TABLE I

SOLUBILITY PRODUCT CONSTANTS OF 16 METALLIC SULFIDES AT 25° AND THE DATA[a] USED IN THEIR CALCULATIONS

Compound	$\Delta F_f°$, kcal. Metallic sulfide	$\Delta F_f°$, kcal. Metallic ion	K_{sp}
PbS	−22.15	− 5.81	8×10^{-28}
Tl_2S	−21.0[b]	− 7.755	7×10^{-20}
ZnS	−47.4	−35.184	8×10^{-25}
CdS	−33.6	−18.58	7×10^{-27}
HgS	−10.22[c]	39.38	3×10^{-52}
Cu_2S	−20.6	12.0	1×10^{-48}
CuS	−11.7	15.53	8×10^{-36}
Ag_2S	− 9.56[d]	18.430	7×10^{-50}
NiS	−18.8[b]	−11.1	2×10^{-21}
CoS	−21.8[b]	−12.3	8×10^{-23}
Co_2S_3	−47.6[b]	29.6	10^{-124}
FeS	−23.32	−20.30	5×10^{-18}
MnS	−47.6[b]	−53.4	1×10^{-11}
Ce_2S_3	−293.0[b]	−170.5	6×10^{-11}
La_2S_3	−301.2[b]	−172.9	2×10^{-13}
Bi_2S_3	−39.4	15	10^{-96}

[a] Except where otherwise noted the free energy data are from F. D. Rossini, *et al.*, *Natl. Bur. Stds. Circ.*, 500 (1950). [b] Calculated from heat content data taken from reference "a" and estimates of entropy made by the method recently proposed by W. M. Latimer, THIS JOURNAL, **73**, 1480 (1951). [c] J. R. Goates, A. G. Cole and E. L. Gray, *ibid.*, **73**, 3596 (1951). [d] J. R. Goates, A. G. Cole, E. L. Gray and Neal D. Faux, *ibid.*, **73**, 707 (1951).

the values of 1×10^{-91} and 1.6×10^{-72}(?) should certainly be discarded.

The value of 7.1×10^{-61} was reported by A. F. Kapustinsky and I. A. Makolkin[8] and was supposed to have been calculated from the $\Delta F_f°_{Bi_2S_3}$ given by Kelley (−39.14 kcal.).[9] It appears, however, that an error was made in these calculations, for the $\Delta F_f°_{Bi^{+++}}$ which corresponds to Kapustinsky and Makolkin's solubility product constant value is the unreasonable value of −9.5 kcal.

The value given in the table was calculated from the $\Delta F_f°_{Bi_2S_3}$ given by the Bureau of Standards[3] and a value for the $\Delta F_f°_{Bi^{+++}}$ that was calculated from data reported by Feitknecht.[10] There is some question as to the accuracy of this last value, but it appears reasonable, and since its effect on the solubility product constant is much less than that of the sulfide ion, the value of the solubility product constant given seems to be a reasonable approximation.

(8) A. F. Kapustinsky and I. A. Makolkin, *Acta Physiochim., U. R. S. S.*, **10**, 259 (1939).

(9) K. K. Kelley, *U. S. Bur. of Mines, Bul.* 406, 63 (1937).

(10) W. Feitknecht, *Helv. Chim. Acta*, **16**, 1307 (1933).

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The Chlorination of Diisopropyl Ether at Low Temperatures[1,2]

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The chlorination of diethyl ether at −20° or lower yields α,α'-dichlorodiethyl ether rather than the α,β-dichlorodiethyl ether obtained at higher temperatures.[3] The present investigation was made to determine whether this low temperature orientation to the α-position is also found with diisopropyl ether. Chlorination of diisopropyl ether under the conditions used with diethyl ether gave no more than traces of α-chlorinated ethers, as determined by hydrolysis of the products and Volhard chloride determinations. The chlorination mixture distilled over a wide range and fractional distillation, both at atmospheric and reduced pressures, failed to give sharp fractions. 1,3-Dichloropropanone was the only substance isolated. This product indicates a cleavage during chlorination not found with diethyl ether.

Henry's method,[4] using isopropyl alcohol and acetone, failed to give α-chlorodiisopropyl ether, desired for comparison with the chlorination products.

