Synthesis and Electrohydrodimerization of *meta*-Substituted Thiocinnamic Acid *S*-Esters

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The synthesis of the novel *m*-substituted *S*-methyl thiocinnamates **1**–**4** is described. Cathodic reductions of *S*-esters **1**–**3**, carried out at constant potentials corresponding to their first voltammetric E_{pc}, in a polar aprotic solvent, led exclusively to the racemic 'all-*trans*'-configured 2,3-diaryl-5-oxocyclopentane-1-carbothioates, as shown by assignments of ^{1}H-NMR coupling constants.

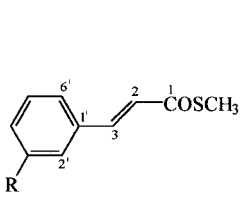
Introduction. – The electrohydrodimerization (EHD) of alkenes, activated towards cathodic reduction by electron-withdrawing groups such as CO_2R, COR, CN, NO_2, and C=NR, is a successful C–C bond-forming reaction [1][2]. The best-known example is the EHD of acrylonitrile (CH_2=CHCN) to give adiponitrile ($NC(CH_2)_4CN$) [3][4] that was developed into a commercial process [5].

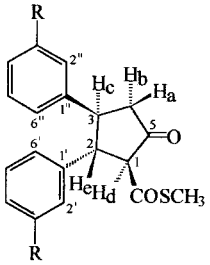
The cathodic reduction of alkyl cinnamates (=alkyl (*E*)-3-phenylpropenoates) in relatively aprotic media was early recognized to involve electrohydrodimerization followed by *Dieckman* condensation under the alkaline conditions of the electrolysis [6]. Only the 'all-*trans*'-configured esters of (±)-2,3-diaryl-5-oxocyclopentanecarboxylic acid are formed, as could be firmly established by assignment of ^{1}H-NMR coupling constants [7] and later confirmed by X-ray crystallography [8].

Our continued interest in the electrochemical behaviour of thiocinnamic acid *S*-esters [9] led us to prepare some *m*-substituted *S*-methyl (*E*)-thiocinnamates **1**–**4** and investigate their cyclic electrohydrodimerization carried out in dimethylformamide (DMF) containing residual water. Compounds **1**–**3** gave in good yields exclusively the cyclic hydrodimers methyl (±)-2,3-diaryl-5-oxocyclopentanecarbothioates **5**–**7** in which the ring substituents are 'all-*trans*'. This extends the scope of an efficient and useful electrochemical C–C bond-forming reaction with subsequent cyclization. The obtained products can be potentially decarboxylated to yield cyclopentanones with C_2 symmetry.

Results and Discussion. – *Syntheses.* The preparation of the *S*-esters **1**–**4** of thiocinnamic acid was achieved by reaction of commercial *m*-substituted (*E*)-cinnamic acids with thionyl chloride in anhydrous Et_2O followed by the treatment with liquefied methanethiol at low temperature (see *Exper. Part* for details).

Cyclic Voltammetry. Single-sweep voltammetry at a Hg-coated Pt-bead cathode in DMF/$(Et_4N)Br$ (0.1 mol·l^{-1} at 0.30 V·s^{-1} revealed for almost all thiocinnamates two reduction peaks (*Table*). The first quasi-reversible one corresponds to the formation of the radical anion **8** and the second irreversible peak to that of the dianion **9** (*Scheme*).





