β-sitosteryl acetate, the fraction containing the soluble acetates was obtained by evaporation of the solvent on the steam-bath. The residue obtained was taken up in ethanol and hydrolyzed by the addition of alcoholic potassium hydroxide in the manner previously described. The solution obtained was worked up in the same manner as given for β-sitosterol. The product was dried and treated with sufficient 3,5-dinitrobenzoyl chloride in order to yield the corresponding esters. Triangular fractionation was again used in an attempt to isolate one of the three known "α-sitosterols," which according to Wallis and Fernholz[13] differ greatly in the solubilities of their 3,5-dinitrobenzoates. The most insoluble of the 3,5-dinitrobenzoates obtained had a m. p. of 222–223°; $[\alpha]^{28}\text{D}$ $-17.3°$ (23.6 mg., 2.1 ml. chloroform, $l = 1$ dm., $\alpha^{28}\text{D}$ $-0.195°$, *average* reading). The regenerated free sterol melted at 155–157°; $[\alpha]^{28}\text{D}$ $-55.8°$ (15.6 mg., 2.1 ml. chloroform, $l = 1$ dm., $\alpha^{25}\text{D}$ $-0.415°$, *average* reading). The acetate of the free sterol was prepared; m. p. 134–135°. The Liebermann-Burchard reaction was positive. Since all the derivatives of all the "α-sitosterols" have a positive value of relatively high magnitude for their optical rotations, the absence of any appreciable amounts of α-sitosterols is indicated, and the presence of an unknown sterol is indicated. A summary of the properties of this unknown sterol is also included in Table I.

5. **Irradiation of the Unsaponifiable Matter.**—A portion of the unsaponifiable matter was dissolved in ethyl ether and irradiated with ultraviolet light. Aliquots of this stock solution were taken for assay by the standard biological method. The results of the assay indicated an activity of 700 U. S. P. units per g. of crude unsaponifiable matter.[14]

Summary

1. The total unsaponifiable matter of the common bean, *Phaseolus vulgaris*, is about 5.9%, or about 0.15% of the air-dry bean.

2. About 60% of the unsaponifiable matter is represented by crude sterols.

3. Stigmasterol and β-sitosterol have been isolated and characterized, the former representing about 25%, and the latter about 6% of the crude sterols.

4. An unidentified sterol with a high negative optical rotation has been isolated.

5. Neither α-sitosterols nor γ-sitosterol, the apparent paraphytosterol of Likiernik, have been found, although the presence of small amounts of these sterols is not precluded.

6. The unsaponifiable matter of the common bean after irradiation has a Vitamin-D activity of 700 U. S. P. units per g.

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[13] Wallis and Fernholz, THIS JOURNAL, **58**, 2446 (1936).

[14] The authors wish to thank Dr. C. A. Hoppert, Professor of Biological Chemistry, for the Vitamin-D assay.

EAST LANSING, MICH. RECEIVED JANUARY 3, 1944

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE UNIVERSITY OF TEXAS AND SOUTHWESTERN LOUISIANA INSTITUTE]

Studies in the Biphenyl Series. IV. The Iodination of the Acetate, Benzoate and Benzenesulfonate of 4-Hydroxybiphenyl[1]

BY HAROLD R. SCHMIDT, CORA MAY SAVOY[2] AND JOHN LEO ABERNETHY

In connection with an investigation of the bactericidal activity of certain halo-4-hydroxybiphenyls, it was of interest to find a more convenient route to 4-hydroxy-4′-iodobiphenyl than had been used previously. Since it is known that chlorination[3,4,5] and bromination[6,7] of certain esters of 4-hydroxybiphenyl give rise to substitution in the 4′-position of the biphenyl nucleus, and subsequent hydrolysis gives the desired 4′-chloro and 4′-bromo compound, it seemed that iodination of these esters might give rise to the corresponding iodo compounds. Hence, 4-acetyloxybiphenyl, 4-benzoyloxybiphenyl and 4-benzenesulfonyloxybiphenyl were subjected to iodination.

