Selective derivatisation of resorcarenes: Part 7. The reason for the diastereoselectivity of Mannich reactions with chiral amines†

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The formation of tetrakis(benzo-3,4-dihydro-1,3-oxazines) **2** by condensation of resorcarenes **1** with various primary amines and an excess of formaldehyde is not only regioselective but, in the case of (*R*)- or (*S*)-1-phenylethylamine and their *para*-substituted (Br, Me) derivatives, also completely diastereoselective. The reaction with the structurally similar (*R*)-1-aminoindane and (*S*)-1-(1-naphthyl)ethylamine, on the other hand, produced only a slight excess of one of the two possible epimers **2** and with (*R*)-1-cyclohexylethylamine no diastereoselectivity was found at all. The presence and the ratio of both diastereomeric structures can be clearly determined by NMR spectroscopy. Inspection of partly converted reaction mixtures suggests that the preferred crystallisation of one of the epimers is responsible for the diastereoselectivity observed in the case of 1-phenylethylamines and not an entirely diastereoselective reaction. The identity of **3**, a cyclic triamine obtained as a side product of the Mannich reaction with (*R*)-1-aminoindane, was established by single crystal X-ray structure analysis.

Resorcarenes **1**, readily available in the form of their *rccc* (all-*cis*) isomers by acid catalysed condensation of resorcinol with various aldehydes, are easily substituted in the 2-position of the resorcinol units by mild electrophiles.[1] For instance, the Mannich reaction with formaldehyde and various secondary amines leads in high yields to tertiary amines.[2] If primary amines are used under similar conditions with a sufficient excess of formaldehyde, tetrabenzoxazines[3] are formed in an entirely regioselective reaction.[4] This reaction is attractive, since it furnishes potential host molecules with an extended (flexible) cavity and inherent chirality (C_4 symmetry). It may be extended to various diamines, leading to 1,2- or 1,3-bridged compounds[5] and, in the case of ethylenediamine, also to tetra-bridged dimers of the carcerand type.[6]

The use of chiral amines introduces additional chiral centres attached to the nitrogen atoms of the benzoxazine rings. Thus, two epimeric, C_4 symmetrical products are possible, differing in the direction of the oxazine rings (Fig. 1). Previous results show that with (*R*)- or (*S*)-1-phenylethylamine only one of these epimers is formed in high yield.[7] This was proved by ^{1}H NMR and additionally shown for two examples by single crystal X-ray analysis. Since the absolute configuration of the asymmetric carbon is known, the direction in which the oxazine rings point could be established as clockwise [for the (*S*)-amine][7a] or counterclockwise [for the (*R*)-amine],[7a,b] if the molecule is regarded from the cavity side.

These epimers, readily obtained under alkaline conditions, are stable in solution only in the absence of acids. With traces of TFA the optical rotation changes (to reach an equilibrium value) and the ^{1}H NMR spectra show the appearance of a second set of signals, most probably due to an acid-catalysed epimerisation. If the mixture thus obtained is treated again under the alkaline conditions of the synthesis, the single epimer is formed again.

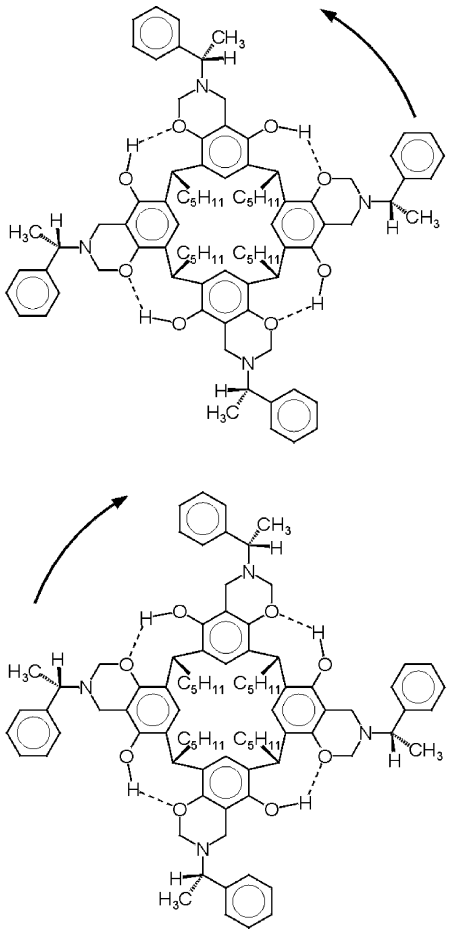

Fig. 1 The two possible epimeric tetrabenzoxazines.

