(13,200), and 300 (8100). An n.m.r. spectrum taken in trifluoroacetic acid showed the benzylic proton as a singlet at τ 3.25.

Residue B consisted of 2-carboxamido-3,4-trimethyleno-1-indanol (11). Movement of the crude product on t.l.c. plates eluted with chloroform–methanol (5:1) showed the presence of only one isomer. Recrystallization of 11 from 95% ethanol yielded white flakes: m.p. 190–191°; λ_{max}^{KBr} 2.95, 3.05, 3.18 μ (OH and NH₂), 5.95, and 6.08 μ (amide CO); $\lambda_{max}^{CHCl_3}$ 2.95, 3.05, 3.1 (OH and NH₂), and 5.95 μ (amide CO).

Anal. Calcd. for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.98; H, 7.09; N, 6.75.

Residue C contained 2-carboxamido-1-acenaphthenone (12) along with traces of the ketoamide 9 and starting material, depending on the reaction conditions. Recrystallization of 12 from 95% ethanol gave an analytical sample: m.p. 221–223°; λ_{max}^{KBr} 2.97, 3.12 (NH₂), 5.85 (CO), and 5.98 μ (amide CO); $\lambda_{max}^{95\% EtOH}$ 228 mμ (ϵ 12,480), 244 (7360), 252 (7360), 280–285 (2660), 303 (2880), 315 (2450), and 335 (1810). An n.m.r. spectrum taken in trifluoroacetic acid showed the single aliphatic proton at τ 5.08.

Anal. Calcd. for $C_{13}H_9NO_2$: C, 73.92; H, 4.27; N, 6.63. Found: C, 73.53; H, 4.19; N, 6.61.

A summary of the R_f values of the above products of the reduction on t.l.c. plates eluted with chloroform–methanol (5:1) is as follows: 1, 0.69; 9, 0.65; 10, 0.49; 11, 0.42; and 12, 0.40.

Reduction of 2-Carboxamido-2a,3,4,5-tetrahydroacenaphthen-1-one (9).—To a solution of 2.17 g. of 9 in 50 ml. of methanol was added 0.38 g. of sodium borohydride in 6 ml. of 1% NaOH and the whole was stirred for 2 hr. The solvent was evaporated and the precipitate was collected to give 2.04 g. (94%) of 11, m.p. 188–190°, by mixture melting point and identity of the infrared spectra. T.l.c. determinations proved the presence of only one isomer.

Reduction of 2-Carboxamido-3-t-butyl-1-indanone (14a).—To a solution of 1.43 g. (6.2 mmoles) of 14a in 25 ml. of methanol was added 0.24 g. (6.3 mmoles) of sodium borohydride in 6 ml. of 1% sodium hydroxide. After stirring for 2 hr., the solvent was evaporated and the precipitate was collected to give 1.40 g. (97%) of the corresponding alcohol 15, m.p. 150–160°. T.l.c. determinations showed the presence of two substances, but several recrystallizations from ethyl acetate gave one isomer with m.p. 199–200°; λ_{max}^{KBr} 2.95–3.05 (OH and NH₂) and 6.05 μ (CONH₂).

Anal. Calcd. for $C_{14}H_{19}NO_2$: C, 72.06; H, 8.21; N, 6.03. Found: C, 72.36; H, 8.41; N, 5.96.

Treatment of 14b under similar conditions resulted in the recovery of 97% of starting material.

Hydrogenation of 1 over Raney Nickel. A.—A mixture of 3 g. of 1, 0.5 teaspoon of wet Raney nickel, and 100 ml. of absolute ethanol was subjected to hydrogenation at 45 p.s.i. at 80° for 40 hr. Filtration and evaporation of the solvent yielded 2.95 g. (96%) of 11, m.p. 153–164°. T.l.c. determinations indicated the presence of two isomers in almost equal proportions. Recrystallizations of the mixture from ethyl acetate yielded the more insoluble isomer of 11, m.p. 190–191°. The R_f value (0.42) of this isomer proved it to be the same as that prepared from the sodium borohydride reduction of 1. By gradually evaporating the mother liquor and periodically collecting the crystals, a crop was finally collected which consisted entirely of the second isomer, m.p. 145–149°. Recrystallization from 95% ethanol gave colorless crystals, m.p. 154–155°. This isomer had an R_f value of 0.45 on t.l.c plates eluted with chloroform–methanol (5:1): λ_{max}^{KBr} 2.98, 3.05, 3.12 (NH and OH), and 5.95 μ (amide CO); $\lambda_{max}^{CHCl_3}$ 2.84, 2.95 (OH and NH₂), and 5.98 μ (amide CO).

