THIO-CLAISEN REARRANGEMENT OF CYCLIC S-ALLYLTHIOIMIDATES[1]

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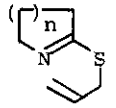
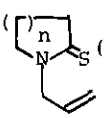
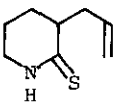
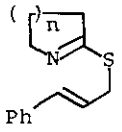
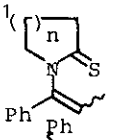
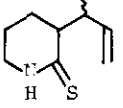
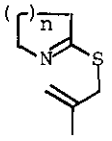
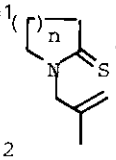
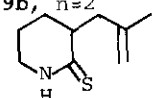
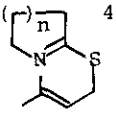
Abstract - Palladium(II)-catalyzed or non-catalyzed thio-Claisen rearrangement of cyclic S-allylthioimidates is described.

The [3,3]-sigmatropic rearrangement is of considerable synthetic utility.[2] There have been many reports on the attempts to improve the usefulness of aliphatic Claisen rearrangement as a tool for organic synthesis by lowering the activation energy using transition metal-catalyzed reaction.[3] In connection with our research on the heterocyclic chemistry using thiolactams,[4] we required a variety of N-allylthiolactams. Yoshida et al. have reported the highly selective S→N allylic rearrangement of S-allylthioimidates using palladium(II) salt as a catalyst.[5] We carried out the thio-Claisen rearrangement of cyclic S-allylthioimidates (**1a-c**) in the presence of 1 mol% of bis(benzonitrile)palladium(II) chloride by refluxing in tetrahydrofuran (THF). Although **1a** and **1c** underwent the S→N allylic to yield N-allyl products (**2a** and **2c**), respectively (Entries 1 and 4), **1b** did the S→C rearrangement to form 3-allylpiperidine-2-thione (**3**) (Entry 2). No trace of N-allyl product (**2b**, n=2) was detected. In addition, Yoshida et al. have reported that the use of harder $Pd(OAc)_2$ instead of $PdCl_2$ resulted in a spectacle change in the ratio of S→C/S→N rearrangement from 81:19 to 4:96 in an acyclic thioimidate.[6,7] Even though $Pd(OAc)_2$ as a catalyst was used, the rearrangement of **1b** furnished only **3**, and **2b** was not isolated (Entry 3). These results prompted us to study the rearrangement of other cyclic S-allylthioimidates.[8]

The S→N rearrangement of S-trans-cinnamylthioimidates (**4a** and **4c**) followed by the isomerization afforded N-vinyl thiolactams (**5a** and **5c**), respectively (Entries 5 and 7). On the other hand, **4b** underwent the S→C rearrangement to produce 3-allylthiolactam (**6**) (Entry 6). In accordance with the previous observations that

Table. Palladium(II)-Catalyzed Rearrangement of Cyclic S-Allylthioimidates[a,b]

Entry	Cyclic S-Allyl-thioimidates	Reaction Times [h]	Products[c]	Yield [%]	mp or bp/ ^{1}H NMR [δ]
1	1a, n=1 	24	**2a**, n=1 	28 (45)[d]	124 °C/9 mmHg
2	**1b**, n=2	43	**3** 	74	74-77 °C 9.60 (1H, br s, NH)
3	**1b**, n=2	40	**3**	66	
4	**1c**, n=3	15	**2c**, n=3	94	83 °C/0.3 mmHg
5	**4a**, n=1 	40	**5a**, n=1 	23 (32)[d]	oil 1.76 (3H, d, J=7.5 Hz, Me) 6.25 (1H, q, J=7.5 Hz, vinyl H)
6	**4b**, n=2	15	**6e** 	58[e] (3)[d]	129-132 °C 9.22 (1H, br s, NH)
7	**4c**, n=3	15	**5c**, n=3	45 (3)[d]	oil 1.79 (3H, d, J=7 Hz, Me)
8	**7a**, n=1 	40	**8a**, n=1 	0 (64)[d]	
9	**7b**, n=2	15	**9b**, n=2 	25 (25)[d]	71-78 °C 1.74 (3H, s, Me) 8.94 (1H, br s, NH)
10	**7c**, n=3	15	**8c**, n=3	8	65 °C/0.4 mmHg
			9c, n=3	8 (13)[d]	105-107 °C 1.73 (3H, s, Me) 9.07 (1H, br s, NH)
11	**10a-c**, n=1,2,3 	48		0[f]	

a All reactions were carried out in the presence of 1 mol% $PdCl_2(PhCN)_2$ by refluxing THF except for Entry 3. In Entry 3, $Pd(OAc)_2$ (5 mol%) as a catalyst was used.

b Although reactions of compounds (**1a-c**, **4b,c**, and **7b,c**) without Pd(II) were carried out under reflux in THF, the rearrangement did not take place.

c All new compounds were fully characterized spectroscopically (IR, ^{1}H NMR, and MS spectra) and combustion or high resolution MS spectra.

