The Beckmann Rearrangement of 1,2-Cyclohexane-dione Dioxime in Liquid Sulfur Dioxide[1]

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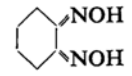
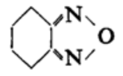
The Beckmann rearrangement of 1,2-diketone dioxime has scarcely been reported on except in the case of benzil dioximes[2]. In the present article the authors wish to reports on the Beckmann rearrangement of 1,2-cyclohexanedione dioxime in liquid sulfur dioxide, which resulted in a variety of interesting products.

Several examples of the Beckmann rearrangement, in which the directions of the course of the rearrangement were affected by difference in the reagents applied or conditions used have been published. In a report of Brown, van Gulic and Schmid[3], for instance, the migratory aptitude of pivalophenone oxime was found to be largely dependent upon the nature of the reagent applied, the oxime being subjected to geometrical isomerization before rearrangement[4]. The present authors have also observed that the Beckmann rearrangement of 1,6-cyclodecanedione dioxime yielded different products accoding to the different reagents used in the rearrangement. Such complicated results have also been reported by McLaren and Schacht[5], and Yukawa and his associates[6]. However, one of the anomalies during the rearrangement, the occurrence of the syn-anti isomerization of the oximes before the rearrangement, can be largely reduced as was reported in a recent article[7] if the reaction is conducted in liquid sulfur dioxide.

In a preceding paper[8], the present authors reported on their unsuccessful attempt at the Beckmann rearrangement of 1,2-cyclohexanedione dioxime (I) with thionyl chloride in liquid sulfur dioxide. They obtained only a dehydrated product, cyclohexano[c]-1,2,5-oxadiazole (II) in a yield of 70 per cent.



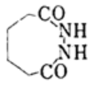
I



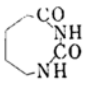
II

Although the reaction with thionyl chloride was unfruitful, however, the bromine in liquid sulfur dioxide and the sulfur trioxide in sulfur dioxide afforded the rearranged products with which the present paper is concerned.

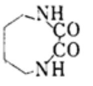
As 1,2-cyclohexanedione dioxime (I) has not been found to have geometrical isomers and as the various reagent examined in this material have given no symptom of the presence of geometrical isomers, the problem of the possible isomer was excluded in this experiment. In view of the authors' experience with the Beckmann rearrangement, it is interesting to examine the formation of the three possible cyclic acidamide III, IV, V or the mixture of these compounds in the reaction products. But the transformation to any of these three has not been observed.



III

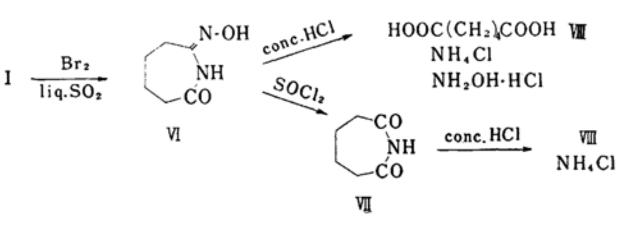


IV



V

Bromine in liquid sulfur dioxide yielded a half-rearranged product as follows:



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[1] The Beckmann Rearrangement in Liquid Sulfur Dioxide. Part VIII.

[2] J. Meisenheimer and W. Lamparter, *Ber.*, **57**, 276 (1924).

[3] R. F. Brown, N. M. van Gulic and G. H. Schmid, *J. Am. Chem. Soc.*, **77**, 1094 (1955).

[4] N. Tokura, R. Tada and K. Suzuki, This Bulletin, **32**, 654 (1958).

[5] A. D. McLaren and R. E. Schacht, *J. Org. Chem.*, **14**, 254 (1949).

[6] Y. Yukawa, "Jikken Kagaku Koza", Vol. 18, Maruzen, Tokyo (1958), p. 426.

[7] R. Tada, Y. Masubuchi and N. Tokura, This Bulletin, **34**, 209 (1961).

[8] Part VII of this series, This Bulletin, **34**, 270 (1961).

