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Synthesis and Characterization of New Benzothiazole-derived Schiff Bases Metal Complexes

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Abstract:

Nitrogen-comprising heterocyclic compounds and their derivatives have empirically been invaluable as therapeutic agents. Fundamentally, 4-chloro-6-nitro-2-amino-1,3-benzothiazole **1** was synthesized via bromination of 2-chloro-4-nitro aniline with ammonium thiocyanate. This new heterocyclic haloorganoamino-1,3-benzothiazole derivative, was a starting material, which condensed and tethered with three different aromatic aldehyde pendant arm in presence of ethanol and glacial acetic acid isolating an interesting sequence of tridentate Schiff bases **2-4**. These compounds were used for complexation reactions in 1:1 (metal: ligand) stoichiometry to obtain heteroleptic Al(III), Ni (II) and K(I) benzothiazole chelates **5-7(a-c)** of the type [Al(L)Cl_2, Ni(L)Cl, K(L) {L = Schiff base derivatives}]. The newly synthesized complexes were characterized by the melting points, IR and some of them by ^{1}H-NMR spectroscopy and only one by X-ray techniques. The structures of complexes were anticipated from the spectroscopic studies.

Keywords: aniline, 1,3-benzothiazole, ligand, metal complexes, Schiff bases.

Introduction:

Benzothiazole is an organic heterobicyclic compound consists of a five-membered 1,3-thiazole ring comprising nitrogen and Sulphur atoms fused to a benzene ring. The benzothiazole ring is weak base, has various positions and is directed according to Sulphur, which is in No.1 position. The nine atoms of the bicycle together with the attached substituents are coplanar. One of the most important parts of scaffolds for the preparation of dyes that are used in the identification of lanthanide metal ions in aqueous media is benzothiazole ring [1].

Benzothiazole derivatives are industrially identified as antioxidant [2], corrosion inhibitors and surface-active chelating agents for mineral processing [3]. Benzothiazole nucleus are valuable for their biological activities and found as anticancer, antimicrobial, antidiabetic, anti-inflammatory, antiviral, antileishmanial, and antiviral [4]. It is known as a plant metabolite, a xenobiotic and an environmental contaminant [5]. Benzothiazole is found as well rarely in marine and terrestrial natural compounds with significant pharmacological properties, as they act as aroma components in tea leaves and cranberries that are formed from *Aspergillus* fungi [6]. Copper complexes of 2-aminobenzothiazole have been used as a versatile material for different derivatives [7]. It has also been found that the selective functionalization of benzothiazole with diverse substituents grows their range of action in many fields. Various recent synthetic processes have been developed for the preparation of benzothiazole compounds associated with green chemistry [8]. Benzothiazole derivatives linked with some heterocyclic ring such as thiadiazole have a high biological activity against some bacterial [9]. Benzothiazole Schiff's base is a nitrogen analogue of an aldehyde/ketone in which the carbonyl group has been switched by an imine or azomethine group. They have been used widely as antioxidant, antimicrobial, antifungal, anti-inflammatory, anticancer and cytotoxic activity [10-13]. In this study we planned to prepare a new

substituted Schiff's base ligands derived from benzothiazole, and combined them with some metal ions [Al(III), Ni(II), K(I)] and characterizing them by spectral methods. We expect this work would grow to design better molecules, which can improve biological specificity, and will be further investigated in the future.

Materials and Methods:

All chemicals are provided by B.D.H and Sigma-Aldrich and used without further purification.

With the Stuart Melting point apparatus, melting points were confirmed and were uncorrected. The key functional groups were identified via Fourier-transform infrared spectroscopy analysis, and recorded in the scanning range of 400−4000 cm^{-1} at room temperature on Shimadzu (FT-IR-8300S) spectrophotometer by KBr disc in Ibn Sina State Company (ISSC). ^{1}H-NMR spectra have been used to confirm the placement of protons stating signals as δ-values in ppm for the achieved compounds, and the values are recorded on a BRUKER (400 MHz) instrument operating at 300 MH_Z with tetra methyl silane as an internal standard in $CDCl_3$ and DMSO-d_6 as solvent, measurements were made at the Chemistry Department, Al Baath University-Syria. One of the resulted complexes was experienced for the first time with X-ray device type Shimadzu LabX-XRD-6000 X-RAY Diffractometer.

