Synthesis and structures of azine-based crown-containing hetarylphenylethenes

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Condensation of methyl-substituted six-membered heteroaromatics containing one or two nitrogen atoms with aldehyde derived from benzo-15-crown-5 ether in DMF in the presence of Bu^tOK afforded 15-crown-5-containing hetarylphenylethenes. According to the results of NMR spectroscopy, these compounds exist as mixtures of *syn* and *anti* conformers in solution (MeCN-d₃). The structures of two compounds were established by X-ray diffraction analysis.

Key words: picoline, quinaldine, lepidine, 4-methylpyrimidine, 2-methylpyrazine, 15-crown-5 ether, complexation.

Ligands based on substituted pyridines, in which the cyclic nitrogen atom can form strong coordination bonds with metal cations and hydrogen bonds with carboxy and ammonium groups of other organic molecules,¹ are widely used for designing supramolecular assemblies.² It is expected that such ligands and supramolecular assemblies based on these ligands can be used for molecular recognition of chiral molecules^{3,4} and the design of molecular devices having good luminescence characteristics^{5,6} and materials for optoelectronics^{7,8} and find application in electrochemical analysis as well.⁹

Hetarylphenylethenes based on pyridine, quinoline, dipyridyl, 3H-indole, benzothiazole, and benzoxazole can be prepared by condensation of methyl-substituted heterocyclic bases with substituted benzaldehydes under basic (Py, ^{10,11} piperidine, ¹² Bu¹OK, ¹³ AlkONa (Alk = Me or Et), ^{14,15} or LDA ¹⁶) or acidic (ZnCl₂, ^{17,18} HCl, ¹⁹ acetic acid, or acetic anhydride^{20,21}) conditions. The synthesis of hetarylphenylethenes by the Wittig reaction was also documented.²²

The synthesis and properties of heterocyclic analogs of stilbene containing a macrocyclic fragment were considered in several publications.^{23–29} It was noted that this class of compounds holds promise for the design of optical sensors for metal cations.³⁰

In the present study, we used six-membered heteroaromatic bases containing one or two nitrogen atoms in the ring (Scheme 1) as the heterocyclic component and analyzed the influence of the structure of the heterocyclic component on the formation of the corresponding crowncontaining hetarylphenylethenes.





Reagents and conditions: AlkOM = MeONa or Bu^tOK; DMSO or DMF as the solvent.

Condensation of azine derivatives 1a-g with 4'-formylbenzo-15-crown-5 ether (2a) or 3,4-dimethoxybenzaldehyde (2b) was carried out at room temperature

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Table 1. Influence of the nature of the solvent and alkali metal alkoxide on the yields of crown-containing hetarylphenylethenes (CHPE) **3a,d,e** at 20 °C

HetMe	AlkOM	Ratio*	Solvent	СНРЕ	Yield of CHPE (%)
1a	MeONa	1:1:1	DMSO	3a	0
	Bu ^t OK	1:1:1	DMSO		12
	Bu ^t OK	5:1:1.5	DMSO		23
	Bu ^t OK	5:1:1.5	DMF		78
1d	MeONa	1:1:1	MeOH	3d	0
	MeONa	1:1:1	DMSO		18
	Bu ^t OK	1:1:1	DMSO		25
	Bu ^t OK	1:1:1	DMF		47
	Bu ^t OK	5:1:1.5	DMF		88
1e	MeONa	1:1:1	MeOH	3e	0
	Bu ^t OK	1:1:1	DMSO		11 + 16**
	MeONa	1:1:0.1	DMSO		15
	Bu ^t OK	1:1:1	DMF		33
	Bu ^t OK	5:1:1.5	DMF		38

* HetMe : AlkOM : 2a.

** The yield of bisheterocyclic by-product 4a.

because heating of the reaction mixture causes resinification. The anhydrous aprotic solvents DMSO and DMF were used in the reactions. In ethanol, the formation of condensation products was not observed. We studied the influence of the nature of alkali metal alkoxide and the solvent on the yields of the products of the condensation reactions (Table 1).

The yields in DMF are much higher than those in DMSO. Among other things, this may be attributed to the involvement of DMSO in condensation with benzalde-hyde. Earlier,¹¹ it has been demonstrated that such side reactions are not associated with the involvement of DMF.

An increase in the basicity of alkoxide leads to an increase in the yield of the target product (see Table 1).

Analogous results were observed in the presence of an excess of the heterocyclic component.

