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Selective Derivatisation of Resorcarenes: 1. The Regioselective Formation of Tetra-Benzoxazine Derivatives

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Abstract: Four 5,6-benzo-1,3-oxazine rings are formed by the condensation of resorcarenes with various aliphatic or aromatic primary amines and formaldehyde. From four possible regioisomers only the C_4 symmetrical compound is isolated in yields of up to 90%. Semiempirical calculations confirm its relative stability, which is due to the possible formation of four intramolecular O-H···O hydrogen bonds. The regioselectivity of the reaction is further established for two examples by single crystal X-ray analysis. A solvent molecule is included in the extended cavity. © 1997 Elsevier Science Ltd.

INTRODUCTION

Resorcarenes, readily available in the all-cis isomer form by acid catalysed condensation of resorcinol with various aldehydes,[1] provide a cavity, which in combination with the four pairs of hydroxyl groups, has the potential to bind various guests such as alcohols ("monools"), diols, sugars and similar compounds.[2] The cavity may be further modified by chemical reactions involving the phenolic hydroxyl groups and/or the 2 position of the resorcinol units. Connection of adjacent oxygens by bifunctional reagents leads to the more rigid cavitands[3] which may be connected to hemicarcerands or carcerands via bridges between the 2 positions.[4] Examples for electrophilic substitutions at the 2 position include bromination,[5] coupling with diazonium salts[6] and aminomethylation.[7] With primary amines and an excess of formaldehyde the condensation leads to the formation of benzoxazine rings in an entirely regioselective way.[7a,8] In addition, with chiral amines bearing the chiral center in the alpha-position the reaction shows a remarkable diastereoselectivity.[9]

We were interested in this condensation of resorcarenes with primary amines and formaldehyde mainly for three reasons, to enlarge the cavity, to introduce further functionalities and, last but not least, to prepare

dissymmetric compounds with inherent chirality. We describe here the synthesis of various tetrabenzoxazines and their spectroscopic characterisation. For two examples a single crystal X-ray analysis was obtained and semiempirical calculations were carried out to compare the relative stability of the different possible regioisomers.

SYNTHESIS

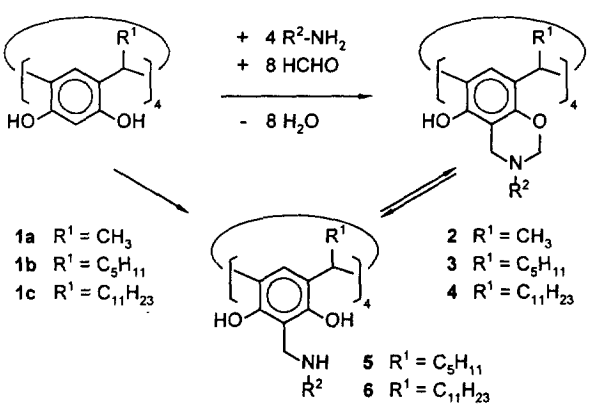
General Considerations

For each resorcinol unit the condensation with the amine and (excess) formaldehyde involves (at least) two steps, the first being the usual Mannich aminomethylation. In the second step the secondary amine thus formed undergoes ring closure by condensation with a second molecule of formaldehyde and one of the two adjacent hydroxyl groups (Scheme 1).

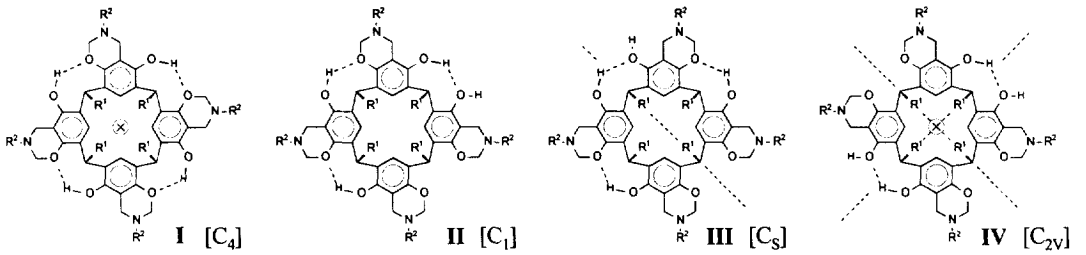
Since two directions exist for the formation of the oxazine ring, four different regioisomers could be formed, as shown in Scheme 2. Isomer **I** has a fourfold axis as the only symmetry element (C_4 symmetry), while isomer **II** (with one of the four oxazine rings "pointing" in the opposite direction) has no symmetry element at all (C_1 symmetry). Both isomers are chiral and two enantiomers should exist therefore. The two other isomers are achiral; **III** has a symmetry plane (C_S symmetry) while two symmetry planes and a twofold axis are present in **IV** (C_{2V} symmetry).

Reaction Conditions

As shown in Scheme 2, four intramolecular O-H···O hydrogen bonds are possible only in **I**. Therefore, its formation should be most favored over the other isomers under conditions, where no competition with intermolecular hydrogen bonds exists (or where such a competition is minimised). Thus, our first attempts were carried out by refluxing the resorcarene with a 5-fold amount of the primary amine and a 10-fold amount of formaldehyde in mixtures of benzene or toluene with the minimum amount of ethanol to achieve a homogeneous reaction mixture. Later we found that (at least in some cases) even better yields were obtained when the reaction is catalysed by the addition of a drop of NaOH or KOH. And finally, the



Scheme 1: Condensation of resorcarenes with primary amines and formaldehyde



Scheme 2: The four possible regioisomers of tetrabenzoxazines and their symmetry classes.

selective formation of isomers **I** was also achieved under mild acid catalysis at room temperature, reaction condition which we now prefer.

Scope and Limitations

Table 1 gives a survey on the tetrabenzoxazines prepared so far. We have used three different resorcarenes (with rccc configuration), but there seems to be no limitation from this side, and tetrabenzoxazines should be available also with other resorcarenes.

Various aliphatic amines (linear, branched, cyclic or bicyclic) have been used, but the reaction was not yet successful with amino acids or in the case of diamines with suppression of the reaction of the second amino group. When aliphatic diamines were applied in stoichiometric amounts under dilution conditions, additional bridging between adjacent benzoxazine rings could be achieved.[10] While no definite reaction product was obtained with aniline itself, the synthesis of tetrabenzoxazines was successful with anilines carrying deactivating substituents like p-nitroaniline, with p-phenoxyaniline (as an example for an aniline with an activating substituent) and also with the sterically hindered 2,4,6-trimethylaniline (mesitylamine).

With chiral amines like 1-phenyl-,[9] 1-(1-naphthyl)-[9c] or 1-cyclohexylethylamine[9c] only one of two possible epimers with the benzoxazines pointing in clockwise or counterclockwise direction is formed. However, this diastereoselectivity disappears, when the stereogenic carbon atom is not directly bound to the nitrogen (Fig. 3).

The tendency to form a tetrabenzoxazine derivative is so pronounced, that it can be isolated in more than 70% yield (with respect to the amine) if **1** is taken in excess. This means that partially converted products cannot be formed in larger amounts. A tentative explanation would be, that the formation of the first benzoxazine ring (or even the first secondary amine structure) leads to a „cleavage" (or weaking) of the intramolecular OH···OH hydrogen bonds (e.g. by small conformational changes), thus making the remaining resorcinol units more reactive.

