2-(Trimethylsilyloxy)furan as a dianion equivalent: a two-step synthesis of functionalised spirocyclic butenolides.

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SUPPORTING INFORMATION

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Instrumentation and procedures.

Routine nuclear magnetic resonance (NMR) spectra were recorded on a VARIAN GEMINI-200, VXR-200 (^{1}H 200 MHz and ^{13}C 50 MHz), VARIAN GEMINI-300 (^{1}H 300 MHz and ^{13}C 75 MHz), BRUKER-300 (^{1}H 300 MHz and ^{13}C 75 MHz) and BRUKER-500 (^{1}H 500 MHz and ^{13}C 125 MHz) spectrometers. Chemical shifts (δ_H) are reported in ppm downfield from internal tetramethylsilane (TMS). ^{13}C NMR spectra were recorded using $CDCl_3$ as the internal standard. Splitting patterns in ^{1}H spectra are designed as s, singlet; d, doublet; t, triplet; b, broad and m, multiplet.

Low resolution mass spectra (EI) were recorded using VARIAN MATT-44 and FINNIGAN MAT-TSQ 70 spectrometers.

Infra-red (IR) spectra were taken as KBr disks, thin films or in solution, on a SHIMADZU Benelux FTIR-8400S spectrometer and recorded in cm^{-1}.

Elemental analyses were performed in Prof. S. Laschat's analytical laboratory (Institut für Organische Chemie, Universität Stuttgart, Germany). High-resolution mass spectra were recorded in Prof. R. Flamant's laboratory (Université de Mons, Belgium).

Thin layer chromatography (TLC) was performed on MERCK silica gel 60 F_{254} aluminum-backed plates. The plates were visualised using 254 nm UV light and developed using an alkaline KMnO4 solution (1% $KMnO_4$/ 5% Na_2CO_3). Flash chromatography was performed using Rocc silica gel 60 (40-63 μm) under pressure with the stated solvents.

All solvents were routinely distilled prior to use. Reactions were performed under a dry, inert atmosphere of argon unless stated otherwise.

The following abbreviations are used: rt, room temperature; hr, hour; min, minute; mmol, millimole; mol, mole; mg, milligram; g, gram; mL, milliliter, μL, microliter; eq., equivalent.

General procedure for the preparation of spirocyclic butenolides 7b-7i.

A solution of the corresponding butenolide ketal (1 mmol, 1 eq.) in 10 mL THF was cooled to 0 °C and treated with 1.3 mmol (1.3 eq.) of either a 2.0 M THF solution of NaHMDS or solid *t*-BuOK. The reaction was stirred until complete conversion of the starting materials and quenched by addition of a saturated aqueous NH_4Cl solution. Following extractive workup, purification by flash chromatography on silica gel (elution with 10% EtOAc/hexane) afforded the desired products.

7b

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33 (d, *J* = 5.7 Hz, 1 H), 6.08 (d, *J* = 5.7 Hz, 3 H), 3.97-3.70 (m, 4 H), 2.25-2.13 (m, 2 H), 2.01-1.79 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.4, 122.8, 116.9, 95.6, 66.5, 65.1, 33.6, 32.3, 18.3; IR(cm^{-1}): 3359, 2921, 1751, 1697, 1391; MS (APCI+ev): *m/z* (%): 197 (100) $[M+H]^{+\cdot}$, 135 (5), 99 (5); Elemental analysis calcd. for $C_{10}H_{12}O_4$ C: 61.26%; H 6.17%; found C 60.82%; H 6.16%.

7c

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (d, *J* = 6.0 Hz, 1 H), 6.08 (d, *J* = 6.0 Hz, 1 H), 4.01-3.77 (m, 4 H), 1.90-1.54 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.7, 122.4, 116.4, 94.9, 65.9, 65.8, 33.4, 29.7, 22.8, 21.5; IR(cm^{-1}): 2968, 1751, 1143; MS (APCI+ev): *m/z* (%): 211 (100) $[M+H]^{+\cdot}$, 149 (15), 121 (5); HRMS (ES) calcd. for $C_{11}H_{14}O_4Na$ (M+Na) : 233.0790; found 233.0795.

7d

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.94 (d, *J* = 2.1 Hz, 1 H), 4.07-3.73 (m, 4 H), 2.23-2.14 (m, 2 H), 1.99-1.81 (m, 4 H), 1.93 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.3, 146.6, 131.4, 116.7, 93.2, 66.4, 65.1, 33.5, 32.4, 18.2, 10.9; IR(cm^{-1}): IR(cm^{-1}): 3360, 2919, 2844, 1759, 1655, 1415; MS (APCI+ev): *m/z* (%): 211 (100) $[M+H]^{+\cdot}$, 149 (10), 99 (5); Elemental analysis calcd. for $C_{11}H_{14}O_4$ C: 61.38%; H 6.80%; found C 61.85%; H 6.71%.

7e

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00 (d, *J* = 1.5 Hz, 1 H), 3.97-3.80 (m, 4 H), 1.91 (d, *J* = 1.5 Hz, 3 H), 1.87-1.83 (m, 3 H), 1.71-1.61 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.0, 148.7, 131.2, 108.7, 66.4, 66.3, 34.2, 34.0, 23.3, 22.1, 11.3; IR(cm^{-1}): 3357, 2923, 2852, 1757, 1660, 1435; MS (APCI+ev): *m/z* (%): 225 (100) $[M+H]^{+\cdot}$, 207 (20), 181 (30), 163 (55), 153

(85), 135 (100), 107 (10); HRMS (ES) calcd. for $C_{12}H_{17}O_4$ (M+H): 225.1127; found 225.1119.

