dimedon procedure was applicable only to 1,2-dihydroxy-3-nitratopropane since the α-nitratoacetaldehyde presumbly formed did not yield a derivative with 5,5-dimethyl-1,3-cyclohexanedione as determined by a mixed melting point determination on the formaldehyde derivative. In the oxidation of 3-chloro-1,2-propanediol, the chloroacetaldehyde derivative is not found in quantitative yield under the conditions of test.

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Selective Mercaptole Formation of Steroid Ketones

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The ease of formation and chemical stability of mercaptoles makes these compounds attractive intermediates in multi-stage syntheses. The studies of Hauptmann,[1] of Ruff and Reichstein[2] and of Fieser[3] on the reaction of steroid ketones with ethanedithiol have demonstrated that this dimercaptan will condense with carbonyl functions at the 3-, 6-, 7-, 12-, 17- and 20-positions: the hindered 11-position is the only site of unreactivity. This situation has been used to advantage in selective formation of 7-mercaptoles from 7,11-diones[4] and 12-mercaptoles from 11,12-diones.[5] A higher order of selectivity is required when the competitive reaction is between the 3- and 6-, the 3- and 17-, or the 3- and 20-positions. There has been a recent description of selective reaction at the 3-position in 3,6-diones.[3] A solution to the 3- and 17-positions case is disclosed in the patent literature[6] where the reaction of 4-androstene-3,17-dione with ethanedithiol in the presence of dry hydrogen chloride is said to yield 4-androstene-3,17-dione 3-ethylene mercaptole. No experimental details or physical constants appear in the patent.

We have previously observed[7] that steroid ketones condense with ethanedithiol under very mild conditions, *i.e.*, acetic acid as a solvent and *p*-toluenesulfonic acid as a catalyst. When these conditions were used with di- and tri-ketones, it was found that reaction took place primarily at the 3-position.

Experimental

4-Androstene-3,17-dione 3-Ethylene Mercaptole.—A solution of 1.42 g. (5 mmoles) of 4-androstene-3,17-dione in 20 ml. of acetic acid was treated with 0.471 g. (5 mmoles) of ethanedithiol and a solution of 0.450 g. of *p*-toluenesulfonic acid monohydrate in 5 ml. of acetic acid. After one hour at room temperature, the pale yellow colored solution was poured into water. The resulting suspension was extracted with chloroform. The chloroform solution was washed with water, 5% sodium hydroxide solution and water. After drying over anhydrous sodium sulfate and evaporation of the solvent, there remained 1.93 g. of pale yellow oil. The oil was chromatographed on silica gel. Elution with 1:2 petroleum ether:benzene gave 0.160 g. of solid melting at 173–175°. Crystallization from acetone afforded 0.139 g. of solid, m.p. 174–176°. This compound gave negative color tests for 17-ketone (Zimmermann) and 4-en-3-one (two-stage Rosenheim) and was 4-androstene-3,17-dione 3,17-bis-(ethylene mercaptole).

Anal. Calcd. for $C_{23}H_{34}S_4$ (438.74): C, 62.96; H, 7.81. Found: C, 63.13; H, 7.66.

Elution with 19:1 benzene:ethyl acetate gave 1.38 g. of solid melting at 173–177°. Crystallization from ethyl acetate gave the analytical sample melting at 173–174.5°. The compound gave a positive Zimmermann reaction and showed no 4-en-3-one absorption in the ultraviolet.

Anal. Calcd. for $C_{21}H_{30}OS_2$ (362.57): C, 69.57; H, 8.34; S, 17.68. Found: C, 69.59; H, 8.32; S, 17.83.

Elution with 4:1 benzene:ethyl acetate gave 0.210 g. of starting material which was identified by melting point and mixed melting point.

4-Androstene-3,11,17-trione 3-Ethylene Mercaptole.—A suspension of 0.60 g. (2 mmoles) of 4-androstene-3,11,17-trione in 8 ml. of acetic acid was treated with 0.185 ml. (2.2 mmoles) of ethanedithiol and a solution of 0.180 g. of *p*-toluenesulfonic acid monohydrate in 2 ml. of acetic acid. When the solution was poured into water (after one hour at room temperature), a solid (0.85 g., m.p. 85–158°) separated. Crystallization from methanol–water afforded 0.40 g. of solid melting at 158–167°. Crystallization from ethyl acetate:petroleum ether to constant m.p. gave 0.232 g. melting at 164–165°.

Anal. Calcd. for $C_{21}H_{28}O_2S_2$ (376.55): C, 66.98; H, 7.49. Found: C, 66.80; H, 7.82; $[\alpha]_D$ +205° (1% in acetone); λKBr, 5.75, 5.88, 9.50 μ.

