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PECULIARITIES OF THE BEHAVIOR OF SUCCINYL DICHLORIDE IN FRIEDEL-CRAFTS REACTION WITH THIOPHENES*

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The reactions of thiophene, 2-methyl-, and 2-bromothiophene with succinyl dichloride in the presence of $AlCl_3$, $TiCl_4$, and $SnCl_4$ have been studied. The effect of the acylation conditions, the relative amounts and nature of the Lewis acid on the ratio and yields of the 1,4-di(2-thienyl)-1,4-diones and 4-oxo-4-(2-thienyl)butyric acids formed have been demonstrated. Under the reaction conditions, the formation of 4,4-di(2-thienyl)but-3-enoic acids (the main products in many cases) and also 4,4-di(2-thienyl)-butyrolactones was demonstrated.

Keywords: 4,4-di(2-thienyl)but-3-enoic acids, 4,4-di(2-thienyl)butyrolactones, 4-oxo-4-(2-thienyl)butyric acids, succinyl dichloride, 1,4-(2-thienyl)butane-1,4-diones, thiophenes, acylation.

1,4-Di(2-thienyl)butane-1,4-diones are convenient starting materials for the preparation of 2,5-di(2-thienyl)pyrroles, -furans, and -thiophenes which, in turn, can serve as precursors of polymers and monomers which show electrical conductivity and particular photochemical properties [1]. The known syntheses of 1,4-dihetarylbutane-1,4-diones are very varied. With regard to the most frequently used of these, the Stetter method is based on a Michael addition of aldehydes to the activated double bond of enones in the presence of cyanide or thiazolium salt [2, 3]. Particularly promising for the preparation of unsymmetrical 1,4-diketones (although somewhat time consuming) is the method due to Kulinkovich *et al.* based on the reaction of methyl- and α-bromomethyl ketones [4]. The reactions of diesters or N,N,N',N'-tetrasubstituted succinic acid diamides with hetaryl lithium [5] or reaction of sodium acetylide with hetarenecarbaldehydes and subsequent conversion of the 1,4-dihetarylbut-2-en-1,4-diol to the corresponding 1,4-diketone in the presence of alcoholic alkali solution [6] are relatively simple but they give low yields.

We consider in more detail the data available for the Friedel-Crafts reaction of thiophene **1a**, 2-methylthiophene **1b**, and 2-bromothiophene **1c** with succinyl dichloride (SDC) as the method for synthesizing the di(2-thienyl)-1,4-dione **2a** and the substituted bis(5-methyl-2-thienyl)-1,4-dione **2b**, and bis(5-bromo-2-thienyl)-1,4-dione **2c**, respectively. This apparently simple and obvious route meets a series of complications,

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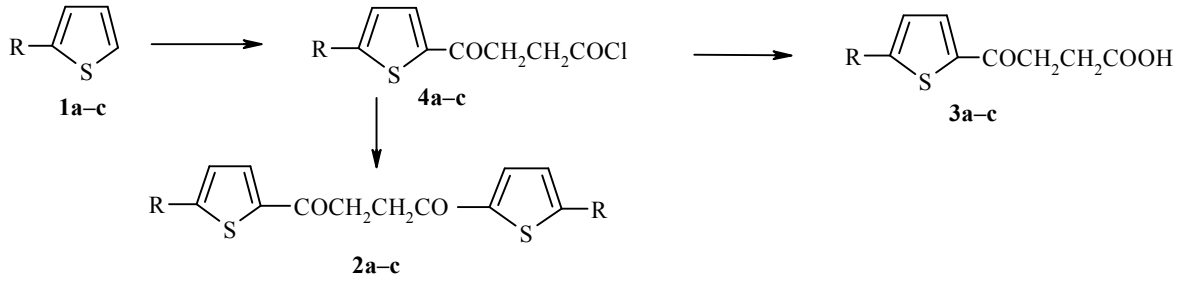
however. Firstly, the reaction of thiophene with succinyl dichloride under conditions standard for the thiophene series (*i.e.* the presence of tin tetrachloride) leads to the monoacylation product, 4-oxo-4-(2-thienyl)butyric acid (**3a**) [7] after work up. Without a detailed discussion of the reason for this occurrence, it should just be noted that it is evidently due to the interaction of two closely spaced COCl groups activated by complex formation with the $SnCl_4$. Indeed, for glutaryl dichloride, the main product is 5-oxo-5-(2-thienyl)pentanoic acid, and reaction to give the bisacylation product, 1,5-di(2-thienyl)pentane-1,5-dione, occurs in only 5% yield [8]. However, the reaction of adipyl dichloride in the presence of $SnCl_4$ occurs smoothly to give the 1,6-di(2-thienyl)hexane-1,6-dione in 80% yield [9, 10].

