Doctoral Thesis

Molecular recognition of anions in protic solvents

Author(s):
Sebo, Lubomir

Publication Date:
1999

Permanent Link:
https://doi.org/10.3929/ethz-a-003822848

Rights / License:
In Copyright - Non-Commercial Use Permitted
Molecular Recognition of Anions in Protic Solvents

A dissertation submitted to the
SWISS FEDERAL INSTITUTE OF TECHNOLOGY ZÜRICH
for the degree of
Doctor of Natural Sciences

presented by
Ľubomír Šebo
Dipl. Chem., Comenius University, Bratislava
born November 10, 1971
citizen of Slovak Republic

accepted on the recommendation of
Prof. Dr. François Diederich, examiner
Prof. Dr. Donald Hilvert, co-examiner

Zürich 1999
Acknowledgments

I would like to thank Professor François Diederich for giving me the opportunity to work in his group, for his kind help and encouragement, and for the freedom I had during my project.

My thanks also go to Professor Donald Hilvert for accepting the co-examination of my thesis and for important corrections of the manuscript.

I would like to thank Dr. Ivan Kompš for the possibility to visit Roche (Basel) and ETH Zürich before the beginning of my Ph. D. work.

I am grateful to Dr. Roland Pieters, my first teacher of supramolecular chemistry, for introducing me to this exciting discipline.

I would like to thank Dr. Carlo Thilgen, Dr. Philipp Lustenberger, Anne-Sophie Droz, and Derk Joester for proof-reading and helping to improve parts of the manuscript.

My thanks go to Prof. Jack Dunitz for fruitful discussions about thermodynamics and X-ray crystallography.

I am grateful to Dr. Miroslav Rozložník for interesting discussions about my mathematical problems and for his help with numerical computer calculations.

I want to thank Dr. Thomas Carell, Dr. Jens Butenandt, and Derk Joester for the introduction to the DNA assays.

I am grateful to all the members of the ETH staff for the valuable services they provided. In particular I would like to thank Dr. Bernhard Schweizer and Professor Volker Gramlich for solving the X-ray crystal structures, the group of Dr. Walter Amrein and especially Rolf Häfliger for excellent mass-spectra.

I would like to thank Ursula Majadi and Irma Näf for their patience, understanding, and help with all administrative problems.

I want also to thank Dr. Luc Patiny for teaching me Macintosh basics.

Many thanks go to all the members of the Diederich group - I have learned a lot from you. I particularly thank Dr. Carlo Thilgen, Dr. Ulrike Obst, Dr. Francesca Cardullo, Dr. Philipp Lustenberger, Anne-Sophie Droz, and Derk Joester.

This work could not be completed without the help of my wife Monika. Thank you for your support, prayers, and your love.
# Table of Contents

### ABBREVIATIONS

### SUMMARY

### ZUSAMMENFASSUNG

1. INTRODUCTION

   1.1. MOLECULAR RECOGNITION OF OXYANIONS IN PROTIC SOLVENTS
   1.1.1. Carboxylate Recognition
   1.1.2. Phosphate Recognition
   1.1.3. Sulfate Recognition
   1.2. CHORISMATE MUTASE MIMICS
   1.3. ANALYSIS OF COMPLEXATION DATA
       1.3.1. 1 : 1 Complexation Model
       1.3.2. 1 : 2 Complexation Model
       1.3.3. Job's Method (1 : 1 Model)
       1.3.4. Job's Method (1 : 2 Model)

2. 1,1'-BINAPHTHALENE RECEPTOR FOR CARBOXYLATES

   2.1. INTRODUCTION
   2.2. DESIGN
   2.3. SYNTHESIS
   2.4. $^1$H-NMR COMPLEXATION STUDIES
   2.5. VARIABLE TEMPERATURE $^1$H-NMR COMPLEXATION STUDIES
   2.6. MICROCALORIMETRIC TITRATIONS
   2.7. SUMMARY

