Synthesis of Azapolycyclic Systems Based on the Indolizino[3,4-*b*]quinoline Skeleton − A Diastereoselective Entry to Potential Oligodentate Artificial Receptors

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A convenient diastereoselective synthetic route to the molecular tweezer bis(indolizino[3,4-*b*]quinolyl)methane **9** and the rigid indolizino[7′,8′:2,3]quinolino[8,7-*h*]indolizino[8,7-*b*]quinolines **14**, **15** as potential receptor molecules has been developed, involving double imine condensation followed by Lewis acid catalyzed biscyclization of prolinal-derived bis(imines) **8** and **13**, respectively. Whereas the use of $SnCl_4$ leads to the formation of the planar polycycle **15**, the corresponding concave product **14** is formed in the presence of $EtAlCl_2$. Both compounds **14**, **15**, as well as tweezer **9** have been characterized by X-ray crystal-structure analysis. Although tris(imines) **20**, **24** derived from 1,3,5-triaminobenzene (**18**) and tris(4-aminophenyl)amine (**23**) could be obtained similarly by molecular sieve-catalyzed condensation, the corresponding triscyclization could not be achieved. However, by attaching preformed indolizino[3,4-*b*]quinoline subunits **25** and **31** to an aromatic core, the bidentate receptors **30**, **33** and the tentacle molecule **28** were accessible.

The design of novel artificial receptor molecules has stimulated much research effort since the discovery of the selective cation-complexing ability of crown ethers and cryptands by Pedersen[1], Lehn[2] and Cram[3]. In order to achieve efficient molecular recognition and to use specific host-guest interactions for applications in catalysis and analytical devices, diverse types of receptor structures have been developed[4]. In particular, molecular clefts[5] and molecular tweezers[6][7] seem to be attracting considerable attention as synthetic targets. One reason for this is that molecular tweezers contain rigid substructures with suitable binding sites that allow strong non-covalent interactions with specific types of guest molecules possessing complementary donor and/or acceptor functionalities. In addition, molecular tweezers are sufficiently flexible to be able to adjust their binding interactions to accommodate different guest molecules, so that the artificial receptor is capable of recognizing a whole class of structurally related compounds rather than a single substrate[8]. In contrast to the large number of nitrogen-containing receptors with either flexible aza-crowns or rigid oligopyridine and aromatic polyaza systems[9], only those aliphatic azapolycycles derived from Tröger's base[10] are known in the literature. However, in order to explore the scope of azapolycyclic skeletons as artificial receptors in general, we thought it desirable to synthesize a series of related receptor structures differing in their flexibility, but with a common rigid binding pocket. Ultimately, this would allow us to study the binding properties of a particular receptor subsystem with respect to shape and functional-group complementarity and flexibility. Thus, it might be possible to quantify the importance of "key and lock"[11] versus "induced fit"[12] features of host-guest interactions. Based on our previously established diastereoselective synthesis of the indolizino[3,4-*b*]quinoline skeleton **1** via Lewis acid catalyzed cyclization of the corresponding *N*-arylimine[13], we felt that this structural motif should be well suited to serve as a potential chiral receptor moiety, e.g. for the optical resolution of carboxylic acids, owing to the presence of two nitrogen atoms with different basicities. Thus, we planned to incorporate this substructure either into rigid concave systems **2**, semi-rigid tweezers **3**, **4**, or flexible tentacle molecules **5** (Scheme 1). We report herein on our synthetic efforts towards this goal.

A convenient synthesis of a flexible polydentate receptor such as **3**−**5** requires either the coupling of two (or more) receptor subunits, formed in a previous step, via a spacer, or the simultaneous build-up of both subunits bound to the spacer. With regard to the synthesis of enantiomerically pure receptors, it should be borne in mind that the latter approach, although it is more concise, requires a higher level of stereocontrol than the first one. Following the latter strategy, we attempted the synthesis of tweezer **4**, having a methylene spacer. As shown in Scheme 2, bis(4-aminophenyl)methane (**6**) was treated with 4-Å molecular sieves and 2 equiv. of (*S*)-*N*-(4-methyl-3-pentenyl)prolinal (**7**), which was prepared in two steps from (*S*)-prolinol[14], to give the bis(imine) **8**. After removal of the molecular sieves by filtration, the bis(imine) **8** was not further isolated or purified, but was immediately treated with 2.5 equiv. of $EtAlCl_2$ at −78°C. Reaction was allowed to proceed for 1 d at room

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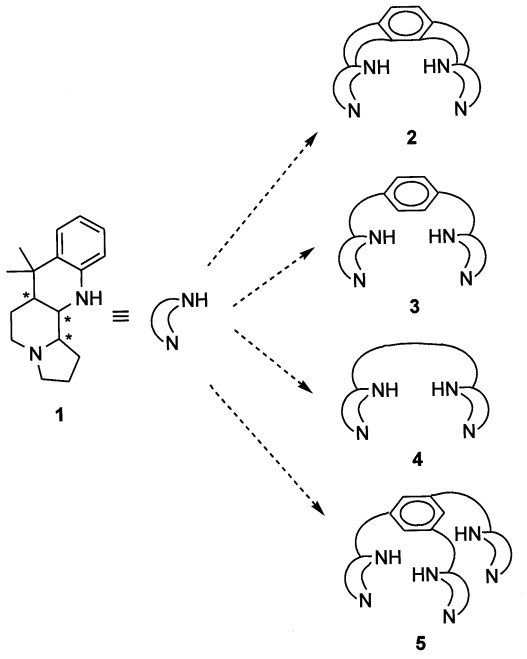
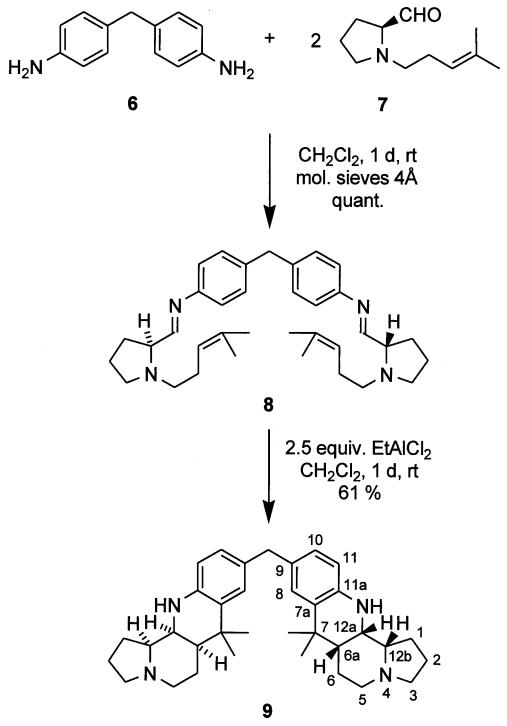
Scheme 1



Scheme 2

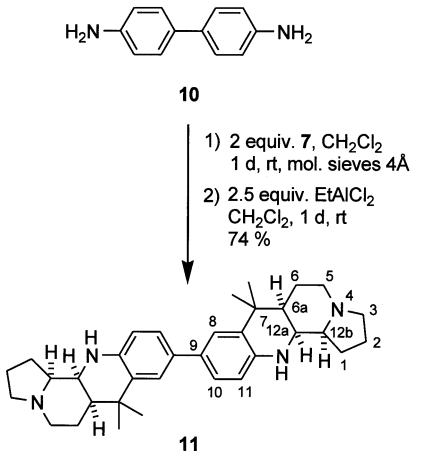


temperature. Although it had previously been found in our laboratory that aromatic diamines such as **6** or 1,5-diaminonaphthalene can be condensed with 3,3,7-trimethyl-6-octenal to give the bis(imines), which cleanly undergo a Lewis acid catalyzed biscyclization[15], we were concerned about the diastereoselectivity of the biscyclization of **8**. It was felt that the two imino moieties might have disturbed each other during Lewis acid complexation, thereby leading to a decrease in the diastereoselectivity. However, after basic hydrolysis and chromatographic purification, bis(indolizino[3,4-*b*]quinolyl)methane (**9**) was obtained in 61% yield as a single diastereomer. Analytical HPLC of the crude product showed, to our delight, that the biscyclization had proceeded with 92% *de*[16]. An X-ray crystal-structure determination of **9** confirmed the all-*cis* configuration (Figure 1)[17], which had been tentatively assigned on the basis of NMR experiments[18].

Figure 1. X-ray crystal structure of compound **9** (one of two almost identical molecules is shown)

Chelation control is still operative even when the two arylamines are connected more directly, as was demonstrated by the conversion of 4,4′-diamino-1,1′-biphenyl (**10**) to the 9,9′-bi(indolizino[3,4-*b*]quinoline) (**11**) (Scheme 3). Again, high diastereoselectivity (> 95% *de*) was obtained.

