

The Stobbe Condensation with Substituted Succinic Esters. II (1) A Synthesis of Benzothiophene Derivatives.

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The condensation of some thienyl carbonyl compounds with dimethyl phenylsuccinate using either sodium hydride or potassium *t*-butoxide as condensing agents, gave a stereoisomeric mixture of (*E*)- and (*Z*)-half-esters (3). The (*E*)-half-esters Ia-c were either cyclised to the corresponding benzothiophene derivatives or hydrolysed to the (*E*)-dibasic acids VIa-c, which were cyclised to the corresponding anhydrides VIIa-c. Methylation of VIIa,c gave the isomeric half-esters VIIIa,c. The (*Z*)-half-ester Id can cyclise easily to the lactone IX.

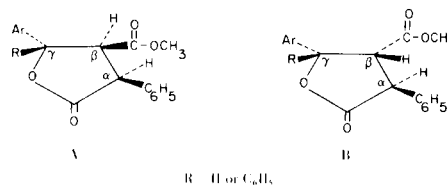
J. Heterocyclic Chem., **13**, 285 (1976).

Two groups of workers have studied the Stobbe condensation of α -phenylsubstituted succinic esters and have come to conflicting conclusions (4,5). The present investigation was intended to give an answer to the question concerning the propensity of the above ester to undergo a normal Stobbe condensation. Thus thiophene-, 5-methylthiophene-2-carboxaldehydes and phenyl 2-thienyl ketone were condensed with dimethyl phenylsuccinate using either sodium hydride (6) or potassium *t*-butoxide (7) as condensing agents, to give a stereoisomeric mixture of (*E*)- and (*Z*)-half-esters Ia-c and Id-f, respectively, in about 70% yield. The ratio of the isomeric half-esters depends upon the temperature of the condensation; higher temperatures (about 75° in the potassium *t*-butoxide method) favoured the formation of the (*E*)-isomers, whereas lower temperatures (5-10°) favoured the predominance of the (*Z*)-isomers to the extent of about 80% of the total yield. However when the condensation was carried out by about 45° (sodium hydride method), almost equal amounts of the stereoisomers were obtained. In all cases the ratio of the two isomers in the original mixture was spectrophotometrically determined (8).

The formation of the two stereoisomeric half-esters can be interpreted by taking in consideration the non-bonded interactions, which are both polar and steric in origin, involved in the formation of the intermediate γ -lactones (9,10). In presenting the role of the polar factor, we take three electric fields into consideration, that of the α -phenyl group, the electronegative field of the carbonyl oxygen in the β -ester group, as well as that of the heterocyclic ring. The formation of the intermediate γ -lactone (A), though favoured by repulsive forces between the

negative field of the heterocyclic ring and the ester group (β,γ -interaction), might be retarded by repulsive forces between the β -methoxycarbonyl and the α -phenyl groups (α,β -interaction). The above mentioned three bulky groups can be also considered in the discussion of the steric effect. It is thus conspicuous that β,γ -interactions (polar and steric) will favour the formation of the intermediate lactone (A), and hence the corresponding (*E*)-half-ester. On the other hand, the α,β -interactions, which can be polar and steric in nature, result in the formation of the intermediate γ -lactone (B) and consequently the corresponding (*Z*)-half-ester.

Experimental results revealed that phenyl-2-thienyl ketone failed to condense with the α -phenylsuccinic ester under mild conditions (low temperature). This can be interpreted by assuming that in addition to the above mentioned interaction, the formation of both intermediates (A or B) can be retarded by the α,γ -interactions (polar and steric), between the two phenyl groups.



The spectral data can be used as diagnostic tool for the elucidation of the structure and configuration of the (*E*)- and (*Z*)-half-esters. The infrared spectra of the (*E*)-half-esters Ia-c (Table I) and the (*Z*)-half-ester Id, show absorption bands which are correlated to saturated carboxylic acids and α,β unsaturated esters (11a,b). The higher vibra-

tional frequencies of **Id** is due to the field effect caused by the interaction of the polarisable negatively charged oxygen of the carbonyl group in the ester and carboxylic groups, and the π -sextet of the phenyl ring. The electronic spectra (Table I) of the half-esters **la,b** support the suggested (E)-configuration and show resemblance to similar (E)-half esters previously prepared (12). The (E)-half-ester **lc**, showed, however, a different behaviour which can be ascribed to the steric interference between the thienyl and the two phenyl rings, so that they are forced out of the plane of the double bond. The extinction coefficients of the (Z)-half-ester **ld** are considerably smaller than that of the corresponding (E)-isomer.

