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Synthesis and identification of mono and bicyclic compounds containing dinitrogen atoms as anesthetic

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Abstract - In this study, mono and bicyclic compounds [1-8] were synthesized by alkalytion of 2-aminothiozoline with carbonyl compounds (succinic acid, chloro aceticacid, 2,5-hexan-dione, 3-chloro propoyl chloride), where as the compounds [9-12] were synthesized by condensation between diketone compounds with (2-amino benzothiazole, guanine). The synthesized compounds structures were characarterized by several methods :{(C.H.N)-analysis, FT.IR-spectra, H.NMR-spectra } and melting points.

Key words - Bicyclic, Pharmaceiutical analgesic

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A systematic investigation of this class of compounds lead revealed that thiazol containing pharmacoactive agents play important role in medicinal chemistry and has a long history of application in agrochemicals and pharmaceiuticals industry as a analgesic and anti-inflammatory drugs are prescribed simultaneously in normal practice.

The target compounds constitute an essential pharmacophore in many naturally occurring and biologically active agents.Thiazoles fused with different compounds that are known to contribut as antitumor and antimicrobial[1,2].

The mono and bicyclic compounds are class of compounds well known for along time as anesthetic drugsin surgery such as diazepine compounds[3-5]which were first introduced for the treatment of anxiety [4-6].

In this study, the synthesized compounds (thiazolo diazepine, benzoimidazol, thiazolo pyrimidone, benzothiazolo pyrimidine, guano pyrimidine) are cyclic compounds in which one or more of nitrogen atoms which contain five, six and seven membered unsaturated rings of mono or bicyclic compounds [3,5].

In this work, the cyclic nitrogen compounds were synthesized by cyclocondensation of amino compounds with carbonyl compounds led to formation of mono and bicyclic compounds [1-12], which used as analgesic, relaxative, hypnotic[7,8] and other uses[9-20].

EXPERIMENTAL METHODOLOGY

– All chemical used were supplied from Fluka and BDH-chemical company .

– All measurements were carried out by :
- Melting points :electro thermal 9300, melting point engineering LTD, U.K .
- FT-IR spectra : fourrier transform infrared shimadzu (8300) (FT-IR), KBr-disc was performed.
- H-NMR spectra and (C.H.N)-analysis.

Synthesis of compounds [1-8] :

A mixture of 2 – amino thiazole (0.02 mole, 2g) was reacted with one of [(0.02 mole, 2.36g) of succinic acid, (0.02 mole, 1.89 g) of chloro acetic acid, (0.02 mole, 2.54g)

