has been established. α-Chlorocholestane has been oxidized to produce α-chloroandrosterone and α-chlorocholanic acid.

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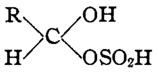
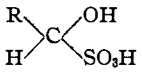
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Constitution of the Bisulfite Addition Compounds of Aldehydes and Ketones

BY WALTER M. LAUER AND CARL M. LANGKAMMERER

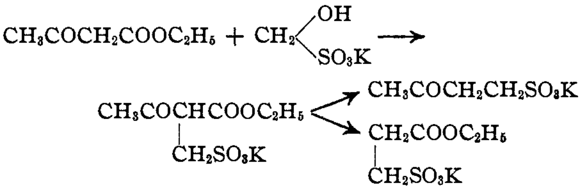
Since the discovery of the first aldehyde and ketone bisulfite addition compounds[1] many difficulties have been encountered in attempting to decide between the α-hydroxysulfite ester formula (I) and the α-hydroxysulfonic acid formula (II) for these compounds.


I

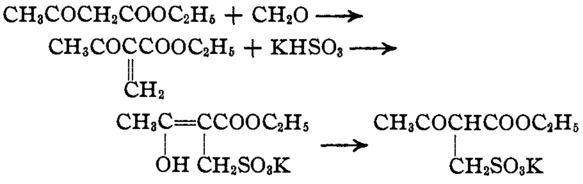

II

Each structure had its proponents[2] and the problem apparently was solved many years ago with the preparation of a "hydroxymethane sulfonic acid" which was not identical with formaldehyde bisulfite.[3] Since then additional "α-hydroxysulfonic acids" have been prepared;[4] they too differed from the corresponding bisulfite addition products. It is natural, therefore, that formation of the α-hydroxynitriles upon treatment of the bisulfite addition compounds with potassium cyanide came to be regarded as characteristic of the –O–SO$_2$H group.[5] These views were current until the time of the exemplary investigations of Raschig and Prahl.[6] These investigators were able to show that the "hydroxymethane sulfonic acid" obtained by Müller on sulfonating methyl alcohol was actually symmetrical acetone disulfonic acid, formed by the sulfonation of acetone present in the methyl alcohol of that early date. The "hydroxymethane sulfonic acid" described by Glimm and by Reinking, Dehnel and Labhardt as the product of the action of sulfuric acid on methyl alcohol was demonstrated to be an isomer, methyl hydrogen sulfate. Likewise, the "α-hydroxyisopropyl sulfonic acid," $(CH_3)_2C(OH)SO_3H$, which Schroeter prepared by the hydrolysis of the diphenyl ester of dimethylmethionic acid, $(CH_3)_2C(SO_2OC_6H_5)_2$, and which was not identical with the acetone bisulfite addition compound, was shown to be the methyl ether of this sulfonic acid.

After thus removing much of the evidence which was damaging to the α-hydroxysulfonic acid structure (II), Raschig and Prahl submitted the reaction



as indicative of structure II, since the cleavage products were definitely sulfonic acids. However, these investigators[7] were not unmindful of the possibility of intermediate formation of methylene-acetoacetic ester with subsequent 1,4-addition of potassium bisulfite but their evidence led them to regard this as unlikely.



$$CH_3COCH_2COOC_2H_5 + CH_2O \longrightarrow \underset{\displaystyle CH_2}{CH_3CO\overset{}{\underset{\|}{C}}COOC_2H_5} + KHSO_3 \longrightarrow \underset{OH}{CH_3\underset{|}{C}}{=}\underset{CH_2SO_3K}{\underset{|}{C}}COOC_2H_5 \longrightarrow CH_3CO\underset{CH_2SO_3K}{\underset{|}{C}H}COOC_2H_5$$

Backer and Mulder[8] a short time ago have introduced independent evidence for the hydroxysulfonic acid structure, for the compound NH$_2$-CH$_2$SO$_3$H (or $NH_3^+CH_2SO_3^-$) obtained by treating formaldehyde bisulfite with ammonia contains a carbon–sulfur linkage since treatment with nitrosyl chloride yields chloromethane sulfonic

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(1) Redtenbacker, *Ann.*, **65**, 37–43 (1848); Tilley, *ibid.*, **67**, 105–15 (1848); Bertagnini, *ibid.*, **85**, 179–196, 268–288 (1853); Limpricht, *ibid.*, **93**, 238–242 (1855).

(2) Mendeleff, *ibid.*, **110**, 241 (1859); Schiff, *ibid.*, **210**, 123 (1881); Eibner, *ibid.*, **316**, 89 (1901).

