

Synthesis and structures of boron complexes of acyl hydroxy coumarins

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New boron chelates were synthesized by the reactions of 3-acetyl-4-hydroxycoumarin and 8-acyl-7-hydroxy-4-methylcoumarins with boron trifluoride etherate and hydroxybenzodioxaborole. The structure of 3-acetyl-4-difluoroboryloxycoumarin containing an intramolecular C=O...B coordination bond was established by X-ray diffraction.

Key words: coumarins, boron complexes, chelates, X-ray diffraction analysis.

Complexes of β -hydroxyenones with boron compounds are characterized by high reactivity, in particular, high mobility of the α -protons of the acyl group. For example, the methyl group in boron complexes of substituted *o*-hydroxyacetophenones, benzoylacetone, and acetylnaphthols is readily involved in condensation with carbonyl compounds and their derivatives, in particular, with acetals and anils. The reactions with DMF produce dimethylaminovinyl derivatives,¹ whereas the reactions with aldehydes afford substituted vinyl derivatives.² The above-mentioned boron complexes react also with trialkyl orthoformates, 1,1,3,3-tetraethoxypropane, and glutaconaldehyde dianil to give symmetrical polymethine dyes showing intense fluorescence.³ The reactions of boron complexes of benzoylacetone and *o*-hydroxyacetophenones with phenylformamidin in acetic anhydride produce hemicyanine dyes. The latter readily react with methylene-active compounds to form unsymmetrical polymethine dyes, which are also characterized by intense fluorescence.

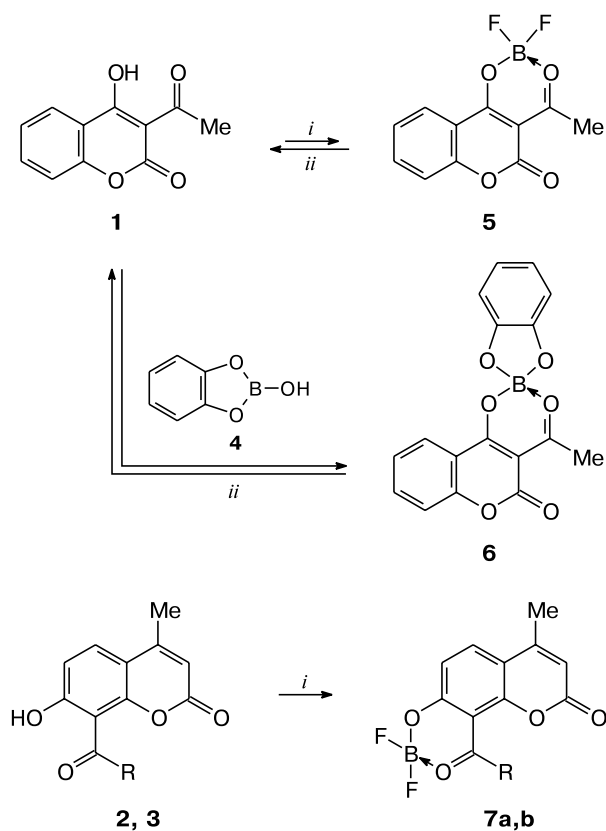
Earlier,⁴ we have observed high reactivity of acyl hydroxy coumarin complexes with boron trifluoride in condensation reactions. In the present study, the synthesis conditions and the structural features of this type of boron complexes were examined in detail.

Results and Discussion

The reactions of 3-acetyl-4-hydroxycoumarin (**1**), 8-acyl-7-hydroxy-4-methylcoumarin (**2**), and 7-hydroxy-4-methyl-8-propionylcoumarin (**3**) with boron trifluoride etherate or 2-hydroxy-1,3,2-benzodioxaborole (**4**)⁵ produced boron complexes **5–7** (Scheme 1).

Difluoroboryl derivatives **5** and **7a,b** were synthesized by refluxing benzene solutions of compounds **1–3** with

Scheme 1



R = Me (**2**, **7a**), Et (**3**, **7b**)

Reagents and conditions: *i.* $\text{BF}_3 \cdot \text{OEt}_2$. *ii.* 1) Na_2CO_3 , EtOH, H_2O ; 2) HCl.

boron trifluoride etherate. Catecholborane derivative **6** was synthesized by the reaction of compounds **1** and **4**.