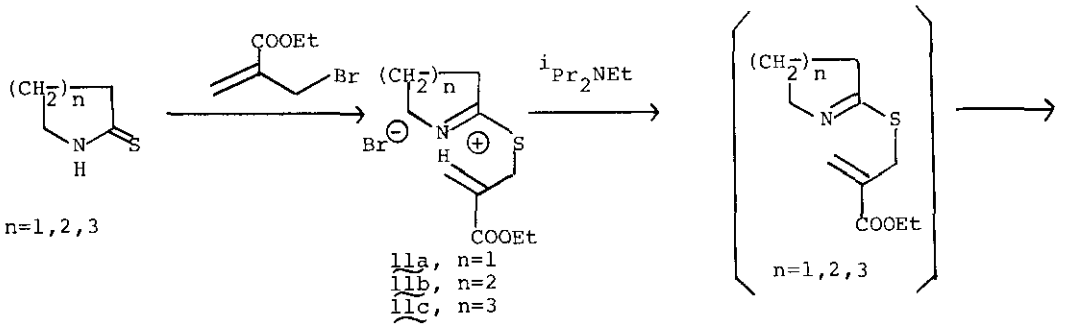
d Yields of the recovery of the starting materials.

e The ratio of erythro:threo is about 1:10 on the basis of ^{1}H NMR spectrum.

f The rearranged products were not detected in ^{1}H NMR spectra.

the rearrangement is related by a substituent (CH_3, Ph, or Cl) at 2-position of the allyl group, S-(2-methyl)allylthioimidates (**7a-c**) were either unreactive (**7a**) or (**7b** and **7c**) rearranged very slowly. The rearrangement of **7b** and **7c** afforded the S→C product (**9b**) and the S→N product (**8c**) together with the S→C product (**9c**), respectively (Entries 9 and 10) in rather low yields. S-(1,1-Dimethyl)-allylthioimidates (**10a-c**) underwent no rearrangement to result in the recovery of the starting materials.

Gompper has reported that the introduction of an electron withdrawing group at the 2-position of the allyl group facilitated the S→N rearrangement via dipolar intermediate.[9] According to the method described, S-allylation of thiolactams with ethyl (α-bromomethyl)acrylate followed by dehydrobromination with Hunig's base at room temperature gave the S→N rearrangement products (**12a-c**) via S-allylthioimidates, respectively. Interestingly, the S→C rearrangement product (**13b**) from **11b** was not isolated. On the other hand, the S→C rearrangement product (**12c**), not obtained by Gompper, was isolated from **11c**.[10]



	Yield	mp or bp		Yield	mp
12a, n=1	59%	38-40 °C	13a, n=1	0%	
12b, n=2	70%	62-65 °C	13b, n=2	0%	
12c, n=3	49%	150-153 °C/0.23 mmHg	13c, n=3	23%	107-109 °C

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) S. J. Rhoads and N. R. Raulins, Org. React., 1975, **22**, 1. b) G. B. Bennet, Synthesis, 1977, 589. c) F. E. Ziegler, Acc. Chem. Res., 1977, **10**, 227.
3. a) R. P. Lutz, Chem. Rev., 1984, **84**, 205. b) L. E. Overman, Angew. Chem. Int. Ed. Engl., 1984, **23**, 579. c) T. G. Schneck and B. Bosnich, J. Am. Chem. Soc., 1985, **107**, 2058.
4. a) H. Takahata, T. Suzuki, and T. Yamazaki, Heterocycles, 1985, **23**, 2213. b) H. Takahata, T. Yamazaki, and K. Aoe, J. Org. Chem., 1985, **50**, 4648. c) H. Takahata, K. Yamabe, T. Suzuki, and T. Yamazaki, Heterocycles, 1986, **24**, 37.
5. Y. Tamaru, M. Kagotani, and Z. Yoshida, J. Org. Chem., 1980, **45**, 5223.
6. Y. Tamaru, M. Kagotani, and Z. Yoshida, Tetrahedron Lett., 1981, **22**, 4245.
7. T. L. Ho, Tetrahedron, 1985, **41**, 3.
8. Thermal thio-Claisen rearrangement of **1c** has been reported. D. S. C. Black, F. W. Eastwood, R. Okraglik, A. J. Poynton, A. M. Wade, and C. H. Welker, Aust. J. Chem., 1972, **25**, 1483.
9. R. Gompper and B. Kohl, Tetrahedron Lett., 1980, **21**, 907.
10. N-Allylthiolactams were prepared as follows. N-Allylation of lactams (allyl halides, pulverized KOH, cat. n-Bu_4NBr, THF) followed by thiation with Lawesson's reagent gave N-allylthiolactams in good yields.

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