

Nuclear Magnetic Resonance Evidence for Restricted Nitrogen Inversion and Nonplanarity in Perfluoro-4-chloro-2-halo-1,2-oxazetidines¹

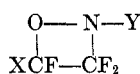
JOSEPHINE D. READIO

Thiokol Chemical Corporation, Reaction Motors Division, Denville, New Jersey 07834

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Perfluoro-4-chloro-2-fluoro-1,2-oxazetidine and perfluoro-2,4-dichloro-1,2-oxazetidine have been prepared. Evidence for a high barrier to nitrogen inversion in these compounds is provided by ¹⁹F nmr results, which demonstrate the presence at room temperature of *cis* and *trans* invertomers. Additional nmr studies have shown that the chemical-shift differences of the geminal fluorines of each invertomer are temperature dependent, indicating equilibrating nonplanar conformers. Values of ΔG for conformers of three invertomers have been determined. Assignments of nmr signals to specific fluorines are discussed.

The tendency of N-halo substituents, particularly bromine and chlorine, to retard inversion of nitrogen in three-membered ring systems has been demonstrated in recent studies involving N-haloaziridines.² We have reported³ similar results for the perfluoro-oxazetidine system and have further found that fluorine is equally effective in restricting nitrogen inversion. This ability of fluorine was revealed in perfluoro-2-fluoro-1,2-oxazetidine (**1**) by the nonequivalence of the geminal fluorines in the ¹⁹F nmr spectrum at 24°. Clearly, this nonequivalence could not be attributed to slow ring inversion, since at this temperature interconversions between possible nonplanar conformations would be rapid. A second manifestation of hindered nitrogen inversion in N-haloperfluoro-oxazetidines would be the likely detection of invertomers for those compounds in which X (structure below) is some group or atom other than fluorine.⁴



- 1, X = F; Y = F
 2, X = Cl; Y = F
 3, X = Cl; Y = Cl
 4, X = F; Y = Cl
 5, X = Cl; Y = H
 6, X = Cl; Y = CF₂CFCIOEt

We wish to present nmr evidence for the presence of two configurational isomers of perfluoro-4-chloro-2-fluoro-1,2-oxazetidine (**2**) and perfluoro-2,4-dichloro-1,2-oxazetidine (**3**) and thus further demonstrate that nitrogen inversion in these compounds even at room temperature has been effectively retarded.

Nmr studies of certain substituted difluorocyclobutanes performed by Lambert and Roberts⁵ indicated that the chemical-shift differences of the geminal fluorines were temperature dependent. These observations were interpreted in terms of a classical equilibrium between puckered ring conformations. We have reported similar evidence for the nonplanarity of the perfluoro-oxazetidines **1** and **4**³ and in this paper will present low-temperature nmr data which suggest that the invertomers of **2** and **3** also exist as equilibrating nonplanar conformers.

(1) This investigation was performed under Contract No. N00019-68-c-0372 for the Naval Air System Command, Department of the Navy, Washington, D. C. 20360, with Mr. John Curtowski as Project Officer.

(2) S. J. Brois, *J. Amer. Chem. Soc.*, **90**, 506, 508 (1968); J. M. Lehn and J. Wagner, *Chem. Commun.*, 148 (1968).

(3) J. D. Readio and R. A. Falk, *J. Org. Chem.*, **35**, 927 (1970).

(4) Lee and Orrell observed the presence of invertomers of perfluoro-4-chloro-2-methyl-1,2-oxazetidine in a ¹⁹F nmr spectrum obtained at -79°: J. Lee and K. G. Orrell, *Trans. Faraday Soc.*, **61**, 2342 (1965).

(5) J. B. Lambert and J. D. Roberts, *J. Amer. Chem. Soc.*, **85**, 3710 (1963); **87**, 3884 (1965).

Results and Discussion

Compounds **2** and **3** were prepared by fluorination and chlorination, respectively, of the parent amine, perfluoro-4-chloro-1,2-oxazetidine (**5**). This latter compound is generated on hydrolysis of the corresponding chloro ether **6**.⁶ Preparative glpc was utilized to obtain pure samples of the N-halooxazetidine products with each collected as a single peak. In neither case did glpc provide evidence for invertomers. The structures of **2** and **3** were confirmed by infrared, mass spectral, and elemental analyses.

