(c) ***p*-Trifluoromethylbenzyl Bromide.**—*p*-Trifluoromethylbenzyl alcohol (35 g., 0.20 mole) was treated with 48% hydrobromic acid (105 g., 0.65 mole). A 90% yield of *p*-trifluoromethylbenzyl bromide was obtained; b. p. 65–66° (5 mm.); $n^{20}D$ 1.4918.

Anal. Calcd. for $C_8H_6F_3Br$: C, 40.00; H, 2.51; Br, 33.43. Found: C, 40.2; H, 2.74; Br, 33.7.

(*p*-Iodomethylphenyl)-trimethylammonium Iodide

(a) ***p*-Dimethylaminobenzyl Alcohol.**—This procedure is far superior to that reported in the literature.[15] *p*-Dimethylaminobenzaldehyde (50 g., 0.33 mole) was treated with lithium aluminum hydride (4.2 g., 0.11 mole) according to the method of Nystrom and Brown.[14] A 75% yield of *p*-dimethylaminobenzyl alcohol was obtained; 38 g.; b. p. 116.5–117° (1 mm.); $n^{20}D$ 1.5795; lit. b. p. 123° (1 mm.); $n^{20}D$ 1.5701.[15]

(b) **(*p*-Hydroxymethylphenyl)-trimethylammonium Iodide.**—*p*-Dimethylaminobenzyl alcohol was treated with methyl iodide in acetone according to the method of Smith and Welch[15]; m. p. 231–232° dec.; lit. m. p. 232° dec.[15].

(c) **(*p*-Iodomethylphenyl)-trimethylammonium Iodide.**—(*p*-Hydroxymethylphenyl)-trimethylammonium iodide (19.5 g., 0.066 mole) was mixed with 57% hydriodic acid (75 ml., 127 g., 0.57 mole) with occasional shaking for two days at 25°. The fine needles which crystallized were filtered, washed with acetone, and dried. Twenty-one grams of product was collected; yield 79%; m. p., after recrystallization, 200–250° dec.

Anal. Calcd. for $C_{10}H_{15}I_2N$: C, 29.80; H, 3.75; N, 3.48. Found: C, 29.7; H, 3.72; N, 3.51.

(15) Smith and Welch, *J. Chem. Soc.*, 730 (1934).

Reaction of Sodium 2-Propanenitronate and *p*-Xylyl Bromide.—Sodium (1.15 g., 0.05 mole) was dissolved in 50 ml. of absolute ethanol. 2-Nitropropane (5.8 g., 0.065 mole) and then *p*-xylyl bromide (9.3 g., 0.05 mole) were added. The mixture was left at room temperature for fifteen hours. The precipitated sodium bromide was filtered and the filtrate was concentrated at atmospheric pressure to remove the ethanol. The resulting mixture was dissolved in ether and water. The ethereal solution was washed with 10% sodium hydroxide solution to remove acetoxime[16] and excess 2-nitropropane, washed with water and then dried with sodium sulfate. The ether was evaporated and the *p*-tolualdehyde was distilled; yield 4.2 g., 70%; b. p. 68–72° (6 mm.); $n^{20}D$ 1.5420.

Summary

A general procedure for the conversion of para-substituted benzyl halides to the corresponding para-substituted benzaldehydes is described. This is effected through the reaction of the halide with sodium 2-propanenitronate. The benzaldehydes are generally obtained in 68–77% yield. *p*-Nitrobenzyl chloride, alone, fails to give the corresponding benzaldehyde in good yield; it is converted mainly to 2-methyl-2-nitro-1-(*p*-nitrophenyl)-propane.

(16) In one exploratory experiment acetoxime was isolated at this point by repeated water extraction followed by continuous extraction of the aqueous solution with ether.

LAFAYETTE, INDIANA RECEIVED JULY 26, 1948

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Stereochemistry of the Sulfation of Optically Active Secondary Butyl Alcohol

BY ROBERT L. BURWELL, JR.

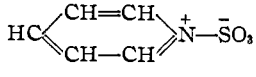
Sulfuric acid, the dioxane sulfur trioxide addition compound, and chlorosulfonic acid react with (+)*s*-butyl alcohol to give (+)barium *s*-butyl sulfate.[1] If, as would appear likely, at least one of these reagents acts without affecting the carbon–oxygen bond of the alcohol, the (+)alcohol is configurationally related to the (+)salt. Since treatment of salt, prepared by action of the dioxane sulfur trioxide complex, with solutions of alkali regenerates an alcohol of opposite but nearly equal rotation, the reaction with dioxane sulfur trioxide proceeds nearly without loss of optical purity.[2] Correspondingly, the configurations in the particular preparations with sulfuric and with chlorosulfonic acids were +22% and +12%.[3]

Other methods of preparing *s*-butyl sulfates have now been investigated. Since barium *s*-butyl sulfate apparently decomposes at room temperatures, the sodium salt has been used as the reference material.

