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Donor–π-acceptor benzothiazole-derived dyes with an extended heteroaryl-containing conjugated system: synthesis, DFT study and antimicrobial activity

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ABSTRACT

A series of novel derivatives containing an electron-donating *N*,*N*-dimethylaminophenyl ring connected to an electron-withdrawing benzothiazole or benzothiazolium moiety via a heteroaryl system (furan, thiophene or *N*-methylpyrrole) and up to two ethenylene groups have been synthesized and characterized. Furthermore, their nonlinear optical (NLO) properties have been investigated at the theoretical level using DFT and time-dependent DFT methods, and their antimicrobial activities were evaluated against a standard set of unicellular organisms. Both benzothiazole and benzothiazolium systems are predicted to exhibit large NLO responses, based on the calculated static molecular quadratic hyperpolarizabilities β_0 as well as intramolecular charge transfer (ICT) transition characteristics. Moreover, the 3-alkyl-benzothiazolium salts were found to display high toxicity against several tested microbes.

1. Introduction

Organic molecules containing both an electron-donating group (donor) and an electron-withdrawing group (acceptor) at opposite ends of a conjugated π-electron system (often referred to as push–pull systems) are of fundamental importance in materials chemistry since they serve as critical components for many advanced technologies, such as nonlinear optical (NLO) devices,[1] organic light-emitting diodes (OLEDs),[2] photovoltaic cells,[3] etc. In such donor–π-acceptor systems, the donor and acceptor moieties provide the necessity of ground-state charge asymmetry, whereas the π-conjugated bridge provides a pathway for the redistribution of electron density under the influence of external electric fields.[4] For the practical application of second-order NLO materials, not only a high molecular quadratic hyperpolarizability β but also a good thermal, chemical and photochemical stabilities are required. It is well known that additional stability of a NLO chromophore can be gained by substitution of the polyene segments by aromatic ones along the conjugation path between a donor and an acceptor. However, such modification leads to a decrease of β values (aromatic rings disfavour an intramolecular charge transfer since it requires them to adopt quinoidal-like structure). Theoretical as well as experimental studies revealed that good thermal and photochemical stabilities of NLO chromophores with preserved high hyperpolarizabilities can be achieved by replacement of an aromatic ring with easily delocalizable heteroaromatics.[5–8]

In respect of these findings, benzothiazole-derived dyes with a donor–π-acceptor setup are promising candidates for NLO applications.[9] Several such systems containing benzothiazole as an (auxiliary) electron-withdrawing group have already been synthesized, and relatively high values of hyperpolarizability β have been reported for them.[10,11] However, a further improvement in β values can be achieved by proper introduction of donor and acceptor substituents onto the benzothiazole core due to its non-symmetric character,[9,10] or by quaternization of the benzothiazole nitrogen.[12,13]

To date, only a few organic salts have been studied for NLO properties, because their electric charge prohibits their use in a poling process. However, donor–π-acceptor organic salts exhibit extremely large NLO responses, substantially higher stabilities and greater chromophore number densities in comparison with organic poled NLO polymers.[14] Furthermore, changing of the counterion

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can influence the crystal packing, with the aim of producing non-centrosymmetric bulk structures, which are a prerequisite for macroscopic second-order NLO effects. Thus, with the progress in fabrication processes of materials, push–pull organic salts also become applicable in NLO devices and could even replace contemporary NLO polymers.

Over the last few years, our research group synthesized a large number of push–pull 3-alkyl-benzothiazolium salts **1** with different number of ethenylene units in a π-conjugated bridge and various donor and alkyl substituents (Fig. 1).[15a–c] As some benzothiazole-derived cyanine dyes were recognized to exhibit interesting biological activities (like e.g., commercially available *dithiazanine*, which is used as an anthelmintic and antiparasitic drug),[16] benzothiazolium salts **1** were primarily studied for their antimicrobial toxicities. Those were analyzed by means of QSAR methods to identify structural blocks responsible for high biological activity.[17] It was shown that the length of the π-conjugated bridge between electron-donating group and benzothiazolium moiety as well as the donor ability have a significant influence.

Recently, Coe et al.[12] reported the results of Hyper-Rayleigh scattering (HRS) measurements for 3-methyl-benzothiazolium salts **1** (n=1–4; R=R′=CH_3) in comparison with the analogous 1-methylpyridinium salts. Experimental measurements revealed that the static molecular quadratic hyperpolarizability β_0 increases with the length of polyene chain, and the benzothiazolium salts exhibit larger NLO responses than their pyridinium analogues.

Aware of above mentioned results, we decided to extend our series of push–pull 3-alkyl-benzothiazolium salts **3** as well as the corresponding non-ionic benzothiazole derivatives **2**, by incorporation of five-membered electron-rich heteroaromatics, namely furan, thiophene or *N*-methylpyrrole, into a π-conjugated bridge (Fig. 2). Such setting could lead to enhanced chemical, photochemical and thermal stabilities, compared to derivatives with a polyenic π-bridge, and even to higher molecular quadratic hyperpolarizabilities β_0.

Herein, we report the synthesis and characterization of title systems **2** and **3**. Furthermore, the structure/NLO–activity relationships in selected systems are investigated using density functional theory (DFT) and time-dependent DFT methods. Calculated hyperpolarizabilities β_0 as well as intramolecular charge transfer (ICT) transition characteristics are confronted with those of the analogous benzothiazolium salts **1aM–dM** (n=1–4; R=R′=CH_3). Also, antimicrobial activities of all compounds prepared in this work are evaluated against a standard set of unicellular organisms.

2. Results and discussion

2.1. Synthesis of target structures

The synthesis of our target structures can be divided into two separate tasks: (a) preparation of neutral (in the sense of non-ionic) chromophores **2a–d** with a direct connection between the benzothiazole and the heteroaryl moiety, and (b) preparation of neutral derivatives **2e–j** and benzothiazolium salts **3**, where these two

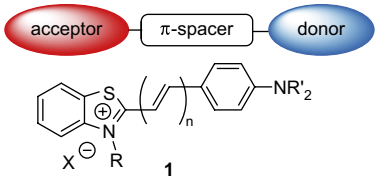


Figure 1. Structure of push–pull 3-alkyl-benzothiazolium salts with a polyenic π-bridge: **1a** (n=1), **1b** (n=2), **1c** (n=3), **1d** (n=4). The *N*-alkyl substituents R are indicated as capitals (M=methyl, A=allyl, P=prop-2-ynyl) appended to the label of corresponding compounds.

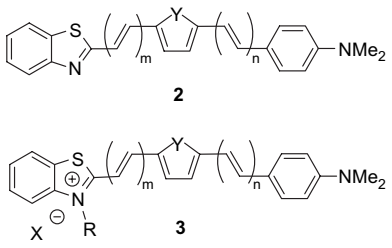
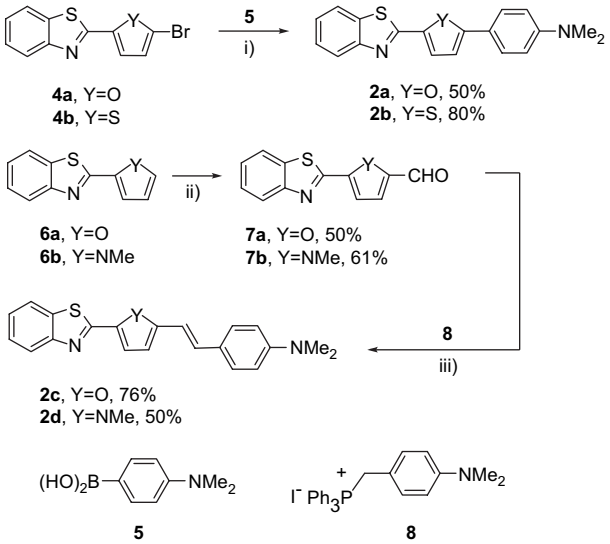


Figure 2. Structures of target compounds. Y=O, S, NMe; R=methyl (M), allyl (A), prop-2-ynyl (P); X=I, Br; m=0, 1; n=0, 1.

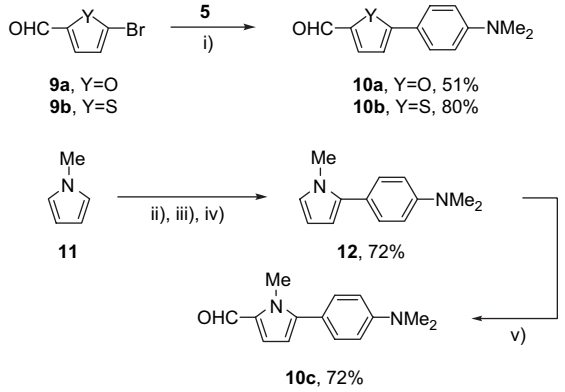
structural units are connected via an ethenylene spacer. In the first class, the synthetic approach starts with 2-heteroaryl-benzothiazoles, readily available via condensation of the corresponding heteroaryl-2-carbaldehydes with 2-amino-thiophenol to form the benzothiazole ring.[18–20] The target compounds without any ethenylene groups in the bridge system were prepared by an aryl–aryl coupling reaction, starting from 2-(5-bromofuran-2-yl)benzothiazole **4a** or 2-(5-bromothiophen-2-yl)benzothiazole **4b**, which were reacted with 4-(dimethylamino)phenylboronic acid **5** under Suzuki-coupling conditions,[21] catalyzed by palladium acetate, to form **2a** and **2b**, respectively, in good yields (Scheme 1). Compounds **2c** and **2d** were built using Wittig olefination.[22] The starting 2-heteroarylbenzothiazoles **6a** and **6b** were formylated by the Vilsmeier–Haack protocol to give the corresponding carbaldehydes **7a** and **7b**.[23] Subsequently, the products smoothly underwent a Wittig reaction with phosphonium iodide **8** (Scheme 1), providing target compounds **2c** (*E*:*Z*=11:1) and **2d** (*E*:*Z*=16:1) in good yields. At this point, it is fitting to mention that the phosphonium iodide **8** can be easily prepared by one-pot reaction of *N*,*N*-dimethylaniline, formaldehyde, PPh_3 and NaI, an approach introduced by Roncali et al.[24] However, the extended reaction time needed (3 weeks) was easily reduced to 2 h, when the reaction was performed under microwave irradiation (see Section 4).



Scheme 1. Preparation of 2-(heteroaryl)benzothiazoles **2a–d**. Reagents and conditions: (i) $Pd(OAc)_2$, PPh_3, aq Na_2CO_3, THF, reflux; (ii) $POCl_3$, DMF, 0 °C to rt; (iii) Na, MeOH, reflux.

To access derivatives **2e–j** and **3a–f** of the second class, with an ethenylene spacer connecting the benzothiazole and the heteroaryl functionalities, an aldol-type condensation reaction between 2-methylbenzothiazole or 2-methyl-3-alkyl-benzothiazolium salts and suitable heteroaryl-2-carbaldehydes was proposed.[15a–c,25] The first set of aldehydes **10a–c** was prepared by aryl–aryl coupling

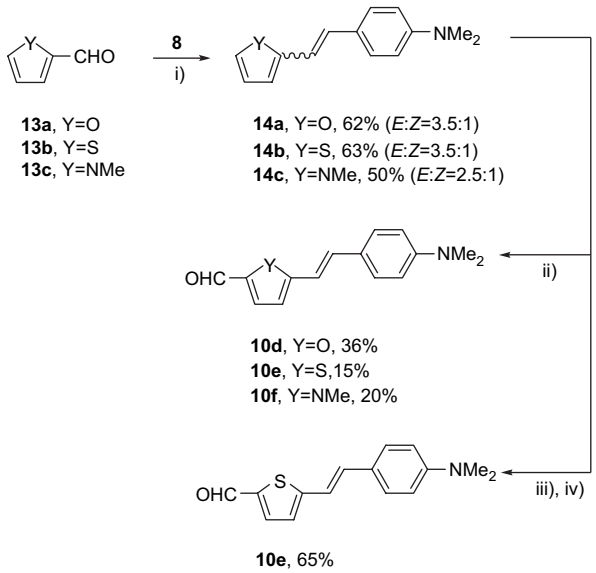
reactions. Under Suzuki-coupling conditions, 5-bromofuran-2-carbaldehyde **9a** and 5-bromothiophene-2-carbaldehyde **9b** reacted with 4-(dimethylamino)phenylboronic acid **5**, yielding carbaldehydes **10a** and **10b**, respectively, in good yields (Scheme 2).



Scheme 2. Preparation of 5-(4-dimethylaminophenyl)-heteroaryl-2-carbaldehydes **10a–c**. Reagents and conditions: (i) $Pd(OAc)_2$, PPh_3, aq Na_2CO_3, THF, reflux; (ii) BuLi, THF, −78 °C to rt; (iii) $ZnCl_2$, THF, rt; (iv) 4-bromo-*N*,*N*-dimethylaniline, $Pd(PPh_3)_4$, THF, reflux; (v) $POCl_3$, DMF, 0 °C to rt.

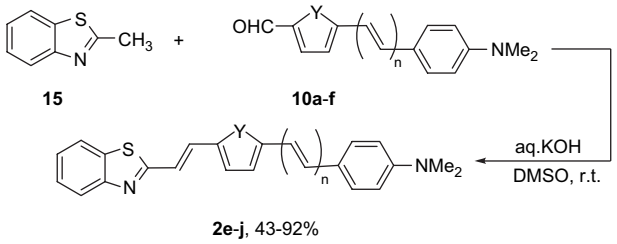
The same approach to form a 2-methylpyrrole **10c** derivative was found to be uneconomical, since 5-bromo-1-methylpyrrole-2-carbaldehyde is not easy to prepare.[26] Much better overall yields were obtained with a Negishi-coupling reaction[27] and a subsequent formylation. *N*-Methylpyrrole was transformed into *N*-methylpyrrole-2-zinc chloride and subsequently coupled with 4-bromo-*N*,*N*-dimethylaniline in a one-pot reaction to give 2-(4-dimethylaminophenyl)-1-methylpyrrole **12** in good yield. This was transformed into the carbaldehyde **10c** by Vilsmeier–Haack reaction in good yield as well (Scheme 2).

