"synthesis of 1-(4-Chlorophenethyl)-3,6-diazahomoadamantane-9-one and Its Substituted Derivatives"

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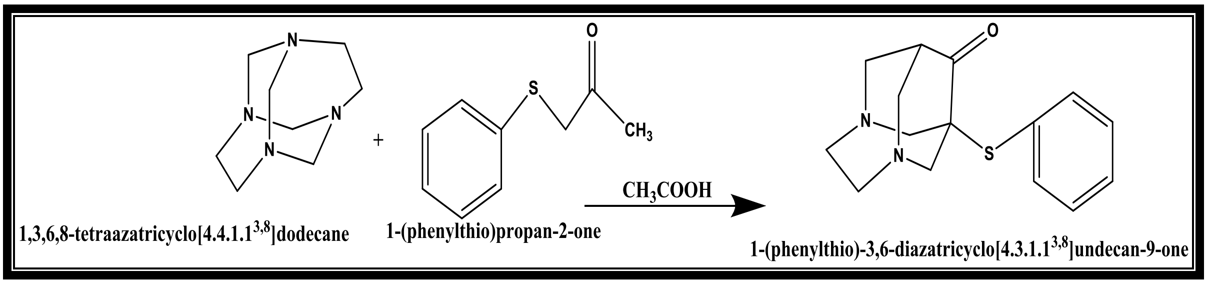
Abstract:
1-(4-chlorophenethyl)-3,6-diazahomoadamantane-9-one was synthesized through the condensation reaction of 5-(4-chlorophenyl)pentane-2-one with diethylene tetra methylene tetra amine (TATD). The C9 bridging atom in this compound and its derivatives have functional groups. were further synthesized via reactions at the carbonyl group of 1-(4-chlorophenethyl)-3,6-diazatricyclo$[4.3.1.1^{3,8}]$undecan-9-one. These derivatives expand the chemical diversity of the parent structure, introducing various functional modifications at the bridging position.

Keywords: diethylene tetramethylene tetramine (TATD) and 5-(4-chloro phenyl) pentane-2-one react; the resultant chemical is dial azahomoadamantanone, hydrazine hydrate, Mannich’s reaction, and different chemical substances.

Introduction

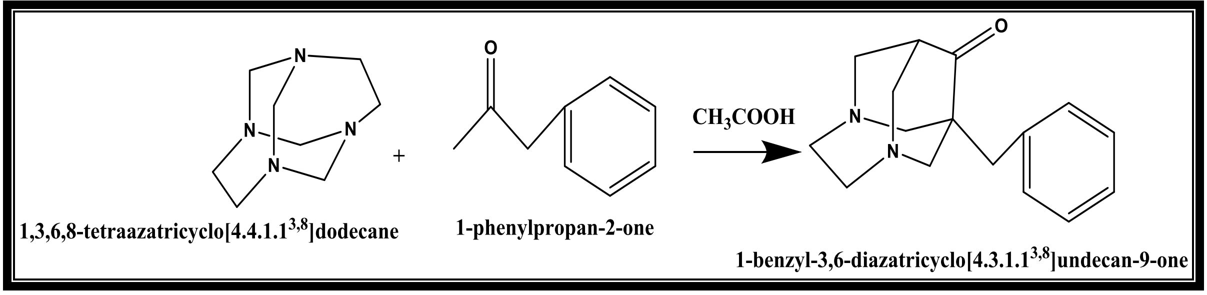
Recent studies on the chemistry of diazahomoadamantane have demonstrated their significance in organic chemistry for several reasons, including their microbial impacts, thermal stability, and functions as accelerators in the rubber industry.

Wolff-Kishner reduction of the resultant diazahomoadamantanones, followed by condensation of ketones with diethylene tetra methylene tetraamine, allowed us to obtain a variety of derivatives of 3,6-diazahomoadamantane substituted at the bridgehead location scheme (1)[1].



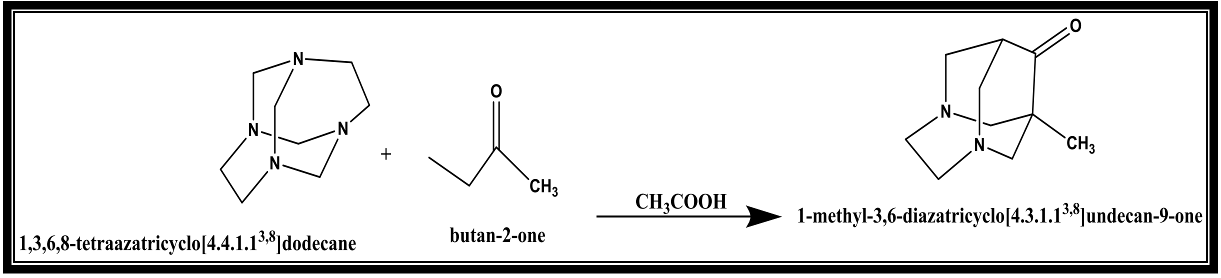
Scheme (1)

A complex molecule with a polycyclic structure is dial azahomoadamantanone. The way that multiple simple molecules group together to form a larger one should first be understood. It is well known that diazahomoadamantanone and its derivatives that have nodal-position substituents can be obtained via Mannich's reaction when a cyclic ketone reacts with diethylene tetra methylene tetra amine (TATD) in 2-propanol in the presence of acetic acid [2]. Continuing our investigation into synthesizing novel 3,6-diazahomoadamantane derivatives, we obtained 4-phenylbutan-2-one by condensation. Tetra methylene diethylene tetraamine is used in this 1-benzyl-3,6-diazahomoadamantan-9-one scheme (2)[3][4].



Scheme (2)

reported on synthesizing and characterizing new 3,6–diazahomoadamantane derivatives. when 2-butanone and cyclododecanone combine to form a novel diazahomoadamantane derivatives scheme(3)[5][6].



