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Review

Metal complexes of saccharin

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Contents

1. Introduction 1981
2. Synthesis and general properties of saccharin 1981
3. Biological effects of saccharin 1982
4. Metal complexes of saccharin 1982
    4.1. Ionic saccharinates 1982
    4.2. Monodentate *N*-coordinated metal complexes 1983
    4.3. Monodentate *O*-coordinated metal complexes 1984
    4.4. Bidentate (N, O) and tridentate (N, O, O)-coordinated metal complexes 1985
    4.5. Saccharinate complexes of the lanthanides 1987
    4.6. Other peculiar (ambidentate) coordination behavior 1987
    4.7. Presence of bonded and non-bonded saccharinate anions and of free saccharin in complex species 1988
5. Brief overview on physicochemical studies of saccharinato complexes 1988
    5.1. Vibrational spectra 1989
    5.2. Electronic and magnetic properties 1990
    5.3. Mössbauer spectra and NMR studies 1990
    5.4. Electrochemical behavior 1990
    5.5. Thermal behavior 1991
6. Theoretical studies 1991
7. Biological effects of saccharinato complexes 1991
8. Metal complexes of thiosaccharin 1992
9. Conclusions and future outlook 1994
Acknowledgements 1995
References 1995

Abbreviations: aeppz, *N*-(2-aminoethyl)piperazine; aepy, 2(2-aminoethyl)pyridine; aim, allylimidazole; ampy, 2-(aminomethyl)pyridine; apy, 4-aminopyridine; ApyH, 2-aminopyridinium; bpy, α,α′-bipyridine; 4-4′-bpy, 4,4′-bipyridine; bpym, bipyrimidine; bzim, benzimidazole; cys, cysteine; dea, diethanolamine; dien, diethylentriamine; dipy, dipyridylamine; dmen, *N*,*N*-dimethylethylenediamine; dmpy, 2,6-dimethanolpyridine; dmso, dimethylsulfoxide; ea, monoethanolamine; en, ethylenediamine; EtOH, ethanol; forth, 2-formylpyridinethiosemicarbazonato; hep, *N*-2-(hydroxyethyl)piperazine; Him, imidazolium cation; Hnic, nicotinic acid; Hpyet, 2-ethanolpyridinium cation; Hsac, saccharin; HydEt-en, *N*-(2-hydroxyethyl)-ethylendiamine; im, imidazole; iqn, isoquinoline; 6mptsc, 6-methyl-2-pyridinecarbaldehydethiosemicarbazone anion; mpy, 4-methylpyridine; nic, nicotinamide; nns, S-methyl-β-*N*-(6-methylpyrid-2-yl)methylenedithiocarbazate; ophen, *o*-phenanthroline; ox, oxalate; prpy, 4-propylpyridine; PPh_3, triphenylphosphine; prz, pyrazole; py, pyridine; pyet, 2-pyridylethanol; pym, 2-pyridylmethanol; pypr, 2-pyridinepropanol; pysme, pyridine-2-carboxaldehyde Schiff base of S-methyldithiocarbazate anion; sac, saccharinate anion; tea, triethanolamine; thf, tetrahydrofuran; tsac, thiosaccharin

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Abstract

Metal complexes of the saccharinate anion, obtained by deprotonation of the N–H moiety of saccharin (*o*-sulfobenzimide) are reviewed. A wide variety of metal species based on mononuclear, binuclear, polynuclear complexes and extended coordination polymers are discussed in relation to the coordination modes of the anion, i.e., monodentate (through the N-atom or the carbonylic O-atom), bidentate, tridentate or bridge forming. 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. With regard to saccharin in food and its health effects, the biological properties of saccharin and its complexes are also summarized. Finally, for comparative purposes, a brief overview on the so far characterized metallic complexes of thiosaccharin is given. This survey demonstrates that saccharinate is a very versatile and polyfunctional ligand in coordination chemistry.

Keywords: Saccharin; Metal complexes; Coordination modes; Metal–saccharinato bonds; Physicochemical properties; Biological properties; Thiosaccharin

1. Introduction

Saccharin (*o*-sulfobenzimide; 1,2-benzothiazole-3(2H)-one 1,1-dioxide; Hsac; Fig. 1) is one of the best known and most widely used artificial sweetening agents. The imino hydrogen is acidic and, thus, the molecule can be easily converted into the corresponding nitranion. It has been shown that the coordination chemistry of this anion is very interesting and versatile, taking into account that it offers different coordination sites to metallic centers, i.e., one N, one O (carbonylic) and two O (sulfonic) atoms. Using these donor atoms the anion can generate either N- or O-monodentate or bidentate (N, O) coordination, and also more complex polymeric species with the participation of all possible donor atoms [1].

Recently, it has also been found that in some compounds the saccharinate anion can be present in both, the complex cation and as a counter-ion, outside the coordination sphere. On the other hand, an important number of compounds in which the saccharinate anion is only present as a counter anion from a complex cation are also known. Besides, the presence of free saccharin in the crystal lattices of certain complexes has also been established [1]. The anion is able to participate in the formation of mixed-ligand complexes, sharing coordination spheres with a great number of different ligands, showing a variety of binding characteristics.

During the last 20 years different research groups have performed 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.

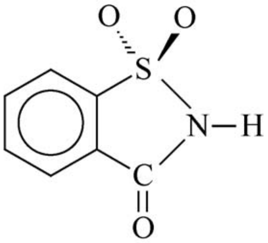


Fig. 1. Schematic structure of saccharin (Hsac).

2. Synthesis and general properties of saccharin

Saccharin was discovered accidentally by Fahlberg in 1878 during an investigation of the oxidation of *o*-toluenesulfonamide [2,3] and published by Remsen and Fahlberg, 1 year later [4,5]. Shortly after its discovery it was produced on an industrial scale (1887) as the first sweetening agent which was not a carbohydrate [2]. As it is not very water soluble it is normally used in the form of the sodium or calcium salt [6] and its sweetening power is about 550 times that of saccharose [2,6–8]. Besides, it exhibits an unpleasant bitter and metallic aftertaste and the sweet taste is still detectable in 1:100,000 dilution [9].

It can be manufactured by two different processes. In one of them, based on the original discovery, toluene is used as the starting reagent. Its treatment with chlorosulfonic acid, followed by interaction with NH_3 generates a mixture of *o*- and *p*-toluenesulfonamide. After separation of the two sulfonamides, the oxidative ring closure of *o*-toluenesulfonamide produces saccharin. In the second process, methyl anthranilate (readily available from phthalic anhydride) is the starting material, and saccharin is obtained after four successive steps (treatments with $NaNO_2$/HCl, SO_2, Cl_2 and NH_3) [6].

Saccharin is relatively insoluble in water. One gram dissolves in 290 ml of water or in 25 ml of boiling water. It is much more soluble in ethanol, acetone and glycerol and slightly soluble also in ether and chloroform [9]. It is usually present in the form of monoclinic crystals which show perfect (1 0 0) cleavage. Its melting point is 228.8–229.7 °C and its density 0.828 g/ml [9]. It is slightly acidic, with a pK_a value of 1.60 [10].

The standard molar enthalpies of combustion, sublimation and formation have only been determined recently by calorimetric methods [11].

The crystal structure of saccharin was published independently by Bart [12] and Okaya [13] quite a long time ago. The results of both studies are comparable, including the final *R*-values, and show that the compound belongs to the monoclinic $P2_1/c$ space group with the unit cell parameters *a*, *b* and *c* close to 9.55, 6.91 and 11.80 Å, respectively, and the monoclinic angle β in the order of 103 °. As in many cyclic imides [14], the structure is molecular, with centrosymmetric dimmer molecules formed by N–H···O hydrogen bonds between the H hydrogen atoms of the imino nitrogen and the carbonyl oxygen atoms, both of the five-membered ring.

3. Biological effects of saccharin

One of the reasons which initially generate important interest on the chemistry of saccharin and its metal complexes, was its suspected carcinogenicity [1]. During years discussions on the health risks of saccharin and other artificial sweetening agents were present in both the scientific literature and the informative media. In the 1970s, there was some basis of concern regarding saccharin when a study showed that rats given high doses developed bladder cancer [15]. As a consequence, the US National Toxicology Program classified saccharin as a "possible carcinogen", suggesting that it might cause cancer in humans.

There are more than 50 publications about the effects of saccharin on rats. A number of these studies investigated its influence over one generation of rats which received high doses (usually 5% of the total consumed food) at least for 1.5 years. The greatest part of these studies could not demonstrate an increasing risk of cancer generation. Later, such experiences were extended to two generations of experimental animals, submitting saccharin to the parents and the following rat generation. These studies demonstrate a certain risk increase towards bladder carcinomas in the second generation (for a brief review of all these studies cf. [16]). A further study, using 2500 rats, demonstrated that the risk for bladder tumors increases at saccharin concentrations higher than 4% [17]. On the basis of these results, the use of saccharin as a food additive was prohibited in Canada [16]. Besides, it could be demonstrated that similar doses of ascorbic acid (Vitamin C) also generate bladder cancers in rats [18]. Rodents present a high urinary osmolality which during the excretion of important amounts of sodium salts, such as sodium ascorbate or saccharinate, favors the precipitation of crystals which may be responsible for the induction of urothelial hyperplasia, *via* micro-abrasion, leading ultimately to bladder tumors [16].

On the other hand, a long-term study (24 years) with monkeys conclusively demonstrated that sodium saccharinate did not cause increased urothelial cell proliferation, bladder tumors or the appearance of crystalline material in the urine of these animals [16,19].

Systematic studies on saccharin risks on humans are relatively more scarce. Some investigations on high and continuous saccharin consumers (for example, diabetic people) do not show any important consequences. It has also been demonstrated that uterine saccharin exposition does not elevate the risk of bladder cancer, at least during the first three decades of life [16,20].

Although the direct extrapolation of results obtained from laboratory animal experiments to humans have often criticized in the here discussed context [21,22], it is possible to state that as a final conclusion of all these studies it becomes evident that the carcinogenicity of sodium saccharinate is essentially specific to the bladder of male rat, with minor effects occurring in the female rat bladder [23,24] and allowing to classify it as a non-genotoxic carcinogen [24,25] which are unlikely to be a human carcinogen [21]. Finally, in 2000 the US National Toxicology Program removed saccharin from the list of carcinogens and saccharin can now be considered safe as proclaimed, for example, in the January/2001 Editorial from Chemistry in Britain [26].

It has also been suggested that saccharin may be potentially useful as an antidote for metal poisoning [27], although this property has not been further explored in a systematic way. Recently, it was also suggested that the weak acidity of saccharin may be exploited in the pharmaceutical chemistry using it as a salt former, which enhances the solubility of certain drugs [28]. These aspects and some other biological properties and activities of the metallic complexes of saccharin shall be discussed in Section 7.

4. Metal complexes of saccharin

The studies commented in the previous section were successfully accompanied by a very rapid and continuous development of the knowledge on the interactions of saccharin with different metallic cations. Initially, most of the prepared and investigated complexes were mixed aqua-saccharinato species. But saccharin shows rapidly its potential as a powerful and versatile polyfunctional ligand and a great number of other simple and mixed-ligand complexes were prepared and thoroughly characterized. Most of these complexes contain the deprotonated saccharin, in the form of its nitranion (the so-called saccharinate anion), which in the following shall be identified as sac, in contrast to the free molecule, identified as Hsac.

