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

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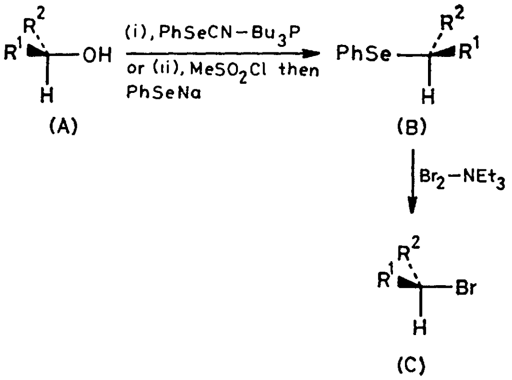
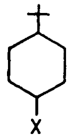
Summary Secondary alcohols can be converted into the corresponding bromides with high stereoselective retention of configuration; this two-step process proceeds by a double inversion involving the intermediate selenides.

WE report here a new method for converting secondary alcohols (A) into the corresponding alkyl bromides (C)[1,2]

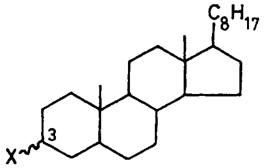


$Me[CH_2]_5CHXMe$

(1) X = OH
(2) X = SePh
(3) X = Br



(4) X = OH
(5) X = SePh
(6) X = Br



(7) X = OH
(8) X = SePh
(9) X = Br
a; 3α–X, b; 3β–X

TABLE.

Starting alcohol[a]	Selenide	Yield/% (method)	$[\alpha]_D^{20}$[b] (Stereochem. purity/%)	Bromide	Yield /%	$[\alpha]_D^{20}$[c] (Stereochem. purity/%)
(−)-(*R*)-(**1**)	(+)-(*S*)-(**2**)	74 (i)	+30·95° (96·8)	(−)-(*R*)-(**3**)	90	− 42·52° (95·5)
(−)-(*R*)-(**1**)	(+)-(*S*)-(**2**)	70 (ii)	+29·89° (93·5)	(−)-(*R*)-(**3**)	88	− 41·32° (92·8)
(+)-(*S*)-(**1**)	(−)-(*R*)-(**2**)	79 (ii)	−29·80° (93·2)	(+)-(*S*)-(**3**)	89	+ 41·20° (92·52)
cis-(**4**)	*trans*-(**5**)	43 (i)	— (>95)	*cis*-(**6**)	95	— (>95)
trans-(**4**)	*cis*-(**5**)	71 (i)	— (>95)	*trans*-(**6**)	25	— (>95)
(**7a**)	(**8b**)	76 (ii)	— (>95)	(**9a**)	93	— (>95)
(**7b**)	(**8a**)	47 (i) 57 (ii)	— (>95)	(**9b**)	22	— (>95)

[a] 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 $[\alpha]_D^{20}$ ±8·15° (refs. 1 and 2). [b] Corrected for optically pure starting material in the case of the octan-2-ols. [c] Overall value for the whole process, corrected for optically pure starting materials in 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‡ takes advantage of the easy synthesis of phenyl selenides (B) from alcohols [PhSeCN–Bu_3P–tetrahydrofuran(THF), 20 °C, 72—100 h, method (i),[3] 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 bromides[4] (Br_2–NEt_3–CH_2Cl_2, 20 °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 ($[\alpha]_D$ for the octyl bromides,[2a,b] ^1H n.m.r. spectroscopy and g.c.[2] for the cyclohexyl bromides,[5a–c] and ^1H n.m.r. spectroscopy for the cholesteryl bromides[5d,e]).

We thank the FNRS (Belgium) for support of this work and for financial support (A. K.) and IRSIA (Belgium) for a doctoral fellowship (M. S.)

(*Received, 1st April* 1980; *Com.* 351.)

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‡ 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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