transformation products formed by the gland are being separated and identified.

THE WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY
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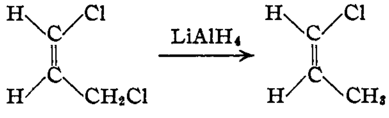
THE CONFIGURATION OF THE 1,3-DICHLOROPROPENES

Sir:

Considerable interest has been shown[1] in the structure of the two isomeric 1,3-dichloropropenes and there has not been complete agreement as to which isomer should be assigned the *cis* configuration and to which the *trans* configuration. This difference of opinion has been caused, in part, by the lack of an unequivocal proof of structure. The configuration of each of the two isomers of 1,3-dichloropropene has now been determined by chemically transforming each isomer into a compound the configuration of which has been established.

The low boiling isomer of 1,3-dichloropene (b. p. 57.5° (150 mm.), n^{25}_D 1.4652, d^{25}_4 1.2048) was refluxed for four hours with sufficient lithium aluminum hydride in isopropyl ether[2] to replace one chlorine atom with a hydrogen atom. By this treatment there was obtained a 50% conversion with a 46% yield of *cis*-1-chloropropene-1 having the following constants: b. p. 32.5° (749 mm.), n^{20}_D 1.4054 (lit.[3] b. p. 32.0–32.2° (747 mm.), n^{20}_D 1.4053). Similar treatment of the high boiling isomer of 1,3-dichloropropene (b. p. 112.2° (760 mm.), n^{25}_D 1.4712, d^{25}_4 1.2139) gave a 56% conversion with a 50% yield of *trans*-1-chloropropene-1, b. p. 37.2° (750 mm.), n^{20}_D 1.4048 (lit.[3] b. p. 36.7° (747 mm.), n^{20}_D 1.4054). In neither reaction was there any indication of the formation of a mixture of *cis*- and *trans*-1-chloropropene-1.

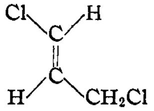
From these experimental data it follows that the low boiling isomer of 1,3-dichloropropene has the following configuration



Low-boiling 1,3-dichloropropene

cis-1-Chloropropene-1

while the high boiling isomer has the remaining configuration



High-boiling 1,3-dichloropropene

This assignment of configuration is in agreement with that proposed by Andrews and Kepner[1b] and not that proposed by Hatch and co-workers.[1a,c]

This method of ascertaining configuration is also being applied to other allylic chlorides which yield compounds of known structure upon replacement of the allylic chlorine atom by a hydrogen atom.

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[1] (a) Hatch and Roberts, THIS JOURNAL, 68, 1196 (1946); (b) Andrews and Kepner, *ibid.*, 69 2230 (1947); (c) Hatch, Gordon and Russ, *ibid.*, 70, 1093 (1948); (d) Smith and King, *ibid.*, 70, 3528 (1948); (e) "Data Sheet" on the 1,3-dichloropropenes published by Shell Chemical Corporation, 8/4/47.

[2] Nystrom and Brown, *ibid.*, 70, 3738 (1948).

[3] Kharasch, Englemann and Mayo, *J. Org. Chem.*, 2, 288 (1938).

PREPARATION OF ADRENAL CORTICAL HORMONES

Sir:

We have made certain observations in the partial synthesis of adrenal cortical hormones which show that it is possible to introduce the 17α-hydroxy group in 11,20-diketo steroids. In addition we have studied the preparation of the dihydroxyacetone side-chain as exemplified by Reichstein's Compounds S and P. Since the reactions appear to be generally applicable, it is possible to prepare adrenal cortical hormones of both the 11-keto series such as Kendall's Compound E and its 11-desoxy analog, Reichstein's Compound S, both of current interest in their medical application.

