DC Electrical Conductivity of Imipramine Hydrochloride, Trimipramine Maleate and Their Ion Pairs*

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This paper describes an experimental study on the electrical conductivity of powder samples of imipramine hydrochloride, trimipramine maleate and their ion-pairs with tetrachlorocuprate, tetrachloromercurate and ammonium reineckate. All studied samples exhibited semiconductor properties. Activation energies (E_a) for the ligands and their ion-pairs were calculated using Arrhenius plots and exhibited the order $CuCl_4^{2-}$ >$HgCl_4^{2-}$ > $[Cr(NH_3)_2(SCN)_4]^-$.

Introduction

Tricyclic antidepressants are a family of structurally similar compounds that constitute an important class of neurotherapeutics, used for the treatment of psychiatric patients suffering from clinical depression(1). Regarding their mechanism of action, it has been proposed that antidepressant agents act by increasing the availability of biogenic amines at their postsynaptic receptor sites in the brain, thereby reversing depression. Among the tricyclic derivatives of pharmacological interest are imipramine hydrochloride and trimipramine maleate . These substances possess a tricyclic ring system with a nitrogen atom and a short hydrocarbon chain carrying a terminal nitrogen atom.The chemical structure of the tricyclic antidepressants derivatives is illustrated Figure 1.

* Paper from chemical studies on some CNS drugs Research performed by the Narcotic Research Department ,supervised by Prof. Dr. Rafic H. Abu-Eittah and Dr. Laila T. Kamel the principal researcher

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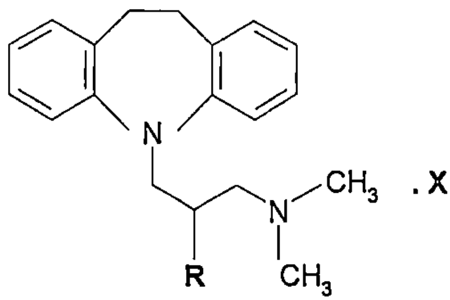

Fig. (1) The Chemical Structure of the Ligands

Where: R = H , X = HCl in imipramine

R = CH_3 , X = $C_4O_4H_4$ in trimipramine

Determination of tricyclic antidepressants by ion-pair extraction is well established by spectrophotometric methods. In this case an ion-pair is formed between these basic compounds and anionic reagents including 2,2 bipyridine[2], ammonium peroxidisulfate and niobium(V) thiocyanate[3], eriochrome cyanine R[4] , 3-methyl-2-benzothiazolone hydrazone in the presence of ferric chloride[5].

Thermal decomposition of imipramine hydrochloride, trimipramine maleate[6] and imipramine ion-pairs [bis(imipraminium) tetrachlorocuprate, bis(imipraminium)tetrachloromercurate and imipraminium reineckate] was investigated thermally and non-isothermally[7]. Few studies for the measurement of DC electrical conductivity of powder imipramine hydrochloride[8] and in aqueous solutions have been reported [9]

Electrical conductivity constitutes one of the most fascinating, recent research topics, deeply involving chemists and relate it to the physicochemical property of materials. It would be very interesting to measure the electrical conductivity of two of the most commonly used antidepressants, imipramine hydrochloride (Imi) and trimipramine maleate (Trim) and their ion-pairs with $CuCl_4^{2-}$, $[Cr(NH_3)_2(SCN)_4]^-$ and $HgCl_4^{2-}$, complex ions, to establish whether the electric properties of these compounds correlate with their pharmacological action or chemical structure and also the effect of their complexation on the π-electrons.

Experimental

Chemicals

Ammonium reineckate, copper chloride and mercuric chloride are Merck grade reagents which were used without further purification. Imipramine hydrochloride and trimipramine maleate were supplied by Sigma Chemical Co. St. Louis, MO, USA.

