

3-Methyl-2,2,5,5-tetrakis(trifluoromethyl)-4-imidazolidinone (15).—A 3% solution of diazomethane in ether was added portionwise to a solution of 5.0 g of **13** in 10 ml of ether until nitrogen evolution ceased. The ether was evaporated under a stream of nitrogen, and the solid residue was recrystallized from alcohol to give 4.0 g of **15** as colorless crystals: mp 164–165° (sealed capillary); ir (KBr) 5.71 μ (C=O); ^{19}F nmr (acetone) δ 72.8 (septet, $J = 4.4$ Hz, 2 CF_3) and 75.3 ppm (septet, $J_{\text{FH}} = 4.4$ Hz, split further to quartets, $J_{\text{FH}} = 0.9$ Hz, 2 CF_3); ^1H nmr (CDCl_3) τ 6.83 (septet, $J = 0.9$ Hz, CH_3) and 3.25 ppm (singlet, NH).

Anal. Calcd for $\text{C}_9\text{H}_4\text{F}_{12}\text{N}_2\text{O}$: C, 25.82; H, 1.08; F, 61.27; N, 7.53. Found: C, 26.05; H, 1.30; F, 61.28; N, 7.81.

Hydrolysis of 4-Amino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (2).—A solution of 100 g of **2** and 25 ml of water in 250 ml of concentrated sulfuric acid was heated at 225° in a sublimation apparatus for 5 days. The sublimate, most of which formed after the first day, was mixed with 200 ml of aqueous 5% sodium hydroxide. The solid that did not dissolve was collected on a filter and washed with water to give 5.8 g of unhydrolyzed **2**. The filtrate was made acidic with 10% hydrochloric acid, and the solid that precipitated was collected on a filter, washed with water, dried, and sublimed at 150° (5 mm) to give 33.2 g (33% conversion, 92% yield) of 2,2,5,5-tetrakis(trifluoromethyl)-4-imidazolidinone (**13**), identical by melting point and ir and nmr spectrum with an authentic sample. The sulfuric acid solution after cooling was poured over 1 l. of crushed ice and the solid that precipitated was collected on a filter, washed with water, and dried to give 58.0 g of unhydrolyzed **2**.

Dimethyl Sulfoxide Complex (19).—Dimethyl sulfoxide, 3.91 g (0.05 mol), was added to a solution of 17.86 g (0.05 mol) of **2** in 25 ml of ether. Heat was evolved, and a white solid precipitated. The solid was collected on a filter, dried in air (17.8 g), and recrystallized from benzene to give 15.7 g (72%) of the 1:1 complex as large, colorless prisms: mp 125–126°; ^{19}F nmr (acetone- d_6) δ 72.1 (septet, $J = 5$ Hz) and 76.7 ppm (septet,

$J = 5$ Hz); ^1H nmr (acetone- d_6) τ 2.70 (NH_2), 3.72 (NH), and 7.42 ppm (singlet, 2 CH_3).

Anal. Calcd for $\text{C}_9\text{H}_5\text{F}_{12}\text{N}_3\text{OS}$: C, 24.83; H, 2.09; F, 52.39; N, 9.66; S, 7.37. Found: C, 25.18; H, 2.17; F, 52.15; N, 9.94; S, 7.47.

Pyrolysis of 2.⁹—Samples of **2** were pyrolyzed over quartz in a glpc-pyrolysis set-up from 200 to 650°. Little decomposition occurred below 500°; at 600° decomposition was moderate and at 750° it was complete. The products were isolated and shown to be a mixture of CF_3CN , CHF_3 , and C_2F_6 by ir analysis.

^{15}N -Labeled 2.—A sample of **2** containing labeled nitrogen in the 4-amino group was prepared using ^{15}N -labeled (98.7%) sodium cyanide: mass spectrum (70 eV) m/e (rel intensity) 358 (0.1, parent - ^{15}N), 339 (5), 289 (100), 220 (47), and 69 (30). Hydrolysis of this sample with sulfuric acid gave the lactam **13**, which contained no ^{15}N as determined from its mass spectrum, which is identical with that of **13** prepared by other methods.

Registry No.—**2**, 23757-42-8; **2** (^{15}N labeled), 23758-03-4; **6**, 14372-88-4; **7**, 23757-44-0; **8**, 23757-45-1; **9**, 23757-46-2; **11**, 23757-47-3; **12**, 23757-48-4; **13**, 23757-49-5; **14**, 14316-86-0; **15**, 23829-37-0; **18**, 23757-51-9; **19**, 23757-52-0; **20**, 23757-53-1; **21**, 23757-96-2; **22**, 23757-97-3; 4-amino-2,5-bis(chlorodifluoromethyl)-2,5-bis(trifluoromethyl)-3-imidazoline, 23757-98-4; 2-amino-6H-hexadecafluoro-6,13-diazadisp[4.1.4.2]tridec-12-ene, 23757-99-5; 4-amino-5-chloro(difluoromethyl)-2,2,5-tris(trifluoromethyl)-3-imidazoline, 23758-00-1; 4-amino-2-chloro(difluoromethyl)-2,5,5-tris(trifluoromethyl)-3-imidazoline, 23758-01-2; 1,2,2,5,5-pentamethyl-4-methylthio-3-imidazoline, 23758-02-3.

Fluorinated Aminoimidazolines. Reactivity of the Nitrogen Functions

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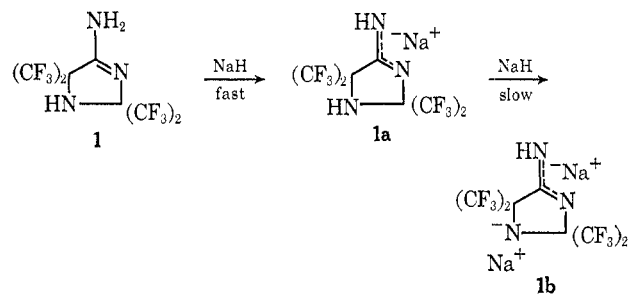
Received August 29, 1969

The very stable amino and amidino functions of 4-amino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (**1**) are attacked by strong acids and bases. Electrophilic alkylating agents such as dimethyl sulfate tend to attack at the 3 position, while nitration and acylation occur on the 4-amino group. Mono- and dianions stable at 25° can be prepared and used to react with **1** at the 1 position and on the 4-amino group. Appropriate combinations of these techniques allowed synthesis of all the nine possible methylated derivatives of **1**. The 4-nitramino and 4-isocyanato derivatives (**10** and **28**) are particularly useful intermediates.

The exceptional stability of 4-amino-2,2,5,5-tetrakis(polyfluoroalkyl)-3-imidazolines and their availability from fluorimines and cyanide ion¹ prompted a study of their properties. The discovery of the pronounced pharmacological activity of 4-amino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (**1**) coupled with low toxicity² provided further incentive for a detailed investigation of the chemistry of these new fluorinated heterocycles.

Anion Formation with Strong Bases.—Although measurement of pH in protic systems established the near neutrality of **1**, the amidine function serves as a donor in the formation of strong hydrogen-bonded

complexes with acceptors such as dimethyl sulfoxide and diethyl oxalate.¹ In aprotic media, salt formation with strong base does occur, so that monoanion **1a** forms easily with 1 equiv of sodium hydride–glyme or sodium methoxide–dimethyl sulfoxide.



Excess (threefold) sodium hydride and **1** in glyme formed **1a** at 25° and dianion **1b** at 60° or higher. Anion **1b** is stable at 25°, and **1b** is moderately stable at 84°

(1) W. J. Middleton and C. G. Krespan, *J. Org. Chem.*, **35**, 1480 (1970).

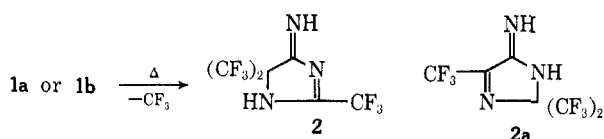
(2) The pharmacological studies on **1** as a skeletal muscle relaxant and central nervous system depressant are being reported separately. See I. M. Levine, P. B. Jossmann, D. G. Friend, and V. DeAngelis, *Chim. Pharmacol. Therap.*, **9**, 448 (1968); J. L. Claghorn and J. C. Schoolar, *Current Therap. Res.*, **10**, 279 (1968); R. Clark, T. E. Lynes, W. A. Price, J. P. Marvel, D. H. Smith, and V. G. Vernier, *The Pharmacologist*, **10**, 197 (1968).

