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An efficient access to (*Z*)-β-fluoroallyl alcohols based on the two carbon homologation of aromatic aldehydes by Horner–Wadsworth–Emmons reaction with 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester followed by reduction with sodium borohydride

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ABSTRACT

We describe a biomimetic approach to (*Z*)-β-fluoroallyl alcohols based on the two carbon homologation of aromatic aldehydes to α-fluorocinnamic thioesters by Horner–Wadsworth–Emmons reaction with 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester, followed by reduction with sodium borohydride in mild conditions. The α-fluorothioesters were obtained in a good yield by condensing the aldehydes with the lithium anion of 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester in THF at −78 °C. The (*E*,*Z*)-α-fluorocinnamic thioester mixtures were then cleanly reduced with double bond isomerisation to the corresponding (*Z*)-β-fluoroallyl alcohols by $NaBH_4$ at room temperature. This methodology may be applied to highly functionalized aldehydes as exemplified by the straightforward access to (*Z*)-β-fluoroconiferin, a strong inhibitor of lignin polymerization from *O*-glucosylated vanillin.

1. Introduction

Fluorinated organic compounds are known to have interesting biological activities.[1] The chemistry of fluorinated organic molecules is unique because of the properties of fluorine, such as strong electronegativity, small size and the low polarisability of the C–F bond. These properties of the fluorine atom can have a considerable impact on the behavior of a molecule in a biological environment. Indeed, an increasing number of drugs contain fluorine, the presence of which often is of major importance to their activity.[2] 2-Fluoropropenol derivatives are a family of fluorinated compounds that have received a considerable attention.[3] The 2-fluoropropenol motif is the key structure of several biologically active compounds.[4] 2-Fluoropropenols are generally obtained from 2-fluoropropenic acid ester by Wittig–Horner condensation with trialkythyl-fluorophosponacetate followed by reduction with a strong reducing reagent like DIBAL-H[5] or $LiAlH_4$.[6] Sodium borohydride may also be used but in harsh conditions, typically $NaBH_4$ (7.4 equiv) in presence of LiCl (10 equiv) in glyme (80 °C, 18 h).[7] When applied to complex molecule containing other ester functions these conditions lead to complex mixtures. During the biosynthesis of lignin monomers like coniferyl alcohol (4-(3-hydroxy-1-propenyl)-2-methoxyphenol), nature uses as intermediate the coenzyme A thioester of the corresponding cinnamic acid, which is first reduced into aldehyde by cinnamoyl-CoA reductase (CCR) and then the aldehyde to the alcohol by cinnanyl alcohol dehydrogenase (CAD).[8] Indeed, thioesters are much more easily reduced than their ester homologues and are reduced by sodium borohydride to the corresponding alcohol at room temperature.[9] In the 3-phenyl-propen-1-ol series, the required cinnamic acid thioester may be obtained either by coupling of a thiol with an activated form of cinnamic acid, like, for example, in the synthesis of caffeoyl coenzyme A thioester[10] or from the corresponding benzaldehyde using a two carbon homologation. The latter is based on the Horner–Wadsworth–Emmons reaction, which was described almost simultaneously by three groups, Coutrot et al.,[11a] Liu et al.[11b] and Schaumann et al.[11c] We present a new biomimetic synthesis of (*Z*)-β-fluoroallyl alcohols based on the preparation of α-fluoro-α,β-unsaturated thioesters using 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester as a new Horner–Wadsworth–Emmons reagent, followed by the reduction of these thioesters to the corresponding (*Z*)-β-fluoroallyl alcohols by $NaBH_4$ in ethanol at room temperature. This methodology enabled us to synthesize the glucoside of β-fluoroconiferyl alcohol, (*Z*)-β-fluoroconiferin, a strong inhibitor of lignin polymerization, in three steps.[7]

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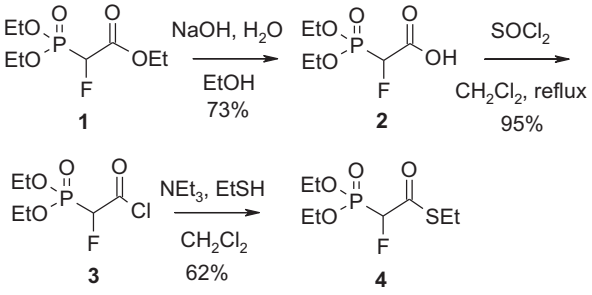
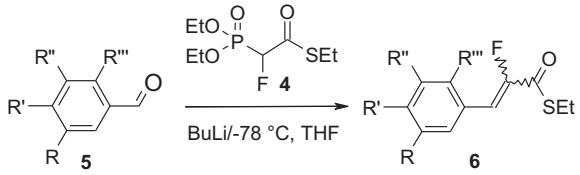
2. Results and discussion

Only a few reports described the preparation of α-fluoro-α,β-unsaturated thioesters contrary to their non-fluorinated homologues.[11,12] Ethyl (*Z*)-2-fluorocinnamothioates are obtained by condensing 3,3-bis(methylthio)-2-fluoropropenal with phenylmagnesium bromide followed by the allylic rearrangement of the 1,1-bis(methylthio)-2-fluoro-3-phenylprop-1-en-3 thus obtained using mercuric chloride in acetonitrile/water.[13] In their approach, Coutrot et al.[11a] prepared a family of 2-[bis(1-methylethoxy)phosphinyl]-ethanethioic acid, *S*-propyl ester substituted in the two position by alkyl groups, aromatic groups and by halogens (chlorine, fluorine). Surprisingly, this family of reagents with bulky substituents on the phosphoryl group and on the thioester gave poor yields in the Horner–Wadsworth–Emmons condensation step and no example was described with the 2-fluorinated Horner–Wadsworth–Emmons reagent. In our approach, we developed a novel Horner–Wadsworth–Emmons reagent: 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester **4** with smaller substituents both on the acid *S*-thioester and on the phosphoryl group, for the preparation of α-fluoro-α,β-unsaturated thioesters. Coupling of **4** with an aromatic aldehydes would provide an efficient method to access a variety of α-fluoro-α,β-unsaturated thioesters. 2-(Diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester **4** was obtained in three steps as described in Scheme 1. Foremost 2-(diethoxyphosphinyl)-2-fluoro-acetic acid **2** was prepared by the saponification of 2-(diethoxyphosphinyl)-2-fluoro-acetic acid, ethyl ester **1** with sodium hydroxide in ethanol/water.[14] Direct conversion of carboxylic acid **2** into acid chloride **3** was achieved in quantitative yields by treatment of **2** with thionyl chloride in dichloromethane.[15] Finally, the reaction between the carboxylic acid chloride **3** and ethanethiol in the presence of triethylamine in dichloromethane gave the desired 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester **4**. Crude acid chloride **3** was used without further purification for this step because this compound decomposed partially during distillation. 2-(Diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester **4** was obtained in a 43% yield from the commercially available 2-(diethoxyphosphinyl)-2-fluoro-acetic acid, ethyl ester **1**.