Merz and Ellinger reported in 1991 a successful acylation of thiophene by succinyl dichloride [11] using dry dichloromethane or 1,2-dichloroethane at room temperature with about 2 mol of $AlCl_3$ per mole of acid chloride (i.e. one mol for each of the COCl groups). The yield of the unpurified diketone **2a** was 55-60%. At the same time and under the similar conditions, a yield of 45% for this product was reported in a patent [12]. In the case of 2-methylthiophene and using the same conditions or with refluxing in dichloromethane, the diketone **2b** was obtained in only 30% yield [13]. When an excess of $AlCl_3$ was used for 2-bromothiophene (~ 3 mol per mol of acid chloride), the yield of diketone **2c** was 61% [14].

According to the data given above, the 4-oxo-4-thienylbutyric acid chlorides **4a-c** formed in the first stage of the acylation as a *nν*–complex with the Lewis acid in the first stage of acylation (in our scheme the complexes are not shown for simplicity) are less active as electrophiles than the starting complex with succinyl dichloride. Thus it is clear why, upon acylation of thiophene and its substituted derivatives, the use of a weak Lewis acid gives mainly the keto acids **3** after hydrolysis of the reaction mixture whereas a strong acid gives the diketone **2** (Scheme 1).

Scheme 1

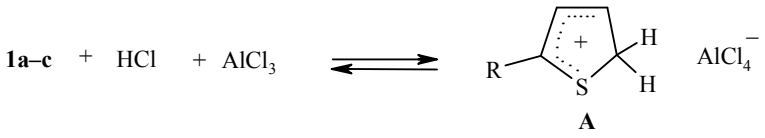


a R = H, **b** R = Me, **c** R = Br

At the same time, the reasons for the modest overall yields of products **2** and **3** obtained in the presence of $AlCl_3$ and also the unexpectedly low yield of diketone **2b** formed from 2-bromothiophene (apparently activated by comparison with thiophene and 2-bromothiophene) remain unclear. It must also be assumed that, in the course of the reaction, there arise some kind of products other than the diketones **2** and keto acids **3** which previously simply could not be found or separated. In this paper we have carried out a detailed study of the composition of the products formed upon acylation of thiophenes **1a-c** using succinyl dichloride in the presence of different amounts of $AlCl_3$, as well as $SnCl_4$ and $TiCl_4$, in order to optimize the synthesis of the diketones **2**. The results obtained are given in Table 1.

In our view one of the reasons for the low yields of the acylation products is the formation of a type **A** σ–complex (Scheme 2). As noted in the studies [15, 16] the hydrogen chloride formed upon acylation of a thiophene series compound in the presence of $AlCl_3$ is not removed from the reaction medium but protonates the starting thiophene to form an approximately equimolar quantity of the type **A** σ-complex. Under standard work up of the reaction mixture this complex is converted to the starting thiophene.

