A Novel Electroneutral Anion Host Based on Organoboron Betaines

Anna Cattani and Franz P. Schmidtchen*

München, Institut für Organische Chemie und Biochemie der Technischen Universität

Received January 13th, 1999

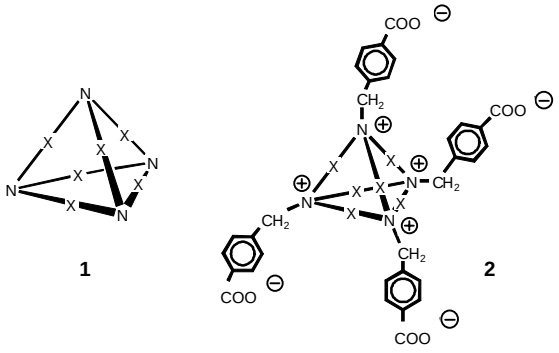
Dedicated to Prof. Fritz Vögtle on the Occasion of his 60th Birthday

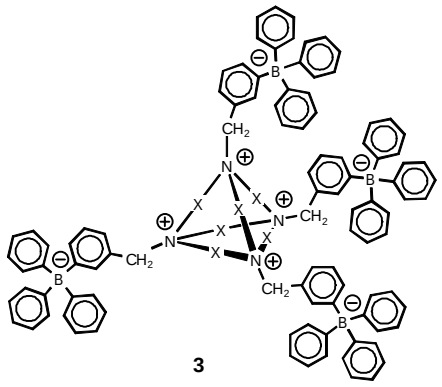
Keywords: Betaines, Boron, Host-Guest chemistry, Inclusion compounds, Supramolecular chemistry

Abstract. Host-guest binding of anions in organic solvents may find attractive applications in ion sensing and transport, if the host can extract the negatively charged guest species from its solvation sphere. The most powerful means to dismantle the anionic guest from solvent molecules that is required for selective binding is to provide positive charges in the host compound. They have to be counterbalanced by negatively charged subsites in order to conserve electroneutrality, but must avoid collapse into ion pairing with the cationic sites. According to this concept the cage compound **3** was constructed by attachment of anionic tetraphenylborate moieties to the parent macrotricyclic amine **1**. The betainic product **3** was shown to be soluble in water-immiscible dipolar organic solvents like propylene carbonate and formed inclusion complexes with chloride and bromide in the gas phase as well as in solution.

The design of artificial molecular hosts for anions [1] heavily depends on the solvation conditions applied in the molecular recognition event. While in strongly solvating solvents (*e.g.* in water or alcohols) the accumulation of positive charge in the host may furnish a viable route for enhancing guest binding affinity and selectivity this path is generally blocked when solvents of low polarity are to be used. This is due to the low solubility of highly charged species in these solvents as well as to the tendency to form ion pairs with whatever anion is present thereby limiting the attainable selectivity. The shining goal of maximum discriminatory power requires a well balanced design of attractive and repulsive interactions in the host–guest complex. In principle a satisfactory host design will be more readily accomplished the larger the individual energetic contributions are (Coulombic-, van der Waals-,solvophobic-, hydrogen bonding-interaction, etc.) in an absolute sense. For this reason strong and far reaching Coulombic attractions resting on full positive charges in the host may be preferable over weaker dipole interactions like hydrogen bonding. Making use of this notion, however, mandates a host design that enables a unique guest binding mode, ensures high charge density, and avoids its annihilation by inter- or intramolecular unspecific ion pairing. On top all charged sites must be readily solvated to allow sufficient solubility in less polar solvents.

Good candidates to meet these requirements are zwitterionic compounds built on the tetrahedral macrocyclic core structure **1**. Cationic derivatives of this cage compound were shown to bind a variety of simple anions in protic solutions [2, 3] by encapsulation [4]. The





electroneutral borane (BH_3) adduct of **1** exploited the attraction of guest anions to a fixed array of dipoles to allow selective anion binding in apolar solvents [5]. An extension of the original idea was the attachment of anionic sites to the macrotricycle [6] to give the zwitterionic compound **2** having a zero overall charge. The

