

The affinity which holds the pyridine in the cobaltous compounds is practically constant over the temperature range 20 to 80°. In the cupric compounds it decreases at the higher temperatures, while in the nickelous and zinc compounds it decreases at the lower temperatures.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

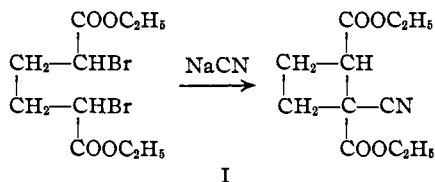
RING CLOSURES IN THE CYCLOBUTANE SERIES. II. CYCLIZATION OF α, α' -DIBROMO-ADIPIC ESTERS

BY REYNOLD C. FUSON, OSCAR R. KREIMEIER AND GILBERT L. NIMMO

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A new method of effecting the closure of the cyclobutane ring has been reported by Fuson and Kao,¹ who obtained diethyl 1-cyanocyclobutane-1,2-dicarboxylate (I) from diethyl α, α' -dibromo-adipate by treatment with sodium cyanide in absolute alcohol.



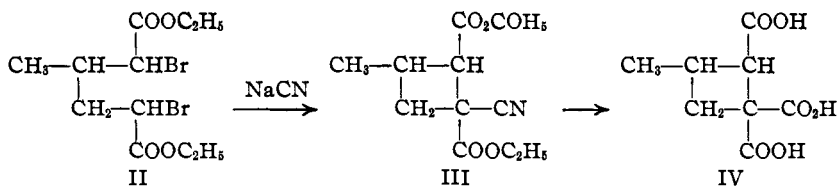
The method has now been tried with other esters of α, α' -dibromo-adipic acid and of β -methyl- α, α' -dibromo-adipic acid. The present article is a report of these experiments.

Since the weight of substituents is known to influence the ease of ring closure, attempts have been made to extend the closure method to α, α' -dibromo-adipic esters in which the alkyl groups were large. For this purpose diphenyl α, α' -dibromo-adipate and di- β -naphthyl α, α' -dibromo-adipate were prepared. The diphenyl ester was prepared from α, α' -dibromo-adipyl chloride by treatment with sodium phenoxide. A somewhat better yield was obtained by heating the acid chloride with phenol. The dinaphthyl ester was prepared by heating α, α' -dibromo-adipyl chloride with β -naphthol.

As was to be expected, these esters could not be studied in ethyl alcohol solutions because of rapid ester interchange. Attempts to replace the absolute alcohol by acetone, ethers, acetonitrile and other solvents led to negative results. Attempts to use other metal cyanides in these solvents were likewise fruitless.

The influence of substituents in the adipic acid chain was then examined. Diethyl α, α' -dibromo- β -methyl adipate (II) was heated for twenty-four hours with powdered sodium cyanide in absolute alcohol.

¹ Fuson and Kao, THIS JOURNAL, 51, 1536 (1929).



The expected cyano ester (III) was obtained in a yield of 62% of the theoretical. The yield is not quite as high as those obtained with diethyl α, α' -dibromo-adipate (70 to 80%). The position of the cyano group in III has not been determined. The compound is a colorless oil which does not decolorize bromine water or dilute alkaline permanganate solution.

Treatment with a solution of barium hydroxide converted the cyano ester into the methylcyclobutane tricarboxylic acid, IV, which was isolated in the form of the barium salt. Here, of course, the structure was indefinite with respect to one of the carboxyl groups.

Experimental Part

Diphenyl α, α' -Dibromo-adipate (from Phenol).—One hundred and forty-six g. (1 mole) of adipic acid was placed in a 1-liter flask equipped with a return condenser and 288 g. (2.4 moles) of thionyl chloride was poured in at once. The mixture was warmed gently (50 to 60°) on a water-bath until solution was complete and the evolution of hydrogen chloride had practically ceased. The excess thionyl chloride was then removed by distillation under diminished pressure. The crude adipyl chloride was brominated by adding 367.5 g. (2.3 moles) of dry bromine and 10 g. of phosphorus tribromide and heating at 50 to 60° for thirty-six to forty-eight hours under a strong light.

To the crude α, α' -dibromo-adipyl chloride was added 188 g. (2 moles) of phenol. The mixture was maintained at a temperature of 50 to 60° for twenty-four hours. To the reaction mixture was then added 500 cc. of benzene; the solution obtained by heating this mixture was cooled and the ester separated in crystalline form. Treatment with charcoal removed the dark color from the benzene solution and the ester was obtained after one additional recrystallization from benzene as colorless crystals melting at 146–148°. The yield was 83 g. or 18.4% of the theoretical.

