

122. Syntheses and Chiroptical Properties of the 13-Membered Spermidine Alkaloids (–)-(S)-Celacinnine, (0)-(S)-Celabenzine, (–)-(S)-Celafurine, and (+)-(S)-Viburnine

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The title alkaloids were prepared from the common chiral precursor (–)-(2S)-2-phenyl-1,5,9-triazacyclotridecan-4-one (**4**) which we had synthesized earlier. The spectral data for the spermidine macrocycles are in good agreement with the data reported for the isolated samples. Our experimental results indicate that the originally reported $[\alpha]_D$ value of -2.6 ($c = 0.10$, MeOH) for natural (S)-viburnine is erroneous and should be $+17.0$ ($c = 0.92$, MeOH). As a result of the chiroptical study conducted, it can be shown empirically that all alkaloids of the 'celacinnine' type have the (S)-configuration.

Introduction. – Around a dozen 13-membered monocyclic spermidine alkaloids have been isolated from plants of different families²⁾. Besides the precursorial polyamine building block, they contain cinnamic- or aliphatic-acid residues which are part of the macrocyclic ring. Prototypes described earlier and also subjects of this report are the related 'celacinnine'-type bases (–)-(S)-celacinnine (**1**), (0)-(S)-celabenzine (**2**)³⁾, and (–)-(S)-celafurine (**3**)⁴⁾. Alkaloid **1** was isolated from *Maytenus arbutifolia* (HOCHST. ex A. RICH.) R. WILCZEK [2], *Tripterygium wilfordii* HOOK. [2], *Maytenus serrata* (HOCHST. ex A. RICH.) R. WILCZEK [3], *M. heterophylla* (ECKL. et ZEYHER) N. ROBSON subsp. *heterophylla* [4], and *Pleurostyliya africana* LOES. [4], all from the same plant family Celastraceae. Compounds **2** and **3** were found in *M. arbutifolia*, *M. serrata*, and *T. wilfordii*. They can all be considered derivatives of the (non-racemic) diaza-lactam **4**, which has been shown to be a preparatively useful intermediate for an entire family of alkaloids [5]. This compound was previously synthesized for the preparation of (–)-(S)-mayfoline (**5**) and (–)-(S)-N(1)-acetyl-N(1)-deoxymayfoline (**6**)⁵⁾; [6]), both isolated from *M. buxifolia* (R. RICH.) GRISEB., Celastraceae [7] [8].

A further target of our synthetic interest is the new macrocyclic lactam alkaloid (S)-viburnine (**7**) from *Viburnum rhytidophyllum* HESSEL (Caprifoliaceae), which was

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²⁾ Based on the two possible orientations of the spermidine unit within the basic skeleton, the alkaloids are classified as of the celacinnine or dihydroperiphylline type [1].

³⁾ The $[\alpha]_D$ value of optically active (0)-(S)-celabenzine is zero. To ensure that it is not misinterpreted as racemic, i.e., (\pm), we use (0).

⁴⁾ Furan-3-carboxylic acid and its derivatives occur rarely in nature; they have been isolated primarily from Celastraceae [3].

⁵⁾ The correct $[\alpha]_D$ value for the N-Ac derivative **6** is -17.4 . The sign and magnitude of rotation given in [6] turned out to be wrong.

isolated quite recently by *Abdallah and Ibraheim* [9]. The plants of the genus *Viburnum* have been described to have many traditional medicinal uses. Several compounds have been already isolated from plants of this genus; however, the recent publication [9] was the first report on the presence of alkaloids in *Viburnum*.

The wide special interest in these materials is principally twofold. Firstly, interest in their therapeutical properties has resulted from the notable and broad biological activity shown by members of the polyamine family [10], and the toxic or cytotoxic effects exhibited by several of these compounds [11]. Secondly, they are challenging materials when testing for new lactamization methods [12]. Our interests lies in the preparation of these natural compounds, at first for the alkaloids **3** and **7**⁶), and in their chiroptical properties which have not yet been thoroughly investigated.

