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New synthesis and cyclopropanation of α-phenylselanyl α,β-unsaturated ketones with non-stabilized phosphorus ylides

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ABSTRACT

A general method for the preparation of α-phenylselanyl enones is described. Phosphorus ylides react with these α-phenylselanyl enones in a 1,4-addition, leading to cyclopropanes and/or dihydrofurans, depending on the substitution pattern. This unusual reactivity is due to the phenylselanyl moiety, hindering the carbonyl of the enone and making it less prone to 1,2-additions or promoting conjugate addition by electronic effects.

1. Introduction

Organoselenium compounds are versatile reagents that can either act as nucleophiles or electrophiles and can generate radicals under mild conditions.[1] Indeed, due to the weakness of the carbon–selenium bond, it is easier to introduce, transform, or eliminate than sulfur. Among these compounds, α-selanylated α,β-unsaturated aldehydes have been shown to be good precursors of α-allenols, -allenamines or -allenyl chlorides after formation of the corresponding diene (Wittig) and allylic rearrangement of the selanylated moiety.[2] Following our studies on such compounds, we turned our attention to the preparation of α-selanylated α,β-unsaturated ketones and studied their reactivity toward phosphorus ylides. We now report on the surprising results that were obtained, as cyclopropanes and sometimes dihydrofurans were formed instead of the expected dienes.

Usually, α-phenylselanyl α,β-unsaturated ketones are prepared by α-selenenylation of the corresponding α,β-unsaturated ketones (PhSeX/amine[3] or $PhSeNR_2/SiO_2$[4]), by reaction of α-diazo-ketones with PhSeX,[5] by oxidation of propargylic phenylselenoderivatives,[6] or by trapping allenol- or enol-ethers by PhSeX.[7] Nevertheless, these methods are limited to non-hindered enones or non-aryl-substituted β-positions in order to achieve good yields, or necessitate the preparation of reactive intermediates. We therefore envisioned introducing the selenium moiety at the enal stage and then further converting enals into diverse enones by addition/oxidation sequence (Scheme 1). Due to the high sensitivity of the selenium atom to oxidation, highly chemoselective oxidation methods of allylic alcohols have to be used.

2. Results and discussion

α-Phenylselanyl α,β-unsaturated aldehydes **2** were prepared following our recently published procedure[2] and submitted to diverse alkyllithium reagents. The corresponding allyl alcohols **3**–**8** were obtained in good yields (57–88%) with methyl-, *n*-butyl-, and aryl-lithium whereas secondary and tertiary alkyllithium reagents (*s*-BuLi, *t*-BuLi) gave rise to lower yields (30–36%), as shown in Table 1. Allyl alcohols were then converted into enones by chemoselective oxidation, without affecting the selanylated moiety, by the mild PhSeSePh/*t*-BuOOH procedure.[8] Enones **9**–**14** were obtained in good yields, except for those in which R^1=H, due to their relative instability (Table 1). When starting enals were Z, substituted enones were obtained mainly (>95%) as *Z* isomers, as determined by ^1H NMR (through NOE experiments when possible) and ^{77}Se NMR spectrometric analyses. Indeed, as previously shown, ^{77}Se NMR is an efficient tool for the determination of the geometry of enals and dienes[2] and we extend this method to enones. Comparison of ^{77}Se chemical shifts (δ ppm) of enones **9**–**14** with those of the starting *Z*-enals **2b** (^{77}Se 261.0 ppm) and **2c** (^{77}Se 301.1 ppm) indicates that the substitution of the aldehyde hydrogen with R^2=Me, *n*-Bu, *s*-Bu, *t*-Bu, or Ph, respectively, generates a homogeneous deshielding of the Se atom of about 35, 36, 45, 80, or 90 ppm, respectively (Table 2).

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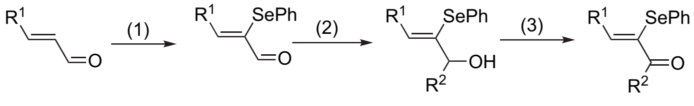


1
1a, R^1=H
1b, R^1=Me
1c, R^1=Ph
1d, R^1=*p*-MeO-C_6H_4

2
2a, R^1=H
2b, R^1=Me
2c, R^1=Ph
2d, R^1=*p*-MeO-C_6H_4

3-8
3a-d, R^2=Ph
4c, R^2=*p*-MeO-C_6H_4
5a-d, R^2=Me
6a-c, R^2=*n*-Bu
7b-c, R^2=*s*-Bu
8b-c, R^2=*t*-Bu

9-14
9a-d, R^2=Ph
10c, R^2=*p*-MeO-C_6H_4
11a-d, R^2=Me
12a-c, R^2=*n*-Bu
13b-c, R^2=*s*-Bu
14b-c, R^2=*t*-Bu

Scheme 1. Synthesis of α-phenylselanylenones **9–14**. (1) (a) Morpholinobenzeneselenamide (MBSe), (b) SiO_2; (2) R^2Li, THF, −70 °C; (3) PhSeSePh, *t*-BuOOH, 80 °C.

