Synthesis of New Asymmetric Phosphonylated Thiazolines and their Use in Olefination Reactions

Nicolas Leflemme, Patrice Marchand, Mihaela Gulea, Serge Masson*

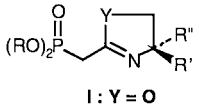
Laboratoire de Chimie Moléculaire et Thioorganique UMR 6507 CNRS, ISMRA-Université de Caen, 6 Bd. Maréchal Juin, 14050 Caen, France

Received 28 January 2000; revised 3 April 2000

Abstract: *N*-(2-Hydroxyalkyl)-2-phosphonoethanethioamides were prepared from a readily accessible phosphonodithioacetate and commercial chiral β-amino alcohols. Taking advantage of both the presence of the hydroxy group (nucleofuge) and of the C=S (nucleophile) in the same molecule, we obtained new chiral phosphonylated thiazolines by an intramolecular cyclisation using the Mitsunobu procedure. These thiazoline-phosphonates were then involved in Horner–Wadsworth–Emmons reaction to give asymmetric vinylic thiazolines.

Key words: phosphonate, dithioester, thioamide, thiazoline, Mitsunobu reaction, Horner–Wadsworth–Emmons reaction

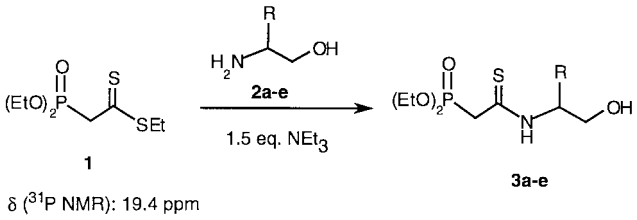
Although less studied than oxazolines,[1] their sulfur analogues, thiazolines, have recently seen an increasing interest due to the presence of this heterocycle in the structure of many biologically active compounds including natural products (such as anguibactin,[2] curacin A,[3] tantazoles and mirabazoles[4]). For example, L-084 (1-β-methylcarbapenem carrying thiazoline ring) is a new oral antibiotic,[5] arylvinyl thiazolines are antihelmintic and antifungal agents[6] and thiangazole alkaloid is the subject of particular attention because of its high potency in HIV inhibition.[4,7] Used several years ago as an aldehyde source by A. I. Meyers,[8] thiazolines continued to find applications as synthetic intermediates.[9] As well as phosphonylated oxazolines **I,**[10] sulfur analogues **II** are convenient Horner–Wadsworth–Emmons (H. W. E.) reagents for the introduction of a thiazoline ring into an organic structure.[6,7] Nevertheless, to the best of our knowledge, only two methods have been described for the synthesis of these thiazolines. The first starts from cyanomethyl phosphonate and either a β-aminoethanethiol[6] or a cysteine derivative.[7] The second, developed in our laboratory, employed phosphonodithioacetate and bromoethyl amine hydrochloride.[11] However, these syntheses cannot be easily generalised because of the limited availability of the starting materials (β-amino thiols or bromides). Therefore, efficient routes are still needed for the preparation of new phosphonylated thiazoline (especially with chiral thiazoline moiety).



I : Y = O
II : Y = S

This report describes a facile synthesis of chiral phosphonylated thiazolines starting from readily accessible ethyl phosphonodithioacetate[12] and commercial β-amino alcohols. The Mitsunobu procedure[13,14] was used to perform the internal cyclisation of intermediate hydroxy substituted thioamides. Some of the resulting phosphonylated thiazolines were then involved in the H·W·E reaction for the synthesis of new vinylic chiral thiazolines.

N-(2-Hydroxyalkyl)-2-phosphonoethanethioamides **3a–e** were readily prepared by amination[12,15] of the phosphonodithioacetate **1** with achiral or enantiopure amino alcohols **2a–e** (Scheme 1). Phosphonylated thioamides **3a–e** were thus obtained in good yields after purification (Table 1).



