

with a water separator. On working up in the manner indicated for glycine, the yield of phthaloyl-DL-phenylalanine, m.p. 176.5–177.5° (lit.,²⁰ m.p. 174–175°), was 5.05 g. (90% yield).

(c) D-Phenylalanine (0.300 g.) and phthalic anhydride (0.254 g.) were heated in 10 ml. of refluxing dimethylformamide for 45 min. The product, isolated by pouring the reaction mixture into 30 ml. of ice and water, weighed 0.43 g. (83.5%) and melted at 175–177°. For a sample recrystallized from aqueous methanol, m.p. 182–183.5°, $[\alpha]_D^{20}$ was +211° (0.0566 g. in 3.5 ml. of ethanol), showing 100% optical purity.

N-Phthaloyl-L-leucine. L-Leucine and phthalic anhydride heated in pyridine at 100–105° for 1 hr. afforded *N*-phthaloyl-L-leucine in poor yield. A sample recrystallized from

(20) J. H. Billman and W. F. Harting, *J. Am. Chem. Soc.*, **70**, 1473 (1948).

aqueous methanol, m.p. 121–122°, showed $[\alpha]_D^{20}$ –25.5° (0.0915 g. in 3.5 ml. ethanol); (lit.,³ m.p. 118.5–119.5°, $[\alpha]_D^{25}$ –24°).

Diethyl N-phthaloyl-L-glutamate. A suspension of 12 g. of diethyl L-glutamate hydrochloride and 7.4 g. of phthalic anhydride in 10 ml. of triethylamine and 150 ml. of toluene was heated under reflux for 2.5 hr. in a flask fitted with a Dean-Stark tube. Nearly the calculated amount of water was collected. The reaction mixture was filtered and the filtrate was washed with dilute hydrochloric acid and then with water and dried over sodium sulfate. On removing the solvent from the dried solution, a light yellow colored, viscous oil was obtained (14.6 g., 88%). A sample was purified by distillation, giving close to quantitative recovery of nearly colorless distillate: n_D^{25} 1.5234; $[\alpha]_D^{25}$ –35.2° (ethanol) [lit.,¹² n_D^{25} 1.5220; $[\alpha]_D^{25}$ –33.5° (ethanol)].

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[CONTRIBUTION FROM E. I. DU PONT DE NEMOURS & CO., INC., EASTERN LABORATORY]

Reaction of Cyclohexane with Nitrosyl Chloride

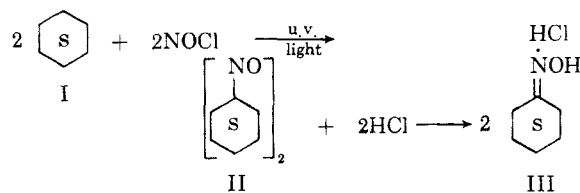
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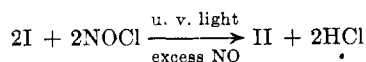
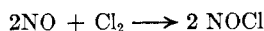
The preparation of nitrosocyclohexane dimer from cyclohexane and nitrosyl chloride is described. Data are presented which may explain the fact that, under the reaction conditions employed, the major reaction product is nitrosocyclohexane dimer and not cyclohexanone oxime hydrochloride.

The reaction of nitrosyl chloride with cyclohexane (I) in the presence of light to yield cyclohexanone oxime hydrochloride (III) has been known for many years.¹ More recently, Mueller and Metz-

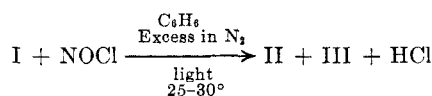
ger² found that they could prepare nitrosocyclohexane dimer (II) by the reaction of cyclohexane (I) with a mixture of nitric oxide and chlorine in the presence of light: Cyclohexyl nitrate and 1-chloro-1-