Scheme (3)

Chemicals and equipment

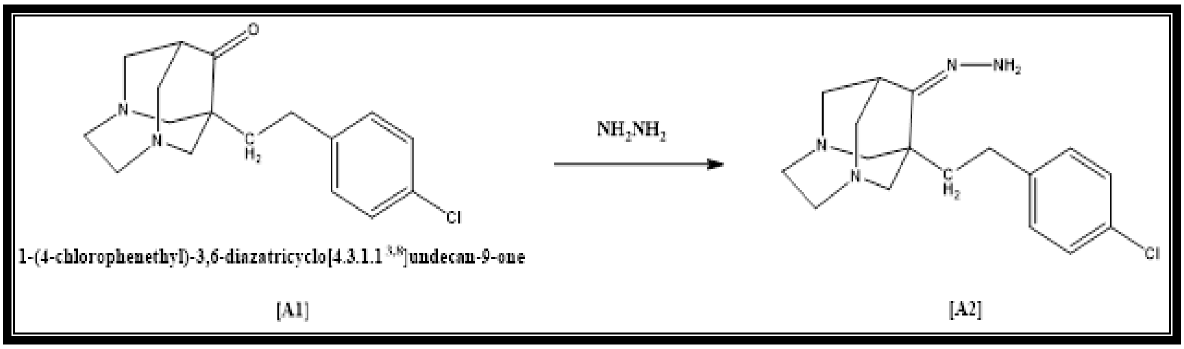
Chemicals were purchased from Merck and Fluka. A Shimadzu FT-IR 8300 Spectropotometer's KBr disc was used to list the FT-IR spectrum at Iraq's Baghdad University. Al-Al-Bayt University in Amman, Jordan, completed micro elemental analysis (C.H.N.S) and the ^{1}HNMR spectrum.

Experiment

1-Synthesis of [1-(4-chlorophenethyl)-3,6-diazatricyclo [4.3.1.1^{3,8}] undecan-9-one] [A$_1$] [7]

In 100 ml circular flask, 20 mmol (3.93 gram) was added of 5-(4-chlorophenyl) pentane-2-one with (20mmol, 3.36gm) of diethylene tetra methylene tetraamine, and the additional solution, which contained 50 mmol, 2.86 ml, and 3 gm of acetic acid, was heated for 30 minutes at 60 to 70°C in 10 ml of isopropanol. After being filtered away, the precipitate was recrystallized from heptane. White crystals, MP 135–137°C, yield (46%). The spectrum of FT-IR, v, cm^{-1}: 1700.03 (C=O); 2954.95, 2924.09 (C-H) aliphatic; (C-H) aromatic Stretch; 3070.91;(C-Cl)779.29; for $C_{17}H_{21}ClN_2O$ Calculated (%):C, 66.99; H, 6.94; Cl, 11.63; N, 9.19; O, 5.25. M =304.82. ^{1}H NMR spectrum, δ, ppm: 1.44 m (1H, CH), 1.45d (2H,$CHCH_2C$), 2.35- 2.46m (12H, 6CH_2). 7.459–7.67 d (4H, Ph). 2.37m (2H, CH_2), 1.752 t (2H, CH_2).

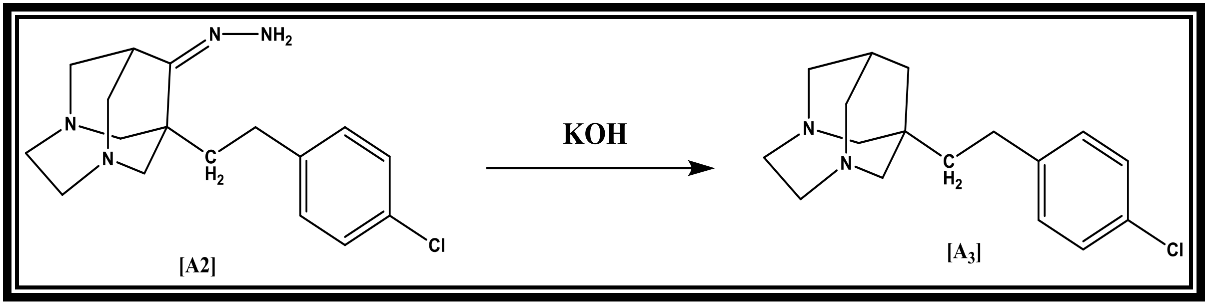
***2- Synthesis of (Z)- 1- (4-chlorophenethyl)- 9-hydrazineylidene-3,6-diazatricyclo [4.3.1.1^{3,8}] undecane[A$_2$]**[8]*. 1.46 g (4.8 mmol) of ketone[A$_1$] was heated in 10 mL of 80% hydrazine hydrate for two hours. The residue was recrystallized from toluene after the reaction mixture was evaporated. White crystals with a yield of 1.2 g(82%), mp 121–122°C.IR spectrum, cm^{-1}: 3180,3312 (NH_2),1665 (C=N),3001 (CH aromatic). ^{1}H NMR spectra, δ, ppm: 1.60 s (2H, CH_2), 2.935 s (1H, CH), 3.003 s (2H, CH_2), 3.122 d (2H, NCH_2C, J 14.0 Hz), 3.172 d (2H, NCH_2C, J 14.0 Hz), 3.259 d (2H, NCH_2C, J 14.0 Hz), 3.315s (4H, NCH_2CH_2N), 3.600 d (2H, NCH_2C, J 14.0 Hz), 7.656-7.961 d (4H, Ph).1.788 t(2H,CH_2), 2,772-2.813 m(2H,CH_2 ph) . Calculated, %:$C_{17}H_{23}ClN_4$, C64.01, H7.25, Cl 11.09, N 17.55.M=318.85.



Scheme (4)

3- Synthesis of [1-(4-chlorophenethyl)-3,6-diazatricyclo [4.3.1.1^{3,8}] undecane] .

After being well mixed, 0.63 g (2 mmol) of compound [A_2] and 0.60 g (11 mmol) of potassium hydroxide were heated for two hours at 220–240°C. After cooling, the mixture was extracted using toluene (3 × 20 ml). Following the evaporation of the solvent, the residue was recrystallized from toluene. Yield: white crystals, mp 64-66°C, 0.30 g (47%). IR spectrum, cm^{-1}, v:2862, 2916(C-H) aliphatic; (C-H) aromatic Stretch;3066,(C-Cl)767; ^{1}H NMR spectrum, δ, ppm2.37 s (2H, CH_2), 2.36 s (1H, CH), 2.35 s (2H, CH_2), 3.122 d (2H, NCH_2C, J 14.0 Hz), 3.172 d (2H, NCH_2C, J 14.0 Hz), 3.259 d (2H, NCH_2C, J 14.0 Hz), 3.315s (4H, NCH_2CH_2N), 3.600 d (2H, NCH_2C, J 14.0 Hz), 7.656=7.961 d (4H, Ph).1.788 t(2H, CH_2), 2,772-2.813 m(2H, CH_2 ph). Calculated, %:$C_{17}H_{23}ClN_4$, C64.01, H7.25, Cl 11.09, N 17.55.M=318.85.

