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HEXAFLUOROACETONE HYDRAZONE CHEMISTRY

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SUMMARY

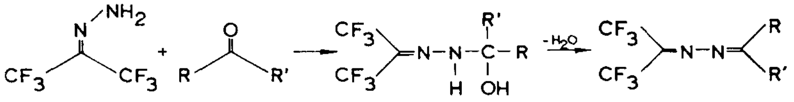
Hexafluoroacetone hydrazone condenses with ketones and aldehydes to give azines. β-Diketones give either azino-enols or hydrazino-ketones depending on the substrate. Aldehydes capable of aldol condensation and some α, β-unsaturated carbonyl compounds give pyrazoles. Isocyanates yield semicarbazones and acid chlorides give hydrazides. Variable-temperature NMR processes in hexafluoroacetone azines are consistent with consecutive nitrogen inversions and intermediate rotation about the nitrogen–nitrogen single bond. Resonance effects lower the barriers in the fluorinated azines.

INTRODUCTION

Hexafluoroacetone hydrazone (HFAH) was first prepared in this laboratory by Middleton and Krespan[1,2], but aside from its facile oxidation to the diazo compound and reaction with sulfur tetrafluoride[3] little chemistry has been explored. This paper presents the reactions of HFAH with carbonyl compounds, cumulated systems and active halides.

RESULTS

HFAH condenses with a variety of carbonyl compounds to form azines (II).



(HFAH) (I) (II)

(a) $R = R' = CH_3$
(b) $R = R' = CH_2Cl$
(c) $R = R' = C_6H_5$

The reactions are typified by the formation of (II(a)), (II(b)) and (II(c)) from simple ketones. The general procedure developed was to heat a slurry of HFAH

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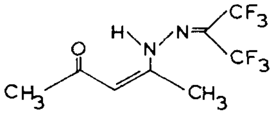
and the carbonyl compound with excess phosphorus pentoxide, either neat or with an inert solvent such as ether or a chlorocarbon. Cyclohexanone, acetophenone and fluorenone reacted analogously.

Other ketones

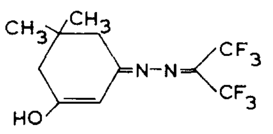
The rate of azine formation decreases as the electronegativity of the groups attached to the carbonyl carbon increases. Although chloro- and 1,3-dichloroacetone reacted normally, heavily halogenated ketones such as hexafluoroacetone or tetrachlorodifluoroacetone gave no azine. Although the reaction with methyl isopropyl ketone proceeded normally, no reaction of HFAH and pinacolone occurred, suggesting steric effects are also important. The major side-reaction from aliphatic ketones was an acid-catalyzed aldol condensation, so yields were generally better with aryl alkyl ketones or diaryl ketones. Although trifluoroacetophenone reacted very slowly, the yield was good because aldol condensation is impossible. α, β-Unsaturated ketones constrained to a *trans* conformation, such as isophorone, reacted to give the expected azine.

Polyketones

HFAH gives 1:1 adducts with α-diketones and β-diketones, but the tautomeric form of the product depends on the substrate. Acetylacetone gives a hydrazino-ketone (III), while dimedone forms an azino-enol (IV).

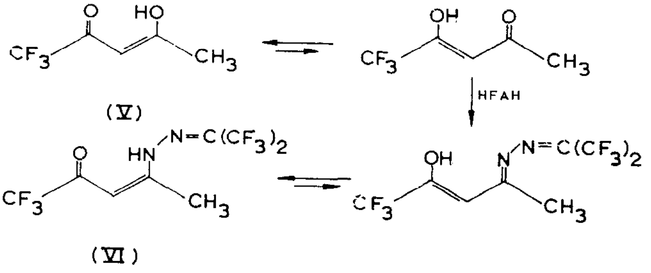


(III)



(IV)

There are two possible sites of attack on 1,1,1-trifluoroacetylacetone and two possible tautomeric products resulting from attack at each. The fluorine magnetic resonance (^{19}F NMR) spectrum of the starting material suggests it is primarily (V). A similar configuration was assigned to the pentafluorophenyl analog of (V)[4]. The structure of the product is (VI), suggesting attack at the carbonyl group of the minor tautomer followed by re-tautomerization to the more stable form.



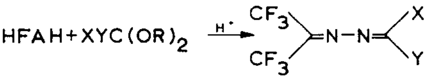
2,3-Butanedione and benzil gave 1:1 hydrazono-ketones, analogous to (II), by reaction of one carbonyl group.

Aldehydes

Aromatic aldehydes such as benzaldehyde give good yields of aldazines. Other aldehydes which cannot undergo aldol condensation such as cinnamaldehyde, isobutyraldehyde, and fluoral also give aldazines. The inital adduct of HFAH and chloral could be isolated in the absence of phosphorus pentoxide but in its presence no pure product could be isolated. Attempted extension of this reaction to linear, aliphatic aldehydes gave anomalous results which will be described below.

Ortho esters and amides

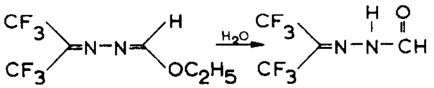
HFAH reacts with ortho esters and amides in the presence of an acid catalyst to give the expected hetero-substituted azines, (VII).



(VII) (a) X = CH_3 Y = OC_2H_5

(b) X = H Y = $N(CH_3)_2$

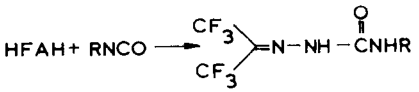
During aqueous workup of the reaction product of HFAH and triethyl orthoformate hydrolysis occurred producing the formyl derivative of HFAH, (VIII).



(VIII)

Cumulated systems

Phenyl isocyanate condenses smoothly with HFAH to give the substituted semicarbazone.



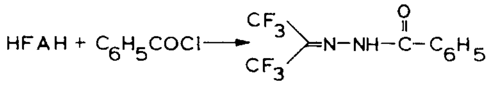
(IX) (a) R = C_6H_5

(b) R = CH_3

Heating HFAH and methyl isocyanate in a sealed tube of 100° overnight returned unreacted starting materials, but when phosphorus pentoxide was added to the solution at room temperature, a quantitative yield of the semicarbazone was rapidly produced.

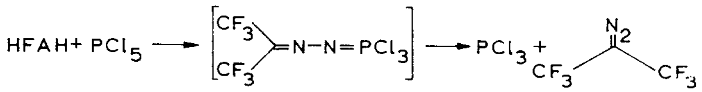
Halides

The benzhydrazide (X) was prepared in low yield from the reaction of HFAH with benzoyl chloride.



