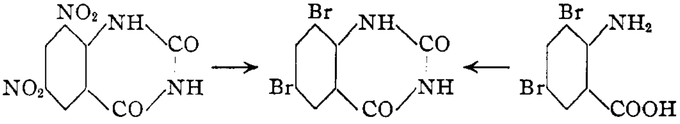
[CONTRIBUTION FROM THE CHEMICAL LABORATORY, CASE SCHOOL OF APPLIED SCIENCE]

6,8-Dibromobenzoylene Urea and the Constitution of Dinitrobenzoylene Urea

BY F. E. SHEIBLEY AND D. P. TURNER

By the direct nitration of benzolyene urea in sulfuric acid solution Bogert and Scatchard obtained a dinitro derivative which exhibited a sharp color change when used in acidimetric titrations. They investigated the limits of this change and dinitrobenzoylene urea has since assumed some importance as an indicator.[1] In a later paper the same authors[2] describe the preparation of 6-nitrobenzoylene urea by nitration with the theoretical amount of nitric acid. This compound was identified through its formation from methyl 2-nitrouramino-5-nitrobenzoate by the action of ammonia, and on further nitration was easily converted into dinitrobenzoylene urea. From the ease with which it is introduced they considered the most probable location of this second entering nitro group to be the 8-position, and an experimental verification of this conclusion is now realized.



I II III

6,8-Dinitrobenzoylene urea (I) was reduced and the resulting diamine[3] completely diazotized, the double diazonium salt thus obtained being converted into 6,8-dibromobenzoylene urea (II) by means of a Sandmeyer reaction. 3,5-Dibromoanthranilic acid (III) was fused with urea and the melt extracted with low-boiling solvents, leaving a residue of 6,8-dibromobenzoylene urea (II) identical with the corresponding substance (II) prepared from dinitrobenzoylene urea (I). Attempts to form the intermediate 3,5-dibromo-2-uraminobenzoic acid by treating acidic solutions of (III) in various solvents with potassium isocyanate were unsuccessful, the dibromoanthranilic acid being recovered unchanged. 5-Bromoanthranilic acid, however, is known to react with isocyanic acid under similar conditions to form the corresponding uramino acid, which can be easily dehydrated[4] to give the alkali-soluble 6-bromobenzoylene urea. The latter compound is now obtained by fusing 5-bromoanthranilic acid with urea. Conversely, and in agreement with the experience of Bogert and Scatchard with 5-nitroanthranilic acid,[5] 3,5-dinitroanthranilic acid was unaffected by fusion with urea, the similarity of the properties of the acid

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(1) Bogert and Scatchard, THIS JOURNAL, **38**, 1606 (1916).

(2) Bogert and Scatchard, *ibid.*, **41**, 2052 (1919).

(3) Ref. 2, p. 2060.

(4) Scott and Cohen, *J. Chem. Soc.*, **123**, 3187 (1923).

(5) Ref. 2, pp. 2053 and 2054.

with those of the product sought rendering improbable the detection of any small amounts of (I) that may have been formed. Other experiments designed to condense urea with 3,5-dinitro-2-chlorobenzoic acid resulted only in the formation of 3,5-dinitroanthranilic acid.

6,8-Dibromobenzoylene urea (II) is a high-melting, inert substance, soluble only in high-boiling solvents. Solutions of sodium and potassium hydroxides fail to dissolve it appreciably due to the formation of sparingly soluble salts. With the hydroxides of the other alkali metals, however, it is more soluble, forming solutions which yield a precipitate of the sodium salt directly when treated with aqueous solutions of sodium salts. The corresponding potassium salt may likewise be precipitated, but the separation is slower and less complete, and requires the use of stronger solutions than is the case with the sodium compound. From a series of comparative precipitation tests the order of increasing solubility of the alkali-metal salts of 6,8-dibromobenzoylene urea is found to be: Na, K, Li, Rb, Cs.

Unlike 6,8-dinitrobenzoylene urea, which could not be alkylated,[6] 6,8-dibromobenzoylene urea reacts with alkylating agents to form alkali-soluble monoalkyl derivatives. Of these, 3-ethyl-6,8-dibromobenzoylene urea possesses the more convenient properties and was studied, the ethyl group being assigned to the 3-position by analogy with previous observations[7] on the alkylation of benzoylene urea.

