Synthesis of some new 3-chloro-4-aryl-2-azitidinone

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Abstract

2-amino benzothiazole (A_1) were synthesized by the reaction of p-toludine with potassium thiocynate in presence of bromine , the reaction of compound (A_1) with hydrazine hydrate and hydrochloric acid in the ethylene glycol gave 2-hydrazinobenzothiazole (A_2) . The compounds (A_{3-7}) were synthesized by the reaction of 2-hedrazinobenzothiazole with substituted benzaldehyde . 3-chloro-4-aryl-2-azitidinone (A_{8-12}) were synthesized by the reaction of compound (A_{3-7}) with chloro acetyl chloride in presence of triethyl amine. The structures of the synthesized compounds were confirmed by I.R, ^{1}H-NMR and ^{13}C-NMR spectra and Some chemical and physical data.

Key word:- azitidinone, 2-hedrazinobenzothiazole,

Introduction:-

Various 2-aminobebzothiazole derivatives have recently received significant importance because of their diverse biological properties. 2-aminobebzothiazole possess various biological activities such as antimicrobial[1],antifungal[2], Parkinson's disease[3],anticandedas[4], anticancer[5] .β-lactam drugs are most widely prescribed antibiotics use in medicine[6]. 2-azetidinone derivative possess wide therapeutic activity like antifungal[7] anticonvulsant[8]antitumour[9] intibictrail[10-12]. In our previous work, we synthesized some azitidinone derivatives from the reaction of 2-hydrazino-6-methylbenzothiazole with substiteuted benzyldehyd to obtain N-(6-mthylbenzothiazole-2-yl-amino)-2-arylidine (A_{3-7}) . the reaction of these compound with chloro acetyl chloride gave 3-chloro-4-aryl-2-azitidinone(A_{8-12}).

Experimental:

Melting point was determined on Electrothermal apparatus. Melting point are uncorrected. The IR absorption spectra were recorded by FTIR model 84005 Shimadzu Japan. Infrared spectrophotometer as KBr disk. $DMSOd_6$ ^{1}H-NMR and ^{13}C-NMR spectra were recorded by Ultra shield 300 MHz. Bruker 2003

1) Synthesis of 2- Amino 6-Methyl Benzothizole (A_1)[13] :

To a solution of(11.10 g , 0.1 mole) Of 4-methylaniline and (19.4 g, 0.2 mole) of potassium thiocyanate in 150 m1 of 96% acetic acid glacial was add dropwise, with stirrings 16g. (0.1 mole) of bromine dissolved in 100 ml of glacial acetic acid while the temperature was kept below (10 C°). After all the bromine solution had been added the mixture was stirred for 10 hr. the mixture filtered and dissolved in warm water. The filtrate neutralized with conc.NaOH The precipitate was collected on a filter and dried recrystllazition from ethanol M.P = 138-140 °C, lit. 140-142°C.

2) Synthesis of 2-hydrazino-6-methyl benzothiazole (A_2)[14] :

2- Amino 6-Methyl Benzothizole (0.001) mole was dissolved in 20ml of ethylene glycol . a mixture of (1ml of HCl and 1ml of $NH_2NH_2.H_2O$) was added dropwise with stirring, the reaction mixture was reflux for 4hrs. after cooling the product was collected and recrystallized from ethanole M.P = 203-205 °C yield = 73% .

3) Synthesis of N-(6-mthylbenzothiazole-2-yl-amino)-2-aryledine(A_{3-7})[15] :

A mixture of 2-hydrazino-6-methyl benzothiazole (0.001) mole and substituted benzyldehyde (0.001) mole was dissolved in 20 ml of absolute ethanol the reaction mixture was refluxed for 1hr. after cooling the product was collected and recrystallized from MeOH, Benzene (1:2). The physical properties of the synthesized compound are given in Table(1).