(X)

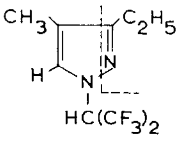
Reaction of HFAH with phosphorus pentachloride gave phosphorus trichloride (identified by gas chromatography and phosphorus magnetic resonance) and the diazo compound (identified by ^{19}F NMR spectroscopy). A possible intermediate, the phosphazene (XI), appears to be unstable with respect to dissociation.



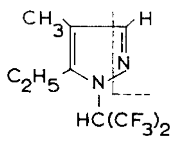
(XI)

Aliphatic aldehydes

Adding n-propanal to a slurry of HFAH and phosphorus pentoxide at 0° produced a vigorous exotherm, and cursory examination of the ^{19}F NMR spectrum of the crude product showed that a new reaction had occurred. Instead of the usual pair of quartets from the non-equivalent geminal trifluoromethyl groups, several doublets with $J = 7$ were seen. Correspondingly, the proton magnetic resonance spectrum showed a septet with $J = 7$ suggesting the grouping $-CH(CF_3)_2$. Two products (XII) and (XIII) were isolated in a pure state by preparative gas chromatography and identified by high resolution mass spectroscopy as isomeric 2:1 adducts which had lost two molecules of water. Consideration of the ^{1}H and ^{19}F NMR spectra led to the pyrazole structures (XII) and (XIII) for the two isomers. The final assignment was made from the high resolution mass spectrum which showed a peak at $M - C_2H_5CN$ (not C_4H_7) and a corresponding ion for loss of HCN from the other isomer.

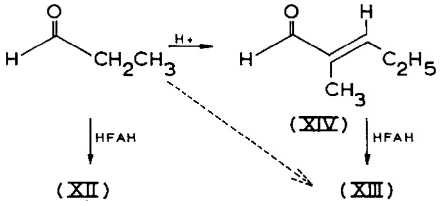


(XII)



(XIII)

Because the aldol dimer (XIV) might be an intermediate in the formation of one or both pyrazoles, (XIV) was prepared independently and treated with HFAH. Only pyrazole (XIII) was detected by ^{19}F NMR spectroscopy of the crude product suggesting that pyrazole (XII) forms directly from the aldehyde.



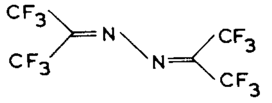
Of the other α,β-unsaturated carbonyl compounds treated with HFAH, only chalcone gave a pyrazole. Cinnamaldehyde and isophorone gave azines while acrolein, crotonaldehyde, benzal acetone, mesityl oxide and methyl vinyl ketone gave mixtures of products which could not be separated. In the strongly acidic medium used to carry out these reactions any of a number of carbonium ion rearrangements and proton transfers may be possible. Because the yields of isolated products from propanal and its aldol condensation product are low, speculation as to the detailed course of the reaction is not warranted.

Physical properties of HFA azines

The physical properties of HFA azines closely resemble those of the aldehydes and ketones from which they are formed, so separations are difficult. Compared with the acetone hydrazones, HFA derivatives are much more soluble in organic media. The more volatile HFA azines have sweet, ester-like odors. Although both acetone azine and HFA azine are colorless, the mixed aliphatic–fluorocarbon azines are yellow because the $n \rightarrow \pi^*$ absorption centered at 295 nm tails into the visible.

Variable-temperature NMR studies

The room-temperature ^{19}F NMR spectrum of hexafluoroacetone azine (XV)



(XV)

shows two featureless absorptions at -65.0 and -68.7 ppm[1]. By comparison with HFA and all other HFA azines a 6–8 Hz fluorine–fluorine coupling was expected.

Three possible explanations for the lack of observable fine structure are: (a) partially relaxed coupling to nitrogen-14[5]; (b) extensive long-range fluorine–fluorine coupling which produces a complicated $A_3A_3'X_3X_3'$ spin system; and (c) a nitrogen inversion process which exchanges the environments of the trifluoromethyl groups.

At $-60°$ the ^{19}F NMR spectrum of (XV) shows two sharp quartets, $J = 5.8$ Hz. As the temperature is raised, the individual peaks of the quartets broaden and the two quartets coalesce at 72° and 56.4 MHz and at higher temperatures sharpen to a singlet. This change is consistent only with a nitrogen-inversion process. Acetone azine shows no temperature variation in its NMR spectrum[6].

The proton spectrum of the mixed azine of HFA and acetone (II(a)) shows two singlets at 1.86 and 2.12 ppm which coalesce at 88° at 60 MHz and sharpen to a singlet at higher temperatures. At 190° and 94.1 MHz the fluorine spectrum is still well below coalescence. The spectra of azines (II(b)) and (II(c)) were briefly studied; their fluorine spectra were similar to (II(a)). At 190° the ^{19}F NMR spectrum of (II(a)) had not shown any broadening, those of (II(b)) and (II(c)) were only slightly below their coalescence temperatures. All spectral changes were reversible. The variable-temperature NMR data are summarized in Table 1.

TABLE 1

COALESCENCE TEMPERATURES OF HEXAFLUOROACETONE AZINES

Compound	$\Delta\delta_{F}{}^{a}$	T_c	$\Delta\delta_{H}{}^{a}$	T_c
(XV); R = CF_3	228^b	73°	—	—
(II(a)); R = CH_3	318^c	$\gg$190°	16^d	88°
(II(b)); R = CH_2Cl	334^c	>190°	14^d	—
(II(c)); R = C_6H_5	334^c	>190°	—	—

[a] In hertz.
[b] At 56.4 MHz.
[c] At 94.1 MHz.
[d] At 60 MHz.

Because of symmetry the barriers to inversion of each nitrogen of (XV) must be the same, but they can be synchronous or consecutive. The independent barriers to inversion of the two nitrogens in the unsymmetrical azine (II(a)) suggest the double nitrogen-inversion process is not concerted[7].

Figure 1 depicts several reaction pathways for consecutive nitrogen inversions. A single nitrogen inversion from a *trans* conformation gives a *cis* conformation. Immediate inversion of the second nitrogen gives a *trans* product with both nitrogens inverted. Only a single NMR process is likely to be observable from this mechanism, representing the inversion with the higher barrier. If inversion takes place from a *trans* conformation, the *cis* conformation which is produced can rotate about the nitrogen–nitrogen bond giving a new *trans* conformation in which only one of the nitrogens has been inverted. For (II(a)), inversion of N_2 leads to exchange of the methyl groups without exchanging the environments of the trifluoromethyl groups. For (XV), a second inversion–rotation process exchanges the environments of all four trifluoromethyl groups.

