aci-9-nitro-2-bromofluorene. Treatment with bromine gave 9-nitro-2,9-dibromofluorene which was also optically inactive.

Methylation of the silver salt of 9-nitro-2-bromofluorene gave an unstable nitronic ester which readily decomposed into 2-bromofluorenone oxime and formaldehyde.

The *aci*-nitro form of 9-nitro-2-bromofluorene readily rearranged to the *normal* form. The latter did not absorb bromine whereas the *aci*-form absorbed 50% of the theoretical amount.

URBANA, ILLINOIS RECEIVED AUGUST 2, 1935

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

Some Derivatives of *p*-Fluorophenyl Sulfinic Acid[1]

BY RAYMOND M. HANN

In connection with a study of the action of certain sulfur compounds as possible chemotherapeutic agents in the treatment of pneumonia, a series of derivatives of *p*-fluorophenyl sulfinic acid has been prepared. The sodium salt of *p*-fluorophenyl sulfinic acid was readily obtained from fluorobenzene by the synthesis of Knoevenagel and Kenner[2] and proved to be a suitable material for the introduction of various substituents in the sulfinic acid group. Such compounds as were applicable in regard to solubility and toxicity were tested upon pneumococcus infections in mice by Dr. Sanford Rosenthal, of the Division of Pharmacology, National Institute of Health, but proved to be without therapeutic effect.

Experimental

Sodium *p*-Fluorophenyl Sulfinate Dihydrate.—Dry hydrochloric acid gas was bubbled through an ice-cold suspension of 15 g. of anhydrous aluminum chloride in a solution of 10 g. of fluorobenzene in 25 cc. of carbon disulfide until it was saturated. Dry sulfur dioxide was then introduced in a slow steady stream until the crystalline aluminum chloride was completely changed to a heavy green oily layer (three hours), which became crystalline on standing overnight at room temperature. The reaction mixture was decomposed with 200 cc. of ice water, 20% sodium hydroxide added to strong alkalinity (about 70 cc.), the suspension digested for an hour on the steam-bath, filtered, the soluble aluminum precipitated by passing in carbon dioxide, and, following a second filtration, the mother liquor concentrated to a volume of 50 cc. when a first crop of 12.7 g. of pure salt separated. A second crop, upon further concentration, brought the total yield to 17.0 g. (75% based on dihydrate). Recrystallized from one part of hot water it separated in glistening diamond shaped crystals of the dihydrate.

Anal. Calcd. for $C_6H_4O_2SNaF \cdot 2H_2O$: Na, 10.5; H_2O, 16.5. Found: Na, 10.4; H_2O, 16.7.

Benzyl-ψ-thiourea Salt of *p*-Fluorophenyl Sulfinic Acid.—Cold solutions of 1 g. of benzyl-ψ-thiourea hydrochloride in 10 cc. of 0.25 *N* hydrochloric acid and of 0.9 g. of sodium *p*-fluorophenyl sulfinate in 10 cc. of water were mixed, the resulting thiourea salt filtered and recrystallized from 25 cc. of 0.25 *N* acid, when it separates in elongated prismatic columns showing a melting point of 161° (corr.).

Anal. Calcd. for $C_{14}H_{15}O_2N_2S_2F$: N, 8.6. Found: N, 8.7.

Benzyl-ψ-thiourea Salt of *p*-Fluorophenyl Sulfonic Acid.—A solution of 1 g. of sodium *p*-fluorophenyl sulfinate in 5 cc. of *N* sodium hydroxide was treated dropwise with 5 cc. of 30% hydrogen peroxide, and following the original heating up and gas evolution, it was heated on the steam-bath for one-half hour to complete the oxidation. The oxidized solution was carefully neutralized with *N* hydrochloric acid and added to a solution of 1.1 g. of benzyl-ψ-thiourea hydrochloride in 10 cc. of 0.25 *N* hydrochloric acid. The precipitated salt was filtered and recrystallized from 15 cc. of 0.25 *N* hydrochloric acid, being obtained in brilliant plates, melting at 166° (corr.).

Anal. Calcd. for $C_{14}H_{15}O_3N_2S_2F$: N, 8.2. Found: N, 8.3.

***p*-Fluorophenylphenacyl Sulfone.**—A solution of 1 g. of sodium *p*-fluorophenyl sulfinate in 5 cc. of water and 15 cc. of 95% alcohol was refluxed for fifteen minutes with 1.1 g. of ω-bromoacetophenone and the precipitate which separated on cooling was recrystallized from 30 cc. of 95% alcohol. The sulfone separates in large elongated colorless plates melting at 151° (corr.).

Anal. Calcd. for $C_{14}H_{11}O_3SF$: S, 11.5. Found: S, 11.3.

***p*-Fluorophenyl *p*-Nitrobenzyl Sulfone.**—This sulfone was obtained from the sulfinate and *p*-nitrobenzyl chloride and crystallized from 95% alcohol in slightly yellow brilliant plates melting at 185° (corr.).

Anal. Calcd. for $C_{13}H_{10}O_4NSF$: N, 4.8. Found: N, 5.0.

