Supporting Information

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One-pot and multi-step syntheses of new 2-(4,5-dihydro-1*H*-pyrazol-1-yl) thiazole derivatives

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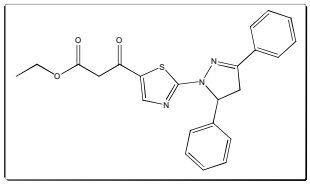
Ethyl 3-(2-(3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)thiazol-5-yl)-3-oxopropanoate (C1)



Color: Yellow, Yield 0.344 g, 82%, mp 158-159 ºC, FT-IR (ATR, cm^{-1}): υ_{max} 3093-3034 (Ar-H); 2989-2901 (aliphatic C-H), 1726 (C=O, ester); 1641 (C=O, ketone); 1566-1489 (C=N and C=C). ^{1}H-NMR (300 MHz; $CDCl_3$, ppm): δ 7.79-7.26 (m, 10H, Ar-H); 7.81 (s, CH, thiazole); 5.74-5.69 (dd, J_{trans}= 5.0 Hz, J_{cis}= 11.7 Hz, 1H, C_5H-pyrazole); 4.18 (q, *J*= 7.1 Hz, 2H, O<u>CH_2</u>CH_3); 4.01-3.91 (dd, J_{gem}= 17.7 Hz, J_{trans}= 11.8 Hz, 1H, C_4H-pyrazole); 3.74 (s, 2H, CH_2); 3.38-3.30 (dd, J_{gem}= 17.7 Hz, J_{cis}= 5.1 Hz, 1H, C_4H-pyrazole); 1.25 (t, *J*= 7.1 Hz, 3H, OCH_2<u>CH_3</u>). ^{13}C-NMR (75 MHz; $CDCl_3$, ppm): δ 183.2 (C=O, ketone); 166.6 (C=O, ester); 161.3; 155.0; 148.9; 140.6; 130.7; 129.1; 128.9; 128.8; 128.2; 126.9; 126.8; 125.7 (C=C and C=N); 63.7 (C_5-pyrazole); 61.5 (OCH_2); 45.8 (CH_2); 43.9 (C_4-pyrazole); 14.1 (CH_3). Elemental analysis calcd: C, 65.85; H, 5.05; N, 10.02; S, 7.64. Found: C, 65.94; H, 5.01; N, 9.78; S, 7.33 %.

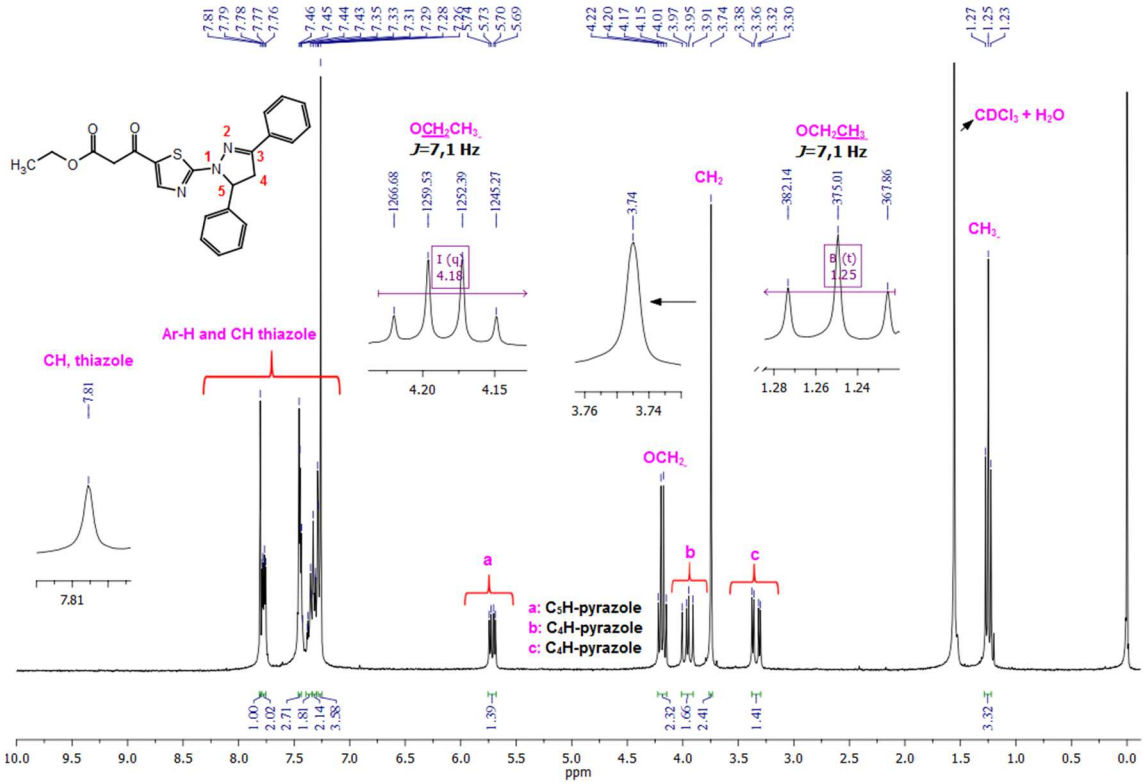


Figure S1: ^{1}H NMR spectra of **C1**

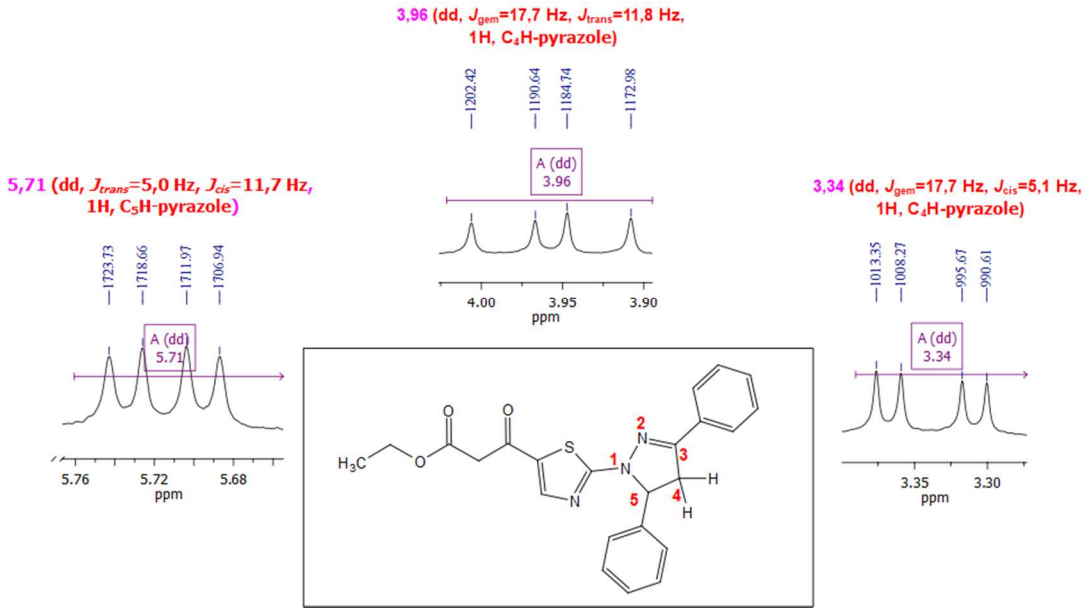


Figure S2: ^{1}H NMR splitting of the pyrazole protons (C_4H- and C_5H-) of compound **C1**

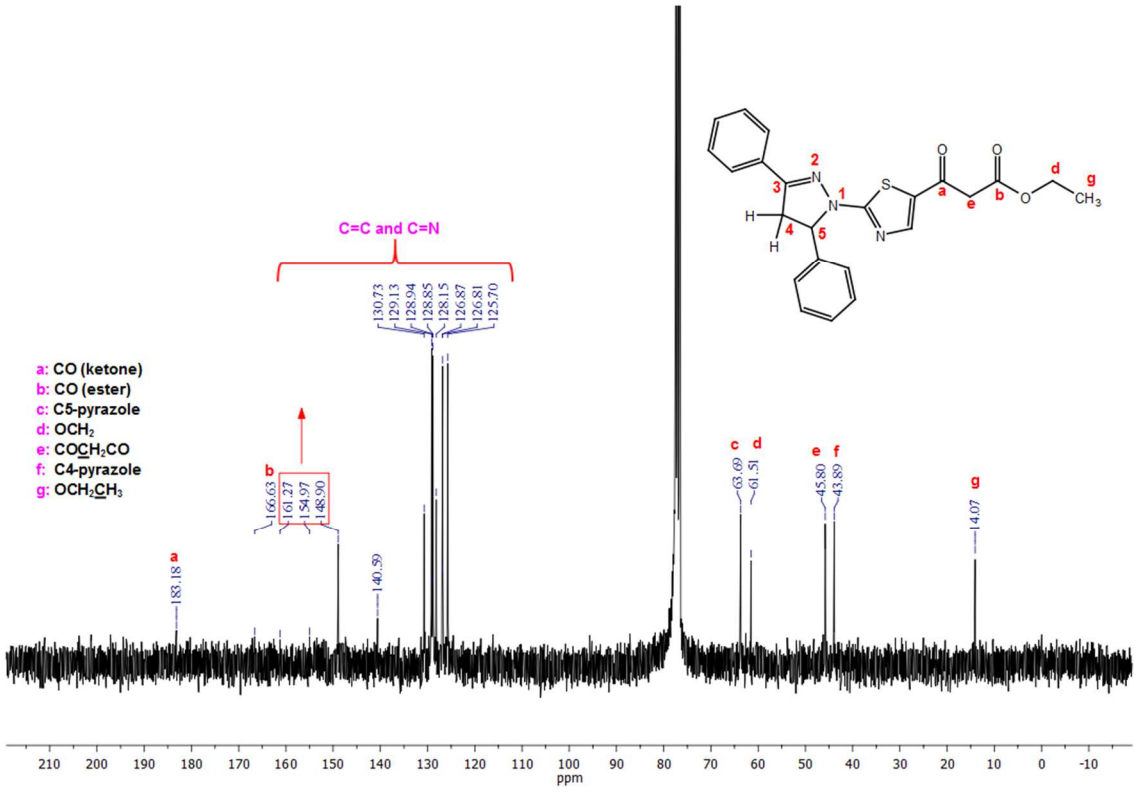
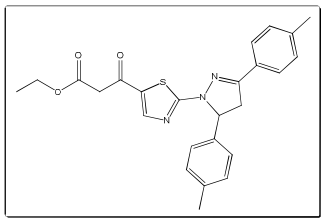


Figure S3: ^{13}C NMR spectra of **C2**

Ethyl 3-(2-(3,5-dip-tolyl-4,5-dihydro-1*H*-pyrazol-1-yl)thiazol-5-yl)-3-oxopropanoate (C2)



Color: Yellow, Yield 0.353 g, 79%, mp 145-146 °C, FT-IR (ATR, cm^{-1}): υ_{max} 3092-3030 (Ar-H); 2984-2868 (aliphatic C-H), 1741 (C=O, ester); 1635 (C=O, ketone); 1612-1500 (C=N and C=C). ^{1}H-NMR (300 MHz; $CDCl_3$, ppm): δ 7.81 (s, CH, thiazole); 7.67-7.15 (m, 8H, Ar-H); 5.68-5.62 (dd, J_{trans}= 5.0 Hz, J_{cis}= 11.7 Hz, 1H, C_5H-pyrazole); 4.18 (q, *J*= 7.1 Hz, 2H, O<u>CH_2</u>CH_3); 3.96-3.86 (dd, J_{gem}= 17.6 Hz, J_{trans}= 11.7 Hz, 1H, C_4H-pyrazole); 3.74 (s, 2H, CH_2); 3.33-3.26 (dd, J_{gem}= 17.6 Hz, J_{cis}= 5.0 Hz, 1H, C_4H-pyrazole); 2.40 and 2.32 (s, 6H, 2 x Ar-CH_3); 1.25 (t, *J*= 7.1 Hz, 3H, OCH_2<u>CH_3</u>). ^{13}C-NMR (75 MHz; $CDCl_3$, ppm): δ 183.1 (C=O, ketone); 170.0 (C=O, ester); 167.2; 155.2; 149.1; 141.2; 137.9; 137.8; 129.8; 129.6; 129.4; 127.9; 126.8; 125.7 (C=C and C=N); 63.4 (C5-pyrazole); 61.5 (OCH_2); 45.8 (CH_2); 44.0 (C4-pyrazole); 21.6; 21.1 (2 x Ar-CH_3); 14.1 (CH_3). Elemental analysis calcd: C, 67.09; H, 5.63; N, 9.39; S, 7.16. Found: C, 67.02; H, 5.33; N, 9.08; S, 7.40 %.

