

Diastereoselective Asymmetric Induction in the Thio-Claisen Rearrangement Over Zeolites.

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Abstract : S-Allyl γ -hydroxy ketene dithioacetals [**1a-1e**] underwent a rapid and diastereoselective thio-Claisen rearrangement into *anti* α -allyl β -hydroxy dithioesters [**2a-2e**] over various zeolites at room temperature in hexane is described. © 1997 Elsevier Science Ltd.

Thio-Claisen rearrangements have been extensively studied in the past under various conditions but not received as much attention as normal Claisen rearrangements.¹ Recently a new Claisen protocol, dealing with the highly diastereoselective thio-Claisen rearrangement of S-allyl ketene dithioacetals and S-methylallyl N-nitro thioacetyl pyrrolidine were reported.^{2,3} Achieving stereocontrol in the construction of acyclic systems is a challenging goal in organic synthesis.⁴ Even though there have been several reports on asymmetric induction in [3,3] sigmatropic rearrangement,⁵ no report is available in the literature in which a zeolite is employed either to promote the thio-Claisen rearrangement or for the chiral induction. The unique characteristics of zeolites such as shape selectivity, thermal stability, acidic and basic properties coupled with the ease of operation have made the interface of organic synthesis and zeolite catalysis an important research area.⁶ In this communication we wish to report the synthetic utility of zeolites (Y, EMT, ZSM-5 and Zeolite beta) as a versatile catalyst for diastereoselective thio-Claisen rearrangement of various S-allyl γ -hydroxy ketene dithioacetals.

The S-allyl γ -hydroxy ketene dithioacetals [**1a-1e**] were prepared from the corresponding β -hydroxy dithioester by treatment with LDA and allyl bromide at -78 °C and the zeolites were synthesized as reported elsewhere.^{2,7} The reaction on HY-Zeolite was optimized with respect to temperature, reaction time and catalyst to substrate ratio. HPLC was performed with a UV (254 nm) detector on a Beckman HPLC pump and a 40 mm x 25 cm silica column (Merck SI 60, 5 μ). Prior to use, zeolites were calcined at 500 °C for 5 h in presence of air.

All S-allyl γ -hydroxy ketene dithioacetals [**1a-1e**] underwent rapid and diastereoselective thio-Claisen rearrangement into *anti* α -allyl β -hydroxy dithioesters [**2a-2e**] in good yield over various zeolites at room temperature in hexane (Scheme 1). The mixture of [**1a**] (0.1 g) and HY-Zeolite (1 g) was stirred in a round bottom flask at room temperature for 2 h in 125 ml of dry hexane under nitrogen pressure, after which it was filtered. The hexane filtrate did not contain any dissolved matter. The products trapped inside the pores of zeolite

were extracted out with methanol (3 x 50 ml). Evaporation of methanol furnished the crude product and was further purified by HPLC using ethyl acetate / n-heptane (95 : 5) furnished *anti* α -allyl β -hydroxy dithioester as only product in 88% yield. Diastereoisomer configuration were deduced from HPLC comparison with a *syn*- rich mixture of the same diastereoisomers prepared by a *syn*- stereospecific aldol condensation of methyl pent-4-enedithioate with the requisite aldehydes. Assignment of the *anti*-configuration to [2a] were confirmed by chemical conversion of the [2a] into the known *syn*- and *anti* -ethyl 2-allyl-3-hydroxybutanoates and by coupling constant measurements [$J_{2,3}$ (*syn*) 4.85 Hz and $J_{2,3}$ (*anti*) 5.35 Hz].⁸ Table 1 summarizes the results obtained with HEMT, HZSM-5 and HZeolite beta. The compounds [1b-1e] were also underwent thio-Claisen rearrangement in presence of various zeolites to [2b-2e] and the results are listed in Table 1.

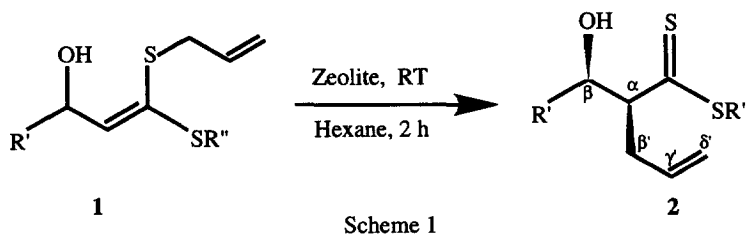


Table 1. Thio-Claisen rearrangement of γ -hydroxy ketene dithioacetals [1a-1e] over different zeolites

