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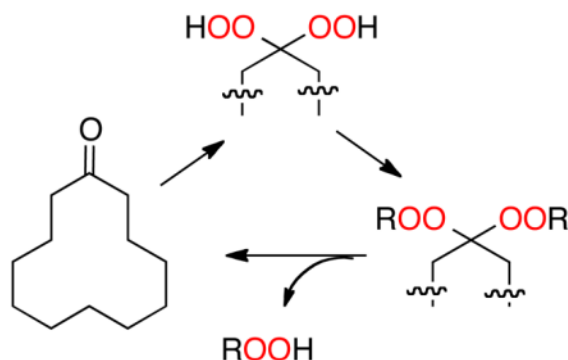
## Synthesis Of Alkyl Hydroperoxides Via Alkylation Of *gem*-Dihydroperoxides

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### Abstract



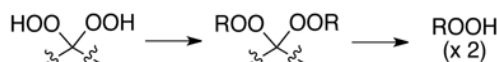
Two-fold alkylation of 1,1-dihydroperoxides, followed by hydrolysis of the resulting bisperoxyacetals, provides a convenient method for synthesis of primary and secondary alkyl hydroperoxides.

A number of methods have been reported for synthesis of alkyl hydroperoxides,<sup>1</sup> with some of the most widely used based upon displacement of a leaving group by a peroxide nucleophile.<sup>1b, 2</sup> Some years ago, we reported a convenient approach to alkyl hydroperoxides based upon alkylation of 2-methoxypropyl-2-yl hydroperoxide followed by deprotection of the resulting monoperoxyacetals.<sup>3</sup> Although the method has seen significant use,<sup>4</sup> it is limited by the need to generate and concentrate a low molecular weight hydroperoxyacetal.<sup>5</sup> Our recent experiences with the synthesis and reactivity of 1,1-dihydroperoxides (DHPs) led us to hypothesize that these species might offer useful alternatives as precursors for alkyl hydroperoxides.<sup>6</sup> We were encouraged by a report from Nojima and coworkers demonstrating alkylations of 1,1-DHPs,<sup>7</sup> and by the demonstrated stability of 1,1-bisperoxyacetals.<sup>7,8</sup> We now report a convenient procedure for synthesis of alkyl hydroperoxides via alkylation of 1,1-dihydroperoxides followed by acidic deprotection of the derived bisperoxyacetals (eq 1).

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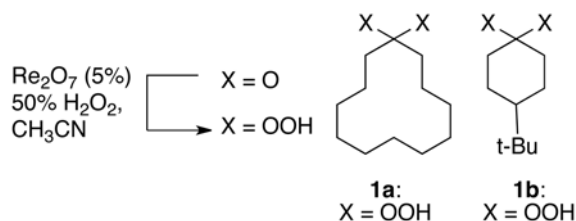
The authors declare no competing financial interest.

Supporting Information. <sup>1</sup>H and <sup>13</sup>C NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.



(1)

As initial substrates, we selected cyclododecanone 1,1 dihydroperoxide (**1a**) and 4-*t*-butylcyclohexanone dihydroperoxide (**1b**), known DHPs possessing sufficient mass to simplify isolation and mitigate safety concerns.<sup>9</sup> **1a** and **1b** were readily prepared via  $\text{Re}_2\text{O}_7$ -catalyzed condensation of the corresponding ketone with aq. hydrogen peroxide (eq 2).<sup>6a</sup>



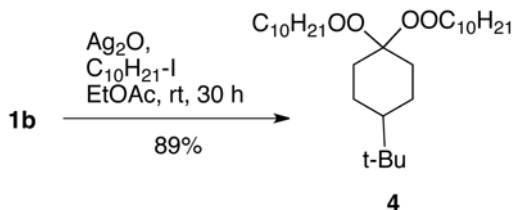
(2)

We chose to initially focus on the cyclododecanone-derived **1a** based upon previous reports demonstrating that this DHP more readily undergoes acid hydrolysis compared with DHPs derived from strain-free ketones; it was our hope that this increased reactivity would extend to derived bisperoxyacetals.<sup>10</sup> Investigations of conditions for alkylation of **1a** are summarized in Table 1. There have been only a few reports describing alkylation of 1,1-dihydroperoxides.<sup>6b, 7</sup> The bisalkylation of **1a** with primary iodides was achieved in good yield using  $\text{Ag}_2\text{O}$ ;<sup>7,11</sup> although the reaction was successful in several solvents, the best yields were obtained in ethyl acetate. The corresponding reaction with a primary bromide was unsuccessful. Attempted alkylation of **1a** by a primary iodide in the presence of cesium hydroxide or cesium carbonate resulted in decomposition with formation of ketone.<sup>7</sup> Silver-promoted benzoylation proceeded in modest yield due to facile Kornblum fragmentation of the peroxide product.<sup>12</sup> No product was observed upon attempted alkylation in the presence of potassium *t*-butoxide in THF or under phase-transfer conditions proven effective for alkylation of simple hydroperoxides.<sup>13</sup>

Neither  $\text{Ag}_2\text{O}$  nor base was successful in promoting alkylation with a secondary iodide. In search of electrophiles that would allow synthesis of secondary peroxides, we investigated alkyl triflates, which have been successfully applied to alkylation of alkyl hydroperoxides.<sup>2e</sup> Alkylation of **1a** with a slight excess (nominally 2.2–3.0 equiv) of primary or secondary triflates took place rapidly in the presence of potassium *tert*-butoxide (entries 10–11, 14–15).<sup>14</sup> We were unable to find any method for two-fold alkylation with a tertiary electrophile. Ag-promoted alkylation with *tert*-butyl bromide furnished a mixture containing mostly recovered starting material and monoalkylated product; only a trace of the desired bisperoxyacetal was observed (entry 16). Attempted alkylation of **1a** with *tert*-butyl bromide in the presence of base resulted in no reaction or decomposition (entries 17, 18).

Differential scanning calorimetry/thermal gravimetric analysis (DSC/TGA) demonstrated that the product bisperoxyacetal (**2a**) undergoes exothermic decomposition, but only upon heating to above 120–125 °C (Figure 1).

The cyclohexanone-derived DHP **1b** also underwent Ag-promoted alkylation with iododecane to generate a good yield of bisperoxyacetal **4** (eq 3).



(3)

## Hydrolysis of bisperoxyacetals: synthesis of alkyl hydroperoxides

Table 2 illustrates screening of conditions for deprotection of bisperoxyacetal **2a**. Little deprotection was observed upon exposure of **2a** to a room temperature ethanolic solution of dilute aqueous  $\text{H}_2\text{SO}_4$  or even upon heating with an excess of sulfuric acid in methanol. In contrast, refluxing **2a** in a methanolic solution containing 50% aqueous  $\text{H}_2\text{SO}_4$  resulted in rapid deprotection to furnish a high yield of decyl hydroperoxide and recovered ketone (entry 3). Application of the same reagent but at room temperature resulted in only a modest yield even after two days of reaction (entry 4). A THF solution of **2a** also proved unreactive towards anhydrous acid (entry 6) but rapidly underwent complete deprotection upon heating with a slight excess of 50% aqueous  $\text{H}_2\text{SO}_4$  (entry 7). Application of the same conditions at room temperature resulted in a prolonged reaction time and lower yield (see entry 8). In no case could we detect any ring-expanded lactone. DSC/TGA analysis of a sample of the purified decyl hydroperoxide product (**3a**) revealed a profile for thermal stability very similar to that described earlier for bisperoxyacetal **2a**, with onset of decomposition occurring well above the temperatures required for acid hydrolysis; details are provided in Supporting Information.

Consistent with our hypothesis regarding the contribution of ring strain to peroxyacetal hydrolysis,<sup>10</sup> bisperoxyacetal **4** could not be completely hydrolyzed under conditions that had proven effective for **2a**. (Table 3).

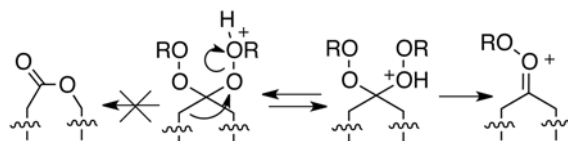
The optimized conditions were next applied to deprotection of bisperoxyacetals **2a-2g** (Table 4) to furnish moderate to good yields of hydroperoxides in highly pure form.

Curious as to the potential for stereospecific displacement of secondary substrates, we repeated the synthesis of 2-hydroperoxyoctane (**3f**) beginning with the triflate derived from enantiomerically enriched *R* (-) 2-octanol (Scheme 1). Phosphine reduction of the derived hydroperoxide furnished 2-octanol possessing a very low specific rotation, suggesting that the displacement of secondary triflates proceeds with little if any stereospecificity.<sup>15</sup>

## Discussion

Our decision to focus on the use of a cyclododecanone-derived bishydroperoxide was based upon the report by Terent'ev investigating hydrolysis of analogous 1,1-dihydroperoxides. In that work, the bis hydroperoxyacetals derived from bulky alicyclic or strained cyclic frameworks underwent hydrolysis more rapidly than those based upon a strain-free backbone.<sup>10</sup> Our results demonstrate that these trends extend to bisperoxyacetals, with **2a** undergoing complete hydrolysis under relatively mild conditions that fail to completely

deprotect cyclohexanone-derived **4**. The lack of ring-expanded products observed during acid hydrolysis suggests that ionization of the acetal center is greatly favored relative to C-to-O migration (eq. 4).



(4)

The displacements of primary halides are anticipated to proceed through an  $S_N2$ -type transition state. In contrast, the displacements of secondary triflates appear to involve a transition state with significant cationic character. Although the successful displacement of highly reactive secondary electrophiles suggests the potential for extension to tertiary systems, this proved not to be the case (Table 1, entries 16–18), presumably due to rapid elimination.

In conclusion, we have demonstrated a convenient synthesis of primary and secondary alkyl hydroperoxides based upon use of 1,1-dihydroperoxides. The reagents are available in one step from commercially available ketones, which can be recovered from the hydrolysis/deprotection step. The ease of generating 1,1-dihydroperoxides and of handling the bisperoxyacetal intermediates suggests the potential for extension of the methodology to solid-phase organic synthesis.

#### Note on safety

Although no safety issues were encountered in the course of this work, any preparative work with peroxides should be conducted with an awareness of the potential for spontaneous and exothermic decomposition reactions.<sup>16</sup>

## EXPERIMENTAL PROCEDURES

1,1-Dihydroperoxides were prepared using a literature procedure.<sup>6a</sup> Alkyl triflates were prepared according to a published procedure and used without column purification.<sup>14</sup> EA = ethyl acetate; Hex = hexane. NMR spectra were acquired at 400 MHz ( $^1\text{H}$ ) or 100 MHz ( $^{13}\text{C}$ ) in  $\text{CDCl}_3$  unless noted.

#### General Procedure (Method-A): Synthesis of 1,1-bisperoxyacetals

To a 0 °C solution of cyclododecanone 1,1 dihydroperoxide (1 mmol) in ethyl acetate (10 mL) was added freshly prepared  $\text{Ag}_2\text{O}$  (3 mmol) followed by alkyl iodide (2.2 mmol). The reaction was stirred at room temperature until starting material could no longer be detected (TLC, 5 – 30 h).<sup>17</sup> The reaction solution was filtered through small pad of Celite and the filtrate concentrated *in vacuo*. The residue was purified by silica chromatography using 1% EA/Hex to furnish pure samples of the bisperoxyacetal.

#### General Procedure (Method-B): Synthesis of Bisperoxyacetal from alkyl triflates

To a 0 °C solution of 1,1 dihydroperoxide (0.5 mmol) in dry THF was added  $\text{KO}^t\text{Bu}$  (2.1 equiv) followed by alkyl triflate (2.2 equiv/equiv DHP for primary triflates, 3 equiv/equiv DHP for secondary triflates). The reaction was allowed to stir until starting material was no longer visible (TLC, 20 min - 1 h) and then quenched with water (15 mL).<sup>17</sup> The combined

EA extracts (25 ml x 2) were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated on a rotary evaporator. The crude product was purified by silica chromatography using 1% diethyl ether and hexane.

### General Procedure: Synthesis of Alkyl hydroperoxides from 1,1-dihydroperoxides

To a room temperature solution of bisperoxyacetal (0.3 mmol) in tetrahydrofuran (3 ml) was added 50% aq. H<sub>2</sub>SO<sub>4</sub> (1.8 mmol, 6 equiv). The reaction was heated at 50–55 °C until starting material could no longer be detected (TLC, 1–3 h).<sup>17</sup> The reaction was then allowed to cool to room temperature and quenched with saturated aq. Na<sub>2</sub>CO<sub>3</sub> (15 mL). The combined EA extracts (25 ml x 2) were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by silica chromatography using 1–3% EA/Hex.

**1,1-Dihydroperoxy cyclododecane (1a)**—White solid; mp 139–141 °C, yield: 78% (909 mg); R<sub>f</sub> (20% EA/Hex): 0.54; <sup>1</sup>H NMR δ (MeOH-D<sub>4</sub>, 300 MHz): 4.84 (s, 2H), 1.59–1.52 (m, 8H), 1.39 (m, 14H). <sup>13</sup>C NMR δ (MeOH-D<sub>4</sub>, 75 MHz): 113.3, 25.8, 25.7, 21.9, 21.6, 18.9.

**4-tert-Butyl 1,1 dihydroperoxy cyclohexane (1b)**—White solid; mp 78–80 °C yield: 85% (174 mg); R<sub>f</sub> (20% EA/Hex): 0.54; <sup>1</sup>H NMR δ (300 MHz): 8.95 (bs, 2H), 2.33 (bd, *J* = 12 Hz, 2H), 1.75 (bd, *J* = 12 Hz, 2H), 1.48 (dt, *J* = 13.3, 3.6 Hz, 2H), 1.27 (dq, *J* = 13.3, 3.6 Hz, 2H), 1.06 (tt, *J* = 12.0, 2.9 Hz, 1H), 0.88 (s, 9H); <sup>13</sup>C NMR δ: 111.0, 47.4, 32.3, 29.7, 27.6, 23.4.

**1,1-Bis(decylperoxy) cyclododecane (2a)**—Thick colorless liquid; yield: 93% (553 mg) R<sub>f</sub> (10% EA/Hex): 0.74; <sup>1</sup>H NMR δ: 4.07 (t, *J* = 6.8 Hz, 4H), 1.75–1.58 (m, 8H), 1.48 (m, 4H), 1.35–1.27 (m, 42H), 0.88 (t, *J* = 6.8 Hz, 6H); <sup>13</sup>C NMR δ: 113.1, 75.0, 31.9, 29.6, 29.5, 29.3, 27.9, 27.0, 26.2, 26.11, 22.7, 22.3, 21.9, 19.4, 14.1; IR (neat) 2922, 2851, 1468, 1054, 989; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>32</sub>H<sub>64</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 535.4702, found 535.4727.

**1,1-Bis(hexylperoxy) cyclododecane (2b)**—Thick colorless liquid; yield: 79% (317 mg); R<sub>f</sub> (10% EA/Hex) = 0.65; <sup>1</sup>H NMR δ: 4.05 (t, *J* = 6.7 Hz, 4H), 1.67–1.57 (m, 8H), 1.50–1.41 (m, 4H), 1.39–1.27 (m, 26H), 0.88 (t, *J* = 6.8 Hz, 6H); <sup>13</sup>C NMR δ: 113.1, 75.0, 31.6, 27.8, 27.0, 26.0, 25.9, 25.7, 22.6, 22.3, 21.9, 19.3, 13.99; IR (neat) 2927, 2852, 1468, 1052, 989; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>24</sub>H<sub>48</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 423.3450, found 423.3465.

**1,1-Bis(benzylperoxy) cyclododecane: (2c)**—White solid; yield: 56% (232 mg); mp 68–70 °C; R<sub>f</sub> (10% EA/Hex) = 0.69; <sup>1</sup>H NMR δ: 7.41–7.32 (m, 10H), 5.11 (s, 4H), 1.73–1.69 (m, 4H), 1.52–1.42 (m, 4H), 1.35 (m, 14H); <sup>13</sup>C NMR δ: 136.0, 129.2, 128.3, 128.2, 113.8, 27.1, 26.1, 22.3, 21.9, 19.4; IR (neat) 2927, 2850, 1706, 1469, 1453, 964; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>26</sub>H<sub>36</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 435.2511, found 435.2508.

**1,1-Bis(9-decenylperoxy) cyclododecane: (2d)**—Thick colorless liquid; yield (method B) 80% (122 mg); (method A) 79% (400 mg); R<sub>f</sub> (10% EA/Hex) = 0.81; <sup>1</sup>H NMR δ: 5.81 (m, 2H), 5.02–4.91 (m, 4H), 4.07 (t, *J* = 6.6 Hz, 4H), 2.04 (q, *J* = 6.8 Hz, 4H), 1.70–1.58 (m, 8H), 1.49–1.31 (m, 38H); <sup>13</sup>C NMR δ: 139.1, 114.3, 113.1, 75.0, 33.8, 29.4, 29.1, 28.9, 27.9, 27.1, 26.2, 26.1, 22.3, 21.98, 19.4; IR (neat) 3076 (weak), 2924, 2852, 1468, 990, 907; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>32</sub>H<sub>60</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 531.4389 found 531.4385.

**1,1-Bis(4-phenylbutylperoxy) cyclododecane: (2e)**—Thick colorless liquid; yield 68% (340 mg); R<sub>f</sub> (10% EA/Hex) = 0.82; <sup>1</sup>H NMR δ: 7.30 (m, 4H), 7.21 (m, 6H), 4.13 (t, *J* = 6.0, 4H), 2.67 (t, *J* = 7.1 Hz, 4H), 1.76–1.69 (m, 12H), 1.51 (m, 4H), 1.39 (m, 14H); <sup>13</sup>C

NMR  $\delta$ : 142.3, 128.4, 128.3, 125.7, 113.2, 74.8, 35.7, 28.0, 27.5, 27.1, 26.1, 22.4, 22.0, 19.4; IR (neat): 2927, 2860, 1495, 1469, 1452, 989; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>32</sub>H<sub>48</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 519.3450 found 519.3439.

