The Reactions of 1, 2-Cyclopentanedione Dioxime and of 1, 2, 3-and 1,3,5-Cyclohexanetrione Trioximes in Liquid Sulfur Dioxide[1]

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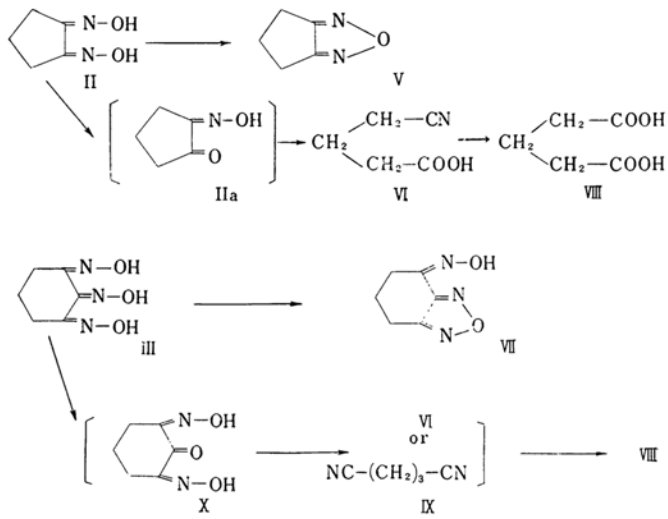
As has been reported in the preceding papers of this series[2,3], 1, 2-cyclohexanedione dioxime, when subjected to Beckmann rearrangement in liquid sulfur dioxide, gives different products according to the reagents applied. Thus, thionyl chloride yielded an oxadiazole (furazan) derivative by condensation of the two neighboring hydroximino groups; bromine yielded a rearranged product, and sulfur trioxide afforded δ-cyanovaleric acid, a product of ring cleavage. The causes of such various reactions have also been discussed.

The result has prompted the present authors to investigate similar reactions with 1, 2-cyclopentanedione dioxime and 1, 2, 3- and 1, 3, 5-cyclohexanetrione trioximes.

1, 2-Cyclopentanedione dioxime (II) was prepared by the method of Belcher et al.[2,4]

1) The Beckmann Rearrangement in Liquid Sulfur Dioxide, Part IX.
2) N. Tokura, R. Tada and K. Yokoyama, This Bulletin, **34**, 270 (1961).
3) N. Tokura, R. Tada and K. Yokoyama, ibid., **34**, 1812 (1961).
4) R. Belcher, W. Hoyl and T. S. West, *J. Chem. Soc.*, **1958**, 2743.



Namely, 2-bromocyclopentanone (I) was converted into 1, 2-cyclopentanedione dioxime by hydroxylamine, but in a low yield, as in the case of 1, 2-cyclohexanedione dioxime[2]. 1, 2, 3-Cyclohexanetrione trioxime (III) was prepared via 1, 2, 3-cyclohexanetrione 1, 3-dioxime by the method of Donald, Batesky and Moon[5]. 1, 3, 5-Cyclohexanetrione trioxime (IV) was prepared from phloroglucinol by the method of Baeyer[6].

In general, the oximes were not completely soluble in liquid sulfur dioxide at first, but they were immediately dissolved to transparent and homogeneous solutions on the addition of the rearranging reagents; the reactions were carried out at room temperature (10~18°C). Because of the unusual instability of the trione trioximes, the addition of the reagents often led to explosive reactions. Therefore, the reactions were sometimes performed at temperature below 0°C. Furthermore, the reactions were accompanied by the formation of large amounts of resinous matters, which has made the quantitative treatment and the discussion of the results difficult.

The reaction of II with thionyl chloride in liquid sulfur dioxide afforded a low melting substance, m. p. 41°C, which was identified as 5, 6-dihydro-4-cyclopenta [*c*] furazan[7] (V) both by analogy with the results disclosed in a preceding paper[2] and from the results of elementary and infrared spectrometric analyses.

The reaction of bromine with II in liquid sulfur dioxide produced only a large amount of a tarry matter, failed to give a product which could be characterized.

The reaction of sulfur trioxide with II in liquid sulfur dioxide afforded the expected γ-cyanobutyric acid (VI) as a product of ring cleavage. However, the yield was very low because of the violent carbonizing and resinifying action of sulfur trioxide. Hydrolysis of VI with aqueous hydrochloric acid gave glutaric acid (VIII). It seems likely that VI was derived through the incipient intermediate (IIa), as has been demonstrated in a preceding paper[2].