When the dienol acetate derived from 3α-hydroxypregnane-11,20-dione (m. p. 200–201°; $[\alpha]^{33}_D$ +105° (chloroform); $C_{27}H_{38}O_6$, calcd.: C, 70.71; H, 8.35; found: C, 70.80; H, 8.21) is treated with perbenzoic acid according to the procedure of Kritchevsky and Gallagher[1] the reaction product after saponification yielded 3α,17α-dihydroxypregnane-11,20-dione, m. p. 198–201°; $[\alpha]^{32}_D$ +66° (acetone). The monoacetate of this compound, m. p. 202–204°, $[\alpha]^{34}_D$ +81° (acetone), upon oxidation with chromic anhydride yielded 3α-acetoxyetiocholane-11,17-dione identical in all respects with the known compound. The enol of the 11-keto group therefore either does not react or reacts to such a negligible extent that isolation of the desired product in good yield is easily possible. This establishes the formation of a 17α-hydroxy derivative from a 20-keto steroid with an 11-keto group.

The preparation of the dihydroxy acetone side-chain characteristic of the most active adrenal hormones is illustrated by the reactions leading to the formation of Reichstein's Compounds P and S. Bromination of 3α-acetoxy-17α-hydroxyallopregnan-20-one with one mole of bromine yielded the 21-bromo derivative, m. p. 184–187°; $C_{23}H_{35}O_4Br$, calcd. Br, 17.76; found: Br, 17.47. Hydrolysis

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[1] Kritchevsky and Gallagher, *J. Biol. Chem.*, 179, 507 (1949).

with 0.05 N sodium hydroxide in 60% ethanol at room temperature in a nitrogen atmosphere for ten minutes resulted in replacement of halogen by a hydroxyl group. Acetylation yielded the diacetate of Reichstein's Compound P, m. p. 206–207°; $[\alpha]^{25}_{\mathrm{D}}$ +48° (chloroform).

The preparation of Reichstein's Compound S was achieved by the following reactions: 3α-formoxy-17α-hydroxypregnan-20-one (m. p. 184–185°; $[\alpha]^{34}_{\mathrm{D}}$ +68° (ethanol), $C_{22}H_{34}O_4$, calcd.: C, 72.89; H, 9.45; found: C, 73.00; H, 9.63) was brominated as in the preceding experiment yielding the 21-bromo compound as a solvate, m. p. 188–190°; $[\alpha]^{35}_{\mathrm{D}}$ +75° (ethanol). The formate was converted to the hydroxy compound, m. p. 202–204°, with methanol and dry hydrogen chloride at 5° for fourteen hours. Oxidation of 3α,17α-dihydroxy-21-bromopregnan-20-one with N-bromoacetamide yielded 17α-hydroxy-21-bromopregnan-3,20-dione, m. p. 203–204°; $[\alpha]^{33}_{\mathrm{D}}$ +81° (ethanol); $C_{21}H_{31}O_3Br$, calcd.: C, 61.31; H, 7.60; Br, 19.43; found: C, 61.02; H, 7.65; Br, 19.59. Hydrolysis of the halogen was accomplished by the procedure described above and, without isolation, the reaction product was acetylated, yielding 21-acetoxy-17α-hydroxypregnan-3,20-dione, m. p. 195–197°; $[\alpha]^{32}_{\mathrm{D}}$ +81° (ethanol). Bromination in acetic acid yielded the 4-bromo derivative (m. p. 196–203°; $[\alpha]^{36}_{\mathrm{D}}$ +83° (chloroform); $C_{23}H_{33}O_5Br$, calcd.: Br, 17.03; found: Br, 17.62) which was dehydrobrominated by a modification of the Mattox and Kendall[2] procedure to yield Reichstein's Compound S acetate, m. p. 237–241°; $[\alpha]_{\mathrm{D}}$ +116° (acetone); ϵ_{2410} = 17,400 (methanol).

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(2) Mattox and Kendall, THIS JOURNAL, **70**, 882 (1948).

(3) Visiting investigator from the University of New Brunswick, Fredericton, N. B.

