[CONTRIBUTION FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS AND CO.]

Synthesis of 2,5-Bis(polyfluoroalkyl)-1,3,4-oxadiazoles and -thiadiazoles

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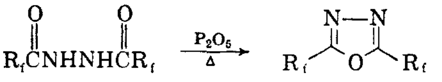
2,5-Bis(polyfluoroalkyl)-1,3,4-oxadiazoles and the 2,5-bis(polyfluoroalkyl)-1,3,4-thiadiazoles have been prepared by heating bis(polyfluoroacyl)hydrazines with excess phosphorus pentoxide and phosphorus pentasulfide, respectively, at 200–300°.

The cyclodehydration of diacylhydrazines by heating alone or with thionyl chloride results in the formation of 2,5-dialkyl-1,3,4-oxadiazoles,[1] and synthesis of the corresponding 2,5-dialkyl-1,3,4-thiadiazoles has been accomplished by reaction of diacylhydrazines with phosphorus pentasulfide.[1,2]

We now report the preparation of new representatives of these two classes of five-member cycles, 2,5-bis(polyfluoroalkyl)-1,3,4-oxadiazoles (I) and 2,5-bis(polyfluoroalkyl)-1,3,4-thiadiazoles (II). The (polyfluoroalkyl)oxadiazoles I, in which R_f = C_3F_7—, C_7F_{15}—, and $H(CF_2)_4$—, were obtained in 50–70% conversions by heating the bis(polyfluoroacyl)hydrazines with excess phosphorus pentoxide at 200–300°.

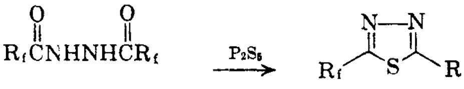


I

In contrast to the behavior of fluorine-free diacylhydrazines,[1] the bis(polyfluoroacyl)hydrazines did not cyclodehydrate when refluxed with thionyl chloride or phosphorus oxychloride. Furthermore, only low yields of 2,5-dialkyl-1,3,4-oxadiazoles were obtained when diacylhydrazines were treated with phosphorus pentoxide, the preferred reagent for dehydrating the bis(polyfluoroacyl)hydrazines. An alternative synthesis of the (polyfluoroalkyl)oxadiazoles was found in the reaction of polyfluoroalkanoic acids with hydrazine hydrate in refluxing benzene to obtain a mixture, presumably consisting of the bis(polyfluoroacyl)hydrazine, the monoacyl hydrazinium carboxylate, and the bis(hydrazinium)dicarboxylate, which was then heated with phosphorus pentoxide. In this way, bis(polyfluoroalkyl)oxadiazoles I with R_f = CF_3—, C_2F_5—, and $H(CF_2)_4$— were obtained in yields of 26%, 49%, and 13%, respectively.

The bis(polyfluoroalkyl)oxadiazoles I are liquids boiling over the range from 65° (R_f = CF_3) to 236° (R_f = C_7F_{15}) without decomposition and are quite stable thermally. The boiling points of the (polyfluoroalkyl)oxadiazoles I are appreciably lower than the boiling points of their alkyl analogs. For example, 2,5-dimethyl-1,3,4-oxadiazole boils at 178°,[1] while 2,5-bis(trifluoromethyl)-1,3,4-oxadiazole (I. R_f = CF_3) boils at 65°, a differential (112°) somewhat greater than one might expect.

The bis(polyfluoroalkyl)thiadiazoles II, in which R_f = C_2F_5— and $H(CF_2)_4$—, were prepared by treating the bis(polyfluoroacyl)hydrazines or the hydrazinium fluorocarboxylates with phosphorus pentasulfide at 250–300°. For example, 1,2-bis(5-hydrooctafluorovaleryl)hydrazine formed 2,5-bis(4-hydrooctafluorobutyl)-1,3,4-thiadiazole (II. R_f = $H(CF_2)_4$—) in 74% conversion, while pentafluoropropionic acid and hydrazine hydrate gave 2,5-bis(pentafluoroethyl)-1,3,4-thiadiazole (II. R_f = C_2F_5—) in 56% yield.



