Electronic Supplementary Material (ESI) for Green Chemistry

Laccase-catalyzed synthesis of catechol thioethers by reaction of catechols with thiols using air as an oxidant

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Electronic Supplementary Information

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1. General remarks

All chemicals were purchased from commercial suppliers. Laccase from *Agaricus bisporus* (6 U / mg) was purchased from ASA Spezialenzyme. Solvents used in 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 precoated silica gel 60 F_{245} aluminium plates (Merck) with visualization under UV light. Flash chromatography was carried out on silica gel MN 60, 0.04-0.053 mm (Macherey & Nagel). 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-spectrometer). ^{1}H and ^{13}C NMR spectra were recorded at 300 (75) MHz on a Varian ^{Unity}Inova using DMSO-d_6. The chemical shifts were referenced to the solvent signals at $\delta_{H/C}$ 2.49 / 39.50 ppm (DMSO-d_6) relative to TMS as internal standards. gHSQC, gHMBC and gCOSY spectra were recorded on a Varian ^{Unity}Inova spectrometer (300 MHz). Coupling constants *J* [Hz] were directly taken from the spectra and are not averaged. Low resolution electron impact mass spectra (EI-LRMS) and exact electron impact mass spectra (HRMS) were recorded at 70 eV on a Finnigan MAT 95 instrument. Low resolution electron spray ionisation mass spectra (ESI-LRMS) and exact electron spray ionisation mass spectra (HRMS) were recorded on a Bruker Daltonics (micro TOFQ) instrument. The intensities are reported as percentages relative to the base peak (I = 100%).

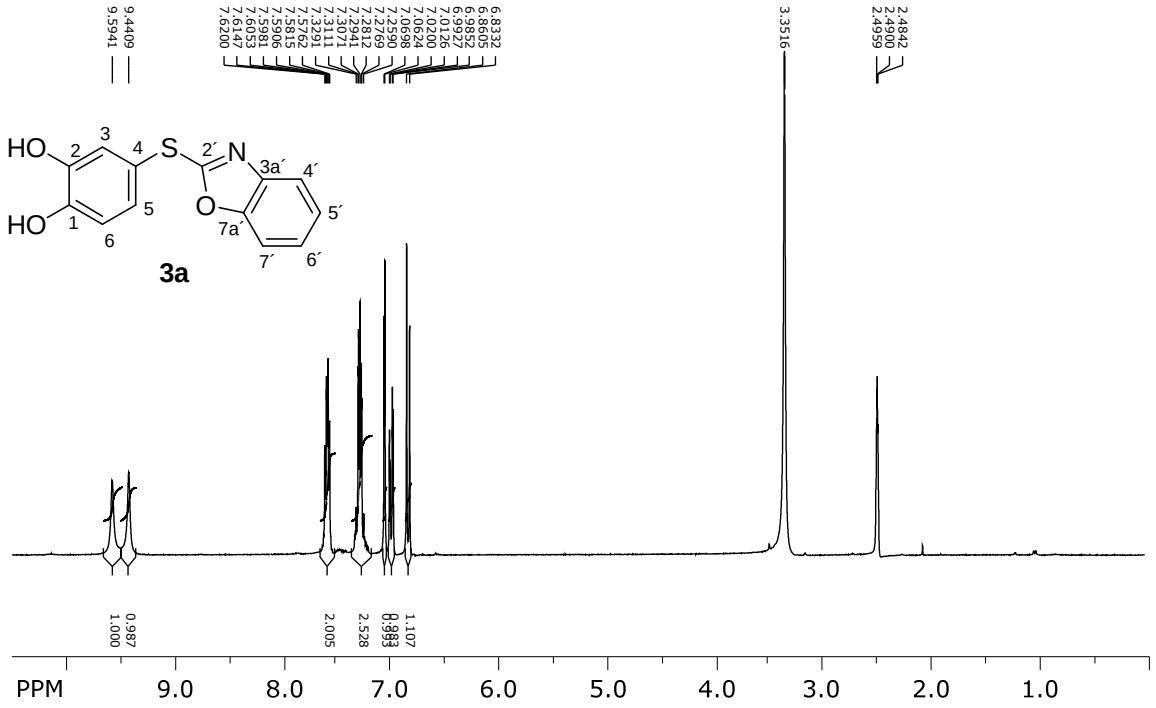
2. General procedure for the laccase-catalyzed domino reaction between catechols and thiols

A 100 mL round bottomed flask with a magnetic stir bar was charged with a solution or suspension of the catechol **1** (0.63 mmol) and the thiol **2** (0.50 mmol) in methanol (3 mL). Phosphate buffer (0.2 M, pH 6, 27 mL) and laccase from *A. bisporus* (10 mg, 6 U/ mg) were added and the mixture was stirred under air at rt for the time given. The reaction mixture was acidified with 2M HCl to pH ~ 4 and saturated with solid NaCl. The precipitated product was filtered with suction using a Buchner funnel. The filter cake was washed with aq NaCl (15%, 25 mL) and water. The crude products obtained after drying exhibit a purity of 90-95% (NMR). Analytically pure products were obtained by column filtration (CH_2Cl_2/EtOAc 5:1 to 1:1) of the crude products.

3. Synthesis and analytical data of catechol thioethers

3.1. Synthesis and analytical data of 4-(benzo[*d*]oxazol-2´-ylthio)benzene-1,2-diol (3a)

According to the general procedure, catechol (**1a**) (69 mg, 0.63 mmol), 2-mercaptobenzoxazole (**2a**) (76 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 16 h. Workup gave 4-(benzo[*d*]oxazol-2´-ylthio)benzene-1,2-diol (**3a**) as a pale brown solid (121 mg, 93%), mp 155–157 °C (lit.[1] 126–126 °C); R_f = 0.54 (CH_2Cl_2/EtOAc = 5:1); λ_{max} (MeCN)/nm 286 (log ε, 4.20), 280 (4.16), 246 (3.17) and 202 (4.62); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3560 – 3160 (OH), 1517, 1493, 1452, 1217 and 1137; δ_H (300 MHz; DMSO-d_6) 6.85 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.1 Hz, 6-H), 7.00 (1H, dd, $^3J_{5\text{-H},6\text{-H}}$ 8.4 Hz, $^4J_{3\text{-H},5\text{-H}}$ 2.1 Hz, 5-H), 7.07 (1H, d, $^4J_{3\text{-H},5\text{-H}}$ 2.4 Hz, 3-H), 7.28 – 7.31 (2H, m, 5´-H and 6´-H), 7.57 – 7.62 (2H, m, 4´-H and 7´-H), 9.44 (1H, s, 1-OH or 2-OH), 9.59 (1H, s, 1-OH or 2-OH); δ_C (75 MHz; DMSO-d_6) 110.26 (C-7´), 113.68 (C-4), 116.58 (C-6), 118.51 (C-4´), 122.05 (C-3), 124.42 (C-5´ or C-6´), 124.63 (C-5´ or C-6´), 126.83 (C-5), 141.40 (C-3a´), 146.20 (C-2), 147.99 (C-1), 151.23 (C-7a´), 163.74 (C-2´); *m/z* (EI, 70 eV) 259 (M$^+$, 100%), 226 (M$^+$ – SH, 9), 151 ($C_7H_5SNO^+$, 20), 119 (10) and 91 (12); HRMS (EI, M$^+$) found: 259.0281; calcd for $C_{13}H_9SNO_3$: 259.0303.



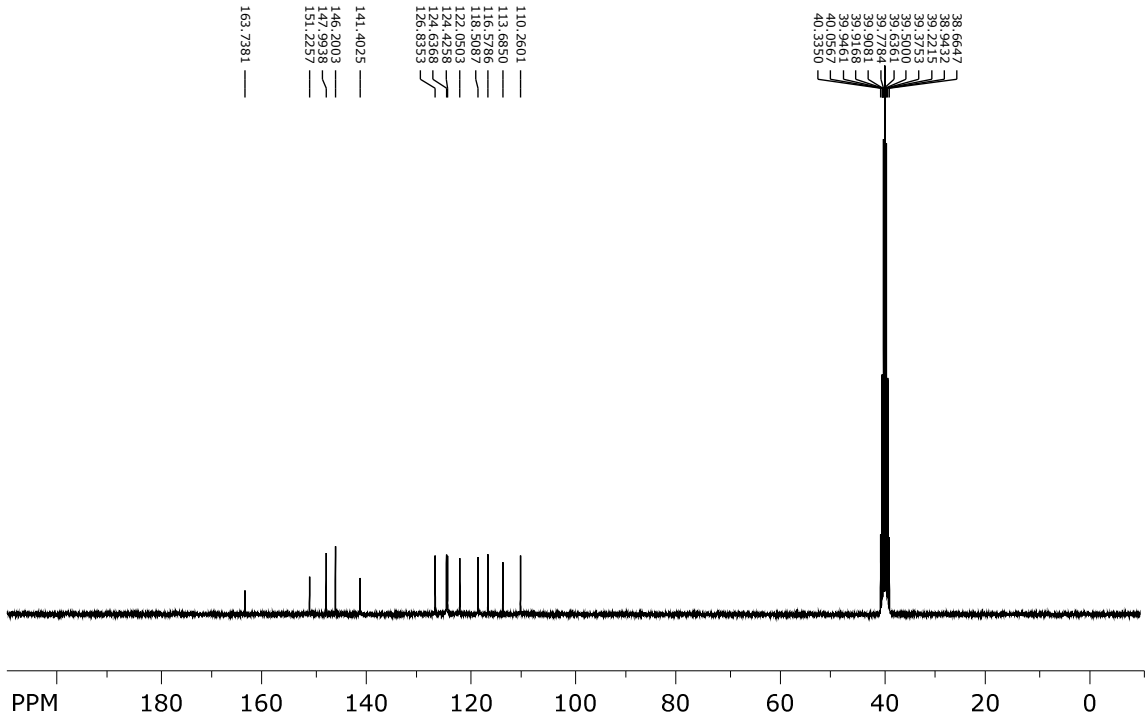


Fig. 1 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3a** in DMSO-d_6

3.2. Synthesis and analytical data of 4-(benzo[*d*]thiazol-2´-ylthio)benzene-1,2-diol (**3b**)

According to the general procedure, catechol (**1a**) (69 mg, 0.63 mmol), 2-mercaptobenzothiazole (**2b**) (84 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave 4-(benzo[*d*]thiazol-2´-ylthio)benzene-1,2-diol (**3b**) as a pale yellow solid (120 mg, 87%); mp 198–200 °C; R_f = 0.53 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 284 (log ε, 4.60) and 206 (4.20); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3426 (OH), 3054 (C-H), 1593, 1415, 1270 and 1030; δ_H (300 MHz; DMSO-d_6) 6.90 (1H, d, $^{3}J_{5\text{-H},6\text{-H}}$ 8.1 Hz, 6-H), 7.07 (1H, dd, $^{3}J_{5\text{-H},6\text{-H}}$ 8.4 Hz, $^{4}J_{3\text{-H},5\text{-H}}$ 2.1 Hz, 5-H), 7.13 (1H, d, $^{4}J_{3\text{-H},5\text{-H}}$ 2.1 Hz, 3-H), 7.29 (1H, ddd, $^{3}J_{5'\text{-H},6'\text{-H}}$ 7.2 or 7.9 Hz, $^{3}J_{6'\text{-H},7'\text{-H}}$ 7.2 or 7.9 Hz, $^{4}J_{4'\text{-H},6'\text{-H}}$ 1.1 Hz, 6´-H), 7.42 (1H, ddd, $^{3}J_{4'\text{-H},5'\text{-H}}$ 7.3 or 8.2 Hz, $^{3}J_{5'\text{-H},6'\text{-H}}$ 7.3 or 8.2 Hz, $^{4}J_{5'\text{-H},7'\text{-H}}$ 1.3 Hz, 5´-H), 7.79 (1H, ddd, $^{3}J_{4'\text{-H},5'\text{-H}}$ 8.1 Hz, $^{4}J_{4'\text{-H},6'\text{-H}}$ 1.2 or 0.6 Hz, $^{5}J_{4'\text{-H},7'\text{-H}}$ 1.2 or 0.6 Hz, 4´-H), 7.89 (1H, ddd, $^{3}J_{6'\text{-H},7'\text{-H}}$ 8.0 Hz, $^{4}J_{5'\text{-H},7'\text{-H}}$ 1.3 or 0.7 Hz, $^{5}J_{4'\text{-H},7'\text{-H}}$ 1.3 or 0.7 Hz, 7´-H) and 9.63 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) 116.66 (C-4), 117.01 (C-6), 121.12 (C-4´), 121.64 (C-7´), 122.45 (C-3), 124.13 (C-6´), 126.27 (C-5´), 127.66 (C-5), 134.75 (C-7a´), 146.61 (C-2), 148.66 (C-1), 153.71 (C-3a´) and 171.99 (C-2´); *m/z* (EI, 70

eV) 275 (M^+, 100%), 242 (M^+ – SH, 5), 167 ($C_7H_5S_2N^+$, 8) and 115 (15); HRMS (EI, M^+) found: 275.0051; calcd for $C_{13}H_9S_2NO_2$: 275.0075.

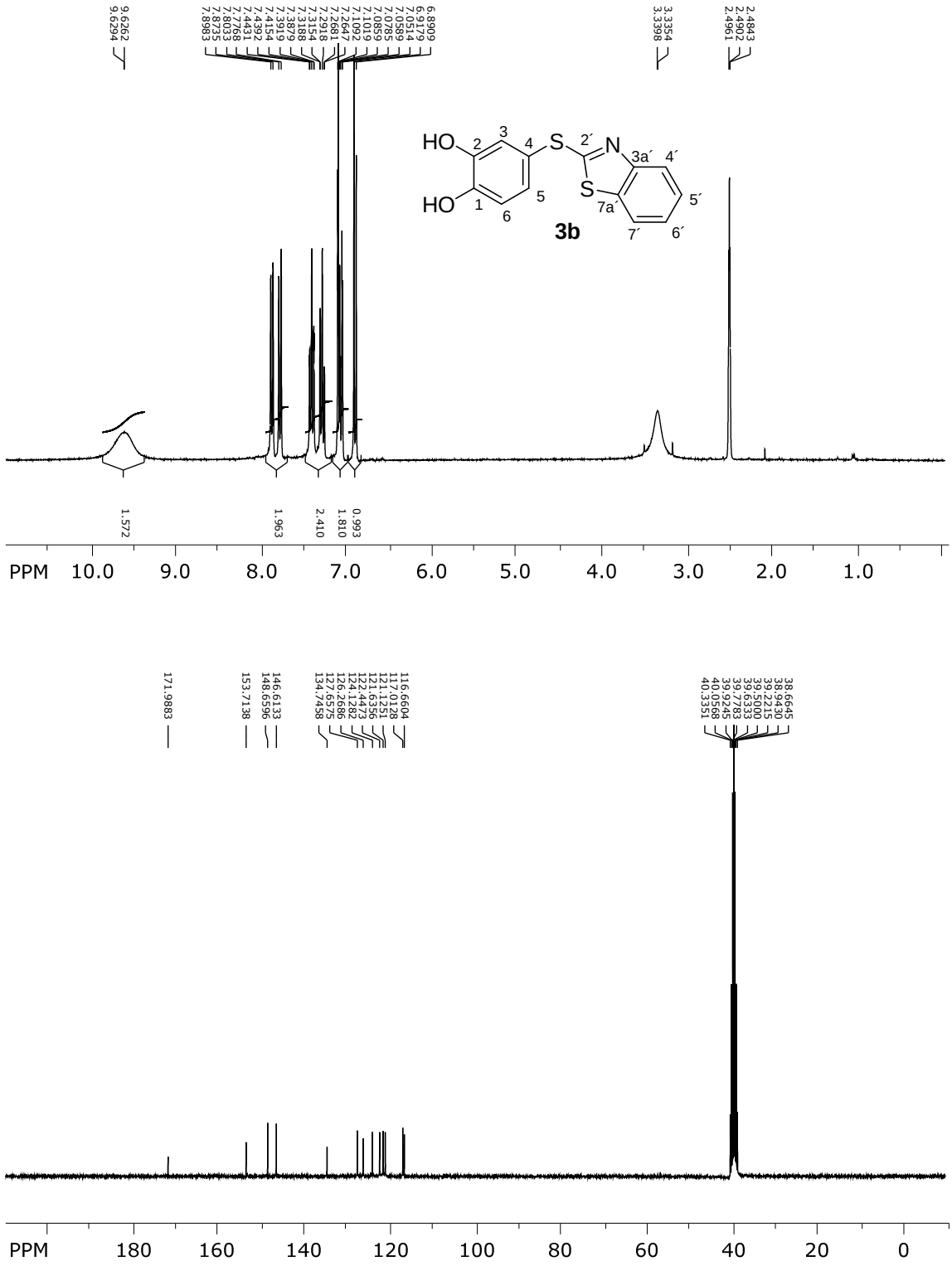


Fig. 2 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3b** in DMSO-d_6

3.3. Synthesis and analytical data of 4-(benzo[*d*]oxazol-2´-ylthio)-3-methylbenzene-1,2-diol (3c) and 5-(benzo[*d*]oxazol-2´-ylthio)-3-methylbenzene-1,2-diol (5c)