The product was contaminated with a large amount of brown resinous matter from which white crystalline substances VI were isolated by acetone extraction in a yield of 32 per cent. A very small amount of II was also found in the mixture. The substance VI, m. p. 155°C, was soluble in water, acid, base, ethyl alcohol and acetone respectively but was insoluble in ether, benzene and chloroform. When VI was subjected to hydrolysis with concentrated hydrochloric acid, adipic acid, ammonium chloride[9] and hydroxylamine hydrochloride[10] were identified in the reaction mixture; no hydrazine salt was found in the mixture[11], however, the infrared spectrum of VI also proved the presence of OH and NH (2900~3200 cm^{-1}, strong and broad) and carbonyl (1620~1600 cm^{-1}, strong) groups. Moreover, the NMR spectrum of VI in dimethylsulfoxide confirmed the presence of =NOH and =NH, as in Fig. 1[12]. The peak of the oximine group was consistent with that of cyclohexanoxime, and the very low and broader absorbancy in the higher field corresponded to that of the imino group.

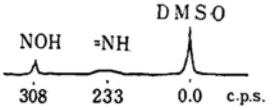
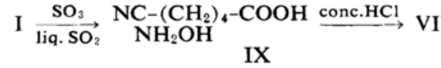


Fig. 1. NMR spectrum of VI in DMSO. c. p. s. was taken with that of DMSO as standard.

Thus the structure of VI was established as 1-aza-7-oximinocyclohepta-2-one. In order to effect the rearrangement of the remaining oximino group of VI, VI was further subjected to a reaction with thionyl chloride in ether. The resultant product seemed likely to be adipic imide (VII)[13], the oximino group being eliminated from VI without accepting further rearrangement. The hydrolysis of VII with concentrated hydrochloric acid afforded adipic acid (VIII) and ammonium chloride. The infrared spectrum of VII was agreeable with that of cyclic imide as reported by Vegstky et al.[14]

The attempted rearrangement with sulfur trioxide in liquid sulfur dioxide was accompanied by a large resinous matter. By extracting the viscous reaction mixture with ether, an orange oil (IX) was obtained. The oil boiled at 181~183°C/17 mmHg, and its yield was 23 per cent.



$$\mathrm{I}\ \xrightarrow[\text{liq. }SO_2]{SO_3}\ \underset{\underset{\text{IX}}{NH_2OH}}{NC\text{-}(CH_2)_4\text{-}COOH}\ \xrightarrow{\text{conc.HCl}}\ \text{VIII}$$

The compound IX was identified as δ-cyanovaleric acid from the elemental analysis, the infrared spectrum, the hydrolysis to adipic acid, the esterification and the saponification value of the ester. The present authors also found hydroxylamine in the residue of the reaction mixture by the diacetyl monoxime method[10]. Thus, the cleavage of I to IX seems likely to pass through an intermediate, 1, 2-cyclohexanedione 2-monoxime (X), which might be derived through partial hydrolysis of an oximino group of I, the so-called Beckmann rearrangement of the second order being followed. An alternative explanation is also conceivable and will be discussed later.

Experimental

Materials.—Commercial sulfur dioxide was dried with concentrated sulfuric acid[15] and distilled.

Bromine was dehydrated with concentrated sulfuric acid and distilled. Sulfur trioxide of extra pure grade was used without further purification. 1,2-Cyclohexanedione dioxime (I) was synthesized[8] from 2-halo-cyclohexanone by reacting with hydroxylamine in yields of 10 to 34 per cent.

Infrared Spectrum.—A Perkin Elmer model 21 infrared spectrophotomer was used.

NMR Spectrum.—A Varian Associates' type V-4300 (40 mc.) nuclear magnetic resonance spectrometer was used.

Reaction of Bromine on I.—The dioxime(I) (14.2 g.) and bromine (35.2 g.) were reacted in 150 ml. of liquid sulfur dioxide at room temperature for one hour. When the reaction was over, the solution was poured into ice-water, the sulfur dioxide was evaporated and the residue was extracted with ether. From the ether extract, colorless crystals were obtained after the condensation of the solution. This substance was identified as cyclohexano-[c]-1, 2, 5-oxadiazole (II), which had already been produced and confirmed by the reaction of thionyl chloride on I in liquid sulfur dioxide[8], by its m. p. and mixed m. p. of 25.5~26.0°C: the yield was 0.6 g. (4%). The residual solution was neutralized with sodium carbonate and extracted with chloroform. Seven grams of resinous material was obtained from the solution, but the nature of this material was obscure.

