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On the Condensation of 2,2-Difluoro-4-methyl-benzo[*d*]-1,3,2-dioxaborines with Cyano Acetic Acid Derivatives. Formation and Transformation of 3-Cyano-4-methyl-benzo[*b*]pyran-2-ones and their 2-Imine Precursors

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Summary. By condensation of 2,2-difluoro-4-methyl-benzo[*d*]-1,3,2-2*H*-dioxaborines (**12**) with cyano acetic acid derivatives in presence of weak bases, 3-cyano-4-methyl-benzo[*b*]pyran-2-ones (**13**) or their 3-cyano-4-methyl-benzo[*b*]pyran-2-imine precursors (**14**) are available in satisfactory yields.

Keywords. 3-Cyano-4-methyl-benzo[*b*]pyran-2-ones; 3-Cyano-4-methyl-benzo[*b*]pyran-2-imines; *Knoevenagel* condensation of 2,2-difluoro-4-methyl-benzo[*d*]-1,3,2-2*H*-dioxaborines.

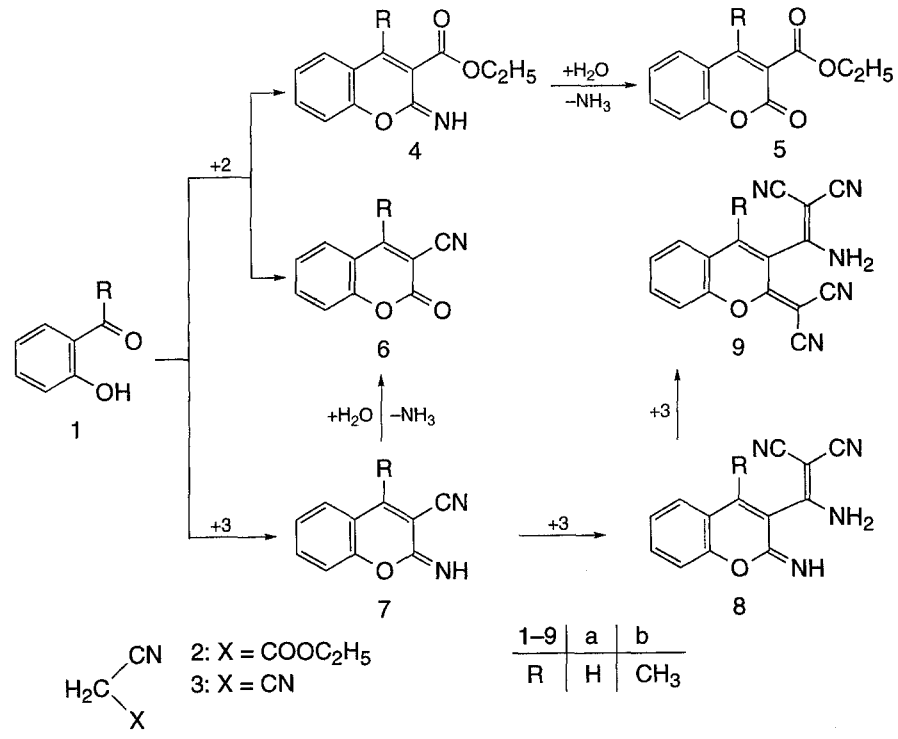
Zur Kondensation von 2,2-Difluor-4-methyl-benzo[*d*]-1,3,2-2*H*-dioxaborinen mit Cyanessigsäure-Derivaten. Bildung und Umwandlung von 3-Cyano-4-methyl-benzo[*b*]pyran-2-onen und ihrer 2-Imino-Vorstufen

Zusammenfassung. Durch Kondensation von 2,2-Difluor-4-methyl-benzo[*d*]-1,3,2-2*H*-dioxaborinen (**12**) mit Cyanessigsäure-Derivaten in Gegenwart von Hilfsbasen entstehen in befriedigenden Ausbeuten 3-Cyan-4-methyl-benzo[*b*]pyran-2-one (**13**) oder ihre 3-Cyan-4-methyl-benzo[*b*]pyran-2-imino-Vorstufen (**14**).

