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Supplementary Information

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Synthesis and Testing of 3-Acetyl-2,5-Disubstituted-2,3-Dihydro-1,3,4-oxadiazole Derivatives for Antifungal Activity Against Selected *Candida* Species

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General procedure for the preparation of 1,3,4-oxadiazoline derivatives (**4a**-**v**)

A mixture of *N*-acylhydrazone **3** (2.0 mmol) and acetic anhydride in excess (10.0 mL) was heated under reflux at a temperature of 140 °C for to 2 h. The reaction mixture was then cooled to a temperature of 80-100 °C, and poured into ice water (30.0 mL) to decompose the excess acetic anhydride. The reaction mixture was stirred vigorously until a precipitate formation, which was filtered, washed twice with aqueous $NaHCO_3$ (5.0%), and then with water. The purification of the compound was performed by recrystallization from ethanol.

(±)-2-(4-Isoproprylphenyl)-3-acetyl-5-(pyridin-4-yl)-2,3-dihydro-1,3,4-oxadiazole (**4b**)

^{1}H NMR (200 MHz, DMSO-d_6) δ 1.17 (d, 6H, *J* 8.0 Hz, 2 × CH_3), 2.27 (s, 3H, H-17), 2.92 (sept, 1H, *J* 6.8 Hz, CH), 7.18 (s, 1H, H-2), 7.29 (d, 2H, *J* 8.2 Hz, H-13,15), 7.39 (d, 2H, *J* 8.4 Hz, H-12,16), 7.72 (d, 2H, *J* 6.2 Hz, H-7,10), 8.74 (d, 2H, *J* 6.0 Hz, H-8,9); ^{13}C NMR (50 MHz, DMSO-d_6) δ 21.3 (C-17), 23.7 ($CH_3CH\boldsymbol{CH_3}$), 33.3 ($CH_3\boldsymbol{CH}CH_3$), 92.9 (C-2), 120.2 (C-7,10), 126.7 (C-12,16), 126.8 (C-13,15), 131.4 (C-11), 133.8 (C-6), 150.5 (C-14), 150.7 (C-8,9), 153.0 (C-5), 167.0 (C=O); FTIR (KBr) ν/cm^{-1} 1257, 1060 (C–O–C), 1504, 1550 (C=C), 1620 (C=N), 1685 (C=O); GC-MS, *m/z* (%) 43 (100), 78 (57), 106 (56), 267 (33), 51 (29), 119 (26), 91 (25), 266 (17), 148 (17), 161 (8), [M]$^+$ (7), 65 (7).

(±)-2-(4-Bromophenyl)-3-acetyl-5-(pyridin-4-yl)-2,3-dihydro-1,3,4-oxadiazole (**4h**)

^{1}H NMR (500 MHz, DMSO-d_6) δ 2.28 (s, 3H, H-17), 7.23 (s, 1H, H-2), 7.46 (d, 2H, *J* 8.6 Hz, H-13,15), 7.65 (d, 2H, *J* 8.4 Hz, H-12,16), 7.73 (d, 2H, *J* 6.0 Hz, H-7,10), 8.75 (d, 2H, *J* 5.8 Hz, H-8,9); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.2 (C-17), 92.1 (C-2), 120.1 (C-7,10), 123.4 (C-14), 128.9 (C-12,16), 131.2 (C-11), 131.8 (C-13,15), 135.5 (C-6), 150.6 (C-8,9), 152.9 (C-5), 167.1 (C=O); FTIR (KBr) ν/cm^{-1} 1068, 1215 (C–O–C), 1670 (C=O), 1624 (C=N), 1593, 1550 (C=C) e 1095 (C_{Ar}-Br); GC-MS, *m/z* (%) 43 (100), 106 (92), 78 (63), 303 (29), 345 [M$^+$] (8).

(±)-2-(2,5-Dimethoxyphenyl)-3-acetyl-5-(pyridin-4-yl)-2,3-dihydro-1,3,4-oxadiazole (**4j**)

^{1}H NMR (200 MHz, DMSO-d_6) δ 2.27 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 6.88 (s, 1H, H-16), 6.99 (d, 1H, *J* 9.2, H-14), 7.06 (d, 1H, *J* 9.2 Hz, H-13), 7.25 (s, 1H, H-2), 7.71 (d, 2H, *J* 5.0 Hz, H-7,10), 8.73 (d, 2H, *J* 5.0 Hz, H-8,9); ^{13}C NMR (50 MHz, DMSO-d_6) δ 21.2 (C-17), 55.5 (OMe), 56.3 (OMe), 90.2 (C-2), 113.4 (C-16), 114.6 (C-14), 115.8 (C-13), 120.2 (C-7,10), 124.3 (C-11), 131.7 (C-6), 150.7 (C-8,9), 151.7 (C-12), 153.0 (C-15), 153.1 (C-5), 166.8(C=O); FTIR (KBr) ν/cm^{-1} 1666 (C=O), 1627 (C=N), 1222, 1041 (C–O–C), 1597, 1550 (C=C); GC-MS (EI) *m/z* (%) 106 (100), 43 (64), 78 (51), 163 (40), 254 (38), 149 (28), 51 (27), 327 [M]$^+$ (12), 135 (11), 91 (11).

(±)-2-(4-Acetoxyphenyl)-3-acetyl-5-(pyridin-4-yl)-2,3-dihydro-1,3,4-oxadiazole (**4l**)

^{1}H NMR (500 MHz, DMSO-d_6) δ 2.27 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 7.21 (d, 2H, *J* 8.46, H-13,15), 7.24 (s, 1H, H-2), 7.55 (d, 2H, *J* 8.52 Hz, H-12,16), 7.74 (d, 2H, *J* 6.06 Hz, H-7,10), 8.75 (d, 2H, *J* 6.12 Hz, H-8,9), ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.8 (CH_3), 21.2 (CH_3), 92.2 (C-2), 120.2 (C-7,10), 122.4 (C-13,15), 128.1 (C-12,16), 131.4 (C-11), 133.8 (C-6), 150.7 (C-8,9), 151.7 (C-14), 153.0 (C-5), 167.2 (C=O), 169.1 (C=O); FTIR (KBr) ν/cm^{-1} 1068, 1195 (C–O–C), 1512, 1590 (C=C), 1616 (C=N), 1670,

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1755 (C=O); GC-MS, *m/z* (%) 43 (100), 78 (40), 106 (37), 123 (28), 51 (20), 241 (15), 283 (M^+ - C_2H_2O, 12), 148 (7).

(±)-2-(4-Acetoxyphenyl)-3-acetyl-5-phenyl-2,3-dihydro-1,3,4-oxadiazole (**4m**)

^{1}H NMR (500 MHz, DMSO-d_6) δ 2.27 (s, 3H, CH_3, H-21), 2.28 (s, 3H, CH_3, H-18), 7.20-7.86 (m, 10H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.9 (C-21), 21.3 (C-18), 91.4 (C-2), 122.4 (C-14,16), 124.0 (C-6), 126.7 (C-7,11), 128.0 (C-8,10), 129.2 (C-13,17), 132.0 (C-9), 134.2 (C-12), 151.6 (C-15), 154.7 (C-5), 166.9 (C-19), 169.1 (C-20); FTIR (KBr) ν/cm^{-1} 1662, 1759 (C=O), 1624 (C=N), 1199, 1064 (C–O–C), 1573, 1512 (C=C); GC-MS (EI) *m/z* (%) 43 (100), 105 (82), 77 (49), 51 (11), 282 (M^+ - C_2H_2O, 6), 122 (5).