(3) Müller, *Ber.*, **6**, 1031 (1873); Glimm, "Inaug.-Diss.," Freiburg, 1902; Reinking, Dehnel and Labhardt, *Ber.*, **38**, 1069 (1905).

(4) Schroeter, *Ann.*, **418**, 161–257 (1919); *Ber.*, **59**, 2341–2343 (1926); *ibid.*, **61**, 1616–1627 (1928).

(5) Knoevenagel, *ibid.*, **37**, 4059–4065 (1904).

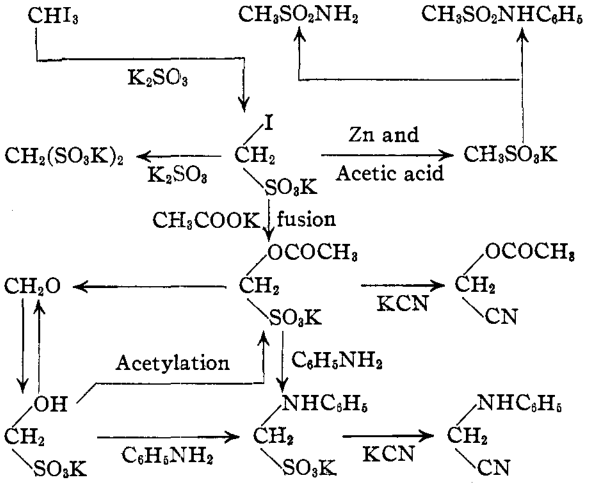
(6) Raschig and Prahl, *Ber.*, **59**, 859–865 (1926); *Ann.*, **448**, 265–312 (1926); *Ber.*, **59**, 2025–2028 (1926); *ibid.*, **61**, 179–189 (1928).

(7) See also Schroeter, *Ber.*, **61**, 1621 (1928).

(8) Backer and Mulder, *Rec. trav. chim.*, **52**, 454–468 (1933); *ibid.*, **53**, 1120–1127 (1934).

acid. In spite of this excellent evidence for structure II, it was thought desirable[9] to add still further and, if possible, equally conclusive proof.

The following series of reactions, which needs but little explanation, has been carried out.



Iodomethane sulfonic acid is definitely a sulfonic acid since it can be transformed into methionic acid and methane sulfonic acid. Fusion (*ca.* 200°) of this compound with potassium acetate and acetylation of the formaldehyde bisulfite addition compound each yields acetoxymethane sulfonic acid. The identity of these two preparations has been demonstrated. This evidence, in conjunction with that submitted by other investigators, supplies ample proof of the hydroxymethane sulfonic acid structure for formaldehyde bisulfite and makes it unnecessary to resort to a "polymolecule formula," (R_2CO), (SO_2), (HOH), of the type suggested by Schroeter.

Experimental

Potassium Iodomethane Sulfonate.—Since the preparations of the salts of iodomethane sulfonic acid are described only in patent literature[10] the details of procedure are included here.

Ninety-five grams (0.6 mole) of potassium sulfite was dissolved in 450 cc. of water in a 1-liter round-bottomed flask and 78.8 g. (0.2 mole) of freshly recrystallized iodoform added so that the iodoform formed a layer above the water. The reaction mixture was refluxed for a period of three to four hours until practically all of the iodoform and methylene iodide had disappeared. After filtering the solution it was evaporated to dryness on a steam-cone. (Blowing a stream of compressed air over the beaker shortens considerably the length of time required for this operation.) The dry solid was extracted with methyl alcohol at room temperature. One extraction with 300 cc. followed by two extractions with 200 cc. of methyl alcohol is sufficient to remove almost all of the inorganic iodide. The residue was then treated with 800 cc. of boiling 80% ethyl alcohol and filtered. The cooled filtrate yielded 38.0 g. (73%) of shiny, white plates which were washed with absolute alcohol and ether and then air dried.

Anal. Calcd. for CH_2ISO_3K: K, 15.03. Found: K, 14.95, 15.05.

The sodium salt was prepared in a similar way; however, in this case it is not necessary to remove the sodium iodide. The evaporated reaction mixture is extracted directly with 300 cc. of 90% ethyl alcohol; yield, 68%.

Anal. Calcd. for $CH_2ISO_3Na \cdot H_2O$: K, 8.78; H_2O, 6.68. Found: K, 8.78; H_2O, 7.16.