***p*-Fluorophenyl Sulfone Acetic Acid.**—A solution of 3 g. of sodium *p*-fluorophenyl sulfinate and 1.6 g. of monochloroacetic acid in 15 cc. of water was neutralized with *N* sodium hydroxide, evaporated over a free flame to crystallization and then to dryness on the steam-bath. The dry salt was taken up in 10 cc. of water, acidified to Congo red

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Knoevenagel and Kenner, *Ber.*, **41**, 3315 (1908).

with hydrochloric acid, extracted with ether and the residue remaining after evaporation of the ether recrystallized from benzene when the free acid was obtained in colorless needles melting at 110–111° (corr.).

Anal. Calcd. for $C_8H_7O_4SF$: S, 14.7. Found: S, 14.4.

Benzyl-ψ-thiourea Salt of *p*-Fluorophenyl Sulfone Acetic Acid.—This salt was obtained in microcrystalline glistening prismatic needles melting at 144° (corr.) with decomposition.

Anal. Calcd. for $C_{16}H_{17}O_4N_2S_2F$: N, 7.3; S, 16.7. Found: N, 7.7; S, 16.6.

***p*-Bromophenacyl Ester of *p*-Fluorophenyl Sulfone Acetic Acid.**—This ester crystallizes from 95% alcohol in colorless glistening needles melting at 126° (corr.).

Anal. Calcd. for $C_{16}H_{13}O_5SBrF$: S, 7.7. Found: S, 8.0.

***p*-Fluorophenylsulfonyl Acetone.**—A suspension of 5.5 g. (10% excess) of finely powdered sodium *p*-fluorophenyl sulfinate in 25 cc. of 95% alcohol containing 2.1 g. of monochloroacetone was refluxed for one-half hour, the alcohol driven off by an air current and the oily residue crystallized by trituration with water; yield quantitative.

The sulfonyl acetone was obtained in elongated needle-like plates melting at 66° (corr.) by recrystallization from 10 parts of 95% alcohol.

Anal. Calcd. for $C_9H_9O_3SF$: S, 14.8. Found: S, 14.7.

α-γ-Di-*p*-fluorophenylsulfonyl Acetone.—The difluorophenylsulfonyl ketone was similarly prepared from α-γ-diiodoacetone and crystallized from 95% alcohol in long colorless needles melting at 144° (corr.).

Anal. Calcd. for $C_{15}H_{12}O_5S_2F_2$: S, 17.1. Found: S, 16.8.

Summary

A series of derivatives of *p*-fluorophenyl sulfinic acid has been prepared and characterized.

WASHINGTON, D. C. RECEIVED AUGUST 27, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Chemistry of the Acetylenes. II. Pharmacological Properties of the Acetylenic Linkage

BY G. BRYANT BACHMAN

Although the number of medicinals containing acetylenic linkages which have been prepared is relatively small, the available evidence points to a lesser pharmacological activity for these substances than for the corresponding olefinic and saturated isologs. Shonle[1] has found this to be true of a group of hypnotics of the barbital series, and Gilman and Pickens[2] still earlier report β-diethylaminoethylphenyl propiolate to be intensely irritating rather than anesthetic in its action. In order to investigate this lesser activity of acetylenic compounds more thoroughly and to study further the relative values of aliphatic novocaine analogs,[3] a number of amino esters of α-octynoic, α-octenoic and octanoic acids have been prepared and tested for local anesthetic action on the sciatic nerves of frogs. From the results obtained it may be said that in so far as sensory anesthesia is concerned, the same order of activity holds for these anesthetics as holds for the hypnotics tested by Shonle. On the motor and sensory nerves of frogs the compounds tested exhibited a potency comparable to or slightly better than that of novocaine. The octanoic acid esters, however, were the best and the octynoic esters the poorest of the entire group. All of the esters were somewhat irritating although not intensely so. Of the esters of any single acid, those were best having the greatest molecular weight and those poorest having the least molecular weight. On the basis of these results it appears that the local anesthetic effectiveness of novocaine analogs in the aliphatic series is directly proportional to the molecular weight of the alcohol portion of the molecule (probably within limits) and inversely proportional to the degree of unsaturation in the acid portion of the molecule. None of the compounds tested in this work exhibited anesthetic action on mucus membranes.

(1) Shonle, *J. Ind. Eng. Chem.*, **23**, 1104 (1931); Shonle and Waldo, THIS JOURNAL, **55**, 4649 (1933).

(2) Gilman and Pickens, *ibid.*, **47**, 245 (1925).

(3) *Cf.* Brill and Bulow, *ibid.*, **55**, 2059 (1933).

Experimental

The esters were prepared by cautiously adding a slight excess of the acid chlorides in an equal volume of benzene to the amino alcohols also in benzene. The mixture was then refluxed for one hour, poured into water and made alkaline with aqueous potassium hydroxide. The benzene solution of the ester was separated, dried and then distilled under diminished pressure.

α-Octenic acid chloride, a new compound, was prepared by reaction of the acid with thionyl chlo-