The reaction of lepidine (1e) with crown-containing benzaldehyde 2a in the presence of Bu^tOK in DMSO at a ratio of 1:1:1 afforded target product 3e along with the known bisheterocyclic derivative 4a,³¹ which is apparently produced as a result of the Michael addition of the second molecule of the heterocyclic base at the double bond (Scheme 2). The reaction with the use of MeONa and the reagents in a ratio of 1:1:0.1 did not afford product 4a, but 3e was obtained in low yield (15%).

The reaction in DMF allowed us to substantially increase the yield of target product **3e**. The formation of **4a** was not observed even in the presence of a fivefold excess of lepidine.

The reaction conditions and the yields of condensation products of methyl-substituted heterocyclic bases **1a-g** with aromatic aldehydes **2a,b** are given in Table 2. Evidently, the yields of crown-containing hetarylphenylethenes (CHPE) **3a-e** depend substantially on the following two factors: the acidity of the methyl group in the heterocyclic component (pK_a^{CH}) and the steric effects. For example, the acidities of the protons of the methyl groups in quinaldine **1d**, lepidine **1e**, and γ -picoline **1a** are sufficiently high for the reactions to occur, whereas the acidities of these protons in α - and β -picolines **1f,g** are low,³² which hinders their involvement in condensation.

The protons of the methyl group in lepidine $1e^{32}$ have the highest acidity (see Table 2). However, the corresponding product 3e is formed in lower yield compared to other crown-containing derivatives. Presumably, this is attributable to steric hindrance due to the presence of the benzene ring in the *ortho* position with respect to the methyl group.

The introduction of the second nitrogen atom into the pyridine ring leads to an increase in the acidity of the methyl group.³² This is associated with the fact that



Scheme 2

X = N (1b, 3b, 4b), CH (1e, 3e, 4a)

Reaction conditions: *i*. DMSO or DMF.

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Scheme 3
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Table 2. Yields of hetarylphenylethenes 3a-g in condensation reactions of 1a-g with 2a,b in DMF; Het-Me : Bu^tOK : 2a = 5 : 1 : 1.5, 20 °C

HetMe	р <i>К</i> _а ^{СН 32}	Benzaldehyde	CHPE	Yield (%)
1a	25	2a	3a	78
1a	25	2b	3f	28
1b	_	2a	3b	41*
1c	_	2a	3c	75
1d	23	2a	3d	88
1d	23	2b	_	_
1e	22	2a	3e	38
1e	22	2b	3g	38
1f	27	2a	_	_
1g	28	2a	—	_

* The ratio HetMe : $Bu^{t}OK : 2a = 1 : 1 : 1$.

deprotonation of the methyl group in 4-methylpyrimidine **1b** leads to stabilization of the carbanion through the involvement of two nitrogen atoms. As a results of high nucleophilicity of the carbanion, the Michael reaction occurs extensively in the presence of an excess of the heterocyclic component to yield bisheterocyclic derivative **4a** (see Scheme 2). This side reaction can be avoided by using reagents in an equimolar ratio (see Table 2).

A comparison of the results of the synthesis of CHPE by condensation of **1a,d,e** with **2a** and its analog **2b** containing two methoxy groups shows that the presence of the crown ether fragment facilitates the reaction. Apparently, the latter reactions, like the synthesis of CHPE from five-membered heterocyclic bases,^{29,30} afford complexes of crown ether with a metal cation (Scheme 3). This facilitates dissociation of the alkali metal cation—alkoxide anion pair, thus promoting generation of the anion and its efficient reaction with the heterocyclic component. The resulting carbanion is sufficiently nucleophilic to add to the carbonyl carbon atom giving rise to alkoxide. Subsequent water elimination occurs readily because it gives rise to a conjugated double bond.

Therefore, the above-described conditions of condensation can successfully be used for the synthesis of crowncontaining hetarylphenylethenes from six-membered heteroaromatic bases containing one or two nitrogen atoms.

As is evident from the spin-spin coupling constants (J=15.8-16.3 Hz) of the olefinic protons, all the CHPEs synthesized have a *trans* configuration. The full assignment of the signals in the NMR spectrum was made using the COSY technique. The mutual arrangement of the structural fragments was determined from the NOESY spectroscopic data.

The above-described compounds can exist as several conformers. Thus, two conformers, **A** and **B**, can exist due to rotation of the heterocyclic fragment of the hetarylphenylethene molecule about the C–C bond (Scheme 4, heavy line).

Scheme 4





Rotation about the second C—C single bond, which is also indicated by a heavy line in Scheme 4, can lead to the transformation of the conformers A and B into the conformers C and D, respectively.

