

Microwave generation and trapping of acetylketene.

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Supporting Information

Experimental Details

Microwave Specifications

All microwave experiments were done in Milestone's START microwave lab station installed with a touch control terminal. All the microwave experiments were carried out in a sealed pressure tube. The program was set such that it had a ramp time of 8 minutes to reach 120 °C, had a temperature of 120 °C for 20 minutes and finally a ventilation time of 10 minutes to reach room temperature. The maximum power was set to 900 W.

General Experimental Methods

All the chemicals were used as purchased unless mentioned. 2,2,6-Trimethyl-4H-1,3-dioxin-4-one and molecular sieves (4 Å) were purchased from Aldrich. HPLC grade ethyl acetate was used as solvent.

All the ¹H NMR spectra were recorded on a Varian Mercury Plus spectrometer at 300 MHz with CDCl₃ as solvent and the solvent peak referenced to 7.26 ppm. *J* values are given in Hz. All the ¹³C NMR spectra were recorded on a Varian Unity Inova spectrometer at 125 MHz with CDCl₃ as solvent and the solvent peak referenced to 77 ppm. IR spectra are recorded on Thermo Nicolet IR spectrometer as a thin film on NaCl salt plates. Elemental analysis was done by Desert Analytics.

General Procedures

Trapping of 2 from microwave heating of 1

To a 15 mL pressure tube dried overnight in an oven, 3 g of 4 Å molecular sieves were added and closed with a septum. Air was removed from the pressure tube by vacuum and then it was flushed with nitrogen. Ethyl acetate (HPLC grade) was added first to the tube (volume needed to make the reaction mixture up to 10 mL was calculated), followed by 0.2 mL of 2,2,6-trimethyl-4H-1,3-dioxin-4-one (**1**) (1.519 mmol) and 20 equivalents (0.0303 mol) of trapping agent. Then vacuum was applied to the pressure tube and it was again flushed with nitrogen. After closing the pressure tube with its cap, it was subjected to microwave radiation. In most of the experiments both the trapping agent and ethyl acetate were removed by rotavapor. A Kugelrohr was used to remove acetophenone and trifluoroacetophenone. Isolated products were obtained by flash chromatography. All compounds were identified using ¹H NMR spectra and compared with reported spectra from the literature. For compounds which were not reported previously ¹³C NMR, IR and elemental analysis were done to establish the product identity.

Trapping of 2 from thermolysis of 1 under reflux

Synthesis of acetoacetates from dioxinone **1** and alcohols in refluxing toluene was also studied. For this reaction 0.2 mL of dioxinone **1** (1.519 mmol), 20 equivalents of alcohol (3.27 mL, 0.0303 mol) and 25 mL of freshly distilled toluene from sodium were used. The reaction mixture was refluxed for 8 h under nitrogen. After the reaction toluene and excess alcohol were removed by rotovapor and isolated product was obtained by flash chromatography (hexane / ethyl acetate = 9:1).

Trapping of 2 from microwave heating of 1 with neat alcohol

In these reactions dioxinone **1** was heated in microwave with alcohol as the solvent. To a 15 mL pressure tube dried overnight in an oven, 0.2 mL of dioxinone **1** (1.519 mmol) and 10 mL of alcohol were added and closed with a septa. No molecular sieves were used for this study. Then vacuum was applied to the pressure tube and it was flushed with nitrogen. After closing the pressure tube with its cap, it was subjected to microwave radiation. The time and power settings were same as those for the usual trapping

experiments above. After the reaction, excess alcohol was removed by a rotovapor and the isolated product obtained by flash chromatography (hexane / ethyl acetate = 9:1).

Experimental data

Dehydroacetic acid¹ (3) was obtained when no trapping agent was added to the reaction mixture. ¹H-NMR (300 MHz, CDCl₃) δ 5.93 (s, 1H), 2.67 (s, 3H), 2.27 (s, 3H).

Isopropyl acetoacetate² (5a): All the β-ketoesters (**5**) were purified by flash chromatography (hexane/ethyl acetate = 7:3). 5a was obtained in 91% isolated yield (0.1980 g). ¹H-NMR (300 MHz, CDCl₃) δ 5.06 (heptet, 1H, *J* = 6.3 Hz), 3.41 (s, 2H), 2.26 (s, 3H), 1.26 (d, 6H, *J* = 6.6 Hz). **Enol tautomer 4a** (approximately 7%): 12.18 (s, 1H), 4.94 (s, 1H), 1.94 (s, 3H). The yield of the thermolysis reaction was 83% (0.1822 g). The yield of neat alcohol reaction was 72% (0.1577 g).