1 R=CH_3
2 R=OCH_3
3 R=Cl
4 R=NO_2

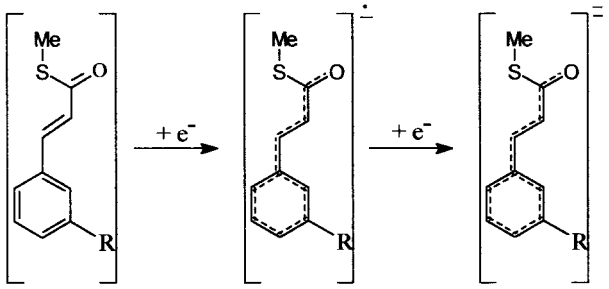
5 R=CH_3
6 R=OCH_3
7 R=Cl

Table. *Cyclic-Voltammetry Experiments with* S-*Methyl Thiocinnamates* **1**–**4**[a])

		$-E_{pc}(1)$[b])[c])	$-E_{pc}(2)$[b])[d])			$-E_{pc}(1)$[b])[c])	$-E_{pc}(2)$[b])[d])
1	R=Me	1.29	–[e])	**3**	R=Cl	1.00	1.57
2	R=MeO	1.15	1.64	**4**	R=NO_2	0.70	1.55

[a]) *S*-Ester concentration 2–4 mmol l^{-1}. [b]) V *vs.* Ag/AgBr. [c]) Quasi-reversible. [d]) Irreversible; pc = potential peak, cathodic. [e]) This value is beyond the measuring range.

Scheme. *Formation of the Radical Anion* **8** *and Dianion* **9**



8 **9**

The differences in the first reduction peak potentials ($|E_{pc}|(\mathbf{1}) - |E_{pc}|(\mathbf{4}) = 0.59$ V) are substantial and probably reflect a difference in the standard reduction potentials (E°). Plots of the first and second E_{pc} against σ_m show linear relationships (*Fig. 1*) which agree with the substituent inductive-effect magnitudes.

Controlled-Potential Electrolyses. These were typically carried out on a 0.3- to 0.5-g scale upon controlled-potential electrolysis, at the first reduction peak potentials ($E_{pc}(1)$ in the *Table*) referred to above, in a conventional cell equipped with a magnetically stirred Hg-pool cathode, a reference electrode (Ag/AgBr), a graphite anode, and an efficient microporous divider. The solvent was DMF containing 0.1 mol·l^{-1} (Et_4N)Br as supporting electrolyte. The cathode compartment was continually flushed with a slow stream of dry N_2.

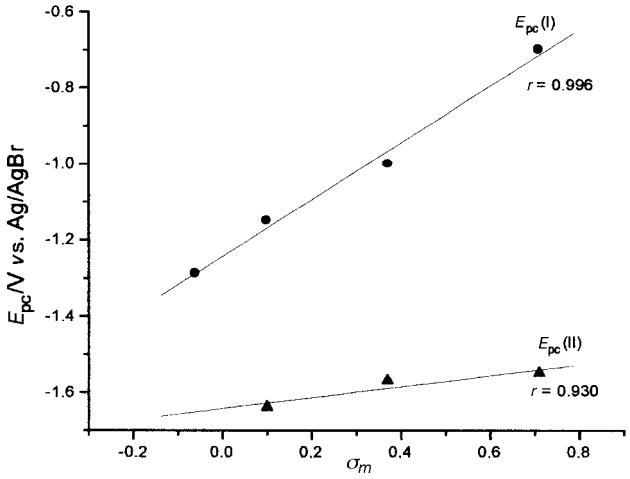


Fig. 1. *Linear relationships between* E_{pc} *and* σ_m

S-Methyl thiocinnamates **1**–**3** were converted to the corresponding cyclic hydrodimers **5**–**7**, and the reactions were complete after the passages of *ca.* $1 \cdot F\ mol^{-1}$, at which point the current had fallen to the background level. The nitro derivative **4** did not show the same behaviour: even after $2\ F \cdot mol^{-1}$, the current was still high, and a complex product mixture was obtained which could not be properly identified. Probably reduction of the nitro group had occurred concomitantly.

