Journal of Fluorine Chemistry, 12 (1978) 439–461
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Received: April 11, 1978

SYNTHESIS OF FLUORINATED α-DIKETONES AND AS-TRIAZINES AND QUINOXALINES

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SUMMARY

Benzylheptafluoropropyl ketone and 1,8-diphenyl-3,3,4,4,5,5,6,6-octafluoro-2,7-octanedione were prepared by the reaction of benzylmagnesium chloride with heptafluorobutyric acid and octafluoroadipic acid, respectively. Oxidation of the methylene ketones with selenium dioxide produced 1-phenyl-3,3,4,4,5,5,5-heptafluoro-1,2-pentanedione and 1,8-diphenyl-3,3,-4,4,5,5,6,6-octafluoro-1,2,7,8-octanetetrone. Both α-diketones were yellow and readily formed crystalline hydrates. Several alternate routes to the synthesis of the fluorinated α-diketones were investigated. The α-diketones were reacted with amidrazones and aromatic *o*-diamines to form *as*-triazines and quinoxalines, respectively.

INTRODUCTION

Fluorine incorporated within polymers generally imparts several attractive properties such as chemical inertness, thermal and thermooxidative stability, and radiation stability. Highly fluorinated or perfluorinated heterocyclic polymers would be promising candidates for use as sealants, coatings, adhesives, and composite matrices in harsh environments demand-

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ing high chemical, radiation, and thermal stability. Several partially fluorinated heterocyclic polymers such as the benzoxazoles [1,2] and the *as*-triazines [3,4] and perfluorinated heterocyclic polymers such as *sym*-triazines [5,6] have been reported. The synthetic route to *as*-triazines polymers involves the reaction of a diamidrazone with a bis(α-diketone). This route provides an avenue to the direct preparation of highly fluorinated and perfluorinated heterocyclic polymers from highly fluorinated bis-(phenyl α-diketones) or perfluorinated bis(α-diketones). In pursuit of this goal, highly fluorinated phenyl α-diketones were prepared. Their synthesis, purification, characterization, and conversion to *as*-triazines and quinoxalines are discussed.

RESULTS AND DISCUSSION

α-Diketones

There are several methods available for the synthesis of α-diketones. A common synthetic route involves the oxidation of ketones with an adjacent benzylic group. Using this route, 1-phenyl-3,3,4,4,5,5,5-heptafluoro-2-pentanone (I) was prepared and subsequently oxidized to 1-phenylheptafluoro-1,2-pentanedione (II) as shown in Eq. 1. The α-diketone was converted to a mono-hydrate (IIa) and a mono-deuterate (IIb). Similarly, 1,8-diphenyl-

$$\begin{tikzcd}
C_3F_7CO_2H + C_6H_5CH_2MgCl \arrow[r] & C_3F_7COCH_2C_6H_5 \arrow[d, "\text{I}"] & \\
C_3F_7COCOC_6H_5 \cdot H_2O & C_3F_7COCOC_6H_5 \arrow[l, "H_2O"'] \arrow[r, "D_2O"] & C_3F_7COCOC_6H_5 \cdot D_2O \\
\text{IIa} & \text{II} & \text{IIb}
\end{tikzcd} \qquad (1)$$

3,3,4,4,5,5,6,6-octafluoro-2,7-octanedione (III) was prepared and converted to 1,8-diphenyl-3,3,4,4,5,5,6,6-octafluoro-1,2,7,8-octanetetrone (IV) as depicted in Eq. 2. The bis(α-diketone) IV readily formed a dihydrate (IVa) and a dideuterate (IVb).

$$\begin{tikzcd}
\mathrm{HO_2C(CF_2)_4CO_2H + C_6H_5CH_2MgCl} \arrow[r] & \underset{\mathrm{III}}{\mathrm{C_6H_5CH_2CO(CF_2)_4COCH_2C_6H_5}} \arrow[d, "\mathrm{SeO_2}"] \\
\mathrm{X_2O\cdot C_6H_5COCO(CF_2)_4COCOC_6H_5\cdot X_2O} & \underset{\mathrm{IV}}{\mathrm{C_6H_5COCO(CF_2)_4COCOCH_2C_6H_5}} \arrow[l, "\mathrm{X_2O}"']
\end{tikzcd} \qquad (2)$$

X = H: IVa

X = D: IVb

Physical and analytical data for the various fluorinated ketones are presented in Table 1; infrared and NMR spectroscopic data for these compounds are shown in Table 2.

The synthesis of compound I in 75% yield from the reaction of benzylmagnesium chloride and heptafluorobutyronitrile has been described [7]. Using this method, compound I was prepared in 56% yield. Since the preparation of heptafluorobutyronitrile from the corresponding acid requires several steps, the synthesis of compound I was modified to use heptafluorobutyric acid or its more readily accessible derivatives according to general procedures described in the literature [8,9]. Reaction of benzylmagnesium chloride with lithium heptafluorobutyrate gave compound I in yields of 22.8 to 37.2%. Somewhat better yields (41.3%) of compound I were obtained from the reaction of benzylmagnesium chloride with heptafluorobutyric acid.

The well-known method for the synthesis of ketones using acyl chlorides and dialkyl cadmium compounds failed entirely, evidently because Tiffeneau rearrangement of benzyl to tolyl compounds (V) ($R_F = C_3F_7$) took place during the treatment of benzylmagnesium chloride with cadmium chloride.

The most straightforward conversion of benzyl heptafluorobutyl ketone (I) to 1-phenylheptafluoro-1,2-pentanedione (II) is oxidation by selenium dioxide. This reaction was accomplished by heating compound (I) with selenium dioxide in boiling acetic anhydride to provide 70-95% yields of a bright yellow α-diketone (II).

