[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA]

# The Oxidation of *N*-Alkyl-2,4-dinitroanilines with Chromic Acid[1a]

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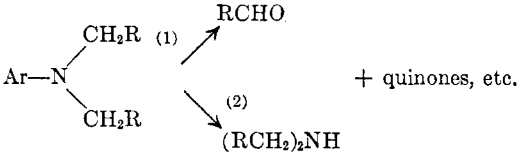
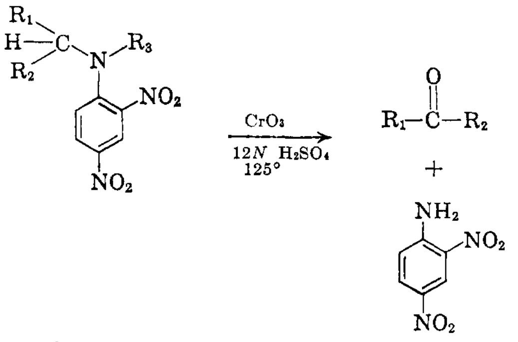
Several *N*-alkyl-2,4-dinitroanilines, which were obtained readily and in high yields by treatment of 2,4-dinitrochlorobenzene with the corresponding aliphatic amines, were oxidized with chromic acid in 12*N* sulfuric acid to the corresponding carbonyl compounds and 2,4-dinitroaniline in good to excellent yields. Treatment of 2,4-dinitroaniline with 12*N* sulfuric acid at 125° gave an almost quantitative yield of 2,4-dinitrophenol. Several unsuccessful attempts were made to isolate the chromic acid amide of *N-t*-butyl-2,4-dinitroaniline.

Neumann and Gould[2] have studied in some detail the oxidation of *N*-alkylarylamines with chromic acid. The majority of amines studied were oxidized to the carbonyl compound corresponding to the *N*-alkyl group (1) in yields up to 37%. Amines containing *para* substituents which tend to promote ring oxidation, *e.g.*, amino and hydroxyl, yielded aliphatic amines (2) with only traces of carbonyl compounds. Also formed were quinones, other oxidation products, and condensation products. Aliphatic amines were not oxidized under the conditions used to effect oxidation of the *N*-alkylarylamines.



The need for a convenient method of converting a primary or secondary aliphatic amine to the corresponding carbonyl compound[2,3] led us to examine the practicality of converting such an amine to a corresponding *N*-alkylaniline prior to oxidation with chromic acid. It was decided to prepare and oxidize the *N*-alkyl-2,4-dinitroaniline derivative since this derivative can be prepared readily and in good yield by treatment of most primary or secondary aliphatic amines with 2,4-dinitrochlorobenzene,[4] and the presence of nitro groups was expected to greatly reduce oxidation of the aromatic ring.

Several primary amines of the type $R_1R_2CHNH_2$ and one secondary amine, di-*n*-propylamine, were converted to the corresponding 2,4-dinitroaniline derivatives (Ia–Ie) in yields ranging from 70 to 84%. These yields were obtained using a ratio of reactants of close to unity, and there is little doubt that the yields can be improved by increasing the amine-aryl halide ratio. Ia–Ie were oxidized with chromic acid in 12*N* sulfuric acid at 125°. The carbonyl compounds were steam distilled as formed and collected as 2,4-dinitrophenylhydrazones or *p*-(phenylazo)phenylsemicarbazones. These derivatives were chosen because they are formed rapidly and in nearly quantitative yields, and the carbonyl compounds can be regenerated readily from these derivatives.[2,5] Further, considerable work has been done on the chromatographic separation of 2,4-dinitrophenylhydrazones,[6] and the use of 2,4-dinitrophenylhydrazine to form derivatives should allow application of the method described here to the conversion of unsymmetrical secondary amines to separable mixtures of carbonyl compounds. The yields from the various oxidations and the melting points of the carbonyl derivatives are given in Table I.



Ia. $R_1 = R_2 = CH_3$; $R_3 = H$
Ib. $R_1 = R_2 = C_2H_5$; $R_3 = H$
Ic. $R_1R_2 = C_5H_{10}$; $R_3 = H$
Id. $R_1 = CH_3$; $R_2 = n\text{-}C_6H_{13}$; $R_3 = H$
Ie. $R_1 = C_2H_5$; $R_2 = H$; $R_3 = CHR_1R_2$

It can be seen from Table I that the yields of ketones from the chromic acid oxidations decrease with increasing boiling point of the ketone formed, undoubtedly because of further oxidation of the ketone in the oxidizing mixture. The yield of acetone was not affected by varying the mole ratio of chromic anhydride and Ia from two to

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[1] (a) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. (b) American Chemical Society–Petroleum Research Fund Fellow, 1961.

