Synthetic Applications of 2-(1,3-Dithian-2-yl)indoles. Part 7. Synthesis of Aspidospermidine

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Synthetic Applications of 2-(1,3-Dithian-2-yl)indoles. 7. Synthesis of Aspidospermidine

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A new method of synthesizing the alkaloid aspidospermidine (**1**), based on building ring E on the pyridocarbazole [ABCD] ring structure, is reported. The preparation of the pyridocarbazole framework of *Aspidosperma* alkaloids is a new three-step synthetic application of 2-(1,3-dithian-2-yl)indoles. A tandem conjugate addition−alkylation reaction starting from indolyldithiane (**4**), 3-methylenelactam **6**, and EtI yields the adduct **17**. Treatment of lactam **17** with DIBALH leads to formation of the naphthyridoindole **18**. Compound **18** isomerizes in aqueous AcOH to yield pyridocarbazole **3**. Finally, closure of ring E and subsequent reduction of the dithiane ring produces aspidospermidine. Pyridocarbazoles **2** and **10** were prepared as models.

Introduction

In the context of our studies on the application of 2-(1,3-dithian-2-yl)indoles to the synthesis of indole alkaloids, we reported the synthesis of 20-epidasycarpidone[1] and several derivatives.[2] The key reactions were the conjugate addition of the indolyldithiane dianion on appropriate Δ^3-piperidein-2-ones and the partial reduction of the lactam adduct with spontaneous cyclization. An appropriate substitution on the piperidine nitrogen atom of these uleine-type structures allows the formation of the pyrrolidine E-ring of the *Strychnos* alkaloids.[3] We have now developed a similar strategy for the synthesis of the pyridocarbazole nucleus of the *Aspidosperma* alkaloids ([ABCD] ring structure). Only a few of the many reported syntheses of *Aspidosperma* alkaloids[4] involve the formation of the pyridocarbazole framework and final closure of the pyrrolidine ring.[5−9]

On the basis of our previous work, we envisaged the formation of pyridocarbazoles by conjugate addition of indolyldithiane (**4**) (Figure 1) on a 3-methylenelactam and treatment of the resulting adduct with DIBALH. A 2-hydroxyethyl chain on the piperidine nitrogen atom would allow us to build the fifth ring of *Aspidosperma* alkaloids by using a nucleophilic attack of the indole to displace the hydroxy group.[10]

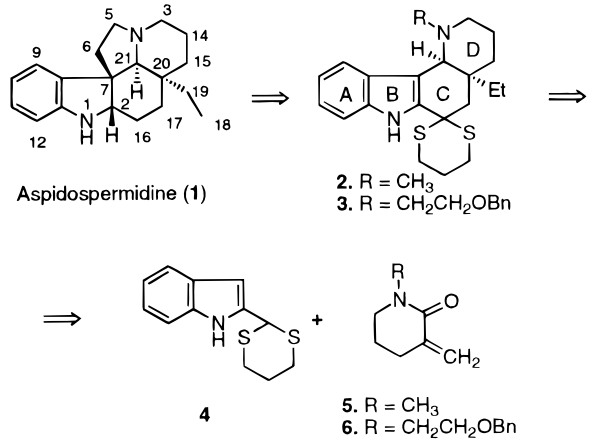

Figure 1.

Results and Discussion

We first tested the method using 1-methyl-3-methylene-2-piperidone (**5**)[11] as the piperidine synthon (Figure 2). Treatment of 2-(1,3-dithian-2-yl)indole (**4**) with 2 equiv of *n*-BuLi in dry THF afforded dianion **7**, which was condensed with **5** in the presence of HMPA to give the lactam adduct **9**, in 64% yield. In the absence of HMPA the condensation was slower and gave dicondensation products.

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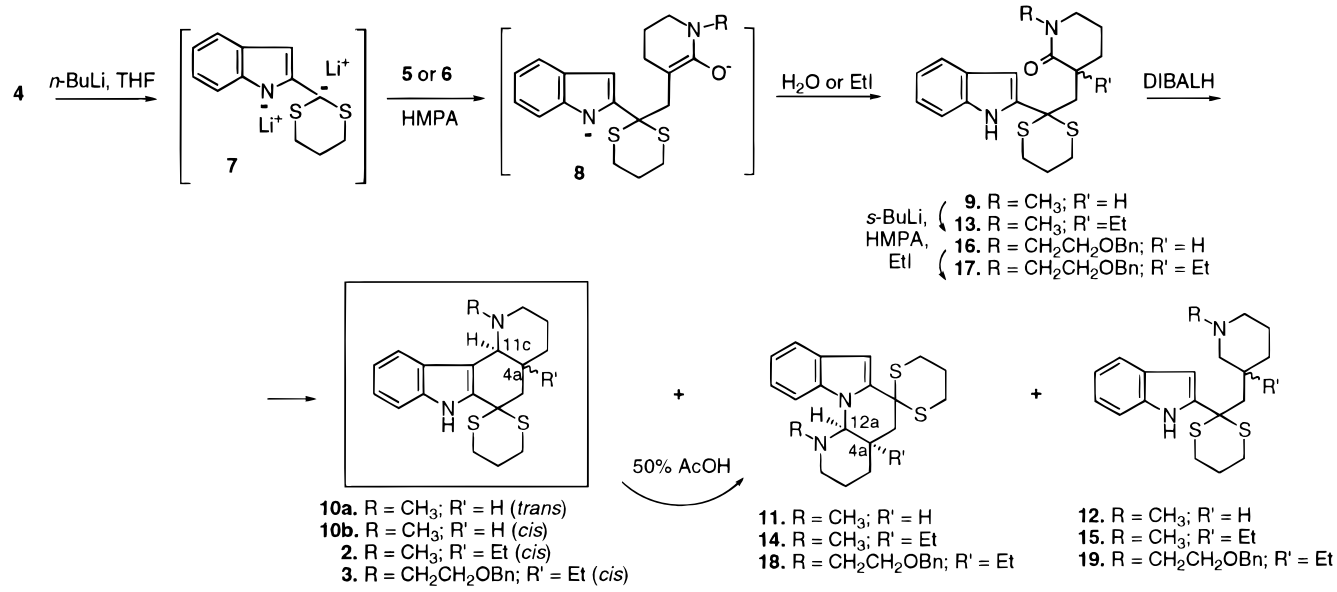

Figure 2.