† For part 6, see, C. Schmidt, T. Straub, D. Falàbu, E. F. Paulus, E. Wegelius, E. Kolehmainen, V. Böhmer, K. Rissanen and W. Vogt, *Eur. J. Org. Chem.*, 2000, 3937.

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Recently, Heaney *et al.* found conditions to methylate the four remaining OH groups (deprotonation by butyllithium in THF at −78 °C, followed by reaction with methyltriflate).[8] This can be considered a break-through in this area, since evidently an epimerisation is impossible for these tetramethyl ethers. Thus, various stable enantiomers are available, which also remain chiral after the removal of the chiral auxiliary groups.

A careful reinspection of the ^{1}H NMR spectrum of the tetrabenzoxazine obtained with (*R*)-1-cyclohexylethylamine[9] showed two sets of signals of equal intensity with a very small difference in their chemical shifts. A reasonable explanation could be the formation of both possible epimers instead of only one. This would mean that the diastereoselectivity of the Mannich reaction with chiral amines is not a general phenomenon, but may occur only under special conditions or with certain amines. In addition it was found that a diastereoselective reaction with 1-phenylethylamine can also be achieved under acid catalysis, which seems to be a contradiction to the acid-catalysed epimerisation mentioned above. To find an explanation for these divergent observations and to get a more general view, we studied the reaction with various chiral amines and under different reaction conditions.

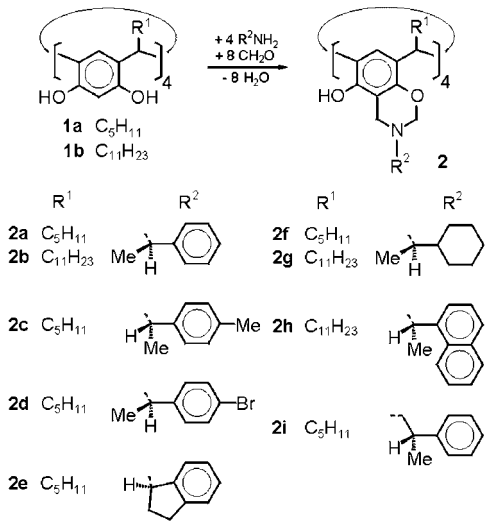
Results and discussion

Synthesis

All the condensation reactions of resorcarenes **1** (Scheme 1) were carried out with an excess of formaldehyde in ethanol at room temperature, catalysed by a small amount of base (sodium hydroxide) or acid (acetic acid or phosphoric acid). The products were directly isolated as a precipitate from the reaction mixture in 63–91% yields.

With (*R*)-1-phenylethylamine and its *para*-substituted analogues only one of the two possible epimeric C_4-symmetric tetrabenzoxazines **2a**–**d** was obtained, which is in agreement with the results reported earlier.[7] This follows unambiguously from their ^{1}H and ^{13}C NMR spectra, showing only one set of signals (see also Fig. 3).

In the case of the structurally similar, but more rigid (*R*)-1-aminoindane, compound **2e** is formed as a 60 : 40 mixture of two similar compounds, most probably the two epimers. The same observation was made for **2h**, prepared with the more bulky (*S*)-1-(1-naphthyl)ethylamine.[9] The ^{1}H NMR spectra unambiguously show two sets of signals, clearly seen for the diastereotopic Ar–CH_2–N and N–CH_2–O protons, for example, showing two pairs of doublets each (Fig. 2). By integration it is possible to attribute nearly all signals for both



