

A COMBINATION OF FRIEDEL-CRAFTS AND LAWESSON REACTIONS TO 5-SUBSTITUTED 2,2'-BITHIOPHENES

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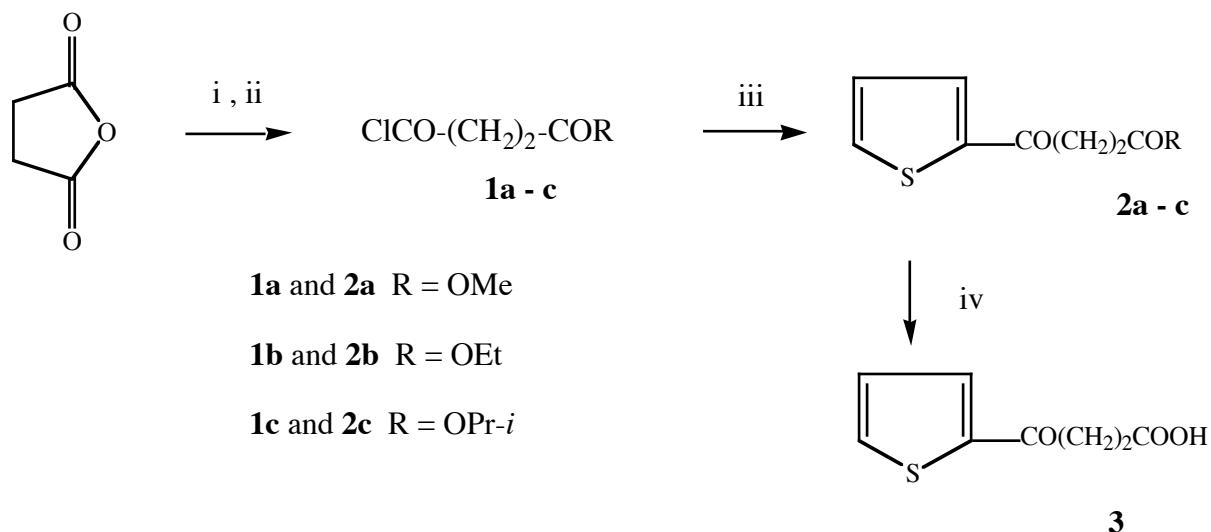
Abstract - γ -Keto esters (**2**) derivatives of thiophene were obtained from hemisuccinic esters and transformed to the corresponding amides (**4**). Lawesson's treatment of **2** and **4** gave the corresponding bithiophenes (**5**) with alkoxy or amino substituents.

In the past few years interest has been focused on new organic materials with non-linear optical properties,¹⁻³ and it was proved that, introduction of the thiophene nucleus enhance these properties.⁴⁻⁶ Thiophenes and oligothiophenes substituted by donor-acceptor groups have been extensively investigated.⁷⁻¹¹ These compounds are often used as energy transfer and light-harvesting systems¹²⁻¹⁴ and for optical and electronic devices.^{6, 10-11} Unsymmetrically substituted bithiophenes are usually synthesised by cross-coupling reactions; Stille,^{8, 15-18} Suzuki,¹⁹ or others²⁰⁻²² and by procedures involving thiophene ring formations.²³⁻²⁴ As part of our continuing interest in non-linear optical material²⁵⁻²⁶ we have synthesised several 5-substituted 2,2'-bithiophenes *via* a combination of Friedel-Crafts and Lawesson reactions.