The residual solution of the chloroform extraction was condensed in vacuo and triturated with acetone. On the evaporation of acetone, 4.6 g. (32%) of colorless crystals resulted. This crystal, VI, melting at 155°C (from water or ethyl alcohol), was soluble in water, acid, base, ethyl alcohol and acetone respectively but was insoluble in ether, benzene and

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9) By Nessler reagent.

10) W. Hirscher and J. A. Verboeff, *Chem. Abstr.*, **17**, 2845 (1923).

11) L. Szebelledy and V. Madis, ibid., **31**, 6128 (1937).

12) The NMR spectrum was taken by the courtesy of Prof. T. Isobe.

13) E. N. Zilbermann, *Chem. Abstr.*, **50**, 8458 (1956): H. K. Hall, Jr. and A. K. Schneider, *J. Am. Chem. Soc.*, **80**, 6411 (1958).

14) A. Vegstky, K. Harada and S. W. Fox, *J. Am. Chem. Soc.*, **80**, 336 (1958).

15) D. Murakami and N. Tokura, This Bulletin, **31**, 431 (1958).

chloroform. The elemental analysis showed no difference to the starting oxime I, suggesting that a rearrangement was undertaken in this reaction.

Found: C, 51.21; H, 6.85; N, 19.68. Calcd. for $C_6H_{10}O_2N_2$: C, 50.69; H, 7.07; N, 19.71%. IR $\nu_{\max}^{\text{KBr}}$ 2900~3200 (strong and broad, -OH and =NH); 1660 (strong and broad, =CO) and 1620 weak, -C=N) cm^{-1}, respectively.

Hydrolysis of VI.—VI (2.0 g.) was refluxed for 2 hr. in concentrated hydrochloric acid. After the reaction, the colorless needles (III) so produced were filtered and recrystallized from ethyl alcohol, 1.1 g., m. p. 151~152°C. The mixed melting point with adipic acid showed no depression.

Found: C, 49.46: H, 6.94. Calcd. for $C_6H_{10}O_4$: C, 49.31: H, 6.90%.

The filtrate was evaporated to dryness. This residue contained ammonium chloride (Nessler test). Also hydroxylamine hydrochloride was identified[10]. No hydrazine salt was found in the residual mixture[11].

Reaction of IV with Thionyl Chloride.—VI(0.5 g.) was refluxed in ether (20 ml.) with thionyl chloride (0.5 g.) for fifteen minutes. The reaction mixture was poured into ice-water, and white powder (0.2 g.), m. p. 166.5°C., was yielded by the ethereal solution. This compound VII was assumed to be adipic acid imide from the elemental analysis, the infrared spectrum and the hydrolysis with concentrated hydrochloric acid to adipic acid (VIII), the melting point and the mixed melting point being 152°C.

Found: N, 1030, Calcd. for $C_6H_9O_2N$: N, 11.02%. IR $\nu_{\max}^{\text{KBr}}$ 3200 and 3350, (strong, =NH), 1700 (=CO) and 2950 (=CH_2) cm^{-1}, respectively. From the reaction mixture of the hydrolysis, after the filtration of the afforded adipic acid, neither hydrazine nor hydroxylamine salt was identified by the procedure described above.

Reaction of I with Sulfur Trioxide.—I (7.1 g.) and sulfur trioxide (10.0 g.) were reacted in 100 ml. of sulfur dioxide for one hour at room temperature. The reaction mixture was poured into ice-water, after which the sulfur dioxide was allowed to evaporate and was then extracted with ether. The ethereal solution was washed with water, dried and evaporated. An orange-colored liquid (IX), boiling at 181~183°C/17 mmHg, $n_D^{17}=1.4452$, 1.6 g. (23%), was obtained and identified as δ-cyano-valeric acid, (literature[16], b. p. 158~160°C/5 mmHg, $n_D^{20}=1.4481$).