7f

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, *J* = 5.7 Hz, 1 H), 6.00 (d, *J* = 6 Hz, 1H), 3.51-3.35 (m, 4 H), 2.26-2.15 (m, 1 H), 2.10-2.04 (m, 2 H), 1.89-1.65 (m, 3 H), 1.16 (t, *J* = 6.6 Hz, 3 H), 1.05 (t, *J* = 7.2 Hz, 3 H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.3, 157.4, 121.2, 110.4, 96.3, 59.6, 57.0, 34.2, 31.1, 18.7, 15.7, 15.4; IR(cm^{-1}): 2954, 2911, 1750, 1677, 1411; MS (APCI+ev): *m/z* (%): 227 (100) $[M+H]^{+\cdot}$, 209 (5), 181 (15); HRMS (ES) calcd. for $C_{12}H_{18}O_4Na$ (M+Na) : 249.1103; found 249.1102.

7g

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16 (m, 1 H), 3.55-3.35 (m, 4 H), 2.27-2.17 (m, 1 H), 2.12-2.02 (m, 2 H), 1.90 (s, 3 H), 1.94-1.64 (m, 3 H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.3, 149.4, 129.6, 110.1, 93.9, 59.6, 56.9, 34.1, 30.8, 18.5, 15.7, 15.4, 10.8; IR(cm^{-1}): 3200, 2920, 1755, 1429 ; MS (APCI+ev): *m/z* (%): 241 (15) $[M+H]^{+\cdot}$, 195 (90), 177 (25), 149 (100), 121 (5), 79 (15); Elemental analysis calcd. for $C_{13}H_{20}O_4$ C: 64.98%; H 8.39%; found C 65.06%; H 8.19%.

7h

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.00 (s, 1 H), 3.86 (s, 3 H), 3.66-3.40 (m, 4 H), 2.21-1.95 (m, 4 H), 1.89-1.61 (m, 2 H), 1.16-1.09 (apparent q, *J* = 7.0 Hz, 6H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 183.2, 171.7, 108.9, 92.1, 88.9, 59.7, 58.5, 57.7, 32.4, 31.9, 17.7, 15.6, 15.3; IR(cm^{-1}): 3050, 2925, 1750, 1438; MS (APCI+ev): *m/z* (%): 257 (10) $[M+H]^{+\cdot}$, 211 (50), 179 (25), 165 (100), 133 (10); HRMS (ES) calcd. for $C_{13}H_{21}O_5$ (M+H): 257.1389; found 257.1401.

7i

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.03 (s, 1 H), 3.90 (s, 3 H), 3.32 (s, 3 H), 3.24 (s, 3 H), 2.23-1.97 (m, 4 H), 1.86-1.63 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 182.9, 171.4, 109.3, 91.8, 89.0, 59.7, 50.9, 49.9, 32.6, 30.9, 17.5; IR(cm^{-1}): 3116, 2837, 1751, 1622, 1456, 1440; MS (APCI+ev): *m/z* (%): 229 (35) $[M+H]^{+\cdot}$, 197 (50), 165 (100); HRMS (ES) calcd. for $C_{11}H_{17}O_5$ (M+H): 229.1076; found 229.1076.

General procedure for the conjugate reduction of spirocyclic butenolides 7b-7c.

A solution of **7b-7c** (1 mmol, 1 eq.) in methanol (3 mL) was cooled to 0ºC and treated with $NiCl_2.6H_2O$ (0.7 mmol, 0.7 eq.). The resulting mixture was stirred at the same temperature for 15 min before the addition of $NaBH_4$ (1 mmol, 1 eq.). The reaction was gradually allowed to reach room temperature, after which it was quenched with a saturated solution of NH_4Cl. Following conventional extractive workup, the products **12b-12c** were obtained in analytically pure form.

12b

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.05-3.96 (m, 4 H), 2.68-2.61 (m, 1 H), 2.54-2.48 (m, 1 H), 2.40 (dtd, *J* = 11.5, 4.0, 3.5 Hz, 1 H), 2.11-2.06 (m, 1 H), 2.02-1.96 (m, 2 H), 1.92-1.81 (m, 3 H), 1.72-1.67 (m, 1 H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.8, 115.6, 92.4, 65.8, 65.2, 33.8, 31.7, 29.1, 26.0, 17.2; IR(cm^{-1}): 2954, 2887, 1770, 1458, 1433; MS (APCI+ev): *m/z* (%): 199 (100) $[M+H]^{+\cdot}$, 149 (40), 137 (50), 109 (20); HRMS (ES) calcd. for $C_{10}H_{15}O_4$ (M+H): 199.0970; found 199.0965.

12c

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.02-3.94 (m, 4 H), 2.74-2.61 (m, 1 H), 2.53-2.34 (m, 2 H), 2.04-1.96 (m, 1 H), 1.88-1.54 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.1, 109.8, 88.6, 65.7, 36.0, 32.2, 29.0, 28.4, 22.6, 21.5; IR(cm^{-1}): 2950, 1771, 1460; MS (APCI+ev): *m/z* (%): 213 (100) $[M+H]^{+\cdot}$, 151 (10), 123 (5); HRMS (ES) calcd. for $C_{11}H_{17}O_4$ (M+H): 213.1127; found 213.1129.

