2.5; N, 2.7; I, 48.3. Found: C, 34.5; H, 2.8; N, 2.5; I, 48.6.

***dl*-α-Amino-β-(3,5-diiodo-4-(3′,5′-diiodo-2′-hydroxyphenoxy)-phenyl)-propionic Acid (X).**—Iodine (0.28 g.) dissolved in 1 *M* aqueous potassium iodide was added, dropwise, to a chilled solution containing 0.277 g. of IX in 10 ml. of 7 *N* ammonium hydroxide, and the reaction mixture allowed to stand at 0° for one-half hour. After the addition of a small amount of sodium bisulfite solution to the reaction mixture, it was adjusted to *p*H 4 with dilute hydrochloric acid. The solid that had precipitated was collected and washed with water and ethanol. The crude amino acid was then recrystallized by dissolving it in 80% ethanol containing the requisite quantity of sodium hydroxide and suddenly acidifying the solution with dilute acetic acid to give 0.33 g. of X, pale pink clusters of needles, m. p. 218–219°, with decomposition.

Anal. Calcd. for $C_{15}H_{11}O_4NI_4$ (776.9); C, 23.2; H, 1.4; N, 1.8; I, 65.3. Found: C, 23.5; H, 1.7; N, 1.9; I, 65.4.

Summary

The synthesis of *dl*-3,5-diiodo-4-(3′,5′-diiodo-2′-hydroxyphenoxy)-phenylalanine, an isomer of thyroxine, is described. This compound is physiologically active, the activity being approximately one twenty-fifth of that of *dl*-thyroxine. This finding is in accordance with an earlier prediction and is taken as evidence in favor of a proposed hypothesis relating chemical structure and thyroxine-like activity.

PASADENA, CALIFORNIA RECEIVED AUGUST 4, 1941

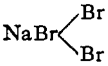
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNITED GAS IMPROVEMENT CO.]

An Anomalous Bromination Reaction. The Analytical Bromination of Styrene and Indene by the Kaufmann Method

BY C. W. JORDAN

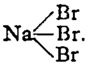
Kaufmann[1,2] developed a method for the determination of bromine numbers of various unsaturated organic compounds using a solution of bromine in methanol saturated with sodium bromide. With pure, water-free reagents a 0.1 *N* solution retained a constant titer over a much longer period of time than any other bromine solution tested. He observed that when bromine was added to methanol saturated with sodium bromide the solution was bright yellow in contrast with the red solutions formed by the same concentration of bromine in carbon tetrachloride, chloroform, glacial acetic acid, etc. The vapor pressure of the bromine appeared to be greatly lowered since the solution had very little odor. This was an important factor in preventing loss of bromine. The physical changes noted led to the conclusion that the halogen no longer existed in a free state but was loosely attached to the sodium bromide forming the tribromide, $NaBr_3$, or in some manner was combined with the methanol, or both.

By analogy with the known compound, sodium triiodide, the constitution was believed to be either



$NaBr{<}^{Br}_{Br}$

or



$Na{\leftarrow}Br_3$.

Kaufmann concluded that this solution was the outstanding titration liquid for use in bromometry in that it was odorless, permanent and easy to pipet in contrast with bromine solutions in carbon tetrachloride, glacial acetic acid, etc. It reacted far more energetically than iodine and completely saturated the double bond without the formation of substitution products.

Analytical Procedure.—The standard bromine solution was prepared by saturating Kahlbaum methanol with pure anhydrous sodium bromide (100 parts of methanol dissolve 12–15 parts of sodium bromide) and then adding bromine in the amount required to form 0.1 *N* solution. The exact normality was established by adding an excess of 0.2 *N* potassium iodide and titrating the liberated iodine with 0.1 *N* sodium thiosulfate. The quantity of sample recommended for test varied between 0.1 g. and 1.0 g. depending upon the magnitude of the bromine number.

The substance under test was weighed from a dropping bottle and put in a dry 300-ml. Erlenmeyer flask containing 15 ml. of chloroform. Chloroform was recommended for use when the substance under test was not freely miscible with the methanol–bromine solution. An excess of bromine solution was then added at room temperature and the mixture allowed to react, usually for two hours. The unreacted bromine was titrated iodimetrically and the bromine or iodine number calculated in the usual manner. The index of reliability of the method was determined by titrating a number of pure unsaturated compounds.

Anomalous Reactions Using Kaufmann Bromine Solution.—Kaufmann verified the method solely by determining the total amount of bromine consumed. Since the values obtained

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[1] H. P. Kaufmann and E. Hansen-Schmidt, *Archiv. der Pharmazie*, **263**, 32 (1925).