(±)-2-(4-Acetoxyphenyl)-3-acetyl-5-(p-tolyl)-2,3-dihydro-1,3,4-oxadiazole (**4n**)

^{1}H NMR (200 MHz, DMSO-d_6) δ 2.26 (s, 3H, CH_3, H-21), 2.27 (s, 3H, CH_3, H-18), 2.36 (s, 3H, CH_3), 7.18-7.22 (d, 3H, H-2,14,16), 7.33 (d, 2H, *J* 8.0 Hz, H-8,10), 7.52 (d, 2H, *J* 8.6 Hz, H-13,17), 7.73 (d, 2H, *J* 8.2 Hz, H-7,11); ^{13}C NMR (50 MHz, DMSO-d_6) δ 20.8 (C-21), 21.1 (CH_3), 21.2 (C-18), 91.0 (C-2), 121.0 (C-6), 122.2 (C-14,16), 126.5 (C-7,11), 127.9 (C-8,10), 129.6 (C-13,17), 134.2 (C-12), 142.1 (C-9), 151.4 (C-15), 154.7 (C-5), 166.6 (C-19), 169.1 (C-20); FTIR (KBr) ν/cm^{-1} 1662, 1759 (C=O), 1620 (C=N), 1215, 1064 (C–O–C), 1508 (C=C); GC-MS (EI) *m/z* (%) 119 (100), 43 (58), 91 (40), 65 (17), 296 (9), 135 (8), 254 (5), 51 (4), 338 $[M]^+$ (4), 77 (4), 161 (2).

(±)-2-(4-Acetoxyphenyl)-3-acetyl-5-(4-nitrophenyl)-2,3-dihydro-1,3,4-oxadiazole (**4o**)

^{1}H NMR (500 MHz, DMSO-d_6) δ 2.27 (s, 3H, CH_3, H-18), 2.30 (s, 3H, CH_3, H-21), 7.21 (d, 2H, *J* 8.5 Hz, H-14,16), 7.26 (s, 1H, H-2), 7.55 (d, 2H, *J* 8.5 Hz, H-13,17), 8.07 (d, 2H, *J* 9.0 Hz, H-7,11), 8.34 (d, 2H, *J* 9.0 Hz, H-8,10); ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.8 (C-21), 21.2 (C-18), 92.3 (C-2), 122.3 (C-14,16), 124.4 (C-8,10), 127.9 (C-7,11), 128.1 (C-13,17), 129.8 (C-6), 133.8 (C-12), 149.1 (C-9), 151.7 (C-15), 153.2 (C-5), 167.2 (C-19), 169.2 (C-20); FTIR (KBr) ν/cm^{-1} 1666, 1755 (C=O), 1,620 (C=N), 1219, 1076 (C–O–C), 1597 (C=C); GC-MS (EI) *m/z* (%) 43 (100), 285 (11), 327 (M^+ - C_2H_2O, 8).

(±)-2-(4-Acetoxyphenyl)-3-acetyl-5-(4-chlorophenyl)-2,3-dihydro-1,3,4-oxadiazole (**4p**)

^{1}H NMR (500 MHz, DMSO-d_6) δ 2.27 (s, 3H, H-18), 2.27 (s, 3H, H-21), 7.20 (d, 2H, *J* 8.4 Hz, H-14,16), 7.21 (s, 1H, H-2), 7.53 (d, 2H, *J* 8.6 Hz, H-13,17), 7.61 (d, 2H, *J* 8.8 Hz, H-7,11), 7.84 (d, 2H, *J* 8.8 Hz, H-8,10); ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.5 (C-21), 20.9 (C-18), 91.4 (C-2), 122.1 (C-14,16), 122.5 (C-6), 127.7 (C-8,10), 128.1 (C-7,11), 129.0 (C-13,17), 133.7 (C-12), 136.4 (C-9), 151.3 (C-15), 153.6 (C-5), 166.7 (C-19), 168.8 (C-20); FTIR (KBr) ν/cm^{-1} 1662, 1755 (C=O), 1631 (C=N), 1215, 1064 (C–O–C), 1604, 1508 (C=C); GC-MS (EI) *m/z* (%) 43 (100), 139 (52), 111 (21), 141 (18), 75 (10), 274 (9), 316 (M^+ - C_2H_2O, 8), 156 (3), 113 (3).

(±)-2-(4-Acetoxyphenyl)-3-acetyl-5-(4-methoxyphenyl)-2,3-dihydro-1,3,4-oxadiazole (**4q**)

^{1}H NMR (500 MHz, DMSO-d_6) δ 2.25 (s, 3H, CH_3, H-18), 2.27 (s, 3H, CH_3, H-21), 3.81 (s, 3H, OCH_3), 7.06 (d, 2H, *J* 9.0 Hz, H-8,10), 7.17 (s, 1H, H-2), 7.20 (d, 2H, *J* 8.6 Hz, H-14,16), 7.51 (d, 2H, *J* 8.4 Hz, H-13,17), 7.78 (d, 2H, *J* 9.0 Hz, H-7,11); ^{13}C NMR (125 MHz, DMSO-d_6) δ 20.8 (C-21), 21.2 (C-18), 55.5 (OCH_3), 90.9 (C-2), 114.5 (C-8,10), 116.0 (C-6), 122.2 (C-7,11), 127.9 (C-14,16), 128.4 (C-13,17), 134.3 (C-12), 151.4 (C-15), 154.7 (C-5), 162.0 (C-9), 166.6 (C-19), 169.1 (C-20); FTIR (KBr) ν/cm^{-1} 1658, 1759 (C=O), 1631 (C=N), 1207, 1064 (C–O–C), 1608, 1573 (C=C); GC-MS (EI) *m/z* (%) 135 (100), 43 (83), 77 (15), 92 (5), 312 ((M^+ - C_2H_2O, 1).

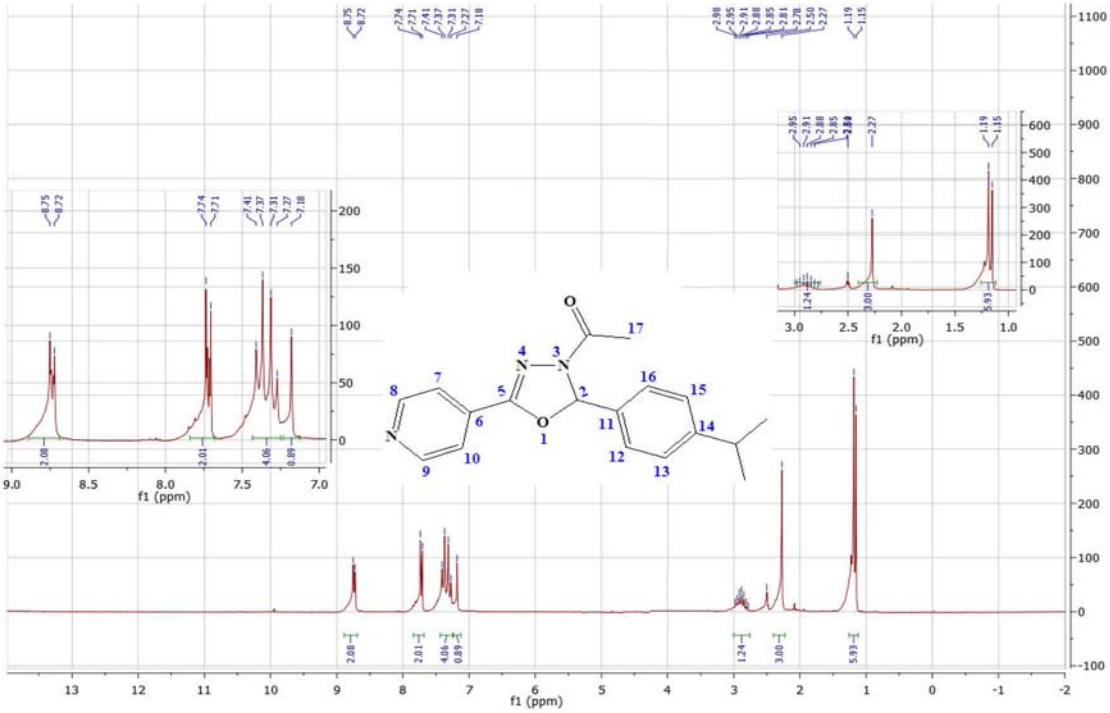

Figure S1. [1]H NMR spectrum (200 MHz, DMSO-d_6) of **4b**.

