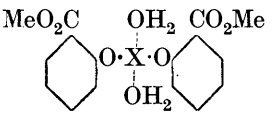
CCCLXV.—*Metallic Derivatives of Hydroxy-esters. Part I. Copper and Nickel Derivatives of Methyl Salicylate.*

By Brian Wilfred Doak and John Packer.

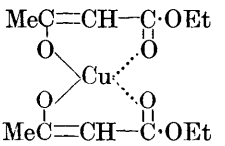
The alkali salts of the complex acids theoretically derived from hydroxy-acids by the replacement (in part at least) of the hydrogen of the hydroxyl groups by various metals have been the subject of many investigations (see Wark, J., 1923, **123**, 1816, 1826; 1924, **125**, 2004; 1927, 1753, for references). It is, however, impossible to assign definite constitutional formulæ to all but the simplest of them owing to the difficulty of distinguishing between the carboxylic and the hydroxylic hydrogen atom and the extent to which each is replaced by the metal of the complex anion.

The metallic derivatives of the corresponding hydroxy-esters appear to have been little investigated. The potassium and barium derivatives of methyl salicylate and various metallic derivatives of ethyl acetoacetate have long been known; sodium and potassium metalloacetoacetates, however, are unknown. Since the completion of the present work Burrows and Wark (this vol., p. 222) have described anhydrous methyl aluminosalicylate, $Al(C_8H_7O_3)_3$, the complex aluminosalicylic acid, $H_2\left[(C_7H_4O_3)_2Al\begin{matrix}OH\\OH_2\end{matrix}\right]$, and a number of its salts: they did not succeed in preparing salts of the type $M_3[(C_7H_4O_3)_3Al]$.

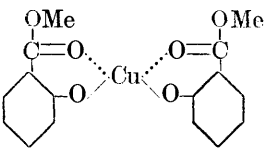
It is to be expected that, as in the case of the sodium salts, the stability and ease of formation of the esters of the complex metal-substituted hydroxy-acids would be greater the more acidic the hydroxylic hydrogen atom. The esters of phenolic acids should therefore yield more stable metallic derivatives than the esters of aliphatic hydroxy-acids, and for this reason salicylic acid was chosen for investigation first. Sodium cuprisalicylate (anhydrous) has been isolated by Wark (J., 1927, 1753), who assigns to it the formula $Na_2[Cu(C_7H_4O_3)_2]$.



(I.)



(II.)



(III.)

Starting with methyl salicylate, the authors have prepared *methyl cuprisalicylate* and *nickelosalicylate* as crystalline dihydrates, and *anhydrous* methyl cuprisalicylate, which differs somewhat from the

hydrated form in its solubility in organic solvents. The constitutions of the hydrates are best represented as in (I; X = Cu or Ni), the two molecules of water being held by co-ordination bonds to the central copper or nickel atom, which has a co-ordination number of four. These hydrates are non-volatile solids, undergoing exothermic decomposition on heating and leaving a quantitative residue of the metallic oxide. In this respect methyl cuprisalicylate dihydrate differs from ethyl cupriacetoacetate, which is not hydrated, is volatile below its decomposition temperature, and shows considerable solubility in liquids of low dielectric constant, such as chloroform, and therefore probably is a co-ordinated copper compound possessing a chelate ring structure as shown in (II), the dotted lines denoting co-ordination bonds (the copper atom sharing a pair of electrons belonging to each carbonyl oxygen atom and thus completing its octet of electrons). The tendency of anhydrous methyl cuprisalicylate towards similar co-ordination with chelate ring formation (III) is apparently small, as shown by its relatively small, although appreciable, solubility in chloroform (in which the hydrate is, however, insoluble) and its non-volatility.

