# Syntheses of β-Hydroxyselenides and Selenides from 1,2,3-Selenadiazoles: Selenophilic Reaction of Phenylmagnesium bromide on α-Selenoketones



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Received October 12, 1985

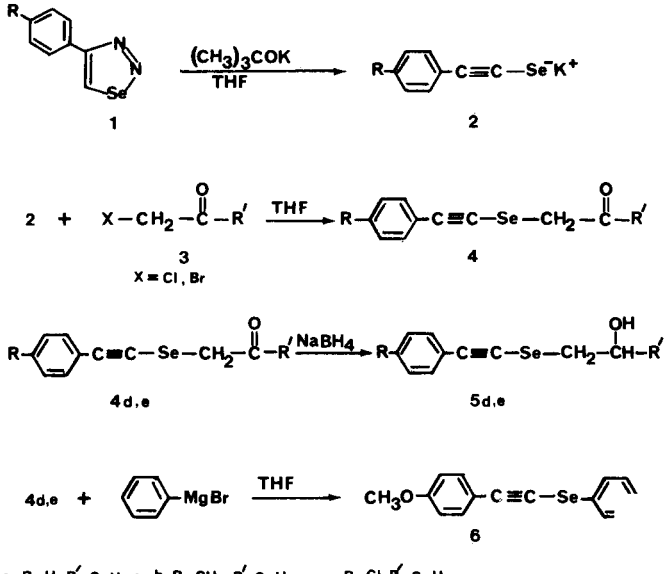
α-Selenoketones were prepared starting from 1,2,3-selenadiazoles and α-haloketones and were reduced to corresponding β-hydroxyselenides. The action of phenylmagnesium bromide on α-selenoketones was studied. Selenium was the site of nucleophilic attack by Grignard reagent.

*J. Heterocyclic Chem.*, **23**, 893 (1986).

Organo-selenium compounds have attracted much attention, mainly as important intermediates in various synthetic transformations [1-5].

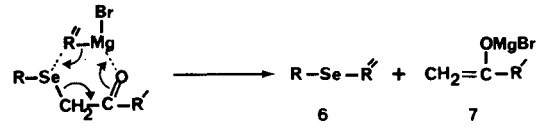
β-Hydroxy selenides can be made by reduction of selenides carrying an α-carbonyl group or from α-selenoaldehydes by treatment with Grignard reagents [6 and 7]. The latter is highly stereoselective but it is not generally applicable to α-selenoketones. Nevertheless, Leonard-Coppens and Krief [7] have described the formation of a β-hydroxy selenide from a reaction between α-selenoacetone and decanylmagnesium bromide, and reported that Grignard reagents do not add to other α-selenoketones under standard conditions. Despite numerous papers concerning selenium compounds, relatively little is known about the fate of organomagnesium reactions with α-selenoketones.

Scheme 1




a, R=H R′=C6H5 ; b, R=CH3 R′=C6H5 ; c, R=Cl R′=C6H5 ; d, R=CH3O R′=C6H5 , e, R=CH3O R′=CH3

Scheme 2




R= p–CH3O–C6H4–C≡C
R′= C6H5 , CH3
R″= C6H5

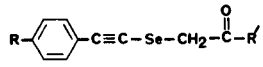
In the present work we prepared α-selenoketones by base-catalyzed decomposition of 4-substituted-1,2,3-selenadiazoles **1** and subsequent nucleophilic substitution reaction of the selenolate anions **2** with α-haloketones **3**. We prepared β-hydroxyselenides **5** by reduction of the α-selenoketones **4** with sodium borohydride and also studied the course of the reaction between α-selenoketones and phenylmagnesium bromide (Scheme 1), **6**.

