Electronic Supplementary Material (ESI) for RSC Advances.

Thienopyrimidine sulphonamide hybrids: Design, synthesis, antiprotozoal activity and molecular docking studies

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SA1. Crystal Data and Structure Refinement for the compounds 4-[4-(Propane- 1- sulphonyl)-piperazine-1-yl] – 5,6,7,8- tetrahydrobenzo [4,5] theino [2,3-d] pyrimidine (9) and 4-[4-Benzenesulphonyl) – piperazine – 1 –yl] -5,6,7,8 –tetrahydro-benzo [4,5] theino [2,3 –d] pyrimidine (13)

	9	13
Formula	$C_{17}H_{24}N_4O_2S_2$	$C_{20}H_{22}N_4O_2S_2$
Formula weight	380.52	414.54
T, *K*	100	100
Wavelength, Å	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	I2a
a/Å	8.4757(6)	16.3801(11)
b/Å	23.0572(18)	10.1789(7)
c/Å	9.7935(8)	24.6397(19)
β/º	103.534(5)	107.967(4)
V/Å^3	1860.8(2)	3907.9(5)
Z	4	8
F_{000}	808	1744
D_{calc}/g cm^{-3}	1.358	1.409
μ/mm^{-1}	0.305	0.297
θ/ (º)	1.77 to 27.88	1.74 to 28.28
R_{int}	0.0322	0.0493
Crystal size/ mm^3	0.60 x 0.55 x 0.39	0.65 x 0.31 x 0.28
Goodness-of-fit on F^2	1.028	1.058
$R_1[I>2\sigma(I)]$ [a]	0.0437	0.0327
wR_2 (all data) [b]	0.1222	0.0876
Largest differences peak and hole (eÅ^{-3})	0.427 and -0.329	0.349 and -0.474

[a] $R_1 = \Sigma \left| |F_o| - |F_c| \right| / \Sigma |F_o|$. [b] $wR_2 = \{\Sigma[w(|F_o|^2 - |F_c|^2)^2]\} / \Sigma[w(F_o^2)^2]\}^{1/2}$

SA2: Bond lengths [Å] and angles [°] for the compounds 4-[4-(Propane- 1- sulphonyl)- piperazine-1-yl] – 5,6,7,8- tetrahydrobenzo [4,5] theino [2,3-d] pyrimidine (9) and 4-[4-Benzenesulphonyl) – piperazine – 1 –yl] -5,6,7,8 –tetrahydro-benzo [4,5] theino [2,3 –d] pyrimidine (13).

Bond lengths	9	13
S(1)-C(8)	1.723(2)	1.7333(14)
S(1)-C(1)	1.739(2)	1.7401(13)
O(1)-S(2)	1.4314(16)	1.4365(11)
S(2)-O(2)	1.437(2)	1.4333(10)
S(2)-N(4)	1.6198(17)	1.6345(11)
S(2)-C(15)		1.7656(14)
S(2)-C(15B)	1.720(10)	
S(2)-C(15A)	1.793(5)	
N(3)-C(10)	1.394(3)	1.3959(16)
N(3)-C(14)	1.466(3)	1.4647(16)
N(3)-C(11)	1.468(2)	1.4765(16)
N(4)-C(13)	1.469(3)	1.4753(16)
N(4)-C(12)	1.469(2)	1.4758(16)

Bond angles	**9**	**13**
C(8)-S(1)-C(1)	91.01(10)	90.71(6)
O(1)-S(2)-O(2)	119.13(11)	120.03(6)
O(1)-S(2)-N(4)	106.51(10)	106.37(6)
O(2)-S(2)-N(4)	106.53(10)	106.50(6)
O(2)-S(2)-C(15)		107.96(7)
O(1)-S(2)-C(15)		107.80(6)
N(4)-S(2)-C(15)		107.62(6)

O(1)-S(2)-C(15B)	108.0(3)	
O(2)-S(2)-C(15B)	98.0(3)	
N(4)-S(2)-C(15B)	119.2(3)	
O(1)-S(2)-C(15A)	106.5(2)	
O(2)-S(2)-C(15A)	112.8(3)	
N(4)-S(2)-C(15A)	104.3(3)	
C(10)-N(3)-C(14)	116.02(17)	115.54(10)
C(10)-N(3)-C(11)	116.39(15)	114.93(10)
C(14)-N(3)-C(11)	109.70(16)	110.42(10)
C(13)-N(4)-C(12)	112.81(16)	111.57(10)
C(13)-N(4)-S(2)	119.40(14)	117.40(9)
C(12)-N(4)-S(2)	118.68(14)	116.86(9)

SA3. Chemistry

The ^{1}HNMR signals for the aliphatic protons of ring **a** appeared in the range of 4.50-1.76 ppm. The hydrogen of the pyrimidine ring (Ring **c**) is deshielded due to the presence of two adjoining nitrogen atoms and appeared as a singlet at around 8.47 ppm in all the compounds. The protons of various substitutions of the sulphonamide group appeared in all the final compounds. The ^{13}C spectra showed common peaks of 4-piperazine-1-yl-5, 6, 7, 8 tetrahydrobenzothiopheno [2, 3-d] pyrimidine in all the compounds. The carbons of the piperazine ring (Ring **d**) appeared at around 50 ppm and 45 ppm. The carbons of the tetrahydrobenzotheinopyrimidine (Ring **a**, **b** & **c**) showed signals at around 168.27, 162.46, 151.49, 135.12, 127.23, 121.44, 26.76, 25.81, 23.00 ppm. The carbons of the aliphatic sulphonamide appeared upfield and for aromatic sulphonamide groups downfield respectively. The elemental analyses were found to be in agreement with the calculated results. The [M+1] peak was observed in mass spectra for all the compounds.

SA4. *Single crystal structure*

*Single crystal structures of **9** and **13***

The asymmetric units of 9 and 13 only contain the piperazine derivatives. The piperazine rings are in a chair form and hence the molecules have an extended conformation. Both ring N atoms are bonded in a configuration which are distinctly pyramidals, with the sum of the C—N—C angles being 342.11(16)º and 350.89 (14)º for 9 and 340.89(10)º and 345.83(10)º for 13 [3]. Crystal data and details of the data collection and refinement for the new compounds are collected in SA1 and SA2 contains selected bond lengths and angles for compound 9 and 13. Stereoisomers by hindered rotation about a single bond singleN(3)-C(10) are present in racemic mixture in the two crystal packing. These stereoisomers, called atropoisomers [4] have a barrier to rotation due to steric strain. In figure 3, we can see the configuration *aR*-9, and in figure 4, the configuration *aS*-13. Figure 5 show the two atropoisomers present in crystal packing of compound 13.

SPECTRAL DATA

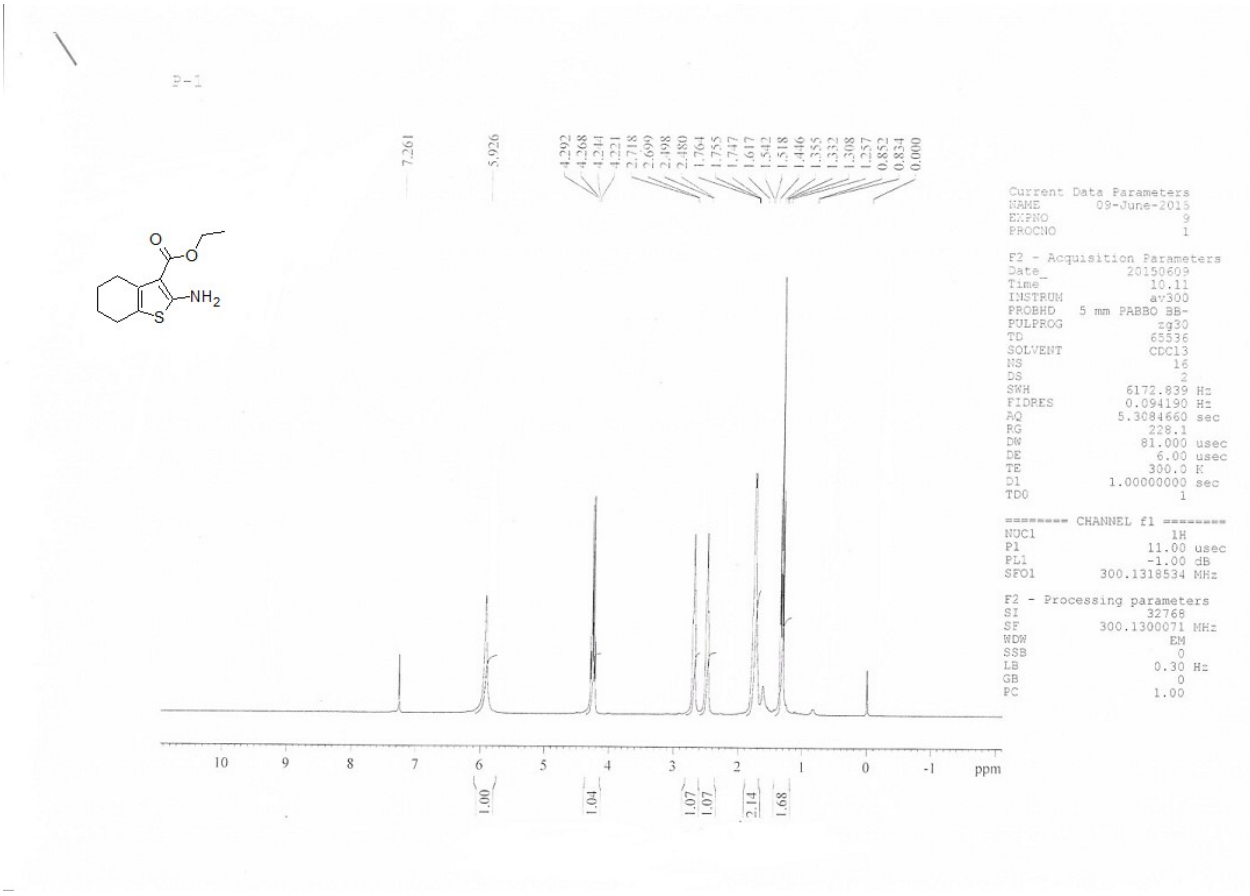

Fig 1. ^{1}H NMR spectrum of compound 1.