Table 1: Survey of tetrabenzoxazines; yields are given for the isolated products

Compd.	R^1	R^2	Yield (%)	Compd.	R^1	R^2	Yield (%)
2a	CH_3	2-phenylethyl	76	**3o**	C_5H_{11}	3,4-dimethoxybenzyl	78
2b	"	2,4,6-trimethylphenyl	91	**3p**	"	2,4,6-trimethylphenyl	90
3a	C_5H_{11}	methyl	62	**3q**	"	4-nitrophenyl	55
3b	"	ethyl	73	**3r**	"	4-phenoxyphenyl	49
3c	"	propyl	81	**3s**	"	(R)-(+)-1-phenylethyl	84
3d	"	*iso*-propyl	77	**3t***	"	(S)-(-)-2-phenylpropyl	81
3e	"	butyl	88	**4a**	$C_{11}H_{23}$	butyl	89
3f	"	*tert*-butyl	81	**4b**	"	6-hydroxyhexyl	69
3g	"	decyl	94	**4c**	"	benzyl	93
3h	"	cyclohexyl	76	**4d**	"	adamantyl	73
3i	"	adamantyl	65	**4e**	"	4-nitrophenyl	62
3j	"	allyl	84	**4f**	"	4-phenoxyphenyl	53
3k	"	2-methoxyethyl	89	**4g**	"	(S)-(-)-1-phenylethyl	89
3l	"	2-(N-morpholino)-ethyl	93	**4h**	"	(R)-(+)-1-phenylethyl	87
3m	"	2-phenylethyl	80	**4i**	"	(S)-1-cyclohexylethyl	81
3n	"	benzyl	75	**4j**	"	(R)-1-(1-naphthyl)ethyl	78

* mixture of the both epimers

Secondary amines **5** and **6** can be prepared by hydrolysis of the benzoxazine structures **2**, **3** and **4** as demonstrated for some examples. By reactions with CH_2O (or CD_2O) they can be transformed into the original benzoxazines again (or their partially deuterated analogues).[7a]

SPECTROSCOPIC STUDIES

The formation of tetrabenzoxazines **2-4** is confirmed in all cases by their mass spectra, and the formation of a single isomer can be concluded from the NMR spectra. The ^1H NMR spectra show for all examples ***one*** singlet for each the OH and the ArH protons, ***one*** triplet (vicinal coupling) for the methine protons Ar-CHR^1-Ar of **3** and **4** (for **2** with $R^1 = CH_3$ one quadruplet is found) and ***one*** pair of doublets (AB-system, geminal coupling) for each pair of diastereotopic protons of the Ar-CH_2- and the N-CH_2-O groups in the benzoxazine rings (Fig. 1, Fig. 2). All the other protons of R^1 and R^2 give signals, which are compatible with a single type of each of these residues. For instance, ***one*** doublet appears for **2** with $R^1 = CH_3$ (vicinal coupling with the adjacent CH), or ***two*** doublets (vicinal coupling) for the two diastereotopic methyl groups of R^2 = -$CH(CH_3)_2$ are found for **3d**.

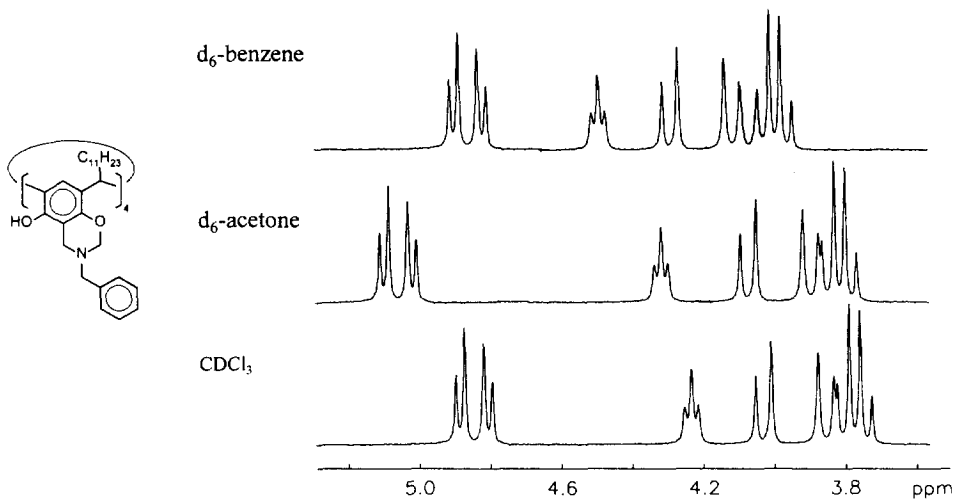


Figure 1: Section of the ^{1}H NMR spectra (400MHz) of **4c** in different solvents.[11]

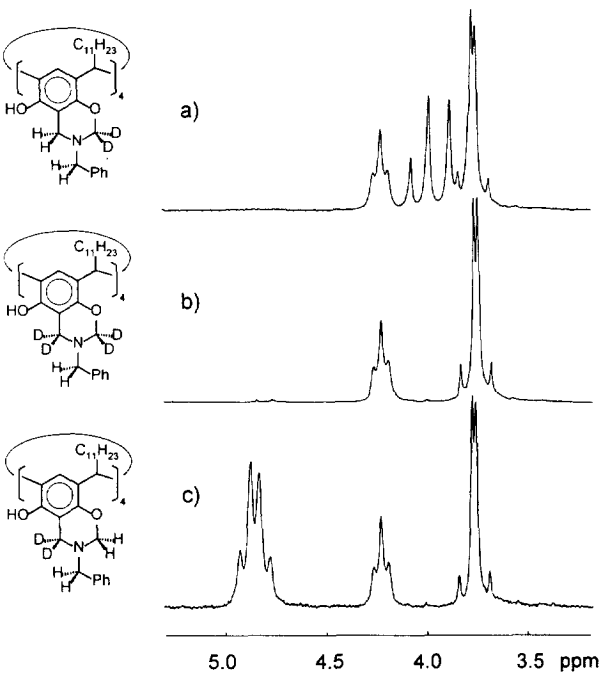


Figure 2: ^{1}H NMR spectra (200 MHz) of **4c** a) after treatment with CD_2O under reflux; b) of a product synthesised with CD_2O; c) after treatment of the latter product with CH_2O under reflux.[11]

As an example a section of the ^{1}H NMR spectrum of **4c** is shown in Fig. 1, where a further AB-system appears for the N-CH_2-Ph protons. The assignment of the protons was easily achieved in this case on the basis of the CH_2/CD_2 exchange experiments shown in Fig. 2.

All these NMR results are in a strict sense *only* in agreement with isomer **I**, while they exclude (more or less entirely) the structures of isomers **II** and **III**. It must be kept in mind, however, that the only group which allows a distinction between the isomers **I** and **IV** is the Ar-CHR^1-Ar group, which is always situated between OH and O-CH_2- in **I** while two groups between two OH and two groups between two O-CH_2- structures would be present in **IV**. Therefore, it is important that only ***one*** triplet for the methine

proton of **4c** is found in quite different solvents like $CDCl_3$, acetone-d_6 or benzene-d_6 (Fig. 1).

Further evidence for isomers **I** comes from ^{13}C NMR, where the methine carbon atom at 30 ppm can be easily identified on the basis of a DEPT experiment, and distinguished by its chemical shift from aromatic carbons (>108 ppm) and the CH_3-carbons (14 ppm). In all cases and all solvents studied, only ***one*** signal was found for this carbon atom.

The appearance of a single pair of doublets for each, the O-CH_2-N and the Ar-CH_2-N protons in **3s** and **4g-j** and one triplet for the methine protons is strong evidence for the formation of a pure epimer in the case of chiral amines, having the stereogenic carbon atom attached directly to the nitrogen[12] (Fig. 3a). The product obtained with (S)-2-phenylpropylamine, however, shows for instance a pair of doublets and a pseudo singlet for the N-CH_2-O protons, two (superimposed) triplets for the methine protons of the resorcarene skeleton and two pairs of doublets for the Ar-CH_2-N protons (Fig. 3b). This can be best explained by the presence of the two possible epimers with opposite direction of the benzoxazines.