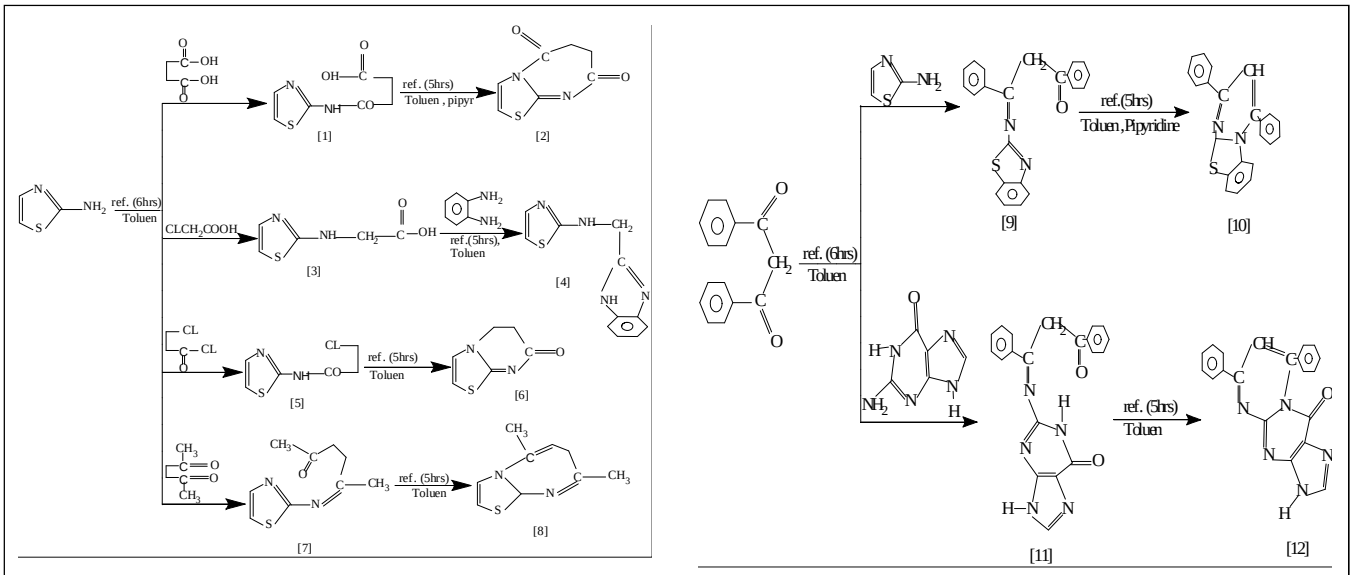


Fig. A : Reaction scheme

of 3 –chloro propoyl chloride, (0.02 mole, 2.28) g of 2, 5-hexane-dione)], respectively, under reflux for (6hrs) in presence of toluene (100ml), the mixture was cooled, the precipitate was filtered off to produce (85-90)%of compounds [1, 3, 5, 7], respectively. Drops of piperidine was heated with one of (0.01 mole, 2g of compounds [1], 0.01 mole, 1.58 g of compound [3] and 0.01 mole, 1.08 g of o-phenylene diamine, 0.01 mole, 1.90 g of compounds [5], 0.01 mole, 1.96 g of compound [7]), respectively, with reflux for (5 hrs) in presence toluene (100ml), precipitate was filtered off and recrystallized to give (79-81)% of compound [2,4,6,8], respectively.

Synthesis of compound [9-12] :

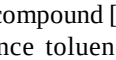
A mixture of dibnzoyl methane (0.02 mole, 4.48 g) was refluxed for (6hrs) with one of (0.02 mole, 3g of 2- amino benzothiazole, 0.02 mole, 3.02 g of guanine), respectively, in presence of toluene (100 ml), the precipitate was filtered off and recrystallized to produce (86, 88) % of compounds [9, 11], respectively .

To prepare compounds [10, 12], drops of piperidine was heated with one of (0.01 mole, 3.56 g of compound [9], 0.01 mole, 3.57 gm of compound [11]), respectively with reflux for (5 hrs) in preseuce of toluene (100 ml), the precipitate was filtered off and recrystallized to give (80, 83) % of compounds [10, 12], respectively .

EXPERIMENTAL FINDINGS AND ANALYSIS

All formated compounds [1-12] have been characterized by their melting points and spectroscopic methods (FT.IR-spectra, (C.H.N)-analysis and H-NMR-spectra) :

FT.IR- spectra :

In FT.IR–spectra, the reaction is followed by appearance carboxyl group (CO-O-) absorption band at (2615) cm^{-1} and at (1696) cm^{-1} due to carbonyl of amide[6] (CO-NH) in compound [1], which disappear and other bands appear at (1625,1678) cm^{-1} due to (C=N azomethine, () carbonyl of lactamrespectively in compound [2].

