Controlled Synthesis of Functionalized Mixed Thiophene/Furan Oligomers

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A novel and simple synthetic route for the preparation of a series of functionalized mixed thiophene/furan oligomers is described. This method, involving a $Mn(OAc)_3$-mediated oxidative addition of β-thienyl-β-keto esters (= β-oxothiophenepropanoates) to methyl 3-thienylprop-2-enoates, allows the construction of highly functionalized heteropolyaromatic oligomers possessing various chain lengths (*Schemes 2*, *4*, and *5*). Moreover, the straightforward transformation of the carbonyl functions appended to the furan rings leads to polycarboxylic acid precursors of H_2O-soluble conducting polymers (*Scheme 6*).

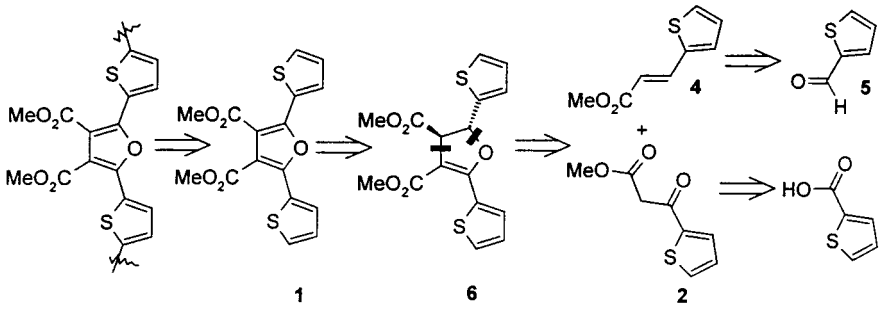
Introduction. – Over the last two decades, the importance of π-conjugated thiophene-based oligomers and polymers has steadily grown. Due to their interesting optical, electrical, and electrochemical properties, these compounds have been thoroughly investigated as materials for organic semiconductors [1] and sensors [2–4]. The 2,5-bis(2-thienyl)heterocyclopentadienes constitute useful starting materials for the preparation of copolymers. They also represent simple models used to predict the properties of the corresponding polymers.

The solubility of conducting polymers is of crucial importance for their potential applications. Unfortunately, the conjugated backbones that allow electron transport in these polymers display poor solubility in common organic solvents. Furthermore, with regard to applications, H_2O-soluble conducting polymers are more attractive than those soluble in organic solvents [5]. The judicious functionalization of oligomers not only can permit accurate modulation of the physical properties of polymers but can also contribute to enhancing the solubility of such materials in organic [6] or aqueous solvents [7–9]. Finally, the presence of carbonyl groups directly linked to the conjugated backbone could help to stabilize the excited quinoid form.

Polythiophenes possessing electron-withdrawing ester groups have already been prepared by polymerization *via* the *Ullmann* reaction with copper in DMF [10], but only examples of unfunctionalized mixed thiophene/furan oligomers have yet been reported [11–13]. Herein, we present a new low-cost synthetic strategy for the preparation of functionalized mixed heteropolyaromatic thiophene/furan oligomers. We thought that the ester functionality was best suited to give access to a wide range of other functionalities such as alcohols, aldehydes, carboxylic acids, and their salts. The furan/thiophene C–C coupling is usually realized by a *Stille* reaction between an organic halide and an organostannane [12], under conditions that are rather incompatible with the presence of carbonyl groups. In this paper, we propose an

unusual *retro*-synthetic analysis of methoxycarbonyl oligomers in which a 2,3-dihydrofuran acts as the furan precursor (*Scheme 1*). This approach is based on the $Mn(OAc)_3$-mediated radical addition of β-keto esters to alkenes in acetic acid, which allows the one-pot synthesis of 2,3-dihydrofurans in good yield [14][15]. The reaction is totally regio- and diastereoselective with cinnamate esters and acetyl- or benzoylacetates as substrates [16]. Therefore, we endeavored to exploit this strategy, switching to cinnamate-like olefins and benzoylacetate-like 1,3-dioxo compounds, each bearing a thiophene in place of the phenyl moiety.

Scheme 1



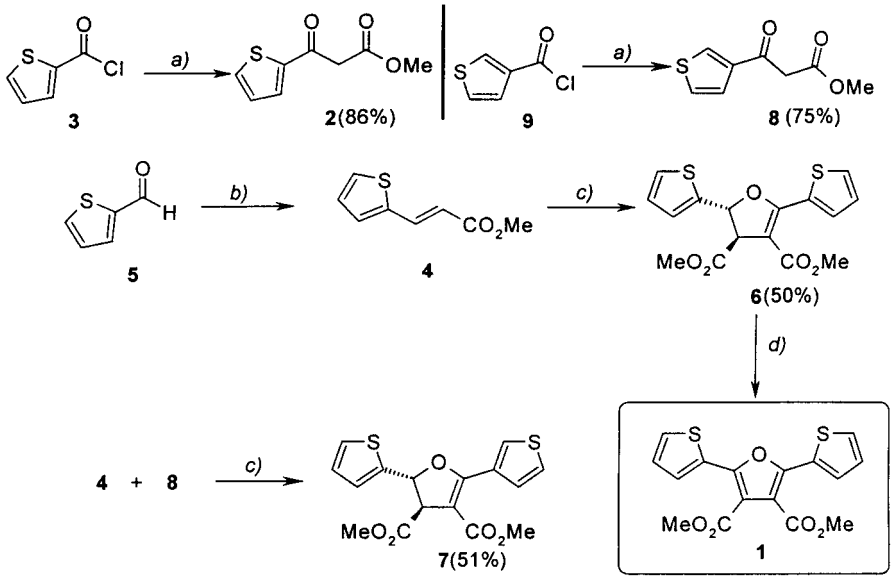
2. Results and Discussion. – 2.1. *Three-Ring Heterocycles* **1** *and* **7**. The required starting materials used in the synthesis of the three-ring heterocycle thiophene/furan/thiophene (TFT) **1** were prepared as described in *Scheme 2*. The β-keto ester **2** was obtained in excellent yield (86%) *via* condensation of thiophene-2-carbonyl chloride (**3**) with potassium monomethyl malonate in the presence of $MgCl_2$ [17]. The (*E*)-α,β-unsaturated ester **4** could be easily obtained by a *Doebner* condensation involving the commercially available thiophene-2-carboxaldehyde (**5**) (75% yield). The Mn^{III}-promoted addition of **2** to **4** led to a single product, *trans*-2,3-dihydrofurandicarboxylate **6**, isolated in good yield (50%).

