Supporting Information

Synthesis, anticancer activity and docking studies of pyrazoline and pyrimidine derivatives as potential epidermal growth factor receptor (EGFR) inhibitors

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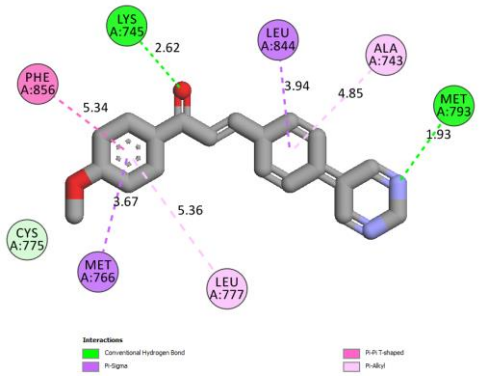
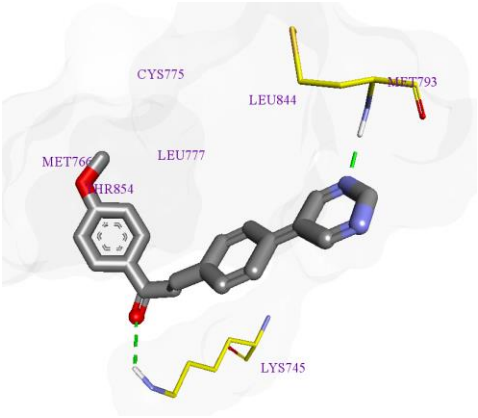
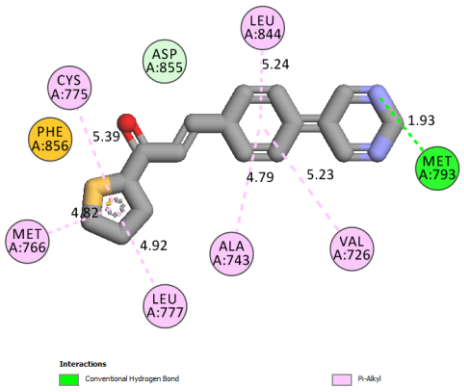
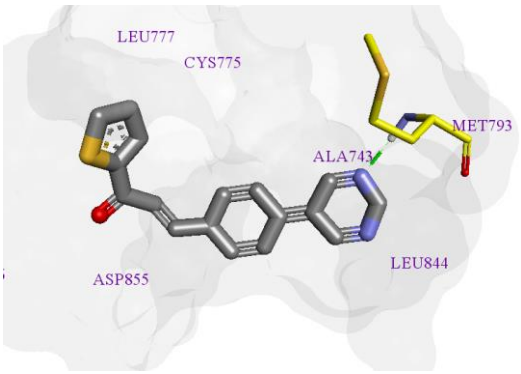
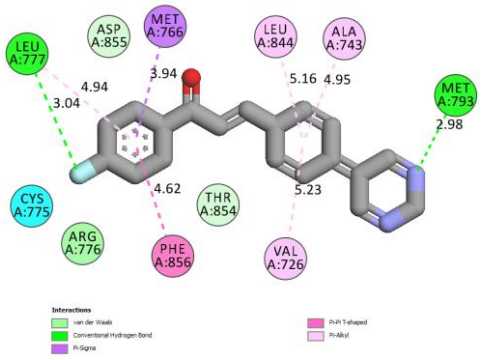
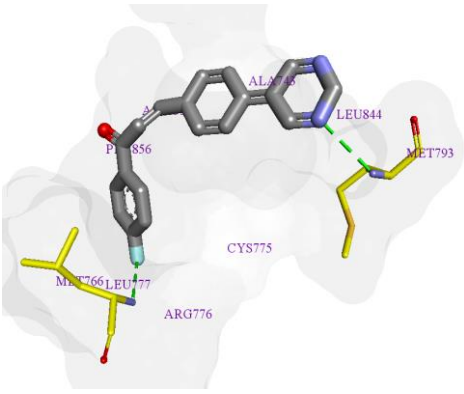
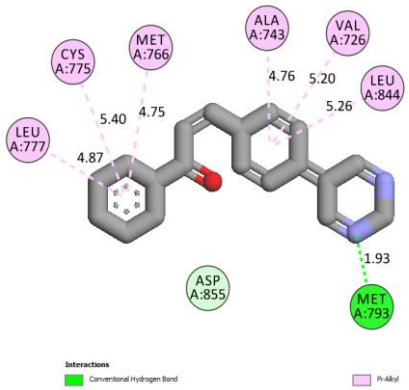
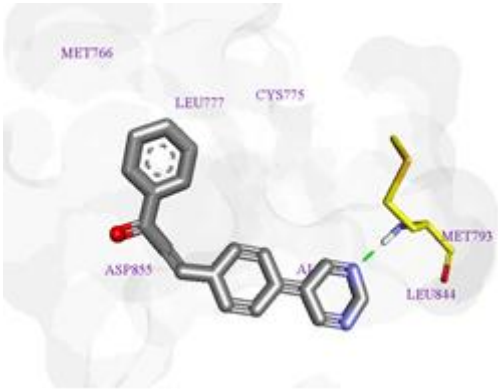
	2D-Intermolecular interactions	3D-Intermolecular interactions
1		
3		
4		
5		

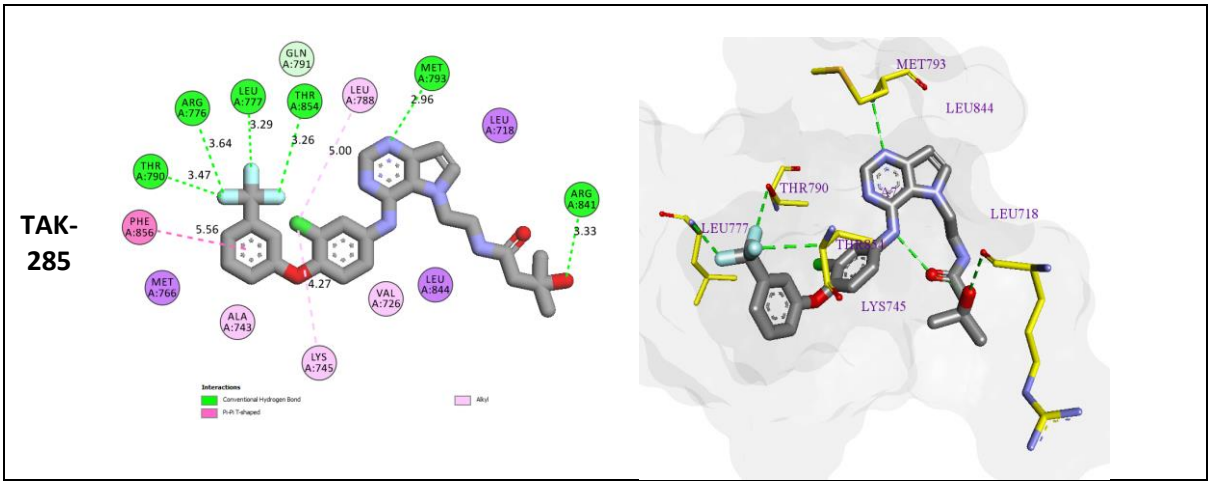


Figure S1.1. 2D & 3D intermolecular interactions between docked chalcone compounds **1, 3, 4** and **5** with 3POZ.PDB. Green and pink coloured amino acids represent their contribution in hydrogen bond and hydrophobic interactions, respectively.

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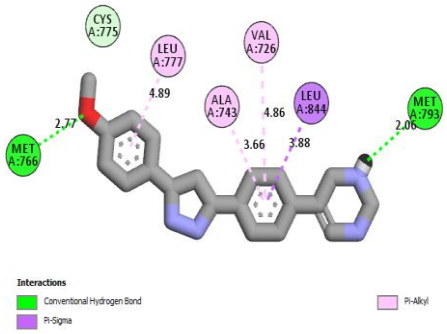
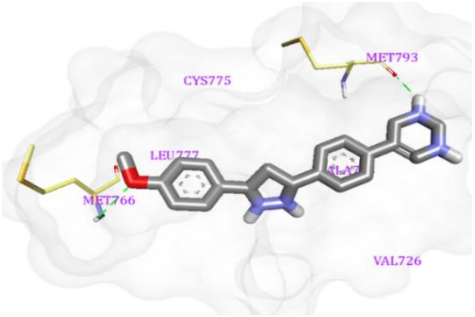
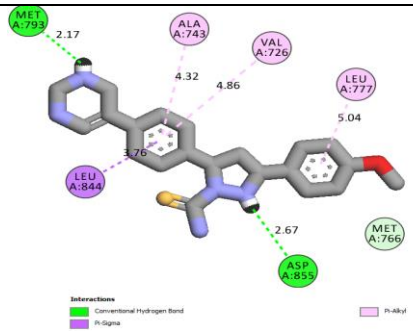
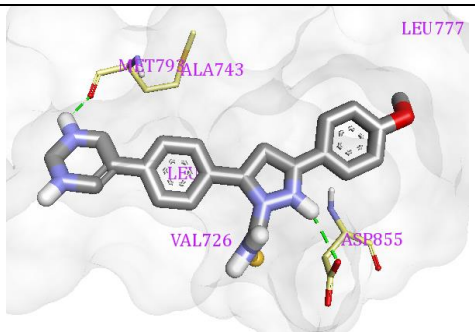
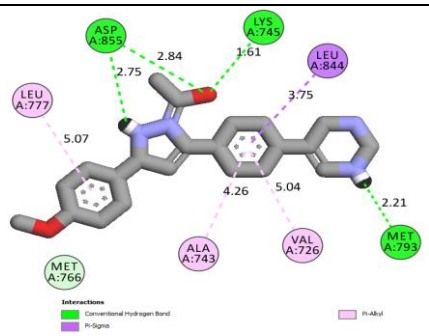
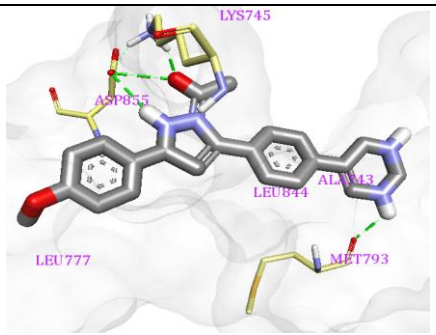
1Ai		
1Aii		
1Aiii		

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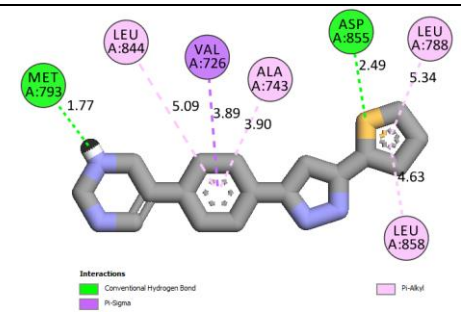

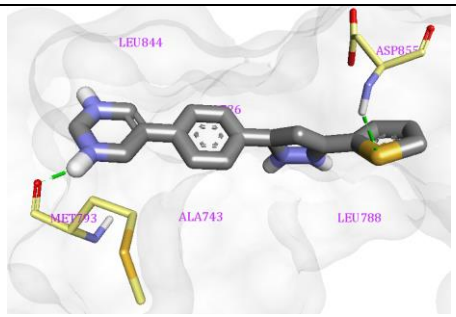

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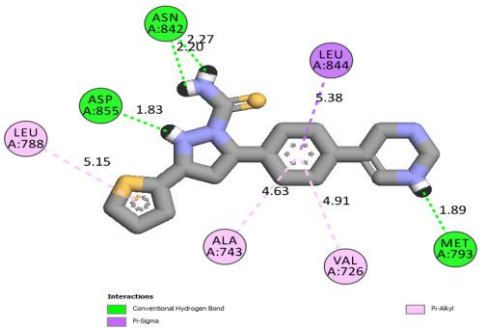

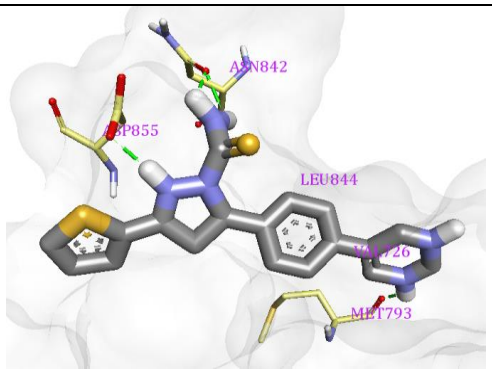

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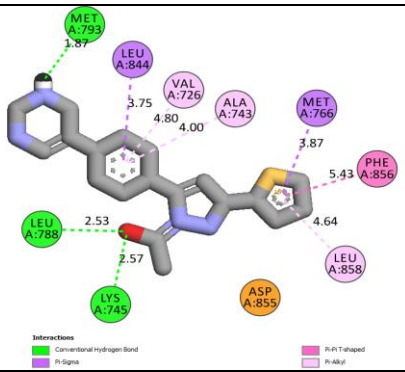

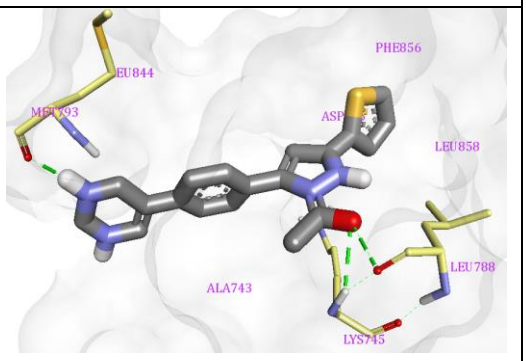

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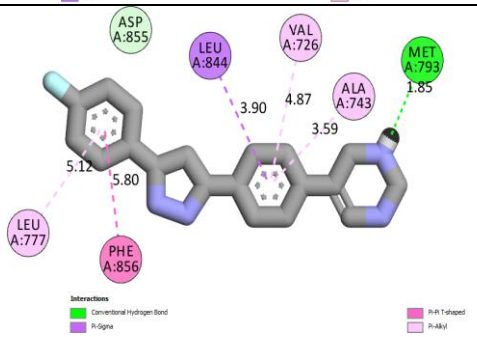

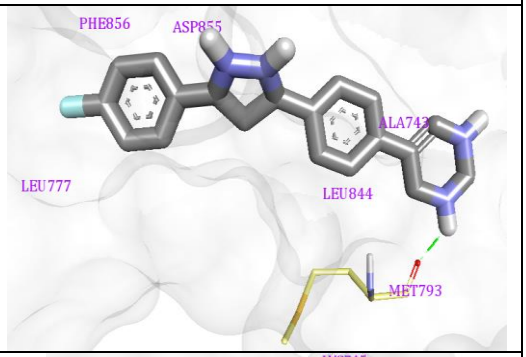

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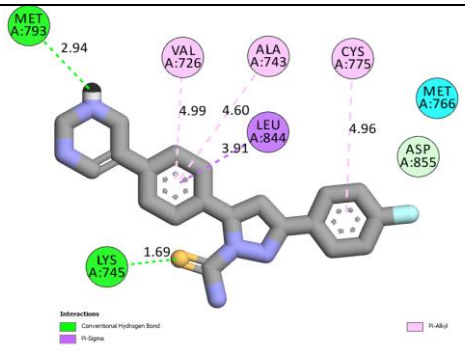
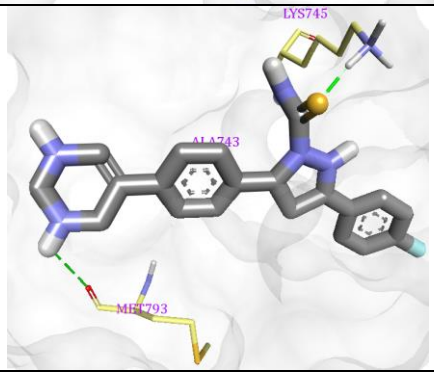




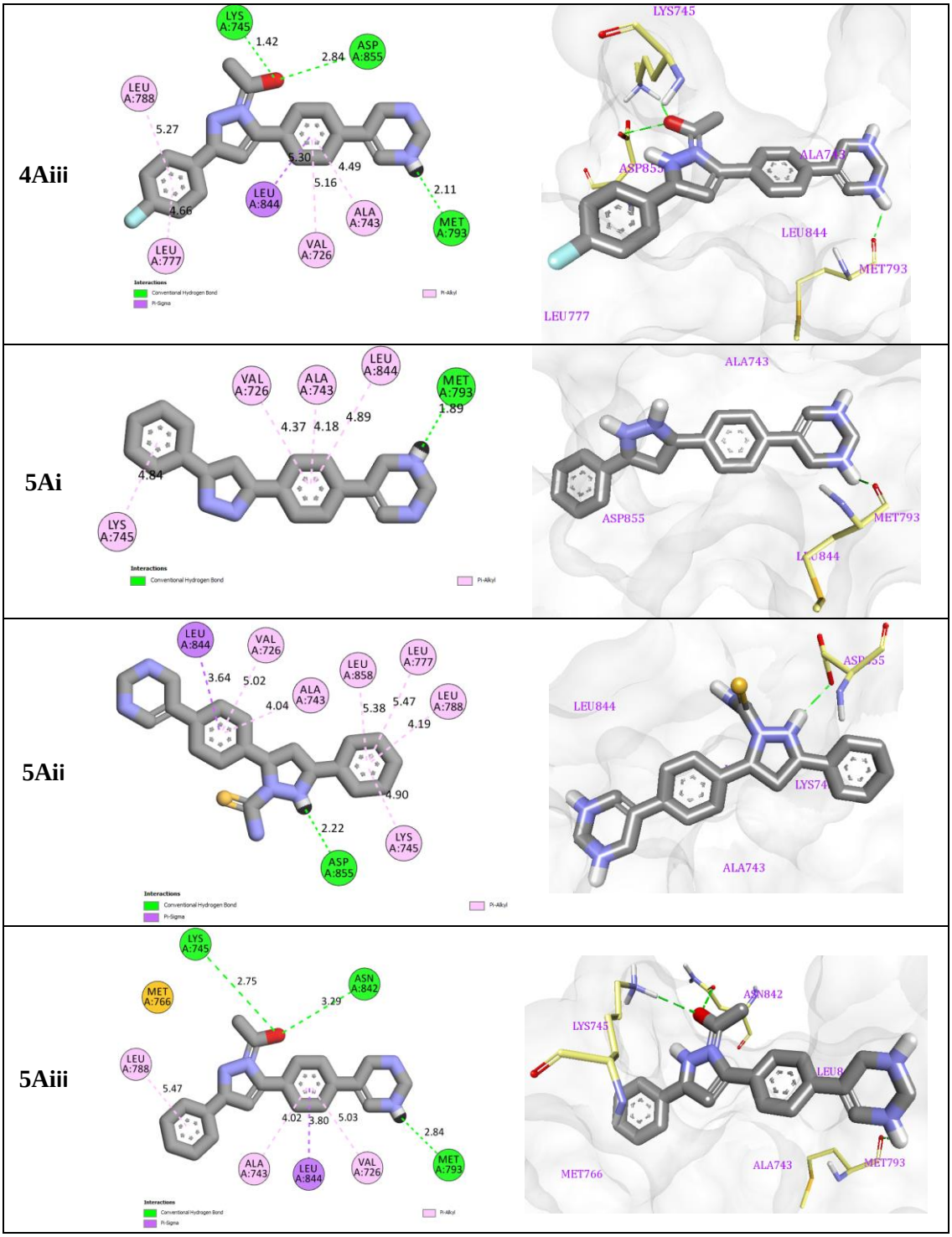
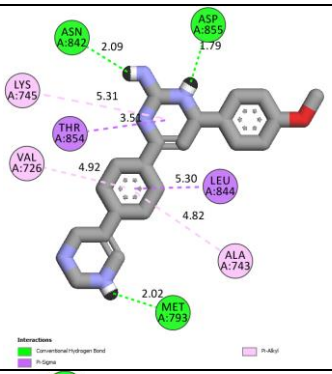
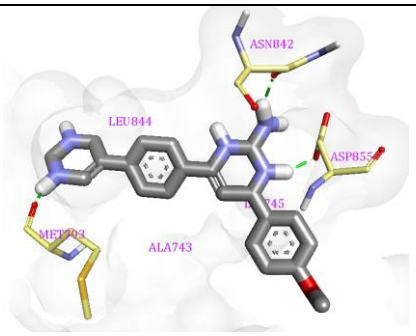
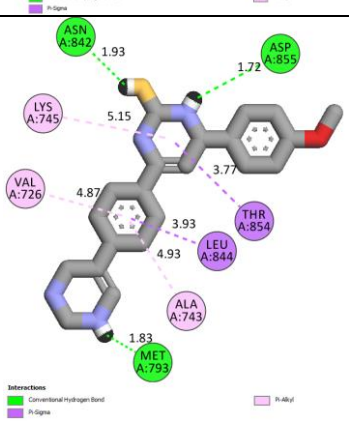
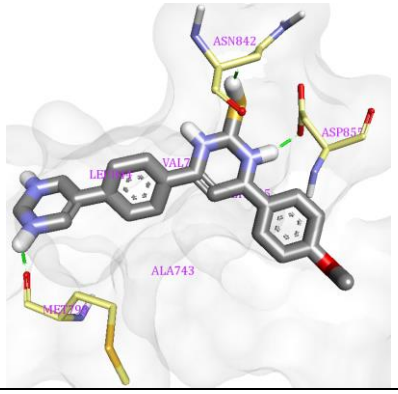
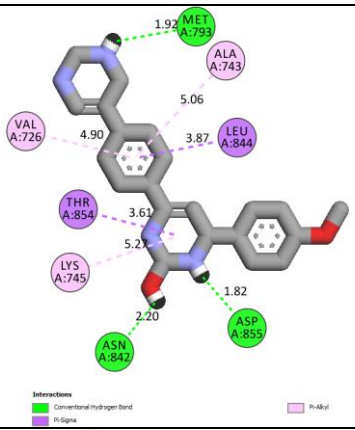
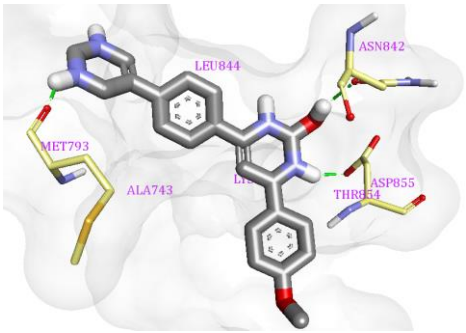
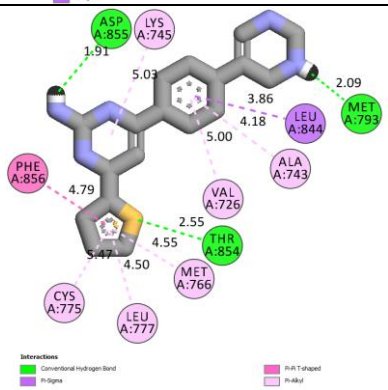
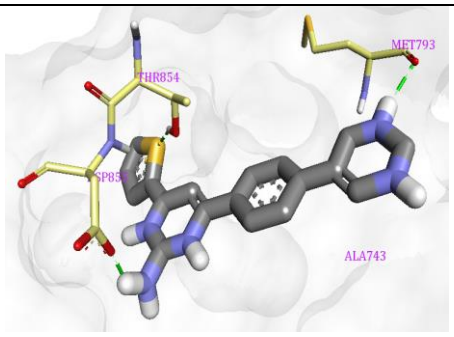
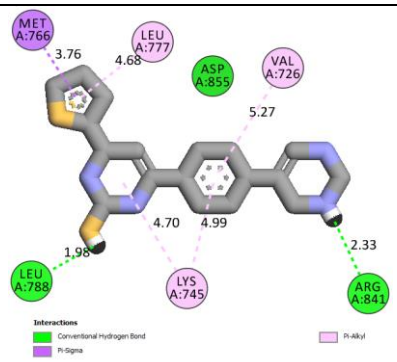
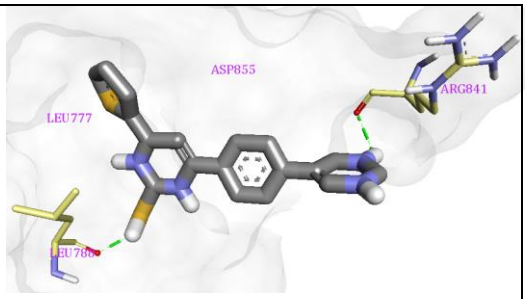
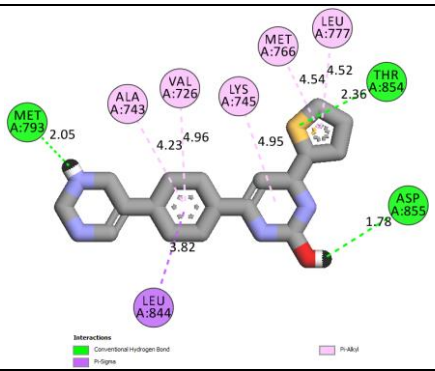
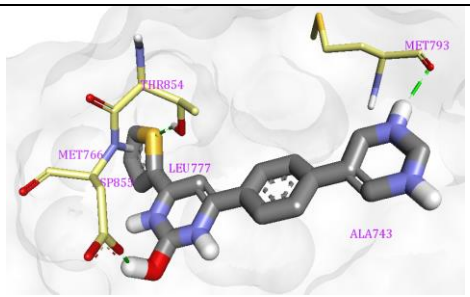
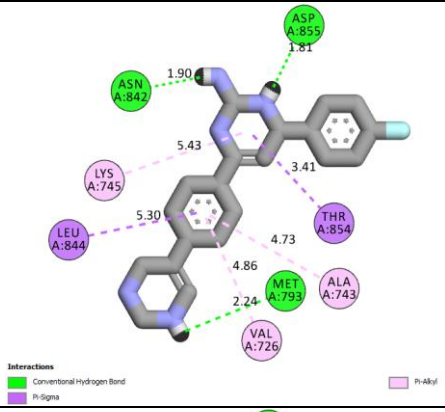
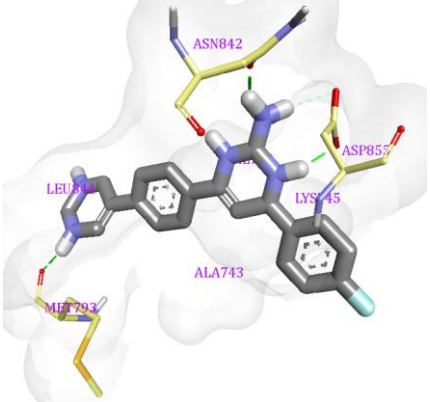
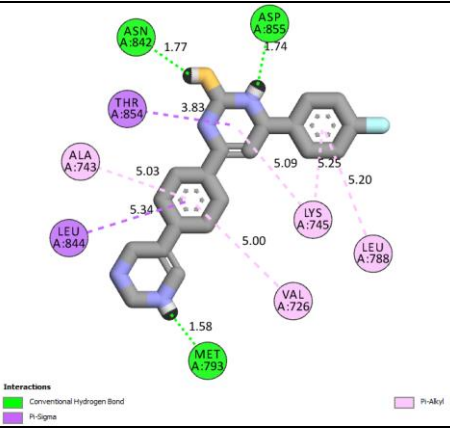
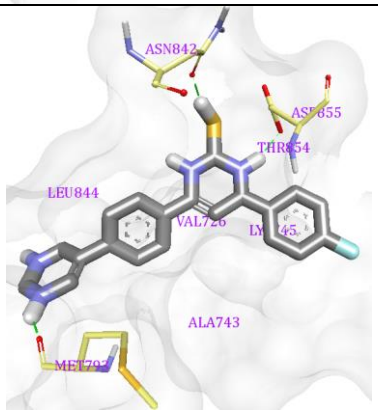


Figure S1.2. 2D & 3D intermolecular interactions between docked pyrazoline compounds **1A(i-iii)** and **(3-5)A(i-iii)** with 3POZ protein. Green and pink colored amino acids represent their contribution in hydrogen bond and hydrophobic interactions, respectively.