The intermediates **10d–f** were prepared from heteroaryl-2-carbaldehydes **13a–c** by Wittig reaction with phosphonium iodide **8**, yielding heteroarylstyrenes **14a–c** in good yields as mixtures of *E* and *Z* isomers, which were in turn formylated (Scheme 3). Under Vilsmeier–Haack conditions, the aldehydes **10d–f** were obtained in only low yields as pure *E* isomers. As a better alternative, the carbaldehyde **10e** was synthesized also by an alternative method. Lithiation of **14b** and following reaction with DMF gave the product in much higher yield, again as pure *E* isomer (Scheme 3).[28]



Scheme 3. Preparation of 5-[4-(dimethylaminophenyl)vinyl]-heteroaryl-2-carbaldehydes **10d–f**. Reagents and conditions: (i) Na, MeOH, reflux; (ii) $POCl_3$, DMF, 0 °C to rt; (iii) BuLi, THF, 0 °C; (iv) DMF, rt.

With the carbaldehyde substrates **10a–f** in hand, the proposed aldol-type condensations were performed (Scheme 4). At first, in reactions with 2-methylbenzothiazole **15**, catalyzed by aqueous KOH in DMSO at rt, 2-ethenylbenzothiazole derivatives **2e–j** were prepared in yields ranging from 43% up to 92% (Table 1).

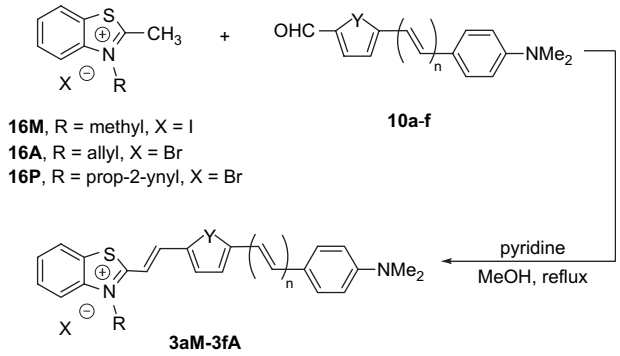


Scheme 4. Aldol-type condensations of heteroarylcarbaldehydes **10a–f** with 2-methylbenzothiazole.

Table 1
Preparation of benzothiazole derivatives **2e–j**

Product	Y	*n*	Reaction time (h)	Yield (%)
2e	O	0	3.5	54
2f	S	0	5	52
2g	NMe	0	16	43
2h	O	1	6	92
2i	S	1	16	79
2j	NMe	1	16	46

Benzothiazolium derivatives **3aM–fA** were obtained in a similar manner from 3-alkyl-2-methylbenzothiazolium salts **16M–P** and carbaldehydes **10a–f** using pyridine as a base catalyst in methanol at reflux (Scheme 5, Table 2). It is important to remark that the products, as well as the starting aldehydes, have a rather low solubility in common solvents, therefore in some cases the 3-alkyl-2-methylbenzothiazolium salts were employed in excess to remove all the aldehyde from the reaction mixture, furnishing the product in good purity (see Section 4).



Scheme 5. Aldol-type condensations of heteroarylcarbaldehydes **10a–f** with 3-alkyl-2-methylbenzothiazolium salts **16M–P**.

2.2. DFT study of molecular structures

As all compounds under investigation (in the case of benzothiazolium salts only the cationic part is assumed) can exist in at least two different conformations, all conformers were taken into account, and the electric properties (static quadratic hyperpolarizabilities β_0, ICT excitation energies E_{max}, adiabatic dipole moment changes between the ground-state and the first excited state $\Delta\mu_{12}$, transition dipole moments μ_{12} and oscillator strengths f_{osc}) were calculated by Boltzmann averaging.[29,30] More details are provided in Supplementary data (Tables S1–S3).

Table 2
Preparation of benzothiazolium salts **3aM**–**fA**

Product[a]	Y	*n*	R	X	Reaction time (h)	Yield (%)
3aM	O	0	Methyl	I	14	58
3aA	O	0	Allyl	Br	14	43
3aP	O	0	Prop-2-ynyl	Br	16	31
3bM	S	0	Methyl	I	35	40
3bA	S	0	Allyl	Br	24	60
3cM	NMe	0	Methyl	I	16	43
3cA	NMe	0	Allyl	Br	17	43
3cP	NMe	0	Prop-2-ynyl	Br	16	64
3dM	O	1	Methyl	I	16	84
3dA	O	1	Allyl	Br	12	38
3eA	S	1	Allyl	Br	20	54
3fA	NMe	1	Allyl	Br	15	54

[a] *N*-alkyl groups abbreviations: M=methyl, A=allyl, P=propargyl (prop-2-ynyl).

It is worthwhile mentioning that in all benzothiazolium salts within the series **1**, there is a significant gap (ΔE_{rel}>15 kJ mol^{-1}) between the energetically lowest lying conformer (*all-s-trans*), that is found in crystal structure,[12,13] and the others, which therefore contribute only marginally to averaged values of electric properties. On the other hand, the energy differences between various conformers of 2-(heteroarylethenyl)benzothiazole derivatives **2e**–**j** and their *N*-alkylated salts **3**, respectively, are smaller and thus contributions from the other conformations are also substantial. The optimized structures of the energetically most favoured conformers of 3-methylbenzothiazolium salts **3aM**–**fM** are depicted in Figure 3. Irrespective of the length and constitution of a π-bridge, the *s-trans* conformation with $\tau_1=\angle(N–C_2–C_9–C_{10})=180°$ is preferred over *s-cis* ($\tau_1=0°$) within series **1** and **3**. In contrast to benzothiazolium salts, neutral benzothiazoles **2e**–**j** energetically prefer the *s-cis* ($\tau_1=0°$) arrangement of benzothiazole with the adjacent ethenylene spacer. Apart from **2g** and **3cM**, which are non-planar due to steric repulsion of *N*-pyrrolic methyl group with an attached phenyl ring (torsion angle is 44° and 34°, respectively), all other energy minima take up a fully planar arrangement (if hydrogen atoms are not assumed). In the case of derivatives **2j** and **3fM** with an extended π-conjugated bridge (*n*=1), the repulsion between the *N*-pyrrolic methyl and olefinic hydrogen atoms H_{10} and H_{15} is less pronounced than in **2g** and **3cM** (*n*=0) due to the larger distance between them, which allows a coplanar arrangement of the 4-dimethylaminostyryl moiety with the pyrrole ring. Here, the *s-cis* orientation of both ethenylene spacers attached to the pyrrole ring with the endocyclic double bonds ($\tau_2=\angle(C_9–C_{10}–C_{11}–C_{12})=0°$; $\tau_3=\angle(C_{13}–C_{14}–C_{15}–C_{16})=0°$) is found to be the most stable. In contrast to *N*-methylpyrrole, the energy minima of furan and thiophene analogues (**2e**–**f**, **2h**–**i**, **3aM**–**bM**, **3dM**–**eM**) favour the *s-trans* arrangement ($\tau_2=180°$; $\tau_3=180°$) of both ethenylene spacers with the endocyclic double bonds in the five-membered heteroaromatics. The stability of these conformers can be attributed to the electrostatic through-space interaction of the lone pairs on oxygen/sulfur atom with the positively charged hydrogens. However, the *s-trans* orientation of $C_{13}=C_{14}–C_{15}=C_{16}$ ($\tau_3=180°$) in both **3dM** and **3eM** is found to be more stable only by 2 kJ mol^{-1} than in analogous conformers with $\tau_3=0°$. This can be rationalized by the less positive charge of vinyl hydrogen H_{16} in comparison with H_9.

2.3. DFT study of static molecular quadratic hyperpolarizabilities

The results of density functional theory (DFT) and time-dependent DFT calculations (both at B3LYP/6-31G* level of theory) of molecular quadratic hyperpolarizabilities β_0 and ICT transition characteristics are summarized in Tables 3 and 4.

Obviously, the relative trends in β_0 values obtained by both approaches, the finite-field (FF) derivative method and the two-state model (cf. Tables 3 and 4), are parallel. That supports the appropriateness of applicability of the simplified two-state model

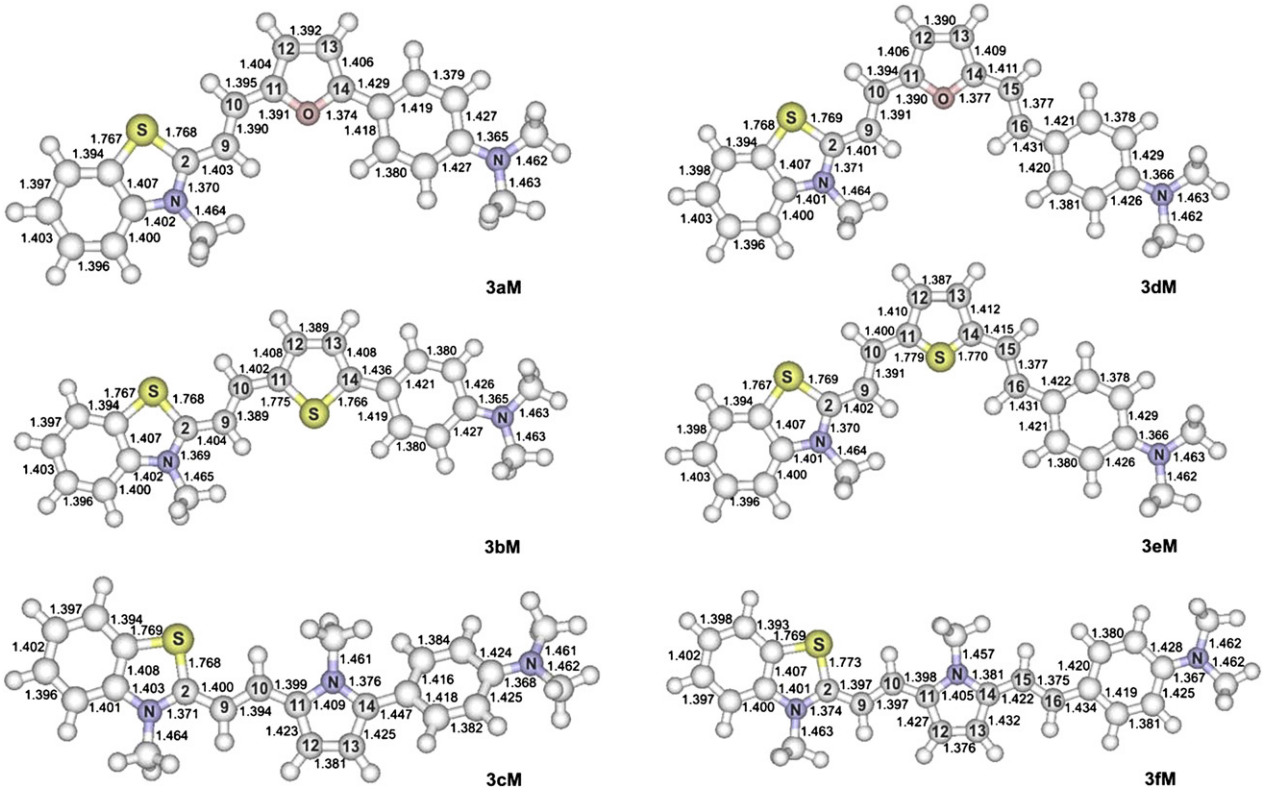


Figure 3. Optimized geometries (bond distances are given in Angstroms) of 3-methylbenzothiazolium salts **3aM**–**fM**; only conformers with the lowest energy are depicted.

Table 3
Calculated static molecular hyperpolarizabilities β_0 (B3LYP/6-31G*) and ICT transition characteristics (time-dependent DFT, B3LYP/6-31G*)

Compound	Y	n	β_0[a] [10^{-30} esu]	E_{HOMO} [eV]	E_{LUMO} [eV]	E_{max} [eV]	Configuration	μ_{12} [D]	$\Delta\mu_{12}$ [D]	f_{osc}	β_0[b] [10^{-30} esu]
2e	O	0	158	−4.71	−1.85	2.72	0.629 (HOMO→LUMO)	11.3	14.6	1.319	296
2f	S	0	193	−4.83	−1.98	2.66	0.631 (HOMO→LUMO)	12.0	15.0	1.465	356
2g	NMe	0	131	−4.65	−1.61	2.90	0.627 (HOMO→LUMO)	11.5	14.7	1.452	271
2h	O	1	227	−4.61	−1.98	2.49	0.624 (HOMO→LUMO)	12.3	15.1	1.445	431
2i	S	1	313	−4.69	−2.13	2.43	0.624 (HOMO→LUMO)	13.6	16.3	1.715	599
2j	NMe	1	249	−4.43	−1.78	2.56	0.619 (HOMO→LUMO)	14.5	14.1	2.036	530

[a] Calculated by using the finite-field numerical derivative method.
[b] Estimated from the two-state model (see Section 4.5).

Table 4
Calculated static molecular hyperpolarizabilities β_0 (B3LYP/6-31G*) and ICT transition characteristics (time-dependent DFT, B3LYP/6-31G*)

Compound	Y	n	β_0[a] [10^{-30} esu]	E_{HOMO} [eV]	E_{LUMO} [eV]	E_{max} [eV]	Configuration	μ_{12} [D]	$\Delta\mu_{12}$ [D]	f_{osc}	β_0[b] [10^{-30} esu]
1aM	—	1	78	−8.18	−5.53	2.72	0.591 (HOMO→LUMO)	12.0	6.2	1.481	141
1bM	—	2	142	−7.78	−5.47	2.45	0.578 (HOMO→LUMO)	14.6	7.8	1.984	324
1cM	—	3	233	−7.45	−5.41	2.23	0.567 (HOMO→LUMO)	17.1	8.8	2.465	604
1dM	—	4	357	−7.18	−5.33	2.05	0.558 (HOMO→LUMO)	19.4	9.8	2.936	1019
3aM	O	0	230	−7.57	−5.46	2.19	0.585 (HOMO→LUMO)	13.0	13.2	1.395	540
3bM	S	0	289	−7.54	−5.49	2.14	0.584 (HOMO→LUMO)	13.9	13.8	1.584	683
3cM	NMe	0	329	−7.44	−5.29	2.14	0.603 (HOMO→LUMO)	12.3	20.4	1.220	782
3dM	O	1	381	−7.28	−5.38	2.00	0.576 (HOMO→LUMO)	14.6	15.2	1.617	943
3eM	S	1	463	−7.25	−5.41	1.96	0.572 (HOMO→LUMO)	16.0	15.0	1.915	1160
3fM	NMe	1	465	−7.09	−5.14	2.05	0.581 (HOMO→LUMO)	15.8	18.4	1.949	1274

[a] Calculated by using the finite-field numerical derivative method.
[b] Estimated from the two-state model (see Section 4.5).

in order to gain a better understanding of the structure–activity relationships in all compounds under investigation.

