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Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

Reductive Removal of Phenylseleno Groups from a-Phenylseleno Carbonyl Compounds by Means of Tellurolate Anions

C. C. Silveira^a, E. J. Lenardão^a & J. V. Comasseto^b ^a Departamento de Química, Universidade Federal de Santa Maria, 97119-900, Santa Maria, RS, Brazil ^b Instituto de Química, Universidade de São Paulo, P. O. Box 20780, São Paulo, SP, Brazil

Available online: 04 Jan 2007

To cite this article: C. C. Silveira, E. J. Lenardão & J. V. Comasseto (1994): Reductive Removal of Phenylseleno Groups from α -Phenylseleno Carbonyl Compounds by Means of Tellurolate Anions, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:4, 575-582

To link to this article: <u>http://dx.doi.org/10.1080/00397919408011508</u>

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Reductive Removal of Phenylseleno Groups from α-Phenylseleno Carbonyl Compounds by Means of Tellurolate Anions

C.C.Silveira*, E.J.Lenardão Departamento de Química,Universidade Federal de Santa Maria 97119-900-Santa Maria-RS-Brazil

> J.V.Comasseto Instituto de Química, Universidade de São Paulo P.O.Box 20780-São Paulo-SP-Brazil

Abstract: α-Phenylseleno carbonyl compounds are reduced to the corresponding selenium free carbonyl compounds by reaction with organic and inorganic tellurolate anions.

Tellurium compounds exhibit unique properties as synthetic reagents¹. Among these properties is the ability of several easily prepared organic and inorganic anionic species of this element to selectively reduce several classes of organic substrates with advantages over the known methods to perform similar transformation^{1d,e}. One of the first uses of such tellurium reagents as reducing agents was the transformation of α -halo-, α -acetoxy-, α -mesyloxy- and α -thiophenylacetophenones into the corresponding ketones by means of thienyltellurolate^{1d,2}. In recent years a few other examples of substituent removal from the α -position of α -substituted carbonyl compounds using tellurium reagents have been reported le.

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In spite of the wide use of α -selenocarbonyl compounds as synthetic intermediates³ no attempts have been made to apply the tellurium methodology to remove the organoselenium moiety from α -selenocarbonyl compounds⁴.

Recently we needed to remove the phenylseleno group from ethyl-(α -phenylseleno)-phenyl acetates in view of the instability of these compounds⁵. We found that a catalytic amount of dithienylditelluride in ethanol and a 5% solution of NaBH₄ in 5% aqueous sodium hydroxide at room temperature promoted the removal of the phenylseleno group and the hydrolysis of the ester group of ethil-(α - phenylseleno)-o,m-dimethyl phenyl acetate, leading to the corresponding arylacetic acid in few minutes in 80% yield. In view of this result we decided to apply the methodology for the reduction of other α -phenylseleno carbonyl compounds and found that the reaction is not as easy as was for the above isolated example. In this paper we describe the scope and limitations of the tellurium species promoted reduction of α -phenylseleno carbonyl compounds.

Procedure A that makes use of the above mentioned conditions⁵ (Eq. 1, Table 1) was employed for the reduction of a number of α -phenylseleno esters.



The products obtained in good yields were the corresponding arylacetic acids free of selenium (entries 1-6, Table 1). Malonic acid was obtained in 70% yield by the reduction of diethyl-(α -phenylseleno) malonate (entry 7a, Table 1). α -Phenylseleno-acetic acid was also efficiently reduced by this method (entry 1a, Table 1). The yield of the reduced acids dropped in the case of the more sterically hindered esters (entries 3a, 4a).

By changing the reaction conditions, generating the tellurium reducing agent from elemental tellurium and sodium hydride in DMF^{1e} (Eq. 2,Method B), it was possible to selectively remove the phenylseleno group without hydrolysis of the ester group. Alternatively the selective removal of the phenylseleno group was effected by generating the tellurium reducing species from

elemental tellurium and sodium borohydride in DMF^{1e} (eq. 2, entries 3b, 4b, 7c, Method C).

PhSe

$$R \longrightarrow OR^{1} \frac{Te/NaH/DMF/140^{0}, \text{ then } 0^{0} \text{ (Method B) or}}{Te/NaBH_{4}/DMF/70^{0}, \text{ then } 0^{0} \text{ (Method C)}} R \longrightarrow OR^{1}$$
(2)

Similar results were obtained using sodium borohydride and catalytic amounts of diphenyl diselenide (Eq. 3, Table 1, entries 2b, 7b, 8, Method E).

$$R = \frac{OR^{1}}{O} = \frac{NaBH_{4}/(PhSe)_{2} (cat.)}{EtOH, r.t., 2min. (Method E)} = R = \frac{OR^{1}}{O}$$
(3)

The removal of the phenylseleno group from α -phenylseleno ketones was more troublesome⁴. By using method A, α -phenylseleno acetophenone was transformed into 1-phenyl ethanol. The selective removal of the phenylseleno group in this case was achieved by using method B (entries 9a,b, Table 1). Method C was used to remove the phenylseleno group from t-butyl-(α -phenylseleno) acetoacetate, leading to t-butyl-3-hydroxy butanoate (entry 8, Table 1).