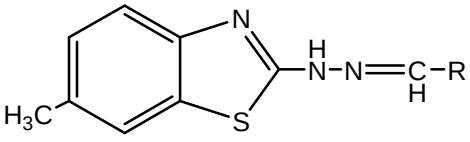


Table (1) the physical properties to compound (A_{3-7})

Compd.No.	R	M.p °C	Yield (%)	Colour
A_3	C_6H_4-4-OCH_3	219-221	80	Yellow
A_4	C_6H_4-4-OH	223-225	63	Yellow
A_5	C_6H_4-4-Cl	255-257	74	Yellow
A_6	C_6H_4-4-Br	270-272	67	Yellow
A_7	C_6H_4-4-$N(CH_3)_2$	233-235	85	Red

4) Synthesis of 1-(6-mthylbenzothiazole-2-yl-amino)-3-chloro-4-aryl-2-azetidinone(A_{8-12})[16] :

An equimolar mixture of compound (A_{3-7}) and chloroacetyl chloride was taken in 25 ml of 1,4-dioxan. To this(4 – 5) drops of triethylamine was added and the mixture was stirred for 12 hrs. and was kept at room temperature for 24hr. It was then poured on crushed ice water. The product was filtered washed dried and recrystallised from EtOH . The physical properties of the synthesized compounds are given in Table(2).

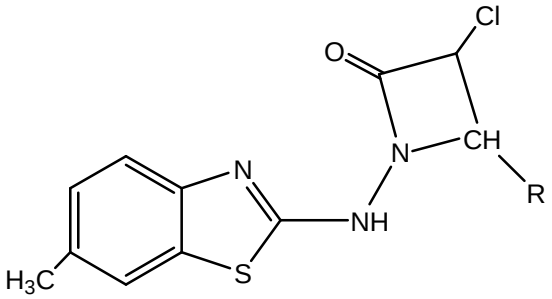


Table (2) the physical properties to compound (A_{8-12})

Compd.No.	R	M.p °C	Yield (%)	Colour
A_8	4-OCH_3-C_6H_4	170-173	45	White
A_9	4-OH-C_6H_4	166-168	40	Yellow
A_{10}	4-Cl-C_6H_4	190-192	70	White
A_{11}	4-Br-C_6H_4	200-202	60	White
A_{12}	4-$N(CH_3)_2$-C_6H_4	197-199	74	Yellow

Results and Discussion

2-amino-6-methylbenzothiazol(A_1) was synthesized by cyclization of 4-methylaniline with Potassium thiocynate in presence of Bromine in ice water bath temperature . the I-R spectrum of (A_1) showed band at (3260 cm^{-1}) due to stretching (N-H) group, band at (1620 cm^{-1}) for (C=N) group, band at (1095 cm^{-1}) for (C-S-C) group .2-Hydrazino-6-methylbenzothiazole (A_2) was synthesized by the reaction of 2-amino-6-methylbenzothiazol (A_1) with hydrazine hydrate and hydrochloric acid the I-R spectrum of (A_2) showed band at (3260-3380 cm^{-1}) due to stretching (N-H) group, band at (1645 cm^{-1}) for (C=N) group, band at (1095 cm^{-1}) for (C-S-C) group . The ^{1}H-NMR spectrum (DMSO-d_6) of compound (A_2) showed signal at (δ 4.6 ppm) for (H, NH) , signal at (δ 2.2 ppm) for (2H, NH_2) , signal at (δ 7.05- 8.1 ppm) for (3H, phenyl) , also the spectrum showed signal at (δ 2.35 ppm) for (3H,CH_3) . The ^{13}C-NMR spectrum (DMSO-d_6) showed signal at (δ 26 ppm) du to (C, CH_3) , signal at (δ 133 ppm) for (C_6) , signal at (δ 169 ppm) for (C_2) . N-(6-mthylbenzothiazole-2-yl-amino)-2-aryledine(A3-7) were synthesized from the reaction of compound (A_2) with substituted benzyldehydes , The structure of synthesis compounds were confirmed by there melting-point and , I-R , ^{1}H-NMR , ^{13}C-NMR data , The spectra characterization data are given in table (3,4,5) . 1-(6-mthylbenzothiazole-2-yl-amino)-3-chloro-4-aryl-2-azetidinone(A_{8-12})were synthesized by the reaction of compound (A_{3-7}) with Chloro acetyl Chloride , The structure of synthesized compounds were confirmed by measuring there melting-point and , I-R , ^{1}H-NMR , ^{13}C-NMR data , spectroscopic data were shown in Table (6,7,8) and figer (1,2) .The synthetic rout of these compounds is presented in Scheme (I) .