It is well known that most of the total hyperpolarizability in donor–π-acceptor organic systems is associated with ICT (intramolecular charge transfer) transitions. The CI (configuration interaction) coefficients calculated by time-dependent DFT reveal that the lowest energy excitations E_{max} correspond in every case with the HOMO–LUMO transitions (cf. Tables 3 and 4). For all compounds studied here, both HOMO and LUMO are π-type orbitals, which appearance is demonstrated for **3fM** in Figure 4. The HOMO is mainly constrained to the donor part, i.e., the 4-dimethylaminophenyl moiety, whereas the LUMO has its largest atomic orbital (AO) coefficients at the atoms of the electron-withdrawing thiazole/thiazolium ring and adjacent ethenylene group. However, other carbon atoms in a π-conjugated bridge with incorporated heteroaromatics also contribute to both HOMO and LUMO, leading to an extensive overlap of those frontier orbitals, and thus to large values of transition dipole moments μ_{12}. Neutral benzothiazole derivatives render a similar picture.

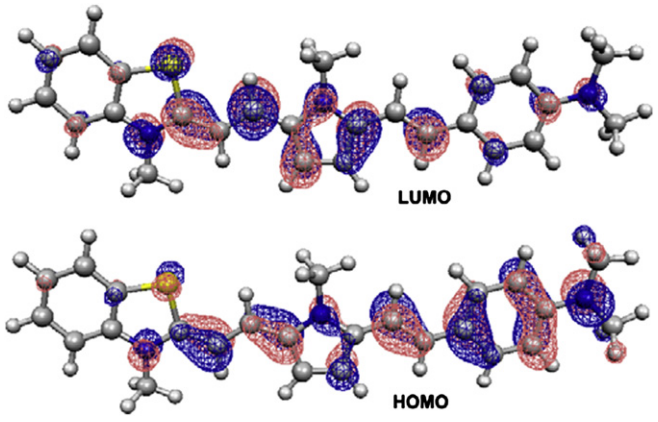


Figure 4. Frontier molecular orbitals HOMO and LUMO (isosurface +/−0.03 a.u.) in the benzothiazolium salt **3fM**.

Some structural aspects that influence the NLO activity are discussed here.

2.3.1. Length of the π-conjugated bridge

Theoretical calculations reproduce the expected optical behaviour in the studied set of compounds. Increasing the length of polyene chain in the set **1aM–dM** (Table 4) is accompanied by the decrease in E_{max}, along with increases in μ_{12}, $\Delta\mu_{12}$, f_{osc}, that leads to enhanced NLO response (larger β_0 values). The same holds also for 2-heteroaryl derivatives within the both series **2** and **3**. The only exception is observed in $\Delta\mu_{12}$ passing from **2g** to **2j** and **3cM** to **3fM**, respectively, which can be rationalized by non-planar structures of **2g** and **3cM**.

2.3.2. Polyene versus heteroaryl-containing spacer

If the five-membered heteroaromatics are viewed as an equivalent of two ethenylene units (or *s-cis*-buta-1,3-diene fragment), it is evident from Table 4, that 2-(heteroarylethenyl)benzothiazolium salts **3** display comparable (Y=O) or even larger (Y=S, NMe) β_0 values compared to their analogues with a genuine polyenic chain **1**. Although smaller transition dipole moments μ_{12} are computed for 2-(heteroarylethenyl)benzothiazolium salts **3**, their enhanced NLO response results from considerable larger change in dipole moment $\Delta\mu_{12}$ upon ICT excitation. This implies a slightly different origin of β_0 values, which can be understood from the following: electron-rich heterocycles (furan, thiophene, *N*-methylpyrrole) in the ground-state suppress an electron transfer from a 4-dimethylamino-phenyl moiety to an electron-withdrawing (benzothiazole/-ium) group due to their aromatic character, and therefore larger change in dipole moment upon ICT excitation is observed. On the other hand, smaller overlap of HOMO and LUMO orbitals, resulted from the same reason as enhancement of $\Delta\mu_{12}$, leads to a smaller transition moment μ_{12}.

2.3.3. Benzothiazole versus benzothiazolium derivatives

Calculated β_0 values indicate somewhat (ca. two times) larger NLO response of ionic **3aM–fM** chromophores compared to their neutral analogues **2e–j** (cf. Tables 3 and 4). Here, enhanced NLO response of benzothiazolium compounds can be explained by their

Table 5
Calculated static molecular hyperpolarizabilities β_0 (B3LYP/6-31G*) and ICT transition characteristics (time-dependent DFT, B3LYP/6-31G*) using PCM solvation model (CH_3OH as a solvent)

Compound	β_0[a] [10^{-30} esu]	E_{max}[b] [eV]	μ_{12} [D]	$\Delta\mu_{12}$ [D]	f_{osc}	β_0[c] [10^{-30} esu]
1aM	289	2.61 (2.37)	12.7	6.5	1.604	180
1bM	628	2.32 (2.19)	15.5	7.8	2.102	408
1cM	1192	2.09 (2.13)	18.1	8.6	2.584	757
1dM	2059	1.90 (2.11)	20.6	9.2	3.059	1259
3aM	871	2.12 (2.13)	13.8	12.1	1.540	598
3bM	1218	2.07 (2.20)	14.9	12.9	1.746	784
3cM	955	2.15 (2.21)	13.6	17.5	1.514	818
3dM	1580	1.90 (2.09)	15.0	13.4	1.630	973
3eM	2299	1.86	16.8	14.0	1.995	1341
3fM	1740	2.00	17.3	15.2	2.255	1335

[a] Calculated by using the finite-field numerical derivative method.
[b] Experimental values are given in parenthesis.
[c] Estimated from the two-state model (see Section 4.5).

much lower excitation energies E_{max}, as well as slightly larger transition moments μ_{12}.

Although non-ionic benzothiazole derivatives **2e–j** are predicted to exhibit smaller static molecular hyperpolarizabilities β_0 compared to their *N*-alkylated analogues, a functionalization of the *N*-alkyl donor with hydroxyethyl groups would allow their use as monomers in the synthesis of interesting NLO polymers.

2.3.4. Character of heteroaryl moiety

According to computed β_0 values, thiophene- and *N*-methylpyrrole-containing derivatives are expected to be the most NLO-active. While the former is more efficient in neutral benzothiazoles, the latter leads to the highest β_0 values in benzothiazolium salts. However, as the calculated β_0 values of pyrrole- and thiophene-containing derivatives are in a narrow range of numerical values, the ordering of the structures according to their calculated NLO responses must not be necessarily consistent with experimental observation.

2.3.5. Solvent effects

Since the hyperpolarizability values are also markedly influenced by the solvent effects, DFT calculations with the inclusion of bulk solvent effects by the polarizable continuum model (PCM) were also performed for benzothiazolium salts (methanol as a solvent; ε=32.63). The results are gathered in Table 5. Generally, β_0 values calculated by employing PCM solvation model are higher in comparison with those in vacuo (cf. Table 4), which can be mainly attributed to smaller excitation energies and larger transition moments μ_{12}. Nevertheless, the trends in β values are parallel with those obtained in vacuo, apart from the fact that finite-field β_0 values are superior to those estimated from the two-state model.

In addition, the calculated E_{max} values are compared with the experimental ones measured in methanol solution (Table 5). Although a qualitative agreement is found, the calculations predict a greater extent of red-shifting of the ICT bands with a π-bridge elongation (for instance, the calculated value of ΔE_{max} on moving from **3aM** to **3dM** is 0.22 eV, whereas that observed is only 0.04 eV).

2.4. Biological activity

Prepared benzothiazole derivatives **2** and benzothiazolium salts **3** were tested in vitro for their antimicrobial activity against unicellular flagellate *Euglena gracilis*, as well as some Gram-positive and Gram-negative bacteria, a yeast and a mould (see Section 4). The log(1000/ED50) values, where ED50 is the dosage producing a desired effect in half the test population (in 10^{-3} mol L^{-1}), and minimum inhibitory concentrations (MIC in μg/mL) are collected in Table 6.

It is evident that all benzothiazolium salts **3** exhibit much higher antimicrobial activities than the neutral benzothiazole derivatives **2**, a fact observed already in our previous studies.[15,17] Better solubility of benzothiazolium salts in a polar medium, and therefore easier transport of the substrate into the cellular environment, is presumably responsible for higher toxicity of these compounds.

Table 6
Antimicrobial activities of tested benzothiazole derivatives **2a–j** and benzothiazolium salts **3aM–fA** in comparison with **1aM–cM**

Compound	*Eugena gracilis*[a]	Gram-positive bacteria		Gram-negative bacteria		Yeast	Mould
		Staphylococcus aureus[b]	*Bacilus subtilis*[b]	*Escherichia coli*[b]	*Pseudomonas aeruginosa*[b]	*Candida albicans*[b]	*Microsporum gypseum*[c]
2a	2.482	50	250	>250	>250	250	>250/250
2b	2.878	50	250	>250	>250	250	>250/250
2c	2.933	50	250	>250	>250	250	>250/250
2e	2.886	50	250	>250	>250	250	>250/250
2f	2.910	50	250	>250	>250	250	>250/250
2g	2.965	50	250	>250	>250	250	>250/250
2h	2.985	50	250	>250	>250	250	>250/250
2i	2.983	50	50	>250	>250	250	>250/250
2j	2.999	50	250	>250	>250	250	>250/250
1aM	6.135	2	50	250	>250	50	50/10
1bM	6.437	10	50	250	>250	50	50/10
1cM	6.976	2	10	50	>250	50	5/2.5
3aM	6.480	10	50	250	>250	250	50/10
3aA	6.428	2	10	250	>250	50	10/2
3aP	6.410	2	10	250	>250	50	10/2
3bM	6.563	10	50	250	>250	250	50/10
3bA	6.533	2	10	250	>250	50	50/10
3cM	6.590	2	10	50	>250	10	10/2
3cA	6.508	2	10	50	>250	10	10/2
3cP	6.612	2	10	50	>250	10	10/2
3dM	6.575	10	50	250	>250	50	50/10
3dA	6.557	2	50	250	>250	50	10/2
3eA	6.571	2	10	50	>250	10	2/0.4
3fA	6.484	2	10	50	>250	10	2/0.4

[a] Values given as log(1000/ED50).
[b] Values for minimum inhibitory concentration (MIC) in μg/mL.
[c] Fungicide/fungistatic concentration in μg/mL.

The toxicity values of the title structures **3** against the unicellular flagellate *E. gracilis* are in general comparable to those of benzothiazolium salts **1aM**–**cM**. The highest toxicities were exhibited by compounds **3cM** (6.590, Y=O, R=Me, n=0) and **3cP** (6.612, Y=NMe, R=Me, n=0) and are somewhat lower compared with the structure **1cM** (6.955, n=3). The inclusion of heteroaryl moiety into a π-conjugated bridge slightly enhances the antimicrobial activity, but not as much as an inclusion of two ethenylene units. Thus, unlike the effect observed in the NLO properties, the five-membered heteroaromatic fragment is not equivalent to two ethenylene units in the terms of resulting toxicity. In general, the sensitivity of Gram-positive bacteria to the tested substances is higher than that of Gram-negative bacteria. The strongest antibacterial effect was found for *Staphylococcus aureus*. Moreover, derivatives **3eA** (Y=S, R=Me, n=1) and **3fA** (Y=NMe, R=Me, n=1) display interesting fungicidal/fungistatic activity against *Microsporum gypseum* and could be considered as new potential antifungal substances.

3. Conclusions

A series of novel donor–π-acceptor benzothiazole-derived dyes (**2** and **3**) with an extended heteroaryl-containing π-conjugated system have been synthesized and characterized. Fast and effective access to the target compounds was accomplished through the combination of palladium-catalyzed aryl coupling reactions, Wittig olefination, Vilsmeier–Haack formylation and aldol-type condensations.

Selected target structures were investigated for their molecular nonlinear optical (NLO) properties at the theoretical level using DFT and time-dependent DFT methods. A pronounced conformational effect on calculated static quadratic hyperpolarizabilities β_0 was found for 2-(heteroarylethenyl)benzothiazole/-ium derivatives (**2** and **3**). Pursuant to this finding, the influence of conformational equilibria on β_0 values should be taken into account in further studies of related systems.

All the compounds under investigation could be considered as efficient NLO-phores due to their very large β_0 values. The benzothiazolium salts **3aM**–**fM** are predicted to exhibit somewhat larger molecular quadratic NLO responses compared to their non-ionic analogues **2e**–**j**. In general, it was shown that inclusion of a five-membered heteroaryl moiety into a π-conjugated bridge substantially enhances the NLO response of the donor–π-acceptor systems. In this respect, benzothiazole-based chromophores containing *N*-methylpyrrole-2,5-diyl or thiophene-2,5-diyl spacer are predicted to be superior to those derived from furan.

In addition, the antimicrobial activities of the title systems (**2** and **3**) were evaluated against a standard set of unicellular organisms. The title structures **3** exhibit high toxicity values against the unicellular flagellate *E. gracilis*, as well as some interesting antibacterial and fungicidal activities. The studied systems were found to be comparably active than the previously prepared benzothiazolium salts containing polyene π-conjugated bridge (**1aM**–**cM**).

Moreover, the prepared heteroaryl-2-carbaldehyde intermediates **10a**–**f** can serve as valuable and versatile building blocks for the synthesis of molecules with an extended π-conjugated system, finding potential application in many fields of material chemistry, such as optical and electronic devices.

4. Experimental

4.1. General

Purchased chemicals and solvents were purified by distillation or crystallization and dried as needed, using standard procedures. For TLC and column chromatography, a mixture of hexane isomers (hexanes, light petroleum) was used in eluent solutions. Solvents were removed by rotary evaporation. The starting compounds **4a**,[18] **4b**,[19] **5**,[31] **6a**,[20] **6b**,[20] **9a**,[32] **9b**,[33] **13b**[33a] and **13c**[34] were prepared according to known literature procedures.

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer, operating at 300 MHz (^{1}H) and 75 MHz (^{13}C) with TMS as internal standard. Chemical shifts δ are referred in terms of parts per million and *J*-coupling constants are given in hertz. Abbreviations for multiplicity are as follows: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet). IR-spectra were recorded on a Carl Zeiss/Jena Specord M 80 instrument or *Perkin Elmer Spectrum One FTIR* with an *Universal ATR Sampling Accessory* and the signals are given by wave numbers (cm^{-1}). UV–vis absorption maxima were measured on a HP Diode Array 8245 spectrometer. Combustion analysis was measured on a Carlo Erba Science 1106 instrument. The melting points were measured using a Kofler apparatus and were not corrected.

