of fluorine so that this ordinarily non-reducible group becomes labile.

Anomalous Maximum Suppression.—Another manifestation of the ortho effect is seen in the different tendency toward maxima exhibited by *o*-nitroiodobenzene as compared to the corresponding meta and para isomers. As shown by the polarograms given in Fig. 2, both the meta and para derivatives yield large maxima while the ortho isomer shows no maximum at the same concentration.

Suppression of the polarographic maximum in the case of *p*-nitroiodobenzene (Fig. 2) yields a *smaller* negative half-wave potential than that obtained from the unsuppressed curve. Behavior in this case appears to be unique by comparison with the more negative half-wave potentials that are usually found[7,8] as a result of maxima suppression.

Experimental

The apparatus, accessories and polarographic characteristics were the same as described in previous communications from this Laboratory.[7,9] All measurements were made at 25.00 ± 0.05° and at a drop-time of 3.00 seconds.

All the iodo compounds investigated polarographically were Eastman Kodak Co. White Label grade with the exception of *m*-iodo- and *p*-iodoanisoles. *m*-Iodoanisole was synthesized by accepted procedure[10,11] from *m*-aminophenol (Eastman Kodak Co. Yellow Label grade). It boiled at 117° at 13 mm., b.p. reported[11] is 123° at 14 mm. *p*-Iodoanisole was prepared by the iodination[12] of anisole. The yield after recrystallization from ethanol was 57.5%, m.p. 50–51°. The reported m.p.[12] is 51–52°.

All iodo compounds were investigated polarographically in a 90% alcohol *p*H 7.00 buffer solution[13] containing 0.060 *M* lithium chloride, 0.024 *M* potassium acetate and 0.013 *M* acetic acid.

Methyl cellulose (1500 cps. viscosity) from Dow Chemical Co. was used as a suppressor and was maintained at a constant ratio of maximum suppressor to iodo compound equal to 5% per molarity. A recent investigation[7] showed the desirability of using a constant ratio of suppressor to reduction material in alcohol–water mixtures.

Acknowledgment.—The authors are indebted to the Research Corporation for supporting this work.

[7] E. L. Colichman, This Journal, **74**, 722 (1952).

[8] E. L. Colichman, *ibid.*, **72**, 4036 (1950).

[9] E. L. Colichman and H. P. Maffei, *ibid.*, **74**, 2744 (1952).

[10] F. Reverdin and A. de Luc, *Ber.*, **47**, 1537 (1914).

[11] E. Votocek and J. Matejka, *ibid.*, **46**, 1755 (1913).

[12] F. F. Blicke and F. D. Smith, This Journal, **50**, 1229 (1928).

[13] Measured with an ordinary Beckman *p*H meter, employing usual aqueous reference cell, thus is an effective *p*H value.

Department of Chemistry
University of Portland
Portland 3, Oregon

Freezing Points of the System Water-Trifluoroacetic Acid

By Howard H. Cady and George H. Cady

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Although trifluoroacetic acid is known to be miscible with water in all proportions and to behave as a strong acid, no report has been made of a systematic study of the system water–trifluoroacetic acid. The purpose of this note is to give the information about freezing points which is summarized in Fig. 1. Numerical data for the points indicated by letters in the figure are listed in Table I. The value observed for the melting point of the pure acid is a little lower than −15.25°, the temperature reported by Swarts.[1]

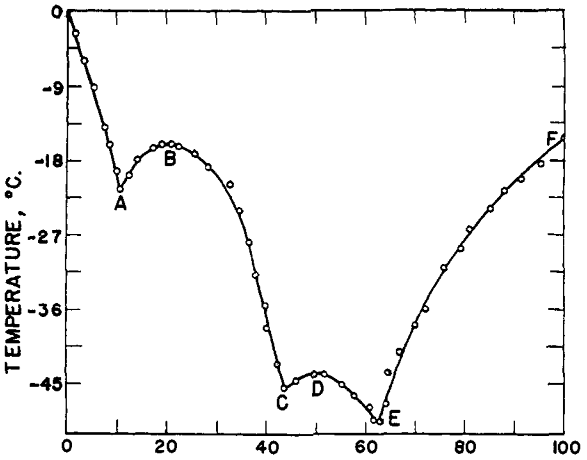

Fig. 1.—System CF_3COOH–H_2O.