Configuration of the Cyclic Hydrodimers. Only the 'all-*trans*' isomers could be observed both in the crude and purified products **5**–**7**. Their ^{1}H-NMR spectra (*e.g.* of **6**, *Fig. 2*) showed that the neighbouring protons (H_a, H_c, H_e, and H_d) at the cyclopentane ring had typical *trans*-coupling constants (*ca.* 12 Hz), whilst protons H_b and H_c had *cis*-coupling constants (*ca.* 7.5 Hz). These observations are consistent with the reported [8] coupling constants for an analogue cyclic hydrodimer ester of which X-ray crystallography confirmed the structure.

Experimental Part

General. Most chemicals were used as received from *Aldrich*. Commercial DMF was dried over anh. $CuSO_4$ for 2 days and then distilled at 44–45°/25 Torr through a 40-cm *Vigreux* column and stored over freshly baked 4-Å molecular sieves. Commercial-grade $(Et_4N)Br$ was baked at 150° overnight before use. Cyclic-voltammetry experiments: USP electronics workshop-constructed triangular wave generator/potentiostat with a *PAR-RE0074-XY* recorder. Controlled-potential electrolysis experiments were carried out using a potentiostat [10] with an electronic charge integrator [11] constructed in our laboratory. IR Spectra: *Perkin-Elmer-1750*-FTIR instrument; only major or important absorptions are given; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker-AC-200* spectrometer at 200 and 50 MHz, resp.; $CDCl_3$ solns.; δ in ppm rel. to $SiMe_4$, *J* in Hz. Elemental analyses: *Perkin-Elmer-2400-CHN* elemental analyser.

S-*Methyl Thiocinnamates* **1**–**4** [12]: *General Procedure.* Thionyl chloride was added dropwise to a stirred soln. of *m*-substituted cinnamic acid in anh. Et_2O (20 ml), the resulting mixture being held under reflux during 4 h. The solvent and excess thionyl chloride were evaporated, and the solid obtained was redissolved in anh. Et_2O (20 ml). This soln. was cooled in a dry-ice/acetone bath, and liquefied methanethiol was added to it in a single portion, followed by pyridine (2.0 ml), added dropwise. After removing the cooling bath, the mixture was

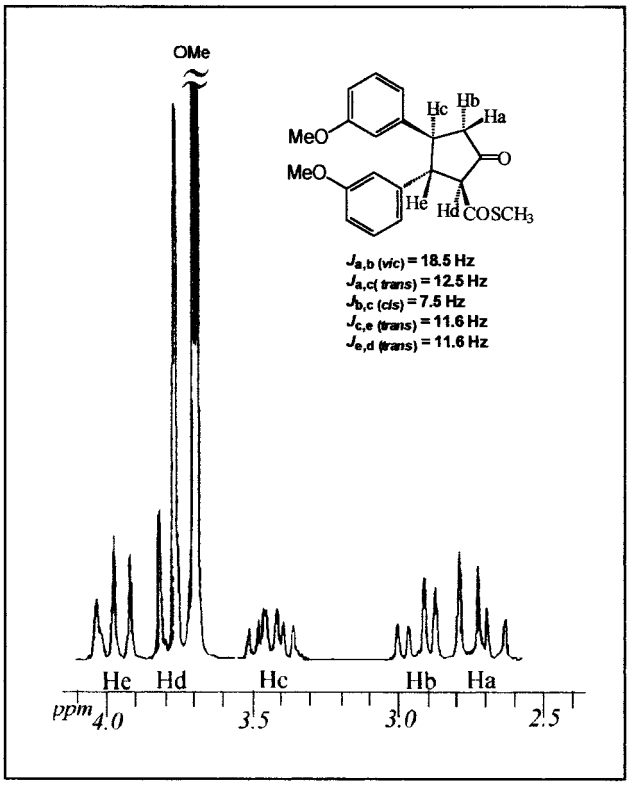


Fig. 2. *Part of* ^{1}*H-NMR spectra of compound* **6**

boiled under reflux for 5 h and then quenched with H_2O and extracted with CH_2Cl_2. The combined extract was dried ($MgSO_4$) and evaporated and the crude product recrystallized from EtOH.

