was considered as a more or less transitory (v) intermediate in the reaction."

This statement was an unintentional oversight on our part of the fact that Hunter, Hinman and Carter[1] had changed their original interpretation as to the significance of this experiment so that in the final draft of their chapter in the Penicillin Monograph the oxazolone hydrobromide was not mentioned as a possible intermediate and no conclusion was drawn as to the structure of the intermediate product. This change in interpretation, of which we had been notified, was at least in part based on data obtained from us after conclusion of the penicillin contract.

SHELL DEVELOPMENT COMPANY
EMERYVILLE, CALIFORNIA RECEIVED JANUARY 21, 1950

Azeotrope in the Bromine–Carbon Tetrachloride System[1]

BY WILLIAM M. SPICER AND JEROME KRUGER[2]

In connection with thermal diffusion experiments on azeotropes, it seemed desirable to use a colored azeotrope in order that the separation could be followed visually. This need led to a search for azeotropes of bromine. Since none was found listed in the literature, a systematic experimental investigation was undertaken.

The number of possible second components is limited by the reactivity of bromine. The first system selected as a probable one in which to find an azeotrope was that of bromine with carbon tetrachloride. The boiling points of these liquids are only 18° apart and their solutions show positive deviations from Raoult's law.[3] These deviations would be expected to be rather large since there are large differences in the internal pressures, which are 5700 and 3070 atm. for bromine and carbon tetrachloride, respectively.[4]

Experimental

The carbon tetrachloride was purified by washing with concentrated sulfuric acid, then with water, and drying over phosphorus pentoxide. It was then fractionated in a five-foot glass helix packed column. A center cut of about 80% of the charge was retained. The boiling point was 76.0° at 739.1 mm. Using an Abbe refractometer, the index of refraction was found at 25° to be 1.4576 as compared with 1.4575 from the literature.[5] J. T. Baker analyzed C. P. bromine was used without further purification.

Weighed samples of the bromine–carbon tetrachloride solutions were analyzed for bromine by titration with standardized sodium thiosulfate solution using iodide and starch indicator.

Liquid–vapor equilibrium data as shown in Table I were obtained using an equilibrium still similar to that described by Jones, Schoenborn and Colburn.[6] The heating of the residue chamber and flash boiler was controlled by a Variac connected to a Sola constant voltage transformer. The equilibrium temperatures, which were measured by means of a calibrated copper–constantan thermocouple using a potentiometer reading to one microvolt, were accurate to approximately 0.1°.

This uncertainty in the temperature as well as the variation in the pressure as noted in Table I were tolerated since the object was not to obtain accurate liquid–vapor equilibrium data but to ascertain whether an azeotrope exists in this system.

TABLE I

LIQUID–VAPOR EQUILIBRIUM DATA FOR SYSTEM BROMINE–CARBON TETRACHLORIDE

Temp., °C.	Pressure, mm.	Mole fraction	
		Bromine in liquid	Bromine in vapor
58.0	741.2	1.0	1.0
57.9	738.1	0.969	0.966
57.7	736.8	.940	.927
57.9	736.8	.865	.874
58.1	736.8	.771	.810
59.9	734.6	.558	.690
61.2	734.6	.441	.606
63.1	738.5	.342	.536
68.6	734.3	.151	.353
71.7	736.7	.070	.199
76.0	738.5	.0	.0

A plot of the data of Table I in the form of mole fraction bromine in the vapor *vs.* mole fraction bromine in the liquid indicated an azeotrope with a composition of approximately 0.89 mole fraction bromine. In order to determine more accurately the composition and boiling point of this azeotrope, solutions near the azeotropic composition were distilled through the fractioning column mentioned previously. The azeotrope, which was approached from both sides, was found to boil at 57.7° at 735.6 mm. and have a composition of 0.884 mole fraction bromine.

It was felt that there was little likelihood of reaction between these liquids at the low temperatures used. However, the following experiment was performed to determine whether reaction had taken place. A bromine–carbon tetrachloride solution containing approximately 11% bromine was fractionated. After the bromine, as azeotrope, had been removed as indicated by the fact that the distillate coming off exhibited the boiling point of carbon tetrachloride, the content of the still pot exhibited the refractive index of pure carbon tetrachloride.

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(1) From the thesis submitted by Jerome Kruger in partial fulfillment of the requirements for the M.S. degree, Georgia Institute of Technology, September, 1949.

(2) Present address: Department of Chemistry, University of Virginia, Charlottesville, Virginia.

(3) Lewis and Storch, THIS JOURNAL, **39**, 2544 (1917).

(4) Ewell, Harrison and Berg, *Ind. Eng. Chem.*, **36**, 871 (1944).

(5) Perce and Evdorinnoff, *Gazz. chim. ital.*, **70**, 723 (1940).

(6) Jones, Schoenborn and Colburn, *Ind. Eng. Chem.*, **35**, 666 (1943).

In order to determine whether there is an increase in volume when these liquids are mixed to form the azeotrope, as is to be expected since there are positive deviations from Raoult's law, the specific gravity was determined and from this the volume of a given weight of the azeotrope calculated. This volume was found to be 4% greater than that calculated assuming ideal behavior.

