[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF MIAMI UNIVERSITY]

Molecular Rearrangements. I. The Base-catalyzed Condensation of Benzil with Urea[1]

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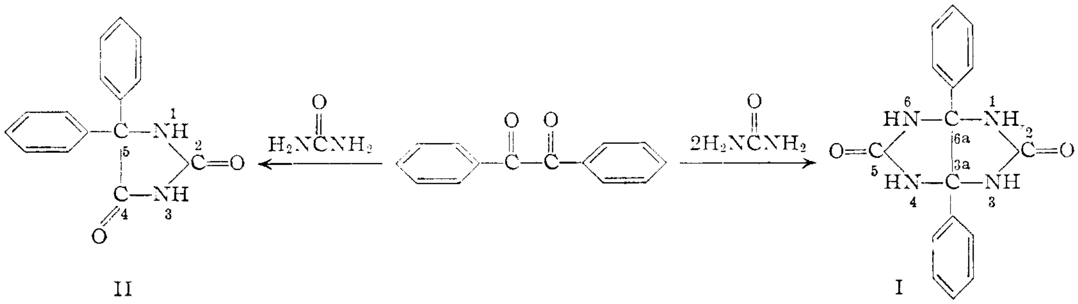
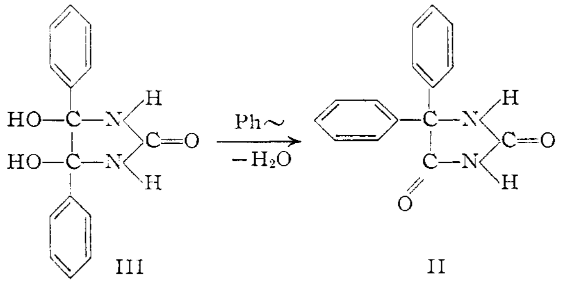
The formation of 5,5-diphenylhydantoin by the condensation of benzyl with urea under the influence of ethanolic potassium hydroxide involves a molecular rearrangement which has hitherto been considered to be a pinacol rearrangement. An investigation of the reaction conditions and the condensation of 4,4′-disubstituted benzils with urea leads us to the conclusion that the rearrangement is that of the benzilic acid type, rather than the pinacol rearrangement. A number of new 5,5-di-(4-substituted phenyl)-hydantoins and 3a,6a-di-(4-substituted phenyl)-glycolurils were prepared.

The condensation of benzil and urea in ethanolic potassium hydroxide solution gives 3a,6a-diphenylglycoluril (I) and 5,5-diphenylhydantoin (II).



The formation of the hydantoin (II) involves a molecular rearrangement in which a phenyl group undergoes a 1,2-shift and has been cited as an example of the pinacol rearrangement.[3,4] It was proposed,[3] and the view is still accepted,[5] that the reaction proceeds stepwise with the formation of the intermediate 4,5-diphenyl-4,5-dihydroxy-2-imidazolone (III) followed by a pinacol rearrangement to the hydantoin (II).

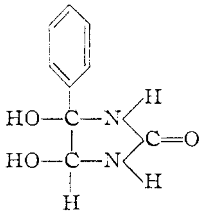


To support this mechanism III was synthesized[6] and found to rearrange to II in alcoholic potassium hydroxide solution. Condensation of III with urea was found to result in the corresponding glycoluril (I).

However, III was never isolated as an intermediate of the reaction between benzil and urea. Analogous reactions[7,8] in which urea and glyoxal were condensed gave corresponding 1,2-dihydroxy intermediates which rearranged to give hydantoins. These reactions, however, were carried out under acidic conditions.

Fisher, Ekeley and Ronzio[9] report condensing urea with phenylglyoxal and obtained 5-phenyl-4,5-dihydroxy-2-imidazolone (IV)

IV



which rearranged under both alkaline and acidic conditions to give its corresponding hydantoin. No mention of further condensation to its glycoluril was made.

