

**REGIOSELECTIVE THIO-CLAISEN REARRANGEMENT VIA S-ALLYL KETENE-S,N-
ACETALS GENERATED FROM CYCLIC S-ALLYLMONOTHIODICARBOXIMIDE SALTS¹**

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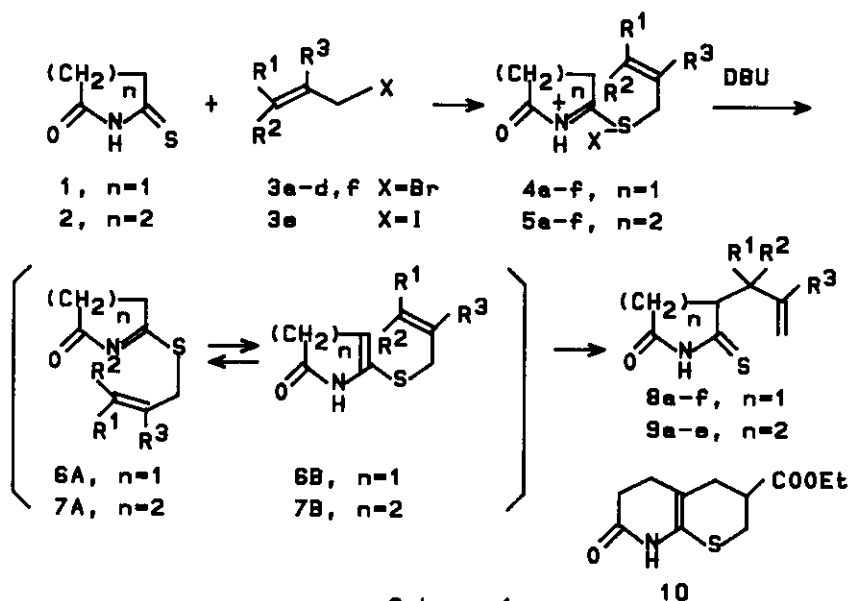
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Abstract - Thio-Claisen rearrangement via S-allyl ketene-S,N-acetals generated from cyclic S-allylmonothiodicarboximide salts with a base furnished the S→C allylic rearranged products exclusively.

The [3,3]-sigmatropic rearrangements are one of the most important transformations in the arsenal of modern synthetic organic chemistry.² Although thio-Claisen rearrangement of S-allylthioimides has been well investigated³, no report has dealt with a study of the rearrangement in S-allyl-N-acylthioamide system. In connection with our research on organic synthesis using thioamide functions⁴, we wish to communicate herein the regioselective thio-Claisen rearrangement via S-allyl ketene-S,N-acetals generated from cyclic S-allylmonothiodicarboximide salts with a base.

The formation of cyclic S-allylmonothiodicarboximide salts (**4a-f** and **5a-f**) by the reaction of cyclic monothiodicarboximides (**1** and **2**) with allyl halides (**3a-f**), followed by dehydrohalogenation with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) underwent the selective S→C allylic rearrangement to yield cyclic allylmonothiodicarboximides (**8a-f** and **9a-e**), respectively (Table 1). The reaction of **5f** gave bicyclic compound (**10**), which would be obtained by the intramolecular Michael reaction of **9f**. No traces of S→N allylic rearranged products were detected. Accordingly, the thermal rearrangement of the S-allyl ketene-S,N-acetal tautomer (**6B** or **7B**) to the C₃-allyl monothiodicarboximide (**8** or **9**) would be a faster process than that of direct rearrangement of S-allylimide tautomer (**6A** or **7A**) to N-allylmonothiodicarboximide or the exclusive rearrangement may proceed due to the predominance of the tautomer (**6B** or **7B**) over **6A** or **7A** form in the equilibrium drawn in Scheme 1. Although it was reported palladium-catalyzed rearrangement

of cyclic S-allylthioimidates produced the S→N allylic rearranged products exclusively due to the further coordination of Pd (II) to the nitrogen atom after the coordination of Pd (II) to the allylic double bond,^{3c,e} the reaction using 4a and 5a in the presence of Pd (II) as a catalyst gave no S→N allylic rearranged products. Because of a conjugation between the adjacent carbonyl and imine, the nitrogen might be unable to coordinate Pd (II).



In order to demonstrate the synthetic utility of allylmonothiodicarboximides thus prepared, proton-induced imino thiolactonization⁵ was carried out. The imino thiolactonizations of 8a and 9a with H₂SO₄ in HCOOH followed by hydrolysis produced the thiolactone-3-carboxylic acids (11 and 12),⁶ respectively (Scheme 2).

