Tetrahedron: *Asymmetry* 22 (2011) 394–398

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Efficient synthesis of *cis*-thiazolidinethiones derived from ephedrines

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ARTICLE INFO

Article history:
Received 4 November 2010
Revised 4 February 2011
Accepted 17 February 2011
Available online 23 March 2011

ABSTRACT

The reaction of chlorodeoxypseudoephedrine or chlorodeoxynorpseudoephedrine hydrochlorides with sodium dithiocarbonate in stirring ethanol at 0 °C to stereoselectively afford the corresponding *cis*-thiazolidinethiones in good yields (81% and 95%) is reported. The in situ formation of a *cis*-aziridine to explain the presence of *trans*-thiazolidinethione as a side product is proposed when the same reaction was carried out at room temperature. In addition, a 70:30 mixture of *trans*-isomers of a thiazolidinethione/isothiazolidinethione was formed when a *cis*-aziridine NH was reacted with carbon disulfide in refluxing ethanol. The analogous reaction with *cis*-aziridine N–Me stereoselectively affords the corresponding *cis*-thiazolidinethione. The ^{1}H and ^{13}C NMR data of the thiazolidinethiones were assigned. *cis*-3,4-Dimethyl-5-phenylthiazolidine-2-thione was crystallized from ethanol and its X-ray diffraction structure was analyzed.

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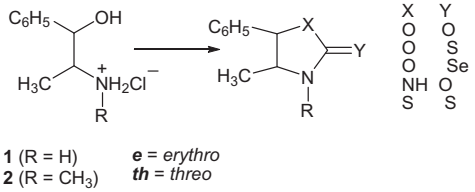
1. Introduction

Ephedrines **1** and **2** and their derivatives are well known to exhibit biological activity and have been widely used in asymmetric synthesis.[1] There are many examples where norephedrines **1** and ephedrines **2**, as a part of a cyclic system, have been used in asymmetric synthesis, mainly those of five-membered rings, such as oxazolidines,[2] oxazaborolidines,[3] oxazolines[4], and particulary oxazolidinones (X = Y = O, R = H),[5] oxazolidinselone (X = O, Y = Se, R = H),[6], and imidazolidinone (X = NH, Y = O, R = Me),[7] Scheme 1.



1 (R = H)
2 (R = CH_3)

e = *erythro*
th = *threo*

Scheme 1. 1,3-Heterazolidines-2-heterounsaturated derived from ephedrines.

Heterocyclic sulfur analogues derived from norephedrines **1** are scarcely used, only one example in which a oxazolidinethione (X = O, Y = S, R = H) was used in the resolution of a racemic mixture of chiral carboxylic acids and aminoacids has been reported.[9] On the other hand, to the best of our knowledge, there are no reports on the use of chiral thiazolidinethione (X = Y = S, R = H) as an asymmetric inductor. However, in recent reports, analogous chiral 4-alkylthiazolidinethiones in the form of *N*-acyl-thiazolidinethiones have been found to be efficiently used as asymmetric inductors for the synthesis of chiral molecules.[10]

Our recent research has been focused on the development of new reactions and reagents to obtain thiazolidinethiones (X = Y = S) from ephedrines **1**,**2**. The synthetic methods of 1,3-heterocycles with 2-one, 2-thione and 2-imine functional groups derived from ephedrines have been reported in the literature, and have recently been reviewed.[8]

With norephedrine ***1e*** and ephedrine ***2e***, Delaunay et al.[11] determined the reaction parameters for directing the formation of the corresponding oxazolidinethiones or thiazolidinethiones and established the mechanism and the stereochemistry of the reactions, that is, 5 equiv of CS_2 in an alkaline medium (KOH), requires 24 and 16 h to obtain thiazolidinethiones in 43% (R = H) and 60% (R = Me) yields, respectively.

On the other hand, methyldithiocarbamates **2** and **3**,[12] aziridines **4** and **5**,[13] and chlorodeoxypseudoephedrines **6** and **7**[14] have been used as intermediates in the synthesis of thiazolidinethiones **8** and **9** (Fig. 1).

