International Journal of Research Publication and Reviews

Saccharine's Metal Complexation

*Saqlain Nabiji **[1]**, Yogesh Harangule**[2]**, Nandkishor B. Bavage**[3]**, Shyamlila B. Bavage**[4]***

[1]B.Pharmacy Final Year Student, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist Latur-413512, Maharashtra, India
[2]Department of Organic Chemistry, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India
[3]Department of Pharmaceutical Analysis, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India
[4]Department of Pharmacognosy, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist.Latur-413512 Maharashtra, India

ABSTRACT

Metal complexes of saccharinate ions obtained by precipitation of the N-H fraction of saccharin (O-sulfonamide) were reviewed. A variety of metal species based on mononuclear, binuclear, polynuclear complexes, and expanded covalent polymers have been discussed in relation to the mode of ionization, i.e. monodentate (via n-atom or carbon monolithic O-atom), or to a trident. The most important physicochemical properties such as vibrational and electronic spectra, thermal, magnetic, and redox properties as well as quantum chemical theoretical studies of these compounds are briefly described. The biological properties of saccharin and its complexes are also summarized in relation to saccharin and its health effects on the diet. Finally, for comparison purposes, a brief overview of the osacran's common metal complexes is given. This survey proves that saccharinate is a very versatile and multifunctional ligand in integrative chemistry.

Keywords: Metal complaxation of saccharine, modes coordination, Physical & Biological properties, Bonds between Metal- Saccharinato.

Introduction

Saccharin (O-sulfobenzamide; 1,2-benzothiazole-3 (2H) -a 1,1-dioxide; Hsac) is one of the most well-known and widely used synthetic sweetening agents. Imino hydrogen is acidic and, therefore, can easily convert a molecule into a corresponding nitrone. The coordination chemistry of this ion has been shown to be very interesting and versatile, providing different coordination sites for metal nuclei, i.e. one N, one O (carbonic) and two O (sulfonic) atoms. Does. These donor molecules can be used to produce ion N- or O-monodontate or bidentate (N, O) synthesis and even more complex polymer species with the participation of all donor molecules.

Recently, it has also been found that the saccharinate ion in some compounds may be complex cation and counter-ion outside the coordinate region. On the other hand, a significant number of compounds are also detected in which the saccharinate ion is only counter-ion from the complex cation. In addition, the presence of free saccharin has been established in the crystal lattice of some complexes. Ion can participate in the formation of mixed-ligand complexes, sharing coordinate regions with a large number of different ligands, showing different types of binding properties.

During the last 20 years different research groups have per- formed systematic studies on these type of systems, obtaining a great number of new and often fascinating saccharinato–metal complexes. Therefore, we have prepared here a general overview on this field of coordination chemistry..
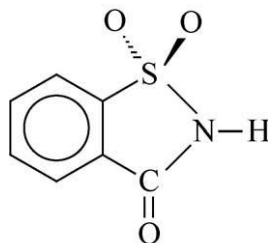
(Schematic structure of saccharin)

SYNTHESIS AND GENERAL PROPERTIES OF SACCHARIN

Saccharin was accidentally discovered by Falberg in 1878 in an oxidation study of Otoluenesulfonamideand published 1 year later by Remsen and Fahlberg. It was produced industrially (1887) shortly after its discovery as the first carbohydrate-free sweetening agent. Because it is insoluble in most

water, it is commonly used as a sodium or calcium salt and has a power of 550 times sweeter than saccharos. In addition, it exhibits an unpleasant bitter and metallic aftertaste and a sweet taste can still be found at 1: 100,000 dilution.

It can be made by two different processes. In one of them, based on the original invention, toluene is used as the starting factor. Treatment with chlorosulfonic acid, followed by interaction with NH, produces a mixture of o- and p-toluenesulfonamide. After separation of the two sulfonamides, saccharin is produced by closing the oxidation ring of -toluene sulfonamide. In the second process, methyl anthranilate (obtained immediately from phthalic anhydride) is the starting material, and saccharin is obtained after four consecutive stages (treatment with NaNO2 / HCl, SO2, Cl2 and NH3).

Saccharin is relatively insoluble in water. One gram is soluble in 290 ml of water or 25 ml of boiling water. It is highly soluble in ethanol, acetone, and glycerol, and slightly soluble in ether and chloroform [9]. It is usually a monoclinic crystal that shows an exact (1 0 0) cleavage. Its melting point is 228.8–229.7 C and its density is 0.828 g / ml. It is slightly acidic with a value of 1.60pKa.

The standard molar enthalpy of combustion, sophistication, and structure has recently been determined by calorie-metric methods. Saccharin's crystal structure was published independently long ago by Bart and Okaya. The results of the two studies are comparable, including the final R-values, and show that the compound belongs to the monoclinic p21 / C space group, with the unit cell parameters being close to A, B, and C

9.55, 6.91 and 11.80 A˚, and the monoclinic angle 103 in order. Like many cyclic imidals, the structure is molecular with centrosymmetric dimer molecules formed by the NH.Imino nitrogen and carbonyl oxygen atom, both five-member rings.

BIOLOGICAL EFFECTS ON SACCHARINE

One of the reasons for the initial considerable interest in the chemistry of saccharin and its metal complexes was its suspected carcinogenicity. Discussions on the health risks of agents of saccharin and other artificial sweeteners have been in the scientific literature and the media for years. In the 1970s, there was some evidence of concern about saccharin when a study showed that mice developed high doses of bladder cancer. As a result, the US National Toxicology Program has classified saccharin as a "potential carcinogen" that may cause cancer in humans.