DEPARTMENT OF CHEMISTRY
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The C-12 Position of the Carbonyl Group in Hecogenin

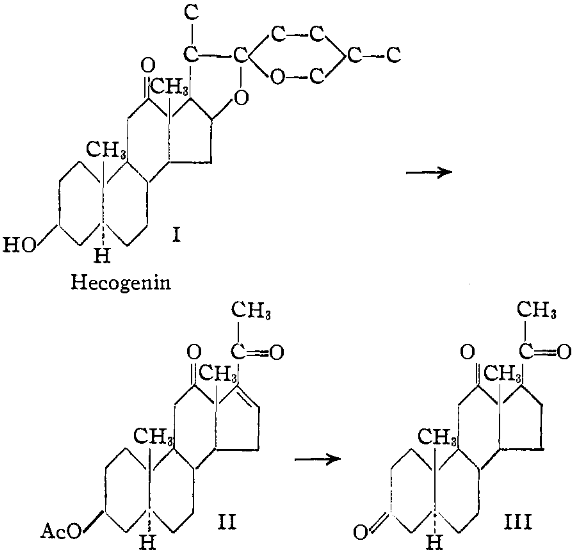
BY R. B. WAGNER, JAMES A. MOORE AND ROBERT F. FORKER

The current interest in cortisone for rheumatoid arthritis has stimulated great interest in the 12-ketosapogenins as possible starting material for its synthesis. The position of the carbonyl group in these substances has been assigned as a result of a systematic elimination of the other possible positions.[1]

It is now possible to give more direct proof for the C-12 oxygen in hecogenin (1) and related sapogenins by converting hecogenin to *allo*-pregnan-3,12,20-trione (III) identical with an authentic sample prepared from 12(α)-acetoxyprogesterone. Treatment of the oxidation product from pseudohecogenin diacetate with a hot aqueous methanolic solution of potassium carbonate followed by acetylation leads to 16-*allo*-pregnen-3(β)-ol-12,20-dione acetate (II). This substance (II) shows an ultraviolet absorption maximum in alcohol at λ230 mμ, log ϵ 3.93, typical for α,β-unsaturated systems. It is noteworthy that the peak is shifted from the position $\lambda^{\text{alc}}_{\text{max}}$ 238–240 mμ, log ϵ 3.9 exhibited by other 16-pregnen-20-ones containing no oxygen at C-12.[1a] Catalytic hydrogenation followed by hydrolysis and mild chromic acid oxidation gives *allo*-pregnan-3,12,20-trione (III). For purposes of comparison, this material and its C-5 isomer have been prepared from degradation products of desoxycholic acid.[2]

Previous efforts for converting hecogenin to this key substance (III) resulted in a product whose structure was not definitely settled.[1,2] Marker has stated that this material is 17-hydroxy-*allo*-pregnan-3,12,20-trione arising by the addition of water to the unsaturated ketone system.[3]

Acknowledgments.—We gratefully acknowledge a generous gift of hecogenin from Merck and Company. We thank Parke, Davis and Company for their help.



Hecogenin

(tentative)

allo-Pregnan-3,12,20-trione

Experimental

16-*allo*-Pregnen-3(β)-ol-12,20-dione Acetate.—To a solution of 2 g. of pseudohecogenin diacetate in 30 ml. of acetic acid was added a solution of 1.2 g. of chromic anhydride in 10 ml. of 80% acetic acid. After the reaction mixture had stood at 25° for ninety minutes, it was diluted with water and the product was extracted with ether. The ethereal solution was washed free from acetic acid and evaporated. The residue dissolved in 16 ml. of hot methanol was treated with 1 g. of potassium carbonate in 10 ml. of hot water, adding additional water to cause a turbid solution. The total time of heating on the steam-bath was ten minutes. The hydrolysis mixture was immediately diluted with cold water and ether extracted. The ethereal solution was dried and evaporated to dryness. The residue was acetylated with a hot pyridine–acetic anhydride mixture and finally crystallized from ether–pentane, m. p. 173–176°; 345 mg. Recrystallization from ether–methanol gave needles, m. p. 177–179°, $[\alpha]^{20}\text{D}$ +126° and $[\alpha]^{20}{}_{5461}$ +159° (dioxane), $[\alpha]^{27}\text{D}$ +138° and $[\alpha]^{27}{}_{5461}$ +177° (chloroform), absorption maximum at 227–230 mμ (log ϵ 3.93 in ethanol).

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.2; H, 8.7. Found: C, 73.9; H, 8.6.

***allo*-Pregnan-3,12,20-trione from Hecogenin.**—The 16-pregnene compound from above, 300 mg., in 200 ml. of ether containing a few drops of acetic acid was shaken with hydrogen and Adams catalyst at forty-five pounds pressure for four hours. This treatment removed the conjugated unsaturated ketone system as shown by the absence of an absorption maximum at λ 230 mμ in the crude product. After hydrolyzing with 2% alcoholic potash in the usual manner, it was oxidized for two hours at room temperature with 0.6 g. of chromic anhydride in acetic acid. The excess oxidizing agent was destroyed with methanol and the acetic acid was removed in vacuum. The residue was extracted with ether and the ethereal solution was washed with water, 10% sodium hydroxide, water and evaporated. The crystalline residue was crystallized from ether to give almost pure material, m. p. 206–208°; yield, 105 mg. Recrystallization from ether gave crystals, m. p. 207–209°, $[\alpha]^{28}\text{D}$ +180° and $[\alpha]^{28}{}_{5461}$ +225 (chloroform). These properties are in good agreement with those of *allo*-pregnan-3,12,20-trione described below. A mixture gave no melting point depression.

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[1] Marker and co-workers, THIS JOURNAL, **69**, 2167 (1947).

[1a] FOOTNOTE ADDED IN PROOF: Ultraviolet absorption data for the pregnene compound from a second 12-ketosapogenin is in agreement with the lower maximum. In view of these data, formula II may not be the exact representation. On the other hand, any assignment must be closely related to account for the formation of *allo*-pregnan-3,12,20-trione (III). The nature of this unsaturated system is under further study.

[2] Wagner, Moore and Forker, THIS JOURNAL, **71**, 3856, 4159 (1949).

[3] Marker, *ibid.*, **71**, 2656, 4149 (1949).