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Stereospecific Synthesis of 2,3-Dimethoxy-naphtho[1,2-b]indolizidine[1)]

Gwan Sun Lee[*], Yong Seo Cho[*)], Sang Chul Shim[*)], Wan Joo Kim[**)], Ernst Eibler[***)], and Wolfgang Wiegrebe[***)]

[*)]Department of Chemistry, Korea Advanced Institute of Science and Technology, P. O. Box 150, Cheongryang, Seoul 130-650, Korea

[**)]2nd Division of Organic Chemistry, Korea Research Institute of Chemical Technology, Daejon, Korea

[***)]Faculty of Chemistry and Pharmacy, University, D-8400 Regensburg

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(11aS)- and (11aR)-2,3-dimethoxy-naphtho[1,2-b]indolizidine (**9a** and **9b**) were synthesized from optically pure L- and D-glutamic acid through several steps (scheme 1). All the intermediates of the route to the optical antipodes of **9** exhibit identical physical and spectral properties except the sign of the optical rotation values. The optical purity of the enantiomers of **6** was checked by ^{1}H-NMR spectra using Eu(tfc)$_3$, that of the enantiomers of **9** by HPLC-separation on a chiral column; the amount of racemization was less than 3% in **9a** and **9b**, respectively.

Stereospezifische Synthese von 2,3-Dimethoxynaphtho[1,2-b]indolizidin

Die (11aS)- und (11aR)-2,3-Dimethoxy-naphtho[1,2-b]indolizidine (**9a**) und (**9b**) wurden, ausgehend von optisch reiner L- bzw. D-Glutaminsäure, synthetisiert (Schema 1). Alle Zwischenprodukte auf dem Weg zu **9** zeigen identische physikalische und spektrale Eigenschaften mit Ausnahme des Drehsinns. Die optische Reinheit der **6**-Enantiomere wurde durch ^{1}H-NMR-Spektroskopie mit Eu(tfc)$_3$ bestimmt, die der **9**-Enantiomere durch HPLC-Trennung auf einer chiralen Säule: die Razemisierungsrate war in **9a** und **9b** <3%.

