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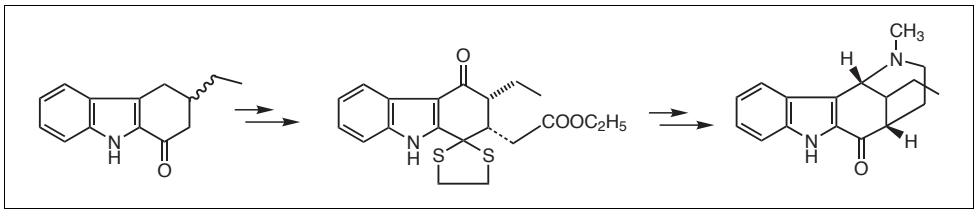

In this study, a new synthetic route to the total synthesis of (±)-20- epidasycarpidone (1b) is described. This route involves acid catalyzed ring closure and the formation of the intermediate 13 in the key step. The relative stereochemistry of 13 has been confirmed by X-ray structure analysis. The tetracyclic intermediate 13 was synthesized through several steps starting from 3. The removal of the protecting group of 13 yielded the lactam 15, which was reduced by Red-Al® to give 16. The synthesis of (±)-20-epidasycarpidone (1b) was finally completed by the oxidation of 16.

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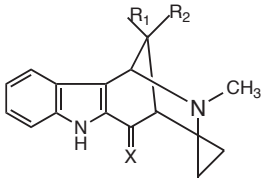
Several total syntheses of uleine (**2a**) [1-8] and its epimer (**2b**) [9-16] have been previously reported. All those synthetic routes for the construction of the uleine and dasycarpidone (**1a**) systems have involved the conversion of either 2-(4-piperidinylmethyl)indole [1,2, 12,14] 3-(2-piperidinylmethyl)indole [4,9-11] or Fischer indolization of 2-azabicyclo[3.3.1]nonane [17]. In our study, an alternative synthetic entry to the tetracyclic ring system of indole alkaloids of the uleine group is presented. Our approach is based on the formation of a tetracyclic core structure **13** formed by the ring closure [18] of the tetrahydrocarbazole derivative **10**, that possesses the required functionality at the C_2- position. The synthesis of the key intermediate **10** has started from the easily available 3-ethyl-1,2,3,4-tetrahydrocarbazole-1-one (**3**) [19].

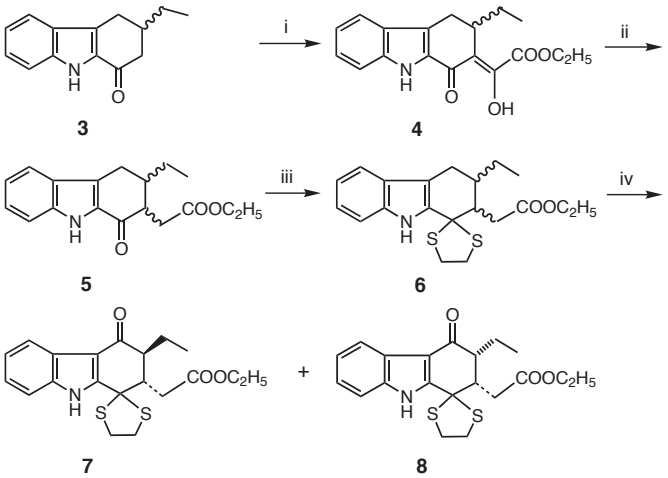


1a X: O	R_1: C_2H_5	R_2: H	dasycarpidone
1b X: O	R_1: H	R_2: C_2H_5	epidasycarpidone
2a X: CH_2	R_1:C_2H_5	R_2:H	uleine
2b X: CH_2	R_1: H	R_2: C_2H_5	epiuleine

Figure 1

The 1-oxo-tetrahydrocarbazole **3** was then converted into ethoxalyl derivative **4** by using sodium hydride and diethyl oxalate [20] in tetrahydrofuran. A mixture of diastereomers of saturated ketoester **5** was obtained by the reaction of **4** with triethylamine and methanesulfonyl chloride followed by the reduction of the resulting mesylate with zinc dust in acetic acid. The ratio of the diastereomers of **5** was determined by GC-MS analysis and was of 66:34 in favour of the 3-β-ethyl isomer to the detriment of the 3-α-ethyl one. Although the separation of the diastereomers by column chromatography was unsuccessful, some amount of the 3-β-ethyl isomer **5** was isolated successfully by crystallization in diethyl ether and its structure was confirmed by single crystal X-ray structure analysis [21]. However, the highly hindered pure 3-β-ethyl isomer of ketone **5** was converted under mild conditions into thioketal **6** by refluxing for 22 h

