Anal. Calcd. for $C_{10}H_{14}N_2O_2 \cdot 2C_6H_3N_3O_7$: C, 41.5; H, 3.2; N, 17.6. Found: C, 41.6; H, 3.0; N, 17.7.

It should be pointed out that neither II, III, nor IV can be satisfactorily extracted from aqueous solution with organic solvents.

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Addition of Alkanethiolic Acids to $\Delta^{1,4,6}$-3-Oxosteroids

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Recently some selective additions to $\Delta^{1,4,6}$-3-oxosteroids have been reported. Nussbaum and coworkers[1] have reported the epoxidation of the 6,7-double bond, and Kirk and Petrow[2] recorded the addition of chlorine to the 1,2-double bond. We have observed mono- and di- additions of alkanethiolic acids to the $\Delta^{1,4,6}$-3-ketones. When 1,4,6-androstatriene-3,17-dione was heated with ethanethiolic acid, a monoadduct separated rapidly from the hot solution. The same product was obtained from a chloroform solution of equimolar amounts of triene and thiolic acid irradiated with an ultraviolet lamp. On the basis of its ultraviolet spectrum ($\lambda_{max}^{methanol}$ 287 mμ, ϵ 23,400) and of analogy to the addition of thiolic acids to $\Delta^{1,4}$-3-oxosteroids,[3] this product was assigned the structure, 1α-acetylthio-4,6-androstadiene-3,17-dione.

In the cases of 17β-acetoxy-1,4,6-androstatrien-3-one, 17α,21-dihydroxy-1,4,6-pregnatriene-3,11,20-trione 21-acetate, and 11β,17α,21-trihydroxy-1,4,6-pregnatriene-3,20-dione 21-acetate, the products isolated were di-adducts (exhibiting maxima in the 240 mμ region characteristic of Δ^4-3-ketones). Again by analogy to monoadditions,[3] these compounds were assigned the 1α,7α-diacylthio structures.

EXPERIMENTAL[4]

1α-Acetylthio-4,6-androstadiene-3,17-dione. 1,4,6-Androstatriene-3,17-dione,[5] 2.00 g., was dissolved in 5.0 ml. of ethanethiolic acid and irradiated and heated with an ultraviolet light for 1 hr. During this time crystals formed. They were separated by filtration, washed with ether, and crystallized from methylene chloride-methanol. In this way 1.00 g. of 1α-acetylthio-4,6-androstadiene-3,17-dione, m.p. 229–229.5° (dec.), was obtained.

Anal. Calcd. for $C_{21}H_{26}O_3S$: C, 70.36; H, 7.31. Found: C, 70.38; H, 7.33. Ultraviolet spectrum: $\lambda_{max}^{methanol}$ 287 mμ, ϵ 23,400. $[\alpha]_D$ +68°.

1α,7α-Dithiol-11β,17α,21-trihydroxy-4-pregnene-3,20-dione 21-acetate 1,7-dipropionate. 11β,17α,21-Trihydroxy-1,4,6-pregnatriene-3,20-dione 21-acetate,[6] 0.87 g., dissolved in 1.0 ml. of propanethiolic acid, was heated on the steam bath for several hours. Most of the excess thiolic acid was removed under vacuum and the residue was chromatographed on silica gel. The column was washed with benzene and mixtures of 5 and 10% ethyl acetate in benzene. Then the column was eluted with 15% ethyl acetate in benzene and the eluants were concentrated to yield 0.20 g. of 1α,7α-dithiol-11β,17α,21-trihydroxy-4-pregnene-3,20-dione 21-acetate 1,7-dipropionate as a glass.

Anal: Calcd. for $C_{29}H_{40}O_8S_2$: C, 59.97; H, 6.94. Found: C, 59.91; H, 7.05. Ultraviolet spectrum $\lambda_{max}^{methanol}$ 239 mμ, ϵ 21,200; $[\alpha]_D$ +37°.

