tilled to obtain the product. The yield was 880 g. (92%), b. p. 120–121° (20 mm.), $n^{25}D$ 1.4977. Pure *p*-ethylphenyl acetate boiled at 113–114° (16 mm.), (226–227°),[4] $n^{25}D$ 1.4970, d^{25}_{25} 1.030.

Anal.[5] Calcd. for $C_{10}H_{12}O_2$: C, 73.3; H, 7.33. Found: C, 73.6; H, 7.60.

***p*-Acetylphenyl Acetate.**—Oxygen was blown through an alundum disperser into 317 g. of *p*-ethylphenyl acetate containing 5% of a 1:1:8 mixture of chromium oxide, cobalt hydrate and calcium carbonate held at 140–145° for fifteen hours. Water was removed by means of a Dean and Stark trap. Upon cooling, the catalyst was removed by filtration and washed with benzene. The combined filtrate and washings were refluxed for two hours with 100 cc. of acetic anhydride containing 10 g. of sodium acetate. This mixture was washed thoroughly with water and then distilled to give 222 g. (70% recovery) of *p*-ethylphenyl acetate, b. p. 109–124° (13 mm.), $n^{25}D$ 1.4961, and 81 g. (24% conversion, 79% yield) of *p*-acetylphenyl acetate, b. p. 157–162° (13 mm.) [160° (22 mm.)].[6]

***p*-(α-Hydroxyethyl)-phenyl Acetate.**—One hundred and nine grams of *p*-acetylphenyl acetate was hydrogenated (2000 lb. initial pressure) in the presence of 11 g. of copper chromite, at 130°. The hydrogenation was stopped as soon as one mole of hydrogen had been taken up. The hydrogenated product boiled at 138–142° (3 mm.), $n^{25}D$ 1.5160; yield was 86 g., 78%. An analytical sample boiled at 89–93° (0.07 mm.), $n^{25}D$ 1.5178, d^{25}_{25} 1.134.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.7; H, 6.67. Found: C, 66.2; H, 6.87.

A sample of this compound was acetylated. The main fraction of the product distilled at 94.5–98.0° (0.09 mm.), (b. p. 145–6° (7 mm.), m. p. 51°),[7] $n^{25}D$ 1.4980, d^{25}_{25} 1.128.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.9; H, 6.31. Found: C, 65.4; H, 6.48.

***p*-Vinylphenyl Acetate.**[8]—Eighty-six grams of *p*-(α-hydroxyethyl)-phenyl acetate, 0.9 g. of potassium bisulfate, and 0.9 g. of hydroquinone were placed in a 500-ml. flask equipped with a Vigreux column and heated by an oil-bath. Hydroquinone was placed in the receiver. The product was distilled as formed at an oil-bath temperature of 175–200° and a pressure of 60-13 mm. This product was twice distilled in the presence of hydroquinone to yield 37 g. (45%) of *p*-vinylphenyl acetate; b. p. 100–105° (4 mm.), (b. p. 83–86° (1 mm.)),[7] $n^{25}D$ 1.5356, ($n^{25}D$ 1.5368),[7] d^{25}_{25} 1.065, (d^{25}_4 1.0586).[7]

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.1; H, 6.18. Found: C, 73.8; H, 6.41.

(4) Clemmensen, *Ber.*, **47**, 53 (1914).

(5) All of the analyses are microanalyses performed by the Arlington Laboratories, Fairfax, Virginia.

(6) Verley, *Bull. soc. chim.*, [3] **19**, 140 (1898).

(7) Alderman and Hanford, U. S. Patent 2,276,138; *C. A.*, **36**, 4732 (1942).

(8) Essentially the method of Brooks, THIS JOURNAL, **66**, 1295 (1944).