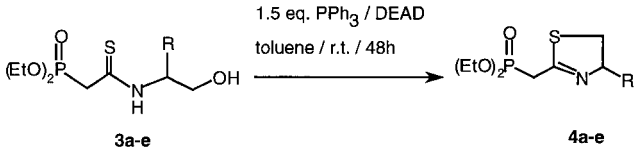
Scheme 1

The resulting thioamides **3a–e** were then treated with 1.5 equivalents of PPh_3/DEAD in toluene (Scheme 2). After 48 hours at room temperature, the reaction was complete

Table 1

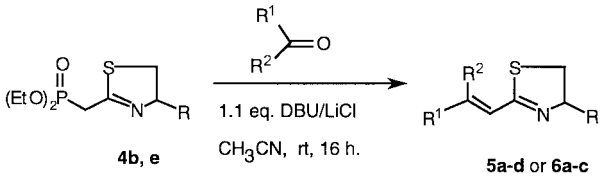
Product	R Amino alcohol	^{31}P NMR ($CDCl_3$), δ (ppm)	Isolated Yield (%)	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)
3a	H ethanolamine	23.2	87	–
3b	C_2H_5 *R*-(−)-2-aminobutanol	23.2	83	+30.9 (c=0.5)
3c	$(CH_3)_2CH$ *S*-(+)-valinol	23.5	79	−36.2 (c=0.5)
3d	C_6H_5 S-(−)-1-phenylglycinol	23.3	71	−87.6 (c=0.5)
3e	$CH_2C_6H_5$ S-(−)-phenylalaninol	22.9	80	−72.1 (c=0.5)

(as proved by ^{31}P NMR spectroscopy). The expected products **4a**–**e** were isolated in satisfactory yields (Table 2). Although the cyclisation seems quantitative according to ^{31}P NMR spectra of the crude reaction products, separation of these thiazolines from residual triphenylphosphine oxide by silica gel column chromatography proved difficult. However, this problem of purification can be easily solved by using PPh_3 fixed on solid support.[16] This increases the yield for **4c** and **4d** to 90% and 78%, respectively.



Scheme 2

The use of these phosphonylated thiazolines as H.W.E reagents was examined using the racemic product **4b**. With NaH as a base,[6] vinylthiazoline **5a** was produced in very low yield (18%). However, using DBU/LiCl in acetonitrile as the deprotonation agent,[7] various aldehydes and acetone could be successfully coupled. The reaction was then performed with the chiral thiazoline phosphonates **4b** and **4e** (Scheme 3). New racemic **5a**–**d** and chiral **5c*, 6a**–**c** vinylic thiazolines were thus obtained in good yields (Table 3). No loss of enantiomeric purity of the products under these basic conditions was confirmed by HPLC analysis on a Chiralpak AD column of the racemic **5c** and enantiopure product **5c***. An excellent selectivity (>99%) in favour of the *trans*-isomer was observed in each case.



Scheme 3

Table 2

Product	R	^{31}P NMR ($CDCl_3$), δ (ppm)	Isolated Yield (%)	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)
4a	H	23.1	51	–
4b	Et	22.9	78	+24.6 (*c* = 1.10)
4c	iPr	23.3	76 (90)[a]	−20.9 (*c* = 0.75)
4d	Ph	22.7	55 (78)[a]	−14.8 (*c* = 0.52)
4e	Bn	22.8	61	−29.4 (*c* = 0.5)

[a] Yields obtained using PPh_3 on solid support.

Table 3

Product	R	R^1	R2	Isolated Yield (%)	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)
5a	Et	Me	H	56	–
5b	Et	*i*-Pr	H	74	–
5c	Et	Ph	H	76	–
5d	Et	Me	Me	32	–
5c*	Et	Ph	Me	75	+12.7 (c = 1.0)
6a	Bn	Me	H	71	−15.1 (c = 0.5)
6b	Bn	*i*-Pr	H	75	−12.2 (c = 1.3)
6c	Bn	Ph	H	88	− 8.8 (c = 0.8)

In conclusion, this work describes an efficient synthesis of new chiral phosphonylated thiazolines using readily available starting materials (phosphonodithioacetate and chiral amino alcohols). These compounds could be used as Horner–Wadsworth–Emmons reagents and new vinylic thiazolines were obtained. Reactivity, complexing properties, and utilisation of these chiral thiazolines derivatives in asymmetric synthesis are under investigation.