	2D-Intermolecular interactions	3D-Intermolecular interactions
1Bi		
1Bii		
1Biii		
3Bi		

3Bii		
3Biii		
4Bi		
4Bii		

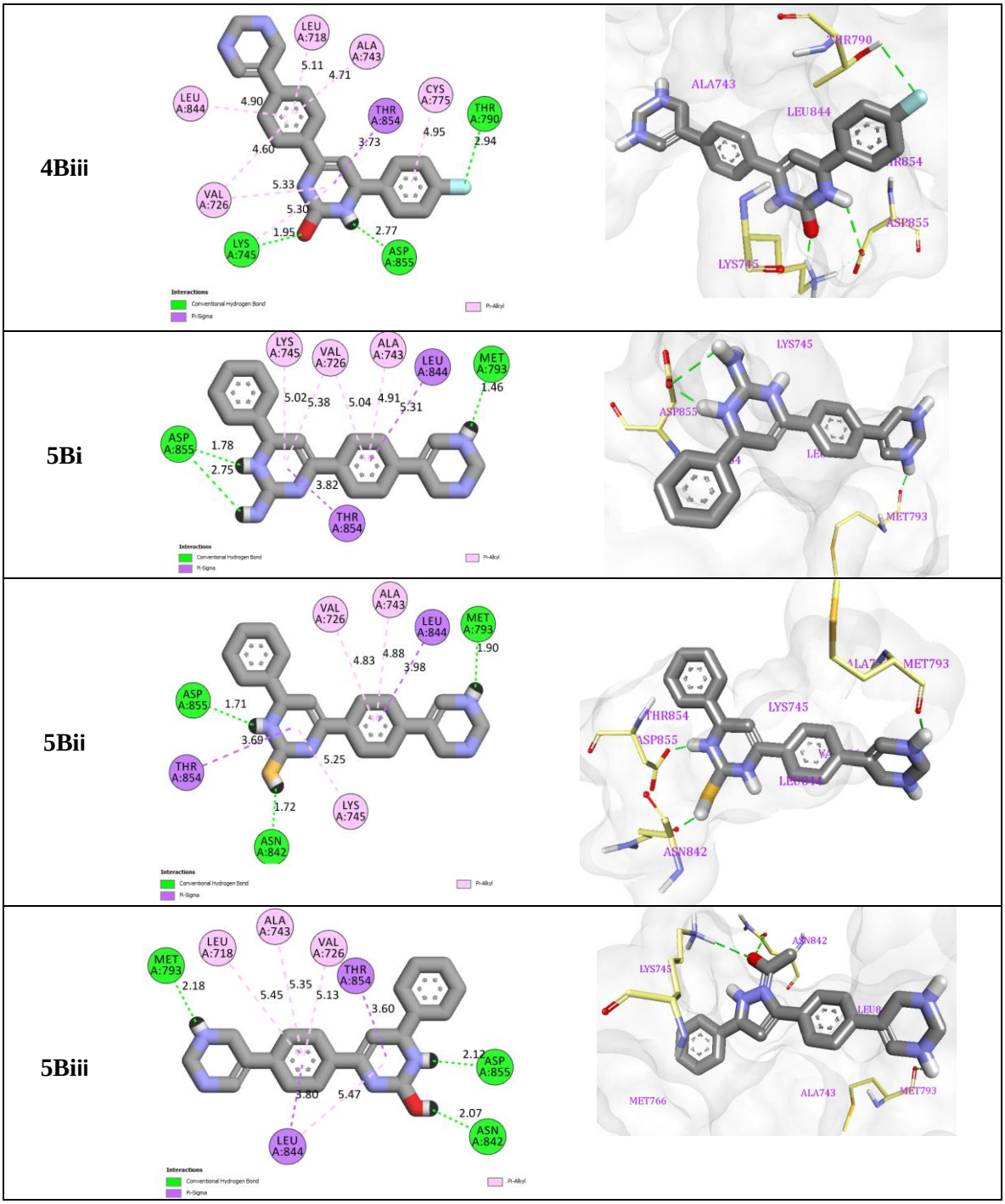
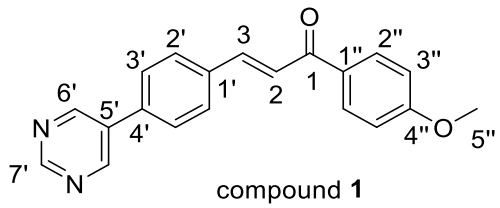
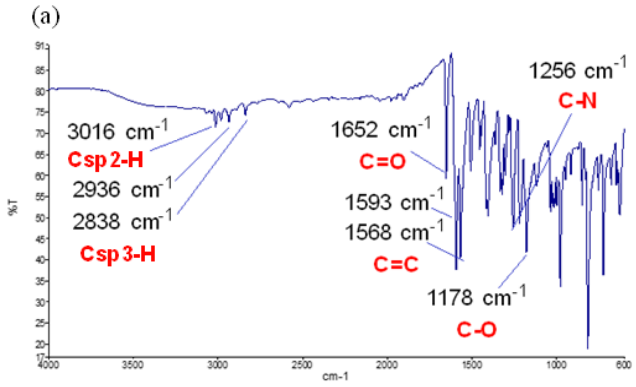
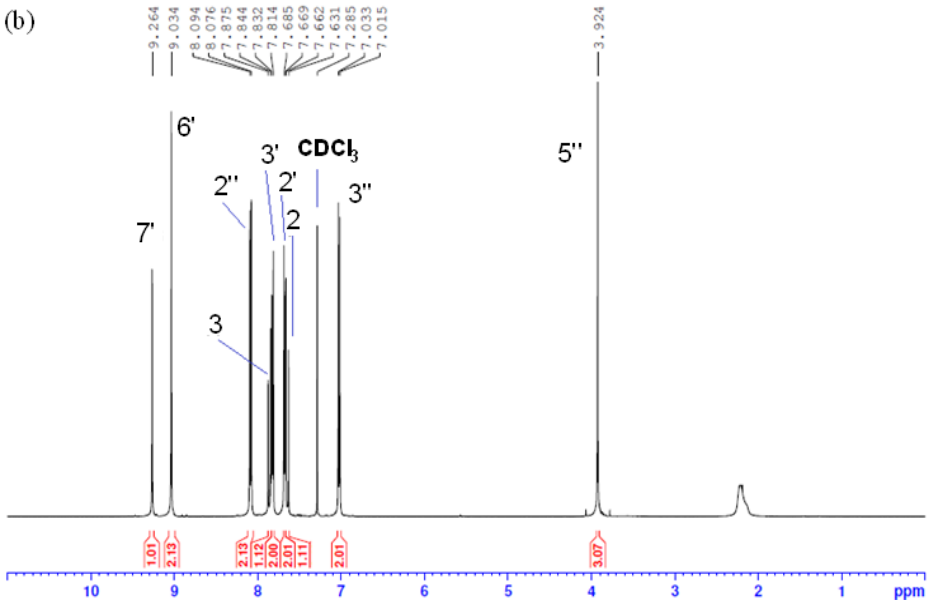


Figure S1.3. 2D & 3D intermolecular interactions between docked pyrimidine compounds **1B(i-iii)** and **(3-5)B(i-iii)** with 3POZ protein. Green and pink colored amino acids represent their contribution in hydrogen bond and hydrophobic interactions, respectively.


O
2'
3
3'
2''
1''
3''
6'
1'
2
1
5'
4'
N
4''
O
5''
7'
N
compound 1


(a)
%T
3016 cm-1
Csp2-H
2936 cm-1
2838 cm-1
Csp3-H
1652 cm-1
C=O
1593 cm-1
1568 cm-1
C=C
1256 cm-1
C-N
1178 cm-1
C-O
4000
3500
3000
2500
2000
1500
1000
600
cm-1


(b)
9.264
9.034
8.094
8.076
7.875
7.844
7.832
7.814
7.685
7.669
7.662
7.631
7.285
7.033
7.015
3.924
6'
3'
CDCl3
2''
2'
3''
7'
2
3
5''
1.01
2.13
2.13
1.12
2.00
2.01
1.11
2.01
3.07
10
9
8
7
6
5
4
3
2
1
ppm

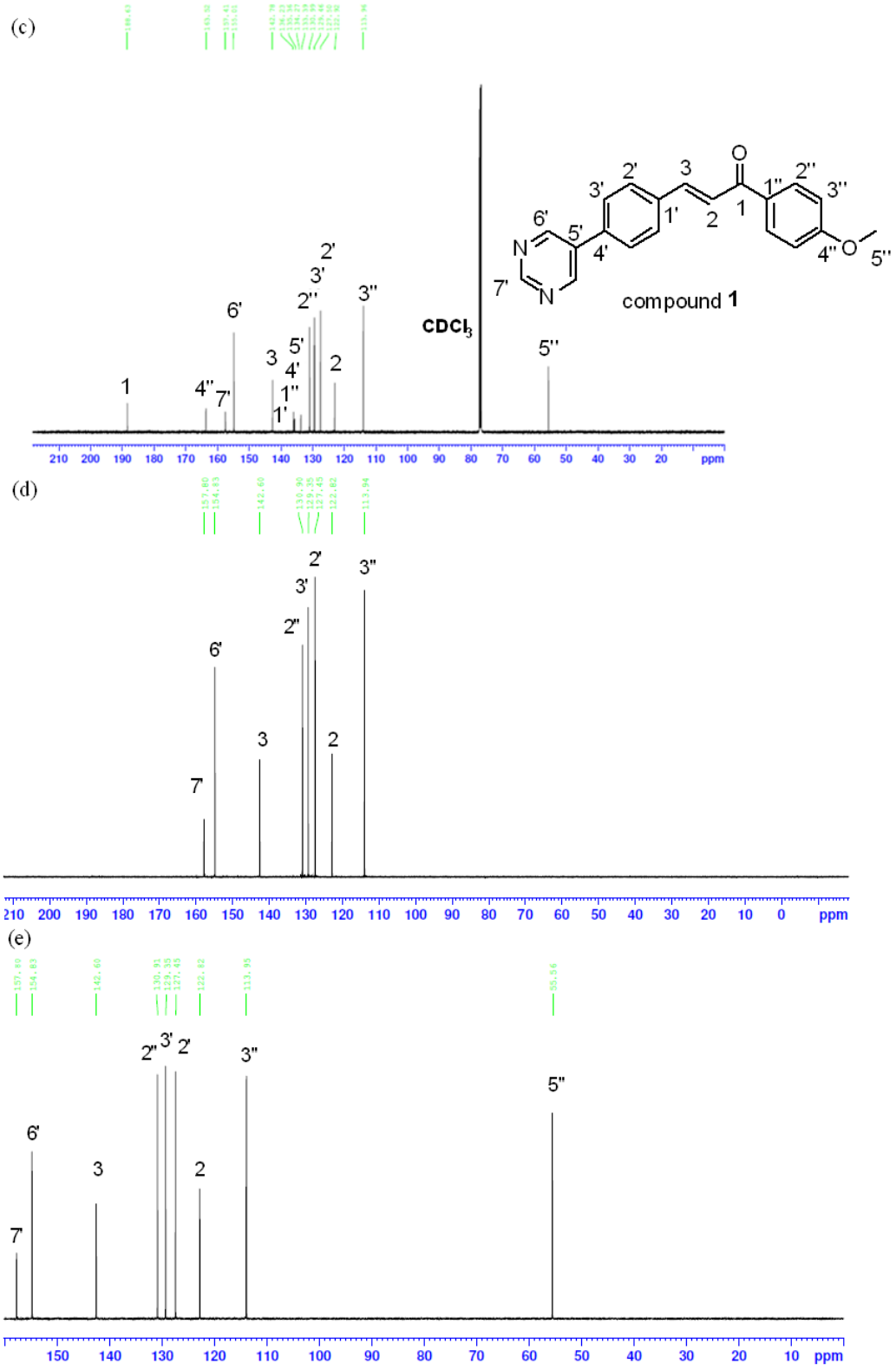
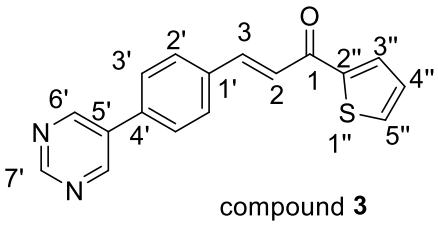
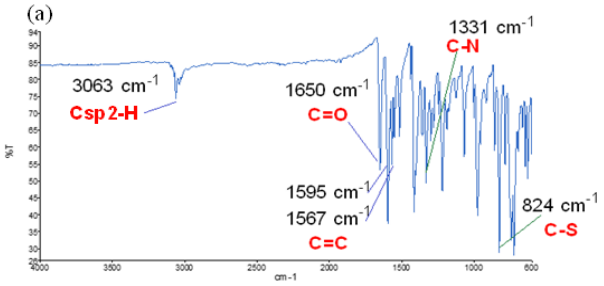
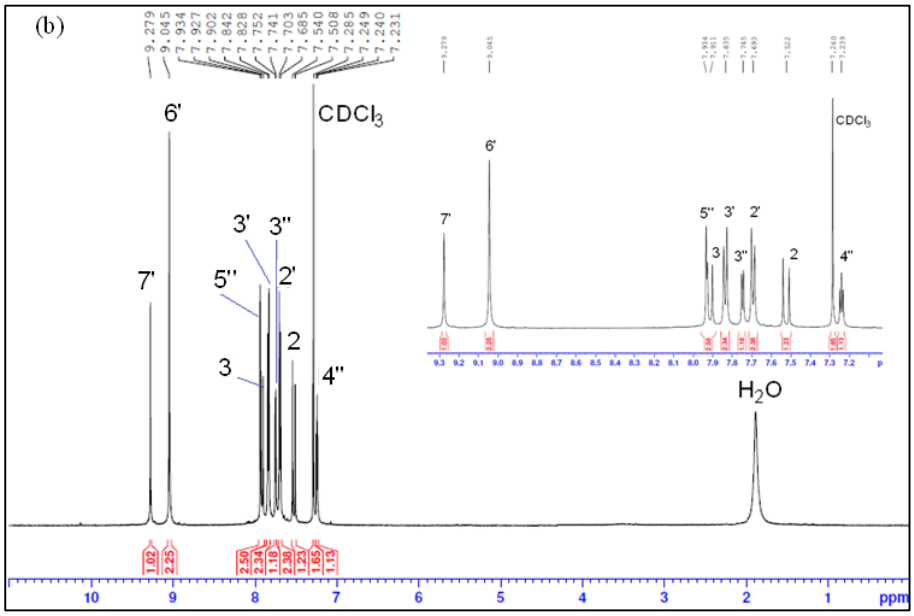


Figure S2.1. (a) IR (b) ^{1}H (C) ^{13}C NMR, (d) DEPT 90 and (e) DEPT135 spectra of chalcone **1** in $CDCl_3$.



compound **3**





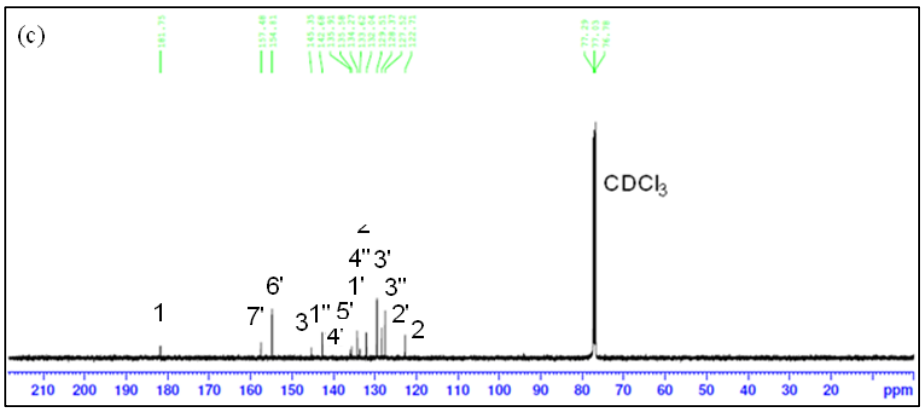
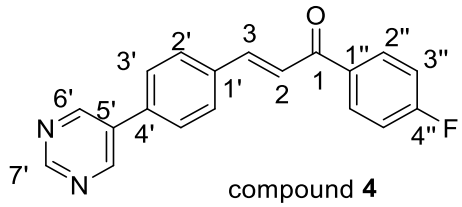
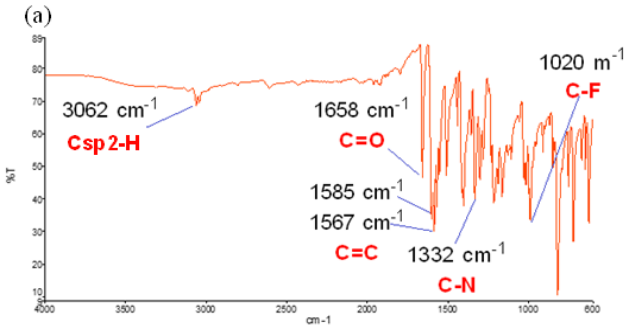


Figure S2.2. (a) IR (b) ^{1}H and (C) ^{13}C NMR spectra of chalcone **3** in $CDCl_3$.



compound **4**



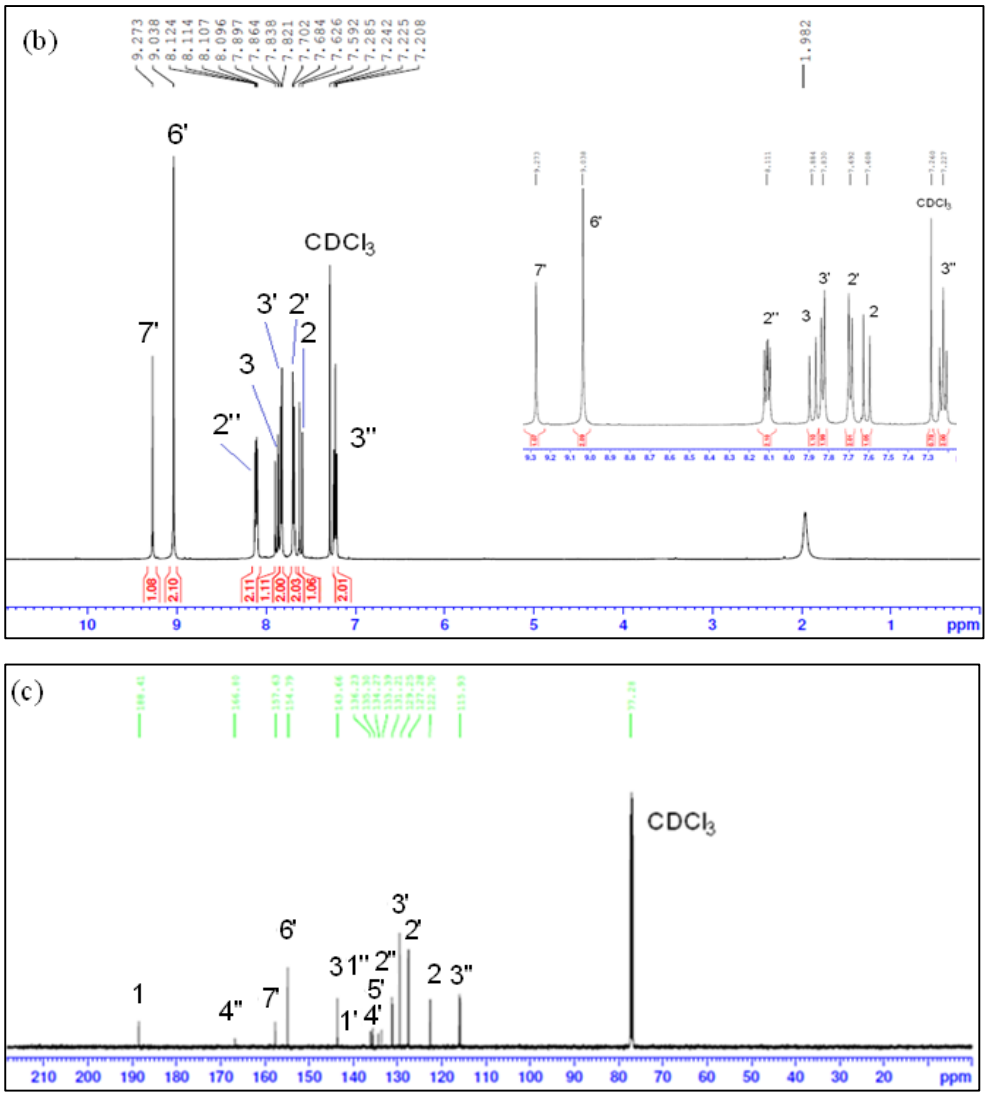


Figure S2.3. (a) IR (b) ^{1}H and (C) ^{13}C NMR spectra of chalcone **4** in $CDCl_3$.

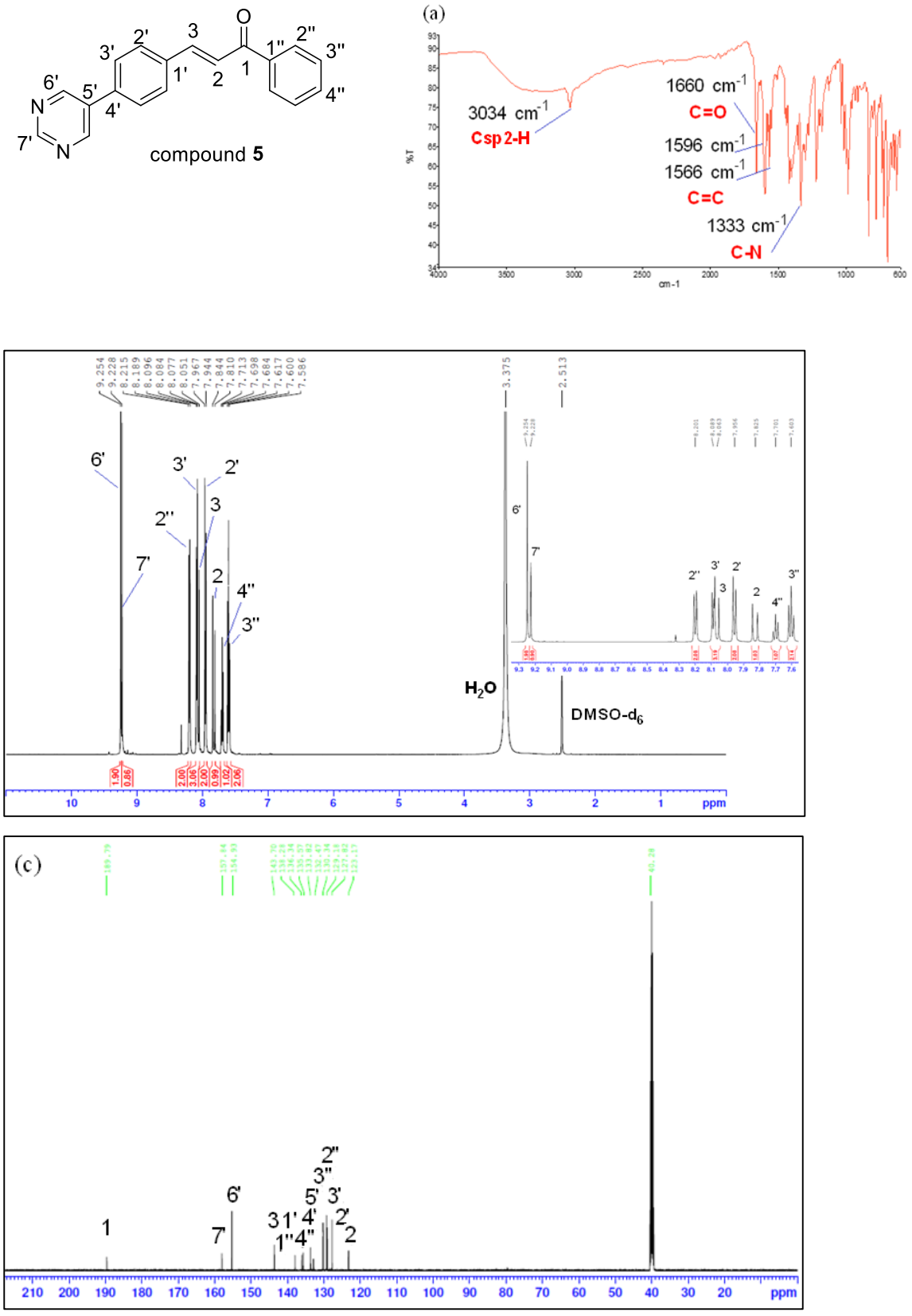


Figure S2.4. (a) IR (b) ^{1}H and (C) ^{13}C NMR spectra of chalcone **5** in DMSO-d_6.