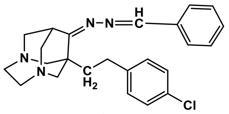
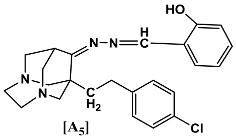
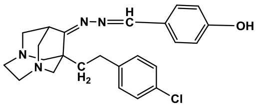
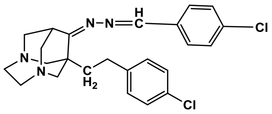
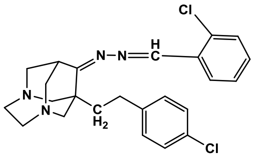


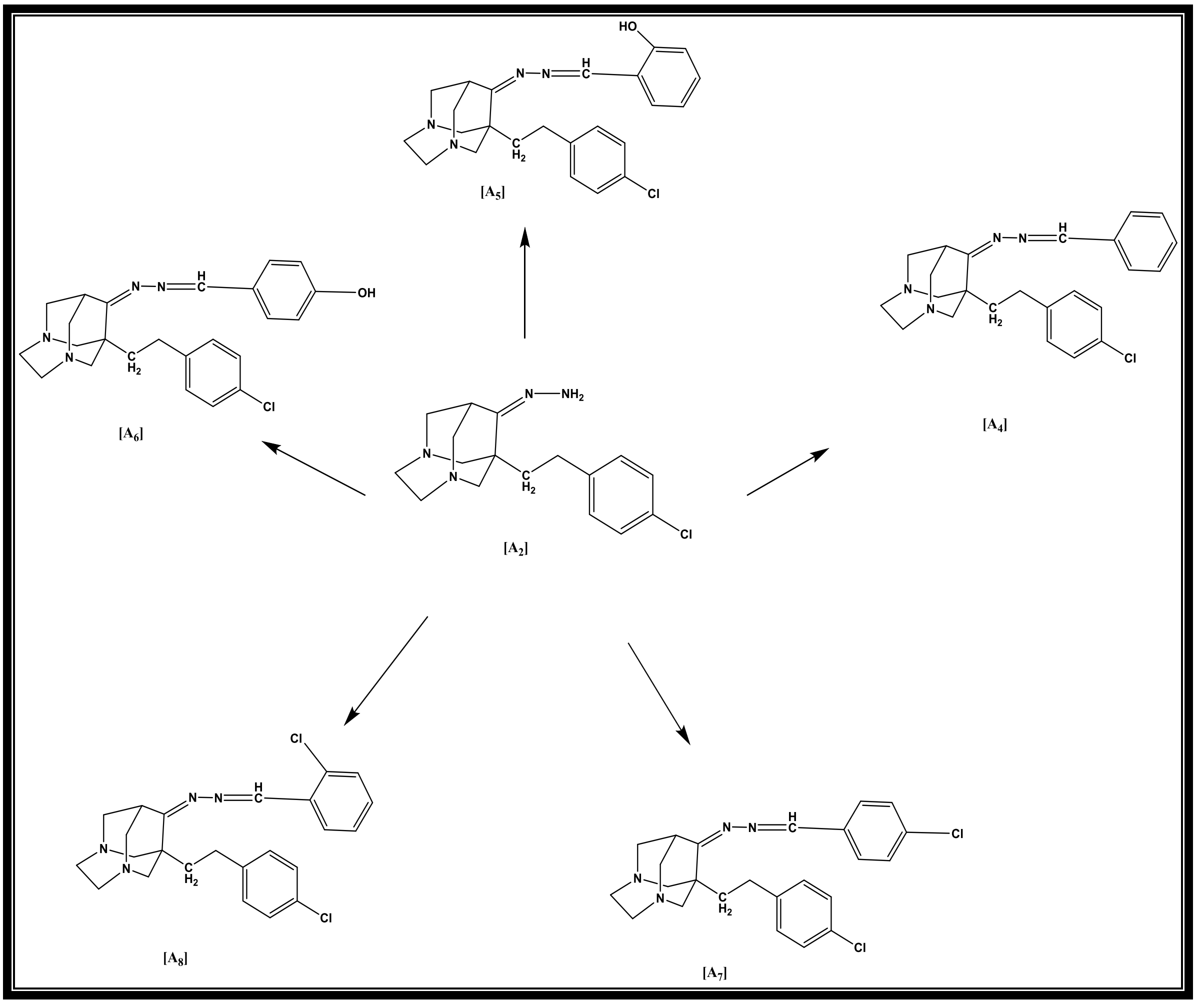
Scheme (5)

Preparation of the Schiff base[9]

An equimolar mixture of aldehyde compound (10 mmol) and (Z)-1-(4-chlorophenethyl)-9-hydrazineylidene-3,6-diazatricyclo [4.3.1.1^{3,8}] undecane (10 mmol) in ethanol (40 ml) were refluxed on a hot plate with stirring for 3 h. FT-IR spectrum and properties of the Schiff bases are summarized in Table1.

Table 1: Synthesized compounds' physicochemical and analytical data [A_4-A_8]

Structure	Color and yield %	M.P (°C)	FT-IR spectrum (cm^{-1})	Molecular formula	C% H% N% Cl% O%
 [A_4]	66 White crystal	88-86	C=N 1630, 1689,	$C_{24}H_{27}ClN_4$	C, 70.83; H, 6.69; Cl, 8.71; N, 13.77
 [A_5]	67 white crystal	77-79	C=N 1629, 1655 C-OH 3450	$C_{24}H_{27}ClN_4O$	C, 68.15; H, 6.43; Cl, 8.38; N, 13.25; O, 3.78
 [A_6]	77 white crystal	73-75	C=N 1633, 1655, C-OH 3310	$C_{24}H_{27}ClN_4O$	C, 68.15; H, 6.43; Cl, 8.38; N, 13.25; O, 3.78
 [A_7]	73 white crystal	78-80	C=N 1627, 1634 C-Cl 622,634	$C_{24}H_{26}Cl_2N_4$	C, 65.31; H, 5.94; Cl, 16.06; N, 12.69
 [A_8]	61 white crystal	80-82	C=N 1625, 1631, C-Cl 626,654	$C_{24}H_{26}Cl_2N_4$	C, 65.31; H, 5.94; Cl, 16.06; N, 12.69



Scheme (6)

