

A NOVEL CONVERSION REACTION OF CHROMONE-3-CARBOXALDEHYDES
TO 3-HALOGENOCHROMONES

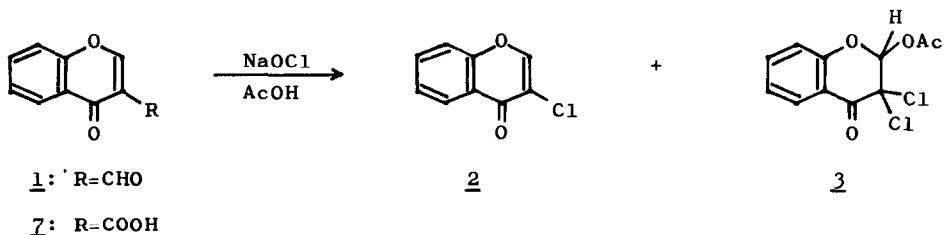
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The synthesis of chromones carrying halogen at C-3 position has been investigated for a long time. The well known method is halogenation of C₂-substituted chromones^{1a} and as another method, Allan-Robinson chromone synthesis with 2'-hydroxy-2-chloroacetophenones and acetic anhydride is rarely employed^{1b}. In the case of C₃-halogenation of C₂-unsubstituted chromones, the desired compounds must be synthesized by the addition of halogen followed by dehydrohalogenation^{1c} to chromone or Friedel-Crafts reaction of α,β -dihalogeno-acrylic acid derivatives with phenols^{1d}. Accordingly it is not so easy.

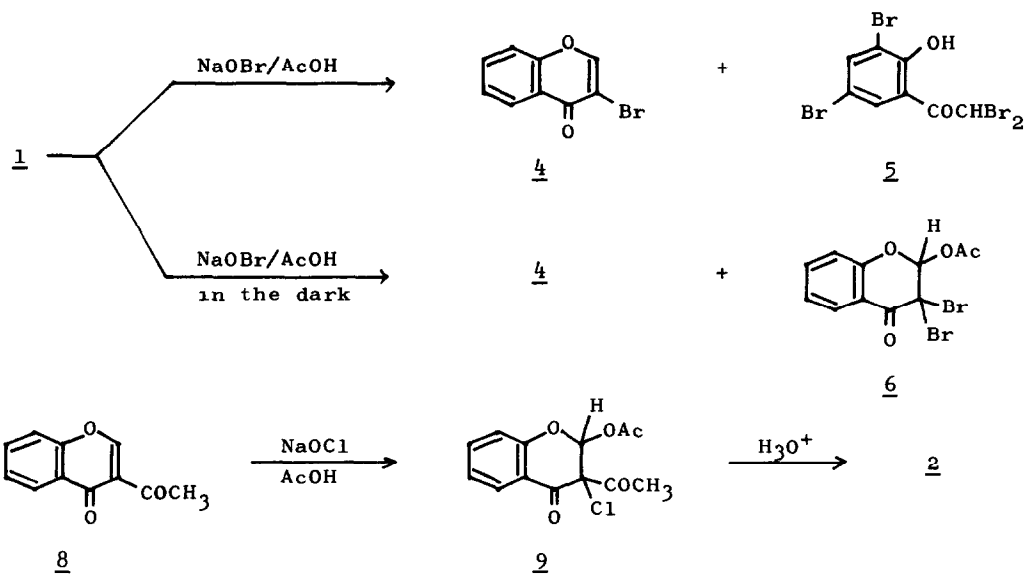
We now wish to report a novel conversion of chromone-3-carboxaldehydes to 3-halogenochromones in one step. Addition of aqueous sodium hypochlorite to the acetic acid solution of chromone-3-carboxaldehyde 1^{2,4} at room temperature gave 3-chlorochromone 2, mp 114-115°, 86% yield, along with 2-acetoxy-3,3-dichlorochromanone 3, mp 86.5-87.5°, 1% yield, mass spectrum m/e 274, 276, 278 (ratio 8:5:1, M⁺); IR (KBr) 1780, 1720 cm⁻¹; UV λ_{\max} (MeOH) 260, 321 nm, similar to o-hydroxyacetophenone; NMR (CDCl₃) δ 8.0 (1H, dd, J 8 and 2 Hz, H₅) 7.4-7.8 (1H, m, H₇), 6.9-7.3 (2H, m, H_{6,8}), 6.72 (1H, s, H₂), 2.10 (3H, s, OAc). The structure of 2 was confirmed by the comparison with authentic sample³.



