

## A NEW METHOD FOR ANNULATION OF THE $\alpha$ -PYRONE RING

V. F. Traven, I. V. Voevodina, A. V. Manaev, and N. Ya. Podkhalyuzina

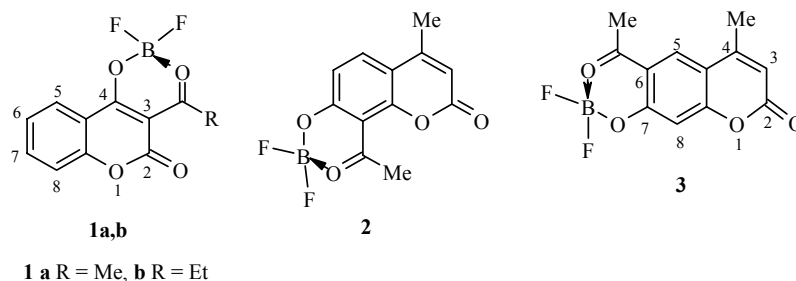
*New derivatives of coumarin, containing annulated  $\alpha$ -pyrone rings, were obtained by reaction of the borate complexes of three isomeric acyl(hydroxy)coumarins with acid anhydrides. It was shown that the borate complex of 3-acetyl-4-hydroxy-2-pyrone also condenses with acetic anhydride to form a derivative containing a new annulated  $\alpha$ -pyrone ring.*

**Keywords:** 3-acetyl-4-hydroxy-2-pyrone, acyl(hydroxy)coumarins, borate complexes,  $\alpha$ -pyrone ring, condensation.

Annulation reactions of the pyrone ring are well known both in benzene derivatives and in heterocyclic compounds—the Kostanecki–Robinson [1, 2], Allan–Robinson [3, 4], and Bargellini [5] reactions. An  $\alpha$ -pyrone but more often a  $\gamma$ -pyrone ring is formed during the reaction, depending on the structure of the reagents and the conditions. For example, 4-methylcoumarin is mostly formed when *o*-hydroxyacetophenone is heated with acetic anhydride in the presence of sodium acetate (the Kostanecki–Robinson reaction), while 2,3-dimethylchromone is obtained when *o*-hydroxypropiophenone is heated under the same conditions [1].

Examples of annulation of the pyrone ring in coumarin derivatives are also known [6, 7]. For example, 4-hydroxy-3-propionyl- and 4-hydroxy-3-phenylacetyl coumarins undergo annulation with the formation of new  $\gamma$ -pyrone rings when heated with acetic anhydride in the presence of sodium acetate. A distinct preference for annulation of the  $\alpha$ -pyrone ring is only observed under the conditions of the Bargellini reaction [5]. When *o*-hydroxyacetophenone, *o*-hydroxybenzophenone, and *o*-hydroxypropiophenone are heated with acetic anhydride in the presence of sodium phenylacetate the corresponding coumarins are mostly formed.

While studying the condensation of the borate complexes of acyl(hydroxy)coumarins [8], we established that their reaction with carboxylic acid anhydrides led to exclusive annulation of the  $\alpha$ -pyrone ring.

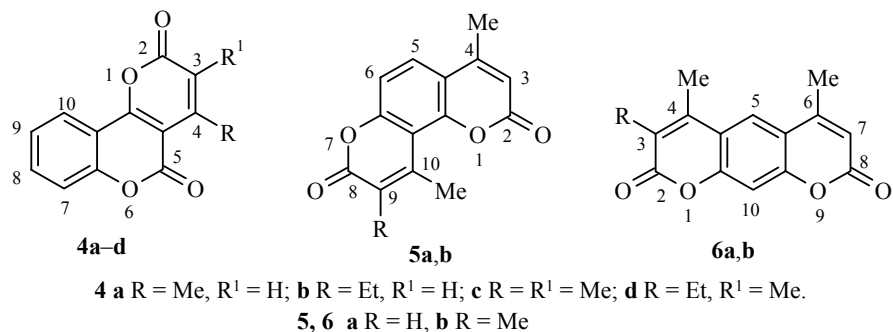


The borate complexes of 3-hydroxycoumarin (complex **1a**), 4-hydroxy-3-propionylcoumarin (complex **2**), and 6-acetyl-7-hydroxy-4-methylcoumarin (complex **3**) were condensed with acetic and propionic anhydrides. Complexes **1-3** were obtained by the reaction of boron trifluoride etherate with the respective acyl(hydroxy)coumarins in benzene [9].