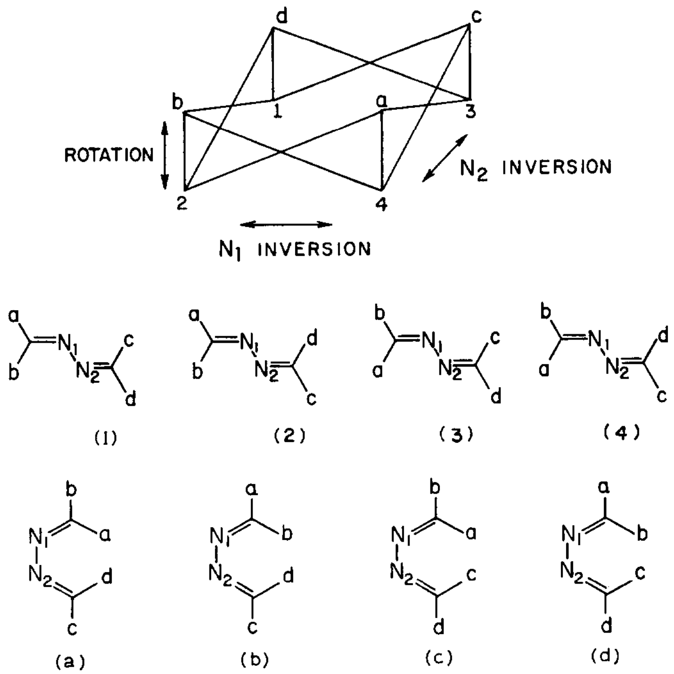
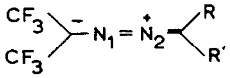


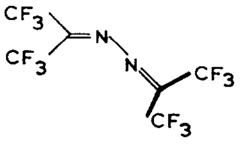
Fig. 1. Nitrogen inversion mechanism in azines.

Because the nitrogen in azines (II(a))–(II(c)) whose inversion is affected most by trifluoromethyl substitution is N_2, resonance structures such as (XVI) may contribute to the transition state and lower the inversion barrier of N_2 more than that of N_1.

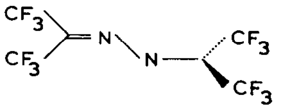


(XVI)

A continuum of possible transition states[8] stretches from pure nitrogen inversion followed by pure rotation about the nitrogen–nitrogen bond to simultaneous rotation–inversion as depicted in (XVII). All paths involving sequential reaction at the two nitrogens lie on the surface of the cube depicted in Figure 1. The problem of defining inversions and rotations would become a moot point if the exchange mechanism is actually rotation about the carbon–nitrogen double bond such as in (XVIII).



(XVII)



(XVIII)

EXPERIMENTAL

Melting points and boiling points are uncorrected. Fluorine NMR spectra were obtained on Varian A56/60 and HA-100 spectrometers and proton magnetic resonance spectra on a Varian A60. Spectra were determined as dilute solutions in carbon tetrachloride or deuteriochloroform to which tetramethylsilane and trichlorofluoromethane had been added for calibration purposes. Infrared spectra were taken on dilute solutions in carbon tetrachloride or chloroform on a Perkin–Elmer 137 instrument. The concentrations used were chosen so that the intense C–F stretch absorptions between 8 and 9 μ remained on scale. Low resolution mass spectra were run on a du Pont CEC 21-103C instrument. High resolution mass spectra were run on a du Pont CEC 21-110B instrument. Preparative gas chromatography of the isomeric pyrazoles was done on a 1.8 m × 1.0 cm SS column of 20% fluoroalkyl pyromellitate on 60–80 GCR. Analytical gas chromatography was done on a 1.8 m × 0.6 cm SS column of 20% silicone No. 200 on Gas Chrom Ra (60–80). All compounds described below are new.

1-[1-Methylethylidenehydrazono]-1-(trifluoromethyl)-2,2,2-trifluoroethane (II(a))

To a solution of 10.0 g HFAH and 21 g acetone at 0° was added in small portions 20 g of phosphorus pentoxide. The solution became yellow and a mild exotherm occurred. After the addition was complete, the reaction was refluxed until no more hydrazone was present. A rapid distillation separated the volatile materials from inorganic phosphorus residues and the product was isolated as a yellow liquid b.p. 100–103° by distillation through a small spinning-band column. Yield 6 g. Calcd. for $C_6H_6F_6N_2$: C, 32.8; H, 2.8%. Found: C, 33.1; H, 3.0%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -65.09$ and $\delta = -68.62$, $J = 6.2$ Hz, and the ^1H NMR spectrum showed two singlets at $\delta = 2.12$ and 1.86. The UV spectrum showed $\lambda_{max} = 238$ nm ($\varepsilon = 4400$) and a shoulder at $\lambda = 295$ nm ($\varepsilon = 142$). The infrared spectra had bands at 7.4, 7.9, 8.0, 8.1, 8.4, and 9.95 μ.

(1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono)cyclohexane

To 4 g cyclohexanone and 3.6 g HFAH in a 100 ml round-bottomed flask was added 5 g phosphorus pentoxide. The solution was heated at 80° for 1 h, then quickly distilled at reduced pressure into a receiver cooled to −78°. Re-distillation through a spinning-band column gave *ca.* 2 g product as a yellow liquid b.p. 67–68°/10 mmHg. Calcd. for $C_9H_{10}F_6N_2$: C, 41.6; H, 3.9%. Found: C, 42.0; H, 3.9%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -64.80$ and $\delta = -68.48$, $J = 6$ Hz. The ^1H NMR spectrum showed a multiplet at $\delta = 2.3$, 4H, and a broad singlet at $\delta = 1.7$, 6H. The infrared spectrum showed bands at 3.40, 3.48, 6.14, 6.28, 6.9, 7.4, 8.0, 8.5, 10.0 and 10.5 μ.

1-[1(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-1-phenylethane

A slurry of 2.5 g acetophenone, 3.6 g HFAH, and 5 g phosphorus pentoxide was heated at 80° for 0.5 h. During this time the liquid became yellow. The solid mass of phosphorus pentoxide was triturated with 3 × 25 ml ether. The combined ether extracts were dried over magnesium sulfate and distilled through a spinning-band column giving 3.1 g of yellow liquid, b.p. 75–78°/3.5 mmHg; m.p. 16.5–18°. Calcd. for $C_{11}H_8F_6N_2$: C, 46.8; H, 2.8%. Found: C, 46.9; H. 3.1%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -65.20$ and $\delta = -68.35$, $J = 5$ Hz. The ^1H NMR spectrum showed a singlet at $\delta = 2.28$, $C\underline{H}_3$, and aromatic multiplets at $\delta = 7.45$, 3H, and $\delta = 7.85$, 2H.

