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FLUORO-KETONES VIII. SYNTHESIS OF SOME FLUOROQUINOXALINE COMPOUNDS FROM FLUOROKETONES

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SUMMARY

The reaction between a perfluoroalkylether α,β-diketone or perfluoroalkyletherketoester and o-phenylenediamine yielding quinoxaline compounds was studied in detail. The various intermediate compounds leading to the formation of the quinoxalines were examined by NMR, MS, GC/MS and IR. 2,3-Perfluoroalkylether substituted quinoxaline is the major product of the reaction. In addition however, the formation of a minor product 3-perfluoroalkylether-2(1H)-quinoxalinone, indicates an alternate reaction path.

INTRODUCTION

Reactions of o-phenylenediamine with perfluoroalkyl α,β-diketones yield 2,3-diperfluoroalkyl substituted quinoxalines [1,2]. Generally, such a reaction is carried out in order to characterize an α,β-diketone by forming a quinoxaline derivative. It has also been suggested as a potential polymer forming reaction for polyperfluoroalkylquinoxaline polymers [2]. Recently we have reported the synthesis of perfluoroalkyl α,β-diketones ($R_fC(O)C(O)R_f$) and perfluoroalkylketoesters ($R_fC(O)C(O)OC_2H_5$) [3]. We have found that both classes of compounds react with o-phenylenediamine to yield quinoxaline derivatives. The results of that study are now being reported.

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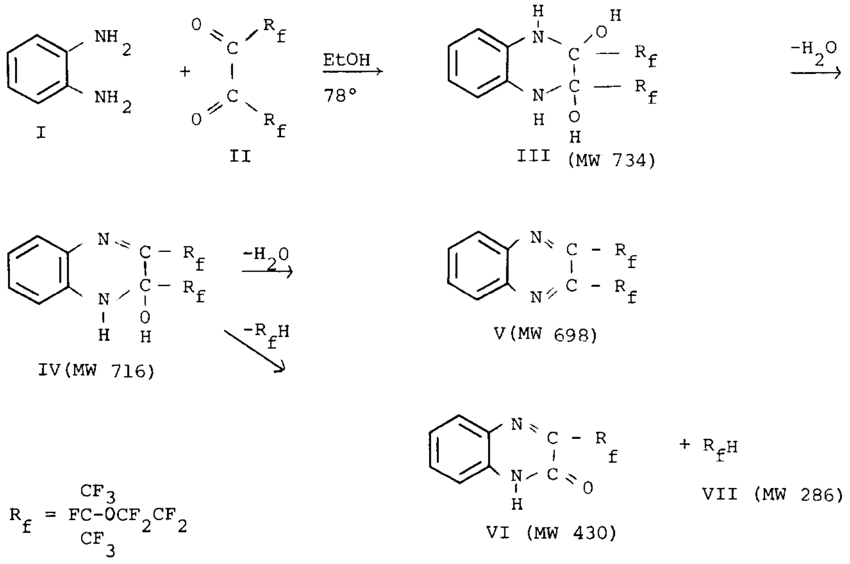
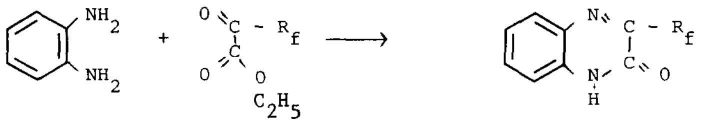
DISCUSSION

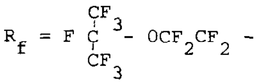
On close examination of the reaction between a perfluoroalkyl α,β-diketone and o-phenylenediamine we have found a mixture of reaction products. As an example, the diketone $[F(CF_3)_2COCF_2CF_2C(O)]_2$ (II) [3] and the diamine I in ethanol at 78° yielded on GC analysis (see however, NMR analysis data) two cyclic products V and VI in a 92:6 (GC area) ratio. In addition $F(CF_3)_2COCF_2CF_2H$, (VII) a low boiling (46°) [4] component was also found by GC/MS analysis of the reaction mixture. Formation of these products can be rationalized by considering the following reaction scheme:



By repeating the experiment at -78° and isolating the reaction product at low temperature (see experimental) the intermediate compound III could be isolated. This compound was characterized by IR, MS, ^1H and ^{19}F NMR and elemental analysis. The compound rapidly decomposes on heating between 45° → 52°. On further heating to 130° the quinoxaline compound V is formed as the principal product. A GC/MS analysis of III indicated compounds III, IV, V, VI and VII. Apparently, on volatilization of III in the gas chromatograph (inlet port), the compound thermally decomposes in part to yield the decomposition products (IV, V, VI and VII) in addition to the undecomposed portion of III. Compound VI can also be synthesized in high yield by an alternate route through the reaction between the diamine I and a ketoester VIII [3].