Results and Discussion:

1. Synthesis and Characterization of 4-chloro-6-nitro-2-amino-1,3-benzothiazole 1. The titled compound **1** presented in this work was combined from 2-chloro,4-nitroaniline and ammonium thiocyanate via bromination, Fig.1, according to published procedures [14]. The structural examination of the complex was based on its melting point and spectral (FT-IR and ^{1}HNMR) records, and the conformation of 4-chloro-6-nitro-2-amino-1,3-benzothiazole **1** has been confirmed. The FT-IR spectrum showed significant two bands at 3390 and 3460 cm^{-1} that could be attributed to asymmetric and symmetric stretching vibrations of the NH_2 group [15]. Also, there is band observed at around 1620 cm^{-1} owing to cyclic (C=N) stretching. Bands obtained at 3062-3053 are due to the aromatic (C-H) stretching and bending. Besides, the appearance of two bands at 1504 and 1539 cm^{-1} belongs to aromatic (C=C) stretching.

A Band noticed at about 1157 cm^{-1} is owing to (C-S-C) stretching. A Band observed at 1431 cm^{-1} is due to the (C-N) stretching vibration [16]. (C-Cl) stretching is observed at 1080 cm^{-1}. ^{1}H-NMR spectrum of compound **1** showed the following characteristic chemical changes (DMSO-d_6, ppm). Five aromatic protons were located at δ 7.36-7.76, which was approximately in agreement with the literature review [17]. Singlet signal of amino protons NH_2 has been located at δ 4.50. Besides, a particular peak at δ 2.5 that was owing to DMSO.

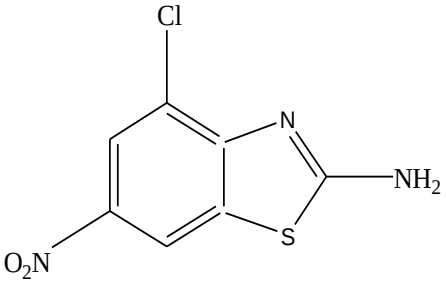


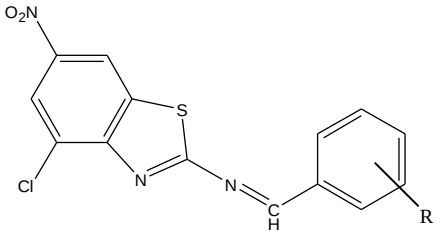
Figure 1. Compound 1

2. Synthesis and Characterization of 4-[(4-chloro-6-nitro-benzothiazol-2-ylimino) methyl]-2-methoxyphenol, N-(4-chloro-6-nitro-benzothiazol-2-yl)-1-(2,4-dichlorophenyl) methanimine and 4-[(4-chloro-6-nitro-benzothiazol-2-ylimino) methyl] phenol.

Generally, condensation reaction between equimolar quantity of compound **1** and appropriate benzaldehydes in absolute ethanol and glacial acetic acid gave the titled compounds **2**,**3** and **4** [18], which was the main route to prepare series of Schiff bases. The structures of these Schiff bases were recognized utilizing their spectral (FT-IR and ^{1}H-NMR) records. The existence of stretching band in the region between 1230-1252 cm^{-1} owned to (=N-N=C-) cyclic group, all the expected bands for olefinic (C-H), (C=C) aromatic, endocyclic (C=N) and exocyclic imine group. In addition, broadening vibrations and out of plane bending of substituted aromatic ring was observed.

The ^{1}H-NMR spectra for compounds **2**,**3** and **4**, are all almost devoid of the NH_2 resonance at 4.50 ppm found in **1** showing full deprotonation of the starting material. This is confirmed by the lack of a NH_2 absorption at 3390-3460 cm^{-1} in the IR spectrum for compounds **2**,**3**,**4** compared with the starting material. Besides, IR spectra revealed the absence of band at 1735 cm^{-1} due to carbonyl (C=O) stretching vibration. However, strong new bands appeared in the range 1633-1639 cm^{-1} (for the three Schiff bases) referred to the frequency of the azomethine group (HC=Nimine) connection [19]. This means that the benzaldehyde and amino moieties of the starting reactants had been transformed to their corresponding Schiff bases Fig.2. Bands at 3022, 3052 and 3064 cm^{-1} along with the bands at 2813, 2863 and 2866 cm^{-1} were attributed to (C-H) aromatic and aliphatic. The bands refer to (C=Caromatic) group were determined at 1466 and

