# FORMATION AND PROPERTIES OF SOME URETEDIONES

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Hofmann (1) found that triethylphosphine converts phenyl isocyanate into a crystalline solid, m.p. 175°, which he called phenyl dicyanate and to which he assigned the formula  $C_{14}H_{10}N_2O_2$ , though he recorded no analytical data to support it. Snape (2) obtained the same compound by boiling a mixture of the isocyanate and pyridine, and analyzed his product for nitrogen only, which gave no information concerning the molecular weight of the polymer. Hofmann had previously attempted to fix this value by a vapor density determination, but was unsuccessful. He states, however, that treatment of the diisocyanate with alcohol converted it into the ester of the corresponding allophanic acid, which indicated that the polymer represented two molecules of the isocyanate. Dennstedt (3) and Frentzel (4) obtained similar results with 4-bromophenyl and 4-tolyl isocyanates, respectively. Structures for the polymers were not suggested.

Much later Warren and Wilson (5) reported that phenylurethan reacts with thionyl chloride to eliminate ethyl chloride, sulfur dioxide, and hydrogen chloride, and produces diphenyl diisocyanate, which they identified with Hofmann's product by melting point determination and analysis for nitrogen. Again, molecular weight measurements were not made, mechanism of formation, and structure for final product were not suggested.

At this point it should be noted that Raiford and Freyermuth (6) have recently shown that Warren and Wilson's observation is specific for phenylurethan. When the aryl radical contained a "negative" substituent, a mixture of the urethan and thionyl chloride underwent no change on standing at room temperature or upon refluxing for several hours. Compounds containing alkyl in the aryl radical formed tars from which nothing could be isolated.

Interest in further study of the formation and properties of such polymers resulted from an observation of Raiford and Shelton (7), who found that hot pyridine caused 2-carbophenoxyamino-4-methyl-6-bromophenyl 4-tolylsulfonate to lose phenol and give a polymerization product. It was assumed that loss of phenol from the starting material left 3-methyl-5-bromo-6-(4-tolyl)sulfonyloxyphenyl isocyanate (not isolated), and that two of these molecules united to give a derivative of the four-membered ring assigned by Staudinger (8) to Hofmann's polymerization product. Analyses of the compound in question for bromine, nitrogen, and sulfur, and molecular weight measurements supported this view. The product was designated as 1,3-di-(3-methyl-5-bromo-6-p-tolylsulfonyloxyphenyl) uretedione. The work of Hale (9) and of Hale and Lange (10) indicates that the existence of four-membered rings of this type is well established.



It was of interest to try to prepare by other means and isolate, if possible, the isocyanate mentioned above. To do this 2-nitro-4-methyl-6-bromophenyl 4-tolylsulfonate (11) was reduced to the corresponding amino compound, and a boiling toluene solution of the latter was saturated with phosgene. There was obtained in this way a 43% yield of purified material that melted at  $208-209^{\circ}$ , and which was identified by mixed melting point determination and molecular weight measurement as Raiford and Shelton's uretedione. When the amine had in the ortho position an exposed hydroxyl group a different type of product was obtained. When 2-amino-4-methyl-6-bromophenol was used as starting material, the isocyanate that was probably formed rearranged immediately into 5-methyl-7-bromobenzoxazolone previously obtained in a different way by Raiford and Inman (12). In no case could the isocyanate be isolated. The relationships are indicated in Figure 1.

In the work now reported the number of molecules of isocyanate involved in this polymerization was determined in most cases by molecular weight measurement. Two difficulties were met with in these experiments. Some of the products were practically insoluble in liquids that could be used for freezing-point determinations, and others were partially depolymerized at the high temperatures required for boiling-point determination in the liquids in which they were soluble. In such cases attempts were made to learn the molecular weights indirectly by study of some derivative of the polymer that was more soluble than the starting material.

Hofmann (13) noted that the phenyl diisocyanate he studied would react with ammonia and primary amines to give biurets, but he recorded no analytical data to support the composition of these products. In the present work it was found that aliphatic amines open the uretedione ring to give the related biurets. The cleavage involved must occur at but one place, otherwise there would be formed



some isocyanate and this would interact with a portion of the amine to give an unsymmetrical urea. To test that possibility here, the melting points, analytical data, and values for molecular weight measurements of the products in question were compared with those required by the related ureas. The importance of this consideration was illustrated in several cases as detailed below.