The pyridine sulfur trioxide complex reacts with optically active *s*-butyl alcohol to give a product whose configuration is substantially + 100%.

While sulfamic acid reacts with primary alcohols to give ammonium alkyl sulfates, it has been reported not to react with secondary alcohols.[4] Actually, however, small yields result from heating *s*-butyl alcohol and sulfamic acid at 100° but the reaction, at any rate, is difficult. The addition of pyridine greatly facilitates the reaction and permits good yields to be obtained. The configuration of the product is substantially + 100%. This is a most convenient way of making the alkali metal *s*-butyl sulfates and presumably those of many other secondary alcohols since sulfamic acid is much easier to handle than sulfur trioxide or chlorosulfonic acid. The sulfamic acid pyridine reagent has been used to sulfate the phenolic hydroxyls of stilbesterol.[5]

Baumgarten[6] has argued plausibly that sulfamic acid is best represented as an inner salt, $\overset{+}{H_3}\overset{}{N}—\overset{-}{SO_3}$, analogous to the pyridine sulfur trioxide addition compound



(1) Burwell, THIS JOURNAL, **67**, 220 (1945).

(2) Burwell and Holmquist, *ibid.*, **70**, 878 (1948).

(3) The + indicates that the reaction proceeds with retention of configuration; the number indicates the per cent. of maximum rotation relative to the starting compound.

(4) Cupery, *Ind. Eng. Chem.*, **30**, 627 (1938).

(5) Short and Oxley, British Patent 577,666, May 27, 1946; *C. A.*, **41**, 2084 (1947).

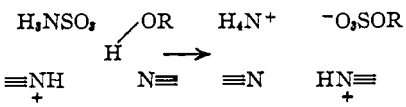
(6) Baumgarten, *Ber.*, **62**, 820 (1929).

Sulfamic acid should, then, be added as the least active member to the sequence suggested by Suter[7]

$(ClCH_2CH_2)_2OSO_3 > O(CH_2CH_2)_2OSO_3 > C_5H_5NSO_3$.

This sequence consists of an addition compound of a Lewis acid with bases of increasing strength. It is possible that acetylsulfuric acid, usually written CH_3COOSO_3H,[8] should be considered as the addition compound of acetic acid and sulfur trioxide and fitted into the series. Although its tautomeric form, H_2OSO_3, may well be involved in the mechanism of sulfation by sulfuric acid (two of the addition compounds in the above sequence are derivatives of this tautomeric form), the position of sulfuric acid in the sequence is anomalous because the greater stability of the ordinary form of sulfuric acid displaces the equilibrium in the direction of sulfuric acid and alcohol. In regard to the activity of the pyridine sulfur trioxide complex, it should be noted that the addition compound as ordinarily made contains excess pyridine. The pure material might be less reactive.

The reaction between sulfamic acid and an alcohol apparently involves displacement of ammonia from the sulfur atom by the oxygen atom of the alcohol and transfer of the proton of the hydroxyl radical to the ammonia to form the ammonium ion. In a simple bimolecular reaction, there is no way in which the proton can get from the oxygen to the nitrogen. In a polymolecular reaction involving the presence of pyridine as a proton acceptor and the pyridinium ion as a proton donor a considerable reduction in activation energy might be possible



Experimental

Materials.—The preparation of most reagents followed previous procedures.[1] A partially resolved *s*-butyl alcohol $\alpha^{25}D$ + 5.60°, was employed save as otherwise noted. Sulfamic acid (Eastman Kodak Company) was dried at 85° before use. The pyridine sulfur trioxide addition compound was prepared following Sobel, Drekter and Natelson.[9]

Procedure.—Rotations of sodium *s*-butyl sulfate were determined in aqueous solution at $C = 26$ in a 2-cm. tube.

In isolating sodium *s*-butyl sulfate, the reaction mixture was neutralized with sodium hydroxide and extracted with benzene. The aqueous layer was evaporated to dryness and the sodium alkyl sulfate extracted with methanol. Upon evaporation of the methanol extract, drying at 65° and redissolving in methanol, a further small quantity of sodium sulfate or sodium sulfamate was removed. To avoid interference from sodium chloride, chloride-free sodium hydroxide must be employed. Evaporation gave sodium *s*-butyl sulfate which if optically active was not recrystallized because of the danger of fractionation. Inactive material was recrystallized from methyl–isopropyl alcohol mixtures.