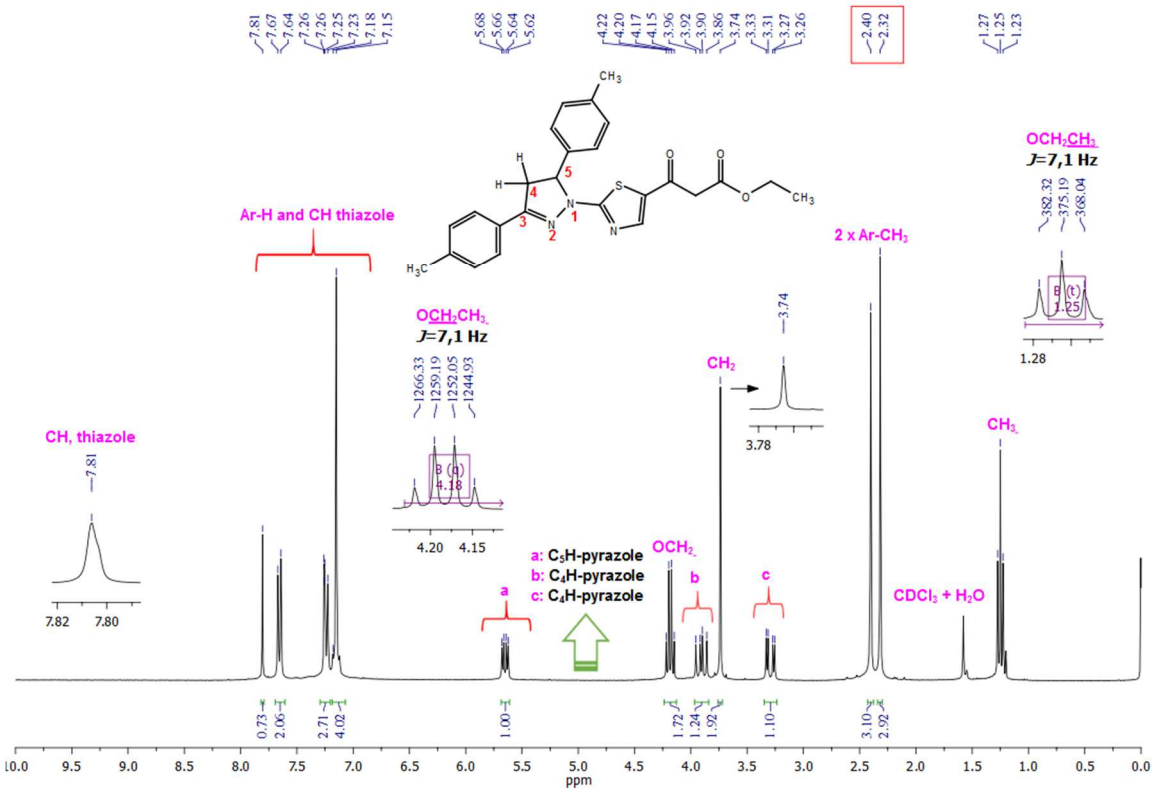


Figure S4: ^{1}H NMR spectra of **C2**

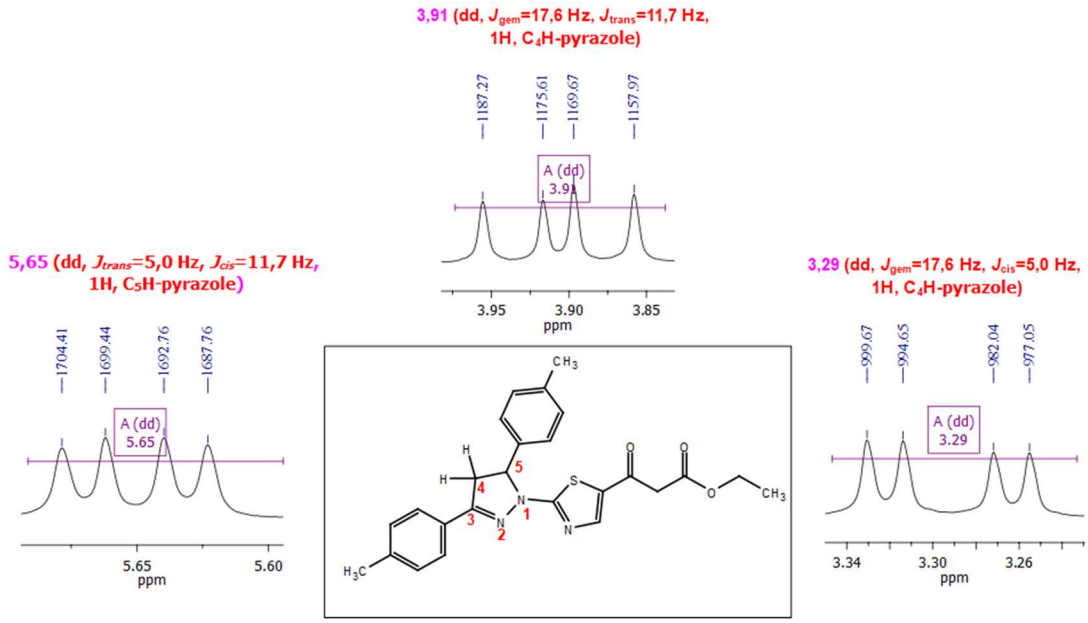


Figure S5: ^{1}H-NMR splitting of the pyrazole protons (C_4H- and C_5H-) of compound **C2**

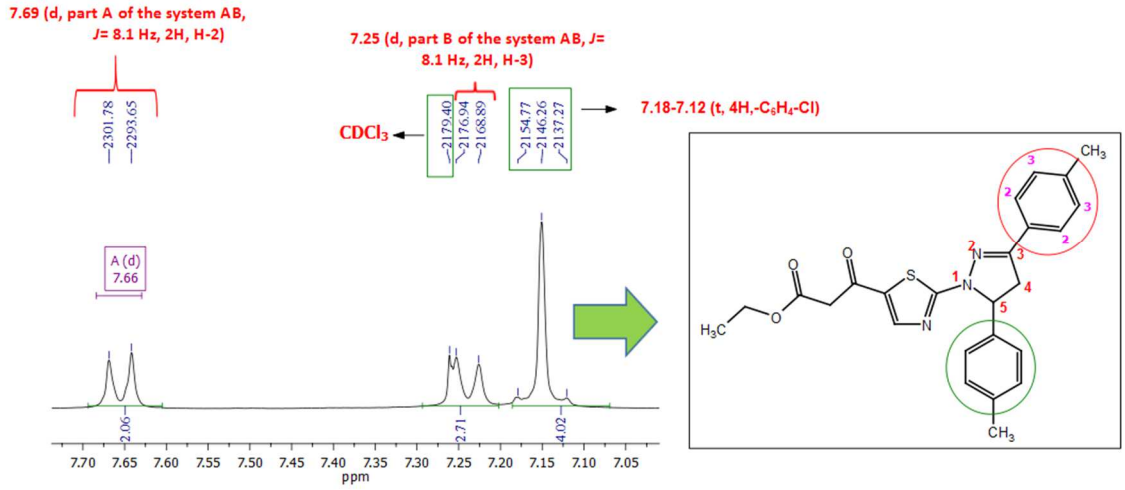


Figure S6: ^{1}H NMR splitting of *p*-disubstituted benzene group protons in compound **C2**

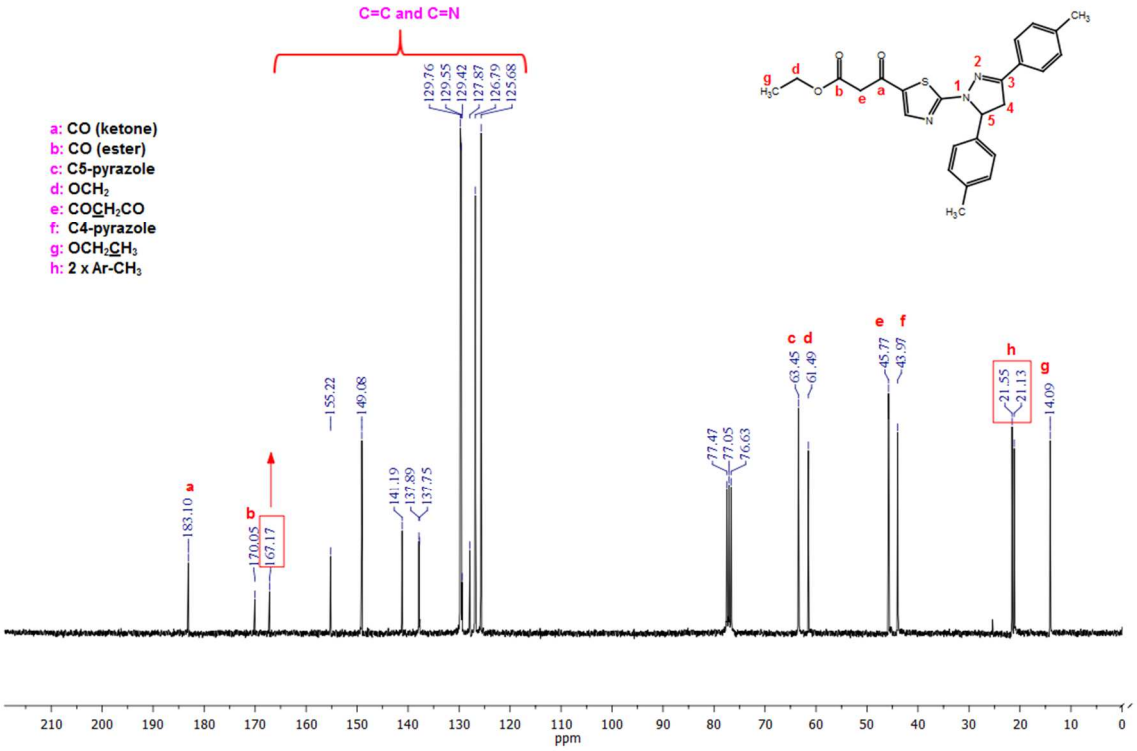
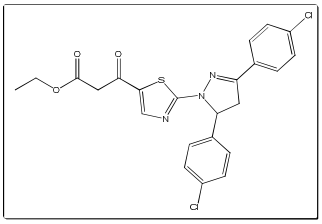