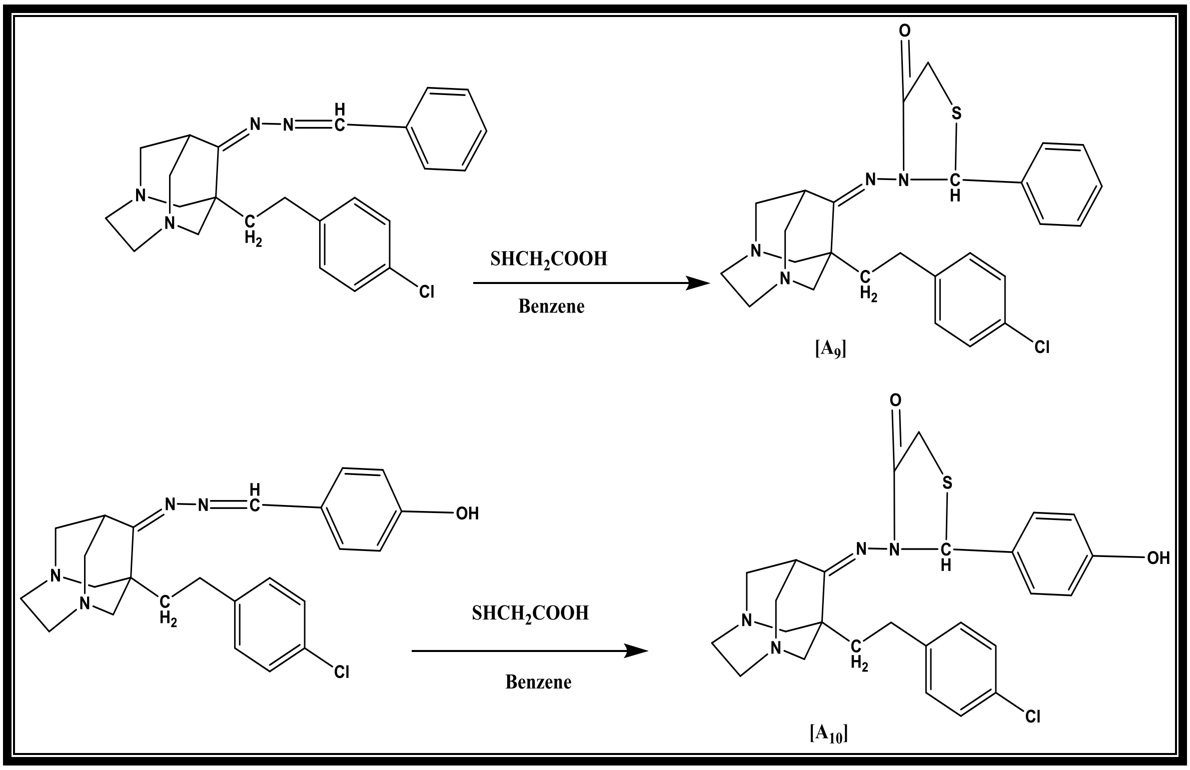
5- Synthesis derivatives of Schiff bases [A_9-A_{10}][10]

One of the Schiff base compounds (1 mmol) is added to 25 ml of benzene and [1 mmol, 0.1 gm] of thioglycolic acid. The mixture refluxed for eight hours. the result was recrystallized from (DMF). ^{1}H NMR spectrum, δ, ppm of compound [A_9]] 2.35 s (2H, CH_2), 2.33 s (1H, CH), 2.36 s (2H, CH_2), 3.122 d (2H, NCH_2C, J 14.0 Hz), 3.182 d (2H, NCH_2C, J 14.0 Hz), 3.289 d (2H, NCH_2C, J 14.0 Hz), 3.223s (4H, NCH_2CH_2N), 3.600 d (2H, NCH_2C, J 14.0 Hz), 1.888 t(2H, CH_2), 2,882-2.812 m(2H, CH_2 ph), 7.662-7.66 d (4H, Ph, J 14.0Hz) 7.4421-7.611d (4H,phCl, J14.0Hz) 3.911s(2H, CH_2S). . ^{1}H NMR spectrum, δ, ppm of compound [A_{10}] 2.35 s (2H, CH_2), 2.33 s (1H, CH), 2.36 s (2H, CH_2), 3.122 d (2H, NCH_2C, J 14.0 Hz), 3.172 d (2H,

NCH_2C, J 14.0 Hz), 3.259 d (2H, NCH_2C, J 14.0 Hz), 3.215s (4H, NCH_2CH_2N), 3.500 d (2H, NCH_2C, J 14.0 Hz), 1.788 t(2H, CH_2), 2,772-2.813 m(2H, CH_2 ph), 7.671-7.955 d (4H, PhOH) 7.431-7551d (4H,phCl) 3.981s(2H, CH_2S) 9.121s(1H, OH).

Table 2: Physicochemical and analytical data of the synthesized compounds[A_9-A_{10}]

Com p.No	**Color and yield%**	**M. P (°C)**	**FT-IR spectrum (cm^{-1})**	**molecular formula**	**C% H% N% Cl% O% S%**
[A_9]	57% white crystals	88-86	1733(C=O) 1655,1649 (C=N), 2855, 2944 (C-H) aliphatic, 3006,3044 (C-H) aromatic, 767(C-Cl), 3255(C-OH)	$C_{26}H_{29}ClN_4O_2S$	C,62.83; H, 5.88; N,11.27; Cl, 7.13; O, 6.44; S,6.45
[A_{10}]	66% white crystals	82-80	1755(C=O) 1661-1510(C=N) 2843,2933(C-H) aliphatic, 3011,3034(C-H) aromatic	$C_{26}H_{29}ClN_4OS$	C,64.92; H, 6.08; N, 11.65; Cl,7.37; O, 3.33; S, 6.66.



Scheme (7)

Results and discussion

We made 1- (4-chlorophenethyl)- 9-hydrazineylidene-3,6-diazatricyclo [4.3.1.1^{3,8}] by using Mannich's process to condense 5-(4-chlorophenyl) pentane-2-one with diethylene tetra methylene tetraamine in 2-propanol with acetic acid, the principal (1) yield can be produced in a yield of around 46%. The (C=O) group in the range 1700 cm^{-1} of compound [A$_1$] caused a stretching vibration band to appear in the FT-IR spectrum. Protons of (1H, CH) are multiple in 1.44 m, (2H, CHCH$_2$C) are doublet in 1.45 d, and (12H, 6CH$_2$) are multiple in 2.35–2.46 m in the HNMR^1 spectrum in (CDCl$_3$). The ring aromatic appears in (7.459–7.67) d (4H, Ph). 2.37 m (2H, CH$_2$).