Experimental

Chlorination of Diisopropyl Ether.—Seventy-two grams (0.710 mole) of purified[5] anhydrous diisopropyl ether were placed in a Pyrex flask fitted with a thermometer, mechanical stirrer and gas inlet tube and protected from moisture. The flask was immersed in a Dry Ice–acetone-bath and irradiated with a 275-watt reflector sun lamp at a distance of 30 cm. Dry chlorine was slowly passed into the ether at −20 to −25° until 53.0 g. (0.746 mole) had been absorbed, requiring 8.5 hours. Gases escaped as the reaction mixture warmed to room temperature, leaving a net gain of 30.8 g. Distillation and redistillation under reduced pressure gave 12.0 g. of material boiling at 83–88° (33 mm.) which solidified in the ice-box. Repeated crystallization from chloroform gave colorless needles with the following properties: m.p. 42.0–43.0° (cor.); b.p. 172–172.5°; n^{25}_D 1.4773; volatile at room temperature; lachrymatory; soluble water, alcohol, ether; reduces Fehling solution. These properties are in agreement with those reported for 1,3-dichloropropanone.[6]

Anal. Calcd. for $C_3H_4Cl_2O$: C, 28.35; H, 3.18; Cl, 55.91; mol. wt., 127.0. Found: C, 28.56; H, 3.18; Cl, 55.40; mol. wt.,[7] 128.4.

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(1) From the Master's thesis of Iclâl Sirel.

(2) This work was carried out under contract with the Office of Naval Research.

(3) G. E. Hall and F. M. Ubertini, *J. Org. Chem.*, **15**, 715 (1950).

(4) L. Henry, *Bull. acad. roy. Belg.*, [3] **25**, 439 (1893); *Ber.*, **26**, Referate, 933 (1893).

(5) A. I. Vogel, *J. Chem. Soc.*, 618 (1948).

(6) E. H. Huntress, "Organic Chlorine Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 91.

(7) Cryoscopic method, *dl*-camphor solvent.

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The Preparation and Spectrophotometric Estimation of 2-Amino-7-hydroxyfluorene[1]

BY HELMUT R. GUTMANN

The preparation and properties of 2-amino-7-hydroxyfluorene are of considerable interest since this phenolamine is a likely intermediate in the metabolism of the carcinogen 2-aminofluorene.

The synthesis of this compound from 2-amino-7-nitrofluorene was first reported by Bielschowsky.[2] 2-Amino-7-hydroxyfluorene melting at 271° was obtained in unrecorded yield. Goulden and Kon[3] prepared 2-amino-7-hydroxyfluorene starting with 2-aminofluorenone.

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(1) This investigation was supported by Research Grant C-1066 from the National Cancer Institute of National Institutes of Health, Public Health Service.

(2) F. Bielschowsky, *Biochem. J.*, **39**, 287 (1945).

(3) F. Goulden and G. Kon, *J. Chem. Soc.*, 930 (1945).

The present method simplifies the existing procedures by utilizing the readily available 2,7-diaminofluorene dihydrochloride as the starting material.[4] 2-Amino-7-hydroxyfluorene, m.p. 265–268°, was obtained in yields ranging from 24–37%.

The quantitative estimation of the compound in solution or in biological materials may be based on the measurement of the red dye which is formed when 2-amino-7-hydroxyfluorene is diazotized and coupled with sodium 2-naphthol-3,6-disulfonate (R-salt). The dye absorbs maximally at a wave length of 530 mμ (Fig. 1). The molar extinction coefficient at 530 mμ is 34,300. The spectrophotometric measurement of the dye under the conditions described in the experimental part permits the detection of as little as 5 micrograms of 2-amino-7-hydroxyfluorene. Beer's law is followed with quantities of 2-amino-7-hydroxyfluorene ranging from 5–80 micrograms. The great sensitivity of of the method makes it particularly suited for the estimation of the compound in metabolic studies.

Experimental

2-Acetylaminofluorene-7-diazonium Chloride.—Thirteen grams of 2,7-diaminofluorene dihydrochloride[4] (0.049 mole) was dissolved in 300 ml. of distilled water with slight warming and filtered. After the solution had attained room temperature 5.6 ml. of freshly distilled acetic anhydride (0.060 mole) was added dropwise with vigorous stirring. After the addition of the acetic anhydride had been completed, stirring was continued for one hour. The 2-amino-7-acetylaminofluorene hydrochloride which had precipitated was filtered with suction and washed with 400 ml. of distilled water. The washed product was dried in air for 12 hours and used without further purification in the next step of the synthesis. All of the material was mixed in small succeeding portions in a Waring blendor with 500 ml. of 0.18 *M* hydrochloric acid and the mixture transferred to a 1-l. beaker. To the rapidly stirred suspension there was added 1.95 g. of sodium nitrite (0.028 mole) in 30 ml. of distilled water. After the suspension had been stirred for 2 hours it was warmed to 60° and filtered with suction. The residue on the filter was washed with 145 ml. of distilled water. The filtrate was made 80% saturated with 200 g. of sodium chloride. After standing at 5° for 12 hours the fine, reddish-brown precipitate was filtered with suction and washed with cold 50% saturated sodium chloride solution. The use of hard filter paper (Whatman No. 52) facilitates the quantitative collection of the compound. The material was recrystallized by dissolving it in methanol (90 ml./g.) and adding sufficient ether (100 ml./g.) to cause incipient precipitation. After standing at 5° for 1 hour the precipitate was filtered with suction and dried over calcium chloride. Additional material was obtained from the mother liquor after standing at 5° for 12 hours. After it had been collected with suction the product was added to the material which had been obtained previously. The compound weighed 3 g. and melted at 143–145°. Ray and Peters[5] report a melting point of 146° for this compound.