According to the general procedure, 3-methylcatechol (**1b**) (78 mg, 0.63 mmol), 2-mercaptobenzoxazole (**2a**) (76 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 24 h. Workup gave a mixture of 4-(benzo[*d*]oxazol-2´-ylthio)-3-methylbenzene-1,2-diol (**3c**) and 5-(benzo[*d*]oxazol-2´-ylthio)-3-methylbenzene-1,2-diol **(5c)** as a brown solid (123 mg, 90%), mp 181–183 °C; R_f = 0.64 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 286 (log ε, 4.25), 279 (4.23), 247 (4.24) and 206 (4.66); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3471 (OH), 1592, 1500, 1452, 1235 and 1138; δ_H (300 MHz; DMSO-d_6) of **3c** 2.21 (3H, s, CH_3), 6.74 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.2 Hz, 6-H), 7.05 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.3 Hz, 5-H), 7.24 – 7.31 (2H, m, 5´-H and 6´-H), 7.55 – 7.58 (2H, m, 4´-H and 7´-H), 8.68 (1H, br, 1-OH or 2-OH) and 9.85 (1H, br, 1-OH or 2-OH); δ_H (300 MHz; DMSO-d_6) of **5c** 2.13 (3H, s, CH_3), 6.94 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 3.0 Hz, 4-H), 6.96 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 3.0 Hz, 6-H), 7.24 – 7.31 (2H, m, 5´-H and 6´-H), 7.55 – 7.58 (2H, m, 4´-H and 7´-H), 8.80 (1H, br, 1-OH or 2-OH) and 9.71 (1H, br, 1-OH or 2-OH); δ_C (75 MHz; DMSO-d_6) of **3c** 14.06 (CH_3), 110.20 (C-7´), 113.29 (C-6), 114.35 (C-4), 118.40 (C-4´), 124.25 (C-5´ or C-6´), 124.57 (C-5´ or C-6´), 127.70 (C-5), 129.39 (C-3), 141.47 (C-3a´), 144.43 (C-2), 147.80 (C-1), 151.23 (C-7a´) and 163.71 (C-2´); δ_C (75 MHz; DMSO-d_6) of **5c** 15.79 (CH_3), 110.26 (C-7´), 112.80 (C-5), 118.40 (C-4´), 119.45 (C-6), 124.41 (C-5´ or C-6´), 124.62 (C-5´ or C-6´), 125.92 (C-3), 128.20 (C-4), 141.47 (C-3a´), 145.54 (C-1), 145.99 (C-2), 151.23 (C-7a´) and 163.82 (C-2´); *m/z* (EI, 70 eV) 273 (M^+, 100%), 240 (M^+ – SH, 7), 166 (18) and 73 (13); HRMS (EI, M^+) found: 273.0445; calcd for $C_{14}H_{11}SNO_3$: 273.0460.

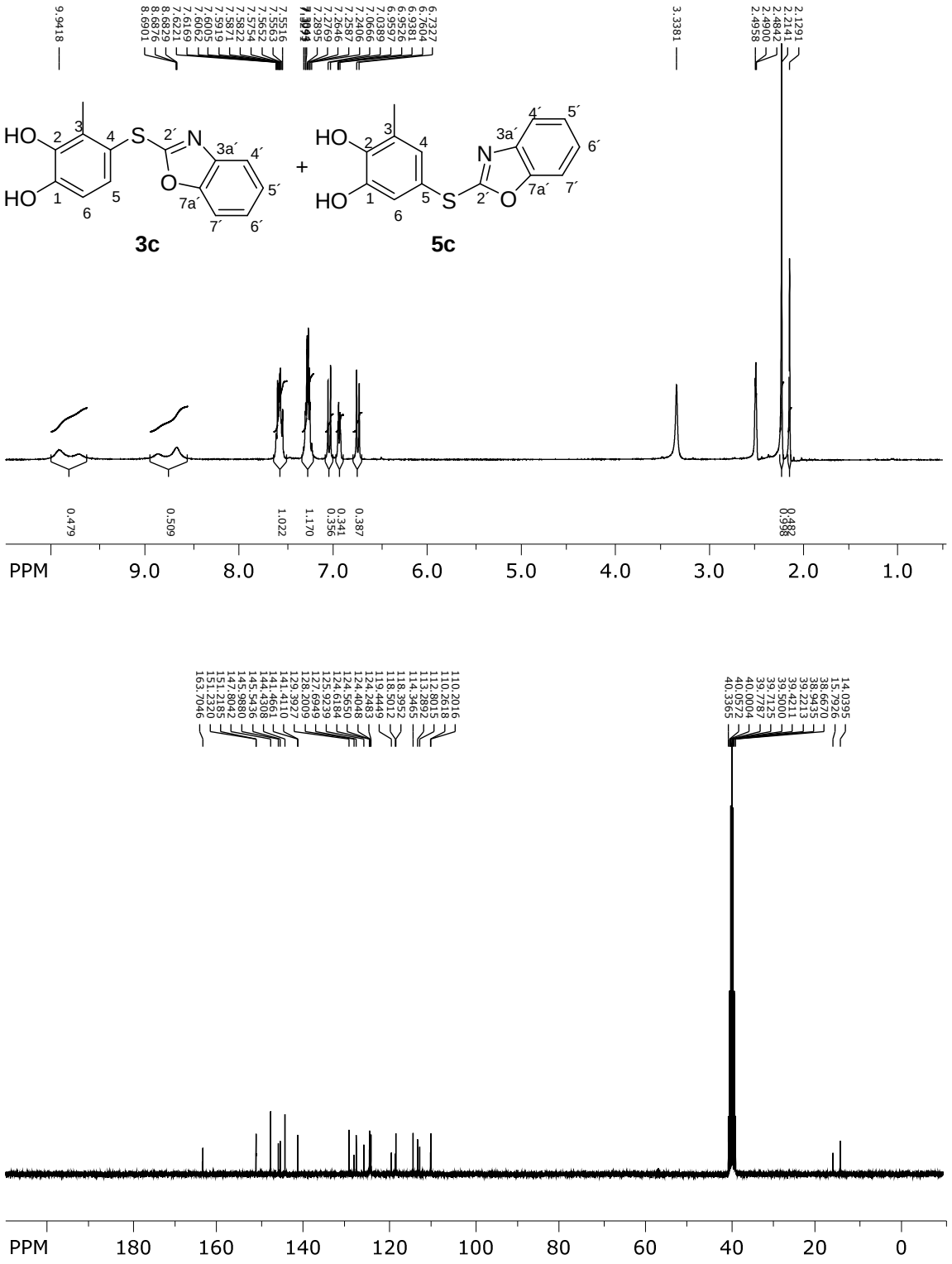


Fig. 3 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3c** and **5c** in DMSO-d_6

3.4. Synthesis and analytical data of 4-(benzo[*d*]thiazol-2´-ylthio)-3-methylbenzene-1,2-diol (3d) and 5-(benzo[*d*]thiazol-2´-ylthio)-3-methylbenzene-1,2-diol (5d)

According to the general procedure, 3-methylcatechol (**1b**) (78 mg, 0.63 mmol), 2-mercaptobenzothiazole (**2b**) (84 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave a mixture of 4-(benzo[*d*]thiazol-2´-ylthio)-3-methylbenzene-1,2-diol (**3d**) and 5-(benzo[*d*]thiazol-2´-ylthio)-3-methylbenzene-1,2-diol (**5d**) as a pale brown solid (138 mg, 95%); mp 186–188 °C; R_f = 0.74 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 289 (log ε, 4.20), 282 (4.21) and 211 (4.59); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3260 (OH), 1453, 1416, 1415, 1270 and 1010; δ_H (300 MHz; DMSO-d_6) of **3d** 2.26 (3H, s, CH_3), 6.81 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.4 Hz, 6-H), 7.11 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.3 Hz, 5-H), 7.27 – 7.31 (1H, m, 6´-H), 7.41 (1H, t like ov, ^3J ~ 8.1 Hz, 5´-H), 7.78 (1H, d like ov, ^3J ~ 8.1 Hz, 4´-H), 7.87 (1H, t like ov, ^3J ~ 8.1 Hz, 7´-H) and 8.78 (2H, br, 1-OH and 2-OH); δ_H (300 MHz; DMSO-d_6) of **5d** 2.15 (3H, s, CH_3), 7.02 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 1.8 Hz, 6-H), 7.04 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 1.8 Hz, 4-H), 7.27 – 7.31 (1H, m, 6´-H), 7.41 (1H, t like ov, ^3J ~ 8.1 Hz, 5´-H), 7.78 (1H, d like ov, ^3J ~ 8.1 Hz, 4´-H), 7.87 (1H, t like ov, ^3J ~ 8.1 Hz, 7´-H) and 9.02 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) of **3d** 13.94 (CH_3), 113.80 (C-6), 117.45 (C-4), 121.07 (C-4´), 121.11 (C-7´), 123.98 (C-6´), 126.24 (C-5´), 128.34 (C-5), 129.48 (C-3), 134.79 (C-7a´), 144.74 (C-2), 148.30 (C-1), 153.88 (C-3a´) and 171.94 (C-2´); δ_C (75 MHz; DMSO-d_6) of **5d** 15.83 (CH_3), 115.83 (C-5), 119.79 (C-6), 121.07 (C-4´), 121.11 (C-7´), 124.10 (C-6´), 126.46 (C-3), 126.21 (C-5´), 128.92 (C-4), 134.76 (C-7a´), 145.90 (C-1), 146.63 (C-2), 153.73 (C-3a´) and 172.14 (C-2´); *m/z* (EI, 70 eV) 289 (M^+, 100%), 256 (M^+ – SH, 68), 210 (16) and 167 ($C_7H_5NS_2^+$, 18); HRMS (EI, M^+) found: 289.0246; calcd for $C_{14}H_{11}NO_2S_2$: 289.0231.

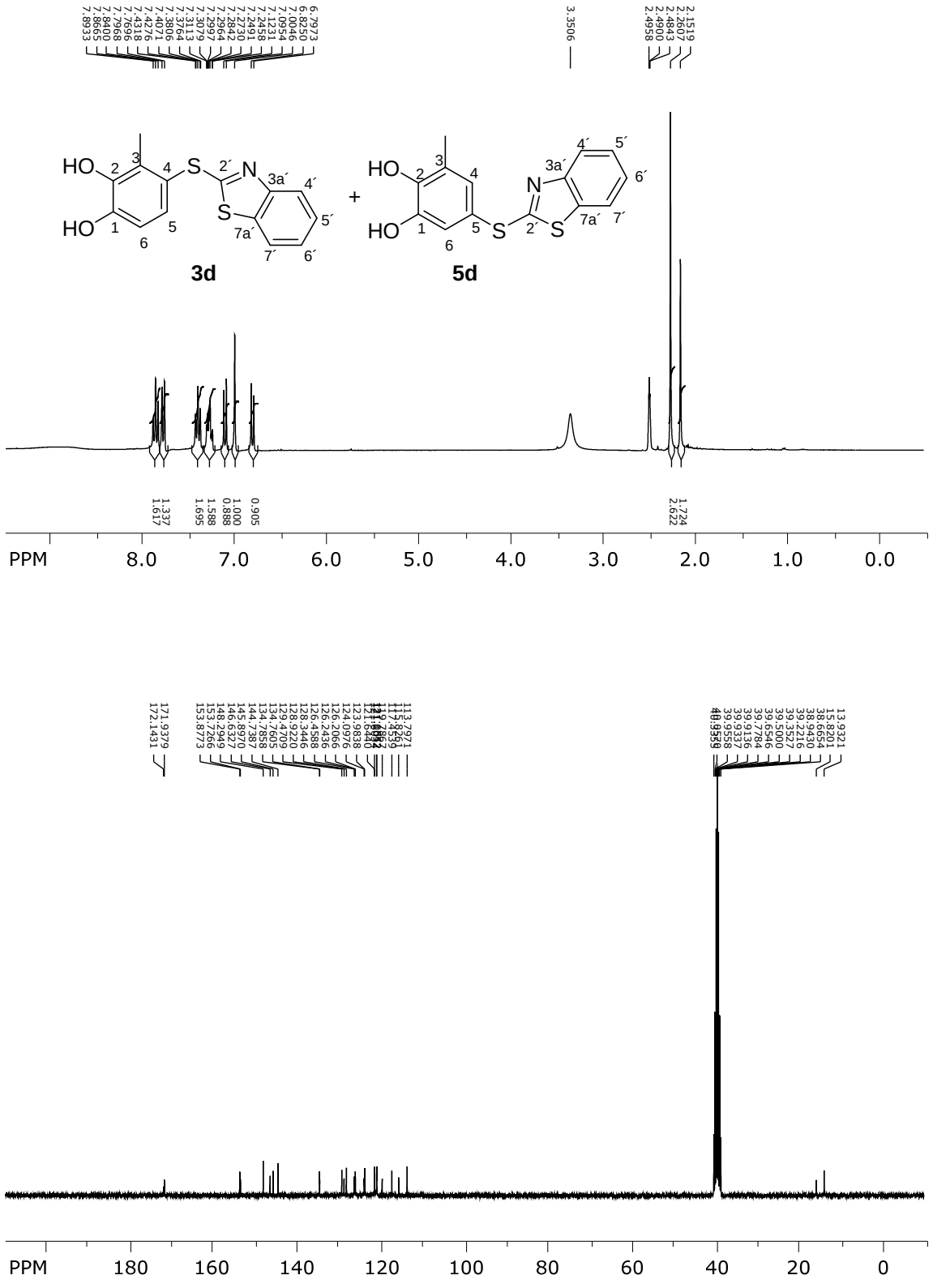


Fig. 4 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3d** and **5d** in DMSO-d_6

3.5. Synthesis and analytical data of 4-(benzo[*d*]oxazol-2´-ylthio)-3-methoxybenzene-1,2-diol (3e) and 5-(benzo[*d*]oxazol-2´-ylthio)-3-methoxybenzene-1,2-diol (5e)

According to the general procedure, 3-methoxycatechol (**1c**) (88 mg, 0.63 mmol), 2-mercaptobenzoxazole (**2a**) (76 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave a mixture of 4-(benzo[*d*]oxazol-2´-ylthio)-3-methoxybenzene-1,2-diol (**3e**) and 5-(benzo[*d*]oxazol-2´-ylthio)-3-methoxybenzene-1,2-diol (**5e**) as a pale brown solid (140 mg, 96%), mp 150–152 °C; R_f = 0.43 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 286 (log ε, 4.18), 279 (4.19), 249 (4.19) and 208 (4.59); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3300 (OH), 2994 (C-H), 1499, 1450, 1200, 1131 and 1095; δ_H (300 MHz; DMSO-d_6) of **3e** 3.68 (3H, s, OCH_3), 6.67 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.5 Hz, 6-H), 6.96 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.4 Hz, 5-H), 7.23 – 7.31 (2H, m, 5´-H and 6´-H), 7.56 – 7.63 (2H, m, 4´-H and 7´-H) and 9.22 (2H, br, 1-OH and 2-OH); δ_H (300 MHz; DMSO-d_6) of **5e** 3.74 (3H, s, OCH_3), 6.79 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 3.0 Hz, 6-H), 6.82 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 3.0 Hz, 4-H), 7.23 – 7.31 (2H, m, 5´-H and 6´-H), 7.56 – 7.63 (2H, m, 4´-H and 7´-H) and 9.22 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) of **3e** 60.16 (OCH_3), 108.22 (C-4), 110.11 (C-7´), 111.71 (C-6), 118.41 (C-4´), 124.26 (C-5´ or C-6´), 124.58 (C-5´ or C-6´), 126.21 (C-5), 139.41 (C-2), 141.50 (C-3a´), 149.37 (C-1), 150.05 (C-3), 151.16 (C-7a´) and 163.63 (C-2´); δ_C (75 MHz; DMSO-d_6) of **5e** 56.05 (OCH_3), 110.20 (C-7´), 110.29 (C-4), 113.11 (C-5), 116.11 (C-6), 118.54 (C-4´), 124.44 (C-5´ or C-6´), 124.64 (C-5´ or C-6´), 136.78 (C-2), 141.44 (C-3a´), 146.38 (C-1), 148.76 (C-3), 151.24 (C-7a´) and 163.59 (C-2´); *m/z* (EI, 70 eV) 289 (M^+, 17%), 287 (M^+ – 2, 100), 274 (M^+ – CH_3, 15), 256 (M^+ – SH, 20), 255 (50) and 240 (60); HRMS (EI, M^+) found: 289.0413; calcd for $C_{14}H_{11}SNO_4$: 289.0409.

