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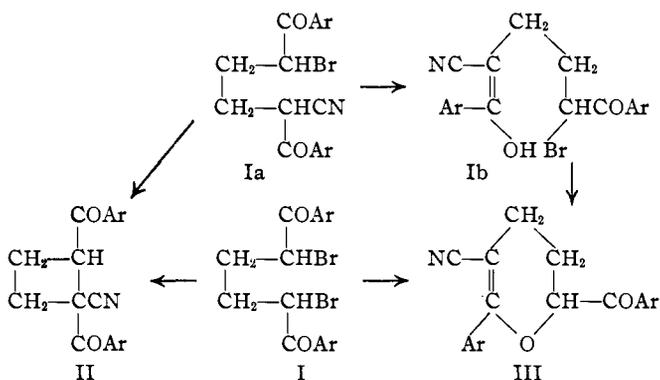
DIHYDRO-1,4-PYRANS. I. THE ACTION OF SODIUM CYANIDE ON 1,4-DIBROMO-1,4-DIAROYLBTANES

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RECEIVED AUGUST 6, 1931

PUBLISHED NOVEMBER 5, 1931

The method used in the preparation of cyclobutane derivatives by the treatment of α,α' -dibromoadipic esters with sodium cyanide¹ has been applied to 1,4-dibromo-1,4-diaroylbutanes. The reaction in these cases has been found to proceed in a manner entirely different from that which might have been expected by analogy with the cyclization of the dibromoadipic esters. When the dibromo ketones (I) are treated with sodium



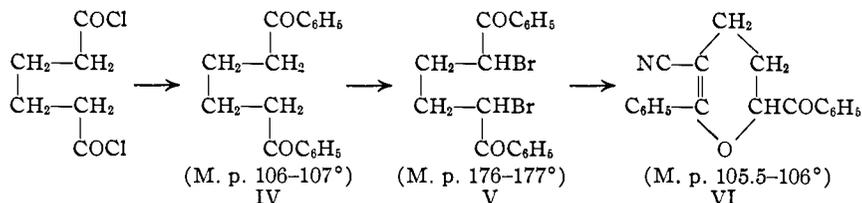
cyanide in absolute alcohol, the product is not the 1-cyano-1,2-diaroyl-cyclobutane derivative (II) but a new type of 1,4-pyran, 2-aryl-3-cyano-6-aryloyl-5,6-dihydro-1,4-pyran (III). 1,4-Dibromo-1,4-dibenzoylbutane (V), 1,4-dibromo-1,4-di-(*p*-toluyl)-butane (VIII) and 1,4-dibromo-1,4-dianisoylbutane (XI) have been prepared and each has been found to undergo ring closure when treated with sodium cyanide in absolute alcohol.² Although the three cases are closely related, the experimental results differed at many points; accordingly, the three series of reactions will be described separately.

1,4-Dibromo-1,4-dibenzoylbutane.—The method of Étaix³ was used for the preparation of 1,4-dibenzoylbutane (IV); by a somewhat revised procedure, yields of 70% were obtained. The diketone was brominated in carbon tetrachloride solution

¹ Fuson and Kao, *THIS JOURNAL*, **51**, 1536 (1929); Fuson, Kreimeier and Nimmo, *ibid.*, **52**, 4074 (1930).

² A mixture of equal amounts of absolute alcohol and ethyl acetate was found to give better results and was used in most of the later experiments.