1557 cm^{-1} [20]. The singlet signal of OH proton vibrate at δ 4.3, three-four aromatic ring protons of phenyl bridged to substituted benzothiazole presented as singlet signals at range δ 6.8 – 8.1 ppm. Furthermore, the singlet signal at δ 10.1 was assigned to (C-H) proton. Therefore, NMR study is adjusted to the results of the previous investigations. Tab. 1 shows all the other spectral data.



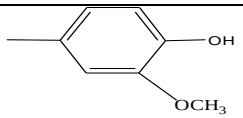
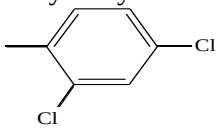
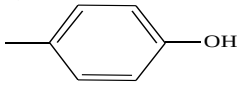
R= 4- hydroxy-3-methoxy **2**
R= 2,4- dichloro **3**
R= 4- hydroxy **4**

Figure 2. Compounds 2,3,4

Table 1. FT-IR υ(KBr) cm^{-1} spectral data of compound 2-4

Comp. No.	$\upsilon_{(C-H)}$ aromatic cm^{-1}	$\upsilon_{(C-H)}$ aliphatic cm^{-1}	$\upsilon_{(C=N)}$ exo cm^{-1}	$\upsilon_{(C=N)}$endo cm^{-1}	Others cm^{-1}
2	3022	2813	1633	1620	$\upsilon(NO_2)$ 1381 υ(OH) 3360 (OCH_3) 2830
3	3052	2863	1635	1642	$\upsilon(NO_2)$ 1398 C-Cl 1080
4	3064	2866	1639	1651	$\upsilon(NO_2)$ 1405 υ(OH) 3375

Table 2. Physical properties and percentage for compounds 2-4

Comp. No.	R	Color	M.p °C	Yield %
2	 4- hydroxy-3-methoxy benzaldehyde	Yellow	182-184	77%
3	 2,4- dichloro benzaldehyde	Light yellow	171-173	73%
4	 4- hydroxy benzaldehyde	Yellow	120-124	72%

3. Synthesis and Characterization of 5,6,7(a-c).

These compounds were combined from the reaction of Schiff bases **2**,**3**,**4** with metal salts ($AlCl_3$, $NiCl_2$ and KBr) in different solvents. Nine configurations are assessed, as schematically shown in Fig. 3. All the present synthesized metal complexes were insensitive towards air/moisture and were prepared by the stoichiometric reaction of the analogous Schiff base in molar ratios M: L 1:1. These complexes were characterized by means of their FT-IR and some of them by ^{1}H-NMR spectroscopic methods. The IR spectra of the Al(III), Ni (II) and K(I) chelates revealed that the three Schiff bases joined the metal atom in three different instructions, therefore showing ligand tridentate performance. The azomethine band appeared at 1633-1623 cm^{-1} shifted to lower frequency providing an evidence for azomethine nitrogen contribution in the complexation. In addition, the nitrogen of the benzothiazole bunch was involved in chelation, which was detected through the transference of (C=N) band located at 1620 cm^{-1} to lower frequency by 10-15 cm^{-1} [21]. Furthermore, conclusive clue for the coordination of the three Schiff bases with the metal atoms (Al, Ni and K) was presented by the attendance of weak low-frequency new band seen at 545-565 cm^{-1} denoted to the metal-nitrogen band. This band only appeared in the spectra of the metal complexes, but not in the spectra of the non-complexed Schiff bases.

