SYNTHESIS OF ENANTIOPURE (*S*)-THIENO[*f*]INDOLIZIDINES

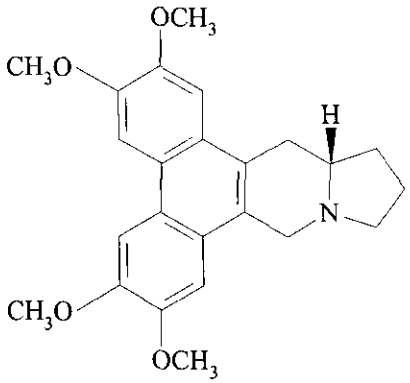
Stefan Marchalin,[a] Fridrich Szemes,[a] Nathalie Bar,[b] and Bernard Decroix*[b]

[a]Department of Organic Chemistry, Slovak Technical University, Radlinského 9, 8123 Bratislava, Slovak Republic

[b*]Laboratoire de Chimie, Faculté des Sciences et Techniques de l'Université du Havre, 30 rue Gabriel Péri, 76600 Le Havre, France

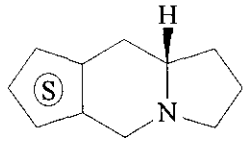
Abstract - The thieno[2,3 (or 3,2)-*f*]indolizidines (**5a**,**b**) were synthesized in four steps from ready available (*S*)-5-oxoprolines (**1a**,**b**) derivatives. The stereospecific reduction of (*S*)-thieno[*f*]indolizinediones (**2a**,**b**) was discussed and the optical purity of each compound was determined.

Tylophorine (**I**) belongs to the phenanthroindolizidine group of alkaloids.[1] Interest in this group of alkaloids stems in particular from their reported antitumor activity, unfortunately tylophorine is also highly toxic.[2] A variety of syntheses of tylophorine in both racemic and optically active form have been reported.[3]



