

6,8-DIIODOBENZOYLENEUREA, AND THE INTERACTION OF 5,7-DIHALOGENOISATOIC ANHYDRIDES WITH AMMONIA AND WITH ETHYLAMINE. 3-ETHYL-6,8-DIHALOGENOBENZOYLENEUREAS

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The reaction of isatoic anhydride and its derivatives with ammonia or primary amines to produce 2-aminobenzamides is sufficiently general (1) for the formation of benzoyleneureas in two instances to have been overlooked. In a study (2) of the behavior of 5,7-dichloroisatoic anhydride with ammonia, it was shown that one of the products of the reaction, previously reported to be 3,5-dichloro-2-aminobenzamide, is actually 6,8-dichlorobenzoyleneurea, and a like mistake was suspected in the case of the dibromo derivatives. This suspicion has been confirmed and the investigation has been extended to include 6,8-diiodobenzoyleneurea and related compounds. The syntheses and reactions of these three series of compounds, respectively dichloro, dibromo, and diiodo derivatives, are similar and are outlined concordantly below.

6,8-Diiodobenzoyleneurea as a Reagent for Sodium

The use of 6,8-dibromo- and especially 6,8-dichloro-benzoyleneurea as reagents for the detection of sodium in the presence of other alkali metals was suggested in previous papers (2, 3). The analogous 6,8-diiodobenzoyleneurea is not a reagent for sodium because of the sparing solubility and ready hydrolysis of its alkali metal salts. Preparations of the sodium salt, obtained by precipitating solutions of the urea in aqueous lithium hydroxide with sodium chloride, have a variable composition and are evidently mixtures of 6,8-diiodobenzoyleneurea and its hydrated monosodium salt. Possibly some of the isomeric dichlorobenzoyleneureas will prove useful as reagents for sodium, and this approach is being investigated.

Fusion of 3,5-Dihalogenoanthranilic Acids with Urea

When 3,5-dihalogenoanthranilic acids (I) are fused with urea, 6,8-dihalogenobenzoyleneureas (V) and 3,5-dihalogeno-2-aminobenzamides (IV) are formed. The detection of both of these products in a single experiment was initially effected (4) with 3,5-dichloroanthranilic acid but subsequent trials with 3,5-diiodoanthranilic acid and a repetition of the fusion of urea with 3,5-dibromoanthranilic acid (3) demonstrate the generality of this reaction for all three of the acids (I). The yields of products (IV, V) from fusions of the three acids (I) with urea, conducted at the same temperature, vary regularly with the increase in weight of the halogen substituents and are compared in Table I.

Nuclear-substituted anthranilic acids, considered as monobasic acids, are an exception to the observation (5) that aromatic monobasic acids do not give

amides on fusion with urea, for recent work (6) has shown that 3-nitro- and 4-nitro-anthranilic acids also furnish the corresponding amides and benzoyleneureas by this treatment although 5-nitro- and 3,5-dinitro-anthranilic acids (7, 8) fail to react. Anthranilic acid itself, fused with 1.5 moles of urea at 120° during two hours, gave 16% of benzoyleneurea, but any *o*-aminobenzamide which may have been formed in the reaction was not detected.

