TABLE II

EQUILIBRIUM CONSTANTS FOR ARGENTATION AND IONIZATION OF ANILINES AT 25.0°

Amine	K_1	K_2	pK_a
Aniline	27.6	1.45	4.62[a]
o-Toluidine	32.4	1.40	4.43[a]
m-Toluidine	29.2	1.68	4.71[a]
p-Toluidine	36.8	1.24	5.12[a]
3,5-Xylidine	43.0	1.09	4.9[b]
2,6-Xylidine	41.6	2.49	4.1[b]
N-Methylaniline	10.0	0.80	4.78[a]

[a] N. F. Hall, THIS JOURNAL, **52**, 5115 (1930). [b] Ref. 14.

Thus, the increase in K_1 values for the homologous series, aniline < toluidines < xylidines, is that anticipated from the known base-strengthening action of nuclear methyl substituents. However, a comparison between K_1 and pK_a values must take into account the different steric requirements of the anilinium[9] and silver ions.[10] *o*-Methyl substituents markedly decrease the basicity of aniline relative to hydrogen ion but have no pronounced effect relative to the silver ion as an acid; the reverse appears to be true with N-methyl substituents.

The coördination of silver ion with the benzenoid nucleus is also influenced by steric and polar factors. The more widely spaced a pair of substituents is around the ring, the greater is the steric hindrance to coördination.[10] On this basis, it is understandable that *p*-toluidine and 3,5-xylidine have the lowest K_2 values in the toluidine and xylidine series, respectively.

It is also possible that the attachment of the first silver ion decreases the basicity of the ring by resonance inhibition in a manner analogous to the effect of N-alkyl substituents on the base strength of aniline.[9] This may account for the fact that the K_2 values, in particular, that of N-methylaniline, are lower than those observed in the argentation of corresponding benzenoid hydrocarbons.[3]

Information of the type given in Table I is helpful in determining whether complex formation can be utilized to enhance separation of mixtures of compounds by fractional extraction procedures.[11,12] A convenient measure of the separability of compounds is the β-value or ratio of partition coefficients.[13] When 1:1 complex formation occurs, the β-value, k'_c/k'_d for a pair of compounds (in the limit of high concentration of complexing agent), is given by the equation

$$k'_c/k'_d = k_cK_d/k_dK_c \qquad (5)$$

where k_c and k_d represent the partition coefficients of the uncomplexed compounds, and K_c and K_d are the complex formation constants.[5] Application of this relationship to the data of Table I shows that in some instances the complexing action aids and in others hinders separation. Thus, the β-value for a mixture of *o*- and *m*-toluidine is slightly decreased by complex formation, whereas that of a mixture of aniline and N-methylaniline is increased by a factor of almost 3.

Experimental

Materials and Procedure.—The source and purity of the aromatic bases are recorded elsewhere.[14]

The procedure for distribution of the bases is the same in all details as that given in the previous paper of this series,[5] except that the concentration of the initial solutions of the amines was 0.005 *M*. The establishment of equilibrium was checked by the procedure of Barry, *et al.*,[15] in which the partition coefficients were measured after application of known numbers of equilibrations. It was found that equilibrium was established after only ten or twenty equilibrations. The data of Table I are, however, based on measurements after 100 to 200 equilibrations.

Acknowledgment.—The author is indebted to Dr. H. C. Brown for valuable suggestions and to George Goldbach for technical assistance.

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(9) H. C. Brown and A. Cahn, THIS JOURNAL, **72**, 2939 (1950).

(10) R. S. Mulliken, *ibid.*, **74**, 811 (1952).

(11) L. C. Craig, *J. Biol. Chem.*, **155**, 519 (1944).

(12) C. Golumbic, *Anal. Chem.*, **23**, 1210 (1951).

(13) K. A. Varteressian and M. R. Fenske, *Ind. Eng. Chem.*, **29**, 270 (1937).

(14) C. Golumbic and G. Goldbach, THIS JOURNAL, **73**, 3966 (1951).

(15) G. T. Barry, Y. Sato and L. C. Craig, *J. Biol. Chem.*, **174**, 209 (1948).

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The Preparation of Methylthiazoles

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The method most generally applicable to the synthesis of alkyl thiazoles involves the reaction of α-halocarbonyl compounds with thioamides. The preparation and purification of the thioamides (from the amide and phosphorus pentasulfide) are sometimes difficult and the yields are generally very poor.[1] A modification introduced by Hromatka[2] avoids isolation of the thioamide. It consists in heating a mixture of the stoichiometric quantities of amide, phosphorus pentasulfide and the α-halocarbonyl compound. By this method Schwarz[3] has prepared 2,4-dimethylthiazole in 45% yield by the reaction of five moles of acetamide, one mole of phosphorus pentasulfide and five moles of chloroacetone in benzene. Ganapathi and Venkataraman have prepared this compound[4] and several other methylthiazoles by this method.

