plex of duroquinone[5] has a comparatively low decomposition temperature. Attempts to prepare a similar complex with *p*-benzoquinone so far were unsuccessful.[6] The nature of bonding in these complexes has been discussed in terms of molecular orbital theory.[7]

We wish to report the synthesis of the first member of a class of nickel(0)complexes containing quinones as ligands. If duroquinone is refluxed with nickel carbonyl in benzene under nitrogen a red, crystalline substance is formed in good yields. According to analysis, this is bis-duroquinone-nickel, (I): Calcd. for $Ni(C_{20}H_{24}O_4)$: Ni, 15.18; C, 62.05; H, 6.25, mol. wt., 387. Found: Ni,15.01; C, 61.87; H, 6.28; mol. wt. (ebullioscopic in CH_2Cl_2), 364.

I is completely stable to air and to dilute non-oxidizing acids. It is sparingly soluble in alcohol, benzene, hexane and acetone; moderate solubility permits recrystallization from chloroform and methylene chloride. When heated under the Kofler microscope it remains unchanged up to a temperature of 205°, above which it decomposes without previous melting. When heated in a high vacuum, slow decomposition with partial sublimation starts at temperatures above 160° producing metallic nickel and duroquinone.

The observed diamagnetism ($\chi_m = -176\cdot10^{-6}$ cm.^{3} g.$^{-1}$)[8] is in accord with the proposed sandwich-type structure. The infrared spectrum of I shows the C=O absorption at 6.34 μ (KBr).[9] As in the cyclopentadienone complexes the lowering of the carbonyl frequency is attributed to the presence of dative π-bonds between the metal d-orbitals and the low-lying, unoccupied molecular orbitals of the organic ligands. When *p*-benzoquinone was treated with nickel carbonyl a black, non-crystalline substance of composition $Ni(Quinone)_2$, (II), was obtained (*anal.* Calcd.: Ni, 21.34. Found: Ni, 21.4). This material starts to decompose at about 150°, yielding nickel and benzoquinone. In contrast to the properties of I, II was found to be insoluble, hygroscopic and paramagnetic (3.31 Bohr magneton). With dilute acids it immediately decomposed, forming Ni((II)-ion and quinhydrone. Consequently, II is to be regarded as a metallic quinhydrone-type compound.[10] Products similar to II were isolated from the reaction of *p*-xyloquinone and naphthoquinone-1,4 with nickel carbonyl. The behavior of these quinones as compared to duroquinone is related to their electron affinities and π-electron densities. Whereas *p*-benzoquinone causes the oxidation of the nickel atom, the introduction of the methyl groups lowers the electron affinity and increases the π-electron densities to such an extent that π-complex formation becomes possible. A detailed description of this work which currently is being extended will be published elsewhere.

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(5) H. W. Sternberg, R. Markby and I. Wender, THIS JOURNAL, **80**, 1009 (1958); *Chemistry and Industry*, 1381 (1959).

(6) E. Weiss and W. Hübel, *J. Inorg. Nucl. Chem.*, **11**, 42 (1959).

(7) D. A. Brown, *ibid.*, **10**, 39, 49 (1959).

(8) The magnetic measurements were performed by Mr. A. Sepp, Technische Hochschule at Munich.

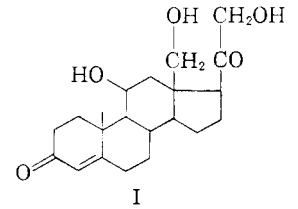
(9) The C=C— stretching frequency overlaps with the C=O absorption of duroquinone (6.14 μ); it could not yet be assigned with certainty.

(10) $Fe_3(CO)_{12}$ also reacts with quinone to produce a black powder of composition Fe(Quinone) ~21. Calcd.: Fe, 20.52. Found: Fe, 22.6.

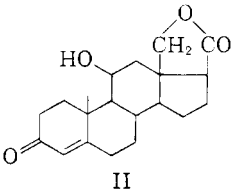
A NEW C-18 OXYGENATED CORTICOSTEROID FROM BULLFROG ADRENALS

Sir:

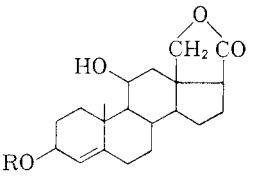
The incubation of C^{14}-progesterone with bullfrog adrenals yielded, in addition to aldosterone,[1,2] an unknown radioactive substance I, which was considerably more polar (R_{Aldo} = 0.24 in toluene–propylene glycol).[3] The possibility that the unknown substance might be another C-18 oxygenated corticosteroid was suggested by the quantitative conversion of I to a less polar neutral product (II) with periodic acid.



