Chelates of Acetylsalicylic Acid with Group IB and IIB Metals -- Spectroscopic and X-Ray Diffraction Studies

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Summary: The chelation of acetylsalicylic acid with group IB and IIB metals is reported. The metal contents in different synthesised compounds were ascertained using atomic absorption technique. Their analytical data, infrared spectra and x-ray diffractographs have also been employed in their characterization.

Introduction

The use of salicylates dates back to the 19th century, when salicylic acid was first obtained in 1838 from salicin, a glycoside present in most willow and poplar bark. Acetylsalicylic acid (aspirin) was prepared in 1853 and was used from around the close of this century for medicinal purposes. Since then numerous derivatives of salicylic acid have been synthesised and evaluated pharmacologically [1]. The use of aspirin in reducing cardiac mortality has been reviewed [2]. In the early years of this century Frankel [3] reported the formation of calcium acetylsalicylic acid. Its manufacturing techniques were filed by Bayer and Company in two independent patents [4]. Ritchter submitted three patents not only for calcium salts of acetylsalicylic acid but for barium and strontium as well [5]. Acetylsalicylates of alkaline earths, particularly those of magnesium and bismuth were patented by Gerngross and Kast [6]. Gerngross and Charlotton [7] had already reported the preparation of potassium, lithium, magnesium, calcium and some other salts of acetylsalicylic acid. Kereztz had

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patented the preparation of a yohimbine salt [8]. Hardman and Holden Ltd prepared pharmacologically active aluminium compounds of acetylsalicylic acid and patented their results [9]. The composition, stability and properties of copper (II) salicylate complexes have been investigated in two separate studies [10,11]. In a Romanian work the administration of liposomes containing copper (II) salicylate has been tested on rabbit skin, which showed a pronounced carrier ability for liposomes [12]. In an other study on rats $Cu(II)_4$ $(acetylsalicylate)_4$ was found to be more effective than the uncomplexed ligand in limiting the inflammation provoked by phlegm. With regard to their ulcerogenic effect, this ligand appeared to be more irritating for gastric mucosa than its copper complex [13]. Acetylato copper (II) complexes of the type $Cu(II)_2$ $(acetylsalicylate)_4$. L_2 have also been obtained with N-containing organic bases [14]. Even composition containing copper(II) acetylsalicylate have been used to treat rheumatoid disorders [15]. Recently, anticold medicines containing zinc acetylsalicylate have been claimed as antipyretics, analgesics and virusides for the treatment of influenza [16]. In an other Chinese patent greater anti-inflammatory activity, increased water solubility and lower acidity than aspirin have been reported for its zinc chelate [17]. Obviously, the combining capacity of various transition metals like copper, silver, zinc,cadmium and mercury has gained considerable importance with various ligands. We have already reported a brief account of medicinal importance of some salicylates [18]. Thus, as a part of our systematic studies of salicylates, this paper describes the synthesis of chelates of acetylsalicyclic acid with group IB and IIB metals. The compounds synthesised have been characterized using combustion analysis, atomic absorption, infrared spectroscopy and x-ray diffraction techniques.

Results and Discussion

In view of the importance of salicylates for medicinal and other purposes, metal derivatives of acetylsalicylic acid were synthesised using salts of Cu^{++}, Ag^{+}, Zn^{++}, Cd^{++} and Hg^{++}. The structures of these salicylates were ascertained using different analytical techniques. The infrared spectra of the compounds obtained recorded in KBr (disc.) and nujol, when compared with the starting ligand, indicated shift in position and intensity of various absorptions due to chelation with various cations. The spectra also included certain new bands, while some peaks vanished. The presence of water was inferred from broad absorption within the range 3600-3200 cm^{-1}, a weak signal between 1640-1610 cm^{-1} and around 910 ± 10 cm^{1}. The metal ligand vibrations (M-O) usually appear below 650 cm^{1} [19].

The x-ray diffractograph of the compound obtained from the reaction of acetylsalicylic acid with copper(II) chloride is shown in Fig. 1. This diffractional pattern does not show the peaks of the starting ligand. Moreover, it affords a large number of reflections for the entire angular range for which it was scanned. Hence, this system appears to have low symmetry. The XRD pattern of the product of reaction of acetylsalicylic acid with zinc (II) chloride is also shown in Fig. 1. The formation of a new compound is evident from its XRD pattern, as it does not have any reflection belonging to the original acid. This diffractograph also has a large number of well defined peaks indicating the formation of low symmetry compound.

