AL-Qadisiyha Journal For Science Vol.19 No. 2 Year 2014
ISSN 1997-2490 Hashim M. \ Hasan T.

*Synthesis and characterization of new macrocyclic compound from 4- amino antipyrine

Rcevied : 17\6\2012 Accpted : 13\8\2012

Hashim M. Sheerali Hasan T. Ghanim
Dep. Of Chemistry, College of Education for Women, University of Kufa, Najaf -Iraq

Abstract :

The target of this work involves synthesis of different new macrocyclic derivatives utilizing two different strategies. The first one involved prepare new azo derivative for (4- amino antipyrine), Through reaction between (4-amino antipyrine) with antipyrine in suitable solvent to form (A1), while the second step involved reaction prepared azo compound with several compounds such as (urea , thiourea , quanidine , o- phenylene diamine) to form (A2, A3, A4, A5) compounds.

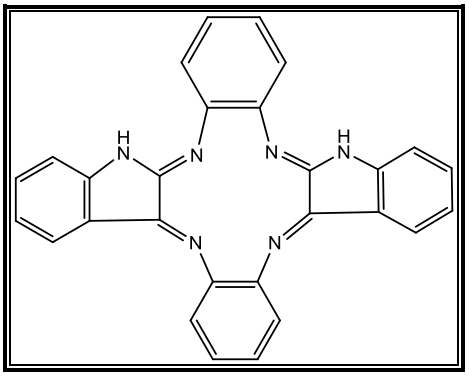
.

Keywords: synthesis, macrocyclic compounds, 4-amino antipyrine.

Introduction

In recent years, there has been a considerable interest in the chemistry of antipyrine and its derivatives. These compounds are reported to exhibit analgesic and anti-inflammatory effects, antiviral, antibacterial, and herbicidal activities [1-5]. Also, they have been used as hair colour additives, in spectrophotometric determination of metal ions and are particularly interesting as promising ligands for the building of polynuclear complexes as models to bioinorganic systems as well as for the discovery of new catalyst precursors[6-10] . Compounds containing an azomethine group are known as imines (Schiff bases). The chelating abilities and analytical and biological applications of these compounds have attracted remarkable attention. These compounds are readily hydrolyzed under acidic conditions leading to active aldehydes which can act as alkylating agents . Besides, several azomethines have been reported to possess remarkable antibacterial, antifungal , anticancer and diuretic activities. Antibiotics such as Streptomycin, Aspergillic acid, Usnic acid and Tetracycline are known to have chelating properties[11].On the other hand the macrocyclic compounds defined as compounds contained nine or more of atoms to form big molecule called macrocyclic[12,13]. This compounds also are called to (super bases) because of contained three or more of dentate atoms, As for instant the compound below[14].:

***The Research is apart of on MSC. Thesis in the case of the First researcher**



Experimental

All the chemicals used were supplied by Merck, Fluka, Himedia and BDH chemicals. FTIR spectra were recorded on SHIMADZU – FTIR 8400 Fourier transform infrared spectrophotometer using KBr discs. Melting point were determined in open capillaries on Thomas Hoover apparatus and were uncorrected. H-NMR spectra (400 MHz) of so samples were recorded in DMSO by employing TMS as internal standard and finally by C.H.N technique, Euro vector S.P.A. E.A 3000-C.H.N. Elemental analyzer .

Preparation (Z)-4,4'-(diazene-1,2-diyl)bis(1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one) (A1).

The titled compound was synthesis from 4-amino antipyrine and antipyrine by diazotization and coupling as given in literature [15],4-amino antipyrine (2.03 gm ,0.01 mol) was converted to the hydrochloric using 1:1 hydrochloric acid and the solution was cooled below (0 C) in an ice-salt bath. A solution of sodium nitrate (0.7 gm , 0.01 mol) in water (20 ml) was chilled using ice-salt bath. The pre-cooled nitrite sodium was then added in small volumes to the cooled amine hydrochloride solution with good stirring. The temperature was always kept in (0-5 C) and small amounts of crushed ice were use when required. The last part of nitrite solution was add slowly and drop wise till a slight access of nitrous acid was present which was indicated by an immediate colour, imparted to a starch potassium iodide paper. After keeping the diazonium chloride solution in ice bath for a few minutes. The (antipyrine) (2.04 gm , 0.01 mol) was dissolved in (5 ml) of sodium carbonate (10%) solution. The solution was then cooled below (5 C) in an ice bath followed by the direct addition of (25 g) of crushed ice. The cold diazonuim chloride was added very slowly to the solution of antipyrine with vigorous stirring.

The colour of solution became brown red and a solid product separation slowly. After the addition of the entire amount of diazo compound, The

Comp no.	M.F	M.wt	m.p	Yield %	Color	Rf (Benz:4 Meth:1)	Time (hrs)	Solvent
A1	$C_{22}H_{22}N_6O_2$	402	196-198	85.7	yellow	-	24	Ethanol
A2	$C_{26}H_{26}N_8$	450	262-264	81.5	brown	0.81	12	Ethanol
A3	$C_{23}H_{23}N_9$	425	232-234	71.8	Red brown	0.66	14	Ethanol
A4	$C_{23}H_{22}N_8S$	442	242-244	80.2	Pale yellow	0.85	14	Ethanol
A5	$C_{23}H_{22}N_8O$	426	248-250	75.3	Pale yellow	0.61	16	Ethanol

mixture was allowed to stand in the bath for 30 min. with occasional stirring. The solid product obtained was then filtered, washed well with cold water and recrystallised from alcohol. Physical properties of compound (A1) are listed in table. (1)**.**

Table (1) : physical properties of the prepared compounds in this work

Preparation (4Z,8aE,14E)-2,3,6,7-tetramethyl-1,8-diphenyl-1,2,7,8-tetrahydrobenzo[f]dipyrazolo[4,3-c:3',4'-i][1,2,5,8]tetrazecine. (A2).