II

The identities of the oxa- and thiadiazoles were established by their elemental composition and by their infrared and NMR spectra. The polyfluoroalkyl oxadiazoles exhibited absorptions in the infrared near 6.35 μ in the —C═N— region. In the alkyl series, 2,5-dimethyl-1,3,4-oxadiazole absorbs in the —C═N region at 6.30 μ and at 5.75 μ.[3] With the polyfluoroalkyl thiadiazoles the infrared absorption shifted to 6.7 μ. The fluorine magnetic resonance was shifted appreciably by the replacement of oxygen by sulfur. Thus, the resonance of the fluorine atoms in the *alpha* position in 2,5-bis(4-hydrooctafluorobutyl)-1,3,4-oxadiazole [I. R_f = $H(CF_2)_4$—] was at 2690 c.p.s. while the corresponding fluorine atoms in 2,5-bis(4-hydrooctafluorobutyl)-1,3,4-thiadiazole [II, R_f = $H(CF_2)_4$—] exhibited a peak at 2080 c.p.s. The fluorine resonance of 2,5-bis(trifluoromethyl)-1,3,4-oxadiazole (I. R_f = CF_3) consisted of a single peak at 45 c.p.s. on the high field side relative to 1,2-difluorotetrachloroethane.

EXPERIMENTAL

All melting points and boiling points are uncorrected.

The infrared spectra were obtained using a Perkin-Elmer Model 21 double-beam spectrophotometer.

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[1] R. Stolle, *J. prakt. Chem.*, II, **68**, 137 (1903); II, **69**, 151, 481 (1904).

[2] R. Stolle and L. Gutmann, *J. prakt. Chem.*, II, **69**, 509 (1904).

[3] M. Milone and E. Barello, *Gazz. chim. ital.*, **81**, 683 (1951).

The NMR spectra were obtained by means of a high-resolution magnetic resonance spectrometer and associated electromagnet, both manufactured by Varian Associates, Palo Alto, Calif., operated at 56.4 mc./sec. and approximately 14,081 gauss. A capillary of 1,2-difluoro-tetrachloroethane was placed in each sample, and the spectra were calibrated in terms of displacement in cycles per second (c.p.s.) from the fluorine resonance of 1,2-difluorotetrachloroethane. All peaks were to the high field side.

1,2-Bis(polyfluoroacyl)hydrazines. 1,2-Bis(5-hydrooctafluorovaleryl)hydrazine.[4] To a stirred solution of 0.14 mole (38 g.) of 5-hydrooctafluorovaleryl chloride in benzene was added 0.14 mole (7 g.) of hydrazine hydrate. After stirring for 1.5 hr., the mixture was refluxed with a water eliminator attached until all the water had been removed. Filtration of the hot benzene mixture removed the hydrazine dihydrochloride. On cooling the benzene solution, there was obtained 22 g. (64% yield) of 1,2-bis(5-hydrooctafluorovaleryl)hydrazine, m.p. 131–132°.

Anal. Calcd. for $C_{10}H_4F_{16}N_2O_2$: C, 24.60; H, 0.82; F, 62.27; N, 5.74. Found: C, 24.44; H, 1.31; F, 61.20; N, 6.19.

The following 1,2-bis(perfluoroacyl)hydrazines were prepared by the same method.

1,2-Bis(perfluorobutyryl)hydrazine. From 0.13 mole (29 g.) of perfluorobutyryl chloride there was obtained 15.6 g. (59% yield) of bis(perfluorobutyryl)hydrazine, m.p. 167–168°.[5]

1,2-Bis(perfluorooctanyl)hydrazine. From 0.09 mole (37.5 g.) of perfluorooctanoyl fluoride there was obtained 28 g. (76% yield) of bis(perfluorooctanyl)hydrazine, m.p. 137–139°.

Anal. Calcd. for $C_{16}H_2F_{30}N_2O_2$: C, 23.31; H, 0.25; N, 3.40. Found: C, 23.76; H, 0.40; N, 3.80.

2,5-Bis(polyfluoroalkyl)-1,3,4-oxadiazoles (I). The following procedures were used for the preparation of the oxadiazoles.

Method A. 2,5-Bis(4-hydrooctafluorobutyl)-1,3,4-oxadiazole [I. $R_f = (CF_2)_4H$]. An intimate mixture of 3.3 mmoles (6.5 g.) of 1,2-bis(5-hydrooctafluorovaleryl)hydrazine and 46 mmoles (6.5 g.) of phosphorus pentoxide was heated at a bath temperature of 250° for 1 hr. The volatile product was distilled under reduced pressure to give 4.8 g. (77% yield) of crude product. Fractionation at atmospheric pressure gave 3.7 g. (59% yield) of 2,5-bis(4-hydrooctafluorobutyl)-1,3,4-oxadiazole, b.p. 193–195°.