| Entry | Substrates | R' | R'' | Products | Yield ^a | | | | |
|-------|------------|--------|-----|----------|--------------------|------|---------------|--------|------------------------|
| | | | | | HY-Zeolite | HEMT | HZeolite beta | HZSM-5 | uncatalysed |
| 1 | 1a | Me | Me | 2a | 88 | 81 | 78 | 84 | 68 (11:1) ^b |
| 2 | 1b | Et | Me | 2b | 84 | 76 | 72 | 68 | 47 (14:1) ^b |
| 3 | 1c | Pr | Me | 2c | 78 | 69 | 64 | 70 | 49 (15:1) ^b |
| 4 | 1d | t-But. | Me | 2d | 83 | 71 | 57 | 80 | 40 (19:1) ^b |
| 5 | 1e | Ph | Me | 2e | 76 | 61 | 55 | 65 | 38 (8:1) ^b |

^a Isolated pure products. ^b *Syn* : *Anti* ratio.

The uncatalysed thio-Claisen rearrangement of [1a-1e] were performed by stirring a solution of S-allyl γ -hydroxy ketene dithioacetals (0.05 g) in dry hexane (50 ml) at room temperature. The progress of the reaction was monitored by HPLC. After 3 days, the reaction mixture was analysed by HPLC and it was found that the distribution of two diastereoisomeric α -allyl β -hydroxy dithioesters with a *syn* : *anti* ratio varying in the range 8 : 1 to 19: 1.⁹⁻¹¹ The results are summarized in Table 1.

In uncatalysed thio-Claisen rearrangement of [1a-1e] the major product is *syn* isomer. Whereas in zeolite mediated rearrangement *anti* isomer is the only product (HPLC chromatogram shows only the peak corresponding to the *anti* isomer). The S-allyl γ -hydroxy ketene dithioacetals can be adsorbed comfortably inside the channels of zeolites in such a way that the bulky groups are away from the catalytic surface. The diastereoselectivity of this rearrangement over zeolites could be due to the transition state model as shown in Fig.1.

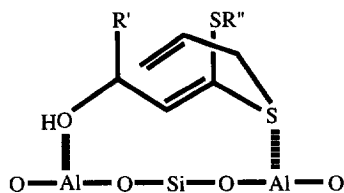


Fig. 1 The transition state model for thio-Claisen rearrangement over zeolites.

It is worth noting the facile and highly diastereoselective occurrence of the thio-Claisen rearrangement S-allyl γ -hydroxy ketene dithioacetals catalysed by zeolites. The easy separation of a solid catalyst from the reaction mixture is one of the main advantages offered by heterogeneous catalysts and an essential prerequisite for their regeneration. Presently described protocol for thio-Claisen rearrangement is advantageous in view of high yield of diastereomerically pure *anti* α -allyl β -hydroxy dithioester, mild reaction conditions, the ease of work up and regeneration of the catalyst.

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9. **2a(Anti)** : $^1\text{H NMR}$: 1.20 (d, 3H), 2.60 (s, 3H), 2.31-2.76 (m, 3H), 3.12 (m, 1H), 3.89 (m, 1H) and 4.75- 5.84 (m, 3H). $^{13}\text{C NMR}$: 19.45 (SCH_3), 21.32 (CH_3), 38.49 (C_β), 66.68 (C_α), 70.25 (C_β),