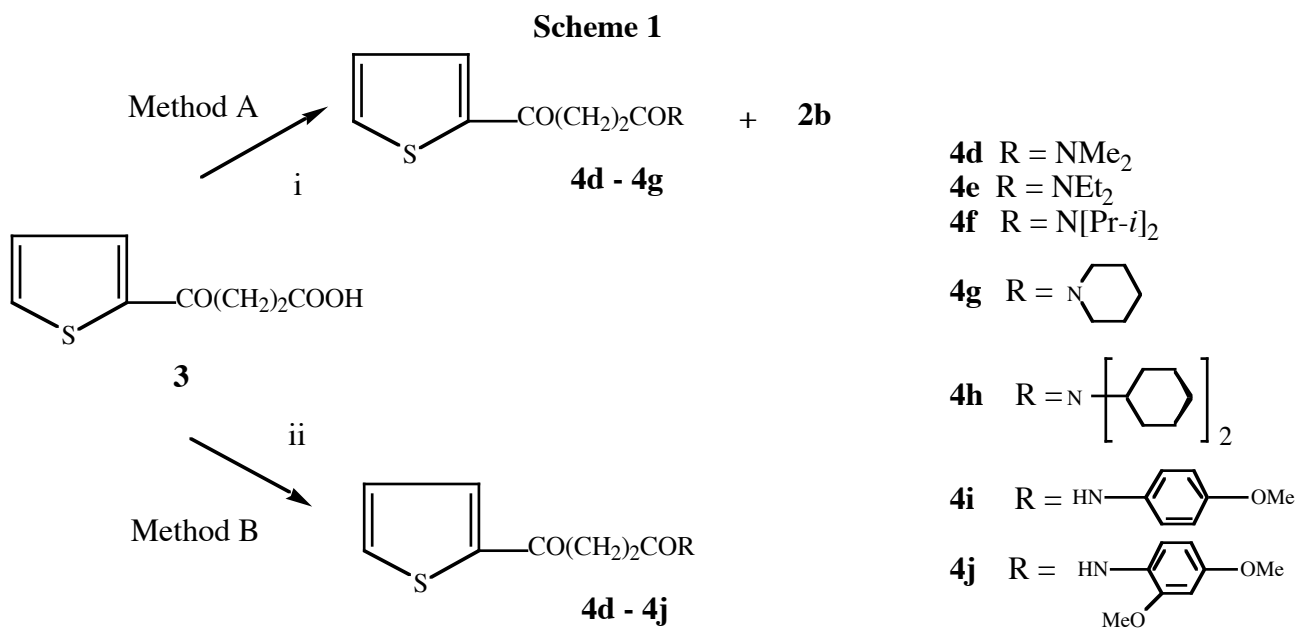
Starting from succinic anhydride, we have prepared the acid chlorides (**1**) which on Friedel-Crafts reaction with thiophene afforded the γ -keto esters (**2**). Hydrolysis of **2** gave the γ -keto acid (**3**) (Scheme 1).²⁷⁻³⁰

Transformation of **3** to amide (**4**) was made *via* two different synthetic routes (Scheme 2). The mixed anhydride was prepared and reacted with the amine in DMF (Method A) (Table 1). In these cases, low

yields and a secondary product, the γ -keto ester (**2b**) were always obtained. Direct amidation of the acid (**3**) with the amine was then run through DCC-BtOH catalysed reaction (Method B). No secondary products were detected and the yields were moderate to good (Table 1).



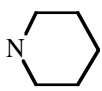
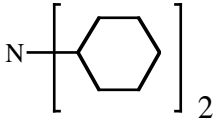
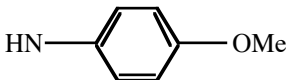
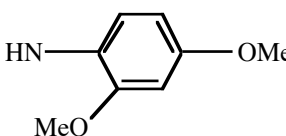
Reagents and conditions: i, RH, reflux; ii, SOCl_2 , CH_2Cl_2 , reflux; iii, Thiophene, SnCl_4 , CH_2Cl_2 ; iv, NaOH, 95% EtOH, reflux.



Reagents and conditions: i, EtOCOCl, NEt₃, DMF, amine; ii, DCC, BtOH, CH_2Cl_2 , amine.

Scheme 2

Table 1 Comparative yields of compounds (**4**) from γ -keto acid (**3**).


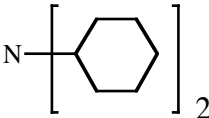

Compound	R	Method A (%)	Method B (%)
4d	NMe ₂	15	70
4e	NEt ₂	40	67
4f	N(Pr- <i>i</i>) ₂	35	33
4g		50	84
4h		----	52
4i		----	62
4j		----	64

Treatment of the esters (**2a-c**) and the amides (**4d-i**) with Lawesson's reagent (LR) afforded the corresponding alkoxy- and aminobithiophenes (**5**) (Scheme 3). The mechanism has been discussed by T. Nisho³¹ and it has been shown that pyrroles may become by-products in the case of secondary amides, this may explain the low field of **5i**.

The yields of alkoxybithiophenes (**5a-b**) were improved on addition of a 20% excess of Lawesson's reagent (Table 2).

In the case of the amides (**4**) no excess of Lawesson's reagent was used and the yields were moderate (Table 3). In fact the reaction runs faster than in the case of the esters.

Table 3 Yields of compounds (**5d - i**) from amides (**4**)

Compound	R	Yield(%)	Reaction time (min)
5d	NMe ₂	69	30
5e	NEt ₂	64	25
5f	N(Pr- <i>i</i>) ₂	53	35
5g		79	35
5h		63	60
5i		14	15

EXPERIMENTAL

¹H NMR spectra were obtained on a Varian Unity Plus Spectrometer at 300 MHz and ¹³C NMR spectra were determined in the same instrument at 75.4 MHz. The solvent are quoted in parenthesis before the chemical shift values (δ relative to internal CDCl₃). Mp were determined on a Gallenkamp apparatus and are uncorrected. IR spectra were recorded as Nujol mulls, on a Perkin Elmer 1600 FTIR Spectrophotometer, unless stated otherwise. UV spectra were recorded in ethanol on a Hitachi U-2000. EI MS were run on a Unicam GC-MS 120. Elemental analyses were made on a Leco CHNS-932. Column chromatography was performed on Merck silica gel 60 (Art 9385). Light petroleum refers to solvent boiling in the range 40-60 °C.

