rated and recrystallized from methanol; yield 0.16 g., m.p. 197–198.5°, $[\alpha]^{20}\mathrm{D}$ −16°, no hydroxyl band in the infrared. The zinc chloride procedure gave somewhat poorer results.

Anal. Calcd. for $C_{30}H_{48}O_4$: C, 76.22; H, 10.24. Found: C, 76.05; H, 10.56.

Under the above conditions or employing zinc chloride, 22-isoallospirostan-2α,3β-diol (III) (gitogenin) was recovered in 80–92% yield.

2α,3α-Oxido-22-isoallospirostan (VIII).—A solution of 10 g. of Δ^2-22-isoallospirosten (V) in 50 cc. of chloroform was treated for 24 hours at room temperature with 200 cc. of a chloroform solution of perbenzoic acid (0.26 g./cc.). After washing with 5% sodium iodide solution, sodium thiosulfate solution and sodium bicarbonate, the chloroform was evaporated and the residue recrystallized from acetone; yield 7.4 g. (71%), m.p. 171–173°, $[\alpha]^{20}\mathrm{D}$ −49°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.21; H, 10.21. Found: C, 78.51; H, 10.47.

22-Isoallospirostan-3α-ol (IXa) (Epitigogenin).—To a mixture of 1.5 g. of lithium aluminum hydride in 75 cc. of ether was added a solution of 3.0 g. of the above oxide VIII in 100 cc. of the same solvent. After refluxing for two hours and decomposing the excess reagent with ethyl acetate, the layers were separated, the ether solution was washed with dilute acid and water, dried and evaporated. Two recrystallizations of the residue from acetone afforded 2.1 g. (70%) of colorless crystals with m.p. 242–245°, $[\alpha]^{20}\mathrm{D}$ −58°; lit.[6] m.p. 242–245°. Chromium trioxide oxidation produced 22-isoallospirostan-3-one, m.p. 208–210°, identical with an authentic sample.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.83; H, 10.65. Found: C, 77.84; H, 10.59.

The acetate IXb possessed m.p. 201–203°, $[\alpha]^{20}\mathrm{D}$ −41°; reported[6] 199–202°.

2β-Bromo-22-isoallospirostan-3α-ol (IXc).—The oxide ring was opened by refluxing 2.0 g. of the α-oxide VIII in 200 cc. of ethanol with 2.4 g. of pyridine hydrobromide[14] for one hour. Dilution with water, filtration of the colorless solid and recrystallization from ether–hexane gave 1.45 g. of the bromohydrin IXc with m.p. 203–205°, $[\alpha]^{20}\mathrm{D}$ −35°.

Anal. Calcd. for $C_{27}H_{43}O_3Br$: C, 65.44; H, 8.75. Found: C, 64.97; H, 8.83.

22-Isoallospirostan-2β,3α-diol 2-Monoacetate (Xc).—The acetolysis was carried out exactly as described for 2α,3α-oxidocholestane[5] by refluxing 4.0 g. of the oxide VIII with 400 cc. of glacial acetic acid for 3 hours. The solution was concentrated under reduced pressure to a volume of *ca.* 100 cc., diluted with water and the product was extracted with ether. Recrystallization of the ether residue from acetone yielded 2.4 g. (52%) of the monoacetate with m.p. 219–222°, $[\alpha]^{20}\mathrm{D}$ −41°.

Anal. Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.19; H, 9.70.

Saponification with methanolic potassium hydroxide followed by recrystallization from acetone afforded in 87% yield **22-isoallospirostan-2β,3α-diol (Xa)** with m.p. 240–242°, $[\alpha]^{20}\mathrm{D}$ −52°. The substance gave a yellowish color with concentrated sulfuric acid.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25. Found: C, 75.23; H, 10.48.

The diacetate Xb was recrystallized from ether–acetone, whereupon it showed m.p. 246–248°, $[\alpha]^{20}\mathrm{D}$ −26°.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.06; H, 9.36. Found: C, 72.36; H, 9.52.

22-Isoallospirostan-2β,3α-diol 2-acetate 3-mesylate (Xd) was prepared in 82% yield from the monoacetate Xc and methanesulfonyl chloride in pyridine solution as described above for the tosylate IV. Recrystallization from acetone led to the analytical sample with m.p. 184–186° (dec., Kofler block), $[\alpha]^{20}\mathrm{D}$ −18°.

Anal. Calcd. for $C_{30}H_{48}O_7S$: C, 65.15; H, 8.75. Found: C, 65.06; H, 8.58.