Ethyl acetoacetate³ (5b) was obtained in 92% isolated yield (0.1816 g). ¹H-NMR (300 MHz, CDCl₃) δ 4.19 (q, 2H, *J* = 6.9 Hz), 3.44 (s, 2H), 2.27 (s, 3H), 1.28 (t, 3H, *J* = 6.9). **Enol tautomer 4b** (approximately 7%): 12.01(s, 1H), 4.98 (s, 1H), 1.95 (s, 3H). The yield of the thermolysis reaction was 84% (0.1651 g) and the yield of the neat alcohol reaction was 85% (0.1688 g).

t-Butyl acetoacetate⁴ (5c) was obtained in 72% isolated yield (0.1726 g). ¹H-NMR (300 MHz, CDCl₃) δ 3.35 (s, 2H), 2.25 (s, 3H), 1.47 (s, 9H). **Enol tautomer 4c** (approximately 7%): 12.21 (s, 1H), 4.90 (s, 1H), 1.91 (s, 3H). The yield of the thermolysis reaction was 58% (0.1381 g) and the yield of neat alcohol reaction was 51% (0.1223 g).

2-tert-Butyl-6-methyl-1,3-dioxin-4-one⁵ (6a) was isolated in 82% isolated yield (0.2113 g) following flash chromatography (hexane/ethyl acetate = 9:1). ¹H-NMR (300 MHz, CDCl₃) δ 5.28 (s, 1H), 5.04 (s, 1H), 2.04 (s, 3H), 1.05 (s, 9H).

2-Isobutyl-6-methyl-1,3-dioxin-4-one (6b) was isolated in 73% isolated yield (0.1875 g) following flash chromatography (hexane/ethyl acetate = 8:2). Another flash column (hexane/ether = 7:3) was performed to obtain a sample for elemental analysis. ¹H-NMR (300 MHz, CDCl₃) δ 5.49 (t, 1H, *J* = 5.7 Hz), 5.29 (s, 1H), 2.03 (s, 1H), 1.96 (hd, 1H, *J* = 6.3 Hz), 1.85 (d, 1H, *J* = 5.7 Hz), 1.82 (dd, *J* = 5.7, *J* = 1.5 Hz), 0.99 (d, 3H, *J* = 6.6 Hz), 0.98 (d, 3H, *J* = 6.6 Hz); ¹³C-NMR (125 MHz, CDCl₃) δ 172.06, 162.83, 100.27, 96.04, 41.60, 23.32, 22.68, 22.56, 19.41; An HMBC spectrum aided in the assignment of peaks. IR ν cm⁻¹ 3056 (sp² C-H), 2964 (sp³ C-H), 1632 (C=C), 740 (cis C=C), 1735 (C=O), 1266 (C-(C=O)-O); Elemental analysis Found: C, 63.1; H, 8.2. C₉H₁₄O₃ requires C, 63.5; H, 8.3%.

2-Isopropyl-6-methyl-1,3-dioxin-4-one (6c) was isolated in 53% yield following flash chromatography (ether/hexane = 2:8). ¹H-NMR (300 MHz, CDCl₃) δ 5.29 (s, 1H), 5.22 (d, 1H), 2.16 (hd, 1H), 2.04 (s, 3H), 1.07 (d, 6H). ¹³C-NMR (125 MHz, CDCl₃) δ 172.09, 162.95, 104.01, 95.81, 31.27, 19.34, 16; IR ν (cm⁻¹) 3059 (sp² C-H), 2973 (sp³ C-H), 1633 (C=C), 737 (cis C=C), 1741 (C=O), 1228 (C-(C=O)-O); Elemental analysis Found: C, 59.3; H, 7.8%. C₈H₁₂O₃ requires C, 61.5; H 7.7% (the elemental analysis results deviated from the calculated values probably because of some inseparable impurity in the product).

2-Trifluoro-2-phenyl-6-methyl-1,3-dioxin-4-one⁶ (8) was obtained in 44% yield (0.1740 g) following a flash chromatography (hexane/ethyl acetate = 8:2). 4Å Molecular sieves were not added to the reaction mixture for this compound synthesis. ¹H-NMR (300 MHz, CDCl₃) δ 7.60 (d, 2H, *J* = 7.65), 7.47 (m, 3H), 5.23 (s, 1H), 2.11(s, 3H)

