Electronic Supplementary Material (ESI) for RSC Advances

The first enzymatic Achmatowicz reaction: selective laccase-catalyzed synthesis of 6-hydroxy-(2*H*)-pyran-3(6*H*)-ones and (2*H*)-pyran-2,5(6*H*)-diones

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Electronic Supplementary Information

Table of contents

		Pages
1	General methods	3
2	Furan-2-yl carbinols **1**	3
2.1	General procedure I for the preparation of furan-2-yl carbinols **1**	3-4
2.2	Synthesis and analytical data for **1a-l**	4-23
3	Oxidation of **1** to **2**	23
3.1	General procedure II for the oxidation of **1** to **2**	23
3.2	Synthesis and analytical data for **2a-h**	23-35
4	Oxidation of **1** to **8**	35
4.1	General procedure III for the oxidation of **1** to **8**	35
4.2	Synthesis and analytical data for **8i-l**	36-41
5	Laccase activity determination	42

6 References 42

1 General methods

All chemicals and the laccase (*Trametes versicolor*) were purchased from commercial suppliers and were used without further purification unless otherwise indicated. Solvents used for extraction and purification were distilled prior to use. The pH of the buffer was adjusted using a pH 330/SET-1 pH-meter. Analytical thin layer chromatography (TLC) was performed on aluminium-backed plates coated with silica gel with F254 indicator (Merck). Compounds were visualized by UV light (254 nm) or with vanillin/H_2SO_4 as a solution in ethanol. Flash chromatography was carried out using silica gel 60 M, 230-400 mesh (Macherey & Nagel). Silica gel deactivated with triethylamine was prepared by treating 80 mL of silica with 1.5 mL of triethylamine. Melting points were determined on a Büchi melting point apparatus B-545 with open capillary tubes and are uncorrected. UV/VIS spectra were recorded with a Varian Cary 50. IR spectra were measured on a Perkin-Elmer *Spectrum One* (FT-IR-spectrum). ^{1}H (^{13}C) NMR spectra were recorded at 300 (75) MHz on a Varian ^{Unity}Inova spectrometer with $CDCl_3$ (δ = 7.26 ppm in ^{1}H NMR spectra and δ = 77.0 ppm in ^{13}C NMR spectra) as internal standards. Coupling constants *J* [Hz] were directly taken from the spectra and not averaged. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), sep (septet) and m (multiplet). All NMR Data were processed with *Spinworks 3.1.8, copyright © 2011, Kirk Marat, University of Manitoba*. Electron impact low resolution mass spectra (EI) and electron impact high resolution mass spectra HRMS) were recorded at 70 eV on a Finnigan MAT 95 instrument. The intensities are reported as percentages relative to the base peak (I = 100%).

2 Furan-2-yl carbinols 1

2.1 General procedure I for the preparation of furan-2-yl carbinols 1[1]

12.5 mmol (8 mL) *n*-butyl-lithium (1.6 M in hexanes) were added drop wise at -50 °C under argon to a solution of 12.5 mmol of furan (**5**) or a furan derivative **5** in 20 mL

diethylether. After refluxing for 2 h, the mixture was cooled to -25 °C; then 12.5 mmol of the corresponding ketone **6** were added drop wise and the mixture was refluxed for 4 h. The reaction mixture was poured into 20 mL of saturated NH_4Cl solution at room temperature and the mixture was stirred until a clear solution was formed. The organic phase was separated and the aqueous phase was extracted with diethylether (3 × 20 mL). The combined organic phases were washed with brine, dried with Na_2SO_4 and evaporated to give the crude product which was purified by flash chromatography over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4 : 1) to afford the furan-2-yl carbinol **1**.

2.2 Synthesis and analytical data for 1a-l

2-(5-Methylfuran-2-yl)propan-2-ol (1a) [2]

According to the general procedure I, 2-methylfuran (**5b**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and acetone (**6a**, 12.5 mmol, 0.9 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4 : 1) afforded **1a** (1.3 g, 9.4 mmol, 75%) as a yellowish oil.

R_f 0.33 (cyclohexane – EtOAc = 8:3); ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.56 (6H, s, 1-H and 3-H), 2.01 (1H, s, OH), 2.27 (3H, s, 1”-H), 5.86 (1H, dq, $^3J_{4'\text{-H},\,3'\text{-H}}$ 3.2 Hz, $^4J_{4'\text{-H},\,1''\text{-H}}$ 0.9 Hz, 4’-H) and 6.04 (1H, d, $^3J_{3'\text{-H},\,4'\text{-H}}$ 3.2 Hz, 3’-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 13.5 (C-1”), 28.6 (C-1 and C-3), 68.6 (C-2), 104.2 (C-3’), 105.8 (C-4’), 151.1 (C-5’) and 158.4 (C-2’) ppm; MS (EI, 70 eV) *m/z* 140 (M^+, 28%), 125 (100, $M^+ - CH_3$) and 43 (43); HRMS (EI, M^+) found: 140.0841, calcd for $C_8H_{12}O_2$: 140.0837.

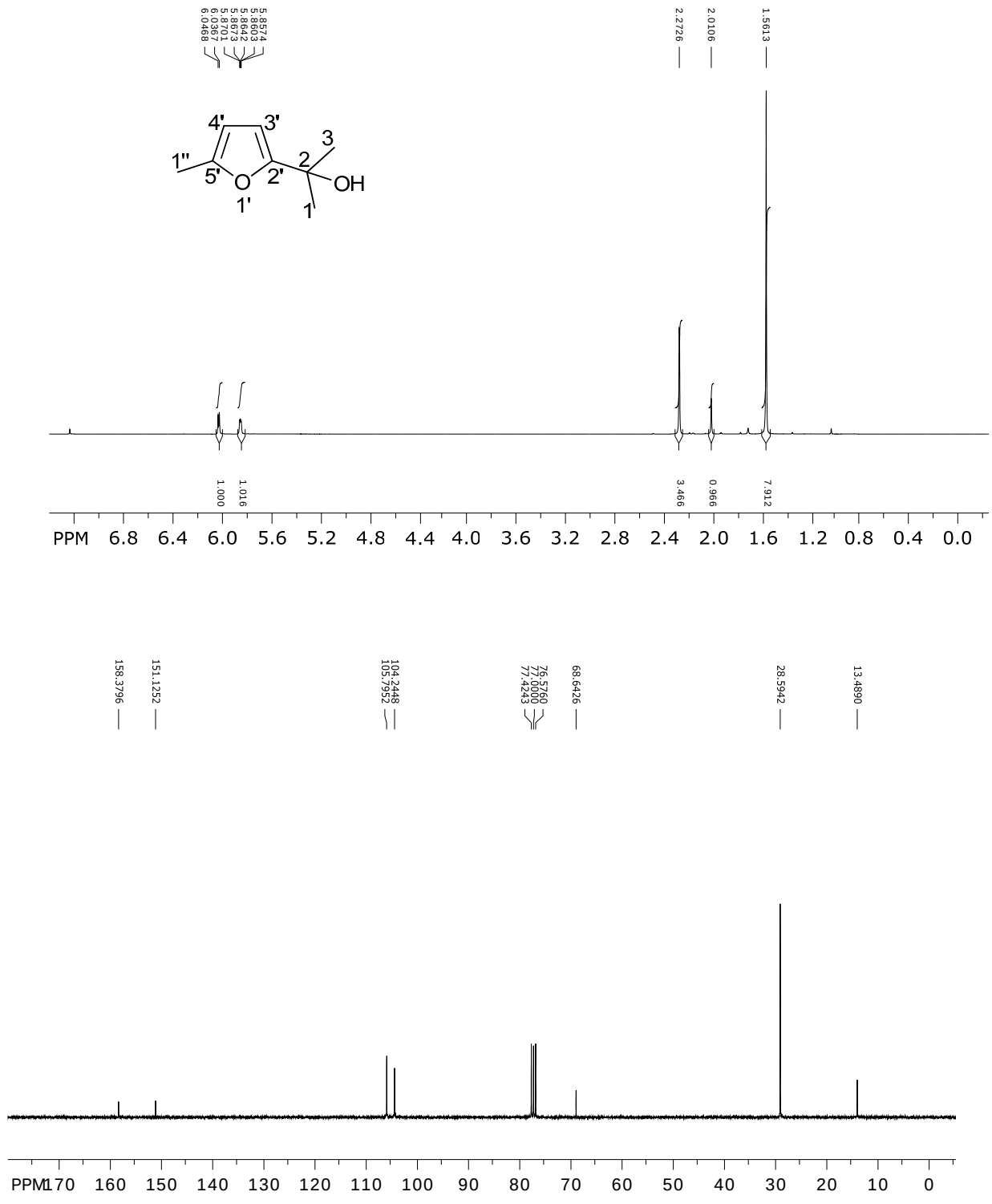
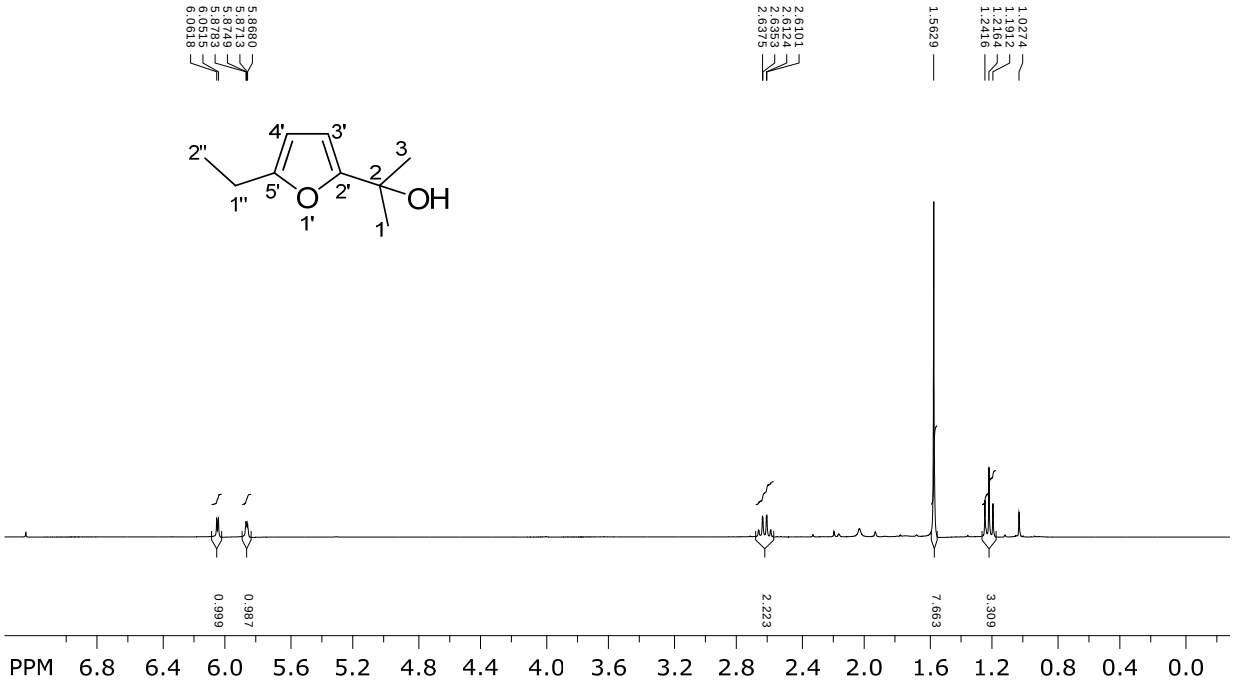


Fig. 1 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1a** in $CDCl_3$.

2-(5-Ethylfuran-2-yl)propan-2-ol (1b)

According to the general procedure I, 2-ethylfuran (**5c**, 12.5 mmol, 1.3 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and acetone (**6a**, 12.5 mmol, 0.9 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4:1) afforded **1b** (1.3 g, 8.8 mmol, 70%) as a yellowish oil.

R_f 0.35 (cyclohexane ─ EtOAc = 8:3); UV λ_{max} (MeCN)/nm 219 (log ε/dm^3 mol^{-1} cm^{-1} 3.87); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3387 (OH), 2980 (CH_3, CH_2), 1372, 1220, 1119, 1021, 944 and 781; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.21 (3H, t, $^3J_{2''\text{-H},\,1''\text{-H}}$ 7.6 Hz, 2''-H), 1.56 (6H, s, 1-H and 3-H), 2.62 (2H, q, $^3J_{1''\text{-H},\,2''\text{-H}}$ 7.6 Hz, 1''-H), 5.87 (1H, dt, $^3J_{4'\text{-H},\,3'\text{-H}}$ 3.2 Hz, $^4J_{4'\text{-H},\,1''\text{-H}}$ 0.9 Hz, 4'-H) and 6.05 (1H, d, $^3J_{3'\text{-H},\,4'\text{-H}}$ 3.2 Hz, 3'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 12.0 (C-2''), 21.3 (C-1''), 28.6 (C-1 and C-3), 68.7 (C-2), 104.0 (C-3'), 104.1 (C-4'), 156.9 (C-5') and 158.2 (C-2') ppm; El. anal. found (%): C 69.93, H 9.47, calcd (%) for $C_9H_{14}O_2$: C 70.10, H 9.15.



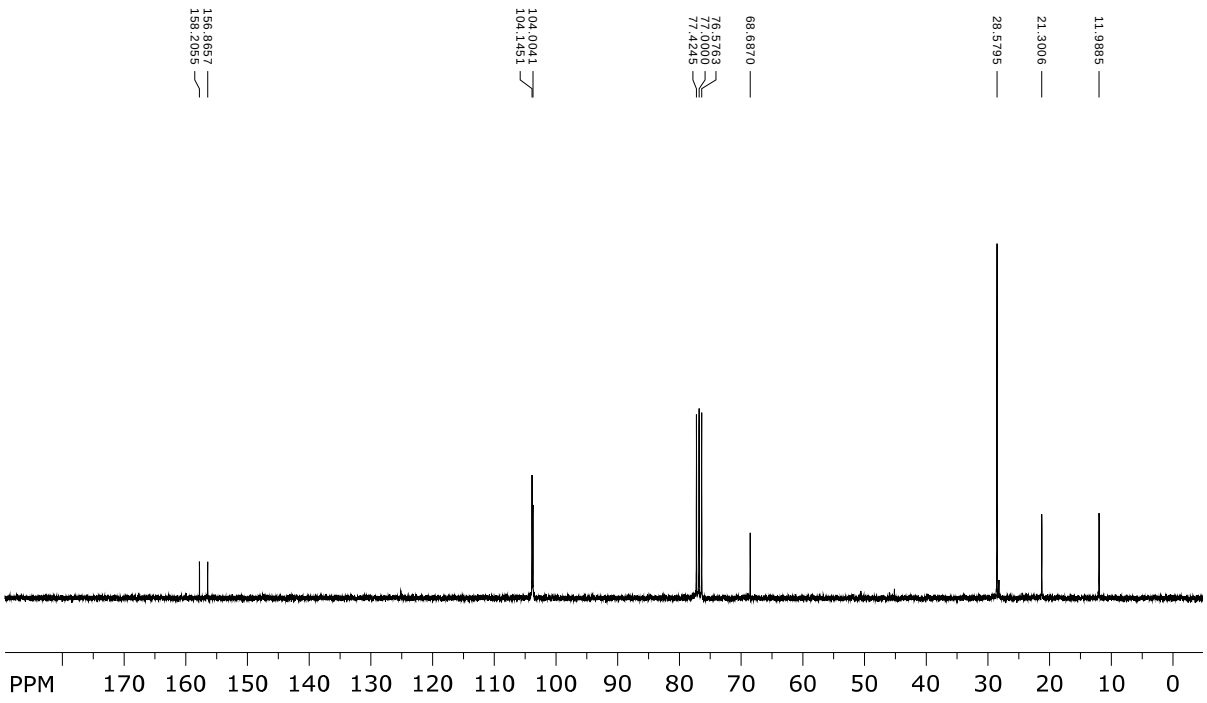


Fig. 2 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1b** in $CDCl_3$.

2-(5-Propylfuran-2-yl)propan-2-ol (1c)

According to the general procedure I, 2-propylfuran (**5d**, 12.5 mmol, 1.6 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and acetone (**6a**, 12.5 mmol, 0.9 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4 : 1) afforded **1c** (1.16 g, 6.9 mmol, 55%) as a yellowish oil.

R_f 0.36 (cyclohexane ─ EtOAc = 8:3); UV λ_{max} (MeCN)/nm 221 (log ε/dm^3 mol^{-1} cm^{-1}, 3.90); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3403 (OH), 2961 (CH_3, CH_2), 1378, 1170, 943 and 780; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.96 (3H, t, $^{3}J_{3''\text{-H, }2''\text{-H}}$ 7.4 Hz, 3''-H), 1.56 (6H, s, 1-H and 3-H), 1.65 (2H, tq, $^{3}J_{2''\text{-H, }1''\text{-H}}$ 7.0 Hz, $^{3}J_{2''\text{-H, }3''\text{-H}}$ 7.4 Hz, 2''-H), 2.56 (2H, t, $^{3}J_{1''\text{-H, }2''\text{-H}}$ 7.6 Hz, 1''-H), 5.88 (1H, $^{3}J_{4'\text{-H, }3'\text{-H}}$ 3.0 Hz, 4'-H) and 6.05 (1H, d, $^{3}J_{3'\text{-H, }4'\text{-H}}$ 3.2 Hz, 3'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 13.7 (C-3''), 21.30 (C-2''), 28.6 (C-1 and C-3), 30.0 (C-1'') 68.7 (C-2), 104.0 (C-3'), 105.0 (C-4'), 155.5 (C-5'), 158.2 (C-2') ppm; MS (EI, 70 eV) *m/z* 168 (M^+, 13%), 153 (100, $M^+ - CH_3$), 82 (13) and 43 (16); HRMS (EI, M^+) found: 168.1151, calcd for $C_{10}H_{16}O_2$: 168.1150.