A mixture of (4.02gm, 0.01mol) of prepared azo (A1) and (*o*-phenylene diamine) (1.08gm, 0.01mol) in 20 ml of ethanol (15ml) was reflux for (12 hrs), After than it is cooled to room temperature, then the precipitate was filtrated and recrystlized from ethanol [(16)]. Physical properties of compound (A2) are listed in table (1)**.**

Preparation (4Z,8aE,11E)-2,3,6,7-tetramethyl-1,8-diphenyl-7,8-dihydro-1H-dipyrazolo[4,3-c:3',4'-h][1,2,5,7]tetrazonin-10(2H)-imine (A3).

A mixture of (4.02gm, 0.01mol) of prepared azo (A1) and (quanidine) (o.56gm, 0.01mol) in 20 ml of ethanol (15ml) was reflux for (14 hrs), After than it is cooled to room temperature, then the precipitate was filtrated and recrystlized from ethanol. Physical properties of compound (A3) are listed in table (1)**.**

Preparation (4Z,8aE,11E)-2,3,6,7-tetramethyl-1,8-diphenyl-7,8-dihydro-1H-dipyrazolo[4,3-c:3',4'-h][1,2,5,7]tetrazonine-10(2H)-thione (A4)

A mixture of (4.02gm, 0.01mol) of prepared azo (A1) and (quanidine) (o.72gm, 0.01mol) in 20 ml of ethanol (15ml) was reflux for (14 hrs), After than it is cooled to room temperature, then the precipitate was filtrated and recrystlized from ethanol. Physical properties of compound (A4) are listed in table (1)**.**

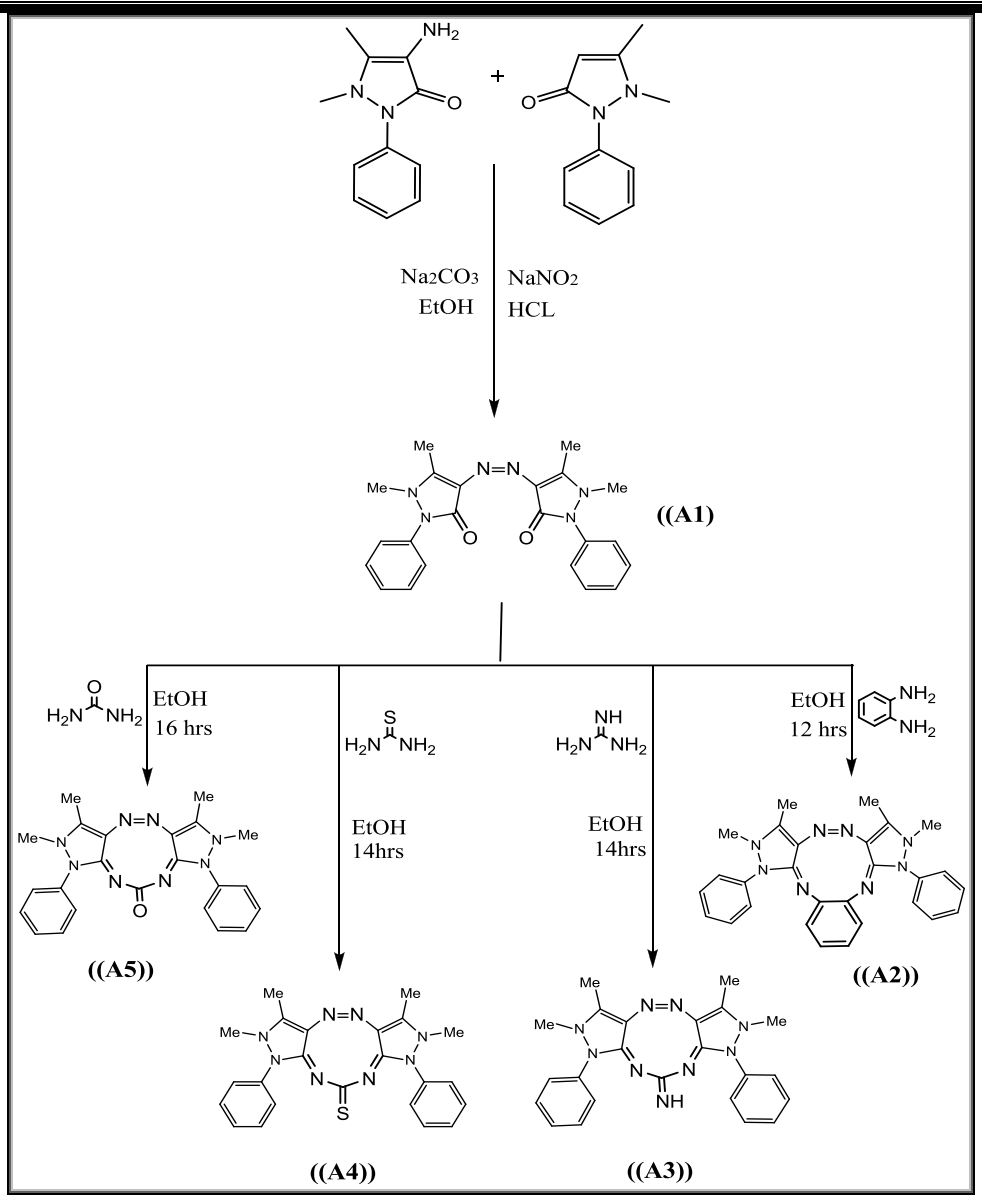
Preparation (4Z,8aE,11E)-2,3,6,7-tetramethyl-1,8-diphenyl-7,8-dihydro-1H-dipyrazolo[4,3-c:3',4'-h][1,2,5,7]tetrazonin-10(2H)-one (A5)