Table 1. Spectral Data of Naphthyridoindoles 11, 14, and 18

H-atom	**11**[a,b]	**14**[a,b]	**18**[a,b]	C-atom	**11**[a]	**14**[a]	**18**[a]
2-Heq	2.98 dd (12,3)	3.01 dm (12)	3.21−3.30 m	C-2	56.0	55.9	53.7
2-Hax	2.40 m	2.32 td (12, 2)	2.39 td (14, 3)	C-3	20.8	20.3	21.1
3-Heq	1.53 m	1.57 dm (12)	1.55 dm (14)	C-4	29.6	33.2	33.2
3-Hax	1.85 m	1.96 tt (12, 4)	1.92 qt (14, 5)	C-4a	33.6	39.4	39.7
4-Heq	1.85 m	1.77 dm (12)	1.73 dm (14)	C-5	35.8	38.6	38.6
4-Hax	1.85 m	1.43 td (12, 5)	1.41 td (14, 5)	C-6	47.7	44.9	44.8
4a-H	2.40 m			C-6a	137.8	137.4	137.8
5-Heq	2.55 dd (12,3)	2.50 d (14)	2.42 d (14)	C-7	104.0	103.0	102.9
5-Hax	3.38 t (12)	3.31 d (14)	3.31 d (14)	C-7a	127.8	127.8	127.8
7-H	6.93 s	6.98 s	6.96 s	C-8	120.9	120.9	120.9
8-H	7.57 dm (7)	7.60 br d (8)	7.59 d (8)	C-9	119.9	120.0	120.1
9-H	7.08 ddd (8,7,1)	7.09 ddd (8, 7, 1)	7.07−7.28 m	C-10	121.6	121.6	121.9
10-H	7.17 ddd (8,7,1)	7.18 ddd (8, 7, 1)	7.07−7.28 m	C-11	110.4	109.8	109.6
11-H	7.41 br d (8)	7.40 br d (8)	7.35 d (8)	C-11a	137.1	137.2	137.0
12a-H	4.42 d (3)	4.08 s	4.26 s	C-12a	72.5	77.5	76.3
SCHeq	2.85 dt (13,4)	2.87 dt (14, 4)	2.85 dt (14, 4)	SCH_2	28.0	28.9	28.6
SCHeq′	2.75 dt (13,4)	2.94 dt (14, 4)	2.97 dt (14, 4)	SCH'_2	29.3	29.2	29.2
SCHax	3.30 ddd (13,11,3)	3.26 ddd (14, 11, 3)	3.18 ddd (14, 11, 3)	$SCCH_2$	24.9	24.9	24.8
SCHax′	3.20 ddd (13,11,3)	3.30 ddd (14, 11, 3)	3.21−3.30 m	CH_2CH_3		28.5	28.5
$SCCH_2$	2.00−2.20 m	2.03−2.25 m	2.05−2.20	CH_2CH_3		7.4	7.3
CH_ACH_3		1.02 m<Tc>	0.96 m	NCH_3	43.2	42.8	
CH_BCH_3		1.16 m	1.11 m	NCH_2			51.9
CH_2CH_3		0.72 t (7)	0.70 t (7)	CH_2OBn			69.8
NCH_3	2.03 s	2.01 s		OCH_2Ph		72.4	
NCH_A			2.27 ddd (13, 7)	C-*i* Ph			138.4
NCH_B			2.65 ddd (13, 7)	C-*o* Ph			127.5
CH_AOBn			2.99 ddd (13, 7)	C-*m* Ph			128.1
CH_BOBn			3.33 ddd (13, 7)	C-*p* Ph			127.2
OCH_APh			4.13 d (12)				
OCH_BPh			4.19 d (12)				

[a] All data are confirmed by COSY (H,H) and (H,C) experiments. [b] Coupling constants are given in parentheses (Hz).

When piperidone **9** was reduced with DIBALH at 0 °C, the expected mixture of *trans*-**10a** (3%), *cis*-**10b** (31%), *cis*-**11** (35%), and piperidine **12** (5%) was obtained, and the compounds were isolated by flash chromatography. The cyclization was demonstrated by the loss from the ^{1}H NMR spectra of the In-3H proton in compounds **10** and of the In-NH proton in compound **11**, as well as by the lack of the carbonyl absorption signal in their IR spectra. The main differences between pyridocarbazoles **10** were the chemical shift and the coupling constant value of the angular proton 11c-H (**10a**: δ_{11c-H} 4.02, J_{11c-4a} = 10 Hz; **10b**: δ_{11c-H} 3.18, J_{11c-4a} = 3.2 Hz), observed in the ^{1}H NMR spectra (Table 2), which corresponds to the assignments described.[9a] The ^{1}H NMR spectrum of naphthyridoindole **11** (Table 1) showed the aromatic 7-H proton at δ 6.93 and the methine aminal-type 12a-H proton as a doublet at δ 4.42. The latter was correlated with the signal at δ 72.5 assigned to C-12a carbon in the COSY (C,H) spectrum. It is also worth mentioning that only the C/D *cis* isomer was obtained, as shown by the coupling constant value of the 12a-H proton (J = 3 Hz).

As in the case of methanodiazocinoindoles obtained in the *Strychnos* series,[1] the isomerization of naphthyridoindole **11** was performed in 50% aqueous AcOH and yielded a 1:3 mixture of pyridocarbazoles *trans*-**10a** and *cis*-**10b**. The fact that the isomerization occurs in the C/D condensed (naphthyridine) as well as in the C/D

Table 2. ^{1}H NMR Data of Pyridocarbazoles 10, 2, 3, and 23[a]

H-atom	*trans*-**10a**[b]	*cis*-**10b**[b]	**2**	**3**[b]	**23**[b]
2-Heq	3.04−3.30 m	2.95 dt (13, 3)	2.97 dm (11)	3.11−3.25 m	3.12 dm (13)
2-Hax	3.04−3.30 m	2.15−2.30 m	2.10−2.25 m	2.25−2.36 m	2.19−2.27 m
3-Heq	1.39 br d (13)	1.55 dt (12, 3)	1.58 dm (13)	1.54 dm (13)	1.62 dm (13)
3-Hax	1.85−2.06 m	1.80−1.90 m	1.97 qt (13, 4)	1.88 qt (13, 4)	1.90 qt (13, 4)
4-Heq	1.84 dm (13)	1.74−1.80 m	1.75 dm (14)	1.73 br d (13)	1.74 dm (13)
4-Hax	1.44 dddd (13, 3)	1.74−1.80 m	1.33 td (14, 5)	1.31 td (13, 5)	1.41 td (13, 5)
4a-H	2.35 masked	2.15−2.30 m			
5-H$_\alpha$	2.08 d (11)	2.53 dd (13, 3)	2.61 d (14)	2.53 d (14)	2.60 d (13)
5-H$_\beta$	2.76 dd (11, 2)	3.25 t (12)	3.29 d (14)	3.33 d (14)	3.35 d (13)
7-H	8.42 br s	8.50 br s	8.55 s	8.58 s	8.60 br s
8-H	7.31 dt (8,1)	7.30 d (7)	7.36 d (8)	7.33 br d (8)	7.35 br s (8)
9-H	7.17 td (7, 1)	7.15 td (7, 1)	7.19 td (8, 1)	7.18 td (8, 1)	7.19 td (8, 1)
10-H	7.07 td (7, 1)	7.10 td (7, 1)	7.11 td (8, 1)	7.07−7.27 m	7.12 td (8, 1)
11-H	7.94 br d (8)	7.55 d (7)	7.58 d (8)	7.57 br d (8)	7.50 br d (8)
11c-H	4.02 d (10)	3.18 d (3, 2)	2.92 s	3.19 s	3.33 s
SCHax	3.04−3.30 m	3.21 ddd (13, 12, 3)	3.38 ddd (15, 13, 3)	3.27−3.40 m	3.27−3.40 m
SCHax′	3.04−3.30 m	3.30 ddd (13, 12, 3)	3.32 ddd (15, 13, 3)	3.11−3.25 m	3.27−3.40 m
SCHeq	2.72 dt (12, 3)	2.72 dt (13, 3)	2.83 dt (15, 3)	2.80 dt (14, 3)	2.83 dt (14, 3)
SCHeq′	2.81 dt (12, 3)	2.81 dt (13, 3)	2.89 dt (15, 3)	2.86 dt (14, 6)	2.90 dt (14, 3)
SCC*H*ax	1.85−2.06 m	1.99 qt (13, 3)	2.01 qt (13, 3)	1.98 qt (14, 3)	2.00 qt (14, 3)
SCC*H*eq	2.19 dm (14)	2.15−2.30 m	2.10−2.25 m	2.18 dm (14)	2.19−2.27 m
C*H*$_A$CH$_3$			0.99 ddd (21, 7)	0.98 m	1.04 m
C*H*$_B$CH$_3$			1.48 ddd (21, 7)	1.45 m	1.38 m
CH2C*H*$_3$			0.73 t (7)	0.72 t (7)	0.72 t (7)
NCH$_3$	2.29 s	2.29 s	2.19 s		
NC*H*$_A$				2.25−2.36 m	2.16 ddd (13, 11, 3)
NC*H*$_B$				3.02 ddd (13, 7)	2.96 ddd (13, 11, 4)
C*H*$_A$OR				3.11−3.25 m	3.07 br t (11)
C*H*$_B$OR				3.27−3.40 m	3.48 td (11, 3)
OC*H*$_A$Ph				4.17 d (14)	
OC*H*$_B$Ph				4.20 d (14)	

