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# ORGANIC REACTIONS AT ALUMINA SURFACES[1]. CHEMOSPECIFIC OXIDATION OF β-HYDROXY SULFIDES AND SELENIDES INTO THE CORRESPONDING β-KETO SULFIDES AND SELENIDES USING CHLORAL ON ACTIVATED ALUMINA.

Gary H. Posner* and Marc J. Chapdelaine
Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

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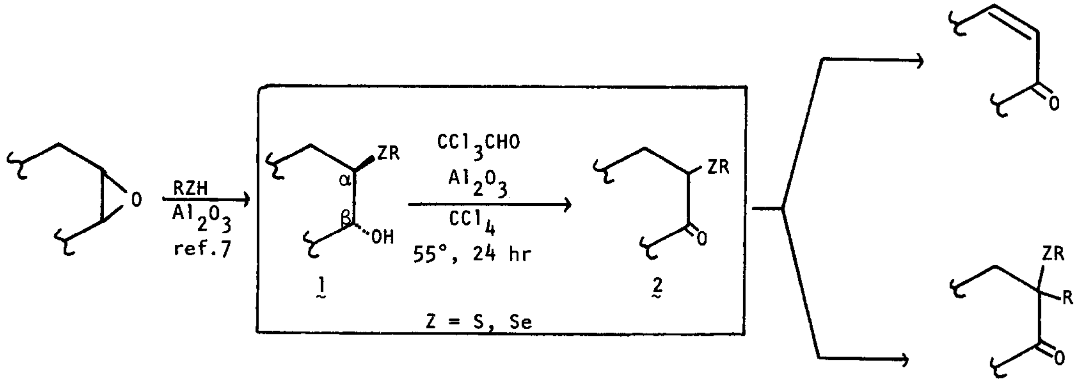
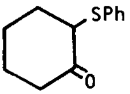
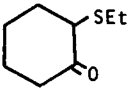
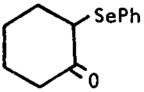
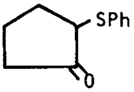
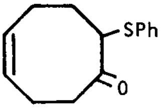
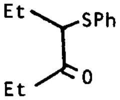
β-Keto sulfides and selenides 2 are used extensively for synthesis of α,β-unsaturated ketones and for regiospecific attachment of electrophiles at the carbon atom bearing the sulfide or selenide group (RZ-, eq. 1)[2-5]. β-Keto sulfides and selenides have been prepared usually from carbonyl precursors either *via* enolate ions and electrophilic sulfur and selenium species or *via* nucleophilic $RZ\bar{C}<$ species and carboxylic acid chlorides or anhydrides[2-5]. Despite the availability of β-*hydroxy* sulfides and selenides 1, no general method has been reported for specific hydroxyl oxidation in these bifunctional compounds containing also easily oxidized sulfur and selenium atoms[6]. We describe here an operationally simple and practical method for chemospecific oxidation of β-hydroxy sulfides and selenides 1 into the corresponding β-keto sulfides and selenides 2 using chloral on activated Woelm chromatographic alumina (eq. 1).



(1)

β-Hydroxy sulfides and selenides 1 were prepared conveniently using our recently reported procedure for alumina promoted epoxide opening by thiols and selenols[7]. Our oxidation results under optimized conditions are summarized in Table 1. Yields were reproducible to within ±5%.

Table 1. Chemispecific oxidation of β-hydroxy sulfides and selenides **1** into ketones **2** via eq. 1.

| Ketone **2** | % Yield[a] | Infrared (CHCl$_3$) $\nu_{CO}$(cm$^{-1}$) | bp[c](mm) or mp |
|---|---|---|---|
|  | 58(78) | 1710 | 100-105°(0.03)<br>(lit[d] 116-120°(0.05)) |
|  | 62(87) | 1700 | 95-100°(18)<br>(lit[e] 119-121°(30)) |
|  | 55(80) | 1700 | 58°<br>(lit[f] 56-57.5°) |
|  | 29(65)[b] | 1735 | 50∿60°(0.04)decomp[g] |
|  | 75(91) | 1710 | 90-95°(0.03)[h] |
|  | 64(74) | 1710 | 65-70°(0.03)[h] |

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a) This yield is of product isolated and purified by preparative tlc; the number in parenthesis represents the yield based on recovered β-hydroxy sulfide or selenide **1**; most reactions were done on a millimole scale; the first reaction was done on a 4-g scale.

b) Reaction conditions were 24 hr at 25° (rather than 55°).

c) Kügelrohr distillation.