General procedure for the preparation of acid chlorides (**1**) .

The acid chlorides (70 mmol) were dissolved in 50 mL of dry dichloromethane and then thionyl chloride (12.5 g, 105 mmol) was added and the mixture was heated at reflux for 4-4.5 h. Evaporation of the solvent

under reduced pressure gave the crude acid chlorides (**1**) which were used without further purification in the Friedel-Crafts reactions.

3-Carbomethoxypropionyl chloride (1a) : colorless oil. Quantitative yield. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 2.80 (2H, t, \underline{J} = 6.6 Hz, CH_2), 3.20 (2H, t, \underline{J} = 6.6 Hz, CH_2), 3.71 (3H, s, OCH_3).

3-Carboethoxypropionyl chloride (1b)²⁷: colorless oil. Quantitative yield. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 1.25 (2H, t, \underline{J} = 6.7 Hz, OCH_2CH_3), 2.65 (2H, t, \underline{J} = 6.7 Hz, CH_2), 3.20 (2H, t, \underline{J} = 6.7 Hz, CH_2), 4.15 (2H, q, \underline{J} = 6.7 Hz, OCH_2CH_3).

3-Carboisopropoxypropionyl chloride (1c) : colorless oil. Quantitative yield. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 1.23 (6H, d, \underline{J} = 6.3 Hz, $\text{OCH}(\text{CH}_3)_2$), 2.63 (2H, t, \underline{J} = 6.3 Hz, CH_2), 3.19 (2H, t, \underline{J} = 6.3 Hz, CH_2), 5.05 (1H, sep, \underline{J} = 6.3 Hz, $\text{CH}(\text{CH}_3)_2$).

General procedure for the Friedel-Crafts reaction.

Acid chloride (**1**) (70 mmol) and thiophene (5.88 g, 70 mmol) in dry dichloromethane (200 mL) were added dropwise to a stirred solution of stannic chloride (20 g, 77 mmol) in dry dichloromethane (200 mL) at 0 °C. After the addition, the mixture was stirred overnight at rt and then poured onto ice-water (1000 mL), acidified with conc. HCl and stirred at 0 °C during 1 h. This mixture was extracted with dichloromethane (3x50 mL) and the combined organic extracts were washed with a solution of 20% NaOH (3x50 mL), water (2x200 mL) and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave the crude γ -keto esters (**2**) as oil which were purified by "flash" chromatography on silica with increasing amounts of ether in light petroleum as eluent.

Methyl 4-(2-thienyl)-4-oxobutanoate (2a)²⁸ : yellow oil. Yield 83%. Anal. Calcd for $\text{C}_9\text{H}_{10}\text{O}_3\text{S}$: C, 54.55; H, 5.05; S, 16.18. Found: C, 54.42; H, 5.18; S, 16.40. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 2.77 (2H, t, \underline{J} = 6.6 Hz, CH_2), 3.27 (2H, t, \underline{J} = 6.6 Hz, CH_2), 3.71 (3H, s, OCH_3), 7.12-7.16 (1H, m, 4'-H), 7.65 (1H, dd, \underline{J} = 5.2 and 1.3 Hz, 5'-H), 7.78 (1H, dd, \underline{J} = 3.9 and 1.3 Hz, 3'-H). MS (EI, 70 eV): m/z (%) 198 (M^+ , 17), 167 (18), 111 (100), 83 (13), 55 (20). IR ν_{max} (liquid film)/ cm^{-1} 1739, 1666.

Ethyl 4-(2-thienyl)-4-oxobutanoate (2b)²⁹ : pale yellow oil. Yield 83%. Anal. Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_3\text{S}$: C, 56.60; H, 5.65; S, 15.11. Found: C, 56.58; H, 5.79; S, 15.47. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 1.27 (3H, t, \underline{J} = 6.7 Hz, OCH_2CH_3), 2.76 (2H, t, \underline{J} = 6.7 Hz, CH_2), 3.26 (2H, t, \underline{J} = 6.7 Hz, CH_2), 4.18 (2H, q, \underline{J} = 6.7 Hz, OCH_2CH_3), 7.12-7.16 (1H, m, 4'-H), 7.65 (1H, dd, \underline{J} = 5.1 and 1.2 Hz, 5'-H), 7.78 (1H, dd, \underline{J} = 4.0 and 1.2 Hz, 3'-H). MS (EI, 70 eV): m/z (%) 213 ($\text{M}^+ + 1$, 12), 212 (M^+ , 57), 167 (5), 83 (100), 69 (23), 55 (19). IR ν_{max} (liquid film)/ cm^{-1} 1730, 1666.