There are more than 50 publications on the effect of saccharin on rats. Most of these studies examined its effect on a generation of mice that received high doses (usually 5% of the total food eaten) for at least 1.5 years. Most of these studies failed to increase the risk of cancer production. Later, such experiences were extended to two generations of experimental animals, the saccharin being passed on to parents and the next generation of rats. These studies increase the risk of bladder carcinoma in the second generation (cf. for a brief review of these studies). Another study using 2500 mice found that the risk of bladder tumors at saccharin concentrations was more than 4%. Based on these results, the use of saccharin as a food additive is banned in Canada. Furthermore, a similar dose of ascorbic acid (vitamin C) has been shown to induce bladder cancer in mice. Mice have a high urinary osmolarity, which is conducive to the precipitation of crystals during the excretion of significant amounts of sodium salts such as sodium ascorbate or saccharinate, which can lead to urothelial hyperplasia by microbial abrasion, which eventually leads to the bladder.

On the other hand, a long-term study (24 years) with monkeys showed that sodium saccharinate did not increase the proliferation of urothelial cells, bladder tumors, or the presence of crystalline substances in these animals.

Systematic studies on saccharin exposure in humans are very rare. Some tests on high and persistent saccharin users (e.g., people with diabetes) do not show significant results. Cervical saccharin exposure has also been shown to increase the risk of bladder cancer, at least in the first three decades of life. Although direct extrapolation of the results of laboratory animal experiments is often criticized in the context discussed here, it can be concluded that the carcinogenicity of sodium saccharinate C must be clear by the conclusion of all these studies. It is specific to the bladder of the male rat, has minor effects on the bladder of the female rat and allows it to be classified as a genotoxiccarcinogen, that is not harmful to humans. Not likely to be carcinogenic. Finally, the US National Toxicology in 2000

The program removed saccharin from the list of carcinogens, and saccharin is now considered safe, for example, in a January / 2001 editorial from Chemistry in the UK.Saccharin has also been suggested to be useful as an antidote to metal poisoning, although this property has not been explored more systematically. Recently, it has also been suggested that the weak acidity of saccharin may be used as a precursor to salt in chemistry, which may increase the solubility of some of the drugs. Is these elements of saccharin's metal complexes and some other biological properties and activities are discussed in Section 7.

SACCHARINES METAL COMPLEXES

The studies commented on in the previous section have successfully developed a very rapid and continuous cognitive development on the interaction of saccharin with various metal cations. Initially, most of the complexes prepared and researched were mixed aqua-saccharinato species. But Saccharin is rapidly showing its potential as a powerful and versatile polygonal ligand, and a large number of other common and mixed-ligand complexes have been developed and fully described. Most of these complexes are in the form of the protonated saccharin nitrone (known as the saccharinate anion), as opposed to the free molecule called HAC, which can be identified as SAC in the following.

A very limited number of systematic studies and generalizations have been made so far about these types of campuses. Many of these structural data have been critically evaluated and some specifics of Ligand's geometric properties and its binding properties are discussed in detail. Some relevant results of these studies, as well as analysis of vibration-spectroscopic data and spectral / structural correlations are also discussed.

As mentioned in Section 1, the sacred ion interacts with metal centers in a variety of ways, a topic that has only recently been briefly reviewed. In the following sections, we provide a detailed analysis of these different types of interactions and discuss the most relevant features and characteristics of complex compounds belonging to these classes.

IONICSACCHARINATES

Saccharinates are a family of derivatives that contain alkaline or alkaline-earth cations, in which cation / ion interaction is predominantly ionic in nature. However, complete crystal-graphic construction information is only available for some of them.

As mentioned above, the most common commercial form of saccharin is the solid hydrate of sodium saccharinate ("sodium saccharin" and "soluble saccharin"). Although this salt has been widely used for over a century and is one of the most commonly used synthetic sweeteners worldwide, its exact composition has not been clearly established until recently.

The re-crystallization of sodium saccharinate from different solvents provided two different hydrates. Structure Na (sock) (2/3) H2O hydrate obtained from 95% ethanol, crystallizes in triclinic space group P 1. The stoichiometry of the monoclinic hydrate of the Na (SAC) (15/8) H2O and P21 / n space group can be obtained from recent water and is similar to that of unclean commercial product. From a crystalline point of view it should form Na64 (shock) 64 120H2O, forming a very large unit cell with a volume of 15560.4 A° 3 and Z = 64, which can be considered for ideal commercial and displacement modulation. Can be considered. (i) The structure with C2 / m, Z = 8, and ai = a, bi = b / 4 and ci = 2, contains a large number of structurally different water molecules. The crystals of this form are very stable if stored in a closed container and mechanical damage is not allowed. However, when exposed to dry air, placed in empty containers or crushed, they become opaque. Its isobaric dehydration begins slightly above room temperature and continues through two intermediates: Na (sac) (9/8) H2O and Na (sac) (2/3) H2O (or Na (sac) (4/9) H2O). The exact formula of the second intermediate has not been definitively established and the structure of 9/8 hydrate has not yet been determined due to its low crystallization [33] and the same is true in the case of the anhydrous compound, Na. (SAC), which clearly shows a specific structural relationship with triclinic hydrate. Triclinic when dehydrated under isobaric conditions

Hydrate Na (sack) (2/3) H2O also gives 4/9 hydrate as a special intermediate, which is stable in the temperature range between 343 and 389 K.

Other ionic saturates available for structural data so far are K (SAC) (2/3) H2O, compound cation salt K2Na (bag) H2O, Mg (II) compound bag of Mg (II) structure).) 2 7H2O and alkaline such as ammonium salt, NH4 (shock). The compound is by far the only structurally classified anhydrous ionic saccharinate. It is composed of ammonium and saccharinate ions formed by a network of hydrogen bonds to form a membrane structure. Each NH4 + cation interacts with four oxygen atoms of different saccharinate ions through four common hydrogen bonds, producing four times as much synergy as this cation, similar to NH4F.

The IR spectra of two cesium saccharinates of the formation of Cs (SAC) 0.5H2O and Cs (SAC) (Hsac) H2O were reported a few years ago, although the composition of these compounds is unknown. Furthermore, some spectroscopic and thermal data are available for Rb (shock) 0.5H2O derived from Rb2CO3 and for saccharin dissolved in hot ethanol More recently, rubidium saccharinate has also been described as a structure of Rb (sac) (Hsac) H2O.