4.2. Synthesis

4.2.1. *(4′-Dimethylaminobenzyl)triphenylphosphonium iodide (**8**)*

A suspension, containing *N*,*N*-dimethylaniline (10 g, 82 mmol, 1 equiv), 37% aqueous formaldehyde solution (8.2 g, 82 mmol, 1 equiv), PPh_3 (21.5 g, 82 mmol, 1 equiv), NaI (12.3 g, 82 mmol, 1 equiv), acetic acid (15.6 mL) and chloroform (60 mL), was stirred for 15 min at rt. Afterwards, a few drops of water were added and the mixture was heated in a microwave reactor (400 W) to reflux for 2 h and subsequently left to stand at rt overnight. The chloroform was evaporated, 150 mL of water was added, the insoluble residue collected by filtration, washed several times with water and diethyl ether and dried in vacuum. The reaction yielded 32.5 g of white solid (76%). Mp 238–239 °C (lit. 240 °C);[24] ^{1}H NMR ($CDCl_3$) δ=7.83–7.75 (m, 3H, Ar–H), 7.69–7.62 (m, 12H, Ar–H), 6.85 (dd, 2H, *J*=8.9, 2.5 Hz, Ar–H), 6.46 (d, 2H, *J*=8.6 Hz, Ar–H), 4.93 (d, 2H, *J*=13.0 Hz, CH_2), 2.88 (s, 6H, NMe_2) ppm.

4.2.2. *5-(Benzothiazol-2-yl)-furan-2-carbaldehyde (**7a**)*

To a solution of furan derivative **6a** (0.8 g, 4 mmol, 1 equiv) in dry DMF (2 mL), cooled in an ice bath, $POCl_3$ (0.84 mL, 1.38 g, 9 mmol, 2.25 equiv) was added with stirring. The reaction mixture was stirred for 1 h at rt and 3 h at 80 °C. After this time, the mixture was allowed to cool and was poured on ice and neutralized with aqueous solution of NaOH. The precipitated solid was collected by filtration. The crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to give 0.45 g of beige solid (50%). Mp 175–176 °C (lit. 176 °C);[23] ^{1}H NMR ($CDCl_3$) δ=9.81 (s, 1H, CHO), 8.12 (d, 1H, *J*=8.2 Hz, H_{BT}), 7.97 (d, 1H, *J*=8.0 Hz, H_{BT}), 7.56 (dt, 1H, *J*=8.2, 1.1 Hz, H_{BT}), 7.47 (ddd, 1H, *J*=8.2, 8.0, 1.1 Hz, H_{BT}), 7.40 (d, 1H, *J*=3.8 Hz, H_{FUR}), 7.36 (d, 1H, *J*=3.6 Hz, H_{FUR}) ppm.

4.2.3. *5-(Benzothiazol-2-yl)-1-methylpyrrole-2-carbaldehyde (**7b**)*

To a solution of pyrrole derivative **6b** (0.3 g, 1.4 mmol, 1 equiv) in dry DMF (5 mL), cooled in an ice bath, $POCl_3$ (0.38 mL, 0.63 g, 4.2 mmol, 3 equiv) was added with stirring. The reaction mixture was stirred for 30 min at rt and 1 h at 80 °C. After this time, the mixture was allowed to cool and was poured on ice and neutralized with aqueous solution of NaOH. The mixture was extracted with chloroform (3×20 mL), combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated to give the crude product, which was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to yield 0.2 g of beige solid (61%). Mp 188–190 °C; ^{1}H NMR ($CDCl_3$) δ=9.71 (s, 1H, CHO), 8.07 (d, 1H, *J*=8.1 Hz, H_{BT}), 7.90 (d, 1H, *J*=8.1 Hz, H_{BT}), 7.52 (t, 1H, *J*=8.2 Hz, H_{BT}), 7.42 (t, 1H, *J*=7.1 Hz, H_{BT}), 6.98 (d, 1H, *J*=4.1 Hz, H_{PYR}), 6.84 (d, 1H, *J*=4.2 Hz, H_{PYR}), 4.49 (s, 3H, CH_3–N) ppm; ^{13}C NMR ($CDCl_3$) δ=179.2, 160.1, 154.4, 133.9, 132.8, 132.5, 125.9, 125.3, 124.5, 122.5, 121.0, 115.1, 34.9 ppm. Anal. Calcd for $C_{13}H_{10}N_2OS$: C 64.44, H 4.16, N 11.56; found: C 64.25, H 4.30, N 11.48%.

4.2.4. 2-[5-(4-Dimethylaminophenyl)-furan-2-yl]-benzothiazole (**2a**)

To a solution containing the boronic acid **5** (0.3 g, 1 mmol, 1.0 equiv), arylbromide **4a** (0.21 g, 1.3 mmol, 1.3 equiv), $Pd(OAc)_2$ (2 mg, 0.01 mmol, 0.01 equiv) and PPh_3 (8 mg, 0.03 mmol, 0.03 equiv), in THF (7 mL) under nitrogen, 2 M aqueous Na_2CO_3 solution (3 mL) was added and the mixture was heated to reflux for 16 h. After this time, 20 mL of water was added and the mixture was extracted with ethyl acetate (2×10 mL), combined organic layers were dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to yield 0.16 g of sightly yellow solid (50%). Mp 188–190 °C; ^{1}H NMR ($CDCl_3$) δ=8.02 (d, 1H, J=8.6 Hz, H_{BT}), 7.87 (d, 1H, J=8.1 Hz, H_{BT}), 7.68 (d, 2H, J=9.0 Hz, H_{2Ph}, H_{6Ph}), 7.47 (t, 1H, J=8.4 Hz, H_{BT}), 7.35 (t, 1H, J=8.1 Hz, H_{BT}), 7.26 (d, 1H, J=3.7 Hz, H_{3FUR}), 6.76 (d, 2H, J=9.0 Hz, H_{3Ph}, H_{5Ph}), 6.62 (d, 1H, J=3.7 Hz, H_{4FUR}), 3.03 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=157.7, 157.3, 153.9, 134.0, 126.5, 126.2, 125.7, 124.6, 124.5, 122.6, 121.9, 121.3, 113.9, 112.0, 104.9, 40.4 ppm; IR (MeOH) ν=2920, 1612, 1596, 1499, 1431, 1362, 1195, 905 cm^{-1}. Anal. Calcd for $C_{19}H_{16}N_2OS$: C 71.22, H 5.03, N 8.74; found: C 71.41, H 5.14, N 8.52%.

4.2.5. 2-[5-(4-Dimethylaminophenyl)-thiophen-2-yl]-benzothiazole (**2b**)

To a solution containing the boronic acid **5** (0.3 g, 1 mmol, 1.0 equiv), arylbromide **4b** (0.20 g, 1.2 mmol, 1.2 equiv), $Pd(OAc)_2$ (2 mg, 0.01 mmol, 0.01 equiv), and PPh_3 (8 mg, 0.03 mmol, 0.03 equiv) in THF (7 mL) under nitrogen, 2 M aqueous Na_2CO_3 solution (3 mL) was added and the mixture was heated to reflux for 16 h. After this time, the mixture was allowed to cool to ambient temperature, the precipitated solid was collected by filtration, washed with diethyl ether and cold acetone and dried under vacuum to give 0.27 g of yellow solid (80%). Mp 219–220 °C (lit. 211–212 °C);[11b] ^{1}H NMR ($CDCl_3$) δ=8.01 (d, 1H, J=8.1 Hz, H_{BT}), 7.83 (d, 1H, J=8.4 Hz, H_{BT}), 7.58 (d, 1H, J=3.7 Hz, H_{3THP}), 7.56 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.45 (ddd, 1H, J=8.2, 7.3, 1.1 Hz, H_{BT}), 7.34 (ddd, 1H, J=8.2, 8.0, 1.1 Hz, H_{BT}), 7.18 (d, 1H, J=4.0 Hz, H_{4THP}), 6.74 (d, 2H, J=8.9 Hz, H_{3Ph}, H_{5Ph}), 3.02 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=161.8, 154.0, 150.8, 149.8, 134.8, 133.8, 130.0, 127.2, 126.5, 125.1, 122.9, 121.9, 121.7, 121.6, 112.6, 40.5 ppm; UV–vis ($CHCl_3$) λ_{max}=406 nm (log ε=6.510); IR (MeOH) ν=1610, 1520, 1460, 1430, 1350, 920 cm^{-1}. Anal. Calcd for $C_{19}H_{16}N_2S_2$: C 67.82, H 4.79, N 8.33; found: C 68.03, H 4.95, N 8.30%.

4.2.6. 2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-furan-2-yl}-benzothiazole (**2c**)

A sodium methanolate solution, prepared from sodium (50 mg, 1.9 mmol, 1.1 equiv) and dry MeOH (5 mL), was added dropwise to a stirred suspension of phosphonium iodide **8** (1 g, 1.9 mmol, 1.1 equiv) in MeOH (5 mL) at rt. The mixture was stirred for 15 min, a solution of aldehyde **7a** (0.4 g, 1.7 mmol, 1 equiv) in MeOH (5 mL) was added and the reaction mixture was then set to reflux for 4 h. After cooling to ambient temperature, the solvent was evaporated, the residue was mixed with water (20 mL) and extracted with chloroform (3×15 mL). Combined organic layers were dried (Na_2SO_4), the solvent was evaporated and the crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to give 0.45 g of yellow solid (*E*:*Z* isomer=11:1, overall yield 76%). (*E*)-isomer: mp 164–166 °C; ^{1}H NMR ($CDCl_3$) δ=8.04 (d, 1H, J=7.7 Hz, H_{BT}), 7.88 (d, 1H, J=8.0 Hz, H_{BT}), 7.48 (ddd, 1H, J=8.2, 7.1, 1.1 Hz, H_{BT}), 7.43 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.36 (ddd, 1H, J=8.2, 8.0, 1.1 Hz, H_{BT}), 7.22 (d, 1H, J=16.2 Hz, C=CH_β), 7.21 (d, 1H, J=3.6 Hz, H_{3FUR}), 6.76 (d, 1H, J=16.2 Hz, C=CH_α), 6.72 (d, 2H, J=9.1 Hz, H_{3Ph}, H_{5Ph}), 6.45 (d, 1H, J=3.6 Hz, H_{4FUR}), 3.01 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=158.0, 157.2, 154.5, 150.9, 147.5, 134.7, 131.0, 128.4, 126.8, 125.3, 125.1, 123.3, 121.9, 114.5, 112.7, 111.7, 109.7, 40.8 ppm; UV–vis ($CHCl_3$) λ_{max}=414 nm (log ε=6.450); IR (MeOH) ν=1520, 1410, 1340, 920 cm^{-1}. Anal. Calcd for $C_{21}H_{18}N_2OS$: C 72.80, H 5.24, N 8.09; found: C 72.58, H 5.07, N 7.80%.

4.2.7. 2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-1-methylpyrrol-2-yl}-benzothiazole (**2d**)

A sodium methanolate solution, prepared from sodium (16 mg, 0.68 mmol, 1.1 equiv) and dry MeOH (2 mL), was added dropwise to a stirred suspension of phosphonium iodide **8** (0.36 g, 0.68 mmol, 1.1 equiv) in MeOH (2 mL) at rt. The mixture was stirred for 15 min, a solution of aldehyde **7b** (0.15 g, 0.62 mmol, 1 equiv) in MeOH (5 mL) was added and the reaction mixture was then set to reflux for 4 h. After cooling to ambient temperature, the solvent was evaporated, the residue was mixed with water (10 mL) and extracted with chloroform (3×10 mL). Combined organic layers were dried (Na_2SO_4), the solvent was evaporated and the crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to give 0.11 g of orange solid (*E*:*Z* isomer=16:1, overall yield 50%). (*E*)-isomer: mp 189–191 °C; ^{1}H NMR ($CDCl_3$) δ=7.92 (d, 1H, J=8.0 Hz, H_{BT}), 7.80 (d, 1H, J=7.7 Hz, H_{BT}), 7.42 (m, 1H, H_{BT}), 7.40 (d, 2H, J=8.5 Hz, H_{2Ph}, H_{6Ph}), 7.29 (ddd, 1H, J=8.5, 8.0, 0.9 Hz, H_{BT}), 6.99 (d, 1H, J=16.2 Hz, C=CH_β), 6.85 (d, 1H, J=4.4 Hz, H_{3PYR}), 6.75 (d, 1H, J=15.7 Hz, C=CH_α), 6.72 (d, 2H, J=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.50 (d, 1H, J=4.4 Hz, H_{4PYR}), 4.23 (s, 3H, CH_3–N_{PYR}), 3.00 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=159.5, 153.4, 137.9, 132.8, 129.2, 129.2, 126.5, 125.8, 124.9, 124.6, 123.2, 121.2, 120.0, 114.7, 111.5, 111.0, 105.5, 39.5, 32.1 ppm; UV–vis ($CHCl_3$) λ_{max}=390 nm (log ε=6.38), 518 nm (log ε=5.60); IR (MeOH) ν=1610, 1550, 1520, 1430, 1360, 910 cm^{-1}. Anal. Calcd for $C_{22}H_{21}N_3S$: C 73.50, H 5.89, N 11.69; found: C 73.33, H 6.05, N 11.48%.

4.2.8. 2-(4-Dimethylaminophenyl)-1-methylpyrrole (**12**)

To a solution of 1-methylpyrrole (0.65 g, 8 mmol, 1 equiv) in dry THF (10 mL) under nitrogen, cooled to −78 °C, a solution of *n*-butyllithium in hexanes (5 mL, 1.6 M, 8 mmol, 1 equiv) was added dropwise. The mixture was stirred for 5 min at −78 °C, allowed to warm to rt and was stirred for another 30 min. Afterwards a solution of $ZnCl_2$ in THF (8 mL, 1 M, 8 mmol, 1 equiv) was added and the mixture was stirred for 90 min at rt. The resulting solution was added via a syringe to a second flask, charged with 4-bromo-*N*,*N*-dimethylaniline (1.6 g, 8 mmol, 1 equiv) and [$Pd(PPh_3)_4$] (185 mg, 0.16 mmol, 0.02 equiv) under nitrogen. The mixture was heated to reflux for 60 h, was allowed to cool and saturated aqueous NH_4Cl solution (5 mL) was added. After a while, the mixture was diluted with water, mixed with aqueous Na_2CO_3 solution (50 mL) and extracted with ethyl acetate (3×50 mL). Combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated. The crude product was purified with column chromatography (SiO_2, hexanes/EtOAc=5:1) to yield 1.16 g of beige solid (72%). Mp 66–67 °C; ^{1}H NMR ($CDCl_3$) δ=7.28 (d, 2H, J=8.9 Hz, H_{2Ph}, H_{6Ph}), 6.76 (d, 2H, J=8.9 Hz, H_{3Ph}, H_{5Ph}), 6.66 (d, 1H, J=3.0 Hz, H_{PYR}), 6.17 (d, 1H, J=2.6 Hz, H_{PYR}), 6.12 (dd, 1H, J=3.0, 2.6 Hz, H_{PYR}), 3.62 (s, 3H, CH_3–N_{PYR}), 2.98 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=149.5, 134.2, 128.7, 120.1, 117.9, 112.4, 110.2, 104.8, 40.4, 34.5 ppm; IR (MeOH) ν=2770, 1570, 1510, 1450, 1420, 1330, 1050, 940 cm^{-1}. Anal. Calcd for $C_{13}H_{16}N_2$: C 77.96, H 8.05, N 13.99; found: C 77.74, H 8.16, N 14.10%.

