

A SIMPLE RELATIONSHIP BETWEEN STEREOSTRUCTURE AND SPECIFIC ROTATION FOR THE
BISBENZYLISOQUINOLINES

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Abstract — Within a stereochemical subgroup of bisbenzylisoquinolines,
the sign of the specific rotation is characteristic of that particular
subgroup. The absolute configuration of tiliamosine has been assigned for
the first time.

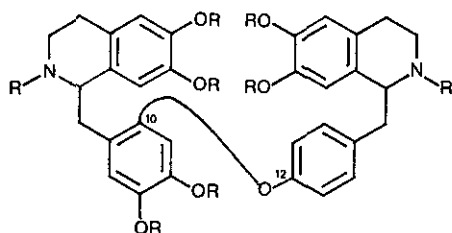
The bisbenzylisoquinoline alkaloids have been the subject of several recent reviews²⁻⁶ covering different aspects of their structure, chemistry, pharmacology and occurrence. In view of their structural variety, it has proven useful to classify them into an increasing number of types^{6,7} on the basis of their oxygenation patterns and the number and nature of the linkages between the benzylisoquinoline halves of the molecule. Although the stereochemistry of nearly all these compounds is now known, this aspect of bisbenzylisoquinoline structure has not been incorporated into their classification. The inclusion of a configurational criterion in defining alkaloid types can be expected to highlight the similarities and differences between these substances, and should facilitate the understanding of biogenetic relationships and the discovery of meaningful bioactivity correlations.

For this purpose, it is convenient to consider major groups of bisbenzylisoquinolines characterized only by the location and type of linkage between the monomeric units, and then further subdivide these classes according to the absolute configurations of the benzylisoquinoline moieties. Thus, the alkaloids with the bonding pattern found in oxyacanthine can all be described as 7*, 11[†]-8*, 12[†] dimers, and within this large group the bases with the (R,R), (S,S), (R,S), and (S,R) configurations can be placed together forming four stereochemical subgroups. Since thalisopine and its congeners possess the same ring system as oxyacanthine, they could be conveniently included within the oxyacanthine main group. In order to accommodate this situation within a unified framework, the previously published rules concerning the classification of the bisbenzylisoquinoline alkaloids can be supplemented with the statement that:

In tail-to-tail coupled dimers, the benzyloquinoline half whose C-12 oxygen atom participates in a diaryl ether bridge always constitutes the right hand side of the molecule.^{6,7}

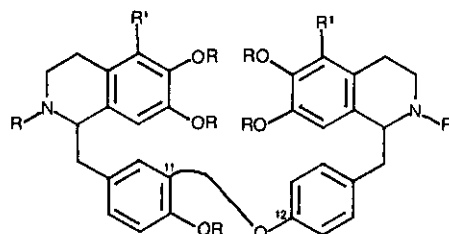
According to the foregoing definition, the major groups of known stereochemistry are the following:

(R' = H or OR).



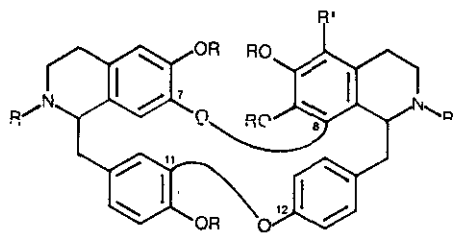
Group 10^{*}-12^{*}

Magnolamine



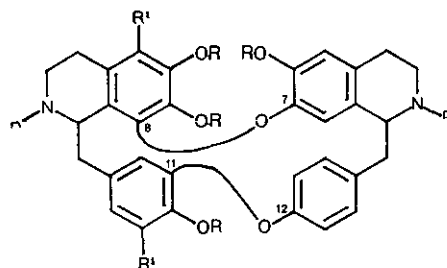
Group 11^{*}-12^{*}

Cuspidaline group



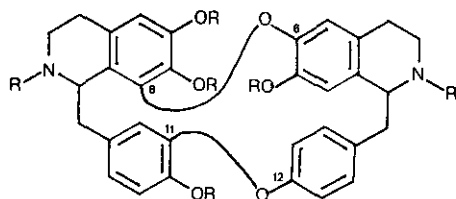
Group 7^{*}, 11[†]-8^{*}, 12[†]