[2] F. W. Neumann and C. W. Gould, *Anal. Chem.*, **25**, 751 (1953).

[3] See E. Muller in Houben-Weyl, *Methoden Der Organischen Chemie*, 4th ed., Vol. 7, Part 1, Georg Thieme Verlag, Stuttgart, 1954, p. 205, and N. Ya. Demyanov and Z. I. Shuikina, *J. Gen. Chem. U.S.S.R.*, **5**, 1213 (1935).

[4] (a) O. L. Brady and F. R. Cropper, *J. Chem. Soc.*, 507 (1950); (b) J. J. Blanksma and H. H. Schreinimachers, *Rec. trav. chim.*, **52**, 428 (1933).

[5] M. Winter, E. Demole, and E. Sundt, *Helv. Chim. Acta*, **40**, 467 (1957).

[6] See ref. (2) and references cited therein.

TABLE I

YIELDS AND MELTING POINTS OF CARBONYL DERIVATIVES OBTAINED FROM OXIDATION OF 2,4-DINITROANILINES WITH CHROMIC ACID IN 12$N$ SULFURIC ACID AT 125°

| 2,4-Dinitro-aniline | Carbonyl Compound (B.P.)[a] | Yield,[b] % | | Melting Points | | | |
|---|---|---|---|---|---|---|---|
| | | 2,4-DNPH[c] | *p*-APS[d] | 2,4-DNPH[c] | Lit.[a] | *p*-APS[d] | Lit. |
| Ia | Acetone (56) | 94 | 96 | 125.5–126.0 | 128 | 212.5–213.0 | 211–213[h] |
| Ib | 3-Pentanone (102) | 75 | 73 | 154.0–155.0 | 156 | 173–174[f] | — |
| Ic | Cyclohexanone (156) | 45 | 43 | 160.0–161.0 | 162 | 221.5–222.0[g] | — |
| Id | 2-Octanone (173) | 21 | 32 | 57.5–58.0 | 58 | 137.0–138.3 | 138[h] |
| Ie | Propanal (49) | 42 | 40[e] | 152.0–153.5 | 155 | 152.0–154.0[e] | 155[i] |

[a] Ref. (15), pp. 582, 663. [b] As recrystallized products. [c] 2,4-Dinitrophenylhydrazone. [d] *p*-(Phenylazo)phenylsemicarbazone. [e] As 2,2-propylidenebis(5,5-dimethyl-1,3-cyclohexanedione) (propanal dimethone). [f] *Anal.* Calcd. for $C_{18}H_{21}N_5O$: C, 66.85; H, 6.54; N, 21.66. Found: C, 66.9; H, 6.60; N, 22.2. [g] *Anal.* Calcd. for $C_{19}H_{21}N_5O$: C, 68.03; H, 6.31; N, 20.88. Found: C, 68.14; H, 6.40; H, 20.90. [h] Ref. (5). [i] Ref. (15), p. 583.

four, and a chromic anhydride–amine mole ratio of about three was used for oxidation of Ia–Id. The optimum mole ratio of chromic anhydride and Ie was found to be two. All the reaction mixtures were heterogeneous because of the low solubilities of the 2,4-dinitroanilines in 12$N$ sulfuric acid at 125°.

