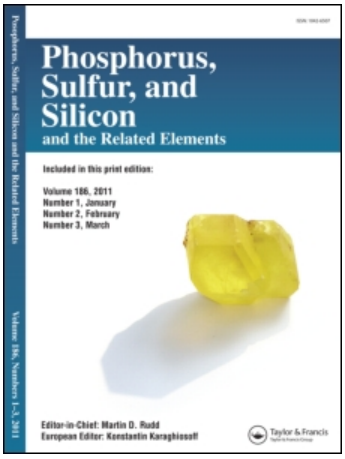

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Jean-Pierre Guemas[a]; Michele Lees[a]; Alain Reliquet[a]
[a] Laboratoire de Chimie Organique II 2, rue de la Houssinière, Nantes Cedex, France

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ADDITION OF ORGANOMETALLICS TO α,β-UNSATURATED THIOCARBONYL COMPOUNDS. III. MICHAEL ADDITION OF ACTIVE METHYLENE COMPOUNDS TO THIOAMIDE AND DITHIOCARBAMATE VINYLOGS

JEAN-PIERRE GUEMAS, MICHÈLE LEES and ALAIN RELIQUET

Laboratoire de Chimie Organique II 2, rue de la Houssinière, 44072 Nantes Cedex, France

(*Received July 20, 1983*)

α,β-Unsaturated thiocarbonyl compounds substituted by a secondary amino group in position β, such as thioamide and dithiocarbamate vinylogs, react with sodium derivatives of active methylene compounds CH_2XY to give 1,4-addition compounds. Methylation of the 1,4-adducts is followed by elimination of the amine and leads to conjugate thioethers and ketene dithioacetals with functional groups X and Y at the end of the chain. Cyclization and hydrolysis of the adduct afford 2H-thiopyran derivatives.

INTRODUCTION

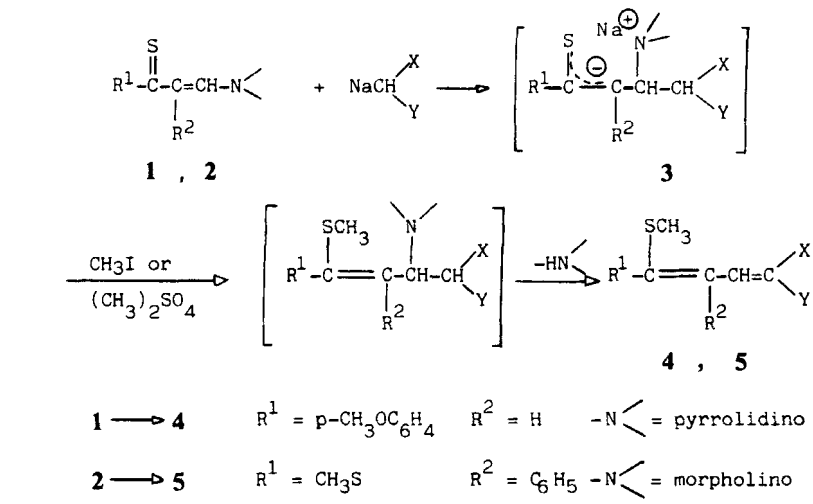
Contrary to carbonyl compounds, α,β-unsaturated thiocarbonyl compounds are little used in Michael condensations, only one study of Tamaru, Harada and Yoshida[1] describes the 1,4-addition reaction of lithium enolates to α,β-unsaturated thioamides. Recently we have shown[2] that vinylogs of thioamides and dithiocarbamates, more correctly β-aminopropenethiones and β-aminopropenedithioates, behave as good Michael acceptors towards lithium enolates of ketones, esters and amides. As an extension of this work, we describe herein the conjugate addition of enolates of active methylene compounds to thioamide and dithiocarbamate vinylogs **1** and **2**.

RESULTS AND DISCUSSION

Formation and Methylation of 1,4-addition Compounds

The α,β-ethylenic thiocarbonyl compounds **1** and **2** react with sodium derivatives of active methylene compounds according to a regioselective 1,4-addition beginning with a nucleophilic attack at the carbon β to the thiocarbonyl group.

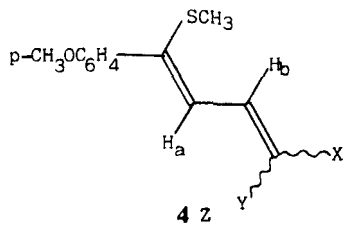
Methylation of the adducts **3** by methyl iodide or dimethyl sulfate occurs at the sulfur atom and is followed by elimination of the amine, pyrrolidine or morpholine, to give dienic compounds **4** and **5**.



