Conjugated Compounds Based on Vinylthiazole Units

Herbert Meier, Frank Nicklas, and Ralf Petermann

Institute of Organic Chemistry, University of Mainz, Duesbergweg 10 – 14, 55099 Mainz, Germany

Reprint requests to Prof. Dr. H. Meier. Fax: 0049-(0)6131-3925396.
E-mail: hmeier@mail.uni-mainz.de

Z. Naturforsch. **2007**, *62b,* 1525 – 1529; received July 2, 2007

Conjugated compounds based on vinylthiazole units show a strong polarization along the π chain, when NR_2 groups as electron donors are attached in the terminal position. The effect can be even more enhanced by a CHO group as electron acceptor in the opposite terminal position. This property makes such oligomers (n = 1, 2, . . .) interesting for applications in linear and nonlinear optics.

Key words: Absorption, Conjugation, Fluorescence, Polarization, Push-pull Effect

Introduction

Conjugated oligomers attract increasing attention because of their interesting properties in materials science [1]. Moreover, they are model compounds for conjugated polymers. Molecules polarized by electronic effects, in particular push-pull systems having terminal donor-acceptor substitution represent a special class of such oligomers [2]. Their major applications are in the field of nonlinear optics (NLO), two-photon absorption (TPA), two-photon induced fluorescence (TPIF), and photorefractive materials (PR). Fig. 1 illustrates known 2,5-thienylenevinylenes with zwitterionic resonance structures **1** (D = NR_2; A = NO_2, CHO, SO_2R; n = 1, 2) [3, 4]. The corresponding compounds **2** with thiazole instead of thiophene rings are unknown.

On the whole, very few 1,2-di(thiazolyl)ethenes were reported. Among the three symmetric (2,2′; 4,4′; 5,5′) and the three unsymmetric (2,4′; 2,5′; 4,5′) linkings of two thiazole rings by a vinylene bridge, only one parent system, namely 1,2-di(2-thiazolyl)ethene has been described [5]. Whereas some derivatives of 1,2-di(4-thiazolyl)ethene [6 – 8], 1,2-di(5-thiazolyl)ethene [9 – 13] and 1-(2-thiazolyl)-2-(4′-thiazolyl)ethene [14] are known, 2,5′- and 4,5′-linkings are – to our best knowledge – unknown.

We report here on 1-(2-thiazolyl)-2-(5′-thiazolyl)ethenes (**2**). The electron donor D is represented by a dihexylamino group, the electron acceptor A can be a thiazole ring (**2a**) or an thiazol bearing a carbonyl group (**2b**).

