(3.0%), 71 (36.1%), 57 (10.9%), 55 (7.8%). Monodeuterated **5b**: 236 (P, 11.3%), 234 (1.7%), 220 (15.7%), 218 (3.2%), 179 (21.4%), 178 (B, 100%), 177 (6.9%), 176 (2.9%), 165 (3.2%), 164 (22.5%), 163 (5.9%), 162 (7.5%), 161 (2.9%), 151 (10.2%), 150 (75.0%), 149 (7.8%), 148 (17.7%), 147 (6.8%), 136 (17.4%), 135 (39.2%), 134 (10.6%), 133 (6.9%), 122 (41.6%), 121 (7.6%), 120 (8.8%), 119 (5.9%), 108 (3.7%), 107 (5.3%), 106 (5.3%), 105 (5.5%), 94 (2.3%), 93 (3.1%)8 92 (4.2%), 91 (6.5%), 79 (2.6%), 77 (2.5%), 71 (38.1%), 57 (14.3%), 55 (3.2%); ^{1}H NMR (100 MHz, $CHCl_3$) δ 0.747 (6-CH_3, 3 H, J(CH,CH_3) = 6.8 Hz), 0.878 (4-CH_3, 9 H), 0.957 (1-CH_3, 6 H), 1.486 (6-CH, 1 H), 1.660 (5-CH_3, 3 H), 1.716 (2,3-CH_3, 6 H), 2.170 (4-CH_2, 2 H), ^{13}C NMR (Me_4Si, 22.63 MHz, $CDCl_3$) 11.71 (6-CH_3), 14.68 (2-CH_3), 16.67 (5-CH_3), 20.34 (3-CH_3), 23.79 and 25.09 (1-CH_3), 30.05 (4-CH_3), 34.42 (4-$C(CH_3)_3$), 36.47 (1-C ring), 39.66 (4-CH_2), 47.70 (6-C ring), 126.8 (5-C ring), 127.9 (2-C ring), 130.9 (3-C ring), 134.4 (4-C ring).[21]

Reaction of *sec*-Butyllithium with Triene 1. This reaction was carried out in similar fashion to those using *n*-butyllithium and *tert*-butyllithium. Thus *sec*-butyllithium (2.3 mL, 4.08 M, 9.48 mmol) in cyclopentane was reacted at 0 °C for 30 min with a solution of triene 1 (1.52 g, 8.02 mmol) in 3 g of dry THF. Quenching with degassed water and separation of products by gas chromatography gave 0.31 g of triene 1 (20.6%), 0.56 g of **5c** (37%), 0.4 g of **6c** (26.2%), and 0.25 g of **4c** (16.2%). Crude samples were purified by high-pressure LC (see above). NMR spectra are summarized in Table I. Mass spectral data: **4c**, *m/e* calcd 218.2034, obsd 218.2039; **5c**, *m/e* calcd 234.2347, obsd 234.2351.[21]

Reaction of 3b with O_2. The glassware consists of a 10-mL round-bottom flask with side arm protected by a 2-mm straight-bore stopcock with serum cap. A glass-covered stirring bar was introduced and the system flamed out in a current of argon. A mixture of triene 1 (0.67 g, 3.79 mmol) and *N*-methylpyrrolidine (0.79 mL, 7.58 mmol) was syringed in via the stopcock. To this solution, at 20 °C, was added by syringe *tert*-butyllithium in cyclopentane (1.5 mL, 2.64 M, 3.98 mmol) over a period of 8 min and the mixture was allowed to stir for an additional 20 min. A 0.4-mL aliquot from this reaction mixture was hydrolyzed with deoxygenated 5% aqueous HCl and the organic layer separated by gas chromatography (5 ft × 0.25 in. column with SE-30 on glass beads, 122 °. This showed >99% conversion to **3b**. Dry oxygen (through $CaSO_4$) was bubbled through the remaining solution of **3b**, which turned from yellow to red and then back to yellow. Samples were removed for NMR (^{1}H and ^{13}C) investigation. The rest was hydrolyzed with D_2O, treated with 10 mL of a solution of 5 g of ammonium chloride in 25 mL of water and the organic layer washed with 5% aqueous HCl. After being dried with sodium acetate and removal of solvent the organic layer gave 0.52 g of a yellow oil, 93% of which gave rise to six components: **25** (56%), *m/e* 232; **26** (8%), *m/e* 232; **27** (9%), *m/e* 232; **28** (5%), *m/e* 248; **29** (1%), *m/e* 248; **30** (14%), *m/e* 248.

(21) Dienes and dienols were insufficiently stable to survive transportation for analysis. However, their NMR spectra show no detectable impurities.

Acknowledgment. This research was supported by grants from the National Science Foundation, GP36633-X2 and CHE-7610909, and in part by the donors of the Petroleum Research Fund, administered by the American Chemical Society, No. 8795-AC4. A grant from the National Science Foundation partly financed the NMR equipment used in this work. We thank Mr. C. R. Weisenberger for his generous help with the mass spectral work.

Registry No. 1, 3043-52-5; 2, 27175-04-8; **3a**, 75961-59-0; **3b**, 75961-60-3; **3c**, 75961-61-4; **4a**, 75934-66-6; **4b**, 56909-25-2; **4c**, 75934-67-7; **5a**, 75948-79-7; **5b**, 75948-80-0; **5b-d**, 75948-81-1; **5c**, 75948-82-2; **6a**, 75948-83-3; **6b**, 75948-84-4; **6b-d**, 75948-85-5; **6c**, 75948-86-6; **7**, 702-98-7; **25** (R = *tert*-butyl), 75934-68-8; **26** (R = *tert*-butyl), 75934-69-9; **27** (R = *tert*-butyl), 75934-70-2; **28** (R = *tert*-butyl), 75934-71-3; **29** (R = *tert*-butyl), 75934-72-4; **30** (R = *tert*-butyl), 75934-73-5; butyllithium, 109-72-8; *tert*-butyllithium, 594-19-4; *sec*-butyllithium, 598-30-1; hexamethylbenzene, 87-85-4; 2-adamantanone, 700-58-3.

