Synthesis of Indolizidinediones Annelated to a Furan Ring

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The furo[2,3(or 3,2)-*f*]indolizidinediones **4a,b** were synthesized in five steps from glutamic acid in good yield. The ketones were converted into *trans* alcohols **5a,b** or oximes **6a,b** (either as *syn-anti* mixture or as single isomer). The selectivity of these reactions is discussed.

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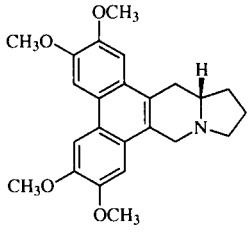
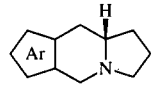
Formulas **I** and **II**



Tylophorine, **I**



Ar = thiophene, furan

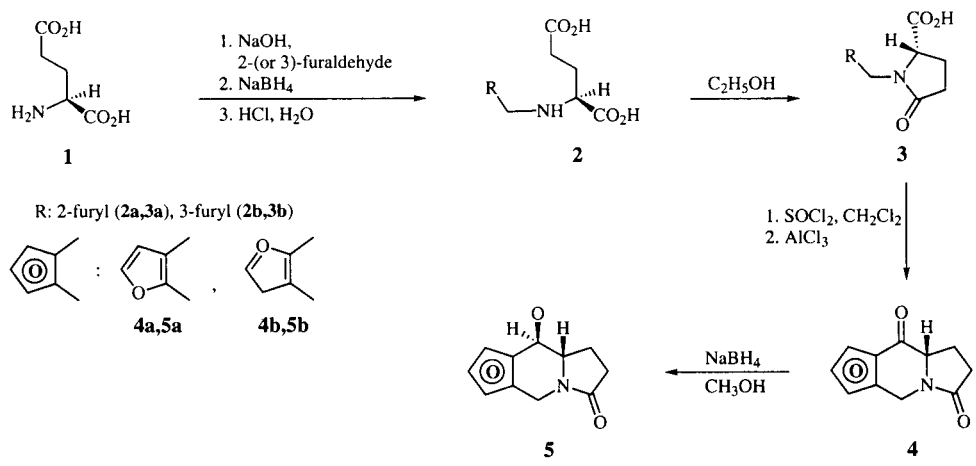
II

In spite of the intense progress in the stereospecific synthesis of phenanthroindolizidine [1,2] or naphthoindolizidine [3] alkaloids there is no report about the stereospecific synthesis of furoindolizidines. For example a variety of synthesis of tylophorine **I** belonging to the phenanthroindolizidine group of alkaloids in both racemic and optically active form have been recently reported [4]. Indeed one of our papers concerned the synthesis of thienoindolizidines **II** (Ar = thiophene) in racemic form [5].

Since we are now able to obtain in very good yields enantiopure (*S*)-*N*-arylmethyl-5-oxoprolines [6] we wish to report herein the synthesis of the furan derivatives **II** (Ar = furan) from (*S*)-glutamic acid **1** *via* the (*S*)-*N*-(furylmethyl)-5-oxoprolines **3**. Finally, to our knowledge, only one paper [7] mentioned a five membered ring including an oxygen atom in a cyclic anhydride form fused to the *f* bond of the indolizidine system (6,7-indolizidinedicarboxylic anhydride).

The synthetic pathway is denoted in Scheme 1. (*S*)-Glutamic acid (**1**) was condensed with 2 (or 3)-furaldehyde to give a Schiff base, which upon treatment with sodium borohydride gave the crude (*S*)-*N*-(furylmethyl)-glutamic acids **2a,b**. Cyclization of acids **2a,b** into oxopro-