General procedure for dihydroxylation of spirocyclic butenolides 7b-7c.

To a vigorously stirred solution of **7b-7c** (0.2 mmol, 1 eq.) in CH_3CN/AcEt (1 mL each) at 0º C was added a solution of $RuCl_3.3H_2O$ (0.014 mmol, 0.07 eq.) and $NaIO_4$ (0.3 mmol, 1.5 eq.) in distilled water (1 mL). The mixture was stirred for 90 seconds after which a saturated solution of $Na_2S_2O_3$ is added. Following extractive workup with AcOEt, the dihydroxylated lactones **13b-13c** are obtained in analytically pure form.

13b

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.62 (d, *J* = 5.2 Hz, 1 H), 4.45 (d, *J* = 5.3 Hz, 1H), 3.98-3.86 (m, 4 H), 2.98 (br s, 1H), 2.68 (br s, 1 H), 2.31-2.25 (m, 1H), 2.08-2.01 (m, 1 H), 1.99-1.95

(m, 1 H), 1.90-1.85 (m, 2 H), 1.78-1.70 (m, 1 H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.0, 115.7, 94.9, 70.3, 69.7, 65.9, 65.5, 32.9, 29.3, 17.6; IR(cm^{-1}): 3367 (br), 2924, 1772, 1132; MS (APCI+ev): *m/z* (%): 231 (100) $[M+H]^{+\cdot}$, 213 (10), 169 (15), 149 (5); HRMS (ES) calcd. for $C_{10}H_{15}O_6$ (M+H): 231.0869; found 231.0871.

13c

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80 (d, *J* = 5.9 Hz, 1 H), 4.40 (d, *J* = 5.9 Hz, 1 H), 3.98-3.94 (m, 4 H), 3.12 (br s, 1H), 2.83 (br s, 1 H), 1.79-1.50 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.1, 109.1, 80.8, 69.3, 69.0, 65.4, 65.2, 32.4, 29.4, 22.5, 21.1; IR(cm^{-1}): 3354 (br), 2911, 1770, 1412; MS (APCI+ev): *m/z* (%): 245 (100) $[M+H]^{+\cdot}$, 201 (15), 183 (5); HRMS (ES) calcd. for $C_{11}H_{17}O_6$ (M+H): 245.1025; found 245.1022.