3. SMALL BISAMIDINIUM RECEPTORS

   3.1. TOWARDS MULTI-AMIDINIUM-FUNCTIONALIZED ACETYLENIC MACROCYCLES
       3.1.1. Synthesis
   3.2. DIPHENYLNAPHTHALENE RECEPTORS
       3.2.1. Synthesis

4. CAVITAND TETRAAMIDINIUM RECEPTOR

   4.1. SYNTHESIS
   4.2. BINDING STUDIES
### Abbreviations

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Å</td>
<td>Angstrom ($1 , \text{Å} = 10^{-10} , \text{m}$)</td>
</tr>
<tr>
<td>Ac</td>
<td>acetyl</td>
</tr>
<tr>
<td>aq.</td>
<td>aqueous</td>
</tr>
<tr>
<td>BHT</td>
<td>2,6-bis(1,1-dimethylethyl)-4-methylphenol</td>
</tr>
<tr>
<td>Bn</td>
<td>benzyl</td>
</tr>
<tr>
<td>Bu</td>
<td>butyl</td>
</tr>
<tr>
<td>°C</td>
<td>degree centigrade ($0 , ^\circ\text{C} = 273.15 , \text{K}$)</td>
</tr>
<tr>
<td>calc.</td>
<td>calculated</td>
</tr>
<tr>
<td>CC</td>
<td>column chromatography</td>
</tr>
<tr>
<td>CD</td>
<td>circular dichroism</td>
</tr>
<tr>
<td>conc.</td>
<td>concentrated</td>
</tr>
<tr>
<td>d</td>
<td>day</td>
</tr>
<tr>
<td>dec.</td>
<td>decomposition</td>
</tr>
<tr>
<td>DMA</td>
<td>N,N-dimethylacetamide</td>
</tr>
<tr>
<td>DME</td>
<td>1,2-dimethoxyethane</td>
</tr>
<tr>
<td>DMF</td>
<td>N,N-dimethylformamide</td>
</tr>
<tr>
<td>dpdf</td>
<td>1,1'-bis(diphenylphosphanyl)ferrocene</td>
</tr>
<tr>
<td>EI</td>
<td>electron impact</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
<tr>
<td>FAB</td>
<td>fast atom bombardment</td>
</tr>
<tr>
<td>g</td>
<td>gram</td>
</tr>
<tr>
<td>h</td>
<td>hour</td>
</tr>
<tr>
<td>HR</td>
<td>high resolution</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz, (s$^{-1}$)</td>
</tr>
<tr>
<td>IR</td>
<td>infrared spectroscopy</td>
</tr>
<tr>
<td>J</td>
<td>coupling constant</td>
</tr>
<tr>
<td>K</td>
<td>Kelvin</td>
</tr>
<tr>
<td>l</td>
<td>liter</td>
</tr>
<tr>
<td>M</td>
<td>molarity (mol l$^{-1}$)</td>
</tr>
<tr>
<td>Me</td>
<td>methyl</td>
</tr>
<tr>
<td>min</td>
<td>minutes</td>
</tr>
<tr>
<td>ml</td>
<td>milliliter</td>
</tr>
<tr>
<td>µl</td>
<td>microliter</td>
</tr>
<tr>
<td>mol</td>
<td>moles</td>
</tr>
<tr>
<td>mmol</td>
<td>millimoles</td>
</tr>
<tr>
<td>µmol</td>
<td>micromoles</td>
</tr>
<tr>
<td>M.p.</td>
<td>melting point</td>
</tr>
<tr>
<td>Ms</td>
<td>methanesulfonate (mesylate)</td>
</tr>
<tr>
<td>MS</td>
<td>mass spectrometry</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>ppm</td>
<td>parts per million</td>
</tr>
<tr>
<td>r.t.</td>
<td>room temperature</td>
</tr>
<tr>
<td>sat.</td>
<td>saturated</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMEDA</td>
<td>N,N,N',N'-tetramethyl-ethylenediamine</td>
</tr>
<tr>
<td>TMSA</td>
<td>trimethylsilylacetylene</td>
</tr>
<tr>
<td>Tris</td>
<td>2-aminio-2-(hydroxy-methyl)-1,3-propanediol</td>
</tr>
<tr>
<td>Ts</td>
<td>para-toluene sulfonate (tosylate)</td>
</tr>
<tr>
<td>UV</td>
<td>ultraviolet</td>
</tr>
</tbody>
</table>
Summary

