Letters to the Editor

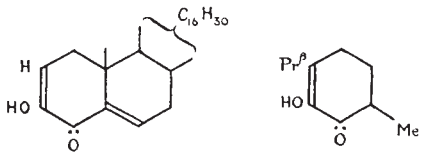
The Editor does not hold himself responsible for opinions expressed by his correspondents. He cannot undertake to return, or to correspond with the writers of, rejected manuscripts intended for this or any other part of NATURE. *No notice is taken of anonymous communications.*

NOTES ON POINTS IN SOME OF THIS WEEK'S LETTERS APPEAR ON P. 1022.

CORRESPONDENTS ARE INVITED TO ATTACH SIMILAR SUMMARIES TO THEIR COMMUNICATIONS.

Cholesterol and the Adrenal Cortical Hormone

THE discovery that carbon atom C_4 of the cholesterol molecule is the first point of attack by oxygen, leading to the formation of *cis* $\Delta^{5:6}$-cholestene-3 : 4-diol, suggested that this reactive primary oxidation product may play an important role in the metabolism of cholesterol and the sexual hormones. Experimental confirmation of this view was obtained by feeding experiments, which showed that the diol, as well as its intermediate dehydration product cholestenone, were converted into coprosterol by the animal organism[1]. We have now obtained by mild oxidation of the 3-monoacetate (or 3-benzoate) of the *cis*-diol what is probably the oxide of 4-ketocholestenol 3-acetate (or 3-benzoate). These compounds yield on hydrolysis a highly reactive substance $C_{27}H_{42}O_2$ (I) which possesses the typical grouping —C=COH—CO— of diosphenol (buchu-camphor) (II).



I II

As the substance, like diosphenol, functions in several tautomeric forms, it would be arbitrary to assign a definite structural designation to it, and we propose to call it *diosterol* (abbreviated from diossterol). Diosterol reduces ammoniacal silver solution, reacts with Schiff's fuchsin reagent and, as a phenol, is extracted by strong alkali from its ether- or benzene solution, forming yellow insoluble sodium or potassium salts (see forthcoming publication in conjunction with W. W. Starling and V. A. Petrow). The intensity of the ultra-violet absorption spectrum of diosterol is $\varepsilon_M = 22{,}000$ at 320 mμ, that is, twice that of diosphenol at 270 mμ [2]. Diosterol was found to be identical with the "substance $C_{27}H_{42}O_2$" of Inhoffen[3] and Butenandt and Schramm[4], which is obtainable by a complex debromination process from certain bromination products of cholestenone.

Since it has now been shown that the same substance arises from cholesterol in definite stages by a process which may easily be visualized as a biological oxidation occurring in the animal organism, a hint is afforded in explanation of the unknown position and function of the fourth oxygen atom in the adrenal cortical hormone. This labile hormone, essential for life, possesses the remarkable property for a steroid of reducing ammoniacal silver solution, usually attributed to the terminal —$CO.CH_2OH$ group in ring IV.

It is tempting to suggest that the diol and its immediate oxidation products may be steps in the biological formation from cholesterol of the labile cortical hormone of the adrenals. A new experimental approach to the system from the sexual hormones and other steroids has become available by the further discovery that the conversion of cholesterol into *cis*-cholestene-3 : 4-diol can be effected by simple treatment of cholesterol dibromide with silver acetate in pyridine at room temperature. This reaction, which is probably a general one, is at present being applied to steroids with a 5 : 6 ethylenic linkage.

O. ROSENHEIM.
H. KING.

National Institute for Medical Research,
London, N.W.3.
May 29.

[1] Rosenheim and Webster, NATURE, **136**, 474 (1935). Rosenheim and Starling, *J. Chem. Soc.*, 377 (1937); cf. Schoenheimer, Rittenberg and Graff, *J. Biol. Chem.*, **111**, 185 (1935).
[2] Walker and Read, *J. Chem. Soc.*, 238 (1934).
[3] Inhoffen, *Ber.*, **69**, 1702 (1936).
[4] Butenandt and Schramm, *Ber.*, **69**, 2289 (1936).

Inhibition of the Gonadotropic Activity of Pregnancy Urine Extract by the Serum of Rabbits injected with an Extract of Male Urine

THE fact, first noted by Bachmann, Collip and Selye[1], that the serum of an animal which has received prolonged treatment with gonadotropic substances may acquire antigonadotropic properties, has been confirmed by many other workers. Twombly[2] was able to produce active antisera by the use of solutions of pregnancy urine extract, most of the initial gonadotropic activity of which had been lost during storage, and his results suggested that the presence of active gonadotropic substance, in the material used for repeated injection, might not be essential. We were able to confirm this supposition.

A precipitate was prepared from the urine of normal male factory workers, by a method known to be suitable for concentration of the gonadotropic substances in pregnancy urine. 3·9 mgm. of this preparation (representing 50 c.c. original urine) yielded no trace of a gonadotropic reaction in immature female rats ; 22·5 mgm. (representing 300 c.c. original urine) produced œstrus in six treated rats, with luteinization in one of them.

An adult female rabbit received 10·0 mgm. daily for 30 days (representing 130 c.c. original urine daily). The ovaries were apparently not influenced by this treatment, for autopsy showed ripe follicles only. Each of six immature female rats then received a total dose of 1·2 c.c. of the blood serum of this rabbit at the same time as 5 units of gonadotropic hormone

© 1937 Nature Publishing Group