The possibility of a benzilic acid rearrangement in the condensation of benzil with urea was rejected[10] when it was found that benzilic acid and urea in alcoholic sodium hydroxide solution failed to produce 5,5-diphenylhydantoin (II).

Discussion and Results

In the exploratory stages of this work we studied the effect of varied reaction conditions on the relative yields of 5,5-diphenylhydantoin (II) and 3a,6a-diphenylglycoluril (I) from the condensation of benzil with urea.

In a series of runs the molar ratio of benzil to urea was varied from 1:1.05 to 1:2.81 (Table I). From the results it appeared that the extent of hy-

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[1] Taken in part from the M.S. thesis of W. R. Dunnavant, Miami University, August, 1954.

[2] Chemistry Research Branch, Aeronautical Research Laboratory, Wright Air Development Center.

[3] H. Biltz, *Ber.*, **41**, 169 (1908).

[4] C. W. Porter, "Molecular Rearrangements," Chemical Catalog Co. (Reinhold Publ. Corp.), New York, N. Y., 1928, p. 96.

[5] K. Hofmann, "Imidazole and Its Derivatives, Part I," Interscience Publishers, Inc., New York, N. Y., 1953, p. 230.

[6] H. Biltz *Ber.*, **41**, 172 (1908).

[7] L. Siemonsen, *Ann.*, **333**, 102 (1904).

[8] H. Pauly and H. Sautei, *Ber.*, **63**, 2063 (1930).

[9] H. Fisher, J. Ekeley and A. Ronzio, THIS JOURNAL, **54**, 4116 (1932).

[10] H. Biltz, *Ber.*, **41**, 1384 (1908).

dantoin formation was not appreciably affected by variation of the molar ratio, but the glycoluril yield gradually increased as the ratio of urea to benzil increased.

Table I

Effect of Varying the Urea Concentration

The runs were conducted by refluxing 0.0095 mole of benzil and 0.0178 mole of potassium hydroxide in ethanol with varying amounts of urea.

Urea, mole	Hydantoin yield, mole	Glycoluril yield, mole
0.010	0.0056 ± 0.0003[a]	0.0012 ± 0.0002
.013	.0066 ± .0001	.0015 ± .0001
.017	.0060 ± .0002	.0022 ± .0003
.023	.0064 ± .0001	.0023 ± .0001
.027	.0054 ± .0006	.0034 ± .0008

[a] Average deviations calculated on a minimum of three runs.

Since the formation of the hydantoin is a base-catalyzed reaction, it seemed desirable to determine what proportion of alkali was needed for optimum hydantoin yields. Accordingly, a series of preparations was made with a constant amount of benzil and urea, and an increasing potassium hydroxide concentration (Table II). It was of interest to note that when no alkali was used, condensation failed to occur and unreacted benzil was recovered. Hydantoin yields increased rapidly with increasing alkali concentration, but the yield became constant when the molar ratio of benzil to potassium hydroxide reached about 1:1.87. The glycoluril yield decreased as the alkali concentration increased and became about constant at the same benzil–potassium hydroxide ratio, 1:1.87. Further increase in alkali concentration gave little change in either hydantoin or glycoluril yields.

Table II

Effect of Varying Alkali Concentration

These runs were carried out by refluxing 0.0095 mole of benzil and 0.0166 mole of urea with varying amounts of potassium hydroxide

KOH, mole	Hydantoin yield, mole	Glycoluril yield, mole
0.000	None[a]	None[a]
.009	0.0054 ± 0.0002[b]	0.0035 ± 0.0003
.018	.0060 ± .0002	.0022 ± .0003
.027	.0060 ± .0001	.0026 ± .0002
.036	.0060 ± .0001	.0023 ± .0004

[a] No reaction occurred. Unreacted benzil was recovered in 97% yield. [b] Average deviations calculated on a minimum of three runs.

A series of preparations was run in which the addition of urea to the reaction mixture was delayed. These runs indicated that as the time interval increased the yields of both the hydantoin and glycoluril decreased (Table III). The results were in agreement with the reported failure[10] of the benzilate ion to condense with urea.