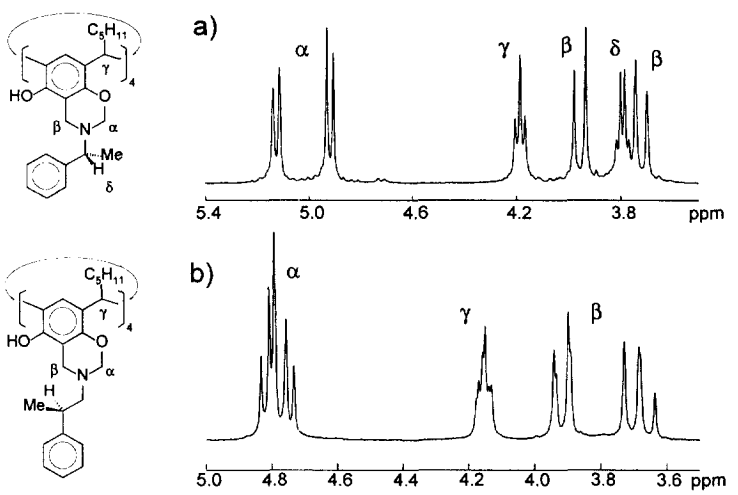


Figure 3: Section of the ^1H NMR spectra of the single enantiomer **3s** (a) and the mixture of epimers **3t** (b). The assignment of protons is indicated.

SEMIEMPIRICAL CALCULATIONS

To characterise the relative stabilities of the four possible regioisomers and to get further insight into the factors determining the observed regioselectivity, semiempirical computations using the PM3 hamiltonian[13] were performed. For these calculations the simpliest example of such a benzoxazine was taken ($R^1 = R^2 = CH_3$) which would be obtained by reaction of **1a** with methylamine. Since the oxazine ring is not planar, it may point towards ("i") and away ("o") from the cavity formed by the resorcarene skeleton. Additionally, the substituent at

the nitrogen (R^2) can assume an axial ("ax") or equatorial ("eq") arrangement with respect to the oxazine ring. Thus, for each of the four regioisomers four basic conformations result, if one assumes the same conformation of all four oxazine rings in the molecule.

From the heats of formation listed in Table 2 it is obvious that the axial arrangement of the N-substituent is energetically strongly favored by approximately 7-9 kcal mol^{-1}. The two conformers (in/out) with axial position of R^2 have always nearly the same energy, the highest difference of 1.2 kcal mol^{-1} being found for the asymmetric (C_1) isomer. For several examples it was also checked that combinations of "in" and "out" gave Δ_fH values in the same range, as shown for the C_4 symmetrical isomer **I** in Table 2, so that the discussion can be restricted to the all-in or all-out arrangement.

Table 2: Heats of formation and geometric parameters calculated for different regioisomeres (compare Scheme 2) of a tetrabenzoxazine with $R^1=R^2=CH_3$. Different orientations of the oxazine ring (in/out) have been considered only for **I** with an axial position of R^2.

Isomer	Δ_fH [kcal mol^{-1}]	$\Delta\Delta_fH$ [kcal mol^{-1}]	Conformation R^2	oxazine	Plane angles [deg]				O···O Distances [Å]			
I	-249.2	0.0	ax	o	130	130	130	129	2.75	2.75	2.75	2.76
	-249.1	0.1	ax	o,o,o,i	130	130	130	130	2.75	2.74	2.75	2.75
	-249.0	0.2	ax	o,o,i,i,	130	130	130	130	2.74	2.74	2.74	2.75
	-249.1	0.1	ax	o,i,o,i	133	126	133	126	2.75	2.75	2.75	2.75
	-248.9	0.3	ax	o,i,i,i	130	130	130	130	2.75	2.74	2.74	2.74
	-248.8	0.4	ax	i	130	130	130	130	2.74	2.74	2.74	2.74
	-241.7	7.5	eq	o	129	131	129	131	2.74	2.74	2.74	2.74
	-240.6	8.6	eq	i	130	130	130	130	2.77	2.76	2.77	2.76
II	-244.5	4.7	ax	o	142	121	143	121	3.16	3.08	2.77	2.76
	-245.7	3.5	ax	i	139	122	135	124	2.92	2.75	2.74	2.74
	-237.7	11.5	eq	o	124	135	123	142	2.76	2.75	2.74	3.12
	-236.6	12.6	eq	i	143	123	135	123	3.04	2.77	2.77	2.75
III	-244.4	4.8	ax	o	125	134	124	140	2.74	2.75	3.09	2.75
	-244.7	4.5	ax	i	130	133	119	131	2.74	2.90	2.75	2.73
	-236.6	12.6	eq	o	125	134	124	140	2.74	2.74	3.09	2.75
	-235.3	13.9	eq	i	132	129	136	130	2.73	2.76	2.99	2.77
IV	-242.8	6.4	ax	o	163	107	163	107	3.54	3.55	3.55	3.54
	-242.4	6.8	ax	i	146	121	144	119	3.12	2.71	3.15	2.75
	-235.8	13.4	eq	o	95	179	91	179	4.18	4.21	4.17	4.23
	-233.3	15.9	eq	i	119	148	119	146	3.19	2.75	3.24	2.71

The C_4 symmetrical isomer turned out to be most stable, followed by the C_1 and the C_S isomer which both have nearly the same stability. The C_{2V} isomer finally is the least stable. This result correlates with the number of possible intramolecular O-H···O hydrogen bonds which is four for the C_4 isomer, three for the C_1 and C_S isomers and only two for the C_{2V} isomer.[14] Obviously the driving force for the observed regioselectivity is the formation of the maximum number of intramolecular hydrogen bonds, and further conformational differences of the resorcarene skeleton (characterised for instance by the different interplanar angles given in Table 2) play only a minor role.

SINGLE CRYSTAL X-RAY ANALYSES

Single crystals suitable for an X-ray analysis were obtained for two tetrabenzoxazines prepared with anilines. Both structures[15] confirm the C_4 symmetrical constitution of the tetrabenzoxazines. (**4e** lies on a twofold crystallographic axis, while **3p** is not on a crystallographic symmetry element.)

For compound **4e** the nitrogen atoms of all benzoxazine rings point towards the cavity and the p-nitrophenyl residues assume, in accordance with the calculations, the axial position. As shown in Fig. 4 they form a cavity with an estimated volume of 250 Å^3 in which a totally disordered acetone molecule (V ≈ 60 Å^3) is included, while a second molecule of acetone is found at a definite position between the four alkyl chains. The size and shape of the molecular cavity may be characterised by the following values:

- the interplanar angles between the resorcinol rings and the best plane through the methine carbons which are 124.9° and 131.4° (indicating a nearly fourfould symmetry)

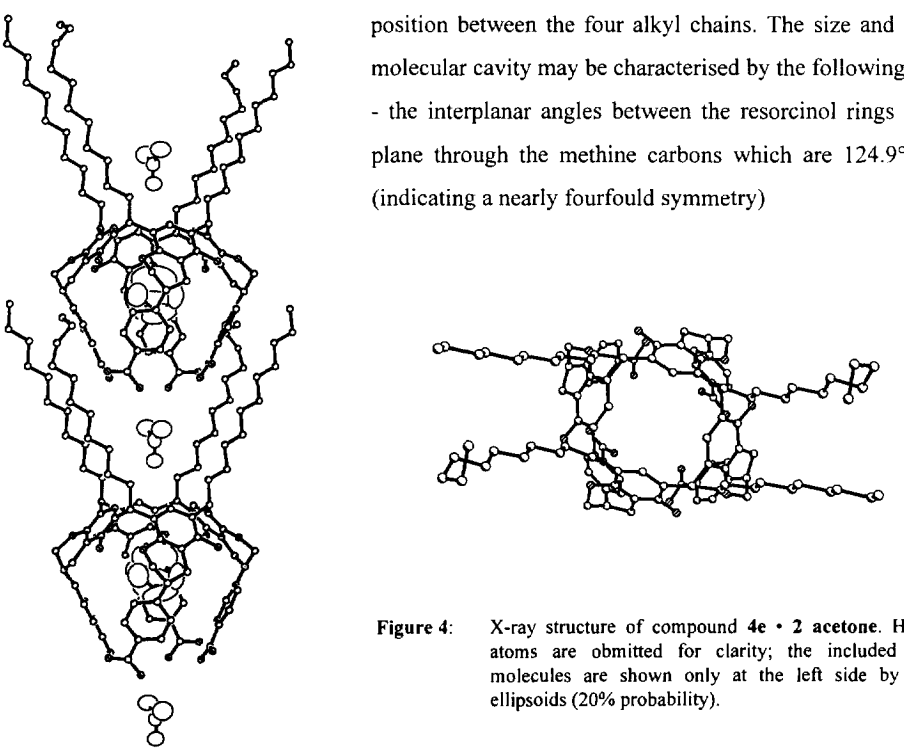


Figure 4: X-ray structure of compound **4e • 2 acetone**. Hydrogen atoms are obmitted for clarity; the included acetone molecules are shown only at the left side by thermal ellipsoids (20% probability).

