Synthesis of crown-containing 2-styrylbenzothiazoles. Effect of alkali metal cations on the condensation of crown-ether benzaldehydes with 2-methylbenzothiazole

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Methods for the synthesis of unknown 2-styrylbenzothiazoles containing crown ether moieties with different combinations of O, S, and N-heteroatoms based on the Wittig reaction or condensation of 2-methylbenzothiazole with crown-ether benzaldehydes in the presence of strong bases or acids are proposed. The condensation in the presence of bases is accompanied by complex formation with participation of the crown ether moiety of the benzaldehyde. The complex formation has a pronounced influence on the yield of the target product and the pattern of condensation of 2-methylbenzothiazole with crown-ether benzaldehydes.

Key words: crown-ether benzaldehydes, 2-methylbenzothiazole, 2-styrylbenzothiazoles, Wittig reaction, condensation, complex formation, alkali metals.

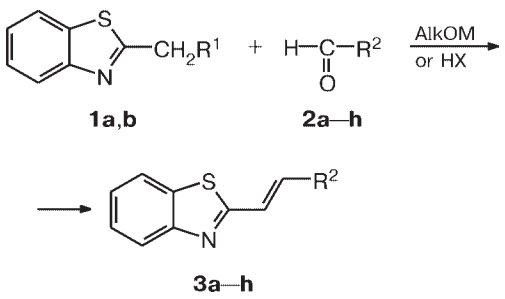
A unique feature of crown ethers is highly selective complex formation with various cations including alkali and alkaline earth metal cations. This feature underlies the use of crown compounds in the chemical synthesis and analytical chemistry and as models of biological systems.[1—3]

The introduction of various functional groups in the macrocycle markedly extends the scope of application of crown ethers. In recent years, in order to prepare reagents for colorimetric or luminescence determination of cations, new crown compounds containing photosensitive groups have been synthesized.[4—8] In particular, crown-containing hetarylphenylethylenes and various styryl dyes has been proposed for this purpose.[9—18]

With the view of performing an extended quest for new promising chromogenic crown compounds, here we developed methods (Scheme 1) for the synthesis of crown-containing 2-styrylbenzothiazoles (CSB, **3b**—**h**) with different combinations of O, S, and N heteroatoms in the macrocycle. Reference compound **3a** devoid of the crown ether moiety was synthesized to elucidate the regularities of condensation of benzothiazole derivatives **1** with aldehyde **2**.

Compounds **3a**—**h** were prepared by condensation of 2-methylbenzothiazole (**1a**) or (benzothiazol-2-ylmethyl)triphenylphosphonium bromide (**1b**) with 3,4-dimethoxybenzaldehyde (**2a**) or with formyl derivatives of benzo-, benzoaza-, and phenylazacrown ethers **2b**—**h** in the presence of alkali metal alkoxides or concentrated acids (see Scheme 1).

Scheme 1

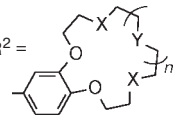


M = Li, Na, K; Alk = Me, Et, Bu^t; X = Cl, H_2PO_4

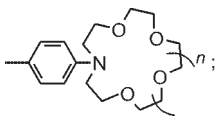
1: R^1 = H (**a**), $P^+Ph_3Br^-$ (**b**)
2a, **3a:** R^2 = 3,4-$(OMe)_2C_6H_3$

2b, **3b:** X = Y = O, *n* = 1
2c, **3c:** X = Y = O, *n* = 2
2d, **3d:** X = O, Y = NMe, *n* = 1
2e, **3e:** X = S, Y = O, *n* = 1
2f, **3f:** X = S, Y = O, *n* = 2

2b—f, **3b—f:** R^2 =



2g,h, **3g,h:** R^2 =



; *n* = 1 (**g**), 2 (**h**)

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Table 1. Yields (%) of compounds **3a**—**h** in the condensation of benzothiazoles **1a**,**b** with aldehydes **2a**—**h**

Entry	Reactants	Product	Condensing reagent					
			MeONa[a]	EtOLi[a]	EtONa[a]	EtOK[a]	Bu^{t}OK[a]	HCl[b]
1	**1a** + **2a**	**3a**	—	7	36	54	—	—
2	**1a** + **2b**	**3b**	53	2	33	19	15	37
	1a + **2b**	**3b**	20[c]	—	—	—	—	24[d]
	1b + **2b**	**3b**[e]	—	12	61	24	—	—
3	**1a** + **2c**	**3c**	72	—	53	70	43	22
4	**1a** + **2d**	**3d**	43	0	45	27	17	20
	1a + **2d**	**3d**	27	—	—	—	—	20
			(54)[d]	—	—	—	—	(68)[d]
	1b + **2d**	**3d**[e]	—	—	60	23	—	—
5	**1a** + **2e**	**3e**	57	—	—	—	—	Resinification
6	**1a** + **2f**	**3f**	56	—	—	—	—	Resinification
7	**1a** + **2g**	**3g**	—	0	0	0	—	46
	1b + **2g**	**3g**	—	—	0	—	—	—
8	**1a** + **2h**	**3h**	—	—	—	—	—	44

[a] Equimolar ratio of the reactants and bases (~20 °C, anhydrous DMSO, 24 h).
[b] Sintering of the reactants for 6 h at 130 °C in the presence of concentrated HCl.
[c] A tenfold excess of MeONa.
[d] A fivefold excess of **1a** (the yield for side product **4** formed under these conditions is given in parentheses).
[e] Equimolar ratio of the reactants and the base (anhydrous DMSO, 1 h at 0 °C and 24 h at ~20 °C).