The action of *n*-propylamine on 1,3-diphenyluretedione gave a 96% yield of a product that melted at 115–116°. But Oliveri-Mandala' and Noto (14) recorded 114–116° for 1-*n*-propyl-3-phenylurea which they had obtained by a method quite different from the one employed here. A sample of their urea, prepared by the interaction of *n*-propylamine and phenyl isocyanate, melted at 115–116°, while a mixture of this and the compound here in question

melted with a depression of 26°. In addition, a molecular weight measurement of the biuret obtained from our polymer gave a value of 284 which compared favorably with the theoretical one of 297, while that required by the urea is 178. The interaction of the above uretedione with *n*-butylamine gave a compound that melted at 79–80°, which suggested that it might be a purer form of a byproduct, m.p. 65°, obtained by Davis and Blanchard (15) by heating a mixture of sym-di-*n*-butylurea and aniline, and which they supposed might be 1-*n*-butyl-3-phenylurea, but which they did not characterize further. To show that our substance was not the urea just named, the latter was prepared by the action of *n*-butylamine on phenyl isocyanate and was found to melt at 129–130°, and to depress the melting point of our biuret.

Difficulties with molecular weight measurements, noted above, were illustrated by the behavior of a compound, m.p. 196–197°, obtained by polymerization of 2-naphthyl isocyanate. Attempts to determine the freezing point of a 1,4dioxane solution were unsuccessful because the solute crystallized out. But partial support for the view that the polymer was a dimer was indicated by noting that it is quite different from a product of the same composition which showed no melting point but began to decompose at 220°, and which was synthesized by Otto (16) by a method which shows that the latter compound is  $\beta$ -trinaphthyl cyanurate, a trimer. Further proof that our product was a dimer was furnished by its interaction with *n*-butylamine, which gave an almost quantitative yield of a compound that gave nitrogen analyses and a molecular weight measurement in close agreement with values required by 1,3-di-(2-naphthyl)-5-*n*-butylbiuret, as shown below.

# EXPERIMENTAL

With the exceptions of the o- and p-chlorophenyl, the p-xenyl and the phenyl-p-azophenyl derivatives, the isocyanates used in this study were Eastman's purest products. Those prepared in this laboratory were made by Hardy's method (17) with such modifications as were required in individual cases.

4-(Phenylazo)phenyl isocyanate. A solution of 35 g. of 4-aminoazobenzene in 400 cc. of toluene was placed in a 500 cc. three-necked flask fitted with a mercury sealed mechanical stirrer, and return condenser. Dry hydrogen chloride was bubbled through the gently boiling liquid until the amine had been converted into the hydrochloride, which separated in finely divided form. Phosgene was then passed in at the rate of about four bubbles per second for three hours, which caused all solid to dissolve. The mixture was cooled and filtered to remove about 2 g. of solid that melted with decomposition at 270°, and which was identified as di-(4-phenylazophenyl)urea (18). About two-thirds of the solvent was distilled from the filtrate, and ligroin (65-70°) was added to the residue to precipitate the isocyanate. In a second experiment the filtrate left after removal of di-(4-phenylazophenyl)urea was mixed with 500 cc. of ligroin and the liquid was saturated with ammonia. This caused the separation of 38.5 g. of orange-yellow solid. Crystallization from ethanol gave orange plates that melted at 231° and which were identified as 4-phenylazophenylurea, previously obtained by Pierron (19) in a different way. The amount of urea isolated corresponded to a 90% yield of isocyanate in the reaction mixture. The isocyanate isolated from the first experiment was crystallized from ligroin and was obtained in very small orange needles that melted at 94-95°.

Anal. (Dumas) Calc'd for C13H9N8O: N, 18.83. Found: N, 18.54.

The catalyst, triethylphosphine, was prepared by the interaction of ethylmagnesium bromide and phosphorus tribromide in accordance with Slotta and Tschesche's (20) adaptation of Hibbert's (21) method, but with the further modification that our product was finally purified by distillation in an atmosphere of nitrogen. It boiled at 126-128°.