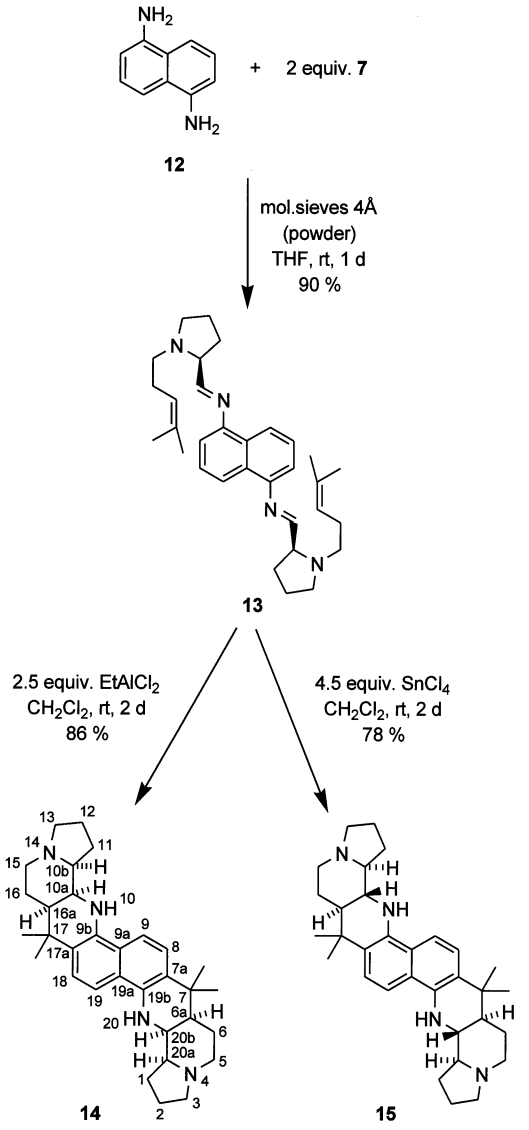
Scheme 3



In order to prepare completely rigid receptors of type **2**, 1,5-diaminonaphthalene (**12**) and aldehyde **7** were condensed to give the bis(imine) **13** in 90% yield (Scheme 4). Even in this case, with the two amino groups being attached to the same aromatic system, the biscyclization of **13** proceeded with high diastereoselectivity. The all-*cis*-configured rigid indolizino[7′,8′:2,3]quinolino[8,7-*h*]indolizino[8,7-*b*]-quinoline **14** was obtained when $EtAlCl_2$ was used for the biscyclization (diastereomeric ratio **14**/**15** = 98:2), while the corresponding all-*trans* product **15** was isolated from the $SnCl_4$-induced reaction (**14**/**15** = 5:95)[19]. X-ray crystal structures of compounds **14** (Figure 2) and **15** (Figure 3) not only proved the relative configurations[17], but also showed that the two products differ in their three-dimensional appearance. Whereas **15** is almost flat, with two receptor moieties on opposite sides of the polycyclic system,

compound **14** has a concave structure with two receptor sites being located inside one large binding pocket. The diameter of the cavity is approximately 6 Å.

Scheme 4



Our next objective was to test the applicability of the triscyclization in the preparation of rigid bowl-shaped receptors by using tris(imine) **20** as a model system (Scheme 5). The required 1,3,5-triaminobenzene (**18**) was prepared in two steps from commercially available 3,5-dinitroaniline (**16**)[20]. Oxidation of **16** with dioxirane[21] gave 1,3,5-trinitrobenzene (**17**)[22]. Clean and quantitative reduction of **17** was achieved by a modification of Gill's method[23], i.e. using Raney Ni in ethyl acetate at 40°C under 40 bar of hydrogen. Although tris(imine) **20** could easily be obtained by condensation of **18** with 3 equiv. of **19**, the attempted triscyclization was not successful[24]. It seems probable that the steric hindrance at C-2, C-4 and C-6 of the aromatic ring prevents the attack of the *gem*-dimethyl-substituted alkene.

Figure 2. (a) X-ray crystal structure of compound **14** (one of two almost identical molecules is shown) and (b) view from the front side (hydrogen atoms are omitted for clarity)

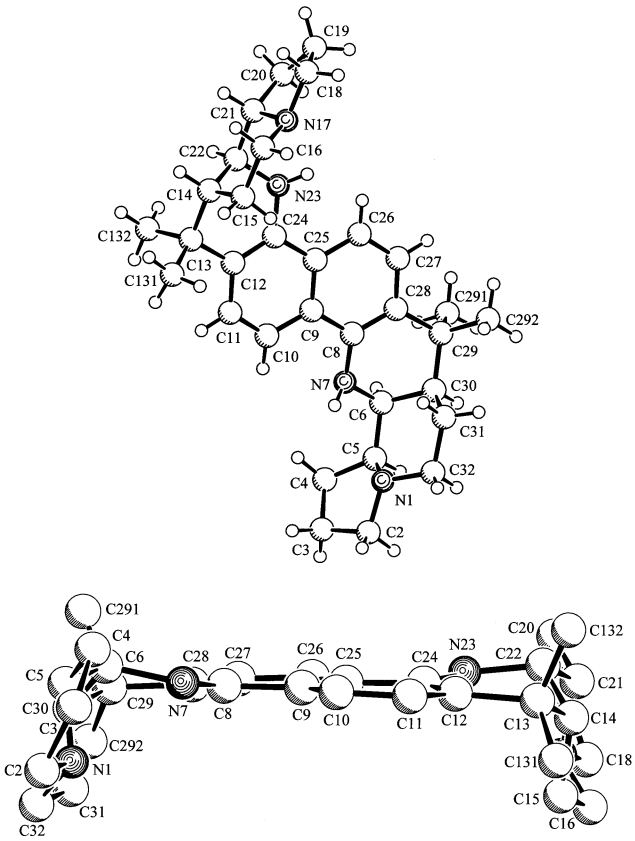
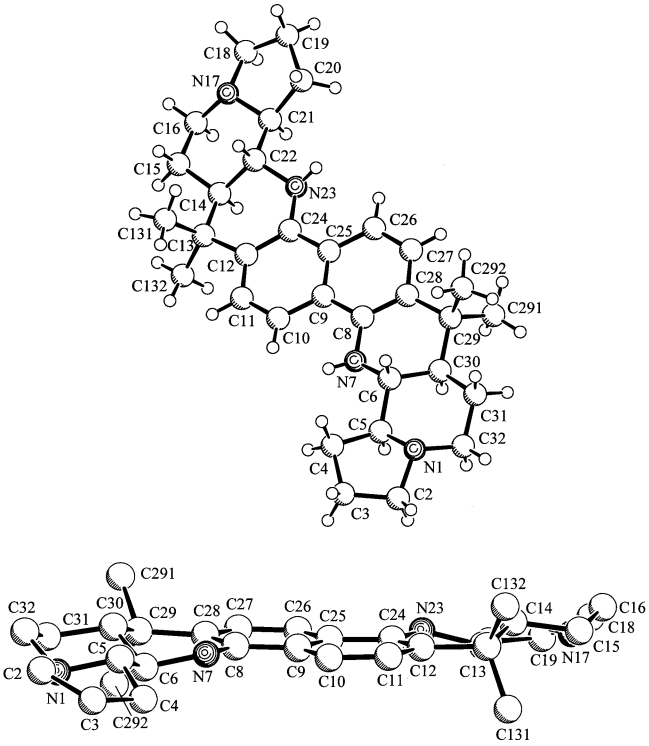
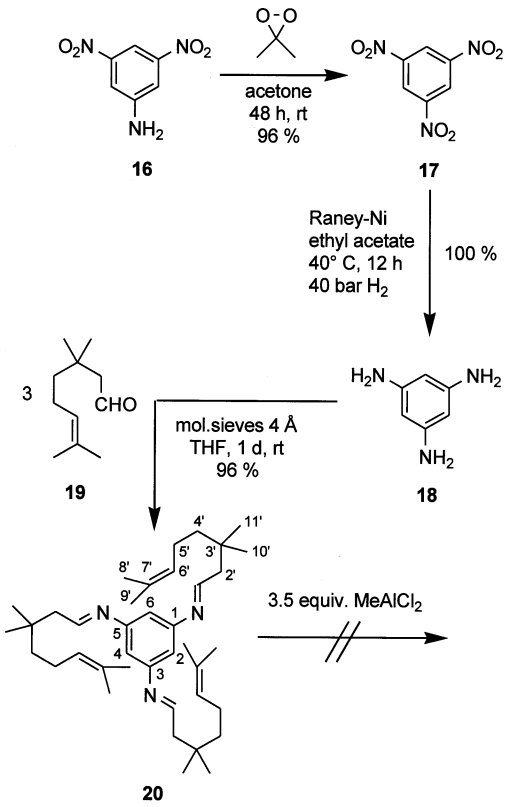


Figure 3. (a) X-ray crystal structure of **15** (one of two almost identical molecules is shown) and (b) view from the front side (hydrogen atoms are omitted for clarity)