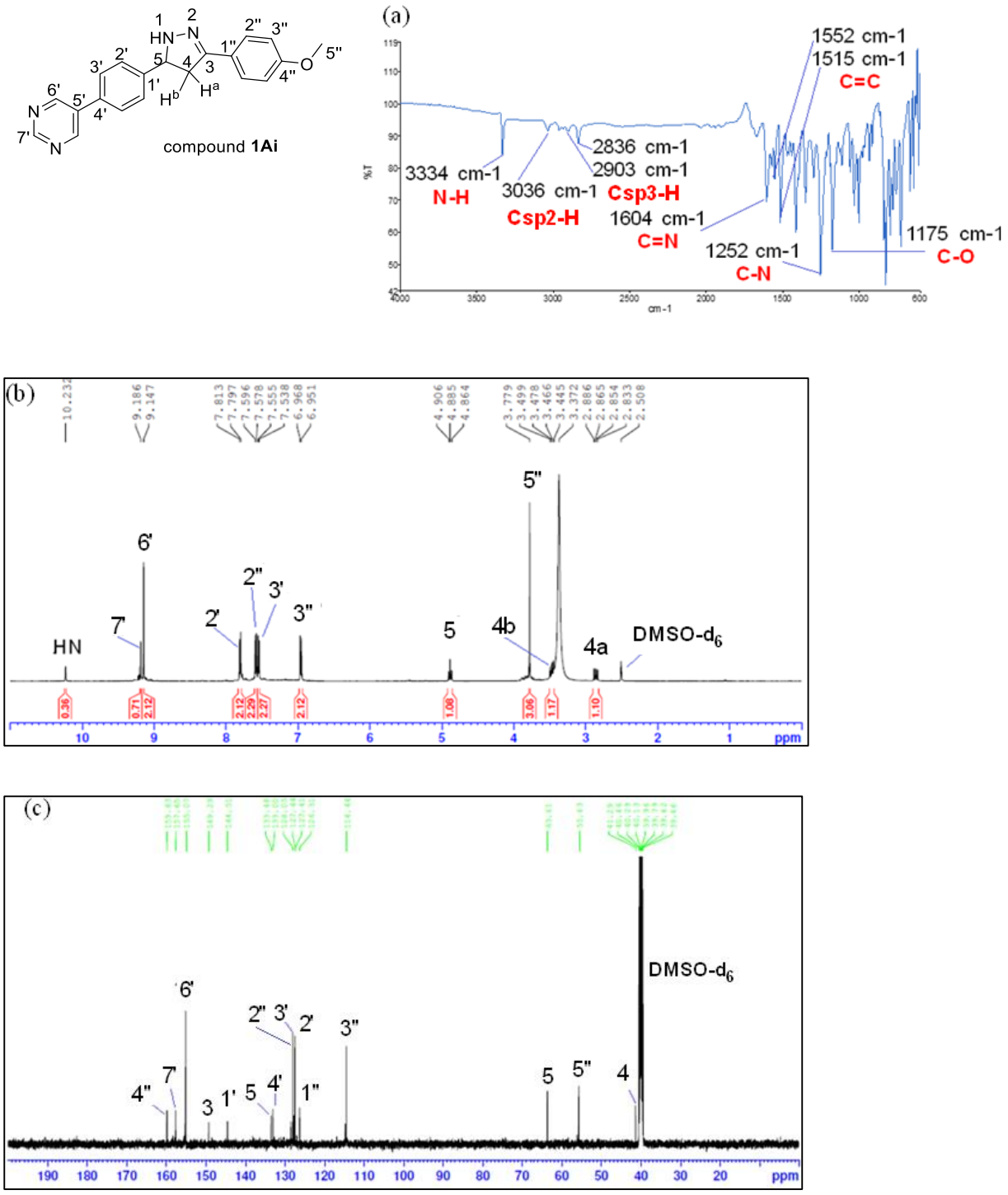


Figure S2.5. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **1Ai** in DMSO-d_6

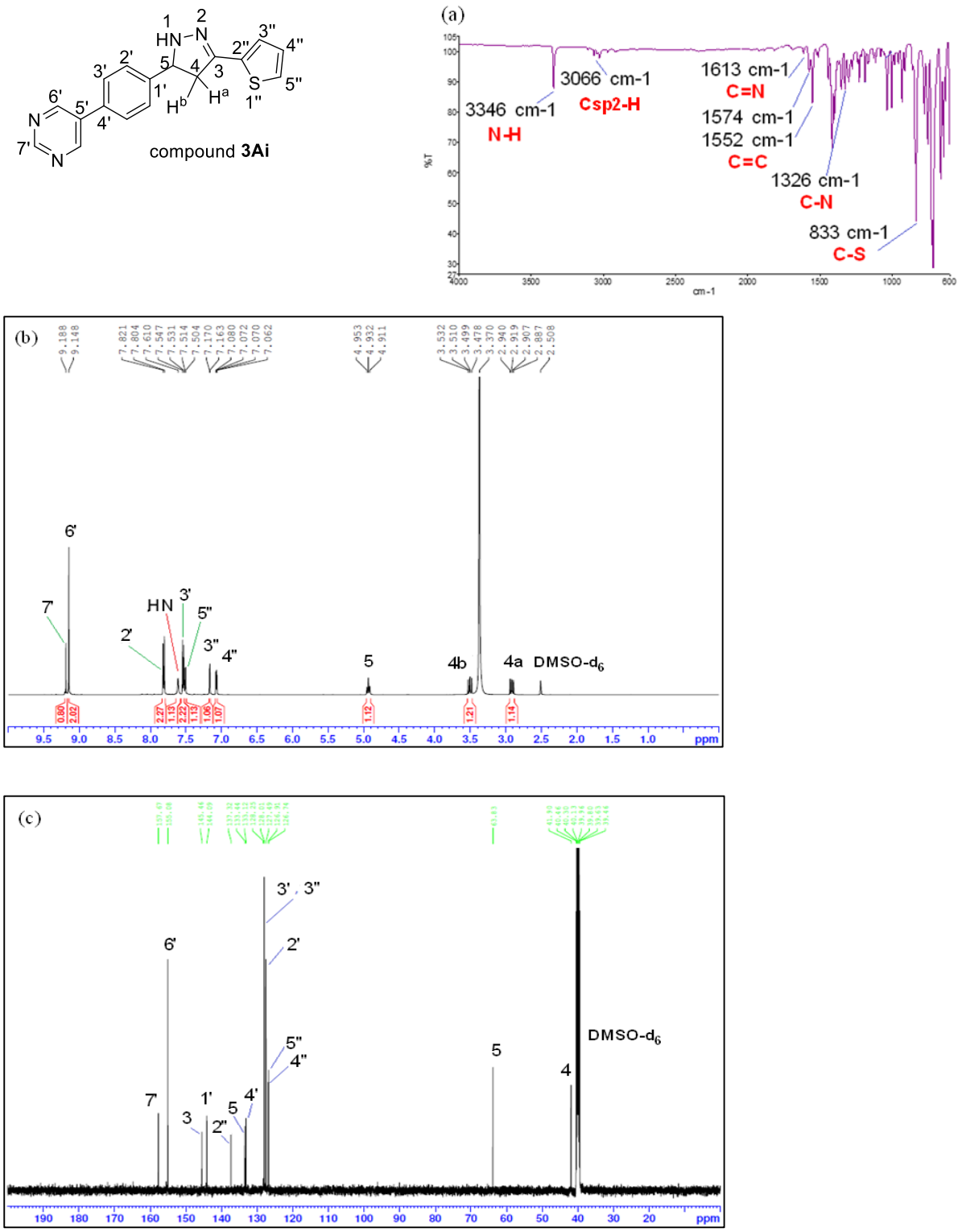


Figure S2.6. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **3Ai** in DMSO-d$_6$

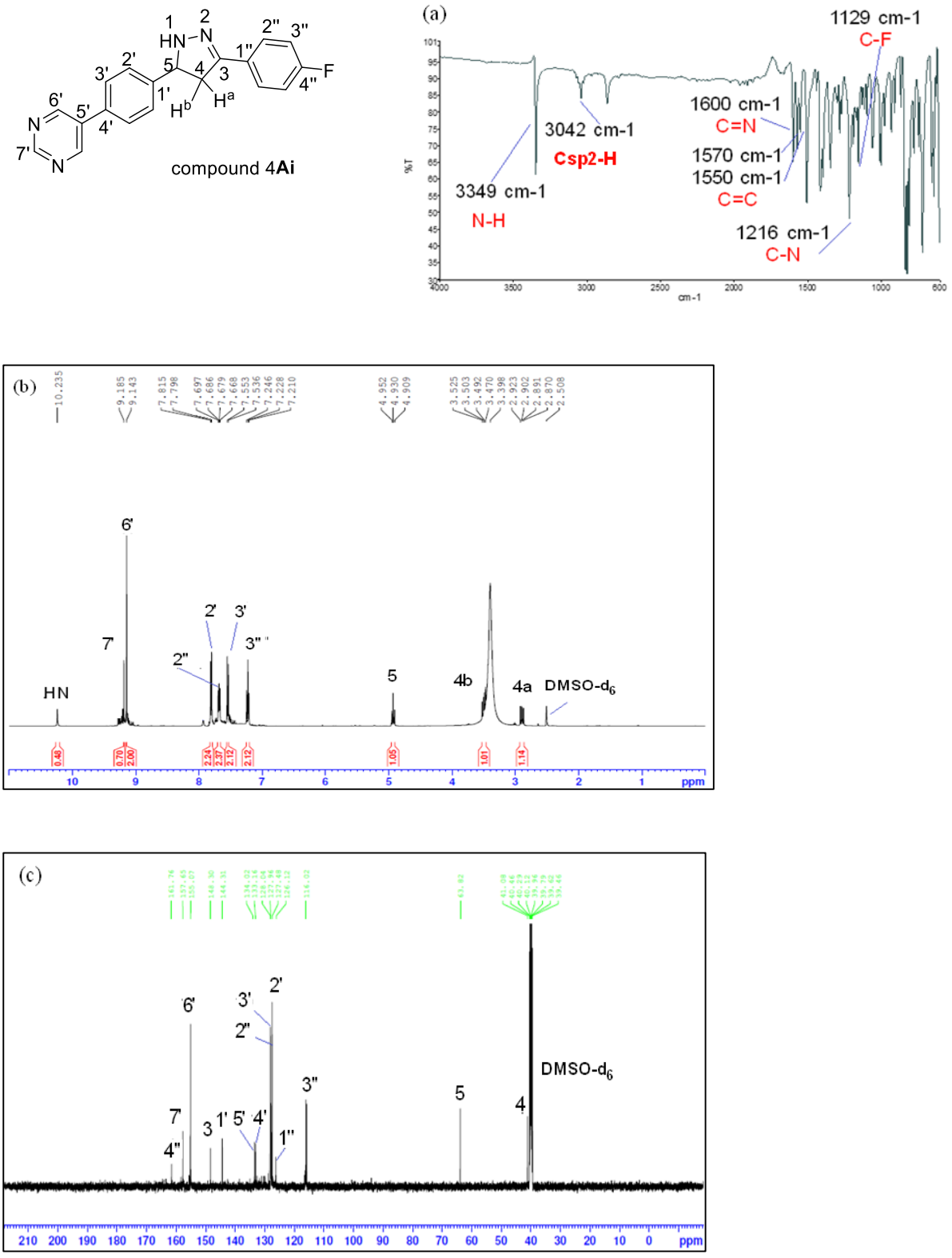


Figure S2.7. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **4Ai** in DMSO-d_6

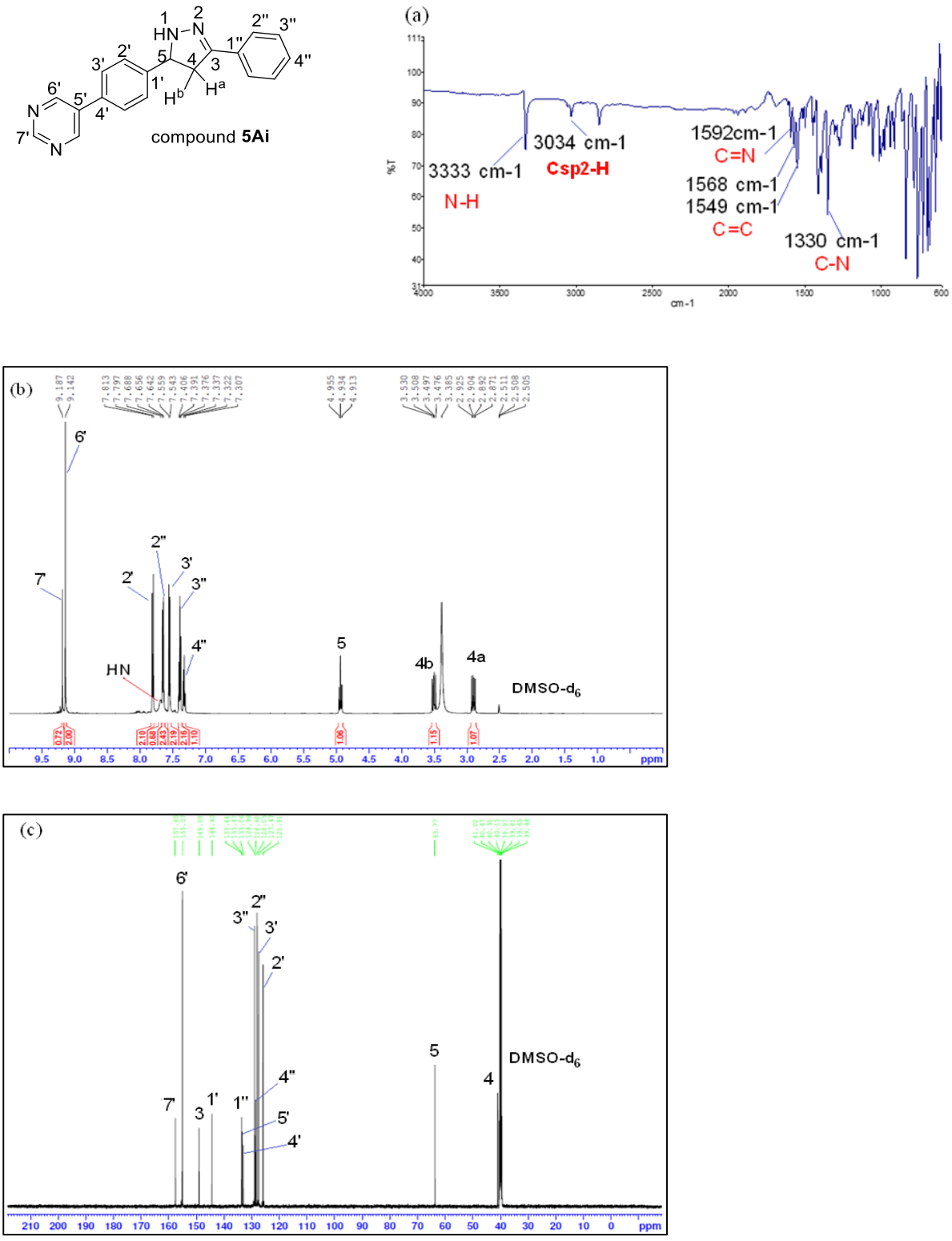


Figure S2.8. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **5Ai** in DMSO-d_6

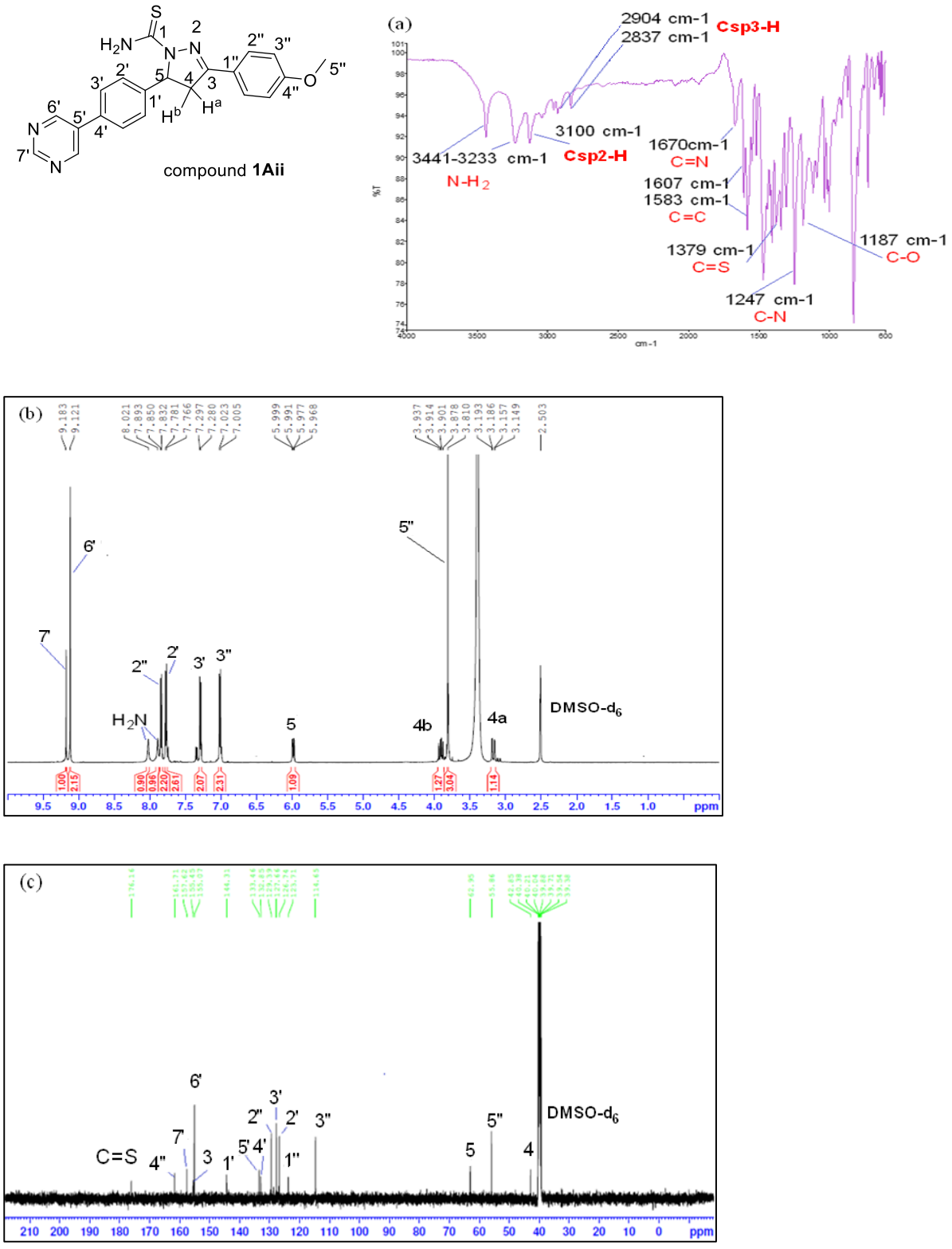


Figure S2.9. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **1Aii** in DMSO-d_6

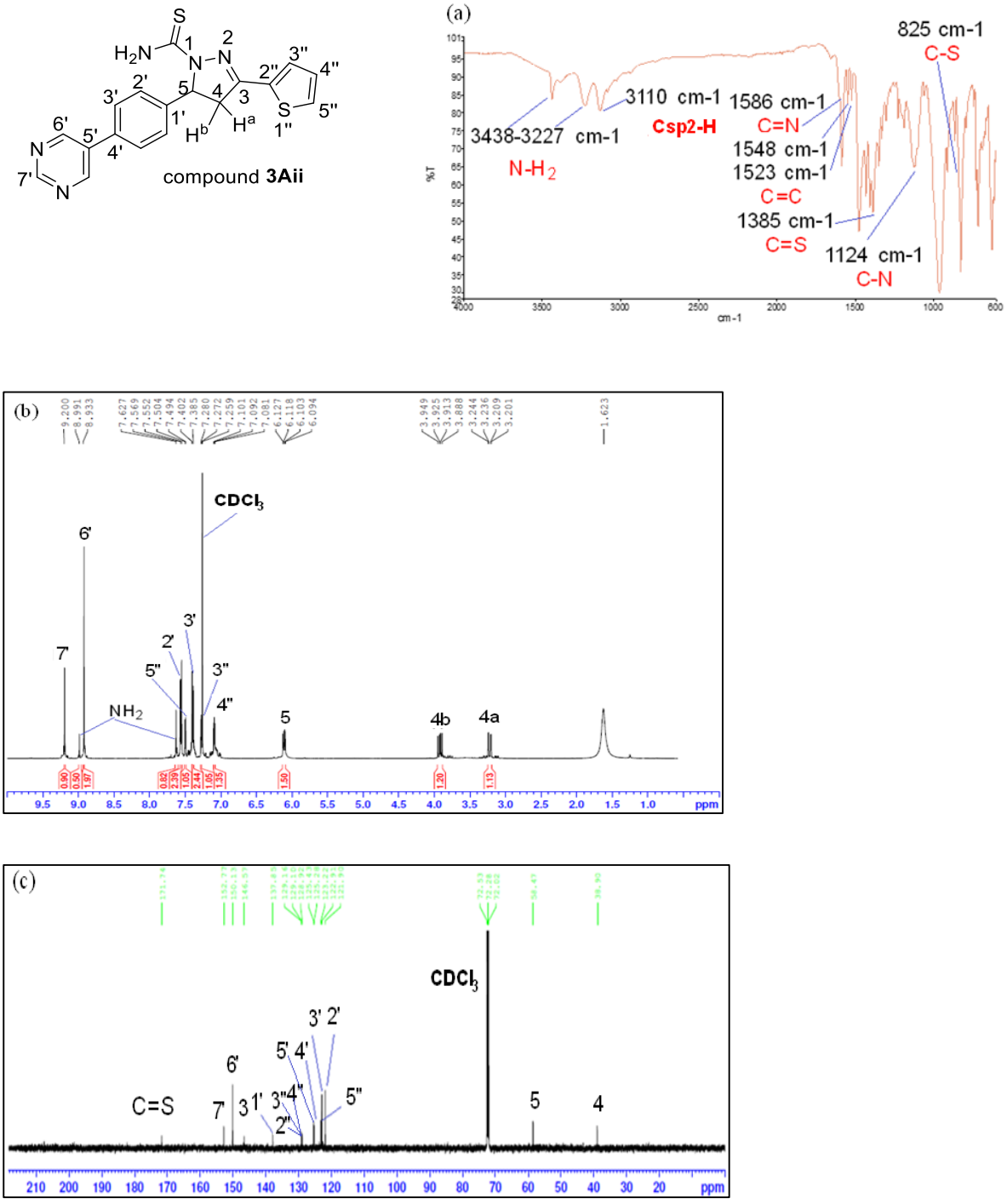


Figure S2.10. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **3Aii** in $CDCl_3$

