(m.p. 56–57°) obtained by chromic acid oxidation of 2,3-dimethylaniline hydrochloride.[11]

The 2,3-dimethylbenzoquinone (1.4 g., 0.010 mole) prepared by hydrogenation as described above was mixed with 40 ml. of water, and the mixture warmed as sulfur dioxide was bubbled into the water for 1 hr. White crystals (1.1 g., 77% yield) were removed by filtration; m.p. 220–221°, lit.,[12] m.p. 221°. The melting point of the product was not depressed when mixed with an authentic sample of 2,3-dimethylhydroquinone.

3,8-Di-α-methylbenzyl-2,3,4,7,8,9-hexahydrobenzo[1,2-e,4,5-e']bis-m-oxazine (Id) *and 2,9-di-α-methylbenzyl-1,2,3,8,9,10-hexahydrobenzo[2,1-e,3,4-e']bis-m-oxazine* (IIb). To a cooled solution of 30 ml. of 37% aqueous formaldehyde (0.40 mole) in 30 ml. of dioxane was added 25.8 ml. of α-methylbenzylamine (0.20 mole) and 11.0 g. of hydroquinone (0.10 mole) and the resulting solution was refluxed for 4 hr. and cooled. The solid (33.2 g., 83% yield) was removed by filtration. It was placed in 400 ml. of boiling methanol and filtered. The residue (Id; 12.4 g., 31% yield, m.p. 179–182°) melted at 191–192° after recrystallization from benzene–methanol. The filtrate was evaporated and cooled. The solid (IIb; 10.7 g., 27% yield, m.p. 163–167°) melted at 176–177° after three recrystallizations from ethyl acetate.

2,5-Bis(cyclohexylaminomethyl)hydroquinone (IVc). 2,5-Bis(dimethylaminomethyl)hydroquinone (4.5 g., 0.020 mole) was dissolved in 46 ml. of cyclohexylamine (0.40 mole) and refluxed for 12 hr. The solvents were removed by distillation under reduced pressure, and the residue cooled. The solid (6.3 g., 94% yield, m.p. 158–163°) was removed by filtration; m.p. 170–171° after recrystallization from ethyl acetate. The melting point of the product was not depressed when mixed with a sample of the Mannich base (m.p. 173–174°) obtained by the hydrolysis of the bis-*m*-oxazine (Ib) from cyclohexylamine.[3]

2,5-Bis(N-cyclohexyl-N-methylaminomethyl)hydroquinone. Formic acid (9.2 ml. of 85% aqueous solution, 0.20 mole) was added dropwise with agitation to 3.6 g. of Ib (0.010 mole) at room temperature. The solution was refluxed for 30 min., then cooled and added dropwise to a slurry of 20 g. of sodium bicarbonate (0.25 mole) in 100 ml. of water. The solid (2.9 g., 80% yield, m.p. 186–188°) was removed by filtration and washed with cold water; m.p. 189–190° after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{22}H_{36}N_2O_2$: C, 73.29; H, 10.07. Found: C, 73.13; H, 9.86.

The melting point was not depressed when the product was mixed with a sample (m.p. 190–191°) prepared by reaction of 2,5-bis(dimethylaminomethyl)hydroquinone with *N*-methylcyclohexylamine or when mixed with the product (m.p. 190–191°) from the condensation of hydroquinone, formaldehyde, and *N*-methylcyclohexylamine in a molar ratio of 1:2:2.

2,5-Bis(N-benzyl-N-methylaminomethyl)hydroquinone. Formic acid (25.0 ml. of 85% aqueous solution, 0.55 mole) was added dropwise to 9.3 g. of Ic (0.025 mole), and the resulting solution was kept at room temperature for 2 hr. The temperature was increased to 75° for 1 hr. The solution was cooled, poured into water, and neutralized with a solution of sodium bicarbonate. The solid (8.8 g., 94% yield, m.p. 173–178°) was removed by filtration; m.p. 181–182° after recrystallization from acetone.

Anal. Calcd. for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.72; H, 7.53; N, 7.37.