The nmr spectra furnish considerable information about the structure of **la-c** (Table I). These show a series of chemical shifts representing protons in different chemical environments; each absorption area is proportional to the number of protons it represents.

Corroboration of the (E)-configuration of the half-esters **la-c** is forthcoming from their cyclisation to the corresponding acetoxy-esters **Ila-c**. Information concerning the occurrence of cyclisation is derivable from chemical and spectroscopic evidence. The infrared spectra of **Ila-c** (Table I) exhibit two bands characteristic of the acetoxy and ester groups (**Ilb**). They show also two bands which are attributed to the aromatic C-H out-of-plane bending vibrations (**Ilc**). The electronic spectra of **Ila-c** (Table I) show resemblance to that of related systems

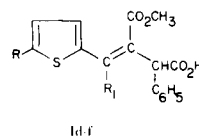
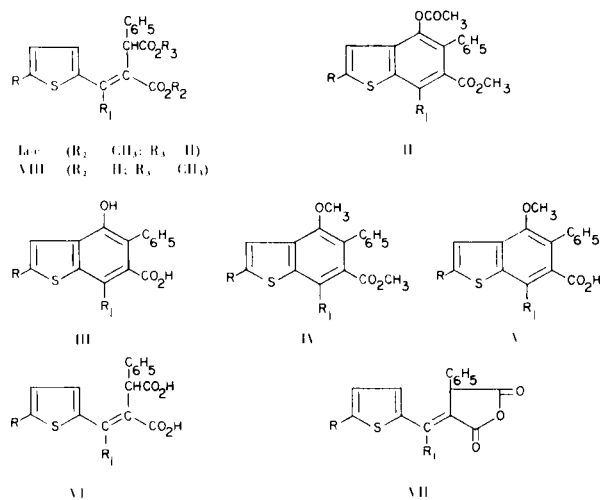
previously prepared (12). In comparison to the parent benzothiophene, these systems show bathochromic shift as well as hypsochromic effect, due to increased conjugation affected by the substituents. The nmr spectra (Table I) lend further support for the proposed structure. Thus each of the acetoxy-esters **Ila,c** show two 3Hs ascribed to the protons of the acetoxy and ester groups. The product **Ilb** shows an additional 3Hs attributed to the methyl group in position 2. They show also other signals characteristic of aromatic and heterocyclic protons at different positions. An elegant evidence for the structure of compounds **Ib** and **c** has been furnished from the study of their mass spectra. These show peaks at m/e 340 (M^+ , 6.2%) and m/e 402 (M^+ , 6.1%), which correspond to the molecular ions of **Ib** and **c** and give exact values for their molecular weights (*Cf.* Experimental).

Further information about the structure of the above acetoxy-esters is forthcoming from their chemical behaviour. Alkaline hydrolysis of these esters produced the corresponding phenolic acids **IIla-c**. The infrared spectra of these acids (Table II) show absorption bands characteristic of aromatic acids (**IIa**) and phenols (**IId**). Methylation of the above acids gave the corresponding methoxy-esters **IVa-c**. These show absorption bands in the infrared region characteristic of aryl esters (**IIb**). Saponification of the latter esters produced the methoxy acids **Va-c**. Their infrared spectra (Table II) show absorption bands which can be correlated to aromatic acids (**IIa**).

Table I

Compound	Ir Spectra (Potassium Bromide)		Uv Spectra (Ethanol)		Nmr Spectra	
	ν C=O cm^{-1}	γ C-H cm^{-1}	λ max	log ϵ	δ	Assignment
la	1718	770	212	3.99	3.80	(s, 3, CO ₂ CH ₃)
	1705	703	270	4.06	5.30	(s, 1, ph-CH)
			315	4.26	8.07	(s, 1, =C-H)
lb	1720	720	210	4.24	2.46	(s, 3, Ar-CH ₃)
	1702	697	270	3.91	3.86	(s, 3, CO ₂ CH ₃)
			315	4.42	5.40	(s, 1, ph-CH)
lc	1715	750	212	4.04	8.0	(s, 1, =C-H)
		700	252	3.37	3.64	(s, 1, ph-CH)
			280	3.27	3.77	(s, 3, CO ₂ CH ₃)
Ila	1768	738	211	4.41	7.41	(m, 13, Ar-H)
	1733	718	240	4.61	1.99	(s, 3, OCOCH ₃)
			268	3.99	3.61	(s, 3, CO ₂ CH ₃)
			315	3.82		
IIb	1740	725	212	4.38	1.90	(s, 3, OCOCH ₃)
	1709	718	242	4.58	2.53	(s, 3, Ar-CH ₃)
			278	4.07	3.50	(s, 3, CO ₂ CH ₃)
			318	3.85		
IIc	1770	768	205	4.46	1.91	(s, 3, OCOCH ₃)
	1732	730	238	4.56	3.18	(s, 3, CO ₂ CH ₃)
		708	275	3.82		
			304	3.74		