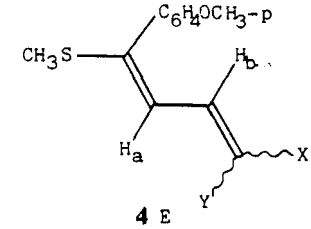
The formation of the adduct **3** is carried out by adding the thioamide or dithiocarbamate vinylog to a solution of the sodium enolate (4 equivalents) prepared by the action of sodium hydride on the active methylene compound. With malonic derivatives containing a cyano group, the reaction occurs at 20°C in THF; with malonic acid esters the condensation is much more difficult and takes place only on heating (Tables I and II).

With malodinitrile, ethyl cyanoacetate, cyanacetamide, dimethyl and diethyl malonic esters, ethyl diethylphosphonatoacetate and fluorene, methylation of the 1,4-addition compounds obtained from 1-*p*-methoxyphenyl-3-pyrrolidino-2-propen-1-thione **1** gives $\alpha,\beta,\gamma,\delta$-dienic thioethers **4**. Results and experimental conditions are summarized in Table I.

Contrary to the 1,4-addition of organomagnesium compounds[3] to thioamide vinylogs **1**, the condensation of the active methylene compounds, followed by methylation, has low stereoselectivity with regard to the ethylenic bond carrying the methylthio group. The proton nuclear magnetic resonance spectra of **4** show distinct signals for the methylthio group (and the hydrogen α to this group), corresponding to the two E and Z isomers. The Z/E ratio, determined on the basis of the singlets observed for the CH_3S group, shows a predominance, of the order of 65 to 75%, of the Z isomer. The coupling constant of about 11.5 Hz between the ethylenic protons H_a and H_b indicates a *s*-trans conformation for the two ethylenic bonds.



4 Z



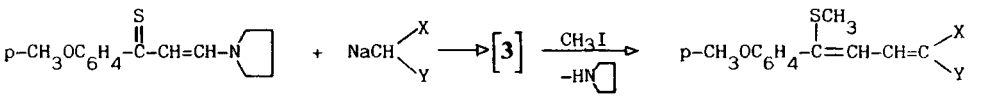
4 E

δ_{CH_3S} = 2.03 to 2.17 ppm ($CDCl_3$) $\quad$ δ_{CH_3S} = 2.32 to 2.50 ppm ($CDCl_3$)

δ_{H_a} = 6.67 to 6.80 ppm ($CDCl_3$) $\quad$ δ_{H_a} = 6.37 to 6.57 ppm ($CDCl_3$)

TABLE I

Methylation of 1,4-addition compounds of active methylene compounds to thioamide vinylog **1**

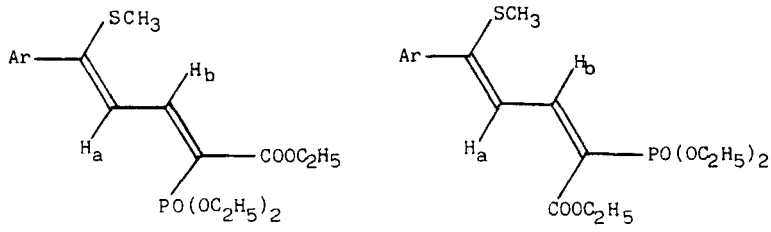


1 **4**

Compound	X	Y	Solvent[a]	Temperature[a] (°C)	Time[a] (h)	Melting point (°C)	Yield (%)	Z/E
4a	CN	CN	THF	20	1	110–117	67	1.8
4b	CN	$COOC_2H_5$	THF	20	1	78–84	73	3.0
4c	CN	$CONH_2$	THF	20	4	189–192	55	1.9
4d[b]	$COOCH_3$	$COOCH_3$	DMF	50	18	68–69	54	2.0
4e	$COOC_2H_5$	$COOC_2H_5$	DMF	50	2	yellow oil	39	3.0
4f	$COOC_2H_5$	$PO(OC_2H_5)_2$	THF(HMPT)	then 20	20	yellow oil	90	2.6
				30	2			
4g[b]	$C_{12}H_8$[c]		DMF	20	1	140–142	96	3.0

[a]Experimental conditions for the formation of 1,4-addition compounds **3**.
[b]Dimethyl sulfate was used as methylating agent.
[c]$C_{12}H_8$ derived from fluorenylidene group $C_{13}H_8$.

In compound **4f**, corresponding to the condensation of ethyl diethylphosphonato acetate, two different values, 44.0 and 22.8 Hz, are observed for the coupling constant $^3J_{PH}$ corresponding to a trans and a cis disposition of the phosphorus atom with respect to the hydrogen H_b. This shows that the elimination of pyrrolidine is not stereospecific.