Limacusine group



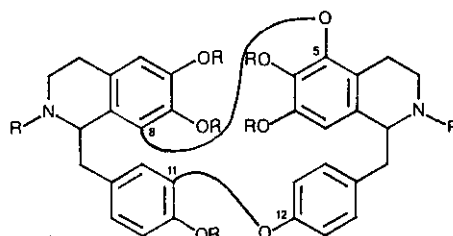
Group 8^{*}, 11[†]-7^{*}, 12[†]

Krukovine group



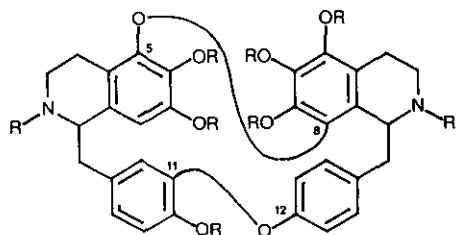
Group 8^{*}, 11[†]-6^{*}, 12[†]

Thalibcerine group



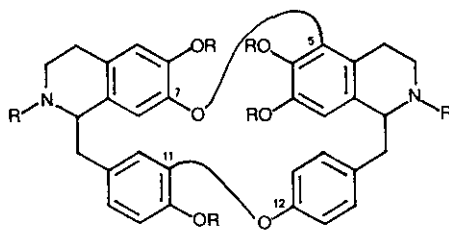
Group 8^{*}, 11[†]-5^{*}, 12[†]

