Synthesis and Characterization of Some Heterocyclic Compound Tetrazole from Schiff Base

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Abstract

A series of five membered ring, the tetrazole have been synthesized via Schiff base with sodium azide in the presence dry acetone at(50-55)C^{o} to give the following compounds:-

1- 10-Methyl-3,6-bis(5-phenyl-1H-tetrazol-1-yl)-4a,10-dihydroacridine
2- 3,6-bis(5-(3,5-dimethylphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.
3- 3,6-Bis(5-(2-Bromophenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10- dihydroacridine.
4- 3,6-bis(5-(3-methoxy,5-hydroxyphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

The derivatives have long been known to possess hypnotics activity and it is may be to get hypnotics activity from the newly prepared compounds.

Chemical classification QD 241- 441

Key Word : tetrazole, sodium azide, Schiff base.

Introduction

Heterocyclic compounds are considered as the most promising molecules for the design of new drug, More than 50% of all known organic compounds are heterocyclic compounds. Heterocyclic systems are important building-blocks for new materials possessing attractive electronic, mechanical or biological properties (1,2).

Tetrazole heterocyclic ring are characterized by five atom heterocyclic ring with two unsaturated bonds, containing 4atoms of nitrogen and one of carbon displayed significant stability in the presence of acid ,alkalis, oxidizing agent and reducing agents ,as these wear used in this process of forming free tetrazole(3)and its derivatives have involved much interest because of their unique structure and applications as antihypertensive, antialergic, antibiotic and anticonvulsant agents(4-9), antinociceptive anti-inflammatory ,antimicrobial (10) , anticancer (11) . The tetrazole heterocyclic was first discovered in 1985 by bladin in upsal university upon formation of dicyan dimethyl hydrazine-a product of reaction dicyan with phenyl hydrazine (12). The preparation of free tetrazole from its derivatives ,.the tetrazole ring is thermodynamically stable ,as it is recovered unchanged after long periods of boiling and heating .upon elimination of proton from the NH group of tetrazole,highly aromatic(A=98) tetrazolate anion is formed ,this leads to the superior explosive properties in many tetrazole derivatives (13) . In general, it has been shown that the breakdown of the tetrazole molecule can differ due to the position and formation of its attached functional groups(14,15).Synthesis of tetrazole derivatives is observably an important task in modern medicinal chemistry, primarily due to its ability to serve as bioequivalent (bioisostere) of the carboxylic acid group(11,16).

EXPERIMENTAL:

All melting points are uncorrected and are expressed in degree(°C), using melting point SMP3 . IR spectra were recorded as KBr disks using shimadzu FT-IR 8400. H^{1}- NMR spectra were recorded using Bruker system AL 400 (400 MHz) and tetramethylsilane (TMS) as internal standard, measurements were made at Chemistry Department, AL-Bait University-Jordin. C.H.N analyzer, Euro EA 1106,Babylon University .

1-Preparation of Schiff Bases(17).

A solution of (0.01mol) of diamines in (40ml)ethanol was added to (0.02mol) of aromatic aldehyde or its derivatives in (20ml) ethanol then the mixture was refluxed for (3hr.). the mixture was cooled to room temperature, filtered and re-crystallized ,Table (1).

General procedure of tetrazole 2a .

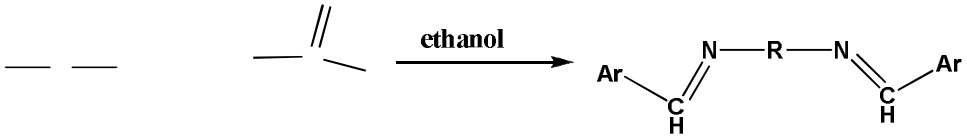
2-Preparation of 10-methyl-3,6-bis(5-substituted-1H-tetrazol-1-yl)-4a,10-dihydroacridine.