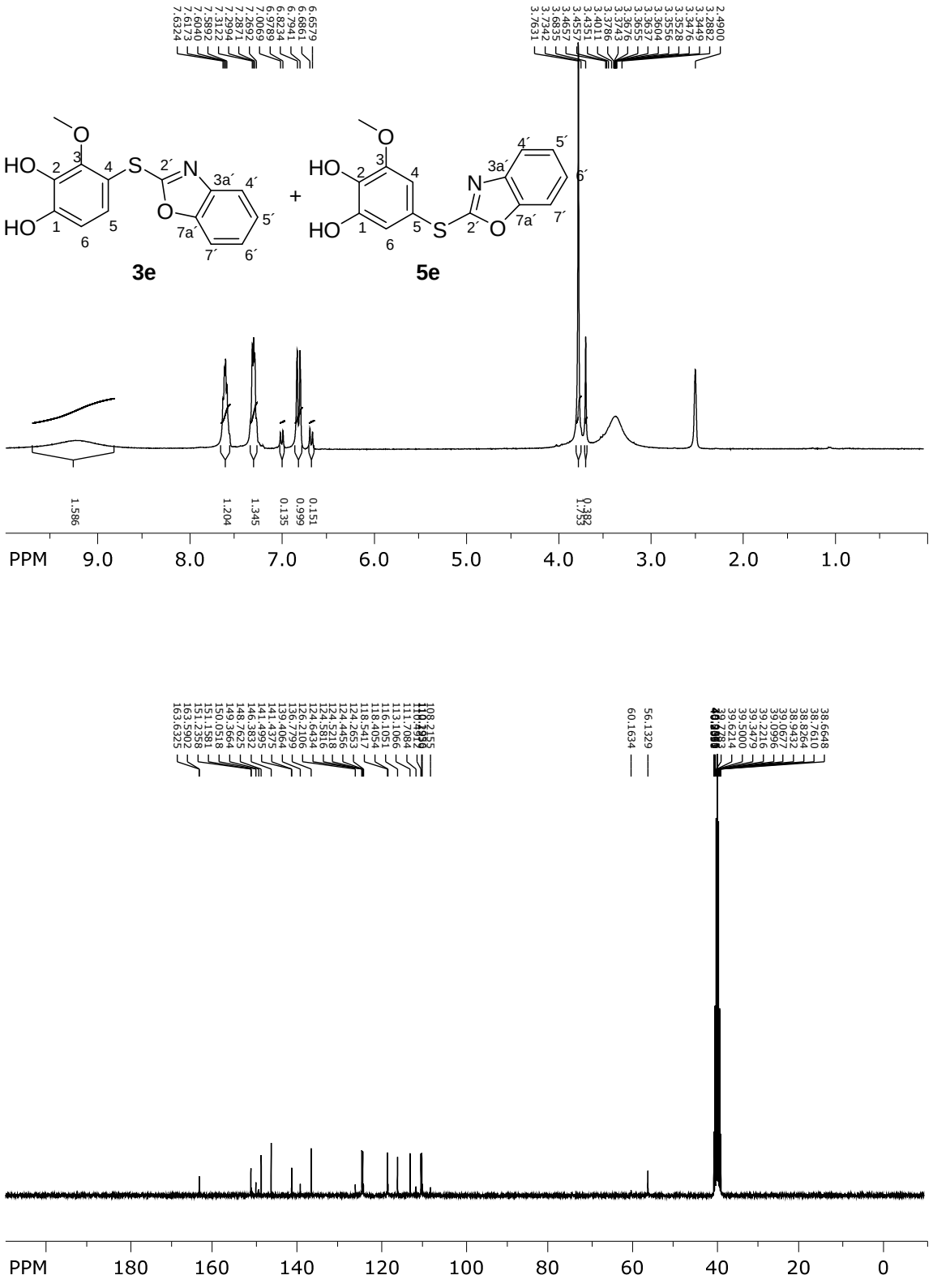


Fig. 5 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3e** and **5e** in DMSO-d_6

3.6. Synthesis and analytical data of 4-(benzo[*d*]thiazol-2´-ylthio)-3-methoxybenzene-1,2-diol (3f) and 5-(benzo[*d*]thiazol-2´-ylthio)-3-methoxybenzene-1,2-diol (5f)

According to the general procedure, 3-methoxycatechol (**1c**) (88 mg, 0.63 mmol), 2-mercaptobenzothiazole (**2b**) (84 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave a mixture of 4-(benzo[*d*]thiazol-2´-ylthio)-3-methoxybenzene-1,2-diol (**3f**) and 5-(benzo[*d*]thiazol-2´-ylthio)-3-methoxybenzene-1,2-diol (**5f**) as a pale brown solid (145 mg, 95%); mp 108–110 °C; R_f = 0.55 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 279 (log ε, 4.19) and 217 (4.55); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3400 (OH), 3058 (C-H), 1599, 1504, 1420, 1196 and 1084; δ_H (300 MHz; DMSO-d_6) of **3f** 3.72 (3H, s, OCH_3), 6.72 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.3 Hz, 6-H), 7.07 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 8.3 Hz, 5-H), 7.31 (1H, t like ov, ^3J ~ 8.0 Hz, 6´-H), 7.42 (1H, t like ov, ^3J ~ 8.0 Hz, 5´-H), 7.78 (1H, d like ov, ^3J ~ 7.8 Hz, 4´-H), 7.90 (1H, d like ov, ^3J ~ 7.8 Hz, 7´-H) and 9.27 (2H, br, 1-OH and 2-OH); δ_H (300 MHz; DMSO-d_6) of **5f** 3.78 (3H, s, OCH_3), 6.84 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 2.0 Hz, 6-H), 6.89 (1H, d, $^4J_{4\text{-H},6\text{-H}}$ 2.0 Hz, 4-H), 7.31 (1H, t like ov, ^3J ~ 8.0 Hz, 6´-H), 7.42 (1H, t like ov, ^3J ~ 8.0 Hz, 5´-H), 7.78 (1H, d like ov, ^3J ~ 7.8 Hz, 4´-H), 7.90 (1H, d like ov, ^3J ~ 7.8 Hz, 7´-H) and 9.27 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) of **3f** 56.18 (OCH_3), 111.04 (C-4), 112.15 (C-6), 121.06 (C-4´), 121.56 (C-7´), 124.03 (C-6´), 126.20 (C-5´), 127.32 (C-5), 134.71 (C-7a´), 139.63 (C-2), 149.72 (C-1), 150.68 (C-3), 153.72 (C-3a´) and 169.92 (C-2´); δ_C (75 MHz; DMSO-d_6) of **5f** 56.92 (OCH_3), 111.01 (C-4), 115.98 (C-5), 116.54 (C-6), 121.13 (C-4´), 121.65 (C-7´), 124.14 (C-6´), 126.26 (C-5´), 134.77 (C-7a´), 137.44 (C-2), 146.74 (C-1), 149.13 (C-3), 153.70 (C-3a´) and 171.88 (C-2´); *m/z* (EI, 70 eV) 307 (M^+ + 2, 45%), 305 (M^+, 100), 290 ($M^+ - CH_3$, 28) and 274 ($M^+ - OCH_3$, 24); HRMS (EI, M^+) found: 305.0122; calcd for $C_{14}H_{11}NO_3S_2$: 305.0180; *m/z* (ESI) 328 (M^+ + Na, 100%) and 306 (M^+ + 1, 30); HRMS (ESI, M^+ + Na) found: 328.0076; calcd for $C_{14}H_{11}NO_3S_2Na$: 328.0073.

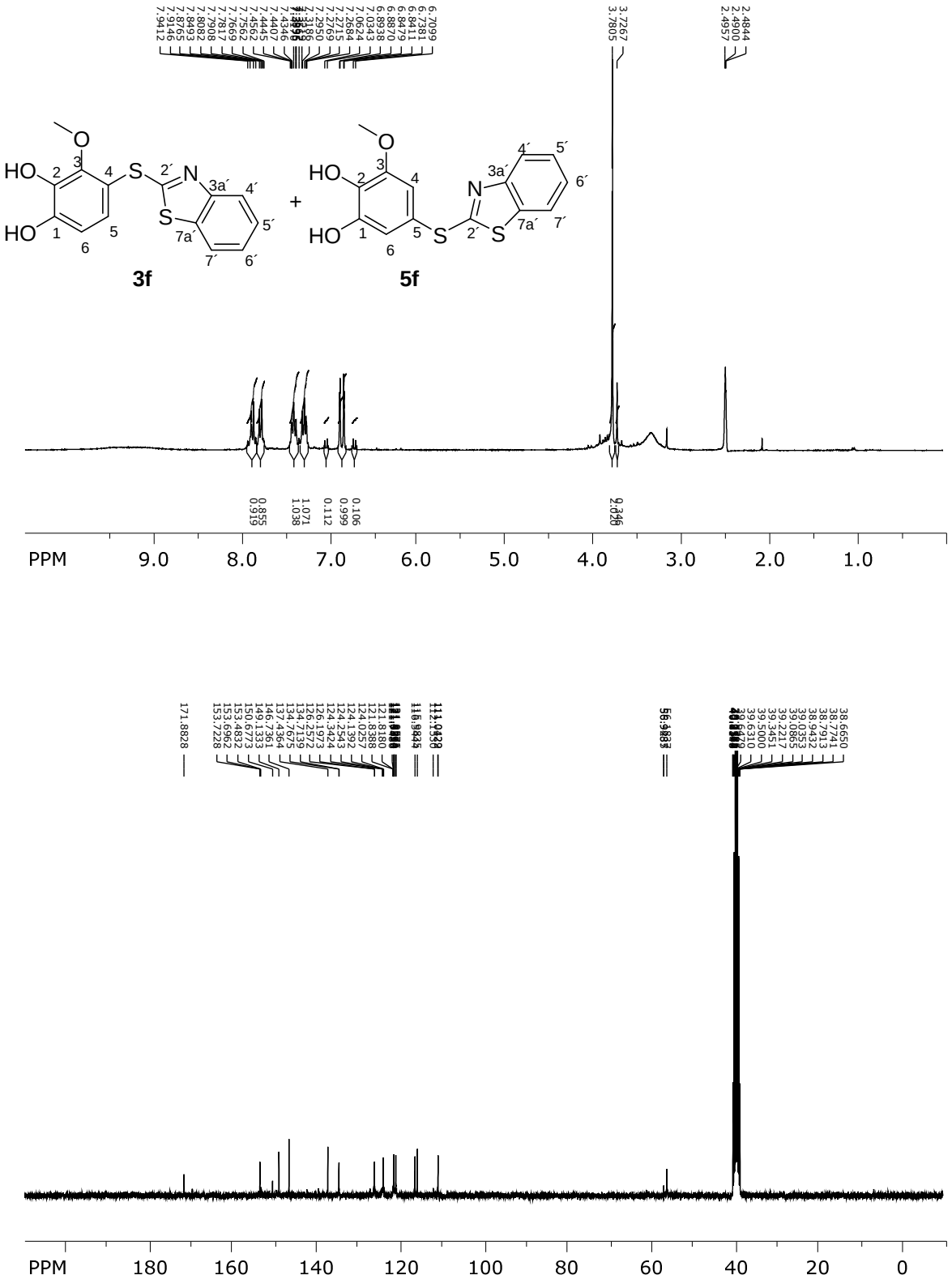


Fig. 6 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3f** and **5f** in DMSO-d_6

3.7. Synthesis and analytical data of 4-(benzo[*d*]oxazol-2´-ylthio)-3-fluorobenzene-1,2-diol (3g) and 5-(benzo[*d*]oxazol-2´-ylthio)-3-fluorobenzene-1,2-diol (5g)

According to the general procedure, 3-fluorocatechol (**1d**) (81 mg, 0.63 mmol), 2-mercaptobenzoxazole (**2a**) (76 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave a mixture of 4-(benzo[*d*]oxazol-2´-ylthio)-3-fluorobenzene-1,2-diol (**3g**) and 5-(benzo[*d*]oxazol-2´-ylthio)-3-fluorobenzene-1,2-diol (**5g**) as a pale yellow solid (125 mg, 90%); mp 183–185 °C; R_f = 0.36 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 285 (log ε, 4.18), 278 (4.18) and 247 (4.21); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3470 (OH), 3064 (C-H), 1500, 1452 and 1138; δ_H (300 MHz; DMSO-d_6) of **3g** 6.73 (1H, dd, $^3J_{5\text{-H},6\text{-H}}$ 8.6 Hz, $^5J_{6\text{-H},F}$ 1.4 Hz, 6-H), 7.06 (1H, dd, $^3J_{5\text{-H},6\text{-H}}$ 8.6 Hz, $^4J_{5\text{-H},F}$ 7.6 Hz, 5-H), 7.27 – 7.34 (2H, m, 5´-H and 6´-H), 7.58 – 7.64 (2H, m, 4´-H and 7´-H) and 9.78 (2H, br, 1-OH and 2-OH); δ_H (300 MHz; DMSO-d_6) of **5g** 7.00 (1H, dd, $^4J_{4\text{-H},6\text{-H}}$ 1.6 or 2.1 Hz, $^5J_{6\text{-H},F}$ 1.6 or 2.1 Hz, 6-H), 7.08 (1H, dd, $^4J_{4\text{-H},6\text{-H}}$ 2.2 Hz, $^3J_{4\text{-H},F}$ 10.1 Hz, 4-H), 7.27 – 7.34 (2H, m, 5´-H and 6´-H), 7.58 – 7.64 (2H, m, 4´-H and 7´-H) and 9.78 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) of **3g** 101.77 (d, $^2J_{C\text{-}4,F}$ 16.9 Hz, C-4), 110.34 (C-7´), 111.88 (d, $^4J_{C\text{-}6,F}$ 2.2 Hz, C-6), 118.56 (C-4´), 124.54 (C-5´ or C-6´), 124.76 (C-5´ or C-6´), 126.28 (br, C-5), 134.45 (d, $^2J_{C\text{-}2,F}$ 14.73 Hz, C-2), 141.32 (C-3a´), 151.24 (d, $^3J_{C\text{-}1,F}$ 6.1 Hz, C-1), 151.31 (C-7a´), 152.30 (d, $^1J_{C\text{-}3,F}$ 240.4 Hz, C-3) and 162.50 (C-2´); δ_C (75 MHz; DMSO-d_6) of **5g** 113.45 (br, C-5), 113.66 (d, $^2J_{C\text{-}4,F}$ 10.6 Hz, C-4), 110.34 (C-7´), 118.08 (d, $^4J_{C\text{-}6,F}$ 2.2 Hz, C-6), 118.64 (C-4´), 124.54 (C-5´ or C-6´) 124.76 (C-5´ or C-6´), 135.97 (d, $^2J_{C\text{-}2,F}$ 13.7 Hz, C-2), 141.32 (C-3a´), 148.18 (d, $^3J_{C\text{-}1,F}$ 6.5 Hz, C-1), 151.31 (C-7a´), 151.64 (d, $^1J_{C\text{-}3,F}$ 240.5 Hz, C-3) and 163.01 (C-2´); *m/z* (EI, 70 eV) 277 (M^+, 85%), 257 (M^+ – HF, 100), 226 (16), 171 (15), 151 ($C_7H_5SNO^+$, 19) and 119 (18); HRMS (EI, M^+) found: 277.0194; calcd for $C_{13}H_8FSNO_3$: 277.0209.

