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REDUCTION OF β-ALKYLTHIO α,β-UNSATURATED KETONES [$R^1COCH=C(R^2)SR^3$] WITH $LiAlH_4$ OR $NaBH_4$: CONVERSION TO α,β-UNSATURATED KETONES ($R^1CH=CHCOR^2$)

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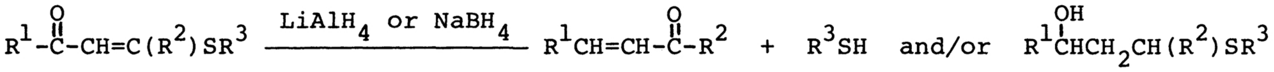
Reduction of β-alkylthio α,β-unsaturated ketones [$R^1COCH=C(R^2)SR^3$] with lithium aluminium hydride ($LiAlH_4$) or sodium borohydride ($NaBH_4$) gave α,β-unsaturated ketones ($R^1CH=CHCOR^2$) in moderate yields. In some cases, the saturated γ-hydroxy sulfide is obtained in high yield.

β-Heteroatom substituted α,β-unsaturated ketones (β-amino, β-alkoxy and β-alkylthio α,β-unsaturated ketones) are common synthetic intermediates being useful not only as protecting groups but also as sources of other functional groups and substituents.[1)] Recent interest concerning the reduction of β-amino α,β-unsaturated ketones with $LiAlH_4$[2)] or with $NaBH_4$-$FeCl_3$[3)] and β-alkoxy α,β-unsaturated ketones with $LiAlH_4$[4)] has led us to study the chemistry of β-alkylthio α,β-unsaturated ketones (1).



$$R^1-\overset{O}{\overset{\|}{C}}-CH=C(R^2)SR^3 \xrightarrow{LiAlH_4 \text{ or } NaBH_4} R^1CH=CH-\overset{O}{\overset{\|}{C}}-R^2 + R^3SH \text{ and/or } R^1\overset{OH}{\overset{|}{C}}HCH_2CH(R^2)SR^3$$

1 2 3 4

a: R^1=Ph R^2=Me R^3=Et b: R^1=Ph R^2=Me R^3=Pr^n c: R^1=Ph R^2=Ph R^3=Et
d: R^1=Ph R^2=Me R^3=Ph e: R^1=Ph R^2=H R^3=Et f: R^1=Ph R^2=H R^3=Ph
g: R^1=Me R^2=Ph R^3=Et h: R^1=Me R^2=Ph R^3=Ph i: R^1=Me R^2=Me R^3=Bu^n
j: R^1=Me R^2=Me R^3=Ph k: R^1, R^2=$(CH_2)_3$ R^3=Et

When 3-ethylthio-1-phenyl-2-buten-1-one (1a) was reduced with $LiAlH_4$ in dry ether and then the reaction products were decomposed under acidic conditions, 4-phenyl-3-buten-2-one (2a) was obtained. Reduction of 1a with $NaBH_4$ in MeOH also gave 2a in moderate yield. In Table 1, the yield of 2a under various conditions is summarized.

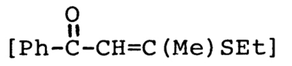


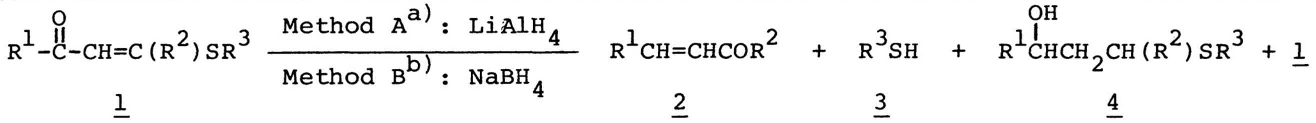
Table 1. Reduction of 1a [$Ph-\overset{O}{\overset{\|}{C}}-CH=C(Me)SEt$] with $LiAlH_4$ or $NaBH_4$ under various conditions

