Synthesis of 2,4-Difuryl-4*H*-3,1-benzothiazines via a Furan Ring Migration Reaction

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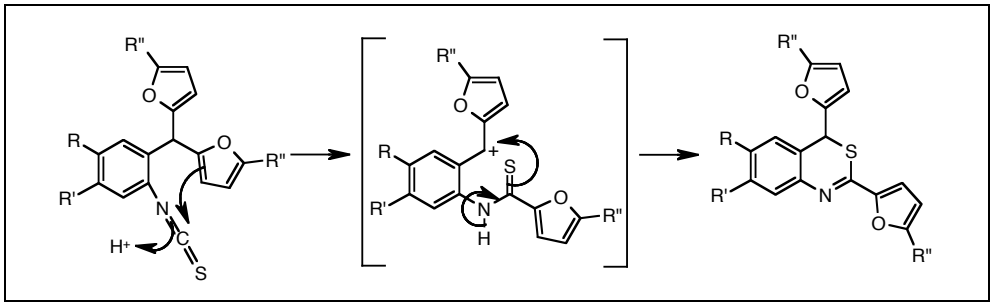

A new simple synthetic approach to 2,4-difuryl-4*H*-3,1-benzothiazines from 2-isothiocyanoaryldifuryl-methanes in the presence of acidic catalyst is described. This rearrangement is a new example of furan ring migration reaction resulting from intramolecular attack with electrophilic carbon.

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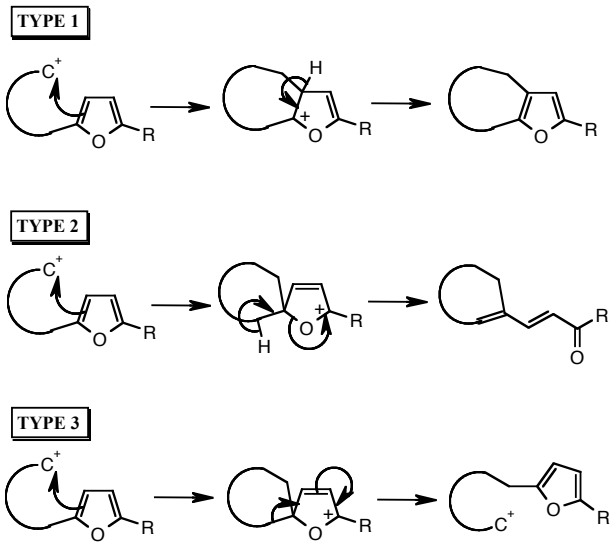
INTRODUCTION

Among the five-membered aromatic heterocycles furan holds leading positions due to unique diversity of its chemical transformations. For example furan compounds can undergo substitution reactions as aromatic compounds, cycloaddition reactions as dienes, can serve as convenient precursors of 1,4-diketones and undergo oxidation reactions. All these transformations are widely used in synthetic practice [1]. It should be noted that reactivity of furan compounds strongly depends on the substrate structure and reaction conditions. Presently, three types of intramolecular reactions of furans with electrophilic carbon are known: cyclization, electrophilic ring opening, and ring transfer (Scheme 1).

The first type, the electrophilic cyclization is probably the common intramolecular furan-carbocation reaction. It includes intramolecular alkylation, acylation and condensation reactions leading to a new ring formation. Furan compounds with alkene side chain are prone to acid catalyzed intramolecular alkylation, and the reaction is commonly used in natural products synthesis. In particular, a synthesis of furanosesquiterpenoid *Pallescensin A* and its derivatives was reported [2] as well as formal total syntheses of *Aphidicolin* [3] and substances structurally related to natural *Guaianolides* and *Pseudoguaianolides* [4]. Katritzky *et al* offered a general and facile synthesis of furocarbazoles based on the intramolecular furan alkylation with benzotriazole as a leaving group [5]. Tanis *et al* synthesized furyl containing alkaloids by intramolecular alkylation of furans with acyliminium ions [6].

Scheme 1



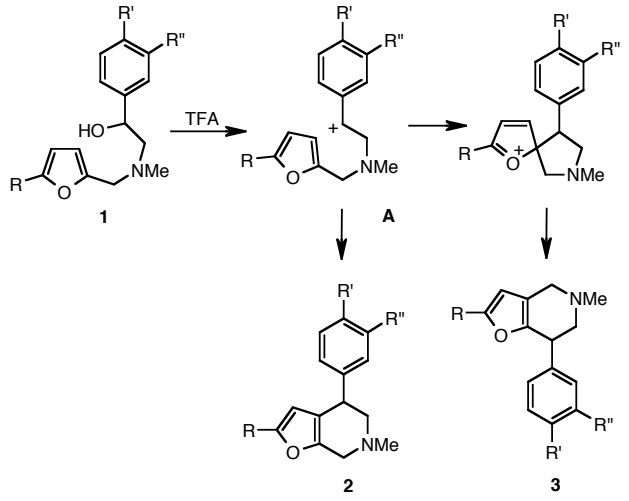
Intramolecular acylation, which takes place in the presence of acidic catalysts and leads to a new benzene ring formation, is widely used in the synthesis of naphthofuran [7] and benzofuran [8] skeletons. Similar intramolecular electrophilic cyclizations are also successfully used to build up naphthofuran [7f, 7g] and benzofuran [9] heterocyclic systems. Recently we applied

the reaction to obtain a number of seven-membered furoannelated carbocycles [10].

