# Iso-neoergosterol.

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It was reported in the previous paper⁽¹⁾ that, along with neoergosterol, a new compound was isolated from the product of pyrolysis followed by the immediate distillation under high vacuum of ergopinacone, the dimolecular derivative prepared by the photochemical dehydrogenation of ergosterol. The new compound was considered to be an isomeride of neoergosterol $C_{27}H_{40}O$ and named iso-neoergosterol. It was then suspected that isoneoergosterol might be a stereoisomeride of neoergosterol, perhaps with regard to the carbon atom 3. However, further investigations have shown that iso-neoergosterol is not an isomeride of neoergosterol, but a molecular compound of the latter with a substance of formula $C_{28}H_{42}O$.⁽²⁾ For convenience the name iso-neoergosterol is retained in this paper, although it is not appropriate to designate a substance not isomeric with neoergosterol.

Iso-neoergosterol is obtained from the more soluble part of the crude product in somewhat smaller quantity than neoergosterol and has a melting point 138–139° (corr.), $[\alpha]_D^{20°} = -59.1°$, and ultraviolet absorption maxima at 264 mμ (unsharp) and 277 mμ (sharp).⁽³⁾ Its acetate melts at 108–109° (corr.), and has a specific rotation $[\alpha]_D^{23°} = -41.6°$.

Iso-neoergosterol yields easily a difficultly soluble digitonide with a decomposition point about 250°, while neoergosterol is not so easily precipitated by digitonin. Iso-neoergosterol gives distinctly the colour reactions of Liebermann-Burchard and of Rosenheim, while neoergosterol appears indifferent to these reactions. Thus it seems that iso-neoergosterol consists of a compound whose constitution is rather similar to that of ergosterol, the methyl group at the carbon atom 10 being yet reserved.

On acylation with 3,5-dinitrobenzoyl chloride and pyridin, iso-neoergosterol was separated into equal quantities of two different dinitrobenzoates:

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(1) Y. Urushibara and T. Ando, this Bulletin, **11** (1936), 757.

(2) The epimeride of neoergosterol, epi-neoergosterol, was recently prepared by A. Windaus and M. Deppe, *Ber.*, **70** (1937), 76.

(3) Cordial thanks are due to Dr. K. Yamasaki for his kindness in taking absorption spectra.

3,5-dinitrobenzoate of neoergosterol, melting point 227–228° (corr.) with decomposition, $[\alpha]_D^{14°} = -6.7°$,⁽⁴⁾ from the less soluble part, and a 3,5-dinitrobenzoate having presumably the composition $C_{35}H_{44}O_6N_2$, melting point 187.5–189.5° (corr.) with decomposition, $[\alpha]_D^{14°} = -72.9°$, from the more soluble part. The formula of the latter substance corresponds to the dinitrobenzoate of a compound $C_{28}H_{42}O$, and may be very probable in view of H. H. Inhoffen's hypothetical equation for the decomposition of ergopinacone:⁽⁵⁾

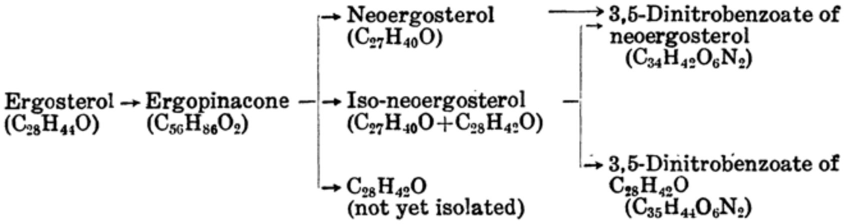
$$\underset{\text{Ergopinacone}}{C_{56}H_{86}O_2} \longrightarrow \underset{\text{Neoergosterol}}{C_{27}H_{40}O} + CH_4 + (C_{28}H_{42}O\,?)\,.$$

Dehydroergosterol $C_{28}H_{42}O$ gave a 3,5-dinitrobenzoate melting at 187.5–188.5° (corr.) with decomposition, namely at the same point as the dinitrobenzoate $C_{35}H_{44}O_6N_2$ from iso-neoergosterol, but a considerable depression of the melting point was observed with a mixture of the two substances.

Thus, iso-neoergosterol seems to be a molecular compound of neoergosterol and a compound $C_{28}H_{42}O$, an isomeride of dehydroergosterol. The isolation and investigation of the free compound $C_{28}H_{42}O$ are now in progress.