The reduction of cyclic α -phenylseleno ketones was not possible using the preceding methods. Only by using lithium butyltellurolate in THF generated under aprotic conditions it was possible to remove the phenylseleno group (entry 10, Table 1). Even using two equivalents of lithium butyltellurolate a part of starting material was recovered after the work up.

In conclusion, it was possible to selectively remove the phenylseleno group from α -phenylseleno carboxylic acids, esters, ketones, β -ketoesters and malonic esters by means of tellurium reagents. However the reaction conditions and reagents have to be conveniently chosen in order to obtain the desired product.

DLC-

	Starting Material	Product ^c	Method [Yield, (%)]	
1.	Ph Se a		1a R = H	A (80)
		OH o	1b R = Et	A (96)
			2 a R = H	Α
2.		$\widehat{\mathbf{O}}$	$2 \mathbf{b} \mathbf{R} = \mathbf{E}\mathbf{t}$	(80)
			2 b R = Et	B (60)
	Ph Se			E (84)
	o a		3 a R = H	A (12)
3.	Ph Se	O O	3 b R = Et	C (86)
			$3 \mathbf{b} \mathbf{R} = \mathbf{E}\mathbf{t}$	B (60)
	a) O		A
4.			4 a R = H	(47)
			$4 \mathbf{b} \mathbf{R} = \mathbf{E}\mathbf{t}$	С
	Sern	\sim		(90)
	a a			
5.	Ú OFt	Ă,		Α
	SePh	I OH		(68)

Table 1 - Reductive Removal of the Phenylseleno Group from α -Phenylseleno Carbonyl Compounds.

	Table 1 continued			
	Starting Material	Product ^c	Method [Yield, (%)]	
6.	Ph Se II O	ОН		A (77)
7.	Ph Se b Et O $\downarrow $ Q Et O Et Q O Et Q O E T O O O E T O O E T O O E T O O E T O O E T O O E T O O E T O O E T O O E T O O E T O O O E T O O E T O O O E T O O O E T O O O O	$ \begin{array}{c} \mathbf{R} \\ \mathbf{R}^{1}\mathbf{O} \\ \mathbf{I} \\ \mathbf{O} \\ \mathbf{O}$	7a R=R ¹ = H 7b R=H R ¹ = Et 7c R=R ¹ = Et	A (70) E (75) C (64)
8.	0 0 b $\downarrow 0 0$ SePh			C (63) E (78)
9.	o b U SePh	X Y	9a X = OH; Y = H 9b X,Y = O	A (92) B (67)
10.	SePh			D (60)

a. Prepared as described in reference 5; b. Prepared by treating the corresponding enolate with phenylselenenyl bromide^{4a}; c. The spectral data agree with the proposed structures; d. Purity of the compounds obtained: 1a: mp 74-76°C (lit.⁶ 77-78.5°C); lb: 100% pure by GC; 2a: mp 110° C (lit.⁷ 105°C); 2b; >83% pure by GC; 3a: mp 163-167°C (lit.⁸ 164°C); 3b: 99% pure by GC; 4a: two peaks by GC, 96% pure; 4b: two peaks by GC, 99% pure; 5: two peaks by GC, 99% pure; 6: as the ethyl ester, GC/MS (100% purity): m/e 263(M-1), 218, 204, 191(100%), 164; 7a: mp 134-137°C (lit.⁹ 135-137°C); 7b:>90% by GC; 7c: 100% by GC; 8: 100% by GC; 9a: 100% pure by GC; 9b: 98% by GC; 10: mp 46-48°C (lit.¹⁰ 47-50°C), 95% by GC.

