(5 H, m), 3.9 (3 H, s), 3.7 (3 H, s), 3.5–3.1 (4 H, m), 2.7–2.35 (4 H, m), 2.3 (3 H, s); IR (neat) 2900 (s), 2750 (s), 1580 (s), 1545 (m), 1475 (s), 1450 (s), 1400 (s), 1375 (s), 1330 (w), 1310 (m), 1280 (s) cm^{-1}; mass spectrum, m/e 363 (M^+). Anal. Calcd for $C_{19}H_{22}ClNO_2S \cdot 0.25H_2O$: C, 56.37; H, 5.85; N, 3.46,; Cl, 17.51. Found: C, 56.40: H, 5.89; N, 3.62; Cl, 17.55.

Method B. The reaction was carried out as described in method A by using 50 mg (0.000 15 mol) of **12** in 3 mL of methylene chloride and 0.05 mL (0.000 67 mol) of sulfuryl chloride in 2 mL of methylene chloride. The identity of the crude product was established as **14** by TLC and mass spectral analyses.

6-Chloro-2,3,4,5-tetrahydro-7,8-dihydroxy-3-methyl-9-(phenylthio)-1*H*-3-benzazepine (6). To a solution of the dimethoxy compound **14** (3 g., 8.3 mmol) in 120 mL of methanesulfonic acid was added 6.9 g (0.046 mol) of L-methionine. The reaction mixture was stirred for 48 h at room temperature, poured into ice–water, and adjusted to pH 7.6 by gradual addition of concentrated ammonium hydroxide. The resulting solid was collected. Methionine was selectively removed from the product by dissolving the bulk of the material in ethanol. The filtrate was concentrated and then partitioned between ethyl acetate and aqueous ammonium hydroxide (pH 9). The aqueous layer was exhaustively extracted with ethyl acetate, and the combined organic extracts were dried with anhydrous sodium sulfate and then concentrated. The resulting solid was treated with decolorizing carbon and recrystallized from Me_2SO to give 0.89 g (32%) of crystals: mp 174–176 °C; NMR (TFA) δ 7.3–6.9 (5 H, m), 4.0–3.1 (8 H, m), 2.8 (3 H, s); IR (Nujol) 3300 (w), 2800 (s), 1560 (m), 1440 (s), 1360 (m), cm^{-1}; mass spectrum, m/e 335 (M^+). Anal. Calcd for $C_{17}H_{18}ClNO_2S \cdot 0.75H_2O$: C, 58.45; H, 5.62; N, 4.01; Cl, 10.15. Found: C, 58.22; H, 5.51; N, 3.94; Cl, 9.95.

6-Chloro-9-[(4-chlorophenyl)thio]-2,3,4,5-tetrahydro-7,8-dimethoxy-3-methyl-1*H*-3-benzazepine (17) and 6-Chloro-9-[(2,4-dichlorophenyl)thio]-2,3,4,5-tetrahydro-7,8-dimethoxy-3-methyl-1*H*-3-benzazepine (18). The reaction was carried out as described prevously by using 90 g (0.261 mol) of **13** in 800 mL of methylene chloride and 86 mL (1.18 mol) of thionyl chloride in methylene chloride. The reaction mixture was worked up after 3 days at room temperature to give the di- and trichlorinated compounds **17** and **18** in yields of 50.8% and 26.3%, respectively, as determined by GC/MS. After a number of unsuccessful column chromatographies (open, wet column, medium-pressure JY column), **17** and **18** were separated by preparative HPLC (two Prepak silica columns, eluting with 3% methanol in methylene chloride) in yields of 2% and 4%, respectively. The dichlorinated compound **17** was converted to a crystalline HCl salt: mp 221–223 °C dec; NMR (Free base, $CDCl_3$) δ 7.2–6.8 (4 H, q), 3.85 (3 H, s), 3.75 (3 H, s)8 3.40–3.25 (4 H, m), 2.6–2.35 (4 H, m), 2.3 (3 H, s); IR (neat) 2800 (s), 2700 (s), 1520 (m), 1450 (s), 1430 (s), 1390 (s), 1350 (s), 1310 (m), 1200 (m), 1275 (s) cm^{-1}; mass spectrum, m/e 397 (M^+). Anal. Calcd for $C_{19}H_{21}Cl_2NO_2S \cdot HCl$: C, 52.48; H, 5.10; N, 3.22; Cl, 24.46. Found: C, 52.45; H, 5.14; N, 3.37; Cl, 24.31. The trichlorinated compound **18** was recrystallized from ethyl acetate: mp 126.5–129 °C; NMR ($CDCl_3$) δ 7.5–6.5 (3 H, m), 4.0 (3 H, s), 3.9 (3 H, s), 3.45–3.25 (4 H, m), 2.8–2.4 (4 H, m), 2.3 (3 H, s); IR (Nujol) 2900 (s), 1540 (w), 1450 (s), 1400 (m), 1360 (2), 1300 (w), 1280 (m) cm^{-1}; mass spectrum, m/e 431 (M^+). Anal. Calcd for $C_{19}H_{20}Cl_3NO_2S$: C, 52.78; H, 4.79; N, 3.14; Cl, 23.85. Found: C, 53.19; H, 4.67; N, 3.25; Cl, 23.86.

6-Chloro-9-[(4-chlorophenyl)thio]-2,3,4,5-tetrahydro-7,8-dihydroxy-3-methyl-1*H*-3-benzazepine (19). The starting dimethoxy compound **17** (1.4 g, 0.0035 mol) was dissolved in 60 mL of methansulfonic acid; L-methionine (2.63 g, 0.0176 mol) was then added all at once. The reaction was stirred at room temperature for 24 h, poured into ice–water and then adjusted to pH 8 with concentrated ammonium hydroxide. The product was extracted into ethyl acetate, and the organic extract was then dried with anhydrous sodium sulfate and concentrated. The crude solid was recrystallized from ethyl acetate to give 440 mg (34%) of product: mp 204 °C dec; NMR (Me_2SO-d_6) δ 7.4–6.9 (4 H, q) 3.4–2.9 (4 H, m), 2.7–2.4 (4 H, m), 2.3 (3 H, s); IR (Nujol) 3200 (w), 2800 (s), 1430 (s), 1345 (s), 1320 (m), 1250 (s), cm^{-1}; mass spectrum, m/e 369 (M^+). Anal. Calcd for $C_{17}H_{17}Cl_2NO_2S$: C, 55.14; H, 4.63; N, 3.78. Found: C, 54.74; H, 4.85; N, 3.58.