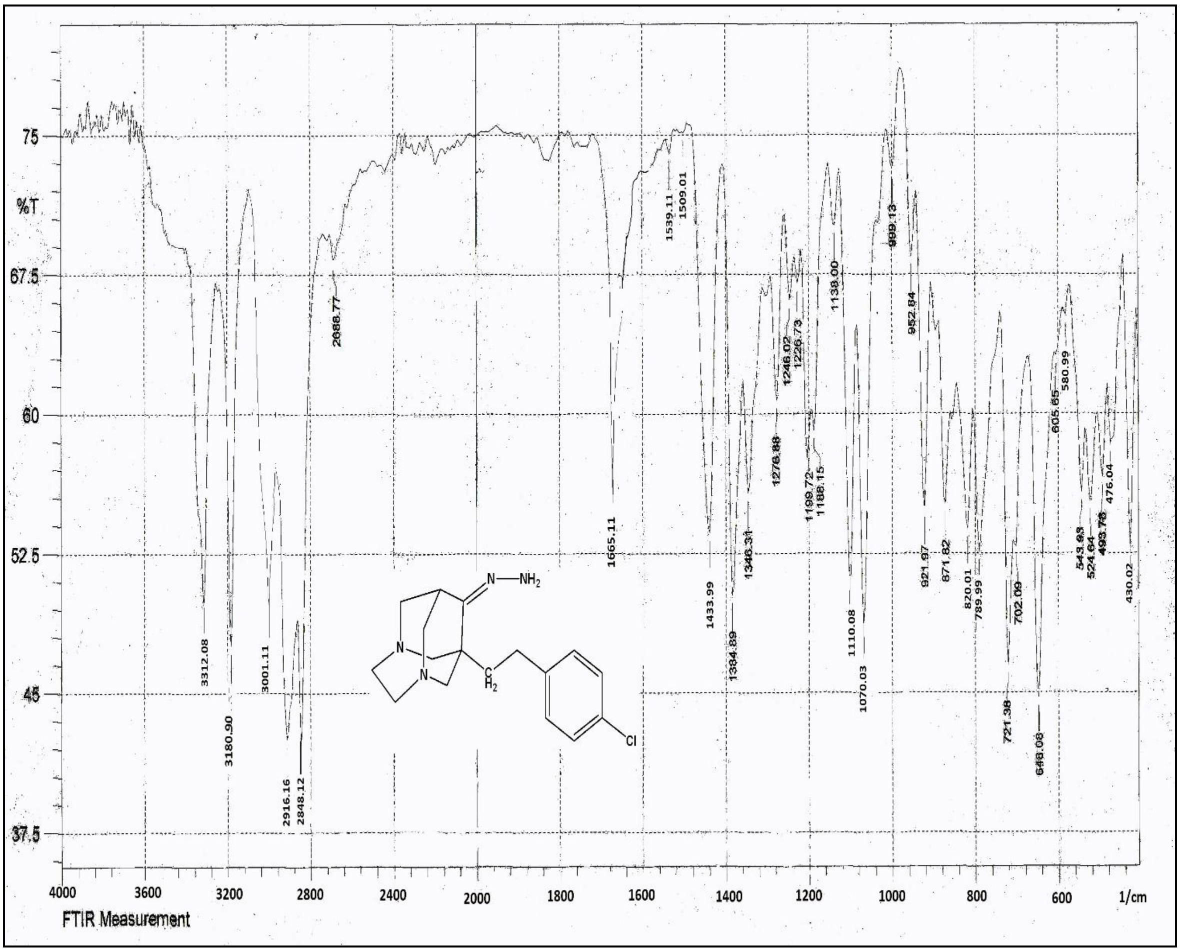


Figure (1) FT-IR spectrum of compound [A_2]

When compound [A_1] reacted with hydrazine hydrate, it exhibited strong absorption bands, as shown in Figure 1. The FT-IR spectrum of compound [A_2] reveals two peaks for the NH_2 group at 3180 and 3312 cm⁻¹, and a single peak for the C=N group at 1665 cm⁻¹. In the ^1H NMR spectrum, the NH_2 group appears as a broad singlet at 5.96 ppm. The azahomoadamantane (aliphatic cycle) shows multiple peaks (m, 13H) in the range of 1.78-5.89 ppm, while the aromatic cycle is represented by a doublet (4H, ph) in the range of 7.27-7.35 ppm, as shown in Figure 2.