Anal. Calcd. for $\text{C}_{13}\text{H}_{16}\text{O}_4\text{Br}_2$: Br, 35.1. Found: Br, 34.7.

Diphenyl α, α' -Dibromo-adipate (from Sodium Phenoxide).—The ester was made also by treating one mole of the crude α, α' -dibromo-adipyl chloride with 232 g. (2 moles) of sodium phenoxide. The chloride was placed in an ice-bath and the sodium phenoxide was added gradually in small portions. Small amounts of benzene (200 cc. in all) were added from time to time and the reactants were thoroughly mixed by shaking. The ester was removed by extracting the solid mass with 800 cc. of boiling benzene. By concentration of the benzene extracts, 31.5 g. of the ester was obtained in nearly pure form. This corresponds to a yield of 7% of the theoretical.

Di- β -naphthyl α, α' -Dibromo-adipate.—To the dibromo-adipyl chloride obtained from one-half mole of adipic acid was added in portions one mole of β -naphthol. The mixture was stirred vigorously during the addition and after being dissolved in 200 to 300 cc. of benzene was allowed to stand. The crude ester which separated after several hours was recrystallized from acetone. It melted at 165–166.8°. The yield was 28.5 g. or 10% of the theoretical.

Anal. Calcd. for $\text{C}_{26}\text{H}_{20}\text{O}_4\text{Br}_2$: Br, 28.7. Found: 28.4.

Diethyl 3-Methyl-1-(or 2)-cyano-1,2-cyclobutane Dicarboxylate.—Eight g. of powdered sodium cyanide was placed in a 200-cc. round-bottomed flask containing a solution of 20 g. of diethyl α, α' -dibromo- β -methyl adipate in 15 cc. of absolute alcohol. The mixture was heated under reflux on the steam-bath for twenty-four hours. It was then cooled and filtered by means of suction to remove solid inorganic substances (sodium bromide and excess sodium cyanide). The solid material was washed with ether and the washings were added to the filtrate, which after the removal of the ether and alcohol boiled at 140 to 143° at 3 mm. The yield of diethyl 3-methyl-1-(or 2)-cyano-1,2-cyclobutane dicarboxylate was 8 g. or 63% of the theoretical; d_4^{20} 1.08854; n_D^{21} 1.44735.

Anal. Calcd. for $C_{12}H_{17}O_4N$: C, 60.2; H, 7.2. Found: C, 59.7; H, 7.2.

Hydrolysis of the Cyano Ester.—The cyano ester was hydrolyzed by treatment with hot barium hydroxide (20%) according to the method of Perkin.² From 8 g. of the ester was obtained 8.5 g. of the barium salt of the tricarboxylic acid; this corresponds to a yield of 67% of the theoretical.

Anal. Calcd. for $C_{16}H_{14}O_{12}Ba_3$: Ba, 50.8. Found: Ba, 50.9.

Summary

Diethyl α, α' -dibromo- β -methyl adipate has been converted by treatment with sodium cyanide in absolute alcohol into diethyl 3-methyl-1-(or 2)-cyano-1,2-cyclobutane dicarboxylate. The latter has been hydrolyzed to the corresponding cyclobutanetricarboxylic acid, which has been isolated in the form of its neutral barium salt.

The diphenyl and di- β -naphthyl esters of α, α' -dibromo-adipic acid have been prepared. Attempts at ring closure were unsuccessful with these esters.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE OKLAHOMA AGRICULTURAL AND MECHANICAL COLLEGE]

THE SYNTHESIS OF SOME NEW COMPOUNDS RELATED TO APOCYNIN AND APOCYNOL¹

BY HENRY P. HOWELLS, B. H. LITTLE AND H. P. ANDERSEN

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The syntheses described herein were undertaken originally with the aim of securing intermediates for a study of the effect of length of side chain upon the physiological properties of certain unstudied phenolic bodies related to guaiacol. In choosing the method of preparation for such intermediates as the acyl substituted guaiacols, the findings of Finnemore² on methods of obtaining acetovanillone appeared to answer our immediate problem. His work³ suggested also new lines of thought that made the

² Perkin, *J. Chem. Soc.*, 65, 580 (1894).

¹ This communication is an abstract of portions of theses submitted by B. H. Little and H. P. Andersen in partial fulfillment of the requirements for the degree of Master of Science at the Oklahoma Agricultural and Mechanical College.

² Finnemore, *J. Chem. Soc.*, 93, 1520 (1908).

³ Finnemore² pointed out that apocynol or α -(4-hydroxy-3-methoxyphenyl)-methyl carbinol and its demethylated product possessed certain structural similarities to epinephrine, and stated that these products were still under investigation since the