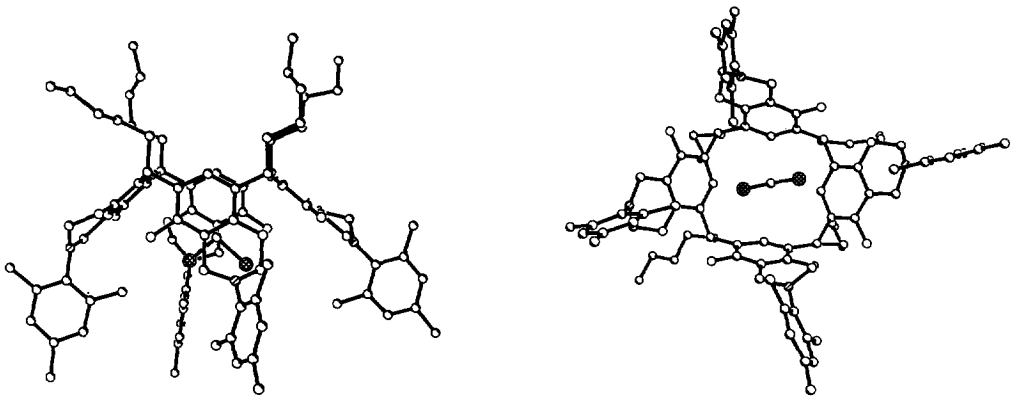


Figure 5: X-ray structure of compound **3p** • CH_2Cl_2; hydrogen atoms are omitted for clarity.

- the diagonal distances of amino nitrogens are 10.49 and 11.18 Å
- the diagonal distances of the nitrogen atoms of the p-nitro groups are 7.02 and 7.61 Å

Intramolecular hydrogen bonds between the OH-groups and the ether oxygens are revealed by O···O distances of 2.77 and 2.79 Å.

Due to their *o*-methyl groups, the aniline residues in **3p** are forced into a position roughly perpendicular to the oxazine rings. Thus, one of these two methyl groups is always pointing towards the cavity. In connection with an included molecule of methylene chloride, this leads to a significantly stronger distortion of the resorcarene skeleton. For **3p** the same characterisation is used as above for **4e**:

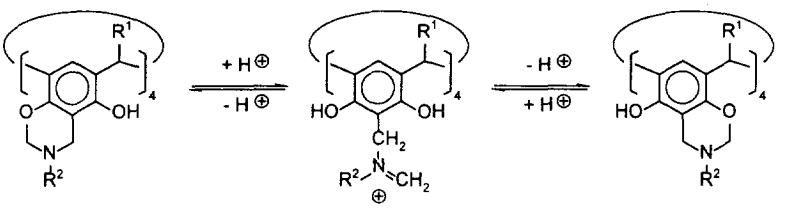
- the interplanar angles are 144.4°, 111.5°, 138.0° and 119.3°
- the diagonal distances of the amino nitrogens are 9.68 and 12.77 Å
- the diagonal distances of the *p*-methyl carbons in the aniline residues are 15.16 and 17.73 Å

Again a solvent molecule (methylene chloride) is included in the cavity.

From the intramolecular O···O distances only three are in the usual range of hydrogen bonds (2.81 - 2.85 Å) while the fourth is slightly longer (2.93 Å).

OPEN QUESTIONS, OUTLOOK

There is now strong evidence from NMR spectra as well as from several X-ray structures[9] that the formation of four benzoxazine rings occurs in a regioselective way, leading exclusively to the chiral, C_4 symmetrical isomer **I**, which is predicted to be the most stable isomer also by the calculations. This high regioselectivity obviously is due to the fact, that the second step in Scheme 1 is reversible, as proved by the CH_2/CD_2 exchange demonstrated in Fig. 3.



Scheme 3: Possible mechanism of the (acid catalysed) isomerisation

However, it was neither possible to split this chiral isomer **I** into the enantiomers (e.g. by chromatographic separation using chiral stationary phases)[9c] nor could any enantioselective host-guest interaction be observed in solution up to date. One reason could be a "sufficiently rapid" equilibrium[9] as indicated in Scheme 3.

This reaction means enantiomerisation in the case of compounds **2**, **3a-r**, **4a-f** derived from achiral primary amines. In the case of **3s-t** and **4g-j** , derived from chiral amines, it means epimerisation and would account for the change in the rotatory power and for the appearance of a second pair of doublets for O-CH_2-N protons in acidified solutions of chloroform.[9c] However, this second epimer has not been isolated in pure form up to now. At the other hand, when a mixture obtained by evaporation of such an acidified solution is refluxed under alkaline catalysis again, the initial pure epimer can be recovered in high yield.

If these considerations are valid, it should be possible to obtain stable enantiomers, by derivatisation of the remaining OH groups in **I**. However, numerous attempts to acylate the remaining OH-groups under various conditions, including those described by Mattay et al[9a] were unsuccessful in our hands.[16] The same is true for an attempted O-alkylation by diazomethane.

EXPERIMENTAL PART

Melting points were determined with a MEL TEMP 2 capillary melting point apparatus and are uncorrected. ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded on a Bruker AC 200; ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AM 400 spectrometer. Coupling constants *J* are given in Hz. Only selected examples of ^{13}C NMR spectra are given in the following. FD mass spectra were recorded with a Finnigan MAT 90 (5 kV/10 mA/min) spectrometer.

General procedure for the acid catalysed preparation of tetrabenzoxazines 2, 3 and 4b

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) a solution of amine (5.4 mmol) in ethanol (5 ml) was added. After 24 - 48 h at room temperature the precipitate (which formed eventually only after adding some drops of water) was filtered off and recrystallised from chloroform-methanol. For compounds **3k** and **3l** no precipitate formed; here 20 ml of water and 20 ml of chloroform were added. The water layer was extracted three times with chloroform and the combined organic layers were washed with water, dried and evaporated. The product thus obtained was usually already pure.