Mechanism of an Acid-Catalyzed Geometric Isomerization about a Carbon-Nitrogen Double Bond[1]

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The mechanism of the hydrogen chloride catalyzed geometric isomerization of (*E*)-*O*-methylbenzohydroximoyl chloride (**1a**) has been investigated. It has been determined that radioactive chloride ($^{36}Cl^-$) is incorporated into the hydroximoyl chloride at a rate equal to one-half the rate of the isomerization. It has also been found that the rate constant for $^{36}Cl^-$ incorporation into the (*E*)-hydroximoyl chloride (**1a**) during isomerization is about 210 times faster than the rate constant for $^{36}Cl^-$ exchange in the (*Z*)-hydroximoyl chloride (**2a**). Based on these observations, it is concluded that the isomerization of **1a** involves nucleophilic attack by $^{36}Cl^-$ on the conjugate acid of **1a** to give a tetrahedral intermediate. The tetrahedral intermediate undergoes stereomutation and thus has a 50–50 chance of losing either $^{36}Cl^-$ or nonradioactive Cl^- to give the conjugate acid of **2a**. The isomerization rates for five (*E*)-hydroximoyl chlorides (**1a–e**) gave a Hammett correlation with σ with a ρ value of –0.66. The rate of isomerization of **1a** was measured in deuterium chloride–dioxane solution and found to be about twice as fast as the isomerization of **1a** in hydrogen chloride (k_H/k_D = 0.44). The low Hammett ρ value and a deuterium isotope effect of 0.44 are consistent with a preequilibrium protonation of **1a** followed by nucleophilic attack by chloride ion. It was found that an *o*-methyl substituent (**1f**) considerably reduces the rate of isomerization.

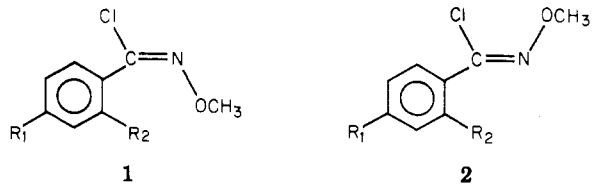
A plethora of studies[3-13] has been carried out on the kinetics and mechanisms of uncatalyzed geometric isomerization of compounds containing a carbon–nitrogen double bond (imines). Although most of these investiga-

(1) Part of this work was presented at the 170th National Meeting of the American Chemical Society, Chicago, IL, Aug 27, 1975; Abstract ORGN-69.

(2) Taken in part from the Ph.D. Dissertation of E. A. Nalley, Texas Woman's University, May 1975, and the M.S. Thesis of N. M. Silk, Texas Woman's University, May 1978.

0022-3263/81/1946-0546$01.00/0

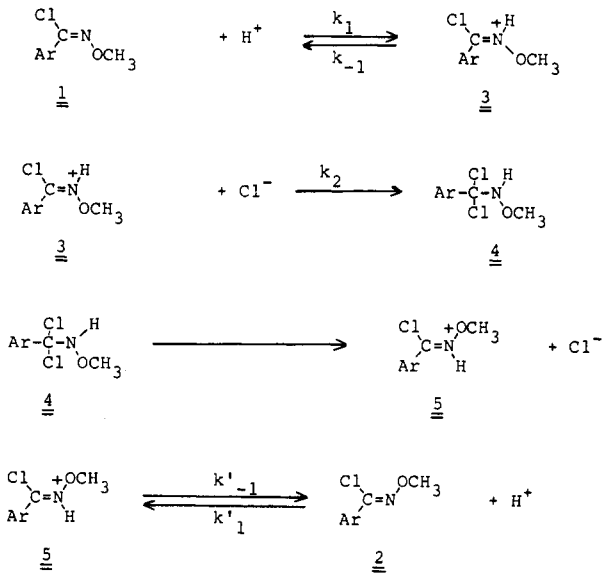
Chart I



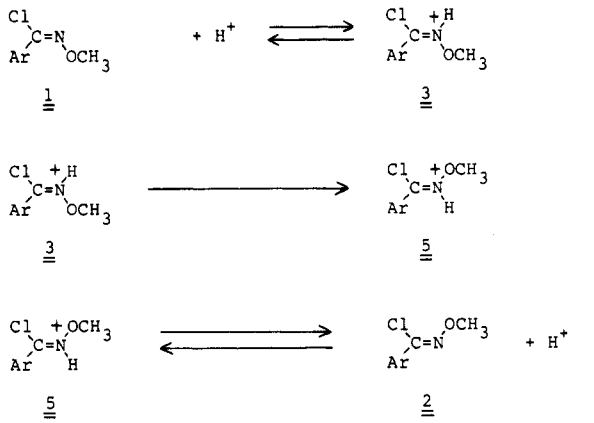
1 **2**

a, $R_1 = R_2 = H$
b, $R_1 = NO_2$; $R_2 = H$
c, $R_1 = CH_3$; $R_2 = H$
d, $R_1 = Cl$; $R_2 = H$
e, $R_1 = OCH_3$; $R_2 = H$
f, $R_1 = H$; $R_2 = CH_3$

Mechanism I. Nucleophilic Catalysis



Mechanism II. Immonium Ion Rotation



tions have been concerned with systems which isomerize rapidly at room temperature, several studies have been carried out on imine derivatives (oximes,[11] oxime anions,[12a] amidoximes,[13] and nitrones[12]) whose geometric isomers are configurationally stable at room temperature. In comparison, there are relatively few studies on the acid-catalyzed isomerization of imine derivatives. It has even been suggested,[11] apparently without regard to many earlier reports[14-16] to the contrary, that oximes do not undergo rapid acid-catalyzed isomerization. This suggestion was based on the observation that phenyl 2-pyridyl ketoxime does not isomerize at a measureable rate in 1 M hydrochloric acid solution at 32 °C. It is likely, however, that the reason for slow isomerization of the pyridyl oxime is simply that protonation occurs on the pyridine nitrogen rather than the oxime nitrogen. Since diprotonation would be unlikely in 1 M acid solution, the oxime functional group is not protonated and does not undergo *E*–*Z* isomerization.

In this report we describe a kinetic and mechanistic investigation on the acid-catalyzed geometric isomerization of (*E*)-*O*-methylbenzohydroximoyl chlorides (Chart I, **1a–f**). Previous work[17,18] has shown that these compounds do not readily undergo thermal isomerization but are isomerized to the *Z* isomers (**2a–f**) in the presence of hydrogen chloride. The acid-catalyzed *E*–*Z* isomerization goes essentially to completion with the equilibrium concentrations being approximately 0.5% *E* to 99.5% *Z*.