TABLE I
SYNTHESES OF METHYLATED 4-AMINO-2,2,5,5-TETRAKIS(TRIFLUOROMETHYL)-3-IMIDAZOLINES AND
4-IMINO-2,2,5,5-TETRAKIS(TRIFLUOROMETHYL)IMIDAZOLIDINES^a

Product	Starting materials	Conditions	Isolation	Yield, %	Mp or bp, °C (mm)	Ir bands, μ
3	Na salt of 1 [from NaH and 7.0 g (0.02 mol) of 1] + 3.5 g of CH ₃ I	Refluxed overnight in 50 ml of glyme	Distillation	40	75 (10)	2.90 (m) and 3.08 (w) for NH; 6.00 (s) for C=N ^b
17	10.0 g (0.028 mol) of 1 + 20 ml of (CH ₃) ₂ SO ₄	Heated rapidly to boiling (ca. 188°)	Hydrolyzed hot with 50 ml of H ₂ O, then neutralized with 10% NaOH; fractional recrystallization from pentane to separate from 18	21 (as mixture with 18)	121–122	2.95 (m) and 3.17 (m) for NH; 5.95 (s) for C=N
17	13.5 g (0.041 mol) of 1 + 6.0 g of (CH ₃) ₃ OBF ₄	Stirred and refluxed for 6 hr in 80 ml of CH ₂ -Cl ₂	Washed with aq Na ₂ CO ₃ ; recrystallized from 1:1 water-ethanol, then from pentane	65
16	Na salt of 8 [from 7.5 g (0.02 mol) and 1.2 g of NaOCH ₃] + 4.5 g of CH ₃ I	10 min at 25° in 50 ml of (CH ₃) ₂ SO	Diluted with 300 ml of H ₂ O and extracted with ether; preparative gc at 100° on silicone 200	32	71.5–73	2.87 (m) and 2.91 (m) for NH; 6.01 (s) for C=N
4	10.0 g (0.028 mol) of 1 + 30 ml of (CH ₃) ₂ SO ₄	8 hr at 200° under autogenous pressure	Hydrolyzed hot with 10 ml of H ₂ O, then neutralized with aq NaOH; portion soluble in ether-pentane isolated by gc along with 18 using silicone 200 column	7	30–33	2.88 (m) for NH; 6.12 (s) for C=N ^c
20	9.25 g (0.025 mol) of 8 + 11 ml of (CH ₃) ₂ SO ₄	Heated rapidly to 170° and exothermic reaction (185°) allowed to occur	Hydrolyzed hot with 10 ml of 35 H ₂ O, neutralized with aq NaOH and steam distilled; preparative gc on silicone 200 column at 100° to separate from 19		Soft, waxy solid	2.96 (m) for NH; 5.95 (s) for C=N ^c
18	See 4 above	66 (as mixture with 17)	48–49	3.0 (m, broad) for NH; 5.92 (s) for C=N
5	10.7 g (0.03 mol) of 1 treated in three separate successive reactions with 1.78 g (0.033 mol) of NaOCH ₃ and 4.97 g (0.035 mol) of CH ₃ I in each reaction	Each reaction run for 10 min at 5° in 75 ml of (CH ₃) ₂ SO	Each diluted with 350 ml of H ₂ O and lower layer collected; product of third treatment purified by preparative gc on silicone 200 at 85°	50	37.5–39	6.13 (s) for C=N
19	Na salt of 18 [from 5.77 g (0.015 mol) and 1.35 g of NaOCH ₃] + 4.5 g of CH ₃ I	20 min at 25° in 35 ml of (CH ₃) ₂ SO	Diluted with 150 ml of H ₂ O; bottom layer purified by preparative gc on silicone 200 at 85°	46	<0	5.85 (s) for C=N ^b
19	See 20 above	29

^a All compounds gave satisfactory elemental analyses. Mass spectra and nmr analyses support the assigned structures. ^b CCl₄ solution. ^c Neat liquid.

(reflux in glyme). Prolonged reflux of 1b in glyme caused slow decomposition to a four-component product mixture. The major component was 2, formed by leavage of a trifluoromethyl anion from one or both of the salts of 1.



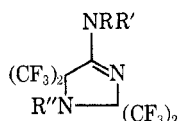
A conjugated structure with two kinds of hydrogen is indicated by the ultraviolet and proton nmr spectra, and structure 2 is favored for the product over alternative structure 2a on the basis of acidity and the fluorine nmr spectrum. Solubility in dilute sodium hydroxide, the means by which 2 is isolated from 1 and by-products, is more in keeping with formation of a completely conjugated anion than the cross-conjugated anion which would result from 2a. Loss of a trifluoro-

methyl group from the 2 position is also indicated by the loss of high-field fluorine nmr signal for 2 compared with 1.¹

Alkylations of Imidazolinium Anions.—All the methylated derivatives of 1 prepared under basic conditions are given in Table I. Alkylation of the salt 1a (prepared with 1 equiv of sodium methoxide in dimethyl sulfoxide) with methyl iodide at 25° gave predominantly the 4-methylamino isomer 3. Although this might be a kinetic result, it is taken as confirmation of delocalized structure 1a rather than that with a charge at the 1 position. Independent evidence that amidine hydrogen is more acidic than amine hydrogen in 1 was obtained by nmr. In deuterioacetone with D₂O, both protons of the 4-amino group of 1 exchanged within 1 hr at 25°, whereas the 1-position proton required catalysis. The preference for substitution in 1a on the 4-amino group rather than at the 3 position apparently results from the considerable steric crowding around the

3 position indicated by Stuart-Briegleb models. The proportions of product methylated at the 4-amino-, 3, and 1 positions was 60:2:1, with intermediate amounts of dimethylated products. Of the dimethylated products, the 4-(N,N-dimethylamino) compound **4** predominated. Repeated methylation of **1** led to the 1-methyl-4-(N,N-dimethylamino) compound **5**.

Anion **1a** derived from **1** with sodium hydride in glyme also was methylated to give mainly **3**. This procedure was used to obtain pure **3** (Table I). Similar alkylations with a spectrum of functionally substituted alkyl halides gave imidazolines monosubstituted on the 4-amino group (**6**) in up to 80% yield (Experimental Section).



3, R = CH₃; R' = R'' = H

4, R = R' = CH₃; R'' = H

5, R = R' = R'' = CH₃

6a, R = CH₂CH₂N(CH₃)₂; R' = R'' = H

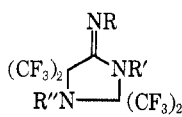
b, R = CH₂C₆H₅; R' = R'' = H

c, R = CH₂CH=CH₂; R' = R'' = H

d, R = CH₂CO₂C₂H₅; R' = R'' = H

9, R = R' = H; R'' = C₂H₅

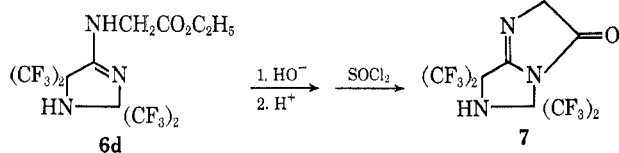
16, R = H; R' = R'' = CH₃



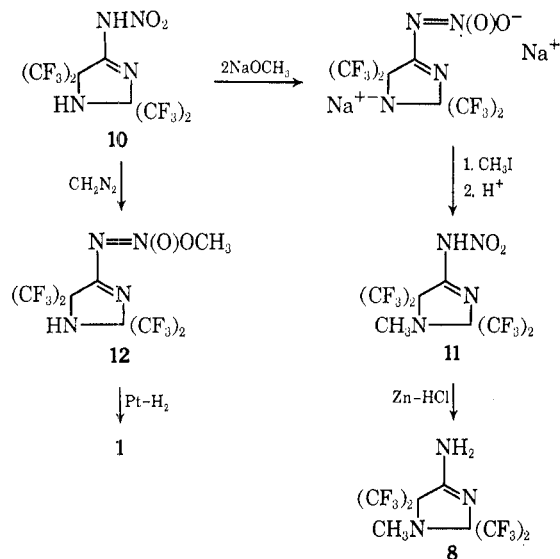
19, R = R' = R'' = CH₃

20, R = H; R' = R'' = CH₃

In addition to correlation of spectral parameters for these products with those of **1** and the preparation of all the possible methylated isomers (Table I), the structure of **6d** is supported by its easy cyclization to lactam **7**.



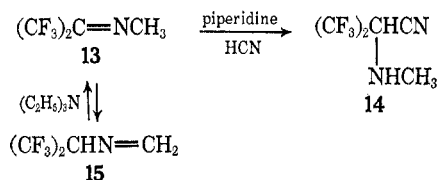
Preparation of the 1-methyl (**8**) and 1-ethyl (**9**) derivatives was accomplished by alkylation of the disodium salt of 4-nitramino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (**10**) (see below). The monoanion of **10** is unreactive toward halides; alkylation of the disodium salt gives the 1-methyl derivative **11** in good yield.



The nitro group was removed by chemical reduction to give 4-amino-1-methyl-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (**8**). A similar procedure gave the 1-ethylated product, **9**.