When ephedrine-*N*-methyldithiocarbamate ***3e*** was refluxed in dichloromethane in the presence of mesyl chloride and pyridine, via an S_N2 process leading to a 2-(SMe)thiazolidinium intermediate and subsequent cleavage of the CH_3–S bond, the corresponding *trans*-thiazolidinethione ***9t*** was produced in 56% yield. Kellogg et al.[13] obtained the *cis*-thiazolidinethione ***9c*** in 81% yield through a ring opening reaction of *trans*-aziridine ***5t*** with CS_2. However, starting from *cis*-aziridine ***5c*** or *trans*-aziridine ***4t***, the same reaction was unsuccessful. Condensation of *dl*-chlorodeoxypseudoephedrine hydrochlorides ***7th***[14a] with potassium ethyl xanthate,

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doi:10.1016/j.tetasy.2011.02.016

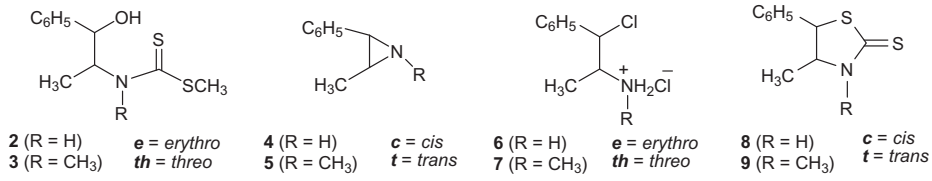


Figure 1. Intermediates used in the synthesis of thiazolidinethiones **8**,**9**.

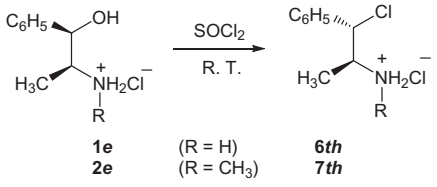
gave low yields (26%) of the corresponding thiazolidinethione **9*c***. The treatment of *erythro*- or *threo*-chlorodeoxynorephedrines·HCl **6*e***, **6*th*** with thiophosgene afforded the respective *erythro*- or *threo*-1-chloro-1-phenyl-2-isothiocyanatepropanes as intermediates. Each isothiocyanate diastereoisomer was reacted with NaSH, the reaction was stereospecific with inversion at the carbon atom to give *cis*- or *trans*-thiazolidinethiones **8*c***, **8*t***, in high yields (90%).[14b]

In 1995, we reported that chlorodeoxypseudoephedrine·HCl **7*th*** reacts with a 33% aqueous solution of sodium trithiocarbonate (Na_2CS_3) in refluxing ethanol to give *cis*-thiazolidinethione **9*c*** in 53% yield.[14c] The same reaction with chlorodeoxynorpseudoephedrine **6*th*** failed to give the corresponding *cis*-thiazolidinethione derivative **8*c***.

In spite of their high potential use in synthesis, thiazolidinethiones **8** have not been exploited because there is not an efficient synthetic method to obtain them and, the regents used are expensive or dangerous. As a result, we are interested in the design of new routes for their synthesis or to improve existing methods in order to increase the yields. With this in mind, we decided to start from either chlorodeoxynorpseudoephedrine **6*th*** or chlorodeoxypseudoephedrine **7*th*** to obtain selectively *cis*- or *trans*-thiazolidinethiones **8** and **9** derived from ephedrines **1** and **2**.

2. Results and discussion

To obtain chlorodeoxynorpseudoephedrine **6*th*** or chlorodeoxypseudoephedrine **7*th*** as starting materials for the synthesis of thiazolidinethiones, a stereoselective chlorination with $SOCl_2$ was used. It is well known that the reaction of hydrochlorides of norephedrine **1*e*** or ephedrine **2*e*** with thionyl chloride at room temperature proceeds stereoselectively with inversion of C-1 configuration (S_N2 mechanism) to give the corresponding hydrochlorides of chlorodeoxypseudoephedrines **6*th***, **7*th***, respectively (Scheme 2).[15]



Scheme 2. Chlorodeoxypseudoephedrine hydrochlorides from chlorination reaction of ephedrines **1*e*** and **2*e***.

