

Synthesis of 2,3,5-triaryl-4-trifluoromethyl thiophenes

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Abstract

Triaryl- β -trifluoromethyl thiophenes are synthesized from 1,3-dithiolium-4-olates and various substituted 1-aryl-3,3,3-trifluoro-1-propynes. The spectroscopic characteristics of the products and the regioselectivity of the reaction are discussed.

Keywords: Trifluoromethyl thiophenes; 1,3-Dipolar cycloaddition; MS spectrometry

1. Introduction

In the last few years fluorinated molecules have attracted the interest of both academic and industrial researchers [1,2]. Several examples demonstrate that the introduction of a fluoroalkyl moiety into a target molecule often improves its performance [3,4].

A number of thiopene derivatives are known to be effective agrochemicals, among these, 3-(4-chlorophenyl)-2,5-diphenyl thiophene is the active ingredient of the miticide "Micromite" [5]. So, in our search for new acaricidal products, we decided to start with a program for the synthesis of triaryl thiophenes incorporating a trifluoromethyl group. Only recently have papers appeared dealing with the preparation of thiophenes bearing a fluoroalkyl group in the β -position [6,7]. The synthesis of 2,5-diphenyl-3,4-bis-(trifluoromethyl)thiophene from mesoionic anhydro-4-hydroxy-2,3,5-triphenylthiazolium hydroxide and hexafluoro-2-butyne has been previously reported [8]. The use of 1,3-thiazolium-4-olates, however, may lead to the formation of another product arising from a competitive reaction pathway during the elimination step, so that this method may not be of general application. Other mesoionic compounds, such as 1,3-oxathiolium-5-olates that, in principle, could be employed, do not appear to be of practical use [9].

Among the methods available for the synthesis of thiophenes, the 1,3-dipolar cycloaddition of mesoionic 1,3-dithiolium-4-olates with alkynes represents a suitable way for our purpose [10,11].

We have thus prepared new β -trifluoromethyl-substituted thiophenes **3** and **4** employing 1-aryl-3,3,3-trifluoro-1-propynes **2** and 1,3-dithiolium-4-olates **1** as shown in Scheme 1 (Table 1). This study gives us the occasion to extend the synthetic usefulness of alkynes **2** in the construction of trifluoromethyl substituted five-membered heterocyclic rings.

2. Results and discussion

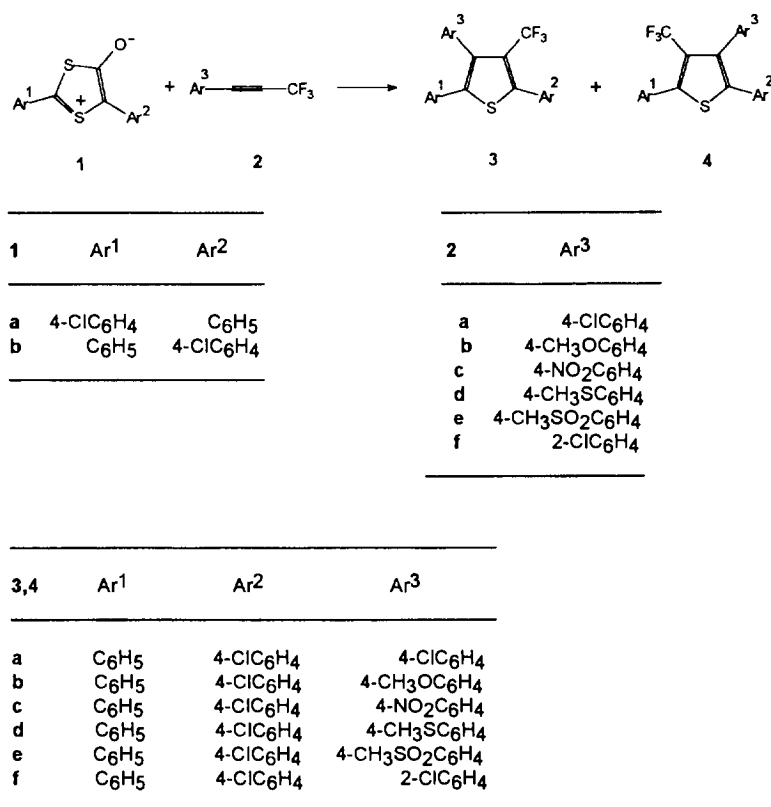
The results collected in Table 1 show that aryltrifluoromethyl alkynes **2a–f** undergo 1,3-dipolar cycloaddition with 1,3-dithiolium-4-olates **1a,b** in fair yields with good regioselectivity. The reaction was accomplished by heating for 20–32 h equimolar amounts of the two reagents in xylene at 120 °C, until the disappearance of the purple color. The progress of the reaction can be controlled by GC and TLC analyses.