Amixture of (0.002 mole) of appropriate Schiff based1a ,dry acetone (20g) and Sodom azide (0.004mole,0.26g) was heated on a water bath ,the temperature of water bath was controlled between (50-55)C° the solid was filtered, washed with water and1N HCL and recrystallized from ethanol .The completion of reaction was monitored by TLC.

RESULTS AND DISCUSSION

Five MEMEBERD RING SYNTHESI:

The Schiff bases were prepare by the reaction of diamines (1mole) with (2mole)of terephthaldehyde in absolute ethanol:

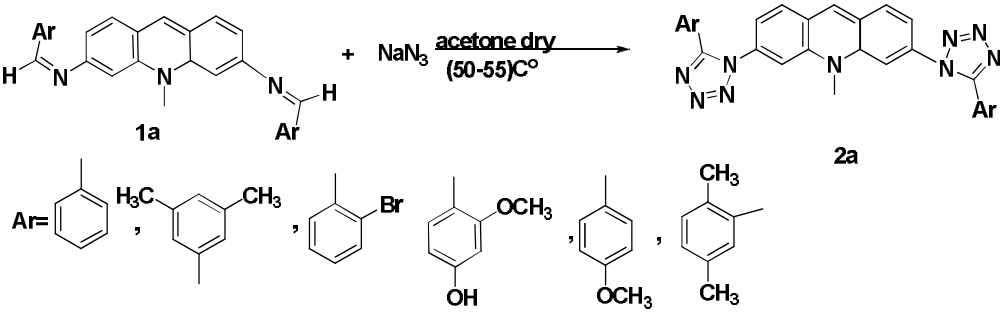


The prepared compounds were characterized by FT-IR spectra ,H-NMR spectra and the melting points were recorded and checked by TLC.

The FT-IR spectrum of Schiff bases showed the appearance of bands at 3250 cm-1 due to amino group. The new band which appears at(1600-1697)cm^{-1} which is attributed to the new azomethine (C=N) group. Besides the appearance of bands at (1475-1456)cm-1and at (1581-1570)cm-1 due to (C=C) aromatic and at (3103-3047)cm-1 attributed to(C-H)aromatic fig.(1).

Structures of tetrazole compound, were confirmed by disappearance of band at(1600-1697)cm^{-1} ,attributed to (C=N) (azomethine group) stretching frequency which was agood evidence for the success of this step of reaction beside this, FTIR spectra of of these compound were devoid of a strong band at (2120-2160) cm^{-1} attributed to stretching frequency of azide group .Aband at the range(1087-1176) cm^{-1} was due to tetrazole ring(18).

The synthesis for preparing compounds (2a) which are our target was carried out in Scheme (1). the reaction was started by condensation of Schiff base (1a) with sodium azide(NaN_3) produced tetrazole derivatives **(2a)** were synthesized by the Staudinger [2 + 3] cycloaddition as shown below Scheme 1.



Scheme 1:The reaction between Sodium azide with Schiff base(1a).

1H-NMR spectrum for compound (1), showed single peak at (3.36) ppm due to(N□C-H)proton of imine group and peaks at (7.4-7.7) ppm attributed to aromatic protons.

1H-NMR spectrum for compound (A_1), showed single peak at (4.2) ppm due to methyl protons ($N-CH_3$) and peak at (8.26-5.76)ppm due to aromatic protons. figs.(6).

1H-NMR spectrum for compound (A_2), showed single peak at (4.2) ppm due to methyl protons($N-CH_3$) , single peak at (2.2-2.6) ppm due to (CH_3 protons) and peak at (6.2-7.5)ppm due to aromatic protons. figs.(7).

1H-NMR spectrum for compound (A_3), showed single peak at (4.2) ppm due to methyl protons ($N-CH_3$) and peak at (6.2-7.7)ppm due to aromatic protons. figs.(8).