The second type, the electrophilic cleavage of furan ring leading to α,β-unsaturated ketones is less known, but represented in several publications. It is described as a result of intramolecular reaction of furan ring with carbenes which are generated from furyl α-diazoketones under catalysis with Cu(II) [11] and Rh(II) [12] or from furyl acetylenes under catalysis with $PtCl_2$ [13]. Most interesting is the synthesis of benzo[*a*]azulenyl- [14] and azuleno[1,2-*b*]thienyl- [15] α,β-unsaturated ketones by Yamamura *et al* based on the reaction of cycloheptatrienyl cation which is connected with furan *via* benzene and thiophene rings respectively.

The third type of furan-carbocation reactions is accompanied with furan ring transfer and as we known it is represented by a single publication. It was reported that treatment of aminoalcohols **1** with trifluoroacetic acid led to the cyclization product **2** with low yield in only one case. The major products of the reaction were identified as isomeric tetrahydrofuro[3,2-*c*]pyridines **3** which resulted from rearrangement and furan ring transfer to carbocation **A** (Scheme 2) [16].

Scheme 2



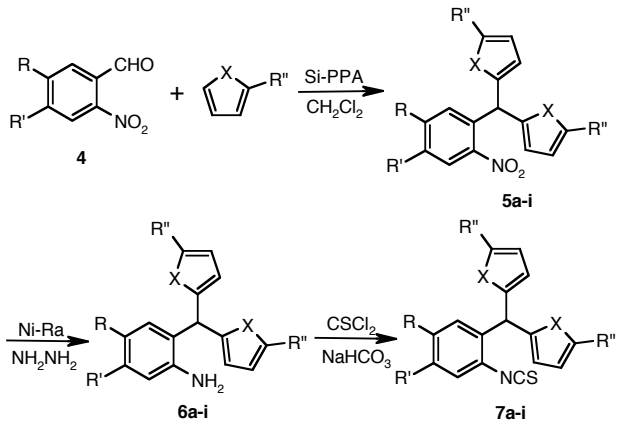
Isothiocyanates are well known reagents for Friedel-Crafts reaction with aromatic and heterocyclic compounds to give thioamides in the presence of acidic catalysts [17], and isothiocyano carbon atom is acting as electrophile in the aromatic substitution. Similar intramolecular cyclization reactions are also known for compounds with isothiocyano group bound with aromatic and heteroaromatic rings *via* alkyl spacers [18].

In a preliminary communication [19], we reported two examples of perchloric acid catalyzed transformation of 2-isothiocyanoaryldifurylmethanes into corresponding 2,4-difuryl-4*H*-3,1-benzothiazine derivatives in 1,4-dioxane. In this case the reaction does not proceed through a classical electrophilic cyclization as initially thought but is accompanied with furan ring transfer and it is therefore a new example of transformations of such type. In the present publication we describe results of detailed investigation of this rearrangement.

RESULTS AND DISCUSSION

Isothiocyanates **7** were the starting compounds for our synthesis of 4*H*-3,1-benzothiazine derivatives (Scheme 3, Table 1). 2-Nitroaryldihetarylmethanes **5** were prepared by condensation of 2-nitrobenzaldehydes **4** with furans and 2-methylthiophene in CH_2Cl_2 in the presence of polyphosphoric acid trimethylsilyl ether (Si-PPA) at r.t., the method earlier reported by our group [20]. The compounds **5** were reduced to corresponding amines **6** with hydrazine hydrate in the presence of Raney nickel. 2-Isothiocyanoaryldihetarylmethanes **7** were synthesized by treatment of amines **6** with thiophosgene in CH_2Cl_2/aq. $NaHCO_3$ biphasic system.

Scheme 3



Treatment of 2-isothiocyanoaryldifurylmethanes **7a-h** with 70% $HClO_4$ in 1,4-dioxane at r.t. leads to 2,4-difuryl-4*H*-3,1-benzothiazine derivatives **8a-h** in with 57-70% yield (Scheme 4, Table 2). Alkyl substituents (methyl, ethyl, *t*-butyl) in the position 5 of furan ring do not influence the course of the reaction. The reaction follows the same reaction pathway with comparable rates and is completed within 5 hours in average. Fluctuations in yields are caused most likely by isolation procedures for a particular compound.

Replacement of alkyl group in the position 5 of furan ring by aromatic group in the compound **7d** also leads to benzothiazine **8d** after rearrangement, with the only difference being an increase in the reaction time to 3 days at r.t. Elevated temperatures resulted in noticeable decomposition of the reaction mixture and lower yields of the target compound.

