Phenyl-di-(p-N^4-acetylsulfanilamidophenyl)-arsenic.—To a solution of 3.36 g. (0.01 mole) of phenyl-di-(p-aminophenyl)-arsenic in 30 cc. of acetone was added 5.9 g. (0.025 mole) of p-acetaminobenzenesulfonyl chloride and 5 cc. of pyridine.[7] After standing for three hours the mixture was diluted with 500 cc. of water, and the oil which separated crystallized on standing. The crystals were washed successively with 5% sodium carbonate solution, 10% hydrochloric acid and water. Recrystallization from 30% ethanol gave 7 g. or a 96% yield of phenyl-di-(p-N^4-acetylsulfanilamidophenyl)-arsenic melting at 184°.

Anal. Calcd. for $C_{34}H_{31}O_6N_4S_2As$: N, 7.68. Found: N, 7.72.

Phenyl-di-(p-sulfanilamidophenyl)-arsenic.—The acetyl derivative was hydrolyzed by boiling 3.6 g. (0.005 mole) with 1 g. of sodium hydroxide in 15 cc. of water for one hour. The resulting 2.7 g. (84%) of crude hydrolysis product was recrystallized from 95% ethanol; m. p. 198°.

Anal. Calcd. for $C_{30}H_{27}O_4N_4S_2As$: N, 8.68. Found: N, 8.80.

Reaction with Phenylphosphorus Dichloride.[8]—p-Aminophenyllithium, prepared from 0.198 mole of n-butyllithium and 11.35 g. (0.066 mole) of p-bromoaniline, was allowed to react with 6 g. (0.033 mole) of phenylphosphorus dichloride under conditions identical with those described for the corresponding arsenic compound. The phenyl-di-(p-aminophenyl)-phosphorus, which separated as an oil upon neutralization of the aqueous hydrochloric acid extract, was extracted with ether, the ether solution dried over sodium sulfate, and the amine hydrochloride precipitated with hydrogen chloride. Since the hydrochloride was extremely hygroscopic and difficult to handle as such, it was suspended in dilute ammonium hydroxide. The amine was again extracted with ether and the ether removed by distillation. Distillation of the amine at 2 mm. could not be accomplished without decomposition. The yield of amine was 6 g. or 93%, based on a 70% interconversion of p-bromoaniline.

Anal. Calcd. for $C_{18}H_{17}N_2P$: P, 10.9. Found: P, 11.2.

Phenyl-di-(p-N-acetylaminophenyl)-phosphorus.—The diacetyl derivative of phenyl-di-(p-aminophenyl)-phosphorus, prepared by a Schotten–Baumann reaction using acetic anhydride and sodium hydroxide, melted at 169° after recrystallization from 50% ethanol.

Anal. Calcd. for $C_{22}H_{21}O_2N_2P$: N, 7.6. Found: N, 7.42.

Phenyl-di-(p-N^4-acetylsulfanilamidophenyl)-phosphorus.—The disulfanilamido derivative, prepared in 94% yield by a procedure similar to that used for the synthesis of the analogous arsenic compound, melted at 186–187°, after recrystallization from 30% ethanol.

Anal. Calcd. for $C_{34}H_{31}O_6N_4S_2P$: P, 4.5. Found: P, 4.72.

Phenyl-di-(p-sulfanilamidophenyl)-phosphorus.—The diacetyl derivative was hydrolyzed by boiling 4 g. (0.0058 mole) with 1 g. of sodium hydroxide in 25 cc. of water. Neutralization of the alkaline solution gave 3 g. (86%) of the free amine. Recrystallization from 95% ethanol gave a product melting at 202–204°.

Anal. Calcd. for $C_{30}H_{27}O_4N_4S_2P$: N, 9.3. Found: N, 9.46.

It is of interest to note that a mixed melting point of the analogous arsenic and phosphorus compounds, melting at 198° and 202–204°, respectively, showed no depression.

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(7) Winterbottom, THIS JOURNAL, **62**, 160 (1940).

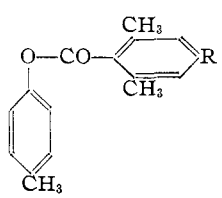
(8) The authors are grateful to Mr. G. E. Brown for the phenylphosphorus dichloride.