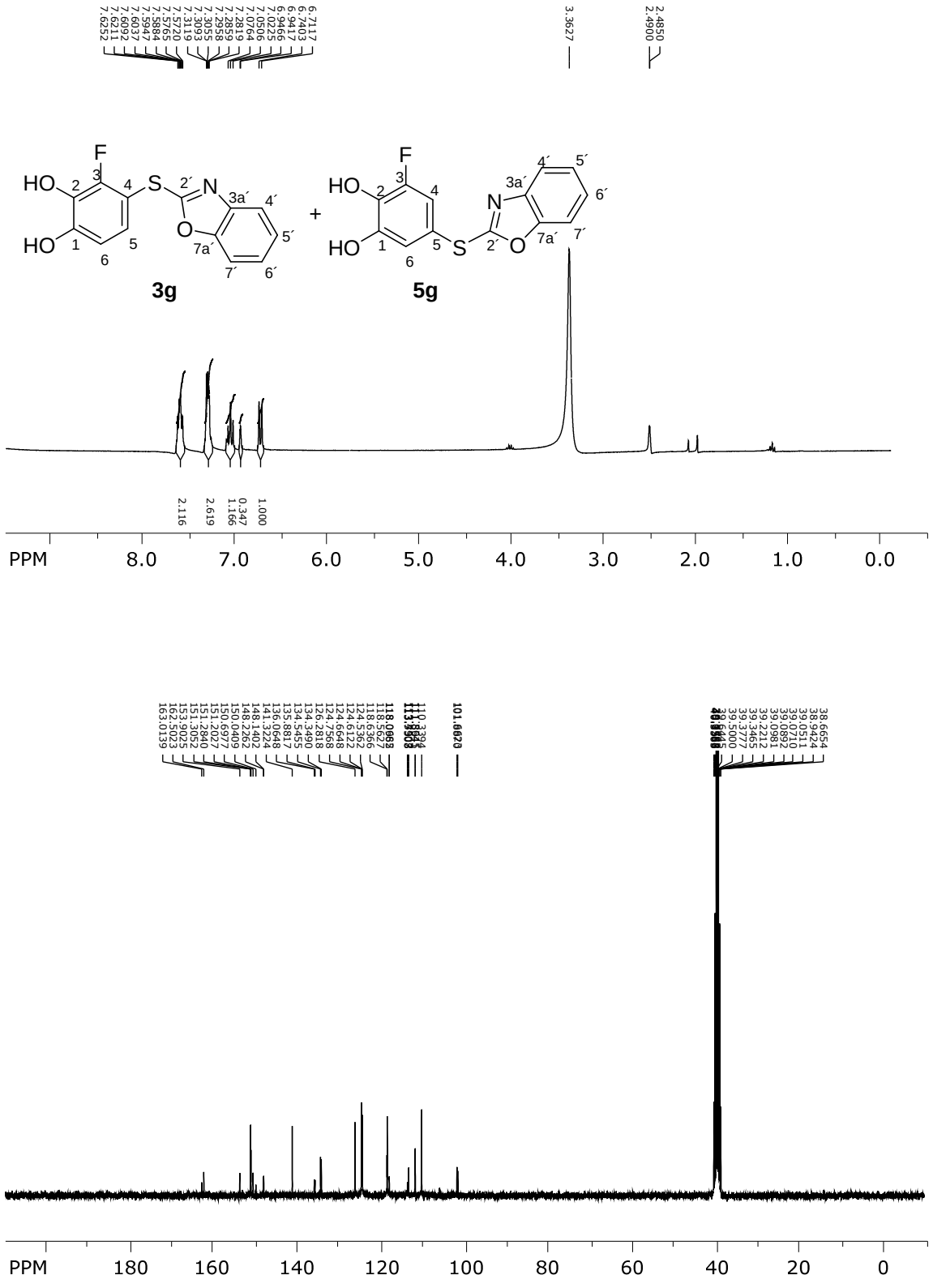


Fig. 7 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3g** and **5g** in DMSO-d_6

3.8. Synthesis and analytical data of 4-(benzo[*d*]thiazol-2´-ylthio)-3-fluorobenzene-1,2-diol (3h) and 4-(benzo[*d*]thiazol-2´-ylthio)-3-fluorobenzene-1,2-diol (5h)

According to the general procedure, 3-fluorocatechol (**1d**) (81 mg, 0.63 mmol), 2-mercaptobenzothiazole (**2b**) (84 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave a mixture of 4-(benzo[*d*]thiazol-2´-ylthio)-3-fluorobenzene-1,2-diol (**3h**) and 5-(benzo[*d*]thiazol-2´-ylthio)-3-fluorobenzene-1,2-diol (**5h**) as a pale yellow solid (127 mg, 86%); mp 177–179 °C; R_f = 0.36 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 277 (log ε, 4.19) and 208 (4.53); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3263 (OH), 1578, 1414, 1276 and 1011; δ_H (300 MHz; DMSO-d_6) of **3h** 6.78 (1H, dd, $^3J_{5\text{-H},6\text{-H}}$ 8.4 Hz, $^5J_{6\text{-H},F}$ 1.4 Hz, 6-H), 7.11 (1H, dd, $^3J_{5\text{-H},6\text{-H}}$ 8.6 Hz, $^4J_{5\text{-H},F}$ 7.7 Hz, 5-H), 7.31 (1H, t like ov, ^3J ~ 7.7 Hz, 6´-H), 7.43 (1H, ddd, $^3J_{4´\text{-H},5´\text{-H}}$ 7.3 or 8.4 Hz, $^3J_{5´\text{-H},6´\text{-H}}$ 7.3 or 8.4 Hz, $^4J_{5´\text{-H},7´\text{-H}}$ 1.4 Hz, 5´-H), 7.81 (1H, d like ov, $^3J_{4´\text{-H},5´\text{-H}}$ 8.1 Hz, 4´-H), 7.90 (1H, ddd, $^3J_{6´\text{-H},7´\text{-H}}$ 7.8 Hz, $^4J_{5´\text{-H},7´\text{-H}}$ 1.3 or 0.7 Hz, $^5J_{4´\text{-H},7´\text{-H}}$ 1.3 or 0.7 Hz, 7´-H) and 9.78 (2H, br, 1-OH and 2-OH); δ_H (300 MHz; DMSO-d_6) of **5h** 7.00 (1H, dd, $^4J_{4\text{-H},6\text{-H}}$ 1.6 or 2.2 Hz, $^5J_{6\text{-H},F}$ 1.6 or 2.2 Hz, 6-H), 7.15 (1H, dd, $^3J_{4\text{-H},F}$ 10.0 Hz, $^4J_{4\text{-H},6\text{-H}}$ 2.1 Hz, 4-H), 7.31 (1H, t like ov, ^3J ~ 7.7 Hz, 6´-H), 7.43 (1H, ddd, $^3J_{4´\text{-H},5´\text{-H}}$ 7.3 or 8.4 Hz, $^3J_{5´\text{-H},6´\text{-H}}$ 7.3 or 8.4 Hz, $^4J_{5´\text{-H},7´\text{-H}}$ 1.4 Hz, 5´-H), 7.81 (1H, d like ov, $^3J_{4´\text{-H},5´\text{-H}}$ 8.1 Hz, 4´-H), 7.90 (1H, ddd, $^3J_{6´\text{-H},7´\text{-H}}$ 7.8 Hz, $^4J_{5´\text{-H},7´\text{-H}}$ 0.7 or 1.3 Hz, $^5J_{4´\text{-H},7´\text{-H}}$ 0.7 or 1.3 Hz, 7´-H) and 9.78 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) of **3h** 104.66 (d, $^2J_{C\text{-4},F}$ 16.7 Hz, C-4), 112.31 (d, $^4J_{C\text{-6},F}$ 2.5 Hz, C-6), 121.27 (C-4´), 121.73 (C-7´), 124.33 (C-6´), 126.38 (C-5´), 126.99 (br, C-5), 134.65 (d, $^2J_{C\text{-2},F}$ 14.9 Hz, C-2), 134.77 (C-7a´), 151.76 (d, $^3J_{C\text{-1},F}$ 6.3 Hz, C-1), 152.32 (d, $^1J_{C\text{-3},F}$ 240.4 Hz, C-3), 153.65 (C-3a´) and 170.10 (C-2´); δ_C (75 MHz; DMSO-d_6) of **5h** 114.28 (d, $^2J_{C\text{-4},F}$ 20.1 Hz, C-4), 116.16 (d, $^3J_{C\text{-5},F}$ 10.3 Hz, C-5), 118.69 (d, $^4J_{C\text{-6},F}$ 1.6 Hz, C-6), 121.27 (C-4´), 121.73 (C-7´), 124.33 (C-6´), 126.38 (C-5´), 134.77 (C-7a´), 136.68 (d, $^2J_{C\text{-2},F}$ 13.8 Hz, C-2), 148.59 (d, $^3J_{C\text{-1},F}$ 6.7 Hz, C-1), 151.18 (d, $^1J_{C\text{-3},F}$ 240.4 Hz, C-3), 153.59 (C-3a´) and 170.62 (C-2´); *m/z* (EI, 70 eV) 293 (M^+, 100%), 273 (M^+ – HF, 79), 260 (M^+ – SH, 4), 244 (8) and 167 ($C_7H_5NS_2^+$, 10); *m/z* (ESI) 316 (M^+ + Na, 100%) and 294 (M^+ + 1, 30); HRMS (ESI, M^+ + Na) found: 315.9893; calcd for $C_{13}H_8FNO_2S_2Na$: 315.9873.

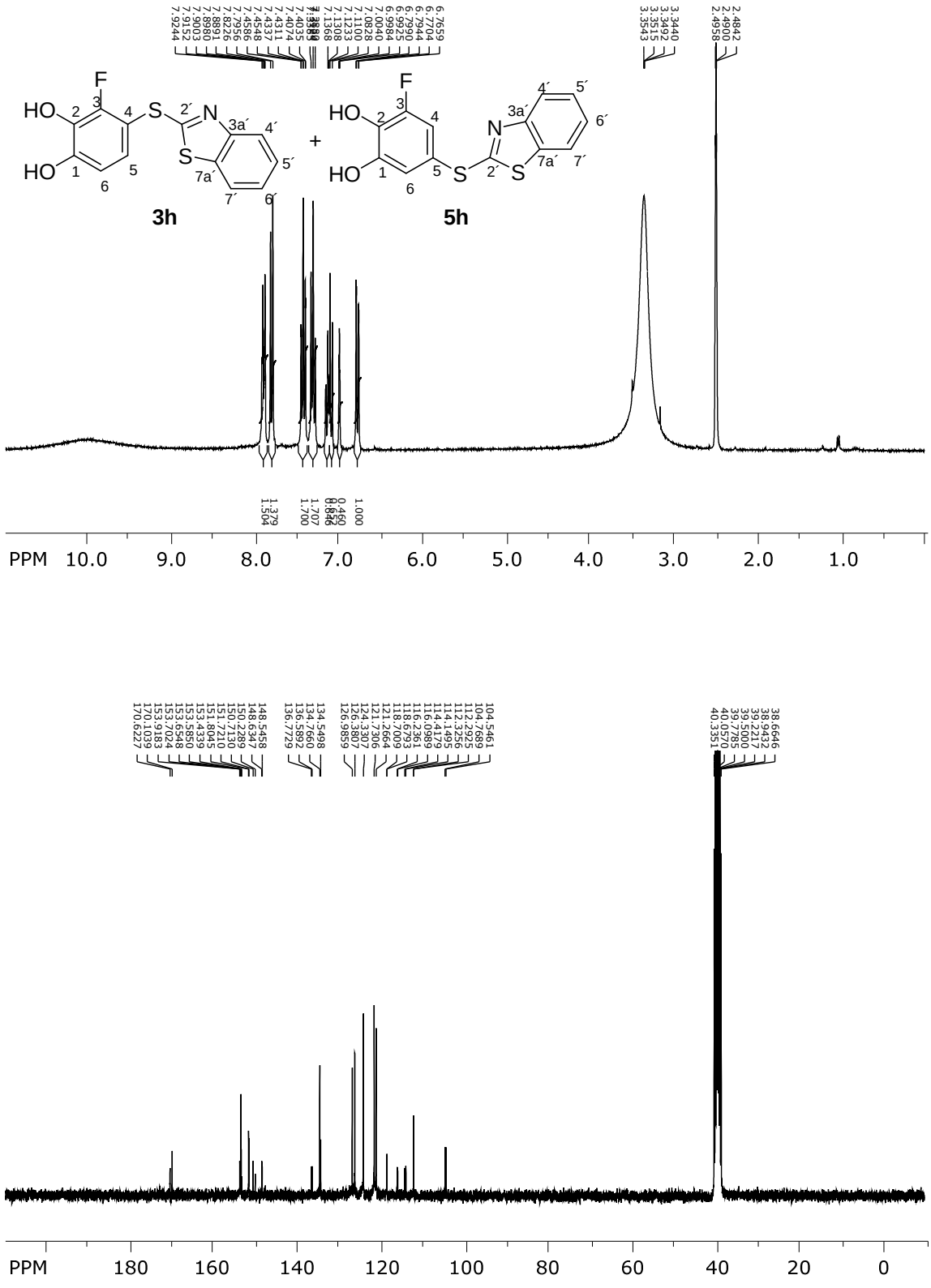
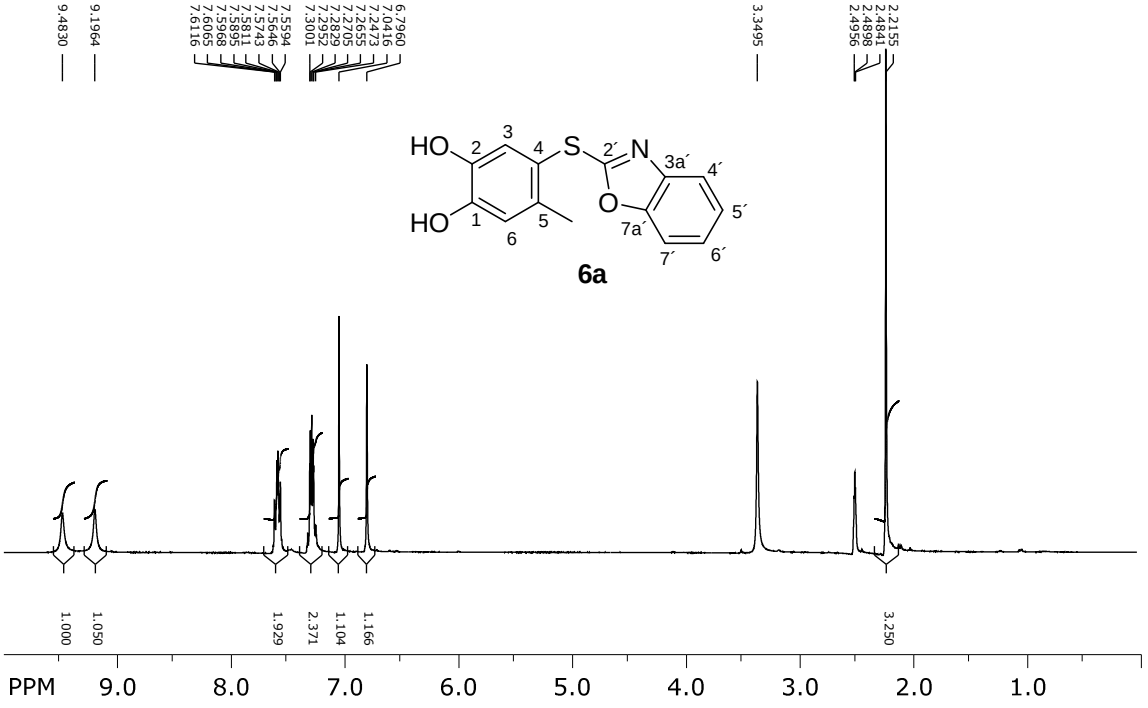


Fig. 8 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3h** and **5h** in DMSO-d_6

3.9. Synthesis and analytical data of 4-(benzo[*d*]oxazol-2´-ylthio)-5-methylbenzene-1,2-diol (6a)

According to the general procedure, 4-methylcatechol (**1h**) (78 mg, 0.63 mmol), 2-mercaptobenzoxazole (**2a**) (76 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave 4-(benzo[*d*]oxazol-2´-ylthio)-5-methylbenzene-1,2-diol (**6a**) as a pale yellow solid (117 mg, 85%); mp 198–200 °C (lit.[1] 198–200 °C); R_f = 0.53 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 287 (log ε, 4.27), 280 (4.23), 246 (4.28) and 206 (4.71); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3200 (OH), 3141, 1496 1453, 1235 and 1132; δ_H (300 MHz; DMSO-d_6) 2.22 (3H, s, CH_3), 6.80 (1H, s, 6-H), 7.04 (1H, s, 3-H), 7.25 – 7.32 (2H, m, 5´-H and 6´-H), 7.56 – 7.61 (2H, m, 4´-H and 7´-H), 9.20 (1H, s, 1-OH or 2-OH), 9.48 (1H, s, 1-OH or 2-OH); δ_C (75 MHz; DMSO-d_6) 19.66 (CH_3), 110.23 (C-7´), 112.76 (C-4), 118.07 (C-6), 118.44 (C-4´), 123.16 (C-3), 124.31 (C-5´ or C-6´) 124.59 (C-5´ or C-6´), 133.58 (C-5), 141.45 (C-3a´), 143.99 (C-2), 148.17 (C-1), 151.25 (C-7a´) and 163.51 (C-2´); *m/z* (EI, 70 eV) 273 (M^+, 100%), 240 (M^+ – SH, 40), 151 ($C_7H_5NSO^+$, 42) and 124 ($C_7H_8O_2^+$, 32); HRMS (EI, M^+) found: 273.0455; calcd for $C_{14}H_{11}NSO_3$: 273.0460.