Scheme 1



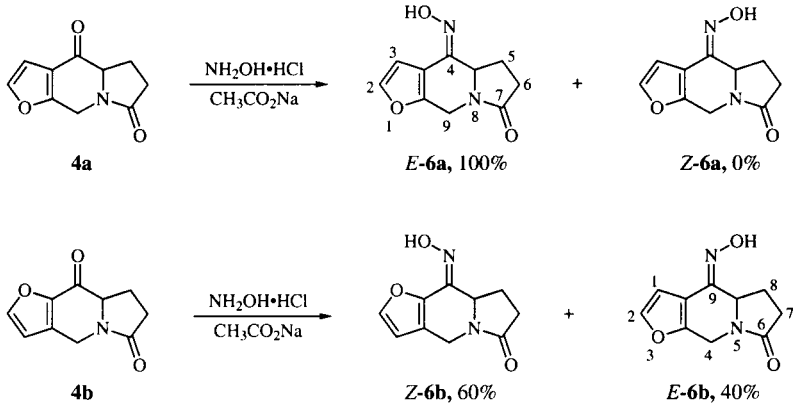
lines **3a,b** was performed in refluxing ethanol in good yields (61 to 75%). These amido acids were conveniently converted to acid chlorides by the action of thionyl chloride in dichloromethane. The resulting acid chlorides under Friedel-Crafts cyclization conditions using aluminium trichloride of high quality as a catalyst gave the expected ketones **4a,b** in moderate yields (39 to 72%). As in the thiophene series [5] the yield was better when the cyclization occured at the 2 position of the furan ring. Amide ketone (*S*)-(-)-**4a** was checked for its optical purity by comparison of its ^{1}H nmr spectrum in the presence of the chiral shift reagent Eu(hfc)$_3$ with the corresponding spectrum of (±)-**4a**.

Reduction to the corresponding alcohol **5** proceeded efficiently by treatment of **4** with sodium borohydride in methanol and gave only one diastereomer **5a** or **5b**. The stereochemical assignments are based on analysis of the nmr spectra. The ^{1}H nmr coupling constants (J = 8.3 Hz for **5a** and J = 7.9 Hz for **5b**) are characteristics of the *trans* diaxial relationship between C*H*-OH and junction proton H_{4a} (or H_{8a}). These are consistent with those of similar compounds [1,8,9]. This result is very interesting since Rapoport [1] had reported the formation of a diastereomeric mixture of alcohols during the reduction of carbonyl group of phenanthroindolizidinediones. The best diastereoselectivity (α-alcohol as the major product) was obtained when K-selectride® or L-selectride ® were used as reducing reagents. Otherwise, in similar conditions (sodium borohydride, methanol) indolizidinedione when ftised to benzene ring gave the β-alcohol as the major product and fused to naphtalene gave the β-alcohol as the minor product. Our result is particularly interesting because we only observe the β-alcohol. This confirmed the result obtained during the reduction of thienoindolizidinediones [10] since the β-alcohol was also the lone reduced product. Examination of molecular models reveals a striking aspect of the three dimensional configuration of the ketones **4a,b** as in thiophene series. 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.

Another aspect of the reactivity of furoindolizidinediones **4a,b** has been investigated in view to compare with the results obtained with the thienoindolizidinediones [5]. The oximes **6a,b** were prepared in the usual manner (hydroxylamine hydrochloride in the presence of sodium acetate) from racemic ketones **4a,b**. Ketone **4a** gave only *E*-isomer and ketone **4b** gave a 60/40 *Z/E* mixture of inseparable isomers. The configuration *Z/E* of these oximes was assigned on the basis of their ^{1}H nmr spectra. Thus, as in the thiophene series [5] the two protons at C_7 and C_8 of *E*-**6b** are not equivalent due to the proximity of the hydroxy group. One of them (at C_7) is shifted downfield (Δδ +0.4 ppm) while another (Δδ +0.4 ppm) is shifted upfield (Δδ -0.2 ppm). These protons are equivalent when the hydroxy group is near to the furan ring.

In conclusion, we have presented an efficient synthesis of enantiopure furo[2,3 (or 3,2)-*f*]]indolizidinediones. The stereospecific reduction of these ketones lead to β-alcohols as a single diasteromers. In the case of furo[2,3-*f*]-indolizidinedione a stereoselective formation of the corresponding *E*-oxime was observed. Beckmann rearrangement of oximes **6** are in progress and the results will be published soon.