The residual solution after the extraction contained a large amount of resinous matter which could not be further examined.

Found: N, 10.53. Calcd. for $C_6H_9O_2N$: N, 11.02%. IR $\nu_{\max}^{\text{liq.}}$, 3000~3300 (strong and broad, -OH), 2260 (medium, -CN) and 1700 (strong, =CO) cm^{-1}, respectively.

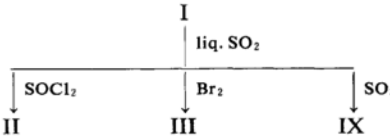
Hydrolysis of IX—IX(0.3 g.) was reacted with 3 ml. of concentrated hydrochloric acid by refluxing. On cooling of the reaction mixture, colorless needles were obtained in the mixture, which on admixture with adipic acid (VIII) showed no depression of the m. p. of 151~152°C.

Esterification of IX.—IX(2.0 g.) and two drops of concentrated sulfuric acid in 4 ml. of absolute ethyl alcohol were refluxed for 24 hr. The mixture was then mixed with water, and the separated oil was dried and distilled. An oil of b. p. 252~256°C 760 mmHg, (reportedly[16] 145~150°C/24 mmHg), was obtained. This oil was consistent with ethyl δ-cyano-valerate.

Found: C, 60.83; H, 8.37; N, 8.44, Calcd. for $C_8H_{13}O_2N$: C, 61.91; H, 8.44; N, 9.03%. Sapon. value, Found, 706.5, Calcd., 722.5.

Discussion

When I was reacted with three different reagents, thionyl chloride, bromine and sulfur trioxide respectively, in liquid sulfur dioxide, for one hour at room temperature, three different products were obtained, viz., cyclohexano[c]-1, 2, 5-oxadiazole (II), 1-aza-7-oximino-cyclohepta-2-one (VI) and δ-cyano-valeric acid (IX) respectively, among which the first has been presented in a preceding paper[8].



If the reactions were performed without sulfur dioxide, no such simple product was obtained. Thus, thionyl chloride yielded much resinous matter, and II was obtained in a yield of zero to ten per cent. Bromine afforded only nitrosobromo compound, the presence of which was recognized by the blue color formation. Sulfur trioxide also produced a large amount of resin. This means that the reaction in liquid sulfur dioxide was greatly favored by the assistance of the solvation of this solvent, which enabled the reaction to be carried out at a lower temperature and to avoid various side reactions.

The results obtained above may be useful to enhance our understanding of the mechanism of the Beckmann rearrangement in liquid sulfur dioxide. Not only were the three products different, but the features of the respective processes were entirely different.

They were a dehydrative condensation, a Beckmann rearrangement of one of the two oximino groups, and a ring cleavage reaction respectively. The Beckmann rearrangement of 1, 2-diphenyl-1, 2-dione dioxime (benzil dioxime) which reportedly consisted of three geometrical isomers, has already been reported[17]. According to Meisenheimer and Lamparten[2], the β-isomer of XI afforded oxanilide XII, both of the two oximino groups rearranging, whereas α- and γ-isomers yielded

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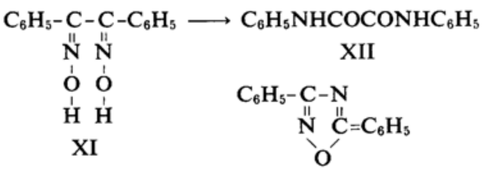
16) R. H. Wiley and H. S. Morgan, Jr., *J. Org. Chem.*, **15**, 800 (1950); W. Reppe, *Ann.*, **596**, 127 (1955).

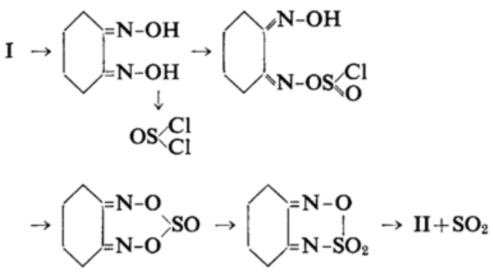
17) a) K. Awers and V. Meyer. *Ber.*, **21**, 810 (1888). b) E. Beckmann and A. Koster, *Ann.*, **274**, 18 (1893). c) E. Gunther, *Ber.*, **21**, 516 (1888); *Ann.*, **257**, 276 (1889).

