Ring Cleavage in Liquid Sulfur Dioxide. I. Cleavage of Cyclic 1,2-Diketone Monoximes

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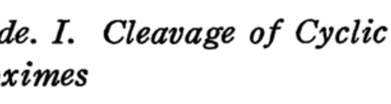
When a 1,2-diketone 1-monoxime is treated under the conditions of the Beckmann rearrangement, it is cleaved into two fragments, a cyano compound and a carboxylic acid[1,2]. This reaction, designated as the Beckmann rearrangement of the second order[2,3], is distinguished from the normal Beckmann rearrangement in its mechanism.

$$R-\overset{\overset{O}{\|}}{C}-\overset{\overset{NOH}{\|}}{C}-R' \longrightarrow RCOOH+R'CN$$

Usually the reaction is conducted in a basic solvent such as pyridine[2,4] at its refluxing temperature with an aromatic sulfonic acid or its chloride as the reagent[2]. Sulfuric acid, phosphoric acid, hydrochloric acid in acetic acid, and phosphorus compounds are used sometimes as the reagents but their use is limited because of inevitable side reactions. For example, 9,10-phenanthrenequinone 9-monoxime (II) gives a fluorenone derivative[1,3].



R=CN or $CONH_2$
(II)

Considering the characteristic properties of liquid sulfur dioxide as solvent, the authors studied ring opening reactions of some cyclic 1,2-dione 1-monoximes in liquid sulfur dioxide, expecting smoother

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[1] a. E. Beckmann and A. Koster, *Ann.*, **274**, 15 (1893). b. E. Beckmann and O. Liesche, *Ber.*, **56**, 1 (1923). c. E. Beckmann and P. Wegerhoff, *Ann.*, **252**, 14 (1889).

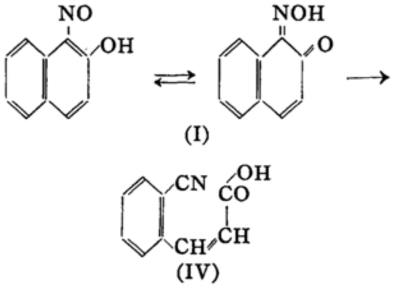
[2] A. Werner and A. Piguet, *Ber.*, **37**, 4293 (1904).

[3] W. Borsche and W. Sander, ibid., **47**, 2825 (1914).

[4] a. M. Gates, *J. Am. Chem. Soc.*, **72**, 228 (1950). b. B. Rapoport and J. Z. Pasky, ibid., **78**, 3788 (1956).

cleavages under milder conditions than in previously reported cases. Three typical diketone monoximes, viz., 1,2-naphthoquinone 1-oxime (I), 9,10-phenanthrenequinone 9-oxime (II) and tetralin-1,2-dione 2-oxime (III), were chosen.

Among various reagents tried, thionyl chloride only was found to effect the ring opening of I to *o*-cyanocinnamic acid (IV) in liquid sulfur dioxide. Toluenesulfonyl chloride and phosphorus pentoxide were slightly effective, but sulfur trioxide, sulfuric acid, phosphorus oxychloride, sulfuryl chloride, phosphorus pentachloride and aluminum chloride gave always resinous matters containing nitrogen.



(I)
(IV)

Effects of the reaction time and temperature were studied with the results listed in Table 1.

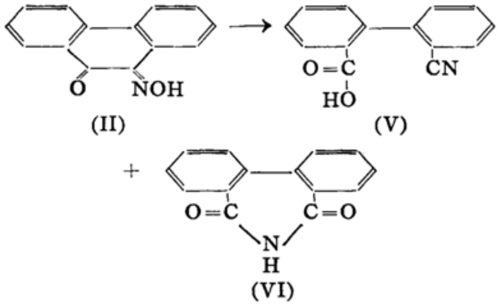
TABLE I

EFFECTS OF REACTION TIME AND TEMPERATURE ON RING OPENING OF 1,2-NAPHTHOQUINONE 1-OXIME IN LIQUID SULFUR DIOXIDE

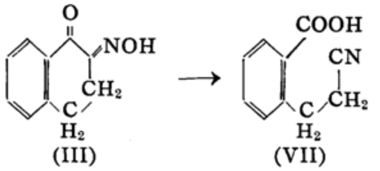
Expt.	Thionyl chloride/ naphthoquinone monoxime (Mole Ratio)	Reaction temp. °C	Reaction time	Yield (%)
1	3	−20	10 days	5
2	1	15	12 hrs.	10
3	1	15	10 days	40
4	1	50	6 hrs.	51
5	1	70	6 hrs.	54
6	2	70	6 hrs.	48
7	1	100	6 hrs.	46

The best yield (54 percent) recorded in Table I is a great improvement if compared with the result obtained by Borsche[3] (1 g. of *o*-cyanocinnamic acid chloride from 17.3 g. of I). The temperature over 100°C caused a decrease in the yield of *o*-cyanocinnamic acid (IV) and an increase in resinous matters in the product.