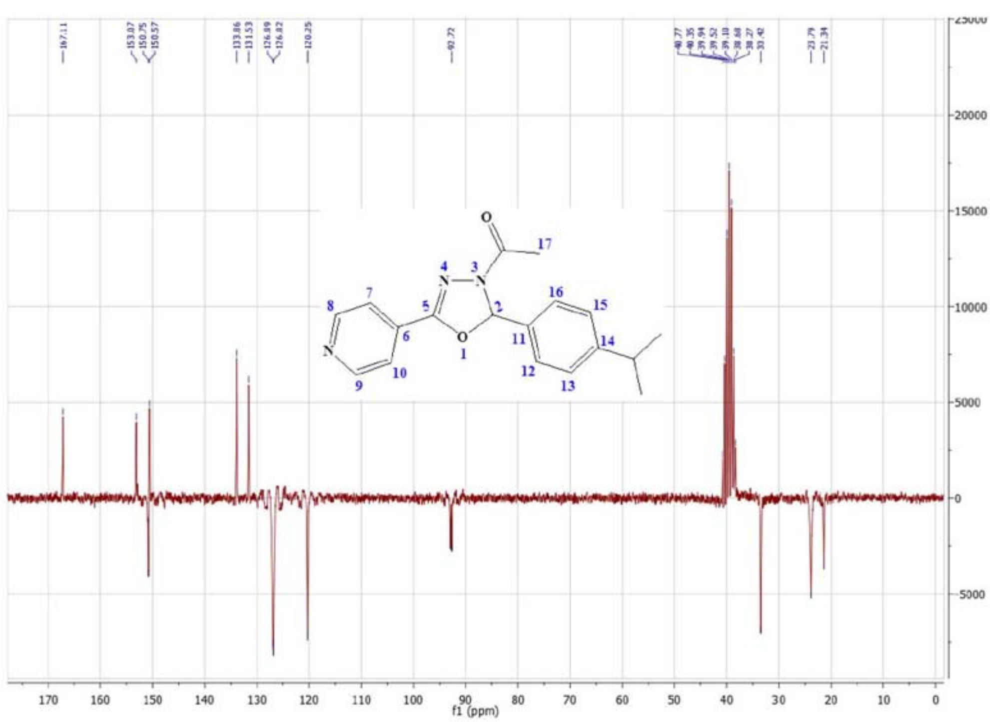

Figure S2. [13]C NMR spectrum (50 MHz, DMSO-d_6) of **4b**.

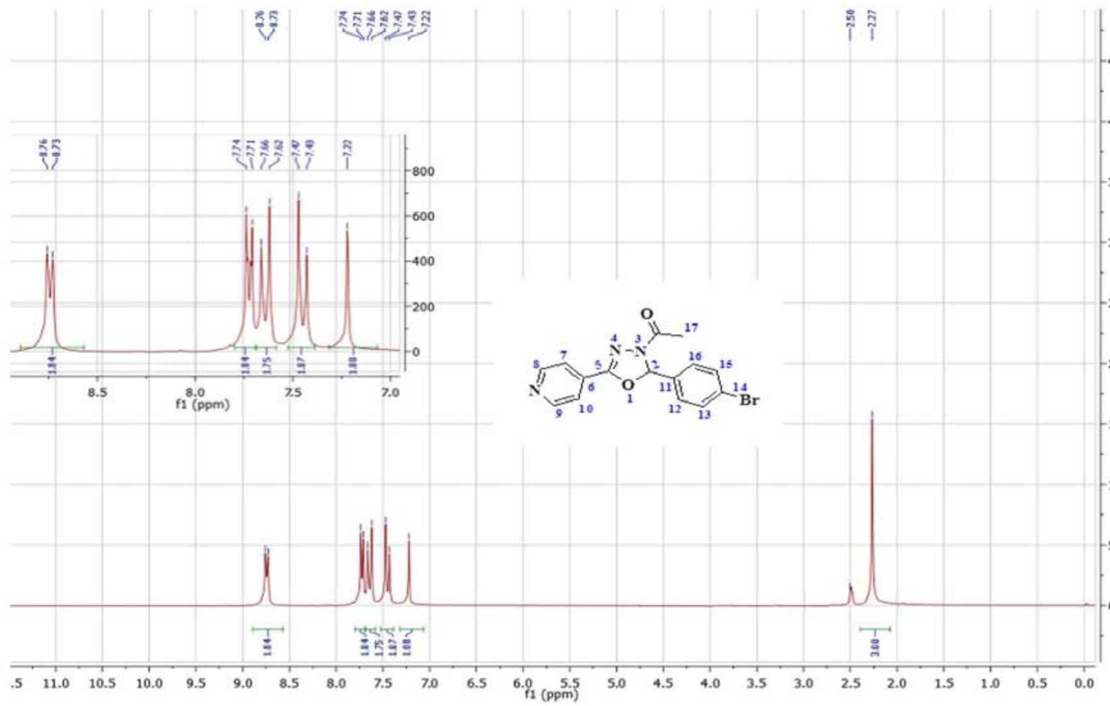

Figure S3. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) of **4h**.

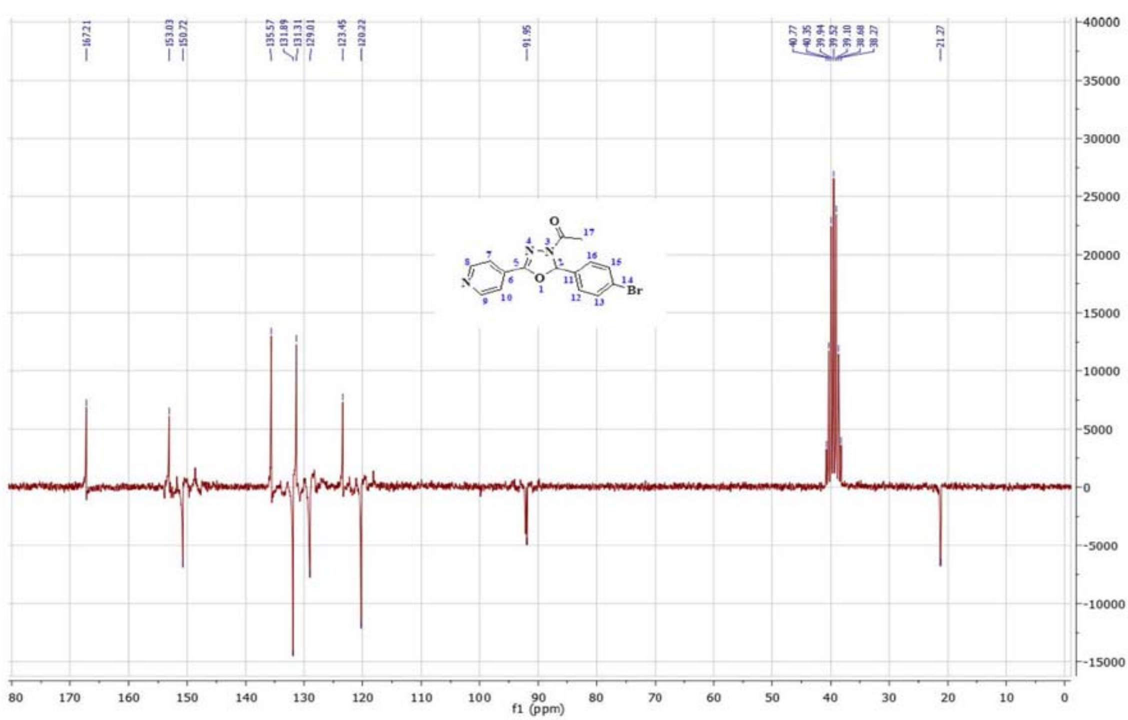

Figure S4. ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of **4h**.