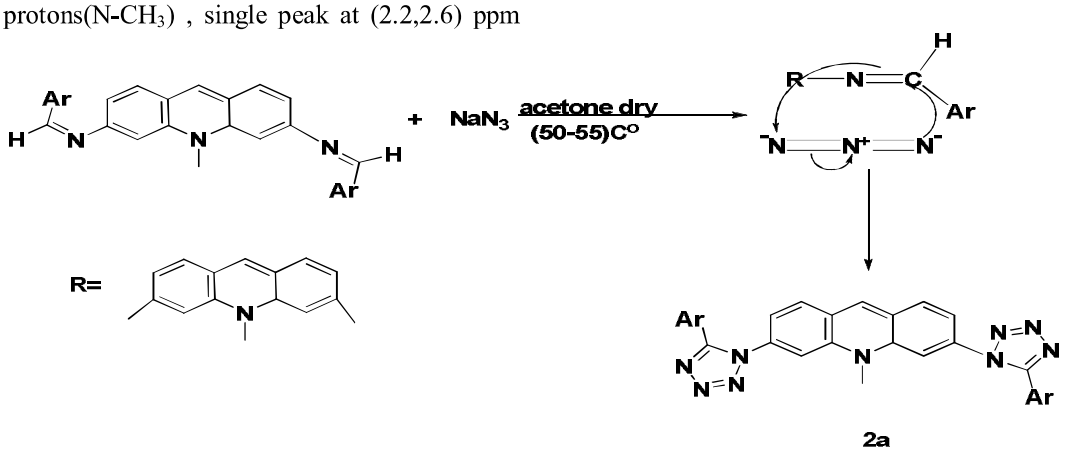
1H-NMR spectrum for compound (A_4), showed single peak at (4.2) ppm due to methyl protons($N-CH_3$) , peak at (3.6) ppm due to (OCH_3 protons) , peak at (5.6) ppm due to (OH

protons) and peak at (6.2-7.8)ppm due to aromatic protons. figs.(9).

1H-NMR spectrum for compound (A_5), showed single peak at (4.2) ppm due to methyl protons(N-CH_3) , peak at (3.8) ppm due to (OCH_3 protons) and peak at (6.3-7.9)ppm due to aromatic protons. figs.(10).

1H-NMR spectrum for compound (A_6), showed single peak at (4.2) ppm due to methyl protons(N-CH_3) , single peak at (2.2,2.6) ppm due to (CH_3 protons) and peak at (6.2-7.5)ppm due to aromatic protons.

The mechanism of reaction is shown in scheme (2) .



scheme 2: The mechanism of Compound 2a.

Table (1): physical propertiesof Schiff bases (1-6).

Co.	Formula	Mp.C°	Yield ٪	Colour
$C_{28}H_{23}N_3$	162-164	85	yellow	**1**
$C_{32}H_{31}N_3$	150-153	65	yellow	**2**
$C_{28}H_{21}Br_2N_3$	180-183	80	yellow	**3**
$C_{30}H_{27}N_3O_4$	124-127	73	yellow-blue	**4**
$C_{30}H_{27}N_3O_2$	110-113	81	yellow	**5**
$C_{32}H_{31}N_3$	150-154	65	yellow	**6**

Table 2: Physical properties of the Prepared compounds(A_1-A_6).

N٪	H٪	C٪	C.H.N	Yiel٪	Mp.C°	Co.
21.95 21.88	4.21 4.15	64.59 64.26	Calc. Foun.	65	202-204	A1
23.36 23.10	5.42 4.54	77.22 70.32	Calc. Foun.	75	255-258	A2
22.82 22.72	3.47 3.38	60.88 60.77	Calc. Foun.	64	212-213	A3
21.60 20.6	4.38 3.46	62.60 61.6	Calc. Foun.	63	238-240	A4
23.19 23.09	4.64 4.52	66.29 66.2	Calc. Foun.	72	224-226	A5
23.36 23.10	5.42 4.54	71.22 70.32	Calc. Foun.	78	258-260	A6