The ¹⁹F nmr data from room-temperature spectra of **2** and **3** are listed in Table I. The spectrum of the

TABLE I
CHEMICAL SHIFTS AND GEMINAL COUPLING CONSTANTS FROM THE ¹⁹F NMR SPECTRA OF **2** AND **3** AT 24°

Assignment	2, Y = F		3, Y = Cl	
	2, $\phi^*{}^a$	2, J_{F-F} Hz	3, $\phi^*{}^a$	3, J_{F-F} Hz
<i>cis</i> CF ₂ N	96.0, 98.2, ^b 102.9, 105.9	128	86.3, 88.2, ^c 96.7, 98.8	116
<i>trans</i> CF ₂ N	98.2, 100.6, ^b 102.4, 104.6	128	91.2	...
<i>cis</i> CFCl	62.4 ^b	...	60.3 ^b	...
<i>trans</i> CFCl	61.7 ^b	...	63.0	...
<i>cis</i> N-F	-26.9
<i>trans</i> N-F	-30.0

^a Chemical shift in parts per million with CCl₄ as internal standard. ^b Each value represents center of doublet of doublets. ^c Each value represents center of doublet.

CF₂N fluorines of **2** at -60° is reproduced in Figure 1, while these same fluorines of **3** at 24° are found in Figure 2. It is evident from these results that each collected sample of **2** and **3** does in fact consist of two configurational isomers, **2** showing a 65:35 invertomer distribution and **3** containing essentially equal quantities of the *cis* and *trans* isomers. These ratios are unchanged in spectra taken over the temperature range of 24 to -125°. The above evidence hence indicates a high barrier to nitrogen inversion in **2** and **3**.

(6) R. A. Falk and J. D. Readio, *J. Org. Chem.*, **34**, 4088 (1969).

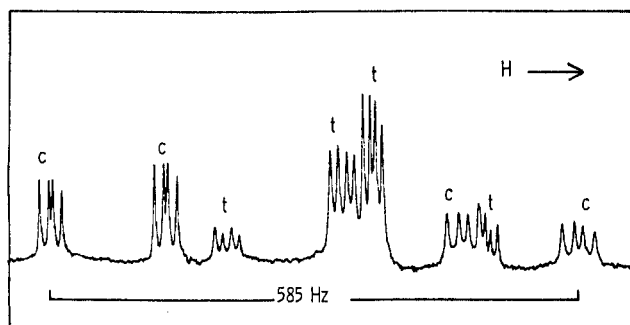


Figure 1.— ^{19}F nmr spectrum of the CF_2N fluorines of **2** at -60° :
c = *cis*; t = *trans*.

The specific assignment of peaks in the spectrum of **2** to the *cis* and *trans* invertomers was primarily based on nmr correlations which are discussed below. These interpretations were most consistent with the conclusion that the more prevalent isomer of **2** had the *trans* configuration. The nonequivalence of the CF_2N fluorines of **2** is indicated by the basic AB patterns in the spectrum (Figure 1). These patterns for both invertomers are clearly resolved at this lower temperature. In addition to the geminal coupling, the CF_2N fluorines also undergo coupling with the adjacent CFCl and N-F fluorines, and consequently each member of the AB quartets appears as a doublet of doublets. This same pattern is likewise observed for the CFCl fluorine of the *cis* invertomer and indicates coupling only with the vicinal CF_2N fluorines.⁷ The CFCl fluorine of the *trans* invertomer of **2** gives a quartet pattern which will be discussed later. The N-F absorptions of the invertomers of **2** are broad and essentially structureless at room temperature, whereas at low temperature (-100°) quartet structures are discernible.