Therefore, the hetarylphenylethenes under consideration can exist as four conformers, **A**, **B**, **C**, and **D**, simultaneously.

There are evident steric restrictions in the arrangement of the H(5) and H_b protons of the conformers **B** and **D** of 4-styrylquinoline derivatives 3e,g, due to which these conformers are unstable (Scheme 5). Actually, as is evident from the NMR spectroscopic data, compounds **3e** and **3g** in MeCN-d₃ exist as mixtures of the conformers **A** and **C**, because the NOESY spectra of both compounds have intense cross-peaks from pairs of coupled protons of these conformers (see Scheme 5).

Scheme 5



Analogous results were obtained for 2-styrylquinoline **3d** and CHPE **3b,c**. All the above compounds exist in solution as mixtures of the conformers **A** and **C**. The simultaneous existence of the *anti,syn* and *anti,anti* conformers is attributed to the fact that the interconversions of these conformers of all the compounds under consideration do not give rise to steric hindrance.

Compound **3a** can exist only as two conformers, **A** (*syn*) and **C** (*anti*), which were detected in solution by NMR spectroscopy (Scheme 6).

Molecular structure (X-ray diffraction data). The molecular structure of 3g and the atomic numbering scheme are shown in Fig. 1. There are noticeable torsional distortions in molecule 3g. The dihedral angles formed by the plane of the ethylene fragment (C(3)-C(10)-C(11)-C(12)) with the planes of the quinoline bicyclic fragment and the benzene ring (C(12)...C(17)) are 15.6 and 16.6°, respectively. The quinoline and benzene systems are twisted in the same



direction. The dihedral angle between the planes of these fragments is as small as 1.4°.

The C(10)-C(11) double bond is substantially localized (1.334(2) Å). The C(3)-C(10) and C(11)-C(12) single bond lengths in the ethylene fragment are 1.462(2) and 1.471(2) Å, respectively. In the C(12)-C(13)-C(14)-C(15) fragment of the dimethoxysubstituted benzene ring, the bonds clearly alternate. The corresponding bond lengths are 1.401(2), 1.380(2), and 1.407(2) Å. By contrast, the bond lengths in the other part of this ring, C(15)-C(16)-C(17)-C(12), are equalized within standard deviations (1.385(2), 1.392(2), and 1.390(2) Å). Apparently, these geometric differences are associated with the conjugation between the lone pairs (LP) of the oxygen atoms located on the p-orbitals and the π system of the benzene ring. This conjugations is also evidenced by other characteristic features of the molecular structure. The bond angles at the oxygen atoms



Fig. 1. Molecular structure of **3g** with displacement ellipsoids drawn at the 50% probability level.

(117.4 and 117.0°) correspond to the sp²-hybridized state of these atoms. The C_{Me} -O- C_{Ar} - C_{Ar} torsion angles at the O(1) and O(2) atoms (-173.8 and -3.0°, respectively) are indicative of the parallel orientation of these orbitals.

Two exocyclic O-C-Cbond angles (O(1)-C(15)-C(16) and O(2)-C(14)-C(13)) increase to 125.3(1) and 125.0(1)°, respectively, whereas two other bond angles (O(1)-C(15)-C(14)) and O(2)-C(14)-C(15) decrease to 115.5(1) and 115.3(1)°, respectively. The character of distortion of these angles is contradictory to that expected in the case of steric repulsion between the oxygen atoms located at a distance (2.58 Å) shorter than twice the van der Waals radius (~2.8 Å). Apparently, the geometry of the fragments in compound 3g is determined by the electronic effects associated with the conjugation between LP of the oxygen atoms and the π system of the benzene ring.

The structures of two crystallographically independent molecules A and B of crown-containing 2-styrylquinoline 3d are shown in Fig. 2.

The conjugated fragments in molecules **A** and **B** have similar geometry, which is, to a large extent, similar to that observed in **3g**. Both these fragments are slightly twisted about the central ethylene bond. The dihedral angles between the planes of the quinoline system and the ethylene fragment (C(12)-C(15)-C(16)-C(17)) in **A** (**B**) and between the planes of the latter fragment and the benzene ring (C(9)...C(14)) are 14.3° (12.8°) and 10.5° (5.9°), respectively. The quinoline and benzene systems are twisted in the same direction, because the dihedral angle between their planes is smaller than each of the above-mentioned angle $(4.9^{\circ} \text{ in } \mathbf{A} \text{ and } 7.3^{\circ} \text{ in } \mathbf{B})$.