9,10-Phenanthrenequinone 9-monoxime (II) was treated in the same way. By six hours' reaction at 70°C 2-cyanobiphenyl-2′-carboxylic acid (V) was obtained in a yield (60 percent) much greater than that reported previously[2]. As a by-product, diphenic acid imide (VI) was obtained in a yield of 11 percent. No fluorenone derivative was found in the reaction products[3].



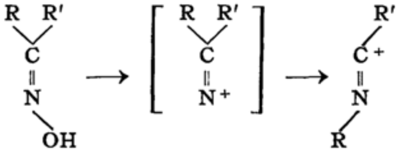
(II) (V)
(VI)



(III) (VII)

No attempt has been reported on the cleavage of tetralin-1,2-dione 2-oxime (III). When the oxime was treated with thionyl chloride at 70°C for six hours in liquid sulfur dioxide, an almost quantitative yield (98%) of *o*-(2-cyanoethyl)benzoic acid (VII) was obtained. The experimental results are summarized in Table II.

The *trans*-migration in the Beckmann rearrangement has long been established[5]. The group in *anti* position to the hydroxyl group may shift to the nitrogen atom by rearrangement, which proceed, as is well recognized, through a nitrogen cation intermediate (IX) and intramolecular migration of the anion R.



(VIII) (IX) (X)

In such a rearrangement it may not be possible for either a bulky group or a sterically strained group to take part. The carbon atom starred in XI could not migrate[6] owing to its double bond strain

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[5] B. Jones, *Chem. Revs.*, **35**, 355 (1944).

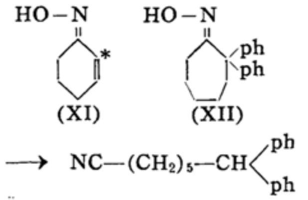
[6] F. J. Donat and A. L. Nelson, *J. Org. Chem.* **22**, 1107 (1957).

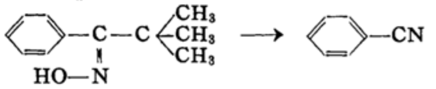
TABLE II

RING-OPENING OF 1,2-DIKETONEMONOXIMES WITH THIONYL CHLORIDE IN LIQUID SULFUR DIOXIDE

Compound	React. temp. (°C)	React. time (hr.)	Product	Yield (%)
1,2-naphthoquinone 1-oxime (I)	70	6	*o*-cyanocinnamic acid (IV)	54
9,10-phenanthrene-quinone 9-oxime (II)	70	6	2-cyanobiphenyl-2′-carboxylic acid (V)	60
			diphenic acid imide (VI)	11
tatralin-1,2-diketone 2-oxime (III)	70	6	*o*-(2-cyanoethyl)-benzoic acid (VII)	98

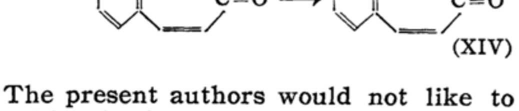
in a ring. Also ketoximes having bulky groups such as phenyl in XII⁽⁷⁾ or *tert*-butyl⁽⁸⁾ in XIII could not yield acid amides, and often gave cyano compounds.





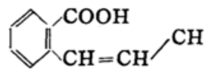
(XIII)

In naphthoquinone monoxime (I), the isonitrosomethylene group is sterically restricted in two ways, namely, by the condensation of a benzene ring and by the ring closure of groups on both its sides. Carbon atom 8a in I is inhibited from taking part in the rearrangement, and it may be impossible for carbon atom 2 to migrate to the nitrogen atom, since a steric interaction may prohibit the hydroxyl group from taking a *syn*-position to the condensed benzene ring, and thus the formation of dicarboxylic acid imide XIV may be improbable.



(XIV)

The present authors would not like to consider the dicarboxylic acid imide (XIV) as a precursor or an intermediate to *o*-cyanocinnamic acid (IV), because then one more final product (XV) would be expected from the imide (XIV).



(XV)

In the present study each cleavage gave only one kind of cyano acid, which resulted from a cleavage between the carbonyl group and the isonitrosomethylene group and a migration of the hydroxyl group. No isonitrile was found in the reaction product.