All attempts to dehydrogenate **6** in the presence of a Pd or Pt catalyst failed. However, this dehydrogenation could be achieved with excellent yield by heating **6** with 4,5-dichloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile (DDQ) in refluxing toluene. Even when the reaction was performed in refluxing xylene, the reaction time (72 h) necessary for the total conversion of **6** to **1** could not be reduced. TFT **1** was thus obtained in a two-step sequence in 45% overall yield. To demonstrate the versatility of this strategy, we also synthesized **8**, a precursor of the TFT oligomer **7** in which one of the thiophene moieties is linked to the furan by its 3-position (*Scheme 2*).

2.2. *Five-Ring Heterocycle* **10** *and Synthons* **16** *and* **17**. 2.2.1. retro-*Synthesis*. We next focused our attention on the preparation of the five-ring pattern TFTFT **10**, which can be envisioned as resulting from two different reaction routes (iterative or convergent) each involving a Mn^{III}-based radical addition as the key step (*Scheme 3*).

The first route consists in the application of a new cycle of oxidative addition/dehydrogenation to an alkene moiety grafted onto **1**. The second pathway is a more

Scheme 2



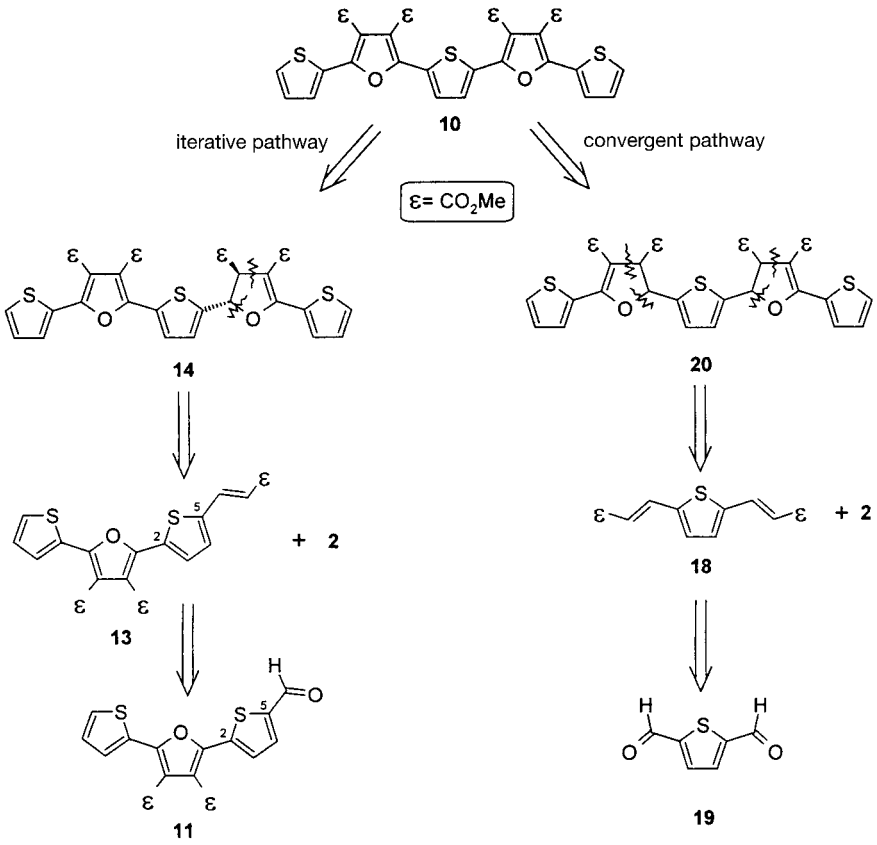
a) Potassium monomethyl malonate, $MgCl_2$, Et_3N, MeCN, r.t., 12 h. *b*) Malonic acid monomethyl ester, piperidine, pyridine, 100°, 3 h; 75%. *c*) **2**, $Mn(OAc)_3 \cdot 2\ H_2O$, AcOH, 70°, 1 h. *d*) DDQ, toluene, reflux, 72 h; 90%.

convergent strategy, namely a double oxidative addition performed with a (thiophene-2,5-diyl)bis[propenoate], followed by a double dehydrogenation.

2.2.2. *Iterative Pathway.* To introduce an alkenyl moiety at the 5-position of thiophene, we first prepared **11** by formylation of **1**. In this case, the *Vilsmeier-Haack* method gave only traces of the desired product; the BuLi/DMF sequence yielded a complex mixture of self-condensation products. A more-efficient synthesis of **11** was thus sought: it involved the treatment of **1** with $TiCl_4$ in CH_2Cl_2 at 0° followed by the addition of 1.3 equiv. of the powerful electrophile Cl_2CHOMe (*Scheme 4*). It should be noted that a careful control of the experimental conditions must be exercised to stop the reaction at the monoformylation stage **11** (70% yield), because prolonged treatment with 2.6 equiv. of Cl_2CHOMe led to the formation of the 5,5′-diformyl compound **12** (59% yield). A classical *Doebner* condensation converted aldehyde **11** to **13** (86% yield). Then, the addition of **2** to **13** in AcOH at 70° furnished the *trans*-2,3-dihydrofurandicarboxylate **14** as the sole product in 52% yield. Finally, the oxidation of **14** by DDQ in refluxing toluene led to the five-ring target TFTFT **10** in 88% yield.