With respect to alkaline-earth saccharinates, other simple compounds other than the Mg (II) complex mentioned above have not yet been fully described, although compounds Ca (Zac) 2 4H2O, Sr (Zac) 2 4H2O and Ba (Zac) 2 8H2O are mentioned in the literature. As shown by our own studies, Ca (II), Sr (II) and Ba (II) saccharinates are highly soluble in water, preventing the synthesis of crystalline materials sufficient for crystalline studies. However, there are some mixed-ligand complexes from this citation   **.**

Recent design and feature. They are described in Sections 4.4 and 4.7. On the other hand, stoichiometry of the B (II) complex of B (SAC) 2H2O obtained by the reaction of beryllium perchlorate and sodium saccharinate solution has been described but poorly classified.

MONODENTATE N-COORDINATED METALCOMPLEXES

The reaction of sodium saccharinate with the first row diva- lent metal ions from V(II) to Zn(II) results in isomorphouscoor- dination compounds with the formula [M(sac)2(H2O)4] 2H2O, where M is V(II), Cr(II) [43–45], Mn(II), Fe(II)

Co(II), Ni(II), Cu(II) and

Zn(II). All these divalent metal cations show a clear preference to interact with the saccharinate anion through its deprotonated and negatively charged N-atom. The crystal structures of these [M(sac)2(H2O)4] 2H2O species were doc- umented about two decades ago and, these octahedral complexes contain two N-bonded sac ligands in trans positions.

For the synthesis of mixed-ligand saccharinate complexes with these metal ions, it became a common practice to apply [M(sac)2(H2O)4] 2H2O as synthetic precursors, since the aqua ligands in these metal complexes are labile and readily displaced by neutral ligands. Therefore, the new complexes are simply pre- pared by the direct reaction of a neutral ligand with the starting aqua-saccharinato complex in solution. The addition of the lig- ands to the solutions of the complexes usually results in the substitution of all four aqua ligands, thereby forming stable new mixed-ligand complexes. In most cases, saccharinate interacts with the metals in mixed-ligand complexes in the same way as in the starting complexes.

Accumulated structural data of mixed-ligand complexes containing these and other metal cations in the solid state show that the N-coordinated saccharinato complexes may be classified according to their coordination geometries. A three-coordinated copper(I) complex containing an N-bonded
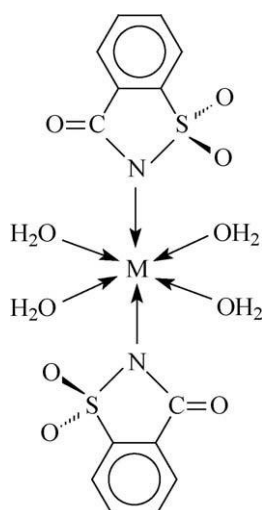
Structure:- [M(sac)$_2$(H$_2$O)$_4$] 2H$_2$O com- plexes (M^{II} = V, Cr, Mn, Fe, Co, Ni, Cu and Zn)

Saccharinato ligand, [Cu (sac) (PPh3) 2], derived from the reaction of the dehydrated initial aqua complex, [Cu (sac) 2 (H2O) 4] triphenylphosphine (PPh3) [54] in CH2Cl2, and other examples of this type of silver Observed with (I): [Ag (sac) (PPh3) 2] , [Ag (sac) (pie)] n (pie = pyridine), [Ag (sac)) (pym)] n (pym = 2-pyridylmethanol), [Ag2 (bag) 2 (dmen) 2] (dmen = N, N-dimethylethylenediamine). Thesedimeric and polymeric silver (I) -sack complexes are formed by relatively strong Ag-Ag interactions.

Tetrahedral coordination is usually in the case of Zn (II), and examples [Zn (sac) 2 (above) 2], [Zn (sac) 2 (im) 2] (im = imidazole) [60], [Zn (II) SAC) 2 (bzim) 2] 2 2EtOH H2O (bzim = benzimidazole; EtOH = ethanol) [60], [Zn (SAC) 2 (aepy)] (aepy = 2- (2-aminoethyl) pyridine) [61]. ApyH [Zn (SAC) 3 (H2O)] (ApyH = 2-aminopyridinium) is the first example of a tetrahedral coordinated mononuclear Tris (saccharinato) complex of a divalent transition metal.

Square-planar coordination geometry is observed in two dimeric Cu (II) - saccharinato complexes, [Cu2 (dea) 2 (sack) 2] (dia = diethanolamine) and [Cu2 (pypr) 2 (sack) 2] (pypr= 2- pyridinepropanoxy ion). Two of the two are Cu (II) ions

The dimers are Cu dissociation of two alkoxo-bridges and relatively small Cu +++ ca. Are connected by. 2.99 (2) A° is a strong. Is responsible

[Cu (ophen) 2 (sock)] as in sock 2H2O (ophen = o-phenathroline) and a, ar-bipyridine, [Cu (bpy) 2 (SAC)] in a complex equivalent to SAC 3H2O both of which are saturated ion three equatorial positions.

Octahedral complexes usually occur in the presence of two neutral chelating co-ligands. Examples :: (bag) 2 (ea) 2] ,

[Cu (sack) 2 (pym) 2], [Cu (sack) 2 (HydEt-en) 2] (HydEt-en = N- (2-hydroxyethyl) -Ethylandium), [Cu (Bag) 2 (amp) 2]

[73], [Zn (ea) 2 (sac) 2], [Zn (sac) 2 (amp) 2] and

[M (shock) (bpy) 2 (H2O)] bag, with M = Mn (II), Co (II), Ni (II) and Zn (II) [87-89]. In addition, [Cu (SAC) 2 (NH3) 4] is a compound with four additional monodontate ligands, one of the rarest examples of octahedral saccharinato complexes, containing two saccharinate ions in transordination. Complexes such as Mn (II), Fe (II), Co (II), Ni (II) and Zn (II) are also clearly drawn, but are not further classified.