4.2.9. 2-[2-(4-Dimethylaminophenyl)-vinyl]-furan (**14a**)

A solution of sodium methanolate, prepared from sodium (0.25 g, 10.4 mmol, 1 equiv) and dry MeOH (20 mL), was added slowly to a suspension of phosphonium iodide **8** (5.45 g, 10.4 mmol, 1 equiv) in MeOH (20 mL). The mixture was stirred for 5 min and a solution of furan-2-carbaldehyde (1 g, 10.4 mmol, 1 equiv) in MeOH (20 mL) was added dropwise with stirring. The mixture was heated to reflux for 3 h, was allowed to cool and the solvent was

evaporated. The residue was mixed with hot water (200 mL) and the insoluble solid product was collected by filtration. The crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=5:1) to yield 1.4 g of yellowish solid (*E*:*Z* isomer=3.5:1, overall yield 62%). (*E*)-isomer: mp 103–106 °C (lit. Mp not given);[36] ^{1}H NMR ($CDCl_3$) δ=7.36 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.35 (d, 1H, *J*=2.2 Hz, H_{5FUR}), 6.97 (d, 1H, *J*=15.7 Hz, C=CH), 6.71 (d, 1H, *J*=15.7 Hz, C=CH), 6.70 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.39 (dd, 1H, *J*=3.3, 2.2 Hz, H_{4FUR}), 6.24 (d, 1H, *J*=3.3 Hz, H_{3FUR}), 2.97 (s, 6H, NMe_2) ppm.

4.2.10. 2-[2-(4-Dimethylaminophenyl)-vinyl]-thiophene (**14b**)

A solution of sodium methanolate, prepared from sodium (0.34 g, 14 mmol, 1 equiv) and dry MeOH (20 mL), was added slowly to a suspension of phosphonium iodide **8** (7.3 g, 14 mmol, 1 equiv) and MeOH (20 mL). The mixture was stirred for 15 min and a solution of thiophene-2-carbaldehyde (1.5 g, 14 mmol, 1 equiv) in MeOH (20 mL) was added dropwise with stirring. The mixture was heated to reflux for 6 h, was allowed to cool and the solvent was evaporated. The residue was mixed with hot water (200 mL) and the insoluble solid product was collected by filtration. The crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to yield 2 g of yellowish solid (*E*:*Z* isomer=3.5:1, overall yield 63%). (*E*)-isomer: mp 147–149 °C (146–148 °C);[37] ^{1}H NMR ($CDCl_3$) δ=7.36 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.11 (dd, 1H, *J*=4.8, 1.8 Hz, H_{5THP}), 7.04 (d, 1H, *J*=16.0 Hz, C=CH), 6.98–6.96 (m, 2H, H_{3THP}, H_{4THP}), 6.86 (d, 1H, *J*=16.0 Hz, C=CH), 6.70 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 2.98 (s, 6H, NMe_2) ppm.

4.2.11. 2-[2-(4-Dimethylaminophenyl)-vinyl]-1-methylpyrrole (**14c**)

To a solution of sodium methanolate, prepared from sodium (0.22 g, 9.2 mmol, 1 equiv) and dry MeOH (10 mL), phosphonium iodide **8** (4.8 g, 9.2 mmol, 1 equiv) was added and the mixture was stirred for 10 min. A solution of 1-methylpyrrole-2-carbaldehyde (1 g, 9.2 mmol, 1 equiv) in MeOH (20 mL) was added dropwise with stirring and the mixture was heated to reflux for 8 h. After cooling to ambient temperature, the solvent was evaporated, the residue was mixed with water and extracted with ethyl acetate (3×50 mL), combined organic layers were dried (Na_2SO_4), evaporated and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc=5:1) to give 0.3 g of *Z* isomer as yellow oil and 0.75 g of *E* isomer as yellowish solid (*E*:*Z* isomer=2.5:1, overall yield 50%). (*E*)-isomer: mp 102–104 °C; ^{1}H NMR ($CDCl_3$) δ=7.35 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 6.82 (d, 1H, *J*=16.0 Hz, C=CH), 6.75 (d, 1H, *J*=16.0 Hz, C=CH), 6.71 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.59 (m, 1H, H_{5PYR}), 6.40 (dd, 1H, *J*=3.7, 1.6 Hz, H_{3PYR}), 6.13 (dd, 1H, *J*=3.7, 2.7 Hz, H_{4PYR}), 3.66 (s, 3H, CH_3–N_{PYR}), 2.97 (s, 6H, NMe_2) ppm. Anal. Calcd for $C_{15}H_{18}N_2$: C 79.61, H 8.02, N 12.38; found: 79.37, H 8.20, N 12.10%.

4.2.12. 5-(4-Dimethylaminophenyl)-furan-2-carbaldehyde (**10a**)

To a solution containing the boronic acid **5** (0.25 g, 1.4 mmol, 1 equiv), arylbromide **9a** (0.3 g, 1.7 mmol, 1.2 equiv), $Pd(OAc)_2$ (3.1 mg, 0.014 mmol, 0.01 equiv) and PPh_3 (11 mg, 0.042 mmol, 0.03 equiv), in THF (9 mL) under nitrogen, 2 M aqueous Na_2CO_3 solution (5 mL) was added and the mixture was heated to reflux for 20 h. After cooling to rt, the mixture was filtered, water was added (20 mL), the organic layer was separated and the aqueous layer was extracted with ethyl acetate (2×10 mL). Combined organic layers were dried (Na_2SO_4), evaporated and the crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to yield 0.23 g of yellow solid (77%). Mp 96–98 °C (lit. 95–98 °C);[35] ^{1}H NMR ($CDCl_3$) δ=9.54 (s, 1H, CHO), 7.70 (d, 2H, *J*=9.2 Hz, H_{2Ph}, H_{6Ph}), 7.29 (d, 1H, *J*=3.7 Hz, H_{3FUR}), 6.72 (d, 2H, *J*=9.2 Hz, H_{3Ph}, H_{5Ph}), 6.62 (d, 1H, *J*=3.7 Hz, H_{4FUR}), 2.92 (s, 6H, NMe_2) ppm.

4.2.13. 5-(4-Dimethylaminophenyl)-thiophene-2-carbaldehyde (**10b**)

To a solution containing the boronic acid **5** (0.57 g, 3 mmol, 1 equiv), arylbromide **9a** (0.75 g, 4.5 mmol, 1.5 equiv), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.01 equiv) and PPh_3 (23 mg, 0.09 mmol, 0.03 equiv), in THF (20 mL) under nitrogen, 2 M aqueous Na_2CO_3 solution (10 mL) was added and the mixture was heated to reflux for 20 h. After cooling to rt, the precipitated solid was collected by filtration. The crude product was purified by crystallization from MeOH to give 0.63 g of yellow solid (92%). Mp 190–192 °C (lit. 189–190 °C);[11b] ^{1}H NMR ($CDCl_3$) δ=9.82 (s, 1H, CHO), 7.68 (d, 1H, *J*=4.0 Hz, H_{3THP}), 7.56 (d, 2H, *J*=9.0 Hz, H_{2Ph}, H_{6Ph}), 7.24 (d, 1H, *J*=4.0 Hz, H_{4THP}), 6.72 (d, 2H, *J*=9.0 Hz, H_{3Ph}, H_{5Ph}), 3.03 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=182.4, 156.0, 151.0, 140.1, 138.1, 121.5, 121.4, 112.2, 40.3, 29.6 ppm. Anal. Calcd for $C_{13}H_{13}NOS$: C 67.50, H 5.66, N 6.06; found: C 67.77, H 5.68, N 6.25%.

4.2.14. 5-(4-Dimethylaminophenyl)-1-methylpyrrole-2-carbaldehyde (**10c**)

To dry DMF (0.32 mL, 0.3 g, 4 mmol, 1 equiv), cooled in an ice bath, $POCl_3$ (0.38 mL, 0.61 g, 4 mmol, 1 equiv) was added dropwise and the mixture was stirred for 10 min. Afterwards, a solution of **12** (0.8 g, 4 mmol; 1 equiv) in DMF (5 mL) was slowly added with cooling, the mixture was allowed to warm up to rt and was stirred for further 2 h. The reaction mixture was subsequently poured on ice, neutralized with aqueous NaOH solution and the precipitate was collected by filtration. The crude product was crystallized from methanol to give 0.65 g of yellowish solid (72%). Mp 112–114 °C; ^{1}H NMR ($CDCl_3$) δ=9.52 (d, 1H, CHO), 7.30 (d, 2H, *J*=9.1 Hz, H_{2Ph}, H_{6Ph}), 6.96 (d, 1H, *J*=4.1 Hz, H_{3PYR}), 6.77 (d, 2H, *J*=9.1 Hz, H_{3Ph}, H_{5Ph}), 6.24 (d, 1H, *J*=3.9 Hz, H_{4PYR}), 3.94 (s, 3H, CH_3–N_{PYR}), 3.02 (s, 6H, CH_3–N) ppm; ^{13}C NMR ($CDCl_3$) δ=179.1, 150.6, 145.6, 132.7, 130.2, 125.0, 118.5, 112.1, 110.2, 40.4, 34.6 ppm; UV–vis ($CHCl_3$) λ_{max}=312 nm (log ε=6.248); IR (MeOH) ν=2780, 1640, 1600, 1540, 1510, 1470, 1450, 1430, 1350, 1040, 920 cm^{-1}. Anal. Calcd for $C_{14}H_{16}N_2O$: C 73.66, H 7.06, N 12.27; found: C 73.63, H 7.35, N 11.99%.

4.2.15. (E)-5-[2-(4-Dimethylaminophenyl)-vinyl]-furan-2-carbaldehyde (**10d**)

To dry DMF (0.4 mL, 0.38 g, 5.2 mmol, 1 equiv), cooled in an ice bath, $POCl_3$ (0.5 mL, 0.8 g, 5.2 mmol, 1 equiv) was added dropwise. The mixture was stirred for 10 min and a solution of **14a** (1.1 g, 5.2 mmol, 1 equiv, *E*:*Z*=4:1) in DMF (5 mL) was added with cooling. The mixture was allowed to warm up to rt and was stirred for further 1 h at rt and 2.5 h at 70 °C. Afterwards, the mixture cooled to ambient temperature and was poured on ice, neutralized with aqueous NaOH and was left to stand overnight. The precipitated solid was collected by filtration, dried and purified by column chromatography (SiO_2, hexanes/EtOAc=5:1) to yield 0.45 g of orange solid (*E* isomer, 36%). Mp 130–131 °C; ^{1}H NMR ($CDCl_3$) δ=9.53 (s, 1H, CHO), 7.41 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.34 (d, 1H, *J*=16.2 Hz, C=CH), 7.24 (d, 1H, *J*=3.8 Hz, H_{3FUR}), 6.73 (d, 1H, *J*=16.2 Hz, C=CH), 6.70 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.43 (d, 1H, *J*=3.8 Hz, H_{4FUR}), 3.01 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=176.5, 160.3, 151.3, 151.0, 134.2, 128.6, 124.8, 124.0, 112.3, 110.4, 109.1, 40.4 ppm; UV–vis ($CHCl_3$) λ_{max}=414 nm (log ε=6.06); IR (MeOH) ν=1660, 1600, 1520, 1480, 1410, 1350, 1010, 920 cm^{-1}. Anal. Calcd for $C_{15}H_{15}NO_2$: C 74.67, H 6.27, N 5.80; found: C 74.84, H 6.27, N 5.74%.

4.2.16. (E)-5-[2-(4-Dimethylaminophenyl)-vinyl]-thiophene-2-carbaldehyde (**10e**)

Method A. To dry DMF (0.44 mL, 0.42 g, 5.7 mmol, 1 equiv), cooled in an ice bath, $POCl_3$ (0.53 mL, 0.87 g, 5.7 mmol, 1 equiv) was added dropwise. The mixture was stirred for 10 min and a solution of **14b** (1.3 g, 5.7 mmol, 1 equiv, *E*:*Z*=3.5:1) in DMF (5 mL) was added with cooling. The mixture was allowed to warm up to rt and

was stirred for further 1 h at rt and 16 h at 70 °C. Afterwards, the mixture cooled to ambient temperature and was poured on ice, neutralized with aqueous NaOH and was left to stand overnight. The precipitated solid was collected by filtration, dried and purified by column chromatography (SiO_2, hexanes/EtOAc=5:1) to yield 0.22 g of red solid (*E* isomer, 15%).

Method B. To a solution of **14b** (0.7 g, 3 mmol, 1 equiv, *E*:*Z*=3.5:1) in dry THF (15 mL), cooled in an ice bath, a 1.6 M solution of *n*-BuLi in hexanes (2.8 mL, 5.2 mmol, 1.7 equiv) was added dropwise with stirring under an atmosphere of nitrogen. The resulting mixture was stirred at 0 °C for 1 h and subsequently dry DMF (0.35 mL, 0.33 g, 4.5 mmol, 1.5 equiv) was added with cooling. Afterwards, the mixture was allowed to warm to ambient temperature and was stirred for further 16 h. Water was added and the mixture was extracted with ethyl acetate (3×20 mL), combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated. The residue was crystallized from methanol to give 0.50 g of red product (*E* isomer, 65%). Mp 178–181 °C; ^{1}H NMR ($CDCl_3$) δ=9.81 (s, 1H, CHO), 7.63 (d, 1H, *J*=3.8 Hz, H_{3THP}), 7.40 (d, 2H, *J*=9.1 Hz, H_{2Ph}, H_{6Ph}), 7.39 (d, 1H, *J*=16.0 Hz, C=CH), 7.06 (d, 1H, *J*=3.8 Hz, H_{4THP}), 7.05 (d, 1H, *J*=16.0 Hz, C=CH), 6.69 (d, 2H, *J*=9.1 Hz, H_{3Ph}, H_{5Ph}), 3.01 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=181.3, 155.6, 148.7, 140.1, 137.3, 132.1, 129.2, 124.5, 122.1, 112.6, 110.5, 40.5 ppm; UV–vis (MeOH) λ_{max}=418 nm (log ε=6.37). Anal. Calcd for $C_{15}H_{15}NOS$: C 70.01, H 5.87, N 5.44; found: C 69.85, H 5.94, N 5.34%.