CENTRAL RESEARCH DEPARTMENT
MONSANTO CHEMICAL COMPANY
DAYTON, OHIO

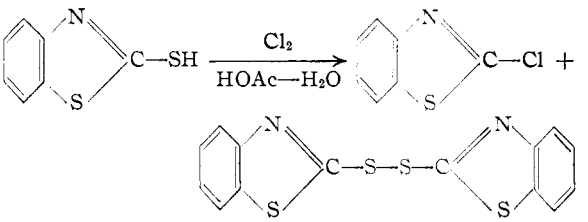
RECEIVED APRIL 5, 1946

The Action of Chlorine on 2-Mercaptobenzothiazole in Aqueous Acetic Acid

BY STEPHEN P. FINDLAY AND GREGG DOUGHERTY

The action of aqueous chlorine on sulfides and disulfides to produce sulfonyl chlorides and thence sulfonic acids is a familiar preparative method.[1,2,3] Under these conditions one mole of 2-mercaptobenzothiazole reacts with half a mole of chlorine to give the corresponding disulfide.[4] However, if the chlorination is conducted in aqueous acetic acid and an excess of the halogen is used, the sulfhydryl group is to a considerable extent replaced by chlorine. Besides 2-chlorobenzothiazole minor quantities of bisbenzothiazolyl 2,2′-disulfide, bisbenzothiazolyl 2,2′-monosulfide, water soluble dyes, and tarry products are formed.

The chlorination of the thiazole in aqueous acetic acid is an exothermic reaction and the best yields of 2-chlorobenzothiazole were obtained when the admission of chlorine to the reaction mixture was so slow that the temperature did not rise above 45°.



Experimental

2-Mercaptobenzothiazole was obtained by treating the commercial product (Captax) with sodium carbonate solution, filtering off the insoluble material, acidifying the filtrate, and separating the precipitated mercaptan. This material after one recrystallization from glacial acetic acid melted at 174–176°.[5]

Procedure.—In a typical run gaseous chlorine was passed slowly for twenty-four hours through a mixture of 50 g. of 2-mercaptobenzothiazole in 200 ml. of glacial acetic acid and 50 ml. of water. The dark-brown product was poured into 350 ml. of water and, after stirring, the heavier phase was separated and steam distilled. The distillate was saturated with salt and extracted with ether. On standing long, pale yellow filaments of the monosulfide separated from the lighter phase and, after two recrystallizations from benzine (b. p. 70°), gave 0.07 g. of pure product, m. p. 99°. Admixture of this with an authentic sample of dibenzothiazolyl 2,2′-monosulfide, prepared by heating in absolute alcohol equimolecular quantities of **2-chlorobenzothiazole** and the potassium salt of 2-mercaptobenzothiazole in the presence of a trace of potassium iodide, did not depress the melting point. Removal of the ether from the extract gave 24 g. (yield 47%) of **2-chlorobenzothiazole**, b. p. 116–122° (3 mm.) and 248° (760 mm.), which, according to Hofmann's directions,[6] yielded a 6-nitro derivative, m. p. 190°. During the steam distillation about 7% of this was hydrolyzed to the hydroxy derivative.

A tarry residue after the steam distillation when recrystallized twice from benzene gave 3.1 g. (6.2%) of **dibenzothiazolyl 2,2′-disulfide**, m. p. 178°.

(1) Lee and Dougherty, *J. Org. Chem.*, **5**, 81–85 (1940).

(2) Schiller and Otto, *Ber.*, **9**, 1638 (1876).

(3) Douglass and Johnson, THIS JOURNAL, **60**, 1486 1489 (1938).

(4) U. S. Patent 2,265,347.

(5) All melting points are uncorrected.

(6) Hofmann, *Ber.*, **13**, 10 (1880).

FRICK CHEMICAL LABORATORY
PRINCETON UNIVERSITY
PRINCETON, N. J.