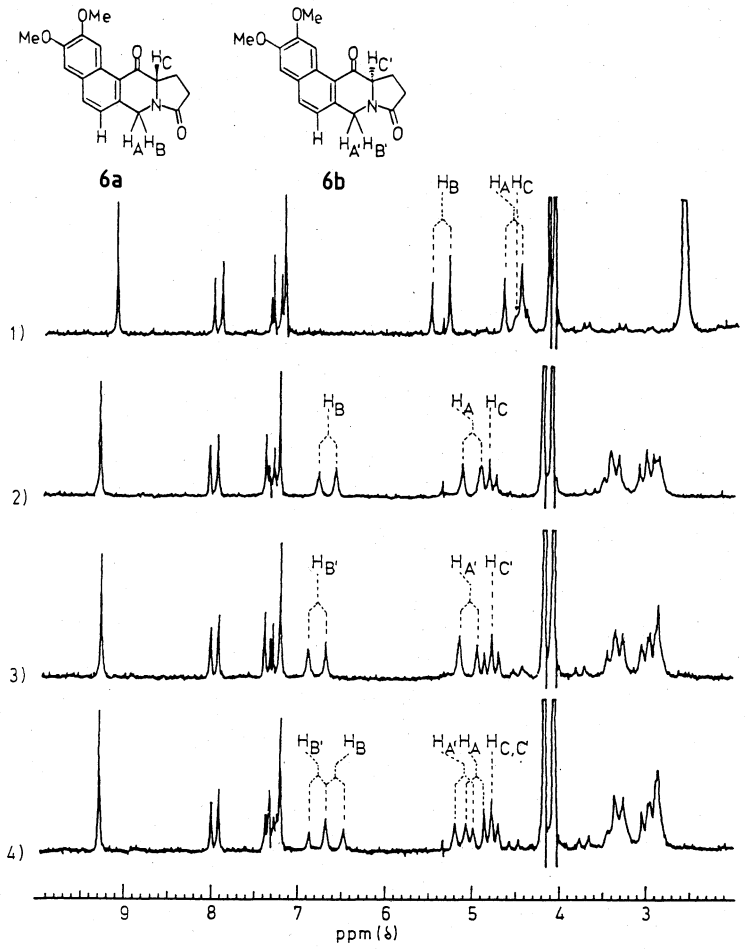

Fig. 1. Normal and Eu(tfc)$_3$ shifted ^{1}H-NMR spectra of **6a** and **6b**. 1) normal spectrum (**6a=6b**) 2) **6a**+Eu(tfc)$_3$ (3:1) 3) **6b**+Eu(tfc)$_3$ (3:1) 4) **6a+6b**+Eu(tfc)$_3$ (1.5:1.5:1).

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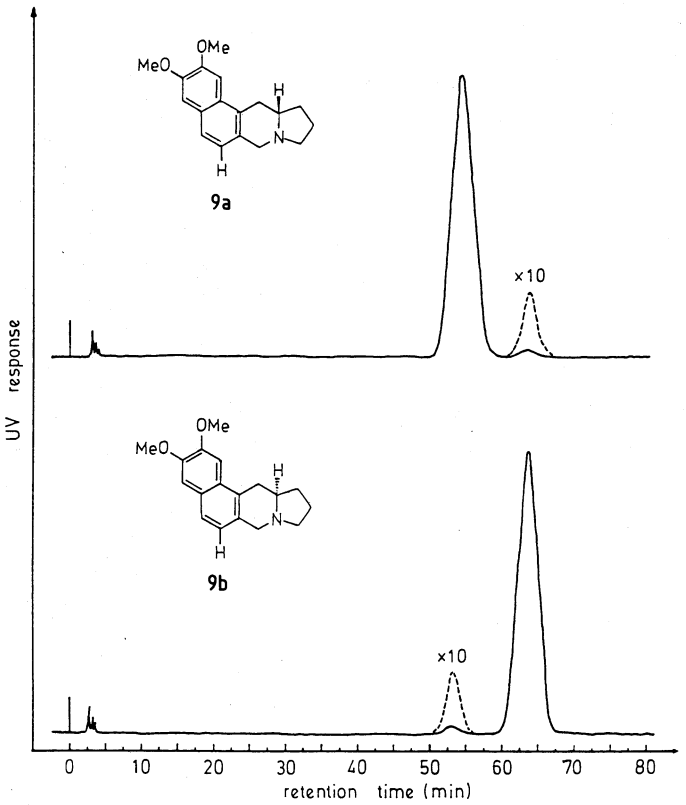
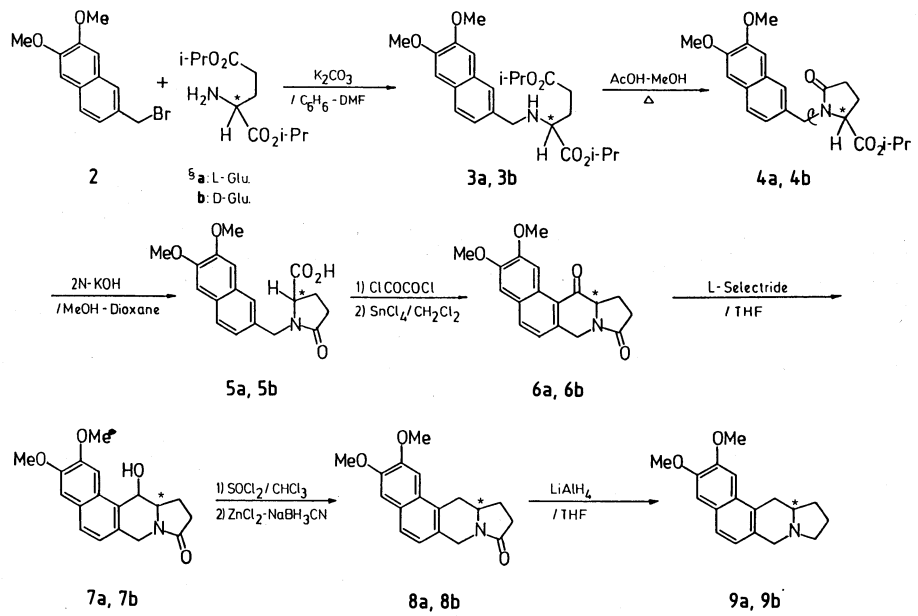


Fig. 2. HPLC chromatogram of **9a** and **9b** on a chiral column (Bakerbond cov. 5(chiral); Eluent:i-PrOH/MeOH/n-Hexane 0.66/1.34/98(v/v/v); flow rate: 1.0 ml/min; Detector:UV(254nm))



Scheme 1. The intermediates with subscription "**a**" were derived from L-glutamic acid, those with "**b**" from D-glutamic acid.

