

A FACILE SYNTHESIS OF CHROMONE-3-CARBOXALDEHYDE*, CHROMONE-3-CARBOXYLIC
ACID* AND 3-HYDROXYMETHYLCHROMONE

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The preparations of chromone-3-carboxaldehydes are little known^{1,2}. Chromone-3-carboxaldehyde was prepared by the reaction of 2-formyl-2'-hydroxyacetophenone derived from o-hydroxyacetophenone with ethyl orthoformate and acetic anhydride¹, and 2,2-difluoro-4-methyl-naphtho-1,3,2-dioxaborin compounds were converted to benzochromone-3-carboxaldehydes by Vilsmeier-Haack reaction². Owing to the synthetic utility of chromone-3-carboxaldehydes, a facile synthetic method was pursued.

We report a novel synthesis of chromone-3-carboxaldehydes from o-hydroxyacetophenones and Vilsmeier reagent, and also new synthetic methods of chromone-3-carboxylic acids* and 3-hydroxymethylchromone from them in this paper.

After the addition of phosphorus oxychloride to the cooled dimethylformamide solution of o-hydroxyacetophenone, the reaction mixture was stood at room temperature for 13 hr and then treated with ice-water to give chromone-3-carboxaldehyde, which was identified with authentic sample¹, in 61% yield. Thus the desired compounds carrying various substituents were prepared by the similar method in one step**.

* Takeda Chemical Industries, Ltd., Belgium Patent No. 769146, 3, Nov., 1971 (OPI).

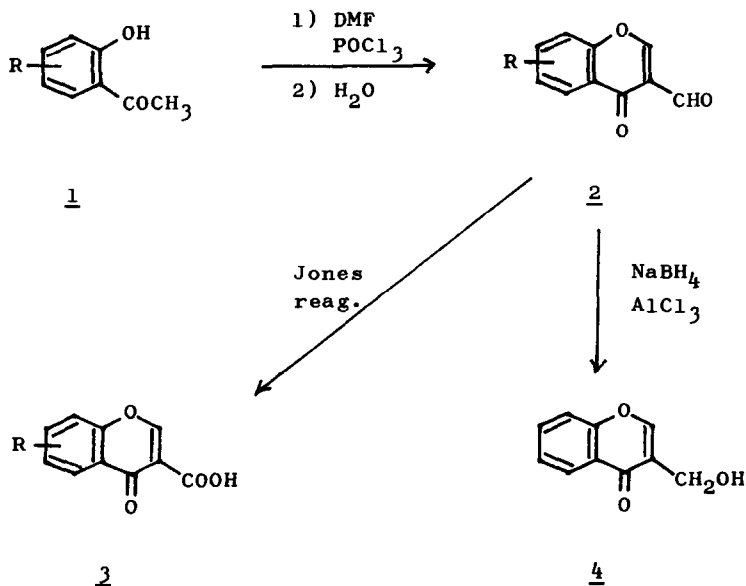
** A similar synthesis was described by H. Harnisch in Ann. Chem., 768, 8 (1972).

Chromone-3-carboxaldehydes 2

R and position	mp (°C)	Yield (%)
6-Methyl-	174 - 175	65
6-Ethyl-	109 - 111	76
6-iso-Propyl-	98 - 99.5	42
5-Methoxy-	115 - 116	61
6-Nitro-	163 - 164	54
6-Chloro-	166 - 168	73
6,8-Dibromo-	177 - 178	40
6-Dimethylamino-	153.5 - 154.5	49
7-Acetoxy-	155 - 156	67
5,7-Diacetoxy-	162 - 163 (dec.)	80
6,7-Diacetoxy-	140 - 141	66
6-Carboxy-	271.5 - 273.5 (dec.)	14

Few of the generally applicable synthetic methods of chromone-3-carboxylic acids³ have been known, and also 3-hydroxymethylchromone derivatives have not been synthesized. So the synthesis of them from chromone-3-carboxaldehydes were tried.

Chromic acid oxidation with Jones reagent of 2 (R=H) at 10-15°C gave chromone-3-carboxylic acid 3 (R=H)⁴, mp 204-205° (decomp.), mass spectrum m/e 190 (M⁺), nmr (d₆-DMSO) δ 9.12 (1H, s, H₂), 8.13 (1H, dd, J 7 and 2 Hz, H₅), 7.4-8.0 (3H, m, H_{6,7,8}), ir (KBr) 1750 (COOH), 1620 (pyrone CO) cm⁻¹, in 39% yield. Similarly, 3 (R=5,7-diacetoxy), mp 155-156° (decomp.), 18.5% yield, mass spectrum m/e 306 (M⁺), ir (KBr) 1780 (OAc), 1750 (COOH), 1635 (pyrone CO) cm⁻¹, nmr (CDCl₃) δ 13.12 (1H, broad, OH), 8.88 (1H, s, H₂), 7.43 (1H, d, J 2 Hz, H₆ or H₈), 7.05 (1H, d, J 2 Hz, H₈ or H₆), 2.42 (3H, s, OAc), 2.37 (3H, s, OAc), and 3 (R=6,7-diacetoxy), mp 189-191° (decomp.), 9.5% yield,



mass spectrum m/e 306 (M^+), ir (KBr) 1785 (OAc), 1765 (COOH), 1625 (pyrone CO) cm^{-1} , nmr (d_6 -DMSO) δ 9.08 (1H, s, H_2), 8.00 (1H, s, H_5), 7.80 (1H, s, H_8), 2.33 (6H, s, OAc), were obtained.

Reduction of 2 (R=H) using sodium borohydride with anhydrous aluminum chloride in tetrahydrofuran afforded 3-hydroxymethylchromone 4, mp 109-111°, mass spectrum m/e 176 (M^+), nmr (CDCl_3) δ 8.20 (1H, dd, J 8 and 2 Hz, H_5), 8.00 (1H, s, H_2), 7.2-7.8 (3H, m, $H_6, 7, 8$), 4.78 (2H, s, CH_2O), 3.47 (1H, broad, OH), ir (KBr) 3350 (OH), 1640 (pyrone CO) cm^{-1} , in 12% yield.

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