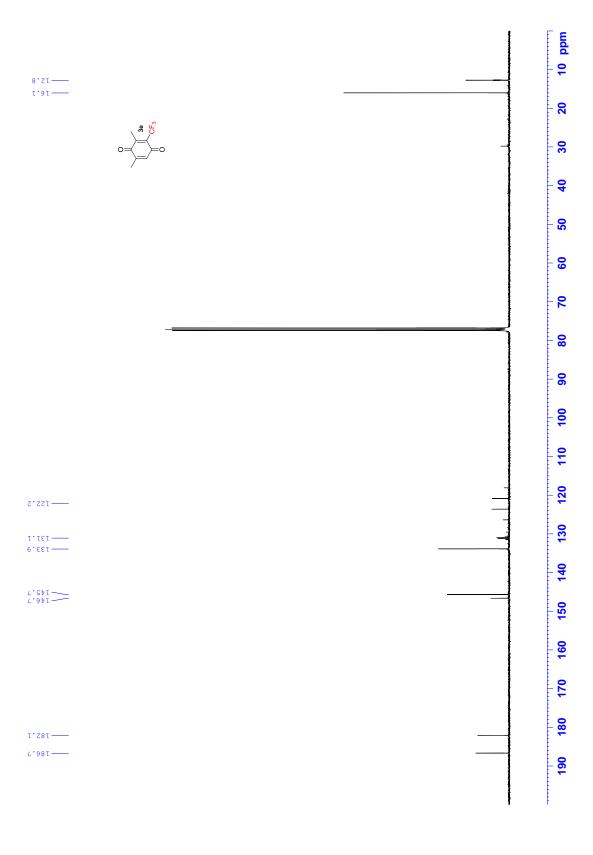
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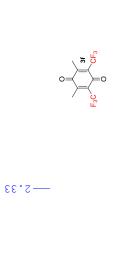
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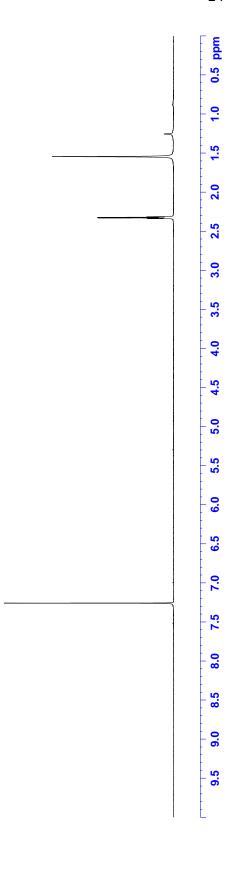
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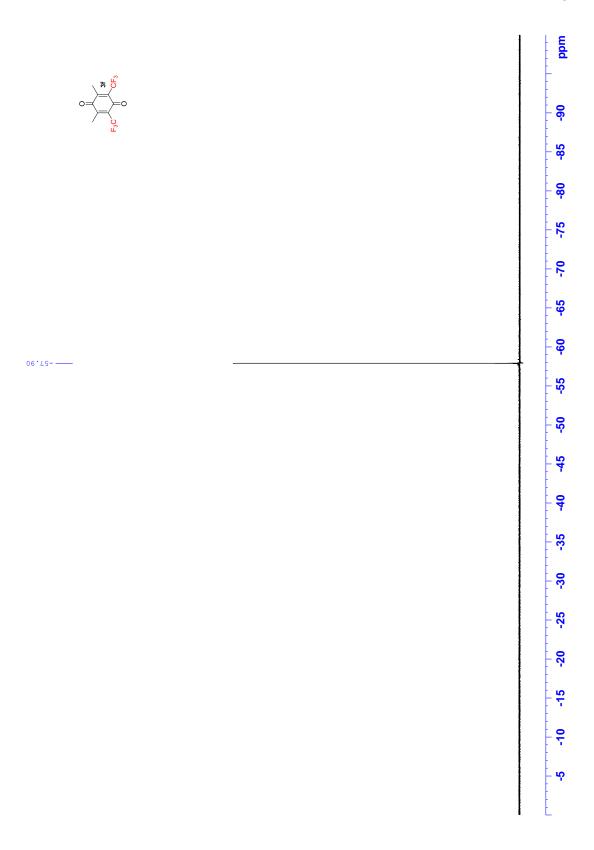