Iodination of 4-acetyloxybiphenyl (I) with iodine in the presence of nitric acid gave rise to 4-acetyloxy-4′-iodobiphenyl (II) when either carbon tetrachloride or glacial acetic acid was used as the solvent. Hydrolysis of the ester gave rise to 4-hydroxy-4′-iodobiphenyl (III) which did not depress the melting point of the known compound prepared from benzidine (IV), by converting IV to 4-amino-4′-iodobiphenyl (V) and then to III, according to the method of van Alphen.[8] Furthermore, acetylation of III produced an ester which did not depress the melting point of the product of iodination of I. It was found that a better yield of the iodinated ester (II) was obtained if nitric acid was added immediately to the reaction mixture rather than dropwise over a period of several hours. The latter procedure gave rise to a considerable amount of nitrated product, along with the iodinated ester.

By means of a similar reaction, 4-benzoyloxybiphenyl (I) was converted to 4-benzoyloxy-4′-iodobiphenyl (II). Benzoylation of III gave rise to this same ester. Hydrolysis of II yielded III. Similarly, iodination of 4-benzenesulfonyloxybiphenyl (I) yielded 4-benzenesulfonyloxy-4′-iodobiphenyl (II), which was proved by benzenesulfonation of III. Hydrolysis of II yielded III.

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[1] A portion of this paper was abstracted from a thesis presented by Harold R. Schmidt to the Graduate Faculty of the University of Texas in partial fulfillment of the requirements for the degree of Master of Arts, August, 1943, and was presented before the Texas Academy of Science, November, 1943, in Austin, Texas.

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[3] Savoy and Abernethy, THIS JOURNAL, **64**, 2219 (1942).

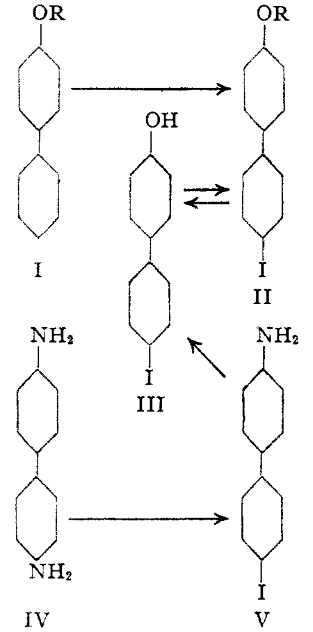
[4] Savoy and Abernethy, *ibid.*, **64**, 2719 (1942).

[5] Schmidt, Savoy and Abernethy, *ibid.*, **65**, 296 (1943).

[6] Hazlet, *ibid.*, **59**, 1087 (1937).

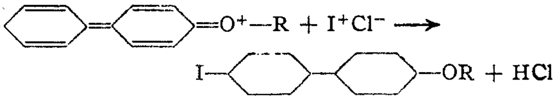
[7] Hazlet, Alliger and Tiede, *ibid.*, **61**, 1447 (1939).

[8] van Alphen, *Rec. trav. chim.*, **50**, 1111 (1931).



R = —$COCH_3$, —COC_6H_5 or —$SO_2C_6H_5$

Iodine monochloride has been found to be a suitable iodinating agent for many organic compounds which contain strong ortho-para directing substituents. Since iodine monochloride has a very high dipole moment, even in solvents of very low dielectric constant,[9] its ability to make an electrophilic attack on positions of relatively high electron density in aromatic compounds is readily explained. As there would be considerable resonance between the benzene rings of the biphenyl nucleus, particularly when the 4-position contains an acetyloxy, benzoyloxy or benzenesulfonyloxy substituent, and as the 3- and 5-positions are hindered by the ester linkages, it was anticipated that substitution by means of this incipiently ionized iodine monochloride would take place with relative ease. Such was found to be the case when either carbon tetrachloride or glacial acetic acid was used as the solvent.



R = —$COCH_3$, —COC_6H_5 or —$SO_2C_6H_5$.

Substituted esters identical with the ones prepared by iodination with iodine and nitric acid were formed.

Acknowledgment.—The authors are indebted to the Research Institute of the University of Texas for a grant which made this investigation possible.