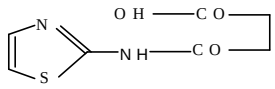
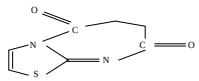
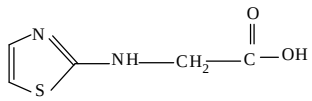
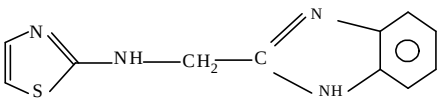
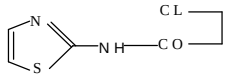
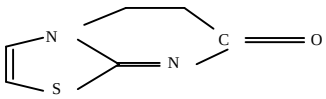
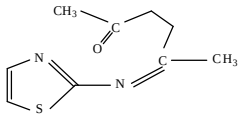
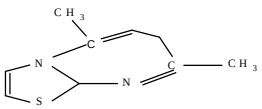
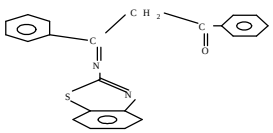
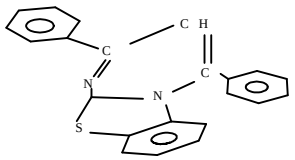
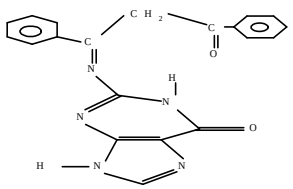
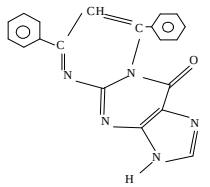
FT.IR–spectra of compound [3] is appear absorption band at (2690) cm^{-1} due to (-OH) in carboxyl group (CO-O-) and (1750)cm^{-1} due to carbonyl (C=O)of carboxyl group, which also disappear and other bands are appear at 1625 cm^{-1} due to (C=N) azomethine group and at (1555, 1470) cm^{-1} due to (C=N) endocyclic of benzoimidazol in compound [4].

FT.IR – spectra of compound [5] is appear absorption band at (1690) cm^{-1} due to[3] carbony of amide[6] (CO-NH) and at (760) cm^{-1} due to (C – Cl) group, which also disappear and other bands are appear at (1635) cm^{-1} due to (C = N) azomethine group and at (1565, 1480) cm^{-1} due to (C –N) endo cyclic of pyrimidone in compound [6].

Compound [7] is appear absorption band at (1630) cm^{-1} due to (C= N) azomethine group and at (1720) cm^{-1} due to (CO-) carbonyl of ketone, which disappear and other bands are appear at (3020) cm^{-1} is due to (= CH_2) and at (1540, 1430) cm^{-1} is due to (C – N) end o cyclic of diazepine in compound [8].

Compound [9] is appear absorption band at (1640) cm^{-1} is due to (C = N) azomethine group[3,6] and at (1725) cm^{-1} is due to (-CO-) carbonyl group of ketone, which disappear

Table 1 : FT.IR data (cm^{-1}) of compounds[1-12]

Comp. No.	Structural formula	Name of compounds	Functional group in every compounds (importance group)
[1]		2-(3-propanoic amido)-thiazoline	υ(-NH-CO-):1696s, (C=N):1512 υ (-OH)of carboxyl:2675 m (C=O)of carboxyl:1750 υ(-NH-)of amide :3276m
[2]		1,2-(thiazolino)-5,6-dihydro-diazepine -4,7-dione	(C=N)azo methine:1625 (-N- C =O):1678 (CH=CH):3000
[3]		2-(amino-acetic)- thiazoline	υ(-NH-CH_2):3300 υ(OH)of caboxyl:2673 (C=O)of carboxyl:1755 (CH=CH):3005
[4]		2-(2-benzoimidazoline methylene-amino)–thiazoline	υ(C=N) azo methine:1625 υ(-NH)endo imidazol cycle :3310 (C-N)endo cycle :1555, 1470 (-NH-):3340 ,3310
[5]		2-(2-chloro ethylene amido) –thiazoline	(O=C-NH-) :1690 (C-Cl):760 ,(-N=C-):1495 (CH=CH):2998
[6]		3,4-tetrahydro thiazolo pyrimidine	(C=N):1635 (O=C–N-):1695 (C-N)endo cycle :1565, 1480 (CH=CH):3000 (CH_2):2910
[7]		2-(2-hexanone–thiazolidine).	(C=N):1630 (O=C–CH_3)ketone :1720
[8]		4,7-dimethyl-1,2- thiazole diazepine	(C=N):1625 , (=CH_2):3020 (C-N) endocyclic :1540,1432
[9]		2-(phenyl acetophenone) – benzothiazolidine.	(C=N)azomethine:1640 , (C=O)Ketone :1725 (-C=N)cyclic:1498 (C-S-C):780
[10]		4,6-(diphenyl)-1,2- (benzothiazole)-pyrimidine	(C=N) azomethine:1635 (C-N) endocycle : 1570 ,1490 (C=C)Alkene:3010 (C=C)Aromatic:1570
[11]		2-(phenylacetophenon) guaninopyrimidine	(C=N):1620s (C=O) Ketone: 1728s , (-NH) endocycle of guanine :3335 br (CO-NH)Carbonyl of amide in guanine cycle :1690
[12]		4,6-(diphenyl)-1,2- guaninopyrimidine	(C=N):1640S , (C-N)endocycle : 1533,1433s (C=N)endocyclic of guanine:1569 s (O=C-N) carbonyl of amide in guanine cycle :1695m (CH=C) alkene :3080 (C=C)Aromatic:1575