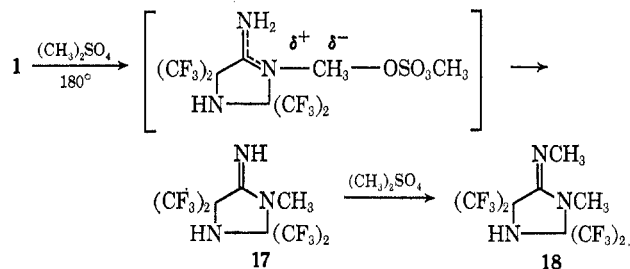
Starting material **10** in these syntheses is derived in good yield from nitration of the very stable parent, **1**, with fuming nitric acid. These vigorous conditions simply convert the 4-amino group in **1** into a nitramino group. The N-nitro compound **10** is very acidic and its anion has low nucleophilicity, but the free acid methylates easily with diazomethane to give **12**, a derivative of the *aci* form. Reductive cleavage of **12** regenerates **1**, showing that methylation occurred at the 4-amino group of **1**.

An alternative possibility for preparation of the methylated imidazolines, in particular the 1-methyl derivatives, was by reaction of cyanide ion with N-methylhexafluoroacetone imine (**13**). The first step in the synthesis, addition of cyanide to form the aminonitrile **14**, was demonstrated. However, attempts to condense more than 1 mol of **13** with cyanide under aprotic conditions gave instead the methylene compound, **15**, in high yield. A base-catalyzed prototropic shift occurred, and under equilibrium conditions, **15** was produced as the major component.



With the 1-methyl derivative **8** as a starting material, alkylation with methyl iodide under basic conditions provided a route to the 1-methyl-4-(N-methylamino) derivative, **16** (Table I).

Alkylations with Strong Electrophiles.—Direct methylation of **1** can be accomplished at high temperatures (170–200°) with dimethyl sulfate. In contrast to the monoalkylation of the anion, attack occurs mainly at the 3 position, presumably because of effective stabilization of positive charge in the transition state leading to **17**. Under the forcing conditions of the reaction, a second methyl group can be introduced, this time on the 4-imino nitrogen, to give 3-methyl-4-(N-methylimino)-2,2,5,5-tetrakis(trifluoromethyl)imidazolidine (**18**). Further methylation of **18** led to the 1,3-dimethyl-4-(N-methylimino) derivative, **19**.



A similar reaction starting with the 1-methyl compound **8** leads to the 1,3-dimethyl derivative **20**, attack at the 3 position again occurring preferentially.

Trimethyloxonium fluoroborate proved to be a better reagent than dimethyl sulfate for introducing a 3-methyl substituent into **1**. Reaction occurred under mild conditions with good selectivity, and yields were

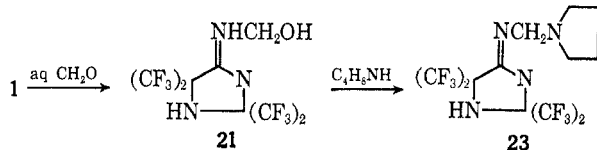
TABLE II
 PRODUCTS FROM 4-ISOCYANATO-2,2,5,5-TETRAKIS(TRIFLUOROMETHYL)-3-IMIDAZOLINE^a

Coreactant	Conditions	Product	Mp or bp, °C (mm)	Yield, %	$\lambda_{\text{max}}^{\text{CH}_3\text{ON}}$, m μ (ϵ)
LiAlH ₄	24 hr at 25° in ether	3 ^b	75 (10)	38	...
CH ₃ OH	Ether solvent	29b	125-129	76	<210
(CH ₃) ₂ NCH ₂ CH ₂ OH	Ether solvent	29c	136-141	62	252 (12,800)
1	Ether solvent	29a	203-205	100	...
CH ₃ CH ₂ SH	Ether solvent	29d	115-117	76	...
C ₆ H ₅ COOCH ₂ CH ₃	Reflux for 3 days, neat, 28 as dimer	32d	80 (0.3)	26	...
<i>p</i> -(CH ₃) ₂ -NC ₆ H ₄ CHO	Reflux for 1 hr, neat, 28 as dimer	32b	138-142	68	258 (7100) 304 (2600) 315 (1900) 420 (38,700)
HCON(CH ₃) ₂	Reflux for 2 hr, neat, 28 as dimer	32c	113-115	84	281 (23,800)
(CH ₃) ₂ NCSN(CH ₃) ₂	Reflux for 1 hr, neat, 28 as dimer	32e	121-129	36	262 (18,000)

^a All compounds gave satisfactory elemental analyses. Nmr spectra support the assigned structures. ^b Product identical with 3 prepared by methylation of 1.

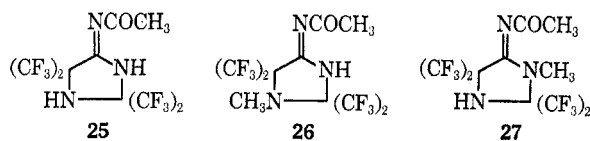
high. This reaction could be extended to ethylation with triethyloxonium fluoroborate, just as the reaction with dimethyl sulfate could also be accomplished with diethyl sulfate. Various combinations of the methods described above were used to prepare all the possible mono-, di-, and trimethyl derivatives of 1. The syntheses are given in Table I.

Mannich Reaction.—Condensation of 1 with formaldehyde proceeded readily to the methylol derivative, 21, and a higher formaldehyde condensation product, the 4-(*N*-hydroxymethoxy) derivative 22. In the presence of various secondary amines, Mannich products were obtained in high yield. As an example, formaldehyde-pyrrolidine converted 1 into the 4-(*N*-pyrrolidylmethylamino) derivative, 23. Compound 23 was converted into water-soluble hydrochloride and methiodide salts.



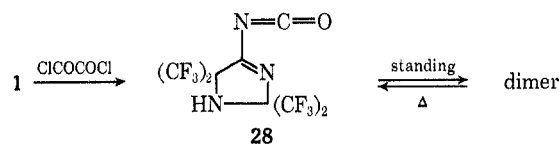
The imidazolines with fluorinated groups other than trifluoromethyl¹ generally undergo the same reactions as 1. An example is the Mannich reaction on 4-amino-2,5-bis(difluoromethyl)-2,5-bis(trifluoromethyl)-3-imidazoline to give 24 (see Experimental Section).

Acylation.—Just as with the Mannich reaction, 1 underwent substitution on the 4-amino group with acid halides. Reaction proceeded slowly because of the very low basicity of 1, but high yields were attained with long reaction times. Acetyl chloride gave with 1 a product formulated as the 4-acetamido compound 25, although the acidity of this product makes the location of the ionizable proton uncertain. A stable tetraethylammonium salt of 25 was readily prepared. The corresponding benzoyl derivative of 1 was prepared, as were many other acylation products.



The 1-methyl compound 8 and the 3-methyl compound 17 also gave acylation products (26 and 27) resulting from attack at the exocyclic nitrogen. Benzenesulfonylation of 1 occurred normally on the 4-amino group.

Formation and Reactions of the Isocyanate.—Oxalyl chloride, as an acid halide, attacked 1 at the 4-amino position to form as the final product 4-isocyanato-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (28). This highly reactive isocyanate dimerized on standing at room temperature. Above the decomposition point of 152-154°, dimer was shown to crack cleanly to regenerate isocyanate 28, thus serving as a convenient source of 28 for many reactions (Table II).

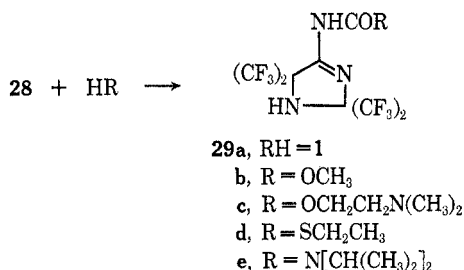


The dimer of 28 may have the normal 1,3-diazetidinedione structure for an isocyanate dimer, as indicated by its pyrolysis back to 28. However, the nmr, infrared, and ultraviolet spectra are also in accord with the isomeric 1,3-oxazetidinedione structure, which can be theoretically derived from cycloaddition of the C=N bond of one isocyanate group to the C=O of a second isocyanate group. The dimer exhibits two ir bands (5.51 and 5.71 μ) which could arise from either coupled vibrations of two small-ring carbonyl groups or a carbonyl group plus an imino group on a small ring. Uv absorption at 228 m μ might result from either structure. Nmr bands for ¹⁹F show the two imidazoline rings to be different, as they would be in an oxazetidinedione and as they might be for steric reasons in a diazetidinedione. An example of the latter case where in two imidazoline rings are fixed in nonequivalent positions in space was found in the urea 29a derived from isocyanate 28. With water or with an equivalent amount of 1, 28 forms the urea 29a in which the ¹⁹F nmr bands are distinct for the trifluoromethyls on each ring.

