TABLE III

MELTING POINTS OF 2,4-DINITROPHENYLHYDRAZONES

| 2,4-Dinitrophenyl-hydrazone of | M.P., °C. Found | M.P., °C. Reported | Reference |
|---|---|---|---|
| Acetaldehyde | 148–148.5 | 147 (162) | 10 |
| Propionaldehyde | 147–148 | 154 | 10 |
| *n*-Butyraldehyde | 122–123 | 122 | 10 |
| Enanthaldehyde | 106.0–106.5 | 106 | 10 |
| Isobutyraldehyde | 182–183 | 182 | 10 |
| α-Ethylbutyraldehyde | 94–95 | 94 | 11 |
| Hydratropaldehyde | 136–137 | 136–137 | 12 |
| Acetone | 126–127 | 126 | 13 |
| Methyl ethyl ketone | 118–119 | 115 | 10 |
| Pinacolone | 126–127 | 125 | 16 |
| Cyclopentanone | 146–146.5 | 146–147 | 13 |
| 4-Methylcyclohexanone | 133.5–134.0 | 134.7–135.1 | 15 |
| Benzylacetone | 127–128 | 125–126.3 | 14 |

TABLE IV

MELTING POINTS OF SEMICARBAZONES

| Semicarbazone of | M.P., °C. Found | M.P., °C. Reported | Reference |
|---|---|---|---|
| Isobutyraldehyde | 118–119 | 125 | 17 |
| α-Ethylbutyraldehyde | 95–96 | 96 | 17 |
| Methyl *n*-amyl ketone | 123–124 | 121–123 | 18 |
| Di-*n*-butyl ketone | 90–91 | 90 | 19 |
| Pinacolone | 157–158 | 157 | 20 |

hyde (7%). The concentrations of the semicarbazone solutions were as follows: isobutyraldehyde 20%, α-ethylbutyraldehyde 15%, methyl *n*-amyl ketone 7%, di-*n*-butyl ketone 14%, pinacolone 10%.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CANISIUS COLLEGE]

# Abnormal Beckmann Rearrangements in Polyphosphoric Acid. I. Benzil Monoxime and Related Oximes[1,2]

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The Beckmann rearrangement of alpha-benzil monoxime and alpha-benzoin oxime in polyphosphoric acid to yield benzonitrile as one of the rearrangement products in each case is reported. These data, together with the direct nitrosation of desoxybenzoin, indicate the rearrangements of these oximes in polyphosphoric acid are examples of the abnormal Beckmann rearrangement rather than the normal Beckmann rearrangement as previously reported. The rearrangement of alpha-benzil dioxime in polyphosphoric acid quantitatively yields 3,5-diphenyl-1,2,4-oxadiazole.

The Beckmann rearrangement of alpha-benzil monoxime and alpha-benzoin oxime has been the subject of extensive study.[4] Although the nature of the products has varied with the acid catalyst used and the conditions of the reaction, in general, each oxime has been shown to yield products which could arise from an initial normal Beckmann rearrangement.[5] It has been reported,[6] that alpha-benzil monoxime (I) in polyphosphoric acid at 120° undergoes the Beckmann transformation to yield initially dibenzamide (II) as shown in Fig. 1. The dibenzamide was believed to be hydrolyzed by the medium to yield the isolated products, namely, benzoic acid and benzamide. These

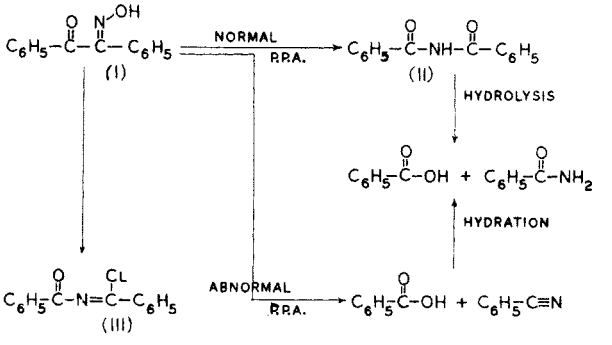


Figure 1

(1) Preliminary results of this investigation are reported in *Tetrahedron*, **3**, 90 (1958).
(2) This work was supported by a Frederick Gardner Cottrell grant from the Research Corp.
(3) Abstracted in part from the thesis submitted by F. A Mikulski to the Department of Chemistry, Canisius College in fulfillment of the requirements for the Bachelor of Science degree.
(4) A. H. Blatt, *Chem. Revs.*, **12**, 215 (1933).
(5) N. V. Sidgwick, *The Organic Chemistry of Nitrogen*, (revised and rewritten by T. W. J. Taylor and W. Baker), Oxford University Press, 1942, p. 182.
(6) E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *J. Am. Chem. Soc.*, **74**, 5153 (1952).