Thaligosidine group



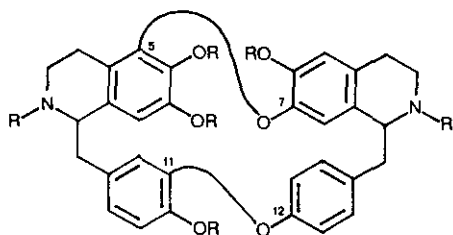
Group $5^*, 11^+ - 8^*, 12^+$

Thalfinine group



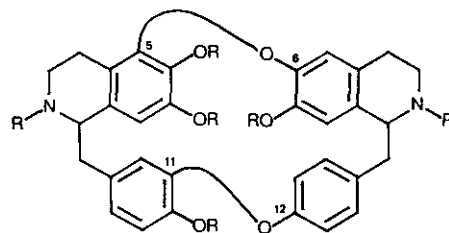
Group $7^*, 11^+ - 5^*, 12^+$

Thalictine group



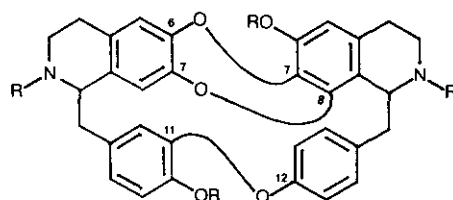
Group $5^*, 11^+ - 7^*, 12^+$

Norpanurensine group



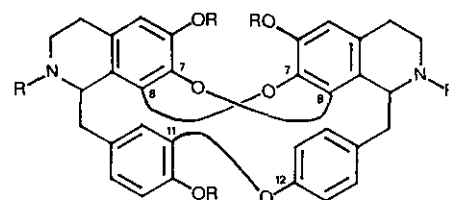
Group $5^*, 11^+ - 6^*, 12^+$

Nemuarine



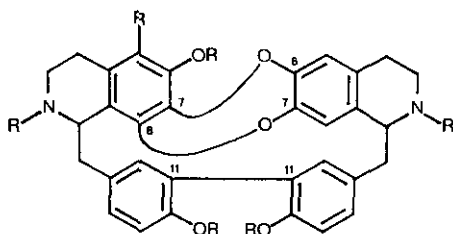
Group $6^*, 7^+, 11^+ - 7^*, 8^+, 12^+$

Micranthine group



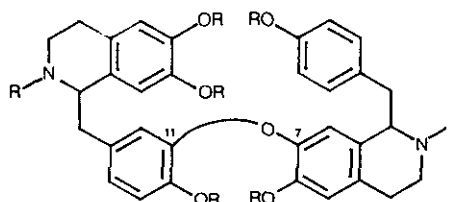
Group $7^*, 8^+, 11^+ - 8^*, 7^+, 12^+$

Gilletine group



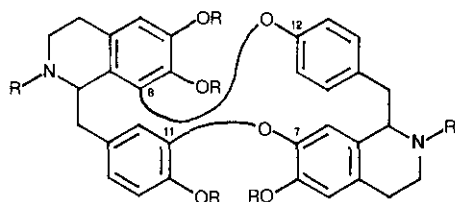
Group $7^*, 8^+ - 6^*, 7^+$ (11-11)

Nortiliacorinine group



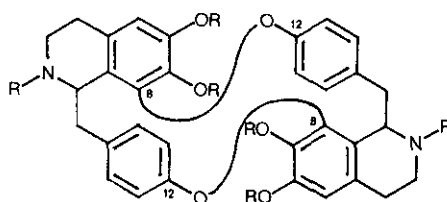
Group $11^* - 7^*$

Liensinine group



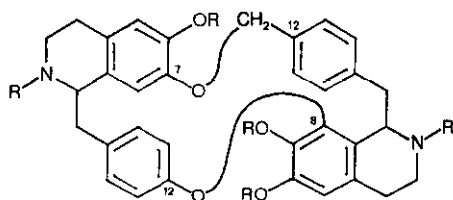
Group 8^{*}, 11[†]-7[†], 12^{*}

Cycleasaurine group



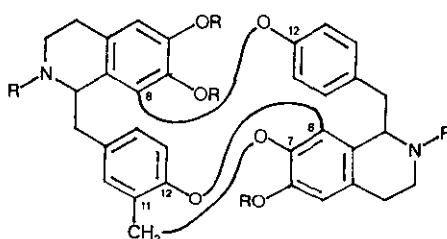
Group 8^{*}, 12[†]-8[†], 12^{*}

Isochondodendrine group



Group 12^{*}-8^{*} [7-12]

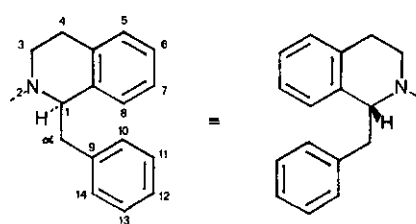
Cissampareine--



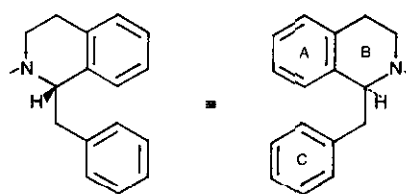
Group 8^{*}, 12[†]-8[†], 12^{*} [11-7]

Insulanoline group

Since some confusion exists in the literature concerning the application of the Cahn-Ingold-Prelog rules to bisbenzylisoquinolines, it is useful to depict the monomeric units in both configurations, in the forms in which they are usually shown when representing dimeric alkaloids.



(R)-configuration



(S)-configuration

Table I lists all the bisbenzylisoquinoline alkaloids whose absolute configuration is known, and a few semisynthetic derivatives, with their published specific rotations at 589 nm. This important physical property has been determined with widely varying accuracy in several solvents with different solvating and hydrogen bonding properties. Solvent polarity may thus lead in some cases to large conformational changes, making direct comparisons of substances whose $[\alpha]_D$'s have been measured in different media less meaningful. Another complicating factor is that phenolic bisbenzyl-

isoquinolines may incorporate intramolecular hydrogen bonding, especially with a basic nitrogen atom, resulting again in conformational changes and thus variations in sign or magnitude of the specific rotation.