Scheme 2



EXPERIMENTAL

Melting points were measured on a Boetius micro hot-stage apparatus and are uncorrected. The infrared spectra were recorded on a Philips analytical PV 9 800 FT IR spectrophotometer (potassium bromide). The nmr spectra were recorded on a Varian XR-300 Spectrometer (300 MHz) in deuteriochloroform and dimethyl-d_6 sulfoxide (compounds **5** and **6**) using tetramethylsilane (^{1}H) or dimethyl-d_6 sulfoxide (^{13}C, δ = 39.5 ppm) as the internal standard. Optical rotations were measured with a Perkin-Elmer 241 polarimeter in a 10 cm cell in methanol (c 1) at 25°.

Ascending thin layer chromatography was performed on precoated plates 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. Mass spectral measurements were recorded on a AEI MS 902 S Spectrometer (70 eV, electron impact). The compounds **3-6** gave the expected molecular ions.

General Procedure for the Preparation of Enantiopure and Racemic *N*-Furylmethyl-5-oxoprolines **3a,b**.

Glutamic acid (**1**) (7.36 g, 50 mmoles) was added at room temperature to a solution of sodium hydroxide (2*M*, 45 ml). To the resulting solution was added dropwise freshly distilled furaldehyde (4.80 g, 50 mmoles). The mixture was stirred for 30 minutes and cooled to 0° and sodium borohydride (0.66 g, 17.5 mmoles) was added in small portions, keeping the temperature at 0-5°. The mixture was stirred for 90 minutes at room temperature, and another portion of furaldehyde (0.96 g, 10 mmoles) was added. After 20 minutes, a second portion of sodium borohydride (0.13 g, 3.5 mmoles) was added as before, and the mixture was stirred for 45 minutes at room temperature. The resulting solution was extracted with ether (3 x 30 ml). The aqueous layer was acidified to *p*H 3 at 0-5° with concentrated hydrochloric acid. The crystalline precipitate was collected, washed with cooled water (10 ml) and dried to give a colorless solid. The suspension of crude *N*-(furylmethyl)glutamic acid **2a,b** in ethanol (120 ml) was heated to reflux for 3 hours. The resulting solution was filtered and concentrated *in vacuo* to give a solid. Crystallization from mixture toluene-ethanol (95:5, v/v) afforded acids **3a,b** as colorless crystals.

(*S*)-(+)-*N*-(2-Furylmethyl)-5-oxoproline ((*S*)-(+)-**3a**).

This compound was obtained from 2-furaldehyde and (*S*)-glutamic acid (**1**) in a yield of 61%, mp 95-97°; $[\alpha]_D$ = +37.2°; ir: ν 1742, 1647 (C=O) cm^{-1}; ^1H nmr: δ 2.10-2.25 (m, 1H, H_3), 2.30-2.68 (m, 3H, H_3 and CH_2), 4.11 (dd, 1H, H_2, J = 3.6, 9.5 Hz), 4.13 (d, 1H, C*H*-N, J = 15.6 Hz), 5.00 (d, 1H, C*H*-N, J = 15.6 Hz), 6.25 (d, 1H, $H_{3'}$, J = 3.3 Hz), 6.29 (dd, 1H, $H_{4'}$, J = 1.8, 3.3 Hz), 7.33 (d, 1H, $H_{5'}$, J = 1.8 Hz), 10.82 (br s, 1H, CO_2H); ^{13}C nmr: δ 22.8 (t, C_3), 29.5 (t, C_4), 38.4 (t, CH_2-N), 58.8 (d, C_2), 109.4 (d, $C_{3'}$), 110.4 (d, $C_{4'}$), 142.8 (d, $C_{5'}$), 148.9 (s, $C_{2'}$), 174.7 (s, *C*O), 176.1 (s, *C*O); ms: m/z 209 (molecular ion).

Anal. Calcd. for $C_{10}H_{11}NO_4$ (209.20): C, 57.41; H, 5.30; N, 6.70. Found: C, 57.26; H, 5.22; N, 6.59.

(±)-*N*-(2-Furylmethyl)-5-oxoproline ((±)-**3a**).

This compound was obtained from 2-furaldehyde and (*R,S*)-glutamic acid (**1**) in a yield of 68%, mp 94-96°.

Anal. Calcd. for $C_{10}H_{11}NO_4$ (209.20): C, 57.41; H, 5.30; N, 6.70. Found: C, 57.29; H, 5.20; N, 6.55.