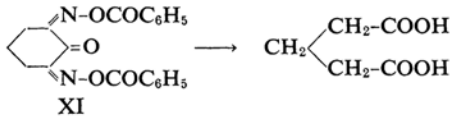
When III reacted with thionyl chloride in liquid sulfur dioxide, a product, m. p. 167~167.5°C, was obtained in a good yield. This was proved to be a cyclodehydrated product like V, and the structure of 7-hydroximino-4, 5, 6, 7-tetrahydrobenzo[*c*]furazan (VII) was assigned to it on the basis of elementary and infrared analyses. The presence of one free hydroximino group and of a furazan ring was deduced from the absorption at 1659 cm^{-1} and from the absorptions at 1622 and 1583 cm^{-1} respectively. The reaction of bromine with III yielded only a small amount of VII with a majority of a resinous matter.

The reaction of sulfur trioxide with III was expected to be of interest, but it turned out to be complicated as well. A small amount of VII was found in the reaction mixture. The residual solution, refluxed with 2 N hydrochloric acid, produced glutaric acid (VIII), but no glutaric acid dinitrile (IX), VI or any other intermediate that would produce VIII by acid hydrolysis, was isolated by extraction of the residual solution with ether.

The only product in the residual solution was apparently a mono-deoximated product,

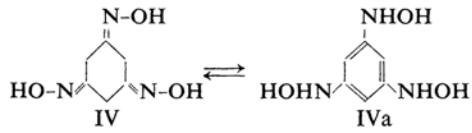
5) D. Donald, C. Batesky and N. S. Moon, *J. Org. Chem.*, 24, 1694 (1959).
6) A. Baeyer, *Ber.*, 19, 159 (1886).
7) Definitive Rules for Nomenclature of Org. Chem. (IUPAC, 1957), *J. Am. Chem. Soc.*, 82, 5545 (1960).
In the preceding papers[2,3], "1, 3, 5-oxadiazole" was used for "furazan".

probably cyclohexanetrione 1, 3-dioxime and not 1, 2-dioxime, for it produced no pink coloration with nickel nitrate solution. One plausible explanation is, therefore, that trioxime III was deoximated to trione 1, 3-dioxime X and the latter was then cleaved to dinitrile IX or to mononitrile VI to be hydrolyzed to VIII. The cleavage of the dibenzoyl derivative (XI) of the 1, 3-dioxime (X) with alkali to glutaric acid has already been reported by Treibs and Kuhn[8].



XI

The reactions of IV with thionyl chloride, with bromine and with sulfur trioxide, all ended in the formation of black nitrogen containing tarry materials, which were not extractable with any organic solvent. Since the following tautomerism in IV may be considered, the formation of a large amount of resinous product from IV may be accounted for by the presence of the reactive tautomer (IVa).



IV IVa

Experimental

Materials.—Commercial sulfur dioxide was dried with concentrated sulfuric acid and distilled. Thionyl chloride and sulfur trioxide were each distilled once. Bromine was dehydrated with sulfuric acid and distilled.

Apparatus and General Procedure.—The procedure and manipulation for the reactions were the same as have been described previously[1,2].

2-Bromocyclopentanone (I)[9].—Bromine (19 ml.) was added to a mixture of cyclopentanone (25 g.), glacial acetic acid (15 ml.) and water (60 ml.) at 55~60°C, and the whole was stirred at this temperature for a while. The reaction mixture was then neutralized with sodium carbonate. The orange oil separated was washed with water. The crude 2-bromocyclopentanone (I) (yield, 34 g.) was oximated without further purification.

1, 2-Cyclopentanedione Dioxime (II).—I (34 g.) was stirred into in small portions to a solution of hydroxylamine hydrochloride (42 g.) and sodium acetate (83 g.) in water (160 ml.), and the mixture was then refluxed for half an hour. After the mixture had been refluxed for twenty minutes more, it was treated with active carbon and filtered while hot. The filtrate was cooled to yield crude crystals of 1, 2-cyclopentanedione dioxime (II), which were then washed with water, thoroughly dried and extracted with 99% ethanol. The crystals obtained on evaporation of ethanol were recrystallized from 50% ethanol, m. p. 205~210°C (lit.: 202~212°C[4]), yield 9.0 g. Found: C, 46.68; H, 5.84; N, 21.66. Calcd. for $C_5H_8O_2N_2$: C, 46.87; H, 6.29; N, 21.87%.

1, 2, 3-Cyclohexanetrione Trioxime (III).—Essentially the method of Donald et al.[5] was employed. 1, 2, 3-Cyclohexantrione 1, 3-dioxime, m. p. 196~197°C, was prepared from cyclohexanone (184 g.), concentrated hydrochloric acid (7.5 ml.) and isoamyl nitrite (250 g.) at −5°C (yield 95 g.). The trione dioxime (31.3 g.) in 50% ethanol was oximated with hydroxylamine hydrochloride (17.4 g.) and sodium carbonate (12.9 g.) to give the 1, 2, 3-trione trioxime (III) (20 g.), m. p. 169.5~170°C (recrystallized from dioxane). Found: C, 42.40; H, 4.50; N, 24.02, Calcd. for $C_6H_9O_3N_3$: C, 42.10; H, 5.30; N, 24.55%.