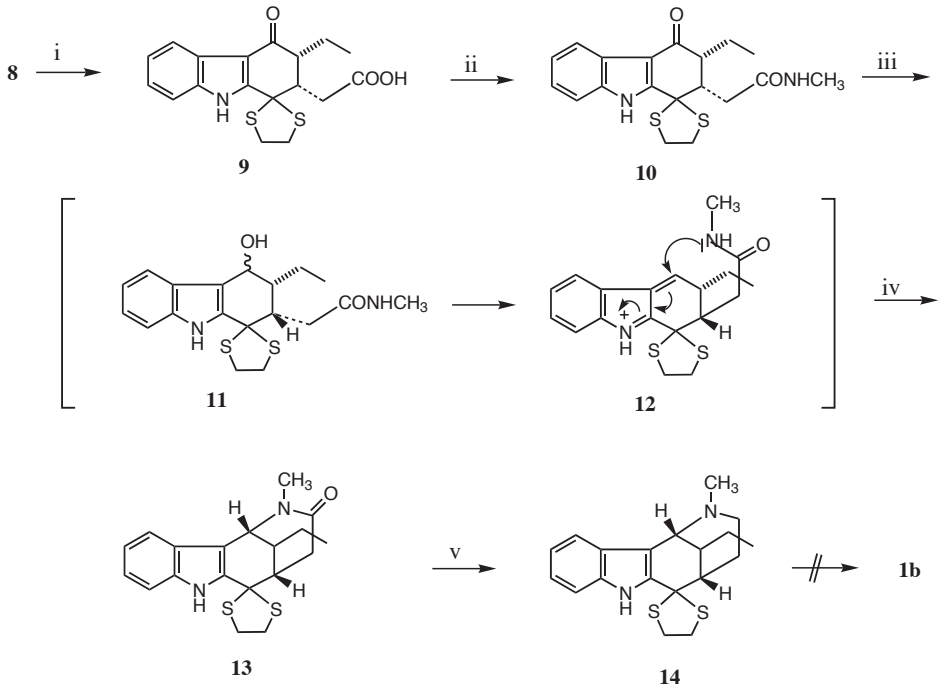
Scheme 1



Reagent and conditions: i) THF, NaH, diethyl oxalate, 60º, 86%; ii): CH_2Cl_2, triethylamine, CH_3SO_2Cl; then Zn, acetic acid, rt, 92%; iii) $CHCl_3$, $HSCH_2CH_2SH$, Zn-triflate, reflux, 66%; iv) THF, DDQ, 0º, 97%.

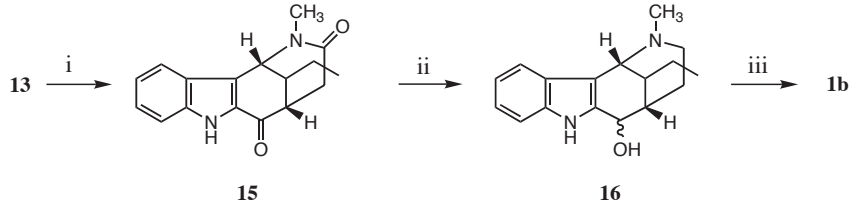
in chloroform with 1,2-ethanedithiol and zinc triflate as a catalyst [22]. Having obtained the pure compound **6**, the conversion of the diastereomers of ketone **5** into **6** under the same condition was also carried out. But unfortunately, the seperation of the diastereomers **6** was not possible and therefore, the mixture of the diastereomers of **6** was used for the next reaction. The mixture of diastereomers of **6** was oxidized [23] with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone at 0º to the corresponding 4-oxo isomers **7** and **8**, which were separated easily by column chromatography. The relative stereochemistry of the isomers *trans* **7** and *cis* **8** was determined by NMR experiments. An X-ray single crystal analysis of **13** confirmed the expected stereochemistry (Figure 2). Hydrolysis of **8** by using 15% potassium hydroxide in methanol-water (3:1) at room temperature gave the acid **9**. However, the amide **10** was obtained by the treatment of **9** with triethylamine and ethyl chloroformate in chloroform, followed by the addition of methylamine. The reduction of the ketone **10** to the corresponding alcohol **11** was carried out with an excess of sodium borohydride in tetrahydrofuran at 55º. The acid-catalyzed ring closure [18] of the rather labile alcohol **11** was accomplished by using trifluoroacetic acid at 5º to give intermediate **12**. The resulting intermediate **12** underwent stereoselectively *syn* cyclization to yield the tetracyclic compound **13**. The most characteristic value of its ^{1}H-NMR spectrum is a doublet of the methine proton on the C-1 position at δ 5.70 ppm, which was comparable to the data observed previously for the analogous methanoazocino-indole structure [24-26]. The lactam **13** was reduced by lithium aluminium hydride in tetrahydrofuran to give compound **14** in a high yield. All attempts to remove the protecting group [27-28] of **14** have led to unidentifiable complex mixtures. Therefore, at this point an alternative

Scheme 2



Reagent and conditions : i) CH_3OH-H_2O, KOH, rt, 84%; ii) $CHCl_3$, $(C_2H_5)_3N$, ethyl chloroformate, CH_3NH_2, -10º, 77%; iii) THF, $NaBH_4$, 55º; iv) CH_2Cl_2, CF_3COOH, 5º, 77%; v) THF, $LiAlH_4$, 35º, 91%.