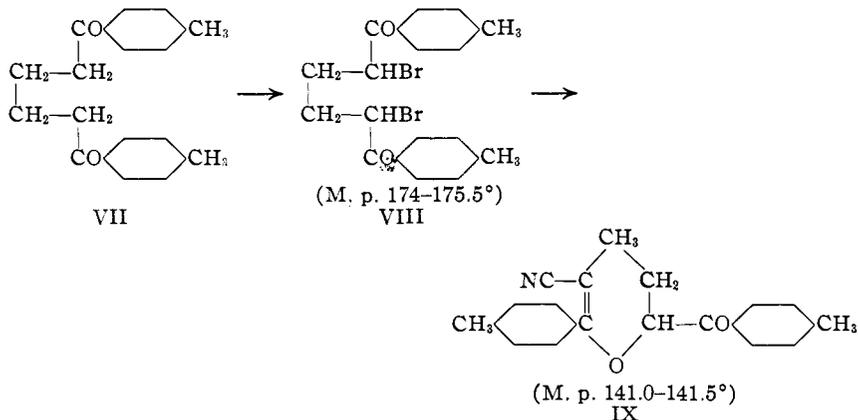
³ Étaix, *Ann. chim. phys.*, [7] **9**, 372 (1896).



and gave a product which after repeated recrystallization from ethyl acetate melted at 176-177,^o with decomposition.⁴ The behavior of the dibromide (V) at its melting point indicated that it was a pure compound. No trace of the theoretically possible isomer could be obtained.

Treatment with sodium cyanide in a mixture of absolute alcohol and ethyl acetate converted the dibromide into a bromine-free, nitrogen-containing compound whose analysis corresponded to that calculated for 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran (VI). The correctness of this structure has been established by a degradation method, a report of which will appear in a subsequent paper. The yield was 50% of the theoretical.

1,4-Dibromo-1,4-di(*p*-toluyl)-butane.—1,4-Di(*p*-toluyl)-butane (VII) was prepared by the method of Borsche⁵ from toluene and adipyl chloride.



Bromination in carbon tetrachloride converted the diketone into a dibromide melting over a wide range. From the melting point it was assumed that the substance was a mixture of the two theoretically possible isomers. By a series of fractional recrystallizations one of the isomers melting at 174-174.5^o (VIII) was obtained.

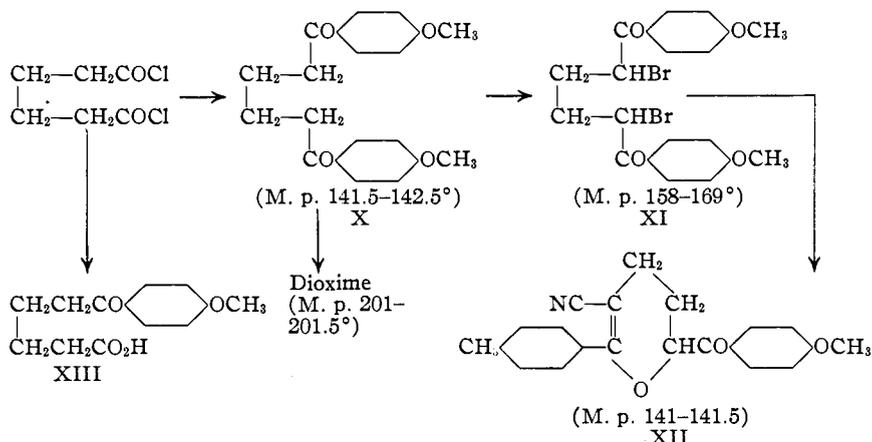
The pure dibromide (VIII) when treated with sodium cyanide in a mixture of absolute alcohol and ethyl acetate gave the expected 2-(*p*-

⁴ Conant and Lutz, [THIS JOURNAL, 49, 1090 (1927)] report a melting point of 171^o for this compound.

⁵ Borsche, *Ber.*, 52, 2080 (1919).

tolyl)-3-cyano-6-(*p*-toluyl)-5,6-dihydro-1,4-pyran (IX) in a 67% yield. It was found that the mixture of dibromides, used directly without any attempt at separation of a pure form, gave the same product in equally good yields.

1,4-Dibromo-1,4-dianisoylbutane.—1,4-Dianisoylbutane (X) was prepared from anisole and adipyl chloride by the method of Friedel and Crafts. Considerable amounts were obtained of a by-product, δ -anisoylvaleric acid (XIII). The diketone readily gave a dioxime.