*4.2.17. (E)-5-[2-(4-Dimethylaminophenyl)-vinyl]-1-methyl-pyrrole-2-carbaldehyde (**10f**)*

To dry DMF (0.4 mL, 0.37 g, 5.0 mmol, 1 equiv), cooled in an ice bath, $POCl_3$ (0.47 mL, 0.77 g, 5.0 mmol, 1 equiv) was added dropwise. The mixture was stirred for 10 min, dry 1,2-dichloroethane was added and subsequently a solution of **14c** (1.14 g, 5.0 mmol, 1 equiv, *E* isomer) in 1,2-dichloroethane (5 mL) was added dropwise with cooling. The mixture was allowed to warm up to ambient temperature and was stirred for 10 min. Afterwards the mixture was heated to reflux for 30 min, cooled to rt and saturated aqueous solution of sodium acetate was added. The mixture was extracted with $CHCl_3$ (3×20 mL), combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography (SiO_2, hexanes/EtOAc=4:1) to yield 0.25 g of yellow solid (20%, *E* isomer). Mp 146–150 °C; ^{1}H NMR ($CDCl_3$) δ=9.44 (s, 1H, CHO), 7.40 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.07 (d, 1H, *J*=16.2 Hz, C=CH), 6.90 (d, 1H, *J*=4.4 Hz, H_{3PYR}), 6.77 (d, 1H, *J*=15.9 Hz, C=CH), 6.71 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.50 (d, 1H, *J*=4.1 Hz, H_{4PYR}), 3.01 (s, 3H, CH_3–N_{PYR}), 3.01 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=178.6, 150.8, 143.2, 133.9, 132.2, 130.1, 128.1, 124.9, 112.4, 110.4, 107.3, 40.5, 32.6 ppm; UV–vis ($CHCl_3$) λ_{max}=342 nm (log ε=6.21); IR (MeOH) ν=1660, 1600, 1520, 1480, 1410, 1360, 920 cm^{-1}. Anal. Calcd for $C_{16}H_{18}N_2O$: C 75.56, H 7.14, N 11.01; found: C 75.72, H 7.05, N 10.78%.

4.3. GP1: condensation reactions of 2-methylbenzothiazole[15c]

To a solution of the corresponding aldehyde (1 equiv) and 2-methylbenzothiazole (1.1 equiv) in DMSO, 50% aqueous solution of KOH was added, the mixture was stirred for 10 min and afterwards left at rt without stirring for the given time. The precipitate was collected by filtration, washed with water (50 mL) and cold methanol (5 mL) and dried in vacuum to yield the product in good purity.

*4.3.1. (E)-2-{2-[5-(4-Dimethylaminophenyl)-furan-2-yl]-vinyl}-benzothiazole (**2e**)*

According to GP1, aldehyde **10a** (0.2 g, 0.9 mmol), 2-methylbenzothiazole (0.15 g, 1.0 mmol), DMSO (5 mL) and 50% aq KOH (2 mL) were used, reaction time 3.5 h, yield 170 mg of orange solid (54%). Mp 160–162 °C; ^{1}H NMR ($CDCl_3$) δ=7.97 (d, 1H, *J*=8.0 Hz, H_{BT}), 7.84 (d, 1H, *J*=8.2 Hz, H_{BT}), 7.63 (d, 2H, *J*=9.1 Hz, H_{2Ph}, H_{6Ph}), 7.46 (ddd, 1H, *J*=8.2, 7.1, 1.1 Hz, H_{BT}), 7.34 (ddd, 1H, *J*=8.0, 6.9, 1.1 Hz, H_{BT}), 7.31 (m, 2H, C=CH_α, C=CH_β), 6.75 (d, 2H, *J*=9.1 Hz, H_{3Ph}, H_{5Ph}), 6.63 (d, 1H, *J*=3.6 Hz, H_{FUR}), 6.53 (d, 1H, *J*=3.6 Hz, H_{FUR}), 3.02 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=167.2, 157.0, 154.3, 150.6, 149.9, 134.6, 126.4, 125.7, 125.1, 124.4, 122.8, 121.6, 118.7, 118.2, 116.1, 112.4, 105.5, 40.5 ppm; UV–vis ($CHCl_3$) λ_{max}=436 nm (log ε=6.47); IR (MeOH) ν=1600, 1490, 1460, 1420, 1350, 1010, 910 cm^{-1}. Anal. Calcd for $C_{21}H_{18}N_2OS$: C 72.80, H 5.24, N 8.09; found: C 72.94, H 5.32, N 7.98%.

*4.3.2. (E)-2-{2-[5-(4-Dimethylaminophenyl)-thiophen-2-yl]-vinyl}-benzothiazole (**2f**)*

According to GP1, aldehyde **10b** (0.15 g, 0.6 mmol), 2-methylbenzothiazole (0.1 g, 0.7 mmol), DMSO (1.7 mL) and 50% aq KOH (1 mL) were used, reaction time 5 h, yield 110 mg of orange solid (52%). Mp 210–214 °C; ^{1}H NMR ($CDCl_3$) δ=7.97 (d, 1H, *J*=8.0 Hz, H_{BT}), 7.84 (d, 1H, *J*=7.7 Hz, H_{BT}), 7.62 (d, 1H, *J*=15.7 Hz, C=CH_β), 7.52 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.46 (ddd, 1H, *J*=8.0, 7.1, 0.8 Hz, H_{BT}), 7.35 (ddd, 1H, *J*=8.0, 6.9, 1.1 Hz, H_{BT}), 7.16 (d, 1H, *J*=3.8 Hz, H_{THP}), 7.12 (d, 1H, *J*=15.7 Hz, C=CH_α), 7.11 (d, 1H, *J*=3.8 Hz, H_{THP}), 6.73 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 3.01 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=167.0, 154.2, 150.6, 147.8, 138.0, 134.5, 131.3, 130.9, 127.1, 126.5, 125.2, 122.9, 122.2, 121.7, 121.6, 119.7, 112.5, 40.6 ppm; UV–vis (MeOH) λ_{max}=430 (log ε=6.46); IR (MeOH) ν=1600, 1510, 1470, 1440, 1420, 1040, 920 cm^{-1}. Anal. Calcd for $C_{21}H_{18}N_2S_2$: C 69.58, H 5.00, N 7.73; found: C 69.15, H 4.90, N 7.38%.

*4.3.3. (E)-2-{2-[5-(4-Dimethylaminophenyl)-1-methylpyrrol-2-yl]-vinyl}-benzothiazole (**2g**)*

According to GP1, aldehyde **10c** (0.1 g, 0.43 mmol), 2-methylbenzothiazole (71 mg, 0.47 mmol), DMSO (2 mL) and 50% aq KOH (1 mL) were used, reaction time 16 h, yield 95 mg of yellow solid (43%). Mp 174–176 °C; ^{1}H NMR ($CDCl_3$) δ=7.93 (d, 1H, *J*=8.0 Hz, H_{BT}), 7.82 (d, 1H, *J*=8.0 Hz, H_{BT}), 7.50 (d, 1H, *J*=15.7 Hz, C=CH_β), 7.44 (ddd, 1H, *J*=8.0, 7.4, 1.1 Hz, H_{BT}), 7.32 (ddd, 1H, *J*=8.0, 7.4, 1.1 Hz, H_{BT}), 7.29 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.12 (d, 1H, *J*=15.7 Hz, C=CH_α), 6.78 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.76 (d, 1H, *J*=4.1 Hz, H_{3PYR}), 6.24 (d, 1H, *J*=3.8 Hz, H_{4PYR}), 3.73 (s, 3H, CH_3–N_{PYR}), 3.01 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=168.1, 154.3, 150.1, 140.2, 134.3, 131.2, 130.2, 126.4, 126.4, 124.8, 122.5, 121.5, 120.5, 116.7, 112.4, 111.2, 109.9, 40.6, 32.7 ppm; UV–vis ($CHCl_3$) λ_{max}=416 nm (log ε=6.45), 550 nm (log ε=5.86); IR (MeOH) ν=1610, 1540, 1520, 1450, 1440, 1420, 1050, 920 cm^{-1}. Anal. Calcd for $C_{22}H_{21}N_3S$: C 73.50, H 5.89, N 11.69; found: C 73.55, H 5.83, N 11.40%.

*4.3.4. (E,E)-2-(2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-furan-2-yl}-vinyl)-benzothiazole (**2h**)*

According to GP1, aldehyde **10d** (0.1 g, 0.41 mmol), 2-methylbenzothiazole (69 mg, 0.46 mmol), DMSO (2 mL) and 50% aq KOH (1 mL) were used, reaction time 6 h, yield 140 mg of red solid (92%). Mp 192–195 °C; ^{1}H NMR ($CDCl_3$) δ=7.97 (d, 1H, *J*=7.7 Hz, H_{BT}), 7.84 (d, 1H, *J*=8.0 Hz, H_{BT}), 7.46 (ddd, 1H, *J*=8.5, 7.1, 1.4 Hz, H_{BT}), 7.41 (d, 2H, *J*=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.36 (d, 1H, *J*=15.7 Hz, C=CH_β), 7.35 (ddd, 1H, *J*=8.0, 6.9, 1.4 Hz, H_{BT}), 7.27 (d, 1H, *J*=15.9 Hz, C=CH_α), 7.15 (d, 1H, *J*=16.2 Hz, C=CH_δ), 6.72 (d, 2H, *J*=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.70 (d, 1H, *J*=16.2 Hz, C=CH_γ), 6.59 (d, 1H, *J*=3.6 Hz, H_{3FUR}), 6.33 (d, 1H, *J*=3.6 Hz, H_{4FUR}), 3.01 (s, 6H, NMe_2) ppm; UV–vis ($CHCl_3$) λ_{max}=448 nm (log ε=6.56); IR (MeOH) ν=1610, 1520, 1420, 1010, 920 cm^{-1}. Anal. Calcd for $C_{23}H_{20}N_2OS$: C 74.16, H 5.41, N 7.52; found: C 73.77, H 5.29, N 7.15%.

*4.3.5. (E,E)-2-(2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-thiophen-2-yl}-vinyl)-benzothiazole (**2i**)*

According to GP1, aldehyde **10e** (0.1 g, 0.39 mmol), 2-methylbenzothiazole (64 mg, 0.43 mmol), DMSO (2 mL) and 50% aq KOH (1 mL) were used, reaction time 16 h, yield 120 mg of orange solid (79%). Mp 209–211 °C; ^{1}H NMR ($CDCl_3$) δ=7.97 (d, 1H, J=7.6 Hz, H_{BT}), 7.84 (d, 1H, J=8.4 Hz, H_{BT}), 7.60 (d, 1H, J=15.7 Hz, C=CH_β), 7.46 (ddd, 1H, J=8.4, 7.3, 1.2 Hz, H_{BT}), 7.39 (d, 2H, J=8.6 Hz, H_{2Ph}, H_{6Ph}), 7.35 (ddd, 1H, J=8.4, 7.3, 1.2 Hz, H_{BT}), 7.12 (d, 1H, J=15.7 Hz, C=CH_α), 7.11 (d, 1H, J=3.8 Hz, H_{3THP}), 7.00 (d, 1H, J=16.0 Hz, C=CH_δ), 6.92 (d, 1H, J=3.8 Hz, H_{4THP}), 6.91 (d, 1H, J=16.0 Hz, C=CH_γ), 6.70 (d, 2H, J=8.7 Hz, H_{3Ph}, H_{5Ph}), 3.00 (s, 6H, NMe_2) ppm; UV–vis ($CHCl_3$) λ_{max}=452 nm (log ε=6.55); IR (MeOH) ν=1600, 1520, 1420, 1350 cm^{-1}. Anal. Calcd for $C_{23}H_{20}N_2S_2$: C 71.10, H 5.19, N 7.21; found: C 70.85, H 5.20, N 6.95%.

*4.3.6. (E,E)-2-(2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-1-methylpyrrol-2-yl}-vinyl)-benzothiazole (**2j**)*

According to GP1, aldehyde **10f** (0.1 g, 0.39 mmol), 2-methylbenzothiazole (65 mg, 0.43 mmol), DMSO (2 mL) and 50% aq KOH (1 mL) were used, reaction time 16 h, yield 70 mg of red solid (46%). Mp 202–205 °C; ^{1}H NMR ($CDCl_3$) δ=7.93 (d, 1H, J=8.0 Hz, H_{BT}), 7.82 (d, 1H, J=8.0 Hz, H_{BT}), 7.47 (d, 1H, J=15.7 Hz, C=CH_β), 7.44 (ddd, 1H, J=8.2, 7.1, 1.4 Hz, H_{BT}), 7.38 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.31 (ddd, 1H, J=8.2, 7.1, 1.4 Hz, H_{BT}), 7.09 (d, 1H, J=15.7 Hz, C=CH_α), 6.93 (d, 1H, J=15.9 Hz, C=CH_δ), 6.79 (d, 1H, J=15.9 Hz, C=CH_γ), 6.75 (d, 1H, J=4.1 Hz, H_{3PYR}), 6.71 (d, 2H, J=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.54 (d, 1H, J=4.1 Hz, H_{4PYR}), 3.76 (s, 3H, CH_3–N_{PYR}), 3.00 (s, 6H, NMe_2) ppm; ^{13}C NMR ($CDCl_3$) δ=167.9, 154.3, 150.3, 137.7, 134.3, 131.2, 129.5, 127.6, 126.4, 125.9, 125.4, 124.8, 122.4, 121.5, 116.7, 112.7, 112.3, 111.8, 107.8, 40.7, 31.0 ppm; UV–vis ($CHCl_3$) λ_{max}=464 nm (log ε=6.52); IR (MeOH) ν=1600, 1520, 1420, 920 cm^{-1}. Anal. Calcd for $C_{24}H_{23}N_3S$: C 74.77, H 6.01, N 10.90; found: C 74.85, H 6.24, N 10.54%.