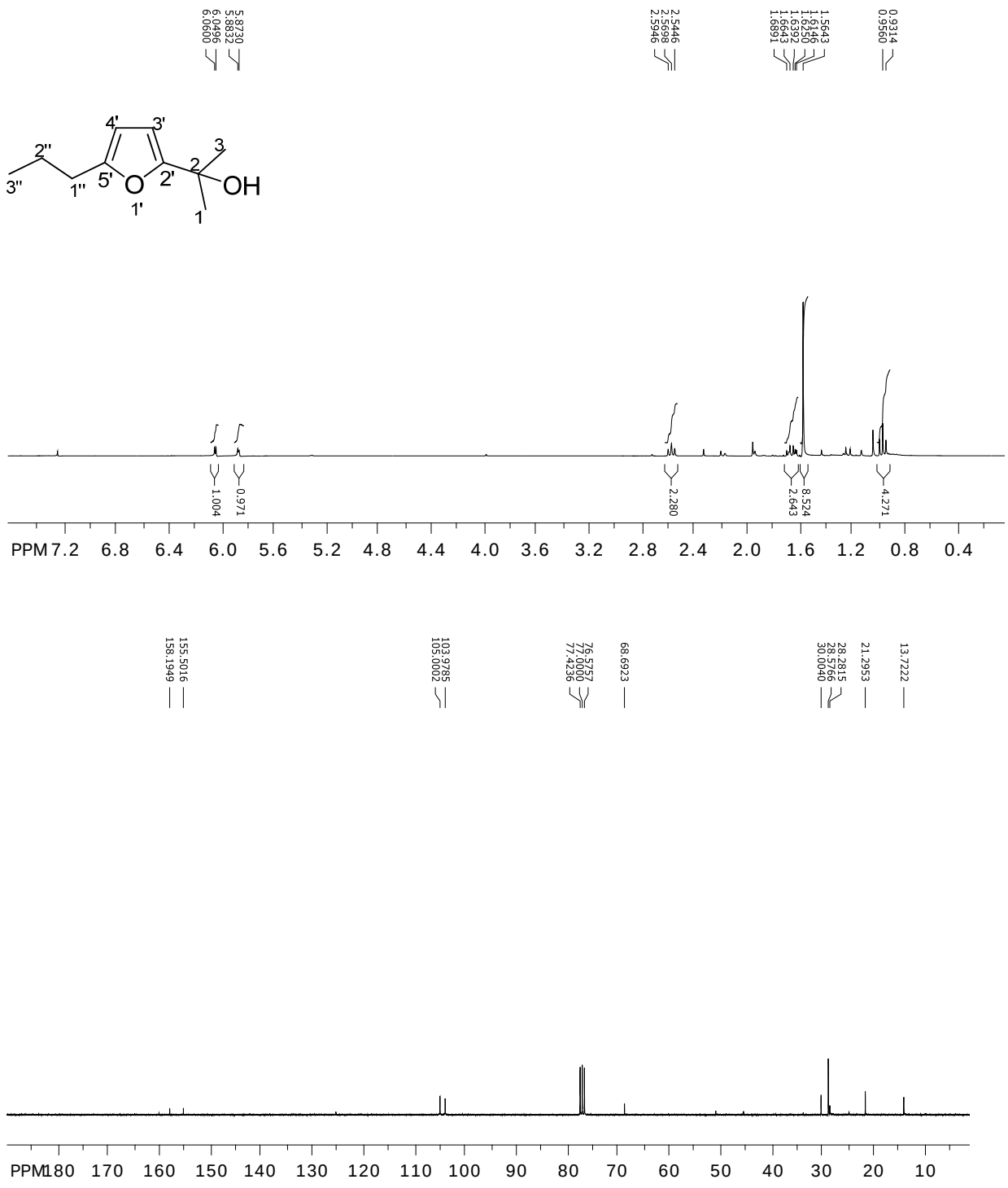
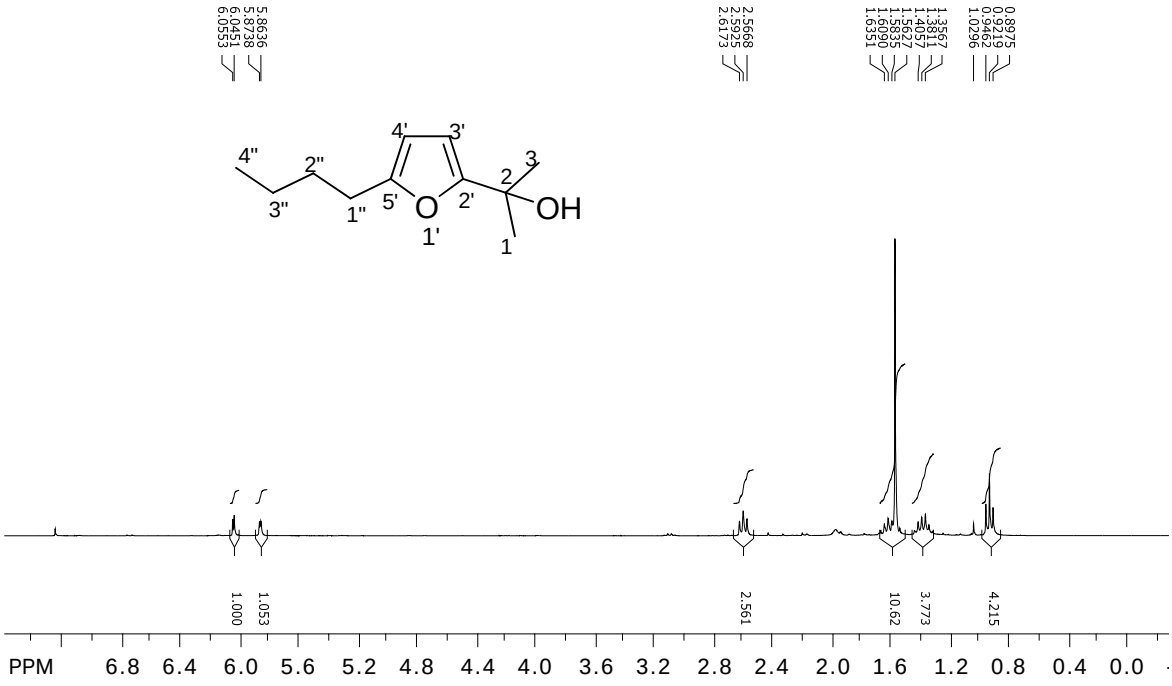


Fig. 3 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1c** in $CDCl_3$.

2-(5-Butylfuran-2-yl)propan-2-ol (1d)

According to the general procedure I, 2-butylfuran (**5e**, 12.5 mmol, 1.9 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and acetone (**6a**, 12.5 mmol, 0.9 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4: 1) afforded **1d** (1.4 g, 7.7 mmol, 62%) as a yellowish oil.

R_f 0.36 (cyclohexane ─ EtOAc = 8:3); UV λ_{max} (MeCN)/nm 219 (log ε/dm^3 mol^{-1} cm^{-1}, 3.91); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3371 (OH), 2958, 2931, 1476, 1377, 1167, 1121, 957 and 780; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.92 (3H, t, $^3J_{4''\text{-H},\ 3''\text{-H}}$ 7.4 Hz, 4''-H), 1.38 (2H, tq, $^3J_{3''\text{-H},\ 4''\text{-H}}$ 7.0 Hz, $^3J_{3''\text{-H},\ 2''\text{-H}}$ 7.4 Hz, 3''-H), 1.56 (6H, s, 1-H and 3-H), 1.61 (2H, tt, $^3J_{2''\text{-H},\ 1''\text{-H}}$ 7.0 Hz, $^3J_{2''\text{-H},\ 3''\text{-H}}$ 7.4 Hz, 2''-H), 2.59 (2H, t, $^3J_{1''\text{-H},\ 2''\text{-H}}$ 7.6 Hz, 1''-H), 5.87 (1H, d, $^3J_{4'\text{-H},\ 3'\text{-H}}$ 3.2 Hz, 4'-H) and 6.05 (1H, d, $^3J_{3'\text{-H},\ 4'\text{-H}}$ 3.2 Hz, 3'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 13.8 (C-4''), 22.3 (C-3''), 27.7 (C-2''), 28.6 (C-1 and C-3), 30.1 (C-1'') 68.7 (C-2), 104.0 (C-3'), 104.9 (C-4'), 155.7 (C-5') and 158.2 (C-2') ppm; MS (EI, 70 eV) *m/z* 182 (M^+, 14%), 167 (100, $M^+ - CH_3$), 164 (38), 21 (100) and 43 (13); HRMS (EI, M^+) found: 182.1309, calcd for $C_{11}H_{18}O_2$: 182.1307.



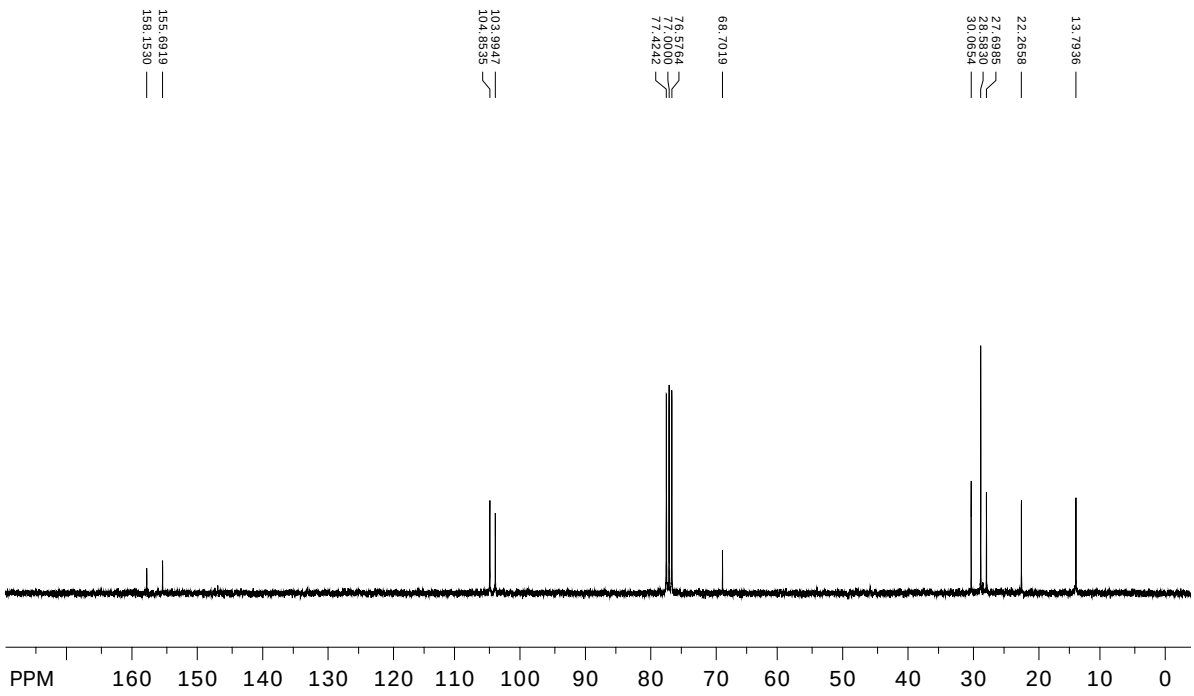


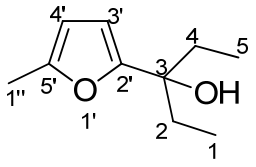
Fig. 4 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1d** in $CDCl_3$.

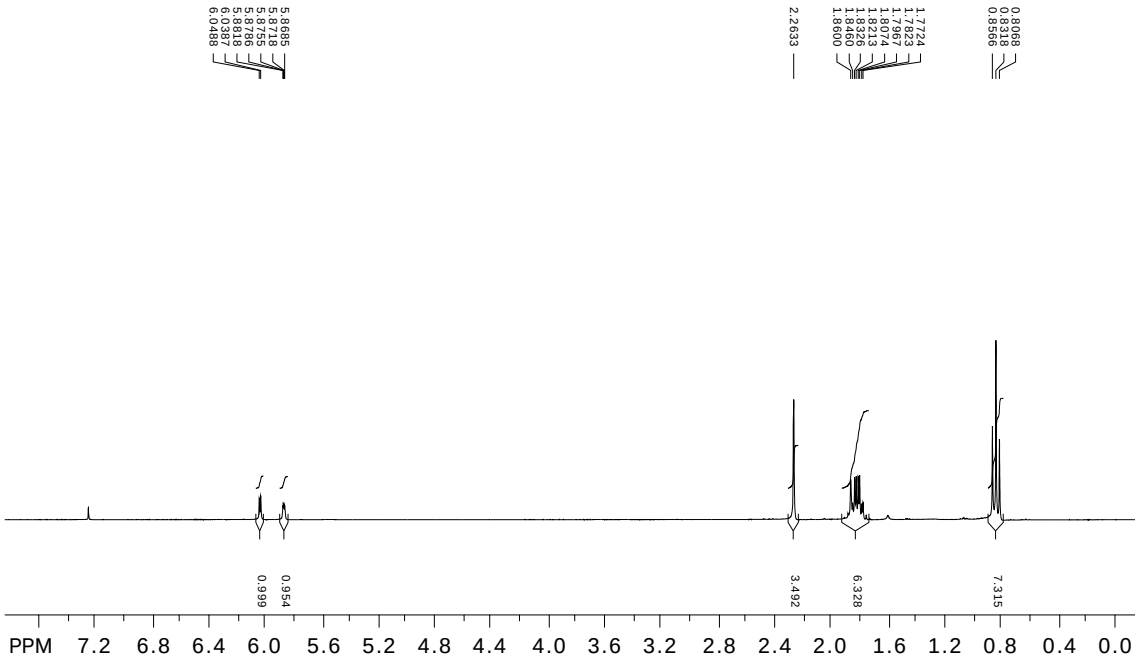
3-(5-Methylfuran-2-yl)pentan-3-ol (1e)

According to the general procedure I, 2-methylfuran (**5b**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and 3-pentanone (**6e**, 12.5 mmol, 1.3 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4: 1) afforded **1e** (1.58 g, 9.4 mmol, 75%) as a yellowish oil.

R_f 0.38 (cyclohexane ─ EtOAc = 8:3); UV λ_{max} (MeCN)/nm 220 (log ε/dm^3 mol^{-1} cm^{-1}, 3.92); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3447 (OH), 2967, 1459 (C=C), 1219, 1020, 946 and 781; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.83 (6H, t, $^{3}J_{1\text{-H, }2\text{-H}}$ and $^{3}J_{5\text{-H, }4\text{-H}}$ 7.6 Hz, 1-H and 5-H), 1.82 (4H, q, $^{3}J_{2\text{-H, }1\text{-H}}$ and $^{3}J_{4\text{-H, }5\text{-H}}$ 7.4 Hz, 2-H and 4-H), 2.26 (3H, s, 5'-Me), 5.87 (1H, dq, $^{3}J_{4'\text{-H, }5'\text{-H}}$ 3.2 Hz, $^{4}J_{4'\text{-H, }1''\text{-H}}$ 0.9 Hz, 4'-H) and 6.04 (1H, d, $^{3}J_{3'\text{-H, }4'\text{-H}}$ 3.2 Hz, 3'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 7.9 (C-1 and C-5), 13.6 (5-Me), 31.6 (C-2 and C-4), 74.7 (C-3), 105.7 (C-3'), 106.1 (C-4'), 150.9 (C-5') and 156.7 (C-2') ppm; (EI, 70 eV) *m/z*

168 (M^+, 13%), 150 (31, M^+-H_2O) 139 (100, M^+−C_2H_5) and 121 (22); HRMS (EI, M^+) found: 168.1154, calcd for $C_{10}H_{16}O_2$: 168.1150.





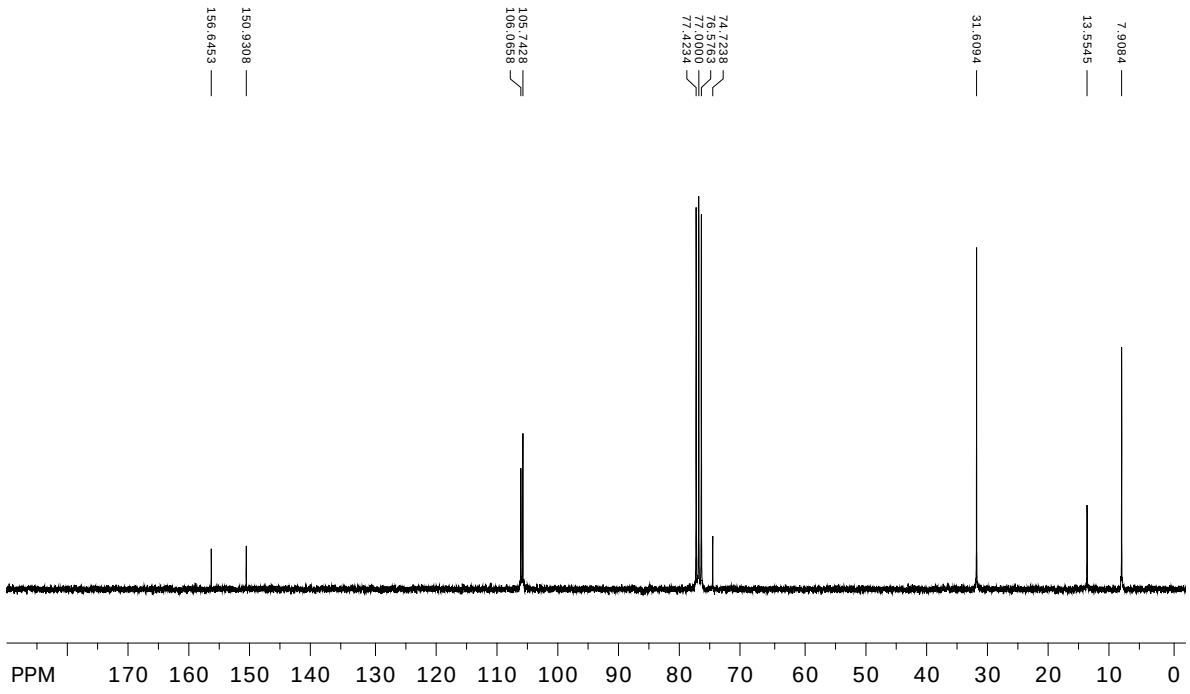


Fig. 5 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1e** in $CDCl_3$.

1-(5-Methylfuran-2-yl)cyclopentan-1-ol (1f)

According to the general procedure I, 2-methylfuran (**5b**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and cyclopentanone (**6f**, 12.5 mmol, 1.1 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4: 1) afforded **1f** (1.3 g, 7.9 mmol, 63%) as a yellowish oil. R_f 0.39 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 220 (log ε/dm^3 mol^{-1} cm^{-1}, 3.93); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3389 (OH), 2956, 1639, 1440, 1382, 1255, 1176, 1020, 971 and 780; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.93 (8H, m, 2-H, 3-H, 4-H and 5-H), 2.27 (3H, s, 1''-H), 5.87 (1H, dq, $^{3}J_{4'\text{-H},\,4'\text{-H}}$ 3.2 Hz, $^{4}J_{4'\text{-H},\,1''\text{-H}}$ 0.9 Hz, 4'-H), 6.07 (1H, d, $^{3}J_{3'\text{-H},\,3'\text{-H}}$ 3.2 Hz, 3'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 13.5 (C-1''), 23.5 (C-3 and C-4), 39.4 (C-2 and C-5), 79.4 (C-1), 104.8 (C-3'), 105.8 (C-4'), 151.2 (C-5') and 157.4 (C-2') ppm; MS (EI, 70 eV) *m/z* 166 (M^+, 43%), 151 (30, M^+─CH_3) 137 (100, M^+─C_2H_5), 124

(48), 109 (52), 95 (20), 55(16) and 43 (27); HRMS (EI, M^+) found: 166.0999, calcd for $C_{10}H_{14}O_2$: 166.0994.

