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ONE-POT SYNTHESIS OF γ-BUTYROLACTONES AND 4,5-DIHYDROFURANS FROM α-CHLORO-α-KETOSULFIDES AND OLEFINS

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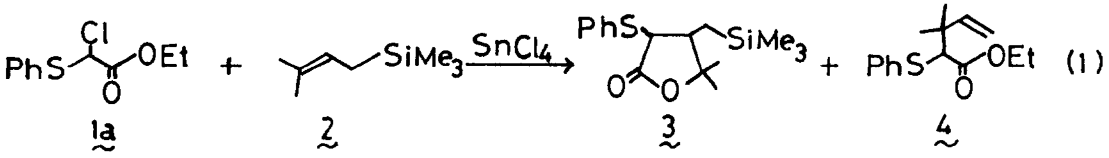
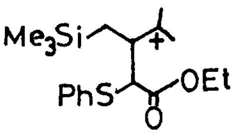
Abstract : Lewis acid ($SnCl_4$) catalyzed reaction of ethyl α-chloro-α-(p-chlorophenylthio)acetate (1b) with several olefins afforded the corresponding γ-butyrolactones (9) in good yields (51 - 92%). Under almost the same conditions, α-(t-butylthio)-α-chloroacetone (1c) reacted with olefins to give the expected 4,5-dihydrofurans (10) in moderate yields (41 - 55%).

In relation to recent attention on reactivity and availability of α-thio-α-ketocarbocations, we have investigated some reaction of α-chloro-α-ketosulfides (1) with allylsilanes in the presence of Lewis acids.[1)] During these experiments, we have noticed that γ, γ-dimethylallylsilane (2) reacted with 1a at β-carbon (abnormal reaction) to give γ-butyrolactone derivative (3 : 19% yield) as well as at γ-carbon (normal reaction) to substitute for chlorine atom (4 : 20% yield) as shown in reaction (1). We ascribed this fact to the presence of competition of stability between intermediate carbocations, i.e., tertiary carbocation (5) vs. secondary carbocation assisted by β-silyl group (6).[2)]



Therefore, in order to simplify the systsm, we tried the reaction of 1a with 2-methyl-2-pentene which should give tertiary carbocation as an intermediate and obtained γ-butyrolactone derivative (7) and thiochromane derivative (8) in a 45% and 41% yield, respectively. In order to prevent the intramolecular Friedel-Crafts reaction to give thiochromane derivative (8),[3] we used ethyl α-chloro-α-(p-chlorophenylthio)acetate (1b), and obtained the expected γ-butyrolactone derivatives (9) from several olefins in good yields via one-pot procedure as shown in reaction (3).



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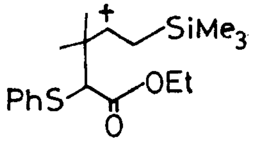

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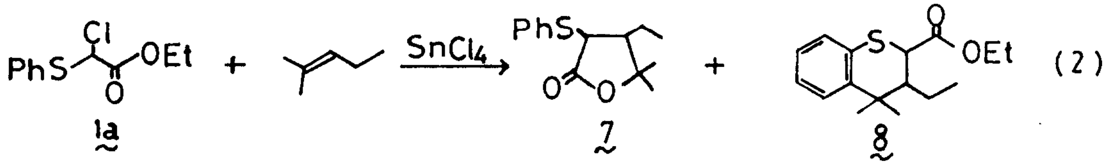
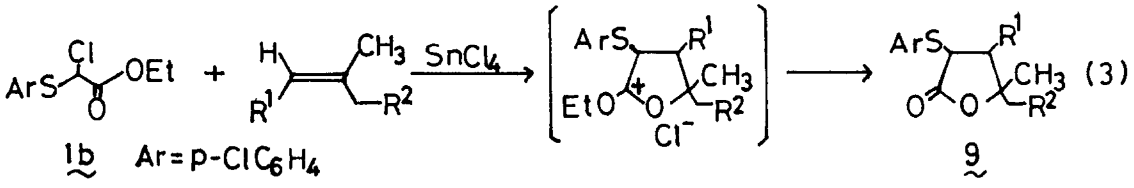




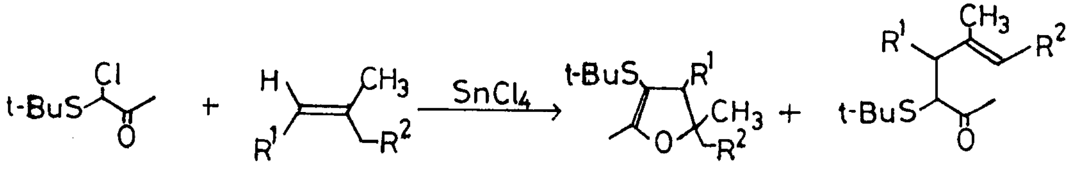
The following procedure for preparation of α-(p-chlorophenylthio)-β, γ, γ-trimethyl-γ-butyrolactone (9a) is representative. Stannic chloride (1.0 mmol) was added to a stirred solution of 1b (1.0 mmol) and 2-methyl-2-butene (1.1 mmol) in CH_2Cl_2 (10 ml) at room temperature under argon. The reaction mixture was stirred at the same temperature for 1 h. The mixture was poured into water and extracted with CH_2Cl_2 and dried. After the solvent was evaporated, the crude (almost pure) product was purified by flash column chromatography on silica gel (Merck Art 9385 ; n-hexane : ethyl acetate = 9 : 1 as eluent) to give 9a (almost 1 : 1 mixture of cis and trans isomers) in a 72% yield.[4]