Molecular recognition of anions is an area of intense interest due to their important role in many chemical and biological processes. This work concentrates more specifically on the binding of oxyanions, such as carboxylates and phosphates, since these are the most important anionic functional groups present in organic molecules. Design of an enzyme mimics for catalysis of the rearrangement of chorismate to prephenate is also presented.

In the initial phase of this project, two o-benzamidinium cationic binding sites were attached to the 6,6'-positions of a 1,1'-binaphthalene unit to explore the recognition of dicarboxylates in protic solvents. The resulting molecular cleft 29 forms complexes with carboxylates, such as isophthalates and glutarate, even in competitive protic solvents. Association constants ranged from 5 000 to 10 000 l mol\(^{-1}\) in CD\(_3\)OD at 300 K, as determined by \(^1\)H-NMR titration experiments. Variable temperature \(^1\)H-NMR titrations with 5-nitroisophthalate revealed that the complexation is endothermic (\(\Delta H^\circ = 7.7\) kJ mol\(^{-1}\)) and thus entropy driven (\(\Delta S^\circ = 96.6\) J mol\(^{-1}\) K\(^{-1}\)) in methanol at 300 K. These thermodynamic data were confirmed using isothermal titration calorimetry.
In order to increase the strength of carboxylate binding more complex multi-amidinium receptors were designed. A rigid resorcinarene cavitand core was selected for its suitable geometry, four-fold symmetry, and facile synthesis. This resulted in the preparation of receptors 74-75. Although formation of a 1 : 1 complex between 75 and AMP was confirmed using FAB-MS techniques, the complexation studies in protic solvents were complicated by low solubility of the complexes. Therefore, four triethyleneglycol monomethyl ether chains were introduced to provide solubility in water. The resulting cavitand receptor 87 was explored in complexation studies with carboxylates, phosphates, and sulfates in protic solvents using 1H-NMR titration techniques. The strong binding of isophthalates in methanol ($K_1 = 350 \text{KJ mol}^{-1}$, $K_2 = 60 \text{KJ mol}^{-1}$, $T = 300 \text{K}$) leads to formation of 1 : 2 host-guest complex, as shown by the Job's method of continuous variation. In aqueous buffers (borate, Tris/HCl), complexation of isophthalates was weaker ($K_a = 4 \text{KJ mol}^{-1}$, $T = 300 \text{K}$), and the 1 : 1 host-guest stoichiometry was confirmed using Job's method. Complexation of nucleotides with the water-soluble receptor 87 was further studied. The nucleotide binding is mostly governed by Coulombic interactions. Thus, the $K_a$ increases with the number of anionic phosphates moieties. For example, tetraanionic ATP is complexed more strongly ($K_a = 660 \text{KJ mol}^{-1}$) than trianionic ADP ($K_a = 48 \text{KJ mol}^{-1}$), dianionic AMP ($K_a = 10 \text{KJ mol}^{-1}$) and monoanionic cAMP ($K_a = 1 \text{KJ mol}^{-1}$) in aqueous Tris/HCl buffer ($pH = 8.3$) at 300 K as determined by 1H-NMR complexation studies. The 1 : 1 stoichiometry of AMP complexation was confirmed by Job's method. Large complexation-induced shifts of the adenine protons indicate inclusion of the nucleobase into the hydrophobic receptor cavity, as supported by molecular modeling. Hydrophobic interactions gained in this way do not contribute substantially to the total binding free energy $\Delta G_{300}^\circ$, which varies little (20.4-23.0 KJ mol$^{-1}$) for complexes formed between 87 and various dianionic nucleotides (AMP, GMP, CMP, TMP, and UMP). Sulfate guests, such as heparin analogs, form stable complexes with 87 in water, but the stoichiometry of this process is rather complex. Using 1H-NMR measurements of the chorismate sample in CD$_3$OD, it was found that the rearrangement of chorismate to prephenate is accelerated by a factor of 7.5 in the presence of receptor 87 at $T = 323 \text{K}$. This is the largest acceleration of this important rearrangement by a non-proteinogenic catalyst.
Zusammenfassung