Methyl cuprisalicylate and nickelosalicylate dihydrates are completely decomposed by mineral acids. They are insoluble in cold water; but when boiled with water, methyl cuprisalicylate undergoes complete hydrolysis to methyl salicylate and copper hydroxide (or oxide), and methyl nickelosalicylate yields methyl salicylate and *methyl hydroxynickelosalicylate* (IV : X = Ni; R = H). The

(IV) $CO_2Me{\cdot}C_6H_4{\cdot}O{\cdot}X{\cdot}OR$

(V) $CO_2Me{\cdot}C_6H_4{\cdot}O{\cdot}Cu{\cdot}O{\cdot}Cu{\cdot}O{\cdot}C_6H_4{\cdot}CO_2Me$

corresponding copper compound (IV : X = Cu; R = H) can be obtained, by less energetic hydrolysis, by passing wet air over methyl cuprisalicylate dihydrate at 100°. This *methyl hydroxycuprisalicylate*, on heating at 100° in a stream of dry air, undergoes dehydration to yield the *basic compound* (V). The hydrolysis of methyl cuprisalicylate, which occurs according to the equation

$$(CO_2Me{\cdot}C_6H_4{\cdot}O)_2Cu + H_2O \rightleftharpoons CO_2Me{\cdot}C_6H_4{\cdot}OH + CO_2Me{\cdot}C_6H_4{\cdot}O{\cdot}Cu{\cdot}OH,$$

is reversible, the hydroxycuprisalicylate slowly absorbing methyl salicylate vapour at the ordinary temperature. That hydrolysis can also proceed very slowly at the ordinary temperature is shown by the facts that methyl cuprisalicylate dihydrate gradually loses weight in a vacuum (2 cm.) to an extent greatly in excess of that corresponding to the loss of its two molecules of water and that methyl cuprisalicylate and nickelosalicylate dihydrates smell quite strongly of methyl salicylate at the ordinary temperature. An-

hydrous methyl cuprisalicylate, however, is stable at temperatures up to 100° in the absence of water vapour.

Methyl cuprisalicylate and nickelosalicylate dihydrates also undergo alcoholysis with methyl and ethyl alcohols. The reaction between methyl cuprisalicylate dihydrate and methyl alcohol occurs (partly at least) at the ordinary temperature, whereas that with ethyl alcohol occurs only on boiling. When boiled with methyl alcohol, both esters yield the respective *methoxymetallosalicylates* (IV: X = Cu or Ni; R = Me) as insoluble residues. The reaction

$$(CO_2Me\cdot C_6H_4\cdot O)_2X + MeOH \rightleftharpoons CO_2Me\cdot C_6H_4\cdot OH + CO_2Me\cdot C_6H_4\cdot O\cdot X\cdot OMe$$

is reversible and the insoluble methoxy-compound can readily be made to pass into methyl-alcoholic or acetone solution as the original metallosalicylate by the addition of methyl salicylate. The reversibility of this reaction is the basis of the method for the preparation of anhydrous methyl cuprisalicylate (see p. 2768).

On boiling with ethyl alcohol, methyl nickelosalicylate dihydrate gives the corresponding insoluble *ethoxy-compound* (IV: X = Ni; R = Et). Methyl cuprisalicylate dihydrate behaves differently, the alcoholysis with boiling ethyl alcohol proceeding a stage further to give small quantities of methyl salicylate and *cupric ethoxide*, $Cu(OEt)_2$. The addition of very little methyl salicylate completely suppresses the alcoholysis in this case.

These alkyloxy-derivatives are stable in the absence of moisture, even at 100°, but undergo hydrolysis in its presence, although only very slowly at the ordinary temperature. Methyl methoxycuprisalicylate, on heating at 100° in a stream of moist air, gives methyl alcohol and the same hydroxycuprisalicylate as is obtained by the hydrolysis of the original cuprisalicylate.