RECEIVED APRIL 15, 1946

Crystalline Racemic Calcium Pantothenate

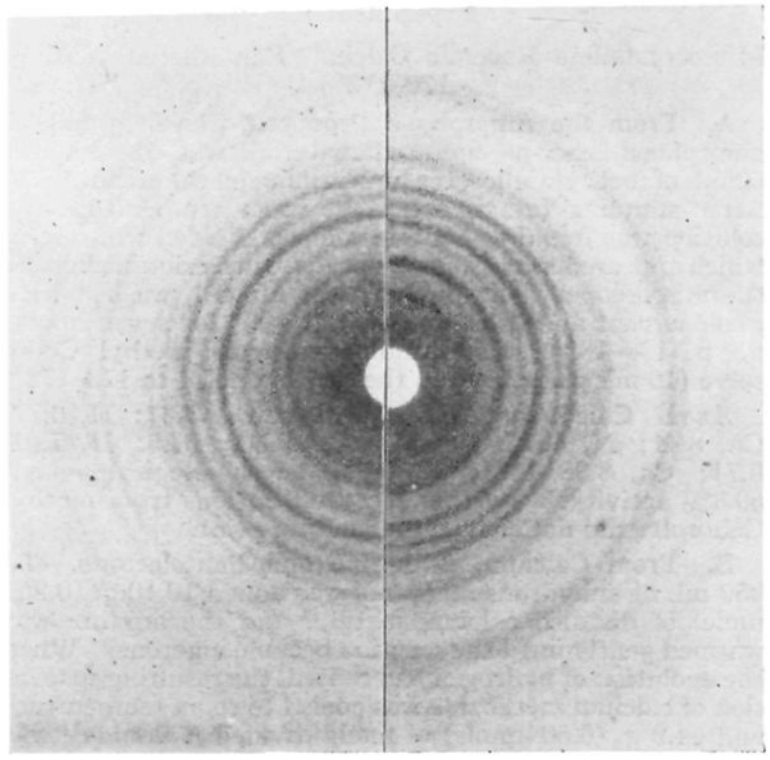
BY JARED H. FORD

The preparation of macrocrystalline calcium (+)-pantothenate has been reported by Levy,

Weijlard and Stiller.[1] Although racemic calcium pantothenate has been prepared by several investigators[2,3,4] no data have been reported which would lead one to believe that crystalline products were obtained. The preparation of pure microcrystalline racemic calcium pantothenate and a macrocrystalline methanol solvate are described in this communication.

Microcrystalline racemic calcium pantothenate was first obtained by dissolving an amorphous ether-precipitated sample[5] in methyl Cellosolve and allowing the solution to stand at room temperature for several weeks. The resulting white powder appeared as slender needles under a microscope and was found to have 50% activity.[6] After recrystallization from methyl Cellosolve it melted at 170–172°. When this microcrystalline product was dissolved in methanol and seeded with macrocrystalline calcium (+)-pantothenate[1] a fluffy mass of needle shaped crystals, some of which were large enough to be seen with the naked eye, formed very slowly. These proved to be a solvate which readily lost all of its methanol upon drying *in vacuo*, forming a microcrystalline product, melting point 187–189°, which also had 50% activity. It is interesting to note that calcium (+)-pantothenate has also been reported to crystallize from methanol as a solvate. Recrystallization of the higher melting product from methyl Cellosolve converted it into the lower melting form.

Both of the microcrystalline products appeared as slender needles under the microscope, but the crystals of the lower melting form were much smaller than those of the higher melting form. A mixture of the 170–172° and 187–189° products melted at 170–187°. Both forms had approximately the same solubility in methyl Cellosolve and both were found to be very soluble in methanol at room temperature if they were shaken vigorously so that solution occurred before crystals of the methanol solvate began to form (see Table I). The possibility that the difference in melting points was caused by an impurity seems unlikely in view of the fact that both forms could be recrystallized to constant melting points and that satisfactory analyses, both chemical and biological, were obtained in each case. The X-ray



M. p. 170–172° M. p. 187–189°

Fig. 1.

powder diagrams (see Fig. 1) indicate clearly that the two forms have different crystal structures.

TABLE I

APPROXIMATE SOLUBILITY[a] OF VARIOUS FORMS OF RACEMIC CALCIUM PANTOTHENATE AT ROOM TEMPERATURE

	Methyl cellosolve	Methanol
Amorphous	>50	>50.0
M. p. 170–172°	0.6	>50.0
M. p. 187–189°	0.6	>12.0
Methanol solvate	....	1.6[b]

[a] Solubility expressed in grams of solute per 100 ml. of solvent. [b] Solubility expressed in solvent-free material. Composition of the solvate not determined.

A convenient method for preparing methanol solutions of calcium pantothenate from metallic calcium, β-alanine and pantolactone is described in the experimental part.[7] By seeding these methanol solutions, pure racemic calcium pantothenate can be obtained in 70–80% yield. Thus it is now possible to make a pure crystalline product without resolving the pantolactone.

Acknowledgments.—The author wishes to express his thanks to Mr. Anthony Bucci for technical assistance, to Mr. Harold Buskirk and Miss Mary Katherine Gee for the microbiological assays, to Dr. George Pish and Mr. Norman Drake for the X-ray powder diagrams, and to Mr. Harold Emerson, Mr. William A. Struck and Miss Celia Triemstra for the microanalyses.