**1,1-Bis(2-octyl peroxy) cyclododecane: (2f)**—Thick colorless liquid; yield 53% (417 mg); R<sub>f</sub> (10% EA/Hex) = 0.85; <sup>1</sup>H NMR  $\delta$ : 4.25–4.06 (m, 2H), 1.71–1.58 (m, 7H), 1.48 (m, 5H), 1.36–1.20 (m, 30H), 1.21 (d, *J* = 6.2 Hz, 6H), 0.90 (t, *J* = 6.4 Hz, 6H); <sup>13</sup>C NMR  $\delta$ : 112.8, 79.6, 79.5, 34.7, 32.1, 31.8, 31.5, 29.4, 27.3, 27.2, 26.2, 26.1, 25.6, 25.5, 25.3, 22.6, 22.4, 22.0, 19.4, 18.8, 14.0; IR (neat): 2927, 2855, 1468, 1055, 989; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>28</sub>H<sub>56</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 479.4076; found, 479.4068.

**1,1-Bis(2-dodecyl peroxy) cyclododecane: (2g)**—Thick colorless liquid; yield 42% (252 mg); R<sub>f</sub> (15% EA/Hex) = 0.84; <sup>1</sup>H NMR  $\delta$ : 4.23 (m, 2H), 1.71–1.59 (m, 6H), 1.48 (m, 4H), 1.36 (m, 18H), 1.28 (m, 30H), 1.21 (d, *J* = 6.3 Hz, 6H), 0.90 (t, *J* = 6.3 Hz, 6H); <sup>13</sup>C NMR  $\delta$ : 112.8, 79.6, 79.5, 34.7, 31.9, 29.8, 29.6, 29.3, 27.3, 26.2, 26.1, 25.7, 25.6, 22.7, 22.3, 22.0, 19.4, 18.86, 18.83, 14.1; IR (neat): 2922, 2851, 1467, 989; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>36</sub>H<sub>72</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 591.5328; found, 591.5319.

**4-tert-Butyl- 1,1 bis (decylperoxy) cyclohexane (4)**—Thick colorless liquid; yield 89% (866 mg); R<sub>f</sub> (10% EA/Hex) = 0.71; <sup>1</sup>H NMR  $\delta$ : 4.11 (t, *J* = 6.7 Hz, 2H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.29 (bd, *J* = 12.0 Hz, 2H), 1.69–1.58 (m, 6H), 1.44–1.19 (m, 33H), 0.89 (t, *J* = 0.89 Hz, 6H), 0.87 (s, 9H); <sup>13</sup>C NMR  $\delta$ : 108.9, 75.4, 75.1, 47.5, 32.3, 31.9, 30.6, 29.6, 29.48, 29.47, 29.3, 27.89, 27.83, 27.6, 26.18, 26.16, 23.5, 22.7, 14.1; IR (neat): 2922, 2853, 1466, 1365, 1060; HRMS (ESI<sup>+</sup>, TOF) calcd for C<sub>30</sub>H<sub>60</sub>NaO<sub>4</sub> (M+Na)<sup>+</sup>: 507.4389; found, 507.4384.

**Decyl hydroperoxide (3a)**—CAS # 4225–91-6; Colorless liquid; yield: 78% (64 mg); R<sub>f</sub> (10% EA/Hex) = 0.44; <sup>1</sup>H NMR  $\delta$ : 8.23 (s, 1H), 4.03 (t, *J* = 6.7 Hz, 2H), 1.64 (quintet, *J* = 6.7 Hz, 2H), 1.37–1.27 (m, 14H), 0.89 (t, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR  $\delta$ : 76.7, 31.9, 29.5, 29.4, 29.3, 27.5, 25.9, 22.7, 14.1.

**Hexyl hydroperoxide (3b)**—CAS # 4312-76-9; Colorless liquid; yield 49% (58 mg); R<sub>f</sub> (10% EA/Hex) = 0.39; <sup>1</sup>H NMR  $\delta$ : 8.36 (s, 1H), 4.03 (t, *J* = 6.7 Hz, 2H), 1.64 (quintet, *J* = 6.8 Hz, 2H), 1.39–1.26 (m, 6H), 0.89 (t, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR  $\delta$ : 76.7, 31.6, 27.5, 25.5, 22.5, 13.9.

**Benzyl hydroperoxide (3c)**—CAS # 3071-34-9; Colorless liquid; yield: 60% (75 mg); R<sub>f</sub> (10% EA/Hex) = 0.22; <sup>1</sup>H NMR  $\delta$ : 8.25 (s, 1H), 7.43–7.39 (m, 5H), 5.02 (s, 2H); <sup>13</sup>C NMR  $\delta$ : 135.7, 129.0, 128.6, 79.2.

**9-Decenyl hydroperoxide (3d)**—CAS # 123369-53-9; Colorless liquid; yield: 62% (107 mg); R<sub>f</sub> (10% EA/Hex) = 0.37; <sup>1</sup>H NMR  $\delta$ : 8.23 (s, 1H), 5.87–5.77 (m, 1H), 5.03–4.92 (m, 2H), 4.03 (t, *J* = 6.7 Hz, 2H), 2.07–2.02 (m, 2H), 1.64 (quintet, *J* = 6.9 Hz, 2H), 1.40–1.25 (m, 10H); <sup>13</sup>C NMR  $\delta$ : 139.1, 114.1, 76.7, 33.7, 29.35, 29.34, 29.0, 28.9, 27.5, 25.9.

**4-Phenylbutyl hydroperoxide (3e)**—CAS# 99172-63-1; Colorless liquid; yield: 79% (133 mg); R<sub>f</sub> (10% EA/Hex) = 0.30; <sup>1</sup>H NMR  $\delta$ : 8.44 (s, 1H), 7.37–7.33 (m, 2H), 7.27–7.24 (m, 3H), 4.09 (t, *J* = 6.1 Hz, 2H), 2.71 (t, *J* = 7.1 Hz, 2H), 1.80–1.71 (m, 4H); <sup>13</sup>C NMR  $\delta$ : 142.2, 128.48, 128.4, 125.8, 76.9, 35.6, 27.7, 27.2.

**2-Octyl hydroperoxide (3f)**—CAS # 32956-90-4; Colorless liquid; yield: 48% (105 mg); R<sub>f</sub> (10% EA/Hex) = 0.37; [ $\alpha$ ]<sub>D</sub> = –0.5 (c = 1.46 gm/100ml, CHCl<sub>3</sub>); <sup>2</sup>H NMR  $\delta$ : 7.89 (s,



1H), 4.07 (m, 1H), 1.64 (m, 1H), 1.44–1.28 (m, 9H), 1.23 (d,  $J = 6.1$  Hz, 3H), 0.89 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR  $\delta$ : 84.7, 34.0, 31.7, 29.3, 25.3, 22.5, 18.1, 14.0.

**2-dodecyl hydroperoxide (3g)**—CAS # 123369-50-6; Colorless liquid; yield: 63% (94 mg);  $R_f$  (15% EA/Hex) = 0.33;  $^1\text{H}$  NMR  $\delta$ : 7.81 (s, 1H), 4.12–4.04 (m, 1H), 1.68–1.61 (m, 1H), 1.45–1.27 (m, 17H), 1.24 (d,  $J = 6.1$  Hz, 3H), 0.89 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR  $\delta$ : 81.7, 34.0, 31.9, 29.69, 29.61, 29.59, 29.55, 29.33, 25.4, 22.6, 18.1, 14.1.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

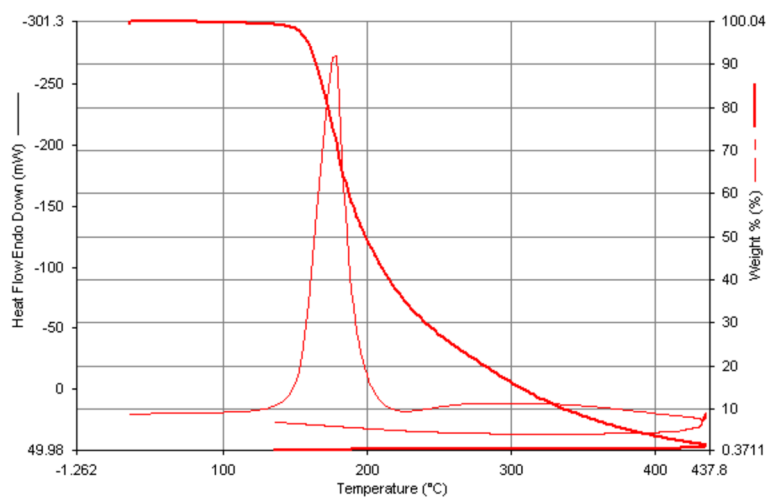
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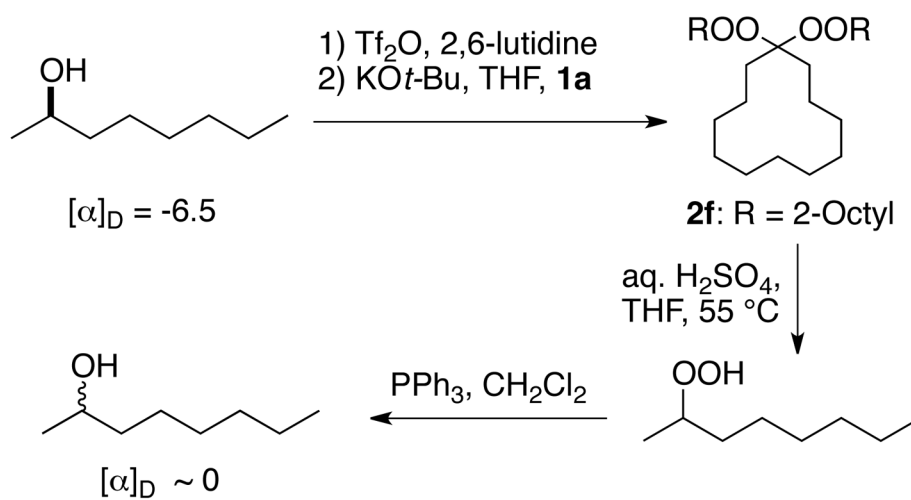


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**Figure 1. Thermal stability of peroxide 2aa**

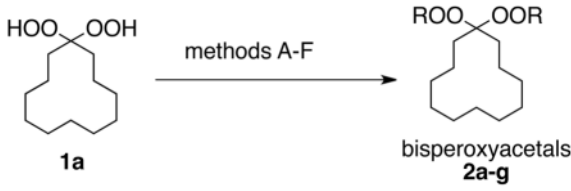
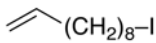
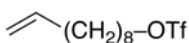
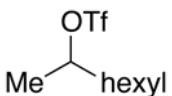
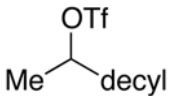
<sup>a</sup> Upper curve is percent of original mass; lower curve indicates heat flow.

**Scheme 1.**

Lack of stereospecificity in alkylation with a 2° triflate.

Table 1

Alkylation of dihydroperoxide **1a**

			
entry	electrophile	method <sup>a</sup>	product (yield)
1	<i>n</i> -C <sub>10</sub> H <sub>21</sub> I	A	<b>2a</b> (93%)
2	<i>n</i> -C <sub>10</sub> H <sub>21</sub> I	C	<b>2a</b> (19%) <sup>b,c</sup>
3	<i>n</i> -C <sub>10</sub> H <sub>21</sub> I	D	<b>2a</b> (7%) <sup>b,c</sup>
4	<i>n</i> -C <sub>10</sub> H <sub>21</sub> Br	A or F	-
5	<i>n</i> -C <sub>10</sub> H <sub>21</sub> I	E	-
7	<i>n</i> -C <sub>6</sub> H <sub>13</sub> I	A	<b>2b</b> (79%)
8	BnBr	A	<b>2c</b> (56%)
9		A	<b>2d</b> (79%)
10		B	<b>2d</b> (80%)
11	Ph(CH <sub>2</sub> ) <sub>4</sub> -OTf	B	<b>2e</b> (68%)
12	2-iodooctane	A	-
13	2-iodooctane	C	<b>2f</b> (trace) <sup>c</sup>
14		B	<b>2f</b> (53%)
15		B	<b>2g</b> (42%)
16	<i>t</i> -BuBr	A	monoalkylation (35%)
17	<i>t</i> -BuBr	G	NR
18	<i>t</i> -BuBr	H	- <sup>c</sup>

<sup>a</sup> A: Ag<sub>2</sub>O, RBr or RI, EtOAc; B: KO<sup>t</sup>Bu, ROTf, THF; C: CsOH•H<sub>2</sub>O (2 equiv), RI (2 eq) DMF; D: CsCO<sub>3</sub> (2 equiv), RI (2 equiv), DMF; E: KO<sup>t</sup>Bu (2.1 equiv), RI (2 equiv), THF; F: 50% KOH (4 equiv), RBr (2 equiv), *n*-Bu<sub>4</sub>NBr (10%), cyclohexane, 50 °C; G: K<sub>2</sub>CO<sub>3</sub>, acetone; H: K<sub>2</sub>CO<sub>3</sub>, DMF, 70 °C.

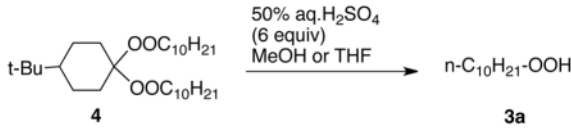
<sup>b</sup> NMR-based yield (internal standard).

<sup>c</sup> Decomposition of **1a** with formation of ketone.

## Optimization of hydrolysis conditions



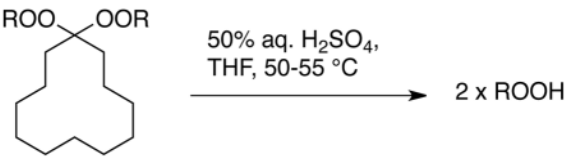
**Table 3**Hydrolysis of cyclohexanone-derived bisperoxyacetal **4**

			
solvent	temp	time (h)	yield
MeOH	reflux	0.25	21%
THF	50–55 °C	6	34% <sup>a</sup>

<sup>a</sup> NMR-based yield

**Table 4**

Hydrolysis to form hydroperoxides

				
entry	acetal	R	hydroperoxide	yield
1	<b>2a</b>	decyl	<b>3a</b>	78%
2	<b>2b</b>	hexyl	<b>3b</b>	49% <sup>a</sup>
3	<b>2c</b>	benzyl	<b>3c</b>	60%
4	<b>2d</b>	9-decenyl	<b>3d</b>	62%
5	<b>2e</b>	Ph(CH <sub>2</sub> ) <sub>3</sub>	<b>3e</b>	79%
6	<b>2f</b>	2-octyl	<b>3f</b>	48%
7	<b>2g</b>	2-dodecyl	<b>3g</b>	63%

<sup>a</sup> volatile compound.



**Supporting Information** for “A New Synthesis Of Alkyl Hydroperoxides Via Alkylation Of *gem*-Dihydroperoxides” (1H and 13C NMR except as noted)

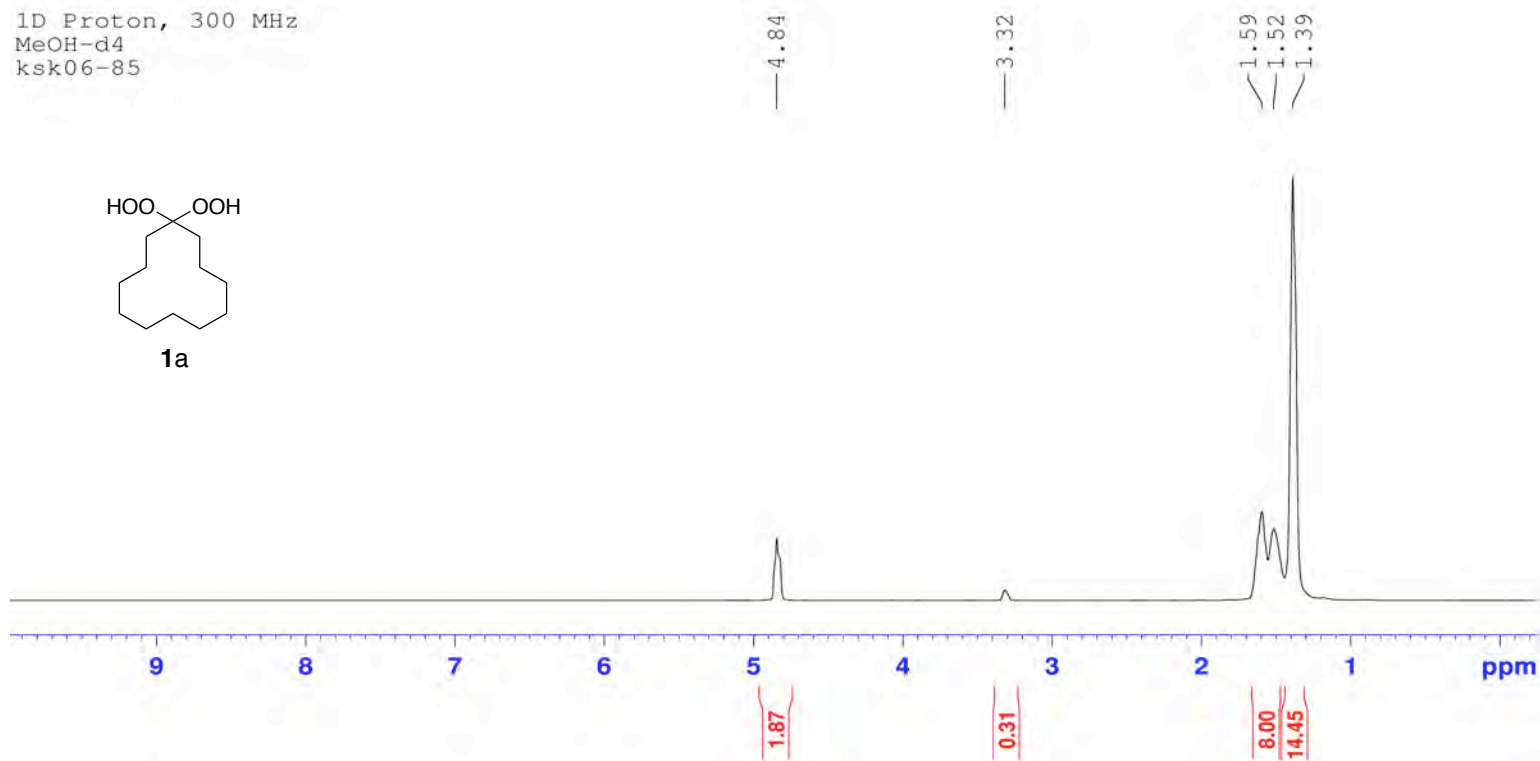
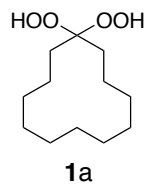
ShivaKumar Kyasa, Benjamin W Puffer, Patrick H Dussault\*.

