and refluxed for 8 hr. and then allowed to stand overnight. It was decomposed by the dropwise addition of 30 ml. of ethyl acetate followed by 300 ml. of 20% sodium potassium tartrate solution. The ether layer was separated from the aqueous layer, which was extracted twice with ether. The combined oil and ether extracts were washed with water, dried and evaporated. The residue was distilled at 95–96 (0.1 mm.) to give 12.5 g. (70%) of a colorless oil, n_D^{30} 1.5430.

Anal. Calcd. for $C_{10}H_{13}NO_2$: N, 7.82. Found: N, 7.84.

The *hydrochloride* salt was recrystallized from absolute ethanol to give a colorless material, m.p. 205–207°.

Anal. Calcd. for $C_{16}H_{14}O_2NCl$: N, 6.49. Found: N, 6.49.

Addition of ether to the above ethanol filtrate caused an isomer of the hydrochloride salt to separate, which after recrystallization from absolute ethanol and ether, melted at 178–180°.

Anal. Calcd. for $C_{10}H_{14}O_2N$: N, 6.49. Found: N, 6.49.

(*b*) *By the reaction of chloride* VI *with ammonia.* According to the procedure of Martini-Betolo, Landi-Victory and Bovet[6] heating 2-chloromethyl-3-methyl-1,4-benzodioxan with 12% ethanolic ammonia at 120° for 12 hr., provided an oily product, b.p. 95–97° (0.1 mm.), n_D^{30} 1.5435, in 21% yield.

Anal. Calcd. for $C_{10}H_{13}O_2N$: N, 7.82. Found. N, 7.76.

2-Aminomethyl-1,4-benzodioxan (Xb). This compound was obtained by lithium aluminum hydride reduction of 1,4-benzodioxan-2-carboxamide (IXb) in a similar manner as that of VIII. Starting with 24 g. of amide, 19 g. (82%) of pure product was provided as a colorless liquid, b.p. 82–83° (0.75 mm.), n_D^{25} 1.5554. The reported[6] b.p. 127–137° (4 mm.) but no per cent of yield mentioned.

Anal. Calcd. for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.18; H, 6.96; N, 8.35.

N-Isopropyl-(3-methyl-1,4-benzodioxan-2-ylmethylamino)-acetamide (IVc). To 9 g. of 2-aminomethyl-3-methyl-1,4-benzodioxan in 200 ml. of toluene was added dropwise 3.4 g. of *N*-isopropylchloroacetamide with stirring and refluxing for a period of 22 hr. The colorless salt which separated was filtered and washed with a little toluene. The toluene solution was evaporated under reduced pressure and the residue was distilled at 175–180°/0.03 mm. to give 4.1 g. (65%) of a thick lemon colored oil.

Anal. Calcd. for $C_{18}H_{22}O_3N$: N, 10.06. Found: N, 9.83.

PHILADELPHIA 44, PA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NORTH CAROLINA COLLEGE AT DURHAM AND THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

The Acyloin Condensation. I. The Syntheses of 1,6-Diphenylhexanedione-3,4 and 2-Carbethoxy-3,4-diphenylcyclopentanone[1]

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The acyloin condensation with ethyl β-phenylpropionate in toluene and xylene under the atmosphere and under nitrogen gave 1,6-diphenylhexanedione-3,4 (hydrocinnamil) (I) in 61% yield; no acyloin could be isolated. The structure was demonstrated by its quinoxaline, dioxime, diphenylhydrazone, and dihydro derivatives and its infrared spectrum. Ethyl *p*-nitrocinnamate under similar conditions was recovered unchanged. Ethyl cinnamate in ether gave a 10% yield of 2-carbethoxy-3,4-diphenylcyclopentanone (III) accompanied by a large amount of high boiling substance. The proof of structure of this product was demonstrated by its 3,5-dinitrobenzoate, phenylhydrazones, and oxime derivatives and by its infrared spectrum. The product was degraded to the known *dl*-3,4-diphenyladipic acid and a mixed melting point taken with a prepared sample. The chromophore of this compound and its derivatives gave very characteristic absorption bands in the carbonyl region.