Compound **4** was prepared *in situ* by refluxing pyrocatechol with boric acid in benzene with azeotropic distillation of water and then used without additional purification.

The structures of the boron complexes were established by ^1H and ^{11}B NMR spectroscopy. In the ^1H NMR spectra of the chelates, the signals for the protons of the methyl group of the acetyl fragment are shifted downfield compared to the signals of the starting acetylhydroxycoumarins due to a lower electron density on the carbonyl oxygen atom. The ^1H NMR spectrum of compound **6** shows a singlet for four protons at δ 6.84 corresponding to the pyrocatechol moiety.

The ^{11}B NMR spectra of compounds **5** and **6** show signals at δ 0.228 and 14.488, respectively, belonging to the four-coordinate boron atom.

The mass spectra of all the compounds under study have molecular ions with an intensity of 100%.

The IR spectrum of compound **5** shows an intense stretching band of the carbonyl group of lactone at 1740 cm^{-1} . This band remains virtually unchanged upon complexation. The band at 1600 cm^{-1} becomes less intense compared to the analogous band in the spectrum of the starting 3-acetyl-4-hydroxycoumarin (**1**), in which this band is more intense and broader than the band of the lactone carbonyl fragment and is a superposition of two bands of the conjugated $\text{C}=\text{C}$ and $\text{C}=\text{O}$ bonds. The change in the intensity is associated with the fact that the stretching band of the carbonyl group in the spectrum of complex **5** is shifted to lower frequencies and is observed at 1560 cm^{-1} . A decrease in the frequency of the $\text{C}=\text{O}$ stretching band of the acetyl group is attributed to its donor-acceptor interaction with the boron atom (*cf.* lit. data⁶). In the $1000\text{--}1100\text{ cm}^{-1}$ range, there is an intense absorption band consisting of two maxima at 1040 and 1065 cm^{-1} , which can be assigned to $\text{C}-\text{O}-\text{B}$ stretching vibrations. The stretching band of the $\text{B}=\text{O}=\text{C}$ donor-acceptor bond is pronounced and observed at 720 cm^{-1} .

The resulting boron complexes differ in hydrolytic stability. For example, storage of boron complex **6** in air is accompanied by its gradual decomposition. On the contrary, boron complex **5** is not only stable during prolonged storage but also does not undergo hydrolysis even on refluxing in water in neutral and acidic media. Hydrolysis was successfully performed only in an aqueous alcoholic solution of sodium carbonate, and compound **1** was recovered in quantitative yield. In turn, complexes **7a,b** containing the functional groups in other positions are unstable to hydrolysis and prolonged storage. Unlike boron complexes of 3-acetyl-4-hydroxycoumarin **5** and **6**, complexes of 7-hydroxy-8-acylcoumarins **7a,b** are colored and show fluorescence both in solution and in the solid state.

Due to high stability of complex **5** to hydrolysis and high proton acidity of its methyl group, this com-

pound can be used in different condensation reactions and for the synthesis of new 3-substituted 4-hydroxycoumarins.

It was of interest to study the electronic and three-dimensional structure of compound **5** and compare its structure with the data obtained earlier for 3-acetyl-4-hydroxycoumarin (**1**).^{7,8}

X-ray diffraction study demonstrated that complexation of compound **1** with BF_3 leads to a pronounced change in the molecular geometry and the bond lengths in the $\text{O}-\text{C}=\text{C}-\text{C}(\text{O})\text{Me}$ fragment (Fig. 1). Earlier, it has been demonstrated^{7,8} that molecule **1** in the crystal is planar, and the acetyl group $\text{C}(11)\text{C}(10)\text{O}(3)$ is rotated relative to the 4-hydroxycoumarin fragment by 6.2° . In compound **5**, the corresponding angle is 9.7° . Unlike the planar H-bonded ring in coumarin **1**, the six-membered boron-containing ring in complex **5** adopts a sofa conformation with the boron atom deviating from the plane through the $\text{O}(3)$, $\text{O}(4)$, $\text{C}(10)$, $\text{C}(8)$, and $\text{C}(7)$ atoms by 0.375 \AA . The bond lengths in the six-membered boron-containing heterocycle are indicative of the presence of conjugation in the $\text{O}-\text{C}=\text{C}-\text{C}=\text{O}$ fragment (Table 1). The observed equalization of the $\text{C}-\text{C}$ and $\text{C}-\text{O}$ bonds is due to formation of the donor-acceptor $\text{B}\dots\text{O}$ bond and a high extent of π delocalization. The $\text{C}(10)-\text{O}(3)$, $\text{C}(7)-\text{O}(4)$ and $\text{C}(10)-\text{C}(8)$, $\text{C}(7)-\text{C}(8)$ bonds in molecule **5** ($1.287(2)$, $1.297(2)$ and $1.412(2)$, $1.395(2)\text{ \AA}$, respectively) are more equalized compared to the analogous