3, 5-diphenyl-1, 2, 4-oxadiazole (XIII), a product of one oximino group rearrangement followed by dehydration. The reagent used were thionyl chloride and phosphorus compounds.

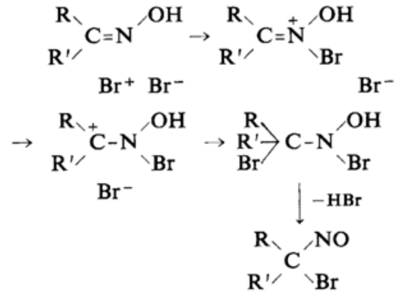

XI XII XIII

That a simple dehydration occurred by thionyl chloride from I to II indicates that the rate of the Beckmann rearrangement of I with thionyl chloride was much less than the rate of condensation with the same reagent in liquid sulfur dioxide. In such a cyclic dioxime as I, the steric impedence by the ring enlargement, if it arose, would be considerable. On the other hand, in the case of XI, no steric hindrance was anticipated, and the formation of azilinium cation favorable for the Beckmann rearrangement may be greatly assisted by the participation of the phenyl group.

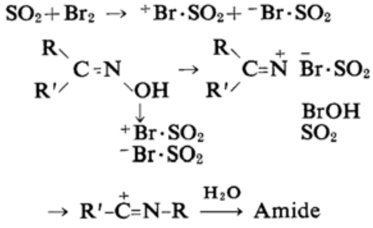
The predominance of the condensation reaction between the two competitive reaction is a result of the nature of the reagent (thionyl chloride). A=N–O·SOCl group formed from a reaction between thionyl choride and a oximino group will easily produce a sulfite linkage XIV by reacting with another oximino group, for these two groups are occupying positions very close to each other. Consecutively, the formation of a sultone via the Bissinger rearrangement[18] and the conversion of the sulfite to II by elimination of the sulfur dioxide molecule would be undertaken. Very recently, Gillis[19] has reported the formation of tetrahydrofuran from 1, 4-tetramethylene glycol with thionyl chloride via the sulfite. The derivation of II from I closely resembles this furan formation.


XIV

Here, the behavior of bromine in liquid sulfur dioxide is very interesting. When the reagent is bromine only, without sulfur dioxide, the bromine cation will attack the nitrogen atom of the oxime:

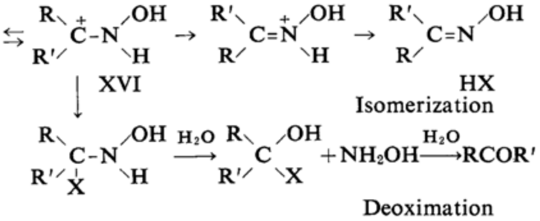

XV

Producing a nitroso bromo compound XV which is characteristically blue in color. However, the bromine in sulfur dioxide[20] may attack the oxygen atom of the oxime, since the voluminous SO_2-solvated bromo-cation is liable to prefer the oxygen atom to the nitrogen atom; this would be followed by the rearrangement:



The reason why only one of the two oximino groups will accept the rearrangement is perhaps due to the steric hindrance.

Generally speaking, the attack of hydrogen acid causes some complex results in the attempted Beckmann rearrangement. The side reactions are the isomerization[5,21] of the oxime and the deoximation of the oxime (ketone formation)[21]. The origin of both arises from the same source, the formation of a carbonium ion, XVI:



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[18] W. Bissinger, F. E. King and C. W. Hamilton, *J. Am. Chem. Soc.*, **70**, 3940 (1948).

[19] R. G. Gillis. *J. Org. Chem.*, **25**, 651 (1960).

[20] N. Tokura, R. Asami and R. Tada, *J. Am. Chem. Soc.*, **79**, 3135 (1957).

[21] R. Tada, Y. Masubuchi and N. Tokura, This Bulletin, **34**, 270 (1961).

