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Pyridine-Substituted Hydroxythiophenes. III. Dimerization of 3-(2-Pyridyl)thiophen-2(5*H*)-one from the Demethylation Reaction of 2-Methoxy-3-(2-pyridyl)thiophene. X-Ray Structure Determination of (±)-(3*R**, 4*S**)-3-(2-Pyridyl)-4-[2-oxo-3-(1,2-dihydropyridin-2-ylidene)-2,3-dihydrothiophen-5-yl]-4,5-dihydrothiophen-2(3*H*)-one

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The demethylation of 2-methoxy-3-(2-pyridyl)thiophene with chlorotrimethylsilane–sodium iodide in refluxing acetonitrile or with boron tribromide in dichloromethane at ambient temperature led to the formation of (±)-(3*R**, 4*S**)-3-(2-pyridyl)-4-[2-oxo-3-(1,2-dihydropyridin-2-ylidene)-2,3-dihydrothiophen-5-yl]-4,5-dihydrothiophen-2(3*H*)-one. A possible mechanism by which the compound is formed is proposed. The structure of the compound has been established by X-ray crystallography.

Aromatic *O*-dealkylation is a synthetically very useful reaction. Therefore, demethylation of methoxythiophenes prepared by a direct ring closure reaction or other approaches, may – in certain cases – offer a preparatively valuable route to hydroxythiophenes and their related compounds.[1–6] In connection with a study of *O*-pyridyl-3-hydroxythiophenes,[7] we have recently investigated the preparation of 3-(2-pyridyl)-2-hydroxythiophene.

Results and discussion

Attempts to prepare 3-(2-pyridyl)-2-hydroxythiophene (**1**) by the demethylation of 2-methoxy-3-(2-pyridyl)thiophene (**2**) with chlorotrimethylsilane–sodium iodide in refluxing acetonitrile as shown in Scheme 1 or with boron tribromide in dichloromethane at ambient temperature led to the formation of (3*R**, 4*S**)-3-(2-pyridyl)-4-[2-oxo-3-(1,2-dihydropyridin-2-ylidene)-2,3-dihydrothiophen-5-yl]-4,5-dihydrothiophen-2(3*H*)-one (±**4**). Compound **2** was synthesized by Pd(0) catalyzed cross-coupling of 2-bromopyridine with 2-methoxy-2-trimethylstannylthiophene (**3**) derived from 2-methoxythiophene via 3,5-dibromo- and 3-bromo-2-methoxy-thiophene (*cf.* Scheme 1).[8]

It is suggested that compound **4** arises from the dimerization of 3-(2-pyridyl)thiophen-2(5*H*)-one (**5**), a tautomeric isomer of **1**, through base-catalyzed Michael addition followed by tautomerization (Scheme 2). The formation of the dimer following the base-catalyzed Michael addition (the silyl ether was hydrolyzed with aqueous sodium carbonate) may be rationalized by the presence of the acidic methylene proton in the 5-position of compound **5**. It is known that 5-alkyl substituted thiophene-2(5*H*)-ones can undergo base-catalyzed Michael addition to form dimers **6** and **7**.[9] Jakobsen and Lawesson have also isolated a dimer **8** from 3-ethoxycarbonyl-2-hydroxythiophene.[10] In this case dimerization occurred spontaneously at room temperature or under the influence of trifluoroacetic acid.[10] For this compound, the most stable form is the enol form and the thiophene structure is thus imposed on the unsaturated ring. It is interesting to observe that in the dimerization of **5**, compound **9**, structurally similar to **8**, was not detected. It seems likely that **4** is thermodynamically more stable than **9**.