Isopropyl 4-(2-thienyl)-4-oxobutanoate (2c): yellow oil. Yield 5%. Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_3\text{S}$: C, 58.41; H, 6.19; S, 14.18. Found: C, 58.41; H, 6.11; S, 14.22. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 1.25 (6H, d, \underline{J} = 6.3 Hz,

OCH(CH₃)₂), 2.74 (2H, t, $J = 6.3$ Hz, CH₂), 3.25 (2H, t, $J = 6.3$ Hz, CH₂), 5.04 (1H, sep, $J = 6.3$ Hz, CH(CH₃)₂) 7.12-7.16 (1H, m, 4'-H), 7.66 (1H, dd, $J = 5.4$ and 1.4 Hz, 5'-H), 7.78 (1H, dd, $J = 4.1$ and 1.4 Hz, 3'-H). MS (EI, 70 eV): m/z (%) 226 (M⁺, 12), 184 (4), 167 (42), 139 (8), 111 (100), 83 (13), 55 (24). IR ν_{\max} (liquid film)/cm⁻¹ 1728, 1667.

4-Oxo-(2-thienyl)butanoic acid (3)³⁰: Ester (**2b**) (1.5 g, 7 mmol) was heated at reflux for 1 h in a solution of sodium hydroxide (0.57 g, 14 mmol) in 95% ethanol (50 mL). The mixture was cooled and after evaporation was poured onto water and extracted with chloroform (3x50 mL). Acidification of the aqueous phase with conc. HCl till pH 1-2 gave **3** as a pale pink solid, mp 119-120.5 °C [lit.,³⁰ 119-120 °C]. Yield (1 g, 78%).

General procedure for the synthesis of amides (4d-g); Method A: EtOCOCI / NEt₃ / DMF.

Triethylamine (4.48 mL, 32.4 mmol) and ethyl chloroformate (3.12 mL, 32.4 mmol) were added dropwise to a stirred solution of the acid (**3**) (2.0 g, 10.8 mmol) in dry dimethylformamide (5 mL) at - 5 °C. After 15 min, the amine (10.8 mmol) was added and the mixture was stirred overnight at rt. Triethylamine hydrochloride was filtered off and washed with dimethylformamide. Evaporation of the solvent under reduced pressure gave the mixture of the amides (**4d-g**) and the γ -keto ester (**2b**) as oils which were isolated by "flash" chromatography on silica with increasing amounts of ether in light petroleum as eluent.

N,N-Dimethyl-4-(2-thienyl)-4-oxobutanamide (4d): The first component eluted was the γ -keto ester (**2b**) as a pale yellow oil. Yield 48%. The second component eluted was the amide (**4d**) as a beige solid mp 96.2-97.7 °C (ether). Yield 15%. Anal. Calcd for C₁₀H₁₃NO₂S: C, 56.88; H, 6.16; N, 6.63; S, 15.18. Found: C, 56.64; H, 6.12; N, 6.50; S, 15.14. ¹H NMR δ_{H} (CDCl₃) 2.78 (2H, t, $J = 6.7$ Hz, CH₂), 2.97 (3H, s, NCH₃), 3.09 (3H, s, NCH₃), 3.31 (2H, t, $J = 6.7$ Hz, CH₂), 7.14 (1H, m, 4'-H), 7.63 (1H, br d, $J = 5.2$ Hz, 5'-H), 7.82 (1H, br d, $J = 3.7$ Hz, 3'-H). MS (EI, 70 eV): m/z (%) 211 (M⁺, 76), 167 (68), 139 (25), 111 (100), 100 (58), 83 (20), 72 (67), 69 (18), 55 (28). IR ν_{\max} /cm⁻¹ 1641.

N,N-Diethyl-4-(2-thienyl)-4-oxobutanamide (4e): The first component eluted was the γ -keto ester (**2b**) as a pale yellow oil. Yield 23%. The second component eluted was the amide (**4e**) as a beige solid, mp 62.5-65 °C (ether). Yield 40%. Anal. Calcd for C₁₂H₁₇NO₂S: C, 60.23; H, 7.11; N, 5.86; S, 13.41. Found: C, 60.44; H, 7.07; N, 5.80; S, 13.34. ¹H NMR δ_{H} (CDCl₃) 1.11 (3H, t, $J = 7.5$ Hz, CH₂CH₃), 1.23 (3H, t, $J = 7.5$ Hz, CH₂CH₃), 2.77 (2H, t, $J = 7.5$ Hz, CH₂), 3.31 (2H, t, $J = 7.5$ Hz, CH₂), 3.40 (4H, m, 2xCH₂CH₃), 7.13 (1H, m, 4'-H), 7.62 (1H, dd, $J = 5.3$ and 1.2 Hz, 5'-H), 7.81 (1H, dd, $J = 4.1$ and 1.2 Hz, 3'-H). MS (EI, 70 eV): m/z (%) 239 (M⁺, 17), 211 (2), 167 (51), 140 (4), 128 (20), 111 (25), 100 (7), 72 (100), 58 (30). IR ν_{\max} /cm⁻¹ 1632.