Scheme 3



Reagent and conditions : i) CH_3CN-H_2O, (90:10), $(CF_3CO_2)_2IPh$, rt, 74%; ii) THF, Red-Al®, rt, 54%; iii) CH_2Cl_2-THF, MnO_2, rt, 71%.

synthetic pathway (Scheme 3) was used where the removal of the protecting group of compound **13** by [bis(trifluoro-acetoxy)iodo]benzene [27-28] was achieved successfully giving rise to compound **15** in good yield (74%). The compound **15** was then successfully converted into its epimeric 6-hydroxy compound **16** by the treatment with sodium bis(2-methoxyethoxy)aluminium hydride (Red-Al®) [29]. Finally, the oxidation [30] of **16** with active manganese(IV)oxide has led to the formation of the alkaloid (±)-20-epidasycarpidone **1b**. The spectral data of (±)-20-epidasycarpidone obtained were identical to those of the natural product reported in the literature [8,12].

Crystal data for **13** $C_{19}H_{22}N_2OS_2$ is: M_r=358.51, monoclinic, a=11.0142(14), b=9.821(3), c=16.1723(17) Å, β=96.646(6)° V=1737.6(6) Å^3, space group $P2_1/c$, Z=4,D_x=1.370 mg m^{-3}, μ=2.34 mm^{-1}. The crystallographic data were collected at room temperature on an Enraf-Nonius CAD-4 diffractometer with CuK_α radiation (λ=1.54184 Å). The structure was solved by direct methods. The final R value was 0.0549 (R_w=0.1591). H16A, H16B, H17A and H17B atoms were positioned geometrically [0.97 (CH_2)] and constrained to ride on their parent atoms with U_{iso}(H)=1.2 U(C). The remaining ones were located in a difference map and refined isotropically [31]. Programs used were SHELXS97 & SHELXL97 [32] and Ortep-3 for windows [33].

Table 1

Selected Bond Distances (Å) and Angles (°)

N2	C3	1.348(4)	N2	C1	1.486(4)
C3	C4	1.502(5)	C4	C5	1.541(5)
C5	C6	1.555(4)	C6a	N7	1.364(4)
C6a	C11b	1.366(4)	C1	C11b	1.497(4)
C1	C12	1.524(5)	C5	C12	1.533(5)
C12	C13	1.532(5)	C13	C14	1.497(7)
N2-C1-C11b		110.0(3)	C11-C5-C4		108.6(3)
N2-C1-C12		110.2(3)	C12-C8-C6		110.4(3)
C11b-C1-C12		110.1(3)	C4-C5-C26		114.6(3)
C6-N7-C7a		109.0(3)	C1-C12-C13		112.2(3)
C1-C12-C5		106.9(3)	C13-C12-C5		114.3 (3)

As a conclusion, these results have demonstrated the feasibility of the construction of dasycarpidone skeleton and the total synthesis of indole alkaloids of the uleine group (±)-20-epidasycarpidone. Further application of this method can be extended to the syntheses of the other members of the Aspidospermatan skeletal type alkaloids.

EXPERIMENTAL

^{1}H-NMR spectra were recorded on a BRUKER 400 spectrometer operating at 400 MHz. Spectra were registered in $CDCl_3$

