Kirkuk University Journal - Scientific Studies , Vol 8, No.3, 2013

Khalid A. Al-Badrany Ayad S. Hamad Ihmood K. Al-Juboori

Synthesis of Some Mannich and 2,5-Disubstituted 4-Thiazolidinone Compounds Derived from 4-amino Sulphamethaoxazole

Khalid A. Al-Badrany Ayad S. Hamad** Ihmood K. Al-Juboori ****

**Sciences Food & Biotechnology Department, College of Agriculture.- University of Tikrit*

*** Chemistry Department, College of Education - University of Tikrit*

**** Chemistry Department, College of Science - University of Tikrit*

Email: khalidazize@yahoo.com

Received date: 31/5/2012 Accepted date: 6/10/2013

Abstract

4-Chloro acetyl amino sulphamethaoxazole (A_1) was synthesized by the reaction of amino sulphamethaoxazole with chloro acetyl chloride, Then refluxed with ammonium thiocyanate to obtain thiazoldine-4-one (A_2) . (A_2) was stirred with formaldehyde and various secondary amines to gain 5 novel compounds Mannich bases(A_{3-7}).and 2,5-Disubstituted thiazolidine-4-one (A_{8-11}) were synthesized by the reaction of substituted benzyldehyd with Compound (A_2) . The structure of the synthesized compounds are confirmed by I.R, ^{1}H-NMR & ^{13}C-NMR spectra and Some chemical physical data.

Key Words: synthesis Mannich bases, 2,5-Disubstituted 4-thiazolidinones.

تحضير عدد من قواعد مانخ و مركبات 5,2-ثنائي معوضات 4-ثايازولدينون المشتقة من 4-امينو سلفاميثااوكسازول

*خالد عبد العزيز عطية البد راني **احمود خلف جبر الجبوري ***اياد سليمان حمد

* جامعة تكريت / كلية الزراعة / قسم علوم الأغذية والتقانات الاحيائية

** جامعة تكريت / كلية العلوم/ قسم الكيمياء

*** جامعة تكريت / كلية التربية/ قسم الكيمياء

تاريخ استلام البحث:2012/5/31 تاريخ قبول البحث:2013/10/6

الخلاصة

يتضمن البحث تحضير عدد من قواعد مانخ وقواعد شيف المناظرة لها من خلال مفاعله 4-امينو سلفاميثاكسازول مع كلورو كلوريد الاستيل للحصول على 4-كلورو اسيتايل امينو سلفاميثاكسازول (A_1) . كذلك تم الحصول على N-(2-مثيل اوكسازول-5-ايل)-4-(4-اوكسوثايازولدين-2-ايلدين ايمينو) بنزين سلفونمايد(A_2) من تفاعل المركب (A_1) مع ثايوسيانات الامونيوم . وتم الحصول على معوضات 4-(5-(ثنائي معوضات امينو)مثيل)4-اوكسوثايازولدين-2-ايلدين ايمينو)- N-(2-مثيل اوكسازول-5-ايل)-4-(4-اوكسوثايازولدين-2-ايلدين ايمينو) بنزين سلفونمايد (A_{3-7}) من تفاعل المركب (A_2) مع معوضات الامين الثانوي والفورمالديهايد.ومعوضاتZ-4-(5-اريلدين-4-اوكسازولدين-2-ايلدين ايمينو)- N-(2-مثيل اوكسازول-5-ايل)-4-(4-اوكسوثايازولدين-2-ايلدين ايمينو) بنزين سلفونمايد (A_{8-11}) من تفاعل المركب (A_2) مع معوضات البنزالديهايد .وتم تشخيص المركبات الناتجة بالطرق الفيزياوية والطيفية المتاحة وقد دلت النتائج على صحة التراكيب المقترحة .

الكلمات المفتاحية : تحضير قواعد مانخ ، 5,2-ثنائي معوضات 4-ثايازولدين .

Introduction

4-thiazolidinone derivatives have various pharmacological activities such as antibacteria1[1], antifungal[2], anticonvulsant[3] and anticancer[4] and herbicidal[5]. It way, we found that Mannich bases had antimicrobial activities [6−9] antifungl [10-11] besides various other activities. Sulpha drug are also referred to as antibacterials[12]. Sulfa drugs represent group of compounds discovered in a conscious search of antibiotics[13], In our previous work, we synthesized some thiazolidinone derivatives from the reaction of sulphamethaxzole with chloro acetyl chloride .and we synthesized and characterized new Mannich bases by refluxing thiazolidine-4-one with formaldehyde and various secondary amines .thiazolidine-4-one react with various aromatic aldehyd to give 2,5-Disubstituted thiazolidine-4-one.

