

ON THE STEREOSELECTIVITY OF THE α -ALKYLATION OF
 β -HYDROXY ESTERS. ENANTIOSELECTIVE SYNTHESIS OF
4,4- AND 6,6-DISUBSTITUTED CYCLOHEX-2-EN-1-ONES.

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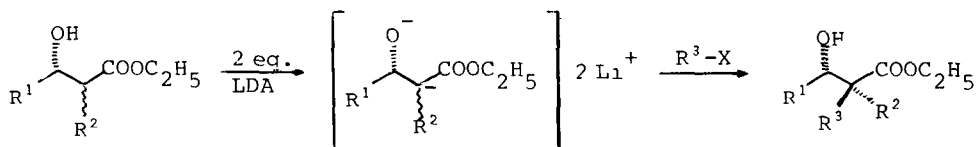
SUMMARY

Stereoselective α -alkylation of the optically active β -hydroxyester 1 gives rise to 2, which was converted to the 1,5-diketone 4. Regioselective aldolcondensation of the latter furnished (S)-5 and (S)-6 respectively, each with an e.e. of 86%.

Recent work of Terashima et al.¹ and Kreiser et al.², respectively, concerning the regioselective aldolcondensation of 1,5-diketones, brings us about to present some of our results.

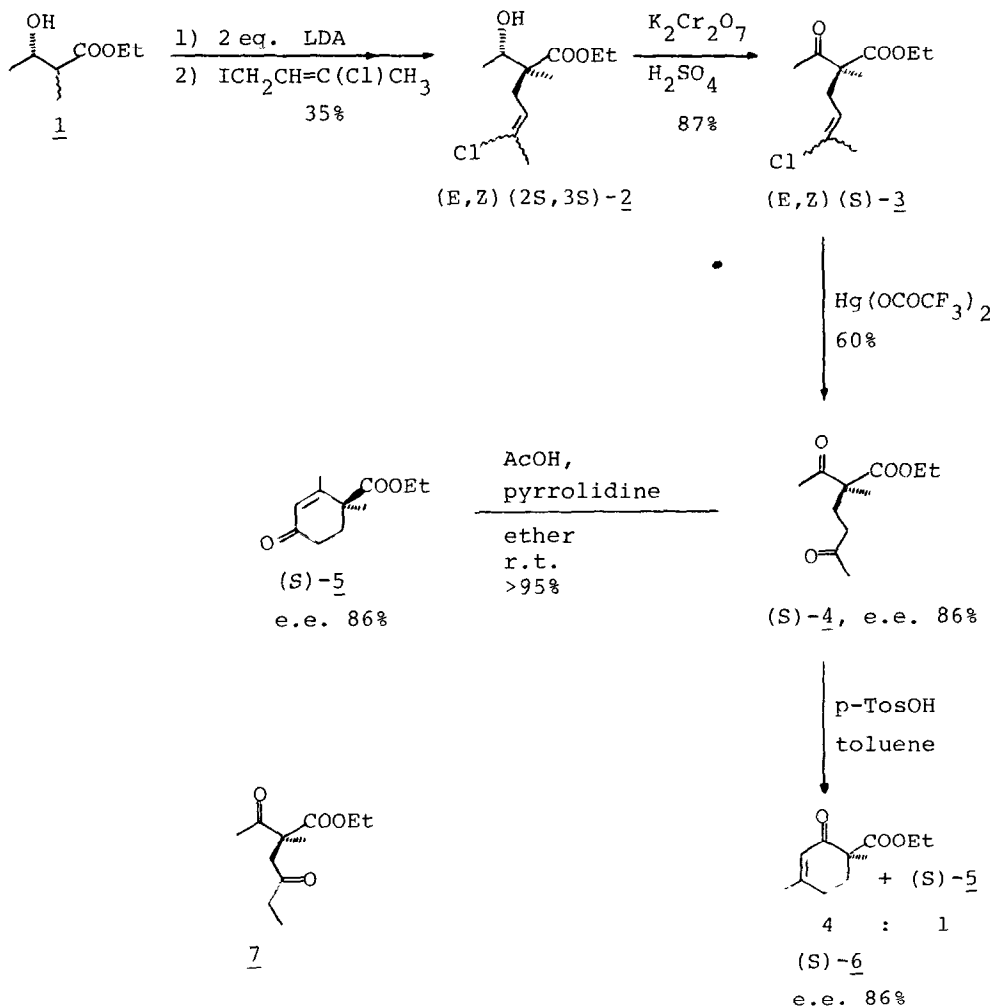
Earlier we have shown³ that the α -alkylation of dianions derived from β -hydroxyesters furnished the threo-product with about 94 : 6 stereoselectivity (scheme 1). This new stereoselective reaction (see also ref.^{4,5}) was found to be useful in the synthesis of a pheromone of *Scolytus multistriatus*⁶ and operative also in the alkylation of ethyl-2-hydroxy-cyclohexanecarboxylate⁷.