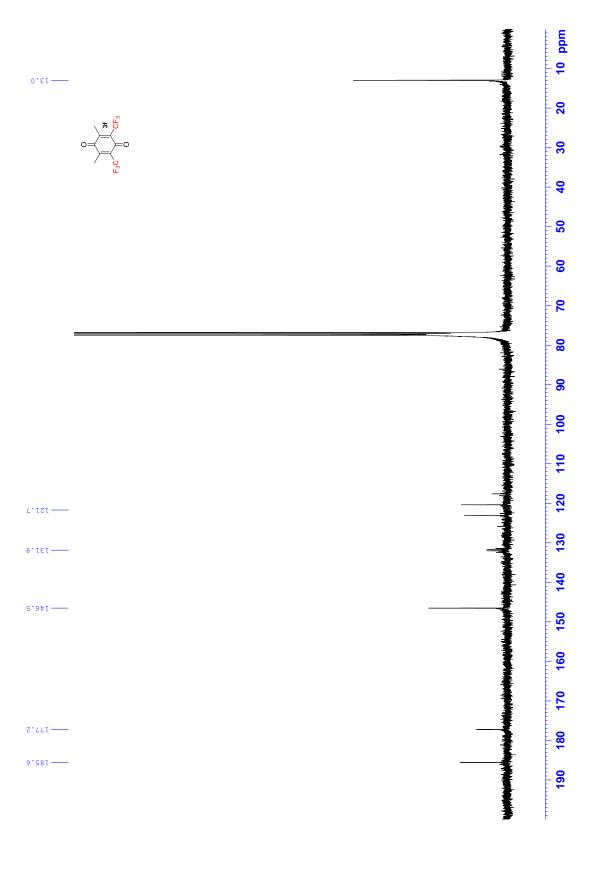




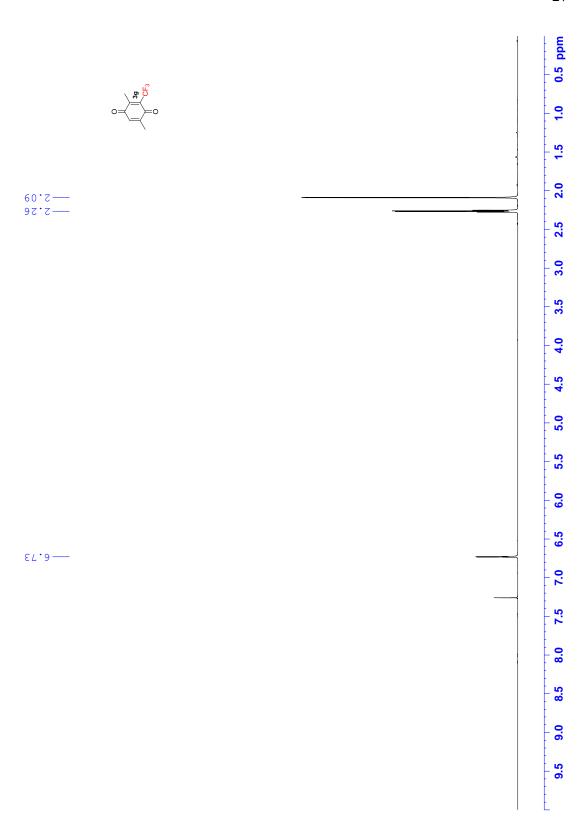










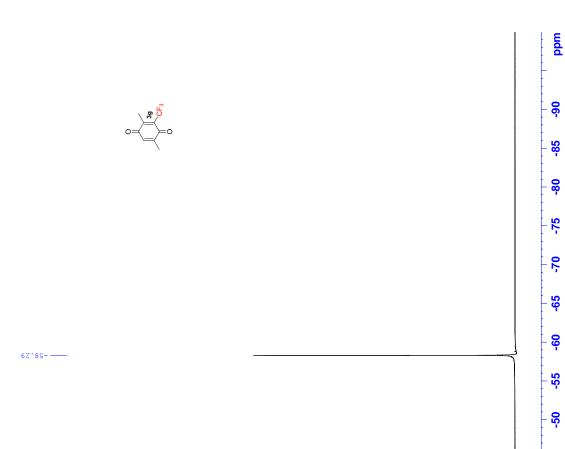


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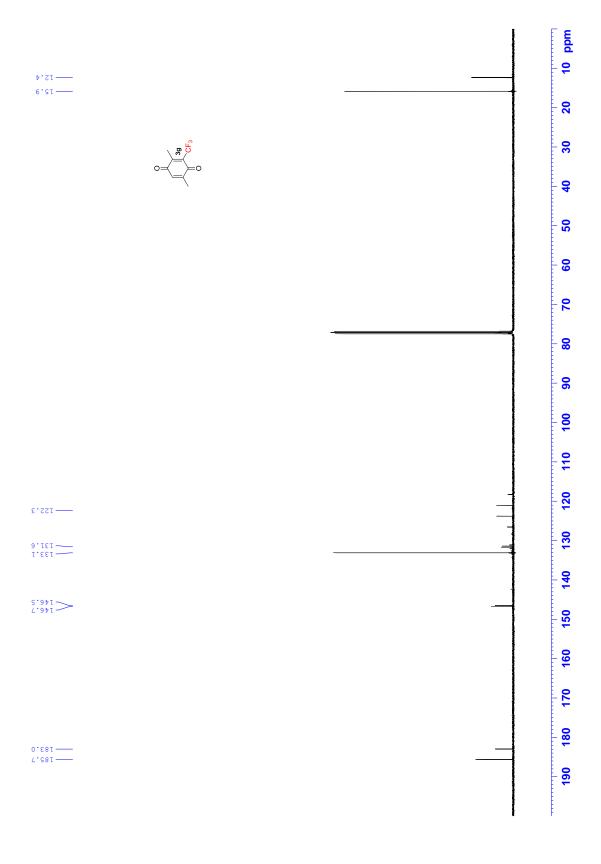
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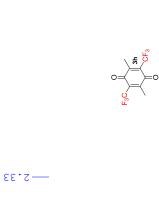