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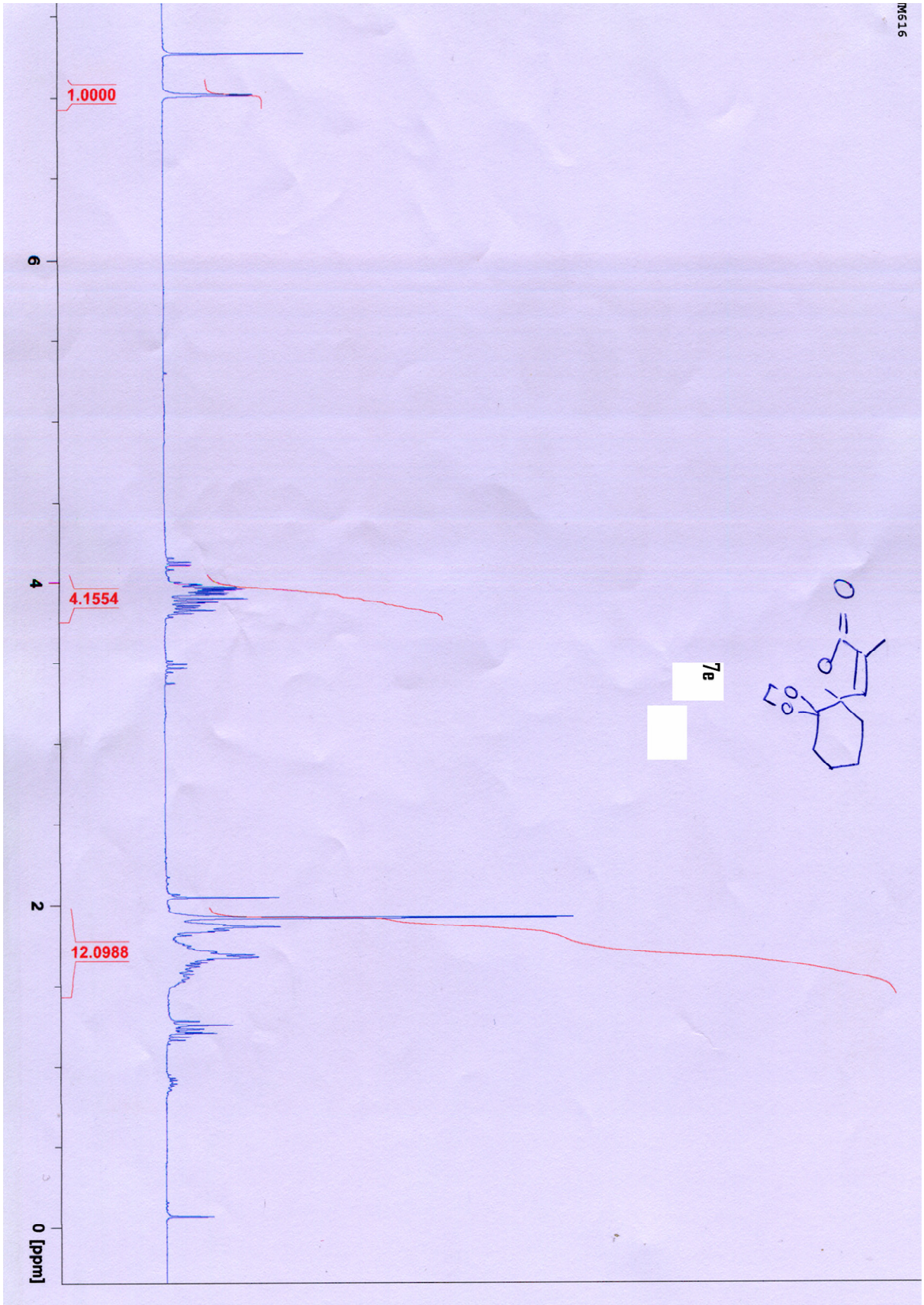
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