---

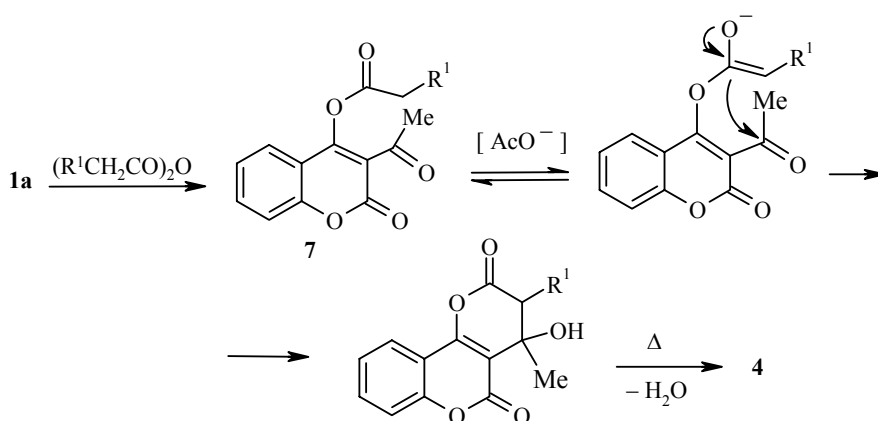
D. Mendeleev University of Chemical Technology of Russia, Moscow, 125047; e-mail: traven@muctr.edu.ru. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 4, pp. 513-517, April, 2007. Original article submitted September 12, 2006.

It was found that the action of heat on the complexes **1-3** both with acetic and with propionic anhydride led to the formation of the respective condensed  $\alpha$ -pyrone structures **4-6**. This reaction path was confirmed by the  $^1\text{H}$  NMR spectra, the mass spectra, and elemental analysis.



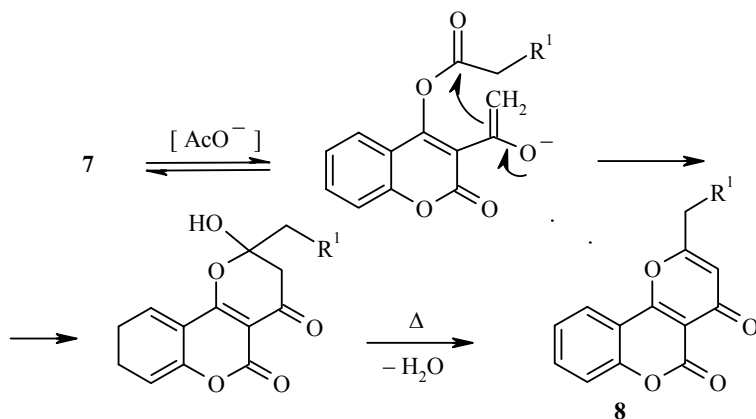
The reaction of acyl(hydroxy)coumarins with acid anhydrides most likely takes place according to the following scheme, shown for the case of the transformation of the complex **1a**.

Scheme 1

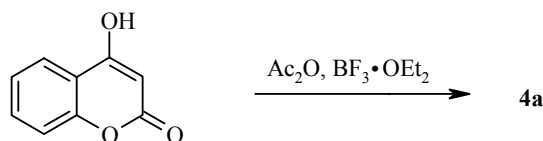


Acylation at the hydroxy group probably takes place at the first stage, and the deciding role in such a reaction path is played by the boron atom coordinated with the oxygen atoms of the acetyl and hydroxyl groups. The obtained ester **7** is enolized at the ester group. Cyclization of the obtained enolate leads to the coumarin derivative **4**, containing an annulated  $\alpha$ -pyrone ring. In the case of enolization of the acetyl group in compound **7** the formation of the  $\gamma$ -pyrone derivatives **8** as final products should be expected, but they were not detected even in trace quantities (scheme 2).