The yields of benzothiazoles **3a**—**h** for various reaction conditions and initial compounds are presented in Table 1 and the spectral and physicochemical characteristics are summarized in Tables 2 and 3.

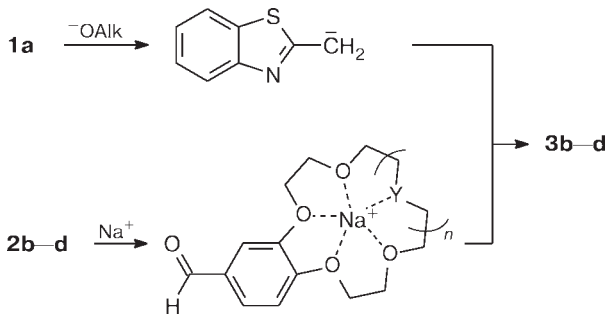
Compounds **3a**—**h** were isolated as *trans*-isomers, as indicated unambiguously from the spin—spin coupling constants of the olefinic protons (15.9—16.2 Hz). Thus, condensation of 2-methylbenzothiazole (**1a**) with benzaldehydes **2a**—**h** and the formation of CSB **3b**,**d** under the Wittig reaction conditions are stereoselective processes.

Comparison of the results of entries *2* and *4* (see Table 1) shows that the Wittig reaction provides better results than the condensation involving 2-methylbenzothiazole; however, the three-step synthesis of the initial salt **1b** reduces the synthetic value of this method.

The variation of the condensation conditions in the presence of bases made it possible to elucidate a number of regular features of reactions involving a crown-containing component. To interpret the results, we assumed that during the reaction, alkali metal alkoxides influence both the heterocyclic component by favoring the proton abstraction and the formation of the reactive methylene derivative and the formyl component (**2b**—**d**) through complexation with the crown ether moieties (Scheme 2).

Thus in entry *1* (see Table 1), which is related to the synthesis of compound **3a** devoid of the crown ether fragment, the yield of the reaction product **3a** increases in the following series of ethoxides: $Li^+ < Na^+ < K^+$. In the synthesis of CSB **3b**,**d** with the same condensing reagents, the yield increases in the sequence $Li^+ < K^+ < Na^+$ (see

Scheme 2



2: Y = O, *n* = 1 (**b**); Y = O, *n* = 2 (**c**); Y = NMe, *n* = 1 (**d**)

Table 1, entries *2* and *4*), while the order observed for CSB **3c** (entry *3*) is the same as that found for **3a**. It is known[2] that the Na^+ cation fits the 15-crown-5 cavity and forms the most stable complexes with the crown ethers having this size; meanwhile, the K^+ cation is bound most strongly to the 18-crown-6 ether. Thus, the results obtained are correlated with the stability of the complexes formed.

We "titrated" crown ether formyl derivatives **2b**,**d**,**g** with a solution of $NaClO_4$ in DMSO-d_6, the process being monitored by ^{1}H NMR spectroscopy. The presence of the salt has no substantial influence on the positions of signals in the spectrum of *N*-(4-formylphenyl)aza-15-crown-5 ether (**2g**). Conversely, for compounds **2b**,**d**, the addition of the salt induces downfield shifts of the signals

