By systematic variations of the conditions the following preferred procedure was finally fixed upon.

To 0.2-g. samples of glycerophosphate, 25 cc. of water, 1.4 cc. of 0.1 *N* hydrochloric acid (0.003 *N*) and 20 cc. of 0.1 *N* lead tetraacetate (0.05 mole per liter) in glacial acetic acid are added and the solutions allowed to stand at room temperature for six hours. Controls containing 20 mg. of sodium dihydrogen phosphate, which prevents the hydrolysis of the lead tetraacetate without causing any reduction, in place of glycerophosphate, are allowed to stand the same length of time. Then 15 cc. of potassium iodide reagent, containing 500 g. of sodium acetate and 20 g. of potassium iodide per liter, is added and the iodine titrated with standard 0.1 *N* sodium thiosulfate solution.

Using this procedure the following results on a mixture of alpha and beta salts were obtained.

TABLE I

| Glycerophosphate in sample, g. Calcium alpha | Sodium beta | % alpha | 0.1 *N* lead tetraacetate reduced, cc. Found | Calcd. | % alpha calcd. |
|---|---|---|---|---|---|
| 0 | 0.20 | 0 | 0.22 | 0 | 0 |
| 0.05 | .15 | 25 | 4.57 | 4.38 | 25.3 |
| .10 | .10 | 50 | 8.82 | 8.76 | 50.2 |
| .15 | .05 | 75 | 13.04 | 13.14 | 74.6 |
| .20 | 0 | 100 | 17.40 | 17.52 | 98.1 |

The advantages of lead tetraacetate over periodic acid are: (a) it is more easily available; (b) it gives a sharper end-point; (c) it does not continue to act as rapidly after the true end-point has been reached and (d) its blank test correction is smaller.


## Summary

Lead tetraacetate can be used successfully for the quantitative determination of α-glycerphosphates in aqueous solutions according to the procedure outlined.


TORONTO, CANADA RECEIVED JUNE 23, 1941

# NOTES

## Sulfapyrazine, Sulfapyrimidine and "Sulfadiazine"*

BY RUDOLPH C. ELLINGSON

It is known that pyrazine monocarboxylic acid is of low toxicity in comparison with the α- and β-carboxylic acids of pyridine.[1] This and other considerations led me to synthesize the pyrazine analog of sulfapyridine, in the expectation that it would carry the desirable feature of low toxicity to the drug.

2-N⁴-Acetylsulfanilamidopyrazine, m. p. 250–252° (dec.), was obtained by allowing *p*-acetaminobenzenesulfonyl chloride to react with 2-aminopyrazine in pyridine. This compound was deacetylated by acid hydrolysis, giving 2-sulfanilamidopyrazine, m. p. 255–257° (dec.). Both compounds are colorless and tasteless. When the latter is suspended in ethanol and treated with sodium hydroxide, sodium 2-sulfanilamidopyrazine monohydrate is obtained.

TABLE I

| Compound | | C | H | N | S | Na | $H_2O$ |
|---|---|---|---|---|---|---|---|
| 2-N⁴-Acetylsulfanilamidopyrazine, $C_{12}H_{12}O_3N_4S$ | Calcd. | 49.3 | 4.1 | 19.2 | 11.0 | | |
| | Found | 49.4 | 4.7 | 18.5 | 11.0 | | |
| 2-Sulfanilamidopyrazine, $C_{10}H_{10}O_2N_4S$ | Calcd. | 48.0 | 4.0 | 22.4 | 12.8 | | |
| | Found | 48.4 | 4.2 | 21.9 | 13.0 | | |
| Sodium 2-sulfanilamidopyrazine monohydrate, $C_{10}H_9O_2N_4SNa \cdot H_2O$ | Calcd. | | | 19.3 | | 7.9 | 6.2 |
| | Found | | | 19.2 | | 7.8 | 6.5 |

The solubilities of 2-sulfanilamidopyrazine and its acetyl derivative in 100 cc. of water at 37° are 5.2 and 5.6 mg., respectively. Thus 2-sulfanilamidopyrazine shares with its isomer, 2-sulfanilamidopyrimidine,[2] a pharmacologically desirable property,[3] not exhibited by most of the sulfa drugs in common use.

The *p*H of a 10% solution of sodium 2-sulfanilamidopyrazine monohydrate in physiological saline was 9.3 (glass electrode, corrected for sodium ion). Comparably, the sodium salts of sulfapyridine, sulfathiazole and sulfapyrimidine gave *p*H values of 10.7, 10.0 and 10.2, confirming Feinstone, *et al.*[4]

To avoid possible confusion between sulfapyridine and sulfapyrimidine, Roblin and co-workers[2] suggest that the latter be called sulfadiazine. Since our "sulfapyrazine" is also a sulfadiazine, it would seem that the use of these abbreviations, although convenient for physicians, is by no means ideal. In theory, there are six possible sulfadia-

* Original manuscript received March 18, 1941.

(1) Bills, McDonald and Spies, *Southern Med. J.*, **32**, 793 (1939).

(2) Roblin, Williams, Winnek and English, THIS JOURNAL, **62**, 2002 (1940).

(3) Northey, *Chem. Rev.*, **27**, 108 (1940).

(4) Feinstone, Williams, Wolff, Huntington and Crossley, *Bull Johns Hopkins Hosp.*, **67**, 430 (1940).

zines—two ortho, three meta and one para—not counting the many additional compounds obtainable by ring substitution. Strictly speaking, our sulfapyrazine is the one and only sulfa-para-diazine, and "sulfadiazine" is one of the three possible sulfa-meta-diazines.

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EVANSVILLE, INDIANA RECEIVED JULY 14, 1941

## The Distribution of Di- and Trimethylamines between Chloroform and Water at 25°

BY W. A. FELSING AND EDDIE BALL

Felsing and Buckley[1] determined the composition of the methylamine complexes of the metal-ammine type by a study of the distribution coefficients of monomethylamine between chloroform and (a) pure water and (b) aqueous copper sulfate solutions. A similar study was made with the di- and trimethylamines; however, the extent of the ammine formation with the cupric ion was too limited to allow of a quantitative estimation of their composition by this method. In the course of the investigation, however, accurate determinations of the distribution coefficients were made; these values are presented here.