Alkaline hydrolysis of the (*E*)-half-esters Ia-c gave the corresponding dibasic acids VIa-c. The infrared spectra of these acids (Table II) show absorption bands which can be ascribed to saturated and unsaturated carboxyl groups (IIa). The electronic spectra of these acids (Table II) show resemblance to that of *trans*-cinnamic acid (13); the bathochromic shift observed can be attributed to enhanced conjugation caused by the unshared electron pair of the hetero atom (14,15). Supporting evidence for the structure of these diacids was also obtained from their cyclisation to the corresponding anhydrides VIIa-c. The infrared spectra of these anhydrides show carbonyl coupling bands charac-



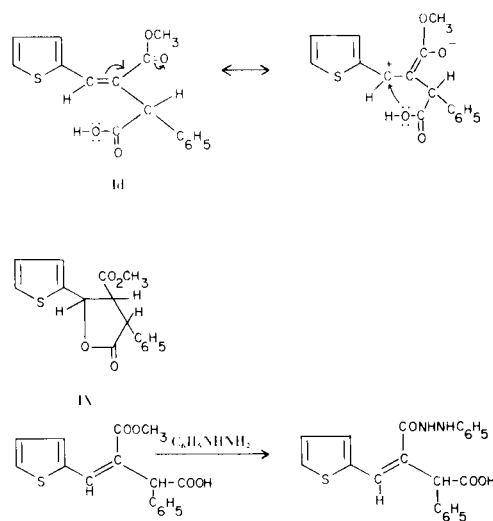
Compound	R	R ₁
IVIIIa	H	H
IVIIIb	C ₆ H ₅	H
IVIIIc	H	C ₆ H ₅

teristic of five-membered ring anhydrides (IIe). Methanalysis of the anhydrides VIIa,c resulted, as expected, in ring cleavage at the non-conjugated carbonyl group to give the corresponding α -half-esters VIIIa,c. The infrared spectra of these half-esters show strong carbonyl bands expected for non-conjugated esters (IIb) and α,β -unsaturated acids (IIa), respectively.

Experimental results revealed that the (*Z*)-half-ester Id has high susceptibility to undergo cyclisation reaction to the corresponding (*Z*)-lactone IX. Construction of space-filling models (Courtauld Atomic Models-Griffin) for the (*Z*)-half-esters indicated the close proximity of the carboxylic oxygen to the unsaturated carbon atom. This might have a profound effect in enhancing the nucleophilic attack of the negatively charged oxygen on the carbonium ion, leading ultimately to the formation of the saturated (*Z*)-lactone. Its infrared spectrum shows carbonyl stretching bands ascribed to saturated esters (IIb) and γ -lactones (IIf). The electronic- and the nmr spectra of IX agree well with the suggested (*Z*)-configuration. A further support for the structure of the (*Z*)-half-ester Id is attained from its tendency to react with phenylhydrazine to give the corresponding hydrazone X.

Table II

Compound	ν C=O	Infrared Spectra		ν OH	λ max	Electronic Spectra	
		γ (C-H) cm ⁻¹ (Potassium Bromide)				(Ethanol)	log ϵ
IIIa	1700	750, 708		3500		---	
IIIb	1688	750, 705		3496		---	
IIIc	1734	763, 708		3520		---	
IVa	1730	755, 710		---		---	
IVb	1735	765, 708		---		---	
	(Chloroform)						
IVc	1735	767, 708		---		---	
Va	1697	728, 698		---		---	
Vb	1698	725, 702		---		---	
Vc	1725	758, 748, 702		---		---	
VIa	1728				207		4.28
	1710				302		4.39
VIb	1745				205		4.11
	1725				265		3.72
VIc	1710				310		4.24
					207		4.56
					245		4.26
					285		4.21



EXPERIMENTAL

Microanalyses were performed by Dr. A. Bernhardt, Mikroanalytisches Laboratorium, B. R. D. The nmr spectra have been run on a T60A spectrometer in deuteriochloroform with TMS as the internal standard. The infrared (potassium bromide or chloroform) and the electronic spectra (ethanol) were taken on a Unicam SP-1000 and a Unicam SP-3000 spectrophotometers, respectively. The mass spectra were kindly done by the Chemistry Department, Swansea University, England.