Scheme 1. Synthesis of 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester.

The Horner–Wadsworth–Emmons condensation between compound **4** and the aromatics aldehydes **5a**–**f** in presence of *n*-butyllithium at −78 °C gave the α,β-unsaturated α-fluorothioesters **6a**–**f** in good yields (64–91%) as a mixture of *E*, *Z* isomers (Scheme 2). With benzaldehyde **5a**, the Horner–Wadsworth–Emmons reagent **4** gave a 90/10 mixture of *E*/*Z* isomers (Table 1, entry a) in agreement with the reactivity previously described for 2-(diethoxyphosphinyl)-2-fluoro-acetic acid, ethyl ester **1** in THF using *n*-BuLi as a base at −78 °C.[16] The Wadsworth–Emmons reagent **1** is well known for its sensitivity to reaction parameters. As reported above, the benzaldehyde gives a nearly pure *E* product whereas crotonaldehyde affords the reverse *Z* geometry.[17] So it is not surprising that the situation is more contrasted with benzaldehyde-bearing substituents (Table 1, entries b–f). A recent paper reports than the reaction Hammett constant ρ for a non-fluorinated Horner–Wadsworth–Emmons reagent is positive in the 2.7–3.6 range showing that the benzaldehyde-bearing electrodonating substituents are reacting faster.[18] Unfortunately, to the best of our knowledge there is no equivalent report for the stereochemistry.[19] No clear trend with the substitution parameters can be seen in our data. As a result, no further attempt was made to control the stereochemistry as the α,β-unsaturated α-fluorothioesters **6a**–**f** were isomerized during the next reduction step to their *Z* isomer. The Horner–Wadsworth–Emmons step works both with non-substituted (Table 1, entry a), slightly or strongly electroattractive groups (Table 1, entry b and c, respectively), electrodonating group (Table 1, entry e) or functionalized groups (Table 1, entry f).



Scheme 2. Synthesis of α,β-unsaturated α-fluorothioesters **6a**–**f**.

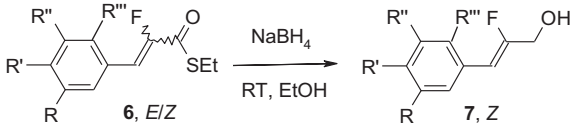
Table 1
Yields of α-fluorothioesters **6a**–**f** from Horner–Wadsworth–Emmons reaction of the corresponding aldehydes

Entry	R	R′	R″	R‴	(*E*/*Z*)[b]	Yield (%)
a	H	H	H	H	90/10	80
b	H	F	H	H	0/100	91
c	H	NO_2	H	H	60/40	66
d	H	H	Br	H	0/100	64
e	H	H	H	CH_3	100/0	81
f	MeO	GluO[a]	H	H	80/20	73

[a] GluO=2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl.
[b] From ^1H and ^{19}F NMR.

The second step of this work is the reduction of the (*E*/*Z*)-α-fluorocinnamic acid thioesters **6a**–**f** mixture to the corresponding (*Z*)-β-fluoroallyl alcohols **7a**–**f**. Thioesters could be reduced by various reagents directly to the corresponding aldehydes. Thioesters are reduced in aldehydes in mild conditions with triethylsilane in the presence of palladium on carbon catalyst (Pd/C 2.0–5.0 mol %),[20a–c] and the reaction may be performed with a lower catalytic amount of catalyst (0.5–1.0 mol %).[20d] Aldehydes could also be obtained from the reduction of thioesters with diisopropylaluminium hydride in dichloromethane at −55 °C[20e] or in toluene at −78 °C.[20f] However, the reduction of thioesters to alcohols is less documented than their reduction to aldehydes. As in the case of esters, $LiAlH_4$ in excess affords the alcohol but this reagent is not compatible with our objective of a mild reduction.[21a,21b] Benzenecarbothioic acid and *S*-phenyl esters are reduced to benzyl alcohol using nickel boride, generated in situ from nickel chloride hexahydrate and sodium borohydride in methanol/THF.[21c] Thioesters are also cleanly reduced to alcohol by zinc borohydride.[21d] However, the best synthetic approach seemed us the simplest, the reduction of the thiol ester by $NaBH_4$ at room temperature, which is compatible with ester, nitrile and epoxyde functions.[9] To the best of our knowledge, for the reduction of α-fluoro-α,β-unsaturated thioesters, only the reduction of methyl (*Z*)-

3-(4′-imidazolyl)-2-fluorothioacrylate to (*Z*)-2-fluoro-3-(4′-imidazolyl)-2-propenol with $NaBH_4$ in a fair yield (51%) has been described in literature.[13] We chose to work under the same mild conditions using $NaBH_4$ in ethanol at room temperature for the reduction of α-fluoro-α,β-unsaturated thioesters **6a**–**f** (Scheme 3). The results of the $NaBH_4$ reductions of α-fluoro-α,β-unsaturated thioesters **6a**–**f** to the corresponding fluoroallyl alcohols **7a**–**f** are listed in Table 2.

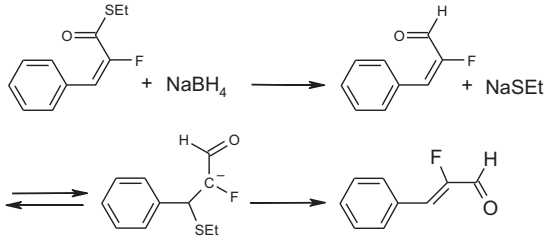


Scheme 3. Reduction of α-fluorothioesters **6a**–**f** by sodium borohydride.