Hydrogenolysis of 2,5-bis(N-benzyl-N-methylaminomethyl)-hydroquinone. 2,5-Bis(*N*-benzyl-*N*-methylaminomethyl)hydroquinone (7.5 g., 0.020 mole) and 2.0 g. of copper–chromium oxide catalyst were mixed with 100 ml. of absolute ethanol and added with hydrogen to a high pressure bomb. The reaction mixture was heated at 225° and 3200 p.s.i. pressure for 2 hr. The catalyst was removed by filtration and washed with ethanol, which was added to the filtrate. The filtrate was mixed with aqueous ferric chloride, extracted twice with benzene, and discarded. The benzene extract was evaporated to dryness. A yellow crystalline solid (0.2 g., 7% yield, m.p. 120–121°) was removed by sublimation. 2,5-Dimethylbenzoquinone is reported[13] to melt at 123°.

3,8-Diallyl-2,3,4,7,8,9-hexahydrobenzo[1,2-e,4,5-e']bis-m-oxazine (Ie). Allylamine (7.5 ml., 0.10 mole) was added dropwise with cooling to a solution of 15 ml. of 37% aqueous formaldehyde (0.20 mole) in 20 ml. of dioxane. Hydroquinone (5.5 g., 0.05 mole) was added, and the resulting solution was refluxed for 3 hr. and then cooled. The solid (11.1 g., 82% yield, m.p. 123–128°, was removed by filtration; m.p. 139–140°, after two recrystallizations from acetone.

SALT LAKE CITY, UTAH

---

[11] O. H. Emerson and L. I. Smith, *J. Am. Chem. Soc.*, **62**, 141 (1940).

[12] E. Nolting and S. Forel, *Ber.*, **18**, 2668 (1885).

[13] H. Von Pechmann, *Ber.*, **21**, 1411 (1888).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMICAL ENGINEERING AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF FLORIDA]

Synthesis of 2,5 Bis(perfluoroalkyl)-1,3,4-oxadiazoles

HENRY C. BROWN, MING T. CHENG, LLOYD J. PARCELL,[1] AND DONALD PILIPOVICH[2]

Received March 8, 1961

2,5-Bis(perfluoroalkyl) 1,3,4-oxadiazoles, in which the perfluoroalkyl groups were CF_3, C_2F_5, C_3F_7, or C_7F_{15}, were prepared by the dehydration of the corresponding *N,N'*-bis(perfluoroacyl)hydrazines. Preparation of the previously unreported intermediate perfluoroalkyl hydrazides and *N,N'*-bis(perfluoroacyl)hydrazines is described.

As a continuation of our interest in the unusual properties of heterocyclic compounds having perfluoroalkyl groups as ring substituents, several 2,5-bis(perfluoroalkyl)-1,3,4-oxadiazoles have been synthesized. In view of the pronounced differences in reactivity[3,4,5] between the perfluoroalkyl-heterocycles and the nonfluorinated heterocycles, a

---

[1] Present address: University of Virginia, Charlottesville, Va.

[2] Present address: Rocketdyne, Canoga Park, Calif.

[3] H. C. Brown and W. L. Reilly, *J. Org. Chem.*, **22**, 698 (1957).

[4] H. C. Brown, *J. Polymer Sci.*, **44**, 9 (1960).

[5] H. C. Brown, *J. Org. Chem.*, **22**, 715 (1957).

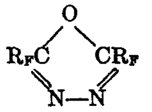
TABLE I

PERFLUOROACYL HYDRAZIDES AND *N*,*N*′-BIS(PERFLUOROACYL)HYDRAZINES

Compound	M.P.	Calcd., %				Found, %			
		C	H	N	F	C	H	N	F
Heptafluorobutyrhydrazide	73–74	21.05	1.32	12.28	58.33	21.27	0.92	12.12	58.53
Pentafluoropropionhydrazide	63–64	20.22	1.69	15.73	53.36	20.20	1.59	15.52	53.68
Trifluoroacethydrazide	143–144	18.75	2.34	21.88	44.53	18.95	2.29	21.84	44.48
N,*N*′-Bis(perfluorobutyryl)hydrazine	164–166	22.64	0.47	6.60	62.74	22.97	0.68	6.87	63.00
N,*N*′-Bis(perfluoropropionyl)hydrazine	142–143	22.22	0.67	8.64	58.64	22.49	0.87	8.53	58.41
N,*N*′-Bis(perfluoroacetyl)hydrazine	176	21.43	0.89	12.50	50.89	21.69	1.14	12.47	50.83
N,*N*′-Bis(perfluorooctanoyl)hydrazine	139–140	23.30	0.24	3.40	69.17	23.33	0.57	3.64	68.97