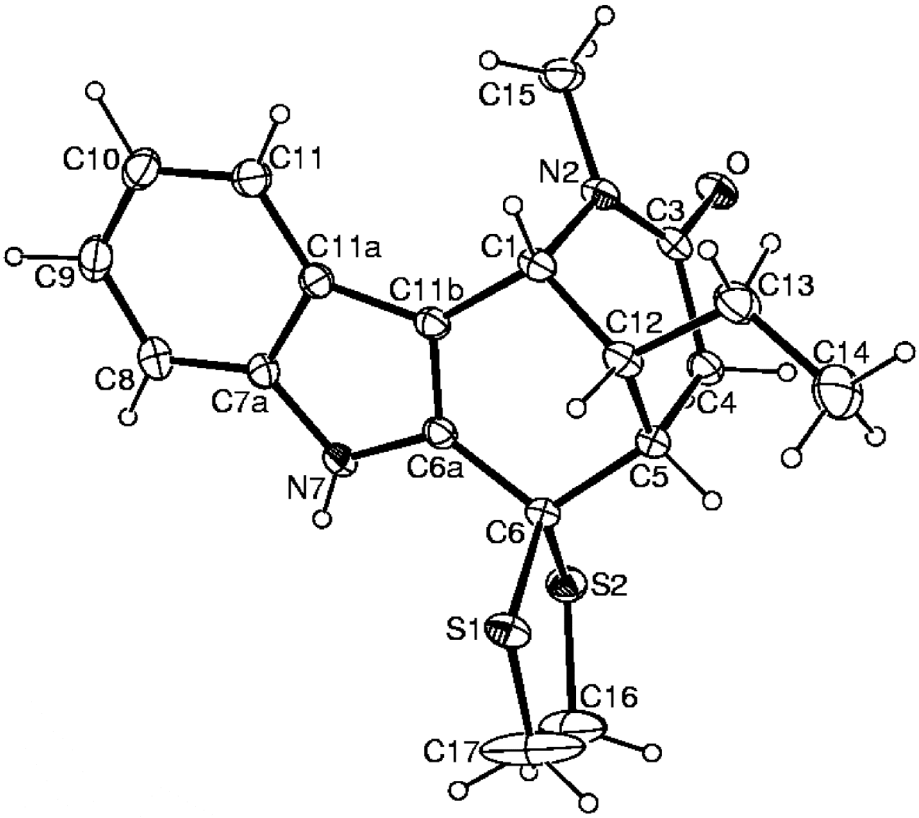


Figure 2. The ORTEP drawing of **13**

and DMSO-d_6, using the solvent as internal standard at 400 MHz for ^{1}H and ^{13}C at 25°. Chemical shifts are expressed in terms of parts per million (δ) and the coupling constants are given in Hz. IR spectra were recorded by using Mattson 1000 FT-IR spectrometer. Mass spectra were determined by means of Agilent 5973 model of GC-MS. Melting points were determined in a capillary tube on Electro thermal IA 9000 apparatus and were uncorrected. Reactions were monitored by thin layer chromatography (silica gel 60 F254). Purification of solvents were performed according to standard methods.

3- Ethyl-2- ethoxalyl-1,2,3,4-tetrahydrocarbazole-1-one (**4**).

To a solution of **3** (30 g, 140.66 mmoles) in dry tetrahydrofuran (200 mL), sodium hydride (11.5 g, 281.32 mmoles, 60% dispersion in oil) was added in several portions and the mixture was stirred under argon atmosphere for 1 h at room temperature. Finally 29.22 g (200 mmoles) of diethyl oxalate was added and stirred for 4 h at 60°. Then the mixture was cooled in an ice bath and 200 mL of 10% hydrochloric acid was added. After the extraction with 300 mL of ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate and evaporated. After crystallization of the residue from diethyl ether/*n*-hexane (1:1), 38 g (86%) of the product (mp 123°) was isolated; ir (potassium bromide): ν 3294, 1724, 1601, 1250, 1201 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.82 (t, 3H, *J*= 7.31 Hz) 1.34 (t, 3H, *J*= 7.08 Hz), 1.44-1.54 (m, 2H), 2.97 (d, 2H, *J*= 3.24 Hz), 3.62 (t, 1H, *J*= 3.44 Hz), 4.29-4.34 (m, 2H), 7.13 (d, 2H, *J*= 8.69 Hz), 7.54 (d, 1H, *J*=8.56 Hz), 7.95 (d, 1H, *J*=8.01 Hz), 8.87 (s, 1H, NH-indole), 14.83 (s, 1H, OH).

Anal. Calcd for $C_{18}H_{19}NO_4$: C, 69.00; H, 6.10; N, 4.47. Found: C, 69.02; H, 6.08; N, 4.44.

Diastereomers of Ethyl (3-ethyl-1-oxo-1,2,3,4,9-tetrahydro-1*H*-carbazole-2-yl)-2-acetate (**5**).

To a solution of **4** (20 g, 63.8 mmoles) in 80 mL of dichloromethane and triethylamine (12.9 g, 127.6 mmoles), under argon atmosphere at 0° methanesulfonyl chloride (14.6 g, 127.6 mmoles) was added dropwise. The mixture was stirred at room temperature for 14 h. The solvent was removed and the residue was dissolved in tetrahydrofuran. To this solution, 20 g of zinc dust was added, and cooled to 0°. While stirring, 50 mL of acetic acid was added dropwise. The mixture was allowed to stir for 4 h at room temperature. Then, the mixture was neutralized with 200 mL of 10% sodium hydroxide and extracted with ethyl acetate (300 mL) and then dried over anhydrous magnesium sulfate. The solvent was evaporated off and the residue was chromatographed using silica gel and ethyl acetate-dichloromethane (1:1) which yielded a mixture of diastereomers of **5**, as a brown oil (17.6 g, 92%). The ratio of diastereomers of **5** was determined by GC-MS analysis and was found to be 3-β-ethyl/3-α-ethyl (66:34). Most of the 3-β-ethyl isomer of compound **5** was isolated by crystallization in diethyl ether to give 7 g as a white solid with mp 158°. 3-β-Ethyl isomer **5**; ir (potassium bromide): ν 3283, 2964, 1705, 1641, 1545, 1431, 1334, 810, 750 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.10 (t, 3H, *J*= 7.43 Hz), 1.34 (t, 3H, *J*= 7.13 Hz), 1.55-1.61 (m, 1H), 1.74-1.80 (m,1H), 2.34-2.36 (m, 1H), 2.77-2.94 (m, 3H), 3.03-3.07 (m, 1H), 3.29 (dd, 1H, *J*= 16.62 and 4.60 Hz), 4.22-4.28 (q, 2H), 7.19-7.23 (m, 1H), 7.41-7.45 (m, 1H), 7.52 (d, 1H, *J*= 8.36 Hz), 7.72 (d, 1H, *J*= 8.03 Hz), 9.41 (s, 1H); ms: m/z 299 (65) $[M]^+$, 270 (8), 254 (34), 225 (58), 211 (100), 196 (88), 182 (31), 168 (30), 154 (14), 129 (31), 102 (10), 77 (8).

Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.06; N, 4.68. Found: C, 72.20; H, 7.04; N, 4.71.

3-α-Ethyl isomer **5;** ms: m/z 299 (70) $[M]^+$, 270 (14), 254 (32), 224 (100), 210 (48), 196 (84), 182 (27), 168 (26), 154 (12), 129 (26), 102 (10), 77 (7).

Diastereomers of Ethyl{3-ethyl-2,3,4,9-tetrahydrospiro[1*H*-carbazole-1,2 '(1,3)dithiolane]-2-yl}-2-acetate (**6**).

A mixture of ketone **5** (2.78 g, 9.28 mmoles) was refluxed with 1,2-ethanedithiol (2 mL, 23.78 mmoles) and zinc trifluoromethanesulfonate (4.01 g, 11.16 mmoles) in 60 mL of chloroform for 22 h. The mixture was treated with 30 mL solution of 15% sodium hydroxide. The organic layer was dried over anhydrous magnesium sulfate and then the solvent was removed to give a dark brown oil, which was purified by column chromatography (dichloromethane). Compound **6** was isolated as a yellow oil, which contained both of diastereomers mixture (2.47 g, 66%). 3-α-Ethyl isomer **6**; ms m/z 375 (38) $[M]^+$, 240 (31), 233 (38), 208 (100), 195 (37), 180 (40), 167 (31), 129 (21). 3-β-Ethyl isomer (**6**); operating as above, pure 3-β-ethyl isomer **5** was converted into 3-β-ethyl isomer **6**, mp 138°; ir (potassium bromide): ν 3402, 2966, 1720, 1458, 1373, 1307, 1236, 1194, 1026, 738 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.94 (t, 3H, *J*= 7.32 Hz), 1.20 (t, 3H, *J*= 7.11 Hz), 1.23-1.33 (m, 1H), 1.61-1.84 (m, 2H), 2.28 (dd, 1H, *J*= 16.02 and 10.00 Hz), 2.54 (dd, 1H, *J*= 16.41 and 7.73 Hz), 2.80-2.86 (m, 1H), 2.88-2.96 (m, 2H), 3.23-3.33 (m, 1H), 3.35-3.44 (m, 2H), 3.51-3.57 (m, 1H), 4.07-4.12 (q, 2H), 6.99 (t, 1H, *J*= 7.35 Hz), 7.06-7.16 (m, 1H), 7.21 (d, 1H, *J*= 8.07 Hz), 7.37 (d, 1H, *J*= 7.75 Hz), 8.01 (s, 1H, NH-indole); ms: m/z 375 (47) $[M]^+$, 240 (27), 233 (40), 212 (36), 208 (100), 195 (40), 180 (37), 167 (28), 129 (18).

Anal. Calcd for $C_{20}H_{25}NO_2S_2$: C, 63.96; H, 6.71; N, 3.73. Found: C, 63.93; H, 6.68; N, 3.76.

Ethyl{3-β-ethyl-4-oxo-2,3,4,9-tetrahydrospiro[1*H*-carbazole-1,2 '(1,3)dithiolane]-2-yl}-2-acetate (**7**) and Ethyl{3-α-ethyl-4-oxo-2,3,4,9-tetrahydrospiro[1*H*-carbazole-1,2'(1,3)dithiolane]-2-yl}-2-acetate (**8**).

To an ice cooled solution of **6** (2.9 g, 7.22 mmoles) in 50 mL of acetonitrile-water (90:10), a solution of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (3.50 g, 15.44 mmoles) in 30 mL acetonitrile was added dropwise. The mixture was stirred in an ice bath for 4 h, then the solution was poured into 100 mL of 10% sodium hydroxide and extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel. Elution with chloroform-ethyl acetate (20:1) gave 1.5 g (54%, mp 113°) of 3-β-ethyl isomer **7** (lower R_f) and 1.22 g (43%, mp 162°) of 3-α-ethyl isomer **8** (higher R_f). 3-β-Ethyl isomer **7**; ir (potassium bromide): ν 3287, 2970, 1730, 1624, 1458, 1279, 1032, 756 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.88 (t, 3H, *J*= 7.35 Hz), 1.20 (t, 3H, *J*= 7.13 Hz), 1.60-1.70 (m, 1H), 2.24-2.34 (m, 1H), 2.51-2.61 (m, 2H), 2.94 (dd, 1H, *J*=16.55 and 5.65 Hz), 3.34-3.49 (m, 4H), 3.52-3.64 (m, 1H), 4.07-4.12 (q, 2H), 7.11-7.23 (m, 2H), 7.28-7.32 (m, 1H), 8.14-8.17 (m, 1H), 8.77 (s, 1H, NH-indole); ms: m/z 389 (100) $[M]^+$, 361 (26), 297 (23), 282 (38), 255 (42), 222 (28), 219 (78), 191 (24), 185 (32), 159 (37), 143 (20).

