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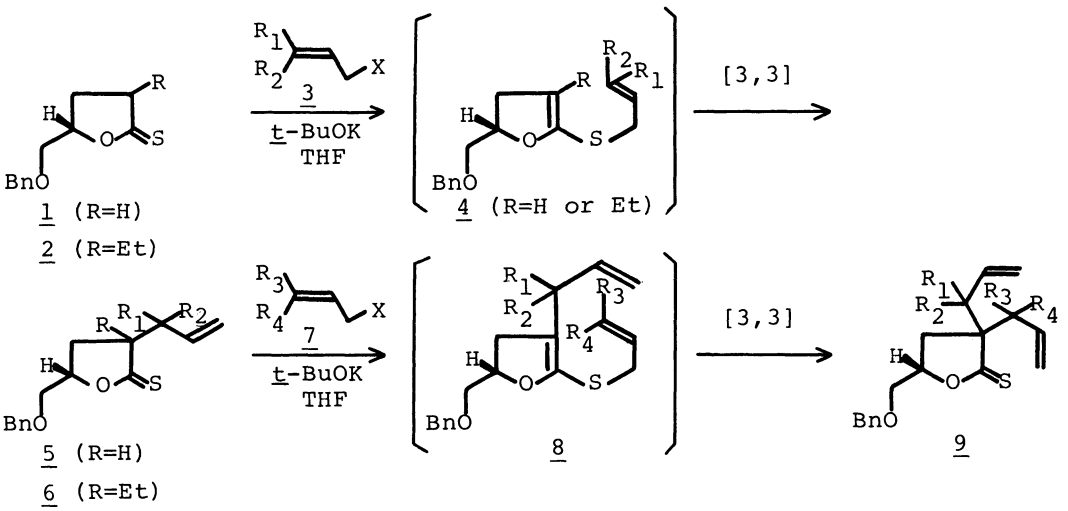
Thionolactone Claisen Rearrangement

Seiichi TAKANO,* Shun'ichi TOMITA, Michiyasu TAKAHASHI, and Kunio OGASAWARA
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980

Thionolactones prepared from the corresponding γ-lactones are found to be good substrates for the Claisen rearrangement.

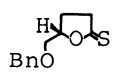
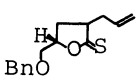
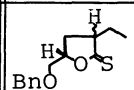
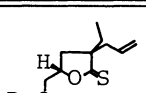
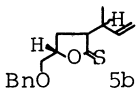
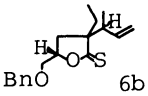
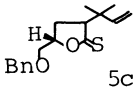
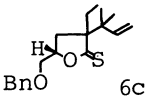
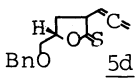
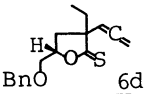
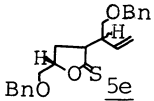
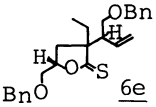
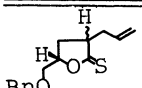
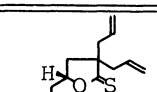
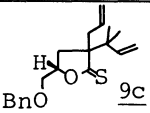
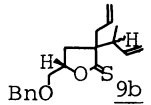
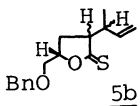
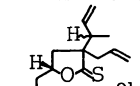
Synthetic utility of thionolactones has not been fully explored to date. We report here the first example of a synthetically promising Claisen type rearrangement using γ-thionolactone substrates, 1 and 2, prepared from the lactone precursors[1] with Lawesson reagent.[2-4] The reaction allows introduction of an allylic substituent on the α-position of the substrates under mild conditions. The reaction may be reiteratively carried out to afford α,α-bis-allylated products. Although the reaction proceeds non-stereoselectively in the first rearrangement generating tertiary center probably due to facile epimerization under the conditions, the second rearrangement takes place predominantly from the less crowded anti face to the γ-substituent.[9] In contrast to thio-amides[5,6] and thiolactams[6-8] the thionolactones are inert to allyl halides without catalyst and therefore activation by potassium t-butoxide is unavoidable to generate a ketene thioacetal intermediate.[10]



A typical procedure is as follows; To a stirred solution of the thionolactone (1, 440 mg, 20 mmol) in THF (12 ml) is added potassium t-butoxide (269 mg, 2.4 mmol) portionwise at -70 °C, and warmed to room temperature for 10 min, and again cooled at -70 °C for 10 min. To the mixture is added allyl bromide (266 mg, 2.2 mmol) dropwise and warmed to -10 °C for 1 h,[9] then 50 °C for 30 min. The mixture is treated with sat. aq. NH_4OH and is extracted with ether. After usual work-up, the product is chromatographically (SiO_2) purified to give the allyl-thionolactone

(5 R_1=R_2=H, 448 mg, 85.5%) as a syn/anti mixture.

Table 1.

Substrate	Allyl halide	Product	Ratio[a] (anti:syn)	Yield %	Substrate	Allyl halide	Product	Ratio[a] (anti:syn)	Yield %
 1	 3a	 5a	1.1:1	85.5	 2	3a	 6a	3.5:1	79.2
1	3b	 5b	1.3:1[b]	70.0	2	3b	 6b	—— [b),c)]	77.9
1	 3c	 5c	X=Br 2.2:1 X=Cl 2.0:1	25.0 31.6	2	3c	 6c	X=Cl 3.2:1	14.6
1	 3d	 5d	3.2:1	8.0	2	3d	 6d	4.4:1	52.0
1	 3e	 5e	1.4:1[b]	39.3	2	3e	 6e	4.4:1[b]	52.0
 5a	3a	 9a		82.7	5a	3c	 9c	X=Cl 1.0:0	15.3
5a	3b	 9b	—— [b),c)]	61.6	 5b	3a	 9b	—— [c)]	50.7

a) Determined by HPLC (EYELA PLC-10, Microsorb (80-115, 4.6 mm x 150 mm), 2% ^{i}PrOH-hexane) and ^{1}H-NMR. b) Stereochemistry and relative ratio of the newly generated allylic center could not be determined. c) Ratio could not be determined.

References

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4) Compounds 1 and 2 were obtained in 75.5 and 94.5% yields, respectively.
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9) Cf. S. Takano and K. Ogasawara, Yuki Gosei Kagaku Kyokai Shi, 40, 1037 (1982).
10) Formation of a ketene thioacetal intermediate may be discernible on a silica gel TLC plate.

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