The yellow color of the reagent was discharged within several seconds. The resulting solution was stirred at room temperature for 0.5 hr, 13 ml of 3 *M* aqueous sodium hydroxide and 26 ml of 0.5 *M* sodium borohydride in 3 *M* sodium hydroxide were added, and stirring was continued for 6 hr. The mixture was decanted away from the mercury, diluted with saturated brine, and thoroughly extracted with ethyl acetate. Evaporation of the solvent afforded 3.45 g of oil: λ_{max}^{film} 2.92 (OH), 6.05 (CO), and 6.19 μ (C=C). This material decomposed with the appearance of metallic mercury during attempted distillation at 110° (0.01 mm).

Registry No.—**4**, 15051-78-2; **5**, 15051-79-3; **6**, 15051-80-6; **7**, 15051-81-7; **8**, 15052-76-3; **9**, 5956-12-7; **10**, 6040-08-0; **11**, 15051-82-8.

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The Reversible Removal of Carbon 2 of 3-Substituted 4-Hydroxycoumarins

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The need for isotopically labeled, optically active 4-hydroxycoumarin anticoagulants prompted the investigation of methods of inserting a radiocarbon atom into the preresolved cold molecule. This approach seemed attractive because of the problems involved in a classical resolution by fractional crystallization of necessarily small quantities of radioactive diastereomers.

The synthetic route taken involves hydrolytic removal and subsequent reinsertion (with labeling) of the 2 carbon of the 4-hydroxycoumarin lactone ring. Methods for performing both of these transformations have been improved. We have also shown that the decarboxylation–carboxylation cycle does not involve racemization of a center attached at position 3 of the 4-hydroxycoumarin.

We also wish to suggest 3 substitution and hydrolytic decarboxylation of 4-hydroxycoumarins as an effective synthetic route to pure *o*-hydroxy ketones with complex side chains.

4-Hydroxycoumarin can be substituted in the 3 position with wide variety of groups. Most useful appear to be the Michael reaction[1] and the displacement reactions described by Ziegler[2] and by Schroeder.[3] In addition the cyclization of substituted phenyl malonates[4] yields a wide variety of 3-substituted 4-hydroxycoumarins. Van Zanten[5] has reveiwed the methods available.

Lactone opening and decarboxylation of 4-hydroxycoumarins has been reported.[6] The use of strongly alkaline solutions leads in some cases to extensive degradation as a side reaction, even as far as to salicylic acid. We have found that decarboxylation is accomplished better by heating pH 9 solutions of the sodium enolates of the 4-hydroxycoumarins to *ca.* 150° in sealed tubes. Wildi[7] has described the stability of the 3-phenyl-4-hydroxycoumarin anion to hydrolysis: we feel that in our procedure hydroxide ion attacks the uncharged 4-hydroxycoumarin since more strongly basic solutions are slower to react. Attempts at decarboxylations in neutral and acid solutions failed, as did attempts to decarboxylate 3-acetyl-4-hydroxycoumarin under any conditions.

Recarboxylation of ring-substituted *o*-hydroxyacetophenones has been discussed by Desai and Sethna.[8] We have found that the presence of α-substituents as large as diphenylmethyl on the acetophenone methyl group do not interfere with base-catalyzed carboxylative cyclization with alkyl carbonates. It appears that this route to 3-substituted 4-hydroxycoumarins is a favorable one provided the *o*-hydroxy ketone is available.

Experimental Section

Decarboxylation. General Procedure.—The 3-substituted 4-hydroxycoumarin was dissolved in a very small excess of 5% aqueous sodium hydroxide and the solution was sealed in a heavy walled Pyrex tube. The tube was heated to 150° in a capped iron pipe in an oven for 48 hr. The reaction mixture was extracted with chloroform and the chloroform was freed of traces of starting material or salicylic acid by washing with aqueous sodium carbonate. The chloroform solution was evaporated. All products except where R = 1-phenyl-2-carboxyethyl were distilled at reduced pressure; when products solidified after distillation, uncorrected melting points are given.

An exception to the general scheme given in Table I was the decarboxylation of warfarin, 3-(α-acetonylbenzyl)-4-hydroxycoumarin.[9] The product of this decarboxylation was 3-(*o*-hydroxyphenyl)-5-phenyl-2-cyclohexen-1-one, as was first shown by Robertson[10] and Link.[11] The decarboxylation was done as above, except that the solid product was filtered from the reaction mixture and crystallized first from acetic acid, then from benzene, mp 161–163°.

Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.9; H, 6.10. Found: C, 82.3; H, 6.00.

The same reaction, carried out with (−)(*S*)-warfarin,[11] $[\alpha]^{25}D$ −148° (*c* 2, 0.5 *N* NaOH), yielded the (+) isomer of the above ketone, $[\alpha]^{23}D$ +100° (*c* 0.8, 0.5 *N* NaOH), mp 145–146°.

Carboxylative Cyclization of *o*-Hydroxy Ketones.—Approximately 1 g of the *o*-hydroxy ketone was added to 1 g of sodium dispersion in 100 ml of benzene. After the evolution of hydrogen had ceased, 6 ml of dimethyl carbonate was added and the mixture was refluxed with stirring until thin layer chromatography on fluorescent silica gel plates showed absence of starting material. The time varied from 24 to 48 hr. The tlc solvent system was in all cases 3:1 v/v of toluene–glacial acetic acid. Excess sodium was consumed with ethyl alcohol and water was added. The aqueous layer was separated and poured into excess dilute

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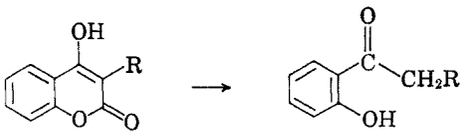
(11) B. D. West, S. Preis, C. H. Schroeder, and K. P. Link, *J. Am. Chem. Soc.*, **83**, 2676 (1961).

TABLE I

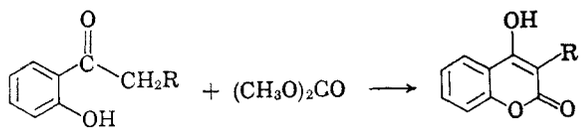


R (references are to coumarins)	Bp (mm) or mp, °C	Formula	% calcd C	% calcd H	% found C	% found H	% yield	Recrystn solvent
H		$C_8H_8O_2$ (1)	*i*				82	
Methyl[a]	225 (630)[e]	$C_9H_{10}O_2$ (2)	71.98	6.71	72.24	6.66	92	
Phenyl[b]	58–59[f]	$C_{14}H_{12}O_2$ (3)	79.23	5.70	79.34	5.71	82	
Benzyl[c]	300 (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-

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