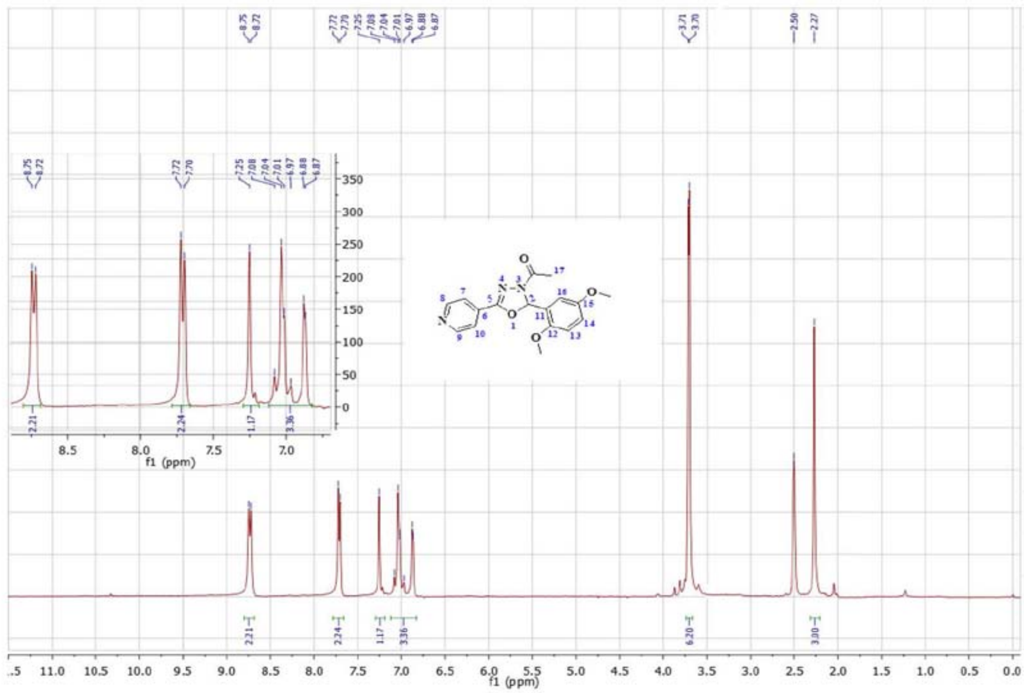

Figure S5. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) of **4j**.

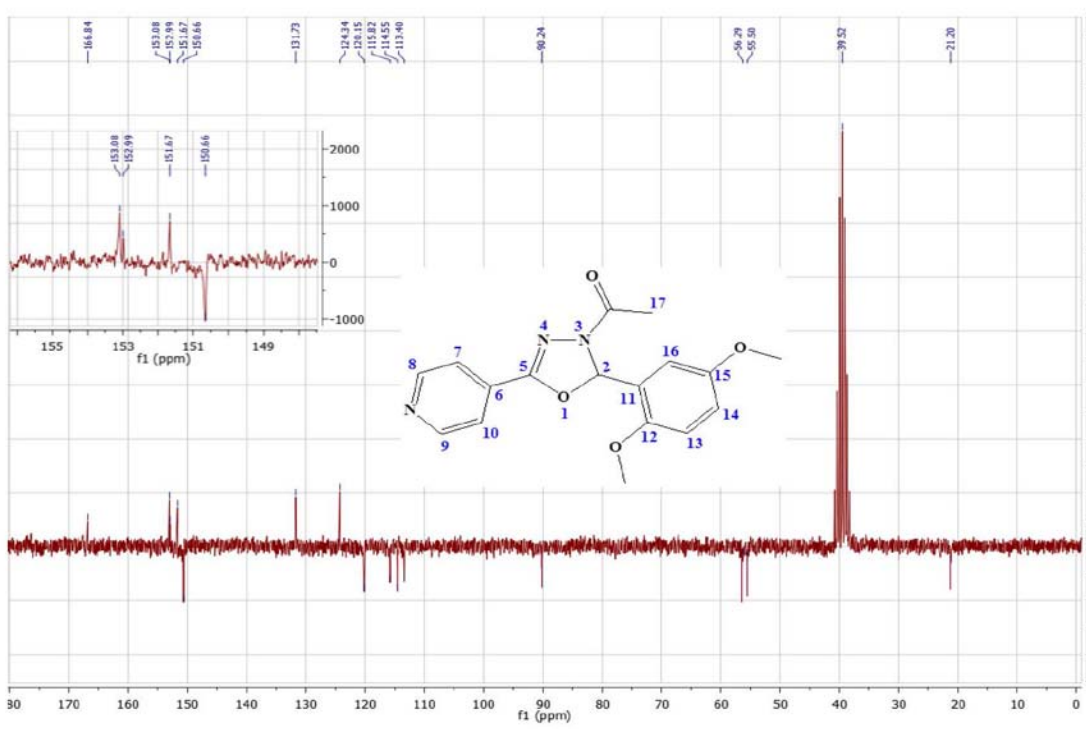

Figure S6. ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of **4j**.

