5-Perfluoroalkyltetrazoles. I. Ring-Opening Reactions[1]

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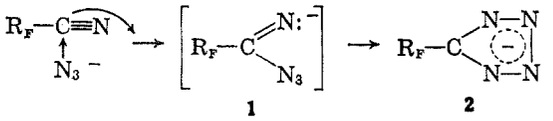
5-Perfluoroalkyltetrazoles and 1,3-bis(5-tetrazolyl)perfluoropropane were prepared; acylation of these compounds with perfluoroacyl chlorides resulted in the formation of 2,5-bis(perfluoroalkyl)-1,3,4-oxadiazoles and 1,3-bis(5-perfluoroalkyl-1,3,4-oxadiazolyl-2)perfluoropropane. 5,5′-Bis(perfluoroalkyl)-2,2′-bi-1,3,4-oxadiazole was prepared from bitetrazole with a perfluoroacyl chloride or from a 5-perfluoroalkyltetrazole with oxalyl chloride. Reaction of perfluoroalkylnitriles with 5-perfluoroalkyltetrazoles gave 3,5-bis(perfluoroalkyl)-1,2,4-triazoles.

The perfluoroalkylnitriles are readily attacked by nucleophiles such as ammonia, hydrazine, hydrogen sulfide, and hydroxylamine to give the stable perfluoroalkylamidines,[2] -hydrazidines,[3] -thioamides,[4] and -amidoximes.[5] A similar reaction with azide ion as the nucleophile resulted in formation of the perfluoroalkyl-substituted tetrazole anion (2) probably through the intermediate, unstable imidazide (1).



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Prior to the appearance of the paper of Norris[6] describing the synthesis of 5-perfluoromethyltetrazole, 5-perfluoropropyltetrazole and 1,3-bis(5-tetrazolyl)perfluoropropane were prepared using a method similar to that described by Mihina and Herbst.[7] Purification of the product, however, required preparation of its silver salt and regeneration of the free tetrazole. The method of Norris gave a product of slightly lower purity, but was much less laborious.

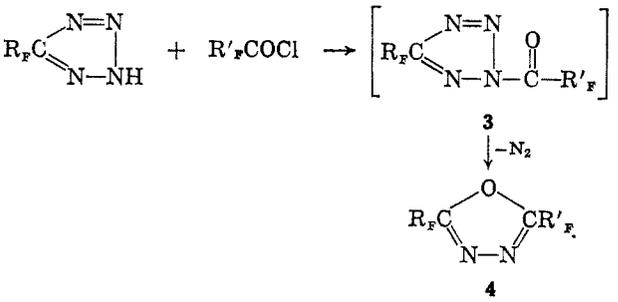
The 5-perfluoroalkyl-substituted tetrazoles are colorless, odorless, strong acids. Pure 1,3-bis(5-tetrazolyl)-perfluoropropane slowly decomposed at 170° while 5-perfluoromethyltetrazole and 5-perfluoropropyltetrazole decomposed at about 180°; the sodium salts of the latter compounds decomposed slowly at 245 and 258°, respectively. Silver 5-perfluoropropyltetrazole undergoes a slow decomposition at 290° which becomes very rapid but not explosive at 350°. Both silver 5-perfluoropropyltetrazole and disilver 1,3-bis(5-tetrazolyl)-perfluoropropane were found to be stable to bright sunlight. Mihina and Herbst[7] reported that several silver tetrazoles were light sensitive but also noted that they occluded silver nitrate. The 5-perfluoroalkyltetrazoles are stable to both hot, aqueous acids and bases and to both alkaline and acidic potassium permanganate at 100°

Huisgen and his co-workers[8-10] recently described the synthesis of 1,3,4-oxadiazoles by the acylation of 5-aryl- and 5-alkyltetrazoles. Huisgen[11] also investigated an analogous reaction with imidoyl chlorides and -tetrazoles which gave substituted 1,2,4-triazoles.