6-Chloro-9-[(2,4-dichlorophenyl)thio]-2,3,4,5-tetrahydro-7,8-dihydroxy-3-methyl-1*H*-3-benzazepine (20). The reaction was carried out as described previously by using 1.63 g (3.78 mmol) of **18**, 2.82 g (0.0189 mol) of L-methionine, and 80 mL of methanesulfonic acid. After the usual workup, the crude solid was recrystallized from ethyl acetate to give 710 mg (46%) of product: mp 202–203 °C dec; NMR (Me_2SO-d_6) δ 7.5–6.4 (3 H, m), 3.3–2.9 (4 H, m), 2.7–2.4 (4 H, m), 2.3 (3 H, s); IR (Nujol) 3200 (w), 2850 (s), 1440 (s), 1350 (m), 1330 (w), 1250 (m), cm^{-1}; mass spectrum, m/e 403 (M^+). Anal. Calcd for $C_{17}H_{16}Cl_3NO_2S$: C, 50.45; H, 3.98; N, 3.46. Found: C, 50.55; H, 4.27; N, 3.32.

Acknowledgment. We are grateful to David Staiger and Gary Zuber for some NMR spectra, Gerald Roberts for mass spectra, Edith Reich, Gail Johnson, and Suzanne Jancski for combustion analyses, and Karl Erhard for his assistance in the HPLC work.

Registry No. 6, 73943-05-2; **7**, 37462-47-8; **8**, 73943-26-7; **9**, 73943-27-8; **10**, 73954-41-3; **11**, 73943-23-4; **12**, 73942-96-8; **13**, 73943-28-9; **14**, 82614-92-4; **17**, 82614-93-5; **18**, 82614-94-6; **19**, 82614-95-7; **20**, 82614-96-8.

Synthesis and Ring-Opening Reactions of Functionalized Spiro-Δ^3-1,2,3-thiadiazoline 1-Oxides and 1,1-Dioxides. A New Approach to Unsymmetrically Disubstituted α-Chloro Azines

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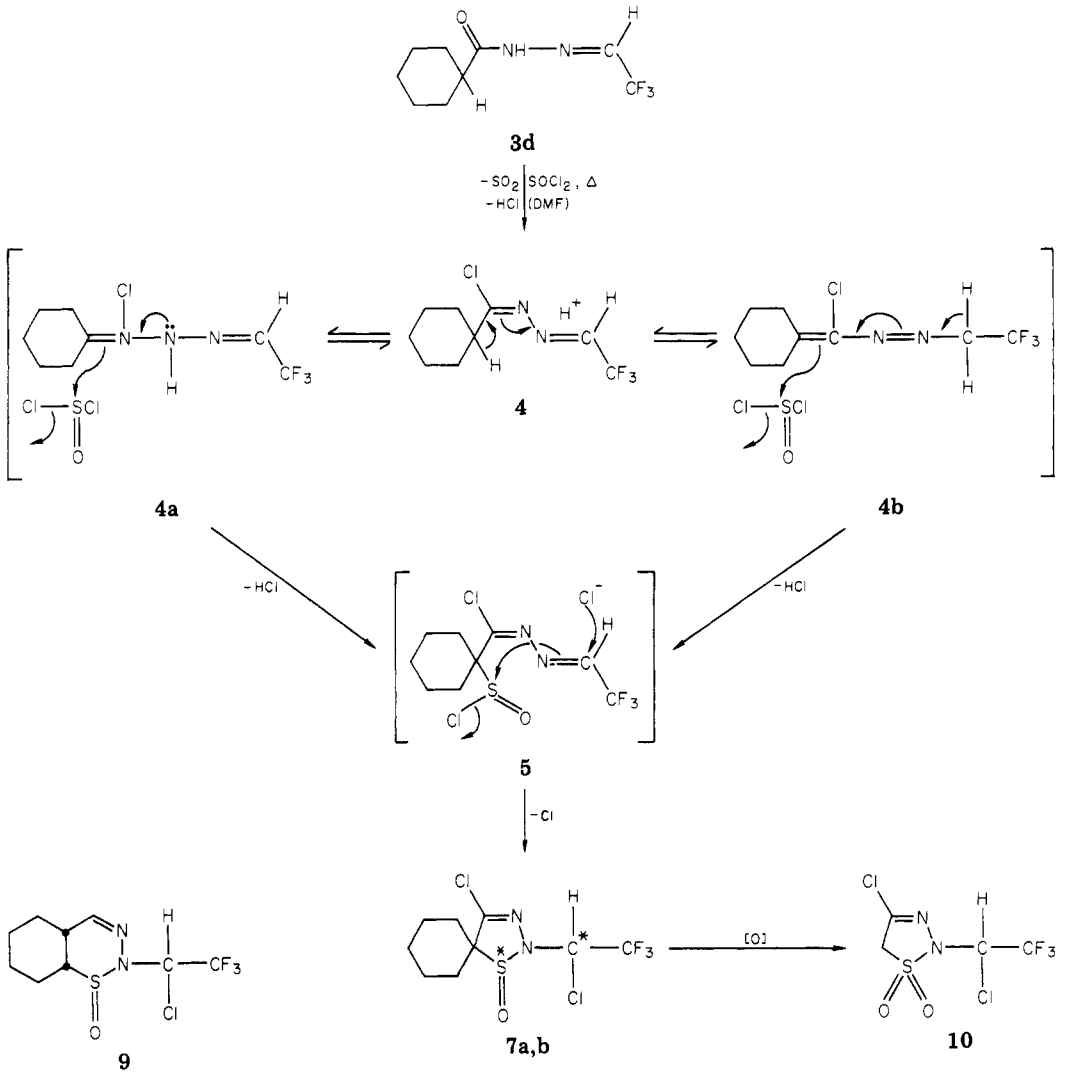
A general procedure for the synthesis of functionalized spiro-Δ^3-1,2,3-thiadiazoline 1-oxides from previously unreported (perfluoroalkylidene)hydrazides derived from cycloalkanecarboxylic acids (**3**) is described. Reaction of **3** with thionyl chloride in the presence of dimethylformamide gives diastereoisomeric pairs of 4-chloro-2-(1-chloroperfluoroalkyl)-spiro-Δ^3-1,2,3-thiadiazoline 1-oxides **6**, **7**, and **8**. Cleavage of **7** lead to 4-chloro-1-thia-2,3-diazaspiro[4.5]dec-3-ene 1-oxide (**14**). Peracid oxidation of **7** gave the corresponding 1,1-dioxide **10**. Both nucleophilic and thermal reactivity of **10** have been investigated. Reaction of **10** with nucleophilic reagents afforded products resulting from initial dehydrochlorination and ring opening to *N*-[(1-cyanocyclohexyl)sulfonyl]trifluoroacetimidoyl chloride (**15**). Thermolysis of **10**, at 110 °C, resulted in dissociation (–SO_2, –HCl) to give *N'*-[(2,2,2–trifluoroethylidene)amino]-1-cyclohexenecarboximidoyl chloride (**20**). Some reactions of **20** are also described.