Table 1
δ^{77}Se of α-phenylselanyl enols **3–8** and α-phenylselanyl enones **9–14**

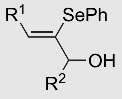
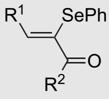
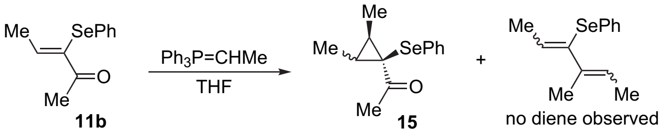
Entry	R^1	R^2						
			No.	Yield (%)	δ^{77}Se	No.	Yield (%)	δ^{77}Se
1	H	Ph	**3a**[9]	60	390.1	**9a**[12]	54	390.8
2	Me	Ph	**3b**	81	269.3	**9b**[4]	88	342.8
3	Ph	Ph	**3c**	88	323.4	**9c**[11,13]	89	404.5
4	*p*-MeO–C_6H_4	Ph	**3d**	85	313.2	**9d**	91	385.4
5	Ph	*p*-MeO–C_6H_4	**4c**	73	327.5	**10c**	80	409.9
6	H	Me	**5a**[9,10]	58	381.0	**11a**[6b,12,14]	54	413.1
7	Me	Me	**5b**	88	254.7	**11b**	85	295.8
8	Ph	Me	**5c**[11]	83	311.3	**11c**[15]	89	337.3
9	*p*-MeO–C_6H_4	Me	**5d**	84	301.4	**11d**	85	325.2
10	H	*n*-Bu	**6a**	57	379.6	**12a**		
11	Me	*n*-Bu	**6b**	75	252.0	**12b**	76	296.9
12	Ph	*n*-Bu	**6c**	66	310.9	**12c**	88	337.4
13	Me	*s*-Bu	**7b**	36	250.9	**13b**	86	304.4
14	Ph	*s*-Bu	**7c**	30	306.9	**13c**	89	349.7
15	Me	*t*-Bu	**8b**	36		**14b**	90	338.0
16	Ph	*t*-Bu	**8c**	31		**14c**	89	388.2

Table 2
δ^{77}Se of α-phenylselanyl enal **2** and α-phenylselanyl enones **9–14**

Enal (δ^{77}Se)	Enone (δ^{77}Se)	Δδ (ppm)	Enal (δ^{77}Se)	Enone (δ^{77}Se)	Δδ (ppm)
Z-**2b** (261.0)	**11b** (295.8)	34.8	**Z-2c** (301.1)	**11c** (337.3)	36.2
	12b (297.0)	36		**12c** (337.4)	36.3
	13b (304.4)	43.4		**13c** (349.7)	48.6
	14b (338.0)	77		**14c** (388.2)	87.1
	9b (342.8)	81.8		**9c** (404.5)	103.4

With enones **9–14** in hand, we explored their reaction with phosphorus ylides and started with enone **11b** (R^1=Me, R^2=Me) as model substrate. Addition of **11b** to a solution of ethylidenetriphenylphosphorane (R^3=Me, R^4=H) at rt in THF, surprisingly, yielded cyclopropane **15** in 12% yield, 47% of PhSeSePh, and no trace of the desired diene. After a brief survey of the reaction conditions (time and temperature), we found that heating the mixture at 50 °C for 12 h was beneficial, increasing the yield in **15** to 65% (along with 15% of PhSeSePh); again, no diene was observed (Scheme 2).

Cyclopropanations via 1,4-addition of phosphorus ylides to enones have been known in the literature for many years, but have never been developed because they generally occur only with highly hindered substrates in which 1,2-additions are not possible or require hard conditions.[16,17] The other methods involving nucleophiles other than phosphorus ylides mainly include sulfur ylides (Corey's ylide), but also ammonium ylides, carbenes, diazomethane, and tellurium derivatives, and have been recently reviewed.[18]



Scheme 2. 1,4-Addition of phosphorus ylide to enone **11b**.

The addition of Corey's ylides to α-phenylthioenones has recently been reported and allows the formation of cyclopropanes or dihydrofurans, depending on both the substituents on the enone and on the oxidation level of the sulfur atom (sulfur, sulfoxide, or sulfone).[19] The advantage of phosphorus ylides lays in the fact that more substituted cyclopropanes can in principle be obtained if alkylphosphorus ylides are used. We thus turned our attention to the cyclopropanation of α-phenylselanyl enones using different phosphorus ylides (Scheme 3, Table 3).

With R^1=Me, cyclopropanes **15–20** and **41–42** are the exclusive products, regardless of R^2 (Me or Ph), R^3, or R^4 (Me, *n*-Pr, butenyl), in yields ranging between 38 and 65%. The isolated amount of $(PhSe)_2$ ranged between 15 and 26%. The substituted cyclopropanes were isolated as cis and trans mixture at carbons 2 (R^1) and 3 (R^3) from 40/60 to 60/40. When R^2=Me, trans isomer is formed