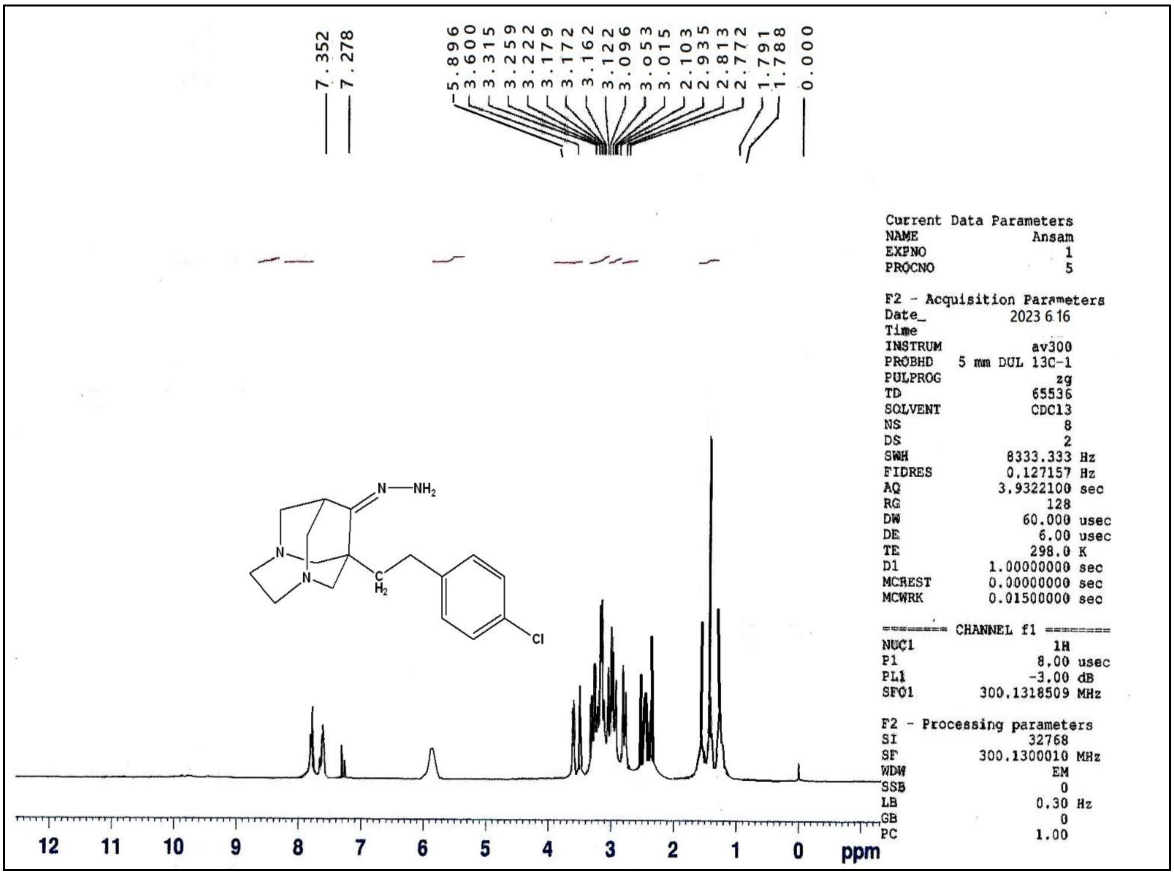


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Figure (2) ^{1}HNMR spectrum of compound[A_2]

When compound [1-(4-chlorophenethyl)-3,6-diazatricyclo[4.3.1.1^{3,8}]undecane] [A_3] reacted with potassium hydroxide, the ^{1}H NMR spectrum shows that the NH_2 group signal disappears. The two peaks corresponding to the NH_2 group in the IR spectrum also vanish, as shown in Figure 3.

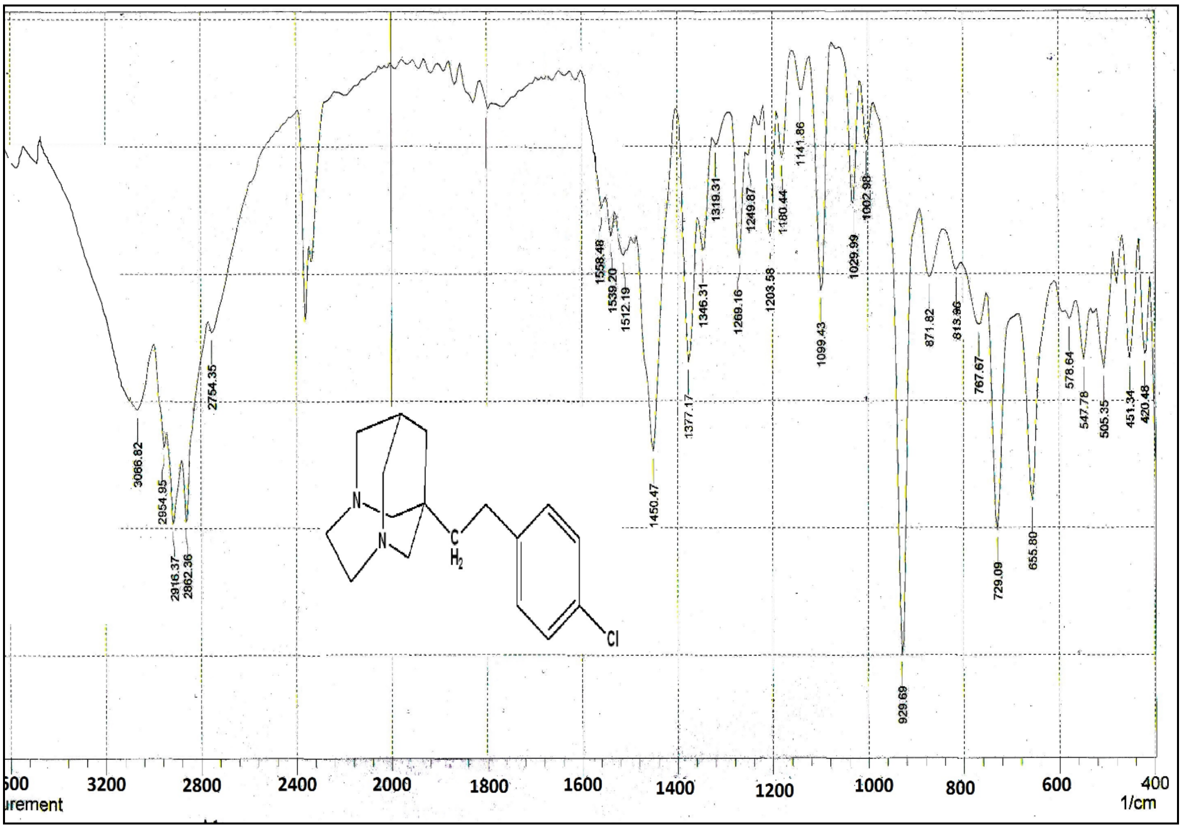
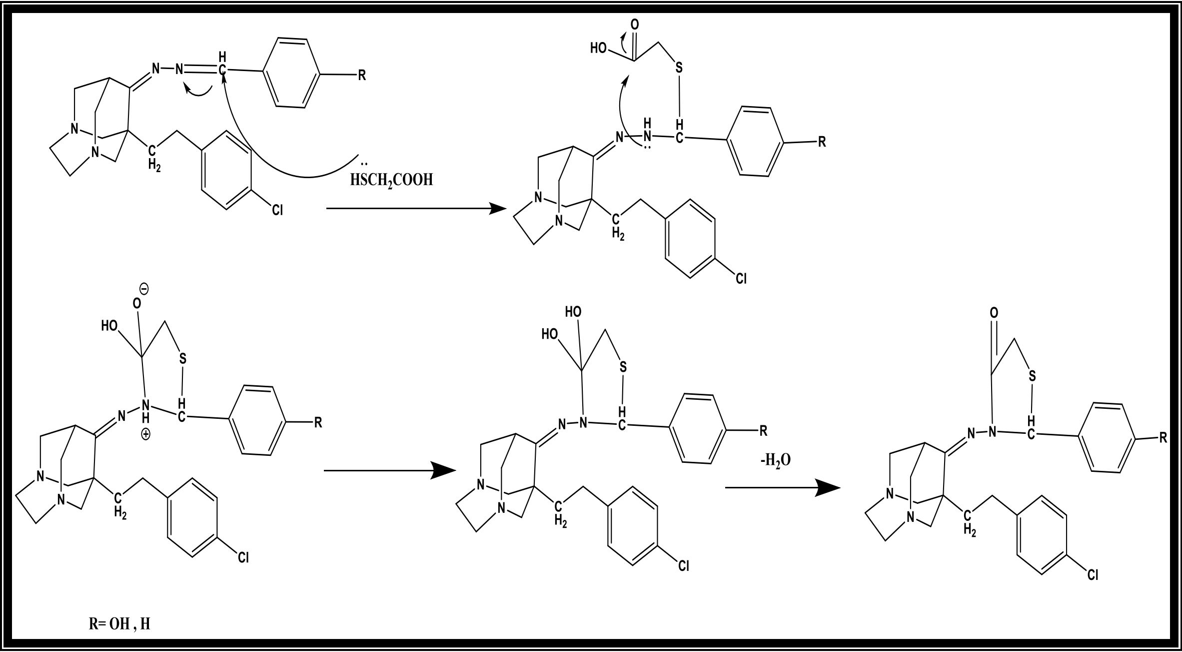