The experimental procedures of Felsing and Buckley[1] were followed throughout. The di- and trimethylamines were liberated by means of potassium hydroxide from their highly purified hydrochlorides. Distribution determinations (16 for each amine) covered an aqueous concentration up to 4 molal for dimethylamine and up to approximately 3 molal for trimethylamine.

The values of the true distribution coefficient, $K_D$, were calculated from experimental determinations by means of the relation

$$K_D = \frac{2C_1 + K_m \pm \sqrt{K_m^2 + 4K_mC_1}}{2C_2}$$

where $C_1$ is the concentration of the amine in the water layer; $C_2$, the concentration in the chloroform layer; and $K_m$, the dissociation constant of the amine hydroxide. The value for $K_m$ for dimethylamine hydroxide[2] was taken as $5 \times 10^{-4}$ and for trimethylamine hydroxide[2] as $6.5 \times 10^{-5}$.

The relation of $K_D$ to the concentrations of the amines in the chloroform layer is given by the linear equations

Dimethylamine: $K_D = 2.75 - 0.109C_2$
Trimethylamine: $K_D = 0.45 + 0.021C_2$

These relations may be compared with that obtained for monomethylamine by Felsing and Buckley[1]

Monomethylamine: $K_D = 11.39 - 2.32C_2$

In each case, the linear relation fails to hold in the very dilute region; for dimethylamine, the average deviation is 0.014 unit with a maximum deviation of 0.030; and for trimethylamine, the average is 0.0030 unit with a maximum of 0.0054. The values of $K_D$ decrease for both mono- and dimethylamine and increase for trimethylamine; as the methyl radicals increase, the solubility in the chloroform layer increases, of course.

CONTRIBUTION NO. 239
DEPARTMENT OF CHEMISTRY
THE UNIVERSITY OF TEXAS
AUSTIN, TEXAS RECEIVED JUNE 9, 1941

(1) Felsing and Buckley, *J. Phys. Chem.*, **37**, 779 (1933).
(2) "I. C. T.," Vol. VI, pp. 263–265.

## The Reaction of Rhenium Trichloride with Methylmagnesium Iodide

BY H. GILMAN, R. G. JONES, F. W. MOORE AND M. J. KOLBEZEN

A previous note on the synthesis of tetramethylplatinum and of hexamethyldiplatinum[1] reported part of a general study concerned with the possible preparation of RM compounds wherein a transitional element is combined exclusively with alkyl or aryl groups. Trimethylrhenium has been described[2] as a colorless liquid, b. p. 60°, heavier than water, and apparently stable in the presence of air or moisture. We have observed, however, that the reaction between rhenium trichloride and methylmagnesium iodide[2] gives a mixture from which methane and ethane are evolved, but from which no organorhenium compound could be isolated. Actually, in one experiment, the yield of methane and ethane accounted for 91.4% of the methylmagnesium iodide initially used.

The formation of methane is common[3] to reactions of salts of transitional elements with methylmetallic compounds like $CH_3MgX$ and $CH_3Li$. Although our rhenium trichloride was analyzed and appeared to be of good quality, it is possible that traces of impurities may have been responsible for the failure to produce trimethylrhenium. In other studies, we have found that small quantities of the salts of copper, iron and other metals are able to decompose quickly the lower aliphatic

(1) Gilman and Lichtenwalter, THIS JOURNAL, **60**, 3085 (1938).
(2) Druce, *J. Chem. Soc.*, 1129 (1934).
(3) See Gilman and Jones, THIS JOURNAL, **62**, 2357 (1940); also unpublished studies.

RMgX and RLi compounds if an organic halide is also present.[4] Actually, rhenium trichloride also catalyzed a reaction between methylmagnesium iodide and methyl iodide.

## Experimental

A sample of rhenium trichloride[5] was freshly resublimed *in vacuo* at 500–550° to give a dark red crystalline solid.[6]

*Anal.*[7] Calcd. for $ReCl_3$: Re, 63.65; Cl, 36.35. Found: Re, 63.82, 64.35; Cl, 36.05, 36.24.

The powdered rhenium trichloride, 2.50 g. (0.0085 mole), dissolved partially in 20 cc. of ether to give a red-violet solution. This mixture was stirred while 27 cc. of 1.09 molar (0.0294 mole) of methylmagnesium iodide was added during ten minutes. An immediate darkening occurred, but there was no noticeable heat evolution. The mixture was stirred at room temperature for thirty minutes, during which time a steady evolution of gas took place. This gas was collected over water, and analysis showed a 27.2% yield of methane and an 8.2% yield of ethane based on the methylmagnesium iodide. After thirty minutes, the mixture (still evolving gas) was cooled in an ice-bath and cautiously hydrolyzed with 50 cc. of 2 *N* hydrochloric acid, to yield an additional 56% of methane, and a trace (0.00073 mole) of hydrogen.

In another experiment, carried out under corresponding conditions, there was isolated 0.00095 mole of hydrogen, in addition to methane, from the hydrolysis. It is probable that the hydrogen resulted from the action of hydrochloric acid on metallic rhenium, which may have been formed by reduction of some of the rhenium trichloride by methylmagnesium iodide.

A mixture of 0.03 mole of methyl iodide, 0.03 mole of methylmagnesium iodide and 0.0005 mole of rhenium trichloride in 50 cc. of ether was allowed to stand for seventy-two hours. During this time 0.0104 mole of methane was evolved. A blank experiment run in the same apparatus but using only methylmagnesium iodide and pure ether, gave 0.0029 mole of methane due to hydrolysis of the methylmagnesium iodide.