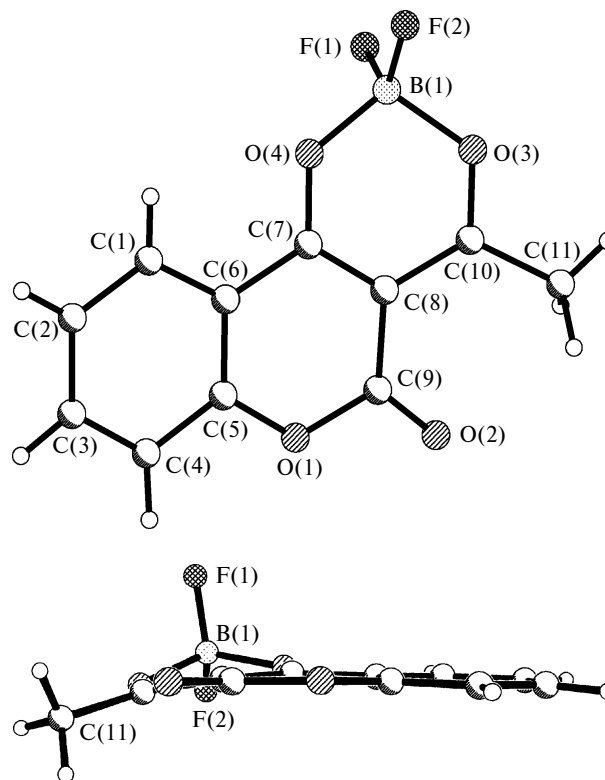


Fig. 1. Overall view of compound **5a** in two projections.

Table 1. Selected bond lengths (*d*) and bond angles (ω) in boron complex **5** determined by X-ray diffraction

Bond	<i>d</i> /Å	Bond	<i>d</i> /Å
F(1)—B(1)	1.355(2)	O(3)—C(10)	1.287(2)
F(2)—B(1)	1.359(2)	O(4)—C(7)	1.297(2)
B(1)—O(3)	1.503(2)	C(6)—C(7)	1.439(2)
B(1)—O(4)	1.483(2)	C(7)—C(8)	1.395(2)
O(1)—C(5)	1.372(2)	C(8)—C(10)	1.412(2)
O(1)—C(9)	1.376(2)	C(8)—C(9)	1.453(2)
O(2)—C(9)	1.204(2)	C(11)—C(10)	1.476(2)
Angle	ω /deg	Angle	ω /deg
C(5)—O(1)—C(9)	122.2(1)	C(8)—C(7)—C(6)	119.8(1)
C(10)—O(3)—B(1)	122.9(1)	C(7)—C(8)—C(10)	118.4(1)
C(7)—O(4)—B(1)	120.5(1)	C(7)—C(8)—C(9)	120.3(1)
F(1)—B(1)—F(2)	113.2(1)	C(10)—C(8)—C(9)	121.0(1)
F(1)—B(1)—O(4)	109.6(1)	O(2)—C(9)—O(1)	115.9(1)
F(2)—B(1)—O(4)	108.9(1)	O(2)—C(9)—C(8)	126.6(1)
F(1)—B(1)—O(3)	107.9(1)	O(1)—C(9)—C(8)	117.4(1)
F(2)—B(1)—O(3)	107.8(1)	O(3)—C(10)—C(8)	119.5(1)
O(4)—B(1)—O(3)	109.3(1)	O(3)—C(10)—C(11)	115.7(1)
O(4)—C(7)—C(8)	122.4(1)	C(8)—C(10)—C(11)	124.8(1)
O(4)—C(7)—C(6)	117.8(1)		

bonds in the H-bonded fragment **A** (1.254(2), 1.303(2), 1.454(2), and 1.392(2) Å).^{7,8} The B—O bonds in complex **5a** are similar in length (1.503(2) and 1.483(2) Å), the B(1)—O(3) bond being slightly elongated. The pseudo-equatorial and pseudoaxial B—F bonds are virtually equal.

