6-positions, one bromine only enters the molecule. This bromine atom appears in the para position of the 2-phenyl group.

With 2,3-diphenylindenone, one or two bromine atoms can be introduced. The first one also enters the para position of the 2-phenyl group. The second takes the 6-position of the indene ring system.

Similarly, with 2,3,4,7-tetraphenylindenone, one bromine atom appears in the para position of the 2-phenyl group.

A mechanism has been proposed to account for these unexpected results.

2,3,5,6-Tetraphenylindenone, the first step in the degradation of the bimolecular product formed by the action of acidic dehydrating agents upon anhydracetonebenzil, has been synthesized.

ROCHESTER, NEW YORK RECEIVED DECEMBER 4, 1942

[CONTRIBUTION NO. 899 FROM THE KODAK RESEARCH LABORATORIES]

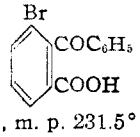
Indanone Ring Closure of Unsymmetrical β,β-Diarylpropionic Acids

BY C. F. H. ALLEN AND J. W. GATES, JR.

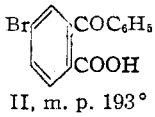
Thirty years ago it was shown[1] that in the Friedel–Crafts reaction, unsaturated acid chlorides gave a variety of products, among which were ketones in the indane series. Cyclic bromo ketones were also obtained with the dihalo acid chlorides. The evidence for the structure of the bromoindanones, so formed, was based upon the nature of the products secured by permanganate oxidation of one of them, but the position of the bromine atom in the oxidation product (a bromobenzoylbenzoic acid) was not determined except by inference from the nature of the starting material and supposed course of the reaction—assumptions that seemed valid and sufficient at that time.

Ten years later, others had occasion to utilize the reaction, but did not secure any of the indanones.[2]

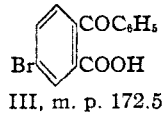
In a study of the behavior of the bromophthalic anhydrides and benzene in the presence of anhydrous aluminum chloride, Stephens[3] obtained three bromobenzoylbenzoic acids, I, II, III, and proved the structures of II and III. The structure assigned to I was in error, but this has been recently corrected.[3a]



I, m. p. 231.5°



II, m. p. 193°

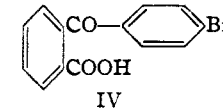


III, m. p. 172.5°

In speaking of the isomer III, Stephens says, "This substance is, no doubt, identical with the one described by Kohler, Heritage and Burnley (m. p. 174°). . . ."

Waldmann[4] obtained but one acid, m. p. 191°, by the same procedure used by Stephens, and by an independent method showed it had the structure II as assigned by Stephens. He assumed that Kohler's acid, m. p. 174°, was impure or had the structure III, and "corrected" the structure of the bromoindanone from which it had been made. The acid, m. p. 192°, has also been obtained as an oxidation product of a bromodiphenylindenone.[5]

The isomeric 4'-bromobenzoylbenzoic acid IV, apparently overlooked by the various authors, also has a melting point of 173°.[6]



IV

During an investigation of an apparently anomalous bromination in the polyphenylated indenone series,[7] several discrepancies between the properties of some of our products and those described in the literature were found. In order to clear up the uncertainty, it became necessary to try to repeat enough of the earlier work to secure specimens for comparison and for mixed melting point determinations.

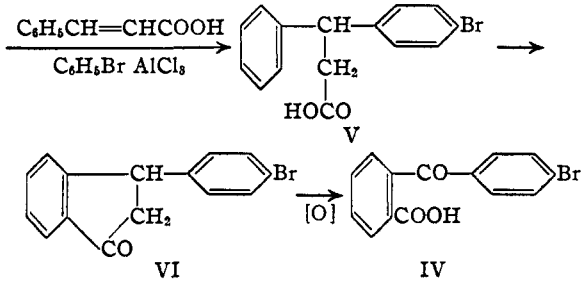
In agreement with McKenzie, but contrary to Kohler, we were unable to obtain the cyclic bromoindanone by the use of anhydrous aluminum chloride with the cinnamoyl chlorides and bromobenzene; in each instance a saturated propionic acid which could be converted to the desired indanone by formation of its acid chloride, followed

(1) Kohler, Heritage and Burnley, *Am. Chem. J.*, **44**, 60 (1910).
(2) McKenzie and Barrow, *J. Chem. Soc.*, **119**, 72 (1921).
(3) Stephens, THIS JOURNAL, **43**, 1050 (1921).
(3a) Huntress, Pfister and Pfister, *ibid.*, **64**, 2846 (1942).
(4) Waldmann and Mathiowetz, *J. prakt. Chem.*, **126**, 69 (1930).
(5) Koelsch, THIS JOURNAL, **58**, 1330 (1936).
(6) Ullmann and Sone, *Ann.*, **380**, 337 (1911).
(7) Allen and Gates, THIS JOURNAL, **65**, 419 (1943).

by ring closure, was found. This failure is attributed to the difference in the quality of the aluminum chloride, *i. e.*, small amounts of unsuspected impurities may alter the nature of a reaction. With the dibromocinnamoyl chloride, however, the indanones were obtained.