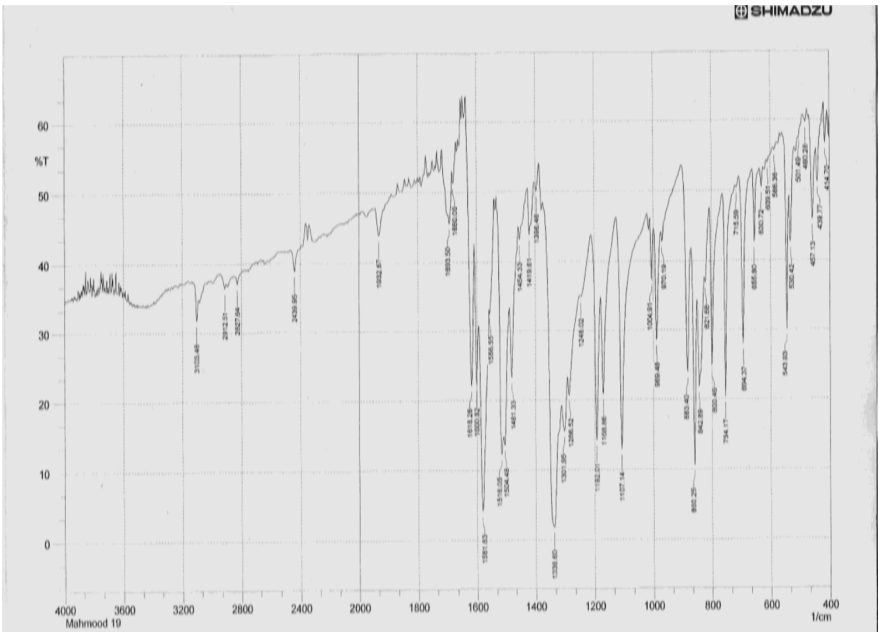


Fig.(1) IR Spectra of Compound(3).

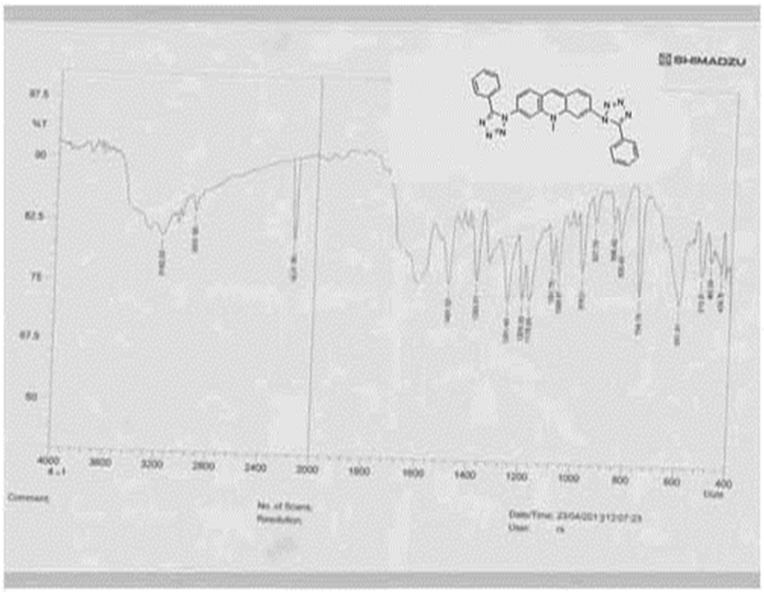


Fig.(2) IR Spectra of 10-methyl-3,6-bis(5-phenyl-1H-tetrazol-1-yl)-4a,10-dihydroacridine.