The infrared spectrum showed absorptions at 3.2, 7.4, 7.7, 8.0, 8.1, 8.45, 10.02 and 10.7 μ.

9-[1-[Trifluoromethyl]-2,2,2-trifluoroethylidenehydrazono]fluorene

A slurry of 4 g HFAH, 3.0 g fluorenone, 5 g phosphorus pentoxide and 25 ml methylene chloride was refluxed for 2 h. The methylene chloride solution was decanted and the residue triturated with methylene chloride until the solvent remained colorless. Evaporation of methylene chloride and recrystallization of the residue from ethanol/water gave 2.8 g of product as yellow-orange needles, m.p. 43.5–45°. Calcd. for $C_{16}H_8F_6N_2$: C, 56.2; H, 2.3%. Found: C, 56.3; H, 2.4%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -64.57$ and $\delta = -68.07$, $J = 6$ Hz. The ^1H NMR spectrum showed only aromatic resonances between $\delta = 7.1$ and 7.9.

The infrared spectrum showed absorptions at 6.9, 7.4, 7.9, 8.0, 8.4, 9.9, 10.0 and 10.9 μ.

1-[1,2-Dimethylpropylidenehydrazono]-1-(trifluoromethyl)-2,2,2-trifluoroethane

A mixture of 1.8 g methyl isopropyl ketone, 3.6 g HFAH and 6 g phosphorus pentoxide was heated for 4 h. The black residue was extracted with methylene chloride and distilled through a small spinning-band column giving 1.8 g of yellow liquid b.p. 65–68°/80 mmHg. Calcd. for $C_8H_{10}F_6N_2$: C, 38.7; H, 4.0%. Found: C, 38.5; H, 4.2%.

The infrared spectrum showed bands at 3.4, 7.4, 8.0, 8.1, 8.5 and 10.0 μ.

The ^1H NMR spectrum showed a doublet, $J = 6$ Hz, at $\delta = 1.16$, $CHC\underline{H}_3$, a singlet at $\delta = 1.77$, $=CC\underline{H}_3$, a septet, $J = 6$ Hz, at $\delta = 2.48$, $C\underline{H}$. The ^{19}F NMR spectrum showed two quartets, $J = 6.5$ Hz, at $\delta = -65.12$ and $\delta = -68.48$.

2-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-1-chloropropane

A slurry of 3.6 g HFAH, 3.0 g chloroacetone and 5 g phosphorus pentoxide was stirred at room temperature. After 1 h, considerable charring had occurred and the residue was extracted with ether and 2.7 g of product isolated as a yellow liquid b.p. 75–78°/100 mmHg. Calcd. $C_6H_5ClF_6N_2$: C, 28.4; H, 2.0%. Found: C, 28.3; H, 2.4%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -65.37$ and $\delta = -68.72$, $J = 6$ Hz. The ^1H NMR spectrum showed two singlets at $\delta = 1.97$ and $\delta = 4.16$ assigned to $C\underline{H}_3$ and $C\underline{H}_2$ respectively.

The infrared spectrum showed bands at 7.4, 8.0, 8.4 and 10.0 μ.

2-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-1,3-dichloropropane (II(b))

A slurry of 5 g HFAH, 2.6 g 1,3-dichloroacetone and 7 g phosphorus pentoxide was heated at 50° for 4 h. Trituration of the solid mass with ether and distillation through a spinning-band column gave 2 g of product as a pale-yellow liquid b.p. ~ 55°/20 mmHg. Calcd. for $C_6H_4Cl_2F_6N_2$: C, 25.0; H, 1.4%. Found: C, 25.5; H, 1.5%.

The ^{19}F NMR spectrum consisted of two quartets at $\delta = -64.82$ and $\delta = -68.72$, $J = 6.5$ Hz. The ^1H NMR spectrum consisted of two singlets at $\delta = 4.15$ and $\delta = 4.38$.

The infrared spectrum showed bands at 7.0, 7.4, 8.0, 8.4 and 10.0 μ.

α-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-α-(trifluoromethyl) toluene

A slurry of 4.9 g α,α,α-trifluoroacetophenone, 5.5 g HFAH and 10 g phosphorus pentoxide was heated at reflux for two days. The progress of the reaction was monitored by ^{19}F NMR spectroscopy and when no trifluoroacetophenone was present the residue was extracted with methylene chloride and distilled through a spinning-band column giving 5.1 g product as a pale-yellow liquid b.p. 71–75°/15 mmHg. Calcd. for $C_{11}H_5F_9N_2$: C, 39.3; H, 1.5%. Found: C, 38.9; H, 1.6%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -65.34$ and $\delta = -68.71$, $J = 6.5$ Hz, and a singlet at $\delta = -68.17$ with $W_{1/2} = 5$ Hz in the ratio of 1:1:1. The ^1H NMR spectrum consisted of a relatively sharp singlet at $\delta = 7.4$.

The infrared spectrum had bands at 7.4, 7.9, 8.0, 8.3, 8.45, 8.65 and 10.0 μ.

[1-Trifluoromethyl]-2,2,2-trifluoroethylidenehydrazonodiphenylmethane (II(c))

A slurry of 3.4 g benzophenone, 3.6 g HFAH and 5 g phosphorus pentoxide in 20 ml methylene chloride was stirred at room temperature overnight. An additional 1.5 g HFAH was added and the solution allowed to stand at room temperature for 3 days. At this point IR spectroscopy revealed the absence of ketone. The solvent was removed on a rotary evaporator and the residual oil recrystallized from ethanol–water to give 4.4 g of yellow needles, m.p. 42–44°. Calcd. for $C_{16}H_{10}F_6N_2 \cdot H_2O$: C, 53.0; H, 3.3; N, 7.7%. Found: C, 53.5; H, 3.0; N, 7.8%.

IR (CCl_4): 3.45, 7.4, 8.0, 8.1, 8.4, 10.0, 10.1 μ.

NMR (CCl_4/TMS/F-11): ^1H NMR spectrum showed only aromatic absorptions between $\delta = 7.4$ and 7.7. The spectrum showed two quartets, $J = 6.3$ Hz, at $\delta = -68.44$ and $\delta = -65.25$.

3-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-1,5,5-trimethylcyclohex-1-ene

To a solution of 2.8 g of isophorone and 4.5 g HFAH was added at room temperature 7 g of phosphorus pentoxide. A vigorous exotherm occurred. The solution was heated at 100° for 1 h. The reaction mixture was cooled to room temperature and then was exhaustively extracted with ether, dried over magnesium sulfate and distilled through a spinning-band column to give 1.3 g of a yellow liquid b.p. 62–63°/0.8 mmHg. Calcd. for $C_{12}H_{14}F_6N_2$: C, 48.0; H, 4.7%. Found: C, 48.4; H, 4.9%.

