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The Formation and Chelate-forming Properties of 2-Chloriminocyclohexanone Oxime and Its Hydrochloride

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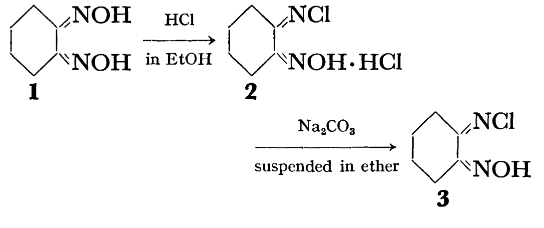
Cyclohexane-1,2-dione dioxime (**1**) in absolute ethanol containing hydrogen chloride was subjected to an irreversible dehydration to afford 2-chloriminocyclohexanone oxime hydrochloride (**2**), which could be liberated by cautious neutralization with sodium carbonate. The novel free and salt-form compounds thus obtained reacted with metal ions, such as Cu(II), Co(II), Ni(II), and Pd(II), to afford stable complexes. The molar ratio and the consecutive stability constants of a Ni(II) complex of **2** were determined and compared with those of a complex of **1** with Ni(II). An approximate linear relationship between the logarithm of the rate constant of the *N*-chlorimination and the acidity function, H_0, was observed.

The ordinary reaction of oximes with hydrogen chloride in nonaqueous solvents affords the corresponding stable salts, which can be reversibly set free with strong bases. Cyclohexanone oxime[1a,b)] and its 2-substituted derivatives,[1c,d)] the substituents of which are alkyl, alkoxyl, hydroxyl, piperidinyl, morpholinyl, and so on, are typical examples. In an attempt to prepare cyclohexanedione dioxime dihydrochlorides, we have found that cyclohexane-1,2-dione dioxime (**1**) can readily be transformed into novel 2-chloriminocyclohexanone oxime hydrochloride (**2**). The conventional synthetic routes to *N*-chlorimines are the chlorination of the corresponding imines with hypochloric acid or its derivatives,[2–5)] the reaction of carbonyl compounds with chloramine[6,7)] and the dehydrochlorination of *N*,*N*-dichloro-*sec*-alkylamines by the action of strong bases.[8–10)] There are few papers[11)] reporting the direct conversion of hydroxyimino group into *N*-chlorimine. The present paper will report the formation of **2** from **1** by the direct displacement of one of the hydroxyl groups of the hydroxyimino groups with chloride and the chemical properties, especially, related to a ligand in chelate complexes.

Results and Discussion

Formation of 2-Chloriminocyclohexanone Oxime and Its Hydrochloride. It was found that when an absolute ethanolic solution of cyclohexane-1,2-dione dioxime (**1**) was, after the introduction of dry hydrogen chloride to saturation at temperatures between −1 and 1 °C, allowed to stand for several days at a low temperature colorless-needle-form crystalline 2-chloriminocyclohexanone oxime hydrochloride (**2**) was precipitated with the formation of its equivalent molar water.



As is shown in Fig. 1, the chloride titrations of **2** with silver nitrate indicates that the ionic chloride in **2** is equal to half of the total chlorine content. The successful liberation of **2** to 2-chloriminocyclohexanone oxime (**3**) proceeded by means of the neutralization of 2 suspended in diethyl ether with an aqueous sodium carbonate solution at temperatures between −10 and 5 °C.

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1) a) H. Saito, K. Nukada, and M. Ohno, *Tetrahedron Lett.*, **1964**, 2124. b) H. Saito, *Nippon Kagaku Zasshi*, **85**, 724 (1964). c) H. Saito and K. Nukada, *J. Mol. Spectrosc.*, **18**, 1 (1965). d) H. Saito, I. Terasawa, M. Ohno, and K. Nukada, *J. Amer. Chem. Soc.*, **91**, 6696 (1969).

2) P. P. Peterson, *Amer. Chem. J.*, **46**, 325 (1911).

3) K. N. Campbell, *J. Amer. Chem. Soc.*, **59**, 2058 (1937).

4) a) H. E. Baumgarten and F. A. Bower, *ibid.*, **76**, 4561 (1954). b) H. E. Baumgarten and J. M. Petersen, *ibid.*, **82**, 459 (1960). c) H. E. Baumgarten, J. M. Petersen, and D. C. Wolf, *J. Org. Chem.*, **28**, 2369 (1963).

5) G. F. Wright, L. K. Jackson, and G. W. R. Smart, *J. Amer. Chem. Soc.*, **69**, 1539 (1947).

6) C. R. Hauser, *ibid.*, **52**, 1108 (1930).

