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TRANSFORMATION OF SELENIDES TO ALKYLHALIDES

NEW ROUTES FOR HOMOLOGIZATION OF PRIMARY ALKYLHALIDES

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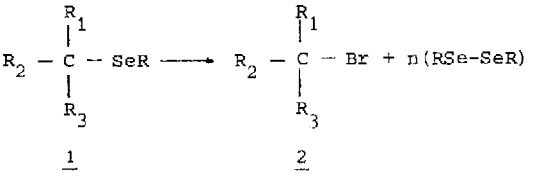
This communication reports two complementary methods for the conversion of selenides 1 to the corresponding alkylhalides 2 (Scheme I). We found [1], for instance, that secondary and tertiary alkyl bromides are formed in good yield (table I), by reacting alkylphenyl or alkyl methyl selenides with bromine (Method A) [2] or N-bromo succinimide (Method B) [3], in water-ethanol solution (20°C, 3h) (table I). The yields in alkyl bromide 2 are generally improved when a methylene chloride solution of the selenide is added to a solution of triethyl amine-bromine (Method C) [4] in the same solvent (20°C, 3h) (table I).

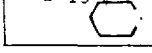
SCHEME I



1 2

R = CH_3 or C_6H_5

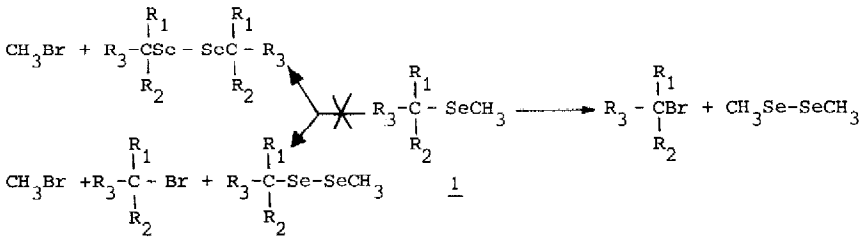
TABLE I

R_1	R_2	R_3	Yield in 2 % (**)	R*
nC_9H_{19}	CH_3	H	70(A)-60(B)-84(C)	C_6H_5
nC_9H_{19}	CH_3	H	50(A)-22(B)-75(C)	CH_3
nC_6H_{13}	C_6H_{13}	H	82(C)	C_6H_5†
nC_6H_{13}	C_6H_{13}	H	63(A)-73(C)	CH_3†
		C_6H_{13}	68(C)	CH_3 †

* substituent on the selenium in the starting selenide 1
** refer to the method of reduction used
† obtained from an α-selenocarbanion (see ref. 5b)

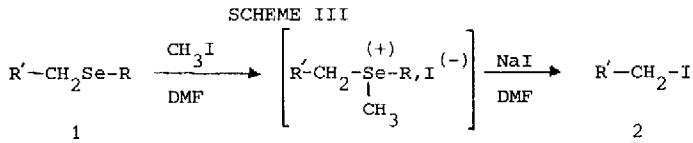
The reaction (methods A, B or C) works poorly when R_3 is an alkyl substituent and R_1,R_2:H (yield ∿20%). This can explain the fact that dimethyl diselenide is formed instead of the other diselenides, which could formally arise, when methyl selenides (R_1,R_2:Alkyl, R_2:H or R_1,R_2,R_3:Alkyl) are reacted (scheme II)

SCHEME II



When the substituents R_1,R_2 are H, in the selenide 1, the desired transformation to primary alkylhalide was efficiently performed (scheme III) using methyliodide and sodium iodide in DMF (method already described by Corey in the analog sulfur case)[4].

SCHEME III

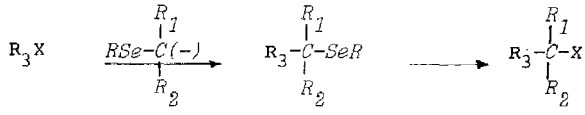


R_3=nC_9H_{19} R:C_6H_5 yield % : 80
R:CH_3 yield % : 65

Nevertheless we found that this procedure is uneffective when the substituent on the selenide is secondary or tertiary alkyl. Indeed, the major product (>90%) is starting selenide which results from the attack of the iodide on the methyl group of the hypothetically formed selenonium salt 3.
This hypothesis was verified in one case : 7-tetradecyl methyl selenide being quantitatively recovered from the reaction of 7-tetradecyl dimethyl selenonium fluoroborate with sodium iodide in DMF.

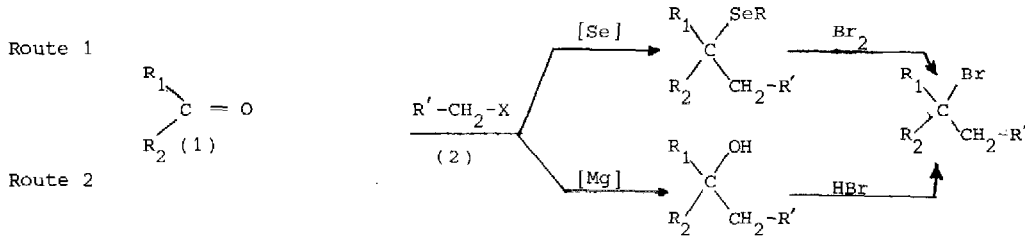
The interest in transforming selenides to alkylhalides is enhanced by the fact that selenides can be obtained in high yield from alkylhalides and α-seleno-carbanions (scheme IV)[5b]. Accordingly the whole process described below is a new and highly effective method for the homologization of alkyl halides (total yield ∿60%).