The data in Table I and the spectrum in Figure 2 clearly indicate that the geminal fluorines of one of the invertomers of compound **3** appear as a single unsplit absorption. The apparent equivalence of these fluorines suggests a certain degree of symmetry more likely encountered in the *trans* configuration; hence the single peak is attributed to the CF_2N fluorines of the *trans* invertomer. Assignment of the upfield CFCl peak to this same invertomer then follows and is based on the absence of appreciable splitting in this absorption. In Figure 2 it may be seen that the CF_2N fluorines assigned to *cis*-**3** are nonequivalent and show the basic AB pattern with each member appearing as a doublet owing to coupling with the adjacent CFCl . This latter fluorine of the same invertomer appears as a doublet of doublets. The coupling constants for the ABX system of *cis*-**3** were calculated: $J_{\text{AB}} = 116$ Hz, $J_{\text{AX}} = 12.7$ Hz, and $J_{\text{BX}} = 10.0$ Hz (spectrum at -58°).⁸

Low-temperature nmr studies of compounds **2** and **3** indicated that the chemical-shift difference, δ , of the geminal fluorines of the invertomers was temperature dependent. The observed values of δ at various temperatures are listed in Table II. As has been previously reported,^{3,5} such effects in four-

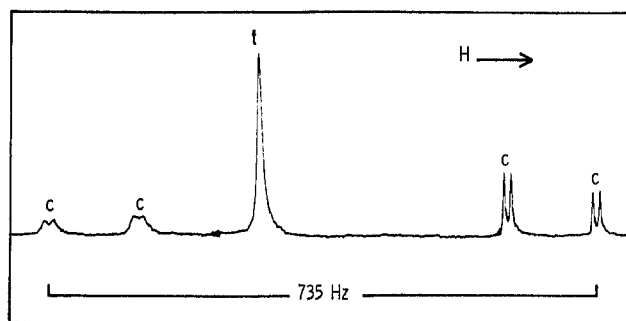


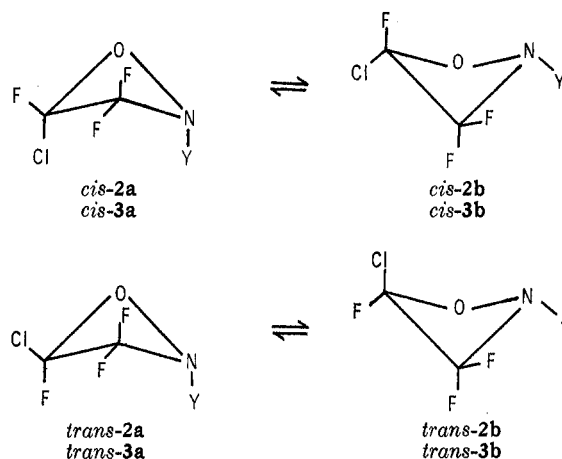
Figure 2.— ^{19}F nmr spectrum of the CF_2N fluorines of **3** at 24° :
c = *cis*; t = *trans*.

TABLE II
FLUORINE-FLUORINE CHEMICAL-SHIFT DIFFERENCES^a

Temp, $^\circ\text{C}$	<i>cis</i> - 2 δ CF_2N , Hz	<i>trans</i> - 2 δ CF_2N , Hz	<i>cis</i> - 3 δ CF_2N , Hz
24	362	191	586
-13	396	154	554
-33	420	127	534
-60	443	102	513
-80	470	80	488
-105	498	55	465
-125	518	—	445

^a These values were found to be essentially independent of changes in concentration (see Experimental Section).

membered ring compounds may be interpreted in terms of equilibrating nonplanar conformers. Since interconversion of conformers is rapid, only an average signal is observed. The puckered conformers involved are represented as follows.



Although the *trans* invertomer of **3** is likely a mixture of two nonplanar conformers, the apparent equivalence of the geminal fluorines throughout the temperature range investigated precluded the determination of δ . However, the single absorption does undergo a change in chemical shift with lowering of temperature, thus suggesting that variations in conformer population are likewise occurring with this invertomer.

For the equilibria above, it is assumed that the a conformation is the less stable owing to destabilization from the 1,3-diaxial chloro- N -halo interaction. The fraction of molecules, p , in conformation b is thus related to the conformational free-energy difference, ΔG , by the expression

$$p/(1-p) = K = e^{-\Delta G/RT}$$

(7) The corresponding CF_2O fluorines of **1** show coupling with both CF_2N and N-F fluorines and give an ABMX₂ pattern.⁹

(8) K. B. Wiberg and B. J. Nist, "Interpretation of NMR Spectra," W. A. Benjamin, Inc., New York, N. Y., pp 21-27.