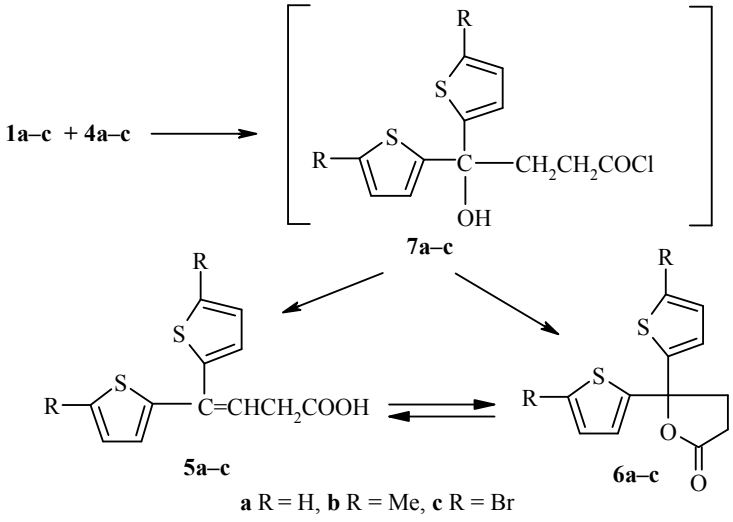
Scheme 2



Bearing in mind that a single molecule of diketone **2** can bind 2 molecules of $AlCl_3$ as the *n*,π-complex and the hydrogen chloride (2 molecules) formed upon acylation can bind a further 2 molecules of $AlCl_3$ as the σ-complex **A** and 2 molecules of thiophene **1**, the yield of the target product **2** with a ratio of compound **1** to $AlCl_3$ to succinyl dichloride of 2:2:1 should not exceed 50%. That the yield of diketone **2** in a number of cases is somewhat higher can be related to a reversibility of the protonation (although the equilibrium is shifted to the right) and the presence of some excess of the starting thiophene compound beyond 2 mol per mol of acid chloride. The lower yields in the case of the 2-methylthiophene can be explained by the higher stability of the **A** type σ-complex due to the effect of the methyl group. However, the fact that the yield of diketone **2b** is always below 50% supports the occurrence of some other reactions beyond those shown in Scheme 1.

Our analysis of the ^{1}H NMR spectra of the mixture of products formed in the system thiophene compound–succinyl dichloride–$AlCl_3$ allowed us to identify a previously unknown reaction route for this system which yielded the 4,4-di(2-thienyl)but-3-enoic acids **5a-c** and also the lactones **6a-c** (Table 1). Acids **5a-c** were quite readily separated by acidification of an alkaline extract of the admixture of reaction products of thiophenes **1a-c** with succinyl dichloride. Purification of the lactones **6a-c** from the mixture with acids **5a-c** caused significant difficulty and was carried out only for the lactone **6b**. The most favourable case for separation of the lactone involved the use of $TiCl_4$ as condensation agent (experiment 12) where the diketone **2b** was not found overall. Fivefold washing of the mixture of reaction products with saturated sodium bicarbonate solution gave a mixture of acid **5b** and the lactone **6b** which still contained 60% of the acid **5b** (^{1}H NMR). Only a further sevenfold washing allowed the preparation of sufficiently pure (> 95%) lactone **6b**. Formation of the indicated products can be regarded as the result of alkylation of thiophenes **1a-c** with the participation of the keto group of the acid chloride and subsequent reaction of the 4-hydroxy-4,4-di(2-thienyl)butyric acid chlorides **7a-c** produced. Dehydration of compounds **7** gives the acids **5** while dehydrochlorination of **7** leads to the γ-lactones **6a-c**. In principle the latter can also be formed from the acids **5a-c** *via* ring-chain tautomerism (Scheme 3).

Scheme 3



a R = H, **b** R = Me, **c** R = Br

TABLE 1. Reactions of 2-R-Thiophenes **1a-c** with Succinyl Dichloride (SDC) under Varying Conditions