To obtain thiazolidinethiones **8**, **9**, the chlorohydrates of chlorodeoxy*pseudo*ephedrines **6*th***, **7*th*** were reacted with one molar equivalent of sodium dithiocarbonate ethanolic solution at room temperature for 6 h. Next, Na_2COS_2 was prepared in situ from two molar equivalents of NaOH and one molar equivalent of carbon disulfide in stirring ethanol at room temperature for 3 h. In the case of chlorodeoxynorpseudoephedrine·HCl **6*th***, a white powder solid precipitated from ethanol. The *cis*- and *trans*-relationships between the phenyl and the methyl groups in thiazolidinethiones **8** were deduced from analysis of their ^{1}H NMR spectra; owing to the magnetic anisotropy of the phenyl substituent, the methyl group in the *cis*-compound **8*c*** is more shielded (1.0 ppm) than in the *trans*-isomer **8*t*** (1.36). In addition, the characteristic ^{13}C NMR chemical shifts of thiocarbonyl carbon appeared at 199.5 ppm for **8*t*** and 200.3 ppm for **8*c***, which is in agreement with data reported in the literature.[14b] On this basis, the product represented a mixture of *cis*/*trans*-thiazolidinethiones of **8** in a 9:1 ratio. A S_N2 mechanism to explain the inversion of configuration at C1 followed by cyclization to give the *cis*-isomer is proposed in Scheme 3. On the other hand, a competitive double S_N2 mechanism on C1, followed by cyclization in which *cis*-aziridine **4*c*** as intermediate is involved to explain the presence of the *trans*-isomer **8*t***. Analogous mechanistic observations have been proposed to stereospecifically obtain thiazolidinethiones from the reaction of vic-iodoalkanecarbamates with potassium ethylxanthate then NaOH.[16]

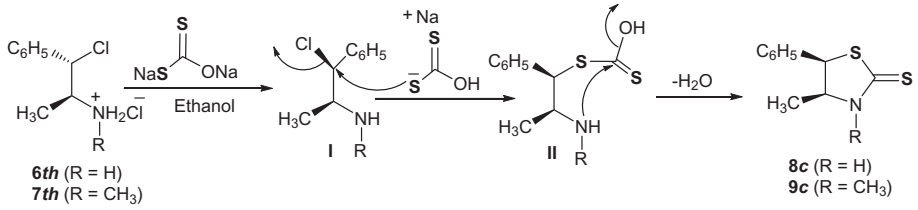
To avoid the formation of the aziridine, the same reaction was carried out at low temperature. After 6 h of stirring at 0 °C, only *cis*-thiazolidinethione **8*c*** was precipitated from ethanol as a white powder in 95% yield.

If the ^{1}H NMR spectra of pure *cis*-thiazolidinethione **8*c*** is recorded in a concentrated solution, the thione tautomeric form is observed (δ NH at 8.3 ppm). However, in diluted solution, the thiol is the observed tautomer, in this case, the SH group appeared at 1.6 ppm.