In spite of the intense progress in the synthesis of phenanthroindolizidine alkaloids especially about their stereospecific synthesis[2,3] there is no report about the stereospecific synthesis of naphthoindolizidines. Several attempts[4,5] were reported concerning the formation of the naphtho[1,2-b]indolizidine ring system. One paper[4] is concerned with the coupling of a naphthalene derivative with proline followed by intramolecular acylation giving no comment about the optical purity. The other one[5] reports *Bischler-Napieralsky* cyclization of racemic 2-naphthylmethylpyrrolidines.

Rapoport et al.[2] reported on a stereospecific synthesis of tylophorine, a phenanthroindolizidine alkaloid, starting from optically pure glutamic acid diester but they did not prove in detail the optical purities.

We developed a stereospecific synthesis of the naphtho[1,2-b]indolizidine ring system **9** varying *Rapoport's* strategy[2]. The synthetic pathway is denoted in scheme 1.

2,3-Dimethoxy-6-bromomethylnaphthalene (**2**)[6] was coupled with diisopropyl glutamate (L- or D-form) to afford the alkylated products **3a** and **3b**, respectively. Compound **3** was cyclized to the pyroglutamate **4** which was hydrolyzed to the acid **5**.

After converting the acid **5** to its acid chloride by oxalyl chloride, intramolecular *Friedel-Crafts* acylation[7] yielded the amide ketone **6** in good yield.

Amide ketone **6a**, an important intermediate in this synthesis, was checked for its optical purity by comparison of its ^{1}H-NMR spectrum in the presence of the chiral shift reagent Eu(tfc)$_3$[8] with the corresponding spectrum of **6b** (Fig. 1).

Striking differences in chemical shifts between the two optical antipodes **6a** and **6b** were observed in the methylene protons adjacent to the nitrogen atom. In **6a**, H_A and H_B appeared at 4.95 and 6.55 ppm as doublets with the same coupling constant (J = 18.0 Hz). The $H_{A'}$ and $H_{B'}$ protons in **6b** were shifted more downfield (5.10 and 6.75 ppm) than those of **6a**, evincing the formation of diastereomeric complexes with Eu(tfc)$_3$.

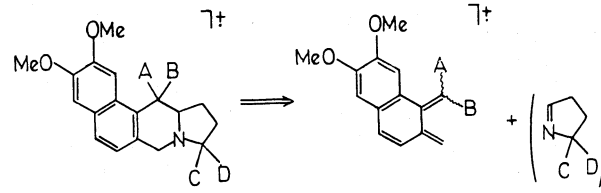
Reduction to the corresponding alcohol **7** proceeded efficiently by treatment of **6** with L-Selectride. Deoxygenation of **7** was effected by reaction with $SOCl_2$ followed by reduction with $ZnCl_2$-modified $NaBH_3CN$[9] to afford amide **8**. **8** was further reduced to **9** with $LiAlH_4$. Physical and spectral data were in agreement with the structures of all the intermediates, the optical rotation value for all the optical antipodes were identical within small error ranges with opposite signs. The optical rotation values are summarized in Table 1.

Final evidence for the naphthoindolizidine ring system was found in the mass spectra showing retro *Diels-Alder* fragmentation as base peaks in compounds **6** - **9** (Scheme 2).

Differences in ^{1}H-NMR chemical shifts were not observed with Eu(tfc)$_3$ in **9a** and **9b**. This indicates that Eu(tfc)$_3$ can not form diastereomeric complexes because there are no lactam groups in these molecules.