The NMR spectra were recorded in $CDCl_3$ with a Bruker AC 250 spectrometer; the chemical shifts (δ) are expressed in ppm relative to TMS for ^1H, ^{13}C nuclei and to H_3PO_4 for ^{31}P nucleus (broad band decoupling); the coupling constants (*J*) are given in Hz; conventional abbreviations are used. Signals corresponding to alcoholic protons are not reported. IR spectra were recorded on a Perkin–Elmer 684 spectrometer. A typical example of spectrum is given for each series of compounds. Elemental microanalyses were obtained from the "Service de Microanalyse ICSN" (Gif sur Yvette). Analyses of sulfur were performed at Caen following Debal and Levy's method (*Bull. Chem. Soc. Fr.* **1968**, 426). High resolution mass spectra (HRMS) were obtained with a JEOL GCmate spectrometer.

N-(2-Hydroxyalkyl)(diethylphosphono)ethanethioamide (3); Typical Procedure

A solution of phosphonodithioacetate **1** (1 mmol) in THF (5 mL) was added to a stirred mixture of amino alcohol **2** (1 mmol) and Et_3N (1.5 mmol) in THF (15 mL). The mixture was allowed to react for 24 h at r.t. The colour changed from orange to pale yellow. The solvent was removed and the residual crude product was purified by column chromatography on silica gel (EtOAc/MeOH, 95:5) to afford phosphonothioamides **3**. The ^{31}P NMR data of **3** are recorded in Table 1 and ^1H and ^{13}C NMR data in Table 4. Satisfactory microanalyses were obtained for **3a**, **b**, **c**, **e** C ± 0.40; H ± 0.20; N ± 0.20; P ± 0.02; S ± 0.19.

3b

IR (NaCl): ν = 3450 (ν_{OH}), 3232 (ν_{NH}), 2972, 2936, 2878, 1554 ($\nu_{N-C=S}$), 1432, 1394, 1236 ($\nu_{P=O}$), 1164 ($\nu_{C=S}$), 1054, 1028, 972 cm^{-1}.

1-[(Diethylphosphono)methyl]-(4,5-dihydro)thiazole (4); General Procedure

A solution of diethyl azodicarboxylate (1.5 mmol) in THF (5 mL) was added dropwise to a stirred mixture of phosphonothioamide **3** (1 mmol) and triphenylphosphine (1.5 mmol) in THF (20 mL). The