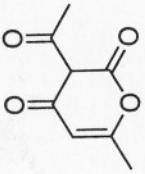
1,1,1-Trifluoro-2-hydroxy-2-phenyl-4-pentanone⁷ (9) was formed under the standard reaction conditions and was isolated in 49% yield (0.1712 g) following flash chromatography (hexane/ethyl acetate = 7:3). ¹H-NMR (300 MHz, CDCl₃) δ 7.56 (d, 2H, *J* = 7.5), 7.38 (m, 3H, *J* = 7.2), 5.43 (s, 1H), 3.37 (d, 1H, *J* = 17.1), 3.20 (d, 1H, *J* = 17.4), 2.21 (s, 3H). Compound **9** was also obtained when 1 mL of water was added to reaction mixture instead of 4Å molecular sieves under the same reaction conditions. For Gudipati, Sadasivam and Birney Page S4 Microwave generation of acetylketene

deuterium incorporation experiment 1 mL of D₂O was added to the reaction mixture instead of 4Å molecular sieves under same reaction conditions. After the reaction ethyl acetate was separated from the H₂O/D₂O layer and dried over magnesium sulphate for an hour. Magnesium sulphate was removed by filtration and the compound was obtained by removing ethyl acetate using a rotovapor.

References

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dehydroacetic acid

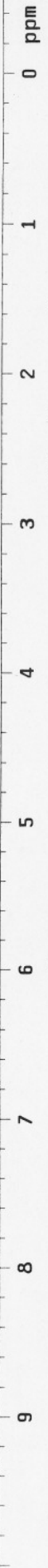


3

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2.673

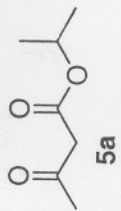


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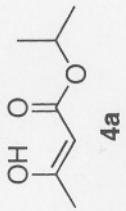
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0.88

