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SYNTHESIS OF γ-BUTYROLACTONES VIA THE ENE REACTION OF ETHYL α-CHLORO-α-PHENYLTHIOACETATE AND 1-ALKENES

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Abstract: Ethyl α-chloro-α-phenylthioacetate reacted with 1-alkenes in CH_2Cl_2 at -78—0 °C in the presence of $SnCl_4$ to afford the ene reaction products (80-90%), which were readily converted into the corresponding γ-butyrolactones.

In our previous report we described one-pot synthesis of γ-butyrolactones and 4,5-dihydrofurans from α-chloro-α-ketosulfides and branched olefins in the presnce of $SnCl_4$,[1)] where tertiary carbocations are generated in situ. During these experiments, we encountered that ene reaction took place as a side reaction. In this communication we wish to report that ethyl α-chloro-α-phenylthioacetate (**1**) reacts with 1-alkenes (**2**) to afford solely an ene reaction product (**3**), which is readily converted into the corresponding γ-butyrolactone. The skeleton of γ-butyrolactone is widely found as a moiety in many naturally occurring compounds, and a number of methods for the synthesis of these compounds have been reported.[2)]

Ethyl α-chloro-α-phenylthioacetate (**1**) was prepared from the corresponding sulfide by treating with N-chlorosuccinimide.[3)] Tin tetrachloride was added to a mixture of **1** and **2** in CH_2Cl_2 under argon atmosphere at -78 °C and the reaction mixture was allowed to warm to room temperature to give **3** as shown in Scheme I and the results of these reactions are summarized in the Table.[4)]

Scheme I

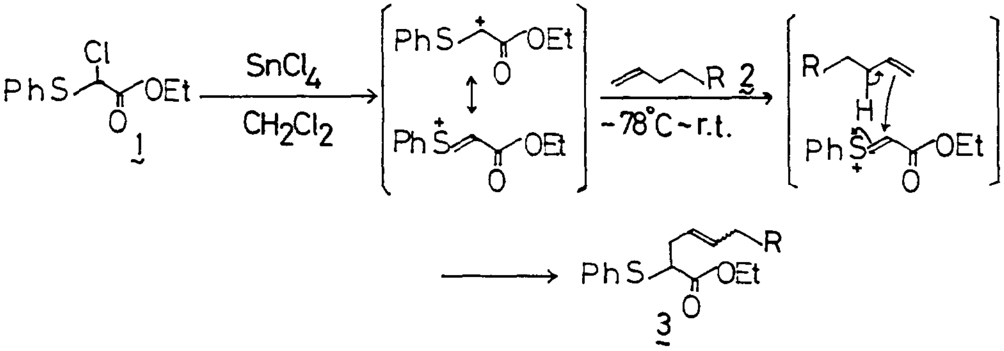


Table Ene Reaction of Ethyl α-Chloro-α-phenylthioacetate (**1**) and 1-Olefins (**2**)$^{a)}$

	1-Olefin (equiv.)	Equiv. of $SnCl_4$	Yield of **3**$^{b)}$ (%)
a	CH_2:$CH(CH_2)_3CH_3$ (1)	1	51
	CH_2:$CH(CH_2)_3CH_3$ (2)	1	72
	CH_2:$CH(CH_2)_3CH_3$ (2)	2	88
b	CH_2:$CH(CH_2)_2CH_3$ (2)	2	81
c	CH_2:$CH(CH_2)_7CH_3$ (2)	2	92
d	CH_2:$CH(CH_2)_{10}CH_3$ (2)	2	92
e	CH_2:$CH(CH_2)_{12}CH_3$ (2)	2	80