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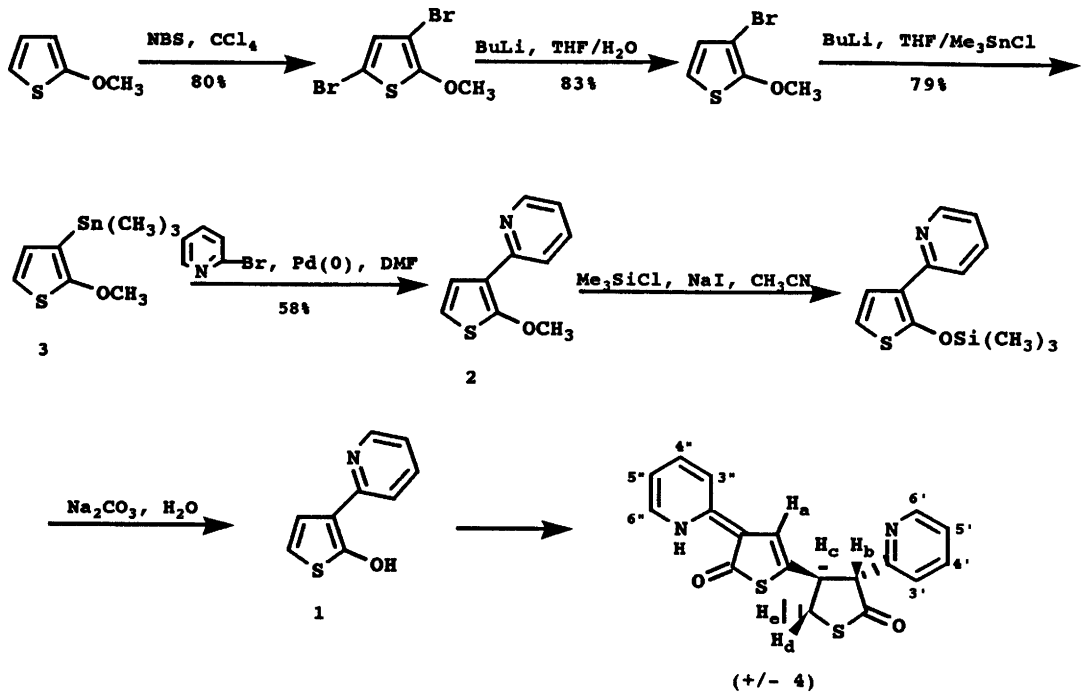
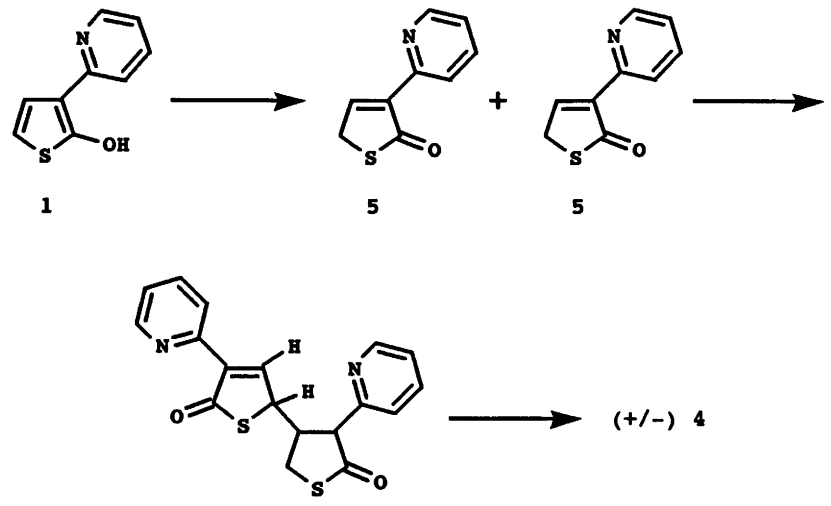
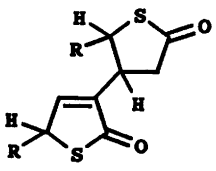


Scheme 1. The yield of the last three steps is 52%.

The structure determination of **4** was based on the following spectroscopic and X-ray investigations. The high resolution mass spectrum showed the formula $C_{18}H_{14}N_2O_2S_2$, in agreement with that of the dimer of **5**. The absorptions at 1680 cm^{-1} and 1625 cm^{-1} in the IR spectrum indicated that the compound had two carbonyl groups with the second one shifting toward lower frequency probably due to conjugation of β,γ-unsaturated γ-thiobutyrolactone ring with the cycloenamine ring, and to hydrogen bonding between the oxygen of carbonyl and the hydrogen on the nitrogen in the cycloenamine ring. Unexpectedly, there is no absorption due to this hydrogen in the IR spectrum, probably due to the hydrogen bonding. However, in the ^1H NMR spectrum of **4** a broad band (δ 1.35–1.80) centered at δ 1.58 was observed, which disappeared upon the addition of deuteriated water. Furthermore, the doublet at δ 6.49 with a splitting of 0.75 Hz indicated that the proton H_a on the β,γ-unsaturated γ-thiobutyrolactone ring couples with the allylic proton H_c on the saturated γ-thiobutyrolactone ring. The signals appearing in the aliphatic region at δ 4.38–3.55 are due to protons H_b, H_c, H_d and H_e on the saturated γ-thiobutyrolactone ring. A doublet with a splitting of 11.5 Hz at δ 3.93 is due to proton H_b, which



Scheme 2.



