The writer has lately succeeded in the synthesis of methylated biflavonyl (XI), which was identical with ginkgetin tetramethyl ether. The course of the synthesis was as follows: 2-Acetyl-3,5-dimethoxyphenyl 3-iodoanisate (V) and 2-acetyl-6-iodo-3,5-dimethoxyphenyl anisate (VI) were respectively isomerized to the diketones (VII (40%), VIII (78%)) by potassium hydroxide in pyridine and then cyclized to the flavones (IX (91%), X (85%)) by sulfuric acid in acetic acid. The two iodinated flavones were finally condensed to biflavonyl (XI) by activated copper powder. In the condensation experiment, a mixture of equal moles of the iodo compounds and equal weight of copper powder to the above were heated in boiling dimethylformamide for 8 hours. To the filtrate of the reaction mixture several volumes of ethanol was added, when the sparingly soluble condensation compound (XI) separated in needles (28%), while 8,8- and 3',3'-*bis* compounds remained dissolved in the filtrate.

Biflavonyl compound (XI) obtained as above forms prismatic crystals (from dimethylformamide), m.p. 238°, scarcely soluble in methanol, ethanol, and dioxane. The dioxime, m.p. 252°. It was proved through elemental analysis, admixture of biflavonyls and their oximes, and infrared absorptions that the synthetic compound is identical with ginkgetin tetramethyl ether.

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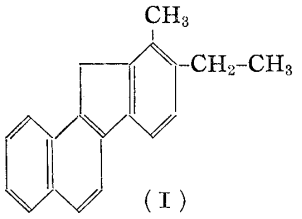
On the Selenium-dehydrogenation of Cynanchogenin

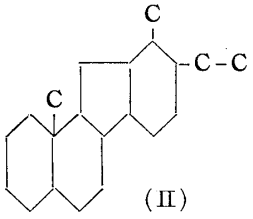
A crystalline aglycone, cynanchogenin, m.p. 167°, $C_{28}H_{42}O_6$, which was isolated from the root of *Cynanchum caudatum* MAX. and gave desacylcynanchogenin ($C_{21}H_{32}O_6$, m.p. 242°) and 2,3-dimethylbutene-1-carboxylic acid[1] on alkaline hydrolysis, was submitted to dehydrogenation with selenium. The aglycone (1.8 g.) was heated with selenium at 310° for 24 hours and the cooled mixture was extracted with ether. The extract was washed successively with dil. sodium hydrogen carbonate solution and water, and evaporation of ether left a neutral oily substance (200 mg.). The neutral portion of dehydrogenation product was chromatographed over neutral alumina and eluted with hexane and benzene to give two crystalline hydrocarbons.

One of them, m.p. 146~150°(A), showed ultraviolet absorption spectra ($\lambda_{max}^{cyclohexane}$ mμ (log ε): 249.5 (4.50), 258 (4.85), 268 (5.02), 304 (4.33), 317 (4.32), 332 (3.37), 348 (2.88)) identical with that of the hydrocarbon first produced by the selenium-dehydrogenation of jervine and veratramine by Jacobs[2] and which was recently proved to be 7-ethyl-8-methyl-1,2-benzofluorene[3] (I). The other crystals (B), which seemed to be a mixture, gave a very similar UV curve to that of the oily hydrocarbon obtained from desisovaleryltetrahydrodrevogenin-A, $C_{22}H_{36}O_6$, which also gave Jacob's hydrocarbon as the main dehydrogenation product and was assured to have a hydrogenated benzofluorene skeleton.[4]

1) The isolation and details of functional groups were reported at the 3rd Hokkaido Local Meeting of the Pharmaceutical Society of Japan, July 27, 1959.
2) W. A. Jacobs, L. C. Craig, G. Lavin: J. Biol. Chem., **141**, 51(1941); W. A. Jacobs, Y. Sato: *Ibid.*, **181**, 55(1949).
3) L. Keller, Ch. Tamm, T. Reichstein: Helv. Chim. Acta, **41**, 1633(1958).
4) R. E. Winkler, T. Reichstein: *Ibid.*, **38**, 721(1954).



(I)



(II)

Hence, angular methyl group is usually removed by dehydrogenation and the most likely structure for desacylcynanchogenin appeared to be the carbon skelton of c-nor-D-homo-pregnane (II). Further work on the structure of cynanchogenin is in progress.

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α-Lipoic Acid-Thiourea Adduct

α-Lipoic acid-thiourea adduct was obtained by crystallization of a mixture of α-lipoic acid and thiourea from butanol or by standing the mixture with a trace of methanol in a plugged flask at 40° for 4 days.

The adduct is odorless, slightly yellow, needle crystals and decomposes at 158°. The adduct consists of 1 mole of α-lipoic acid and 6.3 moles of thiourea, and the ratio is determined by elementary analysis, ultraviolet absorption spectrum, and polarography.

Infrared spectrum of the adduct closely resembles those of thiourea inclusion compounds of cyclohexane,[1] isoöctane,[2] camphor, 9-oxocamphor,[3] ascaridol,[1] etc. The α-lipoic acid in the adduct is extracted with ethanol, leaving behind rhombic thiourea.

From these data, the thiourea adduct of α-lipoic acid may be considered as an inclusion compound of thiourea. However, X-ray powder diffraction pattern of the adduct differs from those of typical inclusion compounds of thiourea. To comfirm the crystal system of the adduct, X-ray photographs of a single crystal were taken and following data were obtained.

Crystal system : Monoclinic — Space group : $C_{2h}^5-P2_1/a$

Unit cell : a = 5.27 Å
b = 14.71 Å (needle axis)
c = 11.9 Å
$\beta = 113.0°$

It is very interesting to note that the crystal system of this adduct differs from those of hitherto known thiourea adducts which belong to rhombohedral $D_{3h}^6-R\bar{3}c$ group.

As the adduct is odorless and α-lipoic acid is very stable in the adduct, it might be convenient to use it for the preparation of powder or tablets containing α-lipoic acid.

Details of these experiments will be published in the near future.

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August 10, 1959

1) H. Mima : Yakugaku Zasshi, **78**, 993(1958).
2) Stewart : J. Chem. Phys., **26**, 248(1957).
3) H. Mima : Yakugaku Zasshi, **77**, 1196(1957).