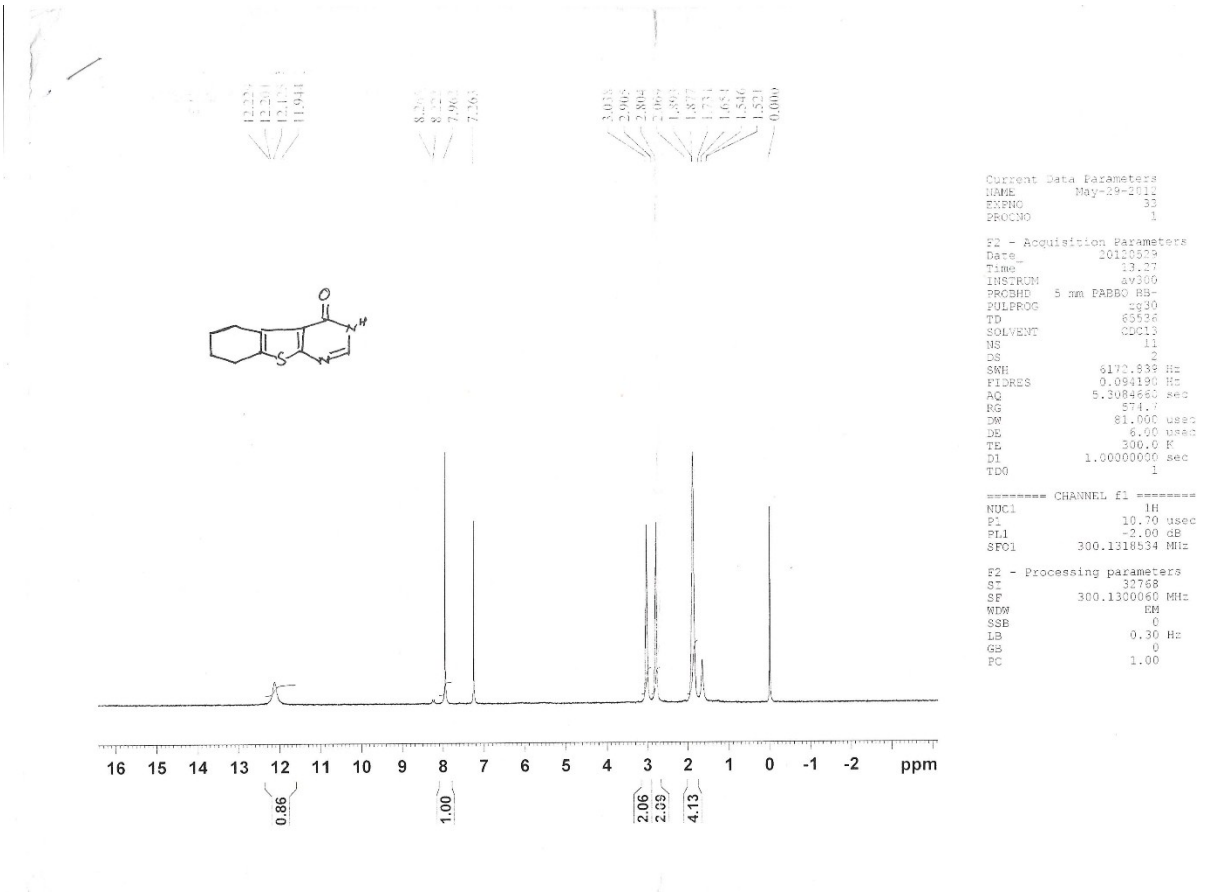

Fig 2. ^{1}H NMR spectrum of compound 2.

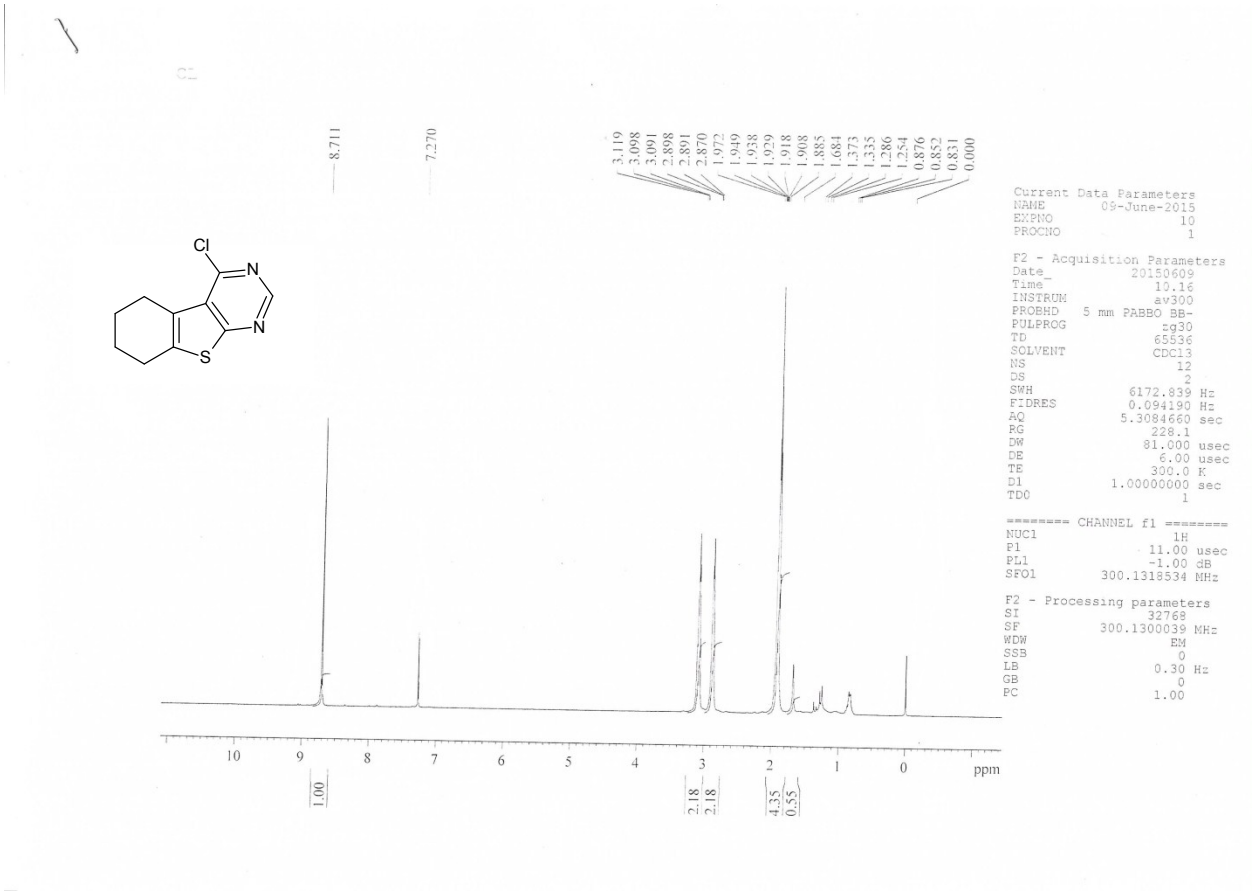

Fig 3. ^{1}H NMR spectrum of compound 3.

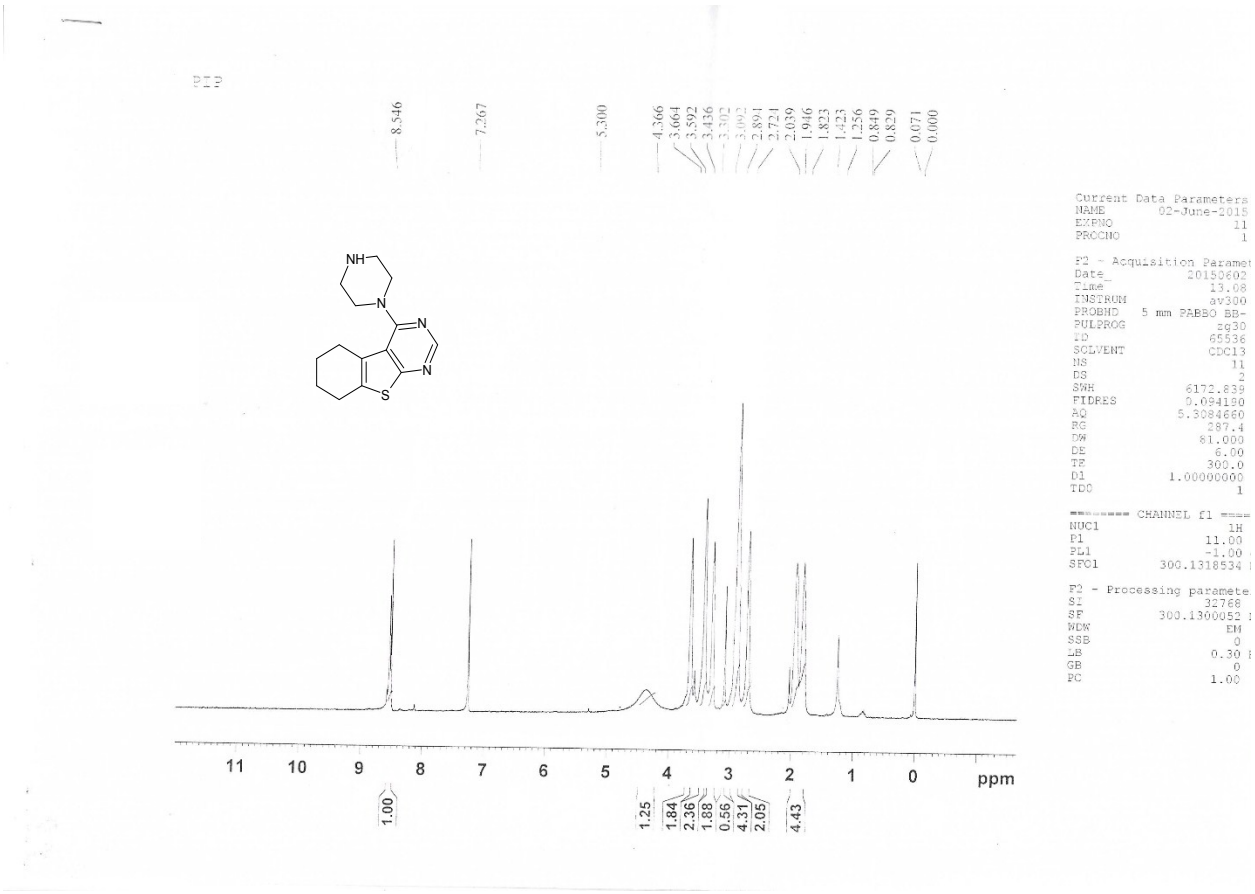

Fig 4. ^{1}H NMR spectrum of compound 4.