Since the yields reported in the syntheses of the methylthiazoles were not too high, the methods used were tedious and difficult to control and large quantities of these substances were required for investigations in the thiazole series, attempts were made to improve the methods of synthesis. Previous workers have assumed that the conversion of acetamide and formamide to the thioamide was quantitative, otherwise no attempt would have been made to react the stoichiometric quantity of haloketone or aldehyde. It is quite obvious, however, on inspection of the reaction mixture, that much tar is produced and that some of the phosphorus pentasulfide remains unreacted. It therefore seemed impractical to use the stoichiometric

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(1) A. G. Pesina, *J. Gen. Chem.* (*U.S.S.R.*), **9**, 804 (1939); *C. A.*, **34**, 425 (1940).

(2) O. Hromatka, U. S. Patent 2,160,867; *C. A.*, **33**, 7320 (1939).

(3) G. Schwarz, *Org. Syntheses*, **25**, 35 (1945).

(4) K. Ganapathi and A. Venkataraman, *Proc. Indian Acad. Sci.*, **22A**, 343, 362 (1945).

quantities of haloketones or aldehydes. This investigation utilized the more reactive bromoketones and by use of five moles of amide and one mole of phosphorus pentasulfide with two to three moles of haloketone great improvements in the yields in the preparation of methylthiazoles have resulted.

When bromopropionaldehyde reacted in the *in situ* procedure, the yields were the same as those obtained when the pure thioamide reacted but a considerable saving in reaction time was achieved. Only 2-methylthiazole was not prepared by the *in situ* procedure. This was prepared by the method of Erlenmeyer[5] by the reaction of thioacetamide and chloroacetaldehyde hydrate.

Experimental

2,4-Dimethylthiazole.—A mixture of 300 g. (5.1 moles) of acetamide, 225 g. (1.01 moles) of phosphorus pentasulfide and 300 ml. of benzene (dried over sodium wire) in a two-liter three-neck flask was heated on the water-bath. When a black oily lower layer formed, 342.5 g. (2.5 moles) of bromoacetone[6] was added dropwise at a rate sufficiently fast to maintain refluxing of the benzene. After completion of the addition, the mixture was refluxed for one hour, 100 ml. of water and 20 ml. of concd. hydrochloric acid were added and the mixture heated one hour more. The mixture was steam distilled to remove the benzene, made basic with 50% sodium hydroxide solution and steam distilled. The distillate was extracted with ether, the ether extract was dried over sodium sulfate and the ether removed by distillation at reduced pressure. Fractionation yielded 215 g. (76%) of 2,4-dimethylthiazole, b.p. 70–73° (50 mm.), lit. b.p. 143–145°.[3]

4,5-Dimethylthiazole.—Phosphorus pentasulfide (67.5 g., 0.32 mole) and 100 ml. of dioxane (refluxed and distilled over sodium wire) were placed in a two-liter three-neck flask fitted with a reflux condenser, dropping funnel and sealed stirrer. Formamide (66 g., 1.47 moles) was added dropwise quite rapidly. When the flask became warm, it was cooled in an ice-water mixture and 151 g. (1.0 mole) of methyl α-bromoethyl ketone[6] was added dropwise at a rate sufficiently fast to maintain reaction but slow enough to prevent rapid refluxing. After completion of the addition and when the reaction subsided, the mixture was refluxed for one hour, 100 ml. of water and 20 ml. of concd. hydrochloric acid were then added and the mixture refluxed one hour more. The mixture was steam distilled to remove most of the dioxane and any other steam distillable organic materials. The mixture was then made basic with 50% sodium hydroxide solution and steam distilled. The steam distillate was saturated with potassium carbonate, extracted with ether, the ether extract dried over sodium sulfate and the ether removed by distillation at reduced pressure. Fractionation of the residue yielded 81.5 g. (72%) of 4,5-dimethylthiazole, b.p. 75° (47 mm.), lit. b.p. 158°.[4]

2,5-Dimethylthiazole.—This compound was prepared in the same manner as 2,4-dimethylthiazole by the action of 200 g. (3.4 moles) of acetamide and 150 g. (0.71 mole) of phosphorus pentasulfide in 200 ml. of benzene with 150 g. (1.1 moles) of α-bromopropionaldehyde.[7] The steam distillate containing 2,5-dimethylthiazole, was saturated with potassium carbonate, extracted with ether and the ether extract was dried over potassium carbonate. The ether was removed by distillation at reduced pressure and fractionation of the residue yielded 42 g. (30%) of 2,5-dimethylthiazole, b.p. 86° (80 mm.), lit. b.p. 148.9–150.9° (734 mm.)[8]

