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The Magnetic Properties of a Series of Copper(II) Aspirinates

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Abstract

The synthesis and magnetic properties for a series of copper(II) aspirinates of the general formula $CuA_2 \cdot nL$ (A = 5-substituted acetylsalicylate, L = H_2O or CH_3OH, and n = 0 or 2) have been investigated. Magnetic susceptibilities were obtained for the temperature range 77–300 K and were interpreted by using a dimetallic model. The compounds are all antiferromagnetic with the singlet ground state ranging from 238 to 371 cm^{-1} below the triplet. Electron paramagnetic resonance measurements confirm the existence of electron spin coupling; the *g* values obtained from the triplet state spectra were used in best-fitting the susceptibility data to the dimetallic model. The compounds were also characterized with infrared and ultraviolet-visible spectral data.

Introduction

The drug produced in the largest quantity is aspirin [1]. While aspirin is effective as an analgesic, antipyretic, and anti-inflammatory drug, it is limited due to its low potency [2]. In certain cases the relief of pain and control of inflammation would require gram quantities of aspirin; such quantities may cause adverse reactions such as peptic ulceration and gastrointestinal bleeding. Recently copper complexes of anti-inflammatory drugs have been suggested to be more effective anti-inflammatory agents than the parent antiinflammatory drug [3]. One of the most potent and relatively non-toxic of these complexes is copper aspirinate [4]. In this article the synthesis and magnetic properties for a series of copper aspirinates are reported.

Experimental

All chemicals were reagent grade and used as received.

Synthesis

The substituted acetylsalicylic acids were prepared by reacting the appropriately substituted salicylic acid with acetic anhydride [5]. The copper compounds were prepared according to the reported general procedure [6]. The substituted acetylsalicylic acid (0.02 mol) was dissolved in 30 ml of water containing potassium bicarbonate (0.02 mol). To this solution was added, dropwise and with constant stirring, a solution of copper sulfate pentahydrate (0.01 mol) in 20 ml of water. The precipitate, which formed immediately, was collected on a filter and washed several times with water. The synthesis of the iodo compound was varied slightly due to the insolubility of 5-iodoacetylsalicylic acid in aqueous potassium bicarbonate. In this case a methanolic solution of KOH was used. All compounds were air-dried at room temperature. Analyses of the compounds were performed by Galbraith Laboratories, Inc. of Knoxville, Tennessee, and the results are listed in Table I.

Physical Measurements

The magnetic susceptibility was determined as a function of temperature by the Faraday method. Mercury tetrathiocyanatocobaltate(II) was used as the magnetic susceptibility standard [7], and diamagnetic corrections were estimated from Pascal's constants [8]. The EPR spectra were obtained with a Varian E109E spectrometer operating near 9.5 GHz. The field was calibrated using diphenylpicrylhydrazyl (DPPH) for which $g = 2.0036$. Cylindrical quartz sample tubes and a Varian E-231 rectangular cavity were employed. Infrared spectra were obtained by using a Nicolet MX-1 instrument. Nujol mull and potassium bromide disc techniques were employed. Electronic spectra were recorded using a Beckman Model DK-2A spectrophotometer. The solid state spectra were recorded from Nujol mulls as described in the literature [9].

Results and Discussion

These complexes appear to be stable over long periods of time if stored over common desiccants

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TABLE I. Analytical Data.

Compound	C(%) Calcd. Found	H(%) Calcd. Found	Cu(%) Calcd. Found	X(%)[a] Calcd. Found
Cu(aspirinate)$_2$	51.21	3.34	15.07	
	51.16	3.44	15.13	
5-Chloroaspirin	50.37	3.29		16.52
	50.23	3.13		16.59
Cu(5-chloroaspirinate)$_2\cdot 2\mathrm{H_2O}$	41.04	3.06	12.06	13.46
	41.04	3.12	12.12	13.68
Cu(5-bromoaspirinate)$_2$	37.30	2.09	10.96	27.57
	37.41	2.20	10.73	27.36
5-Iodoaspirin	35.32	2.31		
	35.10	2.26		
Cu(5-iodoaspirinate)$_2\cdot 2\mathrm{CH_3OH}$	32.56	2.74	8.61	34.40
	32.65	2.72	8.42	34.62
Cu(5-fluoroaspirinate)$_2$	47.22	2.65	13.88	8.30
	47.41	2.87	13.87	8.52
Zn(aspirinate)$_2\cdot 2\mathrm{H_2O}$	47.02	3.95		14.22
	47.27	4.09		14.48

[a] Percent halogen or zinc.