Figure S7: ^{13}C NMR spectra of **C2**

Ethyl 3-(2-(3,5-bis (4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)thiazol-5-yl)-3-oxopropanoate (C3)



Color: Yellow, Yield 0.346 g, 71%, mp 135-137 ^{o}C, FT-IR (ATR, cm^{-1}): υ_{max} 3064-3003 (Ar-H); 2981-2936 (aliphatic C-H), 1737 (C=O, ester); 1642 (C=O, ketone); 1596-1487 (C=N and C=C). ^{1}H-NMR (300 MHz; $CDCl_3$, ppm): δ 7.79 (s, CH, thiazole); 7.69 (d, part A of the system AB, *J*=8.5 Hz, 2H, H-2), 7.41 (d, part B of the system AB, *J*=8.5 Hz, 2H, H-3), 7.32 (d, part A of the system AB, *J*=8.4 Hz, 2H, H-3'), 7.21 (d, part B of the system AB, *J*=8.5 Hz, 2H, H-2'); 5.71-5.65 (dd, J_{trans}= 5.2 Hz, J_{cis}= 11.8 Hz, 1H, C_5H-pyrazole); 4.19 (q, *J*=7.1 Hz, 2H, O$\underline{CH_2}$CH$_3$); 3.98-3.88 (dd, J_{gem}= 17.7 Hz, J_{trans}= 11.8 Hz, 1H, C_4H-pyrazole); 3.75 (s, 2H, CH_2); 3.30-3.22 (dd, J_{gem}= 17.7 Hz, J_{cis}= 5.3 Hz, 1H, C_4H-pyrazole); 1.25 (t, *J*=7.1 Hz, 3H, OCH$_2\underline{CH_3}$). ^{13}C-NMR (75 MHz; $CDCl_3$, ppm): δ 183.3 (C=O, ketone); 170.0 (C=O, ester); 167.0; 153.7; 148.6; 139.0; 136.9; 134.1; 130.2; 129.4; 129.2; 128.9; 128.0; 127.2 (C=C and C=N); 63.3 (C_5-pyrazole); 61.6 (OCH_2); 45.8 (CH_2); 43.6 (C_4-pyrazole); 14.1 (CH_3). Elemental analysis calcd: C, 56.56; H, 3.92; N, 8.60; S, 6.57. Found: C, 56.23; H, 3.97; N, 8.62; S, 6.35 %.

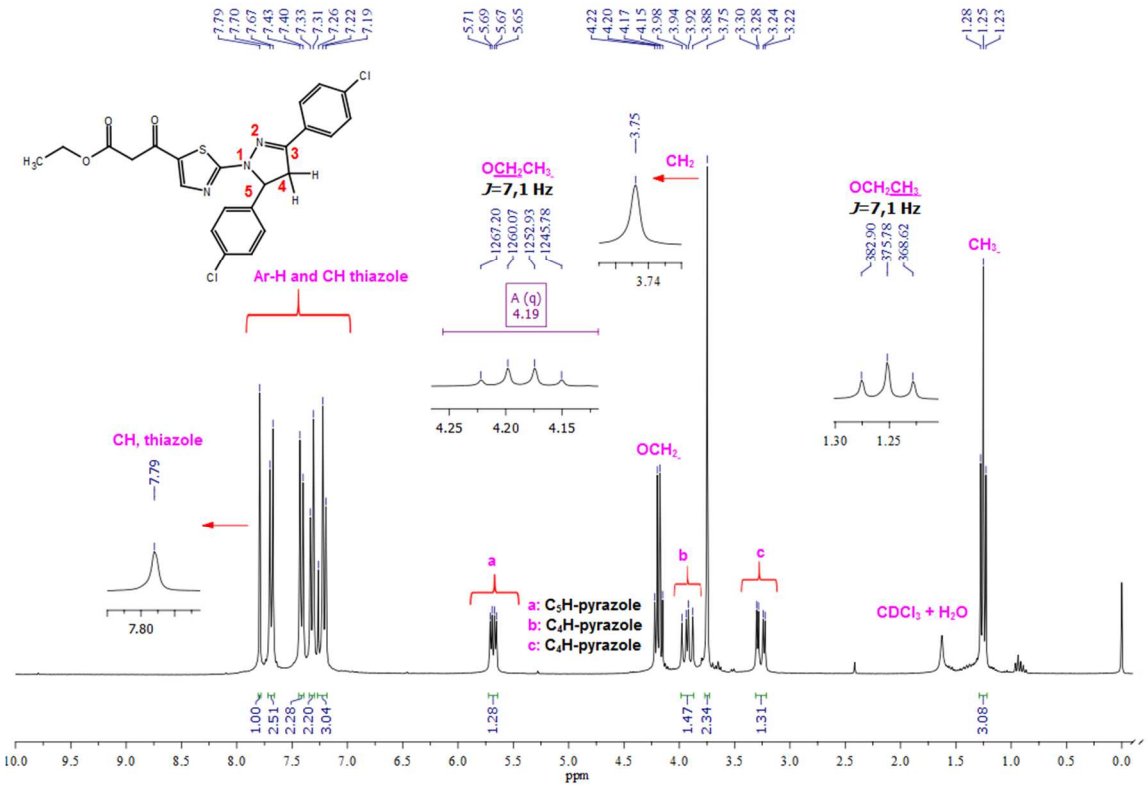


Figure S8: ^{1}H-NMR spectra of **C3**

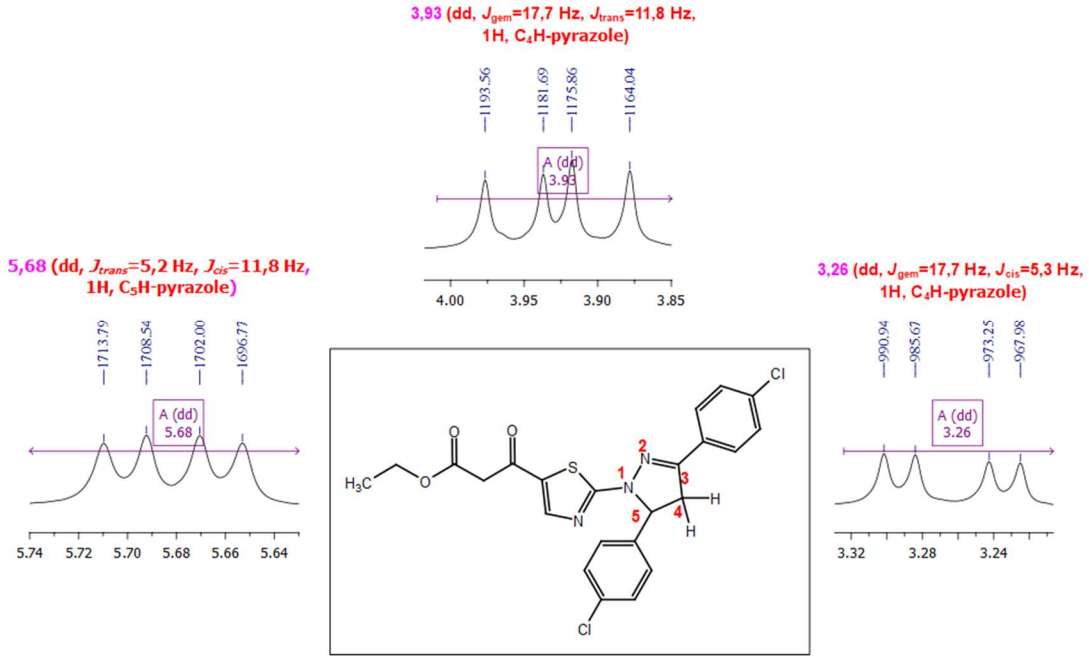


Figure S9: ^{1}H NMR splitting of the pyrazole protons (C_4H- and C_5H-) of compound **C3**

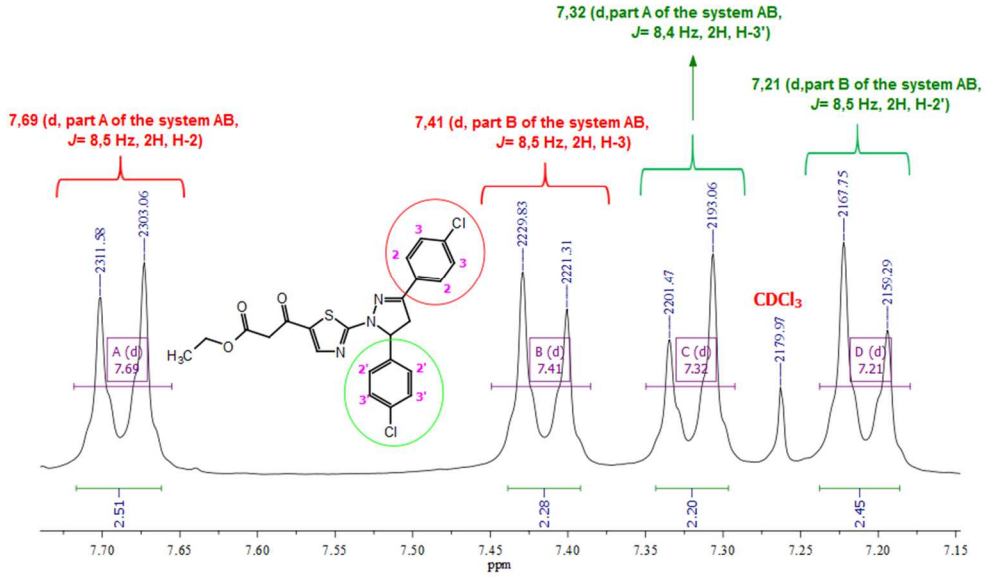


Figure S10: ^{1}H NMR splitting of *p*-disubstituted benzene group protons in compound **C3**

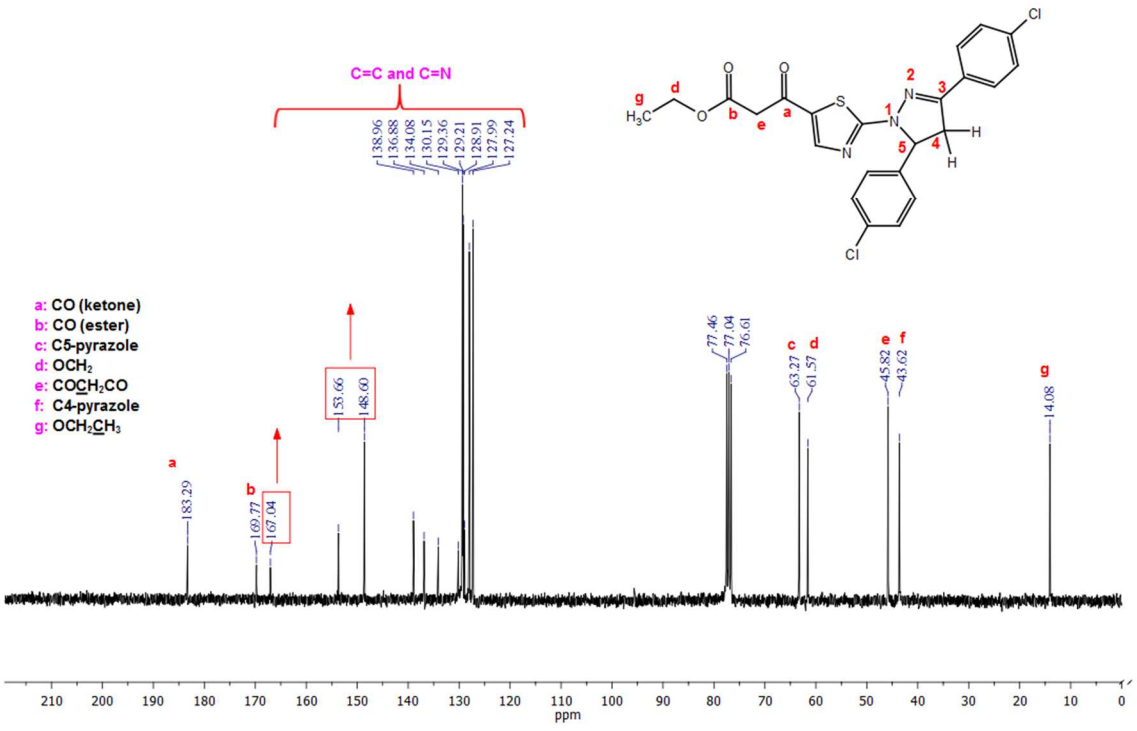
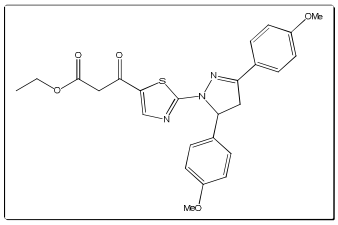