Isocyanate formation and dimerization were general for the fluorinated imidazolines. 4-Isocyanato-2,2,5,5-tetrakis(chlorodifluoromethyl)-3-imidazoline (30) and

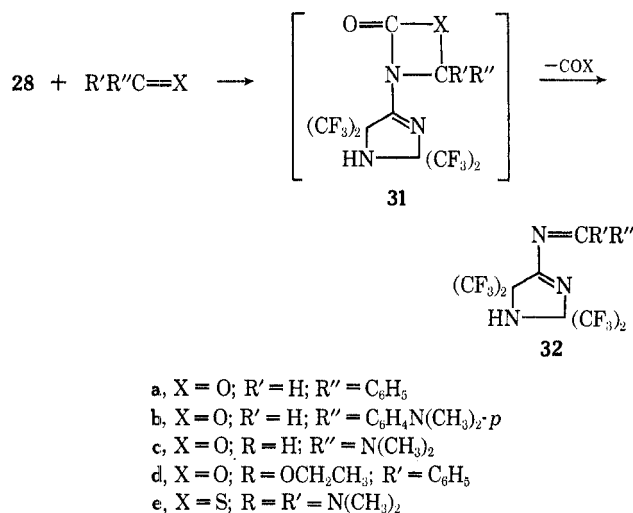
its dimer are described in the Experimental Section as an additional example.

Isocyanate **28** reacted vigorously with active hydrogen compounds to form the corresponding carbamoyl derivatives, **29** (Table II). As noted above, reaction even occurred readily with the amino group in **1**.



The products **29** have an acidic proton, and those derived from amines can give the ammonium salts directly. For example, the diisopropylammonium salt of the N,N-diisopropylurea **29e** was formed from **28** and excess diisopropylamine.

The highly reactive isocyanate group in **28** also reacted easily with carbonyl and thiocarbonyl functions. The initial products in these cases may have been cycloadducts **31**, but loss of CO₂ or COS occurred spontaneously with formation of unsaturated products **32**. Even the ester carbonyl in ethyl benzoate participated in the reaction (Table II).



Reduction of **28** provided a chemical proof of structure for the monomethyl compound **3**. Lithium aluminum hydride converted the isocyanate group, which must be at the 4 position on the imidazoline ring, into an N-methyl compound identical with **3** obtained earlier by methylation under basic conditions.

Spectral Correlations.—In addition to the chemical evidence and to the synthesis of all the possible methylated isomers, spectral correlations tend to confirm the structures assigned to the compounds we have described.

Proton nmr positions for the various NH groups are solvent sensitive, tending to be grouped in the range of τ 5–7 for neat samples and samples in solvents of low polarity. Pronounced shifts to low field occurred with acceptor solvents such as acetone and dimethyl sulfoxide, and resolution of the different types of NH was improved. Examination of the data for alkyl deriv-

atives of **1** shows that in the polar acceptor solvents, hydrogen in the 1 position of either imidazolines or imidazolidines generally appeared in the range of τ 3.7–4.1. The more acidic hydrogen on the 4-amino group of the imidazolines appeared at lower field in the range of τ 2.3–3.0; the 4-imino hydrogen in imidazolidines were at still lower field, *ca.* τ 2.0. The NH chemical shifts in other derivatives are consistent with this classification, with the additional observation that the increased acidity caused by a nitro, acyl, or other negative substituent on the 4-amino group produced a downfield shift for the nearby NH to the region of τ -0.5 to 1.0.

Fluorine nmr shifts, as noted before,¹ were characterized by a higher field position for the trifluoromethyl groups in the 2 position (72–78 ppm) than in the 5 position (67–74 ppm). Long-range coupling between these sets was consistently around 5 Hz. No indication of an AA'BB' pattern was seen.

Infrared absorption bands for the endocyclic imino group attached to an amino group occurred near 5.9 μ . With one alkyl substituent on the 4-amino group, absorption occurred near 6.0 μ , and with a 4-dialkylamino group near 6.1 μ . The exocyclic imino group gave rise to a band near 5.95 μ , while the 4-alkylimino group gave a band near 5.85 μ .

Experimental Section³

4-Imino-2,5,5-tris(trifluoromethyl)-2-imidazoline (2).—To a slurry of 8.1 g (0.34 mol, from 15 g of 54% NaH–Nujol washed with benzene) of sodium hydride in 300 ml of glyme was added a solution of 36 g (0.1 mol) of **1** in 50 ml of glyme at -10°. One equivalent of gas was evolved immediately. The mixture was refluxed for 6 hr while an additional 1.6 equiv of gas were evolved. The resulting dark mixture was cooled and treated at 5° with 10 ml of methanol to destroy excess sodium hydride and then with 200 ml of 2 *N* hydrochloric acid followed by 400 ml of water.

The acidic mixture was extracted with five 75-ml portions of ether and the ethereal solution was concentrated under reduced pressure to give a dark brown tar. Steam distillation afforded 8.2 g of a mixture of starting material and **2**. The crude mixture was dissolved in ether and extracted with three 15-ml portions of 1 *N* sodium hydroxide. The combined basic solutions were extracted twice with ether, neutralized with aqueous HCl, and extracted with ether to afford 4.5 g (16%) of **2**, mp 152–154°. An analytical sample, mp 154–155°, was obtained by three recrystallizations from methylene chloride followed by sublimation at 120° (15 mm): ir 2.88, 3.01 (NH), 5.96, 6.17, and 6.35 μ (C=N); uv $\lambda_{\text{max}}^{\text{ethanol}}$ 285 m μ (ϵ 7300); ¹H nmr τ 0.4 (NH) and 1.0 ppm (NH); ¹⁹F nmr 73.2 (singlet, 1, CF₃) and 73.3 ppm (singlet, 2, CF₃).

Anal. Calcd for C₆H₂F₉N₃: C, 25.1; H, 0.7; F, 59.6; N, 14.6. Found: C, 24.9; H, 1.4; F, 59.5; N, 14.5.

4-(N-Benzylamino)-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (6b).—A 7-g sample (0.02 mol) of **1** dissolved in 10 ml of glyme was added at <10° to 1 g (0.02 mol) of 54% sodium hydride–mineral oil in 50 ml of glyme. The stirred suspension was refluxed for 2 hr. Later studies showed that 1 equiv of H₂ is evolved at ice-bath temperature but that refluxing the sodium salt in glyme, even for several days, has no adverse effect. The suspension was cooled and 4 g (0.023 mol) of benzyl bromide was added at <10°. The mixture was refluxed for 22 hr, cooled, and filtered to remove the sodium bromide formed, and the filtrate

(3) Melting points and boiling points are uncorrected. Proton nmr spectra were obtained with a Varian A-60 spectrometer on deuterioacetone solutions with tetramethylsilane as an internal standard. Peak center positions for ¹H are reported as τ parts per million. Fluorine nmr spectra were obtained with a Varian A56-60 spectrometer on deuterioacetone solutions with trichlorofluoromethane as an internal standard. Peak center positions for ¹⁹F are reported in parts per million upfield from CFCl₃. Ir spectra were determined in KBr wafers with a Perkin-Elmer 21 spectrophotometer. Mass spectra were taken at 70 eV on a CEC 21-103C instrument.

was distilled through a spinning-band column. The product was **6b**: yield 6.3 g (70%); bp 120° (10 mm); ¹H nmr τ 2.35 (broad, 1, NH), 2.68 (5, C₆H₅), 3.85 (broad, 1, NH), and 5.30 ppm (doublet, 2, J_{HH} = 6.0 Hz, CH₂); ¹⁹F nmr 72.8 (septet, 1, J_{FF} = 5.0 Hz, CF₃) and 78.1 ppm (septet, 1, J_{FF} = 5.0 Hz, CF₃).

Anal. Calcd for C₁₄H₉F₁₂N₃: C, 37.6; H, 2.0; F, 51.1; N, 9.4; mol wt, 447. Found: C, 37.6; H, 2.1; F, 50.9; N, 9.4; mol wt, 447 (mass spectrum).

4-(N-Allylamino)-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (6c).—Using the above procedure for **6b**, but substituting 3 g (0.025 mol) of 3-bromopropene for benzyl bromide, a 6.1-g (75%) sample of **6c** was prepared: bp 87° (25 mm); ¹H nmr (CCl₄) τ 3.7–5.1 (multiplet, 4, NH and CH=CH₂), 5.9 (multiplet, 2, CH₂), and 6.4 ppm (1, NH); ¹⁹F nmr 72.8 (septet, 1, J_{FF} = 5.0 Hz, CF₃) and 77.8 ppm (septet, 1, J_{FF} = 5.0 Hz, CF₃).

Anal. Calcd for C₁₀H₇F₁₂N₃: C, 30.2; H, 1.8; F, 57.4; N, 10.6; mol wt, 397. Found: C, 30.2; H, 2.2; F, 56.9; N, 10.4; mol wt, 397 (mass spectrum).