The β-keto ester **16** bearing not only a thiophene unit but also a wholely functionalized polyaromatic TFT system was readily accessible from **11** *via* **15**. Oxidation of **11** by the *Jones* reagent in acetone gave carboxylic acid **15** in good yield. Subsequent treatment of **15** by thionyl chloride in refluxing benzene in the presence of Et_3N furnished the corresponding acid chloride, which was directly converted to β-keto ester **16** in 30% overall yield. On the other hand, dialkenyl derivative **17** was readily

Scheme 3

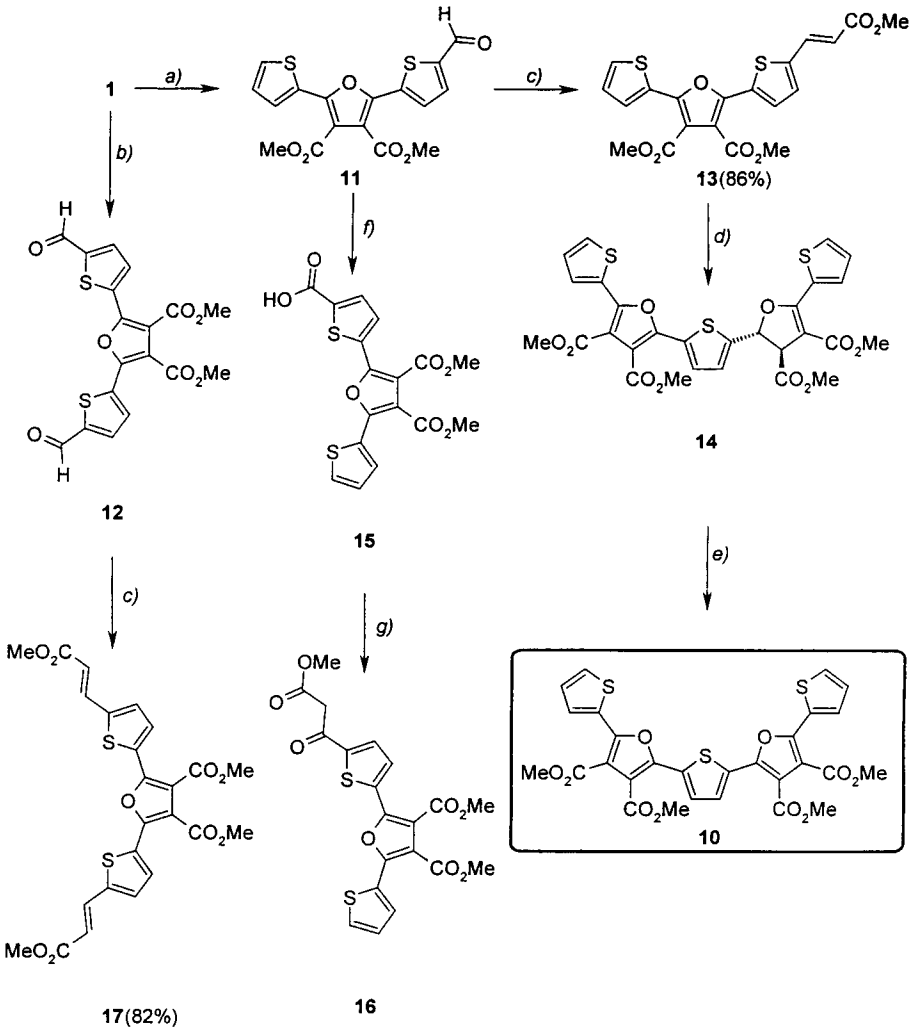


available by a double *Doebner* condensation with **12**. Synthons like **16** and **17** could be used for the rapid construction of long-chain oligomers.

2.2.3. *Convergent Pathway.* The alternative strategy for the synthesis of **10** required the preparation of dialkenyl derivative **18**, which was obtained in good yield (70%) by a one-pot double *Doebner* condensation from commercially available dialdehyde **19** (*Scheme 5*). The addition of **2** (2 equiv.) to **18** in the presence of 4.4 equiv. of $Mn(OAc)_3$ afforded the oily (thiophene-2,5-diyl)bis[2,3-dihydrofuran-3,4-dicarboxylate] **20** in low yield (21%) as a single diastereoisomer in a rare example of a double radical oxidative addition [18][19].

Two structures possible for **20** (**20a** and **20b** or their rotamers) share common symmetry features. As a result, it is impossible to know which of these two stereoisomers is, indeed, formed on the basis of ^{1}H- or ^{13}C-NMR spectra. Nevertheless, this result demonstrates that the first attack of **2** on **18** entails a strict facial selectivity for the second radical addition to the remaining C=C bond. A double oxidation by DDQ of the bis[2,3-dihydrofurandicarboxylate] **20** gave TFTFT **10** in a yield similar to that obtained for TFT **1** (85%).