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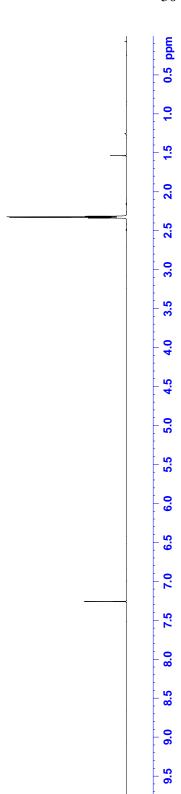
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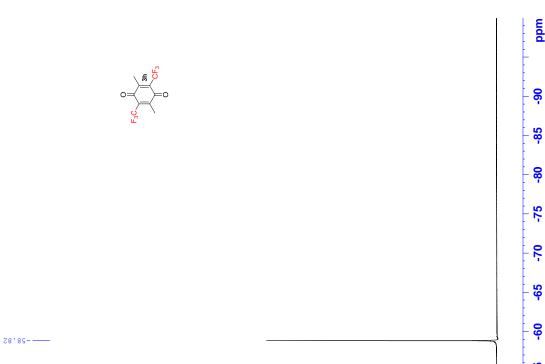
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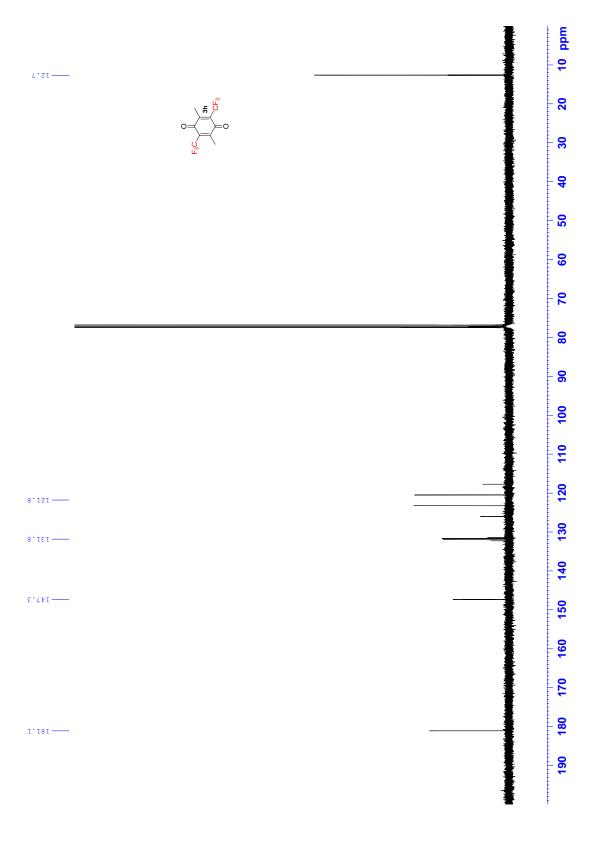
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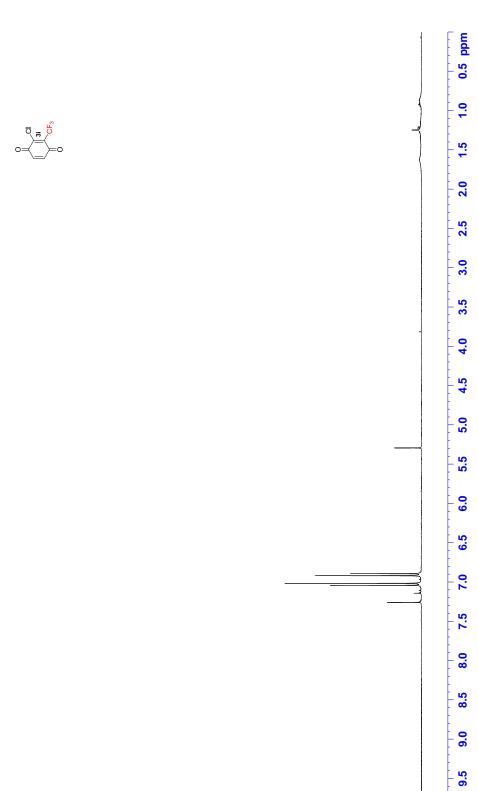