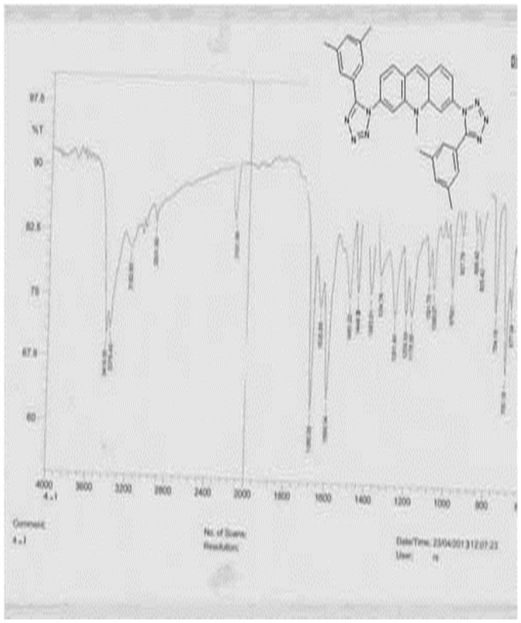


Fig.(3) IR Spectra 3,6-bis(5-(3,5-dimethylphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

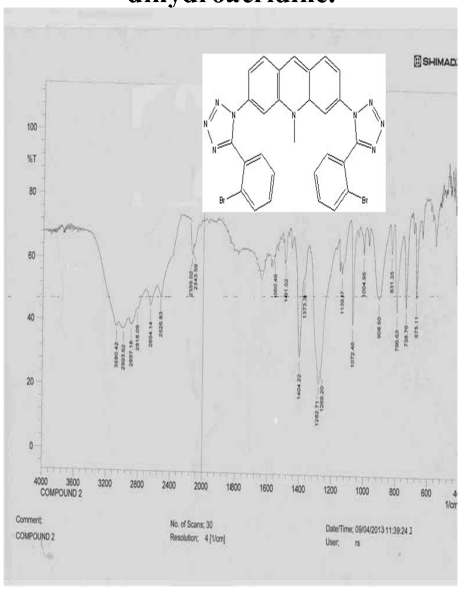


Fig.(4) IR Spectra of 3,6-bis(5-(2-Bromophenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

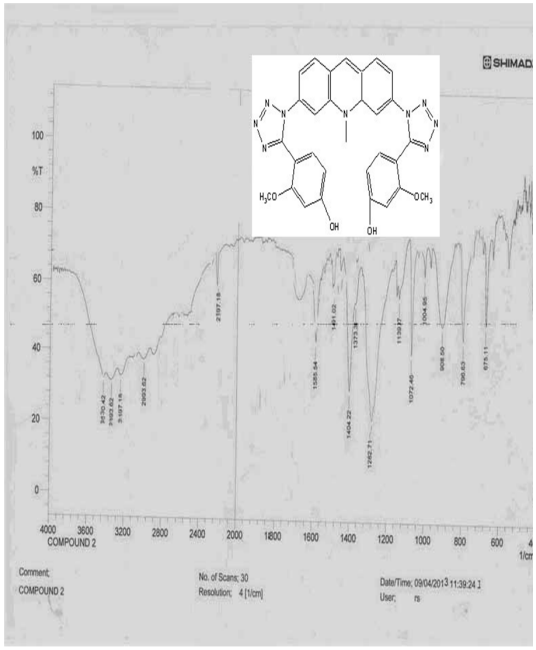


Fig.(5) IR Spectra of 3,6-bis(5-(3-methoxy,5-hydroxyphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