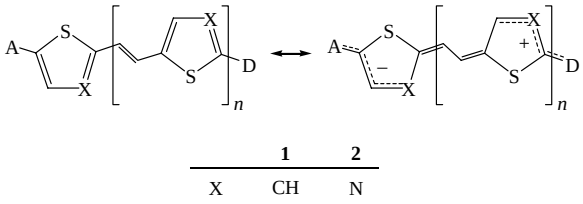


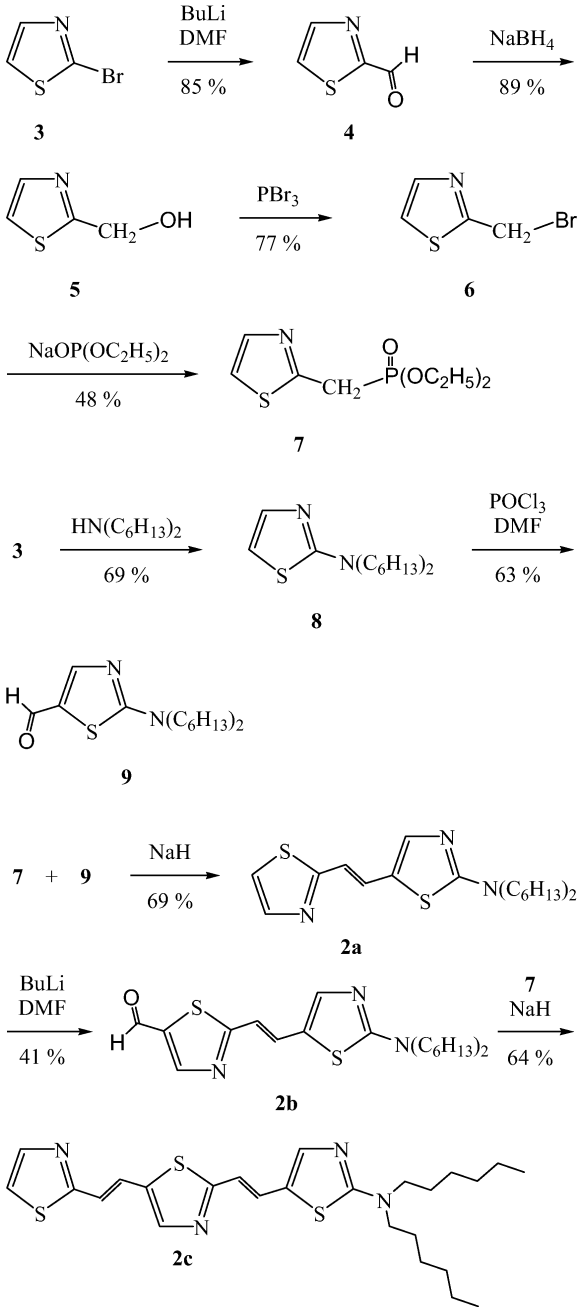
Fig. 1. Push-pull compounds with conjugated 2,5-thienylene-vinylene or thiazole-2,5-diylvinylene building blocks (n = 1, 2, . . .).

Results and Discussion

Scheme 1 shows the synthetic route to the target compounds **2a** – **c**. 2-Bromo-1,3-thiazole (**3**) was subjected to a Bouveault formylation to thiazole-2-carbaldehyde (**4**). Reduction of **4** with $NaBH_4$ yielded alcohol **5**, which was transformed with PBr_3 to 2-(bromomethyl)thiazole (**6**). The variant [15] of the Arbuzov reaction using $NaOP(OC_2H_5)_2$ afforded phosphonate **7**. The reaction of **6** with triethyl phosphite led to the formation of C_2H_5Br, which attacked the nitrogen atom of the thiazole ring and lowered the yield of **7**.

On the other side, thiazole **3** was reacted with dihexylamine to yield 2-dihexylaminothiazole (**8**) [16]. Vilsmeier formylation led to aldehyde **9**, which in a Wittig-Horner reaction with **7** gave the target compound **2a**. Formylation of **2a** with BuLi/DMF afforded the aldehyde **2b**. The reactivity in 5-position of the thiazole ring is much higher than in the two free 4-positions of both thiazole rings. The final step **2b** + **7** → **2c** was achieved by another Wittig-Horner reaction.

0932–0776 / 07 / 1200–1525 $ 06.00



Scheme 1. Preparation of the target compounds **2a**–**c**.

The *trans* selectivity of the double bond formation in a Wittig-Horner olefination is high. The ^{1}H NMR spectra of crude reaction mixtures showed only small amounts (≤ 5 %) of the *cis* isomers [17].

A full spectroscopic characterization of all compounds by FT IR, FD MS, and NMR data is given in the Experimental Section. The ^{1}H and ^{13}C chemical shifts of **2a** are shown as an example in Fig. 2.