The acyloin condensation has been carried out with a variety of esters but little has been reported on the acyloin condensation with esters of the type used in this work. The acyloin condensation with ethyl β-phenylpropionate was expected to give the corresponding acyloin, but the product obtained was a low melting yellow ketone. A considerable amount of sodium remained at the end of the reaction. The product was not further reduced when retreated with sodium under similar conditions. Bredereck and Theilig[4] reported that the acyloin condensation with ethyl β-phenylpropionate gave the corresponding acyloin. These workers, however, did not isolate an acyloin but assigned a structure on the basis that an imidazole was formed by treating the reaction mixture with formamide, since this was a general reaction for acyloins. The product obtained in this work, however, would not form an imidazole when treated with formamide according to the procedure of Bredereck and Theilig.[4] The acyloin condensation was carried out according to a procedure described by Snell and McElvain.[5] The condensation was run in toluene and xylene, under nitrogen and under the atmosphere; the same product was obtained under each condition. The pure product melted at 90–91°. The product gave no acetate or benzoate derivative, but readily gave dioxime, diphenylhydrazone, and quinoxaline derivatives. The product was reduced with sodium borohydride; a compound was ob-

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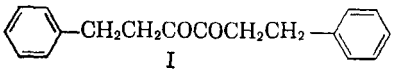
(4) H. Bredereck and G. Theilig, *Ber.*, 86, 88 (1953).

(5) J. M. Snell and S. M. McElvain, *Org. Syntheses*, Coll. Vol. II, 114 (1943).

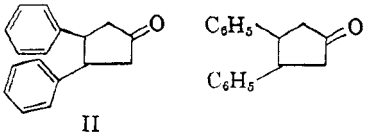
tained which melted at 133°. This corresponded with the m.p. of 1,6-diphenylhexanediol-3,4 of m.p. 132° reported in the literature.[6] The reduced product with acetic anhydride in pyridine gave a compound which melted at 68–70°. The literature reported a m.p. of 70° for the diacetate of 1,6-diphenylhexanediol-3,4.[6] The condensation product was recovered unchanged after refluxing with copper acetate, ammonium nitrate, and acetic acid. The infrared spectrum showed no hydroxyl absorption but absorbed strongly at 5.85 μ, characteristic of α-diketones. The analytical value for carbon was low for this product but the accuracy of the analytical values for carbon and hydrogen of its derivatives helps to make this value acceptable. These facts demonstrated that the acyloin condensation with ethyl-β-phenylpropionate gave 1,6-diphenylhexanedione-3,4. (I)



I

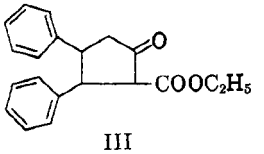
p-Nitroethyl cinnamate was treated with sodium in benzene, toluene, and xylene respectively. In each instance the starting material was recovered practically quantitatively unchanged.[7] No product could be isolated.

The acyloin condensation with ethyl cinnamate was expected to present trouble because of the many possible directions which the rate controlling step could take in the reaction. Bernhauer and Hoffman[8] carried out an acyloin condensation with ethyl cinnamate in xylene. These workers reported two ketones, both having the molecular formula $C_{16}H_{16}O$, melting at 108° and 166°, respectively. The problem of these two ketones was elucidated by Weidlich[9] who showed that they were the isomeric 3,4-diphenylcyclopentanones, and that the molecular formula was $C_{17}H_{16}O$, and the 166° isomer when pure melted at 177°. The acyloin condensation with ethyl cinnamate was run in xylene, toluene, benzene, and ether. With ether as a solvent, a waxy, colorless, crystalline product was finally crystallized from a large mass of high boiling substance. After obtaining seed crystals, consistent yields of 10% were obtained. The pure compound melted at 102–103°, and had an analysis corresponding to the molecular formula $C_{20}H_{20}O_3$. The molecular formula for the acyloin (cinnamoin) is $C_{18}H_{16}O_2$. The product would not form a quinoxaline and showed no hydroxyl absorption in the infrared. The infrared spectrum showed two very strong bands in the carbonyl region—a doublet at 5.7 μ and 5.8 μ. The product readily formed 3,5-dinitrobenzoate, phenylhydrazone, and oxime derivatives. The band at 5.7 μ suggested the presence of an ester. The product was treated very carefully with a 5% solution of alcoholic sodium hydroxide. An acid was obtained which melted at 186°. It had a neutral equivalent of 150.7. This corresponded to the neutral equivalent for 3,4-diphenyladipic acid,[10] which melts at 186°. A mixed m.p. of the acid from the hydrolysis of the condensation product with *dl*-3,4-diphenyladipic acid prepared by the procedure of Badger[10] showed no depression. The condensation product was refluxed in a 1:1 hydrochloric acid–alcohol solution. A ketone which melted at 177° was obtained. The same ketone was obtained when hydrobromic or hydriodic acid was used. This ketone absorbed very strongly in the infrared at 5.75 μ. This ketone and its oxime had an analysis corresponding to a compound of molecular formula $C_{17}H_{16}O$ and had the same properties as the *dl*-ketone of Weidlich.[9] (II)