Anal. Calcd. for $C_{10}H_2F_{16}N_2O$: F, 64.66; N, 5.96. Found: F, 65.14; N, 6.04.

The infrared spectrum showed strong absorptions at 3.32 μ (CF_2—H), 6.35 μ (—C═N—), 7.14 μ, 7.35 μ, 7.6–9.1 μ (C—F), 9.6 μ, 10.02 μ, 10.40 μ, 10.62 μ, 11.2–11.6 μ (broad), 11.68 μ, 12.3–12.8 μ (broad), 13.50 μ, and 14.80 μ.

The fluorine magnetic resonance spectrum consisted of five chemically shifted resonances, a doublet having components at 4108 and 4055 c.p.s. (—CF_2H), and three singlets at 3580, 3290, and 2690 c.p.s. (internal —CF_2—). All the resonances exhibited considerable fine structure.

Other oxadiazoles made by the same general procedure are described below.

2,5-Bis(perfluoropropyl)-1,3,4-oxadiazole (I. $R_f = C_3F_7$). A mixture of 10 mmoles (4.2 g.) of 1,2-bis(perfluorobutyryl)-hydrazine and 30 mmoles (4.3 g.) of phosphorus pentoxide gave 2.8 g. (69% yield) of 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole, b.p. 118–119°.

Anal. Calcd. for $C_8F_{14}N_2O$: F, 65.50; N, 6.90. Found: F, 66.75; N, 6.85.

The infrared spectrum showed absorptions at 6.35 μ (—C═N—), 6.40 μ, 7.08 μ, 7.40 μ, 7.7–9.0 μ (C—F), 8.80 μ, 9.26 μ, 9.85 μ, 10.85 μ, 11.38 μ, and 13.30 μ.

2,5-Bis(perfluoroheptyl)-1,3,4-oxadiazole (I. $R_f = C_7F_{15}$). A mixture of 28.6 mmoles (23.5 g.) of 1,2-bis(perfluorooctanoyl)-hydrazine and 239 mmoles (34 g.) of phosphorus pentoxide gave 12.6 g. (55% yield) of 2,5-bis(perfluoroheptyl)-1,3,4-oxadiazole, b.p. 234–236°.

Anal. Calcd. for $C_{16}F_{30}N_2O$: C, 23.84; F, 70.70; N, 3.48. Found: C, 24.41; F, 69.97; N, 3.87.

The infrared spectrum showed absorptions at 6.38 μ (—C ═N—), 7.13 μ, 7.32 μ, 7.59 μ, 7.9–8.9 μ (C—F), 9.25 μ, 9.65 μ, 9.85 μ, 10.35 μ, 10.45 μ, 11.35 μ, 11.50 μ, 12.05 μ, 12.36 μ, and 13.37 μ.

Method B. 2,5-Bis(trifluoromethyl)-1,3,4-oxadiazole (I. $R_f = CF_3$). A mixture of 0.5 mole (25 g.) of hydrazine hydrate, 0.25 mole (57 g.) of trifluoroacetic acid, and 300 ml. of benzene was refluxed for 1 hr. The mixture was then refluxed for 2 hr. with a water eliminator attached. An additional 0.25 mole (57 g.) of trifluoroacetic acid was added. The resulting mixture was then refluxed for 2 hr. without the water eliminator and 15 hr. with the water eliminator attached. The white solid obtained upon cooling was removed by filtration; it weighed 76 g. and had no definite melting point. An additional 26 g. of product in the form of a viscous liquid was obtained by removing the solvent from the filtrate. A mixture of the solid and 100 g. of phosphorus pentoxide was heated for 2 hr. at 200° under an efficient reflux condenser. 1,2,4-Trichlorobenzene (100 ml.) was added to the reaction mixture which was then heated 3 hr. at 220°. The volatile material was distilled from the reaction flask to give 31.9 g. of crude 2,5-bis(trifluoromethyl)-1,3,4-oxadiazole, b.p. 45–65°. A mixture of the viscous liquid and 100 g. of phosphorus pentoxide was heated 3 hr. at 250° under an efficient reflux condenser. Distillation of the volatile product gave 7 g. of crude 2,5-bis(trifluoromethyl)-1,3,4-oxadiazole, b.p. 45–65°.

The crude products were combined, washed with 20 ml. of ice water, 20 ml. of cold 2% aqueous sodium hydroxide, and dried over anhydrous magnesium sulfate. Careful fractionation gave 26.8 g. (26% yield) of 2,5-bis(trifluoromethyl)-1,3,4-oxadiazole, b.p. 62.5–65°.