A mixture of (4.02gm, 0.01mol) of prepared azo (A1) and (urea) (o.60gm, 0.01mol) in 20 ml of ethanol (15ml) was reflux for (16 hrs), After than it is cooled to room temperature, then the precipitate was filtrated and recrystlized from ethanol. Physical properties of compound (A5) are listed in table (1)**.**

The prepared compounds were colored solids with sharp melting point and offered in good yields.

Results and discussion :

Azo compound and macrocyclic compounds are very important organic compound having wide spectrum of biological activities. The target of this work was performed by following different strategies, .The first one involved prepare new azo derivative for (4- amino antipyrine), Through reaction between (4-amino antipyrine) with antipyrine in suitable solvent to form (A1), while the second step involved reaction prepared azo compound with several compounds such as (urea , thiourea , quanidine , *o*- phenylene diamine) to form (A2, A3, A4, A5) compounds.



FTIR spectra of the prepared compounds in this work are listed in table (2) and figures (1, 2, 3 ,4 ,5)

Table (2) : FTIR spectra of the prepared compounds in this work.

Comp No.	Imine ν (C=N)	Azo ν (N=N)	Alkenes ν(C=C)	Aromatic ν (C- H)	Aliphatic ν (C- H)	Other
A1	-	1539	1647 1591	3091	2993	1680 **ν (C=O)**
A2	1640 1587	1532	1645 1589	3088	2998	-
A3	1660,1600	1529	1650 1585	3055	2978	3407 **ν** (N-H)
A4	1660,1605	1535	1645 1591	3120	2999	1561 **ν (C=S)**
A5	1650 ,1670	1537	1645 1597	3055	2978	1695 **ν (C=O)**

On the other hand (C.H.N) data of the prepared compounds in this work are listed in table (3)

Table (3) C.H.N Analysis for prepared compounds.

Compound NO.	C%		H%		N%		S%	
	calculated	found	calculated	found	calculated	found	calculated	found
A1	65.6	65.5	5.4	5.5	20.8	21.0	-	-
A2	70.8	70.5	5.4	5.5	20.2	21.1	-	-
A5	64.7	64.5	5.1	5.2	26.1	26.2	-	-