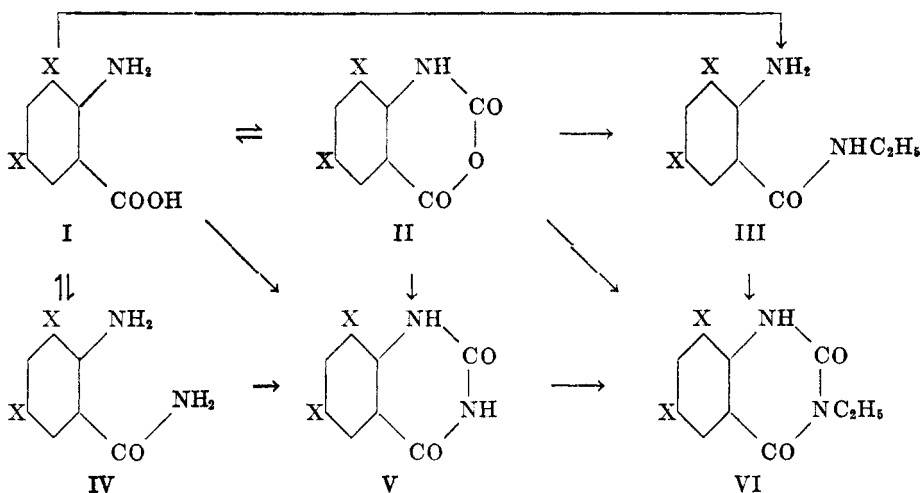


TABLE I

YIELDS OF CRUDE PRODUCTS FROM FUSIONS OF 3,5-DIHALOGENOANTHRANILIC ACIDS AND UREA AT 160°

ANTHRANILIC ACID (I)	MOLAR RATIO, UREA: ACID	TIME, HOURS	BENZOYLENE-UREA (V), %	2-AMINO BENZ-AMIDE, (IV), %
Dichloro ^a	3.43	4	67	11
Dibromo ^b	3.34	7	45	40
Diiodo ^b	3.24	7	23	69

^a Data from (4).

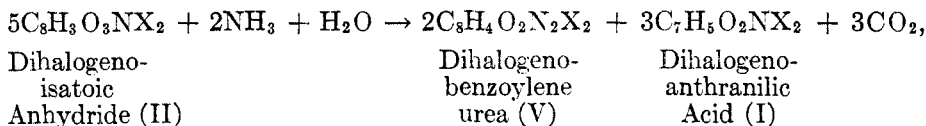
^b This paper.

3,5-Diiodo-2-aminobenzamide has been prepared (9) from diiodoanthranilic acid with phosphorus pentachloride and ammonium carbonate; this method is applicable to the dichloro and dibromo acids (I), but attempts to apply it to anthranilic acid were unsuccessful.¹ The constitution (IV) of the three dihalogenoaminobenzamides is indicated by their alkaline hydrolysis to the parent acids (I) and by their conversion to the benzoyleneureas (V) with ethyl chlorocarbonate (11). Prepared in this way, from the amides and ethyl chlorocarbonate, the benzoyleneureas (V) are pure white in color, a quality which is difficult to attain in these compounds by the other methods of preparation.

¹ The compound, ClCOC₂H₄NHPOCl₂, from anthranilic acid and phosphorus pentachloride, is said (10) to give *o*-aminobenzamide with aqueous ammonia.

Interaction of 5,7-Dihalogenoisatoic Anhydrides and Ammonia

3,5-Dichloro- and 3,5-dibromo-2-aminobenzamide were first recorded in 1885 by Robert Dorsch² who assigned the constitution IV to two products which he obtained by treating 5,7-dichloro- and 5,7-dibromo-isatoic anhydride, respectively, with aqueous ammonia. Repetitions (13) of his experiments, however, invariably yielded the corresponding benzoyleneureas (V) and anthranilic acids (I) in proportions required by the equation,



which applies equally well to the behavior of 5,7-diiodoisatoic anhydride with ammonia. For his dichloro amide Dorsch (14) gave the melting point 284° (an uncorrected melting point of 6,8-dichlorobenzoyleneurea) and a nitrogen determination which is 1.3% high for dichlorobenzoyleneurea; for his dibromo amide he gave the melting point 196–197° and determinations of four elements which are in good agreement with the calculated composition of the amide. But 3,5-dibromo-2-aminobenzamide, prepared from 3,5-dibromoanthranilic acid by fusion with urea or by treatment with phosphorus pentachloride and ammonium carbonate, melts at 215.5° (corrected), the constitution IV being established for this product by its ready conversion to 6,8-dibromobenzoyleneurea with ethyl chlorocarbonate, and by an easy hydrolysis to the anthranilic acid. Dorsch's products, therefore, must have been 6,8-dichloro- and 6,8-dibromo-benzoyleneurea, and the melting point 196–197° is a misprint for 296–297°, an uncorrected melting point of 6,8-dibromobenzoyleneurea. Subsequent investigators (15) were unable to repeat certain parts of Dorsch's work and concluded that the tri- and tetra-bromoanthranilic acids which he described (16) were specimens of tri-bromoaniline (17).