Anal. Calcd for $C_{20}H_{23}NO_3S_2$: C, 61.67; H, 5.95; N, 3.59. Found: C, 61.65; H, 5.93; N, 3.61.

3-α-Ethyl isomer **8**; ir (potassium bromide): ν 3314, 2886, 2928, 1727, 1664, 1458, 764 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.09 (t, 3H, *J*= 7.42 Hz), 1.22 (t, 3H, *J*= 7.1 Hz), 1.28-1.33 (m, 2H), 2.31-2.47 (m, 3H), 3.23-3.46 (m, 1H), 3.47-3.52 (m, 1H), 3.53-3.63 (m, 4H), 4.08-4.13 (m, 2H), 7.23-7.29 (m, 1H), 7.34-7.39 (m, 1H), 8.18 (d, 1H, *J*= 6.46 Hz), 8.86 (s, 1H); ms: m/z 389 (100) $[M]^+$, 297 (33), 282 (46), 255 (44), 219 (88), 185 (43), 159 (53), 143 (33), 115 (24).

Anal. Calcd for $C_{20}H_{23}NO_3S_2$: C, 61.67; H, 5.95; N, 3.59. Found: C, 61.66; H, 5.92; N 3.58.

{3α-Ethyl-4-oxo-2,3,4,9-tetrahydrospiro[1*H*-carbazole-1,2(1,3)dithiolane]-2-yl }-2-acetic acid (**9**).

Compound **8** (2.0 g, 5.13 mmol) was dissolved in 10 mL of 15% potassium hydroxide (methanol-water, 3:1) and stirred at room temperature for 2 h. After removal of the solvent, the residue was treated with 30 mL of 10% hydrochloric acid, and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and the solvent was evaporated to afford an oily residue, which was crystallized in diethyl ether-*n*-hexane to give 1.55 g, 84% of **9**, mp 212°; ir (potassium bromide): ν 3280, 2930, 1709, 1636, 1456, 1279, 751 cm^{-1}; ^1H nmr (deuteriodimethylsulfoxide): δ 1.00 (bs, 3H), 1.15-1.33 (m, 1H), 2.07-2.42 (m, 2H), 2.87-3.12 (m, 1H), 3.17-3.41 (m, 2H), 3.45-.3.80 (m, 4H), 7.15-7.33 (m, 2H), 7.47 (d, 1H, *J*=7.9 Hz), 7.95 (d, 1H, *J*=7.3 Hz), 11.91 (bs, 1H, NH-indole), 12.22 (bs, 1H, OH); ^{13}C nmr (deuteriodimethylsulfoxide): δ 12.48, 19.46, 20.67, 35.46, 39.84, 50.60, 53.26, 69.28, 111.42, 112.79, 121.27, 122.52, 123.93, 124.52, 136.83, 149.32, 173.72, 193.38; ms: m/z 361 (100) $[M]^+$, 333 (18), 300 (23), 268 (57), 219 (78), 191 (32), 185 (44), 159 (55), 143 (33), 115 (27).

Anal. Calcd for $C_{18}H_{19}NO_3S_2$: C, 59.86; H, 5.29; N, 3.87. Found: C, 59.88; H, 5.32; N, 3.89.

(*N*-Methyl){3-α-ethyl-4-oxo-2,3,4,9-tetrahydrospiro[1*H*-carbazole-1,2'(1,3)dithiolane]-2-yl}-2-acetamide (**10**).

Compound **9** (1.5 g, 4.14 mmoles) and 0.83 g (8.2 mmoles) triethylamine were dissolved in 30 mL chloroform, and cooled to –10°. To this mixture was added dropwise 0.91 g (8 mmoles) ethyl chloroformate, and the temperature was kept at –10° for 3 h. After 2 h, 5 mL of 40% methylamine was added and stirred for 12 h. To the mixture 50 mL of 10% sodium hydroxide was poured and then extracted with chloroform. The organic layer was dried over anhydrous magnesium sulfate and the solvent was evaporated off. The resulting residue was crystallized in diethyl ether-*n*-hexan (1:1) to afford 1.2 g (77%) of **10**, mp 238°; ir (potassium bromide): ν 3328, 3181, 2924, 1657, 1635, 1453, 757 cm^{-1}; ^1H nmr (deuteriodimethylsulfoxide): δ 0.98 (bs, 3H), 1.15 (t, 1H, *J*=7.06 Hz), 1.97-2.24 (m, 2H), 2.52 (s, 3H), 2.99 (bs, 1H), 3.31-.3.36 (m, 2H), 3.51-3.76 (m, 4H), 7.13-7.22 (m, 2H), 7.45 (d, 1H, *J*=7.26 Hz), 7.66 (bs,1H, NH-amide), 7.94 (d, 1H, *J*=7.26 Hz), 11.90 (bs, 1H, NH-indole); ^{13}C nmr (deuteriodimethylsulfoxide): δ 12.6, 19.3, 26.4, 36.2, 40.3, 50.1, 53.3, 60.4, 69.1, 111.7, 112.6, 120.3, 122.4, 123.7, 124.1, 136.2, 150.8, 171.6, 193.4; ms: m/z 374 (62) $[M]^+$, 315 (32), 283 (63), 282 (100), 254 (35), 219 (48), 159 (33).