		cis	trans
^{1}H NMR (CCl_4) : δ	α - H (total 1H)	: 3.31 (d, J=12 Hz)	: 3.79 (d, J=8 Hz)
	β - H (total 1H)	: 1.70-2.23 (m)	: 2.43-2.77 (dq, J=7, 8 Hz)
	Me groups (total 9H)	: 1.1-1.5 (five separate peaks)	

IR (neat) : 1760, 1475, 1265, 1090 cm^{-1} ; MS (m/e) 270 (M^+, 70%), 83 (100%)

By the same procedure, 2-methyl-1-pentene and 1-methylcyclohexene gave almost 1 : 1 mixture of cis and trans isomers, *i. e.*, **9b** (51%) and **9c** (54%), and also tetramethylethylene gave the corresponding **9d** (92%). This reaction proceeded with complete regioselectivity so that the tertiary carbon lay at γ-position exclusively. The yields of crude products, which were pure by ^{1}H NMR, were ca. 10% higher than those mentioned above. Among several Lewis acids ($ZnBr_2$, $ZnCl_2$, $TiCl_4$, $AlCl_3$, and $SnCl_4$), $SnCl_4$ was the best choice for the present reaction.

Next, we investigated the reaction of α-(*t*-butylthio)-α-chloroacetone (**1c**) with several olefins under almost the same conditions as above[5)] and found that 4, 5-dihydrofurans (**10**) were obtained directly accompanied by ene reaction products (**11**).[6)]



1c **10** **11** (4)

3-(*t*-Butylthio)-2, 4, 5, 5-tetramethyl-4, 5-dihydrofuran (**10a**) was obtained in a 55% yield. ^{1}H NMR (CCl_4) : δ 0.97 (3H, d, J=7 Hz), 1.18 (3H, s), 1.25 (9H, s), 1.33 (3H, s), 1.87 (3H, d, J=2 Hz), 2.57 (1H, q, J=7 Hz) ; MS : 214 (M^+, 24.5%), 158 (100%). By the same procedure, 2-methyl-1-pentene and methylenecyclohexane gave the expected **10b** (53%) and **10c** (48%), respectively, and also tetramethylethylene afforded the corresponding **10d** (42%).[7)] In each case, a considerable amount of ene reaction product was easily separated by flash column chromatography on silica gel (Merck Art 9385 ; n-hexane : ethyl acetate = 40 : 1 as eluent), i.e., **11a** (21%), **11b** (16%), **11c** (11%), and **11d** (36%). Again, regioselectivity of reaction (4) was so complete that the tertiary carbon lay exclusively at position 5 in 4, 5-dihydrofurans (**10**). When α-chloro-α-(*p*-chlorophenylthio)acetone (**1d**) was used, reaction was slower and yields of the products were lower.

In contrast to the results of reaction (3) and (4), ene reaction products were solely obtained, when **1b** and **1c** were reacted with 4-methyl-1-pentene in which secondary carbocation should be the intermediate.6)

Finally, we have presented one-pot synthesis of γ-butyrolactone and 4, 5-dihydrofuran derivatives which proceeds through intramolecular attack of the oxygen of a carbonyl group to the tertiary carbocation generated *in situ*. Extention of this method to other types of olefin is now underway.

References and Notes

1) M. Wada, T. Shigehisa, and K. Akiba, submitted for publication.

2) For the β-effect of silicon, see : E. W. Colvin, " *Silicon in Organic Synthesis* ", Chapter 3, Butterworth, London, 1981.

3) Y. Tamura, K. Ishiyama, Y. Mizuki, H. Maeda, and H. Ishibashi, *Tetrahedron Lett.*, **22**, 3773 (1981).

4) **9a** decomposed by distillation (110 °C / 0. 1 mmHg). **9a** gave correct elemental analyses. All **9** showed satisfactory NMR, IR, and MS.

5) The reaction was carried out at 0 °C for 5 min under otherwise the same conditions. When the reaction was carried out for longer period, yields of **10** and **11** were lower.

6) Y. Tamura, H.-D. Choi, H. Maeda, and H. Ishibashi, *Tetrahedron Lett.*, **22**, 1343 (1981).

7) All **10** gave satisfactory NMR, IR, and MS but deteriorated slowly on standing in the air. 3-(*p*-Chlorophenylthio) derivative (**10a'**) gave correct elemental analyses.

8) Partial support of this work is acknowledged for Grant-in-Aid for Special Project Research (No. 57218017) administered by Ministry of Education, Science and Culture.

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