11β-Hydroxy-4-androstene-3,17-dione 3-Ethylene Mercaptole.—The reaction of 3.02 g. (10 mmoles) of 11β-hydroxy-4-androstene-3,17-dione with ethanedithiol (11 mmoles) was conducted as described in the previous preparations. Crystallization of the chloroform soluble products from ethyl acetate gave 1.43 g. of the desired compound melting at 247–249°.

Anal. Calcd. for $C_{21}H_{30}O_2S_2$ (378.57): C, 66.62; H, 7.99; S, 16.94. Found: C, 66.69; H, 7.90; S, 16.60; λ $CHCl_3$, 2.75, 5.78 μ.

Chromatography of the mother liquor material from the above crystallization gave an additional 1.29 g. of the desired product, 0.251 g. of starting material, and 0.127 g. of the **bis-(ethylene mercaptole)** melting at 215–218°.

Anal. Calcd. for $C_{23}H_{34}OS_4$ (454.71): C, 60.75; H, 7.54; S, 28.20. Found: C, 61.19; H, 7.73; S, 27.82; λ $CHCl_3$, 2.78 μ.

4-Pregnene-3,20-dione 3-Ethylene Mercaptole.—A mixture of 7.8 g. (25 mmoles) of progesterone, 125 ml. of acetic acid, 2.3 ml. of ethanedithiol and 2.50 g. of *p*-toluenesulfonic acid monohydrate was kept at room temperature for one hour and then poured into water. Isolation of the products by chloroform extraction gave 10.53 g. of solid melting at 142–174°. Crystallization from 2-propanol gave 5.02 g. of solid, m.p. 169–181°. A 2.0-g. portion was chromatographed on silica gel. Elution with 1:2 petroleum ether:benzene gave 0.110 g. of solid melting at 179–181.5°. It was not further investigated. Elution with 19:1 benzene:ethyl acetate gave 1.70 g. of solid, m.p. 183–186°. Crystallization from ethyl acetate afforded 1.16 g., m.p. 184–186°. The compound showed no maximum at 240 mμ.

Anal. Calcd. for $C_{23}H_{34}OS_2$ (390.62): C, 70.72; H, 8.77; S, 16.42. Found: C, 70.81; H, 8.78; S, 16.65; $[\alpha]_D$ +211° (1% in chloroform).

17α-Hydroxy-21-acetoxy-4-pregnene-3,20-dione 3-Ethylene Mercaptole.—A solution of 11.64 g. (30 mmoles) of 17α-hydroxy-21-acetoxy-4-pregnene-3,20-dione in 250 ml. of warm acetic acid was treated with 2.76 ml. (30 mmoles) of ethanedithiol and a solution of 2.7 g. of *p*-toluenesulfonic acid monohydrate in 30 ml. of acetic acid. After 17 hours at room temperature, 7.16 g. of crystalline solid had separated. This material melted at 227–229°. Crystallization from acetone gave an analytical sample of the same m.p.

Anal. Calcd. for $C_{25}H_{36}O_4S_2$ (464.66): C, 64.62; H, 7.81; S, 13.80. Found: C, 64.44; H, 7.69; S, 13.30; $[\alpha]_D$ +154° (1% in chloroform); λKBr, 2.95, 5.80, 7.30, 7.92, 8.08, 9.58 μ.

17α-Hydroxy-21-acetoxy-4-pregnene-3,11,20-trione 3-Ethylene Mercaptole.—Reaction of 12.06 g. (30 mmoles) of cortisone acetate as described in the previous preparation

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gave 9.5 g. of solid melting at 245–247°. The mixed m.p. with starting material was 220–236°. Crystallization from acetone gave the analytical sample, m.p. 256–258°.

Anal. Calcd. for $C_{25}H_{34}O_5S_2$ (478.64): C, 62.73; H, 7.16. Found: C, 62.72; H, 7.00; $[\alpha]_D$ +210° (0.5% in chloroform); λKBr, 2.96, 5.74, 5.82, 5.95, 7.30, 7.91, 8.10, 9.52μ.

Saponification with methanolic potassium bicarbonate solution yielded **17α,21-dihydroxy-4-pregnene-3,11,20-trione 3-ethylene mercaptole** crystallization from acetone: petroleum ether afforded material melting at 210–213°.

Anal. Calcd. for $C_{23}H_{32}O_4S_2$ (436.61): C, 63.27; H, 7.39. Found: C, 63.18; H, 7.29; λKBr, 2.96, 5.88, 9.52 μ.