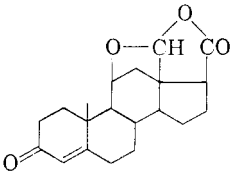
I



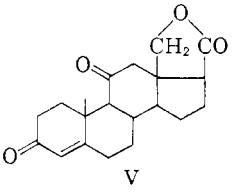
II



III, R = H
IIIAC, R = Ac



IV



V

Compound I (1.2 × 10^6 c.p.m.) (less than 0.02 mg.) was obtained from the incubation of 4.0 × 10^7 c.p.m. of progesterone-4-C^{14} (0.45 mg.) with adrenal slices from nine bullfrogs (*Rana catesbiana*), according to the procedure previously described.[1] Oxidation with periodic acid yielded substance II (R_B = 1.05 in toluene–formamide). Substance II could not be acetylated with acetic anhydride in pyridine. The reduction of II with excess 0.1 *M* $NaBH_4$ in 80% aqueous tertiary butyl

(1) S. Ulick and S. Solomon, THIS JOURNAL, **82**, 249 (1960).

(2) In addition to substance I and aldosterone (5% yield) the other products of the incubation were desoxycorticosterone and corticosterone. There was no evidence of 17α-hydroxylation in this tissue. To be published, S. Ulick, K. Kusch and S. Solomon.

(3) *R* values refer to the distance migrated by the sample on paper chromatograms (run at room temperature) relative to the reference steroid. Radioactive steroids were located with a windowless paper strip scanner and reference steroids with ultraviolet light. Abbreviations for reference steroids: Aldo = aldosterone, B = corticosterone, F = cortisol, DOCA = desoxycorticosterone acetate.

alcohol[4] for 18 hours at room temperature, and then acidification of the reaction mixture with dilute HCl and extraction, yielded a neutral product III-C^{14} (R_F = 1.05 in ethylene dichloride–formamide; = 1.02 in toluene: ethyl acetate 9:1, methanol–water 1:1).

Tritium-labeled III was prepared by the sequence of reactions described by Ham, *et al.*[5] *d*-Aldosterone-7-H^3 [6] was diluted with carrier *dl*-aldosterone and oxidized with HIO_4 to aldosterone etiolactone IV[7] (R_B = 4.2 in methylcyclohexane: toluene 1:1-formamide) m.p.[8] 295–300°. Lactone IV was treated with $NaBH_4$ under the same conditions used for the reduction of II. Acidification and extraction of the reaction mixture yielded III-H^3 in the lactone form.

III-H^3 and III-C^{14} were combined and the mixture was converted to two derivatives. Ac_2O in pyridine yielded IIIAc (R_{DOCA} = 1.1 in methylcyclohexane–dimethylformamide). Oxidation of III with CrO_3-pyridine complex[9] gave the diketo lactone V, which was chromatographed first on paper (R_B = 2.5 in methylcyclohexane:toluene (1:1)-formamide), then on neutral alumina, and eluted with 0.5% ethanol in benzene; m.p. 239–244°, λ_{max}^{EtOH} 238 mμ, $\lambda_{max}^{CHCl_3}$ 5.60, 5.81, 5.97 and 6.14 μ. The properties of lactone V were in agreement with those previously reported.[5,10,11] H^3:C^{14} ratios[12] were determined before and after chromatographic purification of compound III and after the preparation and purification of the acetylated and oxidized derivatives (Table I).

The agreement of all values for H^3:C^{14}, within the precision of measurement, was interpreted to indicate that compound III-C^{14} of adrenal origin and synthetic compound III-H^3 were chemically identical.

The conversion of II and the known etiolactone IV to the same reduction product (III) and the identification of III in turn by oxidation to V, established that II was a 4-etienic acid lactone (20,-18) with additional oxygen functions at C-3 and C-11. Of the possible structures which could have been reduced to III, only II, IV and V did not possess an acetylatable hydroxyl group. Compounds IV and V were prepared and excluded on the basis of their chromatographic properties. This permitted the assignment of the structure 11β,18-dihydroxy-3-keto-4-etienic acid lactone to II and the formulation of I as 18-hydroxycorticosterone.[13]