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h) All new compounds gave satisfactory spectral (ir, nmr, mass) data.

The results in the table show 1) that the R group in the RZ- substituent can be either alkyl or aryl; 2) that both cyclic and acyclic thio- and seleno-alcohols can be oxidized; 3) that 6- and 8-membered cycloalkanols are oxidized in higher yields than cyclopentanols which give many decomposition products when exposed to chloral on alumina for a few hours at 55°; 4) that hydroxyl group oxidation by chloral on alumina proceeds not only in the presence of an adjacent phenylthio group but also in the presence of a carbon-carbon double bond. This last observation is especially significant because such oxidizing agents as ruthenium tetroxide[8] and 1-chlorobenzotriazole[9] react with alkenes as well as with alcohols and because transannular interaction of the cyclooctenyl double bond with the β-hydroxy sulfide portion of the molecule did not occur. The functional group specificity and the absence of double bond participation support our previous evidence (e.g. cyclobutanol oxidation)[10] that chloral on alumina acts as a hydride ion acceptor and thus as a two-electron oxidant. Finally, it is noteworthy that even though selenium undergoes oxidation more easily than sulfur[11], chloral on alumina is able to oxidize trans-2-phenylselenocyclohexanol chemospecifically at the hydroxyl group; to our knowledge, this is the first example of any hydroxy selenide being oxidized into the corresponding keto selenide[12].

Oppenauer oxidation under standard conditions (1:3:150, alcohol:aluminum isopropoxide: acetone in benzene at reflux for 24 hr and at room temperature for 48 hr)[13] did not convert 2-ethylthiocyclohexanol into the desired ketone. Only one β-hydroxy sulfide that we examined failed to react at all with chloral on alumina; cis-2-phenylthiocyclododecanol was recovered in good yield[6a]. The reason for its inertness is unclear.

A typical procedure is provided to illustrate the operational details of this selective oxidation method.

2-Phenylselenocyclohexanone from trans-2-phenylselenocyclohexanol: Woelm W-200 neutral alumina (ICN Pharmaceuticals, Inc., Cleveland, Ohio) was heated in a quartz vessel at 400° and 0.06 torr for 24 hr[14]. About 5 g of this freshly activated alumina was transferred inside a nitrogen-filled glove bag to an oven-dried, tared 25 ml round bottom flask containing a magnetic stirring bar. The flask was then stoppered and removed from the glove bag. About 6 ml of carbon tetrachloride containing 255 mg (1.0 mmol) of trans-2-phenylselenocyclohexanol[7b] was then added. After stirring for 0.5 hr at 25°C, 588 mg (4.0 mmol) of freshly distilled trichloroacetaldehyde in 1 ml of carbon tetrachloride was added and stirring was continued for 24 hrs at 55°C. The reaction was quenched by adding 10 ml of methanol and stirring for 0.25 hr. Vacuum filtration through Celite and washing the alumina with 70 ml of methanol gave crude reaction product. Preparative thin layer chromatography (development with 2:1 petroleum ether:diethyl ether) gave 139 mg (55%) of 2-phenylselenocyclohexanone: mp. 58°C; ir ($CHCl_3$) 3040 (w), 3000 (m), 2940 (s), 1700 (vs), 1580 (m), 1470 (m), 1440 $cm^{-1}$ (m); nmr ($CDCl_3$) $\delta$7.55 (m, 5H), 3.95 (t, 1H, CH-Se-), 2.5-1.5 (b, 8H); mass spectrum (70 eV) m/e 256, 254, 252, 251, 250 (ratio 9:50:25:10:11, molecular ion characteristic family of peaks for selenium due to natural isotopic abundance), and 64 mg (25%) of starting material.

The heterogeneous procedure we have described here makes synthetically valuable β-keto sulfides and selenides more accessible than heretofore and provides a new and effective route for overall conversion of epoxides into β-keto sulfides and selenides and into related structural units.

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