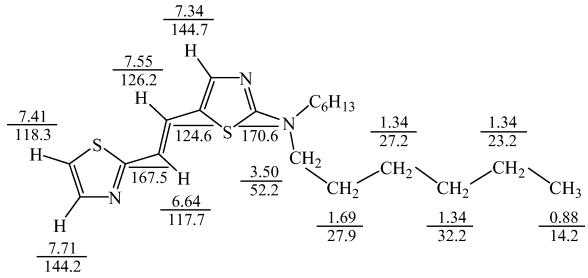


Fig. 2. ^{1}H and ^{13}C NMR data of **2a** (δ values in CD_3COCD_3, TMS as internal standard) [18]. The olefinic protons show a $^3J_{trans}$ coupling of 15.6 Hz. The AB spin system of the thiazole ring has a ^3J coupling constant of 3.2 Hz.

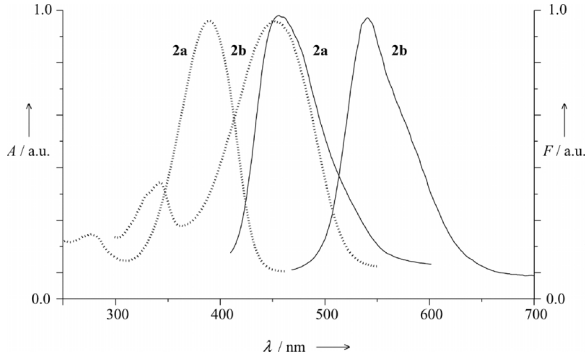


Fig. 3. Absorption (···) and fluorescence (—, normalized intensity) of **2a** and **2b** in CH_2Cl_2.

The polarization along the conjugated chains in compounds **2a**–**c** is revealed by the polarization of the olefinic C=C double bonds. The $\Delta\delta$ values of their ^{13}C chemical shifts provide a reliable indication for this effect [2]. We found for **2a** a $\Delta\delta$ value of 126.2 – 117.7 = 8.5 ppm. The strong push-pull effect in **2b** corresponds to $\Delta\delta$ = 14.1 ppm. The electron-releasing effect of the dihexylamino group is extended along the chain of the dimer **2c** as well; however, its decrease with increasing distance from the NR_2 group is documented by the fact, that the $\Delta\delta$ value for the olefinic double bond on the side of the amino group is much higher than on the other side, namely 10.1 compared to 1.3 ppm.

Formylation of **2c** on the outer, mono-substituted thiazole ring would lead again to a strong push-pull effect. We tried the conditions used for **2a** → **2b**, but **2c** yields a non-uniform product mixture.

Fig. 3 exhibits the absorption and emission spectra of **2a** and **2b**. The strong push-pull effect in **2b** shifts

Table 1. Comparison of the thiazole systems **2a – c** with the corresponding (*E*)-stilbenes having the same endgroups[a].

		Thiazole system **2** (this work)	Stilbenoid system [22, 23]
Absorption: λ_{max} (CH_2Cl_2)	**2a**	390	366
	2b	451	423
	2c	452	403
Chemical shift differences $\Delta\delta$ (in CD_3COCD_3) of the ^{13}C nuclei of the C=C double bonds	**2a**	8.5	6.4
	2b	14.1	10.6
	2c	10.1	6.8
		1.3	0.7

[a] λ in nm, δ in ppm.

the long-wavelength absorption maximum from 390 for **2a** to 451 nm and the fluorescence maximum from 458 to 540 nm. The extension of the conjugated chromophore in **2c** has almost the same effect. Dimer **2c** in CH_2Cl_2 has λ_{max} values of 452 nm (A) and 541 nm (F), respectively. The Stokes shift amounts to 3807, 3654 and 3640 cm^{-1} for **2a**, **2b** and **2c**.

Conclusions

The compounds **2a – c**, which consist of vinylthiazole building blocks, represent a new class of conjugated oligomers. Terminal dihexylamino groups as electron donors induce a polarization along the π chain, which can be further enhanced when a formyl group as electron acceptor is attached to the opposite terminal position. Compared to the corresponding oligo(1,4-phenylenevinylene)s [OPV], which contain benzene instead of thiazole rings but the same endgroups (D, A), **2a – c** exhibit red-shifted UV/vis absorptions. The polarization of the π chains in **2a – c** is stronger than in the corresponding OPVs, as indicated by the $\Delta\delta$ shift differences of the C=C double bonds. Table 1 summarizes this comparison. The extension of the conjugated chain in **2** from $n = 1, 2$ to higher numbers of repeat units ($n = 3, 4, \ldots$) will be of special interest for applications in materials science.