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 1999 1436-9966/99/3410X-291 $ 17.50 + .50/0

internal charge distribution enforced by the covalent molecular skeleton allowed anion binding in much the same way and with similar affinity as realized in the cationic counterparts but avoided interference by counteranions which are inevitably present in the cationic host. A great disadvantage of **2** with respect to potential applications for electrochemical anion sensing or membrane transport is its insolubility in almost all organic solvents except for the lower alcohols. The replacement of the hydrophilic carboxylate groups by more hydrophobic sites could be a remedy, if a number of requirements can be met. The desired anionic moiety must be chemically stable, easy to introduce, exhibit satisfactory solubility in organic solvents and should belong to the group of non-coordinating anions [7a]. The latter feature would open the option to separate ion pairs in organic solvents by complexation of the anionic part leaving the cation in a noncoordinated "naked" and potentially more reactive state. Among the few options available that would comply with the restrictive catalogue of requirements the tetraphenylborate moiety sticks out because of its modifiability and wide-spread use in organic preparative chemistry [7b]. Though no suitable *C*-functionalized tetraphenylborates have been reported so far in the literature, the decoration of **1** with anionic tetraphenylborate moieties to give the zwitterionic compound **3** seemed feasible. Early indications of the presumed anion binding properties of **3** were obtained from molecular modeling. In a molecular dynamics run *in vacuo* (forcefield MM^+, 300 K; Hyperchem 3) a chloride or bromide ion placed initially at some distance to the cage molecule **3** ended up after some time in the interior of the molecular cavity. This encapsulation process was faster for the more polarizable bromide ion and was accompanied by a drop in the total energy of the system reflecting enthalpic attraction in host–guest complex formation (fig. 1). Here, we report on the synthesis and preliminary binding studies of the macrotricyclic zwitterionic host **3** which was designed along these guidelines.

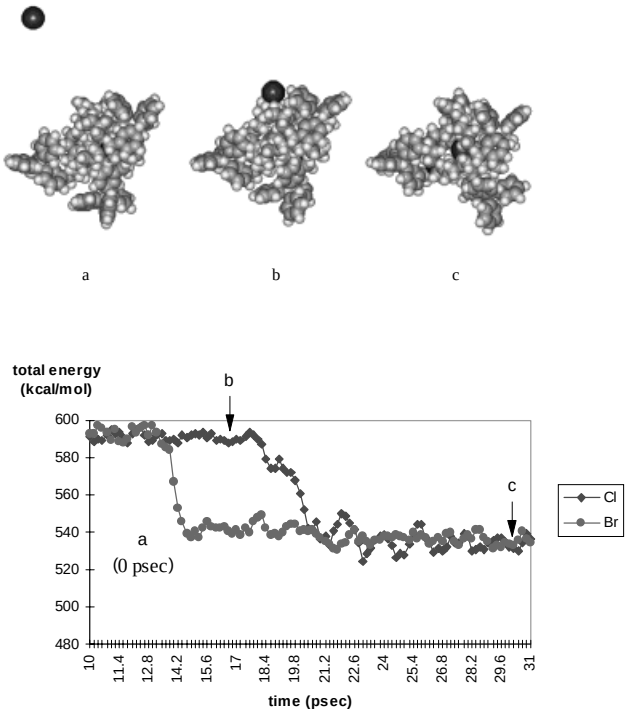
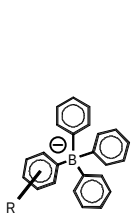


Fig. 1 Molecular dynamics simulation (300 K, MM^+ forcefield, Hyperchem 3) of the encapsulation of bromide and chloride by **3**. The depicted CPK-structures represent the choride complexing process at a) 0 psec, b) 17 psec, c) 30 psec.

Results and Discussion

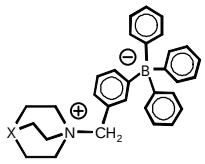
With respect to the synthetic strategy only the convergent approach towards **3** seemed rational using the macrotricyclic amine **1** and a preformed anionic subsite as the parent building blocks. Attachment of the anionic moiety to **1** must then proceed by Menshutkin alkylation [8] forming a chemically quite stable quaternary ammonium salt as the product. Though these nucleophilic substitutions generally give good yields, the four fold reiteration of this process to furnish the tetra-substituted product from **1** might require a particularly reactive alkylation reagent for success. A benzylhalide or mesylate appeared suitable making the benzylbromide **5** first choice as an alkylating agent. Its preparation from the literature known *p*-tolyltriphenylborate **4** [9] by radical bromination appeared straightforward, but all attempts using *N*-bromosuccinimide with chemical (AIBN) or photolytical initiation at reflux in CCl_4 or at ambient temperature invariably resulted in extensive degradation. A more promising access route started with the commercial 4-bromobenzylalcohol **10a** which was silyl-protected and converted to the corresponding borate **6a** by treating the intermittently formed Grignard reagent with triphenylborane according to a standard protocol [9]. Silyl group deprotection by fluoride yielded the alcohol **7a**. Unexpectedly, **7a** and the putative derivative products **8a** or **9a** turned out to be very labile because even at −45 °C under strictly basic conditions the conversion resulted in a complex mixture of products. This chemical sensitivity was attributed to the particular *para*-substitution pattern in the series and was circumvented on using the corresponding *meta* substituted species (series b). Following the analogous route as in the 'a' series the benzylchloride **9b** was finally obtained directly from the alcohol **7b** under standard mesylation conditions thus testifying to the reactivity of the benzylic position towards nucleophilic attack. The enhanced stability of the *m*-substituted phenylborates was also apparent from their HPLC-chromatographic behaviour. Even quite acidic mobile phases (30 mM