Scheme 4

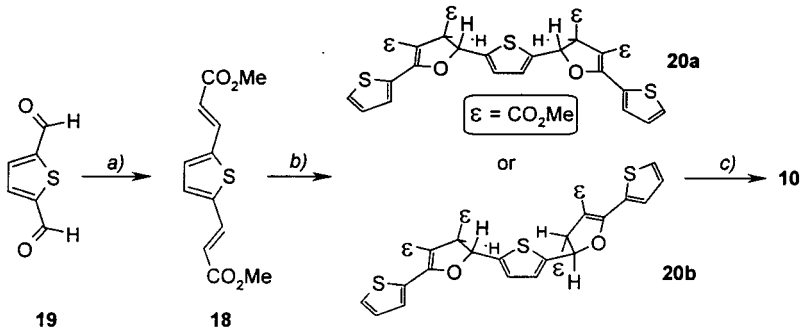


a) 1) 1.3 equiv. of $TiCl_4$, CH_2Cl_2, 0°, 1 h; 2) 1.3 equiv. of Cl_2CHOMe, 0°, 1 h; 70%. *b*) See *a*) with 2.6 equiv. of $TiCl_4$ and Cl_2CHOMe; 59%. *c*) Malonic acid monomethyl ester, pyridine, piperidine, 100°, 4 h. *d*) **2**, $Mn(OAc)_3 \cdot 2\,H_2O$, AcOH, 70°, 3 h; 52%. *e*) DDQ, toluene, reflux, 72 h; 88%. *f*) CrO_3/H_2SO_4, acetone, r.t., 1 h; 65%. *g*) 1) $SOCl_2$, Et_3N, benzene, reflux, 1.5 h; 2) potassium monomethyl malonate, $MgCl_2$, Et_3N, MeCN, r.t., 12 h; 45%.

Thus, the five-ring heterocycle **10** was obtained in 12% overall yield from dialdehyde **19** *via* the convergent pathway and in 14% overall yield from aldehyde **5** *via* the iterative pathway.

2.3. *Properties and Transformations of TFT* **1** *and TFTFT* **10**. The perfect symmetry exhibited by the ^{1}H- and ^{13}C-NMR spectra of **10** and **1** reveals a stereoregularity in

Scheme 5



a) Malonic acid monomethyl ester, pyridine, piperidine, 100°, 4 h; 70%. *b*) **2**, $Mn(OAc)_3 \cdot 2\ H_2O$, AcOH, 70°, 2 h; 21%. *c*) DDQ, toluene, reflux, 72 h; 85%.

these oligomeric structures but does not attribute a head-to-tail or a head-to-head arrangement to them.

The ester functionalities on the tris- and pentakis-heterocycles **1** and **10** could be manipulated so as to readily obtain the corresponding alcohols, aldehydes, or carboxylic acids (*Scheme 6*). For example, diester **1** could be reduced by $LiAlH_4$ in THF at 0° into the polyaromatic diol **21** in quantitative yield. Its subsequent oxidation by pyridinium dichromate (PDC) in CH_2Cl_2 led to the dialdehyde **22**. On the other hand, the saponification of **1** allowed to prepare the diacid **23** in high yield. Likewise, the saponification of **10** furnished the tetraacid **24** in a comparable yield, requiring, however, a longer reaction time. The synthetic interest of these transformations is obvious. For example, the 2,5-di(2-thienyl)furan-3,4-dicarboxaldehyde (**22**) could be used as a potential starting point to increase the conjugation *via* a *Wittig* or a *McMurry* reaction. It should be pointed out that, from a practical point of view, the diacid **23** and tetraacid **24** are fairly soluble in H_2O.

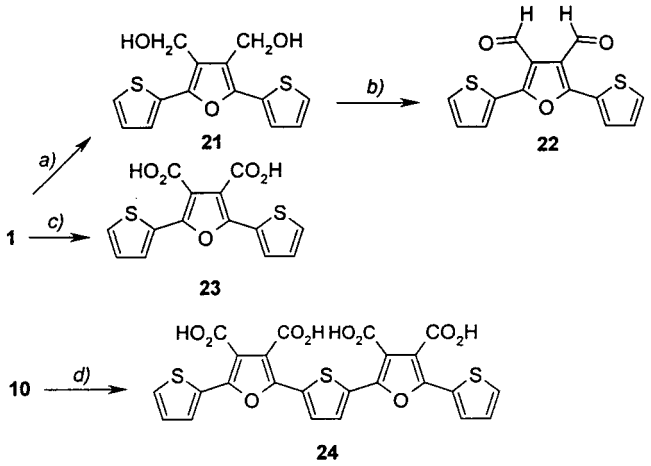
The UV/VIS spectra of these mixed oligomers show a bathochromic λ_{max} shift with increasing chain length as shown in the *Table*. Thus, the tris-heterocycle TFT **1** and the pentakis-heterocycle TFTFT **10** display absorptions at 340 and 418 nm, respectively. No difference in λ_{max} values is observed between oligomers bearing either an ester or the corresponding acid. When compared to the analogous unfunctionalized oligomers [12], only minor differences are observed.

Table. *UV/VIS Spectral Data* ($CHCl_3$)

	TFT Type		TFTFT Type	
	1	**23**	**10**	**24**
λ_{max} nm (eV)	340 (3.65)	342 (3.63)	418 (2.97)	415 (2.99)

Conclusions. – In summary, we have established a new synthetic route to mixed thiophene/furan oligomers. This low-cost and good-yielding strategy is complementary to the generally used *Stille* coupling, allowing the construction of functionalized

Scheme 6



a) $LiAlH_4$, THF, 0°, 10 min; 100%. *b*) PDC, CH_2Cl_2, r.t., 8 h; 71%. *c*) 1) LiOH, MeOH/H_2O 4 : 1, reflux, 15 min; 2) HCl/H_2O; 95%. *d*) See *c*), 6 h; 86%.

systems. By an iterative introduction of functionalized furan moieties, this route makes possible the control of oligomer topology and, consequently, can provide opportunities to tune the oligomer/polymer physical properties. We are currently investigating the chemical polymerization of these mixed subunits to prepare functionalized poly(thiophene/furans) and to study their solvatochromic, ionochromic, and aggregation properties.