2,5-Bis(perfluoroalkyl)-1,3,4-oxadiazoles and 3,5-bis(perfluoroalkyl)-1,2,4-triazoles have been previously synthesized in this laboratory.[12,13] These perfluoroalkyl-substituted heterocycles were stable at high temperatures and were considered to be promising candidates for incorporation into polymer structures in accordance with the previous interest in this laboratory in poly(perfluoroalkylene heterocycles).[14] The preparation of perfluoroalkyl-substituted 1,3,4-oxadiazoles might be a desirable route to new polymer structures, but little information was available concerning the chemical reactivity of the 5-perfluoroalkyltetrazoles; the present study was undertaken to investigate reactions that might be useful for this purpose.

The synthesis of 2,5-bis(perfluoroalkyl)-1,3,4-oxadiazole (4) was accomplished conveniently by the reaction of a 5-perfluoroalkyltetrazole with a perfluoroacyl chloride. (See Scheme I.) Perfluoroalkyl-substituted 1,3,4-oxadiazoles were synthesized by this method in which the perfluoroalkyl groups were either C_3F_7 or CF_3.

SCHEME I



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An attempt was made to isolate the intermediate 2-perfluorobutyryl-5-perfluoropropyltetrazole (3) by acylating the silver salt of the tetrazole at a low temperature in tetrahydrofuran. Even under these very mild conditions the acylated tetrazole was unstable and rearranged with nitrogen elimination to give 3,5-bis(perfluoropropyl)-1,3,4-oxadiazole in 95% yield. This instability of the 2-perfluoroacyl-5-perfluoropropyltetrazole was in sharp contrast to the stability of the

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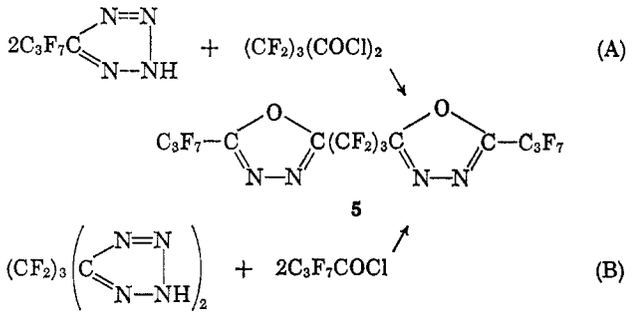
(2) D. R. Husted, U. S. Patent 2,676,985 (1954).
(3) H. C. Brown and D. Pilipovich, *J. Am. Chem. Soc.*, **82**, 4700 (1960).
(4) W. L. Reilly and H. C. Brown, *ibid.*, **78**, 6032 (1956).
(5) H. C. Brown and C. R. Wetzel, *J. Org. Chem.*, **30**, 3734 (1965).
(6) W. P. Norris, *ibid.*, **27**, 3248 (1962).
(7) J. S. Mihina and R. M. Herbst, *ibid.*, **15**, 1082 (1950).
(8) R. D. Huisgen, *Angew. Chem.*, **72**, 366 (1960).
(9) R. Huisgen, J. Sauer, and M. Seidel, *Chem. Ber.*, **93**, 2106 (1960).
(10) J. Sauer, R. Huisgen, and H. J. Sturm, *Tetrahedron*, **11**, 241 (1960).
(11) R. Huisgen, J. Sauer, and M. Seidel, *Chem. Ber.*, **93**, 2885 (1960).
(12) H. C. Brown, M. T. Cheng, L. J. Parcell, and D. Pilipovich, *J. Org. Chem.*, **26**, 4407 (1961).
(13) H. C. Brown and M. T. Cheng, *ibid.*, **27**, 3240 (1962).
(14) H. C. Brown, *J. Polymer Sci.*, **44**, 9 (1960).