H_3PO_4) were tolerated and caused no deterioration as observed in the 'a' series.

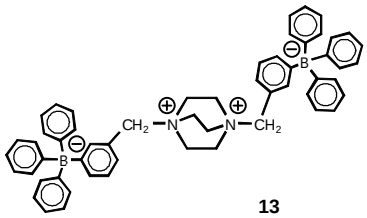


	R a	R b
4	4-CH_3	
5	4-CH_2-Br	
6	4-CH_2-OTBDMSi	3-CH_2-OTBDMSi
7	4-CH_2-OH	3-CH_2-OH
8	4-CH_2-OSO_2CH_3	3-CH_2-OSO_2CH_3
9	4-CH_2-Cl	3-CH_2-Cl

	R a	R b
10	4-CH_2-OH	3-CH_2-OH
11	4-CH_2-OTBDMSi	3-CH_2-OTBDMSi



12a X = CH
12b X = N



13

Quinuclidin and DABCO (diazabicyclooctane) served as model substrates to probe Menshutkin alkylations with **9b**. *N*-methylpyrrolidone (NMP) at first turned out as the solvent of choice since more common solvents regularly used in this type of reactions like ethanol, acetonitrile or chloroform failed to dissolve the product and gave heterogeneous reaction mixtures. If several successive alkylation steps were required as in the prospected preparation of **3**, the precipitation of intermediates most likely would complicate the overall conversion. The solubility properties, however, provided a simple and effective means for purification of the betainic products by reprecipitation from NMP/ethanol mixtures. The monobetainic compounds **12a**, **12b** were obtained in one hour at 80 °C while the introduction of a second phenyloborate into **12b** required prolonged heating for several hours.

Literal transposition of the reaction conditions elaborated in the model reaction to the alkylation of the tetrahedral amine **1** with **9b** led to inhomogeneous mixtures and severe problems in monitoring the multistep conversion. Crucial to success was the elaboration of a ternary gradient HPLC-system that allowed to resolve the various intermediates and made the rapid quantification possible. With this tool at hand the reaction conditions could be optimized. For best results NMP was replaced by propylene carbonate, and relatively short reactions times (2–3 hours) at 150 °C were employed to minimize the degradation of reagents. The assistance of a nonnucleophilic base originally required to maintain the free base form of the macrotricycle was no longer needed under these conditions. Since the product was totally insoluble in organic solvents like toluene, dichloromethane, methanol, THF, acetonitrile or ethyl acetate work up required simple dilution of the crude reaction mixture by one of these solvents to precipitate the tetrakis betainic product **3**. However, with this procedure it proved impossible to remove all of the tetrabutylammonium chloride that was present in the reaction mixture. Exactly one equivalent of this salt copurified with **3** indicating that a rather strong 1:1 host–guest complex might resist disassembly using this technique. On stirring a DMSO solution of the precipitate with mercuric acetate a white precipitate of mercuric chloride formed, and the guest-free tetrasubstituted host **3** was isolated from the supernatant. Chromatographic purification of the target compound **3** suffered from its low solubility and the marked tendency to irreversibly stick to the chromatographic support material. An exception was found using size exclusion chromatography (SEC) at elevated temperature. Preparative separations succeeded on Lichrogel PS 20 taking straight DMF or DMF/acetonitrile mixtures at 78 °C for elution. In this way, low molecular weight salts were separated, and the pure host compound **3** was recovered by high vacuum evaporation of the corresponding fractions.

Preliminary evidence that **3** indeed qualified as an anion receptor emerged also from electrospray mass spectroscopy [10] as well as from isothermal titration calorimetric studies [11]. We were unable to observe the molecular ion peak in the positive or negative ion mode in the ESI-MS spectrum of **3**. On addition of tetrabutylammonium chloride (TBA chloride), however, the signals corresponding to the host–guest complex with 1:1 (*m/z* = 1 925) and 1:2 (*m/z* = 980) stoichiometry were easily identified in the negative ion mass spectrum. High resolution of these signals produced an isotopic distribution pattern that very closely resembled the one predicted on the basis of the natural boron, chlorine and carbon isotopic ratios. Further addition of TBA bromide to the same sample brought up a new signal at *m/z* = 1969 at the expense of the peaks of the chloride complexes and was attributed to the 1:1 bromide host–guest complex. No complexes of higher stoichiometries were observed in this case, but it was obvious that the receptor **3** had a higher affinity for bromide which expelled chloride from its inclusion complex.