2β,3β-Oxido-22-isoallospirostan (XI).—A solution of 0.35 g. of the mesylate Xd and 0.21 g. of potassium hydroxide in 80 cc. of methanol was refluxed for 2 hours, concentrated under diminished pressure, diluted with water and extracted with ether. After washing and drying, the ether was removed and the residue was recrystallized from acetone; yield 0.21 g. (80%), m.p. 198–201°, $[\alpha]^{20}\mathrm{D}$ −33°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.21; H, 10.21. Found: C, 78.68; H, 10.10.

22-Isoallospirostan-2β-ol (XIIa).—The lithium aluminum hydride reduction of 0.3 g. of the β-oxide XI was carried out exactly as described for the α-epimer and after recrystallization from acetone afforded 0.23 g. of alcohol with m.p. 197–199°, $[\alpha]^{20}\mathrm{D}$ −50°. The substance exhibited a free hydroxy band in the infrared.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.83; H, 10.65. Found: C, 77.70; H, 10.82.

The acetate XIIb had m.p. 187–189°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 76.12; H, 10.34.

MEXICO CITY 17, D. F. RECEIVED MAY 7, 1951

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(14) *Cf.* reaction of cholesteryl oxide with pyridine hydrochloride (P. N. Chakravorty and R. H. Levin, THIS JOURNAL, **64**, 2317 (1942)).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

Rhodanine Derivatives in Reactions of the Michael Type[1]

BY CHARLES K. BRADSHER, FRANCES C. BROWN AND R. JACK GRANTHAM

By a suitable choice of conditions, rhodanine can be made to react with either acetaldehyde or 5-ethylidenerhodanine to yield 1,1-bis-(2-thio-4-ketotetrahydro-5-thiazolyl)-ethane. The structure of this product was demonstrated by hydrolysis and hydrogenolysis to yield β-methylglutaric acid. Products analogous to that obtained with acetaldehyde were obtained by the reaction of rhodanine (two moles) with six other aliphatic aldehydes.

While much study has been devoted to the condensation of rhodanine with aromatic aldehydes,[2] condensation with saturated aliphatic aldehydes appear to have received less attention. The reaction of rhodanine with acetaldehyde,[2a,3,4] isobutyraldehyde,[4b] or 3-methylbutyraldehyde[4b] has been shown to yield 5-alkylidenerhodanines (II).

As a continuation of an earlier[5] investigation of the reaction of rhodanine with carbonyl compounds, we restudied the sodium acetate-catalyzed reaction with paraldehyde.[3,4] It was found that in addition to the expected 5-ethylidenerhodanine (II, R = CH_3), an unidentified high-melting product (m.p. 246.5–248.5°) was often produced. Better yields of the high-melting compound were obtained when pure acetaldehyde was allowed to react with *two*

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(1) This research was sponsored in part by the Biological Division, Chemical Corps, Camp Detrick, Frederick, Maryland under Contract no. DA-18-064-CML-120 with Duke University.

(2) *E.g.* (a) M. Nencki, *Ber.*, **17**, 2277 (1884); (b) N. Campbell and J. McKail, *J. Chem. Soc.*, 1251 (1948); and (c) P. Julian and B. Sturgis, THIS JOURNAL, **57**, 1126 (1935).

(3) C. Granacher, M. Gero, A. Ofner, A. Klopfenstein and E. Schlatter, *Helv. Chim. Acta*, **6**, 458 (1923).

(4) (a) R. Andreasch, *Monatsh.*, **39**, 419 (1918); (b) R. Andreasch, *ibid.*, **49**, 122 (1928).

(5) F. Brown, C. K. Bradsher, S. G. McCallum and M. Potter, *J. Org. Chem.*, **15**, 174 (1950).

TABLE I

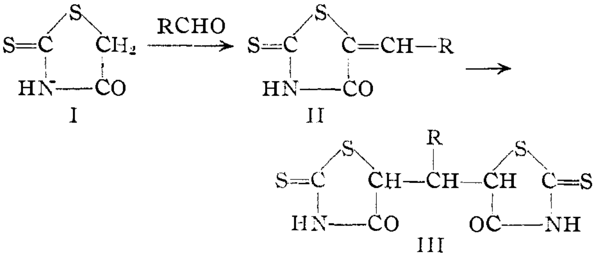
1,1-BIS-(2-THIO-4-KETOTETRAHYDRO-5-THIAZOYL)-ALKANES (III)