Potassium Acetoxymethane Sulfonate (a) from Potassium Iodomethane Sulfonate.—After refluxing potassium acetate and potassium iodomethane sulfonate in aqueous solution for fifteen hours no iodide ion had formed. However, when 10.4 g. (0.04 mole) of potassium iodomethane sulfonate and 5 g. (0.05 mole) of potassium acetate were ground in a mortar and heated to 200–205° in a Wood's metal-bath and held there for an hour with stirring the mass liquefied. The reaction was maintained at this temperature for two and one-half hours. After cooling to room temperature the mass was chipped out of the flask and ground. The solid was extracted with two 200-cc. portions of methyl alcohol and then with one 100-cc. portion, all at room temperature. The methyl alcohol extracts were evaporated to dryness and then dissolved in 100 cc. of water. Titration of a 10-cc. portion with silver nitrate showed that 92% of the iodine in the original compound had been changed to iodide ion.

The solid remaining after the methyl alcohol extraction was treated with 400 cc. of boiling 95% ethyl alcohol. The cooled filtrate produced 1.03 g. of solid. A second extraction yielded 0.55 g. of the same material, yield 20.5%.

Anal. Calcd. for $C_3H_5O_5SK$: K, 20.35. Found: (for 1.03-g. fraction) K, 20.07, 20.11; (for 0.55-g. fraction) K, 20.09.

Potassium Acetoxymethane Sulfonate (b) from the Potassium Bisulfite Addition Compound of Formaldehyde.—Treatment of the potassium bisulfite addition compound of formaldehyde with acetic anhydride according to the procedure of Raschig and Prahl[11] yielded a product the potassium content of which was somewhat too high for potassium acetoxymethane sulfonate. Recrystallization lowered the percentage of potassium but it was still higher than theory. The substance was prepared in the following way.

Twenty grams of the potassium bisulfite addition compound of formaldehyde (K, 26.15; calcd., 26.04) was added to a 200-cc. round-bottomed flask containing 100 cc. of acetic anhydride and 10 cc. of glacial acetic acid. After twenty minutes of refluxing *with constant shaking* the flask was filled with a mass of crystals. Filtered, washed with

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[9] See for example D. Gibson, *Chem. Rev.*, **14**, 431–457 (1934).

[10] German Patents 532,766, 535,652, 546,354, 551,145, 564,211, 562,501; British Patents 353,477, 369,473; French Patents 708,270, 40,169; U. S. Patents 1,842,626, 1,867,793; *Industria chimica*, **7**, 714 (1932).

[11] Raschig and Prahl, *Ann.*, **448**, 305 (1926).

absolute alcohol, followed by ether and then dried, the solid weighed 20.0 g. (75%). The potassium content of the crude product was 20.77%. The solid was recrystallized from 95% alcohol; approximate solubility hot, 0.55 g. per 100 cc. of 95% ethyl alcohol; cold, 0.07 g. per 100 cc. of 95% ethyl alcohol. In larger amounts the substance can be recrystallized satisfactorily from 80% alcohol.

Anal. Calcd. for $C_3H_5O_5SK$: K, 20.35. Found: (for various fractions) K, 20.34, 20.38, 20.17, 20.33.

Comparison of the Potassium Acetoxymethane Sulfonate Prepared by the Two Methods.—The decomposition temperature of the first preparation is 239–245°; that of the second 243–246°. A mixture of the two substances decomposes at 240–246°.

Dr. E. B. Sandell of the division of analytical chemistry of the University of Minnesota kindly submits the following crystallographic comparison. Both substances recrystallized from 95% alcohol form plates and flattened prisms which are anisotropic and exhibit parallel extinction. The index of refraction corresponding to light vibrating parallel to the long direction of the prisms is 1.491 ± 0.002, whereas the index most often exhibited crosswise is 1.521 ± 0.003 *in both samples.*

Potassium Methionate from Potassium Iodomethane Sulfonate.—Twenty-six grams (0.1 mole) of potassium iodomethane sulfonate and 47.5 g. (0.3 mole) of potassium sulfite were dissolved in water and diluted to 500 cc. Placed in a 1-liter round-bottomed flask under a reflux condenser the reaction mixture was heated on a steam-bath. At approximately twenty-four hour intervals 10-cc. portions were removed and extracted with methyl alcohol. The alcoholic extract was evaporated and the resulting solid titrated with silver nitrate solution using eosin as an indicator. At the end of twenty-four hours, 34.3% reaction; forty-eight hours, 49.3%; seventy-two hours, 65.0%; ninety-six hours, 68.8%; one hundred and twenty hours, 76.8%; one hundred and forty-four hours, 87.3%; one hundred and sixty-eight hours, 87.0%. The solution was then evaporated to 150 cc., cooled and the solid filtered off. Recrystallized from 125 cc. of hot water this yielded 15.50 g. of air-dried potassium methionate.

