

Bromination of Diazahomoadamantane with liqiude bromine and Synthesis of New it's Derivatives

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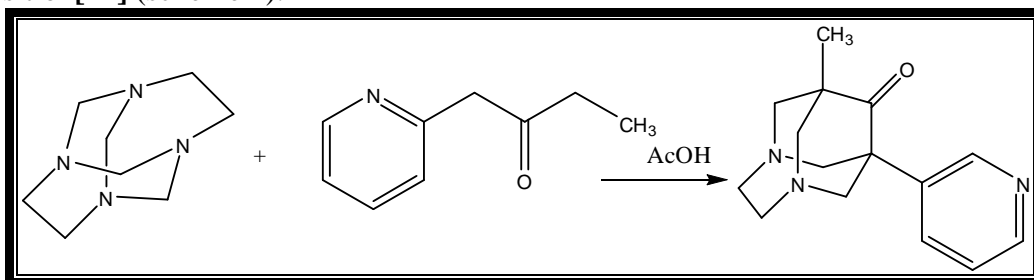
Abstract

In this study, new diazahomoadamantane was prepared by condensation of 2-butanone with 1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}]dodecane and acetic acid in 2-propanol gave new diazahomoadamantanone [1-Methyl-3,6 – diazahomoadamantane -9- one] by mannich's reaction. Also were appeared [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one] with bromine liquid, reaction [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one] with various chemical agents like hydrazine hydrate , hydroxylaminehydrochloride ,and reaction [1-Methyl-3,6 – diazahomoadamantane -9- one] with secondary amine and formaldehyde by mannich's reaction.

KEYWORDS: new diazahomoadamantane, bromine liquid, reaction, various chemical agents, hydrazine hydrate, mannich's reaction.

Introduction

Adamantane is the simplest diamondoid with a chemical formula of C₁₀H₁₆. It consists of four cyclohexane rings in an armchair configuration. To date, seven adamantane derivatives have been applied in clinical usage to treat acne vulgaris [1], Alzheimer's disease[2], as an anti-viral [3–5] and for type-2 diabetes [6–8], adamantane and its derivatives have found applications that range from lubricants to pharmaceuticals [9]. As a result of the high lipophilicity of adamantane molecular, high lipophilicity is reflected on several adamantane – containing derivatives. The lipophilicity of adamantane derivatives enables them to pass through the blood brain barriers leading to the existence of high levels of these derivatives in the central nervous system[10]. Anatoly I .Kuznetsov and Abdel – Amir M. fenjan were reported on the synthesis and characterization of a new 3,6–diazahomoadamantan derivatives[11]. Diazahomoadamantane is acomplex polycyclic framework molecular. First one should realize how several simple molecular organize themselves into a larger one .It is well-know that by condensing a cyclic ketone with 1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}] in the presence of acetic acid by mannich,s reaction can give 3,6-diazahomoadaman-9-one and its derivatives with substituent's in the nodal position[12] (scheme 1).



Scheme (1)

Instrumentation and chemicals

Chemicals were buying from Fluka and Merck chemical companies. The FT-IR spectrum were listed using KBr disc on a Shimadzu FT-IR 8300 Spectrophotometer at Baghdad university in Iraq. micro elemental analysis (C.H.N.S) were completed at Al-Al- Bayt university in Amman –Jordan.

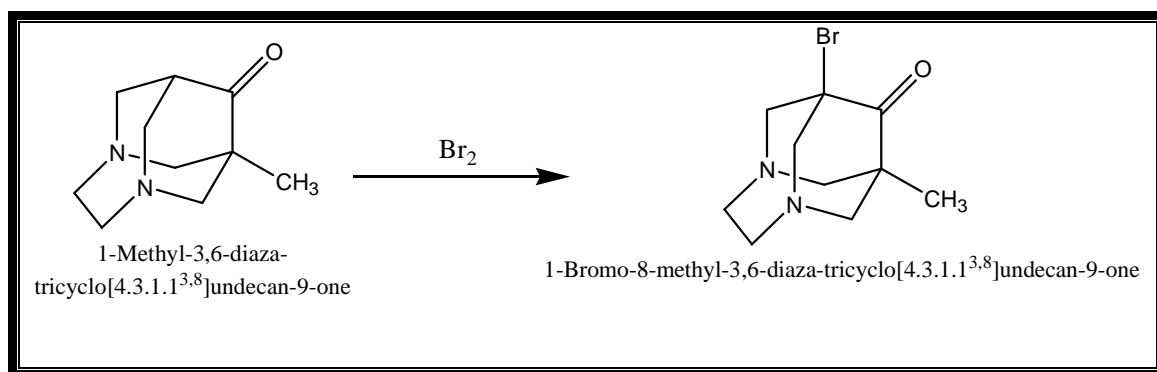
Experimental

Synthesis of [1-Methyl-3,6 – diazahomoadamantane -9- one] (1)