The Stobbe Condensation.

a) Potassium *t*-Butoxide Method.

A mixture of the carbonyl compound (0.1 mole) and dimethyl phenylsuccinate (0.12 mole) in *t*-butyl alcohol (15 ml.) was gradually added during 25 minutes to a heated solution of potassium *t*-butoxide [from potassium (5.8 g.) and *t*-butyl alcohol (85 ml.)] at 70-75°. The mixture was kept at this temperature for an additional hour. The acidic product was extracted with ether, the ether insoluble product was filtered off, and crystallised from the proper solvent to give the (*E*)-half-ester. Upon distillation of the ether, a semi-solid product was left, which was triturated with benzene and left for two days, where a solid product separated out and proved to be the (*E*)-half-ester. Evaporation of benzene left a viscous oil which is the (*Z*)-half-ester. The latter product could not be crystallised owing to its ease of lactone formation on refluxing it with solvents. This procedure favoured the predominance of the (*E*)-half-esters to the extent of about 80%, of the total yield which was found to be about 75%.

b) Sodium Hydride Method.

A mixture of the carbonyl compound (0.1 mole), dimethyl phenylsuccinate (0.15 mole) and sodium hydride (0.2 mole) (50% dispersion in oil) in benzene was stirred at 40-45° for 3 hours and the acid product was worked up as above. The product was a mixture of almost equal amounts of (*E*)- and (*Z*)-half-esters (yield, 75%). When the condensation was repeated by 5-10°, the (*Z*)-half-ester predominated to the extent of about 80%. The ratio of the stereoisomers has been estimated spectrophotometrically according to the method of Dewar and Urch (8). It is noteworthy to mention that phenyl 2-thienyl ketone failed to condense at the latter temperature.

(*E*)- and (*Z*)-3-Methoxycarbonyl-2-phenyl-4-(2'-thienyl)but-3-enoic Acid (Ia,d).

The condensation with thiophene-2-carboxaldehyde (sodium hydride method at 45°) gave a mixture of Ia,d, yield, 75%. The (*E*)-half-ester Ia was crystallised from methanol as white crystals, m.p. 194°, yield, 55% of the total yield.

Anal. Calcd. for C₁₆H₁₄O₄S: C, 63.58; H, 4.67; S, 10.62; OCH₃, 10.28. Found: C, 63.72; H, 4.80; S, 20.40; OCH₃, 10.22.

The (*Z*)-half-ester Id could not be crystallised from any solvent, yield, 45%; ir (chloroform): 1768, 1713 cm⁻¹ (C=O, saturated and α,β-unsaturated carbonyl groups); λ max 207 nm (log ε 3.99), 238 nm (log ε 3.78), 310 nm (log ε 3.68).

On refluxing Id with light petroleum (60-80°) or even on trituration with 1-butanol, a solid product was obtained which proved to be 4-methoxycarbonyl-3-phenyl-5-(2'-thienyl)valerolactone (IX), crystallised from light petroleum (60-80°) as yellow crystals, m.p. 90°; ir (potassium bromide): 1770, 1735 cm⁻¹ (C=O, saturated γ-lactone and saturated ester), 760, 700 cm⁻¹ (γ C-H of 5 Ar-H); λ max 219 nm (log ε 4.02), 233 nm (log ε 4.10); nmr: δ 3.72 (s, 3, CO₂CH₃), 3.70 (q, 1, H-C-CO₂CH₃), 4.39 (d, 1, H-C-ph) and 5.90 (d, 1, H-C-O).

Anal. Calcd. for C₁₆H₁₄O₄S: C, 63.58; H, 4.67; S, 10.62; OCH₃, 10.28. Found: C, 63.46; H, 4.73; S, 10.71; OCH₃, 10.11.

