Registry No.—IV, 16878-41-4; V, 16878-42-5; VI, 16878-43-6; XIV, 16878-44-7; 4-amino-6-chloro-2,7-diphenylpteridine, 16878-45-8; 4-amino-2,7-diphenyl-6-ethoxypteridine, 16878-46-9.

Synthesis of a 10,10a-Dihydro-1H-imidazo-[3,4-*b*][1,2]benzothiazine 5,5-Dioxide

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Chlorosulfonation of an aromatic, followed by treatment of the resulting sulfonyl chloride with ammonia, is a generally useful method for the preparation of aryl sulfonamides.[1] We applied this sequence to 5-(4-chlorophenyl)-5-methylhydantoin (**1**) and its 3-chloro isomer (**4**), with different results in each instance. As anticipated from steric considerations, **1** gave 5-(4-chloro-3-sulfamylbenzyl)-5-methylhydantoin (**2**)[2] in 83% yield, and this was hydrolyzed with barium hydroxide to give 4-chloro-α-methyl-3-sulfamylphenylalanine. However, when **4** was treated with chlorosulfonic acid followed by ammonia, it gave a product in 72% yield; the composition differed from that of **4** by two less hydrogens and an additional SO_2. Barium hydroxide hydrolysis gave a product which displayed a peak at 5.92 μ in its infrared spectrum, characteristic of a carboxylic acid, and which lacked peaks at 6.3 and 6.55 μ, characteristic of amino acids.

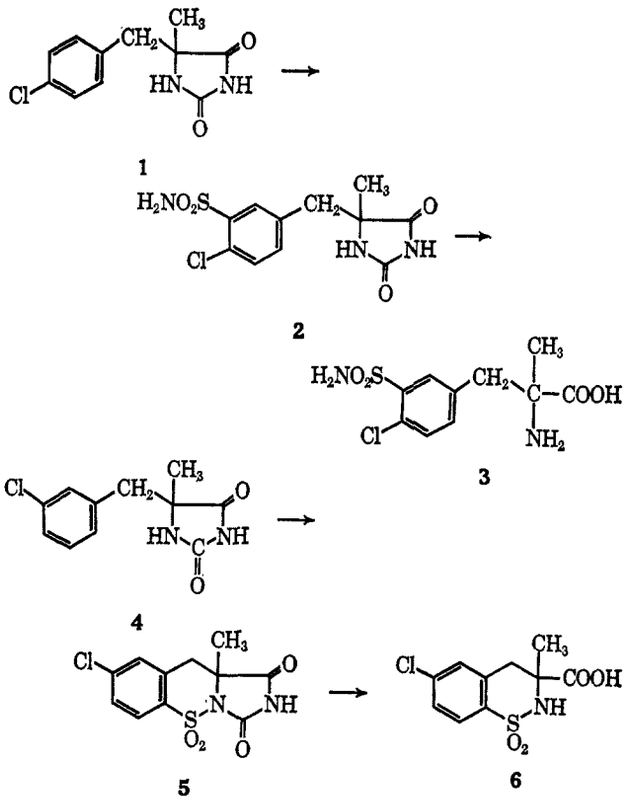
These data are best explained by assuming that the chlorosulfonation of **4** proceeded *para* to the chlorine, and that the sulfonyl chloride cyclized to structure **5** when treated with base. Basic hydrolysis of **5** then opened the hydantoin portion of **5** and the elements of NCO^- were lost, to give 6-chlorobenzo-1,2-thiazine 1,1-dioxide (**6**). The orientation of the chlorosulfonation is confirmed by the nmr spectrum of **5**, which shows a doublet at δ 7.93 (J = 8 Hz). This is expected for an aromatic proton *ortho* to a sulfonyl group which is one of an AB pair.