Experimental

Melting points were determined on Electrothermal. melting point Apparatus are uncorrected.and The IR absorption spectra were recorded by FTIR model 84005 Shimadzu Japan. Infrared spectrophotometer as KBr disk. ^{1}H-NMR & ^{13}C-NMR spectra were recorded by Ultra shield 300 MHz. Bruker 2003.al-albaet university Jordan

1) Synthesis of 2-chloro acetyl amino sulphamethaoxazole(14) (A_1):

Freshly distilled chloro acetyl chloride (2.5ml) dissolved in 1,4-dioxane (10ml) was gradually added to (0.033 mole) 4-amino sulphamethaxazole dissolved in1,4-dioxane (30ml).with 1 ml of triethylamine . The reaction mixture was refluxed on a water bath for 4 hr. then 1,4-dioxan was distilled off , The crude product was washed with water to remove the acid and recrystallized from ethanol to obtain yellow powder yield 73% m.p 195-197 C° .

2) Synthesis of 2-[sulphamethaoxzole]-4-thiazolidinone[15] (A_2):

4-Chloro acetyl amino sulphamethaoxazole (0.05 mol) and 0.1 mol (7.6 g) of ammonium thiocyanate in 50 ml of 96% ethanol were refluxed on a water bath for 1 hr, left overnight, the solution was filtered off and dried in room temperature recrystallized from ethanol to give yellow powder yield 83%, m.p. 208-210 C°

3) Synthesis of 5-(substituted methylene)-2-[sulphamethaoxzole]-4-thiazolidinones[16] (A_{3-7}):

A mixture of 0.5 ml of 37% formaldehyde and 0.002 mol of a secondary amine was added drop wise with vigorous stirring to a suspension of 0.002 mol of (A_2) in absolute ethanol. The mixture was refluxed for 4 hr. Upon cooling, the crude compound was precipitated, filtered off, dried in room temperature and recrystallized from ethanol. The physical properties of the synthesized compound are given in Table(1).

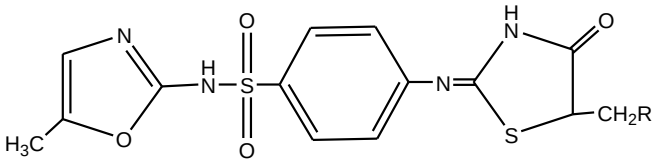


Table (1) physical properties of Compounds (A_{3-7})

Compd. No.	R	M.p °C	Yield %	Color
A_3	$-N(CH_3)_2$	270 dec.	73	White powder
A_4	$-N(C_2H_5)_2$	278 dec.	54	White powder
A_5	$-N(Ph_2)_2$	282 dec.	80	Yellow powder
A_6	$-N-C_{11}H_{12}N_4O$	273 dec.	43	Yellow powder
A_7	$-N-C_7H_4O_3S$	291 dec.	35	Brown powder

4) Synthesis of (Z)-4-(5-(arylidene)-4-oxothiazolidin-2-ylideneamino)-N-(2-methyloxazole-5-yl)benzenesulfonamides[16] (A_{8-12}):

Equimolar solution of the compound (A_2) (0.002 mol) and substituted benzaldehyde (0.002 mol) in dioxane (20 ml) in the presence of sodium ethoxide was reflexed for 6 hr in water bath , after cooling the product was collected and recrystallized from ethanole . The physical properties of the synthesized compounds are given in Table(2).