The hydrazide X of the (*Z*)-half-ester Id was prepared by refluxing 1 g. of the ester and 1 ml. of 85% phenylhydrazine for 15 minutes. Just enough absolute ethanol was added to obtain a clear solution. After the mixture has been heated under reflux for 2 hours, the alcohol was evaporated, the residue cooled and the hydrazide was crystallised from a water-ethanol mixture to give pale yellow crystals, m.p. 151°; ir (potassium bromide): 3020 cm⁻¹ (NH), 1712 cm⁻¹ (C=O, saturated acid), 735, 680 cm⁻¹ (γ C-H of 5 Ar-H).

Anal. Calcd. for C₂₁H₁₈O₃N₂S: C, 66.64; H, 4.53; N, 7.44; S, 8.48. Found: C, 66.31; H, 4.66; N, 7.65; S, 8.54.

(*E*)- and (*Z*)-3-Methoxycarbonyl-2-phenyl-4-(5'-methyl-2-thienyl)-but-3-enoic Acid (Ib,e).

The condensation of 5-methylthiophene-2-carboxaldehyde (sodium hydride method by 40°) gave a mixture of Ib,e. The (*E*)-half-ester Ib was crystallised from methanol as yellow crystals, m.p. 189°, yield, 47% of the total yield.

Anal. Calcd. for C₁₇H₁₆O₄S: C, 66.64; H, 5.10; S, 10.15; OCH₃, 9.82. Found: C, 66.20; H, 4.84; S, 9.83; OCH₃, 9.63.

(*E*)- and (*Z*)-3-Methoxycarbonyl-2-phenyl-4-(2'-thienyl)phenylbut-3-enoic Acid (Ic,f).

The condensation of phenyl 2-thienyl ketone, using the potassium *t*-butoxide method, produced a mixture of Ic,f. The (*E*)-half-ester crystallised from methanol as white crystals, m.p. 210° yield, 77% of the total yield.

Anal. Calcd. for C₂₂H₁₈O₄S: C, 69.82; H, 4.80; S, 8.48; OCH₃, 8.20. Found: C, 69.34; H, 4.76; S, 8.26; OCH₃, 8.51.

Cyclisation of the Half-esters (Ia-c).

A mixture of the half-ester (1 mole), fused sodium acetate (1.2 moles) and acetic anhydride (15 ml./1 g. of sodium acetate) was left overnight at room temperature. The mixture was warmed up to 60-80° during 2 hours, and maintained thereat for further 6 hours and the neutral cyclisation product was isolated; the yield was about 90%.

Methyl 4-Acetoxy-5-phenylbenzothiophene-6-carboxylate (IIa).

The neutral product was crystallised from *n*-hexane to give IIa in orange crystals, m.p. 120°.

Anal. Calcd. for $C_{18}H_{14}O_4S$: C, 66.24; H, 4.33; S, 9.83; OCH_3 , 9.51. Found: C, 66.13; H, 4.32; S, 9.66; OCH_3 , 9.47.

Methyl 4-Acetoxy-2-methyl-5-phenylbenzothiophene-6-carboxylate (IIb).

The neutral product was crystallised from *n*-hexane to give IIb as orange crystals, m.p. 105°; *m/e*: 340 (M^+ , 6.2), 297 (100), 298 (21.5), 263 (32.3) and 43 (12.3).

Anal. Calcd. for $C_{19}H_{16}O_4S$: C, 67.06; H, 4.79; S, 9.43; OCH_3 , 9.13. Found: C, 66.85; H, 4.87; S, 9.64; OCH_3 , 9.46.

Methyl 4-Acetoxy-5,7-diphenylbenzothiophene-6-carboxylate (IIc).

The neutral product was crystallised from *n*-hexane to give IIc as white crystals, m.p. 118°; *m/e*: 402 (M^+ , 6.1), 360 (100), 327 (14), 328 (15), 329 (15), 77 (14) and 43 (97).

Anal. Calcd. for $C_{24}H_{18}O_4S$: C, 71.62; H, 4.57; S, 7.98; OCH_3 , 7.71. Found: C, 71.28; H, 4.32; S, 7.61; OCH_3 , 7.47.

Conversion of the Acetoxy-esters into the Hydroxy Acids.

The acetoxy-esters IIa-c were hydrolysed by refluxing with 10% methanolic potassium hydroxide (15 ml./1 g. of ester) for 3 hours and the acidic product was isolated. The yield was about 95%.

4-Hydroxy-5-phenylbenzothiophene-6-carboxylic Acid (IIIa).