Further purification of 2,5-bis(trifluoromethyl)-1,3,4-oxadiazole was easily carried out employing preparative scale gas chromatography. A column of 0.75 in. × 12 ft. copper tubing packed with 20% fluoroalkylpyromellitate on 35–65 mesh "chromosorb" was used. A column temperature of 105° with a helium back-pressure of 6 lb. eluted the product in 2.8 min. while the small amount of impurity began to come off in 6.5 min. At a loading of 1.5 ml. complete separation was obtained.

Anal. Calcd. for $C_4F_6N_2O$: C, 23.31; F, 55.32; N, 13.60. Found: C, 23.86; F, 56.53; N, 13.40.

The infrared spectrum showed absorptions at 6.25 μ, 6.35 μ (—C═N—), 6.75 μ, 6.88 μ, 7.05 μ, 7.70 μ, 8.0–8.6 μ (C—F). 9.00 μ, 9.94 μ, 10.23 μ, 10.37 μ, 13.10 μ, 13.30 μ and 14.70 μ.

The fluorine magnetic resonance spectrum showed one peak at 45 c.p.s.

2,5-Bis(pentafluoroethyl)-1,3,4-oxadiazole (I. $R_f = C_2F_5$—). A mixture of 0.69 mole (113 g.) of pentafluoropropionic acid and 0.35 mole (17.5 g.) of hydrazine hydrate gave 100 g. of crude reaction product. There was obtained 52 g. (49% yield) of 2,5-bis(pentafluoroethyl)-1,3,4-oxadiazole, b.p. 84–85° after heating the crude reaction product with 100 g. of phosphorus pentoxide.

Anal. Calcd. for $C_6F_{10}N_2O$: C, 23.54; N, 9.16. Found: C, 23.93; N, 9.70.

The infrared spectrum showed absorptions at 6.36 μ (—C═N—), 7.10 μ, 7.48 μ, 8.20 μ, 8.42 μ, 8.65 μ, 8.85 μ, 9.80 μ, 10.30 μ, 10.60 μ, and 13.24 μ.

2,5-Bis(4-hydrooctafluorobutyl)-1,3,4-oxadiazole (I. $R_f = H(CF_2)_4$—). A mixture of 0.2 mole (49.2 g.) of 5-hydrooctafluorovaleric acid and 0.1 mole (5 g.) of hydrazine hydrate gave 35.6 g. of crude reaction product. Upon heating the crude reaction product with 26 g. of phosphorus pentoxide for 2.5 hr. at 300° there was obtained 10.5 g. of crude oxadiazole. Purification as above gave 6.3 g. (13% yield) of 2,5-bis(4-hydrooctafluorobutyl)-1,3,4-oxadiazole, b.p. 192–193°.

2,5-Bis(pentafluoroethyl)-1,3,4-thiadiazole (II. $R_f = C_2F_5$—). A mixture of 0.21 mole (34.5 g.) of pentafluoropropionic acid

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(4) We are indebted to Dr. R. A. Carboni for this experiment.

(5) Private communication, D. C. Remy, m.p. 165–166°.

and 0.11 mole (5.5 g.) of hydrazine hydrate gave 31 g. of crude reaction product. The crude reaction product was mixed well with 46 g. of phosphorus pentasulfide and was then heated under an efficient reflux condenser for 1.5 hr. at 300°. There was obtained 18.8 g. (56% yield) of 2,5-bis-(pentafluoroethyl)-1,3,4-thiadiazole, b.p. 116–118°.

Anal. Calcd. for $C_6F_{10}N_2S$: C, 22.37; F, 58.98; N, 8.70; S, 9.96. Found: C, 22.62; F, 58.75; N, 8.26; S, 9.43.

The infrared spectrum showed absorptions at 6.83 μ (—C=N—), 6.90 μ, 7.45 μ, 8.25 μ (broad), 8.55 μ, 8.88 μ, 9.05 μ, 9.32 μ, 10.60 μ, 12.60 μ, and 13.35 μ.

2,5-Bis(4-hydrooctafluorobutyl)-1,2,4-thiadiazole (II. R_f = $H(CF_2)_4$—). A mixture of 10 mmoles (5.0 g.) of 1,2-bis-(5-hydrooctafluorovaleryl)hydrazine and 23 mmoles (5 g.) of phosphorus pentasulfide was heated at a bath temperature of 250° for 1 hr. The volatile material was removed by distillation. There was obtained 3.6 g. (74% yield) of 2,5-bis(4-hydrooctafluorobutyl)-1,3,4-thiadiazole, approximate b.p. 225°, m.p. 44.5–45.5°.