[2] H. P. Kaufmann, *Zeit. f. Untersuchung der Lebensmittel*, **51**, 3–14 (1926).

were always approximately the same as those calculated by theory, it was assumed that all of the bromine was attached to the two adjacent carbon atoms between which the double bond existed and that substitution products were not formed.

Contrary to this supposition the writer found that considerable hydrobromic acid was present in the bromination flask at the end of a three-minute bromination period. This could be determined after titrating the iodine liberated by reaction of excess bromine with potassium iodide, either by the addition of potassium iodate and again titrating liberated iodine or by titration with 0.1 *N* alkali.

With all substances titrated approximately one half of the total bromine consumed was present in the bromination flask as hydrobromic acid in solution. The original Kaufmann bromine solution used on these tests was free of hydrobromic acid.

Bromination of Synthetic Styrene and Purified Indene by Kaufmann Bromine Solution.—The results obtained in brominating synthetic styrene (by dehydration of β-phenylethyl alcohol) are shown in Table I.

TABLE I

ANALYTICAL BROMINATION OF SYNTHETIC STYRENE AND PURIFIED INDENE USING 0.1 *N* KAUFMANN BROMINE SOLUTION

Substance	Sample, g.	Total Br_2 consumed, m. eq./g.[a]	Subst. Br_2, m. eq./g.	Excess Br_2, m. eq./g.	Addition Br_2, m. eq./g.	*Apparent* Addition Br_2	*% from* Total Br_2 consumed
Styrene	0.1038[b]	18.94	9.11	22.60	9.83	51.19	98.62
Styrene	.1132[c]	18.95	9.03	22.30	9.92	51.65	98.67
Styrene	.2084[b]	19.04	9.53	19.12	9.51	49.52	99.14
Styrene	.2445[c]	19.02	9.29	16.25	9.73	50.67	99.04
Indene	.0917[b]	17.27	7.97	35.30	9.30	54.01	100.30
Indene	.1926[b]	17.33	8.25	49.50	9.08	52.73	100.60

[a] m. eq./g. = milli-equivalents per gram. [b] Fifteen ml. $CHCl_3$ used as solvent. [c] Fifteen ml. CCl_4 used as solvent. Titrations made in diffuse daylight. The reaction time and temperature used in the styrene analyses were, respectively, three minutes and 0° and in the indene analyses, three minutes and 25°.

In contrast with the large amount of apparent substitution bromine obtained with the Kaufmann solution, very little hydrobromic acid was found when titrating styrene and indene with a standard solution of bromine in carbon tetrachloride by the method of McIlhiney.[3] In the case of styrene the substitution bromine was only 0.27 milli-equivalent per milliliter and with indene, 0.48.

Discussion

It is obvious from the relatively large amount of hydrobromic acid formed that reaction product other than styrene dibromide or indene dibromide must be present in the reacted mixture. No attempt was made to systematically study the products formed but sufficient work was undertaken to be worthy of note for future reference.

A slight excess of 0.1 *N* Kaufmann bromine solution was added to a mixture of 10 g. of synthetic styrene and 10 g. of chloroform contained in a 1-liter flask and cooled in a crushed ice-bath. The mixture was allowed to react three minutes, after which 500 ml. of water was added.

A crystalline precipitate which formed was separated and dissolved in chloroform. The remaining diluted reaction products were extracted with several portions of reagent ether. The ether and chloroform extracts were combined, dried, and then distilled through a small Hempel column. After the solvents had distilled off the temperature rose rapidly and about 4 ml. of a light yellow oil was obtained between 200 and 230° at atmospheric pressure. The density of this liquid, $d^{20}{}_4$, was 1.30 and the refractive index, $n^{20}{}_D$ 1.5575. It had a distinct, rather pleasant, flowery odor, but was slightly irritating to the eyes.

The boiling range and density are near those given in the literature for α-bromostyrene and ω-bromostyrene, C_6H_5-CH=CHBr. Beilstein, Vol. V (1922), p. 477, states that α-bromostyrene is an oil having a boiling point of 86–87° at 14 mm. (approximately 210° at 760 mm.). The density was given as 1.38 at 21°. ω-Bromostyrene was stated to be a liquid with a hyacinth-like odor, distilling at ordinary pressure with but little decomposition between 219–221°. The density was given as 1.39 at 24.8°.

No attempt was made to determine the percentage of bromine in the material obtained by distillation.

A quantity of distillate was also obtained between 250–260° which solidified in the condenser tube. After recrystallization from methanol it was found to have a melting point of 71° which is suggestive of styrene dibromide, $C_6H_5CHBrCH_2Br$.