S=strong, M= medium , V=very, br=broad

Table 2 : Melting points, M.F and elemental analysis of compounds[1-12]

Comp. No.	M.F	m.p (c°)	Calc / Found C%	H%	N%
[1]	$C_7H_8N_2O_3S$	160	42.0	4	14
			41.871	3.905	13.836
[2]	$C_7H_6N_2O_2S$	152	46.153	3.296	15.384
			46.026	3.119	15.209
[3]	$C_5H_6N_2O_2S$	148	37.974	3.797	17.721
			37.785	3.628	17.584
[4]	$C_{11}H_{10}N_4S$	154	57.391	4.347	24.347
			57.247	4.214	24.205
[5]	$C_6H_7N_2$ OSCl	145	37.795	3.674	14.698
			37.603	3.485	14.456
[6]	$C_6H_6N_2OS$	136	46.753	3.896	18.181
			46.514	3.718	18.049
[7]	$C_9H_{12}N_2OS$	158	55.102	6.122	14.285
			54.95	6.037	14.148
[8]	$C_9H_{12}N_2$ S	153	60.0	6.666	15.555
			59.81	6.478	15.374
[9]	$C_{22}H_{16}N_2OS$	174	74.157	4.494	7.865
			74.029	4.316	7.657
[10]	$C_{22}H_{16}N_2S$	179	77.647	4.705	8.235
			77.459	4.518	8.087
[11]	$C_{20}H_{15}N_5O_2$	184	67.226	4.201	19.607
			67.098	4.079	19.405
[12]	$C_{20}H_{13}N_5O$	189	70.796	3.834	20.648
			70.558	3.607	20.406