Experiment	Starting 2-R-thiophene	Reaction conditions				Products			
						Molar ratio of products **2,5,6** per 1 mol of keto acid **3**			Overall yield of product **2,5,6** per SDC, %
		T, °C	Reaction time, h	Lewis acid (MX_n)	Molar ratio MX_n:SDC	**2**	**5**	**6**	
1	**1a**	20	3	$AlCl_3$	2.2	25	9.5	0.5	69
2		20	3	$AlCl_3$	6	1.0	0.5	0.02	89
3		20	72	$AlCl_3$	6	1.3	1.3	0	75
4		40	12	$AlCl_3$	6	6.5	3.3	1.5	65
5		20	3	$TiCl_4$	2.2	0	3.5	0.5	85
6		20	3	$SnCl_4$	2.2	0.5	13.0	3.0	91
7	**1b**	20	3	$AlCl_3$	1.1	1.2	6.5	0.5	85
8		20	3	$AlCl_3$	2.2	2.4	11.5	2.0	70
9		20	72	$AlCl_3$	6	1.0	0.8	0	84
10		40	6	$AlCl_3$	6	0.6	0.5	0	87
11		40	12	$AlCl_3$	6	0.9	0.6	0.5	79
12		40	12	$TiCl_4$	2.2	0	9.6	2.0	85
13		20	3	$SnCl_4$	2.2	0	11.0	0	89
14	**1c**	40	3	$AlCl_3$	2.2	7.5	3.7	0	60
15		40	12	$AlCl_3$	6	1.6	0.3	0	74
16		40	24	$AlCl_3$	6	1.5	0.5	0	79
17		20	3	$TiCl_4$	2.2	0.5	11.0	0	85
18		40	12	$TiCl_4$	6	0	8.5	0.7	58

TABLE 2.[1]H NMR Spectra of 1,4-Bis(5-R-2-thienyl)butane-1,4-diones **2**, 4-(5-R-2-Thienyl)-4-oxobutyric Acids **3**, 4,4-Bis(5-R-2-thienyl)but-3-enoic Acids **5**, and 5,5-Di(5-R-2-thienyl)-3,4-dihydrofuran-2-ones **6***

Com-pound	Chemical shifts, δ, ppm (*J*,Hz)							
	$H_{aliph.}$					$H_{thiophene}$		
	CH_2	CH_2CO (t, *J* = 6.6)	CH_2COO (t, *J* = 6.6)	CH= (t)	CH_3	H-3 [H-3']	H-4 [H-4']	H-5 [H-5']
2a	3.40 (s)				—	7.89 (dd, *J* = 3.8, *J* = 1.1)	7.15 (dd, *J* = 5.0, *J* = 3.8)	7.65 (dd, *J* = 5.0, *J* = 1.1)
2b	3.32 (s)				2.54 (s)	7.62 (d, *J* = 3.8)	6.81 (d, *J* = 3.8)	—
2c	3.29 (s)				—	7.55 (d, *J* = 4.0)	7.12 (d, *J* = 4.0)	—
3a		3.27	2.81		—	7.67 (m)	7.15 (m)	7.79 (m)
3b		3.20	2.78		2.53 (s)	7.58 (d, *J* = 3.5)	6.81 (d, *J* = 3.5)	—
3c		3.20	2.80		—	7.58 (d, *J* = 3.9)	7.20 (d, *J* = 3.9)	—
5a	3.32 (d, *J* = 7.4)			6.33 (*J* = 7.4)	—	7.05–7.10 overlapping [6.89 (dd, *J* = 3.6, *J* = 1.2)]	7.05-7.10 overlapping [6.94 (dd, *J* = 5.0, *J* = 3.7)]	7.40 (dd, *J* = 5.0, *J* = 1.3) [7.21 (dd, *J* = 5.1, *J* = 1.3)]
5b	3.33 (d, *J* = 7.2)			6.16 (*J* = 7.2)	2.50 (s) 2.45 (s)	6.83 (d, *J* = 3.3) [6.60 (d, *J* = 3.3)]	6.71-6.72 overlapping	—
5c	3.30 (d, *J* = 7.5)			6.20 (*J* = 7.5)	—	7.04 (d, *J* = 3.8) [6.91 (d, *J* = 3.9)]	6.81 (d, *J* = 3.8) 6.66 (d, *J* = 3.9)	—
6a	2.73 (2H, t, *J* = 7.8), 2.98 (2H, t, *J* = 7.8)				—	7.66 (2H, dd, J_1≈5, J_2≈1, H-5',5)"*[2]		
6b	2.70 (2H, dt, J_1 = 8.0, J_2=1.2), 2.88 (2H, dt, J_1 = 8.0, J_2 = 1.2)				2.46 (6H, d, ^4J = 1)	6.62 (2H, m); 6.84 (2H, d, ^3J = 3.3)		
6c	2.73 (2H, t, *J* = 6.3), 2.85 (2H, t, *J* = 6.3)				—	—*[3]		