The normal course of bromination of styrene (quantitative formation of styrene dibromide which occurs when using pure bromine or solutions of bromine in ordinary solvents) is probably modified by the simultaneous action of molecular bromine and atomic bromine, both of which Kaufmann thought might be present in his unique bromine solution.

The final reaction may be represented by the equation

$$2C_8H_8 + Br_2 + Br + Br \longrightarrow C_8H_8Br_2 + C_8H_7Br + HBr$$

Kaufmann bromine solutions may find useful applications in modifying other common bromination reactions.

Summary

1. A solution of bromine in methanol satu-

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[3] P. C. McIlhiney, THIS JOURNAL, 24, 1109 (1902).

rated with sodium bromide profoundly modifies the addition of bromine to the unsaturated hydrocarbons styrene and indene.

2. The method appears to be quantitative for the formation of the respective dibromides when based on the total bromine consumed.

3. The anomalous feature is that approximately one-half of the total bromine consumed is present in the reaction flask as hydrobromic acid in solution.

4. An equation is suggested in an effort to explain the final mixture reached when titrating styrene.

PHILADELPHIA, PA. RECEIVED JULY 23, 1941

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

Anthochlor Pigments. II. The Pigments of *Coreopsis gigantea*[1,2]

BY T. A. GEISSMAN

Coreopsis gigantea (Compositae) is a perennial common to the coastal areas of California. It blooms during March or April, bearing showy flowers consisting of deep yellow disk-florets and golden-yellow rays. Both the ray- and disk-flowers, as well as the involucral bracts, show the color reaction described by Gertz[3] as being characteristic of a class of pigments known as "anthochlor" pigments,[1,3] one member of which has been shown to be butein (2′,4′,3,4-tetrahydroxychalcone), which has been isolated from *Coreopsis Douglasii*,[2] *Dahlia variabilis*[4] and from *Butea frondosa*[5] (Leguminosae).

Butein is also present in *Coreopsis gigantea.* It was isolated from the ether extract of the dried whole flowers (including the involucral bracts) and was characterized by comparison with a synthetic sample and by conversion into its acetate. The whole flower heads were used because of the difficulty of securing more than a small quantity of material during the flowering season of the present year, and consequently it cannot be stated with certainty whether butein is present in all parts of the flower-head or is localized in the ray- or disk-flowers or the involucral bracts. The qualitative observation of the appearance of a red coloration when a part of the plant is treated with alkali cannot be taken as evidence for the presence of butein since a second substance which could be responsible for this reaction has also been isolated.

This substance, for which no name will be proposed for the present, was isolated from the methanol extract of the dried flowers after exhaustive extraction with ether. It has not yet been obtained in the crystalline state but was converted into a white, crystalline acetate, m. p. 172.5–3°. The amorphous material was in the form of a brown-yellow powder which microscopic examination disclosed to be composed of minute spherical globules of a glassy nature, deep yellow in color. The substance dissolves in aqueous alkali to give an intensely red solution. It is insoluble in ether and somewhat soluble in water, from which butyl alcohol extracts it readily. Its acetate is insoluble in cold, dilute alkali but on warming with alcoholic alkali it dissolves to form an intensely red solution such as is produced when the amorphous pigment dissolves in alkali. The quantity of this material (as acetate) so far available has been small and at present little is known concerning its constitution.

In the preceding paper[2] the remark was made that aqueous extracts of the ether-extracted flowers of *C. Douglasii* contained some water-soluble pigment which gave a red color with alkali. It is therefore probable, in view of the present results, that a second pigment is also present in that flower.

Work on these pigments and on those present in certain other members of the Compositae is being continued.

Experimental

The flowers were collected near the Coast Highway north of Malibu, California, during April. The whole flower

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(1) The use of the term "anthochlor" to describe those pigments whose presence causes certain yellow flowers to turn red when exposed to alkali is to a certain extent undesirable since the term has been used with more than one connotation in the literature. However, since work in progress in this Laboratory on certain Compositae showing this color reaction has so far not given assurance that all the substances responsible belong to a single class of compounds, the use of the term will be continued until a more uniquely descriptive one is found.

(2) First paper of this series, THIS JOURNAL, **63**, 656 (1941).

(3) Gertz, *Kgl. Physiograf. Sällskap, Lund, Förh.*, **8**, 62, 71, 251 (1938).

(4) Price, *J. Chem. Soc.*, 1018 (1939).

(5) Perkin and Hummel, *ibid.*, **85**, 1459 (1904).