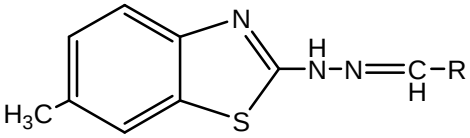


Table (3): IR Data of compound s (A_{3-7})

Comp. No.	R	ν C=C	ν C=N	ν C-H	νArC=C	Others
A_3	4-OCH_3-C_6H_4	1450,1556	1621	2885	3052	-----
A_4	4-OH-C_6H_4	1456,1558	1620	2878	3092	-------
A_5	4-Cl-C_6H_4	1450,1555	1631	2920	3051	ν C- Cl 784
A_6	4-Br-C_6H_4	1456-1556	1620	2960	3090	νC- Br 547
A_7	4-$N(CH_3)_2$-C_6H_4	1450-1550	1610	2890	3100	

Table (4): ^{1}HNMR Data of compound s (A_5,A_7)

Comp. No.	R	^{1}HNMR chemical shift in ppm
A_5	4-Cl -C_6H_4	4.01(H,NH,s, broad) 8.1 N=CH, Ar – H (7.05 –8.2),2.35 CH_3
A_7	4-N$(CH_3)_2$-C_6H_4	4.01 (H,NH, ,s, broad) 8.1 N=CH, Ar – H (7.05 –8.2),2.35-3.2 CH_3

Table (5): ^{13}CNMR Data of compound s (A_5,A_7)

Comp. No.	R	^{13}CNMR chemical shift in ppm
A_5	4-Cl- C_6H_4	12.2 CH_3, 141 N=C,171 $C_{2benzothiazol}$,134C – Cl
A_7	4-N$(CH_3)_2$-C_6H_4	12.2 CH_3,40 N$(CH_3)_2$, 141 N=C,171 $C_{2\text{-}benzothiazol}$,146C – N

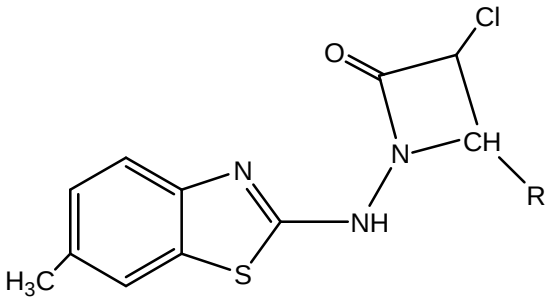


Table (6): IR Data of compound s ($A_{8\text{-}12}$)

Comp. No.	R	ν C=O	νC=N	ν N-H	ν C=C	Others
A_8	4-OCH_3-C_6H_4	1698	1621	3228	1450,1556	1249 As(C-O-C) 1076 Sy(C-O-C)
A_9	4-OH-C_6H_4	1697	1620	3354	1456,1558	3450 for O-H
A_{10}	4-Cl-C_6H_4	1710	1610	3120	1450,1555	
A_{11}	4-Br-C_6H_4	1677	1632	3235	1456-1556	ν C- Br 547
A_{12}	4-N$(CH_3)_2$- C_6H_4	1702	1620	3124	1450-1550	

