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## Note

# A facile synthesis of new 6-acetamido-3-aroyl-2-styryl chromones

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1-(5′-Acetamido-2′-hydroxyphenyl)-3-aryl-1,3-diketones have been refluxed in acetic anhydride in presence of anhydrous sodium acetate to obtain 6-acetamido-3-aroyl-2-methyl chromones. These chromones on condensation with aryl aldehydes in presence of sodium ethoxide in ethanol yield 6-acetamido-3-aroyl-2-styryl chromones. The structures of the newly synthesized compounds have been confirmed on the basis of their elemental and spectral data.

**Keywords**: Facile, styryl chromones, condensation, aryl aldeydes

The chromones and related compounds are widespread in the plant kingdom from algae to conifers. Chromones have been found to be active in a number of plant cycles, including growth regulation, indole acetic acid oxidation and dormancy inhibition as well as exhibiting cytokinin-type behaviour and stimulating oxygen uptake in plant tissues[1]. The furochromones, Khellin has lipid-altering capability[2], while styryl chromone, Homothamnione has been found as potent cytotoxic agent for P388 lymphocytic leukemia and HL-60 human promyelocytic cell lines *in vitro*[3]. The use of chromones as antiviaral[4], anticancer[5] and anti-inflammatory agents[6] is very well known.

Due to the wide range of biological activities associated with the chromone derivatives, significant attention is paid on the synthesis and evaluation of new chromonyl derivatives. Literature survey reveals that there is scanty information on the chemistry of 6-amino/6-acetamido substituted chromones[7]. The biodynamic properties associated with these systems have prompted the synthesis of new chromones having acetamido and styryl moieties to study the additive effect of these moieties on the biological activity of the parent ring.

## Results and Discussion

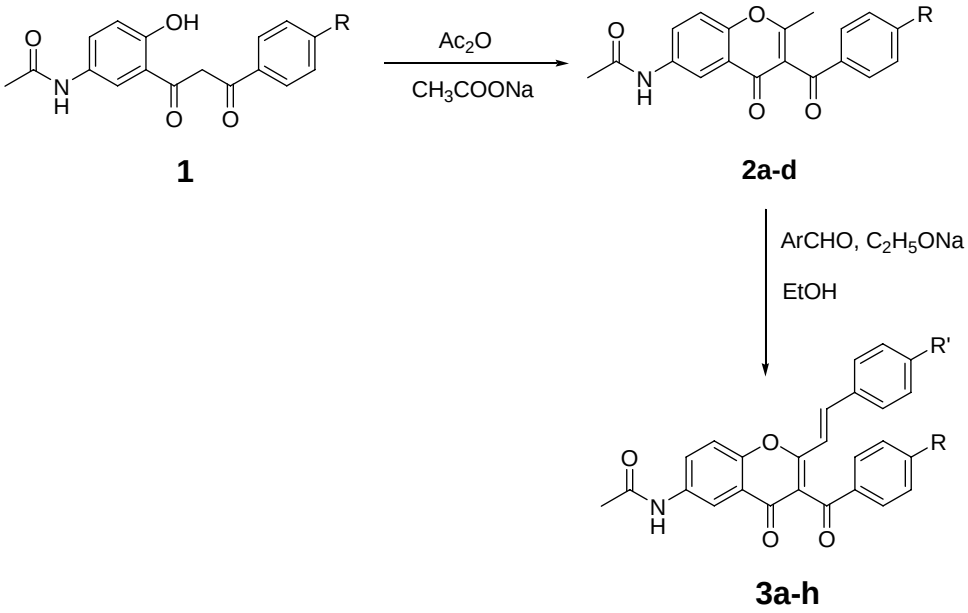
Chromones have been prepared typically from *o*-hydroxyacetophenones in three or more steps *via* either Allan Robinson method[8] or modified Kostanecki Robinson[9] procedure. 2-Styrylchromones have been synthesized either by (i) condensation of cinnamic anhydride and sodium cinnamate with 2,4-dihydroxy phenyl benzyl ketone[10], (ii) condensation of 2-methyl chromones with benzaldehyde in presence of sodium ethoxide[11,12], (iii) Baker-Venkataraman transformation involving the reaction of *o*-hydroxy acetophenones with cinnamoyl chloride in acetone-$K_2CO_3$ medium[13] and (iv) modified Wittig reaction[14].

In an earlier report[15] the synthesis of 1-(5′-acetamido-2′ hydroxyphenyl) -3-aryl-1, 3-diketones **1** is described. These were obtained from 5-acetamido-2-hydroxy acetophenone in two steps. The hydroxyl group of 5-acetophenones was aroylated below 10°C using aroyl chlorides in pyridine to get the corresponding esters. Thereafter, these esters were subjected to B. V. transformation using pyridine and potassium hydroxide to afford 1,3-diketones **1a-d**. These diketones **1a-d** were then refluxed in acetic anhydride in presence of anhydrous sodium acetate to get 6-acetamido-3-aroyl-2-methylchromones **2a-d**. Thus, the obtained chromones **2a-d** were condensed with aryl aldehydes in presence of sodium ethoxide in ethanol to yield the title products, 6-acetamido-3-aroyl-2-styryl chromones **3a-h** (**Scheme I**).

All the newly synthesized compounds were analyzed for CHN and structures were confirmed on the basis of their IR, NMR and mass spectral data.