S-*Methyl (*E*)-3-(3-Methylphenyl)prop-2-enethioate* (**1**): From (*E*)-3-methylcinnamic acid (2.50 g, 15.4 mmol), thionyl chloride (3.40 g, 28.6 mmol), and methanethiol (1.56 g, 32.5 mmol) by the *General Procedure:* yield 58%. White solid. M.p. 39–40°. IR (KBr): 3051, 2920, 1670 (C=O, thioester), 1612 (C=C, alkene), 1044. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.36 (*s*, Me–(3′)); 2.42 (*s*, MeS); 6.72 (*d*, *J* = 16, H–C(2)); 7.17–7.26 (*m*, 4 arom. H); 7.58 (*d*, *J* = 16, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 11.6 (MeS); 21.3 (*Me*–C(3′)); 125 (C(2)); 128–131 (arom. CH); 134 (C(1′)); 139 (C(3′)); 140 (C(3)); 190 (C(1)). Anal. calc. for $C_{11}H_{12}OS$ (192.28): C 68.71, H 6.29; found: C 68.79, H 6.24.

S-*Methyl (*E*)-3-(3-Methoxyphenyl)prop-2-enethioate* (**2**): From (*E*)-3-methoxycinnamic acid (2.50 g, 14.0 mmol), thionyl chloride (3.31 g, 27.8 mmol), and methanethiol (1.56 g, 32.5 mmol) by the *General Procedure:* yield 78%. White solid. M.p. 48°. IR (KBr): 3065, 2923, 1671 (C=O, thioester), 1612 (C=C, alkene), 1262, 1048, 958. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.43 (*s*, MeS); 3.83 (*s*, MeO–C(3′)); 6.71 (*d*, *J* = 16, H–C(2)); 6.94 (*dd*, *J* = 8.0, 2.5, H–C(4′)); 7.05 (*m*, H–C(2′)); 7.13 (*d*, *J* = 8.0, H–C(6′)); 7.29 (*t*, *J* = 8.0, H–C(5′)); 7.58 (*d*, *J* = 16, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 11.6 (MeS); 55.3 (MeO); 113 (C(4′)); 116 (C(2′)); 121 (C(6′)); 125 (C(2)); 130 (C(5′)); 135 (C(1′)); 140 (C(3)); 160 (C(3′)); 190 (C(1)). Anal. calc. for $C_{11}H_{12}O_2S$ (208.28): C 63.43, H 5.81; found: C 63.42, H 5.82.

S-*Methyl (*E*)-3-(3-Chlorophenyl)prop-2-enethioate* (**3**): From (*E*)-3-chlorocinnamic acid (2.50 g, 13.7 mmol), thionyl chloride (3.06 g, 28.7 mmol), and methanethiol (1.47 g, 30.7 mmol) by the *General Procedure:* yield 83%. White solid. M.p. 59°. IR (KBr): 3066, 2923, 1669 (C=O, thioester), 1618 (C=C, alkene), 1081, 959. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.43 (*s*, MeS); 6.70 (*d*, *J* = 16, H–C(2)); 7.26–7.42 (*m*, 4 arom. H); 7.53 (*d*, *J* = 16, H–C(3)). ^{13}C-NMR (50 MHz, $CDCl_3$): 11.6 (MeS); 126 (C(2)); 127–130 (arom. CH); 135

(C(1′)[1])); 136 (C(3′)[1])); 139 (C(3)); 189 (C(1)). Anal. calc. for $C_{10}H_9ClOS$ (212.70): C 56.47, H 4.26; found: C 56.47, H 4.26.