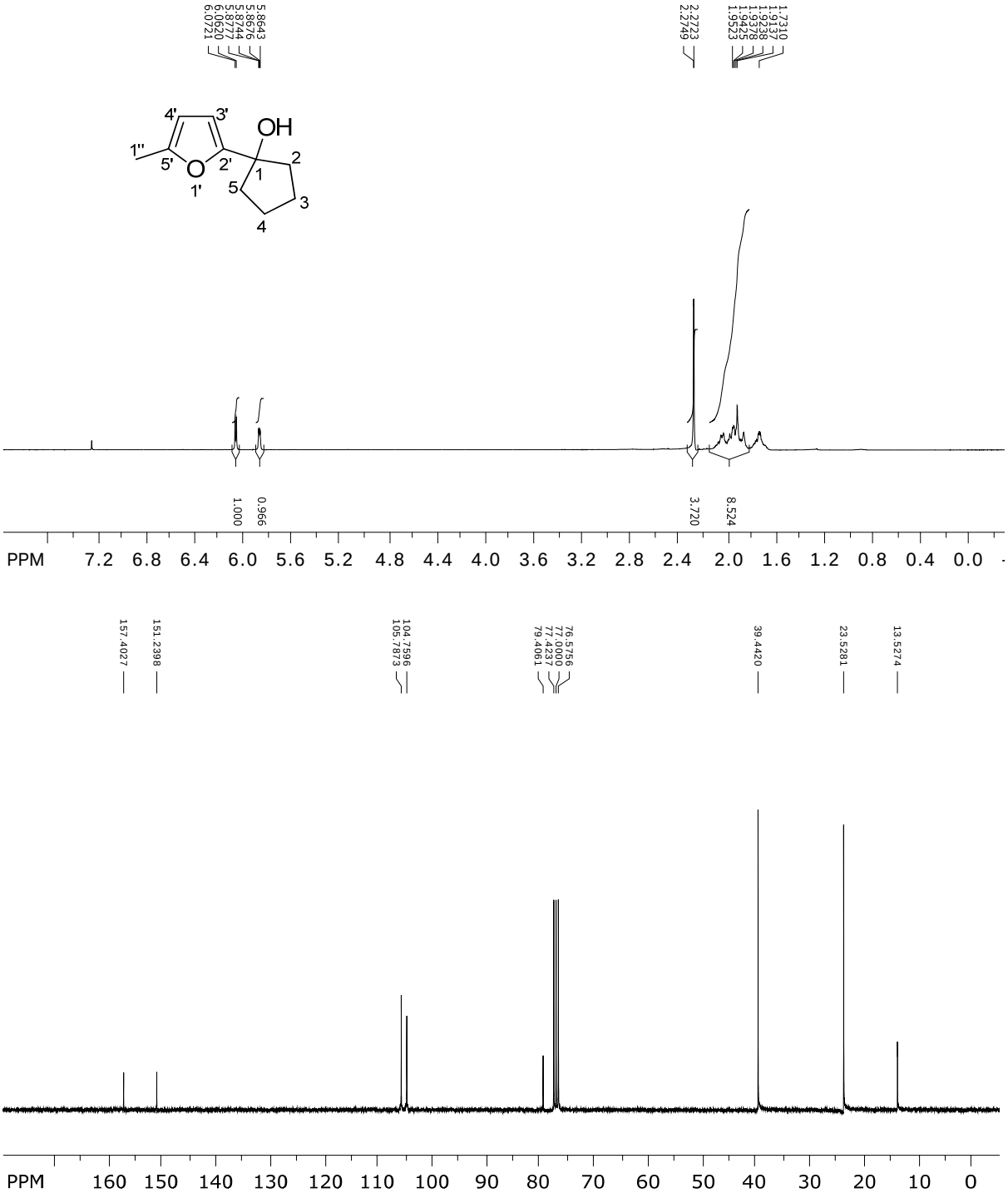
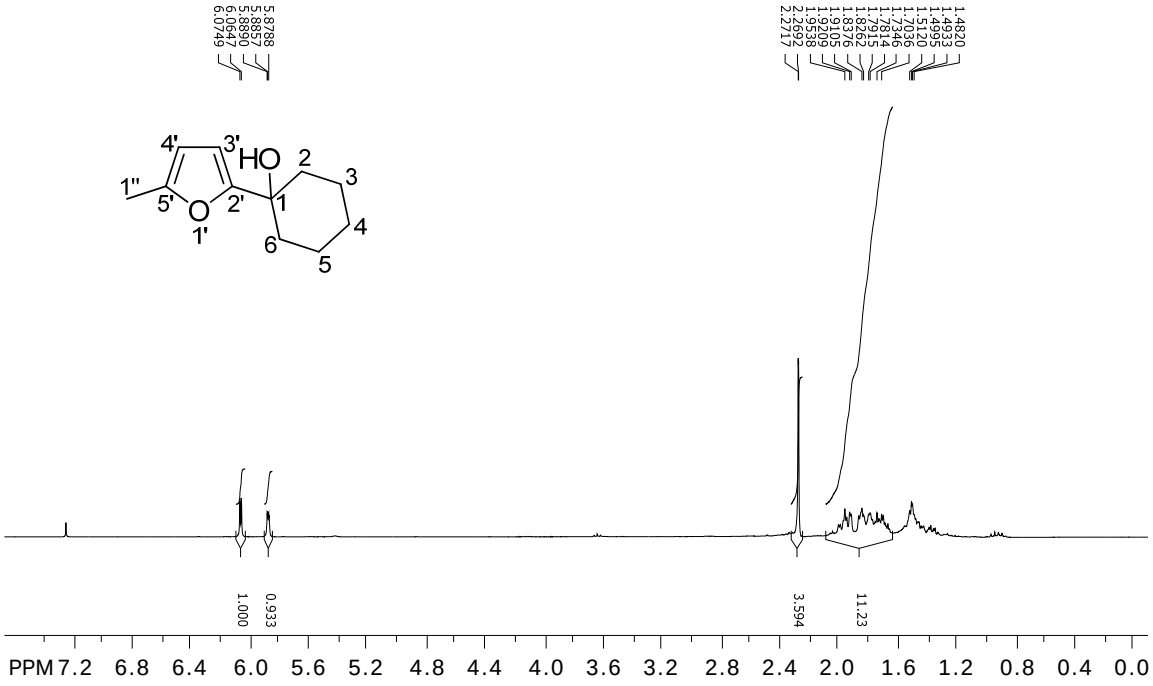


Fig. 6 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1f** in $CDCl_3$.

1-(5-Methylfuran-2-yl)cyclohexan-1-ol (1g)

According to the general procedure I, 2-methylfuran (**5b**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and cyclohexanone (**6g**, 12.5 mmol, 1.3 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4 : 1) afforded **1g** (1.8 g, 10 mmol, 80%) as a white solid. Mp 58-61 °C; R_f 0.40 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 220 (log ε/dm^3 mol^{-1} cm^{-1}, 3.93); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3285 (OH), 2935, 2860, 1446, 1347, 1225, 1061, 959 and 786; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.62-2.10 (10H, m, 2-H, 3-H, 4-H, 5-H and 6-H), 2.27 (3H, s, 1''-H), 5.88 (1H, dq, $^3J_{4'\text{-H, }3'\text{-H}}$ 3.2 Hz, $^4J_{4'\text{-H, }1''\text{-H}}$ 0.9 Hz, 4'-H) and 6.07 (1H, d, $^3J_{3'\text{-H, }4'\text{-H}}$ 3.2 Hz, 3'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 13.5 (C-1''), 22.3 (C-3 and C-5), 22.4 (C-4), 36.6 (C-2 and C-6), 70.0 (C-1), 105.1 (C-3'), 105.8 (C-4'), 151.0 (C-5') and 158.1 (C-2') ppm; MS (EI, 70 eV) *m/z* 180 (M^+, 33%), 137 (100, M^+─C_3H_7), 124 (13), 109 (10); HRMS (EI, M^+) found: 180.1150, calcd for $C_{11}H_{16}O_2$: 180.1150.



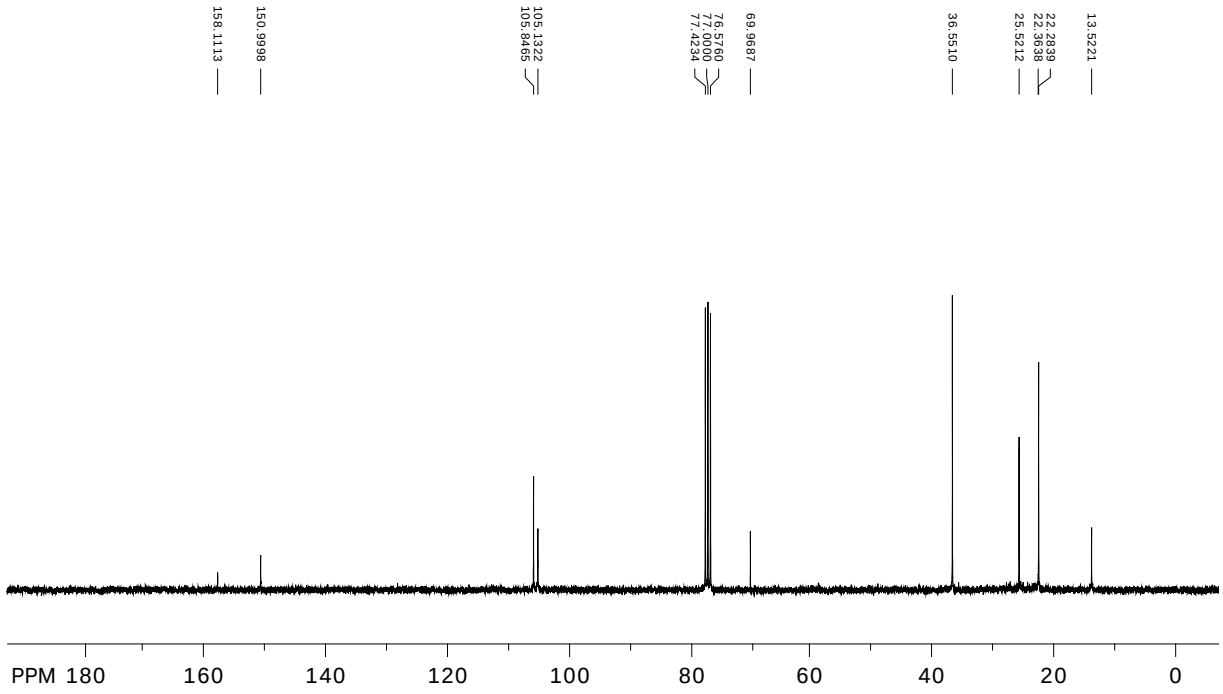


Fig. 7 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1g** in $CDCl_3$.

1-(5-Methylfuran-2-yl)cycloheptan-1-ol (1h)

According to the general procedure I, 2-methylfuran (**5b**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and cycloheptanone (**6h**, 12.5 mmol, 1.5 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4 : 1) afforded **1h** (1.58 g, 8.1 mmol, 65%) as a yellowish solid.

Mp 54-56 °C**;** R_f 0.44 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 219 (log ε/dm^3 mol^{-1} cm^{-1}, 3.94); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3432 (OH), 2927, 2856, 1699, 1456, 1022, and 780; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.50-1.70 (8H, m, 3-H, 4-H, 5-H, 6-H, 7-H), 1.98 (2H, m, 2-H), 2.00 (2H, m, 7-H), 2.27 (3H, s, 1”-H), 5.86 (1H, dq, $^{3}J_{4'\text{-H, }3'\text{-H}}$ 3.2 Hz, $^{4}J_{4'\text{-H, }1''\text{-H}}$ 0.9 Hz, 4’-H) and 6.06 (1H, d, $^{3}J_{3'\text{-H, }4'\text{-H}}$ 3.2 Hz, 3’-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 13.6 (C-1”), 22.1 (C-4 and C-5), 29.5 (C-3 and C-6), 40.0 (C-2 and C-7), 74.0 (C-1), 104.9 (C-3’), 105.7 (C-4’), 151.2 (C-5’) and 158.9 (C-2’) ppm; MS (EI, 70

eV) *m/z* 194 (M^+, 20%), 137 (100, M^+–C_4H_9), 124 (27), 109 (10); HRMS (EI, M^+) found: 194.1311, calcd for $C_{12}H_{18}O_2$: 194.1307.

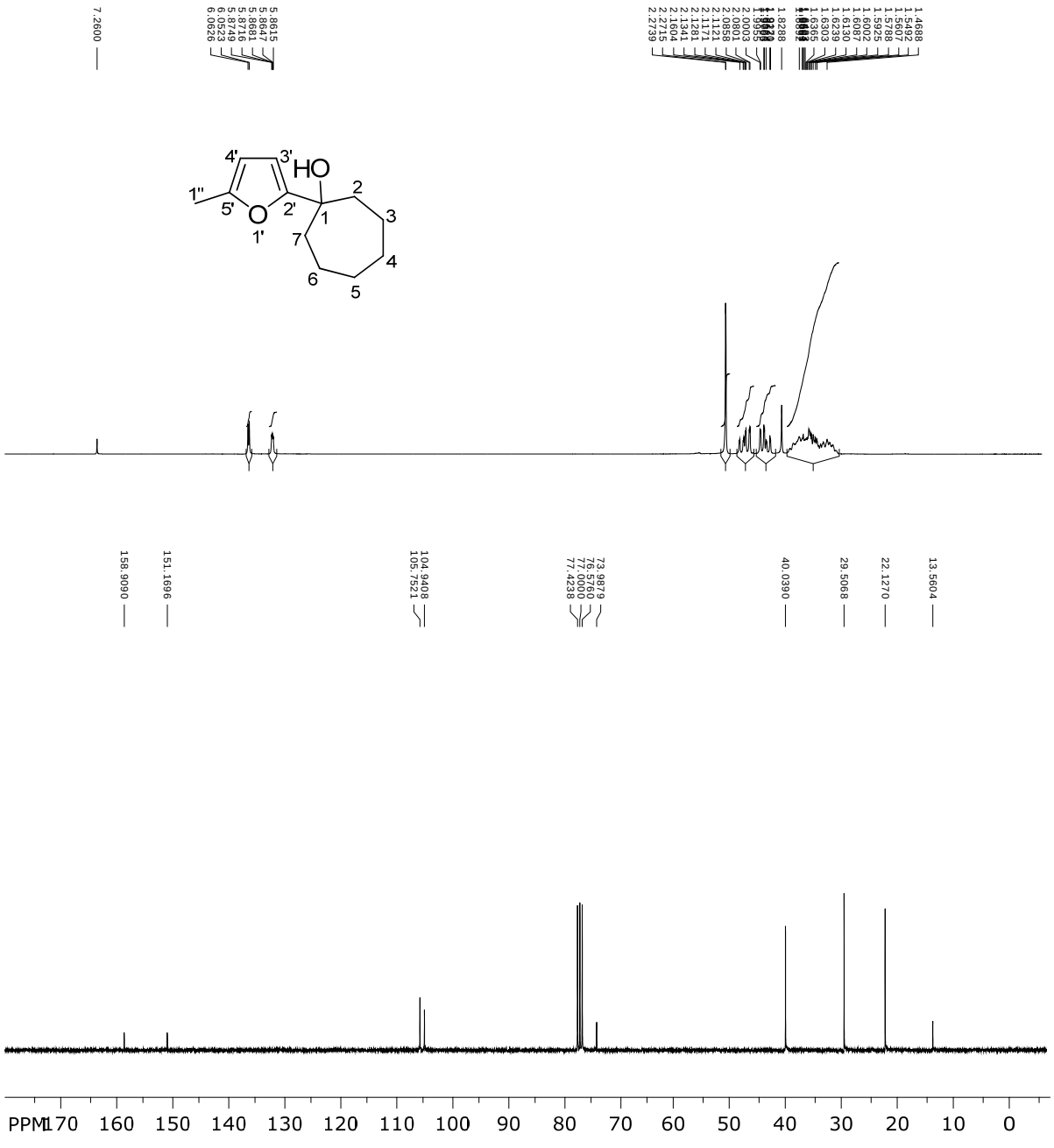
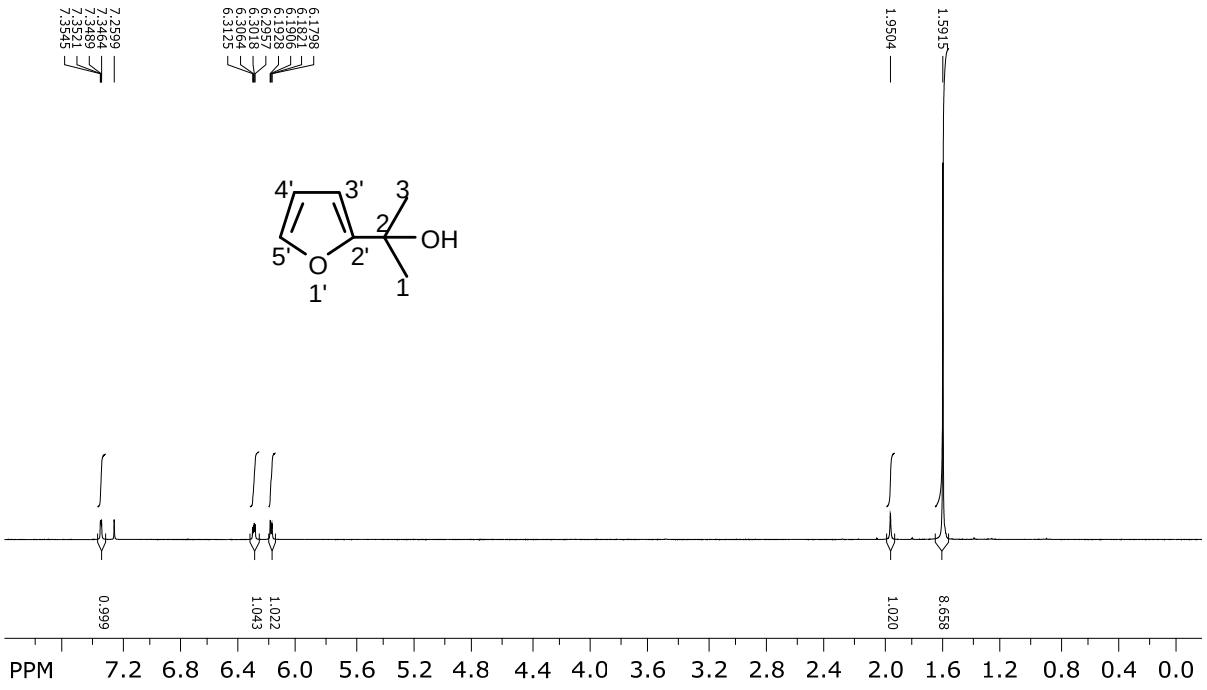


Fig. 8 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1h** in $CDCl_3$.

2-(Furan-2-yl)propan-2-ol (1i)

According to the general procedure I, furan (**5a**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and acetone (**6a**, 12.5 mmol, 0.9 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4:1) afforded **1i** (0.81 g, 6.4 mmol, 51%) as a yellowish oil.