(1) Levy, Weijlard and Stiller, THIS JOURNAL, **63**, 2846 (1941).

(2) Williams, Mitchell, Weinstock and Snell, *ibid.*, **62**, 1784 (1940).

(3) Stiller, Harris, Finkelstein, Keresztesy and Folkers, *ibid.*, **62**, 1785 (1940).

(4) Barnett and Robinson, *Biochem. J.*, **36**, 357 (1942).

(5) Barnett and Robinson[4] reported that they obtained amorphous racemic calcium pantothenate having the theoretical 50% activity[6] by condensing racemic pantolactone (α-hydroxy-β,β-dimethyl-γ-butyrolactone) with the calcium salt of β-alanine in methanol solution and precipitating the product by adding the solution to 6 volumes of dry acetone or ether. In the present investigation numerous attempts were made to duplicate this work but the resulting amorphous products had only 38–44% activity.

(6) Biological activity in comparison with that of pure calcium (+)-pantothenate. Calcium (−)-pantothenate has been reported to be inactive.[1,3]

(7) A similar method has been described by Carlson and Safir in Canadian Patent 417,271 which was issued after the completion of the author's experimental work.

Experimental[8]

Microcrystalline Racemic Calcium Pantothenate (M. p. 170–172°)

A. From the Amorphous Product.—Eleven grams of amorphous ether-precipitated material[4] was dissolved in 50 ml. of methyl Cellosolve by warming on the steam-bath. After standing for six weeks at room temperature the solution was found to contain a finely divided white solid which appeared as very small needles when examined under the microscope. The product was filtered, washed with fresh solvent and dried *in vacuo* at 100° for seven hours; m. p. 166–168°. Recrystallization from methyl Cellosolve (10 ml. per g.) raised the melting point to 170–172°.

Anal. Calcd. for $C_{18}H_{32}N_2O_{10}Ca$: C, 45.37; H, 6.77; Ca, 8.41; N, 5.88. Found: C, 45.50, 45.25; H, 7.01, 6.71; Ca, 8.38, 8.21; N, 5.69; microbiological assay,[9] 50.3% activity.[6] Further recrystallizations from methyl Cellosolve did not change the melting point.

B. From Calcium, β-Alanine and Pantolactone.—To 250 ml. of anhydrous methanol was added 10.10 g. (0.252 mole) of distilled calcium metal,[10] and the mixture was warmed gently until the reaction became vigorous. When the evolution of hydrogen had ceased, the resulting suspension of calcium methoxide was cooled to room temperature and 44.9 g. (0.504 mole) of finely divided β-alanine[11] was added. The resulting mixture was stirred mechanically until a clear solution was obtained (about thirty minutes). A solution of 69.0 g. (0.530 mole) of racemic pantolactone (b. p. 119–122.5° (12.5 mm.)) in 500 ml. of methyl Cellosolve was then added and the methanol was distilled off *in vacuo*. The residual methyl Cellosolve solution was seeded with the crystals described in the preceding paragraph. After standing one month at room temperature, the product was filtered, washed with fresh solvent and dried *in vacuo* at 100°. The yield was 93 g. (77.5%); m. p. 166–169°. Recrystallization from methyl Cellosolve raised the melting point to 170–172°.

Microcrystalline Racemic Calcium Pantothenate (m. p. 187–189°)

A. From the 170–172° Melting Product.—Three grams of the above described microcrystalline salt was dissolved in 10 ml. of dry methanol at room temperature and seeded with crystalline calcium (+)-pantothenate.[1] On standing at room temperature, well defined colorless needles crystallized from the solution. After standing for eleven days the resulting thick slurry of the methanol solvate was filtered, washed with methanol and dried to constant weight *in vacuo* at 100°; m. p. 185–187°. After recrystallization from methanol (5 ml. per g.) it melted at 187–189°.

Anal. Calcd. for $C_{18}H_{32}N_2O_{10}Ca$: C, 45.37; H, 6.77; Ca, 8.41; N, 5.88. Found: C, 45.51; H, 6.58; Ca, 8.59; N, 6.07; microbiological assay, 52.8% activity. Further recrystallizations from methanol did not change the melting point.