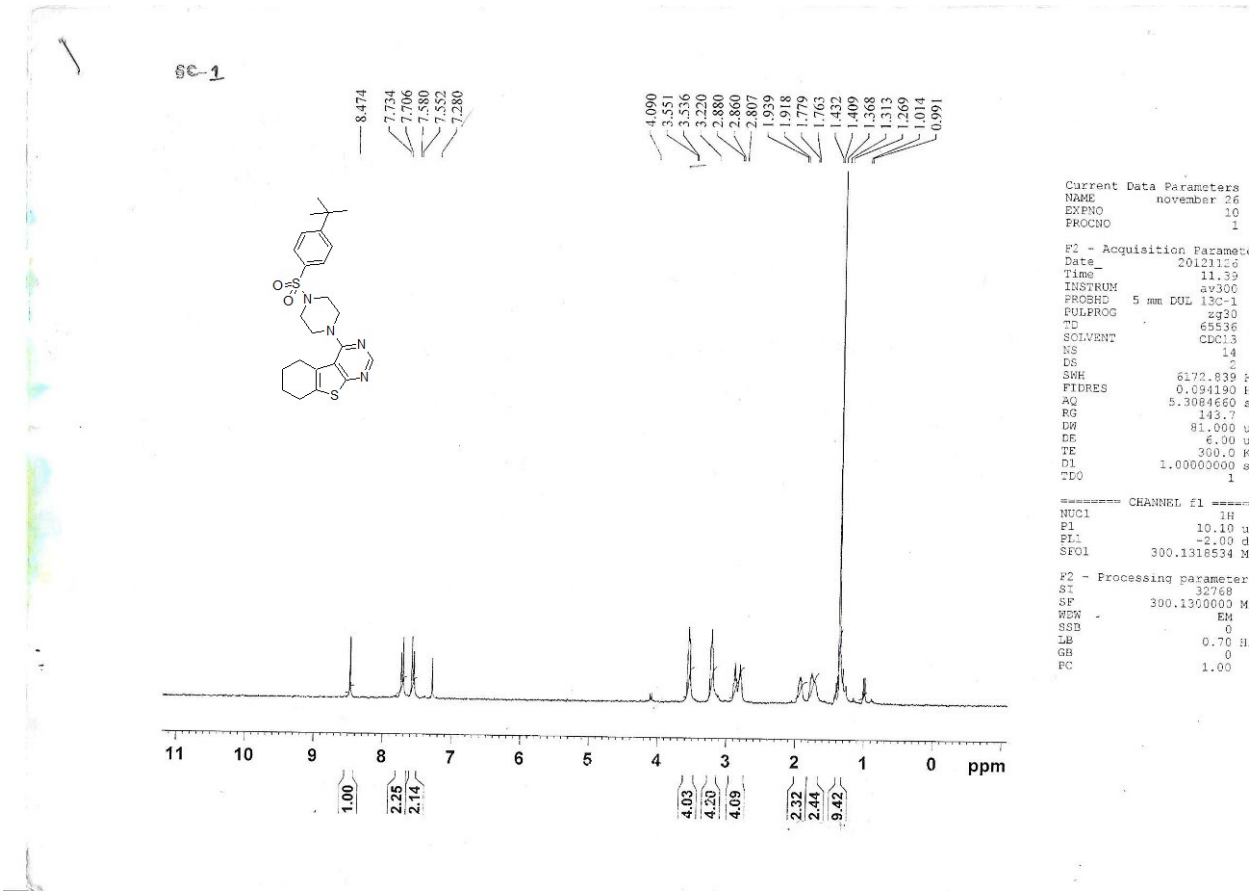

Fig 5. ^{1}H NMR spectrum of compound 5

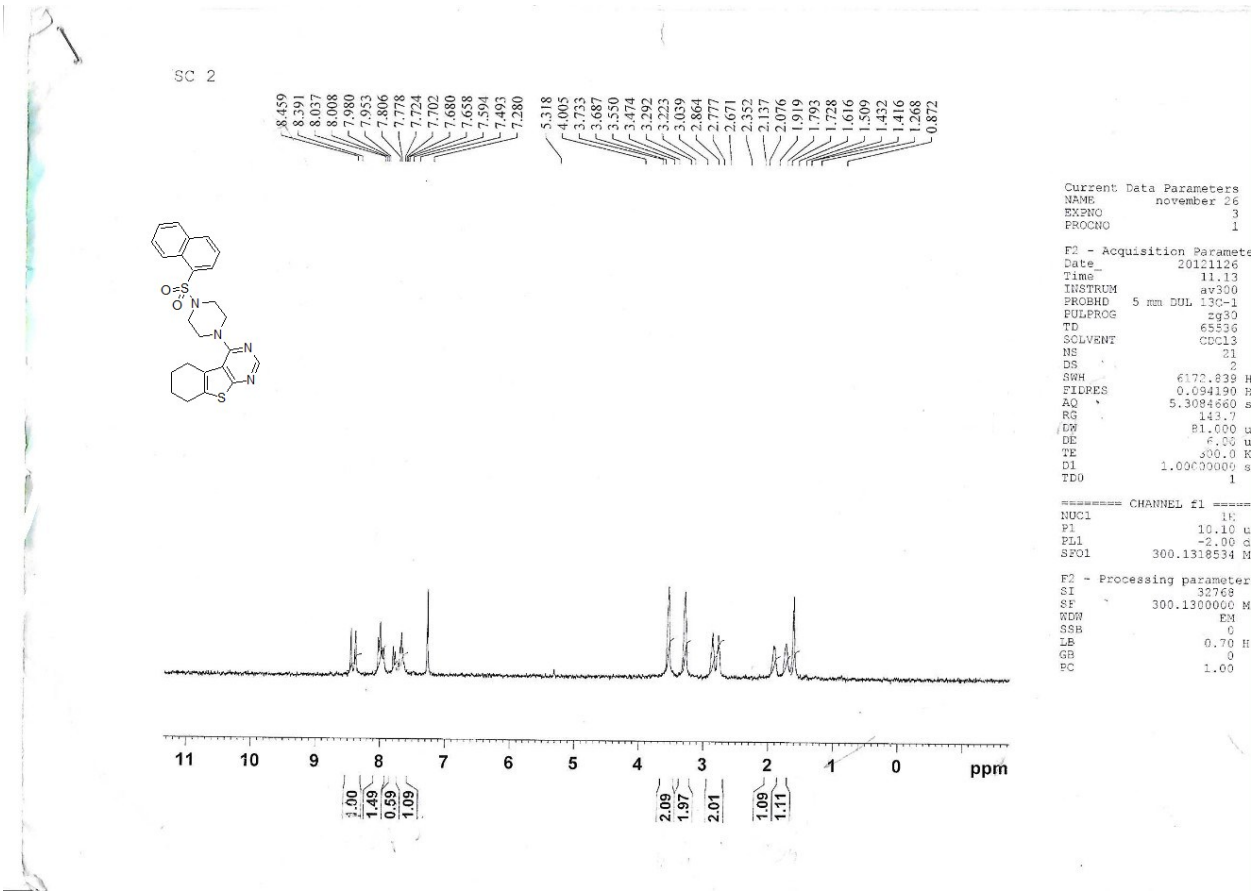

Fig 6. ^{1}H NMR spectrum of compound 6.

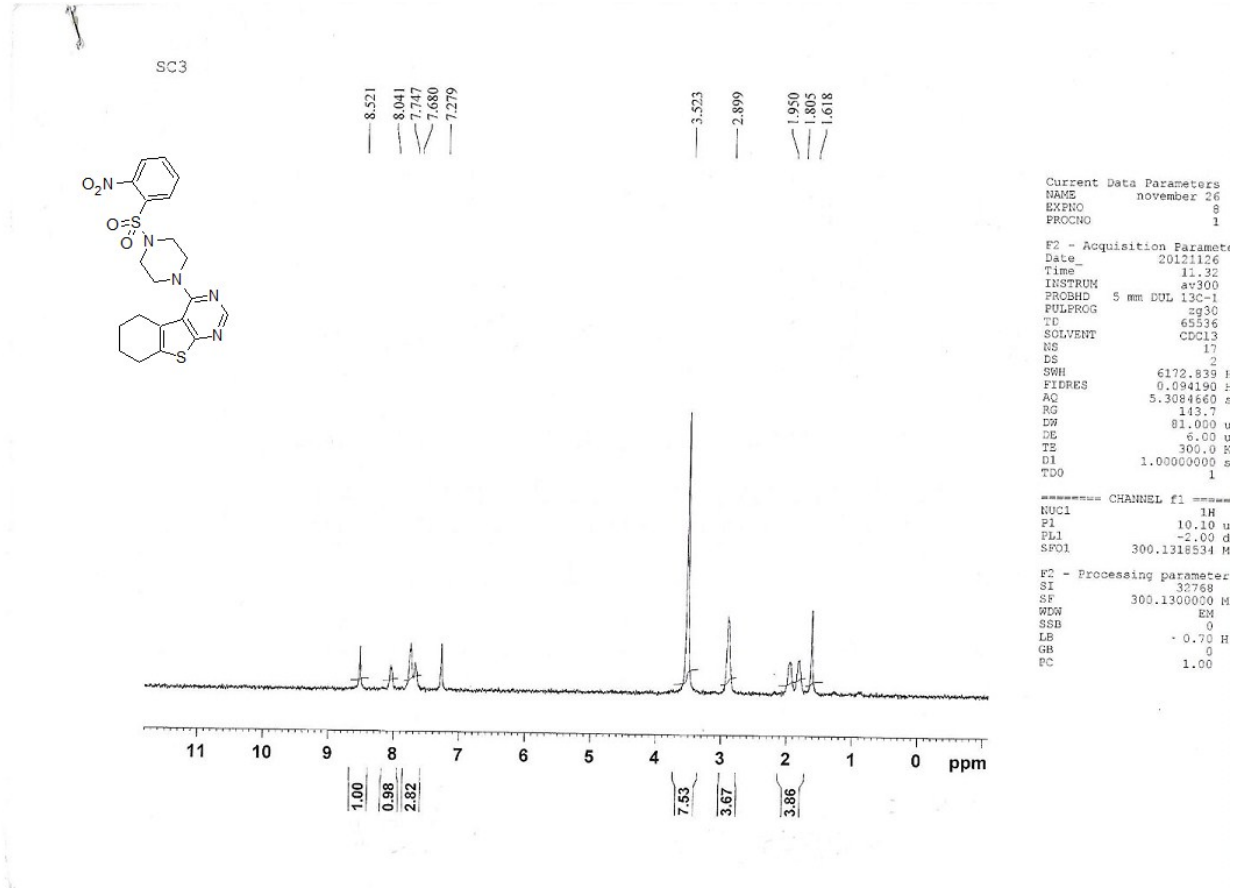

Fig 7. ^{1}H NMR spectrum of compound 7.

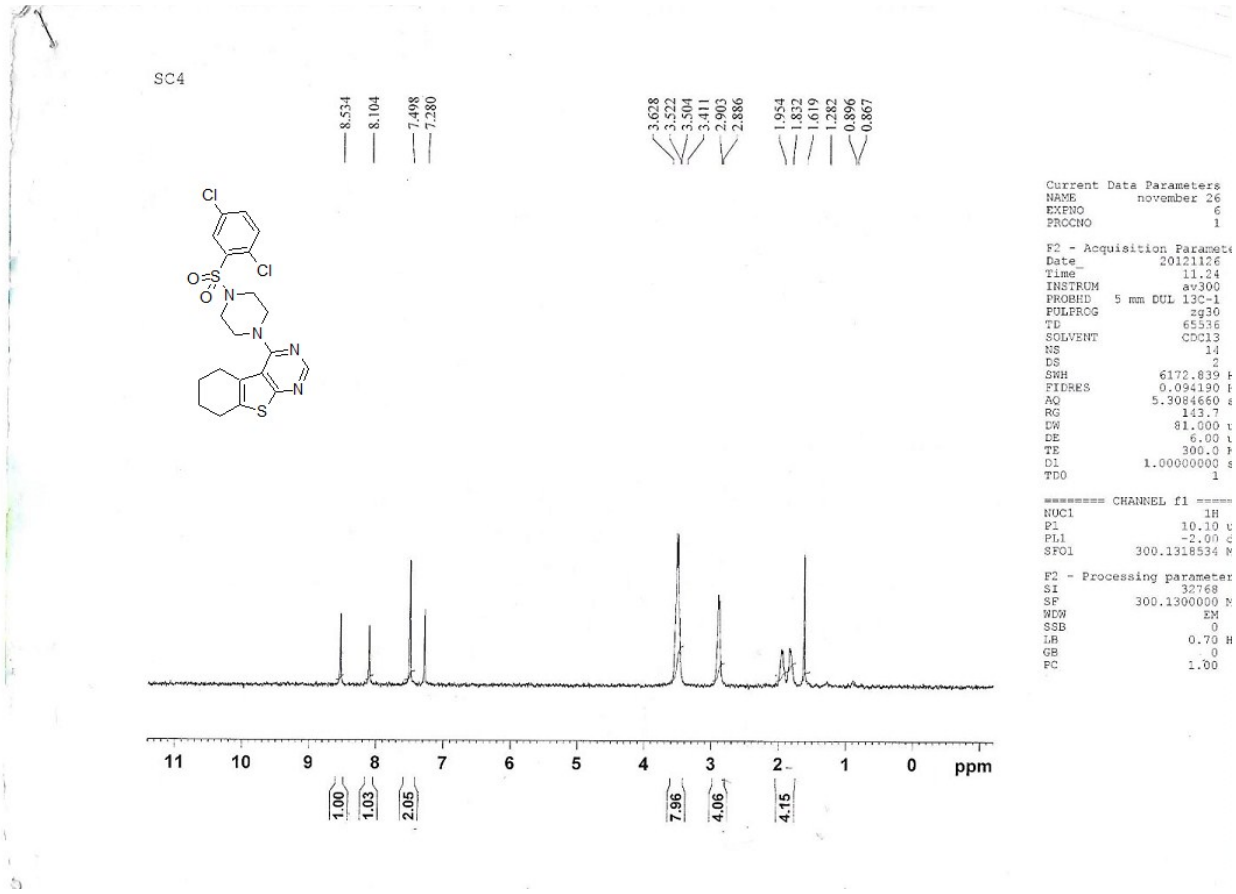

Fig 8. ^{1}H NMR spectrum of compound 8.

