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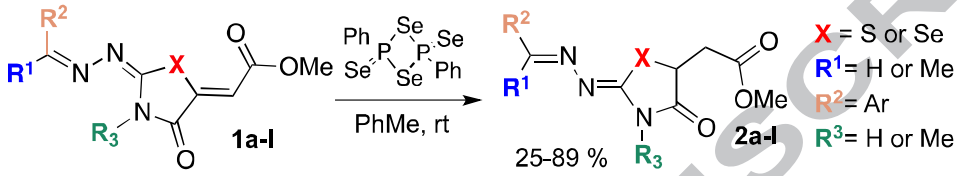

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Woollins' Reagent promotes selective reduction of α,β–unsaturated thiazo and selenazolidinones

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ABSTRACT

In this work we describe the Woollins' reagent as useful for the selective reduction of the double bond of 2-α,β-unsaturated thiazo and selenazolidinones. The reaction took place in toluene at room temperature to give the corresponding saturated heterocycles in good yields, eleven examples are given. The scope of the reaction is also discussed, been esential the conjugated ester to the double bond.

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1. Introduction

Woollins' reagent (WR) is the 2,4-Bis(phenyl)-1,3-diselenadiphosphetane-2,4-diselenide and it plays an essential role in the selenation of organic compounds, see Figure 1.[1] It is described that reacts with secondary and tertiary amides to obtain selenoamides by simple oxygen-selenium exchange.[2] The reaction of arylnitriles with WR/H_2O produces arylselenoamides.[3] It has also been used for the synthesis of selenadiazoles,[4] and P–Se heterocycles.[5] Another application is the C-C bond formation for the reductive coupling reaction of aldehydes and ketones,[6] see Figure 1.

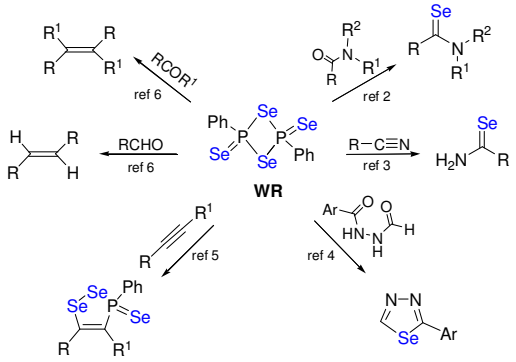
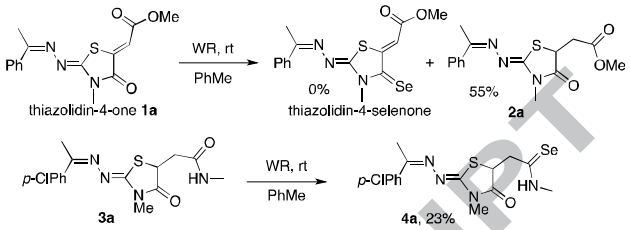


Figure 1. Synthetic applications of Woollins'Reagent (WR).

The advantages of using WR as selenating agent relies on its better stability on air, compared with H_2Se, and that it is either commercially available or easily prepared from $PhPCl_2$ and Na_2Se.[5]

The interest in organoselenium compounds has been growing during the last decades due to its importance as useful intermediates in synthetic chemistry,[7] and as new materials,[8] but the most outstanding field is related to its biological and medicinal significance.[9]

As part of our interest in the preparation and biological evaluation of organoselenium compounds,[10,11] we worked on a general approach towards the synthesis of selenazolyl compounds. Based on the known uses of WR, we decided to explore its utility for the preparation of thiazolidin-selenones.



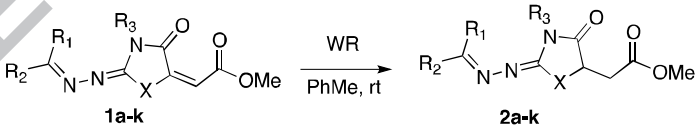
Scheme 1. Selective reduction of the α,β-unsaturated thiazolidinone **1a**, and synthesis of selenoamide **4a**, using WR

When thiazolidinone **1a** was treated with WR in toluene at room temperature, the reduced thiazolidin-4-one **2a** was obtained, instead of the expected thiazolidine-4-selenone, see Scheme 1. When we tryed to obtain the desired seleno derivative starting with the amide derivative **3a**, a selective O-Se exchange occurred at the exocyclic amide instead of the lactame ring, giving thiazolidinone selenoamide **4a**. Adding more equivalents or increasing the reaction time did not led to the O-Se exchange at the ring, see Scheme 1.

In order to gain insight into the reduction reaction, we decided to further explore the utility of WR as a selective reducing agent for α,β-unsaturated heterocycles. For this purpose, thiazolidinones **1b-1j** were treated with WR, using the same conditions used for **1a**, to obtain reduced compounds **2b-2j**.