Introduction

The reaction of salicylic aldehyde (**1a**) with ethyl cyanoacetate (**2**) or malononitrile (**3**) is a well-studied reaction which has been performed in presence of bases and gives rise to the formation of 3-cyano- or 3-ethoxycarbonyl-substituted coumarines (**5a, 6a**) under mild conditions and in satisfactory yields [1,2]. Obviously, the reactions run via the intermediate imino-coumarines **4a** or **7a**, resp., which are isolable as their free bases or, alternatively, as their protonated species [3].

With 2-hydroxy-acetophenone (**1b**) instead of salicylic aldehyde (**1a**), 4-methyl-substituted 3-cyano-coumarine (**6b**) or 3-ethoxycarbonyl-coumarine (**5b**) are formed. The reactions proceed however, in these cases with some difficulties and complications. Whereas the reaction of **1b** with **2** runs nearly analogously to the



Scheme 1

reaction of salicylic aldehyde (**1a**) and gives rise to the formation of 3-cyano-4-methyl-coumarine (**6b**), usually the reaction of **1b** with **3** gives, independent of the ratio of the educts used and the conditions applied, differently substituted products. Thus, by starting with equimolar amounts of **1b** and **3**, the iminocoumarine **7b** is formed in moderate yields only. Using an excess of **3**, the products **8b** and **9b**, together with some other products of unknown structure, are obtained [4]. The reason for the differences in the reactivity between **1a** and **1b** seems to be the lower carbonyl reactivity of **1b** caused by the methyl group at C-4 [5].

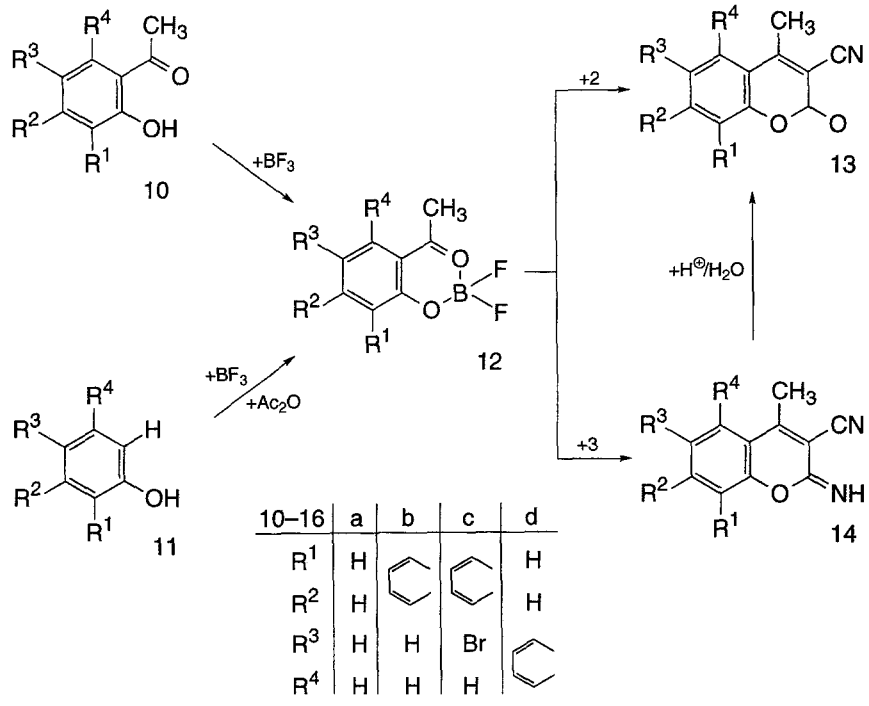
A raising of the carbonyl reactivity in 2-hydroxy-acetophenone as well as in its ring substituted derivatives **10** is expected if these compounds are transformed into 4-methyl-substituted 2,2-difluoro-benzo[*d*]-1,3,2-2*H*-dioxaborines (**12**). These heterocyclic boron containing compounds can be considered as complexed 2-hydroxy-acetophenones and prepared either by the reaction of a 2-hydroxy- acetophenone (**10**) with boron trifluoride in acetic acid solution [6] or by condensation of a suitably substituted phenol (**11**) with acetic acid anhydride in the presence of boron trifluoride [7].

Results and Discussion

As expected, the 4-methyl-substituted 2,2-difluoro-benzo[*d*]-1,3,2-2*H*-dioxaborines **12** condense with ethyl cyanoacetate (**2**) or malononitril (**3**) under the influence of weak bases to give the corresponding 3-cyano-4-methyl-coumarines **13** or their imino derivatives **14**, respectively. The latter compounds can be hydrolyzed to the

parent 3-cyano-4-methyl-benzo[*b*]pyran-2-ones (*3-cyano-4-methyl-coumarines*) **13** by reaction with mineralic acid in aqueous solution.