R_f 0.36 (cyclohexane ─ EtOAc = 3:1), UV λ_{max} (MeCN)/nm 219 (log ε/dm^3 mol^{-1} cm^{-1}, 3.88); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} ; 3411 (OH), 2980, 1654, 1364 1158, 952 and 731; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.59 (6H, s, 1-H and 3-H), 1.95 (1H, s, OH), 6.18 (1H, dd, $^3J_{3'\text{-H, }4'\text{-H}}$ 3.3 Hz, $^4J_{3'\text{-H, }5'\text{-H}}$ 0.8 Hz, 3'-H), 6.31 (1H, dd, $^3J_{4'\text{-H, }3'\text{-H}}$ 3.3 Hz, $^3J_{4'\text{-H, }5'\text{-H}}$ 1.8 Hz, 4'-H) and 7.35 (1H, dd, $^3J_{5'\text{-H, }4'\text{-H}}$ 1.8 Hz, $^4J_{5'\text{-H, }3'\text{-H}}$ 1.8 Hz, 5'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 28.7 (C-1 and C-3), 68.8 (C-2), 103.6 (C-3'), 110 (C-4'), 141.5 (C-5') and 160.2 (C-2') ppm; MS (EI, 70 eV) *m/z* 126 (M^+, 27%), 111 (100, M^+-CH_3) and 43 (47); HRMS (EI, M^+) found: 126.0683, calcd for $C_7H_{10}O_2$: 126.0681.



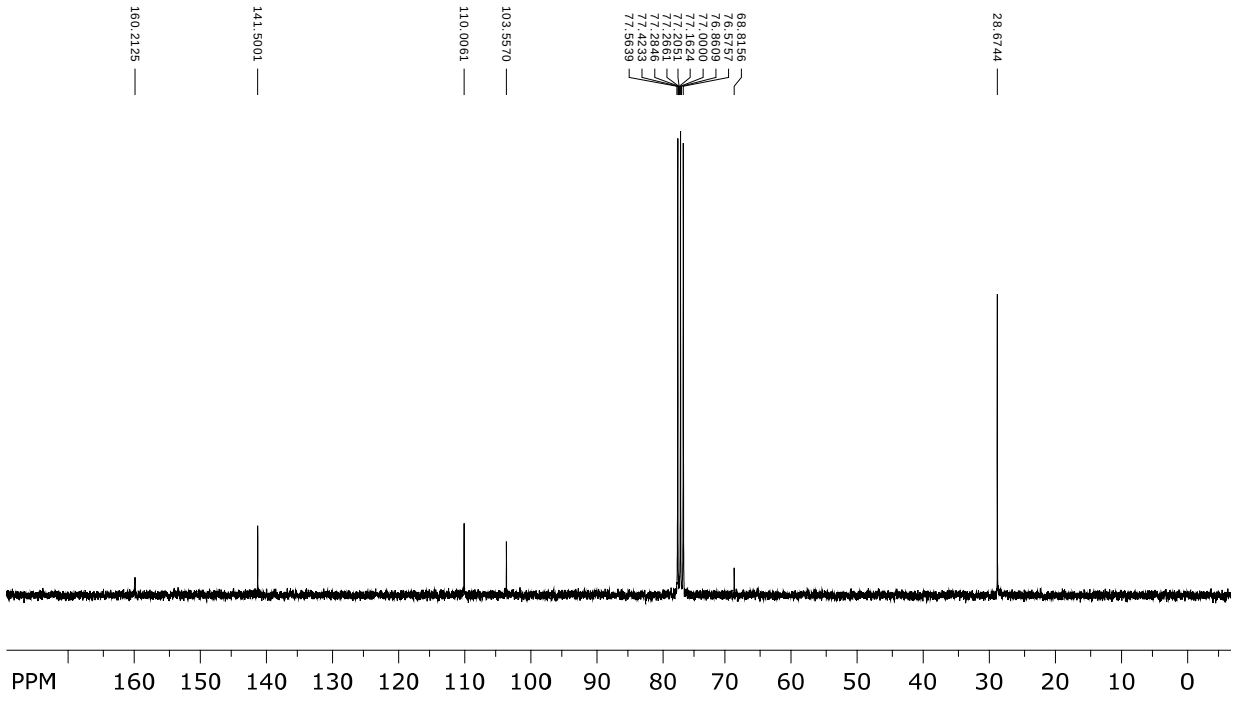


Fig. 9 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1i** in $CDCl_3$.

2-(Furan-2-yl)butanol-2-ol (1j)

According to the general procedure I, furan (**5a**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and butanone (**6b**, 12.5 mmol, 1.1 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4 : 1) afforded **2j** (0.88 g, 6.3 mmol, 50%) as a yellowish oil.

R_f 0.39 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 219 (log ε/dm^3 mol^{-1} cm^{-1}, 3.89); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3425 (OH), 2986, 1647, 1566, 1359, 1154 and 728; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.85 (3H, t, $^{3}J_{4\text{-H, }3\text{-H}}$ 6.2 Hz, 4-H), 1.52 (3H, s, 1-H), 1.89 (2H, q, $^{3}J_{3\text{-H, }4\text{-H}}$ 6.2 Hz, 3-H), 6.18 (1H, dd, $^{3}J_{3'\text{-H, }4'\text{-H}}$ 3.2 Hz, $^{4}J_{3'\text{-H, }5'\text{-H}}$ 0.8 Hz, 3'-H), 6.30 (1H, dd, $^{3}J_{4'\text{-H, }3'\text{-H}}$ 3.2 Hz, $^{3}J_{4'\text{-H, }5'\text{-H}}$ 1.8 Hz, 4'-H) and 7.35 (1H, dd, $^{3}J_{5'\text{-H, }4'\text{-H}}$ 1.8 Hz, $^{4}J_{5'\text{-H, }3'\text{-H}}$ 1.8 Hz, 5'-H) ppm; δ_C (75 MHz; $CDCl_3$) 8.5 (C-4), 25.9 (C-1), 34.4 (C-3), 71.9 (C-2), 104.6 (C-3'), 110.0 (C-4'), 141.4 (C-5') and 159.5 (C-2') ppm; MS (EI, 70 eV) *m/z* 140

(M^+, 13%), 111 (100, M^+-C_2H_5) and 43 (39); HRMS (EI, M^+) found: 140.0839, calcd for $C_8H_{12}O_2$: 140.0837.

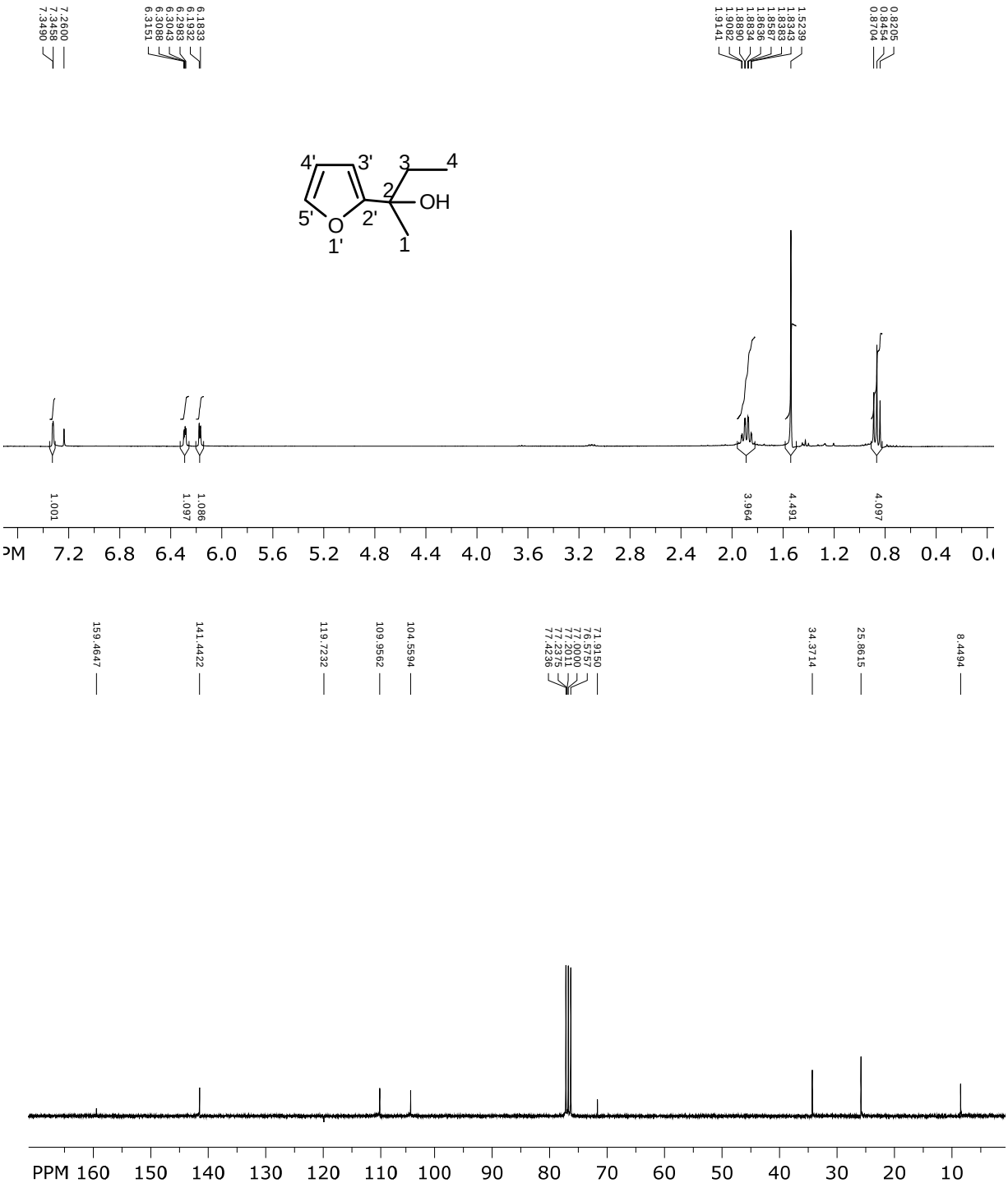
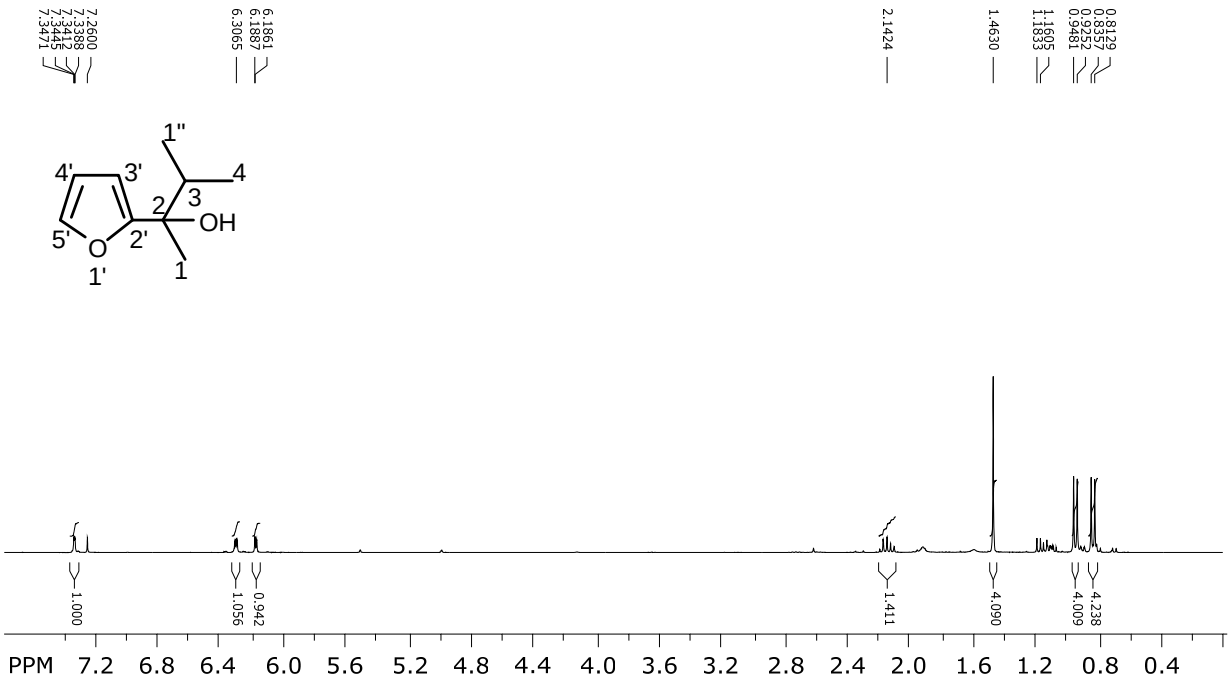


Fig. 10 ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1j** in $CDCl_3$.

2-(Furan-2-yl)-3-methylbutan-2-ol (1k)

According to the general procedure I, furan (**5a**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and 3-methylbutanone (**6c**, 12.5 mmol, 1.3 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4:1) afforded **1k** (0.87 g, 5.6 mmol, 45%) as yellowish oil.

R_f 0.36 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 219 (log ε/dm^3 mol^{-1} cm^{-1}, 3.88); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3427(OH), 2963, 2876, 1370, 1156, 1006 and 729; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.82 (3H, d, $^3J_{4\text{-H, }3\text{-H}}$ 6.5 Hz, 4-H), 0.93 (3H, d, $^3J_{1''\text{-H, }3\text{-H}}$ 6.5 Hz , 1''-H), 1.46(3H, s, 1-H), 2.14 (1H, m, 3-H), 6.19 (1H, dd, $^3J_{3'\text{-H, }4'\text{-H}}$ 3.1 Hz, $^4J_{3'\text{-H, }5'\text{-H}}$ 0.8 Hz, 3'-H), 6.31 (1H, dd, $^3J_{4'\text{-H, }3'\text{-H}}$ 3.1 Hz, $^3J_{4'\text{-H, }5'\text{-H}}$ 1.8 Hz, 4'-H) and 7.35 (1H, dd, $^3J_{5'\text{-H, }4'\text{-H}}$ 1.8 Hz, $^4J_{5'\text{-H, }3'\text{-H}}$ 1.8 Hz, 5'-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 17.0 (C-4), 17.5 (C-1''), 22.4 (C-3), 37.3 (C-2), 105.0 (C-3'), 110.0 (C-4'), 141.1 (C-5'), 160.1 (C-2') ppm; MS (EI, 70 eV) *m/z* 154 (M^+, 12%), 111 (100, M^+-C_3H_7) and 43 (12); HRMS (EI, M^+) found: 154.0994, calcd for $C_9H_{14}O_2$: 154.0994.



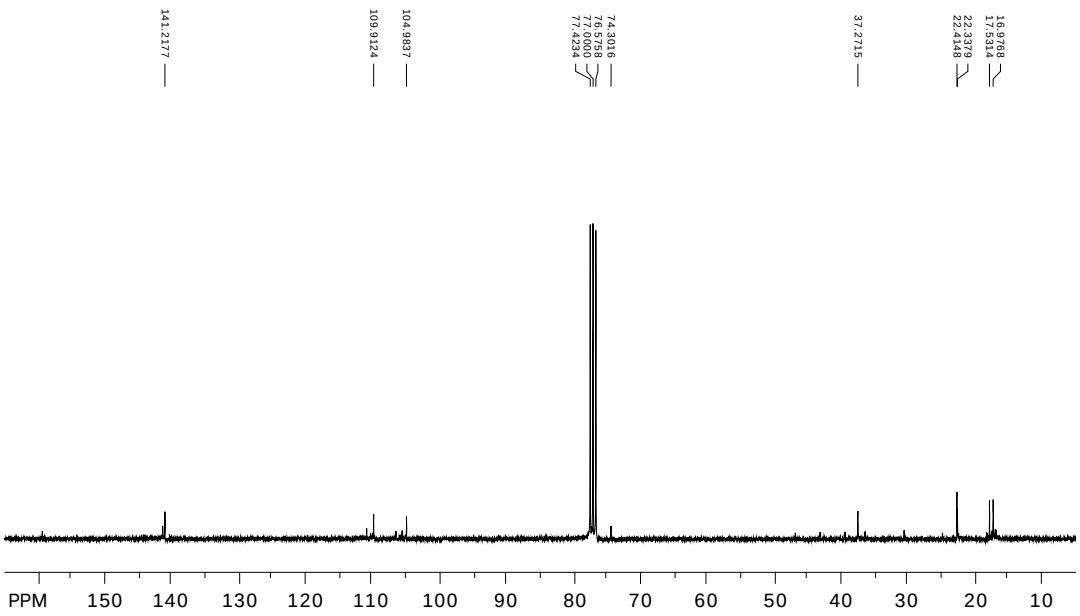


Fig. 11 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1k** in $CDCl_3$.

2-(Furan-2-yl)-4-methylpentan-2-ol (1l)

According to the general procedure I, furan (**5a**, 12.5 mmol, 1.1 mL) was reacted with 8 mL (12.5 mmol) *n*-butyl-lithium solution (1.6 M in hexanes) and 4-methyl-pentan-2-one (**6d**, 12.5 mmol, 1.6 mL). Purification over triethylamine-deactivated silica gel (*n*-pentane ─ Et_2O = 4:1) afforded **1l** (0.84 g, 5 mmol, 40%) as yellowish oil.

R_f 0.36 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 219 (log ε/dm^3 mol^{-1} cm^{-1}, 3.92); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3430 (OH), 2970, 1655, 1536, 1360, 1155 and 730;^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.81 (3H, d, $^{3}J_{5\text{-H, }4\text{-H}}$ 6.2 Hz, 5-H), 0.91 (3H, d, $^{3}J_{1''\text{-H, }4\text{-H}}$ 6.2 Hz, 1''-H), 1.55 (3H, s, 1-H), 1.65 (1H, m, 4-H), 1.79 (2H, dd, $^{2}J_{3\text{-Ha, }3\text{-Hb}}$ 6.2 Hz $^{3}J_{3\text{-H, }4\text{-H}}$ 3.2 Hz, 3-H), 6.18 (1H, dd, $^{3}J_{3'\text{-H, }4'\text{-H}}$ 3.1 Hz, $^{4}J_{3'\text{-H, }5'\text{-H}}$ 0.8 Hz, 3'-H), 6.30 (1H, $^{3}J_{4'\text{-H, }3'\text{-H}}$ 3.4 Hz, $^{3}J_{4'\text{-H, }5'\text{-H}}$ 1.8 Hz, 4'-H) and 7.35 (1H, dd, $^{3}J_{5'\text{-H, }4'\text{-H}}$ 1.8 Hz, $^{4}J_{5'\text{-H, }3'\text{-H}}$ 0.8 Hz, 5'-H) ppm; δ_C (75 MHz; $CDCl_3$) 23.9 (C-4), 24.1 (C-1''), 24.5 (C-5), 27.3 (C-1), 50.4 (C-3), 71.9 (C-2), 104.3 (C-3'), 110.1 (C-4'), 141.2 (C-5') and 159.9 (C-2') ppm; MS (EI, 70

eV) *m/z* 168 (M^+, 11%), 111 (100, M^+-C_4H_9), 101 (22) and 43 (14); HRMS (EI, M^+) found: 168.1154, calcd for $C_{10}H_{16}O_2$: 168.1150.