A number of 4,4′-disubstituted benzils were used in place of benzil in an attempt to determine the relative migratory aptitudes of the substituted phenyl groups. These values were compared to the orders available for the pinacol and benzilic acid series. The validity of these results may be questioned, however, due to the fact that they were obtained from hydantoin yields in a reaction where glycoluril formation is a strong competing reaction. These reactions, in each case, used a molar ratio of benzil to urea of 1:1.84 and resulted in a number of previously unreported 5,5-di-(4-substituted phenyl)-hydantoins and 3a,6a-di-(4-substituted phenyl)-glycolurils (Tables IV and V).

Table III

Effect of Delaying Addition of Urea to Reaction Mixture

These experiments were performed by delaying the addition of 0.0166 mole of urea to refluxing mixtures containing 0.0095 mole of benzil and 0.0178 mole of potassium hydroxide and continuing the reflux for 2 hr. from that time.

Minutes delay	Hydantoin yield, moles	Glycoluril yield, mole
0	1.52 ± 0.07[a]	0.65 ± 0.09
15	1.05 ± .02	.21 ± .05
30	1.16 ± .12	.10 ± .04
45	1.05 ± .12	.01 ± .00

[a] Average deviations calculated on a minimum of three runs.

Table IV

Benzil	Benzil, mole	Hydantoin, mole	Glycoluril, mole	Urea[a] reacting, %	Rearrangement,[b] %
Benzil	0.0095	0.0071	0.0022	98	74.7
4,4′-Dichloro-	.0101	.0075	.0027	101	74.2
4,4′-Dimethyl	.0094	.0068	.0015	88	72.3
4,4′-Dibromo	.0095	.0063	.0015	82	66.3
4,4′-Dimethoxy	.0096	.0060	.0025	89	62.5
4,4′-Diisopropyl	.0095	.0043	.0050	98	45.2
4,4′-Diethoxy	.0084	.0030	.0048	93	35.7
4,4′-Diacetamido	.0094	.0000	.0043	46	00.0
4,4′-Bis-(dimethyl)-amino	.0095	.0000	.0064	67	00.0

[a] Calculated from the amount of benzil required for the hydantoin and glycoluril yields obtained. [b] Calculated as the percentage of starting benzil which has gone to hydantoin.

It was noted that 4,4′-diacetamido- and 4,4′-bis-(dimethylamino)-benzils, previously reported[11] as failing to undergo the benzilic acid rearrangement, also failed to give the corresponding hydantoins in this reaction.

With this information we were able to make a comparison between the relative orders of five groups in the pinacol, benzilic acid and benzil to hydantoin rearrangements. For the pinacol series[12-15] the order is *p*-methoxyphenyl > *p*-methylphenyl > *p*-isopropylphenyl > phenyl > *p*-chlorophenyl. The benzilic acid series[11] gives *p*-chlorophenyl > phenyl > *p*-methylphenyl > *p*-isopropylphenyl > *p*-methoxyphenyl. The order obtained in the benzil to hydantoin rearrangement was found to be phenyl > *p*-chlorophenyl > *p*-methylphenyl > *p*-methoxyphenyl > *p*-isopropylphenyl. It will be seen that the orders of the last two series are almost the reverse of that of the pinacol series.

An attempt was made to condense benzil and urea in an acidic medium. When an ethanol–sulfuric acid mixture was used as the reaction solvent no condensation occurred. This indicates

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(11) F. James and A. Ippolito, *J. Ohio Acad. Sci.*, **53**, 31 (1953).

(12) W. E. Bachman and F. Moser, This Journal, **54**, 1124 (1932).

(13) W. E. Bachman and H. Steinberger, *ibid.*, **55**, 3821 (1933).

(14) W. E. Bachman and H. Steinberger, *ibid.*, **56**, 170 (1934).