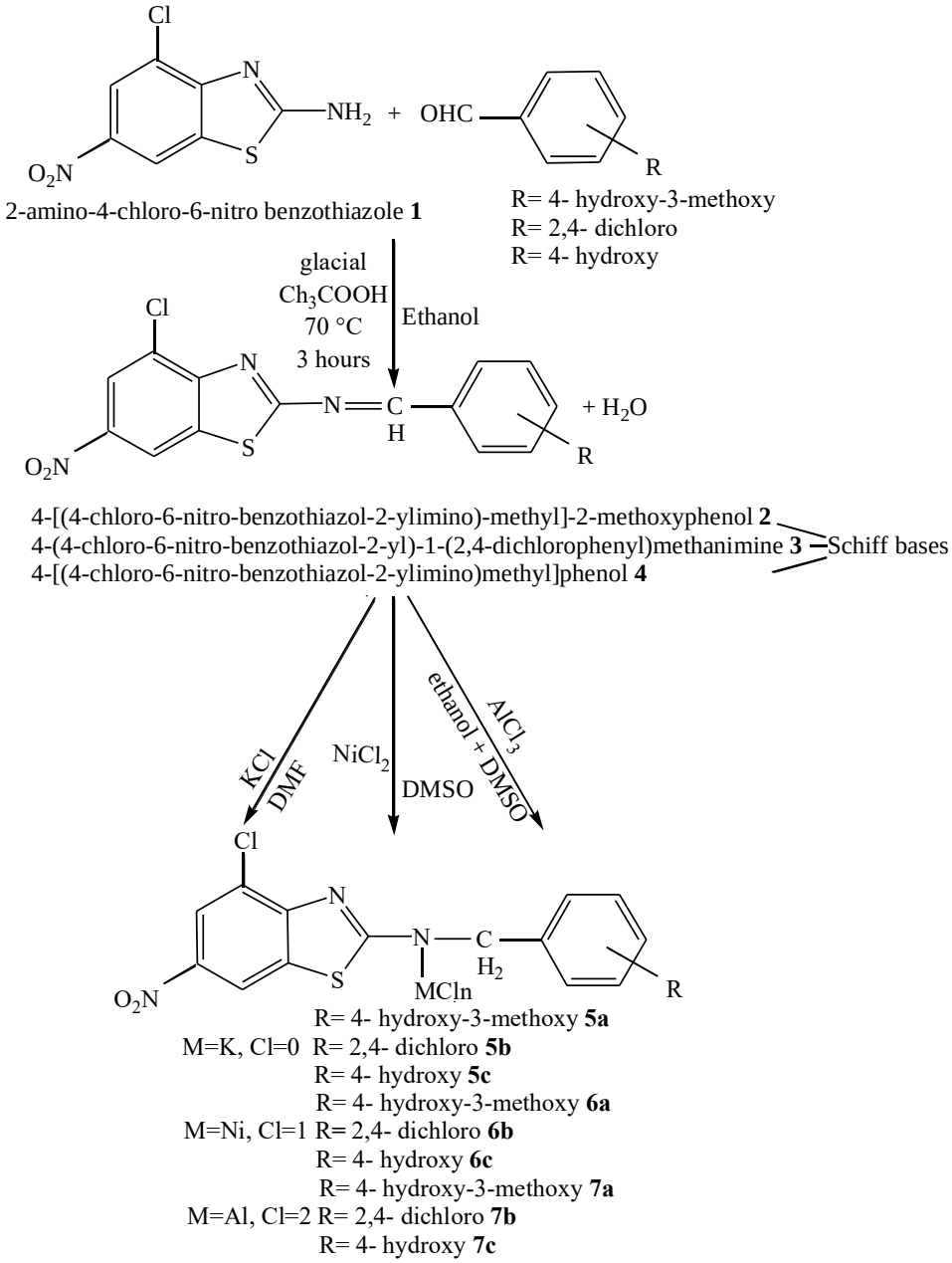


Figure 3. Schematic methodology used for synthesis of benzothiazole derivatives and their complexes

X-ray diffraction (XRD) scans involved powders of one complex **6a** mounted on a no-background N plate. The outcomes of 27 XRD scans employing Cu radiation 5° to 34° 2-theta for most scans displayed that the strongest three peaks were 3.354 Å, 3.421 Å and 3.934 Å Fig. 4. FWHMs represented at range 0.52600-0.46330 (full peak widths at half maximum intensity values in degrees 2 theta). The unit cell parameters need to be examined for further studies. Tab. 3 demonstrates the strongest three peaks.

Table 3. X-ray spectral data of compound 6a.

