CHEMISTRY LETTERS, pp. 855-858, 1975. Published by the Chemical Society of Japan

THE SYNTHESIS AND REACTION OF α,α-BIS(PHENYLTHIO)-γ-BUTYROLACTONE. A CONVENIENT METHOD FOR THE PREPARATION OF 3-SUBSTITUTED 2-BUTEN-4-OLIDE

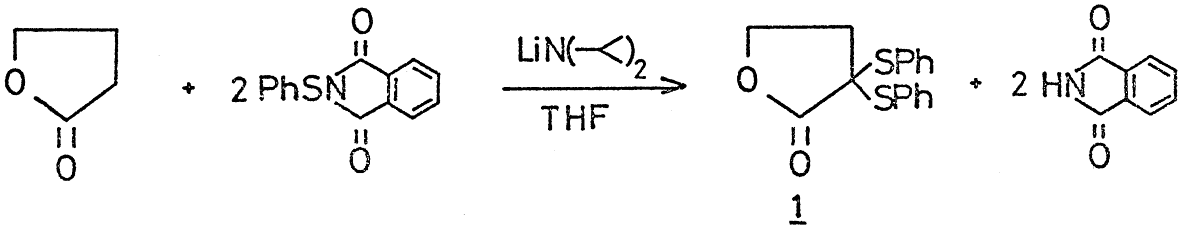
Mikio WATANABE, Kozo SHIRAI, and Takanobu KUMAMOTO
Department of Chemistry, Faculty of Science, Tokai University
Kitakaname, Hiratsuka, Kanagawa 259-12

The reaction of γ-butyrolactone with N-phenylthiophthalimide in the presence of lithium diisopropylamide afforded α,α-bis(phenylthio)-γ-butyrolactone 1 in high yield. Further, a convenient method for the preparation of 3-substituted 2-buten-4-olide was established by the use of 1.

In the past few years there has been a rapid growth of interest in the preparation of butenolides[1)] or methylene lactones[2)] by the use of α-sulfenylated or α-sulfinylated γ-butyrolactones as important synthetic intermediates. For example, H. Uda and co-workers have reported the excellent method for the synthesis of 3-substituted 2-buten-4-olides by the conjugate addition reaction of 3-phenylthio-2-buten-4-olide with organocopper reagents or diethyl malonate[3)].

In the course of our study on the sulfenylation[4)] of active methylene compounds or ketones by the use of sulfenamides, we have reported the preparation of 2,2-bis(phenylthio)cyclohexanone by the use of N-phenylthiophthalimide.