Table 2. Spectral characteristics of compounds **3a—h, 4**

Compound	^{1}H NMR, δ (^3J/Hz)	MS, m/z (I_{rel} (%))
3a	3.95 (d, 6 H, 2 OMe); 6.91 (d, 1 H, H(5′), J = 8.0); 7.16 (m, 2 H, H(6′), H(2′)); 7.31 (d, 1 H, H(a), J = 16.1); 7.37 and 7.48 (both m, 2 H, H(5), H(6)); 7.48 (d, 1 H, H(b), J = 16.2); 7.87 and 7.99 (both d, 2 H, H(4), H(7), J = 7.9, J = 8.0)	297 $[M]^+$ (72), 296 (100), 282 (18), 239 (23), 223 (16), 210 (25), 149 (18), 105 (27), 77 (17), 63 (23), 58 (50), 51 (25)
3b	3.77 (s, 8 H, 4 OCH_2); 3.95 (m, 4 H, 2 OCH_2); 4.20 (m, 4 H, 2 ArOC$\underline{H}_2$); 6.91 (d, 1 H, H(5′), J = 9.0); 7.16 (m, 2 H, H(6′), H(2′)); 7.28 (d, 1 H, H(a), J = 16.2); 7.38 and 7.48 (both m, 2 H, H(5), H(6)); 7.47 (d, 1 H, H(b), J = 16.2); 7.87 and 8.00 (both d, 2 H, H(4), H(7), J = 8.1, J = 7.5)	427 $[M]^+$ (56), 296 (42), 295 (42), 294 (100), 268 (24), 239 (15), 223 (15), 210 (23), 185 (18), 112 (34)
3c	3.71 (s, 4 H, 2 OCH_2); 3.75 (m, 4 H, 2 OCH_2); 3.77 (m, 4 H, 2 OCH_2); 3.96 (m, 4 H, 2 OC$\underline{H}_2CH_2$Ar); 4.22 (m, 4 H, 2 ArOC$\underline{H}_2$); 6.90 (d, 1 H, H(5′), J = 8.7); 7.14 (m, 2 H, H(6′), H(2′)); 7.27 (d, 1 H, H(a), J = 16.2); 7.36 and 7.46 (both m, 2 H, H(5), H(6)); 7.44 (d, 1 H, H(b), J = 16.2); 7.86 and 7.98 (both d, 2 H, H(4), H(7), J = 8.1, J = 8.1)	471 $[M]^+$ (27), 296 (29), 295 (36), 294 (100), 269 (18), 268 (25), 210 (18), 185 (14), 112 (36), 73 (17), 71 (17)
3d	2.37 (s, 3 H, Me); 2.76 (m, 4 H, 2 CH_2N); 3.78 (m, 4 H, 2 OCH_2); 3.92 (m, 4 H, 2 OCH_2); 4.19 (m, 4 H, 2 ArOC$\underline{H}_2$); 6.88 (d, 1 H, H(5′), J = 8.0); 7.14 (m, 2 H, H(6′), H(2′)); 7.27 (d, 1 H, H(a), J = 16.1); 7.37 and 7.47 (both m, 2 H, H(5), H(6)); 7.45 (d, 1 H, H(b), J = 16.1); 7.86 and 7.98 (both d, 2 H, H(4), H(7), J = 7.9, J = 8.0)	440 $[M]^+$ (21), 383 (29), 294 (24), 114 (100), 100 (29), 88 (40), 86 (23), 84 (57), 72 (29), 71 (35), 70 (48)
3e	2.96 (m, 4 H, 2 SCH_2); 3.10 (m, 4 H, 2 SCH_2); 3.80 (m, 4 H, 2 OCH_2); 4.29 (m, 4 H, 2 ArOC$\underline{H}_2$); 6.95 (d, 1 H, H(5′), J = 8.1); 7.15 (m, 2 H, H(6′), H(2′)); 7.28 (d, 1 H, H(a), J = 15.9); 7.35 and 7.50 (both m, 2 H, H(5), H(6)); 7.48 (d, 1 H, H(b), J = 15.9); 7.86 and 7.97 (both d, 2 H, H(4), H(7), J = 8.1, J = 7.5)	459 $[M]^+$ (18), 322 (22), 296 (18), 295 (59), 294 (100), 210 (21), 163 (20), 103 (17), 87 (27), 61 (52), 60 (26)
3f	2.95 (m, 4 H, 2 SCH_2); 3.12 (m, 4 H, 2 SCH_2); 3.60 (m, 4 H, 2 OCH_2); 3.71 (m, 4 H, 2 OCH_2); 4.22 (m, 4 H, 2 OCH_2); 6.83 (d, 1 H, H(5′), J = 8.1); 7.10 (m, 2 H, H(6′), H(2′)); 7.25 and 7.37 (both d, H(a), H(b), J = 15.9, J = 16.2); 7.34 and 7.43 (both m, 2 H, H(5), H(6)); 7.84 and 7.97 (both d, 2 H, H(4), H(7), J = 8.1, J = 7.5)	503 $[M]^+$ (19), 296 (22), 295 (71), 294 (100), 210 (22), 185 (18), 149 (30), 87 (59), 74 (18), 71 (19), 60 (62)
3g	3.61 (m, 12 H, 8 CH_2O); 3.75 (m, 8 H, 4 OCH_2); 6.64 (d, 2 H, H(3′), H(5′)); 7.13 (d, 1 H, H(a), J = 16.1); 7.28 and 7.33 (both m, 2 H, H(5), H(6)); 7.35 (d, 1 H, H(b), J = 16.1); 7.47 (d, 2 H, H(2′), H(6′)); 7.79 and 7.92 (both d, 2 H, H(4), H(7))	454 $[M]^+$ (100), 452 (23), 305 (15), 279 (14), 277 (18), 265 (16), 264 (14), 263 (30), 236 (21), 132 (14)
3h	3.46 (m, 16 H, 8 CH_2O); 3.54 (m, 8 H, 4 OCH_2); 6.76 (d, 2 H, H(3′), H(5′)); 7.24 (d, 1 H, H(a), J = 16.1); 7.33 and 7.37 (both m, 2 H, H(5), H(6)); 7.40 (d, 1 H, H(b), J = 16.1); 7.45 (d, 2 H, H(2′), H(6′)); 7.84 and 7.92 (both d, 2 H, H(4), H(7))	498 $[M]^+$ (100), 497 (11), 496 (25), 321 (11), 279 (15), 277 (12), 265 (18), 264 (19), 263 (38), 236 (19), 132 (12)
4	2.34 (s, 3 H, NMe); 2.71 (s, 4 H, 2 NCH_2); 3.50 and 3.61 (both dd, 2 H, H(a), H(b)); 3.70, 3.75 and 3.84 (all m, 8 H, 4 OCH_2); 3.81 (m, 1 H, ArC$\underline{H}$); 3.95 and 4.07 (both m, 4 H, 2 ArOC$\underline{H}_2$); 6.71 (s, 1 H, H(2″)); 6.75 (d, 1 H, H(5″), J = 8.2); 6.82 (d, 1 H, H(6″), J = 8.3); 7.33 and 7.43 (both m, 4 H, H(6), H(6′), H(5), H(5′)); 7.78 and 7.94 (both d, 4 H, H(7), H(7′), H(4), H(4′), J = 8.0, J = 8.1)	589 $[M]^+$ (4), 296 (12), 148 (100), 147 (26), 108 (26), 101 (42), 100 (43), 71 (20), 69 (15), 57 (14)