TABLE I

COMPARISON OF ISOLATED (C^{14}) AND SYNTHETIC (H^3) SAMPLES OF COMPOUND III FOLLOWING CHROMATOGRAPHIC PURIFICATION AND THE PREPARATION OF DERIVATIVES IIIAc AND V

Substance	Chromatographic system	H^3:C^{14}
III	Before chromatography	16.9 ± 0.5
III	Ethylene dichloride-formamide	16.7 ± .7
III	Toluene-ethyl acetate (9:1)-MeOH:H_2O (1:1)	17.9 ± .5
IIIAc	Methylcyclohexane-dimethylformamide	17.4 ± .1
V	Methylcyclohexane:toluene, (1:1)-formamide	18.2 ± .8
V	Al_2O_3 column	17.6 ± .2
	Mean	17.4 ± .6

These findings support the view[14,15] that hydroxylation of corticosterone at C-18 is an intermediate step in the biological oxidation of the angular methyl group to an aldehyde in the biosynthesis of aldosterone.[16]

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AN EXPLANATION OF AN ANOMALOUS ANTIPODAL SPECIFICITY OF CHYMOTRYPSIN

Sir:

Recently Hein, McGriff and Niemann[1] reported the anomalous finding that α chymotrypsin hydrolyzes the D isomer of 1-keto-3-carbomethoxy-1,2,3,4-tetrahydroisoquinoline (I) much more rapidly than it hydrolyzes the L isomer. These authors suggested several lines of thought along which explanations might be sought. We wish to show here how this observation can be explained simply and plausibly within the framework of the polyaffinity concept without the necessity of invoking new principles.

In the polyaffinity theory it is recognized that although a substrate might exist in a very large number of conformations in solution, when it is bound to the enzyme most of the molecules will assume a well-defined conformation with the contributing groups and the functional group in definite positions in space. This conformation (which we will call the "correct" conformation) is, of course, determined by the reacting sites of the

(4) J. I. Appleby, G. Gibson, J. K. Norymberski and R. D. Stubbs, *Biochem. J.*, **60**, 453 (1955).

(5) E. A. Ham, R. E. Harman, N. G. Brink and L. H. Sarett, THIS JOURNAL, **77**, 1637 (1955).

(6) Dr. James F. Tait kindly provided *d*-aldosterone-7-H^3. We wish to thank Dr. C. H. Sullivan, Ciba Co., for unlabeled aldosterone.

(7) S. A. Simpson, J. F. Tait, A. Wettstein, R. Neher, J. v. Euw, O. Schindler and T. Reichstein, *Helv. Chim. Acta*, **37**, 1200 (1954).

(8) Melting points (uncorrected) were determined on a Kofler type hot stage. The infrared spectrum was recorded on a Perkin Elmer Model 21 spectrophotometer.

(9) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).

(10) J. Schmidlin and A. Wettstein, *Helv. Chim. Acta*, **43**, 973 (1960).

(11) R. Neher and A. Wettstein, *ibid.*, **43**, 623 (1960). These authors also report some chromatographic properties of compounds II and V.

(12) Tritium and C^{14} were determined simultaneously in a Tricarb liquid scintillation spectrometer. Counting efficiencies were approximately 18% for H^3 and 73% for C^{14}. See reference 1 for discriminator and photomultiplier voltage settings.

(13) 18-Hydroxycorticosterone has not been described previously although its 3,20-diethylene ketal derivative was prepared in the course of the synthesis of 11-keto-18-hydroxy-cortexone.[10] Recently, some chromatographic properties of 18-hydroxycorticosterone have been recorded: R. Neher and A. Wettstein, *Helv. Chim. Acta*, **43**, 1171 (1960).

(14) In reference 11, although 18-hydroxycorticosterone itself was not found, the authors were able to isolate lactone II from hog adrenal extracts. This lactone may have been formed from 18-hydroxycorticosterone as an artifact.

(15) P. J. Ayres, J. Eichhorn, O. Hechter, N. Saba, J. F. Tait and S. A. S. Tait, *Acta Endocrinologica*, **33**, 27 (1960).

(16) The extension of results in the amphibian adrenal to higher vertebrates would appear to be justified since the secretory product of the bullfrog adrenal is similar to that of the *sona glomerulosa* of the mammalian adrenal cortex. See footnote 2, also H. Carstensen, A. C. J. Burgers and C. H. Li, THIS JOURNAL, **81**, 4109 (1959).

(1) G. Hein, R. B. McGriff and C. Niemann, THIS JOURNAL, **82**, 1830 (1960).