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REDUCTION OR ALKYLATIVE REDUCTION OF THE CARBONYL GROUP (1)

M. SEVRIN [11], D. VAN ENDE and A. KRIEF+
Department of Chemistry
Facultés Universitaires Notre-Dame de la Paix
61, rue de Bruxelles, B-5000 - Namur (Belgium)

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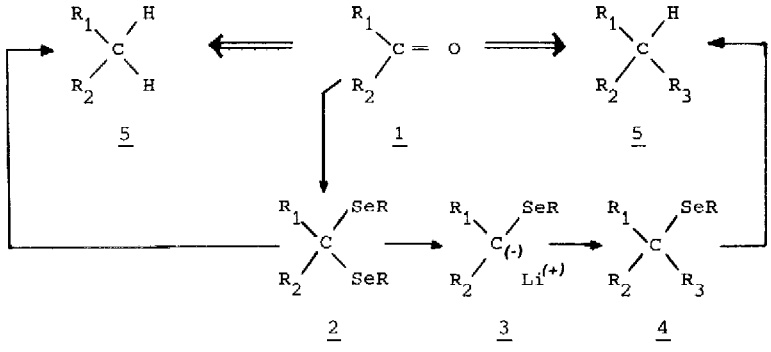
We report here on a new, highly potent method of "reduction" or "alkylative reduction" of carbonyl compounds (aldehyde or ketone)

SCHEME I



This transformation, described in scheme I, takes advantage of:

1) *the high-yield synthesis of seleno-acetals* 2 [3] *from aldehydes and ketones*
2) *the cleavage of the carbone-selenium bond of selenoacetals by n-butyl lithium leading to α-selenocarbanions* 3 [2b,3].
3) *their hydrolysis* [H_2O, D_2O] *or alkylation by alkylhalides producing selenides in high yield* [4]
4) *the transformation of selenides to hydrocarbon using lithium in ethylamine or Raney Nickel.*

These last two transformations (steps 3 and 4) are the concern of this preliminary report.

Selenoacetals 2 are readily cleaved by n-butyl-lithium to α-selenocarbanions (THF, -78°C, 1h) subsequent hydrolysis by H_2O or D_2O leads to the corresponding selenides 4 (R_3:H or D) (Table I). The α-selenocarbanions (R_1,R_2:H or R_1:H, R_2:Alkyl or R_1,R_2:Alkyl) are also easily

transformed to selenides[5] by alkylation with an alkylhalide (bromide or iodide)[5] [THF,-78°C, 2h; 25°C, 2h)]. Better results are obtained when the less stabilised methyl selenocarbanions 3a ($R:CH_3$) are used in place of their selenophenyl analogs 3b ($R:C_6H_5$) [4].

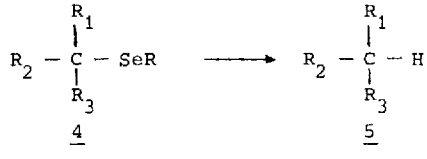
TABLE I

R_1	R_2	R	R_3	Yield in % 4
$nC_{13}H_{27}$	H	CH_3	H	85
			D	87
$nC_{10}H_{21}$	$nC_{10}H_{21}$	CH_3	H	87
			D	87
$nC_{10}H_{21}$	$nC_{10}H_{21}$	C_6H_5	H	92
H	H	CH_3	$nC_{10}H_{21}$	60
nC_6H_{13}	H	CH_3	nC_6H_{13}	85
nC_6H_{13}	H	C_6H_5	nC_6H_{13}	40
nC_6H_{13}	H	CH_3	nC_7H_{15}	75
nC_6H_{13}	H	CH_3	$CH_2-CH=CH_2$	55
CH_3	CH_3	CH_3	nC_6H_{13}	85
		CH_3	nC_6H_{13}	84

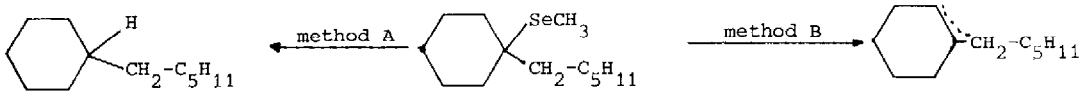
We also found that the carbon selenium bond is easily cleaved by lithium in ethyl amine [6a] (-10°C, 2h) (method A) or by treatment with Raney Nickel [6b] (ethanol, reflux, 24h) (method B). Both methods proved fruitful when performed with sulfur compounds [7] but there are few reports concerning selenium analogs [8].

Under the described [6] conditions, methyl alkyl selenides 4a ($R:CH_3$) and phenyl alkyl selenides 4b ($R:C_6H_5$) (scheme II - table II) as well as the methyl seleno-acetals 2a ($R:CH_3$) or phenyl seleno-acetals 2b ($R:C_6H_5$) (scheme III - table III) lead to the corresponding alkanes 5 in good yield.

SCHEME II



In one case, when selenide 4m is treated with Raney Nickel (method B) a mixture of olefins is formed, similar examples were reported in the case of sulfur [10].



