Naylor [1] has reported that 2, 2, 6, 6-tetramethyltetrahydrothiopyran methiodide is formed only when the initial reactants are allowed to stand cold for a long time; performing the reaction at 100° C leads to the production of trimethylsulfonium iodide as the main product. A similar phenomenon was found in our case, although I proved to be somewhat more stable and did not require cooling during the reaction with methyl iodide.

EXPERIMENTAL

2, 5-Dimethyl-2, 5-hexanediol. From a dropping funnel, 59.2 g (0.34 mole) of diethyl succinate (bp 86° C, 6mm); d_4^{20} 1.040; n_D^{20} 1.4200, in 75 ml of ether was added to the cooled Grignard reagent prepared from 45 g (1.9 g-atom) of magnesium and 270 g (1.9 mole) of methyl iodide in 400 ml of ether.

Then the mixture was boiled for 2 hr and was left overnight. After this it was slowly poured into a previously-prepared solution of ammonium chloride (200 g in 700 ml of water) containing finely crushed ice (2000 g). The ethereal layer was separated off and the aqueous layer was carefully extracted with ether. The combined ethereal extracts were dried with magnesium sulfate. After the ether and volatile products had been distilled off in vacuum (1 mm), 18 g (36.5%) of a product with mp 92° C was obtained. According to the literature [2]: mp 90°–91° C.

2, 2, 5, 5-Tetramethyltetrahydrofuran. A flask fitted with a reflux condenser and a stirrer was charged with a mixture of 18 g (0.12 mole) of 2, 5-dimethyl-2, 5-hexanediol and 150 ml of 2 N sulfuric acid. Stirring and heating (100° C) was carried out for 2 hr. Then the organic layer was separated off and distilled. Colorless liquid with a characteristic odor, yield 7 g (45.5%), bp 115°–118° C, d_4^{20} 0.8336; n_D^{20} 1.4190. According to the literature [3], bp 116°–117° C.

2, 2, 5, 5-Tetramethyltetrahydrothiophene (I). A tube previously purged with nitrogen was charged with 7 g (55 mM) of 2, 2, 5, 5-tetramethyltetrahydrofuran and 24 g (0.11 mole) of phosphorus pentasulfide, sealed, and kept at 100° C for 6 hr. Then the mixture was treated with 30% aqueous alkali and twice extracted with ether. The ethereal extracts were dried with potassium carbonate. After the ether had been driven off, the residue was distilled in vacuum. Yield 4 g (51%).

Redistillation gave a colorless liquid with a sharp smell having bp 56° C (25 mm); d_4^{20} 0.8954; n_D^{20} 1.4670. Found, %: C 67.0; H 11.1; S 22.18; MR_D 44.63. Calculated for $C_8H_{16}S$, %: C 66.7; H 11.1; S 22.20; MR_D 44.44.

IR spectrum: 550 (w); 595 (s); 690 (m); 732 (m); 763 (m); 795 (m); 815 (w); 925 (w); 975 (m); 1013 (m); 1085 (s); 1120 (s); 1139 (v.s); 1185 (w); 1195 (m); 1312 (m); 1379 (s); 1385 (m); 1410 (m); 1460 (s).

Methiodide of I. A mixture of 1.44 g (0.01 mole) of I and 1.4 g (0.01 mole) of methyl iodide was kept at room temperature for 2 days. After recrystallization from ethanol–ether it formed light yellow crystals, mp 161° C (decomp.). The yield was quantitative. Found, %: I 44.76. Calculated for $C_9H_{19}SI$, %: I 44.45.

After I had been kept with an excess of methyl iodide at 80°–100° C for several hours, it was possible to isolate from the reaction mixture only trimethylsulfonium iodide (decomposing at 209° C; according to the literature [4]; decomp. 215° C). Yield 70%. Found, %: I 62.9 Calculated for C_3H_9SI, %: I 62.3.

