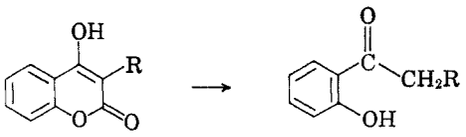
TABLE I

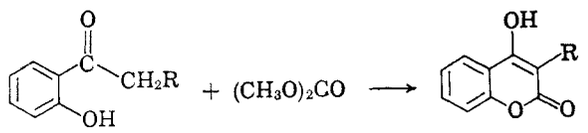


R (references are to coumarins)	Bp (mm) or mp, °C	Formula	% calcd C	% calcd H	% found C	% found H	% yield	Recrystn solvent
H		$C_8H_8O_2$ (1)	*i*				82	
Methyl[a]	225 (630)[e]	$C_9H_{10}O_2$ (2)	71.98	6.71	72.24	6.66	92	
Phenyl[b]	58–59[f]	$C_{14}H_{12}O_2$ (3)	79.23	5.70	79.34	5.71	82	
Benzyl[c]	300 (630)	$C_{15}H_{14}O$ (4)	79.62	6.24	79.69	5.98	72	
Benzhydryl[c]	96–98	$C_{21}H_{18}O_2$ (5)	83.42	6.00	83.51	5.97	89	
1-Phenylpropyl[c]	287 (630)[g]	$C_{17}H_{18}O_2$ (6)	*j*				80	
1-Phenyl-2-carboxyethyl[d]	130–131	$C_{17}H_{16}O_4$ (7)	71.82	5.67	72.07	5.59	97	Ethanol
1-Phenylethyl[c]	75–77	$C_{16}H_{16}O_2$ (8)	79.97	6.71	80.19	6.79	77	

[a] K. N. Trivedi, *J. Sci. Ind. Res.* (India), **21B**, 402 (1962). [b] G. Urbain and C. Mentzer, *Bull. Soc. Chim. France*, **11**, 171 (1944). [c] See ref 3. [d] C. K. Wiener, C. H. Schroeder, B. D. West, and K. P. Link, *J. Org. Chem.*, **27**, 3086 (1962). [e] Lit. 150° (80 mm): I. Heilbron, Ed., "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1953. [f] Lit. 56–57°: *Chem. Abstr.*, **60**, 15808*f* (1964). [g] Lit.[h] 220–225° (15 mm). [h] B. D. West and K. P. Link, *J. Heterocyclic Chem.*, **2**, 93 (1965). [i] The infrared spectrum was identical with a commercial sample. [j] The infrared spectrum was identical with a sample of the (−) isomer.[h]

hydrochloric acid. The products were crystallized from the solvents given in Table II.

TABLE II



R	Mp, °C	Formula	Yield, %	Recrystn solvent
Methyl	230–231[b]	$C_{10}H_8O_3$ (9)	76	*h*
Benzyl	204–206[c]	$C_{16}H_{12}O_3$ (10)	57	*h*
Phenyl	231–232[d]	$C_{15}H_{10}O_3$ (11)	63	*h*
1-Phenylethyl	206–207[e]	$C_{17}H_{14}O_3$ (12)	70	*h*
1-Phenylpropyl[a]	170–171[f]	$C_{18}H_{16}O_3$ (13)	87	*h*
Benzhydryl	181–182[g]	$C_{22}H_{16}O_3$ (14)	58	*i*

[a] See Table I, ref *h*. [b] Lit. mp 230°: ref *a*, Table I. [c] Lit. mp 205°: I. M. Heilbron and D. W. Hill, *J. Chem. Soc.*, 1705 (1957). [d] Lit. mp 240°: ref *b*, Table I. [e] Lit.[3] mp 201–202°. [f] Lit.[3] mp 175–177°. [g] Lit.[3] mp 177–178°. [h] Ethanol–water. [i] Acetic acid.

To show that neither of the above reactions disturbs the asymmetry of an α substituent, (*S*)-*o*-hydroxy-β-phenylcaprophenone,[11] $\alpha^{25}D$ −56.1° (neat), was converted to 3-α-phenylbutyl-4-hydroxycoumarin, $[\alpha]^{24}D$ −136° (*c* 1, 5% aqueous NaOH). Crystallization of this product was not permissible since it is known[11] that the crystals would be enriched in racemic material. Decarboxylation of this product by the above method yielded the original ketone, $\alpha^{25}D$ −55.9° (neat).

Registry No.—**1**, 118-93-4; **2**, 610-99-1; **3**, 2491-31-8; **4**, 3516-95-8; **5**, 15074-13-2; **6**, 2732-23-2; **7**, 15074-15-4; **8**, 15074-16-5; **9**, 15074-17-6; **10**, 15074-18-7; **11**, 1786-05-6; **12**, 15074-20-1; **13**, 435-97-2; **14**, 15074-22-3; 3-(*o*-hydroxyphenyl)-5-phenyl-2-cyclohexen-1-one, 15156-56-6; (+)-3-(*o*-hydroxyphenyl)-5-phenyl-2-cyclohexen-1-one, 15074-23-4; 3α-phenylbutyl-4-hydroxycoumarin, 15074-24-5.