Note. The spectra were recorded in $CDCl_3$ except for compound **3g** (DMSO-d_6).

of all protons, which points to complexation involving the crown ether moiety[19] (Fig. 1).

The data presented in Fig. 1 indicate that the downfield shifts of proton signals are more pronounced in the case of compound **2d**; this points to the formation of a stronger complex with the Na^+ cation and is due to the presence of the highly electron-donating N atom in the macrocycle. The insignificant changes in the chemical shifts of the formyl protons in compounds **2b**,**d** upon complexation imply that the effect of this process on the condensation is not related to activation of the formyl group. Apparently, the presence of the crown ether reactant brings about a situation where the ligand competes successfully with the anion for the cation, thus increasing the concentration of anions not incorporated in ion pairs. A similar phenomenon has been thoroughly studied for reactions proceeding in the presence of crown ethers.[20] It is known,[21,22] for instance, that the Wittig reaction catalyzed by crown ethers as phase transfer catalysts results in high products yields and high homogeneity of the products

Table 3. Physicochemical characteristics of compounds **3a**—**h**, **4**

Compound	M.p./°C	Found / Calculated (%)			Molecular formula
		C	H	N	
2-[(*E*)-2-(3,4-Dimethoxyphenyl)ethen-1-yl]benzothiazole (**3a**)	144—146	68.66 68.46	5.08 5.01	4.71 4.71	$C_{17}H_{15}NO_2S$
15-[(*E*)-(Benzothiazol-2-yl)ethen-1-yl]-2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxacyclopentadecine (**3b**)	139—140	64.76 64.62	5.94 5.89	3.18 3.28	$C_{23}H_{25}NO_5S$
18-[(*E*)-(Benzothiazol-2-yl)ethen-1-yl]-2,3,5,6,8,9,11,12,14,15-decahydro-1,4,7,10,13,16-benzohexaoxacyclooctadecine (**3c**)	126—128	63.81 63.67	6.17 6.19	2.91 2.97	$C_{25}H_{29}NO_6S$
15-[(*E*)-(Benzothiazol-2-yl)ethen-1-yl]-7-methyl-2,3,5,6,8,9,11,12-octahydro-5*H*-1,4,10,13,7-benzotetraoxaazacyclopentadecine (**3d**)	123—125	58.98 59.58	6.92 7.00	5.66 5.52	$C_{24}H_{28}N_2O_4S \cdot 3H_2O$
15-[(*E*)-(Benzothiazol-2-yl)ethen-1-yl]-2,3,5,6,8,9,11,12-octahydro-1,7,13,4,10-benzotrioxadithiacyclopentadecine (**3e**)	137—139	60.01 60.10	5.80 5.48	3.88 3.05	$C_{23}H_{25}NO_3S_3$
18-[(*E*)-(Benzothiazol-2-yl)ethen-1-yl]-2,3,5,6,8,9,11,12,14,15-decahydro-1,7,10,16,4,13-benzotetraoxadithiacyclooctadecine (**3f**)	148—150	60.10 59.94	5.80 5.70	2.78 2.64	$C_{25}H_{29}NO_4S_3 \cdot H_2O$
13-{4-[(*E*)-2-(Benzothiazol-2-yl)ethen-1-yl]phenyl}-2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-tetraoxaazacyclopentadecine (**3g**)	112—113	65.89 66.05	6.73 6.65	6.12 6.16	$C_{25}H_{30}N_2O_4S$
16-{4-[(*E*)-2-(Benzothiazol-2-yl)ethen-1-yl]phenyl}-2,3,5,6,8,9,11,12,14,15-decahydro-1,4,7,10,13,16-pentaoxaazacyclopentadecine (**3h**)	86—87	65.41 65.04	6.98 6.87	5.45 5.62	$C_{27}H_{34}N_2O_5S$
15-[1,3-Bis(benzothiazol-2-yl)ethen-1-yl)]-7-methyl-2,3,6,7,8,9,11,12-octahydro-5*H*-1,4,10,13,7-benzotetraoxaazacyclopentadecine (**4**)	112—114	65.30 65.17	5.97 5.97	6.88 7.12	$C_{32}H_{35}N_3O_4S_2$

(only *trans*-isomers) and ensures suppression of the side Cannizzaro reaction.