[a] Coupling constants are given in parentheses (Hz). [b] All data are confirmed by COSY (H,H) and (H,C) experiments.

bridged (methanodiazocino) compounds confirms the mechanism that we proposed for these acid-induced rearrangements.[1]

We then studied the possibility of inserting the ethyl group by direct alkylation of the intermediate enolate (**8**). Therefore, the conjugate addition of dianion **7** on lactam **5** in the presence of HMPA was quenched by addition of EtI. Lactam **13** was obtained in 51% yield, accompanied with compound **9** (10%). The latter was alkylated in the presence of HMPA using *s*-BuLi as the base and EtI to obtain **13**. The reduction−cyclization reaction of compound **13** with DIBALH yielded a 1:2.7 mixture of piperidine **15** and naphthyridoindole **14**. No pyridocarbazole was obtained in this case. Compound **14** was then transformed to the desired pyridocarbazole **2** by aqueous AcOH treatment. In this case, only the thermodynamically more stable *cis* derivative was obtained (84%).

Concerning the modifications of the dithiane ring (Figure 3), treatment of compound **10b** with $(CF_3CO_2)_2$-IPh in CH_3CN-H_2O (9:1)[12] yielded the acylindole derivative **20** (Tables 4 and 5). The clearest evidence for the presence of the keto group in compound **20** was the carbonyl absorption in its IR spectrum and the ^{13}C NMR signal at δ 192.6. As an alternative, dithianes **10b** and **2** were reduced with Raney Ni in wet EtOH to obtain compounds **21** and **22**. In these cases, a new methylene carbon corresponding to C-6 appeared in the ^{13}C NMR spectra, at *ca.* 20 ppm.

Having shown the validity of the general method, we applied the reaction sequence starting from methylene lactam **6**, which presented the appropriate substituent on the nitrogen atom for assaying the formation of pentacyclic *Aspidosperma* derivatives. Methylene lactam **6** was prepared by *N*-alkylation of ethyl nipecotate with benzyl bromoethyl ether,[13] acid hydrolysis, and subsequent Rapoport rearrangement[11] of the corresponding

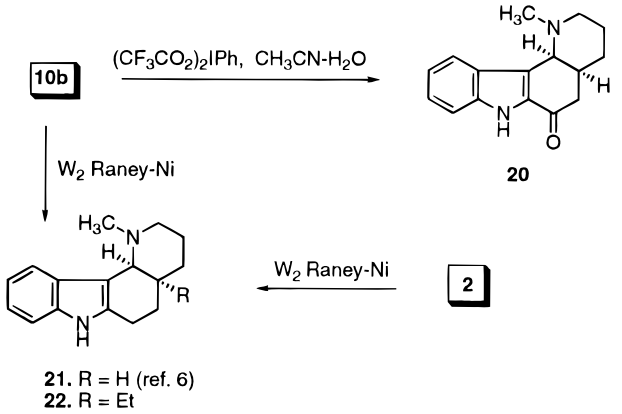

Figure 3.

nipecotic acid to give 3-methylene-2-piperidone **6** (see Experimental Section). The tandem conjugate addition−alkylation reaction of the dithianylindole dianion **7** on lactam **6** furnished the adduct **17**, in 52% yield (Figure 2). As in the previous series, the deethyl analogue **16**, isolated in 10% yield, was quantitatively converted to **17** by alkylation with EtI in the presence of HMPA. The reaction of lactam **17** with DIBALH yielded naphthyridoindole **18** (73%), as well as a small amount of piperidine **19**. Isomerization of naphthyridoindole **18** in aqueous AcOH resulted in the target pyridocarbazole **3** (Tables 2 and 3), in 90% yield: this was identified by comparison of its spectral data with those of the *N*-methyl analogues.

With pyridocarbazole **3** in hand, we proceeded to its conversion to aspidospermidine (**1**).[14] We performed the

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Table 3. ^{13}C NMR Data of Pyridocarbazoles 10, 2, 3, and 23

C-atom	*trans*-**10a**[a]	*cis*-**10b**[a]	**2**	**3**[a,b]	**23**[a]
C-2	54.1	57.3	57.2	54.2	52.4
C-3	19.3	21.9	21.8	21.8	21.9
C-4	31.6	30.2	34.3	34.3	34.0
C-4a	28.3	33.8	39.1	39.6	40.0
C-5	43.6	38.3	39.4	39.3	40.5
C-6	47.6	48.5	46.2	46.4	45.8
C-6a	134.2	135.1	133.5	133.7	133.8
C-7a	136.1	135.8	135.8	135.9	136.0
C-8	110.9	111.2	111.2	111.2	111.5
C-9	122.6	122.3	122.3	122.3	122.5
C-10	119.8	119.8	119.7	119.9	120.0
C-11	121.6	119.5	119.1	119.0	118.4
C-11a	125.9	127.8	128.6	128.5	128.5
C-11b	113.8	masked	113.5	113.6	112.7
C-11c	63.7	59.1	65.4	63.8	63.1
NCH_3	34.1	44.9	45.0		
CH_2CH_3			30.0	29.9	30.1
CH_2CH_3			7.7	7.7	7.6
SCH_2	27.0	26.9	27.9	27.9	27.9
SCH'_2	28.7	28.6	28.3	28.2	28.1
SCH_2CH_2	24.9	24.9	25.0	25.0	25.0
NCH_2				53.6	54.4
CH_2OR				69.4	58.2

[a] All data are confirmed by COSY (H,H) and (H,C) experiments. [b] Signals of the benzyl group in compound **3**: 72.2 (OCH_2Ph), 127.1 (C-*para*), 127.6 (C-*ortho*), 128.1 (C-*meta*), 138.5 (C-*ipso*).