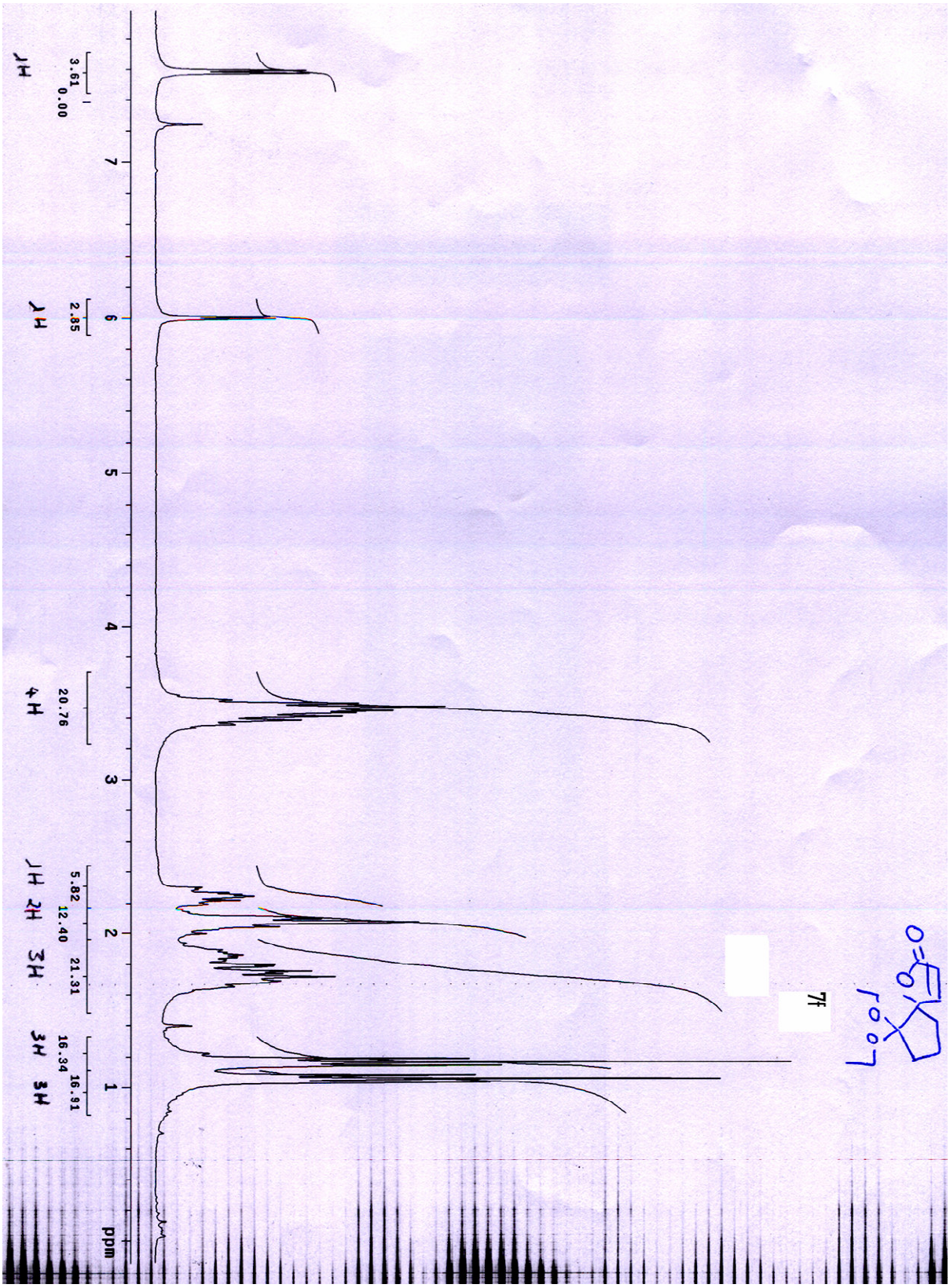
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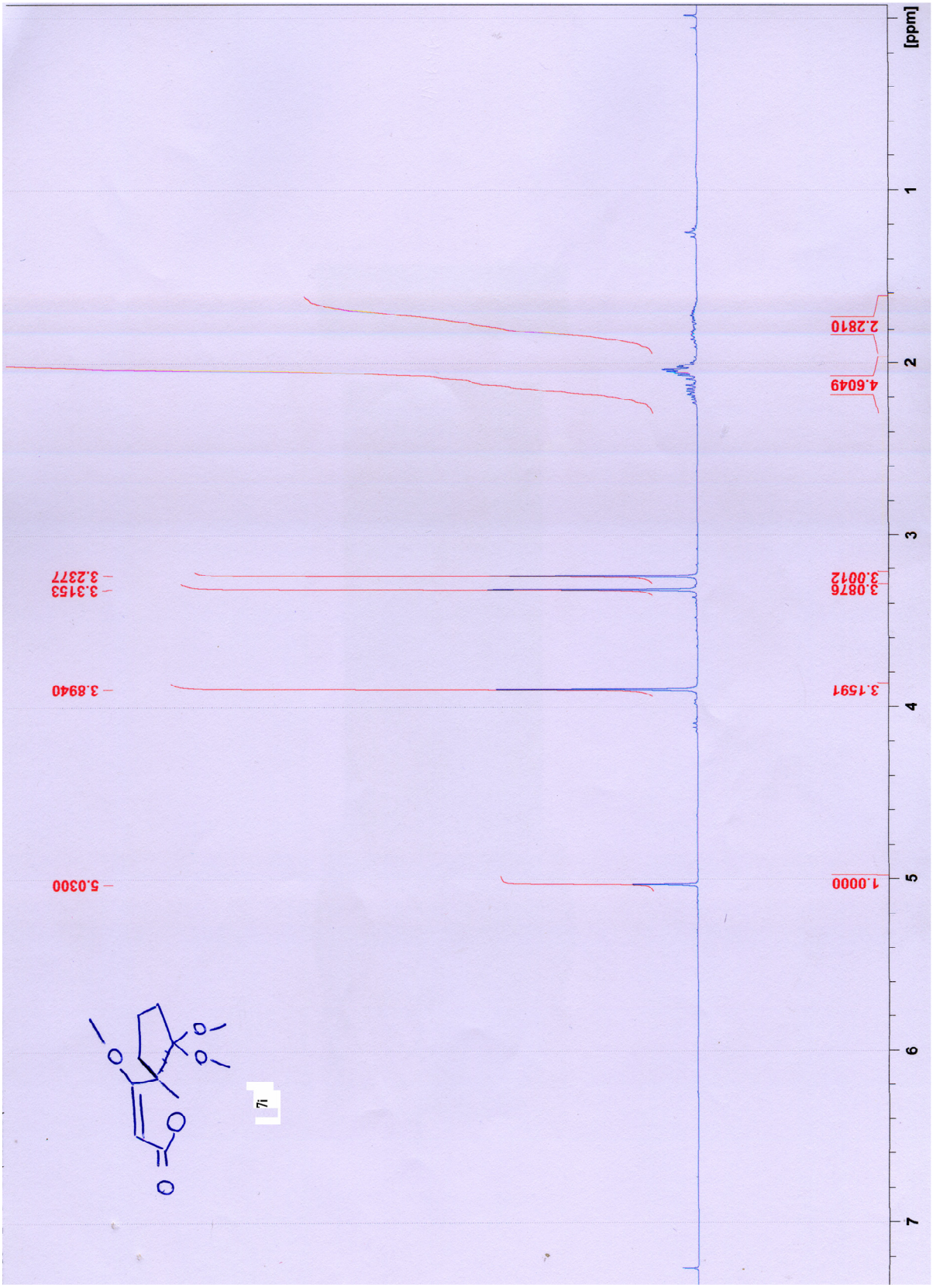
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