In addition, saccharinate interacts with some heavy non-metallic cations such as Cd (II) and Hg (II) [Cd (Sack) 2 (H2O) 4] 2H2O and [Hg (Sack) 2]. , Respectively. Among them, [Cd (SAK) 2 (H2O) 4] • 2H2O iso-Antiferromagnetic coupling in the Cu -Cu pair. Apart from this,

The mononuclear square-planner Pt (II) and Pd (II) complexes also exhibit PtN and PdN bonds in the formula [Mcl (Sac) L2] (L = different phosphine ligands). These are the special saccharinato complexes of the platinum group metals known so far.

Recently, two Au (III) complexes of structure [Au (sac) 2 (H2O) 2] Cl and [Au (sac) 3H2O] have been reported. Based on its IR spectral analysis, they concluded that they also exhibit square-planar coordination with the saccharinate ion by the N-molecule, acting as a monodentate ligand.

Due to the coordinate flexibility of this cation, it is clear that five-coordinate complexes can be obtained with Cu (II). In most cases, these complexes contain aqua ligand, a stable five-coordinate intermediate in the ligand alternative mechanism usually formed during the conversion of the initial compound from octahedral to tetrahedral, the aqua ligand does not change. Examples of square-pyramid complexes with N-bound saccharineto ligands [Cu (sac) 2 (H2O) (above) 2] [Cu (sac) 2 (H2O)(bzim) 2] , [Cu (sack) 2 (H2O) (bzim) (EtOH)] , [Cu (sack) 2 (H2O) (nic) 2] (nic = nicotinamide) , [Cu (sack) 2 (H2O) (Hnic) 2] (Hnic = nicotinic acid) , [Cu (sack) 2 (H2O) (prpy) 2] (prpy = 4-propylpyridine .)) () -Yl)) methyl-dithiocarbaze) , [Cu (pysme) (sack) (MeOH)] (pysme = Pridme-2-carboxaldehyde Schiff base S-methyl-dithiocarbazate ion) and [Cu (Inca) (Shock) (H2O)] 0.5H2O (Forward = 2-Formylpyridinethiosemiccarbazonato).

Tri-dipyramidal coordination is less common in these mixed-ligand complexes. For example, it was also found [Cr (sac) 2 (above) 3] • 2.

Morphology with first-line transition metals.The mixed-ligand Cd (II) and Hg (II) complexes in N-bound saccharinato ligands originate from these species and the complexes reported in this area are: [Cd (Sac) 2 (BPY) 2], [CD (SAC) 2 (DEA) 2], [cd (sack) 2 (hydate-n) 2], [cd (sack) 2 (amp) 2], [cd (sac) 2 (aepe) 2] [92], [cd (sac) 2 (piot) 2] (pit = 2)Pyridylethanol), [Cd (Sac) 2 (H2O) (DMSO) (Pyte)],[Cd (Sac) 2 (H 2 O) 2 (Nic) 2], [Cd (Sac) 2 (NH 3) 4],[Hg (Cl) (sac)] , [Hg (sac) 2 (bpy)] [97], [Hg2 (Cl) 2 (sac) 2 (above) 2], [hg (ea) 2 (sac) 2], [hg (sac) 2 (piot)],[hg (sack) 2 (ampy) 2] and [hg (sack) 2 (apy)].Finally, NG et al. Several five-coordinate trifinylstanilsaccharinates have been reported, including the saccharinate N-bond [102]. In addition, in the T-shaped Ag (I) complexes [Ag (sac) (amp)] and [Ag2 (sac) 2 (monkey) 2], the saccharinate ion forms metal by its N-molecule Coordinates. Monodentate O-coordinated metalcomplexes, As a ligand, the saccharinate ion provides two different donor O-molecules, the carbonyl

and sulfonyl groups, the latter being less basic and rarely involved in bonding, while the former are often involved in synthesis. , Acts as an ion chelating or bridging ligand as discussed later in this review. The monodentate coordination of the carbonyl O-molecule is abnormal and occurs when there are branched or coarse co-ligands. This type of coordination was first perceived in the vanadium (II) complexes [V (sac) 2 (above) 4] 2 and [V (sac) 2 (above) 4] 2nd f and was also established for [Ni (Shock) 2 (above) 4] As shown in Figure 3 above 2, the structures of the vanadium (II) and nickel (II) complexes have four planar pyridine

MONODENTATE O-COORDINATED METALCOMPLEXES

As a ligand, the saccharinate ion provides two different donor O-molecules, the carbonyl and sulfonyl groups, the latter being less basic and rarely involved in bonding, while the former are often involved in synthesis. , Acts as an ion chelating or bridging ligand as discussed later in this review. The monodentate coordination of the carbonyl O-molecule is abnormal and occurs when there are branched or coarse co-ligands. This type of coordination was first perceived in the vanadium (II) complexes [V (sac) 2 (above) 4] 2 and [V (sac) 2 (above) 4] 2nd f and was also established for [Ni (Shock) 2. As shown in Figure 3 above 2, the structures of the vanadium (II) and nickel (II) complexes have four planar pyridine rings at the octahedron equator,
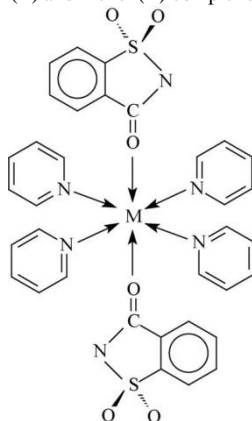

Fig:-[M(sac)$_2$(py)$_4$] (M^{II} = V and Ni).

Saccharinate ligands have to be bound by the carbonyl group. This hypothesis is further confirmed by the [Cu (sock) (H2O) (mpy) 4] (mpy = 4-methylpyridine), [Cu (sock) 2 (iqn) 4] (iqn = isoquinoline) structures, and [Cu (sack) 2 (prz) 4] (prz = pyrazole) [70] have approximately four planar ligands.