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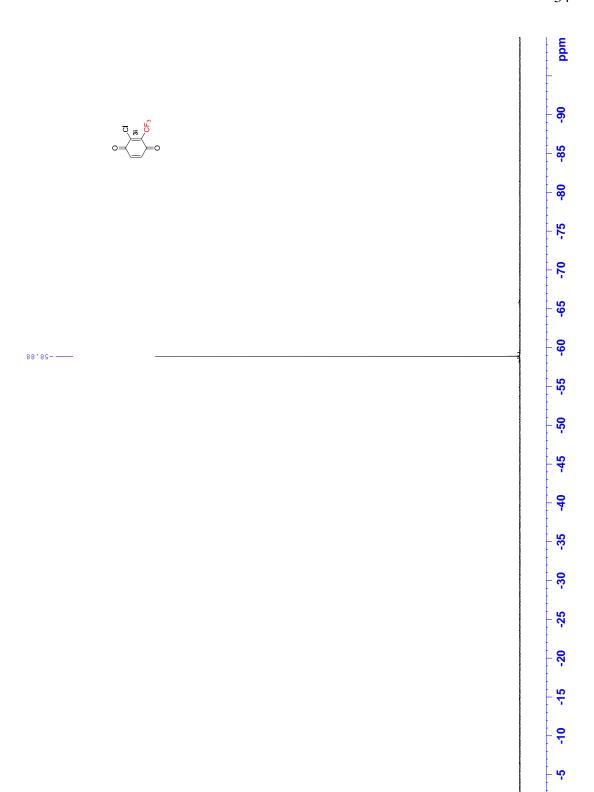


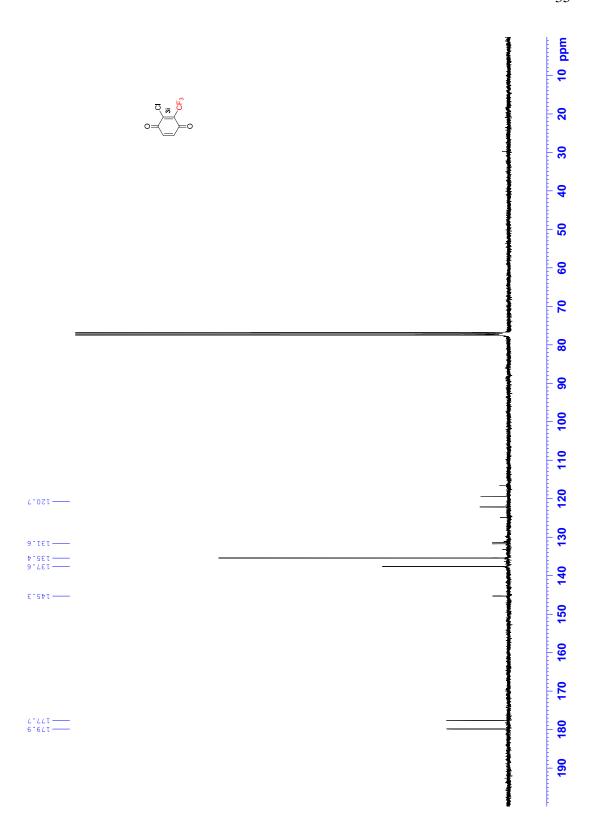


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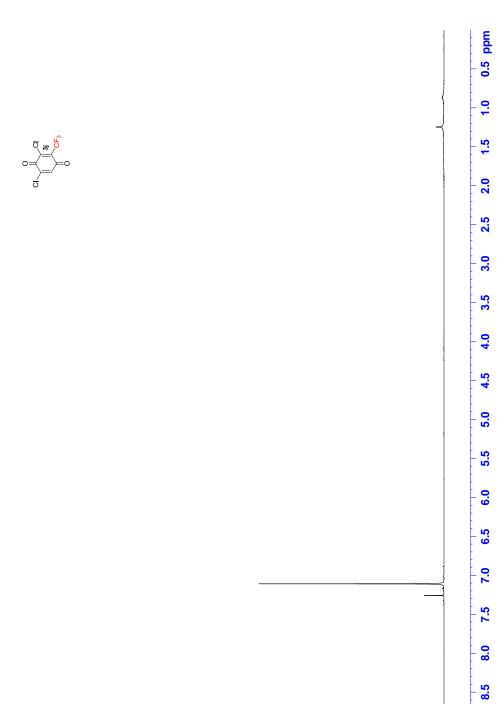






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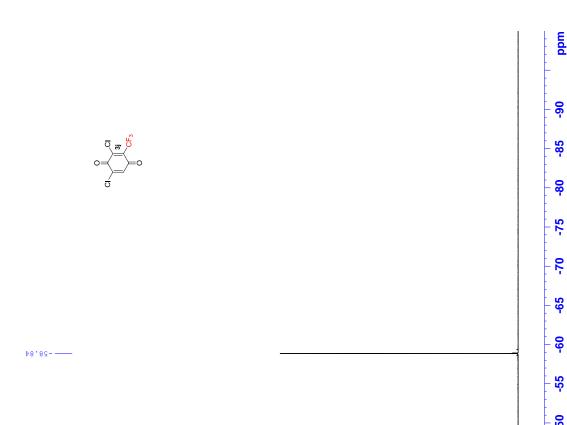