In a circular flask (100 ml) have been added of (20mmol, 1.79ml, 1.44gm) 2-butanone with (20mmol, 3.36gm) of 1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}]-dodecane (teotropine) (1), and added solution consists of (50mmol, 2.86ml, 3gm) of acetic acid in (10ml) of 2-propanol, to the reaction mixture [13] was raised and heat up for 15 minutes at 50°C, remained the mix for 1hr in room temperature. The solvent was rised beneath a lower pressure, then interaction mixture taken away with heptane (3x25 ml), the solution was distilled in filter paper hold(2gm) of aluminum oxide, the solvent was vaporization down a reduced pressure, then the resulting was clarify from heptane. The yield (40%), white crystals, mp. 78-80°C. FT-IR spectrum, ν , cm^{-1} : 1705(C=O); 2955, 2924 (C-H) aliphatic; Calcd for $\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}$ (%):C, 66.63; H,8.95; N,15.54; found %: C,66.60; H,9.05; N,15.41.

Synthesis of [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one](2)

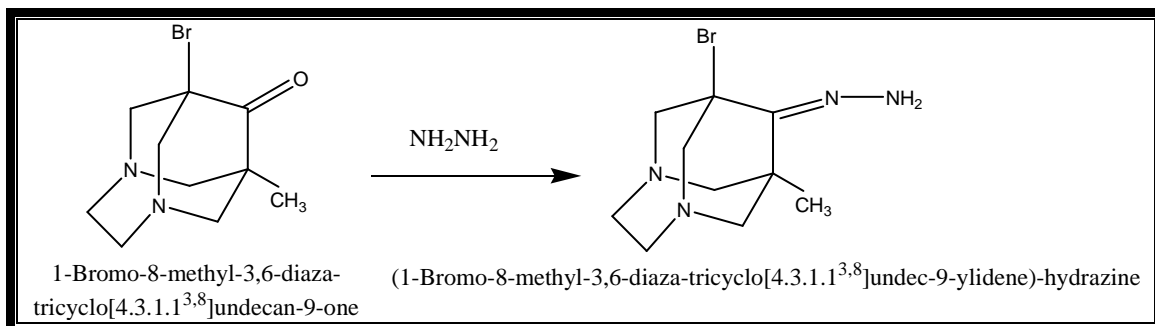
A solution of composite (1-Methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}] undecan-9-one) (6.048gm, 33.6mmol) in mix 30ml(22.5ml CH_3OH and 7.5ml glacial HOAC) add at 0°C Br_2 (2.2ml, 47mmol) [14] in 0°C mixture (3ml CH_3OH + 1ml HOAC) drop by drop. Then it is effects for 4h at 0°C. The mix is concentrated, the remains is stirred with 1N NaOH to resolve solid. Add NaOH to make the aquatic alkaline, the heptane layer is detached the organic is washed with H_2O . Then the yield was recrystallized from heptane. The yield (30%), white crystals, mp. 178-180 °C. FT-IR spectrum, ν , cm^{-1} figure(1): 1708.93(C=O); 2900.94 (C-H) aliphatic, 543.93 (C-Br); 1053.13, 1090.14, 1141.88, 1188.13(C-N) aliphatic ;calcd for $\text{C}_{10}\text{H}_{15}\text{BrN}_2\text{O}$ (%):C,46.35; H,5.83 ; N,10.81 found (%): C,46.05 ; H, 5.50 ; N, 10.51



Scheme (2)

Syntesis of [1-Bromo-8-Methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}] undecan-9-ylidene]-hydrazine(3)

