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Formation and [4 + 2] cycloaddition reactions of 2,3-dimethylene-2,3-dihydrothiophene

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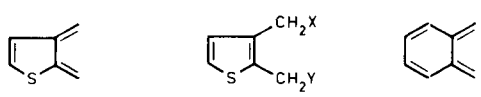
Abstract. 2,3-Dimethylene-2,3-dihydrothiophene (**1**), the thiophene analog of o-xylylene (o-quinodimethane), was generated *in situ* from the (trialkylammoniomethyl)-(trimethylsilylmethyl)thiophene iodides **4** or **5** by fluoride-induced 1,4 elimination, and was trapped by [4 + 2] cycloadditions with a series of dienophiles. The reaction of **1** with dimethyl fumarate was considerably faster than with dimethyl maleate. Unsymmetrical dienophiles gave mixtures of regio-isomers. In the absence of dienophiles, **1** formed [4 + 2] spiro dimers, of which **15a** is the major component, as determined by ^{1}H-NMR comparison with a tetradeutero analog of **15a**. The syntheses of the new precursors of **1** and dideutero-**1**: compounds **4**, **5a,b**, as well as the 3,4-isomer of **4**, are described.

Introduction **

In 1960 2,3-dimethylene-2,3-dihydrothiophene (**1**) was proposed as an intermediate in the formation of a polymer, obtained by pyrolysis of 3-methyl-2-(trimethylammoniomethyl)thiophene hydroxide[1]. Compound **1** did not reappear in the literature until 1987, when several groups reported independently on its synthesis, reactivity and spectroscopic properties[2].



1 2 3

This paper describes details[3] of the *in-situ* generation of **1** by fluoride-induced 1,4 elimination, carried out with two different trimethylsilyl ammonium derivatives of 2,3-dimethylthiophene (Eqn. 1 in Table 1).

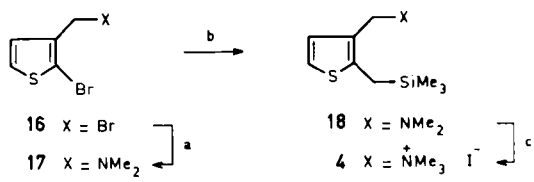
o-Xylylene or *o*-quinodimethane (**3**, the all-carbon analog of **1**) has been studied in great detail, for example, the relation with its valence tautomer benzocyclobutene and its reactivity in [4 + 2] cycloadditions[4]. In particular, intramolecular Diels–Alder reactions of derivatives of **3** are attracting considerable attention in the synthesis of biologically active products[5]. Heterocyclic analogs of **3** bearing nitrogen and oxygen are attracting considerable attention too[6]. Among these are *o*-dimethylene derivatives of pyridines[7a,b], pyrroles[7c,d,e], indoles[7f,g,h], thiazoles, oxazoles and imidazoles[7i], pyrazoles[7j], furans[8a,b] and benzofurans[8c,d].

We became interested in dimethylenethiophene **1** and its derivatives through our work on base-induced ring annulations of sulfonyl- and sulfinyl-substituted thiophene derivatives; reactions of use in the synthesis of benzo[*b*]thiophenes[9], and other bicyclic aromatics[10]. Conceptually, benzo[*b*]thiophenes can be formed also by [4 + 2] cycloaddition reactions of **1**. This is indeed the case, as has been shown by ourselves and other workers[2c,g,i,k,n,p]. Most methods for generating **1** are based on (thermal) 1,4 eliminations of X and Y from **2**, for example X = Y = Cl, Br[2c,o,p], X = H, Y = Cl[2d,f] or $OCOC_6H_5$[2b], X–Y = –CO–O–[2g,k] or SO_2[2i,n].

We have generated **1** from **2** with the substituents X = Me_3N^+ and Y = Me_3Si (**4**), as well as X = Me_3Si and Y = $MeEt_2N^+$ (**5a**). Elimination of Me_3Si and R_3N is induced by F^-, following *Seagusa*'s method[2a,7a] used for the formation of **3**. This method allows the generation of **1** at temperatures of −10°C and below, which is of particular importance due to the strong tendency of **1** to dimerize (or to polymerize)[2a,c,d,e,m,o]. The syntheses of the (new) precursors **4** and **5** are described below (Schemes 1 and 3, respectively).

Results and discussion

Reaction of **4**, or **5a**, with Bu_4NF in the absence of dienophiles rapidly leads to a mixture of products formed



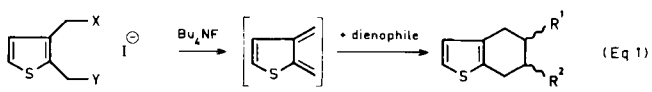
Scheme 1. (a) Me_2NH, 66%; (b) Me_3SiCH_2MgCl, $Ni(PPh_3)_2Cl_2$, Et_2O, heat, 85%; (c) MeI, MeCN, heat, 98%.

** Abbreviations and IUPAC synonyms: benzocyclobutene = bicyclo[4.2.0]octa-1,3,5-triene. DDQ = 2,3-dichloro-5,6-dicyanoquinone = 4,5-dichloro-3,6-dioxo-1,4-cyclohexadiene-1,2-dicarbonitrile. o-quinodimethane = 5,6-dimethylene-1,3-cyclohexadiene. TMEDA = *N,N,N',N'*-tetramethyl-1,2-ethanediamine. tosyl = p-toluenesulfonyl. *o*-xylylene = 5,6-dimethylene-1,3-cyclohexadiene

by dimerization of **1**, as will be discussed below. In the presence of suitable dienophiles, **1** forms Diels–Alder adducts in high yields. Table I presents the results obtained using nine different dienophiles containing a C=C bond or a N=N bond.

Nearly identical results were obtained with dimethyl fumarate and both precursors **4** and **5a** (entries 1 and 2 in Table I). *Trans* adduct **6a** is the expected result of a [4 + 2] cycloaddition of 2,3-dimethylene-2,3-dihydrothiophene (**1**) and dimethyl fumarate. The reaction of

*Table I. [4 + 2] Cycloadducts **6** to **12** synthesized from in-situ generated 2,3-dimethylene-2,3-dihydrothiophene (**1**) and dienophiles listed.*

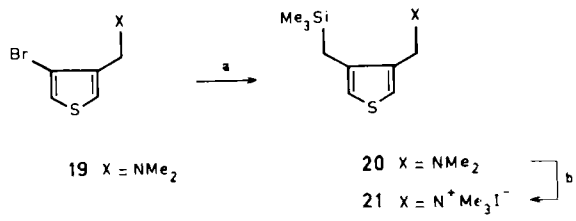


4 X = $\overset{\oplus}{N}Me_3$, Y = Me_3Si **1** **6–12**[a]

5a[b] X = Me_3Si, Y = $\overset{\oplus}{N}Et_2Me$

Entry	Precursor of **1**	Dienophile [c]	Product(s)	Yield [d] (%)	M.p. [e] (°C)
1	**4**	Me_2 fumarate (**13**)	**6a**	81	82.5–84.0
2	**5a**			81	
3	**4**	Me_2 maleate (**14**) [f]	**6a** + **6b**	92 [f]	
4	**4**	Et_2 acetylenedicarboxylate	**7** [g]	56	61–63
5	**4**	*N*-Ph-maleimide	**8**	89	162.0–162.5
6	**4**	Me acrylate [h]	**9a** [h] and **9b** [h]	90	oil
7	**5a**			100	
8	**4**	acrylonitrile [i]	**10a** [i] and **10b** [i]	92	oil
9	**4**	1,4-naphthoquinone [j]	**11** [j]	87	246–247
10	**5a**			41 [k]	
11	**4**	iPr_2 azodicarboxylate	**12a** R = *i*-Pr	82	67–68
12	**5a**			92	
13	**4**	Et_2 azodicarboxylate	**12b**, R = Et	85	oil

[a] For substituents R^1 and R^2, see column 4. For compounds **12a** and **12b**, the ring atoms numbered 5 and 6 are nitrogens. [b] For **5b** with $CD_2N^+Et_2Me$ instead of $CH_2N^+Et_2Me$, see text. [c] Unless stated otherwise, 1.0–1.5 equivalents of dienophile were used. [d] Yield of isolated material after purification. [e] M.p. of analytically pure samples, except for **7**. [f] A mixture of **6a** and **6b** (ratio 4:1) was obtained in 92% yield when 100 equivalents of **14** were used containing 4–5% of **13**; **6b** was not isolated separately. [g] A mixture of isomeric dihydrobenzo[*b*]thiophene-5,6-carboxylates and **7** was formed initially, which was dehydrogenated (DDQ) to **7**[15]. [h] Obtained as a mixture **9a/9b**, ratio 1.8:1, using 55 equivalents of methyl acrylate; product mixture not separated. [i] Obtained as a mixture **10a/10b**, ratio 2.4:1, using 76 equivalents of acrylonitrile; product mixture not separated. [j] Excess of 1,4-naphthoquinone (2 equivalents) used in CH_2Cl_2 as solvent; initial [4+2] adduct air-oxidized to **11**. [k] No dimeric products were detected by TLC.