Anal. Calcd. for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.60; H, 6.98; N, 6.25.

A mixture melting point of the two isomers of 11 melted at 143–150°.

B.—A mixture of 3 g. of 1, 0.5 teaspoon of wet Raney nickel, and 100 ml. of absolute ethanol was subjected to hydrogenation at 45 p.s.i. at room temperature for 16 hr. Filtration of the catalyst and evaporation of the solvent yielded 2.97 g. (98%) of 9, m.p. 174–176°, by identical infrared spectra and R_f values.

Reduction of 2-Carboxamido-2a-nitromethyl-2a,3,4,5-tetrahydroacenaphthen-1-one (16).—16[3a] (0.5 g., 0.0017 mole) in 20 ml. of ethanol was stirred during the dropwise addition of 0.5 g. of sodium borohydride in 5 ml. of 2% sodium hydroxide. The solution was refluxed several hours and cooled overnight. The ethanol was distilled and the residue was cooled to give 0.15 g. (39%) of 11, which, after recrystallization from ethanol, melted at 191–192°. The product was the same as that produced by the reduction of 1 with sodium borohydride as evidenced by the infrared spectrum, mixture melting point, and movement on t.l.c. plates.

Isomerization of 2-Carboxamido-3,4-trimethyleno-1-indenol (10) with Base.—A mixture of 1 g. of 10, 500 ml. of methanol, and 6 ml. of 1% sodium hydroxide was refluxed for 4 hr. Acidification of the resulting solution and evaporation of the solvent yielded 0.8 g. of a precipitate of 9, m.p. 155–159°, as evidenced by its infrared spectrum and movement on t.l.c. plates.

Amine-Catalyzed Isomerization of Nitrosocyclohexane to Oxime

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The subject reaction followed the kinetic expression, rate = k[amine]²[dimer], with an activation energy of 26 kcal. In nine liquid aliphatic amines the rate constant increased with increasing electron density about the amine nitrogen: $k_{max}(Et_3N)/k_{min}(n\text{-}BuNH_2) = 2$. The rate constant increased with decreasing solvent polarity: $k(\text{hydrocarbon})/k(CH_3OH\text{-}H_2O) = 3.5$. An interpretation of the observed results is offered.

In 1958 Gowenlock and Lüttke[1] called attention to the paucity of kinetic data on the dimerization and the isomerization (to oxime) of primary and secondary nitroso compounds. Knowledge of the dimerization reaction was largely limited to the qualitative observation that colorless solutions of nitroso dimers gave, on heating, blue or green solutions of the corresponding monomers which reverted to the colorless dimers on cooling. Recently, Burrell[2] determined the rate of dimerization of nitrosocyclohexane, the constant for monomer–dimer equilibrium, and, hence, the rate of

dimer dissociation over a wide temperature range. It is the only work of this kind reported to date. The opinion was early expressed,[3] and then assumed to be true,[4] that primary and secondary nitroso compounds were unstable and rapidly isomerized to oximes at room temperature. Subsequent work, however, has shown that these compounds are reasonably stable[5-7]; they

(1) D. G. Gowenlock and W. Lüttke, *Quart. Rev.* (London), **12**, 321 (1958).

(2) E. J. Burrell, Jr., *J. Phys. Chem.*, **66**, 401 (1962).

(3) J. Schmidt, *Ber.*, **35**, 2323 (1902); E. Bamberger and R. Seligman, *ibid.*, **36**, 685 (1903).

(4) N. V. Sidgwick, "The Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1937, p. 204; J. Walker in "The Chemistry of Carbon Compounds," Vol. 1A, E. H. Rodd, Ed., Elsevier Publishing Co., Amsterdam, 1951, p. 370.

(5) C. S. Coe and T. F. Dowmani, *J. Am. Chem. Soc.*, **70**, 1516 (1948).

(6) P. Taite, *Bull. soc. roy. sci. Liege*, **22**, 226 (1953).