Tylophorine, **I**

Scheme 1



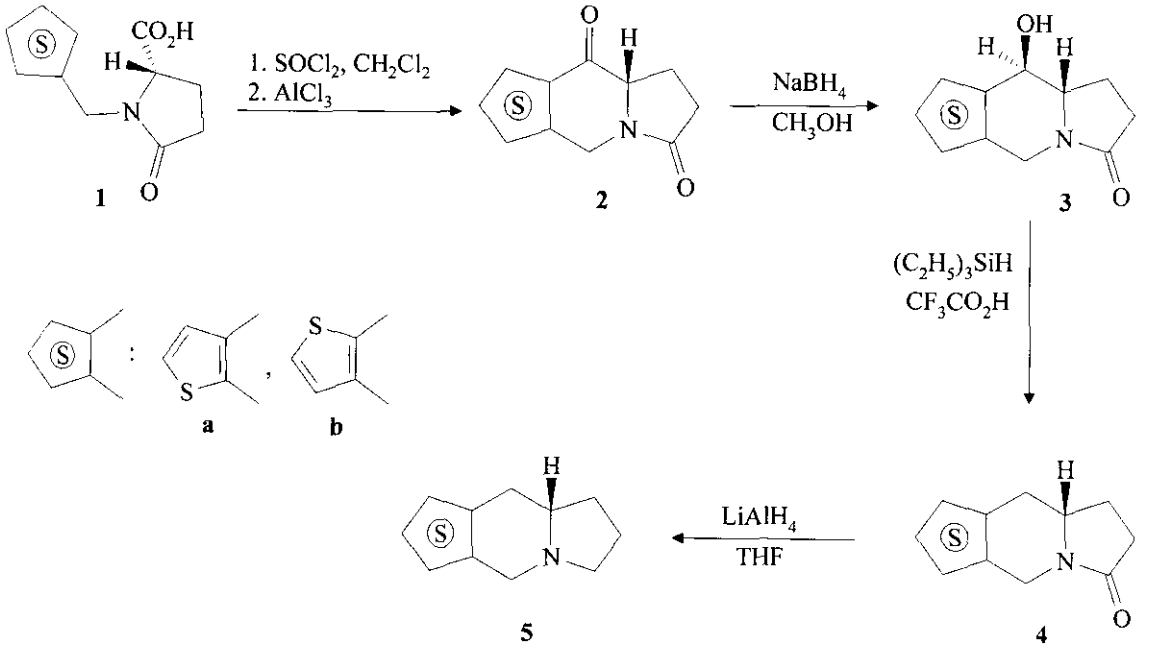
II

With our interest in the synthesis of diversely substituted polycyclic systems in this area we have previously reported indolizidines annulated to thiophene,[4,5] benzothiophene,[5,6] both thiophene and

benzene.[7,8] Now we wish to report herein the synthesis of enantiopure (*S*)-thieno[*f*]indolizidines of type (**II**), closely related compounds of tylophorine.

We have recently described an efficient synthesis of enantiopure *N*-alkylated proline derivatives,[9] which could be used in a large scale. In this way our objective begun with ready available optically pure compounds (**1a,b**) (see Scheme 2). These amido acids were conveniently converted to acid chlorides by the action of thionyl chloride in dichloromethane. The resulting acid chloride in dichloromethane, under Friedel-Crafts cyclization condidtions using aluminium trichloride of high quality as a catalyst gave the expected ketones (**2a,b**) in good yields (65, 70% respectively). Examination of the ^{1}H NMR spectra showed no racemization.

Scheme 2



At this stage it was interesting to test the reduction of amido ketones (**2a,b**). Actually Rapoport[10] has described the reduction of carbonyl group of phenanthroindolizidinediones and reported the formation of a diastereomeric mixture of alcohols. The best diastereoselectivity (α alcohol as the major product) was obtained when K-selectride® or L-selectride® were used as reducing reagents. On the other hand, we have described that the reduction with sodium borohydride of related compounds led to a stereoselective or a stereospecific reduction depending of the position of the fused thiophene ring.[11,12] Interestingly, reduction of amido ketones (**2a,b**) with sodium borohydride in methanol at 0-5 °C gave only one

diastereomer (**3a**) or (**3b**). The stereochemical assignments are based on analysis of the NMR spectra. The ^{1}H NMR coupling constants (8.6 Hz for **3a** and 8.1 Hz for **3b**) are characteristics of the *trans* diaxial relationship between H-9 and junction proton H-8a (see Scheme 2). There are consistent with those of similar compounds.[10,13,14] The β-alcohols (**3a**) and (**3b**) were obtained as optically pure compounds and their optical rotations are given in the Experimental. The enantiopurity of the products was determined by shift-experiments using Eu(hfc)$_3$. In similar conditions ($NaBH_4$, methanol) indolizidine-dione fused to benzene ring gave the β-alcohol as the major product, but indolizidinedione fused to naphtalene gave the β-alcohol as the minor product (20 %). In the phenanthrene series whatever the reductive reagent the α-alcohol was the major product (65 % with $NaBH_4$ and 97 % with L-selectride®). Our result is particularly interesting since we have obtained only the β-alcohol. Since the indolizidine moiety has probably the *cis* cinfiguration as in benzoindolizidinediones examination of molecular models reveals a striking aspect of the three dimensional configuration of the ketones (**2a,b**).[15] Because of the thiophene moiety carbons are coplanar, this results in the formation of two different ketone spatial environments. The central 6-membered heterocycle has a half-chair conformation and the reduction occurred on the carbonyl face leading to an equatorial position of the hydroxy group. This result was similar to those observed elsewhere in the benzoindolizidinedione series.[13] These alcohols (**3a,b**) treated with triethylsilane in trifluoroacetic acid led to the optically pure amides (**4a,b**) in moderate yields (65-67%). The structure of **4a,b** were supported by ^{1}H and ^{13}C NMR analysis as well as their microanalyses. Finally reduction of these amides were achieved using lithium aluminium hydride in refluxing tetrahydrofuran and gave the expected optically pure (*S*)-thieno[*f*]indolizidines (**5a,b**) in good yields (77-91%). Their ^{1}H NMR spectra revealed similar coupling constants to these observed for **4a,b**.