Thiazolidinones **1a-j** were prepared according to a previous one-pot methodology, by condensation of aromatic aldehydes or ketones, thiosemicarbazide or methyl thiosemicarbazide and methyl acetylenedicarboxylate.[12] The reduced derivatives **2a-j** were smoothly obtained in toluene at room temperature using WR (1 eq) with moderated to good yields (25 to 89%), see Table 1.

Table 1. Selective olefin reduction in α,β-unsaturated thiazo and selenazolidinones, using WR



Entry	R^1	R^2	R^3	X	Yield %[a]
1	Ph	Me	Me	S	**2a**, 55
2	*m,p*-diCl Ph	Me	H	S	**2b**, 72
3	*m*-Br Ph	Me	H	S	**2c**, 77
4	*p*-Cl Ph	H	Me	S	**2d**, 68
5	*p*-CF_3 Ph	H	Me	S	**2e**, 79
6	*p*-OMe Ph	H	Me	S	**2f,** 74
7	*p*-OMe Ph	H	H	S	**2g**, 58
8	*m*-Me Ph	H	H	S	**2h**, 25
9	*o,m*-OMe Ph	H	H	S	**2i**, 89
10	Thiophene	H	H	S	**2j**, 50
11	*m,p*-diCl Ph	Me	H	Se	**2k,** 67

[a] Isolated yields.

Generally, N-methyl substituted thiazolidinones gave better yields than the N-unsubstituted ones, as evidenced for compounds **2f** *vs* **2g** (74 and 58% yield, respectively, see entries 6 and 7, Table 1). In this context, the reaction yields seem to be favored when using thiazolidinones derived from aldehydes (R^2 = H), instead of those derived from ketones (R^2 = Me), yields ranging from 68 to 74%, see entries 4-6.

Electron donating or withdrawing groups (EDG and EWG respectively) in the phenyl ring, did not affect the final yields. As an example, strong EDG present in **2i** displays the highest yield (89%, see entry 9, Table 1), but the methyl derivative **2h**, bearing a medium EDG showed the lowest yield (25%, see entry 8, Table 1). A similar behavior is observed when using EWG**.**

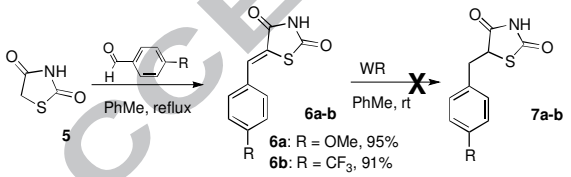
To further evaluate the scope of WR as a reducing agent, we prepared the α,β-unsaturated selenazolidinone **1k**, and the treatment with WR led to the reduced product **2k** in 67% yield (see entry 11, Table 1).

Benzylidenes **6a-b**,[13] were also selected as substrates; see Scheme 2. The main difference in both substrates is the α,β–conjugated group: a benzylidene (**6**) instead of an ester (**2**). When we applied the protocol to **6a-b** after 48 h at rt, or even at reflux, the starting material was recovered and no reduced product was formed, pointing out the needed of the ester as an EWG to reduce the substrate.

Looking for a plausible mechanism for the reduction we explored in literature for antecedents. It is described the use of NaSeH and LiSeH as selective reducing agents of α,β-unsaturated carbonyl compounds.[14] Recently, Alves and co-workers reduced electron deficient olefins as chalcones using PhSe-SePh.[15] WR was also used as a chemoselective reductive agent for diketones, reported by Jaisankar and co-workers.[16]

Based on this background and our findings, we suggested a possible mechanism for the selective reduction, as it is depicted in Scheme 3.

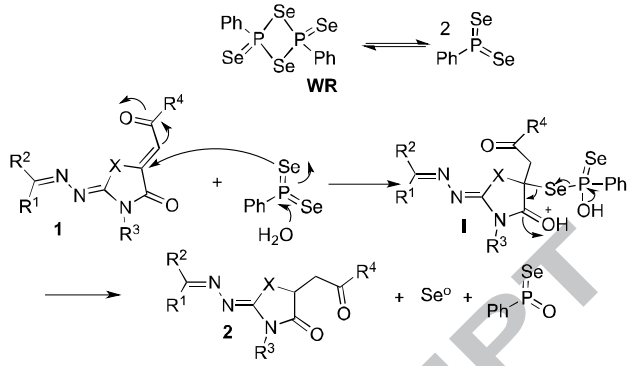
It is reported that WR is in equilibrium with a diselenaphosphorane species, being the reactive one in solution.[17] The conjugated addition of the Se atom to the α,β unsaturated ester gives the intermediate **I**, that could undergo Se^0 to form compound **2** formation.



Scheme 2. Synthesis of thiazolidinones **6a-b** and its attempt to reduction

According to the proposed mechanism for the selective α,β reduction, a 1,4 Se attack of the diselenaphosphorane specie would take place.