(4) A striking illustration is the effect of the quality of magnesium on the yields of cyclohexylmagnesium chloride and bromide: Gilman, Zoellner, Selby and Boatner, *Rec. trav. chim.*, **54**, 584 (1935); see, particularly, pp. 590–593.

(5) The authors are grateful to Dr. George Calingaert for supplying the rhenium trichloride.

(6) Geilmann, Wrigge and Biltz, *Nachr. Ges. Wiss. Göttingen, Math.-physik. Klasse* No. 5, 579 (1932); [*C. A.*, **28**, 60 (1934)].

(7) The rhenium was precipitated as nitron perrhenate which was dried and weighed: Geilmann and Voigt, *Z. anorg. allgem. Chem.*, **193**, 311 (1930).

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA

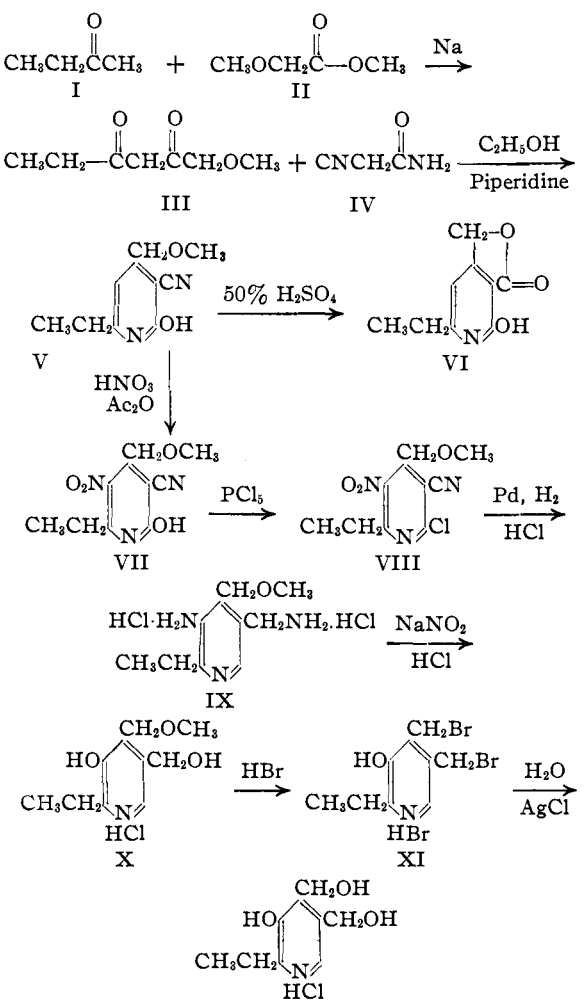
RECEIVED JULY 14, 1941

## Chemistry of Vitamin $B_6$. III. 2-Ethyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine—A Homolog of Vitamin $B_6$

BY STANTON A. HARRIS AND ANDREW N. WILSON

The effect of substitution of various groups of the vitamin $B_6$ molecule on its biological activity has been reported previously from this Laboratory.[1,2,3] It was found[1] that esters of vitamin $B_6$ were fully active on vitamin $B_6$ deficient rats, and that ether derivatives showed less than 10% activity while replacement of an hydroxyl group by hydrogen or the amino group completely inactivated the molecule. It was reported later[2] that substitution of the nitrogen atom by a methyl group also showed inactivation at dose levels fifty times greater than that of vitamin $B_6$.

In continuing this study it was of interest to determine the effect of replacing the methyl group of vitamin $B_6$ with an ethyl group. This compound has been prepared by the set of reactions I → XII which are exactly analogous to those used for the preparation of vitamin $B_6$.[4]




(1) Unna, *Proc. Soc. Exptl. Biol. Med.*, **43**, 122 (1940).

(2) Harris, Webb and Folkers, THIS JOURNAL, **62**, 3198 (1940).

(3) Harris, *ibid.*, **62**, 3203 (1940).

(4) Harris and Folkers, *ibid.*, **61**, 1245 (1939).

The structure of V was proved by treatment with 50% sulfuric acid as described previously[5] for the 2-methyl derivative. The formation of this lactone VI definitely allocated the methoxymethyl group to the 4-position in the pyridine ring.

Tracy and Elderfield[6] reported that ethyl formate condensed with the methylene group of ethyl methyl ketone, while ethyl oxalate condensed with the methyl group. It is evident from the above reactions (III + IV → V → VII) that methyl methoxyacetate reacted with the methyl group of ethyl methyl ketone to give 1-methoxy-3-methyl-2,4-hexadione (III). If the reaction had taken place on the methylene group, the resulting compound, 1-methoxy-3-methyl-2,4-pentadione ($CH_3C(=O)CH(CH_3)C(=O)CH_2OCH_3$, XIII) would have reacted with cyanacetamide to give 2,3-dimethyl-4-methoxymethyl-5-cyano-6-hydroxypyridine. This compound would have been incapable of undergoing the reactions V → VII → XII.

The biological activity of 2-ethyl-3-hydroxy-4,5-bis-(hydroxy-methyl)-pyridine hydrochloride (XII) was determined in the Merck Institute for Therapeutic Research by Dr. Klaus Unna using a single dose curative assay[7] on vitamin $B_6$ depleted rats. Some vitamin $B_6$ activity was found for this sample in dosages of 1000 and 2500 micrograms, but even the larger dose was not sufficient to produce cures which are effected by 50 micrograms of vitamin $B_6$. Thus, the ethyl homolog possesses less than 2% of the activity of vitamin $B_6$ hydrochloride.

## Experimental

Since the reactions are so similar to the published synthesis of vitamin $B_6$,[4] only the physical constants and analyses of the products are given here.

**1-Methoxy-2,4-hexadione** (III).—B. p. 69.5–70° at 7.5 mm. *Anal.* Calcd. for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.37, 58.28; H, 8.34, 8.33.