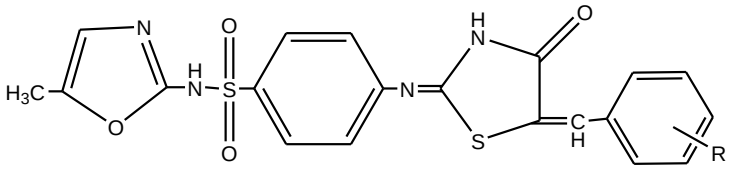


Table (2) physical properties of Compounds (A_{8-12})

Compd. No.	R	M.p °C	Yield %	Color
A_8	$-N(CH_3)_2$	222-224	58	Red powder
A_9	p-Cl	245-247	43	White powder
A_{10}	p-NO_2	238-240	73	Yellow powder
A_{11}	m-Cl	230-232	60	White powder
A_{12}	m-NO_2	227-229	54	Yellow powder

Results and Discussion

2-(Sulfamethaoxazoleeamino)thiazoldine-4-one (A_2) was synthesized by cyclization of 4-Chloroacetyle sulfamethaoxazole (A_1) with ammonium thiosynate in presrnce of ethanole in water bath temperature . The I-R spectrum of (A_2) showed band at (3260 cm^{-1}) due to stretching (N-H) group, band at (1670 cm^{-1}) for (C=O) group, band at (1095 cm^{-1}) for (C-S-C) group and band at (1595 cm^{-1}) to (C=N) group . The ^{1}H-NMR spectrum (DMSO-d_6) of compound (A_2) showed signal at (δ 2.35 ppm) for (3H, $CH_{3(oxazole)}$) , signal at (δ 6.6 ppm) for

(H, $CH_{(oxazole\ ring)}$) , signal at (δ 4.35 ppm) du to (H,$NHSO_2$) , signal at (δ 7.05- 7.9 ppm) for (4H, phenyl) , also the spectrum showed signal at (δ 6.2 ppm) for (H, $NH_{(thazoldinon)}$) , signal at (δ 4.15 ppm) for (2H, $CH_{2(thiazoldinon\ ring\ )}$) . The ^{13}C-NMR spectrum (DMSO-d_6) showed signal at (δ 13 ppm) du to (C, $CH_{3(oxazol)}$) , signal at (δ 163 ppm) for ($C_{5(oxazole\ ring)}$) , signal at (δ 120 ppm) for ($C_{3(oxazle\ ring)}$) , signal at (δ 143 ppm) for ($C_{2(oxazle\ ring)}$) , The ^{13}C-NMR also showed signal at (δ 159 ppm) for ($C_{2(thiazoldinon\ ring\ )}$) , signal at (δ 166 ppm) for ($C_{4(thiazoldinon\ ring)}$) and signal at (δ 38 ppm) for ($C_{5(thiazoldinon\ ring)}$). 5-(substituted methylene)-2-[sulphamethaoxzole]-4-thiazolidinones(A_{3-7}) were synthesized from the reaction of compound (A_2) with substituted secondary amine and formaldehyde , The structure of synthesis compounds were confirmed by there melting-point and , I-R , ^{1}H-NMR , ^{13}C-NMR data , The spectra carctrazetion data are given in table (3) . (Z)-4-(5-(arylidene)-4-oxothiazolidin-2-ylideneamino)-N-(2-methyloxazole-5-yl)benzenesulfonamides(A_{8-12}) were synthesized by the reaction of compound (A_2) with substituted benzyldehyde in presence sodium ethoxid , The structure of prepared compounds were confirmed by measuring there melting-point and , I-R , ^{1}H-NMR , ^{13}C-NMR data , Spectroscopy data were shown in Table (3) .The synthetic rout of these compounds is presented in Scheme (I) .

Table (3) the ^{1}H-NMR , ^{13}C-NMR & (I.R) spectroscopy properties of Compounds (A_{1-12})