Comparing both electron withdrawing groups (ester compounds **1a-k,** and *p*-trifluoromethyl phenyl moiety, compound **6b**), it is noticeable that the conjugation obtained using an α,β ester gets a more activated 4 position, for the attack of the Se, according to the mechanistic proposal. These results



Scheme 3. Proposed mechanism for the selective reduction of α,β-unsaturated thiazo and selenazolidinone compounds.

could explain the importance of the α,β-conjugated ester in the selective reduction mechanism.

A series of heterocycles α,β-unsaturated esters (**1a-1k**) were selectively reduced to the corresponding saturated heterocycles **2a-2k**, using WR and mild reaction conditions.

It seems that the reaction is not sensitive to the electronic effects in the aromatic ring of the thiazolidinones. Therefore, when using either electron-donating (-OMe, -Me) or electron-withdrawing groups (-Br, -Cl), the desired reduction products were obtained in good yields (Table 2, entries 1-10). Besides, the position of the substituent groups did not considerably affect the reactivity.

In this sense, a new applicability of Woollins' reagent is described as a selective reducing agent of thiazo or selenazolidinone olefins conjugated to esters.

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References and notes

1. Woollins, J.D.; Hua, G. *Angew. Chem. Int. Ed.* **2009**, *48*, 1368.
2. Bhattacharyya, P.; Woollins, J.D. *Tetr. Lett.* **2001**, *42*, 5949.
3. Hua, G.; Li, Y.; Slawin, A.M.Z.; Woollins, J.D. *Org. Lett.*, **2006**, 8,5251
4. Ostrowski, W.; Gierczyk, B.; Frański, R. J .*Heterocycl. Chem.* **2012**, *49*, 1266.
5. Gray, I.P; Bhattacharyya, P.; Slawin, A.M.Z.; Woollins, J.D. *Chem. Eur. J.* **2005**, *11*, 6221.
6. Hua, G.; Li, Y.; Slawin, A.M.Z.; Woollins, J.D. *Dalton Trans.* **2007**, *15*, 1477.
7. (a) Liotta, D.; Monahan, R. Science. **1986**, *231*, 356; (b) Wirth, T. *Angew. Chem. Int. Ed*. **2000**, *39*, 3740; (c) Rhoden, C. R. B.; Zeni, G. *Org. Biomol. Chem.* **2011**, *9*, 1301; (d) Levason, W.; Reid, G.; Zhang, W. *Dalton Trans*. **2011**, *40*, 8491.
8. (a) Garían, J. *Adv. Heterocycl. Chem*. **1995**, *62,* 249; (b) Uemoto, T. *Adv. Heterocycl. Chem.* **1995**, *64*, 323; (c) Swapna, K.; Murthy, S. N.; Nageswar, Y. V. D. *Eur. J. Org. Chem.* **2011**, *10*, 1940.
9. (a) Mugesh, G.; du Mont, W. W.; Sies, H. *Chem. Rev*. **2001**, *101*, 2125; (b) Nogueira, C. W.; Zeni, G.; Rocha, T. B. T. Chem. Rev. **2004**, *104*, 6255; (c) Ninomiya, M.; Garud, D R.; Koketsu, M. *Coord. Chem. Rev*. **2011**, *255*, 2968.
10. Pizzo, C.; Faral-Tello, P.; Salinas, G.; Fló, M.; Robello, C.; Wipf, P.; Mahler, S. G. *Med. Chem. Commun*. **2012**, *3*, 362.
11. Pizzo, C.; Faral-Tello, P.; Robello, C.; Mahler, G. *Eur. J. Med. Chem*. **2016**, *109*, 107.

12. Pizzo, C.; Saiz, C.; Talevi, A.; Gavernet, L.; Palestro, P.; Bellera, C.; Blanch, L.B.; Benítez, D.; Cazzulo, J.J.; Chidichimo, A.; Wipf, P.; Mahler, S.G. *Chem. Biol. Drug. Des*. **2011**, *77,* 166.
13. Castillo, V.; Fagúndez, C.; Martínez, V.; Peña, S.; Pizzo, C.; Saiz, C.; Scarone, L.; Mahler, S.G. *ALDEQ*, **2012**, *27*,161.
14. Nishiyama, Y.; Yoshida, M.; Ohkawa, S.; Hamanaka, S. *J. Org. Chem.* **1991**, *56*, 6720.
15. Mesquita, K.D.; Waskow, B.; Schumacher, R.F.; Perin, G.; Jacob, R.G.; Alves, D. *J. Braz. Chem. Soc*. 2014, 25, 1261.
16. Mandal, M.; Chatterjee, S.; Jaisankar, P. Synlett 2012, 23, 2615.
17. Hua, G.; Li, Y.; Slawin, A.M.Z.; Woollins, J.D. *Eur. J. Inorg. Chem.* **2007**, *6*, 891.

Supplementary Material

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