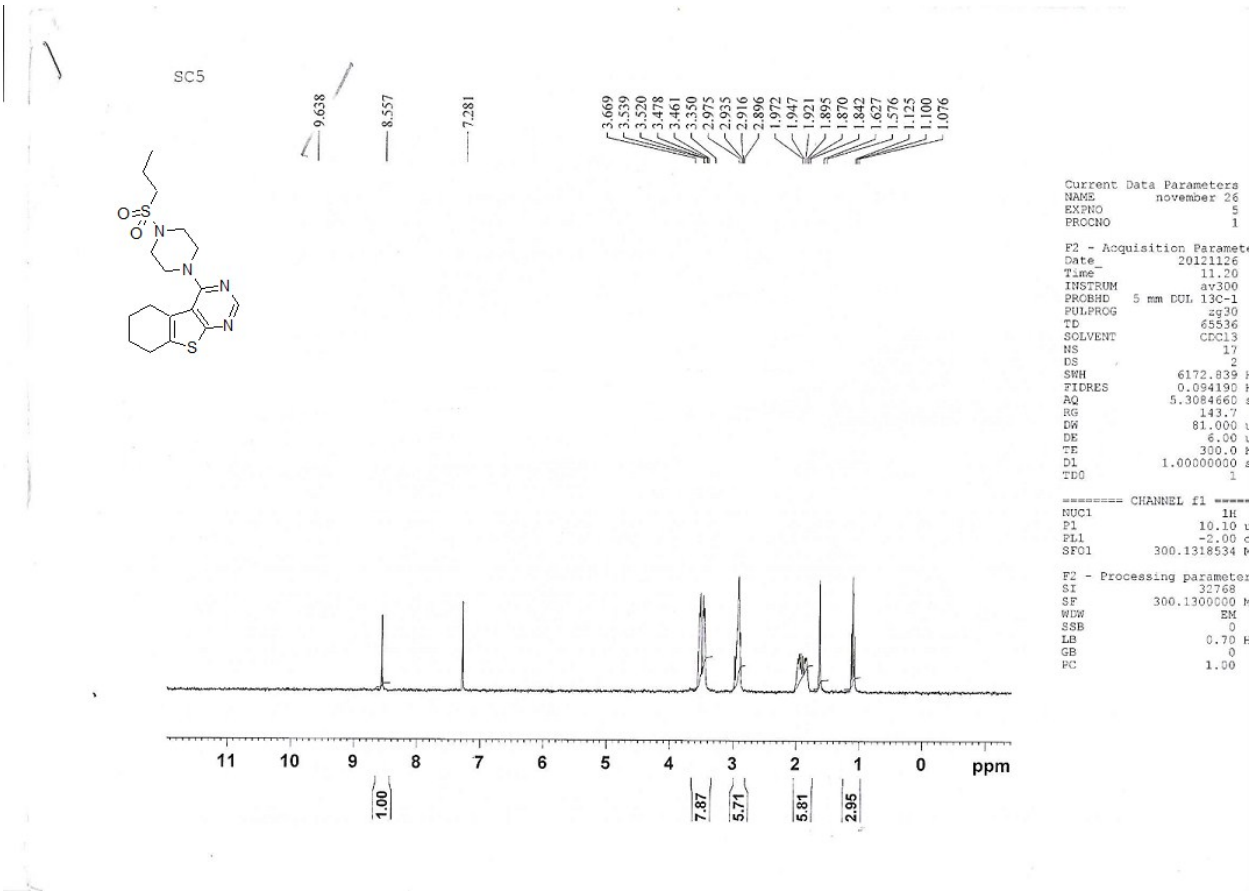

Fig 9. ^{1}H NMR spectrum of compound 9

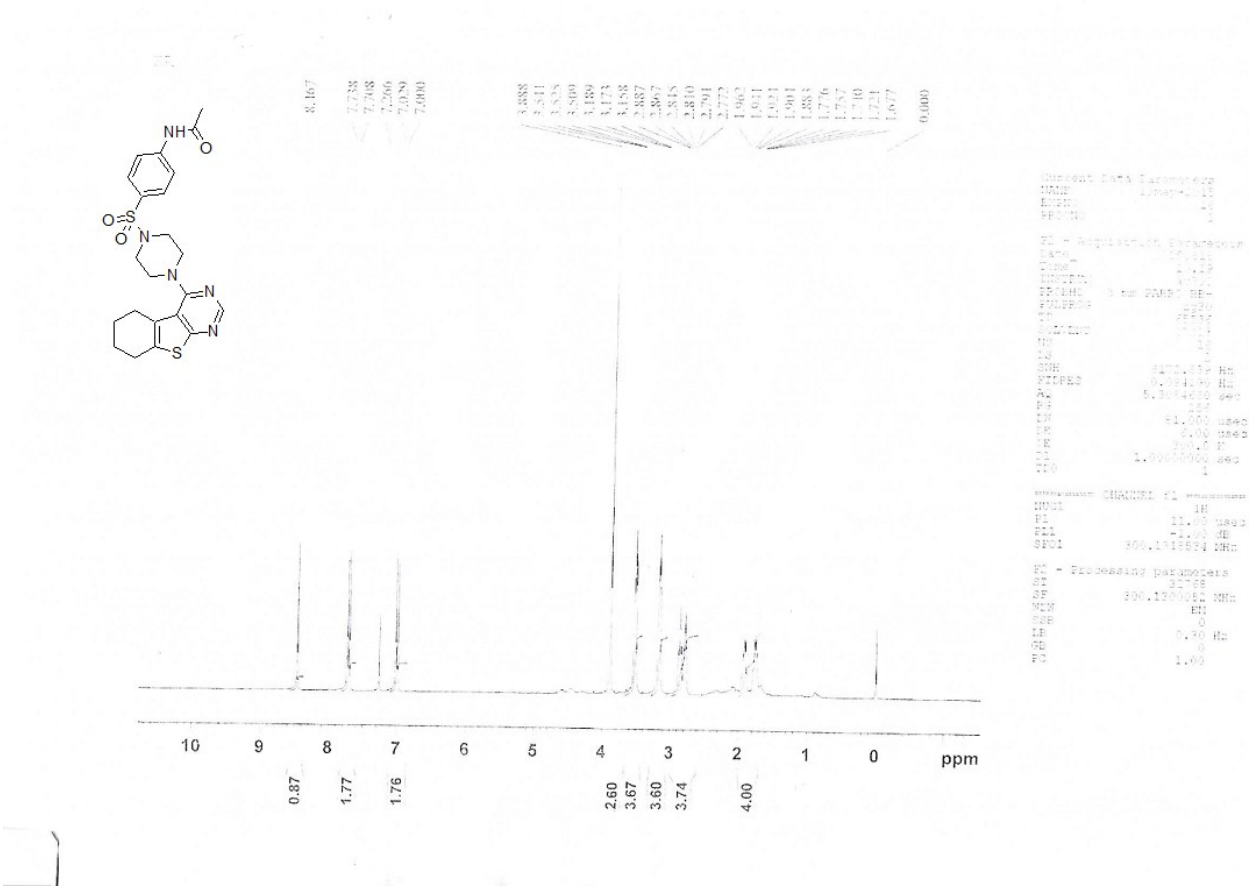

Fig 10. ^{1}H NMR spectrum of compound 10

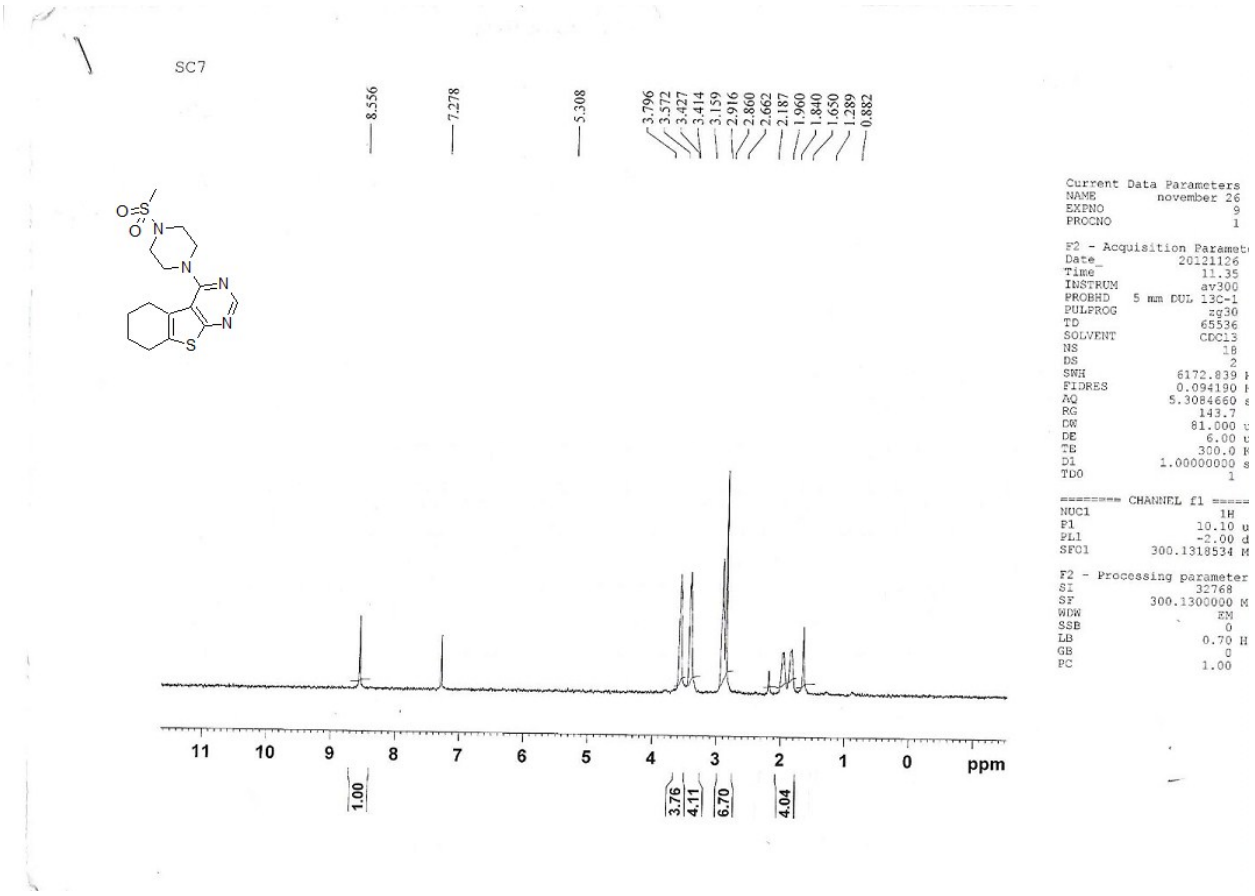

