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.

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[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.

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-

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(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).

TABLE I

PROPERTIES OF SOME AMINO ESTERS OF OCTANOIC, α-OCTENOIC AND α-OCTYNOIC ACIDS

Ester	B. p., °C.	Mm.	n^{20}_D	d^{20}_4	Anal. for N Calcd.	Anal. for N Found	Time, min., for anesthesia Sensory	Time, min., for anesthesia Motor
$C_5H_{11}CH_2CH_2COOCH_2CH_2N(C_2H_5)_2$	162–164	20	1.4390	0.883	5.76	5.63	4	23.5
$C_5H_{11}CH_2CH_2COOCH_2CH_2CH_2N(C_2H_5)_2$	178–181	20	1.4405	.886	5.45	5.19	4	12.5
$C_5H_{11}CH_2CH_2COOCH_2CH_2CH_2N(C_4H_9)_2$	212–215	20	1.4451	.876	4.47	4.21	3.5	11.5
$C_5H_{11}CH{=}CHCOOCH_2CH_2N(C_2H_5)_2$	171–173	20	1.4560	.901	5.81	5.47	6.5	15
$C_5H_{11}CH{=}CHCOOCH_2CH_2CH_2N(C_2H_5)_2$	183–186	20	1.4565	.901	5.49	5.54	5	27.5
$C_5H_{11}CH{=}CHCOOCH_2CH_2CH_2N(C_4H_9)_2$	217–220	20	1.4574	.888	4.50	4.25	4	10
$C_5H_{11}C{\equiv}CCOOCH_2CH_2N(C_2H_5)_2$	150–152	7	1.4723	.916	5.86	5.81	8	24
$C_5H_{11}C{\equiv}CCOOCH_2CH_2CH_2N(C_2H_5)_2$	164–166	7	1.4739	.921	5.53	5.62	6	22
$C_5H_{11}C{\equiv}CCOOCH_2CH_2CH_2N(C_4H_9)_2$	193–195	7	1.4750	.900	4.53	4.41	4.5	10
Novocaine							8	15

ride and has the constants: b. p. 109–111° (30 mm.); n^{20}_D 1.4649; d^{20}_4 0.9841. *Anal.* Calcd. for $C_8H_{13}OCl$: Cl, 22.13. Found: Cl, 22.10, 22.21.

The table lists the properties and analyses of the compounds prepared and shows their relative anesthetic activity as measured by the time elapsed between contact with the drug and complete anesthesia.[4]

Some difficulty was experienced in obtaining satisfactory aqueous solutions of the compounds tested. Apparently excess acid (hydrochloric) was necessary to attain complete solution and undoubtedly this contributed to the irritating qualities noted for each compound. Novocaine is included in the table for the sake of comparison.

Summary

1. A number of amino esters of octanoic, α-octenoic, and α-octynoic acids have been prepared and their local anesthetic powers reported.

2. Within the limits of the compounds here described it appears that the anesthetic power of these amino esters is directly proportional to the molecular weight of the amino alcohol part of the molecule and inversely proportional to the degree of unsaturation of the acid.

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(4) The writer is indebted to Dr. T. H. Rider of the Wm. S. Merrell Company of Cincinnati for the pharmacological testing.

[CONTRIBUTION FROM THE D. I. MENDELEYEFF CHEMICAL-TECHNOLOGICAL INSTITUTE]

Thermodynamical Calculations of Solubilities of Nitrogen and Hydrogen in Water at High Pressures

BY I. R. KRICHEVSKY AND J. S. KASARNOVSKY

Much attention is given nowadays to the experimental investigation of solubilities of gases at high pressures in liquids, chiefly in water and liquid ammonia. This paper gives a method of calculation of solubilities of gases in one special, but very important, case where the solubility of gas is small and the vapor pressure of solvent is not great. The solubilities in water of such important technical gases as hydrogen, nitrogen, carbon oxide, methane, oxygen and helium fall in this classification.

When the concentration of a solute is small the fugacity of the solvent can be calculated by means of Raoult's law, the fugacities of the components being connected according to the equation of Gibbs–Duhem

$$N_1 \mathrm{d} \ln f_1 + N_2 \mathrm{d} \ln f_2 = 0 \qquad (1)$$

(N_1, N_2 and f_1, f_2 are mole fractions and fugacities of either solvent and solute); it is not difficult to prove that there exists direct proportionality between f_2 and N_2, known as Henry's law

$$f_2 = KN_2 \qquad (2)$$

where K is Henry's coefficient.

Wiebe, Gaddy and Heins[1] nevertheless have shown that their experimental data on the solubility of nitrogen in water are poorly expressed by the equation (2). This is also true for the data on the solubility of hydrogen in water. The solubilities of these gases in water are so small, even at a pressure of 1000 atmospheres, that the fugacity of water in solution can be calculated according to Raoult's law. From this, however, it would seem to follow as a thermodynamical

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(1) Wiebe, Gaddy and Heins, THIS JOURNAL, **55**, 947 (1933).