The α-diketone (II) readily formed a white crystalline hydrate (IIa) and a deuterate (IIb) on contact with water or deuterium oxide, respectively. The hydrate was purified by recrystallization from water or from

TABLE 1

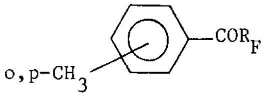
CHARACTERIZATION OF FLUORINATED KETONES

Compound No.	Structure	M.p. °C	Bp, °C/mm	Formula	Elemental analysis* C	H	F
I	$C_6H_5CH_2COC_3F_7$	16-17	80-85/22**	$C_{11}H_7F_7O$	45.72 (45.82)	2.62 (2.45)	—
II	$C_6H_5COCOC_3F_7$	—	80-82/19	$C_{11}H_5F_7O_2$	43.32 (43.72)	2.06 (1.67)	—
IIa	$C_6H_5COCOC_3F_7 \cdot H_2O$	70-71	—	$C_{11}H_7F_7O_3$	41.39 (41.26)	2.01 (2.20)	41.60 (41.54)
IIb	$C_6H_5COCOC_3F_7 \cdot D_2O$	67-68.5	—	$C_{11}H_5D_2F_7O_3$	—	—	—
III	$[C_6H_5CH_2CO(CF_2)_2]_2$	104-105	—	$C_{20}H_{14}F_8O_2$	54.91 (54.80)	3.60 (3.22)	34.30 (34.67)
IV	$[C_6H_5COCO(CF_2)_2]_2$	58-60	155-157/0.35	$C_{20}H_{10}F_8O_4$	51.16 (51.51)	2.06 (2.16)	32.33 (32.59)
IVa	$[H_2O \cdot C_6H_5COCO(CF_2)_2]_2$	122-124.5	—	$C_{20}H_{14}F_8O_6$	48.27 (47.82)	3.02 (2.81)	30.09 (30.26)
IVb	$[D_2O \cdot C_6H_5COCO(CF_2)_2]_2$	127-130	—	$C_{20}H_{10}D_4F_8O_6$	48.61 (47.44)	3.58 (3.58)	29.91 (30.02)
VI	$C_6H_5CHBrCOC_3F_7$	—	50-54/0.7	$C_{11}H_6BrF_7O$	35.02 (35.99)	1.50 (1.62)	—
VIII	$[C_6H_5C(CO_2C_2H_5)_2COCF_2CF_2]_2$	108.5-109	—	$C_{32}H_{30}F_8O_{10}$	52.78 (52.90)	4.14 (4.16)	21.23 (20.92)

*Theoretical values are reported in parentheses
**Ref. [7], B.p. 51°C/3 mm

hexane but partial dehydration occurred during the heating as evidenced by the yellow color of the solutions. In addition products of lower melting points varying from 63 to 71°C were obtained on repeated recrystallizations. Even at room temperature, it is likely that partial reconversion of the hydrate to the anhydrous α-diketone took place. The solutions of the hydrate and deuterate, colorless initially, turned yellow on standing at room temperature, and ^{19}F NMR spectra showed two sets of peaks in ratios varying from 10:1 to 2.5:1. The smaller signals coincided with those of the anhydrous α-diketone. According to preliminary experiments with ^{13}C NMR hydration took place exclusively at the carbonyl group adjacent to the perfluoropropyl group as evidenced by the upfield shift of that carbonyl carbon which showed coupling to fluorine.

As an alternative to the selenium dioxide oxidation, other methods were tried to convert the methylene ketone (I) to the α-diketone (II). Treatment of (I) with nitric acid gave a complex mixture containing mainly benzoic and heptafluorobutyric acid and only a small amount of (II). Another method, dibromination of ketone (I) at the methylene group followed by hydrolysis failed in the first step. Bromination stopped at the stage of the monobromo compound, 1-bromo-1-phenyl-3,3,4,4,5,5,5-heptafluoro-2-pentanone (VI) (63% yield), and oxidative hydrolysis of this compound by lead nitrate was unsuccessful (95% recovery of the bromo compound).



V

$C_6H_5CHBrCOC_3H_7$

VI

Based on the experiences gained from the synthesis of 1-phenylheptafluoro-1,2-pentanedione (II), the preparation of 1,8-diphenyl-3,3,4,4,5,5-6,6-octafluoro-2,7-octanedione (III) was initiated. Surprisingly, the reaction of benzylmagnesium chloride and octafluoroadiponitrile gave mainly tars. Also the commercially available octafluoroadipoyl fluoride could not be used since it reacted with benzylmagnesium chloride to give primarily products of the Tiffeneau rearrangement, the o- and p-tolyl compounds (V) ($R_F = C_4F_8$-) rather than the desired benzyl ketone. The only successful route to the diketone (III) was the reaction of an excess of benzylmagnesium chloride (6 moles) with anhydrous octafluoroadipic acid (1 mole). The best results were obtained by preparing the benzylmagnesium chloride as fast as possible and by reacting it immediately with octafluoroadipic acid in boiling

TABLE 2
SPECTROSCOPIC CHARACTERIZATION OF FLUORINATED KETONES

		NMR Spectra	
Compound	Infrared Spectra*, cm^{-1}	^1H(ppm),TMS	^{19}F (ppm),HFB
$C_6H_5CH_2COC_3F_7$	3040,3000,1750,1600, 1490,1450,1390,1330, 1160-1240,1100,1010, 926,940,710,690	CH_2 3.77(s) C_6H_5 6.90-7.15(m)	CF_3 81.6(t) (J=10) CF_2 42.6(q) (J=9) CF_2 36.4(s)
$C_6H_5COCOC_3F_7$	1755,1690,1600,1580,1450, 1350,1320,1290,1180-1250, 1125,1040,950,850,750, 720,690,600	m,p 7.68-7.96(m) C_6H_5 o 8.10-8.28(m)	CF_3 80.5(t) (J=10) CF_2 42.9(q) (J=9) CF_2 36.0(s)
$C_6H_5COCOC_3F_7 \cdot H_2O$	3560,3360,2610,2500 1675,1590,1440,1340, 1220,1120,950,900,680	m,p 7.26-7.60(m) C_6H_5 o 7.80(dd) 8.12(d) H_2O 4.84(s)	CF_3 80.1(t) (J=10) CF_2 42.2 CF_2 37.0
$C_6H_5COCOC_3F_7 \cdot D_2O$	————————	m,p 7.25-7.62(m) C_6H_5 o 7.84(dd) 8.18(d)	CF_3 80.0(t) (J=10) CF_2 42.0 CF_2 37.0
$[C_6H_5CH_2CO(CF_2)_2]_2$	3020,1760,1490,1450, 1400,1185,1120,1030, 850,690	CH_2 3.93(s) C_6H_5 6.92-7.16(m)	CO ** CF_2 41.5(t) (J=12) CF_2 39.5(t) (J=13)
$[C_6H_5COCO(CF_2)_2]_2$	1780,1750,1685,1600, 1450,1190,1130,1050, 1000,870,850,685	m,p 7.38-7.66(m) C_6H_5 o 7.72-7.89	CO ** CF_2 44.5(t) (J=14) CF_2 41.6(t) (J=13)