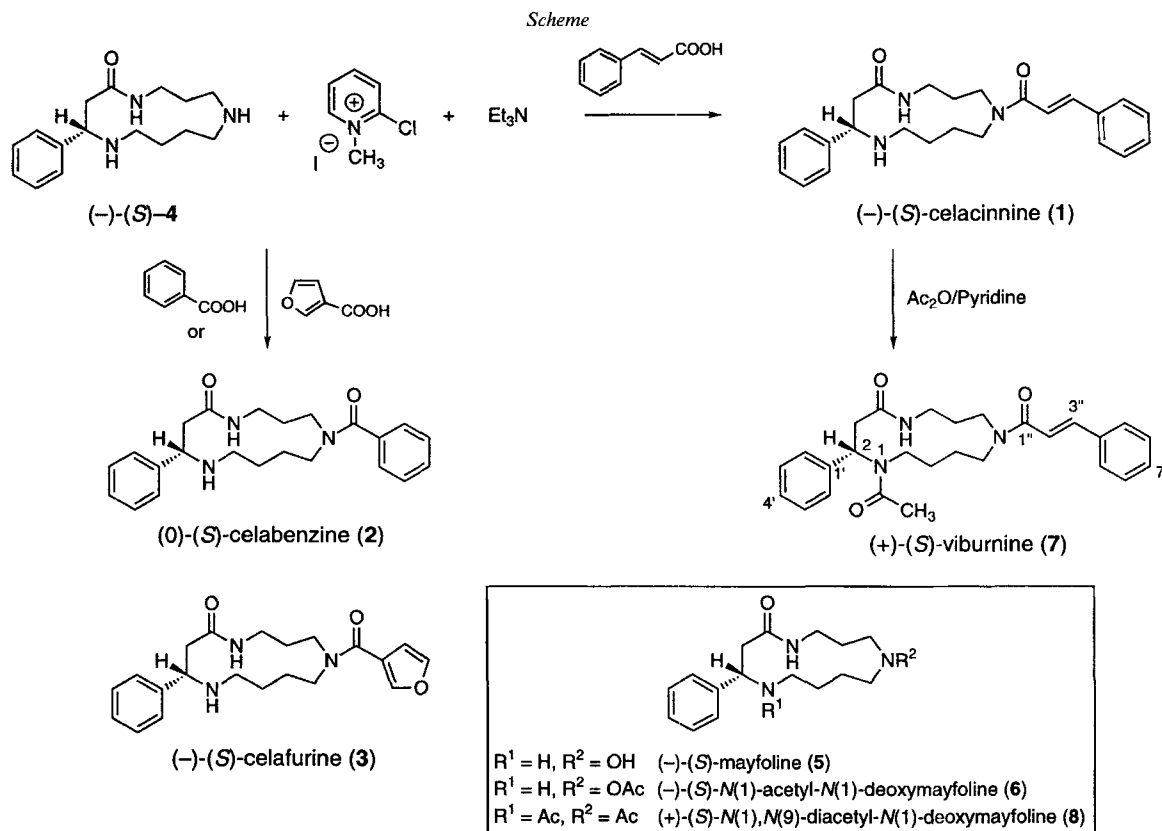
Results and Discussion. – The diaza-lactam **4** was used as starting material for syntheses of the structurally related alkaloids **1–3** and **7** (see the *Scheme*). To couple the three different acids, namely benzoic, cinnamic, and furan-3-carboxylic acid, **4** was added to a solution containing the acid of the corresponding acyl residue, the carboxyl-activating agent 2-chloro-*N*-methylpyridinium iodide, and Et₃N. This *Mukaiyama* procedure has already been employed several times in the preparation of cyclic polyamine alkaloids [12g] [13]. The procedure is simple and requires no special conditions, *i.e.*, strict water-free environment and very 'low temperatures'⁷). The alkaloids were obtained in fair-to-good yields of 55% for (–)-(*S*)-celacinnine (**1**), 67% for (0)-(*S*)-celabenzine (**2**), and 81% for (–)-(*S*)-celafurine (**3**). Acetylation of (–)-(*S*)-celacinnine (**1**) with Ac₂O/pyridine yielded (+)-(*S*)-viburnine (**7**) in a yield of 56%. For a later comparison of the CD properties of **8** with those of **7**, the *N,N*-diacetyl derivative **8** was also prepared using the above-mentioned reagents. Thus, treatment of **4** with an excess of Ac₂O/pyridine gave **8** in almost quantitative yield.

The ¹³C-NMR spectra of the compounds measured at room temperature showed more than the expected number of signals. This is frequently reported by other authors [14], and is due to the *cis/trans* isomerization around the partial C(O)–N double bond. The additional signals could also be caused by existence of conformers in solution as a result of the flexibility of the macrocyclic molecule.