N,N-Diisopropyl-4-(2-thienyl)-4-oxobutanamide (4f): The first component eluted was the γ -keto ester (**2b**) as a pale yellow oil. Yield 23%. The second component eluted was the amide (**4f**) as a beige solid, mp 69-70.5 °C (ether). Yield 35%. Anal. Calcd for C₁₄H₂₁NO₂S: C, 62.93; H, 7.86; N, 5.24; S, 12.0. Found:

C, 62.76; H, 8.00; N, 5.27; S, 12.27. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 1.25 (6H, d, $J = 7.2$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.38 (6H, d, $J = 7.2$ Hz, $\text{CH}(\text{CH}_3)_2$), 2.76 (2H, t, $J = 7.2$ Hz, CH_2), 3.31 (2H, t, $J = 7.2$ Hz, CH_2), 3.90 (1H, m, $\text{CH}(\text{CH}_3)_2$), 4.11 (1H, m, $\text{CH}(\text{CH}_3)_2$), 7.15-7.17 (1H, m, 4'-H), 7.62 (1H, dd, $J = 5.1$ and 1.2 Hz, 5'-H), 7.81 (1H, dd, $J = 3.9$ and 1.2 Hz, 3'-H). MS (EI, 70 eV): m/z (%) 267 (M^+ , 2), 167 (20), 111 (31), 57 (100). IR $\nu_{\text{max}}/\text{cm}^{-1}$ 1636.

Piperidino-4-(2-thienyl)-4-oxobutanamide (4g): The first component eluted was the γ -keto ester (**2b**) as a pale yellow oil. Yield 43%. The second component eluted was the amide (**4g**) as a beige oil. Yield 50%. Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_2\text{S}$: C, 62.16; H, 6.77; N, 5.57; S, 12.76. Found: C, 62.25; H, 6.80; N, 5.55; S, 12.94. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 1.64 (6H, m, $3 \times \text{CH}_2$) 2.78 (2H, br t, $J = 6.4$ Hz, CH_2), 3.30 (2H, br t, $J = 6.4$ Hz, CH_2), 3.47 (2H, t, $J = 5.9$ Hz, NCH_2), 3.56 (2H, t, $J = 5.9$ Hz, NCH_2), 7.12-7.16 (1H, m, 4'-H), 7.63 (1H, dd, $J = 5.3$ and 1.2 Hz, 5'-H), 7.82 (1H, dd, $J = 4.1$ and 1.2 Hz, 3'-H). MS (EI, 70 eV): m/z (%) 251 (M^+ , 12), 167 (17), 139 (9), 125 (4), 111 (45), 97 (12), 84 (100), 56 (40). IR ν_{max} (liquid film)/ cm^{-1} 1638.

General procedure for the synthesis of amides (4d-j); Method B: DCC / BtOH / CH_2Cl_2 .

1,3-Dicyclohexylcarbodiimide (DCC) (6.7 g, 32.6 mmol) and 1-hydroxybenzotriazole (BtOH) (5 g, 32.6 mmol) were added to a stirred solution of the acid (**3**) (5.0 g, 27.2 mmol) in dichloromethane (200 mL) at 0 °C. The mixture was stirred for 30 min at rt after which the amine (27.2 mmol) was added and the mixture was stirred overnight. The by-product formed, dicyclohexylurea (DCU), was separated by filtration affording a pale brown solution. This organic solution was extracted with a solution of citric acid (5%) (4x100 mL), a solution of sodium bicarbonate (5%) (2x100 mL), dried (MgSO_4) and evaporated to give an oily brown residue. "Flash" chromatography on silica with increasing amounts of ether in light petroleum as eluent gave the pure amides (**4d-j**).

N,N-Dicyclohexyl-4-(2-thienyl)-4-oxobutanamide (4h): colorless solid mp 125-126 °C (ether). Yield 52%. Anal. Calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_2\text{S}$: C, 69.17; H, 8.35; N, 4.03; S, 9.23. Found: C, 68.98; H, 8.32; N, 4.12; S, 9.33. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 1.00-2.00 (20H, m, $10 \times \text{CH}_2$) 2.40 (1H, br s, CH), 2.76 (2H, t, $J = 6.8$ Hz, CH_2), 3.31 (2H, t, $J = 6.8$ Hz, CH_2), 3.60 (1H, br s, CH), 7.11-7.14 (1H, m, 4'-H), 7.61 (1H, br d, $J = 4.9$ Hz, 5'-H), 7.80 (1H, br d, $J = 3.8$ Hz, 3'-H). MS (EI, 70 eV): m/z (%) 347 (M^+ , 3), 290 (2), 236 (7), 208 (2), 180 (21), 167 (100), 154 (9), 138 (19), 126 (5), 111 (26), 98 (19), 83 (6), 55 (15). IR ν_{max} (KBr)/ cm^{-1} 1665, 1630.

