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Synthesis of α-Halo β,γ-Unsaturated Esters From γ-Phenylseleno α,β-Unsaturated Esters

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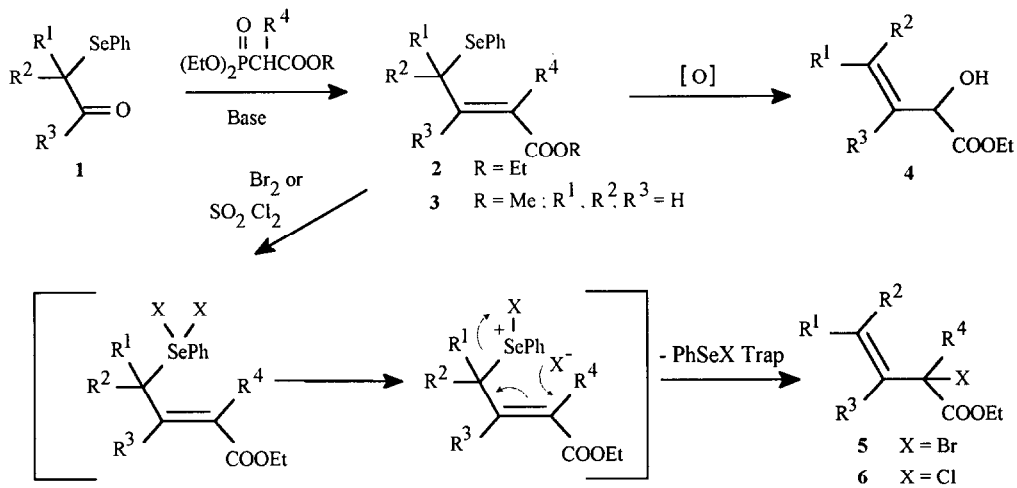
Abstract : γ-Phenylseleno α,β-unsaturated esters, prepared from α-phenylseleno aldehydes by Horner-Emmons reaction and treated with bromine or sulfuryl chloride, form adducts whose decomposition leads to α-halo β,γ-unsaturated esters in fair to good yields.

Some years ago, we prepared, α-hydroxy β,γ-unsaturated esters **4** by a [2,3]-sigmatropic rearrangement[1] of selenoxides derived from the γ-phenylseleno α,β-unsaturated esters **2**.[2] We now report a method for the synthesis of α-halo β,γ-unsaturated esters **5** and **6** simply by treating esters **2** with bromine and sulfuryl chloride respectively (Scheme).

Scheme



1

2 R = Et

3 R = Me ; R^1, R^2, R^3 = H

4

5 X = Br

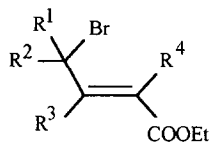
6 X = Cl

A literature survey shown that no general and efficient method exists today for the synthesis of this type of compounds. Alkyl 2-halo 3-butenoates have been prepared from alkyl 2-hydroxy 3-butenoates [3] or by deconjugation of ethyl 2-halo 3-methyl cinnamates with LDA in THF.[4] Other similar deconjugations have been proposed.[5,6] More recently, ethyl 2-chloro 2,3-disubstituted 3-butenoates have been prepared by calcium hypochlorite/acetic acid treatment of ethyl 2,3-disubstituted 2-butenoates.[7]

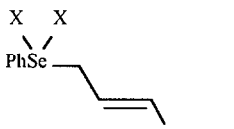
The unsaturated esters **2** were obtained from α-phenylseleno aldehydes **1** (R^3 = H),[8] phenylseleno propanone **1** (R^1, R^2 = H, R^3 = Me) and 2-phenylselenocyclohexanone (R^1 = H, R^2-R^3 = -$(CH_2)_4$-)[9] by Emmons-Horner olefination using triethyl phosphonoacetate[2] or triethyl 2-phosphonopropionate and nBuLi (Table). Methyl 4-phenylseleno 2-butenoate **3** (R^1, R^2, R^3, R^4 = H, R = Me) was prepared as described.[10]

Halogenating agents and alkyl phenylselenide give adducts whose decomposition forms alkyl halide and benzeneselenenyl halide.[11] While the bromination of α-phenylseleno aldehydes gives the α-bromoaldehydes[12], the chlorination of α-phenylseleno-aldehydes[12] and -ketones[13] leads to the formation of α-chloro α-phenylseleno carbonyl compounds.