Table 2
Reduction of **6a**–**f** with $NaBH_4$/EtOH

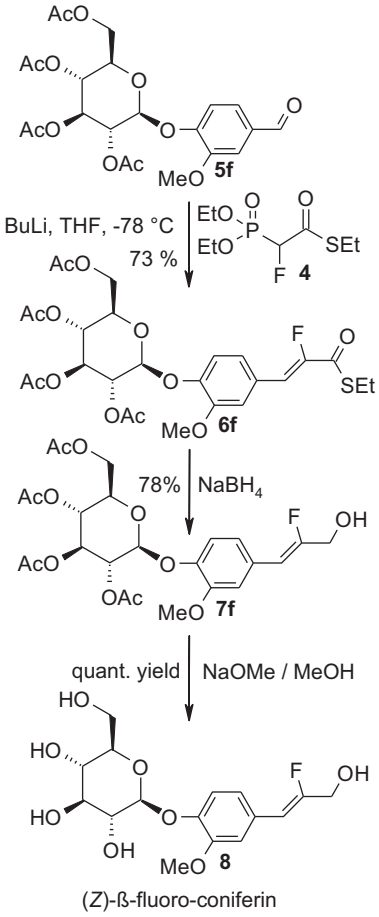
7	R	R′	R″	R‴	Yield (%)
a	H	H	H	H	83
b	H	F	H	H	84
c	H	NO_2	H	H	86
d	H	H	Br	H	82
e	H	H	H	CH_3	90
f	MeO	GluO	H	H	78

A careful inspection of ^1H and ^{19}F NMR spectra shows the presence of one isomer with *Z* geometry. So, starting from an *E*/*Z* mixture of α-fluoro-α,β-unsaturated thioesters **6a**–**e**, the reactions proceeded successfully with complete isomerization of the double bond to give the corresponding stereochemically pure (*Z*)-β-fluoroallyl alcohols **7a**–**f** in good yields (78–90%) and in a convergent way. (*E*)-α-Fluorocinnamic esters may be isomerized to the more stable (*Z*)-isomers using an electrophilic reagent like bromine or iodine.[7,22] (*E*)-α-Fluorocinnamic esters are not so easily isomerized by nucleophilic reagents since they may be reduced without loss of stereochemistry by DIBAL-H to the corresponding alcohol. But according to the DIBAL-H ester reduction mechanism, the free aldehyde is not present in the solution when an excess of DIBAL-H is used, because the reduction of the aldehyde is faster than the reduction of the initial ester.[23] So we may guess that the isomerization is produced by the reversible Michael addition of the ethylthiolate[24] formed during the reduction of the thioester to the intermediate free (*E*)-α-fluorocinnamic aldehyde (Scheme 4).



Scheme 4. Proposed isomerization mechanism during the reduction of α-fluoro-α,β-unsaturated thioesters **6a**–**e** *E*/*Z* mixture to pure (*Z*)-β-fluoroallyl alcohols **7a**–**f**.

This methodology gave a new and straightforward access to (*Z*)-β-fluoroconiferin (Scheme 5). The synthesis was performed in three steps starting from *O*-glucosyl-vanillin **5f**.[25] The corresponding α-fluoroester **6f** was obtained using the Horner–Wadsworth–Emmons reagent, 2-(diethoxyphosphinyl)2-fluoro-ethanethioic acid, *S*-ethyl ester **4**, deprotonated by *n*-BuLi at −78 °C in THF. The reduction of **6f** into alcohol **7f** was accomplished by sodium borohydride in ethanol. A final deprotection step involving the cleavage of the acetyl groups by sodium methylate afforded (*Z*)-β-fluoroconiferin **8** in quantitative yield.[26] From *O*-glucosylated vanillin the (*Z*)-β-fluoroconiferin **8** was obtained in a 57% yield.



Scheme 5. Synthesis of (*Z*)-β-fluoroconiferin **8**.

3. Conclusion

We recently presented a biomimetic strategy for the synthesis of (*Z*)-β-fluoroallyl alcohols based on the palladium-catalyzed formylation by carbon monoxide of α-bromo-α-fluoroolefins obtained by Wittig–Burton reaction, to obtain α-fluoro conjugated aldehydes, which were then reduced to the corresponding alcohols.[27] The new synthesis of (*Z*)-β-fluoroallyl alcohols we present here based on the Horner–Wadsworth–Emmons reaction of benzaldehyde with 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester **4**, followed by reduction with $NaBH_4$, is even simpler since it involves only two steps, compared to three from the same precursor using the formylation by carbon monoxide of α-bromo-α-fluoroolefins approach. All the steps are compatible with highly functionalized molecules. This straightfoward synthesis allowed us to access of pure (*Z*)-β-fluoroconiferin **8**, a strong inhibitor of lignin polymerization.[7] The (*Z*)-β-fluoroconiferin **8** we obtained will be used to further understand the inhibition of lignin biosynthesis in plantlets growing in an artificial medium.[28]

4. Experimental

4.1. General

All commercially available products were purchased from Aldrich (Saint-Quentin Fallavier, France) and used as received.

Deuterated solvents (99.9% or better) were purchased from Eurisotop (Saint-Aubin, France). Tetrahydrofuran (THF) was distilled over sodium benzophenone ketyl under argon before use. For flash chromatography, Merck silica-gel 60 (230–400 mesh ASTM) was used. The melting points were measured on an Electrothermal (Dubuque, Iowa USA) 9100 apparatus and were not corrected. NMR spectra were recorded on a Bruker (Wissembourg, France) AM 300 spectrometer (300, 282 and 75 MHz, for ^{1}H, ^{19}F and ^{13}C, respectively) using $CDCl_3$ or CD_3OD as solvents and TMS as internal standard; chemical shifts and *J* values are given in parts per million and hertz, respectively. Fast atom bombardment (FAB) mass spectra were measured on a JEOL Mass Station 700 spectrometer at the École Normale Supérieure (Paris, France).

