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

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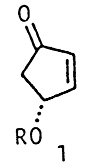
A new method for the synthesis of (R)-4-t-butyldimethylsiloxy-2-cyclopentenone (1, R = t-$BuMe_2Si$) has been developed which involves the effective preparation of the chiral (Z)-γ-iodo allylic alcohol and its conversion into 1 via cycliacylation reaction.

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-$BuMe_2Si$). 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.$^{4)}$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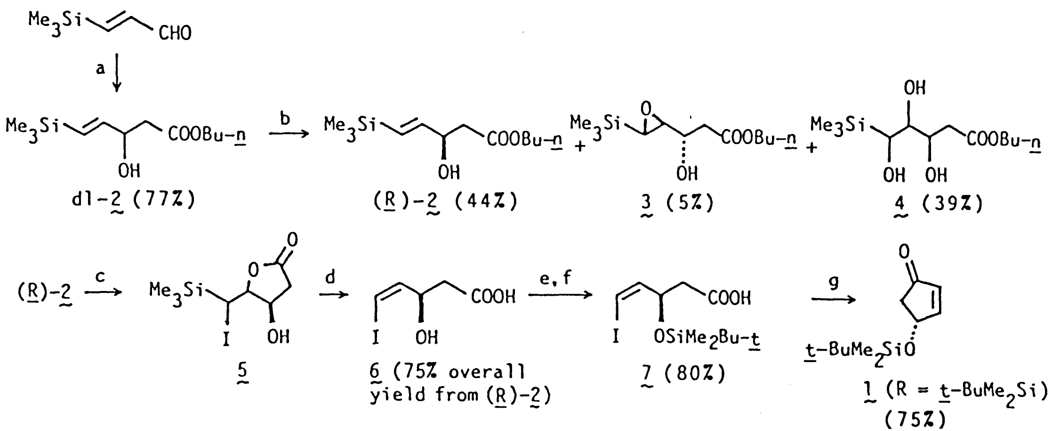
The starting alcohol dl-2 can be readily prepared in 77% yield by the reaction of the lithium enolate derived from butyl acetate with (E)-3-trimethylsilyl-2-propenal.$^{5)}$ Kinetic resolution of dl-2 using t-butyl hydroperoxide (TBHP) (1.5 equiv.), L-(+)-diisopropyl tartrate (L-(+)-DIPT) (1.8 equiv.), and $Ti(O\text{-}i\text{-}Pr)_4$ (1.5 equiv.) in CH_2Cl_2 at -20 °C for 18 h followed by usual work-up (10% aqueous tartaric acid) afforded (R)-2 (>99% ee,$^{6)}$ $[\alpha]_D^{25}$ +6.13° (c 1.63, $CHCl_3$)), 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-Et_2O-MeOH (2:2:1), room temperature, 12 h) followed by the iodolactonization with saturated aqueous $NaHCO_3$ and I_2 (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-Bu_4NF in



a, CH_3COOBu-n, LiN(i-Pr)$_2$, THF; b, TBHP, Ti(O-i-Pr)$_4$, L-(+)-DIPT, CH_2Cl_2; c, 3 mol dm^{-3} NaOH, THF-Et_2O-MeOH then I_2, aq $NaHCO_3$; d, n-Bu_4NF, THF; e, t-$BuMe_2SiCl$, imidazole, DMF; f, K_2CO_3, MeOH-THF-H_2O; g, MeLi then t-BuLi, Et_2O.

Scheme 1.

THF (75% yield from (R)-2).[10] Silylation of 6 with excess t-$BuMe_2SiCl$ (3 equiv.) in DMF followed by selective deprotection of the ester group with K_2CO_3 in MeOH-THF-H_2O (3:1:1)[11] furnished 7 in 80% yield. Finally, the cycliacylation reaction of 7 to 1 (R = t-$BuMe_2Si$) was carried out by treatment with 1 equiv. of MeLi and then with 2 equiv. of t-BuLi at -78 °C in Et_2O (75% yield).[4] The ^1H NMR spectrum, mp and optical rotation of 1 (R = t-$BuMe_2Si$) thus obtained were in good agreement with the literature values (mp 28.5-29.5 °C; $[\alpha]_D^{21}$ +67.3° (c 0.82, MeOH). lit. mp 29 °C,[2a] 30-31 °C;[2b] $[\alpha]_D^{21}$ +66.6° (c 1.0, MeOH),[2a] $[\alpha]_D^{21}$ +67° (c 0.117, MeOH)[2b]).

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6) Optical purity was determined by ^1H NMR analysis of the corresponding MTPA esters.
7) Stereochemistry of the triol 4 was not determined.
8) The resolution using 1.0 equiv. of Ti(O-i-Pr)$_4$ and 1.2 equiv. of L-(+)-DIPT did not proceed to completion.
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10) (Z)-Vinyl iodide 6 was contaminated with about 4% of (E)-isomer.
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