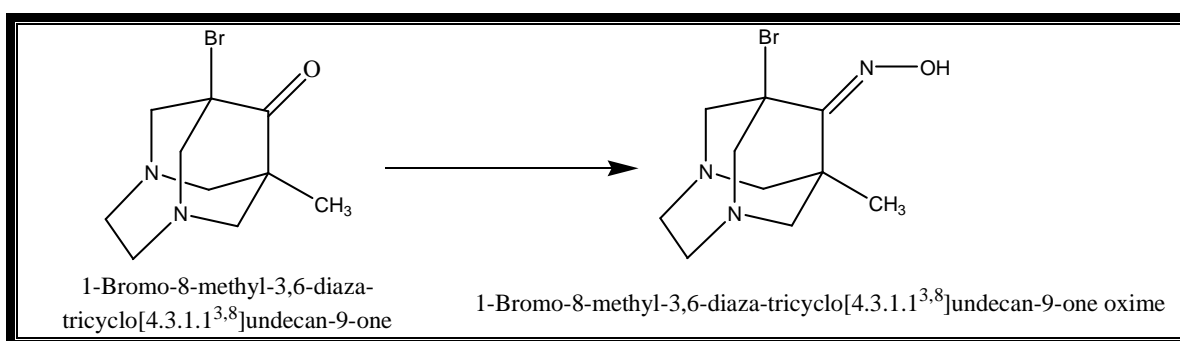
A blend of (5mmol) of (1-Bromo-8-methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one) with (10ml) of hydrazine hydrate %80 [15] was raised and refluxed for 3hrs. The solution was risen and the remnant was recrystallized from toluene. The 80% yield white crystal Mp200-202°C. FT-IR spectrum ν, cm^{-1} ; 3278.99, 3188.40(NH₂); 1647.21(C=N); 540.07(C-Br); 2762.08(C-H) aliphatic ; calcd for C₁₀H₁₇BrN₄ (%): C, 43.97; H, 6.27; N, 20.51 found (%) C, 43.74; H, 5.94; N, 20.21



Scheme(3)

Syntheses of [1-Bromo-8-Methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one oxime(4)

A solution of hydroxylaminehydrochloride[16] (50mmol, 3.47gm) in (9.9ml) of distilled water have been added to a solution of (20mmol) [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one] in (9.9ml) of distilled water at room temperature . The mix stirred and heated at 60-70 °C. A solution of Na₂CO₃ (50mmol, 5.3gm) in (19.8ml) of distilled water was added over 15 minutes. The mix was heated and stirred for 1hr; then the result was recrystallized from ethanol and water (2:1). The yield (90%), white crystals, m.p. 180-182°C. FT-IR spectrum, (ν, cm^{-1}) : 1627.92 (C=N); 3464.15 (OH); 559.36(C-Br); calcd for C₁₀H₁₆BrN₃O (%) : C, 43.81; H, 5.88; N, 15.33 found (%) : C, 43.51; H, 5.55; N , 15.03.



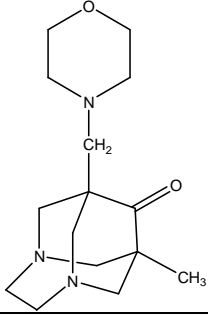
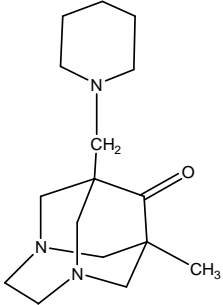
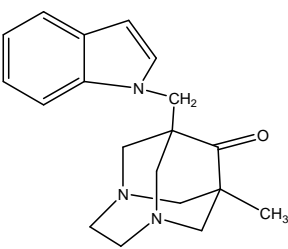
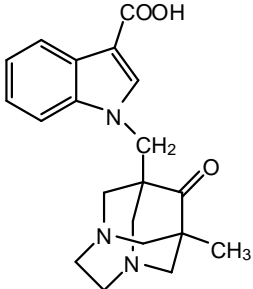
Scheme(4)

Preparation of Mannich Bases (5-8)