1, 3, 5-Cyclohexanetrione Trioxime (IV).[6]—Potassium carbonate (3.2 g.) was added to a stirred solution of phloroglucinol dihydrate (25 g.) and hydroxylamine hydrochloride (32.2 g.) in water (1130 ml.). The mixture was allowed to stand overnight. The greyish white crystals were collected, washed with water and then with acetone, and dried under reduced pressure, m.p. 150°C (decomp.). Found: C, 42.53; H, 5.20; N, 23.51. Calcd. for $C_6H_9O_3N_3$: C, 42.10; H, 5.30; N, 23.15%.

Reaction of 1, 2-Cyclopentanonedione Dioxime (II) with Thionyl Chloride in Liquid Sulfur Dioxide.—Thionyl chloride (4.0 g.) in liquid sulfur dioxide (20 ml.) was added to a suspension of II (3.0 g.) in liquid sulfur dioxide (80 ml.). The oxime dissolved instantly. The mixture was allowed to stand at room temperature for two hours. The reaction mixture was then poured into ice water, sulfur dioxide was allowed to evaporate, and the residue was extracted with ether. The ethereal solution was washed with dilute sodium hydroxide solution and then with water and dried. Evaporation of this solution gave an oily substance, which turned to crystals on cooling, m. p. 40.5~41°C (recrystallized from ether) (yield 2.5 g.). By analogy with the previous experiment[2], and by infrared and elementary analyses, the substance was identified as 5, 6-dihydro-4*H*-cyclopenta[*c*]-furazan (V). Found: C, 54.26; H, 4.91; N, 25.29. Calcd. for $C_5H_6ON_2$: C, 54.54; H, 5.49; N, 25.44%. IR, 1585 (s) cm^{-1} (KBr).

Neutralization of the alkaline extract from the ethereal solution gave no acid product.

Reaction of II with Bromine in Liquid Sulfur Dioxide.—Bromine (12.0 g.) in liquid sulfur dioxide (20 ml.) was added to dioxime II (3.0 g.) in liquid sulfur dioxide (80 ml.). The dioxime dissolved gradually in the solution. The mixture was allowed to stand at room temperature for two hours. No product except a tarry matter was extracted with ether from the reaction mixture.

Reaction of II with Sulfur Trioxide in Liquid Sulfur Dioxide.—Sulfur trioxide (1.5 g.) in liquid sulfur dioxide (20 ml.) was added to dioxime II (3.0 g.) in liquid sulfur dioxide (80 ml.). The oxime dissolved immediately. The mixture was allowed to stand at room temperature for two

8) A. Treibs and A. Kuhn, *Ber.*, **90**, 1691 (1957).
9) R. M. Acheson, *J. Chem. Soc.*, **1956**, 4232.

hours. The reaction mixture was treated as above and extracted with ether. The ethereal solution was washed with water and dried. Evaporation of the ethereal solution afforded an orange oil, which turned to crystals, m. p. 37.5~38°C, on cooling (yieled 0.5 g.). The substance thus obtained was proved to be γ-cyanobutyric acid (VI) by elementary analysis and hydrolysis to glutaric acid (VIII). Found: C, 52.88; H, 5.88; N, 12.60. Calcd. for $C_5H_7O_2N$: C, 53.09; H, 6.24; N, 12.38%.

Hydrolysis of γ-Cyanobutyric Acid (VI).—VI (0.3 g.) was refluxed with 5 N hydrochloric acid for one hour. Then the mixture was extracted with ether. On condensing the ethereal solution, colorless crystals, m. p. 96.5°C, were obtained (yield 0.15 g.). The specimen recrystallized from ethanol showed m. p. 96.5~97.5°C alone and in admixture with authentic glutaric acid (VIII). Found: C, 46.28; H, 5.68. Calcd. for $C_5H_8O_4$: C, 45.45; H, 6.10%.

Reaction of 1, 2, 3-Cyclohexanetrione Trioxime (III) with Thionyl Chloride in Liquid Sulfur Dioxide.—Thionyl chloride (3.4 g.) in liquid sulfur dioxide (40 ml.) was added to trioxime III (5.0 g.) in liquid sulfur dioxide (100 ml.). The dioxime appeared to dissolve into the solution at room temperature in two hours. The reaction mixture was then treated with ice water, and the sulfur dioxide was allowed to evaporate. The residual solution was treated as above. On condensing the ethereal solution, a light yellow substance was obtained. The product, recrystallized from ethanol showed an m. p. of 167~167.5°C (yield 2.4 g.). The melting point was depressed to 156~158°C on admixture with the starting trioxime (III) (m. p. 170°C).