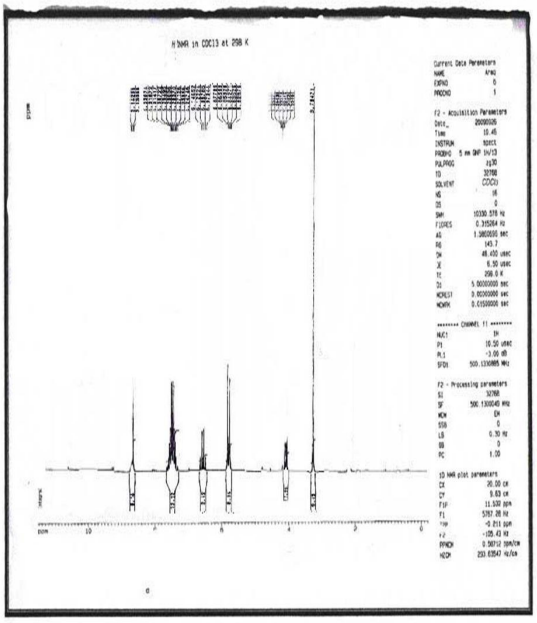


Fig.(6) H^1NMR of 10-methyl-3,6-bis(5-phenyl-1H-tetrazol-1-yl)-4a,10- dihydroacridine.

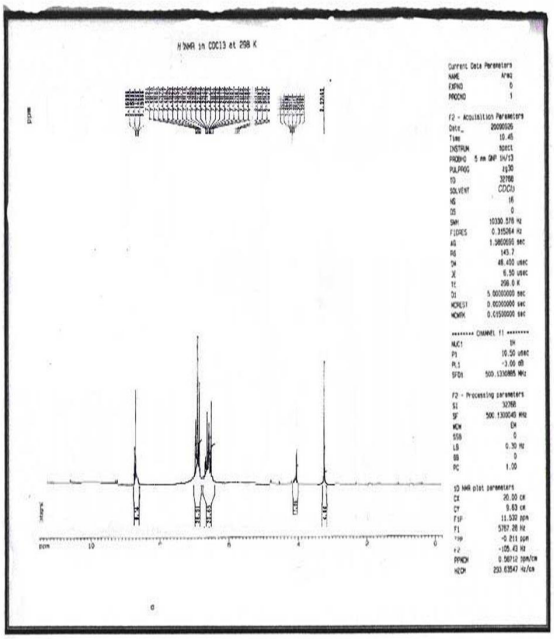


Fig.(7) H^1NMR of 3,6-bis(5-(3,5-dimethylphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

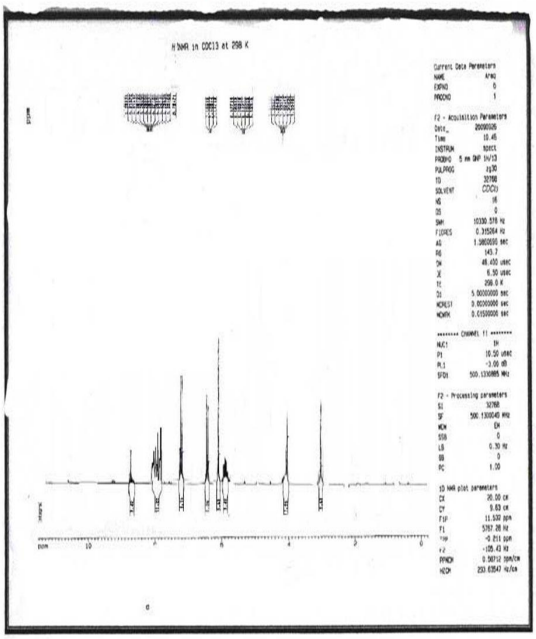


Fig.(8) H^1NMR of 3,6-bis(5-(2-Bromophenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