Experimental Section

FT-IR spectra were collected on a Perkin-Elmer GX/2000 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer. For FD MS and HRMS measurements a Finnigan MAT 95 spectrometer was used. The UV/vis and the fluorescence spectra were obtained on a Zeiss MCS 320/340 and a Perkin-Elmer LS 50 B spectrometer, respectively. The elemental analyses were performed in the microanalytical laboratory of the Chemistry Department of the University of Mainz.

*Thiazole-2-carbaldehyde (**4**)*

The preparation of **4** was performed according to the literature [19, 20]. Pale yellow oil, yield 85 % (lit. [19]: 88 %). – ^1H NMR ($CDCl_3$): δ = 7.75 (dd, ^3J = 2.9 Hz, ^6J = 1.0 Hz, 1H, 5-H), 8.12 (d, ^3J = 2.9 Hz, 1H, 4-H), 10.06 (d, ^6J = 1.0 Hz, 1H, CHO). – ^{13}C NMR ($CDCl_3$): δ = 126.3 (C-5), 145.8 (C-4), 166.2 (C-2), 183.9 (CHO).

*Thiazol-2-yl-methanol (**5**)*

The preparation was carried out according to the literature [5, 19]. Colorless solid, yield 89 % (lit. [19]: 81 %), m. p. 63 °C (lit. [19]: 66 – 67 °C). – ^1H NMR ($CDCl_3$): δ = 4.42 (br. s, 1H, OH), 4.91 (s, 2H, CH_2), 7.28 (d, ^3J = 3.0 Hz, 1H, 5-H), 7.67 (d, ^3J = 3.0 Hz, 1H, 4-H). – ^{13}C NMR ($CDCl_3$): δ = 61.7 (CH_2), 119.2 (C-5), 142.3 (C-4), 171.8 (C-1).

*2-Bromomethyl-thiazole (**6**)*

To a solution of **5** (1.06 g, 9.2 mmol) in $CHCl_3$ (8 mL), PBr_3 (0.29 mL, 0.835 g, 3.1 mmol) was carefully added. After 1 h refluxing, the mixture was treated with aqueous Na_2CO_3 solution till the precipitate initially formed was dissolved. The neutralized water phase was then extracted with $CHCl_3$ (2 × 25 mL). The organic layer was dried with $MgSO_4$ and evaporated. Filtration over a SiO_2 column (7 × 10 cm) with ethyl acetate yielded 1.27 g (77 %) of a light green-yellow oil. (It is advisable to use the compound directly for the next step, since it decomposes fast in the neat form. Storage in diluted solution in $CHCl_3$ in the refrigerator is possible.) [21]. – ^1H NMR ($CDCl_3$): δ = 4.74 (s, 2H, CH_2), 7.37 (d, ^3J = 2.9 Hz, 1H, 5-H), 7.74 (d, ^3J = 2.9 Hz, 1H, 4-H). – ^{13}C NMR ($CDCl_3$): δ = 26.4 (CH_2), 121.3 (C-5), 143.0 (C-4), 165.7 (C-2).