2-acyl-5-aryltetrazoles, which required a temperature of 110–140° for rearrangement to the oxadiazole.[8,15]

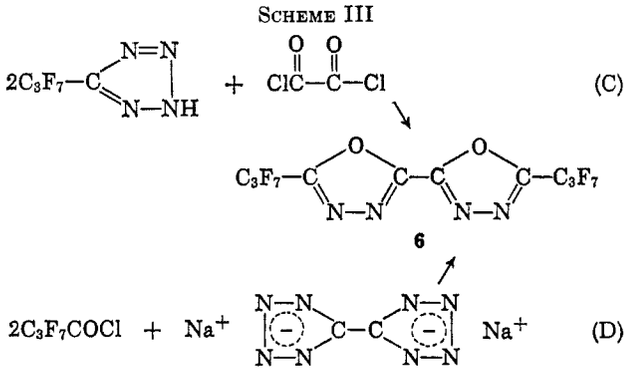
The reaction of fluoroacyl chlorides with fluoroalkyltetrazoles was extended to the synthesis of 1,3-bis(5-perfluoropropyl-1,3,4-oxadiazolyl-2)perfluoropropane (**5**). Two routes were available for this synthesis: the use of a monotetrazole with a diacyl chloride (A), and the use of a difunctional tetrazole with a monoacyl chloride (B). (See Scheme II). 1,3-Bis(5-perfluoropropyl-1,3,4-oxadiazolyl-2)perfluoropropane was prepared by methods A and B in sealed tubes. In theory both reactions should occur with the same ease but in practice method B was preferred since it resulted in both higher yields and a more easily purified product. The infrared spectra of the 1,3-bis(5-perfluoropropyl-1,3,4-oxadiazolyl-2)perfluoropropane showed the same weak absorption at 6.35 and 6.40 μ, previously assigned to cyclic C=N stretching, that was found in the 3,5-bis(perfluoroalkyl)-1,3,4-oxadiazoles.[12]

SCHEME II



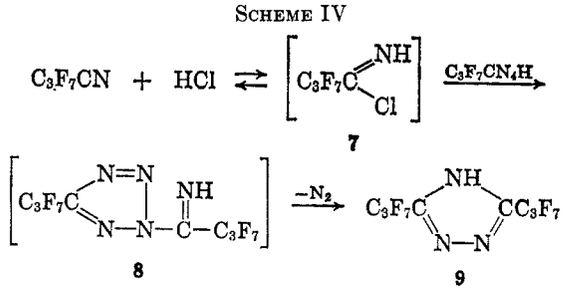
The synthesis of 5,5′-bis(perfluoroalkyl)-2,2′-bi-1,3,4-oxadiazoles (**6**) was carried out also by two synthetic routes as shown at C for the reaction of 5-perfluoropropyltetrazole with oxalyl chloride, or at D for the reaction of perfluorobutyryl chloride with sodium bitetrazole. (See Scheme III.) The yields from method C were much lower than for D. The perfluoroalkyl-substituted bioxadiazole showed several interesting differences from the compounds containing isolated oxadiazole rings. The bioxadiazoles were very high melting by comparison and were more resistant to hydrolysis by hot aqueous alkali. The infrared absorption band at 6.35 μ, characteristic of the 2,5-bis(perfluoroalkyl)-1,3,4-oxadiazoles, did not appear in the spectra of the bioxadiazoles but another, considerably stronger, band appeared at 6.81 μ possibly owing to the absorption of the extended conjugated system C=N—N=C—C=N—N=C. Some degree of conjugation and consequent coplanarity of the rings is indicated by the strong ultraviolet absorption at 230–234 mμ, since the 2,5-bis(perfluoroalkyl)-1,3,4-oxadiazole showed no absorption maxima in the 220–340-mμ region.

SCHEME III



The synthesis of 3,5-bis(perfluoropropyl)-1,2,4-triazole (**9**) was carried out by allowing 5-perfluoropropyltetrazole to react with perfluorobutyronitrile in the presence of an excess of hydrogen chloride. (See Scheme IV.) Although the perfluorobutyrimidoyl chloride (**7**) is not stable, the excess of hydrogen chloride would be expected to shift the equilibrium to the right; reaction with perfluoropropyltetrazole is postulated to involve the intermediate (**8**) analogous to the acylated tetrazole believed to be the intermediate in the formation of the 1,3,4-oxadiazole ring. An intermediate similar to the imidoyl chloride **7**, has been proposed in the hydrogen chloride catalyzed trimerization of perfluoroacetonitrile.[16] In the present study, 3 moles of perfluorobutyronitrile was used for each mole of 5-perfluoropropyltetrazole and the hydrogen chloride–perfluorobutyronitrile ratios ranged from 0.1–1.0 to 4.0–1.0. Increasing the hydrogen chloride concentration definitely increased the yield of the final product, 3,5-bis(perfluoropropyl)-1,2,4-triazole. These reactions were carried out in sealed tubes at temperatures of about 135°; no reaction occurred between 5-perfluoropropyltetrazole and perfluorobutyronitrile under these conditions without the presence of hydrogen chloride.