Table 1: Optical rotation ($[\alpha]_D^{20}$) values of inantiomers

	$[\alpha]_D^{20}$	
cmpd.	a	b
Glu.	+7.59(c,2.00,CH_2Cl_2)	-7.90(c,2.00,CH_2Cl_2)
3	-23.30(c,1.03,CH_2Cl_2)	+23.17(c,1.01,CH_2Cl_2)
4	+36.95(c,2.00,CH_2Cl_2)	-36.83(c,1.01,CH_2Cl_2)
5	+54.10(c,0.61,THF)	-53.00(c,0.61,THF)
6	-207.8(c,1.00,CH_2Cl_2)	+208.9(c,1.00,CH_2Cl_2)
7	-75.90(c,1.00,CH_2Cl_2)	+77.60(c,1.00,CH_2Cl_2)
8	+32.60(c,1.00,CH_2Cl_2)	-30.60(c,1.00,CH_2Cl_2)
9	+129.5(c,0.20,CH_2Cl_2)	-129.0(c,0.80,CH_2Cl_2)



Scheme 2 **6**. A+B=O, C+D=O; m/z=228 **7**. A=OH, B=H, C+D=O; m/z=230 **8**. A=B=H, C+D=O; m/z=214 **9**. A=B=C=D=H; m/z=214

The optical antipodes **9a** and **9b** were successfully separated by HPLC on a chiral column, the result is denoted in Fig. 2. The amount of racemization in **9a** and **9b** was determined to be 2.4% and 2.2%, respectively, by integration of each peak. These values, in the authors' opinion, can be accepted for a stereospecific synthesis.

In a similar work about a phenanthroindolizidine synthesis[3] using N-trifluoroacetylproline as starting material, the amount of racemization was reported to be 2 - 3%.

Experimental Part

General remarks: m. ps. are uncorrected. - Elemental analysis: Microanalysis Laboratory, University of Regensburg. - UV-spectra: Uvikon 810 Kontron, MeOH. - IR-spectra (neat in NaCl cells or KBr pellets): Beckman Acculab 3. - ^{1}H-NMR spectra: Varian EM 390 (90 MHz), or Bruker WM 250 (250 MHz). - Mass spectra: Varian MAT CH 5. - Optical rotation ($[\alpha]_D^{20}$): Perkin-Elmer 241 MC (589 nm).

Diisopropyl(S)-N-[(2,3-dimethoxy-7-naphthyl)methyl]glutamate (**3a**)

To a stirred solution of 2,3-dimethoxy-6-hydroxymethylnaphthalene[6] (3.27 g, 0.018 M) in $CHCl_3$ (150 ml) were added Et_3N (2.48 ml, 0.018 M) and PBr_3 (1.6 ml, 0.018 M) at 0°C. Stirring was continued for 30 min. H_2O (150 ml) was added drop by drop during 30 min, then the org. layer was separated, washed with saturated NaCl solution (150 ml), and dried over Na_2SO_4. After 1 h the solution was filtered and the filtrate was evaporated in vacuo. The residue was dissolved in benzene (75 ml) and DMF (75 ml), and heated to 80°C. K_2CO_3 (8.33 g) and diisopropyl (S)-glutamate (**a**) (5.2 g, 0.0225 M) were added to the hot solution in one portion. Then the mixture was refluxed for 30 min, cooled to room temp. and H_2O (400 ml) and ethyl acetate (400 ml) were added. The upper layer was separated and worked up as usual. Column chromatography (CC) (ethyl acetate : n-hexane 1 : 3) afforded pure **3a** as a colorless liquid. Yield 6.12 g (93.8%). - $C_{24}H_{33}NO_6$ (431.5) Calc. C 66.8 H 7.71 N 3.3 Found C 66.8 H 7.44 N 3.3. - UV (MeOH): λmax (log ε) = 323 (3.53), 309 (3.41), 263 (3.77), 231 nm (4.84). - IR(film): 1730 (CO); 3260 - 3700 cm^{-1} (broad, NH). - ^{1}H-NMR ($CDCl_3$): δ(ppm) = 1.19 (d; J = 6.6 Hz, 6H, isopropyl-CH_3), 1.26 (d; J = 6.6 Hz, 6H, isopropyl-CH_3), 1.83 (s; 1H, -NH-), 1.73 - 2.10 (m; 2H, -CH_2-), 2.30 - 2.60 (m; 2H, -CH_2-), 3.23 (dd; J_1 = 8.4 Hz, J_2 = 5.4 Hz, 1H, -N-CH-), 3.71 (d; J = 12.9 Hz, 1H, H_A in Ar-CH_AH_B-N-), 3.95 (d; J = 12.9 Hz, 1H, H_B in Ar-CH_AH_B-N-), 3.98 (s; 6H, -OCH_3), 5.03 (m; 2H, isopropyl-CH-), 7.10 (s; 2H, Ar-H), 7.32 (d; J = 10.2 Hz, 1H, Ar-H), 7.62 (s; 1H, Ar-H), 7.66 (d; J = 10.2 Hz, 1H, Ar-H). - EI-MS: m/z = 431 (2%, $M^{+\cdot}$), 370 (7), 343 (16), 201 (100, $(M - C_{11}H_{20}NO_4)^+$).