Ar = p-$CH_3OC_6H_4$

4f Z-2, Z-4 $^3J_{PH}$ = 44.0 Hz

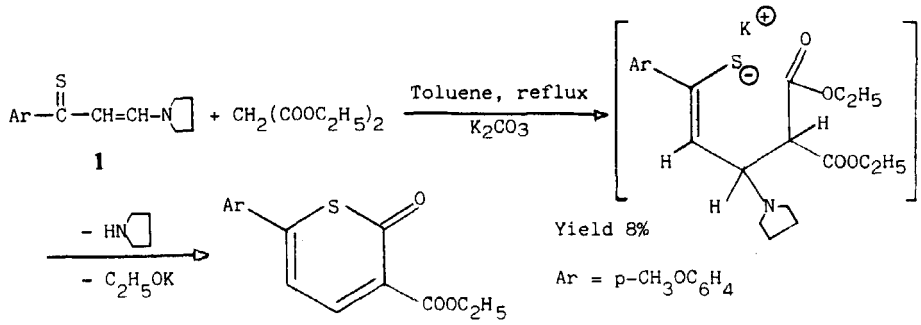
4f E-2, Z-4 $^3J_{PH}$ = 21.8 Hz

Conjugate ketene dithioacetals **5** containing functional groups X and Y at the end of the chain are obtained in an original way, by methylation of the 1,4-adduct **3** resulting from the condensation of malodinitrile, ethyl cyanoacetate, cyanacetamide and dimethyl malonate on methyl 3-morpholino-2-phenylpropenedithioate **2**. Results are given in Table II.

Cyclization of the 1,4-addition Compounds

In certain conditions, cyclization of the 1,4-adduct **3**, obtained from malonic acid esters, occurs giving thiopyran-3-carboxylic acid derivatives.

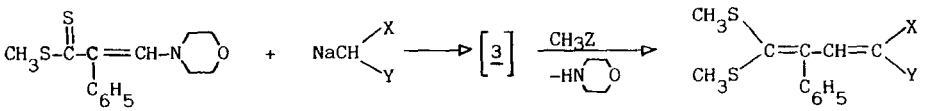
By increasing the temperature of the condensation of diethyl malonate with the thioamide vinylog **1**, ethyl thiopyran-3-carboxylate **6** is obtained resulting from the nucleophilic attack of the thiolate anion on the carbonyl group of one of the ester functions.



An analogous reaction is observed with the dithiocarbamate vinylog **2**: on heating the corresponding adduct **3**, prepared by the addition of dimethyl malonate to **2**,

TABLE II

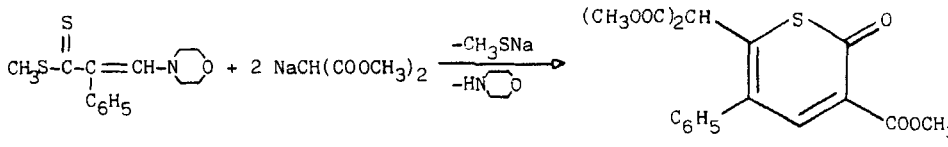
Methylation of 1,4-addition compounds of active methylene compounds to dithiocarbamate vinylogs **2**



2 **5**

Compound	X	Y	Solvent[a]	Temperature[a] (°C)	Time[a] (h)	Z	Melting point (°C)	Yield (%)
5a	CN	CN	THF	20	1	I	103–104	98
5b	CN	$COOC_2H_5$	THF	40	2	I	97–99	87
5c	CN	$CONH_2$	THF	50	2	CH_3SO_4	196–198	80
5d	$COOCH_3$	$COOCH_3$	THF	55	1.5	CH_3SO_4	78–80	31

[a]Experimental conditions for the formation of 1,4-addition compounds **3**.



2 **7**

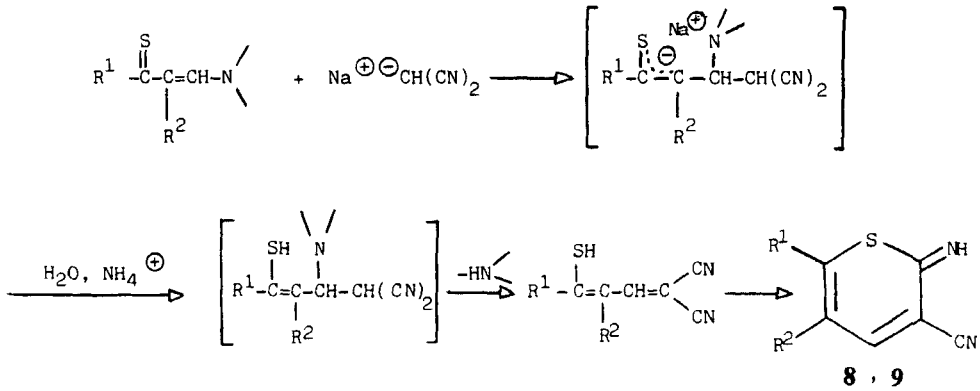
yield 38%

cyclization occurs to give methyl thiopyran-3-carboxylate **7**, in which the methylthio group has been substituted by a second mole of malonate.

A similar type of cyclization was observed by Shibuya[4] in the preparation of 2H-thiopyran-2-one derivatives by condensing active methylene compounds with 3,5-diphenyl-1,2-dithiolylium perchlorate.