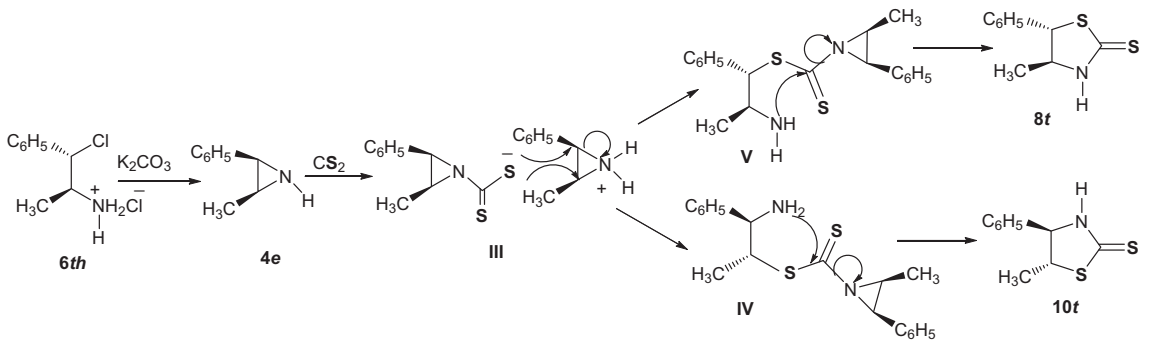
The same reactivity was observed for chlorodeoxypseudoephedrine·HCl **7*th*** using the reaction conditions already mentioned for **6*th***. The reaction of **7*th*** at 0 °C was performed and after 3 days, white orthorhombic crystals of *cis*-thiazolidinethione **9*c*** precipitated from ethanol in 81% yield. The ^{13}C NMR chemical shift at 195.0 ppm of the thiocarbonyl carbon atom, the ^{1}H NMR chemical shift of C–CH_3 at 1.0, and the X-ray diffraction structure are indicative of the formation of the *cis*-isomer. The NMR data of the *trans*-isomer **9*t*** is 195.0 ppm for thiocarbonyl carbon and 1.46 ppm for the methyl hydrogens of the C–CH_3 group.

To confirm that the *cis*-aziridine intermediate is responsible for *trans*-thiazolidinethione formation, Kelloggs method was used with *cis*-aziridine **4*c***, **5*c*** to obtain the corresponding *trans*-thiazolidinethiones **8*t***, **9*t***.

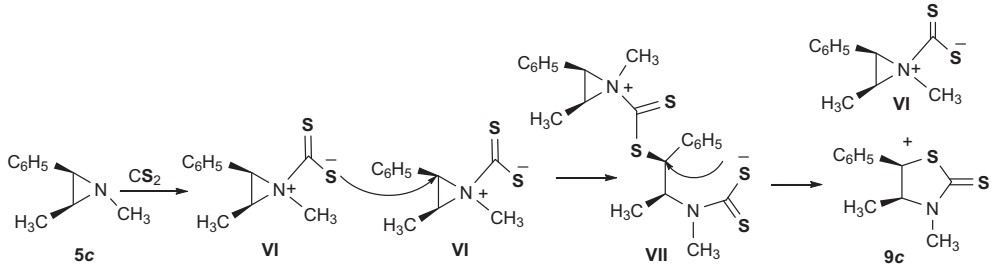
The *cis*-aziridines **4*c***, **5*c*** were obtained when HCl salts of chlorodeoxypseudoephedrines **6*th***, **7*th*** were reacted with three molar equivalents of K_2CO_3 in refluxing ethanol.[17] The corresponding *cis*-aziridine was reacted with CS_2 in stirring ethanol for 48 h at 0 °C. In the case of the reaction of *cis*-aziridine **4*c***, a 70:30 mixture of two compounds were observed in the ^{1}H NMR spectra. The chemical shift of the C–CH_3 of the two resulting compounds was at 1.35 and 1.44 ppm, respectively. After comparison with the reported data, the two compounds were identified as the *trans*-isomers of the thiazolidinethiones.[11] The major heterocycle corresponded to *trans*-thiazolidinethione **8*t*** and the minor heterocycle was assigned to *trans*-isothiazolidinethione **10*t***, whose formation can be explained by ring opening at C3 and C2 of the aziridinium by the aziridinethiocarbamate anion of the intermediate **III**



Scheme 3. Mechanistic transformation to furnish *cis*-thiazolidinethiones from chlorodeoxypseudoephedrines.



Scheme 4. Mechanistic transformation from *cis*-aziridine **4c** into a mixture of *trans*-thiazolidinethione **8t** and *trans*-isothiazolidinethione **10t**.



Scheme 5. Mechanistic transformation for *cis*-aziridine **5c** into *cis*-thiazolidinethione **9c**.