TABLE 2 (continued)

Compound	Infrared Spectra,* cm^{-1}	NMR Spectra ^1H(ppm),TMS	 ^{19}F (ppm), HFB
$[H_2O \cdot C_6H_5COCO(CF_2)_2]_2$	————	C_6H_5 m,p 7.27-7.58 (m) o 8.24(d)	CO ** *** CF_2 43.4 CF_2 41.3
$[D_2O \cdot C_6H_5COCO(CF_2)_2]_2$	————	C_6H_5 m,p 7.44-7.68(m) o 8.30(d)	CO ** *** CF_2 45.3(m) CF_2 44.1(m)
$C_6H_5CHBrCOC_3F_7$	3080, 3050,1770,1700, 1600,1590,1500,1460, 1350,1180-1250,1130, 1020,950,930,910,750, 720,700	CHBr 5.84(s) C_6H_5 7.10-7.44(m)	CF_3 81.4 (t) (J=10) CF_2 44.8 (quintet) (J=10) CF_2 36.4(s)
$C_6H_5CH_2CO(CF_2)_4CO_2H$	————	CH_2 3.93(s) C_6H_5 m,p 7.13-7.24(m) o 6.99-7.07(m) -COOH	CO_2H ** CF_2 42.0(t)(J=11) CF_2 41.6(t)(J=11) CF_2 } 39.2 (m) CF_2 }

*Underscored numbers show strong maxima

**Assignment of signals to the two $-CF_2-$ groups is not unambiguous

***Additional minor signals at 30.0, 32.9, 44.5, 49.1 and 52.0

ether for at least one hour. Even under these precautions the yield of recrystallized diketone (III) was only 38.4 to 41.3%. A portion of the octafluoroadipic acid (12% on the average) had reacted with only one mole of benzylmagnesium chloride to give 7-phenyl-2,2,3,3,4,4,5,5,-octafluoro-6-ketoheptanoic acid (VII). In addition, a small amount ($\sim$2.5%) of unreacted perfluoroadipic acid was recovered. A considerable amount of tars made up the balance.

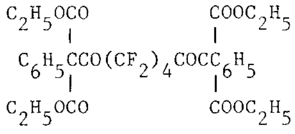
The diketone (III) was converted to the tetraketone (IV) by oxidation with selenium dioxide. When acetic anhydride or glacial acetic acid was used as the solvent, the distilled product was contaminated with a small amount of an acetate impurity (as evidenced by NMR). Purer product was obtained when the oxidation was carried out without solvent by heating the molten diketone (III) with selenium dioxide at 140-150^{o}C. The bright yellow tetraketone (IV) was obtained in 63% yield after purification by distillation or chromatography.

The tetraketone (IV) avidly absorbed water to give a white crystalline dihydrate (IVa). On melting, the white crystals reconverted to the yellow tetraketone (IV). Also during recrystallization from benzene containing a small amount of acetone some dehydration of the dihydrate took place since the colorless solution became pale yellow on heating. Similarly, a dideutrate (IVb) was prepared from (IV) and deuterium oxide.

Since the yields of the tetraketone (IV) were lower than desired, another synthetic approach was tried. Acylation of diethyl phenylmalonate with octafluoroadipoyl fluoride gave 1,8-diphenyl-3,3,4,4,5,5,6,6,-octafluoro-1,1,8,8-tetrakis(ethoxycarbonyl)-2,7-octanedione (VIII) which on ketonic fission and decarboxylation should give the tetraketone (IV). The acylation step gave the desired crystalline product (75% crude, 36% pure) but both acidic and alkaline hydrolysis failed to give the expected diketone (III). From alkaline hydrolysis (25% excess of 3% ethanolic potassium hydroxide at 31-32°) only phenylmalonic acid was isolated. Refluxing of VIII with 20% hydrochloric or 48% hydrochloric acid had no effect whereas treatment with 1% oleum at 25° gave only water soluble byproducts.

$$C_6H_5CH_2CO(CF_2)_4CO_2H$$

VII

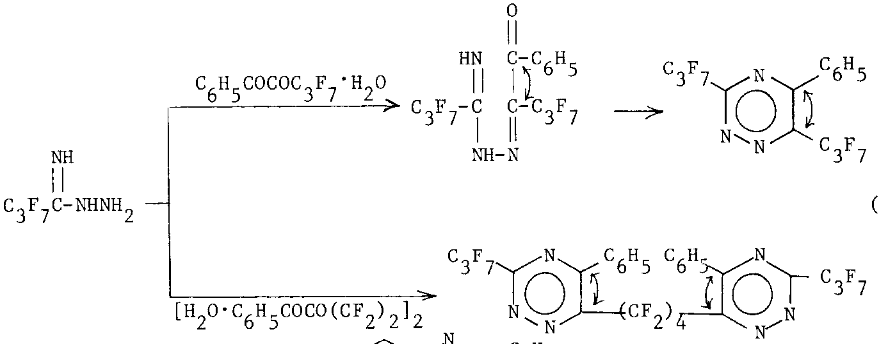


$$C_6H_5\overset{C_2H_5OCO}{\underset{C_2H_5OCO}{C}}CO(CF_2)_4CO\overset{COOC_2H_5}{\underset{COOC_2H_5}{C}}C_6H_5$$