4.2. Synthesis of 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester (4)

*4.2.1. 2-(Diethoxyphosphinyl)-2-fluoro-acetic acid (**2**).* To a solution of sodium hydroxide (4 mmol) in water (5 mL) and ethanol was added a solution of 2-(diethoxyphosphinyl)-2-fluoro-acetic acid, ethyl ester (4.4 mmol) in ethanol (10 mL). The reaction mixture was stirred for 10 h at room temperature, and acidified to pH=1 with 2% HCl. The organic layer was extracted with ether, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure to give the corresponding acid. ^{19}F NMR ($CDCl_3$): δ=−210.2 (dd, $^2J_{HF}$=46.9 Hz, $^2J_{FP}$=72.2 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ=1.34 (t, $^3J_{HH}$=6.7 Hz, 6H), 4.27 (q, $^3J_{HH}$=7.1 Hz, 4H), 5.25 (dd, $^2J_{HF}$=46.9 Hz, $^2J_{HP}$=13.3 Hz, 1H), 10.15 (OH, s, 1H). ^{13}C NMR ($CDCl_3$): δ=16.2 (2C), 64.9 (2C), 84.4 (d, $^1J_{CF}$=195.4 Hz), 165.7. HRMS: calcd for $C_6H_{13}O_5FP$ 215.0476; found 215.0479.

*4.2.2. 2-(Diethoxyphosphinyl)-2-fluoro-ethanethioic acid, S-ethyl ester (**4**).* Thionyl chloride (4 mmol) was added to a solution of compound 2 (2 mmol) in CH_2Cl_2 (5 mL) under argon in a flask fitted with a reflux condenser. The solution was refluxed for 3 h, cooled to room temperature and the solvent was evaporated. A solution of ethanethiol (2 mmol) and triethylamine (2 mmol) in 20 mL of CH_2Cl_2 was then added to the obtained acid chloride. The reaction mixture was stirred for 4 h at room temperature. 20 mL of benzene was added of the residue obtained after evaporation of the solvent and the solution was filtered. The solvent was evaporated and the product was isolated by flash column chromatography using a mixture of ethyl acetate/petroleum ether 60/40 as eluent. ^{19}F NMR ($CDCl_3$): δ=−207.3 (dd, $^2J_{HF}$=46.7 Hz, $^2J_{FP}$=71.5 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ=1.23 (t, $^3J_{HH}$=7.3 Hz, 3H), 1.30 (t, $^3J_{HH}$=6.5 Hz, 6H), 2.92 (q, $^3J_{HH}$=7.2 Hz, 2H), 4.18 (q, $^3J_{HH}$=6.7 Hz, 4H), 5.16 (dd, $^2J_{HF}$=46.7 Hz, $^2J_{HP}$=11.9 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=14.2, 16.2 (2C), 22.8, 64.3 (2C), 91.0 (d, $^1J_{CF}$=158.0 Hz), 193.7 (d, $^2J_{CF}$=25.0 Hz). HRMS: calcd for $C_8H_{17}O_4FPS$ $[M+H]^+$ 259.0563; found 259.0569.

4.3. General procedure for the preparation of α-fluorocinnamic thioesters

To a stirred solution of 2-(diethoxyphosphinyl)-2-fluoro-ethanethioic acid, *S*-ethyl ester (1.50 mmol) in anhydrous THF (10 mL), *n*-butyllithium (1.70 mmol) were added slowly at −70 °C. The solution was stirred at −70 °C for 1 h. A solution of corresponding aldehydes (1.20 mmol) in anhydrous THF (5 mL) was added dropwise, and the reaction mixture was stirred at −70 °C for 4 h and at room temperature for 18 h. The reaction was quenched with water (50 mL), and the mixture was extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography using a mixture of ethyl acetate/petroleum ether to give the product.

*4.3.1. 2-Fluoro-3-phenyl-2-propenethioic acid, S-ethyl ester (**6a**).* Mp 40–41 °C. ^{19}F NMR ($CDCl_3$): δ=−125.1 (*Z*, d, $^3J_{HF}$=36.9 Hz, 1F), −116.7 (*E*, d, $^3J_{HF}$=24.3 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ=1.32 (t, $^3J_{HH}$=7.3 Hz, 3H), 2.85 (q, $^3J_{HH}$=7.3 Hz, 2H), 6.69 (d, *E*, $^3J_{HF}$=24.3 Hz, 0.9H), 6.87 (d, *Z*, $^3J_{HF}$=36.9 Hz, 0.1H), 7.38 (dd, $^3J_{HH}$=7.3 Hz, 1H), 7.42 (dd, $^3J_{HH}$=7.3 Hz, 7.4 Hz, 2H), 7.64 (d, $^3J_{HH}$=7.4 Hz, 2H). HRMS: calcd for $C_{11}H_{12}OFS$ $[M+H]^+$ 211.0587; found 211.0592.

*4.3.2. 2-Fluoro-3-(4-fluorophenyl)-2-propenethioic acid S-ethyl ester (**6b**).* Mp 43–45 °C. ^{19}F NMR ($CDCl_3$): δ=−126.5 (dd, $^3J_{HF}$=36.4 Hz, $^5J_{HF}$=1.4 Hz, 1F), −109.4 (m, 1F). ^{1}H NMR ($CDCl_3$): δ=1.33 (t, $^3J_{HH}$=7.4 Hz, 3H), 3.02 (q, $^3J_{HH}$=7.4 Hz, 2H), 6.77 (d, $^3J_{HF}$=36.4 Hz, 1H), 7.09 (dd, $^3J_{HH}$=8.6 Hz, $^3J_{HF}$=8.6 Hz, 2H), 7.64 (dd, $^3J_{HH}$=8.2 Hz, $^3J_{HF}$=5.6 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ=14.4, 22.9, 111.9, 116.1, 127.1, 132.7, 151.9, 163.3 (d, $^1J_{CF}$=269.3 Hz), 186.5 (d, $^2J_{CF}$=37.6 Hz). HRMS: calcd for $C_{11}H_{11}OF_2S$ $[M+H]^+$ 229.0493; found 229.0494.