Experimental Part

General. All experiments were conducted under N_2 unless indicated otherwise and stirred magnetically. Evaporation was performed on a *Büchi* or a *Heidolph* rotary evaporator. $TiCl_4$ packaged under N_2 (*Aldrich*) was used as received. CH_2Cl_2 was distilled from P_2O_5 and THF from sodium benzophenone-ketyl (=sodium diphenylketyl) immediately prior to use. Flash chromatography (FC): *Merck* silica gel *60 H*. TLC: *Merck* silica gel *60* F_{254}, aluminum-backed plates; visualization by 254-nm UV light and phosphomolybdic acid staining soln. M.p.: *Electrothermal IA-9100* apparatus; uncorrected. UV Spectra: *Beckman DU-640* spectrometer; 10^{-4} M $CHCl_3$ solns. IR Spectra: *Perkin-Elmer 297* spectrometer; film on NaCl plates or $CHCl_3$ solns.; in cm^{-1}. NMR Spectra: *Bruker AC-250* spectrometer (^1H: 250 MHz; ^{13}C: 62 MHz); chemical shifts δ in ppm and coupling constants *J* in Hz.

1. *Acid Chlorides.* Acid chlorides **3** and **9** were prepared by heating the corresponding acid (5 mmol) in freshly distilled $SOCl_2$ (1.5 ml) at 50° for 45 min. After cooling, excess $SOCl_2$ was evaporated under reduced pressure, and the acid chloride was used without further purification.

In the case of **15**, the reaction was carried out in benzene (0.1M soln.) in the presence of 1 equiv. of Et_3N.

2. *β-Keto Esters: General Procedure.* A suspension of potassium monomethyl malonate (328 mg, 2.1 mmol) in MeCN (3.2 ml) was cooled to 5° under N_2. Et_3N (0.44 ml, 3.2 mmol) was added, followed by $MgCl_2$ (238 mg, 2.5 mmol), and stirring was continued for 2.5 h at r.t. A soln. of acid chloride (1 mmol) in MeCN (1 ml) was then added to the cooled mixture (ice/water bath), which turned pale-yellow. After stirring for 12 h at r.t., volatile compounds were evaporated under reduced pressure, and the solid residue was dissolved by addition of toluene (1.7 ml) and 13% aq. HCl soln. (1.4 ml). The aq. layer was extracted with Et_2O (3 × 10 ml), the combined org. layer washed with sat. aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated, and the crude product purified by FC (hexane/AcOEt 16 : 1 → 1 : 1).

Methyl 3-Oxo-3-(2-thienyl)propanoate (**2**): Yield 86%. IR: 3091, 1739, 1653, 1510. ^{1}H-NMR ($CDCl_3$): 3.66 (*s*, 3 H); 3.87 (*s*, 2 H); 7.08 (*d*, *J* = 4.5, 1 H); 7.62–7.68 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 46.0; 52.4; 128.3; 133.4; 135.0; 143.0; 167.32; 184.8.

Methyl 3-Oxo-3-(3-thienyl)propanoate (**8**): Yield 75%. IR: 3095, 1743, 1653, 1520. ^{1}H-NMR ($CDCl_3$): 3.66 (*s*, 3 H); 3.85 (*s*, 2 H); 7.27 (*dd*, *J* = 5.1, 3.1, 1 H); 7.48 (*dd*, *J* = 5.1, 1.3, 1 H); 8.04 (*dd*, *J* = 3.1, 1.3, 1 H). ^{13}C-NMR ($CDCl_3$): 47.1; 52.8; 127.1; 127.2; 133.7; 141.5; 167.9; 186.4.

Dimethyl 2-[5-(3-Methoxy-1,3-dioxopropyl)-2-thienyl]-5-(2-thienyl)furan-3,4-dicarboxylate (**16**): Yield 45%. IR: 3085, 1740, 1650, 1515. ^{1}H-NMR ($CDCl_3$): 3.78 (*s*, 3 H); 3.83 (*s*, 3 H); 3.86 (*s*, 3 H); 3.88 (*s*, 2 H); 7.06 (*dd*, *J* = 4.7, 3.9, 1 H); 7.42 (*dd*, *J* = 4.7, 1.0, 1 H); 7.64 (*AB*, J_{AB} = 4.2, 2 H); 7.77 (*dd*, *J* = 3.9, 1.0, 1 H). ^{13}C-NMR ($CDCl_3$): 29.6; 46.0; 52.3; 52.5; 113.8; 116.3; 127.7; 128.1; 129.0; 129.1; 129.5; 133.2; 138.3; 143.5; 146.6; 150.3; 162.9; 163.0; 167.1; 184.5.

3. *Oxidative Addition of β-Keto Ester* **2** *to Olefins: General Procedure.* A stirred soln. of **2** (184 mg, 1 mmol), olefin (1 mmol), and $Mn(OAc)_3 \cdot 2\ H_2O$ (590 mg, 2.2 mmol) in AcOH (10 ml) was degassed by a stream of N_2. The brown soln. was then heated at 70° under N_2 until decolorization occurred. After cooling, H_2O (10 ml) was added, and the mixture was extracted with Et_2O (3 × 5 ml). The org. extracts were washed with sat. aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated. The crude product was purified by FC (hexane/AcOEt 16:1 → 1:1).

Dimethyl trans-*2,3-Dihydro-2,5-di(2-thienyl)furan-3,4-dicarboxylate* (**6**): Yield 50%. M.p. 73.5–74.0°. IR: 3105, 3077, 1702, 1580, 1437. ^{1}H-NMR ($CDCl_3$): 3.68 (*s*, 3 H); 3.70 (*s*, 3 H); 4.28 (*d*, *J* = 5.8, 1 H); 5.93 (*d*, *J* = 5.8, 1 H); 6.93 (*dd*, *J* = 4.8, 4.4, 1 H); 7.02–7.06 (*m*, 2 H); 7.25 (*dd*, *J* = 4.8, 1.0, 1 H); 7.49 (*dd*, *J* = 4.9, 1.0, 1 H); 8.18 (*dd*, *J* = 3.9, 1.2, 1 H). ^{13}C-NMR ($CDCl_3$): 51.6; 52.9; 58.0; 81.4; 99.8; 125.7; 126.4; 127.1; 127.5; 130.4; 131.7; 133.7; 142.4; 159.8; 164.7; 172.6.