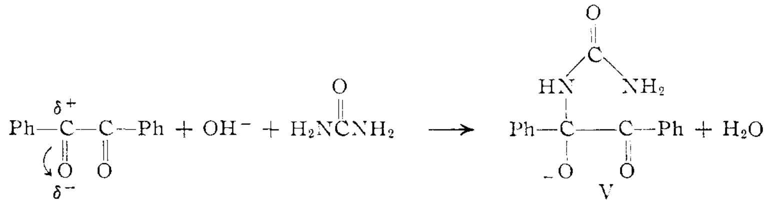
(15) W. E. Bachman and J. Ferguson, *ibid.*, **56**, 2081 (1934).

that the hydroxyl ion is essential in order for condensation to occur.

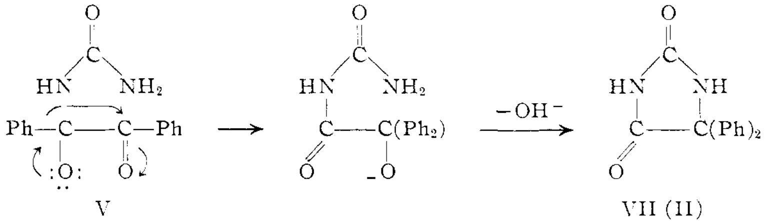
It was found that III rearranged to II in an acidic as well as an alkaline solution. Attempted rearrangement of III by refluxing in ethanol failed to result in the formation of II, eliminating the possibility that the above rearrangements were caused by the temperature at which they were carried out.

The mechanism of the rearrangement involved in the alkaline-catalyzed condensation of benzil with urea is not yet understood. However, there are several possible courses that the reaction might take as indicated by the data.

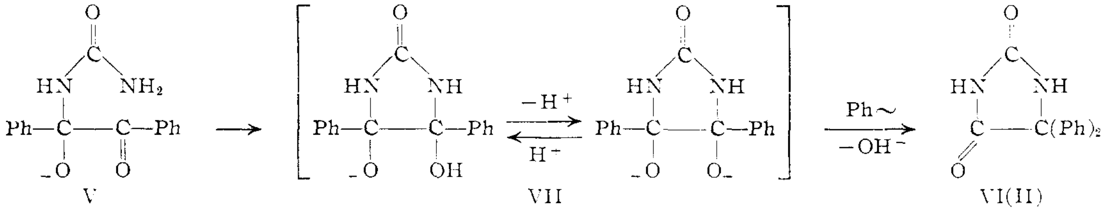
The first step would involve condensation of urea with the benzil by nucleophilic attack on a carbonyl carbon resulting in the formation of V.



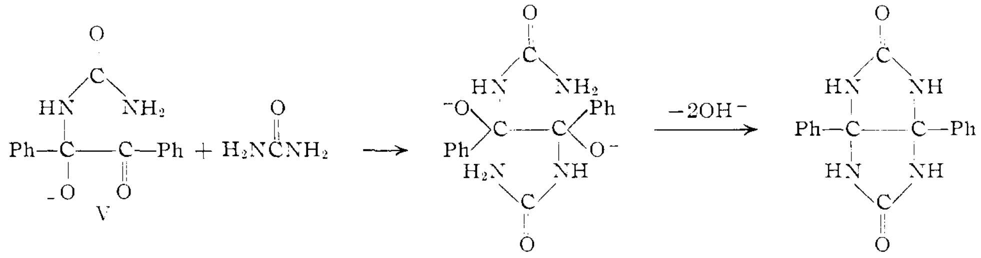
The rearrangement of V followed by ring closure would give the hydantoin VI (II)



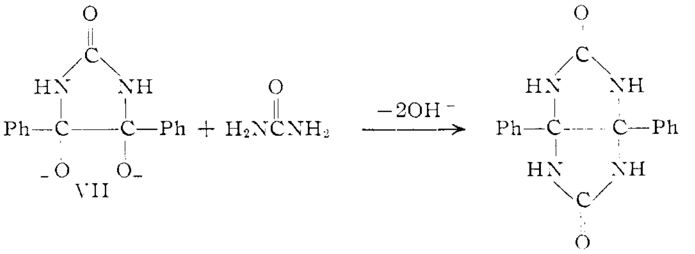
A second route to the hydantoin might be ring closure of V to VII followed by rearrangement.