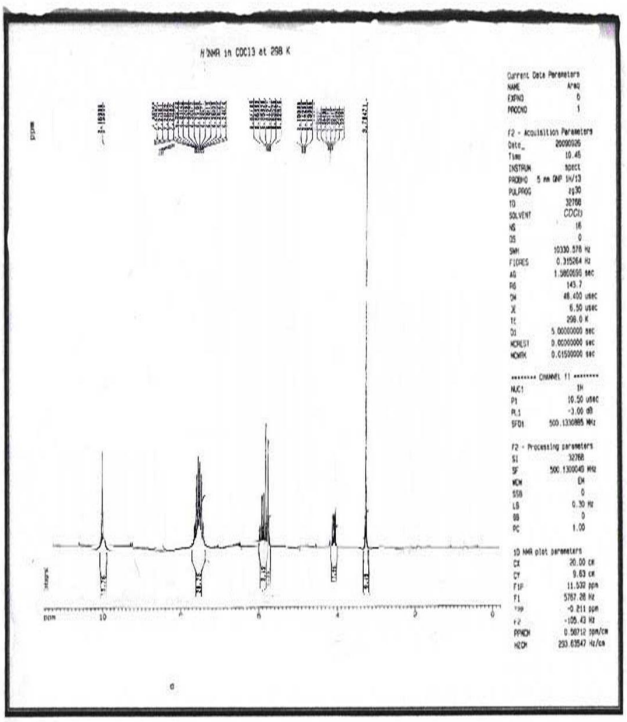


Fig.(9) H^1NMR of 3,6-bis(5-(3-methoxy,5-hydroxyphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

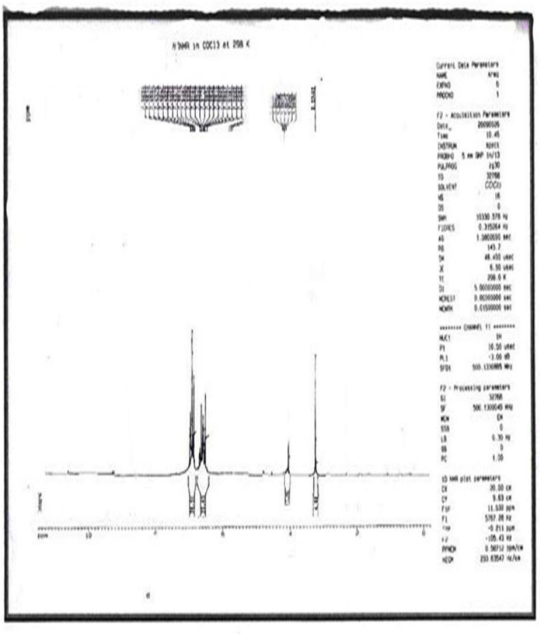


Fig.(10) H^1NMR of 3,6-bis(5-(4-Methoxyphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine

References

1- Satyajit D. S.,(2007), **Chemistry for Pharmacy Students General, Organic and Natural Product Chemistry**, John Wiley & Sons Ltd, England,145.

2-Stephen J.C.,(2012), **Heterocyclic chemistry**, Elsevier: Oxford, UK,Volume 5, p. 157.

3- Engager A.,(2009),**Energetic Derivatives of Tetrazole**, last revision 32,2.

4- Myznikov, L. V., Hrabalek, A.and Koldobskii, G. I.,(2007), **Drugs in tetrazole series**. Chem. Het.Compounds, 43, 1-9.

5- Abdel-Wahad, Z. H., Mashaly M. M. and Faheim A. A., (2005), **Synthesis and characterization of cobalt(II) and cerium (III) complexes of 2,3-dimethyl-1-phenyl-1,3,5-triazine mixed ligand complexes**. Chem. Pap. 59 (1): 25-36.

6- Butter, R. N., Katritzky, A. R., Rees, C. W .(1984) ,**In Comprehensive heterocyclic chemistry**, Vol. 5: Part 4A, Pergamon Press, New York, p. 791 -838.

7- Ostrovskii, V.A.,Koldobskii, G.I., Trifonov, R.E. Tetrazoles.(2008), **In Comprehensive Heterocyclic Chemistry,** III, Elsevier: Oxford, UK, Volume 6, p. 257.

8- Serdar, M., N. Gümrükçü, Ş. Alpay and N. Demirbaş, (2007), **Synthesis of some novel 3,5-diaryl-1,2,4-triazole derivatives and investigation of their antimicrobial activity**. Turk. J. Chem. 31: 315-326.