(7) E. Muller and H. Metzger, *Chem. Ber.*, **88**, 165 (1955).

are converted to the oxime only after prolonged heating in the liquid state. The conversion of secondary bis-nitroso compounds to ketoximes by means of dry hydrogen chloride has been reported; the reaction was catalyzed by ultraviolet light.[8] Gaseous nitroso compounds are stable even at elevated temperatures.[9]

In the present paper the rate of base-catalyzed isomerization of nitrosocyclohexane dimer to cyclohexanone oxime in dilute solution is reported.
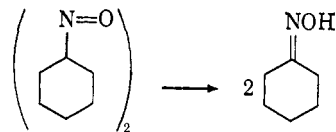
Experimental

Chemicals.—Nitrosocyclohexane dimer was prepared by bromine oxidation of N-cyclohexylhydroxylamine[7]: m.p. 116–117° (lit.[7] 116.5–117°). N-Cyclohexylhydroxylamine was prepared by reduction of nitrocyclohexane with zinc dust in aqueous ammonium chloride solution. Other reagents were obtained from commercial sources.

Procedure.—Isomerization rate data were obtained by measuring the peak absorption of nitrosocyclohexane dimer at 285–290 mμ on a Beckman DK-2 spectrophotometer using a 1-cm. cell. For each run, a master solution was prepared containing 0.03–0.07 g. of nitrosocyclohexane dimer/25 ml. of solution. One-milliliter portions were placed in 2-dram screw-cap vials which were assembled in a rack, and then lowered into a constant-temperature bath. Single vials were periodically removed from the bath starting about 15 min. after immersion. The contents were transferred to a volumetric flask by rinsing with an appropriate solvent (usually methanol or cyclohexane). Fifty-milliliter flasks were normally used; as nitrosocyclohexane concentration decreased, smaller flasks were employed.

Since the rate of dimer disappearance was, in all runs, found to be first order in dimer concentration, absorbance readings were utilized directly to obtain first-order rate constants. Peak absorbance was shown to increase linearly with dimer concentration for readings up to 0.9 (concentration of about 0.02 g./l. in a 1-cm. cell). At higher concentrations, absorbance was slightly higher than the extrapolated value. Most readings were taken in the linear range. A small correction was applied to readings above 0.9.

Results

General.—Nitrosocyclohexane exists in solution almost exclusively as the dimer; calculation based on the known equilibrium constant[2] has shown that under our reaction conditions the fraction dissociated was always negligibly small. In all runs, the rate of dimer disappearance was strictly first order in dimer concentration. The fastest isomerization rates observed were nearly two orders of magnitude slower than the rate of dimer dissociation at the same temperature.[2]

Isomerization and Amine Structure.—The isomerization rates obtained in a number of liquid aliphatic amines are listed in Table I. The rate constant decreased in the order, tertiary > secondary > primary amines. Among the primary amines, rate decreased slightly with type of alkyl group in the order, tertiary > secondary > primary alkyl.

The solid cyclic amines, piperazine and triethylene-diamine, were run in concentrated methanol solutions

at 40°. Again, the isomerization rate was higher with the tertiary amine, triethylenediamine, than with the secondary amine, piperazine (see Table II). In methanol solution, triethylenediamine was not so effective as triethylamine.

TABLE I
ISOMERIZATION RATE OF NITROSOCYCLOHEXANE TO CYCLOHEXANONE OXIME IN VARIOUS AMINES

Amine	Type of amine	Type of alkyl	Temp., °C.	k, min.⁻¹
Ethylenediamine	Prim.	Prim.	40	0.00497
n-Butylamine	Prim.	Prim.	40	0.00506
Cyclohexylamine	Prim.	Sec.	40	0.00592
t-Butylamine	Prim.	Tert.	40	0.00597
Diisopropylamine	Sec.	Sec.	40	0.00903
Triethylamine	Tert.	Prim.	40	0.01199
Cyclohexylamine	Prim.	Sec.	50	0.0255
Diisopropylamine	Sec.	Sec.	50	0.0367
Triethylamine	Tert.	Prim.	50	0.0454
Cyclohexylamine	Prim.	Sec.	60	0.0856
Diisopropylamine	Sec.	Sec.	60	0.1044
Triethylamine	Tert.	Prim.	60	0.1553