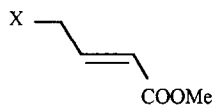
With esters **2**, the bromo and chloro adducts cannot be isolated. The decomposition, at room temperature, in the presence of ethyl vinylether, allows the synthesis of α-halo esters **5** and **6** (Table) except in the cases of two γ-substituents. **2e** and **2f** gave directly the γ-bromo esters **7e** and **7f** respectively[14]. We observed also the formation of γ-bromo esters **7** without addition of the PhSeX trap and the isomerisation **5** → **7** in the presence of a catalytic amount of diphenyldiselenide.



7



8 X = Br
9 X = Cl
10 X = I



11 X = Br
12 X = Cl
13 X = I

The difference in the isomeric nature of the products, when the reaction is achieved in the presence of ethyl vinylether, seems to indicate that the α-attack of the halide ion operates in all cases. Without the trap, the benzeneselenenyl halide formed adds to the double bond of **5**, the PhSe group fixed on the β-carbon, allowing the formation of the conjugated unsaturated esters **7** by a second loss of PhSeX. The mechanism of the isomerisation **5** → **7**, in the reaction conditions, is under investigation. γ-Bromo α,β-unsaturated esters such as **7** are easily prepared by N-bromosuccinimide treatment of the corresponding esters.[15]

The bromine treatment of ester **3** in hexane (- 40°C) furnishes a solid adduct **8** stable at room temperature.[16] The chloro adduct **9** and iodo adduct **10** were obtained using SO_2Cl_2 and I_2 respectively.[16] At more elevated temperatures, these adducts decompose.[17] Even in the presence of ethyl vinylether, a trap for benzeneselenenyl halides, mixtures are formed. They contain the corresponding γ-halo ester **11**, **12** or **13**.[17]

Due to the lack of preparative methods, the synthetic applications of α-halo esters **5** and **6** have not been extensively studied. We note : the thermal allylic rearrangement into γ-bromo esters,[3] the base-catalyzed isomerisation to α-chloro α,β-unsaturated esters,[7, 18, 19] the preparation of alkyl 2-amino 3-butenoates[4] and of vinylcyclopropanes.[20] Reactions with sulfur and nitrogen nucleophiles give α- or γ-substitution products.[7] The action of carbanionic species leads to substituted cyclopentenone and γ-alkyl α,β-unsaturated esters.[21, 22]

Work is in progress to extend this reaction to structures containing other functional groups and substituents, to study some reactions concerning the chemical properties of α-halo β,γ-unsaturated esters **5** and **6**.

Table

γ-Phenylseleno α,β-Unsaturated Esters **2** (R = Et) and α-Halo β,γ-Unsaturated Esters **5** and **6**.

Substrates **2** (R = Et)						Products **5**, **6**	
N°	R^1	R^2	R^3	R^4	Yield %	N°	Yield %
2a	Me	H	H	H	80[2]	**5a**	57
2b	Et	H	H	H	90[2]	**5b**	87
2c	iPr	H	H	H	85	**5c**	89
						6c	52
2d	$-CH(^{Ph}_{Me})$	H	H	H	60 (a)	**5d**	75
						6d	54
2e	$-(CH_2)_5-$		H	H	80	**5e**	0
2f	Et	Me	H	H	78	**5f**	0
2g	H	H	Me	H	81[2] (b)	**5g**	28
2h	H	$-(CH_2)_4-$		H	70[2] (b)	**5h**	79
2i	Me	H	H	Me	82 (b)	**5i**	70
2j	iPr	H	H	Me	61 (b)	**5j**	54

a) mixture of diastereoisomers (1/1) b) all esters were assumed to be E except for : **2g** E/Z : 3/1 ; **2h** E/Z : 7/3 ; **2i** E/Z : 1/1 ; **2j** E/Z : 85/15.