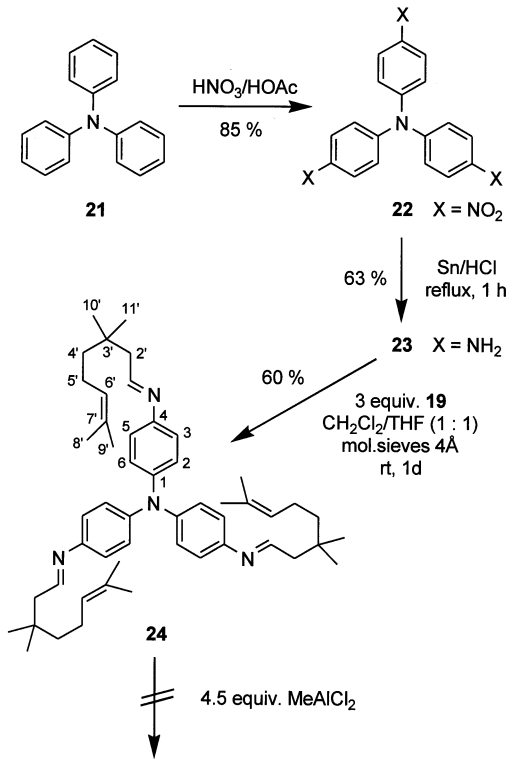


Scheme 5

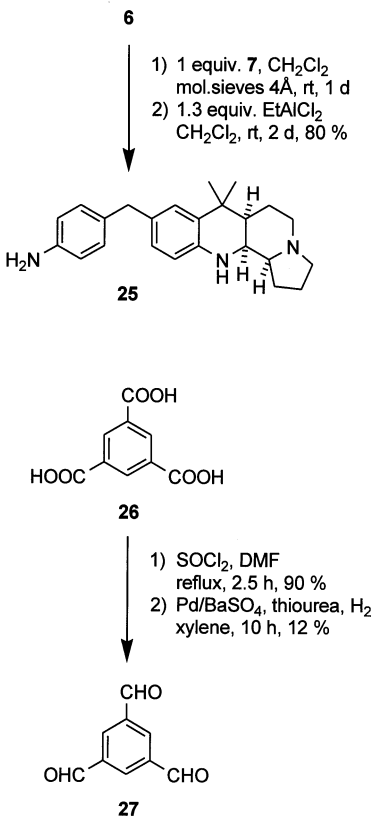


In a different approach, the triscyclization of a more flexible and less sterically congested tris(imine) was envisaged.

Scheme 6



Scheme 7

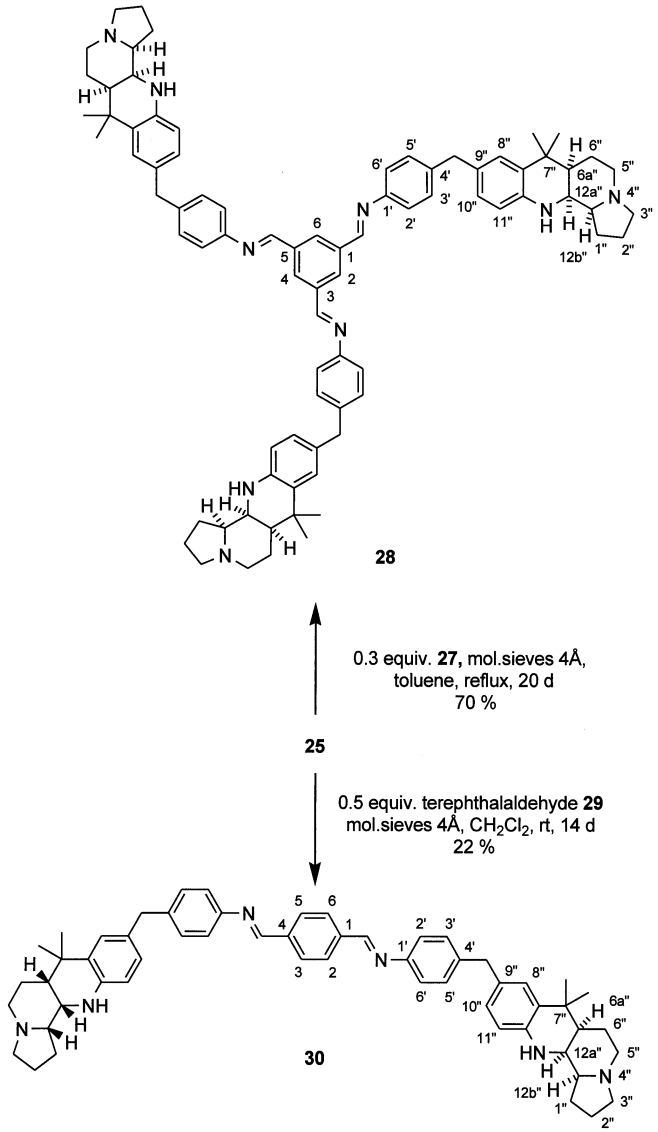


As shown in Scheme 6, triphenylamine (**21**) was treated with a mixture of nitric acid/acetic acid and the resulting trinitro derivative **22** was reduced with Sn/HCl to give tris(4-aminophenyl)amine (**23**) in 54% overall yield[25]. Although the corresponding tris(imine) **24** could be prepared from **23**, the attempted Lewis acid induced triscyclization of **24** was again unsuccessful[24].

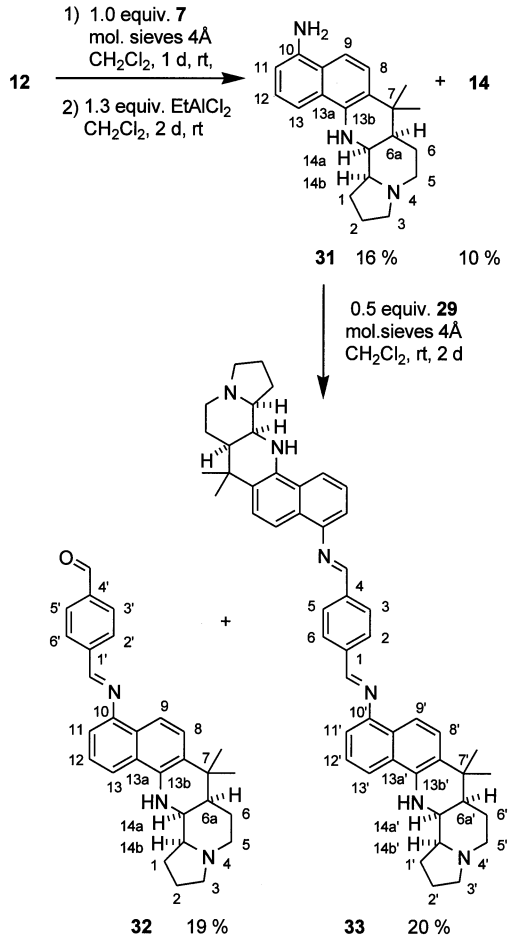
In order to increase the flexibility of the receptor and to avoid the problems of the triscyclization step, we adopted a different strategy. We decided to assemble the tentacle receptor from already functionalized indolizino[3,4-*b*]quinoline moieties and a central 1,3,5-benzenetris(aldehyde) core. The required indolizino[3,4-*b*]quinoline derivative **25** was obtained by monocyclization of bis(4-aminophenyl)methane (**6**) with 1 equiv. of aldehyde **7** in 80% overall yield (> 95% *de*, Scheme 7). The core molecule **27** was isolated in low yield after converting trimesic acid (**26**) to the acid chloride with $SOCl_2$ and catalytic amounts of DMF, and then subjecting this to Rosenmund reduction[26]. The condensation of tris(aldehyde) **27** with 3 equiv. of indolizino[3,4-*b*]quinoline (**25**) required forcing conditions (Scheme 8). After refluxing the mixture for 3 weeks in toluene in the presence of 4-Å molecular sieves, the tentacle molecule **28** was isolated in 70% yield. When terephthalaldehyde (**29**) was treated with **25** under milder conditions, employing 4-Å molecular sieves in CH_2Cl_2 at room temperature, only 22% of the corresponding bis(imine) **30** was isolated.

Unfortunately, the synthesis of receptor **33** was hampered by several problems (Scheme 9). Despite various attempts,

Scheme 8



Scheme 9



a clean imine formation/monocyclization sequence of **12** could not be achieved and a mixture of the desired 10-aminobenzo[*h*]indolizino[8,7-*b*]quinoline (**31**, 16%, > 95% *de*) and the concave biscyclization product **14** (10%) was obtained. Furthermore, treatment of **31** with terephthalaldehyde (**29**) gave a mixture of monoaldehyde **32** (19%) and bis(imine) **33** (20%). Even under the forcing conditions of using excess amine **31**, the formation of bis(imine) **33** could not be driven to completion.

In conclusion, the novel molecular tweezer **9** and cavitand **14** with two indolizino[3,4-*b*]quinoline subunits have been obtained in a highly diastereoselective fashion by a two-step imine condensation/double cyclization procedure. In contrast, the synthesis of a more flexible tentacle-like receptor **28**, bearing three indolizino[3,4-*b*]quinoline moieties (as well as the corresponding systems **30**, **33** with two indolizino[3,4-*b*]quinolines), required the condensation of preformed subunits with a central core. The binding properties of the novel receptors are currently under investigation.