II

The data presented demonstrate that the product isolated from the acyloin condensation with ethyl cinnamate is 2-carbethoxy-3,4-diphenylcyclopentanone (III).



III

The evidence in this work supports a mechanism for the formation of 2-carbethoxy-3,4-diphenylcyclopentanone (III) as proceeding through a bimolecular reduction followed by a Dieckmann cyclization. An identical mechanism for the synthesis of 3,4-diphenylcyclopentane has been suggested by Weidlich[9]; the isolation of 2-carbethoxy-3,4-diphenylcyclopentanone serves as confirmatory evidence for the correctness of Weidlich's mechanism.

Ultraviolet absorption spectra. The ultraviolet absorption spectra of (III), $\lambda_{max}^{C_2H_5OH}$ 330 (ϵ, 325), 315 (ϵ, 361), 283 (ϵ, 3312), 250 (ϵ, 18,139), 240-(ϵ, 21,358) mμ could be expected of such a complex molecule. These different maxima would be expected of a mixture of species which could arise from (III) in solution. Evidence for the possibility of these species in alcohol solution was shown by an immediate positive test with ferric chloride. The test is immediate although a deep color was slow in developing.

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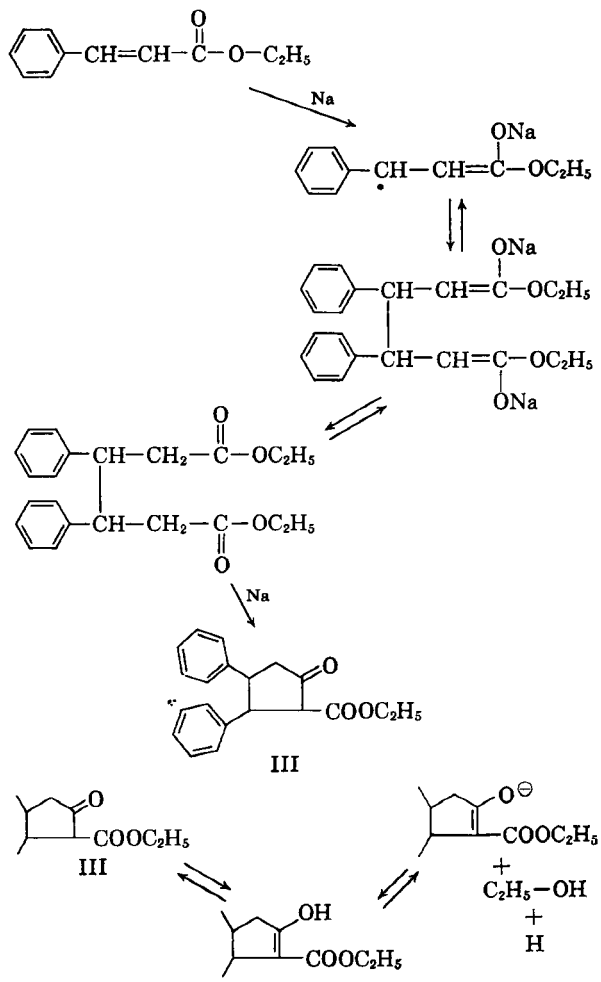