R	Yield,[a] %	M.p., °C.	Formula	Analytical data, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Sulfur Calcd.	Sulfur Found	Nitrogen Calcd.	Nitrogen Found
CH_3	34	246.5–248.5	$C_8H_8O_2S_4N_2$[b,c]	32.86	33.15	2.76	2.76	43.86	44.01	9.58	9.89
C_2H_5	33	208–212	$C_9H_{10}O_2S_4N_2$[b,d]	35.27	34.95	3.29	3.06	41.85	41.58		
C_3H_7	55	217.5–218.5	$C_{10}H_{12}O_2S_4N_2$[e]	37,48	37.60	3.78	3.77			8.74	8.49
C_4H_9	38	190–195	$C_{11}H_{14}O_2S_4N_2$[e]	39,49	39.64	4.22	4.09				
C_5H_{11}	27	189–190.5	$C_{12}H_{16}O_2S_4N_2$[e]	41.35	41.37	4.63	4.65				
C_6H_{13}	33	187–190	$C_{13}H_{18}O_2S_4N_2$[e]	43.06	43.20	5.00	5.02				
C_9H_{19}	22	167–168	$C_{16}H_{24}O_2S_4N_2$[b]					31.70	31.71	6.92	6.92

[a] Yields (recrystallized product) obtained by the ammonium hydroxide–ammonium chloride method. All samples melted with decomposition. [b] Analysis by Clark Microanalytical Laboratory. [c] Neutral equivalent: calcd. 146; found: 146, 147. [d] Molecular weight: calcd., 306; found (by boiling point elevation in acetone) 290, 312. [e] Analysis by Micro-Tech Laboratories.

moles of rhodanine. The reaction could be carried out in the presence of either ammonium hydroxide and ammonium chloride, or acetic acid and sodium acetate.

Analysis of the new product for carbon, hydrogen, nitrogen and sulfur gave results that could best be explained by assuming that one mole of aldehyde had condensed with two of rhodanine with the loss of water. Since it appeared logical to assume that the new compound was formed by a Michael reaction, 5-ethylidenerhodanine (II, R = CH_3) and



rhodanine were allowed to react in the presence of ammonium hydroxide and ammonium chloride. The product was identical with the high-melting compound which had been obtained directly from acetaldehyde and rhodanine.

From the known behavior of rhodanine[6] and 5-alkylidenerhodanine,[4b] it would be expected that alkaline cleavage of the Michael product would yield the unknown α,α'-bis-sulfhydryl-β-methylglutaric acid (IV) or perhaps a mixture of disulfides derived from it. No effort was made to isolate the

$$\text{III} \xrightarrow[\text{2, acid}]{\text{1, NaOH}} \underset{\text{IV (not isolated)}}{CH_3CH(CH(SH)COOH)_2} \xrightarrow{H_2} \underset{\text{(V)}}{CH_3CH(CH_2COOH)_2}$$

bis-sulfhydryl acid as such, but the crude product from the alkaline cleavage was subjected to the action of alkali and Raney nickel alloy under conditions known to effect hydrogenolysis of sulfur compounds.[7] The product was β-methylglutaric acid (V).

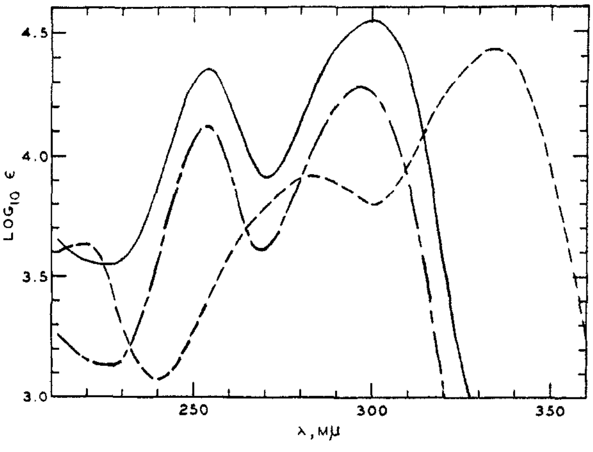


Fig. 1.—1,1-Bis-(2-thio-4-ketotetrahydro-5-thiazolyl)-ethane, ——; 5-ethylrhodanine, – – – –; 5-ethylidenerhodanine, — — — —.

The condensation of one mole of aliphatic aldehyde with two moles of rhodanine appears to be quite general, at least for the straight-chain aldehydes. In Table I are listed the results obtained with seven such aldehydes using the ammonium hydroxide–ammonium chloride procedure. The yields listed are for recrystallized product melting no more than a few degrees below the analytical sample. The melting points in the table are those of the analytical samples, which frequently appeared to melt over a considerable range. While this might be attributed to the presence of stereoisomers, the observed darkening of the compounds on heating suggests that decomposition occurs before the true melting point is reached.

