The Photochemical Dehydrogenation of Ergosterol and 7-Dehydrocholesterol.

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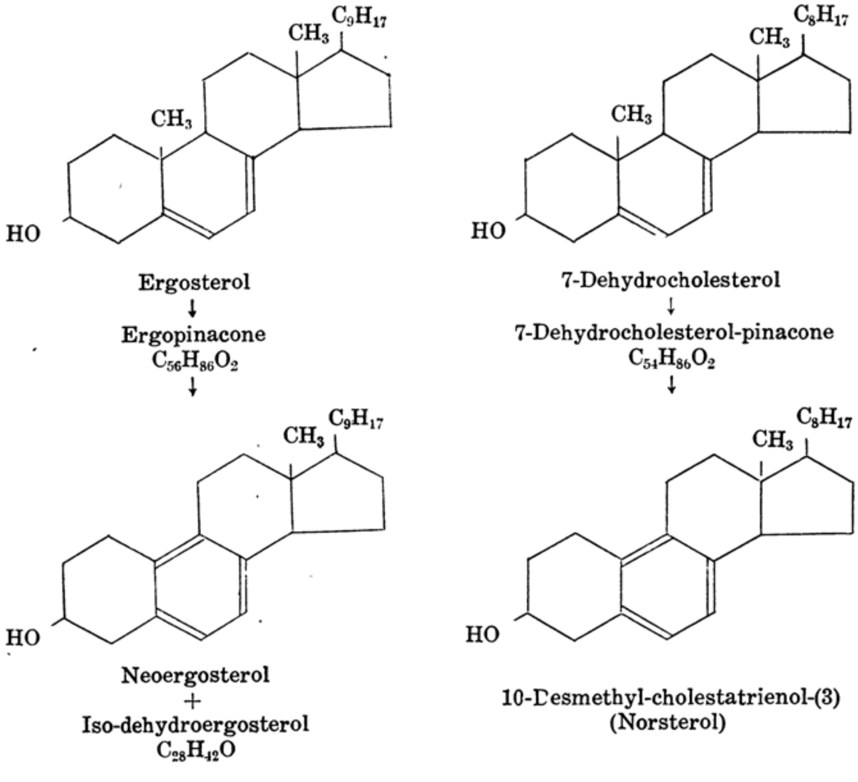
Ergosterol undergoes dehydrogenation when its alcoholic solution containing eosin is exposed to light in the absence of oxygen.(1) The product, $C_{56}H_{86}O_2$, has been unappropriately called ergopinacone. It suffers a characteristic decomposition on submitting it to distillation in vacuum or on heating it with glacial acetic acid or decalin.(2) In this decomposition methane is eliminated, and neoergosterol is formed along with iso-dehydroergosterol, $C_{28}H_{42}O$, which has been isolated and characterized by the present author.(3)



Ergosterol
↓
Ergopinacone
$C_{56}H_{86}O_2$
↓
Neoergosterol
+
Iso-dehydroergosterol
$C_{28}H_{42}O$

7-Dehydrocholesterol
↓
7-Dehydrocholesterol-pinacone
$C_{54}H_{86}O_2$
↓
10-Desmethyl-cholestatrienol-(3)
(Norsterol)

The analogous photochemical dehydrogenation of 7-dehydrocholesterol, with a structure similar to that of ergosterol, to 7-dehydrocholesterol-pinacone, and the decomposition of the latter to 10-desmethyl-cholesta-

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(1) A. Windaus and P. Borgeaud, *Ann.*, **460** (1928), 235.

(2) H. H. Inhoffen, *Ann.*, **497** (1932), 130.