Compd. No.	^{1}H-NMR	^{13}C-NMR	IR υ cm^{-1}(KBr)					
			O ‖ C—N	(C⁻⁻⁻C)	C-N	C=N	C-S-C	Others
A_1			1677	1450,1556	1210	1604	745	
A_2			1690	1456,1558	1227	1598	738	
A_3			1687	1450,1555	1202	1636	745	
A_4	2.4ppm for 4H,CH2 in ethylene, 1ppm for 3H, CH_3 in ethylin ,3.2ppm for H,CH thiazoldin , 3.5-4.1ppm for 2H,CH_2 methylen , 8ppm for H,NH in thiazoldin	12ppm for CH_3 in ethelyn , 44ppm for CH_2 in ethelyn , 53ppm for CH_2 methylin , 49ppm for C5 in thiazoldin	1699	1456-1556	1227	1602	720	
A_5	3.7-5.1ppm for 2H,CH_2,6.2-7.9ppm for 14H,3Ph,8.2ppm for H,NH,3.3ppm for H,CH ,	**159ppm for $C_{2thiazol\ ring}$, 172ppm for $C_{4thazole\ ring}$, 43ppm for $C_{5thiazole\ ring}$, 64ppm for methylene group**	1679	1450-1550	1120	1606	750	
A_6	8.0ppm for $NH_{thiazol}$,3.4-4.1 for (C2,$C6_{piprazin}$) , 4.3-4.9ppm for ($C3,C5_{piprazin}$) , 8.8ppm for C2,C5 in pyridine	51ppm for $C5_{thiazoldin}$,54ppm for methylene , 75ppm for C2,C6in piprazin ,62-63 for C3,C5 in piprazin ,178ppm for C4 in thiazoldin , 159ppm for C2 in thiazoldine	1684	1438,1510	1169	1606	749	
A_7			1700	1465,1557	1220	1600	745	
A_8	6.8ppm For H,CH in aryldine , 2.9ppm for 6H, CH_3 in $N(CH_3)_2$,8ppm for H,NH in thiazoldin , 6.1ppm for H,$NHSO_2$	12ppm for CH_3 in methoxazol, 40ppm for CH_3 in $N(CH_3)_2$, 115ppm for C5 in thiazoldin , 145ppm for CH in aryldin ,	1700	1456,1550	1220	1602	756	
A_9	6.4ppm For H,CH in aryldine ,8ppm for H,NH in thiazoldin , 4ppm for H,$NHSO_2$	12ppm for CH_3 in methoxazol, 115ppm for C5 in thiazoldin , 145ppm for CH in aryldin ,159ppm for C2 in thiazoldin , 168ppm for C5 in thiazoldin	1690	1455,1556	1223	1602	745	649
A_{10}			1697	1456,1556	1226	1606	735	1350 for sy NO_2 1531 for asy NO_2
A_{11}			1699	1435,1556	1220	1636	735	678
A_{12}			1697	1450,1556	1222	1600	735	1350 for sy NO_2 1531 for asy NO_2

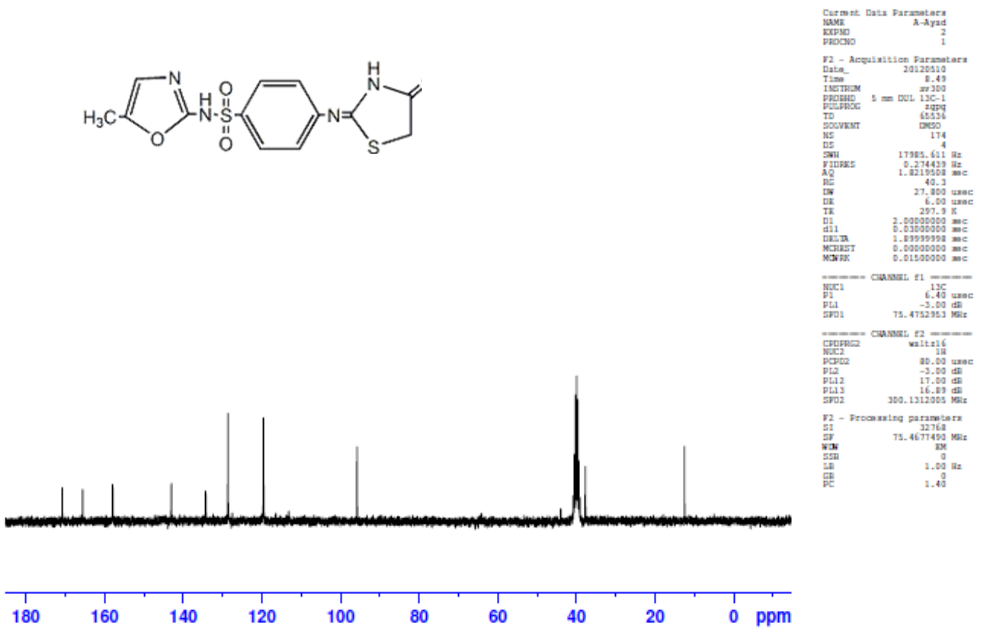


Figure (1)[13] C-NMR for the Compound (A_1)