The ultraviolet absorption spectrum (Fig. 1) of 1,1-bis-(2-thio-4-ketotetrahydro-5-thiazolyl)-ethane (III, R = CH_3) shows a very close similarity to that of 5-ethylrhodanine[8] but not to that of the more highly conjugated 5-ethylidenerhodanine.

Experimental

Ultraviolet Absorption Spectra.[9]—The absorption spectra were measured in 95% ethanol solution using a Beckman model DU quartz spectrophotometer.

1,1-Bis-(2-thio-4-ketotetrahydro-5-thiazolyl)-ethane (III, R = CH_3) (a) From Acetaldehyde by the Ammonium Chloride Method.—In a 3-necked flask equipped with a liquid sealed stirrer, reflux condenser and dropping funnel, 53.5 g. of rhodanine was dissolved in 90 ml. of 5 *M* ammonium hydroxide solution. The resulting solution was heated to about 70° and a solution of 8.8 g. of pure acetaldehyde in 100 ml. of ethanol was added; followed immediately by 30

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(6) I. Ginsburg and S. Bondzynski, *Ber.*, **19**, 113 (1886).

(7) D. Papa, E. Schwenk and H. Ginsberg, *J. Org. Chem.*, **14**, 723 (1949).

(8) C. Redemann, R. Icke and G. Alles, *Org. Syntheses*, **27**, 73 (1947).

(9) We are indebted to Mr. R. A. Potter for these measurements.

g. of ammonium chloride in a small quantity of water. The mixture was heated at 70° and stirred for 80 minutes, cooled and poured into 1.2 l. of ice-cold 1 *N* hydrochloric acid. The slightly gummy yellow solid was recrystallized from alcohol, yielding 19.7 g. (34%) of pale yellow crystals, m.p. 246–249° (dec.). Several recrystallizations from ethanol yielded pale yellow needles, m.p. 246.5–248.5° (dec.).

(b) **From Acetaldehyde by the Sodium Acetate Method.**—To a solution of 26.6 g. of rhodanine in 120 ml. of glacial acetic acid, 4.4 g. of freshly distilled acetaldehyde and 40 g. of anhydrous sodium acetate were added. The resulting mixture was refluxed from three to five hours and then poured into 600 ml. of cold water, yielding 16.6 g. (57%) of an impure yellow solid, m.p. 236–244°. A sample was recrystallized from glacial acetic acid as pale yellow prisms, m.p. 246–248° (dec.).

(c) **From Ethylidenerhodanine.**[2a,8,4]—A mixture containing 2.2 g. of rhodanine, 1.6 ml. of ammonium hydroxide, 3 ml. of water and 40 ml. of ethanol was stirred and heated at 65–70° while 2.6 g. of 5-ethylidenerhodanine in 80 ml. of ethanol was added. Five minutes later, 1.6 g. of ammonium chloride in 10 ml. of water was added and the resulting mixture heated at 65–75° for two hours longer. The reaction mixture was cooled and poured into 650 ml. of ice-cold 1 *N* hydrochloric acid and after standing, a yellow solid precipitated slowly. The precipitate was collected, washed with water and dried, m.p. 241–246° (dec.); yield 3.3 g. (69%). After three recrystallizations, from alcohol, it was obtained as pale yellow crystals, m.p. 247–248.5° (dec.).

The products obtained by each of the three methods were shown to be identical by mixed melting point determinations.

Hydrolysis and Hydrogenolysis of 1,1-Bis-(2-thio-4-keto-tetrahydro-5-thiazolyl)-ethane.—The rhodanine derivative obtained above (III, R = CH_3; 14.6 g.) was dissolved in a solution of 30 g. of sodium hydroxide in 125 ml. of water and the resulting mixture refluxed for three hours. The cooled solution was acidified with hydrochloric acid and extracted with ether and methylene chloride. The solvents were removed on a steam-bath leaving a viscous orange-colored liquid, probably impure α,α′-disulfhydryl-β-methylglutaric acid, which was not purified further. The crude product was dissolved in 300 ml. of 10% sodium hydroxide solution and heated on a steam-bath for 70 hours during which 50 g. of Raney nickel-aluminum alloy was added in small portions.[7] At the end of this period the nickel residue was allowed to settle and the alkaline solution decanted. The solution was strongly acidified and was extracted with ether. The ethereal extract was treated with Norite, and dried over phosphorus pentoxide. Upon removal of the ether, there was obtained 2.3 g. (37%) of a light-orange oil which solidified on standing overnight. On recrystallization from benzene–ligroin and again from cyclohexane, fine white needles, m.p. 84–84.5° (lit.[10] 85–86°), were obtained. This material gave no depression of melting point when mixed with an authentic sample[10] of β-methylglutaric acid, m.p. 84.5–85°.