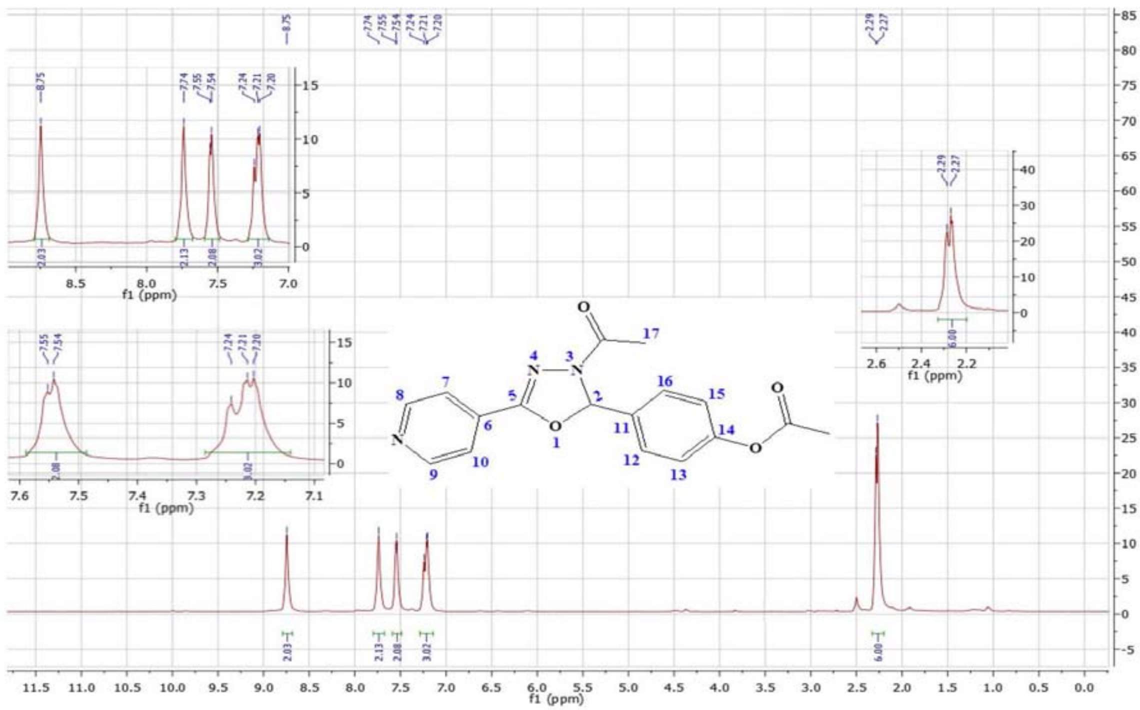

Figure S7. [1]H NMR spectrum (500 MHz, DMSO-d_6) of **4l**.

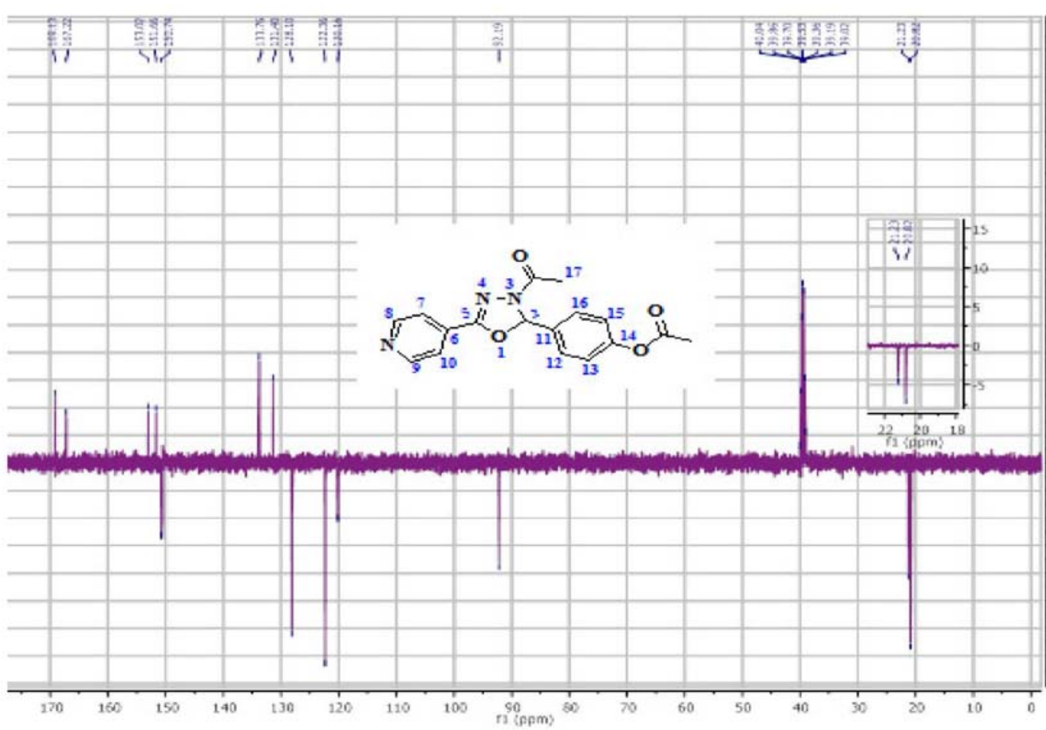

Figure S8. [13]C NMR spectrum (125 MHz, DMSO-d_6) of **4l**.

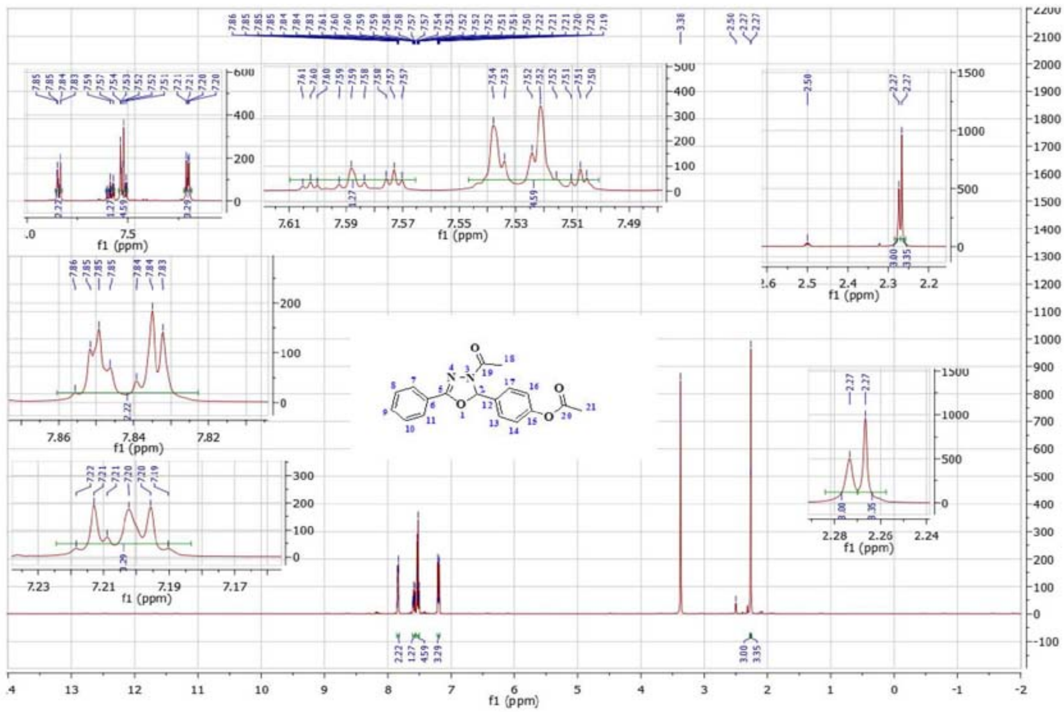

Figure S9. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of **4m**.