I VIII VI



$R_f = F\,C(CF_3)_2 - OCF_2CF_2 -$

Infrared analysis of VI indicates the absence of any significant (detectable) enolization as shown by the lack of an OH stretching vibration and the presence of a C=O stretching vibration. We had considered the possibility of VI being formed by hydrolysis of a $F(CF_3)_2COCF_2CF_2$ group from V. On refluxing V in an aqueous medium, however, no hydrolysis of product occurred. The formation of VI, therefore, must arise from the transient intermediates, e.g. III and IV.

Since the model reaction between a perfluoroalkyl α,β-diketone and a diamine I yields two quinoxaline products, (V and VI) it would suggest that this type reaction would not be a useful polymer forming reaction (as an example between a perfluorotetraketone and a tetraamine) leading to perfluoroalkylquinoxaline polymers as has previously been suggested [2]. The competing reaction forming the hydro-quinoxalinone VI would terminate any further polymer chain growth and thus limit the molecular weight of the quinoxaline polymer.

Mass spectral analysis

The mass spectrum of compound III (sample stored at -15° prior to analysis), obtained by direct probe MS analysis is shown in Fig 1. This compound exhibits a molecular ion at m/e 734, $M-H_2O$ at 716 and a M-F at m/e 715. The ion fragment at m/e 698 is produced as a result of the loss of two molecules of H_2O. The intense ion at m/e 431 is the result of a loss of one molecule of H_2O and a $F(CF_3)_2COCF_2CF_2$ group from III. If compound III is analyzed in the GC/MS mode it is easily thermally decomposed into products via two possible mechanisms. The major mode of decomposition produces V, the result of complete dehydration of III. The mass spectrum of the quinoxaline V is shown in Fig 2. The compound exhibits a molecular ion at m/e 698 and a M-F ion at 679. The most abundant ion is at m/e 463 which is attributed to the loss of a $F(CF_3)_2COCF_2$ group. Other characteristic ions are m/e 513 and m/e 413 indicative of $M-F(CF_3)_2CO$ and $M-F(CF_3)_2COCF_2CF_2$ respectively.

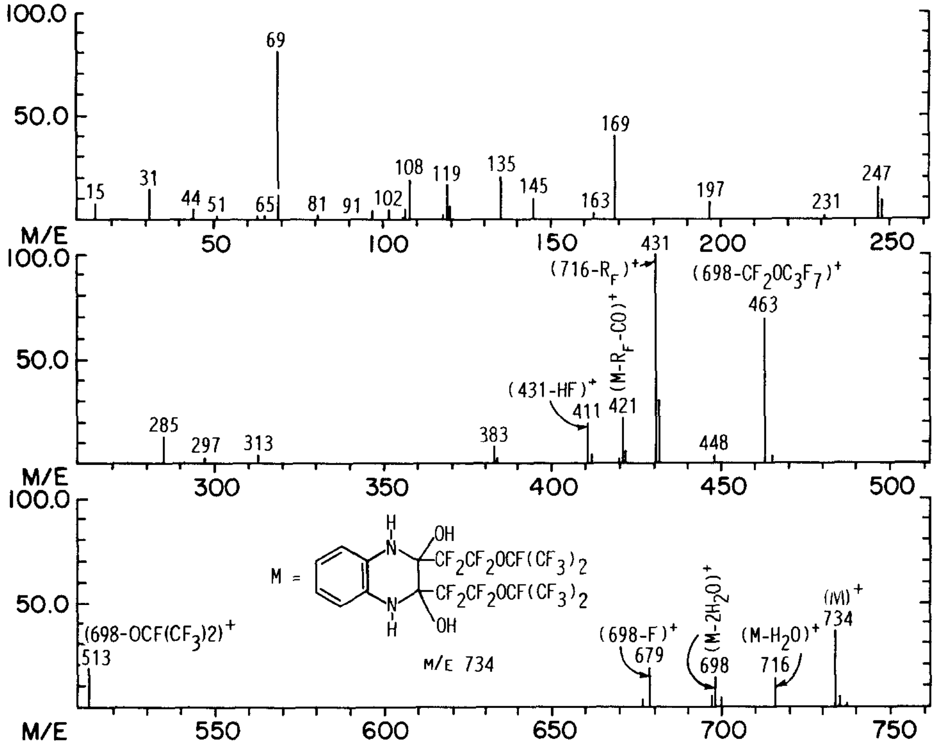


Fig. 1. Mass Spectrum of Compound III.