Reducing reagent	Solvent	Conditions[a]	Mol. ratio Red./1a	Yield of Products (%)[b]	
				2a: PhCH=CHCOMe	1a: Recovered
$LiAlH_4$	Et_2O	r.t. 16 h	1/2	27.0	65.5
$LiAlH_4$	Et_2O	r.t. 2 h reflux 1 h	1/2	21.5	71.5
$LiAlH_4$	Et_2O	r.t. 25 h	1	24.0-28.0	40.0-63.0
$LiAlH_4$	Et_2O	r.t. 2 h reflux 0.5 h	1	49.5	45.5
$LiAlH_4$	Et_2O	reflux 1 h	1	91.0	$\sim$0
$LiAlH_4$	Et_2O	r.t. 5 h	2	72.5-85.0	1.0-13.0
$LiAlH_4$	Et_2O	r.t. 2 h reflux 0.5 h	2	84.0-94.5	1.0-5.5
$LiAlH_4$	Et_2O	r.t. 2 h reflux 0.5 h	4	22.5-23.5	$\sim$0-1.0
$NaBH_4$	MeOH	r.t. 2 h	1	46.0-49.0	30.5-33.5
$NaBH_4$	MeOH	r.t. 112 h	1	47.5	10.5
$NaBH_4$	MeOH	r.t. 2 h	2	46.0	33.5

a) 1a was stirred with reducing reagent and then the reaction mixture was treated with conc. hydrochloric acid. The mixture was diluted with water and extracted with ether or dichloromethane. b) Yields determined by G.L.C..

Similarly, other β-alkylthio α,β-unsaturated ketones (1b, d-e, i-k) were reduced with $LiAlH_4$ and converted in moderate yields into α,β-unsaturated ketones (2b, d-e, i-k). Meanwhile, β-alkylthio α,β-unsaturated ketones (1c, f-h) were reduced with $LiAlH_4$ to give the saturated γ-hydroxy sulfides (4c, f-h) in high yields. The structure of γ-hydroxy sulfides (4c, f-h) was confirmed with their spectrum data and elemental analysis.[5] On reduction with $NaBH_4$ and acid treatment, β-alkylthio α,β-unsaturated ketones (1a, c-d, f-g, i-k) gave the corresponding α,β-unsaturated ketones (2a, c-d, f-g, i-k) in moderate yields (Table 2). $NaBH_4$ is more superior than $LiAlH_4$ for the selectivity for carbonyl group on the reduction. However, the reactivity of $NaBH_4$ is less than that of $LiAlH_4$. The α,β-unsaturated ketone (2) is generated by hydrolysis of hemi-thioacetal formed by allylic rearrangement of β-alkylthio

Table 2. The Yields of Reduction Products (2-4)

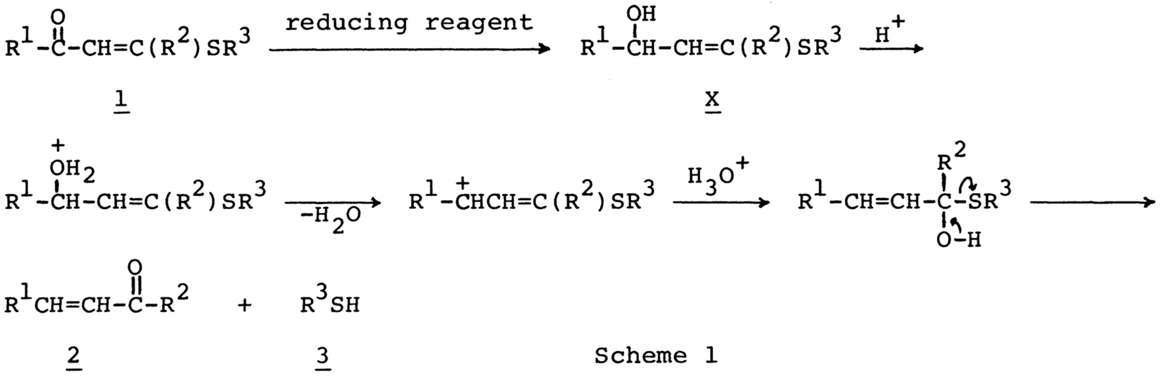


$$\underset{\underline{1}}{R^1-\overset{O}{\overset{\|}{C}}-CH=C(R^2)SR^3} \xrightarrow[\text{Method B}^{b)}:\ NaBH_4]{\text{Method A}^{a)}:\ LiAlH_4} \underset{\underline{2}}{R^1CH=CHCOR^2} + \underset{\underline{3}}{R^3SH} + \underset{\underline{4}}{R^1\overset{OH}{\overset{|}{C}}HCH_2CH(R^2)SR^3} + \underline{1}$$

