Condensation of a Chiral Tetrahydro-2-furanthione with Diazocarbonyl Compounds

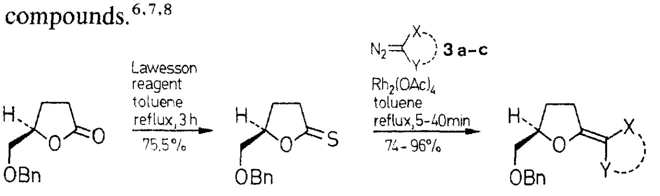
Seiichi Takano,* Shun'ichi Tomita, Michiyasu Takahashi, Kunio Ogasawara

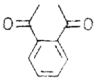
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan

Reaction of (*R*)-5-(benzyloxymethyl)tetrahydro-2-furanthione (**2**), prepared from the corresponding furanone **1**, with the diazocarbonyl compounds **3a–c** in the presence of rhodium(II) acetate afforded the 2-(acylmethylene)tetrahydrofuran derivatives **4a–c** in good yields.

The synthetic utility of thiolactones (i.e. 2-oxacyclanethiones) has not been fully explored to date. In relation to our synthetic investigations utilizing chiral γ-lactone derivatives,[1] we have found a new condensation reaction involving a chiral γ-thiolactone derivative.

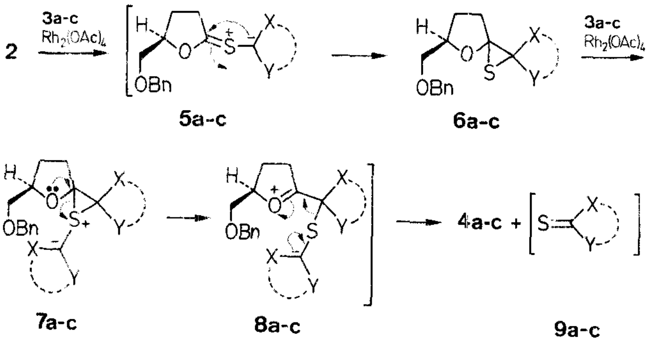
Treatment of the chiral γ-lactone[2] **1** with Lawesson reagent[3,4] in refluxing toluene affords the thiolactone **2** in 75.5 % yield. When **2** is refluxed briefly in toluene with 3 equivalents of the diazoesters **3a–b**, or the diazoketone **3c**, in the presence of a catalytic amount of rhodium(II) acetate,[5] smooth reaction occurs to give rise to the corresponding 2-acylmethylenetetrahydrofurans **4a–c** in good yields (Scheme A). These types of compounds have so far been obtained in much poorer yields by the condensation between lactone acetals and active methylene compounds.[6,7,8]



3,4	X	Y
a	$CO_2C_2H_5$	$CO_2C_2H_5$
b	$CO_2C_2H_5$	$\overset{O}{\overset{\|}{P}}(OC_2H_5)_2$
c		

Scheme A

The reaction may be interpreted as the sequential formation of the corresponding sulfur ylides **5a–c** by reaction of **2** with the carbenoids generated from **3**, isomerization of **5a–c** into the episulfides (**6a–c**), interception of **6a–c** with excess carbenoid generating the ylides **7a–c**, followed by transformation into products **4a–c** and the thioketones **9a–c**, though the latter of which are not isolated (Scheme **B**). The reaction pathway assumed is reminiscent of the Eschenmoser sulfide-contraction reaction[9] using thiolactam substrates.



Scheme **B**

Reactions were carried out under argon. IR spectra were measured with a JASCO A-102 spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL-JNM-FX90A spectrometer. Mass spectra were measured with a JEOL-OISG-2 instrument. Optical rotations were measured with a JASCO-DIP-4 automatic polarimeter.

(*R*)-5-(Benzyloxymethyl)tetrahydro-2-furanthione (2):
A stirred mixture of (*R*)-5-(benzyloxymethyl)tetrahydro-2-furanone (**1**; 1.77 g, 8.59 mmol) and 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane *P*,*P*-disulfide (Lawesson reagent; 2.40 g, 6.45 mmol) in toluene (20 mL) is refluxed for 3 h. The solution is chromatographed on a silica gel column (200 g) using hexane/CH_2Cl_2 (2:1) as eluent to give thione **2** as pale yellow needles; yield: 1.44 g (76%); m.p. 53–55 °C (pet. ether/$CHCl_3$); $[\alpha]_D^{22}$ + 8.11° (*c* 1.01, $CHCl_3$).

$C_{12}H_{14}O_2S$	calc.	C 64.84	H 6.35
(222.2)	found	64.58	6.41

IR (neat): ν = 1200–1100 cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 2.1–2.4 (m, 2 H); 3.0–3.25 (m, 2 H); 3.72 (m, 2 H); 4.58 (s, 2 H); 5.05 (m, 1 H); 7.31 (s, 5 H).

MS (70 eV): *m/e* (%) = 222 (M$^+$), 91 (100).

Ethyl Diazo(diethoxyphosphoryl)acetate (3b):
To a stirred suspension of NaH (2.40 g, 60 mmol) in THF (200 mL) is added ethyl (diethoxyphosphoryl)acetate (11.2 g, 50 mmol) dropwise at 0 °C and, after 20 min, *p*-toluenesulfonyl azide (13.8 g, 70 mmol) portionswise. The mixture, after having been stirred for 40 min at the same temperature, is treated with 5% aq. $NaHCO_3$ (10 mL), and the mixture is evaporated *in vacuo* to remove most of the THF. The residue is then extracted with CH_2Cl_2 (3 × 100 mL), and the extract is washed with 5% aq. $NaHCO_3$ (100 mL), 5% HCl (100 mL), and brine (100 mL), dried ($MgSO_4$), and evaporated *in vacuo*. The residual oil is chromatographed on a silica gel column (250 g) using hexane/EtOAc (1:3) to give pure **3b** as a colorless oil; yield: 9.98 g (80%).