The double bond in the ethylene fragment C(15)-C(16) in **3d** is substantially localized (1.328(6) Å in **A** and 1.334(6) Å in **B**). The C(12)-C(15) and C(16)-C(17) single bond lengths are, respectively, 1.465(6) and 1.485(6) Å in A and 1.472(6) and 1.481(6) Å in B. In these molecules, a slight alternation of the bond lengths is observed in the C(9)-C(14)-C(13)-C(12)fragment of the benzene ring involving the C atoms bound to the oxygen atoms (1.420(5), 1.388(6), and 1.408(6)) Å in A and 1.416(50, 1.383(6), and 1.416(6) Å in B, respectively). This alternation is analogous to that observed in the corresponding fragment in molecule 3g. In the second part of this benzene ring, the bond lengths are equalized within experimental error (1.394(6), 1.397(6),and 1.387(6) Å in A and 1.390(6), 1.387(6), and 1.399(6) Å in **B**).

The character of deformation of the benzene ring in molecule **3d** is analogous to that in molecule **3g**. Actually, the endocyclic $O-C_{Ar}-C_{Ar}$ bond angles in the macrocycle decrease to 114.7(3) and 115.3(3)° in **A** and to 114.7(3) and 115.0(4)° in **B**, whereas the exocyclic bond angles at the C(14) and C(9) atoms increase, respectively, to 125.3(3) and 125.8(4)° in **A** and to 125.5(3) and 125.0(4)° in **B**. The distances between the O(1) and O(5) atoms (2.58 and 2.57 Å in **A** and **B**, respectively) are also shorter than twice the van der Waals radius (~2.8 Å). This effect cannot be related to the contracting effect of



Fig. 2. Structures of two crystallographically independent molecules A and B of crown-containing 2-styrylquinoline 3d.



Fig. 3. Fragment of the crystal packing of compound 3g.

the cyclic system in molecule **3d**, because it is also observed in molecule **3g**, in which the macrocyclic system is absent. Moreover, this effect is always observed in benzocrown ether systems, in which both oxygen atoms have geometry favorable for conjugation between their LP and the π system of the benzene ring.^{33–37} It should be noted that the angles at the oxygen atoms bound to the benzene ring in molecules **3d** (114.8(3) (115.4(4)) and 116.8(3) (117.6(3)°) correspond rather closely to the sp²-hybridized state of these atoms. The C(1)–O(1)–C(14)–C(13) and C(8) - O(5) - C(9) - C(10) torsion angles (-8.0°) (-5.4°) and 1.5° (5.9°)) are close to the ideal value.

The crown ether fragments in two independent molecules differ substantially in the geometry, which reflects the fact of their high conformational mobility.

Crystal packings of compounds 3d and 3g. The crystal packings of compounds provide an insight into the structures of supramolecular associates composed of this type of molecules in solution, although these molecules are less rigorously and rigidly organized in solution compared to the crystalline state.

Molecules **3g** form parallel centrosymmetric dimers (sandwiches), which are packed in a herringbone fashion (Fig. 3). This is one of the typical packings (type *c*) for conjugated molecules according to the known classification.^{**38**} The mean planes of the molecules are strictly parallel to each other, and the distance between the planes (3.41 Å) is typical of stacked conjugated systems (from 3.3 to 3.8 Å).^{**39**}

The C(10B)...C(11A) and C(11B)...C(10A) distances are 3.615 Å, and the ethylene bonds are parallel to each other. This mutual arrangement of two molecules is favorable for photochemical [2+2] cycloaddition reactions giving rise only to the centrosymmetric isomer of cyclobutane. However, this reaction does not occur in the solid state because of the rigid crystal environment of the dimers.

In the crystal packing of molecules 3g, the hydrophobic and hydrophilic regions are separated, which is always observed in the crystal packings of crown-containing styryl dyes and benzocrown ethers.^{33–37}

The crystal packing of compound 3d is shown in Fig. 4.

The hydrophilic layers, which are composed of the crown ether fragments and are perpendicular to the a axis of the crystal, alternate with the layers of the conjugated fragments. The latter form a ladder herringbone packing



Fig. 4. Crystal packing of molecules 3d projected along the c axis.

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within the layers. The ladders contain molecules **A** and **B** located almost perpendicular to each other. Molecules **A**, as well as molecules **B**, are related by a translation along the *c* axis of the crystal. This ladder-type associate is enclosed by the crown ether fragments. In the supramolecular associate, photochemical [2+2]-cycloaddition would not be expected to occur.