This orientation is in accord with the generalization that the *para* directive influence of a halogen in sulfonation is greater than that of a methyl group.[3a] However, the results with the 4-chloro isomer are not in agreement with the generalization[3] that a methyl is more strongly *ortho* directing than halogen.[3b]

Experimental Section[4]

The chromatographic R_f values were determined in the following systems: (1) tlc, silica gel G, chloroform–acetone (1:1); (2) 3 MM Whatman paper, 5.6 N ammonium hydroxide–butanol (125:80); (3) tlc, silica gel G, ethyl acetate–acetic acid (99:1); and (4) tlc, Avicel, 5.6 N ammonium hydroxide–butanol (125:80).

SCHEME I



5-(4-Chlorobenzyl)-5-methylhydantoin (1).—A mixture of 1-(4-chlorophenyl)-2-propanone[5] (8.4 g, 0.05 mol), ammonium carbonate (45 g), potassium cyanide (5.0 g), water (75 ml), and ethanol (75 ml) was heated at 55–60° for 8 hr. After cooling, 50 ml of water was added and the mixture was chilled and filtered to give 10.1 g (84%) of white crystals, mp 215–217°. Recrystallization from ethanol–water gave white crystals: mp 214–215°; R_f 0.43 (system 1).

Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.35; H, 4.64; N, 11.74. Found: C, 55.57; H, 4.77; N, 11.97.

5-(3-Chlorobenzyl)-5-methylhydantoin (4).—Using 1-(3-chlorophenyl)-2-propanone,[6] the above procedure gave 82.4% of product: mp 240–242°; R_f 0.43 (system 1); nmr (D_2O/KOH), δ 1.42 (S, 3, CH_3), 2.89 (S, 2, CH_2), and 7.23 (m, 4).

Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.35; H, 4.64; N, 11.74. Found: C, 55.29; H, 4.69; N, 11.87.

5-(4-Chloro-3-sulfamybenzyl)-5-methylhydantoin (2).—A 32.9-g sample of **1** (0.14 mol) was added in portions to 200 ml of $ClSO_3H$ at 0°. The reaction mixture was then stirred at 100–110° for 3 hr, cooled, and added dropwise to 1500 g of ice. This gave a tan solid, mp 208–210°, which was immediately added to 250 ml of 14 N NH_4OH. After being stirred for 1 hr on a steam bath, the cooled reaction mixture was brought to pH 1 with concentrated HCl, and a tan solid, mp 143–148°, was collected. When this solid was purified by dissolving in dilute NaOH and reprecipitating with HCl, it gave 32.5 g (73%) of white crystals: mp 144–147°; R_f 0.30 (system 1); nmr (D_2O/KOD), δ 1.42 (s, 3, CH_3), 2.98 (d, 2, J = 0.5 Hz, CH_2), 7.34 (q, 1, $J_{5,6}$ = 8 Hz, $J_{2,6}$ = 3 Hz, 6 H of phenyl), 7.57 (d, 1, J = 8 Hz, 5 H of phenyl), and 7.89 (d, 1, J = 3 Hz, 2 H of phenyl).

Anal. Calcd for $C_{11}H_{12}ClN_3O_4S \cdot {}^1/_4H_2O$: C, 41.00; H, 3.91; N, 13.04. Found: C, 40.95; H, 4.06; N, 12.84.

4-Chloro-3-sulfamylphenyl-α-methylalanine (3).—A stirred mixture of 3.2 g (0.01 mol) of **2**, 15.8 g (0.05 mol) of $Ba(OH)_2 \cdot 8H_2O$, and 60 ml of H_2O was refluxed for 48 hr. The cooled

(1) C. M. Suter, "The Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, p 573.

(2) This structural assignment is supported by the difference of δ 0.09 observed for the $-CH_2-$ in the nmr spectra of **2** and **4**. In comparison, the difference of δ between the CH_3 of toluene and the 2-CH_3 and the 5-CH_3 of 2,5-dimethylbenzenesulfonamide is δ 0.37 and 0.085.

(3) (a) See ref 1, p 217. (b) At least 86% of the sulfonation product of 4-chlorotoluene is 3-chloro-6-methylbenzenesulfonic acid: W. P. Wynne and J. Bruce, *J. Chem. Soc.*, 731 (1898).

(4) We wish to thank Mr. R. Warren for nmr spectral data, Miss M. Carroll and staff for microanalytical data, and Mr. A. Post for thin layer and paper chromatographic data.