0.0043 3.39



isopropyl acetoacetate



1.273
1.251

2.264

3.411
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7.260

-0.005

ppm

1

2

3

4

5

6

7

8

9

10

11

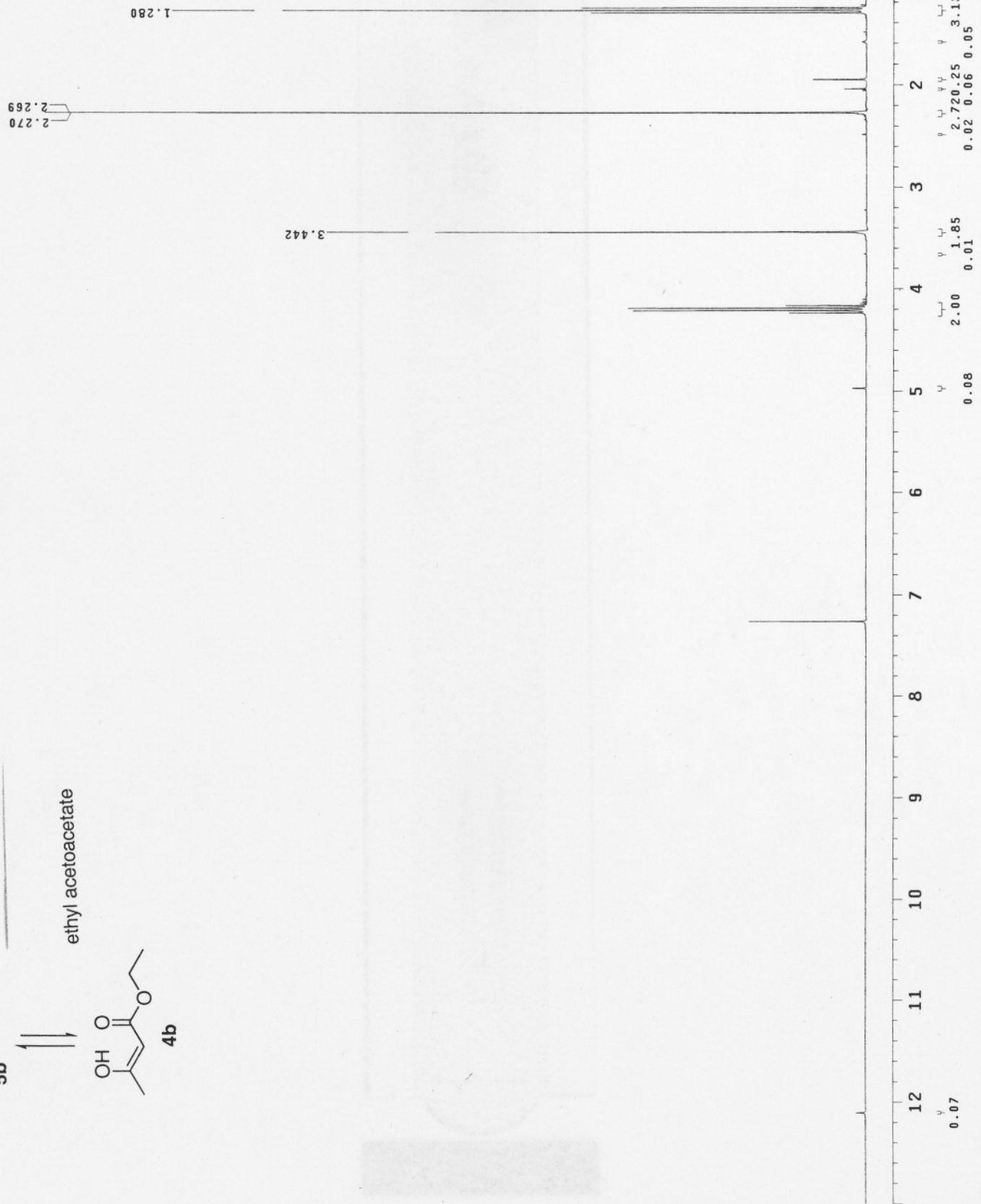
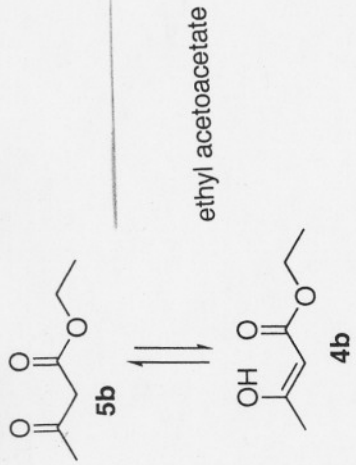