**2-Ethyl-4-methoxymethyl-5-cyano-6-hydroxypyridine** (V).—M. p. 190–191°. *Anal.* Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.30; N, 14.57. Found: C, 62.69, 62.52; H, 6.20, 6.26; N, 14.73.

**The Lactone of 2-Ethyl-3-hydroxymethyl-4-carboxy-6-hydroxypyridine** (VI).—M. p. 285°. *Anal.* Calcd. for $C_9H_9O_3N$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.56; H, 4.98; N, 7.76.

**2-Ethyl-3-nitro-4-methoxymethyl-5-cyano-6-hydroxypyridine** (VII).—M. p. 171–172°. *Anal.* Calcd. for $C_{10}H_{11}O_4N_3$: C, 50.64; H, 4.64; N, 17.72. Found: C, 50.63, 50.81; H, 4.65, 4.54; N, 18.05.

**2-Ethyl-3-nitro-4-methoxymethyl-5-cyano-6-chloropyridine** (VIII).—M. p. 56–57°. *Anal.* Calcd. for $C_{10}H_{10}O_3N_3Cl$: C, 46.96; H, 3.91; N, 16.46. Found: C, 47.12, 46.86; H, 3.89, 3.68; N, 16.34.

**The Dihydrochloride of 2-Ethyl-3-amino-4-methoxymethyl-5-aminomethylpyridine** (IX).—M. p. 214°. *Anal.* Calcd. for $C_{10}H_{19}ON_3Cl_2$: C, 44.78; H, 7.09; N, 15.67. Found: C, 44.81; H, 7.37; N, 15.89, 15.89.

**2-Ethyl-3-hydroxy-4-methoxymethyl-5-hydroxymethylpyridine Hydrochloride** (X).—This compound was not obtained crystalline, but was converted to the dibromide by treatment with constant boiling hydrobromic acid.

**2-Ethyl-3-hydroxy-4,5-bis-(bromomethyl)-pyridine Hydrobromide** (XI).—M. p. 196°. *Anal.* Calcd. for $C_9H_{12}ONBr_3$: C, 27.72; H, 3.10; N, 3.59. Found: C, 27.95; H, 3.19; N, 3.50.

**2-Ethyl-3-hydroxy-4,5-bis-(hydroxymethyl)-pyridine Hydrochloride** (XII).—M. p. 192°. *Anal.* Calcd. for $C_9H_{14}NO_3Cl$: C, 49.12; H, 6.42; N, 6.37. Found: C, 49.11, 49.39; H, 6.44, 6.39; N, 6.36.

The authors wish to express their appreciation to Messrs. D. F. Hayman, W. R. Reiss, R. B. Boos and H. S. Clark for the microanalyses reported in this paper.

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RECEIVED JULY 15, 1941

(5) Harris, Stiller and Folkers, THIS JOURNAL, **61**, 1242 (1939).

(6) Tracy and Elderfield, *J. Org. Chem.*, **6**, 63, 70 (1941).

(7) Reedman, Sampson and Unna, *Proc. Soc. Exptl. Biol. Med.*, **43**, 112 (1940). By this method it has been shown that a single dose of 100 micrograms of vitamin $B_6$ hydrochloride cures 100% of the deficient animals within 14 days, and that a dose of 50 micrograms produces complete cures in 75% of the animals. Lower doses fail to produce complete cures, but signs of partial healing were obtained regularly with 25 micrograms.

# Investigations in the 1-Methylphenanthrene Series. II. Some Substitution Products of 1-Methylphenanthrene

BY TORSTEN HASSELSTROM

The direct nitration of retene yields no crystalline derivatives.[1] On the other hand, it was found in this investigation that 1-methylphenanthrene like phenanthrene gives a crystalline mononitro derivative on nitration in glacial acetic acid. The corresponding amine was produced on reduction with sodium hyposulfite and acetylated. Through the diazo reaction 1-methylphenanthrol was obtained together with minute quantities of a dyestuff of unknown composition. The 1-methylphenanthrol was identified by its acetoxy derivative, which had the same melting point as a 1-

(1) (a) Fehling, *Ann.*, **106**, 390 (1858); (b) Fritzche, *ibid.*, **109**, 251 (1859); (c) Ekstrand, *ibid.*, **185**, 79 (1877); (d) Bamberger and Hooker, *ibid.*, **229**, 116, 144 (1885); (e) Arnot, German Patent 315,623 (1919); *Chem. Zentr.*, **91**, II, 188 (1920); (f) Arnot, British Patent 149,354 (1920); *Chem. Zentr.*, **92**, II, 37 (1921); (g) Wahlforss, Thesis, Helsingfors, 1924, p. 24; (h) Komppa and Wahlforss, THIS JOURNAL, **52**, 5009 (1930).

methylphenanthrol reported by Fieser and Young[2] and did not lower the melting point of this compound in the mixed melting point test. Since these authors conclude their 1-methylphenanthrol to be the 9-derivative, it is assumed that 1-methylphenanthrene on direct nitration produces the 1-methyl-9-nitrophenanthrene.

It is of interest to note that phenanthrene when nitrated under similar conditions yields the 9-derivative.[3] All these facts represent a further support to the suggestion recently made by Campbell and Todd[4] in their work on the constitution of acetylretene of Bogert and Hasselstrom[5] that the phenanthrene nucleus apparently has some inherent orienting influence which overcomes any directing influence of alkyl groups.

**Acknowledgment.**—Thanks are due to Dr. Louis F. Fieser, Department of Chemistry, Harvard University, Cambridge, Massachusetts, for an authentic sample of 1-methyl-9-phenanthrol.

