Synthesis and Reduction of Thieno[2',3'(3',2' or 3',4'):5,6]-azocino[2,1-*a*]isoindole-7,13-diones

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A synthesis of the thieno[2',3'(3',2' or 3',4'):5,6]azocino[2,1-*a*]isoindole-7,13-diones **6a-c** was developed from *N*-thienylethylphthalimides **3a-c** using a Wittig reaction followed by a Friedel-Crafts cyclization of acetic acid derivatives **5a-c**. Reduction of ketones **6a-c** into alcohols **7a-c** was stereospecific.

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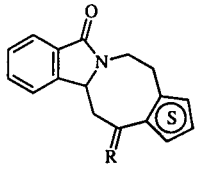
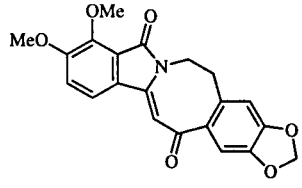
As a part of our continuing studies towards the synthesis of polyheterocycles containing an eight membered ring (as oxazocine or thiazocine), we have described oxazocines [1,2] or thiazocines [1-3] annelated to different rings such as benzene, thiophene or isoindole. Now we wish to report our study concerning the synthesis of thienoazocinoisoindolediones **1** which are analogous to the new class of isoindolobenzazocine alkaloids [4,5] as magallanesine **2** is the first example.



1

R = H, H; H, OH; O



2

The requisite starting phthalimides **3a-c** have been recently described by us [6], and their reduction with sodium borohydride gave the corresponding hydroxylactams **4a-c** in good yields (94-98%). The Wittig reaction using ethoxycarbonylmethylidenetriphenylphosphorane produced an ester, which was immediately hydrolyzed, using a solution of potassium carbonate followed with an acidic treatment, to give the expected substituted acetic acids **5a-c** in good yields (70 to 81%). Cyclization of these acids occurred under Friedel-Crafts conditions. Acids **5a-c** were treated with thionyl chloride in dichloromethane and the resulting acid chlorides in the presence of aluminium trichloride of high quality as a catalyst gave the cyclic ketones **6a-c** in very good yield (87 to 98%). As expected, when the α-position of the thiophene is blocked with a halogen (acid **5c**) cyclization occurred at the β-position.