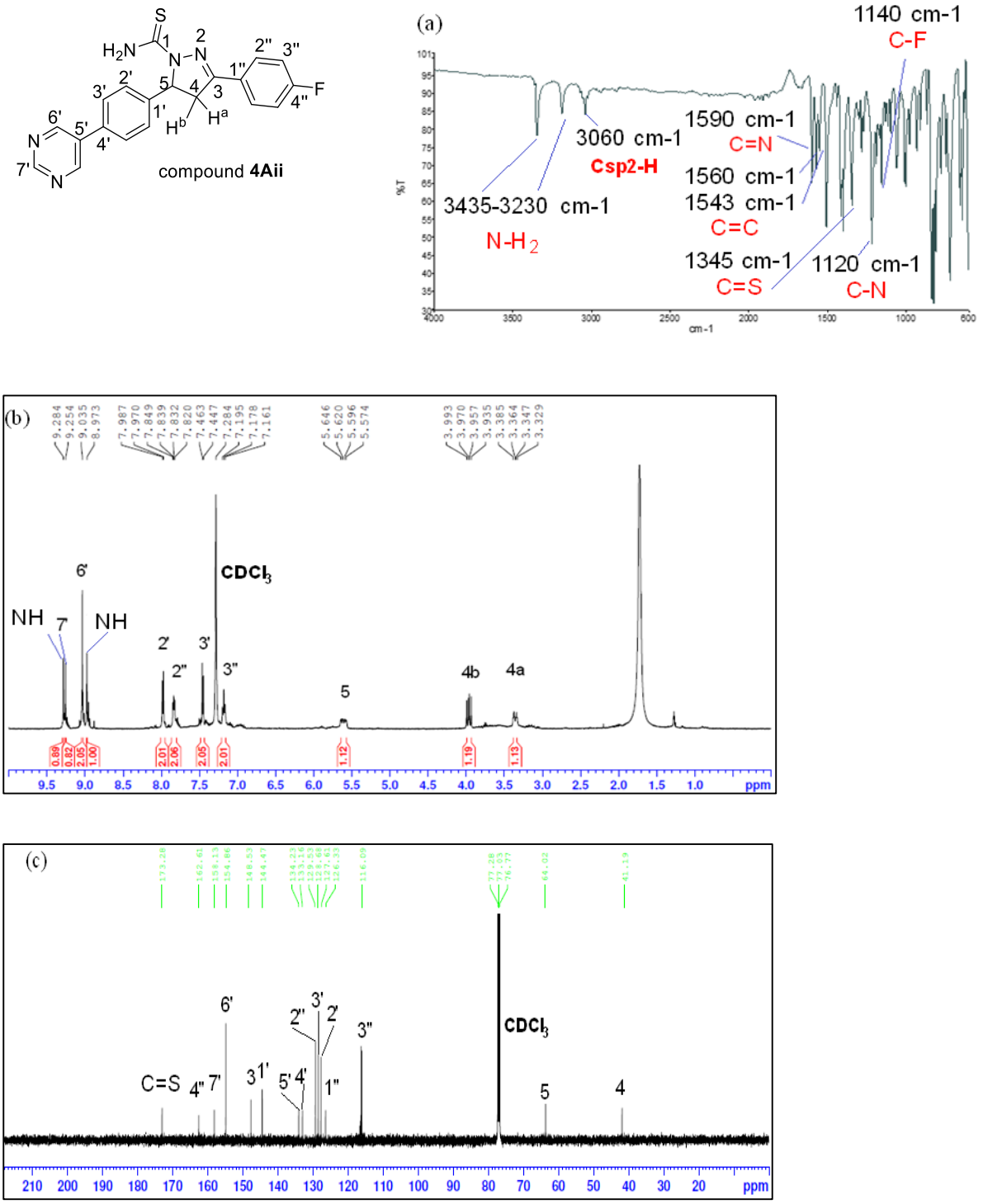


Figure S2.11. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **4Aii** in $CDCl_3$

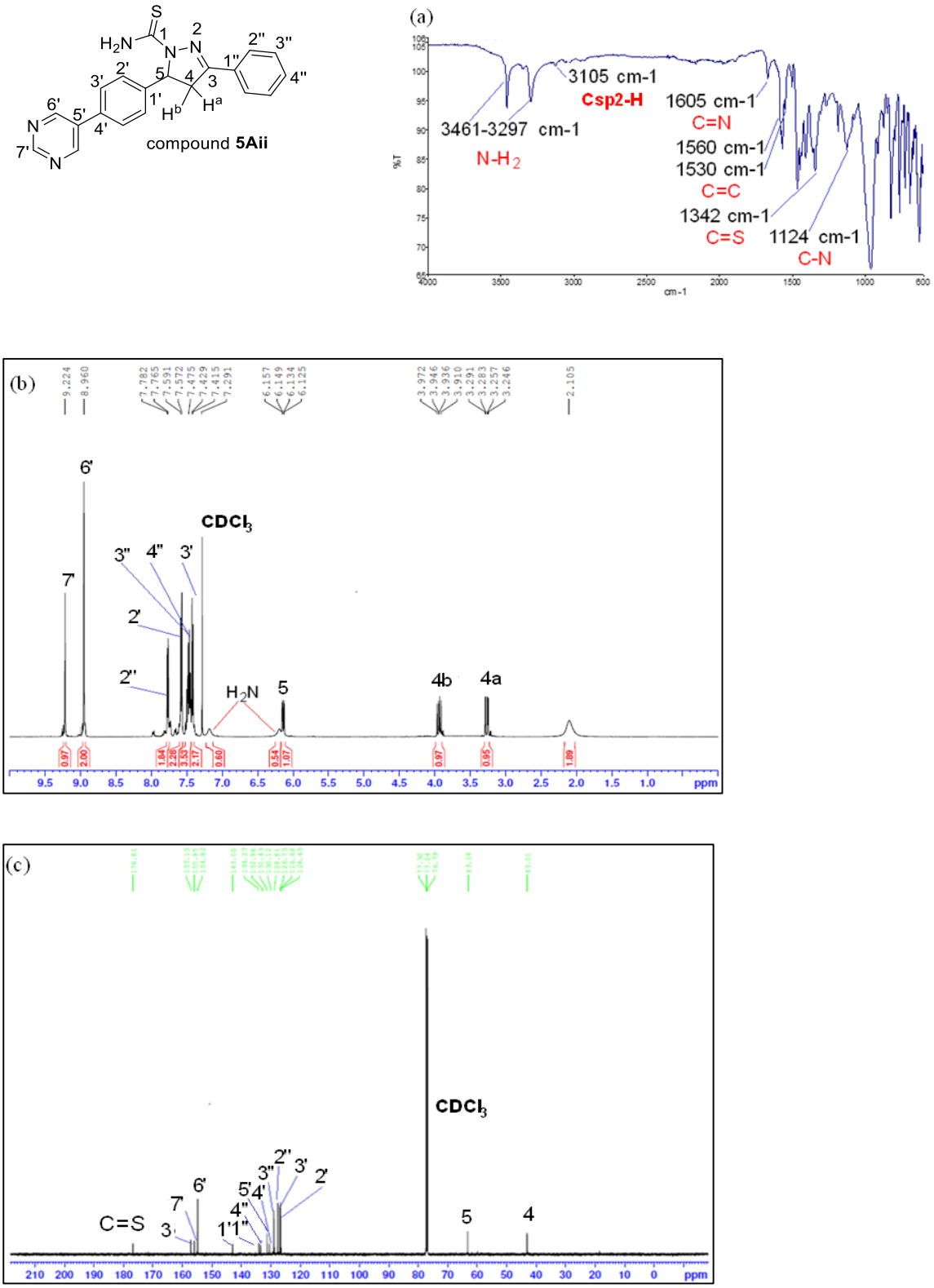
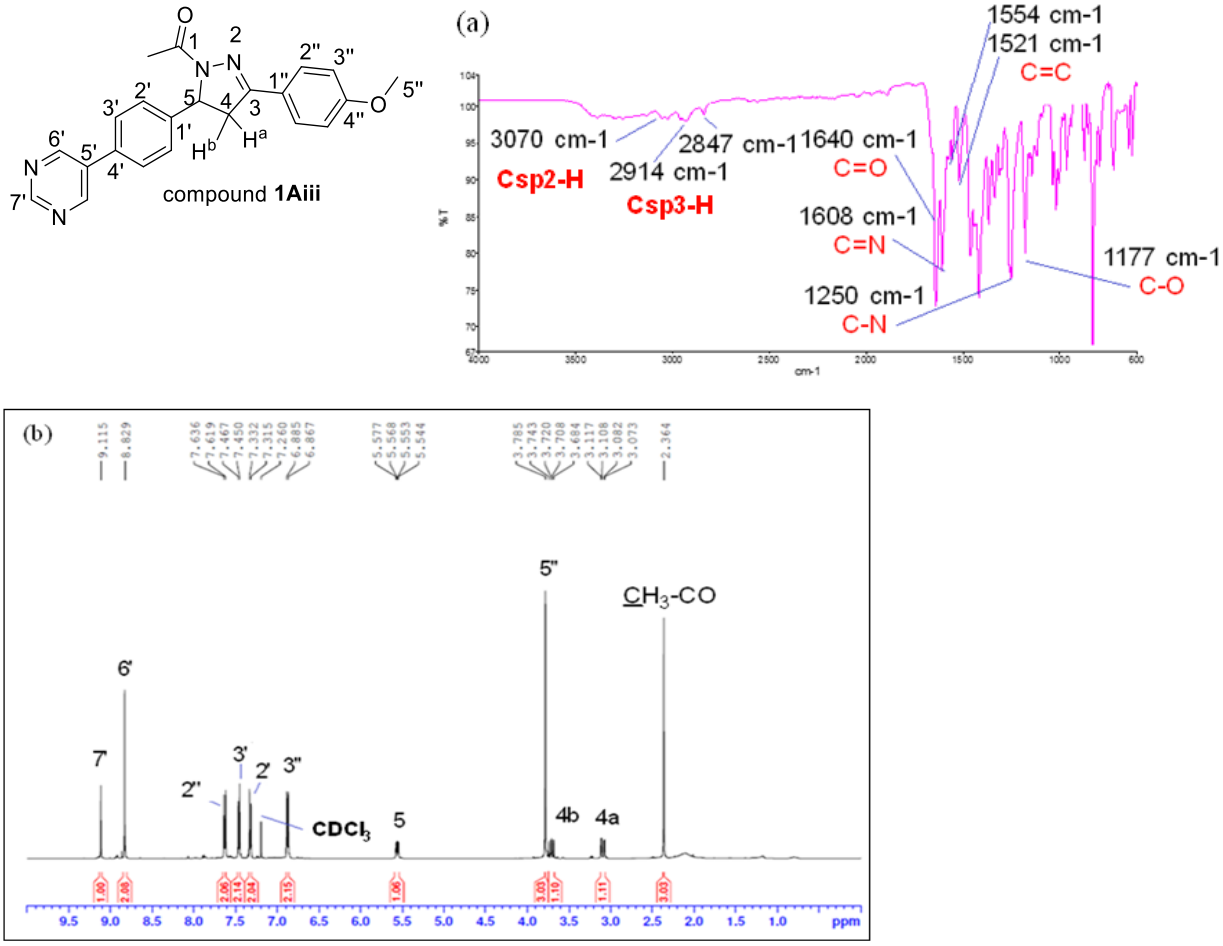


Figure S2.12. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **5Aii** in $CDCl_3$


compound 1Aiii
(a)
3070 cm-1
Csp2-H
2914 cm-1
2847 cm-1
Csp3-H
1640 cm-1
C=O
1554 cm-1
1521 cm-1
C=C
1608 cm-1
C=N
1250 cm-1
C-N
1177 cm-1
C-O
(b)
CDCl3
CH3-CO
ppm

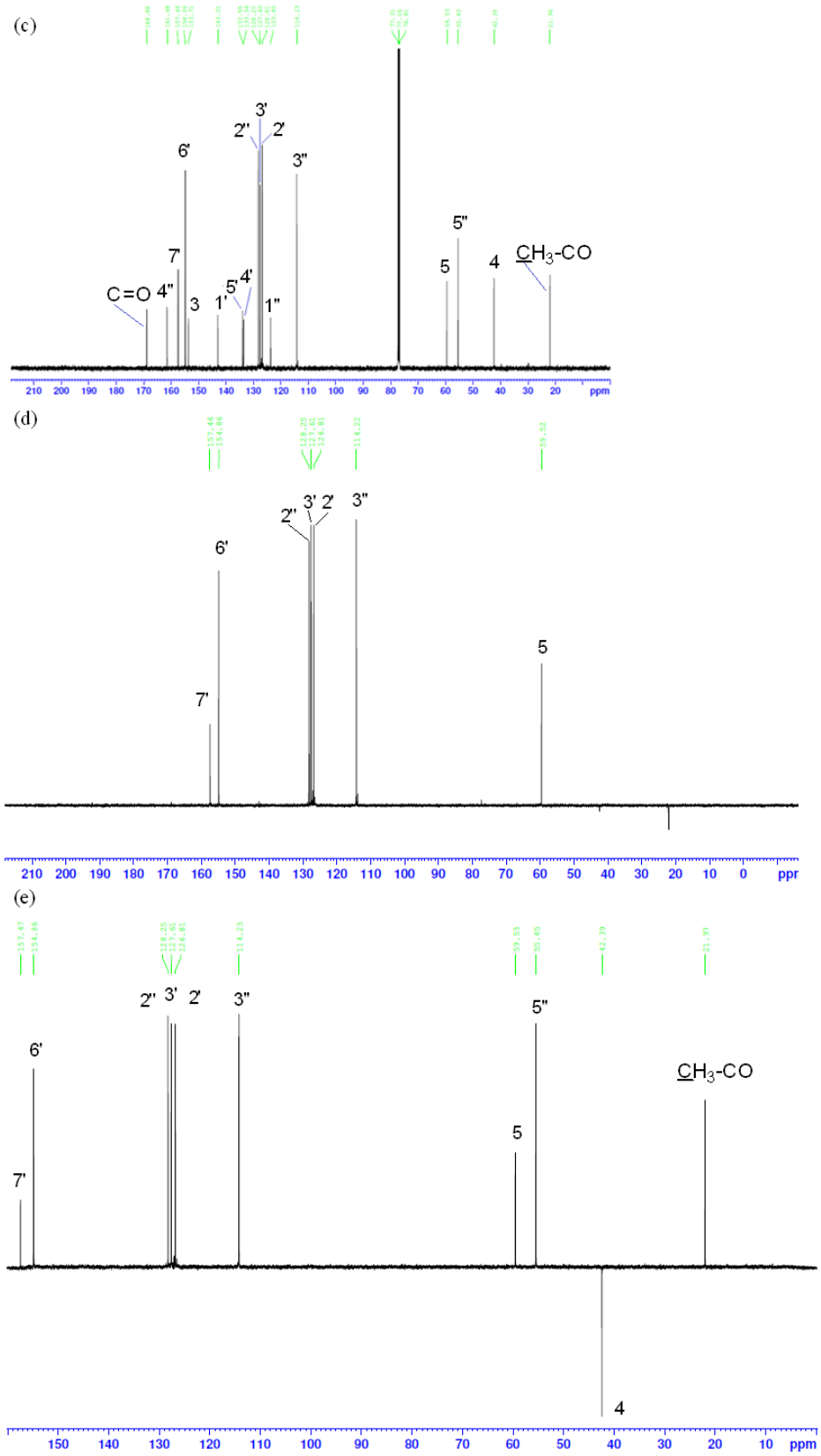


Figure S2.13. (a) IR (b) ^{1}H (c) ^{13}C NMR, (d) DEPT 90 and (e) DEPT135 spectra of pyrazoline **1Aiii** in $CDCl_3$

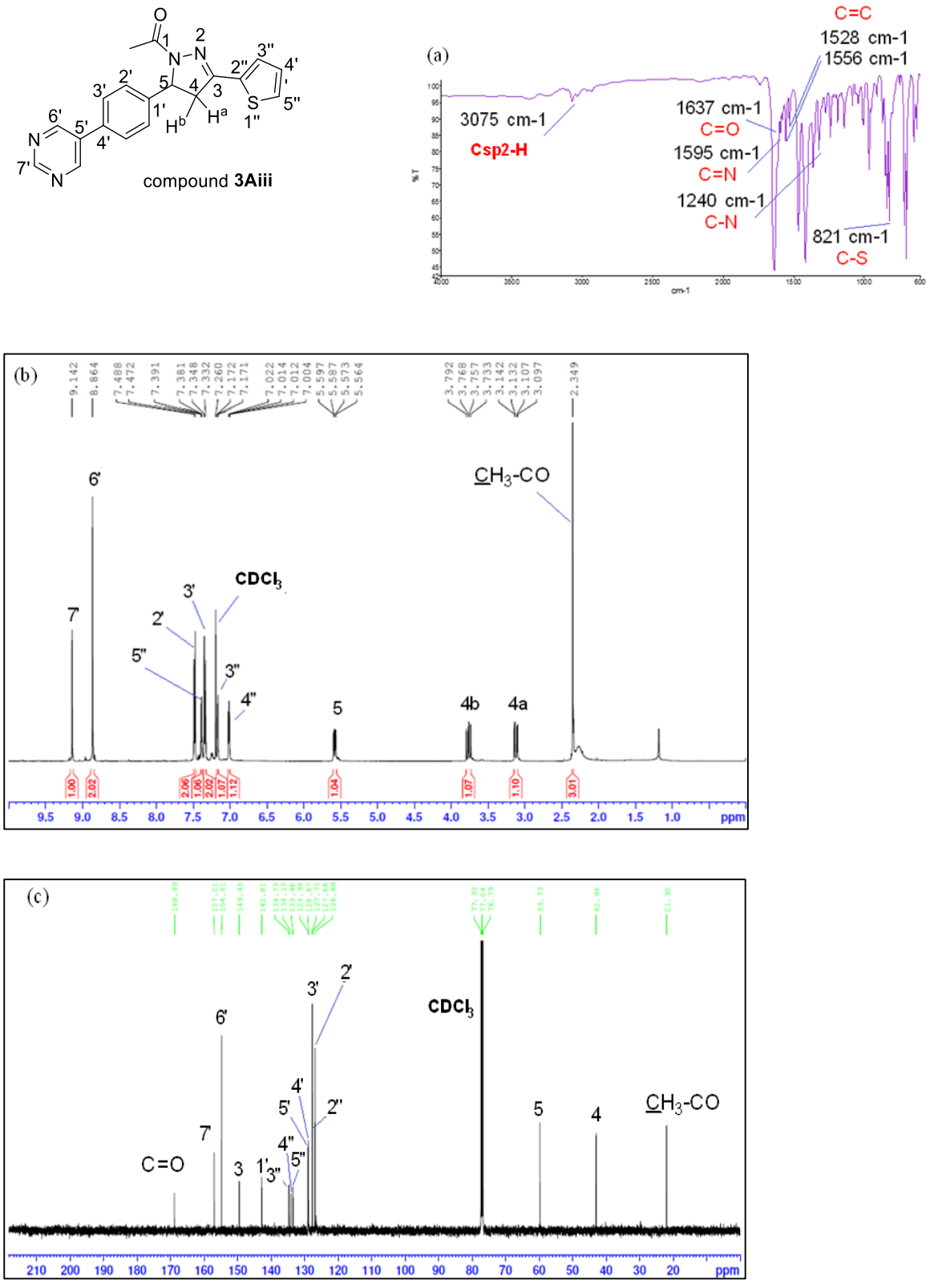


Figure S2.14. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **3Aiii** in $CDCl_3$

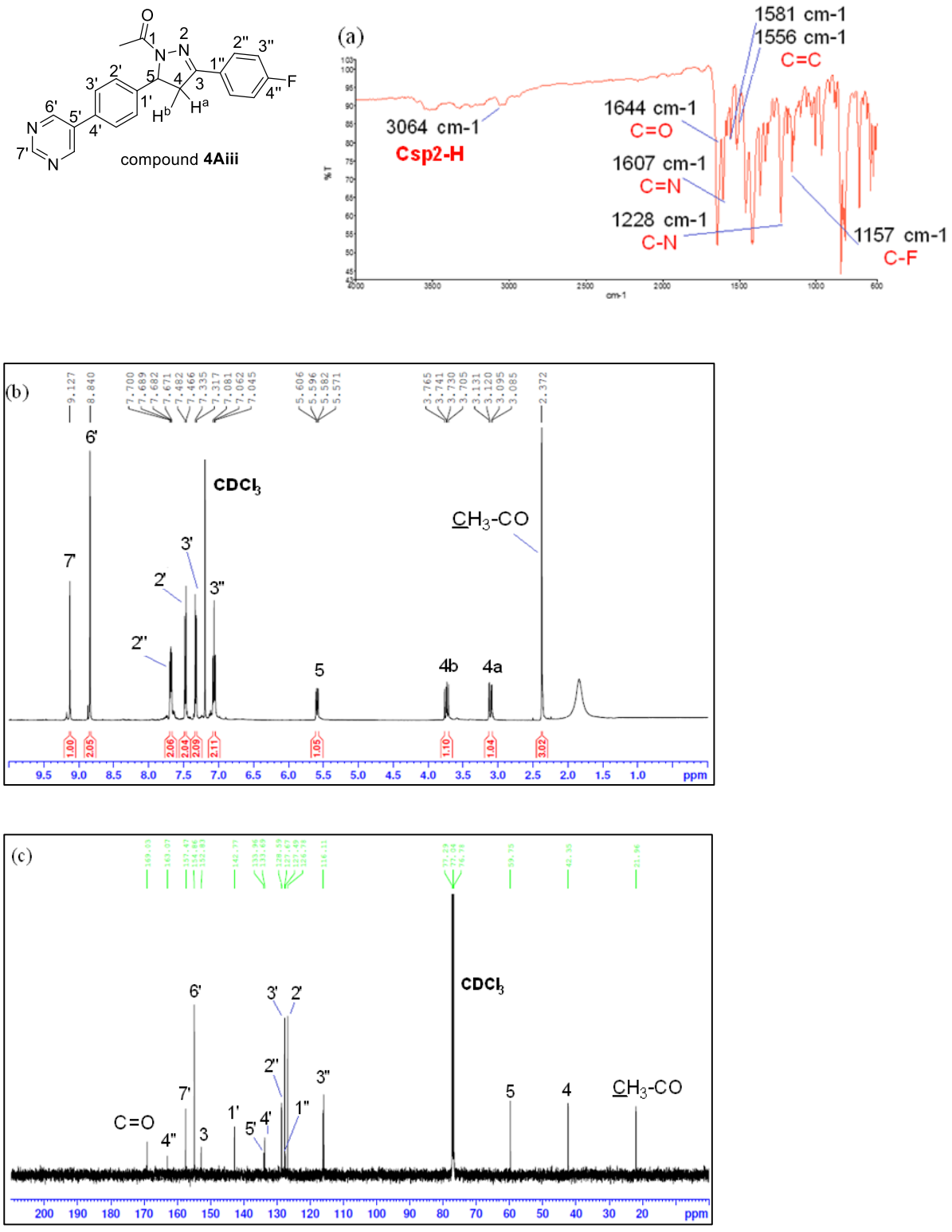


Figure S2.15. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **4Aiii** in $CDCl_3$

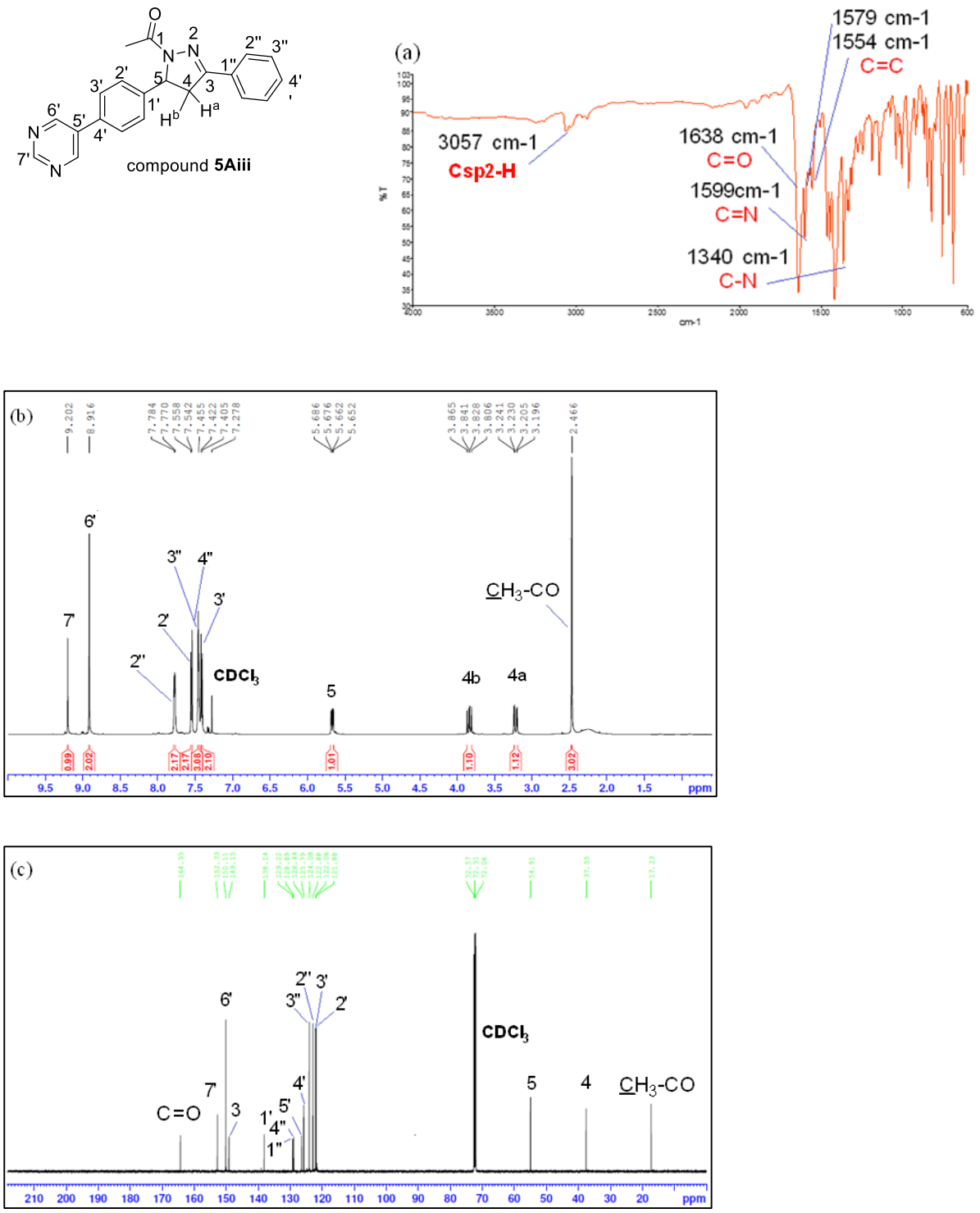


Figure S2.16. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrazoline **5Aiii** in $CDCl_3$