Table 4. ^{1}H NMR Data of Pyridocarbazoles 20−22[a]

H-atom	**20**	**21**[b]	**22**[b]
2-Heq	3.00 dt (12, 2)	2.91 br d (13)	2.95 dm (11)
2-Hax	2.20−2.40 m	2.19 ddd (13, 8, 3)	2.21 td (11, 3)
3-Heq	1.65 dm (13)	1.76−1.92 m	1.58 dm (13)
3-Hax	1.83−2.00 m	1.44−1.52 m	1.95 qt (13, 4)
4-Heq	1.83−2.00 m	1.62−1.70 m	1.73 dm (13)
4-Hax	1.72−1.79 m	1.62−1.70 m	1.38 td (13, 5)
4a-H	2.20−2.40 m	1.76−1.92 m	
5-H_α	2.54 dt (12, 3)	1.44−1.52 m	1.32−1.38 m
5-H_β	3.42 t (13)	2.50−2.60 m	2.56−2.75 m
6-H		2.50−2.70 m	2.56−2.75 m
7-H	9.20 br s	8.20 br s	8.16 br s
8-H	7.44 dt (7, 1)	7.12−7.18 m	7.20 m
9-H	7.33 ddd (8, 7, 1)	6.96−7.04 m	7.07 m
10-H	7.19 ddd (8, 7, 1)	6.96−7.04 m	7.07 m
11-H	7.75 br d (8)	7.44−7.50 m	7.51 m
11c-H	3.43 d (1)	3.13 d (3)	2.83 s
CH_ACH_3			0.94 ddd (14, 7)
CH_BCH_3			1.21 ddd (14, 7)
CH_2CH_3			0.74 t (7)
NCH_3	2.27 s	2.29 s	2.28 s

[a] Coupling constants are given in parentheses (Hz). [b] All data are confirmed by COSY (H,H) and (H,C) experiments.

debenzylation of compound **3** with Me_2S and $BF_3{\cdot}Et_2O$ and obtained aminoalcohol **23** (Figure 4), which was characterized by the hydroxy absorption in its IR spectrum. Compound **23** was then tosylated with TsCl in the presence of an excess of K^{t}BuO, which yielded the expected indolenine system **24**. The structure of compound **24** was shown by the lack of the indole NH proton, the shift of the 5-H and the 6-H protons, and the narrow doublet at δ 2.42 corresponding to the angular methine 21-H proton ($\Delta\delta = -0.91$), observed in the ^{1}H NMR spectrum (Table 6). The most definitive ^{13}C NMR data of indolenine **24** were the olefine carbon signal of C-2 (δ 187.6) and the quaternary C-7 (δ 62.6) (Table 7).

Interestingly, the reduction of **24** with W-2 Raney Ni in EtOH yielded a 1:1 mixture of aspidospermidine and its 1-ethyl analogue **26**. Compound **1** was identified by comparison of its spectral data with those described previously,[15] and **26** was distinguished by the analytical

Table 5. ^{13}C NMR Data of Pyridocarbazoles 20−22

C-atom	**20**	**21**[a]	**22**[a]
C-2	57.1	57.5	57.4
C-3	21.2	21.6	21.8
C-4	29.6	30.5	34.4
C-4a	38.6	35.5	36.3
C-5	39.7	23.2	24.3
C-6	192.6	23.2	20.3
C-6a	131.6	135.9	135.4
C-7a	137.2	136.6	135.9
C-8	112.7	110.4	110.3
C-9	126.6	120.7	120.5
C-10	121.6	119.3	119.1
C-11	120.9	118.3	118.2
C-11a	128.8	128.9	129.8
C-11b	127.3		
C-11c	59.4	59.8	64.9
NCH_3	45.1	45.3	45.6
CH_2CH_3			29.5
CH_2CH_3			7.8

[a] All data are confirmed by COSY (H,H) and (H,C) experiments.

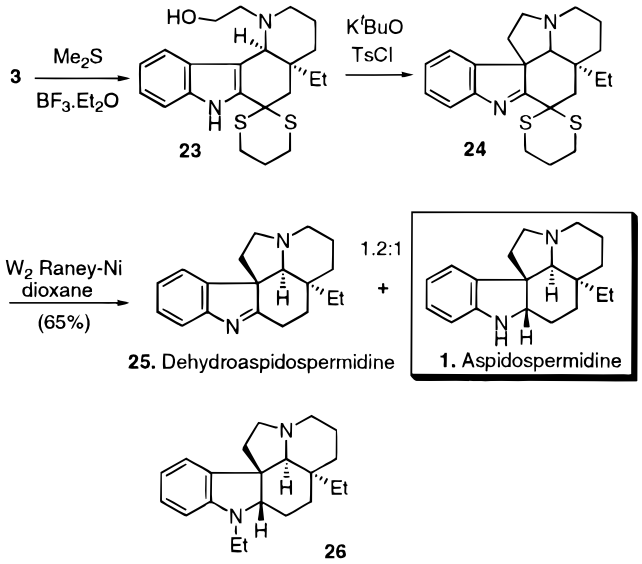

Figure 4.

signals corresponding to the ethyl substituent, and confirmed by MS. The formation of **26** suggested that the EtOH used as the solvent participates in the reaction.[16]

The Raney Ni reduction of **24** was then performed in dioxane, and a 1.2:1 mixture of dehydroaspidospermidine (**25**) and aspidospermidine (**1**) was obtained, in 65% yield. Finally, dehydroaspidospermidine was reduced with $LiAlH_4$ under the described conditions,[7] and yielded aspidospermidine.

Experimental Section[1]

3-[2-(2-Indolyl)-2,2-(propylenedisulfanyl)ethyl]-1-methylpiperidin-2-one (9). To a solution of 2-(2-indolyl)-1,3-dithiane (**4**) (235 mg, 1 mmol) in dry THF (20 mL), cooled at −78 °C and under nitrogen atmosphere, was added *n*-BuLi

(14) For the biogenetic numbering, see: (a) Southon, I. W.; Buckingham, J. *Dictionary of Alkaloids*; Chapman and Hall: London, 1989; p xxxviii. The biogenetic numbering is used in this paper when referring to *Aspidosperma*-type compounds **1**, **24**, and **25**.

(15) Le Ménez, P.; Kunesch, N.; Liu, S.; Wenkert, E. *J. Org. Chem.* **1991**, *56*, 2915−2918.

(16) The *N*-alkylation of pyridine during its Raney Ni reduction in EtOH is well known: Morlacchi, F.; Losacco, V.; Tortorella, V. *J. Heterocycl. Chem.* **1979**, *16*, 297−299 and references cited therein.