Hydrolysis of the 1,4-addition Compounds

Addition of malonitrile to thioamide and dithiocarbamate vinylogs **1** and **2** affords, after hydrolysis, 3-mercaptoallylidenemalonates, giving heterocyclic compounds **8** and **9**.



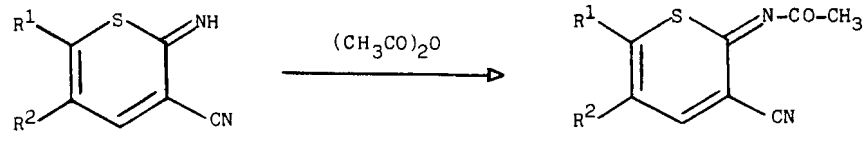
8 , 9

1 ⟶ **8** R^1 = p-$CH_3OC_6H_4$ R^2 = H -N⟨ = pyrrolidino yield 43%

2 ⟶ **9** R^1 = CH_3S R^2 = C_6H_5 -N⟨ = morpholino yield 98%

3-Mercaptoalkylidenemalonates may be obtained by other methods, for example by the action of sodium hydrosulfide on β-chlorovinylacrylonitrile,[5,6] by the condensation of malonitrile with 1,2-dithiolylium perchlorate[4] and by the action of active methylene compounds on the thiourea-thioamide vinylog complexes.[7]

The ^1H NMR spectra of compounds **8** and **9** indicate a 2-imino-2H-thiopyranic cyclic form arising from the nucleophilic addition of the thiol group on one of the nitrile functions. This structure, initially proposed by Liebscher and Hartmann,[6] was confirmed by acetylating compounds **8** and **9** using acetic acid anhydride, which gave the *N*-acetylimino-2H-thiopyrans **10** and **11**.

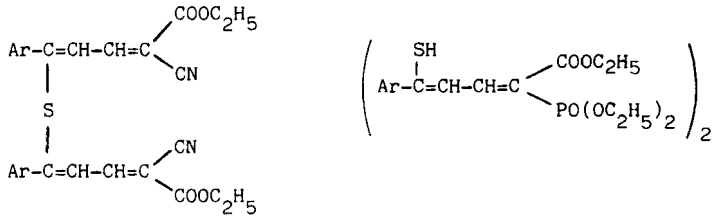


8 , 9 **10 , 11**

8 ⟶ **10** R^1 = p-$CH_3OC_6H_4$ R^2 = H yield 78 %

9 ⟶ **11** R^1 = CH_3S R^2 = C_6H_5 yield 73 %

With ethyl cyanoacetate, the hydrolysis product analogous to compound **8** cannot be isolated because it converts to the sulphide **12** corresponding to the elimination of hydrogen sulphide between two molecules of the 3-mercaptoalkylidenemalonates.



12 Ar = p-$CH_3OC_6H_4$ **13**

Hydrolysis of the 1,4-addition compound prepared by the condensation of ethyl diethylphosphonatoacetate with the thioamide vinylog **1** affords, not the expected ethyl 2-diethylphosphonato-3-mercapto-2,4-pentadienoate, but its dimer. On account of the instability of this dimer, we were not able to elucidate its exact structure, which probably results from the thioketonic tautomeric form of the mercaptoallylidene. Thiopyrans, 1,2 or 1,3-dithiinnes, 1,2 or 1,5-dithiocinnes are possible structures, since α,β-ethylenic thiocarbonyl compounds are known to dimerize giving such heterocycles.[8–13]

EXPERIMENTAL

^{1}H NMR spectra were measured using a Perkin-Elmer R 24 spectrometer or Varian XL 100 spectrometer, ^{13}C NMR spectra were obtained on a Bruker WH 90 spectrometer. Chemical shifts are reported as δ values in parts per million to the internal standard (TMS).

Mass spectra were determined with a Varian MAT 112 spectrometer at 70 eV.

The purity of compounds was tested by thin layer chromagraphy on silica gel plates developed with iodine vapor. Melting points are reported in degrees Celsius and are uncorrected. Elemental analyses were performed by the Central Service of Microanalysis of the C.N.R.S, Vernaison, France.

All reactions between sodium derivatives of active methylene compounds and thiocarbonyl compounds were carried out under an atmosphere of dry nitrogen. Tetrahydrofuran was dried over a mixture of naphthalene–sodium, distilled and stored under nitrogen over molecular sieves. Dimethylformamide was purified by distillation over phosphoric anhydride (P_2O_5).

Preparation of starting materials **1** *and* **2**. 1-*p*-Methoxyphenyl-3-pyrrolidino-2-propen-1-thione **1** was prepared by the action of pyrrolidine on 3-*p*-methoxyphenyl-1,2-dithiolylium perchlorate.[14]

Methyl-(3-morpholino-2-phenyl)-2-propendithioate **2** was prepared according to Smutny[15] by the reaction of morpholine on 3-methylthio-4-phenyl-1,2-dithiolylium iodide.