Two possible mechanisms for the acid-catalyzed isomerization of the (*E*)-hydroximoyl chlorides (**1**) have been considered. The first of these [Mechanism I (nucleophilic catalysis)] involves protonation of **1** on nitrogen to give the (*E*)-immonium ion **3** followed by nucleophilic attack by chloride ion to give the tetrahedral intermediate **4**. The tetrahedral intermediate could collapse to the (*Z*)-immonium ion **5** which on loss of a proton produces the (*Z*)-hydroximoyl chloride (**2**).

Idoux and Sikorski[19] proposed nucleophilic catalysis for the sulfuric acid catalyzed isomerization of α-substituted acetophenone 2,4-dinitrophenylhydrazones in carbon tetrachloride. Unfortunately the only experimental evidence offered to support their conclusion was the observation that aldehyde 2,4-dinitrophenylhydrazones isomerize faster than the corresponding ketone hydrazones. Furthermore, nucleophilic catalysis under their reaction conditions would require nucleophilic attack by sulfate ion (or bisulfate ion) which is unlikely in view of its poor nucleophilicity. It is possible, however, that traces of water in their system were responsible for the nucleophilic catalysis.

More recent reports indicate that nucleophilic catalysis is responsible for the thiol-catalyzed *E*–*Z* isomerization of benzaldehyde semicarbazone[20] and the benzoic acid catalyzed isomerization of the imine **11**.[21]

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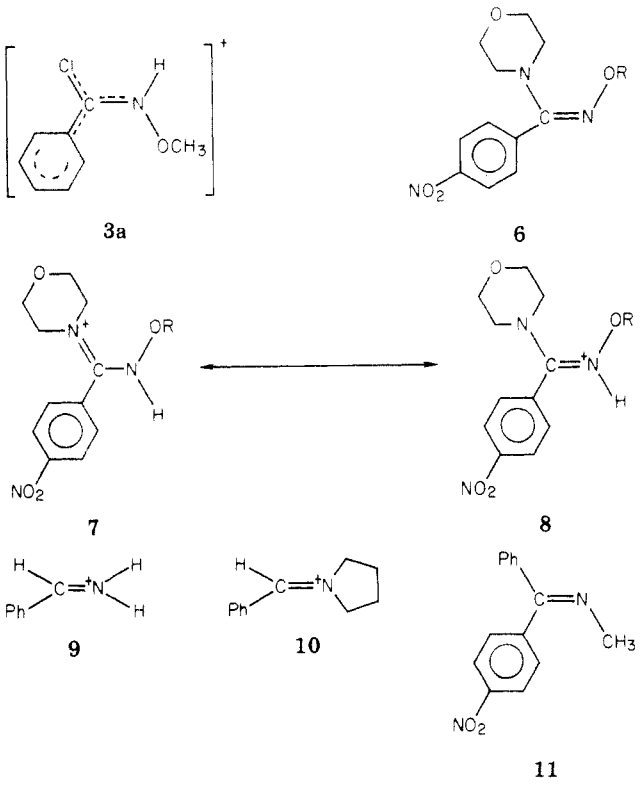
(18) The *E*–*Z* configurational assignments made for the hydroximoyl halides reported in ref 17 must be reversed. The *O*-methyl-*p*-nitrobenzohydroximoyl chloride prepared by reaction of methyl *p*-nitrobenzohydroxamate with phosphorus pentachloride has been determined by X-ray crystallographic analysis to have the *Z* configuration: Bertolasi, V.; Socerdoti, M.; Tassi, D. *Cryst. Struct., Commun.* **1977**, *6*, 335.
(19) Idoux, J. P.; Sikorski, J. A. *J. Chem. Soc., Perkin Trans. 2* **1972**, 921.
(20) Conlon, P. R.; Sayer, J. M. *J. Org. Chem.* **1979**, *44*, 262.

Chart II



In the alternate mechanism [Mechanism II (immonium ion rotation)], the isomerization of 1 occurs by rotation around the immonium ion double bond. This seems to be a reasonable alternative since delocalization of the positive charge by the chlorine atom and the phenyl group (as shown in the resonance hybrid **3a**, Chart II) could substantially lower the rotational barrier in the immonium ion.

The acid-catalyzed isomerization of a wide variety of imine derivatives (oximes,[22,23] amidoximes,[13] amidines,[24] imidates,[25] and *S*-acylisothioureas[26]) are thought to proceed either via rotation about the carbon–nitrogen double bond of the conjugate acid,[13,23,24,26] or through tautomerism mechanisms.[22,25] In only one of these reports,[13] however, has any experimental evidence been offered which rules out isomerization by nucleophilic catalysis either as a concurrent mechanism or as the exclusive process. Dignam and Hegarty[13] found that the rate of acid-catalyzed isomerization of benzamidoximes (**6**) did not increase with an increase in total buffer concentration which demonstrates that the acid counterion is not involved in nucleophilic catalysis. It should be pointed out, however, that benzamidoximes represent a rather special case where resonance stabilization through the nitrogen lone pair of the amino group (resonance structure **7**) of the protonated benzamidoxime (resonance structure **8**) would be expected to be especially important since the resonance structures are equivalent except for substitution. On the other hand, CNDO/2 calculations on **9** as well as dynamic NMR experiments on **10** have shown that these relatively simple immonium ions have high rotational barriers ($\Delta G^{\ddagger} > 27$ kcal/mol at 204 °C).[21] Since addition of benzoic acid to a diphenylamine solution of **11** markedly decreased the coalescence temperature of the *N*-methyl signals in the NMR spectrum, Jennings and Boyd and their co-workers[21] suggested that the isomerization of **11** proceeds by nucleophilic addition of benzoic acid to the immonium ion rather than by a rotation mechanism.