* [1]H NMR spectra of 1,4-diketones **2** agree with the literature data for 1,4-bis(2-thienyl)butane-1,4-dione (**2a**) [13], 1,4-bis(5-methyl-2-thienyl)butane-1,4-dione (**2b**) [13], and 1,4-bis(5-bromo-2-thienyl)butane-1,4-dione (**2c)** [14]; spectra of keto acids **3a,c** agree with data in [27] and [28], respectively, for 4-oxo-4-(2-thienyl)butyric acid (**3a**) and 4-(5-bromo-2-thienyl)-4-oxobutyric acid (**3c)**. The spectra of 4-(5-methyl-2-thienyl)-4-oxobutyric acid (**3b**) and the unsaturated acids **5a-c** and lactone **6b** are reported for the first time

*[2] Other signals were overlapped by the $H_{thiophene}$ signals of compounds **2a, 3a, 5a**.

*[3] Overlapped by the signals for $H_{thiophene}$ in compounds **2c, 3c, 5c**.

Similar transformations are known for Stobbe reaction intermediates involving benzophenone and diethyl succinate where it was possible to separate some of the analogs of lactones **6** [17, 18] and in several cases analogs of the acids **5** also [19] with determination of the ratio of their tautomers [20]. Further, 4,4-diphenylbutyrolactone has been reported as the reaction product of succinyl dichloride with benzene in the presence of $AlCl_3$ [21, 22]. For certain 4,4-diarylbutyrolactones with prolonged heating in acid medium it was possible to record conformation to the corresponding unsaturated acids as analogs of acid **5** [20, 23]. At the same time, 4,4-diphenyl-3-butenoic acid in conc. H_2SO_4 was rapidly converted in 92% yield to 4,4-diphenylbutyrolactone [24]. The fact that the compounds observed and separated by us exist as the acid form **5a-c** was established on the basis of the ^1H NMR spectroscopic data and is found to be in agreement with the results of alkaline titration and elemental analysis.

It should also be noted, in the ^1H NMR spectra of the mixture of succinylation products of the thiophenes **1a-c**, there are present signals for the protons of two CH_2 groups as triplets or doublets of triplets in the ranges 2.70-2.73 and 2.85-2.98 ppm which we assigned to a small amount (~ 5-15 mol. %) of the lactones **6a-c**. The choice between the latter and the corresponding 4-hydroxy-4,4-di(R-thienyl)butanoic acids was made from examination of literature data for similar structures with ^1H NMR spectra showing a characteristic AA'BB' system of signals for a CH_2CH_2 fragment. In the ^1H NMR spectra of the 4,4-diarylbutyrolactones (Ar = Ph, 4-FC_6H_4, 4-$MeOC_6H_4$, or 3,4-$(MeO)_2C_6H_3$) [25] and a single example we found in the literature with substituents relating to the thiophene series (Ar = 2,2':5',2'-terthiophen-5-yl) [11], the A,A'B,B' system is described as two multiplets but in [24] for Ar = Ph as two triplets (the difference evidently being due to variations in instrumental resolution). It is important to note that the spread of chemical shift values for the CH_2 groups for a rather broad series of substituents is small and they vary in the range 2.5 and 2.9 to 2.6 and 2.9 ppm. A shift to high field would be expected for the hydroxy acid **7**. The single related compound we found in the literature as *tert*-butyl 4-hydroxy-4,4-bis(4-dimethylaminophenyl)butyrate [26] shows signals for the CH_2 groups as triplets at 2.25 and 2.51 ppm which markedly differ from the values we observed.

The composition of the reaction mixtures obtained (before their separation) was determined by us using ^1H NMR spectroscopy. The molar ratios of the main product keto acids **3a-c**, diketones **2a-c**, acids **5a-c**, and lactones **6a-c** as well as their overall yields were calculated for each experiment with regard to the weight of the obtained mixture, quantity of succinyl dichloride, variation of reaction conditions, and amounts of reagents (see Table 1). The ^1H NMR parameters for the reaction products which were used for the analysis of the mixtures obtained are given in Table 2.