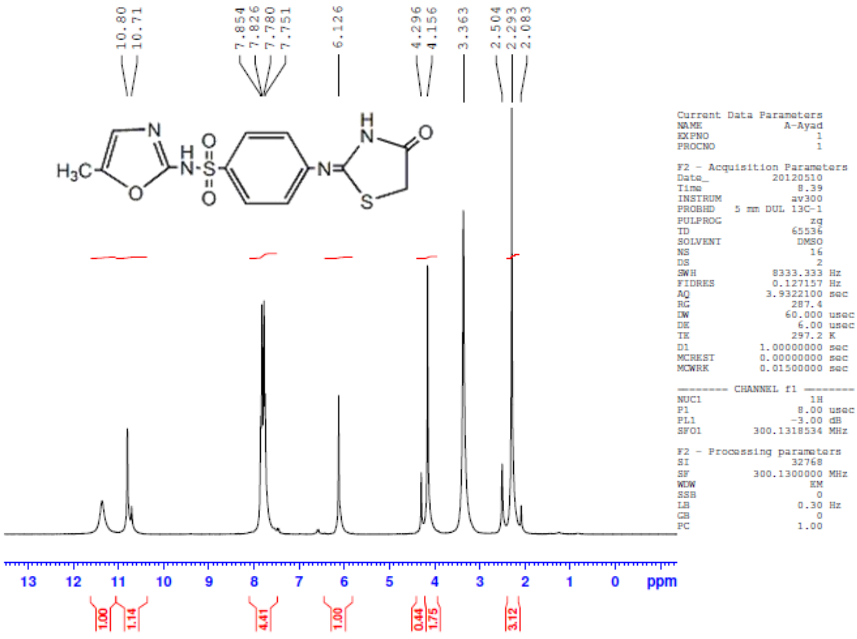


Figure (2)[1]H-NMR for the Compound (A_1)

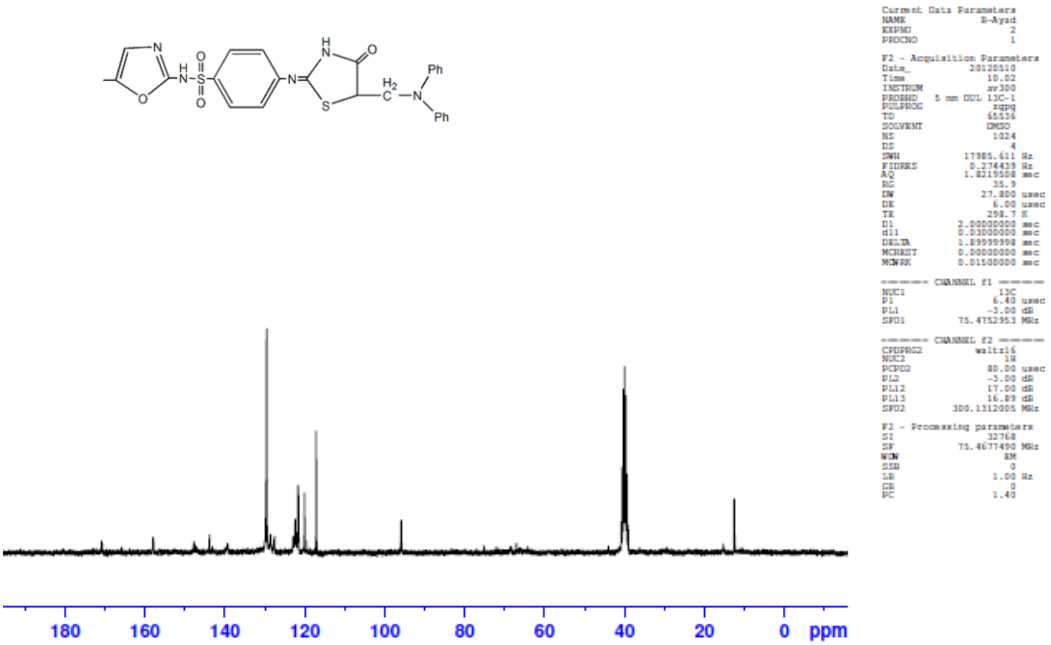


Figure (3)^{13}C-NMR for the Compound (A_5)

