and 100%) and with a constant moisture content (10%), while the weight of the charcoal was 0.3 g. Our studies showed that with increase in the adsorption capacity of the activated charcoal, the adsorption of cocarboxylase also increases, which leads to a decrease in its concentration in the solution (see Fig. 1B). The difference in the cocarboxylase hydrochloride content per ml of solution with a clarifying capacity of charcoal of 75 and 100% was 7.8 mg/ml. Therefore, in production, it is best to use an activated charcoal with a clarifying capacity of 75%. In the case of an increased clarifying capacity of the charcoal, a decrease in the amount of charcoal must be calculated.

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SYNTHESIS OF ADENINE AND HYPOXANTHINE FROM 3-METHYLXANTHINE

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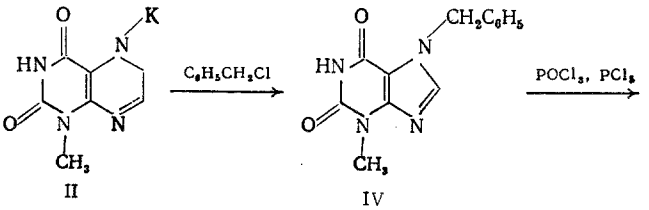
Adenine (I) and hypoxanthine (II) are valuable intermediates in the synthesis of biologically active purine derivatives. Many different syntheses of these compounds are described in the literature. Most of these consist in closing the ring of pyrimidine and imidazole derivatives by the action of different cyclizing agents [1], and other substances, in transformations of the purine derivatives. For example, adenine was prepared from 2,6,8-trichloropurine by substituting chlorine at C_6 with an amino group, followed by the catalytic hydrogenation of the chlorine atoms in positions 2 and 8 over a palladium catalyst [2, 3]. The disadvantage of both methods is the number of stages in the process. Recently, reports have appeared on a single-stage synthesis of adenine from phenylazomalononitrile [4], or from formamide and phosphorus oxychloride [5, 6]. However, these methods require elevated pressure.

We have developed [7] a method for the synthesis of I and II, starting from the readily available potassium salt of 3-methylxanthine (III), an intermediate product in the synthesis of theobromine and caffeine. It consists in converting III, by benzylation, into 3-methyl-7-benzylxanthine (IV), which, in analogy to 2,7-dichloro-7-methylpurine obtained from 3,7-dimethylxanthine (theobromine) [8], is converted in a good yield by the action of phosphorus oxychloride and phosphorus pentachloride into 2,6-dichloro-7-benzylpurine (V). It should be noted that we did not succeed in converting 3-methylxanthine into 2,6-dichloropurine by the action of phosphorus oxychloride and phosophorus pentachloride. For the synthesis of adenine, compound V is converted by heating with aqueous ammonia into 2-chloro-6-hydroxy-7-benzylpurine (VI), from which I is obtained, using catalytic hydrogenation over a palladium catalyst.

For the synthesis of hypoxanthine, the compound V is heated in an aqueous alkali until it dissolves. Upon so doing, 2-chloro-6-hydroxy-7-benzylpurine (VII) is formed, which, without separation, can be converted into II by hydrogenation over a palladium catalyst.



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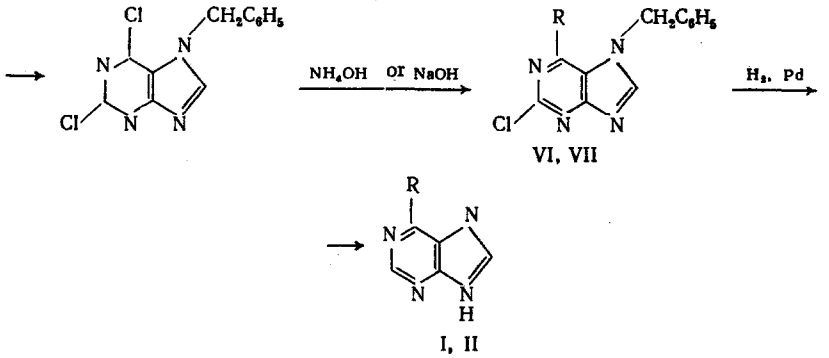

EXPERIMENTAL

3-Methyl-7-benzylxanthine (IV). A 204 g (1 mole) portion of III is boiled for 3 h with 185 ml (1.6 moles) of benzyl chloride in 800 ml of dimethylformamide, and the mixture is then cooled. After 16 h, the precipitate is filtered, washed with water and acetone, and dried. Yield of IV 216 g (84.6%), mp 274-275°C. For analysis, a sample is crystallized from dimethylformamide (1:10), mp 275-276°C. Found, %: C 60.65; H 4.85; N 21.64. $C_{13}H_{12}N_4O_2$. Calculated, %: C 60.93; H 4.71; N 21.88.

2,6-Dichloro-7-benzylpurine (V). A 138 g (0.5 mole) portion of IV is boiled for 7 h with 500 ml of phosphorus oxychloride. Then 208 g (1 mole) of phosphorus pentachloride is added, and boiling is continued for another 6 h. The excess of phosphorus pentachloride is distilled, and the residue is treated with ice, and neutralized with ammonia solution. The precipitate is separated, and crystallized from 70% ethanol or isopropanol. Yield of V 122 g (80.9%), mp 152.4-154.5°C. Found, %: C 51.69; H 2.84; Cl 25.06; N 19.83. $C_{12}H_8Cl_2N_4$. Calculated, %: C 51.61; H 2.87; Cl 25.45; N 20.07.