Scheme 1

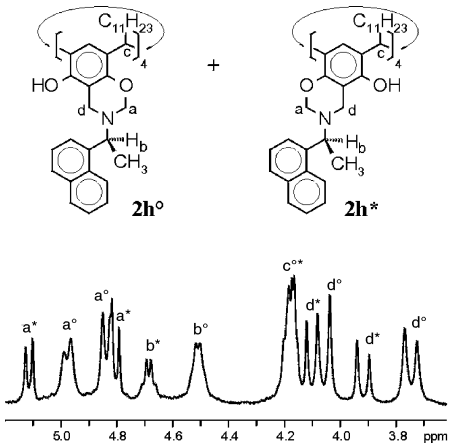


Fig. 2 Section of the ^{1}H NMR spectrum ($CDCl_3$) of **2h**. The signals of the two epimers are indicated (°,*) and assigned to the appropriate protons. The structure of the major epimer is formulated by analogy to the known examples.

epimers, however, it would be desirable to confirm the structure of the minor epimer by an X-ray crystallographic study.[7a,b]

With the non-aromatic (*R*)-1-cyclohexylethylamine, compounds **2f**, **g** are formed without any apparent diastereoselectivity. The ^{1}H NMR spectra of the reaction products show an equal amount of two analogous compounds. In contrast to the aromatic amines, the difference in chemical shifts between the two epimers is very small (*ca.* 0.02 ppm), which can be understood as due to the lack of an anisotropic effect, induced by aromatic rings.

If the distance between the stereogenic centre and the amino group is larger, as for (*S*)-1-amino-2-phenylpropane, the diastereoselectivity is again smaller. The obtained product **2i** is a 60 : 40 mixture of both epimers, as found for **2e**, **h**.

All experiments show that the diastereoselectivity of the reaction strongly depends on the amine. A variation of the reaction conditions, using different solvents (methanol, ethanol, acetone or acetonitrile) and temperatures (RT and 80 °C) shows no significant influence on the ratio of the two epimers. Surprisingly, it was found that under acidic conditions also only one epimer is formed with (*R*)-1-phenylethylamine and its *para*-substituted analogues, in spite of the previously described acid-catalysed epimerisation.[7,10] This led to the idea that the reason for the observed high diastereoselectivity is not the more or less exclusive formation of a single epimer, but the precipitation of one epimer from a reaction mixture in which both exist in equilibrium.

To investigate this idea more deeply, we split a reaction mixture with (*R*)-1-phenylethylamine. After 1 h, when the usual precipitation of the product just starts, a first portion was poured into water, to stop the reaction and the precipitate was collected (**I**). A second portion was reacted for 3 h. The precipitate was filtered off (**II**) and the clear filtrate was poured into water to precipitate the rest (**III**). The ^{1}H NMR spectrum of **I** shows two sets of signals (Fig. 3), which are similar to spectra where both epimers are present. Further signals suggest an additional larger amount of partially reacted resorcarenes (*e.g.* tribenzoxazine), deduced from the characteristic signal at 6.2 ppm for the aromatic proton of the free 2-position. **III** also shows signals for both epimers, but no additional signals for partially reacted resorcarenes are found. In contrast to **I** and **III**, the spectrum of **II**, the usual precipitate from the original reaction solution, shows only one set of signals, which means that in this case only one epimer is present (see Fig. 3). This unambiguously shows that the reaction itself is rather unselective, while the observed diastereoselectivity is mainly the result of the lower solubility of one of the two epimers. It also explains the apparent contradiction

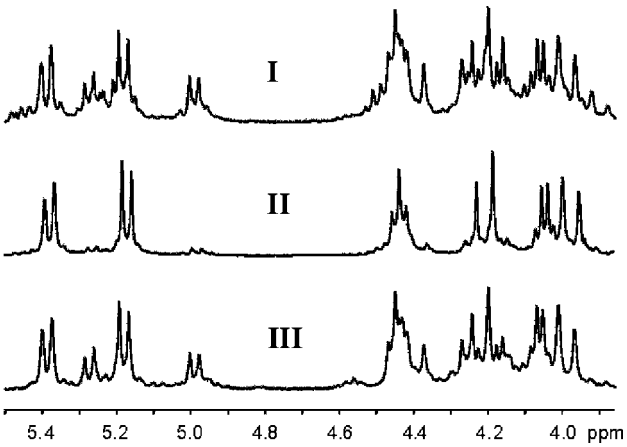


Fig. 3 Sections of the ^{1}H NMR spectra of products isolated during the synthesis of **2a**: (**I**) complete precipitation after 1 h; (**II**) isolation of the usually formed precipitate isolated after 3 h; (**III**) complete precipitation of the filtrate of **II**.

between acid-catalysed epimerisation in homogenous solution and the high diastereoselectivity of the acid-catalysed reaction under preparative conditions.