4.4. GP2: condensation reactions of 3-alkyl-2-methylbenzothiazolium salts[15c]

To a solution of the corresponding aldehyde (1 equiv) and the corresponding 2-methyl-3-alkylbenzothiazolium salt (1 equiv) in dry MeOH, a few drops of pyridine were added and the mixture was heated to reflux for the given time. Afterwards, the mixture was cooled to −10 °C in the refrigerator and the crystallized solid was collected by filtration, washed with cold MeOH and dried in vacuum to give the product in good purity.

*4.4.1. (E)-2-{2-[5-(4-Dimethylaminophenyl)-furan-2-yl]-vinyl-1-yl}-3-methylbenzothiazolium iodide (**3aM**)*

According to GP2, aldehyde **10a** (0.11 g, 0.5 mmol), 2,3-dimethylbenzothiazolium iodide (0.15 g, 0.5 mmol) and MeOH (5 mL) were used, reaction time 14 h, yield 140 mg of dark green solid (58%). Mp=160 °C (decomp.); ^{1}H NMR (DMSO-d_6) δ=8.35 (d, 1H, J=8.1 Hz, H_{7BT}), 8.16 (d, 1H, J=8.4 Hz, H_{4BT}), 8.01 (d, 1H, J=15.2 Hz, C=CH_β), 7.88 (d, 2H, J=9.0 Hz, H_{2Ph}, H_{6Ph}), 7.82 (t, 1H, J=8.4 Hz, H_{5BT}), 7.71 (t, 1H, J=8.1 Hz, H_{6BT}), 7.50 (d, 1H, J=15.2 Hz, C=CH_α), 7.48 (d, 1H, J=3.8 Hz, H_{3FUR}), 7.15 (d, 1H, J=3.8 Hz, H_{4FUR}), 6.81 (d, 2H, J=9.2 Hz, H_{3Ph}, H_{5Ph}), 4.29 (s, 3H, CH_3–N_{BT}), 3.03 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=176.4, 161.1, 151.3, 149.2, 142.0, 132.8, 129.1, 127.1, 126.9, 126.4, 124.0, 116.2, 115.8, 112.0, 108.2, 106.6, 105.6, 35.8 ppm (the CH_3–N signal is overlapped with the DMSO signal); UV–vis (MeOH) λ_{max}=582 nm (log ε=6.64); IR (ATR) ν=2987, 2900, 1591, 1535, 1497, 1462, 1431, 1398, 1369, 1222, 1191, 1028, 914 cm^{-1}. Anal. Calcd for $C_{22}H_{21}IN_2OS$: C 54.10, H 4.33, N 5.74; found: C 54.00, H 4.65, N 5.57%.

*4.4.2. (E)-2-{2-[5-(4-Dimethylaminophenyl)-furan-2-yl]-vinyl}-3-(prop-2-enyl)-benzothiazolium bromide (**3aA**)*

According to GP2, aldehyde **10a** (0.15 g, 0.7 mmol), 3-allyl-2-methylbenzothiazolium bromide (0.19 g, 0.7 mmol) and MeOH (3 mL) were used, reaction time 14 h, yield 140 mg of dark green solid (43%). Mp 165 °C (decomp.); ^{1}H NMR (DMSO-d_6) δ=8.37 (d, 1H, J=8.0 Hz, H_{7BT}), 8.13 (d, 1H, J=8.2 Hz, H_{4BT}), 8.06 (d, 1H, J=15.1 Hz, C=CH_β), 7.88 (d, 2H, J=9.1 Hz, H_{2Ph}, H_{6Ph}), 7.80 (t, 1H, J=8.2 Hz, H_{5BT}), 7.71 (t, 1H, J=7.7 Hz, H_{6BT}), 7.52 (d, 1H, J=3.8 Hz, H_{3FUR}), 7.46 (d, 1H, J=15.1 Hz, C=CH_α), 7.17 (d, 1H, J=3.8 Hz, H_{4FUR}), 6.83 (d, 2H, J=9.1 Hz, H_{3Ph}, H_{5Ph}), 6.18–6.04 (m, 1H, C=CH), 5.57 (d, 2H, J=4.9 Hz, CH_2), 5.37 (d, 1H, J=10.7 Hz, C=CH_2), 5.30 (d, 1H, J=17.3 Hz, C=CH_2), 3.04 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=170.4, 161.4, 151.2, 149.1, 141.0, 133.2, 130.6, 129.0, 127.6, 127.2, 126.9, 126.8, 124.1, 118.9, 116.0, 115.5, 111.8, 108.3, 105.8, 50.0, 39.6 ppm; UV–vis (MeOH) λ_{max}=596 nm (log ε=6.68); IR (ATR) ν=2900, 1593, 1497, 1408, 1369, 1235, 1193, 1031, 942 cm^{-1}. Anal. Calcd for $C_{24}H_{23}BrN_2OS$: C 61.67, H 4.96, N 5.99; found: C 61.36, H 5.11, N 5.87%.

*4.4.3. (E)-2-{2-[5-(4-Dimethylaminophenyl)-furan-2-yl]-vinyl}-3-(prop-2-ynyl)-benzothiazolium bromide (**3aP**)*

According to GP2, aldehyde **10a** (0.15 g, 0.7 mmol), 2-methyl-3-(prop-2-ynyl)-benzothiazolium bromide (0.17 g, 0.7 mmol) and MeOH (5 mL) were used, reaction time 16 h, yield 100 mg of dark green solid (31%). Mp 177 °C (decomp.); ^{1}H NMR (DMSO-d_6) δ=8.37 (d, 1H, J=8.0 Hz, H_{7BT}), 8.20 (d, 1H, J=8.8 Hz, H_{4BT}), 8.10 (d, 1H, J=15.1 Hz, C=CH_β), 7.91 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.85 (t, 1H, J=8.2 Hz, H_{5BT}), 7.73 (t, 1H, J=8.0 Hz, H_{6BT}), 7.58 (d, 1H, J=15.1 Hz, C=CH_α), 7.57 (d, 1H, J=3.8 Hz, H_{3FUR}), 7.21 (d, 1H, J=4.1 Hz, H_{4FUR}), 6.85 (d, 2H, J=9.1 Hz, H_{3Ph}, H_{5Ph}), 5.86 (d, 2H, J=2.2 Hz, CH_2), 3.78 (m, 1H, C≡CH), 3.05 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=171.4, 163.0, 152.3, 150.2, 141.4, 134.6, 130.1, 128.7, 128.8, 128.1, 127.9, 125.2, 116.7, 116.3, 112.8, 109.7, 106.2, 79.3, 76.9, 40.6, 38.7 ppm; UV–vis (MeOH) λ_{max}=612 nm (log ε=6.64); IR (ATR) ν=2901, 1590, 1529, 1494, 1407, 1371, 1335, 1184, 1016, 943 cm^{-1}. Anal. Calcd for $C_{24}H_{21}BrN_2OS$: C 61.94, H 4.55, N 6.02; found: C 62.05, H 4.94, N 5.85%.

*4.4.4. (E)-2-{2-[5-(4-Dimethylaminophenyl)-thiophen-2-yl]-vinyl}-3-methylbenzothiazolium iodide (**3bM**)*

According to GP2, aldehyde **10b** (0.2 g, 0.8 mmol), 2,3-dimethylbenzothiazolium iodide (0.32 g, 1.2 mmol) and MeOH (5 mL) were used, reaction time 35 h, yield 160 mg of dark green solid (40%). Mp 214 °C (decomp.); ^{1}H NMR (DMSO-d_6) δ=8.39 (d, 1H, J=15.4 Hz, C=CH_β), 8.37 (d, 1H, J=7.1 Hz, H_{7BT}), 8.17 (d, 1H, J=8.2 Hz, H_{4BT}), 7.90 (d, 1H, J=3.8 Hz, H_{3THP}), 7.83 (t, 1H, J=8.0 Hz, H_{5BT}), 7.74 (t, 1H, J=7.1 Hz, H_{6BT}), 7.63 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.58 (d, 1H, J=3.8 Hz, H_{4THP}), 7.48 (d, 1H, J=15.1 Hz, C=CH_α), 6.79 (d, 2H, J=8.8 Hz, H_{3Ph}, H_{5Ph}), 4.27 (s, 3H, CH_3–N_{BT}), 3.00 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=171.5, 154.8, 153.8, 142.7, 142.0, 139.4, 136.7, 128.0, 128.7, 128.1, 128.0, 124.9, 124.1, 120.7, 117.2, 113.1, 110.0, 36.9 ppm (the CH_3–N signal is overlapped with the DMSO signal); UV–vis (MeOH) λ_{max}=562 nm (log ε=6.54); IR (ATR) ν=2988, 2901, 1571, 1430, 1411, 1361, 1347, 1275, 1190, 1064, 956 cm^{-1}. Anal. Calcd for $C_{22}H_{21}IN_2S_2$: C 52.38, H 4.20, N 5.55; found: C 52.19, H 4.35, N 5.39%.

*4.4.5. (E)-2-{2-[5-(4-Dimethylaminophenyl)-thiophen-2-yl]-vinyl}-3-(prop-2-enyl)-benzothiazolium bromide (**3bA**)*

According to GP2, aldehyde **10b** (0.2 g, 0.8 mmol), 3-allyl-2-methylbenzothiazolium bromide (0.25 g, 0.9 mmol) and MeOH (5 mL) were used, reaction time 24 h, yield 230 mg of dark green solid (60%). Mp 254 °C (decomp.); ^{1}H NMR (CD_3OD) δ=8.36 (d, 1H, J=15.1 Hz, C=CH_β), 8.18 (d, 1H, J=8.0 Hz, H_{7BT}), 8.04 (d, 1H, J=8.2 Hz, H_{4BT}), 7.81 (t, 1H, J=8.0 Hz, H_{5BT}), 7.74 (d, 1H, J=3.8 Hz, H_{3THP}), 7.72 (t, 1H, J=8.2 Hz, H_{6BT}), 7.65 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}),

7.45 (d, 1H, J=4.1 Hz, H_{4THP}), 7.31 (d, 1H, J=14.9 Hz, C=CH_α), 6.80 (d, 2H J=9.1 Hz, H_{3Ph}, H_{5Ph}), 6.21–6.09 (m, 1H, C=CH), 5.47 (d, 2H, J=5.2 Hz, CH_2), 5.44 (d, 1H, J=10.7 Hz, C=CH_2), 5.24 (d, 1H, J=17.3 Hz, C=CH_2), 3.05 (s, 6H, NMe_2) ppm; satisfactory ^{13}C NMR was not obtained due to very low solubility; UV–vis (MeOH) λ_{max}=580 nm (log ε=6.70); IR (ATR) ν=2905, 1583, 1485, 1405, 1365, 1229, 1071, 947 cm^{-1}. Anal. Calcd for $C_{24}H_{23}BrN_2S_2$: C 59.62, H 4.79, N 5.79; found: C 59.75, H 4.77, N 5.78%.

4.4.6. (E)-2-{2-[5-(4-Dimethylaminophenyl)-1-methylpyrrol-2-yl]vinyl}-3-methylbenzothiazolium iodide (**3cM**)

According to GP2, aldehyde **10c** (0.2 g, 0.88 mmol), 2,3-dimethylbenzothiazolium iodide (0.26 g, 0.88 mmol) and MeOH (3 mL) were used, reaction time 16 h, yield 190 mg of dark green solid (43%). Mp 254 °C (decomp.); ^1H NMR (CD_3OD) δ=8.04 (d, 1H, J=7.7 Hz, H_{7BT}), 7.99 (d, 1H, J=15.1 Hz, C=CH_β), 7.92 (d, 1H, J=8.5 Hz, H_{4BT}), 7.74 (t, 1H, J=8.5 Hz, H_{5BT}), 7.62 (t, 1H, J=7.7 Hz, H_{6BT}), 7.54 (d, 1H, J=4.6 Hz, H_{3PYR}), 7.41 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.33 (d, 1H, J=14.6 Hz, C=CH_α), 6.87 (d, 2H, J=9.0 Hz, H_{3Ph}, H_{5Ph}), 6.55 (d, 1H, J=3.8 Hz, H_{4PYR}), 4.15 (s, 3H, CH_3–N_{BT}), 3.88 (s, 3H, CH_3–N_{PYR}), 3.04 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=169.8, 150.4, 146.1, 141.9, 136.0, 132.3, 129.8, 128.7, 127.0, 126.4, 123.6, 119.8, 117.4, 115.5, 113.5, 112.0, 104.0, 35.2, 32.6 ppm (the CH_3–N signal is overlapped with the DMSO signal); UV–vis (MeOH) λ_{max}=560 nm (log ε=6.79); IR (ATR) ν=2970, 1566, 1435, 1365, 1229, 1201, 1070, 1019, 919 cm^{-1}. Anal. Calcd for $C_{23}H_{24}IN_3S$: C 55.09, H 4.82, N 8.38; found: C 55.39, H 4.98, N 8.47%.

4.4.7. (E)-2-{2-[5-(4-Dimethylaminophenyl)-1-methylpyrrol-2-yl]-vinyl}-3-(prop-2-enyl)-benzothiazolium bromide (**3cA**)

According to GP2, aldehyde **10c** (0.2 g, 0.88 mmol), 3-allyl-2-methylbenzothiazolium bromide, (0.24 g, 0.88 mmol) and MeOH (3 mL) were used, reaction time 17 h, yield 180 mg of dark blue solid (43%). Mp 246 °C (decomp.); ^1H NMR (CD_3OD) δ=8.06 (d, 1H, J=8.0 Hz, H_{7BT}), 7.99 (d, 1H, J=14.6 Hz, C=CH_β), 7.86 (d, 1H, J=8.2 Hz, H_{4BT}), 7.71 (ddd, 1H, J=8.5, 7.4, 1.1 Hz, H_{5BT}), 7.60 (ddd, 1H, J=8.5, 7.4, 1.1 Hz, H_{6BT}), 7.54 (d, 1H, J=4.4 Hz, H_{3PYR}), 7.42 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.24 (d, 1H, J=14.6 Hz, C=CH_α), 6.86 (d, 2H, J=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.57 (d, 1H, J=4.6 Hz, H_{4PYR}), 6.17–6.06 (m, 1H, C=CH), 5.39 (d, 1H, J=10.4 Hz, C=CH_2), 5.33 (d, 2H, J=4.9 Hz, CH_2), 5.20 (d, 1H, J=17.0 Hz, C=CH_2), 3.88 (s, 3H, CH_3–N_{PYR}), 3.04 (s, 6H, NMe_2) ppm; ^{13}C NMR (CD_3OD) δ=171.5, 152.6, 142.7, 137.8, 134.3, 131.3, 131.0, 130.2, 130.0, 128.4, 127.9, 124.4, 122.5, 119.4, 119.0, 116.1, 115.7, 113.3, 103.2, 35.2, 40.4, 33.2 ppm; UV–vis (MeOH) λ_{max}=570 nm (log ε=6.81); IR (ATR) ν=2970, 2886, 1576, 1474, 1350, 1263, 1183, 1058, 943 cm^{-1}. Anal. Calcd for $C_{25}H_{26}BrN_3S$: C 62.50, H 5.45, N 8.75; found: C 62.89, H 5.62, N 8.87%.

