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A new example of dynamic kinetic resolution: aminolysis of α-sulfinyl γ-unsaturated dithioesters

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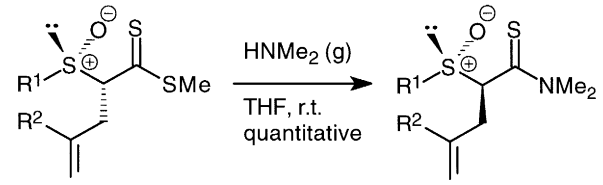
Abstract

The aminolysis of (2*S**,S*S**)-dithioesters **1a**–**d** by dimethylamine proceeded under dynamic kinetic control, affording (2*R**,S*S**)-thioamides **2a**–**d** with reverse configuration at the asymmetric carbon centre. © 2000 Elsevier Science Ltd. All rights reserved.

Kinetic resolution is an efficient method to prepare stereochemically pure compounds[1] but the maximum available yield is 50%. However, if the reacting isomers are able to undergo rapid interconversion, then higher yields can be obtained. Such a process of dynamic kinetic resolution[2] is not commonly encountered and we wish to report here a new example.

We recently developed a new asymmetric version of the Claisen rearrangement affording α-sulfinyl γ-unsaturated dithioesters with high diastereoselectivity (de up to 99%) in the racemic series.[3] With the aim of exploiting these products, we examined their transformation into the corresponding thioamides.

Thioacylation of amines by dithioesters is very easy in contrast to their acylation with esters.[4] The aminolysis of (2*S**,S*S**)-dithioesters **1a**–**d** was carried out at room temperature, in THF, by bubbling dimethylamine. After a reaction time of only 5 min, thioamides **2a**–**d** were quantitatively obtained (Scheme 1).



(2*S**,S*S**)-**1a–d** (2*R**,S*S**)-**2a–d**

Scheme 1.

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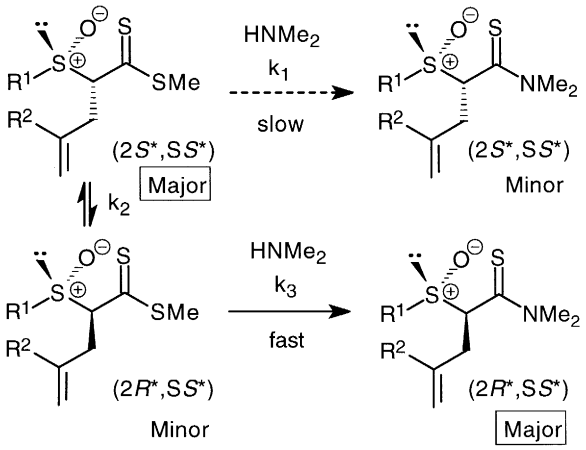
We were surprised to observe an inversion of configuration at the carbon asymmetric centre. Indeed, the (2*S**)/(2*R**) ratio of the resulting thioamides **2a**–**d** ranged from 17:83 to 5:95 while that of the starting dithioesters **1a**–**d** ranged from 80:20 to 99:1 (Table 1). The diastereomeric ratio of **2** was analysed by integration of the signals of the diastereomeric protons. The assignment of the (2*R**,S*S**) configuration to the major isomers of **2a**–**d** was based on a reference sample[5] of enantiopure (2*S*,S*S*)-**2d** and on the observation of similar trends in ^{1}H NMR spectra.[6] Importantly, we had previously shown that the aminolysis of α-sulfinyl dithioacetates proceeded with retention of configuration at sulfur.[7]

Table 1
Aminolysis of dithioesters **1a**–**d**

1	R^1	R^2	(2*S**) / (2*R**)	**2**	(2*S**) / (2*R**)
1a	Me	H	80:20	**2a**	5:95
1b	Me	Me	83:17	**2b**	8:92
1c	*i*Pr	H	99:1	**2c**	14:86
1d	Cy	H	88:12	**2d**	17:83

We checked that thioamides **2a**–**d** did not undergo any epimerisation in the reaction conditions. So the reversal of configuration at carbon was rationalised by suggesting that dithioesters **1a**–**d** underwent rapid equilibration and that the (2*R**,S*S**)-isomers reacted faster than the (2*S**,S*S**)-isomers ($k_3 > k_1$), resulting in the preferential formation of thioamides **2a**–**d** of (2*R**,S*S**) configuration (Scheme 2).



Scheme 2.

In summary, the (2*R**,S*S**)-isomers of thioamides **2a**–**d** were selectively obtained from the aminolysis of (2*S**,S*S**)-dithioesters **1a**–**d** with dimethylamine, under dynamic kinetic control (de up to 90%) while they are the minor isomeric products of the Claisen rearrangement of *S*-allyl aminoketene acetals bearing a vinylic alkylsulfinyl group as chiral auxiliary.[8] So we now have in hand methods for the selective preparation of both diastereomers of thioamides **2**. The synthesis of enantiomerically enriched compounds via the Claisen rearrangement route is in progress.

Acknowledgements

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5. (2*S*,*SS*)-**2d** resulted from the Claisen rearrangement of an enantiopure *S*-allyl aminoketene acetal. Its configuration was assigned according to X-ray diffraction analysis.
6. The signal of the diastereomeric proton of the major isomer of compounds **2** was shifted downfield relative to that of the minor isomer.
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