REFERENCES AND NOTES

1. Sharpless, K.B.; Lauer, R.F. *J. Am. Chem. Soc.*, **1972**, *94*, 7154-5.
2. Lerouge, P.; Paulmier, C. *Bull. Soc. Chim. Fr.*, **1985**, 1225-9.
3. Rambaud, R. *Bull. Soc. Chim. Fr.*, **1934**, 1342-55.
4. Chari, R.V.J.; Wemple, J. *Tetrahedron Lett.*, **1979**, 111-4.
5. (a) Mc Donald, I.A.; Lacoste, J.M.; Bey, P.; Wagner, J.; Zreika, M.; Palfreymann, M.G. *J. Am. Chem. Soc.*, **1984**, *106*, 3354-6 ; (b) Mc Donald, I.A.; Palfreymann, M.G.; Jung, M.; Bey, P. *Tetrahedron Lett.*, **1985**, *26*, 4091-2.
6. Duhamel, L.; Peschard, O.; Plé, G. *Tetrahedron Lett.*, **1991**, *32*, 4695-8.
7. Mathew, J.; Alink, B. *J. Org. Chem.*, **1990**, *55*, 3880-6.
8. Paulmier, C.; Lerouge, P. *Tetrahedron Lett.*, **1982**, *23*, 1557-60.
9. (a) Engman, L. *Tetrahedron Lett.*, **1985**, *26*, 6385-8 ; (b) Petragnani, N.; Comasseto, J.V.; Rodrigues, R.; Brocksom, T.J. *J. Organomet. Chem.*, **1977**, *124*, 1-12.
10. Fitzner, J.N.; Pratt, D.V.; Hopkins, P.B. *Tetrahedron Lett.*, **1985**, *26*, 1959-62.
11. (a) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon Press, **1986**, 102-4 ; (b) Morella, A.M.; Ward, A.D. *Tetrahedron Lett.*, **1984**, *25*, 1997-200 ; *Ibid.*, **1985**, *26*, 2899-

900 ; (c) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron*, **1988**, *44*, 2261-72.

