Rearrangement of Spiro[2*H*-1-benzopyran-2,2'-[2*H*]indoles] to Pyrrolo[1,2-*a*]indole Derivatives

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Heating of 1'-(*N*-substituted carbamoyl)methylspiro[2*H*-1-benzopyran-2,2'-[2*H*]indoles] with potassium hydroxide in ethanol yields diastereomeric 5a,13-methano-6*H*-1,3-benzoxazepino[3,2-*a*]indole-12-carboxamides. Reduction of the latter with sodium borohydride affords 1,2,3,9a-tetrahydro-2-hydroxyaryl-9*H*-pyrrolo[1,2-*a*]indole-3-carboxamides.

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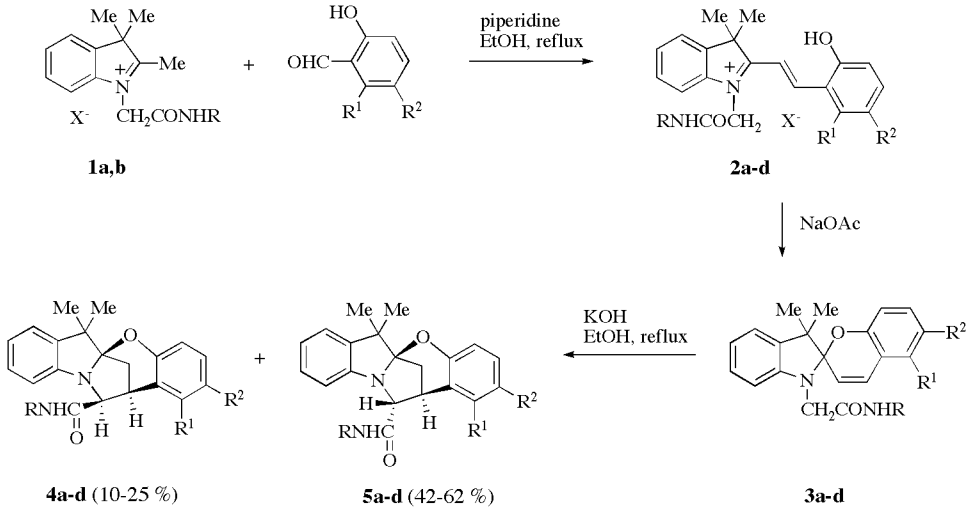
Indoline spiropyrans have been intensively investigated over the years because of their significant practical application, *e.g.*, information imaging and storage [1]. In recent years a number of investigators have reported advances towards synthesis of new indoline spiropyrans and understanding of their reversible photoconversion into coloured merocyanine isomers [2]. However, despite continuous investigations on preparation of new functionalized indoline spiropyrans their chemical properties remain still poorly disclosed.

In the present paper we wish to report a new synthetic method for the preparation of pyrrolo[1,2-*a*]indoles starting from indoline spiropyran derivatives. The pyrrolo[1,2-*a*]indole ring system is closely related to the basic ring system found in the medicinally important mitomycin antibiotics [3]. A number of synthesis of pyrrolo[1,2-*a*]indole derivatives have been developed, including a preparation by 1,3-dipolar cycloaddition of electron deficient dipolarophiles to 3*H*-indolium-*N*-methylides [4], but no direct transformation of indoline spiropyrans into pyrrolo[1,2-*a*]-indoles has been hitherto described.

Condensation of 1-(*N*-phenylcarbamoyl)methyl-2,3,3-trimethyl-3*H*-indolium perchlorate **1a** with salicylaldehyde or 2-hydroxy-1-naphthaldehyde followed by workup of 2-styryl-3*H*-indolium perchlorates **2a,b** under basic conditions gave 1'-(*N*-phenylcarbamoyl)methylindoline spiropyrans **3a,b** (Scheme 1). 1'-(*N*-*tert*-Butylcarbamoyl)-methylindoline spiropyrans **3c,d** were easily prepared by