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Thermal Isomerization of Ergosterol and Dehydrocholesterol

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The thermal rearrangement of 1,3-dienes involving a 1,5-hydrogen shift and concomitant migration of two carbon–carbon double bonds has been widely investigated in acyclic[1,2] and cyclic[3–6] systems.

Pines[7] has shown that 1,3-cyclohexadienes undergo reversible 1,5-hydrogen shifts in the temperature range of 200–400°, but at higher temperature, 450–500°, the cleavage of carbon–carbon single bonds becomes important and is accompanied by extensive skeletal reorganization and aromatization. In this note we report the thermal behavior of ergosterol and $\Delta^{5,7}$-dehydrocholesterol which, as will be seen, is comparable with the behavior of simpler 1,3-cyclohexadienes in the higher temperature range.

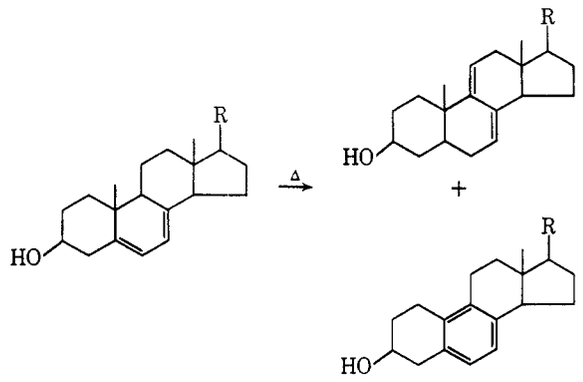
Ergosterol appears to be stable below 350°. We have not been able to detect the isomer resulting from a 1,5-hydrogen shift employing the chromatographic procedures available to us.

Ergosterol is converted into a complicated mixture of sterols on heating to 400 ± 20° for 1–5 min. At the end of 1 min ergosterol is still present in appreciable quantity, but after 3–5 min is largely destroyed. The sterol mixture was subjected to alumina chromatography which led to the isolation of a small amount of nonpolar, fluorescent material which was not char-

(1) J. Wolinsky, M. Baird, and B. Chollar, *J. Am. Chem. Soc.*, **84**, 2775 (1962).
(2) H. M. Frey and R. J. Ellis, *J. Chem. Soc.*, 4770 (1965).
(3) A. P. terBorg, H. Kloosterziel, and N. van Meurs, *Rec. Trav. Chim.*, **82**, 717, 741, 1189 (1963).
(4) W. R. Roth, *Tetrahedron Letters*, 1009 (1964).
(5) J. W. H. Watthey and S. Winstein, *J. Am. Chem. Soc.*, **85**, 3716 (1963).
(6) R. B. Woodward and R. Hoffman, *ibid.*, **87**, 2511 (1965).
(7) H. Pines and R. H. Kozlowski, *ibid.*, **78**, 3776 (1956).

acterized further and various sterol mixtures as indicated by ultraviolet analysis. The sterol fractions were acetylated and chromatographed on silica gel to give a sterol with no absorption in the ultraviolet above 210 mμ which has not been identified and a mixture of ergosteryl acetate and another acetate, λ_{max} 242 and 250 mμ which was isolated in pure form by repeated recrystallization from acetone. The purified acetate exhibited mp 175–175.5°, λ_{max} 235, 242 and 251 mμ, and displayed infrared and nmr spectra identical with those of authentic ergosterol D acetate.[8] The identity was further confirmed by hydrolysis to the parent alcohol followed by spectral and thin layer chromatographic comparison with an authentic sample of ergosterol D.

A fourth acetate was isolated from later fractions and exhibited a singlet aromatic resonance at 6.85 ppm and was shown by infrared and nmr analyses, mixture melting point, and chromatographic behavior to be identical with neoergosteryl acetate.[9]



Evidence that neoergosterol was produced by a demethanation reaction was provided by the mass spectral identification of methane among the gases produced during the thermal reaction.

At 400° it was estimated that ergosterol D is the major component of the sterol mixture, while the amount of neoergosterol seems to increase at higher temperature.

The thermal isomerization of $\Delta^{5,7}$-dehydrocholesterol seemed to be slightly more complicated, but the major product was readily identified as cholesta-7,9(11)-dien-3β-ol.

It can now be claimed that isomerization routes to all the ergosterol isomers (B_1, B_2, B_3 and D) are available.