Table I. Data for the Incorporation of $^{36}Cl^-$ during the H^{36}Cl-Catalyzed Isomerization of 1a at 39.5 °C

% isomerization	theoret specific activity, dpm/mg	obsd specific activity, dpm/mg[a]	% of theory
98 (run 1)[b]	1140 (2a)	1120 ± 10 (2a)	98
98 (run 2)[b]	1140 (2a)	1110 ± 10 (2a)	97
50[c]	1050 (2a)[d]	995 ± 7 (2a)	95
		301 ± 4 (1a)	

[a] The errors in specific activities were estimated at the 95% confidence level [1.96 σ, where σ = (total number of dpm)$^{1/2}$]. [b] 100 mg of 1a in 10.3 g of 0.210 molal H^{36}Cl–dioxane solution with a specific activity of 8.12×10^4 dpm/g. [c] Conditions identical with those in footnote *b* except 393 mg of 1a was used. [d] Corrected for the $^{36}Cl^-$ consumed by 1a. Amount of activity in 2a = $(0.112/0.210)[8.12 \times 10^4 \times 10.3 - (301 \times 197)] \times {}^1/_2 = 2.07 \times 10^5$ dpm. Theoretical specific activity of 2a = 2.07×10^5 dpm/197 mg = 1050 dpm/mg.

In the present work it has been possible to distinguish between nucleophilic catalysis and immonium ion rotation in an unambiguous fashion. It would be expected that radioactive chloride ($^{36}Cl^-$) from the hydrogen chloride catalyst would be incorporated into the hydroximoyl chloride if the nucleophilic catalysis pathway were responsible for the isomerization. Furthermore, if it is assumed that there is an equal probability of loss of either of the two chlorine atoms in the tetrahedral intermediate, then the rate of radioactive chloride incorporation should be one-half the rate of isomerization. Obviously, radioactive chloride should not be incorporated during the isomerization process if rotation about the carbon–nitrogen double bond of the immonium ion is faster than nucleophilic catalysis by chloride ion.

The radioactive chloride incorporation experiments were carried out with **1a** in 10.3-g samples of 0.210 molal hydrogen chloride–dioxane solutions at 39.5 °C for 80 min which corresponds to six isomerization half-lives (98% isomerization). The expected specific activity (dpm/mg, desintegrations per minute per milligram) of the hydroximoyl chloride (100 mg) after isomerization was calculated from the initial specific activity of the 10.3-g sample of HCl–dioxane solution (8.12×10^4 dpm/g) (eq 1 and 2). In

$$\text{amount of activity in 2a after isomerization} = \frac{0.0570 \text{ mol/kg of 2a}}{0.210 \text{ mol/kg of } Cl^-} \times (8.12 \times 10^4 \text{ dpm/g} \times 10.3\text{g}) \times {}^1/_2 = 1.14 \times 10^5 \text{ dpm} \quad (1)$$

$$\text{theoretical specific activity of 2a after isomerization} = \frac{1.14 \times 10^5 \text{ dpm}}{100 \text{ mg}} = 1140 \text{ dpm/mg} \quad (2)$$

this calculation the factor ${}^1/_2$ is the statistical factor which allows for a 50–50 chance of loss of $^{36}Cl^-$ from the tetrahedral intermediate. The factor ${}^1/_2$ assumes the $^{37,35}Cl/^{36}Cl$ kinetic isotope effect in the reaction of **4** → **5** is negligible.

From the results of the $^{36}Cl^-$ incorporation experiments (Table I) it appears that the isomerization is proceeding by nucleophilic catalysis with chloride ion (Mechanism I).

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Table II. First-Order Rate Constants for the Hydrogen Chloride Catalyzed Isomerization of (*E*)-*O*-Methylbenzohydroximoyl Chlorides (1) in Dioxane at 39.5 °C

compd	[HCl], molal	10^2k, min^{-1}
1a	0.210	5.37 ± 0.16
1a	0.155	3.45 ± 0.10
1b	0.155	1.12 ± 0.05
1c	0.155	4.15 ± 0.20
1d	0.155	2.40 ± 0.06
1e	0.155	5.91 ± 0.25
1f	0.923	0.202 ± 0.015
1g	0.155[a]	7.93 ± 0.37

[a] Concentration of DCl.

The isomerization rate (Table II) for the (*E*)-hydroximoyl chloride **1a** was measured in 0.210 molal hydrogen chloride–dioxane solution at 39.5 °C. The reaction gave a good pseudo-first-order plot to greater than 90% of isomerization with a rate constant of 5.37×10^{-2} min^{-1}. Based on the results of the $^{36}Cl^-$ incorporation experiment, the rate constant for $^{36}Cl^-$ incorporation is one-half the rate constant for isomerization, i.e., $k^{36}_{Cl^-}$ incorporation = 2.69×10^{-2} min^{-1} at [HCl] = 0.210 molal.

The conclusion based on the $^{36}Cl^-$ incorporation study would be questionable, however, if the rate of $^{36}Cl^-$ incorporation into the (*Z*)-hydroximoyl chloride **2a** were of the same order of magnitude as the rate of $^{36}Cl^-$ incorporation during the isomerization of the (*E*)-hydroximoyl chloride, **1a**. The possibility was investigated by determining the rate constant of $^{36}Cl^-$ incorporation into the (*Z*)-hydroximoyl chloride (**2a**) according to eq 3, where **2a*** represents the (*Z*)-hydroximoyl chloride containing ^{36}Cl and the symbol **2a** represents the (*Z*)-chloride containing nonradioactive chlorine. Equation 4 is the integrated rate law[27] for this exchange reaction

$$\mathbf{2a} + {}^{36}Cl^- \underset{k}{\overset{k}{\rightleftharpoons}} \mathbf{2a^*} + Cl^- \qquad (3)$$

$$\frac{1}{C} \ln \left(\frac{1}{1 - CX/B} \right) = kt \qquad (4)$$

where

$$B = [\mathbf{2a}]_0[{}^{36}Cl^-]_0$$

$$C = [\mathbf{2a}]_0 + [Cl^-]_t$$

$$X = [\mathbf{2a^*}]$$

$[\mathbf{2a}]_0$ = initial concentration of **2a**

$[{}^{36}Cl^-]_0$ = initial concentration of $^{36}Cl^-$

$[Cl^-]_t$ = total chloride concentration

The derivation of this rate law assumes the radioactive tracer is in low concentration in comparison to the nonradioactive isotopes, i.e., $[Cl^-]_t \gg [{}^{36}Cl^-]$ and $[\mathbf{2a}]_0 \gg [\mathbf{2a^*}]$. This rate law further assumes the kinetic isotope effects for the forward and reverse reactions are equal which is reasonable for a $^{35,37}Cl/^{36}Cl$ exchange process.