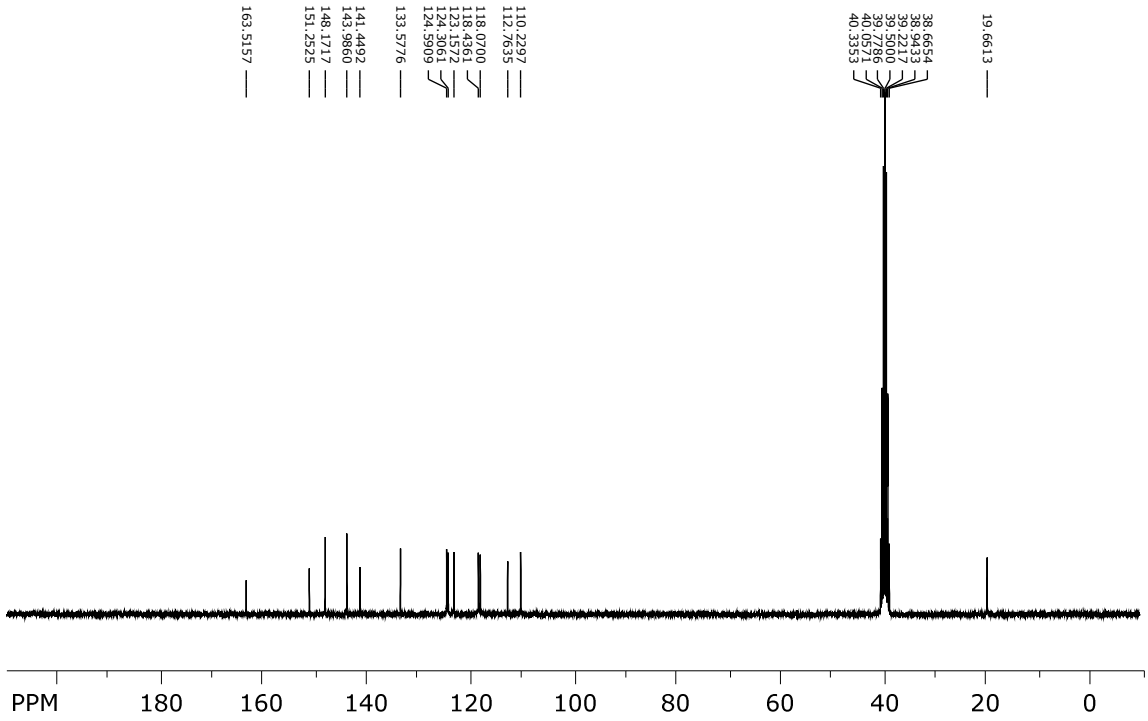


Fig. 9 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **6a** in DMSO-d_6

3.10. Synthesis and analytical data of 4-(benzo[*d*]thiazol-2´-ylthio)-5-methylbenzene-1,2-diol (6b)

According to the general procedure, 4-methylcatechol (**1h**) (78 mg, 0.63 mmol), 2-mercaptobenzothiazole (**2b**) (84 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave 4-(benzo[*d*]thiazol-2´-ylthio)-5-methylbenzene-1,2-diol (**6b**) as a white solid (131 mg, 90%); mp 187–189 °C; R_f = 0.50 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 299 (log ε, 4.15), 290 (4.21), 282 (3.19) and 210 (4.61); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3248 (OH), 3054 (C-H), 1493, 1416, 1278 and 1029; δ_H (300 MHz; DMSO-d_6) 2.25 (3H, s, CH_3), 6.85 (1H, s, 6-H), 7.08 (1H, s, 3-H), 7.26 (1H, ddd, $^{3}J_{5´\text{-H},6´\text{-H}}$ 7.3 or 8.1 Hz, $^{3}J_{6´\text{-H},7´\text{-H}}$ 7.3 or 8.1 Hz, $^{4}J_{4´\text{-H},6´\text{-H}}$ 1.2 Hz, 6´-H), 7.42 (1H, ddd, $^{3}J_{4´\text{-H},5´\text{-H}}$ 7.3 or 8.4 Hz, $^{3}J_{5´\text{-H},6´\text{-H}}$ 7.3 or 8.4 Hz, $^{4}J_{5´\text{-H},7´\text{-H}}$ 1.3 Hz, 5´-H), 7.78 (1H, ddd, $^{3}J_{4´\text{-H},5´\text{-H}}$ 8.1 Hz, $^{4}J_{4´\text{-H},6´\text{-H}}$ 1.1 or 0.6 Hz, $^{5}J_{4´\text{-H},7´\text{-H}}$ 1.1 or 0.6 Hz, 4´-H), 7.87 (1H, ddd, $^{3}J_{6´\text{-H},7´\text{-H}}$ 7.9 Hz, $^{4}J_{5´\text{-H},7´\text{-H}}$ 1.3 or 0.7 Hz, $^{5}J_{4´\text{-H},7´\text{-H}}$ 1.3 or 0.7 Hz, 7´-H) and 9.55 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) 19.52 (CH_3), 115.87 (C-4), 118.39 (C-6), 121.08 (C-4´), 121.64 (C-7´), 123.47 (C-3), 124.04 (C-6´) 126.24 (C-5´), 133.99 (C-5), 134.79 (C-7a´), 144.52 (C-2), 148.88 (C-1), 153.91 (C-3a´) and 171.75 (C-2´); *m/z* (EI, 70 eV) 289 (M^+,

57%), 256 (M^+ – SH, 100), 210 (34), 167 ($C_7H_5NS_2^+$, 34) and 123 (34); HRMS (EI, M^+) found: 289.0237; calcd for $C_{14}H_{11}NO_2S_2$: 289.0231.

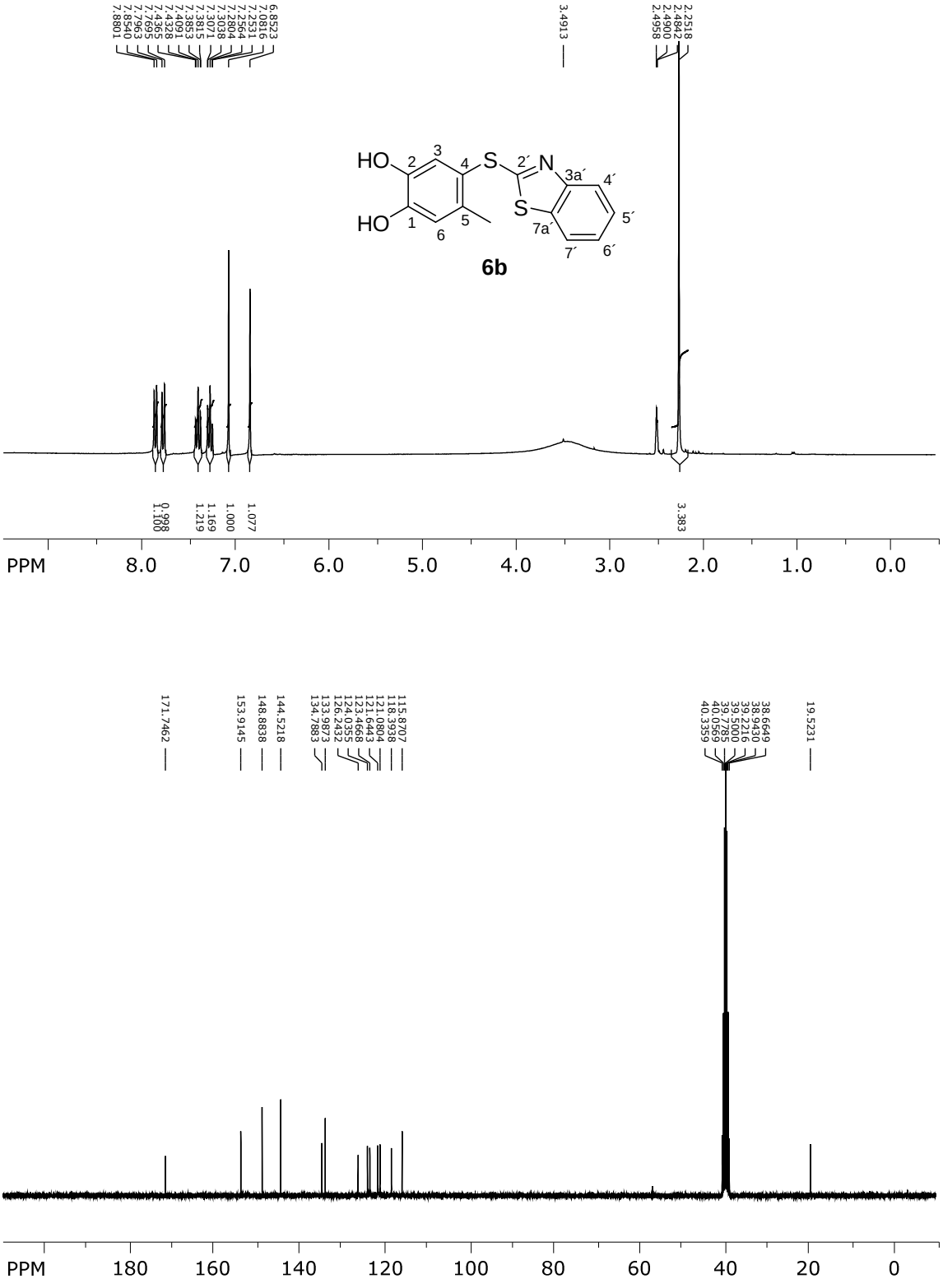
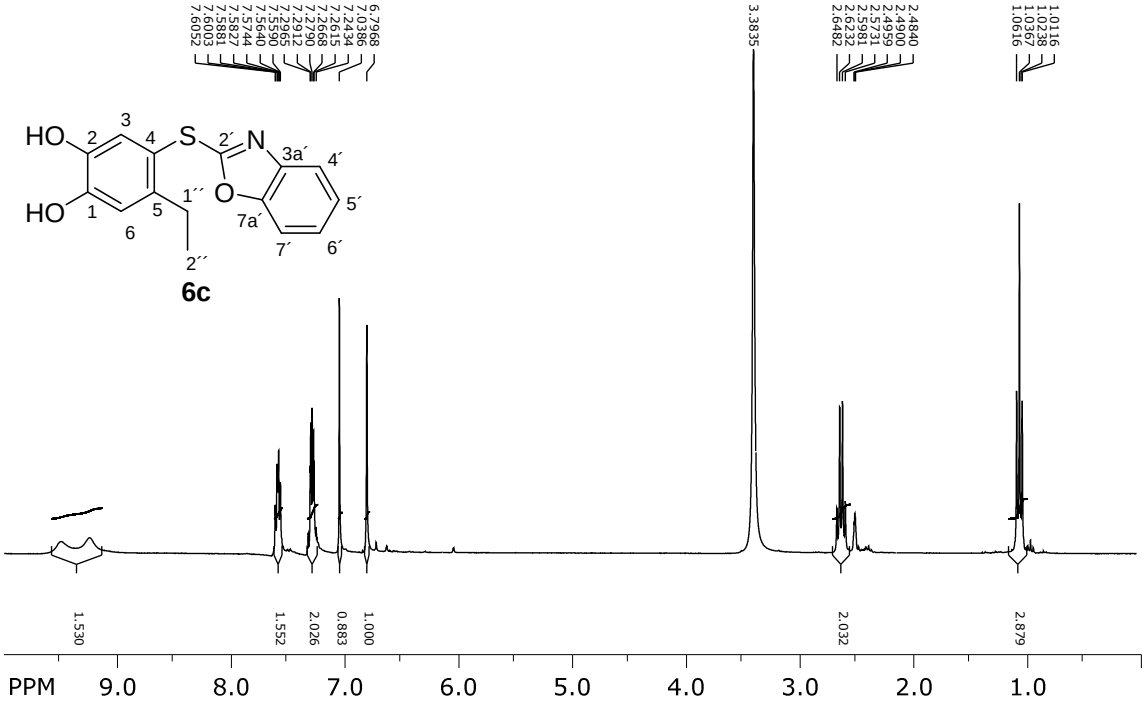


Fig. 10 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **6b** in DMSO-d_6

3.11. Synthesis and analytical data of 4-(benzo[*d*]oxazol-2´-ylthio)-5-ethylbenzene-1,2-diol (6c)

According to the general procedure, 4-ethylcatechol (**1i**) (87 mg, 0.63 mmol), 2-mercaptobenzoxazole (**2a**) (76 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave 4-(benzo[*d*]oxazol-2´-ylthio)-5-ethylbenzene-1,2-diol (**6c**) as a pale yellow solid (120 mg, 83%); mp 141–143 °C; R_f = 0.50 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 287 (log ε, 4.19), 248 (4.13) and 206 (4.55); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3233 (OH), 1502, 1453 and 1133; δ_H (300 MHz; DMSO-d_6) 1.04 (3H, t, $^3J_{1´´\text{-H},2´´\text{-H}}$ 7.5 Hz, 2´´-H), 2.61 (2H, q, $^3J_{1´´\text{-H},2´´\text{-H}}$ 7.5 Hz, 1´´-H), 6.80 (1H, s, 6-H), 7.04 (1H, s, 3-H), 7.24 – 7.30 (2H, m, 5´-H and 6´-H), 7.56 – 7.61 (2H, m, 4´-H and 7´-H), 9.44 (1H, s, 1-OH or 2-OH) and 9.59 (1H, s, 1-OH or 2-OH); δ_C (75 MHz; DMSO-d_6) 15.44 (C-2´´), 26.27 (C-1´´), 110.23 (C-7´), 112.10 (C-4), 116.56 (C-6), 118.47 (C-4´), 123.47 (C-3), 124.34 (C-5´ or C-6´) 124.61 (C-5´ or C-6´), 139.50 (C-5), 141.47 (C-3a´), 144.09 (C-2), 148.43 (C-1), 151.24 (C-7a´) and 163.84 (C-2´); *m/z* (EI, 70 eV) 287 (M^+, 100%), 254 (M^+ – SH, 30), 180 (58), 151 ($C_7H_5NSO^+$, 80) and 123 (44); HRMS (EI, M^+) found: 287.0618; calcd for $C_{15}H_{13}NSO_3$: 287.0616.