III

EXPERIMENTAL[11]

1,6-Diphenylhexanedione-3,4 (I). This compound was prepared by the acyloin condensation as described by Snell and McElvain.[5] A mixture of 18.4 g. (0.80 g.-atom) of powdered sodium in 1200 ml. of dry xylene protected from atmospheric moisture was heated in an oil bath at 110°. From a separatory funnel, 71.3 g. (0.40 mole) of ethyl β-phenylpropionate (ethyl hydrocinnamate) was added slowly with stirring over a period of 1.5 hr. at such a rate that gentle reflux was maintained. After the addition of the ester the reaction mixture was refluxed for 4 hr. longer. The mixture was cooled in an ice bath and 8.5 ml. of cold 37% sulfuric acid was cautiously added with stirring. Sodium sulfate precipitated and was separated by filtration. The water layer was removed from the xylene layer and the water layer extracted with 50 ml. of xylene and the extract added to the xylene layer. The xylene solution was washed with four successive 75-ml. portions of 20% sodium carbonate solution followed by washing with four 100-ml. portions of water and dried over anhydrous sodium sulfate. The xylene was removed under reduced pressure and the residue, a crude sirup, was distilled at 90–100° (50 mm.). The yellow product weighed 33 g., a 61% yield based on ethyl β-phenylpropionate. Purification from alcohol gave a m.p. of 90–91°. The same procedure under nitrogen gave the same product.

Anal. Calcd. for $C_{18}H_{18}O_2$ (266.32): C, 81.17; H, 6.81. Found: C, 80.14; H, 7.20.

(11) (a) All melting points were corrected; they were taken on a Fisher-Johns micro hot stage. (b) Analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Diphenylhydrazone of 1,6-diphenylhexanedione-3,4. To a flask there was added 1.08 g. (0.0075 mole) of phenylhydrazine hydrochloride, 0.58 g. (0.007 mole) of sodium acetate, 8 ml. of water, and 1 g. (0.004 mole) of I dissolved in 18 ml. of absolute alcohol. This was warmed and more alcohol added until the mixture was homogeneous. The solution was refluxed for 1 hr. on a water bath. The phenylhydrazine separated on cooling and was purified from 95% alcohol (m.p. 151–153°).

Anal. Calcd. for $C_{30}H_{30}N_4$ (446.57): C, 80.68; H, 6.77. Found: C, 80.85; H, 6.74.

Quinoxaline of 1,6-diphenylhexanedione-3,4. A mixture of 0.5 g. (0.002 mole) of (I) and 0.22 g. (0.002 mole) of *o*-phenylenediamine (sublimed) was heated on a water bath for 1 hr., cooled, and 5 ml. of methanol added. The pure product from methanol melted at 73–75°.

Anal. Calcd. for $C_{24}H_{22}N_2$ (338.44): C, 85.16; H, 6.56. Found: C, 84.99; H, 6.64.

Dioxime of 1,6-diphenylhexanedione-3,4. Five tenths gram (0.002 mole) of I, 0.28 g. (0.004 mole) of hydroxylamine hydrochloride, 1 ml. of pyridine, and 10 ml. of absolute alcohol were refluxed for 2 hr., cooled, diluted with 10 ml. of water, and cooled in a water bath. The pure product from alcohol melted at 218°.

Anal. Calcd. for $C_{18}H_{20}O_2N_2$ (296.36): C, 72.94; H, 6.80. Found: C, 73.22; H, 6.89.

Reduction of 1,6-diphenylhexanedione-3,4. (*1,6-diphenylhexanediol-3,4*). Two grams (0.0075 mole) of I, 10 ml. of 95% alcohol, and 3 g. (0.10 mole) of sodium borohydride were allowed to stand for 12 hr. with occasional shaking. Ten milliliters of water was added and this heated to boiling. To the cooled mixture 25 ml. of water was added. The aqueous layer was decanted and the product purified from diethyl ether (m.p. 133–134°, lit.[6] m.p. 132°).