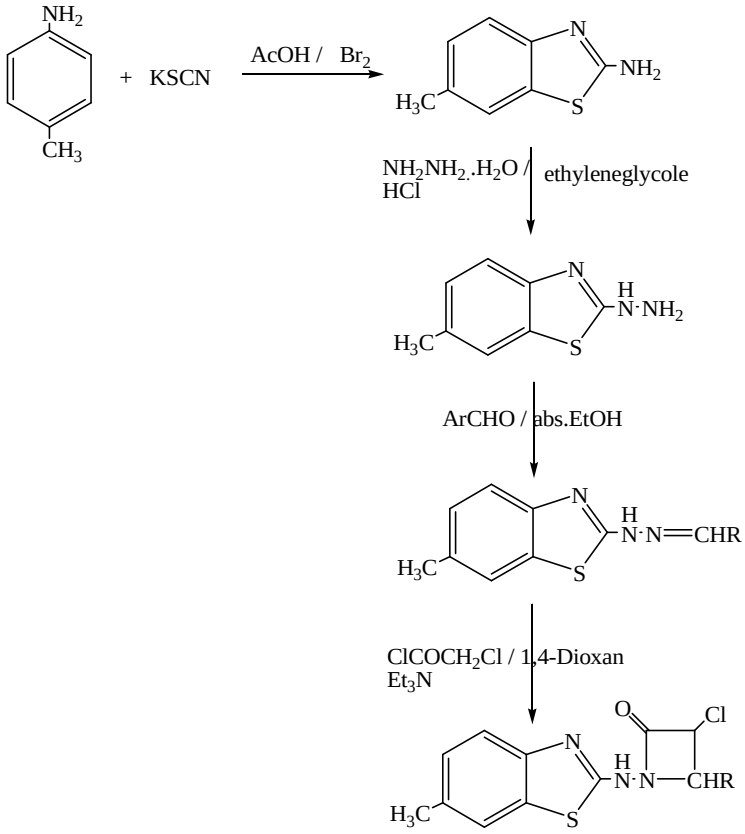
Table (7): ^{1}HNMR Data of compounds (A_{10},A_{12})

Comp. No.	R	^{1}HNMR chemical shift in ppm
A_{10}	4-Cl -C_6H_4	4.01 H,NH, 6.1 CH-Cl,5.1 CH-Ar , (7.05 –8.2) Ar-H, 2.35 CH_3
A_{12}	4-N$(CH_3)_2$-C_6H_4	4.01(H,NH) 6.3 CH-Cl,5.4 CH-Ar , (7.05 –8.1) Ar-H, 2.35-2.85 CH_3

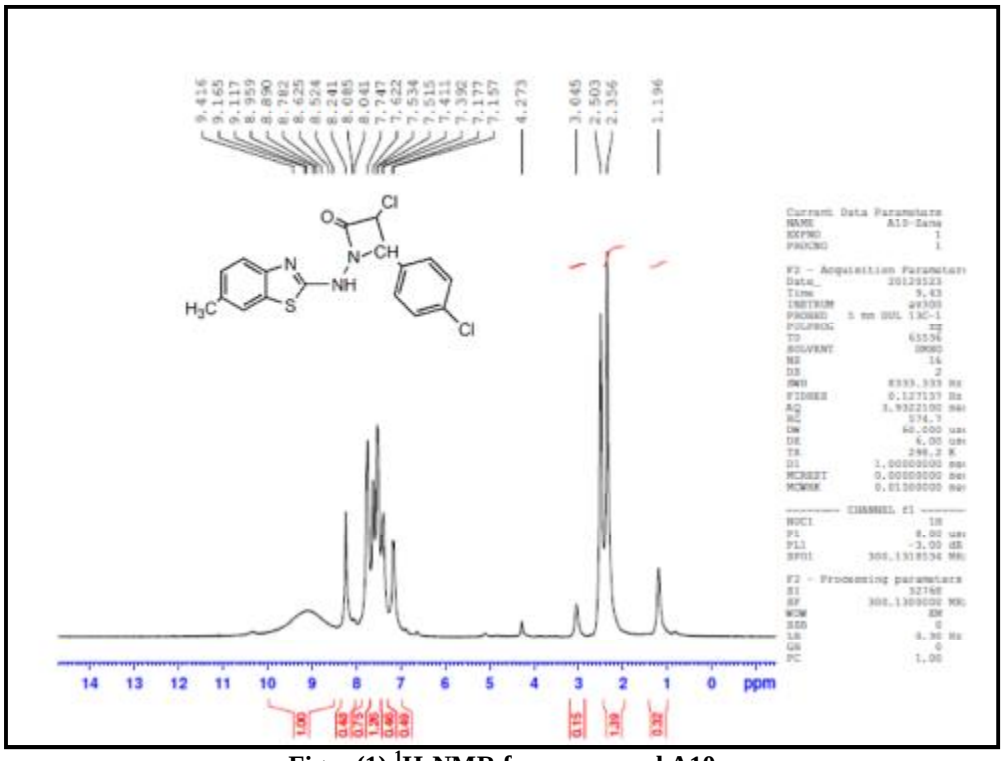
Table (8): ^{13}CNMR Data of compound s (A_{10},A_{12})