4-N-[2-(Dimethylamino)ethyl]amino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (6a).—The sodium salt of **1**, 7.0 g (0.02 mol), was prepared as above. An additional 1 equiv (1 g) of 54% sodium hydride—mineral oil and 4.85 g (0.021 mol) of β-(dimethylamino)ethyl bromide hydrobromide were added successively at <10°. The mixture was refluxed for 24 hr, cooled, and filtered. The product, bp 80–85° (7 mm), yield 5.0 g (58%), solidified on standing, mp 47–53°. A sample was purified *via* the hydrochloride: mp 58–61°; ¹H nmr τ 3.40 (broad, 1, NH), 3.90 (broad, 1, NH), 6.50 (triplet, 2, J_{HH} = 6.0 Hz, CH₂), 7.46 (triplet, 2, J_{HH} = 6.0 Hz, CH₂), and 7.78 ppm (singlet, 6, CH₃); ¹⁹F nmr 75.5 (septet, 1, J_{FF} = 5.0 Hz, CF₃) and 78.6 ppm (septet, 1, J_{FF} = 5.0 Hz, CF₃).

Anal. Calcd for C₁₁H₁₂F₁₂N₄: C, 30.9; H, 2.8; F, 53.2; N, 13.1; mol wt, 428. Found: C, 30.4; H, 2.6; F, 53.4; N, 13.9; mol wt, 428 (mass spectrum).

Preparation of 4-[N-(Ethoxycarbonylmethyl)amino]-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (6d) and Cyclization to 6,7-Dihydro-5,5,7,7-tetrakis(trifluoromethyl)-5H-imidazo[1,5-a]imidazol-3-(2H)-one (7).—A 4-g sample (0.024 mol) of ethyl bromoacetate was substituted for benzyl bromide in the above procedure for **6b** to give 4.8 g (50%) of the 4-N-ethoxycarbonylmethyl derivative: mp 74–78°; ¹H nmr τ 2.60 (broad, 1, NH), 3.80 (broad, 1, NH), 5.81 (doublet, 2, J_{HH} = 5.5 Hz, CH₂), 5.82 (quartet, 2, J_{HH} = 7.0 Hz, CH₂CH₃), and 8.76 ppm (triplet, 3, J_{HH} = 7.0 Hz, CH₂CH₃); ¹⁹F nmr 73.0 (septet, 1, J_{FF} = 5.0 Hz, CF₃), and 78.2 ppm (septet, 1, J_{FF} = 5.0 Hz, CF₃).

Anal. Calcd for C₁₁H₉F₁₂N₃O₂: C, 29.8; H, 2.1; F, 51.5; N, 9.5. Found: C, 30.4; H, 2.2; F, 50.9; N, 9.6.

A 10-g sample (0.023 mol) of **6d** was refluxed with 100 ml of 10% sodium hydroxide solution until the mixture became homogeneous (*ca.* 1 hr). The cooled reaction mixture was mixed with 100 g of ice and acidified to pH 2 with concentrated hydrochloric acid. The solid thus formed was extracted with ether, and the ether extracts were washed with water and dried over magnesium sulfate. Evaporation of the ether gave a residue which was purified by mixing with excess (*ca.* 50 ml) 5% sodium bicarbonate solution. The basic solution was extracted with ether to remove starting material, cooled, and acidified to pH 2. The purified acid was collected on a filter, sucked dry, and washed with pentane. The white acid, pK_a = 5.48, yield 6.48 g (69%), had a melting point of 133–135°.

Anal. Calcd for C₉H₅F₁₂N₃O₂: C, 26.0; H, 1.2; F, 54.9; N, 10.1; neut equiv, 415. Found: C, 26.2; H, 1.2; F, 54.9; N, 10.3; neut equiv, 413.

An 8-g sample (0.019 mol) of the above acid was dissolved in 50 ml of thionyl chloride and the resulting solution was heated at reflux for 8 hr. The reaction mixture was evaporated to dryness under reduced pressure. The yellow residue was sublimed at 150° (1 mm) and then recrystallized from ether–pentane to give 3.1 g (41%) of **7** as a light yellow, crystalline powder: mp 256–259°; ¹H nmr τ 2.16 (1, NH) and 6.88 ppm (singlet, 2, CH₂); ¹⁹F nmr 72.6 (septet, 1, J_{FF} = 4.2 Hz, CF₃) and 75.6 ppm (septet, 1, J_{FF} = 4.2 Hz, CF₃).

Anal. Calcd for C₈H₃F₁₂N₃O: C, 27.2; H, 0.8; F, 57.4; N, 10.6. Found: C, 27.0; H, 1.1; F, 57.0; N, 10.9.

4-Nitramino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (10) and Its Tetramethylammonium Salt.—Red, fuming nitric acid, 50 ml, was added dropwise to a stirred solution of 7.14 g (0.02 mol) of **1** in 50 ml of 20% fuming sulfuric acid at such a rate that the temperature remained at 100–105°. The addition required *ca.* 10 min. The reaction mixture was cooled and poured

over 500 ml of crushed ice. The white solid that formed was collected on a filter, washed with water, and dried in air. Recrystallization from alcohol–water gave 6.8 g (85%) of **10** as colorless needles: mp 176–177° (sealed capillary); ir 6.07 μ (C=N); ¹⁹F nmr 72.9 (septet, 1, J_{FF} = 4.5 Hz, CF₃) and 77.0 ppm (septet, 1, J_{FF} = 4.5 Hz, CF₃); ¹H nmr τ 0.2 (singlet, 1, NH) and 2.8 ppm (singlet, 1, NH). The compound was acidic, pK_a = 2.78 in water.

Anal. Calcd for C₇H₂F₁₂N₄O₂: C, 20.9; H, 0.5; F, 56.7; N, 13.9; neut equiv, 402. Found: C, 21.6; H, 0.6; F, 55.6; N, 14.4; neut equiv, 404.

A solution of 0.5 g of tetramethylammonium chloride in 5 ml of water was mixed with a solution of 0.8 g (0.002 mol) of **10** in 5 ml of 5% aqueous sodium bicarbonate. The reaction mixture was cooled to 0° and the colorless crystals that formed were collected on a filter and washed with water. After drying, there was obtained 0.70 g of the tetramethylammonium salt, mp 207–208°.

Anal. Calcd for C₁₁H₁₃F₁₂N₅O₂: C, 27.8; H, 2.8; F, 48.0. Found: C, 28.1; H, 2.8; F, 47.9.

Preparation and Reduction of 4-(Methoxyazoxy)-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (12).—A 2% solution of diazomethane in ether was added portionwise to a solution of 40.2 g (0.1 mol) of **10** in 100 ml of ether until a faint yellow color persisted. The ether was evaporated under reduced pressure, and the white residue was recrystallized from pentane to give 40.0 g (96%) of **12** as a white solid: mp 68–73°; ir 6.15 and 6.44 μ; ¹⁹F nmr 71.8 (septet, 1, J_{FF} = 4.6 Hz, CF₃) and 76.2 ppm (septet, 1, J_{FF} = 4.6 Hz, CF₃); ¹H nmr τ 5.74 (singlet, 3, CH₃) and 3.46 ppm (broad, 1, NH). Both the melting point and nmr spectra indicate that this sample is contaminated with a few per cent another isomer.

Anal. Calcd for C₈H₄F₁₂N₄O₂: C, 23.1; H, 1.0; F, 54.8; N, 13.5. Found: C, 23.1; H, 0.9; F, 54.4; N, 12.7.

A solution of 12.48 g (0.03 mol) of **12** in 50 ml of ethanol was shaken with 0.2 g of PtO₂ under 2–3 atm of hydrogen pressure until *ca.* 0.09 mol of hydrogen had been absorbed (4 hr). The reaction mixture was filtered, and the filtrate was mixed with 300 ml of water. The white solid that separated was collected on a filter, washed with water, and dried. There was obtained 8.0 g (75%) of a crystalline, white powder identified as **1** by ir.

1-Methyl-4-nitramino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (11).—To a solution of 6.43 g (0.016 mol) of **10** in 75 ml of dimethyl sulfoxide was added with cooling (20°) 1.78 g (0.033 mol) of sodium methoxide. The almost clear solution was treated with 2.17 g (0.017 mol) of methyl iodide added dropwise at 20° over 5 min. After 10 min, the solution was poured into 450 ml of water. The clear solution was diluted to 600 ml and a 100-ml aliquot was treated with 3.0 g of tetraethylammonium chloride. The resulting precipitate (1.1 g) was recrystallized four times from 25-ml portions of water containing 3 ml of ethanol to give 0.73 g (50%) of the tetraethylammonium salt of **11**: mp 132–133°; ir 6.25 μ (strong); uv λ_{max}^{H₂O} 289 mμ (ε 11,600).