By applying this reaction to the various chromone-3-carboxaldehydes⁴, the following results were obtained. All of the compounds described here have been characterized spectroscopically and given satisfactory elemental analysis.

Table 1. Conversion of Chromone-3-carboxaldehydes to 3-Chlorochromones with Sodium Hypochlorite in Acetic Acid

Substituents	mp (°C)	Yield (%)
5,7-Diacetoxy-	123 - 124	69
6,7-Diacetoxy-	139 - 140	82
7-Acetoxy-	151 - 152	69
6-Ethyl-	48 - 49	43
6-Nitro-	148 - 148.5	68



On the other hand, the reaction of 1 and sodium hypobromite instead of hypochlorite under the normal laboratory lighting, afforded 3-bromochromone 4⁵, mp 96-97°, 9% yield, ir (KBr) 1650 cm^{-1} ; uv λ_{max} (MeOH) 231, 250 (sh), 302, 307 nm; nmr (CDCl_3) δ 8.25 (1H, s, H_2), 8.2-8.4 (1H, m, H_5), 7.3-7.8 (3H, m, $\text{H}_{6,7,8}$) and 2,2,3',5'-tetrabromo-2'-hydroxyacetophenone 5⁶, mp 124-125°, 24% yield, mass spectrum m/e 448, 450, 452, 454, 456 (ratio 2:8:11:8:2, M^+), ir (KBr) 1655 cm^{-1} ; uv λ_{max} (MeOH) 225, 273 nm; nmr (CDCl_3) δ 11.88 (1H, s, OH), 8.02 (1H, d, J 2 Hz, H_6), 7.95 (1H, d, J 2 Hz, H_4), 6.66 (1H, s, H_2). The formation of 5 in this reaction is probably caused by a radical reaction. The treatment of 1 with sodium hypobromite in the dark to avoid the radical reaction gave 4 in 32% yield, along with 2-acetoxy-3,3-dibromochromanone 6, mp 101-102°, 28.5% yield, ir (KBr) 1775, 1710 cm^{-1} ; uv λ_{max} (MeOH) 262, 323 nm; nmr (CDCl_3) δ 7.95 (1H, dd, J 7 and 2 Hz, H_5), 7.55 (1H, dt, J 7 and 2 Hz, H_7), 6.9-7.27 (2H, m, $\text{H}_{6,8}$), 6.67 (1H, s, H_2), 2.10 (3H, s, OAc).

The reaction between chromone-3-carboxylic acid 7⁴ and sodium hypochlorite gave 2 in 41% and 3 in 29% yield respectively. From this fact, 7 was presumed as the intermediate of the conversion of 1 to 2, but not detected on TLC (silica gel) during this reaction. The reaction of 7 appears to be similar to Hunsdiecker Reaction which is known as the degradation of a heavy metal salt of a carboxylic acid in anhydrous media by means of halogens to a halide of one less carbon atom. However this reaction proceeded in the presence of water.

The reaction of sodium hypochlorite with 3-acetylchromone 8² afforded only 2-acetoxy-3-acetyl-3-chlorochromanone 9, mp 70-71°, 55% yield, mass spectrum m/e 282, 284 (ratio 3:1, M^+); ir (KBr) 1775, 1730, 1705 cm^{-1} ; nmr (CCl_4) δ 7.93 (1H, dd, J 8 and 2 Hz, H_5), 7.45-7.75 (1H, m, H_7), 6.9-7.3 (2H, m, $\text{H}_{6,8}$), 6.62 (1H, s, H_2), 2.57 (3H, s, Ac), 1.98 (3H, s, OAc). The structure of 9 will be supported by the fact that acid hydrolysis of 9 with 1N hydrochloric acid in methanol gave 2.

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