Single crystal X-ray structure

From a solution of **2e** in a mixture of chloroform and acetonitrile two apparently different sorts of crystals are formed after one day. One of the less abundant crystals was used for an X-ray analysis.[11] Surprisingly, this compound was not the desired minor epimer, but 1,3,5-tris[(*R*)-1-indyl]hexahydro-1,3,5-triazine **3**, which is formed as a side product of the Mannich reaction due to the slight excess of amine and formaldehyde but which can also be prepared in high yield from 1-aminoindane and formaldehyde. The overall geometry of **3** is given in Fig. 4(a); all angles and distances are in the usual range, all hydrogen positions except those of one methylene group could be experimentally determined. The six-membered triamine ring shows an exact chair conformation, in which two of the indyl substituents at the nitrogen atoms are in equatorial positions (N1 and N2), whereas the third is in an axial position (N3). The five-membered rings have an envelope conformation but in two cases (rings 1 and 3) the methylene groups in the 2-position have the usual distance of 0.45 Å from the plane of the other carbon atoms; for ring 2 this distance is only 0.16 Å. The deviation of the local threefold axial symmetry can only be explained by entropical packing effects. The four molecules of the unit cell are shown in Fig. 4(b).

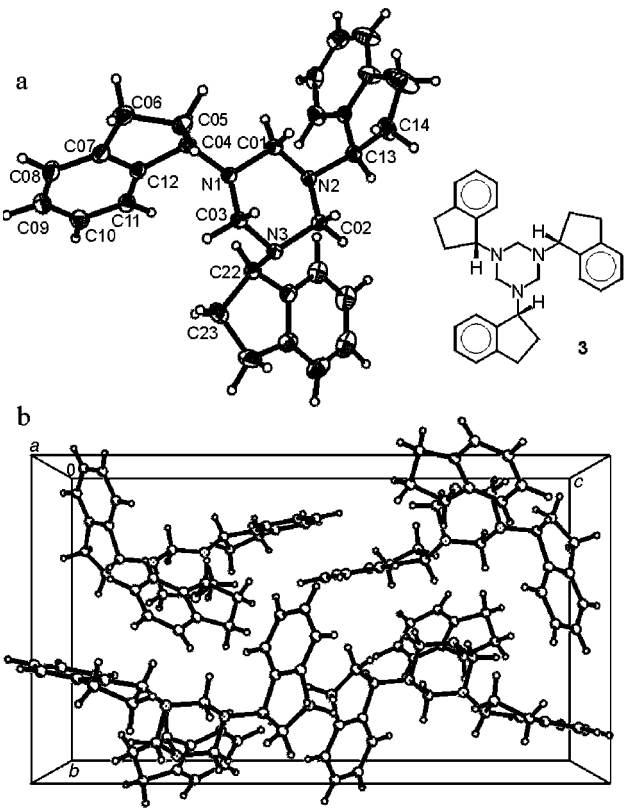


Fig. 4 (a) Molecular conformation of **3** in the crystalline state. The numbering scheme is indicated. Thermal ellipsoids are drawn on the 20% probability level. (b) Projection of the content of the unit cell along the crystallographic *a* axis.

Experimental

General

Resorcarenes **1**[13] were synthesised as described previously. Melting points were determined with a MEL TEMP2 capillary melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC200 (200 MHz) and AM400 (400 MHz) spectrometers. FD mass spectra were recorded with a Finnigan MAT 90 (5 kV and 10 mA min^{-1}) and the optical rotation with a Perkin-Elmer 241 Polarimeter (c = 1.00 g per 100 ml, $CHCl_3$).

General procedure for the synthesis of tetrabenzoxazines 2

To a solution of the resorcarene **1** (1.3 mmol), formaldehyde (35%, 1.5 ml, 17.5 mmol) and glacial acetic acid (0.05 ml) in ethanol (10 ml) was added a solution of the amine (5.4 mmol) in ethanol (5 ml). After 12–48 h at room temperature the precipitate was filtered off and dried. The product thus obtained was normally already spectroscopically pure. Where necessary it was recrystallised from chloroform–methanol.