Interaction of 5,7-Dihalogenoisatoic Anhydrides and Ethylamine

On warming 5,7-dihalogenoisatoic anhydrides (II) with aqueous ethylamine, 3-ethyl-6,8-dihalogenobenzoyleneureas (VI) and 3,5-dihalogeno-2-aminobenzethylamides (III) are formed in variable amounts, depending upon the choice of the halogen substituents. The ethylamides (III) were identified by their synthesis from the anthranilic acids (I) with phosphorus pentachloride and ethylamine, and by conversion to the 3-ethylbenzoyleneureas (VI) on treatment with ethyl chlorocarbonate. The 3-ethylbenzoyleneureas (VI) are identical with the products of direct ethylation of the 6,8-dihalogenobenzoyleneureas (V), obtained by heating the latter with ethyl iodide and alkalies, and confirm the constitution previously assigned (18) to the ethylation product of 6,8-dibromobenzoyleneurea.

² Robert Dorsch, Inaugural-Dissertation, Leipzig, 1885. The text is identical with the published article (12).

Preparation of 5,7-Dihalogenoisatoic Anhydrides

5,7-Dichloro- and 5,7-diiodo-isatoic anhydride (II) were prepared by refluxing the anthranilic acids (I) with ethyl chlorocarbonate. 5,7-Dibromoisatoic anhydride was obtained (13) by oxidizing tetrabromoindigo, but a better method of preparation, now being investigated, is the treatment of dibromoanthranilic acid with phosgene in glacial acetic acid solution. These anhydrides (II) dissolve in warm, aqueous sodium hydroxide, giving solutions which yield precipitates of the anthranilic acids (I) on acidification.

EXPERIMENTAL

3,5-Diiodoanthranilic acid (I). An Eastman preparation was crystallized from alcohol and recrystallized from benzene; needles, m.p. 234.5-235° (corr.).

6,8-Diiodobenzoyleneurea (V) from 3,5-diiodoanthranilic acid (I). Two grams of diiodoanthranilic acid and 1 g. of urea were mixed in a flask equipped with a loose-fitting cork stopper, carrying a vertical exit tube, and heated in an oil-bath at 160° during seven hours. The mixture just melted initially and then resolidified. The acicular sublimate (0.22 g.) which deposited on the flask walls was insoluble in aqueous sodium hydroxide, but the presence of diiodoaminobenzamide in it was not conclusively demonstrated.

The porous, yellow, reaction mixture (2.64 g.) was pulverized and treated with hot, dilute, aqueous sodium hydroxide; the undissolved material remaining from this treatment was warmed with dilute hydrochloric acid, washed with water, and extracted repeatedly with fresh portions of hot aqueous lithium hydroxide until a sample of the extract failed to give a precipitate with hydrochloric acid. The combined extracts crystallized on cooling; they were reheated to boiling and the clear solution was acidified with dilute acetic acid. The precipitate (0.51 g.) of diiodobenzoyleneurea which separated was washed with water, dried, and dissolved in 575 cc. of a boiling 1:1 mixture of acetone and alcohol. The solution was filtered, evaporated slowly on a steam-bath until crystals just began to form, and then allowed to cool; 6,8-diiodobenzoyleneurea (0.44 g.) crystallized in small, pale yellow needles, m.p. 326-327° (corr.) after sintering to larger crystals around 300°. The compound is soluble in hot glycol and crystallizes in flocs on cooling.

Anal. Calc'd for $C_8H_4I_2N_2O_2$: N, 6.77. Found: N, 6.74, 6.99, 6.69.

3,5-Diiodo-2-aminobenzamide (IV). The insoluble residue remaining from the extractions with aqueous lithium hydroxide described above was washed with dilute hydrochloric acid and with water, and dried. The crude, yellow amide (1.39 g.) thus obtained was dissolved in 250 cc. of boiling alcohol and the solution was filtered from a slight amount of deep yellow, insoluble material (possibly a tetraiodoacridone). On cooling, 3,5-diiodo-2-aminobenzamide (1.04 g.) crystallized in yellowish to pale brown, brittle needles, m.p. 241-242° (corr.); at 270° the black melt evolved iodine vapor.

