THIO-CLAISEN REARRANGEMENT OF TROPONOIDS

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Abstract— Several 2-(allylthio)tropones and 2-(propargylthio)tropones gave 2,3-dihydro-(*8H*)-cyclohepta[*b*]thiophen-8-ones and (*8H*)-cyclohepta[*b*]thiophen-8-ones *via* a *thio*-Claisen rearrangement by heating above 180 °C. In cases of γ-substituted allyl derivatives, the results of rearrangement were poor; 2-(prenylthio)tropone gave isoprene by an elimination, similar to 2-(allyloxy)-tropones, while its 3,5,7-trimethyl homolog caused no reaction.

As a part of studies on thermal reactions of troponoids,[1-3] we have investigated the reaction of 2-(allylthio)tropones in order to compare their chemical properties with 2-(allyloxy)tropones. As described below, they have smoothly undergone the *thio*-Claisen rearrangement.

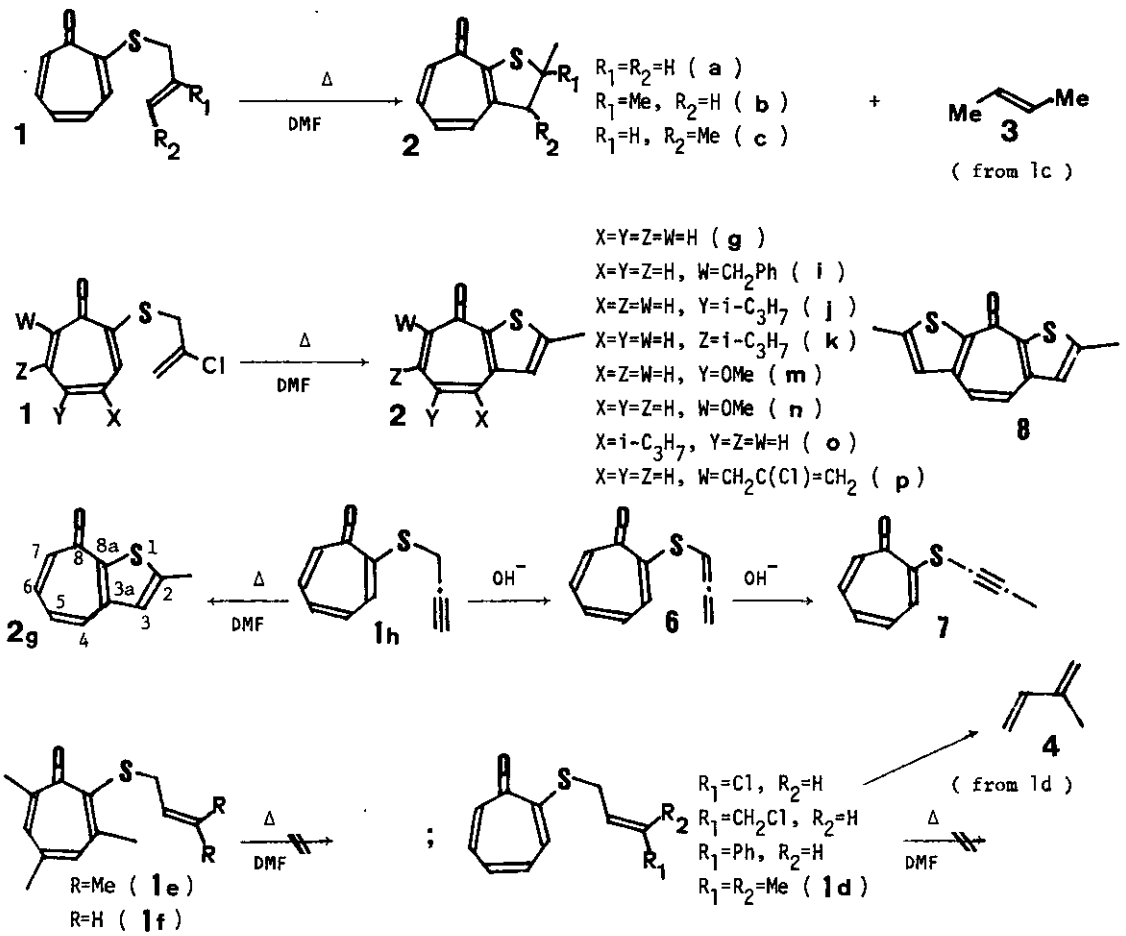
The 2-(allylthio)tropones were conveniently prepared by either base-catalyzed condensation of 2-chlorotropones with appropriate allyl mercaptans or allylation of 2-mercaptotropones with allyl halides.[4]

When 2-(allylthio)tropone(1a, a pale yellow oil)[5] was heated in DMF at 180 °C, a facile reaction has completed within 30 min. Separation of the mixture through a silica-gel column yielded yellow needles, mp 97-98 °C(2a), in 90% yield. Its NMR [δ:[6] 1.44(3H, d, J=7 Hz), 3.04-3.4(1H, br m), 3.5-3.9(2H, m), and 6.6-7.25(4H, m)] was only compatible with that of a dihydrothienotropone, 2-methyl-2,3-dihydro-(*8H*)-cyclohepta[*b*]thiophen-8-one, which should be formed by a cyclization of the *thio*-Claisen rearrangement product. 2-(2-Methyl-2-propenylthio)tropone(1b, a yellow oil) gave 2,2-dimethyl-2,3-dihydro-(*8H*)-cyclohepta[*b*]thiophen-8-one(2b, a yellow oil) in 78% yield.