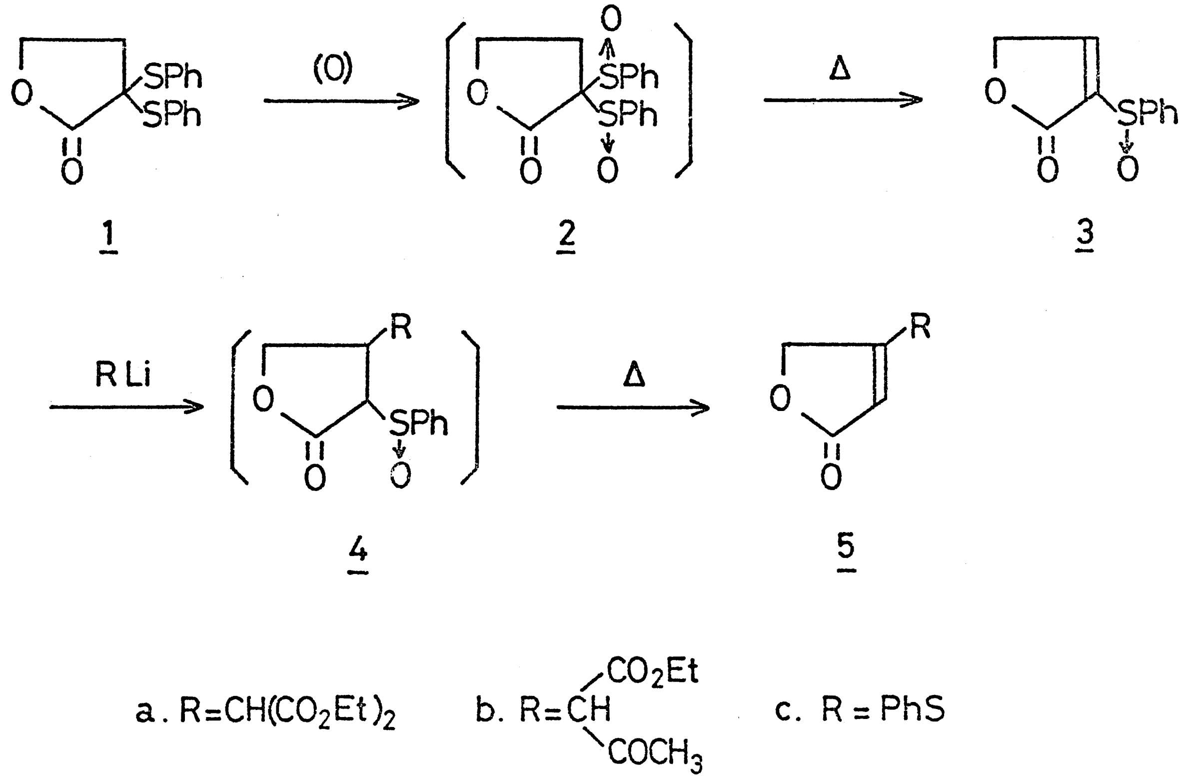
We now wish to report in this paper the preparation of α,α-bis(phenylthio)-γ-butyrolactone 1 and 3-substituted 2-buten-4-olide starting from 1.



Scheme I

To a tetrahydrofuran(THF) solution of lithium diisopropylamide(4.85g, 0.048 mol) was added excess amounts of γ-butyrolactone(2.50g, 0.029 mol) in 10 ml THF at -50°C. After addition of hexamethylphosphoramide(3.58g, 0.02 mol), the lactone enolate was treated with N-phenylthiophthalimide(10.20g, 0.04 mol). The reaction mixture was stirred for 1 hr at -50°C, followed by additional stirring for 1 hr at -20°C and at room temperature for 2 hr. General work-up afforded α,α-bis(phenylthio)-γ-butyrolactone 1(5) in 81% (based on N-phenylthiophthalimide) yield.

Further, a convenient route to the 3-substituted 2-buten-4-olides starting from 1 outlined in scheme II was established.



1 2 3

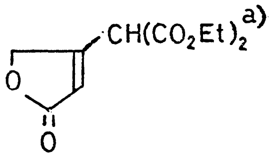
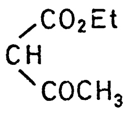
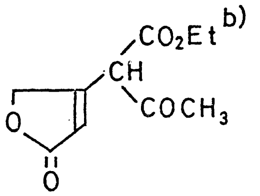
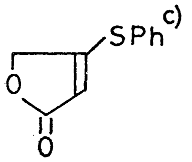
4 5

a. $R=CH(CO_2Et)_2$ b. $R=CH(CO_2Et)(COCH_3)$ c. R = PhS

Scheme II

Oxidation of 1 with 2 equiv of m-chloroperbenzoic acid was carried out in $CHCl_3$ for 1 hr at 0-5°C. The reaction mixture was quenched with aqueous solution of $NaHCO_3$ and $Na_2S_2O_3$, and evaporation of the organic layer gave a crude oil of 2. This crude 2 was thermolized without further purification in refluxing $CHCl_3$ for 1 hr. The reaction mixture was concentrated to an oil; treatment with petroleum ether-ether provided crystals of 2-phenylsulfinyl-2-buten-4-olide(6) in

Table

Substituents R	Conditions of Michael addition	Conditions of thermolysis	Butenolides 5	Overall yield* %
$CH(CO_2Et)_2$	EtOH EtOLi -50°C 40 min	$CHCl_3$-CCl_4 6 hr		76
 $CH(CO_2Et)(COCH_3)$	〃	〃 10 hr		79
PhS	THF n-BuLi -50°C 40 min	〃 6 hr		62