Department of Chemistry, University of Nebraska – Lincoln, Lincoln, NE. 68588-0403

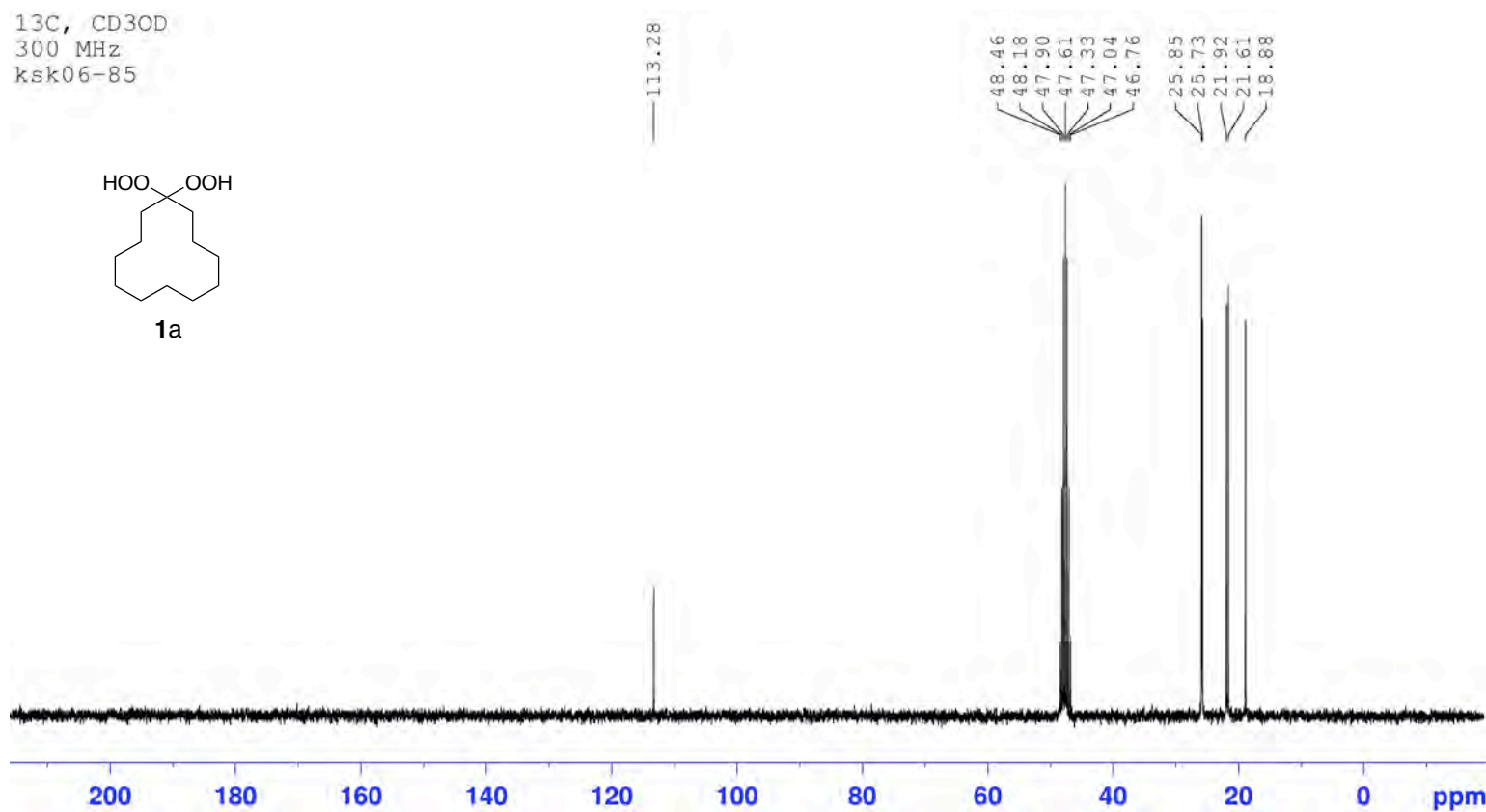
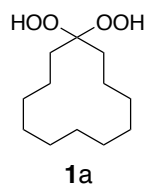
[pdussault1@unl.edu](mailto:pdussault1@unl.edu)

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2c) 1,1 bis(benzylperoxy) cyclododecane .....	6
2d) 1,1 bis(9-decenyl peroxy) cyclododecane .....	7
2e) 1,1-bis(4-phenylbutylperoxy) cyclododecane .....	8
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3f) 2-Octylhydroperoxide .....	18
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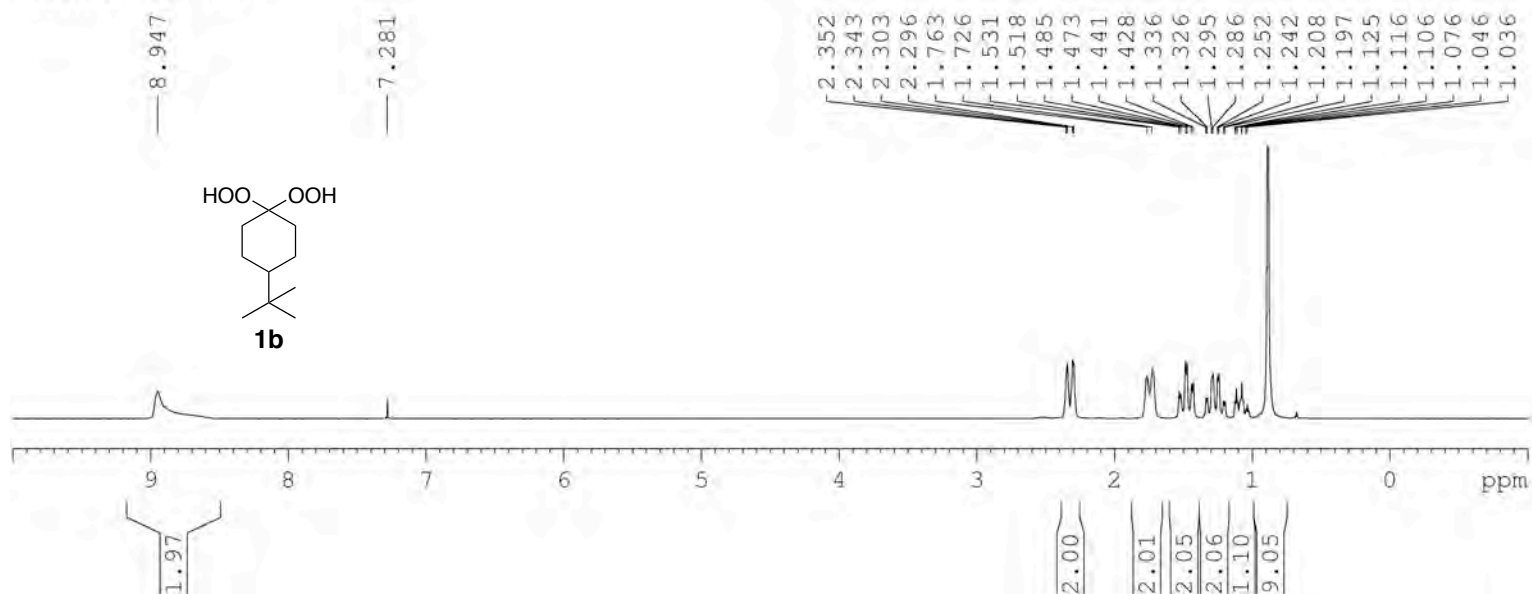
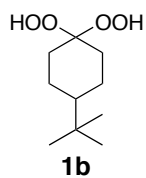
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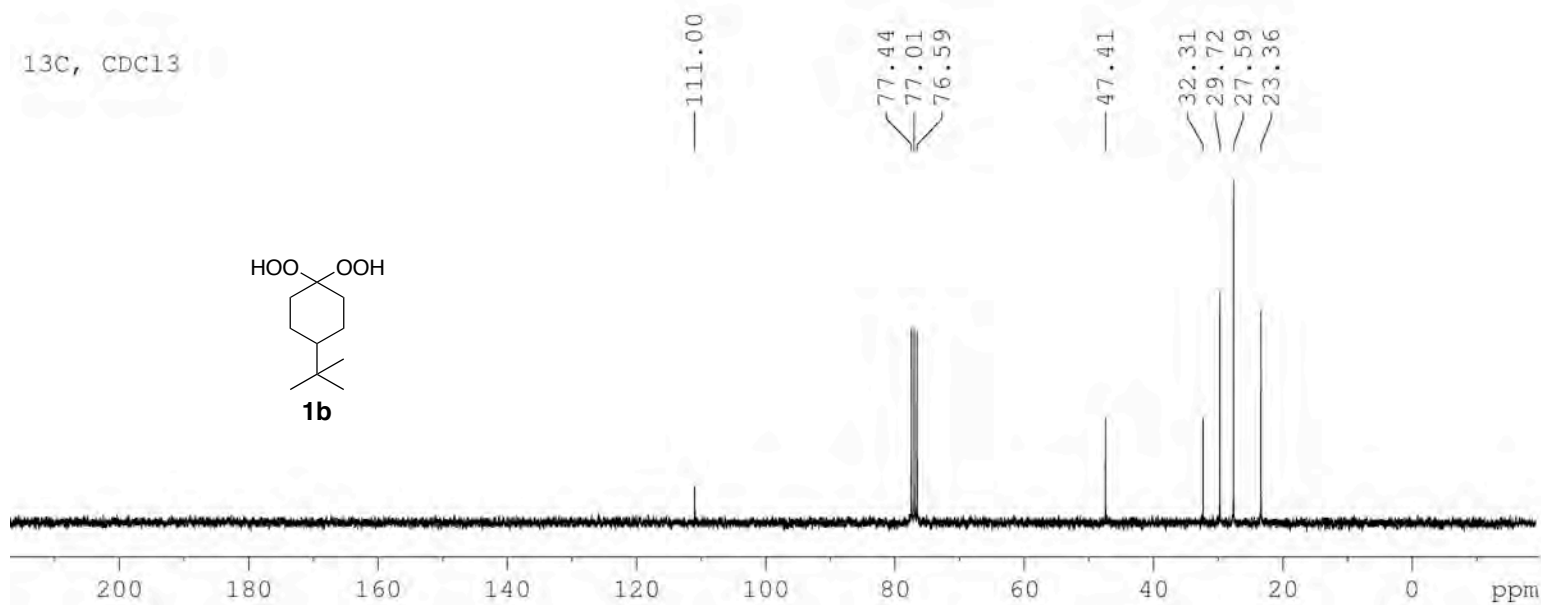
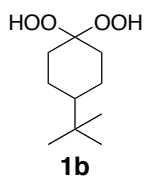
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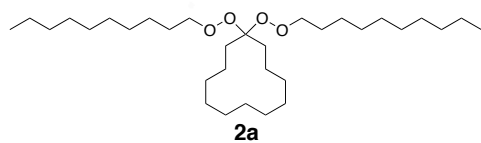
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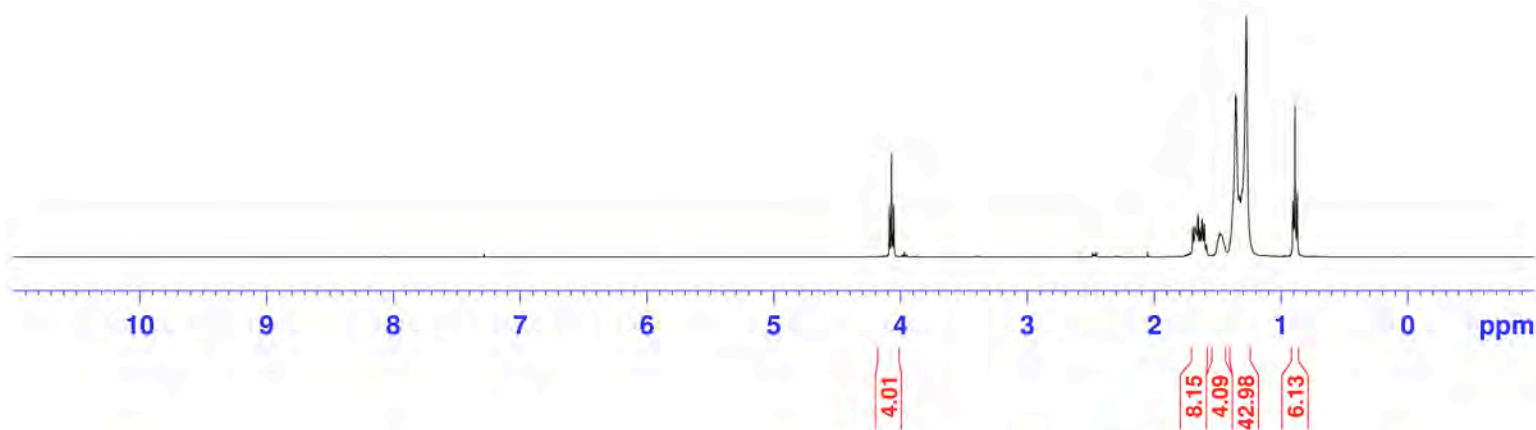
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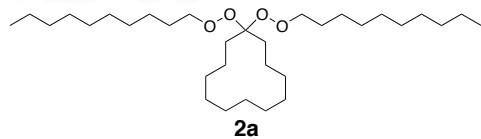
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1.722  
1.694  
1.675  
1.653  
1.639  
1.622  
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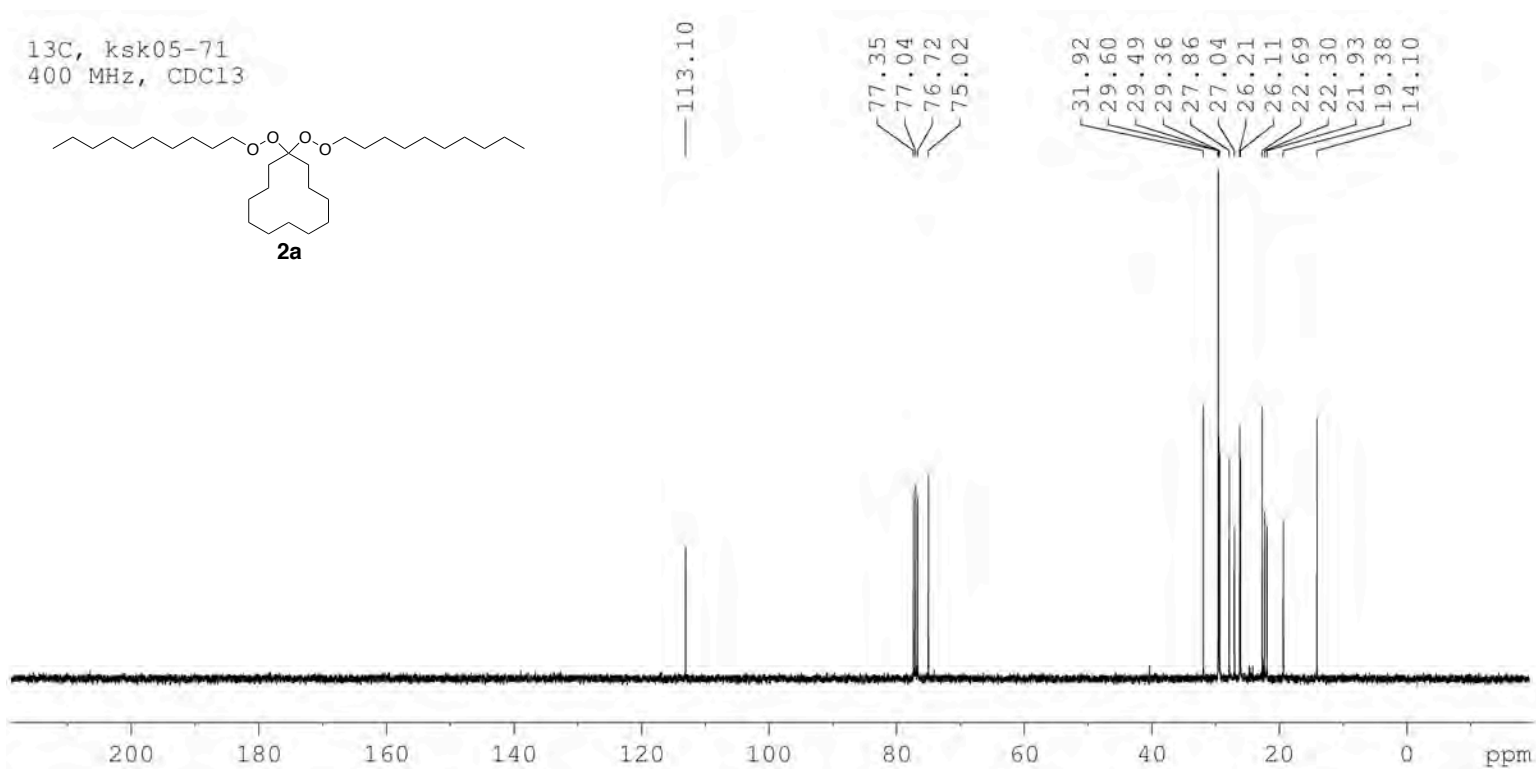