- 117.20 (C_{β}), 134.90 (C_{γ}) and 241.57 (C=S). Anal. calculated for $C_8H_{14}OS_2$: C = 50.49; H = 7.40 and S = 33.68. Found: C = 50.45; H = 7.51 and S = 33.16. **2a(Syn)**: $^1\text{HNMR}$: 1.12 (d, 3H), 2.51 (s, 3H), 2.38-2.68 (m, 3H), 3.06 (m, 1H), 3.94 (m, 1H) and 4.72- 5.78 (m, 3H). $^{13}\text{CNMR}$: 19.24 (SCH₃), 21.10 (CH₃), 36.12 (C_{β}), 67.22 (C_{α}), 71.04 (C_{β}), 116.64 (C_{δ}), 135.62 (C_{γ}) and 241.74 (C=S).
- 2b(Anti)**: $^1\text{HNMR}$: 0.9 (t, 3H), 1.36 (m, 2H), 2.61 (s, 3H), 2.42- 2.81 (m, 3H), 3.21 (m, 1H), 3.71 (m, 1H) and 4.79-5.92 (m, 3H). $^{13}\text{CNMR}$: 10.50 (CH₃), 19.46 (SCH₃), 28.41 (C_{γ}), 38.93 (C_{β}), 65.35 (C_{α}), 76.21 (C_{β}), 117.28 (C_{δ}), 135.01 (C_{γ}) and 241.93 (C=S). Anal. calculated for $C_9H_{16}OS_2$: C = 52.85; H = 7.89 and S = 31.38. Found: C = 52.83; H = 7.87 and S = 31.28. **2b(Syn)**: $^1\text{HNMR}$: 0.89 (t, 3H), 1.42 (m, 2H), 2.57 (s, 3H), 2.61- 2.86 (m, 3H), 3.16 (m, 1H), 3.64 (m, 1H) and 4.74-6.05 (m, 3H). $^{13}\text{CNMR}$: 10.34 (CH₃), 20.18 (SCH₃), 27.72 (C_{γ}), 36.18 (C_{β}), 66.42 (C_{α}), 75.48 (C_{β}), 116.98 (C_{δ}), 135.46 (C_{γ}) and 242.36 (C=S).
10. **2c(Anti)**: $^1\text{HNMR}$: 0.86 (t, 3H), 1.22-1.59 (m, 4H), 2.63 (s, 3H), 2.46-2.82 (m, 2H), 2.94 (br.s, 1H), 2.95-3.18 (m, 1H), 3.75 (m, 1H) and 4.73-6.04 (m, 3H). $^{13}\text{CNMR}$: 13.89 (CH₃), 19.31, 19.45, 37.62, 38.85, 64.95 (C_{α}), 73.82 (C_{β}), 117.24 (C_{δ}), 135.02 (C_{γ}) and 242.0 (C=S). Anal. calculated for $C_{10}H_{18}OS_2$: C = 55.00; H = 8.30 and S = 29.34. Found: C = 54.92; H = 8.46 and S = 29.31. **2c(Syn)**: $^1\text{HNMR}$: 0.89 (t, 3H), 1.19-1.54 (m, 4H), 2.56 (s, 3H), 2.37-2.72 (m, 2H), 2.90-3.24 (m, 1H), 3.69 (m, 1H) and 4.92-6.0 (m, 3H). $^{13}\text{CNMR}$: 12.66 (CH₃), 19.14, 19.25, 36.40, 38.48, 66.26 (C_{α}), 74.42 (C_{β}), 116.56 (C_{δ}), 136.51 (C_{γ}) and 241.36 (C=S). **2d(Anti)**: $^1\text{HNMR}$: 1.01 (s, 9H), 2.62 (s, 3H), 2.51-2.74 (m, 2H), 2.86 (br.s, 1H), 3.34-3.55 (m, 2H) and 4.74-5.82 (m, 3H). $^{13}\text{CNMR}$: 19.48 (SCH₃), 26.94 (3 CH₃), 36.32, 37.20, 62.08 (C_{α}), 82.05 (C_{β}), 117.40 (C_{δ}), 136.38 (C_{γ}) and 242.62 (C=S). Anal. calculated for $C_{11}H_{20}OS_2$: C = 56.85; H = 8.68 and S = 27.60. Found: C = 56.65; H = 8.64 and S = 26.89. **2d(Syn)**: $^1\text{HNMR}$: 0.93 (s, 9H), 2.58 (s, 3H), 2.47-2.81 (m, 3H), 3.40-3.58 (m, 2H) and 4.79-5.86 (m, 3H). $^{13}\text{CNMR}$: 19.32 (SCH₃), 26.98 (3 CH₃), 36.25, 36.94, 61.22 (C_{α}), 81.64 (C_{β}), 116.86 (C_{δ}), 135.84 (C_{γ}) and 241.92 (C=S).
11. **2e(Anti)**: $^1\text{HNMR}$: 2.04-2.42 (m, 2H), 2.48 (s, 3H), 2.94 (br.s, 1H), 3.25-3.78 (m, 1H), 4.63-5.91 (m, 4H) and 7.18 (m, 5H). $^{13}\text{CNMR}$: 19.68 (SCH₃), 38.70 (C_{β}), 66.78 (C_{α}), 77.61 (C_{β}), 117.40 (C_{δ}), 126.28, 127.98, 128.50 (C_6H_5), 134.44 (C_{γ}), 141.48 (C_6H_5), and 241.06 (C=S). Anal. calculated for $C_{13}H_{16}OS_2$: C = 61.8; H = 6.41 and S = 25.43. Found: C = 61.94; H = 6.32 and S = 25.21. **2e(Syn)**: $^1\text{HNMR}$: 2.47 (s, 3H), 2.50-2.74 (m, 2H), 3.02 (br.s, 1H), 3.47-3.65 (m, 1H), 4.81-5.88 (m, 4H) and 7.24 (m, 5H). $^{13}\text{CNMR}$: 19.42 (SCH₃), 35.85 (C_{β}), 67.02 (C_{α}), 76.36 (C_{β}), 116.93 (C_{δ}), 126.127.72, 128.26 (C_6H_5), 135.26 (C_{γ}), 141.46 (C_6H_5), and 241.75 (C=S).

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