2a: 1.11g (76%); mp: 191°C; (Found: C 76.91, H 6.79, N 5.03, $C_{72}H_{76}N_4O_8$ requires C 76.83, H 6.81, N 4.98); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.82 (s, 4H, ArOH), 7.20 (s, 4H, ArH), 7.12 (m, 20H, ArH), 4.91 (s, 8H, OCH_2N), 4.48 (q, J 7.2, 4H, $RCHAr_2$), 4.01, 3.76 (d, J 17.4, each 4H, $ArCH_2N$), 2.80 (m, 16H, CH_2), 1.73 (d, J 7.2, 12H, CH_3); MS (FD) *m/z* 1126.3 [M^+, 1124.6]

2b: 1.40g (91%); mp: 214°C; (Found: C 77.12, H 7.18, N 4.76, $C_{76}H_{84}N_4O_8$ requires C 77.25, H 7.17, N 4.74); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.77 (s, 4H, ArOH), 7.35 (s, 4H, ArH), 6.82 (s, 8H, ArH), 5.10, 4.97 (d, J 8.8, each 4H, OCH_2N), 4.57 (q, J 6.9, 4H, $RCHAr_2$), 4.28, 4,04 (d, J 16.7, each 4H, $ArCH_2N$), 2.22 (s, 24H, CH_3), 2.08 (s, 12H, CH_3), 1.80 (d, J 6.9, 12H, CH_3)

3a: 0.80g (62%); mp: 180°C (dec.); (Found: C 72.76, H 8.41, N 5.58, $C_{60}H_{84}N_4O_8$ requires C 72.83, H 8.56, N 5.67); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.69 (s, 4H, ArOH), 7.10 (s, 4H, ArH), 4.83, 4.77 (d, J 9.5, each 4H, OCH_2N), 4.20 (t, J 7.9, 4H, $RCHAr_2$), 3.91, 3.71 (d, J 17.2, each 4H, $ArCH_2N$), 2.49 (s, 12H, CH_3), 2.16 (br s, 8H, CH_2), 1.32 (br s, 24H, CH_2), 0.88 (t, J 6.0, 12H, CH_3)

3b: 1.00g (73%); mp: 146°C; (Found: C 73.48, H 8.86, N 5.25, $C_{64}H_{92}N_4O_8$ requires C 73.51, H 8.88, N 5.36); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.76 (s, 4H, ArOH), 7.08 (s, 4H, ArH), 4.94, 4.88 (d, J 9.7, each 4H, OCH_2N), 4.19 (t, J 7.9, 4H, $RCHAr_2$), 3.96, 3.78 (d, J 17.3, each 4H, $ArCH_2N$), 2.68 (dq, J 7.2, J 2.3, 8H, CH_2) 2.15 (br s, 8H, CH_2), 1.32 (s, br, 24H, CH_2), 1.11 (t, J 7.2, 12H, CH_3), 0.89 (t, J 6.5, 12H, CH_3); MS (FD) *m/z* 1045.5 [M^+, 1044.7]

3c: 1.16g (81%); mp: 159°C; (Found: C 73.97, H 9.12, N 4.95, $C_{68}H_{100}N_4O_8$ requires C 74.13, H 9.16, N 5.09); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.78 (s, 4H, ArOH), 7.08 (s, 4H, ArH), 4.92, 4.87 (d, J 9.8, each 4H, OCH_2N), 4.19 (t, J 7.4, 4H, $RCHAr_2$), 3.95, 3.75 (d, J 17.3, each 4H, $ArCH_2N$), 2.56 (m, 8H, CH_2) 2.15 (br s, 8H, CH_2), 1.51 (m, 8H, CH_2), 1.32 (br s, 24H, CH_2), 0.86 (br s, 24H, CH_3); MS (FD) *m/z* 1101.4 [M^+, 1100.8]

3d: 1.10g (77%); mp: 151°C; (Found: C 74.03, H 9.12, N 5.08, $C_{68}H_{100}N_4O_8$ requires C 74.13, H 9.16, N 5.09); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.76 (s, 4H, ArOH), 7.07 (s, 4H, ArH), 5.00 (s, 8H, OCH_2N), 4.18 (t, J 7.9, 4H, $RCHAr_2$), 4.00, 3.89 (d, J 7.6, each 4H, $ArCH_2N$), 2.97 (h, J 6.4, 4H, $NCH(CH_3)_2$), 2.14 (br s, 8H, CH_2), 1.32 (br s, 24H, CH_2), 1.12 (d, J 6.4, 12H, $NCH(CH_3)_2$), 1.07 (d, J 6.4, 12H, $NCH(CH_3)_2$), 0.88 (br t, 12H, CH_3); MS (FD) *m/z* 1101.8 [M^+, 1100.8]

3e: 1.32g (88%); mp: 75°C; (Found: C 74.65, H 9.41, N 4.82, $C_{72}H_{108}N_4O_8$ requires C 74.70, H 9.40, N4.84); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.78 (s, 4H, ArOH), 7.07 (s, 4H, ArH), 4.88 (s, 8H, OCH_2N), 4.18 (t, J 7.7, 4H, $RCHAr_2$), 3.96, 3.74 (d, J 17.3, each 4H, $ArCH_2N$), 2.56 (br s, 8H, CH_2), 2.16 (br s, 8H, CH_2), 1.32 (br s, 40 H, CH_2), 0.87 (t, J 7.2, 24H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, RT): δ = 149.84, 148.43, 125.67, 123.78, 120.88, 107.27, 82.67, 50.85, 45.81, 33.89, 32.99, 30.56, 28.07, 23.12, 20.44, 14.44, 13.89; MS (FD) *m/z* 1157.2 [M^+, 1157.7]

3f: 1.22g (81%); mp: 167°C; (Found: C 74.61, H 9.46, N 4.82, $C_{72}H_{108}N_4O_8$ requires C 74.70, H 9.40, N 4.84); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.77 (s, 4H, ArOH), 7.02 (s, 4H, ArH), 5.07, 4.97 (d, J 10, each 4H, OCH_2N), 4.15 (t, J 7.0, 4H, $RCHAr_2$), 4.02, 3.89 (d, J 17.7, each 4H, $ArCH_2N$), 2.11 (br s, 8H, CH_2), 1.29 (br s, 24H, CH_2), 1.10 (s, 36H, CH_3), 0.86 (br t, 12H, CH_3); MS (FD) *m/z* 1157.7 [M^+, 1156.8]

3g: 1.83g (94%); mp: 71°C; (Found: C 77.23, H 10.49, N 3.76, $C_{96}H_{156}N_4O_8$ requires C 77.15, H 10.53, N 3.75); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.78 (s, 4H, ArOH), 7.07 (s, 4H, ArH), 4.92, 4.86 (d, J 10.3, each 4H, OCH_2N), 4.18 (t, J 7.0, 4H, $RCHAr_2$), 3.95, 3.76 (d, J 17.3, each 4H, $ArCH_2N$), 2.58 (m, 8H, CH_2) 2.14 (br s, 8H, CH_2), 1.48 (br s, 8H, CH_2), 1.23 (br s, 80H, CH_2), 0.86 (br s, 24H, CH_3); MS (FD) *m/z* 1494.7 [M^+, 1493.2]

3h: 1.24 (76%); mp: 151°C; (Found: C 76.32, H 8.91, N 4.44, $C_{80}H_{112}N_4O_8$ requires C 76.38, H 8.98, N 4.46); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.71 (s, 4H, ArOH), 7.07 (s, 4H, ArH), 5.06, 5.01 (d, J 9.9, each 4H, OCH_2N), 4.16 (t, J 7.4, 4H, $RCHAr_2$), 4.00, 3.89 (d, J 18.0, each 4H, $ArCH_2N$), 2.53 (br s, 4H, $NCHR_2$), 2.13-1.13 (br s, 64H, CH_2), 0.87 (br t, 12H, CH_3); MS (FD) *m/z* 1262.1 [M^+, 1260.9]

3i: 1.24g (65%); mp: 149°C; (Found: C 78.07, H 8.99, N 3.77, $C_{96}H_{132}N_4O_8$ requires C 78.43, H 9.05, N 3.81); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.71 (s, 4H, ArOH), 7.05 (s, 4H, ArH), 5.09, 5.00 (d, J 11.0, each 4H, OCH_2N), 4.16 (t, 4H, $RCHAr_2$), 4.06, 3.89 (d, J 17.5, each 4H, $ArCH_2N$), 2.17 (br s, 8H, CH_2), 2.02 (br s, 24H, CHR_3), 1.69 (br s, 24H, CH_2), 1.58 (br s, 24H, CH_2), 1.29 (br s, 24H, CH_2), 0.85 (t, 12H, CH_3); MS (FD) *m/z* 1470.6 [M^+, 1470.1]