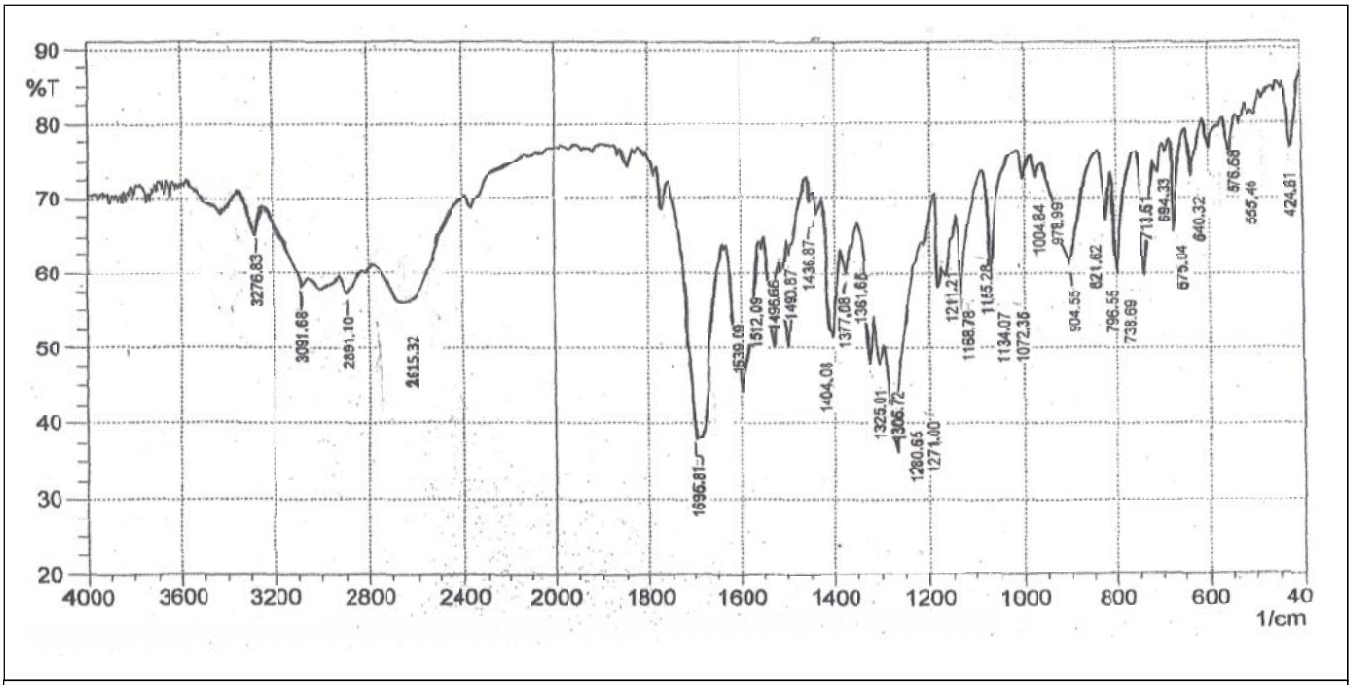


Fig. 1 : FT.IR spectrum of compound [1]

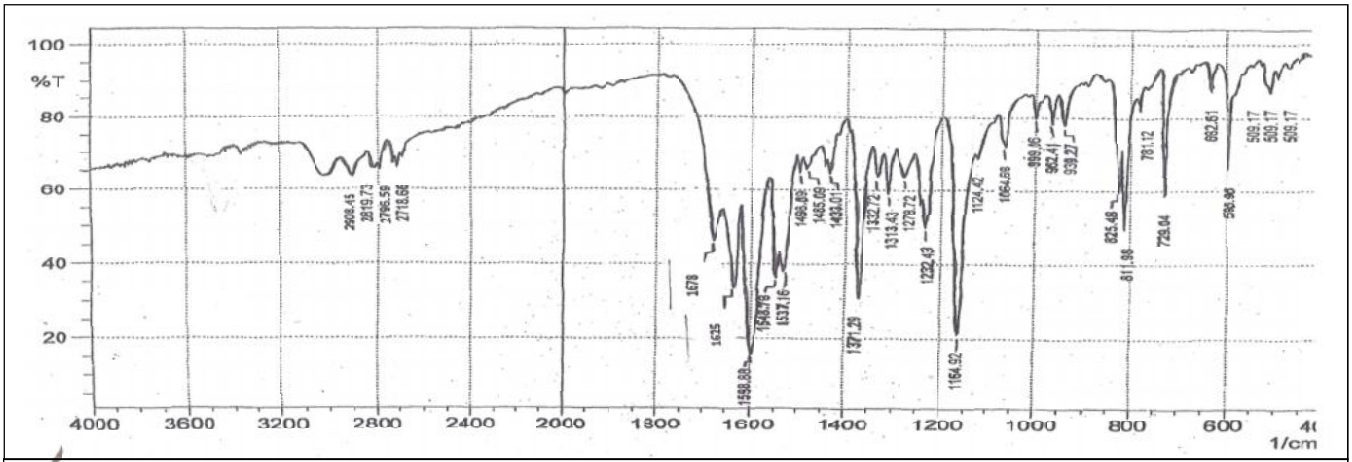


Fig. 2 : FT.IR spectrum of compound [2]