A first calorimetric examination revealed an exother-

mic association of **3** with bromide in DMSO. The heat evolved in the titration was rather small precluding so far the determination of the other thermodynamic state functions. Nevertheless, it is safe to state that the novel electroneutral cage compound **3** serves as an anion host in the gas phase as well as in dipolar organic solvents.

The financial support by Deutsche Forschungsgemeinschaft and Fonds der Chemischen Industrie is gratefully acknowledged. We would like also to thank Dr. E. Fontain for helpful discussions on molecular modeling. We are grateful to Mrs. R. Dumitrescu and Prof. Dr. F. R. Kreißl for the measurement of the FAB spectra.

Experimental

All solvents were dried by standard procedures and distilled before use. Commercial chemicals were used as received. Triphenylborane was freshly prepared from its NaOH complex [12], and the macrotricyclic amine **1** was obtained according to the literature [2b]. NMR measurements used Bruker instruments (AM360; WP200) and were internally calibrated to the solvent signal or to tetramethylsilane; the chemical shifts of the ^{11}B-spectra are referred to external $BF_3O(C_2H_5)_2$; all measurements were performed at 25 °C. For ESI-MS spectra a Finnigan LCQ instrument was used with direct loop injection. For the FAB-MS spectra a Finnigan MAT 90 instrument was used, and nitrobenzylalcohol was employed as matrix. All mass spectra were recorded in negative mode. HPLC separations were done with a Merck-Hitachi L-6200 ternary gradient pump connected to a UV-Vis L-4250 detector. *Columns*: N° 1: 250 × 4mm Nucleosil RP C-18, AB, 5 µm; N° 2: 250 × 4 mm Nucleosil C-CN, 5µm. *Gradients*: N° 1: 50% CH_3CN/H_2O to 70% CH_3CN/H_2O in 10 min to 70% CH_3CN/H_2O in 10 min; N° 2: 10% CH_3CN/H_2O to 50 % CH_3CN/H_2O in 10 min to 90% CH_3CN/H_2O in 10 min to 90% CH_3CN/H_2O in 10 min; N° 3: 50% A 50% B to 100% B in 10 min (A: 10% CH_3CN/H_2O, B: 60% CH_3CN/30% propylene carbonate/10% H_2O); N° 4: 50% A 50% B to 100% B in 15 min to 100% B in 5 min (A: 10% CH_3CN/H_2O, B: 60% CH_3CN/ 30% propylene carbonate/10% H_2O). The eluents contained additives which are specified with the actual separations.

m-Bromobenzyl-tert-butyldimethylsilylether (**11b**)

2.1 g of imidazole (31 mmol) and 2.4 g of *tert*-butyldimethylsilylchloride (16 mmol) were added to a solution of 2.7 g of *m*-bromobenzylalcohol (**10b**) (14 mmol) in anhydrous acetonitrile (60 ml), and the reaction mixture was stirred under nitrogen atmosphere for 3 h. The solvent was then evaporated, and the residue was dissolved in dichloromethane (100 ml). After washing with 2 portions of an aqueous 0.5M solution of ammonium acetate (200 ml), the organic phase was evaporated to give 4.0 g of pure product (yield 95%). HPLC analysis: column n°1, isocratic CH_3CN 70%, NH_4Ac buffer 65 mM, pH 6.8, λ = 254 nm; R_v = 22.4 ml. – ^{1}H NMR (360 MHz, CD_3CN): δ/ppm = 7.38 (m, 4H); 4.73 (s, 2H); 0.94 (s, 9H); 0.11 (s, 6H). – ^{13}C NMR (90 MHz, CD_3CN): δ/ppm = 145.3 (ar-C); 131.1 (ar-C); 130.7 (ar-C); 129.8 (ar-C); 125.8 (ar-C); 122.7 (ar-C); 64.7 (ar-CH_2); 26.2 (*tert*-butyl); 18.9 (*tert*-butyl); –5.2 (Me_2–Si).

p-Bromobenzyl-tert-butyldimethylsilylether (**11a**)

The compound was prepared in complete analogy to **11b**. – HPLC analysis: column n°1, isocratic MeOH 90%, containing 30 mM $NaClO_4$ and 30 mM HCOOH, λ = 254 nm; R_v = 8.0 ml. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.36 (m, 4H); 4.73 (s, 2H); 1.00 (s, 9H); 0.17 (s, 6H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 140.4 (ar-C); 131.2 (ar-C); 127.7 (ar-C); 120.5 (ar-C); 64.2 (ar-CH_2); 25.9 (*tert*-butyl); 18.3 (*tert*-butyl); –5.3 (Me_2–Si).