A minor mode of thermal decomposition of compound III (GC/MS) first produces IV which in turn yields VI and VII. Even though the presence of IV was not detected in this GC/MS mode, it was observed when III was analyzed by the direct probe MS. In this mode the m/e 716 (M-H_2O) is the parent ion and the m/e 697 represents an M-F ion as shown in Fig 1. Even though the direct probe was not heated, the heat from the source (∿ 180°) was sufficient to thermally decompose III so that the intermediate IV was detected as a transient species. In the GC/MS mode the presence of VI and VII was confirmed and their mass spectra are shown in Figures 3 and 4 respectively. Compound VI shows a very strong molecular ion peak at m/e 430 and a M-F at m/e 411. The loss of $F(CF_3)_2COCF_2$ yields the most intense ion at m/e 195 which subsequently loses a CO to yield the ion at m/e 167. Compound VII is highly volatile and was produced in small yield during the thermal decomposition, thus making the mass spectrum less intense but still recognizable. The most intense peaks at m/e 51, 69, 101, 169 and 235 are due

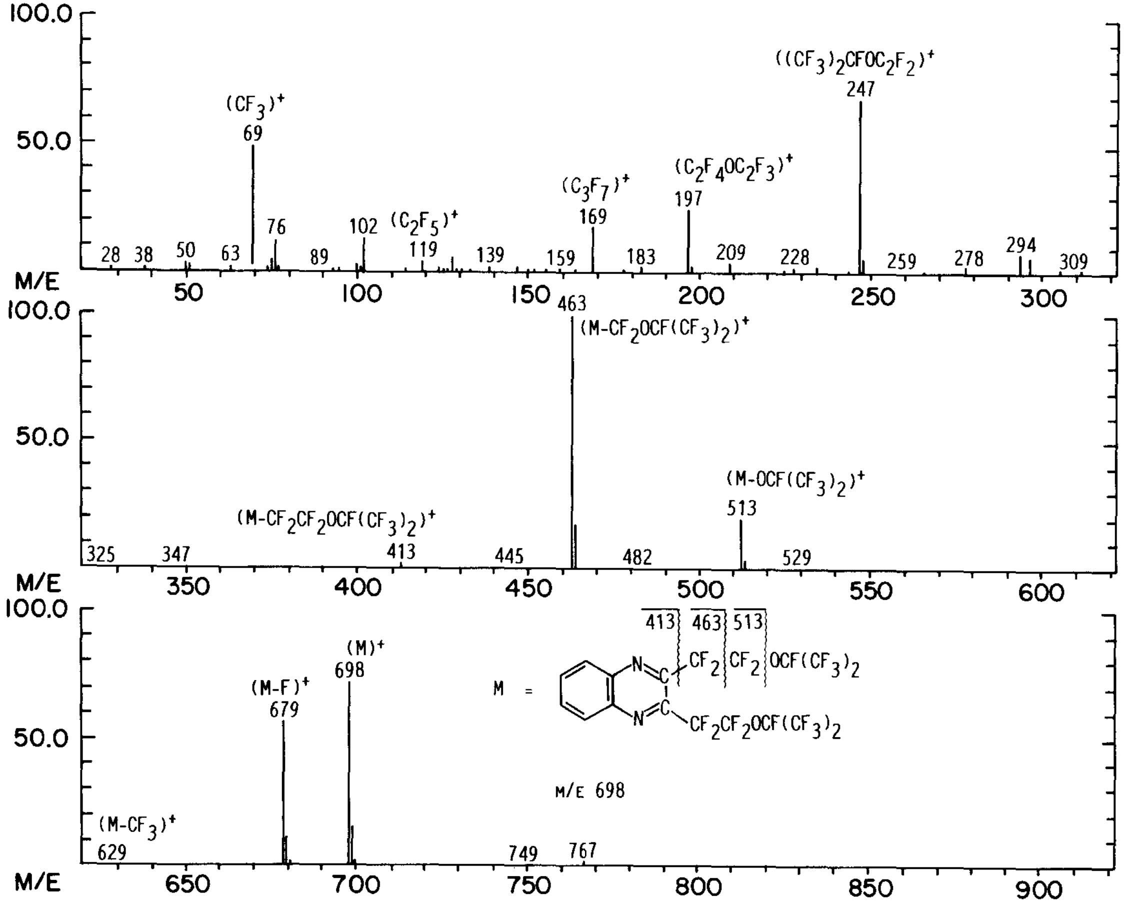


Fig. 2. Mass Spectrum of Compound V.