Anal. Calcd. for $C_{18}H_{22}O_2$ (270.36): C, 79.88; H, 8.20. Found: C, 79.98; H, 8.39.

Diacetate of 1,6-diphenylhexanediol-3,4. In 3 ml. of pyridine, 27 g. (0.001 mole) of I, and 0.26 g. (0.0025 mole) of acetic anhydride were warmed slightly and allowed to remain for 14 hr. at room temperature. The solid which was separated from cold water was purified from 95% alcohol (m.p. 68–70°, lit.[6] m.p. 70°).

2-Carbethoxy-3,4-diphenylcyclopentanone (III). To 25.7 g. (1.12 g.-atoms) of sodium sand in 300 ml. of absolute ether protected by a calcium chloride tube there was added, with stirring, 100 g. (0.56 mole) of ethyl cinnamate over a period of 2 hr. The reaction was refluxed for 2 hr. longer, cooled, and 140 ml. of 35% sulfuric acid was cautiously added with stirring. The ether layer was separated from the aqueous layer and the aqueous layer extracted with four 100-ml. portions of ether. The combined ether layer and extracts were washed with four 50-ml. portions of 20% sodium carbonate followed by washing with 100 ml. of water and dried over anhydrous sodium sulfate. The ether was removed by evaporation until crystals appeared on the wall of the suction flask. The residue was allowed to remain in the deep freeze for several hours. The dried amorphous product weighed 19 g. (m.p. 96°). Recrystallization from 95% alcohol gave a pure product which melted at 102–103°.

Anal. Calcd. for $C_{20}H_{20}O_3$ (308.36): C, 77.89; H, 6.53. Found: C, 78.01, 78.05; H, 6.39, 6.44.

3,5-Dinitrobenzoate of III. 3,5-Dinitrobenzoyl chloride (0.29 g.), 0.132 g. of III, and 0.5 ml. of dry pyridine were heated on a steam bath for 45 min. Ten milliliters of 5% sodium bicarbonate solution was added and the mixture cooled in an ice bath. The product was washed well with water and purified from alcohol (m.p. 121–123°).

Anal. Calcd. for $C_{27}H_{22}N_2O_8$ (502.47): C, 64.45; H, 4.42. Found: C, 64.22; H, 4.51.

Phenylhydrazone of III. For 15 min., 0.132 g. of III, 0.5 ml. of phenylhydrazine, 5 drops of glacial acetic acid, and 5 ml. of water in 15 ml. of 95% alcohol were heated on a steam bath. The product was purified from 95% alcohol (m.p. 129–130°).

Anal. Calcd. for $C_{26}H_{26}N_2O_2$ (398.49): C, 78.36; H, 6.57. Found: C, 78.41; H, 6.50.

Oxime of III. Ten milliliters of 95% alcohol containing 0.246 g. of III, 0.167 g. of hydroxylamine hydrochloride, and 0.5 ml. of pyridine were heated to boiling. The solution was cooled, and the solid which separated was purified from 95% alcohol (m.p. 148–149°).

Anal. Calcd. for $C_{30}H_{21}O_3$ (323.38): C, 74.27; H, 6.55; N, 4.33. Found: C, 74.29; H, 6.40; N, 4.37.

Hydrolysis of III. (*dl-3,4-Diphenyladipic acid*). One gram of III in 10 ml. of 5% sodium hydroxide–ethanol solution was warmed on a steam bath for 1 hr. The solution was allowed to cool and was acidified with hydrochloric acid. Water was added to precipitate the product. The product was purified from 95% alcohol and water (m.p. 186°). A mixed melting point of this compound with known sample prepared by the procedures of Badger[10] showed no depression. Neut. equiv. Calcd. for $C_{18}H_{18}O_4$ (298.32): 149.16. Found: 150.7.

dl-3,4-Diphenylcyclopentanone (II). Five grams of III in 25 ml. of 20% hydrobromic acid and 20 ml. of 95% alcohol was refluxed for 1 hr. The hard lumpy substance was washed with water and purified from 95% alcohol, followed by recrystallization from ether. The colorless sawtooth-like crystals melted at 177°.