Equipments

For electric DC conductivity, samples of 200 mg were thoroughly ground and pressed into circular discs of 12.5 mm diameter and thickness between 0.8-1 mm under 10^4 pascal pressure. To ensure good conductivity contact the two surfaces of the discs were covered with conducting silver paste (FSP 51, Johnson Matthey and Co UK). Compressed pellets were sandwitched between two parallel Cu electrodes. The DC conductivity was carried out from room temperature up to 413K, measured by two probes method using a Keithly electrometer.

Ion-Pairs Complexes

Preparation of imipramine ion–pair complexes:
bis(imipraminium)tetrachlorocuprate(II),bis(imipraminium)tetrachloro-mercurate(II) and imipraminium reineckate were prepared as described previously(10). The same procedure was used to prepare the trimipramine ion-pair complexes.

XRD-Single Crystal

The preparation of bis(imipraminium)tetrachlorocuprate(II) single crystal as well as its XRD spectrum were carried out at the Universität Konstanz, Facultät für Chemie, Germany. The diffractometer used was a Simens p4.

Results and Discussion

Imipramine hydrochloride and trimipramine maleate ion-pair structure was proved by X-ray diffraction of a single crystal. Figures (2,3) show the crystal structure of bis(imipraminium)tetra chlorocuprate(II) and that of bis(trimipraminium)tetrachlorocuprate(II)[11].

The variation in the logarithmic scale electrical conductivity as a function of the reciprocal absolute temperature for the ligands and their ion pairs is represented in Figures (4,5) where activation energies were calculated from the slope . Temperature dependence of the conductivity is expressed by the equation:

$$\sigma = \sigma_0 \exp\left(-E_a/kT\right)$$

where σ_0 is the pre-exponential factor, E_a is the activation energy for this thermally activated process and k is the Boltzmann's constant. The values of the electrical conductivity σ and activation energies (E_a), of these complexes were presented in Tables (1,2).

Compounds under investigation show semiconductivity properties in the temperature under consideration where conductivity increases by increasing temperature. This type of conduction agrees with those of usual organic compounds. The conductivity of the compounds could be attributed to thermal excitations of the lone pair of electrons on the nitrogen-carbon bonds in the side chain of the structure, which makes the delocalization of the π-electrons possible. It is well known that the electronic transport properties of organic semiconductors depends on their chemical structure[12].

As a result the conduction could be explained according to the chemical structure of the compound, the structure has π-electrons which are mobile in the structure, thus the conduction results from the transfer of these π-electrons [13]. The electronic excitation of the rings followed by transfer of an electron to another molecule is considered to be an important step of the conduction process, its electron states are delocalized allowing the electronic transport to be described in terms of hopping conduction.

Change of the slope reflects a change in the activation energy caused by a change in the number of excited carriers [14]. These two activation energies are associated with the intramolecular and intermolecular conductivity process. Low activation energy values (E_{a1}) (at low temperature) are associated with the first step of conduction that starts between inter molecules (intermolecular conductance) while the higher activation energy (E_{a2}) (at high temperatures) corresponds to intra molecular transfer (intramolecular conduction) process. There are two stages in the movement of a current carrier-motion within these compounds, which is in the one molecule and the passage from one molecule to another that is intramolecular and the intermolecular transfer of the current carrier.[15]

The intramolecular transfer of electrons, where electrons can hop one atomic site to another if orbitals exist with the same energy levels between sites. If intermolecular orbital overlap of charges is present, electron or holes can jump from one molecule to another. Therefore π-electrons, can jump from one molecule to another by hopping if orbital with the same energy levels exists between the molecules.

If we assume that excited carriers within intramolecules, are retarded by the barrier molecules, the activation energy of intramolecular conduction process is higher. So the first step of conduction starts between intermolecules and the lower activation energy correspond to intermolecular transfer while the higher activation energy correspond to intramolecular [16]. The main differences in the electrical conductivities of imipramine and trimipramine arises, because these drugs are having different R and X which are expected to vary the inter molecular packing resulting in the electrical conductivity variations.