A very limited number of systematic studies and generalizations about this type of complex has so far been undertaken. Structural data of many of them have been critically evaluated and some peculiarities regarding the geometrical characteristics of the ligand and its bond properties, discussed in detail [29,30]. Some of the most relevant results of these studies together with the analysis of vibrational-spectroscopic data, and of spectral/structure correlations were also discussed [31].

As mentioned in Section 1, the saccharinate anion can interact in different ways with metallic centers, an aspect which has recently been briefly reviewed [1]. In the following sections, we present a detailed analysis of these different forms of interaction, and a discussion of the most relevant properties and characteristics of the complex compounds belonging to each of these classes.

4.1. Ionic saccharinates

There is a family of saccharinate derivatives, containing alkaline or alkaline-earth cations in which the cation/anion interaction is mainly of an ionic nature. However, complete crystallographic structural information is available for only a few of them.

As mentioned above the usual commercial form of saccharin is the solid hydrate of sodium saccharinate ("sodium saccharin" and "soluble saccharin") [9]. Although this salt has been widely used for more than one century and constitutes one of the most used artificial sweeteners around the world, its exact structure was not unequivocally established until very recently.

Recrystallization of sodium saccharinate from different solvents yielded two different hydrates. The hydrate obtained from 95% ethanol, of composition Na(sac)·(2/3)H_2O, crystallizes in the triclinic space group $P\bar{1}$ [32,33]. A monoclinic hydrate of stoichiometry Na(sac)·(15/8)H_2O and belonging to the $P2_1/n$ space group could recently be obtained from water and is identical to the unpurified commercial product [33,34]. From the crystallographic point of view it must be formulated as $Na_{64}(sac)_{64}·120H_2O$, generating a very large unit cell with a volume of 15560.4 Å^3 and $Z = 64$, which may be regarded as an occupational and displaced modulation of an idealized (i) structure with $C2/m$, $Z = 8$, and $a_i = a$, $b_i = b/4$ and $c_i = 2$, containing a large number of structurally different water molecules [33]. Crystals of this form are very stable if stored in a closed vessel and not allowed to suffer mechanical damage. Notwithstanding, when exposed to dry air, placed in an evacuated container or crushed, they turn opaque. Its isobaric dehydration begins slightly above room temperature and proceeds through two intermediates: Na(sac)·(9/8)H_2O and Na(sac)·(2/3)H_2O (or Na(sac)·(4/9)H_2O). The exact formula of the second intermediate could not been established with certainty and the structure of the 9/8 hydrate could so far not be determined due to its low crystallinity [33] and this is also the case of the anhydrous compound, Na(sac), which apparently shows a certain structural relation to the triclinic hydrate [34].

When dehydrated under isobaric conditions the triclinic hydrate Na(sac)·(2/3)H_2O also generates the 4/9 hydrate as the unique intermediate, stable in the temperature range between 343 and 389 K [33,35].

Other ionic saccharinates for which structural data are so far available are K(sac)·(2/3)H_2O [36], the mixed cation salt $K_2Na(sac)·H_2O$ [27], the Mg(II) compound of composition $Mg(sac)_2·7H_2O$ [32] and the alkaline-like ammonium salt, $NH_4(sac)$. This compound is so far the only structurally characterized anhydrous ionic saccharinate [37]. It is composed by ammonium and saccharinate ions, forming a layer structure by a network of hydrogen bonds. Each NH_4^+ cation contacts four oxygen atoms of different saccharinate anions through four normal hydrogen bonds generating a similar four-fold coordination of this cation, which resembles that of NH_4F [38].

The IR spectra of two cesium saccharinates of composition Cs(sac)·0.5H_2O and Cs(sac)(Hsac)·H_2O were reported some years ago [35,39] although the structures of these compounds remain unknown. Besides, also for Rb(sac)·0.5H_2O, obtained from Rb_2CO_3 and saccharin dissolved in warm ethanol, some spectroscopic and thermal data are available [35,40]. Very recently, apparently a rubidium saccharinate of composition Rb(sac)(Hsac)·H_2O could also be characterized [31].

Concerning the alkaline-earth saccharinates, apart from the above mentioned Mg(II) complex, not other simple compounds could so far be thoroughly characterized although compounds with composition $Ca(sac)_2·4H_2O$, $Sr(sac)_2·4H_2O$ and $Ba(sac)_2·8H_2O$ have been mentioned in the literature [31]. As our own studies have shown, Ca(II), Sr(II) and Ba(II) saccharinates are extremely soluble in water, precluding the synthesis of crystalline material adequate for crystallographic studies. However, some mixed-ligand complexes from this cations have recently been prepared and characterized. They shall be described in Sections 4.4 and 4.7. On the other hand, a Be(II) complex, of stoichiometry $Be(sac)_2·2H_2O$, obtained by reaction of beryllium perchlorate and sodium saccharinate solutions, has been described [41] but remains poorly characterized.

4.2. Monodentate N-coordinated metal complexes

The reaction of sodium saccharinate with the first row divalent metal ions from V(II) to Zn(II) results in isomorphous coordination compounds with the formula $[M(sac)_2(H_2O)_4]·2H_2O$, where M is V(II) [42,43], Cr(II) [43–45], Mn(II) [46,47], Fe(II) [48–50], Co(II) [48–50], Ni(II) [48–50], Cu(II) [48–52] and Zn(II) [44,45,48,50,53]. 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 $[M(sac)_2(H_2O)_4]·2H_2O$ species were documented about two decades ago and, as shown in Fig. 2, 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 $[M(sac)_2(H_2O)_4]·2H_2O$ 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 prepared by the direct reaction of a neutral ligand with the starting aqua-saccharinato complex in solution. The addition of the ligands 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

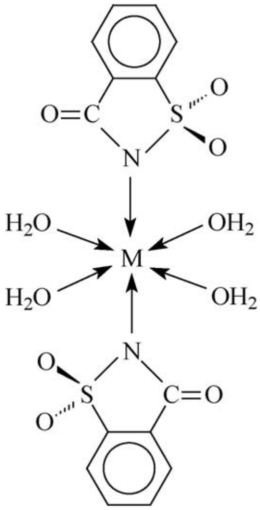


Fig. 2. Schematic drawing of the structure of the $[M(sac)_2(H_2O)_4]·2H_2O$ complexes (M^{II} = V, Cr, Mn, Fe, Co, Ni, Cu and Zn).

saccharinato ligand, $[Cu(sac)(PPh_3)_2]$, was obtained by the reaction of the dehydrated starting aqua complex, $[Cu(sac)_2(H_2O)_4]$, with triphenylphosphine (PPh_3) in CH_2Cl_2 [54], and other examples of this type were observed with silver(I): $[Ag(sac)(PPh_3)_2]$ [55], $[Ag(sac)(py)]_n$ (py = pyridine) [56], $[Ag(sac)(pym)]_n$ (pym = 2-pyridylmethanol) [57], $[Ag_2(sac)_2(dmen)_2]$ (dmen = *N*,*N*-dimethylethylenediamine) [58]. These dimeric and polymeric silver(I)–sac complexes are formed by way of relatively strong Ag–Ag interactions.

Tetrahedral coordination usually occurs in the case of Zn(II), and examples are $[Zn(sac)_2(py)_2]$ [59], $[Zn(sac)_2(im)_2]$ (im = imidazole) [60], $[Zn(sac)_2(bzim)_2]_2\cdot 2EtOH\cdot H_2O$ (bzim = benzimidazole; EtOH = ethanol) [60], $[Zn(sac)_2(aepy)]$ (aepy = 2-(2-aminoethyl)pyridine) [61]. $ApyH[Zn(sac)_3(H_2O)]$ (ApyH = 2-aminopyridinium) is the first example of a tetrahedrally coordinated mononuclear tris(saccharinato) complex of a divalent transition metal [62].

The square-planar coordination geometry was observed in two dimeric Cu(II)–saccharinato complexes, $[Cu_2(dea)_2(sac)_2]$ (dea = diethanolamine) [63] and $[Cu_2(pypr)_2(sac)_2]$ (pypr = 2-pyridinepropanoxy anion) [64]. The two Cu(II) ions in both dimers are linked by two alkoxo-bridges and the relatively short Cu···Cu separation of ca. 2.99(2) Å is responsible for a strong antiferromagnetic coupling in the Cu–Cu pair. Furthermore, mononuclear square-planar Pt(II) and Pd(II) complexes with the formula $[MCl(sac)L_2]$ (L = various phosphine ligands) also exhibit Pt–N and Pd–N bonds [65]. These are so far the unique known saccharinato complexes of platinum group metals.

Recently, two Au(III) complexes of composition $[Au(sac)_2(H_2O)_2]Cl$ and $[Au(sac)_3H_2O]$ have been reported. On the basis of the analysis of its IR spectra it was concluded that they also present a square-planar coordination with the saccharinate anion acting as a monodentate ligand through its N-atom [66].

It is obvious that five-coordinate complexes can be obtained with Cu(II), due to the coordination flexibility of this cation. In most cases, these complexes contain an aqua ligand, suggesting that in the ligand substitution mechanism a stable five-coordinate intermediate usually forms during conversion of the starting compound from octahedral to tetrahedral, leaving one of the aqua ligands unchanged. Examples of square-pyramidal complexes with *N*-bonded saccharinato ligands are $[Cu(sac)_2(H_2O)(py)_2]$ [67], $[Cu(sac)_2(H_2O)(bzim)_2]$ [68], $[Cu(sac)_2(H_2O)(bzim)(EtOH)]$ [68], $[Cu(sac)_2(H_2O)(nic)_2]$ (nic = nicotinamide) [69], $[Cu(sac)_2(H_2O)(Hnic)_2]$ (Hnic = nicotinic acid) [70], $[Cu(sac)_2(H_2O)(prpy)_2]$ (prpy = 4-propylpyridine) [71], $[Cu_2(sac)_2(tea)_2]\cdot 2(CH_3OH)$ (tea = triethanolaminate) [72], $[Cu(sac)_2(H_2O)(aepy)]$ [73], $[Cu(sac)_2(H_2O)(bpy)_2]$ (bpy = α,α′-bipyridine) [74], $[Cu(nns)(sac)(H_2O)]$ (nns = S-methyl-β-*N*-(6-methylpyrid-2-yl)methylenedithiocarbazate) [75], $[Cu(pysme)(sac)(MeOH)]$ (pysme = the pyridine-2-carboxaldehyde Schiff base of S-methyldithiocarbazate anion) [76] and $[Cu(forth)(sac)(H_2O)]\cdot 0.5H_2O$ (forth = 2-formylpyridinethiosemicarbazonato) [77].

The trigonal-bipyramidal coordination seems to be less common for these mixed-ligand complexes. It has been found, for example, in $[Cr(sac)_2(py)_3]\cdot 2py$ [78] as well as in $[Cu(ophen)_2(sac)]sac\cdot 2H_2O$ (ophen = *o*-phenathroline) [79] and in a similar complex with α,α′-bipyridine, $[Cu(bpy)_2(sac)]sac\cdot 3H_2O$ [80,81] in both of which the saccharinate anion occupies one of the three equatorial positions.