As already remarked, similar results were achieved using other dipoles, i.e. nitrile oxides, nitrile imines, sydnone and azides [12–15].

In general, the dipole **1a** gives a lower degree of regioselectivity than that recorded with **1b**. The presence of electron withdrawing groups in the aryl moiety of the dipolarophile (**2c** and **2e**) lowers the regioselectivity by altering the charge distribution in the alkyne. Further, the heavy influence of steric hindrance is observed when employing **2f**.

As previously pointed out inverting the substituents Ar¹ and Ar² in the mesoionic reagent the isomer ratio was completely reversed. In fact, employing **1a** and **2a**, compounds **3a** and **4a** were obtained in 91:9 ratio; whereas by treating **1b** with **2a**, **3a** and **4a** were formed in 2:98 ratio.

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Scheme 1.

Table 1
Yield and regioselectivity of the reaction 1 + 2 to give 3 + 4

Products	Reagents	Yield ^a (%)	Reaction time (h)	Ratio ^b 3/4
3a/4a	1a + 2a	60	20	91:9
3a/4a	1b + 2a	61	20	2:98
3b/4b	1a + 2b	50	20	93:7
3b/4b	1b + 2b	73	20	5:95
3c/4c	1a + 2c	70	20	89:11
3c/4c	1b + 2c	62	20	24:76
3d/4d	1a + 2d	55	20	90:10
3d/4d	1b + 2d	61	20	4:96
3e/4e	1a + 2e	66	32	86:14
3e/4e	1b + 2e	53	32	5:95
3f/4f	1a + 2f	57	20	81:19
3f/4f	1b + 2f	67	20	15:85

^a Yield refers to the mixture 3 + 4 after chromatography.^b The ratios 3:4 were estimated by GC analysis (capillary column SIM-DIST CB, i.d. = 0.32 mm, length 10 m, temperature program 80–320 °C).

A similar behaviour was observed by Gotthardt in the reaction between ethyl 3-phenylpropynoate and anhydro-4-hydroxy-2-(4-methoxyphenyl)-5-phenyl-1,3-dithiolium hydroxide or anhydro-4-hydroxy-5-(4-methoxyphenyl)-2-phenyl-1,3-dithiolium hydroxide, which led to the formation of ethyl 2-(4-methoxyphenyl)-4,5-diphenyl-3-thiophene carboxylate and ethyl 5-(4-methoxyphenyl)-2,4-diphenyl-3-thiophene carboxylate in 97:3 and 6:94 ratios, respectively [11]. The observed regioselectivity can be explained by taking into account Houk's model for the HOMO–LUMO inter-

actions of the reacting species [16–18]. As already established, the cycloadditions involving 1,3-dithiolium-4-olates are HOMO-dipole controlled reactions. In addition, in our case the presence of the electron-deficient withdrawing group CF₃ lowers the LUMO energy of the dipolarophile so that the reaction character is reinforced.

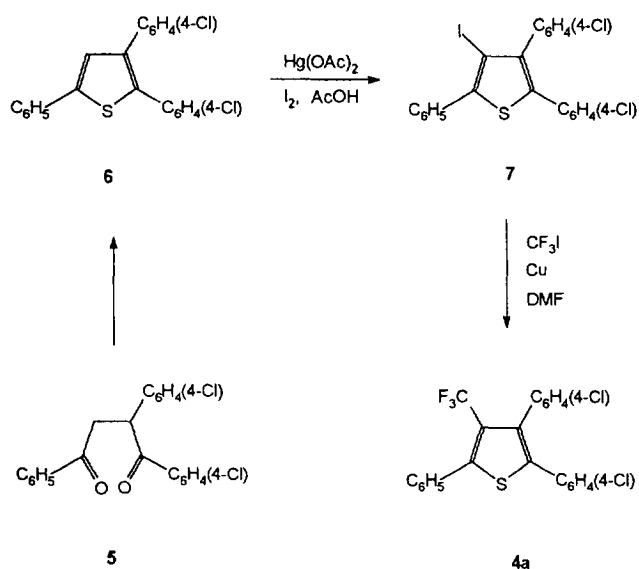
It is known that the 1,3-dithiolium-4-olates **1** possess a larger HOMO atomic orbital coefficient at C5 than at C2 and the alkyne **2** has a larger LUMO atomic orbital coefficient at C1 than at C2. Moreover, the preferred regioisomeric transition state will be the one in which the C5 dipole–C1 dipolarophile and C2 dipole–C2 dipolarophile interactions dominate.

The structure of compounds **3** and **4**, assigned on the basis of their spectroscopic characteristics and FMO predictions, were confirmed by an alternative synthetic route.