Yet another display of influence of complexation on the course of condensation is the effect of the counter-ion present in the condensing reagent. The yield of hetarylphenylethylene in the reaction of **1a**,**b** with **2b**—**d** in the presence of MeONa is higher than that with EtONa, while the yield in the presence of EtOK is higher than that with

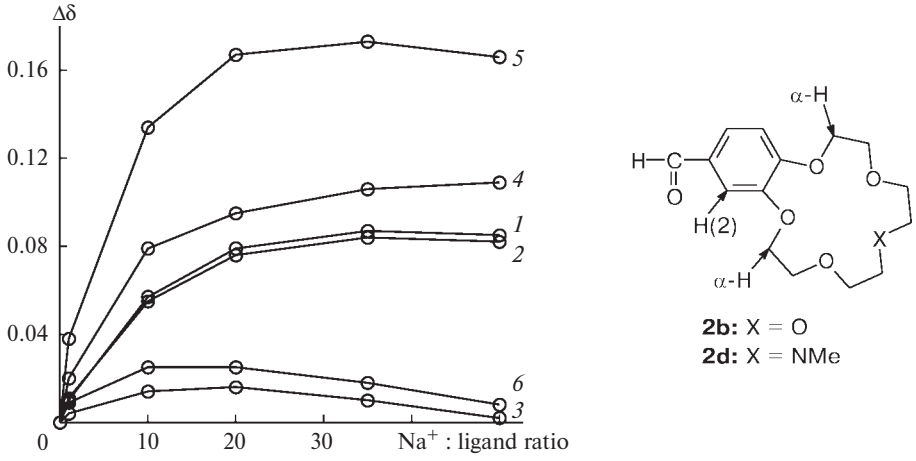
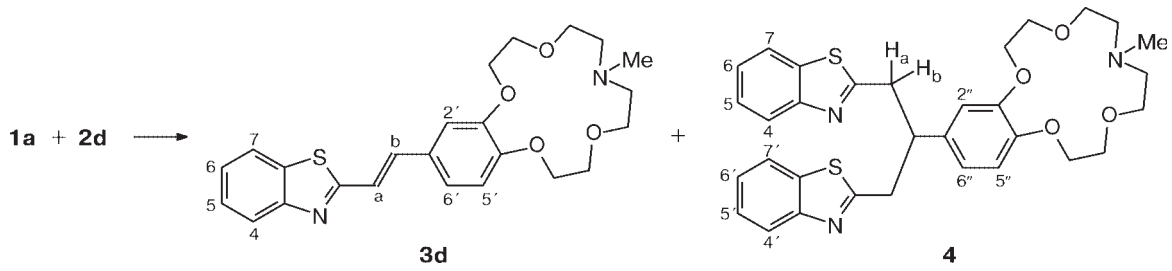


Fig. 1. Change in the proton chemical shifts ($\Delta\delta = \delta_{compl} - \delta_{ligand}$) upon the addition of $NaClO_4$ to a solution of aldehydes **2b**,**d** in DMSO-d_6: $\Delta\delta_H$ for the α-methylene groups in the macrocycles of **2b** (*1*) and **2d** (*4*); $\Delta\delta_H$ for the H(2) proton of the benzene fragment in the macrocycles of **2b** (*2*) and **2d** (*5*); $\Delta\delta_H$ for the formyl-group proton in macromolecules **2b** (*3*), **2d** (*6*).

Scheme 3



Bu^tOK (see Table 1, entries *2*—*4*). The complex formation between crown ether and the metal cation takes place after dissociation of the metal cation—alkoxide ion pair:

$$\text{Crown ether} + \text{AlkO}^-\text{M}^+ \rightleftharpoons [\text{Crown ether}\cdot\text{M}^+] + \text{AlkO}^-.$$

The stronger the ion pair, the lower the degree of its dissociation with liberation of the alkoxide ion participating in the condensation.[23] The strength of the ion pair should depend, among other factors, on the basicity of the alkoxide ion, which increases in the series $MeO^- < EtO^- < Bu^tO^-$. Thus, lower basicity in the given series of anions, all other factors being the same, would promote easier dissociation of the ion pair, the formation of the crown ether complex with the metal cation, liberation of the anion, and efficient condensation.

During the reaction, we were unable to isolate the starting unreacted formyl derivatives of benzocrown ethers **2**. Perhaps, the reaction is partially accompanied by the Cannizzaro reaction giving rise to the corresponding crown-containing acids and alcohols. After the reaction mixture has been quenched by water and the product has been extracted with benzene, the salts of the resulting crown-containing acids and alcohols remain in the aqueous phase.