Whereas the condensation of the 4-methyl-substituted 2,2-difluoro-benzo[*h*]-1,3,2-dioxaborines **12** with the educts **2** or **3** can be performed very easily by adding bases, such as triethylamine, to an equimolar mixture of the mentioned components in acetonitrile solution at room temperature, the hydrolysis of the primarily formed imino coumarines **14** to the corresponding coumarines **13** can be performed by heating the imines **14** with hydrochloric acid in methanol. Usually, the products formed crystallize during the reaction and can be isolated by suction without difficulty.



10–16	a	b	c	d
R^1	H			H
R^2	H			H
R^3	H	H	Br	
R^4	H	H	H	

Scheme 2

Table 1 informs on the 3-cyano-4-methyl-coumarines **13** and their imino derivatives **14** prepared by the above procedures.

Besides the unsubstituted 3-cyano-4-methyl-benzo[*b*]coumarine **13a** and its 2-imine derivative **14a** which are reported in the literature [4], all compounds depicted in Table 1 are new. They exhibit characteristic spectroscopic data which confirm, together with their elemental analytical data (Table 2) their structures.

Thus, the IR spectra of the iminocoumarines **14** show characteristic absorption frequencies at about 2200, 3300, and 1660 cm^{-1} which can be attributed to their cyano and C=NH moieties, resp. Analogously, the coumarines **13** exhibit characteristic absorption frequencies at about 2230 and 1700 cm^{-1} which can be assigned to their cyano and C=O moieties. In the ^1H NMR spectra of the

Table 1. 3-Cyano-4-methyl-benzo[*b*]pyran-2-ones (**13**) and 3-cyano-4-methyl-benzo[*b*]pyran-2-imines (**14**)

R^1	R^2	R^3	R^4	Educts	Product	Yield (%)	m.p. (°C) (Lit. m.p.)	IR (cm^{-1}) in KBr (assignment)	^1H NMR (δ in $CDCl_3$) (assignment)	λ_{max} (nm) (log ε)
H	H	H	H	**12a** + **3**	**13a**	40	148–150 (150 [4])	3303 (NH), 2222 (CN) 1660 (C = N)	2.61 (s, 3H, CH_3), 7.23 (d, 1H, H-7), 7.46 (d, 1H, H-6) 7.52 (d, 1H, H-8), 7.54 (d, 1H, H-5)	302 (3.96) 332 (3.84)
H	H	H	H	**12a** + **2** **13a**	**14a**	62 100	198–199 (194 [5])	2229 (CN), 1722 (CO)	2.76 (s, 3H, CH_3), 7.38 (d, 1H, H-7), 7.42 (d, 1H, H-6) 7.68 (d, 1H, H-8), 7.73 (d, 1H, H-5)	302 (3.80) 342 (3.74) 353 (3.73)
benzo		H	H	**12b** + **3**	**13b**	69	237–239	3271 (NH), 2229 (CN) 1664 (C = NH)	2.68 (s, 3H, CH_3), 7.50 (d, 1H, H-6), 7.67–7.59 (m, 3H, H-7,8,9), 7.83 (d, 1H, H-5), 8.34 (d, 1H, H-10)	319 (4.04) 329 (4.04) 378 (3.87)
benzo		H	H	**12b** + **2** **13b**	**14b**	55 99	291–293	2229 (CN), 1732 (CO)	2.85 (s, 3H, CH_3), 7.64 (d, 1H, H-6), 7.71 (t, 2H, H-8,9), 7.77 (d, 1H, H-5), 7.90 (d, 1H, H-7), 8.56 (d, 1H, H-10)	326 (3.85) 341 (3.83) 390 (3.87)
benzo		Br	H	**12c** + **3**	**13c**	92	236–238	3263 (NH), 2235 (CN) 1658 (C = NH)	2.68 (s, 3H, CH_3), 7.60–7.79 (m, 3H, H-7,8,9), 7.80 (d, 1H, H-5), 8.21 (d, 1H, H-10)	316 (3.96) 330 (3.94) 382 (3.87)
benzo		Br	H	**12c** + **2** **13c**	**14c**	66 98	258–259	2229 (CN), 1628 (CO)	2.82 (s, 3H, CH_3), 7.75 (t, 1H, H-9), 7.85 (t, 1H, H-8), 7.93 (d, 1H, H5), 8.27 (d, 1H, H-7), 8.56 (d, 1H, H-10)	327 (3.69) 342 (3.62) 394 (3.84)
H	H	benzo		**12c** + **3**	**13d**	44	> 148 dec.	3298 (NH), 2218 (CN) 1658 (C = NH)	3.05 (s, 3H, CH_3), 7.23 (d, 1H, H-6), 7.52 (t, 1H, H-9), 7.63 (t, 1H, H-8), 7.86 (d, 1H, H-5), 7.95 (d, 1H, H-7), 8.39 (d, 1H, H-10)	338 (3.91) 376 (4.07) 388 (4.01)
H	H	benzo		**12d** + **2** **13d**	**14d**	82 99	238–240	2224 (CN), 1728 (CO)	3.21 (s, 3H, CH_3), 7.46 (d, 1H, H-6), 7.63 (t, 1H, H-9), 7.74 (t, 1H, H-8), 7.96 (d, 1H, H-5), 8.12 (d, 1H, H-7), 8.51 (d, 1H, H-10)	336 (3.68) 382 (3.78) 391 (3.77)