Scheme 2

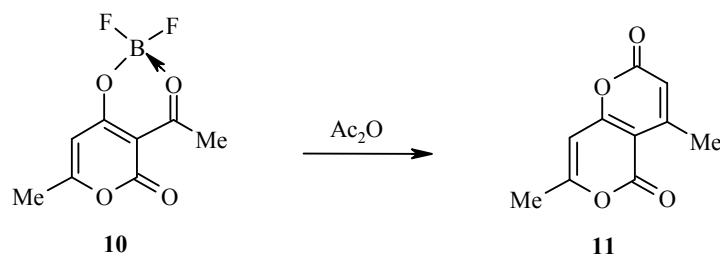


In order to confirm scheme 1 compound **4a** was prepared by an alternative method [6]. The results a mixed melting test with the sample obtained in this way and compound **4a** showed the absence of a melting point depression. The identity of the two samples was confirmed by spectral data. We also obtained compound **4a** in a single stage from 4-hydroxycoumarin, acetic anhydride, and boron trifluoride etherate.



On the other hand, the reaction of 7-hydroxy-4-methylcoumarin with acetic anhydride in the presence of boron trifluoride etherate stops at the stage of O-acylation with the formation of 7-acetoxy-4-methylcoumarin (**9**).

The fact that the new  $\alpha$ -pyrone ring can be annulated with identical success under our investigated conditions both on the side of the pyrone ring in the coumarin (compounds **4a-d**) and on the side of the benzene ring (compounds **5a,b** and **6a,b**) shows that the discussed scheme for annulation of the  $\alpha$ -pyrone ring is universal. This is also demonstrated by the results from study of the reaction of the complex **10** with acetic anhydride. 4,7-Dimethyl-2H, 5H-dihydropyrano[3,2-*c*]pyran-2,5-dione (compound **11**) was isolated with a yield of 72% in full agreement with scheme 1.



## EXPERIMENTAL

The  $^1\text{H}$  NMR spectra were obtained in  $\text{CDCl}_3$  on a Bruker WP-200 SY spectrometer (200 MHz) with TMS as internal standard. The chromatomass spectra were recorded on a PE SCIEX API165 spectrometer (ELSD UV-254), Synergi  $2\mu$  Hydro-RP Mercury column,  $20 \times 2.0$  mm.

The borate complexes **1a** and **2** were obtained as described earlier [9].

**Borate Complexes 1b and 3.** A solution of (0.1 mol) of acyl(hydroxy)coumarin in the smallest amount of dry benzene was boiled until the acyl(hydroxy)coumarin had completely dissolved, (15.62 g, 0.11 mol) of boron trifluoride etherate was added, and the mixture was boiled for 1 h. The precipitate was filtered off, washed with benzene, and dried in air.

**4-Difluoroboryloxy-3-propionyl-coumarin, 3'O $\rightarrow$ B-Chelate (1b).** The yield was 75%; mp 105-107°C (from toluene).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 1.24 (3H, t,  $J = 6.5$ ,  $\text{CH}_2\text{CH}_3$ ); 3.02 (2H, q,  $J = 6.5$ ,  $\text{CH}_2\text{CH}_3$ ); 7.33 (2H, m, H-7,8), 7.87 (1H, t,  $J = 8.3$ , H-6); 8.08 (1H, d,  $J = 8.3$ , H-5). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 266 (45). Found, %: C 54.06; H 3.44.  $\text{C}_{12}\text{H}_9\text{BF}_2\text{O}_4$ . Calculated, %: C 54.14; H 3.38.