The fraction, p , is also related to the chemical-shift difference, since the observed δ is the weighted average of the chemical-shift differences, δ_a and δ_b , of the individual conformers.

$$\delta = \delta_a + p(\delta_b - \delta_a)$$

Values of p at those temperatures shown in Table II were calculated for a range of ΔG 's and were plotted vs. δ at the corresponding temperatures. ΔG values for the equilibria were those for which the best linear relationships were obtained. Values of δ_a and δ_b were readily calculated from the slopes. The determined chemical-shift differences of the conformers and the free-energy differences are listed in Table III.^{9,10}

TABLE III

	CONFORMATIONAL DATA		
	<i>cis</i> -2	<i>trans</i> -2	<i>cis</i> -3
δ_a , Hz	-610	+1265	+1374
δ_b , Hz	+572	-6	+382
ΔG , cal/mol	-900 ± 100	-1000 ± 100	-800 ± 100

Comparison of the ΔG values for the invertomers of 2 and 3 with those of -900 and -1000 cal/mol obtained for 1 and 4, respectively,³ does not reflect much variation. These results suggest that for those oxazetidines studied, the conformer composition at any temperature will be nearly the same for all compounds, with conformer b predominating even at room temperature. In all cases, the proportion of conformer b at -120° would be greater than 0.93.

The relationship between p and the chemical-shift difference, δ , for the invertomers is shown in Figure 3. The negative sign for δ indicates a reversal in relative signal positions of the geminal fluorines. As related to the conformer of *trans*-2, the data suggest that as the temperature is lowered and the population of the more stable conformer b increases, the value of δ would approach 0 and then become slightly negative at $p = 1$. A low-temperature (-100°) spectrum shows that the CF_2N fluorines of *trans*-2 are in fact becoming equivalent, since the inner members of the AB quartet are partially coalesced and the outer members are very small. It is interesting to note that this signal at the lower temperature resembles that of *trans*-3. This fact is consistent with the proposed *trans* configuration of these two invertomers.

The assignment of the CF_2N fluorines of the invertomers to specific nmr peaks was based on considerations made previously for the similar assignment of fluorines of perfluoro-2-fluoro-1,2-oxazetidine (1).³ In the case of 1, it was assumed that the fluorine *cis* to the N-F group would experience the greater variation in chemical shift as the temperature was lowered and the equilibrium favored conformer b. This would result in an increase in the number of molecules having the *cis* fluorine in an axial position or

(9) It is assumed in this treatment that ΔG is constant over the temperature range studied, hence $\Delta S = 0$. Lambert and Roberts note⁹ that although differences in conformer entropies may cause inaccuracies in determined values of ΔG , the demonstrated temperature dependence of δ still represents positive evidence for nonplanarity.

(10) ΔG for the conformers of *trans*-3 could not be calculated. Since the observed chemical shift of the CFCl fluorine of this invertomer is also a weighted average of its shift in either conformer, the above treatment using this one absorption is theoretically possible. However, this signal of *trans*-3 underwent only a very slight change over the temperature range, hence the above procedure was not applicable.

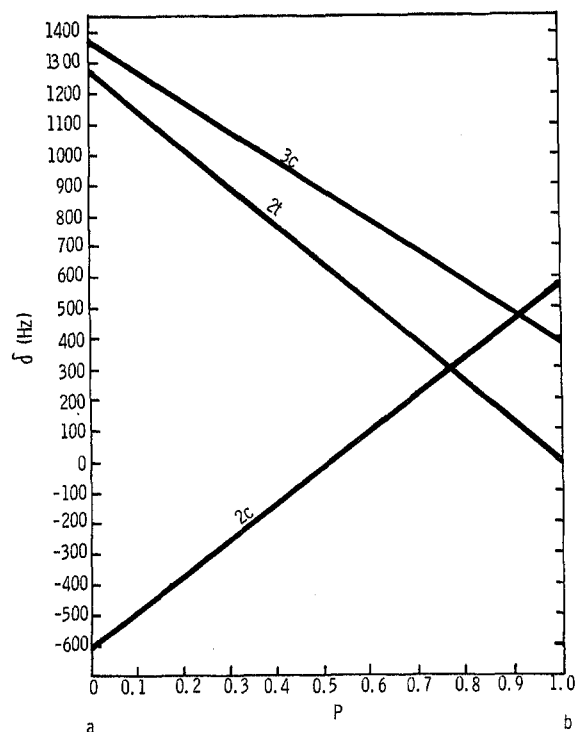


Figure 3.—Chemical-shift difference vs. conformer population.