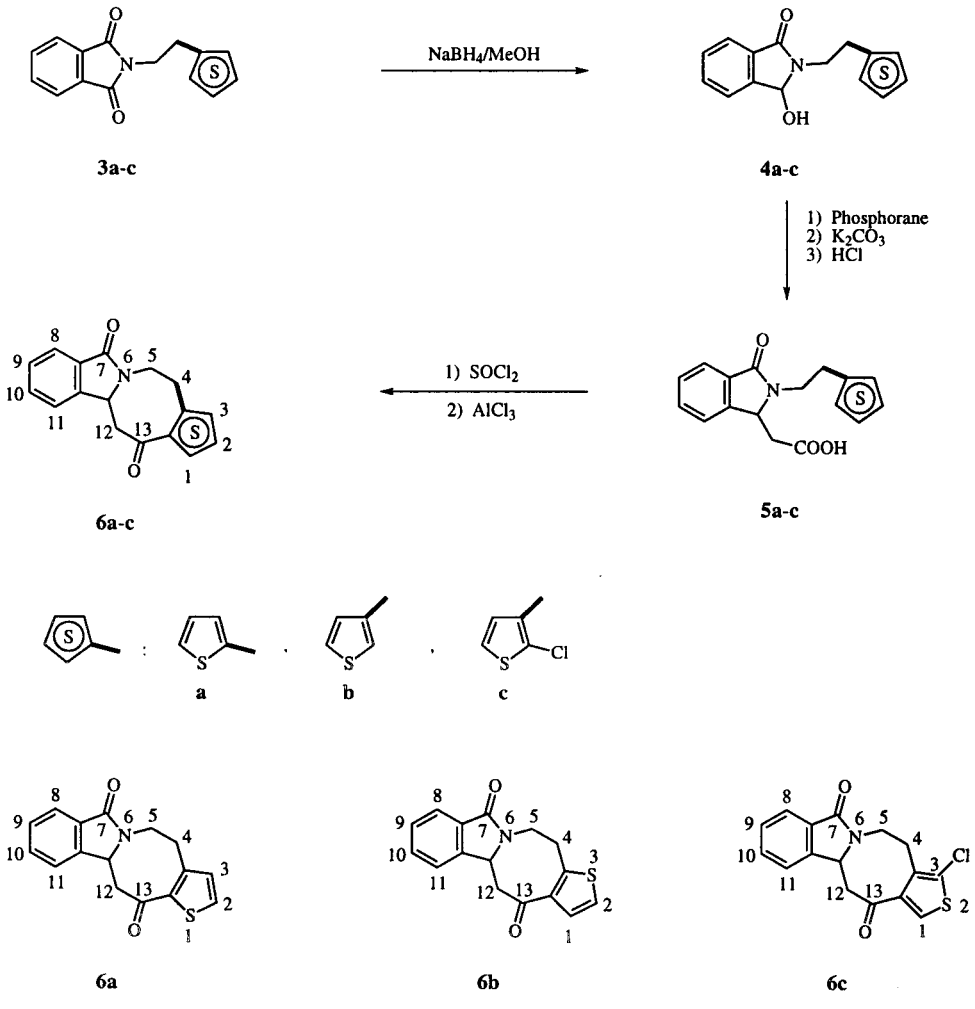
The structure of this new tetracyclic system was supported by the ir and nmr spectra as well as by the microanalysis. The ketones **6a,b** display a characteristic doublet for each proton of an α,β-disubstituted thiophene ring with the usual coupling constant of J = 5.3 Hz. Furthermore, for the ketone **6a** the protons attached to C_4 and C_5 appear as multiplets δH_4 = 3.32-3.51 ppm, δH_5 = 3.71- 3.81, δH_5 = 4.49-4.65. The protons attached to C_{12} are non equivalent and appear as a doublet of doublets with chemical shifts of 3.14 for H_{12pax} (pseudoaxial proton) and 3.89 ppm for H_{12peq} (pseudoequatorial proton) and coupling constants of J = 13.4 Hz (H_{12pax}-H_{12peq}), J = 6.2 Hz (H_{12peq}-H_{11b}), J = 1.9 Hz (H_{12pax}-H_{11b}). Finally, the proton H_{11b} appears as a doublet of doublets (J = 1.9 and 6.2 Hz) with a chemical shift of 4.90 ppm. The spectra of **6b,c** reveal the same remarks (details are reported in the Experimental) and are similar to those observed in the thienoazepinoisoindolediones previously reported [7].

Since, we have observed a stereoselective or a stereospecific reduction of piperidinothienoazepines [8], it appeared interesting to test the reactivity of the amide ketones **6a-c** against sodium borohydride. Actually, this reagent in the presence of methanol does not reduce the amide function [9]. Under these conditions **6a** was stereospecifically reduced into the alcohol **7a** (racemic mixture).

The attack of hydride proceeds from the sterically more accessible side of the carbonyl group and gives amidoalcohols with two asymetric carbon atoms having an S*, S* (from C11b(S*)) or R*, R* (from C11b(R*)) relative configuration. The ^{1}H nmr spectrum of the alcohol **7a** shows a doublet of triplets for H_{12peq} with coupling constants of J = 3 Hz (H_{12peq}-H_{11b}), J = 4 Hz (H_{12peq}-H_{13pax}), J = 14.8 Hz (H_{12peq}-H_{12pax}). Similarly for H_{12pax} we observe a doublet of triplets with coupling constants of J = 7.2 Hz (H_{12pax}-H_{11b}), J = 7.5 Hz (H_{12pax}-H_{13pax}) and J = 14.8 Hz (H_{12pax}-H_{12peq}). These different coupling constants support the proposed structure in which the hydroxyl group has a pseudoequatorial position and a *trans* relationship between H_{11b} and OH. The reduction of ketones **6b,c** gave similar results (details are reported in the Experimental).

Reduction of the ketones **6a,b** into the corresponding methylene compounds was achieved directly from the

Scheme 1



ketones or from the alcohols **7a,b** using triethylsilane in the presence of trifluoroacetic acid (70%). A by-product **9a** or **9b** (10%) was isolated by chromatography on silica gel. The structure of these compounds could be supported by the ^{13}C nmr spectra which revealed the presence of six CH_2 carbons and three CH carbons. The elemental analysis confirmed this structure in which the thiophene ring has been reduced. A similar reduction has already been signaled in the literature when a mixture of triethylsilane and trifluoroacetic acid was used with thiophene derivatives [10].

In summary, a short synthesis of thienoazocinoisoindolediones was described from *N*-thienylethylphthalimides. The stereospecific reduction of these ketones into alcohols was explained.