The structure elucidation of the natural, new macrocyclic spermidine alkaloid **7** was accomplished by spectroscopic methods, especially by comparing the ¹³C-NMR spectral data with those of other spermidine alkaloids and high-resolution mass spectrum. The structure of synthetically obtained **7** was established by IR, CD, NMR, and mass spectrometry. 2D-NMR Techniques (homonuclear and heteronuclear COSY) were applied for complete signal assignments (*vide infra*). The physical and spectral data of synthetic (+)-(*S*)-viburnine (**7**) are identical to those reported for the naturally occurring

⁶) (+)-(*S*)-Viburnine (**7**) was unintentionally prepared earlier by *Kupchan et al.* [3], and *Wagner and Burghart* [4], *via* derivatization of the natural isolate (–)-(*S*)-celacinnine (**1**) by usual methods. The measured optical rotation was given as $[\alpha]_D = +67.7$ ($c = 0.94$, CHCl₃). Note that the $[\alpha]_D$ value given for natural viburnine, measured in MeOH, was found to be -2.6 .

⁷) Almost quantitative yields have been reported [12e] for the selective monoacylations using selected acid chlorides and DMAP in CH₂Cl₂ at -78° . However, in our hands, the procedure described in [12h] was more reliable, although the yields were not as high as reported in [12c].



material, the only exception being the difference in the optical rotation of synthetic and natural **7** recorded in MeOH. This discrepancy could be either due to a small, high-rotating impurity in the isolated natural noncrystalline (*S*)-viburnine (**7**), or the isolate **7** was partly protonated. Differences in the $[\alpha]_D$ values between the free base and its protonated form have also been observed in the case of $(-)-(S)$ -mayfoline [**6**].

Since the compounds differ only in their acyl side chain, it is not possible to use the optical rotation data to draw any conclusions about the configuration at C(2). The optical rotations are listed in the *Table* together with the corresponding literature values. It is interesting to note that most of the optical rotations are negative, and only **7** and **8** (in CHCl_3 , as well as in MeOH) exhibit positive values. This is presumably due to the additional π -electron chromophore in the α -position with respect to the chiral center, which is further augmented by the fact that the Ac residue on a N-atom leads to a reduction of the basicity and conformational freedom. A survey of the literature provides similar results. With the exception of cyclocelabenzine and its congeners, all optically active macrocyclic spermidine and spermine alkaloids possessing a (*S*)- β -amino- β -phenylpropionic acid moiety within the ring system have negative $[\alpha]_D$ values and their *N*(1)-Ac derivatives display primarily positive values.

Table. Optical Rotations in Comparison

Compound	$[\alpha]_D$	Values reported previously		This work	
1	–20.5	($c = 1.15$, CHCl_3)	[4]	–20.7	(c = 0.61, CHCl_3)
	–19.0	($c = 0.16$, CHCl_3)	[2] [3]		
	–5.5	($c = 0.10$, CHCl_3)	[19]		
2	± 0	(CHCl_3)	[2] [3]	± 0	(c = 0.44, CHCl_3)
	± 0	($c = 0.14$, CHCl_3)	[11 c]		
	± 0	($c = 0.73$, CHCl_3)	[12 g]		
3	–11.0	($c = 0.11$, CHCl_3)	[2] [3]	–10.1	(c = 0.99, CHCl_3)
5	–52.2	($c = 1.99$, CHCl_3)	^{a)}	–52.3	(c = 0.64, CHCl_3)
6	–17.8	($c = 1.01$, CHCl_3)	[8]	–17.4	(c = 1.01, CHCl_3)
7	–2.6	($c = 0.10$, MeOH)	[9]	+17.0	(c = 0.92, MeOH)
8	+67.7	($c = 0.94$, CHCl_3)	[4]	+60.6	(c = 0.87, CHCl_3)
				+2.7	(c = 0.84, MeOH)
				+52.9	(c = 0.94, CHCl_3)

^{a)} The corrected value indicated by H. Ripperger in his letter, November, 1996 ($[\alpha]_D^{21} = -52.3$ (c = 0.636, CHCl_3)).