3j: 1.19g (84%); mp: 141°C; (Found: C 74.60, H 8.46, N 5.02, $C_{68}H_{92}N_4O_8$ requires C 74.68, H 8.49, N 5.13); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.70 (s, 4H, ArOH), 7.12 (s, 4H, ArH), 5.84 (m, 4H, *CH*=CH_2), 5.21 (m, 8H, CH=*CH_2*), 4.90 (s, 8H, OCH_2N), 4.22 (t, 4H, $RCHAr_2$), 4.00, 3.78 (d, J 17.5, each 4H, $ArCH_2N$), 3.25 (m, 8H, CH_2), 2.18 (br s, 8H, CH_2), 1.34 (br s, 24H, CH_2), 0.90 (t, J 6.5, 12H, CH_3); MS (FD) *m/z* 1093.7 [M^+, 1092.7]

3k: 1.35g (89%); mp: 104°C; (Found: C 70.15, H 8.61, N 4.75, $C_{68}H_{100}N_4O_{12}$ requires C 70.07, H 8.65, N 4.81); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.69 (s, 4H, ArOH), 7.06 (s, 4H, ArH), 4.95, 4.87 (d, J 9.8, each 4H, OCH_2N), 4.16 (t, J 7.2, 4H, $RCHAr_2$), 3.98, 3.79 (d, J 17.4, each 4H, $ArCH_2N$), 3.45 (t, J 3.6, 8H, CH_2), 3.33 (s, 12H, CH_3), 2.81 (t, J 3.6, 8H, CH_2), 2.12 (br s, 8H, CH_2), 1.29 (br s, 24H, CH_2), 0.86 (t, J 6.2, 12H, CH_3); MS (FD) *m/z* 1165.7 [M^+, 1164.7]

3l: 1.68g (93%); mp: 139°C; (Found: C 69.27, H 8.76, N 8.06, $C_{80}H_{120}N_8O_{12}$ requires C 69.32, H 8.73, N 8.09); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.67 (s, 4H, ArOH), 7.05 (s, 4H, ArH), 4.93, 4.87 (d, J 10.3, each 4H, OCH_2N), 4.15 (t, J 7.5, 4H, $RCHAr_2$), 3.95, 3.75 (d, J 17.3, each 4H, $ArCH_2N$), 3.62 (t, J 4.4, 16H, CH_2), 2.78 (m, 8H, CH_2), 2.48 (t, J 6.4, 8H, CH_2), 2.38 (d, J 3.7, 16H, CH_2), 2.13 (br s, 8H, CH_2), 1.30 (br s, 24H, CH_2), 0.87 (t, J 6.4, 12H, CH_3); MS (FD) *m/z* 1386.9 [M^+, 1384.9]

3m: 1.18g (80%); mp: 122°C; (Found: C 78.27, H 8.11, N 4.07, $C_{88}H_{108}N_4O_8$ requires C 78.30, H 8.06, N 4.14); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.73 (s, 4H, ArOH), 7.27-7.12 (m, 24H, ArH), 4.97 (s, 8H, OCH_2N), 4.19 (t, J 7.1, 4H, $RCHAr_2$), 4.02, 3.75 (d, J 17.5, each 4H, $ArCH_2N$), 2.93-2.76 (m, 16H, CH_2), 2.15 (br s, 8H, CH_2), 1.32 (br s, 24H, CH_2), 0.88 (t, J 7.1, 12H, CH_3)

3n: 1.25g (75%); mp: 108°C; (Found: C 77.83, H 7.70, N 4.29, $C_{84}H_{100}N_4O_8$ requires C 77.99, H 7.79, N 4.33); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.73 (s, 4H, ArOH), 7.30 - 7.17 (m, 24H, Ar H), 4.93, 4.87 (d, J 9.7, each 4H, OCH_2N), 4.25 (t, J 7.5, 4H, $RCHAr_2$), 3.95, 3.76 (d, J 17.5, each 4H, $ArCH_2N$), 3.95 (d, J 13.2, 8H, NCH_2Ar), 2.35 - 2.09 (m, 8H, CH_2), 1.36 (m, 24H, CH_2), 0.91 (t, J 6.5, 12H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, RT): δ = 149.63, 147.92, 137.69, 128.91, 128.29, 127.25, 124.35, 123.56, 121.17, 108.37, 82.12, 64.15, 55.66, 32.69, 33.62, 27.73, 22.65, 14.09; MS (FD) *m/z* 1294.2 [M^+, 1293.7]

3o: 1.55g (78%); mp: 144°C; (Found: C 72.07, H 7.59, N 3.59, $C_{92}H_{116}N_4O_{16}$ requires C 72.02, H 7.63, N 3.65); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.74 (s, 4H, ArOH), 7.18 (s, 4H, ArH), 6.90 (s, 4H, ArH), 6.77 (d, J 8.1, 4H, ArH), 6.61 (d, J 8.1, 4H, ArH), 4.89, 4.81 (d, J 10.0, each 4H, OCH_2N), 4.25 (t, J 7.5, 4H, $RCHAr_2$), 4.21, 3.95 (d, J 17.5, each 4H, $ArCH_2N$), 3.87-3.63 (m, 12H, CH_2), 3.80 (s, 12H, CH_3), 3.76 (s, 12H, CH_3), 2.20 (br s, 8H, CH_2), 1.35 (br s, 24H, CH_2), 0.90 (t, J 6.2, 12H, CH_3); MS (FD) *m/z* 1535 [M^+, 1532.8]

3p: 1.65g (90%); mp: 117°C; (Found: C 78.56, H 8.33, N 4.03, $C_{92}H_{116}N_4O_8$ requires C 78.60, H 8.32, N 3.98); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.72 (s, 4H, ArOH), 7.21 (s, 4H, ArH), 6.83 (s, 8H, ArH), 5.11, 4.98 (d, J 8.9, each

4H, OCH_2N), 4.30 (t, 4H, $RCHAr_2$), 4.28, 4.07 (d, J 16.7, each 4H, $ArCH_2N$), 2.24 (s, 12H, CH_3), 2.22 (s, 12H, CH_3), 2.17 (br s, 8H, CH_2), 2.10 (s, 12H, CH_3), 1.36 (br s, 24H, CH_2), 0.91 (t, J 6.4, 12H, CH_3)

3q: 1.02g (55%); mp: 133°C (dec.); (Found: C 67.63, H 6.13, N 7.80, $C_{80}H_{88}N_8O_{16}$ requires C 67.78, H 6.26, N 7.90); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 8.12 (d, J 9, 8H, ArH), 7.53 (s, 4H, ArOH), 7.06 (s, 4H, ArH), 7.00 (d, J 9, 8H, ArH), 5.42 (s, 4H, OCH_2N), 4.62, 4.42 (d, J 17, each 4H, $ArCH_2N$), 4.16 (t, J 7.4, 4H, $RCHAr_2$), 2.13 (br s, 8H, CH_2), 1.30 (br s, 24H, CH_2), 0.87 (br t, 12H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, RT): δ = 152.81, 148.22, 148.09, 140.59, 125.53, 124.62, 123.61, 120.51, 116.21, 108.9, 76.30, 66.83, 33.73, 31.33, 28.78, 22.89, 14.94; MS (FD) *m/z* 1418.2 [M^+, 1417.6]

3r: 1.02g (49%); mp: 92°C; (Found: C 77.85, H 6.81, N 3.53, $C_{104}H_{108}N_4O_{12}$ requires C 77.78, H 6.78, N 3.49); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.74 (s, 4H, ArOH), 7.31-6.79 (m, 40 H, ArH), 5.44, 5.35 (d, J 10.5, each 4H, OCH_2N), 4.53, 4.39 (d, J 16.2, each 4H, $ArCH_2N$), 4.29 (t, J 7.4, 4H, $RCHAr_2$), 2.25 - 2.01 (m, 8H, CH_2), 1.47 - 1.18 (m, 24H, CH_2), 0.85 (t, J 6.0, 12H, CH_3); MS (FD) *m/z* 1607.2 [M^+, 1606.0]

