chloride ions. The insolubility of thallous chloride in water and dilute solutions of thallic chloride, and the presence of free chlorine in concentrated thallic chloride solutions (3.5 *F*) in which thallous chloride has an appreciable solubility[3] prevented an exact spectrophotometric study of solutions having significant concentrations of thallous and thallic chlorides. We can report however that as successive portions of solid thallous chloride were added to a 3.4 *F* thallic chloride solution containing some (*ca.* 0.03 *F*) free chlorine, the optical density of the resulting solutions decreased (as the chlorine was removed) and became constant at the values: $\lambda = 380$ m$\mu$, $D = 0.065$; $\mu = 360$ m$\mu$, $D = 0.66$, for a solution that contained 0.04 *F* excess Tl(I). Since the optical densities of the solutions never increased as the TlCl was added, there was probably no significant interaction absorption in the solution.

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## The Lactal Ring Structures of Some Synthetic Pyrimidine Nucleosides[1]

BY MARJORIE ZEIGER NEWMARK, IRVING GOODMAN AND KARL DITTMER[2]

The ribosyl, arabinosyl, glucosyl and galactosyl nucleosides of uracil and thymine and the corresponding 5-bromo-uracil derivatives were prepared in our laboratories[3,4] and tested for biological activity[5] on two strains of *Escherichia coli*, two strains of *Neurospora crassa*, a strain of *Lactobacillus casei*, and one of *Streptococcus faecalis* R.

A uracil-requiring mutant of *E. coli* was unaffected by any of the synthetic nucleosides although uracil or natural uridine produced good growth. A uracil-less mutant of *N. crassa* which was shown by Loring to grow well on uracil, uridine or uridylic acid was also unaffected by the synthetic products. Results of studies of *L. casei* and *S. faecalis* R showed a similar lack of biological activity. These studies emphasized the need for complete elucidation of the detailed structure of these synthetic nucleosides.

In order to establish the nature of a possible relationship between structure and activity, a number of naturally occurring and synthetic nucleosides were analyzed by the periodate method as adapted by Davoll, Lythgoe and Todd[6] to determine the ring structures of the sugar component of the nucleosides. In this method glycofuranosyl nucleosides of the pentoses require one mole of periodate per mole of nucleoside for oxidation, whereas glycopyranosides of this type require two moles of periodate. Aldohexoses in the pyranoside form require two moles of periodate for oxidation and liberate one mole of formic acid during the course of the reaction; aldohexoses in the furanoside form also require two moles of periodate for oxidation but liberate no formic acid.

Table I summarizes the results of the periodate oxidation of a number of synthetic pyrimidine nucleosides as well as the naturally occurring pyrimidine nucleosides, uridine and cytidine. All of the synthetic nucleosides here reported possess the pyranoside structure. These results would indicate in part that the known biological activity of uridine and cytidine are dependent upon the furanoside structure.

TABLE I

PERIODATE OXIDATION OF SOME PYRIMIDINE NUCLEOSIDES

| N-Glycoside | Moles $IO_4^-$ / Mole glycoside | Moles HCOOH / Mole glycoside |
|---|---|---|
| Uridine[a] | 1.14 | .. |
| Cytidine[a] | 1.20 | .. |
| 1-D-Ribosyl uracil | 2.02 | ..[b] |
| 1-D-Arabinosyl uracil | 2.07 | ..[b] |
| 1-D-Xylosyl uracil | 1.89 | 0.86 |
| 1-D-Glucosyl uracil | 2.01 | 0.95 |
| 1-D-Galactosyl uracil | 2.03 | ..[b] |
| 1-D-Arabinosylthymine | 2.03 | ..[b] |
| 1-L-Arabinosylthymine | 1.92 | ..[b] |
| 1-D-Galactosylthymine | 2.04 | 0.99 |
| 1-D-Glucosylcytosine | 1.98 | 0.88 |

[a] We are indebted to Dr. H. S. Loring of Stanford University for the samples of uridine and cytidine. [b] The theoretical amount of formic acid expected is 1 mole, but due to limited amounts of material the determinations were not made.

(1) This work was supported in part by a research grant-in-aid from the National Institutes of Health.

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(3) D. Visser, K. Dittmer and I. Goodman, *J. Biol. Chem.*, **171**, 377 (1947).

(4) D. Visser, I. Goodman and K. Dittmer, THIS JOURNAL, **70**, 1926 (1948).

(5) K. Dittmer, I. Goodman, D. Visser and H. P. McNulty, *Proc. Soc. Exp. Biol. Med.*, **69**, 40 (1948).

(6) J. Davoll, B. Lythgoe and A. R. Todd, *J. Chem. Soc.*, 833 (1946).

DEPARTMENT OF CHEMISTRY
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## A Complex Praseodymium Fluoride Readily Soluble in Dilute Acids[1]

BY THEODORE P. PERROS AND CHARLES R. NAESER

The insolubility of praseodymium trifluoride in dilute mineral acids is well known. In the course of investigations concerning this compound a complex potassium–praseodymium–fluoride compound, possibly new, which was easily soluble in dilute acids was prepared.

(1) From the thesis for the M.S. degree of T. Perros, The George Washington University.