The addition of a five- to tenfold excess of alkali metal alkoxides (see Table 1, entries *2* and *4*) to the reaction mixture results in more complete complexation of the cation with the crown-ether component (see Fig. 1) and promotes an additional generation of alkoxide ions and, subsequently, benzothiazolyl anions. The excess benzothiazolyl anions enter into the Michael reaction with hetarylphenylethylene **3d** formed in the reaction mixture to give bis-heterocyclic derivative **4** (Scheme 3).

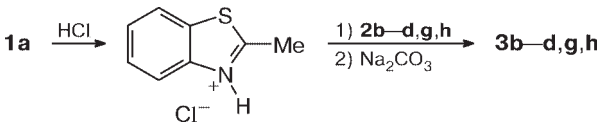
According to the ^1H NMR spectroscopy data, compound **4** has a symmetric structure, *i.e.*, the addition of a second molecule of the heterocyclic base to CSB **3d** proceeds regioselectively to give only one isomer. The regioselectivity is, apparently, due to electronic factors, *i.e.*, it is related to the fact that the electron density on the C_b atom of the ethylene fragment is lower than that on C_a in molecule **3d**.

The presence of a highly electron-donating substituent, dialkylamino group, in the *para*-position to the formyl substituent in aldehydes **2g**,**h** decreases the electron density deficiency on the formyl C atom; hence, these aldehydes do not react with compounds **1a**,**b** under basic conditions (see Table 1, entries *7*, *8*).

Benzaldehydes **2e**,**f** containing dithiacrown ether moieties produce the corresponding CSB **3e**,**f** in good yields (entries *5*, *6*). Since thiacrown ethers are known[24] to have low affinity for alkali metal cations, in the case of compounds **2e**,**f**, complexation seems to influence only slightly the condensation with **1a**. This is confirmed by the fact that CSB **3e**,**f** with different sizes of the crown ether cavity are formed in nearly equal yields in the presence of MeONa (see Table 1, entries *5*, *6*).

We have also studied the condensation of benzothiazole **1a** with crown-ether aldehydes **2b**—**h** in the presence of concentrated acids. By protonating heterocyclic base **1a** at the N atom, acids activate the methyl group toward subsequent condensation (Scheme 4).

Scheme 4



In the presence of concentrated H_3PO_4, the reaction proceeds under mild conditions (sintering at 90 °C); however, the yields of CSB are rather low (5%). In the presence of HCl (sintering at 120—130 °C), hetarylphenylethylenes with oxygen crown ethers are formed in 20—37% yields (see Table 1). This method proved to be suitable for the synthesis of 2-styrylbenzothiazoles **3g**,**h**, containing phenylazacrown ether moieties, which cannot be prepared by condensation under basic conditions (see Table 1). An increase in the reaction temperature (above 90 °C for the reaction with H_3PO_4 or above 120—130 °C in the case of HCl) results in substantial resinification of the reaction mixture. Thiacrown-ether aldehydes **2e**,**f** are completely resinified during condensation in an acid medium.

Condensation of compounds **1a** and **2** in the presence of acids should be carried out at equimolar amounts of the reactants because the use of excess initial heterocyclic derivative induces the Michael reaction and affords a bis-

heterocyclic product (see Table 1, reaction of **1a** with **2d**, entry *4*).

Thus, we propose methods for the synthesis of previously unknown crown-containing styryl dye bases using the condensation of benzothiazole derivatives with crown-ether benzaldehydes in the presence of strong bases or concentrated acids. The condensation in the presence of bases is accompanied by complexation involving the crown ether moiety of the benzaldehyde, which markedly affects the yield of the target product and the pattern of condensation of benzothiazoles with crown-ether benzaldehydes.

Experimental

^{1}H NMR spectra were recorded on a Bruker DRX-500 spectrometer in $CDCl_3$ using Me_4Si as the internal standard. Mass spectra were recorded on a Varian MAT 311A instrument for an ionization energy of 70 eV with direct sample injection. TLC was performed on DC-Alufolien Kieselgel 60 F_{254} plates (Merck).

2,3,5,6,8,9,11,12-Octahydro-1,4,7,10,13-benzopentaoxacyclopentadecine-15-carbaldehyde (**2b**),[25] 2,3,5,6,8,9,11,12,14,15-decahydro-1,4,7,10,13,16-benzohexaoxacyclooctadecine-18-carbaldehyde (**2c**),[25] 7-methyl-2,3,6,7,8,9,11,12-octahydro-5*H*-1,4,10,13,7-benzotetraoxaazacyclopentadecine-15-carbaldehyde (**2d**),[26] 2,3,5,6,8,9,11,12-octahydro-1,7,13,4,10-benzotrioxadithiacyclopentadecine-15-carbaldehyde (**2e**),[15] 2,3,5,6,8,9,11,12,14,15-decahydro-1,7,10,16,4,13-benzotetraoxadithiacyclooctadecine-18-carbaldehyde (**2f**),[15] 4-(1,4,7,10-tetraoxa-13-azacyclopentadecanyl)benzaldehyde (**2g**),[27] 4-(1,4,7,10,13-pentaoxa-16-azacyclooctadecanyl)benzaldehyde (**2h**),[27] and (benzothiazol-2-ylmethyl)triphenylphosphonium bromide (**1b**) [28] were prepared by known procedures. 2-Methylbenzothiazole (**1a**) (Fluka), and $NaClO_4$ (analytical grade) were used as received; DMSO (Merck) was dried by vacuum distillation over BaO.

