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Synthesis & Study of Anesthesia Organic Compounds

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Abstract :
In the present work , mono & bicyclic compounds [1-8] were synthesized as derivatives of analagisic 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 , ^{1}H.NMR-spectra } & melting points .
Keyword: Anesthesia , pharmaceiutical compounds ., diketone

Introduction :

Asystematic 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 & 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 & 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 & bicyclic compounds [1-12] , which used as analgesic , relaxative , hypnotic[(7,8)]& other uses[(9-20)] .

Experimental :

- All chemical used were supplied from Fluka & BDH-chemical company .
- All measurements were carried out by :

1- Melting points :electro thermal 9300 , melting point engineering LTD , U.K .
2- FT-IR spectra : fourrier transform infrared shimadzu (8300) (FT-IR) ,KBr-disc was performed .
3- H-NMR spectra & (C.H.N)-analysis .

Synthesis of compounds [1-8] :

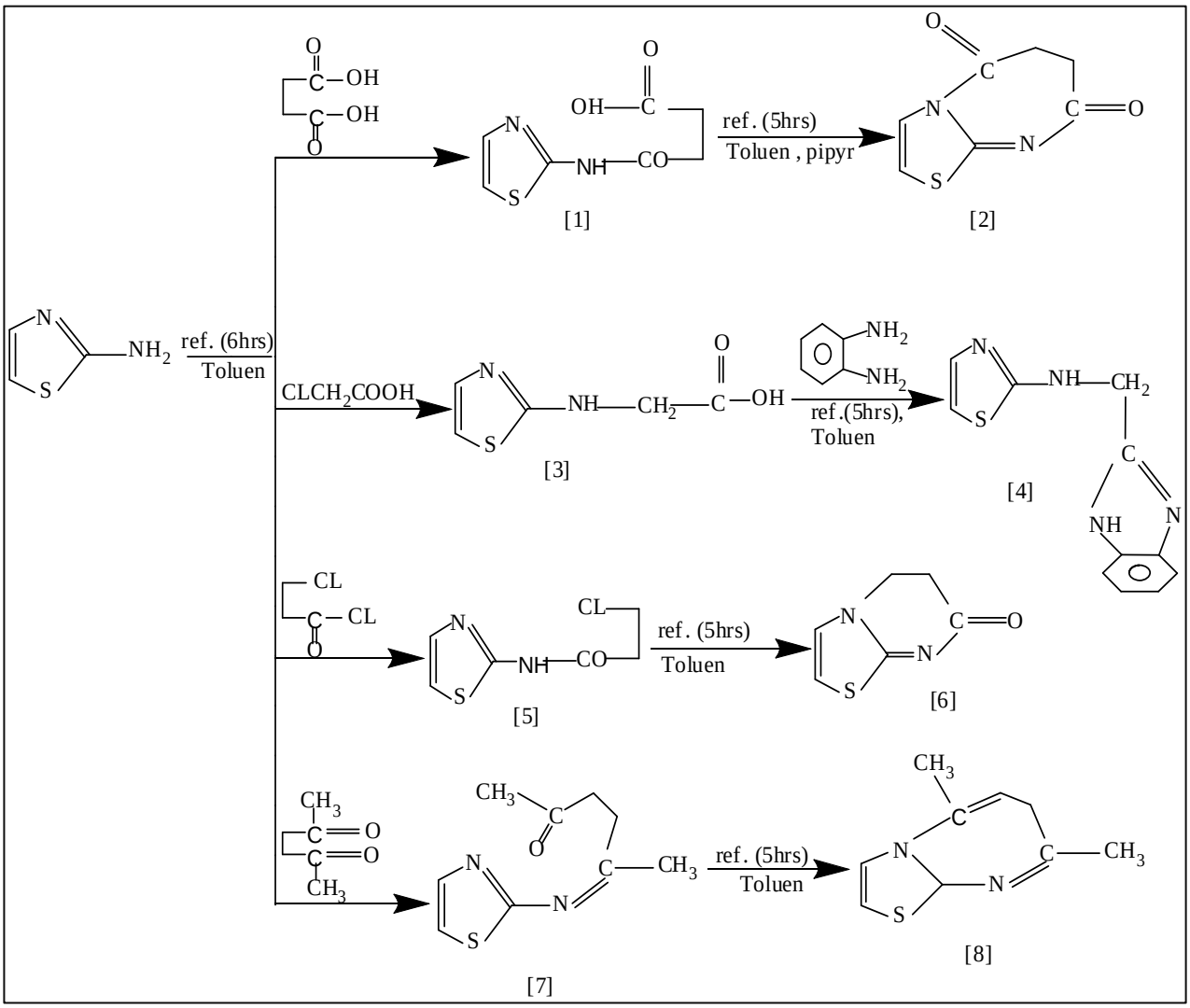
A mixture of 2 – amino thiazole (0.02 mole , 2gm) was reacted with one of [(0.02 mole , 2.36g) of succinic acid .,(0.02 mole , 1.89 g) of chloro acetic acid ., (0.02 mole , 2.54g) of 3 –chloro propoyl chloride ., (0.02 mole , 2.28)g of 2,5-hexane-dione)] , respectively ,under reflux for (6hrs) in presence 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] & 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 &recrystallized to give (79-81)% of compound [2,4,6,8] respectively .