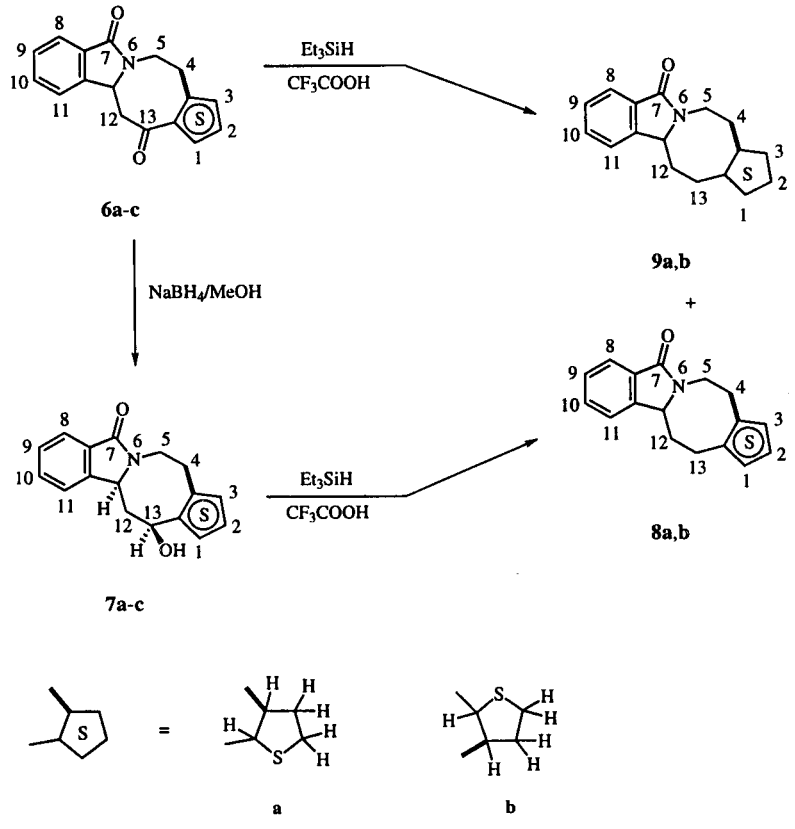
EXPERIMENTAL

Melting points are uncorrected. The infrared spectra of solids (potassium bromide) were recorder on a Perkin Elmer FTIR Paragon 1000 spectrometer. The ^1H and ^{13}C nmr spectra were recorder on a Bruker AC-200 instrument in deuteriochloroform solution and the chemical shifts (δ) are expressed in ppm relative to internal tetramethylsilane. Ascending thin layer chromatography was performed on precoated plates of silica gel 60F 254 (Merck) and the spots visualized using an ultaviolet lamp or iodine vapor. E. Merck silica gel 60F (70-300 mesh) was used for column chromatography. The elemental analyses were carried out by the microanalysis laboratory of INSA at Rouen, F 76130 MT. ST. Aignan.

N-Thienylethylisoindol-3-acetic Acids **5a-c**. General Procedure.

A solution of carbethoxycarbonyltriphenylphosphorane (1 g, 2.87 mmoles), hydroxylactam **4a-c** (2.50 mmoles) in toluene (10 ml) was refluxed with stirring overnight. The solvent was evaporated under reduced pressure and potassium carbonate (0.6 g), water (2 ml) and methanol (8 ml) were added. The mixture was stirred under reflux for 2 hours, then concentrated under reduced pressure. Water and dichloromethane were added and the organic layer was discarded. The aqueous layer was washed with dichloromethane and acidified with hydrochloric acid solution (10%) to *p*H 2. Compounds **5a-c** were extracted

Scheme 2



with dichloromethane, dried on magnesium sulfate and evaporated under reduced pressure. Recrystallization from ethanol gave pure **5a-c**.

2,3-Dihydro-1-oxo-2-(thien-2'-ylethyl)-1*H*-isoindol-3-acetic Acid (**5a**).