SCHEME IV



Experimental Section[17]

5-Perfluoromethyltetrazole.—5-Perfluoromethyltetrazole was prepared by treating perfluoroacetonitrile with sodium azide in anhydrous acetonitrile as described by Norris.[6] The reaction was slow using acetonitrile dried with barium oxide but was catalyzed effectively by a trace of glacial acetic acid. This procedure produced a yield of 54%: bp 82–83° (5.1 mm), pK_a = 1.70.

Anal. Calcd: mol wt, 138. Found (by titration with 0.1000 *N* NaOH): mol wt, 138.

5-Perfluoropropyltetrazole.—Sodium azide (33.75 g, 0.52 mole), methyl cellosolve (120 ml), and glacial acetic acid (150 ml) were mixed and the reaction slurry was cooled in an ice bath and stirred vigorously; 116 g (0.595 mole) of perfluorobutyronitrile was added slowly beneath the surface of the liquid. The reaction mixture was then heated at 70° for 1 hr, cooled, and poured into 200 ml of 20% hydrochloric acid. The crude tetrazole was separated as a slightly viscous oil, washed 10 times with dilute hydrochloric acid, then once with water, and dried under reduced pressure to give 137 g of product.

(15) R. Huisgen, J. Sauer, H. Sturm, and J. Markgraf, *Chem. Ber.*, **93**, 2112 (1960).

(16) E. R. Bissel and R. E. Sprenger, *J. Org. Chem.*, **24**, 1147 (1959).

(17) Elemental Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

The crude 5-perfluoropropyltetrazole was dissolved in 1300 ml of acetone and added with stirring to a solution of 98 g of silver nitrate in 1300 ml of water. A voluminous precipitate of silver 5-perfluoropropyltetrazole formed rapidly and was removed by filtration, washed with water and acetone, and dried at reduced pressure. Free 5-perfluoropropyltetrazole was regenerated from the silver salt by addition of gaseous hydrogen chloride to a slurry of the salt in diethyl ether. The precipitate of silver chloride was removed by filtration and the solvent ether was removed under reduced pressure. A small amount of phosphorous pentoxide was added to the residue and pure 5-perfluoropropyltetrazole was distilled from the mixture: yield 96.2 g (77.6%), bp 60° (0.02 mm), mp 31–34°, pK_a = 1.73.

Anal. Calcd for $C_4HF_7N_4$: C, 20.17; H, 0.41; F, 55.89. N, 23.53; mol wt, 238. Found: C, 20.42; H, 0.55; F, 56.00; N, 23.75; mol wt (by titration with 0.1000 *N* NaOH), 241,

This preparation of 5-perfluoropropyltetrazole was carried out before the appearance of Norris paper on the synthesis of 5-perfluoromethyltetrazole. Since the method of Norris which produces as the initial product the sodium salt of the tetrazole is the more convenient, his procedure was used for preparation of additional amounts of 5-perfluoropropyltetrazole. The product obtained by this method, however, did not solidify and was slightly impure.