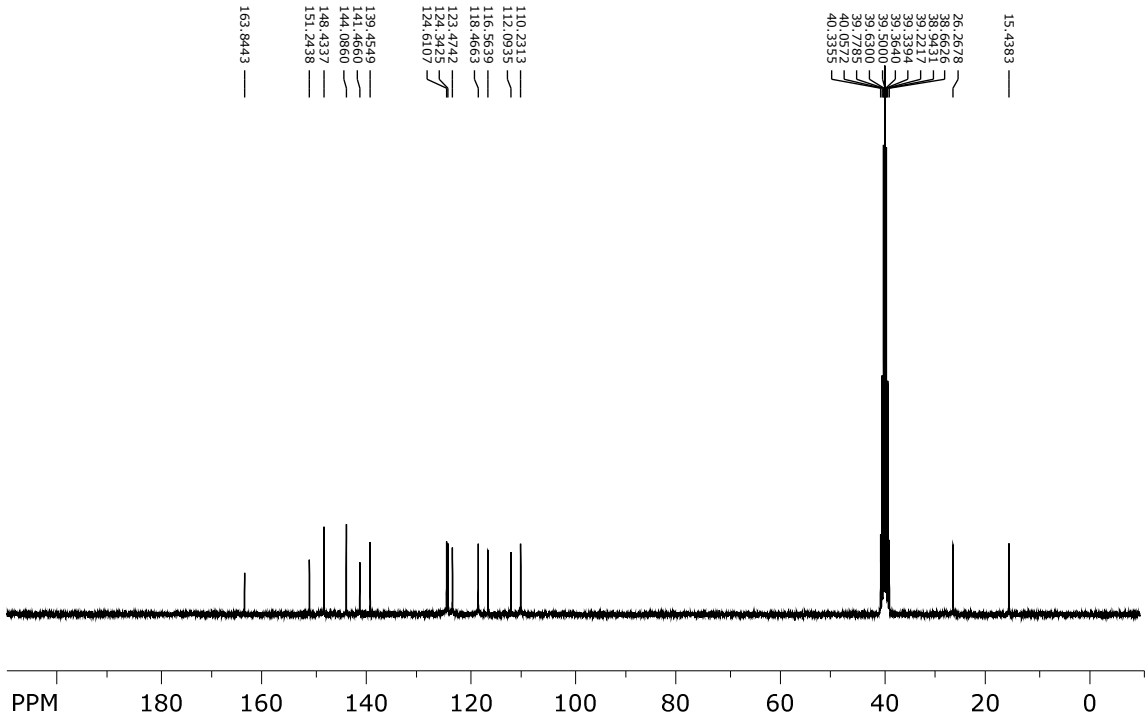


Fig. 11 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **6c** in DMSO-d_6

3.12. Synthesis and analytical data of 4-(benzo[*d*]thiazol-2´-ylthio)-5-ethylbenzene-1,2-diol (6d)

According to the general procedure, 4-ethylcatechol (**1i**) (87 mg, 0.63 mmol), 2-mercaptobenzothiazole (**2b**) (84 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave 4-(benzo[*d*]thiazol-2´-ylthio)-5-ethylbenzene-1,2-diol (**6d**) as a pale yellow solid (126 mg, 83%); mp 152–154 °C; R_f = 0.54 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 290 (log ε, 4.24), 282 (4.24) and 211 (4.63); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3275 (OH), 3054 (C-H), 1498, 1416, 1266 and 1029; δ_H (300 MHz; DMSO-d_6) 1.07 (3H, t, $^{3}J_{1´´\text{-H},2´´\text{-H}}$ 7.2 Hz, 2´´-H), 2.63 (2H, q, $^{3}J_{1´´\text{-H},2´´\text{-H}}$ 7.2 Hz, 1´´-H), 6.85 (1H, s, 6-H), 7.07 (1H, s, 3-H), 7.28 (1H, ddd, $^{3}J_{5´\text{-H},6´\text{-H}}$ 7.2 or 8.0 Hz, $^{3}J_{6´\text{-H},7´\text{-H}}$ 7.2 or 8.0 Hz, $^{4}J_{4´\text{-H},6´\text{-H}}$ 1.1 Hz, 6´-H), 7.41 (1H, ddd, $^{3}J_{4´\text{-H},5´\text{-H}}$ 7.2 or 8.0 Hz, $^{3}J_{5´\text{-H},6´\text{-H}}$ 7.2 or 8.0 Hz, $^{4}J_{5´\text{-H},7´\text{-H}}$ 1.2 Hz, 5´-H), 7.78 (1H, ddd, $^{3}J_{4´\text{-H},5´\text{-H}}$ 8.1 Hz, $^{4}J_{4´\text{-H},6´\text{-H}}$ 1.2 or 0.5 Hz, $^{5}J_{4´\text{-H},7´\text{-H}}$ 1.2 or 0.5 Hz, 4´-H), 7.87 (1H, ddd, $^{3}J_{6´\text{-H},7´\text{-H}}$ 8.0 Hz, $^{4}J_{5´\text{-H},7´\text{-H}}$ 1.3 or 0.6 Hz, $^{5}J_{4´\text{-H},7´\text{-H}}$ 1.3 or 0.6 Hz, 7´-H) and 9.51 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) 15.66 (C-2´´), 26.23 (C-1´´), 115.18 (C-4), 116.86 (C-6), 121.06 (C-4´), 121.63 (C-7´), 123.67 (C-3), 124.02 (C-6´), 126.23 (C-5´), 134.76 (C-7a´), 139.84 (C-5), 144.55 (C-2), 149.05 (C-1),

153.83 (C-3a´) and 172.15 (C-2´); *m/z* (EI, 70 eV) 303 (M^+, 60%), 270 (M^+ – SH, 100), 255 (25), 167 ($C_7H_5NS_2^+$, 42) and 123 (36); HRMS (EI, M^+) found: 303.0381; calcd for $C_{15}H_{13}NO_2S_2$: 303.0388.

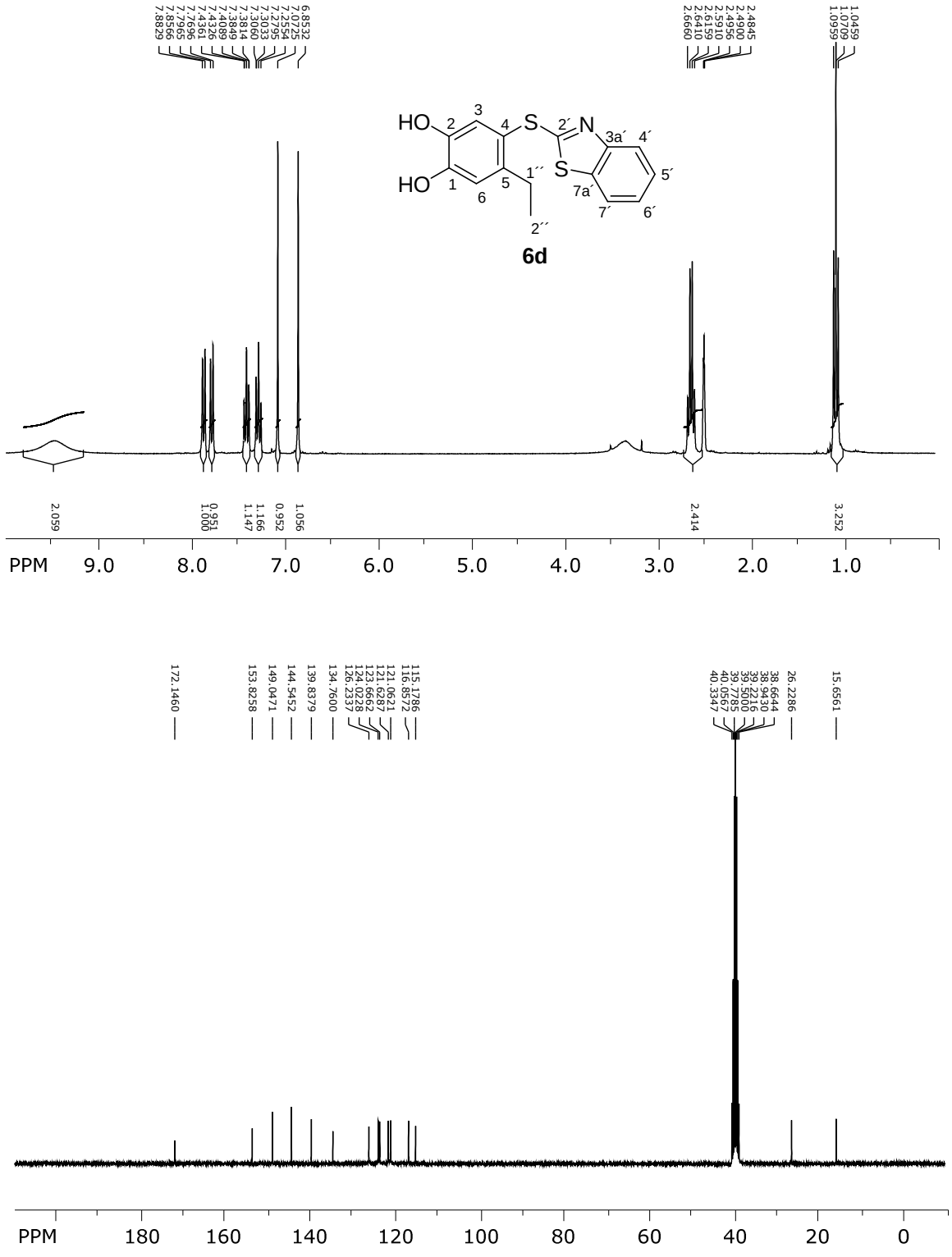
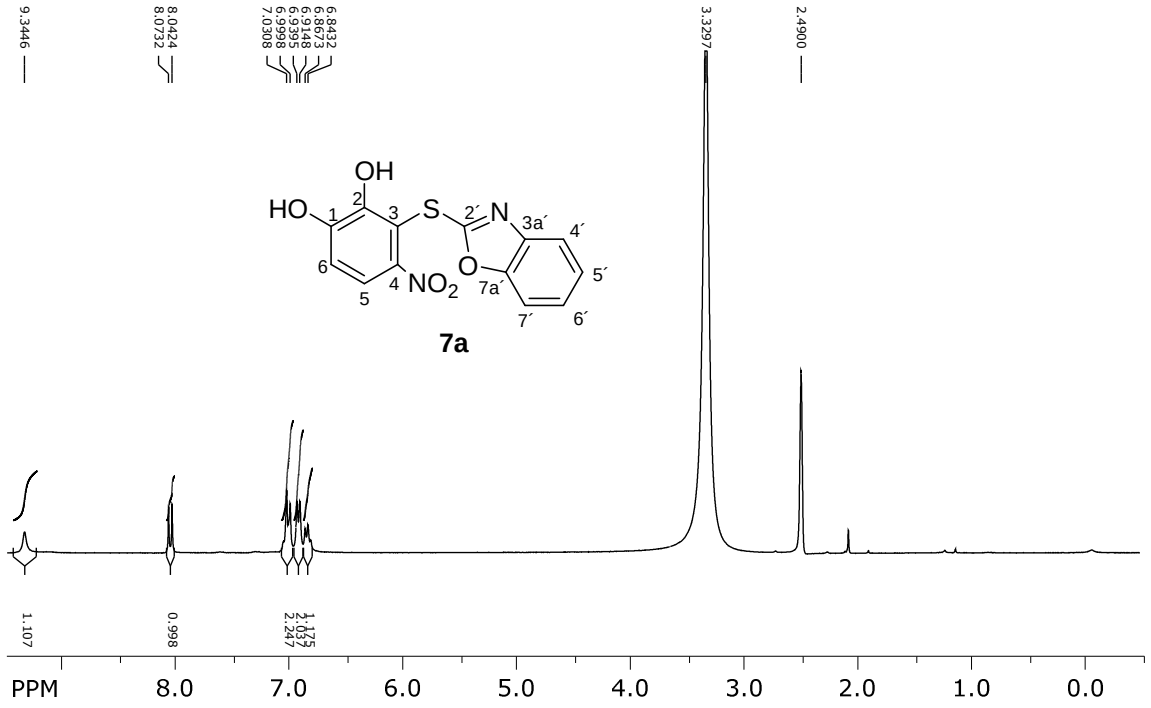


Fig. 12 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **6d** in DMSO-d_6

3.13. Synthesis and analytical data of 3-(benzo[*d*]oxazol-2´-ylthio)-4-nitrobenzene-1,2-diol (7a)

According to the general procedure, 4-nitrocatechol (**1j**) (78 mg, 0.50 mmol), 2-mercaptobenzoxazole (**2a**) (76 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Column filtration (EtOAc/MeOH 1:2) gave 3-(benzo[*d*]oxazol-2´-ylthio)-4-nitrobenzene-1,2-diol (**7a**) as a yellow solid (130 mg, 85%); mp 223–225 °C; R_f = 0.22 (EtOAc/MeOH = 5:1); λ_{max}(MeCN)/nm 314 (log ε, 4.18) and 202 (4.61); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3327 (OH), 1587, 1303 and 1207; δ_H (300 MHz; DMSO-d_6) 6.84 (1H, t like, $^3J_{5´\text{-H},6´\text{-H}}$ 7.1 Hz, 5´-H), 6.93 (2H, d like ov, ^3J ~ 7.5 Hz, 4´-H and 7´-H), 7.00 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 9.2 Hz, 6-H), 7.03 (1H, t like ov, 6´-H), 8.06 (1H, d, $^3J_{5\text{-H},6\text{-H}}$ 9.3 Hz, 5-H) and 9.35 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) 115.11 (C-6), 116.75 (C-7´), 119.84 (C-5´), 121.26 (C-4´), 122.28 (C-5), 123.17 (C-3), 126.11 (C-6´), 133.04 (C-4), 134.70 (C-3a´), 138.17 (C-2), 148.16 (C-7a´), 148.39 (C-1) and 159.83 (C-2´); *m/z* (EI, 70 eV) 304 (M^+, 100%), 258 ($M^+ - NO_2$, 5), 169 (78), 135 (38) and 80 (15); HRMS (EI, M^+) found: 304.0154; calcd for $C_{13}H_8N_2O_5S$: 304.0154.



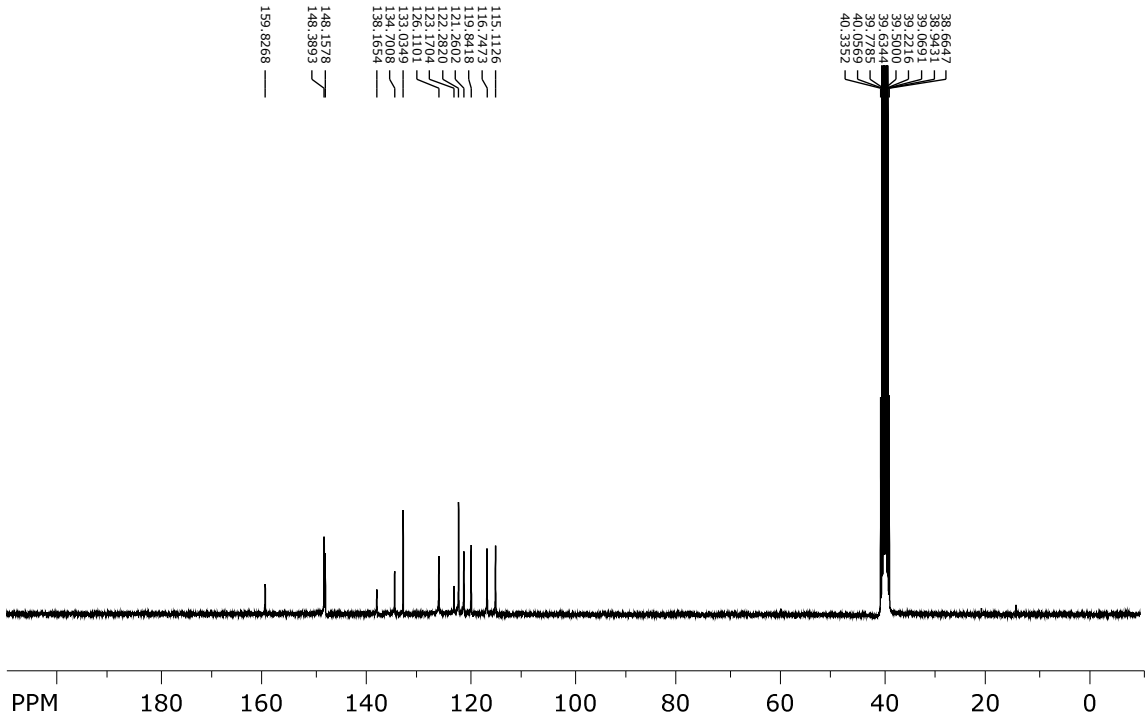


Fig. 13 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **7a** in DMSO-d_6

3.14. Synthesis and analytical data of 4-(4´,5´-dihydrothiazol-2´-ylthio)benzene-1,2-diol (**8a**)

According to the general procedure, catechol (**1a**) (69 mg, 0.63 mmol), 2-mercaptothiazoline (**2c**) (60 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 20 h. Workup gave 4-(4´,5´-dihydrothiazol-2´-ylthio)benzene-1,2-diol (**8a**) as a pale yellow solid (95 mg, 83%); mp 165–167 °C (lit.[2] > 250 °C); R_f = 0.27 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 286 (log ε, 3.23) and 206 (4.14); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3316 (OH), 1546, 1506, 1401, 1251 and 1029; δ_H (300 MHz; DMSO-d_6) 3.26 (2H, t, $^{3}J_{4´\text{-H},5´\text{-H}}$ 8.2 Hz, 5´-H), 4.16 (2H, t, $^{3}J_{4´\text{-H},5´\text{-H}}$ 8.2 Hz, 4´-H), 6.76 (1H, d, $^{3}J_{5\text{-H},6\text{-H}}$ 7.2 Hz, 6-H), 6.87 (1H, dd, $^{3}J_{5\text{-H},6\text{-H}}$ 8.0 Hz, $^{4}J_{3\text{-H},5\text{-H}}$ 2.1 Hz, 5-H), 6.90 (1H, d, $^{4}J_{3\text{-H},5\text{-H}}$ 2.1 Hz, 3-H) and 9.44 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) 34.00 (C-5´), 65.46 (C-4´), 116.08 (C-6), 117.07 (C-4), 122.61 (C-3) 127.37 (C-5), 145.61 (C-2), 147.87 (C-1) and 167.12 (C-2´); *m/z* (EI, 70 eV) 227 (M^+, 74%), 226 (M^+ – 1, 100), 167 (M^+ – C_2H_4S, 47) and 141 (16); HRMS (EI, M^+) found: 227.0090; calcd for $C_9H_9NO_2S_2$: 227.0075.