Direct methylation of sodium cuprisalicylate, $Cu(O\cdot C_6H_4\cdot CO_2Na)_2$ (VI), to methyl cuprisalicylate by means of methyl iodide or sulphate in non-aqueous solvents could not be effected, but the latter reagent converts sodium cuprisalicylate in aqueous or aqueous-alcoholic solution into the basic compound (V) in 70% yield. Now sodium cuprisalicylate undergoes hydrolysis in aqueous solution, as is shown by the appearance of a pale green precipitate after a very short time. If the first stage of the hydrolysis is the production of sodium salicylate and a basic compound analogous to (V) (with Na in place of Me), the formation of (V) by means of methyl sulphate can readily be understood and is in agreement with the simple constitutional formula (VI) assigned to sodium cuprisalicylate by Wark (*loc. cit.*).

When concentrated ammonia is added to alcoholic solutions (containing methyl salicylate) of methyl cuprisalicylate and methyl nickelosalicylate, ammine complexes are formed, but only *methyl diammminenickelosalicylate* has been isolated, two ammonia molecules having replaced the two water molecules of the dihydrate (I; X = Ni). This diammminenickel compound crystallises in three forms, two of which are metastable. On heating with water it undergoes rapid hydrolysis, the basic methyl hydroxynickelosalicylate (IV : X = Ni; R = H), identical with that obtained by the hydrolysis of the dihydrate (I), being produced.

Copper and nickel have a co-ordination number of four in the compounds formulated above. Burrows and Wark (*loc. cit.*) regard the aluminium atoms in methyl and ethyl aluminosalicylates and in the salts of the acid $H_2\left[(C_7H_4O_3)_2Al\begin{matrix}OH\\OH_2\end{matrix}\right]$ as having a co-ordination number of six. The latter salts, however, can be simply formulated as $(CO_2M\cdot C_6H_4\cdot O)_2Al\begin{matrix}OH\\OH_2\end{matrix}$, according to which the aluminium atom has a co-ordination number of four. This is in agreement with the failure of Burrows and Wark to resolve the ion $\left[(C_7H_4O_3)_2Al\begin{matrix}OH\\OH_2\end{matrix}\right]''$ into optical antipodes. The dihydrates and dialcoholates of these salts can then be represented as containing aluminium of co-ordination number six. The properties of methyl aluminosalicylate, $(CO_2Me\cdot C_6H_4\cdot O)_3Al$, do not lend much support to the contention that it is definitely a stable co-ordinated compound of aluminium, although no doubt there is a tendency towards co-ordination (with the C:O of the carbomethoxy-groups) with chelate ring formation. A comparison of methyl or ethyl aluminosalicylate with ethyl aluminomalonate and of methyl cuprisalicylate with ethyl cupriacetoacetate indicates an increased tendency towards co-ordination with the formation of chelate rings on passing from the salicylate to the open-chain compounds, a tendency which is fully developed in the metallic derivatives of acetylacetone.

Experimental.

Methyl Cuprisalicylate Dihydrate (I; X = Cu).—Copper acetate dihydrate (36 g.; slightly less than the theoretical quantity) in aqueous solution and concentrated ammonia (16 c.c.) were added to a solution of methyl salicylate (50 g.) in about five times its volume of 94% ethyl alcohol. *Methyl cuprisalicylate dihydrate*, which rapidly crystallised, was removed, washed with 50% and finally with 80% alcohol, in which it was practically insoluble, and air-dried (yield, 67%) (Found : C, 47·8; H, 4·5; Cu, 15·8; *M*,

ebullioscopic in acetone, 397. $C_{16}H_{18}O_8Cu$ requires C, 47·8; H, 4·5; Cu, 15·8%; *M*, 401·7).

The dihydrate is a green crystalline solid, soluble in acetone (from which it may readily be recrystallised), methyl salicylate, and benzene, very slightly soluble in ether, and insoluble in chloroform. It begins to decompose at 115°, but suffers partial hydrolysis at lower temperatures owing to interaction with its water of crystallisation.

Hydrolysis. In a vacuum, methyl cuprisalicylate dihydrate lost water and methyl salicylate, very slowly at the ordinary temperature and more rapidly at 100°, but the hydrolysis was incomplete. When the dihydrate was heated in air at 100°, the hydrolysis was also incomplete owing to the escape of some of the water of crystallisation.