In einer ersten Phase des Projektes wurden zwei kationische α-Benzamidin-Bindungsstellen in die 6,6'-Stellungen eines 1,1'-Binaphthyls eingeführt, um die Erkennung von Dicarboxylaten in protischen Lösungsmitteln zu untersuchen. Die so erhaltenene "molecular cleft" 29, also ein Rezeptor mit einer spaltenartigen Bindungsstelle, bildet lösliche Komplexe mit Carboxylaten wie Isophthalaten oder Glutaraten sogar in kompetitiven protischen Lösungsmitteln. Bindungskonstanten zwischen 5 000 und 10 000 l mol⁻¹ (T = 300 K) in CD₃OD wurden mithilfe von ¹H-NMR-Titrationsexperimenten bestimmt. Titrationen mit 5-Nitroisophthalat bei verschiedenen Temperaturen zeigten, dass die Komplexbildung bei 300 K in Methanol endotherm (ΔH° = 7.7 kJ mol⁻¹) und somit Entropie-getrieben (ΔS° = 96.6 J mol⁻¹ K⁻¹) ist. Diese thermodynamischen Daten wurden durch isotherme Titrations-Kalorimetrie bestätigt.

Um die Stärke der Carboxylat-Bindung zu erhöhen, wurden dann komplexere Rezeptoren mit mehreren Amidinium-Gruppen vorgeschlagen. Ein steifer...
Resorcinaren-Cavitand wurde aufgrund seiner günstigen Geometrie mit vierzähliger Symmetrieachse und seiner einfachen Synthese ausgewählt. Diese Entscheidung führte zu der Synthese der Rezeptoren 74-75. Die Bildung eines 1 : 1-Komplexes zwischen 75 und AMP konnte mit Hilfe der FAB-Massenspektrometrie nachgewiesen werden. Niedrige Löslichkeit der Komplexe führte aber bei Komplexbindungs-Studien in protischen Lösungsmitteln zu Komplikationen. Deshalb wurden vier Triethylenglykol-monomethylethergruppen in das Molekül eingeführt, um so für Löslichkeit in Wasser zu sorgen. Der daraus resultierende Cavitand-Rezeptor 87 wurde in Komplexierungs-Studien mit Carboxylaten, Phosphaten und Sulfaten in protischen Lösemitteln mit $\text{^1H-NMR-Titrations}$_techniken untersucht. Die starke Bindung von Isophthalaten in Methanol ($K_1 = 350 000 \text{l mol}^{-1}$, $K_2 = 60 000 \text{l mol}^{-1}$, $T = 300 \text{K}$) führte zur Bildung eines 1 : 2 Wirts-Gast Komplexes, wie eine Analyse nach Job zeigte. In wässrigen Pufferlösungen (Borat- und Tris-HCl-Puffer) hingegen war die Komplexierung von Isophthalaten schwächer ($K_a = 4000 - 100 000 \text{l mol}^{-1}$, $T = 300 \text{K}$) und es wurde eine 1 : 1 Stöchiometrie gefunden. Bindung von Nukleotiden wird im wesentlichen von Coulomb-Wechselwirkungen bestimmt. Daher nimmt die Assoziationskonstante $K_a$ mit der Zahl der anionischen Phosphat-Gruppen zu. So wird zum Beispiel in Tris-HCl-Puffer ($\text{pH}=8.3$, $T = 300 \text{K}$) das Tetra-Anion ATP stärker gebunden ($K_a = 660 000 \text{l mol}^{-1}$) als das ADP Trianion ($K_a = 48 000 \text{l mol}^{-1}$), das AMP Dianion ($K_a = 10 000 \text{l mol}^{-1}$) oder cAMP ($K_a = 1 400 \text{l mol}^{-1}$), das nur einfach geladen ist. Diese Messungen, wie auch die Bestimmung der 1 : 1-Stöchiometrie nach der Methode nach Job, wurden mit $\text{^1H-NMR-Titrations}$_techniken durchgeführt. Die großen, durch die Komplexbildung induzierten Verschiebungen der Adenin-Protonen deuten auf einen Einschluss der Nukleobase in der hydrophoben Rezeptor-Bindungstasche hin. Dies wird auch durch Computermodellstudien unterstützt. Die hydrophoben Wechselwirkungen tragen allerdings nicht nennenswert zur freien Bindungsenthalpie $\Delta G^\circ$ bei. Das ergibt sich aus der Beobachtung, dass Komplexe zwischen 87 und natürlichen dianionischen Nukleotiden (AMP, GMP, CMP, TMP und UMP) sehr ähnliche Werte für $\Delta G^\circ_{300}$ zeigen (20.4-23.0 kJ mol$^{-1}$). Sulfate wie zum Beispiel Heparin-Analoga bilden stabile Komplexe mit 87 in Wasser, die Stöchiometrie dieses Prozesses ist jedoch sehr komplex. Schließlich wird die Umlagerung von Chorismat zu Prephenat in Gegenwart von 87 in methanolischer Lösung bei 323 K um einen Faktor 7.5 beschleunigt. Dies stellt die bisher höchste Beschleunigung dieser Reaktion durch einen nichtproteinogenen Katalysator dar.
1. Introduction

