Chemistry of Estrogenic Substances

WE wish to make the following comments on the communication by E. Friedmann in NATURE of April 20 (p. 622) under the above title :-

(1) Dr. Friedmann apparently believes that the æstrogenic activity of synthetic compounds was first observed by Blum-Bergmann¹, and afterwards verified by Cook, Dodds and Hewett² with compounds of analogous structure. The reverse is, of course, the actual sequence of events, as is shown by the reference to our original publication in the paper of O. Blum-Bergmann, wrongly quoted by Dr. Friedmann as O. Blum and E. Bergmann.

(2) If Dr. Friedmann had read our detailed publication³ as well as our preliminary communication¹, he would have realised that the generalisation which he now makes regarding the molecular conditions necessary for æstrogenic activity does not accord with the facts. For example, our series of diols derived from 9: 10-dihydro-1: 2: 5: 6-dibenzanthracene contains inactive members as well as compounds having an extremely high order of œstrogenic activity. Yet if Friedmann's generalisation were true they should all be active. Moreover, we have reported the œstrogenic activity of certain hydrocarbons, which, of course, cannot conform to any rule concerning the relative positions of an aromatic ring and the carbonyl or hydroxyl group. In addition, we observed activity with ergosterol and calciferol, which contain no aromatic or analogous furane ring. In any event, the large doses of 1-keto-1:2:3:4-tetrahydrophenanthrene necessary to produce cestrus (50-100 mgm. in rats) preclude any far-reaching deductions from the inactivity of the isomeric 4-keto compound in similar doses. If, for example, the 1-keto compound had given positive results with doses of 0.1mgm., and the 4-keto compound negative results with 100 mgm., there would have been more adequate basis for generalisation.

Our experiments (in collaboration with Mr. W. Lawson) on the biological effects of diols prepared by the action of Grignard reagents on various quinones continue to yield results of interest, which will be fully reported when they are complete.

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¹ O. Blum-Bergmann, *Naturwiss.*, **21**, 578; 1933. ² Cook, Dodds and Hewett, NATURE, **131**, 56; 1933. ³ Cook, Dodds, Hewett and Lawson, *Proc. Roy. Soc.*, B, **114**, 272; 1934.

Refractive Index of Heavy Hydrogen

In the course of the recovery of some heavy water residues by electrolysis, the gas (D_2) was passed after purification through one side of the double tube (75 cm. in length) of a Rayleigh gas interferometer, while hydrogen gas produced by electrolysis of ordinary water and similarly treated was passed through the other side. A final steady shift of 24 drum divisions of the compensating plate was required to compensate for the difference of refractive index of the two gases. This is equivalent to 1.68 fringes of the mercury line $\lambda = 5461$, and hence the difference of refractive index of ordinary and heavy hydrogen in the visible region is $(123 + 2) \times 10^{-8}$ at 760 mm., ordinary hydrogen being the greater. The gas passed when the final reading was observed was burnt and collected separately, and proved to be within 0.1 of 100 per cent heavy hydrogen (D_2) .

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Deuterium Content of Naturally Occurring Water

THE deuterium content of naturally occurring water has so far been determined by two methodsfrom the mass-spectrogram of the hydrogen derived from it; and from the specific gravity of deuteriumfree water. The former method i gave for the abundance ratio H/D the value 5000+500, while two discrepant values 2,3 have been obtained by the latter, namely 9000 and 5750 ± 250 .

In order to clear up this discrepancy, we have measured the specific gravity increase caused by electrolysing tap-water (+2 per cent caustic soda). This method presupposes a knowledge of the separation coefficient α , and is only susceptible of accuracy if α is not too low and varies between fairly narrow limits. Experiments using water of known deuterium content had shown that for iron cathodes, α (corrected for evaporation) has an unusually high value; in seven experiments α had the extreme values of 8.65 and 11.0.

In three separate experiments, 240 c.e. of tapwater were reduced to 20 c.c. by electrolysis with iron cathodes and the increase in specific gravity measured. Taking $\alpha = 11.0$, the values obtained for the ratio H/D were 6640, 6390 and 6230 respectively, while for $\alpha = 8.65$ the corresponding values were 6230, 5980 and 5840, giving for the most probable value $H/D = 6220 \pm 300$.

This is in agreement with the value 5750 ± 250 obtained by Johnston. His result and ours, taken together, suggest that the mass-spectrographic value is slightly too low, and are irreconcilable with the value of 9000.

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Balliol College and Trinity College Laboratory, Oxford. March 30.

¹ Bleakney and Gould, *Phys. Rev.*, **44**, 265; 1933. ³ Ingold, Ingold, Whitaker and Whytlaw-Gray, NATURE, **134**, 661;

1934. ³ Johnston, J. Amer. Chem Soc., 57, 484; 1935.

Philosophical Interpretation of Science

I HESITATE to reply to Prof. H. Levy's letter in NATURE of April 20 because the questions raised are matter for arm-chairs and midnight oil rather than correspondence. Some comment, however, must be made, so, leaving the justification of my own philosophical outlook for a more convenient occasion, I will simply refer briefly to the charge that I am representing my viewpoint as "a necessary consequence of scientific discovery".

I can only say that I do consider it a necessary consequence of scientific discovery. That, of course, does not prevent me from believing that others hold