SEPARATION OF ZIRCONIUM AND HAFNIUM WITH ANION EXCHANGE RESINS[1]

Sir:

During the course of an investigation of the behavior of negatively charged metal complexes on anion exchange resins, an attempt was made to separate zirconium and hafnium. These elements are generally considered to form negatively charged complexes[2] with certain complexing agents, particularly fluoride and oxalate ions. These elements, furthermore, are generally believed to be in true solution (rather than colloidal solutions) only if they are in the form of ionic complexes.

A separation based on their ability to form negatively charged complexes thus would have the advantage of being specifically designed for operation under conditions where true solution is most probable and complications due to hydrolysis (colloid formation or precipitation) minimized.

The experiments which have been carried out have demonstrated that separation of Zr(IV) and Hf(IV) by anion exchange is feasible, although the separation achieved is by no means at its optimum. Experiments are now under way to improve the efficiency of separation.

Partial separation of Zr(IV) and Hf(IV) at room temperature was achieved using a 107-cm. column of 200–230-mesh Dowex-1 (a quaternary amine anion exchanger) of 0.0226 sq. cm. cross section, and a mixture of 0.5 M hydrofluoric acid–1.0 M hydrochloric acid as eluent. Flow rates of *ca.* 0.3 ml./sq. cm./min. were used. Under these conditions elutions are relatively rapid (complete elution in *ca.* one and one-half days). The experiments were carried out with tracer concentrations of zirconium and 0.2 mg. of hafnium, using Zr^{95} (β-emitter, $T_{1/2}$ = 65 days[3]) and Hf^{181} (β-emitter, $T_{1/2}$ = 55 days[3]) as tracers. Zirconium and hafnium were identified radiochemically and in particular the hafnium content of the various elution fractions was determined by delayed coincidence counting taking advantage of the metastable daughter Ta^{181} (γ-emitter, $T_{1/2}$ = 20μsec.[4]) of Hf^{181}.[5]

The results of a typical experiment are shown in Table I. It may be noticed that the earlier fractions are highly depleted of hafnium, while the last fractions are practically pure hafnium.

TABLE I

SEPARATION OF ZIRCONIUM AND HAFNIUM IN 1.0 M HCl–0.5 M HF

Column length 107 cm., average flow-rate 0.29 ml. cm.$^{-2}$ min.$^{-1}$

No.	Vol., ml.	Spec.[a] act.	Rate[b]	%[c] Hf	No.	Vol., ml.	Spec.[a] act.	Rate[b]	%[c] Hf
4	2.20	16.8	0.08	0.4	9	0.29	510	17	79
5	0.40	290	0.7	3	10	.31	321	22[d]	>95
6	.32	580	1.9	9	11	.31	147	21	>95
7	.27	616	6.6	31	12	.43	30.7	24	>95
8	.31	609	12	56	13	.45	3.3	19[d]	>95

[a] c/min./λ. [b] Coincidence rate per 1000 c./min. [c] Calculated on an activity basis. The initial solution had approximately equal activities of zirconium and hafnium. [d] Radiochemical analyses by S. A. Reynolds did not show presence of Zr^{95}. Estimated purity of the hafnium fractions according to these analyses is better than 95%.

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(1) This document is based on work performed under Contract No. W-7405 eng. 26 for the Atomic Energy Commission at Oak Ridge National Laboratory.

(2) Gmelin's "Handbuch der anorganischen Chemie, Hafnium," Verlag Chemie, Berlin, 1941.

(3) Information from G. T. Seaborg and I. Perlman, "Table of Isotopes," *Rev. Mod. Phys.*, **20**, 585 (1948).

(4) S. DeBenedetti and F. K. McGowan, *Phys. Rev.*, **70**, 569 (1946).

(5) We are indebted to Mr. F. K. McGowan for asssistance in the coincidence counting and for the use of his delayed coincidence circuit.