Table 1

Yields of Compounds **5**, **6** and **7**

Entry	R	R'	R"	X	Yield of **5** (%)	Yield of **6** (%)	Yield of **7** (%)
a		OCH_2O	Me	O	83	92	77
b		OCH_2O	Et	O	85	90	79
c		OCH_2O	*t*-Bu	O	82	95	83
d		OCH_2O	*p*-BrC_6H_4	O	43	85	85
e		OCH_2CH_2O	Me	O	91	94	82
f	OMe	OMe	Me	O	87	88	75
g	H	Br	Me	O	60	78	75
h	H	H	Me	O	84	81	78
i	H	H	Me	S	57	93	85

Scheme 4

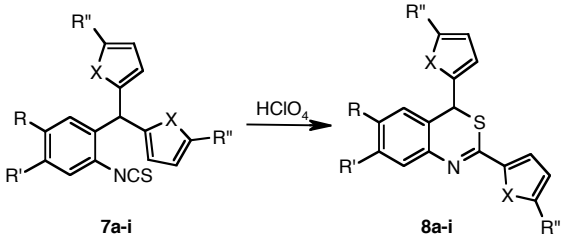


Table 2

Yields of the Compounds **8**

Entry	R	R'	R"	X	Yield of **8** (%)
a	OCH_2O		Me	O	65
b	OCH_2O		Et	O	64
c	OCH_2O		*t*-Bu	O	57
d	OCH_2O		*p*-BrC_6H_4	O	48
e	OCH_2CH_2O		Me	O	65
f	OMe	OMe	Me	O	68
g	H	Br	Me	O	59
h	H	H	Me	O	70
i	H	H	Me	S	45

2,4-Difuryl-4*H*-3,1-benzothiazine derivatives **8a-h** were fully characterized by spectral methods. For unambiguous proof of structure X-Ray analysis was performed for **8e** (Figure 1) [21].

To extend the scope of the reaction, rearrangement to 2,4-dithienyl-4*H*-3,1-benzothiazine was investigated. Treatment of (2-isothiocyanoaryl)dithienylmethane **7i** with 70% $HClO_4$ in 1,4-dioxane at 80-85 °C for 8 hours furnished the corresponding 2,4-dithienyl-4*H*-3,1-benzothiazine **8i** in with 45% yield (Scheme 4, Table 2). The moderate yield of the product stimulated us to explore other reaction conditions. It was found that the catalyst of choice is anh. AlCl3 (1.5 eq.) in 1,2-dichloroethane at r.t. The product **8i** was obtained in 72% yield under these conditions and the reaction time was reduced to 40 min. The same conditions were applied to the rearrangement of aryldifurylmethanes **7a-h**. The yields did not change in this case, but the reaction time could be also reduced to 4 hours for compound **7d** and 30-60 min for the rest of the substrates.

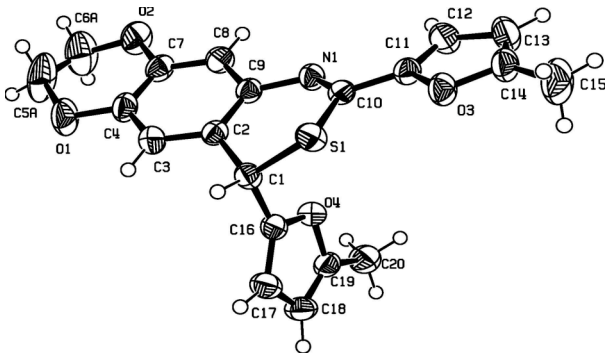
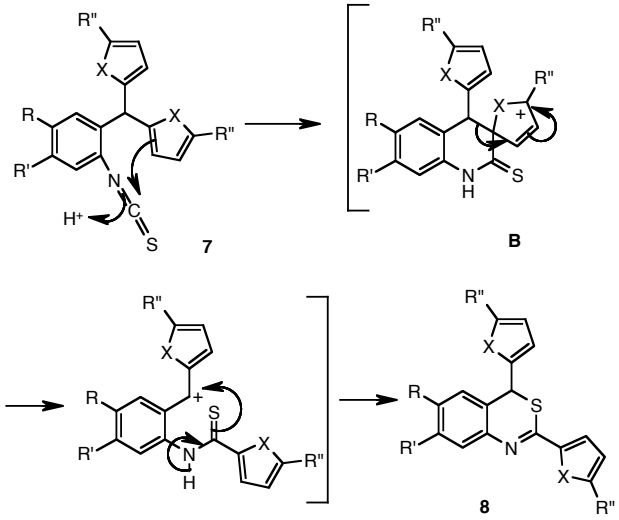


Figure 1. ORTEP diagram of **8e**.

A plausible mechanism for the rearrangement of **7** to **8** is proposed as shown in Scheme 5. We believe that isothiocyano group activated with proton or $AlCl_3$ is able

Scheme 5



to attack the α-position of heterocycle followed by C-C bond cleavage and carbocation **B** formation. Therefore, the first step of the reaction is the transfer of heterocycle from one carbon to another. Subsequent nucleophilic attack of the thioamide sulfur atom to the carbocationic center furnishes the formation of the thiazine cycle.

In conclusion, a new synthetic approach to 2,4-difuryl-4*H*-3,1-benzothiazine derivatives has been developed based on a novel intramolecular furan ring migration reaction as a key step. It was shown that the rearrangement can be extended to the 2,4-dithienyl-4*H*-3,1-benzothiazine derivatives.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on a Bruker AC 200, Bruker AM 300 and Bruker AM 360 spectrometers. Chemical shifts are reported in ppm relative to tetramethylsilane as an internal standard and coupling constants (*J*) are given in absolute values in Hz to the nearest 0.1 Hz. Mass spectra were recorded on a Kratos MS-30 instrument with 70 eV electron impact ionization at 200ºC. IR spectra were recorded on InfraLUM FT-02 and InfraLUM FT-801. Column chromatography was carried out using silica gel KSK (5-40 μm) manufactured by LTD Sorbpolymer. A single crystal of **8e** suitable for X-Ray crystallography was grown from AcOEt-hexane. Compounds **5** were synthesized according published method [20], compounds **6** were synthesized as described [10e].