(*S*)-(+)-(3-*N*-Furylmethyl)-5-oxoproline ((*S*)-(+)-**3b**).

This compound was obtained from 3-furaldehyde and (*S*)-glutamic acid (**1**) in a yield of 71%, mp 125-127°; $[\alpha]_D$ = +49.4°; ir: ν 1736, 1632 (C=O) cm^{-1}; ^1H nmr: δ 2.12-2.66 (m, 4H, $(CH_2)_2$), 3.95 (d, 1H, C*H*-N, J = 15.5 Hz), 4.09 (dd, 1H, H_2, J = 3.3, 9.3 Hz), 4.86 (d, 1H, C*H*-N, J = 15.5 Hz), 6.28 (d, 1H, $H_{4'}$, J = 1.8 Hz), 7.32-7.41 (m, 2H, $H_{2'}$ and $H_{5'}$), 10.37 (br s, 1H, CO_2H); ^{13}C nmr: δ 22.8 (t, C_3), 29.7 (t, C_4), 36.4 (t, CH_2-N), 58.6 (d, C_2), 110.6 (d, $C_{4'}$), 119.2 (s, $C_{3'}$), 141.3 (d, $C_{2'}$), 143.8 (d, $C_{5'}$), 174.6 (s, C_5), 176.3 (s, *C*O); ms: m/z 209 (molecular ion).

Anal. Calcd. for $C_{10}H_{11}NO_4$ (209.20): C, 57.41; H, 5.30; N, 6.70. Found: C, 57.28; H, 5.19; N, 6.48.

(±)-*N*-(3-Furylmethyl)-5-oxoproline ((±)-**3b**).

This compound was obtained from 3-furaldehyde and (*R,S*)-glutamic acid (**1**) in a yield of 75%, mp 124-126°.

Anal. Calcd. for $C_{10}H_{11}NO_4$ (209.20): C, 57.41; H, 5.30; N, 6.70. Found: C, 57.29; H, 5.17; N, 6.51.

General Procedure for the Synthesis of Enantiopure and Racemic Furo[*f*]indolizinediones **4a,b**.

A solution of acid **3** (11.5 g, 55 mmoles) in dry dichloromethane (120 ml) was treated rapidly with thionyl chloride (4.4 ml, 60.5 mmoles). After being refluxed under argon for 5 hours, the chilled solution was treated in portions over 2 hours with high-purity aluminium trichloride (22 g, 165 mmoles) with stirring and external cooling (- 5 to 0°). The mixture was stirred with cooling for 1 hour and 2 hours at room temperature. The mixture was chilled with ice-water and the reaction was quenched by cautious addition of ice chips and then diluted with water. Dichloromethane was added (100 ml) and the mixture was stirred thoroughly until all the solid dissolved. The phases were separated and the aqueous phase was extracted with dichloromethane (2 x 50 ml). The combined organic phase was washed with water (200 ml) and saturated brine (200 ml), dried, filtered and concentrated *in vacuo*. The residual semisolid was subjected to column chromatography (silica gel, 200 g). Elution of the column with isohexane-acetone (2:1, v/v) gave a homogenous residue. Recrystallization of the solid from ethanol gave ketones **5a,b** as pale yellow crystals.

(*S*)-(-)-4,4a,5,6,7,9-Hexahydrofuro[2,3-*f*]indolizine-4,7-dione ((*S*)-(-)-**4a**).

This compound was prepared from acid (*S*)-**3a** in a yield of 39%, mp 112-113°; $[\alpha]_D$ = -0.73°; ir: ν 3150, 3117, 1682 (C=O), 1595 cm^{-1}; ^1H nmr: δ 2.30-2.58 (m, 4H, $2H_5$ and $2H_6$), 4.20 (d, 1H, H_{9ax}, J = 18.3 Hz), 4.23 (t, 1H, H_{4a}, J = 6.6 Hz), 5.24 (d, 1H, H_{9eq}, J = 18.3 Hz), 6.68 (d, 1H, H_3, J = 1.8 Hz), 7.41 (d, 1H, H_2, J = 1.8 Hz); ^{13}C nmr: δ 20.3 (t, C_5), 29.8 (t, C_6), 38.3 (t, C_9), 61.8 (d, C_{4a}), 106.5 (d, C_3), 120.0 (s, C_{3a}), 144.2 (d, C_2), 161.8 (s, C_{9a}), 174.4 (s, C_7), 190.3 (s, C_4); ms: m/z 191 (molecular ion).