Anal. Calcd for C₁₆H₂₃F₁₂N₅O₂: C, 35.2; H, 4.3; F, 41.8; N, 12.8. Found: C, 35.0; H, 4.2; F, 42.0; N, 12.8.

The remaining 500 ml of solution above was acidified with 2 N sulfuric acid, and the crystalline precipitate was collected, washed with water, and dried to give 4.25 g (77%) of crude **11**, mp 104–112°. Four recrystallizations from 50 ml of benzene afforded 2.54 g of an analytical sample: mp 115–116°; ir 2.94 and 3.03 broad, NH), 6.08 (C=N), and 6.49 μ (NO₂); ¹H nmr τ 0.61 (broad, 1, exchangeable with D₂O, NH) and 6.85 ppm (septet, 3, J_{HF} = 1.1 Hz, CH₃); ¹⁹F nmr 70.6 (1, CF₃) and 75.1 ppm (1, CF₃).

4-Amino-1-methyl-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (8).—The 1-methyl derivative can be synthesized from the pure 1-methylnitramino derivative. In practice the crude material was utilized without purification, as described below.

A stirring solution of 32.6 g (0.081 mol) of **10** in 150 ml of dimethyl sulfoxide was treated with 9.65 g (0.179 mol) of sodium methoxide added in small portions while the temperature was maintained at 20–22° in an ice-water bath. Methyl iodide (17.1 g, excess) was added dropwise over 15 min, while the temperature was still kept down. The resulting slurry was stirred for 15 min and poured into 600 ml of ice-water. The clear solution was acidified with 25 ml of 6 N sulfuric acid and the solid was collected and washed with water. The wet crude **11** was dissolved in 375 ml of ethanol and treated with 18 g of zinc dust. To the resulting slurry, stirred while in an ice-water bath, was added 90 ml of concentrated hydrochloric acid. The rate of

addition was such that the temperature was kept below 25° initially and had risen to 40° at the end. The mixture was warmed to 65–70° for 45 min and then filtered. The filtrate was heated to boiling and diluted with water to a cloud point (total volume ca. 900 ml). After cooling in an ice bath, the product was collected, washed with water, and air dried to give 24.2 g (81%) of **8** as white needles, mp 168–170°. An analytical sample, mp 170.5–171°, was obtained by two recrystallizations from 50% ethanol, followed by sublimation at 110° (0.1 mm): ir 2.84 and 3.21 (NH₂), 5.93 (C=N), and 6.27 μ (NH₂); ¹H nmr τ 2.80 (broad, 2, NH₂) and 7.00 ppm (3, CH₃); ¹⁹F nmr 68.7 (septet, 1, J_{FF} = 5.0 Hz, CF₃) and 73.8 ppm (septet, 1, J_{FF} = 5.0 Hz, CF₃).

Anal. Calcd for C₃H₅F₁₂N₃: C, 25.9; H, 1.4; F, 61.4; N, 11.3; mol wt, 371. Found: C, 25.8; H, 1.3; F, 61.4; N, 11.4; mol wt, 371 (mass spectrum).

4-Amino-1-ethyl-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (9).—To a solution of 10.8 g (0.025 mol) of **10** in 50 ml of excess dimethyl sulfoxide was added with cooling 5.4 g (0.01 mol) of sodium methoxide. The resulting slurry was treated with 15.6 g (0.01 mol) of ethyl iodide added dropwise at 20° over 20 min. After 1 hr, the mixture was poured into ice-water and made strongly acidic with 6 N sulfuric acid. The organic product was extracted into ether, washed with water, dried, and concentrated to give 8.9 g of solid. The crude solid was dissolved in 125 ml of ethanol and treated with 6.5 g of zinc dust. To the stirred slurry was added 30 ml of concentrated hydrochloric acid, with warming. After the zinc was consumed (1 hr), water was added to the clear hot solution to the cloud point. After cooling in an ice bath, the crude solid, weighing 2.96 g, was collected and shown to be 90% desired product and 10% unalkylated imidazoline. The experiment was repeated twice and the crude products were combined and recrystallized from 250 ml of 50% aqueous ethanol to give 6.2 g (21%) of **9** as white needles, mp 148–150°. An analytical sample, mp 150–151°, was obtained by two recrystallizations from 50% ethanol followed by sublimation at 110° (0.1 mm): ir 2.86, 3.11, and 3.17 (NH₂), 5.90 (C=N), and 6.21 μ (NH₂); ¹H nmr τ 1.87 (broad, 2, NH₂), 6.55 (quartet, 2, J_{HH} = 7.0 Hz, CH₂), and 8.79 ppm (triplet, 3, J_{HH} = 7.0 Hz, CH₃); ¹⁹F nmr 68.1 (septet, 1, J_{FF} = 5.0 Hz, CF₃) and 73.0 ppm (septet, 1, J_{FF} = 5.0 Hz, CF₃).

Anal. Calcd for C₆H₇F₁₂N₃: C, 28.1; H, 1.8; F, 59.2; N, 10.9. Found: C, 27.8; H, 2.4; F, 59.0; N, 10.9.

N-Methylene-2,2,2-trifluoro-1-(trifluoromethyl)-ethylamine (15).—A solution of 60 g (0.34 mol) of N-methylhexafluoroacetone imine (**13**) and 0.6 ml of triethylamine was warmed to reflux (39°). After 35 min the yellow solution was refluxing at 65°. After 1 hr the mixture was distilled through a spinning-band column to give 50.6 g (85%) of **15**: bp 79°; n_D²⁰ 1.2994; ir 5.97 μ (C=N); ¹H nmr (neat) τ 2.45 (singlet, 2, =CH₂) and 5.90 ppm (septet, 1, J_{HF} = 6.7 Hz, CH); ¹⁹F nmr 71.7 ppm (doublet, J_{HF} = 6.7 Hz, CF₃).

Anal. Calcd for C₄H₅F₃N: C, 26.8; H, 1.7; F, 63.7; N, 7.8; mol wt, 179. Found: C, 27.1; H, 1.8; F, 63.7; N, 8.3; mol wt, 179 (mass spectrum).

3,3,3-Trifluoro-2-trifluoromethyl-2-(methylamino)propionitrile (14).—A mixture of 62 g (0.35 mol) of N-methylhexafluoroacetone imine and 16 ml (11.4 g, 0.50 mol) of hydrogen cyanide was cooled to 5° in a 200-ml flask fitted with a thermometer and a wet ice condenser. To it was added 0.05 ml of piperidine with stirring. The clear liquid was allowed to warm to reflux (28°). As the reflux rate diminished or the temperature started to drop, additional 0.05-ml portions of piperidine were added. After four portions of piperidine had been added, the temperature in the flask had risen to 55°. The reaction mixture was then heated to reflux at 90°. After cooling, the clear orange liquid was distilled through a spinning-band column to give 60.7 g (85%) of **14**: bp 63–65° (185 mm); ir 2.94 (NH) and 4.44 μ (C=N); ¹H nmr (neat) τ 7.62 (broad doublet, 3, J_{HH} = 5.2 Hz, CH₃) and 8.00 ppm (broad, 1, NH); ¹⁹F nmr 87.1 ppm (quadruplet, J_{HF} = 0.8 Hz, CF₃).

Anal. Calcd for C₅H₄F₃N₂: C, 29.1; H, 2.0; F, 55.3; N, 13.6; mol wt, 206. Found: C, 29.4; H, 2.0; F, 55.0; N, 13.5; mol wt, 206 (mass spectrum).

4-[N-(Hydroxymethyl)amino]-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (21).—A mixture of 10 g (0.008 mol) of **1** and 50 ml of 27% aqueous formaldehyde was heated to boiling. The resulting clear solution was cooled to 0°, diluted with 200 ml of cold water, and made strongly basic with 100 ml of 10% sodium hydroxide. The white precipitate that formed was collected on a

filter and recrystallized from ether-pentane (10–90%). There was obtained 6.1 g (56%) of **21** as a white, crystalline powder: mp 90–92°; ir 6.00 (C=N) and 6.44 μ (NH); ¹H nmr τ 2.30 (broad, 1, NH), 3.90 (singlet, 1, NH), and 4.97 ppm (doublet superimposed on broader signal, 3, J_{HH} = 5.4 Hz, CH₂OH); ¹⁹F nmr 72.1 (septet, 1, J_{FF} = 4.8 Hz, CF₃) and 77.1 ppm (septet, 1, J_{FF} = 4.8 Hz, CF₃).

Anal. Calcd for C₈H₅F₁₂N₃O: C, 24.8; H, 1.3; F, 58.9; N, 10.9. Found: C, 25.4; H, 1.5; F, 58.6; N, 11.3.