7) B. Rudner (to W. R. Grace & Co.) U.S. 2894028 (1959).

8) S. L. Reid and D. B. Sharp, *J. Org. Chem.*, **26**, 2567 (1961).

9) G. H. Alt and W. S. Knowles, *ibid.*, **25**, 2047 (1960).

10) S. L. Reid (to Monosonto Co.) U.S. 3137728 (1964).

11) Although Hantzsch[12)] had assumed the formation of *N*-chlorimines as intermediates of the Beckmann rearrangement of oximes in PCl_3, this assumption was denied by Theilacker and Mohl.[13)]

12) A. Hantzsch, *Ber.*, **24**, 23 (1891).

13) W. Theilacker and H. Mohl, *Ann. Chem.*, **563**, 99 (1949).

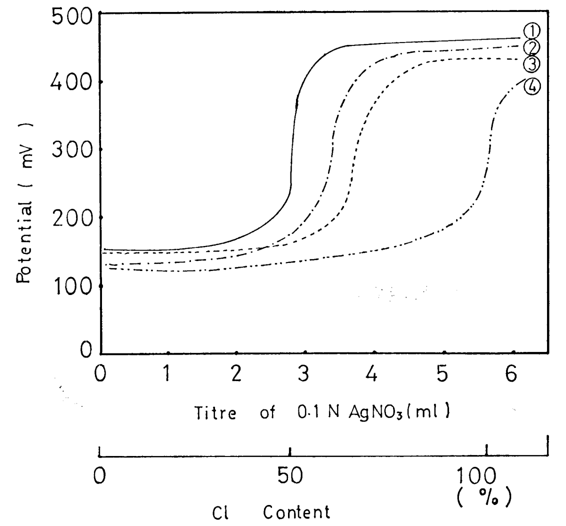
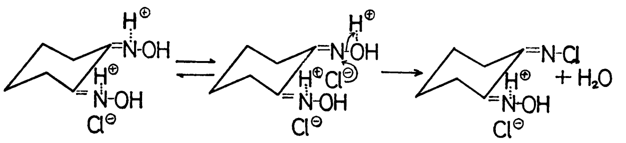


Fig. 1. $AgNO_3$ titration curves of 2-chloriminocyclohexanone oxime hydrochloride.
Condition: Sample 55.5 mg/30 ml H_2O; Temp. 25°C
1: Without buffer solution (pH 2.3); 2: Buffer solution pH 4.6; 3: Buffer solution pH 6.3—7.3; 4: Hydrolysis in alkaline solution.

The structures of **2** and **3** were supported not only by the results of the elemental analysis, the molecular-weight determinations, the titration curves and the UV and IR spectra, but also by the formation of such derivatives as cyclohexane-1,2-dione bis-(2,4-dinitrophenylhydrazone) and 1,2,3,4,6,7,8,9-octahydrophenazine: the latter was obtained by the hydrogenation of **2** in ethanol over palladium chloride. Compounds **2** and **3** also retained such chelate-forming properties as those in **1**.

Acyclic vicinal dioximes, such as dimethylglyoxime, diphenylglyoxime and di-α-furylglyoxime, normally gave the corresponding dihydrochlorides by reactions with hydrogen chloride under the same anhydrous conditions. Cyclohexane-1,3-dione dioxime monohydrochloride was immediately precipitated from an absolute ethanolic solution as soon as dry hydrogen chloride was introduced. Simple dihydrochloride, however, could not be isolated even from the solution saturated with hydrogen chloride. This result is in marked contrast with that of cyclohexane-1,4-dione dioxime, which affords the normal dihydrochloride.

From these results, we can conclude that the *N*-chlorimine formation is limited to **1**. The structure of cyclohexanone oxime hydrochloride has been reported to be one in which proton is donated to the nitrogen atom.[1)] In the case of **1**, the proton transfer to the oxygen atom in one of the hydroxyimino groups is supposed to bring about a partial ionization of the hydroxyimino group as in an intermediate of the Beckmann rearrangement. The electron deficient nitrogen or nitronium thus formed may then be nucleophilically attacked by chloride to afford the *N*-chlorimine.



The peculiar reactivity of **1** may be ascribed to the fact that the rigid co-planarity of vicinal dioxime groups where protons donate and when counter anions, chloride anions, exist, makes the salt unstable and so likely to undergo the α-displacement described above.