Diisopropyl(R)-N-[(2,3-dimethoxy-7-naphthyl)methyl]glutamate (**3b**)

Same procedure as for **3a** using diisopropyl (R)-glutamate (**b**) instead of **a**. Yield 92.1%. - Physical and spectral data: identical with those of **3a**, except the sign of optical rotation.

Isopropyl(S)-N-[(2,3-dimethoxy-7-naphthyl)methyl]pyroglutamate (**4a**)

3a (4.04 g, 9.37 mM) was dissolved in MeOH (150 ml) and glacial AcOH (21.3 ml). The mixture was refluxed for 5 h and evaporated *in vacuo*. Separation by CC (ethyl acetate : n-hexane 2:1) afforded **4a** as a colorless solid. Yield 3.10 g (89.1%). - m.p. 106 - 107°C. - $C_{21}H_{25}NO_5$ (371.4) Calc. C 67.9 H 6.78 N 3.6 Found C 68.0 H 6.90 N 3.8. - UV (MeOH): λmax (log ε) = 323 (3.52), 309 (3.39), 263 (3.81), 230 nm (4.73). - IR(KBr): 1703 (CO); 1727 cm^{-1} (CO). - ^{1}H-NMR ($CDCl_3$): δ(ppm) = 1.20 (d; J = 6.3 Hz, 6H, isopropyl-CH_3), 1.73 - 2.77 (m; 4H, -CH_2-), 3.83 - 4.03 (m; 1H, -CH-N-), 3.98 (s; 6H, -OCH_3), 4.08 (d; J = 14.5 Hz, 1H, H_A in Ar-CH_AH_B-N-), 5.02 (m; J = 6.3 Hz, 1H, isopropyl-CH-), 5.20 (d; J = 14.5 Hz, 1H, H_B in Ar-CH_AH_B-N-), 7.08 (s; 1H, Ar-H), 7.12 (s; 1H, Ar-H), 7.20 (dd; J_1 = 8.4 Hz, J_2 = 1.8 Hz, 1H, Ar-H), 7.53 (d; J = 1.8 Hz, 1H, Ar-H), 7.67 (d; J = 8.4 Hz, 1H, Ar-H). - EI-MS: m/z = 371 (25%, $M^{+\cdot}$), 284 (5, $(M - CO_2C_3H_7)^+$), 201 (100, $(M - C_8H_{12}NO_3)^+$).

Isopropyl(R)-N-[(2,3-dimethoxy-7-naphthyl)methyl]pyroglutamate (**4b**)

Cf. synthesis of **4a**, using **3b** instead of **3a**. Yield 90.3%. - Physical and spectral data: cf. **4a**.