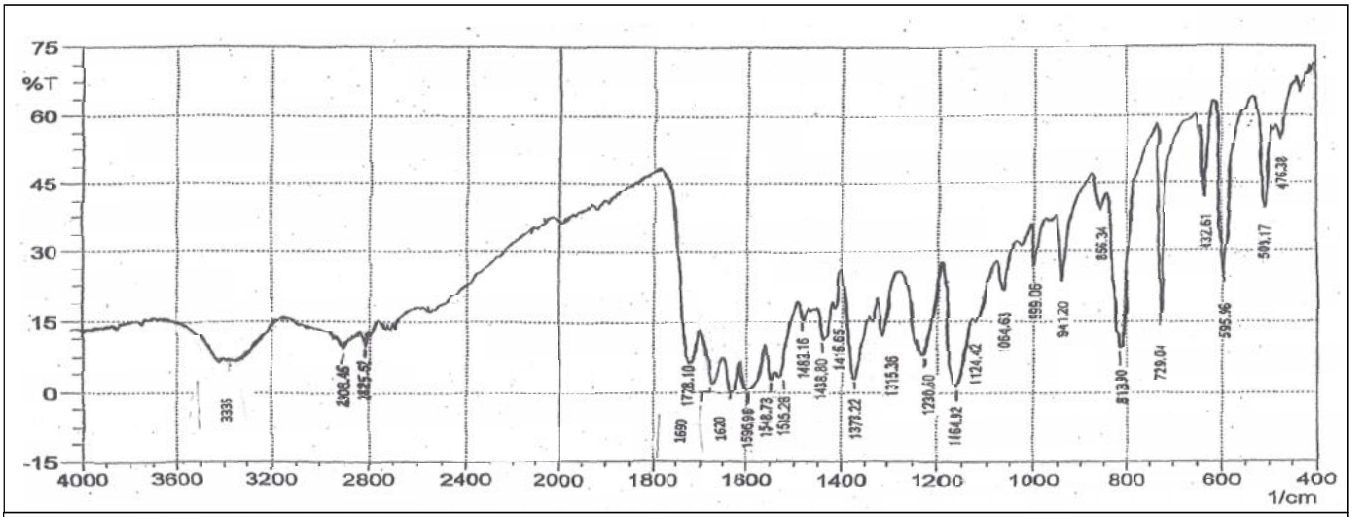


Fig. 3 : FT.IR spectrum of compound [11]

and other bands are appear at (1570, 1490)cm^{-1} is due to (C – N) end o cyclic of pyrimidine in compound [10].

Compound [11] is appear absorption band at (1620) cm^{-1} is due to (C =N) azomethine, at (1690) cm^{-1} is due to (CO-NH) carbonyl of amide and at (1728) cm^{-1} is due to (CO) carbonyl of ketone, which disappear and other bands are appear at (1533, 1433) cm^{-1} is due to (C – N) endo cyclic of pyrimidine, at (3080) cm^{-1} is due to (= CH) in compound [12].

And other data of functional groups show in the following, Table 1 and Fig. 1, 2 and 3.

H.NMR – spectra :

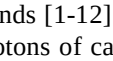
H . NMR – spectra of compounds [1-12] showed :

Singlet signal at ∫10.36 for protons of carboxyl group (- COOH) and at ∫9.8 for proton of amide group (-NH–CO-) in compound [1], which disappear as a result of cyclization in compound [2] .

Singlet signal at ∫10.9 for proton of carboxyl group (-COOH) in compound [3], which disappear and other signals are appear at ∫8.6 for proton of amine.

(-NH-)[3] and at ∫7.1 for protons of phenyl group(-Ph-), signals at ∫2.8 for protons of alkene(CH=CH)in cyclein compound [4] .