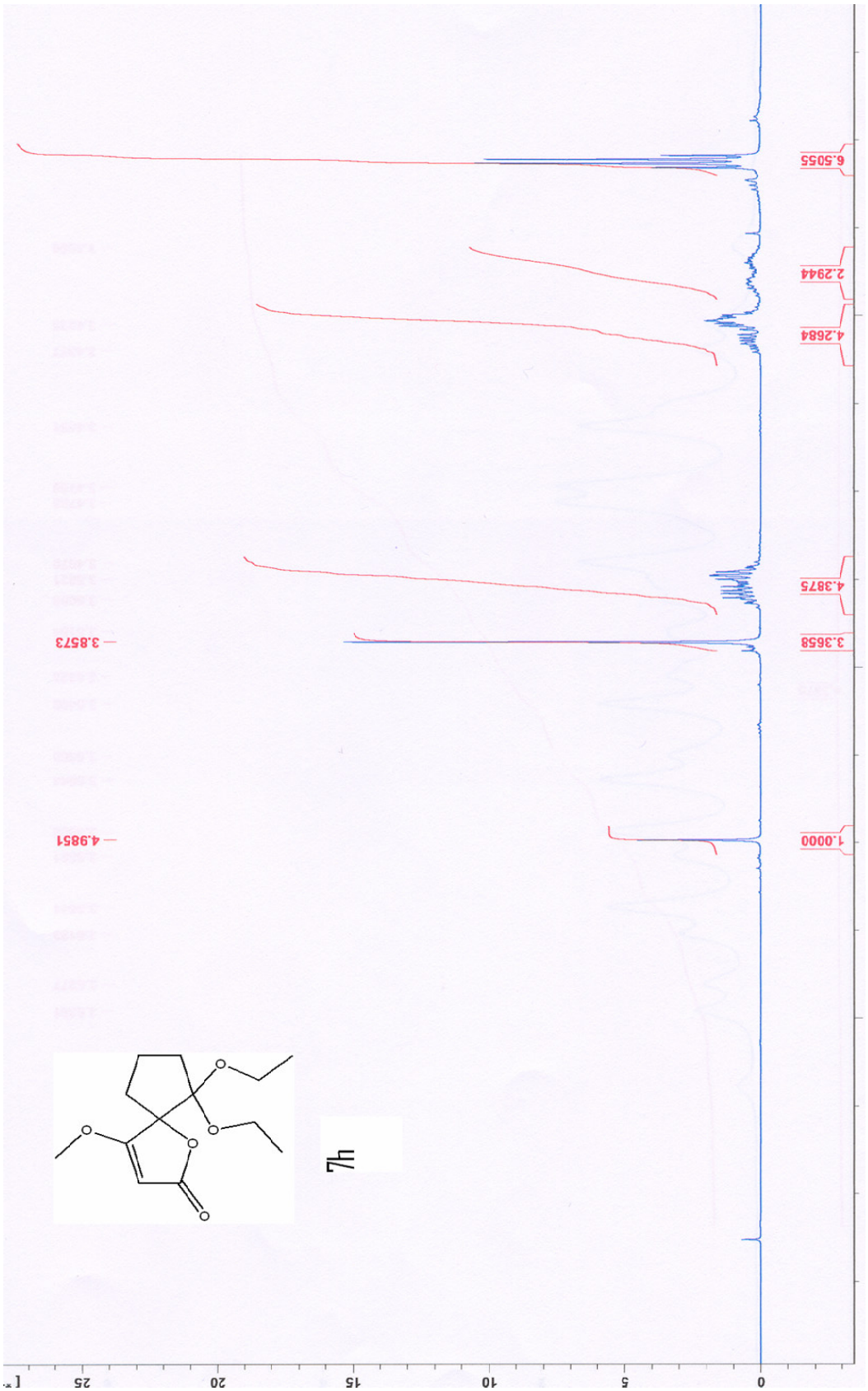
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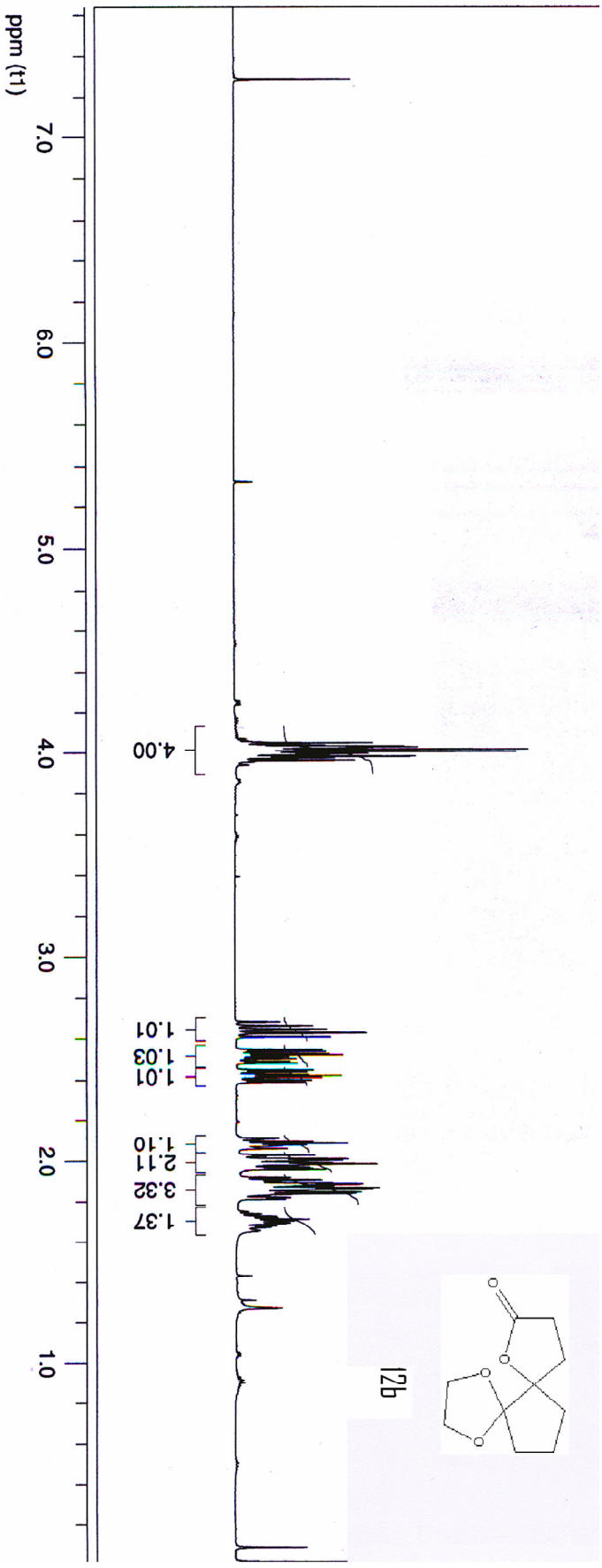