Perfluorinated aliphatic aldehyde aroylhydrazones react with thionyl chloride in the presence of dimethylformamide at reflux to give 1-aryl-1-chloro-4-(perfluoroalkyl) azines.[1] Surprisingly, we find that the acylated hydrazine,

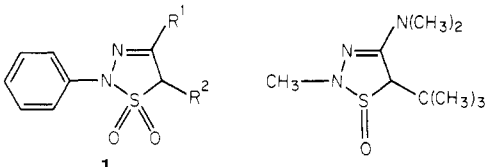
0022-3263/82/1947-3865$01.25/0

Scheme I



3d, derived from cyclohexanecarboxylic acid reacts with thionyl chloride uner similar conditions to give diastereoisomeric spiro-heterocyclic compounds, **7a** and **7b**. The desired chloro azine, **4**, was not obtained (Scheme I).

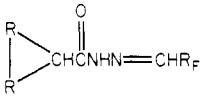
The only known representatives of the Δ^3-1,2,3-thiadiazoline ring system, of which **7a** and **7b** are members, are the *S*,*S*-dioxides,[2] **1**, and the *S*-oxide,[3] **2**. Compounds **1**



1 **2**

were obtained by cyclization of the phenylhydrazones of the salts of β-keto sulfonic acids with the aid of phosphorus pentachloride.[2a,4] Addition of thionyl chloride across the triple bond of 4,4,*N*,*N*-tetramethyl-1-butyn-1-amine followed by treatment with methylhydrazine gave **2**.

Table I. Cycloalkanecarboxylic Acid (Perhaloalkylidene)hydrazides (3)[a]



compd[b]	R-R	R_F	% yield	mp, °C
3a	$(CH_2)_2$	CF_3	64	179-180
3b	$(CH_2)_4$	CF_3	76	147-150
3c	$(CH_2)_5$	CCl_3	97	178-180
3d	$(CH_2)_5$	CF_3	82	154-156
3e	$(CH_2)_5$	C_2F_5	82	134-137
3f	$(CH_2)_5$	n-C_3F_7	83	108-110

[a] Mixtures of geometric isomers (syn and anti). [b] C, H, and N elemental analyses were done for all entries and agreed to ±0.2% of the theoretical values.

Results and Discussion

A solution containing cyclohexanecarboxylic acid (2,2,2-trifluoroethylidene)hydrazide (**3d**), consisting of a mixture of geometric, syn and anti isomers, was refluxed at 82 °C for several hours without noticeable change [by thin-layer chromatography (TLC)]. However, when heating was continued in the presence of catalytic amounts of dimethylformamide (DMF), TLC of the reaction mixture indicated rapid disappearance of **3d**. The reaction

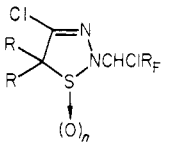
(1) K. H. Pilgram, and R. D. Skiles, *J. Org. Chem.*, **41**, 3392 (1976). K. H. Pilgram, L. E. Wittsell, R. D. Skiles, A. L. James, and J. W. Dawson, *J. Agric. Food Chem.*, **25**, 888 (1977).

(2) (a) P. Mazak and J. Suszko, *Bull. Int. Acad. Pol. Sci.*, 131 (1929); *Chem. Zentralbl.*, 1918 (1929)II. A. P. Terentyev and M. N. Preobrazhenskaya, *J. Gen. Chem., USSR*, **26**, 3468 (1956); *Engl. Transl.*, 3859; *Chem. Abstr.*, **51**, 9633b (1958).

(3) R. Buyle and H. G. Viehe, *Tetrahedron*, **24**, 3987 (1968); *Chem. Abstr.*, **68**, 114025w (1968).

(4) A. P. Terentyev and L. A. Yamovskaya, *J. Gen. Chem. USSR*, **23**, 643 (1953); *Chem. Abstr.*, **49**, 4641 (1955).

Table II. Spiro Compounds



compd[e]	R–R	R_F	n	R_f value	% yield	mp, °C
6	$(CH_2)_4$	CF_3	1	0.34[a]	0.8[b]	114–117
7a	$(CH_2)_5$	CF_3	1	0.37[a]	18	100–102
7b	$(CH_2)_5$	CF_3	1	0.33[a]	32	119–121
8a	$(CH_2)_5$	C_2F_5	1	0.21[c]	5.5	92–94[d]
8b	$(CH_2)_5$	C_2F_5	1	0.15[c]	35	92–95[d]
10	$(CH_2)_5$	CF_3	2	0.53[a]	65	83–85

[a] Solvent (by volume): hexane (80), ethyl acetate (16), tetrahydrofuran (4). [b] Only one isomer was isolated. [c] Solvent (by volume): hexane (90), ether (10). [d] A mixed melting point was depressed: 66–74 °C. [e] C, H, and N elemental analyses were done for all entries and agreed to ±0.2% of the theoretical value.

product consisted of diastereoisomeric 4-chloro-2-(1-chloro-2,2,2-trifluoroethyl)-1-thia-2,3-diazaspiro[4.5]dec-3-ene 1-oxides, **7a** and **7b**, separated by silica chromatography.

The reaction is applicable to a variety of acylated perfluorinated aliphatic aldehyde hydrazones derived from cyclopentane-, e.g., **3b**, and cyclohexanecarboxylic acids, e.g., **3e** and **3f** (Tables I and II). Cyclopropanecarboxylic acid (2,2,2-trifluoroethylidene)hydrazide (**3a**) and cyclohexanecarboxylic acid (2,2,2-trichloroethylidene)hydrazide (**3c**) failed to undergo similar reaction in refluxing thionyl chloride containing catalytic amounts of DMF.

Elemental analysis and mass spectrometry showed that **7a** and **7b** contained one sulfur, two chlorine, and two nitrogen atoms. Their ^{13}C NMR spectra, which are strikingly similar, indicated that five Csp^2 and one spiro carbon atom were present, thus eliminating the fused bicyclic structure **9** from further consideration.

Various combinations of steps can lead to products. We prospose that **7a** and **7b** form from **3d** by the mechanism shown in Scheme I. The first step in the proposed sequence is the reaction of **3d** with thionyl chloride to give α-chloro azine **4**. This reaction, which is catalyzed by DMF, appears to be general for a variety of aroylated aldehyde hydrazones derived from perfluorinated aldehydes.[1] The presence in **4** of an α-hydrogen atomallows for interconvertible isomeric structures such as enhydrazone **4a** and enazo **4b** tautomers[5] which can undergo acylation at the β-carbon (ring) atom followed by ring closure of intermediate **5** as indicated in Scheme I.