Scheme 2. (a) Me_3SiCH_2MgCl, $Ni(PPh_3)_2Cl_2$, Et_2O, heat, 70%; (b) MeI, MeCN, heat, 97%.

dimethyl maleate (entry 3) seems confusing at first glance, since the major product is also the *trans* adduct **6a**, in addition to some *cis* adduct **6b**. The ratio of **6a**/**6b** was 4 : 1. This is not a departure of the suprafacial-suprafacial reaction mode, but the result of some dimethyl fumarate (**13**) present as a standard impurity (4–5%) in the dimethyl maleate (**14**), which was used in large excess (*ca.* 100 equivalents). Apparently, the reaction of **1** is much faster with **13** than with **14**[11]. This is clearly demonstrated by the following observations:

- More than 80% of **6a** is formed in reaction with one equivalent of **13** (entries 1 and 2).
- A large excess of **14** is needed to prevent dimerization of **1** in the reaction leading to **6b** (entry 3).
- *Trans*-**6a** is formed exclusively (87% yield) upon reaction of Bu_4NF with a 1 : 1 : 1 mixture of **4**, **13** and **14**, from which **14** is quantitatively recovered afterwards.

The reaction of **1** with fumarate-free **14** was not investigated[12].

The higher dienophilic reactivity of **13** relative to **14** is probably related to the non-planar ground state of **14**[13]. Due to diminished conjugation, the LUMO of non-planar **14** will have a higher potential energy than the LUMO of **13**. When, however, planar conformations were used for both **13** and **14**, *Koster* and *Nguyen*[14] calculated to substantial differences in the LUMO (and HOMO) energies of **13** and **14**.

The reaction of **1** with diethyl acetylenedicarboxylate leads to a mixture of tautomeric dihydrobenzothiophenes together with about 10% of diethyl benzo[*b*]thiophene-5,6-dicarboxylate[15] (**7**, entry 4). Dehydrogenation (DDQ) of this mixture gave **7** in 56% yield.

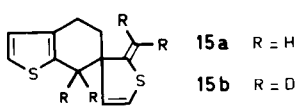
The reactions of **1** with methyl acrylate and with acrylonitrile gave mixtures of regioisomers **9a** and **9b**, and **10a** and **10b**, respectively (entries 6–8). These mixtures have not been separated. As before (entries 1 and 2), the choice of precursor (**4** or **5a**) is of no consequence for yield or product composition (entries 6 and 7). This is good evidence that **1** is a true intermediate for the cycloaddition reactions collated in Table 1[16]. The assignment of structure **9a** to the major isomer of entries 6 and 7 (and by analogy of **10a** in entry 8) is based on comparison with results obtained by *Trahanovsky* et al. with the corresponding 2,3-dimethylene-2,3-dihydrofuran[8a]. Also, *Koster* and *Nguyen* have confirmed this assignment by calculation of the energy levels and orbital coefficients of the HOMOs and LUMOs of **1** and methyl acrylate[14].

Further evidence for the intermediacy of **1** is that nearly identical results were obtained in the sets of experiments of entries 1 and 2, 6 and 7, 9 and 10, despite the fact that **1** is formed faster from **4** (and Bu_4NF) than from **5a**. In a ^{1}H-NMR competition experiment (using 1 equivalent of Bu_4NF and 1.7 equivalents of both **4** and **5a** in $CDCl_3$), it was shown that only **4** was converted to dimers, while **5a** remained unchanged. For this reason, the addition of Bu_4NF was carried out more slowly in experiments using **5a** (instead of **4**), to suppress the formation of dimers (see below). A lower concentration of F^- would lead to lower concentrations of **1**, which would result in less dimer and more cycloadduct with added dienophile. For example, an addition time of $2\frac{1}{2}$ h was used in entry 2, as compared to 30 min in entry 1, to obtain the same yield of **6a**. To explain the observed differences in reactivity between **4** and **5a**, we assume, tentatively, that the developing negative charge brought about by attack of the fluoride anion on silicon, is somewhat better stabilized at the nascent methylene at C2 than at C3[17a]. It should be emphasized, however, that the attack of fluoride is considered the beginning of a more or less concerted 1,4 elimination process[17b].

Adduct **8** of *N*-phenylmaleimide and **1** was obtained in 89% yield using **4** as precursor (entry 5). The corresponding reaction of *N*-phenylmaleimide with **5a**, however, gave no **8** at all, not even on slow addition of Bu_4NF. In this case Bu_4NF appears to react faster with *N*-phenylmaleimide than with **5a**, which leads to highly colored reaction mixtures (polymerization).

The conclusion is that **4** is the preferred precursor for the formation of **1**. However, even with **4** as precursor, a number of attempted cycloadditions were unsuccessful. In these cases, fluoride-induced polymerization of the dienophiles prevails over the formation of **1**. Examples of dienophiles in this category are: maleic anhydride, fumaronitrile, dimethyl methylenebutanedioate, bis(2,2,2-trichloroethyl) azodicarboxylate and 4-phenyl-1,2,4-triazoline-3,5-dione.

The dimerization of **1**, alluded to above, leads to mixtures of dimeric spiro compounds, which are fairly stable in solution, but which tend to polymerize on concentration. Although individual isomers have not been isolated, ^{1}H- and ^{13}C-NMR analysis of the mixtures of dimers obtained from **4**, **5a** and **5b** (*i.e.* the 2-diethylmethylammonio(dideutero)methylene analog of **5a**) suggest that the major product **15a**[18] (> 80% yield) resulted from a [4 + 2] cycloaddition of two molecules of **1** (see Experimental). Comparable spiro compounds have been reported for [4 + 2] cycloadditions of *o*-xylylene[7,19,20], and of 2,3-dimethylene-2,3-dihydroindoles[7k,l]. Dimers resulting from [4 + 4] cycloadditions have been reported for *o*-xylylene[19,20,21] and for 2,3-dimethylene-2,3-dihydrofuran[1,8a,b].



15a R = H

15b R = D

Synthesis of precursors

Schemes 1 and 3 depict the methods used for the synthesis of **4** and **5a**, as well as deuterated **5**, *i.e.* **5b**, which have been used as precursors of **1**, and deuterated **1**. The 3,4-isomer of **4**, *i.e.* **21**, is described also.

Compound **4** was prepared in 3 steps from 2-bromo-3-(bromomethyl)thiophene[22] (**16**) in 50% overall yield. The aliphatic bromine of **16** was selectively substituted with aqueous Me_2NH to give amine **17** (66% yield), followed by a Ni^{II}-catalyzed cross-coupling of the aromatic bromine[23] with Me_3SiCH_2MgCl to **18** (85% yield), which was quaternized quantitatively to **4**. [Amine **17** was previously prepared by a less attractive process from 3-[(dimethylamino)methyl]-2-lithiothiophene and tosyl bromide][24]. The cross-coupling (which was much less successful with the 2-chloro analog of **17**) proved to be the ultimate solution to problems associated with the preparation of **18**, after several unsuccessful other approaches[3b].