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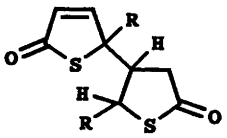

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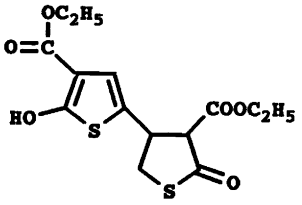
a R = $C(CH_3)_3$

b R = CH_3



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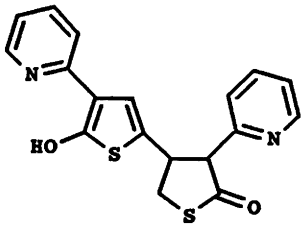

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couples with proton H_c. The band at δ 4.32–4.38 consists of eight pairs of doublets but as two of the coupling constants had the same value the number of lines was reduced to twelve. This absorption was assigned to proton H_c. The signals due to two protons appearing at δ 3.53–3.64 are absorptions from protons H_e and H_d. However, exact assignment for H_e and H_d could not be achieved from the ^1H NMR spectrum. The pyridinic proton H6′ gives a band at δ 8.60 and the splitting pattern is four pairs of doublets. The band at δ 7.69 with a similar splitting pattern is due to proton H6′′ on the cycloenamine ring. Another isolated signal at δ 6.75 is assigned to proton H5′′. The two multiplets at δ 7.60–7.61 and 7.12–7.18 are due to the other pyridinic protons and the protons on the cycloenamine ring; these signals overlapped. The integrations and a ^1H–^1H COSY experiment indicated that one multiplet is attributed to the two protons H4′, and H4′′, the other to the three protons H3′, H3′′ and H5′. However, better separation of these superimposed resonances was achieved by 500 MHz ^1H NMR spectroscopy. Thus, the signals at δ 7.12, 7.17 and 7.18 were assigned to the protons H3′′, H5′ and H3′, respectively, while the signals at δ 7.60 and 7.61 are due to protons H4′ and H4′′, respectively.

The ^{13}C spectrum of compound **4** provided further information for the structure determination. It showed six lines at δ 187.45, 155.96, 149.70, 123.39, 102.69 and 102.68 due to quaternary carbon atoms. Those with the largest δ values belong to the two carbonyl carbon atoms. The shift difference is probably due to the hydrogen bonding mentioned above in connection with the interpretation of the IR spectrum. Signals due to the other twelve carbon atoms in compound **4** were also observed in the ^{13}C spectrum (cf. Experimental).

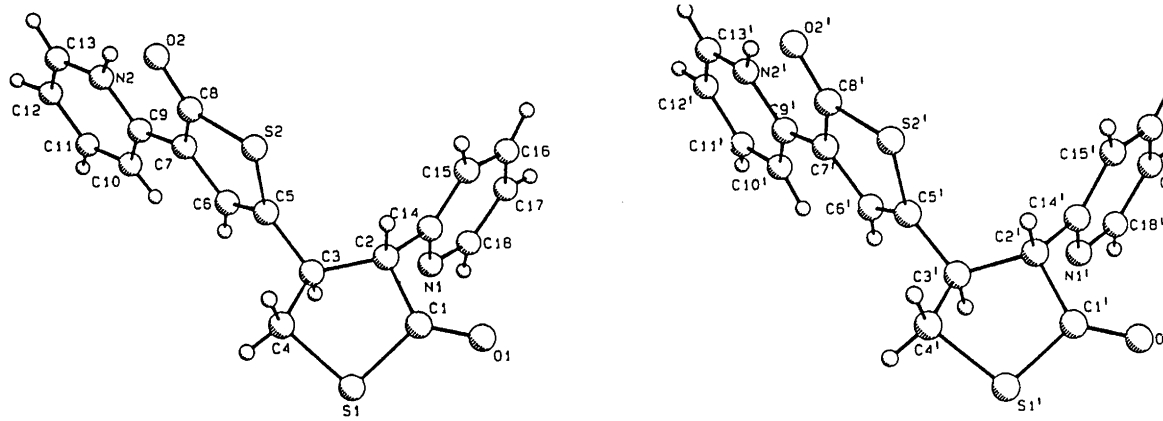

Fig. 1. Perspective view of the two independent molecules with the numbering scheme.