General procedure for the synthesis of isothiocyanates 7a-i. To a stirred solution of the compound (**6**) (5 mmol) in CH_2Cl_2 (15 ml) solutions of $CSCl_2$ (0.5 ml, 6.6 mmol) in CH_2Cl_2 (5 ml) and $NaHCO_3$ (1.5 g, 18 mmol) in water (50 ml) were added simultaneously at r.t. At the end of the reaction (monitored by TLC) the mixture was poured into water (200 ml) and stirred for 6 hours. The organic layer was extracted with CH_2Cl_2 (2 × 40 ml), separated and dried over anhydrous Na_2SO_4. The solvent was evaporated and the oily residue was dissolved in hot hexane and filtered through a pad of silica gel (5-40 μm). The solution was concentrated and left for crystallization.

6-Bis(5-methyl-2-furyl)methyl-1,3-benzodioxol-5-yl isothiocyanate (7a). This compound was obtained according to the general method in 77% yield as pale beige cubes (hexane), mp 78-79 °C; ir (potassium bromide): 2056, 1618, 1561, 1502, 1483, 1386, 1296, 1249, 1212, 1076, 1023, 938, 882, 832, 776 cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 2.27 (s, 6H, CH_3), 5.60 (s, 1H, CH), 5.90 (d, J = 3.2 Hz, 2H, 4-H_{Fur}), 5.97 (d, J = 3.2 Hz, 2H, 3-H_{Fur}), 5.98 (s, 2H, CH_2), 6.67 (s, 1H, H_{Ar}), 6.74 (s, 1H, H_{Ar}). *Anal.* Calcd. for $C_{19}H_{15}NO_4S$: C, 64.58; H, 4.28; N, 3.96. Found: C, 64.35; H, 4.40; N, 4.05.

6-Bis(5-ethyl-2-furyl)methyl-1,3-benzodioxol-5-yl isothiocyanate (7b). This compound was obtained according to the general method in 79% yield as pale yellow oil; ir (Nujol): 2123, 1679, 1620, 1560, 1504, 1481, 1242, 1038, 937, 830, 780 cm^{-1}; ^{1}H nmr (360 MHz, deuteriochloroform): δ 1.20 (t, J = 7.6 Hz, 6H, CH_2CH_3), 2.59 (q, J = 7.6 Hz, 4H, CH_2CH_3), 5.60 (s, 1H, CH), 5.90 (d, J = 3.2 Hz, 2H, H_{Fur}), 5.95 (s, 2H, CH_2), 5.96 (d, J = 3.2 Hz, 2H, H_{Fur}), 6.63 (s, 1H, H_{Ar}), 6.72 (s, 1H, H_{Ar}). *Anal.* Calcd. for $C_{21}H_{19}NO_4S$: C, 66.12; H, 5.02; N, 3.67. Found: C, 66.19; H, 4.91; N, 3.74.

6-Bis[5-(*tert*-butyl)-2-furyl]methyl-1,3-benzodioxol-5-yl isothiocyanate (7c). This compound was obtained according to the general method in 83% yield as pale beige solid (hexane), mp 126-127 °C; ir (potassium bromide): 2127, 1504, 1483, 1461, 1369, 1297, 1249, 1193, 1180, 1124, 1070, 1039, 1018, 979, 939, 871, 784 cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 1.26 (s, 18H, *t*-Bu), 5.61 (s, 1H, CH), 5.88 (d, J = 3.2 Hz, 2H, 4-H_{Fur}), 5.92 (d, J = 3.2 Hz, 2H, 3-H_{Fur}), 5.98 (s, 2H, CH_2), 6.62 (s, 1H, H_{Ar}), 6,74 (s, 1H, H_{Ar}). *Anal.* Calcd. for $C_{25}H_{27}NO_4S$: C, 68.63; H 6.22; N, 3.20. Found: C, 68.78; H 6.17; N, 3.34.

6-Bis[5-(4-bromophenyl)-2-furyl]methyl-1,3-benzodioxol-5-yl isothiocyanate (7d). This compound was obtained according to the general method in 85% yield as pale green solid (hexane), mp 142 °C; ir (potassium bromide) 2125, 2102, 1502, 1477, 1467, 1377, 1242, 1197, 1072, 1033, 1006, 827, 800, 781 cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 5.89 (s, 1H, CH), 6.09 (s, 2H, CH_2), 6.41 (d, J = 3.2 Hz, 2H, H_{Fur}), 6.82 (s, 1H, H_{Ar}), 6.99 (d, J = 3.2 Hz, 2H, H_{Fur}), 7.19 (s, 1H, H_{Ar}), 7.59 (s, 8H, H_{Ar}). *Anal.* Calcd. for $C_{29}H_{17}Br_2NO_4S$: C, 54.83; H, 2.70; N, 2.20. Found: C, 54.70; H, 2.57; N, 2.35.