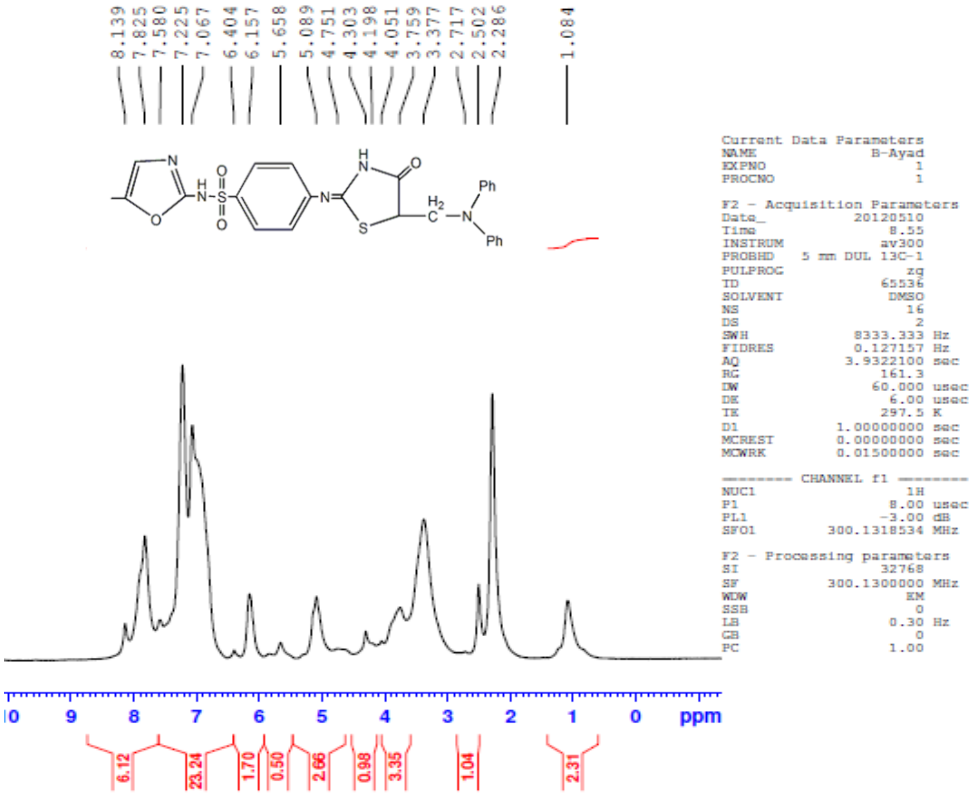


Figure (4)^{1}H-NMR for the Compound (A_5)

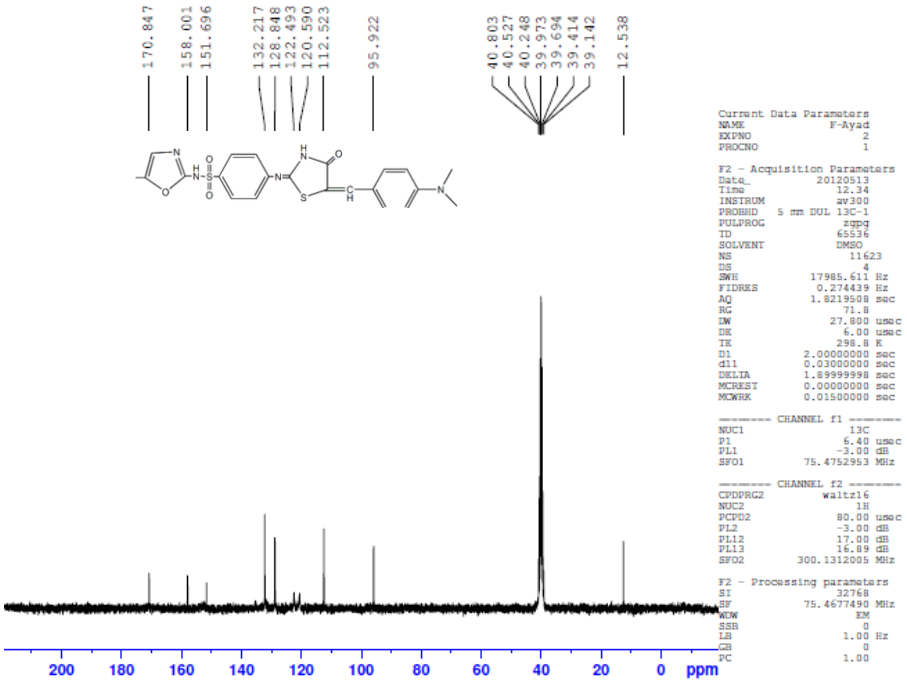


Figure (5)^{13}C-NMR for the Compound (A_8)