Scheme 1



1a,b **2a-d** **4a-d** (10-25 %) **5a-d** (42-62 %) **3a-d**

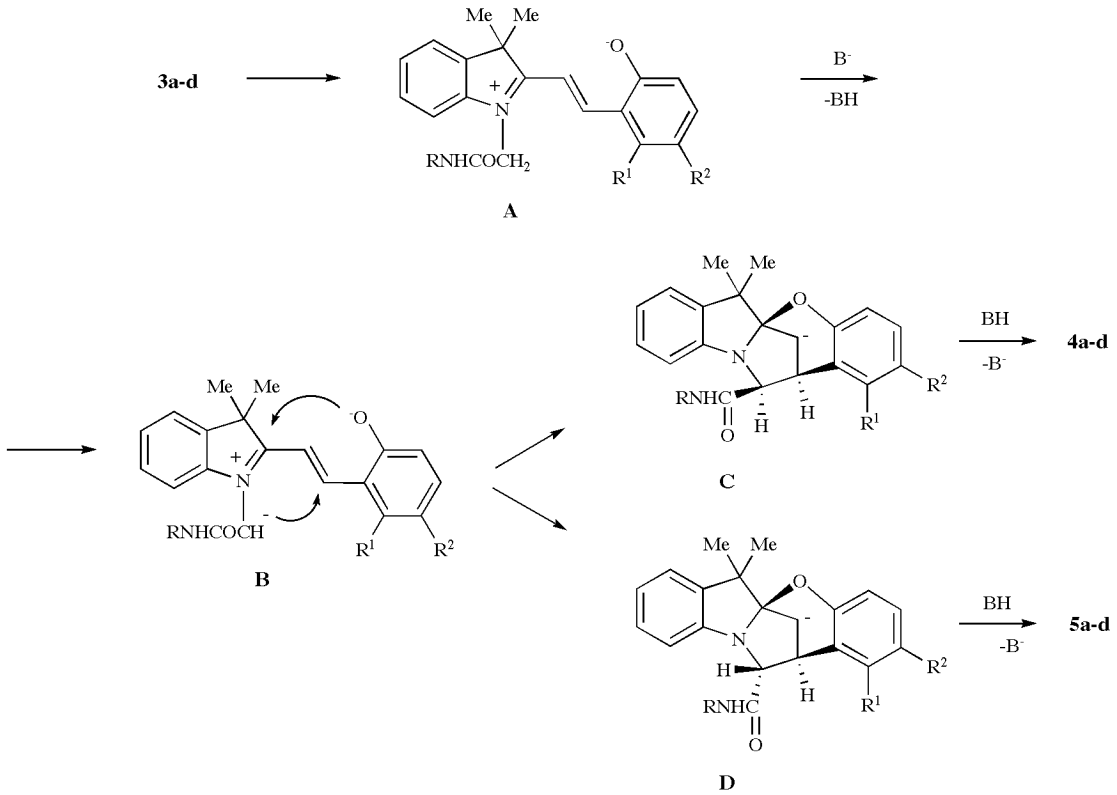
1a R = Ph, X = ClO_4; **b** R = $C(CH_3)_3$, X = Cl
2a R = Ph, $R^1 = R^2$ = H, X = ClO_4; **b** R = Ph, $R^1 + R^2$ = CH=CH-CH=CH, X = ClO_4; **c** R = $C(CH_3)_3$, $R^1 = R^2$ = H, X = Cl; **d** R = $C(CH_3)_3$, $R^1 + R^2$ = CH=CH-CH=CH; X = Cl
3-5a R = Ph, $R^1 = R^2$ = H; **b** R = Ph, $R^1 + R^2$ = CH=CH-CH=CH; **c** R = $C(CH_3)_3$, $R^1 = R^2$ = H; **d** R = $C(CH_3)_3$, $R^1 + R^2$ = CH=CH-CH=CH

the reaction of chloride **1b** with the above aromatic aldehydes in ethanol containing piperidine. The structures of the synthesized **3a-d** are supported by their ^{1}H nmr spectra; for example, vicinal coupling between ethene protons 3-H and 4-H of indoline spiropyran **3a** is 10.0 Hz and evidences their *cis*-allocation [5], while the coupling constant of corresponding ethene protons of 2-[2-(2-hydroxyphenyl)ethenyl]-3*H*-indolium perchlorate **2a** is 16.0 Hz (*trans*-allocation). The protons of NCH_2 group of the compound **3a** are diastereotopic due to the presence of a stereogenic center at C_2 and showed an AB-quadruplet (^2J = 16.0 Hz) at 3.96 ppm.

Heating of compounds **3a-d** with potassium hydroxide in ethanol afforded diastereomeric 5a,13-methano-1,3-benzoxazepino[3,2-*a*]indoles **4a-d** and **5a-d**. The *cis/trans* ratio, determined by ^{1}H nmr, is ~1/3 for the compounds **4a,b, 5a,b** and ~1/5 for **4c,d, 5c,d**. The structural assignment of compounds **4a-d** and **5a-d** was based on their spectroscopic properties, and the distinction of the two diastereomers was based upon vicinal coupling constants. For example, coupling constants between protons 14-H and 15-H of 7a,15-methanonaphth[1',2':6,7][1,3]oxazepino[3,2-*a*]indole derivatives **4b** and **5b** are 4.5 Hz and 0 Hz, respectively. The dihedral angles obtained from MM3 optimized structures are 38° for *cis*-isomer and 91.5° for *trans*-isomer. Using the Karplus equation in the version of by Bothner-By [6] gives coupling constants as 7.4 and 2.0 Hz, respectively. Very similar values were found for the corresponding diastereomers **4a,c,d** and **5a,c,d**. The quantitative discrepancy is probably due to the effect of the substituents and cyclopentane bond angle deformation, as these molecules exhibit very rigid ring structures. Stochastic conformational analysis using MM3 force field shows that there is only one competitive conformation for each diastereomer, and *cis*-isomer is *ca.* 8 kcal/mol more stable than the *trans*-isomer. This relation is the same when low (1.5) or high (25) dielectric constants are used in the electrostatic calculations.

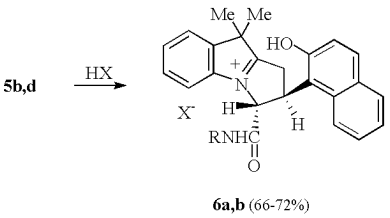
The mechanism of this recyclization reaction can be explained by the formation of an intermediate azomethine ylide (Scheme 2). When the spiro[indoline-pyrans] **3a-d** and a base are refluxed in ethanol, heterolytic cleavage of C-O bond occurs and the zwitter ion **A** is formed. The positively charged nitrogen atom of the indolium ring together with electron-accepting carboxamide group polarizes the C-H bonds of the methylene group, thus enabling for the hydroxide ion to deprotonate it to give the azomethine ylide **B**. The ylide is a strong nucleophile and may attack the partially positive carbon atom. Concerted addition of the oxygen atom to the α-carbon atom of the indole ring gives the two diastereomeric intermediates **C** and **D**, and derivatives **4a-d** and **5a-d** are obtained after reprotonation.

Scheme 2



When *trans*-**5b** was treated with perchloric acid, the heterolytic cleavage of C_{7a}-O bond took place and pyrrolo[1,2-*a*]indolium perchlorate **6a** was formed. Reaction of *trans*-**5d** with tetrafluoroboric acid gave tetrafluoroborate **6b** (Scheme 3). In the ^{13}C nmr spectrum of compound **6b** the signal of the sp^2-hybridized α-carbon atom of the indole ring lies at 203.9 ppm, which is typical of 3*H*-indolium salts [7].