TABLE II

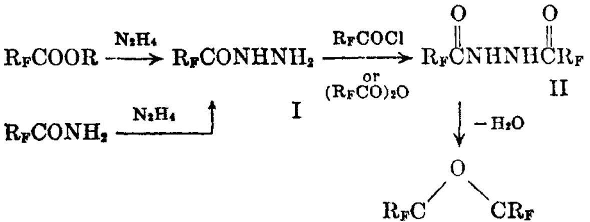
2,5-BIS(PERFLUOROALKYL)-1,3,4-OXADIAZOLES



R	B.P.	n^t	d^t	Calcd., %				Found, %			
				C	N	F	Mol. Wt.	C	N	F	Mol. Wt. (Dumas)
C_3F_7	124.0	1.2980^{30}	1.678^{30}	23.62	6.89	65.50	406	23.91	6.63	65.62	403
C_2F_5	88.0–88.5	1.3000^{25}	1.614^{25}	23.52	9.16	62.09	306	23.66	9.24	62.25	307
CF_3	65.0	1.3088^{25}	1.547^{25}	23.30	13.60	55.34	206	23.12	13.64	55.10	208
C_7F_{15}	116–117 (8 mm.)	1.3121^{24}	1.843^{25}	23.84	3.48	70.70	—	24.05	3.48	70.67	—

general study of the chemical reactions, particularly those involving the ring atoms, of this type of fluorocarbon derivative has been initiated.

Stolle[6] described the preparation of 2,5-dialkyl-1,3,4-oxadiazoles by the dehydration of *N*,*N*′-diacyl hydrazines; this method was found to be applicable to the synthesis of the corresponding perfluoroalkyl derivatives (Equation 1) in which $R_F = CF_3, C_2F_5, C_3F_7,$ or C_7F_{15}.



Either the methyl, or ethyl ester, or the amide of the perfluorocarboxylic acid was treated with hydrazine to form the perfluoroacyl hydrazide (I) which was converted to the *N*,*N*′-bis(perfluoroacyl)-hydrazine (II) by acylation with a perfluoroacyl chloride or a perfluoroacyl anhydride and subsequently dehydrated to 2,5-bis(perfluoroalkyl)-1,3,4-oxadiazole (III).

The perfluoroacyl hydrazides were prepared without difficulty; samples for analysis were purified by sublimation. Acylation of the perfluoroacyl hydrazides was most conveniently carried out by the use of the appropriate perfluorocarboxylic acid anhydride, though the corresponding acyl chloride could be used. The lower molecular weight *N*,*N*′-bis(perfluoroacyl)hydrazines, *N*,*N*′ - bis(perfluoroacetyl)hydrazine, *N*,*N*′-bis(perfluoropropionyl)hydrazine, and *N*,*N*′-bis(perfluorobutyryl)hydrazine exhibited two characteristic maxima in their infrared spectra at 5.60 and 5.85 μ, assigned to C=O stretching. *N*,*N*′-bis(perfluorooctanoyl)hydrazine, $(C_7F_{15}CONH)_2$, gave one strong peak at 5.98 μ for this structural feature. Table I lists the perfluoroacyl hydrazides and the *N*,*N*′-bis(perfluoroacyl)hydrazines prepared.

Since the *N*,*N*′-bis(perfluoroacyl)hydrazines sublimed rather easily, dehydrations to form the perfluoroalkyl oxadiazoles were performed by heating at a comparatively low temperature with phosphorus pentoxide for several hours, then at a higher temperature under reduced pressure to remove the liquid product from excess phosphorus pentoxide. The 2,5-bis(perfluoroalkyl)-1,3,4-oxadiazoles prepared are listed in Table II. These compounds showed two characteristic weak absorption bands in their infrared spectra between 6.30 and 6.42 μ which were assigned to C=N stretching in this cyclic structure.