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Experimental Section

General: All reactions were carried out under argon using standard Schlenk techniques. Solvents were dried and deoxygenated by standard procedures. − Analytical TLC was performed on precoated Merck Si 254 F plates (0.25 mm thickness) and the products were visualized by spraying with a solution of phosphomolybdic acid in EtOH (5%, v/v). Flash chromatography[27] was carried out with Merck silica gel 60 (230−400 mesh). − NMR spectra: Bruker AC 200 P (^{1}H: 200 MHz; ^{13}C: 50 MHz), Bruker ARX 300 (^{1}H: 300 MHz; ^{13}C: 75 MHz) and Varian Unity Plus (^{1}H: 600 MHz; ^{13}C: 150 MHz). Multiplets in the ^{13}C-NMR spectra were assigned with the aid of DEPT and APT experiments. − Melting points (uncorrected): Gallenkamp melting-point apparatus. − IR spectra: Nicolet 5DXC FT-IR spectrometer. − Optical rotations (1-dm cells, 1-ml capacity, room temp.): Perkin-Elmer Model 241 polarimeter. − Mass spectra: Finnigan Model MAT 312 (EI), Finnigan Model MAT 8230 (CI, reacting gas: NH_3). − GC MS: Varian GC 3400 coupled with a Varian Saturn 2 (ion trap) or with a Finnigan MAT 8230 (EI). − GC analysis: HP5 fused-silica capillary column (ID 0.32 mm, length 25 m), HPU2 fused-silica capillary column (ID 0.2 mm, length 25 m). Temperature program: 220°C with 1°C

min^{-1} increments up to 280°C, then isothermal for 20 min. − The following compounds were prepared according to literature procedures: (*S*)-*N*-(4-methyl-3-pentenyl)prolinal (**7**)[13b], 1,3,5-trinitrobenzene (**17**)[21], tris(4-nitrophenyl)amine (**22**)[28], 1,3,5-triformylbenzene (**27**)[26]. − Analytical HPLC was carried out with a Jasco PU-980 gradient pump and a Jasco 875 UV detector at 300 nm, coupled with a Shimadzu C-R6A Chromatopac integrator. Preparative HPLC was performed on a Knauer Compact HPLC with a Knauer variable-wavelength detector at 300 nm. The following conditions were used for HPLC: Analytical: Jasco Si 100 column (5 μm, 4.6 × 250 mm), flow rate: 1.0 ml min^{-1}. Preparative: Jasco Si 100 column (10 μm, 25 × 250 mm), flow rate: 15 ml min^{-1}.

(6aS,12aS,12bS)-Bis(1,2,3,5,6,6a,7,12,12a,12b-decahydro-7,7-dimethylindolizino[3,4-b]quinolyl)methane (**9**): To a solution of aldehyde **7** (4.53 g, 25.0 mmol) and bis(4-aminophenyl)methane (**6**, 2.48 g, 12.5 mmol) in dichloromethane (100 ml) was added powdered 4-Å molecular sieves (25.0 g) and the mixture was stirred for 1 d at room temperature. After filtration through Celite, the solvent was removed in vacuo, the crude product was redissolved in dichloromethane (250 ml), and the resulting solution was cooled to −78°C. $EtAlCl_2$ (31.3 ml, 31.3 mmol, 1 M solution in hexane) was added dropwise over a period of 45 min. The cooling bath was then removed and the mixture was stirred for 1 d at room temperature, before being carefully poured under ice-cooling in 2 N NaOH solution (200 ml). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 250 ml). The combined organic layers were dried with $MgSO_4$, concentrated to dryness, and the residue was subjected to HPLC (eluent: hexane/MeOH/triethylamine, 98:1:1) to give a 96:4 mixture of diastereomers[16] as the crude product. Purification by flash chromatography (hexanes/ethyl acetate/triethylamine, 80:10:10) gave 4.00 g (7.63 mmol, 61%) of a yellow solid; m.p. 148°C; $[\alpha]_D^{22}$ = +152.0 (*c* = 1.00 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3380 cm^{-1}, 3013, 2963, 2933, 1612, 1501, 1295. − ^{1}H NMR (600 MHz, C_6D_6): δ = 7.23 (d, *J* = 1.8 Hz, 2 H, 8-H), 6.98 (dd, *J* = 1.8/7.8 Hz, 2 H, 10-H), 6.55 (d, *J* = 7.8 Hz, 2 H, 11-H), 3.99 (s, 2 H, CH_2), 3.73 (br. s, 2 H, NH), 3.53 (s, 2 H, 12a-H), 2.88−2.80 (m, 4 H, 3-H_{eq}, 5-H_{eq}), 1.82−1.22 (m, 20 H, 1-H, 2-H, 3-H_{ax}, 5-H_{ax}, 6-H, 6a-H, 12b-H), 1.22, 1.23 (s, 12 H, 13-H, 14-H). − ^{13}C NMR (75 MHz, C_6D_6): δ = 141.2 (C-11a), 131.4, 129.5 (C-8a, C-9), 127.6, 126.8, 116.4 (C-8, C-10, C-11), 67.2 (C-12b), 54.3 (C-3), 52.6 (C-5), 47.4, 46.8, 45.0 (CH_2, C-6a, C-12a), 35.7 (C-7), 33.4 (C-13), 26.5 (C-14), 25.2, 23.3, 21.6 (C-1, C-2, C-6). − MS (70 eV); *m/z* (%): 524 (16) [M^+], 509 (12) [$M^+ - CH_3$], 440 (15), 96 (25), 84 (100), 69 (23). − $C_{35}H_{48}N_4$: calcd. 524.3879; found 524.3870 (MS); calcd. C 80.15, H 9.16, N 10.69; found C 80.14, H 8.80, N 10.70. − X-ray crystal-structure analysis of **9**: $C_{35}H_{48}N_4$, M_r = 524.77, crystal size 0.7 × 0.4 × 0.3 mm, *a* = 12.762(1), *b* = 11.179(1), *c* = 22.343(1) Å, β = 102.24(1)°, *V* = 3115.1(4) $Å^3$, $\rho_{calcd.}$ = 1.119 mg m^{-3}, *T* = 293 K, empirical absorption correction based on Ψ-scan data (0.958 < *C* < 0.999), *Z* = 4, monoclinic, space group *P*2(1) (no. 4), λ = 1.54178 Å, ω/2Θ scans, 6977 reflections collected (+*h*, +*k*, ±*l*), [(sinΘ)/λ] = 0.62 $Å^{-1}$, 6675 independent and 5426 observed reflections [$I > 2\sigma(I)$], 724 refined parameters, R = 0.042, ωR^2 = 0.120, max. residual electron density 0.18 (−0.14) e $Å^{-3}$. Data were collected with an Enraf-Nonius CAD4 diffractometer, programs used: MolEN, SHELXS-86, SHELXL-93, SCHAKAL-92. See ref.[17].

(6aS,12aS,12bS)-9,9′-Bi(1,2,3,5,6,6a,7,12,12a,12b-decahydro-7,7-dimethylindolizino[3,4-b]quinoline) (**11**): According to the procedure described for **9**, cyclization of **7** (4.53 g, 25.0 mmol) and 4,4′-diamino-1,1′-biphenyl (**10**, 2.30 g, 12.5 mmol) gave after workup a crude product consisting of a mixture of diastereomers (> 95:5 by ^{1}H NMR)[16]. Flash chromatography yielded 4.72 g (9.25 mmol, 74%) of an orange solid; m.p. 172°C; $[\alpha]_D^{22}$ = +171.0 (*c* = 1.00 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3414 cm^{-1}, 3366, 3021, 2959, 2874, 2788, 1611, 1490, 1280, 1262. − ^{1}H NMR (600 MHz, C_6D_6): δ = 7.65 (d, *J* = 2.4 Hz, 2 H, 8-H), 7.44 (dd, *J* = 2.4/7.8 Hz, 2 H, 10-H), 6.63 (d, *J* = 7.8 Hz, 2 H, 11-H), 3.86 (br. s, 2 H, NH), 3.59 (s, 2 H, 12a-H), 2.91−2.85 (m, 4 H, 3-H_{eq}, 5-H_{eq}), 1.87−1.28 (m, 20 H, 1-H, 2-H, 3-H_{ax}, 5-H_{ax}, 6-H, 6a-H, 12b-H), 1.30, 1.27 (s, 12 H, 13-H, 14-H). − ^{13}C NMR (75 MHz, C_6D_6): δ = 141.8 (C-11a), 132.6, 129.6 (C-8a, C-9), 125.6, 124.6, 116.4 (C-8, C-10, C-11), 67.2 (C-12b), 54.3 (C-3), 52.6 (C-5), 47.4 (C-12a), 45.0 (C-6a), 35.8 (C-7), 33.3 (C-13), 26.4 (C-14), 25.2, 23.3, 21.6 (C-1, C-2, C-6). − MS (70 eV); *m/z* (%): 510 (28) [M^+], 495 (20) [$M^+ - CH_3$], 427 (22), 426 (23), 398 (22), 149 (37), 97 (42), 84 (100), 69 (44). − $C_{34}H_{46}N_4$ (510.77): calcd. C 79.95, H 9.08, N 10.97; found C 79.80, H 9.20, N 11.00.