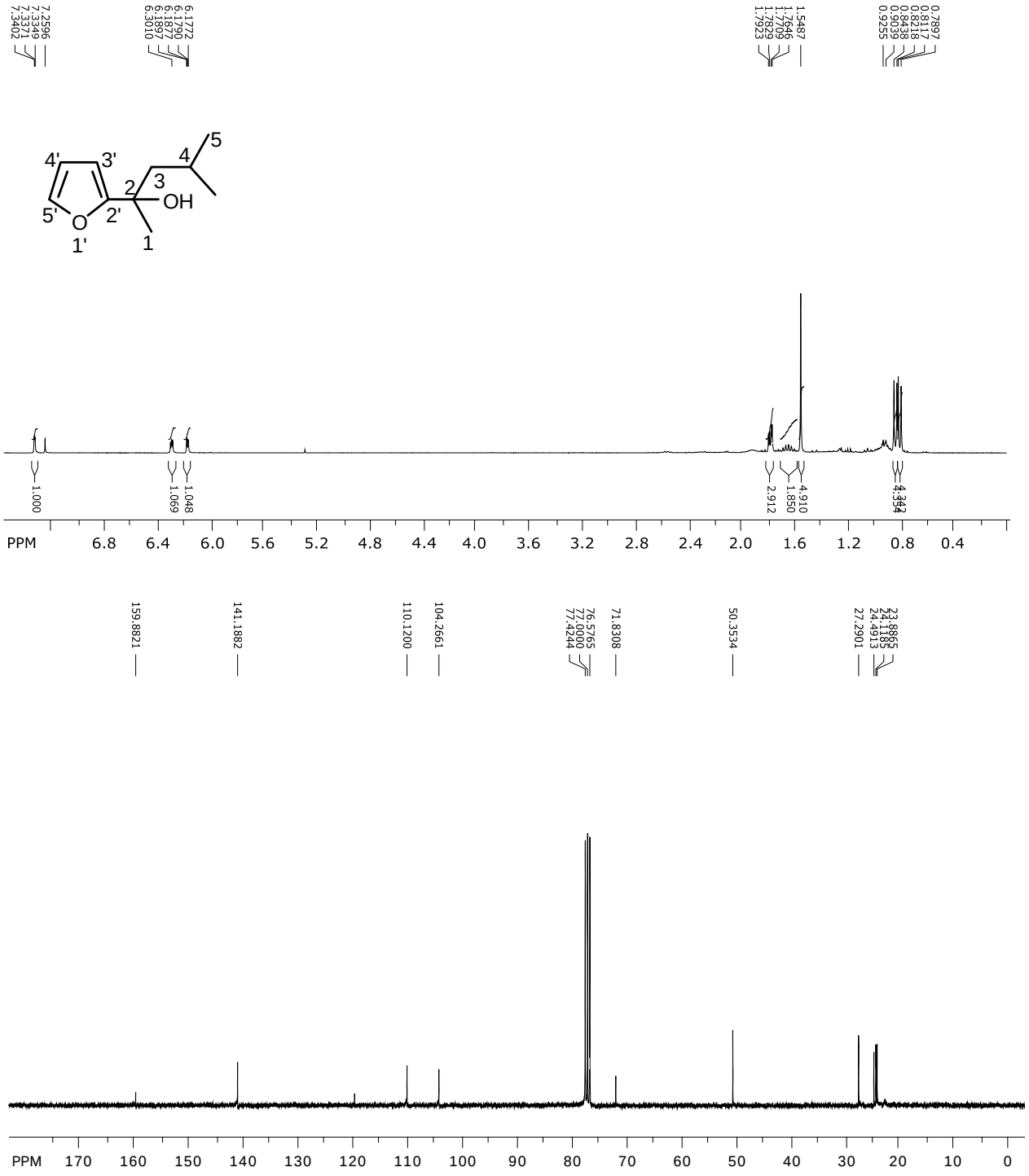


Fig. 12 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **1l** in $CDCl_3$.

3 Oxidation of 1 to 2

3.1 General procedure II for the oxidation of 1 to 2

A 100 mL round bottomed flask was charged with furan-2-yl carbinol **1** (1 mmol), *n*-octane (1 ml), 0.01 M acetate buffer pH 4.5 (10 mL), 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*). The mixture was stirred at rt for the time given. The aqueous phase was saturated with NaCl (1 g) and extracted with CH_2Cl_2 (4 × 25 mL). The combined organic phases were dried over Na_2SO_4. After removal of the solvents *in vacuo*, the crude product was purified by flash chromatography over silica gel (cyclohexane ─ EtOAc = 2:1) to yield the 6-hydroxy-(2*H*)-pyran-3(6*H*)-ones **2**.

3.2 Synthesis and analytical data for 2a-h

6-Hydroxy-2,2,6-trimethyl-2*H*-pyran-3(6*H*)-one (2a)[2]

According to the general procedure II, 2-(5-methylfuran-2-yl)propan-2-ol (**1a**) (140 mg, 1mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 6 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2a** (112 mg, 0.73 mmol, 73%) as a yellowish oil.

R_f 0.18 (cyclohexane ─ EtOAc = 3:1); ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.36 (3H, s, 6-Me), 1.52 (3H, s, 2-Me), 1.59 (3H, s, 2-Me), 2.72 (1H, s, OH), 5.99 (1H, d, $^3J_{4\text{-H, }5\text{-H}}$ 10.3 Hz, 4-H) and 6.80 (1H, d, $^3J_{5\text{-H, }4\text{-H}}$ 10.0 Hz, 5-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 25.9 (2-Me), 28.0 (6-Me), 30.5 (2-Me), 78.7 (C-2), 92.5 (C-6), 124.3 (C-4), 147.6 (C-5) and 199.4 (C-3) ppm.

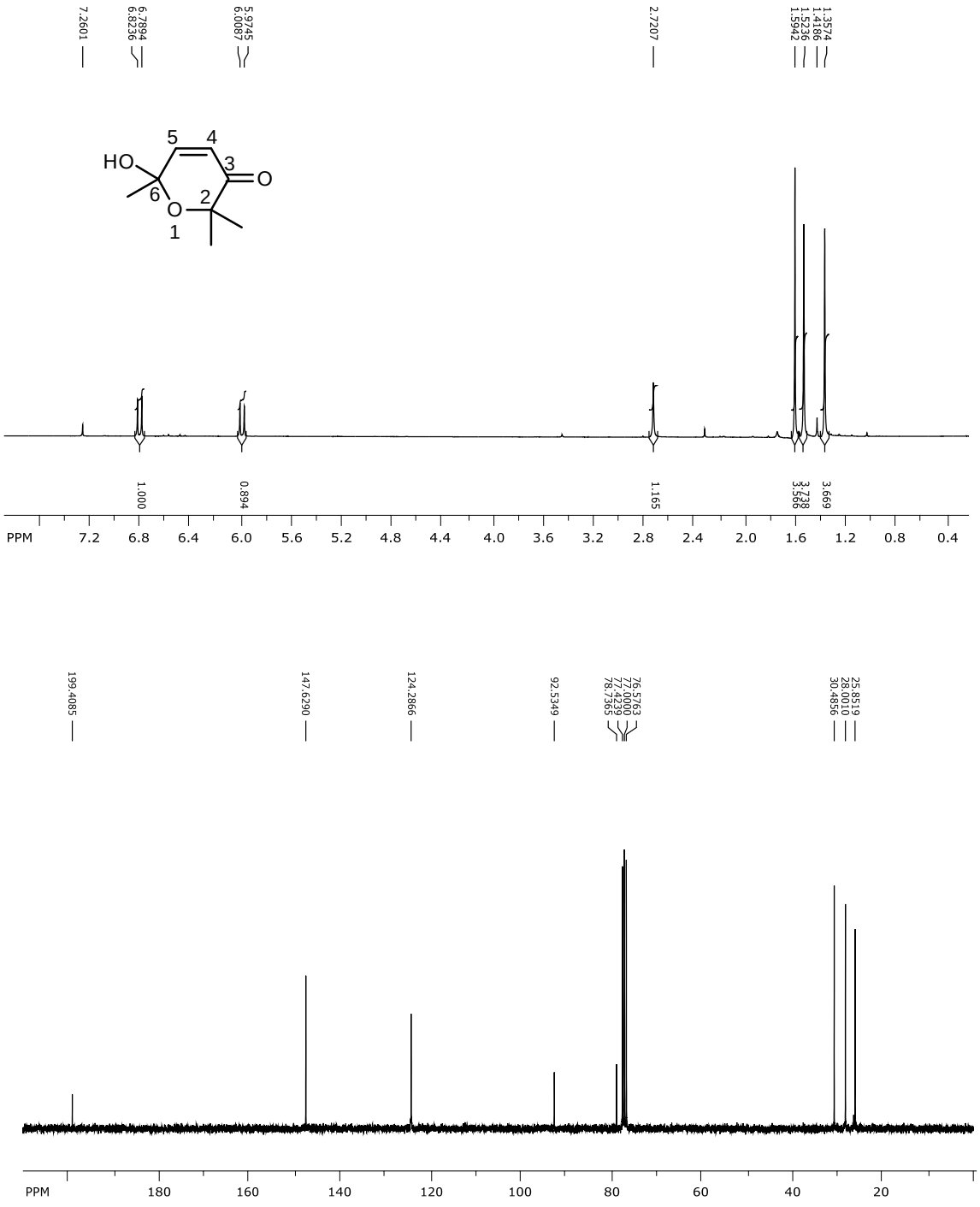
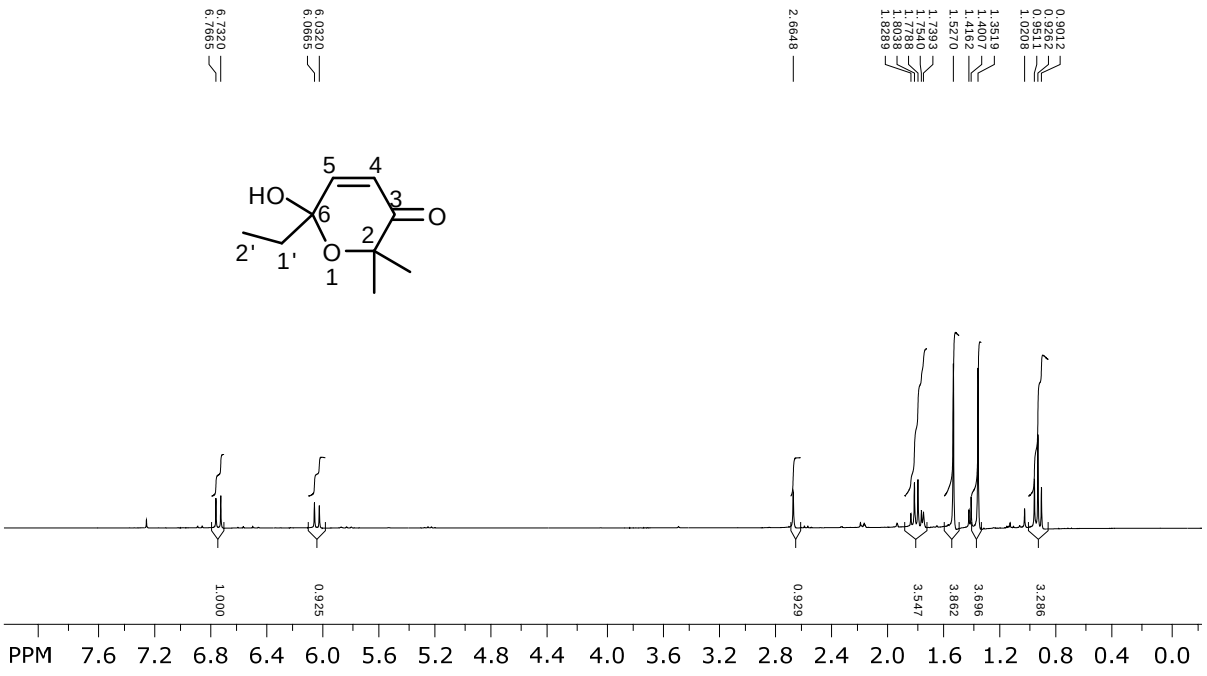


Fig. 13 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2a** in $CDCl_3$.

6-Ethyl-6-hydroxy-2,2-dimethyl-2*H*-pyran-3(6*H*)-one (2b)

According to the general procedure II, 2-(5-ethylfuran-2-yl)propan-2-ol (**1b**) (154 mg, 1 mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 48 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2b** (103 mg, 0.61 mmol, 61%) as a yellowish oil.

R_f 0.22 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 211 (log ε/dm^3 mol^{-1} cm^{-1}, 3.87); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3410 (OH), 2985, 2937, 1683, 1541, 1455, 1375, 1373 and 1171, 1113 and 1084; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.93 (3H, t, $^3J_{2'\text{-H, }1'\text{-H}}$ 7.6 Hz, 2'-H), 1.35 (3H, s, 2-Me), 1.53 (3H, s, 2-Me), 1.80 (2H, q, $^3J_{1'\text{-H, }2'\text{-H}}$ 7.6 Hz, 1'-H), 2.67 (1H, s, OH), 6.05 (1H, d, $^3J_{4\text{-H, }5\text{-H}}$ 10.5 Hz, 4-H) and 6.75 (1H, d, $^3J_{5\text{-H, }4\text{-H}}$ 10.5 Hz, 5-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 8.1 (C-2'), 25.6 (2-Me), 28.2 (2-Me), 36.0 (C-1'), 78.6 (C-2), 94.4 (C-6), 125.4 (C-4), 146.9 (C-5) and 199.6 (C-3) ppm; MS (ESI, pos) *m/z* 141 [(M-C_2H_5)$^+$, 21%)], 123 [26], 112 [100] 97 [28], 83 [26] and 55 [23]; HRMS (ESI, pos) found: 193.0831 [$C_9H_{14}O_3$+Na]$^+$, calcd for $C_9H_{14}O_3$: 170.0943.



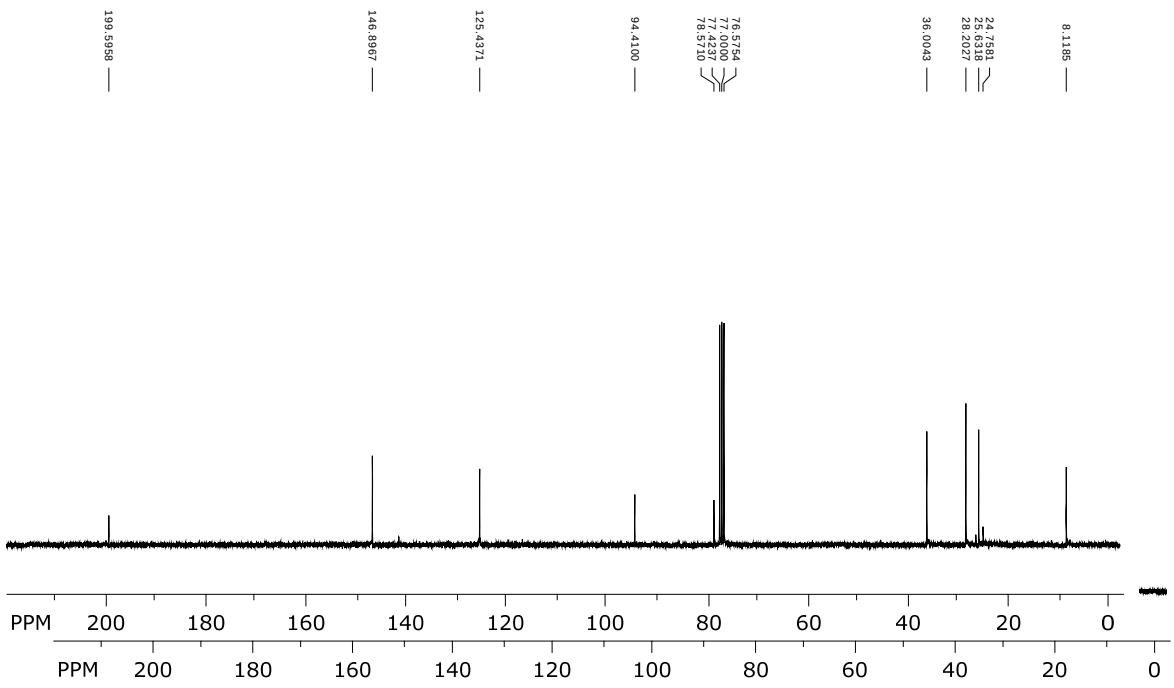


Fig. 14 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2b** in $CDCl_3$.

6-Hydroxy-2,2-dimethyl-6-propyl-2*H*-pyran-3(6*H*)-one (2c)

According to the general procedure II, 2-(5-propylfuran-2-yl)propan-2-ol (**1c**) (168 mg, 1 mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 48 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2c** (114 mg, 0.62 mmol, 62%) as a yellowish oil.

R_f 0.23 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 211 (log ε/dm^3 mol^{-1} cm^{-1}, 3.88); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3446 (OH), 2967, 2934, 2875, 1678, 1629, 1378, 1216, 1168 and 1103; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.93 (3H, t, $^{3}J_{3'\text{-H, }2'\text{-H}}$ 7.6 Hz, 3'-H), 1.35 (3H, s, 2-Me), 1.39 (2H, tq, $^{3}J_{2'\text{-H, }1'\text{-H}}$ 7.6 Hz, $^{3}J_{2'\text{-H, }3'\text{-H}}$ 7.6 Hz, 2'-H), 1.53 (3H, s, 2-Me), 1.80 (2H, t, $^{3}J_{1'\text{-H, }2'\text{-H}}$ 7.8 Hz, 1'-H), 6.03(1H, d, $^{3}J_{4\text{-H, }5\text{-H}}$ 10.4 Hz, 4-H) and 6.76(1H, d, $^{3}J_{5\text{-H, }4\text{-H}}$ 10.4 Hz, 5-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 14.0 (C-2'), 17.3 (C-3'), 25.7 (2-Me), 28.3 (2-Me), 45.3 (C-1'), 78.6 (C-2), 94.1 (C-6), 125.2 (C-4), 147.1 (C-5) and 199.5 (C-3) ppm; MS (ESI, pos) *m/z* 141 [(M^+-C_3H_7, 46%)], 126 [100], 97 [96], 83 [30], 55 [23] and 43 [31]; HRMS (ESI, pos) found: 207.0981 $[C_{10}H_{16}O_3+Na]^+$, calcd for $C_{10}H_{16}O_3$: 184.1099.