(3) Y. Urushibara and T. Ando, this Bulletin **11** (1936), 757; T. Ando, *ibid.*, **13** (1938), 371; **14** (1939), 169.

trienol-(3) (norsterol) corresponding to neoergosterol have been reported independently by Urushibara and the present author(4) and by Schenck, Buchholz, and Wiese.(5) 7-Dehydrocholesterol-pinacone obtained by the present author had a lower melting point (m.p. of anhydrous substance 185.5–186°, corr.) and less water of crystallization ($C_{54}H_{86}O_2+H_2O$) than the substance described by the German authors ($C_{54}H_{86}O_2+1\frac{1}{2}H_2O$, m.p. 196–197°). The pyrolytic decomposition of 7-dehydrocholesterol-pinacone, however, yielded 10-desmethyl-cholestatrienol-(3) apparently identical with norsterol obtained by the German authors by boiling their 7-dehydrocholesterol-pinacone with acetic anhydride. Hence, it seemed possible that 7-dehydrocholesterol-pinacone exists either in two forms differing in the water of crystallization or in two isomerides differing in the configuration or in the positions of the double bonds, the differences having no influence on the constitution of the decomposition product. Ergopinacone has been often prepared in this laboratory, but the known form only has always been obtained.

In the preparation of 7-dehydrocholesterol-pinacone, the author dissolved 7-dehydrocholesterol and eosin in alcohol containing a little benzene and boiled the solution to remove air, while the German authors used alcohol solely and passed carbon dioxide. It was first assumed that such differences might have caused the production of different substances. Now the author has dehydrogenated not only 7-dehydrocholesterol but also ergosterol by these two different methods. The solutions prepared in the two ways were exposed to sunlight for several days. The specimens of the pinacones as well as their diacetates and dibenzoates which have been obtained in the two series of experiments are compared in the accompanying tables.

Table 1. Ergopinacone and Esters.

(A) The boiling method.

Substance	m.p. (corr.)	$[\alpha]_D$	Absorption maxim.
Ergopinacone(6)	200-201°		
Diacetate(6)	207-207.5°	−209° (12°)	267–268 mμ (not sharp)
Dibenzoate	206.5-207.5°	−160° (22°)	

(B) The carbon dioxide method.

Substance	m.p. (corr.)	$[\alpha]_D$	Absorption maxim.
Ergopinacone	200-201°		
Diacetate	206.5-207°	−202° (16°)	267-275 mμ (not sharp)
Dibenzoate	206.5-207.5°	−160° (16°)	280, 273 mμ(7)

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(4) Y. Urushibara and T. Ando, this Bulletin, **11** (1936), 802; **12** (1937), 495.

(5) F. Schenck, K. Buchholz, and O. Wiese, *Ber.*, **69** (1936), 2696.

(6) T. Ando, this Bulletin, **13** (1938), 373. The melting point of the diacetate was given formerly as 205.5-206° (corr.), but it became a little higher on further recrystallization.

(7) The sharp absorptions of the dibenzoates are undoubtedly due to the benzoyl groups.

Table 2. 7-Dehydrocholestrol-pinacone and Esters.

(A) The boiling method.

Substance	m.p. (corr.)	$[\alpha]_D$	Absorption maxim.
7-Dehydrocholesterol-pinacone	184.5-185.5°	−175° (24°) −171° (18°)[10]	254 mμ (indistinct)
Diacetate[8]	190-190.5°	−149° (26°)	
Dibenzoate[9] [10]	183-183.5°	−114° (17°).	

(B) The carbon dioxide method.

Substance	m.p. (corr.)	$[\alpha]_D$	Absorption maxim.
7-Dehydrocholesterol-pinacone	184.5-185.5°	−159° (24°)	254 mμ (indistinct)
Diacetate[8]	191-191.5°	−146° (26°)	
Dibenzoate	182.5-183.5°	−113.5° (26°)	
,, [9]	182.5-183.5°	−101° (25°)	280, 273 mμ[7]

There is no doubt that the substances in the two series A and B are identical each with each. In all cases the identities were confirmed by mixed melting points. 7-Dehydrocholesterol-pinacone showed the lower melting point irrespective of the methods of removing air from the solutions of 7-dehydrocholesterol and eosin.

The pinacones and their esters all showed the colour reactions of Liebermann-Burchard and of Rosenheim as shown in the experimental part.