Figure S11: ^{13}C NMR spectra of **C3**

Ethyl 3-(2-(3,5-bis(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-5-yl)-3-oxopropanoate (C4)



Color: Yellow, Yield 0.354 g, 74%, mp 117-118 °C, FT-IR (ATR, cm^{-1}): υ_{max} 3074-2841 (Ar-H and aliphatic C-H); 1734 (C=O, ester); 1633 (C=O, ketone); 1607-1463 (C=N and C=C), 1248 (C-O). ^{1}H-NMR (400 MHz; $CDCl_3$, ppm): δ 7.83 (s, CH, thiazole); 7.73 (d, part A of the system AB, *J*=8.9 Hz, 2H, H-2), 7.22 (d, part B of the system AB, *J*=8.7 Hz, 2H, H-3), 6.97 (d, part A of the system AB, *J*=8.9 Hz, 2H, H-3'), 6.88 (d, part B of the system AB, *J*=8.7 Hz, 2H, H-2'); 5.67-5.62 (dd, J_{trans}= 4.9 Hz, J_{cis}= 11.6 Hz, 1H, C_5H-pyrazole); 4.20 (q, *J*=7.1 Hz, 2H, OCH_2CH_3); 3.96-3.86 (dd, J_{gem}= 17.6 Hz, J_{trans}= 11.6 Hz, 1H, C_4H-pyrazole); 3.76 (s, 2H, CH_2); 3.34-3.26 (dd, J_{gem}= 17.6 Hz, J_{cis}= 4.9 Hz, 1H, C_4H-pyrazole); 1.27 (t, *J*=7.1 Hz, 3H, OCH_2CH_3). ^{13}C-NMR (100 MHz; DMSO-d_6, ppm): δ 184.3 (C=O, ketone); 169.1 (C=O, ester); 168.0; 161.8; 159.2; 157.1; 151.1; 133.5; 129.2; 128.8; 127.7; 123.2; 114.9; 114.6 (C=C and C=N); 63.2 (C_5-pyrazole); 61.1 (OCH_2); 55.9 and 55.5 (2 x OCH_3); 45.1 (CH_2); 44.1 (C_4-pyrazole); 14.4 (CH_3). Calcd. for $C_{25}H_{25}N_3O_5S$ (479.55): C, 62.61; H, 5.25; N8.76; S, 6.69. Found: C, 62.44; H, 5.37; N, 8.83; S, 6.51 %.

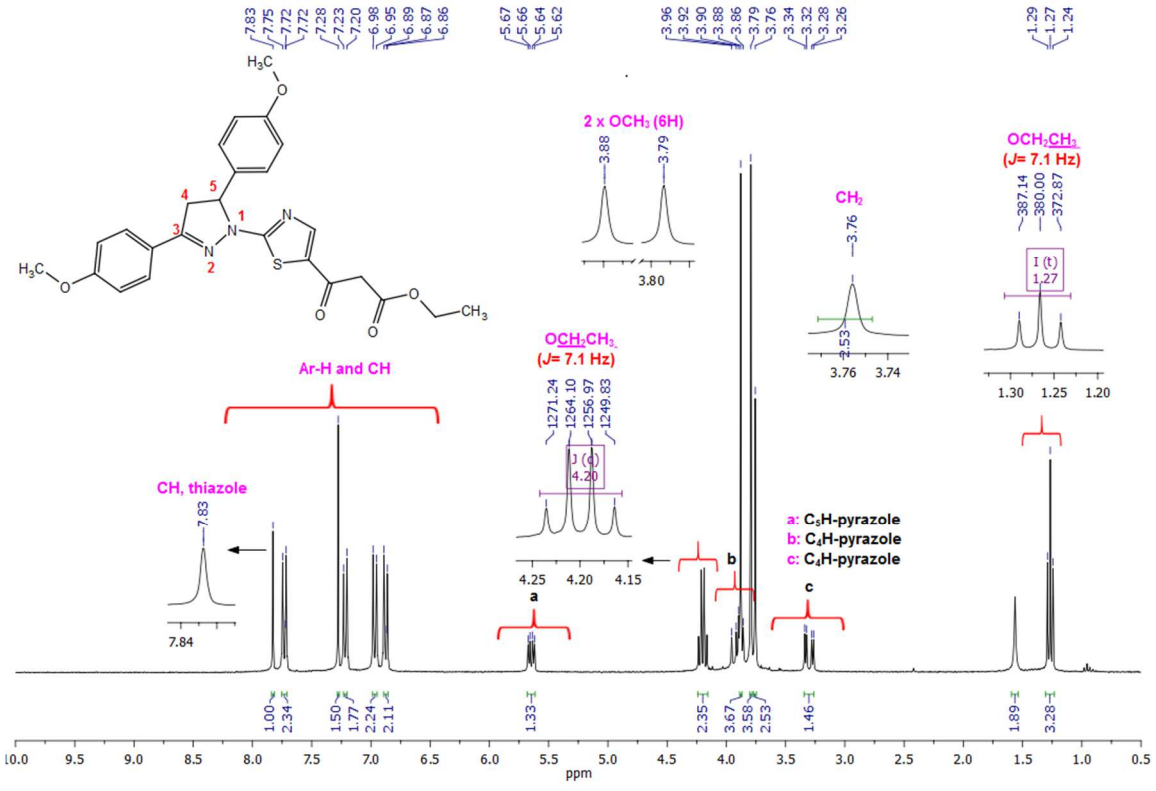


Figure S12: ^{1}H-NMR spectra of **C4**

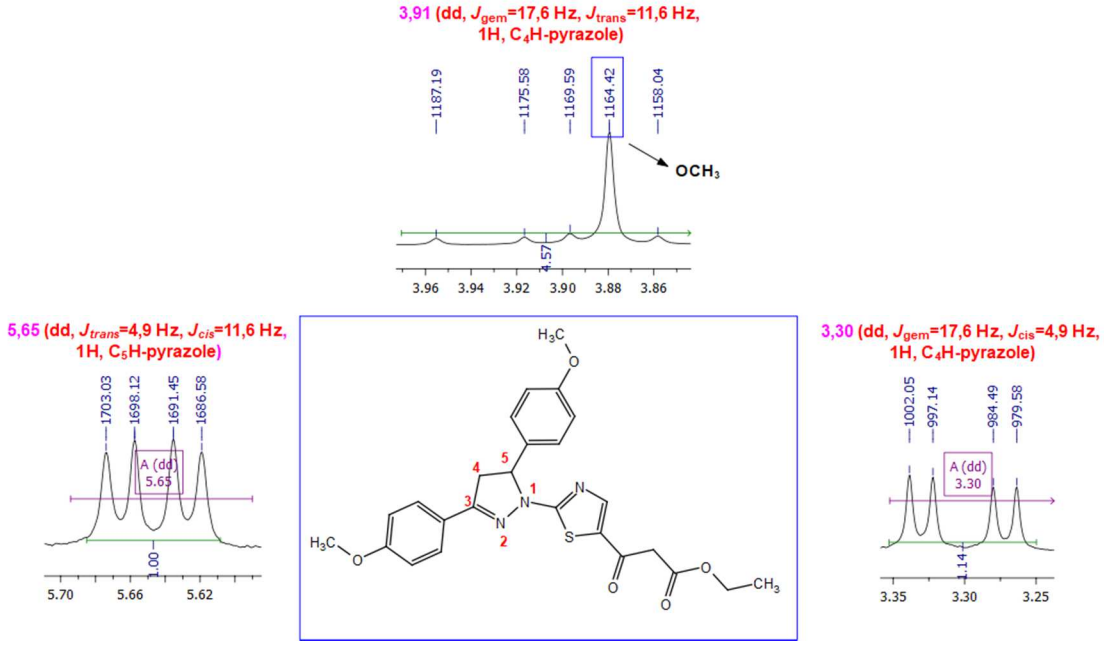


Figure S13: ^{1}H NMR splitting of the pyrazole protons (C_4H- and C_5H-) of compound **C4**

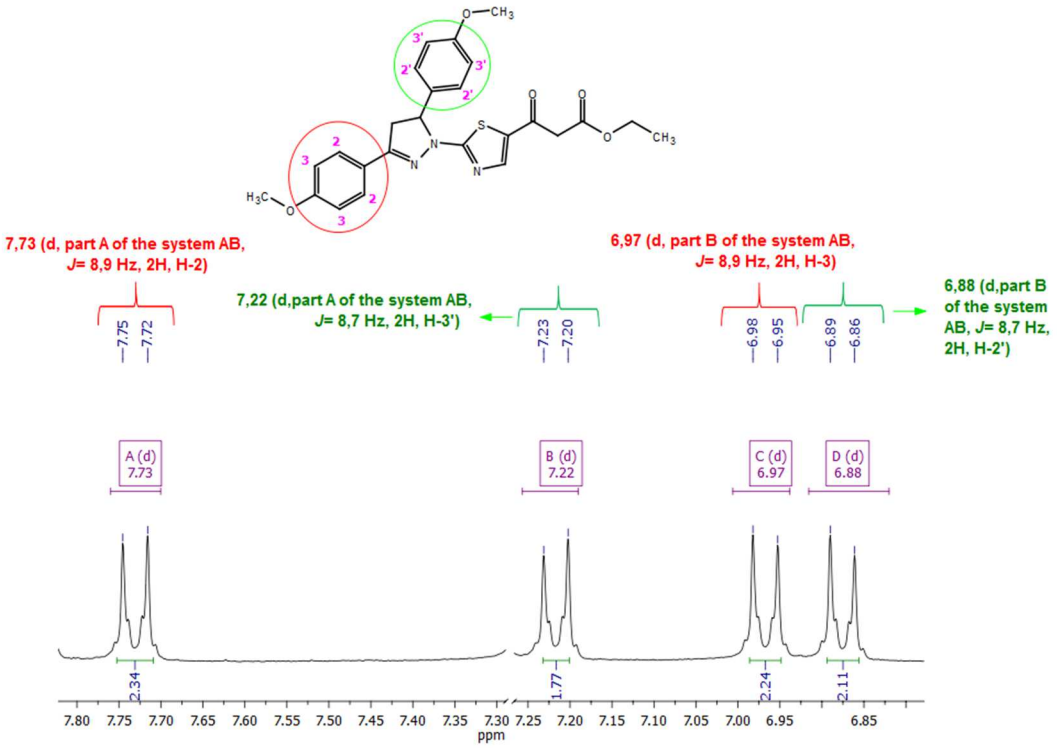


Figure S14. ^{1}H NMR splitting of *p*-disubstituted benzene group protons in compound **C4**