Sodium [3-(tert-butyldimethylsilyloxymethyl)phenyl]triphenylborate (**6b**)

To a slurry of BPh_3 (2.9 g, 11.9 mmol) in dry THF (11 ml) a Grignard solution was added, prepared from *m*-bromobenzyl-*tert*-butyldimethylsilylether (**11b**) (4.0 g, 13.3 mmol) and magnesium turnings (0.33 g, 13.3 mmol) in THF (10 ml). After being stirred for 2 h at room temperature, the solution was poured into a solution of 7 g of Na_2CO_3 in water (40 ml). The THF phase was separated, and the water phase was extracted twice with ethyl acetate (50 ml); the organic phases were combined, and the solvent was removed *in vacuo* The residue was dissolved in ethyl acetate (50 ml), was dried over Na_2SO_4 and filtered. The solvent was removed, and the residue was dried. Yield 5.8 g (99%). The crude product appeared pure enough to be employed in the next synthetic step without further purification. – HPLC analysis: column N°1, gradient N°1, NH_4Ac buffer 65 mM, pH 6.8, λ = 254 nm; R_v = 15.8 ml. – ^{1}H NMR (360 MHz, CD_3CN): δ/ppm = 7.30 (m, ar-H); 7.02 (m, ar-H); 6.87 (m, ar-H); 4.52 (s, 2 H); 0.91 (s, 9H); 0.06 (s, 6H). – ^{13}C NMR (90 MHz, CD_3CN): δ/ppm = 164.7 (B-C); 136.7 (ar-C); 135.7 (ar-C); 135.4 (ar-C); 126.8 (ar-C); 122.7 (ar-C); 121.6 (ar-C); 67.3 (ar-CH_2); 26.4 (*tert*-butyl); 19.0 (*tert*-butyl); –4.9 (Me_2 – Si).

Sodium [4-(tert-butyldimethylsilyloxymethyl)phenyl]triphenylborate (**6a**)

The compound was prepared in complete analogy to **6b**. – HPLC analysis: isocratic, MeOH 90%, column N°1, $NaClO_4/HCO_2H$ buffer 0.030 M, λ = 254 nm; R_v = 9.4 ml. – ^{1}H NMR (200 MHz, CD_3CN): δ/ppm = 7.27 (m, ar-H); 7.02 (m, ar-H); 6.86 (m, ar-H); 4.62 (s, 2H); 0.93 (s, 9H); 0.10 (s, 6H). – ^{13}C NMR (50 MHz, CD_3CN): δ/ppm = 164.7 (B-C); 136.7 (ar-C); 135.4 (ar-C); 126.6 (ar-C); 125.6 (ar-C); 122.8 (ar-C); 66.6 (ar-CH_2); 26.4 (*tert*-butyl); 19.0 (*tert*-butyl); –5.0 (Me_2 – Si).

Tetrabutylammonium [3-(hydroxymethyl)phenyl]triphenylborate (**7b**)

6 g of $NBu_4F{\cdot}2H_2O$ (22.8 mmol) was added to a solution of 5.8 g of sodium [3-(*tert*-butyldimethylsilyloxymethyl)phenyl]triphenylborate (**6b**) (11.9 mmol) in acetonitrile (60 ml). The mixture was stirred at room temperature for 48 h. Water (20 ml) was then added to the solution, and most of the acetonitrile was distilled off to precipitate an amorphous product. After filtration, the solid residue was washed thoroughly with *n*-hexane (60 ml in 3 portions) to isolate, after drying, 6.2 g (yield 88%) of the desired deprotected compound as the tetrabutylammonium salt. – HPLC analysis: column N° 1,

gradient N°1, NH_4Ac buffer 65 mM, pH 6.8, λ = 254 nm; R_v = 6.8 ml. – ^{1}H NMR (360 MHz, CD_3CN): δ/ppm = 7.29 (m, ar-H); 7.18 (m, ar-H); 7.01 (m, ar-H); 6.86 (m, ar-H); 4.40 (s, 2H); 3.06 (m, 8H); 1.58 (m, 8H); 1.35 (m, 8H); 0.98 (t, 12H). – ^{13}C NMR (90 MHz, CD_3CN): δ/ppm = 164.7 (B-C); 136.7 (ar-C); 135.9 (ar-C); 135.4 (ar-C); 127.8 (ar-C); 126.6 (ar-C); 122.7 (ar-C); 121.8 (ar-C); 66.3 (ar-CH_2); 59.3 (NBu_4); 24.3 (NBu_4); 20.3 (NBu_4); 13.8 (NBu_4). – MS (FAB): *m/z* = 349.0 (M^-)