Table I

Point	Nature of the point	Temp., °C.	Acid, mole %
A	Eutectic	−21.55	10.59
B	M.p. of $CF_3COOH \cdot 4H_2O$	−16.06	20.00
C	Eutectic	−45.51	43.9
D	M.p. of $CF_3COOH \cdot H_2O$	−43.73	50.0
E	Eutectic	−49.56	62.5
F	M.p. of CF_3COOH	−15.36	100.0

Data for the part of the system in which ice is the solid phase are given in Table II. Concentrations are in moles per 1000 g. of water.

Table II

m	Freezing temp., °C.	*m*	Freezing temp., °C.	*m*	Freezing temp., °C.
0.0878	−0.34	1.134	−3.75	3.949	−12.52
.1397	−0.50	1.603	−5.12	4.146	−13.20
.1832	−0.68	1.884	−6.00	4.381	−13.92
.2955	−1.03	2.300	−7.32	5.098	−16.10
.7206	−2.36	2.571	−8.20	5.997	−19.38
.8164	−2.70	2.929	−9.22	6.541	−21.53

Materials.—Trifluoroacetic acid was obtained from the Minnesota Mining and Manufacturing Co. Although the acid behaved as a material of high purity as obtained from the manufacturer, it was further purified by distillation. The center cut of the distillate was then frozen, and later as it slowly melted the liquid was drained away from the crystals. After about one third of the acid had been removed in this manner, the remaining solid was allowed to melt and subsequently was used for preparing solutions. The other component was distilled water. In this study no attempt was made to exclude atmospheric gases; therefore, the solutions must have been saturated with air.

Procedure.—Temperatures were measured with a precision of 0.01° using a copper–constantan thermocouple which was found to agree with the standard temperature scale for such a couple to within 0.05° at the sublimation temperature of carbon dioxide, the melting point of carbon tetrachloride, the melting point of ice and the boiling point of water.

Approximately 100 ml. of the solution to be frozen was placed in a 500-ml. wide mouth Dewar flask. As the liquid was stirred, it was partially frozen using as the refrigerant either liquid nitrogen or liquid oxygen held in a test-tube partially immersed in the solution. After all of the refriger-

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[1] F. Swarts, *Bull. soc. chim. Belg.*, **43**, 471 (1934).

ant had evaporated, stirring of the partially frozen mixture was continued for 15 minutes or more; then the temperature was observed, and a sample of the liquid solution was withdrawn at once using a hypodermic syringe and needle. A small glass wool filter at the end of the needle prevented the inclusion of crystals in the sample. This sample was weighed by difference after being transferred to a stoppered flask containing water. The amount of acid was then determined by titration with standardized 0.1 *N* sodium hydroxide. This procedure gave more nearly reproducible values for the composition of a mixture rich in water than for one rich in acid. Changes in composition of the solution were made by adding one of the components or by changing the amount of the solid phase by melting or by freezing.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WASHINGTON
SEATTLE 5, WASHINGTON

N-Phosphorylated Derivatives of Diethanolamine[1]

BY ORRIE M. FRIEDMAN, DONALD L. KLASS AND ARNOLD M. SELIGMAN

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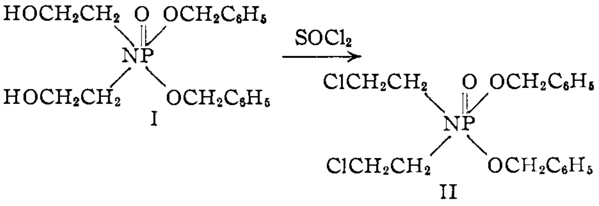
A re-examination[2] of the reported abundance of phosphamidase in malignant tissues as compared to normal tissues[3] has been undertaken with substrates of possible use as chemotherapeutic agents. The substrates prepared for this purpose were N-phosphorylated derivatives of bis-β-chloroethylamine.[2] One approach to the synthesis of compounds of this type appeared to be by way of dibenzyl di-(2-hydroxyethyl)-phosphoramidate (I)[4] which might be partially or totally debenzylated either before or subsequent to chlorination to afford the dibenzyl, monobenzyl and dibasic phosphoric acid derivatives of bis-(β-chloroethyl)-amine.

