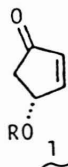


A New Method for the Synthesis of Protected Chiral
4-Hydroxy-2-cyclopentenone

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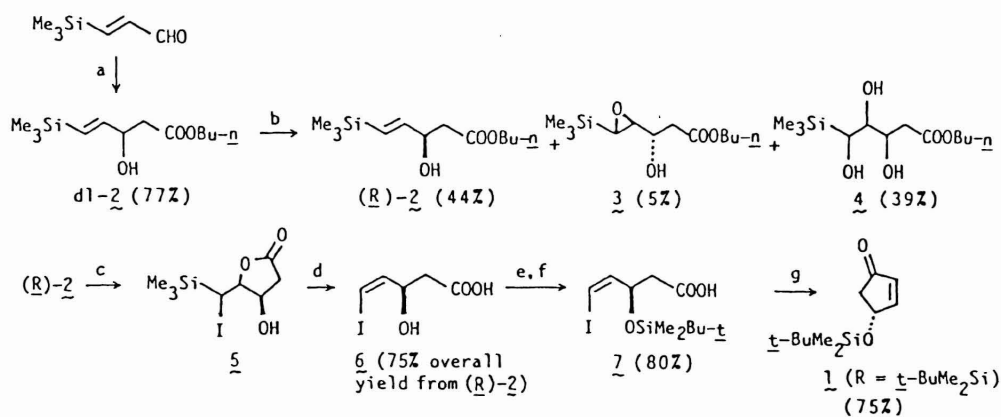
A new method for the synthesis of (*R*)-4-*t*-butyldimethylsiloxy-2-cyclopentenone (**1**, R = *t*-BuMe₂Si) has been developed which involves the effective preparation of the chiral (*Z*)- γ -iodo allylic alcohol and its conversion into **1** via cycliacylation reaction.

Protected 4-hydroxy-2-cyclopentenone with *R*-configuration (**1**) serves as a key building block for the synthesis of prostaglandins via three component coupling process,¹⁾ and thus its enantioselective synthesis has attracted much interest in recent years.²⁾ Herein we report a new method for the synthesis



of **1** (R = *t*-BuMe₂Si). Our procedure illustrated in Scheme 1 involves the preparation of the chiral (*Z*)- γ -iodo allylic alcohol **6** using the Sharpless kinetic resolution of the corresponding racemic (*E*)- γ -trimethylsilyl allylic alcohol **2** as a key step,³⁾ and its conversion into **1** according to the procedure developed by Negishi.⁴⁾

The starting alcohol dl-**2** can be readily prepared in 77% yield by the reaction of the lithium enolate derived from butyl acetate with (*E*)-3-trimethylsilyl-2-propenal.⁵⁾ Kinetic resolution of dl-**2** using *t*-butyl hydroperoxide (TBHP) (1.5 equiv.), L-(+)-diisopropyl tartrate (L-(+)-DIPT) (1.8 equiv.), and Ti(O-*i*-Pr)₄ (1.5 equiv.) in CH₂Cl₂ at -20 °C for 18 h followed by usual work-up (10% aqueous tartaric acid) afforded (*R*)-**2** (>99% ee,⁶⁾ [α]_D²⁵ +6.13° (c 1.63, CHCl₃), epoxy alcohol **3** and triol **4**⁷⁾ in 44%, 5% and 39% yield, respectively.⁸⁾ Noteworthy here is that most of the epoxy alcohol **3** was changed into the very polar triol **4** under this reaction conditions, thus making (*R*)-**2** easily isolable. Hydrolysis of (*R*)-**2** with 3 M NaOH (THF-Et₂O-MeOH (2:2:1), room temperature, 12 h) followed by the iodolactonization with saturated aqueous NaHCO₃ and I₂ (0 °C, 1 h)⁹⁾ afforded γ -lactone **5** as a diastereomeric mixture. The lactone **5** thus prepared was converted into (*Z*)-vinyl iodide **6** by treatment with *n*-Bu₄NF in



a, $\text{CH}_3\text{COOBu-n}$, $\text{LiN}(\text{i-Pr})_2$, THF; b, TBHP, $\text{Ti}(\text{O-i-Pr})_4$, L-(+)-DIPT, CH_2Cl_2 ; c, 3 mol dm^{-3} NaOH, THF-Et₂O-MeOH then I₂, aq NaHCO₃; d, n-Bu₄NF, THF; e, t-BuMe₂SiCl, imidazole, DMF; f, K₂CO₃, MeOH-THF-H₂O; g, MeLi then t-BuLi, Et₂O.

Scheme 1.

THF (75% yield from (R)-2).¹⁰ Silylation of 6 with excess t-BuMe₂SiCl (3 equiv.) in DMF followed by selective deprotection of the ester group with K₂CO₃ in MeOH-THF-H₂O (3:1:1)¹¹ furnished 7 in 80% yield. Finally, the cyclization reaction of 7 to 1 (R = t-BuMe₂Si) was carried out by treatment with 1 equiv. of MeLi and then with 2 equiv. of t-BuLi at -78 °C in Et₂O (75% yield).⁴ The ¹H NMR spectrum, mp and optical rotation of 1 (R = t-BuMe₂Si) thus obtained were in good agreement with the literature values (mp 28.5-29.5 °C; $[\alpha]_D^{21} +67.3^\circ$ (c 0.82, MeOH). lit. mp 29 °C,^{2a}) 30-31 °C;^{2b}) $[\alpha]_D^{21} +66.6^\circ$ (c 1.0, MeOH),^{2a}) $[\alpha]_D^{21} +67^\circ$ (c 0.117, MeOH)^{2b}).

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