Fig 11. ^{1}H NMR spectrum of compound 11

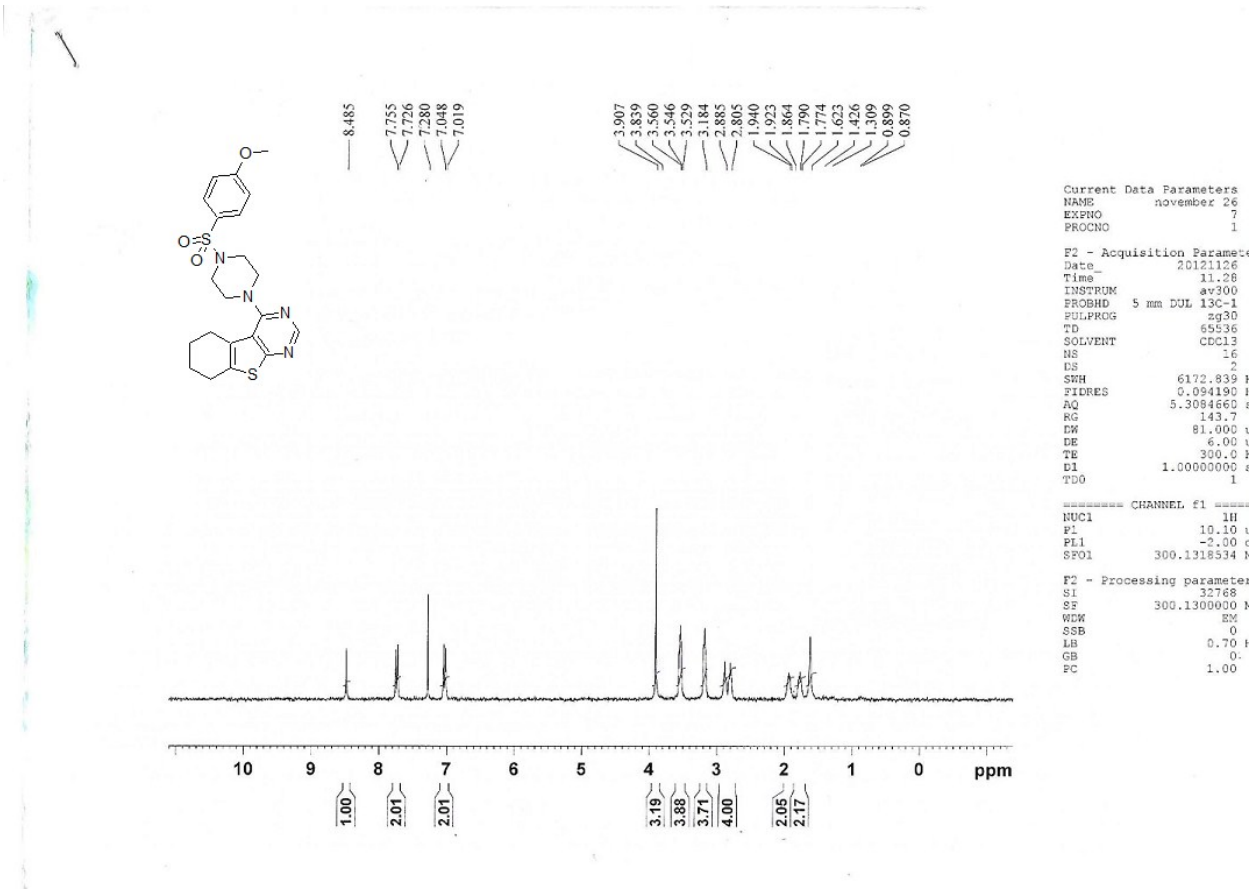

Fig 12. ^{1}H NMR spectrum of compound 12.

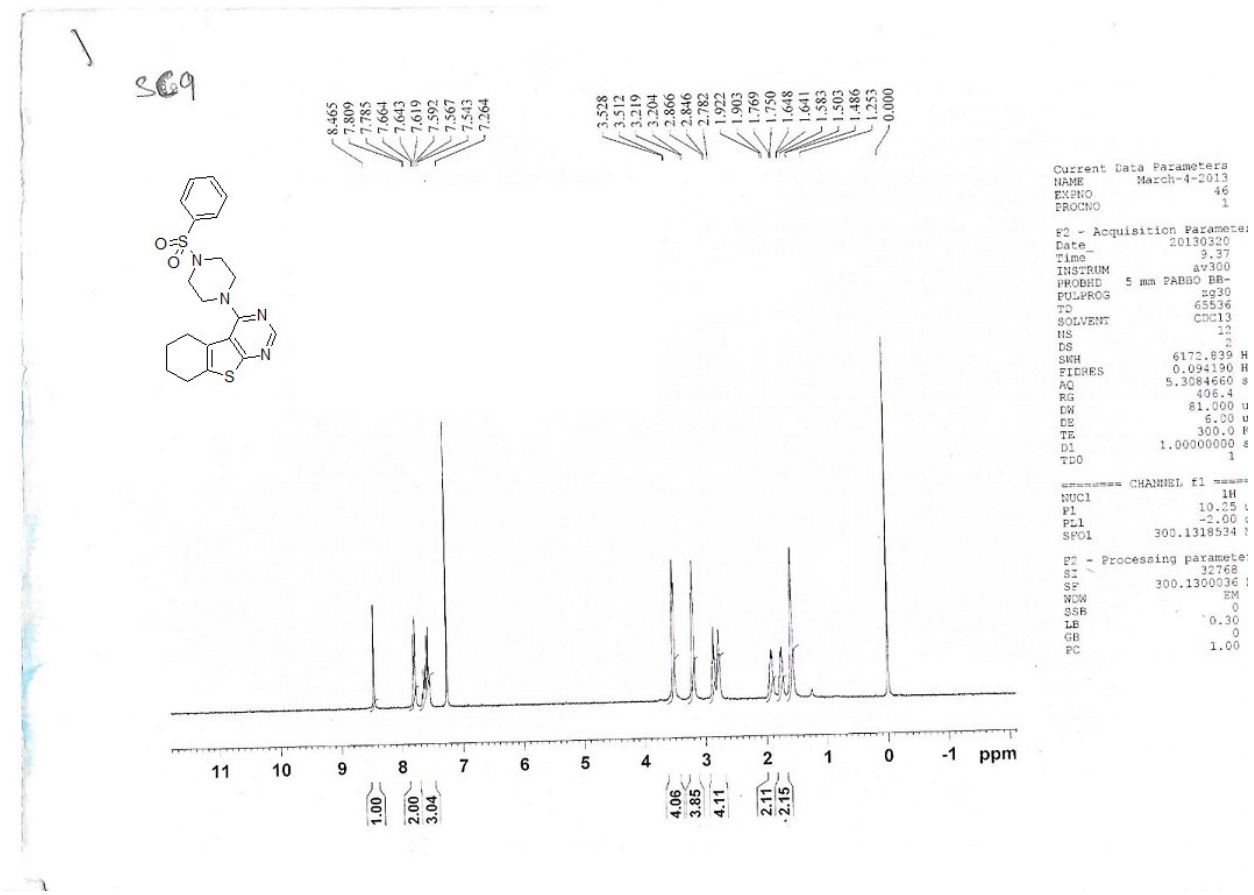

Fig 13. ^{1}H NMR spectrum of compound 13.