2-Chloro-6-amino-7-benzylpurine (VI). A 138 g (0.5 mole) portion of V is heated for 8 h at 110°C in an autoclave with 700 ml (4.5 moles) of a 25% solution of ammonia. The mixture is then cooled, and the precipitate is filtered and washed with alcohol. Yield of VI 120 g (93.9%), mp 233-234°C. For analysis, a sample was crystallized from 30% acetic acid, mp 241-242°C. Found, %: C 55.43; H 4.40; Cl 14.28; N 37.10. $C_{12}H_{10}ClN_5$. Calculated, %: C 55.48; H 3.85; Cl 13.98; N 39.96.

Adenine (I). A 13 g (0.05 mole) portion of VI in 130 ml of water is hydrogenated in the presence of 13 g (0.16 mole) of sodium acetate and 13 g of 5% Pd/C at atmospheric pressure and at 85-90°C until a theoretical amount of hydrogen has been absorbed. The catalyst is separated, and the residue is treated with 45 ml of 1 N sodium hydroxide, and filtered. The filtrate is neutralized to pH 6.0, and after 16 h the adenine which separates is filtered. Yield 4 g (64%), mp 352-353°C (dec.). The UV and IR spectra coincide with those of an authentic sample of adenine.

2-Chloro-6-hydroxy-7-benzylpurine (VII). A 13.8 g (0.05 mole) portion of V in 100 ml of 1 N sodium hydroxide (0.11 mole) is heated to dissolution. The solution is filtered, and neutralized to pH 6.0. The precipitate is washed with water and acetone, and dried. Yield of VII 11.6 g (90%), mp 252-254°C (dec.). Found, %: 55.49; H 3.64; Cl 13.57; N 21.50. $C_{12}H_9ClN_4O$. Calculated, %: C 55.28, H 3.45; Cl 13.63; N 21.48.

Hypoxanthine (II). From V: a 13.8 g (0.05 mole) portion of V in 120 ml of 1 N sodium hydroxide (0.12 mole) is heated to boiling until the material dissolves, 13 g of 5% Pd/C is added, and the mixture is hydrogenated at 85-90°C and at normal pressure up to the absorption of the theoretical amount of hydrogen. The mixture is filtered, the filtrate is neutralized to pH 6.0, and the precipitate filtered. Yield of II 5.3 g (78%), does not melt up to 350°C.

From VII: a 13 g (0.05 mole) portion of VII in 100 ml of 1 N sodium hydroxide is hydrogenated in the presence of 5% Pd/C up to the absorption of the theoretical amount of hydrogen. The catalyst is filtered, the filtrate neutralized to pH 6.0, and 6.1 g (90%) of II is isolated. The UV and IR spectra of samples obtained by the two methods coincide with the spectra of an authentic sample of II.

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SYNTHESIS OF 16-DEHYDRO-16-ALKYL(ARYL) PREGNANES FROM O,N-DIACETATES OF 16-ALKYL(ARYL)PSEUDOSOLASODINES

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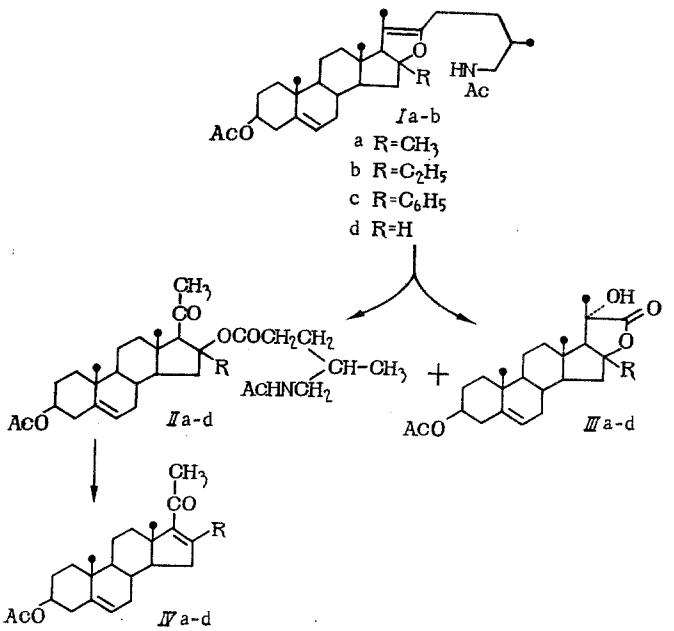
We have already reported [1] on the synthesis of O,N-diacetates of 16-alkyl(aryl)pseudosolasodines (I). In the present work, we report on the conversion of the latter into 16-dehydro-16-alkyl(aryl)pregnanes (IV), which are the starting compounds for the synthesis of several steroid preparations (betamethasone, melengestrol acetate, superlutin) with a β-methyl or methylene group in the 16-position of the molecule.



Compound I was converted into IV by a known method [2], consisting in the oxidation of the double bond of pseudosolasodine O,N-diacetate (Id) with sodium dichromate in acetic acid, followed by splitting of the ester side-chain of the oxidation product by boiling it in glacial acetic acid. This method is used on an industrial scale for the preparation of dehydropregnenolone acetate (IVd) in high yields at the oxidation stage (70-75%), and at the splitting stage (90-95%) [3, 4]. The total yield of IVd based on Id is 65-70%. In the case of 16-alkyl-(aryl)pseudosolasodines (Ia-c), under the above conditions, the end products IVa and c were obtained in lower yields (about 50 and 20%, respectively), while IVb was obtained in trace amounts only. During a chromatographic study of the mother liquors after the crystallization of IVa-c, 16-alkyl(aryl)-3β-acetoxy-20-hydroxy-5-bisnorcholene-22,16-lactones (IIIa-c) were obtained as the side products of the oxidation of Ia-c. We had already obtained similar hydroxylactone (IIId), which is unsubstituted in position 16, during the oxidation of

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