Equimolar amount (0.01mol) of compound (1-Methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}] undecan-9-one) and the specific compounds having secondary amine were thaw in [17] methanol (30ml) in beaker under perfect ice-cold condition and stirred all the time. To this solution ,formaldehyde (0.01mol) was added bit by bit and heated to reflux for (3hrs),the product was perspicuous

recrystallization from toluene. In compound **5**, the yield (70%), white crystals, m.p. 138-140°C. FT-IR spectrum (ν, cm^{-1}): 2972.09 (C-H) aliphatic; 1705.05 (C=O); 1022.27 (C-N); calcd for $\text{C}_{15}\text{H}_{25}\text{N}_3\text{O}_2$ (%): C, 64.49; H, 9.02; N, 15.04, found (%) C, 64.16; H, 8.69; N, 14.71. The FTIR and properties of mannich bases in table (1)

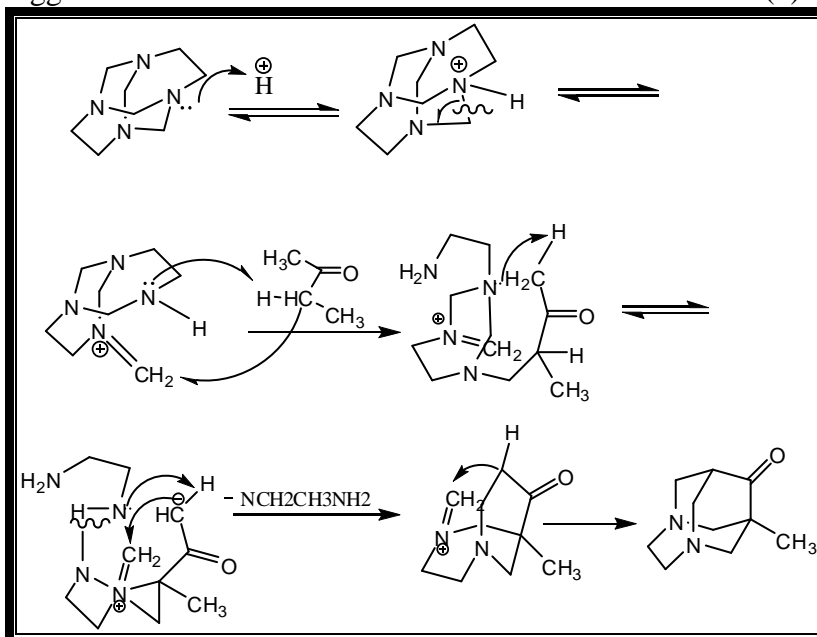
Table 1: Physicochemical and Analytical data of the synthesized compounds 5-8

Comp. No	Structure compound	color Yield%	M.P (°C)	FT-IR Spectra, wave number in (cm-1)			Molecular formula
5		white crystal 70	138-140	C-H aliphatic 2893.2 22972.09 2954.95	C=O 1705.07	C-N 1022.27	$\text{C}_{15}\text{H}_{25}\text{N}_3\text{O}_2$
6		Yellow Oily 50%	-----	C-H aliphatic 2958.80 2924.09 2893.22	C=O 1708.93	C-N 1037.70 1022.27	$\text{C}_{16}\text{H}_{27}\text{N}_3\text{O}$
7		Yellow oily 40%	-----	C-H aliphatic 2959.80 2924.09 2897.08 2850.79	C=O 1712.79	C-H aromatic 3016.67	$\text{C}_{19}\text{H}_{32}\text{N}_3\text{O}$
8		Yellow oil 66%	-----	C-H aliphatic 29881 2885.51	C=O 1770.65 1712.79	OH 3394.72	$\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_2$

Result and Discussion

A survey of diazahomoadamantane[18] chemistry in recent years showed their importance in organic chemistry due to among other reasons their microbial effects,

their roles as accelerators in rubber's industry and their thermal stability. We prepared [1-Methyl-3,6 - diazahomoadamantane -9- one] (1) by condensing 2-butanone and [1,3,6,8-tetraazatricyclo[4.4.1.13,8]dodecane in 2-propanol in the presence of acetic acid by mannich's reaction capable of producing the major (1) approaching 40% yield. The suggested mechanism¹³ of the reaction is shown in scheme(4)



Scheme (4) mechanism steps for preparation of compound (1)

FT-IR spectrum of compound (1) showed band of the stretching vibration due to (C=O) group in region 1705 cm^{-1} , (C-H) aliphatic at $(2939-2858)\text{cm}^{-1}$ and (C-N) band at $(1365-1325)\text{cm}^{-1}$. FT-IR spectrum showed in figer(1)