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A *gem*-Effect in the Addition of 2,4-Dinitrobenzenesulfenyl Chloride to γ,δ-Unsaturated Acids

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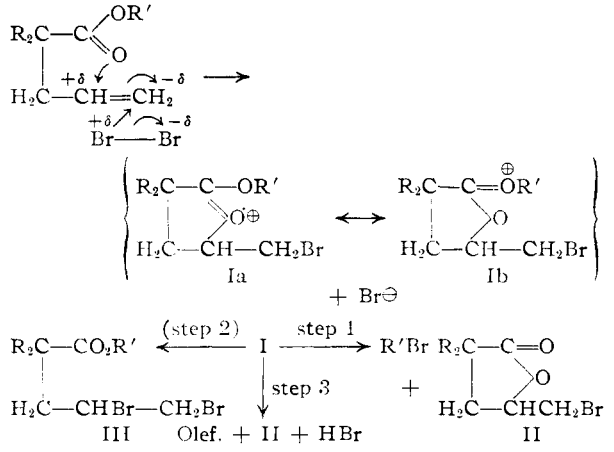
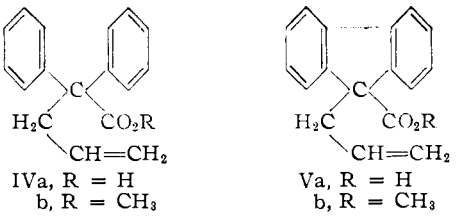
In the reaction of bromine with γ,δ-unsaturated acids and esters the carbonyl oxygen atom is able to participate in the formation of a "resonance stabilized" cyclic oxonium salt (I),[1] in a manner similar to that postulated for the bromination of N-allylbenzamide.[2]

This oxonium salt can undergo three types of transformations: either a bromolactone II or a dibromide III is formed; or, in some cases, the hydrogen bromide formed in the reaction (step 3) can compete with the bromine and simple lactones are formed.[3]



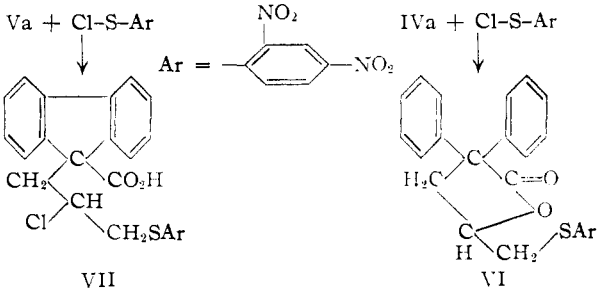
Other electrophilic reagents, like ICN[4] and H^+,[3,5] undergo the same type of reaction.

When methyl 2,2-diphenylpenten-4-oate (IVb) reacts with bromine[3,6] only bromolactone is formed, while the bromination of compound Vb gives rise to a mixture of bromolactone and dibromide.[1]



This seems to indicate that the neighboring carbonyl group of the methyl ester IVb participates as a neighboring group in the reactions involving addition at the γ,δ-double bond to a greater extent than the carbonyl group of methyl 9-allyl-9-fluorene carboxylate.

There is a still greater difference in the behavior of the two acids when they are allowed to react with 2,4-dinitrobenzenesulfenyl chloride. This sulfenyl chloride reacts with olefins giving rise to 2,4-dinitrophenyl β-chloroalkyl sulfides.[7] This is also the result of the reaction of 9-allyl-9-fluorenecarboxylic acid (Va) with 2,4-dinitrobenzenesulfenyl chloride, where a simple addition occurs. However, when the reaction is performed with 2,2-diphenylpenten-4-oic acid (IVa), 2,2-diphenyl-5-(2,4-dinitrophenylmercapto)-4-pentanolactone (VI) is obtained.



This difference in the behavior of the two γ,δ-unsaturated acids is probably due to the fact that in acid Va the fluorene nucleus has a planar configuration whereas in acid IVa the two benzene rings cannot achieve coplanarity,[1] thus occupying a greater space and establishing a conformation of the molecule more favorable for cyclization. This effect is similar to the so-called "*gem*-dimethyl effect" that makes the formation of dimethyl- and tetramethylsuccinic anhydride easier than that of succinic anhydride itself.[8]

In order to compare the behavior of the two acids by means of quantitative data, we measured the reaction of iodine with acids IVa and Va in chloroform solution at 0°. It can be seen from Table I that the values obtained for the rate of reaction agree with the qualitative results, acid IVa reacting much faster than acid Va.

This seems again to indicate that in acid IVa the neighboring carbonyl group participates in the addition reaction to a greater extent, increasing the rate of the reaction. We are studying the reaction

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(7) (a) N. Kharasch, L. Wehrmeister and H. Tigerman, *ibid.*, **69**, 1612 (1947); (b) N. Kharasch and C. M. Buess, *ibid.*, **71**, 2724 (1949); (c) N. Kharasch, *ibid.*, **74**, 3427 (1952).
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