From both *cis*- and *trans*-2-(2-butenylthio)tropones(1c), the same *cis*-and-*trans*-mixture of 2,3-dimethyl-2,3-dihydro-(*8H*)-cyclohepta[*b*]thiophen-8-ones(2c)[7] was obtained in 10% yield (combined), and at the same time *trans*-2-butene(3) was isolated from the mixture in 10% yield.[8] Although 2-(prenylthio)tropone(1d) has caused the rearrangement upon thermolysis, spontaneous elimination led to a formation of only isoprene(4) in 45% yield; expected 2-mercaptotropone(5)[5] could not survive under the conditions.

On the other hand, 3,5,7-trimethyl-2-(prenylthio)tropone(1e) upon the thermolysis recovered the starting material unchanged. The reaction was also attempted with other allylthiotropones such as 2-(3-chloro-2-propenylthio), 2-(4-chloro-2-butenylthio), 2-(cinnamylthio), and 2-(allylthio)-3,5,7-trimethyl(1f) derivatives, but again no product was obtained; irrespective of the kind of substituent, the γ-

substitution on the allyl moiety seems to prevent the rearrangement.
Nextly, a full-conjugated 2-methyl-(*8H*)-cyclohepta[*b*]thiophen-8-one(2g, colorless prisms, mp 87-88 °C), was prepared from 2-(2-chloro-2-propenylthio)tropone(1g, yellow prisms, mp 76-77 °C) in 79% yield or 2-(propargylthio)tropone(1h, yellow plates, mp 94-96 °C) in 90% yield. However preparation of 1h had a difficulty due to its rapid isomerization with bases to 2-(1,2-propadienylthio)tropone(6, a pale yellow oil)[δ: 5.04(2H, d, J=6 Hz), 5.84(1H, t, J=6 Hz), and 6.88-7.45(5H, m). δ(C): 77.5, 82.4, 128.6, 130.5, 132.6, 135.0, 136.4, 158.3, 182.8, and 212.4], and 2-(1-propynylthio)tropone(7, pale yellow needles, mp 107-108 °C)[δ: 2.15(3H, s), 6.8-7.35(4H, m), 7.80(1H, m). δ(C): 5.5, 65.0, 100.7, 129.3, 131.4, 132.7, 134.7, 136.6, 156.5, and 182.3], which are no longer eligible for the rearrangement. The highest yield of 1h from 5 and propargyl bromide was finally achieved to 88%.



On the other hand, preparation of 1g was straightforward from 5 and 2,3-dichloropropene in 82% yield, so 1g is more convenient precursor for 2g. Its spectroscopic data [λ_{max}^{MeOH} 243 nm(log ε=4.25), 290(4.22), 349 (3.54), 364(3.30). δ:[9] 2.57(3H, d, J=1 Hz), 6.84(1H, ddd, J=11, 8, 1.5 Hz), 6.99(1H, ddd, J=12, 1.5, 1 Hz), 7.03 (1H, q, J=1 Hz), 7.20(1H, ddd, J=12, 8, 1 Hz), and 7.41(1H, dt, J=11, 1 Hz). ν^{KBr}:

1620, 1555, 1458, 1030, 925, 838, and 795 cm^{-1}] were in accord to its structure. Several derivatives of 2g could be synthesized from similar allylthiotropones; *i.e.*, 7-benzyl(1i, a pale yellow oil), 5-isopropyl(1j, pale yellow needles, mp 70-71 °C), 6-isopropyl(1k, a yellow oil), 5-methoxy(1m, yellow leaflets, mp 106-107 °C), and 7-methoxy(1n, colorless needles, mp 123-124 °C) derivatives gave thienotropones, 2i(colorless needles, mp 106-107 °C, 93%), 2j(a colorless oil, 77%), 2k(a colorless oil, 84%), 2m(colorless plates, mp 165-166 °C, 83%), and 2n(colorless needles, mp 123.5-125 °C, 59%). As predicted, the conversion of 2-(2-chloro-2-propenylthio)-4-isopropyltropone(1o, yellow plates, mp 64-66 °C) to 4-isopropyl-2-methyl-(*8H*)-cyclohepta[*b*]thiophen-8-one(2o, a colorless oil) needed more severe (220 °C) conditions than those of others due to a steric hindrance, with an inferior (31%) yield. Their ^{13}C-NMR data are compiled in Table 1.

TABLE 1. ^{13}C-NMR FIGURES OF THE CLAISEN REARRANGEMENT PRODUCTS (2).