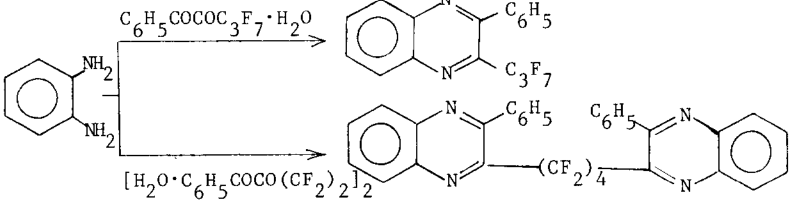
VIII

as-Triazine and Quinoxaline Derivatives

1-Phenyl-3,3,4,4,5,5,5-heptafluoro-1,2-pentanedione hydrate (IIa) and 1,8-diphenyl-3,3,4,4,5,5,6,6-octafluoro-1,2,7,8-octanetetrone dihydrate (IVa) were reacted with various amidrazones and aromatic o-diamines to yield the corresponding as-triazines and quinoxalines, respectively, as shown in Table 3. Representative reaction schemes are shown in Eq. 3 and 4.



(3)



(4)

These compounds were generally prepared by reacting stoichiometric quantities of the two reactants in ethanol at the reflux temperature. In two reactions, an uncyclized intermediate (Table 3) was isolated from the reaction of the amidrazone with the α-diketone in ethanol at ambient temperature. No attempts were made to isolate the uncyclized intermediate in the other reactions. These intermediates underwent cyclodehydration upon melting. When the reactions were conducted at the reflux temperature of the solvent, only the fully cyclized compounds were obtained.

The simplest as-triazine (compound X, Table 3) can have two isomers whereas all the remaining as-triazines in Table 3 can exist as three isomers. For example, compound (XIV) can be present as the following three isomers. This reaction product melted over a six-degree range (37-43°C) suggesting the presence of isomers. The elemental analysis agreed well with the theoretical values. High pressure liquid chromatography (HPLC) showed

TABLE 3

CHARACTERIZATION OF <u>as</u>-TRIAZINE AND QUINOXALINE COMPOUNDS

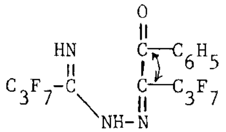
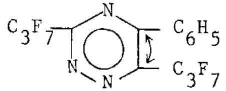
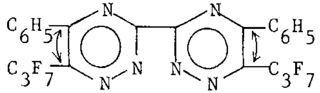
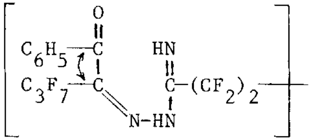
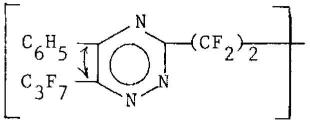
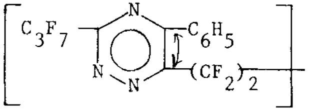
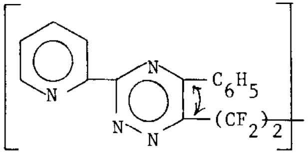
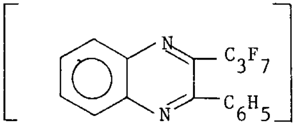
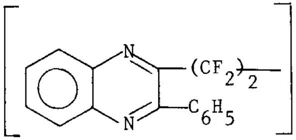
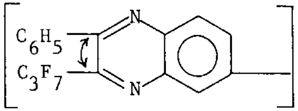
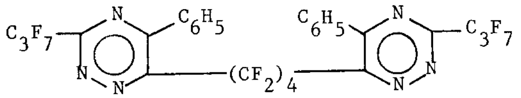
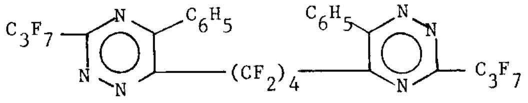
Compound No.	Structure	Form	Mp, °C	Formula	Elemental Analysis, %* C	H	N	F
IX		White solid	157-157.5 dec.	$C_{15}H_7F_{14}NO$	35.02 (35.24)	1.29 (1.38)	8.42 (8.22)	51.79 (52.03)
X		yellow oil	—	$C_{14}H_5F_{14}N_3$	35.21 (34.95)	1.03 (1.05)	9.02 (8.73)	55.06 (55.27)
XI		yellow needles	234-236	$C_{24}H_{10}F_{14}N_6$	44.06 (44.46)	1.67 (1.55)	12.77 (12.96)	40.80 (41.02)
XII		white solid	174-176 dec.	$C_{28}H_{14}F_{22}N_6O_2$	37.88 (38.02)	1.51 (1.60)	9.62 (9.50)	47.02 (47.26)
XIII		yellow solid	64-68 clears at 88	$C_{28}H_{10}F_{22}N_6$	39.47 (39.46)	1.12 (1.19)	10.14 (9.91)	48.83 (49.26)
XIV		waxy yellow solid	37-43	$C_{28}H_{10}F_{22}N_6$	39.86 (39.64)	1.38 (1.19)	10.56 (9.91)	48.37 (49.26)

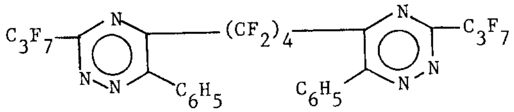
TABLE 3 (continued)

Compound No.	Structure	Form	Mp, °C	Formula	Elemental Analysis, %*			
					C	H	N	F
XV		pale yellow solid	246-256	$C_{32}H_{18}F_8N_8$	57.26 (57.66)	2.90 (2.72)	17.23 (16.82)	22.82 (22.80)
XVI		white needles	103.5-104.5	$C_{17}H_9F_7N_2$	54.68 (54.55)	2.43 (2.42)	7.32 (7.49)	35.79 (35.54)
XVII		white	218-219	$C_{32}H_{18}F_8N_4$	62.64 (62.95)	2.96 (2.97)	9.20 (9.18)	24.72 (24.90)
XVIII		off-white	319-321	$C_{34}H_{16}F_{14}N_4$	54.60 (54.70)	2.42 (2.16)	7.51 (7.50)	35.21 (35.63)

*Theoretical values reported in parentheses







three peaks of 75, 22, and 3% areas (in order of increasing retention time). A preparative separation was performed using HPLC and the components in the three peaks were analyzed by mass spectroscopy. Almost identical mass spectra were obtained for the three components with the molecular ion at 848 (theoretical molecular weight of 848) indicating that the components were isomers. Similar work was also done with compound (XIII) which was shown to contain three isomers of the respective areas of 15, 77, and 8%.