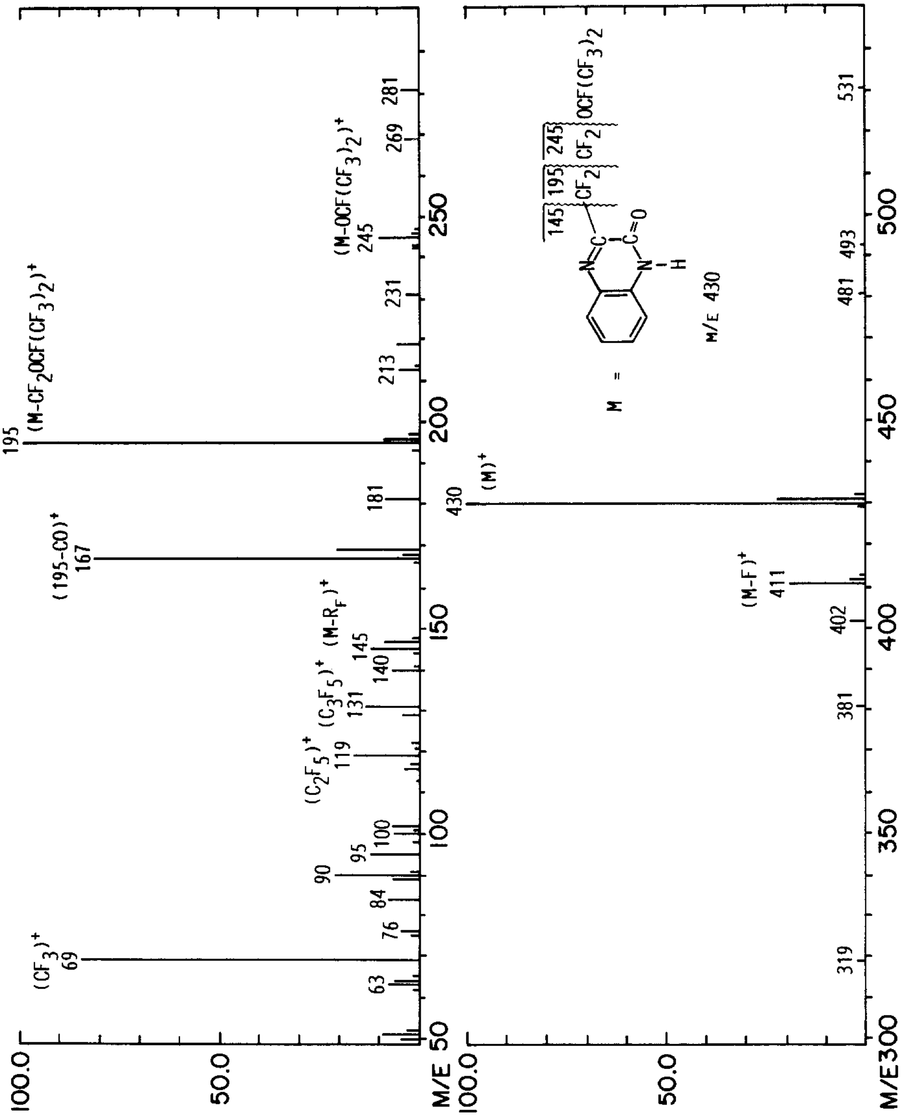


Fig. 3. Mass Spectrum of Compound VI.