(Scheme 4). This aziridinium opening reaction has been observed elsewere.[17,18]

On the other hand, when *cis*-aziridine **5c** was reacted with CS_2 under the same reaction conditions, *cis*-thiazolidinethione **9c** was obtained stereoselectively instead of the expected *trans*-isomer (Scheme 5). In this case, retention of the C1 configuration can be explained by the self attack of the aziridinium thiocarbamate zwitterion **VI** on the benzylic carbon, followed by closure of the intermediate **VII** to recover the initial C1 configuration.*cis*-Thiazolidinethione **9c** was crystallized from ethanol and its molecular structure studied by X-ray diffraction (Fig. 2). The N3–C2(S2)–S1 conjugated system is proposed since the distances are of an intermediate value between a single (1.469 Å) and a double (1.279 Å)[19] N–C bond (N3–C2 = 1.35 Å) and a single (1.789 Å) and a double (1.600 Å) C–S bond (S1–C2 = 1.741 Å and S2–C2 = 1.659). Conjugation allows N3 to be in an sp^2 hybridation, as the angles C(4)-N(3)–C(12) = 119.9(3), C(2)–N(3)–C(4) = 116.2(3) and C(2)–N(3)–C(12) = 121.6(3) show values close to 120°. On the other hand, the torsion angles N(3)–C(2)–S(1)–C(5) of 5.3(3)°, S(2)–C(2)–N(3)–C(12) of −1.8(5)° are very close to 0°, and S(2)–C(2)–S(1)–C(5) of −177.4(2)°, S(1)–C(2)–N(3)–C(12) of 175.1(3) are close to 180°, thus the five membered ring is almost planar.

An intramolecular contact between the hydrogen atom of the N–CH_3 group and the sulfur atom of the thiocarbonyl group occurred to form a five membered ring. The C12H12···S2 distance of 2.72(4) Å [angle of 111(3)°] is in the proper range for a strong interaction of this kind.[20]

3. Conclusions

The reaction of chlorodeoxypseudoepherine hydrochlorides **6th**, **7th** with sodium dithiocarbonate in stirring ethanol at 0 °C, stereoselectively afforded the corresponding *cis*-thiazolidinethiones **8c**, **9c** in high yield. When the same reaction was carried out at room temperature, the formation of a *cis*-aziridine is proposed as an intermediate to explain the presence of *trans*-thiazolidinethiones as the secondary product.

The reaction of *cis*-aziridine **4c** with CS_2 at room temperature affords a 70:30.mixture of the *trans*-isomers of thiazolidinethione **8t**/isothiazolidinethione **10t**, respectively. However, the reaction with *cis*-aziridine **5c** stereoselectively affords the corresponding *cis*-thiazolidinethione **9c**.

Thiazolidinethiones were assigned by ^1H and ^{13}C NMR data. The *cis*- and *trans*-relationships between the phenyl and the methyl groups in thiazolidinethiones were deduced from the analysis of their ^1H NMR spectra; the methyl groups in the *cis*-compounds are more shielded by approximately 0.4 ppm than in the *trans*-isomers. The thiol tautomeric form was observed in the ^1H NMR