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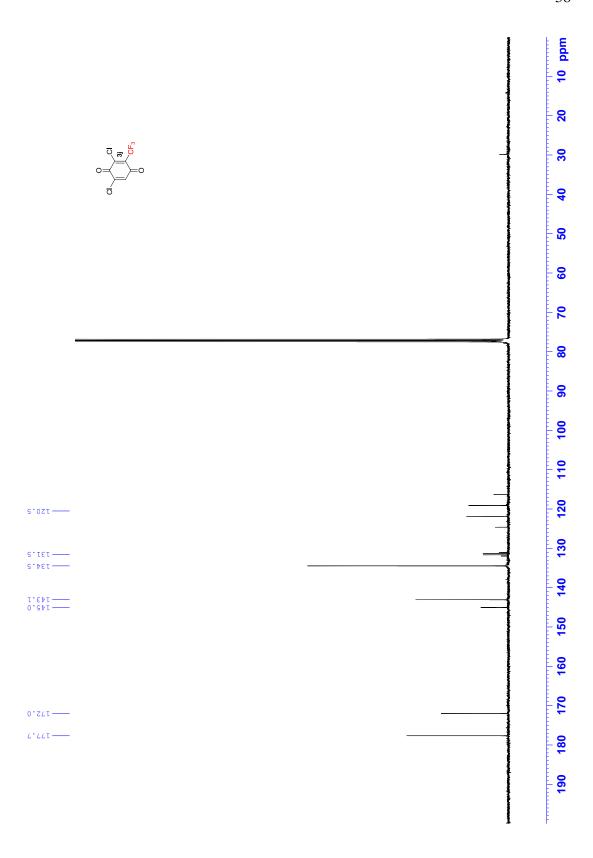
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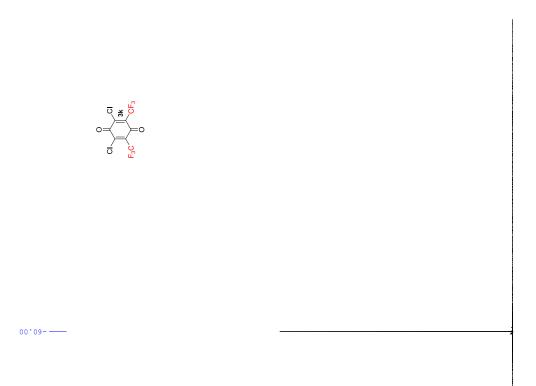
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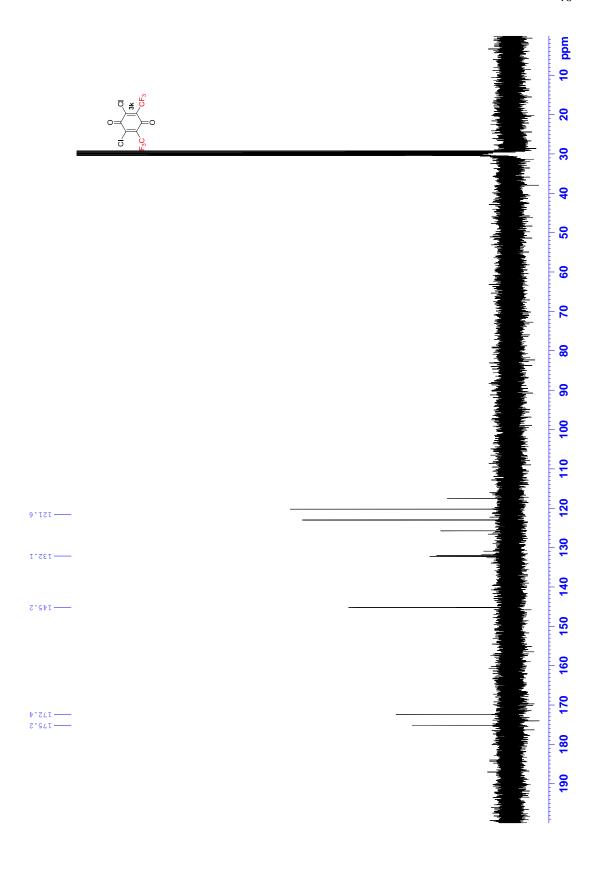