Complexation of drugs with $CuCl_4^{2-}$ and $HgCl_4^{2-}$ increased the electrical conductivity whereas the activation energy decreased. This may be due to the metal ion which can act as a bridge to facilitate the flow of the current[17] The first step in the conduction process is the excitation of a π-electron from the uppermost filled π-orbital to the lowest empty π-molecule orbital[18]. The electron is then assumed to hop to the equivalent empty level of the neighbouring molecule. When it lands on a new site it causes the surrounding ions to adjust their localization and electron or hole trapped temporarily in the potential well thus atomic polarization is produced. The electron resides at its new site until thermally activated, then migrates to another nearby site[16].

On the other hand complexation with $[Cr(NH_3)_2(SCN)_4]^-$, decreased the electrical conductivity this may be due to the presence of bulky anions which occupy much space thus increasing the intramolecular distance between the molecules hindering and weakening the conduction pathway.

Conclusion

Temperature dependence of the electric conductivity of the ligands (imipramine hydrochloride and trimipramine maleate) and their ion-pairs obeys Arrhenius equation with very low conductance values.

Electrical conductivity in the ligand and the ion-pairs can be described by hopping of charge carriers between localized sites.

A general feature, complexation with $CuCl_4^{2-}$ and $HgCl_4^{2}$ increased the ligand conductivity while complexation with $[Cr(NH_3)_2(SCN)_4]^-$ decreased it.

It is clear that the electrical conductivity of the studied drugs and their ion-pairs follows the sequence: $CuCl_4^{2-} > HgCl_4^{2-} > [Cr(NH_3)_2(SCN)_4]^-$.

Electric properties of the antidepressant drugs are connected with their chemical structure of the ring system rather than their pharmaceutical action.

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Table(1)

Activation Energies (E_{a1},E_{a2}) and Conductivity (σ) for Imipramine Hydrochloride and its Ion-Pairs

Compound	E_{a1} (eV) × 10^{-2}	E_{a2} (eV)	σ (S/cm) × 10^{-5}
Imi	0.71	0.64	1.88
$ImiCuCl_4$	0.48	0.22	2.45
$ImiHgCl_4$	0.70	0.42	6.89
$Imi[Cr(NH_3)_2(SCN)_4]$	0.67	0.67	0.71

Table(2)

Activation Energies (E_{a1},E_{a2}) and Conductivity (σ) for Trimipramine Maleate and its Ion-Pairs

Compound	E_{a1} (eV) × 10^{-1}	E_{a2} (eV)	σ (S/cm) × 10^{-5}
Trim	0.96	0.32	2.30
$TrimCuCl_4$	0.98	0.19	8.91
$TrimHgCl_4$	0.98	0.23	3.45
$Trim[Cr(NH_3)_2(SCN)_4]$	0.36	0.40	0.13