TABLE II
ISOMERIZATION RATE OF NITROSOCYCLOHEXANE TO CYCLOHEXANONE OXIME IN VARIOUS SOLVENTS

Amine concn., M	Solvent	Temp., °C.	k, min.⁻¹
	Triethylamine		
4.78ᵃ	Cyclohexane	40	0.0148
2.36	Cyclohexane	40	0.0132
1.187	Cyclohexane	40	0.0115
0.778	Cyclohexane	40	0.0102
0.563	Cyclohexane	40	0.00524
0.324	Cyclohexane	40	0.00172
4.28ᵃ	Nujol	40	0.0136
4.28ᵃ	p-Dioxane	40	0.00750
4.28ᵃ	Methanol	40	0.00472
4.28ᵃ	H₂O-CH₃OHᵇ	40	0.00388
0.322	p-Dioxane	64	0.0773
0.296	Methanol	63	0.0239
0.506	Methanol	64	0.0314
	Triethanolamine		
0.322	p-Dioxane	63	0.0646
0.342	Methanol	64	0.0260
	Piperazine		
4.1ᵃ	Methanol	40	0.00207
	Triethylenediamine		
3.6ᵃ	Methanol	40	0.00308

ᵃ Solution is about 60 vol. % amine. ᵇ Volume ratio, 7:3. This solution was visibly more viscous than any of its three components.

Triethanolamine in dilute solution was slightly less effective than triethylamine under comparable circumstances. Pyridine, in cyclohexane, was about one-tenth as effective as the aliphatic amines in catalyzing the isomerization reaction.[10]

These observations may be summarized by the generalization that catalytic efficiency increases with increasing electron density about the amine nitrogen.

Effect of Solvent.—No measurable isomerization of nitrosocyclohexanone oxime occurred in pure cyclohexane, even after 6 hr. at 80°.[10] Slow isomerization

(8) E. Müller, D. Fries, and H. Metzger, Chem. Ber., 88, 1185, 1188, 1891, (1957).

(9) H. T. J. Chilton and B. G. Gowenlock, J. Chem. Soc., 3232 (1953); 3174 (1954).
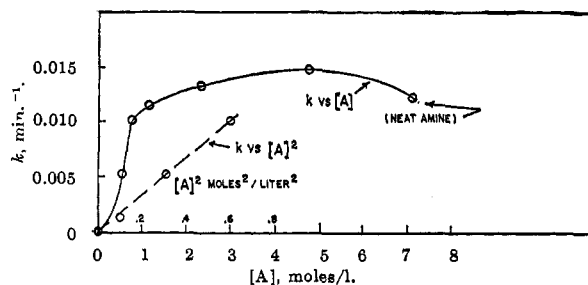
(10) L. G. Donaruma, private communication.

Figure 1.—Rate constant of the isomerization of nitrosocyclo-hexane dimer to cyclohexanone oxime in triethylamine–cyclo-hexane solutions at 40°: [A] = amine concentration.

did occur in p-dioxane and in methanol, however, ($k \sim 0.004$ min.$^{-1}$ at 60° in both instances) and in molten succinonitrile. In the last-named solvent, the rate constant at 65° increased linearly with water content: $10^3 k = 0.55$, 2.3, and 5.0 min.$^{-1}$ in systems containing 0, 16, and 32% water, respectively.

In solvent mixtures consisting roughly of 60 vol. % triethylamine and 40 vol. % second component, the rates at 40° decreased slightly with increasing solvent polarity: cyclohexane $\sim$ Nujol $\gg$ p-dioxane $>$ methanol $>$ water–methanol mixture. Similarly, trieth-anolamine was found to be a more effective catalyst in p-dioxane than in methanol (see Table II).

Effect of Amine Concentration.—Isomerization rate was measured at 40° in a series of cyclohexane solutions containing increasing concentrations of triethylamine (see Table II). A plot of rate constant k vs. amine concentration [A] gave the S-shaped curve shown in Figure 1. At amine concentrations up to 0.8 M, k was proportional to [A]^2.

Effect of Temperature.—The temperature depend-ence of the isomerization rate constant was determined in neat cyclohexylamine, diisopropylamine, triethyl-amine, and in 0.32 M triethylamine in p-dioxane (Figure 2). All systems showed an activation energy of 26 kcal./mole.

Hydroxide Catalysts.—Hydroxide bases were not more effective than aliphatic amines in catalyzing the isomerization reaction. A rate constant of 0.0041 min.$^{-1}$ was obtained in a 20% solution of tetramethyl-ammonium hydroxide in methanol at 40°; in 2 M sodium hydroxide in methanol, $k = 0.0018$ min.$^{-1}$ at 40°.