This compound was obtained in a yield of 75%, mp 134-136°; ir: 2923 (OH), 1715 (C=O), 1639 (C=O) cm^{-1}; ^1H nmr: δ 2.64 (dd, 1H, C*H*$_2$COOH, J = 6.7, 16.5 Hz), 2.85 (dd, 1H, C*H*$_2$COOH, J = 5.4, 16.5 Hz), 3.10-3.48 (m, 3H, C*H*$_2$-C*H*$_2$-N), 4.15-4.29 (m, 1H, CH$_2$-C*H*$_2$-N), 4.84 (dd, 1H, CH-N, J = 5.4, 6.7 Hz), 6.80-6.86 (m, 2H, H arom), 7.07-7.10 (m, 1H, H arom), 7.40-7.56 (m, 3H, H arom), 7.84 (d, 1H, H arom, J = 7.8 Hz); ^{13}C nmr: δ 28.5 (CH$_2$), 37.1 (CH$_2$), 42.3 (CH$_2$), 56.6 (CH), 122.4 (CH arom), 123.7 (CH arom), 123.9 (CH arom), 125.5 (CH arom), 127.0 (CH arom), 128.6 (CH arom), 131.5 (C arom), 131.9 (C arom), 140.5 (C arom), 144.7 (C arom), 168.7 (CO), 173.7 (CO).

Anal. Calcd. for $C_{16}H_{15}NO_3S$: C, 63.77; H, 5.02; N, 4.65. Found: C, 63.80; H, 5.12; N, 4.78.

2,3-Dihydro-1-oxo-2-(thien-3'-ylethyl)-1*H*-isoindol-3-acetic Acid (**5b**).

This compound was obtained in a yield of 81%, mp 145-147°; ir: 2940 (OH), 1708 (C=O), 1642 (C=O) cm^{-1}; ^1H nmr: δ 2.63 (dd, 1H, C*H*$_2$COOH, J = 7, 16.4 Hz), 2.82 (dd, 1H, C*H*$_2$COOH, J = 5.4, 16.4 Hz), 2.88-3.11 (m, 2H, C*H*$_2$-CH$_2$-N), 3.24-3.42 (m, 1H, CH$_2$-C*H*$_2$-N), 4.14-4.28 (m, 1H, CH$_2$-C*H*$_2$-N), 4.80 (dd, 1H, CH-N, J = 5.4, 7 Hz), 6.95-7.00 (m, 2H, H arom), 7.19-7.23 (m, 1H, H arom), 7.44-7.50 (m, 3H, H arom), 7.80 (d, 1H, H arom, J = 7.8 Hz); ^{13}C nmr: δ 28.4 (CH$_2$), 36.6 (CH$_2$), 40.5 (CH$_2$), 55.9 (CH), 121.4 (CH arom), 122.6 (CH arom), 122.8 (CH arom), 126.0 (CH arom), 128.2 (CH arom), 128.3 (C arom), 131.5 (CH arom), 131.6 (CH arom), 139.1 (C arom), 145.2 (C arom), 166.9 (CO), 171.8 (CO).

Anal. Calcd. for $C_{16}H_{15}NO_3S$: C, 63.77; H, 5.02; N, 4.65. Found: C, 63.60; H, 5.10; N, 4.71.

2,3-Dihydro-1-oxo-2-(2'-chlorothien-3'-ylethyl)-1*H*-isoindol-3-acetic Acid (**5c**).

This compound was obtained in a yield of 70%, mp 156-158°; ir: 2924 (OH), 1718 (C=O), 1636 (C=O) cm^{-1}; ^1H nmr: δ 2.56 (dd, 1H, C*H*$_2$COOH, J = 7.2, 16.4 Hz), 2.80 (dd, 1H, C*H*$_2$COOH, J = 5.1, 16.4 Hz), 2.86-3.02 (m, 2H, C*H*$_2$-CH$_2$-N), 3.26-3.46 (m, 1H, CH$_2$-C*H*$_2$-N), 4.01-4.15 (m, 1H, CH$_2$-C*H*$_2$-N), 4.81 (dd, 1H, CH-N, J = 5.1, 7.2 Hz), 6.76 (d, 1H, H thiophene, J = 5.6 Hz), 6.93 (d, 1H, H thiophene, J = 5.6 Hz), 7.35-7.60 (m, 3H, H arom), 7.78 (d, 1H, H arom, J = 7.8 Hz); ^{13}C nmr: δ 26.8 (CH$_2$), 37.0 (CH$_2$), 40.1 (CH$_2$), 56.4 (CH), 122.3 (CH arom), 122.9 (CH arom), 123.7 (CH arom), 126.0 (CH arom), 127.9

(CH arom), 128.7 (CH arom), 131.6 (C arom), 131.9 (CH arom), 135.1 (C arom), 144.6 (C arom), 168.6 (CO), 173.9 (CO).

Anal. Calcd. for $C_{16}H_{14}ClNO_3S$: C, 57.23; H, 4.20; N, 4.17. Found: C, 57.32; H, 4.36; N, 4.21.