Comp. No.	R	^{13}CNMR chemical shift in ppm
A_{10}	4-Cl -C_6H_4	64 C-Cl, 157 C=O,62 C-Ar ,23 CH_3
A_{12}	4-N$(CH_3)_2$-C_6H_4	23 CH_3,40 N$(CH_3)_2$, 163 C=O,59 C-Ar ,140C – N

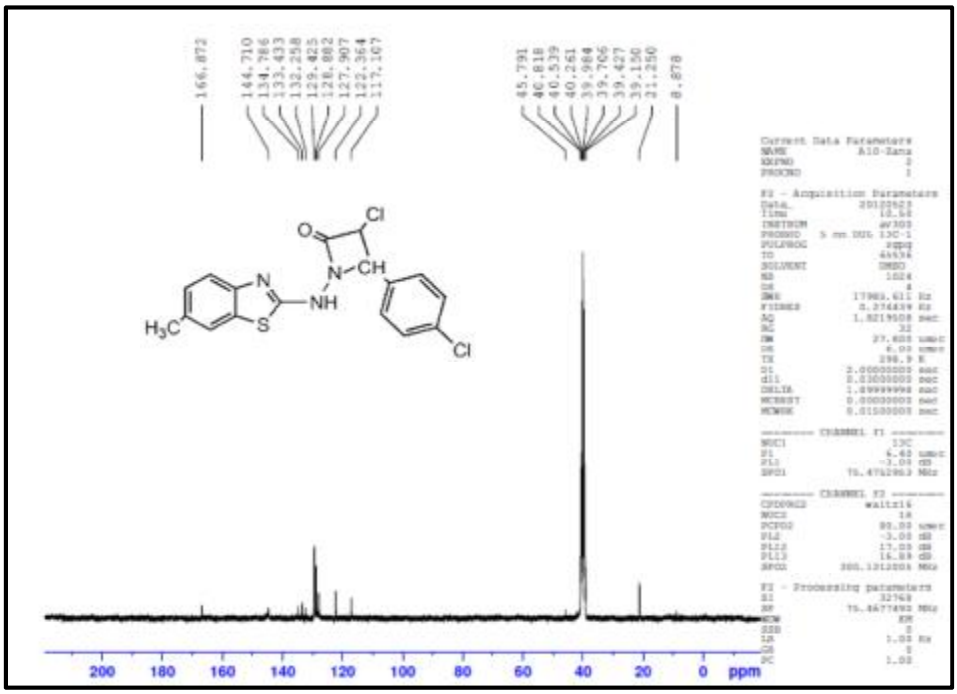
Scheme (I):



R=-4-OCH_3, 4-Cl-C_6H_5 , 4-N(CH_3) -C_6H_4 , -4-Br-C_6H_4 , 4-OH -C_6H_4



Figer (1) ^{1}H-NMR for compound A10



Figer (2) ^{13}C-NMR for compound A10

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تحضير عدد من معوضات 3–كلورو–4–اريل ازتدين–2–اون

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الملخص

يتضمن البحث تحضير 2–امينو–6–مثيل بنزوثايزول(A1) من تفاعل 4–مثيل انيلين مع ثايوسيانات البوتاسيوم بوجود البروم . وتم الحصول على 2–هيدرازينو–6–مثيل بنزوثايازول(A2) من تفاعل المركب (A1) مع الهيدرازين المائي و حامض الهيدروكلوريك المركبات قواعد شف (A3-7) حضرت من تفاعل المركب (A2) مع معوضات البنزالديهايد في الايثانول . ومن خلال مفاعلة قواعد شف مع كلورو كلوريد الاستيل تم الحصول على 3–كلورو–4–اريل–ازتدين–2–اون(A8-12). وتم تشخيص المركبات الناتجة باستخدام طيف الاشعة تحت الحمراء IR وطيف الرنين النووي المغناطيسي ^{13}C-NMR and ^{1}H-NMR وقد دلت النتائج على صحة التراكيب المقترحة .