## Experimental

**1-Methyl-9-nitrophenanthrene**[6].—Fifteen grams of 1-methylphenanthrene[7] was dissolved in 200 cc. of glacial acetic acid. The solution was chilled to 18°, whereby some hydrocarbon separated and with good stirring 30 cc. of nitric acid, of sp. gr. 1.42, was added in the course of twenty minutes. After the first drops were added the mixture was cooled to 5° and kept at 5 to 10° until a clear yellow-colored solution was obtained, which usually required thirty to forty-five minutes. The clear solution was then poured into one liter of water and the sticky brownish resin removed by decanting. This was washed with sodium bicarbonate solution, then with water and stirred with a small quantity of acetone until a thick paste of crystalline material was obtained. Filtration removed some brownish tarry material; yield of solid nitro product 6 g. It was recrystallized from acetone; m. p. 146.5–146.8° (cor.), yellowish needles.

*Anal.*[8] Calcd. for $C_{15}H_{11}NO_2$: N, 5.90. Found: N, 5.72.

**1-Methyl-9-aminophenanthrene.**—One and one-half grams of 1-methyl-9-nitrophenanthrene was suspended in 50 cc. of methanol and 20 cc. of water to which was added 2 g. of commercial sodium hyposulfite. The solution was refluxed for one-half hour until all color of the nitro derivative had disappeared and when the amino product started to separate, the solution was poured into 500 cc. of water containing ammonia. The fluffy white precipitate was filtered off, yield about quantitative; m. p. 138–138.5° (cor.), pale yellow needles from methanol.

*Anal.* Calcd. for $C_{15}H_{13}N$: N, 6.76. Found: N, 7.05.

**1-Methyl-9-diacetaminophenanthrene.**—Acetylation with a boiling mixture of acetic anhydride and fused sodium acetate gave the diacetate, m. p. 193.7–194.3° (cor.) as prismatic white needles from methanol.

*Anal.* Calcd. for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88. Found: C, 78.82; H, 5.90.

**1-Methyl-9-hydroxyphenanthrene.**—A suspension of 2.5 g. of crude 1-methyl-9-aminophenanthrene in 750 cc. of water containing 10 cc. of concentrated hydrochloric acid was cooled to 0–5°. A concentrated aqueous solution of 1 g. of sodium nitrite was added in two portions and the mixture, which turned bright yellow, was allowed to stand for one and one-half hours, when still some yellowish material remained undissolved. After addition of 2.5 g. of urea the mixture was slowly brought to boiling whereby a reddish resin precipitated; yield, 1.7 g. This was suspended in a dilute potassium hydroxide solution and the mixture refluxed for half an hour. The solution was filtered yielding a colorless filtrate and 0.2 g. of a crimson insoluble dye which, recrystallized once from benzene, melted at 283° (cor.), decomp. After cooling, the alkaline filtrate was acidified with dilute hydrochloric acid and the flocculent precipitate of the phenol recrystallized from benzene; yield 1.2 g. of white fluffy crystals, m. p. 199.5–200.5° (cor.). The 1-methyl-9-phenanthrol turned brownish on storage.

*Anal.* Calcd. for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.72; H, 6.03.

**1-Methyl-9-acetoxyphenanthrene.**—Acetylation with acetic anhydride and fused sodium acetate gave the acetoxy derivative, m. p. 99.5–100.3° (cor.), white needles from alcohol.

*Anal.* Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.65; H, 5.92.

In the mixed melting point test with an authentic sample of 1-methyl-9-acetoxyphenanthrene which had darkened somewhat in ten years of standing and melted at 98–99° (cor.) no depression was observed inasmuch as the mixture melted at 98.5–99.5° (cor.).

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RECEIVED JUNE 11, 1941

(2) Fieser and Young, THIS JOURNAL, **53**, 4120 (1931).
(3) Schmidt and Strobel, *Ber.*, **36**, 2511 (1903).
(4) Campbell and Todd, THIS JOURNAL, **62**, 1288 (1940).
(5) Bogert and Hasselstrom, *ibid.*, **53**, 3462 (1931).
(6) When crude retene, m. p. 96–97° (cor.), is subjected to nitration carried out in a similar manner, about 1% of a crystalline nitro product is obtained melting in a crude state at 259–260° (cor.). Investigation of this product will be the subject matter for a separate publication.
(7) Prepared from retene in accordance with procedure described by Hasselstrom, THIS JOURNAL, **63**, 1164 (1941).
(8) All analyses by Mr. S. Gottlieb, Columbia University, New York City, New York.

## The Absorption Spectra of Thiocyano Derivatives of 1,2-Benzanthracene

BY R. NORMAN JONES

The investigation of the influence of substituents on the ultraviolet absorption spectrum of 1,2-benzanthracene[1,2] has been extended to thiocyano derivatives, several of which have been prepared recently in this Laboratory by Wood and Fieser.[3]

(1) Jones, THIS JOURNAL, **62**, 148 (1940).
(2) Jones, *ibid.*, **63**, 151 (1941).
(3) Wood and Fieser, *ibid.*, **63**, 2323 (1941).

The compounds examined included 9-thiocyano-1,2-benzanthracene, 10-thiocyano-1,2-benzanthracene, 9-thiocyano-10-methyl-1,2-benzanthracene, 10-thiocyanomethyl-1,2-benzanthracene, and a thiocyano derivative of 20-methylcholanthrene which, from chemical evidence,[3] very probably has the structure I rather than the alternate possible structure II.