Experimental

Iodination of 4-Acetyloxybiphenyl.—(a) A mixture of 10 g. of 4-acetyloxybiphenyl, prepared from 4-hydroxybiphenyl, 13.1 g. of iodine (10% excess), 100 ml. of carbon tetrachloride and 3 ml. of concentrated nitric acid was refluxed on a steam-bath for five hours and allowed to cool. The solvent was removed by distillation under reduced pressure, and the solid residue was crystallized from ethanol. After purification by recrystallization from ethanol, the pure 4-acetyloxy-4′-iodobiphenyl, which was obtained as lustrous white plates melting at 155° (cor.), weighed 6.1 g. (38.3% yield).

(b) Ten grams of 4-acetyloxybiphenyl and 13.1 g. of iodine were suspended in 100 ml. of glacial acetic acid, and a solution of 3 ml. of concd. nitric acid in 25 ml. of glacial acetic acid was added dropwise over a period of four hours. The mixture was refluxed during the addition of the nitric acid, and for one hour after. The product was cooled, poured into 800 ml. of ethanol, and recrystallized from ethanol. Pure 4-acetyloxy-4′-iodobiphenyl (2.2 g.) (13.8% yield) with m. p. 155° resulted. The rapid addition of nitric acid yielded a product of yellow needles (m. p. 201°) in greater quantity than the iodo compound. Nitration of 4-acetyloxybiphenyl in glacial acetic acid gave rise to the same yellow needles, m. p. 201°.

(c) Fifteen grams of 4-acetyloxybiphenyl was dissolved in 60 ml. of glacial acetic acid. To this solution 14.5 g. of iodine monochloride (Eastman Kodak Co. grade), dissolved in 20 ml. of glacial acetic acid, was added slowly over a period of one-half hour. The mixture was heated gently on a steam-bath during the addition. After all the iodine monochloride had been added the mixture was heated for three hours with constant stirring. Hydrogen chloride was liberated slowly.

At the end of the reaction period the mixture was cooled and poured into a large quantity of ice water. The oil which separated was dissolved in chloroform and the resultant solution was washed thoroughly with sodium bisulfite solution to remove the free iodine and then with water. After drying over anhydrous sodium sulfate, approximately one-third of the chloroform was removed under reduced pressure. Petroleum ether (b. p. 30–35°) was added to the remainder of the solution and 2.5 g. (10.5% yield) of pale yellow crystals separated. These were found to melt at 155–156° and proved to be 4-acetyloxy-4′-iodobiphenyl.

The remaining solution was concentrated further by the above procedure, yielding another precipitate. This solid was found to be soluble in ethanol which indicated that hydrolysis had taken place during the procedure. An attempt was made to benzoylate this solid. An oil formed which could not be solidified, which suggested that a mixture of several different substances was present. Further attempts to separate these products were unsuccessful.

Hydrolysis of 4-Acetyloxy-4′-iodobiphenyl.—Ten grams of 4-acetyloxy-4′-iodobiphenyl, prepared by the iodination of 4-acetyloxybiphenyl, was suspended in a solution of 50 ml. of water, 50 ml. of ethanol, and 10 g. of potassium hydroxide. The mixture was refluxed for one-half hour, cooled, and poured into 250 ml. of water. The solution was acidified, and the white precipitate which formed was filtered and washed with 2 liters of water. This product, obtained in quantitative yield (8.8 g.), melted at 202° (cor.) and did not depress the melting point of 4-hydroxy-4′-iodobiphenyl prepared from benzidine.

4-Hydroxy-4′-iodobiphenyl.—According to the method of van Alphen,[8] 25 g. of benzidine was tetrazotized, and the product obtained was allowed to stand with an additional 25 g. of benzidine at 15° for three days. The 4-amino-4′-biphenyldiazoic acid formed was treated with potassium iodide and subsequently diazotized and heated. The product was extracted from the reaction mixture with a dilute solution of sodium carbonate. Acidification of the solution yielded 3.5 g. (4.4% yield) of 4-hydroxy-4′-iodobiphenyl, which melted at 202° after crystallization from chloroform and petroleum ether (b. p. 35–55°).