The only explanation for such a cleavage was presented by Blatt and Barnes⁽⁹⁾ in 1934. However, little can be said regarding the mechanism of the cleavage reaction of the cyclic dione monoxime system, except some explanation of the cause which hinders the normal Beckmann rearrangement from taking place.

A superior method for preparing cyano-carboxylic acids by the cleavage in liquid sulfur dioxide may find a wide application in synthetic organic chemistry. Experiments in such a direction are now in progress.

Experimental

Solvent, reagents and apparatus.—Commercial liquid sulfur dioxide was distilled after dehydration with concentrated sulfuric acid⁽¹⁰⁾. Commercial reagents of pure grade were used. The reaction was carried out in a glass pressure bottle as reported in the preceding papers⁽¹¹⁾.

1,2-Naphtoquinone 1-oxime (I).—The oxime was synthesized by nitrosation of β-naphthol according to the method of C. S. Marvel and P. K. Porter⁽¹²⁾, and recrystallized from ligroin. Brown crystals, m.p. 108°C. Yield 82%.

Ring cleavage of I to *o*-cyanocinnamic acid (IV).—Into a mixture of 5 g. of oxime I (0.03 mole) and 100 ml. of liquid sulfur dioxide, 5 g. of thionyl chloride (0.03 mole) in 30 ml. of

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7) R. E. Lyle and J. L. Fielding, ibid., **20**, 623 (1955).

8) R. F. Brawn and N. M. Van Gulick, *J. Am. Chem. Soc.*, **77**, 1094 (1955).

9) A. H. Blatt and R. P. Barnes, ibid., **56**, 1148 (1934).

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

11) N. Tokura, R. Asami and R. Tada, *Sci. Rep. of Res. Inst., Tohoku Univ.*, **A8**, 149 (1956).

12) C. S. Marvel and P. K. Porter "Organic Syntheses", Coll. Vol. I, p. 403 (1941).

liquid sulfur dioxide was introduced. The mixture was heated on a water bath at 70°C for 6 hours, when it became dark green in color. After the reaction was completed, sulfur dioxide was removed by evaporation. The residue was dissolved in 150 ml. of chloroform, and the acidic substance was extracted with 250 ml. of 1 N sodium bicarbonate solution. The extract was acidified to pH 3 with concentrated hydrochloric acid. *o*-Cyanocinnamic acid (IV), which separated out, was recrystallized from methanol. White plates, m. p. 254~255°C (reported as 254°C by Werner²⁾). Yield, 2.7 g. (54%).

Anal. Found: C, 69.36; H, 4.24; N, 8.38. Calcd. for $C_{10}H_7O_2N$: C, 69.36; H, 4.07; N, 8.09%.

The results obtained under various conditions are listed in Table I.

To a mixture of 30 ml. of ethanol and 10 ml. of concentrated sulfuric acid was added 0.5 g. of IV and the solution was refluxed for several hours. Ethyl *o*-cyanocinnamate was obtained from the reaction mixture by treating it as usual. White plates (from ethanol), m. p. 57~57.5°C. Yield, 0.3g.

Anal. Found: N, 7.05. Calcd. for $C_{12}H_{11}O_2N$: N, 6.96%.

9,10-Phenanthrenequinone 9-oxime (II).—The quinone was synthesized by oxidizing phenanthrene with chromic acid[13]. The quinone was then monoximated with hydroxylamine hydrochloride by modifying Pschorr's[14] procedure. Five grams of monoxime II was obtained from 10 g. of the quinone.

Ring cleavage of II to 2-cyanobiphenyl-2'-carboxylic acid (V).—In 100 ml. of liquid sulfur dioxide 3 g. (0.015 mole) of the oxime (II) was dissolved and the solution was treated with 1.8 g. (0.015 mole) of thionyl chloride in 30 ml. of liquid sulfur dioxide at 70°C for 6 hours. After evaporating off the solvent, the residue was dissolved in alcohol. The alcoholic solution was filtered and the filtrate was treated with 1 N sodium bicarbonate solution. By acidifying the solution 2-cyanobiphenyl-2'-carboxylic acid (V) was precipitated, and recrystallized from benzene. White pillars, m. p. 169~171°C, (reported[2] m. p. 171~172°C). Yield, 1.8 g. (60%).

Anal. Found: C, 75.06; H, 4.23; N, 6.05. Calcd. for $C_{14}H_9O_2N$: C, 75.32; H, 4.06; N, 6.28%.