Table 4 ^{1}H and ^{13}C NMR Data of Compounds **3**

Product[a]	^{1}H NMR ($CDCl_3$), δ , *J* (Hz)	$^{13}C\{^{1}H\}$NMR ($CDCl_3$), δ , *J* (Hz)
3a	1.35 [t, 6 H, *J* = 6.9, ($C\underline{H}_3CH_2O)_2P$], 3.50 (d, 2 H, *J* = 22.0, $PC\underline{H}_2$), 3.62 (s, 4 H, $NC\underline{H}_2C\underline{H}_2OH$), 4.05−4.25 [m, 4 H, ($CH_3C\underline{H}_2O)_2P$], 9.40 (br s, 1 H, N<u>H</u>)	16.3 [d, *J* = 6.3, ($\underline{C}H_3CH_2O)_2P$], 44.4 (d, *J* = 128.3, $P\underline{C}H_2$), 49.2 ($\underline{C}H_2NH$), 59.7 ($\underline{C}H_2OH$), 63.6 [d, *J* = 6.9, ($CH_3\underline{C}H_2O)_2P$), 192.5 (d, *J* = 6.3, <u>C</u>=S)
3b	0.99 (t, 3 H, *J* = 7.4, $C\underline{H}_3CH_2$), 1.35 [t, 6 H, *J* = 6.9, ($C\underline{H}_3CH_2O)_2P$], 1.72−1.82 (m, 2 H, $CH_3C\underline{H}_2$), 3.45−3.65 (m, 2 H, $PC\underline{H}_2$), 3.75−3.95 (m, 2 H, $C\underline{H}_2OH$), 4.05−4.25 [m, 4 H, ($CH_3C\underline{H}_2O)_2P$], 4.30 (m, 1 H, C<u>H</u>NH), 8.60 (br s, 1 H, N<u>H</u>)	10.5 (s, $\underline{C}H_3CH_2$), 16.3 [d, *J* = 6.1, ($\underline{C}H_3CH_2O)_2P$], 23.1 ($CH_3\underline{C}H_2$), 44.6 (d, *J* = 126.9, $P\underline{C}H_2$), 59.4 (<u>C</u>HNH), 62.5 (s, $\underline{C}H_2OH$), 63.1 & 63.8 [2d, *J* = 6.9, ($CH_3\underline{C}H_2O)_2P$], 192.3 (d, J = 6.4, <u>C</u>=S)
3c	1.01 & 1.02 [2d, 6 H, *J* = 6.8, $(C\underline{H}_3)_2CH$], 1.30 [t, 6 H, *J* = 7.1, ($C\underline{H}_3CH_2O)_2P$], 2.10 [hept, 1 H, *J* = 6.8, $(CH_3)_2C\underline{H}$], 3.45−3.65 (m, 2 H, $PC\underline{H}_2$), 3.75−3.95 (m, 2 H, $C\underline{H}_2OH$), 4.05−4.25 [m, 4 H, ($CH_3C\underline{H}_2O)_2P$], 4.30 (m, 1 H, C<u>H</u>NH), 8.60 (br s, 1 H, N<u>H</u>)	15.2 & 15.3 [2d, *J* = 6.2, ($\underline{C}H_3CH_2O)_2P$], 19.6 & 19.6 [2s, $(\underline{C}H_3)_2CH$], 26.5 [$(CH_3)_2\underline{C}H$], 45.0 (d, *J* = 126.4, $P\underline{C}H_2$), 61.8 (<u>C</u>HNH), 62.8 & 63.1 [2d, *J* = 6.9, ($CH_3\underline{C}H_2O)_2P$], 63.9 (s, $\underline{C}H_2OH$), 192.8 (d, *J* = 6.5, <u>C</u>=S)
3d	1.21 & 1.32 [2t, 6 H, *J* = 7.0, ($C\underline{H}_3CH_2O)_2P$], 3.45−3.65 (m, 2 H, $PC\underline{H}_2$), 3.85−4.35 [m, 7 H, $C\underline{H}_2OH$, ($CH_3C\underline{H}_2O)_2P$, C<u>H</u>NH],; 7.15−7.30 (m, 5 H, $C_6\underline{H}_5$), 8.60 (br s, 1 H, N<u>H</u>)	16.6 & 16.7 [2d, *J* = 6.8, ($\underline{C}H_3CH_2O)_2P$], 45.0 (d, *J* = 127.0, $P\underline{C}H_2$), 62.4 (<u>C</u>HNH), 63.8 & 64.1 [2d, *J* = 6.4, ($CH_3\underline{C}H_2O)_2P$]; 65.3 (d, *J* = 1.5, $\underline{C}H_2OH$), 127.6, 128.0, 128.9, (3s, <u>C</u>Harom), 138.2 (<u>C</u>arom), 192.7 (d, *J* = 6.6, <u>C</u>=S)
3e	1.30 [t, 6 H, *J* = 7.3, ($C\underline{H}_3CH_2O)_2P$], 2.90−3.10 (m, 2 H, $C\underline{H}_2C_6H_5$), 3.35−3.55 (m 2 H, $PC\underline{H}_2$), 3.50−3.80 (m, 2 H, $C\underline{H}_2OH$), 4.05−4.30 [m, 4 H, $CH_3C\underline{H}_2O)_2P$], 4.75 (m, 1 H, C<u>H</u>NH), 7.15−7.35 (m, 5 H, $C_6\underline{H}_5$), 8.95 (br s, 1 H, N<u>H</u>)	16.7 [d, *J* = 6.4, ($\underline{C}H_3CH_2O)_2P$], 35.7 ($\underline{C}H_2C_6H_5$), 44.9 (d, *J* = 128.0, $P\underline{C}H_2$), 59.6 (<u>C</u>HNH), 61.4 ($\underline{C}H_2OH$), 63.5 & 64.2 [2d, *J* = 6.8, ($CH_3\underline{C}H_2O)_2P$], 126.9, 128.9, 129.6 (3s, <u>C</u>Harom), 138.2 (<u>C</u>arom), 192.2 (d, *J* = 6.5, <u>C</u>=S)