We considered alternate pathways such as loss of HCl from **4** followed by addition of $SOCl_2$ to the resulting elongated keteneiminic species and subsequent ring closure. Additionally, $SOCl_2$ could add across the azomethine double bond, —N=CH—, of **4** followed by ring closure involving electrophilic substitution. Since we never observed addition of $SOCl_2$ to conjugated azomethine double bonds[6] in our previous work with 1-aryl-1-chloro azines,[1] such a pathway appears unlikely.

In order to elucidate some of the details of the conversion of cycloalkanecarboxylic acid (perfluoroalkylidene)-hydrazides into spiro compounds, by thionyl chloride, we carried out a limited number of chemical transformations.

Oxidation with *m*-chloroperbenzoic acid of **7a** and **7b**, both independently and in admixture, followed by silica chromatography of the reaction mixture gave the identical *S,S*-dioxide, **10**, having a largely increased R_F value. The *S,S*-dioxide structure is supported by the characteristic absorption in the infrared at 1350 and 1140 cm^{-1} (SO_2) and by its mass spectrum, which shows a strong molecular ion at m/z 338 (M^+). This result agrees with the sulfur atom as being one of the asymmetric centers and agrees with the structural assignments of **7a** and **7b**.

Further structural information about the second asymmetric center was revealed when it was found (by NMR and TLC) that in dimethyl sulfoxide (Me_2SO) solution on prolonged standing at room temperature, **7a** (R_F 0.37) isomerized readily to **7b** (R_f 0.33), whereas the reverse reaction was not observed. Moreover, **7a** lost the side chain, $CHClCF_3$, more readily at room temperature in Me_2SO, whereas **7b** underwent this cleavage much more slowly to give the same cyclic spiro sulfinamide, **14**, having a largely reduced R_f value.

The conversion of both **7a** and **7b** to **14** most likely involves Me_2SO oxidation of iminium ion **11** to **12**, Me_2SO itself getting reduced to dimethyl sulfide; facile hydrolysis of **12** would give **14**. A much more sluggish reaction resulted in the absence of Me_2SO. For example, when **7a,b** was absorbed on silica gel (saturated to capacity with H_2O), conversion to **14** was complete after about 60 days. It is suggested that in this reaction, the presumed intermediate, **11**, is first converted into labile hemi-aminal **13**, followed by dissociation to **14** and trifluoroacetaldehyde (Scheme II).

The chlorine atoms in **10** are predictably susceptible to nucleophilic attack. A brief study of the reaction of a variety of nucleophilic reagents with **10** was, therefore, a logical extension of this work.

Treatment of **10** with excess dimethylamine proceeded exothermically in tetrahydrofuran to give *N'*-[(1-cyanocyclohexyl)sulfonyl]-2,2,2-trifluoro-*N,N*-dimethylethanimidamide (**16**). The infrared spectrum of **16** is characterized by the presence of a very weak band at 2240 cm^{-1} (C≡N).[7] The formation of **16** involves dehydrochlorination as indicated, leading to rupture of the N–N bond to give **15**. This step is accompanied by nucleophilic displacement of the now very reactive imidoyl chlorine atom by dimethylamine to give **16** (Scheme III).

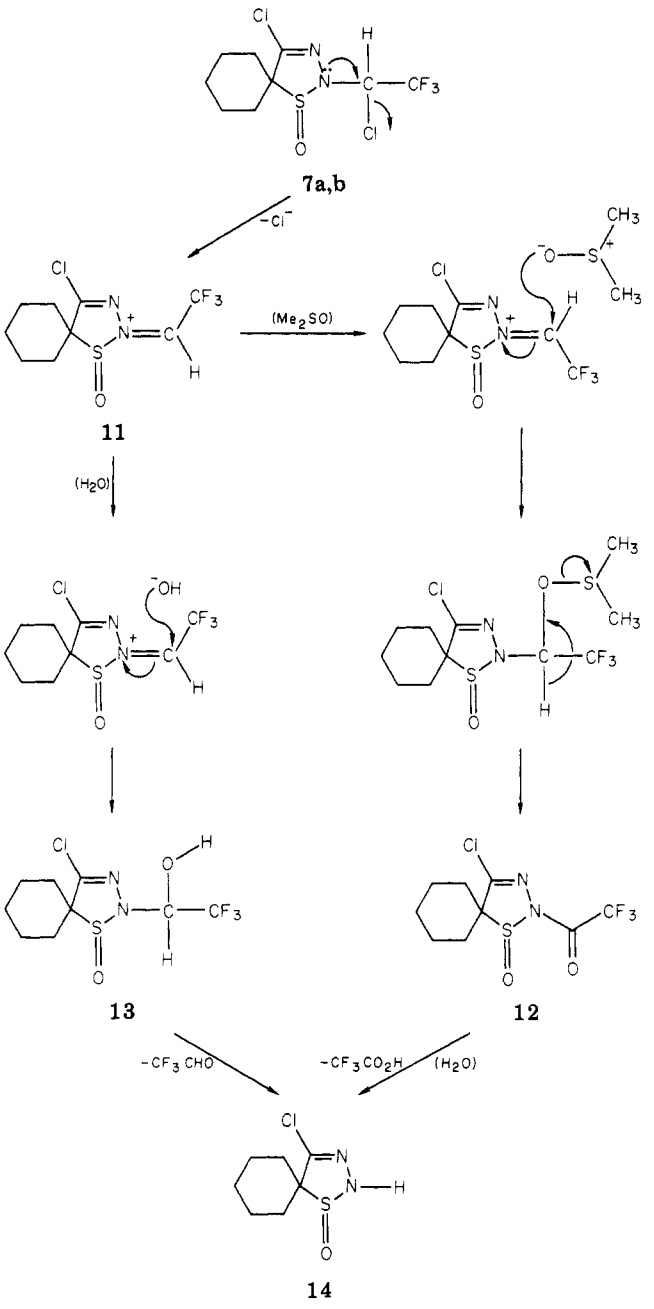
Reaction of **10** with sodium methyl mercaptide in tetrahydrofuran at room temperature (18 h) followed by treatment of the reaction product with diluted hydrochloric acid gave 1-cyanocyclohexanesulfonamide (**18**) in 47%

(5) The equilibrium between azines, $RCH_2CH{=}NN{=}CHCH_2R$, and the enazo form, $RCH{=}CHN{=}NCH_2CH_2R$, has been discussed: M. P. Grammaticakis, *Bull. Soc. Chim.* Fr., 973 (1948).