Anal. Calc'd for $C_7H_6I_2N_2O$: N, 7.22. Found: N, 7.11.

Alkali metal salts of 6,8-diiodobenzoyleneurea are too insoluble to warrant their use as tests for sodium. The urea dissolves in hot aqueous lithium hydroxide to give solutions which rapidly deposit fine needles on cooling. It is slightly soluble in hot aqueous potassium hydroxide, and from the resulting solutions white needles separate in small amounts on cooling and standing. It is least soluble in hot aqueous sodium hydroxide; the solutions hardly crystallize on standing, and yield only slight, flocculent precipitates on acidification.

A solution of 6,8-diiodobenzoyleneurea in lithium hydroxide, sufficiently diluted to avoid rapid crystallization, gave a precipitate with a sodium chloride solution faster and more completely than it did with a solution of potassium bromide, and instantly yielded a gelatinous precipitate of the urea on adding ammonium chloride. A warm, somewhat stronger solution of the urea in lithium hydroxide gave crystalline precipitates with solutions of potassium, rubidium, and cesium chlorides, and also with pure water.

Sodium 6,8-diiodobenzoyleneurea, precipitated from hot solutions of the lithium salt, has

a variable composition and appears to be a mixture of the free urea and its hydrated mono-sodium salt. Equal weights, 0.2 g., of diiodobenzoyleneurea and lithium hydroxide were dissolved in 75 cc. of boiling water, the solution was filtered, and 25 cc. of 0.5 *M* sodium chloride was added. Precipitation began immediately. After the suspension had stood for 1-3 hours, the light, crystalline precipitate was collected, washed with water, and dried at 40° during 2-3 days; yield, 0.21-0.25 g.

In a series of drying experiments conducted with four different samples prepared as described above, the losses, on attaining constant weights, varied from 1.29% after one day at 120° to 4.58% after fifteen days over concentrated sulfuric acid. The hygroscopic products were finally ignited with sulfuric acid and the residues (negative lithium flame tests) weighed as sodium sulfate. The sodium contents, based on the initial samples, varied from 2.68 to 4.17%.

5,7-Diiodoisatoic anhydride (II). A mixture of 0.44 g. of diiodoanthranilic acid and 2 cc. of ethyl chlorocarbonate was gently refluxed over a small flame during 21 hours. A mixture of solid and liquid resulted. Most of the liquid was allowed to evaporate spontaneously, and the solid was crushed, washed with alcohol, and dried; 0.38 g. Crystallization from benzene yielded 0.24 g. of short, glistening, yellow needles, m.p. 264-265° (corr.). Preparations on a larger scale resulted in lower yields. Repeated attempts to prepare the corresponding dibromoisatoic anhydride by this method were unsuccessful and resort was had to the oxidation of tetrabromindigo (13) in order to obtain a supply of this compound. 5,7-Diiodoisatoic anhydride is readily soluble in warm, dilute, aqueous sodium hydroxide, forming solutions which deposit diiodoanthranilic acid on acidification. The acicular habit of diiodoisatoic anhydride was unexpected and contrasts strikingly with the short, clear prisms of the dichloro and dibromo anhydrides.

Anal. Calc'd for $C_8H_3I_2NO_3$: N, 3.38. Found: N, 3.06, 3.29.

6,8-Diiodobenzoyleneurea (V) from 5,7-diiodoisatoic anhydride (II). Suspensions of the anhydride (0.393, 0.5405 g.; 5, 5 moles basis) in 20-cc. portions of aqueous 28% ammonia were refluxed gently on a water-bath during one hour. On cooling, the undissolved residues of diiodobenzoyleneurea (0.122, 0.2225 g.; 1.56, 2.06 moles) were collected, washed with water, and dried. The respective filtrates and washings were acidified hot with dilute acetic acid and the diiodoanthranilic acid was allowed to crystallize (0.227, 0.2915 g.; 3.08, 2.88 moles). These products were identified by crystallizations from the usual solvents and mixture melting points with known specimens.