4.4.8. (E)-2-{2-[5-(4-Dimethylaminophenyl)-1-methylpyrrol-2-yl]-vinyl}-3-(prop-2-ynyl)-benzothiazolium bromide (**3cP**)

According to GP2, aldehyde **10c** (0.2 g, 0.88 mmol), 2-methyl-3-(prop-2-ynyl)-benzothiazolium bromide, (0.24 g, 0.88 mmol) and MeOH (3 mL) were used, reaction time 16 h, yield 270 mg of dark green solid (64%). Mp 240 °C (decomp.); ^1H NMR (CD_3OD) δ=8.03 (d, 1H, J=8.8 Hz, H_{7BT}), 8.00 (d, 1H, J=14.3 Hz, C=CH_β), 7.94 (d, 1H, J=8.2 Hz, H_{4BT}), 7.73 (t, 1H, J=8.5 Hz, H_{5BT}), 7.62 (d, 1H, J=4.7 Hz, H_{3PYR}), 7.60 (t, 1H, J=8.2 Hz, H_{6BT}), 7.43 (d, 2H, J=8.8 Hz, H_{2Ph}, H_{6Ph}), 7.36 (d, 1H, J=14.3 Hz, C=CH_α), 6.86 (d, 2H, J=9.0 Hz, H_{3Ph}, H_{5Ph}), 6.62 (d, 1H, J=4.7 Hz, H_{4PYR}), 5.54 (d, 2H, J=2.5 Hz, CH_2), 3.90 (s, 3H, CH_3–N_{PYR}), 3.15 (m, 1H, C≡CH), 3.04 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=169.9, 151.1, 148.0, 140.9, 137.6, 133.5, 130.5, 129.3, 127.5, 126.7, 124.3, 121.7, 117.5, 115.5, 115.0, 112.5, 103.3, 78.3, 76.8, 37.5, 40.6 ppm (the CH_3–N signal is overlapped with the DMSO signal); UV–vis (MeOH) λ_{max}=578 nm (log ε=6.83); IR (ATR) ν=2910, 1577, 1426, 1264, 1182, 1157, 1058, 1018, 949, 794 cm^{-1}. Anal. Calcd for $C_{25}H_{24}BrN_3S$: C 62.76, H 5.06, N 8.78; found: C 62.44, H 4.91, N 8.58%.

4.4.9. (E,E)-2-(2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-furan-2-yl}-vinyl)-3-methylbenzothiazolium iodide (**3dM**)

According to GP2, aldehyde **10d** (0.15 g, 0.6 mmol), 2,3-dimethylbenzothiazolium iodide (0.17 g, 0.6 mmol) and MeOH (3 mL) were used, reaction time 16 h, yield 260 mg of dark green solid (84%). Mp 237 °C (decomp.); ^1H NMR (CD_3OD) δ=8.15 (d, 1H, J=7.4 Hz, H_{7BT}), 8.06 (d, 1H, J=8.5 Hz, H_{4BT}), 7.90 (d, 1H, J=15.1 Hz, C=CH_β), 7.82 (t, 1H, J=8.5 Hz, H_{5BT}), 7.72 (t, 1H, J=7.7 Hz, H_{6BT}), 7.48 (d, 1H, J=16.2 Hz, C=CH_δ), 7.47 (d, 1H, J=15.1 Hz, C=CH_α), 7.46 (d, 2H, J=8.0 Hz, H_{2Ph}, H_{6Ph}), 7.29 (d, 1H, J=3.6 Hz, H_{3FUR}), 6.89 (d, 1H, J=16.2 Hz, C=CH_γ), 6.74 (d, 2H, J=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.69 (d, 1H, J=3.8 Hz, H_{4FUR}), 4.29 (s, 3H, CH_3–N_{BT}), 3.00 (s, 6H, NMe_2) ppm; ^{13}C NMR (CD_3OD) δ=172.2, 163.3, 152.7, 151.5, 150.1, 143.6, 136.0, 134.1, 130.6, 129.9, 129.3, 128.8, 125.6, 125.4, 124.6, 116. 9, 113.2, 111.0, 107.5, 40.3, 36.2 ppm; UV–vis (MeOH) λ_{max}=592 nm (log ε=6.61). Anal. Calcd for $C_{24}H_{23}IN_2OS$: C 56.34, H 4.51, N 5.45; found: C 56.58, H 4.76, N 5.40%.

4.4.10. (E,E)-2-(2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-furan-2-yl}-vinyl)-3-(prop-2-enyl)-benzothiazolium bromide (**3dA**)

According to GP2, aldehyde **10d** (0.15 g, 0.6 mmol), 3-allyl-2-methylbenzothiazolium bromide (0.16 g, 0.6 mmol) and MeOH (3 mL) were used, reaction time 12 h, yield 90 mg of dark red solid (30%). Mp 218 °C (decomp.); ^1H NMR (DMSO-d_6) δ=8.39 (d, 1H, J=8.0 Hz, H_{7BT}), 8.15 (d, 1H, J=8.2 Hz, H_{4BT}), 8.06 (d, 1H, J=15.1 Hz, C=CH_β), 7.82 (t, 1H, J=8.0 Hz, H_{5BT}), 7.73 (t, 1H, J=8.2 Hz, H_{6BT}), 7.53–7.43 (m, 5H, H_{2Ph}, H_{6Ph}, H_{3FUR}, C=CH_α, C=CH_δ), 7.00 (d, 1H, J=16.2 Hz, C=CH_γ), 6.85 (d, 1H, J=3.6 Hz, H_{4FUR}), 6.76 (d, 2H, J=9.1 Hz, H_{3Ph}, H_{5Ph}), 6.17–6.05 (m, 1H, C=CH), 5.57 (d, 2H, J=4.7 Hz, CH_2), 5.37 (d, 1H, J=10.4 Hz, C=CH_2), 5.30 (d, 1H, J=17.6 Hz, C=CH_2), 3.00 (s, 6H, NMe_2) ppm; satisfactory ^{13}C NMR was not obtained due to very low solubility; UV–vis (MeOH) λ_{max}=606 nm (log ε=6.56); IR (ATR) ν=2988, 2900, 1575, 1525, 1462, 1414, 1363, 1239, 1159, 1026, 943 cm^{-1}. Anal. Calcd for $C_{26}H_{25}BrN_2OS$: C 63.28, H 5.11, N 5.68; found: C 62.97, H 5.32, N 5.51%.

4.4.11. (E,E)-2-(2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-thiophen-2-yl}-vinyl)-3-(prop-2-enyl)-benzothiazolium bromide (**3eA**)

According to GP2, aldehyde **10e** (0.15 g, 0.58 mmol), 3-allyl-2-methylbenzothiazolium bromide (0.24 g, 0.58 mmol) and MeOH (4 mL) were used, reaction time 20 h, yield 160 mg of dark green solid (54%). Mp 210 °C (decomp.); ^1H NMR (DMSO-d_6) δ=8.44 (d, 1H, J=15.1 Hz, C=CH_β), 8.40 (d, 1H, J=7.7 Hz, H_{7BT}), 8.16 (d, 1H, J=8.5 Hz, H_{4BT}), 7.88 (d, 1H, J=3.8 Hz, H_{3THP}), 7.83 (t, 1H, J=8.2 Hz, H_{5BT}), 7.74 (t, 1H, J=8.0 Hz, H_{6BT}), 7.50 (d, 2H, J=9.1 Hz, H_{2Ph}, H_{6Ph}), 7.45 (d, 1H, J=15.1 Hz, C=CH_α), 7.33 (d, 1H, J=4.1 Hz, H_{4THP}), 7.31 (d, 1H, J=15.9 Hz, C=CH_δ), 7.15 (d, 1H, J=15.9 Hz, C=CH_γ), 6.75 (d, 2H, J=8.8 Hz, H_{3Ph}, H_{5Ph}), 6.16–6.03 (m, 1H, C=CH), 5.56 (d, 2H, J=4.4 Hz, CH_2), 5.35 (d, 1H, J=10.4 Hz, C=CH_2), 5.26 (d, 1H, J=17.0 Hz, C=CH_2), 2.98 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=170.8, 153.1, 150.5, 141.6, 140.9, 138.0, 136.4, 133.4, 130.5, 129.2, 128.4, 127.9, 127.8, 127.5, 127.1, 124.1, 123.4, 118.8, 116.2, 112.0, 109.2, 50.2 ppm (the CH_3–N signal is overlapped with the DMSO signal); UV–vis (MeOH) λ_{max}=590 nm (log ε=6.60); IR (ATR) ν=2987, 2900, 1564, 1521, 1407, 1353, 1242, 1159, 1048, 941, 805 cm^{-1}. Anal. Calcd for $C_{26}H_{25}BrN_2S_2$: C 61.29, H 4.95, N 5.50; found: C 61.56, H 5.01, N 5.37%.

4.4.12. (E,E)-2-(2-{5-[2-(4-Dimethylaminophenyl)-vinyl]-1-methylpyrrol-2-yl}-vinyl)-3-(prop-2-enyl)-benzothiazolium bromide (**3fA**)

According to GP2, aldehyde **10f** (0.1 g, 0.4 mmol), 3-allyl-2-methylbenzothiazolium bromide (0.11 g, 0.4 mmol) and MeOH (2 mL) were used, reaction time 15 h, yield 110 mg of dark green solid (54%). Mp 264 °C (decomp.); ^1H NMR (DMSO-d_6) δ=8.21 (d, 1H, J=7.7 Hz, H_{7BT}), 7.91 (d, 1H, J=7.9 Hz, H_{4BT}), 7.88 (d, 1H,

J=14.2 Hz, C=CH_{β}), 7.71–7.66 (m, 2H, H_{3PYR}, H_{5BT}), 7.61–7.54 (m, 3H, H_{2Ph}, H_{6Ph}, H_{6BT}), 7.38 (d, 1H, J=16.0 Hz, C=CH_{δ}), 7.32 (d, 1H, J=14.3 Hz, C=CH_{α}), 7.12 (d, 1H, J=15.9 Hz, C=CH_{γ}), 7.05 (d, 1H, J=4.6 Hz, H_{4PYR}), 6.74 (d, 2H, J=8.9 Hz, H_{3Ph}, H_{5Ph}), 6.11–5.97 (m, 1H, C=CH), 5.35 (d, 2H, J=4.8 Hz, CH_2), 5.32 (d, 1H, J=11.5 Hz, C=CH_2), 5.22 (d, 1H, J=17.1 Hz, C=CH_2), 3.90 (s, 3H, CH_3–N_{PYR}), 2.98 (s, 6H, NMe_2) ppm; ^{13}C NMR (DMSO-d_6) δ=168.4, 150.8, 146.0, 141.0, 135.6, 134.8, 132.7, 130.7, 128.8, 128.6, 126.6, 126.2, 124.1, 123.6, 121.6, 118.5, 114.9, 112.2, 112.0, 110.3, 102.4, 48.6, 30.6 ppm (the CH_3–N signal is overlapped with the DMSO signal); UV–vis (MeOH) λ_{max}=624 nm (log ε=6.98); IR (ATR) ν=2988, 2900, 1566, 1527, 1407, 1376, 1240, 1107, 1048, 946, 803 cm^{-1}. Anal. Calcd for $C_{27}H_{28}BrN_3S$: C 64.03, H 5.57, N 8.30; found: C 63.86, H 5.76, N 7.98%.

4.5. Computational details

All molecular geometries were fully optimized at the BP86 level of theory[38] in combination with the Resolution of Identity approximation (RI-BP86)[39] employing TZVP all-electron basis sets[40] in Turbomole 5.7 program package.[41] The optimized structures were characterized as the true minima on the harmonic potential energy hypersurfaces. The molecular static quadratic hyperpolarizabilities β_0 and electronic transition characteristics were computed in Gaussian 98.[42] The following criteria (*scf=tight*, *grid=fine*) were used in SCF step. β_0 values were calculated at the coupled perturbed Hartree–Fock (CPHF) level (see Supplementary data; Tables S1–S3) as well as at DFT level (B3LYP functional[43]) using the finite-field (FF) numerical derivative method. In both cases, 6-31G(d) basis set (denoted also as 6-31G*) was employed. Moreover, β_0 values were estimated from the two-state model.[44]

$$\beta_0 \approx \frac{3\Delta\mu_{12}(\mu_{12})^2}{(E_{max})^2} \quad (1)$$

The parameters occurring in Eq. 1 were calculated using time-dependent DFT method[45] at B3LYP/6-31G(d) level of theory. The excited state dipole moments were calculated using one particle RhoCI density. Solvent effects on ICT transitions as well as β_0 values were simulated by employing a polarizable continuum model (PCM),[46] assuming methanol as a solvent. Molecular orbitals isosurfaces were plotted using Molekel 4.3 program.[47]

4.6. Biological activity

The toxicity against an autotrophic form of unicellular flagellate *E. gracilis* was monitored in a liquid Cramer–Myers medium containing appropriate concentrations (2.0–300 μg/mL) of the test substances. Fresh solutions of tested substances in DMSO were prepared prior to cultivation. Inoculum of *E. gracilis* was taken from the exponential growth phase and was cultivated for 96 h under permanent illumination at a temperature of 26±1 °C. The ED50 toxicity values (in 10^{-3} mol L^{-1}) were interpolated from nonlinear cubic functions. Antimicrobial properties were tested also against Gram-positive (*S. aureus* CCM 3953, *Bacillus subtilis* 18/64) and Gram-negative bacteria (*Escherichia coli* CCM 3988, *Pseudomonas aeruginosa* CCM 8221) as well as against yeast (*Candida albicans* Pn-10) and mould (*M. gypseum*) were tested by the standard plate diffusion method using Mueller–Hinton and Sabouraud agar, or by standard dilution method in Sabouraud medium.[48]

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Supplementary data

Computational results of static molecular quadratic hyperpolarizabilities β_0 and electronic transition characteristics for all conformers at B3LYP and HF level of theory. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.08.064.

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