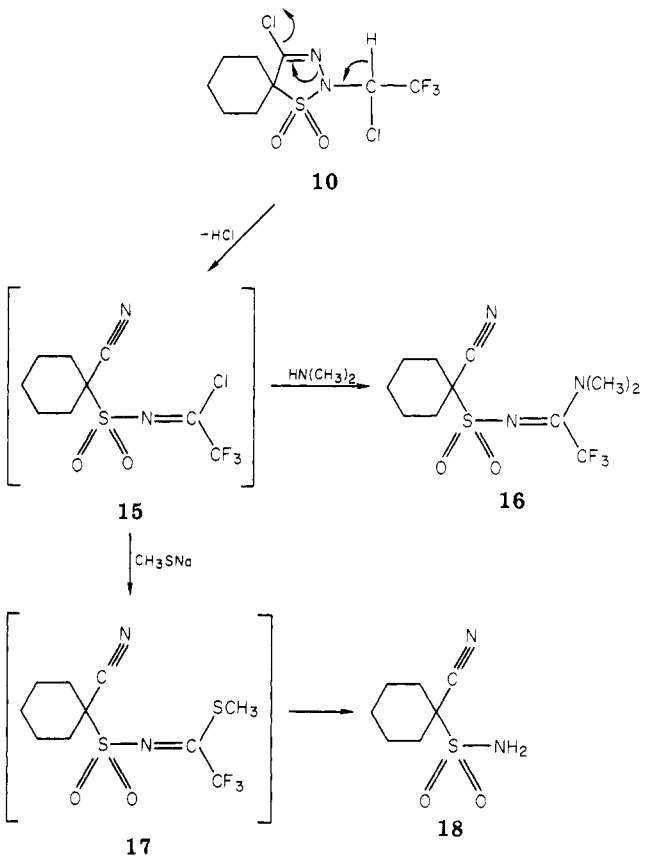
(6) Facile addition of thionyl chloride across polarized carbon–carbon double bonds has been reported: (a) A. J. Krubsack and T. Higa, *Tetrahedron Lett.*, 5149 (1968). (b) A. J. Krubsack, *ibid.*, 4515 (1973).

(7) Intensities of C≡N bonds may vary from strong to undetectable: L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", 2nd ed., Wiley, New York, 1958, Chapter 15(2)b, pp 265–266.

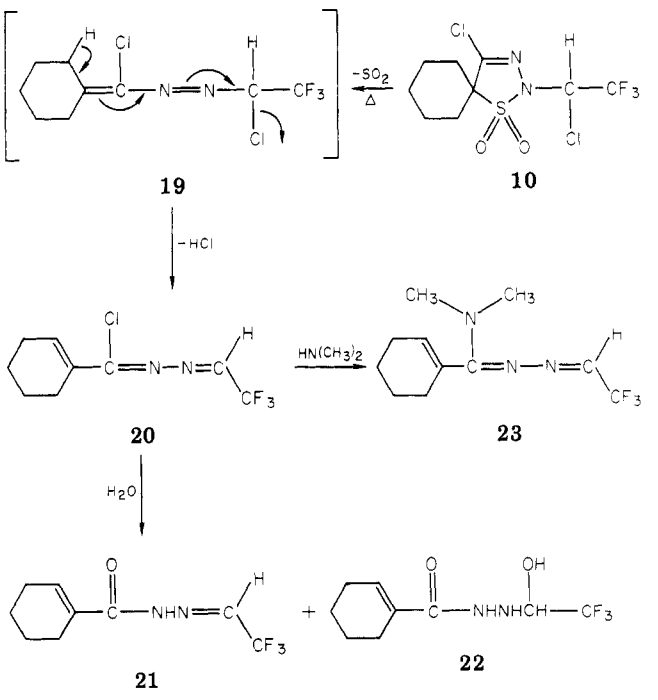
Scheme II



Scheme III



Scheme IV



yield. The formation of **18** most likely is preceded by the formation of thioimidate **17** (Scheme III). *N*-sulfonyl imidates are known to undergo ready hydrolysis under very mild acidic conditions.[8]

When **10** was treated with an equimolar amount of ethyldiisopropylamine (Hünig's base) in refluxing tetrahydrofuran (1 h), the reaction proceeded quite differently. Whereas the reaction with dimethylamine was exothermic at room temperature, reaction with Hünig's base was incomplete after 1 h in refluxing THF. Treatment of the reaction mixture with water followed by silica chromatography lead to the recovery of starting material, **10** (22%), in addition to the isolation in 11% yield of 1-cyclohexenecarboxylic acid 2-(2,2,2-trifluoroethylidene)-hydrazide (**21**; Scheme IV).

In order to elucidate some of the details of the conversion of **10** into **21**, the isolation of **20** was attempted. When heated in refluxing toluene (110 °C, 1 h), **10** underwent fragmentation to deliver **20**, a distillable mobile liquid, in 50–60% yield. Milder conditions, e.g., refluxing benzene (80 °C, 3 h), are not drastic enough to bring about fragmentation.

Reaction of **20** with water proceeded smoothly in tetrahydrofuran to give **21** (36%) in addition to small amounts of the corresponding "hydrazone hydrate" **22** (3%).

(8) K. H. Pilgram, R. D. Skiles, and J. W. Cornforth, German Patent 2227744; *Chem. Abstr.*, 78, 84027k (1973).

A peculiarity of **21** is its pronounced anionic character ($pK_a = \sim 2$) resulting from the influence on the NH group of the adjacent carbonyl and trifluoromethyl groups.

The suggested mechanism for the formation of **20** involves extrusion of sulfur dioxide from **10** to give the intermediate diazabutadiene **19**. Generation of a diene through thermal decomposition of the corresponding 2,5-dihydrothiophene 1,1-oxide (diene sulfone) is well-documented.[9] Observed dissociation temperatures range from 80 to 190 °C.[10] Alkyl substitution in the 2-position of the cyclic sulfone generally decreases the stability of the adduct. Subsequent loss from **19** of hydrogen chloride would lead to the reactive *N'*-[(2,2,2-trifluoroethylidene)-amino]-1-cyclohexenecarboximidoyl chloride (**20**).

Reaction with 2 molar equiv of dimethylamine of **20** proceeded smoothly in ether at 5 °C to give *N,N*-dimethyl-*N'*-[(2,2,2-trifluoroethylidene)amino]-1-cyclohexenecarboximidamide (**23**) in almost quantitative yield.

As would be expected from an α-chloro azine, **20** is easily attacked by nucleophilic reagents other than dimethylamine. Studies of the reaction of **20** and related chloro azines with bifunctional nucleophiles leading to five- and six-membered heterocyclic ring systems is in progress and will be subsequently reported.