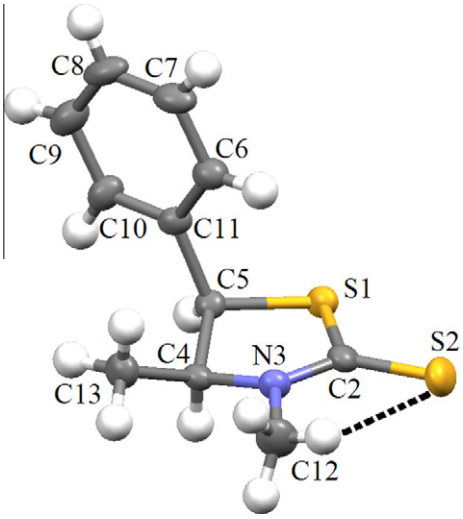


Figure 2. X-ray diffraction structure of *cis*-thiazolidinethione **9c**. Representative bond lengths (Å): S(1)–C(2) = 1.741(3), S(1)–C(5) = 1.828(4), S(2)–C(2) = 1.659(3), N(3)–C(2) = 1.325(4); N(3)–C(4) = 1.471(4), C(4)–C(5) = 1.538(4). Representative bond/valence angles (°): C(2)–S(1)–C(5) = 93.36(14), C(2)–N(3)–C(4) = 116.2(3), C(2)–N(3)–C(12) = 121.6(3), C(4)–N(3)–C(12) = 119.9(3), S(1)–C(2)–S(2) = 119.8(2), S(1)–C(2)–N(3) = 111.8(2), S(2)–C(2)–N(3) = 128.4(3), N(3)–C(4)–C(5) = 107.0(2), N(3)–C(4)–C(13) = 113.0(3), S(1)–C(5)–C(4) = 103.8(2). Representative torsion/dihedral angles (°): S(2)–C(2)–S(1)–C(5) = −177.4(2), N(3)–C(2)–S(1)–C(5) = 5.3(3), S(1)–C(2)–N(3)–C(4) = 12.5(3), S(1)–C(2)–N(3)–C(12) = 175.1(3), S(2)–C(2)–N(3)–C(4) = −164.5(3), S(2)–C(2)–N(3)–C(12) = −1.8(5), C(5)–C(4)–N(3)–C(2) = −27.6(4), N(3)–C(4)–C(5)–C(6) = −97.1(3), C(13)–C(4)–N(3)–C(12) = 42.6(5), C(4)–C(5)–S(1)–C(2) = −19.5(2). Crystal data: formula, $C_{11}H_{13}NS_2$; formula weight, 223.36; crystal system, orthorhombic; space group, P_{212121} (No. 19); *a*, *b*, *c* [Å], 19.3065(17), 7.0924(6), 8.2654(7); *V* [Ang^3], 1131.78(17); *Z*, 4; ρ(calcd) [g/cm^3], 1.311; μ(MoKα) [1/mm], 0.431; *F*(0 0 0), 472; crystal size [mm], 0.26 × 0.41 × 0.50. Data collection: temperature (*K*), 293; radiation [Å], MoKα, 0.71073; theta min–max [°], 2.1, 25.0; dataset, −22:22, −8:8, −9:9; Tot., uniq. data, *R*(int), 10,939, 1989, 0.029; observed data [$I > 2.0\sigma(I)$], 1968. Refinement: Nref, Npar, 1989, 179; *R*, wR_2, *S*, 0.0492, 0.1233, 1.27; $w = 1/[/s^2(Fo^2) + (0.0645\ P)^2 + 0.2906\ P]$, where $P = (Fo^2 + 2Fc^2)/3$; max. and av. shift/error, 0.00, 0.00; flack *x*, 0.01(13); min. and max. resd. dens. [*e*/Å^3], −0.18, 0.33.

spectra, if pure *cis*-thiazolidinethione **8c** is recorded in a dilute solution, whereas the thione tautomer was observed in a concentrated solution.

The molecular structure of *cis*-thiazolidinethione **9c** was confirmed by X-ray diffraction analysis. The intracyclic torsion angle values of *cis*-thiazolidinetione **9c** are close to 0° and 180° and are indicative that the thiazolidine ring is near to being a planar system.

4. Experimental

4.1. General

Melting points were measured on an Electrothermal IA apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 MHz (^{1}H, 300.08; ^{13}C, 75.46 MHz). The spectra were measured with tetramethylsilane as an internal reference following standard techniques. Mass spectrometer HP 5989A, 5890 series II. Crystallographic data (excluding structure factors) for structure of *cis*-thiazolidinethione **9c** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC: 798,828. X-ray diffraction cell refinement and data collection: APEX II Area Detector;[21] data reduction: SAINT;[22] programs used to solve structure: SHELXS-97;[23] software used to prepare material for publication: WINGX.[24]