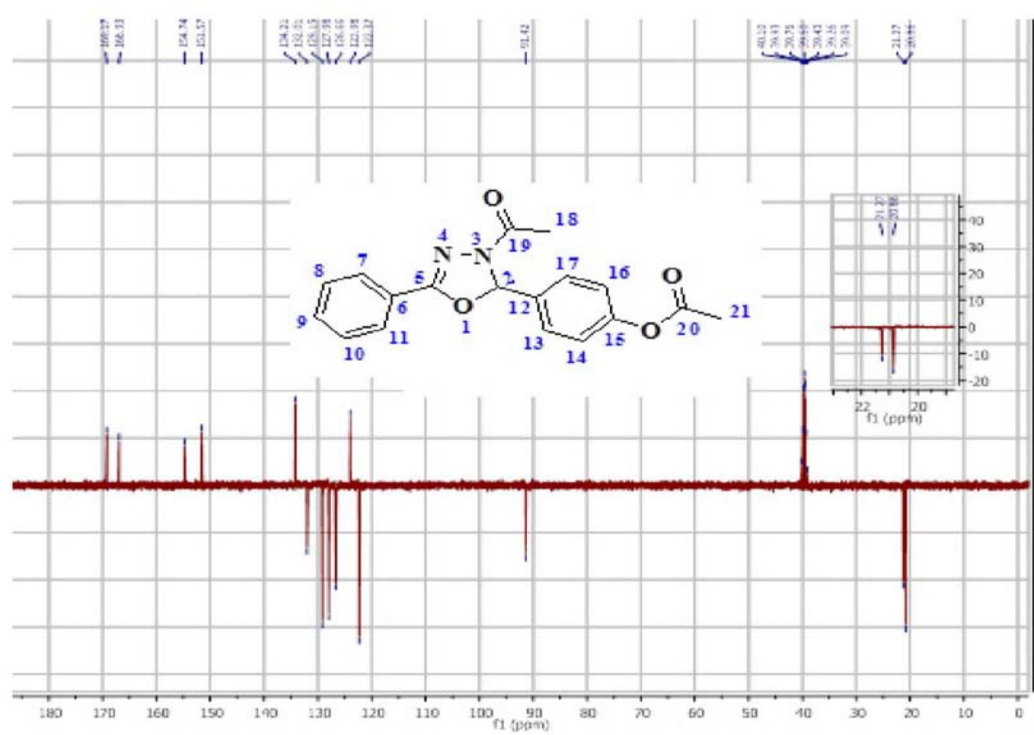

Figure S10. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of **4m**.

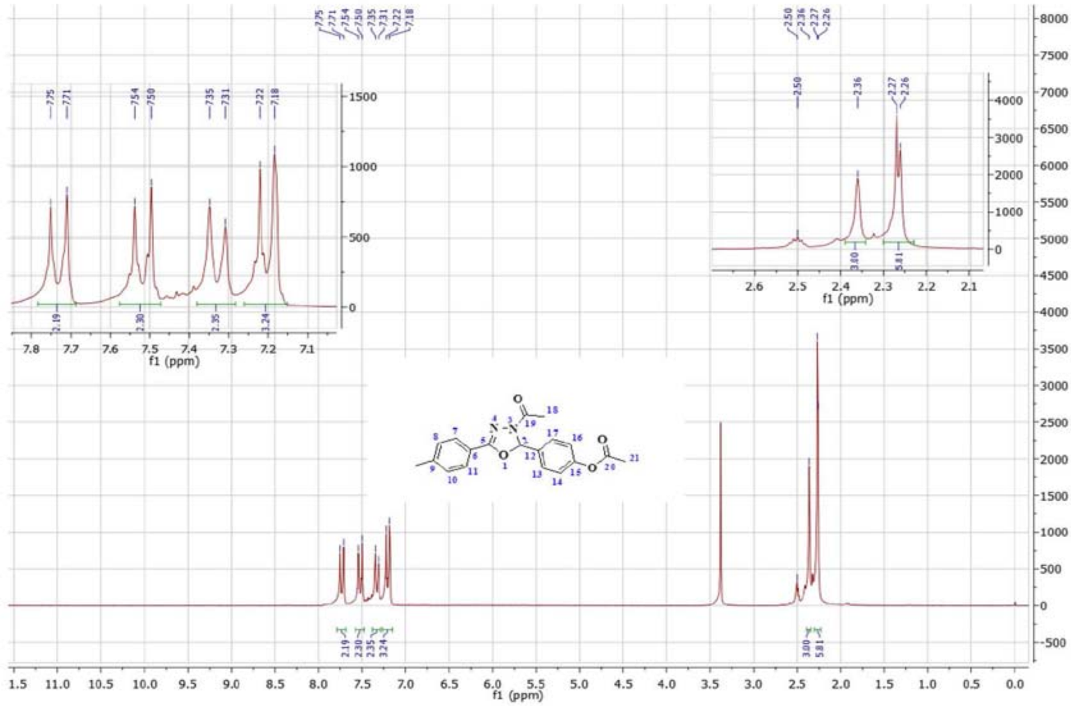

Figure S11. ^{1}H NMR spectrum (200 MHz, DMSO-d_6) of **4n**.

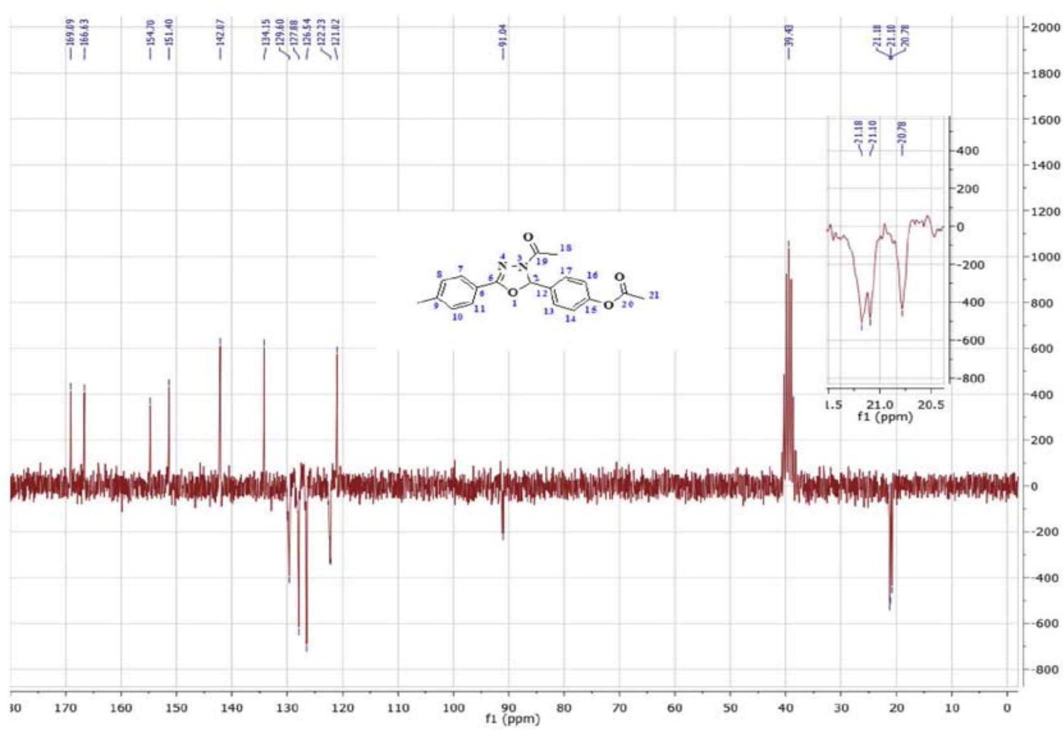

Figure S12. ^{13}C NMR spectrum (50 MHz, DMSO-d_6) of **4n**.