Scheme 1



Now, as a synthetically important extension, we alkylated a mixture of (2R,3S)- and (2S,3S)-ethyl-3-hydroxy-2-methylbutyrate (1)³ with (E,Z)-3-chlorobut-2-enyliodide under the conditions of ref.³. This reaction furnished (E,Z)-2 in moderate yield (35%) with about 94% stereoselectivity (scheme 2). This product was oxidized to (2S)-3 (90% E-, 10% Z-isomer; $[\alpha]_D^{22}$ (CHCl₃, c=1,24) = -27,8°) and the latter converted to (S)-4 ($[\alpha]_D^{22}$ (CHCl₃, c=1,29) = -8,3°) accor-

Scheme 2



ding to the method of Yoshioka et al.¹⁰. Under this conditions (1,5 eq. Hg(OCOCF₃)₂ in nitromethane, 45 h at 20°C, then 10% HCl) beside (S)-4 (60%) also (S)-6 (10%) and 7 (2,5%) could be isolated. Compound (S)-4 exhibited an e.e. of ca. 86%¹¹.

Treatment of (S)-4 in ether with equivalent amounts of acetic acid andpyrrolidine at room temperature for 20 hours furnished (S)-5 ($[\alpha]_D^{22}$ (benzene, c=1,32)=-116°, e.e. 86%¹¹) in essentially quantitative yield. Treatment of (S)-4, however, in toluene with catalytic amounts of p-TosOH at 110°C for 25' gave a 4 : 1 mixture of (S)-6 ($[\alpha]_D^{22}$ (benzene, c=1,07)=+44°, e.e. 86%¹¹) and (S)-5 respectively in 75% yield¹².

NMR-data (360 MHz, CDCl₃, in ppm). (E,Z)(2S,3S)-2 (main isomer): 5,37 (txq; 1H), 4,18 (q, 2H), 3,99 (dxq, 1H), 2,65 (d, OH), 2,6 - 2,4 (AB-m, 2H), 2,1 (m, 3H), 1,28 (t, 3H), 1,16 (d, 3H), 1,14 (s, 3H). (E,Z)(S)-3: 5,33 (txq, 1H), 4,2 (q, 2H), 2,72 (dxq, 2H), 2,16 (s, 3H), 2,09 (m, 3H), 1,35 (s, 3H), 1,26 (t, 3H). (S)-4: 4,23 - 4,16 (m, 2H), 2,45 - 2,39 (m, 2H), 2,16 (s, 3H), 2,14 (s, 3H), 2,15 - 2,0 (m, 2H), 1,34 (s, 3H), 1,27 (t, 3H). (S)-5: 5,92 (q, 1H), 4,2 (q, 2H), 2,53 - 2,38 (m, 3H), 1,96 (d, 3H), 2,0 - 1,9 (m, 1H), 1,43 (s, 3H), 1,28 (t, 3H). (S)-6: 5,9 (q, 1H), 4,15 (q, 2H), 2,51 - 2,38 (m, 2H), 2,3 - 2,2 (m, 1H), 1,95 (m, 3H), 1,91 - 1,83 (m, 1H), 1,47 (s, 3H), 1,23 (t, 3H).

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References and Notes

- ¹ S. Terashima, S. Sato & K. Koga, *Tetrahedron Letters*, 3469 (1979)
- ² W. Kreiser & P. Below, accompanying paper
- ³ Gy. Fráter, *Helv.Chim.Acta*, 62, 2825 (1979)
- ⁴ G.A. Kraus & M.J. Traschnew, *Tetrahedron Letters*, 1977, 4575
- ⁵ D. Seebach & D. Wasmuth, *Helv.Chim.Acta*, 63, 197 (1980)
- ⁶ Gy. Fráter, *Helv.Chim.Acta*, 62, 2829 (1979)
- ⁷ Gy. Fráter, *Helv.Chim.Acta*, 63, 1383 (1980)
- ⁸ All compounds gave correct elemental analysis and showed the expected analytical data (NMR IR)
- ⁹ The absolute configuration was assigned on hand of the proven direction of alkylation ^{3, 6, 7}
- ¹⁰ H. Yoshioka, K. Takasaki, M. Kobayashi & R. Matsumoto, *Tetrahedron Letters*, 1979, 3489
- ¹¹ NMR spectra in the presence of $\text{Eu}(\text{tfc})_3$
- ¹² The structures of (S)-5 and (S)-6 were assigned based on the ¹H-NMR-spectra (360 MHz): in (S)-5 $\text{CH}_3\text{-C}(3)$ is a sharp d, whereas in (S)-6 it is a dxt, due to $J(\text{CH}_3\text{-C}(3), \text{CH}_2(4)) \sim 1\text{Hz}$

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