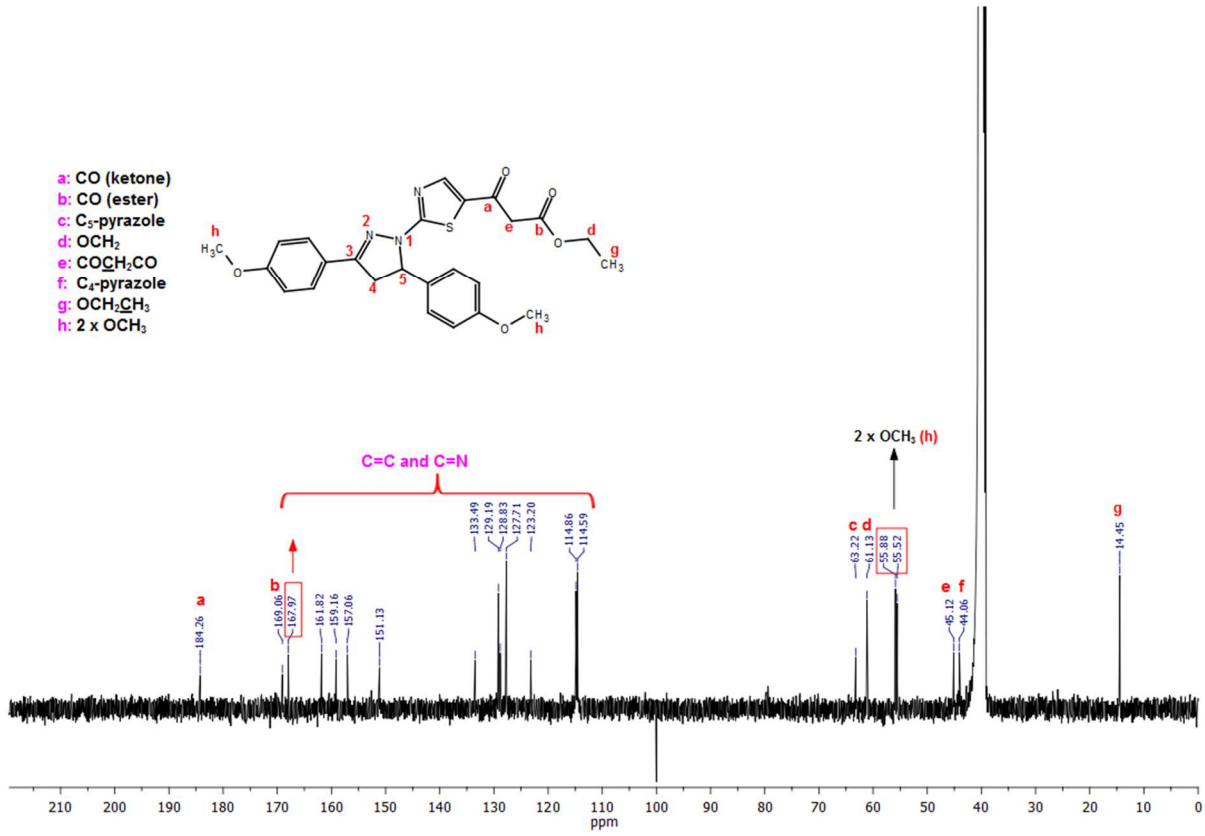
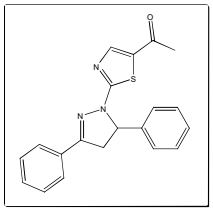


Figure S15: ^{13}C NMR spectra of **C4**

1-(2-(3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)thiazol-5-yl)ethanone (D1)



Color: Yellow, Yield 0.291 g, 84%, mp 227-228 ^{o}C, FT-IR (ATR, cm^{-1}): υ_{max} 3053-2848 (Ar-H and aliphatic C-H); 1626 (C=O, ketone); 1594-1489 (C=N and C=C). ^{1}H-NMR (400 MHz; DMSO-d_6, ppm): δ 8.03 (s, CH, thiazole); 7.83-7.10 (m, 10H, Ar-H); 5.79-5.74 (dd, J_{trans}= 5.0 Hz, J_{cis}= 11.7 Hz, 1H, C_5H-pyrazole); 4.13-4.06 (dd, J_{gem}= 18.1 Hz, J_{trans}= 11.8 Hz, 1H, C_4H-pyrazole); in DMSO-d_6 (dd, 1H, C_4H-pyrazole); 2.36 (s, 3H, CH_3). ^{13}C-NMR (100 MHz; DMSO-d_6, ppm): δ 189.6 (C=O, ketone); 168.8 (C=N, thiazole); 156.4; 149.4; 141.6; 131.2; 130.8; 130.4; 129.4; 129.3; 128.1; 127.3; 126.3 (C=C and C=N); 63.8 (C_5-pyrazole); 44.0 (C4-pyrazole); 26.3 (CH_3). Calcd. for $C_{20}H_{17}N_3OS$ (347.43): C, 69.14; H, 4.93; N, 12.09; S, 9.23. Found: C, 69.28; H, 4.99; N, 12.26; S, 9.37 %.

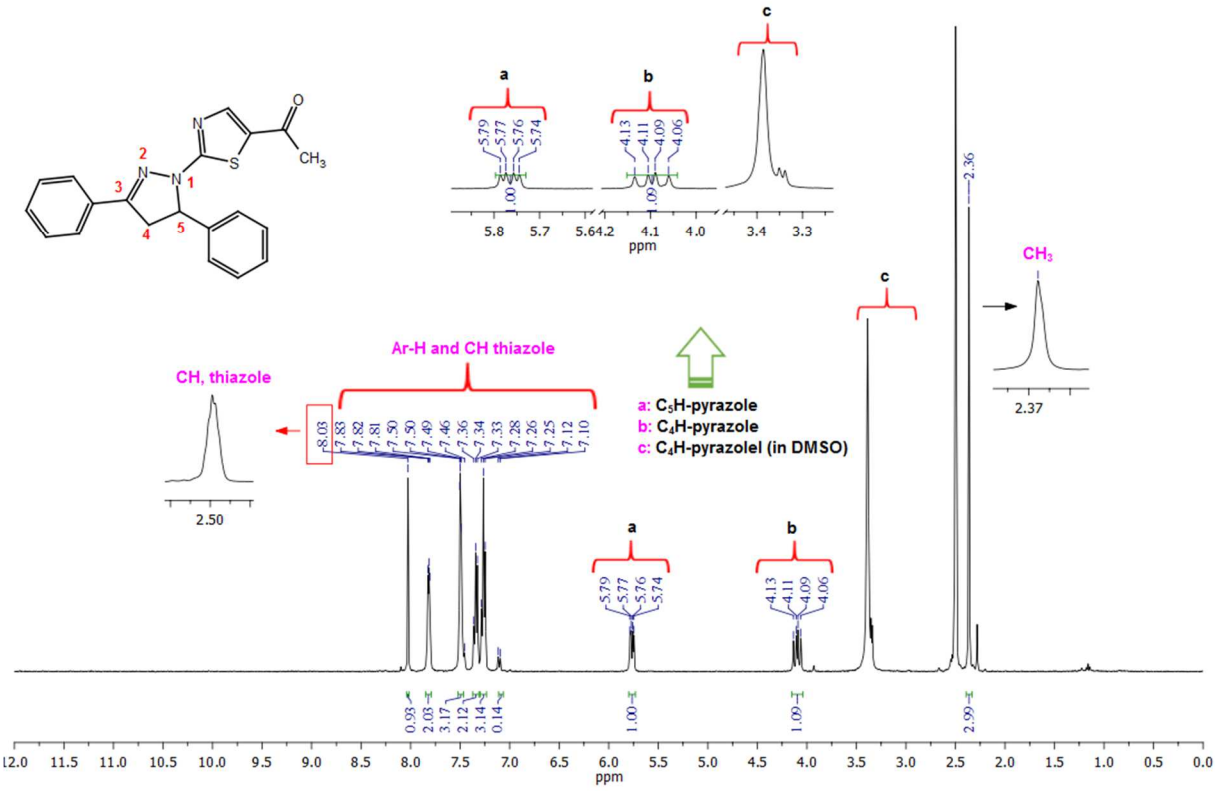


Figure S16: ^{1}H-NMR spectra of **D1**

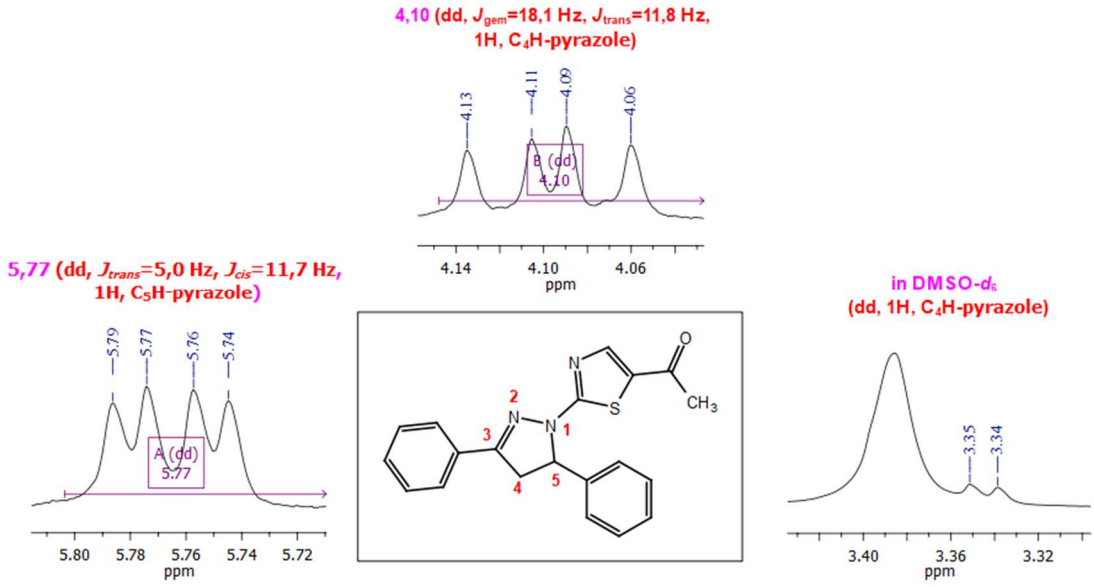


Figure S17: ^{1}H NMR splitting of the pyrazole protons (C_4H- and C_5H-) of compound **D1**