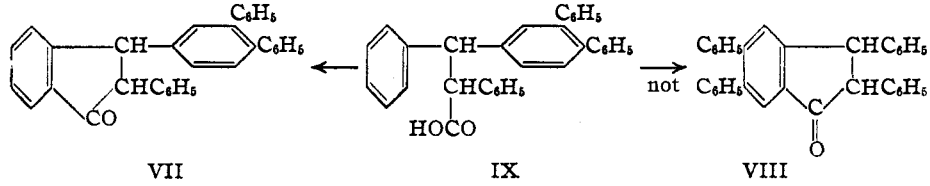
When cinnamic acid was treated with anhydrous aluminum chloride in bromobenzene, β-4′-bromophenyl-β-phenylpropionic acid V was formed. When this was cyclized, via its acid chloride, a bromophenylindanone resulted, having the melting point 60–61° as described by Kohler. Upon oxidation, it gave a bromobenzoylbenzoic acid, m. p. 173°, also in agreement with the same author. However, its crystal form was different from acid III, and a mixed melting point was depressed about 30°; clearly it is not the acid III. However, there was no depression when a mixed melting point was made with Ullmann's acid, IV, and the crystal form was the same. The two bromobenzoylbenzoic acids (Ullmann's and ours) are, thus, identical.

The bromophenylindanone (m. p. 60–61°), therefore, must have the structure VI, and not the one assigned by Kohler; this correction also applies to Waldmann's "correction."



Since it is formed stepwise by ring closure, it follows that cyclization must have taken place between the carboxyl group and the *unsubstituted* benzene ring.

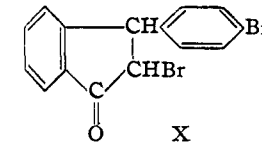
It had been previously concluded in these Laboratories that ring closure took place preferentially with the unsubstituted nucleus in the case of a derivative of *o*-terphenyl, as shown below



since an isomer VII of the known tetraphenylindanone VIII was obtained.

It has been known for some time that, in the presence of anhydrous aluminum chloride, benzene and its monohalogenated substitution products add reversibly to α,β-unsaturated acids, such as cinnamic acid,[8] and that the nature of the product can be controlled by a proper choice of solvent and temperature. The mechanism of Kohler's bromoindanone formation, then, must have been that shown above, rather than by an intramolecular ring closure of benzal-4-bromoacetophenone, as proposed at that time.

Confirmation as to the correctness of these conclusions was afforded by an examination of the dibromophenylindanone X, to which an incorrect structure had also been ascribed. On treatment with methylmagnesium iodide it gave the same 3-(4′-bromophenyl)-indanone VI, the Grignard reagent replacing the bromine in the *alpha* position by hydrogen in the known manner.[9] Therefore, structure X is the true one for the dibromoindanone. The mechanism is the same as for the previous example, with one additional step—the aluminum chloride first dehalogenates the dibromo acid to the α-bromo acid. It has been shown that the α-chloro acid cyclizes to the corresponding chloroindanone under the same conditions.[10]



Experimental

4′-Bromo-2-benzoylbenzoic,[6] 4-bromo-2-benzoylbenzoic[8] and 5-bromo-2-benzoylbenzoic[3] acids were prepared, according to the literature; the recorded melting points were obtained. β-4′-Bromophenyl-β-phenylpropionic acid was secured as follows: a mixture of 30 g. of cinnamic acid and 95 g. of bromobenzene was stirred at 20° during the addition of 55 g. of anhydrous aluminum chloride, and for four hours thereafter. On working up the solution the next day, the alkali-soluble portion was taken up in ether after acidification, and the mixture of acids left, on removal of the solvent, was esterified, using a methyl ester column. Upon fractionation at 2 mm., 10 g. of methyl cinnamate and 15 g. of methyl β-4′-phenyl-β-phenylpropionate, b. p. 170–174° (2 mm.) (220–225° (25 mm.)) were obtained.

(8) Fuson, Kozacik and Eaton, THIS JOURNAL, **55**, 3800 (1933).
(9) Kohler and Tishler, *ibid.*, **57**, 217 (1935).
(10) Auwers and Hügel, *J. prakt. Chem.*, **143**, 159 (1935).

Anal. Calcd. for $C_{16}H_{15}O_2Br$: Br, 25.1. Found: Br, 24.6.

The acid was then prepared by an alkaline hydrolysis of the ester, and crystallization from benzene–ligroin; m. p. 107–108°.