In a series of experiments analogous to Scheme 1, 4-[(trimethylammonio)methyl]-3-[(trimethylsilyl)methyl]thiophene iodide (**21**) was prepared from 3-bromo-4-(bromomethyl)thiophene[25] (Scheme 2). Treatment of **21** with Bu_4NF in the presence of methyl acrylate resulted in protodesilylation rather than cycloaddition[3b]. *Berson* and coworkers have reported earlier on cycloadducts of the expected 3,4-dimethylene-3,4-dihydrothiophene with acrylonitrile and with butenedinitriles, as well as on dimers. The structure of this transient species, which was obtained by pyrolytic and photolytic 1,4 elimination of N_2 from 1,4-dihydrothieno[3,4-*d*]pyridazine, was discussed in detail[26].

A different approach was followed for the synthesis of precursors **5a** and **5b**, via 2-thiophenecarboxamide **25**, which enabled the introduction of deuterium in the 2-substituent of **5b**, used in the structure investigation of dimeric **1** (Scheme 3). The overall yield of **5a** was 70% based on commercially available 3-methyl-2-thiophenecarboxylic acid (**22**). In addition to a nearly quantitative reaction using $SOCl_2$ and Et_2NH[27], **23** was prepared alternatively from 2-bromo-3-methylthiophene[28] in 60% yield using BuLi and *N,N*-diethylcarbamoyl chloride[29]. Silylation of the 3-methyl substituent of **23** could not be achieved without simultaneous silylation at C5 (using *s*-BuLi, TMEDA and Me_3SiCl). However, the silyl group at C5 was specifically removed by treatment with *p*-toluenesulfonic acid. Thus, the overall result was silylation of the 3-methyl group to **25** in 78% yield based on **23**. The amide group of **25** was smoothly reduced to **26a** or **26b** with excess (6 moles) of $LiAlH_4$ or $LiAlD_4$, respectively. With less $LiAlH_4$ partial C–N bond cleavage was observed[30]. Quaternization of the amino groups with MeI to **5a,b** was carried out in the same way as for **4**. Quite recently, *Plant* and *Chadwick* have reported two analogs of precursor **5a**, with Y = N^+Me_2t Bu and N^+Me_2(1-adamantyl)[21].

Conclusions

Compound **4** is an efficient precursor for the *in-situ* generation of **1**, the thiophene analog of *o*-xylylene (**3**), at room temperature and below. Compound **1** is a reactive intermediate, which is of use in Diels–Alder reactions to provide benzothiophene derivatives not previously reported[37].

Experimental

General

Most reactions were carried out under nitrogen, although the [4 + 2] cycloaddition reactions have been carried out occasionally in air without detrimental effects.

^1H NMR: Hitachi–Perkin–Elmer R-24B (60 MHz) or, when mentioned explicitly at 300 MHz: Varian VTR-300; δ (ppm) down field of internal Me_4Si or related via $CDCl_3$ δ 7.24, CD_3OD δ 3.35 and CD_3SOCD_3 δ 2.49. ^{13}C NMR: Nicolet NT-200 (50.3 MHz) or Varian VTR-300 (75.4 MHz): δ (ppm) down field of Me_4Si via $CDCl_3$ δ 76.91 or CD_3OD δ 48.97; the multiplicity of $^1J_{CH}$ is reported only. Mass spectra: AEI MS-902.

Elemental microanalyses: Analytical Department of Groningen University (*A.F. Hamminga, J. Ebels, H. Draayer, J.E. Vos*).

Diethyl ether and tetrahydrofuran (THF) were freshly distilled from Na/benzophenone, and CH_2Cl_2 from P_2O_5. All other solvents were stored over 4Å molecular sieves. TMEDA was distilled from and stored over KOH pellets. Me_3SiCl was distilled and stored under nitrogen. Other commercially available chemicals were used as such.

2-Bromo-3-[(dimethylamino)methyl]thiophene[24] (17)

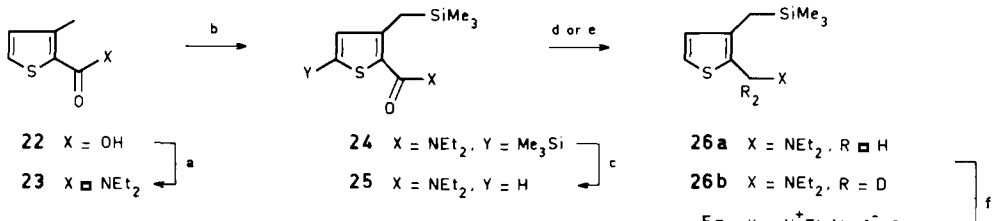
The preparation according to *Slocum* et al.[24] was replaced by an alternative procedure using 2-bromo-3-methylthiophene[28] and 2-bromo-3-(bromomethyl)thiophene[22] (**16**). Crude **16** (46.8 g, 0.18 mol) was added in 10 min to 400 ml of a 40% aqueous solution of Me_2NH (*ca.* 4 mol) at room temperature. After stirring for another 15 min, the mixture was diluted with water (400 ml) and extracted with ether (2×200 ml). The extracts were concentrated and the residue was purified by acid–base separation, using 2N HCl, 15% NaOH and ether. The resulting ether solution was dried (brine and $MgSO_4$) and concentrated. The crude product (27.2 g) was purified by distillation to give 26.7 g (66%) of **17**, b.p. 74–79°C (0.6 mmHg) [lit.[24] b.p. 59–60°C (1.3 mmHg)]. ^1H NMR ($CDCl_3$): δ 2.34 (s, 6H), 3.38 (s, 2H), 6.94 (d, *J* 5.6 Hz, 1H), 7.21 (d, *J* 5.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 44.6 (q), 56.5 (t), 110.3 (s), 124.7 (d), 128.2 (d), 137.7 (s). MS *m/z* (M^+) calcd. 218.972, obsd. 218.973. Anal. calcd. for $C_7H_{10}BrNS$: C 38.19, H 4.58, Br 36.30, N 6.36, S 14.56; found: C 38.15, H 4.54, Br 36.07, N 6.36, S 14.56%.

3-[(Dimethylamino)methyl]-2-[(trimethylsilyl)methyl]thiophene (18)

A solution of Me_3SiCH_2MgCl [prepared from Me_3SiCH_2Cl (25.34 g, 0.208 mol) and Mg (5.52 g, 0.227 mol)][32] in 150 ml of ether was added in 10 min to a solution of **17** (29.1 g, 0.13 mol) and $Ni(PPh_3)_2Cl_2$[33] (0.85 g, 1.6 mol-%) in ether (300 ml; ice bath) and then refluxed for 20 h. Upon cooling, addition of water (100 ml) and saturated NH_4Cl solution (100 ml) and separation, the water layer was extracted with ether (200 ml). The combined ether extracts were dried (brine and $MgSO_4$), concentrated and the residue purified by bulb-to-bulb distillation at 70°C (0.02 mmHg) to give 25.5 g (85%) of **18**. Analytically pure material was obtained by a second distillation, b.p. 60–62°C (0.02 mmHg). ^1H NMR ($CDCl_3$): δ 0.18 (s, 9H), 2.20 (s, 6H), 2.26 (s, 2H), 3.31 (s, 2H), 6.95 (s, 2H). ^{13}C NMR ($CDCl_3$): δ −1.6 (q), 18.2 (t), 45.2 (q), 56.7 (t), 119.2 (d), 129.1 (d), 132.6 (s), 138.4 (s). MS *m/z* (M^+) calcd. 227.116, obsd. 227.119. Anal. calcd for $C_{11}H_{21}NSSi$: C 58.09, H 9.31, N 6.16, S 14.10, Si 12.35; found: C 58.07, H 9.33, N 6.22, S 14.07, Si 12.1%.