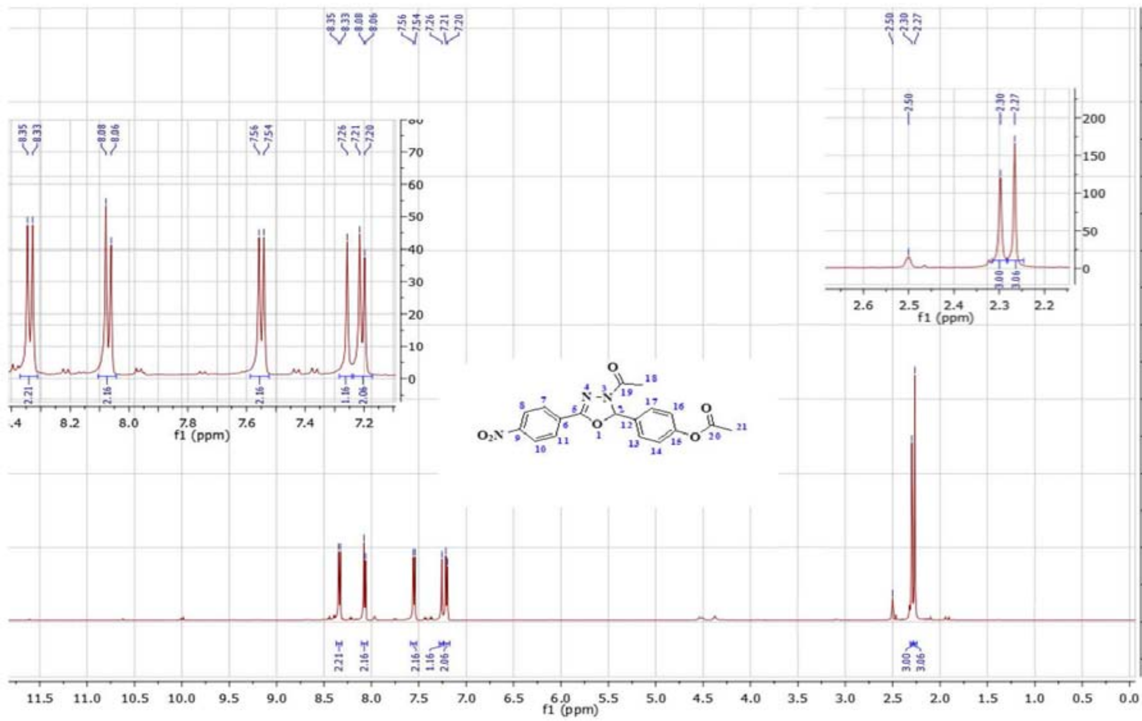

Figure S13. [1]H NMR spectrum (500 MHz, DMSO-d_6) of **4o**.

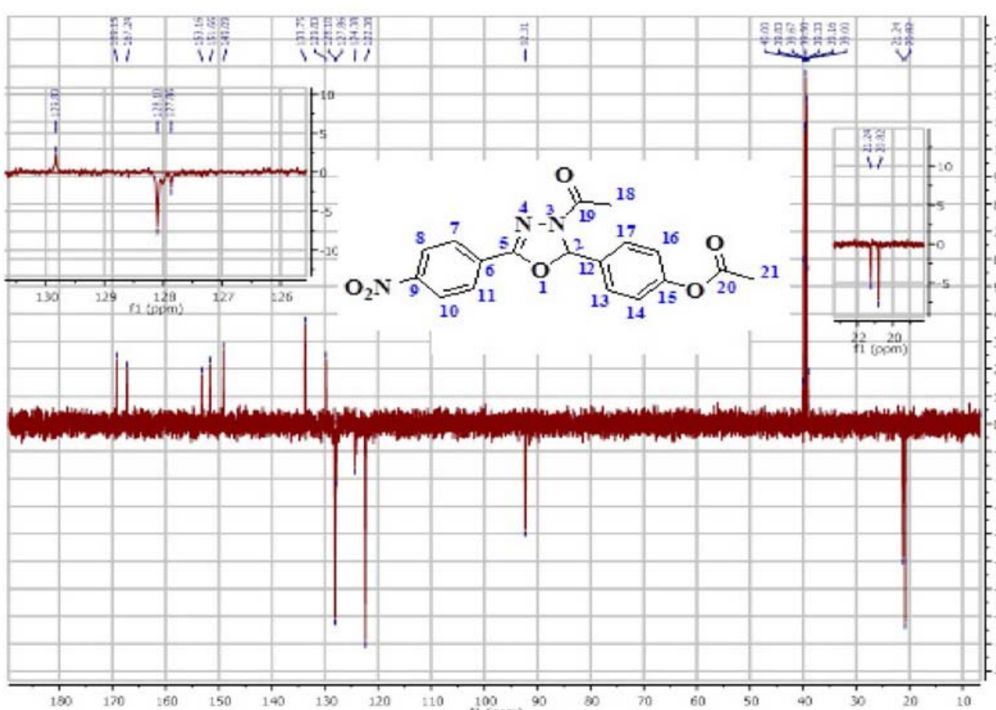

Figure S14. [13]C NMR spectrum (125 MHz, DMSO-d_6) of **4o**.

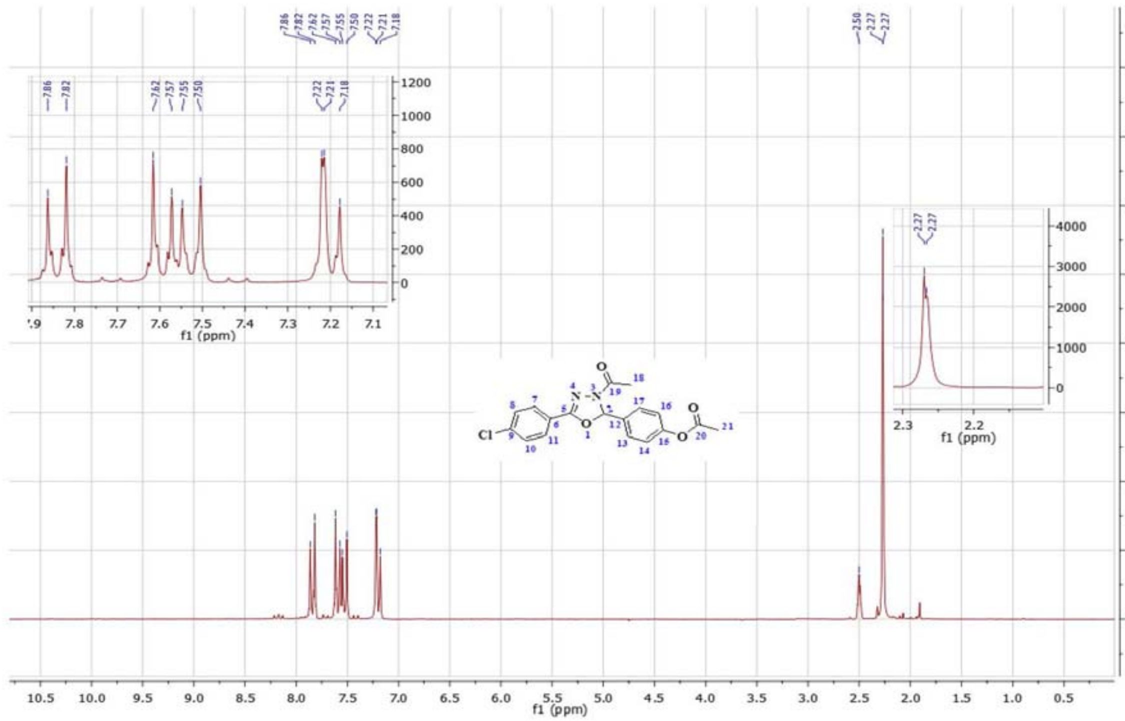

Figure S15. [1]H NMR spectrum (200 MHz, DMSO-d_6) of **4p**.

