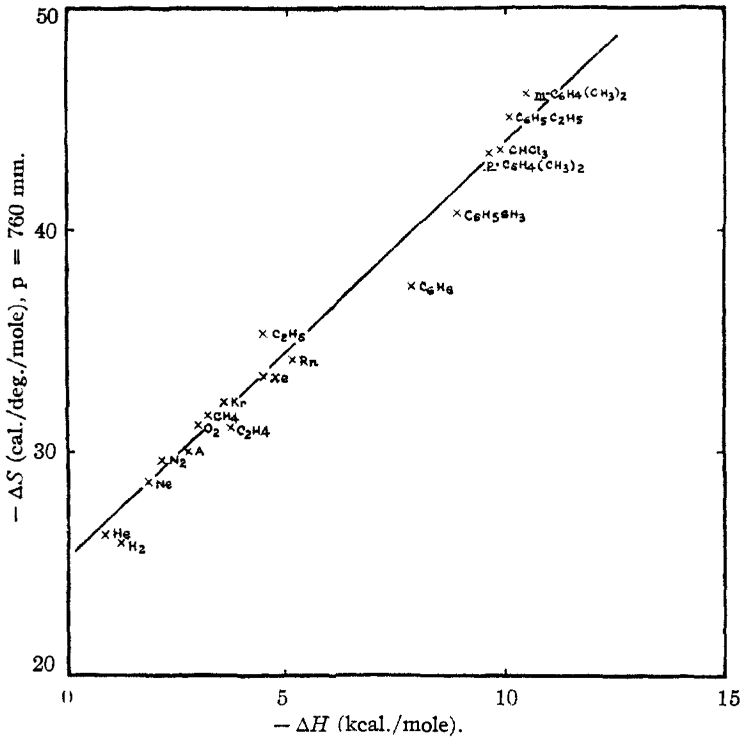

Fig. 2.— $-\Delta S$ plotted against $-\Delta H$ for a number of non-polar substances. All values refer to 25°.

project.[6] In some instances the vapor pressures so calculated involved an extrapolation of the observed data.

Figure 1 shows that the relationship between ΔF and ΔT can be represented by a straight line for each hydrocarbon and hence the values of ΔS and ΔH are almost temperature independent in the range 0 to 40°. This observation indicates that the variation of $\Delta \bar{H}_{sol}$ (equation 1) with temperature arises from the adoption of the liquid hydrocarbon as the standard state and is not to be ascribed to any property of the aqueous hydrocarbon solution. The values of $-\Delta H$ and $-\Delta S(p = 1 \text{ mm.})$ given in Table I were obtained from the slopes of the lines shown in Fig. 1. Column 4 of this table lists the entropy changes when a standard state of $p = 760$ mm. is chosen for the hydrocarbon vapor.

TABLE I

Hydrocarbon	$-\Delta H$, kcal./mole	$-\Delta S(p = 1 \text{ mm.})$, cal./deg./mole	$-\Delta S(p = 760 \text{ mm.})$, cal./deg./mole
Benzene	7.83	50.7	37.5
Toluene	8.85	54.1	40.9
Ethylbenzene	10.03	58.4	45.2
m-Xylene	10.40	59.5	46.3
p-Xylene	9.60	56.9	43.7

In Fig. 2 the values of $-\Delta H$ are plotted against $-\Delta S(p = 760 \text{ mm.})$ for the above compounds together with those for the rare gases and for hydrogen, nitrogen, oxygen, methane, ethane, ethylene and chloroform at 25° quoted by Frank and Evans.[7] The points for the aromatic hydrocarbons follow closely the straight line connecting the $-\Delta S$ and $-\Delta H$ values for the other non-polar substances, but there is however a marked difference between the reported temperature dependence of ΔS for the rare gases and that of the aromatic hydrocarbons. Frank and Evans[7] present a plot of $-\Delta S(p = 760 \text{ mm.})$ against T for the rare gases in the temperature range 0–100° which shows that $-\Delta S$ may have a big temperature coefficient and that for a large atom such as radon in water the partial molar heat capacity exceeds 60 cal./deg./mole. The temperature coefficient of ΔS for these aromatic hydrocarbons is zero within experimental error (see Fig. 1) although these molecules are undoubtedly larger than the radon atom. If the high partial molar heat capacity which has been reported for radon in water is to be attributed to "iceberg" formation[7] then the results for the aromatic hydrocarbons discussed here show that these compounds do not form "icebergs."

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[6] A.P.I.-N.B.S. project 44, Table 5k.