3-[(Trimethylammonio)methyl]-2-[(trimethylsilyl)methyl]thiophene iodide (4)

A solution of **18** (6.82 g, 30 mmol) and MeI (3.0 ml, 48 mmol) in acetonitrile (20 ml) was refluxed for 1 h. After cooling to 20°C and addition of ether (100 ml), the white precipitate was collected, washed with ether to give 10.82 g (98%) of **4** (m.p. 183–186°C, dec.), which was sufficiently pure for use in the preparation of 2,3-dimethylene-2,3-dihydrothiophene (**1**). Analytically pure material was obtained by crystallization from acetonitrile, m.p. 206–208°C (dec.). ^1H NMR ($CDCl_3/CD_3OD$ 1:1): δ 0.10 (s, 9H), 2.52 (s, 2H), 3.14 (s, 9H), 4.50 (s, 2H), 7.14 (d, *J* 5 Hz, 1H), 7.25 (d, *J* 5 Hz, 1H). ^{13}C



Scheme 3. (a) $SOCl_2$, Et_2NH, 96%; (b) s-BuLi / TMEDA (2 equivalents), THF, −78°C, Me_3SiCl, 80%; (c) TosOH, C_6H_6, heat, 97%; (d) $LiAlH_4$, Et_2O, 20°C, 96%; (e) $LiAlD_4$, Et_2O, 20°C, 92%; (f) MeI, MeCN, heat, 95%.

NMR ($CDCl_3/CD_3OD$ 1:1): δ −3.1 (q), 18.2 (t), 51.2 (q), 60.4 (t), 120.8 (s), 120.8 (d), 129.1 (d), 147.4 (s). Anal. calcd for $C_{12}H_{24}INSSi$: C 39.02, H 6.55, N 3.79, S 8.68; found: C 39.10, H 6.55, N 3.87, S 8.73%. The exact mass could not be determined due to Hofmann elimination in the mass spectrometer.

3-Bromo-4-[(dimethylamino)methyl]thiophene (19)

19 was prepared analogously to the procedure described for **17** from impure 3-bromo-4-(bromomethyl)thiophene[25] [b.p. 70–88°C (0.05 mmHg), 20.5 g, *ca.* 53 mmol] and 40% aqueous dimethylamine (100 ml, *ca.* 1 mol). Yield 8.00 g (*ca.* 70%) of **19**, b.p. 67–69°C (0.15 mmHg). ^1H NMR ($CDCl_3$): δ 2.21 (s, 6H), 3.35 (s, 2H), 7.23 (br s, 2H). ^{13}C NMR ($CDCl_3$): δ 45.2 (q), 57.7 (t), 112.2 (s), 122.7 (d), 123.5 (d), 137.8 (s). MS *m/z* (M^+) calcd. 218.972, obsd. 218.973. Anal. calcd for $C_7H_{10}BrNS$: C 38.19, H 4.58, Br 36.30, N 6.36, S 14.56; found: C 38.27, H 4.57, Br 35.82, N 6.34, S 14.74%.

3-[(Dimethylamino)methyl]-4-[(trimethylsilyl)methyl]thiophene (20)

20 was prepared analogously to **18** by refluxing for 23 h a mixture of **19** (3.93 g, 17.8 mmol), $Ni(PPh_3)_2Cl_2$[33] (0.278 g, 4 mol-%) and a solution of Me_3SiCH_2MgCl[32] in ether (27 ml, *ca.* 1 M, from 3.28 g of Me_3SiCH_2Cl) in benzene (70 ml). Bulb-to-bulb distillation at 110°C (0.05 mmHg) gave 2.84 g (70%) of **20**. Analytically pure material was obtained by a second distillation. ^1H NMR ($CDCl_3$): δ −0.07 (s, 9H), 2.18 (s, 2H), 2.33 (s, 6H), 3.43 (s, 2H), 7.07 (d, *J* 3.4 Hz, 1H), 7.47 (d, *J* 3.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ −1.5 (q), 18.2 (t), 45.4 (q), 58.2 (t), 118.1 (d), 122.7 (d), 138.2 (s), 138.9 (s). MS *m/z* (M^+) calcd. 227.116, obsd. 227.117. Anal. calcd for $C_{11}H_{21}NSSi$: C 58.09, H 9.31, N 6.16, S 14.10, Si 12.35; found: C 58.35, H 9.42, N 6.17, S 14.01, Si 12.12%.

3-[(Trimethylammonio)methyl]-4-[(trimethylsilyl)methyl]thiophene iodide (21)

(21) was prepared analogously to **4** using **20** (1.25 g, 5.5 mmol) and MeI (1 ml) in acetonitrile (15 ml). Yield 1.97 g (97%) of **21**, m.p. 199–200°C. Recrystallization from acetone/ethyl-acetate gave analytically pure **21**, m.p. 205–206°C (dec.). ^1H NMR ($CD_3OD/CDCl_3$ 1:1): δ 0.15 (s, 9H), 2.28 (s, 2H), 3.38 (s, 9H), 4.72 (s, 2H), 7.08 (d, *J* 3 Hz, 1H), 8.00 (d, *J* 3 Hz, 1H). ^{13}C NMR ($CD_3OD/CDCl_3$ 1:1): δ −2.8 (q), 17.9 (t), 51.7 (q), 61.0 (t), 119.7 (d), 126.2 (s), 131.1 (d), 139.3 (s). Anal. calcd for $C_{12}H_{24}INSSi$: C 39.02, H 6.55, I 34.35, N 3.79, S 8.68; found: C 38.80, H 6.55, I 34.63, N 3.75, S 8.72%.

N,N-Diethyl-3-methyl-2-thiophenecarboxamide (23)

(*a*) From 3-methyl-2-thiophenecarboxylic acid (**22**). A solution of **22** (8.92 g, 63 mmol) in 65 ml of thionyl chloride was refluxed for 30 min, then concentrated and stripped twice with CCl_4 at reduced pressure. The residue was dissolved in ether (200 ml) and a mixture of Et_2NH[27] (10 ml, 97 mmol) and Et_3N (9 ml, 65 mmol) in ether (100 ml) was added at such a rate that the reaction mixture was gently refluxing. The reaction mixture was stirred for 1 h (20°C). The precipitate was removed and extracted twice with ether. The combined ether solutions were concentrated and the residue was bulb-to-bulb distilled at 135°C (0.25 mm Hg) to give 11.94 g (96%) of **23**. Analytically pure **23** was obtained by a second distillation, b.p. 96–97°C (0.15 mmHg). ^1H NMR ($CDCl_3$) δ 1.17 (t, *J* Hz, 6H), 2.27 (s, 3H), 3.45 (q, *J* 7 Hz, 4H), 6.84 (d, *J* 5.6 Hz, 1H), 7.25 (d, *J* 5.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 13.4 (q), 14.1 (q), 41.6 (br t), 124.5 (d), 129.2 (d), 130.6 (s), 136.3 (s), 164.9 (s). MS *m/z* (M^+) calcd. 197.087, obsd. 197.086. Anal. calcd for $C_{10}H_{15}NOS$: C 60.87, H 7.67, N 7.10, S 16.25; found: C 60.76, H 7.76, N 6.98, S 16.27%.

(*b*) From 2-bromo-3-methylthiophene[29]. Buli (1.6 M in hexane, 6.9 ml, 11 mmol) was added in 5 min to a solution of 2-bromo-3-methylthiophene[28] (1.77 g, 10 mmol) in ether (100 ml) at −70°C. After stirring for 30 min, a solution of diethylcarbamoyl chloride (1.03 ml, 11 mmol) in ether (15 ml) was added rapidly, keeping the temperature between −80 and −70°C. Stirring was continued for 30 min at −70°C, then the temperature was increased to −40°C in 30 min. Saturated NH_4Cl (50 ml) was added, the temperature was further increased to 20°C, and stirring was continued for 30 min. The water layer was extracted with ether (2×25 ml), the combined ether solutions were dried ($MgSO_4$), concentrated and the residue was bulb-to-bulb distilled to collect 1.18 g (60%) of pure amide **23** as the main fraction at 140°C (0.2 mmHg), which was identical to the above preparation by ^1H and ^{13}C NMR.