Figure (3) FT-IR Spectrum of compound [A_3]

A series of 5 new Schiff bases of (Z)- 1- (4-chlorophenethyl)- 9-hydrazineylidene-3,6-diazatricyclo [4.3.1.1^{3,8}] undecane[A_2] derivatives were synthesized by reaction compound [A_2] having NH_2 group with aldehydes and given Schiff bases compounds. NH_2 group bands disappeared and we showed C=N bands of the Schiff bases in Figure (4) to show that.



Scheme (8)

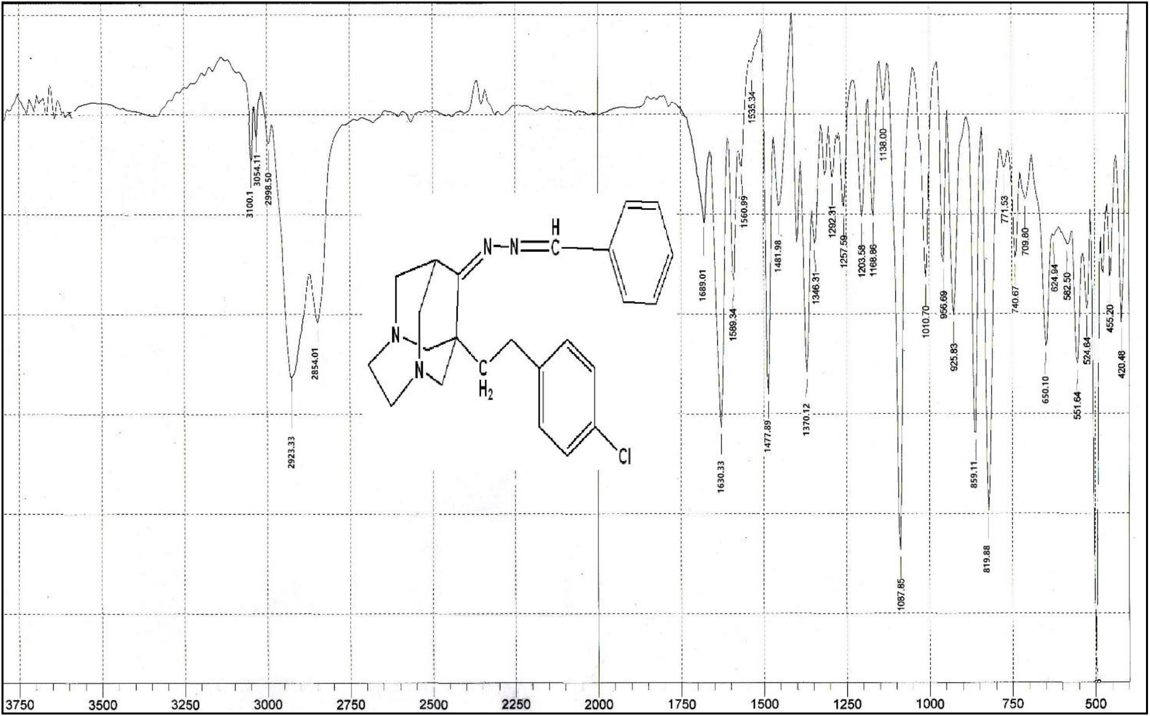


Figure (4) FT-IR Spectrum of compound [A$_4$]

Scheme (8) illustrates the reaction between the Schiff bases compounds ([A_6], [A_4]). Scheme (9) demonstrated a method for the thioglycolic acid we showed, which seems to have a C=O peak in the two molecules.