## Experimental Section

All melting points were determined in open capillary tube and are uncorrected. IR spectra were recorded on a Perkin Elmer FTIR spectrometer. $^1$H NMR spectra were recorded on Bruker FT300 machine at 300 MHz using TMS as internal reference and chemical shifts are expressed in δ, ppm. Mass spectra were obtained using Finnigan 1020 mass spectrometer. The characterization data of newly synthesized compounds are given in **Table I**. The experimental procedures are described as representative cases. Yields of the products were recorded after crystallization.




Where, R= H, $CH_3$, $OCH_3$, Cl

R' = H, Cl

**Scheme I**

**Table I** — Characterization data of compounds **2a-d** and **3a-h**

| Compd | R | R′ | m.p. °C | Yield % | Mol. Formula | Found (Calcd)% C | H | N |
|---|---|---|---|---|---|---|---|---|
| **2a** | H | H | 212 | 70 | $C_{19}H_{15}NO_4$ | 70.85 (71.02 | 4.54 4.67 | 4.24 4.36) |
| **2b** | $CH_3$ | H | 210 | 64 | $C_{20}H_{17}NO_4$ | 71.55 (71.64 | 4.97 5.07 | 4.07 4.18) |
| **2c** | $OCH_3$ | H | 194 | 68 | $C_{20}H_{17}NO_5$ | 68.19 (68.37 | 4.27 4.84 | 3.90 3.99) |
| **2d** | Cl | H | 222 | 61 | $C_{19}H_{14}ClNO_4$ | 64.18 (64.22 | 3.84 3.94 | 3.81 3.94) |
| **3a** | H | H | 275 | 52 | $C_{26}H_{19}NO_4$ | 76.11 (76.28 | 4.56 4.64 | 3.33 4.42) |
| **3b** | H | Cl | 252 | 58 | $C_{26}H_{18}ClNO_4$ | 71.53 (71.64 | 4.01 4.13 | 3.02 3.16) |
| **3c** | $CH_3$ | H | 260 | 56 | $C_{27}H_{21}NO_4$ | 76.50 (76.59 | 4.79 4.96 | 3.22 3.31) |
| **3d** | $CH_3$ | Cl | 263 | 53 | $C_{27}H_{20}ClNO_4$ | 78.73 (70.81 | 4.22 4.37 | 2.89 3.06) |
| **3e** | $OCH_3$ | H | 271 | 61 | $C_{27}H_{21}NO_5$ | 73.7 (73.80 | 4.62 4.78 | 3.03 3.19) |
| **3f** | $OCH_3$ | Cl | 269 | 55 | $C_{27}H_{21}NO_4$ | 68.29 (68.42 | 4.36 4.43 | 2.83 2.96) |
| **3g** | Cl | H | 265 | 51 | $C_{19}H_{15}ClNO_4$ | 70.21 (70.34 | 4.01 4.05 | 3.01 3.16) |
| **3h** | Cl | Cl | 273 | 57 | $C_{26}H_{17}C_{l2}NO_4$ | 65.16 (65.27 | 3.48 3.55 | 2.80 2.93) |

**Synthesis of 6-acetamido-3-benzoyl-2-methyl chromone, 2a**. 1-(6′-Acetamido-2′-hrdroxy)-3-phenyl propane-1,3-dione (10 mmole) was dissolved in acetic anhydride (25 mL). To this solution, fused sodium acetate (50 mmole) was added and the reaction mixture refluxed for 3 hr. The reaction mixture was then cooled to RT and poured over crushed ice. It was further stirred vigorously for 30 min. The solid obtained was filtered, washed with water and purified by recrystallization from ethanol.

IR (Nujol): 3190 (N-H), 1723 (amide C=O) 1670 (C=C) and 1215 $cm^{-1}$ (C-O-C); $^1$H NMR ($CDCl_3$): δ 2.32 (s,3 H, $CH_3$), 2.42 (s,3H,$COCH_3$) and 7.42-8.8 (m, 9H, ArH and NH); MS: *m/z* (%) 321 (100, $M^{+\cdot}$), 320 (57), 306 (77.9), 292 (58.8), 278 (13.6), 250 (12.8), 228 (24.8), 201 (4.3) 178 (8.8) 105 (32.1) and 77 (26.3).

**Synthesis of 6-acetamido-3-benzoyl-2-styryl-chromone, 3a**. Chromone **2a** (10, mmole) was dissolved in ethanol (25 mL).To this solution sodium ethoxide (20 mmole) was added. Benzaldehyde (10 mmole) was then added slowly to the above reaction mixture and then it was stirred at RT for 24 hr. After completion of the reaction, alcohol was removed under reduced pressure and the residue was cooled. The solid obtained was filtered, washed with cold ethanol and purified by recrystalization from ethanol.

IR (Nujol): 3298 (N-H), 1687 ( C=O) 1600 (vinylic) and 1217 $cm^{-1}$ (C-O-C); $^1$H NMR ($CDCl_3$+DMSO-$d_6$): δ 2.16 (s, 3H, $CH_3$), 6.76-8.22 (m, 15H, ArH and vinylic H) and 9.96 (s, 1H, NH); MS: *m/z* (%) 409 (5, $M^{+\cdot}$, unstable), 279 (53.3), 238 (20), 237 (100), 210 (20), 135 (53.3), 134 (22), 107 (24) and 79 (7.3).

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