Thiophene **4a** was unambiguously obtained in the following way. 2,3-bis(4-chlorophenyl)-5-phenyl thiophene (**6**) prepared by treatment of 1,2-bis(4-chlorophenyl)-4-phenylbutane-1,4-dione (**5**) with Lawesson's reagent (4-methoxyphenylthionophosphine sulphide dimer) was converted into its 4-iodo derivative **7** by means of mercuric acetate/iodine and subsequently to the compound **4a** with CF₃I/Cu powder (Scheme 2).

2.1. Spectra

The mass spectra of compounds **3** and **4** have been investigated. Here we summarise some characteristics that allow



us to distinguish between the two regioisomers and give an attempt of rationalisation of the observed experimental results.

The fragmentation pathways give rise to the formation of highly stabilized polycyclic ions [19] (Fig. 1).

For all compounds M^+ is the base peak except in the case of **3f** in which the loss of CF_3 and R from the M^+ ion has double probability to occur. The M^{2+} peak and other doubly charged ions are also present. Both compounds **3** and **4** show the $(M - CF_3 - R)^+$ peak (m/z 344) **8** and its doubly charged ion (m/z 172); further compounds **3** and **4**, after elimination of Cl and R from the M^+ ion, give the ion **9** (m/z 378) besides to its doubly charged ion (m/z 189). Then ion **9** loses CF_3 and H to give the ion **10**, and also in this case the corresponding doubly charged ion (m/z 154) is detected. Moreover ion **10** gain higher stability through the elimination of the sulphur atom to give the ion **11** (m/z 276). Other diagnostic peaks are $C_6H_4CS^+$ (m/z 155) and $C_6H_5CS^+$ (m/z 121). In compounds **3** the m/z 344 peak is more abundant than the m/z 378 peak and the m/z 155 peak is more abundant than the m/z 121 peak. Conversely in compound **4** the m/z 378 and m/z 121 peaks are more abundant than the m/z 344 and m/z 155 peaks respectively. This may be explained by the fact that compounds **4** can give the ion **9** directly from the parent compound. Further fragmentation of **9** leads to $C_6H_5CS^+$. In the case of **3** the formation of **9** requires scrambling of the groups on the thiophene ring. Furthermore, compounds **3** can also give the $(M - R - H)^+$ **12** directly from the parent compound. Further fragmentation of **12** leads to $C_6H_4CS^+$. These differences between the mass spectra of **3** and **4** are amplified in CID experiments.

The ^{19}F NMR spectra of the crude reaction mixtures show, as expected, tiny differences, and when resolved the trifluoromethyl group of **3** resonates at slightly lower field than that of **4**.

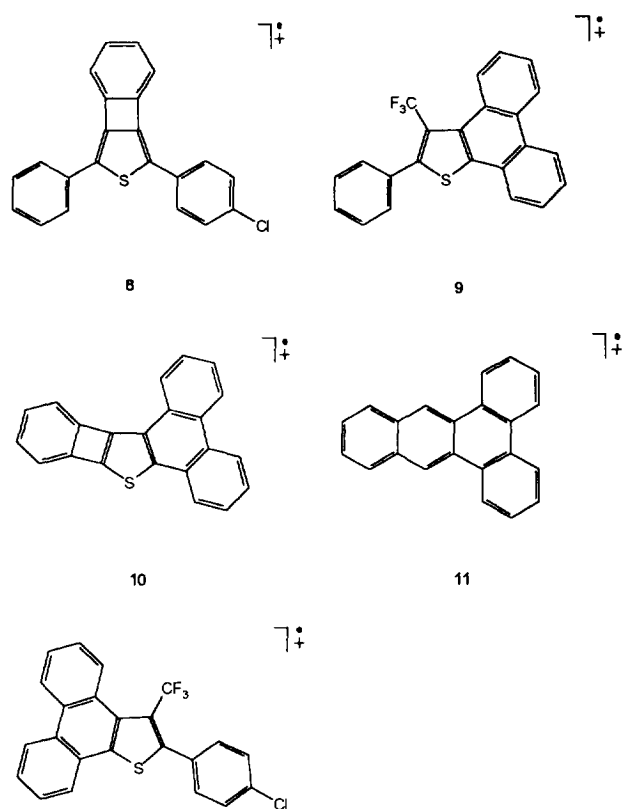


Fig. 1. Polycyclic ions formed in MS analyses.