12. Paulmier, C.; Outurquin, F.; Plaquevent, J.C. *Tetrahedron Lett.*, **1988**, *29*, 5893-6.
13. Engman, L.; Persson, J.; Tilstam, U. *Tetrahedron Lett.*, **1989**, *30*, 2665-8.
14. The adducts formed in hexane at - 40°C decompose at room temperature (10 min). The solution is added to methanol containing triethylamine and ethylvinylether in excess. After concentration, without heating, the α-haloesters **5** and **6** are purified by silicagel chromatography (elution hexane/CH_2Cl_2 9/1) and isolated as oils. ^{1}H-NMR for : **5c:** 4.74 (m, Hα), 5.79 (m, Hβ, Hγ); **6c:** 4.76 (m, Hα), 5.74 (m, Hβ), 6.05 (m, Hγ). J (Hz) : 8.3 (αβ), 5.8 (γδ), 15.4 (βγ); **5d:** 4.78 (m, Hα), 5.93 (m, Hβ, Hγ); **6d:** 4.72 (m, Hα), 5.64 (m, Hβ), 5.85 (dd, Hγ). J (Hz) : 7.8 (αβ), 5.0 (γδ), 15.1 (βγ), 0.8 (βδ). Without a trap of benzeneselenenyl bromide, the decomposition of bromo adducts gives the γ-bromo esters **7**. The compounds **2e** and **2f** give directly the γ-bromo esters **7e** and **7f** respectively which are also purified by chromatography. **7a** :[24] 74 %, **7b** :[24] 60 %, **7c** : 64 %; ^{1}H-NMR ($CDCl_3$) 5.93 (dd, Hα), 7.00 (dd, Hβ), 4.42 (dd, Hγ), 1.96 (m, Hδ). $J_{\alpha\beta}$=15.1 Hz, $J_{\alpha\gamma}$=0.7 Hz, $J_{\beta\gamma}$=9.5 Hz, $J_{\gamma\delta}$=5.5 Hz. The crude product contains 10 % of **5c**. **7e** : 60 %; ^{1}H-NMR ($CDCl_3$) 5.89 (d, Hα), 7.13 (d, Hβ). $J_{\alpha\beta}$=15.6 Hz. **7f** : 63 %; ^{1}H-NMR ($CDCl_3$) 5.89 (d, Hα), 7.08 (d, Hβ). $J_{\alpha\beta}$=15.6 Hz.
15. Moppett, C.E.; Sutherland, J.K. *J. Chem. Soc. (C)*, **1968**, 3040-2.
16. ^{1}H-NMR spectra of adducts ($CDCl_3$) **8:** 6.54 (d, Hα), 7.30 (dt, Hβ), 4.91 (d, Hγ). $J_{\alpha\beta}$=15.6 Hz, $J_{\beta\gamma}$=8.1 Hz; **9:** 6.44 (d, Hα), 7.34 (dt, Hβ), 4.97 (d, Hγ). $J_{\alpha\beta}$=15.5 Hz, $J_{\beta\gamma}$=8.1 Hz; **10:** 5.63 (d, Hα), 6.95 (dt, Hβ), 3.66 (d, Hγ). $J_{\alpha\beta}$=15.4 Hz, $J_{\alpha\gamma}$=8.1 Hz.
17. Adducts **8-10** were decomposed in $CHCl_3$ at reflux. The residue of each reaction contains the γ-haloesters. ^{1}H-NMR ($CDCl_3$) **11**[23]**:** 6.02 (d, Hα), 7.02 (dt, Hβ), 4.01 (d, Hγ). $J_{\alpha\beta}$=15.6 Hz, $J_{\alpha\gamma}$=1.3 Hz, $J_{\beta\gamma}$=6.7 Hz; **12:** 5.98 (d, Hα), 7.96 (dt, Hβ), 4.10 (d, Hγ). $J_{\alpha\beta}$=15.6 Hz, $J_{\alpha\gamma}$=1.6 Hz, $J_{\beta\gamma}$=5.4 Hz; **13:** 5.93 (d, Hα), 7.06 (dt, Hβ), 3.93 (d, Hγ). $J_{\alpha\beta}$=15.6 Hz, $J_{\alpha\gamma}$=0.8 Hz, $J_{\beta\gamma}$=8.1 Hz.
18. Vessière, R. *Bull. Soc. Chim. Fr.*, **1959**, 1645-50.
19. Mialhe, Y.; Vessière, R. *Bull. Soc. Chim. Fr.*, **1968**, 4181-91; *Ibid*, **1969**, 3687-92.
20. Ducher, S.; Sudre, J.P.; Vessière, R. *C. R. Acad. Sc.*, **1973**, 277C, 575-8; *Ibid.*, **1974**, 278C, 537-9.
21. (a) Mathew, J.; Alink, B. *J. Chem. Soc.*, Chem. Commun., **1990**, 684-6; (b) Mathew, J. *J. Org. Chem.*, **1990**, *55*, 5294-7.
22. Mathew, J. *J. Org. Chem.*, **1992**, *57*, 2753-5.
23. Loffler, A.; Norris, F.; Taub, W.; Svanholt, K.L.; Dreiding, A.S., *Helv. Chim. Acta.*, **1970**, *53*, 403-417.
24. Kraus, J.L.; Sturtz, G. *Bull. Soc. Chim. Fr.*, **1974**, (5-6, Pt. 2), 943-52.

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