1,3-Bis(5-tetrazolyl)perfluoropropane.—Sodium azide (8.68 g, 0.133 mole), glacial acetic acid (7.95 ml), and methyl cellosolve (30 ml) were frozen in a flask immersed in liquid nitrogen, the flask was pumped free of air, and perfluoroglutaronitrile (10.0 g 0.0495 mole) was condensed in the reaction flask. The mixture was warmed to 0° and stirred for 30 min, heated at 70° for 15 min, refluxed for 15 min, and then cooled to room temperature. Acetone (25 ml) and concentrated hydrochloric acid (8 ml) were added to the reaction mixture and the precipitated salt was removed by filtration. This procedure was repeated, the solvent was removed under reduced pressure, and the crude product was redissolved in acetone and filtered. Solvent was again removed under reduced pressure and the solid 1,3-bis(5-tetrazolyl)-perfluoropropane was precipitated by the addition of 60 ml of benzene. Yield of crude product was 11.58 g (81%), mp 156–157°. This product was recrystallized from perfluorobutyric acid to give white 1,3-bis(5-tetrazolyl)perfluoropropane: mp 159.8–160.5°, pK_a = 1.70.

Anal. Calcd for $C_5H_2F_6N_8$: C, 20.83; H, 0.67; F, 39.58; N, 38.88; mol wt, 288. Found: C, 21.03; H, 0.84; F, 36.69; N, 39.28; mol wt (by titration with 0.1000 *N* NaOH), 287.

2,5-Bis(perfluoropropyl)-1,3,4-oxadiazole.—5-Perfluoropropyltetrazole (0.51 g, 0.0021 mole) was placed in a heavy-wall, glass tube and the tube was pumped free of air. Perfluorobutyryl-chloride (0.50 g, 0.0022 mole) was condensed in the tube and the tube was sealed and heated at 90° for 6 hr and at 110° for 11.5 hr. The reaction tube was then cooled in liquid nitrogen and opened to the vacuum system, and the evolved nitrogen (0.00105 mole, 50%) was removed. The reaction tube was resealed and heated for 21 hr at 125° and then opened, and the volatile portion of the reaction mixture was transferred to the vacuum system. Separation on the vacuum system gave 0.35 g (25%) of pure 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole, identified by comparison with an authentic sample.[12]

2,5-Bis(perfluoromethyl)-1,3,4-oxadiazole.—5-Perfluoromethyltetrazole (1.47 g, 0.0107 mole) and perfluoroacetyl chloride (1.69 g, 0.0128 mole) were sealed in a glass tube and heated for 30-min periods at 95, 105, and 200°. The tube was then cooled in liquid nitrogen and opened to the vacuum system, and the theoretical amount of evolved nitrogen was recovered. Hydrogen chloride and residual perfluoroacetyl chloride were removed through the vacuum system to leave 2.07 g (95%) of 2,5-bis-(perfluoromethyl)-1,3,4-oxadiazole (bp 65°), identified by comparison with an authentic sample.[12]

1,3-Bis(5-perfluoropropyl-1,3,4-oxadiazolyl-2)perfluoropropane.—1,3-Bis(5-tetrazolyl)perfluoropropane (5.00 g, 0.0173 mole), perfluorobutyryl chloride (8.08 g, 0.0345 mole), and 25 ml of anhydrous methylene chloride were sealed in a reaction tube and heated at 125° for 6.5 hr with continuous agitation. On opening the tube, 85% of the theoretical amount of evolved nitrogen was recovered. Methylene chloride was removed under reduced pressure to leave 10.06 g (93%) of 1,3-bis(5-perfluoropropyl-1,3,4-oxadiazolyl-2)perfluoropropane, mp 36.2–37.5 (after recrystallization from hexane).

Anal. Calcd for $C_{13}F_{20}N_4O_2$: C, 25.02; F, 60.85; N, 8.97. Found: C, 25.30; F, 60.73; N, 8.93.

An alternative synthesis of 1,3-bis(5-perfluoropropyl)1,3,4-oxadiazolyl-2)perfluoropropane was carried out by using 3.06 g (0.0129 mole) of 5-perfluoropropyltetrazole and 1.78 g (0.00643 mole) of perfluoroglutaryl chloride. These reactants were heated in a sealed tube for 18 hr at 125–130°. The crude liquid product was washed with dilute potassium carbonate solution, filtered, washed with water, and dried at reduced pressure. Sublimation at reduced pressure product 1.16 g (30%) of 1,3-bis(5-perfluoropropyl-1,3,4-oxadiazolyl-2)perfluoropropane.