4.2. (1*S*,2*S*)-Chlorodeoxynorpseudoephedrine hydrochloride 6*th*

To the (1*R*,2*S*)-(−)-norephedrine hydrochloride **1e** (1.0 g, 5.33 mmol), $SOCl_2$ (1.43 mL, 19.8 mmol) was added slowly. After stirring for 8 h at room temperature, the excess $SOCl_2$ was removed under vacuum. The resulting white solid was washed with acetone, filtered, and recrystallized from CH_3OH to give **6th** as a white solid (0.80 g, 73%), mp 205–207 °C; $[\alpha]_D^{33} = +10.4$ (*c* 0.1, H_2O); ^{1}H NMR [δ, ppm, DMSO-d_6]: 8.68 (br, 3H, $^+NH_3$), 7.45 (m, 5H, Ph), 5.26 (d, 1H, ^3J = 9.7 Hz, C1-H), 3.83 (dq, 1H, *J* = 9.7, 6.7 Hz, C2-H), 1.03 (d, 3H, ^3J = 6.7 Hz, C2-*C*H$_3$). ^{13}C NMR [δ, ppm, DMSO-d_6]: 138.08 (Ci), 129.9 (Cp), 129.65 (Co), 128.51 (Cm), 65.0 (C1), 52.92 (C2), 16.91 C2–*C*H$_3$; IR (KBr, ν_{max}/cm^{-1}): 3420 (NH_3), 3058, 3014 (Ar), 2996, 2974, 2958 (CH, CH_3), 716, 692 (Cl); Elemental Anal. Calcd C, 52.4461; H, 6.3570; N, 6.7956. Found: C, 53.1263; H, 6.4989; N, 7.5554.

4.3. (1*S*,2*S*)-Chlorodeoxypseudoephedrine hydrochloride 7*th*

The same procedure as for **6th** with (1*R*,2*S*)-(−)-ephedrine hydrochloride **2e** (1.0 g, 4.96 mmol) to get **7th** as a white solid (0.82 g, 75%); mp 198-200 °C; $[\alpha]_D^{30} = +10.5$ (*c* 0.1, CH_3OH), ^{1}H NMR [δ, ppm, DMSO-d_6]: 9.45 (br, 2H, $^+NH_2CH_3$), 7.4 (m, 5H, Ph), 5.45 (d, 1H, ^3J = 9.4 Hz, C1-H), 3.96 (dq, 1H, *J* = 9.4, 6.7 Hz, C2-H), 2.60 (s, 3H, N–CH_3), 1.03 (d, 3H, ^3J = 6.7 Hz, C2-*C*H$_3$). ^{13}C NMR [δ, ppm, DMSO-d_6]: 137.92 (Ci), 129.98 (Cp), 129.71 (Co), 129.71 (Cm), 62.98 (C1), 58.93 (C2), 29.84 (N–*C*H$_3$); 13.59 C2-*C*H$_3$.

4.4. (4*S*,5*R*)-*cis*-4-Methyl-5-phenyl-thiazolidinethione 8*c*

(1*S*,2*S*)-Chlorodeoxynorpseudoephedrine·HCl **6th** (5.0 g, 24.27 mmol) was dissolved in 10 mL of ethanol. To this was added a solution prepared with NaOH (2.0 g, 50 mmol) and, CS_2 (2.5 g, 32.9 mmol) after stirring for 3 h in 10 mL of ethanol. The resulting mixture was stirred for 6 h at room temperature, the precipitate was filtered off, and washed three times with 5 mL of water to eliminate the NaCl to get 4.75 g of **8c** as a white powder in 95% yield: mp = 89–90 °C; *m*/*z*: 117(55%), 123(76%), 166(27%), 209.2(100%); $[\alpha]_D = -33$ (*c* 0.2, $CHCl_3$) ^{1}H NMR [δ, ppm, $CDCl_3$]: 8.28 (br, 1H, NH), 7.2–7.4 (m, 5H, Ph), 4.97 (d, 1H, ^3J = 7.3 Hz, C5-H), 4.63 (dq, 1H, C4-H); 1.0 (d, 3H, ^3J = 6.75 Hz, C4-*C*H$_3$). ^{13}C NMR [δ, ppm, DMSO-d_6]: 201.14 (C=S), 135.6 (C*i*), 129.0 (C*o*), 128.9 (C*p*), 128.6 (C*m*), 63.31 (C4), 57.85 (C5), 15.92 C4–*C*H$_3$.

