

Coumarin-4-carboxylic Acids from Coumaran-2,3-diones

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The synthesis of coumarin-4-carboxylic acids (I) reported so far consists of condensation of phenols with phenols with oxalacetic acid or its equivalent.¹⁻³⁾ During the course of our studies⁴⁾ on the structure and reactions of 4,7-dimethyl-5-ethylcoumaran-2,3-dione (IIg), a pyrolysis product of tetrahydrophysalin A,⁵⁾ we found that coumaran-2,3-diones (II) gave coumarin-4-carboxylic acids (I) under reflux in acetic anhydride containing catalytic amount of pyridine. The results are given in Table 1. This reaction is considered useful for the preparation of I with $R_1=R_4=CH_3$, because, by the earlier method, condensation of 2,5-xylénol with oxalacetate occurred mainly at 4-position of xylénol, affording the maleic acid derivative (III).

TABLE 1. RESULTS OF THE FORMATION OF I FROM II

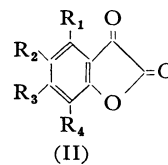
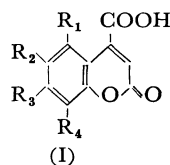
Starting material	Coumarin-4-carboxylic acids obtained (Yield %)	Recovery (%)
IIa ⁶⁾	Ia (12)	5
IIb ⁴⁾	Ib (14)	20
IIc ⁷⁾	Ic (7)	45
IId ⁷⁾	Id (8)	8
IIf ⁴⁾	Ie (12)	43
IIg ⁴⁾	If (19)	50

The mass spectra of I are summarized in Table 2. Compounds I with $R_1=CH_3$ gave a strong peak at m/e *M*-18 as well as at m/e *M*-44 and m/e *M*-45. In contrast to this, I with $R_1=H$ showed no significant peak at m/e *M*-18, suggesting that in the case of I with $R_1=CH_3$ the ion corresponding to m/e *M*-18 has mainly structure IV. From this observation, the mass spectra of various monomethyl derivatives of 1-naphthoic acid were examined. As expected only 8-methyl derivative gave a strong peak at m/e

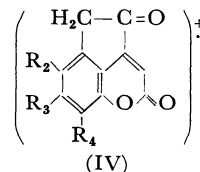
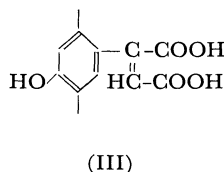
TABLE 2. RELATIVE PEAK HEIGHTS OF THE MASS SPECTRA OF COUMARIN-4-CARBOXYLIC ACIDS

Compound	<i>M</i>	<i>M</i> -18	<i>M</i> -44	<i>M</i> -45
Ia	100	0	6	14
Ib	100	1	25	120
Ic	100	130	105	39
Id	100	170	300	70
Ie	100	180	155	27
If	100	200	155	50

168 (*M*-18). In other cases the peak at m/e 169 (*M*-OH) was stronger than that at m/e 168 (*M*-H₂O). The results are summarized in Table 3.



	R_1	R_2	R_3	R_4
a	H	H	H	H
b	H	Me	H	Me
c	Me	H	H	Me
d	Me	H	Me	H
e	Me	H	Me	Me
f	Me	Me	H	Me
g	Me	H	Et	Me



Experimental

Melting points were uncorrected. IR spectra were measured in KBr. Mass spectra were obtained using a Hitachi RMS-4 mass spectrometer with ionizing voltage of 70 eV.

General Procedure. Coumaran-2,3-dione (II) (ca. 400 mg) was refluxed in acetic anhydride (40 ml) containing a few drops of pyridine for 7–8 hr. The reaction mixture was evaporated *in vacuo* and the residual mass was triturated with water. The crude product was chromatographed on silica gel (3.0 g). First, elution with 5% acetone-light petroleum gave starting material (II), and then with 15% acetone-light petroleum, mainly cou-

1) H. V. Pechmann and E. V. Krafft, *Ber.*, **34**, 421 (1901).

2) B. B. Day, *J. Chem. Soc.*, **107**, 1606 (1915).

3) R. V. Smith and M. D. Bealor, *J. Org. Chem.*, **27**, 3092 (1962).

4) T. Matsuura, M. Kawai and Y. Butsugan, unpublished work.

5) T. Matsuura, M. Kawai, R. Nakashima and Y. Butsugan, *Tetrahedron Lett.*, **1969**, 1083.

6) E. H. Huntress and W. M. Hearon, *J. Amer. Chem. Soc.*, **63**, 2762 (1941).

7) R. Stollé and E. Knebel, *Ber.*, **54B**, 1213 (1921).

TABLE 3. RELATIVE PEAK HEIGHTS OF THE MASS SPECTRA OF VARIOUS MONOMETHYL DERIVATIVES OF 1-NAPHTHOIC ACID

Position of methyl	M (186)	M-17 (169)	M-18 (168)	M-44 (142)	M-45 (141)	M-46 (140)
3	100	37	5	7	19	7
4	100	21	4	8	20	8
5	100	21	7	10	21	19
6	100	23	8	11	19	17
7	100	32	15	15	31	25
8	100	76	98	17	81	91

TABLE 4. ANALYTICAL DATA OF I

Compound	mp (°C) (Solvent of recrystallization)	Formula	Found		Calcd	
			C%	H%	C%	H%
Ia	183—187 (acetone-benzene)	C ₁₀ H ₆ O ₄	62.98	3.05	63.16	3.18
Ib	255—256 (acetone)	C ₁₂ H ₁₀ O ₄	66.07	4.56	66.05	4.62
Ic	188—198 (benzene)	C ₁₂ H ₁₀ O ₄	65.75	4.72	66.05	4.62
Id	219—224 (acetone-light petroleum)	C ₁₂ H ₁₀ O ₄	66.05	4.86	66.05	4.62
Ie	219—223 (benzene)	C ₁₃ H ₁₂ O ₄	66.95	5.18	67.23	5.21
If	226—228 (benzene)	C ₁₃ H ₁₂ O ₄	66.96	5.25	67.23	5.21

marin-4-carboxylic acid (I). When necessary, this fraction was rechromatographed on silica gel (2.0 g) using 10% ether-light petroleum as eluent. Melting points and the results of elementary analysis of I are given in Table 4. The IR spectra of Ia and Ib were identical with those of authentic samples synthesized.^{1,3)}

Condensation of 2,5-Xylenol with Sodium Diethyl Oxalacetate. Intimate mixture of 2,5-xylenol (3.97 g) and sodium diethyl oxalacetate (5.25 g) was added into the ice-cooled concd. H₂SO₄ (25 ml). After 7 hr the reaction mixture was poured into ice-water. The solid separated was dissolved in NaOH aq. solution and carbon dioxide was introduced into it to remove unreacted xylenol by filtration. HCl aq. solution was added to the filtrate and the crude product separated was

recrystallized from acetone giving 650 mg of III, mp 165—70°C.

IR spectrum: 1730, 1690, 1620 and 1575 cm⁻¹. Found: C, 60.73; H, 5.20%. Calcd for C₁₂H₁₂O₅: C, 61.01; H, 5.12%.

Sublimation of III gave an anhydride (mp 169°C). IR spectrum: 1820, 1750, 1615 and 1565 cm⁻¹. (Found: C, 65.87; H, 4.68%).

On thin layer chromatography the mother liquor of III showed no spot corresponding to Ic.

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