Anal. Calcd. for $C_{10}H_9NO_3$ (191.19): C, 62.82; H, 4.74; N, 7.33. Found: C, 62.78; H, 4.56; N, 7.15.

(±)-4,4a,5,6,7,9-Hexahydrofuro[2,3-*f*]indolizine-4,7-dione ((±)-**4a**).

This compound was prepared from acid (±)-**3a** in a yield of 42%, mp 111-113°.

Anal.. Calcd. for $C_{10}H_9NO_3$ (191.19): C, 62.82; H, 4.74; N, 7.33. Found: C, 62.74; H, 4.59; N, 7.18.

(*S*)-(-)-4,6,7,8,8a,9-Hexahydrofuro[3,2-*f*]indolizine-6,9-dione ((*S*)-(-)-**4b**).

This compound was prepared from acid (*S*)-**3b** in a yield of 65%, mp 160-162°; $[\alpha]_D$ = -42.4°; ir: ν 3115, 1700, 1676 (C=O), 1593 cm^{-1}; ^1H nmr: δ 2.30-2.58 (m, 4H, $2H_7$ and $2H_8$), 4.12 (d, 1H, H_{4ax}, J = 18.0 Hz), 4.32 (t, 1H, H_{8a}, J = 6.0 Hz), 5.17 (d, 1H, H_{4eq}, J = 18.0 Hz), 6.49 (d, 1H, H_3, J = 1.8 Hz), 7.65 (d, ^1H, H_2, J = 1.8 Hz); ^{13}C nmr: δ 20.2 (t, C_8), 29.9 (t, C_7), 37.7 (t, C_4), 62.5 (d, C_{8a}), 109.9 (d, C_3), 136.9 (s, C_{3a}), 145.5 (s, C_{9a}), 149.2 (d, C_2), 174.2 (s, C_6), 182.6 (s, C_9); ms: m/z 191 (molecular ion).

Anal. Calcd. for $C_{10}H_9NO_3$ (191.19): C, 62.82; H, 4.74; N, 7.33. Found: C, 62.71; H, 4.61; N, 7.21.

(±)-4,6,7,8,8a,9-Hexahydrofuro[3,2-*f*]indolizine-6,9-dione ((±)-**4b**).

This compound was prepared from acid (±)-**3b** in a yield of 72%, mp 155-157°.

Anal. Calcd. for $C_{10}H_9NO_3$ (191.19): C, 62.82; H, 4.74; N, 7.33. Found: C, 62.76; H, 4.62; N, 7.22.

General Procedure for the Synthesis of Hydroxyhexahydrofuro[*f*]indolizinones **5a,b**.

Sodium borohydride (0.3 g, 7.8 mmoles) was added portionwise to a suspension of ketone **4a,b** (1.5 g, 7.8 mmoles) in methanol (30 ml) at 0-5° for 30 minutes. The mixture was stirred at 0-5° for 2 hours. After removal of the solvent, the residue was diluted with water (20 ml), than it was acidified with diluted hydrochloric acid (10%) to *p*H 6, and extracted with dichloromethane (3 x 30 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 **5a,b** as colorless crystals.

(4*R*,4a*S*)-(+)-4-Hydroxy-4,4a,5,6,7,9-hexahydrofuro[2,3-*f*]-indolizin-7-one ((*R,S*)-(+)-**5a**).