*Diethyl thiazol-2-ylmethylphosphonate (**7**)*

To NaH (60 %, 0.45 g, 11.2 mmol) in THF (37 mL), diethyl phosphite (1.55 g, 11.2 mmol) dissolved in THF (37 mL) was added dropwise within 5 min at 0 °C. After further 30 min stirring at this temperature, **6** (1.95 g, 10.9 mmol) dissolved in THF (8 mL) was added dropwise. After stirring overnight, the reaction was stopped by addition of crushed ice. Extraction with $CHCl_3$ (4 × 50 mL), drying ($MgSO_4$) and evaporation furnished a residue, which was purified by column chromatography (4 × 40 cm silica gel, ethyl acetate / ethanol 10 : 1). Viscous oil, yield 1.24 g (48 %). – FT IR (neat): ν = 3081, 2984, 2910, 1499, 1393, 1256, 1166, 1029, 971, 790, 764 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 1.27 (t, ^3J = 7.3 Hz, 6H, CH_3), 3.63 (d, ^2J (P,H) = 21.0 Hz, 2H, PCH_2), 4.10 (quint., ^3J (P,H) ≈ ^3J (H,H) = 7.3 Hz), 7.27 (dd, ^3J = 3.4 Hz, ^6J = 1.5 Hz, 1H, 5-H), 7.70 (d, ^3J = 3.4 Hz, 1H, 4-H). – ^{13}C NMR ($CDCl_3$): δ = 16.3 (d, ^3J (P,C) = 6.4 Hz, CH_3), 31.9 (d, ^1J (P,C) = 140.5 Hz, PCH_2),

62.7 (d, ^2J (P,C) = 6.4 Hz, OCH_2), 120.1 (d, ^5J (P,C) = 3.2 Hz, C-5), 142.3 (d, ^4J (P,C) = 3.2 Hz, C-4), 160.1 (d, ^2J (P,C) = 9.6 Hz, C-1). – FD MS: *m/z* (%) = 236 (100) $[M+H]^+$. – $C_8H_{14}NO_3PS$ (235.2): calcd. C 40.85, H 6.00, N 5.95, S 13.63; found C 40.63, H 6.12, N 6.15, S 13.78.

*N,N-Dihexyl-(thiazol-2-yl)-amine (**8**)*

Dihexylamine (6.90 g, 37.2 mmol), 2-bromothiazole (**3**) [24] (6.10 g, 37.2 mmol) and K_2CO_3 (1.03 g, 7.5 mmol) were refluxed in DMF (22 mL) for 10 h. Evaporation of the solvent in the vacuum led to a residue, which was washed with 75 mL of 10 % NaOH and extracted with diethyl ether (4 × 25 mL). The organic phase was dried with $MgSO_4$ and evaporated. Purification by column chromatography (4 × 45 cm, silica gel, ethyl acetate / petroleum ether (b. p. 40 – 70 °C) 1 : 20) yielded 6.90 g (69 %) of a colorless oil, which was identical with an authentic probe obtained by the reaction of dihexylthiourea and 2-chloro-1,1-dimethoxyethane [8].

*2-Dihexylamino-thiazole-5-carbaldehyde (**9**)*

The aldehyde **9** was prepared according to ref. [8]. Pale yellow oil; yield 63 % (lit. [8]: 63 %).

*N,N-Dihexyl-[5-((E)-2-thiazol-2-yl-vinyl)thiazol-2-yl]amine (**2a**)*

Phosphonate **7** (493 mg, 2.1 mmol) was treated in DME (4 mL) with NaH (60 %, 100 mg, 2.5 mmol). At the end of the evolution of H_2, aldehyde **9** (620 mg, 2.0 mmol) was added in DME (4 mL). After TLC control (silica gel, diethyl ether) had indicated the consumption of **9**, H_2O (50 mL) was slowly added. Extraction with diethyl ether (5 × 20 mL) gave an organic phase which was dried ($MgSO_4$) and evaporated. Purification by column chromatography (3 × 27 cm, Al_2O_3, petroleum ether (b. p. 40 – 70 °C) / ethyl acetate 8 : 1) yielded 520 mg (69 %) of a yellow oil. – FT IR (neat): ν = 2955, 2857, 1611, 1538, 1478, 1132, 936 cm^{-1}. – FD MS: *m/z* (%) = 378 (100) $[M+H]^+$. – HRMS: *m/z* = 377.1940 (calcd. 377.1946 for $C_{20}H_{31}N_3S_2$, $[M]^+$).