Octahedral complexes usually occur in the presence of two neutral chelating co-ligands. Examples are as follows: $[Ni(sac)_2(ea)_2]$ (ea = monoethanolamine) [82], $[Ni(sac)_2(ampy)_2]$ (ampy = 2-(aminomethyl)pyridine) [83], $[Cu(sac)_2(ea)_2]$ [84], $[Cu(sac)_2(pym)_2]$ [85], $[Cu(sac)_2(HydEt\text{-}en)_2]$ (HydEt-en = *N*-(2-hydroxyethyl)-ethylendiamine) [86], $[Cu(sac)_2(ampy)_2]$ [73], $[Zn(ea)_2(sac)_2]$ [63], $[Zn(sac)_2(ampy)_2]$ [61] and $[M(sac)(bpy)_2(H_2O)]sac$, with M = Mn(II), Co(II), Ni(II) and Zn(II) [87–89]. Besides, $[Cu(sac)_2(NH_3)_4]$ [54] constitutes one of the rare examples of a mixed octahedral saccharinato complex with four additional monodentate ligands, with the two saccharinate anions in *trans* coordination. Similar complexes of Mn(II), Fe(II), Co(II), Ni(II) and Zn(II) have also been apparently prepared, but have not been further characterized [54].

Additionally, saccharinate also interacts with some heavy non-transition metal cations such as Cd(II) and Hg(II) to yield $[Cd(sac)_2(H_2O)_4]\cdot 2H_2O$ [53] and $[Hg(sac)_2]$ [90], respectively. Among them, $[Cd(sac)_2(H_2O)_4]\cdot 2H_2O$ is isomorphous with those of the first-row transition metals. Mixed-ligand Cd(II) and Hg(II) complexes containing *N*-bonded saccharinato ligands are prepared starting from these species and the complexes reported in this field are the following: $[Cd(sac)_2(bpy)_2]$ [89], $[Cd(sac)_2(dea)_2]$ [91], $[Cd(sac)_2(HydEt\text{-}en)_2]$ [86], $[Cd(sac)_2(ampy)_2]$ [92], $[Cd(sac)_2(aepy)_2]$ [92], $[Cd(sac)_2(pyet)_2]$ (pyet = 2-pyridylethanol) [93], $[Cd(sac)_2(H_2O)(dmso)(pyet)]$ [93], $[Cd(sac)_2(H_2O)_2(nic)_2]$ [94], $[Cd(sac)_2(NH_3)_4]$ [54,95], $[Hg(Cl)(sac)]$ [96], $[Hg(sac)_2(bpy)]$ [97], $[Hg_2(Cl)_2(sac)_2(py)_2]$ [98], $[Hg(ea)_2(sac)_2]$ [99], $[Hg(sac)_2(pyet)]$ [100], $[Hg(sac)_2(ampy)_2]$ [101] and $[Hg(sac)_2(aepy)]$ [101].

Finally, Ng et al. reported a number of five-coordinate triphenylstannyl saccharinates in which saccharinate is also N-bonded [102]. Besides, also in the T-shaped Ag(I) complexes $[Ag(sac)(ampy)]$ and $[Ag_2(sac)_2(aepy)_2]$, the saccharinate anion coordinates to the metal through its N-atom [103].

4.3. Monodentate O-coordinated metal complexes

As a ligand, the saccharinate anion offers two different donor O-atoms, namely carbonyl and sulfonyl groups, among which the latter is less basic and is rarely involved in bonding, but the former often participates in coordination, where the anion acts as a chelating or bridging ligand as discussed later in this review.

Monodentate coordination of the carbonyl O-atom is rather unusual and is found when branched or bulky co-ligands are present. This type of coordination was first realized in the vanadium(II) complexes $[V(sac)_2(py)_4]\cdot 2py$ and $[V(sac)_2(py)_4]\cdot 2thf$ [42,43] and also established for $[Ni(sac)_2(py)_4]\cdot 2py$ [104] and is probably also present in $[VO(OH)(sac)(H_2O)_2]Hsac$ [105]. As illustrated in Fig. 3, the structures of these vanadium(II) and nickel(II) complexes show that when the equatorial plane of the octahedron are occupied by four planar pyridine rings,

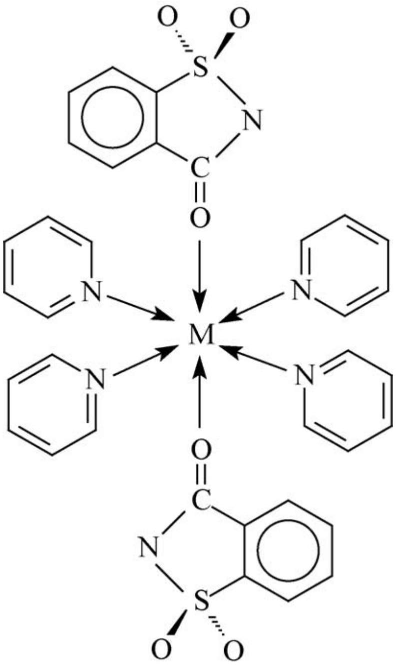


Fig. 3. Schematic drawing of the structures of the mixed-ligand complexes $[M(sac)_2(py)_4]$ ($M^{II} = V$ and Ni).

the saccharinate ligands are forced to bind *via* the carbonyl group. This supposition is further confirmed by the structures of $[Cu(sac)(H_2O)(mpy)_4]$ (mpy = 4-methylpyridine) [71], $[Cu(sac)_2(iqn)_4]$ (iqn = isoquinoline) [71] and $[Cu(sac)_2(prz)_4]$ (prz = pyrazole) [70] containing four nearly planar ligands.

Similar M–O bonds were found in octahedral complexes with bidentate chelating ligands: $[Co(pypr)_2(sac)_2]$ (pypr = 2-pyridinepropanol) [106], $[Cu(pypr)_2(sac)_2]$ [64], $[Ni(sac)_2(pypr)_2]$ [107], $[Ni(sac)_2(aepy)_2]$ [83], $[Ni(sac)_2(aeppz)_2]$ (aeppz = *N*-(2-aminoethyl)piperazine) [108], $Zn(sac)_2(aeppz)_2]$ [109] and $[Cd(sac)_2(aeppz)_2]$ [109]. In these octahedral complexes, secondary ligands are pyridine or piperazine derivatives containing alkylhydroxy and alkylamino groups. The alkyl chains consisting of two- or three-membered C atoms bend rather easily due to the coordination of the end donor atom, increasing consequently the steric crowding around the metal centers. It may be concluded that the coordination of saccharinate through the N-atom becomes difficult due to the increase in the length of alkyl chains. The coordination of other bulky moieties such as PPh_3 and *N*,*N*-dimethylethylenediamine results also in O-bonded saccharinato anions as found in the following complexes: $[Cu(sac)(PPh_3)_3]$ [54] and $[Ni(sac)_2(dmen)_2]$ [110].

4.4. Bidentate (N, O) and tridentate (N, O, O)-coordinated metal complexes

Another possibility is the simultaneous coordination of two or all donor sites of saccharinate where the ligand acts as bi- or tridentate chelating and/or bridging ligand between two or more metal ions.

Two of the most interesting dimeric species showing this type of interactions are $[Cr_2(sac)_4]\cdot 2thf$ [111] and $[Cr_2(sac)_4(py)_2]\cdot 2py$ [78], in which the four saccharinate moieties act as bidentate (N, O) bridges between the two Cr(II) cations and which, therefore, resembles the well known Cr(II)/carboxylate species [112].

The bi- and tridentate coordination modes were observed more frequently with Pb(II) and Ag(I). In the monomeric Pb(II) complex, $[Pb(sac)_2(H_2O)_2(ophen)]$ [113], the two saccharinato moieties act as bidentate chelating ligands, generating an unusual coordination number of eight, together with the other ligands. The first example of bridging saccharinato was the dimeric $[Pb(sac)_2]\cdot H_2O$ in which these two ligands act as a bidentate bridge between the lead(II) centers through the N- and carbonyl O-atoms [114]. In $[Pb_2(sac)_4(H_2O)_2(bpy)_2]$ [115], two of the saccharinato ligands are monodentate N-coordinated, while the others bridge two Pb(II) centers through the N- and carbonyl O-atoms. A similar coordination mode was observed in $[Cd_2(sac)_4(im)_4]$ [116] and $[Cu_2(sac)_4(im)_4]$ [117]. A refinement of this last structure shows that the very short C═O bond distances found for the N-bonded saccharinate ligands was an artifact generated by a disorder in these moieties [118]. Other dimeric species of some first-row transition metals with bridging saccharinato ligands are $[Cu(sac)(PPh_3)]_2$ [54] and $[Cu(6mptsc)(sac)]_2$ complexes (6mptsc = the 6-methyl-2-pyridinecarbaldehydethiosemicarbazone anion) [76].

As mentioned before, the sulfonyl group is less basic and is only occasionally involved in coordination. Saccharinato-bridged complexes, involving N- and sulfonyl O-atoms are known for Ba(II) and Ag(I) in $[Ba_2(sac)_4(triglyme)_2]$ [119] and $[Ag_2(sac)_2(pyet)_2]$ [120], respectively.

The bridging ability of saccharinate sometimes results in the formation of coordination polymers. For example, in $[Pb(H_2O)(OAc)(sac)]_n$, the Pb(II) ions present a pentagonal bipyramidal coordination geometry and are bridged by both saccharinato and acetato (OAc) ligands in a zigzag arrangement, featuring a linear chain with a Pb···Pb distance of ca. 4.25(2) Å [121]. Although usually the saccharinate functions in a single bridging mode as explained in the above examples, occasionally it acts in more than one bridging mode, i.e., a bicoordinating-bridging (or chelate-bridging) mode, as shown in Fig. 4. In such situation, the N-atom is monodentate, while the O-atom is bidentate. The bicoordinate-bridging mode has so far been documented in the eight-coordinated one-dimensional Pb(II) complexes $[Pb(sac)_2(pym)]_n$ [122] and $[Pb(sac)_2(ampy)]_n$ [123]. Besides, these complexes are so far the only examples of simultaneous chelating/bridging coordination of two saccharinates within the same coordination environment: one bidentate (N, O) chelating and one (N, O) bridging saccharinato ligand, respectively.

In the case of Ag(I), polymeric species are favored. $[Ag_2(sac)_2(hep)_2]_n$ (hep = *N*-(2-hydroxyethyl)piperazine) consists of dimeric $[Ag_2(sac)_2]$ units formed by two bridging saccharinato ligands (N, $O_{carbonyl}$) and these dimeric units are further bridged by the hep ligands, forming a one-dimensional coordination polymer with three- and four-coordinate Ag(I) cations [124]. Bridging of the Ag(I) centers by similar saccharinato ligands are also found in a one-dimensional helical chain of $[Ag_2(sac)_2(en)(H_2O)]_n$ and results in a fairly short

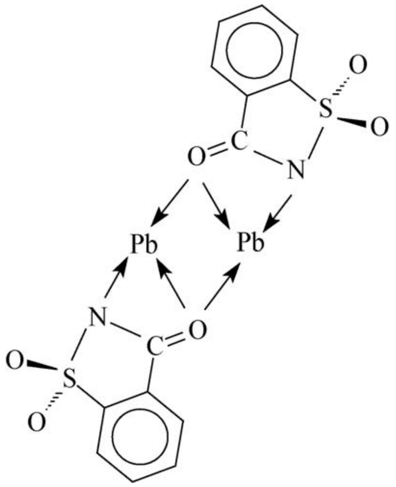


Fig. 4. Bidentate coordinating-bridging mode of the saccharinate ligand.