Preparation of 1,4-addition compounds **3**: *General procedure.* In a flame-dried 500 ml round-bottomed flask, equipped with a magnetic stirrer, a thermometer (−20°C, +100°C), a pressure-equalizing addition funnel and a reflux condenser, was placed 0.60 g (12.5 mmol) of sodium hydride as an oil dispersion (50%). The oil was eliminated by washing twice with 10 ml of dry THF. The sodium hydride was then covered with 20 ml of THF or DMF (Tables I and II).

After cooling to 0°C, 12.0 mmol of the active methylene compound CH_2XY were added with stirring, and the reaction mixture was allowed to warm to 20°C. The solution of the thioamide or dithiocarbamate vinylog **1** or **2** (4.0 mmol in 20–30 ml of solvent) was then added dropwise and the mixture maintained at the temperature and during the time indicated in Tables I and II.

Preparation of compounds **4** *and* **5**: *Methylation of the 1,4-addition compounds.* Methylation of the 1,4-addition compound **3** prepared as described above, was carried out at 20°C by the slow addition of methyl iodide or dimethyl sulfate (16.0 mmol) in solution in 5 ml of THF. The reaction mixture was stirred for 2 h and then hydrolysed using a saturated aqueous solution of ammonium chloride. After extraction with methylene chloride, the organic layers are washed by water, and dried over calcium chloride.

Evaporation of the solvent gave a yellow oil, which was purified by silica gel column chromatography. Elution with a mixture of petroleum ether–ethyl acetate (15 : 1) afforded compound **4** or **5**, which was recrystallized from the appropriate solvent.

(3-*p*-Methoxyphenyl-3-methylthio-allylidene)malonodinitrile **4a**: yellow crystals, mp 110–117°C (ethanol), ^{1}H NMR ($CDCl_3$) δ, isomer Z (65%) 2.15 (s, 3 H, CH_3S), 6.70 (d, H, CH, J = 11.0 Hz), 8.13 (d, H, CH, J = 11.0 Hz), isomer E (35%), 2.50 (s, 3 H, CH_3S), 6.38 (d, H, CH, J = 11.7 Hz), 7.03 (d, H, CH, J = 11.7 Hz); mass spectrum m/e 256 (m^+). Anal. Calcd. for $C_{14}H_{12}N_2OS$: C, 65.59; H, 4.72; S, 12.51. Found: C, 65.53; H, 4.58; S, 12.53.

Ethyl-(2-cyano-5-*p*-methoxyphenyl-5-methylthio)-2,4-pentadienoate **4b**: yellow crystals, mp 78–84°C (ethanol), ^{1}H NMR ($CDCl_3$) δ, isomer Z (75%), 1.37 (t, 3 H, CH_3CH_2, J = 7.0 Hz), 2.13 (s, 3 H, CH_3S), 4.30 (q, 2 H, CH_2CH_3, J = 7.0 Hz), 6.80 (d, H, CH, J = 12.0 Hz), 8.57 (d, H, CH, J = 12.0 Hz), isomer E (25%), 1.30 (t, 3 H, CH_3CH_2), 2.50 (s, 3 H, CH_3S), 4.23 (q, 2 H, CH_2CH_3), 6.47 (d, H, CH, J = 13.0 Hz), 7.77 (d, H, CH, J = 13.0 Hz); mass spectrum m/e 303 (m^+). Anal. Calcd. for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.65; S, 10.57. Found: C, 63.08; H, 5.64; S, 10.71.

2-Cyano-5-*p*-methoxyphenyl-5-methylthio-2,4-pentadienamide **4c**: yellow crystals, mp 189–192°C (ethanol), ^{1}H NMR ($CDCl_3$) δ, isomer Z (66%) 2.17 (s, 3 H, CH_3S), 6.67 (d, H, CH, J = 11.3 Hz), 7.67 (qs, 2 H, NH_2), 8.35 (d, H, CH, J = 11.3 Hz), isomer E (34%), 2.53 (s, 3 H, CH_3S), 6.37 (d, H, CH, J = 11.8 Hz), 7.67 (qs, 2 H, NH_2), 7.54 (d, H, CH, J = 11.8 Hz); mass spectrum m/e 274 (m^+). Anal. Calcd. for $C_{14}H_{14}N_2O_2S$: C, 61.29; H, 5.14; S, 11.69. Found: C, 61.08; H, 5.05; S, 11.85.

Dimethyl(3-*p*-methoxyphenyl-3-methylthio-allylidene)malonate **4d**: white crystals, mp 68–69°C (petroleum ether), ^{1}H NMR ($CDCl_3$) δ, isomer Z (67%), 2.03 (s, 3 H, CH_3S), 3.67 and 3.77 (2s, 6 H, CH_3O), 6.75 (d, H, CH, J = 11.2 Hz), 8.13 (d, H, CH, J = 11.2 Hz), isomer E (33%), 2.35 (s, 3 H, CH_3S), 3.67 and 3.77 (2s, 6 H, CH_3O), 6.57 (d, H, CH, J = 11.8 Hz), 7.36 (d, H, CH, J = 11.8 Hz); mass spectrum m/e 322 (m^+). Anal. Calcd. for $C_{16}H_{18}O_5S$: C, 59.61; H, 5.63; S, 9.94. Found: C, 59.55; H, 5.49; S, 9.99.