Table 6. ^{1}H NMR Data of Compounds 24, 26, and 1[a]

H-atom	**24**[b]	**26**[b,c]	**1**[b]
H-2		3.51 dd (11, 6)	3.50 dd (11, 6)
H-3eq	3.12−3.20 m	3.06 br d (12)	3.06 br d (14)
H-3ax	2.20 dt (12, 3)	1.95 td (12, 3)	1.93 td (14, 3)
H-5$_\alpha$	2.61−2.71 m	2.22 dt (10, 8)	2.19−2.35 m
H-5$_\beta$	3.12−3.20 m	3.11 ddd (10, 8, 1)	3.05−3.15 m
H-6$_\alpha$	1.63−1.73 m	1.41−1.55 m	1.32−1.54 m
H-6$_\beta$	3.12−3.20 m	2.31 dt (13, 8)	2.19−2.35 m
H-9	7.68 d (7)	7.00−7.04 m	7.08 d (7)
H-10	7.23 t (7)	6.60 t (7)	6.73 t (7)
H-11	7.28−7.35 m	7.00−7.04 m	7.01 t (7)
H-12	7.28−7.35 m	6.37 d (7)	6.64 d (7)
H-14eq	1.47−1.57 m	1.41−1.55 m	1.32−1.54 m
H-14ax	1.73−1.84 m	1.67−1.80 m	1.73 qt (13, 4)
H-15eq	1.47−1.57 m	1.63 br d (15)	1.58−1.67 m
H-15ax	1.03 td (13, 5)	1.05−1.20 m	1.10 td (13, 5)
H-16$_\alpha$		1.05−1.20 m	1.05 br d (13)
H-16$_\beta$		1.89 td (13, 3)	1.91−2.01 m
H-17$_\alpha$	1.86 dd (15, 2)	1.15−1.30 m	1.32−1.54 m
H-17$_\beta$	3.06 d (15)	1.67−1.80 m	1.58−1.67 m
H-18	0.61 t (7)	0.63 t (7)	0.63 t (7)
H-19	0.66−0.72 m	1.41−1.55 m	1.32−1.54 m
	0.85−0.91 m	0.79−0.94 m	0.76−0.96 m
H-21	2.42 d (2)	2.20 s	2.22 s
SCHax	3.07 ddd (12, 10, 2)		
SCH'ax	4.25 td (14, 3)		
SCHeq	2.61−2.71 m		
SCH′eq	2.77 dt (14, 3)		
SCCHax	2.00 qt (12, 3)		
SCCHeq	2.18 dm (12)		

[a] Coupling constants are given in parentheses (Hz). [b] All data are confirmed by COSY (H,H) and (H,C) experiments. [c] Signals of the ethyl group in compound **26**: 1.23 (t, J = 7 Hz, 3H, NCH_2CH_3), 2.89−3.00 (m, 1H, NCH_ACH_3), 3.20−3.30 (m, 1H, NCH_BCH_3).

Table 7. ^{13}C NMR Data of Compounds 24−26 and 1[16]

	24[a]	**26**[a]	**25**	**1**[a,b]
C-2	187.6	68.1	192.4	65.7 (65.7)
C-3	51.5	53.8	52.0	53.9 (53.9)
C-5	54.0	53.0	54.5	53.0 (53.0)
C-6	39.8	38.7	35.1	38.8 (38.8)
C-7	62.6	52.3	66.2	53.3 (53.7)
C-8	147.9	136.7	147.0	135.7 (135.7)
C-9	121.3	122.3	120.9	122.8 (122.8)
C-10	126.1	116.8	125.0	119.9 (119.0)
C-11	127.2	127.1	127.4	127.0 (127.1)
C-12	120.6	106.2	120.1	110.3 (110.2)
C-13	152.6	149.8	154.0	149.4 (149.4)
C-14	21.9	21.8	22.0	21.8 (23.0)
C-15	33.0	34.4	33.1	34.5 (34.5)
C-16	47.9	23.0	27.1[c]	23.0 (21.8)
C-17	44.3	22.0	23.7[c]	28.1 (28.1)
C-18	7.4	6.8	7.3	6.8 (6.8)
C-19	28.8	30.1	29.7	30.0 (30.0)
C-20	38.0	35.5	36.2	35.6 (35.6)
C-21	77.1	71.1	79.0	71.3 (71.3)
SCH_2	28.5			
SCH'_2	30.7			
SC*CH2*	24.7			
NCH_2CH_3		37.8		
NCH_2CH_3		13.3		

[a] All assignments have been confirmed by COSY (H,H) and (H,C) experiments. [b] The described assignments[15] are given in parentheses. [c] These assignments are exchangeable.

(1.6 M in hexane, 1.35 mL, 2.2 mmol) dropwise. After 20 min, HMPA (540 μL, 3.1 mmol) and a solution of lactam **5** (125 mg, 1 mmol) in dry THF (5mL) were slowly added, and the mixture was maintained at −78 °C for 1.5 h. The reaction was quenched by addition of HCl until pH = 1. The mixture was basified with K_2CO_3, the layers were separated, and the aqueous phase was extracted with EtOAc. The organic extracts, dried and evaporated, furnished a brown oil that, after chromatography (EtOAc/hexane, 7/3), gave piperidone **9**[17] (230 mg, 64%): mp 211−212 °C (EtOAc−hexane); IR (NaCl) 3400 (NH), 1621 (C=O) cm^{-1}; MS m/z 360 (M$^+$, 67), 254 (100). Anal. Calcd for $C_{19}H_{24}N_2OS_2$: C, 63.30; H, 6.71; N, 7.77. Found: C, 63.20; H, 6.75; N, 7.61.

1-Methyl-6,6-(propylenedisulfanyl)-1,2,3,4,4a,5,6,11c-octahydropyrido[3,2-*c*]carbazoles (10a,b), 1-Methyl-6,6-(propylenedisulfanyl)-1,2,3,4,4a,5,6,12a-octahydro-1,8-naphthyrido[1,2-*a*]indole (11), and 3-[2-(2-Indolyl)-2,2-(propylenedisulfanyl)ethyl]-1-methylpiperidine (12). To a solution of piperidone **9** (228 mg, 0.63 mmol) in dry THF (40 mL) cooled at −20 °C was slowly added a solution of DIBALH (1 M in THF, 633 μL, 0.63 mmol). The reaction mixture was allowed to reach 0 °C, and its evolution was monitored by TLC after 1 h. The procedure was repeated until completion (6 h). The reaction was quenched with H_2O, the phases were separated, and the aqueous layer was extracted with EtOAc. The organic extracts, dried and evaporated, yielded an oil that was flash chromatographed (hexane/EtOAc, 7/3) to isolate compounds **10**−**12**. Compound **11** (higher R_f, 76 mg, 35%): mp 200−201 °C (EtOAc/hexane); MS m/z 344 (M$^+$, 5), 110 (100). Anal. Calcd for $C_{19}H_{24}N_2S_2$: C, 66.24; H, 7.02; N, 8.13. Found: C, 66.37; H, 6.98; N, 8.20. Compound **10a** (second R_f, 7 mg, 3%): IR (NaCl) 3375 (NH) cm^{-1}. Anal. Calcd for $C_{19}H_{24}N_2S_2$: C, 66.13; H, 7.02; N, 8.13. Found: C, 66.13; H, 7.10; N, 8.00. Compound **10b** (third R_f, 68 mg, 31%): MS m/z 344 (M$^+$, 13), 269 (100). Anal. Calcd for $C_{19}H_{24}N_2S_2$: C, 66.24; H, 7.02; N, 8.13. Found: C, 66.11; H, 7.04; N, 7.92. Piperidine **12**[17] (lower R_f, 11 mg, 5%): MS m/z 346 (M$^+$, 10), 97 (100). Anal. Calcd for $C_{19}H_{26}N_2S_2$: C, 65.85; H, 7.56; N, 8.08. Found: C, 65.62; H, 7.58; N, 7.98.