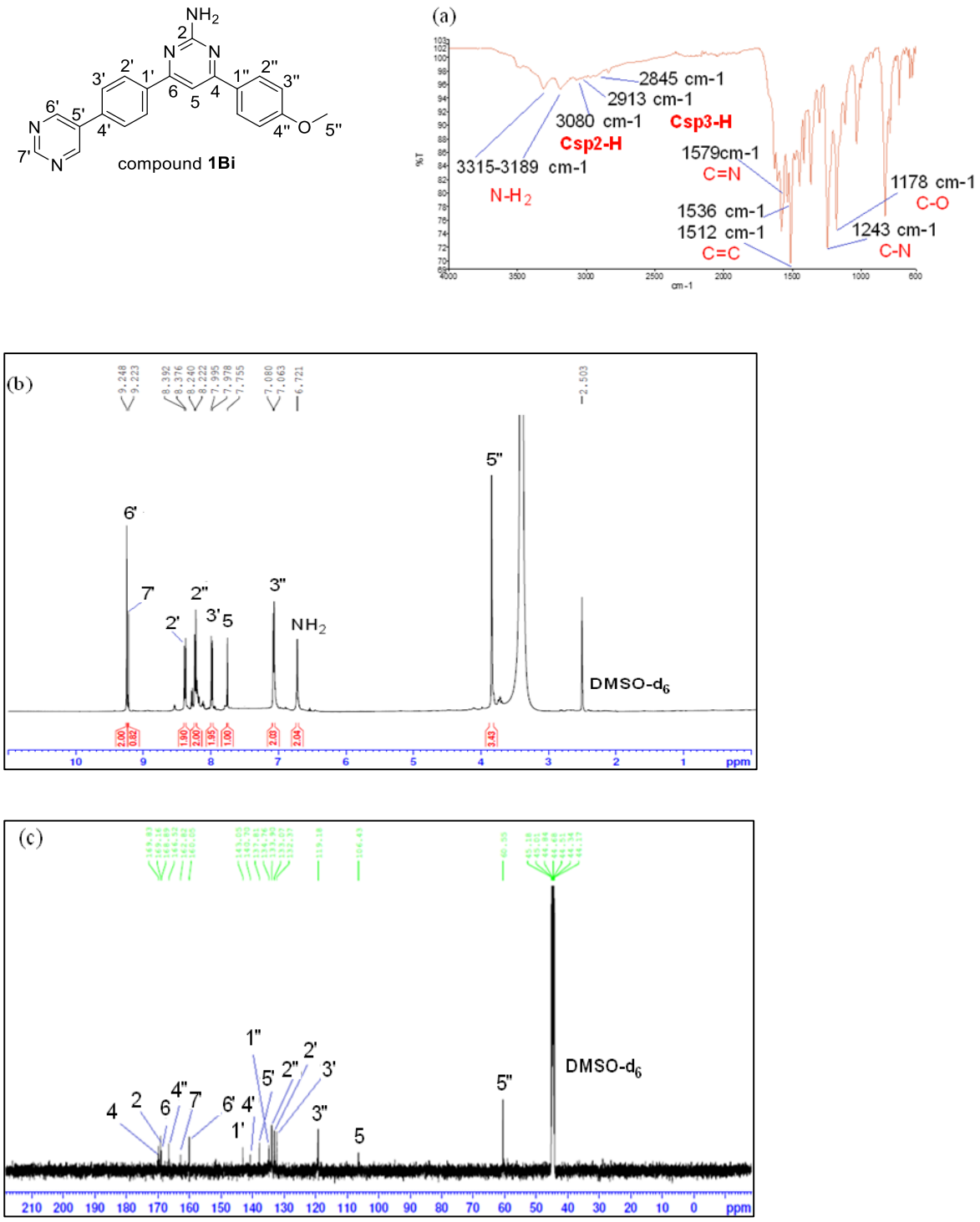


Figure S2.17. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **1Bi** in DMSO-d_6

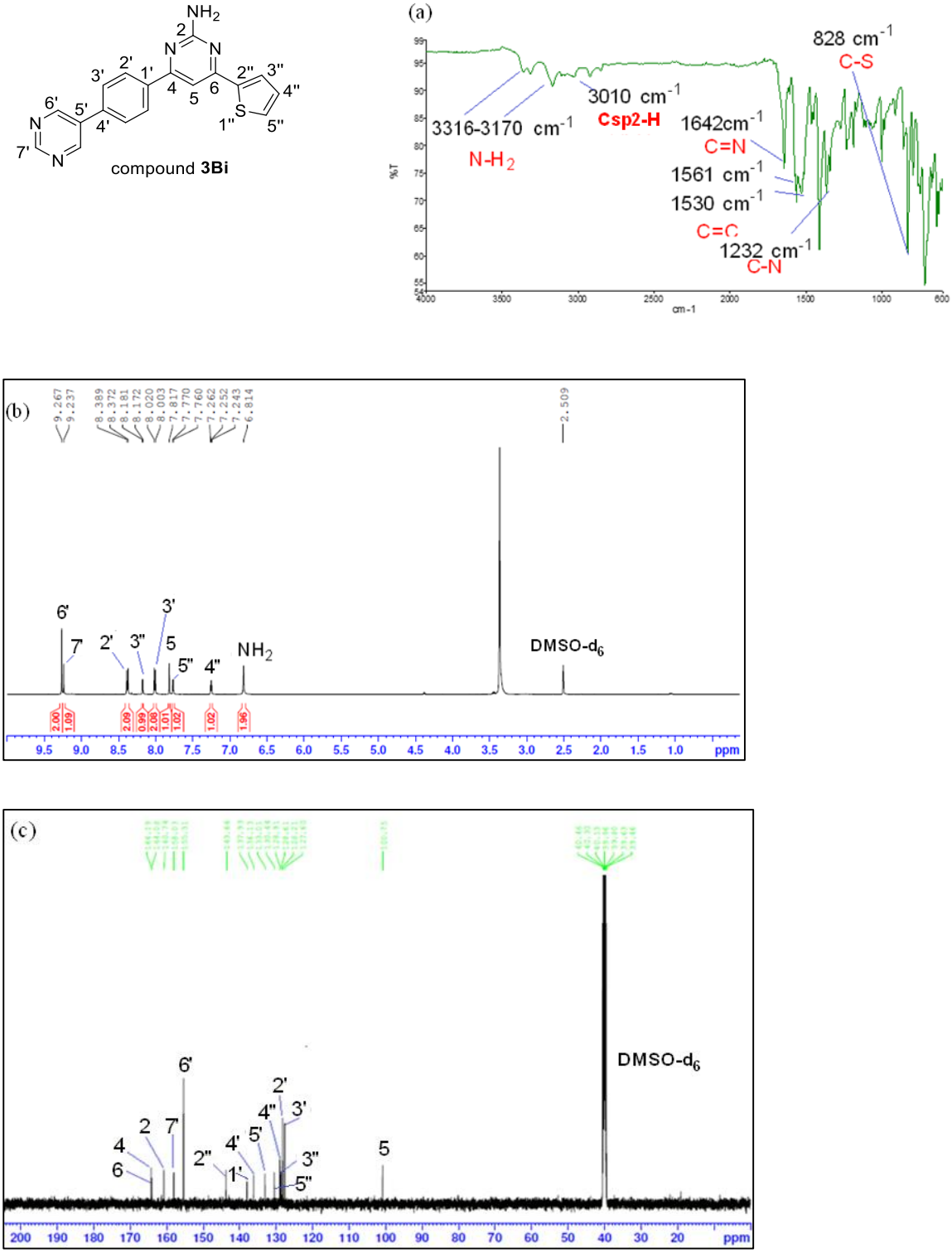


Figure S2.18. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **3Bi** in DMSO-d_6

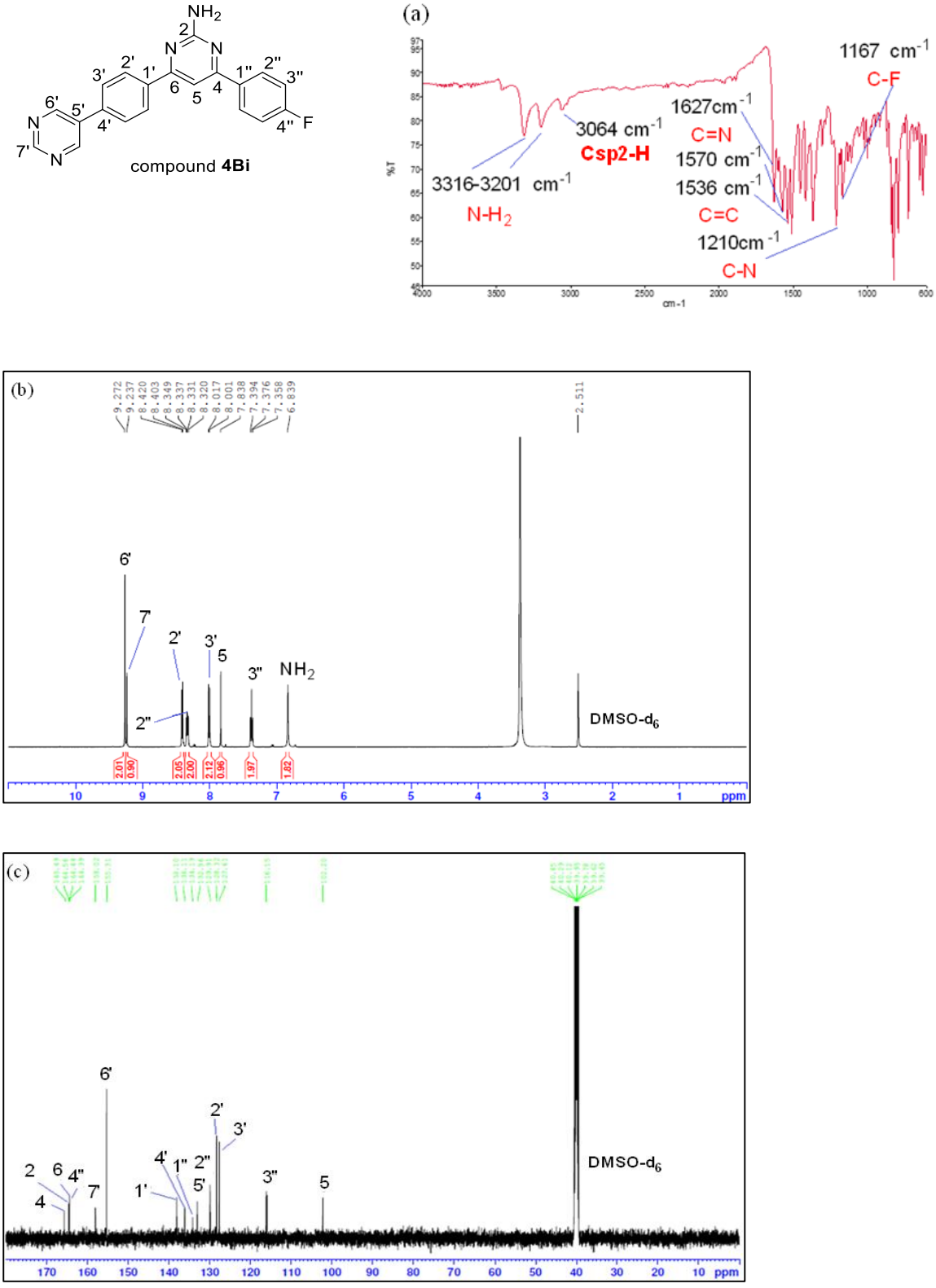


Figure S2.19. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **4Bi** in DMSO-d_6

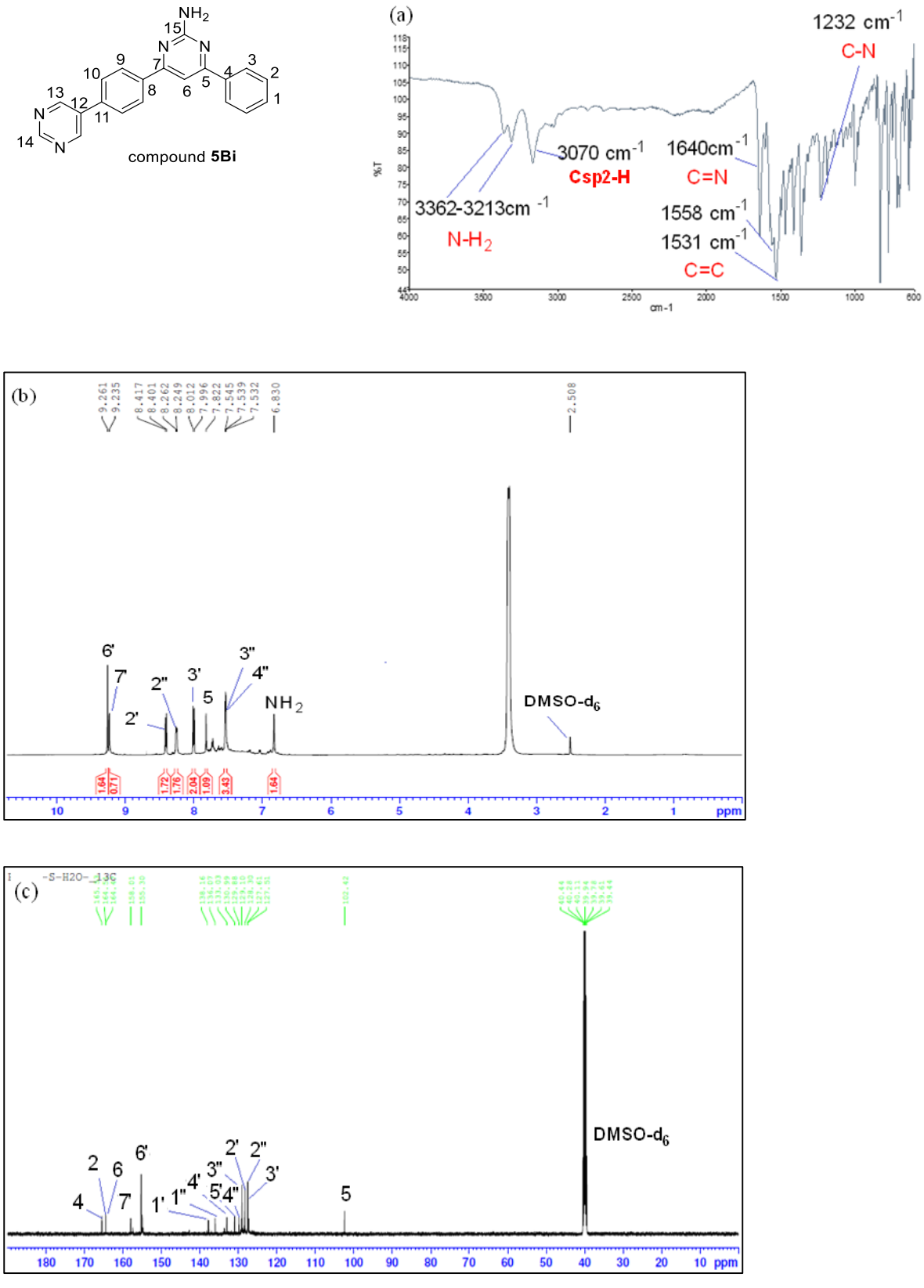


Figure S2.20. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **5Bi** in DMSO-d_6

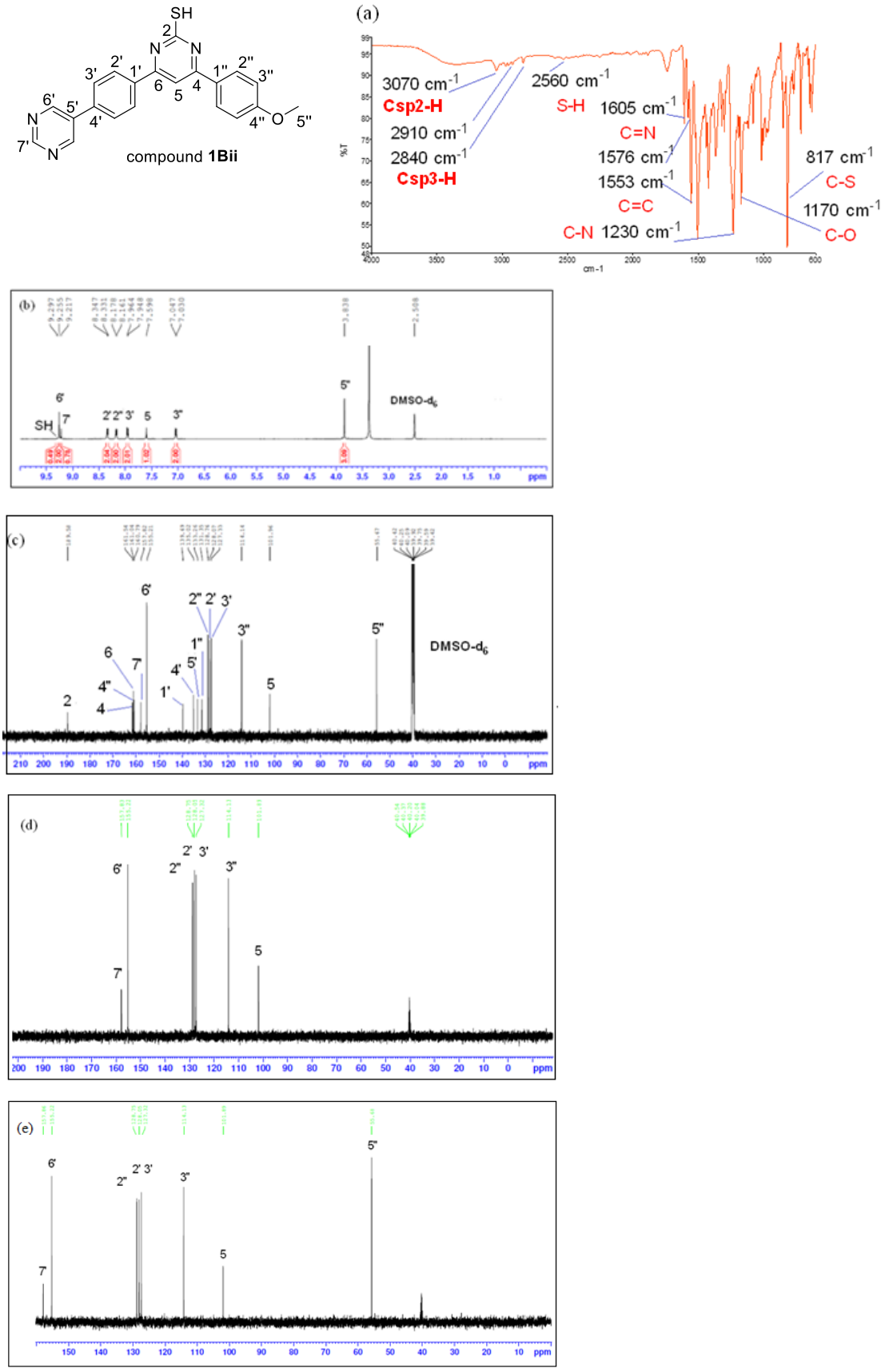


Figure S2.21. (a) IR (b) ^{1}H (c) ^{13}C NMR, (d) DEPT 90 and (e) DEPT135 spectra of pyrimidine **1Bii** in DMSO-d_6

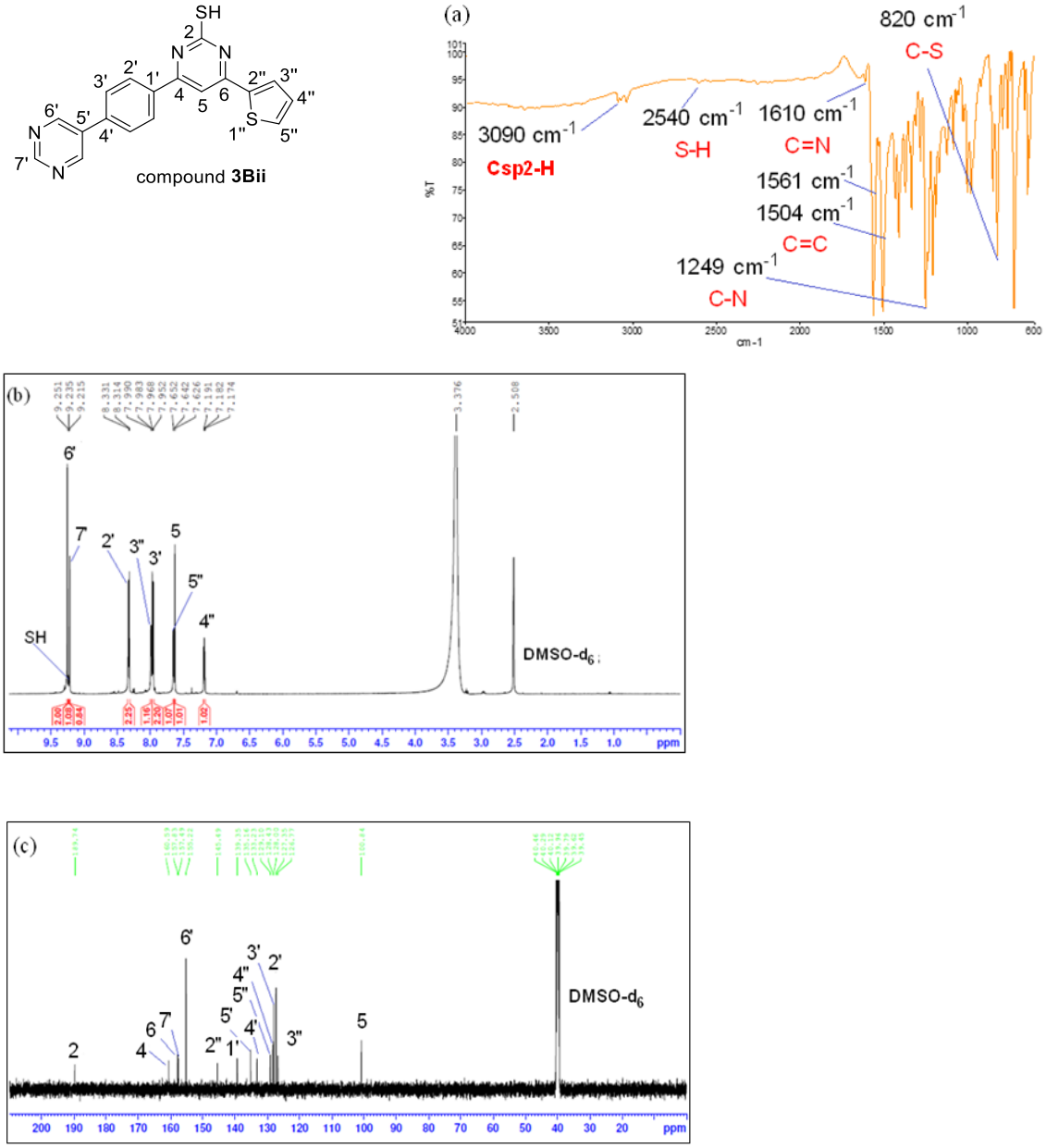


Figure S2.22 (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **3Bii** in DMSO-d_6

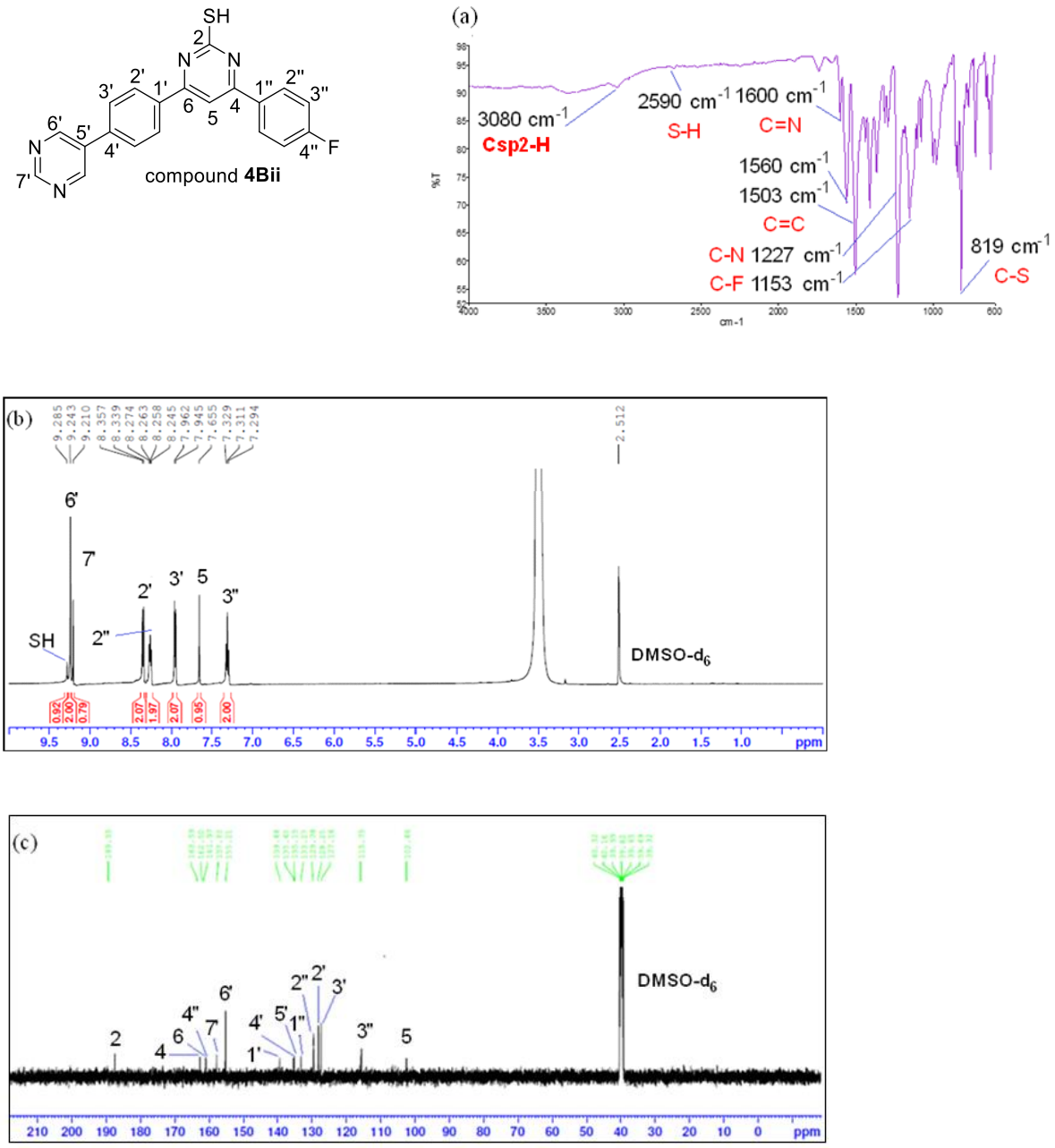


Figure S2.23 (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **4Bii** in DMSO-d_6