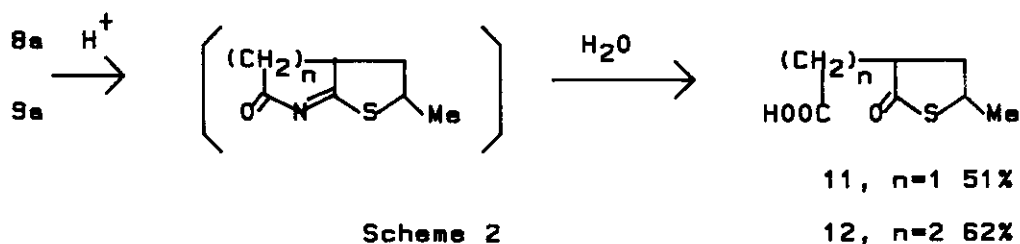


Table 1. The S \rightarrow C rearranged allylic products (8a-f, 9a-e, and 10)^{a)}

Product ^{b)}	R ¹	R ²	R ³	Yield (%)	Mp (°C)	¹ H-NMR (NH)/ppm
8a	H	H	H	67	174-177	10.1
8b	CH ₃	CH ₃	H	34	89-91	9.73
8c	C ₆ H ₅	H	H	35 ^{c,d)}	oil	9.97 10.2
8d	H	H	Br	37	65-68	10.5
8e	H	H	CH ₃	40	56-60	9.93
8f	H	H	COOC ₂ H ₅	66	oil	10.6
9a	H	H	H	72	71-73	9.73
9b	CH ₃	CH ₃	H	52	77-79	9.56
9c	C ₆ H ₅	H	H	49 ^{d,e)}	102-107	9.94
9d	H	H	Br	54	106-108	9.91
9e	H	H	CH ₃	43	77-78	9.47
10	H	H	COOC ₂ H ₅	54	111-114	8.73

a) All reactions were carried out as follows. Allylation of 1 and 2 was carried out in *t*-BuOH for 15 h at room temperature and subsequent dehydrohalogenation was in situ done for 4 h under reflux.

b) All new compounds were fully characterized spectroscopically (IR, ¹H-NMR, and MS spectral) and by combustion.

c) A mixture of erythro:threo (5:6).

d) Stereoisomer ratios determined by ¹H-NMR spectroscopy.

e) A mixture of erythro:threo (1:3).

In summary, this rearrangement proceeded regioselectively with a milder condition compared with that of S-allylthioimides, providing the S \rightarrow C rearranged products, which may be used for the further elaboration.

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REFERENCES AND NOTES

1. This work was presented at the 65th Meeting of the Hokuriku Branch of the Pharmaceutical Society of Japan, Toyama, June 1985.
2. a) R. P. Lutz, Chem. Rev., 1984, **84**, 205. b) L. E. Overman, Angew. Chem. Int. Engl., 1984, **23**, 579 .
3. a) P. J. W. Schuijl and L. Brandsma, Rec. Trav. Chim., 1968, **87**, 929. b) D. S. C. Black, F. W. Eastwood, R. Okragrik, A. J. Poynton, A. M. Wade, and C. H. Welker, Aust. J. Chem., 1972, **25**, 1483. c) Y. Tamaru, M. Kagotani, and Z. Yoshida, J. Org. Chem., 1980, **45**, 5223. d) R. Gompper and B. Kohl, Tetrahedron Lett., 1980, **21**, 907. e) Y. Tamaru, M. Kagotani, and Z. Yoshida, ibid., 1981, **22**, 4245. f) H. Takahata, Y. Banba, M. Mozumi, and T. Yamazaki, Heterocycles, 1986, **24**, 947.
4. a) H. Takahata, A. Anazawa, K. Moriyama, and T. Yamazaki, Chem. Lett., 1986, 5. b) H. Takahata, K. Yamabe, T. Suzuki, and T. Yamazaki, Heterocycles, 1986, **24**, 37. c) H. Takahata, T. Suzuki, and T. Yamazaki, ibid., 1986, **24**, 1247.
5. a) P. A. Bartlett, "Asymmetric Synthesis", J. D. Morrison, Ed., Chapter 6, Vol. 3, Academic Press, 1984. b) M. Mizutani, Y. Sanemitsu, Y. Tamaru, and Z. Yoshida, J. Org. Chem., 1983, **48**, 4585.
6. Compound 11: amorphous; ^1H NMR (CDCl_3) δ : 1.48 (3H, d, $J=6$ Hz, Me), 9.29 (1H, br s, COOH); IR (CHCl_3) ν : 1720, 1700 cm^{-1} ; Mass 155 (M^+).
Compound 12: mp 65-67 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ : 1.47 (3H, d, $J=6.5$ Hz, Me), 9.20 (1H, br s, COOH); IR (CHCl_3) ν : 1700, 1690 cm^{-1} ; Mass 169 (M^+).

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