Isomerization of 1,8-Naphthyrido[1,2-*a*]indole 11 To Give 10. A solution of naphthyridoindole **11** (126 mg, 0,366 mmol) in 50% aqueous AcOH (10 mL) was refluxed for 2 h. The mixture was basified with Na_2CO_3 and extracted with CH_2Cl_2. The organic extracts, dried and evaporated, were flash chromatographed (hexane/EtOAc, 3/7) to give compounds **10a** (20 mg, 16%) and **10b** (56 mg, 44%).

3-Ethyl-3-[2-(2-indolyl)-2,2-(propylenedisulfanyl)ethyl]-1-methylpiperidin-2-one (13). Method A. To a solution of 2-(2-indolyl)-1,3-dithiane (**4**) (470 mg, 2 mmol) in dry THF (25 mL), cooled at −78 °C and under nitrogen atmosphere, was added *n*-BuLi (1.6 M in hexane, 2.8 mL, 4.4 mmol) dropwise. After 20 min, HMPA (1.08 mL, 6.2 mmol) and a solution of lactam **5** (250 mg, 2 mmol) in dry THF (5 mL) were slowly added, and the mixture was maintained at −78 °C for 30 min. EtI (780 μL, 12 mmol) was added, and the mixture was maintained at −78 °C for an additional hour. The reaction was quenched by addition of HCl until pH = 1. Then the mixture was basified with K_2CO_3, the layers were separated, and the aqueous phase was extracted with EtOAc. The organic extracts, dried and evaporated, furnished a brown oil that was flash chromatographed (EtOAc/hexane, 7/3) to isolate compounds **9** (lower R_f, 71 mg, 10%) and **13** (higher R_f, 400 mg, 51%). Lactam **13**:[17] mp 119−120 °C (EtOAc/hexane); IR (NaCl) 3325 (NH), 1616 (C=O) cm^{-1}; MS m/z 388 (M$^+$, 23), 141 (100). Anal. Calcd for $C_{21}H_{28}N_2OS_2$: C, 64.91; H, 7.26; N, 7.21. Found: C, 64.89; H, 7.32; N, 7.10. **Method B.** To a solution of piperidone **9** (360 mg, 1 mmol) in dry THF (25 mL), cooled at −78 °C under nitrogen atmosphere, was added *s*-BuLi (1.3 M in cyclohexane, 1.92 mL, 2.5 mmol) dropwise. After 20 min, HMPA (540 μL, 4 mmol) was added, and the mixture was maintained at −78 °C for 1 h. The reaction was treated as in method A, and lactam **13** was obtained (276 mg, 71%).

***cis*-4a-Ethyl-1-methyl-6,6-(propylenedisulfanyl)-1,2,3,4,-4a,5,6,12a-octahydro-1,8-naphthyrido[1,2-*a*]indole (14) and 3-Ethyl-3-[2-(2-indolyl)-2,2-(propylenedisulfanyl)-ethyl]-1-methylpiperidine (15).** To a solution of piperidone **13** (344 mg, 0.886 mmol) in dry THF (50 mL), cooled at 0 °C, was slowly added a solution of DIBALH (1 M in THF, 3.54 mL) until the reaction was complete. The reaction was quenched with H_2O (30 mL), the phases were separated, and the aqueous layer was extracted with EtOAc. The organic extracts, dried and evaporated, yielded an oil that was flash chromatographed (EtOAc/hexane, 3/7) to isolate compounds

(17) For the NMR data of this compound, see the supporting information.

14 and **15**.[17] **Compound 14** (higher R_f, 185 mg, 56%): mp 185−187 °C (EtOAc/hexane); MS *m*/*z* 372 (M^+, 14), 125 (100). Anal. Calcd for $C_{21}H_{28}N_2S_2$: C, 67.70; H, 7.57; N, 7.52. Found: C, 67.76; H, 7.78; N, 7.38. Piperidine **15** (lower R_f, 70 mg, 21%): IR (NaCl) 3350 (NH) cm^{-1}; MS *m*/*z* 374 (M^+, 3), 125 (100). Anal. Calcd for $C_{21}H_{30}N_2S_2$: C, 67.33; H, 8.07; N, 7.48. Found: C, 67.25; H, 8.05; N, 7.37.

***cis*-4a-Ethyl-1-methyl-6,6-(propylenedisulfanyl)-1,2,3,4,-4a,5,6,11c-octahydropyrido[3,2-*c*]carbazole (2).** Operating as for the isomerization of **11**, from the naphthyridoindole **14** (125 mg, 0.336 mmol) and AcOH (50%, 12 mL) was obtained pyridocarbazole **2** (105 mg, 84%), after flash chromatography (Al_2O_3, CH_2Cl_2), as a white solid: mp 203−204 °C (EtOAc/hexane); IR (KBr) 3430 (NH) cm^{-1}; MS *m*/*z* 372 (M^+, 23), 71 (100). Anal. Calcd for $C_{21}H_{28}N_2S_2 \cdot 2H_2O$: C, 61.73; H, 7.89; N, 6.86. Found: C, 62.07; H, 7.56; N, 6.85.

***cis*-1-Methyl-1,2,3,4,4a,5,6,11c-octahydropyrido[3,2-*c*]-carbazol-6-one (20).** To a solution of compound **10b** (50 mg, 0.145 mmol) in CH_3CN-H_2O (9:1, 5 mL) was added $(CF_3COO)_2IPh$ (144 mg, 0.334 mmol). The mixture was stirred at room temperature for 45 min, poured on aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The organic extracts, dried and evaporated, yielded an oil that was flash chromatographed (CH_2Cl_2/MeOH, 95/5) to give ketone **20** (13 mg, 35%): IR (NaCl) 3350 (NH), 1650 (C=O) cm^{-1}; MS *m*/*z* 254 (M^+, 100). Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.40; H, 7.19; N, 10.93.

***cis*-1-Methyl-1,2,3,4,4a,5,6,11c-octahydropyrido[3,2-*c*]-carbazole (21).**[6] A mixture of **10b** (50 mg, 0.145 mmol) and an excess of W-2 Raney-Ni in EtOH (10 mL) was refluxed for 15 min. The mixture was filtered, and the filtrate was evaporated to give an oil, which, after flash chromatography (CH_2Cl_2/MeOH, 93/7), furnished the tetracyclic system **21** (22 mg, 63%).