Tetrabenzoxazine 2a. 2a was synthesised from **1a** and (*R*)-1-phenylethylamine. Yield: 1.34 g (84%); mp: 102 °C; $[\alpha]_D^{20}$ = 107.8°. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (s, 4H, ArOH), 7.18 (d, J = 7.2, 8H, ArH), 7.08 (s, 4H, ArH), 7.03 (t, J = 7.6, 8H, ArH), 6.93 (t, J = 7.2, 4H, ArH), 5.13 (d, J = 9.8, 4H, OCH_2N), 4.92 (d, J = 9.8, 4H, OCH_2N), 4.15 (t, J = 7.7, 4H, $RCHAr_2$), 3.95 (d, J = 17.3, 4H, $ArCH_2N$), 3.72 (d, J = 17.3, 4H, $ArCH_2N$), 3.79 (q, J = 6.6, 4H, $NCHRAr$), 2.25–2.00 (m, 8H, CH_2), 1.43–1.07 (m, 24H, CH_2), 0.85 (t, J = 6.9 Hz, 12H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.58, 148.76, 144.48, 128.15, 127.37, 127.03, 124.31, 123.48, 121.10, 108.95, 80.99, 58.16, 44.55, 33.77, 32.80, 31.85, 27.72, 22.65, 21.33, 14.09. Anal. calc. for $C_{88}H_{108}N_4O_8$: C 78.30, H 8.06, N 4.14; found: C 78.23, H 8.02, N 4.11%.

Tetrabenzoxazine 2b. 2b was prepared from **1b** and (*R*)-1-phenylethylamine. Yield: 2.00 g (91%); mp: 89 °C; $[\alpha]_D^{20}$ = 101.9°. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 4H, ArOH), 7.19 (d, J = 7.2, 8H, ArH), 7.08 (s, 4H, ArH), 7.02 (t, J = 7.6, 8H, ArH), 6.93 (t, J = 7.2, 4H, ArH), 5.13 (d, J = 9.8, 4H, OCH_2N), 4.93 (d, J = 9.8, 4H, OCH_2N), 4.15 (t, J = 7.7, 4H, $RCHAr_2$), 3.94 (d, J = 17.3, 4H, $ArCH_2N$), 3.72 (d, J = 17.3, 4H, $ArCH_2N$), 3.79 (q, J = 6.6, 4H, $NCHRAr$), 2.25–2.00 (m, 8H, CH_2), 1.43–1.07 (m, 96H, CH_2), 0.84 (t, J = 6.9 Hz, 12H, CH_3).

Tetrabenzoxazine 2c. 2c was synthesised from **1a** and (*S*)-1-(4-methylphenyl)ethylamine. Yield: 1.35 g (79%); mp: 175 °C; $[\alpha]_D^{20}$ = −134.1°. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 4H, ArOH), 7.17 (d, J = 7.8, 8H, ArH), 7.14 (s, 4H, ArH), 7.02 (d, J = 7.8, 8H, ArH), 5.06 (d, J = 10.0, 4H, OCH_2N), 4.85 (d,

$J = 10.0$, 4H, OCH_2N), 4.20 (t, $J = 7.9$, 4H, $RCHAr_2$), 3.95 (d, $J = 17.5$, 4H, $ArCH_2N$), 3.80–3.70 (m, 8H, $ArCH_2N + NCHRAr$), 2.24 (s, 12H, CH_3), 2.20 (br s, 8H, CH_2), 1.45–1.20 (br s, 36H, $CH_2 + CH_3$), 0.90 (t, $J = 6.8$ Hz, 12H, CH_3). MS (FD): m/z 1405.7 [M^+, 1410.0].