The acid was crystallised from light petroleum (100-120°) to give IIIa as red crystals, m.p. 208°.

Anal. Calcd. for $C_{15}H_{12}O_3S$: C, 66.66; H, 3.73; S, 11.88. Found: C, 66.40; H, 3.70; S, 11.44.

4-Hydroxy-2-methyl-5-phenylbenzothiophene-6-carboxylic Acid (IIIb).

The acid was crystallised from light petroleum (100-120°) to give IIIb as light brown crystals, m.p. 209°.

Anal. Calcd. for $C_{16}H_{14}O_3S$: C, 67.61; H, 4.26; S, 11.29. Found: C, 67.53; H, 4.61; S, 11.05.

4-Hydroxy-5,7-diphenylbenzothiophene-6-carboxylic Acid (IIIc).

The acid was crystallised from light petroleum (80-100°) to give IIIc as white crystals, m.p. 118°.

Anal. Calcd. for $C_{21}H_{14}O_3S$: C, 72.82; H, 4.08; S, 9.25. Found: C, 72.47; H, 4.48; S, 9.0.

Methylation of the Hydroxy Acids to the Corresponding Methoxy Esters.

The hydroxy acid (1 mole) was methylated by refluxing with dimethyl sulphate (5 moles) and anhydrous potassium carbonate (8 moles) in excess dry acetone, for a period of 12 hours and the neutral product was isolated.

The hydroxy acids IIIa,b gave oily methoxy esters, which could not be crystallised and thus converted to the corresponding methoxy acids Va,b.

Methyl 5-Methoxy-5,7-diphenylbenzothiophene-6-carboxylate (IVc).

The crude ester was crystallised from *n*-hexane to give IVc as light yellow crystals, m.p. 104°.

Anal. Calcd. for $C_{23}H_{18}O_3S$: C, 73.79; H, 4.85; S, 8.56; OCH_3 , 16.58. Found: C, 73.54; H, 4.98; S, 8.09; OCH_3 , 16.20.

Conversion of the Methoxy Esters to the Methoxy Acids.

The methoxy ester was hydrolysed by refluxing with 10% aqueous methanolic potassium hydroxide (15 ml./1 g ester) for a period of 2 hours and the acidic product was isolated. The yield was about 90%.

4-Methoxy-5-phenylbenzothiophene-6-carboxylic Acid (Va).

The acid was crystallised from light petroleum (60-80°) as yellow crystals, m.p. 173°.

Anal. Calcd. for $C_{16}H_{12}O_3S$: C, 67.61; H, 4.26; S, 11.28; OCH_3 , 10.92. Found: C, 67.39; H, 4.42; S, 11.18; OCH_3 , 10.75.

4-Methoxy-2-methyl-5-phenylbenzothiophene-6-carboxylic Acid (Vb).

The acid was crystallised from benzene as yellow crystals, m.p. 218°.

Anal. Calcd. for $C_{17}H_{14}O_3S$: C, 68.45; H, 4.74; S, 10.91; OCH_3 , 10.41. Found: C, 68.26; H, 4.78; S, 10.91; OCH_3 , 10.25.

4-Methoxy-5,7-diphenylbenzothiophene-6-carboxylic Acid (Vc).

The acid was crystallised from light petroleum (60-80°) as red crystals, m.p. 123°.

Anal. Calcd. for $C_{22}H_{16}O_3S$: C, 73.32; H, 4.48; S, 8.90; OCH_3 , 8.61. Found: C, 73.10; H, 4.98; S, 8.71; OCH_3 , 8.85.

Hydrolysis of the Half-esters to the Corresponding Dibasic Acids.

The half-ester was refluxed with a saturated aqueous alcoholic barium hydroxide solution (15 ml./1 g. of ester) for a period of 3 hours and the acid was isolated; the yield was about 90%.

(E)-3-Carboxy-2-phenyl-4-(2'-thienyl)but-3-enoic Acid (VIa).

The acid was crystallised from acetone-benzene to give white needles, m.p. 185°.

Anal. Calcd. for $C_{15}H_{12}O_4S$: C, 62.34; H, 4.18; S, 10.89. Found: C, 62.49; H, 4.20; S, 11.13.

(E)-3-Carboxy-2-phenyl-4-(5'-methyl-2'-thienyl)but-3-enoic Acid (VIb).

The acid was crystallised from acetone-benzene to give yellow crystals, m.p. 188°.