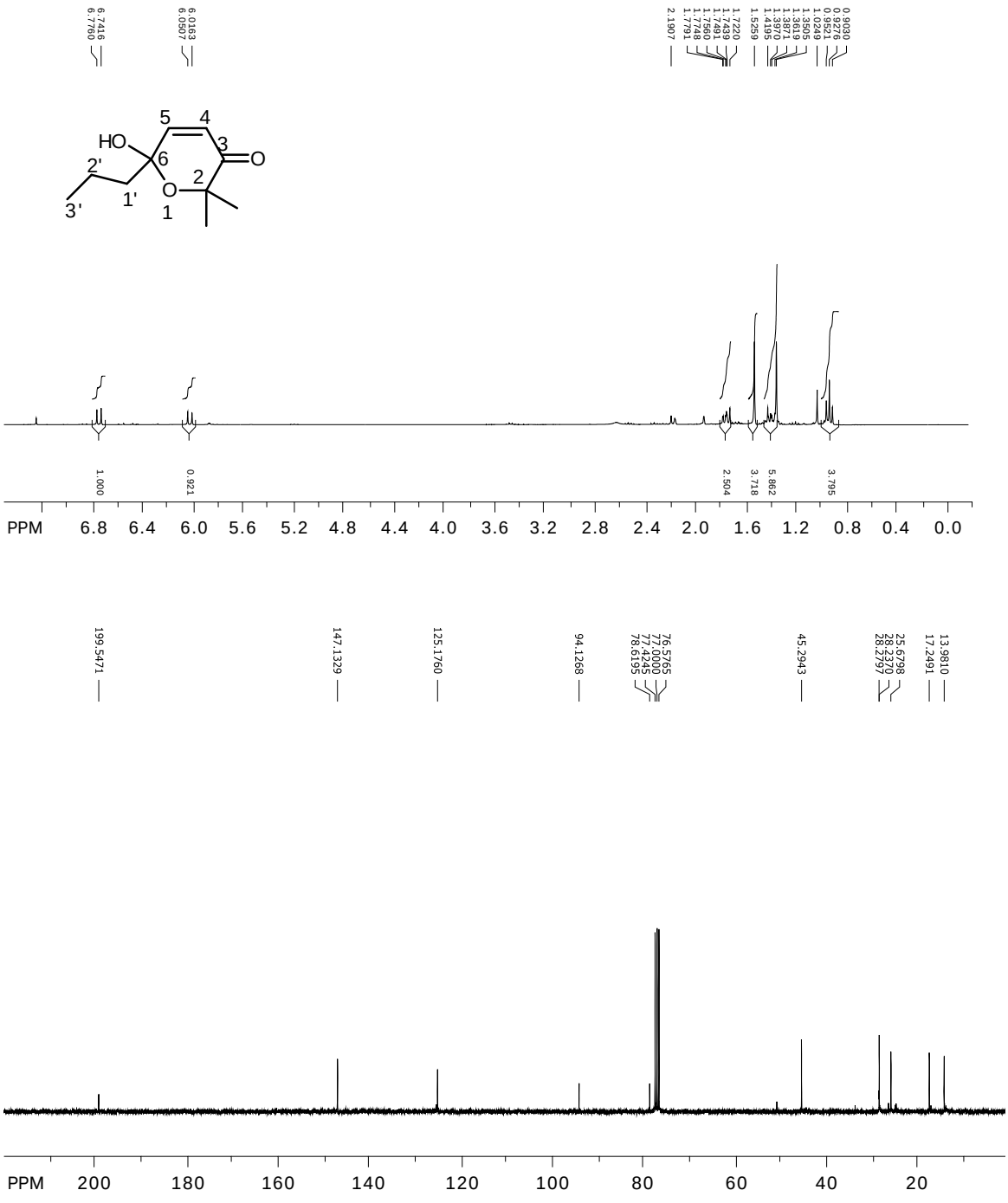
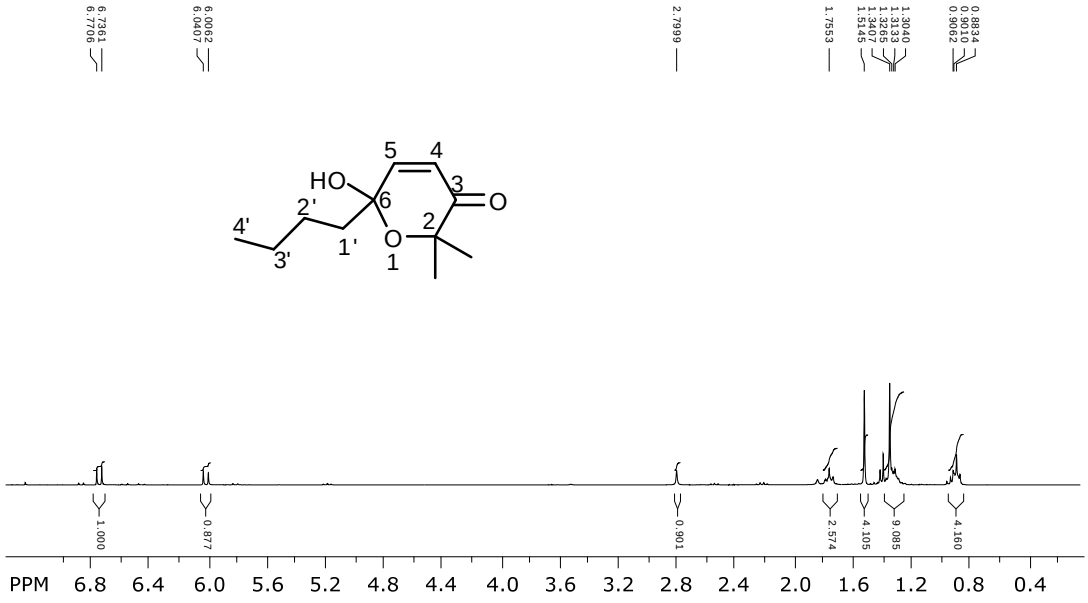


Fig. 15 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2c** in $CDCl_3$.

6-Butyl-6-hydroxy-2,2-dimethyl-2*H*-pyran-3(6*H*)-one (2d)

According to the general procedure II, 2-(5-butylfuran-2-yl)propan-2-ol (**1d**) (182 mg, 1 mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 72 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2d** (65mg, 0.33 mmol, 33%) as a yellowish oil.

R_f 0.24 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 212 (log ε/dm^3 mol^{-1} cm^{-1}, 3.89); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3447 (OH), 2960, 2933, 2872, 1676, 1630, 1585, 1378, 1207 and 1103; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.90 (3H, t, $^3J_{4'\text{-H},\ 3'\text{-H}}$ 7.5 Hz, 4'-H), 1.31 (3H, s, 2-Me), 1.29-1.35 (4H, m, 2'-H and 3'-H), 1.51 (3H, s, 2-Me), 1.75 (2H, t, $^3J_{1'\text{-H},\ 2'\text{-H}}$ 7.6 Hz, 1'-H), 2.80 (1H, s, OH), 6.02 (1H, d, $^3J_{4\text{-H},\ 5\text{-H}}$ 10.3 Hz, 4-H) and 6.75 (1H, d, $^3J_{5\text{-H},\ 4\text{-H}}$ 10.2 Hz, 5-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 13.9 (C-4'), 22.6 (C-2'), 25.7 (C-3'), 26.0 (2-Me), 28.2 (2-Me), 42.8 (C-1'), 78.6 (C-2), 94.1 (C-6), 125.2 (C-4), 147.3 (C-5) and 199.7 (C-3) ppm; MS (ESI, pos) *m/z* 180 [(M^+-H_2O), 8%], 140 [100], 123 [32], 97 [79], 83 [28], 55 [32] and 43 [34]; HRMS (ESI, pos) found: 221.1140 $[C_{11}H_{18}O_3+Na]^+$, calcd for $C_{11}H_{18}O_3$: 198.1256.



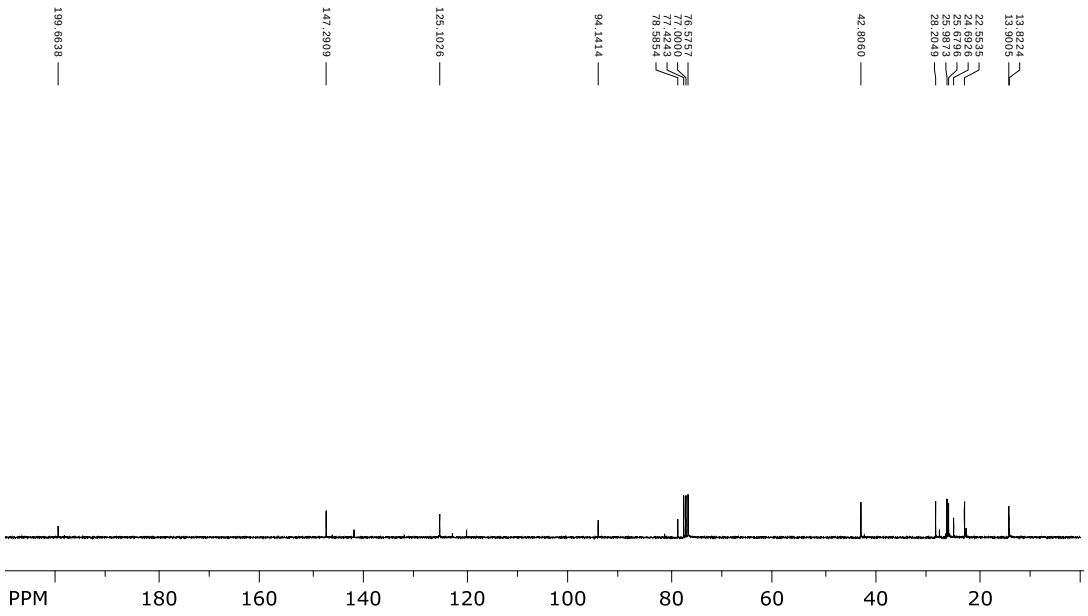


Fig. 16 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2d** in $CDCl_3$.

2,2-Diethyl-6-hydroxy-6-methyl-2*H*-pyran-3(6*H*)-one (2e)

According to the general procedure II, 3-(5-methylfuran-2-yl)pentan-3-ol (**1e**) (168 mg, 1 mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 8 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2e** (138 mg, 0.75 mmol, 75%) as a yellowish oil.

R_f 0.20 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 212 (log ε/dm^3 mol^{-1} cm^{-1}, 3.88); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3422 (OH), 2951, 2970, 2938, 2882, 1677, 1460, 1375, 1085 and 1047; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.79 (3H, t, $^{3}J_{2'\text{-H, }1'\text{-H}}$ 7.6 Hz, 2'-H), 0.89 (3H, t, $^{3}J_{2''\text{-H, }1''\text{-H}}$ 7.6 Hz, 2''-H),1.60 (3H, s, 6-Me), 1.65-1.85 (2H, m, 1'-H), 1.86-1.95 (2H, m, 1''-H), 2.99 (1H, s, OH), 5.97 (1H, d, $^{3}J_{5\text{-H, }4\text{-H}}$ 10.2 Hz, 5-H) and 6.77 (1H, d, $^{3}J_{4\text{-H, }5\text{-H}}$ 10.5 Hz, 4-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 7.5 (C-2'), 7.8 (C-2''), 28.6 (C-1''), 30.2 (C-1'), 31.6 (6-Me), 84.5 (C-2), 92.3 (C-6), 125.2 (C-4), 147.4 (C-5) and 199.7 (C-3) ppm; MS (ESI, pos) m/z 98 [100%], 87 [96], 83 [9], 70 [12], 55 [14] and 43 [7]; HRMS (ESI, pos) found: 207.0994 $[C_{10}H_{16}O_3+Na]^+$, calcd for $C_{10}H_{16}O_3$: 184.1099.

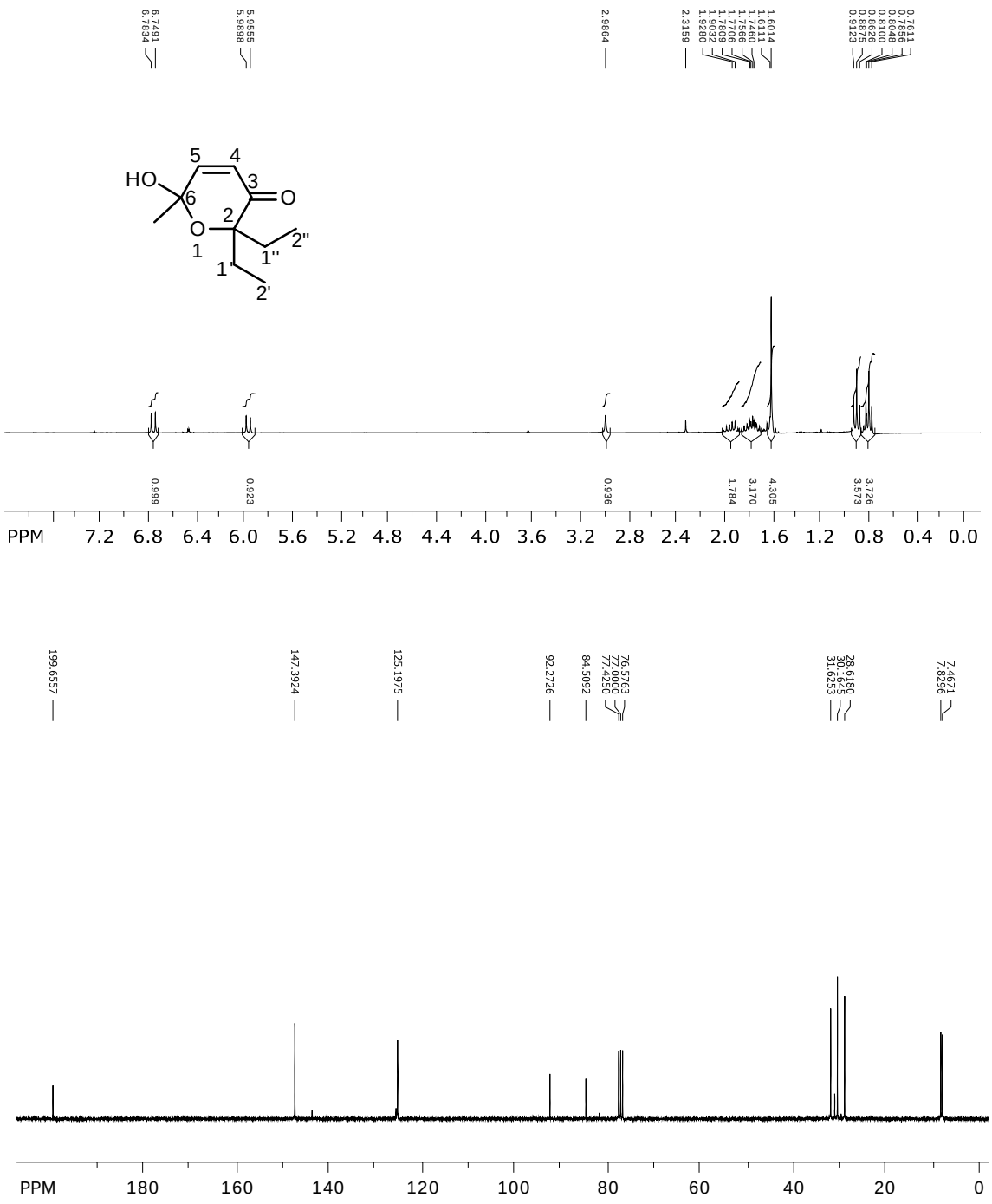
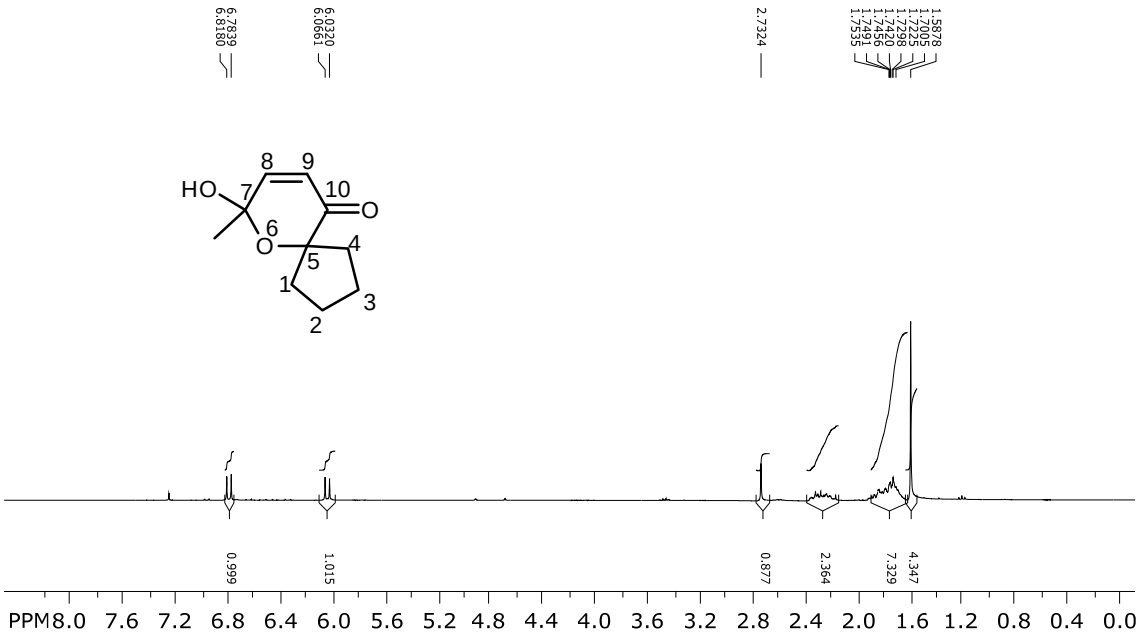


Fig. 17 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2e** in $CDCl_3$.

7-Hydroxy-7-methyl-6-oxaspiro[4.5]dec-8-en-10-one (2f)

According to the general procedure II, 1-(5-methylfuran-2-yl)cyclopentan-1-ol (**1f**) (166 mg, 1 mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 15 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2f** (98 mg, 0.54 mmol, 54%) as a yellowish oil.

R_f 0.25 (cyclohexane ─ EtOAc = 8:3); UV λ_{max} (MeCN)/nm 212 (log ε/dm^3 mol^{-1} cm^{-1}, 3.87); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3326 (OH), 2951, 2873, 1738, 1668, 1370, 1128, 1095 and 928; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.59 (3H, s, 7-Me), 1.62-1.72 (6H, m, 1-H, 2-H, 3-H), 2.20-2.35 (2H, m, 4-H), 2.73 (1H, s, 7-OH), 6.05 (1H, d, $^3J_{9\text{-H, }8\text{-H}}$ 10.2 Hz, 9-H) and 6.80 (1H, d, $^3J_{8\text{-H, }9\text{-H}}$ 10.3 Hz, 8-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 24.4 (C-2 or C-3), 25.1 (C-3 or C-2), 30.2 (7-Me), 37.8 (C-1 or C-4), 40.5 (C-4 or C-1), 88.7 (C-5), 92.8 (C-7), 125.6 (C-9), 147.5 (C-8) and 199.3 (C-10) ppm; MS (EI, 70 eV) m/z 98 (100%), 70 (12), 55 (18) and 43 (10); HRMS (EI, M^+) found: 182.0946, calcd for $C_{10}H_{14}O_3$: 182.0943.