Anal. Calcd. for $C_{17}H_{16}O$ (236.30): C, 86.40; H, 6.80. Found: C, 86.69; H, 6.97.

Oxime of dl-3,4-diphenylcyclopentanone. One gram of II, 2 ml. of pyridine, 0.3 g. of hydroxylamine hydrochloride, and 20 ml. of 95% alcohol was refluxed for 2 hr. The solution was concentrated and the product purified from 95% alcohol (m.p. 117–118°).

Anal. Calcd. for $C_{17}H_{17}NO$ (251.32): C, 81.24; H, 6.81. Found: C, 81.38; H, 6.91.

Acknowledgments. The authors are greatly indebted to Dr. R. H. Eastman for his interest in this work and very helpful discussions. We also wish to thank Miss Brigitte Bach for the infrared and ultraviolet spectral measurements.

STANFORD, CALIF.

[CONTRIBUTION FROM THE DIAMOND ALKALI COMPANY RESEARCH DEPARTMENT]

Chlorinated Derivatives of Butadiene Sulfone and Diels-Alder Reactions of 3,4-Dichlorothiophene 1,1-Dioxide

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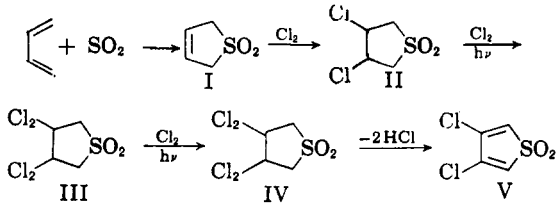
Received May 3, 1960

Chlorination of butadiene sulfone (I) has produced *cis*- and *trans*-3,4-dichlorotetrahydrothiophene 1,1-dioxide (*cis*-II and *trans*-II), 3,3,4-trichlorotetrahydrothiophene 1,1-dioxide (III), and 3,3,4,4-tetrachlorotetrahydrothiophene 1,1-dioxide (IV). Treating *cis*-II and *trans*-II with an equivalent of alkaline material yielded 3-chloro-2,3-dihydrothiophene 1,1-dioxide (VI); alkaline treatment of IV yielded 3,4-dichlorothiophene 1,1-dioxide (V) and 3,3,4-trichloro-2,3-dihydrothiophene 1,1-dioxide (VII). Diels-Alder reactions of 3,4-dichlorothiophene 1,1-dioxide (V) with butadiene, isoprene, and cyclopentadiene each produced two types of products wherein the diene-dienophile relationships were interchanged. Reactions of V with benzoquinone, bicycloheptadiene, two *N*-substituted maleimides, and with itself are also reported.

The investigation of the chemistry and biological activity of chlorinated derivatives of butadiene sulfone was undertaken because of the expected reactivity of such compounds with various substrates. This report concerns the intermediates involved in the preparation of 3,4-dichlorothiophene 1,1-dioxide (V) and Diels-Alder reactions of V. Reports on the biological activity of some of these materials[2,3] have been or will be published elsewhere.

The synthetic route to V is straightforward and is represented by the following series of reactions:



The chlorination of 2,5-dihydrothiophene 1,1-dioxide (I) under a variety of conditions[4–7] produced 3,4-dichlorotetrahydrothiophene 1,1-dioxide (II) as the main product.

Chlorination of I produced a mixture of the *cis* and *trans* isomers of II. Prochazka and Horak[7] reported a 75% yield of *trans*-II *via* chlorination in aqueous hydrochloric acid, but isolation of *cis*-II has not been reported. We have found chlorination conditions which favor formation of each isomer and have isolated both pure isomers. The *cis* isomer was the major product when the chlorination of I was conducted in an essentially nonpolar environment, whereas the *trans* isomer predominated when the chlorination was carried out under polar conditions. Thus, chlorinating a solution or suspension of I in anhydrous carbon tetrachloride using only gaseous chlorine produced the

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