7-Bis(5-methyl-2-furyl)methyl-2,3-dihydro-1,4-benzodioxin-6-yl isothiocyanate (7e). This compound was obtained according to the general method in 82% yield as pale beige needles (hexane), mp 101-102 °C; ir (potassium bromide): 2021, 1506, 1458, 1378, 1309, 1251, 1216, 1199, 1182, 1064, 1022, 939, 891, 804, 796, 786 cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 2.26 (s, 6H, CH_3), 4.24 (s, 4H, CH_2CH_2), 5.55 (s, 1H, CH), 5.89 (d, J = 3.2 Hz, 2H, 4-H_{Fur}), 5.95 (d, J = 3.2 Hz, 2H, 3-H_{Fur}), 6.69 (s, 1H, H_{Ar}), 6.80 (s, 1H, H_{Ar}). *Anal.* Calcd. for $C_{20}H_{17}NO_4S$: C, 65.38; H, 4.66; N, 3.81. Found: C, 65.45; H, 4.81; N, 3.74.

2-Bis(5-methyl-2-furyl)methyl-4,5-dimethoxyphenyl isothiocyanate (7f). This compound was obtained according to the general method in 75% yield as pale beige solid (hexane), mp 88 °C; ir (potassium bromide): 2002, 1604, 1522, 1444, 1351, 1300, 1208, 1116, 1010, 922, 837, 794, 776 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 2.26 (s, 6H, CH_3), 3.79 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 5.60 (s, 1H, CH), 5.90 (d, J = 3.2 Hz, 2H, 4-H_{Fur}), 5.96 (d, J = 3.2 Hz, 2H, 3-H_{Fur}), 6.69 (s, 1H, H_{Ar}), 6.77 (s, 1H, H_{Ar}). *Anal.* Calcd. for $C_{20}H_{19}NO_4S$: C, 65.02; H, 5.18; N 3.79. Found: C, 65.16; H, 5.25; N 3.66.

5-Bromo-2-bis(5-methyl-2-furyl)methylphenyl isothiocyanate (7g). This compound was obtained according to the general method in 75% yield as pale beige solid (hexane), mp 61-62 °C; ir (potassium bromide): 2057, 1909, 1583, 1558, 1475, 1465, 1392, 1378, 1261, 1216, 1166, 1149, 1020, 1000, 964, 950, 881, 827, 792, 783, 727 cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform) δ 2.26 (s, 6H, CH_3), 5.61 (s, 1H, CH), 5.91 (d, J = 3.2 Hz, 2H, 4-H_{Fur}), 5.96 (d, J = 3.2 Hz, 2H, 3-H_{Fur}), 7.07 (d, J = 8.4 Hz, 1H, H_{Ar}), 7.35 (dd, J = 2.0, 8.4 Hz, 1H, H_{Ar}), 7.43 (d, J = 2.0 Hz, 1H, H_{Ar}). *Anal.* Calcd. for $C_{18}H_{14}BrNO_2S$: C, 55.68; H, 3.63; N, 3.61. Found: C, 55.75; H, 3.57; N, 3.52.

2-Bis(5-methyl-2-furyl)methylphenyl isothiocyanate (7h). This compound was obtained according to the general method in 78% yield as pale beige solid (hexane), mp 59 °C; ir (potassium bromide): 2122, 1613, 1563, 1451, 1216, 1022, 936, 779, 751, 713 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform) δ 2.26 (s, 6H, CH_3), 5.67 (s, 1H, CH), 5.91 (d, J = 3.1 Hz, 2H, 4-H_{Fur}), 5.96 (d, J = 3.1 Hz, 2H, 3-H_{Fur}), 7.20-7.27 (m, 4H, H_{Ar}). *Anal.* Calcd. for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53. Found: C, 69.95; H, 4.76; N, 4.63.

2-Bis(5-methyl-2-thienyl)methylphenyl isothiocyanate (7i). This compound was obtained according to the general method in 85% yield as pale beige solid (hexane), mp 62 °C; ir (potassium bromide): 2092, 1575, 1479, 1465, 1450, 1377, 1224, 1164, 1033, 935, 802, 757 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 2.44 (s, 6H, CH_3), 6.01 (s, 1H, CH), 6.60 (d, J = 2.2 Hz, 2H, 4-H_{Th}), 6.63 (d, J = 2.2 Hz, 2H, 3-H_{Th}), 7.21-7.27 (m, 3H, H_{Ar}), 7.30-7.34 (m, 1H, H_{Ar}). *Anal.* Calcd. for $C_{18}H_{15}NS_3$: C, 63.31; H, 4.43; N, 4.10. Found: C, 63.39; H, 4.58; N, 3.98.

General procedure for the synthesis of 4*H*-3,1-benzothiazines 8a-i. Method A. To a solution of isothiocyanate **7** (3 mmol) in 1,4-dioxane (10 mL), $HClO_4$ (70%, 1.0 ml) was added. The reaction mixture was stirred for 5 hours at r.t. (monitored by TLC), then poured into water solution $NaHCO_3$ (1%, 50 ml) and extracted with CH_2Cl_2 (3 × 30 ml). The organic layer was separated, dried over anhydrous Na_2SO_4, the solvent was evaporated to quarter of volume and diluted with hexane. The resulting solution was filtered through a pad of silica gel (5-40 μm). The solvent was evaporated and residue was recrystallized from CH_2Cl_2–hexane (1:10).