This compound was prepared from ketone (*S*)-**4a** in a yield of 67%, mp 202-204°; $[\alpha]_D$ = +0.33°; ir: ν 3222 (OH), 1653 (C=O), 1628 cm^{-1}; ^{1}H nmr: δ 1.94-2.07 (m, 1H, H_{5ax}), 2.18-2.47 (m, 2H, H_{5eq} and H_6, 3.43 (dt, 1H, H_{4a}, J = 3.6, 7.8 Hz), 4.00 (ddd, 1H, H_{9ax}, J = 1.0, 2.0, 16.5 Hz), 4.29 (tdd, 1H, H_4, J = 2.0, 6.4, 8.3 Hz), 4.60 (dd, 1H, H_{9eq}, J = 2.0, 16.5 Hz), 5.60 (d, 1H, OH, J = 6.4 Hz), 6.49 (d, 1H, H_3, J = 1.8 Hz), 7.59 (td, 1H, H_2, J = 1.0, 2.0 Hz); ^{13}C nmr: δ 21.7 (t, C_5), 29.3 (t, C_6), 37.7 (t, C_9), 60.6 (d, C_{4a}), 66.8 (d, C_4), 109.0 (d, C_3), 121.9 (s, C_{3a}), 142.7 (d, C_2), 145.0 (s, C_{9a}), 173.7 (C_7); ms: m/z 193 (molecular ion).

Anal. Calcd. for $C_{10}H_{11}NO_3$ (193.20): C, 62.17; H, 5.74; N, 7.25. Found: C, 62.05; H, 5.59; N, 7.02.

(±)-4-Hydroxy-4,4a,5,6,7,9-hexahydrofuro[2,3-*f*]indolizin-7-one ((±)-**5a**).

This compound was prepared from ketone (±)-**4a** in a yield of 63%; mp 202-203°.

Anal. Calcd. for $C_{10}H_{11}NO_3$ (193.20): C, 62.17; H, 5.74; N, 7.25. Found: C, 62.01; H, 5.57; N, 7.09.

(8a*S*,9*S*)-(+)-9-Hydroxy-4,6,7,8,8a,9-hexahydrofuro[3,2-*f*]-indolizin-6-one ((*S,S*)-(+)-**5b**).

This compound was prepared from (*S*)-**4b** in a yield of 67%, mp 138-140°; $[\alpha]_D$ = +40.7°; ir: ν 3347 (OH), 1651 (C=O), 1620 cm^{-1}; ^{1}H nmr: δ 1.93-2.06 (m, 1H, H_{8ax}), 2.20-2.45 (m, 3H, $2H_7$ and H_{8eq}), 3.54 (dt, 1H, H_{8aq}, J = 3.5, 8.0 Hz), 3.83 (dd, 1H, H_{4ax}, J = 1.2, 16.2 Hz), 4.42 (t, 1H, H_9, J = 7.9 Hz), 4.53 (dd, 1H, H_{4eq}, J = 1.9, 16.2 Hz), 5.86 (d, 1H, OH, J = 6.6 Hz), 6.42 (d, 1H, H_3, J = 1.9 Hz), 7.62 (td, 1H, H_2, J = 0.9, 1.9 Hz); ^{13}C nmr: δ 21.8 (t, C_8), 29.2, (t, C_7), 36.9 (t, C_4), 60.8 (d, C_{8a}), 66.5 (d, C_9), 108.4 (d, C_3), 115.6 (s, C_{3a}), 143.0 (d, C_2), 150.3 (s, C_{9a}), 173.4 (s, C_6); ms: m/z 193 (molecular ion).

Anal. Calcd. for $C_{10}H_{11}NO_3$ (193.20): C, 62.17; H, 5.74; N, 7.25. Found: C, 62.04; H, 5.61; N, 7.08.

(±)-9-Hydroxy-4,6,7,8,8a,9-hexahydrofuro[3,2-*f*]indolizin-6-one ((±)-**5b**).

This compound was prepared from (±)-**4b** in a yield of 78%; mp 169-170°.

Anal. Calcd. for $C_{10}H_{11}NO_3$ (193.20): C, 62.17; H, 5.74; N, 7.25. Found: C, 62.09; H, 5.63; N, 7.11.

Hexahydrooximinofuro[*f*]indolizinediones **6a,b**.

A stirred suspension of the ketones (±)-**4** (0.5 g, 2.62 mmoles) and 95% ethanol (4 ml) was treated with solution of hydroxylamine hydrochloride (0.36 g, 5.24 mmoles), sodium acetate (0.43 g, 5.24 mmoles) and water (5 ml) and was refluxed for 5 hours. Ice-water cooling afforded a crystalline precipitate, which was collected, washed with aqueous ethanol (50%) and recrystallized from ethanol.

