Tetrahedron Letters, Vol. 33, No. 41, pp. 6131-6134, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

# Syntheses of Ketene Thioselenoacetals and of γ-Unsaturated Se-Alkyl Carboxylic Thionoselenoesters

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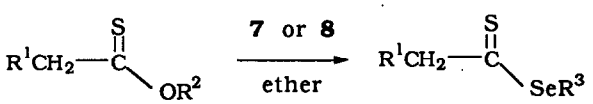
**Abstract:** The alkylation of Se-alkyl carboxylic thionoselenoesters enethiolates stereoselectively leads to ketene thioselenoacetals. When the alkylation is conducted with an allylic halide a thio-Claisen rearrangement is observed.

Dithioesters have proved to be useful reagents in organic synthesis[1]. More particularly, their enethiolates have been used for C-S[2] as well as C-C[3,4] bond formation. In many cases these reactions were found to be stereoselective.

In connection with previous works effected in our group[5] concerning the chemistry of dithioesters, we have recently reported a convenient synthesis of Se-methyl carboxylic thionoselenoesters[6,7] and are now studying their potential in synthesis, especially in comparison with other thiocarbonyl compounds. In this communication, we describe the formation, alkylation and allylation of their enethiolates.

Thionoselenoesters **1-6** (Scheme 1) were prepared by treatment of the corresponding thionoesters with the aluminium reagents **7**[8] or **8**[9] and isolated in good yields[10].




**7** : $Me_2AlSeMe$
**8** : $i\text{-}Bu_2AlSeI\text{-}Bu$

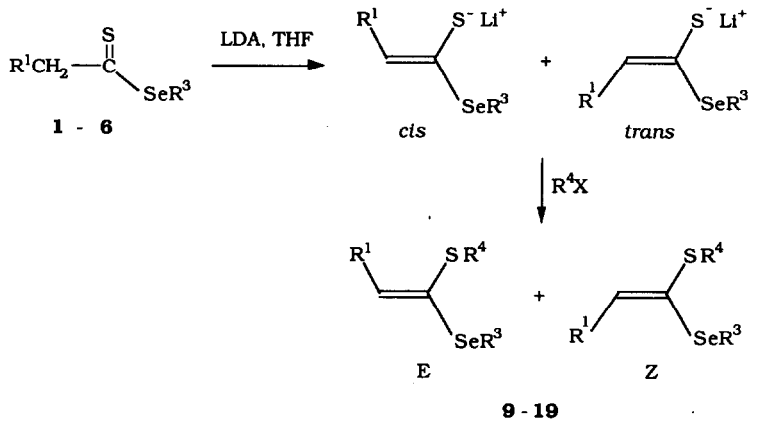
**1 - 6**

| $R^1$ | $R^2$ | $R^3$ | Product | Yield |
|---|---|---|---|---|
| Me | n-Bu | Me | **1** | 61% |
| Me | n-Bu | i-Bu | **2** | 75% |
| Ph | Et | Me | **3** | 94%[6] |
| Ph | Et | i-Bu | **4** | 63% |
| n-Hex | Me | Me | **5** | 98%[6] |
| cyclo-Hex | Me | Me | **6** | 85% |

Scheme 1

As lithium diisopropylamide (LDA) is known to deprotonate many thiocarbonyl compounds under mild conditions, we chose this non-nucleophilic base to enethiolize the thionoselenoesters **1-6** (Scheme 2). Their behaviour follows that of dithioesters. They were deprotonated at low temperature and no C-Se bond cleavage was observed. The reaction was rapidly completed for thioselenopropanoates **1** and **2** but was more difficult for bulkier thioselenoesters such as **3**, **4**, **5** and **6**.

Upon treatment with alkyl halides, the resulting enethiolates were alkylated at the sulfur atom and gave ketene thioselenoacetals **9-19**. In contrast with ketene dithioacetals[11], these are poorly known compounds for which only one synthesis[12] has been proposed before this work. In each case, they were isolated as a mixture of stereoisomers. The ratios were determined by $^1H$ NMR and are reported in Table 1[13].