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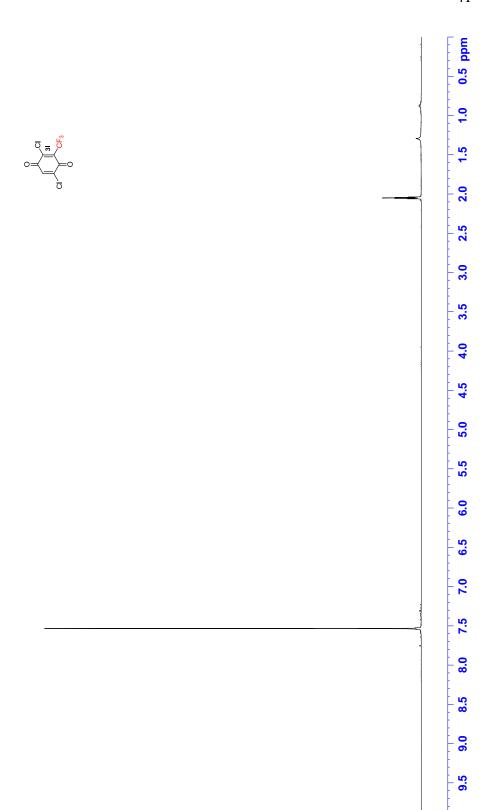






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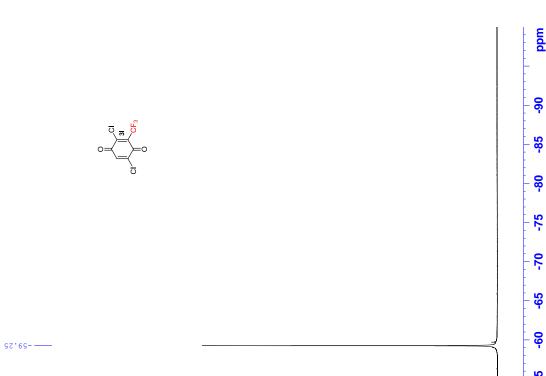
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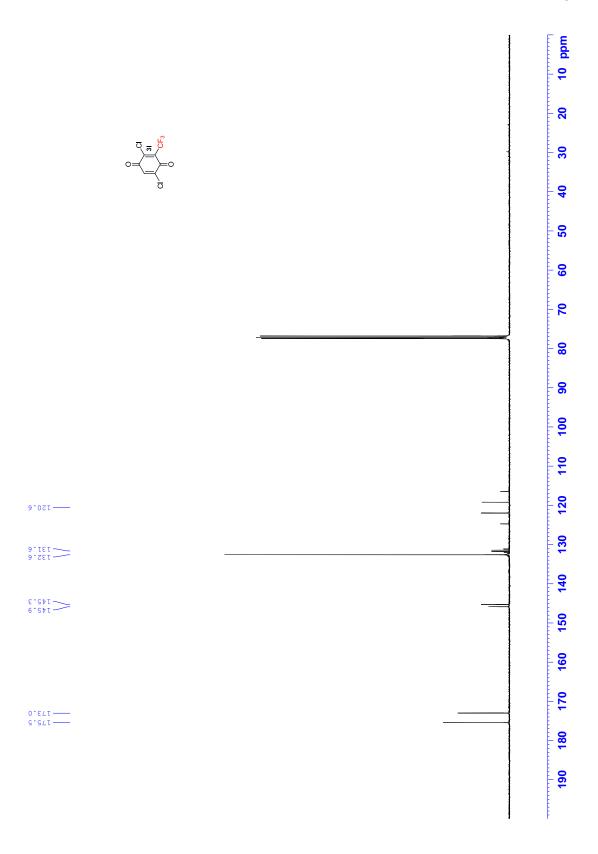
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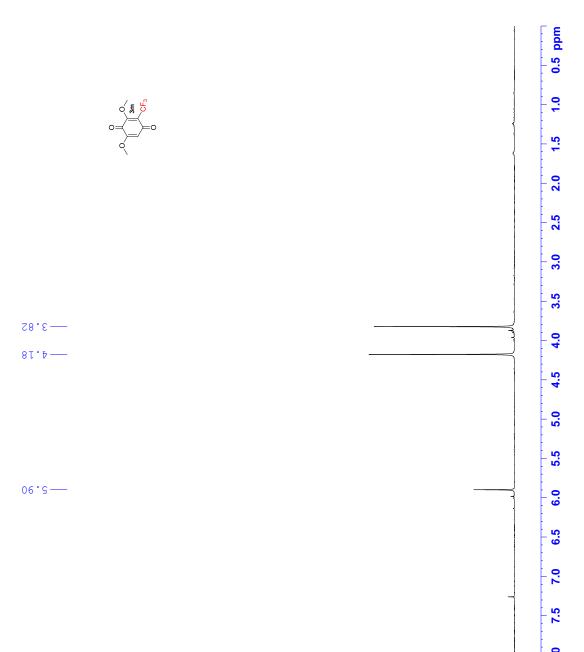