Ag–Ag bond of 2.9920(3) Å [58]. Bidentate-bridging coordination mode involving sulfonyl O-atoms is observed in the Hg(II) complex $[Hg(sac)_4(mpy)_2]_n$, in which two N-bonded saccharinato and two bridging mpy ligands constitute the dimeric units, which are sequentially linked by the sulfonyl oxygens of the bridging saccharinato ligands, generating an infinite chain [85].

Tridentate coordination mode includes coordination of all donor sites of saccharinate and were found in a relatively rare class of complexes. The first reported complex containing tridentate saccharinato ligands was $[Ag(sac)]_n$ [125], which presents an infinite chain structure formed by dimeric units in which two Ag(I) cations are bidentate bridged by two saccharinato anions through the imino N- and carbonyl O-atoms. The dimeric units are further combined in infinite chains by additional participation of the sulfonyl O-atoms. In another, recently reported, polymeric Ag(I) complex of composition $[Ag(sac)(dmpy)]_n$ (dmpy = 2,6-dimethanolpyridine), the [Ag(sac)(dmpy)] units are formed by *N*-coordinated sac and dmpy ligands and these monomeric units are doubly bridged by the two sulfonyl O-atoms of each saccharinato anion, leading to a one-dimensional polymeric chain [57]. In spite of the fact that the Ag–O bonds in this coordination polymer seem to be relatively long, being 2.82–2.94 Å, it represents a nice example of a tridentate saccharinato bonding (see Fig. 5).

The structural analysis of the new compound $Na[Ag(sac)_2]$, containing $[Ag(sac)_2]^+$ cations, shows that its three-dimensional structure is achieved by bi- and tridentate saccharinato bridges between the Ag(I) and Na(I) cations [126]. The most interesting tridentate coordination mode was probably found in the tetrameric $[Ag_4(sac)_4(pypr)_2]$ complex, in which each of the two saccharinato moieties simultaneously bridges three silver(I) centers [120].

An exceptional coordination of saccharinate has been recently documented in a polymeric thallium(I) complex of composition $[Tl_2(sac)_2(H_2O)]_n$ [127]. Its structure shows two structurally different metallic centers, where one of them presents coordination 8 and the other one coordination 5. The saccharinato ligands show an unprecedented coordination behavior as it acts as chelating ligand through its N- and carbonyl O-atoms with the N-atoms interacting simultaneously with both metal centers and also the sulfonyl O-atoms are involved in bonding.

In the recently described $[UO_2(sac)_2]\cdot 3H_2O$ complex an highly improbable bidentate interaction of the ligand, through its carbonyl and sulfonyl oxygen atoms, is postulated on the basis of IR results [66]. This complex was also previously prepared but it was not further characterized [128].

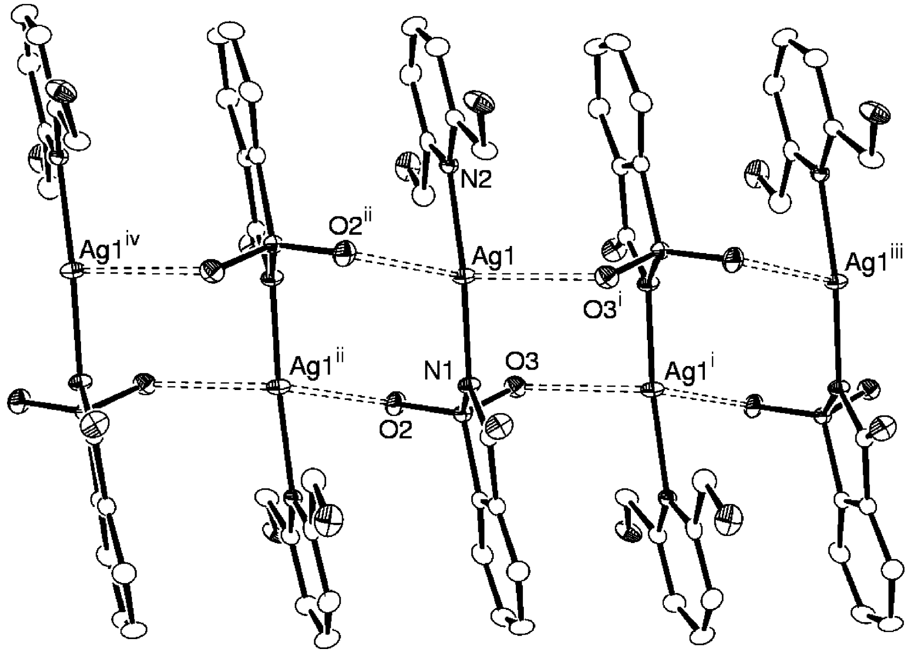


Fig. 5. A fragment of a one-dimensional chain in $[Ag(sac)(dmpy)]_n$, showing tridentate coordination of the saccharinate ligand via the N-atom and the two sulfonyl O-atoms [57].

4.5. Saccharinate complexes of the lanthanides

Trivalent lanthanides and yttrium offer interesting possibilities for systematic studies with coordinating ligands. Due to the continuous decrease of the ionic radii on going from La(III) to Lu(III) [112,129], it is possible to expect variations in the bonding characteristics and metal to ligand interactions along the series [129,130].

About one decade ago, Nabar and Khosla reported a general synthetic procedure for the preparation of lanthanide saccharinates, based on the reaction of the rare earth carbonates with saccharin in hot aqueous solution [131]. They have also investigated the obtained complexes by X-ray powder diffractometry and IR spectroscopy, suggesting the existence of different groups of structurally related complexes, a fact which was confirmed by a recent and systematic study of these compounds [132]. Before them only the structure of the respective Nd(III) complex was known in detail [133].

The above-mentioned investigation of the complete series of lanthanide saccharinates has shown that they belong to three different structural types [132]. In the first family, of composition $[Ln(sac)(H_2O)_8](sac)_2{\cdot}H_2O$, with Ln = La, Ce, Pr, Nd, Sm and Eu, the Ln(III) cation is in a tricapped trigonal prismatic environment with nine-fold oxygen coordination, involving one saccharinato carbonylic O-atom and eight water O-atoms. The second group, of stoichiometry $[Ln(sac)_2(H_2O)_6](sac)(Hsac)$, involving Ln = Gd, Dy, Ho, Er, Yb, Lu and Y constitutes an interesting example of complexes that contain simultaneously saccharin and its anion (in two forms, bonded and not bonded to the metal center) in the crystal lattice (cf. also Section 4.7). In the third group, the Tm(III) and Tb(III) compounds present two closely related structures conformed by three and two $[Ln(sac)(H_2O)_7]^{2+}$ crystallographically independent complexes, respectively, with the $[Tm(sac)(H_2O)_7]_3(sac)_6{\cdot}9H_2O$ and $[Tb(sac)(H_2O)_7]_2(sac)_3{\cdot}6H_2O$ composition.

For all the heavier lanthanides (Gd–Lu) and yttrium the cation presents eight-fold oxygen coordination, involving again the carbonyl O-atom of saccharinate, with the ligands arranged at the corners of a slightly distorted square Archimedean antiprism [132], as shown in Fig. 6 for the terbium complex.

The different structural characteristics of the Tm(III) and Tb(III) complexes in comparison with those of the other heavier lanthanides suggest that some of the saccharinato complexes of these heavier cations may be dimorphic. The stabilization of one or another of the structural modifications is surely dependent on very subtile synthetics and environmental conditions. It is also worthy commenting that the Tb(III) complex is particularly unstable. Under ambient conditions, its crystals rapidly lose water becoming powder [132].

Complexes for lanthanides in other oxidation states different from Ln(III), have not been so far reported. Only a complex of Ce(IV), of composition $Ce(sac)_4{\cdot}8H_2O$ has been mentioned, but without detailed characterization [128]. In this same paper, also the preparation of a related Th(IV) complex, of stoichiometry $Th(sac)_4{\cdot}6H_2O$, was reported [128].

4.6. Other peculiar (ambidentate) coordination behavior

The reported work summarized in Sections 4.2, 4.3 and 4.5 clearly shows that the saccharinato ligand is usually involved in the formation of *N*- or *O*-bonded mononuclear complexes. However, some complexes present a less-common

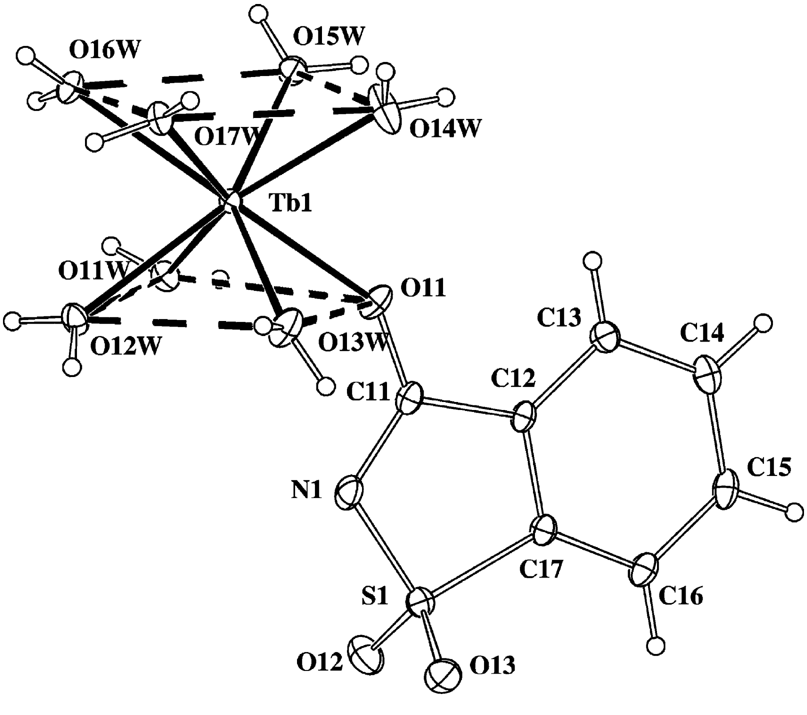


Fig. 6. Structure of one of the two $[Tb(sac)(H_2O)_7]^{2+}$ crystallographically independent complexes in $[Tb(sac)(H_2O)_7]_2(sac)_4{\cdot}6H_2O$, showing the square Archimedean antiprism around Tb(III) [132].