TABLE I

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
<u>Type (S,S) 10[*]-12[*]</u>			
Magnolamine	+180	EtOH	8
<u>Type (R,R) 11[*]-12[*]</u>			
Cuspidaline	-48	CHCl ₃	9
Dauricine	-139	MeOH	10
Dauricinoline	-94.6	MeOH	11
Dauricoline	-105	MeOH	12
Daurinoline	-114	MeOH	13
<u>N'</u> -Desmethyldauricine	-98	MeOH	13
Lindoldhamine	+35	EtOH	14
<u>N,N'</u> -Dimethylindoldhamine (semisynthetic)	-85	CHCl ₃	14
<u>O</u> -Methyldauricine	-78.8	EtOH	15
<u>Type (S,S) 11[*]-12[*]</u>			
Northalibrine	+47	CHCl ₃	16
Thalibrine	+110	CHCl ₃	16
Thaliracebine	+121	MeOH	17
Thalirugine	+92	MeOH	18
Thaliruginine	+104	MeOH	18
Thalirugidine	+112	MeOH	18
Thalirabine	+142	MeOH	17
<u>N</u> -Desmethylthalistyline	+151	MeOH	19
Thalistyline chloride	+146	MeOH	19
Methothalistyline diiodide	+125	MeOH	19

<u>Dimer</u>	<u>[α]_D</u>	<u>Solvent</u>	<u>Reference</u>
<u>Type (R,S) 11[*]-12[*]</u>			
Berberamunine	+87	MeOH	20
	+55.1	Me ₂ CO	20
	+25.6	pyridine	20
Espinine	+25	CHCl ₃	21
Espinidine	+31	CHCl ₃	21
<u>Type (S,R) 11[*]-12[*]</u>			
Grisabine	-60.2	CHCl ₃	22
Magnoline (grisabutine)	-50	CHCl ₃	22
<u>Type (R,R) 7[*],11[†]-8[*],12[†]</u>			
Limacusine	+110	CHCl ₃	9
<u>Type (S,S) 7[*],11[†]-8[*],12[†]</u>			
Demerarine	-162	MeOH-CHCl ₃	23
Cycleaspeltine (farsalaotrine)	-106	CHCl ₃	24
Repandine	-104.3	CHCl ₃	25
<u>O</u> -Methylrepandine	-73	CHCl ₃	26
	-108	0.1 <u>N</u> HCl	26
Johnsonine	-86	CHCl ₃	27
Thalisopidine	-9	EtOH	28
Thalisopine (thaligosine)	-104.9	Me ₂ CO	29
	-71.02	CHCl ₃	29
	-109	MeOH	18
Thaligosinine	-58.5	MeOH	18
Thalrugosaminine (<u>O</u> -methylthalisopine)	-90.4	MeOH	30
<u>Type (R,R) 7[*],11[†]-8[*],12[†]</u>			
Hypoepistephanine (pseudoepistephanine)	+183.8	CHCl ₃	31
(+)-Epistephanine	+226	CHCl ₃	32

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
<u>Type</u> (<u>/</u> , <u>S</u>) 7 [*] , 11 [†] -8 [*] , 12 [†] ^a			
Coclobine	+123	CHCl ₃	33
<u>Type</u> (<u>R</u> , <u>S</u>) 7 [*] , 11 [†] -8 [*] , 12 [†]			
<u>N</u> , <u>N'</u> -Bisnoraromoline	+177	1 <u>N</u> HCl	34
Daphnoline (trilobamine)	+356.6	HOAc	35
Daphnandrine	+480	CHCl ₃	26
Aromoline (thalicrine)	+327	CHCl ₃	36
	+249.5	pyridine	37
Homoaromoline (homothalicrine)	+425.3	CHCl ₃	38
Cepharanoline	+319	CHCl ₃	39
Cepharanthine	+277	CHCl ₃	40
Sepeerine (ocoteamine)	+392	CHCl ₃	23
Oxyacanthine	+285.6	CHCl ₃	41
Baluchistine	+333	MeOH	42
Obaberine (<u>O</u> -methoxyacanthine)	+302	CHCl ₃	43
<u>Type</u> (<u>S</u> , <u>R</u>) 7 [*] , 11 [†] -8 [*] , 12 [†]			
Thalrugosamine	-79	CHCl ₃	44, 45
Macolidine	-320	CHCl ₃	46
Macoline chloride	-60.6	MeOH	46
<u>Type</u> (<u>R</u> , <u>R</u>) 8 [*] , 11 [†] -7 [*] , 12 [†]			
Krukovine	-180	CHCl ₃	47
Limacine	-212	CHCl ₃	9
Pycnamine	-283	CHCl ₃	48
Phaeanthine	-270	CHCl ₃	49
(-)-Nortenuipine	-218	CHCl ₃	26
(-)-Tenuipine	-258	CHCl ₃	26

^a Expressions such as (R,/) and (/,S) refer to the presence of an imino group in the dimer.