Thienoazocinoisoindolediones **6a-c**. General Procedure.

To a mixture of acid **5a-c** (7 mmoles), in dry dichloromethane (30 ml) was added thionyl chloride (0.6 ml) under stirring. The reaction mixture was refluxed for 2 hours. After cooling the solution was evaporated under reduced pressure. The residue was dissolved into dry dichloromethane (40 ml) and was added drop by drop to a stirred solution of aluminium trichloride (99.99%, 3 g, 22 mmoles) and dry dichloromethane (60 ml). Stirring was continued for 1 hour. The solution was poured into cold water and decanted. The aqueous layer was extracted with dichloromethane. The combined organic layer was washed with water, dried on magnesium sulfate, and evaporated. The resulting solids **6a-c** were recrystallized from ethanol.

4,5,11b,12-Tetrahydrothieno[3',2':5,6]azocino[2,1-*a*]isoindole-7,13-dione (**6a**).

This compound was obtained in a yield of 92%, mp 242-244°; ir: 1674 (C=O), 1643 (C=O) cm^{-1}; ^1H nmr: δ 3.14 (dd, 1H, H_{12pax}, J = 1.9, 13.4 Hz), 3.32-3.51 (m, 2H, CH_2-CH_2-N), 3.71-3.81 (m, 1H, CH_2-CH_2-N), 3.89 (dd, 1H, H_{12peq}, J = 6.2, 13.4 Hz), 4.49-4.65 (m, 1H, CH_2-CH_2-N), 4.90 (dd, 1H, H_{11b}, J = 1.9, 6.2 Hz), 6.92 (d, 1H, H thiophene, J = 5.3 Hz), 7.22 (d, 1H, H thiophene, J = 5.3 Hz), 7.38-7.44 (m, 1H, H arom), 7.52-7.57 (m, 2H, H arom), 7.66 (d, 1H, H_8, J = 7.4 Hz); ^{13}C nmr: δ 28.3 (CH_2), 39.6 (CH_2), 45.1 (CH_2), 58.0 (CH), 122.3 (CH arom), 122.4 (CH arom), 123.8 (CH arom), 128.7 (CH arom), 129.2 (CH arom), 131.2 (C arom), 131.9 (CH arom), 140.3 (C arom), 143.2 (C arom), 146.2 (C arom), 168.2 (CO),189.7 (CO).

Anal. Calcd. for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.94. Found: C, 67.71; H, 4.74; N, 5.01.

4,5,11b,12-Tetrahydrothieno[2',3':5,6]azocino[2,1-*a*]isoindole-7,13-dione (**6b**).

This compound was obtained in a yield of 98%, mp 222-224°; ir: 1672 (C=O), 1644 (C=O) cm^{-1}; ^1H nmr: δ 3.20 (dd, 1H, H_{12pax}, J = 2.1, 13.4 Hz), 3.33-3.49 (m, 3H, CH_2-CH_2-N), 3.96 (dd, 1H, H_{12peq}, J = 6.4, 13.4 Hz), 4.45-4.61 (m, 1H, CH_2-CH_2-N), 4.92 (dd, 1H, H_{11b}, J = 2.1, 6.4 Hz), 6.97 (d, 1H, H3, J = 5.3 Hz), 7.36-7.50 (m, 4H, 1H, H arom), 7.56 (d, 1H, H_8, J = 7.4 Hz); ^{13}C nmr: δ 29.0 (CH_2), 38.7 (CH_2), 44.7 (CH_2), 58.0 (CH), 122.4 (CH arom), 123.7 (CH arom), 128.7 (CH arom), 131.2 (C arom), 131.9 (2CH arom), 133.5 (CH arom), 142.2 (C arom), 142.5 (C arom), 143.0 (C arom), 168.2 (CO), 188.4 (CO).

Anal. Calcd. for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.94. Found: C, 68.09; H, 4.54; N, 4.98.

3-Chloro-4,5,11b,12-tetrahydrothieno[3',4':5,6]azocino[2,1-*a*]-isoindole-7,13-dione (**6c**).