*2-[(E)-2-(2-Dihexylamino-thiazol-5-yl)vinyl]thiazole-5-carbaldehyde (**2b**)*

Compound **2a** (520 mg, 1.4 mmol), dissolved in dry THF (5 mL), was treated at −78 °C with 0.51 mL (1.38 mmol) of a 2.7 M solution of BuLi in *n*-heptane and then after about 40 min with 110 mg (1.5 mmol) DMF in dry THF (2.5 mL). Stirring was continued for 1 h at −78 °C and overnight at r. t. A saturated NH_4Cl solution was added to the mixture. Extraction with CH_2Cl_2 (4 × 30 mL) led to an organic phase which was dried with $MgSO_4$ and evaporated. Purification of the residue was achieved by column chromatography (4 × 24 cm, Al_2O_3, petroleum ether (b. p. 40 – 70 °C) / ethyl acetate 8 : 1). Yellow solid, yield 320 mg (41 %), m. p. 75 °C. – FT IR: ν = 3931, 2858, 1668, 1606, 1534, 1408, 1346, 1235, 1145, 953, 813 cm^{-1}. – ^{1}H NMR (CD_3COCD_3): δ = 0.88 (t, 6H, CH_3), 1.34 (m, 12H, CH_2), 1.70 (m, 4H, β-CH_2), 3.53 (m, 4H, α-CH_2), 6.67 (d, ^3J = 15.6 Hz, 1H, olefin. H, carbonyl side), 7.51 (s, 1H, 4-H, amino-substituted thiazole ring), 7.84 (d, ^3J = 15.6 Hz, 1H, olefin. H, amino side), 8.47 (s, 1H, 4-H, formyl-substituted thiazole ring), 10.01 (s, 1H, CHO). – ^{13}C NMR (CD_3COCD_3): δ = 14.2 (CH_3), 23.2, 27.2, 27.8, 32.2 (CH_2), 52.3 (NCH_2), 116.3 (olefin. CH, carbonyl side), 124.5 (C-5, amino-substituted thiazole ring), 130.4 (olefin. CH, amino side), 138.0 (C-5, formyl-substituted thiazole ring), 147.8 (C-4, formyl-substituted thiazole ring), 154.0 (C-4), 171.8 (C-2, amino-substituted thiazole ring), 174.6 (C-2), 183.0 (CHO). – FD MS: *m/z* (%) = 406 (100) $[M+H]^+$. – $C_{21}H_{31}N_3OS_2$ (405.6): calcd. C 62.18, H 7.70, N 10.36, S 15.81; found C 62.11, H 7.65, N 10.21, S 15.83.

*N,N-Dihexyl-(5-{(E)-2-[5-((E)-2-thiazol-2-yl-vinyl)thiazol-2-yl]vinyl}thiazol-2-yl)amine (**2c**)*

The preparation of **2c** was performed as discribed above for **2a**. Phosphonate **7** (74 mg, 0.31 mmol) and aldehyde **9** yielded after the described column chromatography 96 mg (64 %) of a viscous, yellow oil. – IR (neat): ν = 2927, 2865, 1714, 1601, 1537, 1424, 1334, 1231, 1133, 1079, 941, 717, 631 cm^{-1}. – ^{1}H NMR (CD_3COCD_3): δ = 0.88 (t, 6H, CH_3), 1.33 (m, 12H, CH_2), 1.68 (m, 4H, β-CH_2), 3.50 (t, 4H, NCH_2), 6.59/7.58 (AB, ^3J = 15.6 Hz, 2H, olefin. H, amino side), 7.05/7.69 (AB, ^3J = 15.6 Hz, 2H, olefin. H), 7.40 (s, 1H, 4-H, thiazole ring on the amino side), 7.53/7.81 (AB, ^3J = 3.1 Hz, 2H, terminal thiazole ring), 7.88 (s, 1H, 4-H, thiazole ring in the middle). – ^{13}C NMR (CD_3COCD_3): δ = 14.2 (CH_3), 23.2, 27.2, 27.9, 32.2 (CH_2), 52.3 (NCH_2), 117.4, 127.5 (olefin. CH, amino side), 119.9 (HC-5, terminal thiazole ring), 123.3, 124.6 (olefin. CH), 124.8 (C-5, amino substituted thiazole ring), 135.5 (C-5, middle thiazole ring), 144.7, 145.8, 146.1 (C-4 of thiazole rings), 166.3, 167.1, 171.0 (C-2 of thiazole rings). – FD MS: *m/z* (%) = 487 (100) $[M+H]^+$. – HRMS: *m/z* = 486.1944 (calcd. for $C_{25}H_{34}N_4S_3$: 486.1931 $[M]^+$).