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
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Type (S,S) 8^{*}, 11[†]-7^{*}, 12[†]

Atherospermoline	+202	CHCl ₃	50
Fangchinoline	+250	CHCl ₃	51
Penduline	+265	CHCl ₃	52
2-Nortetrandrine	+335.2	CHCl ₃	53
(+)-Tetrandrine	+241.4	CHCl ₃	28
Tetrandrine mono-N-2'-oxide	+198	CHCl ₃	54
Monomethyltetrandrinium-A chloride	+51.5	MeOH	55
Monomethyltetrandrinium-B chloride (semisynth.)	+82	MeOH	55
Tetrandrine dimethiodide (semisynthetic)	+234	MeOH	55
Cycleanorine	+308	CHCl ₃	24
Cycleahomine chloride	+103	CHCl ₃	24
N-Desmethylthalidezine	+280	MeOH	56
Thalidezine	+235	CHCl ₃	57
Hernandezine (thalicsimine)	+250	CHCl ₃	58
N'-Northalibrunine	+79	MeOH	59
Thalibrunine	+160	MeOH	59, 60
(+)-Nortenuipine	+236.3	CHCl ₃	61
(+)-Tenuipine	+223.5	CHCl ₃	61

Type (S,R) 8^{*}, 11[†]-7^{*}, 12[†]

Thalsimidine	+48	CHCl ₃	62
Thalsimine	+22.6	CHCl ₃	63
Thalibrunimine	+28	CHCl ₃	59, 63

Type α -oxo or -hydroxy (S,R) 8^{*}, 11[†]-7^{*}, 12[†]

Oxothalibrunimine	-70	MeOH	59
Thalictrinine	-255	MeOH	59
Dihydrothalictrinine	-125	MeOH	59

Dimer	$[\alpha]_D$	Solvent	Reference
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Type (R,S) 8^{*}, 11[†]-7^{*}, 12[†]

2-N-Norobamegine	+290	CHCl ₃	64
	+146	0.1 N HCl	34
Obamegine (stepholine)	+273	CHCl ₃	65
	+99	CHCl ₃	41
Thalrugosine (thaligine, isofangchinoline)	+87	MeOH	66
2-N-Norberbamine	+117	CHCl ₃	64
Berbamine	+103.1	CHCl ₃	67
Isotetrandrine (O-methylberbamine)	+151	CHCl ₃	68
Isotenuipine	+129	CHCl ₃	69

Type (S,R) 8^{*}, 11[†]-7^{*}, 12[†]

7-O-Demethylpeinamine	-86	MeOH	46
N-Methyl-7-O-demethylpeinamine	-259	CHCl ₃	46
Peinamine	-109	CHCl ₃	70
Isothalidezine	-70	MeOH	56

Type (S,S) 8^{*}, 11[†]-6^{*}, 12[†]

Thalicberine	+231.2	CHCl ₃	71
O-Methylthalicberine (thalmidine)	+244.6	CHCl ₃	71

Type (S,R) 8^{*}, 11[†]-6^{*}, 12[†]

Thalmethine	+200	CHCl ₃	72
O-Methylthalmethine	+237	CHCl ₃	72

Type (R,S) 8^{*}, 11[†]-6^{*}, 12[†]

Belarine	-222	CHCl ₃	73
Isothalicberine	-205	CHCl ₃	74
7-O-Demethylisothalicberine	-230	CHCl ₃	74
O-Methylisothalicberine	-195	CHCl ₃	75