solution became pale yellow and a white precipitate of diethyl hydrazine-*N*,*N*'-dicarboxylate was formed. The mixture was stirred for 48 h at r.t. then pentane (20 mL) was added and the precipitate was filtered off. The solvents were removed in vacuo and the crude mixture was chromatographed on silica gel (Et_2O/acetone, 80:20) to afford the pure phosphonothiazoline **4**. The ^{31}P NMR data of **4** are recorded in Table 2 and ^{1}H and ^{13}C NMR data in Table 5. Satisfactory microanalyses were obtained for **4a**−**e** C ± 0.40; H ± 0.36; N± 0.40; P ± 0.28; S ± 0.10.

4b

IR (NaCl): ν = 2976, 2932, 2876, 1668, 1554, 1460, 1394, 1368, 1246 ($\nu_{P=O}$), 1120, 1098, 1028, 970 cm^{-1}.

Table 5 ^{1}H and ^{13}C NMR Data of Compounds **4**[a]

Product	^{1}H NMR ($CDCl_3$), δ, *J* (Hz)	$^{13}C\{^{1}H\}$NMR ($CDCl_3$), δ, *J* (Hz)
4b	1.02 (t, 3 H, *J* = 7.4, $C\underline{H}_3CH_2$), 1.34 [t, 6 H, *J* = 7.2, ($C\underline{H}_3CH_2O)_2P$], 1.56−1.85 (m, 2 H, $CH_3C\underline{H}_2$), 3.02−3.42 (m, 4 H, $PC\underline{H}_2$, $C\underline{H}_2S$), 4.05−4.25 [m, 4 H, ($CH_3C\underline{H}_2O)_2P$], 4.30−4.47 (m, 1 H, C<u>H</u>N)	11.2 ($\underline{C}H_3CH_2$), 16.7 [d, *J* = 6.3, ($\underline{C}H_3CH_2O)_2P$], 28.2 ($CH_3\underline{C}H_2$), 33.5 (d, *J* = 137.9, $P\underline{C}H_2$), 39.2 ($S\underline{C}H_2$), 62.9 & 63.0 [2d, *J* = 6.4, ($CH_3\underline{C}H_2O)_2P$], 78.9 (d, *J* = 1.6, <u>C</u>HN), 160.5 (d, *J* = 8.6, S-<u>C</u>=N)
4c	0.88 & 0.95 [2d, 6 H, *J* = 6.7, $(C\underline{H}_3)_2CH$], 1.24 [t, 6 H, *J* = 7.1, ($C\underline{H}_3CH_2O)_2P$], 1.95 [hept, 1 H, *J* = 6.7, $(CH_3)_2C\underline{H}$], 3.24−3.45 (m, 4 H, $PC\underline{H}_2$, $C\underline{H}_2S$), 4.05−4.25 [m, 4 H, ($CH_3C\underline{H}_2O)_2P$], 4.30 (m, 1 H, C<u>H</u>N)	13.2 [2d, *J* = 5, $(\underline{C}H_3)_2CH$], 15.3 [d, *J* = 6.2, ($\underline{C}H_3CH_2O)_2P$], 31.8 [d, *J* = 1.5, $(CH_3)_2\underline{C}H$], 32.0 (d, *J* = 137.9, $P\underline{C}H_2$), 35.3 ($S\underline{C}H_2$), 61.3 & 61.5 [2d, *J* = 6.4, ($CH_3\underline{C}H_2O)_2P$], 73.4 (s, <u>C</u>HN), 158.9 (d, *J* = 8.7, S-<u>C</u>=N)
4d	1.26 & 1.35 [2t, 6 H, *J* = 7.2, ($C\underline{H}_3CH_2O)_2P$], 3.25 (d, 2 H, J_{HP} = 21.1, $PC\underline{H}_2$), 3.45 (m, 1 H, SC<u>H</u>H), 3.60 (m, 1 H, SCH<u>H</u>), 4.05−4.15 [m, 4 H, ($CH_3C\underline{H}_2O)_2P$], 5.45 (m, 1 H, C<u>H</u>N), 7.25−7.40 (m, 5 H, $C_6\underline{H}_5$)	15.3 [d, *J* = 6.2, ($\underline{C}H_3CH_2O)_2P$], 32.2 (d, *J* = 137.6, $P\underline{C}H_2$), 41.1 ($S\underline{C}H_2$), 61.6 & 61.65 [2d, *J* = 6.4, ($CH_3\underline{C}H_2O)_2P$], 78.9 (d, *J* = 1.5, <u>C</u>HN), 126.8, 129.2, 129.6 (3s, <u>C</u>Harom), 137.8 (<u>C</u>arom), 161.6 (d, *J* = 8.5, S-<u>C</u>=N)
4e	1.35 [t, 6 H, *J* = 7.1, ($C\underline{H}_3CH_2O)_2P$], 2.7 (m, 1 H, $C_6H_5C\underline{H}H$), 3.1 (d, 2 H, J_{HP} = 21.6, $PC\underline{H}_2$), 3.05−3.45 (m, 3 H, $C_6H_5C\underline{H}H$, $C\underline{H}_2S$), 4.05−4.25 [m, 4 H, ($CH_3C\underline{H}_2O)_2P$], 4.7 (m, 1 H, C<u>H</u>N), 7.00−7.25 (m, 5 H, $C_6\underline{H}_5$)	16.4 [d, *J* = 6.2, ($\underline{C}H_3CH_2O)_2P$], 33.1 (d, *J* = 137.9, $P\underline{C}H_2$), 38.4 ($S\underline{C}H_2$), 39.9 (d, *J* = 2.2, $\underline{C}H_2C_6H_5$), 62.6 & 62.65 [2d, *J* = 6.5, ($CH_3\underline{C}H_2O)_2P$], 78.4 (<u>C</u>HN), 126.8, 129.2, 129.6 (<u>C</u>Harom), 137.8 (<u>C</u>arom), 161.2 (d, *J* = 8.6, S-<u>C</u>=N)

[a] Description of **4a** was already published.[6]