A plot of $[1/C]$ ln $[1/(1 - CX/B)]$ vs. time (Figure 1) gave a rate constant of 6.07 (±0.20) $\times 10^{-4}$ kg mol^{-1} min^{-1} for the exchange reaction. When this rate constant is converted into a pseudo-first-order rate constant by multiplying by the concentration of the hydrogen chloride

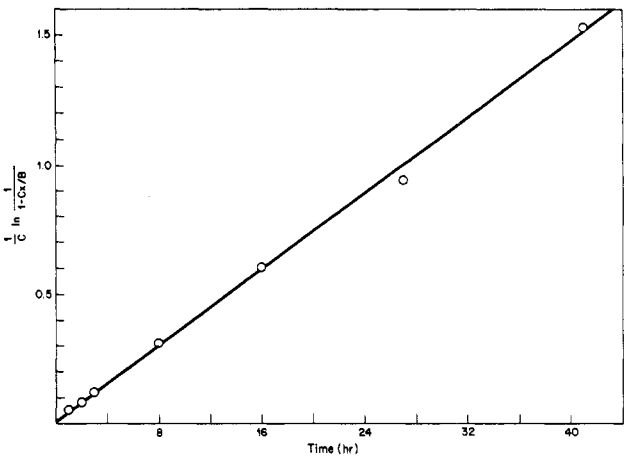
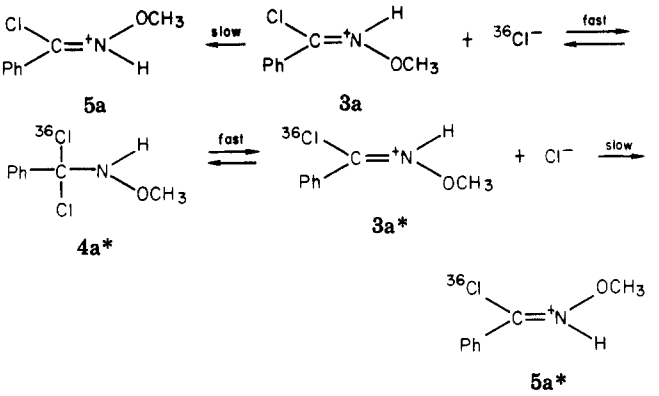


Figure 1. Plot of $(1/C)$ ln $[1/(1 - CX/B)]$ vs. time for the acid-catalyzed exchange of $^{36}Cl^-$ with (*Z*)-*O*-methylbenzohydroximoyl chloride (**2a**) at 39.5 °C.

Scheme I



([HCl] = 0.210 molal) a value of 1.27×10^{-4} min^{-1} is obtained. Thus, the rate constant for $^{36}Cl^-$ incorporation into **1a** during isomerization ($k = 2.69 \times 10^{-2}$ min^{-1}) is over 210 times larger than the rate constant for $^{36}Cl^-$ exchange in the (*Z*)-hydroximoyl chloride. Although we are unable, on the basis of available evidence, to offer a convincing explanation for this large rate difference, it may be that a difference in the base strengths of the (*E*)- and (*Z*)-hydroximoyl chlorides is responsible. If the (*E*)-hydroximoyl chloride **1a** is a stronger base than the *Z* isomer **2a**, then the difference in rate of $^{36}Cl^-$ incorporation would be due to a difference in the values of the equilibrium constants for protonation of **1a** and **2a** ($K_{eq} > K'_{eq}$ where $K_{eq} = k_1/k_{-1}$ and $K'_{eq} = k'_1/k'_{-1}$ in Mechanism I).

It is possible that the $^{36}Cl^-$ incorporation during the isomerization of **1a** occurs by a rapid exchange reaction with the conjugate acid **3a** and that the actual isomerization takes place by rotation around the carbon–nitrogen double bond of **3a** (Scheme I). If this were the case, then it would be expected that an equal amount of ^{36}Cl would be found in the (*E*)- and (*Z*)-hydroximoyl chlorides after one isomerization half-life. When the $H^{36}Cl$-catalyzed isomerization of the (*E*)-hydroximoyl chloride **1a** was carried out to one half-life it was found that **1a** contained about 24% of the total incorporated ^{36}Cl (Table I). Clearly, this observation is inconsistent with a rapid preequilibrium exchange of $^{36}Cl^-$ with **1a**. The fact that there is significant incorporation of $^{36}Cl^-$ into **1a** during the isomerization does not alter our original hypothesis concerning a 50% probability of $^{36}Cl^-$ incorporation since the isomerization of **1a** was carried out with a low concentration of $^{36}Cl^-$ in comparison to nonradioactive chloride $[(^{35}Cl^- + {}^{37}Cl^-)/{}^{36}Cl^- = 6830]$. Thus, it is unlikely that a significant amount of

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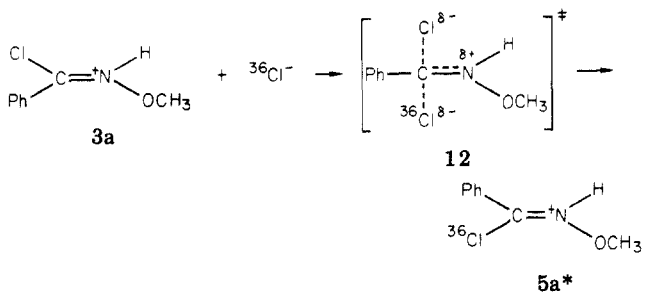
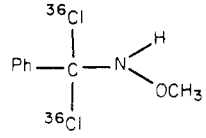
Scheme II



3a 12 5a*

dilabeled tetrahedral intermediate (**4a****) from reaction of **3a*** with $^{36}Cl^-$ would be formed during the isomerization.