In conclusion, we have described a short synthesis of enantiopure (*S*)-thieno[*f*]indolizidines, heteroanalogs of tylophorine. The optical purity of each product was assumed by ^{1}H and ^{13}C NMR analyses by regarding the downfield shifts of the signal which resulted of the addition of Eu(hfc)$_3$ to the chiral compounds compared to those observed with the racemic mixture.

EXPERIMENTAL

Melting points were measured on a Boetius micro hot-stage and are uncorrected. UV spectra were determined in methanol with a Carl-Zeiss Jena M-40 spectrophotometer. The IR spectra were recorded on a Philips analytical PV 9 800 FT IR spectrophotometer (potassium bromide). The NMR spectra were recorded on a Bruker AC-200 Spectrometer (200 MHz) in $CDCl_3$ and DMSO-d_6 (compounds **3a,b**) using tetramethylsilane (^{1}H) or DMSO-d_6 (^{13}C, δ=39.5 ppm) as the internal standart. Optical rotations were

measured with a Perkin-Elmer 241 polarimeter in a 10 cm cell in ethanol (c 1) at 25 °C. Ascending thin layer chromatography was performed on precoated of silica gel 60 F 254 (Merck) and the spots were visualized using UV lamp or iodine vapor. E. Merck silica gel 60 F (70-300 mesh) was used for column chromatography. The elemental analyses were carried out by the microanalysis laboratory of INSA of Rouen, F 76130 $M^T.S^T$. Aignan. MS spectral measurements were recorded on a AEI MS 902 S Spectrometer. The compounds **(2-5)** gave the expected molecular ions. Preparation of the starting (*S*)-(+)-*N*-thienylmethyl-5-oxoprolines **(1a,b)** from (*S*)-glutamic acid is described in a previous paper.[9]

(*S*)-(-)-Thieno[*f*]indolizinediones (2a,b) were prepared from acids **[(*S*)-(+)-1a,b]** by an intramolecular Friedel-Crafts acylation, analogously as described for racemic compounds **(2a,b).**[5]

(*S*)-(-)-4,4a,5,6,7,9-Hexahydrothieno[2,3-*f*]indolizine-4,7-dione [(*S*)-(-)-2a]. This compound was prepared from **(*S*)-1a** in the yield of 65%, mp 151-153 °C (ethanol); $[\alpha]_D$= -18.7°; UV, λ_{max} nm (log ε): 216 (3.29), 254 (3.13); ^{1}H NMR: δ 2.29-2.55 (m, 4H, 2xH-5 and 2xH-6), 4.20-4.43 (m, 1H, H-4a), 4.31 (d, 1H, H-9ax, J=17.5 Hz), 5.40 (d, 1H, H-9eq, J=17.5 Hz), 7.17 (d, 1H, H-3, J=5.1 Hz), 7.37 (d, 1H, H-2, J=5.1 Hz); MS, m/z (%): 208 (8), 207 (M^+, 54), 178 (4), 126 (4), 125 (8), 124 (100), 123 (4), 97 (8), 96 (56), 95 (6), 70 (13), 63 (4), 62 (5), 55 (4), 51 (4). Anal. Calcd for $C_{10}H_9NO_2S$: C, 57.95; H, 4.39; N, 6.76. Found: C, 57.89; H, 4.16; N, 6.79.