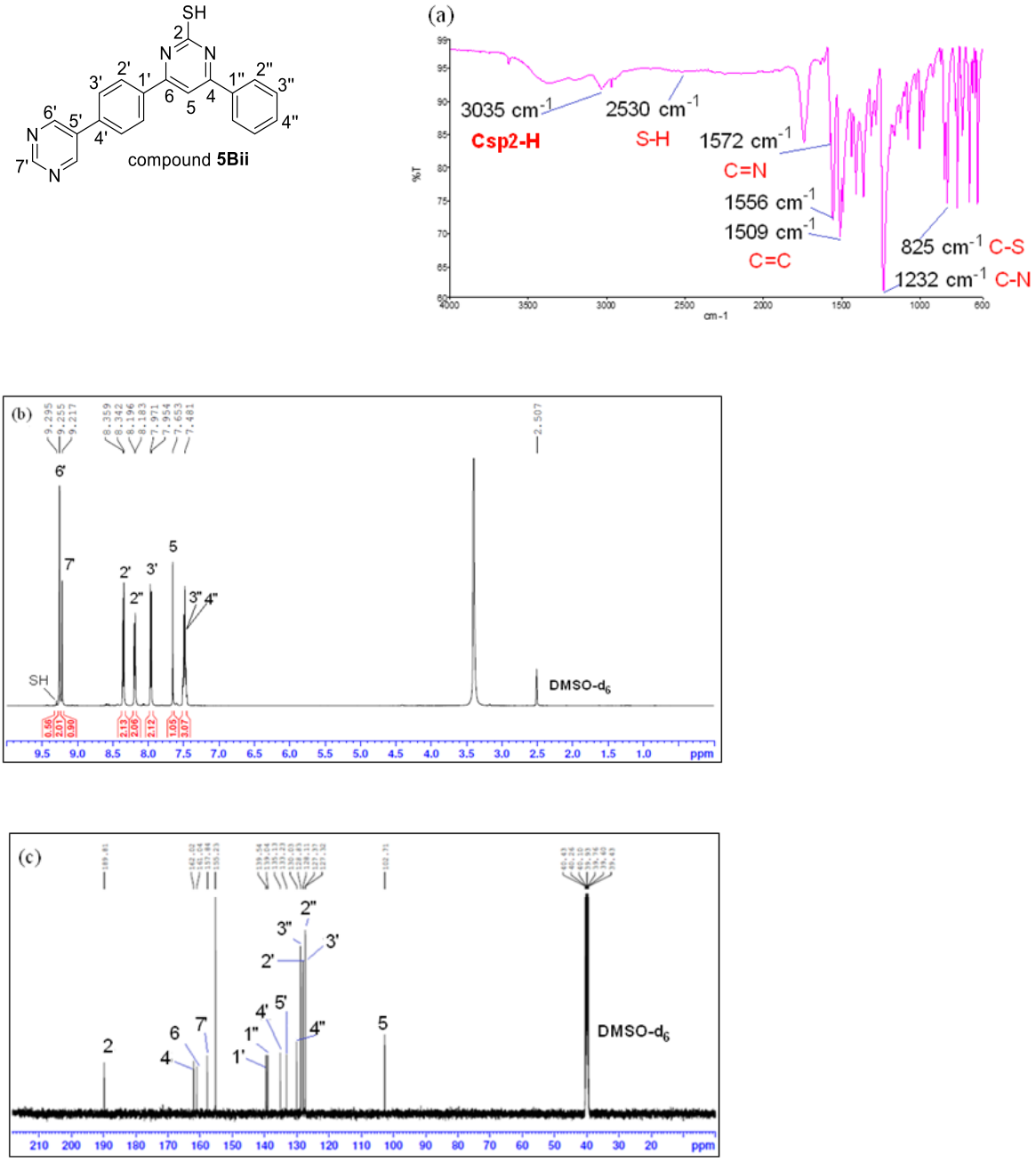


Figure S2.24 (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **5Bii** in DMSO-d_6

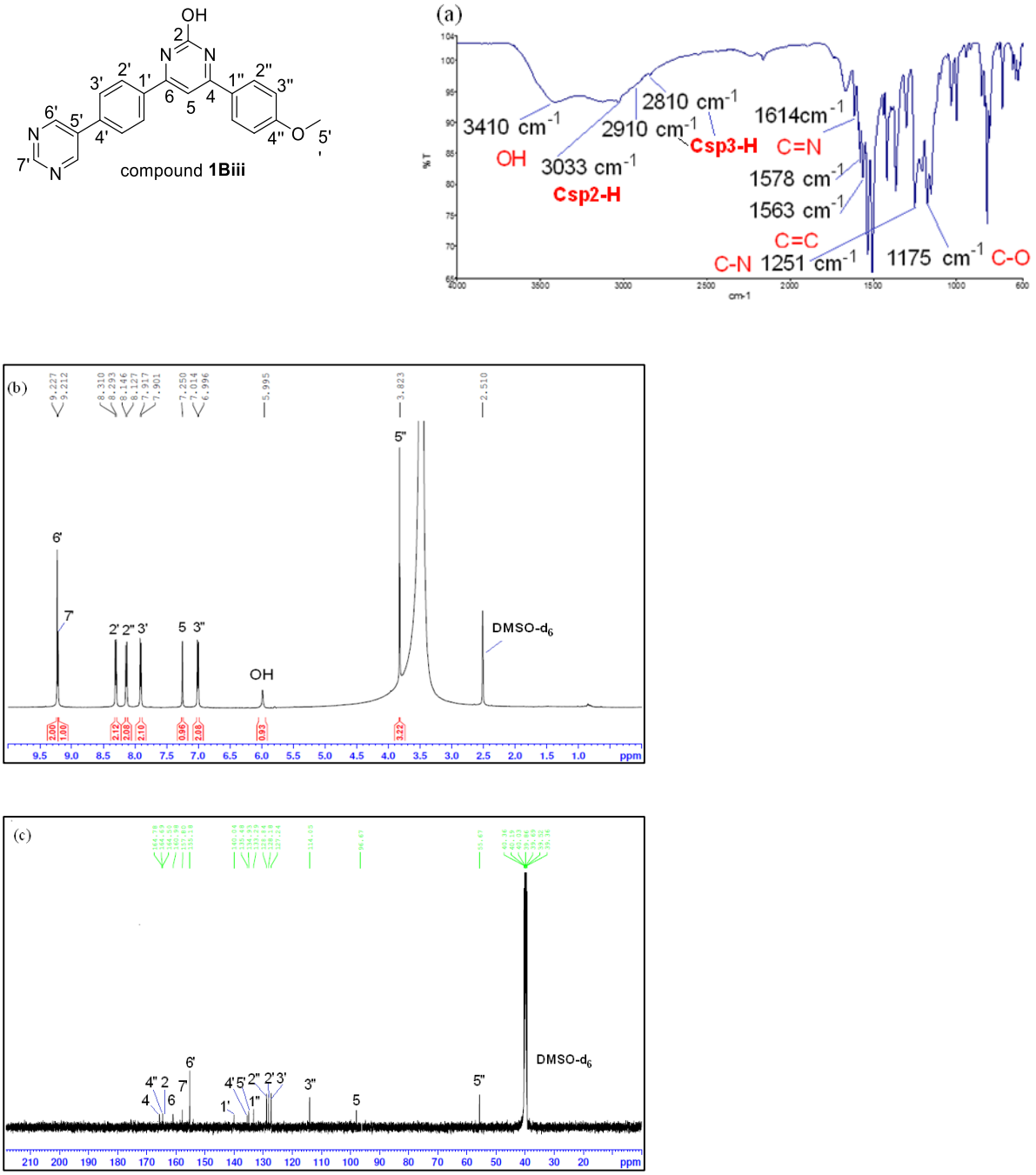


Figure S2.25. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **1Biii** in DMSO-d_6

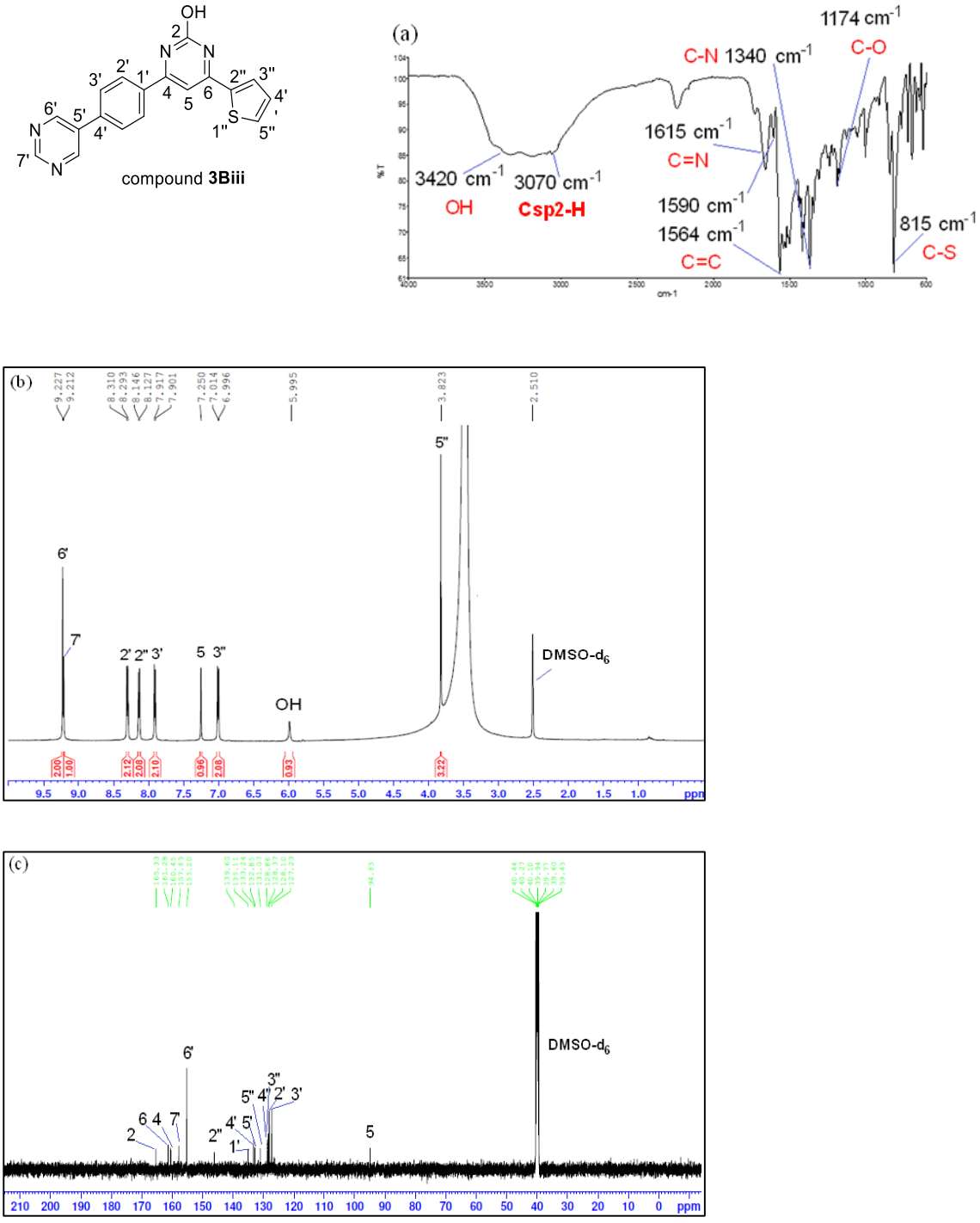


Figure S2.26. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **3Biii** in DMSO-d_6

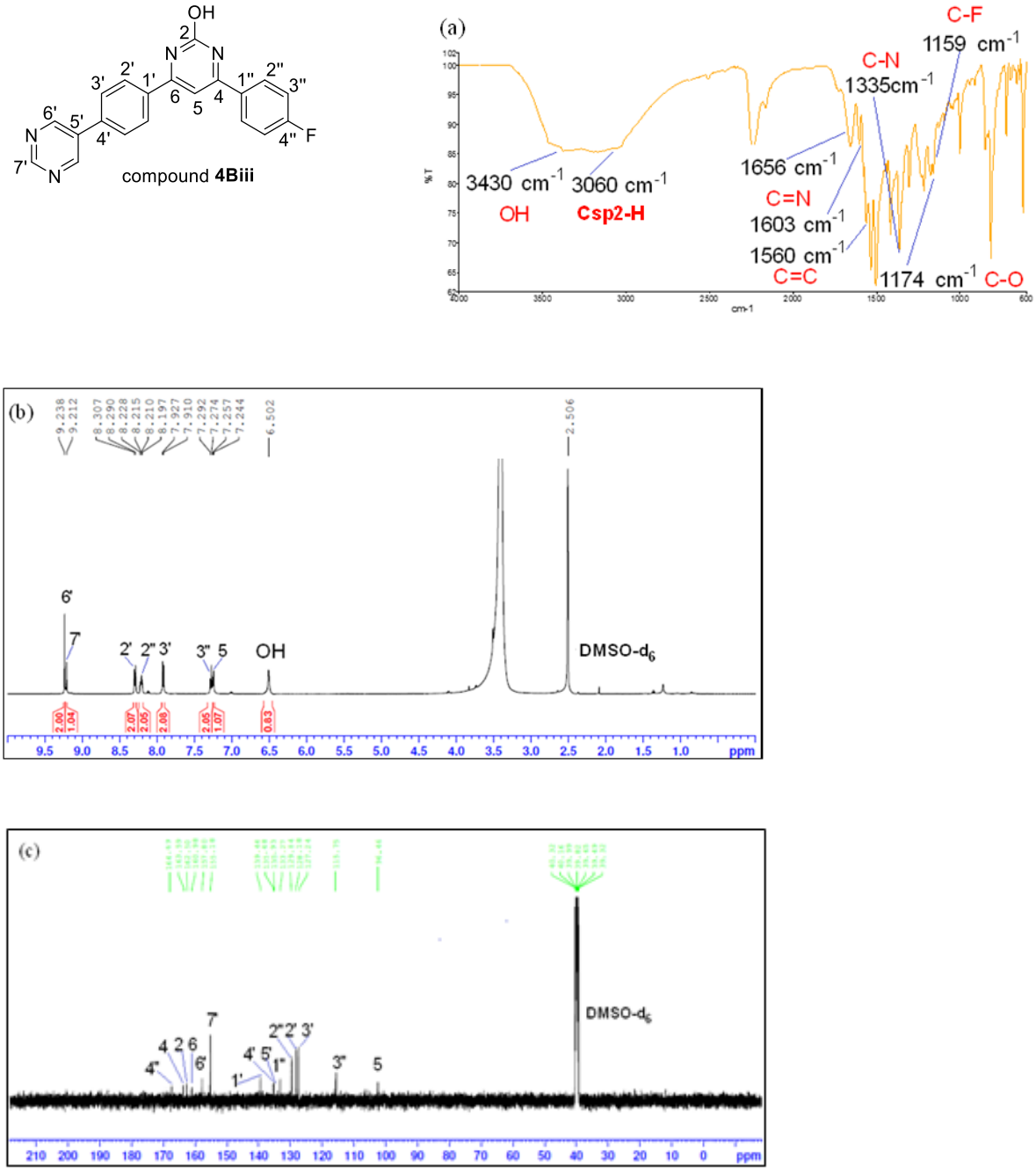


Figure S2.27. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **4Biii** in DMSO-d_6

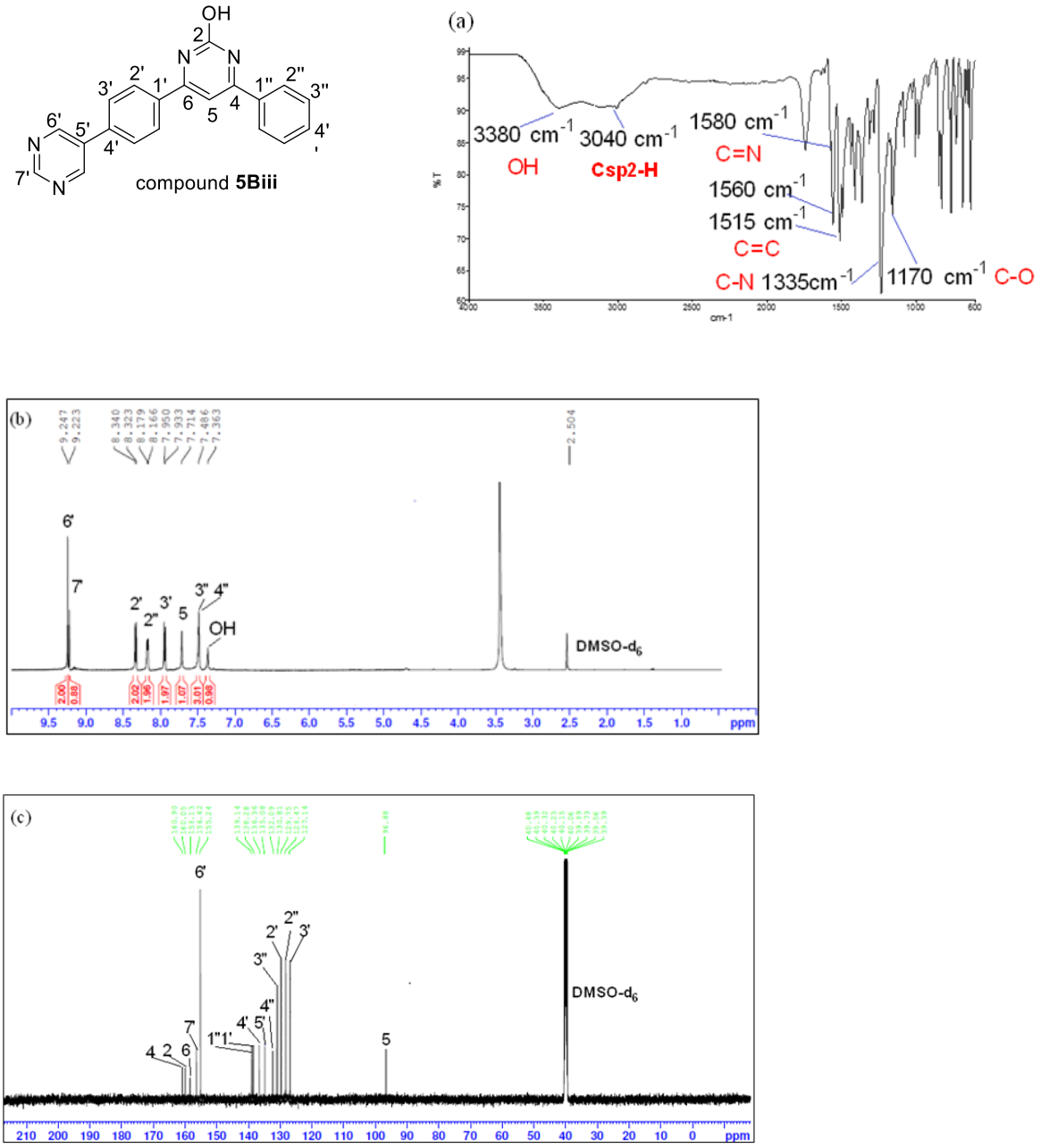


Figure S2.28. (a) IR (b) ^{1}H and (c) ^{13}C NMR spectra of pyrimidine **5Biii** in DMSO-d_6

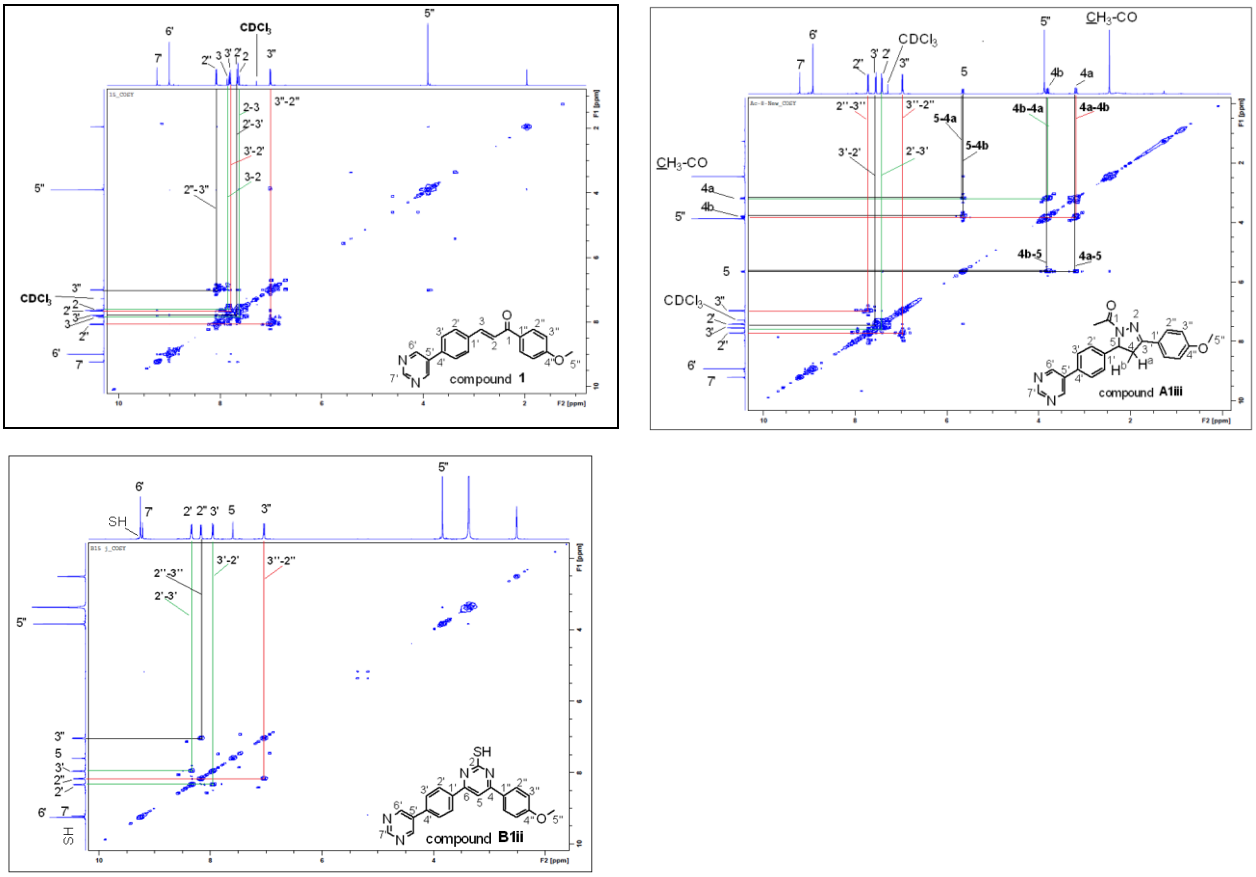
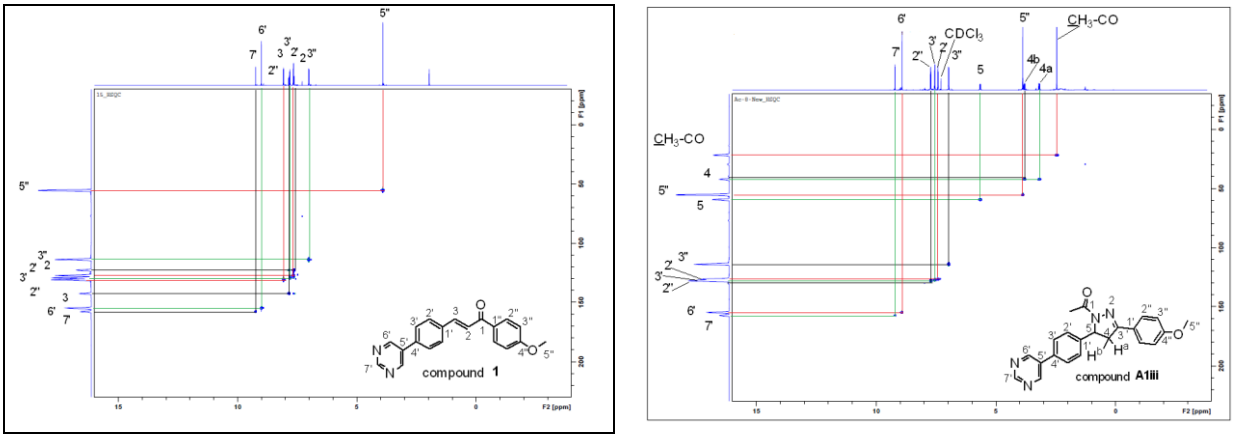


Figure S2.29 ^{1}H-^{1}H COSY NMR spectra of compounds **1**, **1Aiii** and **1Bii** in $CDCl_3$ and DMSO-d_6, respectively



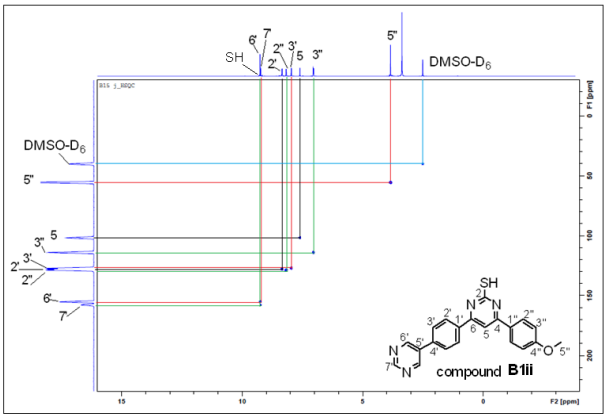


Figure S2.30 ^{1}H-^{13}C HSQC NMR spectra of compounds **1, 1Aiii** and **1Bii** in $CDCl_3$ and DMSO-d_6, respectively.