When treated with two molecules of bromine in carbon tetrachloride, the diketone gave a substance melting over a wide range (158-169°), whose analysis corresponded to that of the expected dibromo compound (XI). It was assumed to be a mixture of the two possible isomers and, in view of the results with the corresponding di-*p*-toluyl compound, no attempt was made at a separation. Treatment with sodium cyanide in absolute alcohol and ethyl acetate gave the expected 2-anisyl-3-cyano-6-anisoyl-5,6-dihydro-1,4-pyran (XII) in yields of 70% of the theoretical.

Discussion

It is interesting to note the difference between the cyclization of the foregoing 1,4-dibromo ketones to dihydro-1,4-pyrans and the formation of cyclobutane derivatives from α,α' -dibromoadipic esters. The latter case corresponds to carbon alkylation and the former to oxygen alkylation. The first step in the reaction may be represented as the replacement of one bromine atom by a cyano group, yielding a compound of the type of Ia. By enolization of Ia compound Ib would result and the latter by loss of a molecule of hydrobromic acid would be transformed into the pyran (III). If the enol, Ib, underwent cyclization by means of carbon alkylation, the cyclobutane type of compound (II) would result. This type is that actually obtained in the case of the dibromoadipic esters. The alkylation

of phenols and enols frequently yields mixtures of the carbon and oxygen alkylation products. In the light of this fact, the production in this process of such diverse substances as cyclobutane derivatives and dihydro-1,4-pyrans from closely related compounds is easily understood.

Experimental Part

1,4-Dibenzoylbutane (IV).—Adipyl chloride was prepared by heating one mole of adipic acid with three moles of thionyl chloride at a temperature not above 60°. When the reaction was complete the excess thionyl chloride was distilled on the water pump. The crude adipyl chloride left as a residue was added in the course of an hour to a mixture of 300 g. of anhydrous aluminum chloride and 1500 cc. of anhydrous benzene, the reaction mixture being cooled by an ice-water bath. The yield of crude 1,4-dibenzoylbutane was 75 to 80% of the theoretical. After one recrystallization from ethyl acetate the product melted at 104–107° and was used without further purification.

1,4-Dibromo-1,4-dibenzoylbutane (V).—Thirty grams of 1,4-dibenzoylbutane was dissolved in 300 cc. of hot carbon tetrachloride and to the solution 36 g. of bromine was added in the course of fifteen to twenty minutes through a capillary tube which extended beneath the surface of the liquid. The reaction mixture gave off hydrogen bromide rapidly and remained colorless until the last few drops of bromine were added. The red solution began at once to deposit crystals. While the mixture was still hot the solvent, together with any bromine and hydrogen bromide, was evaporated under diminished pressure. The residue was washed with petroleum ether and recrystallized twice from ethyl benzoate. The crystals which separated melted at 176–177°, with decomposition. By allowing the mother liquor to stand, additional quantities of product were obtained. The total yield of fairly pure dibromide obtained in this way was 39 g. or 90% of the theoretical. Some tarry material was obtained but there was no indication of the presence of the theoretically possible isomer.

Anal. Calcd. for $C_{18}H_{16}O_2Br_2$: Br, 37.7. Found: Br, 37.8.

2-Phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran (VI).—Thirty grams of the dibromo diketone and 10 g. of powdered sodium cyanide were placed in a mixture of 500 cc. of absolute alcohol and 500 cc. of dry ethyl acetate and the mixture was refluxed for thirty hours. During the course of the reaction the mixture developed a wine-red color. The solvent was evaporated under diminished pressure and the residue was taken up in ethyl acetate. Upon addition of petroleum ether (40–60°) this solution deposited crystals which after recrystallization melted at 105.5–106° (corr.). The compound contained nitrogen but no halogen.