The ^{19}F NMR spectrum showed two sets of two quartets at $\delta = -64.45$ and -64.57 and $\delta = -68.16$ and -68.19, $J = 7$ Hz. The ^1H NMR spectrum consisted of a singlet at $\delta = 1.03$, $C(C\underline{H}_3)_2$, a broad singlet at $\delta = 1.88$, $=C-C\underline{H}_3$, singlets at $\delta = 2.05$, 2.17 and 2.28, $C\underline{H}_2$, and two multiplets at $\delta = 5.72$ and 6.09, $=C\underline{H}$.

The infrared spectrum showed bands at 3.35, 7.4, 8.0, 8.1, 8.5, 10.1 and 10.4 μ.

3-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-2-butanone

A slurry of 1.7 g 2,3-butanedione, 3.6 g HFAH and 5 g phosphorus pentoxide was heated overnight at 80° (probably too long). The black residue was extracted with methylene chloride and distilled through a spinning-band column to give 1.7 g of a yellow liquid b.p. 53°/20 mmHg. Calcd. for $C_7H_6F_6N_2O$: C, 33.9; H, 2.4%. Found: C, 33.4; H, 2.6%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -65.46$ and $\delta = -68.17$, $J = 6.5$ Hz. The ^1H NMR spectrum showed two singlets at $\delta = 1.90$ and $\delta = 2.42$.

The infrared spectrum showed bands at 5.8, 7.4, 8.0, 8.45, 8.95 and 10.0 μ.

2-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-2-phenylacetophenone

A slurry of 1.8 g benzil, 4.6 g HFAH, 8 g phosphorus pentoxide and 10 ml methylene chloride was refluxed for 2 h. The methylene chloride was decanted and the residue triturated with more methylene chloride. Evaporation of the solvent and recrystallization from ethanol/ water gave a product still contaminated by benzil. The crude product was chromatographed on silica gel using hexane as eluent. The early fractions contained 1.3 g product as yellow needles, m.p. 51–52.5°. Calcd. for $C_{17}H_{10}F_6N_2O$: C, 54.8; H, 2.7%. Found: C, 55.3; H, 2.8%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -64.02$ and $\delta = -68.72$, $J = 6$ Hz. The ^{1}H NMR spectrum consisted of aromatic absorptions at $\delta = 7.3$ and $\delta = 7.7$.

The infrared spectrum showed absorptions at 5.9, 6.2, 6.4, 6.9, 7.4, 8.0, 8.1, 8.2, 8.4 and 10.0 μ.

4-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazino]-3-penten-2-one (III)

A slurry of 2 g acetylacetone, 3.6 g HFAH and 5 g phosphorus pentoxide was heated at 100° for 2 h. The residue was extracted with ether and distilled through a spinning-band column giving 3.9 g of a yellow liquid, b.p. 61–63°/3.5 mmHg; m.p. 47–49°. Calcd. for $C_8H_8F_6N_2O$: C, 36.6; H, 3.1%. Found: C, 36.9; H, 3.1%.

The ^{19}F NMR spectrum showed a quartet, $J = 6$ Hz, of doublets, $J = 1.3$ Hz, at $\delta = -65.73$ and a quartet, $J = 6$ Hz, at $\delta = -66.56$. The ^{1}H NMR spectrum showed a singlet at $\delta = 2.12$, $C\underline{H}_3$, a doublet, $J = 1$ Hz, at $\delta = 2.16$, $C\underline{H}_3$, a broad singlet at $\delta = 5.45$, $=C\underline{H}$ and a broad singlet $\delta = 13.95$, $N\underline{H}$.

The infrared spectrum showed bands at 3.3, 6.0, 6.15, 6.23, 6.8, 7.4, 7.8, 8.0, 8.2, 8.7, 9.1, 9.7, 10.0 and 10.3 μ.

4-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazino]-1,1,1-trifluoro-3-penten-2-one (VI)

A slurry of 4.5 g 1,1,1-trifluoroacetylacetone, 3.6 g HFAH and 8 g phosphorus pentoxide was refluxed in 10 ml methylene chloride overnight. The residue was exhaustively extracted with methylene chloride and 4.0 g of product was isolated by distillation through a spinning-band column b.p. 55–56°/2.5 mmHg; m.p. 1–2°. Calcd. for $C_8H_5F_9N_2O$: C, 30.4; H, 1.6%. Found: C, 30.5; H, 1.7%.

The ^{19}F NMR spectrum showed a singlet at $\delta = -78.51$, a quartet, $J = 6$ Hz, at $\delta = -67.18$ and a quartet, $J = 6$ Hz, of doublets, $J = 2$ Hz, at $\delta = -65.53$. The ^{1}H NMR spectrum consisted of singlets at $\delta = 2.33$, 5.75 and 13.5, in the ratio of 3:1:1 assigned to $C\underline{H}_3$, $=C\underline{H}$ and $N\underline{H}$ respectively.

The infrared spectrum showed bands at 6.2, 7.4, 7.5, 7.85, 8.12, 8.3, 8.55, 8.9, 9.3, 9.7 and 10.1 μ.

3-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-5,5-dimethylcyclohex-1-en-1-ol (IV)

A slurry of 2.8 g dimedone, 3.6 g HFAH and 5 g phosphorus pentoxide in 10 ml methylene chloride was heated to 80° for 2 h. The solution became yellow and the phosphorus pentoxide caked. Trituration of the solid with methylene chloride and ether followed by removal of the solvents on the rotary evaporator gave the crude product which was recrystallized as bright-yellow plates from ethanol/water. Yield 3.3 g; m.p. 121–123°. Calcd. for $C_{11}H_{12}F_6N_2O$: C, 43.6; H, 3.9%. Found: C, 43.6; H, 4.0%.

The ^{19}F NMR spectrum showed two quartets at $\delta = -63.53$ and $\delta = -66.33$, $J = 6$ Hz. The ^1H NMR spectrum showed a singlet at $\delta = 1.13$, $C\underline{H}_3$, singlets at $\delta = 2.28$ and $\delta = 2.55$, $C\underline{H}_2$, a singlet at $\delta = 5.84$, $=C\underline{H}$, and a very broad absorption between $\delta = 8.5$ and 10.0 which disappears when the sample is shaken with D_2O, $O\underline{H}$.

The infrared spectrum shows bands at 3.1, 3.4, 6.2, 7.4, 7.6, 8.1, 8.3, 8.6, 9.0 and 10.0 μ.