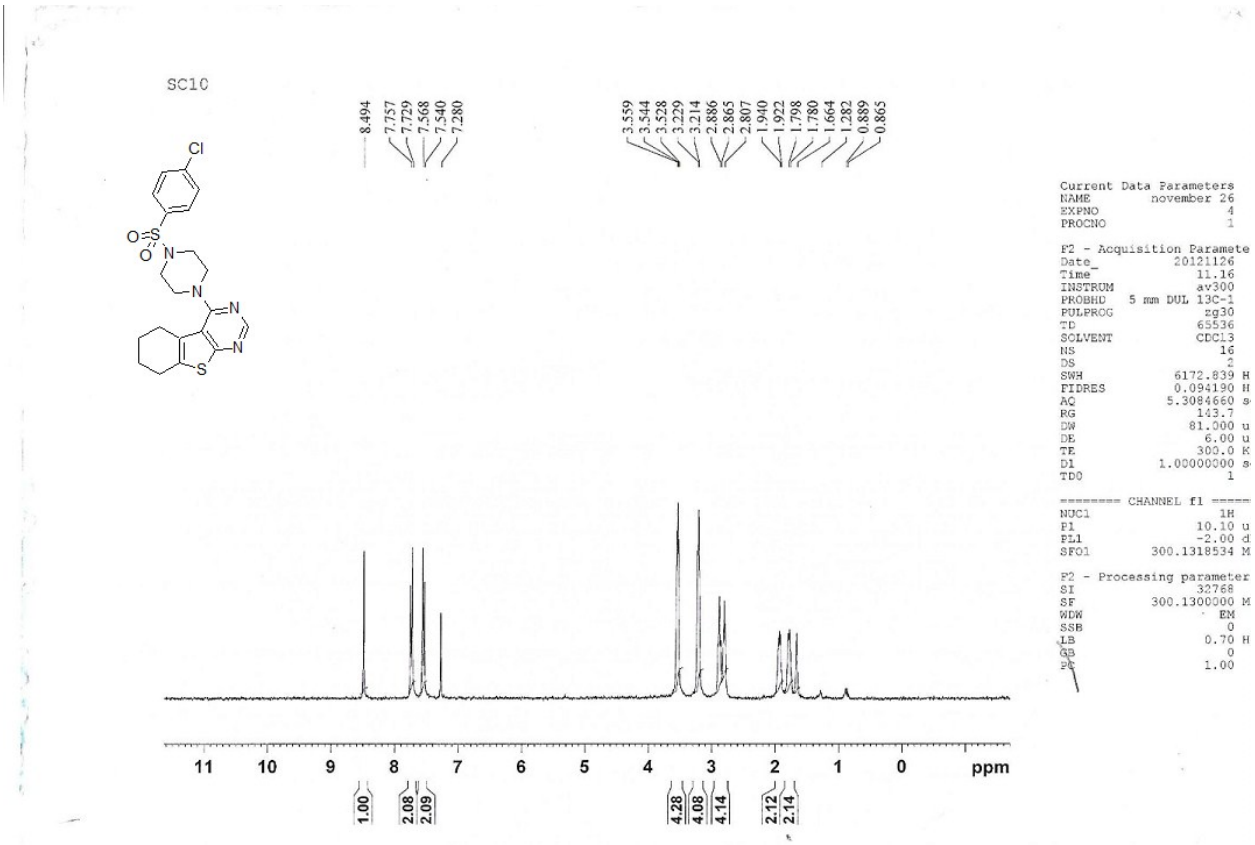

Fig 14. ^{1}H NMR spectrum of compound 14

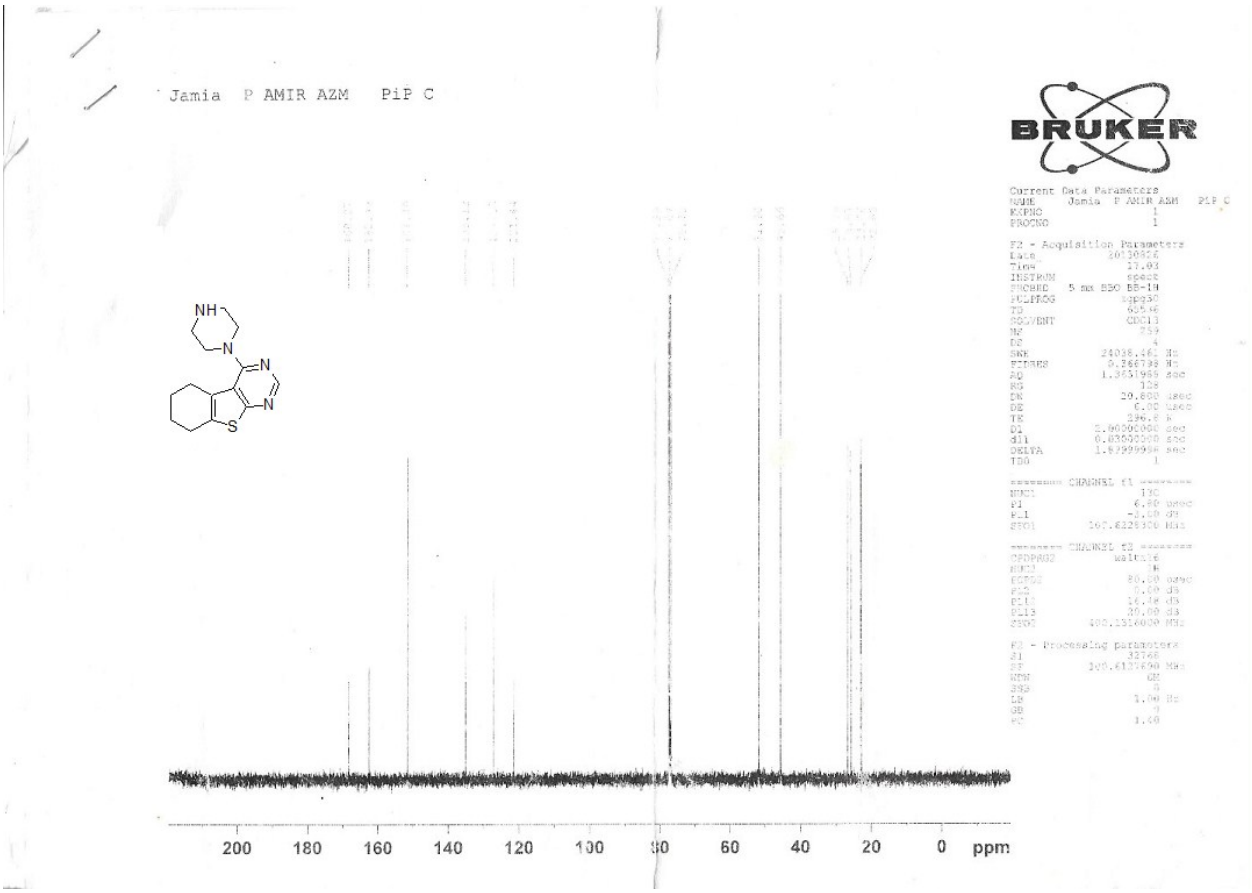

Fig 15. ^{13}C NMR spectrum of compound SCA.

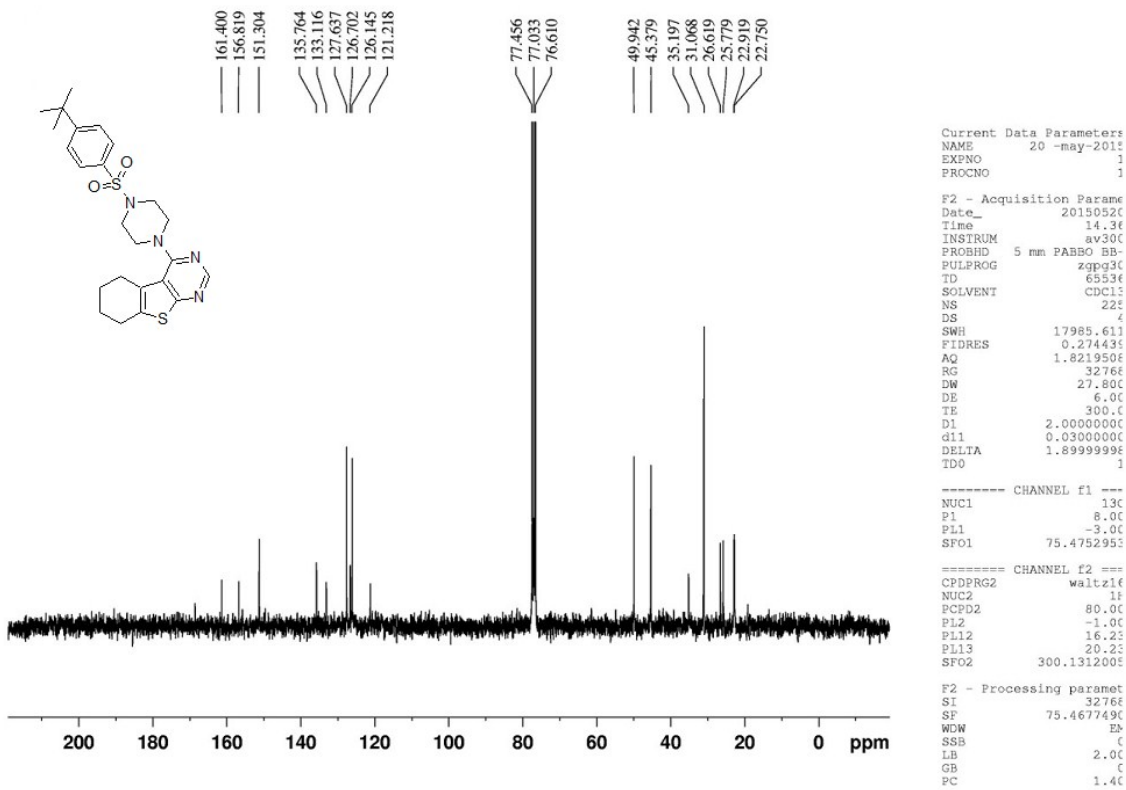

Fig 16. ^{13}C NMR spectrum of compound 5

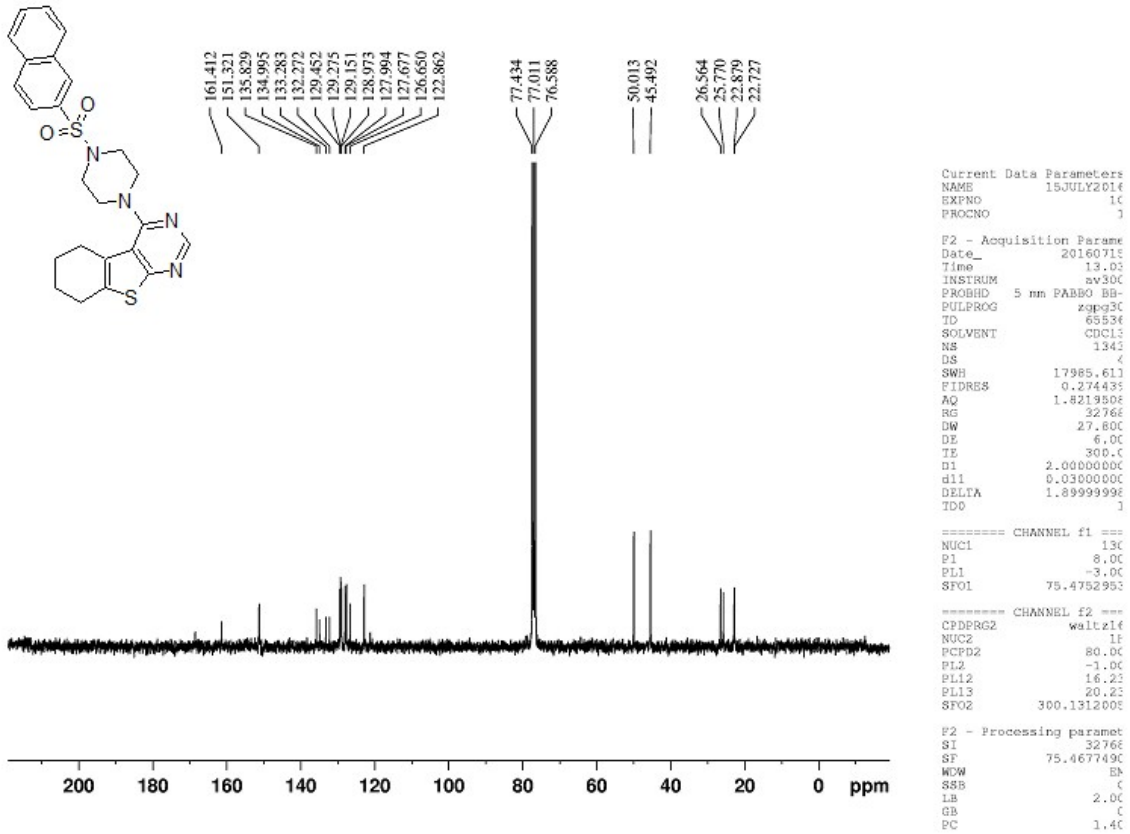

Fig 17. ^{13}C NMR spectrum of compound 6.