S-*Methyl (*E*)-3-(3-Nitrophenyl)prop-2-enethioate* (**4**): From (*E*)-3-nitrocinnamic acid (2.50 g, 13.0 mmol), thionyl chloride (3.08 g, 25.9 mmol), and methanethiol (1.17 g, 24.4 mmol) by the *General Procedure:* yield 85%. Yellow solid. M.p. 158–160°. IR (KBr): 3086, 2934, 1660 (C=O, thioester), 1614 (C=C, alkene), 1527, 1352, 981. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.46 (*s*, MeS); 6.83 (*d*, *J* = 16, H–C(2)); 7.59 (*t*, *J* = 8.0, H–C(5′)); 7.64 (*d*, *J* = 16, H–C(3)); 7.85 (*d*, *J* = 8.0, H–C(6′)); 8.24 (*dd*, *J* = 8.0, 2.5, H–C(4′)); 8.40 (*m*, H–C(2′)). ^{13}C-NMR (50 MHz, $CDCl_3$): 11.8 (MeS); 123 (C(2′)[1])); 125 (C(4′)[1])); 127 (C(2)); 130 (C(5′)); 134 (C(6′)); 136 (C(1′)); 137 (C(3)); 149 (C(3′)); 190 (C(1)). Anal. calc. for $C_{10}H_9NO_3S$ (223.25): C 53.80, H 4.06; found: C 54.05, H 4.06.

Controlled-Potential Electrolyses of Thiocinnamate S-*Esters.* Conditions employed for electrolyses are described above. Workup involved quenching the catholite in an excess of ice-water, neutralization with aq. HCl soln. to pH 6, and extraction with CH_2Cl_2 (3 × 40 ml). The CH_2Cl_2 soln. was washed with H_2O (4 × 50 ml) and dried. The crude solid products were recrystallized from MeOH.

S-*Methyl* t-*2*,c-*3-Bis(3-methylphenyl)-5-oxocyclopentane*-r-*1-carbothioate* (**5**): Yield 78%. White solid. M.p. 82–85°. IR (KBr): 3022, 2918, 1748 (C=O, ketone), 1677 (C=O, thioester). ^{1}H-NMR (200 MHz, $CDCl_3$): 2.17 (*s*, Me–C(3′)[1])); 2.19 (*s*, Me–C(3″)[1])); 2.22 (*s*, MeS); 2.63 (*dd*, $J_{a,c}$ = 12.5, $J_{a,b}$ = 18.5, H_a–C(4)); 2.79–2.85 (*m*, H_b–C(4)); 3.33–3.39 (*m*, H_c–C(3)); 3.70 (*d*, $J_{e,d}$ = 11.6, H_d–C(1)); 3.89 (*t*, $J_{e,c\ or\ d}$ = 11.6, H_e–C(2)); 6.83–7.16 (*m*, 8 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): 12.1 (MeS); 21.2 (*Me*–C(3′), *Me*–C(3″)); 47.2–47.3 (C(3), C(4)); 53.2 (C(2)); 71.0 (C(1)); 124–129 (arom. CH); 138–140 (arom. C); 195 (*C*OSMe); 208 (C(5)). Anal. calc. for $C_{21}H_{22}O_2S$ (338.47): C 74.52, H 6.55; found: C 74.40, H 6.61.