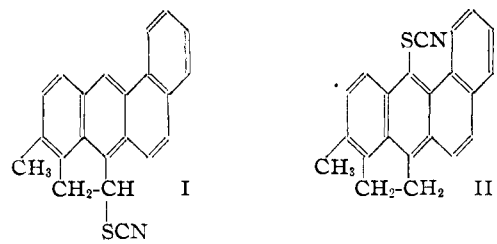


TABLE I

WAVE LENGTHS (Å.) OF THE MAXIMA AND CORRESPONDING INTENSITIES (LOG $E_{molar}$) OF THE SPECTRA OF SOME THIOCYANO DERIVATIVES OF 1,2-BENZANTHRACENE (SOLVENT DIOXANE)

| | Max. | Intensity |
|---|---|---|
| 9-Thiocyano-1,2-benzanthracene | 2620 | 4.45 |
| | 2785 | 4.60 |
| | 2895 | 4.81 |
| | 3020 | 4.89 |
| | 3410 | 3.74 |
| | 3600 | 4.03 |
| | 3795 | 4.23 |
| | (3975)[a] | 4.12 |
| | 4050 | 4.25 |
| 10-Thiocyano-1,2-benzanthracene | 2480 | 4.44 |
| | 2745 | 4.55 |
| | 2840 | 4.82 |
| | 2965 | 4.93 |
| | (3290) | 3.54 |
| | 3460 | 3.79 |
| | 3625 | 3.90 |
| | 3730 | 3.83 |
| | 3795 | 3.75 |
| | 3940 | 3.61 |
| 9-Thiocyano-10-methyl-1,2-benzanthracene | 2750 | 4.70 |
| | 2850 | 4.61 |
| | 2970 | 4.68 |
| | 3110 | 4.69 |
| | (3740) | 3.96 |
| | 3920 | 4.13 |
| | 4155 | 4.15 |
| 10-Thiocyanomethyl-1,2-benzanthracene | 2580 | 4.48 |
| | 2745 | 4.60 |
| | 2840 | 4.86 |
| | 2950 | 4.93 |
| | 3440 | 3.86 |
| | 3590 | 3.98 |
| | 3750 | 3.87 |
| | 3790 | 3.82 |
| | 3925 | 3.46 |
| 15-Thiocyano-20-methylcholanthrene | 2625 | 4.49 |
| | 2750 | 4.54 |
| | 2865 | 4.77 |
| | 2980 | 4.87 |
| | 3255 | 3.72 |
| | 3410 | 3.79 |
| | 3585 | 3.93 |
| | 3775 | 3.82 |
| | 3925 | 3.10 |

[a] Wave lengths in parentheses refer to points of inflection.

The wave lengths and intensities of the maxima in the spectra of these compounds are summarized in Table I and the curves are given in Figs. 1–3. The experimental technique employed has been described previously[1]; the dioxane used as solvent was purified by the method of Hess and Frahm.[4]

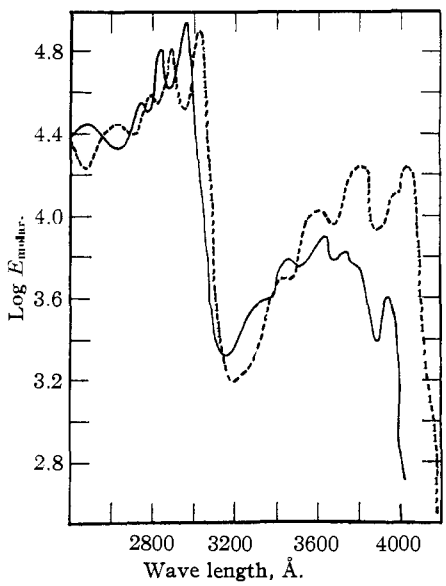


Fig. 1.— ——,10-Thiocyano-1,2-benzanthracene; ---, 9-thiocyano-1,2-benzanthracene.

Examination of the curves showed that the spectra may be divided into two groups. The derivatives in which the thiocyano substituent is not attached at the 9 position possess spectra which are very similar to those of the unsubstituted hydrocarbon. In the spectrum of 9-thiocyano-1,2-benzanthracene, however, the intensities of the maxima at wave lengths greater than 3200 Å. are very considerably increased; in the spectrum of 9-thiocyano-10-methyl-1,2-benzanthracene a change in the relative intensities of the short wave length maxima is also noted in addition to this effect. The similarity of the spectra of 10-thiocyano-1,2-benzanthracene, 10-thiocyanomethyl-

(4) Hess and Frahm, *Ber.*, **71**, 2627 (1938).

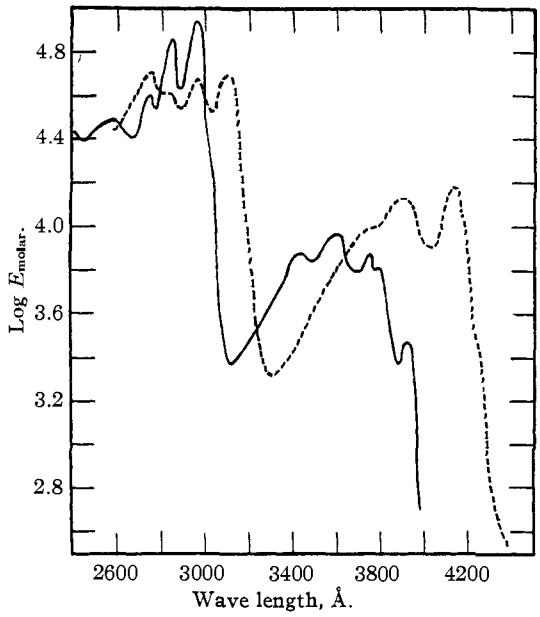


Fig. 2.— ——,10-Thiocyanomethyl-1,2-benzanthracene; ----, 9-thiocyano-10-methyl-1,2-benzanthracene.

1,2-benzanthracene and 1,2-benzanthracene indicates that in spite of the considerable chemical reactivity and unsaturation of the thiocyano group, its introduction does not significantly alter the excitation levels of the electrons of the aromatic ring system, and in this respect may be compared with the isocyanate group, the introduction of which likewise has little influence on the spectrum of 1,2-benzanthracene.[2] The spectra of ethyl thiocyanate and *n*-butyl thiocyanate[5] show only a low intensity maximum near 2500 Å. (log $E$ = 1.6–1.7) and the additive effect of the thiocyano chromophore is negligible in comparison with that of the aromatic system.