Method B. To a solution of isothiocyanate **7** (3 mmol) in 1,2-dichloroethane (10 ml), $AlCl_3$ (0.6 g, 4.5 mmol) was added. The reaction mixture was stirred for 30-60 min at r.t. (monitored by TLC), then poured into water (200 ml) and extracted with CH_2Cl_2 (3 × 40 ml). The organic layer was separated, dried over anhydrous Na_2SO_4, the solvent was evaporated to quarter of volume and diluted with hexane. The resulting solution was filtered through a pad of silica gel (5-40 μm). The solvent was evaporated and residue was recrystallized from CH_2Cl_2–hexane (1:10).

6,8-Bis(5-methyl-2-furyl)-8*H*-[1,3]dioxolo[4,5-*g*][3,1]benzothiazine (8a). This compound was obtained according to the general method A in 65% yield as yellow solid (CH_2Cl_2–hexane), mp 137-138 °C; ir (potassium bromide): 1548, 1477, 1369, 1248, 1149, 1031, 933, 855, 771 cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 2.24 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 5.18 (s, 1H, CH), 5.74 (d, J = 3.0 Hz, 1H, 3-H_{Fur}), 5.76 (d, J = 3.0 Hz, 1H, 4-H_{Fur}), 6.00 (s, 2H, CH_2), 6.12 (d, J = 3.3 Hz, 1H, 4-H_{Fur}), 6.61 (s, 1H, H_{Ar}), 6.97 (d, J = 3.3 Hz, 1H, 3-H_{Fur}), 7.07 (s, 1H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 13.7, 14.2, 39.2, 101.6, 106.7, 106.8, 108.1, 108.7, 109.2, 114.4, 117.0, 139.0, 145.7, 146.7, 148.0, 149.6, 150.3, 152.5, 156.7; ms: *m/z* 353 (M^+, 91), 323 (24), 311 (20), 310 (100), 308 (19), 295 (16), 227 (18), 125 (56), 57 (23), 46 (19), 45 (24), 44 (45), 43 (53), 41 (21), 39 (15). *Anal.* Calcd. for $C_{19}H_{15}NO_4S$: C, 64.58; H, 4.28; N, 3.96. Found: C, 64.66; H, 4.19; N, 4.03.

6,8-Bis(5-ethyl-2-furyl)-8*H*-[1,3]dioxolo[4,5-*g*][3,1]benzothiazine (8b). This compound was obtained according to the general method A in 64% yield as yellow solid (CH_2Cl_2–hexane), mp 138-139 °C; ir (potassium bromide): 1549, 1477, 1368, 1247, 1192, 1148, 1031, 991, 935, 887, 799, 771 cm^{-1}; ^1H nmr (360 MHz, deuteriochloroform): δ 1.19 (t, J = 7.5 Hz, 3H, CH_2CH_3), 1.30 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.59 (q, J = 7.5 Hz, 2H, CH_2CH_3), 2.78 (q, J = 7.5 Hz, 2H, CH_2CH_3), 5.19 (s, 1H, CH), 5.77 (d, J = 3.0 Hz, 1H, 3-H_{Fur}), 5.79 (d, J = 3.0 Hz, 1H, 4-H_{Fur}), 6.00 (s, 2H, CH_2), 6.13 (d, J = 3.4 Hz, 1H, 4-H_{Fur}), 6.60 (s, 1H, H_{Ar}), 6.99 (d, J = 3.4 Hz, 1H, 3-H_{Fur}), 7.07 (s, 1H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 11.9, 12.0, 21.4, 21.8, 39.3, 101.6, 105.1, 106.8, 107.0, 108.1, 109.0, 114.5, 116.7, 139.1, 145.8, 146.7, 147.9, 149.5, 150.2, 158.1, 162.3; ms: *m/z* 381 (M^+, 100), 324 (85), 322 (16), 139 (37), 59 (23), 45 (30), 44 (32), 42 (38), 39 (15). *Anal.* Calcd. for $C_{21}H_{19}NO_4S$: C, 66.12; H, 5.02; N, 3.67. Found: C, 66.01; H, 5.13; N, 3.55.

6,8-Bis[5-(*tert*-butyl)-2-furyl]-8*H*-[1,3]dioxolo[4,5-*g*][3,1]-benzothiazine (8c). This compound was obtained according to the general method A in 57% yield as yellow solid (CH_2Cl_2–hexane), mp 68 °C; ir (potassium bromide): 1621, 1544, 1479, 1366, 1245, 1034, 936, 887, 791, 704 cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 1.24 (s, 9H, *t*-Bu), 1.35 (s, 9H, *t*-Bu), 5.20 (s, 1H, CH), 5.77 (s, 2H, H_{Fur}), 6.00 (s, 2H, CH_2), 6.11 (d, J = 3.4 Hz, 1H, 4-H_{Fur}), 6.60 (s, 1H, H_{Ar}), 6.97 (d, J = 3.4 Hz, 1H, 3-H_{Fur}), 7.03 (s, 1H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 29.0 (3C), 29.1 (3C), 32.7, 33.2, 39.4, 101.6, 102.9, 105.1, 106.7, 108.1, 108.6, 114.6, 115.8, 139.2, 146.4, 146.6, 147.8, 149.6, 150.0, 164.4, 168.2; ms: *m/z* 437 (M^+, 100), 422 (38), 352 (68), 350 (18), 55 (22), 45 (30), 44 (24), 43 (38), 39 (15). *Anal.* Calcd. for $C_{25}H_{27}NO_4S$: C, 68.63; H 6.22; N, 3.20. Found: C, 68.70; H 6.37; N, 3.11.