situated axial and coplanar with the unshared pair of electrons on nitrogen. This particular steric relationship between a hydrogen and free electron pair has been reported to give rise to a pronounced upfield shift of the proton signal,¹¹ and hence might significantly affect the chemical shift of a similarly oriented fluorine. Since the broad unresolved upfield portion of the AB quartet of the CF_2N fluorines of 1 was essentially stationary over the temperature range studied (24 to -115°), the resolved downfield peaks which comprised the other half of the AB pattern and which underwent a substantial downfield shift on cooling were assigned to the *cis* fluorine. As a result of the above, it further appeared that peak broadening provided another basis for configurational assignment.

The present results are completely consistent with the above observations and lend support to the assumptions made. Each AB quartet of the invertomers of 2 shows a noticeably broader portion, although the difference in peak broadness is not as pronounced as in 1. The chemical shifts of the CF_2N fluorines obtained from spectra at several temperatures are given in Table IV, and when compared with the spectrum shown in Figure 1 indicate that the positions of the broader peaks of *cis*-2 and *trans*-2 are virtually unchanged over the temperature range studied.¹² Similarly evident from the data is the fact that the sharper members of the AB quartets of each invertomer move downfield as the temperature is lowered and the proportion of conformer b increases. These results allow for assignment of the fluorines *cis* to N-F to the sharper members and the *trans* fluorines to the broader members. Clearly the effect of temperature on δ for the

(11) H. P. Hamlow, S. Okuda, and N. Nakagawa, *Tetrahedron Lett.*, 2553 (1964); J. B. Lambert, R. G. Keske, R. E. Carhart, and A. P. Jovanovich, *J. Amer. Chem. Soc.*, **89**, 3761 (1967).

(12) The differences in peak broadness are more pronounced in room-temperature spectra.

invertomers of 2 depends upon the relative signal positions of the *cis* and *trans* fluorines, since the *cis* fluorine moves downfield in each case.

The absence of coupling between the CFCl fluorine of *cis*-2 and the fluorine on nitrogen has been noted. This fluorine thus appears as a doublet of doublets owing to coupling with the adjacent geminal fluorines.

TABLE IV

Temp, °C	CF ₂ N FLUORINE PEAK POSITIONS AT SEVERAL TEMPERATURES ^a							
	<i>cis</i> -2		<i>trans</i> -2		<i>cis</i> -3		<i>trans</i> -2	
24	97.4	103.8	99.8	103.1	87.5	97.9	91.3	
-60	96.0	103.8	99.9	101.7	87.4	96.4	90.6	
-105	95.0	103.8	99.8	100.8	87.5	95.7	90.1	
-125	94.7	103.8	87.5	95.4	89.6	

^a Determined chemical shift of each fluorine in parts per million with CFCl₃ as the internal standard.

The initial assignment of configuration to the invertomers of 2 is derived from the observation that the above doublet of doublet pattern resembles very closely that of the same fluorine in *cis*-3. Values of *J*, 10.6 and 12.7 Hz and 9.6 and 12.7 Hz, are obtained for the CFCl fluorines of *cis*-2 and *cis*-3, respectively, from spectra at 24°. Since the proportion of conformers of each invertomer would be nearly the same, similarity of configuration is suggested. The pattern observed for the CFCl fluorine of *trans*-2 suggests that this fluorine is coupled with the vicinal CF₂N fluorines as well as with N-F. Since invertomer *trans*-2 is predominantly represented by conformer b at 24° and since the CF₂N fluorines in this conformer have essentially the same chemical shift, a triplet structure or a doublet of doublets with nearly equal values of *J* would be anticipated in the absence of NF coupling. The observed quartet (*J* = 11 Hz) therefore is more consistent with the interpretation that the CFCl fluorine undergoes equal coupling with the three neighboring fluorines.