These experiments were performed in the laboratory of Dr. N. A. Lange, to whom the authors are indebted.

Experimental Part

Preparation of 6,8-Dibromobenzoylene Urea (II) from 6,8-Dinitrobenzoylene Urea (I).—6,8-Dinitrobenzoylene urea was reduced to the corresponding diamine by means of stannous chloride and concentrated hydrochloric acid, and the hydrochloride thus formed converted into the free base through treatment with ammonia.[3] A suspension of the free base, 6,8-diaminobenzoylene urea, in 30% hydrobromic acid was boiled for a few minutes, allowed to cool, and the insoluble hydrobromide removed by filtration and dried.

To 25 cc. of 30% hydrobromic acid diluted with 125 g. of ice and cooled externally with an ice and salt mixture, was added a cold aqueous solution of 3.75 g. of sodium nitrite. The resulting mixture was then stirred mechanically while 4.3 g. of 6,8-diaminobenzoylene urea hydrobromide suspended in 25 cc. of 30% hydrobromic acid was added slowly. By continuing the stirring and cooling for an hour a clear yellow solution was obtained. Attempts to diazotize the diamino compound by adding sodium nitrite to it in acid solution resulted in the formation of dark red precipitates.

A one liter, three-necked flask was equipped with a water-cooled reflux condenser, a thistle tube and a steam inlet tube both reaching to the bottom of the flask, and a thermometer the bulb of which was immersed in the reaction mixture; following, in general, the directions given elsewhere[8] for effecting a Sandmeyer reaction by the so-called hot method. Two grams of cuprous bromide was added to 80 cc. of 30% hydro-

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(6) Ref. 2, p. 2053.

(7) Lange and Sheibley, THIS JOURNAL, **55**, 2113 (1933).

(8) Fry and Grote, *ibid.*, **48**, 710 (1926).

bromic acid in the flask which was then warmed with a flame and steam passed in until the temperature reached 100°, when the solution of the diazonium salt prepared as described above was slowly introduced through the thistle tube, the temperature being maintained at 100–105°. A vigorous evolution of gas occurred and a pale brown precipitate separated. The mixture was heated and stirred with steam for ten minutes following the addition of all of the diazonium salt, and was then allowed to cool to 70°, after which the 2.1 g. of precipitated 6,8-dibromobenzoylene urea was removed by filtration, washed with water, and dried, m. p. 297°.

Preparation of 6,8-Dibromobenzoylene Urea (II) from 3,5-Dibromoanthranilic Acid (III).—Seven grams of 3,5-dibromoanthranilic acid[9] was fused with 4.1 g. of urea at 140° for about eight hours. The mass resulting on cooling was refluxed with ether, and the insoluble residue extracted successively with five 40-cc. portions of hot nitrobenzene. On allowing these extracts to cool, 6,8-dibromobenzoylene urea crystallized in small yellow needles, the melting points of the succeeding fractions varying from 293 to 295°. This material was collected, washed with ether and dried, the total yield being 5.6 g.

The yields were found to vary considerably with the temperature and duration of heating. In place of the ether and nitrobenzene extractions outlined above two treatments, each with 50 cc. of boiling acetone, in which the product is quite insoluble, may be substituted. The residue from this procedure was dissolved in a large excess of boiling lithium hydroxide solution, filtered and the filtrate acidified with dilute hydrochloric acid. The gelatinous precipitate that separated was collected, washed with water, dried and crystallized twice from hot glycol, yielding glistening, light yellow needles of 6,8-dibromobenzoylene urea, m. p. 305–306° corr.

Anal.[10] Calcd. for $C_8H_4O_2N_2Br_2$: Br, 49.97. Found: Br, 49.72, 49.86.