***cis*-4a-Ethyl-1-methyl-1,2,3,4,4a,5,6,11c-octahydropyrido-[3,2-*c*]carbazole (22).** Operating as for the preparation of **21**, from pyridocarbazole **2** (75 mg, 0.202 mmol), EtOH (10 mL), and W-2 Raney Ni, was obtained pyridocarbazole **22** (40 mg, 75%) after chromatography (Al_2O_3, EtOAc/hexane, 2/8): IR (NaCl) 3450 (NH) cm^{-1}; MS *m*/*z* 268 (M^+, 32), 239 (100). Anal. Calcd for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01; N, 10.44. Found: C, 80.50; H, 9.06; N, 10.35.

***N*-[2-(Benzyloxy)ethyl]-3-methylene-2-piperidone (6).** To a mixture of commercial ethyl nipecotate (3.97 g, 25.3 mmol) and K_2CO_3 (3.34 g, 24.2 mmol) in C_6H_6 (60 mL) was slowly added bromoethyl benzyl ether (6.53 g, 30.4 mmol). The mixture was refluxed for 24 h, cooled, and poured into H_2O (25 mL). The layers were separated, and the solvent was evaporated to give a residue that was flash chromatographed (CH_2Cl_2/MeOH, 98/2) to obtain **ethyl *N*-[2-(benzyloxy)ethyl]-nipecotate** (6.6 g, 89%): ^1H NMR 1.23 (t, J = 7 Hz, 3H, CH_3), 1.41 (qt, J = 12, 4 Hz, 1H, H-4_{ax}), 1.60 (m, 1H, H-5_{ax}), 1.65−1.75 (m, 1H, H-5_{eq}), 1.92 (dd, J = 12, 4 Hz, 1H, H-4_{eq}), 2.02 (td, J = 11, 3 Hz,1H, H-6_{ax}), 2.18 (t, J = 11 Hz, 1H, H-2_{ax}), 2.58 (td, J = 12, 4 Hz, 1H, H-3_{ax}), 2.62 (t, J = 6 Hz, 2H, NCH_2), 2.81 (br d, J = 11 Hz, 1H, H-6_{eq}), 3.05 (dd, J = 12, 3 Hz, 1H, H-2_{eq}), 3.57 (t, J = 6 Hz, 2H, OCH_2), 4.10 (q, J = 7 Hz, 2H, CH_2OBn), 4.52 (s, 2H, OCH_2Ph), 7.2−7.4 (m, 5H, H-Ph); ^{13}C NMR 14.0 (CH_3), 24.3 (C-5), 26.6 (C-6), 41.6 (C-3), 53.8 (C-6), 55.6 (C-2), 57.9 (NCH_2), 60.0 (CH_2OBn), 67.4 (OCH_2), 72.8 (OCH_2Ph), 127.3 (*p*-Ph), 127.4 (*o*-Ph), 128.0 (*m*-Ph), 138.1 (*i*-Ph), 173.9 (C=O). The previous ethyl ester was stirred overnight in 6 N HCl at room temperature. Evaporation of the solvent yielded quantitatively the ***N*-[2-(benzyloxy)ethyl]-nipecotic acid hydrochloride**: IR ($CHCl_3$) 3350−3450 (OH), 1727 (C=O) cm^{-1}; ^1H NMR 1.55 (ddd, J = 12, 8, 3 Hz, 1H, H-4_{ax}), 1.80−2.00 (m, 2H, H-5), 2.17 (br d, J = 12 Hz, 1H, H-4_{eq}), 2.90−3.10 (m, 3H, H-3, H-2_{ax}, and H-6_{ax}), 3.39 (t, J = 5 Hz, 2H, NCH_2), 3.55 (br d, J = 12 Hz, 1H, H-6_{eq}), 3.77 (br d, J = 11 Hz, 1H, H-2_{eq}), 3.84 (t, J = 5 Hz, 2H, OCH_2), 4.57 (s, 2H, OCH_2Ph), 7.25−7.42 (m, 5H, H-Ph); ^{13}C NMR 23.4 (C-5), 26.1 (C-4), 40.4 (C-3), 53.9 (C-6), 54.4 (C-2), 58.1 (NCH_2), 64.5 (CH_2O) 74.1 (OCH_2Ph), 129.0 (*p*-Ph), 129.2 (*o*-Ph), 129.5 (*m*-Ph), 138.7 (*i*-Ph), 174.0 (CO). Anal. Calcd for $C_{15}H_{22}ClNO_3 \cdot 1/4H_2O$: C, 59.21; H, 7.45; N, 4.60. Found: C, 58.97; H, 7.51; N, 4.69. The previous cyclic β-amino acid (8,84 g, 29,6 mmol) was dissolved in Ac_2O. The solution was refluxed for 4 h under N_2 atmosphere, cooled, poured into aqueous K_2CO_3 (300 g in 600 mL of H_2O), and stirred for 4 h at 0 °C. The pH was adjusted to pH = 8 with additional K_2CO_3. The aqueous solution was then extracted with CH_2Cl_2, and the combined organic extracts were dried, filtered, and evaporated to yield lactam **6** (6.2 g, 86%): IR (NaCl) 1634 (CO) cm^{-1}; ^1H NMR 1.75 (qt, J = 4 Hz, 2H, H-5), 2.55 (br t, J = 4 Hz, 2H, H-4), 3.50 (t, J = 4 Hz, 2H, H-6), 3.63 (A_2B_2, 4H, NCH_2CH_2O), 4.50 (s, 2H, OCH_2Ph), 5.26 (dd, J = 1.5, 1 Hz, 1H, $=CH_A$), 6.19 (d, J = 1 Hz, 1H, $=CH_B$), 7.30 (m, 5H, H-Ph); ^{13}C NMR 22.9 (C-5), 29.7 (C-4), 47.6 (NCH_2), 49.9 (C-6), 68.2 (OCH_2), 72.6 (OCH_2Ph), 120.9 ($=CH_2$), 127.1 (*o*-Ph), 127.9 (*m*-Ph and *p*-Ph), 137.5 (*i*-Ph), 137.8 (C-3), 163.7 (C=O); MS *m*/*z* 246 ($M^+ + 1$, 2), 124 (100). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.47; H, 7.75; N, 5.71. Found: C, 73.67; H, 7.51; N, 5.23.