Scheme 3

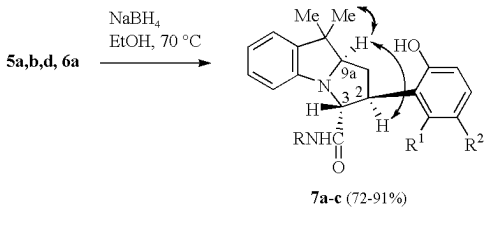


6a,b (66-72%)

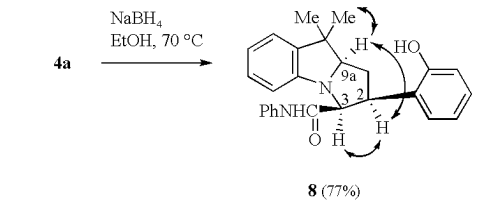
6a R = Ph, X = ClO_4; **b** R = $C(CH_3)_3$, X = BF_4

Reduction of the perchlorate **6a** with $NaBH_4$ in ethanol gave pyrrolo[1,2-*a*]indole derivative **7a** (Scheme 4). Identical product was obtained when compound **5b** was reduced with $NaBH_4$ directly. Pyrrolo[1,2-*a*]indole derivatives **7b,c** were obtained by a similar way from **5a,d**. Reaction of *cis*-**4a** with $NaBH_4$ afforded pyrrolo[1,2-*a*]-indole **8**. However, no reduction was observed in the case of *cis*-**4b**.

Scheme 4



7a-c (72-91%)



8 (77%)

: NOE observed

7a R = Ph, $R^1 + R^2$ = CH=CH-CH=CH; **b** R = Ph, $R^1 = R^2$ = H;
c R = $C(CH_3)_3$, $R^1 + R^2$ = CH=CH-CH=CH

The relative stereochemistry at C_2 and C_{9a} for **7a-c** and **8** was determined by NOESY measurement. Observation of NOEs between protons 2-H and 9a-H proved that they are in a *cis* relationship to each other.

In summary, we have reported a new method for the synthesis of pyrrolo[1,2-*a*]indole system by rearrangement of indoline spiropyran derivatives *via* methylides.

EXPERIMENTAL

All melting points were determined with a Kleinfeld melting point apparatus and are uncorrected. Infrared spectra were recorded on a UR 20 spectrometer. ^1H nmr spectra were recorded with Bruker DPX 200 and Bruker DPX 300 spectrometers at 200 and 300 MHz; ^{13}C nmr spectra were registered at 50 and 75 MHz, respectively. Chemical shifts, expressed in ppm, were relative to tetramethylsilane (TMS). For thin layer chromatographic (TLC) analyses, Merck precoated TLC plates (silica gel 60 F254) were used. Compound **1b** was prepared according to the reported procedure [8].

2,3,3-Trimethyl-1-(*N*-phenylcarbamoyl)methyl-3*H*-indolium perchlorate (**1a**).

To a solution of 2.92 g (10 mmoles) of 2,3-dihydro-3,3-dimethyl-2-methylene-1-(*N*-phenylcarbamoyl)methyl-1*H*-indole [8] in 8 ml of ethanol 60% perchloric acid was added to pH 2. The mixture was stored at -5° for 12 hours, crystalline substance was isolated by filtration and recrystallized from ethanol. Yield of **1a** 2.79 g (71%), mp 207-208°; ir (potassium bromide): 3300 (N-H), 1688 (C=O), 1070-1130, 650 (ClO_4^-) cm^{-1}; ^1H nmr (trifluoroacetic acid): δ 1.30 (s, 6H, 3,3-CH_3), 2.52 (s, 3H, 2-CH_3), 5.29 (s, 2H, CH_2), 6.77-7.60 (m, 10H, Ar-H and NH).

Anal. Calcd. for $C_{19}H_{21}ClN_2O_5$: C, 58.09; H, 5.39; Cl, 9.02. Found: C, 58.44; H, 5.25; Cl, 8.95.

2-[2-(2-Hydroxyphenyl)ethenyl]-3,3-dimethyl-1-(*N*-phenylcarbamoyl)methyl-3*H*-indolium perchlorate (**2a**).

To a solution of 1.96 g (5 mmoles) of perchlorate **1a** and 0.67 g (5.5 mmoles) of salicylaldehyde in 5 ml of ethanol two drops of piperidine were added and the mixture was refluxed for 3 hours. The reaction mixture was poured into 30 ml of 5% sodium acetate solution and extracted with ether (2 x 20 ml). The combined organic layer was washed with water (30 ml), dried over calcium chloride and the solvent was evaporated under reduced pressure. The residue was dissolved in 5 ml of ethanol and perchloric acid (60%) was added to pH 2. The mixture was stored at 0° for 12 hours, crystalline substance was isolated by filtration and recrystallized from ethanol. Yield of **2a** 1.69 g (68%), mp 205-206°; ir (potassium bromide): 3392 (O-H), 3270 (N-H), 1688 (C=O), 1550 (amide II), 1100, 630 (ClO_4^-) cm^{-1}; ^1H nmr (trifluoroacetic acid): δ 1.53 (s, 6H, 3,3-CH_3), 5.37 (s, 2H, CH_2), 6.56-7.61 (m, 15H, Ar-H, NH and C*H*=CH), 8.41 (d, J= 16.0 Hz, 1H, CH=C*H*).

Anal. Calcd. for $C_{26}H_{25}ClN_2O_6$: C, 62.84; H, 5.07; Cl, 7.13; N, 5.64. Found: C, 62.53; H, 5.17; Cl, 7.26; N, 5.62.

2-[2-(2-Hydroxy-1-naphthyl)ethenyl]-3,3-dimethyl-1-(*N*-phenylcarbamoyl)methyl-3*H*-indolium perchlorate (**2b**).