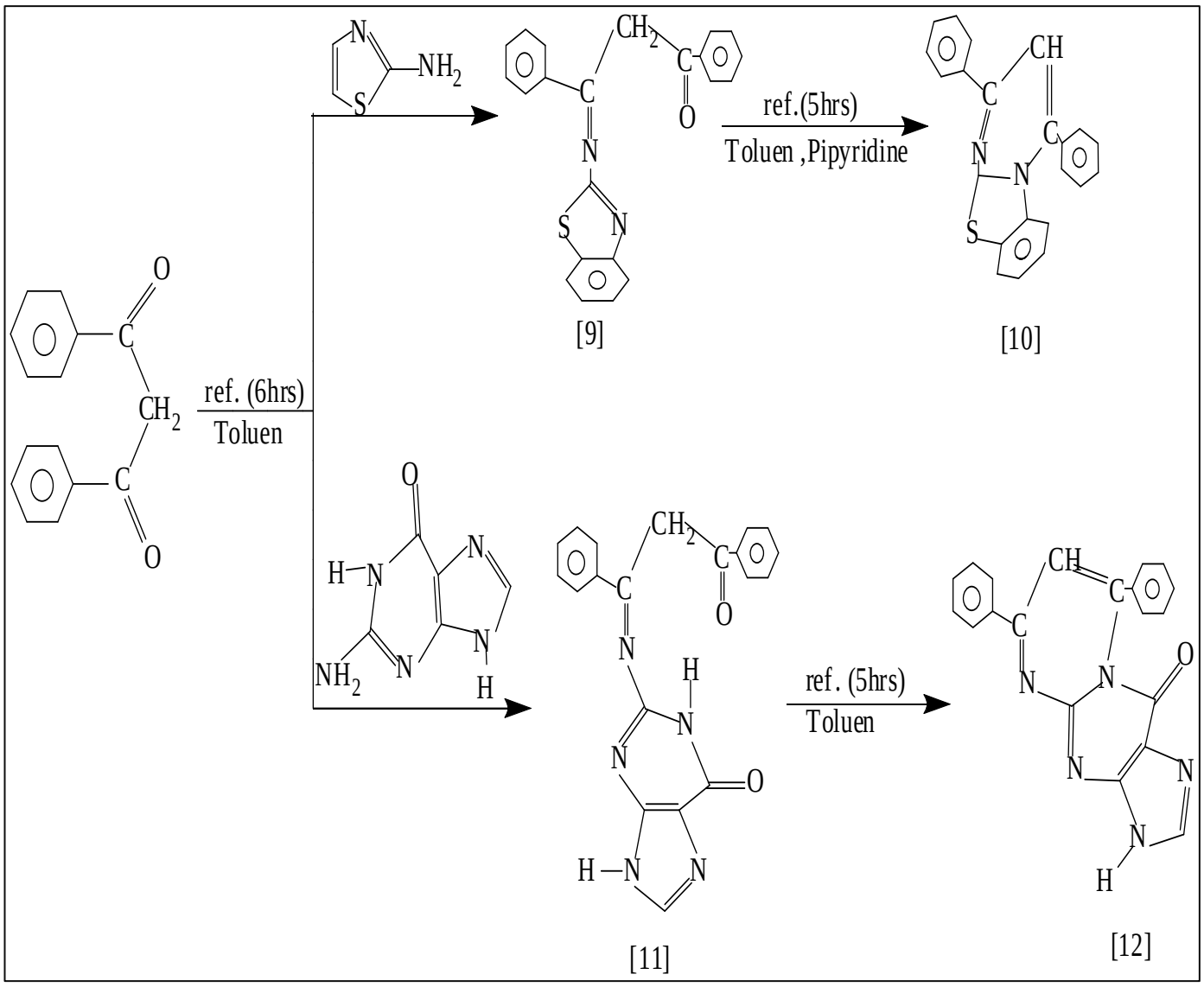
Synthesis of compound [9-12] :

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 gm 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 & recrystallized to give (80 , 83)% of compounds [10,12],respectively .