The glycoluril could be explained by a mechanism involving condensation of the second mole of urea with V



or by condensation of the second mole of urea with VII.



Further work is in progress to determine the identity of the intermediate ion and to choose between these mechanisms.

Experimental[16]

Variation of Reactions of Benzil with Urea.—In each case 0.0095 mole of benzil, 0.0166 mole of urea and 0.0178 mole

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[16] All melting points reported here are uncorrected.

of potassium hydroxide was used except for the variations stated in Tables I, II and III. These materials were added to 40 ml. of U.S.P. ethanol and refluxed on a water-bath for 2 hr. in a 150-ml. r.b. flask fitted with a reflux condenser. The hot reaction mixtures were then poured in ice-water and the 3a,6a-diphenylglycolurils precipitated. These precipitates were filtered onto tared filter papers and dried over calcium chloride in a desiccator for 2 days before weighing. The samples were then recrystallized from glacial acetic acid. The first product obtained was analyzed by nitrogen determination and subsequent products were characterized by their melting points. All samples melted in the range 390–394°. According to the literature[3] 3a,6a-diphenylglycoluril fails to melt at 330°.

Anal. Calcd. for $C_{16}H_{14}O_2N_4$: N, 19.09. Found: N, 18.70.

The filtrates from the glycoluril filtrations were then acidified with concentrated hydrochloric acid and the 5,5-diphenylhydantoins were precipitated. These were isolated and dried as above. The samples were recrystallized from ethanol. The identities of the products were checked in the same manner as were the glycolurils. All samples melted in the range 289–293°. The literature m.p. of 5,5-diphenylhydantoin is given as 293°.[17]

Attempted Condensation of Benzil with Urea in Neutral Solution.—An identical reaction to those previous was run except that no alkali was added. Addition of water to the reaction mixture produced a light yellow precipitate of fine needle-like crystals weighing 1.94 g. and melting at 93–95°, which was identical with the starting benzil.

Attempted Condensation of Benzil with Urea in Acidic Solution.—Another identical reaction was run except that 1 ml. of concentrated hydrochloric acid was substituted for the potassium hydroxide. Addition of water brought down a light yellow precipitate weighing 1.98 g. which melted at 94–96°, again unreacted benzil.

Condensation of 4,4′-Disubstituted Benzils with Urea.—All of the benzils listed in Table IV were refluxed with urea and ethanolic potassium hydroxide. Reaction mixtures consisted of 0.095 mole of the benzil, 0.016 mole of urea and 0.017 mole of potassium hydroxide in 40 ml. of U.S.P. ethanol. They were refluxed for 2 hr. and then worked up in the same manner as the reaction products of benzil and urea. The new products resulting are characterized in Table V.

TABLE V

Compound	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
3a,6a-Di-(4-ethoxyphenyl)-glycoluril	147–149	14.65	14.26
5,5-Di-(4-ethoxyphenyl)-hydantoin	195–198	8.23	8.21
3a,6a-Di-(4-bis-dimethylaminophenyl)-glycoluril	199–201	22.09	22.01
3a,6a-Di-(4-acetamidophenyl)-glycoluril	237–239	20.51	20.50
3a,6a-Di-(4-phenoxyphenyl)-glycoluril	215–217	11.71	10.08
5,5-Di-(4-phenoxyphenyl)-hydantoin	182–185	6.43	6.27
5,5-Di-(4-chlorophenyl)-hydantoin	226–230	8.83	8.81
3a,6a-Di-(4-chlorophenyl)-glycoluril	285–287	15.43	15.43

Rearrangement of III to II in Acidic Solution.—4,5-Diphenyl-4,5-dihydroxy-2-imidazolone (III) was prepared by the method of Breur and Zincke.[18] The material melted at 169–170°. The literature decomposition point[18] is 170°.

