Chirally-labelled Oxirane

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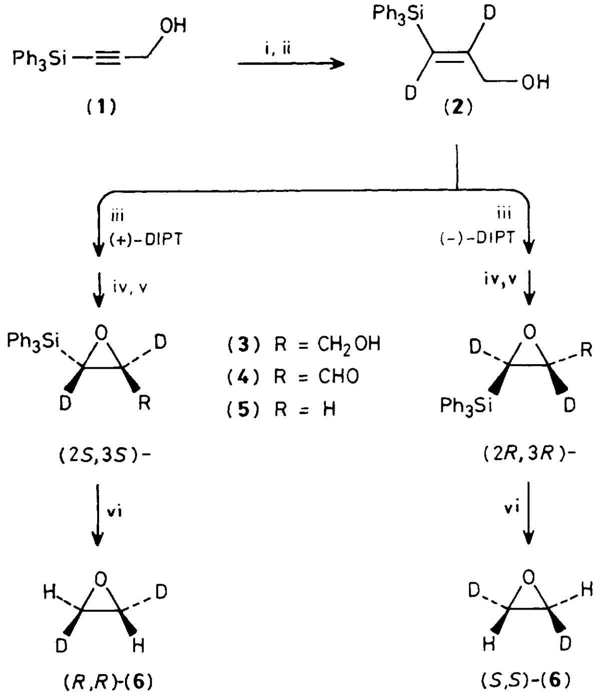
(*R,R*)- and (*S,S*)-[1,2-$^2H_2$]oxiranes have been synthesized from prop-2-yn-1-ol, the key step being asymmetric epoxidation of (*E*)-3-(triphenylsilyl)[2,3-$^2H_2$]prop-2-en-1-ol.

The synthesis of chirally labelled molecules for the study of chemical and enzymatic reaction mechanisms is often complicated by the paucity of readily available, chirally-labelled synthons. To address this need, we now describe the synthesis and configurational analysis of (*R,R*)- and (*S,S*)-[1,2-$^2H_2$]-oxirane.

3-(Triphenylsilyl)prop-2-yn-1-ol[1,2] (**1**) was synthesized in 77% yield by sequential treatment of propargyl alcohol with two equivalents each of ethylmagnesium bromide and chlorotriphenylsilane, with hydrolysis of the resulting bis(triphenylsilyl) intermediate by dilute acetic acid. Reduction of the acetylene with lithium aluminium deuteride,[3] followed by deuterium oxide quench, provided (*E*)-3-(triphenylsilyl)[2,3-$^2H_2$]prop-2-en-1-ol[2,4] (**2**) (96%). This was epoxidized by the Sharpless procedure[5] (90% yield†), using (separately) (+)- and (−)-di-isopropyl tartrate (DIPT). The use of (+)-DIPT gave (2*S*,3*S*)-, while (−)-DIPT provided (2*R*,3*R*)-3-(triphenylsilyl)[2,3-$^2H_2$]oxiranemethanol,[6] (**3**).



Reagents: i, $LiAlD_4$; ii, D_2O; iii, $Ti(OPr^i)_4$/t-butylhydroperoxide; iv, Ag_2CO_3/Celite; v, $(Ph_3P)_3RhCl$; vi, Et_4NF.

Each silylated epoxyalcohol was carried through the following sequence. Oxidation with silver carbonate on Celite[7] led to the aldehyde (42%†), which was decarbonylated[8] (47%†) using Wilkinson's catalyst in benzene. The resulting triphenylsilyloxirane[9,10] samples (**5**) were stable and non-volatile. Finally, desilylation[9] was effected by treatment of (**5**) with tetraethylammonium fluoride in Me_2SO at room temperature. Labelled oxirane was separated from the reaction mixture by entrainment (in a stream of nitrogen) into a solvent-containing flask cooled in dry ice.

For the purpose of demonstrating the configurational integrity of each chirally labelled oxirane sample, the receiver flask was charged with a solution of n-butyl-lithium in diethyl ether. The resulting hexanol samples [isolated in 50% yield from (**5**)] were derivatized as their (−)-camphanic acid esters. These were examined by ^2H n.m.r. spectroscopy, with addition of $Eu(dpm)_3$ (dipivaloylmethanatoeuropium) for separation of the diastereotopic deuteron signals.[11,12] Each camphanate sample was diastereomerically pure (at least to the limits of detection), and the configurations were those predicted from the known enantioselectivity of the epoxidation method.[5]‡

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† Yields are given for the series of reactions leading to (*R,R*)-(**6**). Comparable yields were obtained in the synthesis of (*S,S*)-(**6**).

‡ The identity (*pro-R* or *pro-S*; upfield or downfield) of the $Eu(dpm)_3$-shifted methylene deuteron signal was ascertained in each case by addition of a small amount of [1,1-$^2H_2$]hexyl camphanate to the mixture of chirally-labelled hexyl camphanate and $Eu(dpm)_3$. The larger of the two C-1 deuteron signals in the spectrum of the resulting mixture therefore corresponded to the sole methylene deuteron signal present in the spectrum of the chirally-labelled camphanate ester. (See ref. 12 for a similar experiment.)

It is expected that high enantiomeric purity chirally-labelled oxirane (as well as prior synthetic intermediates) will see widespread application for the synthesis of substances stereospecifically labelled with deuterium and/or tritium. In addition, vibrational circular dichroism (c.d.)[13] and vacuum-u.v.–c.d.[14,15] studies of this minimally-functionalized, chiral species are expected to provide fundamental insights into the relationship between structure and optical activity.

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