Table 6 ^{1}H and ^{13}C NMR Data of Compounds **5** & **6**

Product*	^{1}H NMR ($CDCl_3$), δ , J (Hz)	$^{13}C\{^{1}H\}$NMR ($CDCl_3$), δ
5a	1.03 (t, 3 H, *J* = 7.4, $CH_2C\underline{H}_3$), 1.59−1.86 (m, 2 H, $C\underline{H}_2CH_3$), 1.89 (d, 3 H, *J* = 5.3, $C\underline{H}_3CH$=CH), 2.92−3.33 (m, 2 H, $C\underline{H}_2S$), 4.40 (m, 1 H, C<u>H</u>N), 6.61−6.43 (m, 2 H; <u>H</u>C=C<u>H</u>)	10.0 ($CH_2\underline{C}H_3$), 17.5 ($\underline{C}H_2CH_3$), 27.1 ($\underline{C}H_3CH$=CH), 35.8 ($\underline{C}H_2S$), 77.6 (<u>C</u>HN), 125.7 (CH_3CH=<u>C</u>H), 138.9 ($CH_3\underline{C}H$=CH), 164.8 (S-<u>C</u>=N)
5b	1.04 (t, 3 H, *J* = 7.5, $CH_2C\underline{H}_3$), 1.07 [d, 6 H, *J* = 6.7, $CH(C\underline{H}_3)_2$], 1.62−1,89 (m, 2 H, $C\underline{H}_2CH_3$), 2.48 [m, 1 H, $C\underline{H}(CH_3)_2$], 2.92−3.33 (m, 2 H, $C\underline{H}_2S$), 4.37−4.43 (m, 1 H, C<u>H</u>N), 6.24−6.38 (m, 2 H, <u>H</u>C=C<u>H</u>)	11.6 ($CH_2\underline{C}H_3$), 21.1 ($\underline{C}H_2CH_3$), 21.9 [$CH(\underline{C}H_3)_2$], 37.2 ($\underline{C}H_2S$), 31.5 [$\underline{C}H(CH_3)_2$], 76.3 (<u>C</u>HN), 125.0 [$(CH_3)_2$CH-HC=<u>C</u>H], 151.3 [$(CH_3)_2\underline{C}H$-H<u>C</u>=CH], 163.7 (S-<u>C</u>=N)
5c	1.07 (t, 3 H, *J* = 7.4, $CH_2C\underline{H}_3$), 1.65−1.93 (m, 2 H, $C\underline{H}_2CH_3$), 3.01−3.42 (m, 2 H, $C\underline{H}_2S$), 4.47 (m, 1 H, C<u>H</u>N), 7.06 (d, 1 H, *J* = 16.1, Ph-CH=C<u>H</u>), 7.10 (d, 1 H; *J* = 16.1, Ph-C<u>H</u>=CH), 7.32−7.51 (m, 5 H, $C_6\underline{H}_5$)	11.8 ($CH_2\underline{C}H_3$), 22.6 ($\underline{C}H_2CH_3$), 37.8 ($\underline{C}H_2S$), 77.1 (<u>C</u>HN), 125.4 (Ph-CH=<u>C</u>H), 128.0, 129.2, 129.4 (<u>C</u>Harom.), 134.1 (<u>C</u>arom.), 145.1 (Ph-<u>C</u>H=CH), 164.7 (S-<u>C</u>=N)