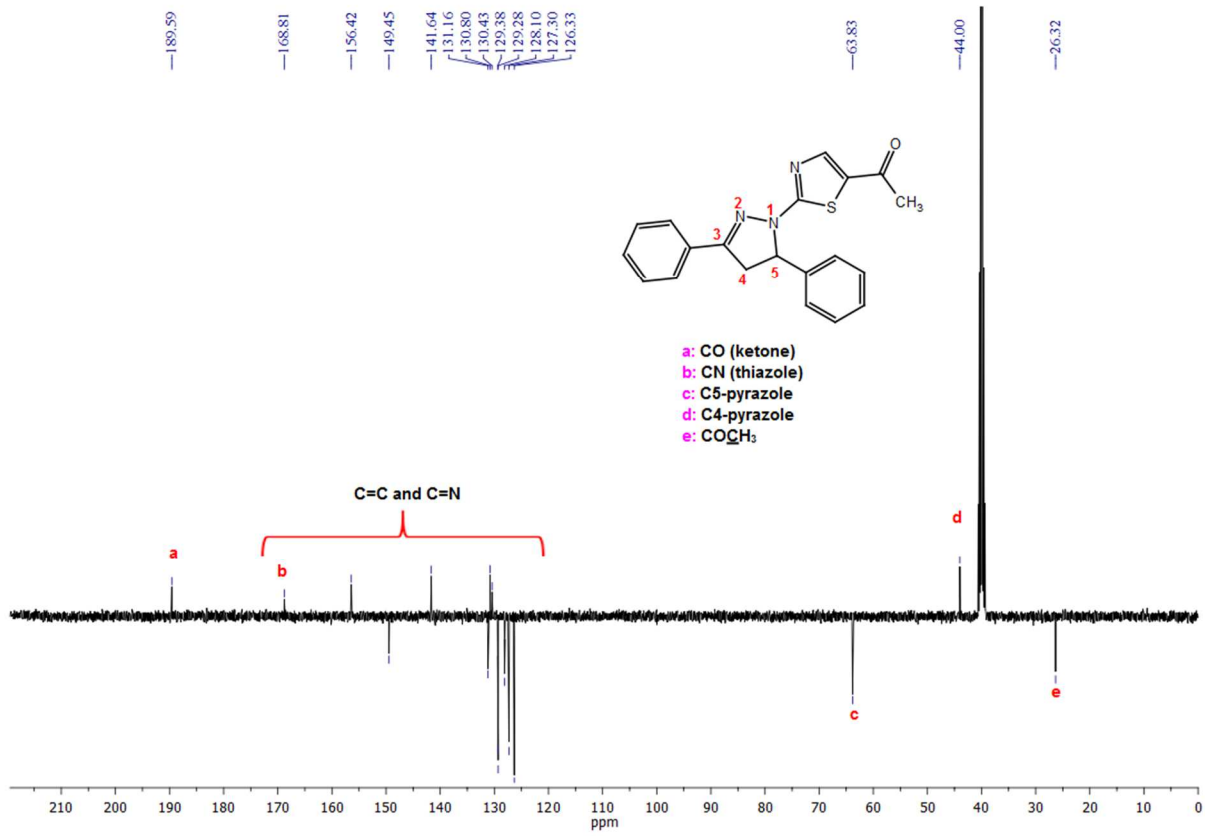
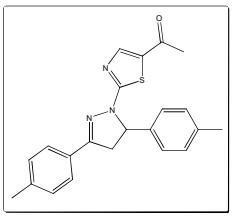


Figure S18: ^{13}C NMR spectra of **D1**

1-(2-(3,5-dip-tolyl-4,5-dihydro-1*H*-pyrazol-1-yl)thiazol-5-yl)ethanone (D2)



Color: Yellow, Yield 0.285 g, 76%, mp 257-258 ºC, FT-IR (ATR, cm^{-1}): υ_{max} 3033-2918 (Ar-H and aliphatic C-H); 1631 (C=O, ketone); 1593-1502 (C=N and C=C). ^{1}H-NMR (300 MHz; $CDCl_3$, ppm): δ 7.75 (s, CH, thiazole); 7.66-7.15 m, 8H, Ar-H); 5.67-5.62 (dd, J_{trans}= 5.1 Hz, J_{cis}= 11.8 Hz, 1H, C_5H-pyrazole); 3.95-3.85 (dd, J_{gem}= 17.6 Hz, J_{trans}= 11.7 Hz, 1H, C_4H-pyrazole); 3.32-3.24 (dd, J_{gem}= 17.6 Hz, J_{cis}= 5.1 Hz, 1H, C_4H-pyrazole); 2.40 (s, 6H, Ar-CH_3), 2.31 (s, 3H, $COCH_3$). ^{13}C-NMR (75 MHz; $CDCl_3$, ppm): δ 189.4 (C=O, ketone); 169.7 (C=N, thiazole); 154.6; 147.9; 141.0; 137.9; 137.8; 130.6; 129.7; 129.5; 128.0; 126.7; 125.7 (C=C and C=N); 63.4 (C_5-pyrazole); 44.0 (C_4-pyrazole); 26.0 (CO-CH_3), 21.5 and 21.1 (2x Ar-CH_3). Calcd. for $C_{22}H_{21}N_3OS$ (375.49): C, 70.37; H, 5.64; N, 11.19; S, 8.54. Found: C, 70.62; H, 5.46; N, 11.50; S, 8.69 %.

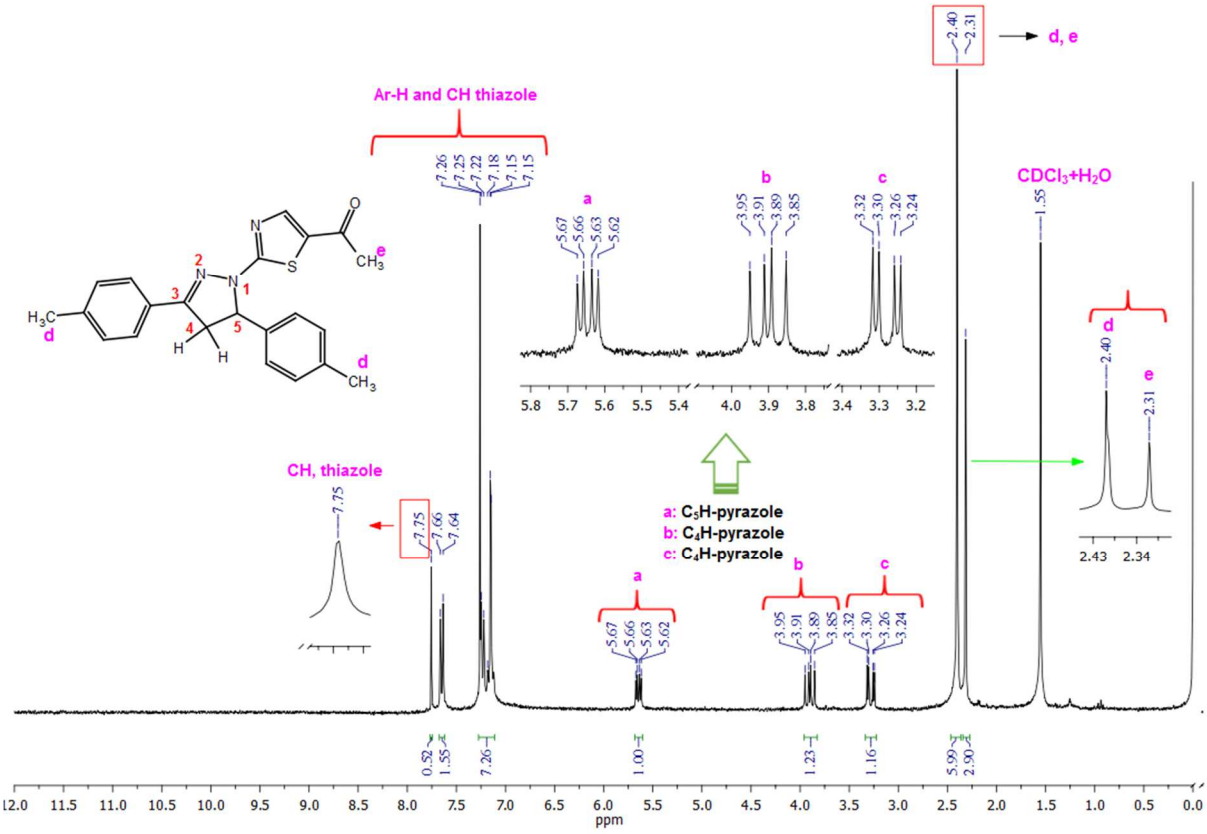


Figure S19: ^{1}H-NMR spectra of **D2**

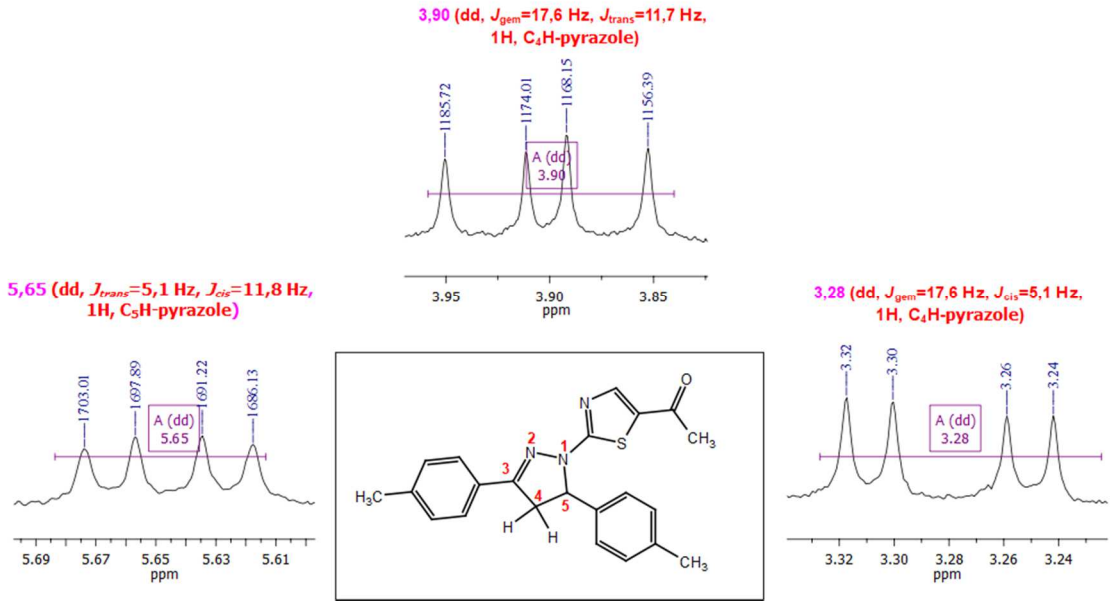


Figure S20: ^{1}H NMR splitting of the pyrazole protons (C_4H- and C_5H-) of compound **D2**