(*S*)-(-)-4,6,7,8,8a,9-Hexahydrothieno[3,2-*f*]indolizine-6,9-dione [(*S*)-(-)-2b]. This compound was prepared from **(*S*)-1b** in the yield of 70%, mp 159-162 °C (ethanol); $[\alpha]_D$= -85.2°; UV, λ_{max} nm (log ε): 270 (3.13); ^{1}H NMR: δ 2.27-2.57 (m, 4H, 2xH-7 and 2xH-8), 4.17 (d, 1H, H-4ax, J=17.8 Hz), 4.25-4.37 (m, 1H, H-8a), 5.27 (d, 1H, H-4eq, J=17.8 Hz), 7.01 (d, 1H, H-3, J=5.1 Hz), 7.73 (d, 1H, H-2, J=5.1 Hz); MS, m/z (%): 208 (9), 207 (M^+, 62), 178 (4), 126 (4), 125 (9), 124 (100), 123 (7), 97 (9), 96 (49), 95 (7), 70 (18), 69 (4). Anal. Calcd for $C_{10}H_9NO_2S$: C, 57.95; H, 4.39; N, 6.76. Found: C, 57.86; H, 4.22; N, 6.59.

Hydroxyhexahydrothieno[*f*]indolizinones (3a,b).

Sodium borohydride (0.83 g, 22 mmol) was added portionwise to a suspension of ketone **(2a,b)** (4.15 g, 20 mmol) in methanol (70 mL) at 0-5 °C for 30 min. The mixture was stirred at 0-5 °C for 2 h. After removal of the solvent, the residue was diluted with water (50 mL), then it was acidified with 10% HCl to pH 4, and extracted with dichloromethane (3 x 100 mL). The combined extracts were washed with brine, dried over magnesium sulfate and concentrated in vacuo to give a residue. Recrystallization of the solid from ethanol gave alcohols **(3a,b)** as colorless crystals.

(4*R*,4a*S*)-(+)-4-Hydroxy-4,4a,5,6,7,9-hexahydrothieno[2,3-*f*]indolizin-7-one[(*R*,*S*)-(+)-3a]. This compound was prepared from **(*S*)-2a** in 65% yield; mp 162-163 °C; $[\alpha]_D$= +68.3°; UV, λ_{max} nm (log ε): 235 (2.89); *IR*, ν cm^{-1}: 3254 *s (OH)*, 3084 *w*, 2896 *w*, 2861 *w*, 1651 *s* (C=O), 1456 *m*, 1439 *m*, 1418 *s*, 1279 m, 1267 m; ^{1}H NMR: δ 1.92-2.11 (m, 1H, H-5), 2.12-2.43 (m, 3H, 2xH-6 and H-5), 3.45 (ddd, 1H, H-4a, J=3.6, 8.6 and 10.5 Hz), 4.13 (d, 1H, H-9ax, J=16.9 Hz), 4.29 (dd, 1H, H-4, J=7.0 and 8.6 Hz), 4.79 (d, 1H, H-9eq, J=16.9 Hz), 5.77 (d, 1H, OH, J=7.0 Hz), 7.03 (d, 1H, H-3, J=5.1 Hz), 7.39 (d, 1H, H-2, J=5.1 Hz); ^{13}C NMR: δ 21.6 (t, C-5), 29.2 (t, C-6), 39.1 (t, C-9), 59.5 (d, C-4a), 68.7 (d, C-4), 124.3 (d), 125.8 (d), 130.8 (s), 140.3 (s), 173.3 (C=O); MS, m/z (%): 209 (M^+, 26), 128 (5), 127 (8), 126 (74), 125 (42), 98 (5), 97 (21), 96 (6), 85 (5), 84 (100), 56 (5), 55 (6), 53 (11) . Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.39; H, 5.31; N, 6.69. Found: C, 57.19; H, 5.19; N, 6.55.

(±)-4-Hydroxy-4,4a,5,6,7,9-hexahydrothieno[2,3-*f*]indolizin-7-one [(±)-3a]. This compound was prepared from **(±)-2a** in 72% yield; mp 192-193 °C. Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.39; H, 5.31; N, 6.69. Found : C, 57.17; H, 5.20; N, 6.51.