One gram of III was added to 30 ml. of U.S.P. ethanol containing 1 ml. of concentrated sulfuric acid. The mixture was thoroughly mixed and refluxed for 2 hr. on a water-bath. Upon pouring into cold water a precipitate of II formed weighing 0.32 g. (34%) which, after recrystallization from ethanol, decomposed at 169–170°.

Attempted Rearrangement of III in Neutral Solution.—The same procedure as above was carried out using 0.5 g. of III and omitting the acid. Upon pouring the reaction mixture into cold water, a white flocculent precipitate formed weighing 0.48 g. and melting at 200° (III).

Acknowledgment.—We are indebted to A. L. Ippolito for the preparation of the 4,4′-disubstituted benzils and to Miami University for financial assistance in conducting this study.

OXFORD, OHIO

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[17] H. Biltz, *Ann.*, **368**, 243 (1909).

[18] A. Breur and T. Zincke, *ibid.*, **198**. 151 (1879).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Stereospecific Reactions of Nucleophilic Agents with Acetylenes and Vinyl-type Halides. I. The Mechanism of the Base-catalyzed Reaction of *cis*-Dichloroethylene with Thiols[1]

BY WILLIAM E. TRUCE, MAX M. BOUDAKIAN, RICHARD F. HEINE AND ROBERT J. MCMANIMIE

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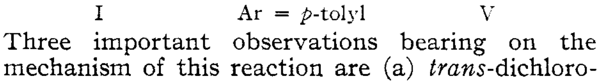
Evidence, both kinetic and chemical, is presented to account for the stereospecific conversion of *cis*-dichloroethylene (I) to *cis*-1,2-bis-(*p*-tolylmercapto)-ethene (V). The proposed reaction sequence is presented in the Introduction as an elimination–addition mechanism. The conversion of chloroacetylene (II) to III, and *p*-tolylmercaptoacetylene (IV) to V, constitute stereospecific *trans* nucleophilic additions across a triple bond.

Introduction

There are several reports that *cis*-dichloroethylene (I) reacts readily with nucleophilic agents such as sodium benzenthiolate,[2,3] sodium *p*-toluenethiolate,[2] sodium 2-methyl-2-propanethiolate[4] and potassium sulfite,[5] while the *trans* isomer, when treated likewise, is recovered unchanged.

The detailed mechanisms of the reactions of nucleophilic agents with the dichloroethylenes were unknown and constitute the purpose of this and later papers. The reaction chosen for this study was the one obtained with the thiolates[2]



I Ar = *p*-tolyl V

Three important observations bearing on the mechanism of this reaction are (a) *trans*-dichloroethylene does not react, (b) sodium ethoxide is necessary in order for any reaction to occur and (c) the final product has exclusively the *cis* structure. The following three mechanisms were considered for the conversion of *cis*-dichloroethylene (I) to *cis*-bis-(arylmercapto)-ethene (V).

A. Nucleophilic Displacement Mechanism.—One possible reaction path is an S_N2 process

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[1] This paper was presented in part before the Division of Organic Chemistry at the Fall 1955 Meeting of the American Chemical Society in Minneapolis, Minn. Abstracted in part from the Ph.D. Thesis of Max M. Boudakian and from the M.S. Thesis of Richard F. Heine.

[2] W. E. Truce and R. J. McManimie, THIS JOURNAL, **76**, 5745 (1954).

[3] W. E. Parham and J. Heberling, *ibid.*, **77**, 1175 (1955).

[4] H. J. Backer and J. Strating, *Rec. trav. chim.*, **73**, 565 (1954).

[5] W. E. Truce and M. M. Boudakian, THIS JOURNAL, **78**, 2752 (1956).