	R^1	R^2	R^3	Method	Mol. ratio Red./1	Yield (%)[c)] 2	3	4	1
1b	Ph	Me	Pr^n	A	2	68.0-78.5	d	-	∿0
1c	Ph	Ph	Et	A	1/2	trace	d	∿0	quant.
1c	Ph	Ph	Et	A	2	trace	d	91.5	∿0
1c	Ph	Ph	Et	B	2	32.5	d	10.5	33.5
1d	Ph	Me	Ph	A	2	40.0	39.0	-	∿0
1d	Ph	Me	Ph	B	2	38.5	9.0	-	50.5
1e	Ph	H	Et	A	2	64.5-71.0	d	-	∿0
1f	Ph	H	Ph	A	2	3.5	7.0	79.5	∿0
1f	Ph	H	Ph	B	2	42.0-49.0	26.0-30.5	-	15.0-20.0
1g	Me	Ph	Et	A	2	-	-	quant.	∿0
1g	Me	Ph	Et	A	1/2	-	-	13.5	60.0
1g	Me	Ph	Et	B	1	15.5-18.5	d	-	69.5-85.5
1h	Me	Ph	Ph	A	2	-	-	quant.	∿0
1h	Me	Ph	Ph	B	2	trace	-	-	∿0
1i	Me	Me	Bu^n	A	2	27.5	d	-	∿0
1i	Me	Me	Bu^n	B	2	14.5	d	-	10.0
1j	Me	Me	Ph	A	2	62.5	6.5	-	7.0
1j	Me	Me	Ph	B	2	22.0	6.0	-	5.5
1k	$(CH_2)_3$		Et	A	2	35.5	d	-	∿0
1k	$(CH_2)_3$		Et	B	1	24.0	d	-	∿0

a) A solution of 1 and $LiAlH_4$ in ether was stirred for 2 h at room temperature and then refluxed for 0.5 h. The reaction mixture was treated with conc. HCl, then diluted with water and extracted with ether. b) A solution of 1 and $NaBH_4$ in MeOH was stirred for 2-24 h at room temperature. The reaction mixture was treated with conc. HCl, then diluted with water and extracted with dichloromethane. c) Yields determined by G.L.C.. d) Alkane thiol could not be detected.

allylic alcohol (X), which is formed by the selective 1,2-reduction. An attempt to isolate β-alkylthio allylic alcohol intermediate (X) was unsuccesful since the intermediate (X) was sensitive to moisture or acid.[4a)] The overall transformation of β-alkylthio α,β-unsaturated ketone (1) to α,β-unsaturated ketone (2) is outlined in Scheme 1.



$$R^1\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH{=}C(R^2)SR^3 \xrightarrow{\text{reducing reagent}} R^1\text{-}\overset{OH}{\overset{|}{C}H}\text{-}CH{=}C(R^2)SR^3 \xrightarrow{H^+}$$

$$R^1\text{-}\overset{\overset{+}{O}H_2}{\overset{|}{C}H}\text{-}CH{=}C(R^2)SR^3 \xrightarrow[-H_2O]{} R^1\text{-}\overset{+}{C}HCH{=}C(R^2)SR^3 \xrightarrow{H_3O^+} R^1\text{-}CH{=}CH\text{-}\underset{O\text{-}H}{\overset{R^2}{C}}\text{-}SR^3 \longrightarrow$$

$$R^1CH{=}CH\text{-}\overset{O}{\overset{\|}{C}}\text{-}R^2 + R^3SH$$

1 X 2 3

Scheme 1

References

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(b) H. Born, R. Pappo, and J. Szmuszkovicz, J. Chem. Soc., 1953, 1779.
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5) Satisfactory elemental analyses were obtained on all compounds.

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