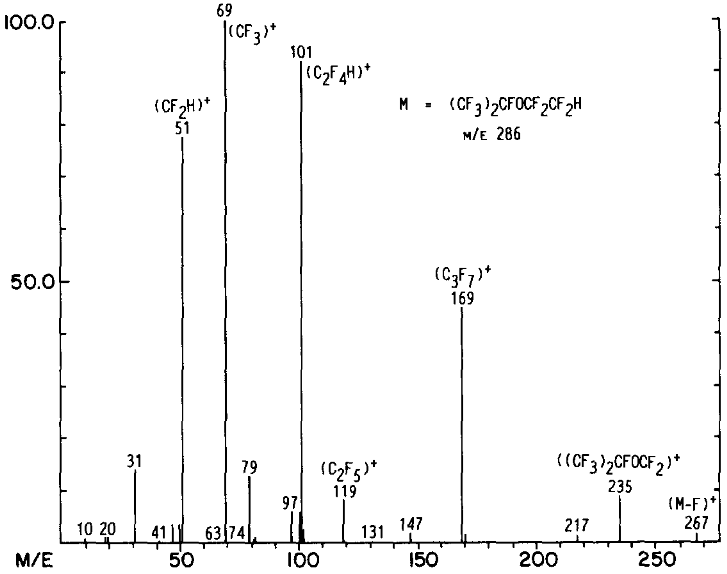


Fig. 4. Mass Spectrum of Compound VII.

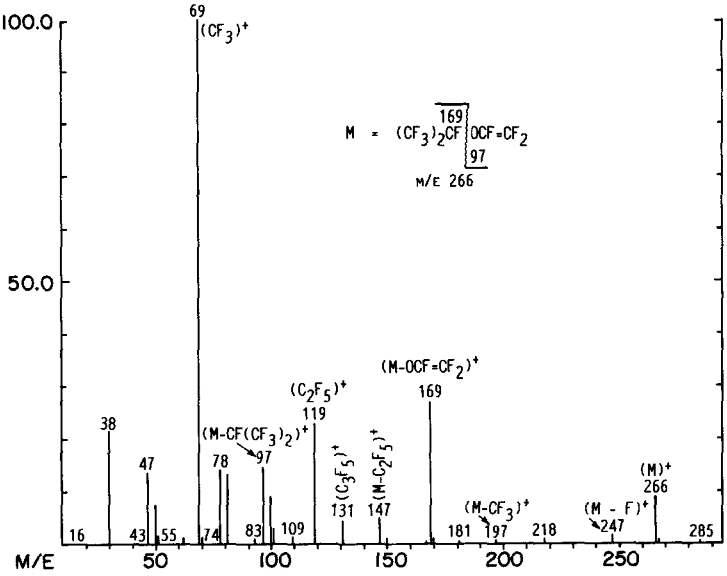


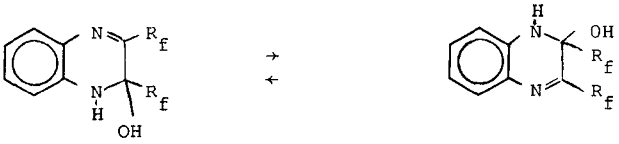
Fig. 5. Mass Spectrum of Compound $C_3F_7OCF = CF_2$.

to CF_2H, CF_3, C_2F_4H, C_3F_7, and $F(CF_3)_2COCF_2$ ion fragments respectively. These fragments compared favorably with the most intense peaks in the mass spectrum of a reference compound $F(CF_3)_2COCF_2CF_2H$ prepared previously [4] as shown in Fig 4. This spectrum is distinctly different from that of $F(CF_3)_2COCF{=}CF_2$ in that the molecular ion for the olefin is shown to be at m/e 266 as shown in Fig 5. There are no fragments found in the mass spectrum of the olefin which can be attributed to the presence of a C-H structure. The thermal decomposition of IV therefore yields $F(CF_3)_2COCF_2CF_2H$ and not the olefin.

Nuclear magnetic resonance analysis

Compound III, (see experimental section) was dissolved in $CDCl_3$. The ^1H spectrum obtained at the ambient probe temperature, 40°, showed that it was actually a mixture of III and IV. Two AA'BB' multiplets centered at δ = 6.7 and δ = 8.1 ppm were evident in the spectrum. Broad absorptions at δ = 3.2, 4.9 and 5.6 ppm due to OH and NH protons were also evident. The δ = 6.7 ppm multiplet is assigned to the aromatic protons of III. The δ = 8.1 ppm multiplet is characteristic of a 2,3 disubstituted quinoxaline (5) and is assigned to IV.

