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REGIOSELECTIVE AND [C,C] CONNECTIVE ROUTES TO OXETANES AND TETRAHYDROFURANES

M. Sevrin and A. Krief [+]
Facultés Universitaires Notre-Dame de la Paix
Department of Chemistry
61, rue de Bruxelles, B-5000 Namur (Belgium)

α-Selenoalkyllithiums already used for the regioselective synthesis of epoxides[1] *are found valuable building blocks for the synthesis of higher homologues namely oxetanes and tetrahydrofuranes. The general synthetic strategy used is schematized below and represent a formal homologization reaction of epoxides and oxetanes by carbene insertion.*

SCHEME I

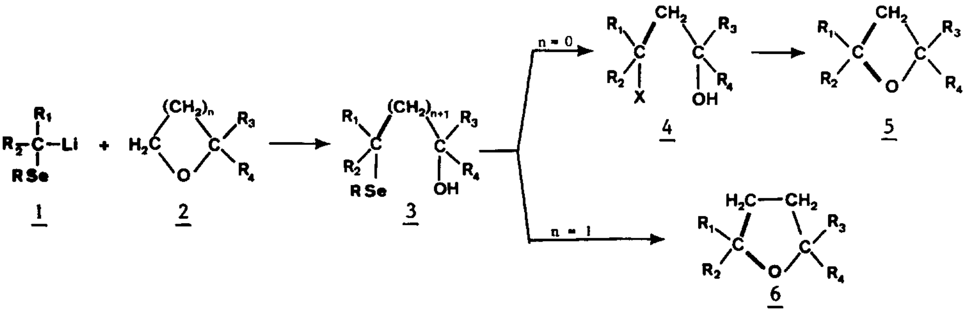
The synthetic approach requires the synthesis of γ and δ-hydroxyselenides 3 (Scheme II) from α-selenoalkyllithiums and epoxides[2] or oxetanes (THF, -78° to +20°, method A, Table). β-Hydroxyselenides were found as side products beside the desired γ-hydroxyselenides when methyl or phenylselenomethyllithiums are reacted. They can be accounted from the reaction, on epoxides of lithioselenolates probably formed by decomposition of α-selenomethyllithiums. However, their formation can be prevented if HMPT is present in the medium (2 in THF/HMPT,1eq. added at -78° on 1 then heated up to +20°, Method B).

δ-Hydroxyselenides (3,n=1) are directly cyclized in good yield to tetrahydrofuranes on reaction with bromine[3] [$Br_2/NEt_3/CH_2Cl_2$, 20°, 0.5 hr (method C) or Br_2/ethanol-water (method D)] . γ-Hydroxyselenides (3,n=0) however do not cyclize to oxetanes under similar (methods C,D) and related reaction conditions[3] [CH_3I/NaI/DMF,$CaCO_3$, 80°, 1hr (method E)] . The reactions stop at the stage of γ-halogenoalcohols[3] which are produced in good yield[3b] (table) and which require a basic media to cyclize to oxetanes 5.

The choice of the right basic system is crucial for the success of the cyclization which is directly related to the number and the nature of the substituants branched on the carbon bearing the halogen atom.
tBuOK/DMSO (20°, method F) is the most valuable system for the cyclization[4] of γ-halogenohydrins bearing the halogen atom at the terminus (R_1,R_2 = H, Table, entries 1 to 3). CH_3MgBr/HMPT (20° to 80°, method G)[5] is the only one among a huge variety of basic systems used[4,6] to allow the desired synthesis when a methyl group is attached at the terminus (R_1=H, R_2=CH_3, Table, entries 4 to 5).

Under these conditions, higher homologues produce low yields of oxetanes (R_1=H, R_2=CH_3 16%; R_1=H, R_2=C_6H_{13} ∿3%) and homoallylalcohols are instead formed[2] (respectively 51% and 70% yields). Work is actually in progress to generalize the oxetane synthesis from epoxides.

SCHEME II



TABLE

					3 yield %		4 yield %		5 or 6 yield %	
entry R$_1$	R$_2$	n	R$_3$	R$_4$	R	(method)	X	(method)	5 or 6	method
1 H	H	0	H	C_6H_{13}	C_6H_5	46(A)[a] 80(B)[b]	I	88(E)	5	70(F)
2 H	H	0	H	C_6H_{13}	CH_3	25(A)[c] 73(B)[d]	I	71(E)	5	70(F)
3 H	H	0	CH_3	C_6H_{13}	C_6H_5	75(B)	I	60(E)	5	70(F)
4 CH_3	H	0	H	C_6H_{13}	C_6H_5	70(A)[e]	Br	67(D)[e]	5	60(G)[e]
5 CH_3	H	0	CH_3	C_6H_{13}	C_6H_5	50(A)[e] 60(B)	Br	55(D)[e]	5	65(G)[e]
6 C_2H_5	H	0	H	C_6H_{13}	CH_3	75(A)[e]	Br	74(D)[e]	5	16(G)[e]
7 C_6H_{13}	H	0	H	CH_3	C_6H_5	84(A)[e]	Br	74(D)[c]	5	3(G)
8 C_6H_{13}	H	1	H	H	CH_3	82(A)			6	77(C)(D)
9 C_6H_{13}	H	1	H	H	C_6H_5	75(A)			6	70(C)(D)
10 C_6H_{13}	H	1	CH_3	H	CH_3	42(A)[e]			6	84(C)[e]
11 C_6H_{13}	CH_3	1	H	H	H	64(A)			6	82(C)

1-seleno 2-hydroxy octane is obtained in a) 26% yield , b) 3% yield, c) 31% yield, d) 10% yield,
e) these derivatives are obtained as a mixture of stereoisomers.

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   b) We are not able at present to achieve the desired transformations (method A or B) when the selenyl moiety is attached to a carbon atom fully substituted.
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