The easy precipitation of iso-neoergosterol by digitonin is undoubtedly due to the component $C_{28}H_{42}O$. However, the separation of iso-neoergosterol into its components by digitonin has not yet been successful, a substance with almost the same melting point as iso-neoergosterol being recovered.

From the quantitative point of view, at least one more compound of the same formula $C_{28}H_{42}O$, which does not combine with neoergosterol, may be expected and may be found in the more soluble part of the decomposition product of ergopinacone. Consequently, the changes involved may be expressed tentatively as follows:



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(4) H. H. Inhoffen gives m. p. 218-220° (corr.), and $[\alpha]_D^{16°} = -13°$, *Ann.*, **497** (1932), 130.

(5) *Naturwissenschaften*, **25** (1937), 125.

## Experimental.

**Ergopinacone.** Prepared from ergosterol (24 g.) according to the directions of H. H. Inhoffen.(4) Colourless silky needles (12.7 g.), m.p. 200–201° (corr.) with decomposition. In the Liebermann-Burchard test it gives red, violet, blue, green, and finally dark green colours; in the Rosenheim test, light pink, light violet, dark violet, then dark brownish violet colours.

**Ergopinacone Diacetate.** A solution of ergopinacone (300 mg.) in pyridin (55 c.c.) was mixed with acetic anhydride (4.5 g.). After a week the mixture was poured into water, the separating crystals were collected, washed with dilute acetic acid and with water, recrystallized twice from benzene-alcohol, and dried over phosphorus pentoxide in vacuum at 110°. Colourless fine needles (253 mg.) m.p. 205.5–206° (corr.) with decomposition (Found: C, 82.99; H, 10.13. Calculated for $C_{60}H_{90}O_4$: C, 82.31; H, 10.37%). $[\alpha]_D^{12°} = -209°$ (11.0 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{12°} = -2.30°$), ultraviolet absorption maximum 267–268 mμ (unsharp) in 0.042% hexane solution. In the Liebermann-Burchard test the diacetate gives red, violet, blue, and then bluish green colours; in the Rosenheim test, pink, light violet, finally dark green colours. The diacetate is far more soluble and stable than the free pinacone.

**Pyrolysis of Ergopinacone.** Ergopinacone (11.3 g.) was subjected in portions of 1 g. to decomposition at 205–210° under the pressure of 0.2–0.3 mm. followed by the immediate distillation at 220–290° under 0.014–0.04 mm. Crystallization of the distillate (9.18 g., 81.3%) from ethanol by seeding yielded crude yellow crystals (5.15 g., 45.6% of ergopinacone, 56.2% of the distillate), m.p. 124–129° (corr.).

**Neoergosterol.** When the crude product (1.50 g.) was fractionally recrystallized from ethanol, pure neoergosterol (330 mg.) was first obtained from the less soluble part in colourless long needles, m.p. 153.5–154.5° (corr.). It gives neither Liebermann-Burchard nor Rosenheim reaction. The precipitation by digitonin occurs only slowly after several hours, and the precipitate melts and decomposes at about 210–260° to red brown liquid. The 3,5-dinitrobenzoate prepared from neoergosterol (80 mg.), recrystallized repeatedly from benzene-methanol, formed light yellow small plates (83 mg.), m.p. 222–223° (uncorr.) or 227–228° (corr.) with decomposition to yellow liquid (Found: C, 70.96; H, 7.39; N, 5.09. Calculated for $C_{34}H_{42}O_6N_2$: C, 71.06; H, 7.37; N, 4.88%). $[\alpha]_D^{12°} = -6.67°$ (15.0 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{12°} = -0.10°$). The acetate of neoergosterol showed m.p. 123.5–124° (corr.), $[\alpha]_D^{28°} = +10.9°$ (13.8 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{28°} = +0.15°$).

**Iso-neoergosterol.** The recrystallization of the more soluble part from methanol and then from acetone gave iso-neoergosterol (287 mg.) in colourless small fine needles, m.p. 138–139° (corr.), $[\alpha]_D^{29°} = -59.1°$ (12.7 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{29°} = -0.75°$), ultraviolet absorption maxima in 0.043% hexane solution 264 mμ (unsharp) and 277 mμ (sharp).(6) In Liebermann-Burchard test it gives red, violet, deep blue, green, and finally dark green colours, while in Rosenheim test pink, light violet, dark bluish green, and finally dark brownish violet colours.