Tetrabutylammonium [4-(hydroxymethyl)phenyl]triphenylborate (**7a**)

The compound was prepared in complete analogy to **7b**. – HPLC analysis: isocratic, MeOH 90%, containing 30 mM $NaClO_4$ and 30 mM HCOOH, column N°1, λ = 254 nm; R_v = 2.8 ml. – ^{1}H NMR (200 MHz, CD_3CN): δ/ppm = 7.29 (m, ar-H); 7.02 (m, ar-H); 6.87 (m, ar-H); 4.46 (s, 2H); 3.05 (m, 8H); 1.58 (m, 8H); 1.35 (m, 8H); 0.98 (t, 12H). – ^{13}C NMR (50 MHz, CD_3CN): δ/ppm = 164.1 (B-C); 136.7 (ar-C); 135.4 (ar-C); 126.6 (ar-C); 125.6 (ar-C); 122.8 (ar-C); 65.7 (ar-CH_2); 59.3 (NBu_4); 24.3 (NBu_4); 20.3 (NBu_4); 13.8 (NBu_4).

Tetrabutylammonium [3-(chloromethyl)phenyl]triphenylborate (**9b**)

0.30 ml of methanesulfonylchloride (3.8 mmol) was added slowly to a solution of 0.5 g of tetrabutylammonium (3-hydroxymethylphenyl)triphenylborate (**7b**) (0.8 mmol) and 0.15 ml of collidine (1.1 mmol) in acetonitrile (2 ml), and the reaction mixture was stirred at 4 °C for 2 days. The solvent was then evaporated, and the residue was washed with a saturated aqueous solution of NBu_4BF_4, then with water and *n*-hexane to obtain the crude product, that crystallized in CH_2Cl_2/EtOH. Yield 0.35 g (72%). Although we were able to obtain a chromatographically pure sample by preparative HPLC (acetonitrile 70%, NH_4Ac buffer), it was impossible to recover the compound from the pooled fractions due to rapid hydrolysis. However, the crude product was pure enough to obtain satisfactory analytical data. – HPLC analysis: gradient N°2, column N° 2, sodium perchlorate/phosphoric acid 0.030M, λ = 254 nm; R_v = 11.4 ml. – ^{1}H NMR (360 MHz, CD_3CN): δ/ppm = 7.40 (m, ar-H); 7.30 (m, ar-H); 7.04 (m, ar-H); 6.96 (m, ar-H); 6.89 (m, ar-H) 4.56 (s, 2 H); 3.04 (m, 8 H); 1.61 (m, 8 H); 1.34 (m, 8 H); 0.98 (t, 12 H). – ^{13}C NMR (90 MHz, CD_3CN): δ/ppm = 164.1 (B-C); 137.2 (ar-C); 136.9 (ar-C); 136.7 (ar-C); 126.8 (ar-C); 126.7 (ar-C); 123.5 (ar-C); 122.8 (ar-C); 59.3 (NBu_4); 49.4 (ar-CH_2); 24.3 (NBu_4); 20.3 (NBu_4); 13.8 (NBu_4). – MS (FAB): *m/z* = 367 (M^-); 332 (M^- – Cl).

N-[3-(Triphenylboranato)benzyl]-1-azoniabicyclo[2.2.2] octane inner salt (**12a**)