Acetylation of 4-Hydroxy-4′-iodobiphenyl.—To a mixture of 2 g. of 4-hydroxy-4′-iodobiphenyl and 3 ml. of acetic anhydride, 5 drops of sirupy phosphoric acid was added. The mixture was refluxed for five minutes on a steam-bath. Water was added slowly to the hot solution until the excess acetic anhydride had decomposed. The

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(9) Fairbrother, *Trans. Faraday Soc.*, **33**, 1507 (1937).

warm solution was poured into ice water whereupon a precipitate separated. Filtration and recrystallization of the precipitate from ethanol yielded 1.8 g. (79% yield) of pure ester[8] melting at 155–156°. The melting point of a mixture of equal amounts of the above prepared ester and the product obtained on iodination of 4-acetyloxybiphenyl caused no depression.

Iodination of 4-Benzoyloxybiphenyl.—(a) A mixture of 10 g. of 4-benzoyloxybiphenyl, prepared from 4-hydroxybiphenyl, 10.1 g. of iodine (10% excess), 10 ml. of concentrated nitric acid, and 100 ml. of carbon tetrachloride was heated on a water-bath for eight hours. After the solvent was removed by distillation under reduced pressure, the solid residue was crystallized three times from glacial acetic acid. Pure 4-benzoyloxy-4′-iodobiphenyl (10.5 g.) (72% yield) was obtained as white plates which melted at 207° (cor.). When glacial acetic acid was used as the solvent for the iodination the yield was reduced to 45%.

(b) To a warm solution of 14.5 g. of 4-benzoyloxybiphenyl in 80 ml. of glacial acetic acid, 15 g. of iodine monochloride in 40 ml. glacial acetic acid was added in fifteen minutes. The mixture was placed on a steam-cone and heated to a temperature at which hydrogen chloride was liberated. Any iodine monochloride which vaporized was condensed in the lower part of the water-cooled condenser. The reaction was allowed to proceed for three hours, at the end of which time it was cooled and poured into ice water. A gummy mass separated. It was taken up in chloroform, washed with sodium bisulfite and water, and dried over anhydrous sodium sulfate.

When the solution was dry it was filtered and the chloroform removed by distillation under reduced pressure until a solid began to separate. The remaining portion was removed from the flask and white plates were caused to precipitate by the addition of petroleum ether. The solid was suspended and digested in hot ethanol. On filtration, 14.2 g. (67.2% yield) of solid was obtained. Recrystallization from acetic acid raised the melting point of 4-benzoyloxy-4′-iodobiphenyl to 207°.

Anal. Calcd. for $C_{19}H_{13}O_2I$: I, 31.75. Found: I, 31.30.

Hydrolysis of 4-Benzoyloxy-4′-iodobiphenyl.—4-Benzoyloxy-4′-iodobiphenyl (5 g.) was suspended in a solution containing 40 ml. of ethanol, 10 ml. of water and 5 g. of potassium hydroxide. The mixture was refluxed for eight hours, cooled, and diluted with an equal volume of water. After the ethanol had been removed by distillation, the solution was chilled and saturated with carbon dioxide. The white solid which separated was extracted with ether. The ether extract was dried with anhydrous sodium sulfate, and the solvent removed by distillation under reduced pressure. The solid residue was crystallized from a mixture of carbon tetrachloride and petroleum ether (b. p. 35–55°). This product, which weighed 2.9 g. (78% yield), melted at 202°. A mixture of the compound thus formed and 4-hydroxy-4′-iodobiphenyl prepared from benzidine melted at 202°.

The aqueous solution previously saturated with carbon dioxide was acidified and again extracted with ether. After the ether extract had been dried with anhydrous sodium sulfate, the ether was removed by distillation under reduced pressure. Upon recrystallization of the residue from water, 0.7 g. (44% yield) of benzoic acid, m. p. 121.5°, resulted.

Benzoylation of 4-Hydroxy-4′-iodobiphenyl.—A mixture of 1 g. of 4-hydroxy-4′-iodobiphenyl, 10 ml. of pyridine and 1 ml. of benzoyl chloride was refluxed for ten minutes. The solution was allowed to cool to room temperature and poured into 100 ml. of ice water. A precipitate separated which was filtered and digested with ethanol. The yield of 4-benzoyloxy-4′-iodobiphenyl was 1.1 g. (82% yield) and its melting point was 206–207°. A mixture of the product obtained by the action of iodine monochloride on 4-benzoyloxybiphenyl and the above ester did not cause a depression of the melting point.