Alkali metal alkoxides were prepared by dissolving metals in the corresponding alcohols followed by evaporation of excess solvent and drying *in vacuo* at 60 °C.

Condensation of 2-methylbenzothiazole (1a) with benzaldehydes 2a—f in the presence of alkali metal alkoxides (general procedure). Compound **1a** (0.2 mmol), compound **2a—f** (0.2 mmol), and alkali metal alkoxide (0.2 mmol) were mixed in 2 mL of anhydrous DMSO and the mixture was allowed to stand for 24 h at ~20 °C. Water (20 mL) was added. Compounds **3a**,**e**,**f** precipitated; the precipitates were filtered off and recrystallized from MeOH. In the other cases, the aqueous solution was extracted with benzene (5×20 mL) and the benzene extract was concentrated. In the synthesis of CSB **3b**, the residue was recrystallized from MeOH. For CSB **3c,d**, no additional purification was required.

In the synthesis of CSB **3d** with a fivefold excess of **1a**, the benzene extract was concentrated *in vacuo* and the residue was chromatographed on Al_2O_3 (150 basisch Typ T, Merck, elution with EtOH (40 : 1)) to give compound **4** (54%).

Condensation of (benzothiazol-2-ylmethyl)triphenylphosphonium bromide (1b) with benzaldehydes 2b,d (general procedure). Compound **1b** (0.2 mmol) was mixed with alkali metal ethoxide in 2 mL of dry DMSO, the mixture was cooled to 0 °C, and a solution of crown ether **2b**,**d** (0.2 mmol) in 5 mL of dry DMSO was added dropwise. The mixture was stirred for 1 h at 0 °C and for 3 h at ~20 °C and allowed to stand for 24 h. Water (20 mL) was added, the mixture was extracted with chloroform, the extract was concentrated *in vacuo*, and the residue was chromatographed on a column with Silica gel L 40/100, Chemapol (elution with benzene—ethyl acetate, 5 : 1). To separate triphenylphosphine oxide, the fraction containing the product was evaporated *in vacuo*, the residue was dissolved in 10 mL of benzene, the solution was extracted with 10% HCl (3×10 mL), the aqueous extract was neutralized by Na_2CO_3 and extracted with benzene (3×20 mL), and the benzene extract was concentrated and dried in *vacuo*.

Condensation of 2-methylbenzothiazole (1a) with formyl derivatives of benzo-, benzoaza- and phenylazacrown ethers (2b—h) in the presence of concentrated acid (general procedure). Compound **1a** (1 mmol) was mixed with concentrated HCl (1.2 mmol), the mixture was concentrated *in vacuo*, and the residue was recrystallized from EtOH to give hydrochloride **1a**·HCl. A mixture of **1a**·HCl (1 mmol), aldehyde **2b—h** (1 mmol), and **1a** (0.06 mmol) was heated for 8 h at 120—130 °C, the sublimed **1a**·HCl being returned at intervals to the reaction mixture. The cooled material was trituratd in Et_2O and extracted with boiling Et_2O (3×20 mL) to remove the remaining starting compounds.

Compounds **3b** and **3g** were isolated as hydrochlorides by recrystallizing the residue from MeCN and MeOH, respectively.

In the synthesis of CSB **3c,d**,**h**, the residue was dissolved in an aqueous solution of Na_2CO_3 and the solution was extracted with benzene (5×20 mL). The benzene extracts were concentrated *in vacuo* and the residue was chromatographed on Al_2O_3 (150 basisch, Typ T, Merck, elution with benzene—EtOH, 40 : 1 for **3d** and heptane—AcOEt, 3 : 1 for **3h**). In the case of compound **3c**, chromatographic purification was not required.

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References

1. *Crown Compounds: Towards Future Application*, Ed. S. R. Cooper, VCH Publishers, Inc., New York, 1992, 51.
2. M. C. T. Fyfe and G. F. Stoodart, *Acc. Chem. Res.*, 1997, **30**, 393.
3. J. S. Bradshow and R. M. Izatt, *Acc. Chem. Res.*, 1997, **30**, 338.
4. M. V. Alfimov and S. P. Gromov, *Applied Fluorescence in Chemistry, Biology, and Medicine*, Eds. W. Rettig, B. Strehmel, S. Schrader, and H. Seifert, Springer-Verlag, Berlin, 1999, 161.
5. J.-F. Letard, S. Delmond, R. Lapouyard, D. Braun, W. Rettig, and M. Kreissler, *Recl. Trav. Chim. Pays-Bas*, 1995, **114**, 517.
6. M. M. Martin, P. Plaza, Y. H. Meyer, L. Begin, J. Bourson, and B. Valeur, *J. Fluoresc.*, 1994, **4**, 271.
7. M. V. Alfimov, A. I. Vedernikov, S. P. Gromov, Yu. V. Fedorov, and O. A. Fedorova, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 2213 [*Russ. Chem. Bull.*, 1997, **46**, 2099 (Engl. Transl.)].