3s: 1.34g (84%); mp: 102°C; $[\alpha]_D^{20}$ = 107.79°; (Found: C 78.23, H 8.02, N 4.11, $C_{88}H_{108}N_4O_8$ requires C 78.30, H 8.06, N 4.14); ^{1}H NMR (200 MHz, $CDCl_3$, RT): 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, 4.92 (d, J 9.8, each 4H, OCH_2N), 4.15 (t, J 7.7, 4H, $RCHAr_2$), 3.95, 3.72 (d, J 17.3, each 4H, $ArCH_2N$), 3.79 (q, J 6.6, 4H, $CH(CH_3)Ph$), 2.25-2.00 (m, 8H, CH_2), 1.43-1.07 (m, 24H, CH_2), 0.85 (t, J 6.9, 12H, CH_3);

4b: 1.18g (69%)mp: 78°C; (Found: C 69.27, H 8.76, N 8.06, $C_{80}H_{120}N_8O_{12}$ requires C 69.32, H 8.73, N 8.09); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.74 (s, 4H, ArOH), 7.06 (s, 4H, ArH), 4.88 (s, 8H, OCH_2N), 4.18 (br t, 4H, $RCHAr_2$), 3.94, 3.73 (d, J 17.3, each 4H, $ArCH_2N$), 3.55 (t, J 6.1, 8H, CH_2), 2.57 (m, 8H, CH_2), 2.15 (br s, 8H, CH_2), 1.49 (br s, 8H, CH_2), 1.24 (br s, 96H, CH_2), 0.86 (br s, 24H, CH_3)

General procedure for the alkali catalysed preparation of tetrabenzoxazines 4a,c-j

A solution of the amine (5.4 mmol) in 10 ml ethanol-toluene (v/v = 1/1) containing three drops of aqueous 2 M KOH is added to a solution of resorcarene **1c** (1.3 mmol) and paraformaldehyde (17.5 mmol) in 10 ml ethanol-toluene (v/v = 1/1). The mixture is refluxed under argon for 20 h. The precipitate is filtered off by suction and recrystallised from chloroform-ethanol.

4a: 1.73g (89%); mp: 89°C; (Found: C 77.25, H 10.59, N 3.80, $C_{96}H_{156}N_4O_8$ requires C 77.16, H 10.52, N 3.75); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.70 (s, 4H, ArOH), 7.08 (s, 4H, ArH), 4.89, 4.80 (d, J 10.3, each 4H, OCH_2N), 4.19 (t, J 7.6, 4H, $RCHAr_2$), 3.96, 3.74 (d, J 17.3, each 4H, $ArCH_2N$), 2.67-2.48 (m, 8H, CH_2), 2.16 (m, 8H, CH_2), 1.60-1.25 (m, 88H, CH_2), 0.88 (t, J 4.0, 12H, CH_3), 0.87 (t, J 3.6, 12H, CH_3); MS (FD) *m/z* 1495.9 [M^+, 1494.2]

4c: 1.96g (93%); mp: 84°C; (Found: C 79.67, H 9.23, N 3.51, $C_{108}H_{148}N_4O_8$ requires C 79.56, H 9.15, N 3.44); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.71 (s, 4H, ArOH), 7.29 - 7.16 (m, 24H, ArH), 4.91, 4.85 (d, J 9.7, each 4H, OCH_2N), 4.23 (t, J 7.7, 4H, $RCHAr_2$), 3.95, 3.77 (d, J 17.4, each 4H, $ArCH_2N$), 3.95 (d, J 13.3, 8H, NCH_2Ar), 2.25 - 2.16 (m, 8H, CH_2), 1.38 - 1.36 (m, 8H, CH_2), 1.24 (m, 64H, CH_2), 0.86 (t, J 6.7, 12H, CH_3); MS (FD) *m/z* 1630.5 [M^+, 1630.4]

4d: 1.72g (73%); mp: 135°C; (Found: C 79.68, H 10.02, N 3.01, $C_{120}H_{180}N_4O_8$ requires C 79.77, H 10.04, N 3.10); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.68 (s, 4H, ArOH), 7.04 (s, 4H, ArH), 5.06, 4.97 (d, J 10.5, each 4H, OCH_2N),

4.17 (t, J 7.3, 4H, $RCHAr_2$) 4.07, 3.87 (d, J 17.6, each 4H, $ArCH_2N$), 2.25-1.91 (m, 20H, CH_2 and CH), 1.77-1.10 (m, 120H, CH_2), 0.85 (t, J 6.9, 12H, CH_3)

4e: 1.37g (62%); mp: 192°C (dec.); (Found: C 71.07, H 7.74, N 6.43, $C_{104}H_{136}N_8O_{16}$ requires C 71.21, H 7.81, N 6.39); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.55 (d, J 9.3, 16H, ArH), 7.51 (s, 4H, ArOH), 7.04 (s, 4H, ArH), 5.41 (s, 8H, OCH_2N), 4.61, 4.40 (d, J 16.9, each 4H, $ArCH_2N$), 4.14 (t, J 7.7, 4H, $RCHAr_2$), 2.15 - 2.09 (m, 8H, CH_2), 1.32-1.21 (m, 72H, CH_2), 0.85 (t, J 6.8, 12H, CH_3); MS (FD) *m/z* 1693 [M^+, 1698.2]

4f: 1.34g (53%); mp: 74°C; (Found: C 78.98, H 8.04, N 2.78, $C_{128}H_{156}N_4O_{12}$ requires C 79.14, H 8.09, N 2.88); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 7.70 (s, 4H, ArOH), 7.25-6.81 (m, 40H, ArH), 5.43, 5.30 (d, J 10.4, each 4H, OCH_2N), 4.58, 4.43 (d, J 17.2, each 4H, $ArCH_2N$), 4.21 (t, J 7.2, 4H, $RCHAr_2$), 2.17 (m, 8H, CH_2), 1.59-1.25 (m, 72H, CH_2), 0.87 (t, J 6.1, 12H, CH_3); MS (FD) *m/z* 1943.9 [M^+, 1942.7]

4g: 1.95g (89%); mp: 72°C; $[\alpha]_D^{20}$ = -89.96°; (Found: C 79.62, H 8.47, N 3.42, $C_{112}H_{156}N_4O_8$ requires C 79.77, H 9.32, N 3.32); ^{1}H NMR (400 MHz, $CDCl_3$, RT): δ = 7.65 (s, 4H, ArOH), 7.17 (d, J 7.2, 8H, ArH), 7.08 (s, 4H, ArH), 7.02 (t, J 7.5, 8H, ArH), 6.93 (t, J 7.3, 4H, ArH), 5.12, 4.90 (d, J 9.9, each 4H, OCH_2N), 4.16 (t, J 7.7, 4H, $RCHAr_2$), 3.94, 3.72 (d, J 17.3, each 4H, $ArCH_2N$), 3.78 (q, J 6.6, 4H, C*H*(CH_3)Ph), 2.30-2.09 (m, 8H, CH_2), 1.43-1.07 (m, 84H, CH_2), 0.87 (t, J 6.9, 12H, CH_3); MS (FD) *m/z* 1686.9 [M^+, 1686.5]