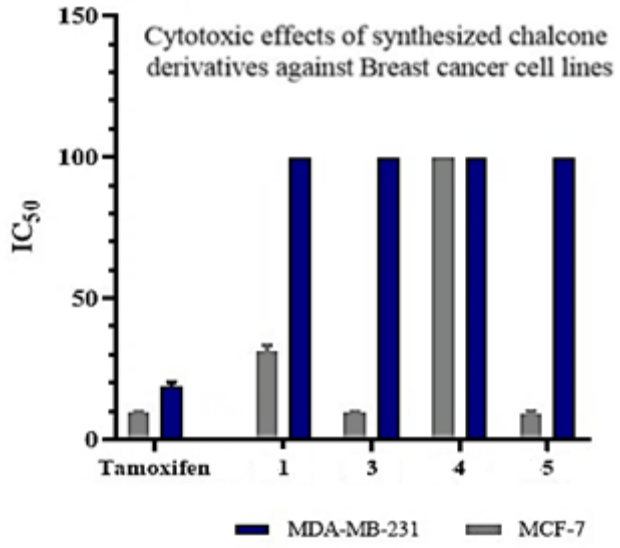


Figure S3.1 Cytotoxic activity of chalcone derivatives at 72 h in the inhibition of MCF-7 and MDA-MB-231 cells based on MTT assay. Data are expressed as mean ± SEM of a representative experiment performed in triplicate (n=3). *Symbol above the bars indicate significant differences. The significance was considered at P< 0.0001

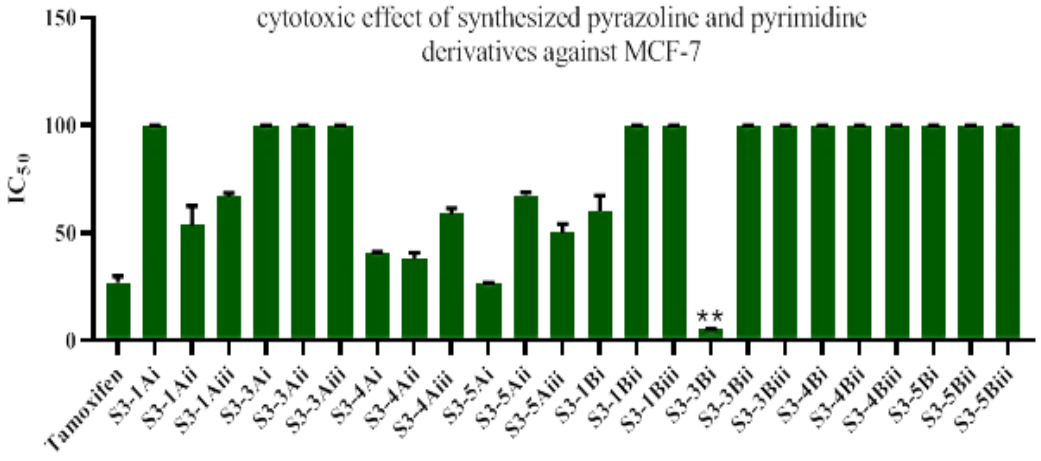


Figure S3.2 Cytotoxic activity of pyrazoline and pyrimidine derivatives at 72 h in the inhibition of MCF-7 cell based on MTT assay.

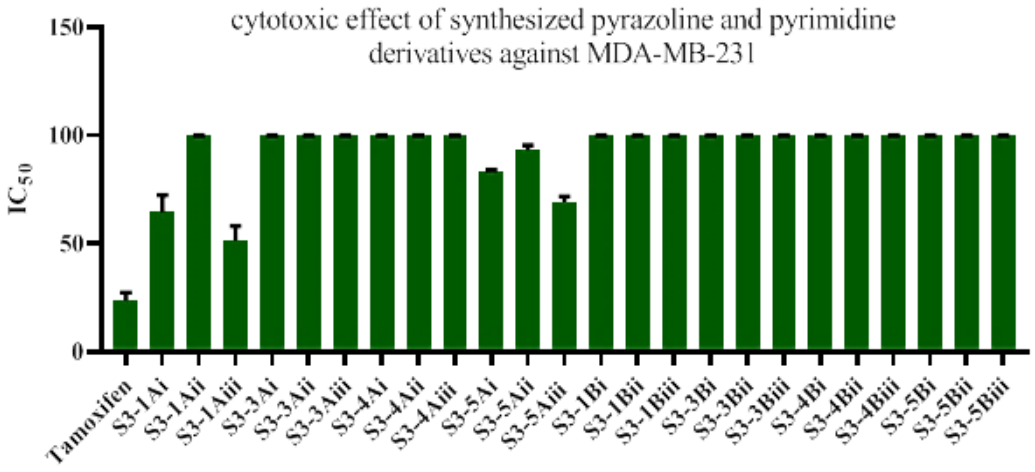


Figure S3.3 Cytotoxic activity of pyrazoline and pyrimidine derivatives at 72 h in the inhibition of MDA-MB-231 cell based on MTT assay.

S4. Characterization data

(*E*)-1-(4-methoxyphenyl)-3-(4-(pyrimidin-5-yl)phenyl)prop-2-en-1-one, **1**

Yield: 90%, bright white powder, m.p.: 187-189 ºC, molecular weight: 316.36. IR (υ_{max}, cm^{-1}): 3016 (C_{sp2}-H str), 2936-2838 (C_{sp3}-H str), 1652 (C=O str), 1593, 1568 (C=C str), 1178 (C-O str), 1256 (C-N str), 1000-975 (CH=CH bend *trans*). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.24 (s, 1H, $H^{7'}$); 9.03 (s, 2H, $H^{6'}$); 8.08 (d, *J*=11.5 Hz, 2H, $H^{2''}$); 7.85 (d, *J*=16.5 Hz, 1H, H^{3}); 7.82 (d, *J*=11.0 Hz, 2H, $H^{3'}$); 7.67 (d, *J*=11.0 Hz, 2H, $H^{2'}$); 7.64 (d, *J*=16.5 Hz, 1H, H^{2}); 7.02 (d, *J*=11.5 Hz, 2H, $H^{3''}$); 3.92 (s, 3H, $H^{5''}$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 55.6 (C-5''), 113.9 (C-3''), 122.9 (C-2), 127.5 (C-2'), 129.4 (C-3'), 130.9 (C-2''), 133.3 (C-5'), 134.2 (C-4'), 135.3 (C-1''), 136.2 (C-1'), 142.7 (C-3), 155.0 (C-6'), 157.4 (C-7'), 163.5 (C-4''), 188.6 (C-1). CHN elemental analysis: $C_{20}H_{16}N_2O_2$ Calculated: C, 75.93%; H, 5.10%; N, 8.86%. Found: C, 76.13%; H, 4.87%; N, 8.64%.

(*E*)-3-(4-(pyrimidin-5-yl)phenyl)-1-(thiophen-2-yl)prop-2-en-1-one, **3**

Yield: 83%, white powder, m.p.: 198-200 ºC, molecular weight: 292.36. IR (υ_{max}, cm^{-1}): 3063 (C_{sp2}-H str), 1650 (C=O str), 1595, 1567 (C=C str), 1331 (C-N str), 824 (C-S str), 1000 (C-O str), 975 (CH=CH bend *trans*). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.27 (s, 1H, $H^{7'}$); 9.04 (s, 2H, $H^{6'}$); 7.93 (d, *J*=3.5 Hz, 1H, $H^{5''}$); 7.91 (d, *J*=15.5 Hz, 1H, H^{3}); 7.83 (d, *J*=7.9 Hz, 2H, $H^{3'}$); 7.74 (d, *J*=3.5 Hz, 1H, $H^{3''}$); 7.69 (d, *J*=7.9 Hz, 2H, $H^{2'}$); 7.52 (d, *J*=15.5 Hz, 1H, H^{2}); 7.32 (t, *J*=5.0 Hz, 1H, $H^{4''}$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 123.1 (C-2), 126.8 (C-2'), 127.6 (C-4''), 129.3 (C-3'), 130.3 (C-3''), 132.6 (C-5''), 134.2 (C-1'), 135.3 (C-5'), 136.3 (C-4'), 142.5 (C-2''), 145.8 (C-3), 155.13 (C-6'), 158.23 (C-7'), 182.2 (C-1). CHN elemental analysis: $C_{17}H_{12}N_2OS$ Calculated: C, 69.84%; H, 4.14%; N, 9.58%. Found: C, 69.74%; H, 3.92%; N, 9.39%.

(*E*)-1-(4-fluorophenyl)-3-(4-(pyrimidin-5-yl)phenyl)prop-2-en-1-one, **4**

Yield: 85%, yellow powder, m.p.: 205-207 ºC, molecular weight: 304.32. IR (υ_{max}, cm^{-1}): 3062 (C_{sp2}-H str), 1658 (C=O str), 1585, 1567 (C=C str), 1332 (C-N str), 1020 (C-F str), 1000-975 (CH=CH bend *trans*). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.27 (s, 1H, $H^{7'}$); 9.03 (s, 2H, $H^{6'}$); 8.11 (q, *J*=6.5 Hz, 2H, $H^{2''}$); 7.88 (d, *J*=17.0 Hz, 1H, H^{3}); 7.83 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.69 (d, *J*=8.0 Hz, 2H, $H^{2'}$); 7.60 (d, *J*=17.0 Hz, 1H, H^{2}); 7.22 (t, *J*=7.5 Hz, 2H, $H^{3''}$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 115.9 (C-3''), 122.7 (C-2), 127.2 (C-2'), 129.2 (C-3'), 131.2 (C-2''), 133.3 (C-5'), 134.2 (C-4'), 135.3 (C-1''), 136.2 (C-1'), 143.6 (C-3), 154.7 (C-6'), 157.6 (C-7'), 166.8 (C-4''), 188.4 (C-1). CHN elemental analysis: $C_{19}H_{13}FN_2O$ Calculated: C, 74.99%; H, 4.31; N, 9.21%. Found: C, 74.79%; H, 4.22%; N, 8.98%.

(*E*)-1-phenyl-3-(4-(pyrimidin-5-yl)phenyl)prop-2-en-1-one, **5**

Yield: 80%, white powder, m.p.: 185-187 ºC, molecular weight: 286.33. IR (υ_{max}, cm^{-1}): 3034 (C_{sp2}-H str), 1660 (C=O str), 1596, 1566 (C=C str), 1333 (C-N str), 995-955 (CH=CH bend *trans*). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.25 (s, 2H, $H^{6'}$); 9.22 (s, 1H, $H^{7'}$); 8.20 (d, *J*=9.0 Hz, 2H, $H^{2''}$); 8.08 (d, *J*=9.0 Hz, 2H, $H^{3'}$); 8.06 (d, *J*=17.0 Hz, 1H, H^{3}); 7.95 (d, *J*=9.0 Hz, 2H, $H^{2'}$); 7.82 (d, *J*=17.0 Hz, 1H, H^{2}); 7.70-7.72 (m, 1H, $H^{4''}$); 7.60 (t, *J*=7.0 Hz, 2H, $H^{3''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 123.1 (C-2), 127.8 (C-2'), 128.8 (C-3'), 129.1 (C-2''), 130.3 (C-3''), 132.4 (C-5'), 133.8 (C-4'), 135.5 (C-4''), 136.3 (C-1'), 138.2 (C-1''), 143.7 (C-3), 154.9 (C-6'), 157.8 (C-7'), 189.7 (C-1). CHN elemental analysis: $C_{19}H_{14}N_2O$ Calculated: C, 79.70%; H, 4.93%; N, 9.78%. Found: C, 79.62%; H, 4.69%; N, 9.55%.

5-[4-(3-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenyl]pyrimidine**, 1Ai**

Yield: 90%, white powder, m.p.: 100-102 ºC, molecular weight: 330.39. IR υ_{max}(neat)/cm^{-1}: 3334 (N-H str), 3036 (C_{sp2}-H str), 2903-2836 (C_{sp3}-H str), 1604 (C=N str), 1552, 1515 (C=C str), 1175 (C-O str), 1252 (C-N str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 10.23 (s, 1H, NH); 9.18 (s, 1H, $H^{7'}$); 9.14 (s, 2H, $H^{6'}$); 7.80 (d, *J*=8.0 Hz, 2H, $H^{2'}$);7.58 (d, *J*=9.0 Hz, 2H, $H^{2''}$); 7.54 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 6.95 (d, *J*=8.5 Hz, 2H, $H^{3''}$); 4.88 (t, *J*=10.5 Hz, 1H, H^{5}); 3.77 (s, 3H, $H^{5''}$); 3.47 (dd, *J*=10.5, 16.5 Hz, 1H, H^{4b}); 2.86 (dd, *J*=10.5, 16.0 Hz, 1H, H^{4a}). ^{13}C-

NMR (125 MHz, DMSO-d_6) δ_C, ppm: 159.8 (C-4''), 157.6 (C-7'), 155.0 (C-6'), 149.2 (C-3), 144.5 (C-1'), 133.4 (C-5'), 133.0 (C-4'), 128.0 (C-2''), 127.4 (C-2'), 127.4 (C-3'), 126.3 (C-1''), 114.4 (C-3''), 63.6 (C-5), 55.6 (C-5''), 41.2 (C-4). CHN elemental analysis: $C_{20}H_{18}N_4O$ Calculated: C, 72.71%; H, 5.49%; N, 16.96%. Found: C, 72.50%; H, 5.30%; N, 16.72%.

5-[4-(3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenyl]pyrimidine, **3Ai**

Yield: 87%, white powder, m.p.: 154-156 ºC, molecular weight: 306.39. IR υ_{max}(neat)/cm^{-1}: 3346 (N-H str), 3066 (C_{sp2}-H str), 1613 (C=N str), 1574, 1552 (C=C str), 1326 (C-N str), 833 (C-S str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.18 (s, 1H, $H^{7'}$); 9.14 (s, 2H, $H^{6'}$); 7.81 (d, *J*=8 Hz, 2H, $H^{2'}$); 7.61 (s, 1H, NH); 7.54 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.50 (d, *J*=5.0 Hz, 1H, $H^{5''}$); 7.16 (d, *J*=3.5 Hz, 1H, $H^{3''}$); 7.07 (dd, *J*=3.7 Hz, *J*=5.0 Hz, 1H, $H^{4''}$); 4.93 (t, *J*=10.5 Hz, 1H, H^5); 3.50 (dd, *J*=10.5, 16.5 Hz, 1H, H^{4b}); 2.91 (dd, *J*=10.5, 16.5 Hz, 1H, H^{4a}). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 157.6 (C-7'), 155.0 (C-6'), 145.4 (C-3), 144.0 (C-1'), 137.3 (C-2''), 133.4 (C-5'), 133.1 (C-4'), 128.2 (C-3'), 128.0 (C-3''), 127.4 (C-2'), 126.9 (C-5''), 126.7 (C-4''), 63.8 (C-5), 41.9 (C-4). CHN elemental analysis: $C_{17}H_{14}N_4S$ Calculated: C, 66.64%; H, 4.61%; N, 18.29%. Found: C, 66.41%; H, 4.39%; N, 18.07%.

5-[4-(3-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl)phenyl]pyrimidine, **4Ai**

Yield: 82%, white powder, m.p.: 135-137 ºC, molecular weight: 318.36. IR υ_{max}(neat)/cm^{-1}: 3349 (N-H str), 3042 (C_{sp2}-H str), 1600 (C=N str), 1570, 1550 (C=C str), 1216 (C-N str), 1129 (C-F str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 10.23 (s, 1H, NH); 9.18 (s, 1H, $H^{7'}$); 9.14 (s, 2H, $H^{6'}$); 7.80 (d, *J*=8.5 Hz, 2H, $H^{2'}$);7.67 (q, *J*=5.5 Hz, 2H, $H^{2''}$); 7.54 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.22 (t, *J*=9.0 Hz, 2H, $H^{3''}$); 4.93 (t, *J*=10.5 Hz, 1H, H^5); 3.49 (dd, *J*=11.0, 16.5 Hz, 1H, H^{4b}); 2.89 (dd, *J*=10.5, 16.0 Hz, 1H, H^{4a}). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 161.7 (C-4''), 157.6 (C-7'), 155.0 (C-6'), 148.3 (C-3), 144.3 (C-1'), 134.0 (C-5'), 133.1 (C-4'), 128.0 (C-3'), 127.9 (C-2''), 127.4 (C-2'), 126.1 (C-1''), 116.0 (C-3''), 63.8 (C-5), 41.0 (C-4). CHN elemental analysis: $C_{19}H_{15}FN_4$ Calculated: C, 71.68%; H, 4.75%; N, 17.60%. Found: C, 71.51%; H, 4.50%; N, 17.37%.

5-[4-(3-phenyl-4,5-dihydro-1*H*-pyrazol-5-yl)phenyl]pyrimidine, **5Ai**

Yield: 80%, white powder, m.p.: 145-147 ºC, molecular weight: 300.37. IR υ_{max}(neat)/cm^{-1}: 3333 (N-H str), 3034 (C_{sp2}-H str), 1592 (C=N str), 1568, 1549 (C=C str), 1330 (C-N str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.18 (s, 1H, $H^{7'}$); 9.14 (s, 2H, $H^{6'}$); 7.80 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 7.68 (s, 1H, NH); 7.64 (d, *J*=7.0 Hz, 2H, $H^{2''}$); 7.54 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.40 (d, *J*=7.5 Hz, 2H, $H^{3''}$); 7.32-7.35 (m, 1H, $H^{4''}$); 4.93 (t, *J*=10.5 Hz, 1H, H^5); 3.49 (dd, *J*=10.5, 16.5 Hz, 1H, H^{4b}); 2.89 (dd, *J*=10.5, 16.0 Hz, 1H, H^{4a}). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 157.6 (C-7'), 155.0 (C-6'), 149.0 (C-3), 144.4 (C-1'), 133.6 (C-1''), 133.4 (C-5'), 133.0 (C-4'),

128.9 (C-3''), 128.6 (C-4''), 128.0 (C-2''), 127.4 (C-3'), 125.9 (C-2'), 63.7 (C-5), 41.0 (C-4). CHN elemental analysis: $C_{19}H_{16}N_4$ Calculated: C, 75.98%; H, 5.37%; N, 18.65%. Found: C, 75.79%; H, 5.10%; N, 18.37%.

3-[(4-methoxyphenyl)-5-(4-(pyrimidin-5-yl)phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide, **1Aii**

Yield: 70%, yellow powder, m.p.: 220-222 ºC, molecular weight: 389.48. IR υ_{max}(neat)/cm^{-1}: 3441-3233 (N-H_2 str), 3100 (C_{sp2}-H str), 2904-2837 (C_{sp3}-H str), 1670 (C=N str), 1607, 1583 (C=C str), 1187 (C-O str), 1247 (C-N str), 1379 (C=S str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.18 (s, 1H, $H^{7'}$); 9.12 (s, 2H, $H^{6'}$); 8.02 (s, 1H, NH); 7.89 (s, 1H, NH); 7.84 (d, *J*=9.0 Hz, 2H, $H^{2''}$); 7.77 (d, *J*=7.5 Hz, 2H, $H^{2'}$); 7.28 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.01 (d, *J*=9.0 Hz, 2H, $H^{3''}$); 5.98 (dd, *J*=4.0, 11.5 Hz, 1H, H^5); 3.90 (dd, *J*=11.5, 18.0 Hz, 1H, H^{4b}); 3.81 (s, 3H, $H^{5''}$); 3.16 (dd, *J*=4.0, 18.0 Hz, 1H, H^{4a}). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 176.1 (C=S), 161.7 (C-4''), 157.6 (C-7'), 155.4 (C-3), 155.0 (C-6'), 144.3 (C-1'), 133.4 (C-5'), 132.8 (C-4'), 129.3 (C-2''), 127.6 (C-3'), 126.7 (C-2'), 123.7 (C-1''), 114.6 (C-3''), 62.9 (C-5), 55.8 (C-5''), 42.8 (C-4). CHN elemental analysis: $C_{21}H_{19}N_5OS$ Calculated: C, 64.76%; H, 4.92%; N, 17.98%. Found: C, 64.51%; H, 4.80%; N, 17.79%.

5-[4-(pyrimidin-5-yl)phenyl]-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide, **3Aii**

Yield: 67%, white powder, m.p.: 244-246 ºC, molecular weight: 365.47. IR υ_{max}(neat)/cm^{-1}: 3438-3227 (N-H_2 str), 3110 (C_{sp2}-H str), 1586 (C=N str), 1548, 1523 (C=C str), 1124 (C-N str), 1385 (C=S str), 825 (C-S str). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.20 (s, 1H, $H^{7'}$); 8.99 (s, 1H, NH); 8.93 (s, 2H, $H^{6'}$); 7.62 (s, 1H, NH); 7.55 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 7.50 (d, *J*=5.0 Hz, 1H, $H^{5''}$); 7.39 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.27 (d, *J*=4.0 Hz, 1H, $H^{3''}$); 7.09 (t, *J*=4.5 Hz, 1H, $H^{4''}$); 6.10 (dd, *J*=4.5, 12.0 Hz, 1H, H^5); 3.91 (dd, *J*=12.0, 18.0 Hz, 1H, H^{4b}); 3.22 (dd, *J*=4.0, 17.5 Hz, 1H, H^{4a}). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 171.7 (C=S), 152.7 (C-7'), 150.1 (C-6'), 146.5 (C-3), 137.8 (C-1'), 129.1 (C-2''), 129.1 (C-3''), 128.9 (C-4''), 125.4 (C-5'), 125.2 (C-4'), 123.2 (C-5''), 122.9 (C-3'), 121.9 (C-2'), 58.4 (C-5), 38.9 (C-4). CHN elemental analysis: $C_{18}H_{17}N_5S_2$ Calculated: C, 58.83%; H, 4.66%; N, 19.06%. Found: C, 58.61%; H, 4.44%; N, 18.79%.

3-(4-fluorophenyl)-5-[4-(pyrimidin-5-yl)phenyl]-4,5-dihydro-1*H*-pyrazole-1-carbothioamide, **4Aii**

Yield: 60%, yellow powder, m.p.: 230-232 ºC, molecular weight: 377.44. IR υ_{max}(neat)/cm^{-1}: 3435-3230 (N-H_2 str), 3060 (C_{sp2}-H str), 1590 (C=N str), 1560, 1543 (C=C str), 1120 (C-N str),

1345 (C=S str), 1140 (C-F str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.28 (s, 1H, NH); 9.25 (s, 1H, $H^{7'}$); 9.03 (s, 2H, $H^{6'}$); 8.97 (s, 1H, NH); 7.97 (d, *J*=8.5 Hz, 2H, $H^{2'}$);7.8.3 (q, *J*=5.0 Hz, 2H, $H^{2''}$); 7.45 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.17 (t, *J*=8.5 Hz, 2H, $H^{3''}$); 5.61 (dd, *J*=11.0, 18.0 Hz, 1H, H^{5}); 3.96 (dd, *J*=11.0, 18.0 Hz, 1H, H^{4b}); 3.35 (dd, *J*=10.5, 18.0 Hz, 1H, H^{4a}). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 173.2 (C=S), 162.6 (C-4''), 158.1 (C-7'), 154.8 (C-6'), 148.5 (C-3), 144.4 (C-1'), 134.2 (C-5'), 133.1 (C-4'), 129.5 (C-2''), 128.6 (C-3'), 127.6 (C-2'), 126.3 (C-1''), 116.0 (C-3''), 64.0 (C-5), 41.1 (C-4). CHN elemental analysis: $C_{20}H_{16}FN_5S$ Calculated: C, 63.64%; H, 4.27%; N, 18.56%. Found: C, 63.41%; H, 4.06%; N, 18.29%.

3-phenyl-5-[4-(pyrimidin-5-yl)phenyl]-4,5-dihydro-1*H*-pyrazole-1-carbothioamide, **5Aii**

Yield: 64%, orange powder, m.p.: 233-231 ºC, molecular weight: 359.45. IR υ_{max}(neat)/cm^{-1}: 3461-3297 (N-H_2 str), 3105 (C_{sp2}-H str), 1605 (C=N str), 1560, 1530 (C=C str), 1124 (C-Nstr), 1342 (C=S str). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.22 (s, 1H, $H^{7'}$); 8.96 (s, 2H, $H^{6'}$); 7.77 (d, *J*=8.5 Hz, 2H, $H^{2''}$); 7.58 (d, *J*=9.5 Hz, 2H, $H^{2'}$); 5.47-5.49 (m, 3H, $H^{3'',4''}$); 7.41 (d, *J*=7.0 Hz, 2H, $H^{3'}$); 7.29 (s, 1H, NH); 7.23 (s, 1H, NH); 6.12 (dd, *J*=4.0, 12.0 Hz, 1H, H^{5}); 3.93 (dd, *J*=13.0, 18.0 Hz, 1H, H^{4b}); 3.27 (dd, *J*=4.0, 18.5 Hz, 1H, H^{4a}). ^{13}CNMR (125 MHz, $CDCl_3$) δ_C, ppm: 176.8 (C=S) , 157.1 (C-3), 155.9 (C-7'), 154.8 (C-6'), 143.0 (C-1'), 134.2 (C-1''), 132.9 (C-4''), 131.4 (C-5'), 130.1 (C-4'), 128.8 (C-3''), 126.7 (C-2''), 126.6 (C-3'), 126.4 (C-2'), 63.1 (C-5), 43.0 (C-4). CHN elemental analysis: $C_{20}H_{17}N_5S$ Calculated: C, 66.83%; H, 4.77%; N, 19.48%. Found: C, 63.61%; H, 4.52%; N, 19.24%.