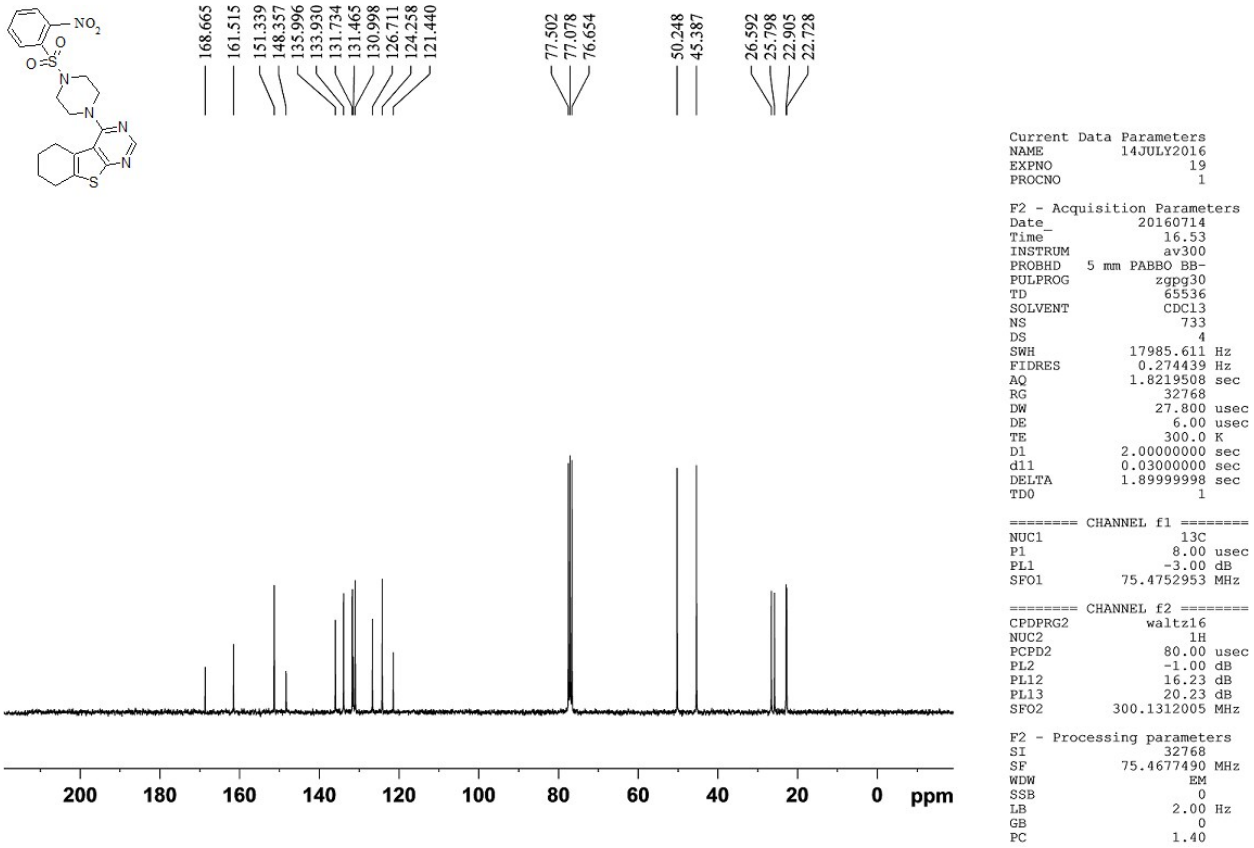

Fig 18. ^{13}C NMR spectrum of compound 7.

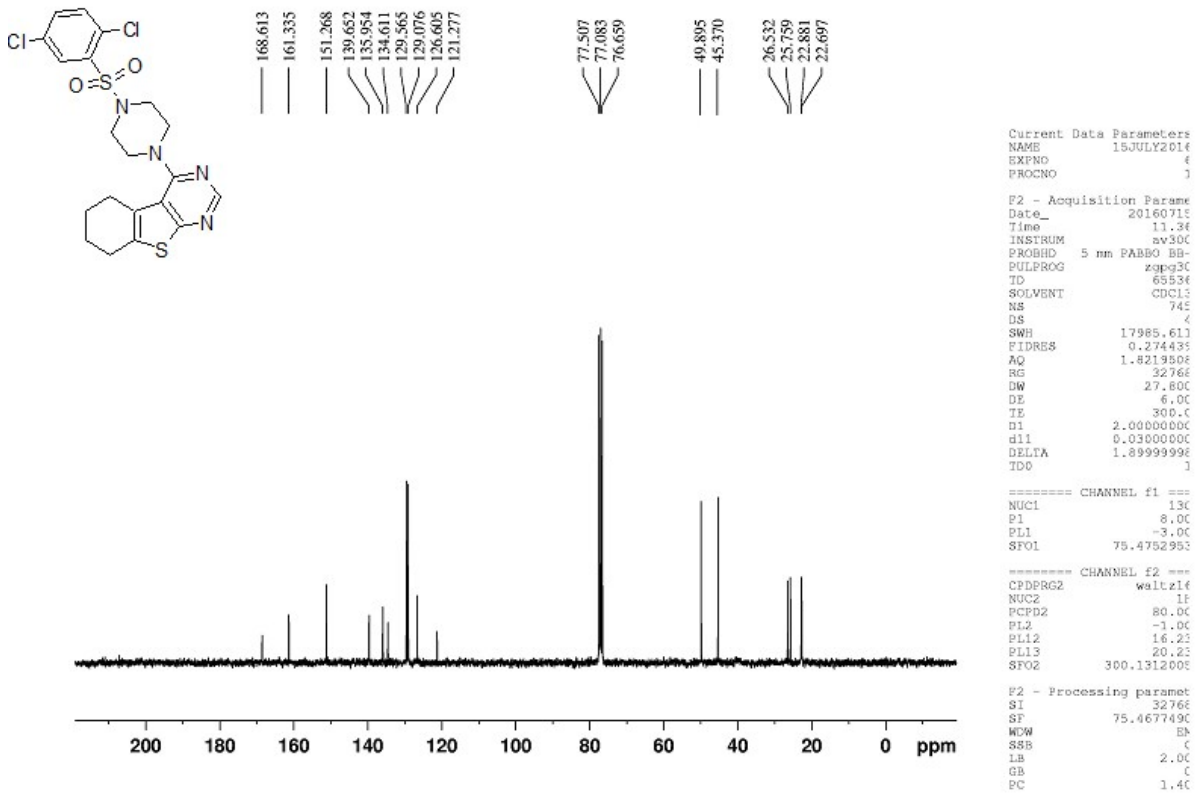

Fig 19. ^{13}C NMR spectrum of compound 8.

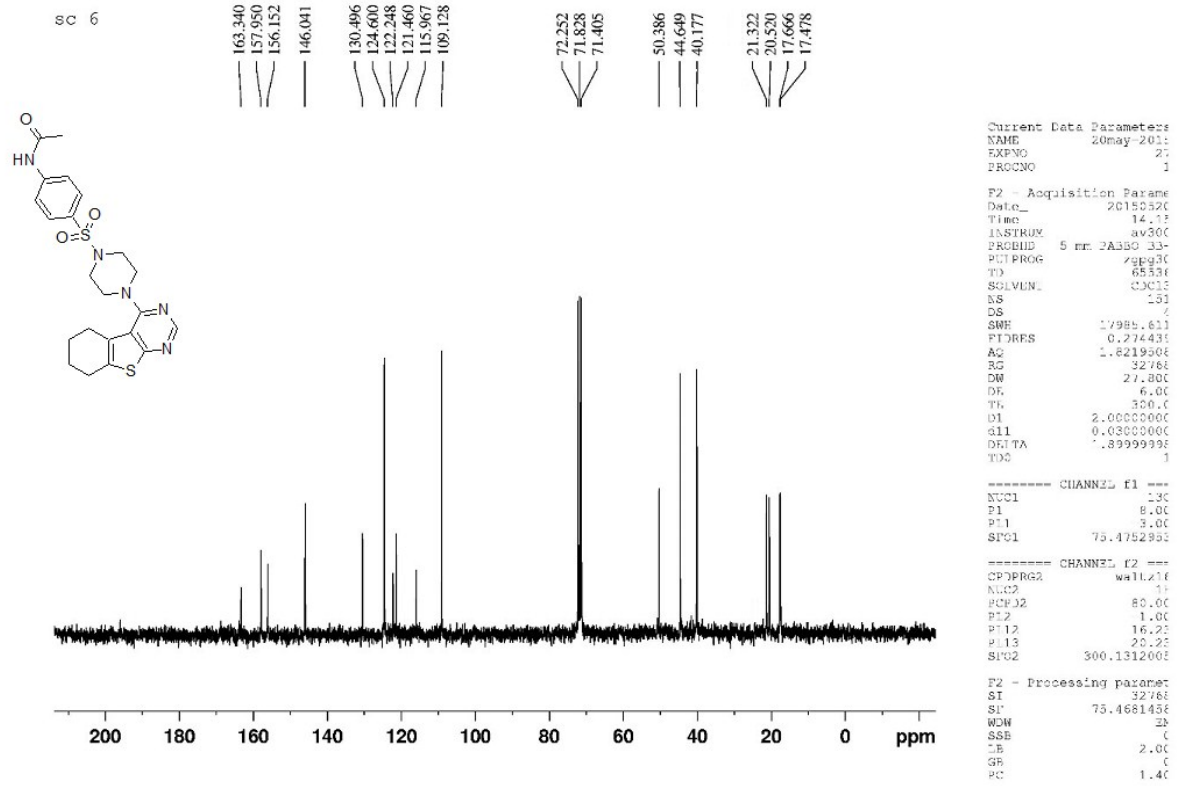

Fig 20. ^{13}C NMR spectrum of compound 10.

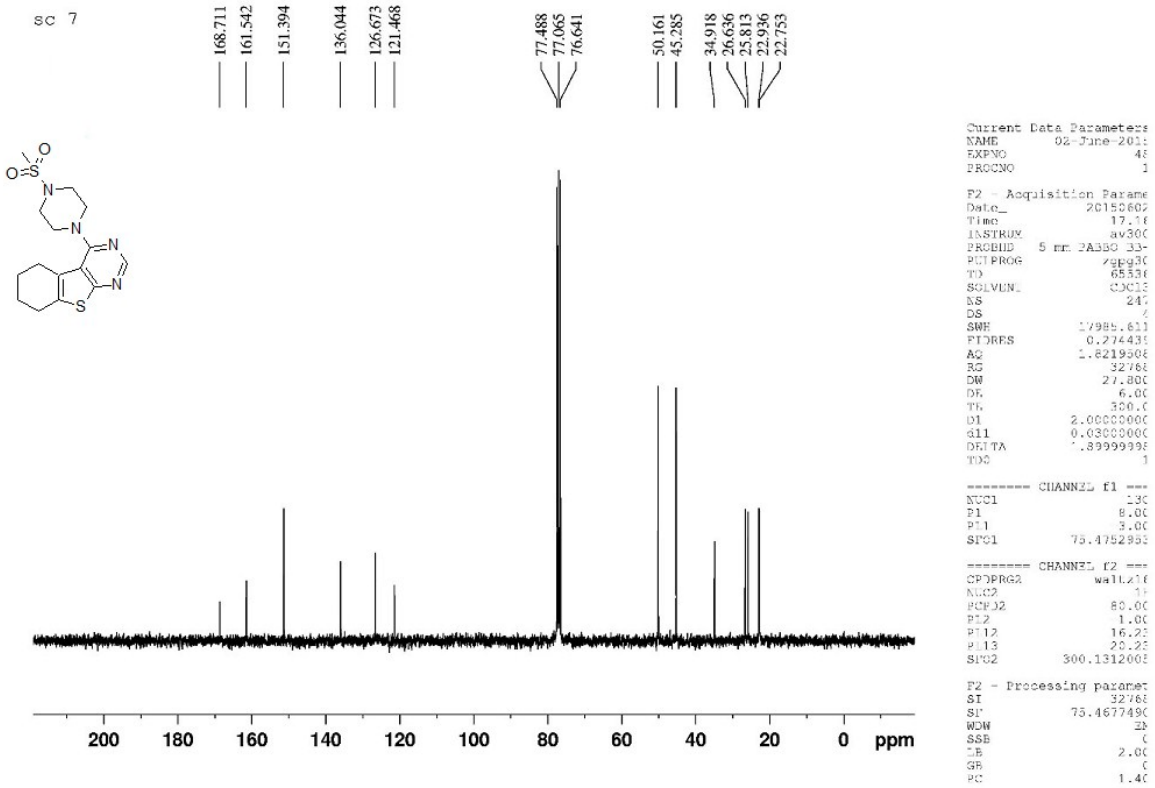

Fig 21. ^{13}C NMR spectrum of compound 11.