4-[N-(hydroxymethoxymethyl)amino]-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (22).—A 10-g sample (0.028 mol) of **1** was dissolved in 50 ml of boiling 37% aqueous formaldehyde. The resulting solution was cooled and diluted with 100 ml of water. The oil that separated was washed with water several times until it solidified. Recrystallization of the solid from ether-pentane gave 8.7 g (74%) of **22** as colorless crystals: mp 106–108°; ir 6.00 (C=N) and 6.44 μ (NH); ¹H nmr τ 2.13 (broad, 1, NH), 3.72 (singlet, 1, NH), 4.57 (triplet, 1, J_{HH} = 7.5 Hz, OH), 4.92 (doublet, 2, J_{HH} = 6.0 Hz, NCH₂O), and 5.15 ppm (doublet, 2, J_{HH} = 7.5 Hz, OCH₂O); ¹⁹F nmr 72.3 (septet, 1, J_{FF} = 4.8 Hz, CF₃) and 77.2 ppm (septet, 1, J_{FF} = 4.8 Hz, CF₃).

Anal. Calcd for C₉H₇F₁₂N₃O₂: C, 25.9; H, 1.7; F, 54.7; N, 10.1. Found: C, 25.9; H, 1.5; F, 54.6; N, 9.9.

4-[N-(Pyrrolidylmethyl)amino]-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (23).—Pyrrolidine, 10 ml, was added to a hot (90°) solution of 10 g (0.028 mol) of **1** in 50 ml of 37% aqueous formaldehyde. The resulting reaction mixture was cooled, and the solid that precipitated was collected on a filter, washed with water, and dried. Recrystallization from pentane gave 9.6 g (78%) of **23** as colorless needles: mp 127–128°; ¹H nmr τ 2.73 (broad, 1, NH), 3.90 (broad, 1, NH), 5.45 (singlet, 2, NCH₂N), 7.3 (multiplet, 4, CH₂), and 8.3 ppm (multiplet, 4, CH₂); ¹⁹F nmr 71.0 (septet, 1, J_{FF} = 4.8 Hz, CF₃) and 77.2 ppm (septet, 1, J_{FF} = 4.8 Hz, CF₃).

Anal. Calcd for C₁₂H₁₂F₁₂N₄: C, 32.7; H, 2.8; F, 51.8; N, 12.7. Found: C, 32.6; H, 3.0; F, 52.3; N, 12.8.

A solution of 3.0 g of **23** in 50 ml of ether was saturated with dry hydrogen chloride gas. The white precipitate that formed was collected on a filter and washed with ether. There was obtained 3.1 g of the hydrochloride as a white, crystalline powder, mp 123–126°.

Anal. Calcd for C₁₂H₁₃F₁₂N₄Cl: Cl, 7.4. Found: Cl, 7.0.

Methyl iodide, 25 ml, was added to a solution of 5.0 g (0.011 mol) of **23** in 25 ml of ether. The solution was allowed to stand for 3 hr at 25°, and the solid that precipitated during this time was then collected on a filter and washed with ether. The solid (5.85 g) was dissolved in acetone and fractionally precipitated by the addition of ether. The first fraction contained no fluorine and was discarded. The methiodide, yield 3.0 g (47%), mp 190–193°, was obtained as the last fraction.

Anal. Calcd for C₁₃H₁₃F₁₂N₄I: C, 26.8; H, 2.6; F, 39.2; I, 21.8; N, 9.6. Found: C, 27.0; H, 2.9; F, 38.7; I, 22.1; N, 9.3.

4-[N-(Pyrrolidylmethyl)amino]-2,5-bis(difluoromethyl)-2,5-bis(trifluoromethyl)-3-imidazoline (24).—A 2.0-g sample (0.0062 mol) of 4-amino-2,5-bis(difluoromethyl)-2,5-bis(trifluoromethyl)-3-imidazoline was dissolved in 5 ml of hot 37% aqueous formaldehyde. The solution was cooled and mixed with 2 ml of pyrrolidine. Water, 100 ml, was added, and the solid that separated was collected on a filter and washed with water. Recrystallization from pentane gave 1.15 g (46%) of **24** as colorless crystals: mp 97–99°; ¹H nmr τ 3.06 (broad, 1, NH), 3.54 (triplet, 2, J_{HF} = 5.4 Hz, CHF₂), 3.95 (singlet, 1, NH), 5.54 (doublet, 2, J_{HH} = 4.5 Hz, NCH₂N), 7.34 (multiplet, 4, CH₂), and 8.31 ppm (multiplet, 4, CH₂); ¹⁹F nmr multiplets at 73.9 (3), 77.8 (3), 126.2 (2), and 131.6 ppm (2).

Anal. Calcd for C₁₂H₁₄F₁₀N₄: C, 35.7; H, 3.5; F, 47.0; N, 13.9. Found: C, 35.8; H, 3.5; F, 46.9; N, 13.5.

4-Acetylimino-2,2,5,5-tetrakis(trifluoromethyl)imidazolidine (25) and Its Tetramethylammonium Salt.—A solution of 5.0 g (0.014 mol) of **1** in 25 ml of acetyl chloride was heated at reflux for 20 hr. The reaction mixture was cooled and poured into 300 ml of cold water to decompose the excess acetyl chloride. The solid that formed was collected on a filter and dried in air. There was obtained 5.32 g (95% yield) of crude **25** as a white powder. Recrystallization from alcohol-water gave colorless needles: mp 154–155° (sealed capillary); ir 5.79, 6.00, and 6.61 μ (conjugated amide); uv λ_{max}^{EtOH} 223 mμ (ε 13,500) and 265 (sh); ¹H nmr τ 0.80 (broad, 1, NH), 3.46 (broad, 1, NH), and 7.63

ppm (singlet, 3, CH₃); ¹⁹F nmr 71.7 (septet, 1, *J*_{FF} = 4.6 Hz, CF₃) and 76.5 ppm (septet, 1, *J*_{FF} = 4.6 Hz, CF₃).

Anal. Calcd for C₉H₁₅F₁₂N₃O: C, 27.1; H, 1.3; F, 57.1; N, 10.5. Found: C, 27.5; H, 1.4; F, 58.1; N, 11.3.

A 10% aqueous sodium hydroxide solution was added dropwise to a suspension of 5.0 g (0.013 mol) of **25** in 25 ml of water until solution was complete. The solution was filtered, and the filtrate was mixed with a solution of 5.0 g of tetramethylammonium chloride in 10 ml of water. The crystalline precipitate that formed upon cooling to 0° was collected on a filter and recrystallized from alcohol-ether. There was obtained 4.1 g (67%) of the tetramethylammonium salt as colorless crystals, mp 225–227°, ir 6.44 μ.

Anal. Calcd for C₁₃H₁₅F₁₂N₄O: C, 33.1; H, 3.4; F, 48.3; N, 11.9. Found: C, 33.4; H, 3.7; F, 47.7; N, 11.6.

4-Acetylimino-1-methyl-2,2,5,5-tetrakis(trifluoromethyl)imidazolidine (26).—A mixture of 3 g (0.008 mol) of **8** and 6 ml of acetyl chloride was heated at reflux for 26 hr. The excess acetyl chloride was evaporated and the residue was sublimed at 80° (0.1 mm) to give 3.29 g (99%) of **26**, mp 159–160°. An analytical sample, mp 159–160°, was obtained by recrystallization from ethanol, followed by sublimation: ir 3.05, 3.09, and 3.17 (NH and CH) and 5.75 and 6.06 μ (C=O and C=N); ¹H nmr τ 0.8 (broad, 1, NH), 6.95 (septet, 3, *J*_{HF} = 1.1 Hz, NCH₃), and 7.60 ppm (singlet, 3, CH₃CO); ¹⁹F nmr 68.4 (septet, 1, CF₃) and 73.4 ppm (septet, 1, CF₃).

Anal. Calcd for C₁₀H₇F₁₂N₃O: C, 29.1; H, 1.7; F, 55.2; N, 10.2. Found: C, 28.7; H, 2.0; F, 55.2; N, 10.5; mol wt, 413 (mass spectrum).

4-Acetylimino-3-methyl-2,2,5,5-tetrakis(trifluoromethyl)imidazolidine (27).—A mixture of 2.0 g (0.0054 mol) of **17** and 5 ml of acetyl chloride was heated at reflux for 30 hr, cooled, and poured over ice. The solid that formed was collected on a filter, washed with water, and recrystallized from alcohol-water. There was obtained 1.85 g (83%) of **27** as colorless crystals: mp 137–139°; ir 5.75 (C=O) and 6.00 μ (C=N); uv λ_{max}^{EIOH} 217 mμ (ε 8300); ¹H nmr (CD₃CN) τ 6.98 (septet, 3, *J*_{HF} = 1.0 Hz, CH₃N), 7.67 (singlet, 1, NH), and 7.83 ppm (singlet, 3, CH₃); ¹⁹F nmr 73.1 (septet, 1, *J*_{FF} = 4.2 Hz, CF₃) and 75.1 ppm (multiplet, 1, CF₃).