Based on limited data, the symmetry of the aromatic multiplet at δ = 8.1 may be explained by rapid exchange of the labile OH and NH protons between the two structures IVa and IVb



IVa IVb

The dehydration of compound III to compound IV was measured by recording and integrating the ^1H spectrum periodically, at 25 min intervals, for 100 min and again the next day (approximately 20 h later). The results of this experiment are shown in Table 1. The relative intensity of the 6.7 and 8.1 ppm absorptions have been converted to mole fractions in the table. The good agreement between calculated and observed values shows that only one equivalent of H_2O is lost as III converts to IV. During the experiment the OH and NH absorptions changed in chemical shift and intensity.

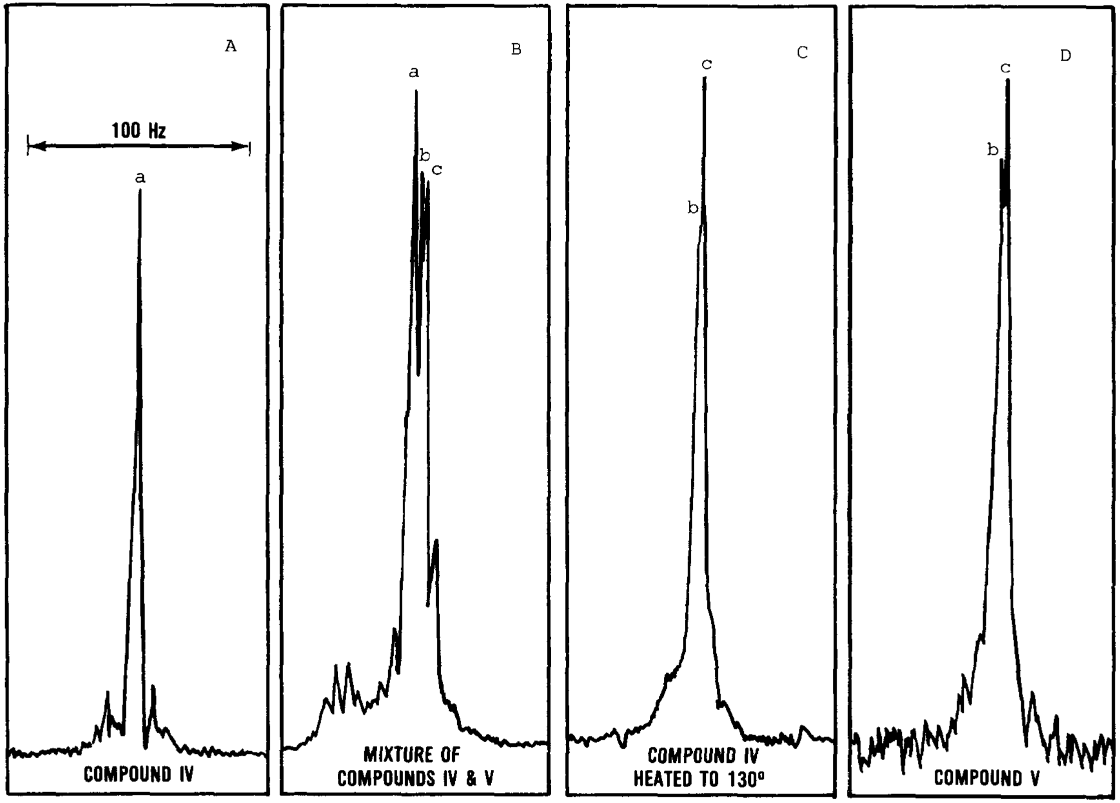


Fig. 6. ^{19}F NMR at 81ppm from $CFCl_3$
A = IV from decay of III (see test)
B = mixture of IV and V (see experimental, at 78°C)
C = mixture of IV and V (see experimental, after 1h at 130°C)
D = V (see experimental, IV and V after 2h at 130°C)

After several days, the multiplet at δ= 6.7 ppm was no longer evident in the ^{1}H spectrum. Only the multiplet at δ= 8.1 and an OH and NH absorption at δ = 2.5 ppm were observed. The rate of conversion of III to IV appears to be partially dependent on the rate of diffusion of water out of the solvent, $CDCl_3$.

^{19}F spectra were useful in characterizing IV and V. Their ^{1}H spectra were similar and could not be readily used to distinguish IV from V. Figure 6 shows the ^{19}F spectra of the CF_3 plus OCF_2 groups for IV, V and mixtures of these two compounds obtained at several times after heat treatment. The CF_3 absorption appears as a singlet in IV and is labeled a. The CF_3 absorption in V appears as a doublet and is labeled b and c.