(S,S)-N,N′-Bis[N-(4-methyl-3-pentenyl)-2-pyrrolidinylmethylene]naphthalene-1,5-diamine (**13**): To a solution of (*S*)-*N*-(4-methyl-3-pentenyl)prolinal (**7**, 4.00 g, 22.0 mmol) and 1,5-diaminonaphthalene **12** (1.70 g, 11.0 mmol) in THF (50 ml) was added powdered 4-Å molecular sieves. After stirring for 1 d at room temp., the mixture was filtered through Celite and the solvent was removed in vacuo to yield 4.80 g (90%) of a brown oil, which was immediately used for the cyclization without further purification; $[\alpha]_D^{22}$ = −45.8 (*c* = 1.00 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 2965 cm^{-1}, 2871, 2800, 1653, 1583, 1532, 783. − ^{1}H NMR (200 MHz, C_6D_6): δ = 8.41 (d, *J* = 8.6 Hz, 2 H, 2-H, 6-H), 7.75 (d, *J* = 6.4 Hz, 2 H, HC=N), 7.30 (dd, *J* = 8.6/7.0 Hz, 2 H, 3-H, 7-H), 6.84 (d, *J* = 7.0 Hz, 2 H, 4-H, 8-H), 5.25 (m, 2 H, 3″-H), 3.34−1.70 (m, 22 H), 1.61, 1.51 (s, 12 H, 5″-H, 6″-H). − ^{13}C NMR (50 MHz, C_6D_6): δ = 168.4 (C=N), 149.5 (C-1, C-5), 132.1, 129.5, 126.0, 122.9, 121.8, 113.8 (C-2, C-3, C-4, C-6, C-7, C-8, C-9, C-10, C-3″, C-4″), 68.8, 55.3, 54.1 (C-1″, C-2′, C-5′), 29.4, 28.4, 25.3, 23.8, 17.2 (C-3′, C-4′, C-2″, C-5″, C-6″). − MS (70 eV); *m/z* (%): 484 (8) [M^+], 252 (27), 169 (55), 152 (86), 84 (62), 70 (100). − $C_{32}H_{44}N_4$: calcd. 484.3565; found 484.3578 (MS).

(6aS,10aS,10bS,16aS,20aS,20bS)-1,2,3,5,6,6a,7,10,10a,10b,11,12,13,15,16,16a,17,20,20a,20b-Eicosahydro-7,7,17,17-tetramethylindolizino[7′,8′:2,3]quinolino[8,7-h]indolizino[8,7-b]quinoline (**14**): To a solution of bis(imine) **13** (4.84 g, 10.0 mmol) in CH_2Cl_2 (200 ml), $EtAlCl_2$ (25.0 ml, 25.0 mmol, 1 M solution in hexane) was added dropwise at −78°C over a period of 30 min. The cooling bath was then removed and the solution was stirred for 2 d at room temp. The mixture was then poured into an ice-cooled 2 N NH_4F solution (200 ml). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 ml). After drying of the combined organic layers with $MgSO_4$ and evaporation of the solvent, the crude product was filtered through SiO_2 (eluent: hexanes/MeOH/triethylamine, 100:3:1) to give 4.16 g (86%) of a violet oil as a mixture of diastereomers (**14**/**15** = 98:2 by HPLC, eluent: hexane/MeOH/triethylamine, 98:1:1). Preparative HPLC (eluent: hexane/MeOH/triethylamine, 94:3:3), followed by slow evaporation of the solvent gave 3.15 g (65%) of red-brown needles; m.p. > 150°C (dec.); $[\alpha]_D^{22}$ = +339.5 (*c* = 1.00 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3430 cm^{-1}, 2964, 2930, 2860, 1601, 1509, 1463, 1438. − ^{1}H NMR (600 MHz, C_6D_6): δ = 7.67 (d, *J* = 8.4 Hz, 2 H, 8-H, 18-H), 7.36 (d, *J* = 8.4 Hz, 9-H, 19-H), 4.40 (d, *J* = 5.4 Hz, 2 H, NH), 3.64 (d, *J* = 5.4 Hz, 2 H, 10a-H, 20a-H), 2.89−2.80 (m, 4 H, 3-H_{eq}, 5-H_{eq}, 13-H_{eq}, 15-H_{eq}), 2.17−2.10 (m, 2 H, 10b-H, 20b-H), 1.91−1.86 (m, 4 H, 3-H_{ax}, 5-H_{ax}, 13-H_{ax}, 15-H_{ax}), 1.78−1.07 (m, 14 H, 1-H, 2-H, 6-H, 6a-H, 11-H, 12-H, 16-H, 16a-H), 1.31 (s, 6 H, 21-H, 23-H), 1.30 (s, 6 H, 22-H, 24-H). − ^{13}C NMR (75 MHz, C_6D_6): δ = 137.8 (C-9b, C-19b), 125.0, 124.1 (C-8a, C-9a, C-17a, C-19a), 123.9, 111.9 (C-8, C-9, C-18, C-19),

67.3 (C-10b, C-20b), 54.3, 52.5 (C-3, C-5, C-13, C-15), 47.6 (C-10a, C-20a), 44.5 (C-6a, C-16a), 35.7 (C-7, C-17), 33.5, 27.0 (C-21, C-22, C-23, C-24), 25.6, 23.2, 21.9 (C-1, C-2, C-6, C-11, C-12, C-16). − MS (70 eV); *m/z* (%): 484 (75) [M^+], 469 (46) [$M^+ - CH_3$], 400 (42), 242 (48), 163 (52), 96 (57), 84 (100) [$C_5H_{10}N^+$], 69 (66). − $C_{32}H_{44}N_4$: calcd. 484.3565; found 484.3554 (MS); calcd. C 79.34, H 9.09, N 11.57; found C 79.47, H 9.28, N 11.25. − X-ray crystal-structure analysis of **14**: $C_{32}H_{44}N_4$, M_r = 484.71, crystal size 0.6 × 0.4 × 0.2 mm, a = 10.903(1), b = 11.601(2), c = 22.973(1) Å, β = 103.27(1)°, V = 2828.2(6) Å^3, $\rho_{calcd.}$ = 1.138 mg m^{-3}, T = 293 K, empirical absorption correction based on Ψ-scan data (0.936 < C < 0.999), Z = 4, monoclinic, space group $P2(1)$ (no. 4), λ = 1.54178 Å, ω/2Θ scans, 6222 reflections collected (±h, +k, −l), [(sinΘ)/λ] = 0.62 Å^{-1}, 6071 independent and 5540 observed reflections [$I > 2\sigma(I)$], 670 refined parameters, R = 0.041, ωR^2 = 0.118, max. residual electron density 0.26 (−0.15) e Å^{-3}. Data were collected with an Enraf-Nonius CAD4 diffractometer, programs used: MolEN, SHELXS-86, SHELXL-93, SCHAKAL-92. See ref.[17].

(6aS,10aR,10bS,16aS,20aR,20bS)-1,2,3,5,6,6a,7,10,10a,10b,11,12,13,15,16,16a,17,20,20a,20b-Eicosahydro-7,7,17,17-tetramethylindolizino[7′,8′:2,3]quinolino[8,7-h]indolizino[8,7-b]quinoline (**15**): According to the same procedure as described for **7**, but using $SnCl_4$ (45 ml, 45.0 mmol of a 1 M solution in CH_2Cl_2) instead of $EtAlCl_2$ gave 3.78 g (78%) of a violet oil as a mixture of diastereomers (**14/15** = 5:95 by HPLC, eluent: hexane/MeOH/triethylamine, 98:1:1). Preparative HPLC (eluent: hexane/MeOH/triethylamine, 94:3:3) followed by slow evaporation of the HPLC solvent gave 2.61 g (54%) of red needles; m.p. > 250°C (dec.); $[\alpha]_D^{22}$ = −445.0 (c = 1.00 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 2982 cm^{-1}, 2932, 2863, 2787, 1515, 1419, 1359. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.32 (d, J = 8.8 Hz, 2 H, 8-H, 18-H), 7.02 (d, J = 8.8 Hz, 2 H, 9-H, 19-H), 4.35 (br. s, 2 H, NH), 3.17−3.01 (m, 6 H, 3-H_{eq}, 5-H_{eq}, 10a-H, 13-H_{eq}, 15-H_{eq}, 20a-H), 2.22−1.62 (m, 20 H, 1-H, 2-H, 3-H_{ax}, 5-H_{ax}, 6-H, 6a-H, 10b-H, 11-H, 12-H, 13-H_{ax}, 15-H_{ax}, 16-H, 16a-H, 20b-H), 1.36, 1.17 (s, 12 H, 21-H, 22-H, 23-H, 24-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 137.4 (C-9b, C-19b), 124.9, 121.7 (C-8a, C-9a, C-17a, C-19a), 124.1, 108.7 (C-8, C-9, C-18, C-19), 69.3 (C-10b, C-20b), 54.8 (C-10a, C-20a), 53.9, 52.2 (C-3, C-5, C-13, C-15), 46.1 (C-6a, C-16a), 34.6 (C-7, C-17), 27.3, 27.2 (C-21, C-22, C-23, C-24), 28.0, 24.6, 21.5 (C-1, C-2, C-6, C-11, C-12, C-16). − MS (70 eV); *m/z* (%): 484 (66) [M^+], 469 (60) [$M^+ - CH_3$], 400 (54), 163 (56), 122 (67), 96 (77), 84 (100) [$C_5H_{10}N^+$], 69 (66), 55 (74). − $C_{32}H_{44}N_4$: calcd. 484.3565; found 484.3554 (MS); calcd. C 79.34, H 9.09, N 11.57; found C 79.43, H 9.24, N 11.33. − X-ray crystal-structure analysis of **15**: $C_{32}H_{44}N_4$, M_r = 484.71, crystal size 0.5 × 0.25 × 0.1 mm, a = 6.999(1), b = 11.959(2), c = 32.930(5) Å, β = 93.74(1)°, V = 2750.4(7) Å^3, $\rho_{calcd.}$ = 1.171 mg m^{-3}, T = 223 K, empirical absorption correction based on Ψ-scan data (0.971 < C < 0.999), Z = 4, monoclinic, space group $P2(1)$ (no. 4), λ = 1.54178 Å, ω/2Θ scans, 5980 reflections collected (±h, +k, −l), [(sinΘ)/λ] = 0.62 Å^{-1}, 5882 independent and 3785 observed reflections [$I > 2\sigma(I)$], 669 refined parameters, R = 0.050, ωR^2 = 0.119, max. residual electron density 0.16 (−0.17) e Å^{-3}. Data were collected with an Enraf-Nonius CAD4 diffractometer, programs used: MolEN, SHELXS-86, SHELXL-93, SCHAKAL-92. See ref.[17].