Iodination of 4-Benzenesulfonyloxybiphenyl.—(a) A mixture of 10 g. of 4-benzenesulfonyloxybiphenyl and 8.9 g. (10% excess) of iodine was suspended in 100 ml. of carbon tetrachloride containing 10 ml. of conc. nitric acid. The suspension was heated on a water-bath for eight hours and allowed to cool. After the solvent had been removed by distillation under reduced pressure, the solid residue was crystallized three times from methanol. The 4-benzenesulfonyloxy-4′-iodobiphenyl, obtained as white needles which melted at 93.5° (cor.), weighed 8.5 g. (60% yield).

Iodination of 4-benzenesulfonyloxybiphenyl was carried out as described above, except that glacial acetic acid was used as the solvent. The same product, 4-benzenesulfonyloxy-4′-iodobiphenyl, resulted in a yield of 51%.

(b) 4-Benzenesulfonyloxybiphenyl (16.7 g.) was suspended in 50 ml. of glacial acetic acid and heated gently on a steam-bath, which caused the ester to dissolve. Fifteen grams of iodine monochloride, dissolved in 20 ml. of glacial acetic acid, was added slowly to the above solution. The reaction was allowed to run for three hours with constant heating and stirring. At the end of this time the solution was cooled and poured into ice water, whereupon a solid separated. The solid was taken up in chloroform after which the iodine was removed with sodium bisulfite solution. The chloroform solution was washed with water and distilled under reduced pressure until approximately one-third of the original volume remained. To this mixture petroleum ether was added causing a precipitate to separate. The solid was recrystallized three times from ethanol, and yielded 5.4 g. (23% yield) of pure 4-benzenesulfonyloxy-4′-iodobiphenyl. The melting point of the above white needle-like crystals was 92–93° (cor.).

Anal. Calcd. for $C_{18}H_{13}SO_3I$: I, 29.10. Found: I, 28.95.

Hydrolysis of 4-Benzenesulfonyloxy-4′-iodobiphenyl.—A suspension of 10 g. of 4-benzenesulfonyloxy-4′-iodobiphenyl in 160 ml. of ethanol, 40 ml. of water, and 10 g. of potassium hydroxide was refluxed for twelve hours, cooled, and diluted with an equal volume of water. The solution was acidified, and the white precipitate which separated was crystallized from a mixture of carbon tetrachloride and petroleum ether (b. p. 35–55°). Six and six-tenths grams of purified product (97% yield), melting point 202°, resulted. A mixture of this compound and 4-hydroxy-4′-iodobiphenyl prepared from benzidine melted at 202°.

Benzenesulfonation of 4-Hydroxy-4′-iodobiphenyl.—Two grams of 4-hydroxy-4′-iodobiphenyl was dissolved in 20 ml. of pyridine and cooled by means of an ice-bath. To this cooled solution, 3 ml. of benzenesulfonyl chloride was added. After the addition the mixture was heated gently on a hot-plate for fifteen minutes, cooled to room temperature and poured into 100 ml. of ice water. The precipitate which separated was filtered and recrystallized from ethanol. The pure product, melting at 93.5° (cor.), weighed 2.7 g. (93% yield). A mixture of the product obtained on iodination of 4-benzenesulfonyloxybiphenyl and the ester as prepared above caused no depression in the melting point.

Summary

Iodination of the acetate, benzoate and benzenesulfonate of 4-hydroxybiphenyl gave rise to substitution in the 4′-position. Both iodine monochloride and iodine and nitric acid were used as iodinating agents. Proof of the structure of these esters was afforded by hydrolysis to the known 4-hydroxy-4′-iodobiphenyl, prepared from benzidine. Furthermore, acetylation, benzoylation and benzenesulfonation of 4-hydroxy-4′-iodobiphenyl gave rise to these same esters.

The ease of iodination of these esters with iodine monochloride has been explained on the basis of

the high dipole moment of iodine monochloride and the resonance between the benzene rings of the biphenyls.

It would appear in each case that iodination with iodine and nitric acid in a carbon tetrachloride solution is the best procedure for iodination of the esters studied.