* Yields given are for isolated products.

a) Anal.(%) Calcd. for $C_{11}H_{14}O_6$: C, 54.54; H, 5.38, Found: C, 54.44; H, 5.62 , NMR(60 MHz, $CDCl_3$): 5.87(s, 1H), 4.78(s, 2H), 4.49(s, 1H), 4.06(q, 4H), 1.26(t, 6H), IR: 1780, 1750 cm^{-1}.

b) This product is insoluble in methanol or chloroform or dimethyl sulfoxide. Mp 166-167°C from benzene. Anal.(%) Calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70, Found: C, 56.48; H, 5.52, IR: 1705 cm^{-1}, MS: m/e 202(202.20).

c) Mp 46-48°C from petroleum ether(boiling range 34-40°C). Anal.(%) Calcd. for $C_{10}H_8O_2S$: C, 62.50; H, 4.20; S, 16.67, Found: C, 62.45; H, 4.37; S, 16.71, NMR(60 MHz, $CDCl_3$): 7.42-6.92(m, 5H), 5.76(s 1H), 4.75(s, 2H), IR: 1780 cm^{-1}.

86% overall yield.

Furthermore, Michael addition reaction of 3 with active methylene compounds or thiophenol followed by thermolysis of resulting adducts 4 afforded 3-substituted 2-buten-4-olide in high overall yield. These results are summarized in the table.

In a typical procedure, to a 10 ml ethanol solution of diethyl lithiomalonate, prepared from lithium ethoxide(3.9 mmol) and diethyl malonate(0.720g, 4.5 mmol), was added crystals of 3(0.624g, 3 mmol) at -50°C, and the mixture was stirred for 40 min at -50°C. Quenching the reaction mixture with 10% HCl followed by evaporation of organic layer afforded a crude oil of 4-a. Thermolysis of the crude 4-a was carried out in refluxing $CHCl_3$-CCl_4(1:3) for 6 hr. After removal of the solvent, the residue was chromatographed on silica gel to give pure 3-[bis(ethoxycarbonyl)methyl]-2-buten-4-olide(0.555g) in 76% overall yield.

Further, application of 3, as a synthetic intermediate, to natural products is now in progress.

References and Notes

1) B. M. Trost and T. N. Salzmann, J. Amer. Chem. Soc., 95, 6840 (1973).

2) P. A. Grieco and J. J. Reap, Tetrahedron Lett.,1097 (1974); R. C. Ronald, Tetrahedron Lett., 3831 (1973); J. L. Herrmann, M. H. Bergar, and R. H. Schlessinger, J. Amer. Chem. Soc., 95, 7923 (1973).

3) K. Iwai, H. Kosugi, and H. Uda, Chem. Lett., 1237 (1974); K. Iwai, M. Kawai, H. Kosugi, and H. Uda, Chem. Lett., 385 (1974).

4) T. Kumamoto, S. Kobayashi, and T. Mukaiyama, Bull. Chem. Soc. Japan, 45, 866 (1972).

5) Mp 57-58°C from ligroin. Anal.(%) Calcd. for $C_{15}H_{14}O_2S_2$: C, 63.57; H, 4.67; S, 21.18, Found: C, 63.48; H, 4.68; S, 21.42, NMR(60 MHz, $CDCl_3$) 7.70-7.15 (m, 10H), 4.20(t, 2H), 2.50(t, 2H), IR: 1760 cm^{-1}. MS: m/e 302(302.3).

6) Washing of crude crystals with petroleum ether-ether(1:1)gave pure crystals of 3(mp 83-85°C). Anal.(%) Calcd. for $C_{10}H_8O_3S$: C, 57.69; H, 3.87: S, 15.40, Found: C, 58.04; H, 3.93; S, 15.57, NMR(60 MHz, $CDCl_3$): 7.92-7.00(m 6H), 4.86(s, 2H), IR: 1750 cm^{-1}.

(Received May 17, 1975)