4.5. (4*S*,5*R*)-*cis*-3,4-Dimethyl-5-phenyl-thiazolidinethione 9*c*

The same procedure as for **8c** with (1*S*,2*S*)-chlorodeoxypseudoephedrine·HCl **7th** (5.0 g, 22.72 mmol). 4.05 g of **9c** crystallized from ethanol (81% yield): mp = 61–62 °C; *m*/*z*: 117(38%), 118(30%), 166(11%), 223 (100%); $[\alpha]_D = -18.8$ (*c* 3.3 × 10^{-3}, $CHCl_3$); ^{1}H NMR [δ, ppm, $CDCl_3$]: 7.2–7.4 (m, 5H, Ph), 5.0 (d, 1H, ^3J = 7.6 Hz, C5-H), 4.41 (dq, 1H, C4-H); 3.27 (s, 3H, N–CH_3), 1.0 (d, 3H, ^3J = 6.75 Hz, C4-*C*H$_3$). ^{13}C NMR [δ, ppm, DMSO-d_6]: 196.31 (C=S), 135.0 (C*i*), 129.1 (C*o*), 129.2 (C*p*), 128.8 (C*m*), 69.2 (C4), 52.66 (C5), 35.24 (N–*C*H$_3$); 14.28 C4-*C*H$_3$.

4.6. (4*S*,5*S*)-*trans*-4-Methyl-5-phenyl-thiazolidinethione 8*t*

(2*S*,3*R*)-*cis*-2-Methyl-3-phenylaziridine **4c** (0.5 g, 3.76 mmol) and 0.23 mL of CS_2 (291.2 mg, 4.5 mmol) were dissolved in 3 mL of ethanol. The resulting mixture was stirred for 48 h on an ice bath in the refrigerator. The ethanol was evaporated to give 0.6 g of an oily residue. The NMR spectra showed a mixture of the *trans*-isomers of thiazolidinethione **8t** and isothiazolidinethione **10t** in a 70:30 ratio. *trans*-Thiazolidinethione **8t** ^{1}H NMR [δ, ppm, $CDCl_3$]:

8.0 (br, 1H, NH), 7.2–7.5 (m, 5H, Ph), 4.70 (d, 1H, ^3J = 8.8 Hz, C5-H), 4.33 (dq, 1H, C4-H); 1.36 (d, 3H, ^3J = 6.16 Hz, C4-*C*H$_3$). ^{13}C NMR [δ, ppm, DMSO-d_6]: 199.7 (C=S), 136.86 (C*i*), 129.37 (C*o*), 129.05 (C*p*), 128.26 (C*m*), 67.73 (C4), 61.63 (C5), 18.72 C4-*C*H$_3$.

4.7. (4*R*,5*R*)-*trans*-5-Methyl-4-phenylthiazolidinethione 10*t*

^{1}H NMR [δ, ppm, $CDCl_3$]: 7.58 (br, 1H, NH), 7.3–7.5 (m, 5H, Ph), 4.78 (d, 1H, ^3J = 8.5 Hz, C5-H), 3.94 (dq, 1H, C4-H); 1.46 (d, 3H, ^3J = 6.75 Hz, C4-*C*H$_3$). ^{13}C NMR [δ, ppm, DMSO-d_6]: 201.1 (C=S), 137.36 (C*i*), 129.1 (C*o*), 129.37 (C*p*), 128.26 (C*m*), 74.97 (C4), 53.64 (C5), 18.87 C4-*C*H$_3$.

Acknowledgments

A.C. thanks Secretaría de Investigación y Posgrado del IPN, Grant SIP-20090455, for financial support.

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