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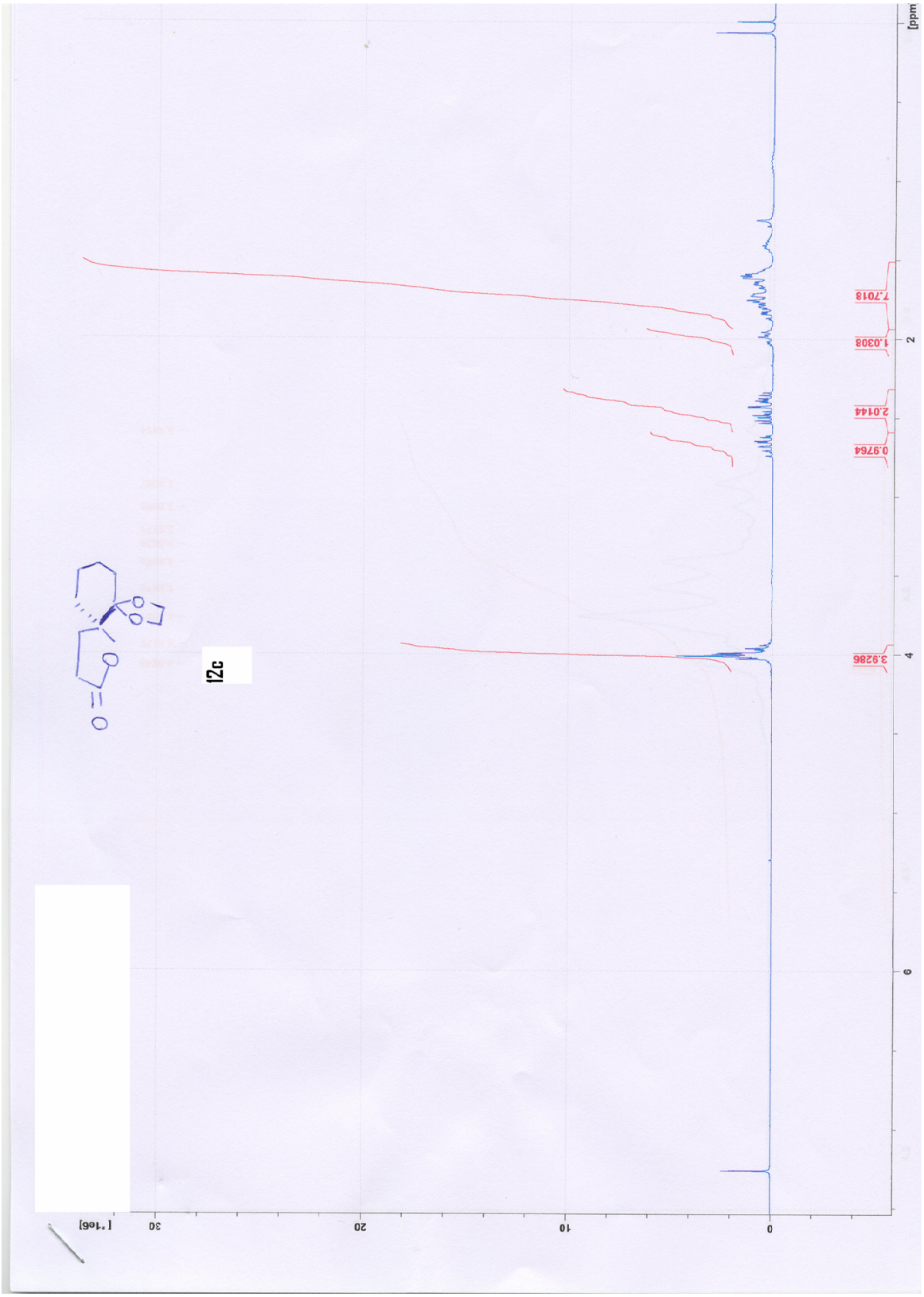
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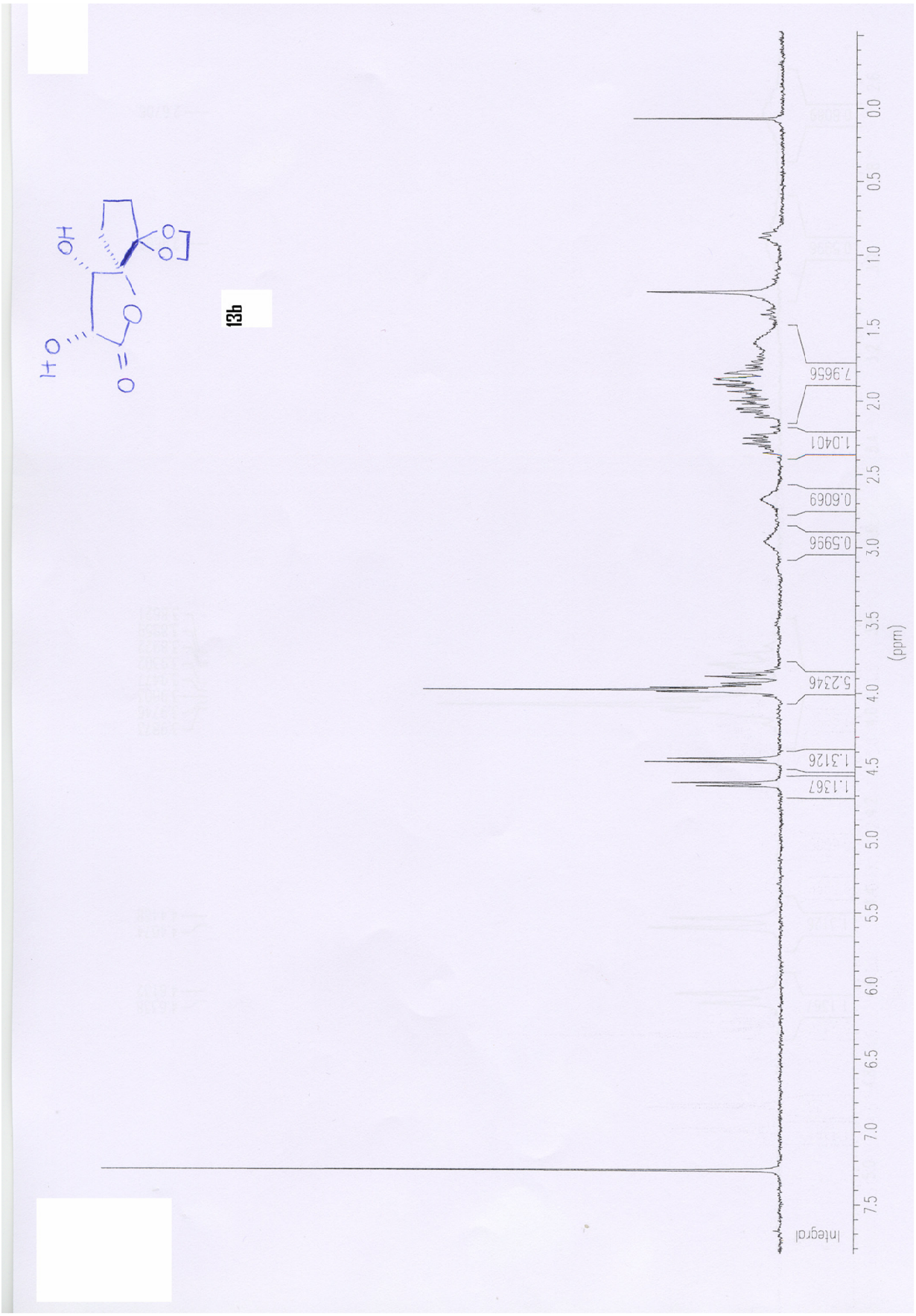