The UV spectrum in iso-octane showed a band at 293 nm ($\varepsilon = 18\,200$) and 234 nm ($\varepsilon = 5130$).

α-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-toluene

To a solution of 2.5 g benzaldehyde and 3.6 g HFAH at room temperature was added in small portions 6 g of phosphorus pentoxide. A potent exotherm was noted and the solution became yellow. The reaction mixture was exhaustively extracted with ether and the combined extracts distilled on a spinning-band column giving 3.9 g of product as a yellow liquid b.p. 88–90.5°/3.5 mmHg. Calcd. for $C_{10}H_6F_6N_2$: C, 44.8; H, 2.2%. Found: C, 44.9; H, 2.5%.

The ^{19}F NMR spectrum showed a quartet, $J = 6$ Hz, of doublets, $J = 0.9$ Hz, at $\delta = -63.39$ and a quartet, $J = 6$ Hz, at $\delta = -68.67$. The ^1H NMR spectrum showed a broad singlet at $\delta = 8.2$, $=C\underline{H}$, and aromatic absorptions at $\delta = 7.8$, 2H and $\delta = 7.43$, 3H.

The infrared spectrum showed bands at 6.2, 6.45, 7.3, 7.4, 8.0, 8.1, 8.4 and 10.3 μ. The UV spectrum consisted of a band at 283 nm ($\varepsilon = 16\,700$) with shoulders at 260 nm ($\varepsilon = 13\,100$) and 340 nm ($\varepsilon = 760$).

3-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-1-phenylprop-1-ene

A slurry of 2.6 g cinnamaldehyde, 3.6 g HFAH and 5 g of phosphorus pentoxide was heated for 30 min at 80° after an initial exotherm had subsided. The residue was extracted with ether and 4.2 g of product isolated as an orange liquid by distillation through a spinning-band column, b.p. 77–78°/0.4 mmHg. Calcd. for $C_{12}H_8F_6N_2$: C, 49.0; H, 2.7%. Found: C, 49.5; H, 3.1%.

The ^{19}F NMR spectrum showed two pairs of two quartets at $\delta = -63.31$ and $\delta = -68.60$, $J = 7$ Hz, intensity 32 and $\delta = -64.56$ and $\delta = -68.30$, $J = 7$ Hz, intensity 7. The ^1H NMR spectrum showed only vinyl and aromatic absorptions between $\delta = 7.1$ and $\delta = 8.1$. Only one vinyl proton was clearly separated from the rest at $\delta = 8.05$, doublet, $J = 6.2$ Hz, of doublets 2.6, $N{=}C\underline{H}-$ of major isomer. Integration of the ^{19}F NMR spectrum of a *neat* sample suggested an isomer ratio of 3:1.

The infrared spectrum showed bands at 6.15, 7.3, 7.45, 8.0, 8.1, 8.4 and 10.25 μ.

1-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-2-methylpropane

A slurry of 5 g isobutyraldehyde, 3.6 g HFAH and 5 g phosphorus pentoxide was heated at 80° for 1 h after an initial exotherm subsided. Extraction of the residue with ether and distillation through a spinning-band column gave 2.4 g of product as a yellow liquid, b.p. 58–62°/92 mmHg. Calcd. for $C_7H_8F_6N_2$: C, 36.0; H, 3.4%. Found: C, 35.7; H, 3.5%.

The ^{19}F NMR spectrum showed a quartet, $J = 7$ Hz, of doublets, $J \sim 0.7$ Hz, at $\delta = -63.35$ and a quartet, $J = 7$ Hz, at $\delta = -68.95$. The ^{1}H NMR spectrum consisted of a doublet, $J = 5$, at $\delta = 7.37$, $=C\underline{H}$, a multiplet at $\delta = 2.62$, $CHC\underline{H}(CH_3)_2$ and a doublet at $\delta = 1.19$, $J = 7$ Hz, $C\underline{H}_3$. The infrared spectrum showed bands at 3.3, 7.35, 8.1, 8.5 and 9.9 μ.

1-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]-2,2,2-trifluoroethane

To a solution of 6.5 g trifluoroacetaldehyde methyl hemiacetal and 9.0 g HFAH at −78° was added in portions 20 g phosphorus pentoxide. The slurry was allowed to warm slowly to room temperature and then refluxed 2 h. The reflux condenser was replaced by a short-path distillation column and the product distilled into a receiver cooled to −78°. Re-distillation of this fraction through a spinning-band column gave 5.2 g of product as a light-yellow liquid b.p. 66–67°. Calcd. for $C_5HN_2F_9$: C, 23.1; H, 0.4%. Found: C, 23.1; H, 0.6%.

The ^{19}F NMR spectrum showed a quartet at $\delta = -63.44$, $J = 7$ Hz, a quartet at $\delta = -69.11$, $J = 7$ Hz, and a doublet, $J = 3.5$ Hz, at $\delta = -70.71$ in the ratio of 1:1:1. The ^{1}H NMR spectrum showed a quartet at $\delta = 7.13$, $J = 3.5$ Hz.

The infrared spectrum showed bands at 6.4, 7.4, 8.0, 8.4, 8.5, 8.6 and 10.0 μ.

1-[(2,2,2-Trichloro-1-hydroxyethyl)hydrazono]-1-(trifluoromethyl)-2,2,2-trifluoroethane

A solution of 5 ml chloral and 3.6 g HFAH was heated at 80° overnight. The product was isolated by distillation through a spinning-band column, b.p. 44–45°/0.3 mmHg, as a pale-yellow liquid. Yield 4.4 g. Calcd. for $C_5H_3Cl_3F_6N_2O$: C, 18.4; H, 0.9%. Found: C, 18.6; H, 1.1%.

The ^{19}F NMR spectrum showed a quartet, $J = 6$ Hz, of doublets, $J = 2.5$ Hz, at $\delta = -64.80$ and a quartet, $J = 6$ Hz, at $\delta = -66.65$. The ^{1}H NMR spectrum showed a singlet at $\delta = 3.65$ which disappears when the sample is shaken with D_2O, $O\underline{H}$, a doublet, $J = 7$ Hz, at $\delta = 5.40$, $C\underline{H}$, and a broad singlet at $\delta = 7.64$, $N\underline{H}$.

1-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidenehydrazono]ethyl ethyl ether (VII(a))

A solution of 3.6 g HFAH and 3.2 g triethyl orthoacetate and 1 g phosphorus pentoxide was heated at 50° for ½ h. Distillation gave 1.6 g of clear liquid b.p. 70–74°/100 mmHg. Calcd. for $C_7H_8F_6N_2O$: C, 33.5; H, 3.2%. Found: C, 33.6; H, 3.4%.