Experimental Section

Melting and boiling points are uncorrected. ^{1}H NMR spectra were recorded at 60 MHz on a Varian EM-360 spectrometer with Me_4Si as an internal standard. ^{13}C NMR chemical shifts were determined on a Bruker WP-60 spectrometer operating at 15.08 MHz. Electron-impact mass spectra were determined at 70 eV on a Finnigan 3200 mass spectrometer by direct introduction via solid probe. Chemical ionization mass spectra were obtained at 70 eV on a Finnigan 4000 mass spectrometer. A Finnigan 6110 data system was used for data acquisition. The high-resolution mass spectrum of **16** was obtained on a Du Pont CEC 21-110 instrument; the sample was introduced via a probe inlet.

The experiments presented in this section are representative of those discussed in this paper.

Cyclopentanecarboxylic Acid (2,2,2-Trifluoroethylidene)hydrazide (3b). A solution of 48.6 g (0.38 mol) of cyclopentanecarboxylic acid hydrazide, mp 112–115 °C, and 80.0 g (0.69 mol) of trifluoroacetaldehyde hydrate in 500 mL of benzene was heated to reflux overnight (18 h). Water was removed azeotropically as formed. The reaction mixture was concentrated to a volume of 200 mL by rotary evaporation, diluted with 600 mL of hexane, and cooled to 5 °C. The product was filtered and dried to give 60 g (76%) of colorless **3b**: mp 147–150 °C; IR (KBr) 3200 (NH), 1680 cm^{-1} (C=O); NMR (Me_2SO-d_6) δ 1.65 (8, $(CH_2)_4$), 3.25 (1, CH=), 7.5 and 7.9 (1, CH=), 11.7 and 11.9 (1, NH).

Cyclohexanecarboxylic Acid (2,2,3,3,3-Pentafluoropropylidene)hydrazide (3e). To a solution of 47.3 g (0.333 mol) of cyclohexanecarboxylic acid hydrazide, mp 150–152 °C, in 250 mL of benzene of cyclohexanecarboxylic acid hydrazide, mp 150–152 °C, in 250 mL of benzene was added with stirring 80.0 g (0.444 mol) of pentafluoropropionaldehyde methyl hemiacetal followed by 20 mL of 14% hydrochloric acid. The mixture was stirred at 50 °C for 1 h and then heated to reflux overnight (18 h) while water was collected in a Dean–Stark tube. The reaction mixture was concentrated by rotary evaporation to a volume of 100 mL, diluted with 300 mL of hexane, and cooled. The product was filtered to give 74.0 g (82%) of colorless solid: mp 134–137 °C; IR (KBr) 3200 (NH), 1680 cm^{-1} (C=O); NMR (Me_2SO-d_6) δ 1.6 (10, $(CH_2)_5$), 2.8 (1, CH), 7.5 and 8.0 (1, CH=), 11.9 (1, NH).

4-Chloro-2-(1-chloro-2,2,2-trifluoroethyl)-1-thia-2,3-diazaspiro[4.5]dec-3-ene 1-Oxide (7a and 7b). A solution containing 51.9 g (0.234 mol) of **3d** in 110 mL of thionyl chloride was refluxed (82 °C) and stirred for 2.5 h without noticeable change (by TLC). Ten drops of dimethylformamide were added, and heating was continued for 2.5 h. At this point, all of the starting material had reacted, and two new spots on the thin-layer plate indicated the formation of two new compounds. The excess thionyl chloride was removed by rotary evaporation, leaving 71 g of residual solid. Recrystallization from hexane, with charcoal decolorization, gave 48 g (64%) of colorless solid, **7a** and **7b** (mixture of isomers), mp 96–101 °C. A 10-g sample was purified by silica chromatography.[7] The first fraction to emerge from the column consisted of 2.75 g (18%) of **7a**: mp 100–102 °C; ^{1}H NMR ($CDCl_3$) δ 1.6 (m, 10, $(CH_2)_5$) and 6.15 (q, 1, CH) (J = 5.2 Hz); ^{13}C NMR ($CDCl_3$) 82.6 (C_1), 23.6 (C_2), 24.2 (C_3), 24.2 (C_4), 24.6 (C_5), 27.0 (C_6), 151.7 (=CCl), 72.0 (J_F = 38.7 Hz, CHCl), 121.3 ppm (J_F = 281.6 Hz, CF_3); electron-impact mass spectrum, m/z 322 (M^+), 287 (M^+ – Cl), 274 (M^+ – SO), 239 (M^+ – SO, Cl), 203 (M^+ – SO, Cl, HCl), 108 ($C_6H_{10}CN^+$, base peak), 69 (CF_3^+), 36 (HCl^+); IR (KBr) no apparent NH, OH, CH=, 1600 (C=), 1110 cm^{-1} (S=O).

The second fraction consisted of 5.5 g (32%) of **7b** (lower R_f value): mp 119–121 °C (mmp with **7a**, 95–101 °C); ^{1}H NMR ($CDCl_3$) δ 1.6 (m, 10, $(CH_2)_5$) and 6.06 (q, 1, CH) (J = 5.0 Hz); ^{13}C NMR ($CDCl_3$) δ 82.7 (C_1), 23.6 (C_2), 24.25 (C_3), 24.5 (C_4), 24.6 (C_5), 27.0 (C_6), 152.4 (=CCl), 70.7 (J_F = 38.6 Hz, CHCl), 121.2 ppm (J_F = 281.7 Hz, CF_3). The IR and mass spectra of **7b** were very similar to those of **7a** (above).

In a second experiment, **7a** and **7b** were obtained in 4.5% and 42% yield, respectively.

4-Chloro-2-(1-chloro-2,2,2-trifluoroethyl)-1-thia-2,3-diazaspiro[4.5]dec-3-ene 1,1-Dioxide (10). To a stirred solution containing 14.0 g (0.0435 mol) of **7a** and **7b** (mixture of isomers) in 100 mL of chloroform was added dropwise within 10 min a solution of 8.8 g (0.0435 mol) of 85% *m*-chloroperbenzoic acid in 100 mL of chloroform. At room temperature (1 h) and at 40 °C (1 h), no observable change was noticed (by TLC). The clear solution was heated at 65–70 °C (1 h), left standing at ambient temperature overnight, extracted with 5% aqueous sodium carbonate, washed with water, dried ($MgSO_4$), and concentrated to give 14 g of amber syrup. Purification by silica chromatography gave 9.5 g (65%) of pink oil that crystallized from hexane to colorless crystals: mp 83–85 °C; IR (CH_2Cl_2) 1350, 1140 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 1.8 (m, 10, $(CH_2)_5$), 5.9 (q, 1, CH); mass spectrum, m/z 338 (M^+), 303 (M^+ – Cl), 274 (M^+ – SO_2).

