phosphate values obtained with the Fiske–SubbaRow[6] and Lowry–Lopez[7] methods.

TABLE II

The complete system contained in 1.0 ml. 10 μM. $MgCl_2$, 40 μM. ATP, 650 μM. *l*-aspartate, and 0.1 ml. enzyme. Both substrates were adjusted to *p*H 8.0 with tris. The incubation was at 30° for 45 minutes. Shown in parentheses are the inorganic phosphate values from which acyl phosphate was calculated.

	Acyl phosphate	
	Hydroxamic acid method, μM.	Fiske–SubbaRow P minus Lowry-Lopez P, μM.
Omit aspartate	0.02	0.1 (0.6–0.5)
Complete system	2.6	2.7 (5.6–2.9)

ADP appears to be the other reaction product, though side reactions prevent its stoichiometric demonstration. Using low initial substrate concentrations, and hydroxylamine as a trapping agent, disappearance of 1 μM. of ATP was accompanied by formation of 1.3 μM. of inorganic phosphate, 1.04 of hydroxamate, 0.64 of ADP, and 0.13 μM. of AMP. This result was not significantly changed by the presence of 0.05 molar potassium fluoride. ATP was determined by the method of Kornberg,[8] ADP and AMP according to Kalckar.[9]

Asparthydroxamic acid derived from the reaction product was characterized as the beta isomer by chromatographic comparison with beta and alpha asparthydroxamic acids. These were prepared by heating the corresponding amides, asparagine and isoasparagine, with hydroxylamine. When mixed with the substance obtained from the enzymatic reaction, only the mixture with alpha isomer could be separated into two hydroxamate fractions.

We wish to express our appreciation to Dr. J. P. Greenstein for a generous gift of isoasparagine.

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RECEIVED MARCH 17, 1953

THE PREPARATION OF SAMARIUM AND YTTERBIUM METALS[1]

Sir:

After many attempts, we have succeeded in preparing massive samarium metal. Previous workers have reported the preparation of this metal by reducing samarium chloride with potassium[2] and by electrolyzing a molten salt-bath containing samarium chloride[3], but neither of these preparations gave a product which permitted characterization of this metal. Attempts to prepare samarium in our laboratory by these methods, while not exhaustive, were not fruitful, and indicated that a better method of preparing samarium was very desirable. Numerous attempts were made to reduce samarium halides by active metals including lithium, sodium, potassium, barium, calcium and magnesium,[4-7] but in each case the divalent halide of samarium was the product, indicating a high position in the electromotive series for the $Sm-Sm^{++}$ couple.

In preparing some of the heavy rare earth metals,[8] several of them were found to be distinctly more volatile than lanthanum. Vapor pressure measurements have been made on lanthanum[5] and dysprosium which indicate that dysprosium has a vapor pressure about 300 times that of lanthanum at the same temperature. Preliminary chemical and metallurgical studies on samarium indicated that it too might be more volatile than lanthanum. This low vapor pressure of lanthanum compared to other rare earth metals, its low melting point and the high heat of formation of its oxide, along with the possible high vapor pressure of samarium, suggested the preparation of samarium by distilling it from a heated mixture of samarium oxide and lanthanum metal.

Using a welded tantalum crucible[9] eight inches long and one inch in diameter with walls 2.5 mils thick, 20 g. of freshly ignited samarium oxide (98% pure, the balance consisting of other rare earths) and 20 g. of freshly prepared lanthanum turnings were heated under a vacuum of less than 1 micron to 1450° and held at this temperature for 30 minutes. The upper half of the crucible extended out of the furnace and had a perforated tantalum lid. On opening, a silvery crystalline metallic deposit was found on the upper walls of the crucible and on the bottom of the cap. Analysis of the deposit showed it to be samarium metal of greater than 98% purity with no lanthanum detectable. In a subsequent preparation, 25 g. of metal was obtained representing a yield of over 80% from the original oxide.

Thirty grams of metal prepared in this manner was melted in a tantalum crucible under a pressure of one atmosphere of purified argon. The melting point as determined with an optical pyrometer was between 1025 and 1050°, which is considerably below the figure of 1300 to 1350° given for previous preparations.[3,10] The bulk density of this fused specimen was found to be 7.53 g./cc., which would represent an atomic volume of 20 cc./mole. This would place samarium in line with the "regular" rare earths on this basis, instead of with europium and ytterbium with which it is chemically associated. Preliminary X-ray diffraction studies on single crystals separated from the condensate indicate that samarium is

(1) Contribution No. 220 from the Institute for Atomic Research and Department of Chemistry, Iowa State College. Work was performed in the Ames Laboratory of the Atomic Energy Commission.
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rhombohedral with $a \cong 8$ Å. and $\alpha \cong 23.5$ Å. The metal is very soft, has the luster of silver and does not tarnish in air after a month of exposure.

Ytterbium has been prepared by this same method and appears to be more volatile than samarium. X-Ray diffraction studies on this metal indicate that it is face-centered cubic with $a = 5.460$ Å.; Klemm and Bommer reported $a = 5.468$ Å. for this metal.

A more complete description of this work will appear in the future.