Another difference in the methods of preparation of 7-dehydrocholesterol-pinacone may be found in the time of exposure to sunlight. The author exposed the solutions for several days, while the German authors for a few hours. Then it is possible that the higher melting product may be formed in short exposure but changeable to the lower melting form during a longer action of sunlight. A preliminary experiment has given an indication to the possibility that it is the case. Ten hours' exposure gave a product melting at 192.5–193.5° (corr.) with decomposition after repeated recrystallization and the melting point was lowered to 187–187.5° (corr.) in a month and to 185.5–186.5° (corr.) in a year, when the substance was reserved in vacuum. Further experiments are required to decide the matter conclusively.

Experimental.

Ergopinacone and Esters.

Dibenzoate from Ergopinacone Prepared by the Boiling Method. Benzoyl chloride (5 g.) was added slowly to a solution of ergopinacone (205 mg.) in pyridine (40 c.c.) with

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(8) The diacetate of the German authors showed m.p. 201-202° and $[\alpha]_D^{22°}$ −161.2°.

(9) Prepared from 7-dehydrocholesteryl benzoate. All the other esters described in the tables were prepared from the pinacones.

(10) Y. Urushibara and T. Ando, this Bulletin, **12** (1937), 495.

cooling and occasional shaking. The mixture was left to stand at room temperature overnight, and poured into ice water. The separating red matter, which solidified completely in a few days, was collected, washed with dilute acetic acid and with water, recrystallized three times from benzene-95% alcohol, and dried in vacuum at 110° over phosphorus pentoxide. Colourless, extremely fine needles (167 mg.), m.p. 201.5-202.5° (uncorr.) or 206.5-207.5° (corr.) with decomposition (Found: C, 84.92; H, 9,82. Calculated for $C_{70}H_{94}O_4$: C, 84,12; H, 9.49%). A considerable depression of the melting point was observed when the substance was mixed with the diacetate with the same melting point, but no depression with the specimen of the dibenzoate described below. $[\alpha]_D^{22^\circ} = -160^\circ$ (13.95 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{22^\circ} = -2.23^\circ$).

Preparation of Ergopinacone by the Carbon Dioxide Method. Carbon dioxide was passed through a solution of ergosterol (1 g.) and eosin (1 g.) in 95% alcohol (about 400 c.c.) for 20 minutes to remove air, and the solution was exposed to sunlight for four days. The separating needles were collected after further a week's standing, washed, and recrystallized twice from benzene-95% alcohol. Colourless silky needles (315 mg.), m.p. 200-201° (corr.) with decomposition. The substance showed the same colour reactions as the specimen prepared by the boiling method.

Diacetate. The above ergopinacone (150 mg.) was acetylated with acetic anhydride and pyridine, and the product was recrystallized twice from benzene-95% alcohol, colourless fine needles (139 mg.), m.p. 201.5-202° (uncorr.) or 206.5-207° (corr.) with decomposition (Found: C, 82.00; H, 10.64. Calculated for $C_{60}H_{90}O_4$: C, 82.31; H, 10.37%). Mixed melting point with the specimen from ergopinacone prepared by the boiling method 204.5-205.5° (corr.). $[\alpha]_D^{16^\circ} = -202^\circ$ (11.45 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{16^\circ} = -2.31^\circ$). Ultraviolet absorption maximum about 267-275 mμ (indistinct) in 0.055% hexane solution. In the Liebermann-Burchard test the diacetate gives red, violet, blue, and bluish green colours, while in the Rosenheim test pink, violet, dark violet, and finally dark green colours.

Dibenzoate. Prepared from the above ergopinacone (250 mg.). Colourless fine needles (217 mg.), melting at 201.5-202.5° (uncorr.) or 206.5-207.5° (corr.) with decomposition alone or in admixture with the specimen described above (Found: C, 84.43; H, 10.16. Calculated for $C_{70}H_{94}O_4$: C, 84.12; H, 9.49%). $[\alpha]_D^{16^\circ} = -160^\circ$ (14.4 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{16^\circ} = -2.31^\circ$). Ultraviolet absorption maxima in 0.041% hexane solution 280 and 273 mμ (both very sharp). In the Liebermann-Burchard test the dibenzoate gives instantly wine-red, bluish violet, and then bluish green colours, while in the Rosenheim test light pink, light violet, and bluish green colours.