Anal. Calcd. for $C_{19}H_{15}O_2N$: C, 78.9; H, 5.2; N, 4.8. Found: C, 79.1; H, 5.4; N, 4.9.

The yield of cyano compound was 50% of the theoretical. The mother liquors contained a sticky viscous red liquid.

1,4-Di-(*p*-toluyl)-butane (VII).—The method of preparation used was that of Borsche⁵ modified in several particulars. Forty grams (0.27 mole) of adipic acid was heated with 78 g. (0.55 mole) of thionyl chloride on a water-bath for three hours at 50–60°. Excess thionyl chloride was removed by heating the solution under diminished pressure and the crude adipyl chloride so obtained was added gradually during the course of thirty minutes to a mixture of 100 g. of anhydrous aluminum chloride and 450 cc. of dry toluene. The reaction mixture was stirred continuously throughout the time of mixing and then for two hours longer, the temperature of the flask being maintained at 50–60°. The mixture was then treated with ice and concd. hydrochloric acid and the diketone was extracted with hot benzene. Four recrystallizations from ethyl acetate

gave a product melting at 144.5–145.0° (corr.). The yields in four runs varied from 25 to 57%.

1,4-Dibromo-1,4-di-(*p*-toluyl)-butane (VIII).—Twenty grams of 1,4-di-*p*-toluylbutane was dissolved in 550 g. of dry carbon tetrachloride by gentle heating. Twenty-four grams of dry bromine was run in slowly during the course of twenty minutes. The solution remained colorless until the end of the reaction. A little excess bromine failed to be decolorized. The crystals which separated when the solution was allowed to cool were filtered and washed with a little cold alcohol. A few additional grams of crude product was obtained by evaporating the mother liquor to dryness and washing the residue with cold alcohol. The total product after one recrystallization from carbon tetrachloride melted at 154–170° (with decomposition). The yield was 85%.

Anal. Calcd. for $C_{20}H_{20}O_2Br_2$: Br, 35.4. Found: Br, 35.6.

A large number of recrystallizations of the above product from ethyl acetate gave a compound melting at 174.0–174.5° (corr.) which was assumed to be one of the two expected isomeric dibromides.

Anal. Calcd. for $C_{20}H_{20}O_2Br_2$: Br, 35.4. Found: Br, 35.5.

2-(*p*-Tolyl)-3-cyano-6-(*p*-toluyl)-5,6-dihydro-1,4-pyran (IX).—Sixteen grams of the dibromide melting at 174.0–174.5° and 5 g. of powdered sodium cyanide were placed in a mixture of 250 cc. of dry ethyl acetate and 250 cc. of absolute alcohol. The mixture was heated under reflux for forty-four hours. During the course of the reaction the solution developed a light brown color. The solvent was evaporated under diminished pressure and the residue was extracted with 500 cc. of boiling ethyl acetate to remove the product. After filtration the hot extract was concentrated to a volume of 50 to 75 cc. and allowed to cool. The addition of low-boiling (40–60°) petroleum ether caused the cyano compound to separate. After four recrystallizations from ethyl acetate it melted at 141.0–141.5° (corr.). The yield was 7.5 g. or 67% of the theoretical.

Anal. Calcd. for $C_{21}H_{19}O_2N$: C, 79.5; H, 6.0. Found: C, 79.4; H, 6.0.

The same procedure was carried out starting with the mixed dibromides and in this case also the yield was 67% of the theoretical.

1,4-Dianisoylbutane (X).—A mole of crude adipyl chloride prepared as indicated above was added over a period of thirty minutes to a mixture of 300 g. of anhydrous aluminum chloride, 220 g. of anisole and 670 cc. of dry carbon disulfide. The temperature of the reaction mixture was not allowed to rise above 60° during the addition of the chloride and was maintained at about this temperature for two hours afterward. During this entire time the mixture was mechanically stirred.