Similar MO bonds have been found in octahedral complexes with bidenet chelating ligands: [Co (Piper) 2 (Sac) 2] (Pipri = 2-Pyridinpropanol), [Cu (Pipr) 2 (Sac) 2], [Ni (Sack) 2

(pypr) 2] [107], [Ni (sac) 2 (aepy) 2], [Ni (sac) 2 (aepz) 2] (aepz = N- (2-aminoethyl) piperine) [108] , Zn (sack) 2 (aepz) 2]

and [cd (sack) 2 (appz) 2]. In these octahedral complexes, the secondary ligands are pyridine or piperazine derivatives, which contain the alkyl hydroxy and alcamino groups. The coordination of the final donor atom causes the alkyl chains consisting of two or three-marked C atoms to bend easily, resulting in increased steric congestion around the metal centers. Increasing the length of the alkyl chains can ensure that the synthesis of saccharinate by the N-molecule becomes difficult. The synthesis of other heavy enzymes, such as PPh3 and N, N-dimethylethylenediamine, also forms O-bonded saccharinato ions as seen in the following complexes: daemon) 2].

BIDENTATE (N, O) AND TRIDENTATE (N,O,O)-COORDINATED METALCOMPLEXES

Another possibility is the simultaneous coordination of two or all donor sites of the saccharinate, where the ligand acts as a double or trident chelating and / or bridging ligand between two or more metal ions.

The two most interesting dimeric species showing such interactions are [Cr2 (sac) 4] ఏ 2nd F and

[Cr2 (sac) 4 (above) 2] 2 above, in which the four sacs act as two (N, O) bridges between the two Cr (II) cations and, therefore, the well-known Cr (II) / carboxylate species.

Bi- and triangular coordinate patterns with Pb (II) and Ag (I) are more frequently observed. In the monomeric Pb (II) complex, [Pb (SAC) 2 (H2O) 2 (ophen), the two Sachari-NATO mutes act as bound chelating ligands, with an exceptional coordination number of eight. Along with other ligands. The first example of a saccharinato bridge was dimeric [Pb (sac) 2] H2O, in which the two ligands act as a bidant bridge between the lead (II) centers through the N- and carbonyl O-atoms. In [pb2 (sac) 4 (H2O) 2 (bpy) 2], two saccharinato ligands bridge the two Pb (II) centers by the other N- and carbonyl O-atoms, while the monodontate is N-coordinated. . A similar coordinate mode has been observed in [Cd2 (sack) 4 (im) 4] and [Cu2 (sack) 4 (im) 4. The refinement of this final structure suggests that the shortest C-O bond distances found for N-banded saccharin ligs are artifacts generated by a disorder in these mutts. The bridge of some first-line transition metals is the saccharinatoligands [Cu (sac) (PPh3)] 2 and [Cu (6mptsc) (shock)] 2 complex (6mptsc = 6-methyl-2-pyridinecarbolidehemiocarmicone).

As mentioned earlier, the sulfonyl group is less basic and is sometimes involved in coordination. Known for the saccharinato-bridge complex, consisting of N- and sulfonyl O-molecules, [Ba2 (sac) 4 (triglyme) 2] and [ag2 (sac) 2 (pite) Ba (II) and Ag (I) 2], respectively.

The bridge capacity of saccharinate sometimes leads to the formation of covalent polymers. For example, in [Pb (H2O) (OAc) (SAC)] n, the Pb (II) ions have a pentagonal pyramidal coordination geometry and both SAC-

The zigzag arrangement is characterized by a straight chain with the PbPb distance of Charninato and Acetato (OAc) ligand, ca. 4.25 (2) a. Usually Saturnate works in single

Bridge mode As described in the examples above, it sometimes operates in more than one bridge mode, i.e. the bicordinate-bridging (or chelate-bridging) mode as shown in Figure 4..Monodentate. , The O-atom is divided into two. The two-coordinate-bridging mode has so far been documented in the eight-coordinate one-dimensional Pb (II) complexes [Pb (SAC) 2 (PIM)] n and [Pb (SAC) 2 (ampy).)] n. Furthermore, these complexes are by far the only examples of simultaneous chelating / bridge coordination of two saccharinates in a single coordinate environment: a bidetate (N, O) chelating and a (N, O) saccharinato ligand bridge, respectively.

In the case of Ag (I), polymer species are preferred. [Ag2 (sack) 2 (hep) 2] n (hep = N- (2-hydroxyethyl) piperazine) Dimeric [Ag2 (sack) 2] consists of two bridging units formed from saccharin ligands (N, ocarbonyl). And these dimeric units are further separated by hep ligands, forming a one-dimensional coordination polymer with three- and four-coordinating Ag (I) cations [124]. Bridging egg (I) centers by similar saccharinato ligands also appear in the dimensional helical chains of [Ag2 (sac) 2 (n) (H2O)] n and the results are significantly lower
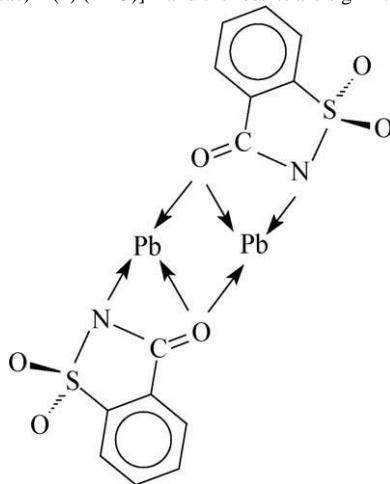
Bidentate coordinating-bridging mode of the saccharinate ligand.