4a**

A possible alternative to nucleophilic catalysis for the acid-catalyzed isomerization of **1a** is a direct S_N2 displacement mechanism by chloride ion at the immonium ion carbon atom (Scheme II). Direct displacement of chloride by $^{36}Cl^-$ on the immonium ion **3a**, through a transition state such as **12**, would invert the configuration of **3a** and give the isomerized immonium ion **5a***. Although direct S_N2 displacements on vinylic substrates have not been observed,[28] it has been suggested by Kevill et al.[29] that the ethanolysis of acyl chlorides proceeds either by exclusive direct displacement or by concurrent direct displacement and a nucleophilic addition elimination route. Furthermore, direct S_N2 displacement could not be unequivocally excluded for the bimolecular reaction of diarylimidoyl chlorides with amines in benzene[30] or acetonitrile.[31] In the isomerization of **1a**, this mechanistic possibility would require that $^{36}Cl^-$ be incorporated every time $^{36}Cl^-$ attack gave the isomerized immonium ion; i.e., the theoretical decay rate would be two times the value calculated for the nucleophilic catalysis mechanism. Since we observed about one-half the amount of $^{36}Cl^-$ incorporation expected for a direct S_N2 displacement, this possibility is ruled out.

The rate of isomerization of **1a** was measured in deuterium chloride–dioxane solution (Table II) and found to be approximately twice as fast as the isomerization in hydrogen chloride (k_H/k_D = 0.44). This observation is consistent with a mechanism involving a rapid preequilibrium proton transfer to **1a**. In aqueous solution the range of deuterium isotope effects for most preequilibrium proton transfers is 0.25–0.50.[32]

The effect of substituents on the rate of isomerization was investigated by measuring isomerization rates of **1a–e** (Table II) in 0.155 molal hydrogen chloride–dioxane solutions at 39.5 °C. A plot of log k_{obsd}/log k_{obsd_0} vs. Hammett σ values gave a ρ value of −0.66 ± 0.15 (Figure 2). The

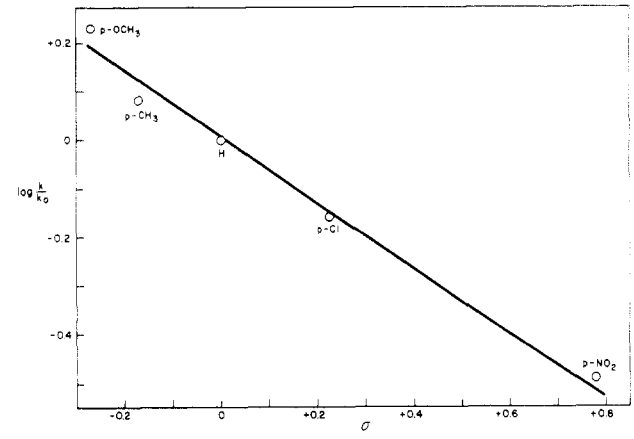


Figure 2. Hammett plot (σ) for the hydrogen chloride catalyzed isomerization of (*E*)-*O*-methylbenzohydroximoyl chlorides (**1**) in dioxane at 39.5 °C.

small ρ value is consistent with a nucleophilic catalysis mechanism, since the overall ρ value for this mechanism is the algebraic sum of the values for two steps ($\rho_1 + \rho_2$) which should be affected in opposite directions by substituents. The preequilibrium step (log K_{eq}/log $K_{eq_0} = \sigma\rho_1$, where $K_{eq} = k_1/k_{-1}$) would be expected to have a negative ρ value, which apparently in the case of hydroximoyl chlorides is partially offset by a positive ρ value for the next step, where chloride ion undergoes nucleophilic attack on the conjugate acid of **1** (log $(k_2/k_{2_0}) = \sigma\rho_2$). A similar compensation of ρ values has been suggested as the reason for the small ρ values observed in the acid-catalyzed hydrolysis of aromatic esters which proceed by the $A_{AC}2$ mechanism.[36]

One might expect that the immonium ion rotation mechanism for acid-catalyzed isomerization of an imine derivative would give large negative ρ values since in this case both the preequilibrium protonation and the rate constant for rotation should have negative ρ values. Dignam and Hegarty,[13b] however, have estimated a Hammett ρ value of +0.28 (using only two compounds) for the isomerization of amidoximes which isomerize by immonium ion rotation.

In order to determine the affect of ortho substituents on this isomerization, the rate of isomerization of the *o*-methyl-substituted (*E*)-benzohydroximoyl chloride (**1f**) was measured (Table II). Introduction of the ortho substituent reduced the rate of isomerization so much that it was necessary to increase the concentration of the hydrogen chloride by a factor of about four in order to get an easily measured rate of reaction. This large decrease in isomerization rate is probably due to a twisting of the *o*-methylphenyl ring out of the plane of the carbon–nitrogen double bond. This would decrease resonance stabilization by phenyl of the immonium ion and would reduce the value of K_{eq}, thus decreasing the rate of isomerization. The twisted *o*-methylphenyl group could also increase the steric effect for nucleophilic attack by chloride ion.

In light of our results, it is of interest to examine the nature of the tetrahedral intermediate in more detail. Attack by $^{36}Cl^-$ on the (*Z*)-immonium ion **3** would give the tetrahedral intermediate **4a1** (Scheme III). If it is assumed that the leaving chloride ion must be trans to a nitrogen lone pair,[33] then the initially formed tetrahedral intermediate **4a1** could lose $^{36}Cl^-$ and return to **3a** or undergo rotation to **4a2** which could lose nonradioactive

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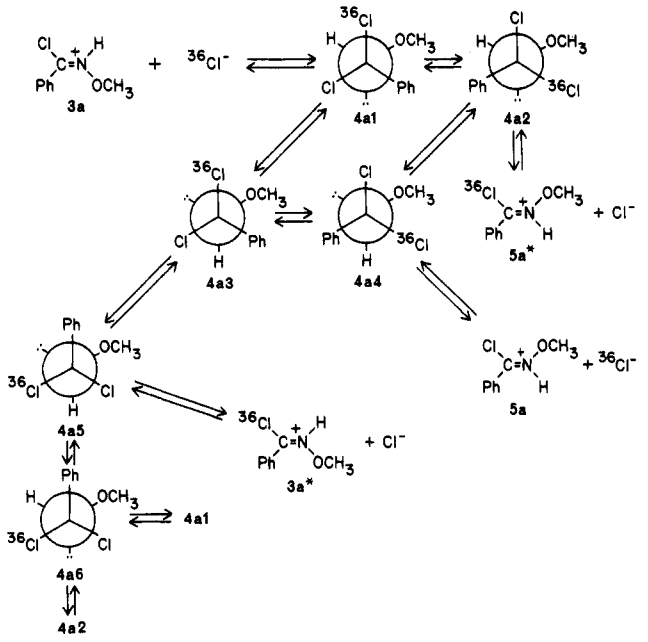
Scheme III