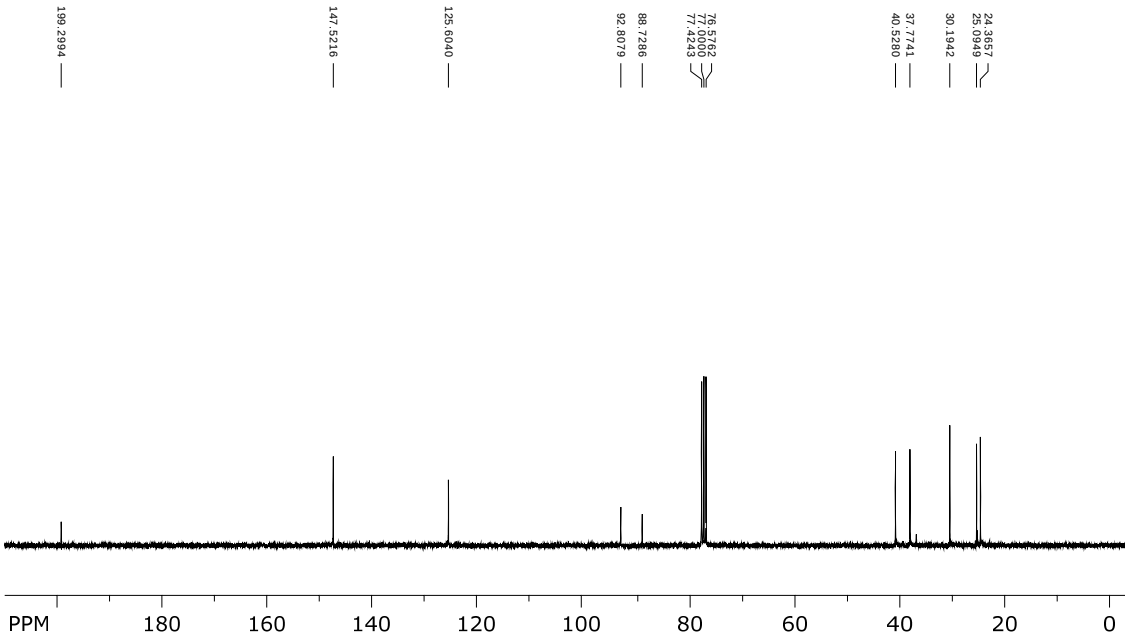


Fig. 18 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2f** in $CDCl_3$.

2-Hydroxy-2-methyl-1-oxaspiro[5.5]undec-3-en-5-one (2g)

According to the general procedure II, 1-(5-methylfuran-2-yl)cyclohexan-1-ol (**1g**) (180 mg, 1 mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 10 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2g** (176 mg, 0.9 mmol, 90%) as a yellowish oil.

R_f 0.28 (cyclohexane ─ EtOAc = 8:3); UV λ_{max} (MeCN)/nm 212 (log ε/dm^3 mol^{-1} cm^{-1}, 3.89); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3447 (OH), 2967, 1459, 1219, 1020, 946 and 781; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.36-1.90 (10H, m, 7-H, 8-H, 9-H, 10-H, 11-H), 1.60 (3H, s, 2-Me), 3.06 (1H, s, OH), 5.95 (1H, d, $^{3}J_{4\text{-H, }3\text{-H}}$ 10.3 Hz, 4-H) and 6.76 (1H, d, $^{3}J_{3\text{-H, }4\text{-H}}$ 10.3 Hz, 3-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 20.5 (C-8), 25.1 (C-10), 30.4 (C-9), 31.6 (2-Me), 33.2 (C-11), 34.8 (C-7), 79.8 (C-6), 92.4 (C-2), 124.4 (C-4), 147.1 (C-3) and 199.9 (C-5) ppm; MS (ESI, pos) m/z 98 [100%], 81 [12], 70 [18], 55 [22] and 43 [11]; HRMS (ESI, pos) found: 219.0977 $[C_{11}H_{16}O_3+Na]^+$, calcd for $C_{11}H_{16}O_3$: 196.1099.

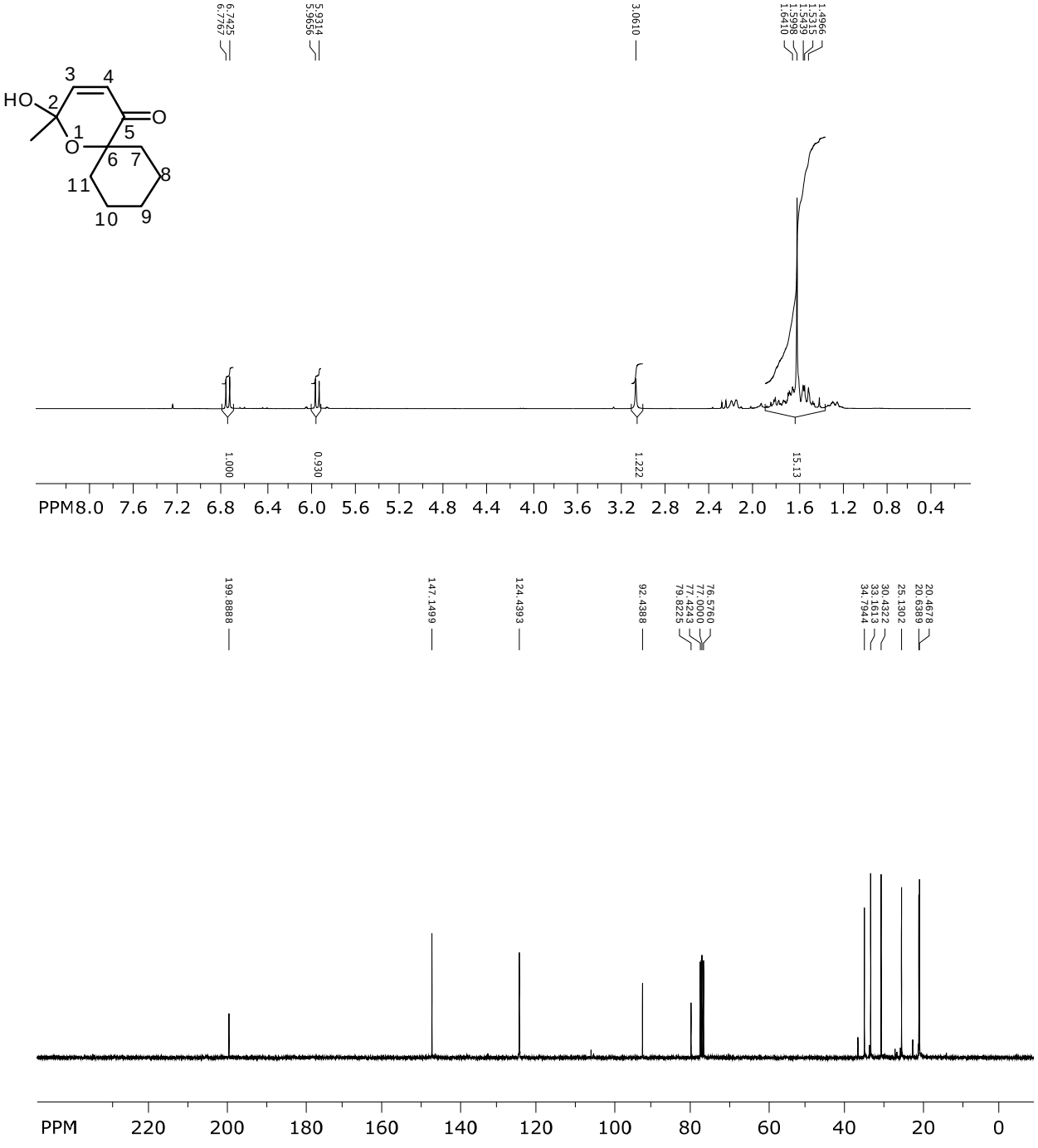
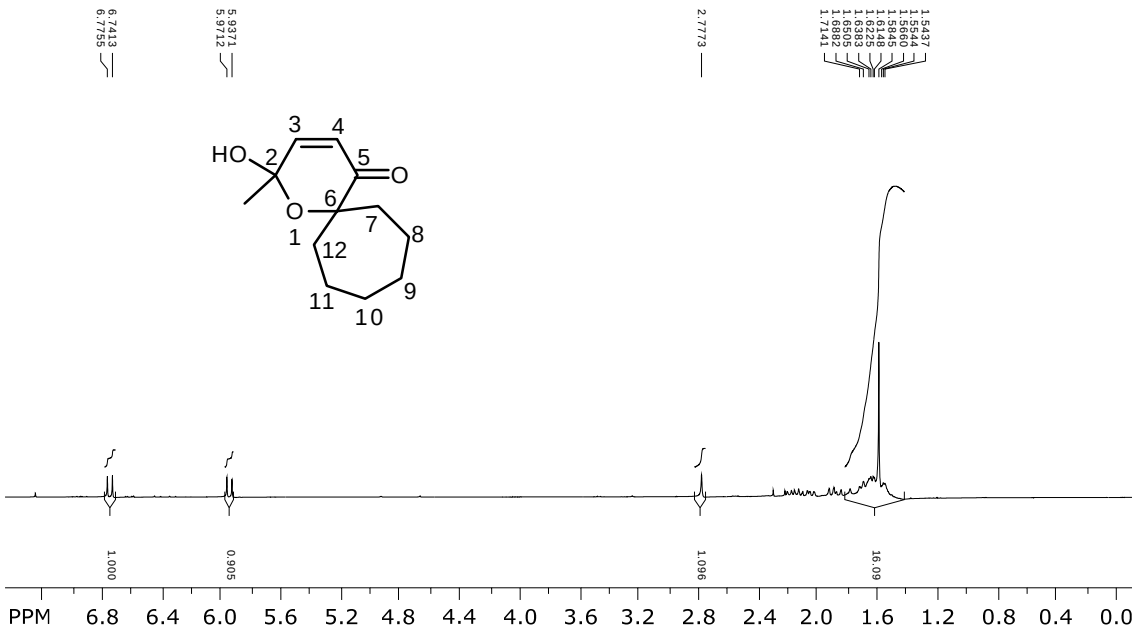


Fig. 19 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2g** in $CDCl_3$.

2-Hydroxy-2-methyl-1-oxaspiro[5.6]dodec-3-en-5-one (2h)

According to the general procedure II, 1-(5-methylfuran-2-yl)cycloheptan-1-ol (**1h**) (194 mg, 1 mmol), was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 36 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **2h** (128 mg, 0.61 mmol, 61%).

R_f 0.28 (cyclohexane ─ EtOAc = 8:3); UV λ_{max} (MeCN)/nm 212 (log ε/dm^3 mol^{-1} cm^{-1}, 3.89); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 3418 (OH), 2924, 2858, 1674, 1459, 1372, 1161, 1092, 1036, 1020 and 927; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.41-2.02 (12H, m, 7-H, 8-H, 9-H, 10-H, 11-H, 12-H), 1.61 (3H, s, 2-Me), 2.78 (1H, s, OH), 5.95 (1H, d, $^3J_{4\text{-H, }3\text{-H}}$ 10.6 Hz, 4-H) and 6.76 (1H, d, $^3J_{3\text{-H, }4\text{-H}}$ 10.3 Hz, 3-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 22.1 (C-8 and C-11), 29.7 (C-9 and C-10), 30.5 (2-Me), 37.5 (C-12), 38.7(C-7), 83.3 (C-6), 92.3 (C-2), 124.4 (C-4), 147.1 (C-3) and 200.1 (C-5) ppm; MS (EI, 70 eV) m/z 210 (M^+,100%), 195 (12), 113 (26), 98 (100), 70 (13), 55 (21)and 43 (12); HRMS (EI, M^+) found: 210.1257, calcd for $C_{12}H_{18}O_3$: 210.1256.



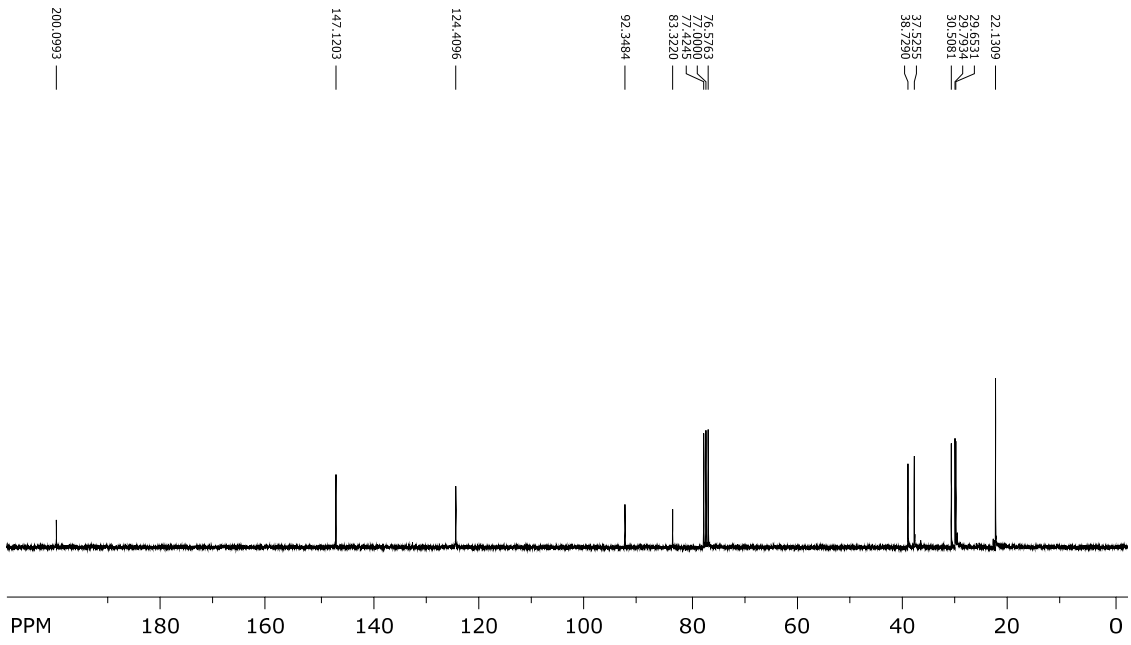


Fig. 20 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **2h** in $CDCl_3$.

4 Oxidation of 1 to 8

4.1 General procedure III for the oxidation of 1 to 8

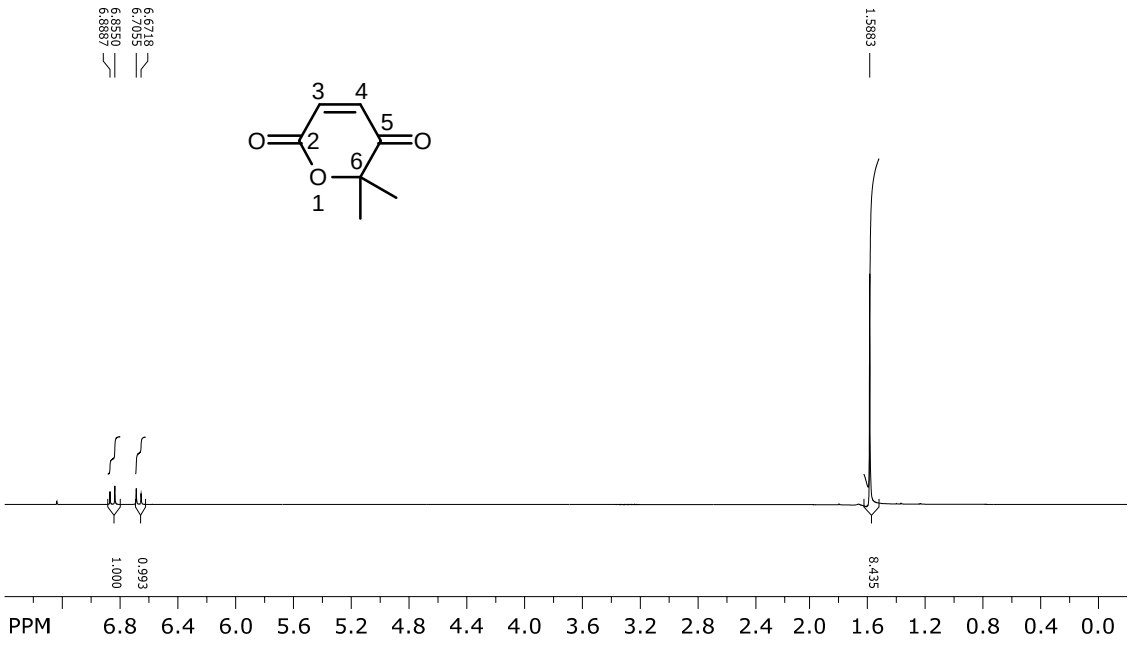
A 100 mL round bottomed flask was charged with furan-2-yl carbinol **1** (1 mmol), *n*-octane (1 mL), 0.01 M acetate buffer pH 4.5 (10 mL), 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*). The mixture was stirred at rt for the time given. The aqueous phase was saturated with NaCl (1 g) and extracted with CH_2Cl_2 (4×25 mL). The combined organic phases were dried over Na_2SO_4. After removal of the solvents *in vacuo*, the crude product was purified by flash chromatography over silicagel (cyclohexane ─ EtOAc = 2:1) to deliver the (2*H*)-pyran-2,5(6*H*)-diones **8**.

4.2 Synthesis and analytical data for 8i-l

6,6-Dimethyl-2*H*-pyran-2,5(6*H*)-dione (8i)

According to the general procedure III, 2-(furan-2-yl)propan-2-ol (**1i**) (126 mg, 1mmol) was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 24 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) **8i** afforded (98 mg, 0.7 mmol, 70 %) as a yellow oil.

R_f 0.32 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 218, 222 and 274 (log ε/dm^3 mol^{-1} cm^{-1}, 4.27, 4.24 and 3.96); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 2981, 1724, 1695, 1285, 1101, 1002 and 850; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 1.59 (6H, s, 6-Me), 6.69 (1H, d, $^3J_{4\text{-H, }3\text{-H}}$ 10.0 Hz, 4-H), 6.87 (1H, d, $^3J_{3\text{-H, }4\text{-H}}$ 10.1 Hz, 3-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 26.5 (6-Me), 87.1 (C-6), 135.3 (C-3), 136.5 (C-4), 160.4 (C-2) and 196.2 (C-5) ppm; MS (EI, 70 eV) *m/z* 140 (M^+, 3%), 82 (100), 54 (33) and 43 (8); HRMS (EI, M^+) found: 140.0487, calcd for $C_7H_8O_3$: 140.0473.



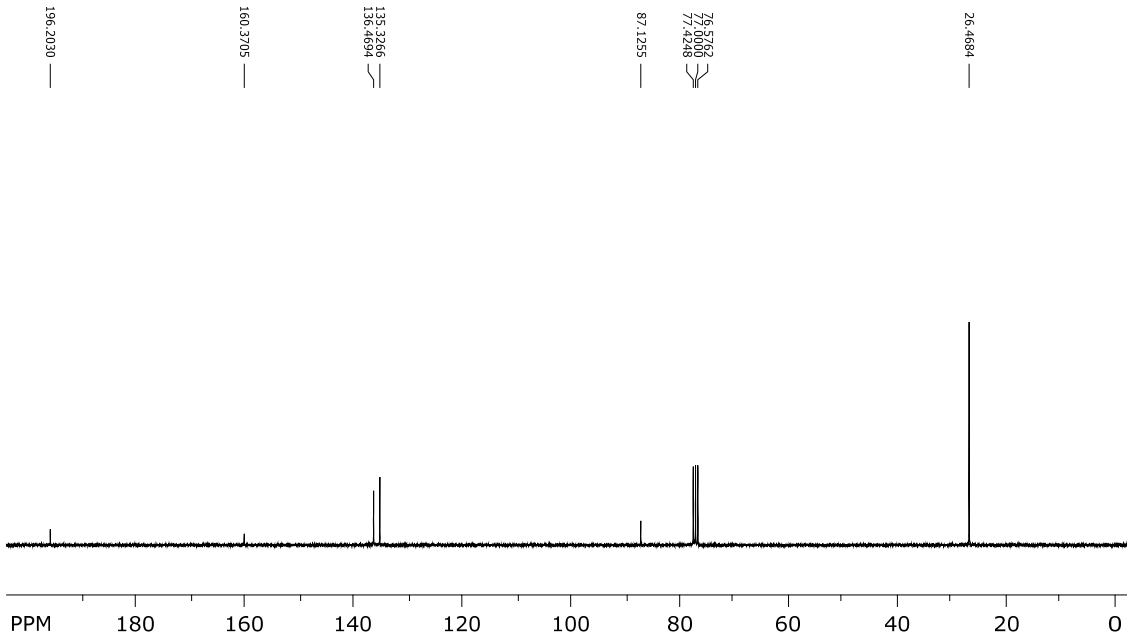


Fig. 21 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **8i** in $CDCl_3$.