Only one of the three quinoxalines in Table 3 can have isomers. Compound (XVIII) was analyzed by HPLC and showed three peaks of 48, 38, and 14% areas (in order of increasing retention time). Preparative separation by HPLC and subsequent analysis by mass spectroscopy showed the components in the three peaks to be isomers.

The relative amounts of the isomers in the *as*-triazines versus the quinoxalines should differ. In the *as*-triazine series, the initial nucleophilic attack should occur between the terminal nitrogen of the hydrazino portion of the amidrazone and the carbonyl adjacent to the perfluoroalkyl portion of the α-diketone. The most nucleophilic portion of the amidrazone is undoubtedly the terminal nitrogen of the hydrazino portion. As a result, one isomer should predominate, which was evident from the HPLC work on the two *as*-triazine products previously discussed. The preponderance of one isomer in the quinoxaline compound was not so great. The nucleophilicity of the amino groups would not be expected to differ substantially. This was substantiated by the HPLC work where compound (XVIII) was resolved into three peaks of 48, 38, and 14%.

In most cases, elemental analyses of the compounds in Table 3 were conducted on crude reaction products. The wide melting points are indicative of mixtures of isomers. The elemental analyses of compounds (XI) and (XVIII) were carried out on high melting fractions which were obtained by recrystallization. No attempt was made to isolate the various isomers in a reaction product by fractional recrystallization.

The mass spectral data for the as-triazine and quinoxaline compounds are presented in Table 4. The most abundant fragment for all of the as-triazine compounds except for compound (XIV) had an m/e of 151 which is attributed to a fluoroalkyl species (C_3F_6H). This fragment apparently arises from cleavage of the perfluoroalkyl(ene) group from the as-triazine ring(s) accompanied by a hydrogen transfer from the phenyl group to the perfluoroalkyl fragment with the loss of a fluorine atom (or CF_2). In those quinoxalines (XVI and XVII) where only a single isomer is possible, the most abundant fragment had an m/e of 205 which corresponded to a phenylquinoxaline species. In quinoxaline (XVIII), the most intense fragment had an m/e of 77 (C_6H_5). The second most intense fragment exhibited an m/e of 577 which corresponded to that resulting from the loss of one perfluoropropyl group from the molecule.

EXPERIMENTAL

Boiling and melting points are uncorrected. Standard silica gel coated plates were used for thin layer chromatography, and silica gel Mallinckrodt CC7 for column chromatography. High pressure liquid chromatography was performed on a Waters Associates Model ALC 202/R401 instrument with a Model 6000 Solvent Delivery System using a Zorbax-Sil column and a 254 nm fixed wavelength ultraviolet detector.

A Finnigan Model 3300 Quadrupole Mass Spectrometer equipped with a Model 6000 Data System was used to obtain the electron-impact spectra of each compound. Samples were introduced into the ion source with a programmable temperature solid inlet probe. Each spectrum was obtained by heating the sample at 2 C^o per minute from the ion source temperature of 100^oC to a temperature where enough sample was vaporized to generate a usable spectrum. Heating to 200^oC was generally sufficient. Each 70 ev spectrum was obtained by repeatedly scanning the 10-1000 amu mass range over a 15-second period while the sample was heated.

Infrared spectra were recorded on Beckman IR20AX and Perkin-Elmer 621 spectrophotometers. Proton and fluorine NMR spectra were obtained on a JEOL PS 100 spectrometer using TMS and HFB as internal standards. Elemental analyses were determined on a Perkin-Elmer 24 Elemental Analyzer and also

TABLE 4

MASS SPECTRA OF *as*-TRIAZINE AND QUINOXALINE COMPOUNDS

Compound No.	m/e (relative abundance)
X	493(10,M^+, 342(14),314(19),270(25),227(22),151(100),119(17),104(36),77(25),69(39)
XI	648(<1,M^+),501(1),270(17),251(1),151(100),101(4),77(2)
XIII	No M^+,651(2),456(1),270(23),151(100),101(3),77(2)
XIV	848(3,M^+),651(4),456(100),381(5),282(6),251(8),151(66),103(12),77(9)
XV	666(8,M^+),533(13),431(30),381(16),282(13),251(18),151(100),105(38),103(12),77(23)
XVI	374(50,M^+),205(100),179(9),151(7),102(26),77(58),51(20)
XVII	610(40,M^+)589(13),305(8),255(16),235(8),205(100),179(14),151(8),102(42),77(86),51(18)
XVIII	746(71,M^+),577(88),457(30),304(10),279(19),204(51),191(23),175(10),152(10),127(10),77(100)

by Galbraith Laboratories, Inc., Knoxville, Tennessee, and by Huffman Laboratories, Inc., Wheatridge, Colorado.

Octafluoroadipic Acid

To 15 ml (0.84 mol) of stirred distilled water, 25 g (0.085 mol) of octafluoroadipoyl fluoride was added dropwise over a period of 25 minutes. The temperature of the reaction mixture rose to about 80°C and crystals of octafluoroadipic acid dihydrate started depositing on the walls of the flask. The mixture was evaporated to dryness at 80°C at 25 mm. The residue was kept overnight in a desiccator over solid potassium hydroxide to remove the hydrofluoric acid and then dried under a water-cooled reflux condenser at 100° and 0.2 mm for 2.5 hours to give 23.2 g (94.5%) of anhydrous octafluoroadipic acid, m.p. 134-135°C [10]. Commercial octafluoroadipic acid had to be dried in the same manner to obtain completely anhydrous material.