S-*Methyl* t-*2*,c-*3-Bis(3-methoxyphenyl)-5-oxocyclopentane*-r-*1-carbothioate* (**6**): Yield 52%. White solid. M.p. 96–98°. IR (KBr): 3057, 2957, 1747 (C=O, ketone), 1670 (C=O, thioester), 1266, 1039. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.30 (*s*, MeS); 2.71 (*dd*, $J_{a,c}$ = 12.5, $J_{a,b}$ = 18.5, H_a–C(4)); 2.94 (*dd*, $J_{b,c}$ = 7.5, $J_{c,e}$ = 11.6, $J_{a,b}$ = 18.5, H_b–C(4)); 3.44 (*td*, $J_{b,c}$ = 7.5, $J_{a,c}$ = 12.5, H_c–C(3)); 3.69 (*s*, Me–C(3′)[1])); 3.70 (*s*, Me–(3″)[1])); 3.80 (*d*, $J_{d,e}$ = 11.6, H_d–C(1)); 3.97 (*t*, $J_{e,d\ or\ c}$ = 11.6, H_e–C(2)); 6.64–6.75 (*m*, 4 arom. H); 7.12–7.22 (*m*, 4 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): 12.1 (MeS); 47.1 (C(4)[1])); 47.3 (C(3)[1])); 53.3 (C(2)); 55.1 (*Me*–C(3′), *Me*–C(3″)); 70.8 (C(1)); 112–114 (C(2′), C(4′), C(2″), C(4″)); 119 (C(6′), C(6″)); 129 (C(5′), C(5″)); 141 (C(1′), C(1″)); 160 (C(3′), C(3″)); 195 (*C*OSMe); 208 (C(5)). Anal. calc. for $C_{21}H_{22}O_4S$ (370.47): C 68.08, H 5.99; found: C 68.23, H 5.96.

S-*Methyl* t-*2*,c-*3-Bis(3-chlorophenyl)-5-oxocyclopentane*-r-*1-carbothioate* (**7**): Yield 66%. White solid. M.p. 112–115°. IR (KBr): 3064, 2926, 1751 (C=O, ketone), 1674 (C=O, thioester), 1084. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.32 (*s*, MeS); 2.69 (*dd*, $J_{a,c}$ = 12.5, $J_{a,b}$ = 18.5, H_a–C(4)); 2.88–2.95 (*m*, H_b–C(4)); 3.43 (*td*, $J_{b,c}$ = 7.5, $J_{c,e}$ = 11.6, $J_{a,c}$ = 12.5, H_c–C(3)); 3.76 (*d*, $J_{e,d}$ = 11.6, H_d–C(1)); 3.96 (*t*, $J_{e,c\ or\ d}$ = 11.6, H_e–C(2)); 7.13–7.26 (*m*, 8 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): 12.2 (MeS); 46.9 (C(4)[1])); 49.6 (C(3)[1])); 55.4 (C(2)); 70.5 (C(1)); 127–128 (arom. CH); 134 (*Me*–C(3′), *Me*–C(3″)); 140 (C(1′), C(1″)); 194 (*C*OSMe); 207 (C(5)). Anal. calc. for $C_{19}H_{16}Cl_2O_2S$ (379.31): C 60.16, H 4.25; found: C 60.05, H 4.42.

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REFERENCES

[1] J. H. P. Utley, *Chem. Soc. Rev.* **1997**, *26*, 157.
[2] M. M. Baizer, in 'Organic Electrochemistry', Ed. H. Lund and M. M. Baizer, Marcel Dekker, New York, 1991, p. 908.
[3] M. M. Baizer, *Chemtech* **1980**, *10*, 161.
[4] D. E. Danly, *Chemtech* **1980**, *10*, 302.
[5] D. Pletcher, 'Industrial Electrochemistry', Chapman and Hall, London, 1982, Chapt. 6.
[6] L. H. Klemm, D. R. Olson, *J. Org. Chem.* **1973**, *38*, 3390.
[7] C. Z. Smith, J. H. P. Utley, *J. Chem. Soc., Chem. Commun.* **1981**, 492.
[8] J. H. P. Utley, M. Güllü, M. Montevalli, *J. Chem. Soc., Perkin Trans. 1* **1995**, 1961.
[9] J. Gruber, F. F. Camilo, *J. Chem. Soc., Perkin Trans. 1* **1999**, 127.
[10] J. Gruber, V. L. Pardini, H. Viertler, *Quim. Nova* **1992**, *15*, 83.
[11] J. Gruber, V. L. Pardini, H. Viertler, I. Gruber, *Anal. Instrum.* **1992**, *20*, 155.
[12] F. F. Camilo, I. P. A. Campos, J. Gruber, *J. Chem. Res., Synop.* **1998**, 270.

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[1]) These assignments may be reversed.