2-Amino-7-hydroxyfluorene.—A solution of 1.7 g. of 2-acetylaminofluorene-7-diazonium chloride (0.0062 mole) in 150 ml. of distilled water was added dropwise to 300 ml. of boiling 3 *M* hydrochloric acid in the course of 1.5 hours. Nitrogen was passed through the solution during the hydrolysis. The hot solution was filtered and the filtrate cooled in an ice-bath. The solution was neutralized with concentrated ammonium hydroxide. The very fine gray precipitate was collected with suction on hard filter paper (Whatman No. 52) and dried *in vacuo* over calcium chloride. There was obtained 0.65 g. of material which melted at 258–263° (with decomposition). The compound was recrystallized from 30 ml. of refluxing absolute ethanol. After standing in the refrigerator for 12 hours the gray, crystalline powder was collected and washed with cold ethanol and ether; m.p. 265–268° (with decomposition).

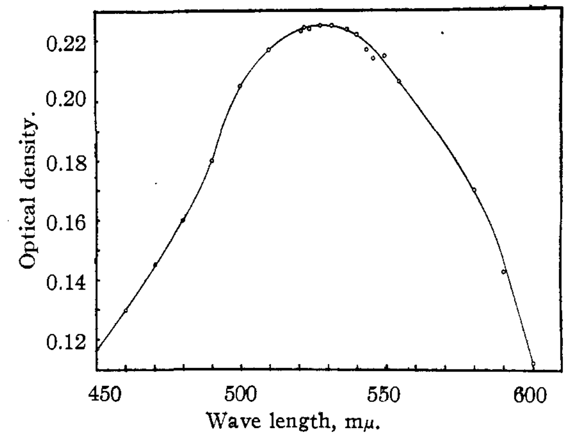

Fig. 1.

Anal. Calcd. for $3_{13}H_{11}ON$: N, 7.11. Found: N, 7.19.

The compound was soluble in acetone, amyl acetate and glacial acetic acid. It darkened quickly on standing in contact with air.

Measurement of the Absorption Spectrum of the Sodium Salt of 7-Hydroxyfluorenyl-2-azo-2′-naphthol-3′,6′-disulfonic Acid.—To 0.0678 mg. of 2-amino-7-hydroxyfluorene in 2 ml. of 4.5 *M* glacial acetic acid and 0.3 ml. of concentrated hydrochloric acid there was added 1 ml. of 0.029 *M* sodium nitrite. The mixture was shaken and, after 1 minute, it was added to 10 ml. of 0.031 *M* sodium 2-naphthol-3,6-disulfonate in 5 *M* aqueous ammonium hydroxide. The solution was cooled to room temperature, 5 ml. of acetone was added and the absorption spectrum of the red dye determined with a Beckman model DU spectrophotometer (Fig. 1).

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O-*p*-Toluenesulfonyl-L-tyrosine, Its N-Acetyl and N-Benzoyl Derivatives

BY ERNEST L. JACKSON

O-*p*-Toluenesulfonyl-L-tyrosine was reported by Fischer[1] as having m.p. 218° (cor., dec.) and $[\alpha]^{20}D$ $-4.6°$ in *N* hydrochloric acid (*c* 6.5). Fischer expressed doubt of the optical purity of the compound, which he prepared by the reaction of hydriodic acid and phosphonium iodide with O,N-di-*p*-toluenesulfonyl-L-tyrosine.

Hydrolysis of the pure methyl ester of O-*p*-toluenesulfonyl-N-acetyl-L-tyrosine with a mixture of hydrochloric and acetic acids yields O-*p*-toluenesulfonyl-L-tyrosine showing m.p. 213–214° (uncor., dec.) and $[\alpha]^{20}D$ $+9.0°$ in *N* hydrochloric acid (*c* 0.42) or $+9.5°$ (*c* 3.16). The rapid separation of crystals from a 6.5% solution of the compound in *N* hydrochloric acid at 20° prevented the determination of the rotation at this concentration. The methyl ester of O-*p*-toluenesulfonyl-N-acetyl-L-tyrosine was prepared by the reaction of *p*-toluenesulfonyl chloride in alkaline acetone solution with the methyl ester of N-acetyl-L-tyrosine, which resulted from acetylation of the known methyl ester of L-tyrosine. Acetylation and benzoylation of O-*p*-toluenesulfonyl-L-tyrosine

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[4] S. Schulman, *J. Org. Chem.*, **14**, 382 (1949).

[5] F. E. Ray and J. H. Peters, *Brit. J. of Cancer*, in press.

[1] E. Fischer, *Ber.*, **48**, 100 (1915).