(8a*S*,9*S*)-(+)-9-Hydroxy-4,6,7,8,8a,9-hexahydrothieno[3,2-*f*]indolizin-6-one [(*S*,*S*)-(+)-3b]. This compound was prepared from **(*S*)-2b** in 67% yield; mp 197-198 °C; $[\alpha]_D$= +88.3°; UV, λ_{max} nm (log ε): 234 (2.94); *IR*, ν cm^{-1}: 3347 *m (OH)*, 2893 *w*, 2855 *w*, 1671 *s*, 1651 *s* (C=O), 1456 *m*, 1435 m, 1404 m, 1273 m, 1251 m; ^{1}H NMR: δ 1.92-2.10 (m, 1H, H-8), 2.12-2.45 (m, 3H, 2xH-7 and H-8), 3.48 (ddd, 1H, H-8a, J=3.5, 8.1 and 10.6 Hz), 3.97 (d, 1H, H-4ax, J=16.9 Hz), 4.44 (t, 1H, H-9, J=8.1 Hz), 4.65 (d, 1H, H-4eq, J=16.9 Hz), 6.09 (d, 1H, OH, J=7.3 Hz), 6.88 (d, 1H, H-3, J=5.1 Hz), 7.44 (d, 1H, H-2, J=5.1 Hz); ^{13}C NMR: δ 21.5 (t, C-8), 29.3 (t, C-7), 39.8 (t, C-4), 60.3 (d, C-8a), 68.7 (d, C-9), 124.8 (d), 125.4 (d), 131.9 (s), 140.2 (s), 173.4 (s, C=O); MS, m/z (%): 209 (M^+, 29), 128 (6), 127 (9), 126 (88), 125 (59), 124 (6), 97 (24), 96 (6), 85 (6), 84 (100), 57 (12), 56 (11), 55 (12), 53 (18). Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.39; H, 5.31; N, 6.69. Found: C, 57.09; H, 5.17; N, 6.52.

(±)-9-Hydroxy-4,6,7,8,8a,9-hexahydrothieno[3,2-*f*]indolizin-6-one [(±)-3b]. This compound was prepared from **(±)-2b** in 76% yield; mp 217-218 °C. Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.39; H, 5.31; N, 6.69. Found: C, 57.11; H, 5.19; N, 6.55.

Hexahydrothieno[*f*]indolizinones (4a,b).

Triethylsilane (2.4 mL, 15 mmol) was added to a stirred solution of alcohol **(3a,b)** (2.1 g, 10 mmol) in trifluoroacetic acid (20 mL) at 0 °C, and the resulting yellow solution was stirred at rt for 2 h. The reaction mixture was concentrated *in vacuo*, diluted with water (50 mL), made alkaline with 10% Na_2CO_3, and then extracted with dichloromethane (3 x 50 mL). The combined extracts were washed with water, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash

chromatography on a silica gel column eluting with dichloromethane. Recrystallization of the solid from cyclohexane gave amides (**4a,b**) as colorless crystals.