As in the case of compound 1,³ the N-F signals for both *cis*-2 and *trans*-2 likewise experience a downfield shift with a lowering of temperature (ϕ -27.6 and -30.6, respectively, at -125°). This observed deshielding (0.7 and 0.6 ppm) may be interpreted as resulting from changes in the proportions of conformers a and b and further may be related to the increase in conformer b over the temperature range 24 to -125°. Thus approximate values representing the difference of the N-F chemical shift in the two possible conformations may be calculated. Values of 298 and 280 Hz for *cis*-2 and *trans*-2 invertomers, respectively, are estimated.¹³

The assignment of the nmr absorptions of the CF₂N fluorines of the invertomer *cis*-3 was based on peak shape and chemical-shift change in a manner analogous to that used for the invertomers of 2. The geminal fluorine AB pattern of *cis*-3 consists of two broad downfield and two sharp upfield members, each of which appears as a doublet (Figure 2). The downfield portion which is attributed to the *trans* fluorine (relative to N-Cl) remained stationary, while the *cis* fluorine peaks moved downfield as the temperature was changed from 24 to -125° (Table IV). Coupling of each geminal fluorine with the adjacent CFCl results in the

splitting at -58° of *J*(*trans*-F) = 12.7 Hz and *J*(*cis*-F) = 10.0 Hz. Since *cis*-3 more closely resembles conformer b at this temperature, these values represent essentially the vicinal F-F equatorial-axial and axial-axial coupling constants, respectively. These results are consistent with those of Feeney, Sutcliffe, and Walker,¹⁴ which related vicinal coupling constants to fluorine conformation as follows: equatorial-axial > axial-axial > equatorial-equatorial.

The single peak observed for the CF₂N fluorines of the invertomer *trans*-3 at 24 and -125° clearly indicates that these fluorines have nearly the same chemical shift at both temperatures. The small value of δ at -125°, coupled with the assumption that *trans*-3 is not too unlike the other three invertomers, hence leads to the conclusion that δ_b is small. That δ_a is likewise small is one manner in which the apparent equivalence of the geminal fluorines at 24° may be explained. In light of the relatively large differences in values of δ_a and δ_b for the other three invertomers, this explanation may at first appear to be somewhat unsatisfactory. However, it should be noted that whereas only one of the geminal fluorines of *cis*-3 and *cis*- and *trans*-2 undergo any significant change in chemical shift with variations in conformer population, both fluorines of *trans*-3, as represented by the single absorption, move upfield as the temperature is increased (Table IV). Similar behavior was observed for compound 4 and is reflected in the relatively small difference in the values of δ_a and δ_b (δ_a = 604 Hz and δ_b = 202 Hz).³ In contrast are the values δ_a = -798 Hz and δ_b = 311 Hz³ obtained for the CF₂N fluorines of 1, fluorines whose chemical shifts respond to changes of conformer population as do those of the three invertomers. The absence of significant coupling between the fluorines of *trans*-3 is not understood. There is only a suggestion of splitting in the CF₂N fluorine signal (<2 Hz), and the CFCl fluorine, which conceivably would appear as a triplet as a result of coupling with the nearly equivalent geminal fluorines, is at best a doublet (*J* = 3 Hz).

Experimental Section

Chromatographic preparative scale separations were accomplished with a Wilkens Autoprep Model A 700 utilizing a column (20 ft × 0.375 in.) containing 20% SF-96 on Chromosorb P.

The elemental analyses were performed by Schwarzkopf Micro-analytical Laboratories, Woodside, N. Y.

Infrared spectra were obtained with a Perkin-Elmer Model 137 double-beam spectrophotometer. Spectra of gaseous samples were obtained with a 7.5-cm gas cell equipped with silver chloride windows.

A Bendix time-of-flight mass spectrometer (Model 12-101) with source elements S14-107 was employed to record the mass spectra at 70 eV.