data were in general agreement with the rearrangement of alpha-diketone monoximes on treatment with other acid catalysts. For example, treatment of alpha-benzil monoxime with phosphorus pentachloride in ether yields *N*-benzoylbenzimido chloride (III) which on hydrolysis yields ammonia and two molecular equivalents of benzoic acid. Recently, it has been reported[7] that certain $\alpha,\alpha$-disubstituted ketoximes rearranges abnormally in polyphosphoric acid. Presumably, these rearrangements proceed through a nitrile intermediate. Also, the behavior of amides in polyphosphoric acid solution[8] indicates that hydrolysis of the postulated dibenzamide intermediate would not have occurred under the conditions of the Beckmann rearrangement. Finally, it has been shown that benzonitrile can be hydrolyzed to benzamide almost quantitatively in polyphosphoric acid at temperatures similar to those used to effect the Beckmann rearrangement.[9] These data indicated that the rearrangement of alpha-benzil monoxime in polyphosphoric acid may proceed *via* the abnormal path as has been observed in the base catalyzed rearrangement of this substance.[10] For example, alpha-benzil monoxime on treatment with benzene–sulfonyl chloride in pyridine or alkali solution undergoes cleavage to yield benzonitrile and benzoic acid. This direct cleavage reaction has been called a second-order Beckmann rearrangement or an abnormal Beckmann rearrangement.

In light of these studies, it was of interest to reinvestigate the Beckmann rearrangement of alpha-benzil monoxime in polyphosphoric acid. However, it was desirable to carry out this investigation under experimental conditions such that the hydrolysis of the nitrile, if produced, would be minimized. It was also of interest to extend the study to include the rearrangement of alpha-benzoin oxime and alpha-benzil dioxime in this medium.

The rearrangement of alpha-benzil monoxime was carried out at three temperatures. These reactions are summarized in Table I. The rearrangement of alpha-benzil monoxime, therefore, initially yields benzonitrile which at higher temperatures is hydrolyzed by the medium to benzamide. This was confirmed by heating alpha-benzil monoxime with polyphosphoric acid for 8 hr. The reaction mixture was then divided into two parts; the first part was hydrolyzed with ice water and the products separated in the usual manner to yield predominantly benzoic acid and benzonitrile, the second part was heated at 120° for 15 min. and the reaction mixtures treated in an identical fashion. The products were benzoic acid and benzamide only. No nitrile could be detected.

TABLE I

VARIATION OF THE PRODUCTS OF THE REARRANGEMENT OF ALPHA-BENZIL MONOXIME WITH TEMPERATURE

| Temp., °C. | Time, Min. | Yield, % | Product |
|---|---|---|---|
| 25 | 420 | 96 | Benzoic acid |
| | | 87 | Benzonitrile |
| | | 3 | Benzamide |
| 65 | 90 | 98 | Benzoic acid |
| | | 80 | Benzonitrile |
| | | 15 | Benzamide |
| 120[a] | 15 | 98 | Benzoic acid |
| | | 92 | Benzamide |
| | | 0 | Benzonitrile |

[a] Ref. 6; report the product distribution under slightly different conditions (temp. 90–115°.C) to be: benzoic acid, 100%; benzamide, 40%; benzonitrile, none detected.

Further substantiation of these results was obtained by the direct nitrosation of desoxybenzoin[11] in polyphosphoric acid at 25°. As expected, the nitroso compound, so produced, rearranged under the acid conditions to the oxime which further rearranged, *in situ*, to yield benzonitrile and benzoic acid. None of the postulated reaction intermediate, dibenzamide, was observed under any of the reaction conditions used in this study.