*4.3.3. 2-Fluoro-3-(4-nitrophenyl)-2-propenethioic acid, S-ethyl ester (**6c**).* Mp 45–46 °C. ^{19}F NMR ($CDCl_3$): δ=−126.1 (d, *Z*, $^3J_{HF}$=35.3 Hz, 1F), −118.5 (d, *E*, $^3J_{HF}$=21.8 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ=1.27 (t, *E*, $^3J_{HH}$=7.3 Hz, 1.8H), 1.33 (t, *Z*, $^3J_{HH}$=7.3 Hz, 1.2H), 2.94 (q, *E*, $^3J_{HH}$=7.4 Hz, 1.2H), 3.04 (q, *Z*, $^3J_{HH}$=7.4 Hz, 0.8H), 6.66 (d, *E*, $^3J_{HF}$=21.8 Hz, 0.6H), 6.84 (d, *Z*, $^3J_{HF}$=35.3 Hz, 0.4H), 7.67 (d, *E*, $^3J_{HH}$=8.8 Hz, 1.2H), 7.78 (d, *Z*, $^3J_{HH}$=8.5 Hz, 0.8H), 7.96 (d, *Z*, $^3J_{HH}$=8.4 Hz, 0.8H), 8.19 (d, *E*, $^3J_{HH}$=8.8 Hz, 1.2H). HRMS: calcd for $C_{11}H_{11}O_3NFS$ $[M+H]^+$ 256.0438; found 256.0441.

*4.3.4. 2-Fluoro-3-(3-bromophenyl)-2-propenethioic acid, S-ethyl ester (**6d**).* Mp 41–43 °C. ^{19}F NMR ($CDCl_3$): δ=−123.1 (d, $^3J_{HF}$=36.2 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ=1.34 (t, $^3J_{HH}$=7.6 Hz, 3H), 3.02 (q, $^3J_{HH}$=7.4 Hz, 2H), 6,74 (d, $^3J_{HF}$=36.2 Hz, 1H), 7.27 (dd, $^3J_{HH}$=7.9 Hz, $^3J_{HH}$=7.7 Hz, 1H), 7.51 (d, $^3J_{HH}$=7.9 Hz, 1H), 7.56 (d, $^3J_{HH}$=7.9 Hz, 1H), 7.82 (s, 1H). ^{13}C NMR ($CDCl_3$): δ=14.4, 23.1, 111.3, 123.0, 129.1, 130.3, 132.8, 132.8, 136.6, 151.3 (d, $^1J_{CF}$=273.6 Hz), 185.5 (d, $^2J_{CF}$=37.5 Hz). HRMS: calcd for $C_{11}H_{11}O^{79}BrFS$ 288.9692 and for $C_{11}H_{11}O^{81}BrFS$ 290.9672; found 288.9694 and 290.9680.

*4.3.5. 2-Fluoro-3-(2-methylphenyl)-2-propenethioic acid, S-ethyl ester (**6e**).* ^{19}F NMR ($CDCl_3$): δ=−117.8 (d, $^3J_{HF}$=21.2 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ=1.29 (t, $^3J_{HH}$=6.9 Hz, 3H), 2.32 (s, 3H), 2.94 (q, $^3J_{HH}$=6.7 Hz, 2H), 6,71 (d, $^3J_{HF}$=21.2 Hz, 1H), 7.24 (d, $^3J_{HH}$=7.1 Hz, 1H), 7.27 (dd, $^3J_{HH}$=7.4, $^3J_{HH}$=7.5 Hz, 1H), 7.35 (d, $^3J_{HH}$=7.4 Hz, 1H), 7.39 (dd, $^3J_{HH}$=7.1, $^3J_{HH}$=7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=14.3, 20.1, 22.7, 116.5, 125.5, 128.9, 129.6, 129.8, 129.9, 136.6, 151.3 (d, $^1J_{CF}$=257.5 Hz), 185.5 (d, $^2J_{CF}$=41.1 Hz). HRMS: calcd for $C_{12}H_{14}OFS$ 225.0749; found 225.0751.

*4.3.6. 2,3,4,6-Tetra-O-acetyl-1-[4-((2Z)-2-fluoro-3-hydroxyprop-1-enyl, 2-propenethioic acid, S-ethyl)-2-methoxyphenyl]-β-D-glucopyranoside (**6f**).* Mp 126–128 °C. ^{19}F NMR ($CDCl_3$): δ=−126.4 (*Z*, d, $^3J_{HF}$=36.6 Hz, 1F), −116.95 (*E*, d, $^3J_{HF}$=25.1 Hz, 1F). ^{1}H NMR ($CDCl_3$): δ=1.25 (t, *E*, $^3J_{HH}$=7.3 Hz, 2.4H), 1.29 (t, *Z*, $^3J_{HH}$=7.3 Hz, 0.6H), 2.04 (s, 3H), 2.08 (s, 6H), 2.10 (s, 3H), 2.96 (q, *E*, $^3J_{HH}$=7.3 Hz, 1.6H), 3.01 (q, *Z*, $^3J_{HH}$=7.3 Hz, 0.4H), 3.78–3.83 (m, 1H), 3.85 (s, 3H), 4.12 (dd, $^2J_{HH}$=14.3 Hz, $^3J_{HH}$=7.1 Hz, 1H), 4.29 (dd, $^2J_{HH}$=12.3 Hz, $^3J_{HH}$=4.9 Hz, 1H), 5.01–5.2 (m, 1H), 5.25–5.32 (m, 3H), 6,61 (d, *E*, $^3J_{HF}$=25.1 Hz, 0.8H), 6.77 (d, *Z*, $^3J_{HF}$=36.6 Hz, 0.2H), 7.09 (d, $^3J_{HH}$=8.4 Hz, 1H), 7.14 (d, $^3J_{HH}$=8.4 Hz, 1H), 7.44 (s, 1H). HRMS: calcd for $C_{26}H_{35}O_{12}NFS$ $[M+NH_4]^+$ 604.1859; found 604.1862.

4.4. General procedures for the reduction of α-fluorocinnamic acid thioesters

$NaBH_4$ (2.5 mmol) was added to a solution of thioesters (0.5 mmol) in EtOH (10 mL). The solution was stirred at room temperature for 24 h, after solvent evaporation, the residue was

extracted with CH_2Cl_2 (2×50 mL). The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The product was isolated by flash column chromatography using dichloromethane as eluent.