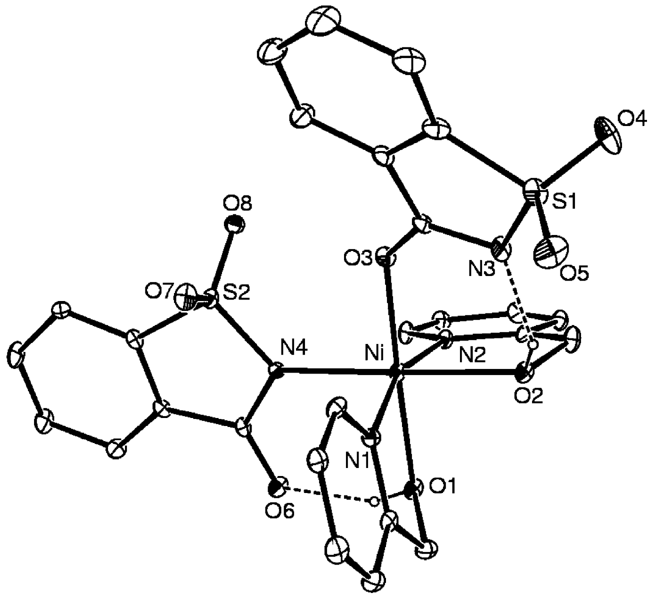


Fig. 7. Molecular view of $[\mathrm{Ni(sac)_2(pym)_2}]$, showing the ambidentate behavior of the saccharinato ligand [85].

coordination characteristic, which exemplify another fascinating aspect of this ligand. This peculiarity was first found in two Cu(II) complexes, namely $[\mathrm{Cu(sac)_2(py)_3}]$ [134] and $[\mathrm{Cu(sac)_2(dipy)(H_2O)}]$ (dipy = dipyridylamine) [70,135] in which both sac ligands are monodentate, but one is *N*-bonded, while the other one is coordinated through the carbonyl O-atom behaving as a ambidentate ligand.

A similar behavior was also observed with some mixed-ligand complexes containing pym, i.e., $[\mathrm{M(sac)_2(pym)_2}]$, where M = Co(II) [85], Ni(II) [85], Zn(II) [136] and Cd(II) [136]. As an example of this kind of ligand arrangement, the molecular structure of the Ni(II) complex [85] is shown in Fig. 7. The ambidentate coordination mode of saccharinato ligands was also found in an unusual tris saccharinato complex, namely $\mathrm{ApyH[Cu(H_2O)_2(sac)_3]}$, where one ligand is *O*-coordinated and the other two are *N*-bonded [62].

4.7. Presence of bonded and non-bonded saccharinate anions and of free saccharin in complex species

Another interesting aspect, recently documented in a variety of compounds, is the fact that the saccharinate anion simultaneously exists as a ligand, coordinating to a metal centre, and as a counter-ion remaining outside the coordination sphere.

Some examples have been presented in Section 4.5, in relation to the complexes of the heavier lanthanides [132]. Other examples are found in the following complexes $[\mathrm{M(sac)(H_2O)(bpy)_2](sac)}$ (M = Mn(II) [137], Co(II) [138], Ni(II) [89] and Zn(II) [89,139]), $[\mathrm{Mn(sac)(H_2O)(phen)_2](sac)}$ [138], $[\mathrm{Cu(sac)(bpy)_2](sac)\cdot 2H_2O}$ [140], $[\mathrm{Cu(sac)(dipy)_2](sac)\cdot 0.25H_2O}$ [135] and $[\mathrm{Cu_2(sac)_2(H_2O)_2(bpym)_3}]\cdot(\mathrm{sac})_2\cdot 4\mathrm{H_2O}$ (bpym = bipyrimidine) [141]. In the above complexes, the coordinated saccharinato ligands are *N*-bonded, whereas in $[\mathrm{Ca(sac)_2(H_2O)_2(Hpyet)_2](sac)_2}$ (Hpyet = the 2-ethanolpyridinium cation) [142], both saccharinato ligands around the calcium(II) are *O*-coordinated.

Obviously, in a large number of complexes, saccharinate is only present as a counter anion outside the coordination sphere. In addition of electrostatic interactions with the complex cation, the anion usually is involved in hydrogen bonding forming supramolecular architectures and additionally reinforcing the crystal structure packing. Some recently reported examples are the following: $[\mathrm{Cu_2(\mu\text{-}ox)(bpy)_2(H_2O)_2}]\mathrm{(sac)_2}$ (ox = oxalate) [143], $[\mathrm{M(H_2O)_4(py)_2](sac)_2}$ [144] (M = Co(II) and Ni(II)), $[\mathrm{Fe(4,4'\text{-}bpy)(H_2O)_4](sac)_2}$ [145], $[\mathrm{M(nic)_2(H_2O)_4](sac)_2}$ (M = Co(II), Ni(II) and Zn(II)) [146,147], $[\mathrm{M(tea)_2](sac)_2}$ (M = Sr(II) [148], Mn(II) [149], Co(II) [72], Ni(II) [150], Zn(II) [151], Cd(II) and Hg(II) [152]), $[\mathrm{M(H_2O)_2(pyet)_2](sac)_2}$ (M = Fe(II) [153], Co(II) [154], Ni(II) [155], Cu(II) [153] and Zn(II) [156]), $[\mathrm{M(dmpy)_2](sac)_2\cdot 2H_2O}$ (M = Co(II) [157], Ni(II) [158], Cu(II) [159] and Zn(II) [158]), $[\mathrm{M(dien)_2](sac)_2\cdot H_2O}$ (dien = diethylenetriamine) (M = Ni(II), Cu(II) and Zn(II)) [159], $[\mathrm{Cd(dien)_2](sac)_2}$ [159], $[\mathrm{Mn(H_2O)_2(phen)_2](sac)_2\cdot H_2O}$ [160], $[\mathrm{Cu(H_2O)_2(apy)_2](sac)_2}$ (apy = 4-aminopyridine) [70], $[\mathrm{Cu(H_2O)_2(aim)_2](sac)_2}$ (aim = *N*-allylimidazole) [71], $[\mathrm{Cu(H_2O)_2(dmen)_2](sac)_2}$ [110], $[\mathrm{Co(im)_4(H_2O)_2](sac)_2}$ [161], $[\mathrm{Ba_2S_2(C_{12}H_{24}O_6)_2(H_2O)_4](sac)_2}$ ($\mathrm{C_{12}H_{24}O_6}$ = the 18-crown-6 ring of 1,4,7,10,13,16-hexaoxacyclooctadecane) [162].

An especially interesting example of systems of this type is the material of composition $[\mathrm{Cu(4,4'\text{-}bpy)_2(H_2O)_2](sac)_2\cdot DMF}$ [163] which is a square grid polymer with the saccharinate anions sandwiched between the complex layers and the dimethylformamide (DMF) molecules filling the square holes. Similarly, $[\mathrm{Cu(H_2O)_2(4,4'\text{-}bpy)_2](sac)_2\cdot CH_2Cl_2}$ [164] is assembled into an infinite two-dimensional rhombic grid clathrating dichloromethane molecules.

The presence of free saccharin in the crystal lattices of certain complexes has been established, as mentioned above in the case of the $[\mathrm{Ln(sac)_2(H_2O)_6](sac)(Hsac)\cdot 4H_2O}$ complexes [132]. The first case in which this situation was found is, apparently, the $\mathrm{VO^{2+}}$ complex of composition $[\mathrm{VO(OH)(sac)(H_2O)_2](Hsac)}$ [105].

Another example recently discussed by two independent research groups is the case of $[\mathrm{Fe(ophen)_3](sac)_2\cdot Hsac\cdot 6H_2O}$ [165,166]. On the other hand, this behavior was also recently described in two alkaline-salts, i.e., $\mathrm{Rb(sac)Hsac\cdot H_2O}$ [31] and $\mathrm{Cs(sac)Hsac\cdot H_2O}$ [38].

5. Brief overview on physicochemical studies of saccharinato complexes

Most of the saccharinato complexes so far investigated and described in the previous sections, whose structures have been usually solved by single crystal X-ray diffractometry, have often been additionally characterized by different physicochemical methods such as IR spectroscopy, thermoanalytical techniques or magnetic measurements. But few systematic studies, using these methodologies have so far been performed and most of them have been devoted to the simple aqua-saccharinato species, $[\mathrm{M(sac)_2(H_2O)_4]\cdot 2H_2O}$. In this section, we present a brief summary of these systematic studies, which widen our perspectives on this interesting type of coordination compound.

5.1. Vibrational spectra

Most experimental studies on the vibrational properties of saccharin or its metallic complexes are based on infrared spectroscopic measurements. Raman spectroscopy has been rarely used.

In this section, only the most general and systematic studies performed on saccharin and on saccharinato complexes, as well as a number of important papers devoted to establish spectra/structure correlations shall be briefly reviewed.

Vibrational spectroscopic studies on saccharin began more than 20 years ago. Interesting improvements to understand the spectral complexity of the ν(NH) region, were possible by application of deuteration techniques [167]. First attempts for the correct analysis of the ν(C=O) vibrations were made by Jovanovski et al. [168,169]. Later, the mid infrared region was analyzed on the basis of the force field derived from a quantum chemical calculation, using the HF3-21G* basis set [170]. Most recently, this vibrational analysis was completed measuring the IR spectra of different saccharinates at room and at liquid nitrogen temperatures, supported by theoretical calculations [40].

In relation to saccharinato complexes an important number of spectral/structure correlations was published during the last years. In particular, the carbonyl and SO_2 stretching vibrations, as well as the vibrations of the hydration H_2O molecules were analyzed in a systematic way.

The ν(C=O) vibration, usually known as an extremely good group frequency, has often been exploited for structural studies. This mode generates a sharp band at 1642 cm^{-1} in sodium saccharinate [59] which shifts to lower frequencies when the carbonyl group participates in metal bonding, an interaction that, evidently, produces a weakening of the carbon–oxygen bond. Some correlations between the position of this vibration and structural peculiarities of the involved complexes were firstly presented in 1988 [171] and complemented most recently, using data for a greater number of compounds [172]. In this last study, the ν(C=O) frequencies were correlated with the C–O and metal–saccharinato distances and the respective formal bond orders (cf. also [31]). Although an approximate ν(C=O) frequency limit for the distinction between N-coordinated and uncoordinated saccharinate in the solid metal complexes was suggested to be 1650 cm^{-1} [31,172], due to intra- and intermolecular interactions such as hydrogen bonds, the ν(C=O) frequency does often not correlate to the coordination mode of the ligand.

The antisymmetric (ν_{as}) and symmetric (ν_s) stretching vibrations of the SO_2 group in sodium saccharinate are observed as two strong IR bands at 1258 and 1150 cm^{-1}, respectively [59]. The assignment of the sulfonyl stretching modes in metal complexes is not so straightforward as that of the carbonyl stretching, due to coupling with other vibrational modes, in particular in the case of the $\nu_s(SO_2)$ mode [31,40]. Notwithstanding, some useful assignment criteria and spectroscopic relations to structural characteristics could be derived in a number of cases [173].