$C_8H_{15}O_5N_2P$	calc.	C 38.38	H 6.04	N 11.20
(250.2)	found	38.33	5.78	11.19

IR (film): ν = 2180, 1705, 1718 cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.24–1.47 (m, 9 H), 4.05–4.41 (m, 6 H).

MS (70 eV): *m/e* (%) = 250 (M$^+$), 109 (100).

(*R*)-5-Benzyloxymethyl-2-[di(ethoxycarbonyl)methylene]tetrahydrofuran (4a):
A stirred mixture of the thione **2** (167 mg, 0.75 mmol) and diethyl diazomalonate[10] (**3a**; 411 mg, 2.25 mmol) in toluene (5 mL) is refluxed for 5 min in the presence of rhodium(II) acetate dimer (6.6 mg, 0.015 mmol). After the solvent has been evaporated *in vacuo*, the residue is chromatographed on a silica gel column (40 g) using EtOAc/hexane (1:3) as eluent to give **4a** as a colorless oil; yield: 257 mg (74%); $[\alpha]_D^{25}$ – 0.95° (*c* 1.05, $CHCl_3$).

$C_{19}H_{24}O_6$	calc.	C 65.50	H 6.94
(348.4)	found	64.92	7.13

IR (neat): ν = 1730, 1705, 1630 cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.28 (2 t, 6 H, *J* = 7.1 Hz); 1.90–2.40 (m, 2 H); 2.85–3.37 (m, 2 H); 4.23 (2 q, 4 H, *J* = 7.1 Hz); 4.56 (s, 2 H); 4.75 (s, 1 H); 7.32 (s, 5 H).

MS (70 eV): *m/e* (%) = 348 (M$^+$), 91 (100).

(*R*)-5-Benzyloxymethyl-2-[ethoxycarbonyl(diethoxyphosphoryl) methylene]tetrahydrofuran (4b):
A stirred mixture of the thione **2** (111 mg, 0.5 mmol) and diazo ester **3b** (375 mg, 1.5 mmol) in toluene (2 mL) is refluxed for 40 min in the presence of rhodium(II) acetate dimer (5.0 mg, 0.014 mmol). After the solvent has been evaporated *in vacuo*, the residue is chromatographed on a silica gel column (40 g) using EtOAc as eluent to give **4b** as a *E*/*Z*-mixture (ca. 1:1) in 96% yield.

$C_{20}H_{29}O_7P$	calc.	C 58.22	H 7.09
(412.2)	found	58.34	7.14

Both isomers can be separated by a silica gel column chromatography using EtOAc as eluent:

Isomer A (less polar); a colorless oil; $[\alpha]_D^{24}$ + 17.14 (*c* 1.05, $CHCl_3$).

IR (neat): ν = 1710, 1625 cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.18–1.43 (m, 9 H); 1.84–2.31 (m, 2 H); 3.10–3.38 (m, 2 H); 3.41–3.80 (m, 2 H); 3.92–4.35 (m, 6 H); 4.57 (s, 2 H); 4.65–4.85 (m, 1 H); 7.32 (s, 2 H).

MS (70 eV): *m/e* (%) = 412 (M$^+$), 91 (100).

Isomer B (more polar); a colorless oil; $[\alpha]_D^{24}$ + 5.78° (*c* 1.02, $CHCl_3$).

IR (neat): ν = 1688, 1575 cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.22–1.43 (m, 9 H); 1.90–2.28 (m, 2 H); 3.04–3.40 (m, 2 H); 3.59 (dd, 1 H, *J* = 11.0, 3.9 Hz); 3.74 (dd, 1 H, *J* = 11.0, 4.2 Hz); 3.90–4.37 (m, 6 H), 4.57 (s, 2 H), 4.80–4.97 (m, 1 H), 7.33 (s, 5 H).

MS (70 eV): *m/e* (%) = 412 (M$^+$), 91 (100)

(*R*)-5-Benzyloxymethyl-2-(1,3-dioxo-2-indanylidene)tetrahydrofuran (4c):
A stirred mixture of the thione **2** (333 mg, 1.5 mmol) and 2-diazo-1,3-indandione[11] (**3c**; 775 mg, 4.5 mmol) in toluene (10 mL) is refluxed for 15 min in the presence of rhodium(II) acetate dimer (13.3 mg, 0.03 mmol). After the solvent has been evaporated *in vacuo*, the residue is chromatographed on a silica gel column (40 g) using ether/hexane (1:2) as eluent to give **4c** as an oil; yield: 368 mg (74%); $[\alpha]_D^{26}$ + 62.68° (*c* 0.97, $CHCl_3$).

$C_{21}H_{18}O_4$	calc.	C 75.45	H 5.43
(334.4)	found	75.11	5.56

IR (neat): ν = 1720, 1675 cm^{-1}.

^{1}H-NMR ($CDCl_3$/TMS): δ = 2.24 (m, 2 H); 3.50 (t, 1 H, *J* = 7.0 Hz); 3.52 (t, 1 H, *J* = 7.0 Hz); 3.69 (dd, 1 H, *J* = 11.0, 3.4 Hz); 3.88 (dd, 1 H, *J* = 11.0, 3.4 Hz); 4.57 (s, 2 H); 5.09 (m, 1 H); 7.28 (s, 5 H); 7.61–7.93 (m, 4 H).

MS (70 eV): *m/e* (%) = 334 (M$^+$), 91 (100).

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