Dimethyl trans-*2,3-Dihydro-2-(2-thienyl)-5-(3-thienyl)-furan-3,4-dicarboxylate* (**7**): Yield 51%. IR: 3062, 1780, 1744, 1650, 1407. ^{1}H-NMR ($CDCl_3$): 3.64 (*s*, 3 H); 3.70 (*s*, 3 H); 4.27 (*d*, *J* = 6.5, 1 H); 5.89 (*d*, *J* = 6.5, 1 H); 6.93 (*dd*, *J* = 4.5, 3.7, 1 H); 7.06 (*d*, *J* = 3.7, 1 H); 7.20–7.26 (*m*, 2 H); 7.70 (*dd*, *J* = 5.0, 1.1, 1 H); 8.46 (*d*, *J* = 1.1, 1 H). ^{13}C-NMR ($CDCl_3$): 51.6; 52.9; 58.0; 81.1; 100.6; 124.9; 125.6; 126.3; 127.2; 128.7; 129.9; 132.0; 142.6; 161.0; 164.8; 172.8.

Dimethyl trans-*2-[5-[3,4-Bis(methoxycarbonyl)-5-(2-thienyl)furan-2-yl]-2-thienyl]-2,3-dihydro-5-(2-thienyl)furan-3,4-dicarboxylate* (**14**): Yield 52%. IR: 3084, 1770, 1750, 1652, 1415. ^{1}H-NMR ($CDCl_3$): 3.70 (*s*, 3 H); 3.73 (*s*, 3 H); 3.80 (*s*, 3 H); 3.82 (*s*, 3 H); 4.31 (*d*, *J* = 5.9, 1 H); 5.93 (*d*, *J* = 5.9, 1 H); 7.00–7.07 (*m*, 3 H); 7.37 (*dd*, *J* = 4.4, 0.9, 1 H); 7.52 (*dd*, *J* = 4.4, 0.9, 1 H); 7.61 (*d*, *J* = 4.4, 1 H); 7.70 (*dd*, *J* = 4.0, 0.9, 1 H); 8.2 (*dd*, *J* = 4.0, 0.9, 1 H). ^{13}C-NMR ($CDCl_3$): 51.5; 52.4; 52.5; 52.9; 57.8; 81.0; 99.7; 113.6; 114.0; 126.0; 127.4; 127.8; 128.3; 128.5; 128.7; 129.9; 130.2; 130.7; 131.7; 133.7; 145.0; 148.4; 149.4; 159.7; 163.4; 163.5; 164.5; 172.2.

Tetramethyl trans,trans-*2,2′-(Thiophene-2,5-diyl)bis[2,3-dihydro-5-(2-thienyl)furan-3,4-dicarboxylate]* (**20**): Yield 21%. IR: 3050, 1739, 1700, 1440, 1262. ^{1}H-NMR ($CDCl_3$): 3.70 (*s*, 6 H); 3.72 (*s*, 6 H); 4.25 (*d*, *J* = 5.9, 2 H); 5.86 (*d*, *J* = 5.9, 2 H); 6.97 (*s*, 2 H); 7.06 (*dd*, *J* = 4.4, 3.5, 2 H); 7.50 (*d*, *J* = 4.4, 2 H); 8.16 (*d*, *J* = 3.5, 2 H). ^{13}C-NMR ($CDCl_3$): 51.4; 52.7; 57.7; 81.0; 99.6; 125.3; 127.3; 130.1; 131.6; 133.6; 143.1; 159.6, 164.4; 172.2.

4. *2,3-Dihydrofuran-3,4-dicarboxylate Oxidation: General Procedure.* A stirred soln. of 2,3-dihydrofuran-3,4-dicarboxylate (1 mmol) in toluene (25 ml) containing DDQ (2.270 g, 10 mmol) was refluxed for 72 h. After cooling, H_2O (20 ml) was added, and the mixture was extracted with AcOEt (4 × 5 ml). The org. extracts were washed with sat. aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated. The crude product was purified by FC (hexane/AcOEt 16:1 → 1:1).

Dimethyl 2,5-Di(2-thienyl)furan-3,4-dicarboxylate (**1**): Yield 90%. M.p. 76.0–76.5°. IR: 3105, 3077, 1702, 1580, 1437. ^{1}H-NMR ($CDCl_3$): 3.85 (*s*, 6 H); 7.04 (*dd*, *J* = 5.0, 3.6, 2 H); 7.37 (*dd*, *J* = 5.0, 0.9, 2 H); 7.71 (*dd*, *J* = 3.6, 0.9, 2 H). ^{13}C-NMR ($CDCl_3$): 52.4; 113.6; 127.8; 128.4; 128.5; 130.2; 149.2; 163.6.

Tetramethyl 2,2′-(Thiophene-2,5-diyl)bis[5-(2-thienyl)furan-3,4-dicarboxylate] (**10**): Yield 85%. M.p. 144.5–145.5°. IR: 3110, 3075, 1720, 1702, 1590, 1580, 1430. ^{1}H-NMR ($CDCl_3$): 3.35 (*s*, 6 H); 3.38 (*s*, 6 H); 7.07 (*dd*, *J* = 4.9, 3.8, 2 H); 7.41 (*dd*, *J* = 4.9, 1.0, 2 H); 7.72 (*s*, 2 H); 7.74 (*dd*, *J* = 3.8, 1.0, 2 H). ^{13}C-NMR ($CDCl_3$): 52.3; 52.4; 113.8; 114.6; 127.7; 128.5; 128.6; 128.7; 129.9; 132.1; 148.2; 149.5; 163.3; 163.4.