1α,7α-Dithiol-17β-hydroxy-4-androsten-3-one triacetate. 17β-Acetoxy-1,4,6-androstatrien-3-one,[5] 1.93 g., was mixed with 2.0 ml. of ethanethiolic acid and heated and irradiated with an ultraviolet light for 45 min. Some of the excess thiolic acid was distilled under vacuum, ether was added to the residue, and the solid which formed was separated by filtration. Two crystallizations of this material from acetone-ether yielded 0.91 g. of 1α,7α-dithiol-17β-hydroxy-4-androsten-3-one triacetate, m.p. 199–200° (dec.).

Anal. Calcd. for $C_{25}H_{34}O_5S_2$: C, 62.73; H, 7.16. Found: C, 62.68; H, 7.46. Ultraviolet spectrum: $\lambda_{max}^{methanol}$ 237.5 mμ, ϵ 20,100; $[\alpha]_D$ −46°.

1α,7α-Dithiol-17α,21-dihydroxy-4-pregnene-3,11,20-trione 1,7,21-triacetate. 17α,21-Dihydroxy-1,4,6-pregnatriene-3,11,-20-trione 21-acetate,[6] 0.54 g., was dissolved in 1.0 ml. of ethanethiolic acid and heated and irradiated with an ultraviolet light for 1 hr. Then part of the excess acid was removed under vacuum and ether was added. The solid which formed was separated by filtration and crystallized from acetone-ether to yield 0.38 g. of 1α,7α-dithiol-17α,21-dihydroxy-4-pregnene-3,11,20-trione 1,7,21-triacetate, m.p. 190–191° (dec.).

Anal. Calcd. for $C_{27}H_{34}O_8S_2$: C, 58.89; H, 6.22. Found: C, 59.05; 58.72; H, 6.70, 6.53. Ultraviolet spectrum: $\lambda_{max}^{methanol}$ 235.5 mμ, ϵ 18,500; $[\alpha]_D$ +80°.

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Synthesis of 1,2,4,5-Tetrachlorobenzene-1-Cl^{36}

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1,2,4,5-Tetrachlorobenzene has been under investigation in this laboratory for use as an agricultural chemical. The compound, labeled with chlorine-36, was desired for residue determinations using an isotope dilution procedure. Since it had not previously been prepared the synthesis was undertaken employing the Sandmeyer reaction.

EXPERIMENTAL

Cuprous chloride-Cl^{36}.[1] To a solution of cupric sulfate pentahydrate (187 mg., 0.75 mmole) and sodium chloride-Cl^{36} (44 mg., 0.75 mmole, specific activity 20.8 μc./mmole) in 0.6 ml. of water was added dropwise with shaking at room temperature, sodium sulfite (96 mg., 0.76 mmole) in 0.3 ml. of water. The mixture was centrifuged, the aqueous phase was removed with a dropper, and the precipitate of cuprous chloride-Cl^{36} was washed once with 0.5 ml. of water to which was added a very small amount of sulfurous acid to prevent oxidation. This aqueous phase was also removed by centrifugation.

The cuprous chloride-Cl^{36} was washed three times each with acetic acid, anhydrous ethanol, and anhydrous ether, centrifugation being used each time to separate the liquid phase. The product was used immediately in the next reaction.

The yield in preliminary runs was quantitative.

1,2,4,5-Tetrachlorobenzene-1-Cl^{36}. 2,4,5-Trichloroaniline (147 mg., 0.75 mmole) was diazotized in the following manner[2]: The aniline derivative was dissolved in 0.75 ml. of concentrated sulfuric acid. To this ice cold solution was added 1.88 ml. of a cold solution of sodium nitrite (1.125 mmole) in concentrated sulfuric acid. Cold 85% phosphoric acid (0.75 ml.) was then added and the dark colored solution was allowed to stand at room temperature for 1.5 hr. Initially and rather slowly, there was some precipitation, but the crystalline material gradually redissolved on intermittent shaking as the reaction progressed. The reaction solution was finally poured onto ice to give a solution with a volume of about 10 ml. The excess nitrous acid was destroyed by addition of small quantities of urea.