1-n-Butyl-3-phenylurea. A solution of 5 g. of phenyl isocyanate in 10 cc. of anhydrous ether was cooled in an ice-bath, and 15 cc. of an ether solution containing 5 g. of *n*-butylamine was slowly added. After ten minutes the solvent was distilled off, the remaining solid was crystallized from ethanol, and was obtained in colorless needles that melted at 129-130°, which is quite different from that of the product mentioned by Davis and Blanchard (15). A mixture of this urea and 1,3-diphenyl-5-*n*-butylbiuret shown in Table II melted at 73-74°. Their analyses, also, show that they are different.

Anal. Calc'd for C<sub>11</sub>H<sub>16</sub>N<sub>2</sub>O: N, 14.58. Found: N, 14.52.

Formation of uretediones. When the starting material was a liquid, two or three drops of the catalyst was added to about 30 g. of the isocyanate under an atmosphere of nitrogen in a suitable vessel. In many cases crystals appeared on the surface of the liquid in a few moments, and within half an hour some mixtures had solidified with the evolution of considerable heat. In a few cases solid isocyanates were melted and the catalyst was mixed with the liquid; while in others it was added to a dry, saturated 1,4-dioxane solution of the isocyanate prepared at room temperature. In all cases the mixtures were allowed to stand overnight in closed vessels, after which the solids were powdered, washed with anhydrous. ether to remove unchanged starting materials, and crystallized from suitable solvents.

1-(4-Chlorophenyl)-3-(4-tolyl) uretedione. To a mixture of 10 g. of 4-tolyl isocyanate and an equimolecular proportion of 4-chlorophenyl isocyanate a few drops of triethylphosphine was added, the mixture was allowed to stand, and was worked up as indicated above. Crystallization from *n*-butyl ether gave an 88% yield of colorless glistening scales that melted at 195°. Mixtures of this product with 1,3-di-(4-chlorophenyl)- and with 1,3-di-(4-tolyl)-uretediones, respectively, melted with pronounced depression.

Anal. Calc'd for C<sub>15</sub>H<sub>11</sub>ClN<sub>2</sub>O<sub>2</sub>: Cl, 12.39; N, 9.77; Mol. wt. 286.5.

Found: Cl, 12.38; N, 9.45; Mol. wt. (freezing point in 1,4-dioxane) 291.

1,3-Di-(1-naphthyl)uretedione. A few drops of triethylphosphine was added to 30 g. of 1-naphthyl isocyanate, the mixture was allowed to stand four days, and the resulting solid was crystallized from nitrobenzene. A 52% yield of colorless microscopic needles was obtained. The product sublimed at about 296°, and the odor of the isocyanate was detected in the vapor. Its insolubility in 1,4-dioxane prevented a molecular weight determination with that solvent, but the difference in properties between this substance and that of the same composition with a melting range of 160-225°, synthesized by Otto (16), shows that they are not identical. Since Otto's product was prepared by a method that proves it to be a cyanurate or trimer, this is partial support for the view that the one here in question is a dimer.

Anal. Calc'd for C<sub>22</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>: N, 8.28. Found: N, 8.49.

1,3-Di-(2-naphthyl)uretedione. Thirty grams of the related isocyanate was melted on an oil-bath and was polymerized by triethylphosphine as described previously. Crystallization from 1,4-dioxane gave large colorless plates that melted at 196-197°. The yield was 87%. Attempts to determine the molecular weight in dioxane solution were unsuccessful because the solute crystallized out. Again, the present product is quite different from Otto's  $\beta$ -trinaphthyl cyanurate (16) which showed no melting point, but began to decompose about 220°.

Anal. Calc'd for C<sub>22</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>: N, 8.28. Found: N, 8.41.

Hydrolysis of 1,3-di-(4-ethoxyphenyl)uretedione. A mixture of 10 g. of this compound and 200 cc. of 10% alcoholic potash was heated on a steam-bath, under reflux, for about ten minutes, the mixture was cooled, the colorless solid that separated was collected and washed with dilute hydrochloric acid. Crystallization from acetic acid gave a 55% yield of colorless needles that melted at 225-226°, and which were identified as sym-bis-(4-ethoxyphenyl)urea, previously obtained by Gattermann and Cantzler (22) by a different reaction.