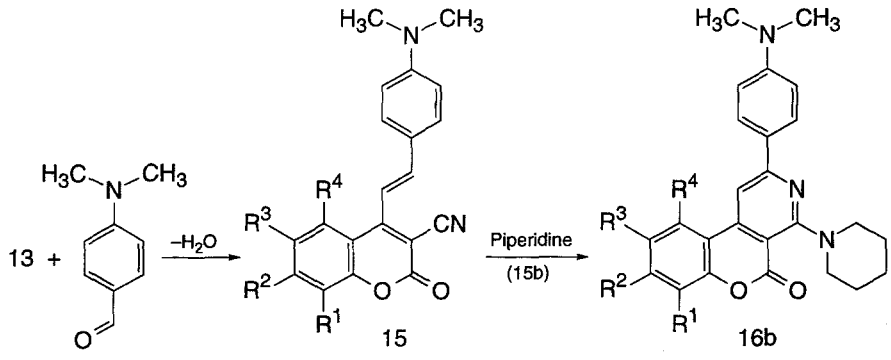
Table 2. Elemental analyses of 3-cyano-4-methyl-benzo[*b*]pyran-2-ones (**13**) and 3-cyano-4-methyl-benzo[*b*]pyran-2-imines (**14**)

	Formula (mol wt.)		C	H	N	Br
13a	$C_{11}H_7NO_2$	calcd.	71.35	3.78	7.57	
	(185.1)	found	71.08	4.07	7.72	
13b	$C_{15}H_9NO_2$	calcd.	76.60	3.83	5.96	
	(235.1)	found	76.23	4.03	5.72	
13c	$C_{15}H_8BrNO_2$	calcd.	57.34	2.55	4.46	25.45
	(314.0)	found	57.11	2.87	4.79	25.63
13d	$C_{15}H_9NO_2$	calcd.	76.60	3.83	5.96	
	(235.1)	found	76.35	4.05	6.15	
14a	$C_{11}H_8N_2O$	calcd.	71.74	4.34	15.22	
	(184.1)	found	72.13	5.04	14.78	
14b	$C_{15}H_{10}N_2O$	calcd.	76.92	4.27	11.96	
	(234.1)	found	76.35	4.71	11.50	
14c	$C_{15}H_9BrN_2O$	calcd.	57.62	2.88	8.95	25.54
	(313.0)	found	57.63	3.53	8.60	25.42
14d	$C_{15}H_{10}N_2O$	calcd.	76.92	4.27	11.96	
	(234.1)	found	77.08	4.72	11.82	

coumarines **13** and their imine precursors **14**, significant signals appear for the protons of their methyl groups at $\delta = 2.6$–3.2 ppm and of their aromatic methine groups at $\delta = 7.2$–8.6 ppm (Table 1).