Strongest 3 peaks							
No.	Peak no.	2Theta(deg)	d(A)	I/I1	FWHM(deg)	Intensity(Counts)	Integrated Int(Counts)
1	27	26.5530	3.35423	100	0.52600	66	1582
2	26	26.0200	3.42171	88	0.44000	58	1104
3	22	22.5783	3.93491	77	0.46330	51	1215

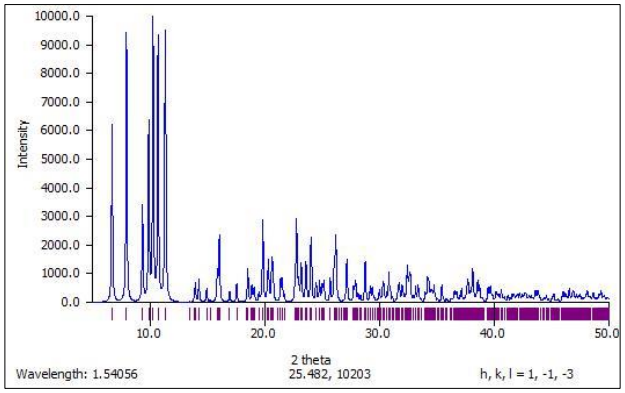
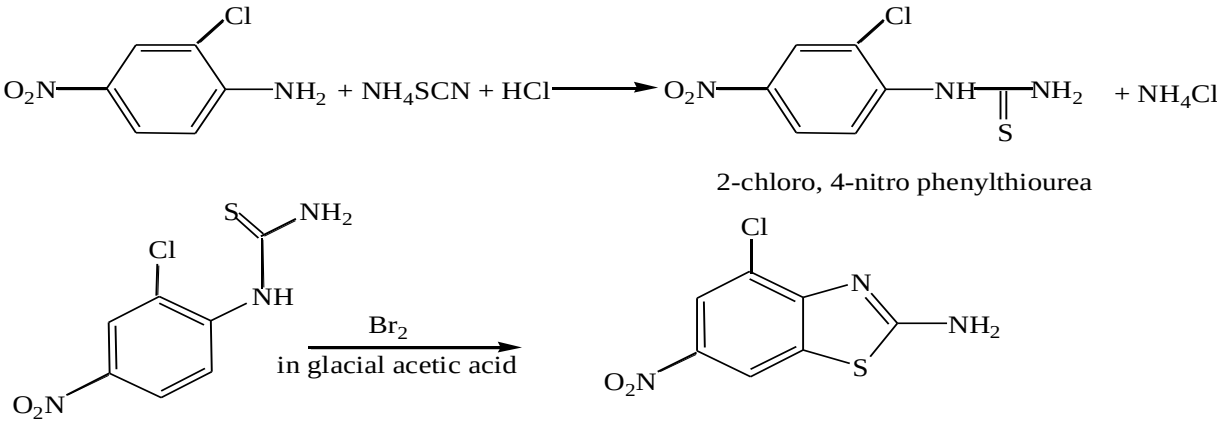


Figure 4. The result of XRD analysis at 0-80° 2-theta of Ni(4-[(4-chloro-6-nitro-benzothiazol-2-ylimino) methyl]-2-methoxyphenol)Cl.

General Method of Synthesis

Equimolar quantities of both components 2-chloro, 4-nitroaniline 3.44 g (172 g/mol, 0.02 mol) and ammonium thiocyanate 1.5 g, 0.02 mol were dissolved in mixture of ethanol and 2 ml of Conc. Hydrochloric acid with stirring for 30 minutes. Followed by addition of bromine 2.7 ml, 0.05 mol in 25 ml of glacial acetic acid and the reaction mixture were refluxed for 1 hour. The mixture was cooled in ice-water bath and the product obtained was filtered with cold water and dried [22]. The brown precipitate was recrystallised from ethanol (Scheme -1). M.p 222-224 °C, yield 85%.