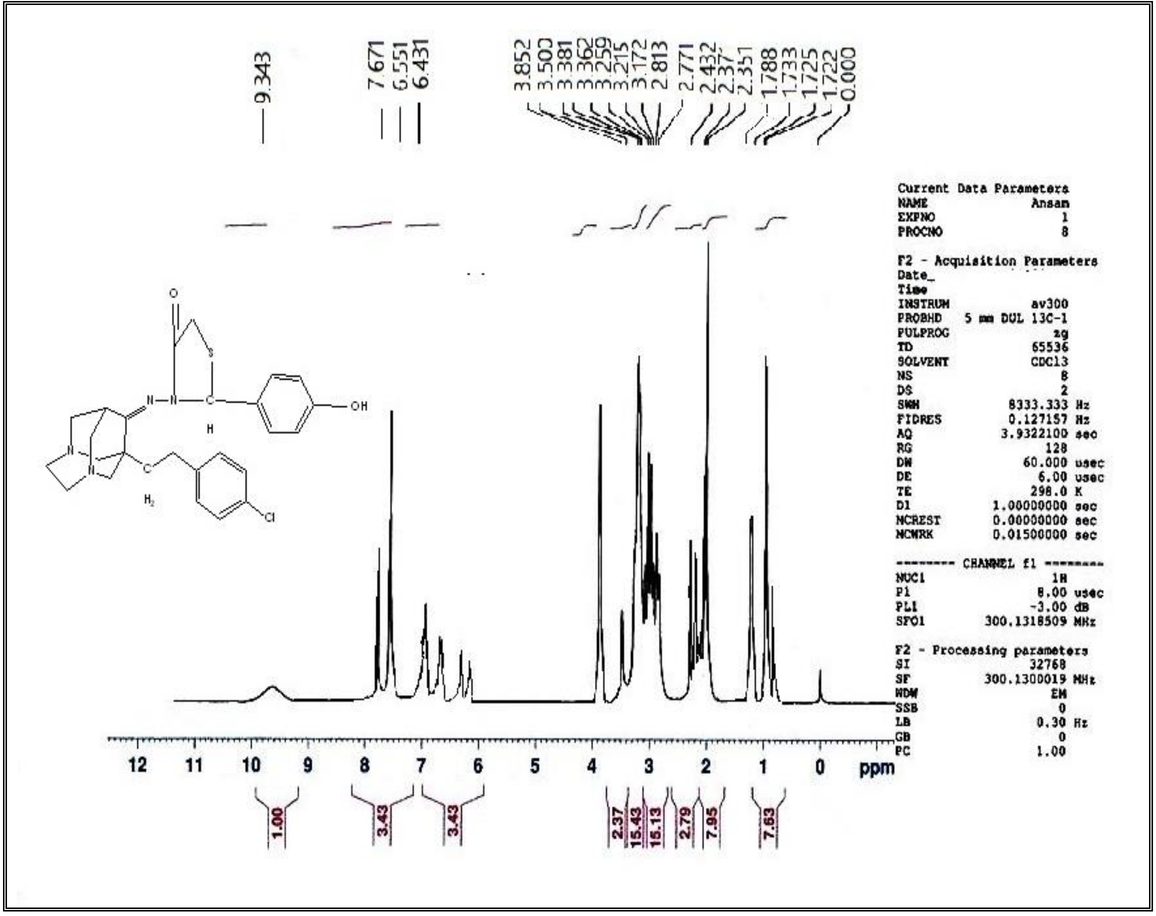


Figure (5) HNMR spectrum of compound [A_{10}]

Conclusions

1. By condensing 5-(4-chlorophenyl) pentane-2-one with diethylene tetra methylene tetraamine in 2-propanol with acetic acid, a novel chemical [1-(4-chlorophenethyl)-3,6-diazatricyclo [$4.3.1.1^{3,8}$] undecan-9-one] [A_1] is created.

2. By reacting compound [A_1] with hydrazine hydrate, a novel molecule (Z)-1 (4-chloro phenethyl) -9-hydrazineylidene-3,6-diazatricyclo [$4.3.1.1^{3,8}$] undecane [A_2] is synthesized.

3. By reacting compound [A_2] with potassium hydroxide, a novel chemical [1-(4-chlorophenethyl)-3,6-diazatricyclo [$4.3.1.1^{3,8}$]undecane] is synthesized.

4. Schiff bases [A_4–A_8] are synthesized by reacting with various aldehyde compounds [A_2].

5. Compounds [A_4-A_6] react with thioglycolic acid in the benzene to synthesize compounds [A_9-A_{10}].

References

1-“Synthesis of 1-Butyl-3,6-diazahomoadamantane’’(2019) ,Rahman.Tama.Alasadi. Ahmed. Al.Yasari. Russian Journal of organic chemistry, 55(3):368-372

2- ‘Synthesis of 3,6-Diazahomoadamantane’’(2012), A. I. Kuznetsov, I. M. Senan, A. Kh. Shukkur,, I. A. Azzheurova, and T. M. Serova,. Russian Journal of Organic Chemistry, 48 (1): 119–122.

3- ‘‘Synthesis and binding affinities of 5-(3-pyridinyl)- and 5-(3-quinolinyl)-4-azahomoa adamantanes to ∝7 nicotinic acetylcholine receptors’’(2002), Dimitris Tataridis, Antonios Kolocouris , George Fytas, Nicolas Kolocouris , George B. Foscolos , Konstantinos Poulas, Socrates J. Tzartos, Il Farmaco (57): 979-984.

4-“Bromination of Diazahomoadamantane with liquids bromine and Synthesis of New it’s Derivatives’’(2016), Ansam. F .Noamane, Noor .N.Saeed. Online International Interdisciplinary Research Journal, Volume-VI: 2249-9598.

5-“Synthesis and Characterization Of [1-Methyl-3, 6 -Diazahomoadamantane -9- One] and some It’s Derivatives”.(2014), Abdel –Amir M. Fenjan, Ansam. Faeak.Noaman. Online International Interdisciplinary Research Journal, Volume-IV:2249-9598.

6- **“**Synthesis and antimicrobial activity of new adamantane derivartives”,(2000),
Andrzej Orzeszko, Renata Gralewska, Bohdan J. Staroœciak and Zygmunt Kazimierczuk,acta biochimica polonica. Vol. 47(1), 87–94.

7- “Synthesis of Diazahomoadamantane Derivative”(2019). Rahman Tama Alasadi, and Zeid Hassan Abood, Research article.

8- “bromo-2-phenylquinoline-4-carboxylic acid تحضير بعض المشتقات الجديدة من ’’ (2015), الاء ماجد صادق ، ا.د.عبدالامير مطلك فنجان , مجلة كلية التربية الاساسية , 87: 93-103.

9- “Crystal structure of the co-crystalline adduct 1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}]dodecane (TATD)–4-bromophenol (1/2)” (2015). Augusto Rivera, Juan Manuel Uribe, Jicli Jose´ Rojas, Jaime Rı´os-Motta and Michael Bolte, Acta cryghllogr communications.71(5) 463–465.

10- ’’Synthesis and Characterization of some new Heterocyclic derivatives from Aromatic Carbonyl Compounds and Carboxylic Acids with Evaluation

Some of Them for Biological Activity''(2024),Shaima Ibraheem Al-Khazraji,, Luma S. Ahamed, Rana Abid Ali, Iraqi Journal of Science, Vol. 65, (4). pp: 1855-1869.

تحضير 1-(4-كلوروفينيثيل)-6,3-ثنائي ازا هومودادامنتان-9-اون ومشتقاته المستبدلة

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مستخلص البحث:

تم تحضير مركب 1-(4-كلوروفينيثيل)-6,3-ثنائي ازاهومودادامنتان-9-اون عبر تفاعل التكثيف بين 5-(4-كلوروفينيل)بنتان-2-ون وثنائي إيثيلين رباعي ميثيلين رباعي امين .

تمثل ذرة الكاربون 9 في هذا المركب وجميع المشتقاته المجموعة الفعالة .وقد اجريت تفاعلات على مجموعة الكاربونيل لهذا المركب ومشتقاته.تسهم هذه المشتقات في توسيع التنوع الكيميائي للبنية الاصلية ، مما يؤدي الى ادخال تعديلات وظيفية متعددة في موقع الربط .