To summarize, we developed a new procedure for the synthesis of hetarylphenylethene derivatives containing six-membered heterocyclic moieties and a benzo-15crown-5 ether fragment under mild conditions in good yields. The influence of the structures of the starting heterocyclic compounds and the reaction conditions of condensation on the yields of the target products was investigated. The structures of the compounds in solution and in the crystalline state were established by NMR spectroscopy and X-ray diffraction analysis.

Experimental

The melting points were measured on a Mel-Temp II instrument. The ¹H NMR spectra were recorded on a Bruker DRX500 spectrometer (500.13 MHz) in CDCl₃ (unless otherwise stated) with Me₄Si as the internal standard. The chemical shifts and the spin-spin coupling constants were measured with an accuracy of 0.01 ppm and 0.1 Hz, respectively. The signals for the protons were assigned based on the 2D COSY and NOESY spectra. The mass spectra were obtained on a Varian MAT 311A instrument with direct inlet of the sample into the ionization source; the ionization energy was 70 eV. Elemental analyses were carried out in the Laboratory of Microanalysis of the A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences (Moscow). The course of the reactions was monitored by TLC on DC-Alufolien Kieselgel 60 F254 (Merck) and DC-Alufolien Aluminiumoxid 60 F₂₅₄ neutral (Typ E) (Merck) plates. Column chromatography was carried out on

Com- pound	M.p./°C	-	Found (%) Calculated		Molecular formula	λ _{max} /nm	ϵ_{max} /L mol ⁻¹ cm ⁻¹
_		С	Н	Ν			
3a	112—114	<u>68.04</u> 67.91	<u>6.76</u> 6.78	<u>3.66</u> 3.77	$\mathrm{C}_{21}\mathrm{H}_{25}\mathrm{NO}_{5}$	331	21340
3b	107—109	$\frac{64.31}{64.50}$	<u>6.44</u> 6.50	<u>7.48</u> 7.52	$C_{20}H_{24}N_2O_5$	346	24176
3c	101-103	<u>64.19</u> 64.50	<u>6.39</u> 6.50	<u>7.44</u> 7.52	$C_{20}H_{24}N_2O_5$	350	24036
3d	119—121	<u>71.21</u> 71.24	<u>6.30</u> 6.46	<u>3.24</u> 3.32	C ₂₅ H ₂₇ NO ₅	358	37951
3e	85—87	<u>70.97</u> 71.24	<u>6.68</u> 6.46	$\frac{3.12}{3.32}$	C ₂₅ H ₂₇ NO ₅	354	26736
3f	113—115	<u>74.64</u> 74.67	<u>6.24</u> 6.27	<u>5.81</u> 5.80	C ₁₅ H ₁₅ NO ₂	333	20156
3g	130-132	<u>78.36</u> 78.33	<u>5.77</u> 5.88	<u>4.74</u> 4.81	C ₁₉ H ₁₇ NO ₂	354	25032
4b	58-60	<u>64.20</u> 64.36	$\frac{6.43}{6.48}$	$\frac{11.49}{12.00}$	$C_{25}H_{30}N_4O_5$	—	_

Table 3. Characteristics of compounds 3a-g and 4b

Table 4. Spectroscopic characteristics of compounds 3a-g and 4b

Com- pound	¹ H NMR, δ (³ <i>J</i> /Hz), 30 °C*	$MS, m/z (I_{rel} (\%))$
3a	3.77 (m, 8 H, 4 OCH ₂); 3.94 (m, 4 H, 2 OCH ₂); 4.20 (m, 4 H, 2 ArOC <u>H₂</u>); 6.88, 7.23 (both d, 2 H, H _a , H _b , $J_1 = 16.3$, $J_2 = 16.3$); 6.90 (d, 1 H, H(6 [°]), $J = 8.3$); 7.09 (m, 2 H, H(2 [°]), H(5 [°])); 7.34 (d, 2 H, H(3), H(5), $J = 5.7$); 8.56 (d, 2 H, H(2), H(6), $J = 5.7$)	371 [M] ⁺ (31), 240 (47), 239 (100), 224 (32), 183 (29), 182 (32), 154 (37), 153 (58), 129 (38), 83 (47)
3b	3.77 (m, 8 H, 4 OCH ₂); 3.94 (m, 4 H, 2 OCH ₂); 4.20 (m, 4 H, 2 ArOC <u>H₂</u>); 6.89 (d, 1 H, H(5 [']), $J = 8.2$); 6.97, 7.85 (both d, 2 H, H _a , H _b , $J_1 = 15.8$, $J_2 = 15.9$); 7.17 (s, 1 H, H(2 ['])); 7.20 (d, 1 H, H(6 [']), $J = 8.2$); 7.39, 8.67 (both d, 2 H, H(5), H(6), $J_1 = J_2 = 5.0$); 9.14 (s, 1 H, H(2))	372 [M] ⁺ (58), 371 (19), 283 (15), 240 (43), 239 (100), 213 (17), 45 (54), 44 (22), 43 (72), 40 (25)