Singlet signal at ∫9.9 for proton of amide group (-NH–CO-) in compound [5], which disappear as a result of formation of cycle in compound [6].

Triplet signal at ∫3.7 for protons of (CO-CH_2-CH_2-) in compound [7], which disappear and other signals appear at ∫2.9 is due to methyl in () and at ∫7.9 is due to proton of thiazol[1] () in compound [8] .

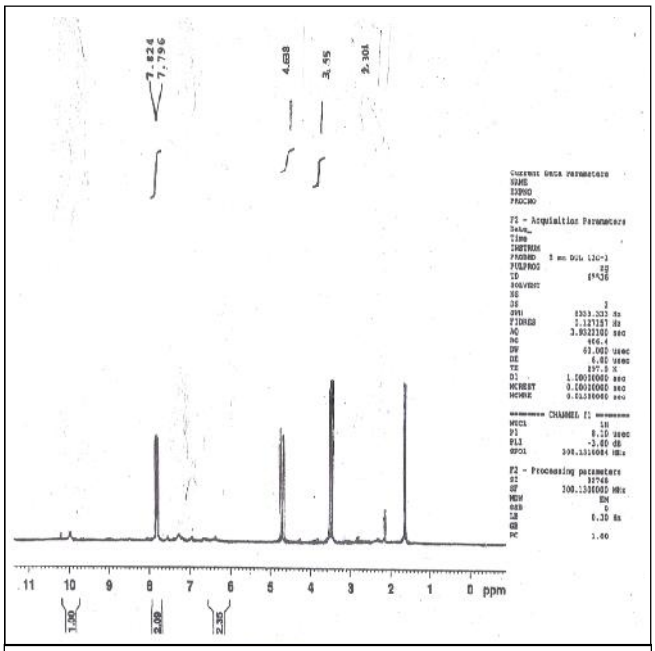


Fig. 4 : H.NMR-spectrum of compound [2]

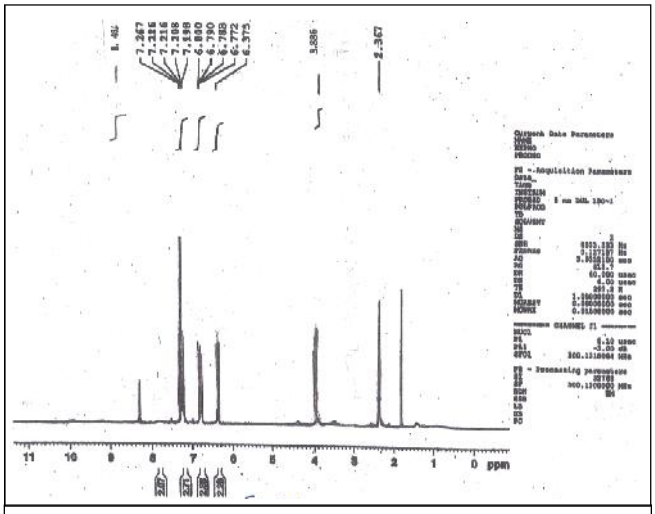


Fig. 5 : H.NMR-spectrum of compound [12]

Singlet signal at ∫4.1 for protons of (-CH_2-CO-) in compound [9], which disappear and other signals appear at ∫3.2 for proton of (—CH═C<) and at ∫7.8 is due to proton of thiazol (<N, S, CH—) in compound [10] .

Singlet signal at ∫9.7 for proton of amide (- NH–CO -) and at ∫4.3 is due to protons of (-CO-CH_2-) in compound [11], which disappear and othersignal is appear at ∫3.8 is due to proton of (—CH═C<) in compound [12], and other peaks shown in the following Fig. 4 and 5.

(C.H.N)–Analysis :

It was found from compared the calculated data with experimentally data of these compounds, the results were compactable, the data of analysis, M.F and melting points are listed in Table 2.

Appearance of (H.NMR, FI.IR, C.H.N)-spectra results are strong evidence to synthesized compounds[1-12].

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