Tetrabenzoxazine 2d. 2d was synthesised from **1a** and (*R*)-1-(4-bromophenyl)ethylamine. Yield: 1.36 g (63%); mp: 171 °C; $[\alpha]_D^{20} = 161.9°$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 4H, ArOH), 7.34 (d, $J = 8.5$, 8H, ArH), 7.15 (d, $J = 8.2$, 8H, ArH), 7.13 (s, 4H, ArH), 5.05 (d, $J = 10.2$, 4H, OCH_2N), 4.85 (d, $J = 10.2$, 4H, OCH_2N), 4.17 (t, $J = 7.9$, 4H, $RCHAr_2$), 3.95 (d, $J = 17.6$, 4H, $ArCH_2N$), 3.77 (*d*, $J = 6.5$, 4H, $ArCH_2N$), 3.74 (d, $J = 6.5$, 4H, $ArCH_2N$), 3.63 (d, $J = 17.6$, 4H, $ArCH_2N$), 2.20 (m, 8H, CH_2), 1.40–1.20 (m, 24H, CH_2), 0.90 (t, 12H, $J = 7.1$ Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.52, 148.58, 143.66, 131.47, 128.78, 124.33, 123.48, 121.12, 120.72, 108.70, 80.57, 57.38, 44.78, 33.64, 32.67, 31.82, 27.70, 22.58, 21.15, 14.01. Anal. calc. for $C_{88}H_{116}Br_4N_4O_8$: C 63.01, H 6.97, N 3.34; found: C 63.15, H 6.89, N 3.25%. MS (FD): m/z 1667.4 [M^+, 1665.4].

Tetrabenzoxazine 2e. 2e was prepared from **1a** and (*R*)-1-indylamine and gave a 60° : 40* mixture of epimers. Yield: 1.56 g (86%); mp: 166 °C; $[\alpha]_D^{20} = -43.4°$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 4H, ArOH), 7.31–7.27 (m, 4H, ArH), 7.20–7.08 (m, 16H, ArH), 4.98–4.96°* (m, 12H, OCH_2N), 4.87* (d, $J = 9.7$, OCH_2N), 4.50° (t, $J = 7.1$, 4H, $NCHRAr$), 4.49 (t, $J = 6.5$, 4H, $NCHRAr$), 4.22–4.16°* (m, 12H, $RCHAr_2$), 3.97° (d, $J = 17.6$, 4H, $ArCH_2N$), 3.90* (d, $J = 17.6$, 4H, $ArCH_2N$), 3.80* (d, $J = 18.1$, 4H, $ArCH_2N$), 3.75° (d, $J = 17.7$ Hz, 4H, $ArCH_2N$), 2.93–2.87* (m, 4H, CH_2), 2.82–2.75° (m, 4H, CH_2), 2.74–2.67* (m, 4H, CH_2), 2.59–2.51° (m, 4H, CH_2), 2.27–2.00 (m, 12H, CH_2), 1.93–1.84* (m, 4H, CH_2), 1.81–1.72° (m, 4H, CH_2), 1.42–1.22 (m, 4H, CH_2), 0.92–0.87°* (m, 24H, CH_3).

Tetrabenzoxazine 2f. 2f was prepared from **1a** and (*R*)-1-cyclohexylethylamine and gave a 50 : 50 mixture of epimers. Yield: 1.23 g (69%); mp: 140 °C; $[\alpha]_D^{20} = 28.5°$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 4H, ArOH), 7.76 (s, 4H, ArOH), 7.05 (s, 4H, ArH), 7.03 (s, 4H, ArH), 4.97 (d, $J = 9.5$, 4H, OCH_2N), 4.95 (d, $J = 9.5$, 4H, OCH_2N), 4.92 (d, $J = 10.0$, 4H, OCH_2N), 4.89 (d, $J = 9.8$, 4H, OCH_2N), 4.17 (t, $J = 7.5$, 4H, $RCHAr_2$), 4.14 (t, $J = 7.8$, 4H, $RCHAr_2$), 3.90 (d, $J = 17.5$, 4H, $ArCH_2N$), 3.88 (d, $J = 17.3$, 4H, $ArCH_2N$), 3.80 (d, $J = 17.3$, 4H, $ArCH_2N$), 3.77 (d, $J = 17.5$, 4H, $ArCH_2N$), 2.58 (m, 4H, $NCHR_2$), 2.16 (m, 4H, CH_2), 2.08 (m, 4H, CH_2), 1.75–1.55 (m, 20H, $CH_2 + CHR_3$), 1.40–1.10 (m, 48H, CH_2), 0.96 (d, $J = 6.6$, 12H, CH_3), 0.89 (d, $J = 6.6$, 12H, CH_3), 0.86 (t, $J = 6.6$ Hz, 12H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.14, 149.05, 149.02, 148.91, 124.13, 123.81, 123.74, 120.86, 120.80, 110.30, 110.23, 82.56, 82.31, 60.12, 61.00, 43.54, 43.45, 41.69, 41.36, 33.68, 32.76, 31.93, 31.91, 30.90, 30.73, 28.49, 28.42, 27.78, 26.78, 26.63, 26.53, 26.49, 22.69, 14.54, 14.28, 14.10. MS (FD): m/z 1374.1 [M^+, 1374.0].

