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# 4,4'-SPIRODICHROMAN-2-ONES AS UNEXPECTED PRODUCTS FROM THE CONDENSATION OF RESORCINOLS AND DIMETHYL ACETONEDICARBOXYLATE

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*As a result of the reaction of resorcinols with dimethyl acetonedicarboxylate under the conditions of the Pechmann reaction derivatives of 4,4'-spirodichroman-2-one were isolated as anomalous condensation products. Their structure was demonstrated by spectral methods. A mechanism was proposed for the formation of the spirodilactone system.*

**Keywords:** coumarins, coumarin-4-acetic acids, spirodilactones, 4,4'-spirodichroman-2-one, Pechmann reaction.

The reaction of phenols and the esters of β-keto acids in the presence of dehydrating agents such as concentrated sulfuric acid is known as the Pechmann reaction [1]. This condensation has found widespread use in the synthesis of compounds based on the benzopyran-2-one system [2, 3]. The course of the reaction and the structure of the products depend on the nature of the phenols and the β-keto esters and also on the nature of the condensing agent. The Pechmann reaction can also give other products and, in particular, chromones, diarylglutamic acids and their anhydrides, dilactones, etc. [1, 4].

In the reaction of resorcinol and dimethyl acetonedicarboxylate in methanol in the presence of concentrated sulfuric acid as condensing agent, in addition to the expected product of the Pechmann reaction [methyl 7-hydroxycoumarin-4-acetate (**1**)] we also obtained a 16% yield of the product **2**, which differed from the benzopyran-2-one derivatives in its spectral characteristics. In the UV spectrum of compound **2** there is one strong absorption maximum at 204 nm, whereas the derivatives of the 7-hydroxycoumarins have two strong maxima at 210-225 and 310-325 nm [5]. In the IR spectrum of compound **2** there are strong bands at 1745 (characteristic of the saturated lactone) and 3435 $cm^{-1}$ (due to the stretching vibrations of the phenol group). The $^1H$ NMR spectrum of the product **2** in the region of the aromatic protons contains a system of ABX protons, a broad one-proton singlet for the hydroxy group at 9.81 ppm, and two one-proton doublets with $J = 15.0$ Hz at 2.97 and 3.16 ppm. The $^{13}C$ NMR spectrum contains a signal at 38.20 ppm for the quaternary carbon atom. A molcular-ion peak of high intensity with $m/z$ 312 $[M]^+$ (96%) is observed in the mass spectrum of compound **2**. Compound **2** is consequently 4,4'-spirodi[7-hydroxychroman-2-one].

During the condensation of 2-methylresorcinol and dimethyl acetonedicarboxylate under analogous conditions methyl 7-hydroxy-8-methylcoumarin-4-acetate (**3**) and 4,4'-spirodi[7-hydroxy-8-methylchroman-2-one] (**4**) were isolated with yields of 64 and 11% respectively.

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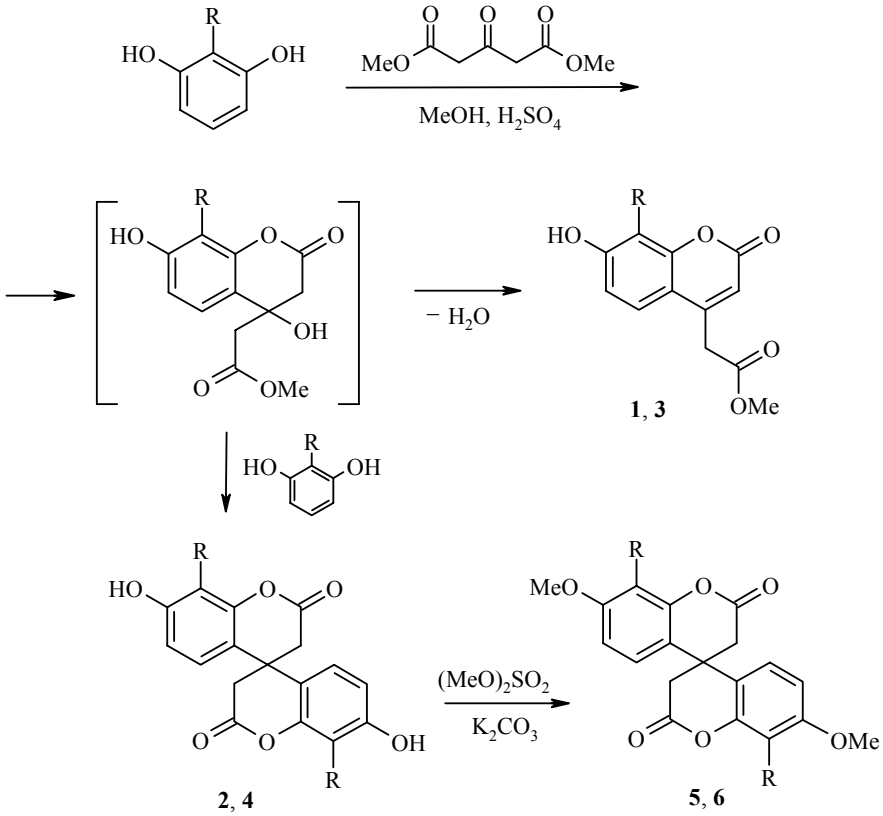
It can be supposed that the reaction of resorcinols and dimethyl acetonedicarboxylate takes place through electrophilic alkylation and lactonization with the formation of a derivative of 4,7-dihydroxychroman-2-one as intermediate compound. Dehydration of the latter with concentrated sulfuric acid leads to the formation of coumarin-4-acetate esters **1** and **3**. Condensation of the intermediate with another molecule of resorcinol leads to the formation of the 4,4'-spirodichroman-2-one system. It should be noted that the use of two mols of the resorcinol to one mol of the dimethyl acetonedicarboxylate in the condensation leads to an insignificant increase in the yield of the respective 4,4'-spirodichroman-2-one **2**, and the main product of the Pechmann reaction is the coumarin-4-acetate ester **1**.