Experimental Section

Typical experiments for the phenylseleno group removal are as follows:

a. <u>Method A</u>: To a solution of the ethyl α -phenylseleno phenyl acetate (0.319g, 1 mmol) and dithienylditelluride (0.01g, 0.024mmol) in ethanol (8mL) under nitrogen at r.t. was added a solution of 5% NaBH₄ (in aqueous 5% NaOH) until the red color of the solution was faded. After 5 min stirring at r.t. the reaction was diluted with H₂O, acidified with 3N HCl, extracted with ethyl acetate and dried over MgSO₄. After the solvent evaporation the residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate (9 : 1). Yield of 1a: 0.11g (80%); mp 74-76 °C (lit.⁶ 77-78.5°C); IR 2930 cm⁻¹ (vOH), 1690 cm⁻¹ (v CO).¹H NMR (80 MHz, CDCl₃) 3.63(s,2H); 7.29(s,5H); 9.36(bs,1H).

b. Method B: A mixture of elemental tellurium (0.127g, 1mmol) and sodium hydride (0.0528g;2.2mmol) in dimethylformamide (3mL) was heated at 140°C under nitrogen and magnetic stirring for 1h. The resulting violet solution was cooled to 0°C in an ice bath and treated dropwise with a solution of ethyl α -(phenylseleno) mesityl acetate (0.361g, 1mmol) in DMF (2mL). A vigorous reaction occurred and the color of the solution changed from violet to dark brown. After the addition the mixture was diluted with diethyl ether and filtered on celite, the filtrate was washed 3 times with water and dried with MgSO₄. The solvent was evaporated and the residue was purified as above. Yield of 3b: 0.12g (60%); GC/MS (>99% putity):m/e 206 (M⁺), 160, 133 (100%), 105, 91; IR (neat) vmax. 1738cm⁻¹; ¹H NMR (80MHz, CDCl₃) 1.16 (t,3H,j=7.2Hz); 2.18 and 2.21 (2s,9H); 3.48 (s,2H); 4.01 (q,2H,j=7.2Hz); 6.70 (s,2H).

c. <u>Method C</u>: A mixture of elemental tellurium (0.0127g, 0.1mmol) and NaBH₄ (0.12g, 3mmol) in DMF (3mL) under nitrogen and magnetic stirring was heated at 70°C for 0.5h. Then the violet solution was cooled to 0°C and a solution of the α -(phenylseleno)t-butyl acetoacetate (0.313g, 1mmol) in ethanol (1mL) was added

dropwise. A vigorous reaction occurred, the color of the reaction mixture changing from violet to bright brown. Then water (3mL) was added and the mixture was acidified with 3N hydrochloric acid (10mL) and extracted with diethil ether (3x25mL). The organic layer was dried with magnesium sulfate and the solvent was evaporated. The residue was purified as above. Yield of 8: 0.10g (63%);GC/MS (100% purity): m/e 161 (M+2), 127, 105, 87, 57 (100%); IR (neat) 3432 cm⁻¹ (vOH), 1727 cm⁻¹ (vCO); ¹H NMR (60 MHz, CCl₄) 1.1 (d,3H,j=6.9Hz); 1.39 (s,9H); 2.22 (d,2H,j=6.9Hz); 3.4 (1H,-OH); 3.98 (sext,1H,j=6.9Hz).

d. Method D: Through a suspension of elemental tellurium (0.191g, 1.5mmol) in THF (6mL) was bubbled nitrogen during a few minutes. Then the flask was closed and n-BuLi (1.1mmol of a 2.48M solution in hexane) was slowly added at room temperature. The mixture was stirred for 40 minutes at room temperature, resulting in a yellow solution. Then the α -(phenylseleno) t-butyl cyclohexanone (0.309g, 1mmol) in THF was added causing the darkening of the reaction mixture. Addition of water (5mL) followed by extraction with methylene dichloride (3 x 25mL), drying with magnesium sulfate and evaporation of the solvent gave an oil, which was purified by column chromatography on silica gel eluting with hexane/ethyl acetate (9 : 1). Yield of 10: 0.092g (60%); mp 46-48 °C (lit.¹⁰ 47-50 °C); ¹H NMR (60 MHz, CCl₄) 0.92 (s,9H); 1.10-2.44 (m,8H).

e. <u>Method E</u>: To a solution of diphenyldiselenide (0.01g) and the diethyl α -(phenylseleno) malonate (0.315g, 1mmol) in ethanol (3mL) at room temperature was added sodium borohydride (0.04g, 1mmol). A vigorous instantaneous reaction was observed. The reaction mixture was treated with 3N hydrochloric acid (10mL) and extracted with ethyl acetate. The organic layer was dried with magnesium sulfate, evaporated and the residue was purified by column chromatography on silica gel eluting with hexane to remove the diphenyldiselenide and with hexane/ethyl acetate (9 : 1) to remove the product. Yield of 7b: 0.12g (75%); IR (neat) 1750, 1728 cm⁻¹;GC/MS(> 99% purity): m/e 160(M + 1, 100%), 133, 115, 87, 69, 60; ¹H NMR (80 MHz, CDCl₃) 1.27 (t,6H,j=7.2Hz); 3.23 (s,2H); 4.15 (q,4H,j=7.2Hz).

Acknowledgments: The authors thank the following agencies for support: FAPERGS, PADCT, GTZ, CNPq and FAPESP.

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(Received in the USA 04 May 1993)

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