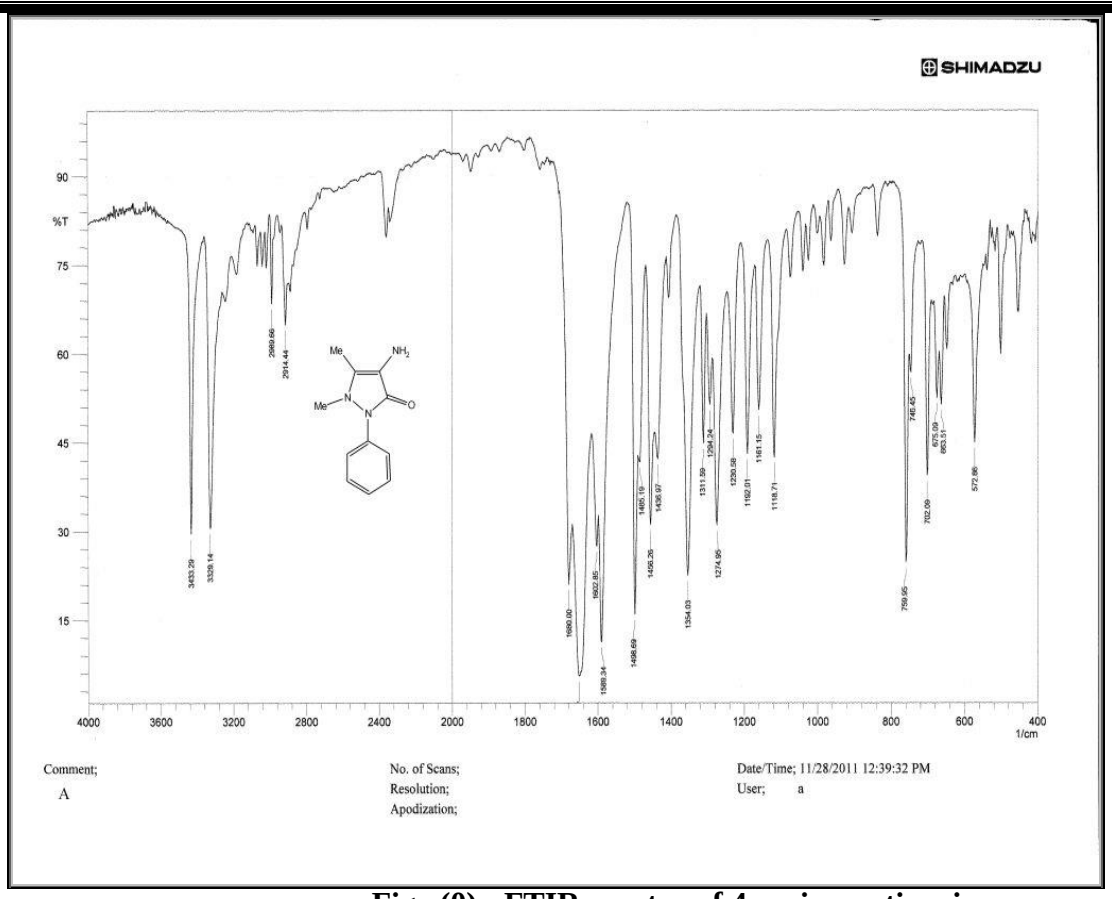


Fig. (0) : FTIR spectra of 4-amino antipyrine

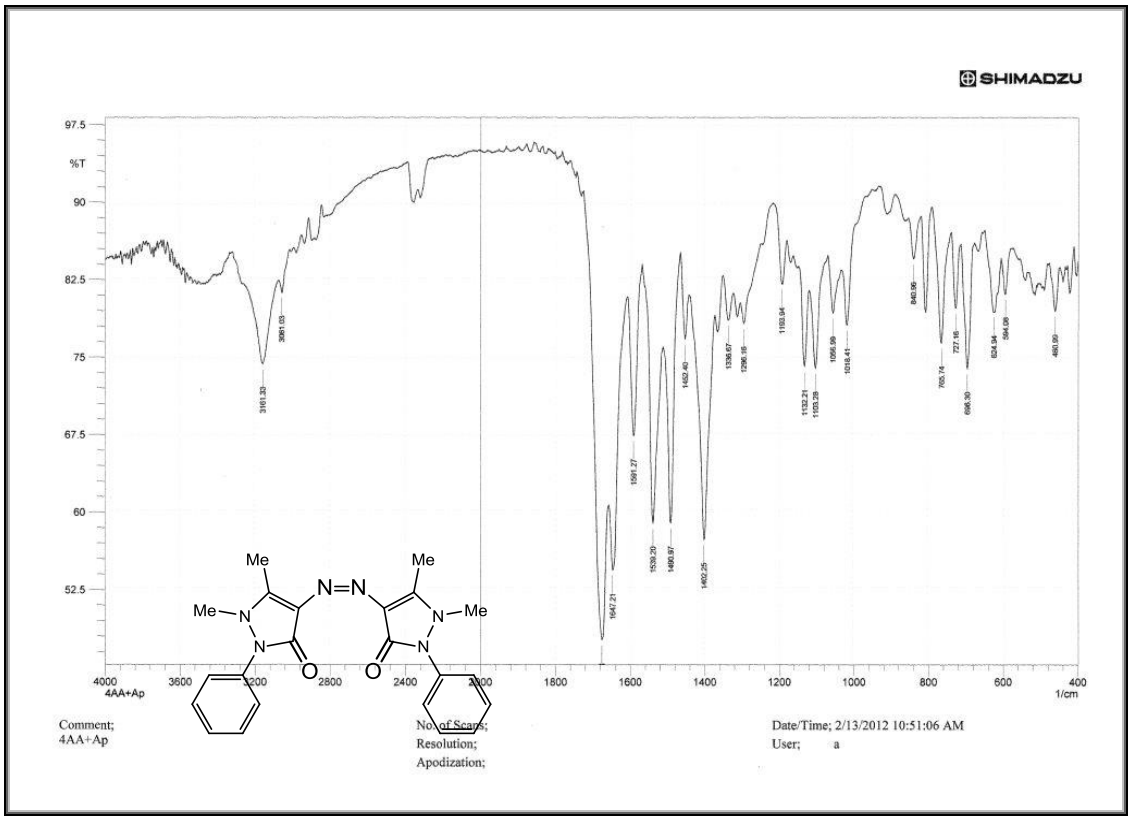


Fig. (1) : FTIR spectra of A1 compound

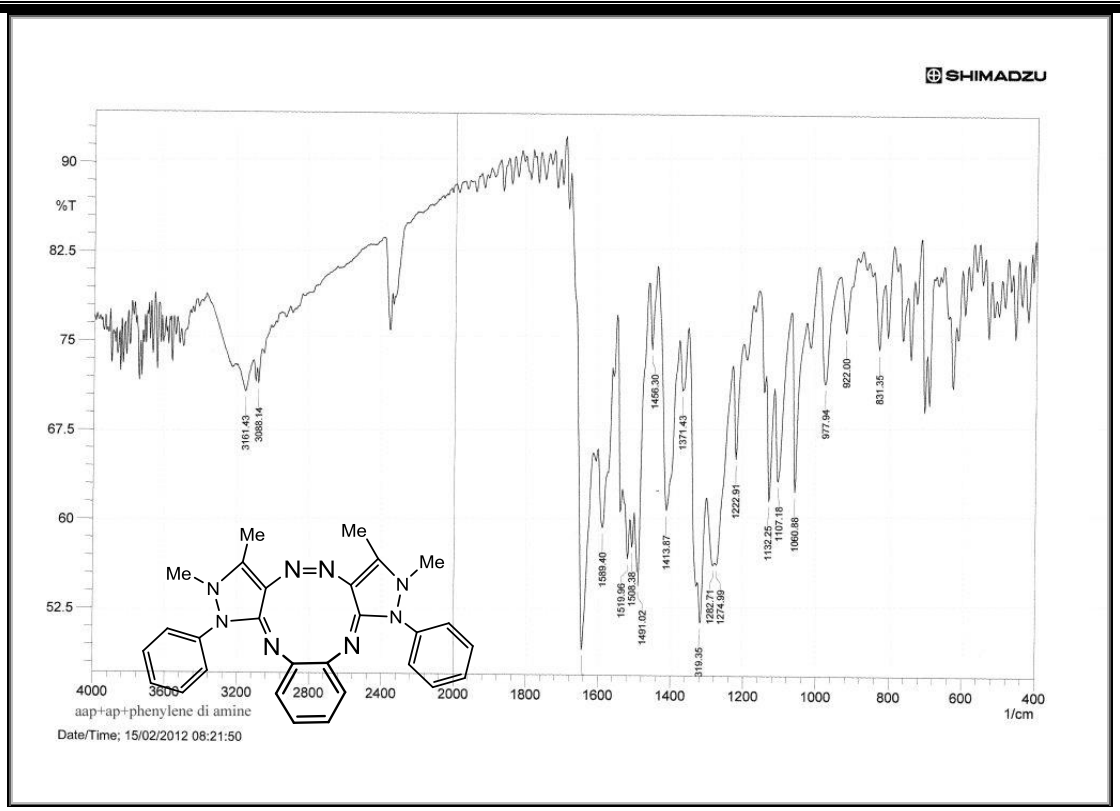


Fig. (2) : FTIR spectra of A2 compound

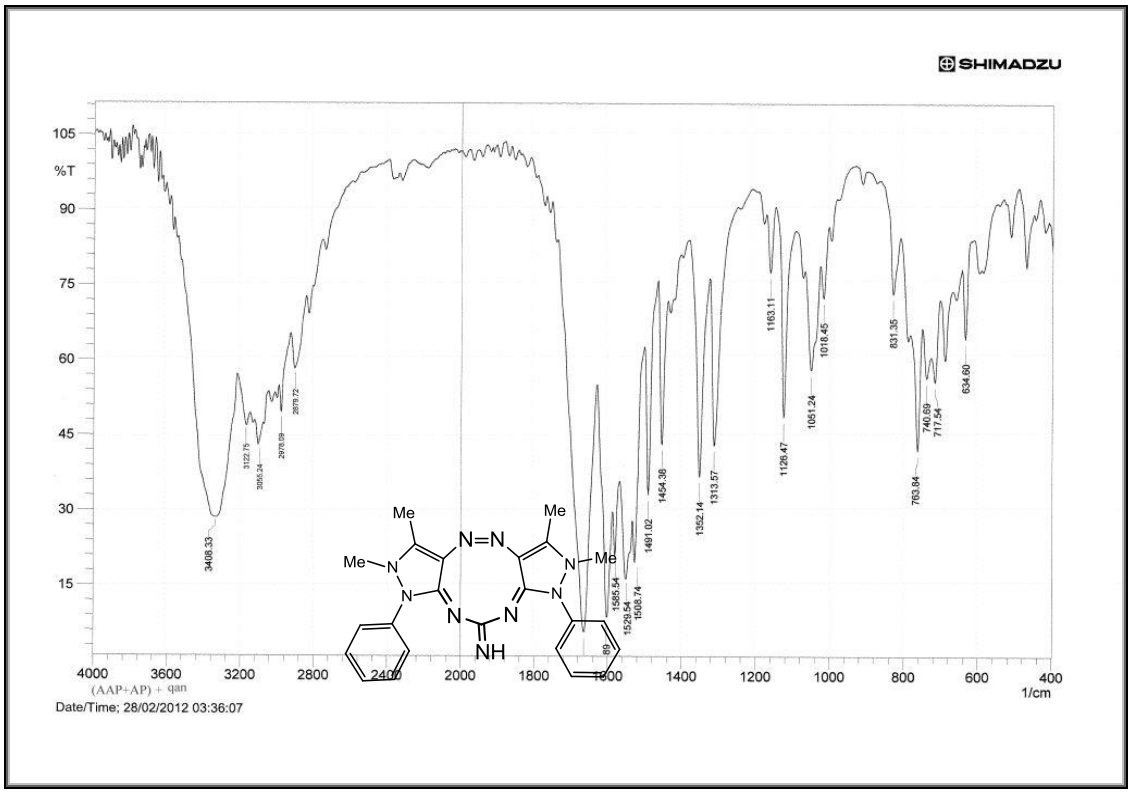


Fig. (3) : FTIR spectra of A3 compound

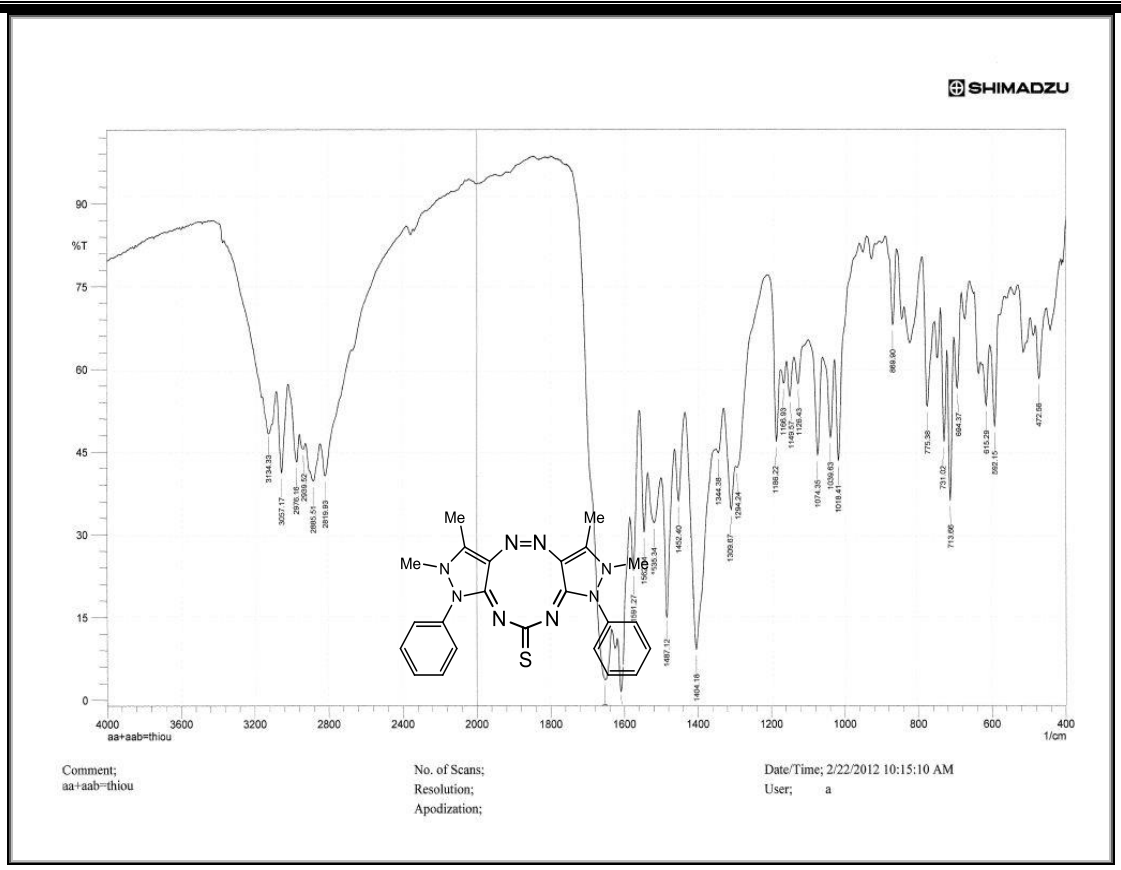


Fig. (4) : FTIR spectra of A4 compound

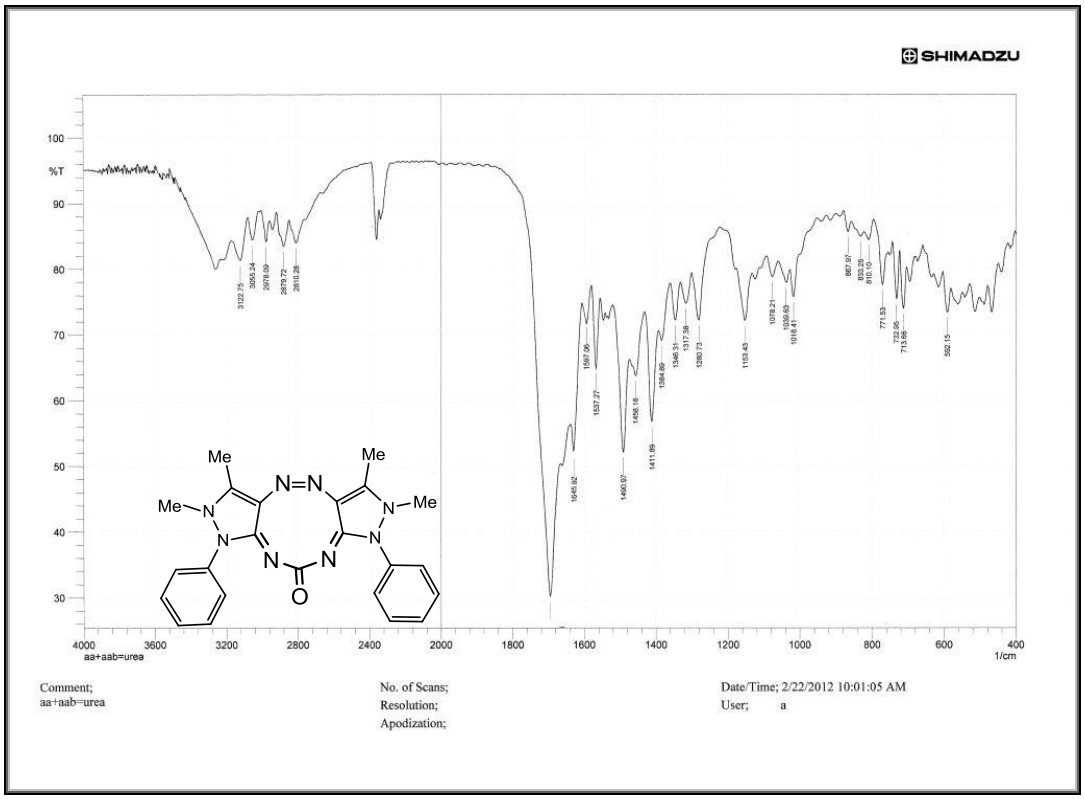


Fig. (5) : FTIR spectra of A5 compound

On the other hand ^{1}H-NMR spectrum of compound [A1] showed singlet signals at δ=(2.3, 3,3) ppm belong to (-CH_3) groups proton of (antipyrine) and multiplet signals at δ=(7.2-7.5) ppm which were assigned to aromatic protons of antipyrine.

^{1}H-NMR spectrum of compound [A2] showed singlet signal at δ=(2.2, 3.0)ppm belong to (-CH_3) groups proton of (antipyrine) and multiplet signals at δ=(7.2-7.5)ppm which were assigned to aromatic protons of (antipyrine) and (o- phenylene diamine).

^{1}H-NMR spectrum of compound [A5] showed singlet signal at δ=(2.4, 3.9)ppm belong to (-CH_3) groups proton of (antipyrine) and multiplet signals at δ=(7.3-7.5)ppm which were assigned to aromatic protons of (antipyrine) and (o- phenylene diamine).

^{1}H-NMR spectra of the prepared compounds in this work are showed in diagrams No. (6, 7 and 8).