This compound was obtained similarly to compound **2a** from 1.96 g (5 mmoles) of perchlorate **1a** and 0.95 g (5.5 mmoles) of 2-hydroxy-1-naphthaldehyde. The yield of **2b** 1.78 g (65%), mp 165-167°; ir (potassium bromide): 3480 (O-H), 3320 (N-H), 1695 (C=O), 1550 (amide II), 1100, 650 (ClO_4^-) cm^{-1}; ^1H nmr (trifluoroacetic acid): δ 1.63 (s, 3H, 3,3-CH_3), 5.22 (s, 2H, CH_2),

6.68-7.66 (m, 17H, Ar-H, NH and C*H*=CH), 7.81 (d, J= 16.0 Hz, 1H, CH=C*H*).

Anal. Calcd. for $C_{30}H_{27}ClN_2O_6$: C, 65.87; H, 4.98; Cl, 6.48; N, 5.12. Found: C, 65.49; H, 5.03; Cl, 6.77; N, 5.32.

1',3'-Dihydro-3',3'-dimethyl-1'-(*N*-phenylcarbamoyl)methylspiro[2*H*-1-benzopyran-2,2'-[2*H*]indole] (**3a**).

A solution of perchlorate **2a** (1.49 g, 3 mmoles) in 10 ml of ethanol was poured into 50 ml of 5% potassium hydroxide and extracted with ether. The organic layers were washed with water and dried over calcium chloride. After removing of the solvent under reduced pressure, the residue was crystallized from ethanol to afford 1.02 g (86%) of **3a**, mp 139-140°; ir (potassium bromide): 3275 (N-H), 1680 (C=O), 1550 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.23 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 3.96 (*AB*-q, J = 16.0 Hz, 2H, CH_2), 5.71 (d, J = 10.0 Hz, 1H, C*H*=CH), 6.48-7.56 (m, 14H, Ar-H and CH=C*H*), 8.51 (br s, 1H, NH).

Anal. Calcd. for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.01; N, 7.07. Found: C, 79.0; H, 5.85; N, 7.35.

1,3-Dihydro-3,3-dimethyl-1-(*N*-phenylcarbamoyl)methylspiro-[2*H*-indole-2,3'-[3*H*]naphth[2,1-*b*]pyran] (**3b**).

This compound was obtained similarly to compound **3a** from 1.64 g (3 mmoles) of perchlorate **2b**. The yield of oily **3b** was 1.14 g (85%); ^1H nmr (deuteriochloroform): δ 1.06 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 3.73 (*AB*-q, J= 16.0 Hz, 2H, CH_2), 5.63 (d, J = 10.0 Hz, 1H, C*H*=CH), 6.39-7.90 (m, 16H, Ar-H and CH=C*H*), 8.37 (br s, 1H, NH).

Anal. Calcd. for $C_{30}H_{26}N_2O_2$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.93; H, 6.01; N, 6.11.

1'-(*N*-*tert*-Butylcarbamoyl)methyl-1',3'-dihydro-3',3'-dimethylspiro[2*H*-1-benzopyran-2,2'-[2*H*]indole] (**3c**).

To a solution of 3.09 g (10 mmoles) of chloride **1b** and 1.34 g (11 mmoles) salicylaldehyde in 10 ml of ethanol, three drops of piperidine were added and the mixture was refluxed for 5 hours. The reaction mixture was poured into 50 ml of 5% sodium acetate and extracted with ether. The organic layers were washed with water, dried over calcium chloride and the solvent was evaporated under reduced pressure. The residue was crystallized from ethanol to afford 2.22 g (59%) of **3c**, mp 144-145°; ir (potassium bromide): 3380 (N-H), 1680 (C=O), 1520 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.20 (s, 3H, CH_3), 1.29 (s, 9H, $C(CH_3)_3$), 1.34 (s, 3H, CH_3), 3.71 (*AB*-q, J = 17.4 Hz, 2H, CH_2), 5.62 (d, J = 10.2 Hz, 1H, C*H*=CH), 6.48-7.19 (m, 8H, Ar-H), 6.54 (br s, 1H, NH), 6.87 (d, J = 10.2 Hz, 1H, CH=C*H*); ^{13}C nmr (deuteriochloroform): δ 20.11, 25.85, 28.43 (3C), 48.78, 50.63, 51.91, 104.06, 107.36, 114.93, 118.07, 118.27, 120.44, 120.75, 121.86, 127.04, 127.76, 130.09, 130.46, 136.44, 146.06, 153.46, 169.03.

Anal. Calcd. for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.60; H, 7.62; N, 7.25.

1-(*N*-*tert*-Butylcarbamoyl)methyl-1,3-dihydro-3,3-dimethylspiro[2*H*-indole-2,3'-[3*H*]naphth[2,1-*b*]pyran] (**3d**).

This compound was obtained similarly to compound **3c** from 0.92 g (3 mmoles) of chloride **1b** and 0.52 g (3 mmoles) of 2-hydroxy-1-naphthaldehyde. The yield was 0.64 g (50%), mp 202-203° (ethanol); ir (potassium bromide): 3210 (N-H), 1680 (C=O), 1530 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.24 (s, 3H, 3-CH_3), 1.29 (s, 9H, 3 x CH_3), 1.36 (s, 3H, 3-CH_3), 3.79 (*AB*-q, J= 17.0 Hz, 2H, CH_2), 5.75 (d, J= 10.0 Hz, 1H, C*H*=CH), 6.41-8.13 (m, 12H, Ar-H, CH=C*H* and NH).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 79.18; H, 7.15; N, 6.72.

General Procedure for the Rearrangement of **3** to **4, 5**.

To a solution of indoline spiropyrans **3** (1 equiv.) in ethanol fine powdered potassium hydroxide (3 equiv.) was added and the mixture was refluxed for 2 hours and then was allowed to reach room temperature. The precipitated crystals of *cis*-**4** were collected by filtration, washed with water to remove sodium hydroxide and recrystallized from ethanol. The filtrate was poured into water and extracted with ether. The organic layers were washed with water and dried over calcium chloride. The solvent was evaporated under reduced pressure and the residue crystallized from ethanol to afford *trans*-**5**.