Anal. Calcd. for $C_{10}H_2F_{16}N_2S$: N, 5.76; S, 6.61. Found: N, 5.65; S, 6.44.

The infrared spectrum showed absorptions at 6.85 μ (—C=N—), 7.10 μ, 7.65 μ, 8.15 μ, 8.52 μ (broad), 8.94 μ, 9.85 μ, 11.55 μ, 11.22 μ, 11.30 μ, 12.37 μ, and 13.07 μ.

The fluorine magnetic resonance spectrum consisted of four chemically shifted resonances, a doublet having components at 4015 and 3965 c.p.s. (—CF_2H), and three singlets at 3495, 3170, and 2080 c.p.s. (internal —CF_2—). All the resonances exhibited considerable fine structure.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY, SICEDISON S.P.A.]

Preparation and Absorption Spectra of 2-Methyl-4-vinyl- and 2-Methyl-6-vinylpyridine

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2-Methyl-4-vinyl- and 2-methyl-6-vinylpyridine were prepared by catalytic dehydrogenation of the corresponding ethyl derivatives. Ultraviolet and infrared spectra were reported and discussed.

2 - Methyl - 6 - vinylpyridine (2M6VP) and 2-methyl - 4 - vinylpyridine (2M4VP) were prepared with a view to comparing their properties, especially their absorption spectra, with other vinyl pyridines deriving, as by-products, from the preparation of 2-methyl-5-vinylpyridine through 2-methyl-5-ethylpyridine dehydrogenation.[1] 2-Methyl-4-vinylpyridine and 2-methyl-6-vinylpyridine were prepared by catalytic dehydrogenation of the corresponding ethyl derivatives.

Analyses and separations were performed by gas chromatography. The substances were identified by spectral analysis; molecular weight resulted from mass spectrometry determinations. The position of the substituent groups was determined by the identification of oxidation products (by paper chromatographic analysis); it was also confirmed by the analysis of hydrogenation products.

2-Methyl-6-vinylpyridine had already been prepared[2] by reaction of formaldehyde on 2,6-lutidine.

Ultraviolet Spectra. 2-Methyl-6-vinylpyridine. Two bands are present in all solutions (methanol, hydrochloric acid, sodium hydroxide). In the case of both methanolic and basic solutions, they are located at 282 mμ and 236 mμ (*p*H 10.02: ϵ_{282} 6570, ϵ_{236} 9450), while in the case of the acid solution, they lie at 292 mμ and 235 mμ (*p*H 3.35: ϵ_{292} 11400, ϵ_{235} 6280). As is already known,[3] these bands can be attributed to bathochromic shifts through conjugation of such pyridine absorption as normally lies around 195 mμ (E band) and in the 250–260-mμ region (B band). The ultraviolet spectra of 2-methyl-6-vinylpyridine are reported in Fig. 1, in which the *p*H 3.35 and *p*H 10.02 absorption curves only are reported. The other measurements taken at *p*H 0.20 and *p*H 13.45, however, do not disclose the presence of an isosbestic point.

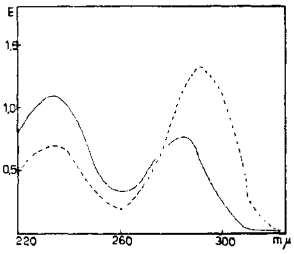

Fig. 1. Ultraviolet spectra of 2-methyl-6-vinylpyridine in acid (*p*H 3.35) (——) and base (*p*H 10.02) (-) solutions (*c*, 0.12 mmole/l.). E denotes the optical density

2-Methyl-4-vinylpyridine. The basic and methanolic solutions show two bands at 281 and 242 mμ (*p*H 10.60: ϵ_{281} = 2910, ϵ_{242} 13,200). The acid solution, on the contrary, shows a broad absorption band only at 264 mμ (*p*H 3.35: ϵ_{264} 13,900). In our opinion, this probably arises from the lack of resolution of two very near bands (type E and B,

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(1) G. B. Gechele, A. Nenz, C. Garbuglio, and S. Pietra, *Chim. e Ind.* (*Milan*), **42**, 959 (1960).

(2) J. Michalski and K. Studniazski, *Roczniki Chemii*, **29**, 1141 (1955).

(3) M. Swain, A. Eisner, C. F. Woodward, and B. A. Brice, *J. Am. Chem. Soc.*, **71**, 1341 (1949).