5d	1.04 (t, 3 H, *J* = 7.4, $CH_2C\underline{H}_3$), 1.59−1.84 (m, 2 H, $C\underline{H}_2CH_3$), 1.87 & 2.06 [2d, 6 H, *J* = 6.8, $(C\underline{H}_3)_2$C=CH], 2.98−3.34 (m, 2 H, $C\underline{H}_2S$), 4,39 (m, 1 H, C<u>H</u>N), 5.97 (s, 1 H, C=C<u>H</u>)	11.5 ($CH_2\underline{C}H_3$), 21.0 ($\underline{C}H_2CH_3$), 27.6 & 28.6 [2s, $(\underline{C}H_3)_2$C=CH], 38.0 ($\underline{C}H_2S$), 78.8 (<u>C</u>HN), 119,6 [$(CH_3)_2$C=<u>C</u>H], 146.7 [$(CH_3)_2\underline{C}$=CH], 164.1 (S-<u>C</u>=N)
6a	1.90 (d, 3 H, *J* = 5.0, $C\underline{H}_3$CH=CH), 2.75 (m, 1 H, CH<u>H</u>Ph), 3.00 (m, 1 H, CH<u>H</u>S), 3.17 (m, 1 H, C<u>H</u>HS), 3.23 (m, 1 H, C<u>H</u>HPh), 4.62−4.73 (m, 1 H, C<u>H</u>N), 6.30−6.44 (m, 2 H, <u>H</u>C=C<u>H</u>), 7.26−7,31 (m, 5 H, $C_6\underline{H}_5$)	18.5 ($\underline{C}H_3$-CH=CH), 36.4 ($\underline{C}H_2S$), 40.3 ($\underline{C}H_2Ph$), 78.0 (<u>C</u>HN), 126.5 (CH_3-CH=<u>C</u>H), 126.6, 128.5 & 129.3 (3s, <u>C</u>Harom), 138.6 (<u>C</u>arom), 140.2 (CH_3-<u>C</u>H=CH), 166.6 (S-<u>C</u>=N)
6b	1.08 [d, 6 H, *J* = 6.8, $CH(C\underline{H}_3)_2$], 2,49 [m, 1 H, $C\underline{H}(CH_3)_2$], 2.75 (m, 1 H, CH<u>H</u>Ph), 3.00 (m, 1 H, CH<u>H</u>S), 3.18 (m, 1 H, C<u>H</u>HS), 3.24 (m, 1 H, C<u>H</u>HPh), 4.70 (m, 1 H, C<u>H</u>N), 6.26−6.40 (m, 2 H, <u>H</u>C=C<u>H</u>), 7.26−7.32 (m, 5 H, $C_6\underline{H}_5$)	21.9 [$CH(\underline{C}H_3)_2$], 31.8 ($\underline{C}H(CH_3)_2$), 36.8 ($\underline{C}H_2S$), 40.7 ($\underline{C}H_2Ph$), 78.4 (<u>C</u>HN), 122.9 [$(CH_3)_2$CH-CH=<u>C</u>H], 126.9, 129.0, 129.6 (3s; <u>C</u>Harom), 139.0 (<u>C</u>arom), 152.1 [$(CH_3)_2$CH-<u>C</u>H=CH], 167.6 (s, S-<u>C</u>=N)
6c	2.81 (m, 1 H, CH<u>H</u>Ph), 3.07 (m, 1 H, CH<u>H</u>S), 3.21−3.32 (m, 2 H, C<u>H</u>HS, C<u>H</u>HPh), 4.77−4.89 (m, 1 H, C<u>H</u>N), 7.07 (d, 1 H, *J* = 16,2, PhCH=C<u>H</u>), 7.10 (d, 1 H, *J* = 16,2, PhC<u>H</u>=CH), 7.26−7.57 (m, 10 H, 2 × $C_6\underline{H}_5$)	37.1 ($\underline{C}H_2S$), 40.7 ($\underline{C}H_2Ph$), 78.6 (<u>C</u>HN), 123.2 (PhCH=<u>C</u>H), 126.9, 127.9, 129.0, 129.3, 129.7, 129.9 (6s, <u>C</u>Harom), 135.8 & 138.9 (2s, <u>C</u>arom), 141.6 (Ph<u>C</u>H=CH), 167.2 (S-<u>C</u>=N)