In 10 ml. of methanol 0.3 g. of V was dissolved and hydrogen chloride was introduced into the mixture. By cooling, methyl 2-cyano-biphenyl-2'-carboxylate was precipitated. Recrystallized from 50% ethanol, white pillars, m.p. 79~80°C. (reported[2] m.p., 79~80°C). Yield, 0.2 g.

From the part insoluble in cold ethanol, a white crystalline subtance, m.p., 217~218°C, was obtained by sublimation in a yield of 0.5 g. (11%) and proved to be diphenic acid imide (VI) by the mixed melting point with an authentic specimen[15].

Anal. Found: N, 6.04. Calcd. for $C_{14}H_9O_2N$: N, 6.28%.

When the reaction was conducted at 15°C, the yields of V and VI decreased to 33% and 5%, respectively.

Tetralin-1,2-dione 2-oxime (III).—Tetralone was prepared from tetralin by air oxidation[16] and the ketone was then treated with isoamyl nitrite to give tetralin-1, 2-dione 2-oxime (III) according to the method of Straus and Eckhard[17] with a slight modification. Pale yellow crystals, m.p. 140~142°C. Yield, 45%.

Cleavage of III to *o*-(2-cyanoethyl) benzoic acid (VII).—A mixture of 3 g. (0.017 mole) of III and 2 g. (0.017 mole) of thionyl chloride in 130 ml. of liquid sulfur dioxide was treated for 6 hours at 70°C as stated above. After evaporating off the solvent, the residue was washed with dilute sodium bicarbonate solution and the solution was acidified. Recrystallization of the precipitates from water afforded 2.9 g. (98%) of *o*-(2-cyanoethyl) benzoic acid (VII). White plates, m. p. 111~112°C.

Anal. Found: C, 68.71, H, 5.04, N, 8.15. Calcd. for $C_{10}H_9O_2N$: C, 68.56, H, 5.18, N, 8.00%.

As a proof of the structure of VII, VII was decarboxylated to β-phenylpropionitrile (XVI), which was then hydrolyzed to β-phenylpropionic acid (XVII) in the following way.

Decarboxylation of VII to β-phenylpropionitrile (XVI).—A mixture of 2 g. (0.012 mole) of VII, 1 g. of copper powder and 30 g. of quinoline was refluxed with stirring for four hours. Evolution of carbon dioxide was observed. The mixture was filtered and the filtrate was diluted with 200 ml. of chloroform. The solution was washed with 5 percent hydrochloric acid and with 2 percent aqueous sodium hydroxide solution successively, and dried with anhydrous sodium sulfate. After the evaporation of the solvent (chloroform), the residue was subjected to a distillation in vacuo and β-phenylpropionitrile (XVI) was obtained as a pale yellow liquid of b.p. 115~117°C (7 mm.) (reported[18] b.p., 114~118°C (8 mm.)). Yield, 1.1 g, (73%).

Anal. Found; C, 77.75, H, 6.27, N, 9.19. Calcd. for C_9H_9N; C, 82.40, H, 6.92, N, 10.68%.

XVI was not pure enough for analysis. It was hydrolyzed to β-phenylpropionic acid (XVII).

Hydrolysis of XVI to β-phenylpropionic acid (XVII).—A mixture of 0.5 g. of XVI in 5 ml. of 10 percent alcoholic potash was refluxed for ten hours. Then the reaction mixture was poured onto ice water and extracted with chloroform. The solution was dried and evaporated. The residue was recrystallized from water to obtain 0.3 g. (53%) of XVII as white needles, m. p. and mixed m.p. with an authentic specimen, 48~49°C. (reported[19] m. p. 47.5~48.0°C).

Anal. Found: C, 70.42, H, 6.68. Calcd for $C_9H_{10}O_2$: C, 71.98, H, 6.71%.

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[13] R. Wendland and J. LaLonde, *Org. Synth.*, **34**, 76 (1954).

[14] R. Pschorr, *Ber.* **35**, 2734 (1902).

[15] N. Tokura and S. Anazawa, *Sci. Rep. of Res. Inst. Tohoku Univ.*, **A9**, 239 (1957).

[16] R. B. Thompson, "Organic Syntheses" Coll. Vol. II, 995 (1943).

[17] F. Straus and W. Eckhard, *Ann.*, **444**, 162 (1925).

[18] V. Grignard, E. Bellet and Ch. Courtot, *Annales de chimie et de physique*, [9], **4**, 43 (1915).

[19] A. W. Ingersoll, "Organic Syntheses", Coll. Vol, I, p. 311 (1941).

Summary

1,2-Diktone monoximes were subjected to treatment with thionyl chloride in liquid sulfur dioxide to obtain cyanocarboxylic acids in good yields.

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