1,3,5-Triaminobenzene (**18**): To a solution of 1,3,5-trinitrobenzene (**17**, 100 mg, 0.47 mmol) in ethyl acetate (10 ml) was added Raney Ni (3.00 g) and the mixture was stirred for 12 h at 40°C under 40 bar of hydrogen in a steel autoclave. The mixture was then filtered through a fritted funnel under argon into a Schlenk flask. Upon cooling of the filtrate overnight in a freezer, 58 mg (100%) of colorless needles was obtained; m.p. 112°C. Analytical data were in accordance with those reported in ref.[23].

N,N′,N″-Tris(3′,3′,7′-trimethyl-6′-octenylidene)-1,3,5-triaminobenzene (**20**): A solution of 1,3,5-triaminobenzene (**18**, 123 mg, 1.00 mmol) and 3,3,7-trimethyl-6-octenal (**19**, 504 mg, 3.00 mmol) in THF (50 ml) was treated with powdered 4-Å molecular sieves (3.00 g) and the mixture was stirred at room temp. for 1 d. After filtration through Celite, the solvent was removed in vacuo to give 550 mg (0.96 mmol, 96%) of a brown oil. − IR (KBr): $\tilde{\nu}$ = 2940 cm^{-1}, 2923, 2875, 1651, 1592, 1507, 1385, 1327. − ^{1}H NMR (200 MHz, C_6D_6): δ = 7.86 (t, J = 5.6 Hz, 3 H, HC=N), 6.90 (s, 3 H, 2-H, 4-H, 6-H), 5.20 (m, 3 H, 6′-H), 2.24 (d, J = 5.6 Hz, 6 H, 2′-H), 1.98−1.22 (m, 12 H, 4′-H, 5′-H), 1.63, 1.54 (s, 18 H, 8′-H, 9′-H), 0.87 (s, 18 H, 10′-H, 11′-H). − ^{13}C NMR (50 MHz, C_6D_6): δ = 164.9 (HC=N), 155.1 (C-1), 130.9 (C-6′), 125.0 (C-2), 110.2 (C-7′), 54.5, 48.1, 42.8, 34.0, 27.5, 27.2, 23.1, 17.6 (C-2′, C-3′, C-4′, C-5′, C-8′, C-9′, C-10′, C-11′). − MS (70 eV); *m/z* (%): 573 (17) [M^+], 147 (56), 132 (65), 106 (42), 69 (100), 55 (72). − $C_{39}H_{63}N_3$: calcd. 573.1368; found 573.1352 (MS).

Tris(4-aminophenyl)amine (**23**): A mixture of tris(4-nitrophenyl)-amine (**22**, 3.00 g, 8.00 mmol) and tin granules (27.0 g, 0.41 mol) in 6 N HCl (144 ml) was refluxed for 1 h. After cooling to room temp., the insoluble residue was removed by filtration. The filtrate was diluted with H_2O (90 ml) and washed with Et_2O (3 × 30 ml). The aqueous layer was adjusted to pH = 12 by the addition of 2 N NaOH and then extracted with CH_2Cl_2 (3 × 30 ml). The combined organic layers were dried with KOH and the solvent was removed in vacuo to give 1.50 g (63%) of a purple solid; m.p. 229°C. The analytical data were in accordance with those reported in ref.[25].

4,4′,4″-Tris(3′,3′,7′-trimethyl-6′-octenylideneamino)triphenylamine (**24**): A solution of tris(4-aminophenyl)amine (**23**, 73 mg, 0.25 mmol) in CH_2Cl_2/THF (10 ml, 1:1) was treated with powdered 4-Å molecular sieves (1.00 g) and the mixture was stirred at room temp. for 1 d. After filtration through Celite, the solvent was removed in vacuo to give 108 mg (60%) of a brown oil. − IR (KBr): $\tilde{\nu}$ = 2950 cm^{-1}, 2895, 2857, 1645, 1498, 1315, 1265, 836. − ^{1}H NMR (200 MHz, C_6D_6): δ = 7.83 (t, J = 5.5 Hz, 3 H, HC=N), 7.14−7.00 (m, 12 H, 2-H, 3-H, 5-H, 6-H), 5.15 (m, 3 H, 6′-H), 2.27 (d, J = 5.5 Hz, 6 H, 2′-H), 2.00 (m, 6 H, 5′-H), 1.65, 1.56 (s, 18 H, 8′-H, 9′-H), 1.33−1.24 (m, 6 H, 4′-H), 0.90 (s, 18 H, 10′-H, 11′-H). − ^{13}C NMR (50 MHz, C_6D_6): δ = 162.9 (HC=N), 148.1, 146.2 (C-1, C-4), 130.9 (C-6′), 125.3, 125.0 (C-2, C-3, C-5, C-6), 122.0 (C-7′), 48.2, 42.8, 34.1, 27.6, 25.8, 23.2, 17.6 (C-2′, C-3′, C-4′, C-5′, C-8′, C-9′, C-10′, C-11′). − MS (70 eV); *m/z* (%): 741 [M^+], 590 (31), 575 (24), 342 (23), 149 (38), 85 (54), 69 (100). − $C_{51}H_{72}N_4$: calcd. 740.5757; found 740.5784 (MS).

(6aS,12aS,12bS)-9-(4-Aminobenzyl)-1,2,3,5,6,6a,7,12,12a,12b-decahydro-7,7-dimethyl-indolizino[8,7-b]quinoline (**25**): According to the procedure described for **9**, cyclization of **7** (2.72 g, 15.0 mmol) and bis(4-aminophenyl)methane (**6**, 2.97 g, 15.0 mmol) in the presence of 1.3 equiv. of $EtAlCl_2$ gave after work-up a crude product consisting of a mixture of diastereomers (98:2 by HPLC, eluent: hexane/MeOH/triethylamine, 98:1:1). Flash chromatography on SiO_2 (hexane/$CHCl_3$/triethylamine, 9:3:1 → 5:3:1) yielded 4.30 g (80%) of a pale-yellow solid: m.p. 137°C; $[\alpha]^d22$ = +115.0 (c = 1.00 in CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3416 cm^{-1}, 3352, 3015, 2965, 2788, 1616, 1512, 1502, 1384, 1298, 810, 736. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.95 (m, 3 H, 3′-H, 5′-H, 8-H), 6.75 (dd, J = 8.1/1.8 Hz, 1 H, 10-H), 6.52 (m, 3 H, 2′-H, 6′-H, 11-H), 3.76 (s, 3 H, CH_2, NH), 3.68 (s, 1 H, 12a-H), 3.45 (br. s, 2 H, NH_2), 3.08 (m, 2 H, 3-H_{eq}, 5-H_{eq}), 2.05−1.73 (m, 10 H, 1-H, 2-H, 3-H_{ax}, 5-H_{ax}, 6-H, 6a-H, 12b-H), 1.30, 1.24 (s, 6 H, 13-H, 14-H). − ^{13}C

NMR (50 MHz, $CDCl_3$): δ = 143.9, 140.3, 131.9, 129.9, 129.2, 129.1, 128.5, 126.7, 115.0, 114.9 (C-1′, C-2′, C-3′, C-4′, C-5′, C-6′, C-8, C-8a, C-9, C-10, C-11, C-11a), 66.9 (C-12b), 53.9, 52.3 (C-3, C-5), 46.6 (C-12a), 44.8 (C-6a), 40.2 (CH_2), 35.1 (C-7), 33.6, 26.0 (C-13, C-14), 24.7, 22.8, 20.8 (C-1, C-2, C-6). − MS (70 eV); *m/z* (%): 361 (22) [M^+], 346 (10) [$M^+ - CH_3$], 277 (15), 249 (14), 106 (36), 84 (100) [$C_5H_{10}N^+$], 69 (18). − $C_{24}H_{31}N_3$: calcd. 361.2518; found 361.2525 (MS); calcd. C 79.25, H 9.05, N 11.70; found C 79.15, H 9.01, N 11.84.