Diethyl(3-*p*-methoxyphenyl-3-methylthio-allylidene)malonate **4e**: yellow oil, ^{1}H NMR ($CDCl_3$) δ, isomer Z (75%), 1.30 (t, 6 H, CH_3CH_2, J = 7.0 Hz), 2.03 (s, 3 H, CH_3S), 4.23 (q, 4 H, CH_2CH_3, J = 7.0 Hz), 6.76 (d, H, CH, J = 11.5 Hz), 8.42 (d, H, CH, J = 11.5 Hz), isomer E (25%), 1.20 and 1.33 (2t, 6 H, CH_3CH_2, J = 7.0 Hz), 2.33 (s, 3 H, CH_3S), 4.13 and 4.27 (2t, 4 H, CH_2CH_3, J = 7.0 Hz), 6.57 (d, H, CH, J = 12.0 Hz), 7.33 (d, H, CH, J = 12.0 Hz); mass spectrum m/e 350 (m^+). Anal. Calcd. for $C_{18}H_{22}O_5S$: C, 61.69; H, 6.33; S, 9.15. Found: C, 61.40; H, 6.47; S, 9.03.

Ethyl-(2-diethylphosphonato-5-*p*-methoxyphenyl-5-methylthio)-2,4-pentadienoate **4f**: yellow oil, ^{1}H NMR ($CDCl_3$) δ, 2-Z, 4-Z and 2-E, 4-Z isomers (72%), 1.30, 1.33 and 1.37 (3t, 9 H, CH_3CH_2, J = 7.0 Hz), 2.07 and 2.08 (2s, 3 H, CH_3S), 4.17 (q, 6 H, CH_2CH_3, J = 7.0 Hz), 7.33 (d, CH, J = 11.4 Hz), 7.70 (d, CH, J = 11.7 Hz), 8.27 (dd, CH, $^3J_{HH}$ = 11.4 Hz, $^3J_{PH}$ = 21.8 Hz), 8.67 (dd, CH, $^3J_{HH}$ = 11.7 Hz, $^3J_{PH}$ = 44.0 Hz), 2-Z, 4-E and 2-E, 4-E isomers (28%), 1.32 (t, 9 H, CH_3CH_2, J = 7.0 Hz), 2.47 (s, 3 H, CH_3S), 4.17 (q, 6 H, CH_2CH_3, J = 7.0 Hz), CH masked; mass spectrum m/e 414 (m^+).

3-Fluorenylidene-1-*p*-methoxyphenyl-1-methylthiopropene **4g**: yellow crystals, mp 140–142°C (ethanol–ethyl acetate), ^{1}H NMR ($CDCl_3$) δ, 2.07 (s, 3 H, CH_3S, Z isomer, 73%) 2.32 (s, 3 H, CH_3S, E isomer, 27%) 7.0–8.10 (m, 10 H, aromatics and ethylenics); mass spectrum m/e 356 (m^+). Anal. Calcd. for $C_{24}H_{20}OS$: C, 80.86; H, 5.66; S, 8.99. Found: C, 80.94; H, 5.51; S, 9.02.

[3,3-Bis(methylthio)-2-phenylallylidene]malonodinitrile **5a**: yellow crystals, mp 103–104°C (ethanol–hexane), ^{1}H NMR ($CDCl_3$) δ, 2.22 and 2.46 (2s, 6 H, CH_3S) 7.07–7.47 (m, 5 H, aromatics) 8.27 (s, H, CH); mass spectrum m/e 272 (m^+). Anal. Calcd. for $C_{14}H_{12}N_2S_2$: C, 61.73; H, 4.44; S, 23.55. Found: C, 61.86; H, 4.43; S, 23.41.

Ethyl-(2-cyano-5,5-bis(methylthio)-4-phenyl)-2,4-pentadienoate **5b**: yellow crystals, mp 97–99°C (ethanol), ^{1}H NMR ($CDCl_3$) δ, 1.28 (t, 3 H, CH_3, J = 7.0 Hz) 2.20 and 2.47 (2s, 6 H, CH_3S) 4.23 (q,

2 H, CH_2, J = 7.0 Hz) 7.03–7.47 (m, 5 H, aromatics) 8.73 (s, H, CH); mass spectrum m/e 319 (m^+). Anal. Calcd. for $C_{16}H_{17}NO_2S_2$: C, 60.16; H, 5.36; S, 20.08. Found: C, 60.16; H, 5.28; S, 20.19.