Recently we reported the synthesis of ethynylselenocarboxylic acids [8] and selenium analogs of glycerol [9] by the nucleophilic attack of 2-arylethynylselenolates **2** on α-bromoesters and epichlorohydrin respectively. Accordingly, 1,2,3-selenadiazoles **1** were prepared from selenium dioxide oxidation of arylketone semicarbazones, following the reported procedures [10]. Selenolate anions **2** were generated *in situ* by the addition of potassium *t*-butoxide to a solution of 1,2,3-selenadiazoles **1** in tetrahydrofuran. Immediately after the evolution of nitrogen gas, 10-15 seconds, the corresponding α-haloketones **3** were added. It is important to observe the time limitation because delay in adding the α-haloketones would result in dimerization of selenolate anions to corresponding 1,4-diselenafulvenes [11]. The structure of all α-selenoketones **4** were confirmed by analytical and spectroscopic methods. The results are tabulated in Table I.

Reduction of the α-selenoketones **4d,e** by sodium borohydride afforded the corresponding β-hydroxysele-

Table I

α(2-[*p*Substitutedphenyl]ethynyl)selenoketones **4**



| No. | R | R' | Mp °C | Yield % | Formula | Elemental Analysis Calcd. C% | (Found) H% | IR, cm$^{-1}$ C≡C | C=O | $^1$H-NMR, ppm |
|---|---|---|---|---|---|---|---|---|---|---|
| **4a** | H | $C_6H_5$ | 52-53 [a] | 67 | $C_{16}H_{12}OSe$ | 64.21 (63.95) | 4.04 (4.04) | 2190 | 1670 | 4.5 (s, 2H), 7.5-8.0 (m, 10H) |
| **4b** | $CH_3$ | $C_6H_5$ | 53-54 [a] | 92 | $C_{17}H_{14}OSe$ | 65.18 (65.25) | 4.50 (4.51) | - | 1665 | 2.4 (s, 3H), 4.4 (s, 2H), 7.1-8.2 (m, 9H) |
| **4c** | Cl | $C_6H_5$ | 78-79 [b] | 97 | $C_{16}H_{11}ClOSe$ | 57.59 (57.48) | 3.32 (3.32) | - | 1670 | 4.3 (s, 2H), 7.3-8.1 (m, 9H) |
| **4d** | $CH_3O$ | $C_6H_5$ | 110-111 [b] | 65 | $C_{17}H_{14}O_2Se$ | 62.01 (62.12) | 4.29 (4.28) | 2190 | 1670 | 4.0 (s, 3H), 4.6 (s, 2H), 7.2-8.1 (m, 9H) |
| **4e** | $CH_3O$ | $CH_3$ | 54-55 [c] | 70 | $C_{12}H_{12}O_2Se$ | 53.95 (53.93) | 4.53 (4.52) | 2190 | 1700 | 2.4 (s, 3H), 3.6 (s, 2H), 3.8 (s, 3H), 6.8 (d, 2H), 7.4 (d, 2H) |

[a] Purified by flash chromatography, acetone-hexane (1.2:8.8). [b] Recrystallized from ethanol. [c] Purified by flash chromatography, ethyl acetate-hexane (2.8:7.2).

nides **5d,e** in excellent yield. The choice of sodium borohydride, as a reducing agent, was to preserve the nature of the acetylenic group in the molecule.

In a further study we reacted the α-selenoketones **4d,e** with phenylmagnesium bromide in tetrahydrofuran. After reaction work up we were not able to detect any β-hydroxyselenides. Instead, after purification by flash chromatography, the selenide **6** was obtained in both cases. This indicates that the selenium, rather than the carbonyl group, was attacked by the nucleophilic organic group of the Grignard reagent. This observation represents a nucleophilic substitution at selenium with the carbon atom playing the role of the leaving group. The driving force seems to be the stability of enolate anion formed. Hence the structural features favorable to this incipient enolate will facilitate the selenophilic reactions. A 6-centered cyclic transition state can account for this transformation (Scheme 2).

## EXPERIMENTAL

Infrared spectra were determined on a Perkin Elmer Infracord spectrophotometer using mineral oil mulls or as a thin film. The $^1$H nmr spectra were obtained on a Perkin Elmer R-12 instrument. Chemical shifts are reported on δ scale relative to TMS in deuteriochloroform. Melting points were taken on Fisher-Johns hot stage apparatus. The 4-aryl-1,2,3-selenadiazoles **1** used as starting material were prepared by previously described methods [10].