N,N-Diethyl-5-(trimethylsilyl)-3-[(trimethylsilyl)methyl]-2-thiophenecarboxamide (24)

s-BuLi (1.20 M[34] in a 10:1 mixture of cyclohexane/isopentane, 83 ml, 100 mmol)[35] was added dropwise (5 min) to a solution of **23** (9.86 g, 50 mmol) and TMEDA (15 ml, 100 mmol) in 500 ml of THF at −70°C. After stirring for 20 min, Me_3SiCl (18 ml, 150 mmol) was added all at once, and the temperature was raised to −20°C in 30 min. Saturated NH_4Cl solution (1 l) was added, the temperature was increased to 20°C, and the water layer was extracted with ether (2×100 ml). The combined ether solutions were dried (brine, $MgSO_4$) and concentrated. Bulb-to-bulb distillation at 135°C (0.05 mmHg) of the residue gave 13.6 g (80%) of **24**. ^1H NMR ($CDCl_3$): δ −0.03 (s, 9H), 0.30 (s, 9H), 1.18 (t, *J* 7.4 Hz, 6H), 2.10 (s, 2H), 3.44 (q, *J* 7.4 Hz, 4H), 6.84 (s, 1H). ^{13}C NMR ($CDCl_3$): δ −1.9 (q), −0.6 (q), 13.2 (q), 19.3 (t), 39.5 (br t), 131.9 (d), 135.7 (s), 138.7 (s), 141.1 (s), 165.0 (s). MS *m/z* (M^+) calcd. 341.166, obsd. 314.167. Anal. calcd for $C_{16}H_{31}NOSSi_2$: C 56.25, H 9.15, N 4.10, S 9.32; found: C 56.97, H 9.27, N 4.10, S 9.32%.

N,N,-Diethyl-3-[(trimethylsilyl)methyl]-2-thiophenecarboxamide (25)

Crude amide **24** [9.42 g (containing *ca.* 10% of trisilylamide **27**)[36], *ca.* 24.3 mmol] and *p*-toluenesulfonic acid·H_2O (5.25 g, 27.6 mmol) were refluxed for 2½ h in 200 ml of benzene. After cooling to 20°C, the mixture was washed with 3N NaOH (2×20 ml), dried ($MgSO_4$), and concentrated. The residue was bulb-to-bulb distilled at 130°C (0.05 mmHg) to give 7.21 g (*ca.* 97%) of **25** (containing *ca.* 10% of *N,N*-diethyl-3-[bis(trimethylsilyl)methyl]-2-thiophenecarboxamide), which was purified by flash chromatography (silica gel, ether/hexane 1:2). Analytically pure **25** was obtained by bulb-to-bulb distillation at 140°C (0.05 mmHg). ^1H NMR ($CDCl_3$): δ −0.10 (s, 9H), 1.12 (t, *J* 7.4 Hz, 6H), 2.11 (s, 2H), 3.38 (q, *J* 7.4 Hz, 4H), 6.67 (d, *J* 5.6 Hz, 1H), 7.16 (d, *J* 5.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ −1.7 (q), 13.3 (q), 19.9 (t), 40.4 (br t), 124.3 (d), 127.0 (s), 129.0 (d), 140.2 (s), 165.1 (s). MS *m/z* (M^+) calcd. 269.127, obsd. 269.127. Anal. calcd for $C_{13}H_{23}NOSSi$: C 57.94, H 8.60, N 5.20, S 11.90; found: C 57.88, H 8.72, N 5.16, S 11.76%.

2-[(Diethylamino)methyl]-3-[(trimethylsilyl)methyl]thiophene (26a)

A solution of amide **25** (879 mg, 3.27 mmol) in ether (20 ml) was added in 5 min to a slurry of $LiAlH_4$ (740 mg, 20 mmol) in ether (60 ml). The mixture was stirred for 1½ h. After the addition of a few drops of 15% NaOH and water (2 ml), the mixture was stirred for another 15 min and then dried ($MgSO_4$). The solids were removed and extracted with ether. The combined ether solutions were concentrated and the residue was bulb-to-bulb distilled at 100°C (0.15 mmHg) to give 800 mg (96%) of **26**. ^1H NMR ($CDCl_3$): δ 0.05 (s, 9H), 1.10 (t, *J* 7.4 Hz, 6H), 2.07 (s, 2H), 2.60 (q, *J* 7.4 Hz, 4H), 3.62 (s, 2H), 6.70 (d, *J* 5.0 Hz, 1H), 7.13 (d, *J* 5.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ −1.4 (q), 11.8 (q), 19.1 (t), 46.7 (t), 50.4 (t), 122.3 (d), 128.9 (d), 134.5 (s), 135.1 (s). MS *m/z* (M^+) calcd. 255.148, obsd. 255.147. Anal. calcd for $C_{13}H_{25}NSSi$: C 61.11, H 9.86, N 5.48, S 12.55; found: C 60.99, H 9.73, N 5.42, S 12.44%.

2-[(Diethylamino)dideuteromethyl]-3-[(trimethylsilyl)methyl]thiophene (26b)

The procedure of **26a** was followed using $LiAlD_4$, instead of $LiAlH_4$, and a reaction time of 20 h. The yield of **26b**, after bulb-to-bulb distillation at 100°C (0.03 mmHg), was 92%. ^1H NMR ($CDCl_3$): δ −0.01 (s, 9H), 1.03 (t, *J* 7 Hz, 6H), 2.02 (s, 2H), 2.57 (q, *J* 7 Hz, 1H), 6.69 (d, *J* 5.6 Hz, 1H), 7.10 (d, *J* 5.6 Hz, 1H), no signal at δ 3.6 thus incorporation of D ≥ 95%. ^{13}C NMR ($CDCl_3$) δ −1.4 (q), 11.9 (q), 19.2 (t), 46.6 (t), 49.6 (quintet), 122.5 (d), 129.0 (d), 134.4 (s), 135.1 (s). MS *m/z* (M^+) calcd. 257.160, obsd. 257.160. Anal. calcd for $C_{13}H_{23}D_2NSSi$: C 60.63, H 9.00, D 1.57, N 5.44, S 12.45; found: C 60.13, H 9.03, D 1.57 (based on a D:H ratio 1:11.5), N 5.33, S 12.26%.

2-[(Diethylmethylammonio)methyl]-3-[(trimethylsilyl)methyl]thiophene iodide (5a)

5a was prepared analogously to **4** from 1.5 mmol of **26a** in 96% yield, m.p. 127–131°C (dec.), which was used as such for the generation of **1**. Analytically pure **5a**, m.p. 138–139 (dec.; from acetone/ethyl-acetate). ^1H NMR (CD_3OD): δ 0.13 (s, 9H), 1.50 (br t, *J* 7.6 Hz, 6H), 2.43 (s, 2H), 3.10 (s, 3H), 3.58 (q, *J* 7.6 Hz, 4H), 7.05 (d, *J* 5.8 Hz, 1H), 7.73 (d, *J* 5.8 Hz, 1H). ^{13}C NMR (CD_3OD): δ −1.1 (q), 9.0

(q), 21.1 (t), 47.2 (q), 56.4 (t), 58.8 (t), 119.7 (s), 129.4 (d), 131.0 (d), 146.9 (s). Anal. calcd for $C_{14}H_{28}INSSi$: C 42.31, H 7.10, I 31.93, N 3.52, S 8.07; found: C 42.14, H 7.20, I 32.14, N 3.56, S 8.19%.

*2-[(Diethylmethylammonio)dideuteromethyl]-3-[(trimethylsilyl)methyl]thiophene iodide (**5b**)*

5b was prepared analogously to **5a** from **26b** in 95% yield, m.p. 133–135°C (dec.), which was used as such for the generation of 2-(dideuteromethylene)-3-methylene-2,3-dihydrothiophene. Analytically pure **5b**, m.p. 139–140°C (dec.; from acetone/ethyl-acetate). ^{1}H NMR (CD_3OD): δ −0.11 (s, 9H), 1.50 (br t, *J* 7.8 Hz, 6H), 2.40 (s, 2H), 3.11 (s, 3H), 3.57 (q, *J* 7.8 Hz, 4H), 7.07 (d, *J* 5.8 Hz, 1H), 7.80 (d, *J* 5.8 Hz, 1H). ^{13}C NMR (CD_3OD): δ −1.1 (q), 8.9 (q), 21.0 (t), 47.1 (q), 56.3 (t), 58.4 (quintet), 119.6 (s), 129.4 (d), 130.9 (d), 146.9 (s). Anal. calcd for $C_{14}H_{26}D_2INSSi$: C 42.10, H 6.56, D 1.01, I 31.77, N 3.51, S 8.03; found: C 42.07, H 6.67, D 1.03 (based on a D/H ratio 1:13), I 31.69, N 3.52, S 8.04%.