3,5-Dibromoanthranilic acid (I) was prepared exactly as described by Wheeler and Oates (19), and was shown to be identical (mixture melting point) with the acid, m.p. 235-236° (corr.) previously obtained (13) by the action of ammonia on 5,7-dibromoisatoic anhydride.

3,5-Dibromo-2-aminobenzamide (IV). (a) A mixture of 2 g. of dibromoanthranilic acid and 1.36 g. of urea was maintained at 160° during seven hours as described above for the preparation of diiodobenzoyleneurea. The mixture melted and bubbled just below this temperature and then slowly solidified to a yellow mass. The white, acicular sublimate (0.41 g.), washed with water, dried, and crystallized from alcohol, was found to consist principally of dibromoaminobenzamide. The yellow residue (2.52 g.) was powdered and extracted three times with hot, aqueous lithium hydroxide, an acidified test portion from the final extraction remaining clear. The combined extracts were acidified and the resulting precipitate was collected, washed with water, and extracted with warm, aqueous sodium hydroxide. The insoluble sodium salt, washed with water and treated with warm, dilute hydrochloric acid, yielded 0.97 g. of crude 6,8-dibromobenzoyleneurea, m.p. 291-292° after washing and drying. Acidification of the sodium hydroxide extract precipitated 0.10 g. of material not identical with dibromoanthranilic acid.

The residue (0.79 g.) insoluble in lithium hydroxide was taken up in boiling alcohol, only a small amount of yellow material remaining undissolved. From the alcoholic solution, on cooling, 3,5-dibromo-2-aminobenzamide separated in long, flat, glistening prisms; m.p. 215.5-216° (corr.).

Anal. Calc'd for $C_7H_6Br_2N_2O$: N, 9.53. Found: N, 9.20, 9.73.

(b) Two-tenths gram of phosphorus pentachloride was added to a suspension of 0.25 g. of dibromoanthranilic acid in 10 cc. of benzene and the mixture was allowed to stand in a stoppered flask at room temperature during five hours, with occasional shaking. The solution was filtered from undissolved solids and allowed to stand overnight with an excess of powdered ammonium carbonate. The white solids were collected, washed with benzene, dried, and the ammonium salts leached out with water. The water-insoluble residue, crystallized from alcohol, did not depress the melting point of a sample of the 3,5-dibromo-2-aminobenzamide described under (a).

3,5-Dichloro-2-aminobenzamide (IV), identical with an authentic specimen (2), was similarly prepared from dichloroanthranilic acid and phosphorus pentachloride except that the bulk of the product, in this case, was found in the benzene solution rather than in the ammonium salt residues.

Alkaline hydrolysis of the amides (IV). 3,5-Dibromo-2-aminobenzamide was completely dissolved after two hours of refluxing with aqueous sodium hydroxide, whereas the diiodo compound required twelve hours of the same treatment to effect complete solution. The dichloro amide is approximately intermediate (2) between these extremes. Acidification of the alkaline solutions produced precipitates of the corresponding anthranilic acids. The dibromo acid thus obtained was crystallized once from benzene; m.p. 235.5–236° (corr.) in exact agreement with the observation of Bogert and Hand (20).

Interaction of the amides (IV) with ethyl chlorocarbonate. 6,8-Diiodobenzoyleneurea (V) from 3,5-diiodo-2-aminobenzamide (IV). Twelve cc. of ethyl chlorocarbonate was added to 0.95 g. of the diiodo amide, and the mixture was gently refluxed during three hours. Reaction took place readily but frequent shaking was necessary in order to prevent the voluminous, fine white particles of product from coating the larger crystals of amide. The suspension was boiled with 20 cc. of alcohol, allowed to cool, and the white, insoluble diiodobenzoyleneurea (0.72 g.) was washed with alcohol.

The dibromo- and dichloro-aminobenzamides reacted similarly, the corresponding benzoyleneureas being obtained and identified, after crystallizations from acetone-alcohol or alcohol, by mixture melting points with known specimens. All three of these products were pure white in color.