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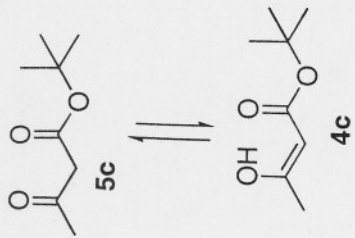
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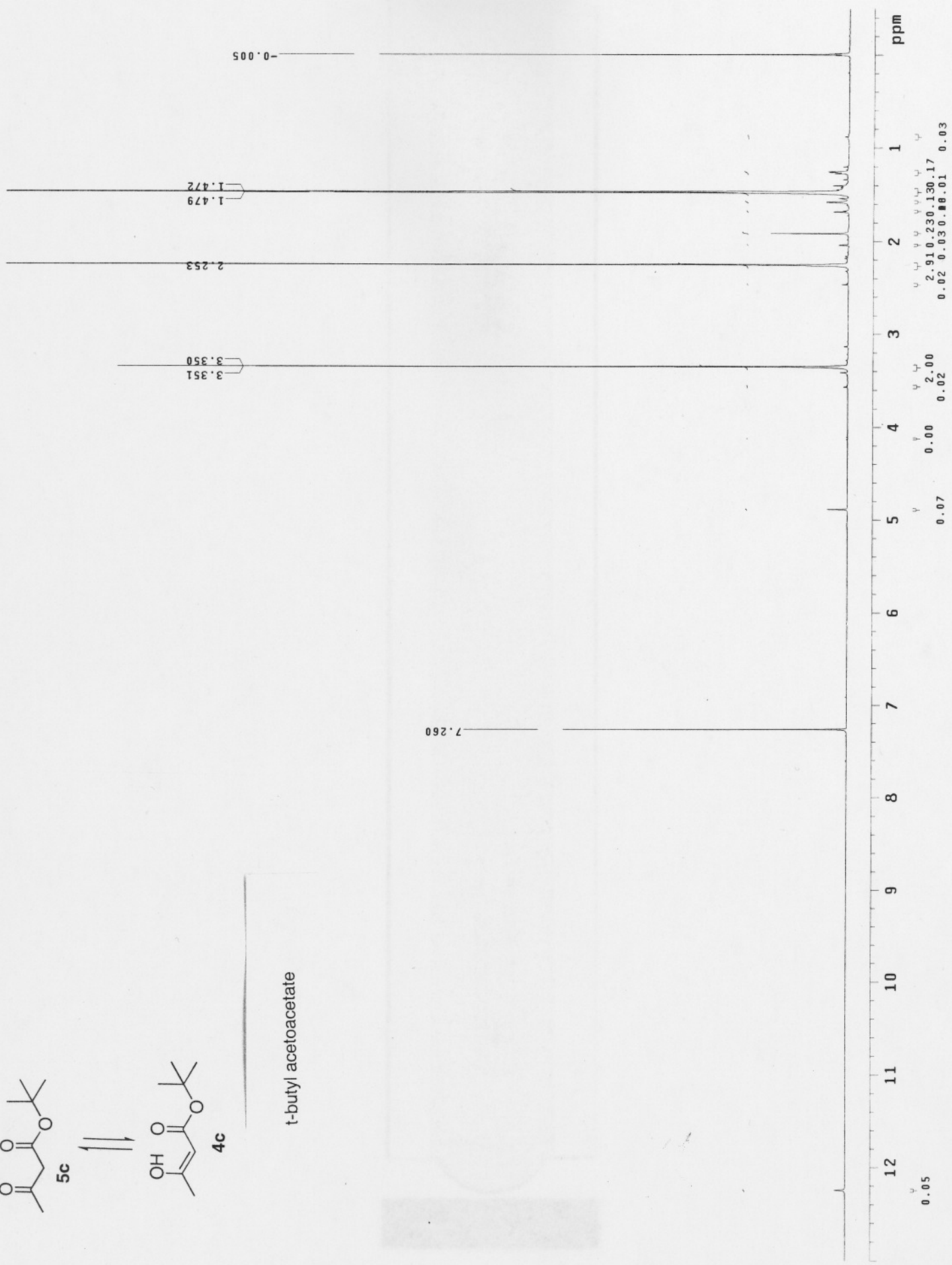
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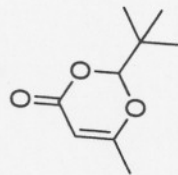