To estimate whether a distortion of the boron-containing ring in complex **5** is a characteristic feature of this compound or it is caused by the crystal packing effects, we performed quantum chemical calculations (B3LYP/6-311G*) with the use of the G98W program.⁹ According to the calculations, the boron-containing ring in the isolated molecule, like that in the crystal, is nonplanar. The rotation angle of the acetyl group is 4.3°. The deviation of the boron atom is 0.235 Å. The bond lengths in the boron-containing ring in the isolated molecule (calculated data), like those in the crystal, are substantially equalized (the C(10)—O(3), C(7)—O(4) and C(10)—C(8), C(7)—C(8) bond lengths are 1.286, 1.277 and 1.413, 1.421 Å, respectively). The observed differences in the geometry of isolated molecule **5** (calculated data) and the molecule in the crystal (experimental data) are apparently attributed to both the difference in the degree of distortion of the boron-containing ring and an elongation of the B—O bonds (1.532 and 1.515 Å), which is a general characteristic of donor-acceptor bonds involving the boron atoms.¹⁰ Therefore, it can be concluded that complexation with the boron atom is accompanied by equalization of the C—C and C=O bonds due to delocalization of π bonds.

Experimental

The ¹H NMR spectra were recorded on a Bruker WP-200-SY instrument in CDCl₃ with Me₄Si as the internal standard. The ¹¹B NMR spectra were measured on a Bruker WM-250 instrument in DMSO-d₆ with boron trifluoride etherate as the external standard. The electronic absorption spectra were recorded on a Specord UV-VIS spectrometer in chloroform. The IR spectra were measured on a Specord IR-71 instrument in Nujol mulls and in KBr pellets. The mass spectra were obtained on a MAT-112 mass spectrometer; the ionizing electron energy was 80 eV, the ion source temperature was 250 °C, and the inlet temperature was 240 °C.

3-Acetyl-4-difluoroboryloxycoumarin (5). Boron trifluoride etherate (9.8 g, 0.18 mol) was added dropwise to a boiling solution of 3-acetyl-4-hydroxycoumarin (**1**)¹¹ (14 g, 0.17 mol) in dry benzene (50 mL). After 10 min, crystallization started. The reaction mixture was then refluxed for 1 h. The precipitate that formed was filtered off, washed with benzene, and dried in air. Compound **5** was obtained in a yield of 12 g (72%) as colorless needle-like crystals with m.p. 198–199 °C. In condensation reactions, this compound was used without additional purification. An analytically pure sample was obtained by recrystallization from benzene, m.p. 199–200 °C. Found (%): C, 52.45; H, 2.76; B, 4.32; F, 15.10. C₁₁H₇BF₂O₄. Calculated (%): C, 52.43; H, 2.80; B, 4.29; F, 15.08. ¹H NMR (CDCl₃), δ : 3.00 (s, 3 H, Me); 7.30 (d, 1 H, C(8)H, *J* = 9.0 Hz); 7.44 (t, 1 H, C(7)H); 7.87 (t, 1 H, C(6)H); 8.23 (d, 1 H, C(5)H, *J* = 9.0 Hz). ¹¹B NMR (DMSO-d₆), δ : -0.228. MS, *m/z* (%): 252 (93).

3-Acetyl-4-(1,3,2-benzodioxaborol-2-yloxy)coumarin (6). 3-Acetyl-4-hydroxycoumarin (**1**) (2.04 g, 10 mmol) and dry benzene (10 mL) were placed in a flask equipped with a Dean–Stark trap. The reaction mixture was heated to reflux. After complete dissolution of compound **1**, 2-hydroxy-1,3,2-benzodioxaborole (**4**)⁵ (1.35 g, 10 mmol) was added. The reaction mixture was refluxed for 3 h with distillation of a water–benzene azeotrope, dry benzene being gradually added to maintain the volume of the mixture of ~15 mL. After ~3 h, an orange solid precipitated. The reaction mixture was cooled, and the precipitate was filtered off and dried in air. The compound with m.p. 243–244 °C was obtained in a yield of 2.77 g (86%). After recrystallization from benzene, orange crystals had m.p. of 244–245 °C. Found (%): C, 63.42; H, 3.47; B, 3.32. C₁₇H₁₁BO₆. Calculated (%): C, 63.40; H, 3.44; B, 3.36. ¹H NMR (CDCl₃), δ : 2.99 (s, 3 H, —CH₃); 6.84 (m, 4 H, pyrocatechol); 7.35 (m, 2 H, C(7)H, C(8)H); 7.83 (t, 1 H, C(6)H); 8.25 (d, 1 H, C(5)H). ¹¹B NMR (DMSO-d₆), δ : 14.488. MS, *m/z* (%): 322 (100).