3-(4'-Bromophenyl)-indanone VI.—To a solution of 7.9 g. of the above acid in 50 cc. of carbon disulfide was carefully added 5.2 g. of phosphorus pentachloride, and, after warming, all the solvent was removed by reducing the pressure. The residual oily chloride was taken up in 100 cc. of carbon disulfide, and, at 10–15°, 6.7 g. of anhydrous aluminum chloride was added. After stirring the mixture at room temperature for three hours and appropriate manipulation, 5 g. of the indanone, m. p. 59–60°, was secured, recrystallizing from benzene–petroleum ether.

Oxidation.—To a boiling solution of 4 g. of the indanone in 30 cc. of acetic acid was added 4 g. of chromium trioxide; the 4'-bromo-2-benzoylbenzoic acid, m. p. 172–173°, was isolated in the usual way. A mixed melting point with an authentic sample[6] showed no depression.

2-Bromo-3-(4'-bromophenyl)-indanone X was secured in both stereoisomeric forms as described.[1] The reduction to VI was carried out by adding the substance to an ethereal methylmagnesium iodide solution, refluxing for two hours, and appropriate manipulation. The indanone VI was readily isolated. Since one of the stereoisomers can be converted into the other, this fixes the structure of both forms of the dibromoindanones.

Summary

When unsymmetrical β,β-diarylpropionic acids are cyclized to indanones, by the use of anhydrous aluminum chloride on their acid chlorides, ring closure takes place with the unsubstituted phenyl group.

Certain discrepancies in the literature have been cleared up, and corrected structures assigned to two bromoindanones.

ROCHESTER, NEW YORK RECEIVED DECEMBER 4, 1942

[CONTRIBUTION FROM THE LABORATORY OF PHYSICAL CHEMISTRY, UNIVERSITY OF WISCONSIN]

The Sedimentation and Diffusion Behavior of Certain Nucleic Acid Preparations[1]

BY HOWARD G. TENNENT AND CHARLES F. VILBRANDT

Introduction

Nucleic acids have a marked influence on biological processes because of their position in cell nuclei. As Hammarsten has pointed out, a large part of this influence is exerted through their physical properties. These have received much less attention than the organic chemistry of nucleic acids. Hammarsten[1a] measured the osmotic pressures, freezing points, viscosities, conductivities and Donnan equilibria of aqueous solutions of sodium thymonucleate, and considered the effect of added electrolytes on some of these properties. Later experiments showed that addition of large quantities of various salts caused a parallel decrease in the viscosity of sodium thymonucleate solutions and in the intensity of their streaming birefringence; this effect was reversible on removal of the salts.[2] The electrophoretic behavior of thymonucleic acid has been reported.[3] From diffusion measurements the following molecular weights have been calculated: 3000 for pancreas polynucleotide,[4] 37,000 for tobacco mosaic virus nucleic acid,[5] 17,000 for one preparation of yeast nucleic acid,[5] and 1300 for another.[4] The sedimentation behavior of sodium thymonucleate in the ultracentrifuge was found to depend upon the method by which the material was prepared.[6] Sodium thymonucleate has been shown to exist in solution as long thin rods of high molecular weight (200,000–500,000) by viscosity and streaming birefringence measurements[7] and by sedimentation and diffusion experiments.[8] Astbury and Bell[9] have made X-ray diffraction analyses of several nucleic acids.

In this report we present the results of sedimentation velocity, diffusion and partial specific volume measurements with solutions of sodium thymonucleate, thymonucleic acid, yeast nucleic acid, pancreas polynucleotide and barium thymate samples. From these data information as to their molecular sizes and shapes has been obtained.

(1) More complete details of this work are to be found in Theses of the authors submitted to the faculty of the University of Wisconsin in partial fulfillment of the requirements for the Ph.D. degree in June, 1942.

(1a) E. Hammarsten, *Biochem. Z.*, **124**, 353 (1924).

(2) J. P. Greenstein and W. V. Jenrette, *J. Nat. Cancer Inst.*, **1**, 77 (1940).

(3) E. Stenhagen and H. Teorell, *Trans. Faraday Soc.*, **35**, 743 (1939).

(4) K. Myrbach and E. Jorpes, *Z. physiol. Chem.*, **237**, 159 (1935).

(5) H. S. Loring, *J. Biol. Chem.*, **128**, lxi (1939).

(6) G. Schmidt, E. G. Pickels and P. A. Levene, *ibid.*, **127**, 251 (1939).

(7) R. Signer, T. Caspersson and E. Hammarsten, *Nature*, **141**, 122 (1938).

(8) K. O. Pedersen, in Svedberg and Pedersen, "The Ultracentrifuge," Oxford University Press, Oxford, 1940.

(9) W. T. Astbury and F. O. Bell, "Cold Spring Harbor Symposia on Quantitative Biology," Vol. VI, 109 (1938).