The abnormal behavior of the 9-thiocyano derivatives may be attributed, most probably, to steric effects, the relatively large thiocyano group being under considerable restraint due to interference with the hydrogen atom at the 1′ position. This effect is not observed in 9-methyl-1,2-benzanthracene, probably on account of the smaller size of the methyl group, the spectrum of 4,5-dimethylchrysene, however, in which comparable steric conditions occur, differs from that of chrysene in a very similar manner.[6]

The spectrum of the thiocyano derivative of 20-methylcholanthrene closely resembles that of 1,2-benzanthracene and shows none of the abnormalities associated with a thiocyano substituent

(5) Pestemer and Litschauer, *Monatsh.*, **65**, 239 (1935).
(6) Jones, THIS JOURNAL, **63**, 313 (1941).

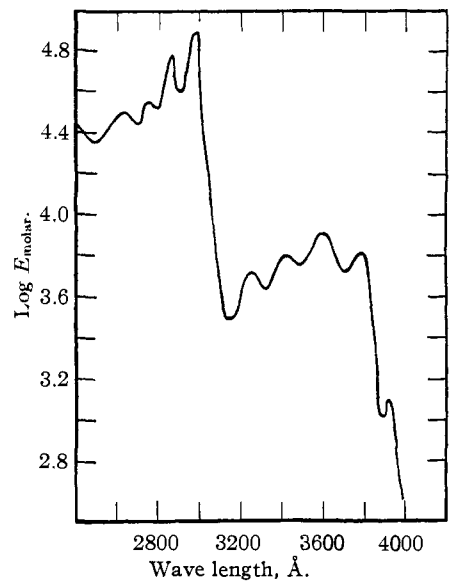


Fig. 3.—15-Thiocyano-20-methylcholanthrene.

at the hindered meso position. The spectrographic evidence therefore favors the structure I in preference to II.

On irradiation with ultraviolet light in a dark room these compounds showed no fluorescence with the exception of the 10-thiocyano derivative which fluoresced bright green in the solid state and blue in solution. A sample of 9-methyl-10-thiocyano-1,2-benzanthracene showed similar fluorescence.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED MAY 28, 1941

## Chlorophyll-Pheophytin: Temperature Coefficient of the Rate of Pheophytin Formation

BY G. MACKINNEY AND M. A. JOSLYN

As reported previously,[1] chlorophyll *a* reacts with acid 8–9 times as rapidly as chlorophyll *b*, in aqueous acetone solution. Measurements have now been made at various temperatures from 0–51° with suitable concentrations of oxalic acid. The pure chlorophyll components were prepared and measurements made as before.[1] At the higher temperatures, the solutions in stoppered test-tubes were rapidly cooled in an ice-bath immediately before measurement. In all cases, acid-free controls were measured under the same conditions. The reaction for each chlorophyll was run at three temperature levels with various concentrations of oxalic acid. Somewhat surprisingly, the plot of ln $k/N$ ($k$ is the first

(1) Mackinney and Joslyn, THIS JOURNAL, **62**, 231 (1940).

order rate constant, $N$ the normality of acid) against $1/T$, the reciprocal of the absolute temperature, gave two virtually parallel curves, Fig. 1. We therefore prepared more chlorophyll *a*, the more abundant and more easily purified component, and repeated measurements at three intermediate temperatures. In view of the number of measurements at different time intervals, for the various acid concentrations, we are confident that the averages for $k/N$, Table I, are substantially correct.

TABLE I

EFFECT OF TEMPERATURE ON RATE CONSTANT

| $T$, °K. | $N$ | $k$ | $k/N$ | Av. |
|---|---|---|---|---|
| | | Chlorophyll *a* | | |
| 273 | 0.01 | 0.410 | 41 | |
| | .002 | .098 | 49 | 45 |
| 280 | .01 | .522 | 46 | |
| | .005 | .222 | 52 | 49 |
| 295 | .002 | .221 | 110.5 | |
| | .001 | .108 | 108 | 109 |
| 301.5 | .01 | 1.39 | 139 | |
| | .007 | 0.907 | 129 | |
| | .004 | .539 | 135 | |
| | .002 | .211 | 105.5 | 127 |
| 310 | .002 | .676 | 338 | |
| | .001 | .373 | 373 | 356 |
| 324 | .001 | 1.725 | 1725 | 1725 |
| | | Chlorophyll *b* | | |
| 273 | 0.05 | 0.23 | 4.6 | |
| | .02 | .04 | 2.00 | 3.3 |
| 301.5 | .10 | 1.69 | 16.9 | |
| | .05 | 0.804 | 16.1 | |
| | .02 | .328 | 16.4 | |
| | .01 | .148 | 14.8 | 16.1 |
| 324 | .01 | 1.47 | 147 | 147 |

Explanations for the deviations of ln $k$ at the higher temperatures (Fig. 1) from the expected straight line relationship include the possibility that secondary reactions occur without being detected. As pointed out by Zscheile and Comar,[2] a considerable proportion of the chlorophyll could be allomerized without affecting the phase test. Variation in the effect of solvent with chlorophyll may also be involved. Regardless, however, of the true explanation, there is no significant difference in the energies of activation for the two chlorophylls whatever basis we select for our calculations.

If we ignore the values for the higher temperatures, and take the slopes of the lines of best fit, we find from the expression

$$\mathrm{d} \ln k = -(E/R)\mathrm{d}(1/T)$$

(2) Zscheile and Comar, *Bot. Gaz.*, **102**, 463 (1941).