1-[2-(Benzyloxy)ethyl]-3-[2-(2-indolyl)-2,2-(propylenedisulfanyl)ethyl]piperidin-2-one (16) and 1-[2-(Benzyloxy)ethyl]-3-ethyl-3-[2-(2-indolyl)-2,2-(propylenedisulfanyl)ethyl]piperidin-2-one (17). Operating as for the preparation of lactam **13**, from dithiane **4** (941 mg, 4 mmol), THF (55 mL), *n*-BuLi (1.6M, 5.3 mL, 8.8 mmol), HMPA (3.5 mL, 20 mmol), lactam **6** (980 mg, 4 mmol), and EtI (1.56 mL, 24 mmol) was obtained a mixture of 2-piperidones **16** and **17**, which was separated by chromatography (EtOAc/hexane, 7/3). Lactam **16**[17] (lower R_f, 192 mg, 10%): IR (NaCl) 3300 (NH), 1624 (C=O) cm^{-1}; MS *m*/*z* 480 (M^+, 32), 374 (100). Anal. Calcd for $C_{27}H_{32}N_2O_2S_2$: C, 67.47; H, 6.71; N, 5.83. Found: C, 67.16; H, 7.14; N, 5.36. Lactam **17**[17] (higher R_f, 1.068 g, 52%): mp 123−124 °C (EtOAc/hexane); IR (NaCl) 3300 (NH), 1619 (C=O) cm^{-1}; MS *m*/*z* 508 (M^+, 5), 262 (100). Anal. Calcd for $C_{29}H_{36}N_2O_2S_2$: C, 68.47; H, 7.13; N, 5.51. Found: C, 68.39; H, 7.34; N, 5.36.

***cis*-1-[2-(Benzyloxy)ethyl]-4a-ethyl-6,6-(propylenedisulfanyl)-1,2,3,4,4a,5,6,12a-octahydro-1,8-naphthyrido[1,2-*a*]indole (18) and 1-[2-(Benzyloxy)ethyl]-3-ethyl-3-[2-(2-indolyl)-2,2-(propylenedisulfanyl)ethyl]piperidine (19).** Operating as for the reduction of lactam **13**, from piperidone **17** (448 mg, 0.882 mmol), THF (50 mL), and DIBALH (1 M in THF, 3.53 mL) was obtained a mixture of compounds **18** and **19**, which was chromatographed (Al_2O_3, EtOAc/hexane, 2/8). Naphthyridoindole **18** (higher R_f, 318 mg, 73%): mp 140−141 °C (EtOAc/hexane); MS *m*/*z* 492 (M^+, 10), 245 (100). Anal. Calcd for $C_{29}H_{36}N_2OS_2 \cdot 1/4H_2O$: C, 70.05; H, 7.40; N, 5.63. Found: C, 69.88; H, 7.31; N, 5.58. Piperidine **19** (lower R_f, 45 mg, 10%): mp 109−110 °C (EtOAc/hexane); IR 3400 (NH) cm^{-1}; MS *m*/*z* 494 (M^+, 2), 245 (100). Anal. Calcd for $C_{29}H_{38}N_2OS_2$: C, 70.40; H, 7.74; N, 5.66. Found: C, 70.42; H, 7.90; N, 5.63.

***cis*-1-[2-(Benzyloxy)ethyl]-4a-ethyl-6,6-(propylenedisulfanyl)-1,2,3,4,4a,5,6,11c-octahydropyrido[3,2-*c*]carbazole (3).** Operating as for the isomerization of **11**, from naphthyridoindole **18** (200 mg, 0.406 mmol) and AcOH (50%, 20 mL) was obtained pyridocarbazole **3** (180 mg, 90%), after chromatography (Al_2O_3, EtOAc/hexane, 1/9), as a white solid: mp 131−133 °C; IR (NaCl) 3250−3350 (NH) cm^{-1}; MS *m*/*z* 492 (M^+, 4), 371 (100). Anal. Calcd for $C_{29}H_{36}N_2OS_2$: C, 70.69; H, 7.36; N, 5.69. Found: C, 70.46; H, 7.35; N, 5.48.

***cis*-4a-Ethyl-1-(2-hydroxyethyl)-6,6-(propylenedisulfanyl)-1,2,3,4,4a,5,6,11c-octahydropyrido[3,2-*c*]carbazole (23).** To a solution of **3** (150 mg, 0.305 mmol) in dry CH_2Cl_2 (8 mL) were added Me_2S (671 μL, 9.15 mmol) and $BF_3 \cdot Et_2O$ (4.21 μL, 3.35 mmol). The reaction mixture was heated at 35 °C for 2 h. The reaction was quenched by addition of $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts, dried and evaporated, gave a yellow solid that was chromatographed (Al_2O_3, CH_2Cl_2) to yield **23** (105 mg, 86%) as a white solid: mp 242−243 °C (CH_2Cl_2); IR (KBr) 3375, 3225 (NH, OH) cm^{-1}; MS *m*/*z* 402 (M^+, 3), 371 (100). Anal. Calcd for $C_{22}H_{30}N_2OS_2$: C, 65.63; H, 7.51; N, 6.96. Found: C, 65.61; H, 7.57; N, 6.80.

16,16-(Propylenedisulfanyl)-1,2-didehydroaspidospermidine (24). To a solution of **23** (110 mg, 0.274 mmol) in dry THF (20 mL) were added K-*t*-BuO (92.2 mg, 0.822 mmol) and TsCl (104.5 mg, 0.548 mmol). After 1 h at room temperature, the reaction was quenched by addition of H_2O and extracted

with EtOAc. The organic extracts, dried and evaporated, furnished a yellow oil, which after chromatography (Al_2O_3, EtOAc/hexane, 5/95) gave indolenine **24** (81 mg, 77%) as a white foam: mp 132−134 °C; IR (NaCl) 1550 (C═N) cm^{-1}; MS *m*/*z* 384 (M^+, 23), 124 (100). Anal. Calcd for $C_{22}H_{28}N_2S_2$: C, 68.71; H, 7.34; N, 7.28. Found: C, 68.63; H, 7.34; N, 7.24.

(±)-Aspidospermidine (1).[16] **Method A.** Operating as for the preparation of **21**, from **24** (84 mg, 0.219 mmol) and W-2 Raney-Ni in EtOH (10 mL) was obtained a 1:1 mixture of *N*-ethylaspidospermidine (**26**) and aspidospermidine (**1**) after 30 min of reaction, which was flash chromatographed (Al_2O_3, EtOAc/hexane, 1/9) to isolate the products. Compound **26** (higher R_f, 17 mg, 25%): MS *m*/*z* 310 (M^+, 19), 282 (10), 124 (100). Anal. Calcd for $C_{21}H_{30}N_2$: C, 81.29; H, 9.67; N, 9.03. Found: C, 81.43; H, 9.54; N, 9.25. **1**[16] (lower R_f, 14 mg, 23%): IR (NaCl) 3375 (NH) cm^{-1}; MS *m*/*z* 282 (M^+, 20), 254 (20), 124 (100). **Method B.** A mixture of compound **24** (32 mg, 83 μmol) and excess W-2 Raney-Ni in dioxane (8 mL) was refluxed for 30 min. The mixture was filtered, and the filtrate was evaporated to give an oil, which was flash chromatographed (Al_2O_3, EtOAc/hexane, 1/9) to isolate the products: dehydroaspidospermidine (**25**, higher R_f, 8.13 mg, 35%) and aspidospermidine (**1**, lower R_f, 7.02 mg, 30%).

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Supporting Information Available: Copies of the ^1H and ^{13}C NMR of compounds **1**, **25**, and **26** are available, as well as copies of the 2D COSY (H,H) and (H,C) of compounds **1** and **26**. The detailed NMR data of lactams **9**, **13**, **16**, and **17** and of piperidines **12**, **15**, and **19** are listed in Tables 8−10 (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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