1.1. Molecular Recognition of Oxyanions in Protic Solvents

Anions play essential roles in many processes - both chemical and biological - which makes their recognition an area of intense interest [1]. Amino acids, peptides, and nucleotides are representative examples of organic anions in living organisms. In fact, 70% of all enzyme substrates are negatively charged. This work concentrates more specifically on the binding of oxyanions, such as carboxylates and phosphates, since these are the most important anionic functional groups present in organic molecules.

The recognition of oxyanions is based on a combination of Coulombic interactions and hydrogen bonds between the anionic moiety and a suitable positively charged hydrogen bond donor, such as an ammonium, guanidinium, or amidinium group.

As this topic was recently reviewed [2,3], only a short overview of oxyanion receptors is presented here.
1.1.1. Carboxylate Recognition

The first attempts to develop receptors for carboxylates concentrated on protonated macrocyclic oligoamines. Kimura et al. [4] and Lehn and co-workers [5] independently showed that the carboxylate affinities of receptors such as 1 and 2 are mostly governed by Coulombic interactions, so that carboxylate binding becomes stronger as the number of protonated host nitrogen atoms increases. For example, citrate trianion is complexed by 1 with $K_a = 5 \times 10^4$ mol$^{-1}$ ($T = 293$ K) and by 2 with $K_a = 4 \times 10^7$ mol$^{-1}$ in an aqueous solution of Me$_4$N$^+$Cl$^-$ (0.1 mol l$^{-1}$) as determined by pH-metric titration [5].

Macrocycles 3 and 4 were designed for complexation of dicarboxylates [6]. Clear size-selectivity was shown. Among the homologous $\text{O}_2\text{C-(CH}_2_m\text{)CO}_2^-$ guests, receptor 3 forms the most stable complexes with glutarate ($m = 3$), whereas 4 prefers pimelate ($m = 5$) as guest.

![Diagram of macrocycles 1, 2, 3, and 4](image)

Similar structural selectivity was found in the complexation of benzenedicarboxylates with macrocycle 5 [7]. The corresponding association constants in aqueous solution have been determined by $^1$H-NMR and fluorescence titration. Receptor 5 preferentially binds the terephthalate anion ($K_a = 1.6 \times 10^5$ mol$^{-1}$, $T = 296$ K) due to complementary Coulombic and hydrophobic interactions. Crystal structures of the terephthalate and isophthalate inclusion complexes with macrocyclic receptor 6 were recently published [8].