Some systematic studies have also been performed in relation to the H_2O vibrations in hydrated ionic saccharinates and in aqua-saccharinato complexes. Thus, the infrared spectra of the two hydrates of sodium saccharinate and that of hydrated potassium saccharinate, as well as those of their partially deuterated hydrates were recorded at room and at liquid nitrogen temperatures and the behavior of the O–H and O–D stretching vibrations could be analyzed in detail [174]. A similar study was also performed for the series $[M(sac)_2(H_2O)_4]\cdot 2H_2O$ (M = Mn, Fe, Co, Ni, Zn and Cd) [175]. Later, using different theoretical models, the anharmonicity constants and the harmonic eigenvalues of the O–H and O–D stretching vibrations for this same isomorphous series (now including also Cr(II) and Cu(II)) were calculated on the basis of IR frequencies of isotopically isolated OH and OD species [176].

Besides, some particular and detailed vibrational spectroscopic studies devoted to a single complex or to a group of related compounds can also be mentioned here. The FTIR spectra at room and liquid nitrogen temperatures, as well as the Raman solid-state spectra of protonated and deuterated NH_4sac and of a series of alkaline-saccharinates were investigated and analyzed in great detail [40], constituting one of the most solid references of the vibrational behavior of the saccharinate anion. Other interesting studies are those of $Pb(sac)_2\cdot H_2O$ [177], Agsac [178], those of the mixed-ligand complex $[Cu(sac)_2(py)_2(H_2O)]$ [179] and those of the complexes $[M(im)_4(H_2O)_2](sac)_2$ and $[M(py)_2(H_2O)_4](sac)_2$, with M = Co(II) and Ni(II) [180].

As commented above, very few Raman studies on these systems have so far been performed. The first detailed Raman investigation of a saccharinato complex was performed on solid $[Fe(sac)_2(H_2O)_4]\cdot 2H_2O$, complemented with comparisons to the behavior of the structurally related Cu(II) and Ni(II) complexes. In this study, also the excitation profiles of the vibrational modes that show pre-resonance on excitation with laser lines within the electronic bands are reported. On this basis, and with the aid of a semi-empirical extended Hückel MO calculation, a first assignment of the metal–ligand vibrations in these complexes could be advanced [181].

Another very complete Raman study was performed some years later on the binuclear $[Cu_2(im)_4(sac)_4]$ complex, complemented with measurements on $[Cu(sac)_2(H_2O)_4]\cdot 2H_2O$, $[Cu(bpy)_2(sac)]sac\cdot 2H_2O$, sodium saccharinate and molecular saccharin [182]. These measurements allowed a wider experimental insight into the general vibrational properties of saccharin, its anion and the complexed moiety.

An important aspect which remains to be solved, is the precise location of the vibrations related to the M–N(sac) bonds. Based on the results of pre-resonance Raman experiments, complemented with theoretical calculations, a very strong band found at 402 cm^{-1} in the spectrum of $[Fe(sac)_2(H_2O)_4]\cdot 2H_2O$ was assigned to this mode [181]. Notwithstanding, later studies, suggested that this band could be expected at lower frequencies [40,59,60,182]. On the basis of the most recent Raman investigation it seems reasonable to accept that in Cu(II)/saccharinate complexes this ν(Cu–N) band lies at 220–235 cm^{-1} [182].

Another aspect which remains to be explored with saccharin and its complexes is the measurement of surface enhanced

Raman scattering (SERS) spectra. As far as we know, only one paper devoted to this methodology has been recently published [183]. In this study, the infrared reflectance spectra of sodium saccharinate adsorbed on Ag powder and its SERS spectra on cellulose acetate doped with fine silver particles were measured. The spectra suggested that the nitranion is bonded to the metal surface through the carbonyl O- and the imide N-atoms and tilts at the surface [183].

5.2. *Electronic and magnetic properties*

Electronic absorption spectra of a series of $[M^{II}(sac)_2(H_2O)_4]\cdot 2H_2O$ complexes, with M^{II} = Mn, Fe, Co, Ni and Cu have been investigated and discussed in terms of its tetragonally distorted octahedral coordination [184]. The electronic transitions were assigned by comparison with those of the respective $[M(H_2O)_6]^{2+}$ complexes. From the analysis of these spectra it was concluded that the 10 Dq values of both series are comparable, showing that the replacement of two of the water molecules in the hexaaqua moieties by two saccharinate N-atoms has only a very small effect on the crystal field of these cations. The spectroscopic results also show that the distortive effects on the overall octahedral symmetry are very low [184]. In the case of the $[Fe(sac)_2(H_2O)_4]\cdot 2H_2O$ complex the electronic spectrum was also measured with the solid crystalline material [185], and a more detailed analysis, with the aid of semi-empirical extended Hückel MO calculations was performed later [181].

Magnetic susceptibility measurements for the above mentioned $[M^{II}(sac)_2(H_2O)_4]\cdot 2H_2O$ complexes, performed in the temperature range between 4.2 and 300 K, show a normal paramagnetic behavior in the full temperature range [184]. These measurements were also complemented, in some cases, with EPR spectra of the crystalline powders [184].

In the case of $[Cu(sac)_2(H_2O)_4]\cdot 2H_2O$ a more detailed EPR study was performed with single crystals as a function of the magnetic field orientation. From these spectra, it was possible to make an estimation of the magnitude of the exchange couplings between copper ions in this lattice [186].

Other similar studies were performed with powders and single crystals resulting in the doping of $[Zn(sac)_2(H_2O)_4]\cdot 2H_2O$ [187] as well as $[Cd(sac)_2(H_2O)_4]\cdot 2H_2O$ and $[Cd(sac)_2(HydEten)_2]$ [188] with Cu(II). In the first two cases, the results of the spectral analyses show the presence of two magnetically non-equivalent Cu(II) sites whereas in the third one, only a single site was detected [187,188].

Most recently, similar measurements were performed with powdered and single crystals of $[Co(sac)_2(H_2O)_4]\cdot 2H_2O$ doped with Cu(II) and VO^{2+} [189]. In both cases, two inequivalent magnetic sites were found for both substituents. Interestingly, no interactions between the paramagnetic Co(II) ion and the doping cations were found at room temperature and the saccharinate complex behaves like a diamagnetic host [189].

Charge transfer spectra of the intra-ligand or ligand-to-metal types, for saccharin, sodium saccharinate and a number of metal saccharinato complexes have been obtained by photoacustic spectroscopy [190].

Very few detailed studies of these types have been so far attempted with mixed-ligand saccharinato complexes and only some data, derived from analyses of electronic spectra are available [80,191].

Intra-ligand transitions have been measured in methanolic solutions of sodium saccharinate and five absorption maxima could be detected (in parentheses, molar absortivity coefficients in $L\,mol^{-1}\,cm^{-1}$): 208 nm (13,540), 216 nm (shoulder, 11,200), 221 nm (10,800), 227 nm (shoulder, 9640) and 271 nm (1230) [41].

A very interesting luminescence study of the interaction of Eu(III) with saccharinate in water was recently published [192], demonstrating that in aqueous solution one saccharinate ligand binds to the trivalent lanthanide cation, in the same way as described in the solid state [132]. Besides, this study also allowed the determination of the binding constants of the Eu(III)/sac system as a function of temperature [192].

5.3. *Mössbauer spectra and NMR studies*

These techniques have been rarely applied to the investigation of saccharinato complexes. Only the ^{57}Fe-Mössbauer spectrum of $[Fe(sac)_2(H_2O)_4]\cdot 2H_2O$ has been so far investigated in detail, showing the presence of Fe(II) as a high spin species [193].

The electronic structure of saccharin in aqueous solution was explored using ^{17}O, ^{15}N and ^{13}C two-dimensional NMR spectroscopy. Analyzing these spectra in the presence of varying concentrations of H^+, Na^+, K^+, Ca^{2+}, Mg^{2+}, CO_3H^- and urate, it was concluded that at physiological levels none of these ions alters significantly the electronic structure of the molecule [194].

On the other hand, the ^{13}C NMR spectra of saccharin, sodium saccharinate and the simple saccharinates of Mg(II), Zn(II), Cd(II), Pb(II) and Hg(II) were measured in dimethylsulfoxide–d_6 solutions. From the chemical shifts some inferences about the bonding characteristics could be made [195].

5.4. *Electrochemical behavior*

The electrochemical behavior of the $[M^{II}(sac)_2(H_2O)_4]\cdot 2H_2O$ complexes (with M^{II} = Fe, Co, Ni, Cu and Zn) was investigated by cyclic voltammetry in dimethylformamide solutions using a glassy carbon electrode [196]. The oxidation and the reduction of the Fe(II) and Cu(II) centers was shown to occur in one-electron steps, and are quasi-reversible. The second electron transfer in $[Cu(sac)_2(H_2O)_4]\cdot 2H_2O$ is followed by decomposition of the complex associated with the loss of the ligand and copper electrodeposition. For the Ni(II), Co(II) and Zn(II) complexes only reduction of the ligand could be observed at highly negative potentials [196].

Sodium saccharinate (10^{-3} M solution in dimethylformamide) is electrochemically inactive in the potential range between +1.1 and −1.9 V [196].

An interesting application of electrochemical techniques to this type of systems was shown by Çakir et al. [197]. They investigated the square-wave voltammetric behavior of cysteine (cys) and saccharinate in the presence of Cu(II) ions at a static mercury dropping electrode. It was possible to determine the stability constants of the binary complexes, as well as the formation and stability of a ternary $[Cu(sac)_2(cys)_2]$ complex [197].

5.5. Thermal behavior

Thermal data of numerous complexes reviewed within this paper were often reported as a part of broader synthetic and structural investigations. Notwithstanding, there is a number of studies devoted exclusively to this aspect. One of the earliest work in this field was the paper of Magri et al. [198] devoted to the investigation of the thermal decomposition of the simple Co(II) and Cu(II) aquo-saccharinato complexes and some of their pyridine adducts. The similar Ni(II) and Zn(II) complexes were investigated some years later [199].

A systematic reinvestigation of the first row transition metal complexes of the type $[M(sac)_2(H_2O)_4]\cdot 2H_2O$ (M = Mn, Fe, Co, Ni, Cu and Zn), was undertaken most recently using thermogravimetric (TG) and differential thermal analysis (DTA) techniques [200]. In this study, the kinetics of first stage of decomposition, which corresponds to the dehydration process, was investigated in detail and the stability of the hydrates was discussed in relation to the values of the ionic radii of the involved metal cations. The final pyrolysis residues, collected at about 750 °C, were identified by X-ray powder diffractometry, as the respective metal oxides (i.e., Mn_2O_3, Fe_2O_3, Co (or Co_3O_4 at higher temperatures), NiO, CuO and ZnO, respectively) [200].

In another interesting study, it was shown that a sharp color change from yellow to brown was observed during the dehydration of $[Fe(sac)_2(H_2O)_4]\cdot 2H_2O$ at 141 °C. The anhydrous brown product was stable up to 250 °C. The Mössbauer and EPR spectra of the dehydration product showed the presence of a high-spin Fe(III), suggesting that a thermally induced intramolecular electron transfer reaction occurred in the solid state during the dehydration process [201].

A detailed TG/DTA analysis, complemented by differential scanning calorimetry (DSC) measurements, for the alkaline (except Li)-saccharinates and $NH_4(sac)$ was also recently performed [35]. The decomposition temperature of the saccharinate anion is about 130 °C higher than that of pure saccharin.