B. From Calcium, β-Alanine and Pantolactone.—The methanol solution was prepared by the same method as that described above using 50.10 g. (1.25 mole) of calcium, 222.8 g. (2.50 mole) of β-alanine, 328.5 g. (2.525 mole) of racemic pantolactone (m. p. 84–85°)[12] and 2.5 liters of dry methanol. The solution was seeded with some of the crystals described in the preceding paragraph. After standing for six weeks at room temperature the resulting slurry was filtered, washed with methanol and dried *in vacuo* at 100° for eight hours. The yield was 419 g. (70%); m. p. 180–184°.

Anal. Calcd. for $C_{18}H_{32}N_2O_{10}Ca$: Ca, 8.41. Found: Ca, 8.39; microbiological assay, 47.2% activity.

The time required for the above recrystallizations may be shortened considerably by operation at slightly elevated temperatures (30–40°). Cooling to 0° was found to inhibit the crystallization completely.

RESEARCH LABORATORIES, THE UPJOHN COMPANY
KALAMAZOO, MICHIGAN
RECEIVED[13] MAY 9, 1946

(8) Melting points on calcium pantothenate depend somewhat upon the rate of heating. Those reported in this paper were taken on finely powdered samples in Pyrex capillary tubes with the bath temperature increased at about 2° per minute.

(9) Strong, Feeney and Earle, *Ind. Eng. Chem., Anal. Ed.*, **13**, 566 (1941).

(10) Obtained from the Electro Metallurgical Company, 30 E. 42nd St., New York, N. Y.

(11) Ford, THIS JOURNAL, **67**, 876 (1945).

(12) Pure racemic pantolactone melts at 90–91°. See Ford, THIS JOURNAL, **66**, 20 (1944).

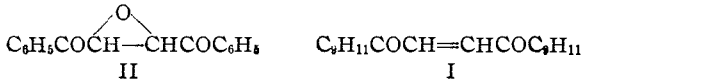
(13) Original manuscript received May 24, 1945.

Coupling of Aryl Methyl Ketones by the Action of Sodium Hypohalite Solutions

BY REYNOLD C. FUSON AND ROBERT JOHNSON

When it was discovered that the diiodo derivatives of highly hindered aryl methyl ketones could be made by treating the ketones with limited amounts of sodium hypoiodite[1] an attempt was made to prepare the corresponding chloro iodo ketones by subjecting the monochloro ketones to the action of the hypoiodite. When the reaction was tried with α-chloroacetomesitylene, however, it was found to take a different course. Treatment with sodium hypochlorite or hypobromite converted the ketone to a halogen-free compound which proved to be the coupling product, *sym*-dimesitoylethylene (I). Both this compound and the ethane made from it by reduction had properties which corresponded to those reported by Conant and Lutz.[2]

It was found that acetophenone could be coupled in a similar manner. The product in this case, however, was the oxide (II) of the expected olefin, *sym*-dibenzoylethylene. The oxide had been made earlier by Lutz and Wilder.[3] Its structure was confirmed by synthesis. It was made by the action of phenylglyoxal on phenacyl bromide.[4]



II I

Experimental

α-Chloroacetomesitylene and Sodium Hypolodite.—Twenty grams of iodine dissolved in aqueous potassium iodide solution was added slowly, with stirring, to a mixture of 5 g. of α-chloroacetomesitylene, 100 ml. of 10% sodium hydroxide solution, 150 ml. of water and 70 ml. of dioxane. The addition was complete in thirty minutes. The product obtained by ether extraction was recrystallized from methanol and then from ethanol. The product melted at 173–174.5° and was shown by the mixed melting point method to be identical with the *sym*-di-(2,4,6-trimethylbenzoyl)-ethylene previously prepared by Conant and Lutz.[2] By use of the method of these authors the ethylene was reduced to the ethane melting at 136–137.5°.

By using sodium hypochlorite and α-chloroacetomesitylene a similar result was obtained. The yield of the ethyl-

(1) Johnson and Fuson, THIS JOURNAL, **57**, 919 (1935).

(2) Conant and Lutz, *ibid.*, **45**, 1303 (1923).

(3) Lutz and Wilder, *ibid.*, **56**, 1987 (1934).

(4) Bodforss, *Ber.*, **51**, 192 (1918); Kleucker, *ibid.*, **55B**, 1634 (1922).