**1 - 6** **9 - 19**

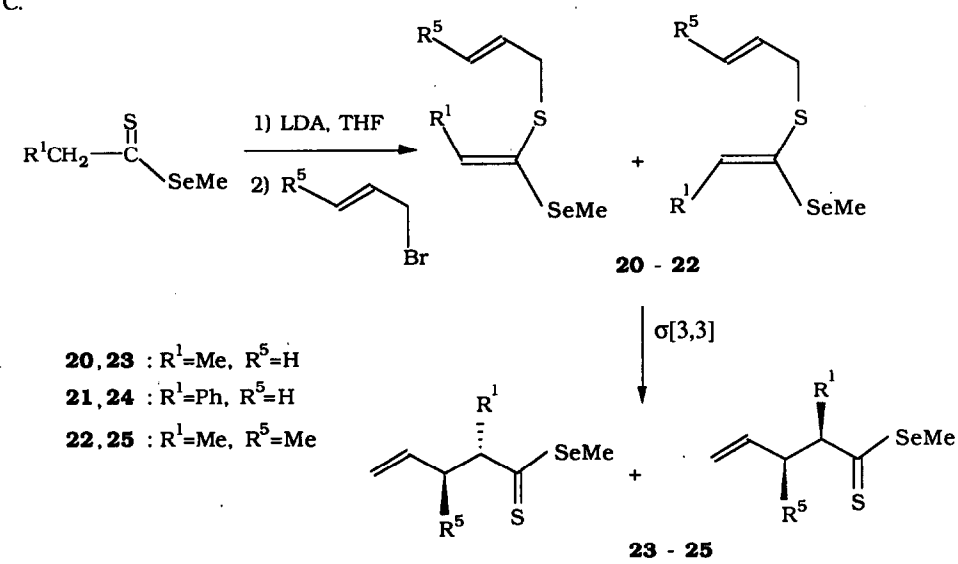
Scheme 2

| starting material | deprotonation conditions | $R^4X$ | Alkylation conditions | Product | Yield% | *E/Z* |
|---|---|---|---|---|---|---|
| **1** | -78°C, 15mn | MeI | -78°C, 1h | **9** | 47 | 85/15 |
| | | EtI | -78 to 0°C, 1h | **10** | 57 | 90/10 |
| | | $PhCH_2Br$ | -78 to -20°C, 18h | **11** | 89 | 92/8 |
| **2** | -78°C, 15mn | MeI | -78°C, 1h | **12** | 59 | 85/15 |
| | | $PhCH_2Br$ | -78 to -20°C, 18h | **13** | 72 | 83/17 |
| **3** | -78°C, 2h | MeI | -78°C, 1h | **14** | 60 | 86/14[13] |
| **4** | -78°C, 2h | MeI | -78°C, 1h | **15** | 58 | 77/23 |
| **5** | -78°C, 2h | MeI | -78°C, 1h | **16** | 60 | 67/33[13] |
| | | EtI | -78 to 0°C, 1h | **17** | 95 | 93/7 |
| | | $PhCH_2Br$ | -78 to -20°C, 18h | **18** | 77 | 95/5 |
| **6** | -20°C, 3h | EtI | -78 to 0°C, 1h | **19** | 63 | 80/20[13] |

Table 1

This synthesis is stereoselective, with stereoselectivities varying from 67/33 to 95/5. Most thiocarbonyl compounds are known to give mainly *cis* enethiolates. This is also probably the case for thionoselenoesters **1-6**, and as the S-alkylation does not alter the configuration of the enethiolates[3], the major ketene S,Se-acetal must be of *E* configuration. It is noteworthy that the stereoselectivity of the deprotonation of **1** is higher than that of corresponding dithioesters in the same conditions (*cis/trans* : 81/19 for $EtCS_2i\text{-}Pr$)[3].

When the alkylating agent is an allylic halide, the obtained ketene S,Se-acetal can be expected to undergo a thio-Claisen rearrangement (Scheme 3)[14]. This is indeed the case. The ketene S,Se-acetal **20**, a non-isolable compound, rearranged to the thioselenoester **23** at room temperature (yield 65%). For compounds **21** and **22** the rearrangement was slow at 20°C but was completed after heating for three hours in refluxing $CCl_4$. To our knowledge, **23, 24** (yield 71%) and **25** (78%) are the first synthesized thionoselenoesters bearing a C=C double bond[6,7]. They are stable and can be stored for at least some weeks at -18°C.




Scheme 3

Compound **25** was obtained as a 80/20 mixture of isomers. The major one was attributed an *anti* structure by comparison of its $^1H$ NMR spectrum with that of the corresponding known dithioesters[4,15]. As it is established that the thio-Claisen rearrangement (a [3,3] sygmatropic process) occurs stereospecifically[16] *via* a six membered chair-like transition state, the stereochemistry of the starting material can be deduced from the geometry of the final products. In our case, formation of *anti* **25** must occur from the *E,E* precursor **22**. This is a proof for the major *cis* structure of the enethiolate derived from the thionoselenoester **1**, and therefore a clear confirmation of the *E* geometry of the ketene S,Se-acetals **9-11**.

We expect that ketene thioselenoacetals and carboxylic thionoesters will advantageously replace dithioacetals and dithioesters in some of their applications, especially by making use of the particular reactivity of the C-Se bond[17].

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9 A 1M solution of **8** was obtained by refluxing commercially available i-$Bu_3Al$ with 1 eq. of selenium in toluene for 2h.
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13 $^1H$ NMR spectra were recorded on a JEOL apparatus (270 MHz). For instance: **14*E***: $^1H$ NMR ($CDCl_3$): 2.30 (s, 3H), 2.33 (s, 3H), 7.03 (s, 1H), 7.2-7.6 (m, 5 aromatic H). **14*Z***: 2.21 (s, 3H), 2.41 (s, 3H), 6.86 (s, 1H), aromatic H masked by those of the E isomer. As in some cases an equilibration was obseved in $CDCl_3$, the spectra must be recorded as soon as possible after the isolation of the products. For example: **19**, after extraction: 80/20, 15 days after: 40/60. This isomerization can explain the abnormally low ratio for compound **16**.
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15 **25:** 2 Me groups ($R^1$ and $R^5$) *anti* 0.99, 1.26 *syn*: 1.07, 1.30 ppm
corresponding dithioester[4] *anti* 0.96, 1.20 *syn*: 1.03, 1.28 ppm
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(Received in France 10 July 1992)