PHYSICOCHEMICAL STUDIES OF SACCHARINATO COMPLEXATION

Most of the saccharinato complexes that have been researched and described so far in the previous sections, their structures are usually fixed by single crystal X-ray diffractometry, which are often extrapolated by various physicochemical methods such as IR spectroscopy, thermoanalytic techniques or magnetic. Dimensions.Described from.But so far some systematic studies have been done using these methods and most of them are dedicated to the simplest aqua-saccharinato species, [M (Sac) 2 (H 2 O) 4] • 2 H 2 O. In this section, we provide a summary-Mary in these systematic studies, broadens our perspective on this interesting type of coordination complex.

VIBRATION SPECTRA

Most experimental studies on the vibrational properties of saccharin or its metal complexes are based on infrared spectroscopic measurements. Raman spectroscopy is rarely used. In this section, only the most general and systematic studies conducted on the Sacharin and Sacharinato complexes, as well as several important papers dedicated to establishing spectro / structural correlations will be briefly reviewed.

Vibrational spectroscopic studies on saccharin began 20 years ago. Interesting improvements in the spectral complexity of the U (NH) region have been made possible by the application of duration methods. The first attempts at proper analysis of U (CO) vibrations were made by Jovanovsky et al. Next, the mid-infrared region was analyzed based on the energy field obtained from quantum chemical calculations using the HF3-21G * basis set. Recently, this vibrational analysis room has been set up to measure the IR spectrum of various saccharinates at liquid nitrogen temperatures, supported by theoretical calculations.

A significant number of spectral / structural correlations have been published in relation to the Saccharinato complex in recent years. In particular, the carbonyl and SO2 stretching vibrations, as well as the vibrations of the hydration H2O molecules were systematically analyzed.

U (CO) vibrations, which usually have a very good group frequency, are often used for structural studies. This mode produces a sharp band at 1642 cm in sodium saccharinate, which converts to lower frequencies when the carbonyl group is involved in the metal bond, weakening the carbon-oxygen bond by interaction. Some correlations between the structural features of this vibrational state and the complex were first demonstrated in 1988 and have recently been replaced using data for a large number of compounds. In this final study, the U (CO) frequency enci coefficients Si -O and the metal-saccharinato distances are related to the corresponding official bond order (cf also). Although the estimated U (CO) frequency range for the difference between N-coordinated and coordinated saturated in solid metal complexes is 1650 cm - 1, due to intra- and intermolecular interactions such as hydrogen bonds, the U (CO) frequency is often likened. Not relevant.

MOSSBAUER SPECTRA AND NMR STUDIES

These methods are rarely applied to the research of saccharinato complexes. [Fe (Sac) 2 (H2O) 4] Only the 57Fe-Mo¨ssbauer spectrum of 2H2O has been researched in detail so far, indicating the presence of Fe (II) as a high spin species.

The electronic structure of saccharin in aqueous solution was detected using two-dimensional NMR spectroscopy of 17O, 15N and 13C. Analyzing this spectrum in the presence of different concentrations of H +, Na +, K +, Ca2 +, Mg2 +, CO3H− and urate, it was concluded that at the physiological level none of these ions significantly altered the electronic structure of the molecule. Does not change. On the other hand, the 13C NMR spectrum of common saccharinates of saccharin, sodium saccharinate and Mg (II), Zn (II), Cd (II), Pb (II) and Hg (II) is measured in dimethyl sulfoxide-d6 solution. Some conclusions can be drawn about the bonding properties from the chemical change.

THERMALBEHAVIOR

Thermal data of many of the complexes reviewed in this paper are often reported as part of a comprehensive synthetic and structural investigation. However, there are many studies dedicated specifically to this topic. One of the earliest works in this area was the paper by Magri and others. Dedicated to the research of the thermal decomposition of the Simple Co (II) and Cu (II) aquo-saccharinato complexes and some pyridine products in them. A few years later, similar Ni (II) and Zn (II) complexes were investigated.

[M (shock) 2 (H2O) 4] 2H2O (M = Mn, Fe, Co, Ni, Cu and Zn) Systematic reorientation of first row transition metal complexes Recent thermogravimetric (TG) and differential thermal analysis (DTA) techniques. In this study, the dynamics of the first stage of decomposition corresponding to the dehydration process were examined in detail and the stability of hydrates with respect to the ionic radii values of the metal cations was discussed. Final pyrolysis residues collected at approximately 750 C were identified by X-ray powder diffractometry as corresponding metal oxides (i.e., Mn 2 O 3, Fe 2 O 3, CO (or CO 3 O 4 at high temperature),NiO, CuO). And ZnO), respectively.

In another interesting study, a sharp color change from yellow to brown was observed during dehydration of [Fe (SAC) 2 (H2O) 4] 2H2O at 141 C. The Mo¨ssbauer and EPR spectra of the dehydration product showed the presence of high-spin Fe (III), indicating that a heat-induced intra-molecular electron transfer reaction occurred in the solid state during the dehydration process [201].

Detailed TG / DTA analysis, complemented by differential scanning calorimetry (DSC) measurements, has also been performed recently for alkaline (excluding Li) -succharines and NH4 (Sac). The decomposition temperature of saccharinate ions is 130C higher than that of pure saccharin.

Various other systematic studies have also been conducted

Various mixed-ligand saccharinato complexes, for example, pyridine A, β-bipyridine, O-phenanthroline, imidazole, hydrogen and ethylenediamine or

A series of cationictriethanolaminecomplexes containingmonoethanoletylenediamineas well as the counter ion saccharinate. Interestingly, during the thermolysis of these final complexes and operating in the N2 environment, elemental metals were obtained as final residues.

THEORETICALSTUDIES

Although the various approximations used in quantum chemical calculations often lead to sharp differences between the calculated and experimentally observed values of molecular parameters, it is widely accepted that such calculations can be made

In fact those parameters give reliable images of trends and / or differences and are also useful in the analysis of spectral data, chemical reactivity and similar issues.

Over the years, several theoretical studies have been conducted for the molecular saccharin and the saccharinate ion. Binev et al. Developed theoretical calculations at the Hartree-Fock level with a relatively small HF3-21G * base set. These calculations provide a good explanation of the spectral changes in the conversion of saccharin to nitron-ion and provide good support for the vibrational functions mentioned in Section 5.1.