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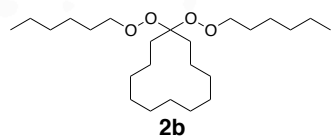


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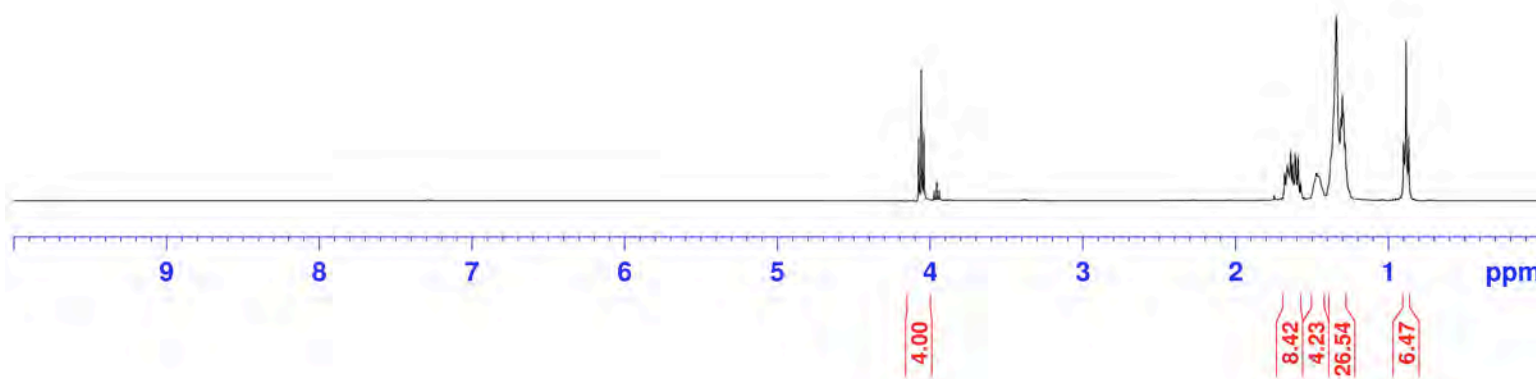


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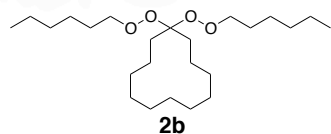


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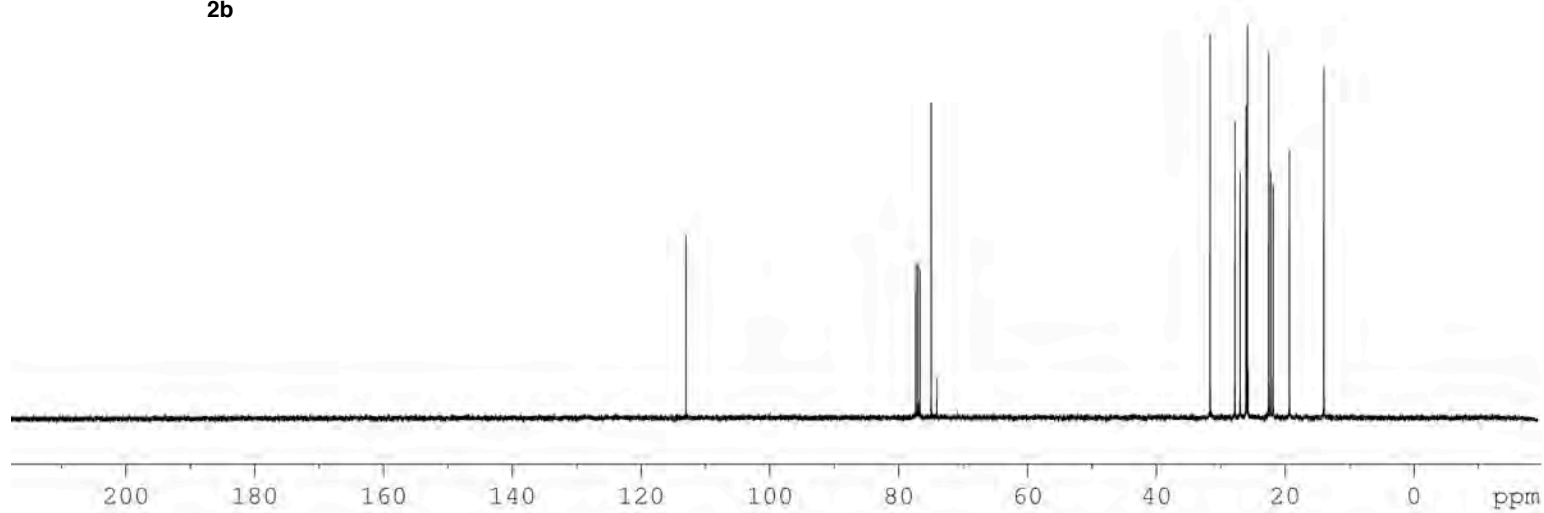
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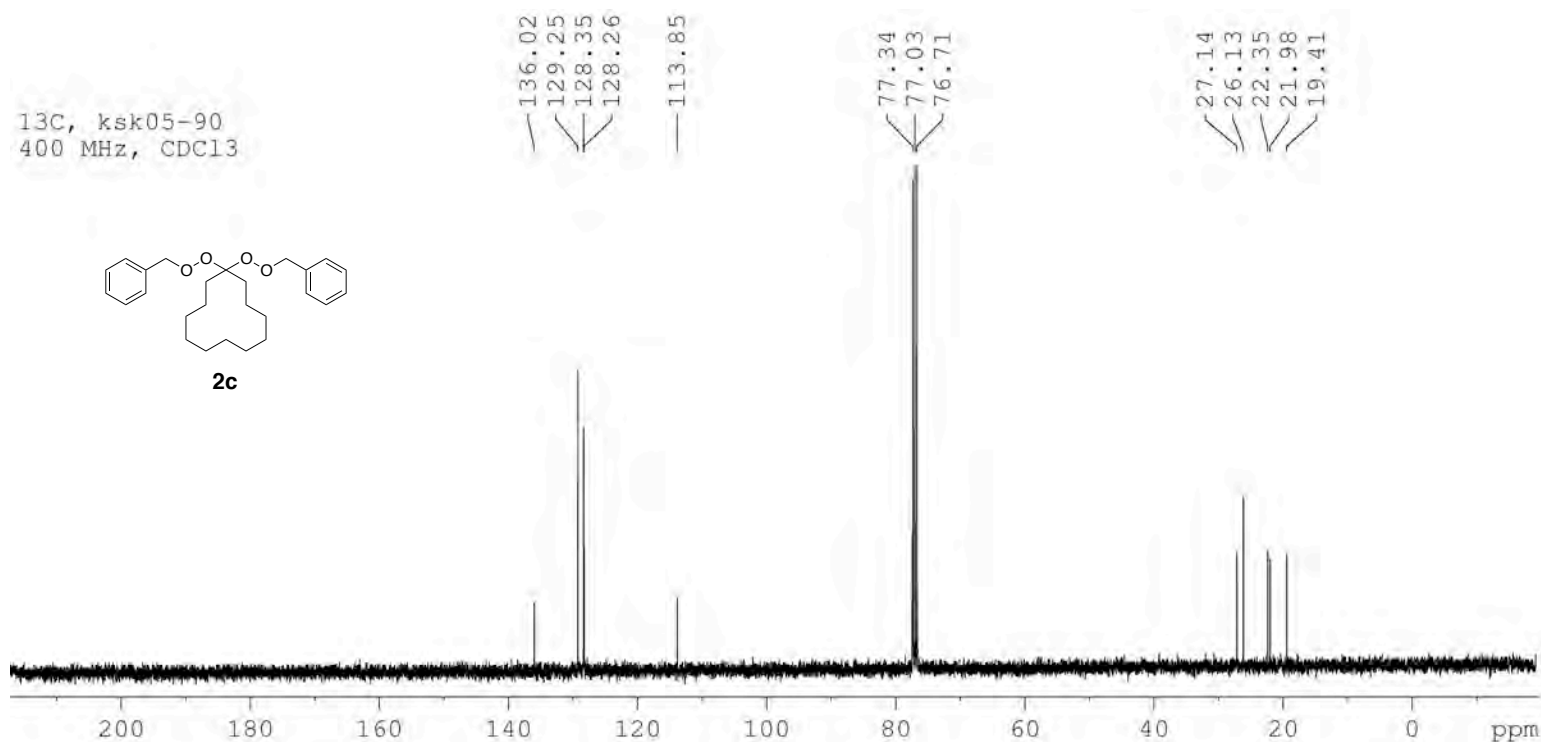
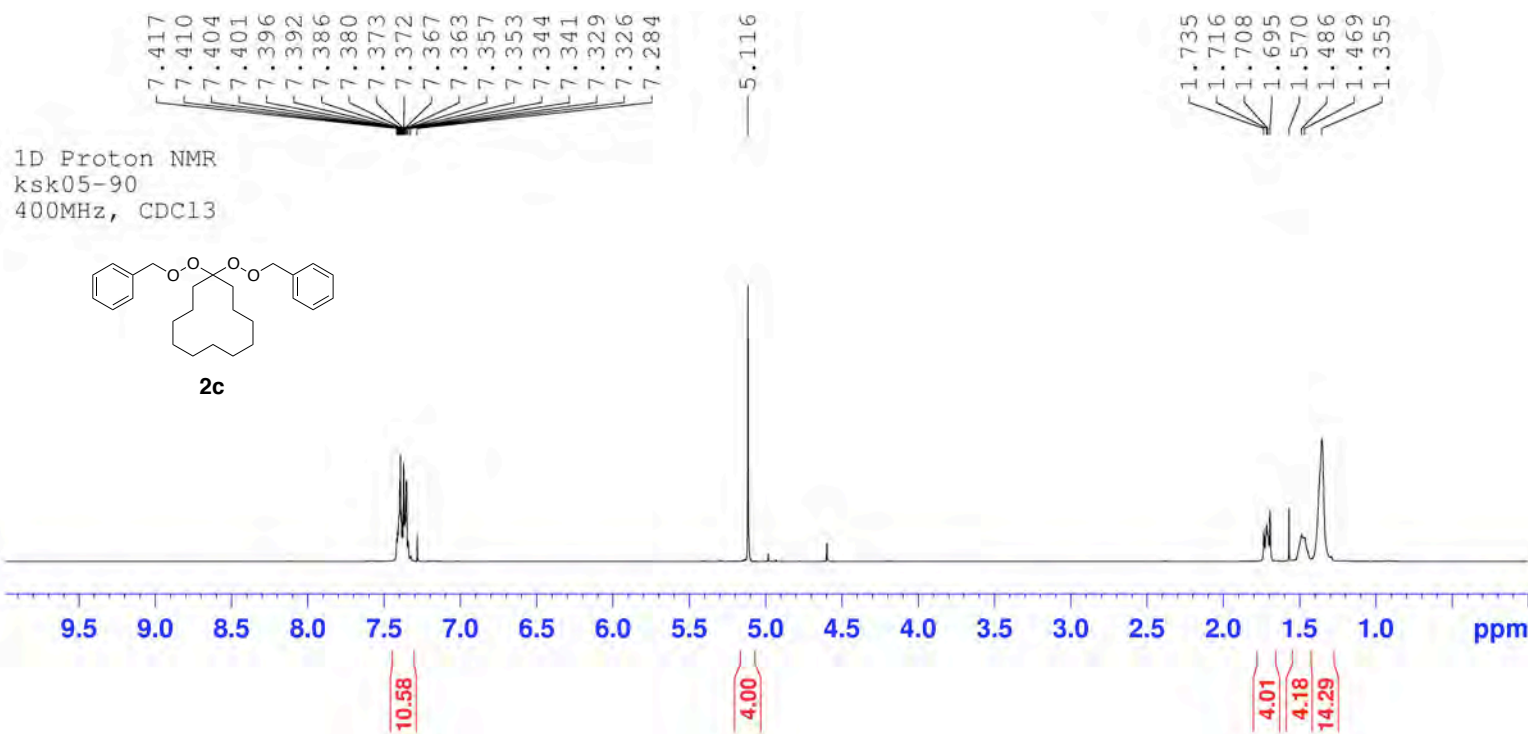


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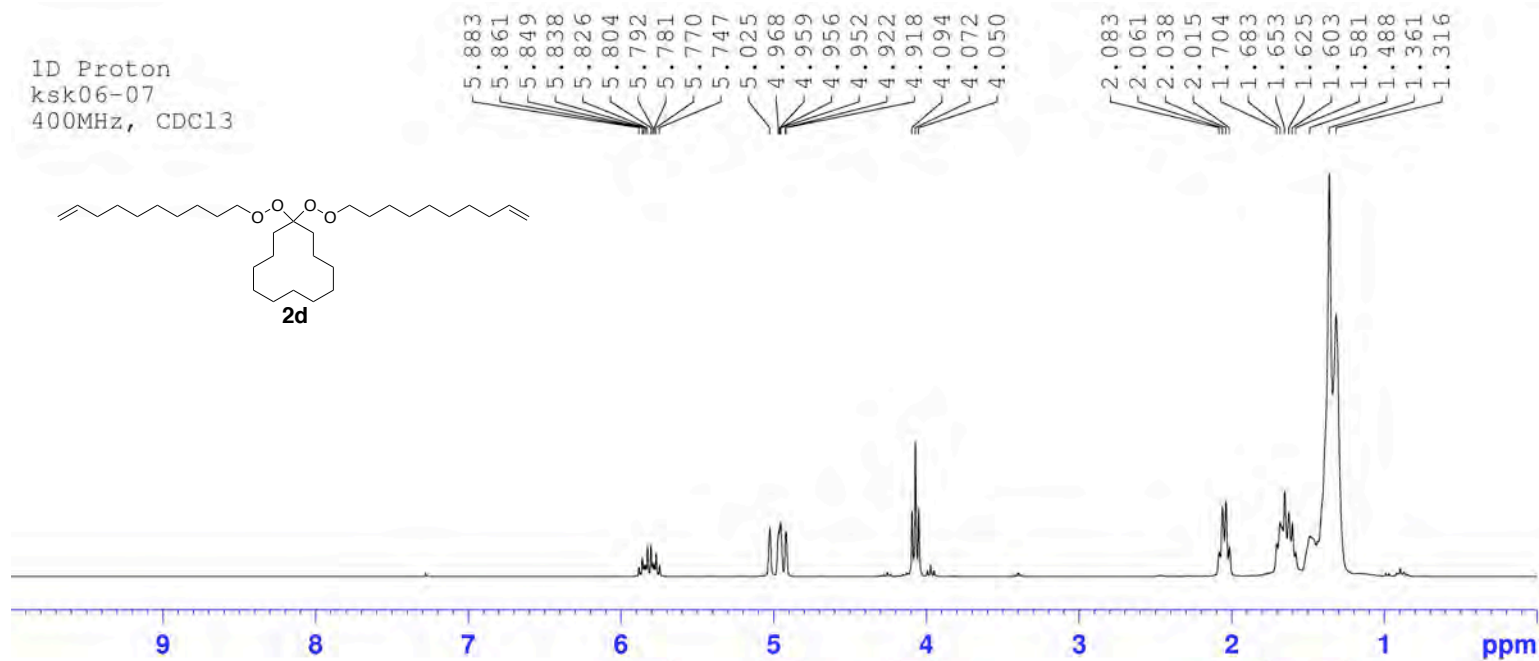
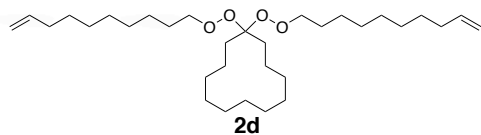
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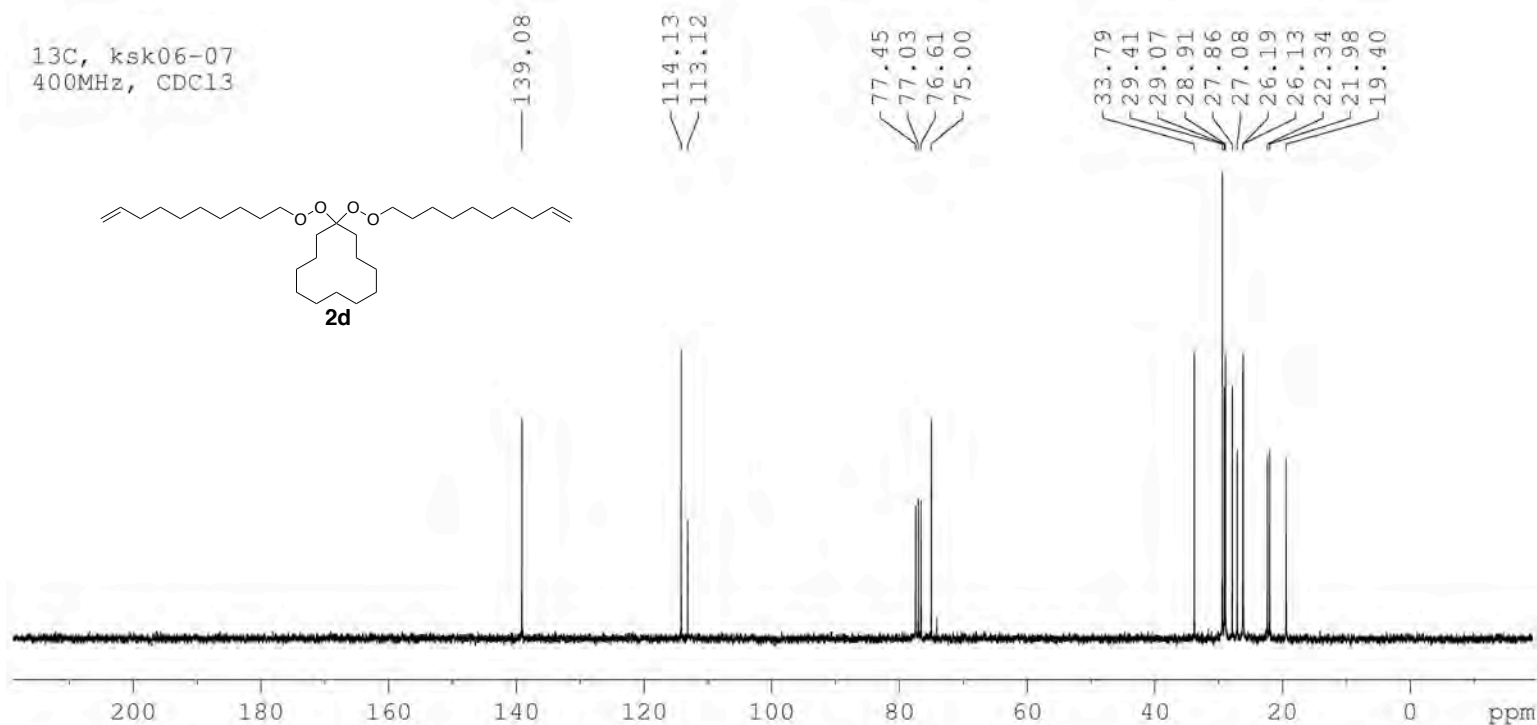
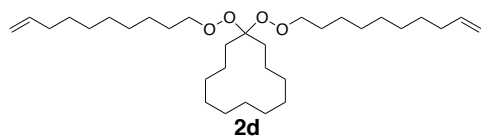