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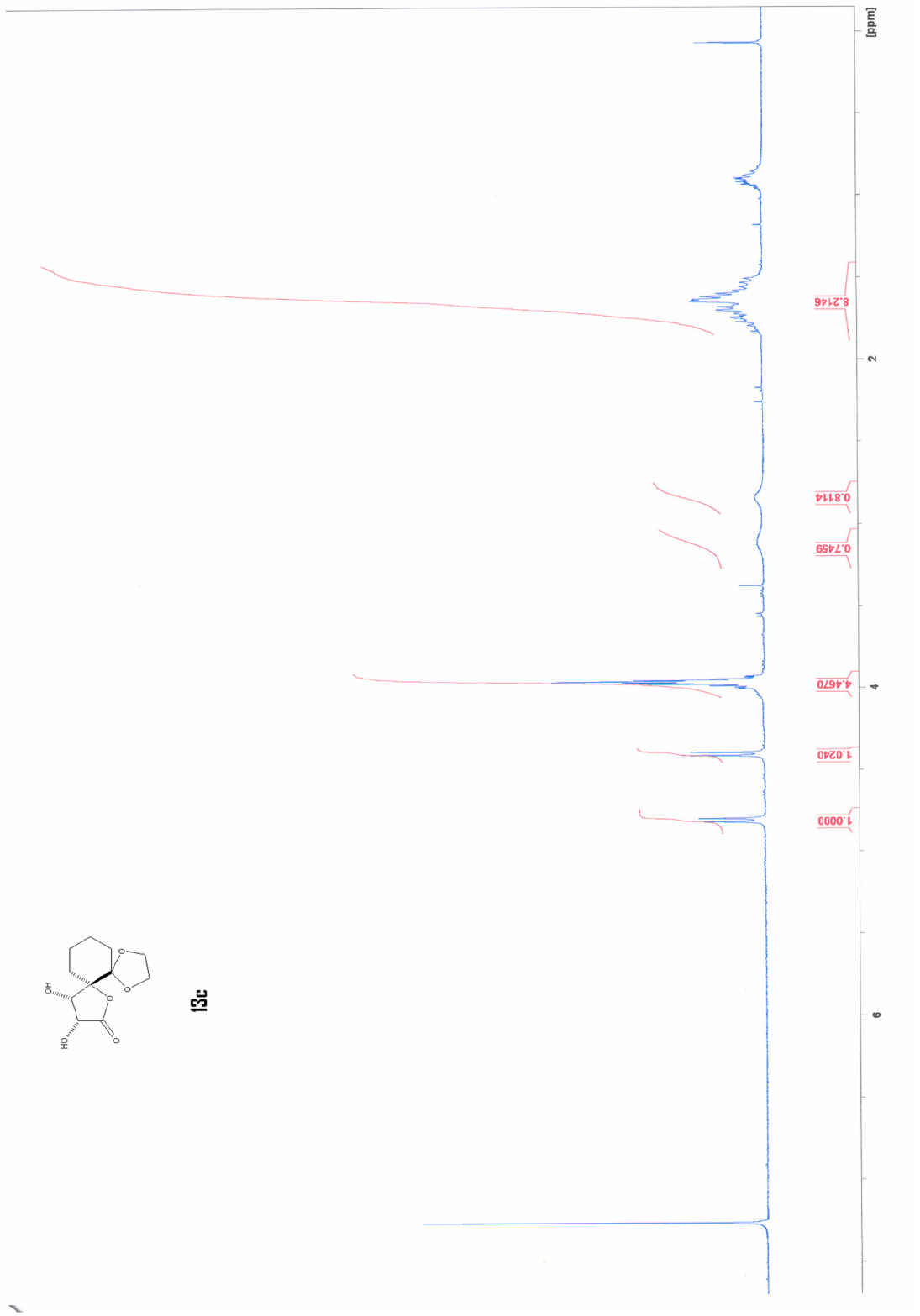
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