TABLE II. Solid State Electronic Spectral Data.

Compound	Band I	Band II	Band III
Cu(aspirinate)$_2$	665[a]	375	310
Cu(5-fluoroaspirinate)$_2$	675	350	306
Cu(5-chloroaspirinate)$_2\cdot 2\mathrm{H_2O}$	705	350	305
Cu(5-bromoaspirinate)$_2$	677	–	310
Cu(5-iodoaspirinate)$_2\cdot 2\mathrm{CH_3OH}$	690	405	305
Cu(aspirinate)$_2$[b]	665(177)[c]	–	304(3,900)
Cu(acetate)$_2\cdot \mathrm{H_2O}$	705	375	301
Zn(aspirinate)$_2\cdot 2\mathrm{H_2O}$	–	–	–

[a] Wavelengths in nm. [b] Pyridine solution. [c] Molar absorptivity.

such as calcium chloride or in typical sample vials. An elemental analysis was performed on the fluoro complex approximately one year after preparation, and the results were the same as those from its previous analysis. All of the copper complexes exhibited various shades of turquoise in color. The elemental analyses indicate the presence of two moles of aspirinate to one mole of metal ion. The comparison of the IR spectra of the substituted acetylsalicylic acid and the corresponding copper(II) complex confirmed the presence of the substituted acetylsalicylate in the complex and revealed the expected shifts for the carboxyl groups. The assignments of all the bands have not been made, but the assignments of the antisymmetric and symmetric carboxyl stretching frequencies are straightforward. For Cu(aspirinate)$_2$ the antisymmetric COO stretch occurs at 1729 cm^{-1} and the symmetric stretch at 1404 cm^{-1}. As for the acetate [10], it is noted that both of the COO stretching bands are shifted in the same direction upon coordination of the aspirinates. IR spectra also confirmed the presence of solvation in the cases for the chloro and iodo aspirinates of copper and the zinc aspirinate. Some additional assignments are: for Cu(aspirinate)$_2$; 1760 (ester C=O), 1729 (carboxyl C=O), 1404 (C–O), 1244 (C–O), 1194 (C–O), and 504 (Cu–O) cm^{-1}; for aspirin; 1755 (ester C=O), 1680 (carboxyl C=O), 1300 (C–O), 1215 (C–O), and 1180 (C–O) cm^{-1}. IR spectra are similar for all the complexes including that for the zinc compound.

The crystal structure of copper(II) aspirinate has been reported [6], and contains dimetallic units of [Cu(aspirinate)$_2$]$_2$ interconnected by acetyl oxygens

TABLE III. Resonances and EPR Parameters at 294 K.

Compound	H_{z_1}[a]	$H_{\perp_2}$	H_{z_2}	D[b]	$g_\perp$	g_z	$\langle g \rangle$
Cu(aspirinate)$_2$	401	4776	6364	0.36	2.08	2.28	2.15
Cu(5-fluoroaspirinate)$_2$	453	4761	5762	0.37	2.09	2.55	2.25
Cu(5-chloroaspirinate)$_2$·2H$_2$O	437	4728	5566	0.37	2.11	2.64	2.30
Cu(5-bromoaspirinate)$_2$	456	4753	5785	0.37	2.10	2.54	2.26
Cu(5-iodoaspirinate)$_2$·2CH$_3$OH	494	4762	6280	0.37	2.09	2.34	2.18

[a] Field in gauss. [b] In cm^{-1} units.

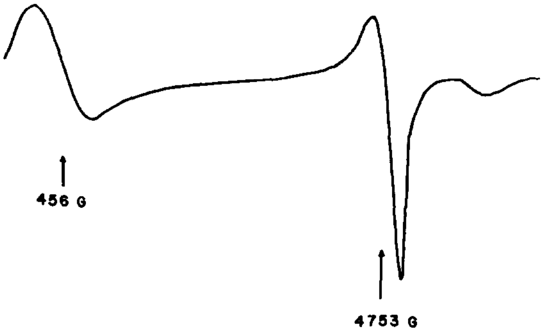

Fig. 1. EPR spectrum of Cu(5-bromoaspirinate)$_2$ recorded on a polycrystalline sample at 20 °C.

from neighboring dimetallic units. The stereochemistry of the dimetallic unit resembles that found in copper(II) acetate monohydrate [11]. The electronic absorption spectral data taken on Nujol mulls are shown in Table II. As noted in Table II the spectra are similar to that of dimetallic copper(II) acetate monohydrate. Band II appears as a shoulder on the more intense Band III and in some cases is not observed. The ultraviolet and visible spectra of many dimetallic copper(II) alkanoates have been measured in the solid state and in solution [12]. Band I has been identified with d–d transitions of the copper ions, but the origin of Band II, originally suggested to be due to the copper–copper linkage, has been controversial. Band II has been attributed to a transition between Cu–Cu molecular orbitals [13] and various types of d–d transitions. Band II has also been considered to be characteristic of the bridging system rather than the Cu–Cu linkage [14]. Band III has been assigned [15] to a carboxyl–copper(II) charge-transfer absorption; this is in agreement with the molar absorptivity of 3,900 for the pyridine solution of Cu(aspirinate)$_2$.