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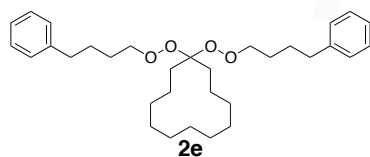


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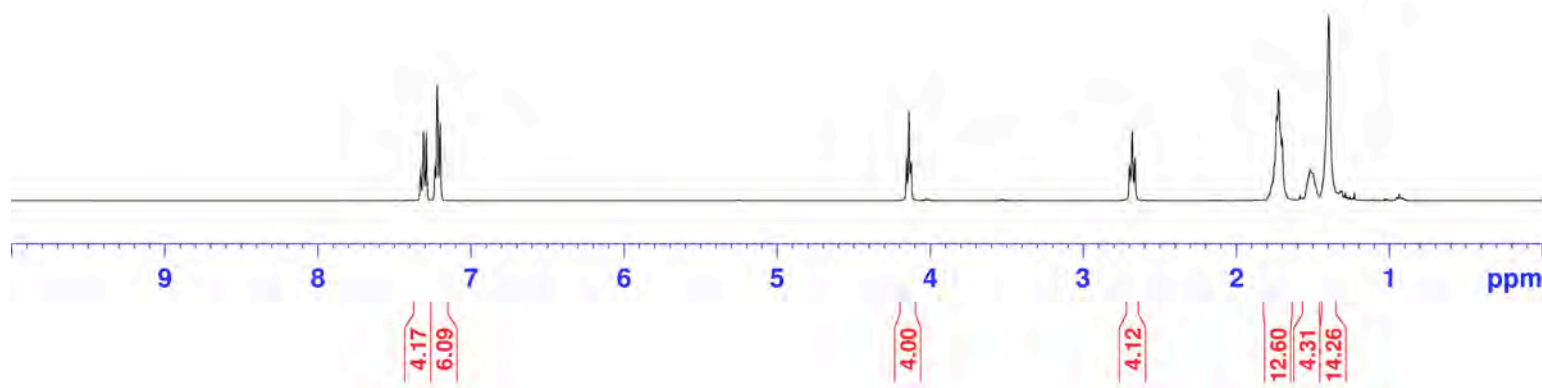


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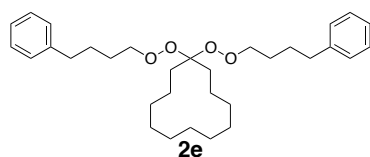
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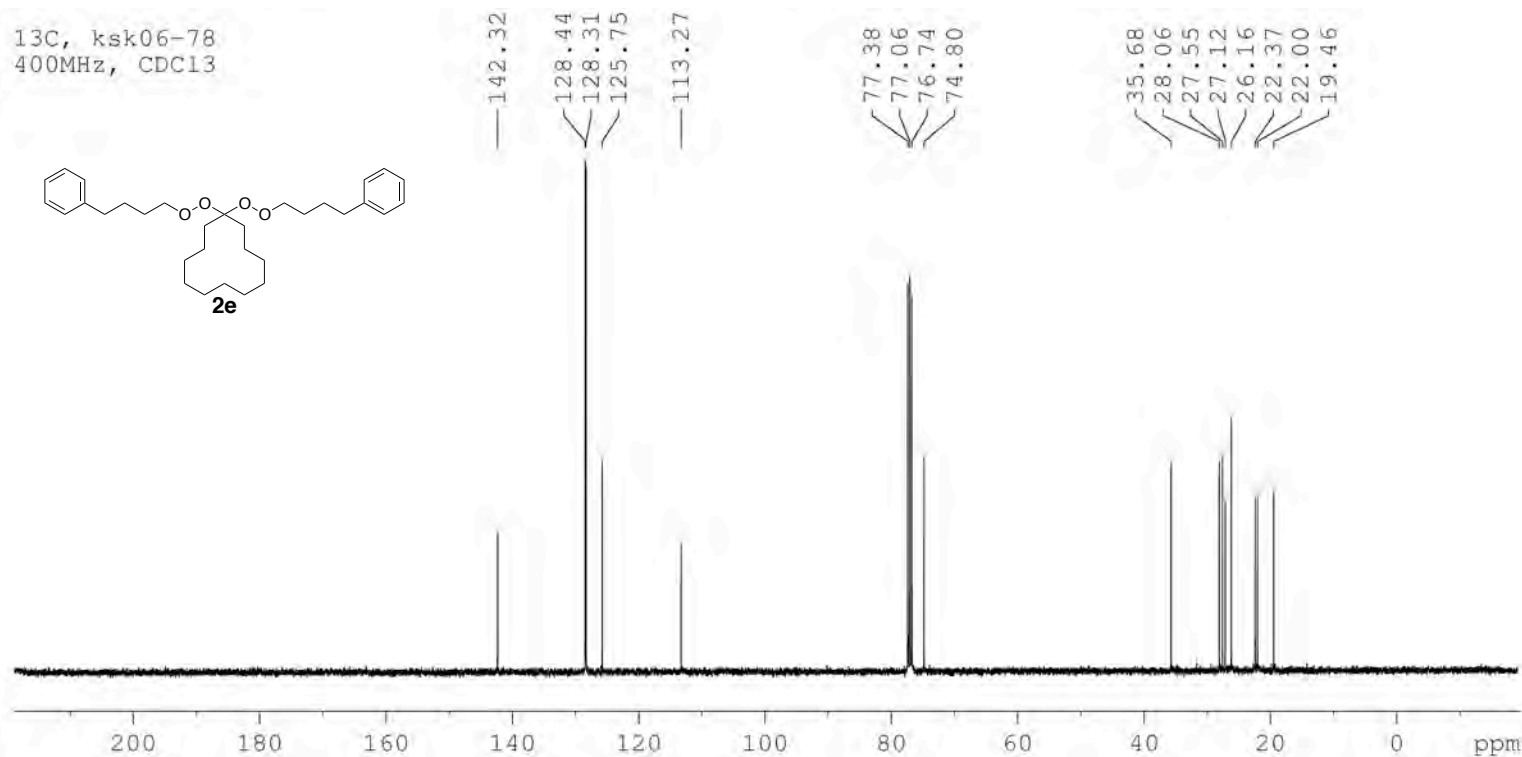
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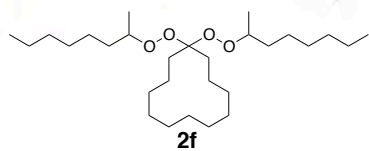
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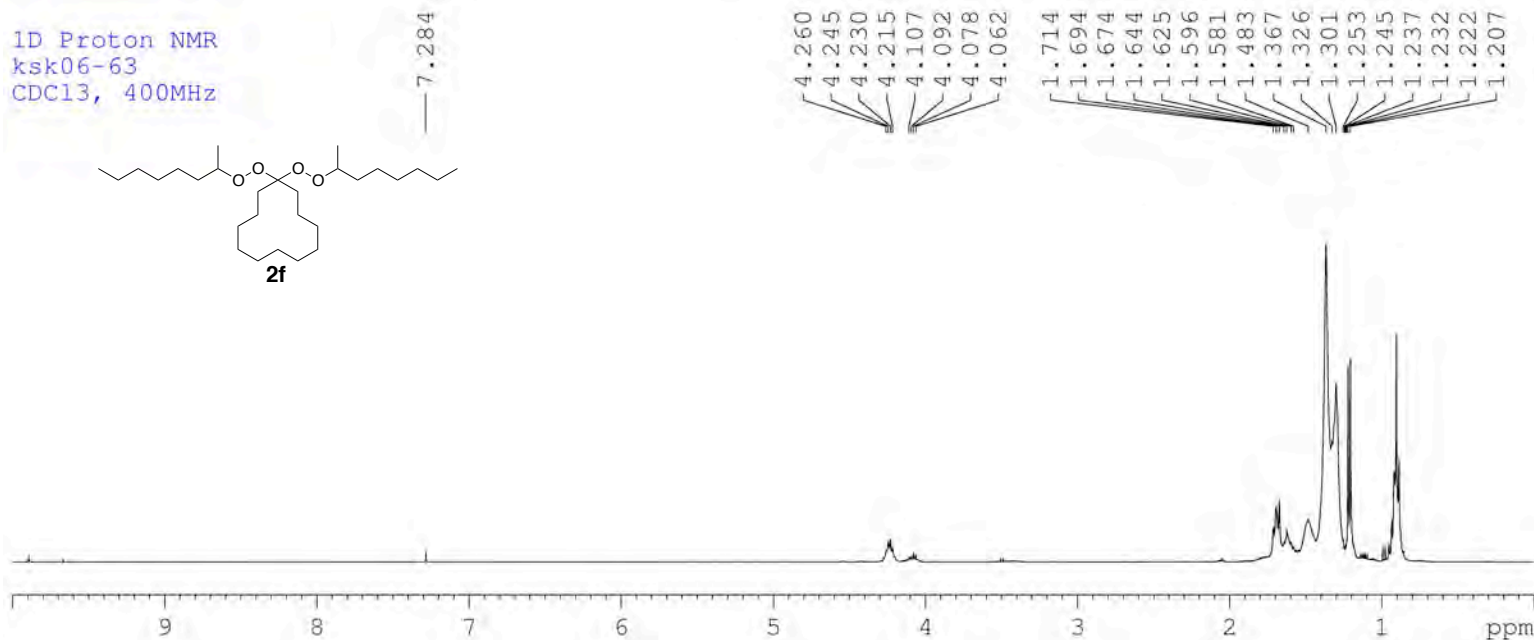
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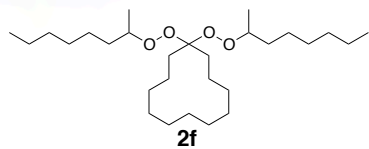
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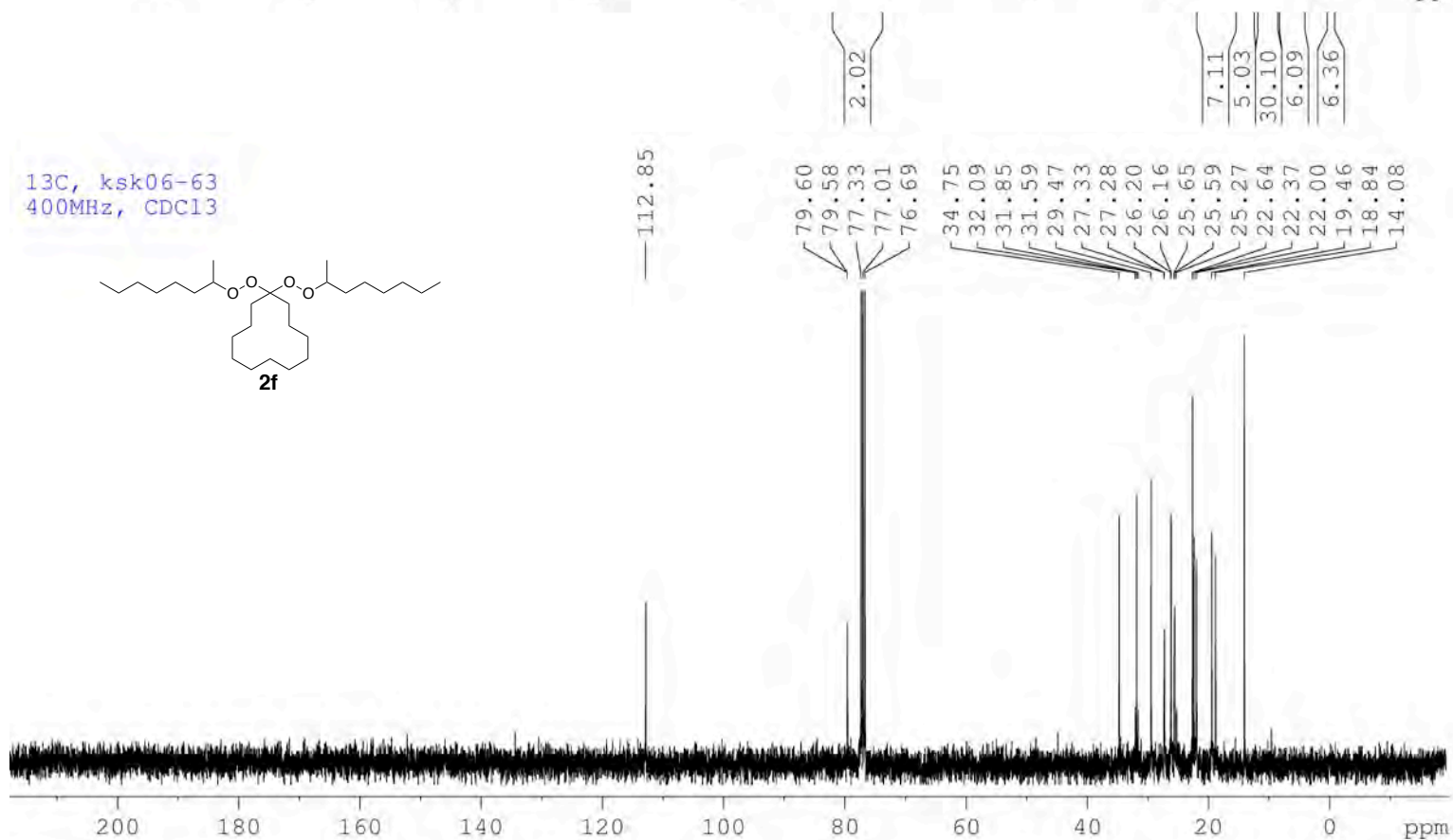
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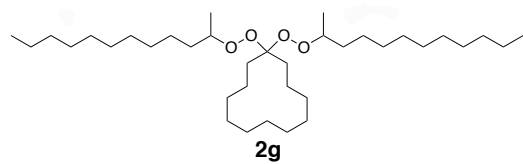
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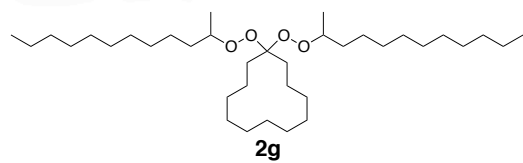
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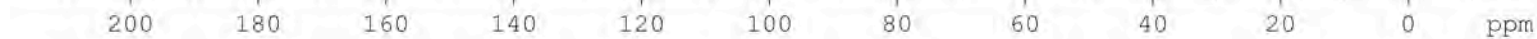
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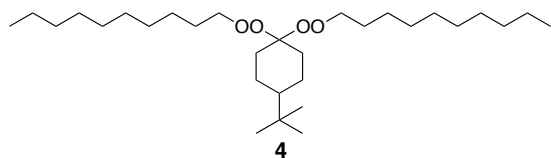
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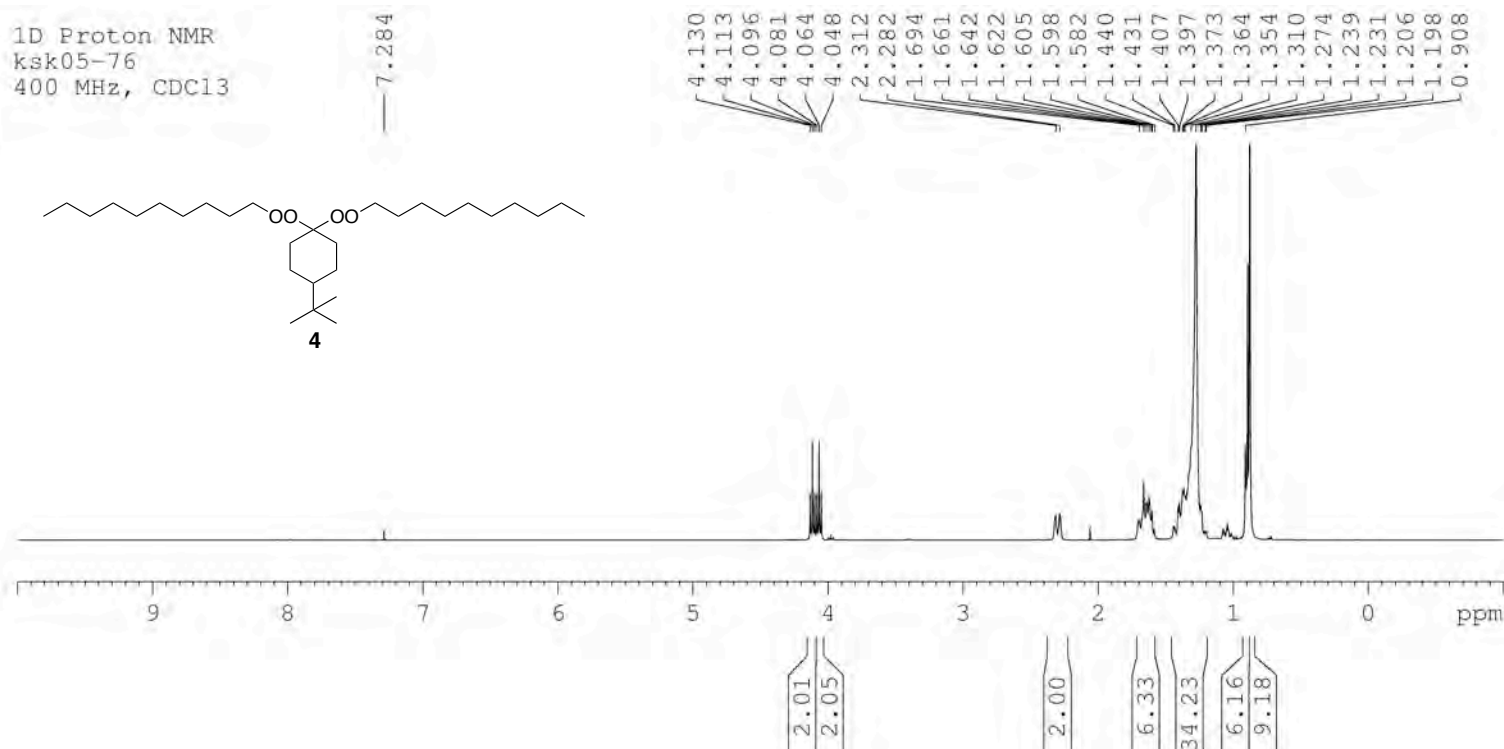
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18.84  
14.11