For a configuration of +100% relative to alcohol of $\alpha^{25}D$ +5.60°, the specific rotation of sodium *s*-butyl sulfate is taken as $[\alpha]^{25}D$ +5.47°, the value most consistent with the data presented below. Taking pure (+)*s*-butyl alcohol as $\alpha^{25}D$ +10.97°, for optically pure (+)sodium *s*-butyl sulfate, $[\alpha]^{25}D$ +10.7°.

Sulfamic Acid and Pyridine.—Sulfamic acid, *s*-butyl alcohol and pyridine in mole proportions of 2:1:1.2 were heated on the water-bath for one hour; about 0.05 mole of alcohol was employed. In several experiments yields ranged from 60 to 70%. Variation of the pyridine proportion within the limits 0.8 to 1.5 had no gross effect on the yield.

Pulverizing the sulfamic acid was undesirable. The fine material consolidated into an unreacted mass at the bottom of the flask. The use of 8–20 mesh sulfamic acid gave better results. The effect of stirring or of adding the sulfamic acid in portions was not investigated though these expedients would no doubt increase yields.

Upon employing 8–20 mesh sulfamic and (−)*s*-butyl alcohol, $\alpha^{25}D$ −2.10°, the yield of the sodium salt was 83%, configuration +103%. Upon using sulfamic acid which passed 40 mesh and the usual (+)*s*-butyl alcohol, a yield of 59% was obtained, configuration +101%.

Anal. Calcd. for $C_4H_9SO_4Na$: Na_2SO_4, 40.3. Found by ignition followed by reignition with added H_2SO_4: Na_2SO_4, 40.4.

The salt was hydrolyzed in basic solution[2] to give an alcohol of configuration −96% relative to the original alcohol.

When the sulfamic acid and pyridine mixture was heated on the steam-bath for 1.7 hours, alcohol then added and heated continued twelve hours, the yield was 72%.

Sulfamic Acid Alone.—Upon omitting the pyridine and heating for two hours at 100°, a 22% yield of sodium *s*-butyl sulfate was obtained. Its identity was confirmed by its X-ray diffraction pattern.

Sulfur Trioxide and Dioxane.—Into a solution of 0.44 mole of ethylene dichloride and 0.29 mole of dioxane was distilled 0.069 mole of sulfur trioxide and to this was added 0.058 mole of (+)*s*-butyl alcohol. Part of the reaction mixture was converted to (+)barium *s*-butyl sulfate monohydrate by pouring onto barium carbonate, filtering and evaporating, $[\alpha]^{25}D$ +4.38° ($C = 36$ on anhydrous salt).

Anal. Calcd. for $C_8H_{18}S_2O_8Ba \cdot H_2O$: $BaSO_4$, 50.6. Found by ignition: $BaSO_4$, 50.5.

The remainder was converted to the sodium salt, configuration + 100%.

Anal. Calcd. for $C_4H_9SO_4Na$: Na_2SO_4, 40.3. Found by ignition: Na_2SO_4, 40.8.

Sulfur Trioxide and Pyridine.—To 600 cc. of benzene was added 0.196 mole of (+)*s*-butyl alcohol and 0.34 mole of pyridine sulfur trioxide. After heating at 100° one hour, the reaction mixture was processed; yield, 90%; configuration +96%. On adding sodium hydroxide to the reaction mixture, a deep red substance was formed presumably by ring cleavage in residual addition compound.[10] Upon bringing the *p*H to 2 with sulfuric acid, this material precipitated.

Acknowledgment.—Some experiments preliminary to certain ones described here were run by Mr. Howard E. Holmquist in the course of his Senior Research for the Honors Degree at Northwestern.

Summary

Sulfamic acid reacts with *s*-butyl alcohol at 100° to give poor yields of sodium *s*-butyl sulfate. The addition of pyridine permits excellent yields to be obtained. It is suggested that pyridine may serve to transfer the hydrogen ion.

(7) Suter, "The Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, 1944, p. 6.

(8) Ref. 7, p. 144, Kuhn and Corwin, THIS JOURNAL, **70**, 3370 (1948).

(9) Sobel, Drekter and Natelson, *J. Biol. Chem.*, **115**, 381 (1936).

(10) Baumgarten, *Ber.*, **59**, 1166 (1926).

The sulfamic acid and pyridine reagent and also the sulfur trioxide pyridine addition compound convert optically active *s*-butyl alcohol to salts of hydrogen *s*-butyl sulfate with retention of configuration and maintenance of optical purity.