Experimental Section

Thermal Rearrangement of Ergosterol.—A 3.0-g sample of recrystallized ergosterol, mp 160–161°, was placed in a 50-ml, round-bottom flask equipped with a condenser and maintained under a nitrogen atmosphere. The flask was submerged in a Woods metal bath at 400 ±10° for 5 min. The yellow solid which resulted on cooling was dissolved in a minimal amount of benzene and applied to a column containing 300 g of neutral alumina. Elution with benzene and 10% ether–benzene gave four fractions: (a) 0.40 g which showed no absorption in the ultraviolet above 210 mμ; (b) 0.056 g of an oil; (c) 2.40 g of sterol mixture; and (d) 0.154 g, mp 160–161°, whose melting point was not depressed on admixture with ergosterol. The acetate of this fraction exhibited mp 170–172° and an infrared spectrum identical with that of authentic ergosteryl acetate.

Fraction c was kept with a large excess of acetic anhydride and a trace of pyridine for 24 hr. The volatile reactants were removed under diminished pressure and thin layer chromatography of the residue on silica gel G showed a minimum of three spots. A small portion was placed on a silica gel column and eluted with 12.5% benzene in pentane to give the following fractions. (a) A solid, mp 148–151°, no absorption in the ultraviolet above 220 mμ, which was not investigated further. (b) A solid, λ_{max} 242 mμ (ε 12,300), which after repeated recrystallization from acetone showed mp 175–175.5°, λ_{max} 235, 242, and 251 mμ (ε 12,800, 15,000, and 10,300, respectively). The melting point of this sample was not depressed on admixture with an authentic sample of ergosterol D acetate and its infrared spectrum proved to be identical with that of the authentic sample. Hydrolysis of the acetate afforded an alcohol: mp 164–165°; λ_{max} 235, 242 (16,300), and 251 mμ. This sample did not depress the melting point of an authentic sample of ergosterol D, and its infrared spectrum was identical with that of the authentic sample. (c) A solid which after recrystallization from ether–methanol showed mp 117–117.5°, $[\alpha]^{32}$ −6.5°, λ_{max} 269 and 278 mμ (ε 440), was obtained as the third fraction. This solid did not depress the melting point of an authentic sample of neoergosteryl acetate. This solid also showed the same R_f value as neoergosteryl acetate on thin layer chromatography. Hydrolysis with alkali afforded a solid, mp 152–153°, $[\alpha]^{28}$ −8.3°, λ_{max} 269 (435) and 278 mμ, whose nmr and infrared spectra were identical with those of an authentic sample of neoergosterol.

A similar separation of the sterol acetates was achieved using alumina, except in this instance neoergosteryl acetate eluted before ergosterol D acetate. It was estimated, by ultraviolet analysis of various chromatographic fractions, that fraction c contained 70–77% ergosterol D and 15–18% neoergosterol.

Thermal Rearrangement of 7-Dehydrocholesterol.—A 3.0-g sample of 7-dehydrocholesterol was heated at 400° for 5 min. Column chromatography using alumina gave five fractions: (a) 50 mg of oil showing no ultraviolet absorption; (b) 100 mg of oil which could not be crystallized; (c) 800 mg of solid, mp 102–110°, λ_{max} 235, 242 (ε 16,000), and 250 mμ (lit., for cholesta-7,9(11)-dien-3β-ol, mp 107–110°,[10] λ_{max} 235, 243 (ε 16,100), and 251 mμ);[11] (d) 1.5 g of solid, mp 148–150°, whose infrared and ultraviolet spectra were identical with those of $\Delta^{5,7}$-dehydrocholesterol; and (e) 0.5 g of oil which was not characterized.

Registry No.—Ergosterol, 57-87-4; dehydrocholesterol, 434-16-12.

(8) We wish to express our appreciation to Dr. E. M. Chamberlin for making this sample available.

(9) We wish to express our appreciation to Dr. Y. Sato for making available a sample of neoergosterol.

(10) L. F. Fieser and J. E. Herz, *J. Am. Chem. Soc.*, **75**, 121 (1953).

(11) R. Antonucci, S. Bernstein, D. Giancola, and K. J. Sax, *J. Org. Chem.*, **16**, 1891 (1951).

Kinetics of Bromination of Benzene and Methylbenzenes in Acetic and Trifluoroacetic Acids[1,2]

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As part of a general investigation of rapid halogenation reactions, kinetic studies of the bromination in water of aromatic amines,[3] of anisoles,[4] and of benzene

(1) Paper II in a series: Bromination of Polymethylbenzenes.

(2) Paper I: P. Alcais, F. Rothenberg, and J. E. Dubois, *J. Chim. Phys.*, 1443 (1966).

(3) (a) J. E. Dubois, P. Alcais, and G. Barbier, *Compt. Rend.*, **254**, 3000 (1962); (b) J. E. Dubois and R. Uzan, *Tetrahedron Letters*, 2397 (1964); (c) *ibid.*, 309 (1965); (d) J. E. Dubois, P. Alcais, and G. Barbier, *Bull. Soc. Chim. France*, in press.

(4) (a) J. E. Dubois and J. J. Aaron, *Compt. Rend.*, **258**, 2313 (1964); (b) *J. Chim. Phys.*, 1354 (1964).