This compound was obtained in a yield of 87%, mp 220-222°; ir: 1674 (C=O), 1660 (C=O) cm^{-1}; ^1H nmr: δ 3.16 (dd, 1H, H_{12pax}, J = 2.1, 13.4 Hz), 3.36-3.52 (m, 3H, CH_2-CH_2-N), 3.94 (dd, 1H, H_{12peq}, J = 6.4, 13.4 Hz), 4.44-4.62 (m, 1H, CH_2-CH_2-N), 4.92 (dd, 1H, H_{11b}, J = 2.1, 6.4 Hz), 7.37-7.58 (m, 3H, H arom), 7.66 (d, 1H, H_8, J = 7.4 Hz), 7.71 (s, 1H, H thiophene); ^{13}C nmr: δ 26.0 (CH_2), 39.4 (CH_2), 44.8 (CH_2), 58.5 (CH), 122.3 (CH arom), 123.7 (CH arom), 128.0 (C arom), 128.7 (CH arom), 130.5 (CH arom), 131.3 (C arom), 132.0 (CH arom), 132.8 (C arom), 140.3 (C arom), 143.0 (C arom), 168.1 (CO), 189.4 (CO).

Anal. Calcd. for $C_{16}H_{12}ClNO_2S$: C, 60.47; H, 3.81; N, 4.41. Found: C, 60.58; H, 3.92; N, 4.60.

Reduction of Ketones **6a-c** into Alcohols **7a-c**.

A solution of the ketoamide **6a-c** (2 mmoles) in methanol (10 ml) was cooled at 0°, and sodium borohydride (100 mg, 2.6 mmoles) was added and stirring was continued at room temperature for 1 hour. The mixture was diluted with water (15 ml), and acidified with 10% hydrochloric acid solution, and was extracted with dichloromethane (3 x 10 ml). The combined extracts were washed with brine, dried and concentrated. Recrystallization of the solid from ethanol gave alcohols **7a-c**.

4,5,12,13-Tetrahydro-13-hydroxy-11b*H*-thieno[3',2':5,6]azocino-[2,1-*a*]isoindol-7-one (**7a**)

This compound was obtained in a yield of 94%, mp 180-182°; ir: 3307 (OH), 1669 (C=O) cm^{-1}; ^1H nmr: δ 2.21 (dt, 1H, H_{12pax}, J = 7.2, 14.8 Hz), 2.76 (dt, 1H, H_{12peq}, J = 4, 14.8 Hz), 3.26-3.32 (m, 2H, CH_2-CH_2-N), 3.39-3.48 (m, 1H, CH_2-CH_2-N), 4.42-4.56 (m, 1H, CH_2-CH_2-N), 4.67 (dd, 1H, H_{13}, J = 4, 7.2 Hz), 5.21 (dd, 1H, H_{11b}, J = 4, 7.2 Hz), 6.94 (d, 1H, H_1, J = 5.4 Hz), 7.03 (d, 1H, H_2, J = 5.4 Hz,), 7.40-7.53 (m, 3H, H arom), 7.72 (d, 1H, H_8, J = 7.2 Hz); ^{13}C nmr: δ 26.9 (CH_2), 42.2 (CH_2), 43.8 (CH_2), 59.7 (CH), 69.0 (CH), 122.0 (CH arom), 122.9 (CH arom), 123.7 (CH arom), 127.4 (CH arom), 128.2 (CH arom), 131.0 (C arom), 131.7 (CH arom), 134.0 (C arom), 140.6 (C arom), 146.8 (C arom), 170.1 (CO).

Anal. Calcd. for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.39; H, 5.36; N, 5.02.

4,5,12,13-Tetrahydro-13-hydroxy-11b*H*-thieno[2',3':5,6]azocino-[2,1-*a*]isoindol-7-one (**7b**).

This compound was obtained in a yield of 98%, mp 170-172°; ir: 3354 (OH), 1656 (C=O) cm^{-1}; ^1H nmr: δ 2.16 (dt,1H, H_{12pax}, J = 7.5, 14.8 Hz), 2.83 (dt, 1H, H_{12peq}, J = 4, 14.8 Hz), 3.01-3.29 (m, 2H, CH_2-CH_2-N), 3.40-3.53 (m, 1H, CH_2-CH_2-N), 4.30-4.48 (m, 1H, CH_2-CH_2-N), 4.71 (dd, 1H, H_{13}, J = 4, 7.5 Hz), 5.41 (dd, 1H, H_{11b}, J = 4, 7.5 Hz), 6.80 (d, 1H, H_3, J = 5.1 Hz), 7.07 (d, 1H, H_2, J = 5.1 Hz), 7.36-7.52 (m, 3H, H arom), 7.73 (d, 1H, H_8, J = 7.2 Hz); ^{13}C nmr: δ 26.9 (CH_2), 44.3 (CH_2), 47.6 (CH_2), 59.0 (CH), 66.9 (CH), 122.4 (CH arom), 122.5 (CH arom), 122.7 (CH arom), 127.9 (CH arom), 129.7 (CH arom), 130.7 (C arom), 131.6 (CH arom), 132.1 (C arom), 145.7 (C arom), 147.5 (C arom), 169.9 (CO).