Acknowledgement

We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

[1] Selected monographs and reviews: a) J. M. Tour, *Chem. Rev*. **1996**, *96*, 537 – 553; b) J. S. Moore, *Acc. Chem. Res*. **1997**, *30*, 402 – 413; c) L. Jones II, J. S Schumm, J. M. Tour, *J. Org. Chem*. **1997**, *62*, 1388 – 1410; d) J. Roncali, *Chem. Rev*. **1997**, *97*, 173 – 205; e) A. Kraft, A. C. Grimsdale, A. B. Holmes, *Angew. Chem*. **1998**, *110*, 416 – 443; *Angew. Chem. Int. Ed*. **1998**, *37*, 403 – 428; f) *Electronic Materials: The Oligomer Approach* (Eds.: K. Müllen, G. Wegner) Wiley-VCH, Weinheim, **1998**; g) T. M. Swager, *Acc. Chem. Res*. **1998**, *31*, 201 – 207; h) P. F. H. Schwab, M. D. Levin, J. Michl, *Chem. Rev*. **1999**, *99*, 1863 – 1933; i) U. Scherf, *Top. Curr. Chem*. **1999**, *201*, 163 – 222; j) R. E. Martin, F. Diederich, *Angew. Chem*. **1999**, *111*, 1440 – 1469; *Angew. Chem. Int. Ed*. **1999**, *38*, 1350 – 1377; k) J. J. Wolff, R. Wortmann, *Adv. Phys. Org. Chem*. **1999**, *32*, 121 – 217; l) U. H. F. Bunz, *Chem. Rev*. **2000**, *100*, 1605 – 1644; m) J. L. Segura, N. Martin, *J. Mater. Chem*. **2000**, *10*, 2403 – 2435; n) J. Roncali, *Acc. Chem. Res*. **2000**, *33*, 147 – 156; o) J. M. Tour, *Acc. Chem. Res*. **2000**, *33*, 791 – 804; p) U. H. F. Bunz, *Acc. Chem. Res*. **2001**, *34*, 998 – 1010; q) S. Tretiak, S. Mukamel, *Chem. Rev*. **2002**, *102*, 3171 – 3212; r) S. Szafert, J. A. Gladysz, *Chem. Rev*. **2003**, *103*, 4175 – 4205; s) H. Meier in *Carbon-Rich Compounds*: (Eds.: M. M. Haley, R. R. Tykwinski), Wiley-VCH, Weinheim, **2006**, pp. 476 – 528.

[2] H. Meier, *Angew. Chem*. **2005**, *117*, 2536 – 2561; *Angew. Chem. Int. Ed*. **2005**, *44*, 2482 – 2506 and refs. cited therein.

[3] V. P. Rao, A. K.-Y. Jen, K. Y. Wong, K. J. Drost, *Tetrahedron Lett*. **1993**, *34*, 1747 – 1750.

[4] S.-S. P. Chou, D.-J. Sun, J.-Y. Huang, P.-K. Yang, H.-C. Lin, *Tetrahedron Lett*. **1996**, *37*, 7279 – 7282.