(to be continued)

Table 4 (continued)

Com-	¹ H NMR, δ (³ <i>J</i> /Hz), 30 °C*	MS,
pound		$m/z (I_{\rm rel} (\%))$
3c	3.78 (m, 8 H, 4 OCH ₂); 3.94 (m, 4 H, 2 OCH ₂); 4.18 (m, 2 H, ArOC <u>H₂</u>);	372 [M] ⁺ (14), 371 (62),
	4.21 (m, 2 H, ArOC \underline{H}_2); 6.88 (d, 1 H, H(5'), $J = 8.0$); 7.07, 7.76 (both d, 2 H, H_a ,	370 (5), 282 (4), 239 (19),
	$H_{b}, J_{1} = J_{2} = 16.1$; 7.18 (d, 1 H, H(6'), $J = 8.3$); 7.27 (s, 1 H, H(2'));	238 (100), 212 (10), 185 (5),
	8.45, 8.54 (both m, 2 H, H(5), H(6)); 8.71 (s, 1 H, H(2))	154 (8), 45 (10)
3d	3.78 (m, 8 H, 4 OCH ₂); 3.95 (m, 4 H, 2 OCH ₂); 4.20 (m, 4 H, 2 ArOC <u>H₂</u>); 6.88 (d, 1 H,	421 [M] ⁺ (100), 420 (32),
	$H(5')$, $J = 8.2$; 7.16 (d, 1 H, H(6'), $J = 8.2$); 7.26, 7.59 (both d, 2 H, H _a , H _b , $J_1 = 16.2$,	290 (26), 289 (49), 288 (99),
	$J_2 = 16.2$; 7.37 (s, 1 H, H(2')); 7.49, 7.69 (both m, 2 H, H(6), H(7)); 7.69, 7.78 (both d,	263 (26), 262 (39), 204 (41),
	2 H, H(3), H(4), $J_1 = 8.0$, $J_2 = 8.0$; 8.06, 8.12 (both d, 2 H, H(5), H(8), $J_1 = 8.4$, $J_2 = 8.6$)	178 (25), 108 (42)
3e	3.79 (m, 8 H, 4 OCH ₂); 3.96 (m, 4 H, 2 OCH ₂); 4.20 (m, 4 H, 2 ArOC <u>H₂</u>); 6.92 (d, 1 H,	421 [M] ⁺ (100), 323 (32),
	$H(5'), J = 8.0$; 7.19 (m, 2 H, $H(2'), H(6')$); 7.28, 7.67 (both d, 2 H, $H_a, H_b, J_1 = 16.0$,	290 (79), 289 (74), 288 (51),
	$J_2 = 16.0$; 7.59, 7.74 (both m, 2 H, H(6), H(7)); 7.60 (d, 1 H, H(3), $J = 4.5$);	263 (42), 217 (28), 216 (29),
	8.14, 8.23 (both d, 2 H, H(5), H(8), <i>J</i> = 8.3, <i>J</i> = 8.3); 8.89 (d, 1 H, H(2), <i>J</i> = 4.5)	204 (49), 109 (39)
3f	3.92 (m, 3 H, OMe); 3.97 (m, 3 H, OMe); 6.89, 7.26 (both d, 2 H, H_a , H_b , $J_1 = 15.9$,	241 [M] ⁺ (100), 226 (87),
	$J_2 = 15.9$; 7.03 (d, 1 H, H(6'), $J = 8.1$); 7.10 (m, 2 H, H(2'), H(5'));	198 (13), 167 (14), 166 (24),
	7.35, 7.37 (both m, 2 H, H(3), H(5)); 8.56, 8.57(both m, 2 H, H(2), H(6))	165 (21), 154 (20), 77 (15),
		58 (45), 51 (27)
3g	3.81, 3.87 (both m, 3 H each, OMe); 7.01 (d, 1 H, H(5'), $J = 8.3$); 7.30 (d, 1 H,	291 [M] ⁺ (100), 290 (27),
	$H(6')$, $J = 8.3$; 7.50 (s, 1 H, $H(2')$); 7.54, 7.96 (both d, 2 H, H_a , H_b , $J_1 = 16.1$,	276 (28), 261 (26), 260 (60),
	$J_2 = 16.1$; 7.66, 7.78 (both m, 2 H, H(6), H(7)); 7.81 (d, 1 H, H(3), $J = 4.6$);	233 (21), 217 (21), 216 (31),
	8.03, 8.55 (both d, 2 H, H(5), H(8), $J_1 = 8.4$, $J_2 = 8.4$); 8.86 (d, 1 H, H(2), $J = 4.6$)	205 (21), 204 (45)
4b	3.40 (m, 3 H, 2 CH ₂); 3.74 (m, 8 H, 4 CH ₂ O); 3.87 (m, 4 H, 2 CH ₂ O);	_
	4.04, 4.08 (both m, 2 H each, ArOCH ₂); 4.16 (m, 1 H, CH); 6.55 (d, 1 H, H(5"),	
	<i>J</i> = 8.0); 6.65 (br.d, 1 H, H(6"), <i>J</i> = 8.0); 6.69 (s, 1 H, H(2")); 7.24 (d, 2 H, H(5),	
	H(5'), J = 4.7); 8.68 (d, 2 H, H(6), H(6'), J = 4.9)	