The procedure used differed from that of Neumann and Gould in several respects. We used a semimicro procedure and a reaction temperature of about 125°, whereas they used a micro procedure and a much lower reaction temperature (60–75° in most cases). In our procedure, the concentration of sulfuric acid is considerably greater than that used by Neumann and Gould. Although they found that better yields of carbonyl compounds were obtained when the oxidation mixture was buffered at a *p*H of about 1.7 by the addition of sodium sulfate, we did not study the effects of added salts on yields. When Ie was oxidized using the method of Neumann and Gould, only a trace of propanal (as the dimethone derivative) was obtained, whereas our procedure gave a 40% yield of propanal (based on two moles of propanal from each mole of Ie). The difference in results is believed to be due in part to the difference in solubility of Ie in 12$N$ sulfuric acid at 125° and in 1.2$N$ sulfuric acid–1.5$M$ sodium sulfate at 75°. This seems reasonable since when a homogeneous solution of Ia in glacial acetic acid was treated with an excess of chromic anhydride at 97° for one hour, at least 43% of Ia was oxidized. It is interesting to note that cyclohexylamine was oxidized at room temperature by a mixture of chromic anhydride and 12$N$ sulfuric acid, whereas Neumann and Gould reported that aliphatic amines were not oxidized under the reaction conditions that they used. Unfortunately, at least one other carbonyl compound was formed together with cyclohexanone during the oxidation of cyclohexylamine. The carbonyl compounds were converted to a mixture of 2,4-dinitrophenylhydrazones, and cyclohexanone 2,4-dinitrophenylhydrazone was identified by paper chromatography. The pure cyclohexanone derivative could not be obtained by several crystallizations of the mixture of 2,4-dinitrophenylhydrazones from ethanol. Treatment of cyclohexylamine at 125° with chromic anhydride in 12$N$ sulfuric acid failed to yield any carbonyl compounds in the steam distillate.

Our expectation that the presence of two nitro groups on the aromatic ring would greatly slow oxidation of the aromatic ring was found to be fully justified. When Ia was oxidized with chromic acid below the boiling temperature of 12$N$ sulfuric acid, a nearly quantitative yield of 2,4-dinitroaniline was obtained.

The steam distillates from mixtures of Ia–Ie and the oxidizing solution were pale yellow. During a preliminary experiment with Ia, steam distillation was continued after all the acetone had been formed. A yellow solid, identified as 2,4-dinitrophenol, began to steam distill when the concentration of sulfuric acid approached 20$N$. It was found that 2,4-dinitroaniline, under the same conditions, was converted in 80% yield to 2,4-dinitrophenol.

By analogy with what is known of the oxidation of alcohols by chromic acid,[7] it can be postulated that the oxidation of a 2,4-dinitroaniline proceeds *via* the chromic acid amide of the amine (*e.g.*, II). Several unsuccessful attempts were made to prepare the chromic acid amide of $N$-*t*-butyl-2,4-dinitroaniline (III)[8] by treatment of excess III in glacial acetic acid with potassium dichromate at and

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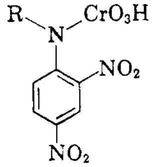
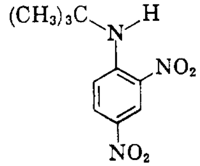
(7) F. Holloway, M. Cohen, and F. Westheimer, *J. Am. Chem. Soc.*, **73**, 65 (1951).

(8) The sample of III prepared by us had m.p. 153°, whereas that prepared by Brady and Cropper[4a] had m.p. 119°. We are certain that the compound prepared by us is III because of the method of preparation, its elemental analysis, and its NMR spectrum in acetone and in benzene. In addition to a broad band and $\tau$ 1.46,[9] due to the amino hydrogen, and aromatic-hydrogen bands at $\tau$ 1.08, 1.70, 1.86, 2.48, and 2.64, the NMR spectrum of III possessed only a singlet at $\tau$ 9.05 ± 0.02 (in benzene) due to the *t*-butyl hydrogens. The NMR spectrum of 2,4-dinitroaniline (in acetone) possessed a broad band at $\tau$ 2.17 due to the amino hydrogens, and aromatic-hydrogen bands at $\tau$ 1.06, 1.76, 1.92, 2.65, and 2.81. The difference in melting points reported for III may be due to polymorphism.

(9) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).



II



III

below room temperature.[10] It was noted that the solutions slowly changed in color from orange to green without the formation of a precipitate. When III was treated with chromic anhydride in 12*N* sulfuric acid at 115°, 2,4-dinitroaniline was formed together with a gas (presumed to be isobutene) that decolorized bromine without evolution of hydrogen bromide.

It is of interest that an α-hydrogen of Ie-1-*t* is apparently removed at about the same rate as the α-tritium of Ie-1-*t* in the rate-determining step of the oxidation with chromic acid in 14*N* sulfuric acid at 125°.[11] The observed kinetic isotope effect ($k_H/k_T \cong 1.2$) is much less than the hydrogen-deuterium isotope effect observed in the oxidation of isopropanol with chromic acid.[12] Further discussion of the mechanism of oxidation of 2,4-dinitroanilines with chromic acid is deferred until more is known of the kinetics and stereochemistry of the reaction.