*4.4.1. (2Z)-2-Fluoro-3-phenyl-2-propen-1-ol (**7a**).* ^{19}F NMR ($CDCl_3$): δ=−110.9 (dt, $^3J_{HF}$=38.9 Hz, $^3J_{HF}$=14.8 Hz). ^1H NMR ($CDCl_3$): δ=4.56 (d, $^3J_{HF}$=14.8 Hz, 2H), 5.55 (d, $^3J_{HF}$=38.9 Hz, 1H), 7.25 (m, 1H), 7.31 (d, $^3J_{HH}$=8.4 Hz, 2H), 7.50 (d, $^3J_{HH}$=8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ=61.2 (d, $^2J_{CF}$=28.8 Hz), 102.3, 128.2, 128.9, 130.2, 132.0, 157.9 (d, $^1J_{CF}$=265.9 Hz). HRMS: calcd for $C_9H_{10}OF$ $[M+H]^+$ 153.0710; found 153.0707.

*4.4.2. (2Z)-2-Fluoro-3-(4-fluorophenyl)-2-propen-1-ol (**7b**).* ^{19}F NMR ($CDCl_3$): δ=−114.8 (dt, $^3J_{HF}$=37.9 Hz, $^3J_{HF}$=14.3 Hz, 1F), 113.9 (m, 1F). ^1H NMR ($CDCl_3$): δ=4.26 (d, $^3J_{HF}$=14.5 Hz, 2H), 5.76 (d, $^3J_{HF}$=37.9 Hz, 1H), 7.01 (dd, $^3J_{HF}$=8.7 Hz, $^3J_{HH}$=8.7 Hz, 2H), 7.47 (dd, $^3J_{HH}$=8.7 Hz, $^4J_{HF}$=5.4 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ=61.9 (d, $^2J_{CF}$=32.6 Hz), 106.5 (d, $^2J_{CF}$=6.8 Hz), 115.6 (d, $^2J_{CF}$=21.5 Hz), 128.8, 130.3 (dd, $^3J_{CF}$=8.4 Hz, $^4J_{CF}$=8.4 Hz), 157.5 (d, $^1J_{CF}$=263.8 Hz), 162.4 (d, $^1J_{CF}$=247.5 Hz). HRMS: calcd for $C_9H_9OF_2$ $[M+H]^+$ 171.0616; found 171.0614.

*4.4.3. (2Z)-2-Fluoro-3-(4-nitrophenyl)-2-propen-1-ol (**7c**).* ^{19}F NMR ($CDCl_3$): δ=−107.5 (dt, $^3J_{HF}$=37.9 Hz, $^3J_{HF}$=11.2 Hz). ^1H NMR ($CDCl_3$): δ=4.35 (d, $^3J_{HF}$=11.2 Hz, 2H), 5.86 (d, $^3J_{HF}$=37.9 Hz, 1H), 7.62 (d, $^3J_{HH}$=8.8 Hz, 2H), 8.19 (d, $^3J_{HH}$=8.8 Hz). ^{13}C NMR ($CDCl_3$): δ=61.3 (d, $^2J_{CF}$=33.9 Hz), 105.1, 123.8, 129.1, 139.4, 146.5, 161.2 (d, $^1J_{CF}$=272.7 Hz). HRMS: calcd for $C_9H_9O_3NF$ $[M+H]^+$ 198.0561; found 198.0560.

*4.4.4. (2Z)-2-Fluoro-3-(3-bromophenyl)-2-propen-1-ol (**7d**).* ^{19}F NMR ($CDCl_3$): δ=−111.2 (dt, $^3J_{HF}$=38.2 Hz, $^3J_{HF}$=14.0 Hz, 1F). ^1H NMR ($CDCl_3$): δ=4.30 (d, $^3J_{HF}$=14.0 Hz, 2H), 5.73 (d, $^3J_{HF}$=38.2 Hz, 1H), 7.20 (dd, $^3J_{HH}$=7.9 Hz; 7.43 Hz, 1H), 7.38 (d, $^3J_{HH}$=7.5 Hz, 1H), 7.42 (d, $^3J_{HH}$=7.9 Hz, 1H), 7.68 (s, 1H). ^{13}C NMR ($CDCl_3$): δ=61.6 (d, $^2J_{CF}$=33.0 Hz), 106.1, 122.5, 127.2, 129.9, 130.5, 131.5, 134.6, 159.1 (d, $^1J_{CF}$=268.7 Hz). HRMS: calcd for $C_9H_9O^{79}BrF$ 230.9815 and for $C_9H_9O^{81}BrF$ $[M+H]^+$ 232.9795; found 230.9820 and 232.9802.

*4.4.5. (2Z)-2-Fluoro-3-(2-methylphenyl)-2-propen-1-ol (**7e**).* ^{19}F NMR ($CDCl_3$): δ=−115.6 (dt, $^3J_{HF}$=37.9 Hz, $^3J_{HF}$=20.3 Hz, 1F). ^1H NMR ($CDCl_3$): δ=2.31 (s, 3H), 4.91 (d, $^3J_{HF}$=20.3 Hz, 2H), 5.92 (d, $^3J_{HF}$=37.9 Hz, 1H), 7.14 (d, $^3J_{HH}$=7.1 Hz, 1H), 7.17 (dd, $^3J_{HH}$=7.4 Hz; 7.5 Hz, 1H), 7.24 (d, $^3J_{HH}$=7.4 Hz, 1H), 7.39 (dd, $^3J_{HH}$=7.1 Hz; 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ=18.1, 61.3 (d, $^2J_{CF}$=31.8 Hz), 105.2, 111.7, 114.6, 125.7, 128.2, 132.0, 135.1, 157.7 (d, $^1J_{CF}$=265.6 Hz) ppm. HRMS: calcd for $C_{10}H_{12}OF$ $[M+H]^+$ 167.0872; found 167.0875.