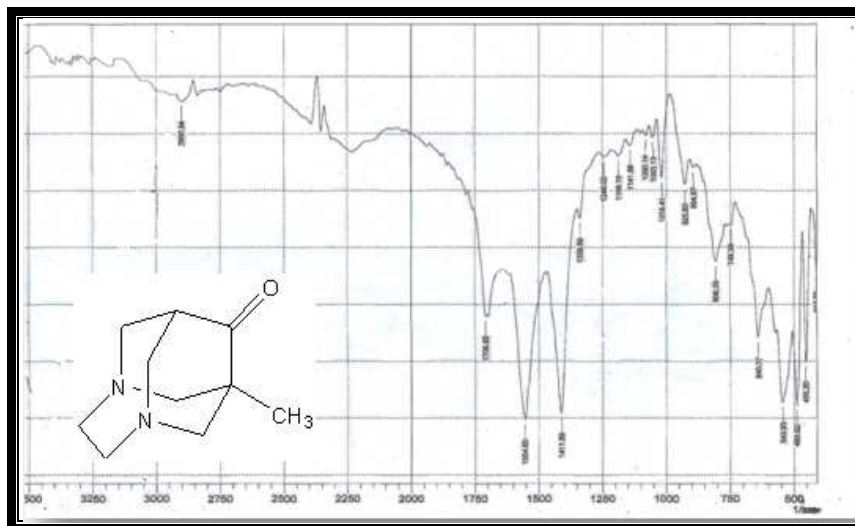


Figure (1) FT-IR spectrum compound (1)

We prepare [1-Bromo-8-methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one] by reaction compound (1) [19] with bromine liquide , the FT-IR spectrum of compound(2) show the appearance stretching vibration (C-Br) at $(690-515)\text{ cm}^{-1}$, (C-H) aliphatic at $(2996-2925)\text{ cm}^{-1}$, and (C-N) band at $(1392-1323)\text{ cm}^{-1}$. FT-IR spectrum showed in figer(2).

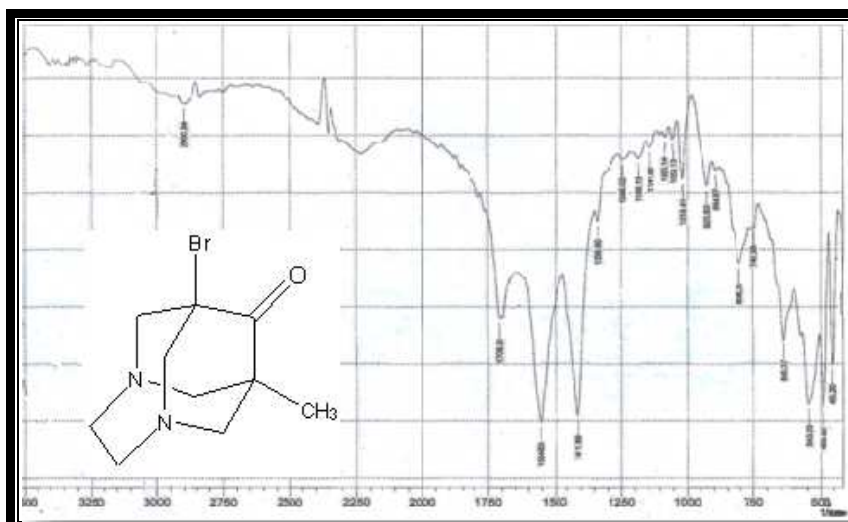
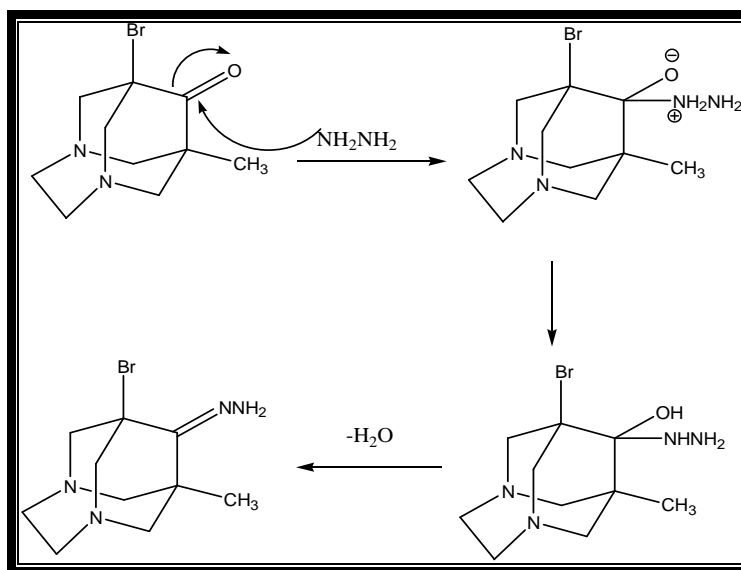