The CD curves (see Fig.) indicate that the measured compounds show similar simple negative *Cotton* effects, with minima between 200 and 220 nm⁸⁾ for the alkaloids 1–3 and for the *N*(1),*N*(9)-diacyl compounds 7 and 8. This feature of the CD curves is in agreement with the fact that electronic absorption of amides starts with a weak but broad $n \rightarrow \pi^*$ transition around 210 nm. With the exception of the spectrum of 7, the nearly missing contribution is that of the long-wavelength absorption between 225 and 295 nm, expected for the Ph chromophore. It is apparent from the spectra that a change in the intensity is observed with a change in the substituent. All five compounds display the same negative *Cotton* effect, in accordance with the lactam rule proposed by Nagao *et al.* [15] [16]. Thus, the spectra indicate that the investigated alkaloids possess, as expected, the same configuration.

Conclusion. – Identification of the synthetic targets as being equivalent to the natural products was effected by comparison of our data with those published. The single discrepancy found in the value of optical rotation of natural vs. synthetic viburnine (7) could be explained as resulting from an experimental error.

The CD spectra of the synthesized compounds with similar structure are also illustrated (Fig.). It is noteworthy that the CD spectrum of the synthetic (0)-(*S*)-celabenzine (2) displays no optical rotation at the $[\alpha]_D$ line⁹⁾. It has been observed before that isolated spermidine alkaloids occur as racemates, since the molecule shows neither optical rotation nor a CD effect [17]¹⁰⁾. As the decisive result of this work and that reported in [6], we could show that all alkaloids of this type have the (*S*)-configuration.

⁸⁾ The transparency cut-off of EtOH and the commercial spectrometer used limited the lower range of the CD measurements of 7 to 207 nm (see Fig.).

⁹⁾ Because of the missing CD spectrum of the natural 2, its absolute configuration cannot be deduced as yet.

¹⁰⁾ It has also been reported in [18], that CD measurements conducted in acidic conditions resulted in complete disappearance of the CD effect.

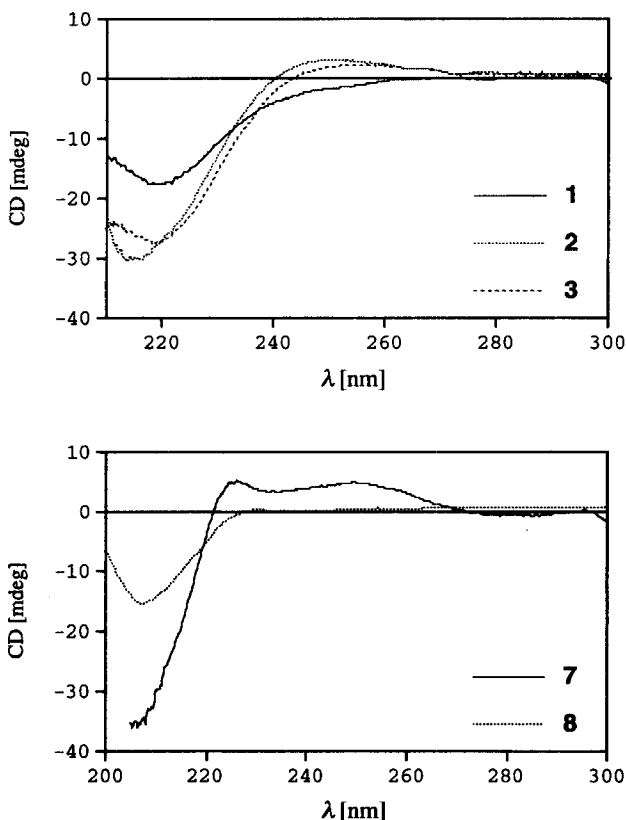


Figure. CD Spectra of the alkaloids 1–3, 7, and 8 measured in EtOH

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Experimental Part

General. See [6].