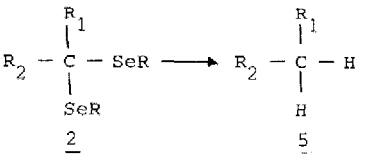
77 % 4m 80 %

TABLE II

R_1	R_2	R_3	Yield in % 5 (**)	R *
$nC_{13}H_{27}$	H	H	90 (A)	CH_3 †
$nC_{13}H_{27}$	H	D	75 (A)	CH_3 †
$nC_{10}H_{21}$	$nC_{10}H_{21}$	H	93 (A)	CH_3 †
$nC_{10}H_{21}$	$nC_{10}H_{21}$	D	74 (A)	CH_3 †
$nC_{10}H_{21}$	$nC_{10}H_{21}$	H	80 (A)	C_6H_5 †
$nC_{11}H_{23}$	CH_3	H	82 (A) -65 (B)	CH_3
$nC_{11}H_{23}$	CH_3	H	80 (A) -65 (B)	C_6H_5
nC_6H_{13}	nC_7H_{15}	H	75 (B)	CH_3 ††
nC_6H_{13}	nC_6H_{13}	H	76 (A)	CH_3 ††
nC_6H_{13}	nC_6H_{13}	H	74 (A)	C_6H_5 ††
		nC_6H_{13}	77 (A)	CH_3 ††

* substituant on the selenium in the starting selenide 4
** refer to the method of reduction used
† obtained from α-selenocarbanion by hydrolysis (see Table I)
†† obtained from α-selenocarbanion by alkylation (see Table I)

SCHEME III



2 5

TABLE III

R_1	R_2	Yield in 5 % (**)	R*
$nC_{13}H_{27}$	H	85 (A) -81 (B)	CH_3
$nC_{10}H_{21}$	$nC_{10}H_{21}$	84 (A) -80 (B)	CH_3
$nC_{10}H_{21}$	$nC_{10}H_{21}$	85 (A)	C_6H_5

* substituant on the selenium in the starting acetal 2
** refer to the method of reduction used

As compared to other published methods of reduction of carbonyl compounds (e.g. Clemmensen, Wolff Kishner, reduction of sulfoacetals), the whole process described in scheme I in this report has the advantage to be effective for the reduction as for the "alkylative reduction" of the carbonyl groups (total yield 1 → 5 ∿50 - 60 %)

References

1) A preliminary report of this work was presented by A. Krief :
- 25th IUPAC Congress held in Jerusalem (Israel) July 1975
- Premières Journées Belges de Chimie Organique - 10,11 Nov.1975 - Knokke-le-Zout (Belgium)

2) a) D. Seebach and N. Peleties, Chem. Ber., 105, 511 (1972) and references cited herein
b) D. Van Ende, W. Dumont and A. Krief, Angew. Chem. Int. Ed. 14, 700 (1975)

3) a) W. Dumont, P. Bayet and A. Krief, Angew. Chem. Int. Ed., 13, 805 (1974)
b) D. Seebach and A.K. Beck, Angew. Chem. Int. Ed., 13, 806 (1976)

4) The hydrolysis or deuteriolysis,as well as some alkylation of two α-phenylseleno carbanions have been already reported in the literature by D. Seebach, see ref. 3b; for other references, see ref. 1

5) *Synthesis of selenides 4 from seleno acetals 2*

nBuLi, 5,5 mm (2N in hexane, Merck) is slowly added to a precooled (-78°C) solution of the selenoacetal (5.00 mm) in anhydrous THF (10 ml); the resulting solution is stirred for 1h at -78°C then treated as in a or b

a) alkylation: the alkylhalide (5.0 mm) in THF (5 ml) is added at -78°C. The solution is then stirred 2h (-78°C) and 2h at 25°C, hydrolyzed, extracted and dried. The selenide is purified by distillation

b) H_2O or D_2O is then added and the solution is stirred for 0.5h at 25°C, hydrolyzed, extracted and dried. The selenide is purified by distillation.

6) *Reduction of selenides 4 or acetals 2 to hydrocarbon 5*

6a) *Method A*

The selenide 4 (1 mm) or the acetal 2 (0.5mm) is dissolved in ethylamine (freshly distilled from lithium). Lithium (0,2 g) is then added in small portions at -15°C. The mixture becomes deep blue after 15 mn. After stirring an additional hour the color disappears.
Ammonium chloride (0.7 g) is added, stirring is continued for 15 min, then the mixture is hydrolyzed, extracted with pentane, washed with brine and dried; the hydrocarbon is purified by distillation.

6b) *Method B*

Raney Nickel (suspension in water - Merck 820876) 4g is washed with ethanol (3 x 2 ml). The resulting precipitate is suspended in ethanol (6 ml) and saturated with hydrogen. The selenide (1 mmole) or the selenoacetal (0.5 mmole) is then dissolved and the mixture is heated at reflux for 24h; the Raney nickel is filtered at this time on cellite, and the solution is washed with water, extrated with pentane. After drying, the solvent is removed and the residue is distilled.

7) H.O. House, Modern Synthetic reactions, 2d edition, W.A. Benjamin Inc. 1972, Chapter I see p. 15 and 17

8) Raney Nickel does not destroy the tetrahydroselenophene ring of the selenobiotine. Private communication from A. Marquet

9) Sodium in liquid ammonia effectsclean debenzylation of alkyl benzyl selenide to selenol. See for example, L.B. Agenas, Arkiv. Kemi, 23, 37, 463 (1965).

10) R.L. Augustine "Catalytic Hydrogenation", Marcel Dekker, Inc., New York (1965) p. 132.

11) 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.