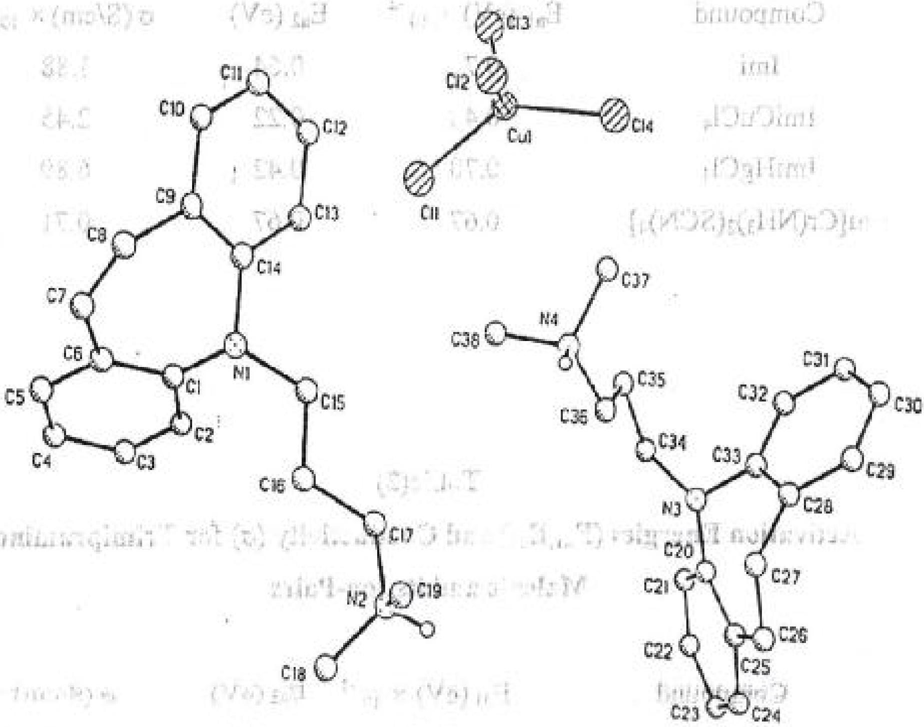


Fig (2) The diagram of bis(imipraminium)tetrachlorocuprate (II) in the asymmetric unit

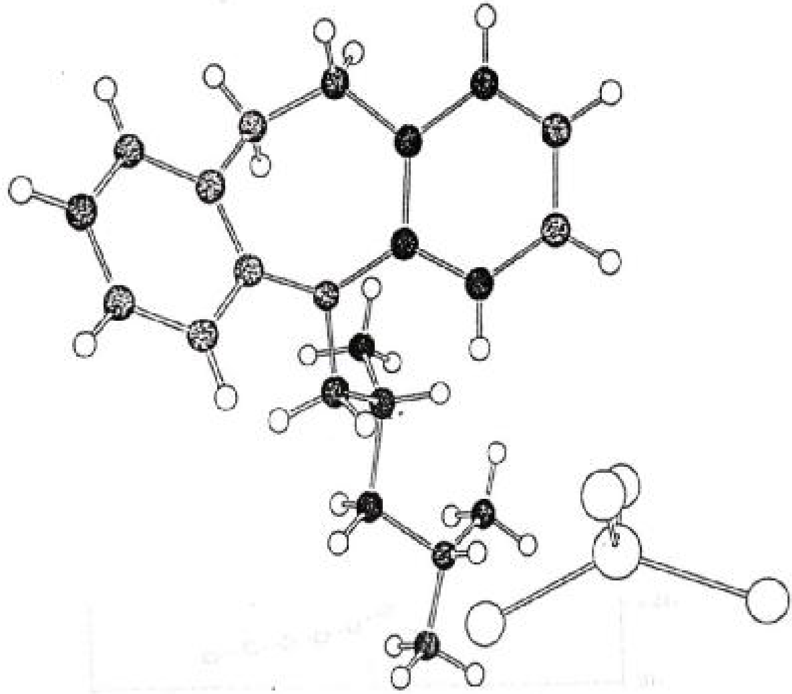
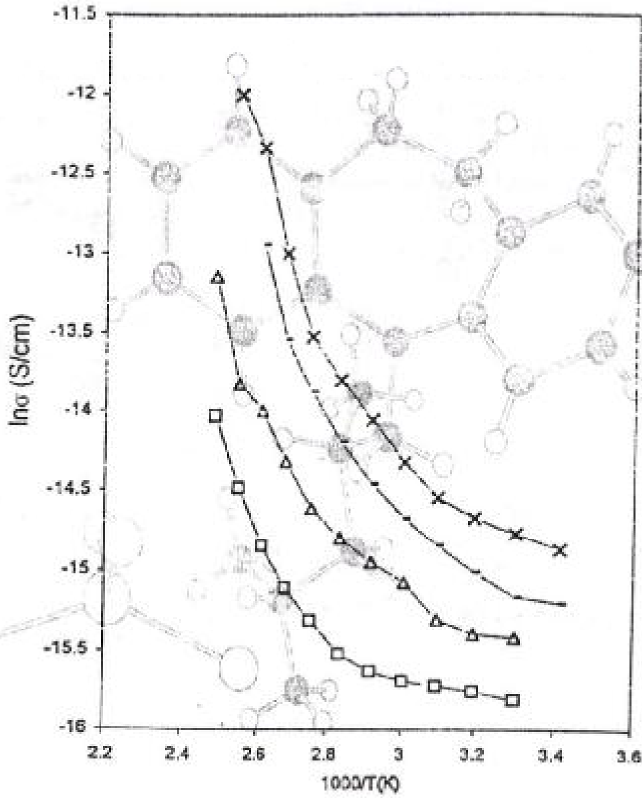
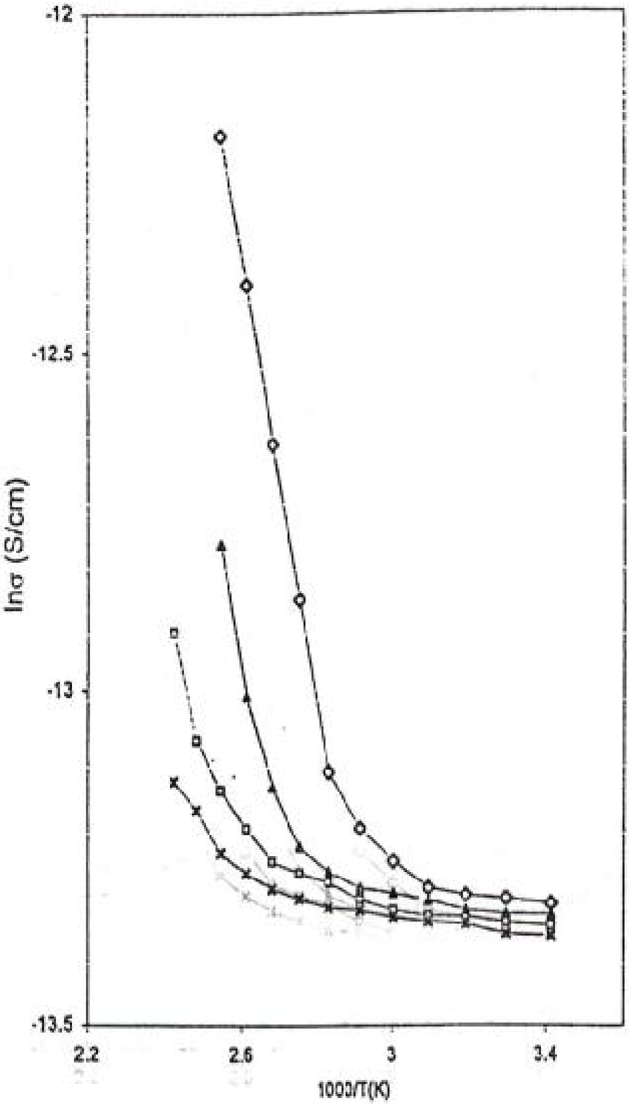