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
<u>Type</u> (<u>S</u> , <u>S</u>) 8 [*] ,11 [†] -5 [*] ,12 [†]			
Thaligosidine	-45	MeOH	18
Thalrugosidine	-185	MeOH	76
Thalfoetidine (thalictrinine)	-88.6	CHCl ₃	77
Thalidasine	-70	MeOH	78
<u>Type</u> (<u>S</u> , <u>S</u>) 5 [*] ,11 [†] -8 [*] ,12 [†]			
Thalfinine	+115	EtOH	79
	+141	MeOH	80
<u>Type</u> (<u>S</u> , <u>R</u>) 5 [*] ,11 [†] -8 [*] ,12 [†]			
Thalfine	+69	EtOH	79
<u>Type</u> (<u>S</u> , <u>R</u>) 5 [*] ,11 [†] -8 [*] ,12 [†]			
Epithalfinine (semisynthetic)	+46	MeOH	80
<u>Type</u> (<u>S</u> , <u>S</u>) 7 [*] ,11 [†] -5 [*] ,12 [†]			
Thalictine	-15.8	CHCl ₃	81
Thalmine	-64.5		82
<u>O</u> -Methylthamine (semisynthetic)	-68.5	CHCl ₃	83
<u>O</u> -Methylthamine dimethiodide (semisynthetic)	+48	MeOH	83
<u>O</u> -Ethylthamine dimethiodide (semisynthetic)	+56	CHCl ₃	83
<u>Type</u> (<u>R</u> , <u>S</u>) 7 [*] ,11 [†] -5 [*] ,12 [†]			
Lauberine	-481	CHCl ₃	75
<u>Type</u> (<u>S</u> , <u>R</u>) 7 [*] ,11 [†] -5 [*] ,12 [†]			
Dryadodaphnine	+390	MeOH	84
Dryadine	+486	CHCl ₃	84

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
<u>Type</u> (R,R) 5 [*] , 11 [†] -7 [*] , 12 [†]			
Norpanurensine	-250	CHCl ₃	85
Panurensine	-245.6	CHCl ₃	85
<u>Type</u> (R,R) 5 [*] , 11 [†] -6 [*] , 12 [†]			
Nemuarine	-42.7	CHCl ₃	86
<u>Type</u> (R,R) 6 [*] , 7 [†] , 11 [‡] -7 [†] , 8 [†] , 12 [‡]			
Micranthine	-221	CHCl ₃	51
O-Methylmicranthine	-208	CHCl ₃	51
N,O-Dimethylmicranthine	-230	CHCl ₃	51
<u>Type</u> (S,S) 6 [*] , 7 [†] , 11 [‡] -7 [*] , 8 [†] , 12 [‡]			
Cocsoline	+204	CHCl ₃	52
Cocsuline (eferine, trigilletine)	+280	CHCl ₃	52
12'-O-Demethyltrilobine	+332	pyridine	87
Trilobine	+304	CHCl ₃	88
Isotrilobine (homotrilobine)	+293.1	CHCl ₃	89
Tricordatine	+247.9	pyridine	90
<u>Type</u> (R,R) 6 [*] , 7 [†] , 11 [‡] -7 [*] , 8 [†] , 12 [‡]			
1,2-Dehydromicranthine	-105	CHCl ₃	91
<u>Type</u> (R,S) 6 [*] , 7 [†] , 11 [‡] -7 [*] , 8 [†] , 12 [‡]			
Dehydroapateline	+137	CHCl ₃	92
Dehydrotelobine	+172	CHCl ₃	92
<u>Type</u> (S,R) 6 [*] , 7 [†] , 11 [‡] -7 [*] , 8 [†] , 12 [‡]			
Trigilletimine	-285.7	CH ₂ Cl ₂	93