**6-Acetyl-7-difluoroboryloxycoumarin, 6'-O $\rightarrow$ B-chelate (3).** The yield was 63%; mp 188-190°C (from toluene).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 2.47 (6H, s,  $2\text{CH}_3$ ); 7.23 (1H, s, H-3); 7.71 (1H, s, H-5); 8.25 (1H, s, H-8). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 266 (55). Found, %: C 54.23; H 3.29.  $\text{C}_{12}\text{H}_9\text{BF}_2\text{O}_4$ . Calculated, %: C 54.14; H 3.38.

**Condensation of Borate Complexes of Acylhydroxycoumarins with Acid Anhydrides.** A solution of 1 g of the borate complex **1**, **2**, or **3** in 7 ml of the anhydride was boiled for 1 h. The precipitate was filtered off and washed on the filter first with water and then with alcohol. The product was recrystallized from alcohol.

**4-Methyl-2H,5H-pyrano[3,2-c]chromene-2,5-dione (4a).** The yield was 79%; mp 243-244°C (mp 243°C [6]).

**4-Ethyl-2H, 5H-pyrano[3,2-c]chromene-2,5-dione (4b).** The yield was 72%; mp 126-128°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm (*J*, Hz): 1.28 (3H, t, *J* = 7.3, CH<sub>2</sub>CH<sub>3</sub>); 3.09 (2H, q, *J* = 7.3, CH<sub>2</sub>CH<sub>3</sub>); 6.25 (1H, s, H-3); 7.39 (2H, m, H-7,8); 8.02 (1H, t, H-9); 8.14 (1H, d, *J* = 7.9, H-10). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 246 (100). Found, %: C 69.25; H 4.07. C<sub>14</sub>H<sub>10</sub>O<sub>4</sub>. Calculated, %: C 69.42; H 4.13.

**3,4-Dimethyl-2H,5H-pyrano[3,2-c]chromene-2,5-dione (4c).** The yield was 71%; mp 222-224°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm (*J*, Hz): 2.10 (3H, s, 4-CH<sub>3</sub>), 2.52 (3H, s, 3-CH<sub>3</sub>); 7.46 (2H, m, H-7,8); 7.82 (1H, t, *J* = 7.9, H-9), 7.96 (1H, d, *J* = 7.8, H-10). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 246 (85). Found, %: C 69.27; H 4.19. C<sub>14</sub>H<sub>10</sub>O<sub>4</sub>. Calculated, %: C 69.42; H 4.13.

**4-Ethyl-3-methyl-2H,5H-pyrano[3,2-c]chromene-2,5-dione (4d).** The yield was 65%; mp 145-147°C, <sup>1</sup>H NMR spectrum,  $\delta$ , ppm (*J*, Hz): 1.26 (3H, t, *J* = 7.1, 4-CH<sub>2</sub>CH<sub>3</sub>); 2.81 (3H, s, 3-CH<sub>3</sub>); 3.04 (2H, q, *J* = 7.1, CH<sub>2</sub>CH<sub>3</sub>); 7.36-8.11 (4H, m, H-7,8,9,10). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 260 (95). Found, %: C 70.46; H 4.57. C<sub>15</sub>H<sub>12</sub>O<sub>4</sub>. Found, %: C 70.31; H 4.69.

**4,10-Dimethyl-2H,5H-pyrano[3,2-f]chromene-2,8-dione (5a).** The yield was 74%; mp 241-243°C (mp 242°C [10]).

**4,9,10-Trimethyl-2H,8H-pyrano[2,3-f]chromene-2,8-dione (5b).** The yield was 63%; mp 256-258°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm (*J*, Hz): 2.27 (3H, s, 10-CH<sub>3</sub>); 2.48 (3H, s, 4-CH<sub>3</sub>); 2.83 (3H, s, 9-CH<sub>3</sub>); 6.27 (1H, s, H-3); 7.23 (1H, d, *J* = 8.8, H-5); 7.65 (1H, d, *J* = 8.8, H-6). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 260 (70). Found, %: C 70.18; H 4.53. C<sub>15</sub>H<sub>12</sub>O<sub>4</sub>. Calculated, %: C 70.31; H 4.69.