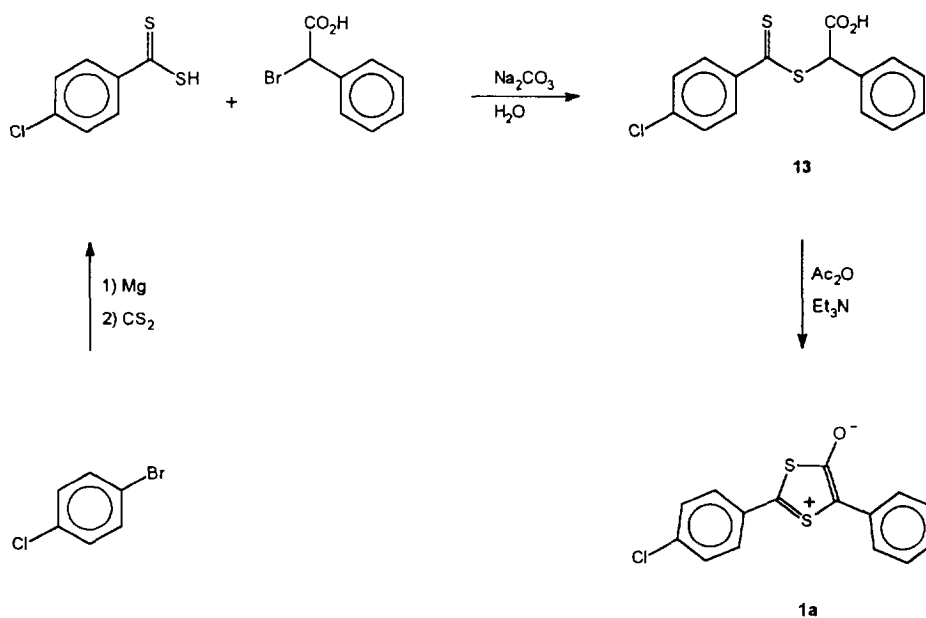
3. Experimental details

Analytical TLC plates and silica gel (230–400 mesh) were purchased from Merck. Melting points were determined using a Buchi SMP-20 apparatus and are reported uncorrected. GC analyses were carried out on a Carlo Erba HRGC 5300 chromatograph. Microanalyses were obtained using a Perkin-Elmer 2400 CHN element analyser. Mass spectra were obtained using a Finnigan MAT INCOS 50 spectrometer with an electron impact source at 70 eV, a Finnigan MAT 8400 double-focusing reversed-geometry mass spectrometer for DIP-EI (70 eV) and CID (argon) experiments. MS/MS experiments were performed on a Finnigan MAT TSQ 700 triple-quadrupole instrument. IR spectra were obtained using a Perkin-Elmer 1420 spectrophotometer. The NMR spectra were recorded with a Bruker AC 200 spectrometer at 200.13 MHz (1H) and 188.3 MHz (^{19}F) with $CDCl_3$ as the solvent. TMS was used as the internal standard for the 1H NMR spectra and $CFCl_3$ as the internal standard for the ^{19}F NMR spectra.

All reagents were of commercial quality. Anhydrous solvents were dried on molecular sieves.

Lawesson's reagent, 4-bromochlorobenzene, α -bromophenylacetic acid and 2-bromoacetophenone was purchased from Aldrich.

Aryl trifluoromethylalkynes **2a–f** [12,15], anhydro-4-hydroxy-5-(4-chlorophenyl)-2-phenyl-1,3-dithiolium



Scheme 3.

hydroxide (**1b**) [20] and 1,2-bis(4-chlorophenyl) ethanone [21] were prepared as described previously.

3.1. Anhydro-4-hydroxy-2-(4-chlorophenyl)-5-phenyl-1,3-dithiolium hydroxide (**1a**) (Scheme 3)

To a stirred mixture of magnesium turnings (2.6 g, 107.0 mmol) in anhydrous ethyl ether (200 ml), 4-bromochlorobenzene (20.4 g, 107.0 mmol) dissolved in anhydrous ethyl ether (20 ml) was added dropwise in 20 min. After consumption of magnesium, the resulting mixture was cooled at 0 °C and treated with carbon disulfide (16 ml, 265.6 mmol) dissolved in anhydrous ethyl ether (16 ml).

The mixture was stirred at 0 °C for 3 h then allowed to stand overnight at room temperature. The mixture was filtered over celite pad and the filtrate was washed several times with ethyl ether. The red aqueous solution thus obtained was treated at 0 °C with a solution of α -bromophenylacetic acid (14.30 g, 66 mmol) and sodium carbonate (3.5 g, 33 mmol) in water (60 ml). The mixture was stirred at 0 °C for 4 h then allowed to stand overnight at 4 °C. The solid was filtered and crystallized from methyl alcohol to give the pure product **13**. Yield: 10.8 g (31% based on 4-bromochlorobenzene). m.p., 160–161 °C. ¹H NMR: δ 5.70 (s, 1H); 6.60 (bs, 1H); 7.25–7.46 (m, 7H); 7.92–7.96 (d, 2H). IR (Nujol): 1720(s), 1595(w) cm⁻¹.