In order to confirm the structure and to determine the stereochemistry of **4**, an X-ray crystallographic investigation was carried out. The two independent molecules in the asymmetric unit, shown in Fig. 1, have the same configuration. They show, however, somewhat different conformations of the saturated γ-thiobutyrolactone, one is a twist (primed) and the other is close to a half-chair (Fig. 2). Details of the structure determination are given in the Experimental section and fractional atomic coordinates and equivalent isotropic temperature factors for the non-hydrogen atoms are given in Table 1. Selected bond distances, angles and torsion angles are presented in Table 2. The bond distances of two carbonyl groups (C = O) in the saturated and the unsaturated γ-thiobutyrolactone rings are 1.200(5) Å and 1.263(5) Å for the twist conformer, 1.203(5) Å and 1.253(5) Å for the half-chair conformer, respectively. The differences in the two types of bond distance of C = O for each conformer are 0.063 Å and 0.050 Å, respectively. The bond distance C(7) = C(9) of 1.143(6) Å/1.411(6) Å is slightly larger than normal sp^2–sp^2 C = C double bond distance,[11] while the bond distance C(7)–C(8) of 1.405(6) Å/1.406 Å is somewhat smaller than for a normal single bond between two sp^3 hybridized carbons.[12] These phenomena for the bond distances can be explained by the fact that in the two independent molecules, the unsaturated γ-thiobutyrolactone ring and the cycloenamine ring are coplanar with maximum deviations of 0.05 Å and 0.04 Å, respectively, from the least-squares planes. The ring system is stabilized by hydrogen bonds N–H···O with N–O distances of 2.655(5) Å/2.673(5) Å and angles N–H···O of 147(4)/144(3)° for the two conformers. The different values of the angles of C(9)–N(2)–C(13) [123.7(5)/124.8(5)°] and C(14)–N(1)–C(18) [116.6(5)°] clearly show two different nitrogen-containing moieties in compound **4**, while these two moieties in compound **9** should be very similar. The most important information obtained from X-ray crystallography is the configuration of the saturated γ-thiobutyrolactone ring. When examining the saturated γ-thiobutyrolactone ring, the unsaturated γ-thiobutyrolactone ring with the cyclic enamine part is *trans* to the pyridine ring. Consequently, the same is true for the protons H_b and H_c which have an NMR coupling constant of 11.5 Hz. For most of the five-membered rings studied, it has been possible to determine only the sum of *cis* and *trans* coupling constants. In a few cases, the coupling constants have been determined individually. Abraham and Thomas[13] have found that in dihydro-thiophene and -furan, the cou-

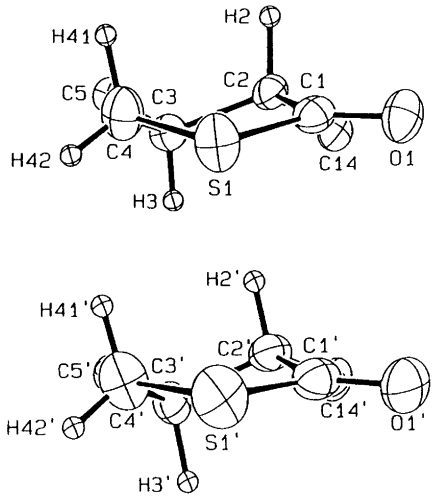

Fig. 2. Perspective drawing of the saturated γ-butyrolactone ring in the two molecules with thermal ellipsoids of vibration (35% probability).

Table 1. Fractional atomic coordinates and *B*(eq) for the non-hydrogen atoms in compound **4** with estimated standard deviations in parentheses.