A stream of air saturated with water vapour was passed over methyl cuprisalicylate dihydrate heated at 100—105°. After 10 days the weight of the residual *methyl hydroxycuprisalicylate* (IV : X = Cu; R = H) was almost constant (Found : loss, 37·6. Calc. loss due to hydrolysis, 42·3%). The stream of moist air was then replaced by one of dry air; the weight again decreased and became constant after a further 6 days, the *basic compound* (V) having been formed (Found : C, 43·1; H, 3·3; Cu, 28·5. $C_{16}H_{14}O_7Cu_2$ requires C, 43·1; H, 3·2; Cu, 28·6%). The total loss in weight was 44·4% (calc., 44·6%).

Alcoholysis of Methyl Cuprisalicylate Dihydrate.—(i) *With methyl alcohol. Formation of methyl methoxycuprisalicylate* (IV : X = Cu; R = Me). When methyl cuprisalicylate dihydrate was treated with cold methyl alcohol, the green colour changed to blue; very little material dissolved, however, even on boiling. Methyl cuprisalicylate dihydrate was treated with methyl alcohol in a Soxhlet apparatus until the extract was colourless : methyl salicylate and a very little methyl cuprisalicylate dihydrate were identified in the extract. The residue after extraction was *methyl methoxycuprisalicylate* (Found in air-dried material : C, 43·9; H, 4·2; Cu, 25·9; *M*, ebullioscopic in chloroform, 238. $C_9H_{10}O_4Cu$ requires C, 43·9; H, 4·1; Cu, 25·9%; *M*, 245·6).

Methyl methoxycuprisalicylate is a blue solid, non-volatile but decomposed on heating, soluble in chloroform but insoluble in water, methyl alcohol, ether and acetone. It is decomposed by mineral acids. Boiling water completely hydrolyses it to methyl salicylate, methyl alcohol, and copper oxide, but in moist air the methoxy-group only is attacked. When heated at 100° in a stream of wet air (4 days) and thereafter in dry air (4 days), it gave successively methyl hydroxycuprisalicylate (Found : loss, 5·7. Calc.,

5·7%) and the basic compound (V) (Found : total loss, 9·3. Calc., 9·4%. Found in final material : C, 43·1 ; H, 3·3 ; Cu, 28·5. Calc. for $C_{16}H_{14}O_7Cu_2$: C, 43·1 ; H, 3·2 ; Cu, 28·6%).

(ii) *With ethyl alcohol.* When methyl cuprisalicylate dihydrate was boiled with ethyl alcohol the bulk of it dissolved to give a deep green solution, but there was a small residue of *cupric ethoxide*, probably contaminated with cupric oxide (Found in air-dried material : C, 31·3 ; H, 6·5 ; Cu, 42·6. $C_4H_{10}O_2Cu$ requires C, 31·4 ; H, 6·6 ; Cu, 41·4%). On further boiling, the green solution turned brown and a small quantity of copper oxide, no doubt formed by hydrolysis by the small amount of water present, separated.

Anhydrous Methyl Cuprisalicylate.—Methyl methoxycuprisalicylate (24·5 g.) was dissolved in a solution in anhydrous acetone of the theoretical quantity of methyl salicylate (15·2 g.). Anhydrous methyl cuprisalicylate separated and was dried over calcium chloride (Found : C, 52·4 ; H, 4·0 ; Cu, 17·4. $C_{16}H_{14}O_3Cu$ requires C, 52·2 ; H, 3·9 ; Cu, 17·4%). It is a green solid which does not crystallise well, is slightly soluble in chloroform and insoluble in acetone, and gives with methyl alcohol the methoxy-derivative (IV : X = Cu ; R = Me).

Methylation of Sodium Cuprisalicylate.—Sodium cuprisalicylate (5 g.), prepared by Wark's method (*loc. cit.*), was dissolved in water (50 c.c.), an excess of methyl sulphate (2 c.c.) immediately added, and the whole shaken at 40° for 15 minutes. The basic compound (V) separated as a dull green solid ; it was washed with water and acetone and air-dried (Found : C, 43·0 ; H, 3·2 ; Cu, 28·6%).