*4.4.6. 2,3,4,6-Tetra-O-acetyl-1-[4-((2Z)-2-fluoro-3-hydroxyprop-1-enyl)-2-methoxyphenyl]-β-D-glucopyranoside (**7f**).* Mp 133–134 °C. ^{19}F NMR ($CDCl_3$): δ=−114.67 (dt, $^3J_{HF}$=38.5 Hz, $^3J_{HF}$=14.3 Hz, 1F). ^1H NMR ($CDCl_3$): δ=2.00 (s, 6H), 2.04 (s, 6H), 3.63–3.70 (m, 1H), 3.80 (s, 3H), 4.15 (dd, $^2J_{HH}$=14.3 Hz, $^3J_{HH}$=7.1 Hz, 1H), 4.20 (dd, $^2J_{HH}$=12.3 Hz, $^3J_{HH}$=4.9 Hz, 1H), 4.22 (d, $^3J_{HF}$=14.3 Hz, 2H), 5.07–5.17 (m, 2H), 5.24–5.29 (m, 2H), 5.65 (d, $^3J_{HF}$=38.5 Hz, 1H), 6.92 (d, $^3J_{HH}$=7.8 Hz, 1H), 7.02 (d, $^3J_{HH}$=8.0 Hz, 1H), 7.08 (s, 1H). ^{13}C NMR ($CDCl_3$): δ=20.6, 56.0, 61.6 (d, $^2J_{CF}$=32.7 Hz), 61.9, 68.4, 71.2, 72.0, 72.7, 100.6, 106.6, 112.9, 119.7, 121.5, 128.6, 145.3, 150.3, 158.1 (d, $^1J_{CF}$=266.2 Hz), 169.4, 170.3, 170.7. HRMS: calcd for $C_{24}H_{33}O_{12}NF$ $[M+NH_4]^+$ 546.1981; found 546.1990.

4.5. 1-[4-((2*Z*)-2-fluoro-3-hydroxyprop-1-enyl)-2-methoxyphenyl]-β-D-glucopyranoside, (*Z*)-β−fluoroconiferin (8)

2,3,4,6-tetra-*O*-acetyl-1-[4-((2*Z*)-2-fluoro-3-hydroxyprop-1-enyl)-2-methoxyphenyl]-β-D-glucopyranoside (0.5 mmol) **7f** was dissolved in 40 mL of a mixture of MeOH/THF (50:50). A solution of sodium methoxide, prepared from 10 mg of sodium metal in methanol (10 mL) was added. When the deprotection was completed, the solution was neutralized by adding 2.0 g of an ion-exchange resin (H^+ form). The agitation was maintained for 30 min, and then the resin was filtered. The methanol was eliminated by vacuum evaporation, at room temperature. The product was isolated by chromatography on a C18 cartridge (LC-SPE) using a mixture of MeOH/H_2O 30/70 as eluent. Mp 141–142 °C. ^{19}F NMR (CD_3OD): δ=−113.1 (dt, $^3J_{HF}$=38.9 Hz, $^3J_{HF}$=15.4 Hz, 1F). ^1H NMR (CD_3OD): δ=3.25–3.45 (m, 4H), 3.62 (m, 1H), 3.71 (m, 1H), 3.83 (s, 3H), 4.20 (d, $^3J_{HF}$=15.4 Hz, 2H), 4.82 (d, $^3J_{HH}$=7.0 Hz, 1H), 5.80 (d, $^3J_{HF}$=38.9 Hz, 1H), 7.04 (d, $^3J_{HH}$=8.3 Hz, 1H), 7.13 (d, $^3J_{HH}$=8.1 Hz, 1H), 7.18 (s, 1H). ^{13}C NMR (CD_3OD): δ=56.7, 61.8 (d, $^2J_{CF}$=32.2 Hz), 62.5, 71.3, 75.0, 77.8, 78.1, 102.6, 107.7, 114.0, 117.7, 123.2, 129.6, 147.3, 150.5, 159.9 (d, $^1J_{CF}$=265.9 Hz). HRMS: calcd for $C_{16}H_{25}O_8NF$ $[M+NH_4]^+$ 378.1559; found 378.1555.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2012.02.039. These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

1. (a) Boehm, H.-J.; Banner, D.; Bendels, S.; Kansy, M.; Kuhn, B.; Mueller, K.; Obst-Sander, U.; Stahl, M. *ChemBioChem* **2004**, *5*, 637–643; (b) Jeschke, P. *ChemBioChem* **2004**, *5*, 570–589; (c) Ojima, I. *ChemBioChem* **2004**, *5*, 628–635.
2. Kirk, K. L. *J. Fluorine Chem.* **2006**, *127*, 1013–1029.
3. (a) Yanai, H.; Taguchi, T. *Eur. J. Org. Chem.* **2011**, *2011*, 5939–5954; (b) Landelle, G.; Bergeron, M.; Turcotte-Savard, M.-O.; Paquin, J.-F. *Chem. Soc. Rev.* **2011**, *40*, 2867–2908.
4. (a) Burkhart, J. P.; Weintraub, P. M.; Gates, C. A.; Resvick, R. J.; Vaz, R. J.; Friedrich, D.; Angelastro, M. R.; Bey, P.; Peet, N. P. *Bioorg. Med. Chem.* **2002**, *10*, 929–934; (b) Michel, D.; Schlosser, M. *Tetrahedron* **2000**, *56*, 4253–4260; (c) Poulter, C. D.; King, C. H. R. *J. Am. Chem. Soc.* **1982**, *104*, 1422–1424; (d) Wei, H.-X.; Schlosser, M. *Eur. J. Org. Chem.* **1998**, 2603–2607.
5. (a) Luo, F.; Wang, P.; Gong, Y. *Tetrahedron Lett.* **2010**, *51*, 1693–1695; (b) Pierry, C.; Zoute, L.; Jubault, P.; Pfund, E.; Lequeux, T.; Cahard, D.; Couve-Bonnaire, S.; Pannecoucke, X. *Tetrahedron Lett.* **2009**, *50*, 264–266; (c) Engman, M.; Diesen, J. S.; Paptchikhine, A.; Andersson, P. G. *J. Am. Chem. Soc.* **2007**, *129*, 4536–4537.
6. Pierry, C.; Cahard, D.; Couve-Bonnaire, S.; Pannecoucke, X. *Org. Biomol. Chem.* **2011**, *9*, 2378–2386.
7. Daubresse, N.; Chupeau, Y.; Francesch, C.; Lapierre, C.; Pollet, B.; Rolando, C. *Chem. Commun.* **1997**, 1489–1490.
8. (a) Wengenmayer, H.; Ebel, J.; Grisebach, H. *Eur. J. Biochem.* **1976**, *65*, 529–536; (b) Humphreys, J. M.; Chapple, C. *Curr. Opin. Plant Biol.* **2002**, *5*, 224–229.
9. (a) Barron, E. J.; Mooney, L. A. *Anal. Chem.* **1968**, *40*, 1742–1744; (b) Nagao, Y.; Kawabata, K.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1978**, 330; (c) Liu, H. J.; Bukownik, R. R.; Pednekar, P. R. *Synth. Commun.* **1981**, *11*, 599–603; (d) Liu, H. J.; Luo, W. *Can. J. Chem.* **1992**, *70*, 128–134.
10. Day, A.; Neutelings, G.; Nolin, F.; Grec, S.; Habrant, A.; Cronier, D.; Maher, B.; Rolando, C.; David, H.; Chabbert, B.; Hawkins, S. *Plant Physiol. Biochem.* **2009**, *47*, 9–19.
11. (a) Coutrot, P.; Charbonnier, C.; Grison, C. *Synthesis* **1991**, 23–26; (b) Liu, H. J.; Rose, P. A.; Sasaki, D. J. *Can. J. Chem.* **1991**, *69*, 934–936; (c) Schaumann, E.; Mergardt, B.; Fittkau, S. *Synthesis* **1990**, 47–51.
12. (a) Keck, G. E.; Boden, E. P.; Mabury, S. A. *J. Org. Chem.* **1985**, *50*, 709–710; (b) Lucast, D. H.; Wemple, J. *Tetrahedron Lett.* **1977**, 1103–1106; (c) van Zijl, A. W.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2008**, *73*, 5651–5653; (d) den Hartog, T.; van Dijken, D. J.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron: Asymmetry* **2010**, *21*, 1574–1584.
13. Pirrung, M. C.; Rowley, E. G.; Holmes, C. P. *J. Org. Chem.* **1993**, *58*, 5683–5689.