* The spectra were recorded in CDCl₃, except for compounds **3g** and **4b** (DMSO-d₆).

Azine (<i>x</i> /mmol)	Substituted benzaldehyde	Base (z/mmol)	Solvent	τ* /days	Method of puri-	Product	Yield (%)
	(y/mmol)				fication**		
1a (0.6)	2a (0.6)	Bu ^t OK (0.6)	DMSO	1	Ι	3a	12
1a (3.0)	2a (0.6)	Bu ^t OK (0.9)	DMSO	3	Ι	3a	23
1a (3.0)	2a (0.6)	Bu ^t OK (0.9)	DMF	1	Ι	3a	78
1b (3.0)	2a (0.6)	Bu ^t OK (0.9)	DMF	1	II	3b	11
						4b	13
1b (0.6)	2a (0.6)	Bu ^t OK (0.6)	DMF	3	III	3b	41
1c (3.0)	2a (0.6)	Bu ^t OK (0.9)	DMF	1	III	3c	75
1d (0.6)	2a (0.6)	MeONa (0.6)	DMSO	1	IV	3d	18
1d (0.6)	2a (0.6)	Bu ^t OK (0.6)	DMSO	1	IV	3d	25
1d (0.6)	2a (0.6)	Bu ^t OK (0.6)	DMF	1	IV	3d	47
1d (3.0)	2a (0.6)	Bu ^t OK (0.9)	DMF	1	IV	3d	88
1e (3.6)	2a (3.6)	MeONa (0.36)	DMSO	1	IV	3e	15
1e (0.6)	2a (0.6)	Bu ^t OK (0.6)	DMF	1	IV	3e	33
1e (3.0)	2a (0.6)	Bu ^t OK (0.9)	DMF	1	IV	3e	38
1a (3.0)	2b (0.6)	Bu ^t OK (0.9)	DMF	1	IV	3f	28
1e (3.0)	2b (0.6)	Bu ^t OK (0.9)	DMF	1	V	3g	38

Table 5. Reagents and conditions of the synthesis of hetarylphenylethenes 3a-g

* The reaction time.

** I, recrystallization from *n*-heptane; II, column chromatography on SiO₂, a 5 : 1 C₆H₆-EtOH mixture of the eluent; III, recrystallization from MeOH; IV and V, column chromatography on Al₂O₃, a C₆H₆-EtOH mixture, EtOH (IV), and C₆H₆ (V) as the eluents.

Compound	3d	3g
Molecular formula	C ₂₅ H ₂₇ NO ₅	C ₁₉ H ₁₇ NO ₂
Molar weight	421.48	291.34
/g mol ⁻¹		
Crystal system	Mono	oclinic
Space group	P2	c_1/c
a/Å	16.396(1)	10.5854(6)
b/Å	33.194(3)	10.9357(7)
c/Å	7.8165(7)	12.6356(6)
β/deg	91.798(5)	99.005(2)
$V/Å^3$	4252.1(7)	1444.65(14)
Ζ	8	4
$\rho_{calc}/g \text{ cm}^{-3}$	1.317	1.339
<i>F</i> (000)	1792	616
$\mu(Mo-K\alpha)/mm^{-1}$	0.092	0.087
Crystal dimensions/mm	0.36×0.34×0.18	0.28×0.16×0.12
T/K	120.0(2)	120.0(2)
Scan mode/scan	$\omega/1.23 - 28.00$	ω/1.95-27.50
range, θ/deg		
Ranges of indices of	$-21 \le h \le 21,$	$-13 \le h \le 9,$
measured reflections	$-43 \le k \le 41,$	$-13 \le k \le 14,$
	$-5 \le l \le 10$	$-16 \le l \le 10$
Number of measured reflections	32831	7335
Number of independent	10259	3245
reflections		
R _{int}	0.1599	0.0278
Number of reflections	4770	3245
with $I > 2\sigma(I)$		
Number of parameters	776	267
in refinement		
<i>R</i> factor using reflections		
with $I \ge 2\sigma(I)$		
R_1	0.1028	0.0448
wR_2	0.2355	0.1167
R factor using all		
reflections		
R_1	0.2162	0.0666
wR_2	0.2764	0.1253
Goodness-of-fit on F^2	0.988	1.076
Residual electron density $(min/max)/e \text{ Å}^{-3}$	-0.547/0.622	-0.191/0.382