TABLE 1. RATE CONSTANTS OF 2-CHLORIMINOCYCLOHEXANONE OXIME HYDROCHLORIDE FORMATION FROM CYCLOHEXANE-1,2-DIONE DIOXIME[a)] IN ETHANOL

Temperature (°C) (±0.1)	Rate constants $(hr^{-1}) \times 10^{-2}$ From the dioxime	From H_2O formed	Mean
0.0	1.72	1.48	1.60
10.0	2.88	3.22	3.05
20.0	7.66	5.27	6.45

a) The concentration of hydrogen chloride was 34.0—34.8% by weight.

TABLE 2. DETERMINATION OF THERMODYNAMIC QUANTITIES IN THE FORMATION OF 2-CHLORIMINOCYCLOHEXANONE OXIME HYDROCHLORIDE

Solvent	E_a (kcal/mol)	(e.u.)$\Delta S^{\neq}$	Concentration of HCl (wt%)
Ethanol	11.1	−19.4	34
Dioxane	19.4	− 8.4	10
Cyclohexanone oxime dihydrochloride	7.1	−39.1	36

Kinetics. The rate of the conversion of **1** into **2** was of the first order in a non-aqueous solution at a given concentration of hydrogen chloride. Table 1 shows that the decreasing rate of **1** was approximately equal to the rate of the formation of water. The activation energy was measured in ethanol, dioxane and cyclohexanone oxime;[14)] the results are shown in Table 2. These substances are all solvent-dependent, *i.e.*, smaller in more polar solvents. The rate of the *N*-chlorimination increased with an increase in the concentration of hydrogen chloride in absolute ethanol, but there was no linear relationship between them. However, when the acidity function, H_0, was measured in an absolute ethanol solution of hydrogen chloride at 10 °C, an approximate linear relationship between the logarithm of the rate constant, k, and the acidity function, H_0, was observed (Fig. 2). In discussing the probable transition state from the relationship between the rate constant and the acidity function, H_0, Hammett[15)] suggested that when the conjugate acid of the reactant takes part in the rate-determining step, the $\log k = -H_0 + \text{const.}$ relation should hold. This prediction of the unit slope relationship was not realized in the authors' experiments, but there may be some significance in the approximate linear relationship between log k and H_0.

Chelate-forming Properties. The *N*-chlorimines **2** and **3** co-ordinate to various metal ions, *e.g.*, copper-

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[14)] Cyclohexanone oxime dihydrochloride forms an oily material.[1a,1b)]

[15)] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y. (1940), p. 273.

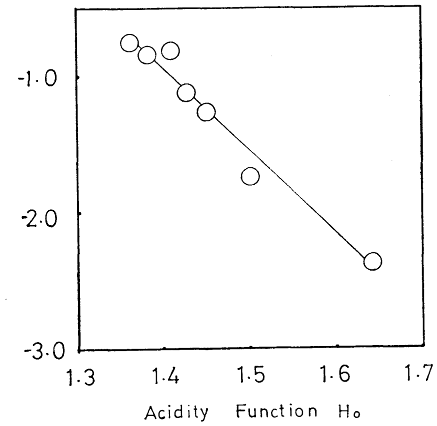
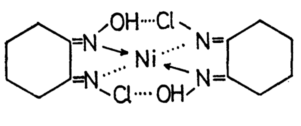


Fig. 2. The relationship between acidity H_0 and log k in 2-chloriminocyclohexanone oxime hydrochloride formation.

(II), nickel(II), cobalt(II), and palladium(II) ions, such as **1** does. However, the *N*-chlorimines are not polarographically active.

Copper(II) Complex of 2. The absorption spectra change on the change in the molar ratio of **2** to the copper(II) ion and the pH of its aqueous solution. In a neutral solution, the complex has its maximum absorption at 264 nm in the presence of an excess of copper(II) ion. However, when the molar ratio is higher than two, the complex shows its maximum at 545 nm ($\varepsilon=1.03\times10^2$). At pH values below three, the complex is not formed. A stable violet complex solution is obtained at pH value from 5 to 6. By Job's continuous variation method,[16] the molar ratio was determined to be two in the stable complex in solution.