chloride ion to give the (*Z*)-immonium ion **5a***. It is likely, however, that proton exchange on nitrogen would be as fast or faster[34] than rotation about the carbon–nitrogen single bond in the tetrahedral intermediate. Thus, one would expect the pathways **4a1** → **4a3** → **4a4** → **5a**, **4a1** → **4a2** → **4a4** → **5a**, and **4a1** → **4a3** → **4a4** → **4a2** → **5a*** which involve proton exchange to be competitive with the pathway **4a1** → **4a2** → **5a***. If the rate formation of **5a*** and **5a** from **4a2** and **4a4** were equal, there would be an equal probability of incorporating $^{36}Cl^-$ and nonradioactive chloride during isomerization of **1a** to **2a**, which is consistent with our observations. Although nitrogen inversion in **4a1** followed by rotation could also account for randomizing the ^{36}Cl in the tetrahedral intermediate, it has been demonstrated that nitrogen inversion is relatively slow in hydroxylamines[35] and presumably it would not compete favorably with proton transfer and C–N rotation.

It is noteworthy that two of the tetrahedral structures, **4a2** and **4a4**, that are in equilibrium through proton exchange, will give the (*Z*)-immonium ion (**5a** and **5a***). A similar proton exchange does not exist for the formation of the (*E*)-immonium ion; i.e., proton exchange with **4a1** or **4a5** does not give a tetrahedral intermediate capable of directly forming the (*E*)-immonium ion (**3a** or **3a***) via trans elimination.

The slower rate of formation of **3a*** when compared to that of **5a*** during isomerization of **2a** may be due to any one or a combination of the following: (1) there are fewer available pathways which lead to **3a*** as compared to **5a***; (2) the pathway **3a** → **4a1** → **4a3** → **4a5** → **3a*** involves a rotation where bulky phenyl eclipses the methoxy group (**4a3** → **4a5**) whereas there are available pathways leading to **5a*** in which a chlorine atom eclipses the methoxy group; and (3) the rate of loss of chloride ion from **4a5** may be slower than the loss of chloride from **4a2**.

In conclusion, the hydrogen chloride catalyzed geometric isomerization of (*E*)-*O*-methylbenzohydroximoyl chloride (**1a**) has been shown to involve nucleophilic attack on the conjugate acid of **1a** to give a tetrahedral intermediate. Our results rule out an isomerization mechanism via immonium ion rotation which may be important only in special systems where there is considerable delocalization of the positive charge on the immonium ion (such as in benzamidoximes). Furthermore, our results exclude a direct S_N2 displacement process for the isomerization, which may have mechanistic implications in the substitution reactions of imidoyl chlorides and acid chlorides.

Experimental Section

Materials. The dioxane was obtained from Burdick and Jackson (distilled in glass) and was used without further purification. A sample of the dioxane purified by refluxing in contact with sodium metal followed by distillation through an 18-in. Vigreux column gave the same kinetic results as the commercial solvent which had received no further purification. The hydroximoyl chlorides **1a–f** and **2a–f** were prepared according to published procedures.[17] For kinetic experiments the hydroximoyl chlorides **1a**, **2a** and **1c–f** were purified by preparative gas–liquid chromatography (PGLC) followed by micromolecular distillation and the hydroximoyl chloride **1b** was purified by preparative thin-layer chromatography followed by recrystallization from methanol.

Preparation of HCl–Dioxane Solutions. The nonradioactive hydrogen chloride solutions were prepared by bubbling hydrogen chloride gas (reagent grade, Matheson Gas Products) through concentrated sulfuric acid and then into dioxane. The concentrations of the solutions were determined by titrating with standard tetra-*n*-butylammonium hydroxide in 10% methanol–benzene, prepared by the procedure of Cundiff and Markunas.[37] The tetra-*n*-butylammonium hydroxide was standardized against primary standard benzoic acid (Mallinckrodt), using thymol blue as the indicator. Samples of HCl–dioxane solutions were pipetted into 80 mL of 10% methanol–benzene and then titrated, using thymol blue as the indicator. The titrations were also followed with a pH meter by recording the change in millivolts vs. milliliters of titrant. The densities of the HCl–dioxane solutions were determined so that the concentrations of the solutions could be calculated in molality.

Preparation of DCl–Dioxane Solution. Anhydrous reagent-grade sodium chloride (40 g) was placed in a three-neck round-bottom flask fitted with a separatory funnel and an exit tube leading to a three-neck flask containing dioxane. All openings were capped with rubber septum caps. The system was purged with dry nitrogen for 15 min and then 25 mL of sulfuric acid-d_2 (Bio Rad, 99.5 atom % D, 98% D_2SO_4 in D_2O) was transferred by a syringe to the separatory funnel through a septum cap. The sulfuric acid was released dropwise through the separatory funnel into the sodium chloride and as the deuterium chloride was generated it was bubbled into the dioxane. The concentration of the DCl–dioxane solution was determined as described above.

Preparation of H^{36}Cl–Dioxane Solution. A 25 μCi solution of sodium chloride-36 in water (Amersham/Searle Corp.) was placed in a round-bottom flask. The water was evaporated and a hydrogen chloride–dioxane solution was added. The mixture was heated and stirred for several days. The radioactive hydrogen chloride–dioxane solution was then removed from the flask by suction through a gas dispersion tube fitted with a fritted cylinder. The concentration of the H^{36}Cl–dioxane solution was determined as described above.

