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LETTERS TO THE EDITOR

CONVENIENT METHOD FOR SYNTHESIS OF 3-(HET)-ARYL-8-FORMYL-7-HYDROXY-CHROMONES

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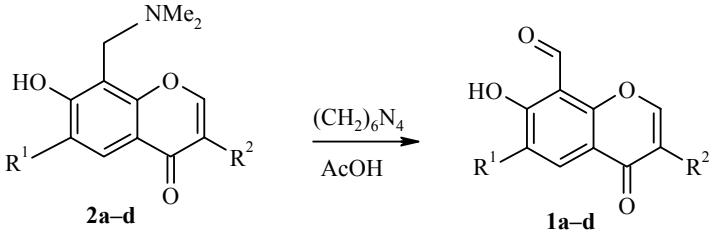
The main method of formylating 7-hydroxychromones (flavones, isoflavones) is the Duff reaction, enabling products of type **1** to be obtained in 32-59% yield [1]. In [2] the synthesis of 8-formyl-7-hydroxy-2,3-dimethylchromone was presented starting from a Mannich base under the conditions of the Duff reaction in low yield (17%).



1, **2 a** R^1 = H, R^2 = 2-ClC_6H_4, **b** R^1 = Et, R^2 = 5-methoxycarbonyl-2-methylfur-3-yl, **c** R^1 = *n*-Pr, R^2 = 2-benzothiazolyl, **d** R^1 = Me, R^2 = 3-isoxazolyl

We decided to check the range of application of this method to isoflavones and their heterocyclic analogs. On boiling 8-dimethylaminomethyl derivatives of 7-hydroxychromones for 1 h with aryl (**2a**), furyl (**2b**), benzothiazolyl (**2c**), and isoxazolyl (**2d**) substituents in position 3 of the chromone ring with an excess (1.75 fold) of hexamethylenetetramine (urotropin) in acetic acid, with subsequent acid hydrolysis, the corresponding 8-formyl derivatives **1a-d** were isolated in high yield (76-80%). It was thus shown that this method is rapid and convenient for the synthesis of formyl derivatives of isoflavones and their analogs bearing residues of oxygen-, sulfur-, and nitrogen-containing five-membered heterocycles in position 3 of the chromone system.

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3-(2-Chlorophenyl)-8-formyl-7-hydroxychromone (1a). Yield was 76%; mp 165°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.09 (1H, d, *J* = 9.2, H-6); 7.35-7.50 (4H, m, H Ar); 8.23 (1H, d, *J* = 9.2, H-5); 8.31 (1H, s, H-2); 10.53 (1H, s, CHO); 12.27 (1H, s, OH). Found, %: Cl 11.68. $C_{16}H_9ClO_4$. Calculated, %: Cl 11.79.

6-Ethyl-8-formyl-7-hydroxy-3-(5-methoxycarbonyl-2-methyl-3-furyl)chromone (1b). Yield was 76%; mp 179°C (MeCN). ^{1}H NMR spectrum, δ, ppm: 1.27 (3H, t, *J* = 7.6, 6-C<u>H</u>$_3$CH$_2$); 2.41 (3H, s, 2'-CH$_3$); 2.74 (2H, q, *J* = 7.6, 6-CH$_3$C<u>H</u>$_2$); 3.83 (3H, s, 5-CH$_3$CO$_2$); 7.34 (1H, s, H-4'); 8.12 (1H, s, H-5); 8.43 (1H, s, H-2); 10.53 (1H, s, CHO); 12.82 (1H, s, OH). Found, %: C 64.33; H 4.35. $C_{19}H_{16}O_7$. Calculated, %: C 64.04; H 4.53.

3-(Benzothiazol-2-yl)-8-formyl-7-hydroxy-6-propylchromone (1c). Yield was 80%; mp 242-243°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00 (3H, t, *J* = 7.2, 6-C<u>H</u>$_3$CH$_2$CH$_2$); 1.69 (2H, m, 6-CH$_3$C<u>H</u>$_2$CH$_2$); 2.70 (2H, t, *J* = 7.2, 6-CH$_3$CH$_2$C<u>H</u>$_2$); 7.39 (1H, t, *J* = 8.0, H-6'); 7.50 (1H, t, *J* = 8.0, H-5'); 7.99 (1H, d, *J* = 8.0, H-7'); 8.67 (1H, d, *J* = 8.0, H-4'); 8.21 (1H, s, H-5); 9.35 (1H, s, H-2); 10.57 (1H, s, CHO); 12.83 (1H, s, OH). Found, %: N 3.92; S 8.69. $C_{20}H_{15}NO_4S$. Calculated, %: N 3.83; S 8.77.

8-Formyl-7-hydroxy-3-(isoxazol-3-yl)-6-methylchromone (1d). Yield was 80%; mp 263°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.34 (3H, s, 6-CH$_3$); 7.07 (1H, d, *J* = 1.6, H-4'); 8.17 (1H, s, H-5); 8.84 (1H, s, H-2); 8.88 (1H, d, *J* = 1.6, H-5'); 10.54 (1H, s, CHO); 12.77 (1H, s, OH). Found, %: N 5.15. $C_{14}H_9NO_5$. Calculated, %: N 5.16.

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