Preparation of α-Selenoketones **4a-e**. General Procedure.

To a stirred solution of 4-aryl-1,2,3-selenadiazole (**1**, 0.01 mole) in dry tetrahydrofuran (30-50 ml) potassium *t*-butoxide (0.01 mole) was added. After the evolution of nitrogen gas has ceased (15-20 seconds), the appropriate α-haloketone (**3**, 0.01 mole) was added in one portion. The mixture was stirred for one hour at room temperature. The solvent was evaporated under reduced pressure, water (50 ml) was added to the residue and extracted with ether (3 x 50 ml). After drying the organic solution on magnesium sulfate, the solvent was removed. The solid was purified either by recrystallization or by flash chromatography. For physical and spectroscopic data see Table I.

Reduction of α-Selenoketones **4d,e** to β-Hydroxyselenides **5d,e**.

To a hot solution of α-selenoketone (**4d** or **4e**, 0.002 mole) in ethanol (200 ml), sodium borohydride (0.004 mole) was added. After 15 minutes water was added (30 ml) and was heated to the boiling point. It was filtered and the filtrate was cooled to room temperature. The solvent was evaporated under reduced pressure. To the residue water (50 ml) was added and the mixture extracted with chloroform (3 x 30 ml). The organic solution was dried on magnesium sulfate and the solvent was removed under reduced pressure.

1-Phenyl-2-(2-[*p*-methoxyphenyl]ethynylselenomercapto)ethanol (**5d**).

This compound was obtained as an oil, yield 93%, purified by flash chromatography (acetone-hexane 3:7); ir (film): ν max = 3500 (OH), 2190 cm$^{-1}$ (C≡C); nmr (deuteriochloroform): δ = 2.8 (br s, OH), 3.3 (br d, 2H), 3.9 (s, 3H), 5.4 (m, 1H), 7.2-7.7 ppm (m, 9H).

*Anal.* Calcd. for $C_{17}H_{16}O_2Se$: C, 61.64; H, 4.87. Found: C, 61.47; H, 4.94.

1-(2-[*p*-Methoxyphenyl]ethynylselenomercapto)-2-propanol (**5e**).

This compound was obtained as an oil, yield 80%, purified by flash chromatography (ethyl acetate-hexane 1:3); ir (film): ν max = 3500 (OH),

2160 $cm^{-1}$ (C≡C); nmr (deuteriochloroform): δ = 1.3 (d, 3H), 2.5 (br s, OH), 2.9 (br d, 2H), 3.75 (s, 3H), 4.3 (m, H), 6.8 (d, 2H), 7.3 ppm (d, 2H).

Reaction of α-Selenoketones **4d,e** with Phenylmagnesium Bromide.

α-Selenoketones (**4d** or **4e** 0.004 mole) in anhydrous tetrahydrofuran (15 ml) was added to a solution of phenylmagnesium bromide (0.005 mole) in tetrahydrofuran (15 ml) in 10 minutes, at room temperature, and under dry nitrogen gas. The mixture was refluxed for one hour. After cooling to room temperature, it was hydrolyzed by pouring the content over 10% sulfuric acid and crushed ice. It was extracted with ether (3 x 30 ml), washed with sodium bicarbonate, and after drying the organic solution on magnesium sulfate the solvent was evaporated under reduced pressure. The oily residue was subjected to flash chromatography using ethyl acetate-hexane 8:92 as eluent. In both cases, when **4d** and **4e** were used as starting material only one compound, (2-[*p*-methoxyphenyl]-ethynyl)phenylselenide (**6**), was recovered in pure form.

Compound **6** had mp = 43°, yield 30% in both cases, ir (Nujol): ν max = 2190 $cm^{-1}$ (C≡C); nmr (deuteriochloroform): δ 3.8 (s, 3H), 6.8-7.8 ppm (m, 9H).

*Anal.* Calcd. for $C_{15}H_{12}OSe$: C, 62.73; H, 4.21. Found: C, 62.87; H, 4.22.

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