4h: 1.91g (87%); mp: 72°C; $[\alpha]_D^{20}$ = 89.76°; (Found: C 79.73, H 9.06, N 3.42, $C_{112}H_{156}N_4O_8$ requires C 79.77, H 9.32, N 3.32); ^{1}H NMR (400 MHz, $CDCl_3$, RT): δ = 7.65 (s, 4H, ArOH), 7.16 (d, J 7.3, 8H, ArH), 7.08 (s, 4H, ArH), 7.03 (t, J 7.5, 8H, ArH), 6.94 (t, J 7.4, 4H, ArH), 5.11, 4.90 (d, J 10.1, each 4H, OCH_2N), 4.17 (t, J 7.7, 4H, $RCHAr_2$), 3.94, 3.71 (d, J 17.4, each 4H, $ArCH_2N$), 3.78 (q, J 6.6, 4H, C*H*(CH_3)Ph), 2.31 - 2.08 (m, 8H, CH_2), 1.43 - 1.09 (m, 84H, CH_2), 0.86 (t, J 6.8, 12H, CH_3); MS (FD) *m/z* 1686.9 [M^+, 1686.5]

4i: 1.79g (81%); mp: 76°C; $[\alpha]_D^{20}$ = 75.18°; (Found: C 78.52, H 10.43, N 3.25, $C_{112}H_{180}N_4O_8$ requires C 78.64, H 10.61, N 3.28); ^{1}H NMR (400 MHz, $CDCl_3$, RT): δ = 7.78 (s, 4H, ArOH), 7.05 (s, 4H, ArH), 4.97, 4.92 (d, J 9.6, each 4H, OCH_2N), 4.15 (t, J 7.4, 4H, $ArCH_2N$), 3.91, 3.78 (d, J 17.4, 8H, $ArCH_2N$), 2.62-2.54 (m, 4H, C*H*(CH_3)Ph), 2.28-0.96 (m, 136H, CH_2), 0.86 (t, J 6.7, 12H, CH_3); MS (FD) *m/z* 1710.4 [M^+, 1710.7]

4j: 1.91g (78%); mp: 89°C; $[\alpha]_D^{20}$ = 91.72°; (Found: C 82.15, H 9.12, N 3.07, $C_{126}H_{164}N_4O_8$ requires C 81.49, H 8.76, N 2.97); ^{1}H NMR (400 MHz, $CDCl_3$, RT): δ = 7.69 (s, 4H, ArOH), 7.59-7.09 (m, 28H, ArH), 5.07, 4.88 (d, J 10.0, 8H, OCH_2N), 4.15 (t, J 7.6, 4H, $ArCH_2N$), 3.96, 3.75 (d, J 17.5, 8H, $ArCH_2N$), 3.76 (q, J 6.9, 4H, C*H*(CH_3)Ph), 2.28-2.09 (m, 8H, CH_2), 1.50-1.12 (m, 84H, CH_2), 0.83 (t, J 6.7, 12H, CH_3); MS (FD) *m/z* 1886.9 [M^+, 1886.7]

General procedure for the preparation of secondary amines 5 and 6

A solution of the tetrabenzoxazine (0.25 mmol), 2 ml conc. hydrochloric acid and 4 ml water in 50 ml isopropanol was heated under reflux. While water and formaldehyde were removed by azeotropic distillation two times 2 ml conc. hydrochloric acid and 4 ml water were added. The remaining isopropanol was finally evaporated and the crude product recrystallised from chloroform-methanol.

5: obtained from tetrabenzoxazine **3f**; 370 mg (89%); mp: 153°C; ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 9.35 (s, 8H, NH_2^+), 7.52 (br s, 8H, OH), 7.17 (s, 4H, ArH), 4.29 (t, J 7.1, 4H, $RCHAr_2$), 4.11 (br s, 8H, NCH_2Ar), 2.14 (br s, 8H, CH_2), 1.56 (s; 36H, CH_3), 1.31 (br s, 24H, CH_2), 0.86 (t, J 7.1, CH_3).

6a: obtained from tetrabenzoxazine **4a**; 275 mg (69%); mp: 143°C; (Found: C 69.47, H 10.19, N 3.37, $C_{92}H_{156}N_4O_8$ • 4 HCl requires C 69.41, H 10.13, N 3.52); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 9.24 (s, 8H, NH_2^+), 7.77 (br s, 8H, OH), 7.18 (s, 4H, ArH), 4.29 (t, J 7.4, 4H, $RCHAr_2$), 4.17 (br s, 8H, NCH_2Ar), 3.10 (br s, 8H, CH_2), 2.31-2.05 (m; 8H, CH_2), 1.93-1.24 (m; 88H, CH_2), 0.92 (t, J 7.3, CH_3), 0.87 (t, J 6.4, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$, RT): δ = 150.25, 126.36, 124.90, 108.81, 49.19, 43.55, 34.33, 32.79, 31.95, 29.73, 29.41, 28.01, 27.53, 22.71, 19.92, 14.13, 13.51.

6b: obtained from tetrabenzoxazine **4c**; 300 mg (77 %); mp: 201-208°C; (Found: C 72.91, H 8.58, N 3.15, $C_{104}H_{148}N_4O_8$ • 4 HCl requires C 72.28, H 8.87, N 3.24); ^{1}H NMR (200 MHz, $CDCl_3$, RT): δ = 9.07 (s, 8H, NH_2^+), 7.10 (br s; 8H, OH), 7.66 (d, J 3.7, 8H, ArH), 7.38 (br s, 12H, ArH), 7.10 (s, 4H, ArH), 4.28 (br s, 8H, NCH_2Ar), 4.20 (t, J 7.3, 4H, $RCHAr_2$), 4.16 (br s, 8H, NCH_2Ph), 2.27-1.95 (m, 8H, CH_2), 1.45-1.01 (m, 72H, CH_2), 0.84 (t, J 6.4, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$, RT): δ = 150.40, 130.43, 129.73, 129.46, 129.06, 126.31, 124.55, 108.54, 51.73, 41.62, 34.33, 33.23, 31.93, 29.69, 29.38, 27.89, 22.69, 14.12.

X-ray crystal structure analyses: Single crystals of **3p** were obtained from dichloromethane/acetonitrile, $C_{92}H_{116}N_4O_8$ • CH_2Cl_2, M_r = 1490.81, orthorhombic, space group $Pna2_1$, a = 16.084(1), b = 18.770(3), and c = 28.904(5) Å, V = 8726(2) Å^3, Z = 4, D_x = 1.135 g cm^{-3}, λ (Cu Kα) = 1.54184 Å, $F(000)$ = 3208, T = 293 K. Data collection with an Enraf-Nonius CAD4 diffractometer. The structure was solved by direct methods and refined on F^2 using SHELXL-93.[17] Refinement led to R = 0.1033, wR = 0.2862 and S = 1.023 for $I>2\sigma(I)$.

Single crystals of **4e** were obtained from acetone/ethanol, $C_{104}H_{136}N_8O_{16}$ • $2CH_3COCH_3$, M_r = 1870.4, monoclinic, space group $C2/c$, a = 20.259(1), b = 17.036(1), and c = 31.617(1) Å, β = 105.73(1)°, V = 10503(5) Å^3, Z = 4, D_x = 1.183 g cm^{-3} , λ (Mo Kα) = 0.71073 Å, μ = 0.08 mm^{-1}, $F(000)$ = 4032.0, T = 293 K. Data collection were performed on a computer controlled three circle diffracometer equipped with a CCD area detector and a rotating anode (focus: 0.5 x 5 mm, 50 kV, 120mA). Refinement of $(F_0^2-F_C^2)^2$ based on all 6229 unique reflections led to R = 0.0756, wR = 0.175 and S = 1.037. All calculations were done with the programs SHELX86, SHELXTL-PLUS, and SHELXL.[17]

Calculations: The semiempirical calculations were performed with the PM3 Hamiltonian[13a] in the MOPAC 6.0[13b] package. The geometries were fully optimised using increased precision (keyword PRECISE) without applying any constraints. For the building of the structures and visualisation of the results the SYBYL[18] software was used. The programs were run on either a SGI Crimson VGXT or an IBM RISC/6000 workstation.

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