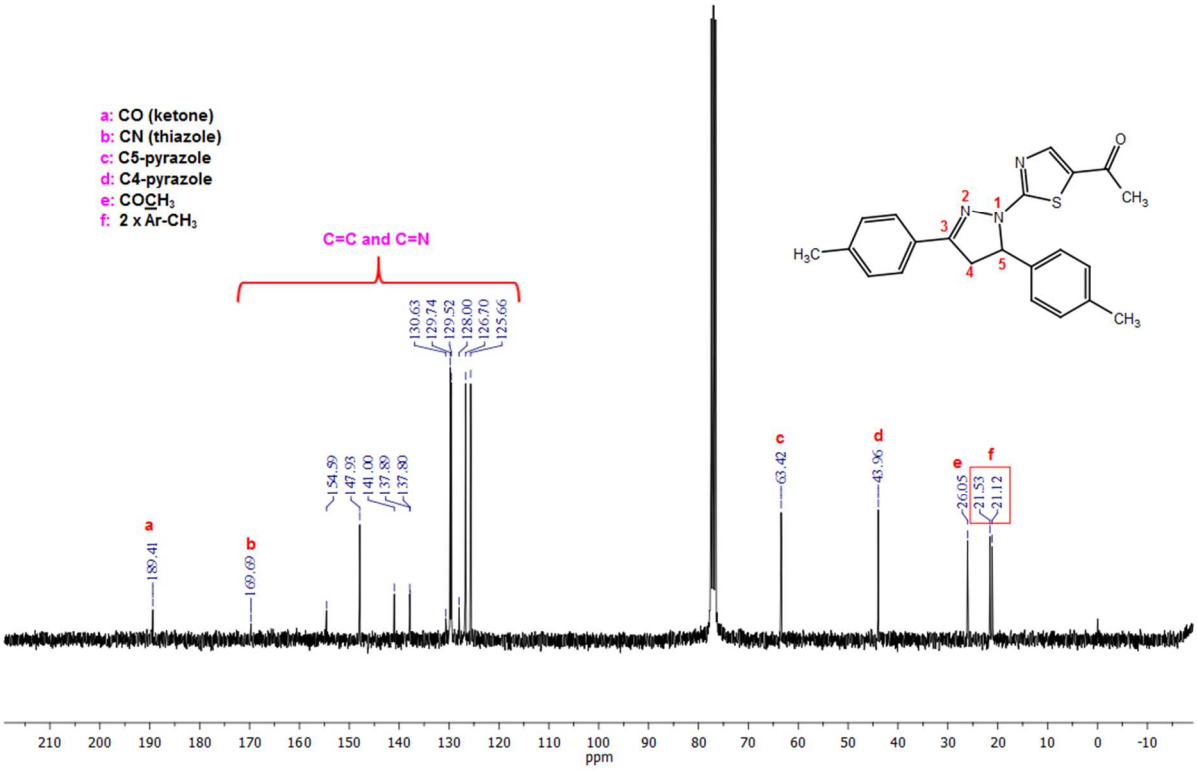
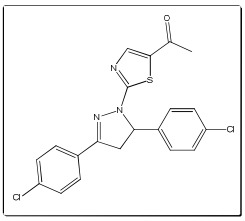


Figure S21: ^{13}C NMR spectra of **D2**

1-(2-(3,5-bis(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)thiazol-5-yl)ethanone (D3)



Color: Yellow, Yield 0.308 g, 74%, mp 260-261 ºC, FT-IR (ATR, cm^{-1}): υ_{max} 3065-2935 (Ar-H and aliphatic C-H); 1631 (C=O, ketone); 1598-1486 (C=N and C=C). ^{1}H-NMR (300 MHz; $CDCl_3$, ppm): δ 7.76 (s, CH, thiazole); 7.71-7.21 (m, 8H, Ar-H); 5.72-5.66 (dd, J_{trans}= 5.3 Hz, J_{cis}= 11.9 Hz, 1H, C_5H-pyrazole); 3.98-3.88 (dd, J_{gem}= 17.6 Hz, J_{trans}= 11.9 Hz, 1H, C_4H-pyrazole); 3.30-3.23 (dd, J_{gem}= 17.6 Hz, J_{cis}= 5.4 Hz, 1H, C_4H-pyrazole); 2.43 (s, 3H, -$COCH_3$). ^{13}C-NMR (75 MHz; DMSO-d_6, ppm): δ 189.7 (C=O, ketone); 168.7 (C=N, thiazole); 155.4; 149.3; 140.5; 135.7; 132.7; 130.7; 129.7; 129.5; 129.2; 129.0, 128.5 (C=C and C=N); 63.4 (C_5-pyrazole); 43.7 (C_4-pyrazole); 26.4 (CH_3). Calcd. for $C_{22}H_{21}N_3OS$ (416.32): C, 57.70; H, 3.63; N, 10.09; S, 7.70. Found: C, 57.74; H, 3.36; N, 10.28; S, 7.78 %.

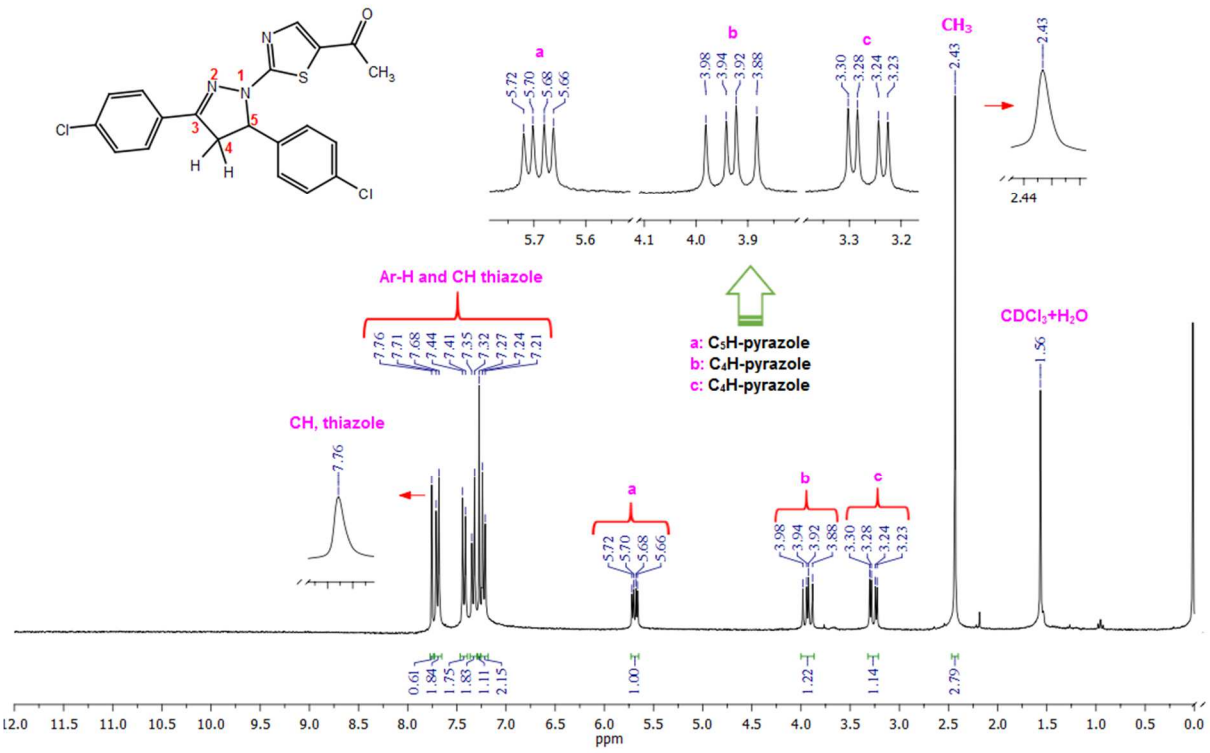


Figure S22: ^{1}H-NMR spectra of **D3**

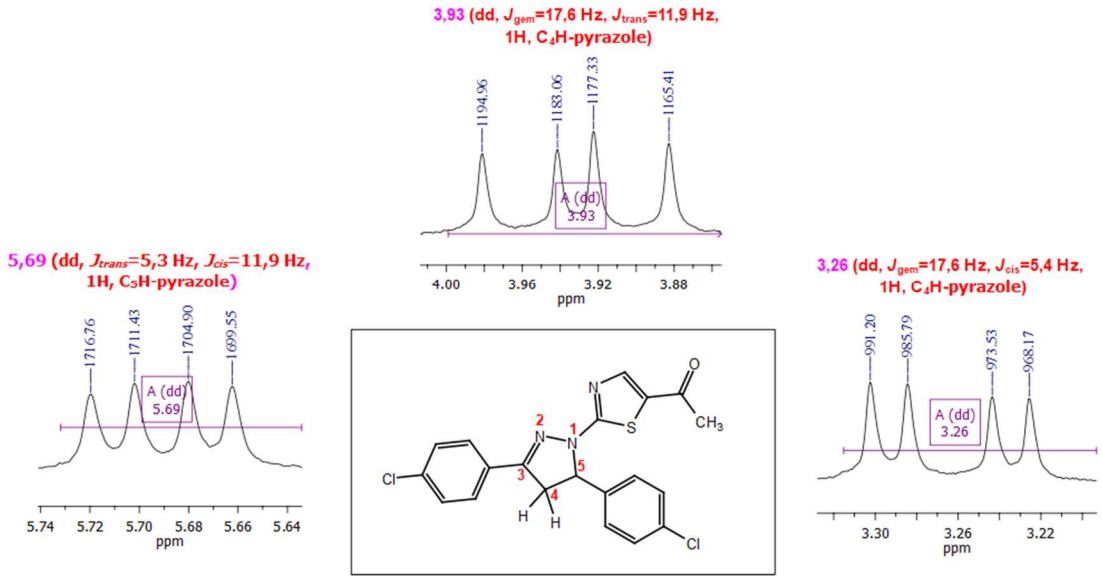


Figure S23: ^{1}H NMR splitting of the pyrazole protons (C_4H- and C_5H-) of compound **D3**

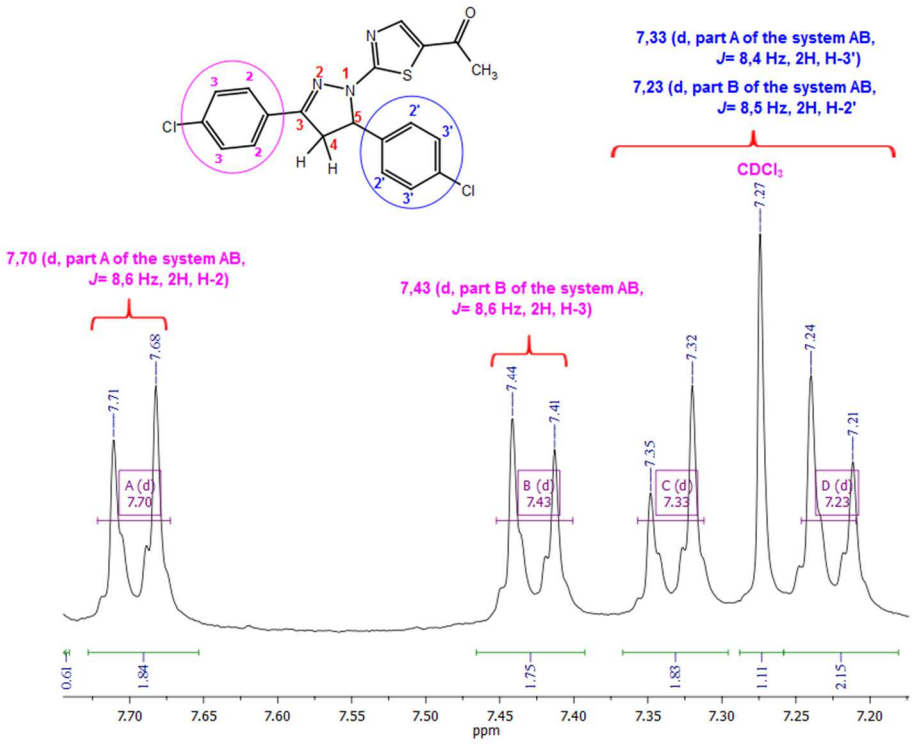


Figure S24: ^{1}H NMR splitting of *p*-disubstituted benzene group protons in compound **D3**