To a solution of 100 mg (0.164 mmol) of tetrabutylammonium [3-(chloromethyl)phenyl]triphenylborate (**9b**) in *N*-methylpyrrolidone (0.4 ml), 15.3 mg of quinuclidine (0.135 mmol) was added, and the reaction mixture was stirred at 120 °C for 2.5 h. Water was then added to the solution to precipitate a yellow product. The solid was separated and washed with acetonitrile at reflux to obtain a pure crystalline product, 40 mg (yield 70%). – HPLC analysis: column N° 2, gradient N° 3, perchlorate/phosphoric acid 0.030M, λ = 240 nm R_v = 7.4 ml. – ^{1}H NMR (360 MHz, [D_6]-DMSO): δ/ppm= 7.08 (m, 19 ar-H); 4.16 (s, 2H); 3.26 (m, 6H, αquin.); 2.01 (m, 1H, γquin.); 1.80 (m, 6H, β quin.). – ^{13}C NMR (90 MHz, [D_6]-DMSO): δ/ppm = 162.6 (B-C); 141.2 (ar-C); 136.4 (ar-C); 135.3 (ar-C) 126.0 (ar-C); 125.8 (ar-C); 125.4 (ar-C); 123.7 (ar-C); 121.7 (ar-C); 68.2 (ar-CH_2); 53.2 (αquin.); 23.2 (βquin.); 19.6 (γquin.). – ^{11}B NMR (115 MHz, [D_6]-DMSO): ^{1}H-decoupled δ/ppm = –6.5 (1 B).

N,N'-Bis[3-(triphenylboranato)benzyl]-1,4-azoniabicyclo [2.2.2]octane inner salt (**13**)

110 mg of tetrabutylammonium [3-(chloromethyl)phenyl]triphenyl borate (**9b**) (0.18 mmol) was added to a solution of 16 mg of DABCO (0.14 mmol) in freshly distilled *N*-methylpyrrolidone (0.5 ml). The mixture was stirred at 80 °C, and the reaction was followed by HPLC. After 1/2 h the adduct was completely converted into the monosubstituted product. Tetrabutylammonium [(3-chloromethyl)phenyl]triphenylborate was added in small portions, and the reaction mixture was stirred at 80 °C till the conversion into the desired disubstituted product was complete. Water (1 ml) was then added to the reaction mixture to precipitate an oily residue, that was washed with CH_2Cl_2 (2 ml) and a few drops of CH_3CN to isolate the desired product as a white solid, 70 mg (yield 65%). – HPLC analysis: column N°1, gradient N°1, NH_4Ac buffer 65 mM, pH 6.8, λ = 254 nm; R_v = 20.8 ml; (monosubstituted R_v = 12.6 ml). – ^{1}H NMR (360 MHz, CD_3CN): δ/ppm = 7.55 (m, ar-H); 7.34 (m, ar-H); 7.30 (m, ar-H); 7.19 (ar-H); 7.03 (m, ar-H); 6.95 (m, ar-H); 6.88 (m, ar-H); 4.35 (s, 4H); 3.46 (s, 12 H). – ^{13}C NMR (90 MHz, [D_6]-DMSO): δ/ppm = 162.6 (B-C); 140.8 (ar-C); 137.4 (ar-C); 135.3 (ar-C) 126.1 (ar-C); 125.6 (ar-C); 125.4 (ar-C); 122.6 (ar-C); 121.7 (ar-C); 68.7 (ar-CH_2); 49.8 (CH_2 octane).

1,8,15,22-Tetrakis[3-(triphenylboranato)benzyl]-1,8,15,22-tetraazoniatricyclo[13.13.6.6^{8,22}]tetracontane inner salt (**3**)

43 mg of tetrahedral amine **1** (0.077 mmol) and 300 mg of tetrabutylammonium [(3-chloromethyl)phenyl]triphenylborate (**9b**) (0.49 mmol) were mixed in propylene carbonate (3 ml, HPLC grade), and the reaction mixture was stirred at 150 °C for 4 h while followed by HPLC. The solution was then concentrated by a jet of nitrogen to reduce the volume to half. This concentrated solution was poured into a solution of diethylether (8 ml) and ethanol (20 ml) in order to precipitate a first amount of the product, that was separated and dried. The remaining solution was then further heated after adding water (8 ml) to precipitate a second amount of product. These two samples were then collected and proved to be mainly a mixture (ca. 1:2) of tris- and tetrafunctionalized tetrahedron compounds (recovery 60%).

Part of the product mixture isolated in this way was then chromatographed twice on a SEC column (Merck Lichrogel PS 20, 5 µm, DMF, 78 °C) in order to obtain a pure sample of the desired tetrafunctionalized compound (ca. 30 mg). – HPLC analysis: gradient N°4, column N° 1, sodium perchlorate/phosphoric acid 0.030M, λ = 230 nm; R_v = 17.6 ml. – ^{1}H NMR (360 MHz, [D_6]-DMSO): δ/ppm = 7.09 (m, 19H, arom.); 4.29 (s, 8H); 3.01 (m, 24H, α tetrah.); 1.58 (m, 24H, β tetrah.); 1.24 (m, 24H, γ tetrah.). – ^{13}C NMR (90 MHz, [D_6]-DMSO): δ/ppm = 162.3 (B-C); 139.8 (ar-C); 137.1 (ar-C); 135.1 (ar-C) 126.0 (ar-C); 125.7 (ar-C); 125.0 (ar-C); 123.6

(ar-C); 121.5 (ar-C); 63.5 (ar-CH_2); 57.1 (α tetrah.); 24.9 (β tetrah.); 20.4 (γtetrah.). – ^{11}B NMR (115 MHz, [D_6]-DMSO): ^{1}H-decoupled δ/ppm = –6.5 (1 B).