*Dimethyl trans-4,5,6,7-tetrahydrobenzo[b]thiophene-5,6-dicarboxylate (**6a**)*

(*a*) Using 3-[(trimethylammonio)methyl]-2-[(trimethylsilyl)-methyl]-thiophene iodide (**4**) as precursor of **1**. A solution of Bu_4NF (350 mg, 1.1 mol) in acetonitrile (10 ml) was added dropwise (30 min) to a slurry of **4** (369 mg, 1.0 mmol) and dimethyl fumarate (**13**, 144 mg, 1.0 mmol) in 10 ml of acetonitrile at 20°C. The mixture was stirred for 30 min. The solvent was removed at reduced pressure, and the residue was treated with ether (30 ml). The precipitate was removed and extracted with ether (2×10 ml). The combined ether solution was concentrated and the residue (234 mg of a white solid) was crystallized from petroleum ether (b.p. 40–60°C) to give 205 mg (81%) of **6a**, m.p. 81–84°C. Analytically pure material was obtained by recrystallization from the same solvent, m.p. 82.5–84.0°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.70–2.83 (m, 1H), 2.85–3.01 (m, 1H), 3.01–3.27 (m, 4H), 3.75 (s, 6H), 6.75 (d, *J* 5.7 Hz, 1H), 7.10 (d, *J* 5.7 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 27.3 (t), 27.9 (t), 41.9 (d), 42.4 (d), 51.8 (q), 51.9 (q), 123.0 (d), 126.6 (d), 132.2 (s), 132.6 (s), 174.2 (s), 174.5 (s). MS *m/z* (M^+) calcd. 254.061, obsd. 254.063. Anal. calcd for $C_{12}H_{14}O_4S$: C 56.68, H 5.55, S 12.61; found: C 56.57, H 5.66, S 12.60%.

(*b*) Using 2-[(diethylmethylammonio)methyl]-3-[(trimethylsilyl)methyl]thiophene iodide (**5a**) as precursor of **1**. An identical result, as above, was obtained when Bu_4NF (380 mg, 1.2 mmol) in acetonitrile (35 ml) was added in 2½ h to a slurry of **5a** (397 mg, 1.0 mmol) and dimethyl fumarate (144 mg, 1.0 mmol) in acetonitrile (10 ml); 206 mg (81%) of **6a**, m.p. 81–83°C.

*Dimethyl trans- and cis-4,5,6,7-tetrahydrobenzo[b]thiophene-5,6-dicarboxylate (**6a**, **6b**)*

Analogously to the procedure described above for **6a** (from **4**), Bu_4NF (315 mg, 1.0 mmol) in acetonitrile was added to a slurry of **4** (150 mg, 0.41 mmol) in an excess of dimethyl maleate (**14**, 5 ml, 40 mmol) at 20°C. After stirring for 1 h and removal of acetonitrile, excess dimethyl maleate was removed by bulb-to-bulb distillation at 80°C (0.4 mmHg). The residue was flash chromatographed (silica gel, ether) to give 95 mg (92%) of a *trans/cis* mixture of **6a** and **6b**, m.p. 70–72.5°C, *trans/cis* ratio 82:18. Two recrystallizations from petroleum ether (b.p. 40–60°C) gave the same analytically pure (*trans*) **6a** described above. The 300-MHz ^{1}H NMR of the *cis/trans* mixture shows two methyl singlets at δ 3.70 and δ 3.75. The ^{13}C NMR ($CDCl_3$) provided the *trans/cis* ratio given above; the signals only of the *cis*-isomer are reported here: 25.2 (t), 25.9 (t), 40.3 (d), 40.9 (d), 51.8 (q), 122.8 (d), 126.9 (d), 132.7 (s), 132.8 (s), 172.4 (s), 172.5 (s).

*Reaction of **1** with a 1:1 mixture of dimethyl fumarate (**13**) and dimethyl maleate (**14**)*

Following the procedure given above for **6a**, Bu_4NF (400 mg, 1.27 mmol) was added to a solution of **13** (144 mg) and **14** (155 mg, containing 4–5% of **13**), which amounts to 1.05 mmol of **13** and 1.02 mmol of **14**, and of **4** (369 mg, 1.0 mmol). Flash chromatography (silica gel, CH_2Cl_2/hexane 1:1, then ether) gave 329 mg (first fraction) as a mixture of **6a**, **13** and **14** in a ratio of 53, 11 and 36%, respectively, as determined by integration of the ^{1}H NMR signals at δ 7.04 (**6a**), 6.80 (**13**) and 6.18 (**14**). According to ^{13}C NMR, no **6b** was formed. A second fraction gave 59 mg of **14**. The overall result was a yield of 87% of **6a**, together with recovery of 12% of **13** and 97% of **14**.

*Dimerization of **1**: Reaction without dienophile to 4,5-dihydro-2'-methylenespiro[benzo[b]thiophene-6(7H),3'(2H')thiophene] (**15a**)[18]*

Bu_4NF (700 mg, 2.22 mmol) was added all at once to a solution of **4** (738 mg, 2.0 mmol) in acetonitrile (10 ml). After stirring for 1 min, work-up as described above (concentration, addition of ether, filtration over 4 cm of silica gel) gave a colorless oil (217 mg), which became brown on standing (the product mixture remains colorless when kept in solution). The oil shows the following NMR signals: ^{1}H NMR ($CDCl_3$): δ 1.70–2.30 (m, 1.5 H), 2.48–3.20 (m, 4.5 H, with singlets at 2.75, 2.99 and 3.19), 5.08 (br s) + 5.18 (br s, together 1.8 H), 5.58 (d, *J* 6.6 Hz, 0.9 H), 6.12 (d, *J* 6.6 Hz, 0.9 H), 6.50–6.90 (m, 1.4 H), 7.00 (d, *J* 5.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 23.2 (t), 34.6 (t), 37.8 (t), 55.5 (s), 103.7 (t), 105.2 (t), 121.8 (d), 122.4 (d), 127.0 (d), 128.7 (d), 133.8 (s), 155.5 (s). Similar results were obtained when **1** was generated from **5a**. When 2-(dideuteromethylene)-3-methylene-2,3-dihydrothiophene was generated similarly from **5b**, the major difference in the product ^{1}H NMR was the absence of a (broad) singlet at δ 2.75, 5.58 and 6.12, indicating that **15a** is the main product.

*Generation of **1** from a mixture of precursors **4** and **5a**; competition experiment*

The ^{1}H NMR spectrum of a solution of **4** (17 mg, 0.05 mmol) and **5a** (18 mg, 0.05 mmol) in $CDCl_3$ confirmed the 1:1 ratio of the solutes by integration of the signals at δ 2.28 (**5a**) and 2.50 (**4**), respectively. The NMR spectrum taken immediately after the addition of this solution to Bu_4NF (10 mg, 0.03 mmol) in $CDCl_3$ showed peaks indicative of the formation of dimers (see above), and of Me_3N at δ 2.11; the peaks of **4** at δ 2.50 and 4.78 were diminished to 40%, whereas those of **5a** remained unchanged.