E-(±)-4,4a,5,6,7,9-Hexahydrofuro-4-oximinofuro[2,3-*f*]-indolizin-7-one ((±)-**6a**).

This compound was prepared from (±)-**4a** in a yield of 62%, mp 255-257°; ir: ν 3252, 3225 (OH), 1659 (C=O) cm^{-1}, 1588; ^{1}H nmr: δ 2.26-2.38 (m, 4H, $2H_5$ and $2H_6$), 4.22 (d, 1H, H_{9ax}, J = 17.4 Hz), 4.45 (t, 1H, H_{4a}, J = 6.6 Hz), 4.83 (d, 1H, H_{9eq}, J = 17.4 Hz), 7.06 (d, 1H, H_3, J = 1.9 Hz), 7.73 (d, 1H, H_2, J = 1.9 Hz), 11.19 (s, 1H, =N-O*H*); ^{13}C nmr: δ 21.2 (t, C_5), 29.8 (t, C_6), 38.2 (t, C_9), 56.0 (d, C_{4a}), 111.5 (d, C_3), 112.3 (s, C_{3a}), 143.1 (d, C_2), 145.2 (s, C_4), 152.3 (s, C_{9a}), 173.6 (s, C_7); ms: m/z 206 (molecular ion).

Anal. Calcd. for $C_{10}H_{10}N_2O_3$ (206.20): C, 58.25; H, 4.89; N, 13.59. Found: C, 58.07; H, 4.72; N, 13.39.

(±)-4,6,7,8,8a,9-Hexahydro-9-oximinofuro[3,2-*f*]indolizin-6-one ((±)-**6b**).

A mixture of *Z* and *E* isomers was obtained from (±)-**4b** in a yield of 58%, mp 235-240°; ir: ν 3289, 3135 (OH), 1667 (C=O), 1663 cm^{-1}.

Isomer *Z* had ^{1}H nmr: δ 2.16-2.48 (m, 4H, $2H_7$ and $2H_8$), 4.01 (d, 1H, H_{4ax}, J = 17.4 Hz), 4.52 (t, 1H, H_{8a}, J = 6.3 Hz), 4.76 (d, 1H, H_{4eq}, J = 17.4 Hz), 6.62 (d, 1H, H_3, J = 1.8 Hz), 7.85 (d, 1H, H_2, J = 1.8 Hz), 11.22 (s, 1H, =N-O*H*); ^{13}C nmr: δ 21.2 (t, C_8), 29.7 (t, C_7), 37.3 (t, C-4), 56.4 (d, C_{8a}), 109.2 (d, C_3), 125.0 (s, C_{3a}), 140.8 (s, C_9), 141.3 (s, C_{9a}), 145.7 (d, C_2), 173.2 (s, C_6).

Isomer *E* had ^{1}H nmr: δ 1.92-2.08 (m, 1H, H_8), 2.16-2.48 (m, 2H, $2H_7$), 2.78-2.91 (m, 1H, H_8), 3.87 (d, 1H, H_{4ax}, J = 16.8 Hz), 4.73 (t, 1H, H_{8a}, J = 6.6 Hz), 4.85 (d, 1H, H_{4eq}, J = 16.8 Hz), 6.58 (d, 1H, H_3, J = 1.8 Hz), 7.73 (d, 1H, H_2, J = 1.8 Hz), 11.29 (s, 1H, =N-O*H*); ^{13}C nmr: δ 25.1 (t, C_8), 29.9 (t, C_7), 36.2 (t, C_4), 55.8 (d, C_{8a}), 109.4 (d, C_3), 122.9 (s, C_{3a}), 143.1 (d, C_{9a}), 144.9 (d, C_2), 145.0 (s, C_9), 172.8 (s, C_6).

Anal. Calcd. for $C_{10}H_{10}N_2O_3$ (206.20): C, 58.25; H, 4.89; N, 13.59. Found: C, 58.01; H, 4.69; N, 13.38.

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