## EXPERIMENTAL

Melting points and boiling points are uncorrected. Infrared spectra were obtained with a Beckman IR-4 spectrophotometer. NMR spectra were obtained at 60 mc. with a Varian Associates HR-60 system using samples contained in 5-mm. o.d. tubes. Microanalyses were performed by Mr. V. H. Tashinian, Berkeley, Calif., and by Drs. Weiler and Strauss, Oxford, England.

*N-Alkyl-2,4-dinitroanilines.* Ia–Ie were prepared in essentially the same manner from recrystallized 2,4-dinitrochlorobenzene, m.p. 53.0–54.0°, and commercially available, reagent grade amines. A typical procedure follows. To a rapidly stirred, boiling solution of 21.0 g. (0.102 mole) of 2,4-dinitrochlorobenzene and 100 ml. of ethanol was added dropwise in 30 min., a solution prepared from 10.0 g. (0.115 mole) of 3-aminopentane, 10 g. (0.12 mole) of sodium acetate, 30 ml. of ethanol, and 50 ml. of water. The stirred mixture was heated at reflux for 3 hr. and cooled in an ice bath. On cooling, a dark brown oil separated which crystallized when allowed to stand overnight. The crude product was recrystallized from ethanol to yield pale gold, flocculent crystals of *N*-(3-pentyl)-2,4-dinitroaniline (Ib). For the preparation of *N*-*t*-butyl-2,4-dinitroaniline (III), the mole ratio of amine and 2,4-dinitrochlorobenzene was 3 instead of about 1:1, no sodium acetate was used, and the reflux period was 6 hr. instead of 3 hr. The yields and melting points of the 2,4-dinitroanilines are given in Table II.

*Oxidation of Ia–Ie in 12N sulfuric acid and characterization of carbonyl products.* The following is typical of the procedure used. A mixture of 0.50 g. (2.2 mmoles) of *N*-isopropyl-2,4-dinitroaniline (Ia), 0.70 g. (7.0 mmoles) of chromic anhydride, 10 mg. of stearic acid, and 60 ml. of 12*N* sulfuric acid was heated to boiling (*ca.* 125°), and the pale yellow distillate was collected in a receiver immersed in an ice-salt bath. The formation of acetone was essentially complete in 15 min., *i.e.*, after 10 ml. of distillate had been collected. The aqueous distillate was added with stirring to a solution of 20 ml. of 2,4-dinitrophenylhydrazine reagent solution[13] and 1 ml. of 60% perchloric acid. The mixture was allowed to stand overnight, the 2,4-dinitrophenylhydrazone was collected by filtration and recrystallized from absolute ethanol. The aqueous distillate from another oxidation of Ia was made up to a volume of 2 l. with water, and 70 ml. of 98% formic acid containing 0.58 g. (2.3 mmoles) of *p*-(azophenyl)phenylsemicarbazide was added. The mixture was allowed to stand overnight and was extracted four times with 75-ml. portions of chloroform. The chloroform extracts were combined, and the solvent was evaporated. The residue was recrystallized once from aqueous formic acid and once from absolute alcohol. The yields of carbonyl compounds, as recrystallized 2,4-dinitrophenylhydrazones, and the melting points of these derivatives are given in Table I.

TABLE II

YIELDS AND MELTING POINTS OF 2,4-DINITROANILINES PREPARED FROM AMINES AND 2,4-DINITROCHLOROBENZENE

| 2,4-Dinitroaniline | Yield,[a] % | M.P. | Lit. M.P. | Ref. |
|---|---|---|---|---|
| Ia | 84 | 94.0–95.0 | 94–95 | [e] |
| Ib | 84 | 58.0–59.0[b] | — | — |
| Ic | 82 | 155.5–156.0 | 156 | [f] |
| Id | 70 | 51.5–52.5[c] | — | — |
| Ie | 78 | 41.0–42.0 | 40 | [g] |
| III | 93 | 153.0–153.5[d] | 119 | 4a |