7-Dehydrocholesterol-pinacone and Esters.

Preparation of 7-Dehydrocholesterol-pinacone by the Boiling Method. As described in the previous papers,(4) an alcohol-benzene solution of 7-dehydrocholesterol (383 mg.) and eosin (383 mg.) was boiled to remove air, and exposed to sunlight for several days. Silky long needles (117 mg.) were obtained, and recrystallization from benzene-alcohol gave colourless needles, m.p. 184.5-185.5° (corr.) with decomposition, $[\alpha]_D^{24^\circ} = -175^\circ$ (6.8 mg. in 1 c.c. pyridine solution, $l = 1$ dm., $\alpha_D^{24^\circ} = -1.19^\circ$). No depression of the melting point was observed when the substance was mixed with the specimen prepared by the carbon dioxide method. The melting point, however, was lowered to 180.5° (corr.) after standing in vacuum half a year.

Diacetate. The above 7-dehydrocholesterol-pinacone (35 mg.) was dissolved in pyridine (7 c.c.) and acetic anhydride (0.7 g.) was added. After standing at room temperature for ten days, the slightly yellowish mixture was poured into ice water, the separating crystals were collected after standing overnight, washed with water, with dilute acetic acid, and again with water, recrystallized twice from benzene-95% alcohol, and dried in vacuum at 110° over phosphorus pentoxide. Colourless fine needles (30 mg.), m.p. 185.5-186° (uncorr.) or 190-190.5° (corr.) with decomposition (Found: C, 81.87; H, 10.53. Calculated for $C_{58}H_{90}O_4$: C, 81.81; H, 10.66%). $[\alpha]_D^{26^\circ} = -149^\circ$ (6.7 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{26^\circ} = -1.00^\circ$). Ultraviolet absorption maximum in 0.052% hexane solution 254 mμ (narrow but indistinct), anothor very dim band at about 268 mμ. The substance showed no depression of the melting point when mixed with the specimen of the diacetate described below.

Preparation of 7-Dehydrocholesterol-pinacone Dibenzoate from 7-Dehydrochlesteryl Benzoate by the Boiling Method.(10) 7-Dehydrocholesterol-pinacone dibenzoate (38 mg.) was obtained from 7-dehydrocholesteryl benzoate (158 mg.) in a week's exposure to sunlight. M.p. 183-183.5° (corr.) with decomposition. $[\alpha]_D^{17°} = -114°$. No depression of the melting point was observed when the substance was mixed with the specimen of the dibenzoate described below. In the Liebermann-Burchard test the substance gives red, violet, blue, and after standing overnight dark green colours, while in the Rosenheim test pink, dark violet, dark green, and after standing overnight dark brownish violet colours.

Preparation of 7-Dehydrocholesterol-pinacone by the Carbon Dioxide Method. Carbon dioxide was passed through a solution of 7-dehydrocholesterol (383 mg.) and eosin (383 mg.) in 95% alcohol (150 c.c.) for 30 minutes to remove air, and the solution was exposed to sunlight for several days. Small needles which separated out were collected and washed, m.p. 182.5-183° (corr.), yield 180 mg. Recrystallized twice from benzene-alcohol, and dried in vacuum at 110° over phosphorus pentoxide. Colourless needles, m.p. 181-182° (uncorr.) or 184.5-185.5° (corr.) with decomposition, $[\alpha]_D^{24°} = -159°$ (6.8 mg. in 1 c.c. pyridine solution, $l = 1$ dm., $\alpha_D^{24°} = -1.08°$). The melting point was lowered to 182.5° (corr.) on standing in vacuum half a year.