The thermal stability of the bis(perfluoroalkyl)-1,3,4-oxadiazole ring was unexpectedly high. No decomposition was evident on heating 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole in a previously evacuated sealed glass tube at 350° for fifteen hours, than at 400° for one hour. The bis(perfluoroalkyl)-oxadiazoles were hydrolyzed slowly to the salt of

---

(6) R. Stolle, *Ber.*, 32, 797 (1899).

the parent carboxylic acid by refluxing with aqueous sodium hydroxide; hydrolysis with concentrated sulfuric acid produced a mixture of the corresponding bis(perfluoroacyl)hydrazine and perfluorocarboxylic acid.

Although the thermal stability of this heterocyclic ring system is high, we have failed to find a distinct absorption maxima in the ultraviolet region of 220–340 mμ that might indicate some degree of aromaticity. Two conjugated $C{=}N$ bonds might be expected to show a maxima at about 210 mμ; further delocalization of these bonds in an aromatic ring should produce a shift to the region studied. Spectra of the bis(perfluoroalkyl)oxadiazoles in acetonitrile, cyclohexane, isooctane, or ethyl ether showed no clear maxima, though there is possibly an inflection in the curve at 235–240 mμ.

The oxadiazole ring in the perfluoroalkyl substituted compounds is easily attacked by nucleophilic reagents as would be expected from the electron deficiency due to the inductive effect of the perfluoroalkyl groups. Studies of the reactions with nucleophiles will be reported in a subsequent publication.

EXPERIMENTAL[7]

Materials. Perfluoroalkyl carboxylic acid esters were prepared by sulfuric acid-catalyzed reaction with alcohol of the corresponding perfluoroalkyl acids obtained from Columbia Organic Chemicals. Hydrazine (95%) and hydrazine hydrate were obtained from Olin Matheson Co. and used as received.

Heptafluorobutyrhydrazide. Method A. Into a 500-ml. round-bottom flask were placed 228 g. (1.0 mole) of methyl heptafluorobutyrate, 32 g. (1.0 mole) of hydrazine (95%), and 80 ml. of methyl alcohol. The flask was shaken gently to mix the liquids and then allowed to stand at room temperature for 4 hr. Removal of the solvent alcohol yielded 228 g. of crude solid product which was sublimed at atmospheric pressure to give 205 g. (90% yield) of white, crystalline heptafluorobutyrhydrazide, m.p. 73–74° (lit., m.p. 76°, no preparation given[8]).

Method B. As an alternative procedure for the preparation of perfluorobutyrhydrazide, 142 g. (0.67 mole) of perfluorobutyramide was dissolved in 250 ml. of ethyl ether and placed in a 500-ml. flask equipped with a water-cooled reflux condenser and magnetic stirring bar. Hydrazine hydrate, 33.5 g. (0.67 mole) was added through the reflux condenser, and the mixture was refluxed for 2 hr. with vigorous stirring. After this time evolution of ammonia had ceased, indicating completion of the reaction. The solvent ether was removed under reduced pressure, and the solid product recrystallized from ethyl alcohol to give 131 g. (85% yield) of perfluorobutyrhydrazide, m.p. 73–74°.

Pentafluoropropionhydrazide and trifluoroacethydrazide. Pentafluoropropionhydrazide was prepared by method A or B described above for preparation of perfluorobutyrhydrazide. Trifluoroacethydrazide was prepared by method A above.

N,N′-Bis(perfluorobutyryl)hydrazine. Heptafluorobutyrhydrazide, 166 g. (0.73 mole), in 50 ml. of heptafluorobutyric acid was placed in a 500-ml. round-bottom flask cooled by an ice bath and equipped for magnetic stirring. Heptafluorobutyric anhydride, 382 g. (20 mole % excess), was added slowly with stirring. Removal of the heptafluorobutyric acid and excess heptafluorobutyric anhydride under reduced pressure gave a white solid product which was recrystallized from heptafluorobutyric acid to yield 259 g. (86% yield) of *N,N′*-bis(perfluorobutyryl)hydrazine, m.p. 164–166°.