Decomposition of the 1:1 3/Chloride Host-guest Complex

75 mg of tetrafunctionalized compound **3** contaminated by 1 equivalent of tetrabutylammonium chloride was solubilized in DMSO (1 ml), and 100 mg of $Hg(OAc)_2$ was added. A precipitate soon formed. The mixture was stirred at room temperature for 1.5 h and then separated by centri-fugation; the solid residue was further washed with DMSO (1 ml), and the two solutions were pooled. The addition of ethanol (8 ml) to the DMSO solution caused, after leaving in the refrigerator for 2 h, the precipitation of the desired product, that was rapidly washed with water (4 ml) to obtain the pure receptor.

References

[1] a) F. P. Schmidtchen, M. Berger, Chem. Rev. **1997**, *97*, 1609; b) M. M. G. Antonisse, D. N. Reinhoudt, Chem. Commun. **1998**, 443; c) A. Bianchi, K. Bowman-James, E. Garcia-España,"Supramolecular Chemistry of Anions", Wiley-VCH, New York 1997

[2] a) F. P. Schmidtchen, Angew. Chem. Int. Ed. Engl. **1977**, *16*, 720; Angew. Chem. **1977**, *89*, 751; b) F. P. Schmidtchen, Chem. Ber. **1980**, *113*, 864; c) F. P. Schmidtchen, J. Chem. Soc. Perkin Trans. 2 **1986**, 135; d) F. P. Schmidtchen, Angew. Chem. Int. Ed. Engl. **1981**, *20*, 466; Angew. Chem. **1981**, *93*, 469; e) F. P. Schmidtchen, Top. Curr. Chem. **1986**, *132*, 101; f) F. P. Schmidtchen, J. Am. Chem. Soc. **1986**, *108*, 8249; g) F. P. Schmidtchen J. Molec. Catal. **1986**, *37*, 141

[3] a) M. A. Hossain, K. Ichikawa, Tetrahedron Lett. **1994**, *35*, 8393; b) M. A. Hossain, K. Ichikawa, Chem. Lett. **1996**, 553; c) K. Ichikawa, M. A. Hossain, Chem. Commun. **1996**, 1721; d) K. Ichikawa, M. A. Hossain, T. Tamura, N. Kamo, Supram. Chem. **1995**, *5*, 219

[4] F. P. Schmidtchen, G. Muller, J. Chem. Soc. Chem. Commun. **1984**, *117*, 115

[5] K. Worm, F. P. Schmidtchen, A. Schier, A. Schäfer, M. Hesse, Angew. Chem. Int. Ed. Engl. **1994**, *33*, 327; Angew. Chem. **1994**, *106*, 360

[6] K. Worm, F. P. Schmidtchen, Angew. Chem. Int. Ed. Engl. **1995**, *34*, 65; Angew. Chem. **1995**, *107*, 71

[7] a) S. H. Strauss, Chem. Rev. **1993**, *93*, 927; b) L. Jia, Y. Xinmin, C. L. Stern, T. J. Marks, Organometallics **1997**, *16*, 842

[8] J.-L. M. Abboud, R. Notario, Prog. Phys. Org. Chem. **1993**, *19*, 1

[9] K. Siegmann, P. S. Pregosin, L. M. Venanzi, Organometallics **1989**, *8*, 2659

[10] M. Przybylski, M. O. Glocker, Angew. Chem. Int. Ed. Engl. **1996**, *35*, 806; Angew. Chem. **1996**, *108*, 878

[11] a) I. Wadsö, Chem. Soc. Rev. **1997**, 79; b) J. E. Ladbury, B. Z. Chowdhury, Chem. Biol. **1996**, *3*, 791

[12] N. M. Yoon, K. E. Kim, J. Org. Chem. **1987**, *52*, 5564

Address for correspondence:
Prof. Dr. Franz P. Schmidtchen
Institut für Organische Chemie und Biochemie
Technische Universität München
Lichtenbergstr. 4
D-85747 Garching
Fax: Internat. code (0)89-289-13345
e-mail: FPSchmid@nucleus.org.chemie.tu-muenchen.de