### Experimental

About 10 g. of technical grade potassium hydrogen fluoride was placed in a platinum crucible and heated over a burner until molten. Approximately 0.5 g. of praseodymium trifluoride was placed in the melt and stirred with a platinum rod. Within five minutes the praseodymium fluoride had dissolved completely, giving a pale yellow-green color to the melt. After the melt had cooled and solidified to a hard, brittle mass, it was placed in a beaker and water (containing a few drops of ammonium hydroxide solution) was added to dissolve the excess potassium fluoride and potassium hydrogen fluoride. After several leachings with water, a pale green residue mixed with dark particles of impurities from the potassium hydrogen fluoride remained. The washings, even after concentration, gave no evidence for the presence of praseodymium ions. However, light reflected from the green residue gave the characteristic absorption spectrum of praseodymium ions.

This green residue, but not the black particles, was readily soluble in 3 *N* hydrochloric acid when slightly warmed. This behavior is quite different from that of praseodymium trifluoride.

Purification of potassium hydrogen fluoride by crystallization eliminated the dark impurities. The purified material with praseodymium trifluoride gave a residue completely soluble in the 3 *N* hydrochloric acid. This marked difference in solubility of the two praseodymium–fluoride compounds indicates the formation of a complex ion containing both praseodymium and fluorine.

When $Pr_6O_{11}$ was added to fused potassium hydrogen fluoride a vigorous reaction took place, and the final green residue showed the same characteristics as that obtained by treatment of the praseodymium trifluoride with potassium hydrogen fluoride.

Investigations to determine whether the composition of this substance is similar to the $KLaF_4$ described by W. H. Zachariasen[2] and also to determine the properties of this substance are being continued.

(2) Zachariasen, THIS JOURNAL, **70**, 2147 (1948).

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## Acid Catalyzed Reaction of Diarylformamidines with Ethyl Orthoformate

BY ROYSTON M. ROBERTS

Ethyl N-phenylformimidate (I) was first prepared by Comstock and Clapp[1] from ethyl iodide and the silver salt of formanilide; the yield was low, and although it has been improved by Smith and Nichols[2] the procedure is expensive and tedious. Claisen[3] prepared this compound from aniline and ethyl orthoformate. He reported that the preparation was accomplished only after numerous unsuccessful attempts and that his directions must be followed exactly; even so, the yield he obtained was only 44% from a reaction mixture heated nine hours. Our attempt to repeat this work resulted in a yield of 11%. Claisen postulated a two-step mechanism for the reaction: first, the formation of N,N′-diphenylformamidine (rapid), and second, reaction of this compound with a second mole of ethyl orthoformate (much slower).

(1) Comstock and Clapp, *Am. Chem. J.*, **13**, 527 (1891).
(2) Smith and Nichols, *J. Org. Chem.*, **6**, 489 (1941)
(3) Claisen, *Ann.*, **287**, 363 (1895).

$$2C_6H_5NH_2 + (C_2H_5O)_3CH \longrightarrow C_6H_5N{=}CH{-}NH{-}C_6H_5 + 3C_2H_5OH \quad (A)$$

$$C_6H_5{-}N{=}CH{-}NH{-}C_6H_5 + (C_2H_5O)_3CH \rightleftharpoons 2C_6H_5N{=}CHOC_2H_5 + C_2H_5OH \quad (B)$$

I

There is no doubt regarding the ease with which the first step (A) takes place, but we have found that the second step (B), is practically completely dependent on acid catalysis. This undoubtedly explains the many unsuccessful experiments mentioned by Claisen and also our first attempt in which we took some care to avoid traces of acid. When we heated pure N,N′-diphenylformamidine with ethyl orthoformate containing a little anhydrous potassium carbonate for twenty-four hours, we found practically no alcohol was produced and the N,N′-diphenylformamidine was recovered unchanged. Prompted by the observation of acid catalysis in the reaction of ethyl N-phenylformimidate with amines (to be published separately) we added a small amount of aniline hydrochloride to the ethyl orthoformate and N,N′-diphenylformamidine and found that the calculated amount of ethanol was evolved rapidly and a 96% yield of ethyl N-phenylformimidate was produced. Other acids are also effective in catalyzing the reaction; sulfuric and *p*-toluenesulfonic acids gave comparable results and even acetic acid was fairly effective. Ethyl N-*p*-tolylformimidate[4] was produced from *p*-toluidine or N,N′-di-*p*-tolylformamidine under similar conditions. The formamidines need not be isolated when the aromatic amine is the starting material. In fact, the acid catalyzed reaction of orthoformate with aromatic amine may not proceed by intermediate formamidine formation but may be more direct. The mechanism of this reaction will be discussed more completely in a subsequent paper. It is interesting to note that reaction (B) is apparently reversible and has previously been described as it occurs in the opposite direction from that reported here! Knott[5] treated ethyl N-phenylformimidate in alcoholic solution with carboxylic and sulfonic acids; he obtained N,N′-diphenylformamidine salts and was able to identify ethyl orthoformate as the other product in one case.

Recently Hamer, Rathbone and Winton have reported modifying Claisen's procedure obtaining yields of 81–85% by "including aniline hydrochloride to inhibit the formation of carbylamine."[6] Their reason for choosing aniline hydrochloride for this function is not given and there is no mention of acid catalysis.

It is perhaps pertinent to recall attention to the fact that in 1941 Smith and Nichols[2] showed that the reaction of Grignard reagents with ethyl N-phenylformimidate was the most satisfactory general method for the synthesis of aromatic

(4) Wheeler and Johnson, *Ber.*, **32**, 35 (1899).
(5) Knott, *J. Chem. Soc.*, 686 (1945).
(6) Hamer, Rathbone and Winton, *J. Chem. Soc.*, 954 (1947).