In subsequent calculations, the geometry of saccharin and its ion was optimized using the AM1 and PM3 semi-empirical methods, and the full geometry was optimized using the 6-31G * basis. A good relationship is formed between the calculated geometric parameters and the average geometry obtained from the experimental structural data. Also - The ionization of the vibrational spectra of some ionic saccharinates is further supported by these calculations [40].

Recently, a DFT study on the electronic structure of saccharin, thiosacrane (1,2-benzisothiazole-3- (2H) -thion-1,1-dioxide) and their corresponding ions was performed using 6-31G **. Base set. In this case, geometry optimization methods were introduced from experimental architecture data [208]. From the results of this study, it appears that there are significant differences in the molecular and electronic structures of the five-member rings of saccharin and thiosacrine, and that these differences provide significant rationale for the different chemical behavior of these ligands (cf. also section 8). .

Another similar DFT study for theosacaran was conducted independently. The obtained geometric parameters of the isolated molecule and its nitrone agree well with the structural data determined for thiosacrine and its sodium and potassium salts.

Some quantum chemical calculations have been performed for 24N-alternative saccharin as well as for some structurally related molecules, thalmide and succinimide. The results of these calculations are also of interest to better understand the geometric and electronic properties of saccharin.

BIOLOGICAL EFFECTS OF SACCHARINATOCOMPLEXES

In Section 3, we will briefly discuss the biological effects of saccharin, especially in relation to previously suspected carcinogenic activity. In the present section, some aspects related to the biological, biochemical and pharmacological effects of saccharinato complexes are discussed.

Complexes [Zn (SAC) 2 (H2O) 4] 2H2O and [Cu (SAC) 2- (H2O) 4] 2H2O have a definite inhibitory effect on carbon anhydrase in vitro. The

potential Zn (II) complex has been researched as a potential therapeutic additive for dentifrice.

A series of poorly classified common saccharinato complexes such as dioxuranium (VI), oxovenadium (IV), Ce (IV), Hg (II) and Pb (II) are also strong inhibitors of carbonic anhydrase in vitro.

[M (Shock) 2 (H2O) 4] The 2H2O (M = Mn, Fe, Co, Ni, Cu and Zn) type of dual-metal metal aqua-saccharinato complexes have superoxide dismutase-like activity. Detection was performed using the nitroblutetrazolium / superoxide reduction test. The results show that all these complexes have the ability to decompose into O2 ions. Interestingly, the copper (II) complex provides the most important functionality, and its behavior is also supported by its redox properties. Significant antibacterial activity of the egg (I) complex with sulfadiazine is derived from the polymeric nature of the compound and its insoluble state, which is conducive to slow silver release. In the search for new similar complexes of this type, it has been found that silver anthranilite and silver saccharinate present in polymeric structures also have sufficient solubility properties to be considered useful slow cations. Silver Release Agent Formulation.

Human leukocyte elastase (HLE), cathepsin G (Cat G) and proteinase 3 (PR3) are serine endopeptidases stored in the aurophilic granules of neurophiles. Growing evidence suggests that these enzymes may play a major role in the pathophysiology of various inflammatory diseases. Therefore, agents that act as selective inhibitors of these enzymes have potential therapeutic value. Various derivatives of saccharin, for example, with R-acetoxy groups or amino acid, show interesting activity towards N-substitute saccharin HLE. As noted in Section 3, saccharin has been suggested to be useful as an antidote to metal poisoning. Although this property has not been explored in detail, the stability of some polymer saccharinato complexes, for example, Pb (II), Tl (I) or Ag (I), is quite surprising in this context. Creates perspective. , Indicating a promising advantage of the saccharinate

LIGAND FOR CHELATION THERAPY

In recent years, various novel biological effects of lanthanides have been discovered and are of significant clinical significance. These observations open up interesting perspectives for the ultimate medical applications of lanthanide saccharinates that deserve in-depth research of nt medicinal properties. Thiosacrine and its derivatives have also been found to have some potent antimicrobial activity. Also this topic deserves further study in the future.

The formation of co-crystals is of particular practical importance in the solid-state chemistry of drugs, especially in the field of drug distribution, especially its increasing aqueous solution-utility. Saccharin appears to be a good co-crystal because it acts as a hydrogen bond donor (NH) and hydrogen bond acceptor (CO or SO). Recent studies done in, With higher pH values (pH 5-6) than hydrochloride and other common salt formulations (pH 2-3), injectable forms of such drugs can cause skin irritation and other undesirable side effects.