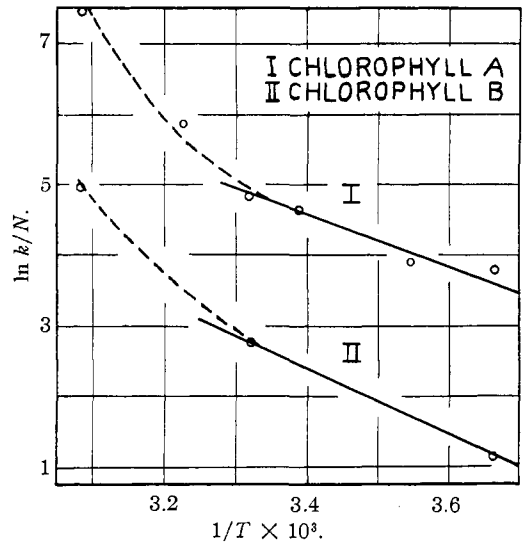


Fig. 1.—First order rate constants as a function of temperature: I, chlorophyll *a*; II, chlorophyll *b*.

energies of 7500 and 9000 cal. for chlorophylls *a* and *b*, respectively. If the values at 0 and 51° be selected, in the two cases, we obtain values of 12,500 and 13,000 cal., respectively. The similarity of these results indicates that the higher rate constant for chlorophyll *a* cannot be explained on the basis of a greater reactivity, and the most plausible explanation is the possibility of steric hindrance in the case of chlorophyll *b*. Phytol also, for example,[3] is less readily split off the chlorophyll *b*.

It is of interest that the stability of the magnesium is markedly affected by the state of oxidation of the isocyclic ring. Preliminary experiments indicate that the effect of a few drops of hydrogen peroxide is to cause a rapid increase in the reaction rate. We hope to report later on the effect of various oxidizing and reducing agents on the stability of magnesium, as this may provide clues to the remarkable ease with which chlorophyll disappears in many biological systems, under conditions as yet ill-defined.

(3) Weast and Mackinney, *J. Biol. Chem.*, **133**, 551 (1940).

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RECEIVED MAY 19, 1941

## The Preparation of Hydrosols by Freezing

BY THOMAS J. SHEA, WILLIAM E. DOOLEY AND CLAUDE SCHWOB

In a previous investigation in this Laboratory[1] hydrosols of active charcoal were prepared by a

(1) Schwob, THIS JOURNAL, **58**, 1115 (1936).

modification of von Weimarn's procedure. These sols are contaminated with considerable amounts of sodium chloride or other "diluent" used in the grinding. Subsequent work showed a need for a substantially electrolyte-free charcoal hydrosol. One of us (T. J. S.) suggested that freezing the water in the capillaries of wet charcoal should cause enough expansion to give the required subdivision. This was found to be the case. Several other substances, such as Patrick's silica gel, which are easily wet by water were found to produce hydrosols when an aqueous paste was rapidly frozen and treated with water. This Laboratory not being equipped for precise colloidal work, it has been decided to forego any attempt to study the nature of the systems so obtained. A description of the general methods used by us is given here.

The charcoal or other solid is covered with water and wet by boiling or evacuation or both. Excess water is then decanted, and the resulting paste frozen in a beaker or flask immersed in a freezing mixture. The usual dry-ice–acetone mixture is very satisfactory for this purpose. The mass is thawed and frozen several times and then mixed with a large volume of distilled water. Alternately, after each freezing, about 200 cc. of water per g. of charcoal may be added to the frozen mass and the resulting sol decanted.

Many varieties of commercial carbons and sugar charcoals were found to give fairly stable sols of low concentration. Often better results were obtained if the water was made slightly acid or basic. The usual protective colloids seem to have very little effect.

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RECEIVED JUNE 16, 1941

## Preparation of 3,4-Dimethylaniline

BY W. A. WISANSKY AND S. ANSBACHER

In the synthesis of riboflavin, the preparation of 3,4-dimethylaniline is an important step. This xylidine is usually obtained by the method of Karrer, *et al.*,[1] comprising nitration of *o*-xylene, isolation by repeated fractionation of the 4-nitro-*o*-xylene and subsequent catalytic hydrogenation of the latter compound. In our hands, Karrer's procedure proved to be tedious and gave relatively low yields; in fact, we confirmed Karrer's 15% yield of xylidine. James, *et al.*,[2] likewise made use of a nitration and reduction method; they obtained a 27% yield of 4-nitro-*o*-xylene by conducting the nitration at a higher temperature. These workers adopted Karrer's laborious fractionation procedure for their subsequent steps of the process.

We have found that 4-bromo-*o*-xylene, obtained from *o*-xylene by bromination and subsequent vacuum distillation in 85% yield, according to Ghigi,[3] may be transformed to 3,4-dimethylaniline, when subjected to high pressure ammonolysis by the procedure of Groggins and Stirton[4] for the conversion of aromatic halides to the corresponding amines. Using pure *o*-xylene as the basic material, 4-bromo-*o*-xylene is obtained free from isomers. Hence, the finally resulting 1,2-dimethyl-4-aminobenzene will likewise be practically free of isomers.

In a bomb of a high-pressure hydrogenator, 200 g. of 4-bromo-*o*-xylene, 14 g. of copper wire and 600 ml. of 28–29% ammonia containing 12 g. of cuprous chloride were placed and treated at 195° and 900–1000 lb. pressure for fourteen hours under agitation by tilting back and forth. The bomb was emptied after cooling, the two layers were separated and 40 ml. of 40% alkali was added to the organic layer. The product was steam distilled and the crude xylidine, which crystallized on cooling, was further purified by dissolving it in 500 ml. of 8% hydrochloric acid and extracting the acid solution twice with 100-ml. portions of ether. The acid solution was made alkaline with 160 ml. of 40% alkali and steam distilled. The distillate was cooled and filtered and the dry product thus obtained was further purified by vacuum distillation at 116–118° and 22–25 mm.

The yield was 103 g. of 3,4-dimethylaniline (79%). A mechanically stirred autoclave may be more suitable than the apparatus employed, since more uniform mixing appears to result in a better yield. It is not known whether a large excess of ammonia is necessary for the reaction.

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(1) Karrer, Becker, Benz, Frei, Salomon and Schöpp, *Helv. Chim. Acta*, **18**, 1435 (1935).

(2) James, Snell and Weissberger, THIS JOURNAL, **60**, 2084 (1938).

(3) Ghigi, *Ber.*, **71**, 684 (1938).

(4) Groggins and Stirton, *Ind. Eng. Chem*, **28**, 1051 (1936).