2-Cyano-5,5-bis(methylthio)-4-phenyl-2,4-pentadienamide **5c**: yellow crystals, mp 196–198°C (ethanol), ^1H NMR ($CDCl_3$) δ, 2.22 and 2.47 (2s, 6 H, CH_3S) 6.13 (qs, 2 H, NH_2) 7.07–7.53 (m, 5 H, aromatics) 8.83 (s, H, CH); mass spectrum m/e 290 (m^+). Anal. Calcd. for $C_{14}H_{14}N_2OS_2$: C, 57.90; H, 4.86; S, 22.08. Found: C, 58.07; H, 4.83; S, 21.94.

Dimethyl[3,3-bis(methylthio)-2-phenylallylidene]malonate **5d**: yellow needles mp 78–80°C (hexane) ^1H NMR ($CDCl_3$) δ, 2.12 and 2.40 (2s, 6 H, CH_3S) 3.03 and 3.72 (2s, 6 H, CH_3O) 7.22 (qs, 5 H, aromatics) 8.13 (s, H, CH); mass spectrum m/e 338 (m^+). Anal. Calcd. for $C_{16}H_{18}O_4S_2$: C, 56.78; H, 5.36; S, 18.95. Found: C, 57.08; H, 5.26; S, 18.83.

Ethyl-(6-*p*-methoxyphenyl-2-oxo-2H-thiopyran)-3-carboxylate **6**: A mixture of 1.0 g (4.0 mmol) of 1-*p*-methoxyphenyl-3-pyrrolidino-2-propen-1-thione **1**, 2.56 g (16.0 mmol) of diethyl malonate, 2.76 g (20.0 mmol) of potassium carbonate and 100 ml of dry toluene was heated under reflux over a period of 18 h. After cooling, the reaction mixture was hydrolysed using a saturated aqueous solution of ammonium chloride. After extraction with methylene chloride, the organic layer was washed with water and dried over calcium chloride. Concentration of the solution on a rotary evaporator under reduced pressure gave the crude crystalline product, which by recrystallization from ethanol afforded 0.78 g of the starting material **1**. The mother liquid was concentrated and recrystallized from ethanol to give 0.10 g (global yield 8%) of compound **6** as yellow needles mp 126–128°C; ^1H NMR ($CDCl_3$) δ, 1.35 (t, 3 H, CH_3, J = 7.2 Hz) 3.40 (s, 3 H, CH_3O) 4.30 (q, 2 H, CH_2, J = 7.2 Hz) 6.93 (d, H, CH, J = 8.0 Hz) 8.08 (d, H, CH, J = 8.0 Hz) 6.87 and 7.45 (2d, 4 H, aromatics, ΣJ = 8.7 Hz); mass spectrum m/e 290 (m^+). Anal. Calcd. for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.86; S, 11.05. Found: C, 61.95; H, 4.88; S, 11.22.

Dimethyl(3-methoxycarbonyl-2-oxo-5-phenyl-2H-thiopyran-6-yl)malonate **7**: Dimethyl malonate (16.0 mmol, 2.11 g) was condensed with the methyl 3-morpholino-2-phenylpropendithioate **2** (1.12 g, 4.0 mmol) according to the general procedure described above. After adding the dithiocarbamate vinylog, the reaction mixture was heated to 60°C and maintained with stirring at this temperature for 24 h. After cooling to 20°C, the mixture was hydrolysed and extracted as for compound **6**. The resulting crude product was chromatographed on a silica gel column; elution with methylene chloride–diethyl ether (20 : 1) gave after recrystallization from ethanol, 0.57 g (yield 38%) of white needles, mp 134–135°C; ^1H NMR ($CDCl_3$) δ, 3.73 (s, 3 H, CH_3) 3.80 (s, 6 H, CH_3) 4.82 (s, H, malonic CH) 7.93 (s, H, thiopyranic proton); mass spectrum m/e 376 (m^+). Anal. Calcd. for $C_{18}H_{16}O_7S$: C, 57.44; H, 4.28; S, 8.52. Found: C, 57.42; H, 4.35; S, 8.47.

Hydrolysis of the 1,4-addition compounds. The 1,4-addition compound **3** of the active methylene compound, malodinitrile, ethyl cyanacetate, ethyl diethylphosphonatoacetate, was prepared according to the general procedure.

Hydrolysis of the 1,4-adduct was carried out rapidly at 20°C by the addition of a saturated aqueous solution of ammonium chloride.

The reaction mixture was then extracted three times with 100 ml portions of benzene. The benzene extracts were combined, washed with water, dried (Na_2SO_4) and concentrated under reduced pressure on a rotary evaporator. The resulting crude product was chromatographed on a Merck 60 silica gel column.