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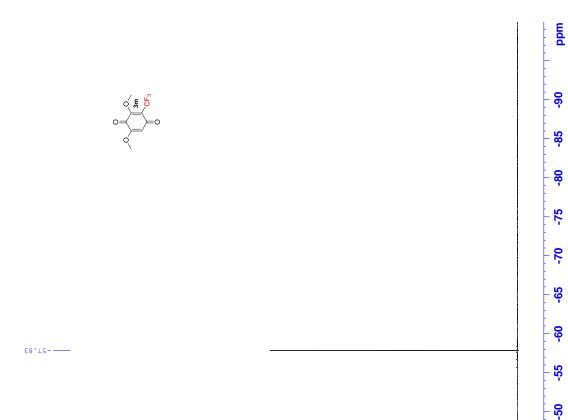
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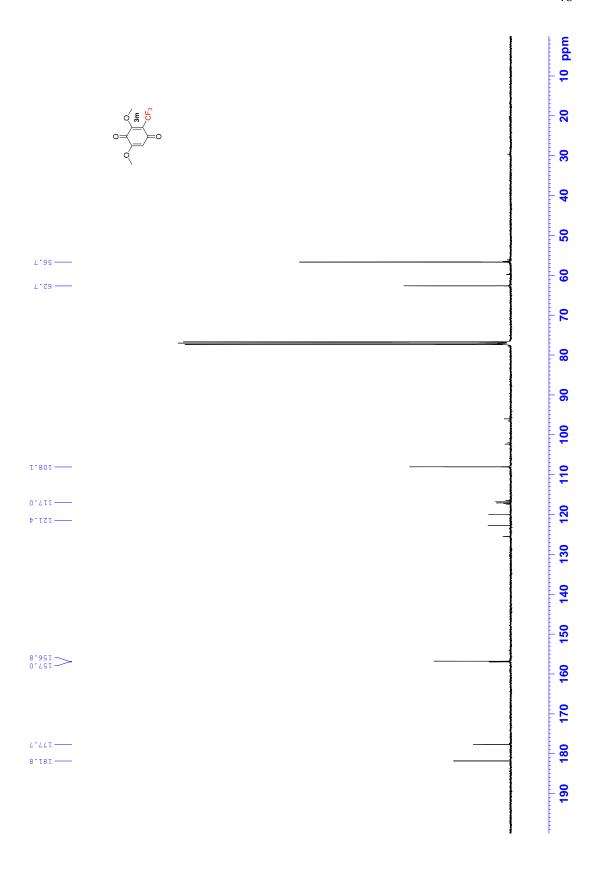
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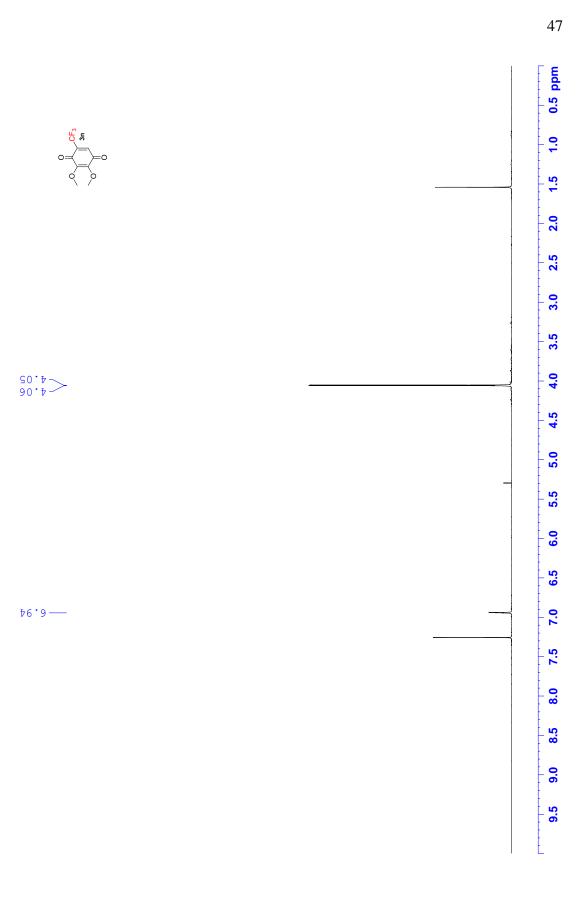