[7] Frank and Evans, *J. Chem. Phys.*, **13**, 507 (1945).

Synthesis of 3,4-Difluorophenylarsonic Acid

BY ARTHUR F. HELIN AND CALVIN A. VANDERWERF

As part of our program on the synthesis and testing of fluorine containing compounds of pharmacological interest, we have synthesized 3,4-difluorophenylarsonic acid, an analog of stovarsol. Several projected routes for the preparation of the critical intermediate, 3,4-difluoroaniline, were explored. In one of these *p*-fluoroaniline was nitrated in good yield to give 3-nitro-4-fluoroaniline, which, after acetylation, was hydrogenated catalytically to 3-amino-4-fluoroacetanilide. Attempted conversion of this product to 3,4-difluoracetanilide *via* the Schiemann reaction was, however, unsuccessful because of the rapid decomposition of the diazonium fluoborate to yield an intractable tar. This fact is in line with the general observation[1] that the presence of amino group lowers the yields obtained in the decomposition of diazonium fluoborates.

Preparation of 3,4-difluoronitrobenzene by means of the Schiemann reaction as applied to 2-fluoro-5-nitroaniline was likewise thwarted by the fact that the diazonium fluoborate decomposed explosively with extensive carbonization when warmed even slightly. The sweet-tasting 2-fluoro-5-nitroaniline used as an intermediate was obtained by selective reduction of the 2-nitro group in 2,4-

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[1] A. Roe in Adams, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 206.

dinitrofluorobenzene by means of stannous chloride and hydrochloric acid.[2]

The successful approach to 3,4-difluoroaniline involved the catalytic reduction of 3,4-difluoronitrobenzene, which was prepared by nitration of *o*-difluorobenzene.[3] The difluoro compound was obtained by means of the Schiemann reaction on *o*-fluoroaniline, which, in turn, was synthesized from *o*-fluorobenzoic acid by means of the Schmidt reaction or, less satisfactorily, from *o*-nitroaniline in a two-step process, (1) the Schiemann reaction, followed by (2) catalytic reduction. Conversion of 3,4-difluoroaniline to 3,4-difluorophenylarsonic acid was achieved by means of the Bart reaction.

Experimental

3,4-Difluoroaniline.—Exactly 142 g. (0.89 mole) of 3,4-difluoronitrobenzene, b.p. 85° (13 mm.), in 150 ml. of absolute ethanol was hydrogenated in a Parr apparatus at 60° and 3 atmospheres pressure in the presence of 2 g. of Raney nickel catalyst. Reduction proceeded slowly and fresh catalyst was twice added during the total 48-hour period. The catalyst was then removed by filtration, the solvent by distillation, and the residue distilled under reduced pressure to yield 107 g. (93%) of 3,4-difluoroaniline, b.p. 77° (7 mm.), n^{25}D 1.5110.

Anal. Calcd. for $C_6H_5NF_2$: C, 55.8; H, 3.9; N, 10.9. Found: C, 55.7; H, 3.9; N, 11.0.

3,4-Difluoroaniline hydrochloride was prepared by passing dry hydrogen chloride into a solution of the free base in absolute ether. The white crystalline product sublimed rapidly above 220°.

Anal. Calcd. for $C_6H_6NF_2Cl$: C, 43.5; H, 3.6; N, 8.5. Found: C, 43.9, 43.8; H, 3.6, 3.6; N, 8.6.

3,4-Difluorophenylarsonic Acid.—A mixture of 1 l. of ethanol, 52 g. (0.40) of 3,4-difluoroaniline, 40 g. of concentrated sulfuric acid and 112 g. (0.62 mole) of arsenic trichloride was cooled to 0°, and 28 g. (0.40 mole) of sodium nitrite in saturated aqueous solution was added with stirring while the temperature was maintained below 5°. When diazotization was complete, 4.0 g. of cuprous bromide was added, the solution was stirred for 30 minutes in the cold, and finally heated on a steam-bath until evolution of nitrogen ceased. The mixture was steam distilled and the residue evaporated to 200 ml. and then allowed to stand for 12 hours. The small amount of amorphous material which precipitated was removed by filtration and discarded. The filtrate was concentrated to a volume of 100 ml. and cooled; the colorless crystals which formed were washed, first with alcohol and then with ether, and dried to yield 30 g. (31%) of 3,4-difluorophenylarsonic acid, which did not melt below 300°. An analytical sample was prepared by recrystallization from water.

Anal. Calcd. for $C_6H_5O_3F_2As$: C, 30.3; H, 2.1. Found: C, 30.4; H, 2.3.