[a] As recrystallized product. [b] *Anal.* Calcd. for $C_{11}H_{15}N_3O_4$: C, 52.17; H, 5.97; N, 16.60. Found: C, 52.14; H, 5.93; N, 16.59. [c] *Anal.* Calcd. for $C_{14}H_{21}N_3O_4$: C, 56.93; H, 7.16; N, 14.23. Found: C, 56.63, H, 7.24; N, 14.31. [d] *Anal.* Calcd. for $C_{10}H_{13}N_3O_4$: C, 50.20; H, 5.48; N, 17.57. Found: C, 50.74; H, 5.70; N, 17.34. [e] A. Mulder, *Rec. trav. chim.*, **25**, 108 (1906). [f] M. Busch and F. Gebelein, *J. prakt. Chem.*, [2] **115**, 111 (1927). [g] P. van Ronburgh, *Rec. trav. chim.*, **8**, 248 (1889).

When the reaction mixture containing Ia, chromic acid, and 12*N* sulfuric acid was distilled until 30 ml. of distillate was collected, a yellow solid was noted to form in the condenser. Continued distillation of the reaction mixture allowed the isolation of 0.17 g. of material which had a melting point of 109.0–110.2° after recrystallization from methanol, and infrared (potassium bromide pellet) and ultraviolet (in ethanol) spectra identical with those of 2,4-dinitrophenol, lit. m.p. 111.6°,[14] 114°.[15a]

*Oxidation of* Ia *with chromic acid in glacial acetic acid.* A solution of 2.25 g. (0.01 mole) of Ia, 1.0 g. (0.01 mole) of chromic anhydride, and 100 ml. of glacial acetic acid was heated in a water bath of 97° for 1 hr. The reaction mixture was cooled and poured into a beaker containing about 200 g. of crushed ice. The yellow solid was collected and dried. It weighed 1.13 g. and had m.p. 73–83°. A saturated carbon tetrachloride solution of the substance had an infrared spectrum almost identical with that of a saturated carbon tetrachloride solution of Ia. The acidic solution was brought to *p*H 4 by the addition of sodium hydroxide and extracted with ether. The ether was evaporated and the crude, dry residue (0.97 g.) was recrystallized from aqueous acetone.

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(10) *Cf.* L. F. Fieser and G. Ourisson, *Bull. soc. chim. France*, 1152 (1953).

(11) A. T. Bottini and R. E. Olsen, *J. Am. Chem. Soc.*, *in press*.

(12) F. H. Westheimer and N. Nicolaides, *J. Am. Chem. Soc.*, 71, 25 (1949).

(13) F. Duke and R. Witman, *Anal. Chem.*, **20**, 490 (1948).

(14) I. Heilbron, *Dictionary of Organic Compounds*, Vol. 1, Oxford University Press, New York, 1943, p. 999.

(15) (a) N. D. Cheronis and J. B. Entrikin, *Semimicro Qualitative Organic Analysis*, 2nd ed., Interscience Publishers, Inc., New York, 1957, p. 684; (b) p. 608.

The material had a melting point of 168–175° and an infrared spectrum (potassium bromide pellet) identical with that of 2,4-dinitroaniline, lit.[15b] m.p. 180° (188°).

*Oxidation of cyclohexylamine.* Excess cyclohexylamine was added to a solution of chromic anhydride in $12N$ sulfuric acid, and the mixture was allowed to stand overnight at room temperature. The color of the mixture changed from orange to murky brown. The mixture was extracted with ether, the ether solution was dried with magnesium sulfate, and the ether was removed by distillation. The residue, which was water white, was added to a solution of 2,4-dinitrophenylhydrazine in aqueous perchloric acid.[13] The orange crystals had a melting point of 110–130°. After two recrystallizations from ethanol, the crystals had a melting point of 122–142°. Paper chromatography of the mixture of 2,4-dinitrophenylhydrazones, using acetone-hexane as the eluent, resolved the mixture into two components. One component was red and did not move appreciably on the chromatograph. The other component moved at the same rate as cyclohexanone 2,4-dinitrophenylhydrazone.