SCHEME IV

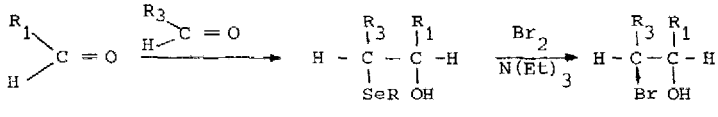


Carbonyl compounds can also be transformed to alkyl halides using the reactions summarized below (route 1) selenium activation (carbonyl compound $\xrightarrow{RSeH}$ selenoacetal $\xrightarrow[2)\,R'\text{-}CH_2X]{1)\,BuLi}$ selenide $\xrightarrow[NEt_3]{Br_2}$ alkylhalide). The same transformation can sometimes be performed using the classical magnesium activation (route 2) (carbonyl compound $\xrightarrow[2)\,H_2O]{1)\,R'\text{-}CH_2X+Mg}$ alcool $\xrightarrow{HBr}$ alkylhalide)

SCHEME V



The carbon atom C(1) on the carbonyl group and the carbon atom C(2) on the alkylhalide are both electrophilic. The magnesium activation allows the activation of C(2) as a nucleophile and the selenium method allowing the activation of C(1) as a nucleophile. The concept could be sometimes very useful as an attractive synthetic methodology; the formation of bromohydrin which is not regiospecific when magnesium is used [7], was realised using selenium ($\overset{R_3}{H}\!>\!C{=}O$ is activated as a selenocarbanion)[5a].



R_1	R_3	R	Method	Yield %
C_3H_7	C_3H_7	C_6H_5	A(1hr) B(24hrs)	72 70
C_3H_7	C_3H_7	CH_3	A(1.5hr)	40

This new regiospecific method of bromohydrin synthesis from β-hydroxyselenide[5a], opens also a new route to the regiospecific synthesis of α-bromoketone (oxidation of the bromohydrin using Jone's reagent).

References

1) a) O.K. Edwards, W.R. Gaythwaite, J. Kenyon and H. Phillips, J. Chem. Soc., 2293 (1928) have described the reaction of bromine on phenyl methyl selenide leading to phenyl methyl selenide dibromide which is decomposed by heating at 100°C to methyl bromide and bromoselenobenzene. Their conditions are much more drastic than ours.

b) reaction of bromine with diaryl selenide to yield selenide dibromide is described by O. Behaghel and H. Hofmann, Chem. Ber., 72, 697 (1939).

c) reaction of bromine with an aryl vinyl selenide and phenyl benzyl selenide are described to produce respectively a vinylic bromide and benzyl bromide. G. Hölzle and W. Jenny, Helv. Chim. Acta, 712 (1958).

d) several authors have used the reaction of bromine in ethanol on aryl methyl selenide for the synthesis of bromoselenoarene. They have not reported the formation of the bromo methane counterpart.

2) Bromine (1 mmole) (Method A) or N.bromo succinimide (2 mmoles) (Method B) is slowly added to a solution of selenide (1 mmole) in ethanol-water (1.5 - 0.5ml). The solution is stirred at 25°C for 10 to 48h (Method A or B) or heated at 80°C for 1h (Method A), the red solution is washed with $NaHCO_3$, water, then dried. The alkyl bromide (rf.:0.85) is purified by PLC (preparative chromatography plates Merck 2mm, SiO_2).

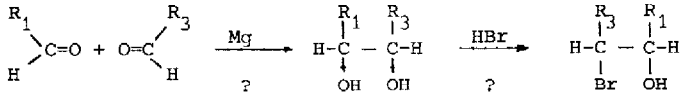
3) Method C : a CH_2Cl_2 (1,5 ml) solution of selenide 1 (0.5 mmole) is slowly added to a stirred suspension of triethyl amine (10 mmoles)/bromine (1 mmole) in CH_2Cl_2 at 20°C. Stirring is continued one more hour. Then ether (15 ml) is added and the solution is washed with $NaHCO_3$ then with water. The ether solution is dried. After evaporation of the solvent, the residue is distilled.

4) E.J. Corey and M. Jautelat, Tet. Lett., 5787 (1968).

5a) For the synthesis of β-hydroxyselenides, see D. Van Ende, W. Dumont and A. Krief, Angew. Chem. Int. Ed., 14, 700 (1975); 5b) M.Sevrin, D.Van Ende and A.Krief, see accompanying paper.

6) The authors are grateful for a fellowship to M. Sevrin from I.R.S.I.A. (Belgium) - Institut pour la Recherche Scientifique dans l'Industrie et l'Agriculture; this work will be included in the Ph.D. thesis of M. Sevrin.

7) The magnesium activation produces the desired glycol 8 [8] along with the glycols [9] arising from the dimerisation of each carbonyl compound 6 or 7 (scheme IV), moreover it is generally impossible to introduce the bromine atom to one specific carbon atom of the glycol 8 to produce one bromohydrine 9.



6 7 8 9

8) H.O. House, Modern Synthetic reactions, 2d edition, W.A. Benjamin Inc. 1972, p. 168

9) E.J. Corey, R.L. Danheiser, S. Chandrasekaran, J. Org. Chem., 41, 260 (1976), succeded in some unsymmetrical reductive coupling reactions