Fig (3) The diagram of bis(trimipraminium)tetrachlorocuprate(II) in the asymmetric unit



Fig(4) The electrical conductivity of trimipramine maleate and its ion-pairs

bis(trimtetrachloromercurate) —□— trim-reineckate
—△— trimipramine maleate —×— bis(trimtetrachlorocuprate)



Fig(5) The electrical conductivity of imipramine hydrochloride and its ion-pairs

التوصيل الكهربائي المستمر لمسحوق من هيدروكلوريد الأيميبرامين والترايميبرامين ماليات والأزواج الأيونية الخاصة بها

ليلـــــى كامـــــل

تعرض هذه الورقة دراسة تجريبية على التوصيل الكهربائى لمسحوق من هيدروكلوريد الأيميبرامين والترايميبرامين ماليات والأزواج الأيونية الخاصة بها مع المتراكبات النحاسية والزنبقية رباعية التكافؤ ورينيكبت الأمونيوم .
أظهرت الدراسة أن جميع العينات لها خصائص أشباه الموصلات . كما تم حساب الطاقة المنشطة (Ea) للعينات باستخدام طريقة أرهينيس ، وكانت على الترتيب المتراكبات النحاسية رباعية التكافؤ ، تليها المتراكبات الزنبقية رباعية التكافؤ ، ثم رينيكيت الأمونيوم .