To a stirred suspension of (α -carboxybenzyl)-4-chlorophenyldithiobenzoate **13** (10 g, 31 mmol) in Ac₂O (20 ml), Et₃N (20 ml) was added dropwise with cooling. The mixture was stirred at 8–10 °C for 2 h, then allowed to stand overnight at room temperature. The product was filtered and washed with a cold 1:1 mixture of cyclohexane–ethyl ether. Crystallization from CH₃CN affords the pure product **1a**. Yield: 5.2 g (55%). m.p., 163–164 °C. ¹H NMR: δ 7.25–7.85 ppm (m, arom.). IR (Nujol): 1605(s), 1585(s) cm⁻¹. Mass spectrum

m/z (%): 304 (M⁺, 15); 155 (ClC₆H₄CS⁺, 6); 121 (C₆H₅CS⁺, 100).

Analysis, found (calc.): C, 58.72 (59.11); H, 3.08 (2.98).

3.2. 2,3,5-Triaryl-4-trifluoromethyl thiophenes **3a–f** and **4a–f**: general procedure

1,3-dithiolium-4-olates **1a,b** (0.61 g, 2 mmol) and alkynes **2a–f** (2 mmol) were suspended in anhydrous xylenes (2 ml). The mixture was heated at 120 °C for the time indicated in Table 1. The solvent was evaporated at reduced pressure and the crude reaction mixture was subjected to column chromatography, then crystallized to give the pure regioisomers **3a–f** or **4a–f**. Analytical data for the compounds obtained are as follows:

3a: m.p., 167–168 °C (*n*-hexane). ¹⁹F NMR: δ –52.61 ppm. IR (Nujol): 1602 (w), 1112 (s) (cm⁻¹). Mass spectrum m/z (%): 448 (M⁺, 100); 413 (M⁺ – Cl, 8); 412 (M⁺ – HCl, 6); 378 (M⁺ – 2Cl, 7); 344 (M⁺ – Cl – CF₃, 32); 308 (M⁺ – Cl – CF₃ – HCl, 15); 276 (4), 189 ((M – 2Cl)²⁺, 3); 172 ((M – CF₃ – Cl)²⁺, 10); 155 (ClC₆H₄CS⁺, 20); 154 (10); 121 (C₆H₅CS⁺, 6). Analysis, found (calc.): C, 61.31 (61.48); H, 2.95 (2.91); F, 12.98 (12.68).

4a: m.p., 158–159 °C (*n*-hexane). ¹⁹F NMR: δ –52.65 ppm. IR (Nujol): 1605 (w), 1118 (s) (cm⁻¹). Mass spectrum m/z (%): 448 (M⁺, 100); 413 (M⁺ – Cl, 3); 412 (M⁺ – HCl, 4); 378 (M⁺ – 2Cl, 17); 344 (M⁺ – Cl – CF₃, 25); 308 (M⁺ – Cl – CF₃ – HCl, 20); 276 (5), 189 ((M – 2Cl)²⁺, 27); 172 ((M – CF₃ – Cl)²⁺, 22); 155 (ClC₆H₄CS⁺, 19); 154 (23); 121 (C₆H₅CS⁺, 45). Analysis, found (calc.): C, 61.52 (61.48); H, 2.96 (2.91); F, 12.91 (12.68).