The ¹⁹F nmr spectra were obtained with a Varian Model V-4302B spectrometer operating at 56.4 MHz. The spectra were calibrated by the side-band modulation technique using a Hewlett-Packard wide-range oscillator. Chemical shifts and coupling constants represent the average of at least eight measurements. Errors of ±0.1 ppm and ±1 Hz, respectively, were estimated. For low-temperature studies, the variable-temperature accessory supplied by Varian was used. Temperature measurements were made both before and after recording spectra by means of a copper-constantan thermocouple immersed in a tube filled with a Kel-F oil. The temperature measurements are

(13) A value of 217 Hz was obtained for compound 1.³

(14) J. Feeney, L. H. Sutcliffe, and S. M. Walker, *Trans. Faraday Soc.*, **62**, 2650 (1966).

believed to be accurate to $\pm 1^\circ$. The chemical-shift differences (Table IV) obtained from nmr spectra of CFCl_3 solutions of **2** and **3** were essentially unchanged with the weight per cent of **2** varied from 30 to 75 and that of **3** varied from 35 to 75.

Perfluoro-4-chloro-1,2-oxazetidene (5) was prepared by hydrolysis of compound **6** as described previously.³

Perfluoro-4-chloro-2-fluoro-1,2-oxazetidene (2).—A 2-l. steel reactor (passivated with fluorine) was charged with NaF pellets (10 g), perfluoro-4-chloro-1,2-oxazetidene (**5**, 5.0 g, 34 mmol), and fluorine (43 mmol) at -196° . The mixture was allowed to react for 5 hr and the excess fluorine was pumped off at -196° . Product **2** was collected as one peak by preparative glpc at 20° . Compound **3** could also be obtained from the reaction mixture, since it was initially present as an impurity in **5**. The infrared spectrum of **2** showed bands at 7.30 (s, ring), 7.75 (s), 8.3 (shoulder), 8.5 (s), 8.95 (s), 9.4 (s), 10.8 (w), and 12.3 μ (s). The mass spectrum of **2** showed peaks at m/e (rel intensity, ion) 130 (9.3, $\text{C}_2\text{F}_4\text{NO}^+$), 118 and 116 (10.6, 30.9, $\text{C}_2\text{F}_3\text{Cl}^+$), 97 (2.1, $\text{C}_2\text{F}_3\text{O}^+$), 87 and 85 (1.8, 5.3, CF_2Cl^+), 83 (4.6, CF_3N^+), 69 (10.1, CF_3^+), 66 (6.9, CF_2O^+), 64 (7.4, CF_2N^+), 50 (20.4, CF_2^+), 47 (100, COF^+), 45 (9.0, CFN^+), 37 and 35 (4.3, 14.9, Cl^+), 31 (62.8, CF^+), 30 (91.5, NO^+), and 26 (4.4, CN^+).

Anal. Calcd for $\text{C}_2\text{F}_4\text{ClNO}$: C, 14.52; H, 0.00; F, 45.92; N, 8.46. Found: C, 14.55; H, 0.00; F, 45.67; N, 8.10.

Perfluoro-2,4-dichloro-1,2-oxazetidene (3) was prepared by reaction of **5** (5.0 g, 34 mmol) and chlorine (32 mmol) in a 2-l.

flask at room temperature for 5 hr. Product **3** was collected as one peak by preparative glpc at 20° . Its infrared spectrum showed bands at 7.40 (s, ring), 7.94 (s), 8.5 (s), 9.0 (s), 9.8 (s), 12.7 (m), and 13.3–13.4 μ (vs, broad). The mass spectrum of **3** showed peaks at m/e (rel intensity, ion) 181 (trace, $\text{C}_2\text{F}_2\text{Cl}_2\text{NO}^+$), 129 and 127 (0.6, 1.9, $\text{C}_2\text{F}_2\text{ClNO}^+$), 118 and 116 (6.2, 21.9, $\text{C}_2\text{F}_3\text{Cl}^+$), 101 and 99 (2.2, 7.5, CF_2NCl^+), 87 and 85 (1.1, 3.6, CF_2Cl^+), 82 and 80 (2.7, 7.5, CFCIO^+), 69 (7.8, CF_3^+), 66 (2.2, CF_2O^+), 65 (0.6, COCl^+), 64 (8.0, CF_2N^+), 63 (2.6, COCl^+ or CNCl^+), 61 (2.4, CNCl^+), 50 (13.5, CF_2^+), 51 (2.4, CCl^+), 49 (9.6, NOF or CCl^+), 47 (100, COF^+), 45 (6.0, CFN^+), 37 and 35 (8.5, 30, Cl^+), 31 (40.6, CF^+), 30 (90, NO^+), and 26 (6.9 CN^+).