TABLE 1

Conversion of compound III to IV from ^{1}H NMR spectra

Time	Mole fraction of III*	Mole fraction of IV*	Calculated ** ratio of $\frac{OH + NH}{aromatic\ H}$ III + 1/2 IV	Observed *** ratio of $\frac{OH + NH}{aromatic\ H}$
25 min	0.62	0.38	0.81	0.83
50 min	0.58	0.42	0.79	0.80
75 min	0.46	0.54	0.73	0.74
100 min	0.41	0.59	0.71	0.71
20 h	0.21	0.79	0.61	0.57

*Relative intensity of 6.7 ppm and 8.1 ppm absorptions used to calculate mole fractions.

**If III is converting to IV, the ratio of OH + NH protons to aromatic protons should be equal to the mole fraction of III plus 1/2 the mole fraction of IV since the ratio of OH + NH protons to aromatic protons is 1 for III and 1/2 for IV. If III is converting to V, the ratio of OH + NH protons to aromatic protons should be equal to the mole fraction of III since the ratio of OH + NH protons to aromatic protons is 1 for III and 0 for V.

***Ratio of integrated intensity of OH + NH protons to aromatic protons.

Since the chemical shift difference between CF_3 plus OCF_2 is very small in IV and V, the spectra are more complex than the first order spectrum obtained for compound VI. Hydrogen bonding between CF_3 and the labile OH and NH as well as a reduction in the coupling between the OCF and CF_3 fluorines due to hindered rotation causes the ^{19}F spectra to be distinctive for the two compounds, although complex. Similar effects of hydrogen bonding and hindered rotation on the ^{19}F spectra of quinoxalines and other nitrogen heterocyclic compounds have been reported [6].

Table 2 shows the ^{1}H and ^{19}F chemical shifts and coupling constants for compounds IV, V and VI.

TABLE 2

^{1}H and ^{19}F NMR spectra of IV, V and VI

Compound	^{1}H Chemical shifts[a]		^{19}F Chemical shifts[c]			
	Aromatic H	OH+NH	CF_3	OCF_2	CCF_2	OCF
III	6.7	3.2,4.9,5.6	80.7	78.4	119.3,120.2,120.7	145.6
IV	8.1[b]	2.5	81.0	81.0	108.8	145.9
V	8.1[b]		81.1	81.1	108.8	145.9
VI	7.6[b]	12.9	80.7	81.7	115.6	145.4

Compound	^{19}F Coupling constants					
	$^{3}J_{CF_3CFO}$	$^{5}J_{CF_3\text{-C-O-}CF_2}$	$^{6}J_{CF_3\text{-C-O-}CCF_2}$	$^{3}J_{OCF_2CF_2}$	$^{4}J_{CF_2OCF}$	$^{5}J_{CF_2\text{-C-O-CF}}$
III	2	4.0	0	0	24	0
IV	2[d]	2.5[d]	0	0[e]	18	0
V	2[d]	0	0	0[e]	18	0
VI	2.5	5.5	0	2.7	25	0

[a] Measured from internal TMS.

[b] Center of multiplet. Partial analysis of the AA'BB' spectrum gives a chemical shift difference between A and B of 11.6 Hz and 10.3 Hz for $J_{AB} + J_{AB'}$. Analysis of the complex ABCD spectrum of VI was not done.

[c] Measured from internal $CFCl_3$.

[d] Estimated values. Analysis of the complex multiplet (see text) would be needed to obtain exact values.

[e] The CF_2 absorption is a singlet in IV and V. Molecular models show that there is steric hindrance to rotation of the CF_2 group. The CF_2 absorption is a triplet in VI.

EXPERIMENTAL

General comments

All reactions were carried out in oven-dried glassware under an atmosphere of dry nitrogen. All melting and boiling points are uncorrected. Gas chromatographic analyses (GC) were performed on a Perkin-Elmer Sigma 1 using 6' stainless steel columns (1/4" o.d.) packed with 10% SE-30 on Chromosorb W. Mass spectra were obtained on a DuPont Model 21-491 magnetic mass spectrometer using the electron impact mode. Infrared spectra were recorded on a Perkin-Elmer Model 600 computing infrared spectrophotometer. ^{1}H and ^{19}F spectra were obtained on a Varian A56/60 NMR spectrometer equipped with a Varian 620I computer and spectrosystem 100 interface. $(CH_3)_4Si$ and $CFCl_3$ were used as internal standards for ^{1}H and ^{19}F chemical shift measurements respectively. The multiscan averaging and integral plotting capability of the system was used to enhance the signal to noise ratio since the compounds were measured in dilute solutions. Five scans were averaged for each spectrum to obtain the mole fraction values shown in Table 2. The resolution is approximately ± 0.5 Hz so that coupling constants of less than 1 Hz were not resolved and are reported as 0. The solvent $CDCl_3$ was dried by passing it through a silica gel column.