Acknowledgment.—These studies were aided by a contract between the Office of Naval Research, Department of Navy, and the University of Kansas.

[2] J. J. Blanksma, W. J. Van den Broek and D. Hoegen, *Rec. trav. chim.*, **65**, 329 (1946).

[3] J. G. McNally and J. R. Byers, U. S. Patent 2,391,179, Dec. 18, 1945.

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Anilinephthalein

BY MAX H. HUBACHER

In the course of a study of compounds with possible laxative properties,[1] it was decided to test anilinephthalein or 3,3-bis-(*p*-aminophenyl)-phthalide.

Baeyer[2] synthesized this compound from 3,3-bis-(phenyl)-phthalide and reported it to have a melting point of 180°. This synthesis was confirmed by v. Pechmann,[3] who, however, did not present any experimental evidence, and by Fischer and Römer,[4] who claimed to have obtained dimethylanilinephthalein from Baeyer's compound. On the other hand, Schwarzenbach and Brandenberger,[5] as well as we in our laboratory, failed to obtain the anilinephthalein which melted at 180° by following Baeyer's procedure.

More recently, Schwarzenbach and Brandenberger[5] described two new syntheses of anilinephthalein which they obtained as a compound melting at 204°. By their first method, starting from 3,3-bis-(*p*-tolyl)-phthalide, they obtained it in very low over-all yields. In their second and more efficient method, they condensed phthalyl chloride with *s*-diphenylurea and then hydrolyzed the intermediary amorphous condensation product with concd. hydrochloric acid at 140° in sealed glass tubes. This method was investigated further in our laboratory and an improved procedure was evolved, based on the observation that the condensation product can be hydrolyzed by a refluxing mixture of acetic and sulfuric acid.

Several new derivatives of anilinephthalein (I) were prepared, and further proof was obtained that I actually is the 3,3-bis-(*p*-aminophenyl)-phthalide. When reduced, anilinephthalin (II) is formed. On decarboxylation, this yields 4,4'-diaminotriphenylmethane (III).

In a similar manner, a toluidinephthalein (V) which melted at 197° was prepared from *s*-di-*o*-tolylurea. It was proved to be 3,3-bis-(*p*-amino-*m*-tolyl)-phthalide, as follows: By eliminating the two amino groups a ditolylphthalide (VI), which has different properties than those of the known *o*- and *p*-ditolylphthalides, was isolated. Compound VI must, therefore, be the 3,3-bis-(*m*-tolyl)-phthalide, which was further proved by synthesis.

Experimental[6]

Condensation Product from *s*-Diphenylurea and Phthalyl Chloride.—A 2-liter flask was charged with 500 ml. of nitrobenzene and 100 g. (0.75 mole) of aluminum chloride (anhydrous, technical or pure grade). After cooling to 25°, 40.6 g. (0.2 mole) of phthalyl chloride and finally 42.4 g. (0.2 mole) of *s*-diphenylurea (m.p. 239–243°) were added. The mixture was heated over a period of two hours from room temperature to 80° and kept at 80° for 30 minutes. The reddish-brown solution was then poured on an ice–hydrochloric acid mixture and the nitrobenzene removed by steam distillation. After the hard, brown residue had been pulverized and submitted to further steam distillation to remove traces of nitrobenzene, it weighed 60–68 g. It starts to melt at 260° and is not entirely melted at 300°. It is insoluble in common solvents and could not be obtained in crystalline form.

Anilinephthalein (I).—A mixture of 60–68 g. of the condensation product, 400 ml. of acetic acid, 5 ml. of water and

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[1] (a) S. Loewe and M. Hubacher, *Arch. intern. pharmacodynamie*, **65**, 297 (1941); (b) M. H. Hubacher, THIS JOURNAL, **64**, 2538 (1942); **66**, 255 (1944); (c) M. H. Hubacher and S. Doernberg, *J. Am. Pharm. Assoc.*, **37**, 261 (1948).

[2] A. Baeyer, *Ann.*, **202**, 66 (1880).

[3] H. v. Pechmann, *Ber.*, **14**, 1866 (1881).

[4] O. Fischer and F. Römer, *ibid.*, **42**, 2934 (1909).

[5] G. Schwarzenbach and M. Brandenberger, *Helv. Chim. Acta*, **20**, 1253 (1937), and in more detail in "Untersuchungen in der Phtaleinreihe," Inauguraldissertation von Mark Brandenberger, Universität Zürich, 1936.

[6] All the melting points are corrected. Elementary analysis by Oakwold Laboratories, William Saschek and Francine Schwarzkopf.