6,8-Bis[5-(4-bromophenyl)-2-furyl]-8*H*-[1,3]dioxolo[4,5-*g*]-[3,1]benzothiazine (8d). This compound was obtained according to the general method A in 48% yield as yellow solid (CH_2Cl_2–hexane), mp 180-181 °C; ir (potassium bromide): 1543, 1475, 1369, 1245, 1072, 1027, 924, 886, 825, 791, 771 cm^{-1}; ^1H nmr (200 MHz, dimethyl sulfoxide-d_6): δ 5.85 (s, 1H, CH), 6.01 (d, J = 3.1 Hz, 1H, H_{Fur}), 6.10 (s, 2H, CH_2), 6.82 (d, J = 3.1 Hz, 1H, H_{Fur}), 6.99 (s, 1H, H_{Ar}), 7.04 (s, 1H, H_{Ar}), 7.22 (d, J = 3.5 Hz, 1H, H_{Fur}), 7.29 (d, J = 3.5 Hz, 1H, H_{Fur}), 7.50 (d, J = 8.7 Hz, 2H, H_{Ar}), 7.56 (d, J = 8.7 Hz, 2H, H_{Ar}), 7.67 (d, J = 8.6 Hz, 2H, H_{Ar}), 7.76 (d, J = 8.6 Hz, 2H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 39.2, 101.8, 106.7, 107.0, 108.0, 108.3, 110.5, 113.6, 117.0, 121.3, 122.6, 125.3 (2C), 126.2 (2C), 128.7, 129.4, 131.9 (2C), 132.0 (2C), 139.0, 145.2, 147.1, 148.3, 150.7, 152.5, 153.0, 155.9; ms: *m/z* 637/635/633 (M^+, 2/4/2), 605/603/601 (61/100/64), 452/450 (90/91), 265 (15), 185/183 (21/29), 46 (16), 45 (35), 42 (35), 40 (46). *Anal.* Calcd. for $C_{29}H_{17}Br_2NO_4S$: C, 54.83; H, 2.70; N, 2.20. Found: C, 54.69; H, 2.78; N, 2.15.

2,4-Bis(5-methyl-2-furyl)-7,8-dihydro-4*H*-[1,4]dioxino[2,3-*g*]-[3,1]benzothiazine (8e). This compound was obtained according to the general method A in 65% yield as yellow solid (CH_2Cl_2–hexane), mp 139-140 °C; ir (potassium bromide): 1573, 1545, 1490, 1310, 1248, 1204, 1063, 1010, 879, 795, 749 cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 2.24 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.28 (s, 4H, CH_2CH_2), 5.20 (s, 1H, CH), 5.75 (d, J = 3.0 Hz, 1H, 3-H_{Fur}), 5.77 (d, J = 3.0 Hz, 1H, 4-H_{Fur}), 6.11 (d, J = 3.4 Hz, 1H, 4-H_{Fur}), 6.64 (s, 1H, H_{Ar}), 6.97 (d, J = 3.4 Hz, 1H, 3-H_{Fur}), 7.12 (s, 1H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 13.7, 14.2, 38.8, 64.4, 64.5, 106.7, 108.6, 109.1, 114.8, 115.3, 116.2, 116.7, 138.0, 142.9, 143.7, 145.9, 149.8, 150.6, 152.4, 156.6; ms: *m/z* 367 (M^+, 100), 336 (17), 324 (41), 268 (18), 125 (22), 44(26), 43(32), 40(16). *Anal.* Calcd. for $C_{20}H_{17}NO_4S$: C, 65.38; H, 4.66; N, 3.81. Found: C, 65.43; H, 4.78; N, 3.86.

6,7-Dimethoxy-2,4-bis(5-methyl-2-furyl)-4*H*-3,1-benzothiazine (8f). This compound was obtained according to the general method A in 68% yield as yellow solid (CH_2Cl_2–hexane), mp 154-155 °C; ir (potassium bromide): 1609, 1552, 1508, 1459, 1349, 1257, 1227, 1118, 1016, 951, 868, 789, 748, 725 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 2.24 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 5.23 (s, 1H, CH), 5.68 (d, J = 3.0 Hz, 1H, 3-H_{Fur}), 5.77 (d, J = 3.0 Hz, 1H, 4-H_{Fur}), 6.12 (d, J = 3.3 Hz, 1H, 4-H_{Fur}), 6.64 (s, 1H, H_{Ar}), 6.97 (d, J = 3.3 Hz, 1H, 3-H_{Fur}), 7.14 (s, 1H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 13.7, 14.2, 38.9, 56.1 (2C), 106.7, 108.7, 109.1, 109.8, 111.0, 112.5, 116.8, 137.7, 145.5, 148.3, 149.1, 149.7, 150.9, 152.4, 156.6; ms: *m/z* 369

(M^+, 90), 354 (15), 338 (100), 326 (56), 268 (21), 244 (16), 243 (22), 125 (58), 95 (33), 46 (17), 45 (20), 43 (36), 42 (23). *Anal.* Calcd. for $C_{20}H_{19}NO_4S$: C, 65.02; H, 5.18; N 3.79. Found: C, 64.93; H, 5.30; N 3.65.