(5) C. G. Overberger and H. Biletch, *J. Amer. Chem. Soc.*, **73**, 4880 (1957).

(6) J. H. Biel, A. E. Drukker, T. F. Mitchell, E. P. Sprengeler, P. A. Nuhfer, A. C. Conway, and A. Horita, *ibid.*, **81**, 2805 (1959).

mixture was brought to pH 1 with 2 N H_2SO_4 and the insoluble product was collected by filtration. The filtrate was concentrated *in vacuo* and the residue was dissolved in 40 ml of H_2O and neutralized with 40% NaOH. Chilling gave 2.4 g (82%) of crystals, mp 305–308°. These crystals were purified by dissolving them in 25 ml of H_2O made basic with diethylamine; the solution was treated with charcoal and then neutralized with acetic acid. Chilling gave 1.6 g of a white solid: mp 299–301°; R_f 0.28 (system 2).

Anal. Calcd for $C_{10}H_{13}ClN_2O_4S$: C, 41.03; H, 4.48; N, 9.57. Found: C, 41.10; H, 4.56; N, 9.33.

8-Chloro-10a-methyl-10,10a-dihydro-1H-imidazo[3,4-*b*][1,2]-benzothiazine-1,3(2H)-dione 5,5-Dioxide (5).—A mixture of 11.9 g (0.05 mol) of **4** in 75 ml of $ClSO_3H$ was stirred at 25° for 3 hr. The mixture was added dropwise with stirring to 500 g of ice, and a white solid, mp 143–154°, was collected by filtration. This was immediately added to 150 ml of concentrated NH_4OH, and the mixture was heated on a steam bath for 1 hr. After standing for 18 hr at 25° the pH was brought to 1 with concentrated HCl, and the resulting solid was collected by filtration. This was dissolved in dilute NH_4OH, treated with charcoal, and reprecipitated at pH 1 to give 10.8 g (72%) of product, mp 265–268°. Another base–acid purification gave white crystals: mp 267–269°; R_f 0.71 (system 3); nmr (CF_3COOH), δ 1.92 (S, 3, CH_3), 3.58 (S, 2, $-CH_2-$), 7.56 (m, 2) and 7.93 (d, 1, J = 8 Hz).

Anal. Calcd for $C_{11}H_9ClN_2SO_4$: C, 43.93; H, 3.02; N, 9.32. Found: C, 43.87; H, 3.16; N, 9.15.

6-Chloro-3-methyl-3,4-dihydro-2H-benzothiazine-3-carboxylic Acid 1,1-Dioxide (6).—A stirred mixture of 7.5 g (0.025 mol) of **5** and 39.4 g (0.25 mol) of $Ba(OH)_2 \cdot 8H_2O$ in 150 ml of H_2O was refluxed for 48 hr. After cooling, the pH was adjusted to 1 with concentrated H_2SO_4. The solid was collected and stirred for 30 min with ethanol. Concentration of the ethanol gave an oil which crystallized when triturated with dilute HCl to give 4.4 g of product, mp 127–152°. This was purified by dissolving in dilute NaOH and reprecipitating at pH 1 with dilute HCl. Two such treatments gave 3.7 g (53%) of product: mp 158–160°; R_f 0.72 (system 4).

Anal. Calcd for $C_{10}H_{10}ClNO_4S$: C, 43.56; H, 3.66; N, 5.08. Found: C, 43.80; H, 3.77; N, 4.86.

The nmr peaks (CF_3COOH) for **2,5-dimethylbenzenesulfonamide** were at δ 2.38 (S, 3, 5-CH_3), 2.67 (S, 3,2-CH_3), 7.45 (broad S, 2), and 8.02 (S, 1). The nmr peak for the CH_3 of toluene (CF_3COOH) is at δ 2.30.

Registry No.—**1**, 16793-24-1; **2**, 16793-21-8; **3**, 16793-22-9; **4**, 16793-23-0; **5**, 16793-19-4; **6**, 16793-20-7.