1. (–)-(2*S*)-9-(1-*Oxo*-3-phenylprop-2-enyl)-2-phenyl-1,5,9-triazacyclotridecan-4-one (= (–)-(S)-Celacinine, **1**). *N*-Methyl-2-chloropyridinium iodide (67 mg, 0.26 mmol) and Et₃N (53 mg, 0.52 mmol) were added to a soln. of cinnamic acid (32 mg, 0.22 mmol) in CH₂Cl₂ (5 ml). The mixture was stirred for 30 min, followed by the addition of (–)-(2*S*)-2-phenyl-1,5,9-triazacyclotridecan-4-one (**4**, 60 mg, 0.22 mmol) [6] dissolved in CH₂Cl₂ in one portion. After stirring for several hours at r.t., usual workup and chromatography on silica gel gave **1** (48 mg, 55%). Colorless solid. *R*_f (CHCl₃/hexane/MeOH 75:20:5) 0.32. M.p. (CH₂Cl₂/hexane) 196.7–198.1°. [α]_D²¹ = –20.7 (*c* = 0.61, CHCl₃). IR: 3450w, 3320w (br.), 3060w, 2990m, 2930m, 2860w, 1650s, 1600s, 1545m, 1495m, 1455s, 1435s, 1375m, 1360m, 1325m, 1305m, 1190m, 1160w, 1120w, 1010w, 1010w, 1000w, 990w, 975m, 910w, 855w, 700m, 670m (sh). ¹H-NMR: 7.65 (*m*, 0.5 C(O)NH); 7.63 (*d*, *J* = 15.3, PhCH=CH); 7.47–7.09 (*m*, 10 arom. H, 0.5 C(O)NH); 6.76 (*d*, *J* = 15.4, 0.5 PhCH=CH); 6.74 (*d*, *J* = 15.4, 0.5 PhCH=CH); 3.94–3.86 (*m*, H–C(2)); 3.75–2.99 (*m*, 6H); 2.65–2.29 (*m*, 4H); 2.10–1.22 (*m*, 7H). ¹³C-NMR: 172.31, 172.11 (2s, CO); 166.35 (*s*, CO); 142.91, 142.73 (2*d*, 1 C); 139.80, 135.57 (2*s*, 2 arom. C); 129.77, 129.07, 128.01, 127.73, 126.36 (5*d*, 10 arom. C); 117.76 (*d*, 1 C); 61.07 (*d*, C(2)); 47.03, 45.45, 44.95, 43.67, 37.39, 36.88, 30.26, 28.25, 25.58, 24.98, 24.81, 23.56 (12*t*, 8C). ESI-MS: 428 ([*M* + Na]⁺), 406 ([*M* + H]⁺).

2. (0)-(2*S*)-9-Benzoyl-2-phenyl-1,5,9-triazacyclotridecan-4-one (= (0)-(S)-Celabenzine, **2**). Preparation analogous to *Exper. 1*. From benzoic acid (22.1 mg, 0.18 mmol), 2-chloro-*N*-methylpyridinium iodide (56 mg, 0.22 mmol), Et₃N (44 mg, 0.43 mmol), **4** (50 mg, 0.18 mmol), and CH₂Cl₂ (6 ml), **2** (46 mg, 67%) was obtained

in pure form. Colorless solid. R_f ($\text{CH}_2\text{Cl}_2/\text{MeOH}/25\%$ aq. NH_3 97:3:0.5) 0.18. M.p. ($\text{CH}_2\text{Cl}_2/\text{hexane}$) 168.2–172.4°¹¹). $[\alpha]_D^{21} = \pm 0$ ($c = 0.44$, CHCl_3). IR: 3450w, 3219w, 3065w, 3005m, 2940m, 2861w, 2360w, 1660s, 1621s, 1579m, 1544m, 1521m, 1497m, 1471m, 1456m, 1431m, 1379w, 1361w, 1316m, 1264m, 1110w, 1074w, 1029w, 1002w, 918w, 864w, 694m, 657w. $^1\text{H-NMR}$ (7.83 (br. s, ca. 0.5 C(O)NH); 7.50 (br. s, ca. 0.5 C(O)NH); 7.42–7.15 (m, 10 arom. H); 4.00–3.88 (m, H–C(2)); 3.85–2.80 (m, 6H); 2.70–2.26 (m, 4H); 2.20–1.23 (m, 7H). $^{13}\text{C-NMR}$: 171.94, 171.53 (2s, CO); 142.56 (s, CO); 136.82 (s, 1 arom. C); 129.27, 128.71, 128.38, 127.38, 126.21, 126.05 (6d, 10 arom. C); 105.89 (s, 1 arom. C); 60.60 (d, C(2)); 47.69, 45.04, 44.37, 42.54, 42.05, 36.93, 28.65, 27.46, 24.43, 23.79, 22.44 (11t, 8C). ESI-MS: 402 ($[M + \text{Na}]^+$), 380 ($[M + \text{H}]^+$).