The infrared absorption spectra of *N,N*-bis(perfluorobutyryl)hydrazine (mull in Kel-F Polymer Oil) shows absorption at 5.72 and 5.82 μ, assigned to $C{=}O$ stretching.

N,N′-Bis(perfluoropropionyl)hydrazine. Pentafluoropropionyl chloride, 96 g. (0.54 mole) was condensed in a 500-ml. three-neck flask cooled by Dry Ice and equipped with an addition funnel and Dry Ice–cooled reflux condenser. Chloroform, 150 ml., was added as a solvent and 8.3 g. (0.26 mole) of hydrazine added slowly with stirring. After completion of of the exothermic reaction from which hydrogen chloride was evolved, the solvent chloroform was removed under reduced pressure to yield 45 g. (55% yield) of *N,N′*-bis-(perfluoropropionyl)hydrazine as white crystals, m.p. 142.0–143.5°. The infrared absorption spectra showed characteristic bands for $C{=}O$ at 5.62 and 5.77 μ (mull in Kel-F Polymer Oil).

N,N′-Bis(perfluoroacetyl)hydrazine. This compound was prepared by the method described above for *N,N′*-bis(perfluorobutyryl)hydrazine.

N,N′-Bis(perfluorooctanoyl)hydrazine. Perfluorooctanoyl chloride 83 g. (0.19 mole) was dissolved in 100 ml. of chloroform and placed in a 500-ml. flask fitted with a reflux condenser and addition funnel. Hydrazine, 3.08 g. (0.10 mole) was added slowly, and the mixture then refluxed for 15 min. Removal of the chloroform under reduced pressure gave 67 g. (86% yield) of crude *N,N′*-bis(perfluorooctanoyl)hydrazine. A portion of this product was washed with water and recrystallized from a water-ethanol mixturd to give pure *N,N′*-bis(perfluorooctanoyl)hydrazine, m.p. 139–140°. The infrared spectra of this product showed only one absorption band (at 5.98 μ) for $C{=}O$.

2,5-Bis(perfluoropropyl)-1,3,4-oxadiazole. *N,N′*-Bis-(perfluorobutyryl)hydrazine, 108 g. (0.25 mole), and 200 g. of phosphorus pentoxide were placed in a 1-l. flask and thoroughly mixed. Approximately 75 g. of phosphorus pentoxide was then placed in a layer over the top of the mixture. The flask was connected to Dry Ice-cooled trap protected from atmospheric moisture. The solid mixture was heated at 100° for 24 hr., then at 350° for 2 hr. The exit line from the trap was then connected to the vacuum line, the trap cooled by liquid air, and the pressure in the system reduced to 10 mm. With the temperature of the reaction flask maintained at 350°, approximately 1 hr. was required for the crude product to collect in the trap. The crude liquid, after being washed with dilute sodium bicarbonate solution and dried, was fractionated to give 78 g. (76.5% yield) of 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole, b.p. 124°; n^{30} 1.2980; d^{30} 1.678.

The infrared absorption spectra of 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole shows two weak absorption bands at 6.35 and 6.40 μ, assigned to $C{=}N$ in cyclic structures. No other significant absorption at wave lengths shorter than 6 μ was apparent.

2,5-Bis(perfluoroethyl)-1,3,4-oxadiazole, 2,5-bis(perfluoromethyl) - 1,3,4 - oxadiazole, and 2,5-bis(perfluoroheptyl)-1,3,4-oxadiazole. These compounds were prepared by the method described above for the synthesis of 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole.

Acknowledgment. This investigation was supported in part by the Chemistry Branch, Office of Naval Research under Contract NONR-580(03) and in part by National Institutes of Health Grant Cy 5083 SSS. Reproduction in part or in whole is permitted for any purpose of the U. S. Government.

GAINESVILLE, FLA.

---

(7) Microanalyses by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(8) Minnesota Mining and Manufacturing Company, *New Products Bulletin*, "Heptafluorobutyric Acid."