Atom	*x*	*y*	*z*	*B*(eq)
S(1)	0.6154(1)	−0.1619(1)	−0.07443(9)	4.88(6)
S(2)	0.7910(1)	0.0797(1)	0.24554(8)	3.83(5)
O(1)	0.6728(3)	−0.3828(3)	−0.0562(2)	4.5(1)
O(2)	0.8912(3)	0.2957(3)	0.3881(2)	4.3(1)
N(1)	0.9845(4)	−0.2451(4)	0.0182(3)	4.9(2)
N(2)	1.1025(4)	0.4555(4)	0.3741(3)	3.6(2)
C(1)	0.6914(4)	−0.2645(5)	−0.0234(3)	3.4(2)
C(2)	0.7829(4)	−0.1831(4)	0.0641(3)	2.9(2)
C(3)	0.8128(5)	−0.0417(5)	0.0634(3)	3.5(2)
C(4)	0.6855(6)	−0.0135(5)	0.0185(4)	4.7(2)
C(5)	0.8697(4)	0.0639(4)	0.1524(3)	2.9(2)
C(6)	0.9725(5)	0.1609(5)	0.1696(3)	3.3(2)
C(7)	0.9968(4)	0.2576(4)	0.2575(3)	2.8(2)
C(8)	0.9029(5)	0.2299(4)	0.3094(3)	3.3(2)
C(9)	1.0961(4)	0.3723(4)	0.2893(3)	3.0(2)
C(10)	1.1885(5)	0.4111(5)	0.2408(4)	3.8(2)
C(11)	1.2784(5)	0.5250(6)	0.2784(4)	4.8(2)
C(12)	1.2791(6)	0.6058(6)	0.3645(4)	5.0(2)
C(13)	1.1919(6)	0.5693(5)	0.4117(4)	4.6(2)
C(14)	0.9030(4)	−0.2463(4)	0.0764(3)	3.0(2)
C(15)	0.9228(6)	−0.3032(5)	0.1405(4)	4.4(2)
C(16)	1.0319(7)	−0.3668(6)	0.1448(5)	6.0(3)
C(17)	1.1155(6)	−0.3663(6)	0.0857(5)	5.7(3)
C(18)	1.0897(6)	−0.3062(6)	0.0243(5)	5.7(3)
S(1′)	−0.4691(2)	−0.3477(1)	−0.4213(1)	6.06(7)
S(2′)	−0.4017(1)	0.0824(1)	−0.18436(8)	4.06(5)
O(1′)	−0.2378(4)	−0.2984(4)	−0.4710(2)	6.2(2)
O(2′)	−0.4552(3)	0.3062(3)	−0.0762(2)	4.0(1)
N(1′)	−0.2623(4)	−0.0024(4)	−0.4758(3)	4.5(2)
N(2′)	−0.5940(4)	0.4470(4)	−0.1509(3)	3.3(2)
C(1′)	−0.3185(6)	−0.2525(5)	−0.4274(3)	4.5(2)
C(2′)	−0.3074(5)	−0.1089(5)	−0.3678(3)	3.8(2)
C(3′)	−0.4499(5)	−0.0848(4)	−0.3655(3)	3.6(2)
C(4′)	−0.5265(6)	−0.2067(5)	−0.3515(4)	5.1(2)
C(5′)	−0.4659(5)	0.0421(4)	−0.2981(3)	3.3(2)
C(6′)	−0.5322(5)	0.1331(5)	−0.3124(3)	3.1(2)
C(7′)	−0.5378(4)	0.2425(4)	−0.2340(3)	2.7(2)
C(8′)	−0.4695(4)	0.2309(4)	−0.1557(3)	3.1(2)
C(9′)	−0.6005(4)	0.3518(4)	−0.2323(3)	2.9(2)
C(10′)	−0.6695(5)	0.3753(5)	−0.3054(3)	3.8(2)
C(11′)	−0.7233(6)	0.4870(6)	−0.2932(4)	5.3(3)
C(12′)	−0.7121(6)	0.5808(6)	0.2084(4)	5.1(2)
C(13′)	−0.6459(5)	0.5579(5)	−0.1384(4)	4.3(2)
C(14′)	−0.2188(5)	−0.0162(4)	−0.3975(3)	3.5(2)
C(15′)	−0.0958(6)	0.0500(6)	−0.3466(4)	5.1(2)
C(16′)	−0.0162(7)	0.1299(6)	−0.3796(5)	5.9(3)
C(17′)	−0.0592(7)	0.1444(6)	−0.4587(5)	5.3(3)
C(18′)	−0.1808(7)	0.0799(6)	−0.5038(4)	5.2(3)

Table 2. Selected bonds lengths (Å), angles (°) and torsion angles (°) in **4**. Standard deviations in parentheses.

	Unprimed molecules	Primed molecules
S1–C1	1.769(5)	1.776(6)
S1–C4	1.804(6)	1.800(6)
C1–O1	1.200(5)	1.203(5)
C1–C2	1.523(6)	1.527(6)
C2–C3	1.522(6)	1.525(6)
C2–C14	1.508(6)	1.490(6)
C3–C4	1.529(7)	1.537(7)
C3–C5	1.510(6)	1.498(6)
C1–S1–C4	93.1(3)	93.7(3)
S1–C1–C2	111.5(4)	109.5(5)
C1–C2–C3	106.8(4)	105.8(5)
C2–C3–C4	106.9(5)	105.7(5)
C3–C4–S1	105.7(5)	106.8(5)
S1–C1–C2–C3	−17.9(4)	−29.0(5)
S1–C1–C2–C14	−144.3(3)	−156.0(3)
S1–C4–C3–C2	−40.4(5)	−41.2(5)
S1–C4–C3–C5	−169.4(3)	−168.2(4)
C1–S1–C4–C3	26.1(4)	21.2(4)
C1–C2–C3–C4	37.1(5)	44.5(5)
C1–C2–C3–C5	163.4(4)	169.5(4)
C2–C1–S1–C4	−4.9(4)	4.4(4)
C4–C3–C2–C14	160.4(4)	169.5(4)