Scheme -1. Synthesis of 2-amino-4-chloro-6-nitro benzothiazole 1

Preparation of the Schiff Base Ligands

To synthesize a bulky 4-[(4-chloro-6-nitro-benzothiazol-2-ylimino)-methyl]-2-methoxyphenol **2**, the first step is to add equimolar amount 0.01 mole of 2-amino-4-chloro-6-nitrobenzothiazole in ethanol (15 ml) gradually to a hot absolute ethanol solution 15 ml of 4-hydroxy-3-methoxy-benzaldehyde. After that 5 drops of glacial acetic acid were added and the mixture was heated up to 70 °C under reflux in 250 ml round bottom flask for 3 hours. On cooling, filtration was performed after a solid product formed and washed with ethanol, then with ether and dried. The obtained white crystals were recrystallized from ethanol and put in an ice path for 3 hours in order to achieve the complete crystallization. Same rout was applied for the preparation of 3 and 4 using the corresponding substances in the molar ratio [22].

Preparation of Al(III), Ni (II) and K(I) Complexes (5,6,7) (a-c)

A warm ethanol solution 20 ml of equimolar amounts of Schiff base ligand 0.01 mol was added to a magnetically stirred solution of ($AlCl_3$ in ethanol + DMSO, $NiCl_2$ in DMSO and KBr in DMF) salts until it makes a pure solution then the reaction stopped. A precipitation appeared after cooling without an interruption. The solvents were to some extent evaporated by rotatory evaporator. A solid product shaped, thus was filtered, washed with ether and dried. The desired metal complexes **5,6,7 (a-c)** were created and then purified by recrystallization from the appropriate solvent (aqueous ethanol).

Conclusion:

In the present research, 4-chloro-6-nitro-2-amino-1,3-benzothiazole was prepared by bromination of 2-chloro-4-nitro aniline with ammonium thiocyanate, then reacted with three aldehyde pendant arms generating Schiff base ligands. The three new products were used for complexation with metals chloride of Al(III), Ni(II), K(I) by nucleophilic substitution and condensation reaction in presence of various solvents (ethanol, DMSO, DMF). These complexes were characterized by physical and spectral studies. Some diffractometer data for one of the complexes are reported in this study. The ligands proposed to be chelated metal ions through the nitrogen atoms

of the azomethine group of imine or the benzothiazole ring. Finally, we believe that the structural variation of the Schiff base benzothiazole metal complexes can permit promising derivatives with a wide range of biological activity to be done in the future.

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Iraq, for their assistance, encouragement and permission to carry out this research.

Authors' declaration:
- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are mine ours. Besides, the Figures and images, which are not mine ours, have been given the permission for re-publication attached with the manuscript.
- Ethical Clearance: The project was approved by the local ethical committee in University of Baghdad.

Author's contributions statement:
(Wasan Abdul Razzaq Mahmood) certify that she has participated in the following roles: design, collected the sample, analyzed all parameters, acquisition of data and submitting the MS. (Areej Kamal Assim Aldabbagh) certify that she has participated in the following roles: analysis, interpretation, drafting the MS, revision and proofreading. (Muhanned A. Mahmoud) certify that he has participated in the following roles: conception of research, design, acquisition of data.

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تحضير وتشخيص معقدات معدنيه حلقية غير متجانسة مشتقة من قواعد شف للبنزوثايوزول

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الخلاصة :

تضمنت الدراسة تحضير معقدات جديده غير متجانسة الحلقة. تشمل هذه المركبات مشتق -2امينو 3، 1 بنزوثايازول المعوض 1 (4-كلورو-6-اوكسيد النتروز-2امينو 3، 1- بنزوثايازول (من 2-كلورو-4-اوكسيد نتروزالانيلين)) كمادة اولية ومفاعلته مع ثلاث الديهايدات اروماتية مختلفة بوجود الكحول المثيلي لتحضير قواعد شف ثلاثية السن 4-2. ثم مفاعلة مركبات البنزوثايازول ومشتقاته مع ايونات البوتاسيوم (I)والنيكل (II) والالمنيوم (III) لتكوين المعقدات المخلبيه7-5 (c-a). تم تشخيص تراكيب المعقدات الجديدة المحضرة بواسطة قياس درجه الانصهار، اطياف الاشعة تحت الحمراء والبعض منهم بواسطة الرنين النووي المغناطيسي البروتوني وحيود الأشعة السينية ومن نتائج الاطياف تم اقتراح شكل البنية الأساسية للمعقدات. نتوقع من هذا العمل ان يكون له اهميه في تصنيع وتطوير مواد علاجيه.

الكلمات المفتاحية: الانيلين، 3,1-بنزوثيازول، ليكاند، معقدات المعادن، قواعد شف.