During the 1.5 hr. required for the diazotization reaction to take place, the cuprous chloride-Cl^{36} was prepared as described above. Following this, a solution of the cuprous chloride-Cl^{36} (0.75 mmole) and sodium chloride-Cl^{36} (65 mg., 1.13 mmole) in hydrochloric acid-Cl^{36} (0.6 ml. of 1.64 N acid, 0.98 mmole, specific activity 20.8 μc./mmole) was prepared. This solution contained a total of 2.86 mmole of chloride-Cl^{36}. Preliminary work had made it clear that a one-to-one stoichiometry, chloride to diazotized amine, gave a very poor yield of product.

The cuprous chloride-Cl^{36} solution was heated on the steam bath and the diazonium solution at room temperature was rapidly poured onto it with shaking. After 15 min. of intermittent shaking at room temperature, the product was isolated by hot benzene extraction. The benzene solution was placed in a porcelain crucible (3.3 cm. i.d. at the top) and the benzene was removed using the steam bath and a gentle stream of air. This evaporation was carried out carefully to prevent loss of product since tetrachlorobenzene sublimes very easily.

The product was purified by sublimation at atmospheric pressure in the following manner: The crucible containing the crude product was covered with a piece of Whatman No. 1 filter paper (4.25 cm.) through which were punched a large number of pin holes. This paper served to prevent sublimed product from falling back into the crucible and, more important, acted as a condensing surface for colored byproducts which do not sublime, but distill. The paper and crucible were covered with an inverted watch glass (4.2 cm.) which served as the condensing surface. The watch glass was cooled with a gentle stream of air. The crucible was heated at 275–285° for 1 hr. with the hot stage from a melting point apparatus. The tetrachlorobenzene condensed as long white needles, m.p. 137° (lit.[3] 137–141°). The yield was 92 mg. (57%); the specific activity was 20.8 μc./mmole. There was no depression in a mixed m.p. with an authentic sample of 1,2,4,5-tetrachlorobenzene.

The excess chloride-Cl^{36} used in this synthesis was recovered from the reaction mixture by treatment with barium hydroxide solution to precipitate the sulfate and phosphate, conversion to hydrochloric acid-Cl^{36} by means of Dowex-50 exchange resin in the acid form, and finally, titration of the eluate with dilute sodium hydroxide solution followed by evaporation to dryness.

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Stereochemistry of 8,10-Dimethyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene

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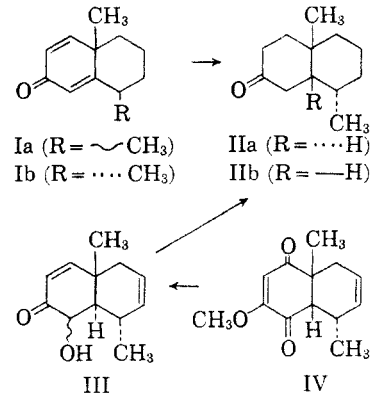
In the reported synthesis of 8,10-dimethyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene (Ia) the relationship between the methyl groups was unassigned.[1] The work described in this note establishes the missing stereochemical link and allows the assignment of (Ib) for the cyclohexadienone.



Reduction of the cyclohexadienone with lithium in ammonia gave an oily saturated ketone which is shown in the sequel to be identical with *trans*-2-keto-8α-10β-dimethyldecalin (IIa) synthesized from IV. The Diels-Alder adduct IV, in which the methyl groups are fixed in the desired manner, was made from the reaction of 4-methoxy-2,5-toluquinone with *trans*-1,3-pentadiene.[2,3] The adduct on

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(2) The *trans*-1,3-pentadiene employed in this study was not separated from any *cis* contaminant (*vide infra*). Several prior investigations have shown that the *cis*-1,3-pentadiene does not give a normal Diels-Alder adduct. For example, *cis*-1,3-pentadiene gives only polymeric material on reaction with maleic anhydride. See D. Craig, *J. Am. Chem. Soc.*, 65, 1006 (1943); R. L. Frank, R. D. Emmick and R. S. Johnson, *J. Am. Chem. Soc.*, 69, 2313 (1947); S. J. Averill and H. L. Trumbull, *J. Am. Chem. Soc.*, 76, 1159 (1954) for a description of the dienophiles and the conditions employed. These facts led us to conclude that the *cis* isomer would give *only* polymeric material on reaction with 4-methoxy-2,5-toluquinone.