6-Bromobenzoylene urea was similarly obtained by fusing 7 g. of 5-bromoanthranilic acid[9] with 4.5 g. of urea. The brown porous solid that resulted was extracted with a hot solution of 2 g. of sodium hydroxide in 300 cc. of water, and the clear filtered extract acidified with hydrochloric acid, when the product separated as a thick flocculent precipitate. The compound was collected and dried and amounted to 6.6 g. of a yellow powder which did not crystallize satisfactorily from various solvents. Its hot saturated solution in dilute sodium hydroxide was allowed to crystallize, and the separated sodium salt redissolved in hot water and decomposed with acetic acid, which precipitated the 6-bromobenzoylene urea as a granular, light yellow solid, m. p. 357–358° corr. (dec.).[11]

6,8-Dibromobenzoylene urea is insoluble in the usual organic solvents and requires the use of high-boiling solvents in order to dissolve it. From its solution in cold concentrated sulfuric acid water precipitates it unchanged. Crystallization from glacial acetic acid was unsatisfactory, but crystallization from glycol is a convenient means of rapidly obtaining the pure substance. The products from both of the methods of preparation, *i. e.*, from dinitrobenzoylene urea and from dibromoanthranilic acid, were each subjected to such processes of purification as extraction of alkali-soluble impurities with sodium hydroxide and crystallization from nitrobenzene or an ethyl benzoate–alcohol mixture, and the preparations compared. In all cases they were identical and mixed melting points (305° corr.) between them showed no depression. Repeated attempts to determine the bromine content of these various preparations, using the method of Carius, gave low and inconsistent results.

Salts of 6,8-dibromobenzoylene urea with the alkali metals result directly on treating the free dibromo compound with aqueous solutions of the alkali hydroxides.

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(9) Wheeler and Oates, THIS JOURNAL, **32**, 772 (1910).

(10) Micro-Pregl determinations by Mr. R. S. Wobus.

(11) Haslinger, *Ber.*, **41**, 1453 (1908), gives m. p. 354°.

Strangely enough, the sodium salt is practically insoluble in water, and is by far the least soluble member of the group. The lithium salt, however, is somewhat more soluble and affords a convenient means of precipitating the sodium salt of dibromobenzoylene urea directly from aqueous solutions of sodium salts. A reagent was prepared by treating a mixture of 0.1 g. of dibromobenzoylene urea and 0.3 g. of lithium hydroxide with 5 cc. of water, heating to the boiling point, and diluting with 55 cc. of hot water. The suspension thus formed was boiled for a minute, when an almost clear solution resulted; this was stoppered and allowed to stand overnight and then filtered repeatedly until lithium carbonate ceased to precipitate and cloud the solution.

Half molar ($M/2$) solutions of cesium nitrate, rubidium chloride, potassium chloride, and sodium chloride were each diluted with an equal volume of the reagent: the sodium chloride solution became turbid and a white crystalline precipitate consisting of minute needles separated almost immediately; the other solutions remained clear. Molar solutions behaved similarly, excepting potassium chloride which precipitated within an hour; 2 M potassium chloride required only a few minutes. A $M/5$ sodium chloride solution was precipitated after a few minutes while a $M/10$ solution took a somewhat longer time to precipitate. A mixture of equal volumes of the $M/2$ sodium and potassium chloride solutions, when treated with a volume of the reagent, was also precipitated within a few minutes. These sodium salt precipitations are sometimes hastened by rolling the tubes between the hands; adding alcohol and shaking causes the precipitate to dissolve. Sodium nitrate, sodium sulfate, and sodium hydroxide solutions were likewise precipitated, but sodium salts of organic acids did not respond well to the test.

Ammonium hydroxide was not precipitated by the reagent but solutions of ammonium chloride and ammonium nitrate instantly gave white precipitates which, from their melting points, appear to be free dibromobenzoylene urea. The latter compound is very slightly soluble in boiling ammonium hydroxide (sp. gr. 0.9), from which solution a gelatinous precipitate separates slowly on cooling. Barium chloride, barium nitrate, and thallous sulfate, with the reagent, yielded heavy white precipitates.