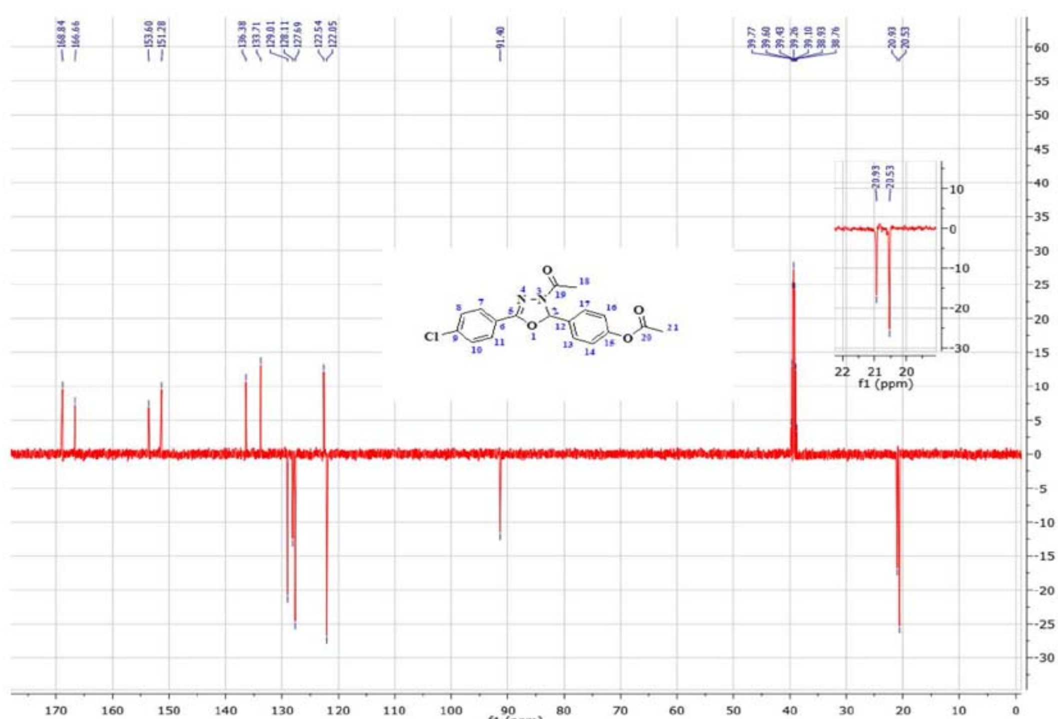

Figure S16. [13]C NMR spectrum (50 MHz, DMSO-d_6) of **4p**.

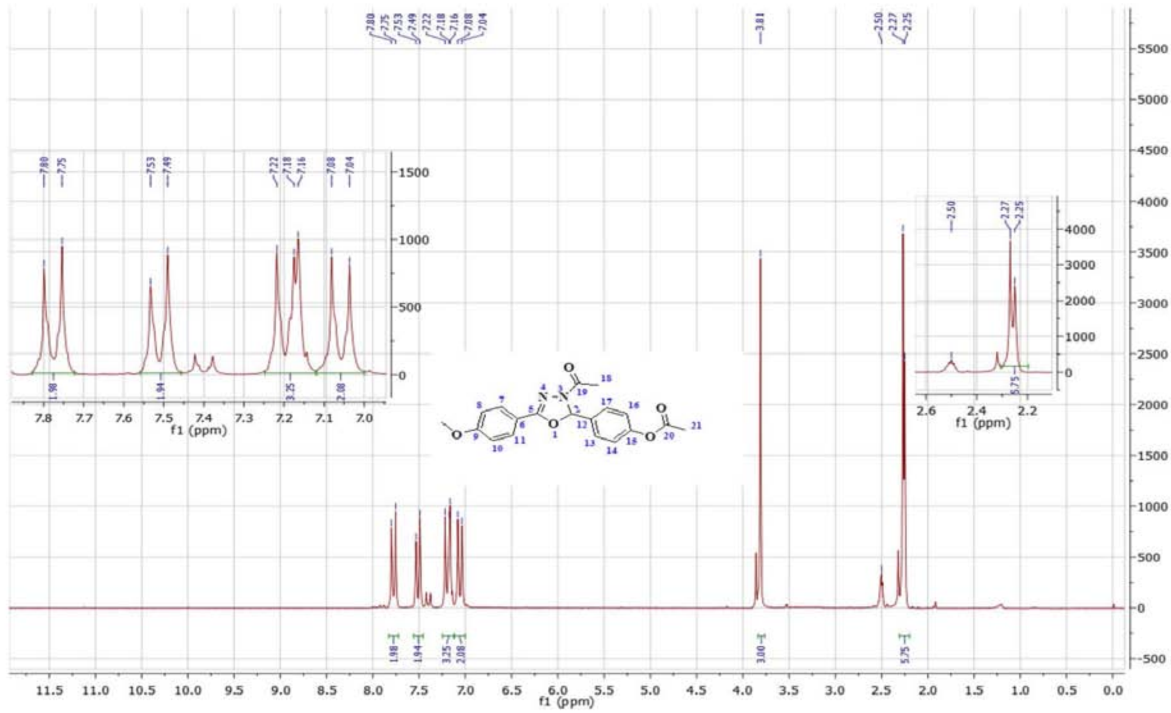

Figure S17. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of **4q**.

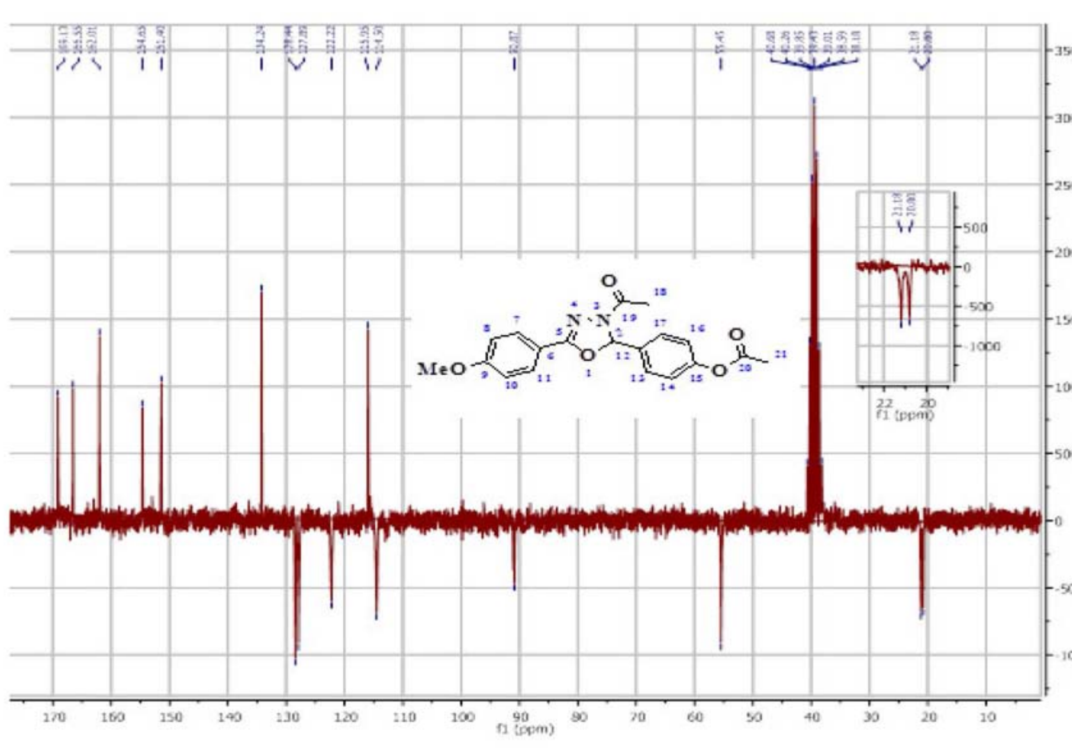

Figure S18. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of **4q**.