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## New Stereoselective Routes from Alcohols to Secondary Alkyl Bromides with Retention of Configuration

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Summary Secondary alcohols can be converted into the corresponding bromides with high stereoselective retention of configuration; this two-step process proceeds by a double inversion involving the intermediate selenides.

WE report here a new method for converting secondary alcohols (A) into the corresponding alkyl bromides  $(C)^{1,2}$ 





TABLE.

Starting alcohol <sup>*</sup> (-)-(R)-(1) (-)-(R)-(1) (+)-(S)-(1) cis-(4) trans-(4) (72)	Selenide (+)-(S)-(2) (+)-(S)-(2) (-)-(R)-(2) trans-(5) cis-(5) (Pb)	Yield/% (method) 74 (i) 70 (ii) 79 (ii) 43 (i) 71 (i) 76 (ii)	$ \begin{array}{c} [\alpha]_{\mathbf{D}}^{20b} \text{ (Stereochem.} \\ & \text{purity} / \% \text{)} \\ + 30.95^{\circ} (96\cdot8) \\ + 29\cdot89^{\circ} (93\cdot5) \\ - 29\cdot80^{\circ} (93\cdot2) \\ & - (>95) \\ - (>95) \\ & - (>95) \\ & - (>95) \end{array} $	Bromide (-)-(R)-(3) (-)-(R)-(3) (+)-(S)-(3) cis-(6) trans-(6) (9a)	Yield /% 90 88 89 95 25 93	$ \begin{array}{c} [\alpha]_D^{20} \stackrel{e}{\circ} (\text{Stereochem.} \\ purity/\%) \\ - 42 \cdot 52^\circ (95 \cdot 5) \\ - 41 \cdot 32^\circ (92 \cdot 8) \\ + 41 \cdot 20^\circ (92 \cdot 52) \\ - (>95) \\ - (>95) \\ - (>95) \\ - (>95) \end{array} $
(7a)	( <b>8b</b> )	76 (ii)	— (>95)	( <b>9a</b> )	93	(>95)
(7b)	(8a)	47 (i) 57 (ii)	— (>95)	( <b>9b</b> )	22	— (>95)

• Purchased from Aldrich. The octanols used had the following  $[\alpha]_D^{20}$  values: (+)-(S)-octan-2-ol 7.52° (optical purity 92.3%, ref. 2), (-)-(R)-octan-2-ol -7.00° (optical purity 85.8%). Optically pure octanols have  $[\alpha]_D^{20} \pm 8.15°$  (refs. 1 and 2). • Corrected for optically pure starting material in the case of the octan-2-ols. • Overall value for the whole process, corrected for optically pure starting material is the case of the octan-2-ols.

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with high (>92%) stereoselective retention of configuration at the substituted carbon atom. This unusual reaction t takes advantage of the easy synthesis of phenyl selenides (B) from alcohols [PhSeCN-Bu<sub>3</sub>P-tetrahydrofuran(THF), 20 °C, 72-100 h, method (i),<sup>3</sup> or  $MeSO_2Cl$ -ether, 0°C, followed by substitution by PhSeNa in THF-hexamethylphosphoric triamide, 20 °C, method (ii)] and their further transformation into the corresponding bromides4 (Br2-NEt3- $CH_2Cl_2,\ 20\ ^\circ C)\,;$  both stages were found to proceed with high stereoselectivity and inversion of configuration at the substituted carbon atom.

The overall yields were usually good (ca. 60%; Table) except for the equatorial alcohols trans-(4) and (7b); in these cases there was a competing elimination reaction during the selenide-alkyl bromide reaction.

The stereochemical purity of the bromides was ascertained by comparison with samples prepared unambiguously by known methods ([ $\alpha$ ]<sub>D</sub> for the octyl bromides,<sup>2a,b</sup> <sup>1</sup>H n.m.r. spectroscopy and g.c.<sup>2</sup> for the cyclohexyl bromides,  ${}^{\mathbf{5a}-\mathbf{c}}$  and  ${}^{1}\!H$  n.m.r. spectroscopy for the cholesteryl bromides {}^{5d}, e).

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t Alkyl chlorides, however, can be prepared from alcohols and thionyl chloride with varying degrees of inversion or retention of configuration depending on the reaction conditions (ref. 1).

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