The dibenzyl di-(2-hydroxyethyl)-phosphoramidate (I) was prepared by reaction of dibenzyl phosphite with two molar equivalents of diethanolamine in carbon tetrachloride.[5] Dibenzyl phosphite was prepared crystalline in over 80% yield by modification of the procedure of Atherton, Oppenshaw and Todd[6] which obviated the hazardous distillation. Pyridine was substituted for dimethylaniline and the distillation time for removal of benzyl chloride from the product was increased. On chlorination with thionyl chloride the dihydroxyphosphoramidate I afforded the corresponding dichlorophosphoramidate II. Hydrogenolysis of this product II over palladium–carbon, however, either when allowed to go to completion, or when terminated after the uptake of one molar equivalent of hydrogen, did not give isolable products. Attempts to prepare the debenzylated dibasic acid, di-(2-hydroxyethyl)-phosphoramidic acid, by other means have been similarly unsuccessful[2] presumably owing to instability of the product.



Partial hydrolysis of dibenzyl di-(2-hydroxyethyl)-phosphoramidate with dilute aqueous alkali resulted in hydrolysis of the P–N bond rather than in ester cleavage. Several attempts were made to isolate benzyl hydrogen di-(2-hydroxyethyl)-phosphoramidate from reactions with 1.5 to 2 molar equivalents of alkali heated to reflux for periods varying from 15 minutes to 1.5 hours. In all cases dibenzylphosphoric acid was obtained in good yield without a trace of the desired product. The preferential hydrolysis of the phosphamide bond in the diester monoamide I is surprising since triesters of phosphoric acid are in general known to be sensitive to alkali.

Several attempts were made to monodebenzylate dibenzyl di-(2-hydroxyethyl)-phosphoramidate (I) with lithium chloride in ethyl cellosolve under various modifications of the conditions which Clark and Todd[7] used to prepare benzyl hydrogen phenylphosphoramidate from dibenzyl phenylphosphoramidate. During the course of the reaction a lithium salt separated in relatively good yield depending upon length of time and heating. This product could not be recrystallized and on analysis the crude material gave a value for nitrogen less than one third of that required for lithium benzyl hydrogen di-(2-hydroxyethyl)-phosphoramidate. Moreover when the crude products were worked up separately or with the reaction mixtures, the only product that could be obtained appeared from the analytical results to be benzylphosphoric acid isolated as the monocyclohexylamine salt.

Experimental[8]

Dibenzyl Phosphite.[6]—To a solution of 88 cc. (138 g.) of phosphorus trichloride in 75 cc. of dry benzene well cooled in ice, a mixture of 158 cc. of dry pyridine and 208 cc. of dry benzyl alcohol was added slowly with vigorous stirring over a period of three hours. After the mixture was stirred for an additional 30 minutes, 104 cc. of benzyl alcohol was added over a period of 20 minutes. The mixture was then allowed to stand at room temperature for 16 hours. The benzene solution was washed in turn with three 500-cc. portions of water, two 500-cc. portions of 5 *N* ammonium hydroxide, two 500-cc. portions of water and finally dried with sodium sulfate. Removal of the benzene under reduced pressure left a light-colored yellow oil from which all traces of benzyl chloride were removed on the steam-bath at 1–3 mm. for 10 hours. The product, a light-yellow oil, crystallized as a solid white mass when stored in the cold; 216.5 g. (82.6%).

Dibenzyl Di-(2-hydroxyethyl)-phosphoramidate (I).—A solution of 41.6 g. of dibenzyl phosphite and 30.4 cc. of diethanolamine in a mixture of 160 cc. of carbon tetrachloride and 160 cc. of chloroform was stirred at room temperature for 19 hours. The reaction mixture became warm during the first hour and turned turbid. When stirring was discontinued, diethanolamine hydrochloride appeared as an orange oil and was separated. The carbon tetrachloride–chloroform solution was shaken with water to remove ex-

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(1) This investigation was supported by a research grant from the National Cancer Institute of the National Institutes of Health, Public Health Service, Federal Security Agency, and (in part) by a research grant from Mrs. Albert B. Lasker.

(2) O. M. Friedman and A. M. Seligman, THIS JOURNAL, **76**, 655 (1954).

(3) G. Gomori, *Proc. Soc. Exp. Biol. Med.*, **69**, 407 (1948).

(4) The system of nomenclature adopted is in accord with the recommendations of the American Chemical Society Committee on Nomenclature, A.C.S. Official Reports, *Chem. Eng. News*, October (1952).

(5) F. R. Atherton and A. R. Todd, *J. Chem. Soc.*, 674 (1947).

(6) F. R. Atherton, H. T. Oppenshaw and R. A. Todd, *ibid.*, 382 (1945).

(7) V. M. Clark and A. R. Todd, *ibid.*, 2030 (1950).

(8) Microanalyses by S. M. Nagy and colleagues, Microchemical Laboratory, Massachusetts Institute of Technology. All melting points are corrected.