6-Ethyl-6-methyl-2*H*-pyran-2,5(6*H*)-dione (8j)

According to the general procedure III, 2-(furan-2-yl)butan-2-ol (**1j**) (140 mg, 1mmol) was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 48 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **8j** (92 mg, 0.6 mmol, 60%) as a yellow oil.

R_f 0.34 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 217, 222 and 274 (log ε/dm^3 mol^{-1} cm^{-1}, 4.28, 4.23 and 3.99); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 2972, 1725, 1687, 1294, 1104, 1034 and 853; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, $^{3}J_{2'\text{-H, }1'\text{-H}}$ 7.4 Hz, 2'-H), 1.56 (3H, s, 6-Me), 1.75-1.85 (1H, m, 1'-H), 1.95-2.05 (1H, m, 1'-H), 6.71 (1H, d, $^{3}J_{4\text{-H, }3\text{-H}}$ 10.0 Hz, 4-H) and 6.89 (1H, d, $^{3}J_{3\text{-H, }4\text{-H}}$ 10.2 Hz, 3-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 7.9 (C-2'), 25.3 (6-Me), 33.3 (C-1'), 90.4 (C-6), 135.5 (C-3), 137.4 (C-4), 160.8 (C-2) and 196.4 (C-5) ppm; MS (EI, 70 eV) *m/z* 154 (M^+, 5%), 82 (100), 54 (20), 43 (8); HRMS (EI, M^+) found: 154.0630, calcd for $C_8H_{10}O_3$: 154.0630.

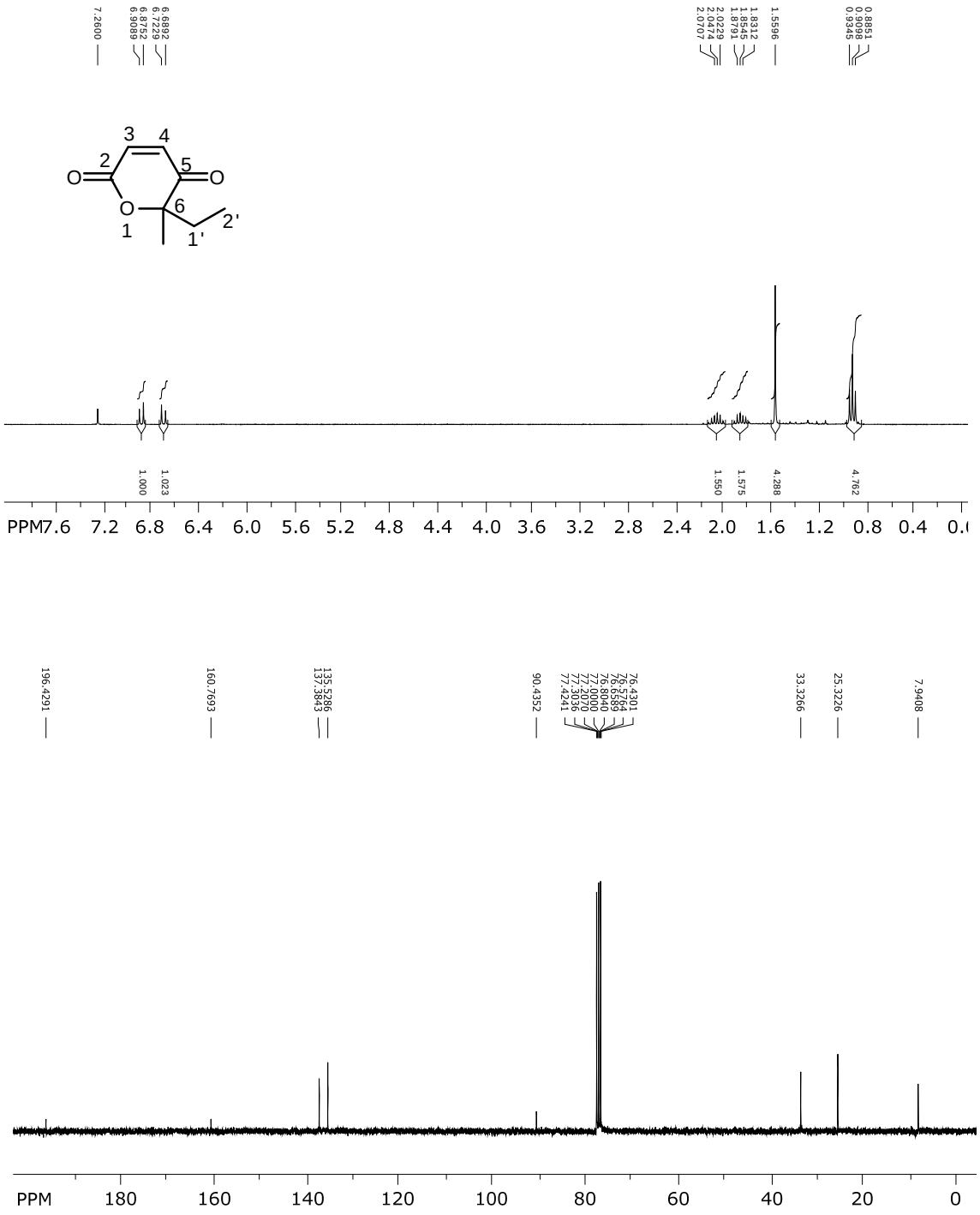
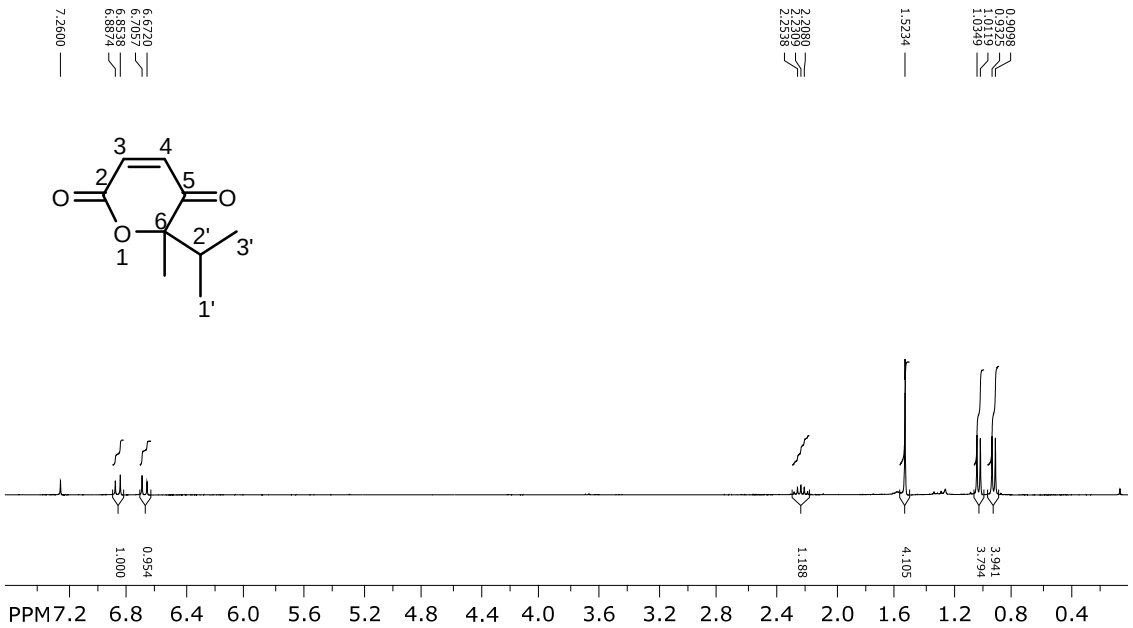


Fig. 22 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **8j** in $CDCl_3$.

6-Isopropyl-6-methyl-2*H*-pyran-2,5(6*H*)-dione (8k)

According to the general procedure III, 2-(furan-2-yl)-3-methylbutan-2-ol (**1k**) (154 mg, 1mmol) was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 48 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **8k** (89 mg, 0.53 mmol, 53%) as a yellow oil.

R_f 0.41 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 218, 223 and 274 (log ε/dm^3 mol^{-1} cm^{-1}, 4.43, 4.42 and 4.27); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 2981, 1724, 1691, 1286, 1100, 1002 and 850; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.92 (3H, d, $^3J_{1'\text{-H, }2'\text{-H}}$ 6.8 Hz, 1'-H), 1.02 (3H, d, $^3J_{3'\text{-H, }2'\text{-H}}$ 6.9 Hz, 3'-H), 1.52 (3H, s, 6-Me), 2.18-2.23 (1H, m, 2'-H), 6.69 (1H, d, $^3J_{4\text{-H, }3\text{-H}}$ 10.2 Hz, 4-H) and 6.86 (1H, d, $^3J_{3\text{-H, }4\text{-H}}$ 10.2 Hz, 3-H) ppm; NMR δ_C (75 MHz; $CDCl_3$) 15.8 (C-1'), 17.2 (C-3'), 23.4 (6-Me), 37.0 (C-2'), 92.3 (C-6), 135.2 (C-3), 137.6 (C-4), 160.9 (C-2) and 196.9 (C-5) ppm; MS (EI, 70 eV) *m/z* 168 (M^+, 5%), 126 (28), 98 (14), 82 (100), 54 (14) and 43 (13); HRMS (EI, M^+) found: 168.0790, calcd for $C_9H_{12}O_3$: 168.0786.



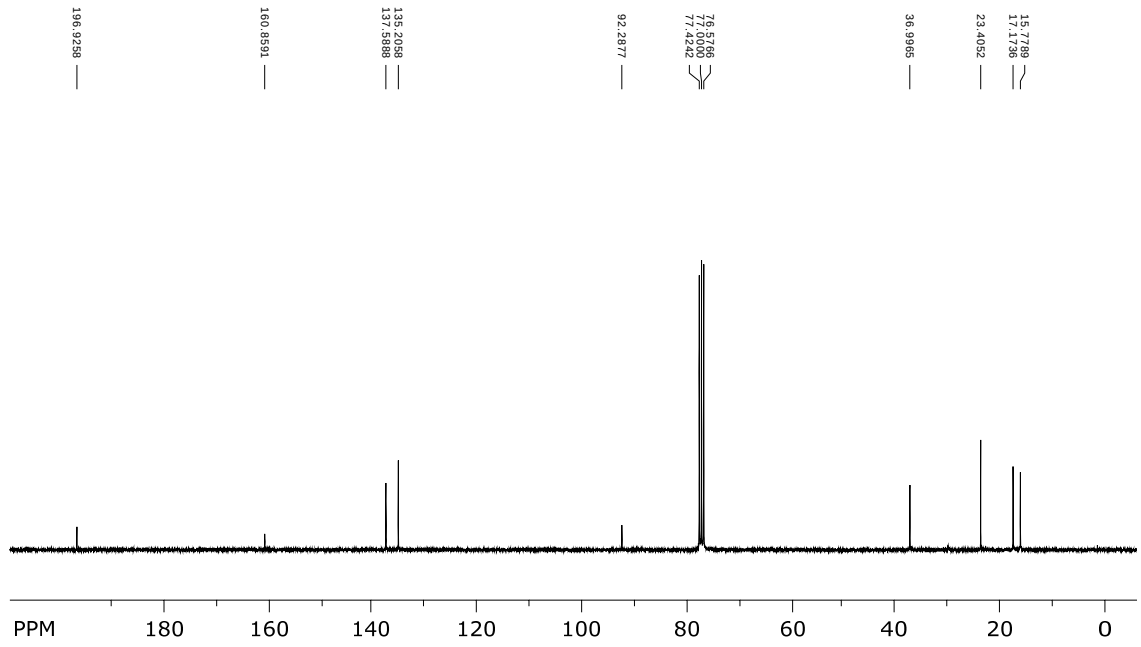


Fig. 23 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **8k** in $CDCl_3$.

6-Isobutyl-6-methyl-2*H*-pyran-2,5(6*H*)-dione (8l)

According to the general procedure III, 2-(furan-2-yl)-4-methylpentan-2-ol **1l** (168 mg, 1 mmol) was reacted with 4-acetamido-TEMPO (42 mg, 0.2 mmol) and 420 U laccase (*Trametes versicolor*) in acetate buffer for 72 h. Purification over silica gel (cyclohexane ─ EtOAc = 2:1) afforded **8l** (64 mg, 0.35 mmol, 35%) as a yellow oil.

R_f 0.49 (cyclohexane ─ EtOAc = 3:1); UV λ_{max} (MeCN)/nm 218, 222 and 274 (log ε/dm^3 mol^{-1} cm^{-1}, 4.23, 4.27 and 4.07); IR (ATR) $\tilde{\nu}_{max}$/cm^{-1} 2958, 2872, 1728, 1692, 1292, 1104 and 853; ^{1}H NMR δ_H (300 MHz; $CDCl_3$) 0.83 (3H, d, $^{3}J_{1'\text{-H, }2'\text{-H}}$ 6.8 Hz, 1'-H), 0.94 (3H, d, $^{3}J_{1'\text{-H, }2'\text{-H}}$ 6.9 Hz, 1'-H), 1.56 (3H, s, 6-Me), 1.85-1.93 (2H, m, 3'-H), 1.98-2.10 (1H, m, 2'-H), 6.72 (1H, d, $^{3}J_{4\text{-H, }3\text{-H}}$ 10.2 Hz, 4-H) and 6.89 (1H, d, $^{3}J_{3\text{-H, }4\text{-H}}$ 10.2 Hz, 3-H) ppm; ^{13}C NMR δ_C (75 MHz; $CDCl_3$) 23.7 (6-Me), 23.8 (C-1'), 24.4 (C-1'), 27.3 (C-3'), 48.1 (C-2'), 90.1 (C-6), 135.3 (C-3), 137.3 (C-4), 160.6 (C-2) and 196.4 (C-5) ppm; MS (EI, 70 eV) *m/z* 182 (M^+, 5%), 126 (5), 97 (3), 82 (100), 54 (13) and 43 (7); HRMS (EI, M^+) found: 182.0944, calcd for $C_9H_{12}O_3$: 182.0943.

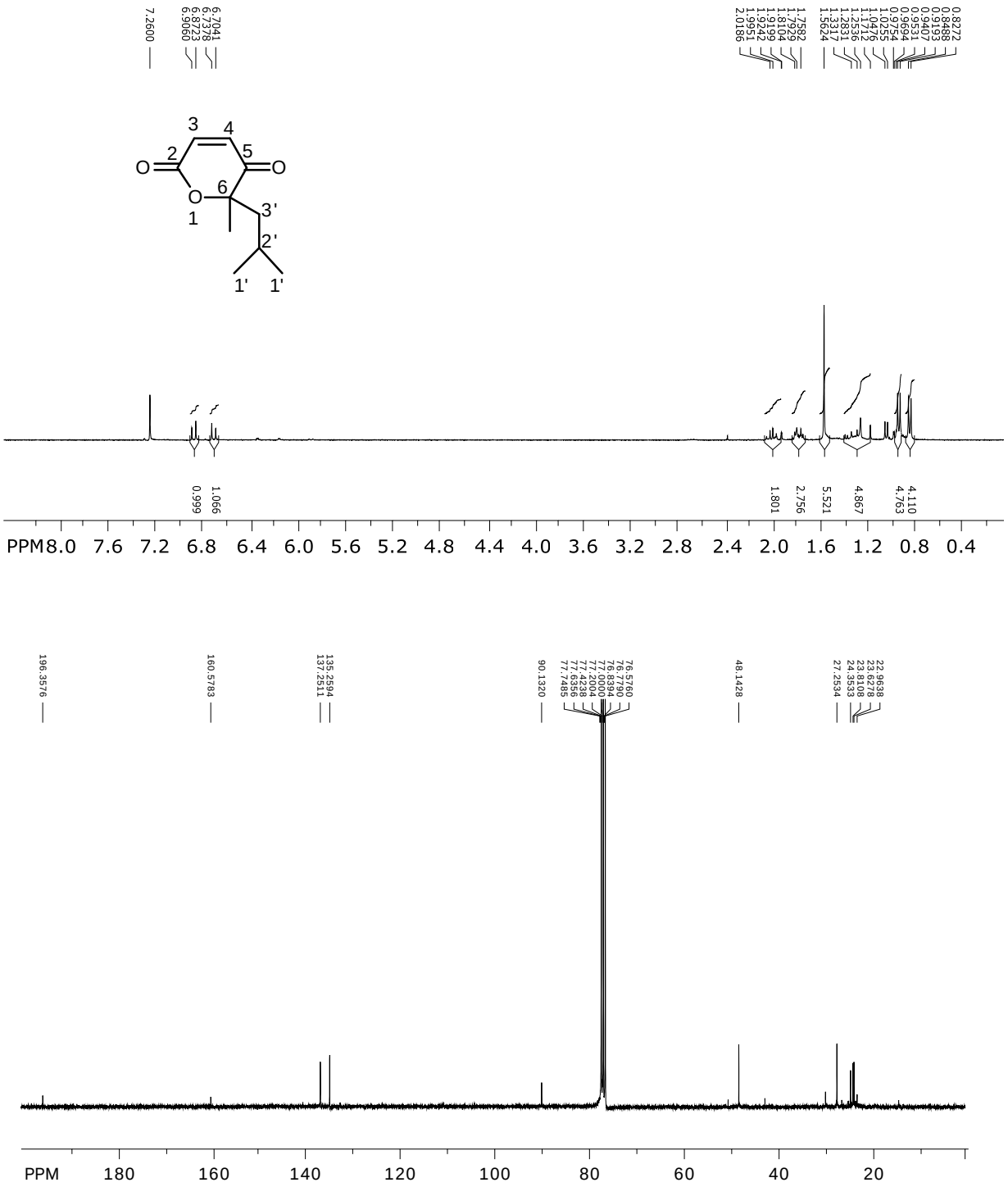


Fig. 24 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **8l** in $CDCl_3$.

5 Determination of laccase activity [3]

A 0.1 M solution of ABTS (0.3 mL) in 0.01 M acetate buffer (pH = 4.5) was diluted with 0.01 M acetate buffer (2.6 mL, pH = 4.5) and treated with a solution of laccase in the same buffer (0.1 mL). The change in absorption was followed *via* UV/Vis spectroscopy (λ= 414 nm). One unit was defined as the amount of laccase (*Trametes versicolor*, Fluka) that converts 1 mmol of ABTS per minute at pH = 4.5 at r.t.

6 References

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