t-butyl acetoacetate

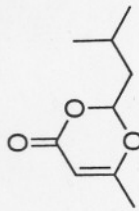


2-tert-butyl-6-methyl-1,3-dioxin-4-one



6a

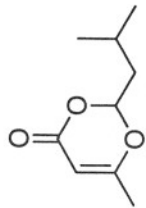




6b

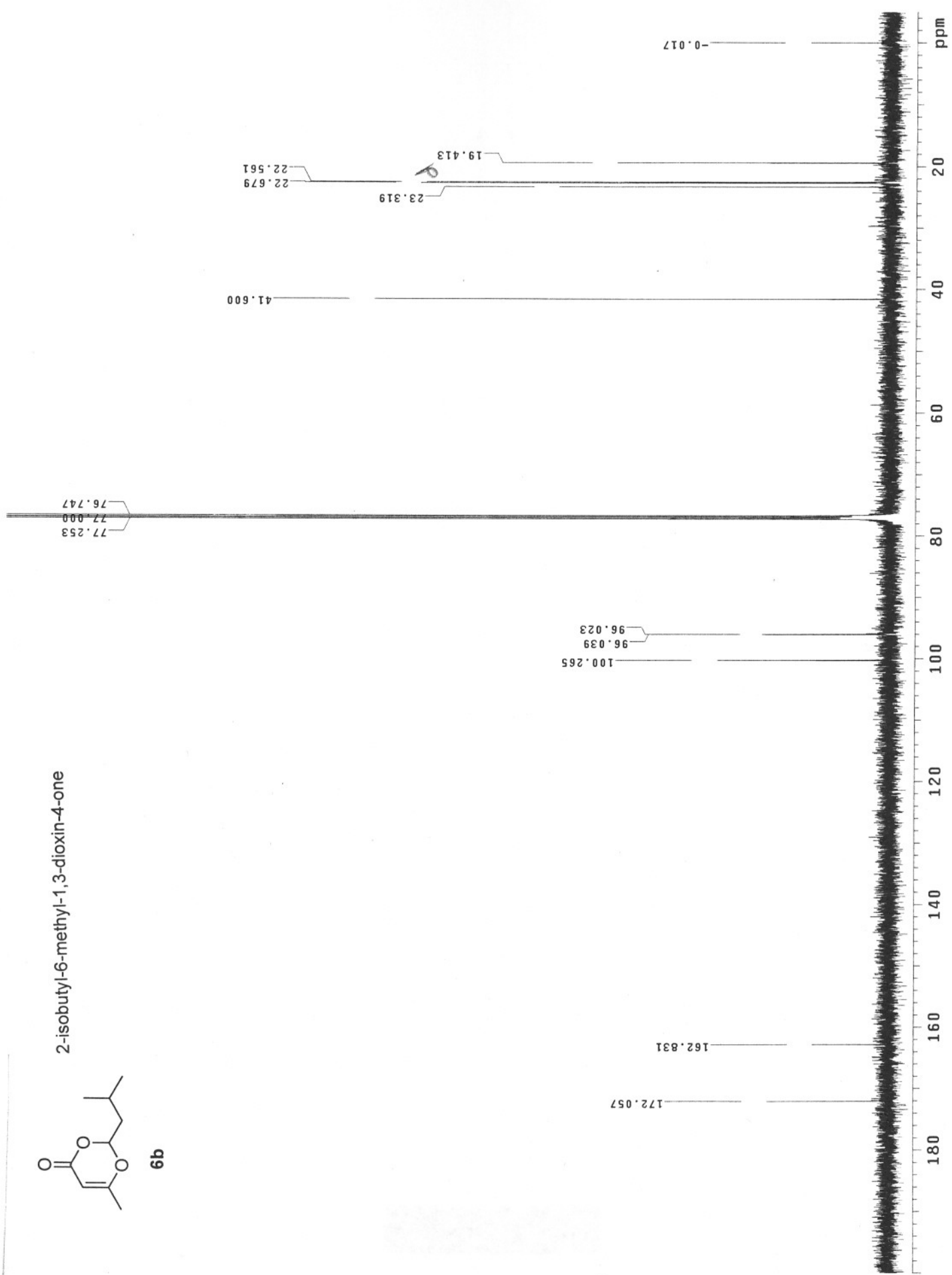
2-isobutyl-6-methyl-1,3-dioxin-4-one

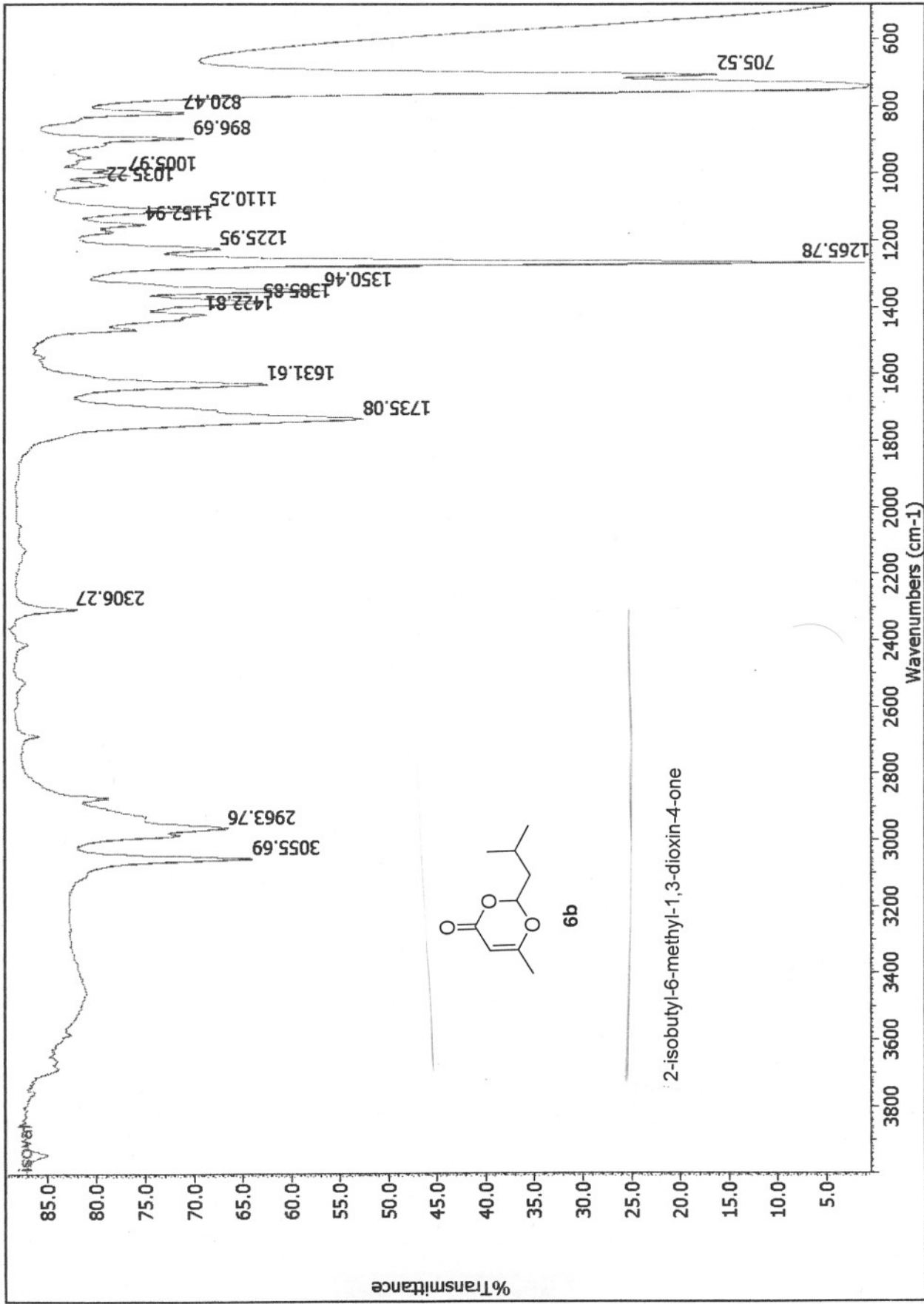


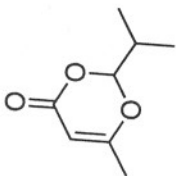


6b