Anal. Calcd for $C_9H_{11}Cl_2F_3N_2O_2S$: C, 31.9; H, 3.2; N, 8.3. Found: C, 31.8; H, 3.3; N, 8.3.

4-Chloro-1-thia-2,3-diazaspiro[4.5]dec-3-ene 1-Oxide (14). a. On Silica Gel. Twenty-four grams (0.073 mol) of **7a** and **7b** (mixture of isomers) was dissolved in ether and absorbed on 300 g of silica gel (no. 62). The solvent was allowed to evaporate, and the silica was left standing for 2 months exposed to the atmosphere. Chromatography over silica of the above silica[6b] gave 11.0 g (73%) of a syrup that crystallized from ether–hexane (1:5) to give colorless crystalline solid: mp 67–69 °C; IR (KBr) 3240 (NH), 1090 cm^{-1} (S=O); NMR ($CDCl_3$) δ 1.7 (m, 10, $(CH_2)_5$), 8.05 (1, NH); in the electron-impact mass spectrum, the molecular ion is not observed; chemical-ionization mass spectrum, m/z 207 ($M + H)^+$.

Anal. Calcd for $C_7H_{11}ClN_2OS$: C, 40.7; H, 5.3; N, 13.6. Found: C, 40.2; H, 5.3; N, 13.3.

b. In Me_2SO. A solution containing 16.1 g (0.05 mol) of **7a** and **7b** in 50 mL of Me_2SO was left standing at ambient temperature. After 3 days, the mixture was diluted with 200 mL of water and extracted with methylene chloride (3 × 200 mL). The combined extracts were washed with water (2 × 300 mL), dried ($MgSo_4$), filtered, and concentrated. The residual light yellow syrup (17.3 g) was purified by silica chromatography to give 4.8 g (46%) of **14**, identical (by elemental analysis (C, H, N, Cl, S), R_f value, and NMR, IR, and mass spectrum) with the product obtained by method a above.

***N'*-[(1-Cyanocyclohexyl)sulfonyl]-2,2,2-trifluoro-*N,N*-dimethylethanimidamide (16).** To a solution of 7.0 g (0.021 mol) of **10** in 50 mL of tetrahydrofuran was added 2.8 g (0.063 mol) of dimethylamine (anhydrous). The solution was placed in a glass cylinder, sealed, and heated on a steam bath (10 min). The cooled reaction mixture was poured into water and filtered. Purification of the filter cake (3.0 g) by silica chromatography

(9) S. D. Turk and R. L. Cobb in "Organic Reactions", J. Hamer, Ed., Academic Press, New York, 1967, Vol. 8, Chapter 2.

(10) The observed dissociation temperature of 2,5-dihydro-3,4-phenylthiophene 1,1-dioxide is 188–190 °C: C. C. Holt and H. J. Backer, *Recl. Trav. Chim. Pays-Bas* **55**, 898 (1936).

Table III. High-Resolution Mass Spectral Data for 16

nominal m/z	exact mass	suggested empirical formula	calcd exact mass	error in mmu
311	311.09225	$C_{11}H_{16}F_3N_3SO_2$	311.09152	0.73
203	203.01141	$C_4H_6F_3N_2SO_2$	203.01019	1.22
187	187.01661	$C_4H_6F_3N_2SO$	187.01528	1.33
139	139.04993	$C_4H_6F_3N_2$	139.04829	1.64
125	125.03422	$C_3H_4F_3N_2$	125.03264	1.58
110	110.02277	$C_3H_3F_3N$	110.02174	1.03

gave 1.0 g (15%) of tan solid: mp 115–117 °C (from ether); IR (KBr) no apparent NH, 2240 (weak, C≡N),[7] 1620 cm^{-1} (C=N and/or CF_3, very intense); NMR ($CDCl_3$) δ 1.4–2.7 (m, 10, $(CH_2)_5$), 3.3 (s, 6, $(CH_3)_2N$); EIMS, m/z 311 (M^+).

Anal. Calcd for $C_{11}H_{16}F_3N_3SO_2$: C, 42.4; H, 5.1; N, 13.5; S, 10.3. Found: C 42.5; H, 5.1; N, 13.1; S, 10.2.

1-Cyanocyclohexanesulfonamide (18). To a stirred and cooled (0 °C) solution containing 6.8 g (0.02 mol) of **10** was added a slurry containing 4.2 g (0.06 mol) of sodium methyl mercaptide in 50 mL of tetrahydrofuran. After 18 h at room temperature, the reaction mixture was concentrated to dryness. The residual solid was treated with 200 mL of water and extracted with with ether (2 × 200 mL). The aqueous layer was acidified (HCl) and extracted with ether (2 × 200 mL). The latter ether extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residual oil, 5 g, was crystallized from ether–hexane to give 1.8 g (47%) of white crystalline solid that had mp 99–101 °C, which resolidified and melted at 113–115 °C; IR (KBr) 3340 and 3240 (NH), 2260 cm^{-1} (C≡N); ^{13}C NMR ($CDCl_3$) 64.21 (C_1), 30.40 (C_2 + C_6), 22.76 (C_3 + C_5), 24.25 (C_4), 117.44 ppm (C≡N).

Anal. Calcd for $C_7H_{12}N_2SO_2$: C, 44.7; H, 6.4; N, 14.9. Found: C, 44.5; H, 6.5; N, 14.9.

***N*-[(2,2,2-Trifluoroethylidene)amino]-1-cyclohexenecarboximidoyl Chloride (20).** A mixture of 28.0 g (0.083 mol) of **10** in 150 mL of toluene was refluxed until the evolution of SO_2 and HCl had ceased (2 h, 110 °C). The solvent was removed under rotary evaporation. The residual liquid was purified by distillation to give 14 g (71%) of **20** as a pale-yellow liquid; bp 77–80 °C (0.2 mm); GLC shows the distillate to be approximately 99% pure; IR (CH_2Cl_2) no apparent NH and C≡N; ^{13}C NMR ($CDCl_3$) 21.76, 22.34, 25.97, 26.52 (4, $(CH_2)_4$), 119.6 (J_F = 272.461 Hz, CF_3), 143.7 (J_F = 38.086 Hz, HC=N), 133.34 (CCl), 133.34 (C=), 140.4 ppm (HC=); ^1H NMR ($CDCl_3$) δ 1.7, 2.35 (m, 8, $(CH_2)_4$), 6.7–7.4 (2, $(CH=)_2$); CIMS, m/z 239 $(M + H)^+$, 203 ($(M + H)^+$ – HCl); EIMS, m/z 238 (M^+), 203 (M^+ – Cl), 169 (M^+ – CF_3), 106 ($C_6H_8CN^+$), 79 (C_6H_7, base peak), 69 (CF_3^+), 65, 53.