1-[3-(4-methoxyphenyl)-5-[4-(pyrimidin-5-yl)phenyl]-4,5-dihydro-1*H*-pyrazol-1-yl]ethan-1-one, **1Aiii**

Yield: 85%, white powder, m.p.:164-166 ºC, molecular weight: 372.43. IR υ_{max}(neat)/cm^{-1}: 3070 (C_{sp2}-H str), 2914-2847 (C_{sp3}-H str), 1640 (C=O str), 1608 (C=N str), 1554, 1521 (C=C str), 1177 (C-O str), 1250 (C-N str). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.11 (s, 1H, $H^{7'}$); 8.82 (s, 2H, $H^{6'}$); 7.62 (d, *J*=8.5 Hz, 2H, $H^{2''}$); 7.45 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.32 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 6.87 (d, *J*=9.0 Hz, 2H, $H^{3''}$); 5.55 (dd, *J*=4.5, 12.0 Hz, 1H, H^{5}); 3.78 (s, 3H, $H^{5''}$); 3.71 (dd, *J*=12.0, 17.5 Hz, 1H, H^{4b}); 3.09 (dd, *J*=4.5, 17.5 Hz, 1H, H^{4a}); 2.36 (s, 3H, C$\underline{H_3}$-CO). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 168.8 (C=O), 161.4 (C-4''), 157.4 (C-7'), 154.8 (C-6'), 153.7 (C-3), 143.0 (C-1'), 133.9 (C-5'), 133.5 (C-4'), 128.2 (C-2''), 127.6 (C-3'), 126.8 (C-2'), 123.8 (C-1''), 114.2 (C-3''), 59.5 (C-5), 55.4 (C-5''), 42.3 (C-4), 21.9 ($\underline{CH_3}$-CO). CHN elemental analysis: $C_{22}H_{20}N_4O_2$ Calculated: C, 70.95%; H, 5.41%; N, 15.04%. Found: C, 70.71%; H, 5.19%; N, 15.10%.

1-[5-(4-(pyrimidin-5-yl)phenyl]-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl]ethan-1-one, **3Aiii**

Yield: 82%, pink powder, m.p.: 106-108 ºC, molecular weight: 348.42. IR υ_{max}(neat)/cm^{-1}: 3075 (C_{sp2}-H str), 1637 (C=O str), 1595 (C=N str), 1528, 1556 (C=C str), 1240 (C-N str), 821 (C-S str). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.14 (s, 1H, H$^{7'}$); 8.86 (s, 2H, H$^{6'}$); 7.47 (d, *J*=8.0 Hz, 2H, H$^{2'}$); 7.38 (d, *J*=5.0 Hz, 1H, H$^{5''}$); 7.33 (d, *J*=8.0 Hz, 2H, H$^{3'}$); 7.17 (d, *J*=4.0 Hz, 1H, H$^{3''}$); 7.01 (dd, *J*=3.8, 5.0 Hz, 1H, H$^{4''}$); 5.57 (dd, *J*=5.0, 12.0 Hz, 1H, H^{5}); 3.75 (dd, *J*=12.0, 17.5 Hz, 1H, H^{4b}); 3.12 (dd, *J*=5.0, 17.5 Hz, 1H, H^{4a}); 2.34 (s, 3H, $\underline{CH_3}$-CO). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 168.8 (C=O), 157.0 (C-7'), 154.8 (C-6'), 149.4 (C-3), 142.8 (C-1'), 134.7 (C-3''), 134.1 (C-4''), 133.4 (C-5''), 128.9 (C-5'), 128.8 (C-4'), 127.7 (C-3'), 127.6 (C-2'), 126.8 (C-2''), 59.7 (C-5), 42.9 (C-4), 21.9 ($\underline{CH_3}$-CO). CHN elemental analysis: $C_{19}H_{16}N_4OS$ Calculated: C, 65.50%; H, 4.63%; N, 16.08%. Found: C, 65.22%; H, 4.42%; N, 15.80%.

1-(3-(4-fluorophenyl)-5-(4-(pyrimidin-5-yl)phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one, **4Aiii**

Yield: 80%, white powder, m.p.: 120-122 ºC, molecular weight: 360.39. IR υ_{max}(neat)/cm^{-1}: 3064 (C_{sp2}-H str), 1644 (C=O str), 1607 (C=N str), 1581, 1556 (C=C str), 1228 (C-N str), 1157 (C-F str). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.12 (s, 1H, H$^{7'}$); 8.84 (s, 2H, H$^{6'}$); 7.68 (q, *J*=5.5 Hz, 2H, H$^{2''}$); 7.47 (d, *J*=8.0 Hz, 2H, H$^{2'}$); 7.32 (d, *J*=9.0 Hz, 2H, H$^{3'}$); 7.06 (t, *J*=9.5 Hz, 2H, H$^{3''}$); 5.58 (dd, *J*=5.5, 12.0 Hz, 1H, H^{5}); 3.73 (dd, *J*=12.0, 17.5 Hz, 1H, H^{4b}); 3.11 (dd, *J*=5.5, 17.5 Hz, 1H, H^{4a}); 2.37 (s, 3H, C$\underline{H_3}$-CO). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 169.0 (C=O), 163.0 (C-4''), 157.4 (C-7'), 154.8 (C-6'), 152.8 (C-3), 142.7 (C-1'), 133.9 (C-5'), 133.6 (C-4'), 128.5 (C-2''), 127.6 (C-3'), 127.4 (C-1''), 126.7 (C-2'), 116.1 (C-3''), 59.7 (C-5), 42.3 (C-4), 21.9 ($\underline{CH_3}$-CO). CHN elemental analysis: $C_{21}H_{17}FN_4O$ Calculated: C, 69.99%; H, 4.75%; N, 15.55%. Found: C, 69.72%; H, 4.52%; N, 15.31%.

1-(3-phenyl-5-(4-(pyrimidin-5-yl)phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one, **5Aiii**

Yield: 83%, bright white powder, m.p.: 160-162 ºC, molecular weight: 342.40. IR υ_{max}(neat)/cm^{-1}: 3057 (C_{sp2}-H str), 1638 (C=O str), 1599 (C=N str), 1579, 1554 (C=C str), 1340 (C-N str). ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H, ppm: 9.20 (s, 1H, H$^{7'}$); 8.91 (s, 2H, H$^{6'}$); 7.77 (d, *J*=7.0 Hz, 2H, H$^{2''}$); 7.54 (d, *J*=8.0 Hz, 2H, H$^{2'}$); 7.45-7.47 (m, 3H, H$^{3'',4''}$); 7.41 (d, *J*=8.5 Hz, 2H, H$^{3'}$); 5.66 (dd, *J*=5.0, 12.0 Hz, 1H, H^{5}); 3.83 (dd, *J*=12.0, 18.0 Hz, 1H, H^{4b}); 3.21 (dd, *J*=5.5, 18.0 Hz, 1H, H^{4a}); 2.46 (s, 3H, C$\underline{H_3}$-CO). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C, ppm: 164.3 (C=O), 152.7 (C-7'), 150.1 (C-6'), 149.1 (C-3), 138.1 (C-1'), 129.2 (C-1''), 128.8 (C-4''), 126.4 (C-5'), 125.7 (C-4'), 124.0 (C-3''), 122.8 (C-2''), 122.0 (C-3'), 121.8 (C-2'), 54.9 (C-5), 37.5 (C-4), 17.2 ($\underline{CH_3}$-CO). CHN elemental analysis: $C_{21}H_{18}N_4O$ Calculated: C, 73.67%; H, 5.30%; N, 16.36%. Found: C, 73.50%; H, 5.11%; N, 16.15%.

4-(4-methoxyphenyl)-6-(4-(pyrimidin-5-yl)phenyl)pyrimidin-2-amine, **1Bi**

Yield: 70%, dark beige powder, m.p.: 210-212 ºC, molecular weight: 355.40. IR υ_{max}(neat)/cm^{-1}: 3315-3189 (NH_2 str), 3080 (C_{sp2}-H str), 2913-2845 (C_{sp3}-H str), 1579 (C=N str), 1536, 1512 (C=C str), 1178 (C-O str), 1243 (C-N str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 6.72 (s, 2H, NH_2); 9.24 (s, 2H, $H^{6'}$); 9.22 (s, 1H, $H^{7'}$); 8.38 (d, *J*=8.0 Hz, 2H, $H^{2'}$); 8.23 (d, *J*=9.0 Hz, 2H, $H^{2''}$); 7.98 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.75 (s, 1H, H^5); 7.07 (d, *J*=8.5 Hz, 2H, $H^{3''}$); 3.80 (s, 3H, $H^{5''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 169.8 (C-4), 169.1 (C-2), 168.8 (C-6), 166.5 (C-4''), 162.8 (C-7'), 160.0 (C-6'), 143.0 (C-1'), 140.7 (C-4'), 137.8 (C-5'), 134.7 (C-1''), 133.9 (C-2''), 133.0 (C-2'), 132.3 (C-3'), 119.1 (C-3''), 106.4 (C-5), 60.6 (C-5''). CHN elemental analysis: $C_{21}H_{17}N_5O$ Calculated: C, 70.97%; H, 4.82%; N, 19.71%. Found: C, 70.70%; H, 4.61%; N, 19.45%.

4-(4-(pyrimidin-5-yl)phenyl)-6-(thiophen-2-yl)pyrimidin-2-amine, **B3i**

Yield: 67 %, brown powder, m.p.: 200-202 ºC, molecular weight: 331.40. IR υ_{max}(neat)/cm^{-1}: 3316-3170 (NH_2 str), 3010 (C_{sp2}-H str), 1642 (C=N str), 1561, 1530 (C=C str), 1232 (C-N str), 828 (C-S str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 6.81 (s, 2H, NH_2); 9.26 (s, 2H, $H^{6'}$); 9.23 (s, 1H, $H^{7'}$); 8.37 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 8.17 (d, *J*=4.5 Hz, 1H, $H^{3''}$); 8.01 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.81 (s, 1H, H^5); 7.75 (d, *J*=5.0 Hz, 1H, $H^{5''}$); 7.25 (t, *J*=5.0 Hz, 1H, $H^{4''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 164.1 (C-6), 164.0 (C-4), 160.7 (C-2), 158.0 (C-7'), 155.3 (C-6'), 143.6 (C-2''), 137.9 (C-1'), 136.1 (C-4'), 133.0 (C-5'), 130.4 (C-5''), 128.9 (C-4''), 128.6 (C-3''), 128.2 (C-2'), 127.6 (C-3'), 100.7 (C-5). CHN elemental analysis: $C_{18}H_{13}N_5S$ Calculated: C, 65.24%; H, 3.95%; N, 21.13%. Found: C, 65.01%; H, 3.73%; N, 20.93%.

4-(4-fluorophenyl)-6-(4-(pyrimidin-5-yl)phenyl)pyrimidin-2-amine, **4Bi**

Yield : 60%, yellow powder, m.p.: 280-282 ºC, molecular weight: 343.37. IR υ_{max}(neat)/cm^{-1}: 3316-3201 (NH_2 str), 3064 (C_{sp2}-H str), 1627 (C=N str), 1570, 1536 (C=C str), 1210 (C-N str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 6.83 (s, 2H, NH_2); 9.27 (s, 2H, $H^{6'}$); 9.23 (s, 1H, $H^{7'}$); 8.41 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 8.33 (q, *J*=6.0 Hz, 2H, $H^{2''}$); 8.00 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.83 (s, 1H, H^5); 7.37 (t, *J*=9 .0 Hz, 2H, $H^{3''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 165.4 (C-4), 164.5 (C-2), 164.4 (C-6), 164.3 (C-4''), 158.0 (C-7'), 155.3 (C-6'), 138.1 (C-1'), 136.1 (C-4'), 134.1 (C-1''), 132.9 (C-5'), 129.9 (C-2''), 128.3 (C-2'), 127.6 (C-3'), 116.1 (C-3''), 102.2 (C-5). CHN elemental analysis: $C_{20}H_{14}FN_5$ Calculated: C, 69.96%; H, 4.11%; N, 20.40%. Found: C, 69.70%; H, 3.93%; N, 20.13%.

4-phenyl-6-(4-(pyrimidin-5-yl)phenyl)pyrimidin-2-amine, **5Bi**

Yield: 58%, yelow powder, m.p.: 260-262 ºC, molecular weight: 325.38. IR υ_{max}(neat)/cm^{-1}: 3362-3213 (NH_2 str), 3070 (C_{sp2}-H str), 1640 (C=Nstr), 1558, 1531 (C=C str), 1232 (C-N str).

^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 6.83 (s, 2H, NH_2); 9.26 (s, 2H, $H^{6'}$); 9.23 (s, 1H, $H^{7'}$); 8.40 (d, *J*=8.0 Hz, 2H, $H^{2'}$); 8.25 (d, *J*=6.5 Hz, 2H, $H^{2''}$); 8.00 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.82 (s, 1H, H^{5}); 7.53-7.55 (m, 3H, $H^{3'',4''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 165.5 (C-4), 164.5 (C-2), 164.4 (C-6), 158. 0 (C-7'), 155.3 (C-6'), 138.1 (C-1'), 136.0 (C-1''), 133.0 (C-4'), 130.9 (C-5'), 129.8 (C-4''), 129.1 (C-3''), 128.3 (C-2'), 127.6 (C-2''), 127.5 (C-3'), 102.4 (C-5). CHN Elemental analysis: $C_{20}H_{15}N_5$ Calculated: C, 73.83%; H, 4.65%; N, 21.52%. Found: C, 73.66%; H, 4.43%; N, 21.33%.

4-(4-methoxyphenyl)-6-(4-(pyrimidin-5-yl)phenyl)pyrimidine-2-thiol, **1Bii**

Yield: 85%, yelow powder, m.p.: >300 ºC, molecular weight: 372.45. IR υ_{max}(neat)/cm^{-1}: 3070 (C_{sp2}-H str), 2910-2840 (C_{sp3}-H str), 2560 (S-H str), 1605 (C=N str), 1576, 1553 (C=C str), 1170 (C-O str), 1230 (C-N str), 817 (C-S str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.30 (s, 1H, SH); 9.25 (s, 2H, $H^{6'}$); 9.21 (s, 1H, $H^{7'}$); 8.33 (d, *J*=8.0 Hz, 2H, $H^{2'}$); 8.16 (d, *J*=8.5 Hz, 2H, $H^{2''}$); 7.95 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.59 (s, 1H, H^{5}); 7.03 (d, *J*=8.5 Hz, 2H, $H^{3''}$); 3.83 (s, 3H, $H^{5''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 189.5 (C-2), 161.5 (C-4), 161.0 (C-4''), 160.7 (C-6), 157.8 (C-7'), 155.2 (C-6'), 139.6 (C-1'), 135.0 (C-4'), 133.2 (C-5'), 131.3 (C-1''), 128.0 (C-2'), 128.7 (C-2''), 127.3 (C-3'), 114.1 (C-3''), 101.9 (C-5), 55.6 (C-5''). CHN elemental analysis: $C_{21}H_{16}N_4OS$ Calculated: C, 67.72%; H, 4.33%; N, 15.04%. Found: C, 67.50%; H, 4.07%; N, 14.85%.

4-(4-(pyrimidin-5-yl)phenyl)-6-(thiophen-2-yl)pyrimidine-2-thiol, **3Bii**

Yield: 80%, yelow powder, m.p.: 226-228 ºC, molecular weight: 348.44. IR υ_{max}(neat)/cm^{-1}: 3090 (C_{sp2}-H str), 2540 (S-H str), 1610 (C=N str), 1561, 1504 (C=C str), 1249 (C-N str), 820 (C-S str) . ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.25 (s, 1H, SH); 9.23 (s, 2H, $H^{6'}$); 9.21 (s, 1H, $H^{7'}$); 8.32 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 7.98 (d, *J*=3.5 Hz, 1H, $H^{3''}$); 7.95 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.64 (d, *J*=5.0 Hz, 1H, $H^{5''}$); 7.62 (s, 1H, H^{5}); 7.18 (t, *J*=4.5 Hz, 1H, $H^{4''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 189.7 (C-2), 160.5 (C-4), 157.8 (C-6), 157.4 (C-7'), 155.2 (C-6'), 145.4 (C-2''), 139.3 (C-1'), 135.1 (C-5'), 133.2 (C-4'), 129.1 (C-5''), 128.4 (C-4''), 128.0 (C-3'), 127.3 (C-2'), 126.7 (C-3''), 100.8 (C-5). CHN elemental analysis: $C_{18}H_{12}N_4S_2$ Calculated: C, 62.05%; H, 3.47%; N, 16.08%. Found: C, 61.80%; H, 3.27%; N, 15.85%.

4-(4-fluorophenyl)-6-(4-(pyrimidin-5-yl)phenyl)pyrimidine-2-thiol**, 4Bii**

Yield: 70%, yellow powder, m.p.: 240-242 ºC, molecular weight: 360.41. IR υ_{max}(neat)/cm^{-1}: 3080 (C_{sp2}-H str), 2590 (S-H str), 1600 (C=N str), 1560, 1503 (C=C str), 1227 (C-N str), 1153 (C-F), 819 (C-S str) . ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.28 (s, 1H, SH); 9.24 (s, 2H, $H^{6'}$); 9.21 (s, 1H, $H^{7'}$); 8.34 (d, *J*=9.0 Hz, 2H, $H^{2'}$); 8.25 (q, *J*=6.5 Hz, 2H, $H^{2''}$); 7.95 (d, *J*=8.5

Hz, 2H, $H^{3'}$); 7.65 (s, 1H, H^5); 7.31 (t, *J*=9.0 Hz, 2H, $H^{3''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 189.5 (C-2), 163.5 (C-4), 162.5 (C-6), 161.9 (C-4''), 157.8 (C-7'), 155.2 (C-6'), 139.4 (C-1'), 135.4 (C-4'), 135.1 (C-5'), 133.2 (C-1''), 129.7 (C-2''), 128.2 (C-2'), 127.1 (C-3'), 115.7 (C-3''), 102.4 (C-5). CHN elemental analysis: $C_{20}H_{13}FN_4S$ Calculated: C, 66.65%; H, 3.64%; N, 15.55%. Found: C, 66.50%; H, 3.43%; N, 15.33%.

4-phenyl-6-(4-(pyrimidin-5-yl)phenyl)pyrimidine-2-thiol, **5Bii**

Yield: 77%, yellow powder, m.p.: >300 ºC, molecular weight: 342.42. IR υ_{max}(neat)/cm^{-1}: 3035 (C_{sp2}-H str), 2530 (S-H str), 1572 (C=N str), 1556, 1509 (C=C str), 1232 (C-N str), 825 (C-S str) . ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 9.29 (s, 1H, SH); 9.25 (s, 2H, $H^{6'}$); 9.21 (s, 1H, $H^{7'}$); 8.35 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 8.18 (d, *J*=8.0 Hz, 2H, $H^{2''}$); 7.96 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.65 (s, 1H, H^5); 7.48-7.50 (m, 3H, $H^{3'',4''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 189.8 (C-2), 162.0 (C-4), 161.0 (C-6), 157.8 (C-7'), 155.2 (C-6'), 139.5 (C-1'), 139.0 (C-1''), 135.1 (C-4'), 133.2 (C-5'), 130.0 (C-4''), 128.8 (C-3''), 128.1 (C-2'), 127.3 (C-2''), 127.3 (C-3'), 102.7 (C-5). CHN elemental analysis: $C_{20}H_{14}N_4S$ Calculated: C, 70.15%; H, 4.12%; N, 16.36%. Found: C, 69.96%; H, 4.01%; N, 16.13%.

4-(4-methoxyphenyl)-6-(4-(pyrimidin-5-yl)phenyl)pyrimidin-2-ol**, B1iii**

Yield: 80%, dark beige powder, m.p.: 296-298 ºC, molecular weight: 356.39. IR υ_{max}(neat)/cm^{-1}: 3410 (OH str), 3033 (C_{sp2}-H str), 2910-2810 (C_{sp3}-H str), 1614 (C=N str), 1578, 1563 (C=C str), 1175 (C-O str), 1251 (C-N str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 5.99 (s, 1H, OH); 9.22 (s, 1H, $H^{6'}$); 9.21 (s, 2H, $H^{7'}$); 8.30 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 8.13 (d, *J*=9.5 Hz, 2H, $H^{2''}$); 7.90 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.25 (s, 1H, H^5); 7.00 (d, *J*=9.0 Hz, 2H, $H^{3''}$); 3.82 (s, 3H, $H^{5''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 164.7 (C-4), 164.6 (C-4''), 164.5 (C-2), 160.9 (C-6), 157.8 (C-7'), 155.1 (C-6'), 140.0, (C-1') 135.4 (C-4'), 134.9 (C-5'), 133.2 (C-1''), 128.8 (C-2''), 128.1 (C-2'), 127.2 (C-3'), 114.0 (C-3''), 96.6 (C-5), 55.6 (C-5''). CHN elemental analysis: Calculated $C_{21}H_{16}N_4O_2$: C, 70.77%; H, 4.53%; N, 15.72%. Found: C, 70.60%; H, 4.32%; N, 15.55%.

4-(4-(pyrimidin-5-yl)phenyl)-6-(thiophen-2-yl)pyrimidin-2-ol, **B3iii**

Yield: 75%, dark beige powder, m.p.: >300 ºC, molecular weight: 332.38. IR υ_{max}(neat)/cm^{-1}: 3420 (OH str), 3070 (C_{sp2}-H str), 1615 (C=N str), 1590, 1564 (C=C str), 1174 (C-O str), 1340 (C-N str), 815 (C-S). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 5.43 (s, 1H, OH); 9.24 (s, 2H, $H^{6'}$); 9.21 (s, 1H, $H^{7'}$); 8.28 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 7.93 (d, *J*=6.5 Hz, 1H, $H^{3''}$); 7.91 (d, *J*=8.0 Hz, 2H, $H^{3'}$); 7.61 (d, *J*=5.0 Hz, 1H, $H^{5''}$); 7.25 (s, 1H, H^5); 7.16 (t, *J*=4.5 Hz, 1H, $H^{4''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 165.3 (C-2), 161.2 (C-6), 160.4 (C-4), 157.8 (C-7'), 155.2 (C-6'), 139.6 (C-2''), 135.11 (C-1'), 133.2 (C-4'), 132.8 (C-5'), 131.0 (C-5''), 128.8 (C-

4''), 128.3 (C-3''), 128.1 (C-2'), 127.2 (C-3'), 94.8 (C-5). CHN elemental analysis: $C_{18}H_{12}N_4OS$ Calculated: C, 65.05%; H, 3.64%; N, 16.86%. Found: C, 64.90%; H, 3.57%; N, 16.65%.

4-(4-fluorophenyl)-6-(4-(pyrimidin-5-yl)phenyl)pyrimidin-2-ol**, B4iii**

Yield: 73%, dark beige powder, m.p.: >300 ºC, molecular weight: 344.35. IR υ_{max}(neat)/cm^{-1}: 3430 (OH str), 3060 (C_{sp2}-H str), 1656 (C=N str), 1603, 1560 (C=C str), 1174 (C-O str), 1335 (C-N str), 1159 (C-F). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 6.50 (s, 1H, OH); 9.23 (s, 2H, $H^{6'}$); 9.21 (s, 1H, $H^{7'}$); 8.30 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 8.21 (q, *J*=6.5 Hz, 2H, $H^{2''}$); 7.91 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.27 (t, *J*=9.0 Hz, 2H, $H^{3''}$); 7.24 (s, 1H, H^5). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 164.6 (C-4''), 163.5 (C-4), 162.5 (C-2), 160.9 (C-6), 157.8 (C-6'), 155.1 (C-7'), 139.4 (C-1'), 135.4 (C-4'), 135.9 (C-5'), 133.2 (C-1''), 129.8 (C-2''), 128.1 (C-2'), 127.2 (C-3'), 115.7 (C-3''), 96.4 (C-5). CHN elemental analysis: $C_{20}H_{13}FN_4O$ Calculated: C, 69.76%; H, 3.81%; N, 16.27%. Found: C, 69.55%; H, 3.57%; N, 16.05%.

4-phenyl-6-(4-(pyrimidin-5-yl)phenyl)pyrimidin-2-ol, **B5iii**

Yield: 70%, dark beige powder, m.p.: 294-296 ºC, molecular weight: 326.36. IR υ_{max}(neat)/cm^{-1}: 3380 (OH str), 3040 (C_{sp2}-H str), 1580 (C=N str), 1560, 1515 (C=C str), 1170s (C-O str), 1335 (C-N str). ^{1}H-NMR (500 MHz, DMSO-d_6) δ_H, ppm: 7.36 (s, 1H, OH); 9.24 (s, 2H, $H^{6'}$); 9.22 (s, 1H, $H^{7'}$); 8.33 (d, *J*=8.5 Hz, 2H, $H^{2'}$); 8.16 (d, *J*=6.5 Hz, 2H, $H^{2''}$); 7.94 (d, *J*=8.5 Hz, 2H, $H^{3'}$); 7.71 (s, 1H, H^5); 7.48-7.50 (m, 3H, $H^{3'',4''}$). ^{13}C-NMR (125 MHz, DMSO-d_6) δ_C, ppm: 160.9 (C-4), 160.0 (C-2), 158.1 (C-6), 156.4 (C-7'), 155.2 (C-6'), 139.1 (C-1''), 138.2 (C-1'), 136.3 (C-4'), 135.0 (C-5'), 132.0 (C-4''), 130.8 (C-3''), 129.7 (C-2'), 128.4 (C-2''), 127.1 (C-3'), 96.8 (C-5). CHN elemental analysis: $C_{20}H_{14}N_4O$ Calculated: C, 73.61%; H, 4.32%; N, 17.17%. Found: C, 73.43%; H, 4.15%; N, 16.95%.