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THE REACTION OF SODIUM SALTS OF URACILS WITH CHLORIDES OF ACIDS OF PHOSPHORUS. I

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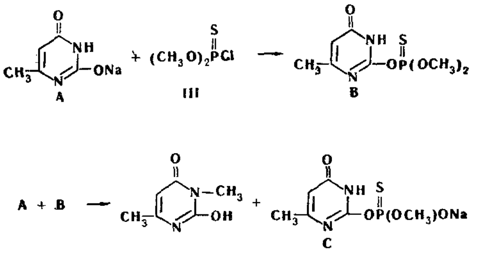
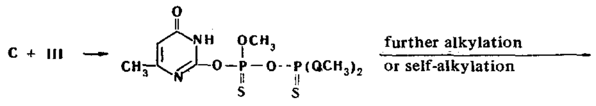
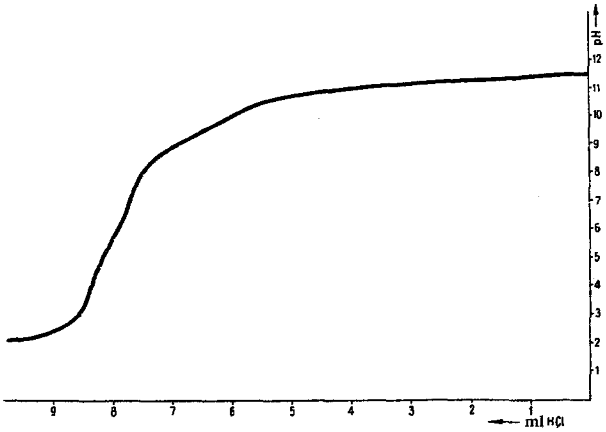
The reaction of the sodium salts of 6-methyluracil (I) and 3, 6-dimethyluracil (II) with methyl and ethyl phosphorochloridates and phosphorochloridothioates give the corresponding N-methyl- and N-ethyluracils. The reaction of I with dimethyl phosphorochloridothioate has given a phosphorus-containing reaction product the structure of which has not been established.

The reaction of the Na salts of 6-methyluracil (I) and 3, 6-dimethyluracil (II) with dimethyl phosphorochloridothioate (III), diethyl phosphorochloridate, and ethyl ethylphosphonochloridothioate leads to the vigorous alkylation of the pyrimidine nucleus, particularly in the case of III. Thus, the reaction of III with I in dimethylformamide yielded 3, 6-dimethyluracil and 1, 3, 6-trimethyluracil, and the reaction of III with II yielded 1, 3, 6-trimethyluracil. The formation of these compounds can be represented by the following scheme.





The reaction of ethyl ethylphosphonochloridothioate with II in benzene gave 3, 6-dimethyl-1-ethyluracil.



Potentiometric titration curve of the products of the alkaline hydrolysis of compound IV. Sample 0.1533 g in 10 ml of H_2O + 40 ml of 0.1 N NaOH. Sample for titration 10 ml. Titration with 0.1N HCl.

In benzene at temperatures of 10°–20° C, the reaction takes place very slowly. The oil obtained under these conditions cannot be distilled: at a temperature above 40° C a strongly exothermic reaction begins which forms the same compounds as when the reaction is carried out in dimethylformamide—uracil, N-methylated uracils, and dark viscous uncrystallizable oils with a revolting smell.

In the case of the reaction of I and III, by careful hydrolysis of the oil obtained it was possible to isolate a solid substance (IV) with mp 274 –276° C. The elementary analysis best agrees with the empirical formula $C_{10}H_{21}N_2P_5O_{12}S_5 \cdot 5H_2O$. This shows that one molecule of the initial uracil is bound to five phosphorothioic acid residues.