2,4,5-Trimethylthiazole.—This compound was prepared in the same manner as 2,4-dimethylthiazole by the reaction of 300 g. (5.1 moles) of acetamide and 225 g. (1.01 moles) of phosphorus pentasulfide in 300 ml. of benzene with 403.2 g. (2.67 moles) of methyl α-bromoethyl ketone. The yield of 2,4,5-trimethylthiazole obtained was 240 g. (71%), b.p. 65–67° (20 mm.), lit. b.p. 166.5–167.5° (717.5 mm.).[9]

4-Methylthiazole.—This compound was prepared in the same manner as 4,5-dimethylthiazole by the reaction of 66 g. (1.47 moles) of formamide and 67.5 g. (0.32 mole) of phosphorus pentasulfide in 150 ml. of dioxane with 137 g. (1.0 mole) of bromoacetone. The yield of 4-methylthiazole obtained was 73 g. (73%), b.p. 70° (90 mm.), lit. b.p. 133–134° (760 mm.).[10]

5-Methylthiazole.—This compound was prepared in the same manner as 4,5-dimethylthiazole by the reaction of 66 g. (1.47 moles) of formamide and 67.5 g. (0.32 mole) of phosphorus pentasulfide in 150 ml. of dioxane with 137 g. (1.0 mole) of α-bromopropionaldehyde. The yield of 5-methylthiazole obtained was 30 g. (30%), b.p. 57° (32 mm.), lit. b.p. 70–72° (41 mm.).[11]

2-Methylthiazole.—This compound was prepared by the reaction of thioacetamide[1] and chloroacetaldehyde hydrate in the presence of benzene and acetic anhydride.[5] The chloracetaldehyde hydrate used was obtained by addition of anhydrous calcium chloride, with cooling and stirring, to a 40% aqueous solution of chloracetaldehyde (Dow). A separation into two layers occurred and the chloroacetaldehyde hydrate layer obtained was used in the preparation of 2-methylthiazole, b.p. 65–67° (80 mm.), lit. b.p. 129–130° (760 mm.),[5] 49% yield.

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[5] H. Erlenmeyer, *et al.*, *Helv. Chim. Acta*, **31**, 1142 (1948).

[6] J. R. Catch, *et al.*, *J. Chem. Soc.*, 272 (1948); J. F. Norris, *J. Ind. Eng. Chem.*, **11**, 817 (1919).

[7] J. U. Nef, *Ann.*, **335**, 247 (1904).

[8] K. Hubacher, *ibid.*, **259**, 228 (1890).

[9] T. Roubleff, *ibid.*, **259**, 253 (1890).

[10] L. Arapides, *ibid.*, **249**, 7 (1888); A. Hantzsch, *ibid.*, **250**, 257 (1889).

[11] H. Erlenmeyer and P. Schmidt, *Helv. Chim. Acta*, **29**, 1957 (1946).

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The Absorption Spectra of $\Delta^{10,10'}$-Bianthrone, Helianthrone and Mesonaphthobianthrone in Concentrated Sulfuric Acid

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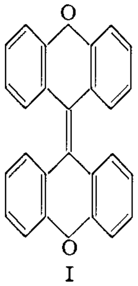
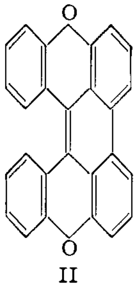
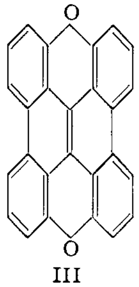
It is commonly known that $\Delta^{10,10'}$-bianthrone (I), and mesonaphthobianthrone (III) give deep red colored solutions in concentrated sulfuric acid while helianthrone (II) gives a deep blue-green solution.


I


II


III

Eckert and Tomaschek[1] reported the absorption spectra of III in concentrated sulfuric acid from 458–615 mμ. Meyer, Bondy and Eckert[2] published the absorption spectra of I, II and III in concentrated sulfuric acid from 515–683 mμ. All curves, except that of I, agreed qualitatively with this research.

Experimental

$\Delta^{10,10'}$-Bianthrone was made by a modification of the method of Schonberg and Ismail[3] in which anthrone was

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[1] A. Eckert and R. Tomaschek, *Monatsh.*, **39**, 839 (1918).

[2] H. Meyer, R. Bondy and A. Eckert, *ibid.*, **33**, 1447 (1912).

[3] A. Schonberg and A. F. A. Ismail, *J. Chem. Soc.*, 307 (1944); M. B. Goren, Doctoral Dissertation, Harvard University, 1949.