140°, $[\alpha]^{25}D$ −51.4, was identical with the antibiotic obtained from the *Streptomyces* fermentation.

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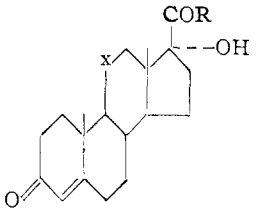
ALDEHYDES DERIVED FROM CORTISONE AND HYDROCORTISONE

Sir:

Cortisone (I) and hydrocortisone (X), Kendall's compounds E and F, have been converted to the corresponding 21-aldehydes, Δ^4-3,11,20-triketo-17α-hydroxypregnene-21-al (V) and Δ^4-3,20-diketo-11β,17α-dihydroxyprenene-21-al (XIII), which are biologically active.

On treatment of cortisone (I) with *p*-toluenesulfonyl chloride a mixture of the pyridinium *p*-toluenesulfonate and chloride (II, III) was obtained. The latter salt was treated with *p*-nitrosodimethylaniline to give the nitrone (IV), isolated in two forms, red plates and yellow needles, having identical decomposition points. The nitrone was hydro-



	X	R	M. p., °C.	$[\alpha]^{25}D$ (CH_3OH, $c=2$)
I	C=O	CH_2OH		
II	C=O	$CH_2Py^+OTs^-$	285–290 dec.	
III	C=O	$CH_2Py^+Cl^-$	290–291 dec.	+231°
IV	C=O	$CH{=}N(O)C_6H_4N(CH_3)_2$	189–190 dec.	
V	C=O	CHO	210–215 dec.	
VI	C=O	$CH(OH)_2$	*ca.* 225 dec.	+182°
VII	C=O	$CH(OCH_3)_2$	142	+176°
VIII	C=O	$CH(OC_2H_5)_2$	77	+165°
IX	C=O	$CH(OCOCH_3)_2$	169	+ 99°
X	CHOH	CH_2OH		
XI	CHOH	$CH_2Py^+Cl^-$	295–296 dec.	+232°
XII	CHOH	$CH{=}N(O)C_6H_4N(CH_3)_2$	186–188 dec.	
XIII	CHOH	CHO		
XIV	CHOH	$CH(OH)_2$	155–160 dec.	+155°

lyzed by dilute acid to cortisone-21-aldehyde (V), which crystallized from aqueous acetone as the colorless hydrate (VI). (*Anal.* (after drying at 25° (1 mm.) 4 hr.) Calcd. for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 67.01; H, 7.75). The yellow free aldehyde was regenerated from the hydrate by several hours drying at 110° (1 mm.). (*Anal.* Calcd. for $C_{21}H_{26}O_5$: C, 70.36; H, 7.31. Found: C, 70.09; H, 7.52).

By an analogous procedure, hydrocortisone (X) was converted *via* the pyridinium chloride (XI) and nitrone (XII) to hydrocortisone-21-aldehyde hydrate (XIV). (*Anal.* Calcd. for $C_{21}H_{30}O_6$: C, 66.64; H, 7.99. Found: C, 66.94; H, 7.69).

The ultraviolet absorption spectra of cortisone aldehyde hydrate (max. 2380 Å., E_m 15,700) and hydrocortisone aldehyde hydrate (max. 2420 Å., E_m 16,000) in methanol resemble those of cortisone and hydrocortisone. Cortisone free aldehyde in anhydrous chloroform has an additional band at 4500 Å. (E_m 36) which is characteristic of α-dicarbonyl compounds. Chemically the hydrates behave as typical aldehydes. Positive Schiff and silver mirror tests are observed and three derivatives involving the aldehyde group have been prepared from cortisone aldehyde, the dimethyl and diethyl acetals (VII, VIII) and the diacetate (IX).

The aldehyde hydrates have approximately the same activity as cortisone and hydrocortisone in rat liver glycogen deposition tests.[1] The nitrone and diacetate in the cortisone series are also active, while the acetals appear to be inert. It has, furthermore, been noted that cortisone and hydrocortisone aldehyde hydrates cause adrenal atrophy and thymus involution similar to that resulting upon administration of the parent hormones.[2] The approximate equivalence in biological activity of cortisone and hydrocortisone with the corresponding 21-dehydro compounds is in contrast to results with desoxycorticosterone and the related 21-aldehyde. This aldehyde is only one twenty-fifth as effective as desoxycorticosterone in the Everse–deFremery work test.[3]

(1) Several modifications of the procedure of Pabst, Sheppard and Kuizenga (*Endocrinology*, **41**, 51 (1947)) have been employed by Drs. C. C. Porter and R. H. Silber of the Merck Institute for Therapeutic Research, to whom we are indebted for the reported results.

(2) We are obliged to Dr. C. A. Winter, Merck Institute for Therapeutic Research, for these tests.

(3) H. Reich and T. Reichstein, *Helv. Chim. Acta*, **22**, 1124 (1939).

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A NEW STREPTOMYCES ANTIBIOTIC[1]

Sir:

A new antibiotic, exhibiting highly specific *in vitro* activity against *Mycobacteria*, has been isolated from a species of *Streptomyces*. The antibiotic may be recovered by successive *n*-butanol extractions of the culture broth after filtration from the mycelium at *p*H 2.0. The butanol extracts are combined and the acidic antibiotic extracted with sodium carbonate solution. The alkaline solution is adjusted to *p*H 4.5, and then repeatedly extracted with butyl acetate. Evaporation of the butyl acetate leaves a dark brown sirup which is dissolved in hot ethylene dichloride, treated with activated carbon, and filtered. On cooling, the antibiotic crystallizes in long white needles. Recrystallization can be effected from hot water, warm acetone, or methanol.

This new antibiotic is a monobasic acid, *pK* 5.1. Titration and molecular weight data are in agreement with the formula $C_9H_{15}O_3NS$, m.p. 139–140°, $[\alpha]^{23}D$ −54 (*c* 1, methanol). (*Anal.* Calcd. for $C_9H_{15}O_3NS$: C, 49.77; H, 6.91; N, 6.45; S, 14.75. Found: C, 49.96; H, 7.09; N, 6.51; S, 14.83).

Solutions of the pure material exhibit a blue fluorescence on exposure to ultraviolet light. There is no characteristic ultraviolet spectrum. The

(1) Since the completion of this work, we have learned that this antibiotic (actithiazic acid) has been independently isolated and synthesized by a group at Abbott Laboratories.