By analogy with the previous experiment[2], and by infrared and elementary analyses, the product was identified as 7-hydroximino-4, 5, 6, 7-tetrahydrobenzo[*c*]furazan (VII).

Found: C, 45.57; H, 4.20; N, 27.20, Calcd. for $C_6H_7O_2N_3$: C, 47.05; H, 4.61; N, 27.44%. Mol. wt., Found: 156 (benzene), Calcd.: 153. IR ν_{max}^{KBr}, 1622(w) and 1583(s) (furazan), 1659 (=NOH) cm^{-1}.

The alkaline solution was neutralized with an acid, but extraction with ether gave nothing.

Reaction of III with Bromine in Liquid Sulfur Dioxide.—Bromine (14.0 g.) in liquid sulfur dioxide (40 ml.) was added to trioxime III (5.0 g.) in liquid sulfur dioxide (100 ml.), and the mixture was allowed to stand at room temperature for two hours. The mixture, containing a large amount of a tarry matter, was treated as above. From the ethereal extract of the residual reaction mixture, a small quantity (1.3 g.) of crystals was obtained, m. p. 166~167°C (recrystallized from ether). The product showed no melting point depression on admixture with the VII described previously. Found: C, 47.20; H, 4.35; N, 26.72. Calcd. for $C_6H_7O_2N_3$: C, 47.05; H, 4.61; N, 27.44%.

Reaction of III with Sulfur Trioxide in Liquid Sulfur Dioxide.—Sulfur trioxide (1.4 g.) in liquid sulfur dioxide (20 ml.) was added to trioxime III (3.0 g.) in liquid sulfur dioxide (80 ml.), and the mixture was kept at −5~−7°C for one hour. The mixture was then treated and extracted as described above. VII (0.3 g.) was obtained from the ethereal solution, m. p. and mixed m. p. 165~166°C. Found: C, 47.78; H, 4.40; N, 27.04. Calcd. for $C_6H_7O_2N_3$: 47.05; H, 4.61: N, 27.44%. The residual solution was again triturated with three times the ether used at first, and the ethereal solution was washed with water, dried and evaporated. The orange substance thus obtained was analyzed, but the specimen was too small to reward further examination. Found: C, 45.48; H, 5.34. Calcd. for $C_6H_8O_3N_2$ (a trione dioxime): C, 46.15; H, 5.16%. There was positive color reaction with nickel nitrate solution.

The residual solution was then refluxed with 2 N hydrochloric acid for five hours. The solution was extracted with ether. Colorless crystals were obtained and recrystallized from ethanol, m. p. 95~96°C (yield 0.4 g.). No melting point depression was observed when the substance was mixed with authentic acid (VIII). Found: C, 46.68; H, 6.03, Calcd. for $C_5H_8O_4$; C, 45.45; H, 6.10%. IR ν_{max}^{KBr}, 2940 (s), (-OH), 1705 (-COOH) cm^{-1}.

Reaction of 1, 3, 5-Cyclohexanetrione Trioxime (IV) in Liquid Sulfur Dioxide.—Thionyl chloride (4.2 g.), bromine (5.7 g.) and sulfur trioxide (1.7 g.) in liquid sulfur dioxide (20 ml.) were added in turn to trioxime IV (3.0 g.) in liquid sulfur dioxide (80 ml.), but only dark and insoluble resinous matters were produced in all cases.

Summary

1, 2-Cyclopentanedione dioxime (II), 1, 2, 3-cyclohexanetrione trioxime (III) and 1, 3, 5-cyclohexanetrione trioxime (IV) were treated with reagents and exhibited different and characteristic behaviors in liquid sulfur dioxide. The formation of 5, 6-dihydro-4*H*-cyclopenta-[*c*]furazan (V) from II with thionyl chloride by a condensation reaction and of γ-cyanobutyric acid (VI) from II with sulfur trioxide by a cleavage reaction were observed. 7-Hydroximino-4, 5, 6, 7-tetrahydrobenzo[*c*]furazan (VII) was found in the the reaction mixtures from III and thionyl chloride and from III and bromine, accompanied by large amounts of resinous matter.

Mono-deoximation by sulfur trioxide was suggested. 1, 3, 5-Cyclohexanetrione trioxime (IV) gave only black tarry matter, which may be attributable to the instability of IV.

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