CONCLUSION

Through this review we have attempted to give a clear insight into the peculiarities and versatility of the saccharinate anion as a ligand in coordination chemistry. The analysis of the examples presented, clearly demonstrates the potential of this simple but polyfunctional moiety, capable of interacting with metal centers in very different ways, and also of generating relatively strong
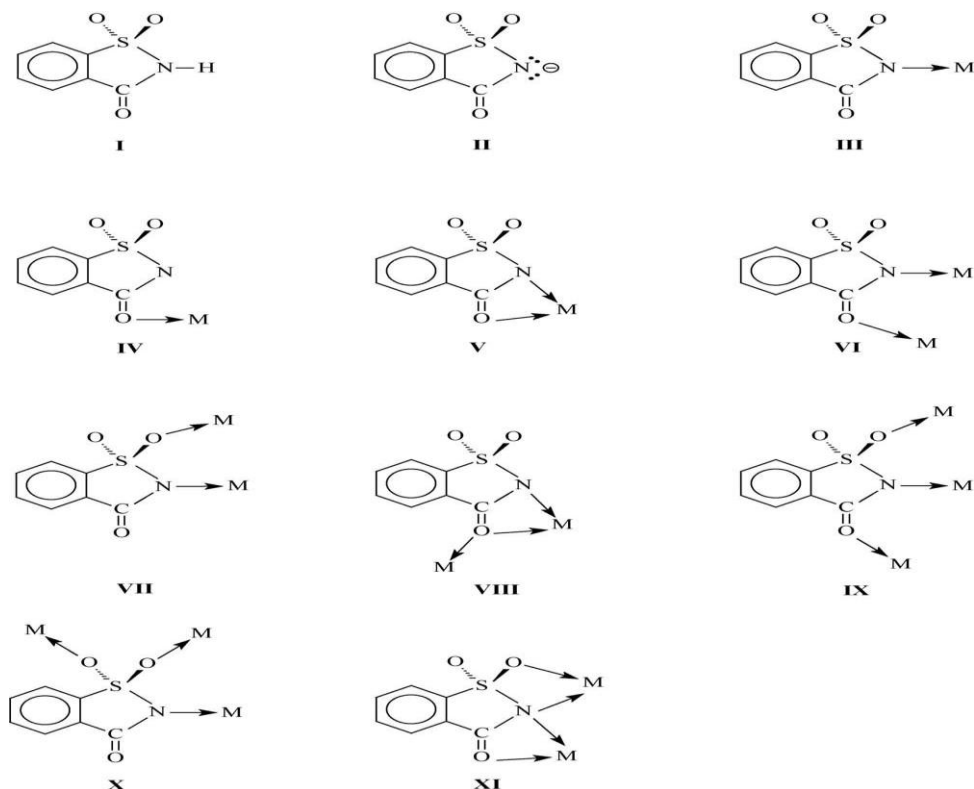
Coordination modes of the saccharinato ligand.Interactions in the crystalline environment, mostly by hydrogen bonding.The structural information collected so far allows to verify its involvement in a variety of ligand-to-metal and molecular interactions, summarized in Figure 8 and includes:Fully ionic interactions between the saccharinate ion (II) (obtained by precipitation of saccharin (I)) and various cations, are discussed in Section 4.1.Monodentate binding by diprotonated N-molecule (III), discussed in Section 4.2. Monodontate bonding by carbonyl O-atom (IV), discussed in Sections 4.3 and 4.5.Binding to single metal center (V) by N- and O (carbonic) -atams, discussed in Section 4.4.Identification of two metal centers by N- and O (carbonyl) -atom (VI), or N- and O (sulfonyl) -atom (VII) -bridging, discussed in Section 4.4.The O-atom, consisting of N- and O (carbonyl) - atoms, simultaneously acts as a bridge to the second metal nucleus (VIII), discussed in Section 4.4.The design of polymeric structures involving trident-bridging modes (IX and XI) is discussed in Section 4.4.Bicordinate-bridging with the N-atom attached to the metal core gives a double bridge (X) with two sulfonyl O-atoms, which are discussed in Section 4.4.-Ambient Coordination Behavior: The formation of Mn and Mo bonds with two different saccharin ligands in the same complex discussed in Section 4.6.-The simultaneous presence of saccharinate (II) as a coordinating ligand and counter ion in complex species is discussed in Sections 4.5 and 4.7. The simultaneous presence of saccharinate (II) and free saccharin (I) discussed in sections 4.5 and 4.7.

REFERENCES

1. R. Mazur, Kirk–Othmer Encyclopedia of Chemical Technology, vol. 22,thirded.,Wiley,NewYork,1983,p.448.
2. J.Jungel,Deutsch.Lebensm.-Rundschau47(1951)7.
3. G.A.Iacobucci,Ind.Qu´m.334(1998)18.
4. The Merck Index, 30th ed., Merck & Co. Inc., Withehouse St., NJ, 2001.
5. R.P.Bell,W.C.E.Higginson,Proc.R.Soc.197A(1949)141.
6. M.A.R. Matos, M.S. Miranda, V.M.F. Forais, J.F. Liebman, Mol. Phys. 103 (2005)221.
7. J.C.J. Bart, J. Chem. Soc. B (1968) 376.
8. Y. Okaya,ActaCrystallogr.B25(1969)2257.
9. G.Argay,L.Fábian,A.Kálmán,Croat.Chem.Acta72(1999)551.
10. M.J. Price, G.C. Biava, L.B. Oser, E.E. Vogin, J. Steinfeld, L.H. Ley, Science 167 (1970)1131.
11. M.R.Weihrauch,V.Diehl,H.Bohlen,Mediz.Klin.96(2001)670.
12. O.M.Jensen,C.Kamby,Int.J.Cancer29(1982)507.
13. S.M.Cohen,Toxicology102(1995)149.
14. J.Zurlo,R.A.Squire,J.Natl.CancerInst.90(1998)2.
15. J.Whysner,G.M.Williams,Pharmacol.Ther.71(1996)127.
16. S.D. Turner, H. Tinwell, W. Piegosrch, P. Schmerzer, J. Ashby, Muta- genesis 16 (2001)329.
17. L.B. Ellwein, S.M. Cohen, Crit. Rev. Toxicol. 20 (1990) 311. [26] Chem. Br. 37 (2001)18.
18. K.M.A. Malik, S.Z. Haider, M.A. Hossain, M.B. Hursthouse, ActaCrystallogr. C40 (1984)1696.
19. P.M. Bhatt, N.V. Ravindra, B. Banerjee, G.R. Desiraju, Chem. Com- mun. (2005)1073.
20. V.T. Yilmaz, Y. Topcu, F. Yilmaz, C. Thoene, Polyhedron 20 (2001) 3209.
21. V.T. Yilmaz, S. Hamamci, O. Andac, C. Thoene, W.T.A. Harrison, Trans.Met.Chem.28(2003)676.
22. W. Henderson, B.K. Nicholson, L.J. McCaffrey, Inorg. Chim.Acta 285 (1999)145.
23. S.M.Teleb,J.Argent.Chem.Soc.92(2004)31.
24. G.Jovanovski,P.Naumov,O.Grupče,B.Kaitner,Eur.J.SolidStateInorg. Chem. 35 (1998)231.