Anal. Calcd for $C_9H_{10}ClF_3N_2$: C, 45.3; H, 4.2; Cl, 14.9; N, 11.7; S, 0.0. Found: C, 44.9; H, 4.2; Cl, 14.9; N, 11.3; S, <0.3.

1-Cyclohexenecarboxylic Acid 2-(2,2,2-Trifluoroethylidene)hydrazide (21) and 1-Cyclohexenecarboxylic Acid (2-(1-Hydroxy-2,2,2-trifluoroethyl)hydrazide (22). a. From 10. A solution containing 6.8 g (0.02 mol) of **10** and 2.6 g (0.02 mol) of ethyldiisopropylamine was stirred at room temperature for 2 h and then heated to reflux (65 °C) for 1 h. The reaction product was poured into ice water and extracted with three 100-mL portions of ether. The combined extracts were washed with 100 mL of cold diluted HCl and then with water. The ethereal layer was dried, absorbed on silica gel, and arranged for silica chromatography, using the solvent mixture (by volume): hexane (80), ethyl acetate (16), THF (4).

The first fraction consisted of 1.5 g (22%) of **10** starting material): mp 78–81 °C; mixture melting point with **10** was not depressed.

The second fraction consisted of 0.5 g (11%) of **21**, a white solid: mp 181–183 °C (from ether–hexane); IR (KBr) 3230 (NH), 1670 (C=O), 1630 cm^{-1} (C=N); EIMS, m/z 220 (M^+), CIMS, m/z 221 $(M + H)^+$; ^{13}C NMR ($CDCl_3$) 21.14, 21.66, 23.9, 25.0 (4, $(CH_2)_4$), 132.21 (C=), 135.57 (HC=), 165.62 (C=O), 132.998 (J_F = 37.598 Hz, HC=N), 138.826 ppm (J_F = 270 Hz, CF_3).

Anal. Calcd for $C_9H_{11}F_3N_2O$: C, 49.5; H, 5.0; N, 12.7. Found: C, 49.6; H, 5.2; N, 12.5.

b. From 20. A solution containing 3.0 g (12.6 mmol) of **20** and 1.0 g (60 mmol) of water in 40 mL of THF was heated at 50 °C for 10 min. The solvent was removed in vacuo, and the residue was triturated with 50 mL of water and 50 mL of ether. The organic layer was dried ($MgSO_4$) and concentrated. The residue crystallized from ether–hexane (1:1) to give 0.1 g (3%) of **22**: mp 110–113 °C; EIMS, m/z 220 (M^+ – H_2O), 151 (M^+ – H_2O, CF_3), 123 (M^+ – H_2O – CF_3CHO), 109 ($C_6H_9CO^+$), 81 ($C_6H_9^+$), 69 (CF_3^+).

Anal. Calcd for $C_9H_{13}F_3N_2O_2$: C, 45.4; H, 5.5; N, 11.8. Found: C, 45.1; H, 5.5; N, 11.7.

The above mother liquor was concentrated to dryness. The residual viscous oil crystallized to give 1.0 g (36%) of **21** as a white solid: mp 187–189 °C; IR (KBr) 3230 (NH), 1670, 1630 cm^{-1} (C=O); EIMS, m/z 220 (M^+), 151 (M^+ – CF_3), 123 (M^+ – CF_3CO), 109 ($C_6H_9CO^+$), 81 ($C_6H_9^+$), 65, 53; CIMS, m/z 221 $(M + H)^+$.

Anal. Calcd for $C_9H_{11}F_3N_2O$: C, 49.1; H, 5.0; N, 12.7. Found: C, 48.8; H, 5.0; N, 12.8.

***N*,*N*-Dimethyl-*N'*-[2,2,2-trifluoroethylidene)amino]-1-cyclohexenecarboximidamide (23).** To a cold (5 °C) solution of 1.1 g (25.2 mmol) of dimethylamine in 30 mL of ether was added 3.0 g (12.6 mmol) of **20**. The mixture became immediately cloudy, and a precipitate was forming. After 24 h at 20 °C, the reaction mixture was washed with 30 mL of water, dried, and concentrated to give 3.1 g (99%) of **23** as a light-yellow oil; TLC shows one spot; IR (CH_2Cl_2) no apparent C≡N and NH; NMR ($CDCl_3$) δ 3.0 (s, 6, $(CH_3)_2$), 7.4 (m, 1, =$CHCF_3$), 5.5 (m, 1, CH=), 1.65–2.1 (m, 8, $(CH_2)_4$); EIMS, (m/z 247 (M^+), 228 (M^+ – F), 203 (M^+ – N-$(CH_3)_2$), 179 (M^+ – CF_3), 158 (M^+ – CF_3CHNH), 122 ($C_7H_{10}N_2^+$), 108, 79 ($C_6H_7^+$), 69 (CF_3^+), 53; CIMS, m/z 248 $(M + H)^+$.

Anal. Calcd for $C_{11}H_{16}N_3F_3$: C, 53.4; H, 6.5; Cl, 0.0; N, 17.0. Found: C, 53.7; H, 6.8; Cl, <0.3, N, 17.1.

Registry No. (*E*)-**3a**, 82691-67-6; (*Z*)-**3a**, 82691-81-4; (*E*)-**3b**, 82691-68-7; (*Z*)-**3b**, 82691-82-5; (*E*)-**3c**, 82691-69-8; (*Z*)-**3c**, 82691-83-6; (*E*)-**3d**, 82691-70-1; (*Z*)-**3d**, 82691-84-7; (*E*)-**3e**, 82691-71-2; (*Z*)-**3e**, 82691-85-8; (*E*)-**3f**, 82691-72-3; (*Z*)-**3f**, 82691-86-9; **6**, 80967-54-0; **7** (isomer 1), 80967-61-9; **7** (isomer 2), 80967-56-2; **8** (isomer 1), 80967-62-0; **8** (isomer 2), 80967-58-4; **10**, 80967-59-5; **11**, 82691-79-0; **14**, 82691-73-4; **16**, 82691-74-5; **18**, 82691-75-6; **20**, 82691-76-7; **21**, 82691-77-8; **22**, 82691-78-9; **23**, 82691-80-3; cyclopropanecarboxylic acid hydrazide, 6952-93-8; cyclopentanecarboxylic acid hydrazide, 3400-07-5; cyclohexanecarboxylic acid hydrazide, 38941-47-8; trifluoroacetaldehyde, 75-90-1; pentafluoropropionaldehyde methyl hemiacetal, 59872-84-3.