The acetate of iso-neoergosterol, m.p. 108–109° (corr.), $[\alpha]_D^{28°} = -41.6°$ (13.7 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{28°} = -0.57°$), gives in Liebermann-Burchard

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(6) Neoergosterol has an ultraviolet absorption maximum at about 268 mμ, H. H. Inhoffen, see note (4).

test violet, blue, dark green, and dark brownish violet colours, while in Rosenheim test, pink, light violet, greenish blue, dark green, and dark brownish violet colours.

**Separation of Iso-neoergosterol into Components in the Forms of 3,5-Dinitrobenzoates.** Iso-neoergosterol (250 mg.) was heated on a boiling water bath for 45 minutes with 3,5-dinitrobenzoyl chloride (390 mg.) and pyridin (3 c.c.) and the mixture was left to stand overnight. The crystals which separated out were collected, washed with cold methanol, with dilute acetic acid and with water, boiled with methanol, and then fractionally recrystallized from chloroform-methanol or benzene-methanol. Pure neoergosteryl 3,5-dinitrobenzoate was first obtained from the less soluble part in glittering light yellow small plates (150 mg.), melting at 227–228° (corr.) with decomposition to yellow liquid alone and in admixture with the specimen prepared from pure neoergosterol (Found: C, 71.01; H, 7.28; N, 5.03. Calculated for $C_{34}H_{42}O_6N_2$: C, 71.06; H, 7.37; N, 4.88%). $[\alpha]_D^{14°} = -6.74°$ (17.8 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{14°} = -0.12°$).

From the more soluble part another 3,5-dinitrobenzoate was obtained in light yellow small plates (110 mg.), m.p. 184–186° (uncorr.) or 187.5–189.5° (corr.) with decomposition to wine-red liquid (Found: C, 71.57, 71.29; H, 7.60, 7.34; N, 4.80. Calculated for $C_{35}H_{44}O_6N_2$ or $C_6H_3(NO_2)_2COOC_{28}H_{41}$: C, 71.37; H, 7.54; N, 4.76%). $[\alpha]_D^{14°} = -72.9°$ (16.2 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{14°} = -1.18°$). When mixed with the 3,5-dinitrobenzoate of dehydroergosterol, a depression of melting point was observed (mixed melting point 174.5–181.5°, corr.).

On adding water to the pyridin mother liquor of the crude 3,5-dinitrobenzoates and recrystallizing the precipitates repeatedly, a more quantity of 3,5-dinitrobenzoate identical with the above was obtained (37 mg.), m.p. 187.5–189.5° (corr.), $[\alpha]_D^{15°} = -72.1°$ (8.6 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{15°} = -0.62°$).

The yield of neoergosteryl 3,5-dinitrobenzoate (150 mg.) was equal to that of the other 3,5-dinitrobenzoate $C_{35}H_{44}O_6N_2$ (147 mg. in total).

**3,5-Dinitrobenzoate of Dehydroergosterol.** Dehydroergosterol, m.p. 147–148° (corr.), prepared according to the directions of A. Windaus and O. Linsert,(7) was heated on a boiling water bath for 20 minutes with 3,5-dinitrobenzoyl chloride and pyridin. The crystals separating out on adding water to the reaction mixture were washed with dilute acetic acid and with water, boiled with methanol, and recrystallized repeatedly from benzene-methanol. Yellow small needles, m.p. 184–185° (uncorr.) or 187.5–188.5° (corr.) with decomposition to deep red liquid (Found: N, 4.92. Calculated for $C_{35}H_{44}O_6N_2$: N, 4.76%).

**Digitonin and Iso-neoergosterol.** When digitonin (315 mg.) dissolved in 95% alcohol (35 g.) was added to a solution of iso-neoergosterol (92 mg.) in 95% alcohol (10 g.), there appeared instantly precipitates, the quantity of which increased rather rapidly. The digitonide was collected, washed with 95% alcohol and with ether, and then dried. Yield 272 mg. (68%). It sinters at about 196°, melts and decomposes gradually at about 203–254° (uncorr.). As K. Bonstedt(8) described that the digitonide of neoergosterol was easily decomposed to its components by extraction with benzene, the present author extracted the above digitonide first with benzene, dissolved the residue in pyridin and added ether. The precipitated digitonin was filtered off and

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(7) *Ann*, **465** (1928), 148.

(8) *Z. physiol. Chem.*, **185** (1929), 165.

the filtrate was evaporated. The crystals which remained were repeatedly recrystallized from dilute acetone, colourless silky needles melting at 136–138.5° (corr.), and at 135–138.5° (corr.) in admixture with iso-neoergosterol. The yield was too poor to be investigated further.

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