The XRD pattern of the complex resulting from the interaction of acetylsalicylic acid with silver(I) nitrate, depicted in Fig. 2, indicates the formation of a new compound, since the data don't have the peaks of the original ligand. This pattern shows relatively small number of peaks, as compared with products mentioned in the preceeding paragraph. This suggests that the formation of this new compound is associated with rather high symmetry. The x-ray diffractograph of the new compound formed by mutual reaction of acetylsalicylic acid and cadmium (II) chloride is also presented in Fig. 2(b). It is evident that no peaks of the starting ligand are present in this diffractograph. The new product has a small number of peaks. Again, this indicates the formation of high symmetry product. Moreover, the XRD pattern arising from the chelate obtained from the same acid and mercury(II) acetate, also included in Fig. 2(b), supports the formation of a compound of high symmetry.

Experimental

Acetylsalicylic acid, copper(II) chloride, zinc (II) chloride, silver (I) chloride, cadmium (II) chloride, mercury (II) acetate and potassium carbonate were of analytical grade. The solvents

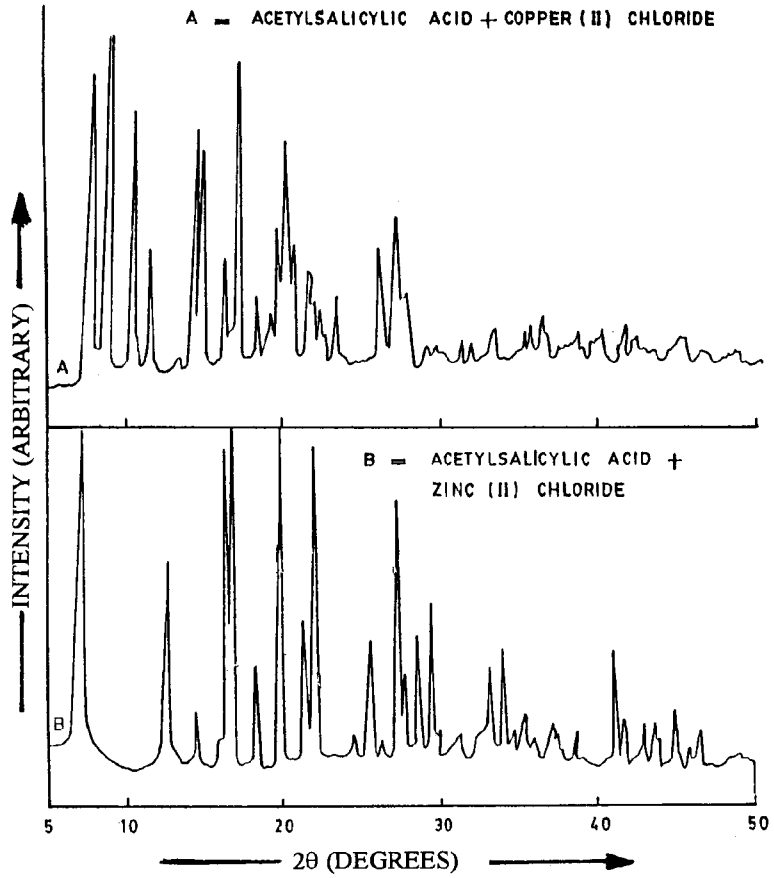

Fig. 1: XRD patterns of chelates of acetylsalicyclic acid with (A) copper (II) chloride and (B) zinc (II) chloride.

employed included acetone, methanol, chloroform, carbon tetrachloride, N,N-dimethylformamide, N,N-dimethylacetamide, tetrahydrofuran, dioxan, petroleum ether (40-60°C), which were subjected to fractional distillation before use.

The following instruments were used to characterize the synthesised chelates:

i) Atomic absorption spectrophotometer (Hitachi 270-30)
ii) Atomic absorption spectrophotometer (Hitachi Polarized Zeeman).
iii) X-ray Diffractometer (Fagaku D-Max/IIA).

Reaction of acetylsalicylic acid with copper(II) chloride

Potassium bicarbonate (2.02 g; 0.02 mole), dissolved in water (30 mL), was added to acetylsalicylic acid (3.60 g; 0.02 mole) followed by slow addition of aqueous solution (25 mL) of copper(II) chloride (3.40 g; 0.02 mole), with constant stirring. The aquamarine crystals thus obtained were filtered off, washed several times with hot water and finally with hot methanol. The product was dried in air and kept in vacuum for 48 hours to afford complex (I) (6.50 g; 21%) which had m.p. 265°). It was soluble in N,N-dimethylsulphoxide and N,N-dimethylformamide.