The rearrangement of alpha-benzoin monoxime was carried out under the same time-temperature conditions as were used for alpha-benzil monoxime (Table I). In all cases, an appreciable amount of tarring of the reaction mixture took place. However, at 25°, benzaldehyde was isolated in 33% yield and benzonitrile in 26% yield by column chromatography over activated alumina, which separated the benzonitrile-benzaldehyde fraction from the tars, followed by micro fractional distillation. At 120°, a small amount of benzaldehyde was isolated (as the 2,4-dinitrophenylhydrazone derivative) and a small amount of a yellow solid, identified *via* its infrared spectrum as benzamide, was also obtained. Further attempts to separate and identify components of the reaction mixture were not undertaken. It is clear, however, that the nitrile is produced in appreciable amounts and that the rearrangement most probably follows the "abnormal" path in polyphosphoric acid.

The rearrangement of alpha-benzil dioxime (IV) in polyphosphoric acid at 25° yields predominantly 3,5-diphenyl-1,2,4-oxadiazole (V). However, frac-

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(8) (a) R. T. Conley, doctoral dissertation, Princeton University (1957); (b) R. K. Hill, *J. Org. Chem.*, **22**, 830 (1957); (c) C. T. Elston, doctoral dissertation, University of Illinois (1954).

(9) H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.*, **76**, 3039 (1954).

(10) (a) A. Werner and A. Piquet, *Ber.*, **37**, 4295 (1904); (b) O. Diels and M. Stern, *Ber.*, **40**, 1629 (1907).

(11) It has come to our attention since the submission of the preliminary results of this investigation, Ref. 1, that a similar experiment was performed by C. T. Elston, Ref. 8c. At that time this author concluded the Beckman rearrangement of alpha-benzil monoxime did not proceed normally as reported by Horning, Stromberg, and Lloyd, Ref. 6 [See F. D. Popp and W. E. McEwen, *Chem. Revs.*, **58**, 372 (1958).]

tional crystallization of the crude product from absolute alcohol yielded *N*-phenyl-*N*-benzoylurea (VI) (4%). At 120°, only 3,5-diphenyl-1,2,4-oxadiazole could be isolated (99%). These data are summarized in Fig. 2. The rearrangement in this

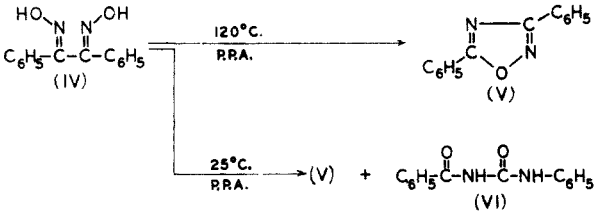


Figure 2

case undoubtedly follows the normal Beckmann path. Rearrangement occurs at one oximino-group followed by cyclization to form the oxadiazole ring. At the lower temperature, however, a small amount of a doubly rearranged product was obtained. This product could not have arisen from the alpha-dioxime.[4] Therefore, it must be assumed that a small amount of inversion of configuration must have occurred during the rearrangement since the product would be expected to be formed only from the gamma-dioxime on the basis of a trans migration of the phenyl groups.

From the results of this study, it is quite clear that the monoximes of both benzil and benzoin follow the abnormal Beckmann rearrangement path in polyphosphoric acid rather than the normal rearrangement previously postulated by Horning, Stromberg, and Lloyd.[6] Further studies of the rearrangement of alpha-diketoximes in polyphosphoric acid are presently being carried out and will be reported at a later time.

Examples of typical rearrangement procedures are given in the Experimental section. The rearrangement products were identified in all cases with authentic samples prepared by reported procedures. The criteria of identity were two; no depression in mixed melting point and identical infrared spectra.

## EXPERIMENTAL

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are corrected. The infrared spectra used for comparison were determined using a Baird, model 2-B, double beam, recording spectrophotometer. The reactants were obtained from commercial sources and purified by repeated crystallization.