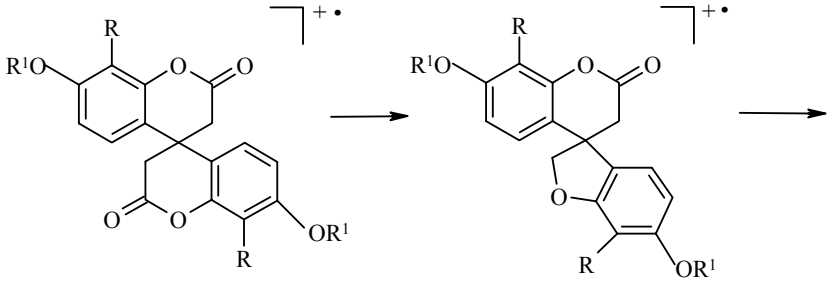
Alkylation of the phenolic hydroxyls of compounds **2** and **4** under the conditions of the Williamson reaction by the action of dimethyl sulfate in acetone leads to the formation of the corresponding methyl ethers **5** and **6**.




**1**, **2**, **5** R = H, **3**, **4**, **6** R = Me

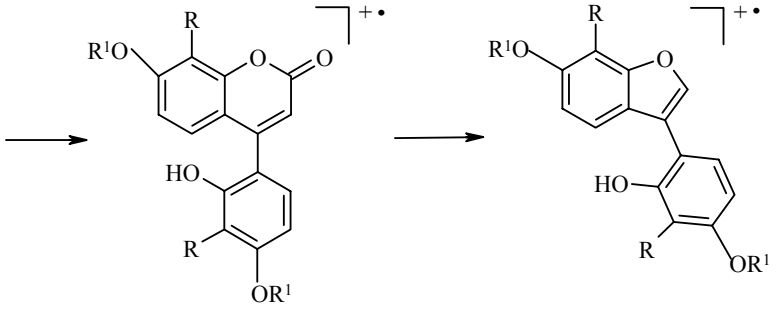
The structure of the isolated side products from the Pechmann condensation and their methyl ethers was confirmed by the data from mass spectrometry. The mass spectra of compounds **2** and **4-6** contain strong molcular-ion peaks corresponding to their empirical formulas. The fragmentation of the compounds under electron impact is fairly general in nature. The presence of the [M−28], [$M^+$−42], and [$M^+$−70] peaks in the mass spectra of compounds **2** and **4-6** makes it possible to suggest the main paths for the fragmentation of the molcules under electron impact.

It should also be noted that the formation of 4,4'-spirodichroman-2-ones is not observed during the condensation of phloroglucinol, pyrogallol, and orcinol with dimethyl acetonedicarboxylate, and the reaction takes place with the exclusive formation of the corresponding methyl coumarin-4-acetates.



**2** *m/z* 312 (96%)
**4** *m/z* 340 (100%)
**5** *m/z* 340 (100%)
**6** *m/z* 368 (100%)

**2** *m/z* 284 (10%)
**4** *m/z* 312 (4%)
**5** *m/z* 312 (8%)
**6** *m/z* 340 (15%)



**2** *m/z* 270 (59%)
**4** *m/z* 298 (71%)
**5** *m/z* 298 (72%)
**6** *m/z* 326 (83%)

**2** *m/z* 242 (100%)
**4** *m/z* 270 (83%)
**5** *m/z* 270 (63%)
**6** *m/z* 298 (36%)

## EXPERIMENTAL

The reactions and the individuality of the compounds were monitored by TLC on Merck 60 F254 plates with 9:1 and 95:5 chloroform–methanol solvent systems as eluants. The melting points were determined on a Kofler hot bench. The IR spectra were measured on a Nicolet FTIR Nexus 475 spectrometer, and the UV spectra were obtained on a Specord M-40 spectrometer. The $^{1}H$ and $^{13}C$ NMR spectra were recorded on Varian VXR-300 (300 and 75 MHz respectively) and Varian Mercury-400 (400 and 100 MHz respectively) in DMSO-$d_6$ with TMS as internal standard. The mass spectra were recorded on a Varian MAT-311A instrument with ionization energy 70 eV.