Interaction of the dihalogenoisatoic anhydrides (II) with ethylamine: 3-Ethyl-6,8-dihalo-benzoyleneureas (VI), and 3,5-dihalogeno-2-aminobenzethylamides (III). One-half gram of the anhydride was treated with 15 cc. of aqueous, 22% ethylamine (an immediate reaction was evident), and the resulting suspension was heated, with frequent shaking, under a reflux condenser on a water-bath during one hour. A part or all of the solids dissolved, but after 20 minutes, crystals began to separate from the hot solution. Sixty cc. of aqueous 0.4 M sodium hydroxide was added; the mixture was boiled, allowed to cool, and the undissolved residue of dihalogenoaminobenzethylamide removed. When diiodoisatoic anhydride was used the filtration was performed with the hot solution since the sodium salt of ethyldiiodobenzoyleneurea crystallizes readily on cooling, and the by-product, ethylamide, is not appreciably soluble; the dichloro and dibromo ethylamides are slightly soluble under these conditions. Addition of acetic acid to the alkaline filtrate precipitated the ethyldihalogenobenzoyleneurea. The yields of crude products, properties, and analytical data observed with these ethyl derivatives are given in Table II.

3,5-Diiodo-2-aminobenzethylamide (III). Two grams of diiodoanthranilic acid and 1.2 g. of phosphorus pentachloride were suspended in 15 cc. of benzene. After standing for one hour at room temperature, shaking frequently, the solution was filtered from undissolved solids and treated slowly, while shaking, with 25 cc. of aqueous, 12% ethylamine. A white precipitate rapidly formed and, after aging overnight, was collected, pressed, washed with water, and dried at 100°; yield 1.45 g. Evaporation of the water-washed, yellow benzene layer gave an additional 0.39 g. of impure product. From these crude products hot, dilute, aqueous sodium hydroxide removed small amounts of alkali-soluble material, precipitable by acids. The residues insoluble in alkali were crystallized from a mixture of benzene and petroleum ether and then repeatedly crystallized from dilute alcohol. 3,5-Diiodo-2-amino-

TABLE II
REACTION PRODUCTS OF 5,7-DIHALOGENOISATOIC ANHYDRIDES WITH ETHYLAMINE

COMPOUNDS	% YIELD, CRUDE	APPEARANCE	M.P., °C., CORR.	FORMULA	ANALYSES ^a			
					Calc'd		Found	
					C	H	C	H
3-Ethylbenzoyleneureas 6,8-Dichloro-	71	Long, slender needles from alcohol	244.5-245	$C_{10}H_8Cl_2N_2O_2$	46.35	3.11	46.66	3.79
	86	Like dichloro	252.5-253	$C_{10}H_8Br_2N_2O_2$	N, 10.83	2.32	N, 10.72	2.46
	87	Scales from glycol	275-276	$C_{10}H_8I_2N_2O_2$	34.51	1.82	34.91	2.07
2-Aminobenzethylamides 3,5-Dichloro-	15	Silky, hair-like needles from petroleum ether	161.5	$C_9H_{10}Cl_2N_2O$	46.37	4.32	46.45	— ^b
	8.2	Sheaves of short needles from benzene + petroleum ether	174-174.5	$C_9H_{10}Br_2N_2O$	33.57	3.13	46.37	3.45
3,5-Diiodo-	5.5	Papery mass of small needles from dilute alcohol	213	$C_9H_{10}I_2N_2O$	25.98	2.42	25.93	2.65 ^c
							25.54	2.83

^a Determinations by J. S. McNulty.

^b This compound was triboelectric and difficult to burn, and good hydrogen values were not obtained.

^c Sample prepared directly from diiodoanthranilic acid.

benzethylamide was not appreciably attacked by long heating with strong, aqueous sodium hydroxide; the material which did dissolve was precipitated by acid but was not identical with 3,5-diiodoanthranilic acid.

The corresponding dibromo- and dichloro-aminobenzethylamides were similarly prepared, except that these compounds remained dissolved in the benzene layers. All three of these substances proved to be identical (mixture melting points) with the alkali-insoluble products obtained, as described above, by the action of ethylamine on the corresponding dihalogenoisatoic anhydrides.