The IR spectrum of IV has a strong band in the region of the absorption of the P=O bond (1240–1260 cm^{-1}). The formation of a P=O bond can be explained by thione-thiol isomerization of the phosphorothioic acid anion taking part in the reaction [1] (see scheme). Strong absorption bands at 1070 and 940–970 cm^{-1} are most probably connected with the vibrations of P—O—alkyl and P—O—P units, respectively.

On the basis of the reaction scheme and the IR spectrum, it may be assumed that pyrophosphate groupings are present in reaction product IV.

To evaluate the correctness of a pyrophosphate structure for IV, we used acid-base potentiometric titration. A weighed sample of the product was subjected to alkaline hydrolysis in an excess of NaOH at 100° C for 13 hr. It was assumed that complete alkaline hydrolysis would give a mixture of salts of phosphorothioic acids and the Na salt of uracil in some excess of alkali. On subsequent titration of the acid the salts of the strong acids (with pK < 2) should remain untitrated and, thus, the number of equivalents of strong acid salt could be calculated from the difference $C_{tot} \cdot v_{tot} - C_A \cdot v_A$. It can be seen from the potentiometric titration curve (figure) that the back-titration of 10 ml of the hydrolyzate consumed 8.38×0.1 meq of hydrochloric acid, i.e. $3.8 \cdot 10^{-2}$ meq more than the alkali taken. This magnitude corresponds to the number of equivalents of uracil formed during the titration of its Na salt ($4.0 \cdot 10^{-2}$ meq). However, the fact that on back-titration with acid no untitrated salts of strong acids remained in the solution contradicts a pyrophosphate structure for compound IV. A direct titration of IV with alkali showed the presence of groups titrating at pH ≈ 2.5–9, but gave no information on their structure.

EXPERIMENTAL

The sodium salts I and II were prepared by the reaction of the corresponding uracils with NaOH in water with heating. To eliminate water of crystallization, the salts were dried at 150°–170° C in a vacuum of 15–25 mm for 15–20 hr.

The IR spectra were taken on a UR-10 spectrophotometer, the samples being prepared in the form of mulls in paraffin oil. The UV spectra were taken on a SFD-2 spectrophotometer.

Reaction of the sodium salt I with III. In drops, 10 g (0.0623 mole) of III was rapidly added to a suspension of 9.23 g (0.0264 mole) of the Na salt I in 100 ml of dry dimethylformamide at 80°–86° C. The suspended matter dissolved and the solution darkened. The reaction mixture was left for a day at room temperature, and then the solvent was distilled off in vacuum. The residual oil was boiled with 250 ml of dry chloroform and centrifuged. From the extract 1, 3, 6-trimethyluracil with mp 111°–112° C (from benzene) [2] was isolated. The residue from the centrifugation was extracted with 200 ml of cold methanol. The substance insoluble in methanol was centrifuged off. From the solid phase were isolated 3, 6-dimethyluracil with mp 259.5°–260.5° C (from aqueous methanol) and the initial 6-methyluracil with mp 308°–309° C (from aqueous methanol). After 2 days, the methanolic solution set to a gel. It was centrifuged and the solid phase was carefully pressed out, washed with methanol, and dried in vacuum. This gave 1.2 g of IV in the form of a flesh-colored powder decomposing at 274°–276° C and insoluble in boiling methanol, dimethylformamide, methyl cellosolve, and benzene, and dissolving in water with decomposition. Found, %: C 15.49; 15.72; H 2.96; 2.79; N 3.60; 3.37; P 20.59; 20.84. IR spectrum: 450–600, 720, 790–820, 940–980, 1070–1090, 1240–1280, 1360, 1430, 1460, 1640, 1680–1730, 2450–2800, 3100–3600 cm^{-1}. UV spectrum: a 0.0238% solution of IV at pH 2 has two maxima, at <218 nm (D ≈ 1) and 261.5 nm (D = 0.275). The spectrum of a 0.0613% solution of the products of alkaline hydrolysis at pH 11.5 have two maxima: 222.5 nm (D > 3) and 277.5 nm (D = 2.9).

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