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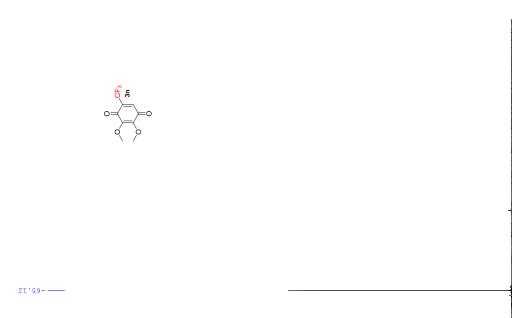
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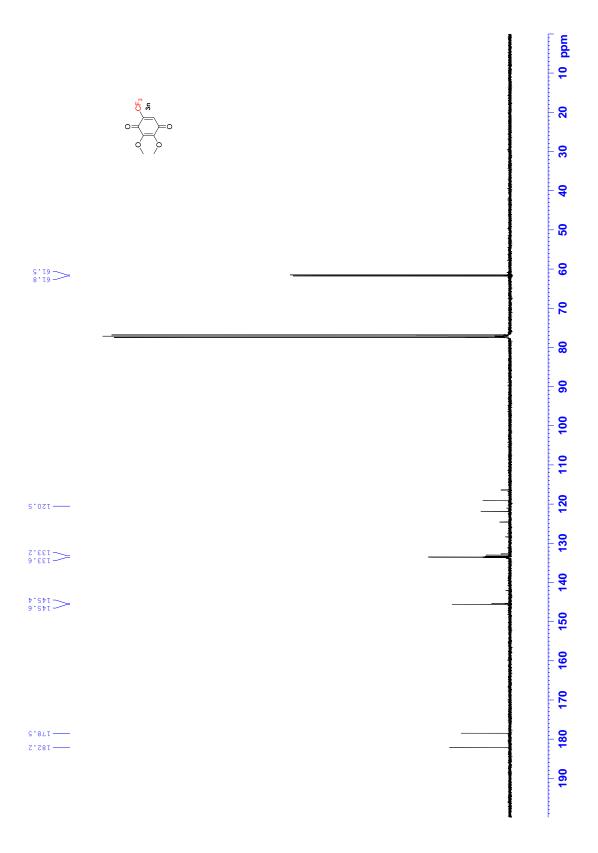
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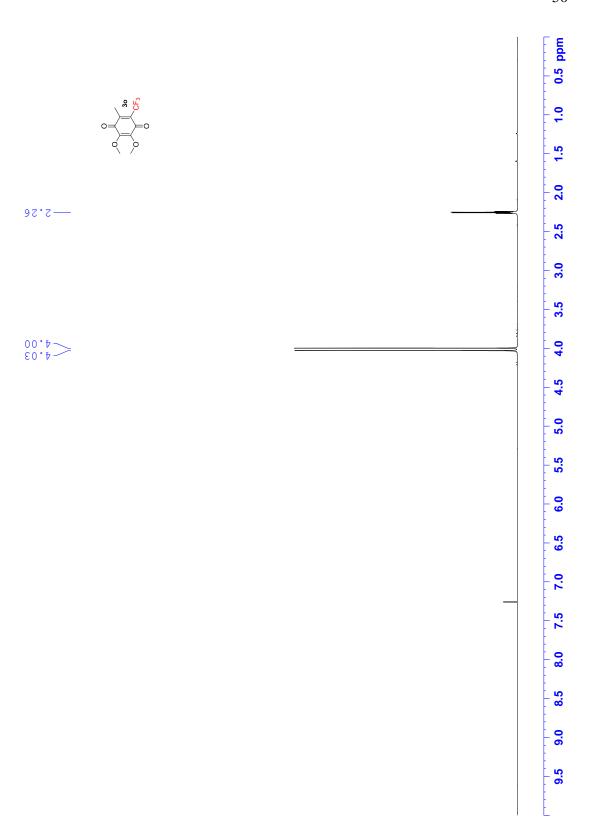
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