5,5′-Bis(perfluoropropyl)-2,2′-bi-1,3,4-oxadiazole.—Dry disodium bitetrazole[13] (3.30 g, 0.0181 mole), methylene chloride (15 ml), and perfluorobutyryl chloride (11.1 g, 0.0478 mole) were sealed in a tube and heated at 95° for 4 hr, and at 125° for 3 hr with constant agitation. On opening the tube, approximately the theoretical amount of nitrogen was found to have evolved. The crude product was recrystallized twice from toluene, then sublimed at reduced pressure to give 6.15 g (75%) of 5,5′-bis(perfluoropropyl)-2,2′-bi-1,3,4-oxadiazole: mp 165.0–165.8°; λ_{max} 234.0 mμ (log ϵ_{max} 4.09) (isopropyl alcohol).

Anal. Calcd for $C_{10}F_{14}N_4O_2$: C, 25.33; F, 56.12; N, 11.80. Found: C, 25.55; F, 56.00; N, 11.70.

An alternative synthesis of 5,5′-bis(perfluoropropyl)-2,2′-bi-1,3,4-oxadiazole was carried out by placing 2.50 g (0.0105 mole) of 5-perfluoropropyltetrazole, 2 ml of dry methylene chloride, and 0.667 g (0.0053 mole) of oxalyl chloride in a glass tube and heating the tube at 100° with agitation for 5.5 hr. The volatile materials were removed from the tube under reduced pressure and the remaining solid product was recrystallized twice from toluene and sublimed under reduced pressure to give 1.37 g (55%) of 5,5′-bis(perfluoropropyl)2,2′-bi-1,3,4-oxadiazole, identical with the product of the preceding preparation.

3,5-Bis(perfluoropropyl)-1,2,4-triazole.—Three experiments in which 5-perfluoropropyltetrazole was allowed to react with perfluorobutyronitrile in the presence of hydrogen chloride were performed under identical conditions, the exception being the amount of hydrogen chloride present. 5-Perfluoropropyltetrazole (0.50 g, 0.0021 mole) was placed in each of three heavy-wall glass tubes of approximately 50-ml capacity. The tubes were then connected to the vacuum system and pumped free of air, and 1.28 g (0.0063 mole) of perfluorobutyronitrile was added. The following amounts of hydrogen chloride were placed in the tubes: tube 1, 0.024 g (0.00063 mole); tube 2, 0.48 g (0.0126 mole); tube 3, 0.96 g (0.0252 mole). The tubes were sealed and heated for 11 hr at 135° with agitation, then immersed in liquid nitrogen and opened to the vacuum system. The following amounts (per cent of theory) of evolved nitrogen were found in the tubes: 49% (tube 1), 83% (tube 2), 100% (tube 3).

The reaction tubes were pumped free of hydrogen chloride to leave a crude mixture of solid and liquid products. The solid portion of the crude product, principally 3,5-bis(perfluoropropyl)-1,2,4-triazole, was separated from the liquid by mixing the crude product with methylene chloride and filtering immediately. From tubes 2 and 3 were obtained 0.18 and 0.30 g, respectively, of 3,5-bis(perfluoropropyl)-1,2,4-triazole identified by comparison with an authentic sample;[13] no triazole was separated by this procedure from tube 1.

The filtrates of the original reaction products were concentrated and analyzed by gas–liquid partition chromatography and estimated to contain 0.20, 0.11, and 0.055 g of 3,5-bis-(perfluoropropyl)-1,2,4-triazole from tubes 1, 2, and 3, respectively. The total yields of triazole were 23%, (tube 1), 35% (tube 2), and 42% (tube 3).

Registry No.—5, 5199-35-9; 6, 10221-20-2; 9, 7355-81-9; 5-perfluoromethyltetrazole, 10221-22-4; 5-perfluoropropyltetrazole, 10221-23-5; 1,3-bis(5-tetrazolyl)perfluoropropane, 10221-24-6; 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole, 647-79-0.

(18) W. Friederick, U. S. Patent 2,710,297 (1955).