(5a*R**,12*S**,13*S**)-12,13-Dihydro-5a,13-methano-6,6-dimethyl-6*H*-1,3-benzoxazepino[3,2-*a*]indole-12-(*N*-phenylcarboxamide) (*cis*-**4a**) and its (5a*R**,12*R**,13*S**)-isomer (*trans*-**5a**).

Following the general procedure, the spiropyran **3a** (1.98 g, 5 mmoles), potassium hydroxide (0.84 g, 15 mmoles) in ethanol (15 ml) gave *cis*-**4a** (0.50 g, 25%) and *trans*-**5a** (0.83 g, 42%). Isomer *cis*-**4a**: mp 183-184°; ir (potassium bromide): 3295 (N-H), 1680 (C=O), 1535 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.55 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 2.22 (dd, J = 3.7 and 11.3 Hz, 1H of CH_2), 2.28 (d, J = 11.3 Hz, 1H of CH_2), 3.78-3.81 (m, 1H, 13-H), 4.06 (d, J= 4.3 Hz, 1H, 12-H), 6.61-7.23 (m, 13H, Ar-H), 8.64 (br s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 18.37, 21.56, 23.10, 26.43, 33.05, 42.59, 44.98, 78.44, 109.74, 110.57, 115.63, 120.72, 120.89, 122.19, 122.58, 124.35, 124.66, 128.28, 128.36, 128.62, 128.98, 136.49, 138.74, 148.88, 152.43, 168.84.

Anal. Calcd. for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.01; N, 7.06. Found: C, 78.69; H, 5.78; N, 7.32.

Isomer *trans*-**5a**: mp 174-175°; ir (potassium bromide): 3315 (N-H), 1680 (C=O), 1530 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.37 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.15 (d, J = 11.2 Hz, 1H of CH_2), 2.51 (dd, J = 2.3 and 11.2 Hz, 1H of CH_2), 3.85 (d, J = 2.3 Hz, 1H, 13-H), 4.53 (s, 1H, 12-H), 6.40-7.62 (m, 14H, Ar-H and NH); ^{13}C nmr (deuteriochloroform): δ 20.57, 28.19, 28.69, 44.79, 46.97, 68.30, 77.21, 106.90, 107.22, 116.77, 119.72, 119.79, 120.12, 122.91, 124.82, 126.82, 127.64, 127.99, 128.71, 129.07 (2C), 136.93, 140.99, 141.92, 153.19, 168.25.

Anal. Calcd. for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.01; N, 7.06. Found: C, 78.53; H, 6.07; N, 7.31.

(7a*R**,14*S**,15*S**)-14,15-Dihydro-7a,15-methano-8,8-dimethyl-8*H*-naphth[1',2':6,7][1,3]oxazepino[3,2-*a*]indole-14-(*N*-phenylcarboxamide) (*cis*-**4b**) and its (7a*R**,14*R**,15*S**)-isomer (*trans*-**5b**).

Following the general procedure, the spiropyran **3b** (2.23 g, 5 mmoles), potassium hydroxide (0.84 g, 15 mmoles) and 15 ml of ethanol gave *cis*-**4b** (0.36 g, 16%) and *trans*-**5b** (1.0 g, 45%). Isomer *cis*-**4b**: mp 206-207°; ir (potassium bromide): 3300 (N-H); 1660 (C=O); 1530 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.56 (s, 3H, CH_3), 1.62 (s, 3H, CH_3), 2.29 (dd, J = 1.1 and 11.0 Hz, 1H of CH_2), 2.34 (dd, J = 3.8 and 11.0 Hz, 1H of CH_2), 4.20 (d, J = 4.5 Hz, 1H, 14-H), 4.58-4.60 (m, 1H, 15H), 6.65-8.08 (m, 15H, Ar-H), 8.50 (br s, 1H, NH). ^{13}C nmr (deuteriochloroform): δ 23.28, 26.43, 33.04, 37.52, 44.89, 78.97, 109.52, 110.66, 116.99, 117.37, 120.89 (2C), 122.24, 122.62, 122.77, 123.52, 124.43, 126.64, 128.00 (2C),

128.36, 128.44, 128.98, 129.46, 131.31, 136.30, 138.83, 148.92, 150.07, 168.75.

Anal. Calcd. for $C_{30}H_{26}N_2O_2$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.35; H, 5.74; N, 6.46.

Isomer *trans*-**5b**: mp 201-203°; ir (potassium bromide): 3320 (N-H), 1660 (C=O), 1530 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.44 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 2.24 (d, J = 11.2 Hz, 1H of CH_2), 2.60 (dd, J = 3.8 and 11.2 Hz, 1H of CH_2), 4.56 (d, J = 3.8 Hz, 1H, 15-H), 4.57 (s, 1H, 14-H), 6.34-8.13 (m, 16H, Ar-H and NH); ^{13}C nmr (deuteriochloroform): δ 20.57, 28.18, 28.42, 42.01, 44.70, 68.08, 107.14 (2C), 118.71, 119.35, 119.70, 119.71 (2C), 121.19, 122.97, 123.34, 124.85, 126.93, 128.06, 128.82 (2C), 128.90, 129.11 (2C), 130.57, 137.04, 141.03, 141.97, 150.82, 168.37.

Anal. Calcd. for $C_{30}H_{26}N_2O_2$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.94; H, 6.03; N, 6.01.

(5a*R**,12*R**,13*S**)-12,13-Dihydro-5a,13-methano-6,6-dimethyl-6*H*-1,3-benzoxazepino[3,2-*a*]indole-12-(*N*-*tert*-butylcarboxamide) (*trans*-**5c**).