Compds: 2a Carbons	2b	2c	2g	2o	2j	2k	2i	2m	2n	8
2	51.0	57.3	57.0	141.5	141.2	142.1	141.0	141.2	141.0	142.4	141.3
3	39.8	50.9	46.6	127.5	123.3	128.5	129.3*	127.1	129.3	128.5	129.7
3a	141.2	141.4	145.4	148.6	147.9	148.3	148.1	148.5	149.0	149.0	148.0
4	131.5	131.8	131.6	132.6	152.3[a]	130.0	131.3	130.7	107.3	126.0*[b]	126.0
5	129.3	129.2	129.6	129.7	126.6	148.0	129.5*	128.9	158.3	125.8*	—
6	135.6*	135.7*	135.5*	135.9	136.0	137.4	156.5	135.0	133.7*	111.8	—
7	135.4*	135.3*	135.4*	134.3	131.8	134.2	131.3	145.8	133.9*	157.9	—
8	180.4	180.4	180.9	180.3	180.4	179.8	179.9	178.9	179.0	173.6	173.3
8a	161.3	161.5	160.0	150.1	151.8	147.6	149.6	150.0	149.0	146.6	143.1
Me	22.0	29.5	22.3 18.8	15.9	16.3	16.0	16.0	16.0	16.0	16.0	16.1

a) Underlined figures are chemical shifts for those carrying the substituent.
b) Asterisked (*) figures may be reversed.

This rearrangement was applicable for a tricyclic dithienotropone synthesis; 2,7-di(2-chloro-2-propenylthio)tropone(1p), prepared from 1m and 2-chloro-2-propenethiol, smoothly afforded, in DMF at 180 °C for 30 min, 2,7-dimethyl-(*9H*)-cyclohepta[*2,1-b;4,5-b'*]dithiophen-9-one(8, colorless granules, mp 211-213 °C), in 88% yield. However, 2,5-di(2-chloro-2-propenylthio)tropone could not be prepared.
It would be not surprising that a literature described an unsuccessful attempt of *thio*-Claisen rearrangement with 1a;[5] the present results are reproducible only in DMF, a polar aprotic solvent. Some results obtained in the reaction with other solvents are shown in Table 2.
Now, we like to point the sharp contrast between the allyloxy and allylthio ethers of 3,5,7-trimethyltropone: By heating, 2-(allyloxy)-3,5,7-trimethyltropone(A)[10] has been reported to cause the rearrangement and further intramolecular Diels-Alder reaction, while 3,5,7-trimethyl-2-(prenyloxy)tropone(B)[3] has shown to give the elimination product, 4, *via* the rearranged intermediate. Thus, in both A and B the Claisen rearrangement was operative, in a contrast, the thio ethers, 1e and 1f, have been recovered unchanged, as mentioned, after heating at 180 °C for 2 h. This

inertness could be explained in terms of a steric hindrance.

TABLE 2. ATTEMPTED THIO-CLAISEN REARRANGEMENT OF DERIVATIVES OF 1 IN VARIOUS SOLVENTS.

Starting Materials	Solvents	Conditions (Temperature, time)	Expected Products	Yields/%
1a	Decalin	180 °C, 60 min	2a	0[a)]
1b	Dioxane	180 °C, 130 min	2b	0[b)]
1a	DMSO	180 °C, 30 min	2a	61
1b	DMSO	180 °C, 30 min	2b	0[a)]
1b	DMSO	140 °C, 180 min	2b	20
1h	DMSO	180 °C, 10 min	2g	0

a) An extensive decomposition of the starting material occurred.
b) No change was observed in respect of NMR spectrometry.

In conclusion, present results on the facile preparation of these novel and fundamental derivatives by the Claisen rearrangement[11] should offer a convenient entry for related non-benzenoid heterocycles.

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6) The NMR spectra were measuren in $CDCl_3$ solutions otherwise stated, and the chemical shifts were expressed in the δ unit from the internal standard, Me_4Si.

7) The stereoisomeric mixture was easily separated by means of a high-pressure liquid chromatography, but in Table 1, only the ^{13}C-NMR data of the major *trans*-component were provided.

8) This unexpected formation of 3 seems to indicate an involvement of a radical process, and detail of which will be a matter of independent investigations. Its identity with authentic sample was confirmed by direct comparisons in respects of glc and spectroscopic data [$\delta^{DMF\text{-}d_7}$: 1.54(6H, d) and 5.57(2H, q). $\delta(C)^{DMF\text{-}d_7}$: 17.9 and 126.2].

9) The H-NMR spectra of all thienotropone derivatives (2) resembled each other, and those figures will be included in a full paper.

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11) Recently, K. Satake, M. Kimura, and S. Morosawa (*Chemistry Lett.*, 145(1983)) reported the synthesis of an *aza*-analog of this thienotropone, 7-chloro-(*8H*)-thieno[*3,2-c*]azepin-8-one. Other than this, previously known related compound is 8-hydroxythieno[*3,2-b*]tropolone (5,8-dihydroxy-(*4H*)-cyclohepta[*b*]thiophen-4-one) synthesized by W. Heyer and W. Treibs (*Ann. Chem.*, 595, 203 (1955)).

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