5. *Dimethyl 2-(5-Formyl-2-thienyl)-5-(2-thienyl)furan-3,4-dicarboxylate* (**11**). A soln. of **1** (90 mg, 0.258 mmol) in anh. CH_2Cl_2 (1 ml) was cooled to 0°, and $TiCl_4$ (0.036 ml, 0.335 mmol, 1.3 equiv.) was added dropwise under N_2. The soln. was stirred for 1 h at 0° and dichloromethyl methyl ether (30 µl, 0.335 mmol, 1.3 equiv.) was added dropwise by means of a syringe. The deep red mixture was further stirred for 1 h at 0° and then allowed to warm to r.t. The soln. was poured onto crushed ice (10 ml) and stirred for 30 min. The aq. layer was extracted wtih CH_2Cl_2 (3 × 2 ml), the combined org. layer washed with H_2O, dried ($MgSO_4$), and evaporated, and the crude product purified by FC (hexane/AcOEt 16:1 → 1:1): 68 mg (70%) of **11**. IR: 3098,

1660, 1520, 1418, 1215. ^{1}H-NMR ($CDCl_3$): 3.54 (*s*, 3 H); 3.57 (*s*, 3 H); 7.07 (*dd*, *J* = 4.8, 3.7, 1 H); 7.43 (*dd*, *J* = 4.8, 1.1, 1 H); 7.76 (*AB*, J_{AB} = 4.3, 2 H); 7.88 (*dd*, *J* = 3.7, 1.1, 1 H); 9.87 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 52.6; 52.8; 113.9; 116.9; 128.0; 128.2; 129.3; 129.4; 129.7; 136.2; 138.6; 144.4; 147.0; 150.7; 163.1; 163.2; 183.0.

6. *Dimethyl 2,5-Bis(5-formyl-2-thienyl)furan-3,4-dicarboxylate* (**12**). As described in *Exper. 5*, with 2.6 equiv. of dichloromethyl methyl ether and 2.6 equiv. of $TiCl_4$. Yield 59%. M.p. 192.0–193.0°. IR: 3084, 1663, 1536. ^{1}H-NMR ($CDCl_3$): 3.90 (*s*, 6 H); 7.74 (*AB*, J_{AB} = 4.1, 4 H); 9.90 (*s*, 2 H). ^{13}C-NMR ($CDCl_3$): 52.8; 116.9; 129.0; 136.0; 137.7; 145.0; 148.4; 162.6; 182.9.

7. Doebner *Condensation: General Procedure.* A soln. of malonic acid monomethyl ester (118 mg, 1 mmol), aldehyde (0.5 mmol), and piperidine (15 µl) in pyridine (2 ml) was stirred at 100° for 3 h. The soln. was then cooled to r.t., and volatile compounds were evaporated. The residue was dissolved in CH_2Cl_2 (5 ml) and the soln. washed with 5% aq. HCl soln. and with H_2O until neutrality, dried ($MgSO_4$), and evaporated. The crude α,β-unsaturated ester was purified by FC (hexane/AcOEt 16:1 → 1:1).

*Methyl (2*E*)-3-(2-Thienyl)prop-2-enoate* (**4**): Yield 75%. M.p. 54.5–55.5°. IR: 3051, 1702, 1620, 1434, 1260. ^{1}H-NMR ($CDCl_3$): 3.71 (*s*, 3 H); 6.15 (*d*, *J* = 16.0, 1 H); 6.96 (*dd*, *J* = 4.9, 3.7, 1 H); 7.16 (*d*, *J* = 3.7, 1 H); 7.28 (*d*, *J* = 4.9, 1 H); 7.70 (*d*, *J* = 16.0, 1 H). ^{13}C-NMR ($CDCl_3$): 51.9; 116.8; 128.3; 128.7; 131.2; 137.5; 139.7; 167.5.

*Dimethyl 2-[5-[(1*E*)-3-Methoxy-3-oxoprop-1-enyl]-2-thienyl]-5-(2-thienyl)furan-3,4-dicarboxylate* (**13**): Yield 86%. IR: 3060, 1718, 1645, 1410, 1210. ^{1}H-NMR ($CDCl_3$): 3.74 (*s*, 3 H); 3.85 (*s*, 3 H); 3.86 (*s*, 3 H); 6.24 (*d*, *J* = 15.3, 1 H); 7.06 (*dd*, *J* = 5.1, 4.3, 1 H); 7.17 (*d*, *J* = 4.3, 1 H); 7.40 (*dd*, *J* = 5.1, 1.1, 1 H); 7.64 (*d*, *J* = 4.3, 1 H); 7.68 (*d*, *J* = 15.3, 1 H); 7.72 (*dd*, *J* = 4.3, 1.1, 1 H). ^{13}C-NMR ($CDCl_3$): 51.9; 52.4; 52.5; 113.5; 115.0; 117.8; 127.9; 128.7; 128.8; 128.9; 129.9; 131.3; 132.3; 136.6; 141.5; 148.1; 149.7; 163.3; 163.4; 167.1

*Dimethyl 2,5-Bis[5-[(1*E*)-3-methoxy-3-oxoprop-1-enyl]-2-thienyl]furan-3,4-dicarboxylate* (**17**): Yield 82%. M.p. 137.5–138.0°. IR: 3095, 1740, 1641, 1410. ^{1}H-NMR ($CDCl_3$): 3.74 (*s*, 6 H); 3.83 (*s*, 6 H); 6.22 (*d*, *J* = 15.8, 2 H); 7.17 (*d*, *J* = 3.6, 2 H); 7.64 (*d*, *J* = 3.6, 2 H); 7.68 (*d*, *J* = 15.8, 2 H). ^{13}C-NMR ($CDCl_3$): 51.8; 52.5; 115.0; 118.0; 129.1; 131.3; 131.9; 136.4; 141.8; 148.5; 163.1; 167.0.