A characteristic property of the 3-cyano-4-methyl-coumarines **13** is, *inter alia*, the acidity of the methyl group at C-4. Thus, these compounds are able to condense with aromatic aldehydes under the influence of bases. With 4-dimethylamino-benzaldehyde and catalytic amounts of piperidine, the 4-dimethyl-amino-substituted styryl derivatives **15a**–**15c** are available. These compounds are able, as exemplified with compound **15b**, to react with amines, such as piperidine, to give pyrido[3,4-*c*]benzo[*h*]pyran-2-one derivatives **16**.

Similar to the pyrido[3,4-*c*]benzo[*h*]pyran-2-one derivative **16b** which is a red coloured compound and has been synthesized either by adding an excess of



Scheme 3

piperidine to the reaction mixture of **13b** and 4-dimethylamino-benzaldehyde or by addition of piperidine to a solution of **15b** in acetonitrile, the styryl coumarines **15** are deeply coloured compounds which exhibit intense absorption bands in the visible region at about 500 nm. Their absoptions are strongly influenced by the polarity of the solvent. Therefore, the styryl coumarines **15** are promising candidates for manifacturing materials with non-linear optical properties. Efforts in this direction are in progress [8].

The structures of the styryl coumarines **15** have been confirmed by means of their ^{1}H NMR spectra which exhibit a characteristic doublet at about 7.2–7.9 ppm with a coupling constant of about 15 Hz, indicating the presence of a vinyl moiety with *E*-configuration.

Experimental

Melting points were determined using a Boetius heating-table microscope. The IR spectra were recorded in potassium bromide pellets with a Philips FTIR spectrometer model PU 9624, the ^{1}H NMR spectra with a Varian 300 MHz Gemini 300 spectrometer, and the UV/Vis spectra with a Perkin Elmer Lambda 2 spectrometer. The elemental analytical data were determined with a LECO analyser CHNS 932.

The 4-methyl-2,2-difluoro-benzo[*d*]-1,3,2-2*H*-dioxaborine educts **12a**, and **12d** were prepared according to the literature [6,7].

6-Bromo-4-methyl-2,2-difluoro-naphtho[1,2-d]-1,3,2-2H-dioxaborine (**12c**)

To a mixture of 2.3 g (0.01 mol) 2,2-difluoro-4-naphtho[1,2-*d*]-1,3,2-2*H*-dioxaborine (**12b**) in 150 ml dichloromethan, 0.5 ml (0.01 mol) Br_2 are added. The mixture is stirred until the colour of bromine has vanished (about 3 days). Then the solvent is evaporated, and the precipitate is recrystallized from acetic acid.

Yield: 2.8 g (90%); m.p.: 228–229 °C; ^{1}H NMR: δ(ppm, *TMS*) = 2.97 (s, 3H, CH_3), 7.80 (t, 1H, H-9), 7.90 (d, 1H, H-5), 8.02 (t, 1H, H-8), 8.26 (d, 1H, H-7), 8.75 (d, 1H, H-10); $C_{12}H_8BBrF_2O_2$ (312.8); calcd.: C46.06, H 2.58, Br 25.54; found: C 45.96, H 2.73, Br 24.94.

Preparation of 3-cyano-4-methyl-benzo[b]pyran-2-ones (**13**)

Method A

To a mixture of 0.01 ml of a 2,2-difluoro-4-methyl-benzo[1,2-*d*]-1,3,2-2*H*-dioxaborine (**12**) and 0.012 mol ethyl cyanoacetate (**2**) in 20 ml acetonitrile 5 drops of triethylamine are added under stirring. After obtaining a clear solution, the product sometimes crystallizes and can by isolated by suction.

Method B

A mixture of 0.005 mol of a 3-cyano-4-methyl-benzo[*b*]pyran-2-imine (**14**), 20 ml ethanol, and 5 ml concentrated hydrochloric acid is refluxed for 30 min. After cooling the reaction mixture, the product crystallizes and can be isolated by suction.

Preparation of 3-cyano-4-methyl-benzo[b]pyran-2-imines (**14**)

To a mixture of 0.01 ml of a 2,2-difluoro-4-methyl-benzo[1,2-*d*]-1,3,2-2*H*-dioxaborine (**12**) and 0.012 mol malononitrle (**3**) in 20 ml acetonitrile, 5 drops of triethylamine are added under stirring. After obtaining a clear solution, the product sometimes crystallizes and can be isolated by suction.