Figure (2) FT-IR spectrum compound (2)

Hydrazine is well known as a key building block for the preparation of many heterocyclic compounds via condensation with a range of [20]difunctional electrophile and being a good nucleophile¹² as well, and also it is a good antioxidant (oxygen scavenger), 1-Bromo-8-methyl-3,6-diaza-tricyclo[4.3.1.1.3]undecan-9-one was refluxed with hydrated hydrazine in ethanol for 3h to get a white crystals of compound(3). The suggested mechanism of the reaction is shown in scheme(5)



Scheme (5) mechanism steps for preparation of compound (3)

Confirmation of the product structure was proved by FT.IR spectrum revealing band at 3278.99 cm^{-1} , 3188.40 cm^{-1} as a doublet for (NH_2) . Bands at 1608 cm^{-1} , 1647.21 cm^{-1} for $(\text{C}=\text{N})$, 1465 cm^{-1} $(\text{N}-\text{N str.})$, 1361 cm^{-1} $(\text{C}-\text{N bend})$. FT-IR spectrum showed in figer(3)

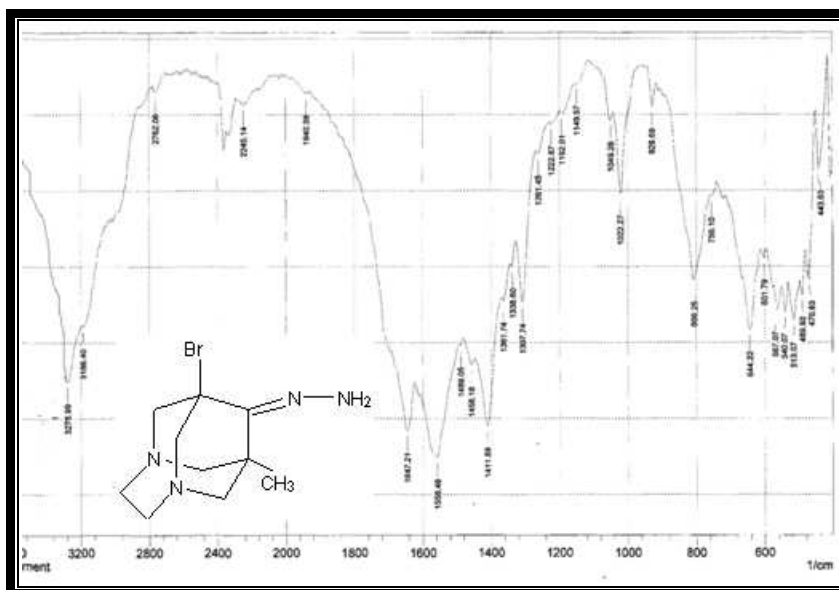
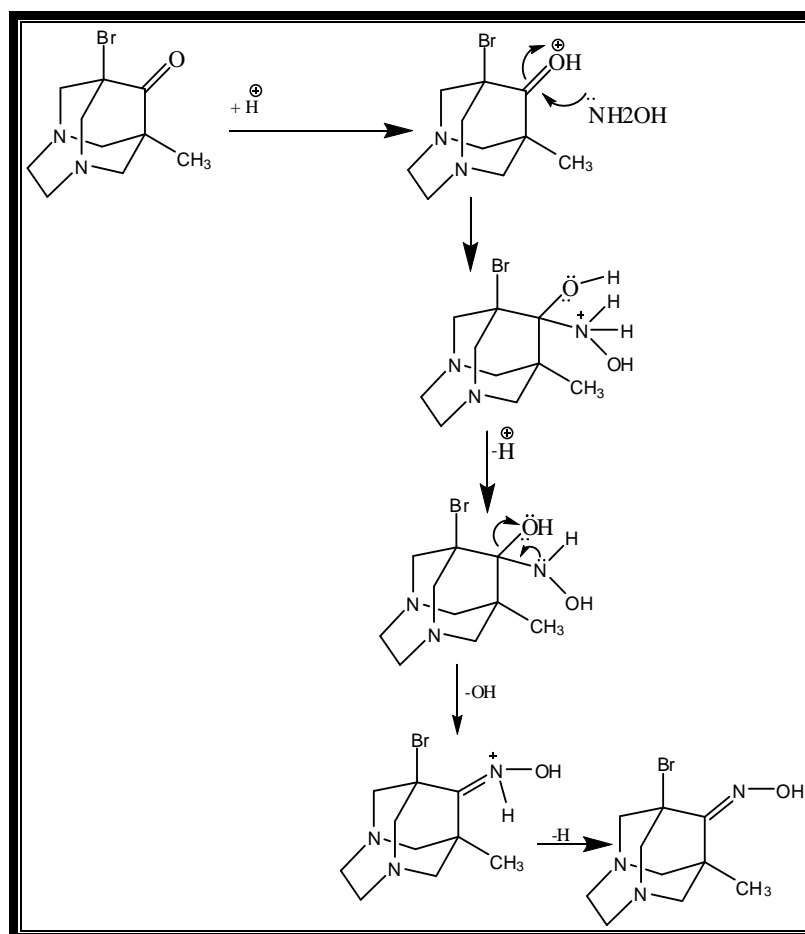