*Dimethyl (2*E*,2′*E*)-3,3′-(Thiophene-1,5-diyl)bis[prop-2-enoate]* (**18**): According to the *General Procedure*, but with 2 mmol of malonic acid monomethyl ester, 30 µl of piperidine, and 4 ml of pyridine. Yield 70%. IR: 3047, 1702, 1615, 1440, 1256. ^{1}H-NMR ($CDCl_3$): 3.65 (*s*, 6 H); 6.10 (*d*, *J* = 15.4, 2 H); 7.02 (*s*, 2 H); 7.55 (*d*, *J* = 15.4, 2 H). ^{13}C-NMR ($CDCl_3$): 51.9; 118.3; 131.7; 136.6; 141.8; 166.9.

8. *5-[3,4-Bis(methoxycarbonyl)-5-(2-thienyl)furan-2-yl]thiophene-2-carboxylic Acid* (*= 2-(5-Carboxy-2-thienyl)-5-(2-thienyl)furan-3,4-dicarboxylic Acid Dimethyl Ester* **15**). To a stirred soln. of **11** (45 mg, 0.12 mmol) in acetone (5 ml), a 4N soln. of *Jones* reagent was added at r.t. until the red color persisted. The excess *Jones* reagent was then destroyed by addition of propan-2-ol (→ green). The mixture was diluted with H_2O (5 ml), the aq. layer extracted with CH_2Cl_2 (2 × 5 ml) and the combined org. layer washed with brine, dried ($MgSO_4$), and evaporated: 31 mg (65%) of crude **15**, which was used in the next step without further purification. IR: 3200 (br.), 1580, 1418, 1240. ^{1}H-NMR ($CDCl_3$): 3.83 (*s*, 3 H); 3.86 (*s*, 3 H); 5.00 (br. *s*, 1 H); 7.06 (*m*, 1 H); 7.42 (*d*, *J* = 5.1, 1 H); 7.70 (*d*, *J* = 3.8, 1 H); 7.72 (*AB*, J_{AB} = 3.5, 2 H).

9. *2,5-Di(2-thienyl)furan-3,4-dimethanol* (**21**). A soln. of **1** (50 mg, 0.14 mmol) in anh. THF (2 ml) was added dropwise to a suspension of $LiAlH_4$ (22 mg, 0.57 mmol) in THF (2 ml) at 0°. The mixture was stirred for 10 min at 0° and quenched by careful addition of H_2O (22 µl), 15% aq. NaOH soln. (22 µl), and H_2O (44 µl). The white precipitate of aluminium salts was filtered through a thin pad of *Celite*, and the org. layer was evaporated: pure **21** (41 mg, quant.). M.p. 134.0–134.5°. IR: 3336 (br.), 2927, 1418, 1156. ^{1}H-NMR ($CDCl_3$): 3.08 (br. *s*, 2 H); 4.74 (*s*, 4 H); 7.02 (*t*, *J* = 4.3, 2 H); 7.26 (*d*, *J* = 4.3, 4 H). ^{13}C-NMR ($CDCl_3$): 55.4; 121.5; 125.1; 125.6; 127.6; 131.8; 145.1.

10. *2,5-Di(2-thienyl)furan-3,4-dicarbaldehyde* (**22**). To a stirred suspension of PDC (246 mg, 0.64 mmol) in CH_2Cl_2 (5 ml), a soln. of **21** (45 mg, 0.16 mmol) in CH_2Cl_2 (1 ml) was added at r.t. After stirring for 8 h, H_2O (10 ml) was added, the aq. phase extracted with CH_2Cl_2 (2 × 5 ml), the combined org. layer washed with H_2O, dried ($MgSO_4$), and evaporated, and the crude product purified by FC (hexane/AcOEt 16:1 → 1:1). Yield 71%. IR: 3098, 2830, 1664, 1520, 1416. ^{1}H-NMR ($CDCl_3$): 7.15 (*dd*, *J* = 4.5, 3.6, 2 H); 7.53 (*dd*, *J* = 4.5, 1.1, 2 H); 7.94 (*dd*, *J* = 3.6, 1.1, 2 H); 10.45 (*s*, 2 H).

11. *Saponification: General Procedure.* A soln. of ester (0.14 mmol) and $LiOH \cdot H_2O$ (35 mg, 0.84 mmol) in MeOH/H_2O 4:1 (3 ml) was refluxed under N_2. After complete disappearance of the ester, the soln. was diluted by addition of H_2O (3 ml) and extracted with CH_2Cl_2 (3 × 4 ml). The aq. layer was cooled in an ice/water bath, acidified by addition of 10% aq. HCl soln. (pH 2), and then extracted with CH_2Cl_2 (3 × 4 ml). The org. layer was dried ($MgSO_4$) and evaporated: the crude product was used without further purification.

2,5-Di(2-thienyl)furan-3,4-dicarboxylic Acid (**23**): Reaction time 15 min. Yield 95%. M.p. 228°. IR: 3447 (br.), 3101, 1683, 1553, 1483. ^{1}H-NMR ((D$_6$)acetone): 7.08 (*dd*, *J* = 5.1, 3.7, 2 H); 7.58 (*dd*, *J* = 5.1, 1.0, 2 H); 7.80 (*dd*, *J* = 3.7, 1.0, 2 H). ^{13}C-NMR ((D$_6$)acetone): 114.6; 128.4; 129.5; 129.7; 130.7; 150.0; 164.5.

2,2′-(Thiophene-2,5-diyl)bis[5-(2-thienyl)furan-3,4-dicarboxylic Acid] (**24**): Reaction time 6 h. Yield 86%. M.p. > 400°. IR: 3363 (br.), 2910, 1633, 1401. ^{1}H-NMR ((D$_6$)acetone): 7.11 (*dd*, *J* = 4.9, 3.83, 2 H); 7.62 (*dd*, *J* = 4.9, 0.8, 2 H); 7.85–7.87 (*m*, 4 H).

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