14. (a) Inagaki, H.; Takeda, T.; Miyauchi, R. N.; Kawakami, K.; Takahashi, H.; Takemura, M. *Heterocycles* **2004**, *63*, 699–706; (b) Zhao, S.; He, Y.-h.; Wu, D.; Guan, Z. *J. Fluorine Chem.* **2010**, *131*, 597–605.
15. (a) Coutrot, P.; Ghribi, A. *Synthesis* **1986**, 661–664; (b) Teichert, A.; Jantos, K.; Harms, K.; Studer, A. *Org. Lett.* **2004**, *6*, 3477–3480.
16. (a) Etemad-Moghadam, G.; Seyden-Penne, J. *Bull. Soc. Chim. Fr.* **1985**, 448–454; (b) Sano, S.; Teranishi, R.; Nagao, Y. *Tetrahedron Lett.* **2002**, *43*, 9183–9186.
17. Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1990**, *55*, 4639–4642.
18. Appel, R.; Loos, R.; Mayr, H. *J. Am. Chem. Soc.* **2009**, *131*, 704–714.
19. Romanenko, V. D.; Kukhar, V. P. *Chem. Rev.* **2006**, *106*, 3868–3935.
20. (a) Fukuyama, T.; Lin, S. C.; Li, L. *J. Am. Chem. Soc.* **1990**, *112*, 7050–7051; (b) Fukuyama, T.; Tokuyama, H. *Aldrichimica Acta* **2004**, *37*, 87–96; (c) Tokuyama, H.; Yokoshima, S.; Lin, S.-C.; Li, L.; Fukuyama, T. *Synthesis* **2002**, 1121–1123; (d) Kimura, M.; Seki, M. *Tetrahedron Lett.* **2004**, *45*, 3219–3223; (e) van Zijl, A. W.; Szymanski, W.; Lopez, F.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2008**, *73*, 6994–7002; (f) Evans, D. A.; Connell, B. T. *J. Am. Chem. Soc.* **2003**, *125*, 10899–10905.
21. (a) Beak, P.; Becker, P. D. *J. Org. Chem.* **1982**, *47*, 3855–3861; (b) Tsunoda, T.; Nagaku, M.; Nagino, C.; Kawamura, Y.; Ozaki, F.; Hioki, H.; Ito, S. *Tetrahedron Lett.* **1995**, *36*, 2531–2534; (c) Back, T. G.; Baron, D. L.; Yang, K. *J. Org. Chem.* **1993**, *58*, 2407–2413; (d) Kotsuki, H.; Yoshimura, N.; Ushio, Y.; Ohtsuka, T.; Ochi, M. *Chem. Lett.* **1986**, 1003–1004.
22. (a) Pawson, B. A.; Chan, K. K.; DeNoble, J.; Han, R. J.; Piermattie, V.; Specian, A. C.; Srisethnil, S.; Trown, P. W.; Bohoslawec, O.; Machlin, L. J.; Gabriel, E. *J. Med. Chem.* **1979**, *22*, 1059–1067; (b) Jin, Y.; Williams, D. C.; Croteau, R.; Coates, R. M. *J. Am. Chem. Soc.* **2005**, *127*, 7834–7842.
23. Ducry, L.; Roberge, D. M. *Org. Process Res. Dev.* **2008**, *12*, 163–167.
24. Ranu, B. C.; Mandal, T. *Aust. J. Chem.* **2007**, *60*, 223–227.
25. Daubresse, N.; Francesch, C.; Rolando, C. *Tetrahedron* **1998**, *54*, 10761–10770.
26. Daubresse, N.; Francesch, C.; Mhamdi, F.; Rolando, C. *Synthesis* **1998**, 157–161.
27. Zemmouri, R.; Kajjout, M.; Castanet, Y.; Eddarir, S.; Rolando, C. *J. Org. Chem.* **2011**, *76*, 7691–7698.
28. Rolando, C.; Daubresse, N.; Pollet, B.; Jouanin, L.; Lapierre, C. *C. R. Biol.* **2004**, *327*, 799–807.