*Rearrangement of alpha-benzil monoxime.* A mixture of 10 g. (0.045 mole) of alpha-benzil monoxime and 120 g. of polyphosphoric acid was stirred intermittently in a 250-ml. Erlenmeyer flask for 8 hr. at 25°C. The mixture was hydrolyzed over crushed ice and water. The hydrolysis mixture was extracted 6 times with 150-ml. portions of ether. The combined ether extracts were washed 3 times with 50-ml. portions of 10% sodium hydroxide solution. Acidification of the basic wash solution with dilute hydrochloric acid in the cold yielded 5.28 g. (96%) of benzoic acid, m.p. 121.5–122°. A mixed melting point with an authentic sample showed no depression, m.p. 121.5–122°.

The combined ether extracts were dried over magnesium sulfate, filtered, and evaporated. The products, obtained as a light yellow oil, were chromatographed over a small column of activated alumina in petroleum ether (65–70° fraction). Elution of the column with 1:1 petroleum ether–diethyl ether mixture yielded on evaporation of the solvents 3.94 g. (87%) of benzonitrile, characterized by its infrared spectrum, conversion to benzoic acid and ammonia with hot 25% potassium hydroxide solution, and hydration to benzamide, m.p. 128–130° with polyphosphoric acid, according to the method described by Snyder and Elston.[9] Elution of the column with 1:1 chloroform–diethyl ether yielded on evaporation of the solvents 0.16 g. (3%) of benzamide, m.p. 128–130°. Mixed melting point with an authentic sample showed no depression, m.p. 128.5–130°. Further elution of the column with first chloroform and then ethyl alcohol did not remove further material from the column.

*Nitrosation of desoxybenzoin in polyphosphoric acid.* A mixture of 9.80 g. (0.05 mole) of desoxybenzoin, 3.45 g. zoin, 3.45 g. (0.05 mole) of sodium nitrite, and 125 g. of polyphosphoric acid was stirred at 25° for 7.5 hr. The mixture was hydrolyzed over crushed ice and water. A thick, brown paste separated. The aqueous mixture was extracted 5 times with 100-ml. portions of ether.

The combined ether extracts were washed 3 times with 50-ml. portions of 10% sodium hydroxide solution. On acidification of the combined base washings, 4.60 g. (75%) of benzoic acid was obtained m.p 118.5–121°. The ether extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated. The residue was distilled *in vacuo* to yield 3.40 g. (67%) of benzonitrile, b.p. 68–70°/10 mm. and 2.4 g. of residue which on cooling solidified. The low melting, solid residue was taken up in a minimum amount of chloroform and passed thru a small alumina column to yield on evaporation of the chloroform solution 2.1 g. (21.4%) of desoxybenzoin, m.p. 55–56°. No depression of the mixed melting point with the starting material was observed, m.p. 55–56.5° and the infrared spectra of the two were identical.

*Rearrangement of alpha-benzoin oxime.* A mixture of 5.0 g. (0.022 mole) of alpha-benzoin oxime and 90 g. of polyphosphoric acid was stirred intermittently for 8 hr. at 25°. The black reaction mixture was hydrolyzed in the usual fashion. A black, viscous mass separated. The aqueous mixture was thoroughly extracted with ether. The ether extracts were combined, dried over anhydrous magnesium sulfate, filtered, and evaporated. The residue was taken up in a minimum amount of chloroform and chromatographed over an activated alumina column packed in ether. The column was eluted with 1:1 chloroform ether. On evaporation, of the first 150 ml. of eluent, a light yellow benzaldehyde-benzonitrile mixture was obtained. This mixture was distilled *in vacuo* to yield 0.76 g. (33%) of benzaldehyde, b.p. 60–63°/10 mm., characterized by its 2,4 dinitrophenylhydrazone derivative, m.p. 236–237.5° and its semicarbazone derivative, m.p. 222.5° (neither derivative showed depression on mixed melting point determination with derivatives prepared from an authentic sample of benzaldehyde) and 0.58 g. (26%) of benzonitrile. No separation of the tarry residue remaining on the column could be effected by elution with successively more polar solvent mixtures.

*Rearrangement of alpha-benzil dioxime.* A mixture of 5.2 g. (0.021 mole) of alpha-benzil dioxime and 80 g. of polyphosphoric acid were heated together at 120° for 12 min. The reaction mixture was hydrolyzed in the usual manner. A flocculent white precipitate formed immediately. After filtration and vacuum drying 4.62 g. (99%) of 3,5- diphenyl-1,2,4-oxadiazole was obtained, m.p. 108–108.5°. Repeated recrystallization from absolute ethanol or sublimation did not alter the melting point.