Interaction of the 3,5-dihalogeno-2-aminobenzethylamides (III) with ethyl chlorocarbonate: 3-Ethyl-6,8-dihalogenobenzoyleneureas (VI). All three of the N-ethylamides dissolved readily in warm ethyl chlorocarbonate. The solutions were evaporated to dryness on a steam-bath and the white, crystalline residues taken up in hot, aqueous sodium hydroxide. The alkaline solutions were filtered from small amounts of insoluble, red-brown, crystalline materials, and acidified, the 3-ethylbenzoyleneureas which precipitated were washed with water, dried (yields 65-72%), and crystallized from suitable solvents before comparison with the identical products by the other two methods of preparation.

Direct ethylation of 6,8-dihalogenobenzoyleneureas (V): 3-Ethyl-6,8-dihalogenobenzoyleneureas (VI). Ethylations were effected by heating the benzoyleneureas with solutions of ethyl iodide and caustic alkalies in dilute alcohol, following the procedure described previously (18) for the preparation of 3-ethyl-6,8-dibromobenzoyleneurea. Potassium hydroxide was used with the dichloro, and lithium hydroxide with the dibromo and diiodo compounds. The yields of precipitated dichloro, dibromo, and diiodo products were 80, 83 (18), and 55%, respectively. These ethylated compounds are identical with and did not depress the melting points of the corresponding alkali-soluble products obtained from the isatoic anhydrides with ethylamine, and from the aminobenzethylamides with ethyl chlorocarbonate.

Color reactions of the benzoyleneureas. Mixtures of approximately equal bulks of the benzoyleneureas and resorcinol were moistened with concentrated sulfuric acid and heated until fumes issued from the mouths of the containers. The cold melts were taken up in water (only the melt with benzoyleneurea dissolved completely) and made alkaline with sodium hydroxide. Benzoyleneurea and dichlorobenzoyleneurea gave yellow colors. Dibromobenzoyleneurea gave a yellow color which turned pink within a few minutes. Diiodobenzoyleneurea gave a pale pink color. These colors fluoresced slightly; they faded with hydrochloric acid and were not completely restored by alkali.

The marked fluorescent property usually exhibited by solutions of the dichloro compounds, the amide, the acid, and the benzoyleneurea (2), is lacking in solutions of the dibromo and diiodo derivatives.

SUMMARY

6,8-Diiodobenzoyleneurea is not a reagent for sodium because of the low solubility and ready hydrolysis of its alkali metal salts. 6,8-Dichlorobenzoyleneurea remains more suited to this purpose.

The fusion of 3,5-dihalogenoanthranilic acids (dichloro, dibromo, and diiodo) with urea yields 6,8-dihalogenobenzoyleneureas and 3,5-dihalogeno-2-aminobenzamides. The latter also result on reacting the anthranilic acids with phosphorus pentachloride and ammonium carbonate, and are converted to the benzoyleneureas by treatment with ethyl chlorocarbonate.

5,7-Dihalogenoisatoic anhydrides, formed (excepting the dibromo derivative) by prolonged heating of the anthranilic acids with ethyl chlorocarbonate, react with ammonia to give the corresponding benzoyleneureas and anthranilic acids in yields of 40 and 60%, respectively. The dibromo and dichloro aminobenz-

amides reported by Dorsch in 1885 to result from this reaction were undoubtedly specimens of the benzoyleneureas.

When ethylamine instead of ammonia acts on 5,7-dihalogenoisatoic anhydrides the reaction follows an altered course, yielding 3-ethyl-6,8-dihalogenobenzoyleneureas and 3,5-dihalogeno-2-aminobenzethylamides in variable amounts. The 2-aminobenzethylamides result directly from the anthranilic acids by successive treatments with phosphorus pentachloride and ethylamine, and react with ethyl chlorocarbonate to give the 3-ethylbenzoyleneureas. The latter are obtained directly on ethylation of the parent 6,8-dihalogenobenzoyleneureas.

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