Table 6. Principal crystallographic data and characteristics of X-ray diffraction study

silica gel (Kieselgel 60, 0.063–0.200 mm, Merck) and aluminum oxide (Aluminiumoxide 150 basic, Typ E, 0.063–0.200 mm, Merck).

4-Methylpyridine (1a), 4-methylpyrimidine (1b), 2-methylpyrazine (1c), 2-methylquinoline (1d), 4-methylquinoline (1e), and 3,4-dimethoxybenzaldehyde (2b) were purchased from Aldrich and used without additional purification. 4'-Formylbenzo-15-crown-5 ether (2a) was prepared according to a known procedure.⁴⁰ The solvents DMSO (Merck) and DMF (Merck) were dried by distillation over BaO *in vacuo*. Alkali metal alkoxides were prepared by dissolution of metals in the corresponding alcohols followed by evaporation of the excess solvent and drying *in vacuo* at 60 °C.

The melting points, elemental analysis data, and the data from ¹H NMR and UV spectroscopy and mass spectrometry are given in Tables 3 and 4. (The atomic numbering schemes are presented in Schemes 5 and 6.)

Synthesis of hetarylphenylethenes 3a-g and 4b (general procedure). Azine A (x mmol) was mixed with 2a or 2b (y mmol) and Bu^tOK (z mmol) in dry DMSO or DMF (2-5 mL), and the mixture was allowed to stand for a certain time at room temperature. Then distilled water (20 mL) was added to the reaction mixture, the mixture was extracted with benzene, chloroform, or CH₂Cl₂ (4×30 mL), and the organic extract was concentrated in vacuo. The residue was purified by column chromatography or recrystallization. The reagents and conditions of the synthesis of compounds 3a-g are given in Table 5. The following compounds were prepared: 4-[(E)-2-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecin-15-yl)ethen-1yl]pyridine (3a), 4-[(E)-2-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecin-15-yl)-ethen-1yl]pyrimidine (3b), 4-[2-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecin-15-yl)-3-(4-pyrimidinyl)propyl]pyrimidine (4b), 2-[(E)-2-(2,3,5,6,8,9,11,12octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecin)ethen-1yl]pyrazine (3c), 2-[(E)-2-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecin-15-yl)ethen-1yl]quinoline (3d), 4-[(E)-2-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecin-15-yl)ethen-1yl]quinoline (3e), 4-[(E)-2-(3,4-dimethoxyphenyl)ethen-1yl]pyridine (3f), and 4-[(E)-2-(3,4-dimethoxyphenyl)ethen-1vllauinoline (3g).

X-ray diffraction study of crystals of 3d,g. Single crystals of compounds 3d and 3g were grown by crystallization from an acetonitrile solution, coated with perfluorinated oil, and mounted on a Bruker SMART-CCD diffractometer under a stream of cooled nitrogen. The experimental X-ray intensity data were collected from single crystals (Mo-K α radiation, $\lambda = 0.71073$ Å) using ω -scanning technique. The crystallographic parameters and characteristics of X-ray diffraction study are given in Table 6.

The X-ray intensity data were processed using the Bruker SAINT software.⁴¹

Both structures were solved by direct methods and refined anisotropically by the full-matrix least-squares method against F^2 . The hydrogen atoms were located from difference Fourier syntheses and refined isotropically. All calculations were carried out using the SHELXTL-Plus program package.⁴²

The complete X-ray diffraction data were deposited with the Cambridge Structural Database (CCDC refcodes 275180 and 275181).*

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^{*} These data can be obtained, free of charge, on application to Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. (fax: +44(0) 1223-336033, e-mail: deposit@ccdc.cam.ac.uk).

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