(4a*S*)-(+)-4,4a,5,6,7,9-Hexahydrothieno[2,3-*f*]indolizin-7-one [(*S*)-(+)-4a]. This compound was prepared from **(*S*,*S*)-3a** in 62% yield; mp 100-102 °C; $[\alpha]_D$= +39.9°; UV, λ_{max} nm (log ε): 235 (2.88); IR, ν cm^{-1}: 3077 m, 2934 w, 2915 w, 1682 s (C=O), 1455 m, 1441 m, 1431 s, 1412 s, 1366 m, 1298 s; ^{1}H NMR: δ 1.68-1.92 (m, 1H, H-5), 2.33 (td, 1H, H-5pax, J=7.8 and 15.6 Hz), 2.40-2.47 (m, 2H, H-6), 2.49 (tdd, 1H, H-4ax, J=1.9, 10.8 and 15.3 Hz), 2.90 (ddd, 1H, H-4eq, J=1.4, 4.3 and 15.3 Hz), 3.71-3.88 (m, 1H, H-4a), 4.16 (d, 1H, H-9ax, J=16.7 Hz), 5.00 (d, 1H, H-9eq, J=16.7 Hz), 6.72 (d, 1H, H-3, J=5.1 Hz), 7.12 (d, 1H, H-2, J=5.1 Hz); ^{13}C NMR: δ 24.4 (t, C-5), 29.7 (t, C-6), 32.4 (t, C-4), 39.6 (t, C-9), 53.7 (d, C-4a), 123.3 (d), 126.5 (d), 130.1 (s), 132.7 (s), 173.3 (s, C=O); MS, m/z (%): 194 (5), 193 (M^+, 38), 192 (5), 136 (5), 112 (5), 111 (10), 110 (100), 109 (5), 84 (5), 66 (7), 65 (5), 55 (5). Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.75; N, 7.25. Found: C, 62.01; H, 5.63; N, 7.05.

(±)-4,4a,5,6,7,9-Hexahydrothieno[2,3-*f*]indolizin-7-one [(±)-4a]. This compound was prepared from **(±)-3a** in 67% yield; mp 108-110 °C. Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.75; N, 7.25. Found: C, 61.97; H, 5.60; N, 7.09.

(8a*S*)-(+)-4,6,7,8,8a,9-Hexahydrothieno[3,2-*f*]indolizin-6-one [(*S*)-(+)-4b]. This compound was prepared from **(*S*,*S*)-3b** in 65% yield; mp 136-138 °C; $[\alpha]_D$= +100.8°; UV, λ_{max} nm (log ε): 231 (2.87); IR, ν cm^{-1}: 3069 w, 2938 w, 2911 w, 2845 w, 1676 s (C=O), 1455 m, 1439 s, 1414 s, 1304 s, 1267 s; ^{1}H NMR: δ 1.71-1.88 (m, 1H, H-8), 2.35 (td, 1H, H-8, J=7.8 and 15.6 Hz), 2.40-2.55 (m, 2H, H-7), 2.66 (tdd, 1H, H-9ax, J=1.7, 10.6 and 15.5 Hz), 3.02 (ddd, 1H, H-9eq, J=1.1, 4.3 and 15.5 Hz), 3.75-3.93 (m, 1H, H-8a), 4.06 (d, 1H, H-4ax, J=16.8 Hz), 4.87 (dd, 1H, H-4eq, J=1.7 and 16.8 Hz), 6.77 (d, 1H, H-3, J=5.1 Hz), 7.11 (dd, 1H, H-2, J=0.9 and 5.1 Hz); ^{13}C NMR: δ 24.7 (t, C-8), 30.1 (t, C-7), 32.1 (t, C-9), 40.7 (t, C-4), 54.6 (d, C-8a), 123.7 (d), 124.9 (d), 130.8 (s), 131.9 (s), 174.1 (s, C=O); MS, m/z (%): 194 (7), 193 (M^+, 41), 192 (5), 136 (7), 112 (7), 111 (10), 110 (100), 109 (7), 97 (5), 84 (7), 77 (5), 69 (6), 66 (10), 65 (8), 58 (5). Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.75; N, 7.25. Found: C, 62.03; H, 5.53; N, 7.01.

(±)-4,6,7,8,8a,9-Hexahydrothieno[3,2-*f*]indolizin-6-one [(±)-4b]. This compound was prepared from **(±)-3b** in 72% yield; mp 146-148 °C. Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.75; N, 7.25. Found: C, 61.94; H, 5.59; N, 7.11.

Hexahydrothieno[*f*]indolizines (5a,b).