Tetrabenzoxazine 2g. 2g was synthesised from **1b** and (*R*)-1-cyclohexylethylamine and gave a 50 : 50 mixture of epimers. Yield: 1.76 g (79%); mp: 98 °C; $[\alpha]_D^{20} = 54.2°$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 4H, ArOH), 7.78 (s, 4H, ArOH), 7.06 (s, 4H, ArH), 7.04 (s, 4H, ArH), 4.98 (d, $J = 9.4$, 4H, OCH_2N), 4.95 (d, $J = 9.6$, 4H, OCH_2N), 4.93 (d, $J = 9.6$, 4H, OCH_2N), 4.90 (d, $J = 9.4$, 4H, OCH_2N), 4.18 (t, $J = 7.5$, 4H, $RCHAr_2$), 4.15 (t, $J = 7.8$, 4H, $RCHAr_2$), 3.92 (d, $J = 17.5$, 4H, $ArCH_2N$), 3.90 (d, $J = 17.3$, 4H, $ArCH_2N$), 3.81 (d, $J = 17.3$, 4H, $ArCH_2N$), 3.78 (d, $J = 17.5$, 4H, $ArCH_2N$), 2.59 (m, 4H, $NCHR_2$), 2.18 (m, 4H, CH_2), 2.09 (m, 4H, CH_2), 1.78–1.55 (m, 20H, $CH_2 + CHR_3$), 1.45–1.10 (m, 96H, CH_2), 0.98 (d, $J = 6.6$, 12H, CH_3), 0.91 (d, $J = 6.6$, 12H, CH_3), 0.88 (t, $J = 6.6$ Hz, 12H, CH_3). Anal. calc. for $C_{112}H_{180}N_4O_8$: C 78.64, H 10.61, N 3.28; found: C 78.70, H 10.55, N 3.18%. MS (FD): m/z 1710.1 [M^+, 1710.7].

Tetrabenzoxazine 2h. 2h was synthesised from **1b** and (*S*)-1-(1-naphthyl)ethylamine and gave a 60° : 40* mixture of epimers. Yield: 2.13 g (87%); mp: 90 °C; $[\alpha]_D^{20} = -247.5°$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.9–7.1 (m, 36H, ArH + ArOH), 5.11° (d, $J = 10.0$, 4H, OCH_2N), 4.98* (d, $J = 9.5$, 4H, OCH_2N), 4.83* (d, $J = 9.6$, 4H, OCH_2N), 4.80° (d, $J = 10.2$, 4H, OCH_2N), 4.68° (q, $J = 6.6$, 4H, $NCHRAr$), 4.51* (q, $J = 6.1$, 4H, $NCHRAr$), 4.18° (t, $J = 7.1$, 4H, $RCHAr_2$), 4.17* (t, $J = 7.8$, 4H, $RCHAr_2$), 4.14* (d, $J = 17.8$, 4H, $ArCH_2N$), 4.06° (d, $J = 17.5$, 4H, $ArCH_2N$), 3.92° (d, $J = 17.5$, 4H, $ArCH_2N$), 3.75* (d, $J = 17.8$, 4H, $ArCH_2N$), 2.30–2.10 (m, 8H, CH_2), 1.40–1.20 (m, 50H, $CH_2 + CH_3$), 0.86° (t, $J = 7.00$, 12H, CH_3), 0.85* (t, $J = 7.0$ Hz, 12H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.54, 149.51, 148.93, 148.74, 139.69, 139.40, 134.25, 133.99, 131.33, 128.87, 128.47, 127.87, 127.67, 125.57, 125.44, 125.33, 125.28, 125.04, 124.85, 124.51, 124.23, 124.05, 123.80, 123.67, 123.64, 121.07, 109.08, 109.03, 81.23, 80.99, 55.11, 55.06, 44.91, 33.79, 32.85, 32.02, 29.89, 29.83, 29.48, 28.28, 28.20, 28.16, 22.76, 20.64, 20.13, 14.18.