Different other systematic studies were also performed with different mixed-ligand saccharinato complexes, for example, with pyridine [202] α,α'-bipyridine [203], *o*-phenanthroline [204], imidazole [205], hydrazine and ethylenediamine [206] or monoethanolethylendiamine [207] as well as a series of cationic triethanolamine complexes with saccharinate as the counter anion [207]. Interestingly, in the thermolysis of some of these last complexes, and working under a N_2 atmosphere, the elemental metals were obtained as the final residues [207].

6. Theoretical studies

Although the various approximations used in quantum chemical calculations can often lead to severe discrepancies between the calculated and experimentally observed values of the molecular parameters, it is widely accepted that such calculations can indeed give reliable pictures of the trends and/or differences in those parameters and may also be useful in the analysis of spectral data, chemical reactivity and similar problems.

In the last years, a number of theoretical studies were performed for molecular saccharin and the saccharinate anion. Binev et al. developed theoretical calculations at the Hartree–Fock level with the relatively small HF3-21G* basis set [170]. These calculations gave a good description of the spectral changes that accompany the conversion of saccharin to its nitranion, and gave a good support to the vibrational assignments, as commented in Section 5.1.

In latter calculations, the geometries of saccharin and its anion were optimized with the AM1 and PM3 semi-empirical methods and the full geometries were optimized using the 6-31G* basis set [29]. A good correlation between the calculated geometrical parameters and the average geometries derived from experimental structural data could be established. Also the analysis of the vibrational spectra of some ionic saccharinates was supported by this type of calculations [40].

Most recently, a DFT study of the electronic structure of saccharin, thiosaccharin (1,2-benzisothiazol-3-(2H)-thione-1,1-dioxide), and their respective anions, was performed using the 6-31G** basis set. In this case, the geometry optimization procedures were started from experimental structural data [208]. From the results of this study, it is clear that important differences exist in the molecular and electronic structures of the five-member rings of saccharin and thiosaccharin and these differences provide an adequate rationalization of the different chemical behavior of these ligands (cf. also Section 8).

Another similar DFT study for thiosaccharin was independently performed. The obtained geometrical parameters of the isolated molecule and its nitranion agree well with the structural data determined for thiosaccharin and its sodium and potassium salts [209].

Some quantum chemical calculations were performed for 24 N-substituted saccharins [210] as well as for some structurally related molecules, such as phthalimide [211] and succinimide [212]. The results of these calculations are also of interest for a better understanding of the geometrical and electronic characteristics of saccharin.

7. Biological effects of saccharinato complexes

In Section 3, we have briefly discussed the biological effects of saccharin, especially in relation with its formerly suspected carcinogenic activity. In the present section, some aspects related to biological, biochemical and pharmacological effects of saccharinato complexes shall be commented.

The complexes $[Zn(sac)_2(H_2O)_4]\cdot 2H_2O$ and $[Cu(sac)_2(H_2O)_4]\cdot 2H_2O$ showed a certain inhibitory effect, in vitro, over carbonic anhydrase [213]. This same Zn(II) complex has been investigated as a possible therapeutic additive for dentifrices [214].

Another series of simple saccharinato complexes, including the poorly characterized complexes of dioxouranium(VI), oxovanadium(IV), Ce(IV), Hg(II) and Pb(II) are also relatively strong inhibitors of carbonic anhydrase in vitro [41,128].

The superoxide dismutase-like activity of a series of the divalent metal aqua-saccharinato complexes of the type $[M(sac)_2(H_2O)_4]\cdot 2H_2O$ (with M = Mn, Fe, Co, Ni, Cu and Zn) has been investigated using the nitrobluetetrazolium/superoxide reduction assay [215]. The results show that all these complexes possess the ability to dismutate the O_2^- anion. Interestingly, the copper(II) complex presents the most important activity [215], a behavior which is also supported by its redox properties [196].

The important antibacterial activity of the Ag(I) complex with sulfadiazine, originates in part on the polymeric nature and insolubility of this compound, which favors a slow liberation of silver [216,217]. In the search for new similar complexes of this type, it was found that silver anthranilate and silver saccharinate, which present polymeric structures [125,218] have also adequate solubility characteristics to be considered as potentially useful slow silver releasing agents in pharmaceutical formulations [219].

Human leukocyte elastase (HLE), cathepsin G (Cat G) and proteinase 3 (PR 3) are serine endopeptidases that are stored in the azurophilic granules of neutrophils. Increasing evidence suggests that these enzymes play a major role in the pathophysiology of different inflammatory diseases [220]. Thus, agents that function as selective inhibitors of these enzymes are of potential therapeutic value. Different derivatives of saccharin, for example, N-substituted saccharins with R-acetoxy groups [221] or with amino acids [222] show interesting activity towards HLE.

As mentioned in Section 3, it was suggested that saccharin may be potentially useful as an antidote for metal poisoning [27]. Although this property has not been explored in detail, it becomes apparent that the stability of certain polymeric saccharinato complexes, for example, those of Pb(II), Tl(I) or Ag(I) generates extremely amazing perspectives in this context, suggesting the potential usefulness of saccharinate as a promising ligand for chelation therapies [217,223,224].

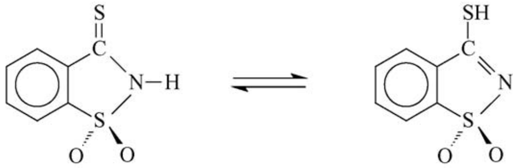
In recent years, different novel biological effects of the lanthanides have been discovered and many of them have important medical significance [225,226]. These observations open interesting perspectives for eventual medical applications of the lanthanide saccharinates, which pharmacological properties deserves a deeper investigation. It has also be commented, that thiosaccharin and some of its derivatives have potent antimicrobial activity [209]. Also this aspect merits further studies in the future.

In the solid-state chemistry of pharmaceutical drugs the formation of so-called co-crystals is of great practical importance in the field of drug delivery, particularly enhancing its water solubility. Saccharin appears as a good co-crystal former because it acts as a hydrogen bond donor (N–H) and as a hydrogen bond acceptor (C=O or S=O) [227]. Recent studies performed in this context have shown that saccharin acts as a weak acid when it is co-crystallized with drugs that contain an adequate basic centre. In these cases, saccharinate salts can be obtained and this suggests a new general use of saccharin as a weak acid in pharmaceutical chemistry, generating highly soluble saccharinates [28]. The high water solubility of the saccharinates of different important drugs allows its use in both injectible and drop formulations. Besides, as saccharin is a potent sweetener, it masks the bitter taste of many drugs. As the saccharinate solutions present higher pH values (pH ~ 5–6) than those of hydrochlorides and other common salt formulations (pH ~ 2–3), injectible forms of such drugs are less likely to cause irritation and other undesirable side effects on the skin [28].

8. Metal complexes of thiosaccharin

Thiosaccharin (Htsac, 1,2-benzisothiazol-3(2H)-thione-1,1-dioxide) is a molecule closely related to saccharin, which presents a thiocarbonyl (C=S) group instead of the carbonyl (C=O) moiety. It can be prepared using some general procedures available for the thionation of organic compounds. In particular, two procedures are commonly used: (a) the treatment of saccharin, dissolved in an appropriate organic solvent, with P_2S_5 [228,229]; (b) the reaction of saccharin, with Lawessons's reagent ($C_{14}H_{14}O_2P_2S_4$: 2-4-bis(4-methoxyphenyl)2-4-dithioxo-1,3,2,4-dithiadiphosphetane) in hot toluene [230].

Thiosaccharin may present two tautomeric forms in solution:



As predicted by theoretical studies [208] and confirmed by recent NMR measurements performed in deuterated dimethylsulfoxide [231], the predominance of the thiol form in solution becomes clearly evident. The theoretical study has also pointed out other important differences between saccharin and thiosaccharin. Upon deprotonation, the negative charge at the N-atom of thiosaccharin is decreased while it remains invariable in saccharin, but the negative charge at the mono-coordinated chalcogen atom is notably increased in the former than in the latter. Therefore, this situation allows to predict favorable interactions of the thiocarbonylic S-atom (a soft base) with heavy metal cations such as Cd(II), Hg(II), Tl(I) or Pb(II) (soft acids) [232,233]. On the other hand, these structural and electronic peculiarities of thiosaccharin, with a reduced formal negative charge on the N-atom, precludes its interaction with first row divalent transition metal cations, which occurs easily with saccharin, as previously shown.

Free thiosaccharin exists in two polymorphic forms (denominated α- and β-thiosaccharin) [234]. The β-form is less stable and after a relatively short time is transformed into the more stable α-modification. The crystal structure of this stable polymorph has been investigated by single crystal X-ray diffractometry and infrared spectroscopy. It crystallized in the orthorhombic space group *Fdd*2 with $a = 26.591(3)$, $b = 25.058(3)$, $c = 4.934(5)$ Å and $Z = 16$ [234]. The structure consists of thiosaccharin molecules bonded to each other through relatively weak N–H···O inter-molecular hydrogen bonds (d(N–H···O) = 2.999(4) Å). Simultaneously, the infrared spectrum of the molecule, as well as that of partially deuterated samples, were investigated in detail in the N–H, N–D and C=S stretching regions [235].

The spectral and structural changes taking place in the course of the conversion of thiosaccharin to its anion have been inves-

Table 1
Structural data of the known metallic thiosaccharinates

No.	Formula	Crystallographic data[a]	Reference
1	Na(tsac)·H_2O	Orthorhombic, $P2_12_12_1$, $Z = 4$ $a = 7.499(3)$ $b = 26.895(10)$ $c = 4.705(2)$	[236]
2	K(tsac)·H_2O	Orthorhombic, *Pbca*, $Z = 8$ $a = 8.873(1)$ $b = 27.108(6)$ $c = 8.708(1)$	[237]
3	[Cd(tsac)$_2$(H_2O)]	Monoclinic, $C2/c$, $Z = 4$ $a = 12.236(3)$ $b = 8.919(3)$ $c = 16.655(3)$ $\beta = 96.18(2)$	[238]
4	[Cd(tsac)$_2$(py)$_3$]	Monoclinic, $C2/c$, $Z = 8$ $a = 27.174(7)$ $b = 12.005(2)$ $c = 19.008(2)$ $\beta = 99.54(1)$	[239]
5	[Cd(tiosac)$_2$(im)$_2$]	Monoclinic, $P2_1$/a, $Z = 4$ $a = 7.9430(1)$ $b = 11.2050(1)$ $c = 26.6170(4)$ $\beta = 90.5660(5)$	[240]
6	(Him)[Cd(tsac)$_2$(H_2O)]	Triclinic, $P\bar{1}$, $Z = 2$ $a = 8.1720(2)$ $b = 12.8618(3)$ $c = 14.7676(4)$ $\alpha = 84.265(1)$ $\beta = 75.427(1)$ $\gamma = 82.763(1)$	[240]
7	[Tl(sac)]	Monoclinic, $P2_1$/a, $Z = 4$ $a = 7.7171(1)$ $b = 10.6202(2)$ $c = 11.1644(2)$ $\beta = 104.866(1)$	[241]
8	[Tl(tsac)(ophen)]	Monoclinic, $C2/c$, $Z = 8$ $a = 23.2338(5)$ $b = 10.4097(2)$ $c = 15.0406(3)$ $\beta = 97.466(1)$	[241]

[a] Cell lengths in Å; angles in °.

tigated on the basis of both infrared spectroscopy and ab initio HF 6-31G(d) and BLYP 6-31G(d,p) force field calculations. The geometries calculated for the molecule and the anion agree well with those obtained crystallographically for thiosaccharin and some of its salts [209].