Following the general procedure, heating of spiropyran **3c** (0.94 g, 2.5 mmoles) with potassium hydroxide (0.42 g, 7.5 mmoles) in 15 ml of ethanol gave a mixture of two diastereomers, from which only *trans*-**5c** was separated with the yield 0.58 g (62%) by crystallization of the mixture from ethanol. Isomer *trans*-**5c**: mp 151-152°; ir (potassium bromide): 3380 (N-H), 1680 (C=O), 1550 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.26 (s, 9H, $C(CH_3)_3$), 1.31 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 2.08 (d, J= 11.0 Hz, 1H of CH_2), 2.38 (dd, J= 4.0 and 11.0 Hz, 1H of CH_2), 3.72 (d, J = 4.0 Hz, 1H, 13-H), 4.27 (s, 1H, 12-H), 5.60 (br s, 1H, NH), 6.32-7.20 (m, 8H, Ar-H); ^{13}C nmr (deuteriochloroform): δ 20.73, 28.04, 28.66 (4C), 44.67, 46.59, 51.41, 68.67, 106.79, 107.30, 116.66, 119.38, 120.03, 122.75, 126.80, 127.70, 128.06, 128.49, 141.30, 141.81, 153.30, 168.93.

Anal. Calcd. for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.70; H, 7.61; N, 7.41.

(7a*R**,14*S**,15*S**)-14,15-Dihydro-8,8-dimethyl-8*H*-7a,15-methanonaphth[1',2':6,7][1,3]oxazepino[3,2-*a*]indole-14-(*N*-*tert*-butylcarboxamide) (*cis*-**4d**) and its (7a*R**,14*R**,15*S**)-isomer (*trans*-**5d**).

Following the general procedure, the spiropyran **3d** (2.14 g, 5 mmoles), potassium hydroxide (0.17 g, 15 mmoles) and 15 ml of ethanol gave *cis*-**4a** (0.21 g, 10%) and *trans*-**5a** (1.11 g, 52%). Isomer *cis*-**4d**: mp 134-135°; ir (potassium bromide): 3350 (N-H), 1675 (C=O), 1520 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.66 (s, 9H, $C(CH_3)_3$), 1.54 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 2.24 (dd, J = 4.1 and 11.6 Hz, 1H of CH_2), 2.26 (d, J = 11.6 Hz, 1H of CH_2), 3.95 (d, J = 4.8 Hz, 1H, 14-H), 4.48-4.50 (m, 1H, 15-H), 6.54-8.06 (m, 10H, Ar-H), 6.59 (br s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 23.86, 26.77, 28.23 (3C), 33.28, 37.79, 45.24, 50.40, 79.29, 109.71, 110.88, 117.75, 117.88, 122.20, 122.89, 123.61, 123.87, 126.90, 128.24, 128.64, 129.42, 129.46, 132.15, 139.27, 149.56, 150.58, 169.64.

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.53; H, 7.43; N, 6.51.

Isomer *trans*-**5d**: mp 189-190°; ir (potassium bromide): 3400 (N-H), 1660 (C=O), 1520 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.28 (s, 9H, $C(CH_3)_3$), 1.37 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 2.20 (d, J = 10.5 Hz, 1H of CH_2), 2.52 (dd, J = 4.5 and 10.5 Hz, 1H of CH_2), 4.41 (s, 1H, 14-H), 4.52 (d, J = 4.5 Hz, 1H, 15-H), 5.74 (br s, 1H, NH), 6.33-8.18 (m, 10H, Ar-H); ^{13}C nmr (deuteriochloroform): δ 20.54, 27.97, 28.21, 28.63 (3C), 41.49, 44.42, 51.31, 68.20, 106.80, 107.12, 118.55, 119.32, 119.52, 121.28, 122.72, 123.16, 126.70, 127.64, 128.43, 128.49, 128.75, 130.60, 141.15, 141.74, 150.65, 169.03.

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.48; H, 7.22; N, 6.76.

(2*R**,3*S**)-1,2-Dihydro-2-(2-hydroxy-1-naphthyl)-9,9-dimethyl-3-(*N*-phenylcarbamoyl)-3*H*,9*H*-pyrrolo[1,2-*a*]indolium perchlorate (**6a**).

To a solution of *trans*-**5b** (1.12 g, 2.5 mmoles) in 6 ml of ethanol, perchloric acid was added to pH 1 and the solution was stored at 5° for 14 hours. The precipitated crystals were isolated by filtration and recrystallized from ethanol to yield 0.99 g (72%) of perchlorate **6a** with m.p. 250-251°; ir (potassium bromide): 3300 (O-H), 3250 (N-H), 1700 (C=O), 1065-1130, 750 (ClO_4^-) cm^{-1}; ^1H nmr (deuteriodimethyl sulfoxide): δ 1.42 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.74 (d, J= 11.1 Hz, 1H of CH_2), 3.09 (dd, J = 3.7 and 11.1 Hz, 1H of CH_2), 4.44 (d, J = 3.2 Hz, 1H, 2-H), 5.36 (s, 1H, 3-H), 6.21-8.13 (m, 15H, Ar-H), 10.43 (s, 1H, OH), 10.51 (br s, 1H, NH).

Anal. Calcd. for $C_{30}H_{27}ClN_2O_6$: C, 65.87; H, 4.98; Cl, 6.48; N, 5.12. Found: C, 65.73; H, 5.12; Cl, 6.78; N, 5.39.

(2*R**,3*S**)-3-(*N*-*tert*-Butylcarbamoyl)-1,2-dihydro-2-(2-hydroxy-1-naphthyl)-9,9-dimethyl-3*H*,9*H*-pyrrolo[1,2-*a*]-indolium tetrafluoroborate (**6b**).