*Oxidation of N-t-butyl-2,4-dinitroaniline* (III). A heterogeneous mixture of 0.50 g. (2.1 mmoles) of III, 0.50 g. (5.0 mmoles) of chromic anhydride, and 50 ml. of $12N$ sulfuric acid, through which was passed a slow stream of nitrogen, was heated in an oil bath at 115° for 1 hr. The effluent gases were passed into 25 ml. of cold carbon tetrachloride. The reaction mixture changed in color from orange to dark green during the heating period, and the carbon tetrachloride solution rapidly decolorized bromine. The reaction mixture was poured on 50 g. of crushed ice, and the yellow solid that separated was collected and recrystallized from aqueous acetone. It weighed 0.30 g. (1.6 mmoles, 80%), m.p. 171–179°, and had an infrared spectrum identical with that of 2,4-dinitroaniline.

*2,4-Dinitrophenol from 2,4-dinitroaniline.* A mixture of 1.00 g. (5.5 mmoles) of 2,4-dinitroaniline, m.p. 184–185°, and 60 ml. of $12N$ sulfuric acid was distilled until 40 ml. of distillate was collected. The yellow solid (2,4-dinitrophenol) that steam distilled was collected and recrystallized from methanol. It weighed 0.40 g. (2.2 mmoles) and had a melting point of 109.5–110.3°. The residue in the reaction flask was poured into 20 ml. of ice water, and the resulting mixture was made alkaline by the careful addition of cold $6N$ sodium hydroxide. The alkaline solution was extracted with 50 ml. of ether, the ether was evaporated, and the residue was recrystallized from aqueous acetone. The recrystallized material weighed 0.12 g., m.p. 166–170°, and had an infrared spectrum (potassium bromide pellet) superimposable on that of 2,4-dinitroaniline.

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DAVIS, CALIF.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE PAINT DIVISION, PITTSBURGH PLATE GLASS CO.,
AND S. C. JOHNSON & SON, INC.]

# The Condensation of Pyruvic Acid with Phenols[1]

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The condensation of pyruvic acid with phenol in sulfuric acid was reinvestigated. Contrary to the report of Böttinger,[3] the product was found to be not 2,2′-bis(*p*-hydroxyphenyl)propionic acid (Ia) but rather a polymeric material whose possible structure is discussed. Authentic Ia was prepared from phenol and pyruvic acid in acetic acid with hydrogen chloride catalyst. The dimethyl ether of Ia was synthesized unequivocally by oxidation of 3,3′-bis(*p*-methoxyphenyl)-2-butanone with sodium hypochlorite. The condensation of pyruvic acid with certain substituted phenols was also investigated, and the nature of the products is discussed.

It has been reported by Böttinger[3] that the addition of phenol to a solution of pyruvic acid in concentrated sulfuric acid near 0° afforded "diphenopropionic acid," presumably compound Ia. Other phenols and phenolic ethers were claimed to react similarly. Diphenopropionic acid was described as a granular, amorphous white solid, insoluble in benzene and chloroform, but soluble in acetone, ethyl acetate, and in bases. It did not melt below 268° but decomposed at elevated temperatures. The carbon and hydrogen analyses appeared to fit the formula for Ia as a monohydrate. Bromination in chloroform solution gave a bromo derivative alleged to have the formula $C_{15}H_{12}Br_2O_4$.

The condensation of pyruvic acid with phenol was reinvestigated. By following Böttinger's procedure a substance was obtained whose properties were in good agreement with those reported. The evidence showed distinctly, however, that the substance was not 2,2′-bis(*p*-hydroxyphenyl)propionic acid (Ia). Furthermore, authentic Ia was prepared and its structure established by an unequivocal synthesis. Bromination by the method[4] of Ingberman resulted in the uptake of 1.5 atoms of bromine based on Ia.

Doubts as to the assigned structure of Ia became evident when (1) it was observed that the infrared spectrum displayed a strong lactone band at 1800 cm.$^{-1}$ in addition to the carboxyl band at 1695 cm.$^{-1}$, (2) a lack of a definite melting point was observed, and (3) an uptake of only 1.5 atoms of bromine per mole was found when it would be

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[1] Presented before the Division of Organic Chemistry, 137th Meeting of the American Chemical Society, Cleveland, Ohio, April 1960.

[2] (a) Pennsalt Chemicals Corp., Philadelphia, Pa.; (b) Paint Division, Pittsburgh Plate Glass Co.; (c) S. C. Johnson & Son, Inc., 3024 Chatham, Racine, Wisconsin.

[3] C. Böttinger, *Ber.*, **14**, 1595 (1881); *Ber.*, **16**, 2071 (1883).

[4] A. K. Ingberman, *Anal. Chem.*, **30**, 1003 (1958).