Benzyl Heptafluoropropyl Ketone (I)

(a) From lithium heptafluorobutyrate

Benzylmagnesium chloride was prepared from 2.7 g (0.11 mol) of magnesium, 14.0 g (0.11 mol) of benzyl chloride, and 90 ml of ether. The solution was decanted from a negligible amount of unreacted magnesium and was added dropwise over a period of 45 minutes to a stirred and cooled (5-10°C) suspension of 22 g (0.1 mol) of anhydrous lithium heptafluorobutyrate in 100 ml of ether. The mixture was stirred at room temperature overnight, then cooled in an ice-bath, and decomposed with dilute sulfuric acid. The ether layer was separated and the aqueous layer was extracted with 75 ml of ether. The combined ether layers were washed with 20 ml of water, with 40 ml of a saturated solution of sodium carbonate, dried with magnesium sulfate, and evaporated under reduced pressure to give 17.3 g of a yellow oil. Distillation afforded 10.7 g (37.2%) of benzyl heptafluoropropyl ketone (I), b.p. 85-95°C/21 mm, which solidified in a refrigerator; m.p. 16-17°C. Lit. b.p. 51°C/3 mm.

(b) From heptafluorobutyric acid

Benzylmagnesium chloride was prepared from 10 g (0.416 mol) of magnesium, 50.6 g (0.4 mol) of benzyl chloride, and 250 ml of anhydrous ether.

The Grignard solution was cooled in an ice-bath to 10°C, and 31 g (0.133 mol) of heptafluorobutyric acid diluted with 30 ml of ether was added dropwise over a period of 0.5 hr at 10-12°C with vigorous stirring. The stirring was continued while the reaction mixture was allowed to warm to room temperature. The resulting green-gray suspension was decomposed by adding portionwise 20 ml of water while the reaction flask was cooled with ice water to 15-20° C. After adding 40 ml of concentrated hydrochloric acid and additional 20 ml of water to dissolve the salt, the aqueous layer was separated and extracted with 50 ml of ether. The combined ether solutions were washed with 20 ml of water, approximately 70 ml of a saturated solution of sodium carbonate, again with water, dried with magnesium sulfate, and evaporated under reduced pressure to give 35 g of a yellow oil. Distillation afforded benzyl heptafluoropropyl ketone (I), which solidified in a refrigerator; m.p. 10-13° C, b.p. 80-85° C/22 mm; yield 18.8 g (41.3%).

1-Phenylheptafluoro-1,2-pentanedione (II) (nc)

A mixture of 10.6 g (0.037 mol) of benzyl heptafluoropropyl ketone, 6.3 g (0.057 mol, 50% excess) of selenium dioxide, and 11.5 ml of acetic anhydride was stirred and heated under reflux at 140-150° for 4 hours. A brown solution was decanted from a black sediment, the sediment was washed three times with 10 ml portions of benzene, and the combined benzene solutions were evaporated under reduced pressure (20 mm) at a temperature up to 40° C. The residue was distilled to yield 8.3 g (74%) of a bright yellow oil, 1-phenylheptafluoro-1,2-pentanedione, b.p. 87-96°/13 mm.

Hydrate of II (nc)

The diketone (II) (2.2 g, 0.00765 mol) was triturated with 0.2 ml of water. The mixture warmed up and soon solidified to give 1.9 g (80%) of white crystals. Recrystallization from hexane yielded 1.5 g (65%) of the hydrate (IIa), m.p. 63-64° C. Another recrystallization from hexane raised the m.p. to 63-65° C.

Deuterate of II (nc)

The diketone (II) (8.3 g, 0.0275 mol) and 0.5 ml (0.0275 mol) of deuterium oxide were thoroughly mixed with a spatula in a 25 ml Erlenmeyer flask capped by a septum to prevent access of moisture. The mixture warmed up to 40-45° C. After cooling, the mixture solidified to a white crystalline mass. Recrystallization from hexane gave 5.0 g (57%) of the deuterate (IIb), m.p. 67-68.5° C. Another recrystallization from 10 ml of hexane gave 4.8 g of (IIb), m.p. 64-65.5° C.

1-Bromo-1-phenyl-3,3,4,4,5,5,5-heptafluoro-2-pentanone (VI) (nc)

A solution of 3.7 ml (11.7 g, 0.073 mol) of bromine in 10 ml of carbon tetrachloride was added over a period of 5.5 hours to a solution of 10.5 g (0.0365 mol) of the ketone (I) in 20 ml of carbon tetrachloride. The reaction mixture was refluxed and irradiated for 41.5 hours with a 100 watt bulb at a distance of 5 cm. The unreacted bromine and the solvent were evaporated under reduced pressure and the residue (12.5 g) was distilled to give 8.6 g (64%) of (VI), b.p. 50-54° C/0.7 mm.

1,8-Diphenyl-3,3,4,4,5,5,6,6-octafluoro-2,7-octanedione (III) (nc)

In a conventional apparatus fitted with a calcium chloride tube, 6.4 g (0.267 mol, 6 equivalents) of magnesium and 0.08 g of iodine were heated with a free flame until iodine vapors filled the reaction flask. When the flask cooled, 10 ml of absolute ether was fed into the flask from the dropping funnel followed by a solution of 33.5 g (0.265 mol, 6 equivalents) of benzyl chloride in 190 ml of anhydrous ether. The solution was added at a rate to maintain reflux (15 min.). The reaction mixture continued to boil for 15 more minutes. It had a green-gray color and contained only a small amount of undissolved magnesium. To this mixture a solution of 12.8 g (0.0441 mol) of anhydrous perfluoroadipic acid (m.p. 130-134° C) in 50 ml of anhydrous ether was added dropwise at a rate that kept the reaction mixture boiling (5 min). After the addition had been completed, the mixture was refluxed and stirred for an additional 1.5 hours. The mixture separated into a gray thick lower layer and an almost colorless upper layer. It was decomposed after cooling in an ice water bath to 8° C by the addition of a mixture of 20 ml of concentrated hydrochloric acid and 20 ml of water. The resulting milky suspension separated into two layers after adding an additional 15 ml of water and 5 ml of concentrated hydrochloric acid. The aqueous solution was separated and extracted with three 30 ml portions of ether. The ether extracts were combined with the original ether layer and the ether solution was washed successively with 10 ml of water and with a saturated solution of sodium bicarbonate until neutral. After drying with magnesium sulfate, the ether solution was evaporated to give 16.0 g of a semicrystalline residue. Recrystallization from 20 ml of hexane yielded 7.98 g (41.3%) of the diketone (III), m.p. 101-103° C. Another crystallization from hexane raised the melting point to 104-105° C. The mother liquor from the first crop of (III) was distilled at 135-150° C at 0.5-1.1 mm to provide an additional 5% of the diketone (III), m.p. 100-102° C. The bicarbonate washings were acidified with hydrochloric acid and extracted with ether. Concentration of the ether extract afforded 12% of 7-phenyl-2,2,3,3,4,4,5,5-octafluoro-6-ketoheptanoic acid (VII), m.p. 62-66° C. This compound is a deliquescent solid, and no correct elemental analysis could be obtained. Its structure is based on the NMR spectra.