Discussion

The principal features of the amine-catalyzed iso-merization reaction are the following: the rate is second order in amine concentration (at concentra-tions below 0.8 M) and first order in dimer concentra-tion. This implies that two molecules of amine and either one molecule of nitroso dimer or two molecules of nitroso monomer are involved before or during the rate-determining step. The rate constant increases slightly with increasing electron density about the amine nitrogen and with decreasing solvent polarity. Two possible mechanisms consistent with these ob-servations are discussed below.
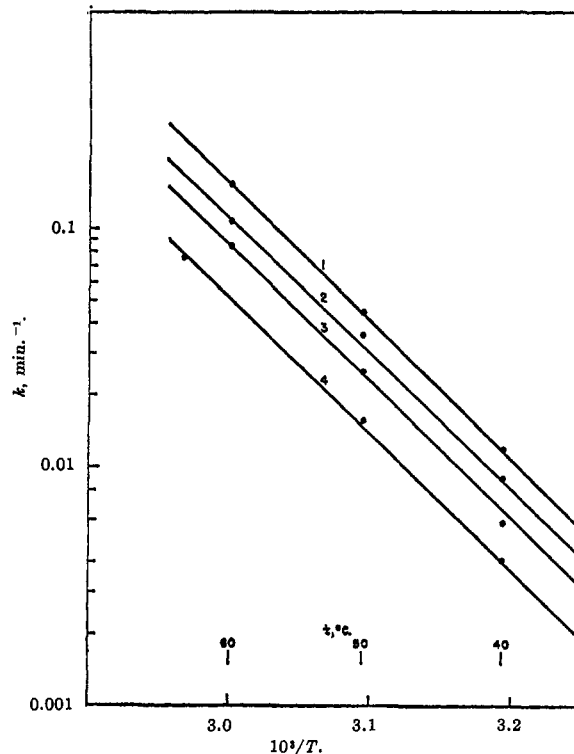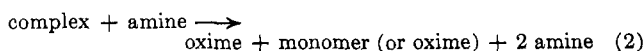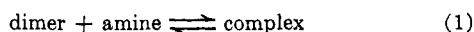
Assume that

$$\text{dimer} + \text{amine} \rightleftharpoons \text{complex} \qquad (1)$$

$$\text{complex} + \text{amine} \longrightarrow$$
$$\text{oxime} + \text{monomer (or oxime)} + 2 \text{ amine} \qquad (2)$$


Figure 2.—Rate constant of the isomerization of nitrosocyclo-hexane dimer to cyclohexanone oxime vs. reciprocal tempera-ture: 1, in triethylamine; 2, in diisopropylamine; 3, in cyclo-hexylamine; 4, in 0.32 M triethylamine in p-dioxane.

in which the equilibrium of eq. 1 is rapidly established, and eq. 2 is the rate-determining step. The rate ex-pression would then be $dX/dt = k_2 CA = k_2 K_1 A^2 D$ where k_2 is the rate constant for eq. 2, K_1 is the equi-librium constant for eq. 1, and X, C, A, and D are the concentrations of oxime, complex, amine, and dimer, respectively.

Equation 1 is assumed to be the removal of one tertiary proton from the nitroso dimer; the resulting anion may be represented by the following electronic structures where dashes represent electron pairs,
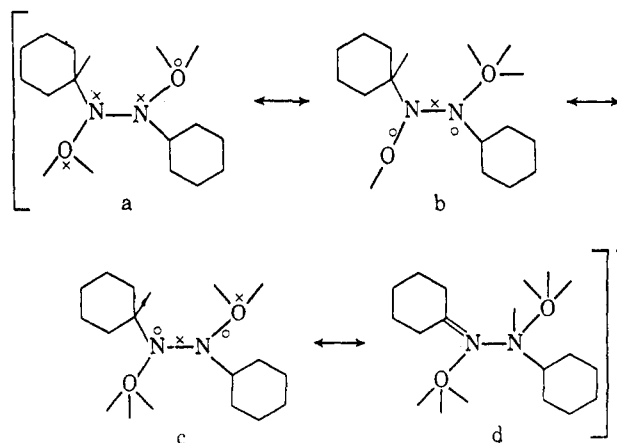

crosses (×) single electrons of one spin, and circles (○) single electrons of opposite spin. In structures a, b, and c we retained the most reasonable electronic structure of the ONNO group of the dimer, as assigned by Linnett and Rosenberg to nitrosobenzene dimer.[11]

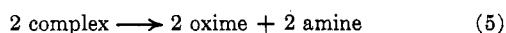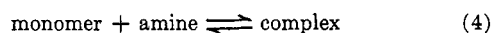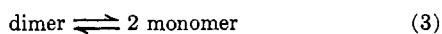(11) J. W. Linnett and R. M. Rosenberg, *Tetrahedron*, **20**, 53 (1964).