The dimetallic nature of these copper(II) aspirinates is also indicated by the EPR data. The EPR spectrum taken on a polycrystalline sample of Cu(5-bromoaspirinate)$_2$ is representative of these complexes and is shown in Fig. 1; complete data for the complexes are given in Table III. The method of analysis for the parameters of such polycrystalline samples has been presented [16–18]. The spin Hamiltonian for the triplet state of dimetallic copper complexes is given by,

$$\mathcal{H} = \beta HgS + DS_z^2 + E(S_x^2 - S_y^2) - 2D/3 \qquad (1)$$

where D and E are zero field splitting parameters, β is the Bohr magneton, and x, y, and z are the principal axes coordinate system fixed with respect to the Cu–Cu bond. Operating upon the usual triplet spin functions with this Hamiltonian, the Hamiltonian matrix can be derived and easily solved for those three cases where the external field H is along one of the principal axes. As shown by Wasson, Shyr, and Trapp [18], from the energy levels thus obtained two transitions allowed by the selection rule $\Delta m_s = \pm 1$ will result in each principal direction, and six resonance fields can be determined. Although it is impossible to align the magnetic field along the principal axes in a polycrystalline sample, and the spectra obtained are, therefore, a sum of random orientations, still the shape of the derivative curve gives special prominence to those resonance fields in which the external field coincides with one of the principal axes of the dimer. Finally, when D is significantly larger than hν and $E = 0$ (which implies axial symmetry), only three absorptions are expected to occur.

$$\begin{aligned} h\nu &= D - g_z\beta H_{z_1} \\ h\nu &= -D + g_z\beta H_{z_2} \qquad (2) \\ h\nu &= -\frac{D}{2} + \left[\frac{D^2}{4} + g_\perp^2\beta^2 H_{\perp_2}^2\right]^{1/2} \end{aligned}$$

The zero field splitting parameter D for all the compounds compares well with those found for copper(II) acetate monohydrate [16] of 0.34 cm^{-1}, copper(II) benzoate [19] of 0.33 cm^{-1}, copper(II) cyanoacetate [18] of 0.39 cm^{-1}, and copper(II) propionate monohydrate [20] of 0.33 cm^{-1}.

TABLE IV. Magnetic Susceptibility Data.

Compound	$10^6\ \chi_M^{\text{corr. a}}$	$\mu_{\text{eff}}^{\text{b}}$	$-E_{ST}^{\text{c}}$
Cu(aspirinate)$_2$	758	1.34	363
Cu(5-fluoroaspirinate)$_2$	835	1.40	343
Cu(5-chloroaspirinate)$_2 \cdot 2H_2O$	1065	1.58	289
Cu(5-bromoaspirinate)$_2$	727	1.31	371
Cu(5-iodoaspirinate)$_2 \cdot 2CH_3OH$	1101	1.61	238

[a] Room temperature, cgs units. [b] Room temperature, B.M. units. [c] Singlet-Triplet splitting, cm^{-1} units.

The Cu–Cu separation in copper aspirinate is 2.62 Å [6]. Using this value and the relationship [21]

$$D_{dd} = \frac{0.650\, g_z^2}{R^3} \tag{3}$$

where the Cu–Cu separation is R, the dipole–dipole contribution to the experimental D is estimated to be about 0.19 cm^{-1}. The experimental D is given by

$$D_{\text{expt}} = D_{dd} + D_{\text{exchange}} \tag{4}$$

where the sign of D_{expt} is experimentally unknown although D_{dd} is expected to be negative and D_{exchange} positive since, from the magnetic susceptibility data, as discussed below, the system is known to have an antiferromagnetic interaction. Thus D_{exchange} is expected to be +0.55 cm^{-1}. Bleaney and Bowers [16] give the equation

$$D_{\text{exchange}} = \frac{-E_{ST}}{8}\,[\tfrac{1}{4}(g_z - 2)^2 - (g_\perp - 2)^2] \tag{5}$$

where $-E_{ST}$ is the energy separation between the singlet ground state and the first excited triplet state. From this equation, $-E_{ST}$ is estimated to be about 330 cm^{-1} which is in good agreement with the value of 363 cm^{-1} found from the magnetic susceptibility measurements.