pling constants are 10.0 Hz and 7.5 Hz, and 10.7 Hz and 8.3 Hz, respectively. Unfortunately, their interpretation did not indicate which values are due to the *cis* and which are due to the *trans* couplings. In compound **4**, the dihedral angles H_b–C3–C4–H_c, H_c–C4–C5–H_d and H_c–C4–C5–H_e[†] are observed to be 167(3)/180(3)°, 171(3)/175(3)° and 41(4)/45(4)° for twist/half-chair conformers. According to the Karplus equation,[14] a coupling constant of 11.5 Hz between H_b and H_c *trans* to each other should be reasonable. Furthermore, a coupling constant of 10.95 Hz between protons H_c and H_d *trans* to each other and a coupling constant of 6.5 Hz between protons H_c and H_e *cis* to each other should be explicable. The sum of J_{cd} and J_{ce}, 17.45 Hz, is in excellent agreement with the value (17.50 Hz) of $J_{cis}+J_{trans}$ obtained from dihydrothiophene.[13] Thus, we could safely assign the signal at δ 3.63 to proton H_e and the signal at δ 3.55 to proton H_d. Coupling constants of the same magnitude between *vicinal* protons were also observed in structurally similar compounds such as 3-pyridyl-4,5-dihydrothiophen-2(3*H*)-ones obtained from demethylation of 2-methoxy-3-pyridylthiophenes with phenyl methaneselenolate.[15] ^{1}H NMR spectroscopy showed that the difference in the chemical shifts between protons H4 and H5 in compounds **2** and **3**, 0.9 ppm and 0.3 ppm, respectively, is too small to give definite assignments for them. HETCOR experiments were therefore performed. In the case of compound **2**, the spectrum showed that the ^{13}C shifts at δ 126.95 and 110.38 interacted with the proton signals at δ 7.53 and 6.63. In the ^{1}H-coupled ^{13}C spectrum, the carbon resonance at δ 126.95 showed a splitting of 170.10 Hz and that at δ 110.38, 189.80 Hz. These values fall in the region characteristic for β-CH and α-CH coupling constants in thiophenes.[16] Thus, the signal at δ 7.53 in the proton spectrum was assigned to the proton in the 4-position and the signal at δ 6.63 to that in 5-position. When the same experiment was performed for compound **3**, the δ-values 6.77 and 6.74 were assigned to the protons in the 4- and 5-positions, respectively. The ^{13}C shifts for these positions were δ 130.30 and 113.38, and the coupling constants 166.55 Hz and 189.95 Hz, respectively.

[†] In Fig. 2 these angles are given as H(2)–C(2)–C(3)–H(3), H(3)–C(3)–C(4)–H(41) and H(3)–C(3)–C(4)–H(42), respectively.

Experimental

Melting points are uncorrected. IR spectra were recorded on a Perkin Elmer 298 spectrophotometer. The NMR spectra (^{1}H, ^{13}C, HETCOR, COSY) were recorded on a Varian XL 300 spectrometer and on a Bruker ARX 500 spectrometer. The high resolution mass spectrum was recorded on a JEOL JMS-SX 102 spectrometer. GLC analyses were carried out on a Varian 1400 gas chromatograph using an OV-17 (3%, 2 m) column. Elemental microanalyses were performed at Dornis und Kolbe, *Mikroanalytisches Laboratorium*, Mülheim a.d. Ruhr, Germany.