The Fries Rearrangement of Esters of Hindered Acids

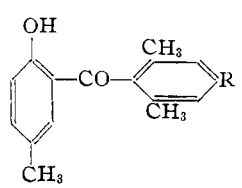
BY REYNOLD C. FUSON, S. L. SCOTT AND S. B. SPECK

The mechanism suggested by Skraup and Poller[1] for the Fries rearrangement of aryl esters involves preliminary fission to the corresponding phenol and acid chloride. If the cleavage involves preliminary addition to the carbonyl group, steric hindrance might be expected to suppress it.

To test this idea we have heated p-tolyl 2,6-xylate (I, R = H) and p-tolyl mesitoate (I, R = CH_3) with aluminum chloride. Rearrangement took place in each case; the methyl groups ortho to the ester group had no marked effect on the ease or extent of the reaction.



I



II

Experimental

p-Tolyl 2,6-Xylate.—To 3 g. of p-cresol was added 4.6 g. (0.025 mole) of 2,6-dimethylbenzoyl chloride. Hydrogen chloride was evolved and the reaction mixture became hot. It was shaken until the evolution of hydrogen chloride ceased, then poured into 50 cc. of a 10% sodium hydroxide solution. The upper layer was extracted with ether, and the ether solution was washed several times with water and dried over magnesium sulfate. The ester crystallized from methanol in long, white needles; yield 4.8 g.; m. p. 62.5–63°.

Anal.[2] Calcd. for $C_{16}H_{16}O_2$: C, 79.96; H, 6.72. Found: C, 80.06; H, 6.77.

p-Tolyl Mesitoate.—This ester was made by a procedure similar to the foregoing. After crystallization from alcohol, it melted at 73°; yield, 85% of the theoretical amount.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.27; H, 7.13. Found: C, 80.29; H, 7.10.

(1) Skraup and Poller, *Ber.*, **57**, 2033 (1924).

(2) Microanalyses by Mr. L. G. Fauble and Miss Mary S. Kreger.

2-(2,6-Xyloyl)-4-methylphenol (II, R = H).—The procedure followed for Fries rearrangement was that described for *o*- and *p*-propiophenol in "Organic Syntheses."[3] To a suspension of 7.3 g. (0.055 mole) of aluminum chloride in 75 cc. of carbon disulfide was added 4.4 g. (0.018 mole) of *p*-tolyl 2,6-dimethylbenzoate. The mixture was heated under reflux with stirring for two hours. Then the carbon disulfide was removed and the mixture was heated, with stirring, to 150° and kept at this temperature for one hour. When cooled to room temperature, the reaction mixture formed a hard cake. It was decomposed by heating with dilute hydrochloric acid on the steam-cone. The aqueous mixture was extracted with benzene, and the benzene layer was washed repeatedly with dilute sodium hydroxide solution and finally with water. The benzene solution was treated several times with norite, then evaporated to dryness. The light brown residue separated from methanol as slightly yellow crystals; yield 1 g.; m. p. 89.7–90.7° (cor.).

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.96; H, 6.72. Found: C, 79.90; H, 6.88.

The phenol was insoluble in aqueous sodium hydroxide; it reacted readily with bromine in carbon tetrachloride, with the evolution of hydrogen bromide.

2-Mesitoyl-4-methylphenol (II, R = CH_3).—A mixture of 12.7 g. (0.05 mole) of *p*-tolyl mesitoate and 15 g. (0.1 mole) of anhydrous aluminum chloride was heated for two hours at 150°. The mixture was decomposed with hydrochloric acid and the 2-mesitoyl-4-methylphenol purified by treatment with norite and recrystallization from aqueous alcohol; m. p. 86°; yield 8 g.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.29; H, 7.13. Found: C, 80.36; H, 7.15.

The phenol was slightly soluble in aqueous sodium hydroxide solution and gave a blue color with ferric chloride solution.

(3) "Organic Syntheses," Vol. XIII, John Wiley and Sons, Inc., New York, N. Y., 1933, p. 90.

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Crystalline Calcium Pantothenate

BY HAROLD LEVY, JOHN WEIJLARD AND ERIC T. STILLER

The calcium salts of (+)-, (−)- and *dl*-pantothenic acid have been described in a recent paper from this Laboratory,[1] as microcrystalline, hygroscopic powders which were readily soluble in water and the lower alcohols. The macrocrystalline sodium[2] and other salts[3–5] have been described.