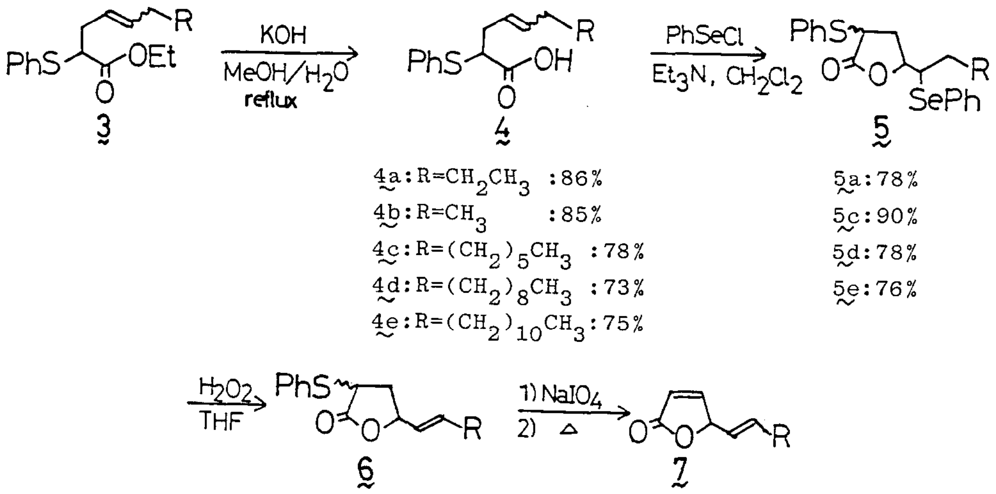
a) A standard procedure is as follows : to a mixture of 2.0 mmol of **1** and 4.0 mmol of **2** in 5 ml of CH_2Cl_2 was added 4.0 mmol of $SnCl_4$ at -78 °C under argon. The mixture was allowed to warm to room temperature with stirring. The reaction mixture was treated with water followed by extraction with CH_2Cl_2. After removal of CH_2Cl_2, the crude product was purified by flash column chromatography on silica gel (Merck Art 9385, hexane:ethyl acetate=19:1)

b) Satisfactory IR, ^1H NMR, MS and elemental analyses data were obtained for these compounds. Data for selected **3a** : IR (neat) 2950, 1725, 1430, 1140, 1015, 960, 735, and 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (t, 3H, J=6.6Hz), 1.14 (t, 3H, J=7.3Hz), 1.35 (sex, 2H, J=6.6Hz), 1.75-2.15 (m, 2H), 2.30-2.80 (m, 2H), 3.66 (t, 1H, J=7.3Hz), 4.08 (q, 2H, J=7.3Hz), 5.20-5.70(m, 2H), and 7.00-7.63 (m, 5H); MS (m/e) 278 (M^+, 100%), 196 (50), 169 (80), and 123 (90); Calcd for $C_{16}H_{22}SO_2$: C, 69.03 H, 7.97; Found: C, 68.95; H, 8.14. The IR spectrum revealed an absorption band at 960 cm^{-1} due to E configuration of the double bond, and the detailed ^1H NMR analysis showed that **3a** was a mixture of E and Z isomers and E isomer was major (the coupling constant of the vinyl proton : 15Hz). The ratio of E to Z isomer of **3a** was about 85:15 by HPLC analysis.

As is evident from the Table, use of two equivalents of $SnCl_4$ and 1-olefins gave good results and γ-butyrolactones were not detected at all, which should be produced by intramolecular attack of the secondary carbocation to the oxygen of a carbonyl group.[1]

The ene reaction product (3) could readily be converted into γ-butyrolactone (5)[5] by hydrolysis with KOH in aq MeOH followed by phenylselenolactonization of the resulted carboxylic acids 4[6] using phenylselenyl chloride and triethylamine in CH_2Cl_2.[7] The final stage of the synthesis of γ-butyrolactones (7) is elimination of the selenyl and the sulfenyl groups as shown in Scheme II.[8] This was carried out by the well known procedures : a) oxidation with H_2O_2 followed by fragmentation of the selenoxides at room temperature,[7] b) oxidation with $NaIO_4$ and successive pyrolysis of the resulting sulfoxides.[9]

Scheme II



4a:R=CH_2CH_3 :86%
4b:R=CH_3 :85%
4c:R=$(CH_2)_5CH_3$:78%
4d:R=$(CH_2)_8CH_3$:73%
4e:R=$(CH_2)_{10}CH_3$:75%

5a:78%
5c:90%
5d:78%
5e:76%

6c:96%
6d:92%
6e:90%

7c:72%
7d:53%
7e:71%

Finally, the present synthesis has the following advantages : a) the starting material can readily be synthesized, b) the reagents are readily available, c) ene reaction with 1-alkenes proceeds in high yields, d) ene reaction products are converted into the corresponding γ-butyrolactones under simple procedures.