In agreement with the failure of cesium nitrate to precipitate with the reagent, cesium hydroxide in aqueous solution dissolves considerably more dibromobenzoylene urea than does lithium hydroxide. A saturated solution, prepared by using an excess of cesium hydroxide, precipitated solutions of lithium chloride and lithium hydroxide within a few minutes, and acted in other respects like the solution of the dibromo compound in lithium hydroxide. It rapidly precipitated $M/10$ sodium chloride, while $M/2$ solutions of rubidium chloride and potassium chloride were precipitated slowly.

When the reagent in lithium hydroxide was allowed to stand for a few days it turned yellow to orange in color and gradually lost its power of precipitating sodium salts.

Sodium 6,8-dibromobenzoylene urea, precipitated by adding sodium hydroxide to a solution of the dibromo compound in aqueous lithium hydroxide, was collected, washed with water, and dried at 100° for two hours. Thus obtained, the salt forms a white powder consisting of microscopic hair-like needles, and has the composition of a monohydrate. It is insoluble in water or alcohol, slightly soluble in hot water, and soluble in dilute (1:1) alcohol. Attempts to determine its solubility in water at 25° gave consecutively lower results and indicated that a slight hydrolysis of the sample was taking place; the initial figure was 42 mg. of dissolved solids per 100 cc. of saturated solution. The compound becomes anhydrous during five days at 100°, or after twenty hours at 140°. When dried at 300° it decomposed. The analyses were made with four different preparations.

Anal. Calcd. for $C_8H_3O_2N_2Br_2NaH_2O$: Na, 6.39; H_2O, 5.01. Found: Na, 6.33, 6.34, H_2O, 4.87; Na, 6.06; Na, 6.22, 6.32; Na, 6.42, 6.25, H_2O, 5.07.

Lithium 6,8-dibromobenzoylene urea was obtained as a white solid on warming dibromobenzoylene urea with a small amount of aqueous lithium hydroxide solution. It is fairly soluble in water but, like the sodium salt, more soluble in dilute alcohol. Saturated solutions in water or dilute alcohol slowly deposited the salt in rosets of slender white needles. The compound was collected, washed with water and dried at 100°. Four analyses made with both the solid and crystallized material from different preparations gave results varying from 1.46 to 2.96% lithium; the mean of these four determinations is given.

Anal. Calcd. for $C_8H_3O_2N_2Br_2Li$: Li, 2.13. Found: Li, 2.16.

Preparation of 3-ethyl-6,8-dibromobenzoylene urea, $\overline{\mathrm{NC_2H_5COC_6H_2Br_2NHC}}\mathrm{O}$.—One gram of dibromobenzoylene urea mixed with 0.4 g. of lithium hydroxide was treated with 60 cc. of water, boiled, and diluted with 60 cc. of alcohol. Five cc. of ethyl iodide was added and the clear solution refluxed on a steam-bath for ten hours, after which the alcohol was removed by evaporation and the resulting generally acidic mixture diluted with 30 cc. of water. Complete precipitation was assured by the addition of a few cc. of hydrochloric acid, and the 1.1 g. of precipitate which had separated was collected, washed with water, dried, and extracted with a hot solution of 1 g. of sodium hydroxide in 80 cc. of water. The alkaline solution was filtered from undissolved sodium salts, and the 3-ethyl derivative precipitated by acidifying the fitrate with hydrochloric acid. The product was removed by filtration, washed with water, and dried, and amounted to about 0.9 g. It was dissolved in 60 cc. of hot glycol, filtered and allowed to crystallize, when it separated in lustrous white satiny needles, m. p. 251° corr. The compound is sparingly soluble in hot alcohol from which it crystallizes in long thin needles on cooling. Hot concentrated hydrochloric acid is without effect, but cold concentrated sulfuric acid dissolves it readily to give a solution from which water precipitates it unchanged. It is soluble in warm solutions of sodium hydroxide, needles of the sodium salt separating slowly on cooling. For analysis the products from two different preparations were crystallized from glycol, washed with alcohol, and dried at 100°. The sodium salt was washed with cold water and dried at 100° for four days.

Anal. Calcd. for $C_{10}H_8O_2N_2Br_2$: Br, 45.94. Found: Br (Carius), 45.17, 44.45. Calcd. for $C_{10}H_7O_2N_2Br_2Na$: Na, 6.22. Found: Na, 6.40.