The present paper describes the method of obtaining the macrocrystalline calcium salts, which are non-hygroscopic and much less soluble in water and the lower alcohols.

(1) Stiller, Harris, Finkelstein, Keresztesy and Folkers, THIS JOURNAL, **62**, 1785 (1940).

(2) Gätzi-Fichter, Reich and Reichstein, *Helv. Chim. Acta*, **24**, 185 (1941).

(3) Kuhn and Weiland, *Ber.*, **73**, 971 (1940); **73**, 1134 (1940).

(4) Grüssner, Gätzi-Fichter and Reichstein, *Helv. Chim. Acta*, **23**, 1276 (1940).

(5) Stiller and Wiley, THIS JOURNAL, **63**, 1237 (1941).

Calcium (+)-Pantothenate

Crystallization from Methanol.—Microcrystalline calcium (+)-pantothenate was dissolved in 10 volumes of 99.5% methanol and allowed to stand for several days at room temperature with frequent stirring. Fine needles were gradually deposited and finally a mass of matted fine needles was obtained. The product was filtered, washed with methanol and dried at 80° *in vacuo*. The solvent of crystallization was readily removed at that temperature: $[\alpha]^{24}D$ +28.2° (*C*, 1% in H_2O); biological potency 108%; m. p. 195–196°. The crystalline salt was recrystallized twice from methanol and showed no change in physical properties.

Anal. Calcd. for $Ca(C_9H_{16}O_5N)_2$: C, 45.35; H, 6.77. Found: C, 45.21; H, 6.69.

Crystallization from Ethanol.—The salt was crystallized from absolute ethanol as above and dried at 100° *in vacuo;* m. p. 195–196°; $[\alpha]^{25}D$ +25.8 (*C*, 1% H_2O).

Anal. Calcd. for $Ca(C_9H_{16}O_5N)_2$: C, 45.35; H, 6.77. Found: C, 45.40; H, 6.70.

Crystallization from Isopropanol.—The salt crystallized well in clusters of fine needles, which contained ½ molecule of isopropanol of crystallization. This alcohol of crystallization could not be removed by drying at 80° (1 mm.); m. p. 200–201°; $[\alpha]^{25}D$ +25.5° (*C*, 0.4% in H_2O).

Anal. Calcd. for $Ca(C_9H_{16}O_5N)_2 \cdot 0.5C_3H_8O$: C, 46.23; H, 7.16; N, 5.53. Found: C, 46.04; H, 7.18; N, 5.57.

When this material was recrystallized from methanol or ethanol it crystallized with isopropanol of crystallization which could not be removed by drying at 100° *in vacuo*. In order to obtain anhydrous calcium (+)-pantothenate from the isopropanol solvated salt, it was dissolved in water and concentrated to a sirup. This treatment was repeated in order to remove all of the isopropanol. The residual water was removed by distillation with methanol and the residue was crystallized from methanol as above. The product was dried at 100° *in vacuo* and had m. p. 195–196°; $[\alpha]^{28.5}D$ +27.6° (*C*, 1% in H_2O); biological potency 106%.

Anal. Calcd. for $Ca(C_9H_{16}O_5N)_2$: C, 45.35; H, 6.77. Found: C, 45.48; H, 6.89.

Recrystallization of the Anhydrous Crystalline Salt.—Because of its slight solubility in alcohols, the crystalline salt was first dissolved in water and concentrated to a sirup *in vacuo*. The sirup was then dissolved in methanol and evaporated to dryness in order to remove the water; the methanol treatment was repeated. The residue was dissolved in 10 parts of methanol and allowed to crystallize as above; $[\alpha]^{23.5}D$ +27.7° (*C*, 1% in H_2O). For analysis and assay the sample was dried *in vacuo* at 100°. It showed a biological potency of 110% and m. p. 195–196°.

Anal. Calcd. for $Ca(C_9H_{16}O_5N)_2$: C, 45.35; H, 6.77. Found: C, 45.25; H, 6.75.

Calcium (−)-Pantothenate

One-half gram of the microcrystalline calcium (−)-pantothenate was moistened with 0.2 cc. of water,