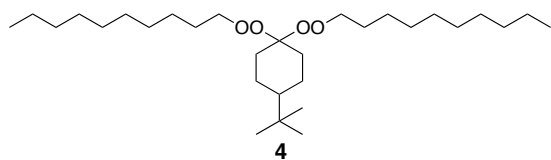
1D Proton NMR  
ksk05-76  
400 MHz, CDC13



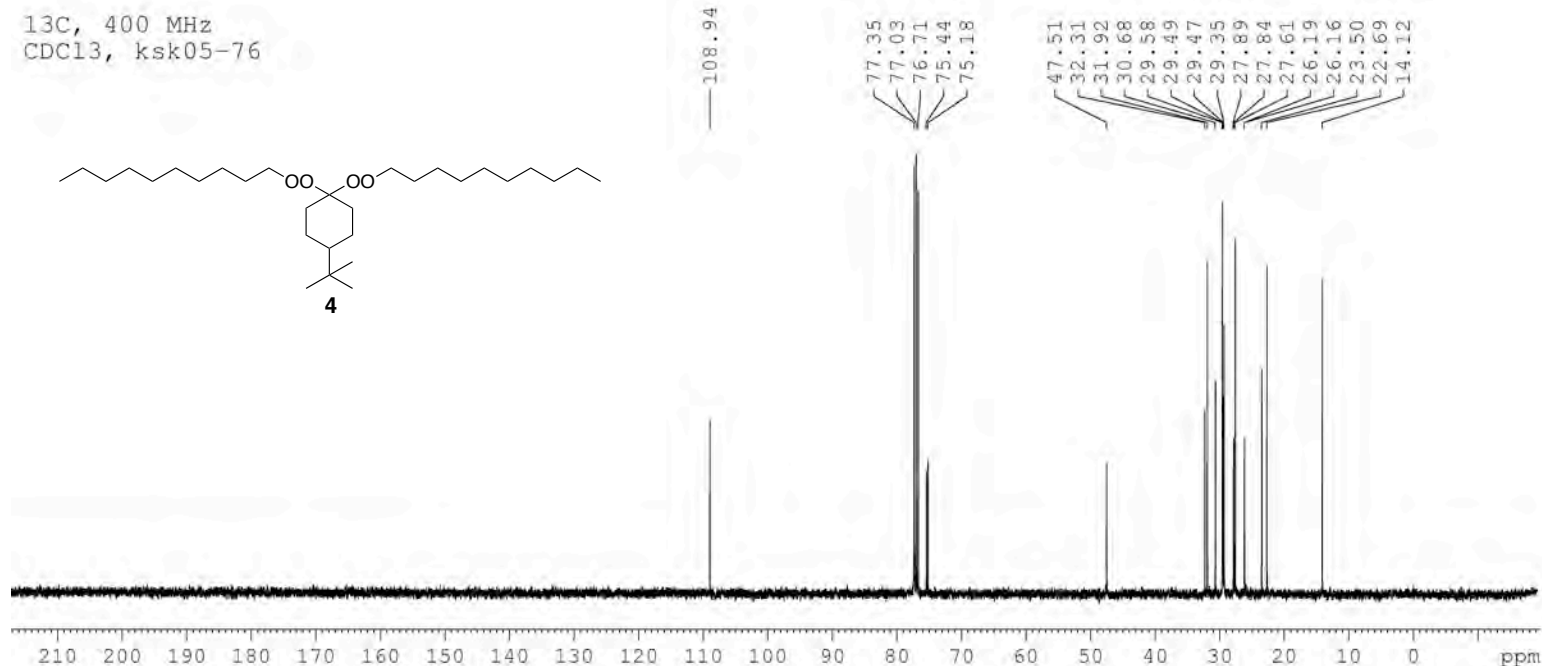
— 7.284



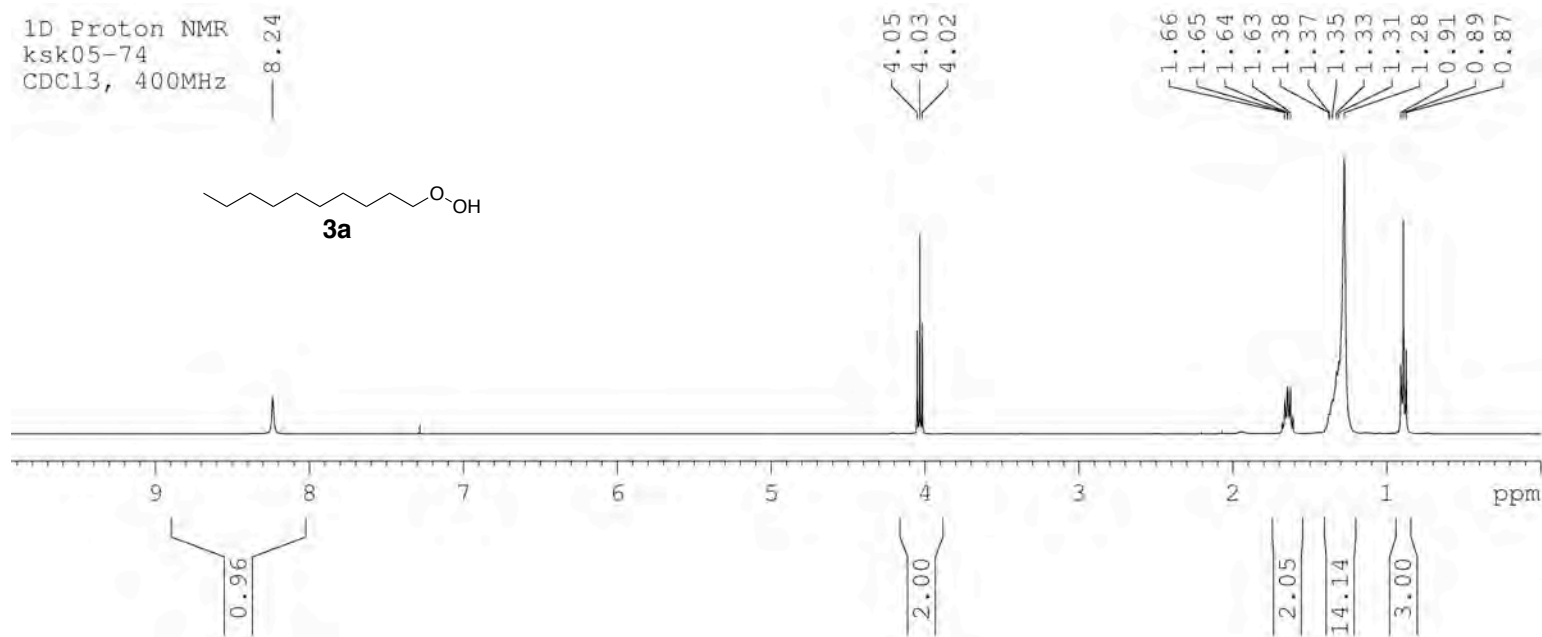
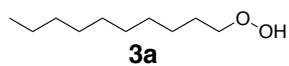
13C, 400 MHz  
CDC13, ksk05-76



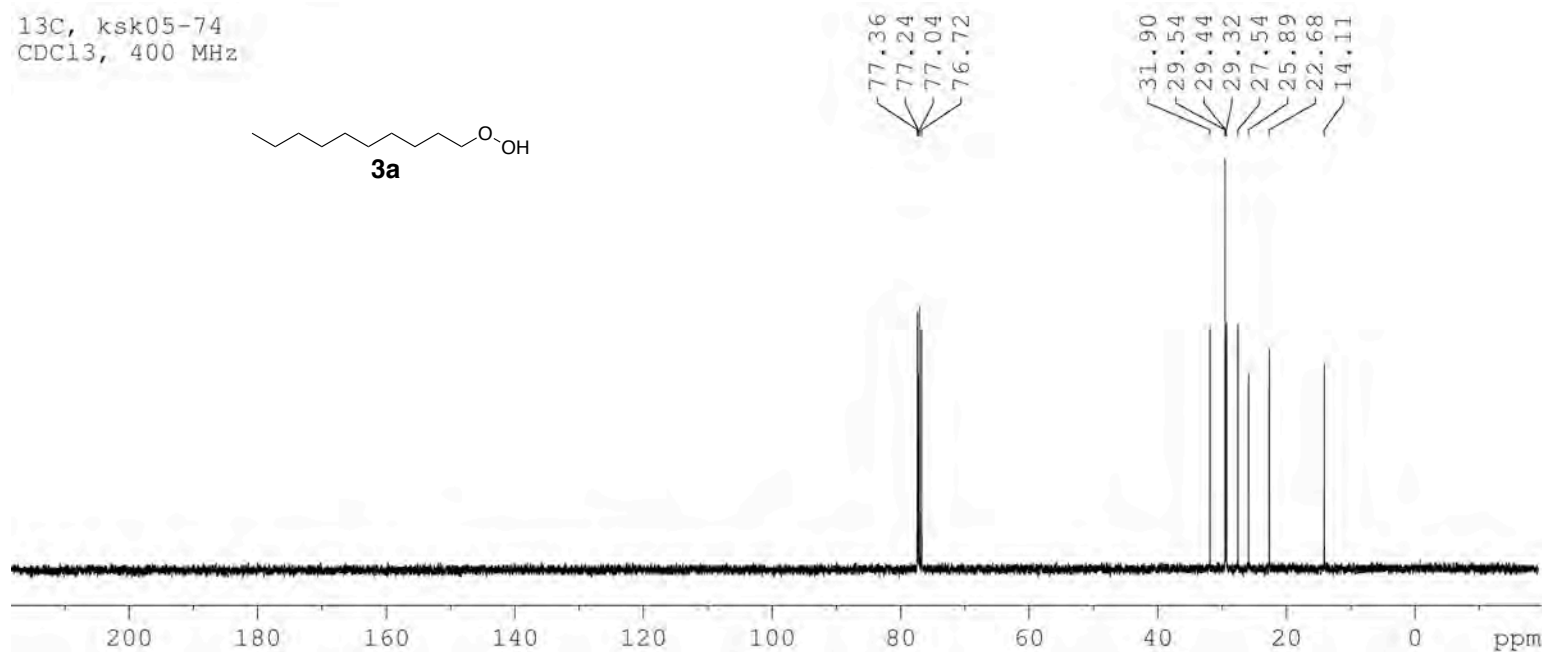
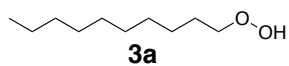
— 108.94



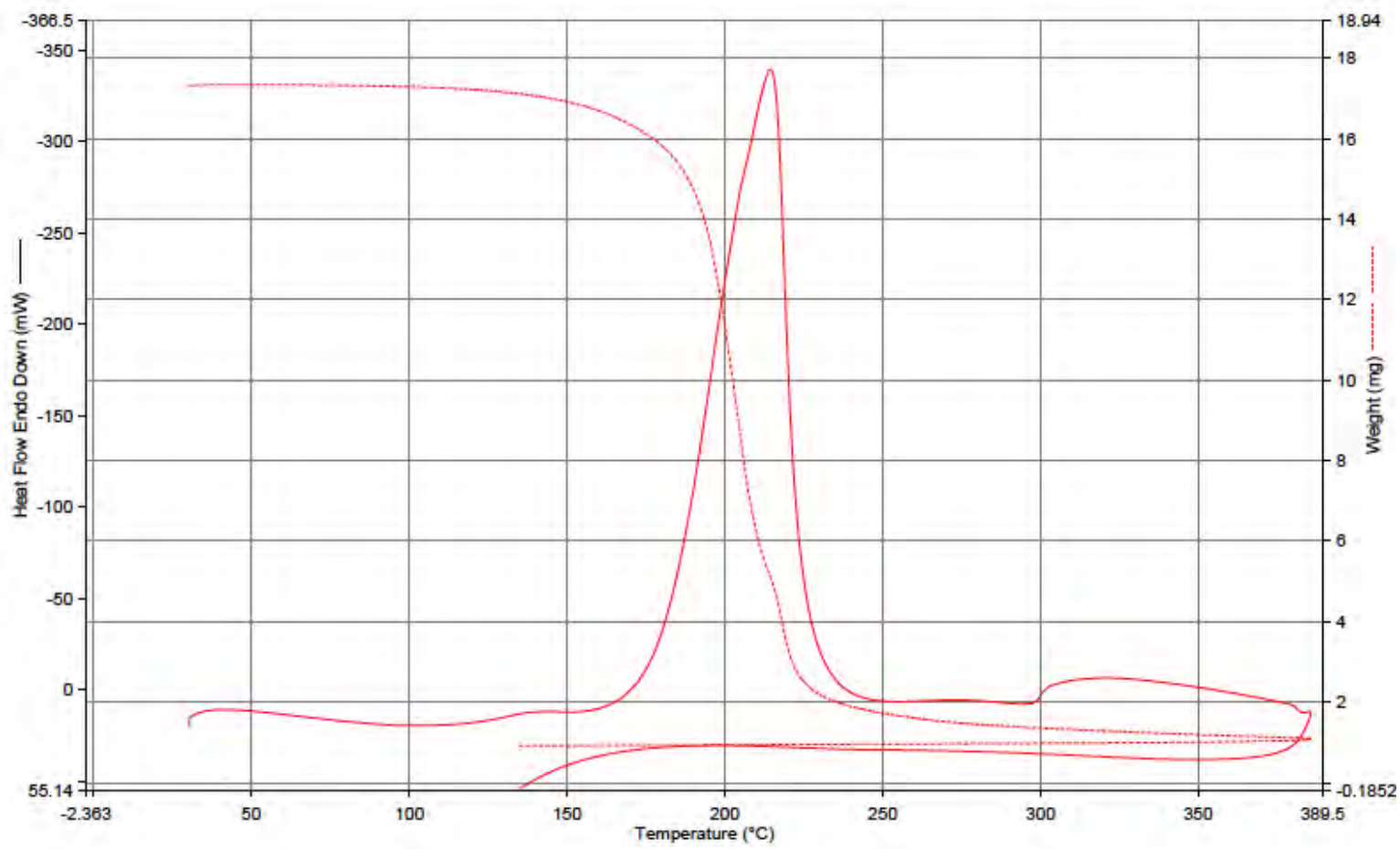
1D Proton NMR  
ksk05-74  
CDCl<sub>3</sub>, 400MHz



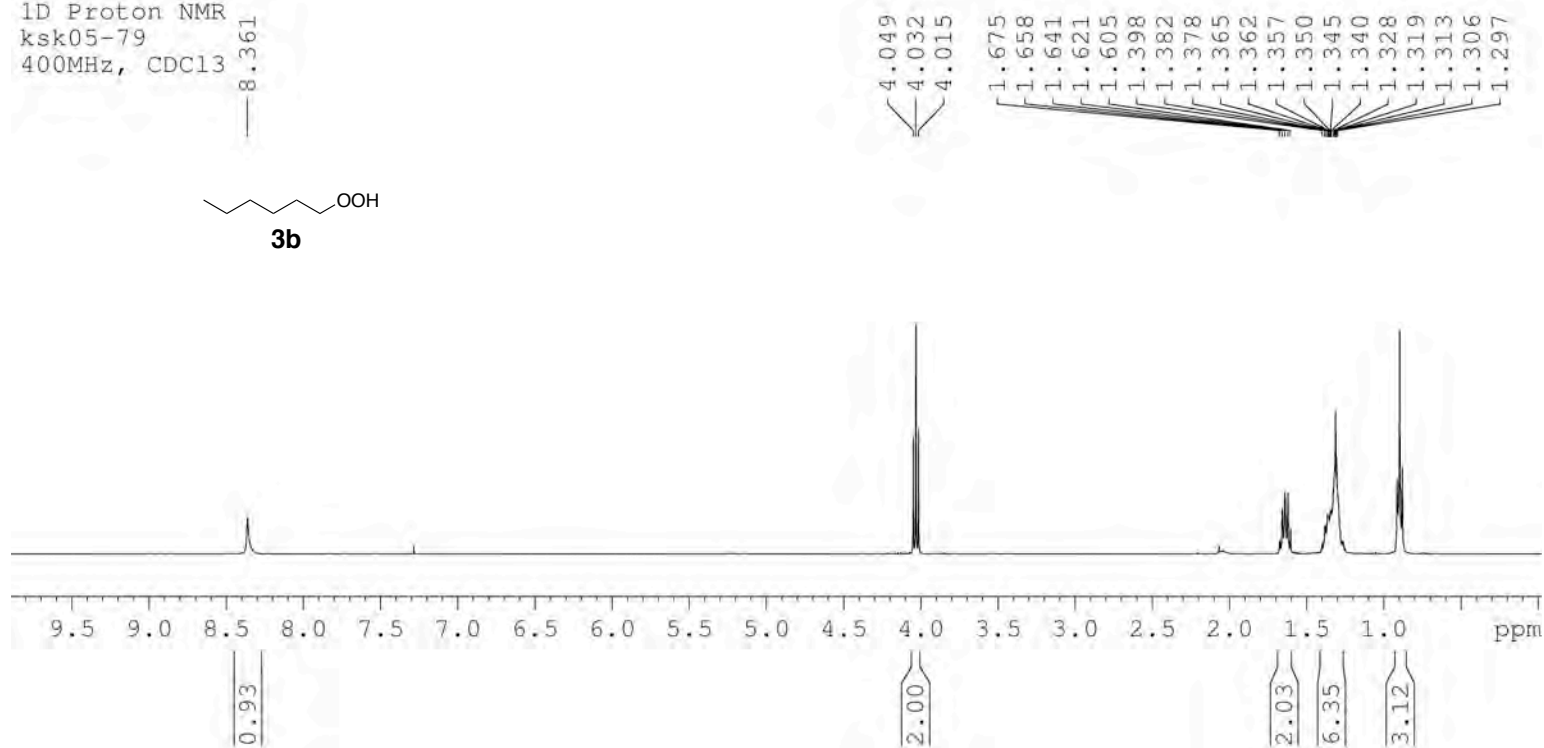
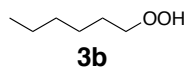
13C, ksk05-74  
CDCl<sub>3</sub>, 400 MHz