Fluoroalkylpyridines. A Novel Rearrangement

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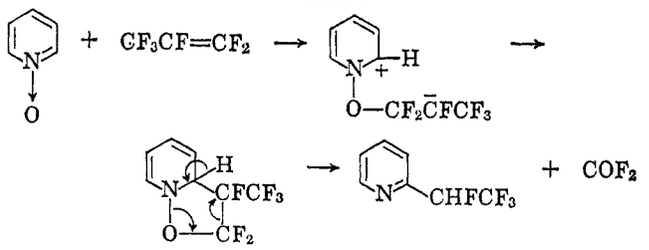
Rearrangements have been shown to occur in pyridine N-oxide chemistry.[1] For instance, pyridine N-oxide and acetic anhydride produced 2-pyridyl acetate, while 2-picoline N-oxide and acetic anhydride yielded 2-pyridylmethyl acetate and 6-methyl-2-pyridinol. Although the reaction of pyridine N-oxide and 2-bromopyridine to give 1-(2-pyridyl)-2-(1H)-pyridone is not a rearrangement, it does show the cyclization that occurs in pyridine N-oxide reactions. Other rearrangements in pyridine N-oxide reactions are also known.[1]

(1) E. N. Shaw, "The Chemistry of Heterocyclic Compounds, Pyridine and Its Derivatives," Part II, E. Klingsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1961, Chapter 4.

The similarity of pyridine N-oxides to nitrones should also be mentioned because it further supports the intermediates postulated below. For example, nitrones of the 1-pyrroline N-oxide type have been treated with olefinic compounds to form isoxazolidines.[2,3]

The novel rearrangement described below furnishes another preparative method for certain alkylpyridines. Alkylpyridines have been obtained previously in a variety of ways: from natural sources, by cyclizations of N-containing compounds; and by alkylation of the pyridine nucleus. These have been reviewed and have been reported by many investigators.[4–7] Our new method of alkylation produces 2-polyfluoroalkylpyridines. Treatment of pyridine N-oxides with terminally unsaturated perfluoroalkenes has yielded 2-polyfluoroalkylpyridines, probably through rearrangement of a postulated isooxazolidine intermediate. For example, pyridine N-oxide and hexafluoropropylene have yielded 2-(1,2,2,2-tetrafluoroethyl)pyridine. One possible mechanism that can account for the product is represented in Scheme I.

SCHEME I



Carbonyl fluoride was found in the off-gases but not in stoichiometric or large amounts, however. Whether some carbonyl fluoride had reacted to give other products was not investigated. Furthermore, solids were always obtained in the short-path distillation of the crude reaction mixture. These air-sensitive solids, when added to water and worked up, provided additional product. No attempt was made to identify these solids. It was later found that the crude reaction mixture could be added directly to water and the resulting mixture then either steam distilled or extracted with an organic solvent. No other reaction variables were investigated.

Mass spectral and nuclear magnetic resonance (F and H) data are consistent with the structures of the 2-polyfluoroalkylpyridines derived from the N-oxides of pyridine and the three picolines. In the case of the 3-picoline product, nmr data indicate it to be an 80:20 mixture of 2- and 6-substituted 3-picoline, respectively.

Experimental Section

Gases were analyzed on a vapor phase fractometer containing a column of DC 200 on Chromosorb P; liquids were analyzed, identified, and isolated on a column containing SE-30 on Chromosorb W. Only medium and strong absorbance bands are re-

(2) G. R. Delpierre and M. Lamchen, *J. Chem. Soc.*, 4693 (1963).
(3) B. G. Murray and A. F. Turner, *ibid., C.*, 1338 (1966).
(4) L. E. Tenenbaum, "The Chemistry of Heterocyclic Compounds, Pyridine and Its Derivatives," Part II, E. Klingsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1961, Chapter 5.
(5) D. Bryce-Smith, *et al.*, *Chem. Ind.* (London), 495 (1964).
(6) R. C. Myerly and K. G. Weinberg, *J. Org. Chem.*, **31**, 2008 (1966).
(7) G. J. Janz and A. R. Monahan, *ibid.*, **29**, 569 (1964).