Reaction of acetylsalicylic acid with silver(I) nitrate

Silver(I) nitrate (1.70 g; 0.01 mole) dissolved in water (30 mL) was gradually added to the solution of acetylsalicylic acid (1.80 g; 0.01 mole) dissolved in water (30 mL). The reaction was stirred for about ten minutes. The white crystalline product thus obtained was filtered off, washed with hot water and finally with a little cold alcohol. The product was

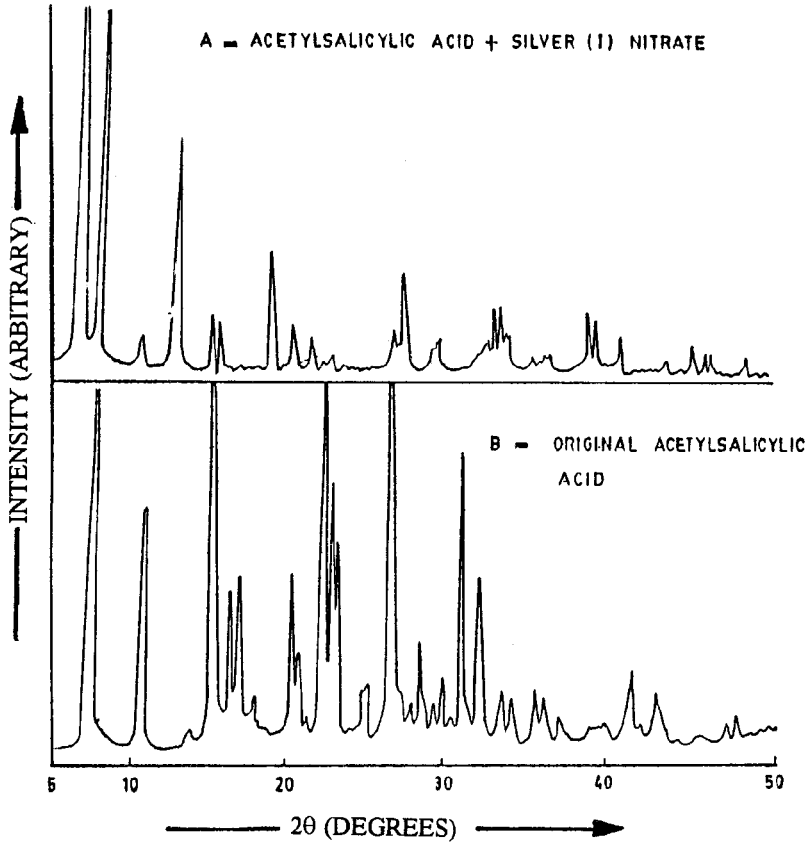

Fig. 2a: XRD patterns of chelate of acetylsalicylic acid with (A) silver (I) nitrate and (B) original acetylsalicylic acid.

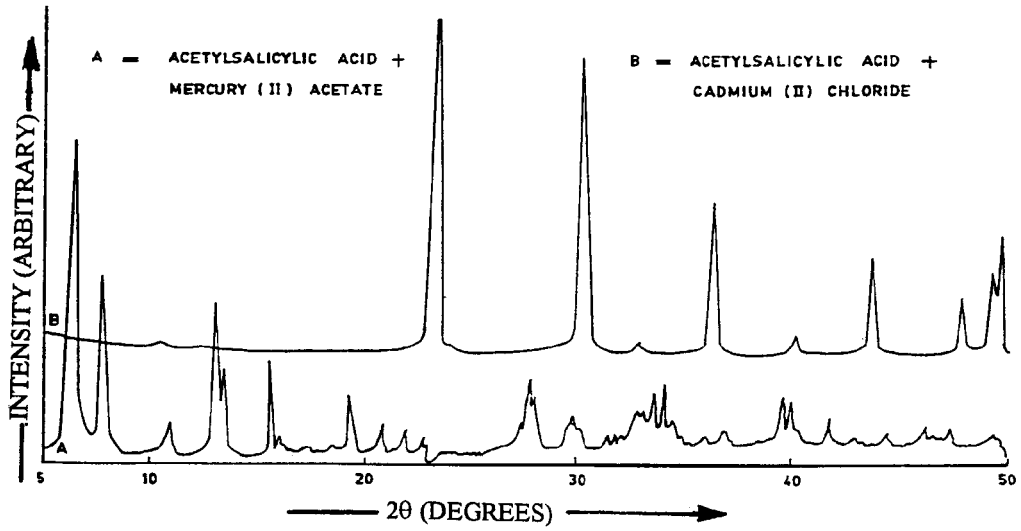

Fig. 2b: XRD patterns of chelates of acetylsalicylic acid with (A) mercury (II) acetate and (B) cadmium (II) chloride.

initially air dried and then kept under vacuum to provide white complex (II) (2.49 g; 81%) having m.p. 243°C. It was soluble in alcohol, chloroform, N,N-dimethylsulphoxide and N,N-dimethylformamide.