(S)-N-[(2,3-Dimethoxy-7-naphthyl)methyl]pyroglutamic acid (**5a**)

To a stirred solution of **4a** (2.74 g, 7.3 mM) in dioxane (20 ml) and MeOH (20 ml) was added 2N-KOH (20 ml) at 0-5°C. The temp. was raised to 20 - 25°C and the mixture was stirred for 1 h. H_2O (150 ml) was dropped to it and the pH of the solution was adjusted to 3 - 4 with H_3PO_4. After stirring for 30 min at 0 - 5°C, the white crystals were filtered, washed with H_2O and dried *in vacuo*. Yield 2.25 g (92.6%). - m.p. 220 - 221°C. - $C_{18}H_{19}NO_5$ (329.4) Calc. C 65.6 H 5.82 N 4.3 Found C 65.5 H 5.91 N 4.0. - UV (MeOH): λmax (log ε) = 323 (3.51), 309 (3.36), 263 (3.75), 230 nm (4.78). - IR (KBr): 1630 (CO, acid); 1722 (CO, amide); 2300 - 3200 cm^{-1} (broad, OH of CO-OH). - ^{1}H-NMR ($CDCl_3$ + DMSO-d_6): δ(ppm) = 2.00 - 2.67 (m; 4H, -CH_2-), 3.87 - 4.03 (m; 1H, -CH-N-), 3.98 (s; 6H, -OCH_3), 4.07 (d; J = 14.7 Hz, 1H, H_A in Ar-CH_AH_B-N-), 5.23 (d; J = 14.7 Hz, 1H, H_B in Ar-CH_AH_B-N-), 7.08 (s; 2H, Ar-H), 7.20 (d; J = 8.5 Hz, 1H, Ar-H), 7.53 (s; 1H, Ar-H), 7.63 (d; J = 8.5 Hz, 1H, Ar-H), 7.00 - 8.30 (broad s; 1H, COOH). - EI-MS: m/z = 329 (76%, $M^{+\cdot}$), 284 (8, $(M - COOH)^+$), 273 (5, $(M - C_2H_4CO)^+$), 201 (100, $(M - C_5H_6NO_3)^+$).

(R)-N-[(2,3-Dimethoxy-7-naphthyl)methyl]pyroglutamic acid (**5b**)

Cf. synthesis of **5a**, using **4b** instead of **4a**. Yield 91.2%. - Physical and spectral data: cf **5a**.

(S)-2,3-Dimethoxynaphtho[1,2-b]-9,12-indolizidinedione (**6a**)

To a stirred solution of **5a** (2.0 g, 6.08 mM) in CH_2Cl_2 (40 ml) at 0 - 5°C were added DMF (1 drop) and oxalyl chloride (0.67 ml, 7.3 mM), and the reaction mixture was refluxed for 2 h. $SnCl_4$ (1.45 ml, 12.16 mM) was dropped for 10 min and reflux was continued for 4 h. To the cooled reaction mixture was dropped 3N-HCl (60 ml) and the org. layer was separated, washed with saturated NaCl solution, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was stirred with MeOH (20 ml) for 80 min. The precipitates formed were collected to afford **6a** as a light yellow crystalline solid. Yield 1.57 (83.3%). - m.p. 200 - 203°C (dec.). - $C_{18}H_{17}NO_4$ (311.3) Calc. C 69.4 H 5.50 N 4.5 Found C 69.6 H 5.46 N 4.3. - UV (MeOH): λmax (log ε) = 3 50 (3.91), 2 20 nm (4.64). - IR(KBr): 1685 (CO); 1700 cm^{-1} (CO). - ^{1}H-NMR ($CDCl_3$): δ(ppm) = 2.43 - 2.60 (m; 4H, -CH_2-), 3.98 (s; 3H, -OCH_3), 4.05 (s; 3H, -OCH_3), 4.23 - 4.50 (m; 1H, -CH-N-), 4.48 (d; J = 18.0 Hz, 1H, H_A in Ar-CH_AH_B-N-), 5.32 (d; J = 18.0 Hz, 1H, H_B in Ar-CH_AH_B-N-), 7.12 (s; 1H, Ar-H), 7.20 (d; J = 9 Hz, 1H, Ar-H), 7.90 (d; J = 9 Hz, 1H, Ar-H), 9.08 (s; 1H, Ar-H). - EI-MS: m/z = 311 (77%, $M^{+\cdot}$), 283 (22, $(M - CO)^{+\cdot}$), 185 (21, $(200 - CH_3)^+$), 157 (9, $(185 - CO)^{+\cdot}$).