From our data presented in Table 1 the 4,4-di(2-thienyl)but-3-enoic acids **5a-c** proved, in most cases, to be main components of the mixture formed upon succinylation of the thiophenes **1a-c**. The use of titanium or tin tetrachlorides as condensing agents which cannot promote formation of the diketones **2a-c** leads to a mixture of products with an acid **5a-c** content of 70-80%. It is most likely that the reason why the latter were not identified is their loss during work up. The formation of σ-complexes of type **A** in reactions with $AlCl_3$ agrees with the recovery of up to 20% of starting thiophene compound in experiments 1-4, 7-11, and 14-16. In addition, such σ-complexes can be partially decomposed by the water evolved upon formation of acids **5** and lactones **6**. The maximum yields of diketones **2a-c** are achieved upon prolonged refluxing of a solution of the starting components in dichloromethane which contains 6 mol of $AlCl_3$ per mol of succinyl dichloride. These conditions evidently enable liberation of the thiophene compound from the σ-complex **A** and ensure a fuller use of the former in the acylation reaction.

EXPERIMENTAL

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 300 radio frequency spectrometer (300 and 75 MHz respectively) using $CDCl_3$ with TMS or the residual signal of chloroform at δ 7.265 ppm as

internal standard. EI mass spectra were obtained on a Kratos instrument (70 eV). Monitoring of the reaction course and the purity of the products obtained was carried out by TLC on Silufol UV-254 plates (Kavalier, Czech Republic) using the system ethyl acetate–hexane (1:4) and dichloromethane–petroleum ether (40-60ºC) (1:2) and were displayed using iodine vapor. Preparative separation of the products was carried out on a Merck SiO_2-60 silica gel column (0.060-0.200 mm) using petroleum ether (40-60ºC), ethyl acetate, dichloromethane, methanol or their mixtures as eluents. Melting points were measured on a Boetius microscope stage.

The 2-methylthiophene and 2-bromothiophene used in this work came from the Acros Company and the remaining reactants are native products. Succinyl dichloride was prepared by method [29].

Reaction of Thiophenes 1a-c with Succinyl Dichloride (**General Method** used in experiments 1-18). A solution of succinyl dichloride (1 ml, 9.08 mmol) and the thiophene **1a**, 2-methylthiophene **1b**, or 2-bromothiophene **1c** (19.5 mmol) in dry dichloromethane (6 ml) was added with cooling and stirring to a suspension or solution of the Lewis acid (20.0 mmol) in dry dichloromethane (25 ml). The mixture obtained was stirred for 3 h at room temperature. The product was poured onto ice (100 g), conc. HCl (2 ml) was added, and the product was then stirred for 1 h before removing the organic layer. The aqueous layer was extracted with dichloromethane (2×30 ml) and the combined extract was washed with 2N HCl, then twice with water, dried over Na_2SO_4, and filtered. The filtrate was evaporated on a rotary evaporator and the residue was examined by ^{1}H NMR. The methods for synthesis or separation of the individual products are given below.

1,4-Di(2-thienyl)butane-1,4-dione (2a). A solution of thiophene **1a** (17.4 ml, 217.9 mmol) and succinyl dichloride (10 ml, 90.8 mmol) in dry dichloromethane (25 ml) was stirred vigorously over 40 min with addition of a suspension of $AlCl_3$ (29 g, 211.8 mmol) in dry dichloromethane (30 ml). The temperature was maintained in the range 0-8ºC by cooling with ice/salt. The reaction mixture became dark-red in color. Stirring was continued for a further 3 h, the reaction mixture was poured onto ice (400 g), conc. HCl (10 ml) was added, and the emulsion produced was stirred for 30 min. The dark-green colored organic layer was separated and the aqueous layer was extracted with dichloromethane (3×50 ml). The combined extract was washed with 2 N HCl solution (20 ml), water (2×50 ml), and then $NaHCO_3$ solution (20 ml), dried over Na_2SO_4, and filtered. The filtrate was evaporated on a rotary evaporator to give a mixture of products (18 g). The latter was triturated with a small amount of alcohol, filtered, washed twice on the filter, and dried in air to give the product (15.9 g) which was recrystallized from ethanol (400 ml) to give the pale-blue diketone **2a** (9.65 g, 42.5%); mp 127-129ºC (mp 130-131ºC [8]).