Anal. Calcd for $C_{19}H_{22}N_2O_2S_2$: C, 60.94; H, 5.91; N, 7.48. Found: C, 60.92; H, 5.94; N, 7.51.

12-Ethyl-2-methyl-6,6-ethylenedithio-1,2,3,4,5,6-hexahydro-1,5-methano-2-azocino[4,3-*b*]indole-3-one (**13**).

To a solution of 1.0 g (2.6 mmoles) of **10** in 40 mL of tetrahydrofuran, 0.75 g (20 mmoles) sodium borohydride was added. The mixture was stirred at 55° for 6 h and poured into a 50 mL of 10% sodium hydroxide solution. After the extraction with dichloromethane, the organic layer was dried over anhydrous magnesium sulfate and evaporated. The residue was dissolved in dichloromethane, and 1 mL of trifluoroacetic acid was added. The mixture was allowed to stand in a refrigerator overnight, washed with 10% potassium carbonate solution and then dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was purified by silica gel chromatography using dichloromethane-acetone (10:1) to give, 720 mg, 77% of **13**, mp 296°; ir (potassium bromide): ν 3219, 2924, 1614, 1452, 743 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.10 (3H, t, *J*=7.42 Hz), 1.56-1.74 (2H, m), 2.51-2.57 (2H, m), 2.67-2.87 (2H, m), 3.18 (3H, s), 3.28-.3.62 (4H, m), 4.42 (1H, d, *J*=0.75 Hz), 7.01-7.25 (2H, m), 7.34 (1H, d, *J*=8.11 Hz), 7.56 (1H, d, *J*=7.9 Hz), 8.58 (1H, s, NH-indole); ^{13}C nmr (deuteriochloroform): δ 11.86, 24.25, 34.05, 34.95, 40.27, 40.32, 41.26, 42.86, 47.74, 52.48, 112.10, 114.61, 119.12, 119.76, 122.58 125.46, 134.77, 137.22, 168.98; ms: m/z 358 (100) $[M]^+$, 330 (45), 298 (43), 241 (36), 240 (51), 212 (68), 209 (76), 180(54), 167(37).

Anal. Calcd for $C_{19}H_{22}N_2OS_2$: C 63.65; H 6.17; N 7.81. Found: C 63.63; H 6.21; N 7.85.

12-Ethyl-2-methyl-6,6-ethylenedithio-1,2,3,4,5,6-hexahydro-1,5-methano-2-azocino[4,3-*b*]indole(**14**).

To a stirred suspension of 0.1 g (2.6 mmoles) of lithium aluminum hydride in 25 mL of dry tetrahydrofuran, a solution of **13** (100 mg, 0.27 mmole) in 15 mL of tetrahydrofuran under argon atmosphere was added dropwise. The mixture was stirred at 35° for 4 h. The excess hydride was decomposed with methanol. The mixture was poured into water and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and evaporated. The residue was purified by column chromatography on silica gel, eluting with dichloromethane-acetone (10:1) to give 87 mg, (91%) of **14**, mp 169° (methanol-*n*-hexane); ir (potassium bromide): ν 3379, 2926, 1622, 1442, 741 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.06 (t, 3H, *J*=7.44 Hz), 1.22-1.62 (m, 4H), 2.21-2.54 (m, 1H), 2.44 (d, 1H, *J*=5.65 Hz), 2.87 (s, 3H), 3.38-.3.69 (m, 4H), 4.17 (t, 1H, *J*=1.3 Hz), 4.64-4.68 (m, 1H), 5.70 (bs, 1H), 7.09-7.19 (m, 2H), 7.32 (d, 1H, *J*=8.00 Hz), 7.59 (d, 1H, *J*=7.78 Hz), 8.33 (s, 1H); ^{13}C nmr (deuteriochloroform): δ 11.74, 24.85, 29.70, 40.33, 40.85, 40.96, 41.64, 46.67, 50.65, 73.59, 94.35, 110.96, 111.98, 119.00 119.74, 122.22, 126.98, 134.85, 136.47; ms: m/z 342 (100) $[M^+-2]$, 313 (60), 281 (52), 249 (21), 220 (20), 205 (19), 122 (12).

Anal. Calcd for $C_{19}H_{24}N_2S_2$: C, 66.23; H, 7.01; N, 8.13. Found: C, 66.27; H, 6.98; N, 8.15.

12-Ethyl-2-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-2-azocino-[4,3-*b*]indole-3,6-dione (**15**).