EVANSTON, ILLINOIS RECEIVED DECEMBER 27, 1948

[CONTRIBUTION FROM THE JOHN HARRISON LABORATORY OF THE UNIVERSITY OF PENNSYLVANIA]

Analogs of Dihydroionone

BY E. C. HORNING, M. G. HORNING AND E. JANE PLATT[1]

The structural relation between ionone and irone has recently been defined through the proof of structure and synthesis of *dl*-α-irone by Ruzicka. Both α- and γ-irone possess a characteristic fresh violet odor, and this is evidently a specific property of the 6-methyl-α- and γ-ionone structure; 6-methyl-β-ionone (β-irone) has an ionone odor. The saturation of the exocyclic double bond in compounds of this group generally leads to complete or almost complete loss of odor, but cyclohexene unsaturation is less necessary for odor. This is indicated by the fact that the condensation product of dihydrocyclocitral and acetone has an intense odor.

The location of the methyl groups is an important factor in determining the character of the odor in these compounds, and we have been interested in a study of several anologs of dihydroionone in which the ring methyl groups are modified in number and position, and in which exocyclic unsaturation is retained. The general method employed for the preparation of these compounds is shown in Fig. 1. Model experiments carried out with 3,5-dimethylcyclohexanone (I, R_1R_2 = H, R_3R_4 = methyl) indicated that the Darzens method gave a satisfactory over-all yield of the corresponding hexahydrobenzaldehyde. The glycidic ester was obtained in 78% yield; hydrolysis under alkaline conditions gave the glycidic acid in 99% yield of crude material, and this gave on pyrolysis a 65% yield of the aldehyde. The condensation of 3,5-dimethylhexahydrobenzaldehyde with acetone was carried out in the usual way,[2] but the result was a mixture which included the aldol product, and it was necessary to carry out a separate dehydration step (with hydrobromic acid) to obtain the unsaturated ketone.

These steps were repeated with 2,3-dimethylcyclohexanone (I, R_2R_4 = H, R_1R_3 = methyl) and with 2,2,3-trimethylcyclohexanone (I, R_4 = H, $R_1R_2R_3$ = methyl). The introduction of methyl groups in positions adjacent to the carbonyl group led to greatly lowered yields in the Darzens procedure. An attempt to obtain 2,2,3,6-tetramethylhexahydrobenzaldehyde (for the proposed preparation of a dihydroirone) was not successful. The introduction of three α-methyl substituents into a cyclohexanone structure (as in 2,2,3,6-tetramethylcyclohexanone) provides sufficient steric hindrance to prevent completely the Darzens condensation.

The dihydroionone analogs obtained in this way did not posses a floral odor, except for 1-(2′,2′,3′-trimethylcyclohexyl)-1-butenone-3, and in this case the odor was not violet-like.

Most of the necessary cyclohexanones were made by methylation methods. 2,3-Dimethylcyclohexanone was prepared from 3-methyl-4-carbethoxy-2-cyclohexen-1-one by sodamide alkylation, followed by hydrolysis, decarboxylation and catalytic reduction. Using the enol ether method,[3] with potassium amide alkylation, 2,2,3-trimethylcyclohexanone was prepared from 2,3-dimethylcyclohexanone. A potassium amide alkylation of 2,2,3-trimethylcyclohexanone provided 2,2,3,6-tetramethylcyclohexanone.

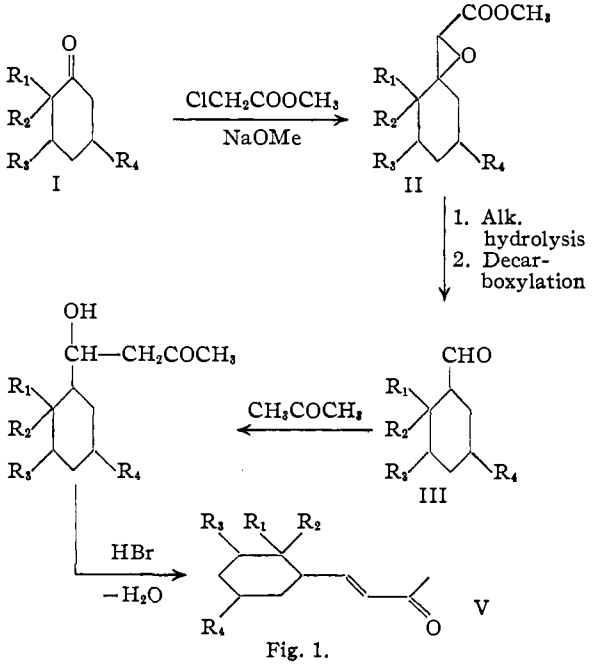


Fig. 1.

Acknowledgment.—We are indebted to Mrs. Sarah M. Woods for the analyses reported here.

Experimental

All melting points are corrected.

Methyl 5,7-Dimethyl-1-oxaspiro[2,5]octane-2-carboxylate.—A mixture of 108 g. (0.86 mole) of 3,5-di-

(1) Rohm and Haas Research Assistant.

(2) "Organic Syntheses," **23**, 78 (1943).

(3) Johnson and Posvic, THIS JOURNAL, **69**, 1361 (1947).