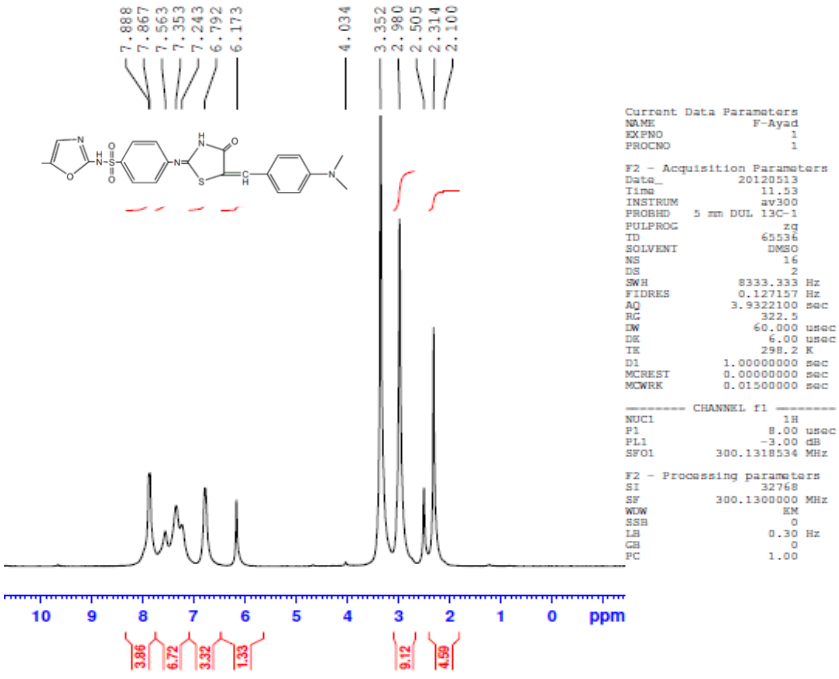
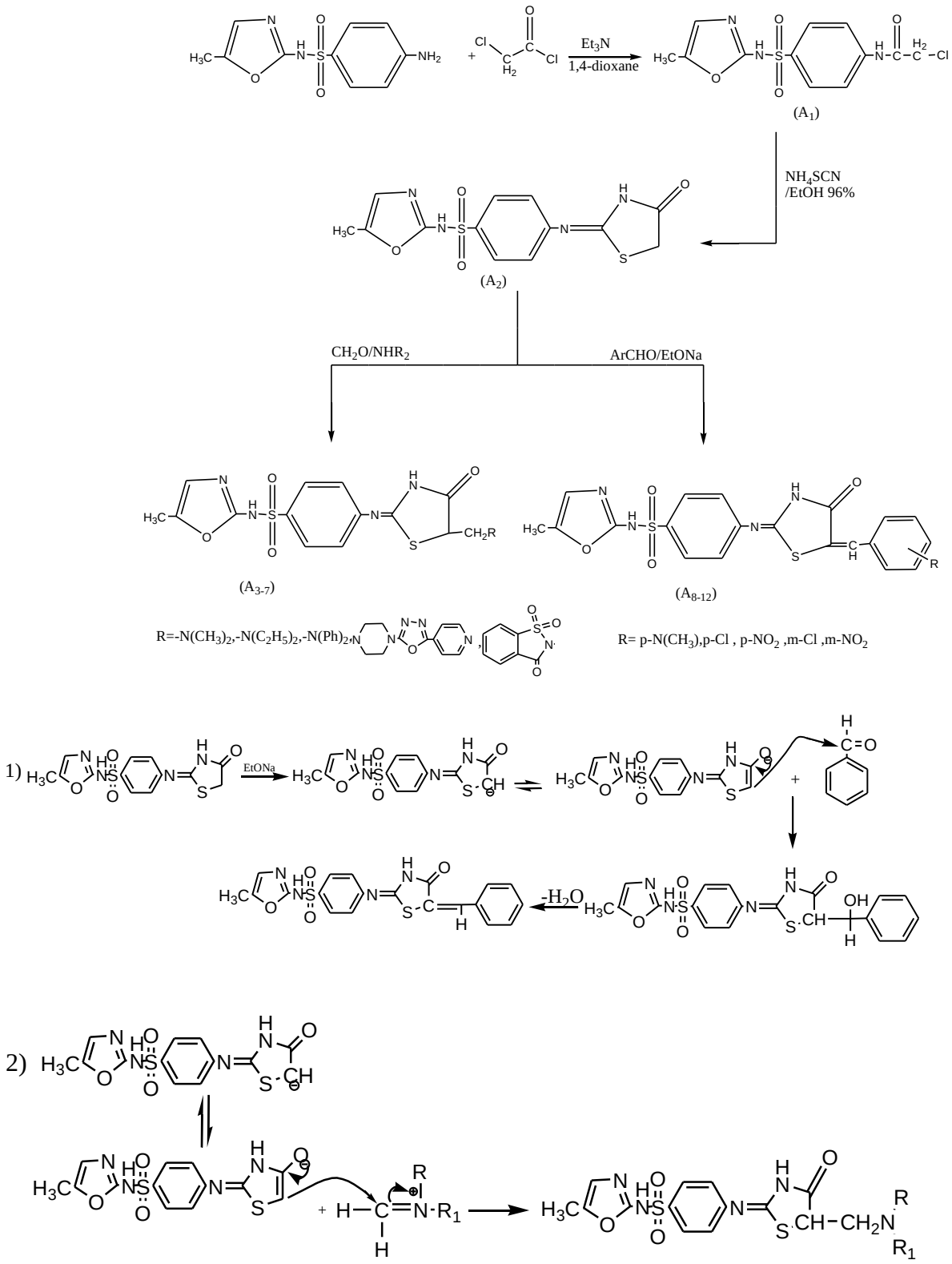