Since the dimetallic units of copper(II) aspirinate are reasonably isolated in the polymeric system of the crystal, it is appropriate to apply a dimetallic model for the interpretation of the magnetic data. The temperature dependence of the magnetic susceptibility of exchanged-coupled d^9 Cu(II) ions of the dimer may be described by the Van Vleck equation [22]

$$\chi_M^{\text{corr}} = \frac{Ng^2\beta^2}{3kT}\,[1 + 1/3\exp(-E_{ST}/kT)]^{-1} + N\alpha \tag{6}$$

where E_{ST} is the singlet-triplet splitting and Nα the temperature-independent paramagnetism. A summary of the magnetic susceptibility data is given in Table IV; the temperature-dependent magnetic susceptibility of the 5-fluoro compound, which is representative of the group, is shown in Fig. 2. Table IV shows experimental magnetic moments, $\mu_{\text{eff}} = 2.83(\chi_M^{\text{corr}} \times T)^{1/2}$, and magnetic susceptibilities, χ_M^{corr}, for room temperature. The singlet–triplet splitting parameters, E_{ST}, were determined by a least-squares best fit of the experimental susceptibilities* for each compound to the Van Vleck equation. The ⟨g⟩ values obtained from the EPR data were used as constants in the fitting process. Also, Nα was assumed to be 60 × 10^{-6} cgs units, a value often found in many other 'octahedral' copper(II) compounds [23].

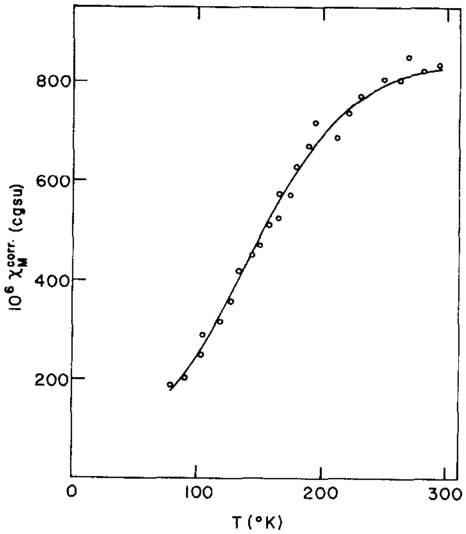

Fig. 2. Magnetic susceptibility *versus* temperature for Cu(5-fluoroaspirinate)$_2$. The circles represent experimental data while the solid line represents the least-squares best fit to the Van Vleck equation.

The absolute values of E_{ST} reported here are of similar order to those observed for other copper(II) carboxylates where the dimeric structure has been established by X-ray structural examination. In anhydrous copper acetate, copper acetate mono-

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*Tables containing magnetic susceptibilities as a function of temperature are available from the authors.

hydrate, and the copper acetate–monopyridine adduct, the observed $|E_{ST}|$ values are 302 [24], 286 [24], and 325 cm^{-1} [23], respectively. It is noted that the E_{ST} values obtained for the copper aspirinates do not correlate with any of the substituent constants which are commonly used. It should also be noted that for a dimetallic complex the exchange-coupling constant is a measure of the energy separation between the singlet and triplet states and is not necessarily a measure of the strength of the exchange interaction. Hoffmann and co-workers [25] have shown that the singlet-triplet splitting is given by

$$E_T - E_S = -2K_{ab} + (e_1 - e_2)^2/(J_{aa} - J_{ab}) \qquad (7)$$

where K_{ab} is the molecular exchange integral, J_{aa} and J_{ab} are the one- and two-center Coulomb repulsion integrals, and e_1 and e_2 are the one-electron energies of the orbitals that are involved in the exchange coupling. Hoffmann and co-workers have pointed out that the exchange and Coulomb integrals are relatively insensitive to subtle structural distortion and substituent effects, and as a result, the singlet–triplet splitting is largely determined by the energy differences ($e_1 - e_2$). It has been noted that this term is determined by the structure of the bridging unit [25–31]. It may be observed from Table IV that the unsolvated compounds have similar magnetic parameters while the solvated compounds have parameters which are notably different. Attempts to rationalize this difference in the absence of detailed structural information for all the compounds require extensive speculation and, therefore, will not be presented here.

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