AUSTIN, TEXAS RECEIVED NOVEMBER 26, 1943

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY, BUREAU OF AGRICULTURAL AND INDUSTRIAL CHEMISTRY, AGRICULTURAL RESEARCH ADMINISTRATION, UNITED STATES DEPARTMENT OF AGRICULTURE]

Pyrolysis of Lactic Acid Derivatives. Production of Phenyl and *o*-Tolyl Acrylate*

BY E. M. FILACHIONE, J. H. LENGEL AND C. H. FISHER

In recent years considerable interest has been shown in the production of acrylic esters by the pyrolysis of esters of acetoxypropionic acid. These esters can be made from lactic acid by the reactions

$$CH_3CHOHCOOH + ROH \longrightarrow CH_3CHOHCOOR + H_2O$$

$$CH_3CHOHCOOR + (CH_3CO)_2O \longrightarrow CH_3CH(OCOCH_3)COOR$$

Methyl acetoxypropionate[1,2] has been pyrolyzed to give high yields of methyl acrylate. Satisfactory yields of acrylic esters have been obtained also by pyrolysis of the benzyl[1] and tetrahydrofurfuryl[3] esters of acetoxypropionic acid. Other esters of acetoxypropionic acid, including the ethyl,[1] butyl,[1] allyl,[4] and methallyl[4] esters, have been pyrolyzed, but the yields of the corresponding acrylic esters are low, since a predominant side reaction takes place, *i. e.*, the aliphatic alcohol radical is decomposed into the corresponding olefin. For example, ethylene, carbon monoxide, acetaldehyde and acetic acid are formed when ethyl acetoxypropionate is pyrolyzed. Because of this or other side reactions, the satisfactory preparation of acrylic esters by the pyrolytic method appears limited to acetoxypropionic esters that have relatively stable alkyl groups.

Recent work[5] has shown that α-acetoxyisobutyric esters can be converted by pyrolysis into methacrylic esters more readily than α-acetoxypropionic esters can be transformed into acrylic esters.

Phenol is thermally stable, and because of their structure phenyl and substituted phenyl esters of acetoxypropionic acid would be expected to be incapable of the side reaction that occurs with ethyl acetoxypropionate and related esters. Results given in the present paper demonstrate that this expectation was reasonable.

Phenyl and *o*-tolyl acetoxypropionates were prepared by the following series of reactions and also by the methods described in the experimental section: (1) Aqueous 80% lactic acid was acetylated with acetic acid, benzene being used as an entraining agent to remove the water of esterification continuously.[6] The yields of acetoxypropionic acid were as high as 77%. (2) Acetoxypropionic acid was converted by means of thionyl chloride into acetoxypropionyl chloride in 80 to 82% yields. (3) Acetoxypropionyl chloride was converted by treatment with phenol (or *o*-cresol) into phenyl (or *o*-tolyl) acetoxypropionate in yields of almost 90%. (4) Pyrolysis of phenyl acetoxypropionate (or the corresponding *o*-tolyl ester) produced the aryl acrylate (75 to 80% yields).

Phenyl α-acetoxypropionate was pyrolyzed at temperatures and contact times that ranged from 440 to 600° and from 0.77 to 20 seconds. A pressure of 18 to 19 mm. was used in one experiment, atmospheric pressure for the others (Table I). The yield of acetic acid was always higher than the yield of phenyl acrylate. Carbon monoxide and carbon dioxide were formed in some experiments in considerable amounts. Styrene, obtained in yields as high as 20%, presumably was formed prior to decomposition of phenyl acetoxypropionate into phenyl acrylate since it has been reported by Skraup and Nietzen[7] that phenyl acrylate yields phenol, acetylene, and carbon monoxide on pyrolysis.

o-Tolyl acetoxypropionate was pyrolyzed at temperatures ranging from 500 to 591° (Table II). *o*-Tolyl acrylate was obtained in yields as high as 75%; the yields of acetic acid were even higher. No real attempt was made to detect *o*-methylstyrene in the reaction products.

Possibly because of the presence of small amounts of phenol or some other inhibitor, the phenyl acrylate purified by distillation showed little tendency to polymerize. Samples of phenyl acrylate that had been washed with dilute sodium

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* Not copyrighted. This paper was presented before the Division of Industrial and Engineering Chemistry of the 106th meeting of The American Chemical Society at Pittsburgh, Pa., Sept., 1943.

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