Anal. Calcd for C₁₀H₇F₁₂N₃O: C, 29.1; H, 1.7; F, 55.2; N, 10.2. Found: C, 29.4; H, 2.0; F, 54.9; N, 10.2.

4-Isocyanato-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (28) and Its Dimer.—A solution of 30 g (0.084 mol) of **1** in 100 ml of oxalyl chloride was stirred at 25° for 3 days and then distilled. There was obtained 26.05 g (81%) of the isocyanate as a colorless liquid, bp 67–67.5° (49 mm).

The isocyanate can also be prepared in ether solution and used as such or isolated by distillation.

A three-necked flask attached to the bottom of a spinning-band column was equipped with a magnetic stirrer, nitrogen inlet, and dropping funnel. The equipment was flame-dried and cooled and 15 ml of oxalyl chloride and 75 ml of anhydrous ether were introduced into the flask under positive nitrogen pressure. A solution of 30 g (0.084 mol) of **1** dissolved in 100 ml of ether was added over 30 min with vigorous stirring. After an additional 20 min, the mixture was distilled to give 25.7 g (80%) of product isocyanate, bp 78° (75 mm). The isocyanate reacts readily with moist air: ir 4.35 μ (NCO); ¹H nmr (neat) τ 6.4 ppm (broad, NH); ¹⁹F nmr 73.3 (septet, 1, *J*_{FF} = 5.0 Hz, CF₃) and 78.0 ppm (septet, 1, *J*_{FF} = 5.0 Hz, CF₃).

Anal. Calcd for C₈HF₁₂N₃O: C, 28.1; H, 0.3; N, 11.0. Found: C, 28.6; H, 0.8; N, 11.5.

The isocyanate dimerized spontaneously at 25° over a period of days. The solid dimer, mp 152–154° dec, no longer has a band for isocyanate in its infrared spectrum: ir 2.89 and 3.02 (NH), 5.51 (small ring C=O), 5.71 (C=O or C=N *exo* to small ring), and 5.95 μ (imidazoline C=N); uv λ_{max}^{CH₃CN} 228 mμ (ε 2700); ¹H nmr τ 2.35 (1, NH) and 2.90 ppm (1, NH); ¹⁹F nmr 70.3 (septet, 1, *J*_{FF} = 5.0 Hz, CF₃), 72.8 (multiplet, 1, CF₃), 73.3 (multiplet, 1, CF₃), and 75.0 ppm (septet, 1, *J*_{FF} = 5.0 Hz, CF₃). Pyrolysis to the original isocyanate occurs in high yield above 155°, so that the easily stored dimer can be used as a source of the reactive isocyanate.

Anal. Calcd for (C₈HF₁₂N₃O)₂: C, 28.1; H, 0.3; F, 59.5; N, 11.0. Found: C, 25.1; H, 0.5; F, 59.5; N, 11.0.

4-Isocyanato-2,2,5,5-tetrakis(chlorodifluoromethyl)-3-imidazoline (30) and Its Dimer.—A solution of 5.0 g (0.012 mol) of 4-amino-2,2,5,5-tetrakis(chlorodifluoromethyl)-3-imidazoline in 20 ml of ether was added dropwise over 30 min to a stirred mixture of 3 ml of oxalyl chloride and 10 ml of ether. The reaction mixture was stirred for 20 min and distilled to give 3.4 g (63%) of **30**: bp 78° (1.5 mm); ir 4.34 μ (NCO); ¹H nmr (CCl₄) τ 5.96 ppm (NH); ¹⁹F nmr complex multiplets at 53.0 (1), 53.6 (1), 58.1 (1), and 58.7 ppm (1).

Anal. Calcd for C₈HCl₄F₈N₃O: C, 21.9; H, 0.2. Found: C, 21.8; H, 0.7.

The isocyanate solidified on standing for several days. The isocyanate was regenerated when the solid was heated above its apparent melting point, 120–140°: ir isocyanate bands typical of dimer and no isocyanate; uv λ_{max}^{CH₃CN} 233 mμ (ε 9800); ¹H nmr τ 2.90 (1, NH) and 3.15 ppm (1, NH).

Anal. Calcd for (C₈HCl₄F₈N₃O)₂: C, 21.9; H, 0.2; F, 33.9; N, 9.4. Found: C, 21.9; H, 0.6; F, 33.9; N, 9.2.

4-Benzylideneamino-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (32a).—A 30-g sample (0.078 mol) of the 4-isocyanato derivative was heated at reflux for 0.5 hr under a nitrogen atmosphere with 50 g of benzaldehyde. Distillation gave 28 g (80%) of **32a**: bp 91° (1.0 mm); uv λ_{max}^{CH₃CN} 235 mμ (sh, ε 5250), 245 (4600), 273 (600), and 280 (600); ¹H nmr τ 3.60 (1, NH) and ca. 3.0 ppm (multiplet, 5, aromatic CH); ¹⁹F nmr 72.7 (multiplet, 1, CF₃) and 77.9 ppm (multiplet, 1, CF₃). This compound is very easily hydrolyzed to a mixture of **1** and benzaldehyde.

Anal. Calcd for C₁₄H₇F₁₂N₃: C, 37.8; H, 1.6; F, 51.2; N, 9.4. Found: C, 36.9; H, 1.6; F, 51.5; N, 9.3.

4-(N,N-Diisopropylureido)-2,2,5,5-tetrakis(trifluoromethyl)-3-imidazoline (29e) and Its Diisopropylammonium Salt.—A 1.9-g sample (0.005 mol) of the isocyanate was added in one portion at room temperature to 7.5 g (large excess) of diisopropylamine dissolved in 100 ml of ether. After an exothermic reaction occurred, the ether and excess amine were evaporated, giving 2.6 g (84%) of the diisopropylammonium salt: mp 76–81° dec; ¹H nmr τ 3.30 (singlet, 2, NH₂⁺), 4.4 (1, NH), 5.8 (broad, 2, CH), 6.76 (septet, 2, *J*_{HH} = 13.0 Hz, CH), 8.78 [doublet, 12, *J*_{HH} = 14.5 Hz, CH(CH₃)₂], and 8.82 ppm [septet, 12, *J*_{HH} = 13.0 Hz, CH(CH₃)₂]; ¹⁹F nmr 71.8 (septet, 1, *J*_{FF} = 4.0 Hz, CF₃) and 76.7 ppm (septet, 1, *J*_{FF} = 4.0 Hz, CF₃). The salt was not stable to storage.

Anal. Calcd for C₂₀H₃₁F₁₂N₅O: C, 41.0; H, 5.3; F, 38.9; N, 12.0. Found: C, 40.6; H, 5.2; F, 41.7; N, 11.8.

Acidification of a sample of the above salt with 3 *N* hydrochloric acid-ice gave **29e** a white solid which was isolated by ether extraction: mp 123–126°; uv λ_{max}^{EIOH} 250 mμ (ε 8400) and 226 (10,900); ¹H nmr τ 0.3 (broad, 1, NH), 3.3 (broad, 1, NH), 5.77 (septet, 2, *J*_{HH} = 14.0 Hz, CH), and 8.73 ppm [doublet, 12, *J*_{HH} = 14.0 Hz, CH(CH₃)₂]; ¹⁹F nmr 72.7 (septet, 1, CF₃) and 77.8 ppm (septet, 1, CF₃).

Anal. Calcd for C₁₄H₁₆F₁₂N₄O: C, 34.7; H, 3.3; F, 47.1; N, 11.6. Found: C, 34.6; H, 3.4; F, 47.2; N, 11.6.

Registry No.—**2**, 23757-54-2; **3**, 14373-01-4; **6a**, 14373-02-5; **6b**, 14372-99-7; **6c**, 14373-00-3; **6d**, 23757-59-7; **7**, 23757-60-0; **8**, 23757-51-9; **9**, 23757-62-2; **10**, 23757-63-3; **10** tetramethylammonium salt, 12408-04-7; **11**, 23757-64-4; **11** tetraethylammonium salt, 12408-05-8; **12**, 23829-38-1; **14**, 23757-65-5; **15**, 23757-66-6; **21**, 14373-03-6; **22**, 14373-04-7; **23**, 14373-05-8; **23** hydrochloride, 14704-55-3; **23** methiodide, 23757-70-2; **24**, 14373-10-5; **25**, 14373-12-7; **26**, 23757-73-5; **27**, 14373-14-9; **28**, 14491-96-4; **29a**, 23757-76-8; **29b**, 23757-77-9; **29c**, 23753-55-1; **29d**, 23757-78-0; **29e**, 23757-79-1; **29e** diisopropylammonium salt, 23829-40-5; **30**, 23757-80-4; **32a**, 23757-81-5; **32b**, 23757-82-6; **32c**, 23757-83-7; **32d**, 23757-84-8; **32e**, 23757-85-9; **25** tetramethylammonium salt, 12408-06-9.