2-Imino-6-*p*-methoxyphenyl-2H-thiopyran-3-carbonitrile **8**: elution with benzene–ethyl acetate (20 : 1), yield 43%, brown crystals mp 141–142°C (ethyl acetate); ^1H NMR (CF_3COOD) δ, 3.90 (s, 3 H, CH_3) 7.01 and 7.64 (2d, 4 H, aromatics, ΣJ = 8.8 Hz) 7.63 (d, H, CH, J = 8.6 Hz) 8.21 (d, H, CH, J = 8.6 Hz), NH not visible; mass spectrum m/e 242 (m^+). Anal. Calcd. for $C_{13}H_{10}N_2OS$: C, 64.44; H, 4.16; N, 11.56; S, 13.24. Found: C, 63.76; H, 4.24; N, 11.54; S, 12.98.

2-Imino-6-methylthio-5-phenyl-2H-thiopyran-3-carbonitrile **9**: elution with benzene–ethyl acetate (20 : 1), yield 98%, red oil; ^1H NMR ($CDCl_3$) δ, 2.38 (s, 3 H, CH_3) 7.08 (s, H, CH) 7.23 (qs, 5 H, aromatics) 8.06 (broad s, H, NH); mass spectrum m/e 258 (m^+).

Dimer **12**: elution with ethyl acetate, yield 25%, yellow oil, ^1H NMR ($CDCl_3$) δ, 1.07–1.60 (m, 18 H, CH_3) 3.73 and 3.78 (2s, 6 H, CH_3O) 3.93–4.40 (m, 14 H, 6 CH_2 and 2 CH) 6.73–7.10 and 7.33–7.63 (2m, 10 H, aromatics and ethylenics) 7.93–8.53 (m, 2 H, ethylenics); mass spectrum m/e 800 (m^+).

Diethyl 2,2′-dicyano-5,5′-di(*p*-methoxyphenyl)-5,5′-thiodi(2,4-pentadienoate) **13**: elution with benzene, yield 39%, yellow needles, mp 215–218°C (acetonitrile); ^1H NMR ($CDCl_3$) δ, 1.40 (t, 3 H, CH_3, J = 7.0 Hz) 3.75 (s, 3 H, CH_3O) 4.36 (t, 2 H, CH_2, J = 7.0 Hz) 6.67 and 6.91 (2d, 4 H, aromatics, ΣJ = 8.8 Hz) 6.81 (d, H, CH, J = 11.5 Hz) 8.57 (d, H, CH, J = 11.5 Hz); mass spectrum m/e 544 (m^+). Anal. Calcd. for $C_{30}H_{28}N_2O_6S$: C, 66.15; H, 5.18; S, 5.89. Found: C, 65.66; H, 5.23; S, 6.12.

2-(*N*-Acetylimino)-6-*p*-methoxyphenyl-2H-thiopyran-3-carbonitrile **10**: Compound **8** (1.0 g, 4.13 mmol) was dissolved in 20 ml of acetic acid anhydride, and the solution was heated under reflux for 30 min. After cooling, the crude product was precipitated by adding diethyl ether, then recrystallized from DMSO-acetonitrile to give 0.91 g (yield 78%) of orange crystals, mp 213–216°C; ^1H NMR (CF_3COOD) δ, 2.60 (s, 3 H, CH_3CO) 3.93 (s, 3 H, CH_3O) 7.00 and 7.73 (2d, 4 H, aromatics, ΣJ = 8.8 Hz) 8.03 (d, H,

CH, J = 8.5 Hz) 8.47 (d, H, CH, J = 8.5 Hz); ^{13}C NMR (DMSO) δ, 27.3 and 182.0 (CH_3CO) 118.4 (CN) 106.9, 149.3, 155.6, 162.2 and 165.1 (thiopyranyl ring) 55.7, 115.3, 127.8, 129.1 and 162.2 ($CH_3OC_6H_4$); mass spectrum m/e 284 (m^+). Anal. Calcd. for $C_{15}H_{12}N_2O_2S$: C, 63.36; H, 4.25; S, 11.28. Found: C, 63.30; H, 4.27; S, 11.34.

2-(*N*-Acetylimino)-6-methylthio-5-phenyl-2H-thiopyran-3-carbonitrile **11**: prepared from **9** as described for **10**, yield 73%, green crystals, mp 195–200°C (DMSO-Acetonitrile); ^{1}H NMR ($CDCl_3$) δ, 2.43 (s, 3 H, CH_3) 2.63 (s, 3 H, CH_3) 7.15–7.43 (m, 5 H, aromatics) 7.63 (s, H, CH); ^{13}C NMR ($CDCl_3$) 15.9 (CH_3S) 27.4 and 183.2 (CH_3CO) 116.1 (CN) 105.3, 131.4, 147.9, 159.6 and 165.2 (thiopyranyl ring) 128.8, 129.2, 129.3 and 136.5 (phenyl ring); mass spectrum m/e 300 (m^+). Anal. Calcd. for $C_{15}H_{12}N_2OS_2$: C, 59.97; H, 4.02; S, 21.35. Found: C, 59.85; H, 3.79; S, 21.51.

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