8-Acetyl-7-difluoroboryloxy-4-methylcoumarin (7a) was synthesized according to an analogous procedure. 8-Acetyl-7-hydroxy-4-methylcoumarin (**2**)¹² (0.413 g, 2 mmol) was dissolved in benzene (10 mL) and then boron trifluoride etherate (0.3 g, 2.05 mmol) was added. A yellow-green luminescent compound was obtained in a yield of 0.39 g (73%) with m.p. 228–229 °C. Found (%): C, 54.21; H, 3.42; B, 4.02; F, 14.31. C₁₂H₉BF₂O₄. Calculated (%): C, 54.18; H, 3.41; B, 4.06; F, 14.28. ¹H NMR (CDCl₃), δ : 2.46 (d, 3 H, C(4)Me, *J* = 1.1 Hz); 3.22 (s, 3 H, C(O)Me); 6.25 (d, 1 H, C(3)H, *J* = 1.1 Hz); 7.05 (d, 1 H, C(6)H, *J* = 9.1 Hz); 7.96 (d, 1 H, C(5)H, *J* = 9.1 Hz). MS, *m/z* (%): 266 (85).

7-Difluoroboryloxy-4-methyl-8-propionylcoumarin (7b) was synthesized according to an analogous procedure. 8-Propionyl-7-hydroxy-4-methylcoumarin (**3**)¹² (0.47 g, 2 mmol) was dissolved in benzene (10 mL) and then boron trifluoride etherate (0.3 g, 2.05 mmol) was added. A yellow-green luminescent compound was obtained in a yield of 0.4 g (72%) with m.p. 206–207 °C. Found (%): C, 55.72; H, 3.96; B, 3.90; F, 13.54. C₁₃H₁₁BF₂O₄. Calculated (%): C, 55.76; H, 3.96; B, 3.86; F, 13.57. ¹H NMR (CDCl₃), δ: 1.43 (t, 3 H, CH₂Me); 2.46 (d, 3 H, C(4)Me, *J* = 1.1 Hz); 3.78 (q, 2 H, CH₂); 6.25 (d, 1 H, C(3)H, *J* = 1.1 Hz); 7.04 (d, 1 H, C(6)H, *J* = 9.1 Hz); 7.95 (d, 1 H, C(5)H, *J* = 9.1 Hz). MS, *m/z* (%): 280 (89).

X-ray diffraction study of compound **5** (C₁₁H₇BF₂O₄) was carried out on an automated four-circle Enraf-Nonius CAD-4 diffractometer. At 298 K, crystals of **5** are monoclinic, space group *P*2₁/*c*, *a* = 10.194(2) Å, *b* = 5.390(1) Å, *c* = 18.815(4) Å, β = 91.54(3)°, *V* = 1033.4(4) Å³, *Z* = 4 (*Z'* = 1), *d*_{calc} = 1.620 g cm⁻³, μ(Mo-Kα) = 1.43 cm⁻¹, *F*(000) = 512. The intensities of 2011 reflections were measured at 298 K (Mo-Kα (λ = 0.71073 Å), graphite monochromator, θ/2θ-scanning technique, 2θ < 50°), and 1834 independent reflections (*R*_{int} = 0.0131) were used in the refinement. The structure was solved by direct methods and with the use of successive electron density maps. All hydrogen atoms were located in difference electron density maps. The refinement was performed against *F*²_{*hkl*} with anisotropic displacement parameters for nonhydrogen atoms and isotropic displacement parameters for hydrogen atoms. The final *R* factors were as follows: *R* = 0.0373 based on 1430 reflections with *I* > 2σ(*I*), *wR*₂ = 0.1132, GOOF = 1.048 based on all measured reflections. All calculations were carried out with the use of the SHELXTL 5.10 program package.¹³

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Received November 11, 2005;
in revised form September 6, 2006