1,4-Bis(5-methyl-2-thienyl)butane-1,4-dione (2b) and 4,4-Bis(5-methyl-2-thienyl)but-3-enoic acid (5b). A solution of 2-methylthiophene (15 ml, 151.8 mmol) and SDC (7 ml, 63.25 mmol) in dry dichloromethane (20 ml) was added with vigorous stirring over ~ 40 min to a suspension of $AlCl_3$ (20.2 g, 151.8 mmol) in a mixture of dry dichloromethane (22 ml) and petroleum ether (14 ml). The temperature was maintained at 5-15ºC by cooling in ice. Stirring was continued at room temperature for a further 5 h. The reaction mixture was poured onto ice (300 g), conc. HCl (8 ml) was added, and the emulsion obtained was stirred for 60 min. The organic layer was separated and the aqueous layer was worked up as described above for diketone **2a**. Evaporation on a rotary evaporator gave a mixture of products (17 g) which was dissolved in dichloromethane and filtered through a layer (15 g) of silica gel. The filtrate was evaporated to give an oil (11 g) which was dissolved at 0ºC in methanol (5 ml) and the solution was held for ~16 h at 4ºC. The green crystals (3.12 g) were filtered off and recrystallized from ethyl acetate to give blue crystals of the diketone **2b** (1.2 g, 7.5%) with mp 170-171ºC (mp 176ºC [13]). The diketone **2b** was obtained in 10% yield by a method analogous to the above for the synthesis of diketone **2a** from the 2-methylthiophene (3.3 g, 21.8 mmol), SDC (1 ml, 9.08 mmol), and $AlCl_3$ (2.905 g, 21.8 mmol); mp 168-170ºC (mp 176ºC [13]).

Addition of petroleum ether to the mother liquor obtained when separating diketone **2b** (see above) gave brown crystals of acid **5b** (1.6 g, 9.4%) which were recrystallized from a mixture of ethyl acetate and petroleum ether (1:1); mp 101-102ºC. ^{13}C NMR spectrum, δ, ppm: 15.99; 16.14; 35.68; 119.91; 125.67;

126.06; 126.73; 133.10; 136.83; 140.33; 141.48; 143.98; 178.66 (COOH). Mass spectrum, *m/z*: 278 [M]. Found, %: C 59.99; H 5.04; S 22.91. $C_{14}H_{14}S_2O_2$. Calculated, %: C 60.40; H 5.07; S 23.04.

1,4-Bis(5-bromo-2-thienyl)butane-1,4-dione (2c). A mixture of SDC (2 ml, 18.15 mmol), 2-bromothiophene (4.1 ml, 41.7 mmol), and dry dichloromethane (9 ml) was added slowly, dropwise, and with cooling to 0-10ºC to a suspension of $AlCl_3$ (5.81 g, 43.5 mmol) in dry dichloromethane (10 ml). The product was stirred for a further 2.5 h at room temperature, and then refluxed for 30 min. The cooled reaction product was poured onto ice (200 g), conc. HCl (2 ml) was added, and stirring continued for 1 h. The organic layer was separated and the aqueous layer was worked up as described for diketone **2a**. Evaporation on a rotary evaporator gave a mixture of products as an oil (6.7 g) which was dissolved in hot ethanol. The crystals formed on cooling were filtered off and dried in air to give diketone **2c** (2.73 g, 37%); mp 175-176ºC (mp 181ºC [14]; mp 177ºC [30]).