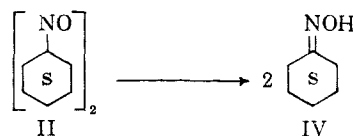
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nitrosocyclohexane were formed as by-products of the reaction. They used a nitric oxide-chlorine volume ratio of 8:1. It seemed logical that the flow of gas through the system resulted in the removal, by entrainment, of the hydrogen chloride formed before it could isomerize the nitroso compound (II)



action was carried out by entraining nitrosyl chloride, with a stream of dry nitrogen, into an irradiated solution of cyclohexane (I) in benzene. In this manner good yields (30–50%) of nitrosocyclohexane dimer (II) and small amounts of cyclohexanone oxime hydrochloride (III) were obtained. If the flow of the gas stream was slow, or if the gas stream was passed into the bottom of a container holding a benzene-cyclohexane solution of considerable depth, the major product was the oxime salt (III). These observations prompted us to measure the rate of isomerization of the nitroso dimer (II) to cyclohexanone oxime (IV) in various media. Table I



shows the results obtained from the measurement of the rate of isomerization of nitrosocyclohexane dimer to cyclohexanone oxime in cyclohexane and in the presence of several different catalysts.

Surprisingly, the data in Table I show that the nitroso dimer (II) did not isomerize to cyclohex-

(1) German Appln. **W5051** (1952), (to Matheson Chemical Corp.); *French Patent 992,772* (1951) (to Svit, Narodni Podnik). W. Zerneck and H. Ritter, (to Cassella Farberwerke Maunkur), Ger. Appln., **C, 2,405** (1952); B. B. Brown (to Olin Matheson), U. S. Patent **2,719,116** (1955); M. A. Naylor and A. W. Anderson, *J. Org. Chem.*, **18**, 115 (1953).

(2) E. Mueller and H. Metzger, *Chem. Ber.*, **88**, 165 (1955).

TABLE I

DATA OBTAINED BY MEASUREMENT OF THE RATE OF ISOMERIZATION OF NITROCYCLOHEXANE DIMER TO CYCLOHEXANONE OXIME IN VARIOUS MEDIA

Temperature, °C.	Reaction Medium	10 ³ k (Min. ⁻¹)
50.2	Cyclohexane	Very small
69.7	Cyclohexane	Very small
80.0	Cyclohexane	Very small
89.8	Cyclohexane-CH ₃ CO ₂ H ^a	4.80
23.5	Cyclohexane-HCl ^b	.640
23.0	Cyclohexane-Cyclohexylamine ^a	1.24
38.8	Cyclohexane-Cyclohexylamine ^a	10.5
24.6	Cyclohexane-Pyridine ^a	.232
59.5	Cyclohexane-Pyridine ^a	9.25

^a Catalyst concentration = 28.6% by volume. ^b Catalyst concentration = 0.2 g./100 ml.

anone oxime (IV) in cyclohexane solution over the concentration range of 0.1–0.2 g./100 ml. even at 80°. After heating the solution at 50° for twenty-seven hours and at 70° and 80° for several hours, no detectable drop in the concentration of II was observed. The data also show that by the addition of suitable acids or bases the isomerization will proceed in cyclohexane solution. Hydrogen chloride is not a good isomerization catalyst at or near room temperature. This latter observation explains why under the conditions employed for the reaction of nitrosyl chloride with cyclohexane (I) the major product was II and not III. Below 70°, glacial acetic acid was not a good isomerization catalyst. After heating at 69–70° for two hours in an acetic acid–cyclohexane mixture, no change in the concentration of II in cyclohexane occurred. Under similar conditions at 89.8°, the nitroso compound (II) was isomerized to the oxime (IV). The best catalyst found to effect the isomerization in cyclohexane was cyclohexylamine. Pyridine was slightly less effective.

Studies of the rate of isomerization of nitrosocyclohexane dimer to cyclohexanone oxime also were carried out in methanol. The results of these investigations are shown in Table II.