1,3,5-Tris{(6aS,12aS,12bS)-4-[9-(1,2,3,5,6,6a,7,12,12a,12b-decahydro-7,7-dimethylindolizino[8,7-b]quinolyl)methyl]phenylaminomethylene}benzene (**28**): A solution of 1,3,5-triformylbenzene (**27**, 16.2 mg, 0.10 mmol) and amine **25** (108 mg, 0.30 mmol) in toluene (10 ml) was treated with 4-Å molecular-sieve beads (1.00 g) and the mixture was refluxed for 20 d. After filtration through Celite, the solvent was removed in vacuo to give 83 mg (70%) of a yellow amorphous solid; $[\alpha]_D^{22}$ = +114.3 (*c* = 1.00 in CH_2Cl_2). − IR (KBr): ṽ = 2957 cm^{-1}, 2921, 2870, 1622, 1501. − ^1H NMR (200 MHz, C_6D_6): δ = 8.50 (s, 3 H, 2-H), 8.19 (s, 3 H, HC=N), 7.30−7.10 (m, 15 H, 8″-H, 2′-H, 3′-H, 5′-H, 6′-H), 6.92 (d, *J* = 8.1 Hz, 3 H, 10″-H), 6.68 (d, *J* = 8.1 Hz, 3 H, 11″-H), 3.91−3.85 (m, 9 H, CH_2, NH), 3.53 (s, 3 H, 12a″-H), 2.90−2.75 (m, 6 H, 3″-H_{eq}, 5″-H_{eq}), 1.80−1.10 (m, 30 H, 1″-H, 2″-H, 3″-H_{ax}, 5″-H_{ax}, 6″-H, 6a″-H, 12b″-H), 1.25, 1.22 (s, 18 H, 13″-H, 14″-H). − ^{13}C NMR (50 MHz, C_6D_6): δ = 158.0 (HC=N), 149.9 (C-11a″), 141.6, 141.2, 137.9, 131.4, 130.0, 129.4, 127.5, 126.8, 121.6, 116.3, 115.3 (C-1, C-2, C-1′, C-2′, C-3′, C-4′, C-5′, C-6′, C-8″, C-7a″, C-9″, C-10″, C-11″), 67.3 (C-12b″), 54.3, 52.6 (C-3″, C-5″), 47.4 (C-12a″), 44.8 (C-6a″), 41.6 (CH_2), 35.7 (C-7″), 33.4, 26.5 (C-13″, C-14″), 25.2, 23.3, 21.5 (C-1″, C-2″, C-6″). − TOF MS (LDI); *m/z* (%): 1191 [M^+]. − $C_{81}H_{93}N_9$ (1192.7): calcd. C 81.57, H 7.86, N 10.57; found C 81.38, H 8.02, N 10.60.

1,4-Bis{(6aS,12aS,12bS)-4-[9-(1,2,3,5,6,6a,7,12,12a,12b-decahydro-7,7-dimethylindolizino[8,7-b]quinolyl)methyl]phenylaminomethylene}benzene (**30**): To a solution of terephthalaldehyde (**29**, 67 mg, 0.50 mmol) and indolizino[3,4-*b*]quinoline (**25**, 321 mg, 1.00 mmol) in CH_2Cl_2 was added 4-Å molecular-sieve beads (10 g) and the mixture was stirred for 14 d at room temp. After filtration through Celite and evaporation of the solvent, the crude product was purified by flash chromatography on SiO_2 (eluent: isohexane/$CHCl_3$/triethylamine, 5:3:1) to give 90 mg (22%) of a pale-yellow solid; m.p. >300°C (dec.); $[\alpha]_D^{22}$ = +170.0 (*c* = 0.10 in CH_2Cl_2). − IR (KBr): ṽ = 3036 cm^{-1}, 3017, 2989−2787, 1622, 1602, 1501, 1472, 1384, 1299, 837, 810, 736. − ^1H NMR (300 MHz, C_6D_6): δ = 8.14 (s, 2 H, HC=N), 7.82 (s, 4 H, 2-H, 3-H, 5-H, 6-H), 7.18 (m, 10 H, 8-H, 2′-H, 3′-H, 5′-H, 6′-H), 6.91 (dd, *J* = 8.1/2.0 Hz, 2 H, 8″-H), 6.54 (d, *J* = 8.1 Hz, 2 H, 10″-H), 4.27 (s, 2 H, NH), 3.91 (s, 4 H, CH_2), 3.75 (s, 2 H, 12a″-H), 3.54 (s, 2 H, 12b″-H), 2.87−2.80 (m, 4 H, 3″-H_{eq}, 5″-H_{eq}), 1.90−1.42 (m, 12 H, 3″-H_{ax}, 2″-H, 1″-H, 5″-H_{ax}), 1.25, 1.22 (s, 12 H, 13″-H, 14″-H), 1.15−0.98 (m, 2 H, 6a″-H). − ^{13}C NMR (75 MHz, C_6D_6): δ = 176.0 (HC=N), 158.3 (C-3′, C-5′), 141.6, 141.0, 140.9, 134.2 (C-4′, C-11a″, C-1, C-7a″), 130.1, 126.8, 116.5 (C-8″, C-9″, C-10″), 129.9 (C-1′, C-7a″), 129.2, 121.4 (C-2, C-6, C-2′, C-6′), 67.2 (C-12b″), 54.3 (C-3″), 52.6 (C-5″), 47.4 (C-12a″), 44.9 (C-6a″), 41.5 (CH_2), 35.7 (C-7″), 33.3 (C-13″), 26.5 (C-14″), 25.2 (C-2″), 23.3 (C-6″), 21.6 (C-1″). − MS (70 eV); *m/z* (%): 820 (20) [M^+], 736 (6) [$M^+ - C_5H_{10}N^+$], 111 (17), 97 (36), 84 (100) [$C_5H_{10}N^+$], 57 (65). − $C_{56}H_{64}N_6$: calcd. 820.5192; found 820.5210 (MS); calcd. C 81.91, H 7.86, N 10.23; found C 81.73, H. 7.90, N 9.86.

(6aS,14aS,14bS)-10-Amino-1,2,3,5,6,6a,7,14,14a,14b-decahydro-7,7-dimethylbenzo[h]indolizino[8,7-b]quinoline (**31**): According to the procedure described for **9**, cyclization of **7** (6.55 g, 36.0 mmol) and **12** (5.75 g, 36.0 mmol) gave after work-up and flash chromatography on SiO_2 (hexane/$CHCl_3$/triethylamine, 5:3:1) 1.74 g (3.60 mmol, 10%) of a violet solid (**14**) as the first fraction and 1.80 g (5.60 mmol, 16%) of a red solid (**31**) as the second fraction; m.p. 217°C; $[\alpha]_D^{22}$ = +93.0 (*c* = 0.10 in CH_2Cl_2). − IR (KBr): ṽ = 3343 cm^{-1}, 2989, 2928, 2792, 1622, 1517, 1432, 1401, 786, 734. − ^1H NMR (600 MHz, C_6D_6): δ = 7.39 (d, *J* = 9.0 Hz, 1 H, 9-H), 7.36 (d, *J* = 8.4 Hz, 1 H, 11-H), 7.23 (dd, *J* = 7.2/8.4 Hz, 1 H, 12-H), 7.19 (d, *J* = 9.0 Hz, 1 H, 8-H), 6.70 (d, *J* = 7.2 Hz, 1 H, 13-H), 4.36 (d, *J* = 4.2 Hz, 1 H, NH), 4.07 (br. s, 2 H, NH_2), 3.77 (s, 1 H, 14a-H), 3.10 (dd, *J* = 9.0/8.4 Hz, 1 H, 3-H_{eq}), 3.05 (ddd, *J* = 12.0/2.2/2.4 Hz, 1 H, 5-H_{eq}), 2.21−2.18 (m, 1 H, 14b-H), 2.13−2.06 (m, 2 H, 3-H_{ax}, 2-H_{eq}), 1.98 (ddd, *J* = 12.0/12.0/3.0 Hz, 1 H, 5-H_{ax}), 1.95−1.87 (m, 2 H, 2-H_{ax}, 1-H_{eq}), 1.84−1.80 (m, 1 H, 1-H_{ax}), 1.55 (ddd, *J* = 12.0/3.0/2.4 Hz, 1 H, 6-H_{eq}), 1.41 (s, 3 H, 15-H), 1.38−1.37 (m, 1 H, 6a-H), 1.36 (s, 3 H, 16-H), 1.24 (ddd, *J* = 12.0/12.0/2.2 Hz, 1 H, 6-H_{ax}). − ^{13}C NMR (150 MHz, C_6D_6): δ = 142.3 (C-10), 137.3 (C-13b), 125.3 (C-7a), 125.0 (C-12), 124 (C-9a), 123.8 (C-11), 122.6 (C-13a), 111.7, 110.3 (C-8, C-9), 109.2 (C-13), 67.1 (C-14b), 54.0 (C-3), 52.3 (C-5), 47.2 (C-14a), 44.2 (C-6a), 35.6 (C-7), 33.6, 26.5 (C-15, C-16), 25.2 (C-2), 22.8 (C-6), 21.3 (C-1). − MS (70 eV); *m/z* (%): 321 (62) [M^+], 306 (23) [$M^+ - CH_3$], 237 (14) [$M^+ - C_5H_{10}N^+$], 209 (18), 97 (32), 84 (100) [$C_5H_{10}N^+$], 69 (27), 57 (31). − $C_{21}H_{27}N_3$: calcd. 321.2205; found 321.2196 (MS).