3. (–)-(2S)-9-[Furan-3-yl]carbonyl]-2-phenyl-1,5,9-triazacyclotridecan-4-one (= (–)-(S)-Celfafurine, 3). Preparation analogous to *Exper. 1*. From furan-3-carboxylic acid (33 mg, 0.29 mmol), 2-chloro-*N*-methylpyridinium iodide (111 mg, 0.43 mmol), Et_3N (71 mg, 0.70 mmol), **4** (80 mg, 0.29 mmol), and CH_2Cl_2 (10 ml), (109 mg, 81%) was obtained in pure form. Colorless solid. R_f ($\text{CH}_2\text{Cl}_2/\text{MeOH}/25\%$ aq. NH_3 97:3:0.5) 0.25. M.p. ($\text{CH}_2\text{Cl}_2/\text{hexane}$) 156.2–157.3°. $[\alpha]_D^{21} = -10.1$ ($c = 0.99$, CHCl_3). IR: 3450w, 3340w (br.), 2990m, 2930m, 2850w, 1660s, 1615s, 1570m, 1505m, 1455m, 1430m, 1380m, 1360m, 1320m, 1255m, 1175m, 1165m, 1110m, 1075w, 1020w, 910w, 875m, 695m, 660w, 600m. $^1\text{H-NMR}$ ((D_6) DMSO, 383 K): 7.87 (dd, $J = 0.8$, 0.8, 1 furyl H); 7.73 (br. s, C(O)NH); 7.61 (t, $J = 1.7$, 1 furyl H); 7.37–7.29 (m, 4 arom. H); 7.26–7.19 (m, 1 arom. H); 6.61 (dd, $J = 0.91$, 0.91, 1 furyl H); 3.99 (dd, $J = 11.4$, 3.4, H–C(2)); 3.59–3.43 (m, 3H); 3.38–3.26 (m, 2H); 3.04–2.95 (m, 1H); 2.63–2.49 (m, 1H); 2.46–2.25 (m, 3H); 1.97–1.22 (m, 7H). $^{13}\text{C-NMR}$ ((D_6) DMSO, 383 K): 170.26 (s, CO); 162.66 (s, CO); 143.61 (s, 1C); 142.26, 141.84, 127.53, 125.85, 125.63 (5d, 5C); 121.27 (s, 1C); 109.60 (d, 1C); 78.35 (s, 1C); 59.51 (d, C(2)); 45.25, 44.76, 44.11, 42.92, 35.38, 27.77, 23.86, 23.45 (8t, 8C). ESI-MS: 392 ($[M + \text{Na}]^+$), 370 ($[M + \text{H}]^+$).

4. (+)-(2S)-1-Acetyl-9-(1-oxo-3-phenylprop-2-enyl)-2-phenyl-1,5,9-triazacyclotridecan-4-one (= (+)-(S)-Viburnine, 7). Ac_2O (3 equiv.) and pyridine (3 equiv.) were added to a soln. of **1** (75 mg, 0.19 mmol) in CH_2Cl_2 (8 ml). The mixture was heated at reflux for 8 h. Then, the solvent was evaporated and the residue purified by CC: **7** (46 mg, 56%). Colorless amorphous solid. R_f (AcOEt/MeOH 9:1) 0.24. M.p. ($\text{CHCl}_3/\text{cyclohexane}$) 112.1–114.7°. $[\alpha]_D^{20} = +17.0$ ($c = 0.92$, MeOH) or +60.6 ($c = 0.87$, CHCl_3). IR (CHCl_3): 3440w (br.), 2995m, 2960m, 2850w, 1710w (br.), 1665s, 1645s, 1595s, 1510m, 1475m, 1450m, 1420s, 1360m, 1345m, 1320m, 1300m, 1260m, 1165w, 1150w, 1090m, 1010m, 990m, 975m, 855w, 695m. $^1\text{H-NMR}$ (CDCl_3): 7.67 (d, $J = 15.3$, H–C(3'')); 7.47–7.41 (m, 2 arom. H); 7.34–7.17 (m, 6 arom. H); 7.06–7.03 (m, 2 arom. H); 6.77 (d, $J = 15.3$, H–C(2'')); 6.43 (br. s, NH); 5.64 (dd, $J = 11.7$, 3.13, H–C(2)); 4.35–4.25 (m, H_a –C(8)); 4.00–3.75 (m, H_a –C(6), H_b –C(10), H_a –C(13)); 3.15–2.98 (br., m, H_b –C(6), H_b –C(10)); 2.95–2.85 (m, H_a –C(3), H_b –C(8)); 2.45–2.20 (m, H_b –C(3), Me, H_b –C(13)); 2.00–1.90 (m, H_a –C(7)); 1.75–1.47 (br. m, H_b –C(7), 2H–C(11), H_a –C(12)); 1.45–1.37 (br. s, H_b –C(12)). $^{13}\text{C-NMR}$ (CDCl_3): 172.03 (s, MeCO); 167.91 (s, C(4)); 167.61 (s, C(1'')); 141.69 (d, C(3'')); 138.08 (s, C(1'')); 133.92 (s, C(4'')); 128.93 (d, C(7'')); 127.89 (d, C(6'')), C(8'')); 127.82 (d, C(3'')); 126.85 (d, C(5'')), C(9'')); 126.64 (d, C(4'')); 125.16 (d, C(2'')), C(6'')); 116.79 (d, C(2'')); 56.61 (d, C(2)); 51.11 (t, C(8)); 49.60 (t, C(10)); 40.30 (t, C(13)); 38.76 (t, C(6)); 38.14 (t, C(3)); 27.94 (t, C(7)); 27.81 (t, C(11)); 27.35 (t, C(12)); 21.26 (q, Me). EI-MS: 447 (73, M^+), 405 (27), 404 (98), 316 (68), 258 (20), 178 (22), 169 (27), 131 (100), 112 (22), 104 (39), 103 (50), 91 (25), 77 (17), 70 (19). ESI-MS: 470 ($[M + \text{Na}]^+$), 448 ($[M + \text{H}]^+$).