Vinylic Thiazolines 5 and 6; General Procedure

A solution of phosphonothiazoline **4** (1 mmol) dissolved in MeCN (5 mL) was added dropwise to a stirred mixture of diazabicycloundecene (1.1 mmol) and LiCl (1.1 mmol). Aldehyde (1.2 mmol) in MeCN (5 mL) was added and the mixture was stirred for 16 h at r.t. In the case of (R_1 = Me) pure acetaldehyde was added at 0 °C and the reaction carried out at this temperature for 20 h. After filtration of the salts and evaporation of the solvent, the crude mixture was chromatographed on silica gel (EtOAc) to afford the pure vinylic thiazoline **5** or **6**. The ^{1}H and ^{13}C NMR data of **5** and **6** are recorded in Table 6.

IR (NaCl): ν = 2962, 2930, 2872, 1632, 1582, 1450, 1188, 960, 752, 692 cm^{-1}.

Enantiopure thiazoline **5c*** was analysed by HPLC (Chiralpak AD analytical column (Daicel); eluting with hexane/propan-2-ol (90:10), flow rate 1 mL/min, 234 nm, t_R = 9.8 min). The HPLC separation was calibrated using racemic product **5c** (t_{R1} = 6.7 min, t_{R2} = 9.8 min).

Satisfactory analyses were obtained for **5c**.

HRMS (EI): *m/z* calcd for $C_{13}H_{15}NS$ (M^+) 217.0925. Found: 217.0948.

Anal. Calcd for $C_{13}H_{15}NS$: S, 13.86. Found: S, 13.69.

Acknowledgement

We warmly thank M. Lemarié who conducted the HPLC analysis. This work was supported by the RINCOF (Contrat de plan Etat-Bassin Parisien-Régions Haute-Normandie et Basse-Normandie) which is gratefully acknowledged.

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Article Identifier:
1437-210X,E;2000,0,08,1143,1147,ftx,en;P01100SS.pdf