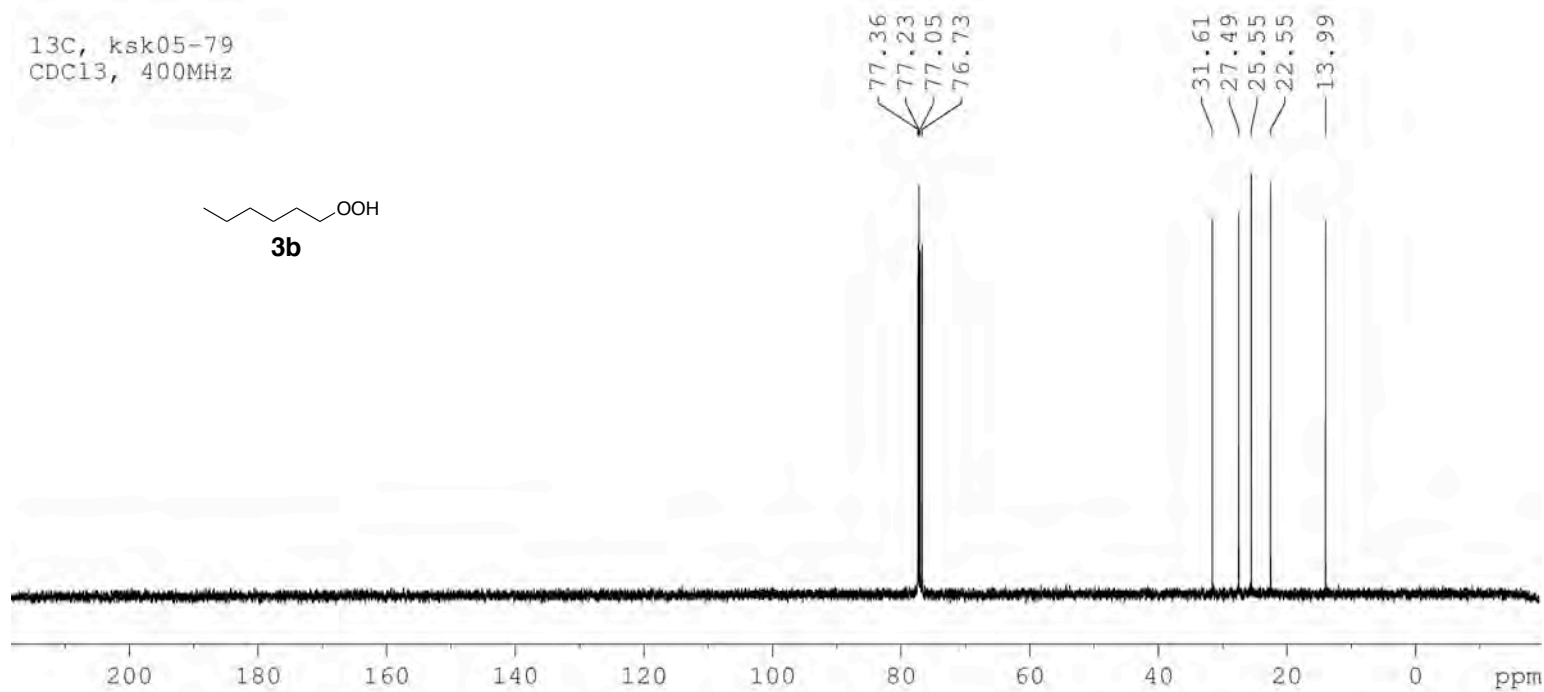
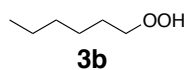
## TGA/DSC of *n*-Decylhydroperoxide



1D Proton NMR  
ksk05-79  
400MHz, CDC13

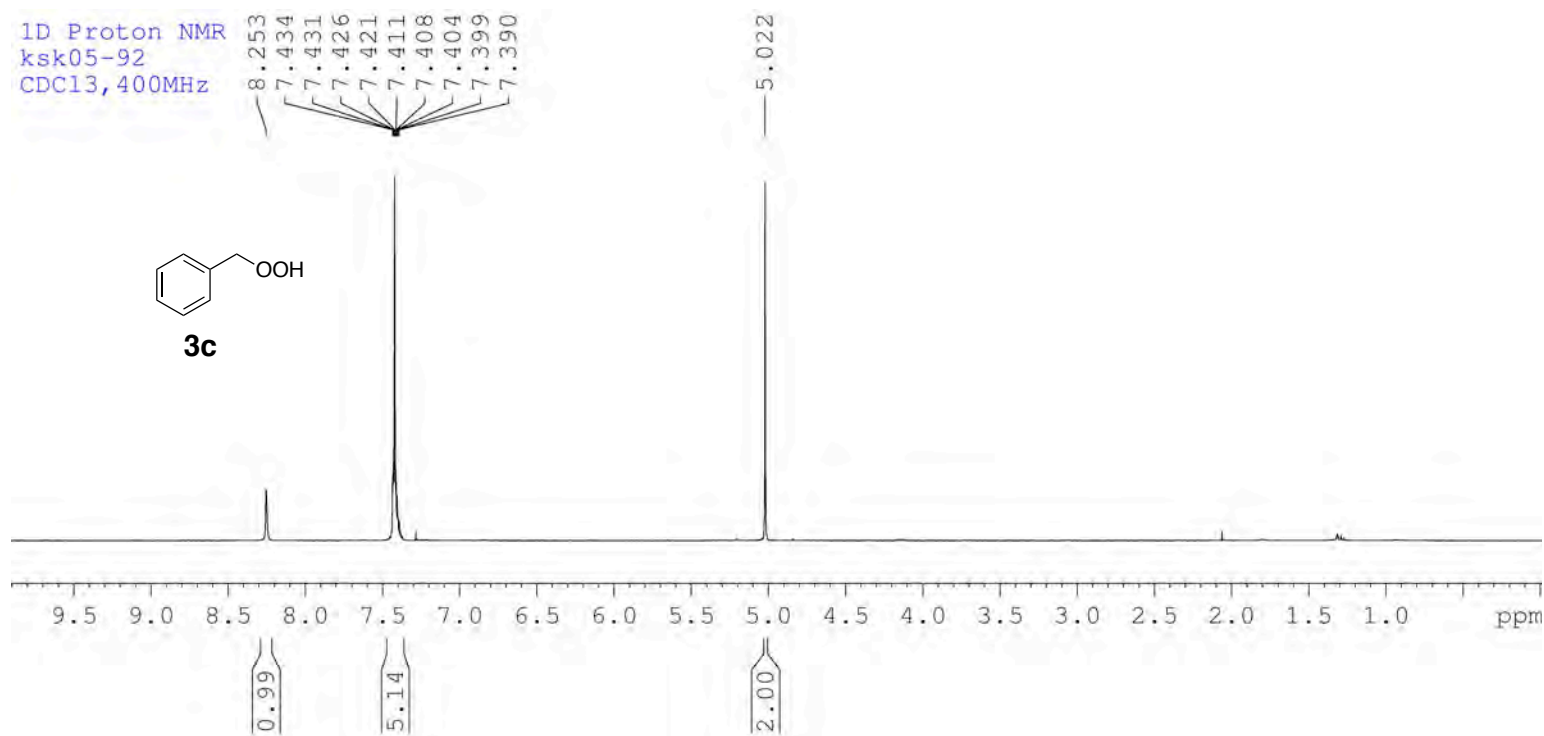
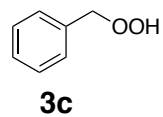


13C, ksk05-79  
CDC13, 400MHz

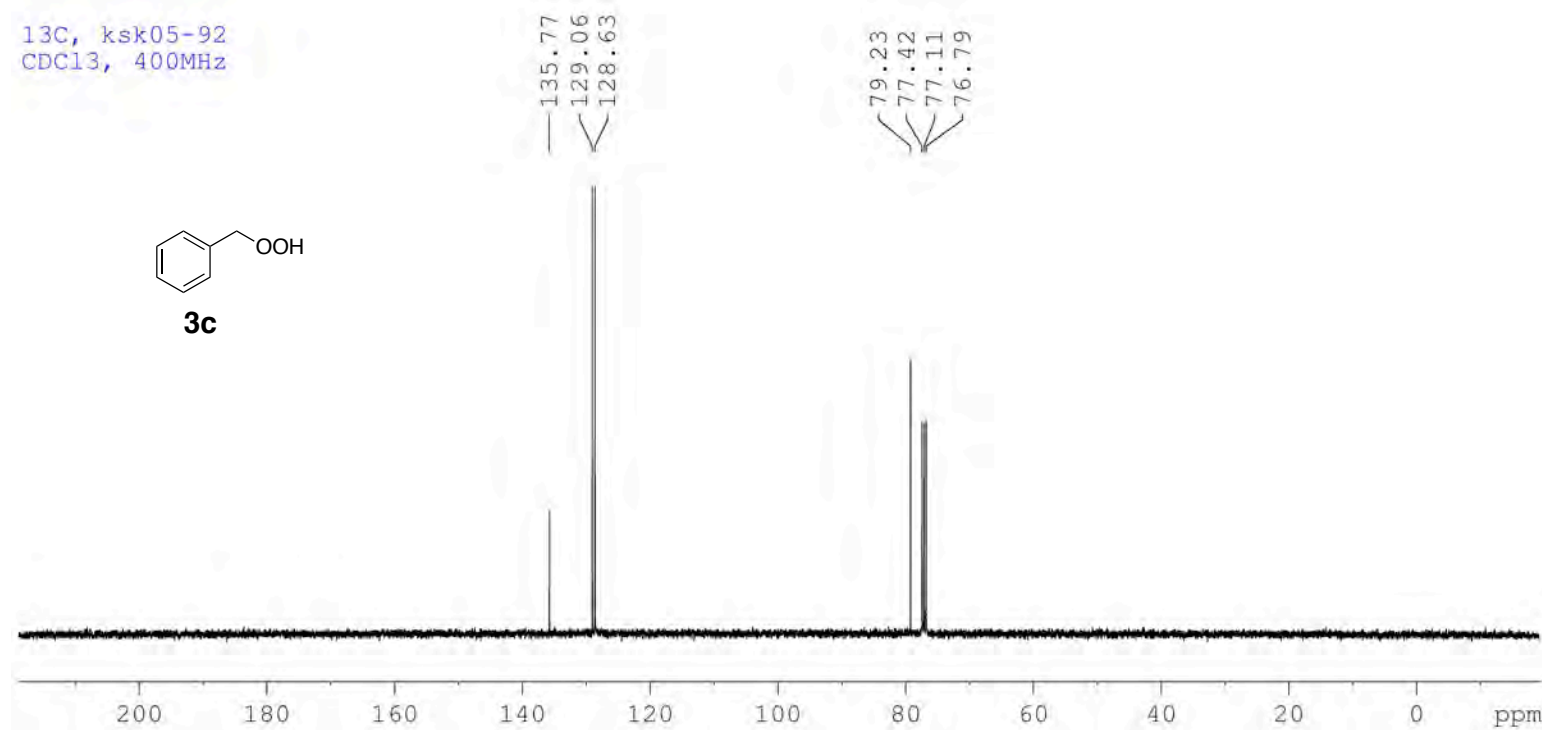
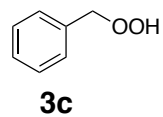




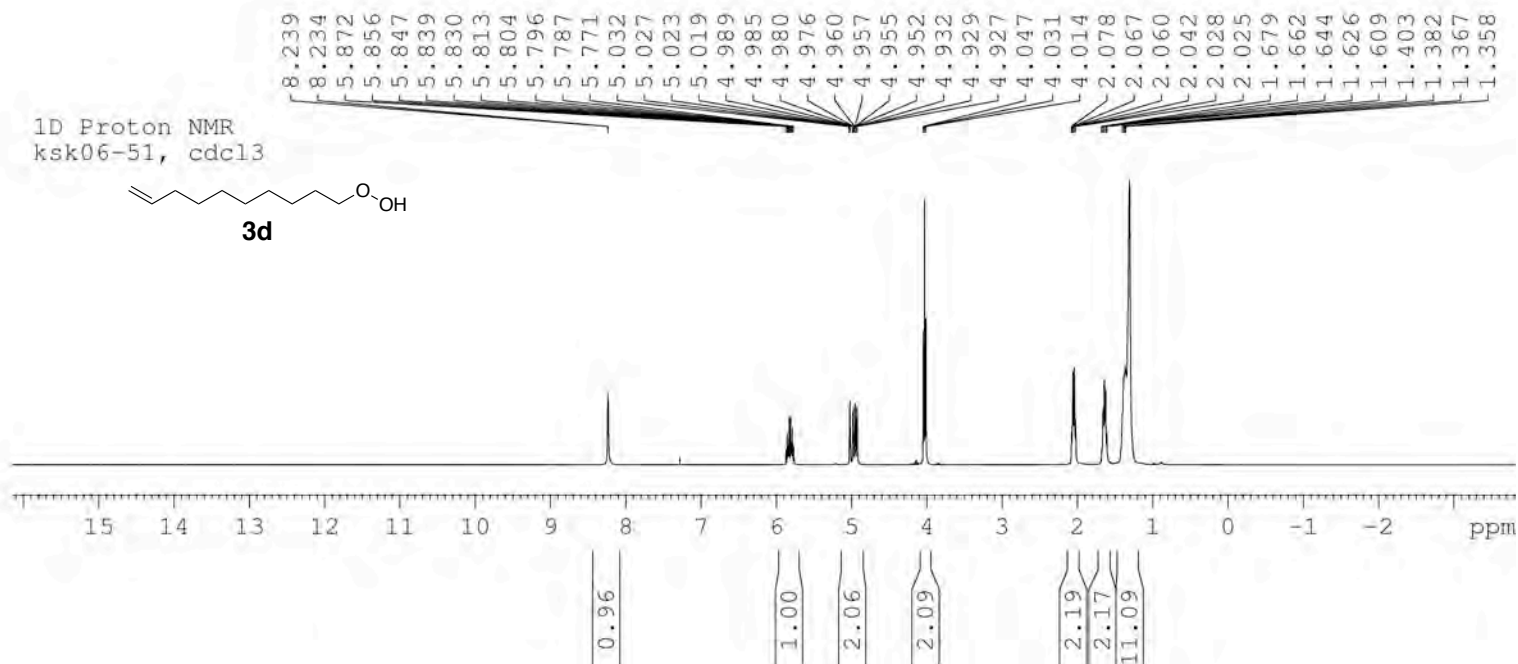
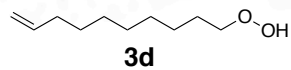
1D Proton NMR  
ksk05-92  
CDCl<sub>3</sub>, 400MHz