*Diethyl benzo[b]thiophene-5,6-dicarboxylate (**7**)*

7 was prepared analogously to the procedure described for **6a**, from **4** (1.48 g, 4.0 mmol), diethyl acetylenedicarboxylate (0.816 g, 4.8 mmol) and Bu_4NF (1.40 g, 4.4 mmol) in 2 h. The residue, obtained after work-up, was purified by bulb-to-bulb distillation (100°C/0.05 mmHg). Flash chromatography (silica gel, petroleum ether (b.p. 40–60°C/ether 2:1) of the residue gave a mixture of diethyl dihydrobenzo[b]thiophene-5,6-dicarboxylates and **7** (ca. 10%) as a slightly yellow oil (678 mg). This mixture (678 mg) was dehydrogenated with DDQ (691 mg, 3.0 mmol) by refluxing for 17 h in benzene (30 ml). After cooling, filtration and removal of solvent, the residue (1.25 g) was purified by filtration over a layer of silica gel using ether/hexane 1:1, yielding **7** as a slightly yellow solid (619 mg, 56%), m.p. 61–63°C. ^{1}H NMR (CCl_4): δ 1.30 (t, *J* 7.0 Hz, 6H), 4.23 (q, *J* 7.0 Hz, 4H), 7.22 (d, *J* 6.0 Hz, 1H), 7.45 (d, *J* 6.0 Hz, 1H), 7.93 (s, 1H), 8.07 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 13.9 (q), 60.6 (t), 61.1 (t), 123.5 (d), 123.8 (d), 124.1 (d), 127.3 (s), 128.4 (s), 130.4 (d), 140.5 (s), 141.2 (s), 167.2 (s), 167.9 (s). MS *m/z* (M^+) calcd. 278.061, obsd. 278.060.

Benzo[b]thiophene-5,6-dicarboxylic acid[31]

Diester **7** (100 mg, 0.36 mmol) was refluxed for 1 h in a mixture of dioxane (5 ml) and 15% aqueous NaOH (5 ml). After removal of dioxane and acidification (4N HCl to pH 1), a white precipitate [62 mg, 81%, m.p. 243°C (dec.)] was collected and recrystallized from water to give the title compound in pure state, m.p. 250°C (dec.), identical with an authentic sample[31] by m.p. and ^{1}H NMR.

*2-Phenyl-3a,4,8,8a-tetrahydro-thieno[2,3-f]isoindole-1,3(2H)-dione (**8**)[2c,i,n]*

8 was prepared analogously to the procedure described for **6a** from **4** (369 mg, 1.0 mmol), *N*-phenylmaleimide (208 mg, 1.2 mmol) and Bu_4NF (460 mg, 1.5 mmol) in 1 h. Work-up using flash chromatography, as with **6a,b** using silica gel and CH_2Cl_2 then ethyl acetate, gave (second fraction) 252 mg (89%) of **8** as a white solid, m.p. 159–162°C. Analytically pure material, m.p. 162.0–162.5°C (from CH_2Cl_2/ether) (lit.[2i] 164–165°C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.76–2.88 (m, 1H), 2.94–3.04 (m, 1H), 3.35–3.53 (m, 4H), 6.87 (d, *J* 5.5 Hz, 1H), 6.98 (d, *J* 6.3 Hz, 2H), 7.08 (d, *J* 5.5 Hz, 1H), 7.38 (d, *J* 6.3 Hz), 7.30–7.46 (m, together with doublet 3H). ^{13}C NMR ($CDCl_3$): δ 24.8 (t), 25.3 (t), 40.2 (d), 40.6 (d), 122.5 (d), 126.2 (d), 126.7 (d), 128.4 (d), 128.9 (d), 131.6 (s), 132.4 (s), 134.4 (s), 178.1 (s), 178.4 (s). MS *m/z* (M^+) calcd. 283.067, obsd. 283.068. Anal. calcd. for $C_{16}H_{13}NO_2S$: C 67.82, H 4.62, N 4.94, S 11.32; found: C 67.70, H 4.65, N 4.92, S 11.22%.

Methyl 4,5,6,7-tetrahydrobenzo[b]thiophene-6-carboxylate (9a) and methyl 4,5,6,7-tetrahydrobenzo[b]thiophene-5-carboxylate (9b)

(*a*) Using **4** as precursor of **1**. This mixture was prepared analogously to the procedure of **6a**, from **4** (369 mg, 1.0 mmol), excess methyl acrylate (5 ml, 55 mmol), and Bu_4NF (630 mg, 2.0 mmol). Work-up as described for **6a** and flash chromatography (silica gel, ether) gave 177 mg (90%) of a mixture of **9a** and **9b** as a colorless oil, which is unstable at room temperature. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.81–2.02 (m, 1H), 2.18–2.33 (m, 1H), 2.60–3.15 (m, 5H), 3.75 (s, 3H), 6.78 (d, *J* 5.4 Hz, 1H), 7.09 (d, *J* 5.4 Hz, 1H). ^{13}C NMR ($CDCl_3$) **9a**: δ 24.5 (t), 25.7 (t), 27.1 (t), 40.3 (d), 51.6 (q), 122.2 (d), 126.9 (d), 133.2 (s), 134.2 (s), 175.1 (s); **9b**: δ 23.9 (t), 26.2 (t), 27.9 (t), 39.7 (d), 51.6 (q), 122.4 (d), 127.1 (d), 133.3 (s), 134.2 (s), 175.4 (s); the ratio **9a/9b** 1.8:1 was determined by ^{13}C NMR. MS *m/z* (M^+) calcd. 196.056, obsd. 196.055. No attempts were made to separate the mixture of **9a** and **9b**, which gave one spot on TLC. A solution of **9a,b** in $CDCl_3$ was stable for several weeks at −25°C.

(*b*) Using **5a** as precursor for **1**. Identical results were obtained when the same procedure described under (*a*) was followed using **5a** (199 mg, 0.5 mmol), methyl acrylate (5 ml, 55 mmol) and Bu_4NF (215 mg, 0.7 mmol). Yield 98 mg (100%) of **9a/9b**, ratio 1.8:1.

4,5,6,7-Tetrahydrobenzo[b]thiophene-6-carbonitrile (10a) and 4,5,6,7-tetrahydrobenzo[b]thiophene-5-carbonitrile (10b)[2c]

These compounds were prepared analogously to the procedure of **9a,b**, from **4** (739 mg, 2.0 mmol), excess of acrylonitrile (10 ml, 152 mmol) and Bu_4NF (1.00 g, 3.2 mmol) in 2 h. Work-up as described for **6a** and flash chromatography (silica gel, ether) gave 299 mg (92%) of a mixture of **10a** and **10b**, ratio 2.4:1, as a colorless unstable oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.02–2.29 (m, 2H), 2.65–2.78 (m, 1H), 2.80–3.25 (m, 5H), 6.75 (d, *J* 5.4 Hz, 1H), 7.10 (d, *J* 5.4 Hz, 1H). ^{13}C NMR ($CDCl_3$) **10a**: δ 22.6 (t), 25.0 (d), 25.3 (t), 27.8 (t), 121.0 (s), 122.3 (d), 126.8 (d), 130.0 (s), 132.7 (s); **10b**: δ 22.1 (t), 24.5 (d), 25.9 (t), 28.2 (t), 121.2 (s), 122.2 (d), 126.2 (d), 130.3 (s), 132.7 (s); the ratio **10a/10b** 2.4:1 was determined by ^{13}C NMR. MS *m/z* (M^+) calcd. 163.046, obsd. 163.043. The mixture of **10a,b** can be stored in solution for several weeks at −25°C. No attempts were made to separate the mixture, which showed one spot on TLC.

Anthra[2,3-b]thiophene-5,10-dione (11)

(*a*) Using **4** as a precursor for **1**. Dione **11** was prepared analogously to the procedure described for **6a** from **4** (369 mg, 1.0 mmol), 1,4-naphthoquinone [316 mg, 2.0 mmol, technical grade, was recrystallized from petroleum ether (b.p. 80–110°C), m.p. 123.5–125.0°C] and Bu_4NF (400 mg, 1.3 mmol) using CH_2Cl_2 as solvent, instead of acetonitrile. After addition of the Bu_4NF, air was bubbled through the solution for 1 h. After removal of the solvent, acetonitrile was added. A brown solid was collected and washed with acetonitrile, yielding **11** (230 mg, 87%), m.p. 244–246°C. Crystallization (from Me_2SO) gave analytically pure material, m.p. 246–247°C. ^1H NMR ($CDCl_3$): δ 7.45–7.95 (m, 4H), 8.15–8.55 (m, 2H), 8.72 (s, 1H), 8.82 (s, 1H). ^{13}C NMR ($CDCl_3$, only C-H-coupled signals were observed) δ 122.5 (d), 123.2 (d), 125.1 (d), 127.2(d), 132.3 (d), 133.9 (d). IR (KBr) 3090, 1670, 1575, 1329, 1290, 1170, 965, 770, 710 cm^{-1}. MS *m/z* (M^+) calcd. 264.024, obsd. 264.025. Anal. calcd for $C_{16}H_8SO_2$: C 72.21, H 3.05, S 12.13; found: C 72.45, H 3.25, S 12.10%.

