acid have been shown[6] to possess the D configuration, the results in Figure 2 also confirm the correctness of the D configuration deduced[5,7] for natural 9-hydroxy-12-octadecenoic acid and the derived 9-hydroxyoctadecanoic acid on the basis of mixture melting point data. The D configuration may now similarly be assigned to natural helenynolic acid (I).[8]

In order to furnish proof of the validity of the rotatory dispersion curves in Figure 2, (−)-methyl-12-D-hydroxyoctadecanoate was inverted by formation of the tosylate, conversion of this to the acetate, and mild hydrolysis of the latter to yield the enantiomeric (+)-methyl 12-L-hydroxyoctadecanoate, using an adaptation of the method of Schroepfer and Bloch.[10] The L-(+) ester [identical with its D-(−) isomer in melting point and infrared spectrum] is seen (Figure 2) to have a rotatory dispersion curve which is the exact mirror image of that of the D-(−) compound.

Experimental Section[11]

Rotatory dispersion curves were determined with a Bendix Model 460-C or a Cary Model 60 spectropolarimeter using 1-mm. or 1-cm. cells (*c* 0.06–6.0, 95% ethanol) at 25°. Rotations are given below only for (1) the highest and lowest wave lengths measured, and (2) peaks and troughs. Results were reproducible to within 5%.

Methyl helenynolate had $[\alpha]_{600}$ −7° (*c* 3.6, ethanol); O.R.D. (*c* 0.06, ethanol) $[\alpha]_{323}$ −75.5°, $[\alpha]_{243.5}$ 1115° (peak), $[\alpha]_{240}$ 512° (trough), $[\alpha]_{232.5}$ 2795° (peak), $[\alpha]_{226}$ 1241° (trough), $[\alpha]_{204}$ 2150°.

Hydrogenation of Methyl Helenynolate.—A solution of 30 mg. of the acetylenic ester in 10 ml. of methanol was hydrogenated in presence of 60 mg. of 10% palladium on charcoal at 15 p.s.i. and room temperature for 1 hr. Filtration and evaporation under reduced pressure gave a white solid, m.p. 45–50°, which was chromatographed on silicic acid (activated by heating to 90° for 24 hr.). The fraction eluted with pentane–ether (9:1) gave 24 mg. (80% yield) of methyl 9-hydroxyoctadecanoate, m.p. 50–51° (*Anal.* Calcd. for $C_{19}H_{38}O_3 \cdot 0.25H_2O$: C, 71.54; H, 12.16. Found: C, 71.55, 71.57; H, 11.85, 12.11.). Its infrared spectrum showed ν_{max} 3350 (OH), 1640 (OH), and 1740 cm.$^{-1}$ ($COOCH_3$). Gas–liquid partition chromatography, using a column (1.8 m. × 3 mm.) packed with 3% S.E. 30 Silicone on Gas-chrom A at 200° with argon (24 p.s.i.) as the carrier gas, showed a single peak of retention time 5.28 min., $[\alpha]_D$ −0.18° (*c* 10.0, ethanol). The racemic ester is reported[12] to have m.p. 51–52°.

Methyl 9-D-Hydroxyoctadecanoate.—A solution of 15 mg. of 9-D-hydroxyoctadecanoic acid[5] in ether was left with diazomethane for 4 hr. at room temperature. Removal of solvent and chromatography of the residue on silicic acid gave a quantitative yield of methyl 9-D-hydroxyoctadecanoate, m.p. 51–52°. A mixture melting point with the sample (m.p. 50–51°) obtained from methyl helenynolate was undepressed, and the infrared spectra and O.R.D. curves of the two samples were identical. The compound showed a single peak with the same retention time (5.28 min.) on gas chromatography both when injected alone and when admixed with the hydrogenation product: $[\alpha]_D$ −0.18° (*c* 10.0, ethanol); O.R.D. (*c* 10.0, ethanol) $[\alpha]_{580}$ −0.20°, $[\alpha]_{240}$ −2.50°.

(−)-Methyl 12-D-hydroxyoctadecanoate had $[\alpha]_D$ −0.37° (*c* 12.2, $CHCl_3$); O.R.D. (*c* 9.0, ethanol) $[\alpha]_{580}$ −0.33°, $[\alpha]_{240}$ −2.31°.

(+)-Methyl 12-L-Hydroxyoctadecanoate.—Prepared from the preceding ester by an adaptation of the method of Schroepfer and Bloch,[10] this had $[\alpha]_D$ +0.36° (*c* 8.8, ethanol); O.R.D. (*c* 8.8, ethanol) $[\alpha]_{580}$ +0.38°, $[\alpha]_{240}$ +2.32°.

(6) (a) K. Serck-Hanssen, *Chem. Ind.* (London), 1554 (1958); (b) K. Serck-Hanssen and E. Stenhagen, *Acta Chem. Scand.*, **9**, 866 (1955).

(7) F. D. Gunstone, *J. Chem. Soc.*, 1274 (1952).