Anal. Calcd. for $CH_2O_6S_2K_2$: K, 30.99. Found: K, 30.91.

A further crop of 3.7 g. potassium methionate was obtained by working up the filtrates; total yield, 19.2 g. (84.6%).

Potassium Methane Sulfonate from Potassium Iodomethane Sulfonate.—Twenty-six grams (0.1 mole) of potassium iodomethane sulfonate, 20 g. of glacial acetic acid and 25 g. of zinc dust were placed in 380 cc. of 50% alcohol and refluxed for two and one-half hours. The excess zinc dust was filtered off and the solution evaporated to 200 cc. The zinc sulfide formed on saturating the solution with hydrogen sulfide was filtered off and the filtrate evaporated to dryness. An extract with 150 cc. of methyl alcohol was discarded. The remaining solid was recrystallized from 150 cc. of 80% ethyl alcohol; total yield (3 crops), 9.8 g. (73%).

Anal. Calcd. for CH_3SO_3K: K, 29.14. Found: K, 28.90.

The amide prepared in the customary manner melted at 89–90°.[12] The sulfonanilide melts at 102–103°.[13]

Acetoxyacetonitrile from Potassium Acetoxymethanesulfonate.—19.2 g. of potassium acetoxymethanesulfonate (0.1 mole) and 6.5 g. (0.1 mole) of potassium cyanide were dissolved in 50 cc. of water and allowed to stand at room temperature for thirty minutes. An oil formed on the surface and was extracted with ether (200 cc.) and the ether extract dried over anhydrous sodium sulfate. The ether was removed on a water-bath and the oil remaining distilled: 105–178°, 1.65 g.; 178–179°, 1.70 g.; total yield 33.9%; after redistillation $n^{20}D$ 1.4040°. Henry[14] reports a boiling point of 179–180° and $n^{20}D$ 1.4107 for acetoxyacetonitrile prepared by the action of potassium acetate on chloracetonitrile.

Potassium Anilinomethane Sulfonate from Potassium Acetoxymethane Sulfonate.—3.84 g. (0.02 mole) of potassium acetoxymethane sulfonate and 40 cc. of aniline were refluxed until the reaction mixture set almost to a solid mass. The flask was cooled to room temperature and an equal volume of absolute alcohol added. The solid after filtration weighed 3.88 g. (85%). Recrystallized from methyl alcohol it analyzed for potassium anilinomethane sulfonate.

Anal. Calcd. for $C_7H_8O_3NSK \cdot H_2O$: H_2O, 7.41; K, 16.07. Found: H_2O, 6.79; K, 16.31.

Treatment with potassium cyanide yielded an oil which was presumably anilinoacetonitrile. Since difficulty was experienced in crystallizing this oil a small part of it was converted to phenylglycine the melting point (124–126°) of which was not depressed on adding authentic phenyl glycine.

Hydrolysis of Potassium Acetoxymethane Sulfonate.—One gram of potassium acetoxymethane sulfonate was dissolved in 25 cc. of water in a 50-cc. distilling flask, 1 cc. of concentrated sulfuric acid was added and the solution distilled slowly into 1 g. of dimethyl dihydroresorcinol dissolved in 75 cc. of water. A precipitate was formed which melted below the melting point of dimethyl dihydroresorcinol. After filtering off this solid the filtrate was treated with potassium bicarbonate and the precipitate recrystallized from a small amount of acetone. The melting point and mixed melting point with a sample of formaldehyde dimethone melting at 191–192°, was 191–192°.

The authors gratefully acknowledge a grant from the Graduate School Fund of the University of Minnesota, which made this work possible.

Summary

It has been shown that the bisulfite addition compound of formaldehyde and presumably all aldehyde and ketone bisulfites are salts of α-hydroxysulfonic acids, $R_2C(OH)SO_3Me$.

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(12) Duguet [*Rec. trav. chim.*, **21**, 76 (1902)] reports 90° for the melting point of methyl sulfonamide.

(13) Duguet, *loc. cit.*, reports 99° for the melting point of methyl sulfonanilide.

(14) Henry, *Rec. trav. chim.*, **24**, 169 (1905).