4-Oxo-4-(2-thienyl)butyric Acid (3a). A solution of SDC (9 g, 50 mmol) in chlorobenzene (40 ml) was added dropwise over 2.5 h to a solution of thiophene (8.4 g, 100 mmol) and $SnCl_4$ (26 g, 100 mmol) in chlorobenzene (100 ml) maintained at 2-4ºC. The mixture obtained was stirred for 1 h and then at 10-15ºC and a solution of HCl (4%, 100 ml) was added. The organic layer was separated and extracted with a 20% solution of Na_2CO_3 (3x10 ml). Acidification of the alkaline extract with HCl gave the acid **3a** (6.1 g, 66%); mp 117-119ºC (water) (mp 119-120ºC [31]).

4-(5-Methyl-2-thienyl)-4-oxobutyric Acid (3b). The mixture of reaction products obtained in experiment 9 was separated by flash chromatography on silica gel eluting with, in sequence, a mixture of dichloromethane and petroleum ether (1:1.5), dichloromethane, and a mixture of ethyl acetate and methanol (10:1) and monitored by TLC. The final fraction was evaporated, the oil obtained was triturated with ether, and the crystals produced were filtered and dried in air to give the acid **3b** (0.261 g, 7.3%); mp 106-108ºC (hexane) (mp 108-109ºC [3]).

4,4-Di(2-thienyl)-3-butenoic Acid (5a). The mixture of products obtained from experiment 4 from SDC (9.08 mmol) was dissolved in methylene chloride and the solution obtained was washed with Na_2CO_3 solution (5%, 3×10 ml). The combined aqueous layer was acidified to pH 3 with conc. HCl and extracted with ethyl acetate (3×20 ml). The extract was evaporated on a rotary evaporator to give an oil (0.76 g) which was extracted three times by refluxing for 1 h with hexane (20 ml). The hot hexane extract was decanted each time. Evaporation of the combined hexane extracts on a rotary evaporator gave acid **5a** (0.4 g, 18%); mp 80-81ºC (hexane). ^{13}C NMR Spectrum, δ, ppm: 35.65; 121.61; 125.68; 126.79; 127.08; 127.60; 127.92; 128.95; 132.70; 139.23; 146.24; 178.01 (COOH). Found, %: C 57.41; H 4.03. $C_{12}H_{10}S_2O_2$. Calculated, %: C 57.57; H 4.03.

4,4-Bis(5-bromo-2-thienyl)-3-butenoic Acid (5c). The mixture of products obtained in experiment 18 was dissolved in dichloromethane, washed with Na_2CO_3 solution, the aqueous layer was acidified with HCl (see the preparation of acid **5a**), and then extracted with dichloromethane (3×20 ml). Solvent was evaporated on a rotary evaporator to give a viscous, brown oil which, as in the case of acid **5a**, was extracted with hexane. The hexane extract was evaporated and the residue was triturated in a minimal volume of dichloromethane to give the acid **5c** (0.29 g, 7.8%); mp 119-120ºC (hexane). ^{13}C NMR spectrum, δ, ppm: 35.56; 112.98; 114.23; 122.62; 127.05; 129.66; 130.60; 131.48; 139.83; 146.67; 177.62 (COOH). Found, %: C 35.41; H 1.92. $C_{12}H_8Br_2O_2S_2$. Calculated, %: C 35.31; H 1.98.

5,5-Bis(5-methyl-2-thienyl)dihydrofuran-2(3H)-one (6b). The mixture of products obtained in experiment 12 from SCD (9.08 mmol) was dissolved in dichloromethane, the solution was washed with a saturated solution of $NaHCO_3$ (12×20 ml), dried over Na_2SO_4, and evaporated on a rotary evaporator to give an oil (1.05 g) which contained an admixture of acid **5b** according to ^{1}H NMR data. Column chromatography of this oil (0.6 g) on silica gel (eluent petroleum ether and dichloromethane, 3:1) gave lactone **6b** (0.14 g, 9.5%) as a viscous oil. ^{13}C NMR spectrum, δ, ppm: 15.16; 29.33; 37.99; 85.76 (C–O); 124.64; 125.39; 128.02; 139.23; 140.97; 143.26; 175.20 (CO). Found, %: C 60.76; H 5.55. $C_{14}H_{14}S_2O_2$. Calculated, %: C 60.40; H 5.07.

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