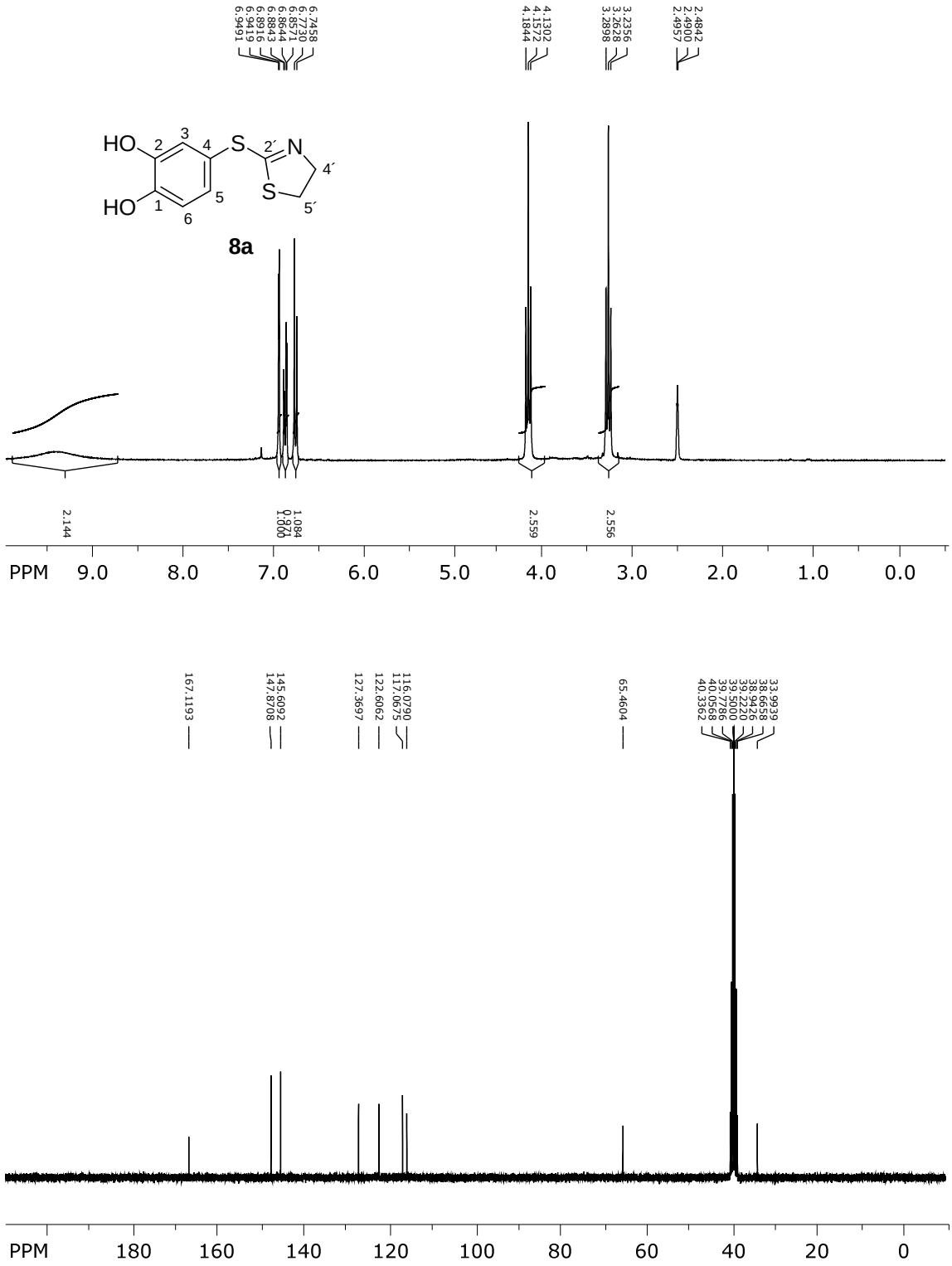
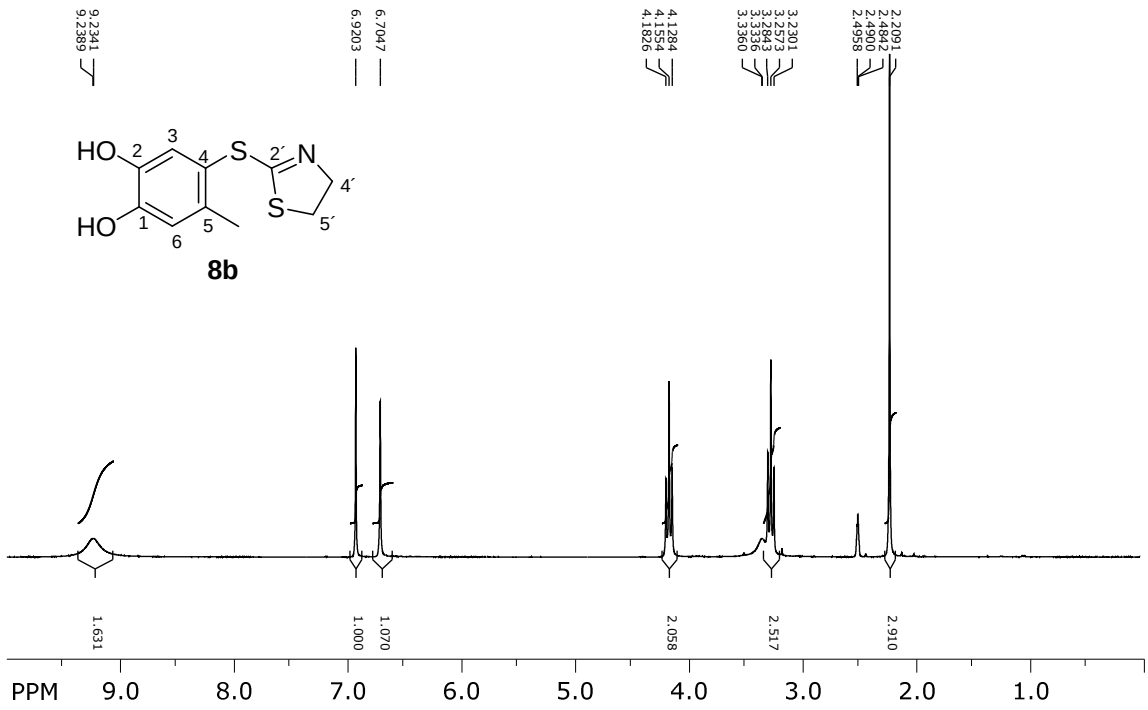


Fig. 14 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **8a** in DMSO-d_6

3.15. Synthesis and analytical data of 4-(4´,5´-dihydrothiazol-2´-ylthio)-5-methylbenzene-1,2-diol (8b)

According to the general procedure, 4-methylcatechol (**1h**) (78 mg, 0.63 mmol), 2-mercaptothiazoline (**2c**) (60 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave 4-(4´,5´-dihydrothiazol-2´-ylthio)-5-methylbenzene-1,2-diol (**8b**) as a white solid (90 mg, 74%); mp 192–194 °C (lit.[2] 179–180 °C); R_f = 0.25 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 291 (log ε, 3.68) and 209 (4.59); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3270 (OH), 1562, 1426, 1401, 1288 and 1002; δ_H (300 MHz; DMSO-d_6) 2.21 (3H, s, CH_3), 3.26 (2H, t, $^3J_{4´\text{-}H,5´\text{-}H}$ 8.1 Hz, 5´-H), 4.16 (2H, t, $^3J_{4´\text{-}H,5´\text{-}H}$ 8.2 Hz, 4´-H), 6.71 (1H, s, 6-H), 6.90 (1H, s, 3-H) and 9.24 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) 19.88 (CH_3), 33.95 (C-5´), 65.51 (C-4´), 116.37 (C-4), 117.63 (C-6), 123.49 (C-3) 133.84 (C-5), 143.45 (C-2), 148.01 (C-1) and 166.82 (C-2´); *m/z* (EI, 70 eV) 241 (M^+, 100%), 226 (M^+ – CH_3, 36), 208 (M^+ – SH, 22), 194 (50) and 154 (32); HRMS (EI, M^+) found: 241.0204; calcd for $C_{10}H_{11}NO_2S_2$: 241.0231.



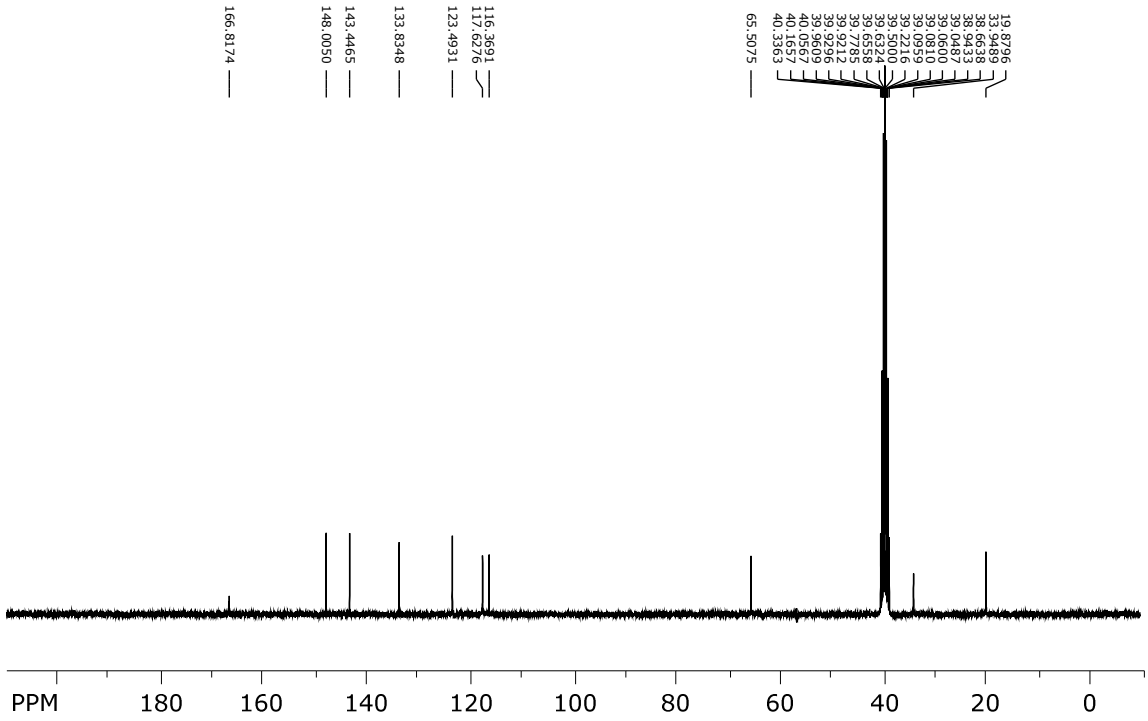


Fig. 15 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **8b** in DMSO-d_6

3.16. Synthesis and analytical data of 4-(4´,5´-dihydrothiazol-2´-ylthio)-5-ethylbenzene-1,2-diol (8c)

According to the general procedure, 4-ethylcatechol (**1i**) (87 mg, 0.63 mmol), 2-mercaptothiazoline (**2c**) (60 mg, 0.50 mmol), methanol (3 mL), phosphate buffer (0.2 M, pH 6.0, 27 mL) and laccase (60 U, 10 mg, *A. bisporus*) were reacted for 17 h. Workup gave 4-(4´,5´-dihydrothiazol-2´-ylthio)-5-ethylbenzene-1,2-diol (**8c**) as a pale yellow solid (105 mg, 82%); mp 169–171 °C; R_f = 0.24 (CH_2Cl_2/EtOAc = 5:1); λ_{max}(MeCN)/nm 290 (log ε, 3.61) and 210 (4.53); $\tilde{\nu}_{max}$ (atr)/cm^{-1} 3252 (OH), 1567, 1435, 1290 and 1003; δ_H (300 MHz; DMSO-d_6) 1.08 (3H, t, $^{3}J_{1´´\text{-H},2´´\text{-H}}$ 7.5 Hz, 2´´-H), 2.60 (2H, q, $^{3}J_{1´´\text{-H},2´´\text{-H}}$ 7.5 Hz, 1´´-H), 3.25 (2H, t, $^{3}J_{4´\text{-H},5´\text{-H}}$ 8.4 Hz, 5´-H), 4.15 (2H, t, $^{3}J_{4´\text{-H},5´\text{-H}}$ 8.4 Hz, 4´-H), 6.71 (1H, s, 6-H), 6.91 (1H, s, 3-H) and 9.24 (2H, br, 1-OH and 2-OH); δ_C (75 MHz; DMSO-d_6) 15.48 (C-2´´), 26.31 (C-1´´), 34.04 (C-5´), 65.51 (C-4´), 115.67 (C-4), 116.11 (C-6), 123.85 (C-3), 139.63 (C-5), 143.49 (C-2), 148.24 (C-1) and 167.29 (C-2´); *m/z* (EI, 70 eV) 255 (M^+, 50%), 222 (M^+ – SH, 17), 208 (44) and 123 (100); HRMS (EI, M^+) found: 255.0417; calcd for $C_{11}H_{13}NO_2S_2$: 255.0388.