(8) This compound has the *S* configuration on the convention of Cahn, Ingold, and Prelog.[9] It should be pointed out here that the use of the *R–S* convention makes natural (+)-methyl ricinoleate and the derived (−)-methyl 12-hydroxyoctadecanoate members of the *R* series owing to the operation of the sequence rule.

(9) (a) R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956); (b) R. S. Cahn, *J. Chem. Educ.*, **41**, 116 (1964).

(10) (a) G. J. Schroepfer, Jr., and K. Bloch, *J. Am. Chem. Soc.*, **85**, 3310 (1963); (b) G. J. Schroepfer, Jr., and K. Bloch, *J. Biol. Chem.*, **240**, 54 (1965).

(11) The mention of firm names or trade products does not imply that they are endorsed or recommended by the U. S. Department of Agriculture over other firms or similar products not mentioned.

(12) S. Bergström, *Arkiv Kemi, Mineral. Geol.*, **A21**, No. 15, 1 (1945).

Coumarins from 2-Hydroxyaryl Acids and Malonic Acid

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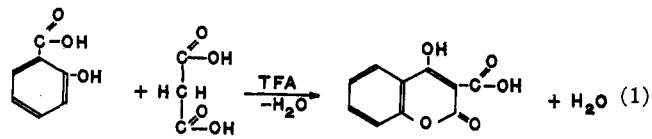
Received June 29, 1965

In previous papers it has been shown that coumarins can be prepared by the action of cyanoacetic acid on certain polyhydroxyaryl acids.[2] Subsequently, coumarins were prepared by the action of aldehydes on malonic acid in basic media.[3] In this contribution, a new method of preparing coumarins is presented in which 2-hydroxyaryl acids react with malonic acid in the presence of trifluoroacetic acid at carefully controlled temperatures to form 4-hydroxy-3-coumarin-carboxylic acids—a rare subclass of coumarins.[4]

Since we have been unable to accomplish attack by an ester or acid on a phenol or monohydroxyphenol containing a powerful electrophilic group on the ring in the presence of trifluoroacetic acid, we have concluded that it is the carboxyl group of the aryl acid which has attacked the very active methylene group of the malonic acid which by the principle of vinylology is activated from two directions.

Attempts to decarboxylate compound I by the method of Adams and Bockstahler[5] failed, which is entirely understandable since a 4-hydroxycoumarin-3-carboxylic acid is the enolic form of a 3-carboxylic acid of a 2-pyronone which would not be decarboxylated by such mild reagents.

The equation for the reaction as visualized for compound I is expressed by eq. 1 and may be used as the



I

model for the other members of the series. In Table I some of the properties of the compounds are given. A tabulation of spectral characteristics of compounds I–VI is given in Table II along with the *p*-bromophenacyl derivatives.

It should be noted that the compounds whose synthesis is described in this report do not have any pronounced fluorescence, do not show any absorption

(1) The person to whom all communications regarding this contribution should be directed.

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(4) M. Covello and E. Piscopo, *Gazz. chim. ital.*, 88 (1958).

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TABLE I

COUMARINS FROM 2-HYDROXYARYL ACIDS

Compd.[a]	Acid used	% yield	M.p., °C.	Formula	Calcd., % C	H	N	Halogen	Found, % C	H	N	Halogen
I	Salicylic	61	162.5–163	$C_{10}H_6O_5$	58.26	2.93			58.58	3.21		
II	5-Chlorosalicylic	70	172.5–173.5	$C_{10}H_5ClO_5$	49.91	2.09		14.73	49.45	2.36		14.39
III	5-Bromosalicylic	80	179.5–180.5	$C_{10}H_5BrO_5$	42.13	1.76		28.03	41.76	2.19		27.71
IV	5-Nitrosalicylic	39	268–269	$C_{10}H_5NO_7$	47.78	2.00	5.57		47.57	2.19	5.74	
V	3-Nitrosalicylic	40	142–143	$C_{10}H_5NO_7$	47.78	2.00	5.57		47.59	2.14	5.40	
VI	2,4-Dihydroxybenzoic	36	232–233	$C_{10}H_6O_6$	54.06	2.72			53.49	3.00		

[a] I, 4-hydroxycoumarin-3-carboxylic acid; II, 6-chloro-4-hydroxycoumarin-3-carboxylic acid; III, 6-bromo-4-hydroxycoumarin-3-carboxylic acid; IV, 4-hydroxy-6-nitrocoumarin-3-carboxylic acid; V, 4-hydroxy-8-nitrocoumarin-3-carboxylic acid; and VI, 4,7-dihydroxycoumarin-3-carboxylic acid.