Figure (3) FT-IR spectrum compound (3)

Reaction of aldehyde or ketone with hydroxyl amine[21] gives oxime. The nucleophilicity of nitrogen on the hydroxyl amine is increased by the presence of oxygen. Successive proton transfer allows for elimination of water. Oximes generally form a mixture of geometric isomers. The reaction path is illustrated in scheme(6)



Scheme (6) mechanism steps for preparation of compound (4)

The FT-IR spectrum of compound (4) in figure (4) shows disappearance absorption band at $(1704) \text{ cm}^{-1}$ due to asymmetric and symmetric stretching vibration of $(\text{C}=\text{O})$ group and appearance the $(\text{O}-\text{H})$ at $(3464) \text{ cm}^{-1}$ stretching, $(\text{C}=\text{N})$ at $(1627) \text{ cm}^{-1}$ and $(\text{N}-\text{O})$ at $(928) \text{ cm}^{-1}$.

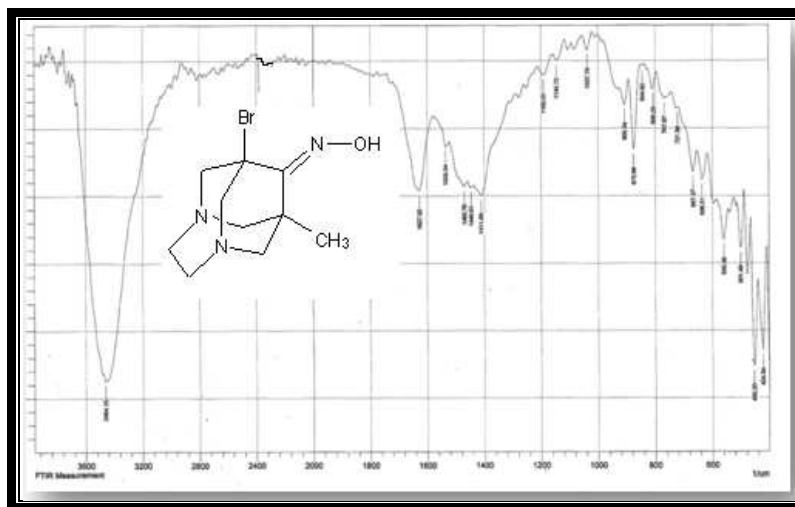
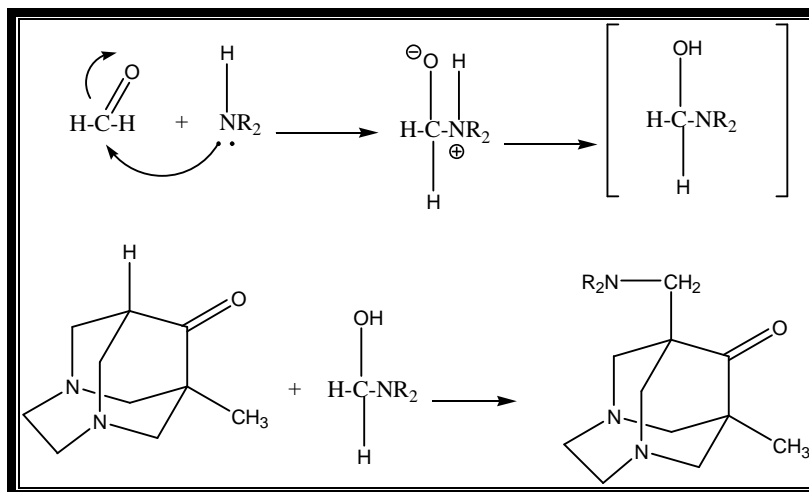