Kinetic Method. The HCl–dioxane solutions were thermostated in a constant temperature bath at 39.5 °C (±0.01 °C). The hydroximoyl chloride was weighed into a 10-mL volumetric flask and 3.0 mL of the thermostated HCl–dioxane solution was pipetted into the flask. The flask was quickly weighed to determine the weight of the HCl–dioxane solution used in each run. The volumetric flask was kept in a constant temperature bath at 39.5 °C for 2 min and then 100-μL aliquots were taken from the flask at timed intervals. The aliquots were quenched in an ether–triethylamine solution (200 μL/350 μL), the precipitated triethylamine hydrochloride was filtered, and the solutions were analyzed by GLC (20% SE-30 on Chromosorb W, 30 ft × 0.375 in. column) or high-performance LC (Corasil column with hexane as the eluant). Normalization factors for the GLC and high-performance LC peak areas were determined by analyzing samples containing known amounts of the (*E*)- and (*Z*)-hydroximoyl chlorides. Some of the isomerization reactions were followed in an NMR spectrometer (Varian Model A-60A) at 39.5 °C. The

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methoxy singlets of the (*E*)- and (*Z*)-hydroximoyl chlorides were integrated at a sweep width of 100 Hz. The first-order rate constants and the Hammett value were calculated by a least-squares evaluation of the data and the error limits were calculated at the 95% confidence level.

Rate of $^{36}Cl^-$ Exchange with (*Z*)-*O*-Methylbenzohydroximoyl Chloride (2a). Eight samples (100 mg each) of **2a** were dissolved in 0.210 molal $H^{36}Cl$–dioxane (10.3 g) which had been thermostated at 39.5 °C. Each reaction was quenched by pouring the reaction mixture into 0.20 M sodium hydroxide (25 mL). The hydroximoyl chloride was extracted with ether (4 × 10 mL) and the ether extracts were washed with water (4 × 10 mL) and dried over anhydrous magnesium sulfate. The magnesium sulfate was filtered by gravity and the filter paper and the magnesium sulfate were thoroughly washed with ether. The ether was removed by means of rotary evaporation and the residue was dissolved in 5 mL of scintillation fluid [3.0 g of 2,5-diphenyloxazole and 0.3 g of 1,4-bis(5-phenyloxazol-2-yl)-benzene/L of toluene]. Each sample was counted three times (10 min each time) with either a Beckman Model 1650 or a Beckman Model LS 9000 liquid scintillation counter using a ^{32}P window. The raw activity data were corrected for counting efficiencies and a blank was run without **2a** in order to correct for background radioactivity. A 1.03-g and 2.06-g sample of the $H^{36}Cl$–dioxane solution in 5 mL of scintillation fluid was counted in order to obtain the initial activity of this solution. The rate constant was calculated by a least-squares evaluation of the data and the error was estimated at the 95% confidence level.

Incorporation of $^{36}Cl^-$ during $H^{36}Cl$-Catalyzed Isomerization of (*E*)-*O*-Methylbenzohydroximoyl Chloride (1a). A 100-mg sample of **1a** was dissolved in 0.210 molal $H^{36}Cl$–dioxane (10.3 g) which had been thermostated at 39.5 °C. The solution was kept at 39.5 °C for 80 min and then quenched by addition of 0.20 M sodium hydroxide (25 mL). The reaction mixture was worked up as described above. In the experiment which was run to only one half-life a larger sample of **1a** (393 mg) was dissolved in 10.3 g of 0.210 molal $H^{36}Cl$–dioxane solution. This reaction was quenched with 0.20 M sodium hydroxide and the reaction mixture was worked up in the usual way. The residual mixture of **1a** and **2a** was separated by PGLC (20% SE-30 on Chromosorb W, 30 ft × 0.375 in. column).

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Registry No. 1a, 41071-34-5; **1b**, 41071-36-7; **1c**, 57139-26-1; **1d**, 57139-27-2; **1e**, 57139-29-4; **1f**, 57139-30-7; **2a**, 41071-35-6; **2b**, 41071-37-8; **2c**, 57139-33-0; **2d**, 57139-34-1; **2e**, 57139-36-3; **2f**, 57139-37-4.

Deamination via Nitrogen Derivatives of Sulfonic Acids: *N*-Alkyl-*N*-nitroso-4-toluenesulfonamides, *N*-Alkyl-*N*-nitro-4-toluenesulfonamides, and *N*-Alkyl-*N'*-(4-toluenesulfonyloxy)diimide *N*-Oxides

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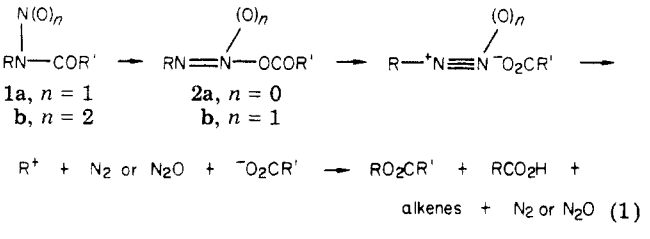
The thermal decomposition of several *N*-alkyl-*N*-nitroso-4-toluenesulfonamides, *N*-alkyl-*N*-nitro-4-toluenesulfonamides, and *N*-alkyl-*N'*-(4-toluenesulfonyloxy)diimide *N*-oxides was undertaken to determine whether the basicity of the negatively charged counterion in deamination reactions was a reaction variable. The nitrososulfonamides decompose following first-order kinetics to give the corresponding esters with retention of configuration. The reaction characteristics are very similar to those of the *N*-nitrosocarboxamides, and the reaction mechanisms are presumably very similar also. The *N*-nitrosulfonamides required high temperatures for decomposition, and they gave an anomalous set of products: amide (by denitration) and olefins, but no nitrous oxide or toluenesulfonate esters. The *N'*-toluenesulfonoxydiimide *N*-oxides, isomeric to the nitrosulfonamides, proved to be surprisingly stable compounds; they decompose by first-order kinetics to yield the corresponding esters and nitrous oxide.

The rate-determining step in the thermal decomposition of *N*-nitroso and *N*-nitrocarboxamides of primary alkylamines **1** is a rearrangement to the diazo or diazoxy ester **2**, respectively; subsequent fast steps lead to the corresponding ester, olefin products, and nitrogen or nitrous oxide (eq 1).[1-4] The range of products, the stereochemical course of the reaction (principally retention of configuration in R), and the extent of scrambling of ^{18}O in the carboxylate groups are virtually the same whether nitrogen or nitrous oxide is the gas molecule formed and also whether the *E* or *Z* isomer of **2a** is the reaction intermediate.[5] The present study, involving the rearrangement of nitroso- and nitrosulfonamides, was designed to determine whether the basicity of the counterion (carboxylate vs. sulfonate) was a reaction variable.



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