Only a limited number of ionic thiosaccharinates and of metallic complexes containing this ligand have so far been structurally characterized. The available structural information is summarized in Table 1 and is briefly commented, as follows:

- The monohydrated sodium and potassium thiosaccharinates (**1** and **2**) are the only structurally characterized ionic salts and show close relationships to the similar salts of saccharin, discussed in Section 4.1. Their IR spectra as well as those of the partially deuterated analogues were recorded at room and liquid nitrogen temperatures, and discussed in detail [242].
- In [Cd(tsac)$_2$(H_2O)] (**3**) the cation is located on a crystallographic two-fold axis presenting the rather uncommon CdS_2O_3 environment, and is five-fold coordinated to the sulfur atoms of two symmetry related thiosaccharinato anions, to two sulfoxide oxygen atoms of other two, symmetry related, thiosaccharinato ligands, and to the oxygen atom of a water molecule. In fact, the ligand acts as a bridging one, generating a layered structure parallel to the *ab* plane; each Cd(II) bonded to the thiocarbonyl moiety interact with another cation through the O-sulfonyl atom and vice versa. The Cd–S bonds (2.467(1) Å) are in the order of the shortest known metal–sulfur distances of covalently bonded thiolates or thioamidates, confirming the existence of an important charge on the S-atom, as pointed out by the theoretical calculations [208].
- In the mixed-ligand [Cd(tsac)$_2$(py)$_3$] complex (**4**) the Cd(II) cation is at the center of a square-bipyramidal environment, equatorially coordinated to two thiosaccharinato anions, through their S-atoms and one of them acting as a bidentate ligand involving also its N-atom in bonding. Nitrogen atoms of pyridine molecules occupy the fourth equatorial position and the two axial ones.
- In [Cd(tsac)$_2$(im)$_2$] (**5**) the cation presents a distorted CsS_2N_2 tetrahedral environment and is coordinated by two thiosaccharinato anions through their sulfur atoms and two neutral imidazole molecules. The [Cd(tsac)$_3$(H_2O)]$^+$ cation in the (Him)[Cd(tsac)$_3$(H_2O)] salt (**6**) presents a similar geometry, with three Cd–S bonds, each to one of the three thiosaccharinato ligands, and one Cd–O bond, involving the water molecule.
- The environment of Tl(I) in [Tl(tsac)] (**7**) is relatively complicated, presenting a distorted eight-fold coordination which involves an interaction to a bidentate thiosaccharinato moiety, through its S- and N-atoms, completed with two longer Tl–S bonds and four Tl···O contacts with five symmetry related neighboring thiosaccharinato anions.
- The other known Tl(I) complex, [Tl(tsac)(ophen)] (**8**), presents a rather simpler environment, with the cation interacting again with a bidentate (N, S) thiosaccharinato anion and completing the coordination sphere with the two N-atoms of the *o*-phenanthroline molecule.

All of the above described Cd(II) and Tl(I) complexes were characterized by IR spectroscopy [238–241] and in the case of the complexes (**3**) and (**4**) also the thermal behavior was investigated by means of thermogravimetric and differential thermal analysis [238,239].

Apart of the mentioned complexes, those of some other metals have been described in the literature but they remain to be structurally characterized. This is the case of the anhydrous M(tsac)$_2$ complexes (M = Mg, Co, Ni, Zn), obtained as polycrystalline powders by direct interaction of an alcoholic solution of thiosaccharin with aqueous solutions of salts of the respective cations [243]. The four complexes appear as members of an isomorphous series, as deduced from their X-ray powder diffractograms, but not definitive evidences about the metal-to-ligand interactions could be derived from the performed IR spectral analysis [243].

Most recently, a Pd(II) complex of stoichiometry Pd(tsac)$_2$·H$_2$O could be prepared and characterized by IR and ^{1}H and ^{13}C NMR spectroscopy. These spectral studies confirmed interaction of the metal center with the thiosaccharinato anions acting as bidentate ligands through their S- and N-atoms [231].

To conclude, the so far available information about the coordination behavior of thiosaccharinate shows certain similarities and differences in comparison with that of saccharinate. In the same way as saccharinate, thiosaccharinate can act as mono, bidentate or bidentate-bridging ligand. However, in monodentate binding the preferred interaction seems to be M–S, a behavior which generates easier complex formation with heavy metals.

9. Conclusions and future outlook

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

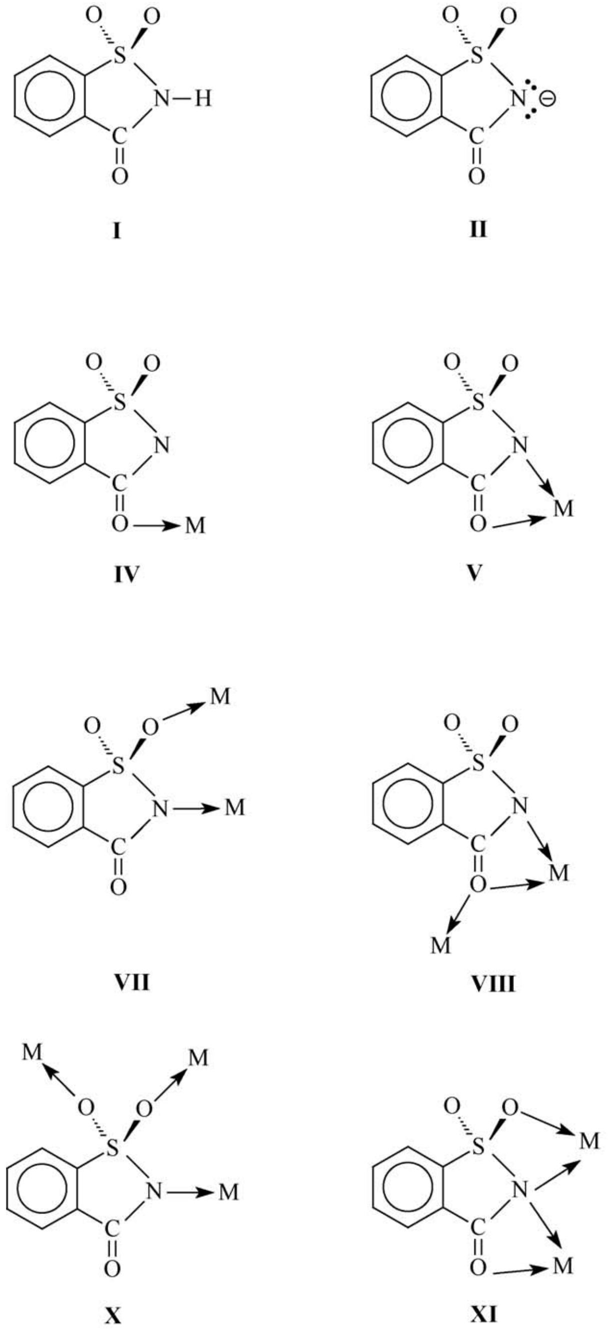


Fig. 8. Coordination modes of the saccharinato ligand.

interactions in crystalline environments, mostly through hydrogen bonding.

The structural information so far accumulated allow us to confirm its participation in different forms of ligand-to-metal and molecular interactions, which are briefly summarized in Fig. 8 and involve:

(a) Purely ionic interactions between the saccharinate anion (**II**) (obtained by deprotonation of saccharin (**I**)) and different cations, discussed in Section 4.1.
(b) Monodentate binding through the deprotonated N-atom (**III**), discussed in Section 4.2.
(c) Monodentate binding through the carbonyl O-atom (**IV**), discussed in Sections 4.3 and 4.5.
(d) Bidentate binding through the N- and O (carbonylic)-atoms to a single metallic center (**V**), discussed in Section 4.4.
(e) Bidentate-bridging of two metallic centers through N- and O (carbonyl)-atoms (**VI**), or through N- and O (sulfonyl)-atoms (**VII**), discussed in Section 4.4.
(f) Bidentate-bridging involving the N- and O (carbonyl)-atoms, with the O-atom acting simultaneously as a bridge to another metal center (**VIII**), discussed in Section 4.4.
(g) Generation of polymeric structures, involving tridentate-bridging mode (**IX** and **XI**), discussed in Section 4.4.
(h) Bicoordinating-bridging with one N-atom bonded to a metal center, with the two sulfonyl O-atoms generating double bridges (**X**), discussed in Section 4.4.
(i) Ambidentate coordination behavior: formation of M–N and M–O bonds with two different saccharinato ligands in the same complex, discussed in Section 4.6.
(j) Simultaneous presence of saccharinate (**II**) as a coordinating ligand and as a counter anion in a complex species, discussed in Sections 4.5 and 4.7.
(k) Simultaneous presence of saccharinate (**II**) and free saccharin (**I**), discussed in Sections 4.5 and 4.7.

On the basis of the so far available, rather limited, data, the related thiosaccharinato ligand presents similar coordination behavior. Notwithstanding, an important difference seems to be the particularly high reactivity of the soft thiocarbonyl S-atom towards soft metallic centers, which probably conditions to a great extent the coordinating abilities of this ligand. Besides, in the case of $[Cd(tsac)_2(H_2O)]$, the ligand presents a bidentate/bridging behavior [238] not found in any other saccharinato complex (cf. Section 8).

This detailed analysis clearly shows that the saccharinate anion is highly flexible to steric requirements, and has demonstrated its versatility in a great number of cases and in the presence of an important number of other ligands with rather different chemical characteristics and properties.

On the other hand, the information so far accumulated on this type of complex shows some important gaps that may be considered as attractive fields for future research. From the spectroscopic point of view, more studies using Raman spectroscopy appear as particularly important for a better understanding of the vibrational properties of these systems. A deeper insight into the bonding characteristics, especially in the case of the mixed-ligand systems may be attained in much cases by NMR measurements, also including NMR spectroscopy of metallic nuclei, or using photoelectron spectroscopy. What is more, the very simple and useful electronic spectroscopy has been rarely applied to these systems.

There also exists a total absence of stability constants and speciation studies and very few data on the redox behavior. This information may be extremely useful in the exploration of possible applications of saccharin and some of its complexes. In particular, the potential usefulness of saccharinate as a chelating ligand in metal detoxification processes would be improved on the basis of such information. On the basis of the limited available data on the possible biological effects of saccharinato complexes, such as those commented in Section 7, more detailed biological and biochemical studies in vitro with these compounds seem justified.

A deeper exploration of the structure and other physicochemical properties of thiosaccharinato complexes would be interesting. As suggested by our own experience, one of the main problems found with this ligand lies in the difficulty to attain single crystals adequate for crystallographic studies. Therefore, the search of experimental procedures adequate for this purpose should be intensified.

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