*2-Methoxy-3-trimethylstannylthiophene (**3**).* To a stirred solution of 3-bromo-2-methoxythiophene[8] (8.00 g, 41.5 mmol) in anhydrous diethyl ether (40 ml) at −70°C under nitrogen butyllithium (20 ml, 2.06 M in hexane) was added dropwise at such a rate that the temperature did not exceed −70°C. The solution was stirred at the same temperature for 30 min, whereupon trimethylstannyl chloride (9.10 g, 45.6 mmol) dissolved in 50 ml of anhydrous diethyl ether was added dropwise at such a rate that the temperature did not exceed −70°C, and then the reaction mixture was allowed slowly to warm to ambient temperature. Water was added and the phases were separated. The aqueous phase was extracted with diethyl ether, the combined ether phases were washed with water and dried over anhydrous sodium sulfate and evaporated. Distillation of the residue under reduced pressure gave 9.1 g (79%) of the title compound, b.p. 65–66/0.8 mmHg. Anal. $C_8H_{14}OSSn$: C, H, S. ^{1}H NMR ($CDCl_3$): δ 0.28 [s, 9 H, $Sn(CH_3)_3$], 3.89 (s, 3 H, OCH_3), 6.71 (d, 1 H, H5, *J* 5.45 Hz), 6.74 (d, 1 H, H4, *J* 5.45 Hz). ^{13}C NMR ($CDCl_3$): δ −9.01 [$Sn(CH_3)_3$], 61.99 (OCH_3), 113.38 (C5), 116.09 (C3), 130.29 (C4), 170.52 (C2).

*2-Methoxy-3-(2-pyridyl)thiophene (**2**).* A 250 ml three-necked flask, equipped with condenser, magnetic stirring bar and nitrogen inlet, was charged with 2-bromopyridine (1.58 g, 10.0 mmol), 2-methoxy-3-trimethylstannyl-

thiophene (**3**) (3.05 g, 11.0 mmol), tetrakis(triphenylphosphine)palladium (0.95 g, 0.50 mmol) and DMF (70 ml). The mixture was vigorously stirred under nitrogen at 100°C for 35 h and monitored by GLC. After being cooled to ambient temperature, the mixture was evaporated, and diethyl ether (100 ml) was added to the residue. The precipitate was filtered off, and the filtrate was washed with water and dried over anhydrous sodium sulfate. After evaporation, the residue was purified by chromatography on a Silica Gel 60 column using petroleum ether (b.p. 60–70°C)–ethyl acetate (7:3) as the eluent to give 1.11 g (58%) of the title compound as an oil. Anal. $C_{10}H_9NOS$: C, H, N. ^{1}H NMR ($CDCl_3$): δ 4.05 (s, 3 H, OCH_3), 6.63 (d, 1 H, H5, *J* 5.94 Hz), 7.10 (ddd, 1 H, H5′, *J* 7.46, 4.88, 1.17 Hz), 7.53 (d, 1 H, H4, *J* 5.94 Hz), 7.67 (ddd, 1 H, H4′, *J* 8.09, 7.46, 1.88 Hz), 7.91 (ddd, 1 H, H3′, *J* 8.09, 1.17, 1.07 Hz), 8.60 (ddd, 1 H, H6′, *J* 4.88, 1.88, 1.07 Hz). MS: *m/z* 191 (M^+), 162, 148, 104, 78. ^{13}C NMR ($CDCl_3$): δ 163.95 (C2), 153.09 (C2′), 149.19 (C6′), 136.19 (C4′), 126.95 (C4), 122.01 (C3′), 120.75 (C3), 120.75 (C5′), 110.38 (C5), 61.74 (OCH_3).