(6aS,14aS,14bS)-10-(4-Formylbenzylidene)amino-1,2,3,5,6,6a,7,14,14a,14b-decahydro-7,7-dimethylbenzo[h]indolizino[8,7-b]-quinoline (**32**): According to the procedure described for **30**, condensation of **29** (201 mg, 1.50 mmol) and **31** (1.29 g, 4.00 mmol) gave after work-up and flash chromatography (isohexane/$CHCl_3$/triethylamine, 8:3:1) 219 mg (0.30 mmol, 20%) of a red solid (**33**) as the first fraction and 128 mg (0.29 mmol, 19%) of a red solid (**32**) as the second fraction; m.p. 110°C; $[\alpha]_D^{22}$ = +66.0 (*c* = 0.10 in CH_2Cl_2). − IR (KBr): ṽ = 3015 cm^{-1}, 2985, 2779, 2748, 2729, 1701, 1621, 1605, 1511, 1502, 1466−1442, 1381−1366, 829, 800, 745. − ^1H NMR (300 MHz, C_6D_6): δ = 9.65 (s, 1 H, HC=O), 8.13 (s, 1 H, HC=N), 8.12 (d, *J* = 8.8 Hz, 1 H, 8-H), 8.04 (d, *J* = 8.3 Hz, 1 H, 11-H), 7.75 (d, *J* = 8.1 Hz, 2 H, 2′-H, 6′-H), 7.55 (d, *J* = 8.1 Hz, 2 H, 3′-H, 5′-H), 7.51 (d, *J* = 8.8 Hz, 1 H, 9-H), 7.26 (dd, *J* = 8.3/7.1 Hz, 1 H, 12-H), 6.79 (d, *J* = 7.1 Hz, 1 H, 13-H), 4.38 (d, *J* = 5.5 Hz, 1 H, NH), 3.59 (s, 1 H, 14a-H), 2.89−2.80 (m, 2 H, 3-H_{eq}, 5-H_{eq}), 2.15−2.05 (m, 1 H, 14b-H), 1.91−1.88 (m, 2 H, 3-H_{ax}, 2-H_{eq}), 1.80−1.45 (m, 5 H, 1-H, 2-H_{ax}, 5-H_{ax}, 6-H_{eq}), 1.28 (s, 3 H, 15-H), 1.27 (s, 3 H, 16-H), 1.20−1.00 (m, 2 H, 6-H_{ax}, 6a-H). − ^{13}C NMR (75 MHz, C_6D_6): δ = 191.3 (HC=O), 158.7 (HC=N), 149.9 (C-4′), 142.0 (C-10), 138.8 (C-13b), 138.0 (C-1′), 129.8, 129.3 (C-2′, C-6′, C-3′, C-5′), 129.3, 127.1, 126.3 (C-7a, C-9a, C-13a), 125.8, 125.3, 120.7 (C-11, C-12, C-13), 115.3, 112.9 (C-8, C-9), 67.6 (C-14b), 54.7, 52.9 (C-3, C-5), 48.1 (C-14a), 44.8 (C-6a), 36.4 (C-7), 34.0 (C-15), 27.2 (C-16), 26.0, 23.6, 22.2 (C-2, C-6, C-1). − MS (70 eV); *m/z* (%): 437 (58) [M^+], 422 (11) [$M^+ - CH_3$], 353 (6) [$M^+ - C_5H_{10}N^+$], 325 (12), 218 (6), 149 (19), 111 (23), 97 (48), 84 (92) [$C_5H_{10}N^+$], 71 (49), 69 (55), 60 (100). − $C_{29}H_{31}N_3O$: calcd. 437.2467; found 437.2459 (MS).

1,4-Bis{(6aS,14aS,14bS)-10-(1,2,3,5,6,6a,7,14,14a,14b-decahydro-7,7-dimethylbenzo[h]indolizino[8,7-b]quinolyl)aminomethylene}benzene (**33**): Red solid, which was obtained during preparation of **32** (see above); m.p. > 300°C (dec.); $[\alpha]_D^{22}$ = +170.0° (*c* = 0.10 in CH_2Cl_2). − IR (KBr): ṽ = 3015 cm^{-1}, 2973, 2786, 1620, 1568, 1514, 1508, 1471, 1440, 1393, 1365, 813, 801, 748. − ^1H NMR (300 MHz, C_6D_6): δ = 8.27 (d, *J* = 8.3 Hz, 2 H, 8-H), 8.25 (s, 2 H, HC=N), 8.10 (d, *J* = 8.5 Hz, 2 H, 11-H), 7.95 (s, 4 H, 2′-H, 3′-H), 7.31 (dd, *J* = 8.5/7.3 Hz, 2 H, 12-H), 6.86 (d,

J = 7.3 Hz, 2 H, 13-H), 4.42 (d, J = 5.9 Hz, 2 H, NH), 3.63 (d, J = 5.7 Hz, 2 H, 14a-H), 2.97−2.77 (m, 4 H, 3-H_{eq}, 5-H_{eq}), 2.22−1.50 (m, 16 H, 14b-H, 3-H_{ax}, 2-H, 1-H, 5-H_{ax}, 6-H_{eq}), 1.40−1.05 (m, 4 H, 6a-H, 6-H_{ax}), 1.30 (s, 6 H, 15-H), 1.29 (s, 6 H, 16-H). − ^{13}C NMR (75 MHz, C_6D_6): δ = 159.1 (C=N), 150.0 (C-10), 139.4 (C-1′), 137.5 (C-13b), 129.5 (C-12), 129.0 (C-7a), 128.3 (C-11), 126.8 (C-9a), 125.8 (C-13a), 125.3, 125.0 (C-2′, C-3′), 119.9, 115.2 (C-8, C-9), 112.6 (C-13), 67.3 (C-14b), 54.3 (C-3), 52.6 (C-5), 47.7 (C-14a), 44.4 (C-6a), 36.0 (C-7), 33.6, 26.8 (C-15, C-16), 25.6, 23.2, 21.9 (C-2, C-6, C-1). − MS (70 eV); *m/z* (%): 740 (62), 725 (10) [$M^+ - CH_3$], 656 (6) [$M^+ - C_5H_{10}N^+$], 321 (5), 163 (14), 122 (9), 97 (32), 84 (100) [$C_5H_{10}N^+$], 69 (20). − $C_{50}H_{56}N_6$: calcd. 740.4566; found 740.4539 (MS); calcd. C 81.04, H 7.62, N 11.34; found C 81.05, H 7.71, N 11.24.

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[16] The corresponding all-*trans* product was obtained as the minor diastereomer.

[17] Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100751. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44(0)1223/336033; E-mail: deposit@ccdc.cam.ac.uk].

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[19] Although we anticipated the formation of "mixed products" bearing one all-*cis* and one all-*trans* unit, no trace of these by-products were found by HPLC analysis of the crude product.

[20] Any attempts to achieve direct reduction of **16** to **18** using Raney-Ni/H_2 were not successful. The high lability of triamine **18** towards acids and the high water solubility are probably the reason for the low yields reported in alternative literature procedures. See for example: [20a] I. Arai, Y. Sei, I. Muramatsu, *J. Org. Chem.* **1981**, *46*, 4597−4599. − [20b] T. Yamaoka, S. Nagakura, *Bull. Chem. Soc. Jpn.* **1970**, *43*, 355−358. − [20c] L. Picket, P. Barbier, *Bull. Soc. Chim. Fr.* **1895**, *13*, 29−35. − [20d] W. Hepp, *Justus Liebigs Ann. Chem.* **1882**, *215*, 348−351. − [20e] A. K. Macbeth, *J. Chem. Soc.* **1922**, 1116−1121.

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[22] ***CAUTION:*** For safety reasons the preparative scale of compound **17** was kept below 2 mmol.

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