**Pechmann Condensation** (General Procedure). To a cooled solution (0°C) of 200 ml of the respective polyphenol and dimethyl acetonedicarboxylate (20 mmol, 29.5 ml) in 30 ml of absolute methanol with vigorous stirring and cooling we added dropwise 20 ml of concentrated sulfuric acid. The reaction mixture was stirred until completely solid and left at room temperature overnight. The mixture was transferred to 500 ml of iced water, the precipitate was filtered off and crystallized from methanol, and compound **1** or **3** was obtained. The methanol mother solution was evaporated under the vacuum of a rotary evaporator, the oily residue was crystallized from acetonitrile, and compound **2** or **4** was isolated.

**Methyl 2-(7-Hydroxy-2- oxochromen-4-yl) acetate (1).** The yield was 60%; mp 215-217 ºC (mp 220 ºC [6, 7], 221-223 ºC [8]). IR spectrum, ν, $cm^{-1}$: 3360 (OH), 1726 (C=O), 1690 (C=O), 1680, 1604 (C=C), 1400, 1342, 1204, 1140. UV spectrum (MeCN), $\lambda_{max}$ (log ε): 202 (4.78), 218 (4.34), 322 (4.25). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.66 (3H, s, $COOCH_3$), 3.95 (2H, s, $CH_2$-4), 6.24 (1H, s, H-3), 6.74 (1H, d, *J* = 2.1, H-8), 6.81 (1H, dd, *J* = 2.1, *J* = 8.7, H-6), 7.52 (1H, d, *J* = 8.7, H-5), 10.56 (1H, br. s, OH-7).

**Methyl 2-(7-Hydroxy-8-methyl-2-oxochromen-4-yl)acetate (3).** The yield was 64%; mp 190-193 ºC. IR spectrum, ν, $cm^{-1}$: 3228 (OH), 2956, 1724 (C=O), 1692 (C=O), 1602 (C=C), 1576, 1320, 1258, 1090, 874, 850, 726. UV spectrum (MeCN), $\lambda_{max}$ (log ε): 203 (4.67), 220 (4.21), 322 (4.14). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.18 (3H, s, 8-$CH_3$), 3.65 (3H, s, $COOCH_3$), 3.86 (2H, s, $CH_2$-4), 6.16 (1H, s, H-3), 6.82 (1H, d, *J* = 8.7, H-6), 7.27 (1H, d, *J* = 8.7, H-5), 10.33 (1H, br. s, OH-7). The ester (**3**) was then used without further purification.

**4,4'-Spirodi[7-hydroxychroman-2-one (2).** The yield was 16%, mp. 308.5-309.5 ºC. IR spectrum, ν, $cm^{-1}$: 3435 (OH), 1745 (C=O), 1620 (C=C), 1441, 1330, 1285, 1256, 1190, 1075. UV spectrum (EtOH), $\lambda_{max}$ (log ε): 204 (4.90). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.97 (1H, d, *J* = 5.0, H-3a), 3.16 (1H, d, *J* = 15.0, H-3b), 6.51 (1H, dd, *J* = 2.1, *J* = 8.7, H-6), 6.55 (1H, d, *J* = 2.1, H-8), 6.74 (1H, d, *J* = 8.7, H-5), 9.81 (1H, br. s, OH-7). $^{13}$C NMR spectrum, δ, ppm: 38.20 (C-4), 40.19 (C-3), 105.56 (C-8), 112.69 (C-6), 118.42 (C-5a), 126.84 (C-5), 152.03 (C-8a), 158.66 (C-7), 167.11 (C-2). Mass spectrum (EI), *m/z* ($I_{rel}$, %): 312 $[M]^+$ (96), 284 (10), 270 (59), 253 (14), 242 (100), 225 (13), 213 (15), 197 (7), 185 (5), 157 (3). Found, %: C 65.12; H 3.61. $C_{17}H_{12}O_6$. Calculated, %: C 65.39; H 3.87.