(R)-2,3-Dimethoxynaphtho[1,2-b]-9,12-indolizidinedione (**6b**)

Cf. synthesis of **6a** using **5b** instead of **5a**. Yield 85.4%.- Physical and spectral data: cf. **6a**.

(11aS)-12-Hydroxy-2,3-dimethoxynaphtho[1,2-b]-9-indolizidinone (**7a**)

To a stirred solution of **6a** (0.825 g, 2.65 mM) in THF (32 ml) at -70°C was added L-Selectride (5.3 ml, 5.3 mM) during 30 min. Stirring was continued for 2 h at that temp. The mixture was allowed to warm to 0°C, then 2N-KOH (3 ml) and 30% H_2O_2 solution (3 ml) were added and the reaction mixture was stirred for 30 min. at 0 - 5°C. THF was evaporated *in vacuo* and the residue was partitioned between H_2O (50 ml) and EtOAc (50 ml). Usual work-up of the EtOAc layer afforded **7a** as pale yellow crystals. Yield 0.69 (83%). - m.p. 218 - 223°C (dec.). - $C_{18}H_{19}NO_4$ (313.4) Calc. C 69.0 H 6.11 N 4.5 Found C 68.6 H 6.17 N 4.2. - UV (MeOH): λmax (log ε) = 325 (3.56), 311 (3.43), 267 (3.73), 232 nm (4.78). - IR(KBr): 1670 (CO); 3418 cm^{-1} (OH). - ^{1}H-NMR ($CDCl_3$): δ(ppm) = 1.80 - 2.65 (m; 4H, -CH_2-), 3.22 (d; J = 9.0 Hz, 1H, OH), 3.70 - 3.90 (m; 1H, -CH-N), 3.95 (s; 3H, -OCH_3), 4.01 (s; 3H, -OCH_3), 4.15 (d; J = 17.8 Hz, 1H, H_A in Ar-CH_AH_B-N-), 4.92 (d; J = 17.8 Hz, 1H, H_B in Ar-CH_AH_B-N-), 5.15 (dd; J_1 = 9.0 Hz, J_2 = 2.3 Hz, 1H, -CH-O-), 7.03 (d; J = 8.4 Hz, 1H, Ar-H), 7.06 (s; 1H, Ar-H), 7.45 (s; 1H, Ar-H), 7.63 (d; J = 8.4 Hz, 1H, Ar-H). - EI-MS: m/z = 313 (84%, $M^{+\cdot}$), 230 (100, $(M - C_4H_5NO)^{+\cdot}$, retro *Diels-Alder*), 202 (50, $(230 - CO)^+$), 187 (18, $(202 - CH_3)^+$), 159 (12, $(187 - CO)^+$).

(11aR)-12-Hydroxy-2,3-dimethoxynaphtho[1,2-b]-9-indolizidinone (**7b**)

Cf. synthesis of **7a** using **6b** instead of **6a**. - Physical and spectral data: cf. **7a**.

(11aS)-2,3-Dimethoxynaphtho[1,2-b]-9-indolizidinone (**8a**)