Methyl Nickelosalicylate Dihydrate (I ; X = Ni).—An aqueous solution of nickel chloride was added to an alcoholic solution of methyl salicylate (theoretical quantities), the whole being made neutral by the addition of concentrated ammonia solution. The *methyl nickelosalicylate dihydrate* did not crystallise nearly as readily as the copper compound and the yield was much less (Found in air-dried material : C, 48·3 ; H, 4·7 ; Ni, 14·7. $C_{16}H_{18}O_8Ni$ requires C, 48·4 ; H, 4·5 ; Ni, 14·8%).

Methyl nickelosalicylate dihydrate is a light green, crystalline substance, insoluble in water and chloroform but soluble in acetone.

Hydrolysis. When the dihydrate was boiled with water, the colour changed to a darker green and *methyl hydroxynickelosalicylate* (IV : X = Ni ; R = H) was formed (Found in air-dried solid : C, 42·1 ; H, 3·6 ; Ni, 25·9. $C_8H_8O_4Ni$ requires C, 42·3 ; H, 3·5 ; Ni, 25·9%).

Alcoholysis. When the dihydrate was boiled with methyl or ethyl alcohol, a portion dissolved, leaving a green residue of *methyl*

methoxynickelosalicylate (IV : X = Ni; R = Me) (Found in air-dried material : C, 44·8; H, 4·2; Ni, 24·2. $C_9H_{10}O_4Ni$ requires C, 44·9; H, 4·2; Ni, 24·3%) or *methyl ethoxynickelosalicylate* (Found in air-dried material : C, 46·0; H, 4·8; Ni, 23·0. $C_{10}H_{12}O_4Ni$ requires C, 46·1; H, 4·7; Ni, 23·0%), respectively. These two substances are insoluble in acetone but soluble in chloroform.

Methyl Diamminenickelosalicylate.—When an excess of concentrated aqueous ammonia was added to a mixture of the theoretical quantities of an aqueous solution of nickel chloride and an alcoholic solution of methyl salicylate, the colour changed from green through blue to deep purple; purple octahedral crystals of *methyl diamminenickelosalicylate* slowly separated and were washed with aqueous alcohol containing ammonia and dried in an atmosphere containing ammonia (Found: C, 48·6; H, 5·2; N, 7·1; Ni, 14·8. $C_{16}H_{20}O_6N_2Ni$ requires C, 48·6; H, 5·2; N, 7·1; Ni, 14·9%). By the addition of a considerable excess of ammonia in this preparation, the diammine compound was obtained in two metastable forms, *viz.*, very fine needles and many-faced crystals of undetermined form, both of which changed fairly rapidly in contact with the solution into the stable octahedral form. Analyses of mixtures of these forms gave figures identical with the above.

Methyl diamminenickelosalicylate is a bright purple, crystalline solid which smells slightly of ammonia and methyl salicylate on exposure to the air, is insoluble in hot or cold acetone, ether and chloroform, and is only slightly attacked by boiling methyl and ethyl alcohols, in which it is insoluble. Heated in a stream of dry air or ammonia, it lost over 40% by weight; only a portion of the ammonia present in the original diammine compound was evolved as such.

Hydrolysis. The diammine compound dissolved in cold water to give a blue (concentrated) or green (dilute) solution which was unstable owing to hydrolysis and immediately started to throw down a green, flocculent precipitate. On boiling, it gave ammonia, methyl salicylate, and a green residue of methyl hydroxynickelosalicylate (Found in the air-dried solid : C, 42·2; H, 3·6; Ni, 25·8. Calc. for $C_8H_8O_4Ni$: C, 42·3; H, 3·5; Ni, 25·9%).

Other metallic derivatives of methyl salicylate are under investigation.

CANTERBURY COLLEGE,
UNIVERSITY OF NEW ZEALAND. [*Received, July 23rd,* 1928.]