Anal. Calcd for $\text{C}_2\text{F}_2\text{Cl}_2\text{NO}$: C, 13.20; H, 0.00; F, 31.33; N, 7.70. Found: C, 13.45; H, 0.00; F, 31.60; N, 7.49.

Registry No.—*cis*-**2**, 23025-21-0; *trans*-**2**, 23025-22-1; *cis*-**3**, 23025-23-2; *trans*-**3**, 23025-24-3.

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Organic Reactions in Liquid Hydrogen Fluoride.

I. Synthetic Aspects of the Ritter Reaction in Hydrogen Fluoride¹

JOHN R. NORELL

Phillips Research Center, Phillips Petroleum Company, Bartlesville, Oklahoma 74003

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Liquid hydrogen fluoride effectively condenses an olefin and nitrile (Ritter reaction) to form N-substituted amides at ambient conditions. With linear monoolefins, *i.e.*, 1-octene and acetonitrile, three isomeric secondary amides are produced in yields of 80–90% when 0–10% water is present in the HF. Branched olefins, *i.e.*, 2-methyl-2-butene, which give tertiary carbonium ions, require 25–40% water in the reaction medium to obtain high yields of amides. With an olefin in which the tertiary carbon is remote from the point of unsaturation, as in the case of 3-methyl-1-butene, the major product is the amide derived from the tertiary carbonium ion *via* isomerization. The reaction has been applied to a variety of monoolefins and substituted nitriles, including HCN. Diolefins, in general, react poorly, giving viscous gums, although 2,5-dimethyl-1,5-hexadiene gave 2,5-diacet-amido-2,5-dimethylhexane and norbornadiene gave N-3-nortricyclacetamide.

Hydrogen fluoride, long known as a catalyst in alkylation reactions,² has received little attention as a solvent for organic reactions. This is undoubtedly due to the hazards associated with handling HF such as its toxicity and the rapid attack on glass. However, its volatility (bp 20°), its strong acid character ($H_0 = -9.9$), and the fact that it can be handled conveniently in polyethylene labware or Monel reactors suggest that HF could have distinct advantages over commonly used acid solvent systems such as sulfuric, polyphosphoric, etc.² We have examined several classes of reactions which normally are carried out in strong acids and wish to report our findings concerning the Ritter condensation of olefins and nitriles.

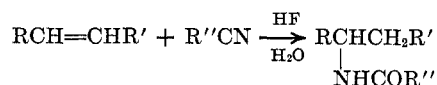
The acid condensation of an olefin, alcohol, or halide with a nitrile to form N-alkylamides has been extensively studied.³ In most cases sulfuric acid was used either alone or with solvents such as acetic acid, but

prior to this work no reports concerning the use of hydrogen fluoride as a solvent system has been noted.⁴

In the present study it was found that hydrogen fluoride is an excellent solvent system for the preparation of N-alkylamides and can be used at room temperature and atmospheric pressure for a variety of olefins and nitriles. Since conditions for optimum yields vary, these are discussed for linear olefins, which form secondary carbonium ions; branched olefins, which form tertiary carbonium ions; and cyclic and bicyclic olefins.

Results and Discussion

Linear Olefins.—Linear monoolefins react smoothly with nitriles, including hydrogen cyanide, in hydrogen fluoride containing from 0 to 10% water to produce N-substituted amides at ambient conditions. Table



(1) Portions of this paper were presented at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968.

(2) G. A. Olah, "Friedel-Crafts and Related Reactions," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1963, p 317 ff.

(3) (a) L. I. Krimen and D. J. Cota, *Org. Reactions*, **17**, 213 (1969); (b) J. J. Ritter and P. P. Minieri, *J. Amer. Chem. Soc.*, **70**, 4045 (1948); (c) E. N. Zil'berman, *Russ. Chem. Rev.* (Engl. Transl.), 311 (1960).

(4) During the course of this research, a patent was issued describing the use of hydrogen fluoride for preparing secondary alkyl, primary amines from linear olefins and nitriles: R. H. Potts, E. J. Miller, and A. Mais (to Armour and Co.), U. S. Patent 3,338,967 (1967).