Anal. Calcd. for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.66; H, 5.41; N, 4.84.

3-Chloro-4,5,12,13-tetrahydro-13-hydroxy-11b*H*-thieno[3',4':5,6]-azocino[2,1-*a*]isoindol-7-one (**7c**).

This compound was obtained in a yield of 96%, mp 198-200°; ir: 3363 (OH), 1656 (C=O) cm^{-1}; ^1H nmr: δ 1.92 (dt, 1H, H_{12pax}, J = 7.5, 15 Hz), 2.77-2.95 (m, 2H, CH_2-CH_2-N), 3.23 (dt, 1H, H_{12peq}, J = 3, 15 Hz,), 3.33-3.44 (m, 1H, CH_2-CH_2-N), 4.36-4.50 (m, 1H, CH_2-CH_2-N), 4.64 (dd, 1H, H_{13}, J = 3, 7.5 Hz), 5.07 (dd, 1H, H_{11b}, J = 3, 7.5 Hz), 6.93 (s, 1H, H_1), 7.36-7.56 (m, 3H, H arom), 7.71 (d, 1H, H_8, J = 7.2 Hz); ^{13}C nmr: δ 25.1 (CH_2), 42.7 (CH_2), 44.9 (CH_2), 59.2 (CH), 69.8 (CH), 116.9 (CH arom), 122.1 (CH arom), 123.7 (CH arom), 127.2 (C arom), 128.4 (CH arom), 131.4 (C arom), 131.8 (CH arom), 132.5 (C arom),

143.6 (C arom), 146.4 (C arom), 170.8 (CO).

Anal. Calcd. for $C_{16}H_{14}ClNO_2S$: C, 60.09; H, 4.41; N, 4.38. Found: C, 60.32; H, 4.50; N, 4.44.

Reduction of Azocinones into Compounds **8** and **9**.

Trifluoroacetic acid (10 ml) was added to a stirred mixture of **6a,b** (4 mmoles) and triethylsilane (3 ml, 18 mmoles). The resulting solution was stirred at room temperature for 3 days. The reaction mixture was concentrated *in vacuo,* diluted with water, washed with 10% potassium carbonate solution and extracted with dichloromethane (3 x 10 ml). The combined extracts were washed with water, dried and concentrated. The residue was subjected to chromatography (silica gel-dichloromethane), to give **8a,b** (90%) and **9a,b** (10%).

4,5,12,13-Tetrahydro-11b*H*-thieno[3',2':5,6]azocino[2,1-*a*]isoindol-7-one (**8a**).

Compound **8a** (0.6 g, 55%) was the first eluted, mp 130-132°; ir: 1673 (C=O) cm^{-1}; ^1H nmr: δ 2.05-2.20 (m, 1H, H_{12}), 2.39-2.78 (m, 3H, H_{12} and H_{13}), 3.23-3.55 (m, 3H, H_4 and H_5), 4.34-4.45 (m, 1H, H_5), 4.66 (dd, 1H, H_{11b}, J = 3.5, 7.2 Hz), 6.60 (d, 1H, H_1, J = 5.1 Hz), 6.95 (d, 1H, H_2, J = 5.1 Hz), 7.33-7.52 (m, 3H, H arom), 7.77 (d, 1H, H_8, J = 7.2 Hz); ^{13}C nmr: δ 24.0 (CH_2), 27.7 (CH_2), 32.4 (CH_2), 42.5 (CH_2), 60.6 (CH), 121.7 (2CH arom), 123.5 (CH arom), 128.1 (CH arom), 130.6 (CH arom), 131.5 (CH arom), 132.3 (C arom), 133.9 (C arom), 136.9 (C arom), 145.9 (C arom), 169.4 (CO).

Anal. Calcd. for $C_{16}H_{15}NOS$: C, 71.35; H, 5.61; N, 5.20. Found: C, 71.20; H, 5.68; N, 5.26.

4,5,12,13-Tetrahydro-11b*H*-thieno[2',3':5,6]azocino[2,1-*a*]-isoindol-7-one (**8b**).