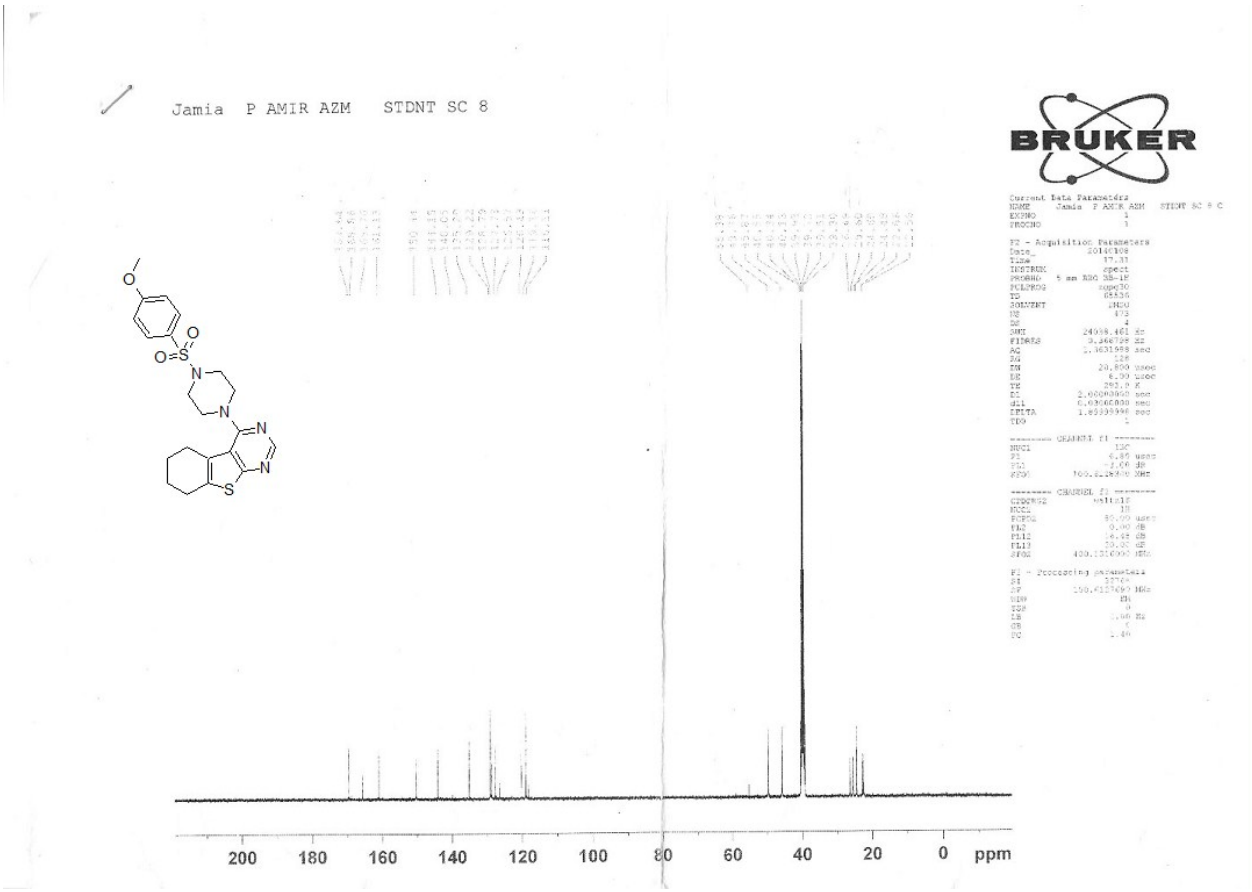

Fig 22. ^{13}C NMR spectrum of compound 12.

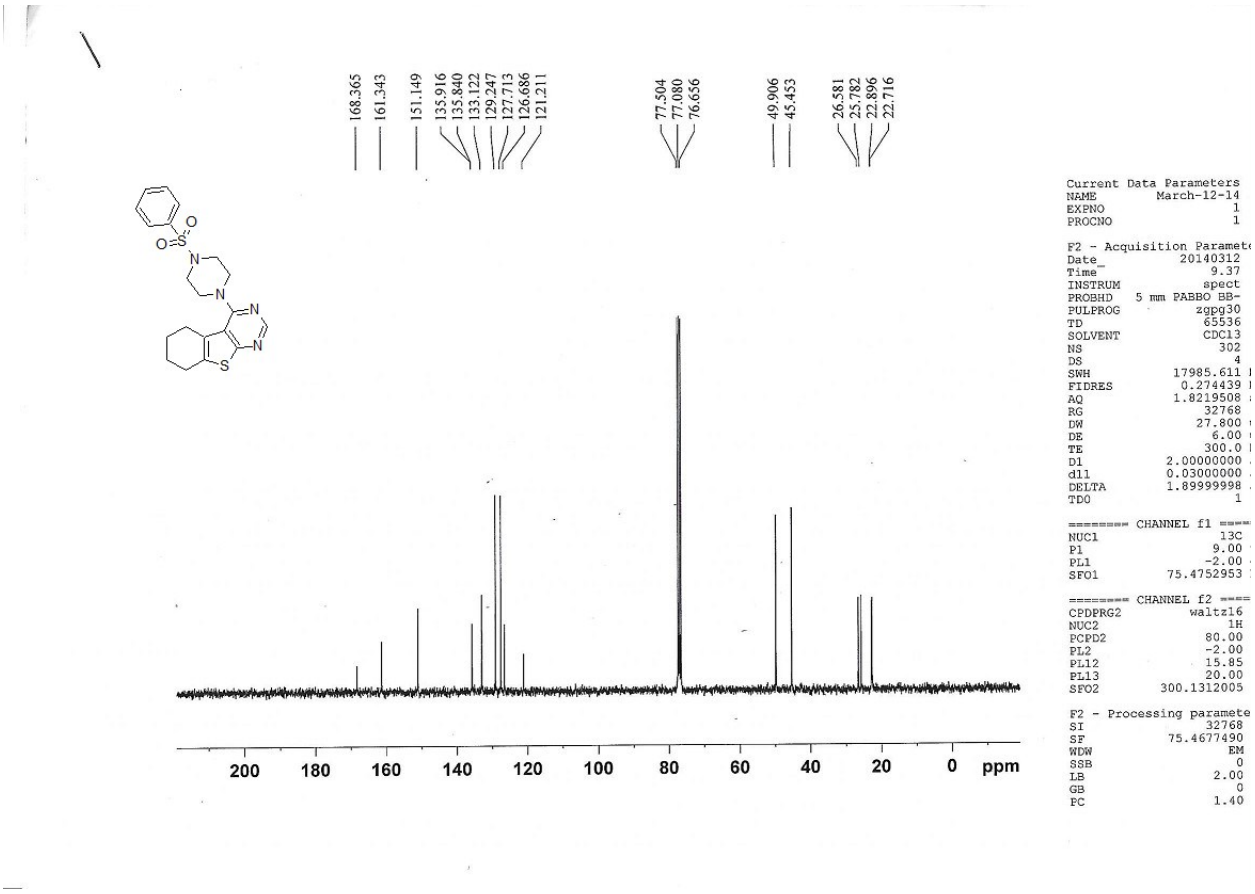

Fig 23. ^{13}C NMR spectrum of compound 13.

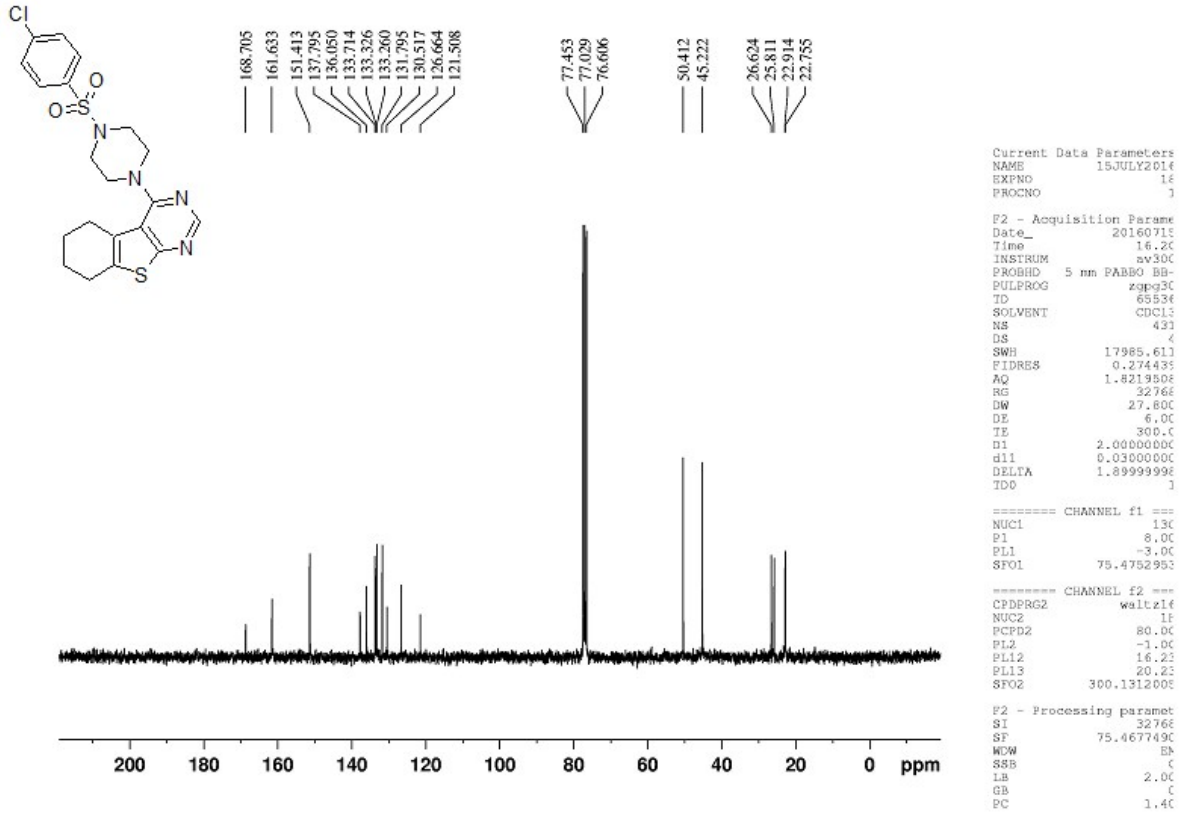

Fig 24. ^{13}C NMR spectrum of compound 14.

References

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[3] M. S. Balakrishna, P. P. George, J. T. Mague, *J. Chem. Res.,* S (2003) 576-577.

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