TABLE I	
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SUBSTITUTION PRODUCTS OF 1,3-DIPHENYLURETEDIONE

MOL. WT.	DETERMINATION	Calc'd Found	238 237	266 264	266 277	326 332	U	307 314	307 293	396 435	v		U		U U	
	ogen	Found	ą	10.57	Ą	8.54	9.20	9.20	9.12		16.78		7.24		18.95	
YSES	Nitr	Calc'd		10.52		8.58	9.12	9.12	9.12		17.07		7.18		18.83	
ANAL	gen	Calc'd			_		23.12	23.04	22.91	40.42						
	Halo	Found					23.12	23.12	23.12	40.40						
	FORMULA		C14H10N2O2	C16H14N2O2	C16H14N2O2	C <sub>18</sub> H <sub>18</sub> N <sub>2</sub> O <sub>4</sub>	$C_{14}H_8Cl_2N_2O_2$	C <sub>14</sub> H <sub>8</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>2</sub>	C <sub>1</sub> ,H <sub>8</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub>	$C_{14}H_8Br_2N_2O_2$	C <sub>14</sub> H <sub>8</sub> N <sub>4</sub> O <sub>6</sub>		$C_{26}H_{18}N_2O_2$		C26H18N6O2	
	м.р., °С		175	159 - 160	185	181-182	234 - 235	153-154	155 - 156	203 - 204	Subl. at	300	270	(dec.)	281-282	(dec.)
	CRYSTAL FORM		Colorless plates	Colorless leaflets	Colorless needles	Colorless prisms	Colorless plates	Colorless needles	Colorless plates	Colorless leaflets	Yellow needles		Colorless flakes		Orange prisms	
	SOLVENT		<i>n</i> -Butyl ether	<i>n</i> -Butyl ether	n-Butyl ether	<i>n</i> -Butyl ether	Acetic acid	<i>n</i> -Butyl ether	<i>n</i> -Butyl ether	<i>n</i> -Butyl ether	Nitrobenzene		Nitrobenzene		Nitrobenzene	
	VIELD, 7/0 <sup>4</sup>		8	67	70	95	37	72	85	87	67		384		Ncarly	quant.
	SUBSTITUENTS IN PHENYL		Unsubst.	3-Methyl-	4-Methyl-	4-Ethoxy-	2-Chloro-	3-Chloro-	4-Chloro-	4-Bromo-	4-Nitro-		4-Phenyl-	-	4-Phenylazo-	

Refer to purified materials.
Previously analyzed.

<sup>c</sup> Due to insolubility in 1,4-dioxane and other suitable solvents molecular weights could not be determined.

<sup>d</sup> High temperature required caused partial depolymerization, and a low yield of product.

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DERIVATIVES OF 1,3-DIPHENYLBIURET

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IN PHENYL RADI- CALS	NITROGEN IN POSITION 5	VIELD,	CRYSTAL FORM <sup>b</sup>	м.Р., °С	FORMULA	Halo	gen	Nitro	gen		
						Calc'd	Found	Calc'd	Found	Calc'd	Found
Unsubst.	Methyl	57	Colorless needles	144-145	C <sub>15</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>			15.61	15.57	269	271
	Ethyl	61	Colorless needles	88-88	C <sub>16</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub>			14.84	14.90	283	284
_	n-Propyl	96	Colorless needles	115-116°	C <sub>17</sub> H <sub>19</sub> N <sub>3</sub> O <sub>2</sub>			14.14	14.13	297	284
	n-Butyl	68	Colorless needles	p08-62	$C_{18}H_{21}N_3O_2$			13.50	13.50	311	308
	iso-Amyl	73	Colorless prisms	62-64	C <sub>19</sub> H <sub>23</sub> N <sub>3</sub> O <sub>2</sub>			12.92	13.07	325	332
	Allyl	40	Large colorless prisms	94-95	$C_{17}H_{17}N_aO_2$			14.23	14.05	295	285
	5,5'-Ethylene	45	Small colorless prisms	171-172	$C_{30}H_{28}N_6O_4$			15.67	15.70	v	
	Piperidyl	8	Colorless needles	135-136	C <sub>19</sub> H <sub>21</sub> N <sub>3</sub> O <sub>2</sub>			13.00	12.76	323	316
3-Methyl-	n-Butyl	86	Colorless needles	102-103	$C_{20}H_{25}N_{3}O_{2}$			12.38	12.22	339	339
4-Methyl-	n-Butyl	94	Colorless needles	131-132	$C_{20}H_{25}N_{3}O_{2}$			12.38	12.46	339	332
4-Methyl-	4-Tolyl	53	Colorless needles	265	$C_{23}H_{23}N_{3}O_{2}$			11.26	11.40		
4-Ethoxy-	Methyl	8	Ncarly colorless needles	1110-111	$C_{19}H_{23}N_{3}O_{4}$	_		11.76	11.54	357	346
3-Chloro-	n-Butyl	37	Colorless needles	119-120	C18H19Cl2N3O2	18.67	18.61	11.05	11.05		
4-Chloro-	n-Butyl	57	Colorless square columns	104-105	C <sub>18</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	18.67	18.67	11.05	11.04	380	373
4-Bromo-	n-Butyl	840	Small colorless prisms	118-120	$\mathrm{C}_{18}\mathrm{H}_{19}\mathrm{Br}_{2}\mathrm{N}_{3}\mathrm{O}_{2}$	34.11	34.03	8.95	8.74	469	415
<sup>a</sup> Values re	present purified m	naterial	unless otherwise indicated.				-	-	-	-	