[5] A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *Tetrahedron* **1988**, *44*, 2021 – 2031.

[6] A. Silberg, M. Ruse, E. Hamburg, I. Cîrdan, *Chem. Ber*. **1969**, *102*, 423 – 426.

[7] A. Gellis, P. Vanelle, M. Kaafarani, K. Benakli, M. P. Crozet, *Tetrahedron* **1997**, *53*, 5471 – 5484.

[8] H. Meier, R. Petermann, *Helv. Chim. Acta* **2004**, *87*, 1109 – 1118.

[9] S. Iwata, Y. Ishihara, C.-P. Qian, K. Tanaka, *J. Org. Chem*. **1992**, *57*, 3726 – 3227.

[10] K. Uchida, T. Ishikawa, M. Takeshita, M. Irie, *Tetrahedron* **1998**, *54*, 6627 – 6638.

[11] T. Nussbaumer, C. Krieger, R. Neidlein, *Eur. J. Org. Chem*. **2000**, 2449 – 2457.

[12] T. Nussbaumer, R. Neidlein, *Helv. Chim. Acta* **2000**, *83*, 1161 – 1167.

[13] M. Giraud, A. Leaustic, M.-F. Charlot, P. Yu, M. Cesario, C. Philouze, R. Pansu, K. Nakatani, E. Ishow, *New J. Chem*. **2005**, *29*, 439 – 446.

[14] M. C. Bagley, J. W. Dale, R. L. Jenkins, J. Bower, *Chem. Commun*. **2004**, 102 – 103.

[15] See for example: S. D. Taylor, C. C. Kotoris, A. N. Dinaut, M. J. Chen, *Tetrahedron* **1998**, *54*, 1691 – 1714.

[16] The attempt to synthesize **8** by the reaction of thiazol-2-yl-amine with 1-bromohexane failed, because hexyl-[3-hexyl-3*H*-thiazol-2-ylidene]amine was obtained. The single alkylation of both nitrogen atoms of thiazol-2-yl-amine is preferred in comparison to the double alkylation of the NH_2 groups.

[17] When crude **2a** was used for the formylation, 5 % (*Z*)-configurated **2b** was formed and could be enriched by column chromatography (Al_2O_3, petroleum ether (40 – 70 °C) / ethyl acetate 8 : 1). (*Z*)-**2b** has the following ^{1}H NMR data in CD_3COCD_3: δ = 0.88 (t, 6H, CH_3), 1.34 (m, 12H, CH_2), 1.70 (m, 4H, β-CH_2), 3.53 (t, 4H, α-CH_2), 6.30/6.97 (AB, ^3J = 12.2 Hz, olefin. H), 7.67 (s, 1H, 4-H), 8.56 (s, 1H, 4′-H), 10.04 (s, 1H, CHO).

[18] Correlation based on 2D measurements (COSY, HMQC).

[19] A. Dondoni, D. Perrone, *J. Org. Chem*. **1995**, *60*, 4749 – 4754.

[20] P. E. Iversen, H. Lund, *Acta Chem. Scand*. **1966**, *20*, 2649 – 2657.

[21] For an alternative preparation of **6** by NBS bromination of 2-methylthiazole see: L. Yang, G. Moriello, K. Leung, T. Jacks, K. Cheng, K. D. Schleim, R. Smith, A. A. Patchett, *Bioorg. Med. Chem. Lett*. **1999**, *9*, 1761 – 1766; *Chem. Abstr*. **1999**, *131*, 193714r.

[22] G. P. Bartholomev, M. Rumi, S. J. K. Pond, J. W. Perry, S. Tretiak, G. C. Bazan, *J. Am. Chem. Soc*. **2004**, *126*, 11529 – 11542.

[23] H. Meier, J. Gerold, H. Kolshorn, B. Mühling, *Chem. Eur. J*. **2004**, *10*, 360.

[24] Commercially avaliable.