TABLE II

RATE OF ISOMERIZATION OF NITROCYCLOHEXANE DIMER TO CYCLOHEXANONE OXIME IN METHANOL

Temperature, °C.	10 ³ k (Min. ⁻¹)
50.3	0.702
65.0 (Refluxing methanol)	5.48

The data in Table II indicate that methanol is a much better solvent for the isomerization than cyclohexane and that perhaps methanol is a catalyst for the isomerization.

EXPERIMENTAL

Materials. Nitrosocyclohexane dimer (II) was prepared by

the oxidation of *N*-cyclohexylhydroxylamine² or by the action of nitrosyl chloride on cyclohexane. It was purified by recrystallization from cyclohexane. The pure dimer melted at 116–118°.

The cyclohexane used as a solvent in the rate studies was distilled through a 12-inch Vigreux column. Undistilled cyclohexane was unsatisfactory for the infrared analyses.

The methanol used in the isomerization studies was Baker Analyzed Reagent Grade (99.5% methanol).

The cyclohexylamine, pyridine, and acetic acid used as catalysts were purified by repeated distillation. The gaseous hydrogen chloride employed as a catalyst was generated from concentrated aqueous hydrochloric acid.

Apparatus. The constant temperature bath was capable of holding the temperature within one-tenth degree of the desired temperature. A stainless steel basket divided into twelve compartments held the samples. The basket was agitated by a shaft which was attached in an offset manner to a flywheel powered by a motor. The sample containers were 10-ml. flat-bottomed cylindrical flasks fitted with individual reflux condensers.

Analyses. The samples employed in the isomerization studies in methanol and pure cyclohexane were analyzed by methods based on the absorption maximum of nitrosocyclohexane dimer (II) at a wave length of 290 millimicrons ($m\mu$) in the ultraviolet region of the spectrum. Working curves were set up for the analysis of II by the measurement of its absorbance at 290 $m\mu$ for both methanol and cyclohexane solutions. Both curves obeyed Beer's Law. The working curves were checked with solutions of known concentration, and the results were within the experimental error.

The samples from the acid and base catalyzed isomerizations were analyzed for nitrosocyclohexane dimer (II) by the infrared method described in a previous publication.³

Procedures. The experiments in pure cyclohexane and methanol were carried out by dissolving 0.05–0.2 g. of the nitroso-dimer (II) in the appropriate solvent and diluting the solution to 100 ml. Two to five milliliters of the stock solution was placed in each of the twelve containers and, if desired, the requisite amount of catalyst was added. The basket was then lowered into the bath at the proper temperature. The samples were allowed 5 min. to reach the reaction temperature. The zero time sample was removed and timing of the other samples started. When the reaction mixtures involving pure methanol or cyclohexane were removed, the reaction was stopped by the addition of cold methanol (–10°) or cold cyclohexane (10°) to the samples. The sample was then diluted to 100 ml. and analyzed by the ultraviolet methods. The acid or base catalyzed isomerizations were stopped by removing the catalyst. Pyridine and cyclohexylamine were removed by washing the sample with 4 20-ml. portions of distilled water. The acid catalysts were removed by washing the samples successively with 10 ml. of water, 10 ml. of saturated aqueous sodium bicarbonate solution, and 10 ml. of water. The washed samples were passed through filter paper to remove traces of water and analyzed by the infrared method.³ The washing technique had no appreciable effect on the concentration of nitrosocyclohexane dimer.

Catalyst Removed	Nitrosocyclohexane Dimer (G./100 ML.)	
	Before wash	After wash
Acetic acid	0.0520	0.0512
Hydrogen chloride	0.0690	0.0690
Cyclohexylamine	0.0478	0.0465
Pyridine	0.0490	0.0478

All reactions ran were at least 65% complete. The yield of cyclohexanone oxime in these reactions ranged from

(3) L. G. Donaruma and D. J. Carmody, *J. Org. Chem.*, **22**, 1024 (1957).