7-Bromo-2,4-bis(5-methyl-2-furyl)-4*H*-3,1-benzothiazine (8g). This compound was obtained according to the general method A in 59% yield as yellow solid (CH_2Cl_2–hexane), mp 114 °C; ir (potassium bromide): 1547, 1488, 1360, 1241, 1178, 1079, 1024, 924, 759, 733 cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 2.24 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 5.27 (s, 1H, CH), 5.73 (d, J = 3.0 Hz, 1H, 3-H_{Fur}), 5.79 (d, J = 3.0 Hz, 1H, 4-H_{Fur}), 6.15 (d, J = 3.5 Hz, 1H, 4-H_{Fur}), 7.02 (d, J = 8.2 Hz, 1H, H_{Ar}), 7.06 (d, J = 3.5 Hz, 1H, 3-H_{Fur}), 7.38 (dd, J = 1.9, 8.2 Hz, 1H, H_{Ar}), 7.74 (d, J = 1.9 Hz, 1H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 13.7, 14.3, 38.9, 106.8, 109.0, 109.5, 118.0, 120.2, 122.1, 128.6, 130.1, 130.4, 145.1, 149.2, 149.5, 149.8, 152.8, 157.5; ms: *m/z* 389/387 (M^+, 27/27), 346/344 (15/15), 308 (100), 265 (18), 125 (38), 57 (72), 45 (22), 43 (24), 42 (21). *Anal.* Calcd. for $C_{18}H_{14}BrNO_2S$: C, 55.68; H, 3.63; N, 3.61. Found: C, 55.81; H, 3.54; N, 3.69.

2,4-Bis(5-methyl-2-furyl)-4*H*-3,1-benzothiazine (8h). This compound was obtained according to the general method A in 70% yield as yellow solid (CH_2Cl_2–hexane), mp 97-98 °C; ir (potassium bromide): 1604, 1545, 1508, 1446, 1191, 1022, 950, 905, 853, 780, 761, 745 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 2.24 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 5.31 (s, 1H, CH), 5.71 (d, J = 3.0 Hz, 1H, 3-H_{Fur}), 5.77 (d, J = 3.0 Hz, 1H, 4-H_{Fur}), 6.14 (d, J = 3.4 Hz, 1H, 4-H_{Fur}), 7.04 (d, J = 3.4 Hz, 1H, 3-H_{Fur}), 7.13-7.17 (m, 1H, H_{Ar}), 7.23-7.31 (m, 1H, H_{Ar}), 7.37-7.45 (m, 1H, H_{Ar}), 7.55-7.59 (m, 1H, H_{Ar}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 13.7, 14.2, 39.3, 106.7, 108.8, 109.3, 117.3, 121.2, 127.3, 127.5, 127.7, 128.9, 143.7, 147.8, 149.7, 150.4, 152.5, 156.9; ms: *m/z* 309 (M^+, 100), 266 (96), 223 (37), 57 (25), 45 (28), 42 (48). *Anal.* Calcd. for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53. Found: C, 69.95; H, 4.73; N, 4.61.

2,4-Bis(5-methyl-2-thienyl)-4*H*-3,1-benzothiazine (8i). This compound was obtained according to the general method A in 45% yield as yellow solid (CH_2Cl_2–hexane), mp 76 °C; ir (potassium bromide): 1547, 1440, 1373, 1203, 1052, 894, 805, 761 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 2.37 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 5.47 (s, 1H, CH), 6.46 (d, J = 2.2 Hz, 1H, 4-H_{Th}), 6.52 (d, J = 2.2 Hz, 1H, 3-H_{Th}), 6.78 (d, J = 2.3 Hz, 1H, 4-H_{Th}), 7.17-7.20 (m, 1H, H_{Ar}), 7.24-7.29 (m, 1H, H_{Ar}), 7.37-7.42 (m, 1H, H_{Ar}), 7.48-7.51 (m, 1H, H_{Ar}), 7.55 (d, J = 2.3 Hz, 1H, 3-H_{Th}); ^{13}C nmr (50 MHz, deuteriochloroform): δ 15.4, 16.0, 41.8, 123.5, 124.8, 125.7, 126.3, 126.9, 127.3, 127.6, 128.8, 130.4, 140.3, 141.2, 142.5, 143.5, 146.3, 151.9; ms: *m/z* 341 (M^+, 100), 326 (57), 308 (37), 57 (17), 55 (16), 46 (17), 45 (29), 44 (48), 43 (38), 41 (16). *Anal.* Calcd. for $C_{18}H_{15}NS_3$: C, 63.31; H, 4.43; N, 4.10. Found: C, 63.42; H, 4.33; N, 4.04.

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[21] Crystal data of compound **8e**: $C_{20}H_{17}NO_4S$, triclinic, space group P-1; a = 8.311(2) Å, b = 10.194(2) Å, c = 11.232(2) Å, α = 90.02(3)°, β = 98.44(3)°, γ = 112.23(3)°, V = 869.7(3) Å^3, Z = 2, D_{calcd} = 1.403 Mg/m^3, F(000) = 384; 2894 reflections collected, 2249 unique (R_{int} = 0.0125); final R indices (2249 observed collections $I > 2\sigma I$): R_1 = 0.0280, wR_2 = 0.0793; final R indices (all data): R_1 = 0.0280, wR_2 = 0.0793. Crystallographic data (excluding structure factors) for the structure in this article have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 642230. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax; +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uc]. Each request should be accompanied by the complete citation of this paper.