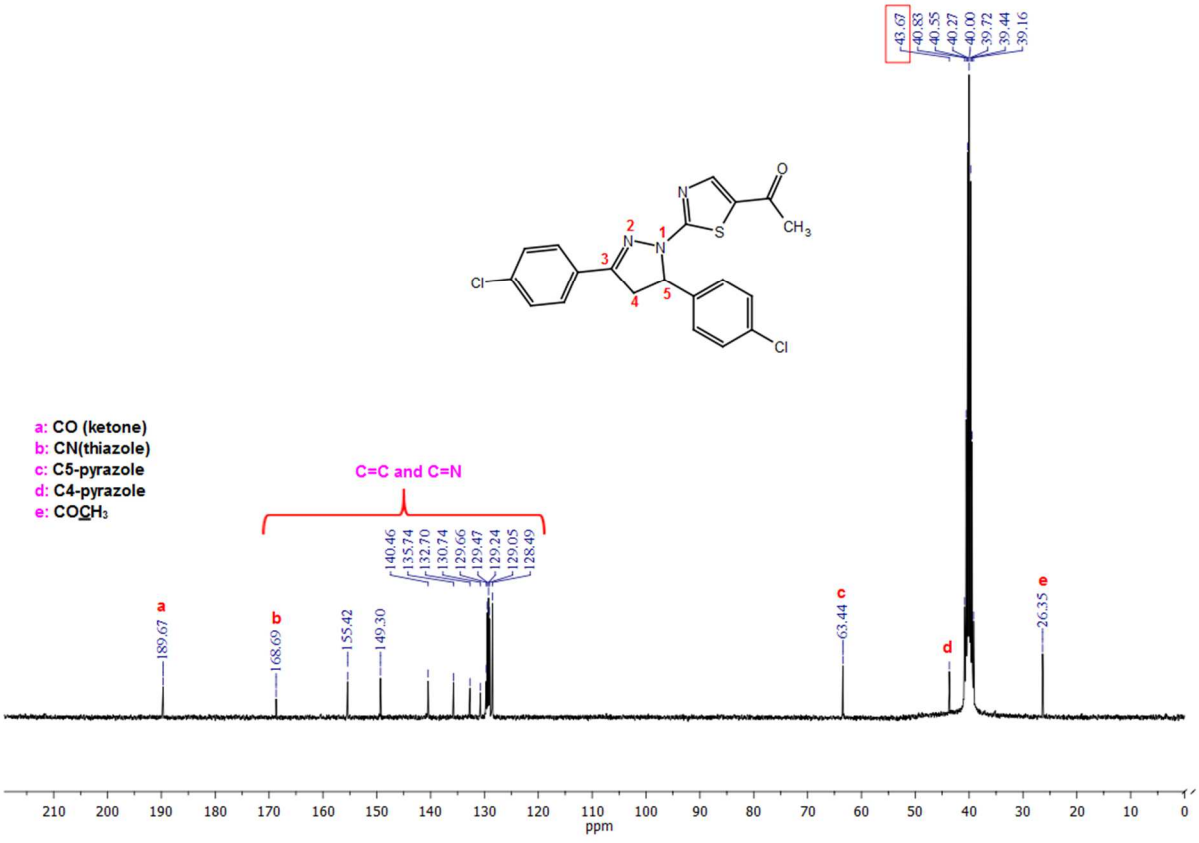
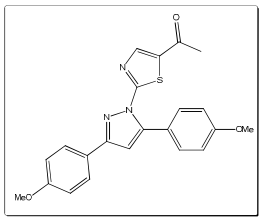


Figure S25: ^{13}C NMR spectra of **D3**

1-(2-(3,5-bis(4-methoxyphenyl)-1*H*-pyrazol-1-yl) thiazol-5-yl)ethanone (D4)



Color: Yellow, Yield 0.275 g, 68%, mp 167-168 °C, FT-IR (ATR, cm^{-1}): υ_{max} 3112-2839 (Ar-H and aliphatic C-H); 1650 (C=O, ketone); 1614-1455 (C=N and C=C), 1252 (C-O). ^{1}H-NMR (400 MHz; $CDCl_3$, ppm): δ 7.91 (s, 1H, CH-thiazole), 6.68 (s, 1H, CH-pyrazole), 7.87-6.95 (m, 8H, Ar-H), 3.88 and 3.87 (s, 6H, 2 x OCH_3), 2.52 (s, 3H, -$COCH_3$). ^{13}C-NMR (100 MHz; DMSO-d_6, ppm): δ 191.2 (C=O, ketone); 166.0; 160.6; 160.4; 154.0; 147.4; 146.3; 137.2; 131.4; 127.9; 123.8; 122.0; 114.8; 113.9; 109.4; 55.7 (2 x OCH_3); 27.0 ($CO\underline{C}H_3$). Calcd. for $C_{22}H_{19}N_3O_3S$ (405.47): C, 65.17; H, 4.72; N, 10.36; S, 7.91. Found: C, 65.02; H, 4.85; N, 10.46; S, 8.19 %.

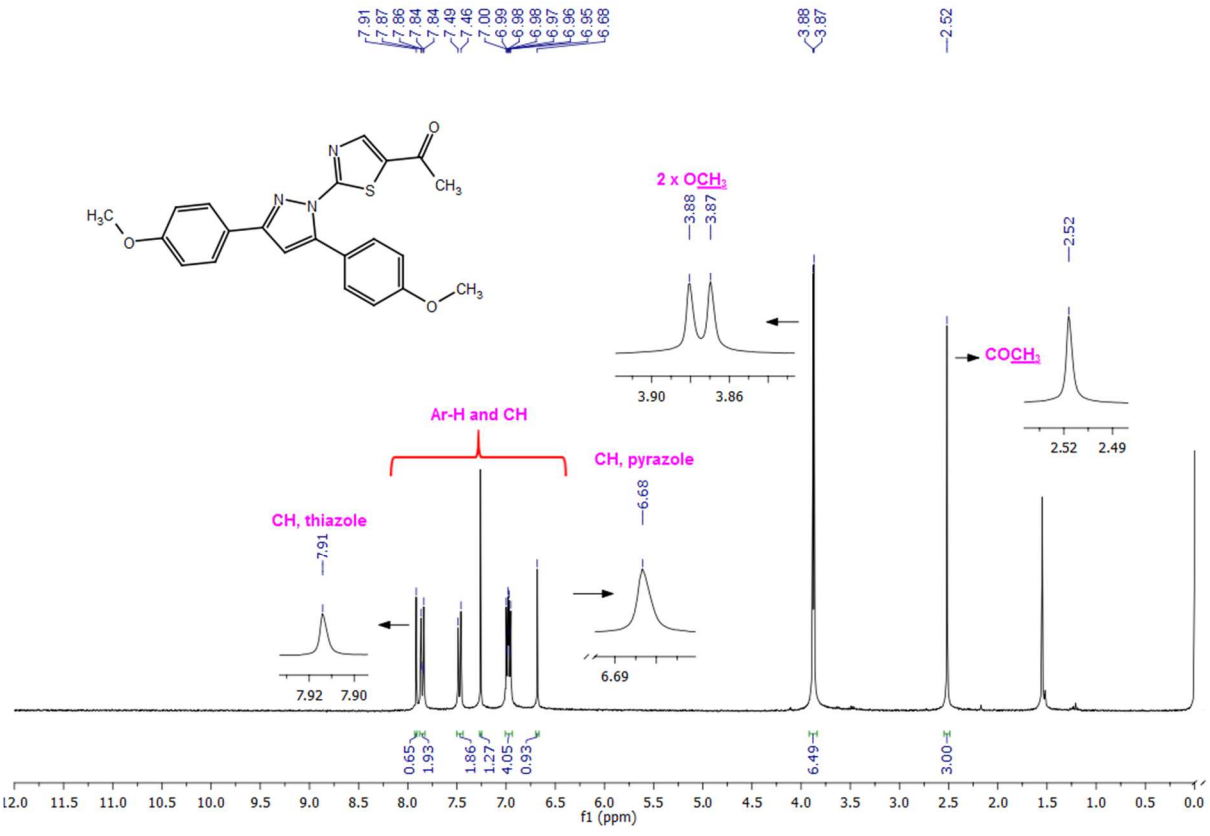


Figure S26: ^{1}H-NMR spectra of **D4**

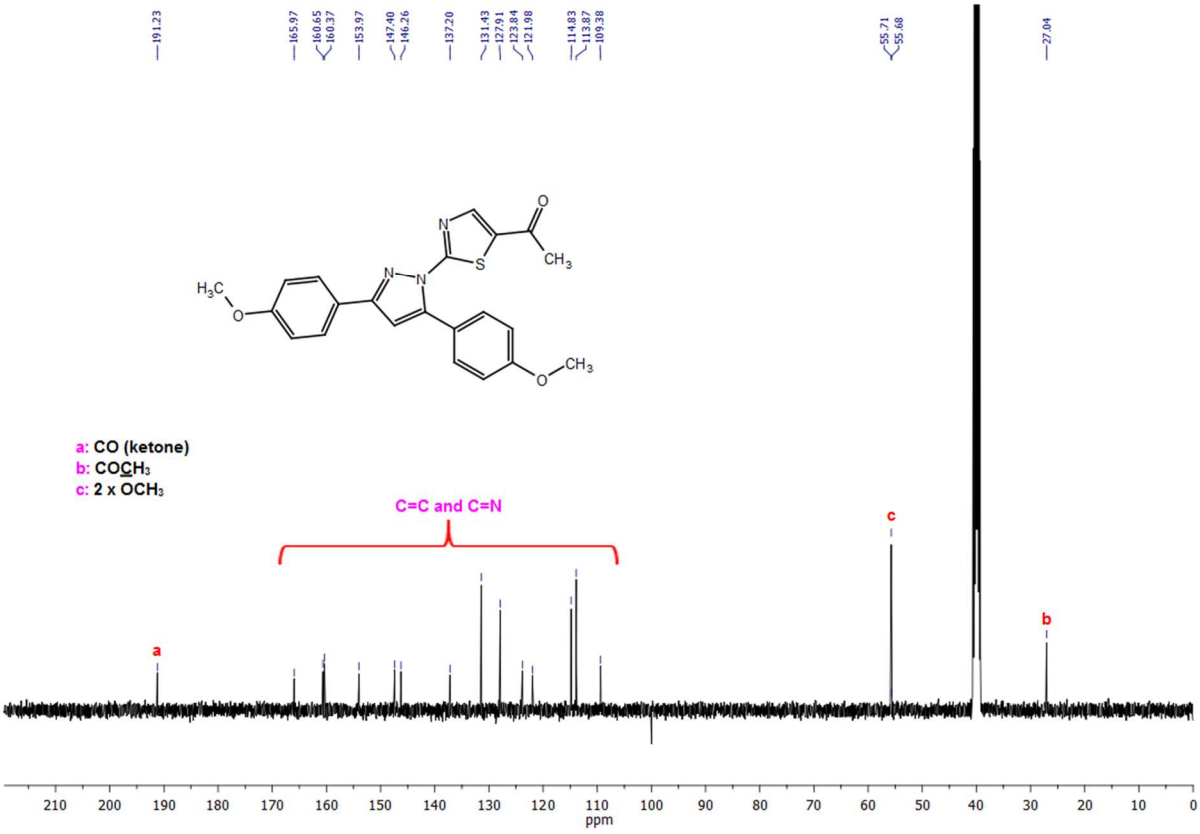


Figure S27: ^{13}C NMR spectra of **D4**