Nickel(II) Complex of 2. The formation of the nickel(II) complex was considerably affected by the pH, and the chelate could be formed only in the alkaline range. The absorption spectrum has no maximum at pH 10, but a shoulder at 420 nm ($\varepsilon=7.10\times10^2$). In a buffer solution at pH 8.0, the molar ratio was determined to be two by Job's method. By means of Bjerrum's pH measurement method[17] and Block-McIntyre calculations[18] the consecutive stability constants were measured in 75% aqueous dioxane at 20 °C and found to be $\log k_1=7.90$ and $\log k_2=4.81$. Accordingly, appreciable amounts of the mono complex must exist in the presence of an excess of nickel(II). In contrast, vicinal dioximes give the $k_1<k_2$[19] stability constants. Especially, the nickel(II) complex of **1** has stability constants at 25 °C $\log k_1=8.52$ and $\log k_2=8.82$. Therefore, the overall stability constant ($\log k_1\cdot k_2=12.71$) of the nickel(II) complex of **2** is much smaller than that ($\log k_1\cdot k_2=17.34$) of the corresponding complex of **1**. From analogy with the metal (II)-vicinal dioxime complexes,[20] the complex was supposed to have the following structure:



The relative instability of the nickel(II) complex of **2** and the $k_1 \gg k_2$ relationship can be attributed to the weaker hydrogen bonding in the –OH···Cl bond in the complex than in the –OH···O bond in the nickel(II) complex of **1**, and to the steric effect of chlorine.

Cobalt(II) and Palladium(II) Complexes. The *N*-chlorimine **2** formed a stable complex with the cobalt(II) ion in an alkaline solution, the absorption spectrum of which had neither maximum nor shoulder. The molar ratio was also shown to be two. The palladium(II) ion readily reacted with **2** to precipitate a yellow complex.

Experimental

Apparatus. The IR spectra were measured on a Shimadzu IR spectrometer IR-27A. The electronic spectra were recorded by means of a Hitachi Spectrometer EPS-2. The pH measurements were made with a Horiba pH Meter, type M. The potentiometric titration curves were obtained by the use of a Metrohm Potentiograph E-336. The molecular weights were determined by means of a Mechrolab Vapor-pressure Osmometer.

Materials. The cyclohexanedione dioximes were prepared by the procedure described in a previous paper.[21] The copper(II), nickel(II), cobalt(II), and palladium(II) ions used were $Cu(OCOCH_3)_2\cdot H_2O$, $NiCl_2\cdot 6H_2O$, $CoCl_2\cdot 6H_2O$, and $PdCl_2$ respectively, all were of analytical grade purity and were used without further purification.

2-Chloriminocyclohexanone Oxime Hydrochloride (2). To a solution of **1** (90 g) in absolute ethanol (200 ml) on a brine bath at −1—1 °C, we introduced dry hydrogen chloride until the point of saturation (about 33—34% by weight). After the mixture had stood for several days in a refrigerator, colorless needle crystallines were precipitated; they were filtered off and washed with anhydrous diethyl ether. Yield, 80 g (64%). Mp 130 °C (decomp.). UV (ethanol): 224 ($\log\varepsilon=4.66$), 265 nm ($\log\varepsilon=4.46$). IR (KBr): 3240 (OH), 2600 (N^+–H), 1665 cm^{-1} (C=N). Found: C, 36.45; H, 4.95; O, 8.65; N, 13.69; Cl, 36.64. Calcd for $C_6H_{10}N_2OCl_2$: C, 36.57; H, 5.11; O, 8.12; N, 14.22; Cl, 36.64%. The potentiometric titration curves obtained by the use of silver nitrate are shown in Fig. 1. No such polarographic activity as that of **1**[22] was observed.

2-Chloriminocyclohexanone Oxime (3). Into a suspension of **2** (10.5 g) in diethyl ether (100 ml) on a brine bath at −5—−10 °C, was added drop an aqueous 10% sodium carbonate solution with stirring to bring the pH of the aqueous phase to about 10. After the separation of the ether phase the aqueous phase was extracted with four 25 ml portions of diethyl ether. The ether fractions were then combined and dried over anhydrous sodium sulfate. The solvent was

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[16] P. Job, *Ann. Chim.*, **9**, (10) 113 (1928).

[17] J. Bjerrum, "Metal Ammine Formation in Aqueous Solution". P. Haase & Son. Copenhagen (1941).

[18] B. P. Block and G. H. McIntyre, Jr., *J. Amer. Chem. Soc.*, **75**, 5667 (1953).

[19] C. V. Banks, The Proceeding of the International Symposium, Analytical Chemistry, held at Birmingum University (U.K.). p. 131, April, 1962.

[20] C. V. Banks, *Record Chem. Progr*, **25**, (2) 85 (1964).

[21] Y. Kobayashi and S. Wakamatsu, *Tetrahedron*, **23**, 115 (1967).