To a solution of 1.0 g (2.79 mmoles) of the thioketal **13** in 40 mL of acetonitrile-water (9:1), 2.99 g (6.97 mmol) [bis(trifluoroacetoxy)iodo]benzene was added. The mixture was stirred at room temperature for 2 h. Then, it was poured into

10% sodium hydoxide solution and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and evaporated. The crude product was chromatographed on silica gel column with a mixture of dichloromethane-acetone (4:1) as eluent to give 0.58 g (74%) of **15**, mp 167º; ir (potassium bromide): ν 3218, 2928, 1659, 1629, 1468, 747 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.12 (t, 3H, *J*=7.44 Hz), 1.65-1.83 (m, 2H), 2.49-2.54 (m, 2H), 2.89-2.96 (m, 1H), 3.03 (d, 1H, *J*=8.73 Hz), 3.14 (s, 3H), 4.66 (s, 1H), 7.23-7.28 (m, 1H), 7.41-7.50 (m, 2H), 7.78 (d, 1H, *J*=8.0 Hz), 9.15 (bs, 1H); ^{13}C nmr (deuteriochloroform): δ 11.32, 23.34, 31.54, 34.86, 44.19, 45.92, 54.10, 113.07, 120.82, 121.71, 124.54, 127.62, 129.20, 130.82 137.99, 167.93, 192.84.

Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.42; N, 9.92. Found: C, 72.34; H, 6.40; N, 9.89.

12-Ethyl-6-hydroxy-2-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-2-azocino[4,3-b]indole (**16**).

A solution of 0.5 g (1.77 mmoles) of **15** were cooled to -10º. To this solution, 2 mL of Red Al® (40% solution in toluene) under argon atmosphere was added dropwise and the mixture was stirred at room temperature for 6 h. The excess Red-Al® was decomposed with ethanol and the mixture was poured into water and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and evaporated. The residue was crystallized in diethyl ether to give 0.26 g (54%) of **16**, mp 193º; ir (potassium bromide): ν 3254, 2976, 1568, 742 cm^{-1}; ^1H nmr (deuteriodimethylsulfoxide): δ 0.95 (t, 3H, *J*=7.24 Hz), 1.54-1.62 (m, 2H), 1.65-1.73 (m, 1H), 1.78 (dd, 1H, *J*=3.88 and *J*=11.27 Hz), 1.85 (bs, 1H), 1.87-1.91 (m, 1H), 1.93-1.99 (m, 2H), 2.10 (s, 3H), 2.15-2.19 (m, 1H), 3.83 (s, 1H), 4.85 (d, 1H, *J*=6.23 Hz), 6.90-7.00 (m, 2H), 7.30 (d, 1H, *J*=7.92 Hz), 7.46 (d, 1H, *J*=7.44 Hz), 10.87 (s, 1H); ^{13}C nmr (deuteriodimethylsulfoxide): δ 12.49, 24.16, 31.13, 36.58, 44.22, 54.29, 60.71, 67.43, 72.69, 111.55, 118.96, 119.19, 120.69, 125.33, 127.96 136.59, 140.10; ms: m/z 271 (15) $[M^+ +1]$, 253 (52), 196 (100), 168 (7), 124 (12).

Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.19; N, 10.35. Found: C, 75.58; H, 8.17; N, 10.28.

(±)-20- Epidasycarpidone (**1b**).

To a solution of 60 mg (0.22 mmole) of the 6-hydroxy compound **16** in 20 mL anhydrous dichloromethane-tetrahydrofuran (1:1), 200 mg (2.3 mmoles) of active manganese(IV)oxide was added. The mixture was stirred at room temperature for 2 h and filtered through Celite. The filtrate was chromatographed on silica gel column with dichloromethane-acetone (4:1) as eluent. The compound **1b** was isolated by crystallization from *n*-hexane to give 42 mg (71%), as a white solid with mp 167º (Lit. [7-8]. mp 168-169º, mp 164-166º); ir (potassium bromide): ν 3250, 1643 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 1.04 (t, 3H, *J*=7.45 Hz), 1.67-1.77 (m, 2H), 1.99-2.08 (m, 2H), 2.23-2.31 (m, 2H), 2.28 (s, 3H), 2.48 (bdd, 1H, *J*=11.5 Hz), 2.65 (t, 1H, *J*=2.38 Hz), 4.19 (d, 1H, *J*=1.78 Hz), 7.23 (td, 1H, *J*=11.83 Hz), 7.40 (td, 1H, *J*=7.7 Hz), 7.52 (d, 1H, *J*=8.37 Hz), 7.73 (d, 1H, *J*=8.12 Hz), 10.1 (bs, 1H); ^{13}C nmr (deuteriochloroform): δ 11.74, 23.40, 23.56, 44.62, 45.08, 46.20, 46.40, 54.80, 112.78, 120.92, 122.06, 124.45, 126.78, 127.10, 133.39 138.10, 195.33; ms: m/z 268 (88) $[M]^+$, 239 (40), 225 (39), 211 (100), 198 (60), 183 (55), 168 (38), 154 (17), 130 (22), 115 (6), 77 (4); hr-ms: Calcd for $C_{17}H_{20}N_2O$: 268.15702. Found: 268.1570.

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.08; H, 7.51; N, 10.43. Found: C, 76.12; H, 7.48; N, 10.46.

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