**4,4'-Spirodi[7-hydroxy-8-methylchroman-2-one] (4).** The yield was 11%, mp 320-321 ºC. IR spectrum, ν, $cm^{-1}$: 3444 (OH), 1748 (C=O), 1620 (C=C), 1432, 1332, 1290, 1270, 1256, 1198, 1076. UV spectrum (EtOH), $\lambda_{max}$ (log ε): 207 (4.75). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.09 (3H, s, 8-$CH_3$), 2.99 (1H, d, *J* = 15.2, H-3a), 3.19 (1H, d, *J* = 15.2, H-3b), 6.59 (1H, d, *J* = 9.2, H-6), 6.62 (1H, d, *J* = 9.2, H-5), 9.84 (1H, br. s, OH-7). $^{13}$C NMR spectrum, δ, ppm: 9.16 ($CH_3$-8), 38.42 (C-4), 40.01 (C-3), 111.44 (C-8), 112.81 (C-6), 116.84 (C-5a), 123.32 (C-5), 150.16 (C-7), 156.76 (C-8a), 167.27 (C-2). Mass spectrum (EI), *m/z* ($I_{rel}$, %): 340 $[M]^+$ (100), 312 (4), 298 (71), 297 (71), 281 (14), 270 (83), 253 (22), 241 (9), 227 (6), 198 (5). Found, %: C 66.92; H 4.53. $C_{19}H_{16}O_6$. Calculated, %: C 67.05; H 4.74.

**4,4'-Spirodi[7-methoxychroman-2-ones] 5 and 6.** To a solution of 5 mmol of the hydroxy derivative **3** or **4** in 20 ml of absolute acetone, containing 2.76 g (20 mmol) of freshly calcined potassium carbonate, while stirring and heating we added 0.95 ml (10 mmol) of dimethyl sulfate. The reaction mixture was kept at 50-60°C for 1-2 h. (The end of the reaction was determined by TLC.) After cooling to room temperature the mixture was transferred to 200 ml of a 1 N solution of sulfuric acid, and the precipitated product was filtered off and crystallized from aqueous methanol.

**4,4'-Spirodi[7-methoxychroman-2-one] (5).** The yield was 94%; mp 194-195.5 °C. IR spectrum, ν, $cm^{-1}$: 1776 (C=0), 1620 (C=C), 1584 (C=C), 1512, 1504, 1440, 1264, 1162, 1120, 978. UV spectrum (EtOH), $\lambda_{max}$ (log ε): UV spectrum (MeCN), $\lambda_{max}$ (log ε): 205 (4.85). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.10 (H, d, *J* = 14.8, H-3a), 3.32 (H, d, *J* = 14.8, H-3b), 3.77 (3H, s, 7-$CH_3$0), 6.78 (H, dd, *J* = 2.4, *J* = 8.8, H-6), 6.87 (H, d, *J* = 2.4, H-8), 6.89 (H, d, *J* = 8.8, H-5). $^{13}$C NMR spectrum, δ, м. д.: 38.17 (C-4), 40.24 (C-3), 56.20 (7-$CH_3$0), 103.36 (C-8), 111.66 (C-6), 118.10 (C-5a), 127.04 (C-5), 152.16 (C-8a), 160.76 (C-7), 166.88 (C-2). Mass spectrum (EI), *m/z* ($I_{rel}$, %): 340 $[M]^+$ (100), 312 (8), 298 (72), 281 (13), 270 (63), 255 (45), 239 (35), 227 (5), 211 (5), 199 (4). Found, %: C 69.79; H 4.66. $C_{19}H_{16}O_6$. Calculated, %: C 67.05; H 4.74.

**4,4'-Spirodi[7-methoxy-8-methylchroman-2-one] (6).** The yield was 95%; mp 259-260.5 °C. IR spectrum, ν, $cm^{-1}$: 1784 (C=0), 1618 (C=C), 1592 (C=C), 1496, 1430, 1304, 1252, 1180, 1116, 1076. UV spectrum (EtOH), $\lambda_{max}$ (log ε): 208 (4.88). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.13 (3H, s, 8-CH3), 3.05 (H, d, *J* = 15.2, H-3a), 3.27 (H, d, *J* = 15.2, H-3b), 3.80 (3H, s, 7-$OCH_3$), 6.76 (H, d, *J* = 8.8, H-6), 6.81 (H, d, *J* = 8.8, H-5). $^{13}$C NMR spectrum, δ, ppm: 9.16 (8-$CH_3$), 38.55 (C-4), 40.24 (C-3), 56.41 (7-$CH_3$0), 107.39 (C-8), 114.38

(C-6), 118.54 (C-5a), 123.72 (C-5), 149.76 (C-7), 158.36 (C-8a), 166.99 (C-2). Mass spectrum (EI), *m/z* ($I_{rel}$, %): 368 $[M]^+$ (100), 340 (15), 326 (83), 325 (84), 309 (13), 298 (36), 283 (31), 267 (55), 255 (6), 184 (9), 165 (22), 149 (20). Found, %: C 68.21; H 5.21. $C_{21}H_{20}O_6$. Calculated, %: C 68.47; H 5.47.

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