1,8-Diphenyl-3,3,4,4,5,5,6,6-octafluoro-1,2,7,8-octanetetrone (IV) (nc)

1,8-Diphenyl-3,3,4,4,5,5,6,6-octafluoro-2,7-octanedione (8.57 g, 0.0196 mol, m.p. 103-104° C) was melted in a 50 ml flask, 6.0 g (0.054 mol, 2.75 equiv., 38% excess), of selenium dioxide was added, and the mixture was stirred in an oil bath at 140-150° C for 4 hours. After cooling, the warm mixture was digested with six 10 ml portions of benzene. The extracts were filtered, and the yellow filtrate was evaporated at 60° C at 30 mm to give a bright yellow oil. The oil crystallized slowly after cooling leaving only 0.25 g of a liquid. This was pipetted off and the residue was distilled to provide 4.67 g of the tetraketone (IV), b.p. 164-169° C/ 0.45-0.5 mm, and 1.03 g of a somewhat less pure fraction of (IV), 175-180° C/ 0.6 mm. The total yield was 5.70 g (62.3%).

Purification by Chromatography

The crude tetraketone (IV) as obtained by evaporation of the benzene solution (2.39 g, 0.005 mol) was chromatographed over 65 g of silica gel. Elution with 600 ml of hexane gave 0.16 g of a noncrystalline oil. Elution with 1600 ml of benzene gave oily residues of the tetraketone (IV). The bulk of pure tetraketone (IV) was obtained on elution with 350 ml of ether: 1.50 g (64%) of a bright yellow oil. Distillation of the oil gave 0.54 g of (IV) at 0.15 mm at 170-180°C (bath temperature); m.p. 50-54°C.

1,8-Diphenyl-3,3,4,4,5,5,6,6-octafluoro-1,2,7,8-octanetetrone Dihydrate (IVa)

Tetraketone (IV) (4.67 g, 0.010 mol) was dissolved in 45 ml of acetone containing 2.3 ml (0.13 mol) of distilled water. The intense yellow color faded to pale yellow. After 15 hours the solution was evaporated to dryness at 25-30° C at 30 mm. In order to remove excessive water, 20 ml of hexane was added and the mixture was evaporated at 35° C and 25 mm. The white residue (m.p. 114-123° C) was stirred with 25 ml of hexane at room temperature for 3 hours and then boiled for 30 seconds. The hot yellow supernatant liquid was decanted and the residue was boiled briefly with another 10 ml of hexane. The hexane was decanted and the residue was evaporated at 33° C and 25 mm to give 4.74 g (94.5%) of the white dihydrate (IVa) (nc) of the tetraketone, melting at 115-122° C to a bright yellow liquid. The compound was found chromatographically pure on TLC (R_F in Et_2O-C_6H_6 = 0.74). The melting point can be raised to 122-124.5° C by recrystallization from benzene with a small amount of acetone but the operation is tedious and is accompanied by a considerable loss of material.

Dideuterate of IV (nc)

Distillation of the dihydrate (IVa) at 0.5 mm from a microflask and the addition of 0.3 ml of deuterium oxide to the yellow liquid distillate gave, after 24 hours, a solid dideuterate (IVb) with the following melting points of different samples: 121-127° C, 127-130° C, and 139-141° C (yellow melts). All the samples were reconverted to IV by vacuum distillation.

1,8-Diphenyl-3,3,4,4,5,5,6,6-octafluoro-1,1,8,8-tetrakis(ethoxycarbonyl)-2,7-octanedione (nc)

A 50% dispersion of sodium hydride (2.0 g, 0.042 mole) was added portionwise to a stirred solution of diethyl phenylmalonate (9.68 g, 0.041 mol) in 40 ml of benzene in a 100 ml flask. When the evolution of hydrogen subsided, 5.9 g (0.02 mol) of octafluoroadipoyl fluoride was added dropwise over a period of 3 minutes. The temperature of the mixture rose to 55° C and a transient precipitate was formed but disappeared on stirring. After 20 hours at room temperature, the light brown solution was evaporated to dryness at 50° C at 18 mm. The semisolid residue was treated with 100 ml of ether to form a white suspension which was stirred with 20 ml of water.

The aqueous layer containing sodium fluoride was separated, diluted with 20 ml of water, and extracted with two 50 ml portions of ether. The combined ether solutions were washed with 10 ml of water, dried over magnesium sulfate, and evaporated to dryness at 50° C and 18 mm. A semi-solid residue (10.96 g, 0.015 mol) was recrystallized from ethanol to afford a 36% yield of 1,8-diphenyl-3,3,4,4,5,5,6,6-octafluoro-1,1,8,8-tetrakis(ethoxycarbonyl)-2,7-octanedione (VIII), m.p. 105-106.5° C). Another crystallization raised the m.p. to 108.5-109°C.

Aromatic 1,2-diamines

1,2-Diaminobenzene and 3,3',4,4'-tetraaminobiphenyl were obtained commercially and recrystallized. The latter amine was recrystallized under nitrogen from deoxygenated water (30 g/liter) containing a pinch of sodium dithionite. The yellow solution was treated with charcoal, filtered, and cooled to afford light tan needles (21 g, 70% recovery), m.p. 176-177.5°C. Lit. m.p. 179-180° C [11].