Reaction Scheme :





Results & Discussion :

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

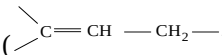
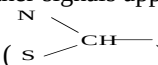
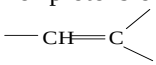
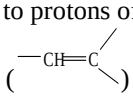
FT.IR- spectra :

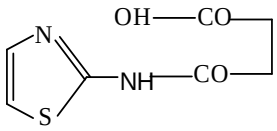
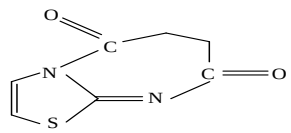
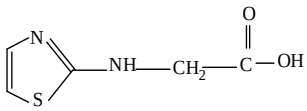
In FT.IR –spectra ,the reaction is followed by appearance carboxyl group (CO-O-) absorption band at (2615)cm^{-1}& at (1696)cm^{-1} due to carbonyl of amide[6] (CO-NH) in compound [1] , which disappear & other bands appear at (1625,1678)cm^{-1} due to (C=N azomethine ,( )carbonyl of lactam respectively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

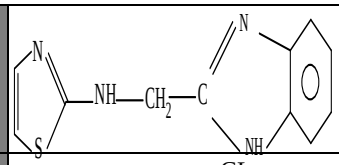
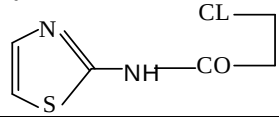
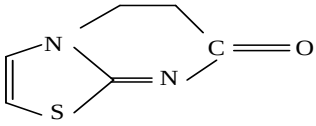
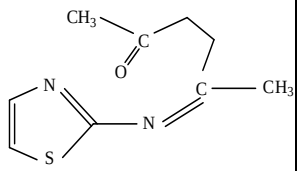
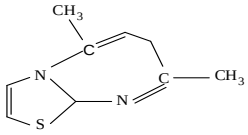
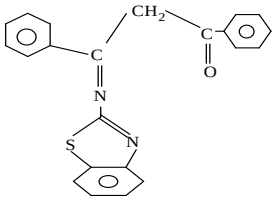
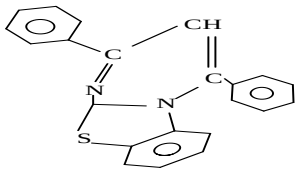
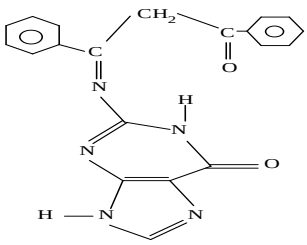
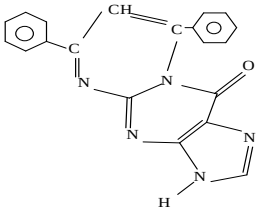
FT.IR–spectra of compound [3] is appear absorption band at (2690)cm^{-1} due to (-OH) in carboxyl group (CO-O-) and (1750)cm^{-1} due to carbonyl(C=O)of carboxyl group , which also disappear and other bands are appear at 1625 cm^{-1} due to (C=N) azomethine group and at (1555, 1470)cm^{-1} due to (C=N) 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 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) 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] .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 () and at ∫ 7.8 is due to proton of thiazol () 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 () in compound [12]
(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].
Acknowledgement:
I would like to express my thanks to ((United Arabic Company)) and ((Zaidan Company of Chemical)) in Jordan for supplied some materials.And express thank to Mr.Audai in Jordan for providing (C.H.N)-element analytical ,H.NMR-spectra and Melting points.
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) :phesical properties 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 41.871	4 3.905	14 13.836
[2]	$C_7H_6N_2O_2S$	152	46.153 46.026	3.296 3.119	15.384 15.209
[3]	$C_5H_6N_2O_2S$	148	37.974 37.785	3.797 3.628	17.721 17.584
[4]	$C_{11}H_{10}N_4S$	154	57.391 57.247	4.347 4.214	24.347 24.205
[5]	$C_6H_7N_2$ OSCl	145	37.795 37.603	3.674 3.485	14.698 14.456
[6]	$C_6H_6N_2OS$	136	46.753 46.514	3.896 3.718	18.181 18.049
[7]	$C_9H_{12}N_2OS$	158	55.102 54.95	6.122 6.037	14.285 14.148
[8]	$C_9H_{12}N_2$ S	153	60.0 59.81	6.666 6.478	15.555 15.374
[9]	$C_{22}H_{16}N_2OS$	174	74.157 74.029	4.494 4.316	7.865 7.657
[10]	$C_{22}H_{16}N_2S$	179	77.647 77.459	4.705 4.518	8.235 8.087
[11]	$C_{20}H_{15}N_5O_2$	184	67.226 67.098	4.201 4.079	19.607 19.405
[12]	$C_{20}H_{13}N_5O$	189	70.796 70.558	3.834 3.607	20.648 20.406

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