Diacetate. Prepared from the above 7-dehydrocholesterol-pinacone (35 mg.). Colourless fine needles (33 mg.), m.p. 186.5-187° (uncorr.) or 191-191.5° (corr.) with decomposition (Found: C, 82.21, 82,28, 82.04; H, 10.40, 10.68, 10.97. Calculated for $C_{58}H_{90}O_4$: C. 81.81; H, 10.66%). $[\alpha]_D^{26°} = -146°$ (7.25 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{26°} = -1.06°$). Ultraviolet absorption maximum in 0.050% hexane solution 254 mμ (narrow but indistinct), another extremely dim band at approximately 268 mμ. In the Rosenheim test the diacetate gives light pink, light violet, then dark green colours.

Dibenzoate. An ice-cooled solution of the above 7-dehydrocholesterol-pinacone (35 mg.) in pyridine (7 c.c.) was mixed with benzoyl chloride (0.8 g.) and the mixture was shaken occasionally for 20 minutes. After standing for a week at room temperature, the mixture was poured into ice water and left to stand for several days. The separating crystals were collected, washed, and recrystallized twice from benzene-alcohol. Colourless needles (31 mg.), m.p. 182.5-183.5° (corr.) with decomposition (Found: C, 83.92; H, 9.45. Calculated for $C_{68}H_{91}O_4$: C, 83.70; H, 9.72%). $[\alpha]_D^{23°} = -113°$ (12.6 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{26°} = -1.43°$).

Preparation of 7-Dehydrocholesterol-pinacone Dibenzoate from 7-Dehydrocholesteryl Benzoate by the Carbon Dioxide Method. A solution of 7-dehydrocholesteryl benzoate (279 mg., m.p. 141.5-143°, clear at 157°, corr.) and eosin (279 mg.) in 95% alcohol (400 c.c.) was exposed to sunlight after removing air by passing carbon dioxide. After a week's irradiation the deposit was collected, washed, recrystallized twice from benzene-alcohol, and dried in vacuum at 110° over phosphorus pentoxide. Colourless fine needles (109 mg.), m.p. 179-180° (uncorr.) or 182.5-183.5° (corr.) with decomposition (Found: C, 83.66; H, 9.51. Calculated for $C_{68}H_{91}O_4$: C, 83.70; H, 9.72%). No depression of the melting point was observed in admixture with other specimens of the dibenzoate described above. $[\alpha]_D^{25°} = -101°$ (12.95 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{25°} = -1.31°$). Ultraviolet absorption maxima in 0.053% hexane solution 280 and 273 mμ (both very sharp). In the Rosenheim test the substance gives light pink, dark violet, dark green, and finally dark brownish violet colours.

Preparation of 7-Dehydrocholestrol-pinacone by the Quick Method. A solution of 7-dehydrocholesterol (227 mg.) and eosin (227 mg.) in 95% alcohol (100 c.c.) was exposed to sunlight after removing air by passing carbon dioxide. After ten hours' irradiation the deposit (75 mg., m.p. 189.5-190.5°, corr.) was collected, purified repeatedly, and dried as usual. Colourless fine needles, m.p. 189-190° (uncorr.) or 192.5-193.5° (corr.) with decomposition. In the Liebermann-Burchard test the substance gives red, violet, and blue colours, while in the Rosenheim test light pink, light red, reddish violet, and finally violet colours. The melting point was lowered with the lapse of time even though the substance was reserved in vacuum: It showed m.p. 187-187.5° (corr.) with decomposition after a month, and m.p. 185.5-186° (corr.) with decomposition after a year. The one year old substance showed a depression of the melting point when mixed with the specimen (m.p. 184.5-185.5°, corr.) prepared by the long 'exposure method (mixed m.p. 181.5-182.5, corr.).

Summary.

Ergopinacone and 7-dehydrocholesterol-pinacone have been prepared by two different methods, viz., the boiling method and the carbon dioxide method. The products obtained by the two methods as well as diacetates and dibenzoates derived from them have been compared. It has been indicated that the two methods yield the same products.

In conclusion the author wishes to express his hearty thanks to Prof. Y. Urushibara for his kind guidance and encouragement. He acknowledges also his indebtedness to Dr. K. Yamasaki for his advice and kindness in taking absorption spectra, and to Mr. Yasohachi Yamaguchi and to Ozi Seisi Co. for generous help.

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