The dark colored reaction mixture was then poured slowly and with constant stirring into a mixture of 1000 g. of cracked ice and 250 cc. of concd. hydrochloric acid. The crude dianisoylbutane separated in lumps which were removed by a suction filtration. The yield of crude product varied in three runs from 46 to 53% of the theoretical. The melting point after four recrystallizations from ethyl acetate was 141.5–142.5° (corr.).

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.6; H, 6.8. Found: C, 73.4; H, 6.8.

Dioxime.—The dioxime was recrystallized from ethyl acetate and melted at 201–201.5° (corr.).

Anal. Calcd. for $C_{20}H_{24}O_4N_2$: C, 67.4; H, 6.7. Found: C, 67.1; H, 6.8.

δ -Anisoylvaleric Acid (XIII).—This acid was obtained by treating the filtrate from the preceding preparation with a solution of sodium carbonate. The carbonate solution after filtration was acidified to precipitate the δ -anisoylvaleric acid. The compound after recrystallization from ethyl acetate melted at 126° (corr.). The yield from several preparations varied from 12 to 16% of the theoretical.

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.1; H, 6.8. Found: C, 65.8; H, 6.8. *Neutral equivalent.* Calcd.: 236. Found: 239.

1,4-Dibromo-1,4-dianisoylbutane (XI).—The bromination was carried out in hot carbon tetrachloride solution in the manner previously described for the dibenzoyl compound. The dibromide after one recrystallization from carbon tetrachloride melted at 158–169°, with decomposition. The yields from three runs varied from 67 to 90% of the theoretical. No attempt was made to separate the meso and racemic isomers.

Anal. Calcd. for $C_{20}H_{20}O_4Br_2$: Br, 33.0. Found: Br, 33.2.

2-Anisyl-3-cyano-6-anisoyl-5,6-dihydro-1,4-pyran (XII).—Sixteen grams of 1,4-dibromo-1,4-dianisoylbutane was treated with sodium cyanide in the manner outlined for the dibenzoyl compound. The product after four recrystallizations from ethyl acetate melted at 141–141.5° (corr.). The yields from two runs were 67 and 73% of the theoretical.

Anal. Calcd. for $C_{21}H_{19}O_4N$: C, 72.2; H, 5.5. Found: C, 72.1; H, 5.5.

Summary

2-Phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran, 2-(*p*-tolyl)-3-cyano-6-(*p*-toluy)-5,6-dihydro-1,4-pyran and 2-anisyl-3-cyano-6-anisoyl-5,6-dihydro-1,4-pyran have been prepared from 1,4-dibromo-1,4-dibenzoylbutane, 1,4-dibromo-1,4-di-(*p*-toluy)-butane and 1,4-dibromo-1,4-dianisoylbutane, respectively. The closure of the ring was effected in each case by heating the dibromo compound for twenty-four to forty-eight hours with powdered sodium cyanide in a mixture of absolute alcohol and ethyl acetate. The yields varied from 50 to 73% of the theoretical.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

5-BROMOFURYLACETYLENE

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RECEIVED AUGUST 10, 1931

PUBLISHED NOVEMBER 5, 1931

Introduction

Furylacetylenes are rare and uncommonly difficult of preparation. The parent type, furylacetylene, was prepared by Moureu, Dufraisse and Johnson¹ after a long and difficult study by the action of alcoholic potassium hydroxide on furylbromoethylene. Their success was due in part to the use of the anti-oxidants or stabilizers elaborated by Moureu and co-workers in connection with polymerization studies on the related styrenes and other compounds. Long before those studies, Gibson and Kahnweiler² used the same reaction for the preparation of bromofurylacetylene, which they never succeeded in isolating in a pure condition.

Incidental to our studies on furan compounds, a need arose for 5-bromo-

¹ Moureu, Dufraisse and Johnson, *Ann. chim.*, **7**, 1, 14 (1927).

² Gibson and Kahnweiler, *Am. Chem. J.*, **12**, 314 (1890).