The infrared spectrum showed bands at 3.3, 6.4, 6.5, 7.1, 7.3, 7.45, 7.6, 8.0, 8.2, 8.5 and 9.6 μ.

The ^{1}H NMR spectrum showed a triplet, $J = 7$ Hz, at $\delta = 1.37$, $C\underline{H}_3$, a singlet at $\delta = 2.21$, $C\underline{H}_3C=$, and a quartet, $J = 7$ Hz, at $\delta = 4.37$, $C\underline{H}_2$. The ^{19}F NMR spectrum showed two quartets, $J = 6.5$ Hz, at $\delta = -64.66$ and $\delta = -68.32$.

[1-[Trifluoromethyl]-2,2,2-trifluoroethylidenehydrazono]-N,N-*dimethylaminomethane (VII(b))*

To 2.4 g *N,N*-dimethylformamide dimethyl acetal was added 3.6 g HFAH. An exotherm took place and a yellow color developed. An additional 1 g HFAH and 0.5 g phosphorus pentoxide were added and the mixture was heated at 50° overnight. The crude product was dissolved in methylene chloride and extracted with 2 × 25 ml water, dried over magnesium sulfate and distilled through a short spinning-band column giving 2.2 g of product b.p. 66–67°/2.5 mmHg. Calcd. for $C_6H_7F_6N_3$: C, 30.7; H, 3.0%. Found: C, 30.9; H, 3.1%.

The infrared spectrum showed bands at 3.3, 6.0, 6.4, 7.0, 7.4, 7.7, 8.15, 8.3, 8.7, 9.0, 9.55, 10.3 and 11.5 μ.

The ^{1}H NMR spectrum showed a singlet at $\delta = 3.13$, $C\underline{H}_3$, and a singlet at $\delta = 8.05$, $=C\underline{H}$. The ^{19}F NMR spectrum showed a doublet, $J = 0.65$ Hz, of quartets, $J = 6.5$ Hz, at $\delta = -64.36$ and a quartet, $J = 6.5$ Hz, at $\delta = -66.81$.

2'-[1(Trifluoromethyl)-2,2,2-trifluoroethylidene]-formohydrazide (VIII)

A slurry of 3.6 g HFAH, 3.0 g triethyl orthoformate, 0.5 g phosphorus pentoxide and 10 ml methylene chloride was refluxed for 1 h. The methylene chloride solution was extracted with water and then dried, and solvent was removed at reduced pressure. The residue was sublimed at 150 mmHg to give 1 g of white, lachrymatory solid, m.p. 72.5–74°. Calcd. for $C_4H_2F_6N_2O$: C, 23.1; H, 1.0; N, 13.4%. Found: C, 23.4; H, 1.3; N, 13.9%.

The IR spectrum (CCl_4) showed bands at 2.9, 3.0, 3.05, 3.4, 5.65, 6.05, 6.1, 7.3, 7.7, 8.4, 8.6, 8.9 and 10.05 μ.

The ^{1}H NMR spectrum showed a sharp singlet at $\delta = 8.65$, $C\underline{H}$, and a broad singlet at $\delta = 10.25$, $N\underline{H}$.

The ^{19}F NMR spectrum showed a doublet, $J = 0.4$ Hz, of quartets, $J = 6$ Hz, at $\delta = -64.84$ and a quartet, $J = 6$ Hz, at $\delta = -67.55$.

1-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidene]-4-phenyl-semicarbazide (IX(a))

To a solution of 2.2 g phenyl isocyanate and 3.6 g HFAH was added 6 g phosphorus pentoxide. The slurry was heated overnight. After cooling to room temperature the slurry was extracted with methylene chloride to give a crude product. Recrystallization from methylene chloride/petroleum ether gave 5 g white needles, m.p. 141–143°. Calcd. for $C_{10}H_7F_6N_3O$: C, 40.1; H, 2.3%. Found: C, 39.7; H, 2.5%.

The ^{19}F NMR spectrum showed a quartet, $J = 6$ Hz, of doublets, $J = 1$ Hz, at $\delta = -64.54$ and a quartet, $J = 6$ Hz, at $\delta = -66.93$. The ^{1}H NMR spectrum showed an aromatic multiplet at $\delta = 7.2$–7.6 and two broad singlets at $\delta = 7.95$ and $\delta = 9.68$ assigned to $N\underline{H}$. The infrared spectrum had absorptions at 2.9, 3.1, 5.7, 5.75, 6.5, 6.9, 7.4, 7.65, 8.1, 8.45 and 8.85 μ.

1-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidene]-4-methyl-semicarbazide (IX(b))

A solution of 3.6 g HFAH and 1.2 g methyl isocyanate was heated in a sealed tube at 100° for 15 h. NMR spectroscopic examination of the reaction mixture showed no reaction had occurred. To the cooled solution was added 5 g phosphorus pentoxide. A mild exotherm was noted during the addition. The slurry was heated at 50° for 30 min, cooled and extracted with methylene chloride. Evaporation of the solvent gave a white solid which was recrystallized from methylene chloride/petroleum ether to give 2.4 g of product m.p. 81–82°. Calcd. for $C_5H_5F_6N_3O$: C, 25.3; H, 2.1%. Found: C, 25.5; H, 2.3%.

The ^{19}F NMR spectrum showed a broadened quartet at $\delta = -64.70$, $J = 6$ Hz, and a sharper quartet at $\delta = -66.90$, $J = 6$ Hz. The ^{1}H NMR spectrum showed a doublet, $J = 5$ Hz, at $\delta = 3.13$, $C\underline{H}_3$, and broad singlets at $\delta = 6.16$ and $\delta = 10.60$, $N\underline{H}$.

The infrared spectrum showed bands at 2.8, 3.1, 3.3, 5.7, 6.1, 6.5, 7.0, 7.3, 7.9, 8.1, 8.6, 8.9 and 10.0 μ.

2′-[1-(Trifluoromethyl)-2,2,2-trifluoroethylidene]benzohydrazide (X)

A mixture of 2.8 g benzoyl chloride and 3.6 g HFAH was heated at 80° for 2 days. On cooling, the reaction mixture solidified. The solid was filtered, washed with pentane, and recrystallized from ethanol/water to give 1 g of white needles m.p. 86–87°. Calcd. for $C_{10}H_6F_6N_2O$: C, 42.2; H, 2.1%. Found: C, 42.2; H, 2.2%.

The ^{19}F NMR spectrum showed a quartet, $J = 6$ Hz, of doublets, $J = 2$ Hz, at $\delta = -63.76$ and a quartet, $J = 6$ Hz, at $\delta = -66.95$. The ^{1}H NMR spectrum showed aromatic absorptions at $\delta = 7.5$ and $\delta = 7.8$ and an $N\underline{H}$ absorption at $\delta = 9.85$.

