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.

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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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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 5×10^{-4} and for trimethylamine hydroxide[2] as 6.5×10^{-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.

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

(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.