- 3b:** m.p., 135–136 °C (*n*-hexane). ^{19}F NMR: δ –52.77 ppm. IR (Nujol): 1620 (m), 1253 (s) 1119 (s) (cm^{-1}). Mass spectrum m/z (%): 444 (M^+ , 100), 429 ($\text{M}^+ - \text{CH}_3$, 3); 413 ($\text{M}^+ - \text{CH}_3\text{O}$, 2); 374 ($\text{M}^+ - \text{CF}_3 - \text{H}$, 7); 360 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3$, 5); 344 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{O}$, p); 331 (19); 295 (8); 222 (M^{2+} , 2); 180 ($(\text{M} - \text{CF}_3 - \text{CH}_3)^{2+}$, 7); 172 ($(\text{M} - \text{CF}_3 - \text{CH}_3\text{O})^{2+}$, 6); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 10); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 4). Analysis, found (calc.): C, 64.99 (64.79); H, 3.83 (3.62); F, 12.98 (12.81).
- 4b:** m.p., 154–155 °C (*n*-hexane). ^{19}F NMR: δ –52.83 ppm. IR (Nujol): 1618 (m), 1255 (s), 1138 (s) (cm^{-1}). Mass spectrum m/z (%): 444 (M^+ , 100), 429 ($\text{M}^+ - \text{CH}_3$, 1); 394 ($\text{M}^+ - \text{Cl} - \text{CH}_3$, 3); 374 ($\text{M}^+ - \text{CF}_3 - \text{H}$, 2); 366 (10); 344 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{O}$, 6); 331 (5); 297 (23); 222 (M^{2+} , 5); 205 (17); 172 ($(\text{M} - \text{CF}_3 - \text{CH}_3\text{O})^{2+}$, 14); 170 (39); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 10); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 22). Analysis, found (calc.): C, 65.03 (64.79); H, 3.68 (3.62); F, 13.04 (12.81).
- 3c:** m.p., 174–175 °C (*n*-hexane–ethylacetate 8:2). ^{19}F NMR: δ –52.45 ppm. IR (Nujol): 1608 (m), 1527 (s) 1126 (s) (cm^{-1}). Mass spectrum m/z (%): 459 (M^+ , 100); 413 ($\text{M}^+ - \text{NO}_2$, 5); 412 ($\text{M}^+ - \text{HNO}_2$, 4); 378 ($\text{M}^+ - \text{Cl} - \text{NO}_2$, 3); 344 ($\text{M}^+ - \text{NO}_2 - \text{CF}_3$, 26); 308 ($\text{M}^+ - \text{NO}_2 - \text{CF}_3 - \text{HCl}$, 20); 276 (4), 189 ($(\text{M} - \text{Cl} - \text{NO}_2)^{2+}$, 2); 172 ($(\text{M} - \text{NO}_2 - \text{CF}_3)^{2+}$, 9); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 8); 154 (10); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 6). Analysis, found (calc.): C, 62.31 (62.24); H, 2.85 (2.95); F, 12.88 (12.84).
- 4c:** m.p., 192–193 °C (*n*-hexane–ethylacetate 8:2). ^{19}F NMR: δ –52.42 ppm. IR (Nujol): 1605 (w), 1516 (s), 1110 (s) (cm^{-1}). Mass spectrum m/z (%): 459 (M^+ , 100); 378 ($\text{M}^+ - \text{Cl} - \text{NO}_2$, 21); 344 ($\text{M}^+ - \text{NO}_2 - \text{CF}_3$, 12); 308 ($\text{M}^+ - \text{NO}_2 - \text{CF}_3 - \text{HCl}$, 19); 276 (4), 189 ($(\text{M} - \text{Cl} - \text{NO}_2)^{2+}$, 10); 172 ($(\text{M} - \text{NO}_2 - \text{CF}_3)^{2+}$, 5); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 3); 154 (8); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 10). Analysis, found (calc.): C, 62.59 (62.24); H, 3.01 (2.95); F, 13.07 (12.84).
- 3d:** m.p., 163–164 °C (*n*-hexane–ethylacetate 9:1). ^{19}F NMR: δ –52.63 ppm. IR (Nujol): 1602 (w), 1114 (s) (cm^{-1}). Mass spectrum m/z (%): 460 (M^+ , 100); 445 ($\text{M}^+ - \text{CH}_3$, 2); 412 ($\text{M}^+ - \text{CH}_3\text{S} - \text{H}$, 8); 378 ($\text{M}^+ - \text{CH}_3\text{S} - \text{Cl}$, 2); 344 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{S}$, 18); 308 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{S} - \text{HCl}$, 11); 230 (M^{2+} , 5); 189 ($(\text{M} - \text{CH}_3\text{S} - \text{Cl})^{2+}$, 7); 172 ($(\text{M} - \text{CF}_3 - \text{CH}_3\text{S})^{2+}$, 24); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 17); 154 (13); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 6). Analysis, found (calc.): C, 62.68 (62.54); H, 3.52 (3.50); F, 12.60 (12.36).