Perfluorobutyramidrazone

Perfluorobutyronitrile (50 g, 0.26 mol) was bubbled during 2 hours into a stirred solution of 97% hydrazine (25 ml) in 2-propanol (250 ml) at 5° C. After complete addition, the 2-propanol was removed under vacuum at <30° C to provide a white precipitate which was filtered, washed with cold 2-propanol, and recrystallized from cyclohexane (41 g in 1.5 l). Perfluorobutyramidrazone was obtained as white platelets (35 g, 59% yield), m.p. 68.5-69.5° C. Lit. m.p. 69.5-70° C [12].

2-Picolinamidrazone

2-Cyanopyridine was reacted with hydrazine in ethanol according to a known procedure [13] to yield a pale yellow solid. Recrystallization from benzene afforded 2-picolinamidrazone as almost white needles, m.p. 94-95° C. Lit. m.p. 95-96° C [13].

Perfluoroadipamidrazone

The diamidrazone was prepared as previously reported [4] from the reaction of perfluoroadiponitrile with hydrazine in 2-propanol. White crystals, m.p. 183-184°C dec. (introduced into a preheated oil bath at 170°C) were obtained after recrystallization from aqueous 2-propanol.

Oxalamidrazone

Following a known procedure [14], dicyanogen was bubbled into a cold solution of hydrazine in ethanol to provide pale yellow crystals, m.p. 178-179° C dec. (introduced into a preheated oil bath at 160° C). Lit. m.p. 179-180° C dec. [14].

Since the experimental procedures for the preparation of the as-triazine and quinoxaline compounds are very similar, the synthesis of a representative compound in each series is presented.

3-Octafluorotetramethylenebis(5-phenyl-6-heptafluoropropyl-as-triazine) and isomers (XIII) (nc)

Perfluoroadipamidrazone (0.4743 g, 1.5 mmol) and 1-phenylheptafluoro-1,2-pentanedione hydrate (0.9605 g, 3.0 mmol) were stirred in ethanol (15 ml) at ambient temperature for 2 days to form a white precipitate. A portion of the reaction mixture was filtered to isolate the uncyclized intermediate (compound XII, Table 3) as a white solid, m.p. 174-176° C dec. This material was readily converted to compound (XIII) upon melting or by refluxing in ethanol. The remainder of the reaction mixture was heated to reflux and maintained at the reflux temperature for 4 hours to yield a yellow solution. The yellow solution was concentrated to dryness to provide a residual yellow gum which solidified after several days to a yellow solid (compound XIII), m.p. 64-68° C, clearing at 88° C. The elemental analysis and mass spectral data are given in Tables 3 and 4, respectively.

Other as-triazines (nc)

All of the as-triazines in Table 3 were prepared in ethanol except for compound (XI). This material was prepared by refluxing stoichiometric quantities of oxalamidrazone and 1-phenylheptafluoro-1,2-pentanedione hydrate for 4 hr in a 1:1 mixture (20 ml) of ethanol and benzene. The yellow reaction mixture was concentrated to dryness to yield an orange solid (0.92 g, 95% yield) which sintered at 125° C and underwent major melting at

160-176° C. The solid was extracted with boiling cyclohexane (50 ml). An insoluble yellow powder (0.2 g), m.p. 234-236° C (compound XI, Table 3) and yellow filtrate were isolated. The cooled yellow filtrate provided yellow needles (0.26 g) which sintered at 120° C, melted at 140-146° C, and cleared at 188° C. The mass spectra of the yellow powder and yellow needles were essentially identical, indicating the presence of isomers.

2,2'-Octafluorotetramethylenebis (3-phenylquinoxaline) and isomers (XVII) (nc)

1,2-Diaminobenzene (0.2162 g, 2.0 mmol) and 1,8-diphenyl-3,3,4,4,5,5,-6,6-octafluoro-1,2,7,8-octanetetrone dihydrate (0.5023 g, 1.0 mmol) were refluxed in ethanol (10 ml) for 16 hr. Turbidity developed after refluxing for 1 hr, and a precipitate appeared after another 0.5 hr. The cooled reaction mixture was filtered to isolate a white solid (0.6 g, 98% yield) (compound XVII, Table 3), m.p. 218-219° C. The elemental analysis and mass spectral data are given in Tables 3 and 4, respectively.

Other Quinoxalines (nc)

Compounds (XVI) and (XVIII) were also prepared in ethanol. Stoichiometric quantities of 3,3',4,4'-tetraaminobiphenyl and 1-phenylheptafluoro-1,2-pentanedione hydrate were refluxed in ethanol for 4 hours. The orange solution was concentrated to dryness to yield a yellow solid which sintered at 198° C, softened at 217° C, and melted at 225-270°C. The yellow solid was dissolved in hot benzene and the solution was treated with charcoal, filtered and cooled to provide an off-white solid (compound XVIII, Table 3), m.p. 319-321° C. Elemental analysis and mass spectral data are presented in Tables 3 and 4, respectively. The filtrate was concentrated to dryness to provide a tan solid which sintered at 177° C, underwent major melting at 181-186° C and cleared at 231° C. The mass spectra of the off-white solid and the tan solid were essentially identical, suggesting the presence of isomers.

ACKNOWLEDGEMENTS

The assistance of the following people is gratefully acknowledged: Mr. G. F. Sykes and Dr. P. R. Young of NASA Langley Research Center for the mass spectroscopic work and the HPLC work, respectively. Mr. T. E. Glass, Mr. R. S. Stringham and Dr. H. C. Dorn of Virginia Polytechnic

Institute and State University for the NMR spectroscopic work, the elemental analyses, and valuable discussions, respectively. A portion of this work was funded under NASA Langley Grant NAS1-13175 to VPI & SU.

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Note Added in Proofs.

When instead of 6 equivalents, 8 equivalents of benzylmagnesium chloride were used per one equivalent of octafluoroadipic acid, the yield of the diketone III was raised to 64.8%.