To a stirred solution of **7a** (0.55 g, 1.76 mM) in CH_2Cl_2 (50 ml) was added $SOCl_2$ (0.21 ml, 2.11 mM) at 0°C. Then it was stirred for 2 h at room temp. The mixture was diluted with Et_2O (30 ml) and THF (30 ml). In another vessel was prepared a $ZnCl_2$ modified $NaBH_3CN$ solution using $NaBH_3CN$ (0.22 g, 3.52 mM) and freshly fused $ZnCl_2$ (0.50 g, 3.52 mM) in Et_2O (30 ml) according to the known procedure[9]. To this solution was added the reaction solution during 10 min at room temp., then it was stirred for 30 min. After cooling the mixture to 0 - 5°C saturated $NaHCO_3$ solution (30 ml) was added drop by drop, then Et_2O and THf were evaporated. The residue was extracted with CH_2Cl_2 (2 x 30 ml) and the extract was washed with H_2O (30 ml) and saturated NaCl solution (30 ml), dried over Na_2SO_4 and filtered. The filtrate was evaporated in vacuo and the residue was crystallized from acetone (10 ml) to afford **8a** as a white crystalline powder. Yield 0.43 g (82%). - m.p. 219 - 222°C (dec.). - $C_{18}H_{19}NO_3$ (297.4) Calc. C 72.7 H 6.44 N 4.7 Found C 72.6 H 6.56 N 4.3. - UV (MeOH): λmax (log ε) = 325 (3.41), 311 (3.30), 276 (3.72), 228 nm (4.61). - IR(KBr): 1685 cm^{-1} (CO). - ^{1}H-NMR ($CDCl_3$): δ(ppm) = 1.77 - 2.63 (m; 4H, -CH_2-CH_2-CO-), 2.63 - 3.60 (m; 2H, -CH_2-), 3.70 - 4.03 (m; 1H, -N-CH-), 4.00 (s; 3H, -OCH_3), 4.03 (s; 3H, -OCH_3), 4.35 (d; J = 18.0 Hz, 1H, H_A in Ar-CH_AH_B-N-), 5.05 (d; J = 18.0 Hz, 1H, H_B in Ar-CH_ACH_B-N-), 7.07 (d; J = 8.7 Hz, 1H, Ar-H), 7.14 (s; 2H, Ar-H), 7.58 (d; J = 8.7 Hz, 1H, Ar-H). - EI-MS: m/z = 297 (68%, $M^{+\cdot}$), 282 (3, $(M - CH_3)^+$), 266 (3, $(M - OCH_3)^+$), 214 (100, $(M - C_4H_5NO)^{+\cdot}$, retro *Diels-Alder*), 199 (8, $(214 - CH_3)^+$).

(11aR)-2,3-Dimethoxynaphtho[1,2-b]-9-indolizidinone (**8b**)

Cf. synthesis of **8a** using **7b** instead of **7a**. Yield 84%. - Physical and spectral data: cf. **8a**.

(11aS)-2,3-Dimethoxynaphtho[1,2-b]indolizidine (**9a**)

To a stirred solution of **8a** (0.186 g, 6.26 x 10^{-4} M) in THF (10 ml) was added $LiAlH_4$ (0.048 g, 1.25 mM) at 0 - 5°C. The resulting suspension was refluxed for 1 h under N_2. Then it was cooled to 0°C and saturated Na_2SO_4 solution (5 ml) was added cautiously. After stirring for 1 h at 0°C, the solvent was evaporated *in vacuo*. Usual work-up afforded **9a** as a pale yellow crystalline powder. Yield 0.15 g (87%). - m.p. 167 - 168°C. - $C_{18}H_{21}NO_2$ (283.4) Calc. C 76.3 H 7.47 N 4.9 Found C 76.4 H 7.61 N 4.8. - UV (MeOH): λmax (log ε) = 325 (3.46), 311 (3.35), 269 (3.74), 229 nm (4.67). - IR(KBr): 1605; 1626 cm^{-1} (aromatic C=C). - ^{1}H-NMR ($CDCl_3$): δ(ppm) = 1.50 - 2.50 (m; 4H, $-CH_2-$), 2.60 - 3.00 (m; 1H, -N-CH-), 3.20 - 3.40 (m; 2H, -N-$\underline{CH_2}$-CH_2-), 3.51 (d; J = 15.0 Hz, 1H, H_A in Ar-CH_AH_B-N-), 3.98 (s; 3H, $-OCH_3$), 4.01 (s; 3H, $-OCH_3$), 4.23 (d; J = 15.0 Hz, 1H, H_B in Ar-CH_AH_B-N-), 7.03 (d; J = 8.4 Hz, 1H, Ar-H), 7.08 (s; 1H, Ar-H), 7.15 (s; 1H, Ar-H), 7.49 (d; J = 8.4 Hz, 1H, Ar-H). - EI-MS: m/z = 283 (33%, $M^{+\cdot}$), 214 (100, (M - $C_4H_7N)^{\cdot+}$, retro *Diels-Alder*), 199 (10, (214 - $CH_3)^+$).

(11aR)-2,3-Dimethoxynaphtho[1,2-b]indolizidine (**9b**)

Cf. synthesis of **9a** using **8b** instead of **8a**. Yield 89%. - Physical and spectral data: cf. **9a**.

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