- 4d:** m.p., 143–144 °C (*n*-hexane–ethylacetate 9:1). ^{19}F NMR: δ –52.69 ppm. IR (Nujol): 1608 (w), 1132 (s) (cm^{-1}). Mass spectrum m/z (%): 460 (M^+ , 100); 445 ($\text{M}^+ - \text{CH}_3$, 2); 412 ($\text{M}^+ - \text{CH}_3\text{S} - \text{H}$, 4); 378 ($\text{M}^+ - \text{CH}_3\text{S} - \text{Cl}$, 14); 344 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{S}$, 9); 308 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{S} - \text{HCl}$, 13), 230 (M^{2+} , 7); 189 ($(\text{M} - \text{CH}_3\text{S} - \text{Cl})^{2+}$, 9); 172 ($(\text{M} - \text{CF}_3 - \text{CH}_3\text{S})^{2+}$, 14); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 9); 154 (10); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 15). Analysis, found (calc.): C, 62.64 (62.54); H, 3.48 (3.50); F, 12.48 (12.36).
- 3e:** m.p., 190–191 °C (*n*-hexane–ethylacetate 8:2). ^{19}F NMR: δ –52.33 ppm. IR (Nujol): 1605 (w), 1159 (s), 1132 (s) (cm^{-1}). Mass spectrum m/z (%): 492 (M^+ , 100); 413 ($\text{M}^+ - \text{CH}_3\text{SO}_2$, 8); 412 ($\text{M}^+ - \text{CH}_3\text{SO}_2 - \text{H}$, 6); 378 ($\text{M}^+ - \text{CH}_3\text{SO}_2 - \text{Cl}$, 4); 344 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{SO}_2$, 46); 308 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{SO}_2 - \text{HCl}$, 26); 246 (M^{2+} , 1); 189 ($(\text{M} - \text{CH}_3\text{SO}_2 - \text{Cl})^{2+}$, 5); 172 ($(\text{M} - \text{CF}_3 - \text{CH}_3\text{SO}_2)^{2+}$, 22); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 18); 154 (19); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 5). Analysis, found (calc.): C, 58.37 (58.48); H, 3.22 (3.27); F, 11.82 (11.56).
- 4e:** m.p., 190–191 °C (*n*-hexane–ethylacetate 8:2). ^{19}F NMR: δ –52.36 ppm. IR (Nujol): 1609 (w), 1321 (s), 1159 (s), 1121 (s) (cm^{-1}). Mass spectrum m/z (%): 492 (M^+ , 100); 378 ($\text{M}^+ - \text{CH}_3\text{SO}_2 - \text{Cl}$, 3); 344 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{SO}_2$, 20); 308 ($\text{M}^+ - \text{CF}_3 - \text{CH}_3\text{SO}_2 - \text{HCl}$, 24); 189 ($(\text{M} - \text{CH}_3\text{SO}_2 - \text{Cl})^{2+}$, 5); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 3); 154 (10); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 16). Analysis, found (calc.): C, 58.58 (58.48); H, 3.34 (3.27); F, 11.72 (11.56).
- 3f:** m.p., 69–70 °C (*n*-hexane–ethylacetate 8:2). ^{19}F NMR: δ –54.20 ppm. IR (Nujol): 1604 (w), 1328 (s), 1175 (s), 1123 (s) (cm^{-1}). Mass spectrum m/z (%): 448 (M^+ , 68); 412 ($\text{M}^+ - \text{HCl}$, 7); 344 ($\text{M}^+ - \text{Cl} - \text{CF}_3$, 100); 308 ($\text{M}^+ - \text{Cl} - \text{CF}_3 - \text{HCl}$, 29); 276 (4), 224 (M^{2+} , 5); 189 ($(\text{M} - 2\text{Cl})^{2+}$, 15); 172 ($(\text{M} - \text{CF}_3 - \text{Cl})^{2+}$, 36); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 29); 154 (24); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 8). Analysis, found (calc.): C, 61.42 (61.48); H, 3.04 (2.91); F, 12.66 (12.68).
- 4f:** m.p., 94–95 °C (*n*-hexane). ^{19}F NMR: δ –54.22 ppm. IR (Nujol): 1325 (s), 1174 (s), 1123 (s) (cm^{-1}). Mass spectrum m/z (%): 448 (M^+ , 100); 412 ($\text{M}^+ - \text{HCl}$, 6); 378 ($\text{M}^+ - 2\text{Cl}$, 33); 344 ($\text{M}^+ - \text{Cl} - \text{CF}_3$, 66); 308 ($\text{M}^+ - \text{Cl} - \text{CF}_3 - \text{HCl}$, 32); 276 (3), 224 (M^{2+} , 7); 189 ($(\text{M} - 2\text{Cl})^{2+}$, 17); 172 ($(\text{M} - \text{CF}_3 - \text{Cl})^{2+}$, 14); 155 ($\text{C}_6\text{H}_4\text{CS}^+$, 7); 154 (13); 121 ($\text{C}_6\text{H}_5\text{CS}^+$, 23). Analysis, found (calc.): C, 61.30 (61.48); H, 2.99 (2.91); F, 12.86 (12.68).