**4,6-Dimethyl-2H,8H-pyrano[3,2-g]chromene-2,8-dione (6a).** The yield was 75%; mp 318-320°C (mp 319-320°C [10]).

**3,4,6-Trimethyl-2H,8H-pyrano[3,2-g]chromene-2,8-dione (6b).** The yield was 67%; mp 289-291°C. <sup>1</sup>H NMR spectrum,  $\delta$ , ppm (*J*, Hz): 2.25 (3H, s, 6-CH<sub>3</sub>); 2.46 (3H, s, 4-CH<sub>3</sub>); 2.50 (3H, s, 7-CH<sub>3</sub>); 6.30 (1H, s, H-7); 7.26 (1H, s, H-5); 7.74 (1H, s, H-10). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 260 (75). Found, %: C 70.42; H 4.76. C<sub>15</sub>H<sub>12</sub>O<sub>4</sub>. Calculated, %: C 70.31; H 4.69.

**Reaction of 3-Acetyl-4-hydroxy- and 8-Acetyl-7-hydroxy-4-Methylcoumarins with Acetic anhydride in the Presence of BF<sub>3</sub>·(OEt)<sub>2</sub>.** A solution of (0.01 mol) of hydroxycoumarin in 10 ml of acetic anhydride was boiled until the hydroxycoumarin had completely dissolved, and (3.12 g, 0.022 mol) of boron trifluoride etherate was added drop by drop. The reaction mass was boiled for a further 5 h until traces of the hydroxycoumarin and its borate complex had completely disappeared. The reaction mixture was cooled, and the crystals that separated were filtered off and washed on the filter with water and alcohol. The product was recrystallized from ethanol.

**7-Acetoxy-4-methylcoumarin (9).** The yield was 78%; mp 150-152°C (mp 150-151°C [11]).

**3-Acetyl-4-difluoroboryloxy-6-methylpyran-3-one, 3'-O→B-Chelate (10).** This compound was obtained as described earlier [12].

**Reaction of the Borate Complex of 3-Acetyl-4-hydroxy-7-methyl-2-pyrone (10) with Acetic Anhydride.** A solution of (1 g) of the borate complex **10** in 6 ml of the anhydride was boiled for 1 h. The precipitate was filtered off, washed on the filter with water and then with alcohol, and recrystallized from alcohol.

**4,7-Dimethyl-2H, 5H-dihydropyrano[3,2-c]pyran-2,5-dione (11).** The yield was 72%; mp 211-213°C (mp 212-213°C [13]).

## REFERENCES

1. S. Von Kostanecki and A. Rozyelci, *Ber.*, **34**, 102 (1901).
2. T. Szell, L. Dozsai, M. Zarandy, and K. Menyharth, *Tetrahedron*, **25**, 715 (1969).
3. J. Allan and R. Robinson, *J. Chem. Soc.*, **125**, 2192 (1924).
4. T. Horie, M. Tsukayama, Y. Kawamura, and M. Seno, *J. Org. Chem.*, **52**, 4702 (1987).
5. G. Bargellini, *Gazz. Chim. Ital.*, **55**, 945 (1925).
6. A. Mustafa, O. H. Hishmat, and A. A. Nawar, *Tetrahedron*, **19**, 1831 (1963).
7. D. Cook and J. S. McInture, *J. Org. Chem.*, **33**, 1746 (1968).
8. V. F. Traven, A. V. Manaev, and T. A. Chibisova, *Dyes and Pigments*, **58**, 41 (2003).
9. V. F. Traven, A. V. Manaev, and T. A. Chibisova, *J. Electron Spectra and Related Phenomena*, **149**, 6 (2005).
10. C. P. Bapat, M. V. Paradkar, and S. V. Sohoni, *Indian J. Chem.*, **21**, 1123 (1982).
11. C. H. Mohindra, C. J. Jonny, and R. S. Mittal, *Bull. Soc. Chim. Fr.*, **11**, 82 (1989).
12. T. D. Cyr and G. A. Poulton, *Can. J. Chem.*, **56**, 1796 (1978).
13. A. K. Müller, F. Raninger, and E. J. Ziegler, *Liebigs Ann. Chem.*, 400 (1976).