2-isobutyl-6-methyl-1,3-dioxin-4-one







6c

2-isopropyl-6-methyl-1,3-dioxin-4-one

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1.086

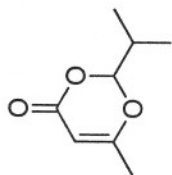
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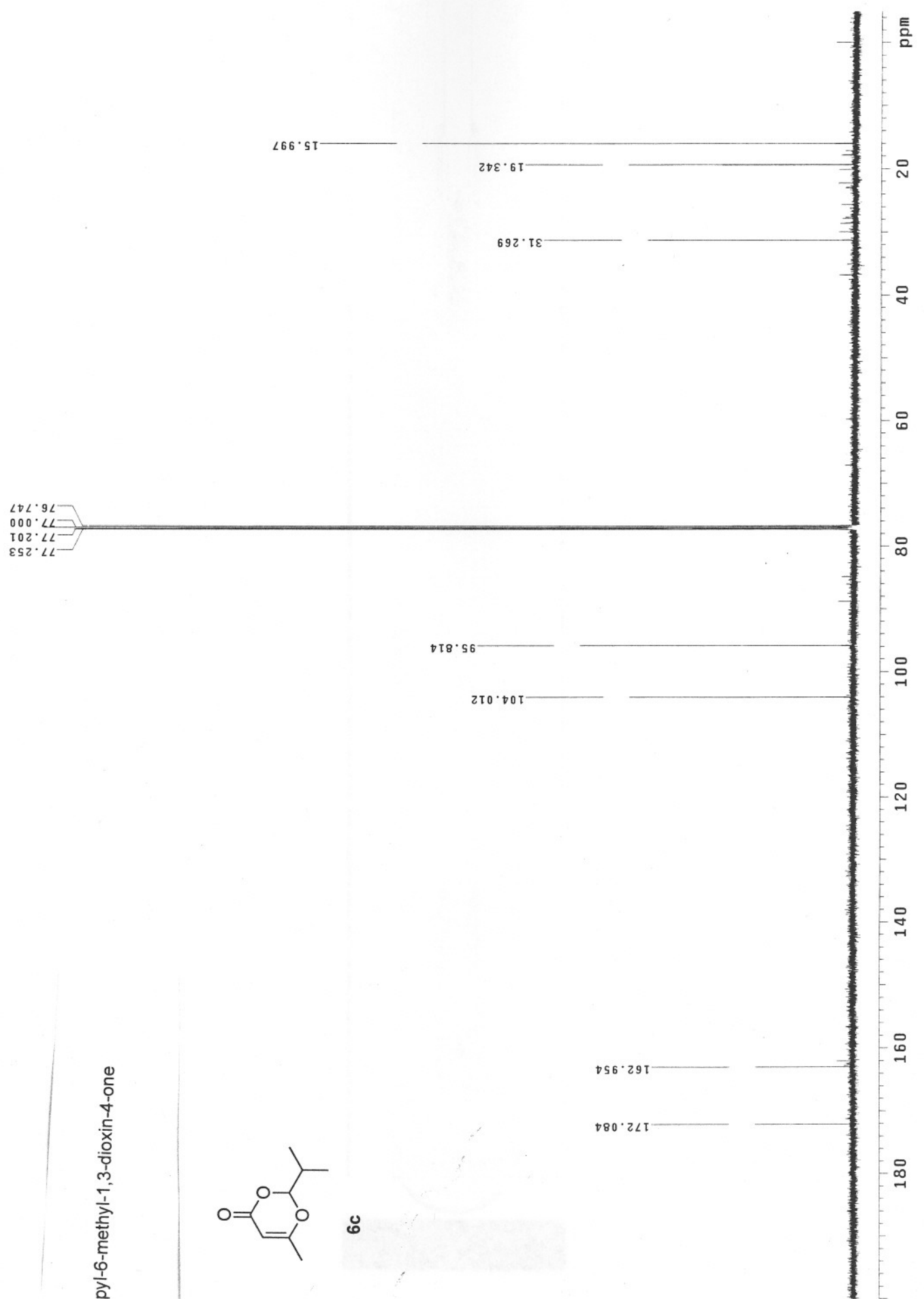
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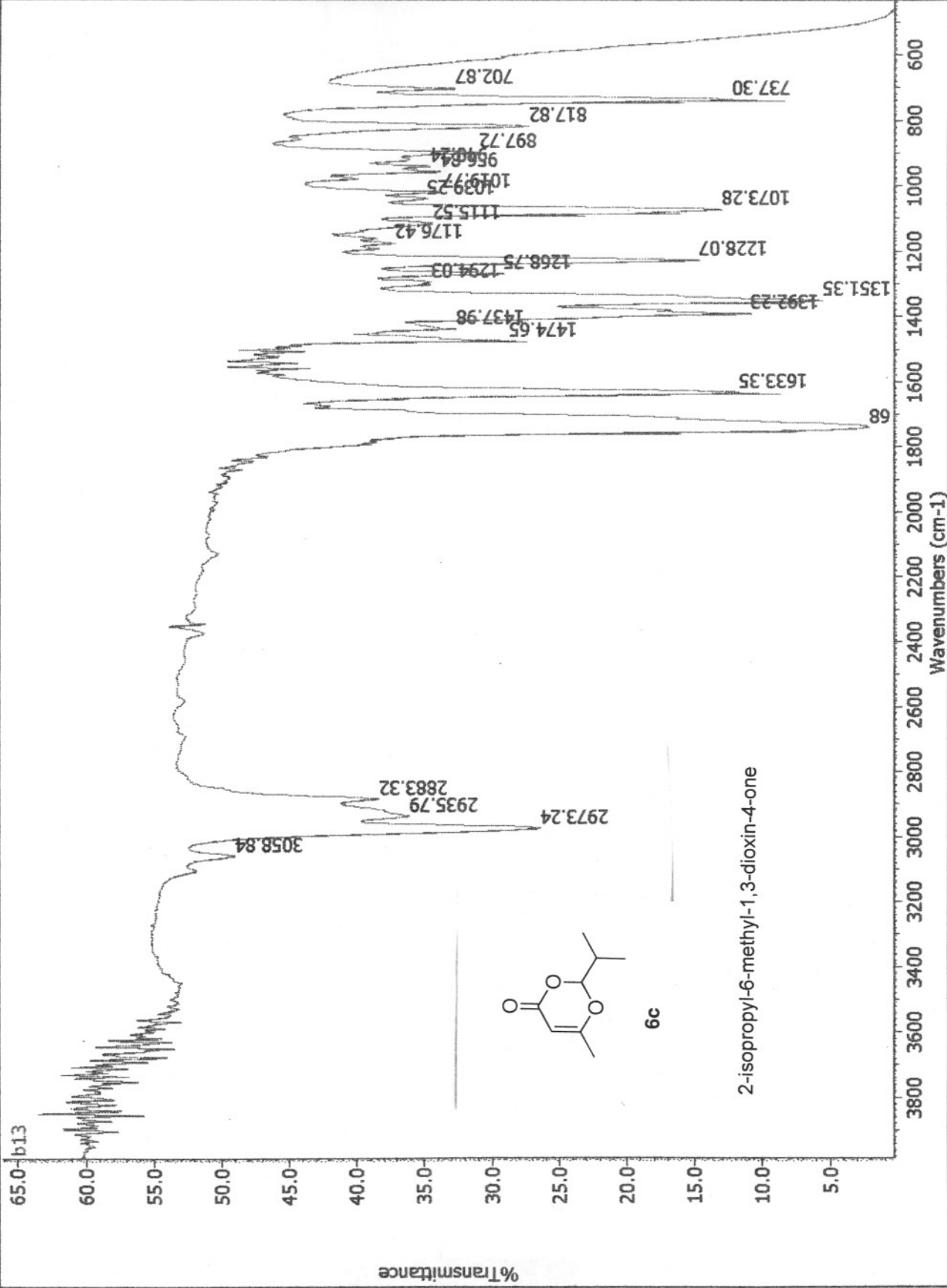
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0.01	0.01	0.09	1.03	1.00	0.03	0.06	0.04	0.22	0.15	0.21	0.42	0.5	0.42

2-isopropyl-6-methyl-1,3-dioxin-4-one

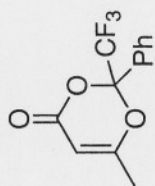


6c





2-trifluoro-2-phenyl-6-methyl-1,3-dioxin-4-one



8



1,1,1-trifluoro-2-hydroxy-2-phenyl-4-pentanone