4-Methoxyphenyl-4-(2-thienyl)-4-oxobutanamide (4i): pale gray solid mp 139-140.5 °C (ethanol). Yield 62%. Anal. Calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_3\text{S}$: C, 62.29; H, 5.19; N, 4.84; S, 11.1. Found: C, 62.1; H, 5.21; N, 4.71; S, 11.5. $^1\text{H NMR } \delta_{\text{H}}$ (CDCl_3) 2.79 (2H, t, $J = 6.7$ Hz, CH_2), 3.41 (2H, t, $J = 6.7$ Hz, CH_2), 3.79 (3H, s, OCH_3), 6.85 (2H, d $J = 8.9$ Hz, 3'' and 5''-H), 7.15 (1H, m, 4'-H), 7.41 (2H, d $J = 8.9$ Hz, 2'' and 6''-H), 7.56 (1 H, br s, NH), 7.67 (1H, dd, $J = 5.1$ and 1.2 Hz, 5'-H), 7.80 (1H, dd, $J = 3.8$ and 1.2 Hz, 3'-H). MS (EI, 70 eV): m/z (%) 289 (M^+ , 5), 167 (8), 122 (9), 111 (63), 81 (14), 73 (29), 69 (71), 55 (100). IR ν_{max} (liquid film)/ cm^{-1} 1659.

2, 4-Dimethoxyphenyl-4-(2-thienyl)-4-oxobutanamide (4j): colorless solid mp 106-107.5 °C (ether). Yield 64%. Anal. Calcd for C₁₆H₁₇NO₄S: C, 60.20; H, 5.32; N, 4.38; S, 10.0. Found: C, 60.16; H, 5.39; N, 4.27; S, 10.3. ¹H NMR δ_H (CDCl₃) 2.83 (2H, t, *J* = 6.7 Hz, CH₂), 3.40 (3H, t, *J* = 6.7 Hz, CH₂), 3.79 (3H, s, OCH₃), 3.87 (3H, s, OCH₃), 6.51-6.55 (2H, m, 3'' and 5''-H), 7.12-7.17 (1H, m, 4'-H), 7.65 (1H, dd *J*=4.9 and 1.2 Hz, 5'-H), 7.78 (1H, dd, *J* = 3.2 and 1.2 Hz, 3'-H), 7.83 (1 H, br s, NH), 8.20 (1H, d, *J* = 8.6 Hz, 6''-H). MS (EI, 70 eV): *m/z* (%) 319 (M⁺, 1), 256 (3), 213 (2), 185 (2), 153 (9), 111 (6), 83 (20), 69 (67), 55 (100). IR ν_{max}(liquid film)/cm⁻¹ 1662.

General procedure for the synthesis of bithiophenes (5a-c) from the γ-keto esters (2a-c).

A mixture of the Lawesson's reagent (4.8 g, 12 mmol) and the γ-keto esters (2a-c) (10 mmol) was heated at reflux in toluene (50 mL) for the time indicated in Table 2. The mixture was cooled and the solvent was evaporated under reduced pressure to give the crude bithiophenes (5a-c) as oil, which were purified by "flash" chromatography on silica with increasing amounts of ether in light petroleum as eluent.

5-Methoxy-2,2'-bithiophene (5a)⁸ : pale yellow liquid. Yield 43%. Anal. Calcd for C₉H₈OS₂: C, 55.09; H, 4.08; S, 32.68. Found: C, 55.24; H, 4.21; S, 32.70. ¹H NMR δ_H (CDCl₃) 3.92 (3H, s, OCH₃) 6.13 (1H, d, *J* = 4.0 Hz, 4-H), 6.81 (1H, d, *J* = 4.0 Hz, 3-H), 6.96-7.00 (1H, m, 4'-H), 7.02 (1H, dd, *J* = 3.3 and 1.2 Hz, 3'-H), 7.14 (1H, dd, *J* = 4.5 and 1.2 Hz, 5'-H). ¹³C NMR δ_C (CDCl₃) 60.25, 104.37, 121.31, 122.28, 123.22, 123.72, 127.56, 138.00, 165.48. MS (EI, 70 eV): *m/z* (%) 196 (M⁺, 4), 149 (3), 83 (10), 69 (100), 60 (82), 56 (92). IR ν_{max}(liquid film)/cm⁻¹ 1564, 1523, 1487, 1450, 1424, 1353, 1320, 1252, 1228, 1198, 1151, 1079, 1052, 996, 835, 818, 771, 744, 721, 693. UV λ_{max}/nm (log ε_{max}/dm³mol⁻¹cm⁻¹) 319 (14994), 239 (4595), 207 inf. (5443).