In structure d the negative charge on the carbon has been removed; it is probably the most stable form of the anion. The complex of eq. 1 may be taken either as the anion or as an ion pair with the ammonium cation.

The rate-determining step represented by eq. 2 is the removal of the second tertiary proton and the simultaneous cleavage of the N–N bond to accommodate the excess electronic charge.
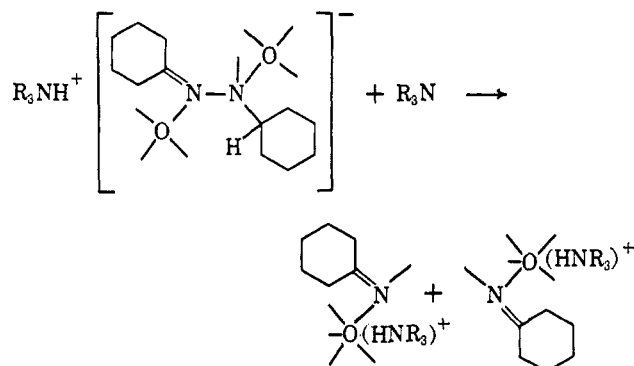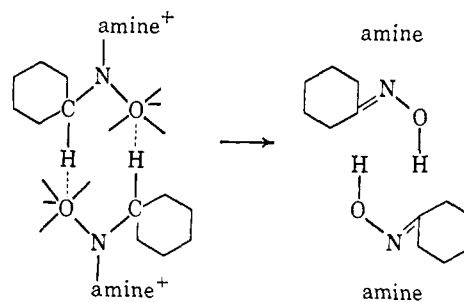

A high electron density about the amine nitrogen should facilitate removal of both the first and second tertiary hydrogens, and thus lead to the observed increase in rate constant with increasing electron density. Separation of the two oxime-like anions in the transition state of the rate-determining step should be furthered by electrostatic repulsion between the two halves of the transition state molecule. Accordingly, the isomerization rate should be highest in media of low dielectric constant. The equilibrium constant of eq. 1 should favor complex formation in polar solvents, however. The product of these two effects, which is equal to the observed rate constant, is consistent with the observed slight decrease in rate constant with increasing solvent polarity.

Alternatively, first-order dependence in dimer concentration also results if two molecules of nitrosocyclohexane monomer are involved before or during the rate-determining step. Assume that

$$\text{dimer} \rightleftharpoons 2 \text{ monomer} \tag{3}$$

$$\text{monomer} + \text{amine} \rightleftharpoons \text{complex} \tag{4}$$

$$2 \text{ complex} \longrightarrow 2 \text{ oxime} + 2 \text{ amine} \tag{5}$$

in which the equilibria of eq. 3 and 4 are rapidly established, and eq. 5 is the rate-determining step. The rate expression would then be $dX/dt = k_5C^2 = k_5 \cdot$

$K_4{}^2K_3A{}^2D$ where k_5 is the rate constant for eq. 5 and K_3 and K_4 are the equilibrium constants for eq. 3 and 4. The transition state for eq. 5 may be represented by a structure composed of two complexes, which breaks down to give the oxime.

A high electron density about the amine nitrogen should favor formation of the amine–nitroso monomer complex, consistent with the observed increase in rate constant with increasing electron density. Formation of the complex, since it involves a charge separation, should be favored by polar solvents; decomposition of the transition state to the oxime, which involves a destruction of charge, should proceed more readily in nonpolar solvents. The net result of these two opposing effects is consistent with the observed slight decrease in rate constant with increasing solvent polarity.

As seen in Figure 1, the second-order dependence of the rate constant on the amine concentration is valid only for amine concentrations below 0.8 M. Neither mechanism affords a ready explanation for the abrupt change in the dependence of the rate constant on amine concentrations above 0.8 M. The slight decrease in rate constant at very high amine concentrations is probably due to increasing polarity of the reaction medium.

Two alternate mechanisms, which might appear plausible in the absence of the present work, are briefly discussed below. If isomerization occurred rapidly through the monomer and dimer dissociation were the rate-determining step, isomerization rate would be equal to the dissociation rate, and no dependence on amine concentration would be evident. If only one molecule of nitrosocyclohexane monomer were involved before or during the rate-determining step, the isomerization rate would depend on the one-half power of the dimer concentration, instead of the first power as observed.