(3R, 4S*)-3-(2-Pyridyl)-4-[2-oxo-3-(1,2-dihydropyridin-2-ylidene)-2,3-dihydrothiophen-5-yl]-4,5-dihydrothiophen-2(3H)-one (±* **4**). *Method A*. To a stirred solution of 2-methoxy-3-(2-pyridyl)thiophene (**2**) (191 mg, 1.0 mmol), sodium iodide (330 mg, 2.2 mmol) in acetonitrile (2.0 ml) was added chlorotrimethylsilane (239 mg, 2.2 mmol) dropwise with a syringe under nitrogen at ambient temperature. The mixture was refluxed for 24 h and monitored by GLC and then allowed to reach ambient temperature. An aqueous solution of sodium carbonate (1.0 M) was added to make the mixture alkaline (pH 7–8). The mixture was stirred for 30 min and then extracted with dichloromethane. The combined dichloromethane phases were washed with water and saturated sodium chloride solution and dried over anhydrous sodium sulfate. After evaporation, the residue obtained was flash chromatographed on a Silica Gel 60 column using dichloromethane–methanol (99:1) as the eluent and purified further by recrystallization from methanol to afford 92.1 mg (52%), m.p. 203–205°C. Peak matching on M^+. Calc. for $C_{18}H_{14}N_2O_2S_2$: 354.0497. Found: 354.0496. IR spectrum (KBr): 1625 (C=O), 1680 cm^{-1} (C=O). MS: *m/z* 354 (M^+), 177, 148, 104, 78. ^{1}H NMR ($CDCl_3$): δ 1.58 (br, 1 H, NH, disappeared after addition of deuterium oxide), 3.55 (t, 1 H, H_d, *J* 10.95, 10.95 Hz), 3.63 (dd, 1 H, H_e, *J* 11.15, 6.50 Hz), 3.93 (d, 1 H, H_b, 11.55 Hz), 4.35 (tdd, 1 H, H_c, *J* 10.95, 10.95, 6.50, 0.75 Hz), 6.49 (d, 1 H, H_a, *J* 0.75 Hz), 6.75 (ddd, 1 H, H5″, *J* 7.05, 6.15, 1.10 Hz), 7.12 (dt, 1 H, H3″, *J* 8.90, 1.00, 1.00 Hz), 7.17 (ddd, 1 H, H5′, *J* 7.60, 4.80, 1.15 Hz), 7.18 (dt, 1 H, H3′, *J* 7.80, 1.00, 1.00 Hz), 7.60 (td, 1 H, H4′, *J* 7.65, 7.65, 1.85 Hz), 7.61 (ddd, 1 H, H4″, *J* 8.90, 7.10, 1.60 Hz), 7.69 (ddd, 1 H, H6″, *J* 6.20, 1.55, 0.95 Hz), 8.60 (ddd, 1 H, H6′, *J* 4.80, 1.80, 0.95 Hz). ^{13}C NMR ($CDCl_3$): δ 36.60, 47.66, 77.22, 102.68, 102.69, 114.09, 116.57, 119.33, 122.60, 123.39, 125.27, 134.65, 136.67, 139.97, 149.70, 149.89, 155.96, 187.45.

Method B. The same procedure as described for method A was carried out except that the silyl ether was hydrolyzed with water (1 h at ambient temperature). A result similar to that from method A was obtained.

Method C. To a stirred solution of 2-methoxy-3-(2-pyridyl)thiophene (191.0 mg, 1.0 mmol) in anhydrous dichloromethane (5 ml) was added dropwise boron tribromide (627.5 mg, 2.5 mmol) with a syringe under nitrogen. The mixture was stirred at ambient temperature for 8 h and monitored by GLC, and then it was poured into cold water with stirring. Aqueous sodium carbonate (1 M) was added with stirring to make the solution alkaline (pH 7–8). The mixture was extracted with dichloromethane. The combined dichloromethane phases were washed with water and saturated sodium chloride solution and dried over anhydrous sodium sulfate. After evaporation, the residue was flash chromatographed on a Silica Gel 60 column using dichloromethane–methanol (99:1) as the eluent and then recrystallized from methanol to yield 83.2 mg (47%). The melting point was identical with that of the compound obtained by method A.

Crystal data for **4**, $C_{18}H_{14}N_2O_2S_2$, triclinic, space group P_1, $a = 10.292(2)$, $b = 10.802(2)$, $c = 15.919(3)$ Å, $\alpha = 108.11(1)$, $\beta = 96.77(2)$, $\gamma = 97.40(2)°$, $V = 1644.5(4)$ Å^3, $Z = 4$, $D_c = 1.43$ g cm^{-3}, μ (Mo Kα) = 3.22 cm^{-1}, $T = 296$ K; yellow crystal of dimensions $0.45 \times 0.20 \times 0.08$ mm obtained by recrystallization from methanol.

Data collection, analysis and refinement The X-ray diffraction data were collected on a computer-controlled Enraf-Nonius CAD4 diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71069 Å). The ω–2θ scan technique was employed with a maximum scan time of 120 s and a scan width of $(1.00 + 0.50 \tan\theta)°$. Of the 4535 measured independent reflections with $\theta \leq 23.0°$, 2410 with $I > 3\sigma(I)$ were considered as observed. The intensities of two test reflections, remeasured every second hour, showed no sign of crystal deterioration during the data collection. All intensities were corrected for LP and absorption effects.

The structure was solved by direct methods and the model obtained was refined by a full-matrix least-squares method, using the program TEXSAN,[17] minimizing $w(\Delta F)^2$ with $w^{-1} = [\sigma^2(F_o) + (0.03F_o)^2]$. In the final refinement, which gave $R = 0.036$, all non-hydrogen atoms were refined with anisotropic temperature factors and the hydrogen atoms with isotropic ones. The maximum shift/error was 0.01 and final Δρ excursions < 0.26 e Å^{-3}. Lists of anisotropic temperature factors, hydrogen atom parameters, bond distances and angles and structure factors are available from the authors.

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