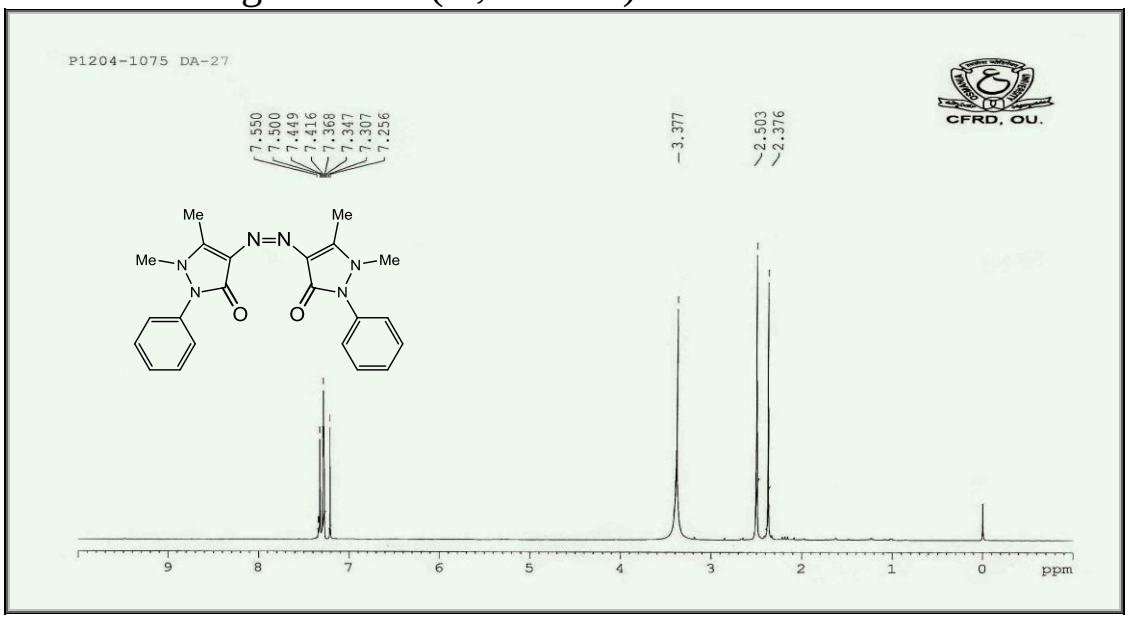


Fig. (6) : H-NMR spectra of A1 compound

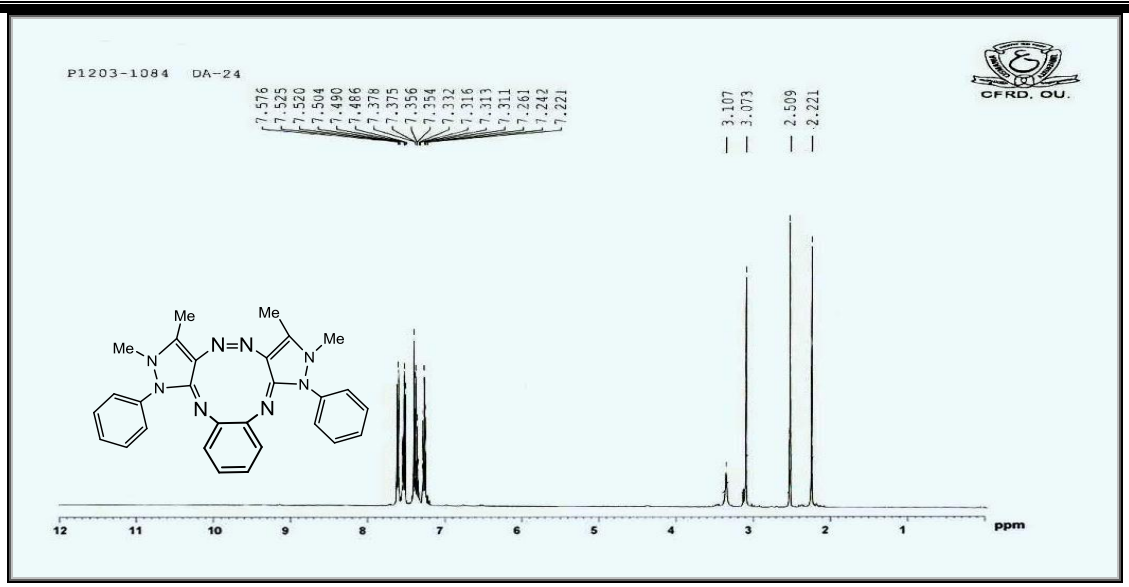


Fig. (7) : H-NMR spectra of A2 compound

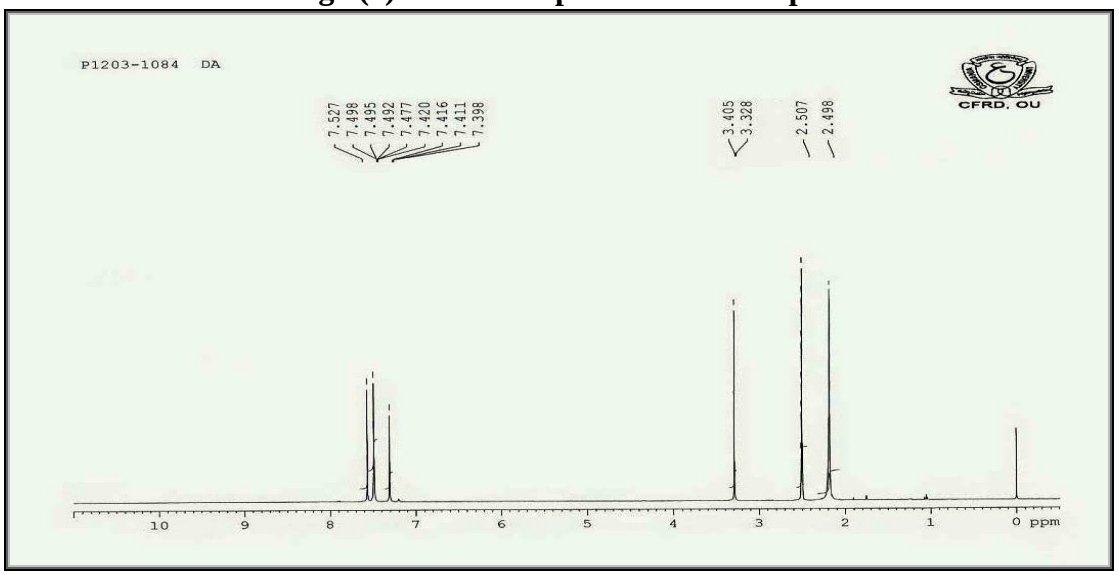


Fig. (8) : H-NMR spectra of A5 compound

Reference

[1] Sayed, C. H.; Hamed, A. A.; Meligi, G. A.; Boraie, W. E.; Shafik, M. *Molecules* **2003**, *8*, 322.
[2] Zhang, Y.; Yizhi, L.; Hanbin, T.; longgen, Z. *Acta Cryst.***2002**, *E 58*, 24.
[3] Turan-Zitouni, G.; Sivaci, M.; Kilic, F. S.; Erol, K. *Eur. J Med. Chem.* **2001**, *36*, 685.
[4] Sondhi, S. M.; Sharma, V. K.; Singhal, N.; Verma, R. P.; Shukla, R.; Ranghubir, R.; Dubey, M. P. *J. Phosphorus Sulfur,Silicon and Relat. Elem.* **2000**, *56*, 21.
[5] Burdulene, D.; palaima, A.; Stumbryavichyute, Z.; Talaikite, Z. *Pharm. Chem. J.* **1999**, *33*, 191.
[6] Evstopov, A. N.; Yavorovskaya, V. E.; Vorobev, E. S.; Kudonogova, Z. P.; Gritsenko, L. N.; Schmidt, E. N.; Medevedeva, S. G.; Filimonov, D. V.; Prishchep, T. P.; Saratikov, A. S. *Pharm. Chem. J.* **1992**, *26*, 426.

[7] Sayed, G. H.; Radwan, A.; Mohamed, S. M.; Shiba, S. A.; Kalil, M. *Chin. J. Chem.* **1992**, *10*, 475.
[8] Daoudi, M.; Larbi, N. B.; Benjelloun, D.; Kerbal, A.; Launay, J. P.; Bonvoisin, J.; Jaud, J.; Mimouni, M.; Hadda, J.B. *Molecules* **2003**, *8*, 269.
[9] Sorrell, T. N.; Vankai, V. A.; Garrity, M. L. *Inorg. Chem.***1991**, *30*, 207.
[10] Togni, A.; Venanzi, L. M. *Angew. Chem. Int. Ed. Eng.* **1994**, *33*, 497.