9- Farghaly, A. R., E. D. Clercq and H. El-Kashef,(2006), **Preparation of pyrazolo[3,4-d]pyrimidines with modification of the substituents at 1-position**. ARKIVOC. x: 137-142.

10- Pradip D., and Berad B.N.(2008), **Synthsis characterization and antimicrobial study of substituted bis-[1, 3, 4]-oxadizole, bis-[1, 3, 4]-thiadizole and bis- [1, 2, 4]- triazole derivatives**, *J.Indian Chem*. Soc. 85:pp. 1153-1158.

11- Butter, R. N., Katritzky, A. R., Rees, C. W.(1984) ,**In Comprehensive heterocyclic chemistry**, Vol. 5: Part 4A, Pergamon Press, New York, p. 791 -838.

12- Etiene. Y., Soulas. R. and Lumbroso. H.,(1964), **The chemistry of Heterocyclic compounds**, Vol. 11: Part 19,Interscience, New York.

13- Miller A.E., Feenev D.J., Ma Y. (1990), **\Synthesis of *N*-(5-Tetrazolyl)-N -(aryl acetyl)urea**.Syn. Commun., *20*, 217–226.

14- Wilson C.O. and Givold O., (1966),**Text book of Organic Medicinal and pharmaceutical Chemistry**, 5th Edition, Ptiman Medical Publishing Co.London coppy right .Cby. J.B. Lippin Cott Company.

15- Voitekhovich S. V., Vorobiev A. N., Gaponik P. N., Ivashkevich O. A. , (2003), **Chemistry of Heterocyclic Compounds** ,Engl. Transl., in press.

16- Burger, A. (1991**),Isosterism and bioisosterism in drug design**. Prog. Drug Res., 37, 287-371.

17- Ruaa M. A., (2012), **Synthesis and Characterization of Some Heterocyclic Compounds (Oxazepine, Tetrazole) Derived from Schiff Bases,** J. of Al-Nahrain University Vol.15 (4), December, pp.60-67.

18-Mastafa M. I., Abass M. and Hassan M., (2000), **Fourth International Electronic Conferences on Synthesis Organic Chemistry** (ECSOC-4),Septermber:1-30.

تحضير وتشخيص بعض المركبات الحلقية الغير متجانسة كالتترازول من قواعد شيف

تاريخ الاستلام 2014/12/25 تاريخ القبول 2016/4/24

حلا شخير لهيمص الشمري , فردوس سامي
قسم الكيمياء \ كلية العلوم \ جامعة بابل

الخلاصة

تم تحضير سلسلة من المركبات خماسية غير المتجانسة كالتترازول من تفاعل قواعد شيف مع ازيد الصوديوم بوجود الأسيتون الجاف وبدرجة (50-55)م^0 ليعطي المركبات الآتية:-

1- 10-Methyl-3,6-bis(5-phenyl-1H-tetrazol-1-yl)-4a,10-dihydroacridine.
2- 3,6-bis(5-(3,5-dimethylphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine
3- 3,6-Bis(5-(2-Bromophenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.
4- 3,6-bis(5-(3-methoxy,5-hydroxyphenyl)-1H-tetrazol-1-yl)-10-methyl-4a,10-dihydroacridine.

شخصت المركبات بعد تحضيرها وتنقيتها بواسطة طيف الرنين النووي المغناطيسي وطيف الأشعة تحت الحمراء ، وأظهرت نتائج التحليل الدقيق للعناصر (C.H.N) توافقا بين النسب المحسوبة نظريا والنتائج التي تم الحصول عليها عمليا .ومن المحتمل إن تكون لهذه المركبات فعالية بايلوجية وأهمية طبية أسوة بالمركبات الخماسية غير المتجانسة الأخرى.

الكلمات المفتاحية:- تترازول، ازيد الصوديوم،قواعد شيف .