To a solution of *trans*-**5d** (1.07 g, 2.5 mmoles) in 6 ml of ethanol, tetrafluoroboric acid was added to pH 1 and the solution was stored at 5° for 18 hours. The precipitated crystals were isolated by filtration and recrystallized from ethanol to yield 0.85 g (66%) of tetrafluoroborate **6b** with mp 238-239°; ir (potassium bromide): 3350-3200 (O-H and N-H), 1685 (C=O), 1545 (amide II), 1100 (BF_4^-) cm^{-1}; ^1H nmr (a mixture of trifluoroacetic acid and deuteriobenzene): δ 1.31 (s, 9H, $C(CH_3)_3$), 1.66 (s, 3H, 9-CH_3), 1.72 (s, 3H, 9-CH_3), 3.64 (m, 1H of CH_2), 3.78 (m, 1H, of CH_2), 5.18 (m, 1H, 2-H), 5.76 (m, 1H, 3-H), 7.18-7.92 (m, 11H, Ar-H and NH); ^{13}C-nmr (a mixture of trifluoroacetic acid and deuteriobenzene): δ 20.54, 21.73, 26.74 (3C), 34.51, 41.98, 50.23, 54.11, 71.37, 114.47, 115.22, 117.27, 120.10, 123.53, 123.96, 127.87, 129.11, 129.33, 129.51, 130.59, 131.35, 132.00, 136.39, 145.34, 152.52, 167.19, 203.92.

Anal. Calcd. for $C_{28}H_{31}BF_4N_2O_2$: C, 65.38; H, 6.07; N, 5.45. Found: C, 65.55; H, 5.77; N, 5.28.

General Procedure for the Reduction of *cis*-**4a** and *trans*-**5a,b,d**.

To a solution of 5a,13-methano-6*H*-1,3-benzoxazepino[3,2-*a*]indole (5 mmoles) in 20 ml of ethanol was added sodium borohydride (0.57 g, 15.0 mmoles) and the mixture was heated at 70° for 1 hour. The reaction mixture was poured into 100 ml of water and was extracted with ether. The organic layers were washed with water and dried over calcium chloride. The solvent was removed by distillation and the residue crystallized from ethanol.

(2*R**,3*S**,9a*S**)-1,2,3,9a-Tetrahydro-2-(2-hydroxy-1-naphthyl)-9,9-dimethyl-9*H*-pyrrolo[1,2-*a*]indole-3-(*N*-phenylcarboxamide) (**7a**).

Method A.

To a solution of perchlorate **6a** (1.37 g, 2.5 mmoles) in 15 ml of ethanol was added sodium borohydride (0.28 g, 7.5 mmoles) and the mixture was heated at 70° for 1 hour. The reaction mixture was poured into 100 ml of water and extracted with ether. The organic

layers were washed with water and dried over calcium chloride. The solvent was removed by distillation and the residue was crystallized from ethanol to afford 0.85 g (76%) of **7a** with mp 228-229°; ir (potassium bromide): 3400-3180 (N-H and O-H), 1665 (C=O), 1520 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.39 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.96 (ddd, J = 6.0, 7.1 and 11.5 Hz, 1H of CH_2), 2.58 (ddd, J = 11.4, 11.5 and 12.0 Hz, 1H of CH_2), 3.90 (dd, J = 7.9 and 11.4 Hz, 9a-H), 4.57 (ddd, J= 7.1, 7.7 and 12.0 Hz, 2-H), 4.80 (d, J = 7.7 Hz, 3-H), 6.73-7.70 (m, 10H, Ar-H), 8.04 (br s, 1H, NH), 9.37 (s, 1H, OH).

Anal. Calcd. for $C_{30}H_{28}N_2O_2$: C, 80.33; H, 6.29; N, 6.25. Found: C, 80.08; H, 6.21; N, 6.52.

Method B.

Following the general procedure, reduction of *trans*-**5b** (2.23 g, 5 mmoles) with sodium borohydride (0.58 g, 15.0 mmoles) in ethanol gave 1.82 g (81%) of **7a**.

(2*R**,3*S**,9a*S**)-1,2,3,9a-Tetrahydro-2-(2-hydroxyphenyl)-9,9-dimethyl-9*H*-pyrrolo[1,2-*a*]indole-3-(*N*-phenylcarboxamide) (**7b**).

Following the general procedure, reduction of *trans*-**5a** (1.98 g, 5 mmoles) with sodium borohydride (0.57 g, 15.0 mmoles) in ethanol gave 1.81 g (91%) of **7b** with mp 184-185° (ethanol); ir (potassium bromide): 3415-3210 (N-H and O-H), 1670 (C=O), 1520 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.44 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 1.93 (ddd, J = 6.2, 6.9 and 13.0 Hz, 1H of CH_2), 2.38-2.56 (m, 1H of CH_2), 4.02 (dd, J= 5.0 and 10.7 Hz, 1H, 9a-H), 4.16-4.24 (m, 1H, 2-H), 4.62 (d, J = 9.0 Hz, 1H, 3-H), 6.35-7.21 (m, 13H, Ar-H), 7.51 (s, 1H, OH), 7.71 (br s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 26.15, 28.09, 29.65, 42.39, 47.02, 63.59, 75.96, 108.84, 116.02, 119.14, 120.62, 122.35 (2C), 123.08, 125.26, 125.50, 127.86 (2C), 128.62, 129.02 (2C), 136.63, 142.91, 147.42, 154.70, 170.35.

Anal. Calcd. for $C_{26}H_{26}N_2O_2$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.52; H, 6.85; N, 7.09.

(2*R**,3*S**,9a*S**)-1,2,3,9a-Tetrahydro-2-(2-hydroxy-1-naphthyl)-9,9-dimethyl-9*H*-pyrrolo[1,2-*a*]indole-3-(*N*-*tert*-butylcarboxamide) (**7c**).