[11] N. Raman, L. Mitu, A. Sakthivel. and M.S.S. Pandi "Studies on DNA Cleavage and Antimicrobial Screening of Transition Metal Complexes of 4-Aminoantipyrine Derivatives of N2O2 Type " *J. Iran. Chem. Soc.*, Vol. 6, No. 4, December (2009), pp. 738-748.
[12] V. Arun , *Ph.D Cochin University of Science and Technology*, JUNE **2009**.
[13] D. P. Singh, V. G. Krishan and K. Jain; *J. Serb. Chem. Soc.* **(2011)** *76 (3) 385–393***.**
[14] D. P. Singh, R. Kumar ,*Acta Chim. Slov*, ,**(2008),** 34 , 3, 238–240 ,.
[15] M. L. Harikumaran Nair and A. Shella."Synthsis,spectral, thermal and electrochemical studies of oxomolybdenum(V) and dioximolybdenum(VI) complexes of an azo dye derived from 4-amino antipyrine "*Indian Journal* , Vol 47A,dec **2008**, pp. 1787-1792.
[16] Ahmad. T. Salem, " Synthesis and characterization of new heterocyclic compound from some heterocyclic amines and study of biological activity of some of these compounds" P.hD thesis *AL-Nahrain university*, (**2008)**.

*تحضير وتشخيص مركبات حلقية كبيرة من 4-امينو انتي بايدين

تاريخ الاستلام : 2012\6\17 تاريخ القبول 2012\8\13

هاشم مشتاق جعفر حسن ثامر غانم
جامعة الكوفة \ كلية التربية للبنات

الخلاصة

هدف البحث : تحضير مشتقات حلقية كبيرة جديدة للمركب (4-amino antipyrine) ويتم ذلك من خلال اتجاهين، **الاتجاه الأول**: يتضمن تحضير مشتق ازو جديد للمركب (4-amino antipyrine) من خلال تفاعل الأخير مع الركب (antipyrine) في مذيب مناسب لتكوين المشتق **(A1)**.
أما **الاتجاه الثاني** : يتضمن تفاعل الازو المحضر مع عدد من المركبات المختلفة مثل (urea , thiourea , quanidine , o- phenylene diamine) لتكوين المركبات (A2, A3, A4, A5) .

*البحث مستل من رسالة ماجستير للباحث الاول