The infrared spectrum showed bands at 5.85, 7.8, 7.9, 8.5 and 8.9 μ.

1-(1,1,1,3,3,3-Hexafluoro-2-propyl)-3-ethyl-4-methylpyrazole (XII)

To a solution of 5 g propionaldehyde and 4.6 g HFAH at 0° was added slowly with stirring 8 g phosphorus pentoxide. The solution was allowed to warm to room temperature, and the solid mass extracted with ether and the ether extract distilled through a spinning-band column. The fraction boiling at 87°/100 mmHg contained a mixture of product and starting hydrazone. The product was purified by preparative gas chromatography. Calcd. for $C_9H_{10}F_6N_2$: Mol. wt. 260. Found: Mass spec. 260. Fragment ions were seen at $m/e = 245$ $(M-CH_3)$, 231 $(M-F)$, 191 ($M-CF_3$), 151 ($CH(CF_3)_2$), 109 ($M-CH(CF_3)_2$) and 69 (CF_3). From the high resolution mass spectrum an ion at M−55 was identified as $M-C_2H_5CN$.

The ^{19}F NMR spectrum showed a doublet, $J = 7$ Hz, of doublets, $J = 1$ Hz, at $\delta = -71.19$. The ^1H NMR spectrum showed a triplet, $J = 7$ Hz, at $\delta = 1.20$, $CH_2C\underline{H}_3$, a singlet at $\delta = 2.00$, $=CC\underline{H}_3$, a quartet, $J = 7$ Hz, at $\delta = 2.5$, $C\underline{H}_2CH_3$, a septet, $J = 7$ Hz, at $\delta = 5.45$, $C\underline{H}(CF_3)_2$, and a broad singlet at $\delta = 7.15$, $=C\underline{H}$.

The infrared spectrum showed bands at 7.35, 7.8, 7.9, 8.1, 8.4, 8.5, 8.75, 9.0, 11.1, 11.35, 11.8 and 14.5 μ.

The ^1H NMR spectrum of the crude reaction mixture before distillation suggested the presence of 2-methylpent-2-enal propionaldehyde aldol condensation product. The ^{19}F NMR spectrum of this crude product showed no azine, but suggested the presence of another minor component with the partial structure $-CH(CF_3)_2$ by a doublet at $\delta = -68.99$. This component could also be isolated by gas chromatography, but could be more conveniently prepared as described below.

1-(1,1,1,3,3,3-Hexafluoro-2-propyl)-4-methyl-5-ethylpyrazole (XIII)

To a slurry of 3.6 g HFAH and 4 g phosphorus pentoxide in 10 ml methylene chloride at room temperature was added drop-wise with stirring 2.0 g 2-methylpent-2-enal (XIV). The phosphorus pentoxide caked and the solution turned yellow. After the addition was complete, the mixture was stirred at room temperature for several hours, the liquid decanted and the solid residue extracted with methylene chloride and the combined solutions were distilled through a spinning-band column. The major fraction boiled at 89.5–90°/40 mmHg. The ^{19}F NMR spectrum showed a doublet, $J = 7$ Hz, at $\delta = -68.99$. The ^1H NMR spectrum showed a triplet, $J = 5$ Hz, at $\delta = 1.15$, $CH_2C\underline{H}_3$, a singlet at $\delta = 2.02$, $=CC\underline{H}_3$, a quartet, $J = 5$ Hz, at $\delta = 2.65$, $C\underline{H}_2CH_3$, a septet, $J = 7$ Hz, at $\delta = 5.02$, $C\underline{H}(CF_3)_2$, and a broad singlet at $\delta = 7.37$, $=C\underline{H}$.

The infrared spectrum showed absorptions at 7.4, 7.5, 7.7, 7.8, 7.9, 7.95, 8.1, 8.3, 8.6, 8.7, 9.0, 9.1, 10.0, 10.1, 11.0, 11.3, 11.6 and 14.3 μ. The mass spectrum showed a significant ion at M−HCN.

1-[1,1,1,3,3,3-Hexafluoro-2-propyl]-3,5-diphenylpyrazole

A mixture of 4.6 g HFAH, 4.2 g chalcone, and 6 g phosphorus pentoxide in 10 ml methylene chloride was heated for 1 h. The solution was decanted from the phosphorus residues and solvent removed on the rotary evaporator. The crude product was recrystallized from ethanol/water to give 3.7 g of yellow plates, m.p. 81–84°. Calcd. for $C_{18}H_{12}F_6N_2$: C, 58.4; H, 3.2; N, 7.5%. Found: C, 58.1; H, 3.2; N, 7.3%.

The infrared spectrum showed bands at 6.7, 6.8, 6.9, 7.2, 7.4, 7.5, 7.7, 7.8, 7.9, 8.1, 8.3, 8.8, 9.0, 11.0, 11.3, 11.5, 13.3 and 14.3 μ.

The ^1H NMR spectrum showed a septet, $J = 6.3$ Hz, at $\delta = 5.08$, $-C\underline{H}$, a singlet at $\delta = 6.67$, $=C\underline{H}$, an aromatic multiplet at $\delta = 7.3$, 8H, and at $\delta = 7.82$, 2H. The ^{19}F NMR spectrum showed a doublet at $\delta = -68.88$, $J = 6.5$ Hz.

The UV spectrum (methanol) showed $\lambda_{max.} = 305$ ($\varepsilon = 1140$); $\lambda_{max.} = 285$ ($\varepsilon = 1680$) and $\lambda_{max.} = 245$ ($\varepsilon = 27\,400$).

REFERENCES

1 W. J. Middleton and C. G. Krespan, *J. Org. Chem.*, *30* (1965) 1398.
2 W. J. Middleton and D. M. Gale, *Org. Synth.*, *50* (1970) 6.
3 O. Glemser and S. P. Von Halasz, *Chem. Ber.*, *102* (1969) 3333.
4 R. Filler, Y. S. Rao, A. Biezais, F. N. Miller and V. D. Beaucaire, *J. Org. Chem.*, *35* (1970) 930.
5 L. Cavalli and P. Piccardi, *Chem. Comm.*, (1969) 1132.
6 D. Wurmb-Gerlich, F. Vögtle, A. Mannschreck and H. A. Staab, *Justus Liebig's Ann. Chem.*, *708* (1967) 36.
7 J. E. Anderson and J. M. Lehn, *J. Amer. Chem. Soc.*, *89* (1967) 81.
8 M. Raban and E. Carlson, *J. Amer. Chem. Soc.*, *93* (1971) 685.