TABLE II

SPECTRAL ABSORBANCE CHARACTERISTICS AND *p*-BROMOPHENACYL DERIVATIVES OF THE I–VI SERIES

Compd. used	Infrared absorption bands 1800–1500 cm.$^{-1}$[a]	Ultraviolet absorption bands, mμ (log ε)[b]	Phenacyl ester Formula	M.p., °C.	Calcd. % C	H	Br	Found, % C	H	Br
I	1661, 1613	241 (3.56), 310.5 (3.51)	$C_{18}H_{11}BrO_6$	145–146	53.62	2.75	19.81	53.39	2.88	19.64
II	1667, 1608, 1575	237.5 (3.74), 321 (3.53)	$C_{18}H_{10}BrClO_6$	163.5–164	49.39	2.30		49.10	2.52	
III	1667, 1605	236 (3.93), 315 (3.80)	$C_{18}H_{10}Br_2O_6$	167–168	44.84	2.09	33.15	44.59	2.22	33.37
IV	1667, 1623, 1575	232 (3.95), 321 (4.00)	$C_{18}H_{10}BrNO_8$	149.5–150	48.23	2.24	17.82	48.04	2.11	17.97
V	1686, 1600	238.5 (3.65), 316 (3.50)	$C_{18}H_{10}BrNO_8$	186–186.5	48.23	2.24	17.82	47.95	2.37	18.07
VI	1667, 1626	226 (4.04), 259 (4.10), 298 (3.98)	$C_{18}H_{11}BrO_7$	196–197	51.57	2.64	19.06	50.92	2.91	19.22

[a] Spectra were determined on Beckman IR-5 using KBr pellets. [b] Spectra were determined on Bausch and Lomb Spectronic 505 in Spectrograde methanol.

for the carboxyl radical in their infrared spectra, and, in general, give expected ultraviolet absorption patterns. Compound VI, however, differs in that it gives three absorption maxima in the range of 200–350 mμ which was indeed the spectral range examined for all of the six compounds reported here.

The reaction of compound I with resorcinol in the presence of trifluoroacetic acid provides an easy—if somewhat time consuming—method to prepare hydroxyaryl ketones of the coumarin acids.

Experimental Section[6]

Preparation of 4-Hydroxy-3-coumarin Acids.—A mixture consisting of 0.1 mole of the 2-hydroxyaryl acid, 0.1 mole of malonic acid, and 30 ml. of trifluoroacetic acid was heated in an all-glass reflux assembly immersed in a Fisher Hitemp oil bath set so that the temperature remained between 95 and 100° and was never permitted to exceed 100°.

The mixture was heated for 20 hr., diluted with 100–150 ml. of water, chilled, and filtered, and the precipitates were dried in air.

The analytical samples were obtained by recrystallizing the compounds twice from heptane or by taking the compounds up in the smallest amount of tetrahydrofuran possible and precipitating them with heptane. The latter process was repeated for a second precipitation.

Preparation of *p*-Bromophenacyl Derivatives of the Compounds of the I–VI Series.—Two grams of the compound, 1 g. of sodium bicarbonate and 2 g. of the 2,4′-dibromoacetophenone were refluxed in 100 ml. of absolute ethanol for 3 hr. The solutions were filtered while boiling hot. The filtrate was chilled and the precipitates thus obtained were recrystallized twice from absolute ethanol.

Preparation of 3-(2,4-Dihydroxybenzoyl)-4-hydroxycoumarin.—A mixture of 0.01 mole of compound I, 0.01 mole of resorcinol, and 10 ml. of trifluoroacetic acid was refluxed for 8 hr., poured into water, chilled, and filtered. The precipitate was dried in air and recrystallized once from boiling heptane: m.p. 162.5–163°.

Anal. Calcd. for $C_{16}H_{10}O_6$: C, 62.34; H, 3.27. Found: C, 62.10; H, 3.44.

(6) All analyses were performed by Dr. Carl Tiedcke, Teaneck, N. J. All melting points were taken on Fisher-Johns melting point blocks.

Acknowledgment.—The authors acknowledge with gratitude the financial assistance of the Robert A. Welch Foundation on this project. We also acknowledge the assistance of Mr. J. Davis in the laboratory preparations.

Synthetic Furocoumarins. VII. Oxazolocoumarins from 6-Hydroxy-4-methylcoumarin

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Received May 3, 1965

The preceding paper[1] in this series describes the conversion of 6-hydroxy-4-methylcoumarin (IVa) to two angular furocoumarins (I). Owing to the reactivity of the 5-position, 6-hydroxy-4-methylcoumarin cannot be converted directly to a linear furocoumarin (II). The linear compound is of greater interest because of its structural similarity to psoralene (III, see Chart I), which possesses unique biological photosensitizing activity.[2] A similar problem in the synthesis of psoralenes was overcome by blocking the reactive 8-position of a 7-hydroxycoumarin with an acetamido group, which was removed after formation of the furan ring fused to the 6- and 7-positions.[3] The present paper describes an attempt to utilize the same sequence of reactions for the conversion of 6-hydroxy-4-methylcoumarin (IVa) to a linear furocoumarin by blocking the reactive 5-position with an acetamido group.

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