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References and Notes

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4. For the similar ene reaction, see : Y. Tamura, H.-D. Choi, H. Maeda, and H. Ishibashi, *Tetrahedron Lett.*, **22**, 1343 (1981); Y. Tamura and H. Ishibashi, *Yuki Gosei Kagaku Kyokai Shi*, **40**, 658 (1982).
5. Satisfactory IR, ^{1}H NMR, and MS data were obtained for these compounds, however, ^{1}H NMR was complicated because the lactones (**5**) were a mixture of diastereomers. Selected ^{1}H NMR signals of **5d** : δ 2.90-3.30 (m, 1H, PhSe-C$\underline{H}$-), 3.80-4.08 (m, 1H, PhS-C$\underline{H}$-), and 4.20-4.64 (m, 1H, -O-C$\underline{H}$-C-SePh).
6. These compounds were identified by IR, ^{1}H NMR, MS, and elemental analyses data. Selected ^{1}H NMR signals of **4a** : δ 3.53 (t, 1H, J=7.2Hz, PhS-C$\underline{H}$-), 5.07-5.87 (m, 2H, -C$\underline{H}$=C$\underline{H}$-), and 12.10 (bs, 1H, -COO$\underline{H}$).
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8. Satisfactory IR, ^{1}H NMR, and MS data were obtained for **6** and **7**. The lactones (**6**) are a mixture of cis and trans isomers while the geometry of the exocyclic double bond is E configuration based on the coupling constant of the vinyl proton. Selected ^{1}H NMR signals of trans **6d** : δ 1.75-2.16 (m, 3H, -C=C-C$\underline{H}_2$- and PhS-C-C$\underline{H}$-), 2.73 (ddd, 1H, J=10.5, 9.0, 7.0Hz, PhS-C-C$\underline{H}$-), 3.94 (dd, 1H, J=10.5, 8.8Hz, PhS-C$\underline{H}$-), 4.74 (ddd, 1H, J=9.0, 6.5, 6.5Hz, -O-C$\underline{H}$-C=C-), 5.32 (ddt, 1H, J=16, 6.5, 1.5Hz, -O-C-C$\underline{H}$=C-), and 5.79 (dt, 1H, J=16. 6.0Hz, -O-C-C=C$\underline{H}$-). Selected ^{1}H NMR signals of cis **6d** : δ 2.36 (dd, 2H, J=6.7, 6.5Hz, PhS-C-C$\underline{H}_2$-), 3.88 (t, 1H, J=6.5Hz, PhS-C$\underline{H}$-), 4.80 (dt, 1H, J=6.7, 6.5Hz, -O-C$\underline{H}$-C=C-), 5.38 (dd, 1H, J=15, 6.5Hz, -O-C-C$\underline{H}$=C-), and 5.78 (dt, 1H, J=15, 6.0Hz, -O-C-C=C$\underline{H}$-). Selected ^{1}H NMR signals of **7d** : δ 5.10-5.50 (m, 2H, -O-C-C=C$\underline{H}$- and -O-C$\underline{H}$-C=C-), 5.90 (dd, 1H, J=15, 6.0Hz, -O-C-C$\underline{H}$=C-), 6.09 (dd, 1H, J=6.0, 1.7Hz, O=C-C$\underline{H}$=C-), and 7.38 (dd, 1H, J=6.0, 1.4Hz, O=C-C=C$\underline{H}$-).
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