Compound **8b** (0.6 g, 55%) was the second eluted, mp 120-122°; ir: 1664 (C=O) cm^{-1}; ^1H nmr: δ 2.12-2.20 (m, 1H, H_{12}), 2.42-2.80 (m, 3H, H_{12} and H_{13}), 3.40-3.55 (m, 3H, H_3 and H_5), 4.38-4.46 (m, 1H, H_5), 4.65 (dd, 1H, H_{11b}, J = 4, 7.2 Hz), 6.76 (d, 1H, H_3, J = 5.1 Hz), 6.99 (d, 1H, H_2, J = 5.1 Hz), 7.35-7.54 (m, 3H, H arom), 7.77 (d, 1H, H_8, J = 7.4 Hz); ^{13}C nmr: δ 23.6 (CH_2), 28.7 (CH_2), 33.8 (CH_2), 41.2 (CH_2), 60.0 (CH), 121.4 (CH arom), 121.6 (CH arom), 123.2 (CH arom), 128.1 (CH arom), 130.3 (CH arom), 131.4 (CH arom), 133.7 (C arom), 134.1 (C arom), 139.6 (C arom), 145.7 (C arom), 169.0 (CO).

Anal. Calcd. for $C_{16}H_{15}NOS$: C, 71.35; H, 5.61; N, 5.20. Found: C, 71.10; H, 5.76; N, 5.01.

4,5,12,13-Tetrahydro-11b*H*-tetrahydrothieno[3',2':5,6]azocino-[2,1-*a*]isoindol-7-one (**9a**).

Compound **9a** (0.1g, 9%) was the first eluted, mp 124-126°; ir: 1640 (C=O) cm^{-1}; ^1H nmr: δ 1.60-2.23 (m, 8H, 6H tetrahydrothiophene, 2H, CH_2-CH_2-CHN), 2.50-2.86 (m, 3H, 2H, CH_2-CH_2-CHN and 1H, CH_2-CH_2-N), 3.25-3.46 (m, 2H, CH_2-CH_2-N), 4.20-4.29 (m, 1H, CH_2-CH_2-N), 4.44 (dd, 1H, H_{11b}, J = 4, 7.2 Hz), 7.34-7.52 (m, 3H, H arom), 7.80 (d, 1H, H_8, J = 6.7 Hz); ^{13}C nmr: δ 25.5 (CH_2), 28.5 (CH_2), 31.6 (CH_2), 32.4 (CH_2), 35.7 (CH_2), 41.4 (CH_2), 46.5 (CH), 47.1 (CH), 62.2 (CH), 121.7 (CH arom), 123.5 (CH arom), 128.1 (CH arom), 131.5 (CH arom), 131.6 (C arom), 146.2 (C arom), 169.5 (CO).

Anal. Calcd. for$C_{16}H_{19}NOS$: C, 70.29; H, 7.00; N, 5.12. Found: C, 70.31; H, 7.08; N, 5.19.

4,5,12,13-Tetrahydro-11b*H*-tetrahydrothieno[2',3':5,6]azocino[2,1-*a*]isoindol-7-one (**9b**).

Compound **9b** (0.1 g, 9%) was the second eluted, mp 126-128°; ir: 1640 (C=O) cm^{-1}; ^1H nmr: δ 1.60-2.24 (m, 8H, 6H tetrahydrothiophene, 2H, CH_2-CH_2-CHN), 2.49-2.91 (m, 3H, 2H, CH_2-CH_2-CHN and 1H, CH_2-CH_2-N), 3.23-3.48 (m, 2H, CH_2-CH_2-N), 4.19-4.38 (m, 1H, CH_2-CH_2-N), 4.45 (dd, 1H, H_{11b}, J = 4, 7.2 Hz), 7.34-7.56 (m, 3H, H arom), 7.80 (d, 1H, H_8, J = 6.7 Hz); ^{13}C nmr: δ 22.3 (CH_2), 27.8 (CH_2), 29.3 (CH_2), 29.9 (CH_2), 39.1 (CH_2), 42.5 (CH_2), 45.9 (CH), 51.4 (CH), 60.2 (CH), 121.7 (CH arom), 123.3 (CH arom), 128.2 (CH arom), 131.4 (CH arom), 133.0 (C arom), 145.0 (C arom), 168.6 (CO).

Anal. Calcd. for $C_{16}H_{19}NOS$: C, 70.29; H, 7.00; N, 5.12. Found: C, 70.34; H, 7.11; N, 5.18.

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