Anal. Calcd. for $C_{16}H_{14}O_4S$: C, 63.58; H, 4.67; S, 10.62. Found: C, 63.59; H, 4.73; S, 10.38.

(E)-3-Carboxy-2-phenyl-4-(2'-thienyl)phenylbut-3-enoic Acid (VIc).

The acid was crystallised from acetone-benzene to give yellow needles, m.p. 209°.

Anal. Calcd. for $C_{21}H_{16}O_4S$: C, 69.22; H, 4.43; S, 8.80. Found: C, 69.50; H, 4.71; S, 8.36.

Conversion of the dibasic acids to the corresponding anhydrides.

The acid was refluxed with acetyl chloride (10 ml./1 g. of acid) for 3 hours, and the neutral product was isolated; the yield was about 95%.

(E)-3-Carboxy-2-phenyl-4-(2'-thienyl)but-3-enoic Anhydride (VIIa).

The anhydride was crystallised from light petroleum (100-120°) to give yellow crystals, m.p. 152°; *ir* (potassium bromide): 1830, 1765 cm^{-1} (C=O) and 728, 694 cm^{-1} (γ C-H of 5 Ar-H).

Anal. Calcd. for $C_{15}H_{10}O_3S$: C, 66.66; H, 3.73; S, 11.88. Found: C, 66.23; H, 4.12; S, 11.62.

(E)-3-Carboxy-2-phenyl-4-(5'-methyl-2'-thienyl)but-3-enoic Anhydride (VIIb).

The anhydride was crystallised from light petroleum (60-80°) as yellow crystals, m.p. 167°; *ir* (potassium bromide): 1830, 1750 cm^{-1} (C=O) and 725, 697 cm^{-1} (γ C-H of 5 Ar-H).

Anal. Calcd. for $C_{16}H_{12}O_3S$: C, 67.61; H, 4.26; S, 11.29. Found: C, 67.28; H, 4.57; S, 10.93.

(E)-3-Carboxy-2-phenyl-4-(2'-thienyl)phenylbut-3-enoic Anhydride (VIIc).

The anhydride was crystallised from methanol to give white crystals, m.p. 156°; ir (potassium bromide): 1855, 1770 cm^{-1} (C=O) and 740, 705 cm^{-1} (γ -C-H or 5 Ar-H).

Anal. Calcd. for $\text{C}_{21}\text{H}_{14}\text{O}_3\text{S}$: C, 72.82; H, 4.08; S, 9.25. Found: C, 72.47; H, 4.42; S, 8.84.

Methanolysis of the Anhydrides.

The anhydride was refluxed in methanol (20 ml./1 g.) for a period of 6 hours and the acidic product was isolated; the yield was about 80%.

Methyl (E)-3-Carboxy-2-phenyl-4-(2'-thienyl)but-3-enoate (VIIIa).

The half-ester was crystallised from light petroleum (100-120°) to give yellow crystals, m.p. 120°; ir (potassium bromide): 1715, 1698 cm^{-1} (C=O, saturated ester and α,β -unsaturated acid), 730, 700 cm^{-1} (γ C-H of 5 Ar-H).

Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{O}_4\text{S}$: C, 63.58; H, 4.67; S, 10.62; OCH_3 , 10.28. Found: C, 63.32; H, 4.31; S, 10.41; OCH_3 , 10.05.

Methyl (E)-3-Carboxy-2-phenyl-4-(2'-thienyl)phenylbut-3-enoate (VIIIc).

The half-ester was crystallised from light petroleum (60-80°) as white crystals, m.p. 69°; ir (potassium bromide): 1748, 1710 cm^{-1} (C=O, saturated ester and α,β -unsaturated acid), 760, 700 cm^{-1} (γ C-H of 5 Ar-H).

Anal. Calcd. for $\text{C}_{22}\text{H}_{18}\text{O}_4\text{S}$: C, 69.82; H, 4.80; S, 8.48; OCH_3 , 8.20. Found: C, 69.50; H, 4.98; S, 8.11; OCH_3 , 8.50.

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- (3) The nomenclature of the *cis/trans* isomers used herein follows the IUPAC Tentative Rules, Section E, Fundamental Stereochemistry, *J. Org. Chem.*, **35**, 2849 (1970). Thus, (E) = *trans*-(heterocyclic ring/ CO_2CH_3), and (Z) = *cis*-(heterocyclic ring/ CO_2CH_3).
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