5-Ethoxy-2,2'-bithiophene (5b) : yellow liquid. Yield 49%. Anal. Calcd for C₁₀H₁₀OS₂: C, 57.13; H, 4.76; S, 30.50. Found: C, 57.22; H, 4.91; S, 30.82. ¹H NMR δ_H (CDCl₃) 1.44 (3H, t, *J* = 6.0 Hz, OCH₂CH₃), 4.13 (2H, q, *J* = 6.0 Hz, OCH₂CH₃), 6.13 (1H, d, *J* = 4.0 Hz, 4-H), 6.80 (1H, d, *J* = 4.0 Hz, 3-H), 6.95-6.99 (1H, m, 4'-H), 7.01 (1H, dd, *J* = 3.3 and 1.2 Hz, 3'-H), 7.13 (1H, dd, *J* = 4.5 and 1.2 Hz, 5'-H). δ_C (CDCl₃) 14.7, 69.4, 105.4, 121.3, 122.2, 123.1, 123.7, 127.5, 138.1, 164.4. MS (EI, 70 eV): *m/z* (%) 210 (M⁺, 60), 181 (100), 153 (35), 109 (12), 69 (12), 45 (10). IR ν_{max}(liquid film)/cm⁻¹ 1560, 1520, 1486, 1469, 1424, 1385, 1317, 1249, 1195, 1052, 878, 835, 766, 689. UV λ_{max}/nm (log ε_{max}/dm³mol⁻¹cm⁻¹) 319.5 (14517), 240 (3892), 210 (3875).

5-Isopropoxy-2,2'-bithiophene (5c) : yellow oil. Yield 39%. Anal. Calcd for C₁₁H₁₂OS₂: C, 58.91; H, 5.35; S, 28.60. Found: C, 59.12; H, 5.43; S, 28.55. ¹H NMR δ_H (CDCl₃) 1.39 (6H, d, *J* = 6.1 Hz, OCH(CH₃)₂), 4.39 (1H, sep, *J* = 6.1 Hz, CH(CH₃)₂), 6.16 (1H, d, *J* = 4.0 Hz, 4-H), 6.81 (1H, d, *J* = 4.0 Hz, 3-H), 6.96-6.99 (1H, m, 4'-H), 7.01 (1H, dd, *J* = 4.2 and 1.4 Hz, 3'-H), 7.13 (1H, dd, *J* = 4.9 and 1.4 Hz, 5'-H). ¹³C NMR δ_C (CDCl₃) 21.89, 77.61, 107.81, 121.18, 122.19, 123.15, 124.43, 127.56, 138.19, 163.27. MS (EI, 70 eV): *m/z* (%) 224 (M⁺, 7), 182 (99), 153 (14), 111 (42), 69 (100), 58 (100), 55 (99).

IR ν_{\max} (liquid film)/ cm^{-1} 2977, 1562, 1518, 1481, 1429, 1384, 1372, 1317, 1249, 1195, 1174, 1137, 1106, 1047, 1036, 923, 823, 773, 691. UV λ_{\max} /nm ($\log \epsilon_{\max}/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1}$) 320 (14056), 242.5 (2944), 213 (966).

General procedure for the synthesis of bithiophenes (5d-i) from the amides (4d-i).

A mixture of the Lawesson reagent (7.3 g, 18 mmol) and the amides (**4d-i**) (18 mmol) was heated at reflux in toluene (100 mL) for the time indicated in Table 3. The mixture was cooled and the solvent was evaporated under reduced pressure to give the crude bithiophenes (**5d-i**) as oils, which were purified by "flash" chromatography on silica with increasing amounts of ether in light petroleum as eluent.

5-*N,N*-Dimethylamino-2,2'-bithiophene (**5d**)⁸: yellow solid, mp 34-36 °C. Yield. 69%.

5-*N,N*-Diethylamino-2,2'-bithiophene (**5e**)³²: yellow liquid. Yield 64%.

5-*N,N*-Diisopropylamino-2,2'-bithiophene (**5f**): yellow liquid. Yield 53%. Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{NS}_2$: C, 63.38; H, 7.16; N, 5.28; S, 24.17. Found: C, 63.41; H, 7.27; N, 5.30; S, 24.16. ^1H NMR δ_{H} (CDCl_3) 1.22 (12H, d, $J = 6.7$ Hz, 4x CH_3), 3.61 (2H, sep, $J = 6.7$ Hz, 2x CH), 6.15 (1H, d, $J = 3.7$ Hz, 4-H), 6.89 (1H, d, $J = 3.7$ Hz, 3-H), 6.96 (1H, m, 4'-H), 7.00 (1H, dd, $J = 3.7$ and 1.2 Hz, 3'-H), 7.09 (1H, dd, $J = 4.8$ and 1.2 Hz, 5'-H). ^{13}C NMR δ_{C} (CDCl_3) 20.87, 50.88, 113.44, 121.40, 121.96, 122.39, 125.53, 127.50, 138.82, 153.10. MS (EI, 70 eV): m/z (%) 265 (M^+ , 54), 250 (16), 222 (27), 208 (26), 180 (54), 69 (100). IR ν_{\max} (liquid film)/ cm^{-1} 3070, 2970, 2930, 2870, 1557, 1511, 1489, 1380, 1366, 1331, 1316, 1271, 1247, 1230, 1190, 1157, 1125, 1055, 1014, 920, 885, 839, 798, 757, 688. UV λ_{\max} /nm ($\log \epsilon_{\max}/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1}$) 341.0 (11494), 246.5 (4481), 213.5 (3633).