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
<u>Type (R,S) 6[*],7[†],11[‡]-7[*],8[†],12[‡]</u>			
Telobine	+188	CHCl ₃	51
<u>N</u> -Methyltelobine (semisynthetic)	+240	CHCl ₃	90
<u>N</u> -Acetyltelobine (semisynthetic)	+115	CHCl ₃	90
Apateline	+270	CHCl ₃	90
<u>N</u> -Methylapateline (semisynthetic)	+212	CHCl ₃	90
<u>N</u> -Methylnorapateline	+235	CHCl ₃	27
<u>Type (S,S) 7[*],8[†],11[‡]-7[†],8[*],12[‡]</u>			
Gilletine	+294.29	MeOH	94
Cocculinine	+312	CHCl ₃	52
<u>Type (S,S) 7[*],8[†]-6[*],7[†] (11-11)</u>			
Nortiliacorinine-A	+268.8	pyridine	95
	+325	CHCl ₃	96
<u>N</u> -Acetylnortiliacorinine-A (semisynthetic)	+588	CHCl ₃	97
Nortiliacorinine-B	+356.2	pyridine	95
Tiliacorinine	+310	pyridine	95
<u>N</u> -Acetyltillamosine (semisynthetic)	+530	CHCl ₃	97
<u>Type (R,S) 7[*],8[†]-6[*],7[†] (11-11)</u>			
Dinklacorine	+42.55	CHCl ₃	98
<u>O</u> -Acetyldinklacorine (semisynthetic)	+20.45	CHCl ₃	98
Dinklacorine methiodide (semisynthetic)	+117.39	MeOH	98
Nortiliacorine-A (isotiliarine)	+194.5	CHCl ₃	96
Tiliacorine	+71.2	pyridine	95
<u>O</u> -Methyltiliacorine (semisynthetic)	+32.60	CHCl ₃	98
<u>O</u> -Acetyltiliacorine (semisynthetic)	+86.73	CHCl ₃	98
<u>O</u> -Methyltiliacorine dimethiodide (semisynth.)	+113.64	MeOH	98

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
<u>Type (R,R) 11[*]-7[*]</u>			
Liensinine	+15.85	Me ₂ CO	99
Isoliensinine	+49.3	Me ₂ CO	100
	-43.3	CHCl ₃	100
Neferine	-37.8	CHCl ₃	101
<u>Type (R,R) 8[*],11[†]-7[†],12[*]</u>			
Cycleacurine	-202	MeOH	24
(-)-Curine ((-)-bebeerine)	-280	0.1 N HCl	102
	-337	pyridine	103
12-O-Methyl(-)-curine (12'-O-methylcurine)	-303	CHCl ₃	104
Chondrofoline	-280.6	0.1 N HCl	105
<u>Type (S,S) 8[*],11[†]-7[†],12[*]</u>			
(+)-Curine ((+)-bebeerine)	+345.7	0.1 N HCl	105
12-O-Methyl(+)-curine (4"-O-methylcurine)	+273	CHCl ₃	106
<u>Type (R,S) 8[*],11[†]-7[†],12[*]</u>			
Chondrocurine ((+)-tubocurine)	+200	0.1 N HCl	102
(+)-Tubocurarine chloride	+215	H ₂ O	106
Chondocurarine iodide	+150	H ₂ O	106
<u>Type (S,R) 8[*],11[†]-7[†],12[*]</u>			
Hayatidine	-109	pyridine	107
<u>Type (R,R) 8[*],12[†]-8[†],12[*]</u>			
Isochondodendrine (isobebeerine)	+120	0.1 N HCl	102
	+59	pyridine	103
(-)-Norcycleanine	-22.50	CHCl ₃	107
	-26.54	MeOH	108

<u>Dimer</u>	$[\alpha]_D$	<u>Solvent</u>	<u>Reference</u>
<u>Type</u> (<u>R,R</u>) $8^*, 12^+-8^+, 12^*$ (continued)			
<u>O</u> -Methylnorcycleanine	-10.85	MeOH	108
Cycleanine (methylisochondodendrine)	-15.94	CHCl ₃	109
	-14.04	MeOH	108
<u>Type</u> (<u>//,R</u>) $8^*, 12^+-8^+, 12^*$			
Sciadoline	+46	CHCl ₃	110
<u>Type</u> (<u>S,S</u>) $8^*, 12^+-8^+, 12^*$			
Sciadenine	-43	pyridine	111
	+15	CHCl ₃	111
<u>Type</u> (<u>//,R</u>) $12^*-8^+[7-12]$			
Cissampareine	-111	CHCl ₃	112
<u>Type</u> (<u>R,R</u>) $8^*, 12^+-8^+, 12^*[11-7]$			
Insulanoline	+48.6	MeOH	108
Insularine	+11.36	EtOH	109
	+57.89	MeOH	108