The same compound was obtained when a solution of dibromobenzoylene urea and potassium hydroxide in warm glycol was treated with ethyl iodide, although the latter is practically immiscible with glycol. By the action of dimethyl sulfate on the dibromo compound suspended in cold aqueous solutions of sodium or potassium hydroxide, a supposed 3-methyl derivative, m. p. 268° corr., and only slightly soluble in sodium hydroxide, resulted. With *n*-propyl iodide and lithium hydroxide in dilute *n*-propyl alcohol, a probable 3-*n*-propyl derivative, m. p. 225° corr., was formed.

Summary

By reduction, diazotization and a Sandmeyer reaction, the dinitro derivative resulting from the direct nitration of benzoylene urea has been converted into a dibromobenzoylene urea identical with the 6,8-dibromobenzoylene urea obtained by fusing 3,5-dibromoanthranilic acid with urea. The dinitro compound is, therefore, 6,8-dinitrobenzoylene urea.

On fusion with urea, 5-bromo- and 3,5-dibromoanthranilic acids yield the corresponding substituted benzoylene ureas; the analogous nitro- and dinitroanthranilic acids are not affected by this treatment.

Whereas 6,8-dinitrobenzoylene urea cannot be alkylated, 6,8-dibromobenzoylene urea undergoes alkylation to form monoalkyl derivatives. Especially characteristic of 6,8-dibromobenzoylene urea is its insolubility in the ordinary caustic alkalies, and the formation of a sparingly soluble sodium salt which can be precipitated from aqueous solutions at room temperature. This salt offers possibilities to investigators who are interested in the microchemical detection of sodium.

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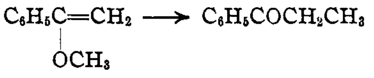
The Molecular Rearrangement of Alpha,Beta-Unsaturated Ethers[1]

BY WALTER M. LAUER AND MARVIN A. SPIELMAN[2]

It has long been known that certain α,β-unsaturated ethers rearrange on heating to form ketones. For the first example we are indebted to Claisen,[3] who found that α-ethoxystyrene readily forms phenyl propyl ketone "on short superheating such as boiling for a few hours under two atmospheres' pressure." Only a few such rearrangements have been recorded,[4] and the reaction is not general, since ethyl β-ethoxycrotonate, α-methoxymesityl oxide and phenyl vinyl ether, substances which might be expected to rearrange, failed to show such behavior.[5]

Previous studies have been confined to the establishment of rearrangement while the present one was undertaken in order to bring into sharper relief certain features dealing with the mechanism of the transformation. The α-alkoxy-styrenes lent themselves admirably to this purpose in view of the ease with which they may be prepared and the simplicity of the products which they form.

A. The Course of the Reaction.—When α-methoxystyrene was heated to temperatures in the neighborhood of 250–275° for an hour or more the chief product was always propiophenone formed by the normal rearrangement



$$C_6H_5C(OCH_3){=}CH_2 \longrightarrow C_6H_5COCH_2CH_3 \qquad (1)$$

but it was also evident that the reaction was more complicated than we had anticipated. On unsealing the tube in which the rearrangement was

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[1] The work described in this paper constituted part of the thesis submitted to the graduate faculty of the University of Minnesota by Marvin A. Spielman in partial fulfilment of the requirements for the degree of Doctor of Philosophy in June, 1933.

[2] Du Pont Fellow in Chemistry 1932–1933.

[3] Claisen, *Ber.*, **29**, 2931 (1896).

[4] Claisen and Haase, *ibid.*, **33**, 3778 (1900); Claisen, *ibid.*, **45**, 3157 (1912); Haller, *Compt. rend.*, **136**, 788 (1903); Staudinger and Ruzicka, *Helv. Chim. Acta.*, **7**, 386 (1924); Wislicenus and Schroeter, *Ann.*, **424**, 215 (1921).

[5] Wislicenus, *Ber.*, **33**, 1469 (1900); Pauly and Lieck, *ibid.*, **33**, 503 (1900); Powell with Adams, THIS JOURNAL, **42**, 646 (1920); Lauer and Spielman, *ibid.*, **55**, 1572 (1933).