There are many examples of carbonium ion formation from oxime with hydrogen acid, such as hydrochloric acid, sulfuric acid and hydrogen cyanide[21,22]. Such a carbonium ion (XVI) cannot undertake the Beckmann rearrangement. To carry out the rearrangement, an ion-pair formation

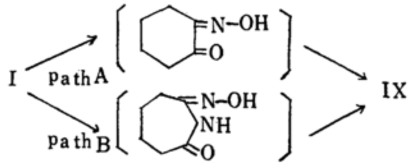
$$=N-O- \rightarrow =\overset{+}{N}\ \overset{-}{O}-$$

between the two atoms is necessary[23].

The cleavage of I to IX is presumed to pass through an intermediate, 1,2-cyclohexanedione monoxime (X), which may result from a partial deoximation of I, the so-called Beckmann rearrangement of the second order being followed (path A). A small amount of water remaining in the solvent (sulfur dioxide) may be responsible for the deoximation by serving as a source of the proton,

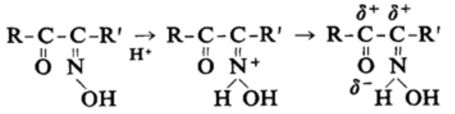
$$SO_3+H_2O+H^++SO_4H^-$$

An alternate path B might be considered.



However, path B must be ruled out because this route cannot explain the presence of hydroxylamine in the reaction mixture.

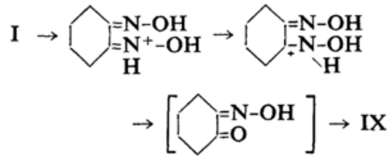
The dioxime I has two oximino group sterically interferring with each other, and the elimination of one of the oximes would be a natural consequence. It is a plausible conclusion that I was cleaved to IX, via the stage of cyclohexanedione monoxime (X), the deoximation being effected by sulfuric acid mentioned above. As the result of the material balance of the IX formation, a large amount of resinous matter was recognized. Such a resinification by a dehydration reaction would supply enough water to make the proton source available for the deoximation. The Beckmann rearrangement of the second order, a well-discussed phenomenon[24], may be explained as:



$$R-\underset{\underset{O}{\|}}{C}-\underset{\underset{N\diagdown OH}{\|}}{C}-R' \xrightarrow{H^+} R-\underset{\underset{O}{\|}}{C}-\underset{\underset{\underset{H\ OH}{\diagup\diagdown}}{\underset{N^+}{\|}}}{C}-R' \rightarrow R-\underset{\underset{O}{\|}}{\overset{\delta^+}{C}}-\underset{\underset{\underset{\delta^-H\ OH}{\diagup\diagdown}}{\underset{N}{\|}}}{\overset{\delta^+}{C}}-R'$$

$$\rightarrow R\cdot\overset{+}{C}O + R'CN \xrightarrow{OH^-} RCOOH + R'CN$$

Summarizing the above discussion, the formation of δ-cyanovaleric acid (XI) may be visualized as:



X

Summary

Three different reagents, thionyl chloride, bromine and sulfur trioxide in liquid sulfur dioxide were reacted on 1,2-cyclohexanedione dioxime to yield cyclohexano[c]-1,2,5-oxadiazole, 1-aza-7-oximinocyclohepta-2-one and δ-cyanovaleric acid respectively. Only the bromine in liquid sulfur dioxdie effected the Beckmann rearrangement. Thionyl chloride caused a dehydrative condensation, as has been reported previously. Sulfur trioxide yielded a product resulting from a deoximative cleavage. The reasons for the different processes and the different products have been discussed.

The authors are grateful to Befu Chemical Industries Inc., for the donation of liquid sulfur dioxide.

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[22] O. L. Brady and E. P. Dunn, *J. Chem. Soc.*, **109**, 656 (1916); G. Munch, *Ber.*, **29**, 62 (1896).

[23] M. Kuhara, Y. Toda, *Memoirs Col. Kyoto Univ.*, **2**, 387 (1910).

[24] D. Murakami and N. Tokura, This Bulletin, **31**, 1044 (1958); R. T. Conley and F. A. Mikulski, *J. Org. Chem.*, **24**, 97 (1959); A. F. Ferris, ibid., **24**, 580 (1959).