[22] a) M. Ishibashi, T. Fujinaga, and K. Kawamura, This Bulletin, **26**, 513 (1953). b) P. E. Wenger, D. Monnier, and W. Backmann-Chapuis, *Anal. Chim. Acta*, **20**, 444 (1959). c) D. Monnier and W. Haerdi, *Helv. Chim. Acta*, **41**, 2205 (1958).

distilled off, and the residue was recrystallized from water to afford colorless needles. Yield, 6.8 g (85%). Mp 115.0—116.5 °C. UV (water): 265 nm ($\log\varepsilon=3.99$), IR (KBr); 1655 cm^{-1} (C=N). (mol. wt. by vapor-pressure osmometry in ethanol): 162 (Calcd for 160.2). Found: C, 44.55; H, 5.68; N, 17.47; O, 10.36; Cl, 22.07%. Calcd for $C_6H_9N_2OCl$: C, 44.87; H, 5.65; N, 17.44; O, 9.96; Cl, 22.08%.

*Cyclohexane-1,2-dione-bis-(2,4-dinitrophenylhydrazone) from **2**.* To a solution of 2,4-dinitrophenylhydrazine (2.0 g) in 95% ethanol (140 ml), conc. hydrochloric acid (100 ml) and **2** (2.0 g) were successively added. The mixture was then refluxed for 30 min with occasional stirring. After the mixture had stood overnight in a refrigerator, an orange precipitate was formed; this was filtered off and recrystallized from ethanol. Yield, 4.9 g. Mp 220—222.5 °C (decomp.); undepressed by admixture with an authentic sample derived from **1** (lit,[23] mp 220 °C). IR: superimposable with that of an authentic sample. Found: C, 45.47; H, 4.02%. Calcd for $C_{18}H_{16}O_8N_8$: C, 45.77; H, 3.42%.

*1,2,3,4,6,7,8,9-Octahydrophenazine from **2**.* Nine grams of **2** in absolute ethanol (220 g) were hydrogenated by palladium chloride (0.6 g as Pd) under atmospheric pressure at room temperature with constant shaking. About 2.7 l of hydrogen was absorbed. After the removal of the catalyst, the solvent was distilled off and benzene was added. The precipitated ammonium chloride was then filtered off, and the filtrate was neutralized with sodium hydroxide solution and steam-distilled. The water was removed *in vacuo*, and the residue was recrystallized from benzene or acetone to afford colorless plate crystalline: 1,2,3,4,6,7,8,9-octahydrophenazine hydrochloride hydrate (0.65 g). Mp 124—126 °C. UV (ethanol): 214 ($\log\varepsilon=3.76$), 291 ($\log\varepsilon=3.90$), 310 nm ($\log\varepsilon=3.93$). IR (KBr): 2380, 1980 cm^{-1} (N$^+$-H), H_2O content: 8.1% (requires 7.42%), as determined by Karl Fischer's method. Found: C, 59.06; H, 7.89; N, 11.53; Cl, 14.86; O, 5.65%. Calcd for $C_{12}H_{16}N_2\cdot HCl\cdot H_2O$: C, 59.37; H, 7.89; N, 11.54; Cl, 14.61; O, 6.59%. The base was successfully liberated by neutralization with an anionic exchanger Amberlite CG-400 (OH type), followed by steam distillation. Mp 109 °C (lit,[24] 108—109 °C). Found: C, 76.73; H, 8.44; N, 14.26%. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 14.88%.

*Determination of the Rate Constants of the Dehydration Reaction of **1** with HCl.* To a 200 ml Erlenmeyer flask with a grinding stopper containing absolute ethanol (150 ml) saturated with dry hydrogen chloride, **1** (4.5 g) was introduced with vigorous shaking. The flask was then placed in a desiccator and kept in a refrigerator at a constant temperature. The contents of both **1** and water were determined at given intervals.

*Determination of **1**.* About 2 g of the sample were pipetted out, accurately weighed, and then poured into water (200 ml). A 20% ammonium acetate solution was added to adjust the pH to 5.5—6.0. Then, 10 ml portion of an aqueous nickel(II) chloride solution (1 mg as Ni(II)/ml) was added, and the whole was kept standing for 3—4 hr at 40 °C. The red precipitates were filtered off with a glass-filter G4 and gravimetrically determined.

Determination of the Water Formed. About 5 g of the sample were pipetted out, poured into a mixture of absolute ethanol (10 ml) and anhydrous pyridine (5 ml), and accurately weighed. The water concentration in the solution was determined by Karl Fischer's method.

Determination of the Acidity Function, H_0. The acidity functions of the absolute ethanol–hydrogen chloride system were determined spectrophotometrically with *p*-nitroaniline at 360 nm.

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[23] D. D. E. Newmann and L. N. Owen, *J. Chem. Soc.*, **1952**, 4713.

[24] O. Wallach, *Ann. Chem.*, **437**, 177 (1927).