Lithium aluminium hydride (0.48 g, 12.6 mmol) was added to a solution of amide (**4a,b**) (0.60 g, 3.1 mmol) in dry tetrahydrofuran (30 mL) at rt and the mixture was heated under reflux for 1 h. The

resulting mixture was cooled and water was added cautiously until the lithium complex was destroyed. Then the mixture was diluted with water (20 mL) and dichloromethane (50 mL). The dichloromethane layer was separated, and the aqueous layer was extracted with dichloromethane (2 x 50 mL). The combined extracts were washed with brine, dried over magnesium sulfate, and concentrated *in vacuo* to give a residue. Recrystallization of the solid from hexane gave amines **(5a ,b).**

(4a*S*)-(+)-4,4a,5,6,7,9-Hexahydrothieno[2,3-*f*]indolizine [(*S*)-(+)-5a]. This compound was prepared from **(*S*)-4a** in 77% yield; mp 69-70 °C; $[\alpha]_D$= +28.2°; UV, λ_{max} nm (log ε): 235 (2.75); IR, ν cm^{-1}: 2955 m, 2913 m, 2870 w, 2780 m, 2734 w, 1441 m, 1374 m, 1337 m, 1320 m, 1291 m; ^{1}H NMR: δ 1.41-1.65 (m, 1H, H-5), 1.73-2.15 (m, 3H, 2xH-6 and H-5), 2.29 (q, 1H, H-7pax, J=8.9 Hz), 2.31-2.56 (m, 2H, H-4a and H-4ax), 2.88 (dd, 1H, H-4eq, J=1.8 and 11.8 Hz), 3.25 (dt, 1H, H-7peq, J=2.4 and 8.3 Hz), 3.38 (d, 1H, H-9ax, J=14.3 Hz), 4.16 (d, 1H, H-9eq, J=14.3 Hz), 6.74 (d, 1H, H-3, J=5.1 Hz), 7.07 (d, 1H, H-2, J=5.1 Hz); ^{13}C NMR: δ 22.0 (t, C-6), 30.2 (t, C-5), 32.4 (t, C-4), 51.8 (t, C-9), 54.1 (t, C-7), 60.9 (d, C-4a), 122.5 (d), 126.7 (d), 133.1 (s), 134.4 (s); MS, m/z (%): 180 (6), 179 (M^+, 34), 178 (11), 112 (6), 111 (11), 110 (100), 109 (6), 84 (9), 77 (6), 66 (12), 64 (8). Anal. Calcd for $C_{10}H_{13}NS$: C, 66.98; H, 7.32; N, 7.81. Found: C, 66.89; H, 7.19; N, 7.65.

(±)-4,4a,5,6,7,9-Hexahydrothieno[2,3-*f*]indolizine [(±)-5a]. This compound was prepared from **(±)-4a** in 86% yield; mp 72-73 °C. Anal. Calcd for $C_{10}H_{13}NS$: C, 66.98; H, 7.32; N, 7.81. Found: C, 66.81; H, 7.21; N, 7.69.