Tetrabenzoxazine 2i. 2i was prepared from **1a** and (*S*)-1-amino-2-phenylpropane and gave a 60° : 40* mixture of epimers. Yields: 1.47 g (81%); mp: 105 °C; $[\alpha]_D^{20} = -151.2°$. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (s, 4H, ArOH), 7.25–7.10 (m, 20H, ArH), 7.05 (s, 4H, ArH), 4.83–4.73 (m, 8H, OCH_2N), 4.18–4.12 (m, 4H, $RCHAr_2$), 3.92° (d, $J = 17.4$, 4H, $ArCH_2N$), 3.91* (d, $J = 17.3$ Hz, 4H, $ArCH_2N$), 3.73–3.64 (m, 4H, $ArCH_2N$), 2.96–2.62 (m, 12H, $ArCH_2N + NCH_2R$), 2.12 (m, 8H, CH_2), 1.28–1.18 (m, 36H, $CH_2 + CH_3$), 0.86 (m, 12H, CH_3). Anal. calc. for $C_{92}H_{116}N_4O_8$: C 78.60, H 8.32, N 3.98; found: C 78.49, H 8.25, N 3.90%. MS (FD): m/z 1405.9 [M^+, 1406.0].

Synthesis of 1,3,5-tris[(*R*)-1-indyl]hexahydro-1,3,5-triazine 3

A solution of 1 ml (*R*)-1-aminoindane and 1 ml formaldehyde (35%) in 30 ml ethanol was stirred for 1 day. The precipitate was filtered off and dried under reduced pressure. The obtained product was spectroscopically pure. Yield: 120 mg (71%); mp: 198 °C; $[\alpha]_D^{20} = -22.4°$. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.44 (d, $J = 6.4$, 3H, ArH), 7.24–7.11 (m, 12H, ArH), 4.49 (t, $J = 6.3$ Hz, 3H, $NCHRAr$), 3.58 (s, 6H, NCH_2N), 3.03–2.66 (m, 6H, CH_2), 2.04 (m, 6H, CH_2).

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9 This was also considered as a single epimer (R. Arnecke, PhD Thesis, University of Mainz, Germany, 1996). See also ref. 7(*c*).
10 Additional experiments show that the equilibrium ratio between the two epimers, after epimerisation, varies for different solvents. For example, **2a** and **2e** both show a 60 : 40 ratio in chloroform, while the ratio is 75 : 25 (**2a**) and 55 : 45 (**2e**) in cyclohexane and 55 : 45 (**2a**) and 70 : 30 (**2e**) in benzene.
11 Crystal data for **3**: $C_{30}H_{32}N_3$, $M_w = 434.59$, orthorhombic, space group $P2_12_12_1$, $a = 9.191(1)$, $b = 12.292(1)$, $c = 21.682(2)$ Å, $U = 2449.5(4)$ Å^3, $Z = 4$, $D_e = 1.178$ g cm^{-3}. Data collection was performed on a computer-controlled four-circle diffractometer equipped with a CCD area detector (Bruker AXS) and a rotating anode (Bruker AXS, focus: 0.5 × 5 mm, 50 kV, 120 mA) using Mo-Kα radiation (graphite monochromator, $\lambda = 0.7107$ Å). Refinement of $(F_o^2 - F_c^2)^2$ based on all 4274 unique reflections ($R_{int} = 0.0217$ with in all 13 061 reflections) led to $R_1 = 0.0413$, $wR_2 = 0.0848$ and $S = 0.927$; $R_1 = 0.0329$, $wR_2 = 0.0819$ and $S = 0.927$ for $F_o > 4\sigma(F)$ (3429 reflections). All calculations were done with SHELX programs.[12] CCDC reference number 440/256. See http://www.rsc.org/suppdata/nj/b0/b010210p/ for crystallographic files in .cif format.
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