5. (+)-(2S)-1,9-Diacetyl-2-phenyl-1,5,9-triazacyclotridecan-4-one (= (+)-(S)-N(1),N(9)-Diacetyl-N(1)-deoxymayfoline, 8). Dissolved in a mixture of pyridine (1 ml) and Ac_2O (1 ml), **4** (34.2 mg, 0.124 mmol) was stirred at r.t. for 16 h. The solvent was then evaporated and the residue purified by CC to yield **8** (44 mg, 98%). Colorless resin. R_f ($\text{CH}_2\text{Cl}_2/\text{MeOH}/25\%$ aq. NH_3 95:5:0.2) 0.22. $[\alpha]_D^{22} = +2.7$ ($c = 0.84$, MeOH) or +52.9 ($c = 0.94$, CHCl_3). IR: 3660w, 3530w, 3440m, 3410m, 3350w, 3000s, 2940m, 2860w, 2460w, 1700m, 1665vs, 1630vs, 1510m, 1495m, 1445s, 1420s, 1365m, 1340m, 1315m, 1275m, 1260m, 1240m (sh), 1170w, 1150w, 1090m, 1060w, 1020m, 975w, 965w, 910w, 860w, 695m. $^1\text{H-NMR}$ ((D_6) DMSO): 8.35–8.25 (br. s, 0.5 H, CONH); 8.20–8.05 (br. m, 0.5 H, C(O)NH); 7.40–7.20 (m, 5 arom. H); 5.55–5.45 (br., m, 0.7 H, H–C(2)); 3.70–2.80 (m, 7.5 H); 2.75–2.60 (m, 1H); 2.48–2.40 (m, 1H); 2.29 (d, $J = 13.4$, Me); 2.05–1.88 (m, 3.5 H, overlapping d, $J = 13.4$, Me); 1.80–1.30 (m, 6H). $^{13}\text{C-NMR}$ ((D_6) DMSO): 171.57, 170.05, 169.69, 169.58 (4s, 3 CO); 140.29 (s, 1 arom. C); 128.80, 128.15, 127.44, 126.57, 126.47 (5d, 4 arom. C); 57.05, 56.86 (2d, C(2)); 49.72, 45.37, 43.66, 41.29, 40.46, 40.18, 37.94, 37.74, 37.13, 36.99, 29.07, 28.44, 27.72, 27.58, 26.12 (15t, 8C); 24.86, 22.57, 22.36, 21.93, 21.79 (5q, 2 Me). ESI-MS: 360 ($[M + \text{H}]^+$), 382 ($[M + \text{Na}]^+$), 398 ($[M + \text{K}]^+$).

¹¹) Celabenzine was described as a material which is difficult to purify and its unusual melting behavior was mentioned before [11c][12b]. The m.p. values reported in the literature (in order of appearance as reported): 156–158° [2] [3], 150–155° [12b], 172–173° [12e], 163–167° [11c], 170–173° [12g].

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