(8a*S*)-4,6,7,8,8a,9-Hexahydrothieno[3,2-*f*]indolizine [(*S*)-(+)-5b]. This compound was prepared from **(*S*)-4b** in 81 % yield; mp 73-75 °C; $[\alpha]_D$= +124.2°; UV, λ_{max} nm (log ε): 234 (2.90); IR, ν cm^{-1}: 2954 m, 2917 m, 2799 m, 2774 m, 2749 m, 1447 m, 1429 m, 1401 s, 1331 m, 1312 s; ^{1}H NMR: δ 1.45-1.67 (m, 1H, H-8), 1.76-2.16 (m, 3H, 2xH-7 and H-8), 2.28 (q, 1H, H-6pax, J=8.9 Hz), 2.35-2.53 (m, 1H, H-8a), 2.65 (tdd, 1H, H-9ax, J=1.2, 10.2 and 15.0 Hz), 3.00 (ddd, 1H, H-9eq, J=1.9, 3.8 and 15.0 Hz), 3.23 (dt, 1H, H-6peq, J=2.2 and 8.9 Hz), 3.24 (dd, 1H, H-4ax, J=1.9 and 14.0 Hz), 4.06 (dd, 1H, H-4eq, J=1.2 and 14.0 Hz), 6.71 (d, 1H, H-3, J=5.1 Hz), 7.05 (d, 1H, H-2, J=5.1 Hz); ^{13}C NMR: δ 22.0 (t, C-7), 30.3 (t, C-8), 32.0 (t, C-9), 52.6 (t, C-4), 54.0 (t, C-6), 61.1 (d, C-8a), 122.8 (d), 124.9 (d), 134.0 (s), 134.2 (s); MS, m/z (%): 180 (5), 179 (M^+, 36), 178 (9), 136 (5), 112 (5), 111 (9), 110 (100), 109 (5), 97 (5), 84 (9), 77 (5), 66 (11), 65 (5). Anal. Calcd for $C_{10}H_{13}NS$: C, 66.98; H, 7.32; N, 7.81. Found: C, 66.86; H, 7.17; N, 7.69.

(±)-4,6,7,8,8a,9-Hexahydrothieno[3,2-*f*]indolizidine [(±)-5b] This compound was prepared from **(±)-4b** in 88 % yield; mp 62-63 °C. Anal. Calcd for $C_{10}H_{13}NS$: C, 66.98; H, 7.32; N, 7.81. Found: C, 66.89; H, 7.19; N, 7.65.

REFERENCES AND NOTES

1. E. Gellert, 'Alkaloids: Chemical and Biological Perspectives,' Vol. 5, ed. by S. W. Pelletier, Wiley, New York, 1987, pp. 55-132.
2. R. C. Bick and W. Sinchai, 'The Alkaloids,' Vol. 19, ed. by R. G. A. Rodrigo, Academic Press, New York, 1981, pp. 193-220.
3. W. H. Pearson and R. Walavalkar, *Tetrahedron*, 1994, **50**, 12293.
4. D. Lebosquain and B. Decroix, *Heterocycles*, 1993, **36**, 2303.
5. S. Marchalin, B. Decroix, and J. Morel, *Acta Chem. Scand.*, 1993, **47**, 287.
6. A. Daich and B. Decroix, *J. Heterocycl. Chem.*, 1996, **33**, 873.
7. P. Pigeon and B. Decroix, *Tetrahedron Lett.*, 1996, **37**, 7707.
8. M. Othman, P. Pigeon, and B. Decroix, *Tetrahedron*, 1997, **53**, 2495.
9. S. Marchalin, K. Kadlecikova, N. Bar, and B. Decroix, *Synth. Commun.*, submitted.
10. T. F. Buckley III and H. Rapoport, *J. Org. Chem.*, 1983, **48**, 4222.
11. D. Berkes and B. Decroix, *Bull. Soc. Chim. Fr.*, 1994, **131**, 986.
12. M. Othman, P. Netchitailo, and B. Decroix, *Heterocycles*, 1998, **48**, 335.
13. H. Budzikiewicz, L. Faber, E. G. Herrmann, F. F. Perrolaz, U. P. Schlunegger, and W. Wiegrebe, *Liebigs Ann. Chem.*, **1979**, 1212.
14. A. Kubo, T. Nakai, Y. Koizumi, Y. Kitahara, N. Saito, Y. Mikami, K. Yazawa, and J. Uno, *Heterocycles*, 1996, **42**, 195.
15. A. Kolocouris, N. Kolocouris, G. B. Foscolos, G. Fytas, A. Hempel, N. Camerman, A. Camerman, and S. J. Hamodrakas, *J. Cryst. Spectroscopic Research*, 1993, **23**, 663.

Received, 20th April, 1998