8. M. V. Alfimov, S. P. Gromov, Yu. V. Fedorov, O. A. Fedorova, A. I. Vedernikov, A. V. Churakov, L. G. Kuz´mina, J. A. K. Howard, S. Bossmann, A. Braun, M. Woerner, D. F. Sears, and J. Saltiel, *J. Am. Chem. Soc.*, 1999, **121**, 4992.
9. S. Fery-Forgues, M.-T. Le Bris, J.-P. Guette, and B. Valeur, *J. Phys. Chem.*, 1988, **92**, 6233.
10. L. Cazaux, M. Faher, C. Picard, and P. Tisnes, *Can. J. Chem.*, 1993, **71**, 1236.
11. S. Fery-Forgues, M.-T. Le Bris, J.-P. Guette, and B. Valeur, *J. Chem. Soc., Chem. Commun.*, 1988, 384.
12. J. Bourson and B. Valeur, *J. Phys. Chem.*, 1988, **92**, 3871.
13. S. P. Gromov, O. A. Fedorova, E. N. Ushakov, O. B. Stanislavskii, and M. V. Alfimov, *Dokl. Akad. Nauk SSSR*, 1991, **321**, 104 [*Dokl. Chem.*, 1991 (Engl. Transl.)].
14. E. Yu. Kryukov, A. V. Feofanov, V. A. Oleinikov, V. V. Vereshchetin, S. Yu. Zaitsev, S. P. Gromov, O. A. Fedorova, S. A. Maskevich, L. N. Kivach, V. P. Zubov, I. R. Nabiev, and M. V. Alfimov, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2490 [*Russ. Chem. Bull.*, 1996, **45**, 2362 (Engl. Transl.)].
15. M. Alfimov, Yu. Fedorov, O. Fedorova, S. Gromov, R. Hester, I. Lednev, J. Moore, V. Oleshko, and A. Vedernikov, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1441.
16. S. P. Gromov, O. A. Fedorova, E. N. Ushakov, I. I. Baskin, A. V. Lindeman, E. V. Malysheva, T. A. Balashova, A. S. Arsen´ev, and M. V. Alfimov, *Izv. Akad. Nauk, Ser. Khim.*, 1998, 99 [*Russ. Chem. Bull.*, 1998, **47**, 97 (Engl. Transl.)].
17. S. P. Gromov, E. N. Ushakov, O. A. Fedorova, V. A. Soldatenkov, and M. V. Alfimov, *Izv. Akad. Nauk*, 1997, 1192 [*Russ. Chem. Bull.*, 1997, **46**, 1143 (Engl. Transl.)].
18. S. P. Gromov, O. A. Fedorova, E. N. Ushakov, A. V. Buevich, and M. V. Alfimov, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 2225 [*Russ. Chem. Bull.*, 1995, **44**, 2131 (Engl. Transl.)].
19. O. A. Fedorova, S. P. Gromov, and M. V. Alfimov, *Dokl. Akad. Nauk*, 1995, **341**, 219 [*Dokl. Chem.*, 1995 (Engl. Transl.)].
20. W. P. Weber and G. W. Gokel, *Phase Transfer Catalysis in Organic Synthesis*, Springer Verlag, Berlin—Heidelberg—New York, 1977.
21. R. M. Boden, *Synthesis*, 1975, 784.
22. M. Mikolajczyk, S. Greejszczak, W. Midura, and A. Zatorski, *Synthesis*, 1975, 278.
23. *Ions and Ion Pairs in Organic Reactions*, Ed. M. Szwarc, Wiley Interscience, Wiley and Sons Inc., New York—London—Sydney—Toronto, 1972.
24. S. P. Gromov, O. A. Fedorova, A. I. Vedernikov, Yu. V. Fedorov, and M. V. Alfimov, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 1007 [*Russ. Chem. Bull.*, 1997, **46**, 967 (Engl. Transl.)].
25. F. Wada, H. Hirayama, H. Namiki, K. Kikukawa, and T. Matsuda, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1473.
26. Z. I. Zhilina, V. I. Mel'nik, S. A. Andronati, T. N. Dmitrieva, and V. N. Ganevich, *Zh. Org. Khim.*, 1989, **25**, 1070 [*J. Org. Chem. USSR*, 1989, **25** (Engl. Transl.)].
27. M. C. Etter, R. B. Kress, J. Berstein, and J. Cash, *J. Am. Chem. Soc.*, 1984, **106**, 6921.
28. E. B. Knott, *J. Chem. Soc.*, 1965, 3793.

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