Preparation of 3-cyano-4-(4-dimethylamino-stryryl)-benzo[b]pyran-2-ones (**15**)

After addition of 3 drops of piperidine to a mixture of 0.005 mol of a 3-cyano-4-methyl-benzo[*b*]pyran-2-one (**13**) and 0.006 mol (0.9 g) 4-dimethylamino-benzaldehyde in 50 ml acetonitrile, the mixture is refluxed for 2 to 3 h. After cooling, the product crystallizes and can be isolated by suction.

3-Cyano-4-(4-dimethylamino-styryl)-benzo[b]pyran-2-one (**15a**)

Yield: 42%; m.p.: 205 °C; ^{1}H NMR: δ (ppm, *TMS*) = 3.06 (s, 6H, CH_3), 6.68 (d, 2H, H-3′), 7.15 (d, 1H, H_{vinyl}; J_{vinyl} = 15.9 Hz), 7.35 (d, 1H, H-8), 7.37 (d, 1H, H-6), 7.53 (d, 2H, C-2′), 7.66 (d, 1H, H-7), 7.79 (d, 1H, H_{vinyl}), 7.95 (d, 1H, H-5); $C_{20}H_{16}N_2O_2$ (316.4); calcd.: C 75.95, H 5.92, N 8.96; found: C 75.82, H. 5.92, N 8.57.

3-Cyano-4-(4-dimethylamino-styryl)-naphtho[1,2-b]pyran-2-one (**15b**)

Yield: 50%; m.p.: 266–268 °C; ^{1}H NMR: δ (ppm, *TMS*) = 3.06 (s, 6H, CH_3), 6.68 (d, 2H, H-3′), 7.20 (d, 1H, H_{vinyl}; J_{vinyl} = 16.3 Hz), 7.55 (d, 2H, H-2′), 7.64–7.74 (m, 3H, H-6, 8, 9), 7.77 (d, 1H, H_{vinyl}), 7.85 (d, 1H, H-5), 7.88 (d, 1H, H7), 8.55 (d, 1H, H-10); $C_{24}H_{18}N_2O_2$ (366.3); calcd: C 78.69, H 4.92, N 7.65; found: C 78.73, H 4.38, N 7.89.

6-Bromo-3-cyano-4-(4-dimethylamino-styryl)-naphtho[1,2-b]pyran-2-one (**15c**)

Yield: 65%; m.p.: 293–294 °C; ^{1}H NMR: δ (ppm, *TMS*) = 3.09 (s, 6H, CH_3), 6.73 (d, 2H, H-3′), 7.29 (d, 1H, H_{vinyl}; J_{vinyl} = 14.5 Hz), 7.60 (d, 2H, H-2′), 7.74 (d, 1H, H-9), 7.84 (d, 1H, H_{vinyl}), 7.89 (d, 1H, H-8), 8.16 (d, 1H, H-5), 8.26 (d, 1H, H-7), 8.60 (d, 1H, H-10); $C_{24}H_{17}BrN_2O_2$ (445.2); calcd.: C 64.73, H 3.82, N 6.29, Br 17.60; found: C 64.06, H 3.57, N 6.43, Br 17.86.

5-(4-Dimethylaminophenyl)-3-(1-piperidino)-naphtho[1,2-b]pyrido[4,3-d]pyran-2-one (**16b**)

A mixture of 1.2 g (0.005 mol) 3-cyano-4-methyl-naphtho[1,2-b]pyran-2-one (**13b**), 0.9 g (0.006 mol) 4-dimethylamino-benzaldehyde, and 0.6 ml (0.006 mol) piperidine in 10 ml acetonitrile is heated on the steam bath for 6 h. After cooling the product precipitates and can be isolated by suction.
Yield: 0.95 g (42%); m.p.: 281–282 °C; ^{1}H NMR: δ (ppm, *TMS*) = 1.92 (m, 6H, CH_2), 3.15 (s, 6H, CH_3), 3.66 (m, 4H, NCH_2), 7.43 (d, 2H, H-7,8), 7.52 (d, 2H, H-3′), 7.66 (t, 2H, H-10, 11), 7.89 (d, 1H, H-9), 8.16 (d, 2H, C-2′), 8.20 (d, 1H, H-12), 8.56 (s, 1H, H-6); $C_{29}H_{26}BrN_3O_2$ (528.2); calcd.: C 65.91, H 4.92, N 7.95; found: C 65.53, H 4.64, N 8.18.

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