(*b*) Using **5a** as precursor for **1**. The procedure described above was followed, using **5a** (397 mg, 1.0 mmol), 1,4-naphthoquinone (316 mg, 2.0 mmol) and Bu_4NF (350 mg, 1.1 mmol, which was added in the course of $2\frac{1}{2}$ h). Yield 107 mg (41%) of **11**, m.p. 244–246°C.

Diisopropyl 4,5,6,7-tetrahydrothieno[2,3-d]pyridazine-5,6-dicarboxylate (12a)

(*a*) Using **4** as precursor for **1**. A procedure analogously to the one described for **6a** was followed using **4** (738 mg, 2.0 mmol), diisopropyl azodicarboxylate (404 mg, 2.0 mmol) and Bu_4NF (670 mg, 2.13 mmol). Work-up as described for **6a** gave, by flash chromatography (silica gel, ether/pentane 1:1), 509 mg (82%) of **12a** as a colorless oil, which solidified on standing, m.p. 63–65°C. Analytically pure material was obtained by bulb-to-bulb distillation at 170°C (0.02 mmHg), m.p. 67–68°C. ^1H NMR ($CDCl_3$): δ 1.26 (d, *J* 5.9 Hz, 12H), 4.09–4.65 (br m, 2H), 4.75–5.47 (br m) and 5.05 (septet, *J* 5.9 Hz, together 3H), 6.92 (d, *J* 5.8 Hz, 1H), 7.30 (d, *J* 5.8 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 23.3 (q), 45.0 (t), 45.6 (t), 71.3 (d), 71.5 (d), 125.0 (d), 125.6 (d), 126.1 (s), 132.5 (s), 156.2 (s). MS *m/z* (M^+) calcd. 312.114, obsd. 312.110. Anal. calcd for $C_{14}H_{20}N_2O_4S$: C 53.83, H 6.45, N 8.97, S 10.26; found: C 53.87, H 6.69, N 8.88, S 10.10%.

(*b*) Using **5a** as precursor for **1**. The procedure described above was followed, using **5a** (199 mg, 0.50 mmol), diisopropyl azodicarboxylate (151 mg, 0.75 mmol) and Bu_4NF (230 mg, 0.73 mmol, which was added in the course of 100 min). The reaction mixture was stirred overnight. After work-up, 144 mg (92%) of **12a** was isolated, m.p. 63–65°C.

Diethyl 4,5,6,7-tetrahydrothieno[2,3-d]pyridazine-5,6-dicarboxylate (12b)

12b was prepared analogously to the procedure of **6a**, using **4** (748 mg, 2.0 mmol), diethyl azodicarboxylate (348 mg, 2.0 mmol) and Bu_4NF (787 mg, 2.5 mmol). The reaction was monitored by TLC (silica gel, ether) until dienophile was no longer detectable (*ca.* 1 h). After work-up and purification by flash chromatography (silica gel/ether), **12b** was isolated as a colorless oil, which was unstable in neat state. Yield 485 mg (85%). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.28 (t, *J* 7.2 Hz, 6H), 4.11–4.63 (br m, 6H), 4.93–5.30 (br m, 2H), 6.80 (d, *J* 5.5 Hz, 1H), 7.20 (d, *J* 5.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 14.3 (q), 44.3 (br t), 62.3 (t), 62.5 (t), 123.7 (d), 124.2 (d), 128.5, 130.6 (br s), 155.2 (br s). MS *m/z* (M^+) calcd. 284.083, obsd. 284.083.

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[12] Commercial dimethyl maleate (**14**; Fluka) contains 4–5% of dimethyl fumarate (**13**). It appears difficult to achieve fumarate-free **14** due to isomerization and close boiling points; see (a) *H. P. Kaufmann* and *W. Wolf*, Fette und Seife **50**, 519 (1943), (Chem. Abstr. **39**, 205 (1945)); (b) *R. P. Linstead* and *M. Whalley*, J. Chem. Soc. 4839 (1952). A recent Japanese patent, dealing with the purification of **14**, reports a purity of 99.53% obtained in the preparation from maleic anhydride: *H. Yoshida, H. Tawara, M. Kamioka, M. Baba* and *A. Okubo*, Jpn. Kokai Tokkyo Koho Jp 61,246,147 [86,246,147] (Chem. Abstr. **106**, 119301w (1987)). Our own attempts to purify commercial **14** by selectively removing **13** on the basis of the fast reaction with **1** were only partially successful; about 2% of **13** was still present after two treatments with **1**, this percentage did not decrease upon a third treatment (Ref. 3b).

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[14] *G. Koster* and *M. T. Nguyen*, Dept. of Organic Chemistry, Groningen University, personal communication: MO calculations by *ab-initio* SCF method (HF 3-21 G level) (*cf.* Ref. 3b).

[15] The initial formation of a small amount of **7** is explained by an oxidation–reduction process with diethyl acetylenedicarboxylate to give some diethyl fumarate and diethyl maleate (1:1) (for further details, see Ref. 3b).

[16] Spectroscopic evidence of **1** has meanwhile been procured by *Schweig* et al.[2f] and by *Trahanovsky* et al., to be published (also Ref. 2m).

[17a] A higher acidity of 2-methylthiophene over 3-methylthiophene would be consistent with the suggested explanation. However, no pK_a values are available. The only potential relevant information at this point may be that the 2-methyl peak in ^{1}H NMR is at about 0.2 ppm at lower field as compared to 3-methylthiophene: see *e.g. S. Gronowitz* and *A-B. Hörnfeldt* in "The Chemistry of Heterocyclic Compounds, Vol. 44", "Thiophene and its Derivatives", Part 4 (*S. Gronowitz*, Ed.) Wiley 1991, p. 1–295, in particular p. 61 ff;

[b] One referee has suggested that the diminished reactivity of **5a** could also be explained by assuming "that Et_2MeN is a somewhat poorer leaving group". This may be true indeed. In aqueous solution Et_2MeN is a stronger base than Me_3N by about 0.5 pK unit[38], which in terms of electronic effects is consistent with this suggestion. Inasmuch as a greater relief of steric strain is involved with the $Et_2MeN^+CH_2$ group, differences in leaving group ability between Et_2MeN and Me_3N, however, will decrease.

[18] The dimeric structures tentatively proposed in our preliminary work[3a] are incorrect. The revised structure **15a** is based on ^{1}H-NMR comparison with deuterated analogs: a tetradeuterated one (**15b**, this paper) and a dideuterated one by *Trahanovsky* et al., to be published (also Ref. 2b). The ^{1}H-NMR spectrum of the major component (**15a**) of the mixture of spiro dimers showed two broad singlets at δ 5.08 and 5.18 (=CH_2, absent in **15b**), two AB quartets at δ 5.58, 6.12 (H11+H12) and δ 6.70, 7.00 (H2+H3), and a broad multiplet between δ 2.5–3.5 (H5+H6) with a singlet at δ 2.8 (H8, absent in **15b**). The regioisomeric structure for **15**, *i.e.* product of reaction of same 3-methylene group as dienophile in reversed direction, would require the singlet at δ 2.8 (in that case due to 2 H5) to remain intact in the tetradeurated spiro dimer. Furthermore, structure **15a** is the preferred one on the basis of calculated energies of activation of formation of the various dimers[14]. For the structure of a related dimer, stabilized with two methyl carboxylate groups, see Ref. 2o.

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[36] See procedure of **24** and footnote 35.

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