Figure (4) FT-IR spectrum compound (4)

A series of 4 new mannich bases of (1-Methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}] undecan-9-one) derivatives were synthesized using mannich reaction by the reaction between compounds having secondary amine and formaldehyde. The mechanism of the reaction depends on the nucleophilic addition of amine to the carbon of formaldehyde followed by condensation of the mannich base on reaction with (1-Methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}] undecan-9-one) gives the final product, the suggested mechanism is shown in scheme (7).



Scheme (7) mechanism steps for preparation of compounds (5-8)

The FT-IR spectrum show the appearance stretching vibration $(\text{C}-\text{H})$ aromatic at $(3096-3025) \text{ cm}^{-1}$, $(\text{C}-\text{H})$ aliphatic at $(2988-2885) \text{ cm}^{-1}$, and $(\text{C}-\text{N})$ band at $(1392-1323) \text{ cm}^{-1}$

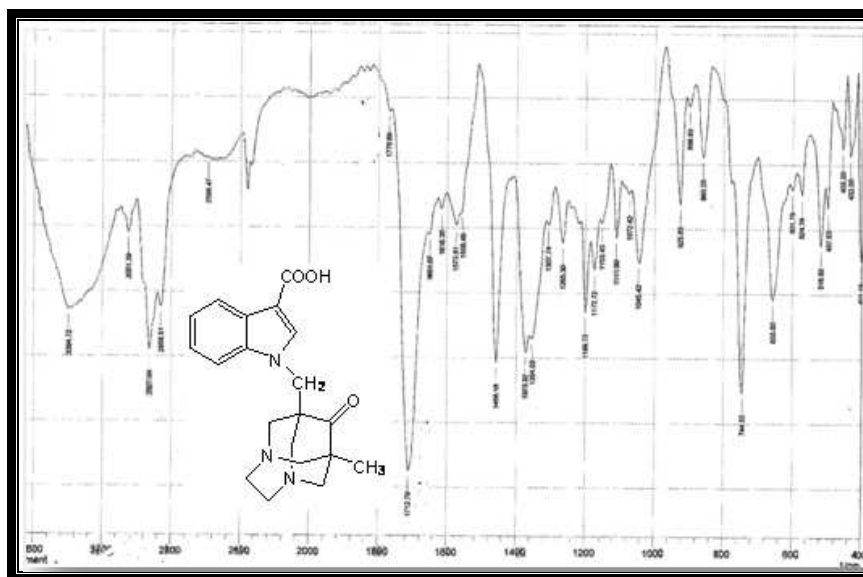


Figure (5) FT-IR spectrum compound (8)

Conclusions

1. Synthesis of a new diazahomoadamantane-9-one [1-Methyl-3,6 – diazahomo adamantane -9- one] by the condensation of 2-butanone with 1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}]dodecane.
2. Synthesis of a new [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one] by reaction [1- Methyl-3,6 – diazahomo adamantane -9- one] with bromine liqide.
3. Synthesis of a new compound [1-Bromo-8- Methyl-3,6-diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-ylidene]-hydrazine by reaction [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one] with hydrazine hydrate 80% .
4. Synthesis of a new [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-oneoxime] by reaction [1- Methyl-3,6 – diazahomo adamantane -9- ylidene]-hydrazine with hydroxylamine hydrochloride.
5. Synthesis of some new mannich bases from [1-Bromo-8-Methyl-3,6 – diaza-tricyclo[4.3.1.1^{3,8}]undecan-9-one] .

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