*Anal.* Calcd. for $C_{14}H_{10}N_2O$: C, 52.65; H, 8.82; N, 24.52. Found: C, 52.60; H, 8.76; N, 24.23.

Mixed melting point with an authentic sample prepared

by the method outlined by Beckmann[12] showed no depression, m.p. 108–108.5°.

*Acknowledgments:* The authors wish to thank Professor R. K. Hill of Princeton University for his many comments and suggestions in connection with these investigations and Canisius College for a Faculty Research Grant to R.T.C. to aid in the preparation of this communication.

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BUFFALO 8, N. Y.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI]

# Substituted γ-Lactones. II. Some Electrophilic Substitution Reactions of α-Benzylidene-γ-butyrolactone

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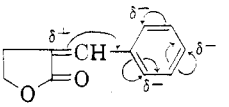
In electrophilic substitution reactions, α-benzylidene-γ-butyrolactone (I) is similar to cinnamic acid. It can be nitrated predominantly in the para position. With chlorosulfonic acid it gives the *p*-chlorosulfonyl derivative (VIII). The structures of the substitution products have been verified by oxidative degradation. The reduction of the three isomeric α-nitrobenzylidene-γ-butyrolactones and the preparation of several derivatives of the α-aminobenzylidene-γ-butyrolactones obtained is described.

In a previous paper[2] the condensation of several aldehydes with butyrolactone was described. It has been found that this reaction did not proceed well with nitrobenzaldehydes or with *p*-acetamidobenzaldehyde, which compounds gave small yields or substantially no yields at all. However, nitro- and amino-substituted α-benzylidene- γ-butyrolactones and some of their derivatives were desired in order to investigate their pharmacological properties; therefore, a nitration of the readily available[3] α-benzylidene-γ-butyrolactone (I) was attempted. The nitration products obtainable from this reaction could serve as intermediates in the preparation of the corresponding amino compounds and derivatives thereof. We also were interested in sulfonic acid derivatives of I and hence ran a sulfochlorination of I.

Reaction of I with potassium nitrate in concentrated sulfuric acid at low temperature[4] furnished a 60% yield of α-(*p*-nitrobenzylidene)-γ-butyrolacrone (II) and a lesser amount of the *o*-isomer (III). The structures of the compounds obtained were proven by oxidative degradation to the corresponding nitrobenzoic acids, and, in the case of II, by comparison with an authentic sample, obtained by a condensation between *p*-nitrobenzaldehyde and butyrolactone.[2] In one experiment which was carried out with an excess of potassium nitrate, a small yield of a dinitro product, presumably α-(2,4-dinitrobenzylidene)-γ-butyrolactone (IV), was obtained.

These experiments show that in I electrophilic substitution occurs in the *p*- and *o*-positions. This can be explained by assuming that during the attack of the nitrating agent a time-variable electromeric electron shift occurs similarly to that observed in the nitration of cinnamic acid,[5] thus, activating the ortho and para positions towards an electrophilic attack: The ratio of the yields of II




and III is about 3.3:1. Underwood and Kochmann,[5b] in the nitration of cinnamic acid, observed a para: ortho ratio of about 2.5:1. The greater tendency of I towards para-substitution can be explained by the appreciable amount of steric hindrance imposed by the lactone ring on the ortho positions. Accordingly the sulfochlorination of I gave predominantly the *p*-chlorosulfonyl derivative (VIII). The corresponding ortho derivative could not be isolated. Probably due to increased steric hindrance, its formation might occur only to a minor extent, if any.

Reduction of II, III, and of α-(*m*-nitrobenzylidene)-γ-butyrolactone (V)[2] with stannous chloride and concentrated hydrochloric aicd gave solid complexes which on treatment with aqueous ammonia and subsequent extraction with an organic solvent such as chloroform or tetrahydrofuran gave the corresponding amino derivatives in high

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(2) H. Zimmer and J. Rothe, *J. Org. Chem.*, **24**, 28 (1959).

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