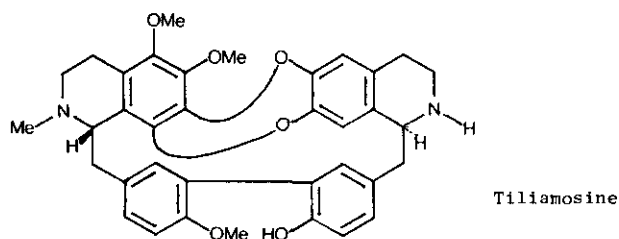
In spite of the above, several striking regularities are evident from the table. In nearly all the configurationally defined subgroups, the optical rotations of the constituent bases have the same sign regardless of the solvents in which they were determined, and within a particular subgroup the $[\alpha]_D$ values seem to cluster around low (10-150), moderate (150-300) or large (300-600) values. When the rotations are small, the signs of the specific rotations within a subgroup of identical stereochemistry may be positive and/or negative depending upon the substituents present and the solvent used. Indeed, in the (R,R) 11^*-7^* subgroup the $[\alpha]_D$ values are positive in acetone and negative in chloroform, even for the same compound, isoliensinine. Sciadenine, the only (S,R) $8^*, 12^+-8^+, 12^*$ alkaloid, is levorotatory in pyridine and dextrorotatory in chloroform. These observations suggest that the conformations of bisbenzylisoquinolines may be quite sensitive to solvent

polarity. Structural changes in a dimer, such as N- or O-methylation, may also lead to changes in the preferred conformation in solution which should be particularly noticeable when the $[\alpha]_D$ values are small. This happens when (R,R) 11^{*}-12^{*} (+)-lindoldhamine is N,N'-dimethylated to a levorotatory derivative,¹⁴ or when (S,S) 7^{*},11⁺-5^{*},12⁺ (-)-O-alkylthalamine ethers are converted to their dextrorotatory dimethiodides.⁸³ (R,R) 8^{*},12⁺-8⁺,12^{*} (+)-Isochondodendrine and its O-methyl derivative (-)-cycleanine may be examples of changes in conformation attributable to the blocking of a phenolic hydroxyl. Noteworthy also is the fact that isochondodendrine has $[\alpha]_D$ +59 in pyridine but is appreciably more dextrorotatory (+120) in an acidic medium, where it is protonated.

Thalisamine is an alkaloid whose structure has not been clearly established.¹¹³ In the latest reviews^{2,3} it is listed as an (S,S) 8^{*},11⁺-7^{*},12⁺ dimer on the basis of a tentative identification of its N-methyl derivative as hernandezine (TLC, IR).¹¹³ Its reported specific rotation, however, is -138 (CHCl₃). If this rotation is correct, it seems unlikely that thalisamine should belong in a subgroup composed of moderately dextrorotatory alkaloids. It is clear, therefore, that the rather meager experimental data on this alkaloid must be supplemented before any final decision regarding its structure can be reached. In particular, remeasurement of the specific rotation of thalisamine is warranted.

Calafatine is the first 6,7,8^{*},10,11⁺,12-6,7^{*},12⁺ bisbenzylisoquinoline to be reported.¹¹⁴ Due to lack of material, it was not possible to determine the configurations of the sodium-liquid ammonia cleavage products, but its positive rotation of +280 (CHCl₃) strongly suggests that it is either an (R,S) or an (S,S) dimer of the 8^{*},11⁺-7^{*},12⁺ group.

As a consequence of the elegant proof of the absolute configurations of tiliacorine and tiliacornine,¹¹⁵ the stereochemistry of nortiliacorine, dinklacorine, and the nortiliacornines is now known. This series is characterized by small positive rotations for the (R,S) bases and much higher positive values for the (S,S) dimers. Although tiliamosine has not been correlated with either of the above two subgroups by chemical or chiroptical means, considering the rigidity of the triply linked 7^{*},8⁺-6^{*},7⁺ (11-11) dibenzo-p-dioxin system and the high positive rotation of N-acetyltiliamosine, it is safe to state that its configuration is (S,S):



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