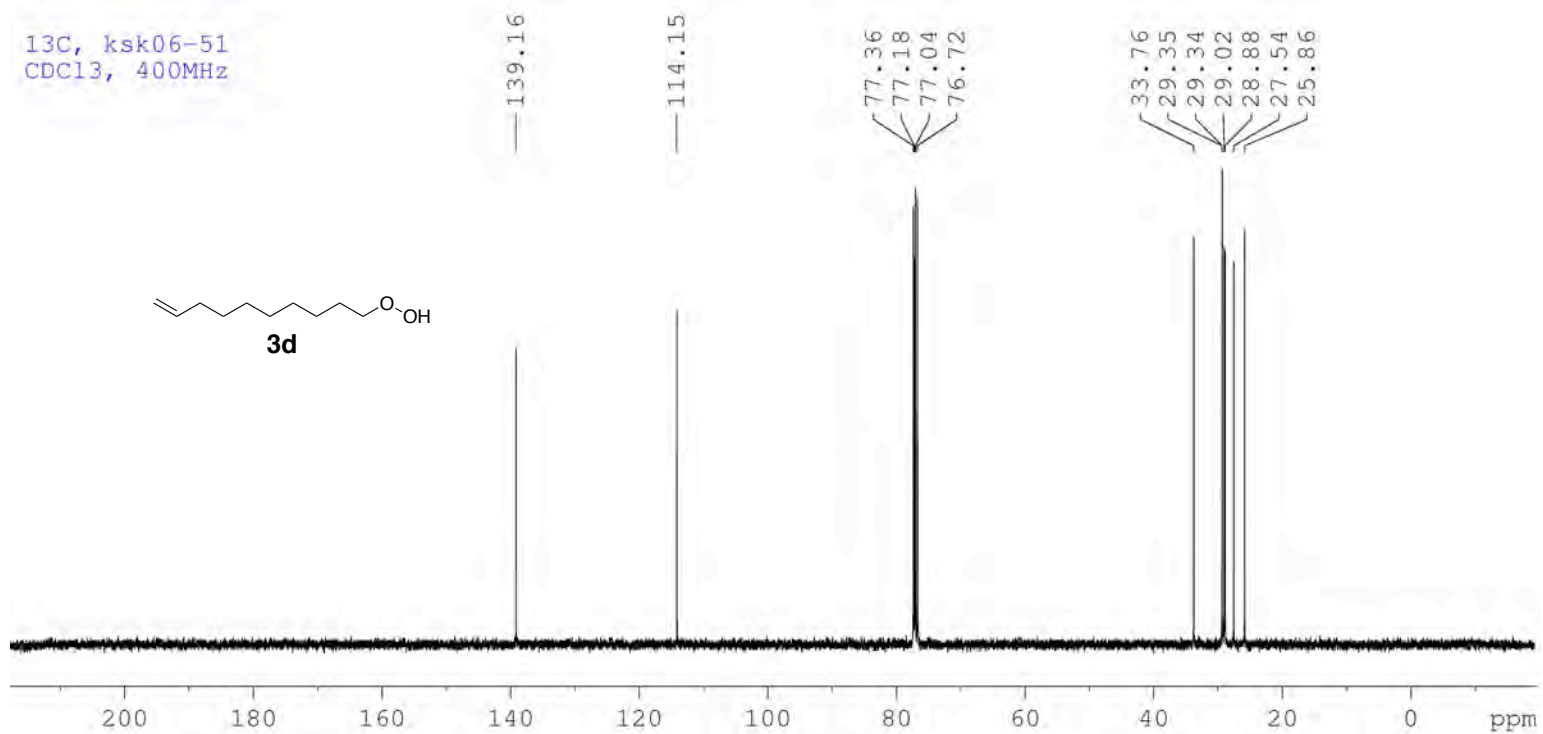
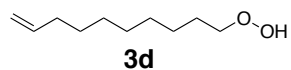
13C, ksk05-92  
CDCl<sub>3</sub>, 400MHz



1D Proton NMR  
ksk06-51, cdcl3



13C, ksk06-51  
CDCl3, 400MHz

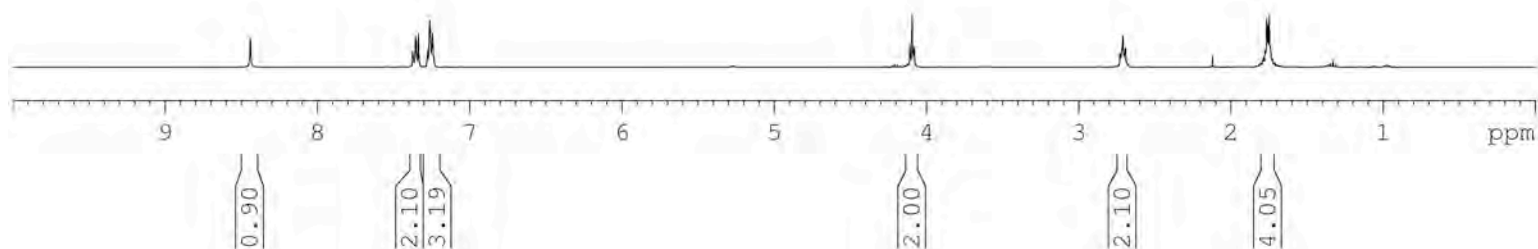
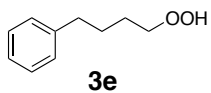


1D Proton NMR  
ksk06-79  
CDCl<sub>3</sub>, 400MHz

8.441  
7.374  
7.370  
7.360  
7.355  
7.353  
7.345  
7.336  
7.274  
7.262  
7.257  
7.243

4.111  
4.095  
4.080

2.729  
2.711  
2.694  
1.808  
1.795  
1.791  
1.785  
1.777  
1.774  
1.766  
1.760  
1.757  
1.749  
1.736  
1.730  
1.725  
1.720  
1.713

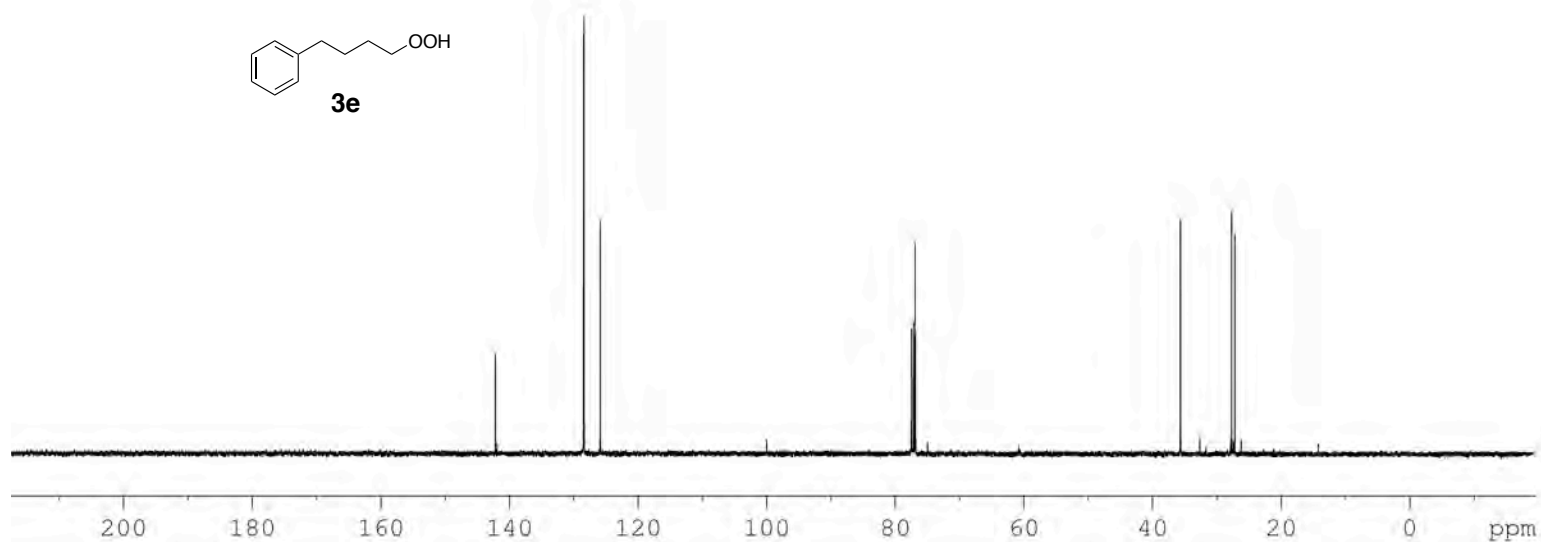
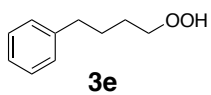


13C, ksk06-79  
400MHz, CDCl<sub>3</sub>

142.19  
128.48  
128.40  
125.89

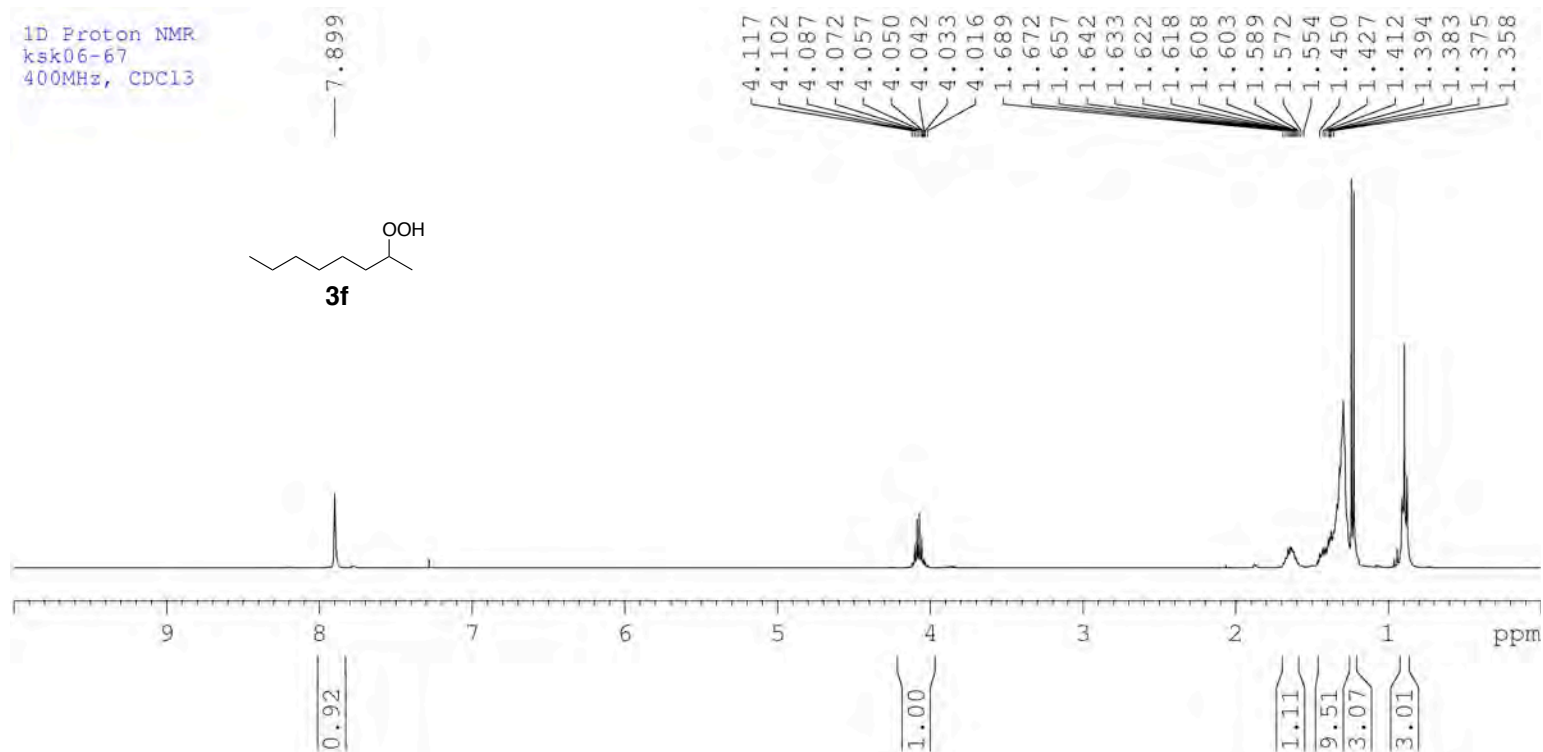
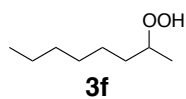
77.50  
77.18  
76.95  
76.86

35.66  
27.71  
27.22

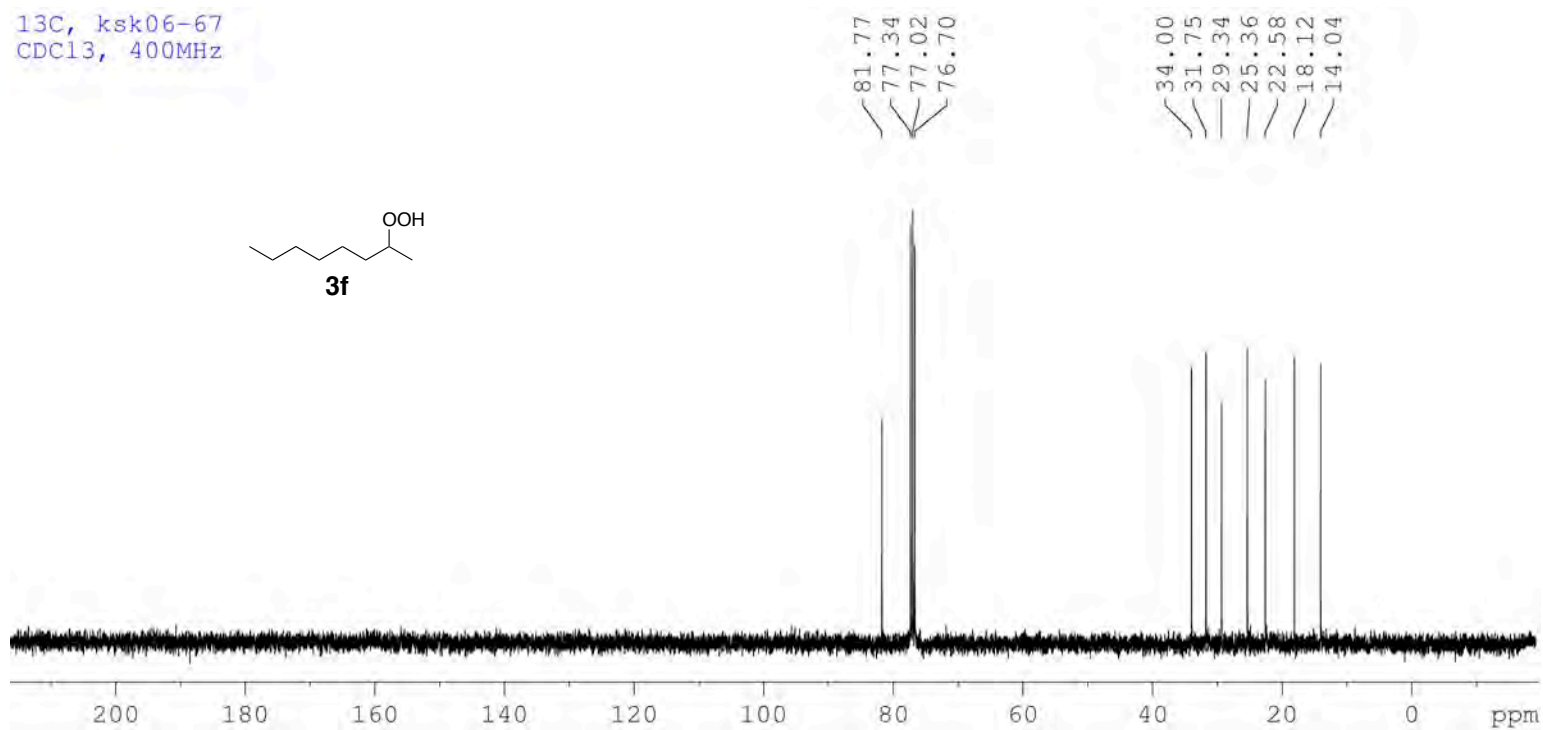
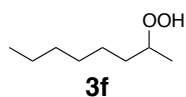


1D Proton NMR  
ksk06-67  
400MHz, CDCl<sub>3</sub>

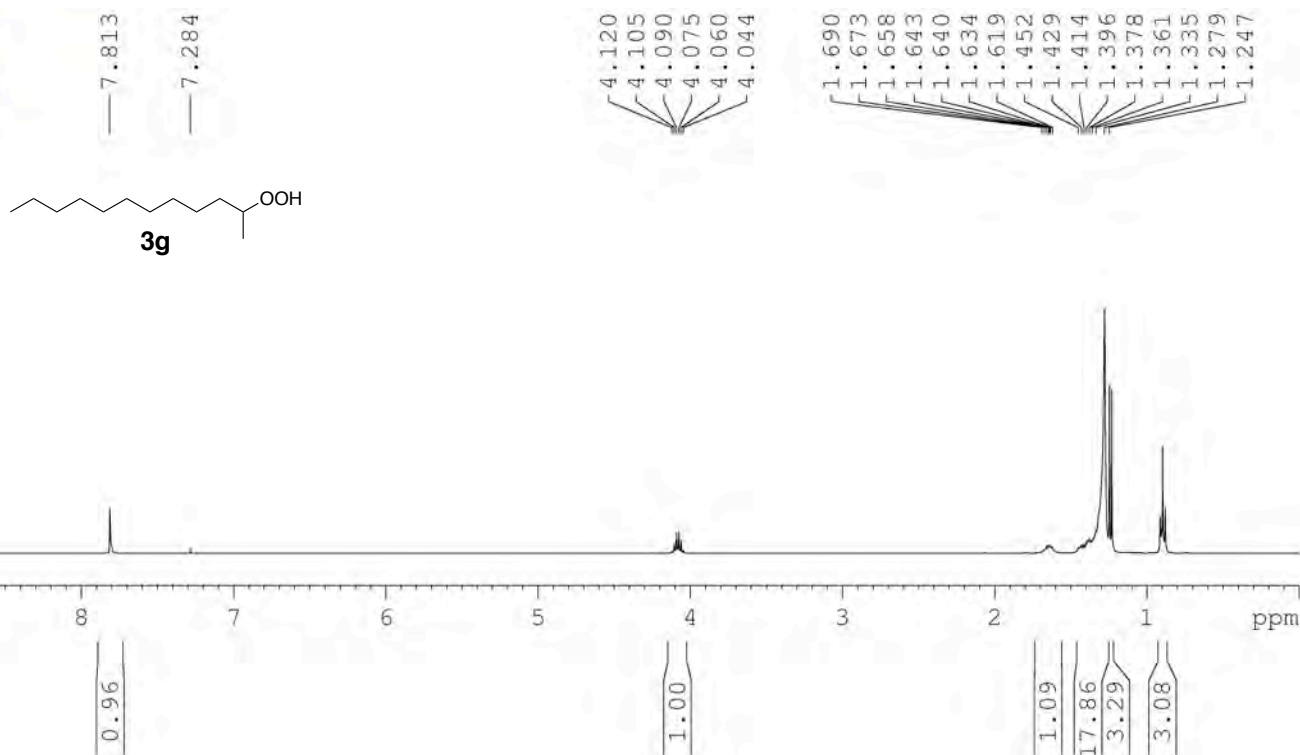
7.899



13C, ksk06-67  
CDCl<sub>3</sub>, 400MHz



1D Proton NMR  
ksk06-76  
400MHz, CDC13



13C, ksk06-76  
CDC13, 400MHz