Dianilide of β-Methylglutaric Acid.—A sample of the acid obtained by hydrogenolysis was heated with aniline for three hours at 190–200°. The product was recrystallized from ethanol as fine white needles, m.p. 213.5–214°. This was identical with a sample prepared from authentic β-methylglutaric acid.

Anal. Calcd. for $C_{18}H_{20}O_2N_2$: C, 72.95; H, 6.80. Found: C, 73.03; H, 6.75.

The di-*p*-toluidide of β-methylglutaric acid was prepared in a similar manner and crystallized from ethanol as fine white needles, m.p. 221–221.5°. This was identical with a sample prepared from authentic β-methylglutaric acid.

Anal. Calcd. for $C_{20}H_{24}O_2N_2$: C, 74.04; H, 7.46. Found: C, 74.21; H, 7.50.

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[10] R. E. Kent and S. M. McElvain, *Org. Syntheses*, **23**, 60 (1943).

DURHAM, N. C. RECEIVED APRIL 21, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF FLORIDA]

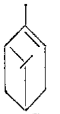
The Preparation of Ocimene from α-Pinene[1]

BY J. ERSKINE HAWKINS AND HARRY G. HUNT

Consideration of the available information led to the conclusion that ocimene is formed as an intermediate product when α-pinene is converted to alloöcimene. A method of obtaining ocimene in this reaction is presented. The refractive index of ocimene at 25° is evaluated and the application of refractive index measurements to the analysis of dipentene–ocimene mixtures is illustrated. The rate of conversion of ocimene to alloöcimene, at 159.5 and 189.5°, and the heat of activation for this conversion are determined.

In the study of the kinetics[2,3] of the thermal isomerization of *d*-α-pinene (I) it became evident that the products, predicted by a simple mechanism[4] for the reactions, would be l-α-pinene (II), dipentene (III) and ocimene (IV).

The reaction has been considered to produce alloöcimene (V) as a primary product. Arbuzov,[5] Dupont and Dulou,[6] Goldblatt and Palkin,[7] Savich and Goldblatt,[8] and Fuguitt and Hawkins[2,9] found large amounts of alloöcimene but reported no ocimene in their products of isomerization of α-pinene. Since the completion of this work, Goldblatt has stated that he recently has detected small amounts of ocimene.[10] Arbuzov in 1934[11] suggested a mechanism for the production of alloöcimene from α-pinene in which a cyclobutane ring with an unsaturated side chain was the intermediate. Rice and Rice discussing free radicals[12] men-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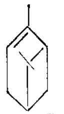
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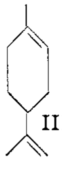
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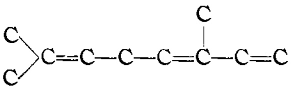
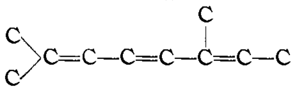

$$(C)_2C{=}C{-}C{-}C{=}\overset{C}{C}{-}C{=}C$$
IV


$$(C)_2C{=}C{-}C{=}C{-}\overset{C}{C}{=}C{-}C$$
V

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[1] The material included in this paper is based upon a partial abstract of a dissertation presented to the Graduate Council of the University of Florida, by Harry G. Hunt, in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1950, and was presented at the Southeastern Regional Meeting of the ACS which was held at Wilson Dam, Ala., Oct. 18–20, 1951.

[2] R. E. Fuguitt and J. E. Hawkins, THIS JOURNAL, **69**, 319 (1947).

[3] H. G. Hunt and J. E. Hawkins, *ibid.*, **72**, 5618 (1950).

[4] J. E. Hawkins, H. G. Hunt and R. E. Fuguitt, unpublished.

[5] B. Arbuzov, *J. Gen. Chem.* (*U. S. S. R.*), **3**, 21 (1933); *Ber.*, **67B**, 563 (1934).

[6] G. Dupont and R. Dulou, *Compt. rend.*, **201**, 219 (1935).

[7] L. A. Goldblatt and S. Palkin, THIS JOURNAL, **63**, 3517 (1941).

[8] T. R. Savich and L. A. Goldblatt, *ibid.*, **67**, 2027 (1945).

[9] R. E. Fuguitt and J. E. Hawkins, *ibid.*, **67**, 242 (1945).

[10] Private communication.

[11] B. Arbuzov, *Ber.*, **67B**, 571 (1934).

[12] F. O. Rice and O. K. Rice, "The Aliphatic Free Radicals," The Johns Hopkins Press, Baltimore, Md., 1935, pp. 163–164.