5-Piperidino-2,2'-bithiophene (**5g**): pale yellow solid, mp 59-60 °C (light petroleum). Yield 79%. Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{NS}_2$: C, 62.64; H, 6.02; N, 5.62; S, 25.73. Found: C, 62.59; H, 6.09; N, 5.56; S, 26.03. ^1H NMR δ_{H} (CDCl_3) 1.50-1.64 (2H, m, CH_2), 1.68-1.80 (4H, m, 2x CH_2), 3.10-3.20 (4H, m, 2x CH_2), 6.00 (1H, d, $J = 4.0$ Hz, 4-H), 6.89 (1H, d, $J = 4.0$ Hz, 3-H), 6.95-7.00 (2H, m, 3' and 4'-H), 7.05-7.11 (1H, m, 5'-H). ^{13}C NMR δ_{C} (CDCl_3) 23.60, 25.09, 52.58, 105.48, 121.39, 122.43, 123.04, 127.51, 138.48, 158.44. MS (EI, 70 eV): m/z (%) 249 (M^+ , 100), 69 (9), 57 (14). IR ν_{\max} (liquid film)/ cm^{-1} 2939, 2826, 1556, 1514, 1488, 1446, 1301, 1276, 1242, 1192, 1121, 1068, 1013, 894, 826, 810, 769, 682. UV λ_{\max} /nm ($\log \epsilon_{\max}/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1}$) 343.0 (18039), 241.5 (4914), 214.0 (6102).

5-*N,N*-Dicyclohexylamino-2,2'-bithiophene (**5h**): pale yellow solid, mp 52-55 °C (light petroleum). Yield 63%. ^1H NMR δ_{H} (CDCl_3) 0.90-1.82 (20H, m, 10x CH_2), 3.00-3.20 (2H, m, CH), 6.19 (1H, d, $J = 3.7$ Hz, 4-H), 6.86 (1H, d, $J = 3.7$ Hz, 3-H), 6.90-7.25 (2H, m, 3' and 4'-H), 7.04 (1H, br d, $J = 5.2$ Hz, 5'-H). MS (EI, 70 eV): m/z (%) 345 (M^+ , 100), 302 (4), 263 (31), 236 (5), 220 (9), 205 (8), 192 (5), 180 (57), 153, (5), 121 (8), 96 (14), 81 (11), 55 (30). IR ν_{\max} (liquid film)/ cm^{-1} 2940, 2860, 1520, 1480, 1450, 1380, 1340, 1260, 1240, 1200, 1130, 1120, 1110, 1050, 1020, 980, 900, 840, 800, 760, 715, 690.

5-(4-Methoxyanilino)-2,2'-bithiophene (5i): pale green solid, mp 113-115 °C (ether). Yield 14%. Anal. Calcd for C₁₅H₁₃NOS₂: C, 62.71; H, 4.52; N, 4.87; S, 22.32. Found: C, 62.84; H, 4.61; N, 4.81; S, 22.72. ¹H NMR δ_H (CDCl₃) 3.80 (3H, s, OCH₃), 6.50 (1H, d, *J* = 3.7 Hz, 4-H), 6.85 (2H, d, *J* = 8.9 Hz, 2'' and 6''-H or 3'' and 5''-H), 6.94 (1H, d, *J* = 3.7 Hz, 3-H), 6.97 (2H, d, *J* = 8.9 Hz, 3'' and 5''-H or 2'' and 6''-H), 7.00 (1H, m, 4'-H), 7.05 (1H, dd, *J* = 3.6 and 1.2 Hz, 3'-H), 7.16 (1H, dd, *J* = 5.0 and 1.2 Hz, 5'-H). ¹³C NMR δ_C (CDCl₃) 55.62, 114.74, 115.49, 117.54, 122.35, 122.45, 123.34, 127.63, 127.92, 137.99, 138.36, 147.29, 154.27. MS (EI, 70 eV): *m/z* (%) 287 (M⁺, 100), 272 (70), 210 (9), 185 (11), 121, (13), 96 (14), 77 (6), 63 (7). IR ν_{max}(liquid film)/cm⁻¹ 1514, 1462, 1441, 1349, 1298, 1249, 1165, 1102, 1040, 916, 835, 789. UV λ_{max}/nm (log ε_{max}/dm³mol⁻¹cm⁻¹) 365.5 (19900), 245.0 (10596), 203.5 (31029).

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