Reaction of acetylsalicylic acid with zinc(II) chloride

Zinc (II) chloride (2.72 g; 0.02 mole) solution in water (30 mL) was gradually added with stirring to acetylsalicylic acid (1.80 g; 0.01 mole) dissolved in the aqueous solution (30 mL) of potassium bicarbonate (1.01 g; 0.01 mole). The reaction mixture yielded a white crystalline product, which was filtered off and washed with hot water followed by washing with a small portion of cold alcohol. The air-dried compound was kept under vacuum to afford white complex (III) (3.06 g; 32%) melting at 240°C. It was soluble in N,N-dimethylsulphoxide and N,N-dimethylformamide.

Reaction of acetylsalicylic acid with cadmium (II) chloride

A solution of cadmium (II) chloride (2.28 g; 0.01 mole) in water (25 mL) was slowly added with constant stirring to an aqueous solution (30 mL) of acetylsalicylic acid (1.80 g; 0.01 mole) prepared in potassium bicarbonate (2.02 g; 0.02 mole). The resulting white crystalline product was filtered off, washed several times with portions (5 mL) of hot alcohol. The product (IV) (0.76 g; 14%) was obtained after air and vacuum drying, which had m.p. 320°C and was soluble in N,N-dimethylsulphoxide and N,N-dimethylformamide.

Reaction of acetylsalicylic acid with mercury (II) acetate

Mercury (II) acetate (3.10 g; 0.01 mole), dissolved in water (25 mL), was gradually added to the aqueous solution (30 mL) of acetylsalicylic acid (1.80 g; 0.01 mole) prepared in potassium bicarbonate (1.01 g; 0.01 mole). The reaction mixture was refluxed for two hours to afford white crystalline material. It was filtered off, washed many times with hot water, air-dried and finally kept under vacuum over-night to afford complex (V) (1.18 g; 17%), melting at 240°C. It was soluble in chloroform, N,N-dimethylsulphoxide and N,N-dimethylformamide.

The details of analytical data and infrared spectra of all the chelates synthesised have been shown in Table-1 and Table-2 respectively.

Table-1: Analytical data of complexes

S.No.	Molecular formula		Analysis %	
			Calcd	Found
I.	$(C_9H_7O_4)_2Cu(H_2O)_2$	C	47.21	47.25
		H	03.93	03.91
		Cu	13.77	13.75
II	$(C_9H_7O_4)Ag(H_2O)_2$	C	33.40	32.98
		H	03.43	03.40
		Ag	34.44	33.95
III	$(C_9H_7O_4)_2Zn(H_2O)_3$	C	45.28	45.20
		H	04.19	03.98
		Zn	13.62	13.58
IV.	$(C_9H_7O_4)_2Cd(H_2O)_3$	C	41.22	41.28
		H	03.81	03.80
		Cd	21.38	21.32
V	$(C_9H_7O_4)_2Hg(H_2O)_7$	C	31.50	31.49
		H	04.09	04.15
		Hg	29.34	29.29

Table-2: Infrared spectra

S.No.	Compounds	Band (cm^{-1}) and intensity
	Acetylsalicylic acid	2950s, 2900s, 1770m, 1620m, 1516sh, 1480s, 1390m, 1270w, 1230w, 1200m, 1150w, 1110w, 1020w, 980w, 930m, 900sh, 850w, 800w, 770m, 730w, 720w, 710w.
I.	$(C_9H_7O_4)_2Cu(H_2O)_2$	3450b, 2940s, 2930s, 2730w, 1760m, 1740s, 1630s, 1580sh, 1470s, 1410sh, 1370m, 1160sh, 920w, 860sh, 660sh
II	$(C_9H_7O_4)_2Ag(H_2O)_2$	3420b, 2950s, 2780s, 1770m, 1744s, 1602m, 1580m, 1500s, 1460s, 1380s, 1300w, 1240sh, 1190m, 1160w, 1090m, 1010w, 810w, 760m, 710w, 680sh, 650sh
III	$(C_9H_7O_4)_2Zn(H_2O)_3$	3375b, 2940s, 2860s, 1740m, 1600w, 1560w, 1460s, 1410sh, 1380m, 1230m, 1200sh, 1150w, 1100w, 1040sh, 925w, 870w, 760w, 720sh, 690w, 660sh
IV	$(C_9H_7O_4)_2Cd(H_2O)_3$	3390b, 2920s, 2710m, 1750m, 1630m, 1460w, 1370m, 1300w, 1240m, 1180 1040w, 950m, 830m, 720m, 710m, 640m
V	$(C_9H_7O_4)_2Hg(H_2O)_7$	3440b, 2960s, 2940s, 1760m, 1605w, 1580m, 1510s, 1460s, 1100m, 925w, 820w, 760m, 680m

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