<sup>b</sup> All products were crystallized from ethanol.

\* A mixture of this product and 1-propyl-3-phenylurea, m.p. 114-116° (14), which could have been formed here if the uretedione ring had opened at two places, melted with a depression of about 26°.

<sup>d</sup> A mixture of this and 1-n-butyl-3-phenylurea, synthesized especially for this comparison, melted at 73-74°. • Solute crystallized out in attempted freezing point determinations.

I Reaction mixture was refluxed twenty-four hours.

" Crude yield.

Action of Grignard reagent on uretedione. When a solution of 20 g. of 1,3-diphenyluretedione in 250 cc. of anhydrous pyridine was slowly dropped into an ether solution containing somewhat more than two molecular proportions of ethylmagnesium bromide, a colorless solid precipitated. The mixture was poured into cracked ice and an excess of dilute hydrochloric acid was added with constant stirring. The ether layer was separated and the remaining solid was collected on a filter. Crystallization from ethanol gave long colorless needles that melted at 238-240°. The product was identified as sym-diphenylurea. Hentschel (23) recorded 235° for this product made in a different way.

Anal. Calc'd for C13H12N2O: N, 13.20. Found: N, 13.28.

The use of methylmagnesium iodide as reagent gave the same result.

Data for other uretediones are shown in Table I.

Preparation of biurets. These compounds were usually obtained by heating an ethanol solution of the uretedione and two molecular proportions of the required amine on a steambath for fifteen to thirty minutes, although the tritolyl derivative was prepared in 1,4-dioxane solution and refluxing was continued for twenty-four hours. Also, in at least one case heat was not required. When unsubstituted diphenyluretedione was mixed with methylamine solution, reaction took place spontaneously with the evolution of heat. Molecular weight measurements were made by the freezing point method in 1,4-dioxane which had been purified as directed by Oxford (24).

1,3-Di-(2-naphthyl)-5-n-butylbiuret. A 1,4-dioxane solution of 10 g. of the required uretedione was heated on a steam-bath with two molecular proportions of *n*-butylamine. The product that separated on cooling was purified by repeated crystallization from ethanol and was obtained in colorless needles that melted at 117-118°.

Anal. Calc'd for C<sub>26</sub>H<sub>25</sub>N<sub>3</sub>O<sub>2</sub>: N, 10.21; Mol. wt, 411.

Found: N, 10.31; Mol. wt. (freezing point in dioxane) 423. Data for other biurets are given in Table II.

## SUMMARY

1. The effect of nuclear substituents on the stability of aryl isocyanates obtained by the action of phosgene on aromatic primary amines was tested. The isocyanate obtained from 3-methyl-5-bromo-6-(4-tolylsulfonyloxy)aniline could not be isolated. It dimerized at once into 1,3-di-(3-methyl-5-bromo-6-*p*-tolylsulfonyloxyphenyl)uretedione. When the starting amine contained an exposed hydroxyl group in the ortho position, the isocyanate formed rearranged immediately, by ring closure, into 5-methyl-7-bromobenzoxazolone.

2. Several new uretediones have been obtained by polymerization of the required isocyanates in the presence of triethylphosphine as catalyst. A mixture of two different isocyanates treated in this way gave an unsymmetrical uretedione.

3. Many of these compounds are but little soluble in the usual organic solvents. They react with primary aliphatic amines to form 1,3,5-trisubstituted biurets.

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