Following the general procedure, reduction of *trans*-**5d** (2.13 g, 5 mmoles) with sodium borohydride (0.57 g, 15.0 mmoles) in ethanol gave 1.54 g (72%) of **7c** with mp 192-193° (ethanol); ir (potassium bromide): 3350 (N-H), 3250 (O-H), 1660 (C=O), 1520 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.38 (s, 3H, 9-CH_3), 1.41 (s, 12H, 9-CH_3, $C(CH_3)_3$), 1.92 (ddd, J = 6.0, 6.4 and 12.4 Hz, 1H of CH_2), 2.58 (ddd, J= 11.3, 11.4 and 12.4 Hz, 1H, of CH_2), 3.76 (dd, J= 6.4 and 11.3 Hz, 1H, 9a-H), 4.44 (ddd, J= 6.0, 8.0 and 11.4 Hz, 1H, 2-H), 4.50 (d, J= 8.0 Hz, 1H, 3-H), 6.68-7.70 (m, 10H, Ar-H), 7.42 (br s, 1H, NH), 9.17 (s, 1H, OH).

Anal. Calcd. for $C_{28}H_{32}N_2O_2$: C, 78.47; H, 7.53; N, 6.54. Found: C, 78.37; H, 7.22; N, 6.68.

(2*R**,3*R**,9a*S**)-1,2,3,9a-Tetrahydro-2-(2-hydroxyphenyl)-9,9-dimethyl-9*H*-pyrrolo[1,2-*a*]indole-3-(*N*-phenylcarboxamide) (**8**).

Following the general procedure, the compound *cis*-**4a** (0.79 g, 2 mmoles), sodium borohydride (0.23 g, 6 mmoles) and 10 ml of ethanol gave 0.61 g (77%) of **8** with mp 186-187° (ethanol); ir (potassium bromide): 3410-3200 (N-H and O-H), 1670 (C=O), 1520 (amide II) cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.41 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.96-2.18 (m, 2H, CH_2), 3.71 (dd, J= 13.2 and 6.0 Hz, 1H, 9a-H), 3.99 (ddd, J = 7.0, 8.3 and 11.2 Hz, 1H, 2-H), 4.11 (d, J = 8.3 Hz, 1H, 3-H), 6.57-7.38 (m, 13H, Ar-H), 9.21 (br s, 1H, NH), 9.40 (br s, 1H, OH); ^{13}C nmr (deuteriochloroform): δ 21.13, 30.19, 33.76, 42.07, 42.72, 73.55, 77.10, 109.78, 118.41, 119.51 (2C), 120.12, 121.11, 122.60, 124.62, 125.01, 127.55 (2C), 128.12, 128.60 (2C), 136.07, 137.31, 149.87, 154.80, 173.31.

Anal. Calcd. for $C_{26}H_{26}N_2O_2$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.42; H, 6.79; N, 7.37.

REFERENCES AND NOTES

[1] R. C. Bertelson, in Photochromism, Techniques of Chemistry, Vol. **3**, G. H. Brown, ed, Wiley Interscience, New York, 1971, pp. 45; R. Guglielmetti, in Photochromism - Molecules and Systems, Studies in Organic Chemistry, Vol. **40**, H. Dürr and H. Bouas-Laurent, ed, Elsevier, Amsterdam, 1990, pp. 314; H. Dürr, *Angew. Chem., Int. Ed. Engl.*, **28**, 413 (1989).

[2] H. Dürr, Y. Ma and G. Cortellaro, *Synthesis*, 294 (1995); R. Blonder, S. Levi, G. Tao, I. Ben-Dov and I. Willner, *J. Am. Chem. Soc.*, **119**, 10467 (1997); H. Görner, *Chemical Physics*, **222**, 315 (1997); A. K. Chibisov and H. Görner, *Chemical Physics*, **237**, 425 (1998); Y. J. Cho, K. Y. Rho, S. R. Keum, S. H. Kim and C. M. Yoon, *Synth. Commun.*, **29**, 2061 (1999); X. Li, Y. Wang, T. Matsuura and J. Meng, *Heterocycles*, **51**, 2639 (1999); G. Berkovic, V. Krongauz and V. Weiss, *Chem. Rev.*, **100**, 1741 (2000).

[3] K. Takahashi and T. Kametani, *Heterocycles*, **13**, 411 (1979); K. Jones and J. M. D. Storey, *Tetrahedron*, **49**, 4901 (1993); S. Lee, H.-J. Lim, K. L. Cha and G. A. Sulikowski, *Tetrahedron*, **53**, 16521 (1997); A. P. Dobbs, K. Jones and K. T. Veal, *Tetrahedron*, **54**, 2149 (1998); C. J. Moody and C. L. Norton, *J. Chem. Soc., Perkin Trans. 1*, 2639 (1997); B. G. Jones, M. Guzel and J. E. Mathews, *Tetrahedron Lett.*, **41**, 1123 (2000).

[4] C. W. G. Fishwick, A. D. Jones, M. B. Mitchell and C. Szantay, *Tetrahedron Lett.*, **29**, 5325 (1988); C. W. G. Fishwick, A. D. Jones and M. B. Mitchell, *Tetrahedron Lett.*, **30**, 4447 (1989); C. W. G. Fishwick, A. D. Jones, M. B. Mitchell, D. S. Eggleston and P. W. Baures, *Synlett*, 359 (1990).

[5] S.-R. Keum, K.-B. Lee, P. M. Kazmaier, R. A. Manderville and E. Buncel, *Magn. Reson. Chem.*, **30**, 1128 (1992).

[6] A. A. Bothner-By, *Adv. Magn. Res.*, **1**, 195 (1965).

[7] E. Kleinpeter and R. Borsdorf, *J. Prakt. Chem.*, **315**, 765 (1973);W.Grahn, *Tetrahedron*, **32**, 1931 (1976).

[8] A. A. Sackus and J. A. Degutis, *Khim. Geterotsikl. Soedin.*, **11**, 1485 (1986).