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RECEIVED APRIL 8, 1953

SYNTHESIS OF 17α-HYDROXYCORTICOSTERONE AND ITS 9α-HALO DERIVATIVES FROM 11-EPI-17α-HYDROXYCORTICOSTERONE

Sir:

The ready availability of 11-epi-17α-hydroxycorticosterone (I) by microbiological hydroxylation[1,2,3] of Reichstein's Compound S suggests as an attractive possibility the utilization of I as an intermediate in the synthesis of 17α-hydroxycorticosterone. We wish to report such a synthesis, a distinguishing feature of which is that it dispenses with the protective derivatization of the 3- and 20-keto groups required in previous syntheses[4,5,6] during operations in ring C. Key intermediates in this synthesis are the 9α-haloderivatives of 17α-hydroxycorticosterone, which we have found to be highly active in the rat liver glycogen assay for 11-oxygenated corticoids.[7] Their activities as well as those of the corresponding cortisone derivatives are listed in Table I.

TABLE I

	Activity in rat liver glycogen test, cortisone acetate = 1
9α-Chloro-17α-hydroxycorticosterone acetate	~4.0 ± 0.6
9α-Chlorocortisone acetate	3.5 ± 0.4
9α-Bromo-17α-hydroxycorticosterone acetate	0.28 ± 0.04
9α-Bromocortisone acetate	0.54 ± 0.08
9α-Iodo-17α-hydroxycorticosterone acetate	~0.1

Acetylation of (I) with one mole of acetic anhydride followed by tosylation gave Δ^4-pregnene-11α,17α,21-triol-3,20-dione 21-acetate 11α-tosylate (II), m.p. 165–166° (dec.); $[\alpha]^{23}D$ +106° (*c*, 1.0 in $CHCl_3$); (*Anal.* Calcd. for $C_{30}H_{38}O_8S$: C, 64.51; H, 6.81; S, 5.73. Found: C, 64.55; H, 6.84; S, 5.77), which on treatment with sodium acetate in boiling glacial acetic acid yielded $\Delta^{4,9(11)}$-pregnadiene-17α,21-diol-3,20-dione 21-acetate (III) m.p. 236–237°; $[\alpha]D$ +117° (*c*, 1.0 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 238 mμ (ϵ = 15,500); (*Anal.* Calcd. for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.31; H, 7.80). Reaction of (III) with N-bromoacetamide[8] in aqueous dioxane in the presence of perchloric acid[9] afforded Δ^4-9α-bromopregnene-11β,17α,21-triol-3,20-dione 21-acetate (9α-bromo-17α-hydroxycorticosterone acetate) (IV), m.p. 130–131° (dec.); $[\alpha]D$ +133° (*c*, 0.75 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 243 mμ (ϵ = 14,500); (*Anal.* Calcd. for $C_{23}H_{31}O_6Br$: C, 57.17; H, 6.42; Br, 16.52. Found: C, 57.40; H, 6.56; Br, 16.11). Oxidation of (IV) with chromic acid yielded 9α-bromocortisone acetate, m.p. 219° (dec.); $[\alpha]^{23}D$ +235° (*c*, 0.61 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 237 mμ (ϵ = 16,100); (*Anal.* Calcd. for $C_{23}H_{29}O_6Br$: C, 57.41; H, 6.03; Br, 16.61. Found: C, 57.30; H, 6.16; Br, 16.15), which on reduction with zinc in acetic acid yielded cortisone acetate identified by comparison with an authentic sample of the latter. IV on treatment with potassium acetate in boiling alcohol gave Δ^4-pregnene-9β,11β-oxido-17α,21-diol-3,20-dione acetate (V),[10] m.p. 210–12°; $[\alpha]^{23}D$ +41° (*c*, 0.69 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 243 mμ (ϵ = 15,500); (*Anal.* Calcd. for $C_{23}H_{30}O_6$: C. 68.63; H, 7.51. Found: C, 69.02; H, 7.42), which with HBr in acetic acid–carbon tetrachloride reverted to IV. Reaction of V with hydrochloric acid in chloroform at 0° yielded 9α-chloro-17α-hydroxycorticosterone acetate, m.p. 200–201° (dec.); $[\alpha]^{23}D$ +139° (*c*, 0.86 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 241 mμ (ϵ = 15,800); (*Anal.* Calcd. for $C_{23}H_{31}O_6Cl$: C, 62.93; H, 7.12; Cl, 8.07. Found: C, 63.23; H, 7.41; Cl, 7.70), which on oxidation with chromic acid yielded 9α-chlorocortisone acetate, m.p. 257–58° (dec.); $[\alpha]^{23}D$ +252° (*c*, 1.1 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 236 mμ (ϵ = 16,600); (*Anal.* Calcd. for $C_{23}H_{29}O_6Cl$: C, 63.22; H, 6.54; Cl, 8.11. Found: C, 62.97; H, 6.61; Cl, 8.13). Reaction of V with hydriodic acid[11] at −20° for 20 minutes gave 9α-iodo-17α-hydroxycorticosterone acetate (VI), m.p. 100–110° (dec.); $[\alpha]^{22}D$ +145° (*c*, 1.05 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 243 mμ (ϵ = 11,000); (*Anal.* Calcd. for $C_{23}H_{31}O_6I$: C, 52.08; H, 5.89; I, 23.93. Found: C, 52.54; H, 6.44; I, 22.60). Both IV and VI with

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(9) Using sulfuric acid in this reaction as suggested by Sarett (*J. Biol. Chem.*, **162**, 601 (1946)) gave yields in the vicinity of 45%, the remainder of III having been transformed into a water-soluble substance, presumably the 11β-sulfuric acid ester of IV. The use of perchloric acid in place of sulfuric acid increased the yield to over 90%.

(10) The corresponding 9α,11α-oxide, m.p. 248–249°; $[\alpha]^{23}D$ +99° (*c*, 1.09 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 238 mμ (ϵ = 16,000); (Found: C, 68.74; H, 7.38) was prepared from III with perbenzoic acid.

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