Figure (6)^{1}H-NMR for the Compound (A_8)



Scheme(I):The rout of synthesis Compounds and mechanisms.

References

[1] B.B. Subudhi , P.K. panda , B.K. Tosh , S.Sahu and P. Majhi., Dhaka unvi. J. Pharm. Sci. , 4(2) , (2005),pp(87-92) .

[2] J. B. Patel and A. Desai ., Int. J. Ind. Chem. , 2 , 1 , (2011) ,pp(45-51) .

[3]S.K. Srivustava , S. Srivustava and S. D. Srivustava .,Ind. J. Chem., 14B, (2002) ,pp(1973-1945) .

[4] H.H. Parekh , K.A. Parekh and A. R. Parekh., J. of Sci. Iran., 15 , 2 , (2004) pp(143-148) .

[5] G. Li , X. Qien , J. Cui , Q. Hueng , D. Cui , R. Zhang , F. Liu ., J of fluorine Chem., 22 , (2006) ,pp(182-186) .

[6] S.Verma, S.K. Servestava and p. Samadhiya ., Int. J. of Pharm. Res. and Deve., 2, 11 , (2011) ,pp(73-81) .

[7] H. Payrak , A. Demirbas , S. A. Karaoglu and N. Demerbas., European J. of Med. Chem. , 44 , (2009) ,pp(1057-1066).

[8]U. K. Singh , S. N. Pandya , A. Singh , B. K. Srivastava. and M. Pandya ., Int. J. of pharm. Sci. and Drug Res. , 2 ,2 , (2010),pp(151-154) ,.

[9] S. S. Chhajed and M. S. Padwal., Int. J. of Chem. Tech. Res., 2,1, (2010),pp(209-213).9

[10] V. Ravichandran , S. Mohan and S. K. Kumar., Arkovic (xiv) , (2007),pp(51-57) .

[11] S.N. Pandya, D. Sriram and G. Nath., European J. Med. Chem. , 35 , (2000),pp(249-255) .

[12] J. Yuan and Sh. Yao ., Talanta., 58 , (2002),pp (641-648).

[13] I. A. Yass, Kerbela J. of Pharm. Sci., 1, (2010),pp(49-58).

[14] A. S. Hamad ., Dyala J. of Sci. , (2011) .

[15] H. Al-tantash , O. Ates , S. Birtekaz , G. Otuk , M. Uzun and D. Satabna., Turk J. of Chem. ., 29 , (2005),pp(425-435).

[16] M. R. Chartria , A. K. Sharma & Surendra K. Sharma., J. Ind. Chem. Sco., LVIII , (2005),pp(687-689).