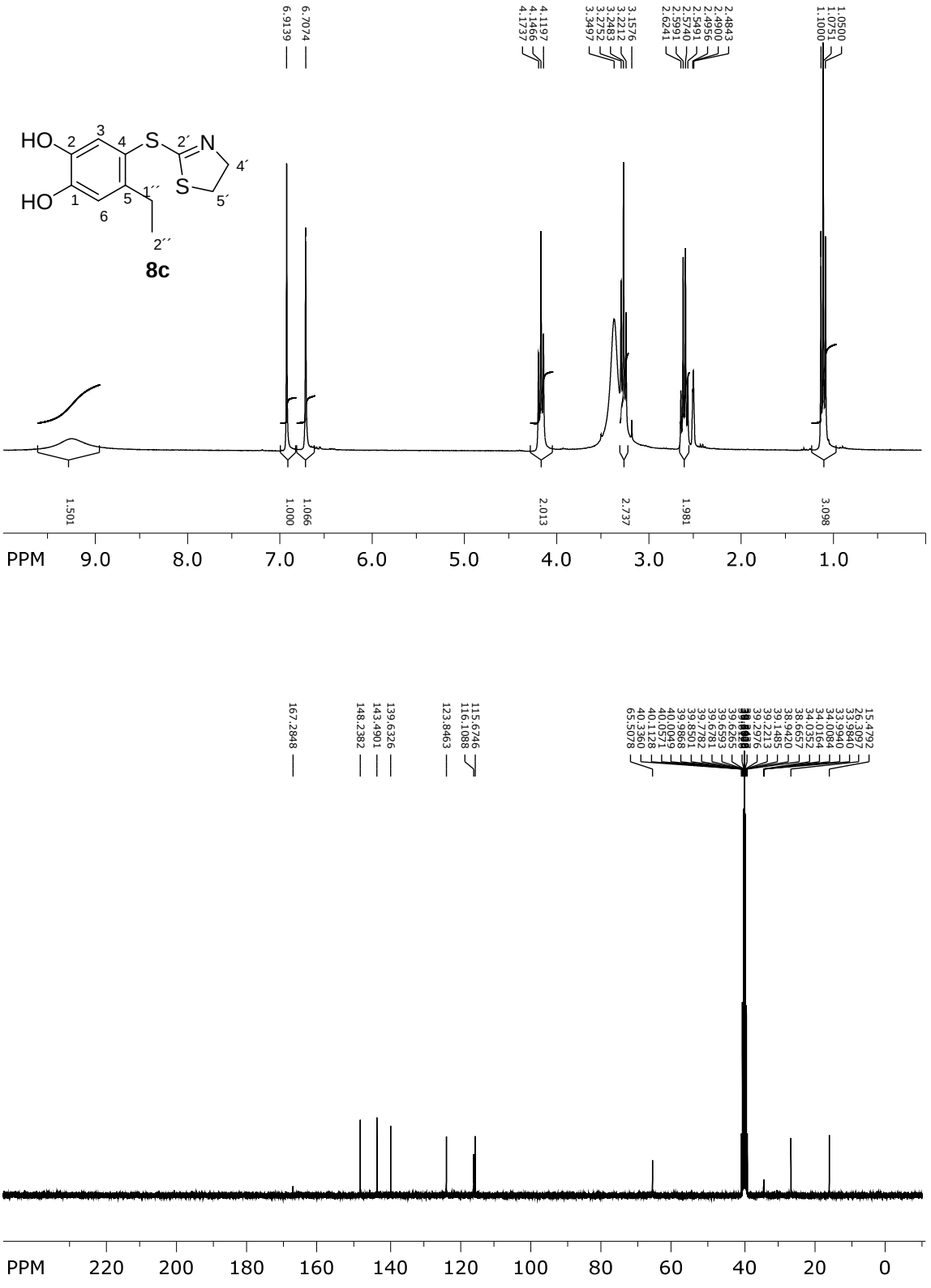


Fig. 16 ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **8c** in DMSO-d_6

4. Computational studies of compounds 3a and 3b

Calculations reported in this paper were performed within Density Functional Theory, using the Gaussian 03 package.[3] ^{13}C NMR chemical shifts of selected compounds **3a** and **3b** were calculated as follows: the structures were optimized with the MM2 force field implemented in Chem3D Pro.[4] In the second step, the optimized structures were subsequently reoptimized at the AM1 level followed by the RHF/3-21G level and finally by B3LYP/6-31G(d) level of theory within the Gaussian 03 package. In the final step, the ^{13}C NMR chemical shielding of the reoptimized geometries were computed once at the mPW1PW91/6-311+G(2d,p)//mPW1PW91/6-31G(d) level of theory in the gas phase.[3] The references TMS and benzene for the MSTD approach according to Sarotti and Pellegrinet[5] were computed in the same manner as for **3a** and **3b**. For comparison with the experimental ^{13}C NMR chemical shifts the computationally derived ^{13}C NMR chemical shifts were calculated as follows:

$\delta_a = \sigma_{ref\ gas\ pahse} - \sigma_{a\ gas\ phase} + \delta_{ref}$

where σ_{ref} and σ_a are the calculated NMR isotropic magnetic shielding tensors of the reference compound and carbon a of the compound of interest: σ_{TMS} = 185.81 ppm and $\sigma_{benzene}$ = 54.41 ppm at the mPW1PW91/6-311+G(2d,p)// mPW1PW91/6-31G(d) level gas phase; δ_{ref} represents the chemical shift of the reference compound in deuterated DMSO: δ_{TMS} = 0 ppm; $\delta_{benzene}$ = 128.27 ppm. An HP Compaq with a 2.39 GHz processor and 2 GB RAM was used for the calculations.

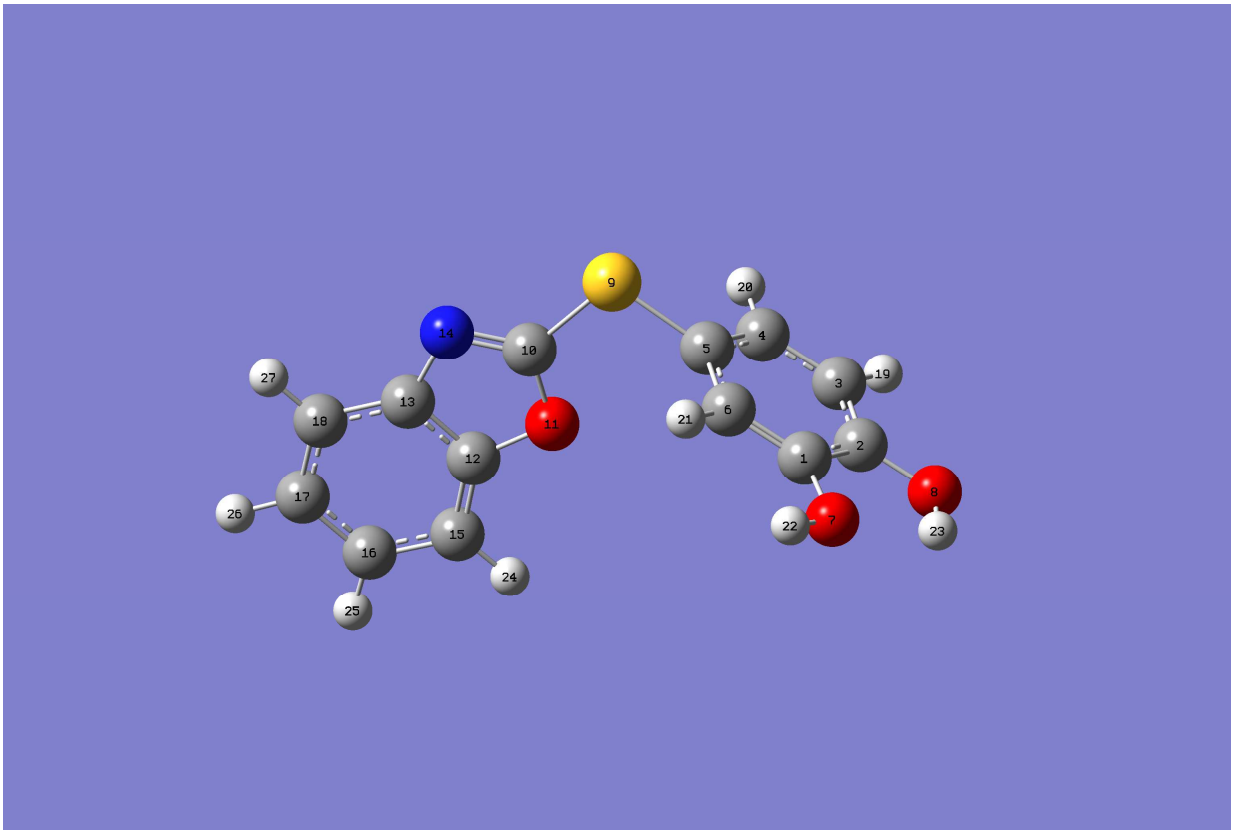


Fig. 17 3D structure of **3a**

4.1. Cartesian of 3a

Symbol	X	Y	Z
C	3.1477780	-0.4840430	0.8295260
C	3.7115840	-0.7013480	-0.4388140
C	3.1897990	-0.0396640	-1.5419860
C	2.1125270	0.8291420	-1.3922370
C	1.5546830	1.0388110	-0.1340220
C	2.0830170	0.3849680	0.9855140
O	3.7429190	-1.1818460	1.8430090
O	4.7555080	-1.5451120	-0.5803500
S	0.2325240	2.2118320	0.0726940
C	-1.1829770	1.1810650	0.0722950
O	-1.0498810	-0.1314110	-0.2668520
C	-2.3317350	-0.6126240	-0.1923470
C	-3.1565960	0.4496740	0.1852060

N	-2.3753490	1.5881030	0.3514700
C	-2.7811200	-1.8964340	-0.4331550
C	-4.1528990	-2.0909980	-0.2788750
C	-5.0047980	-1.0434210	0.0984610
C	-4.5253010	0.2406870	0.3371720
H	3.6378600	-0.2170330	-2.5129140
H	1.7044430	1.3423680	-2.2549740
H	1.6560410	0.5595050	1.9687240
H	3.2976850	-0.9959560	2.6786990
H	4.9673860	-1.8999870	0.2965670
H	-2.1112100	-2.6961140	-0.7256430
H	-4.5695060	-3.0767610	-0.4563580
H	-6.0660090	-1.2420720	0.2062490
H	-5.1817780	1.0520870	0.6293810

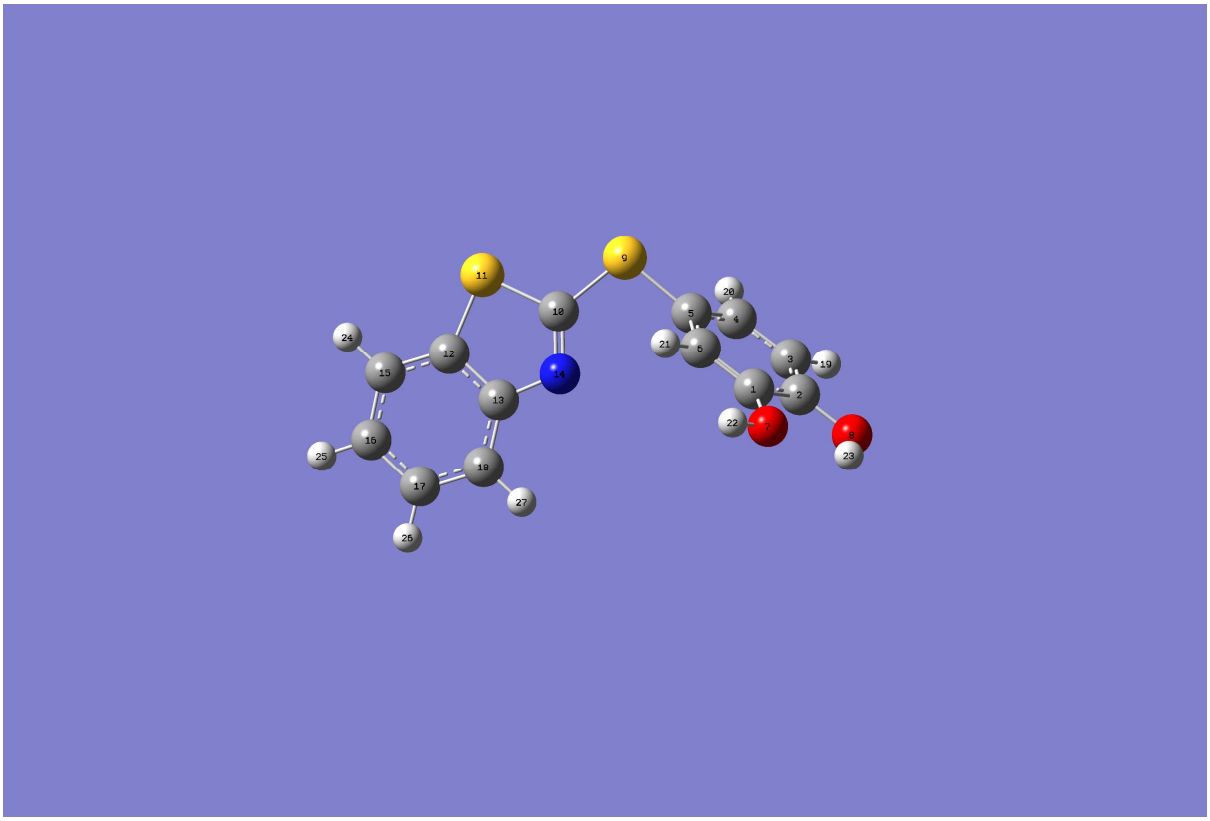


Fig. 18 3D structure of **3b**

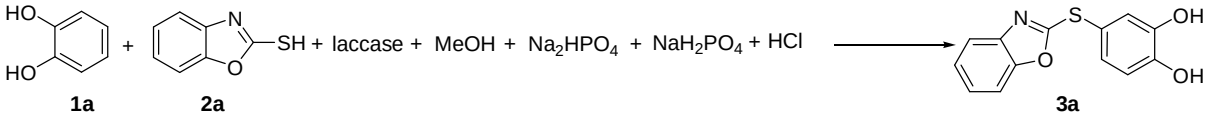
4.2. Cartesian of 3b

Symbol	X	Y	Z
C	-3.3044020	0.6986710	0.7179180
C	-3.9989020	0.6038130	-0.4996440
C	-3.5753440	-0.3043180	-1.4598500
C	-2.4660530	-1.1104230	-1.2186480
C	-1.7847920	-1.0143530	-0.0085760
C	-2.2126120	-0.1108720	0.9703280
O	-3.8094270	1.6232650	1.5900760
O	-5.0708460	1.3919960	-0.7303230
S	-0.4262420	-2.1097620	0.3206890
C	0.9619470	-1.0407230	0.1412380
S	2.5669660	-1.7853290	0.2125980
C	3.2525780	-0.1941630	0.0079470
C	2.2090290	0.7492550	-0.1030000
N	0.9284430	0.2360160	-0.0180700
C	4.5901870	0.1859100	-0.0532420
C	4.8779310	1.5336260	-0.2293890
C	3.8523580	2.4806910	-0.3422380
C	2.5205900	2.1001980	-0.2809250
H	-4.1201130	-0.3633400	-2.3950630
H	-2.1296160	-1.8117070	-1.9731540
H	-1.6807220	-0.0393470	1.9138900
H	-3.2426750	1.6842680	2.3686100
H	-5.1910660	1.9565140	0.0485330
H	5.3863190	-0.5454140	0.0321680
H	5.9132820	1.8537990	-0.2811200
H	4.1046820	3.5267900	-0.4807770
H	1.7163040	2.8218210	-0.3687010

5. Calculation of the E-factor, atom economy, TON and TOF of the laccase-catalyzed domino reaction between catechol (1a) and 2-mercaptobenzoxazole (2a)

Yield of **3a** = 93%

5.1. Calculation of the E-factor[6]



1a **2a** **3a**

69 mg 76 mg 10 mg 237.54 mg 125 mg 542.3 mg 14.4 mg 121 mg

Total amount of the reactants (taking into account a loss of 10% of the solvent used) = 69 mg + 76 mg + 10 mg + 237.54 mg + 125 mg + 542.3 mg + 14.4 mg = 1074.24 mg.

Amount of the final product = 121 mg.

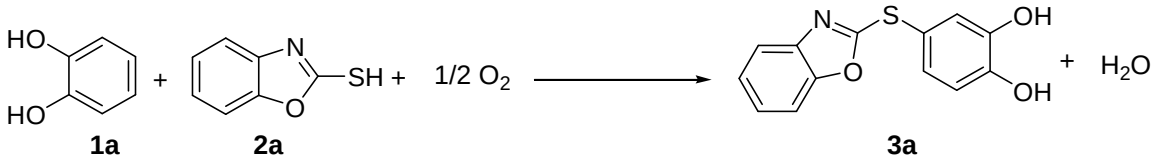
Amount of waste = 1074.24 - 121 = 953.24 mg

E-factor = Amount of waste [kg]/Amount of product [kg] = 953.24/121 = **7.88 kg kg^{-1}**.

5.2. Calculation of the atom economy[7]

The atom economy of the reaction was calculated according to the following equation:

$$\%\ \text{Atom economy} = 100 \times \frac{\text{Molecular weight of the desired product}}{\text{Molecular weight of all reactants}}.$$



1a **2a** **3a**

110 g/mol 151 g/mol 16 g/mol 259 g/mol

Atom economy = 100 × 259/277 = **94%**

5.3. Calculation of TON

Molecular weight of laccase from *A. bisporus* = 96 000 g/mol.[8]

Specific activity of the laccase = 6 U/mg.

60 U Laccase corresponds to 10 mg, ie 1.0417 × 10^{-7} mol = 1.0417 × 10^{-4} mmol.

TON = Amount of the substrate consumed [mmol] / Amount of catalyst [mmol].

TON = 0.47 [mmol] / 1.0417 × 10^{-4} [mmol] = **4512**.

5.4. Calculation of TOF

$$\text{TOF} = \frac{\text{TON}}{\text{Time}}.$$

TOF = 4512 / 16 h = **282 h^{-1}.**

6. References

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