Synthesis of compound III

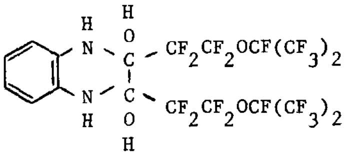
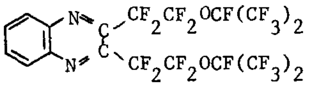
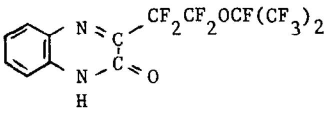
To an ethanol (15 ml) solution of o-phenylenediamine (0.345 g, 3.19 mmol) was added $[F(CF_3)_2COCF_2CF_2C(O)\rceil_2$ (2.0 g, 3.19 mmol) at -78°, and the reaction solution was allowed to warm to -30°. After 10 min, the ethanol was removed by distillation at reduced pressure at 0°. The resulting pale brown residue was washed with precooled (0°) n-hexane (3x1 ml), to yield compound III, 1.5 g (66%). Compound III was kept in a freezer at -15° to prevent any decomposition by dehydration. See Table 3.

Synthesis of compound V

An ethanol (25 ml) solution of $[F(CF_3)_2COCF_2CF_2C(O)\rceil_2$ (4.0 g, 6.39 mmol) and o-phenylenediamine (0.69 g, 6.39 mmol) was heated to reflux temperature for 3 h. The ethanol was removed under vacuo leaving a viscous product. GC/MS analysis of this material indicated two major compounds V (92 GC relative area %) and VI (6 GC relative area %) and the minor product VII. The mixture was passed through a silica gel (1 x 5 cm) column using diethyl ether/n-hexane mixture as the eluent. The colored solution thus obtained was

TABLE 3

Analyses of compounds

Compound		b.p., m.p. or decomp. (°C)	IR (cm^{-1})	MS	Combustion data % calc'd/found C	H	N
	(III) (nc)	decomp. 45 - 52	3535(OH)[b] 3430(NH)	$734(M)^+$ $716(M-H_2O)^+$ $698(M-2H_2O)^+$	29.44/29.36	1.10/0.96	3.82/4.35
	(V) (nc)	b.p. 270 [a]	1610(C=C)[c,e] 1560(C=N)	$698(M)^+$	30.96/30.73	0.58/0.66	4.01/4.05
	(VI) (nc)	m.p. 142	1670(C=O)[d] ∿ 3200(NH) 1560(C=N) 1610(C=C)	$430(M)^+$	36.30/36.21	1.17/1.17	6.51/6.52

[a] Micro-boiling point determined by Swiwoloboff's method and differential thermal analysis.

[b] CCl_4 solution.

[c] Neat liquid.

[d] KBr pellet.

[e] Aromatic C=C ring vibration.

washed with water (3 x 2 ml) and the colorless organic layer dried ($MgSO_4$). The solution was concentrated under vacuo leaving a crude product (3.8 g, 85% yield). GC analysis of this product indicated one compound V. ^{19}F NMR of this product however, indicated two possible compounds IV and V (see NMR discussion). Apparently injection of the product into the GC injection port (280°) dehydrated IV into V so that only one compound was indicated. In order to convert the mixture of IV and V into a single compound V, the mixture was heated at 130° for 2 h. The mixture was analyzed by ^{19}F NMR after 1 and 2 h to follow the progress of dehydration. After 2 h, the conversion of IV into V was complete. See Table 3.

Synthesis of compound VI

An ethanol (30 ml) solution of $F(CF_3)_2COCF_2CF_2C(O)C(O)OC_2H_5$ (9.42 g, 24.4 mmol) and o-phenylenediamine (2.64 g, 24.4 mmol) was heated to 78° for a period of 2 days. The solvent was removed to almost dryness at reduced pressure. The residue was washed with n-hexane (3 x 10 ml) to yield the crude product (10.3 g). The crude product was recrystallized from a mixture of diethyl ether and petroleum ether (37° → 58°) to afford a white crystalline product VI 8.1 g (77%). See Table 3.

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