3.3. 1,2-Bis(4-chlorophenyl)-4-phenylbutane-1,4-dione (5)

To a stirred solution of sodium ethylate prepared from Na (0.48 g, 20.8 mmol) in ethyl alcohol (30 ml), 1,2-bis(4-chlorophenyl) ethanone [21] (5.4 g, 20.0 mmol) was

added. After 10 min 2-bromoacetophenone (4.0 g, 20.0 mmol) was added in one portion. The mixture was heated at 78 °C for 2 h, then poured into water and extracted with ethylacetate. The organic layer was washed with water and dried with sodium sulfate. The solvent was evaporated at reduced pressure and the crude product mixture was chromatographed on a silica gel column, eluted with *n*-hexane–ethyl acetate 85:15. Crystallization from *n*-hexane gave the pure product (**5**); yield: 5.1 g (57%). m.p. 134–135 °C. ¹H NMR: δ 3.23–3.34 (dd, 1 H, *J* = 18.0 Hz, *J* = 3.8 Hz; H-2); 4.09–4.23 (dd, 1H, *J* = 18.0 Hz, *J* = 9.9 Hz; H-3); 5.20–5.27 (dd, 1H, *J* = 9.9 Hz, *J* = 3.8 Hz; H-3); 7.14–7.98 (m, 13H; aryl protons).

Mass spectrum *m/z* (%): 382 (M⁺, 35); 243 (M⁺ – ClC₆H₄CO, 5); 139 (ClC₆H₄CO⁺, 100); 111 (19); 105 (37); 77 (38).

3.4. 2,3-Bis(4-chlorophenyl)-5-phenyl thiophene (**6**)

A 250 ml stainless-steel bomb was charged with 1,2-bis(4-chlorophenyl)-4-phenylbutane-1,4-dione (**5**) (3.0 g, 7.8 mmol), Lawesson's reagent [22] (3.6 g, 8.9 mmol) and anhydrous toluene (20 ml). The bomb was cooled to –78 °C, charged with hydrogen sulfide (3.4 g, 100 mmol) and heated to 120 °C under magnetical stirring. After 4 h at 120 °C the bomb was cooled and the crude mixture was chromatographed on a silica gel column, eluted with *n*-hexane–ethyl acetate 95:5. Crystallization from methanol–chloroform 8:2 gave the pure product **6**; yield: 1.85 g (62%). m.p., 143–144 °C. ¹H NMR: δ 7.20–7.65 (m, aryl protons). Mass spectrum *m/z* (%): 380 (M⁺, 100); 344 (M⁺ – HCl, 12); 310 (M⁺ – 2HCl, 34); 189 (13); 173 (15); 155 ((M – 2HCl)²⁺, 77); 154 (42); 121 (C₆H₅CS⁺, 24); 77 (18).

3.5. 2,3-Bis(4-chlorophenyl)-4-iodo-5-phenyl thiophene (**7**)

To a stirred solution of 2,3-bis(4-chlorophenyl)-5-phenyl thiophene **6** (1.8 g, 4.7 mmol) and mercury(II) acetate (1.6 g, 5 mmol) in acetic acid (30 ml), iodine (1.27 g, 0.5 mmol) was added. The mixture was heated at 100 °C for 1 h, then poured into water and extracted with ethyl ether. The organic layer was treated with an aqueous solution of potassium iodide, washed with water and dried with sodium sulfate. Evaporation of the solvent and crystallization from ethyl alcohol affords 1.2 g (50%) of pure product **7**. m.p., 198–199 °C. ¹H NMR: δ 6.80–7.58 (m, aryl protons). Mass spectrum *m/z* (%): 506 (M⁺, 29); 380 (M⁺ – HI, 4); 344 (M⁺ – I – Cl, 21); 309 (M⁺ – I – 2Cl, 26); 308 (M⁺ – I – Cl – HCl, 26); 253 (M²⁺, 4); 172 ((M – I – Cl)²⁺, 37); 155 ((M – I – 2Cl)²⁺, 48); 154 ((M – I – Cl – HCl)²⁺, 100); 121 (C₆H₅CS⁺, 17); 111 (C₆H₄Cl⁺, 13).

3.6. 2,3-Bis(4-chlorophenyl)-4-trifluoromethyl-5-phenyl thiophene (**4a**)

A 100 ml stainless-steel bomb was charged with 2,3-bis(4-chlorophenyl)-4-iodo-5-phenyl thiophene **7** (1.0 g, 2.0 mmol), copper powder (0.64 g, 10 mmol) and anhydrous *N,N*-dimethylformamide. The bomb was closed, cooled to –50 °C and evacuated. Trifluoromethyl iodide (1.17 g, 6.0 mmol) was introduced and the bomb was gradually heated to 120 °C under magnetical stirring. After 48 h at 120 °C the bomb was cooled and the mixture was filtered over Celite, diluted with water and extracted with ethyl ether. The organic phase was washed with an aqueous solution of sodium thiosulfate and with water, dried with sodium sulfate and concentrated at reduced pressure. The crude product was crystallized twice from *n*-hexane to give 0.12 g of pure product, confirmed to be identical to **4a** by melting point, GC retention time and GC–MS spectrum.

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