![Diagram of macrocycles 5 and 6](image)

$^1$H-NMR titrations in aqueous solution showed that cryptand 7 binds the well-fitting adipate ($m = 4$) more strongly than other $\alpha,\omega$-dicarboxylates, and terephthalate even...
better due to additional π - π interactions. The crystal structure of the terephthalate complex was determined [9], it shows that the terephthalate anion is located inside the molecular cavity, where it is bound by NH⁺−O⁻ hydrogen bonds between each carboxylate group and the three ammonium sites. Water-soluble cryptand 8 containing three fluorogenic acridine units was described later [10]. Its fluorescence is strongly affected by complex formation with various organic anions. Selectivity of carboxylate complexation is almost the same as in the case of cryptand 7.

Macrotricyclic quarternary ammonium salts 9 and 10, developed by Schmidtchen et al., bind carboxylates such as formate, acetate, and benzoate, among a variety of other anions [11]. Although these receptors do not allow for hydrogen bonding interactions, their well-localized cationic centers provide stabilizing charge-charge interactions with the guest, independent of the acidity of the medium.

The polyammonium receptors 1-8 are efficient only at low pH, when all the nitrogen atoms are protonated. In order to overcome this limitation, guanidinium macrocycles 11-13 were prepared by Lehn and co-workers for carboxylate recognition [12]. The guanidinium unit (pKₐ = 13.5) remains protonated up to a high pH value and is ideal for extending the pH range over which anion complexation occurs. On the other hand, anion binding by macrocycles 11-13 was considerably weaker than in the case of their polyammonium analogues, as a result of excess flexibility and charge delocalization.
Bis(alkylguanidinium) receptor 14 was reported by Hamilton and co-workers [13]. Binding of glutarate was observed using $^1$H-NMR titrations in 12% D$_2$O/(CD$_3$)$_2$SO ($K_a = 8 \times 10^3$ 1 mol$^{-1}$, $T = 295$ K) and even in 25% D$_2$O/(CD$_3$)$_2$SO ($K_a = 5 \times 10^2$ 1 mol$^{-1}$). Apparently, the guanidinium moieties are very effective in competing with D$_2$O for the H-bonding sites of the anionic guest.

A chiral bicyclic guanidinium unit, originally developed by de Mendoza, Lehn and co-workers [14], was exploited in dicarboxylate receptor 15 prepared by Schiessl and Schmidtchen [15]. Due to its flexible framework, it binds dianions that range in size from carbonate to 3,3'-(benzene-1,4-diyl)bispropenoate with a maximum association constant for malonate and 5-nitroisophthalate ($K_a = 1.65 \times 10^4$ 1 mol$^{-1}$, $K_a = 1.45 \times 10^4$ 1 mol$^{-1}$, respectively), as determined by $^1$H-NMR titrations in the competitive solvent CD$_3$OD ($T = 300$ K).
Tridentate guanidinium-based receptor 16 shows a high affinity \( (K_a = 6.9 \times 10^3 \text{ mol}^{-1}, T = 300 \text{ K}) \) and selectivity for the citrate trianion as determined by \(^1\)H-NMR titration in pure \( \text{D}_2\text{O} \) [16]. A novel citrate sensor was prepared by mixing 16 and carboxyfluorescein 17, which is fluorescent and binds weakly to the receptor. When citrate is added to the mixture, it displaces 17, which is released from the complex and undergoes a considerable change in its emission properties. This way, a sensory response is obtained upon addition of citrate. The sensor is able to detect the concentration of citrate accurately even in the presence of other anions, such as ascorbate or phosphate [17].

1.1.2. Phosphate Recognition

Receptors for phosphates are structurally very similar to carboxylate receptors. Often, it is just their application that is different. Thus, the macrocycles 1 and 2 were successfully used for nucleotide binding in aqueous solution [5]. The driving force for complexation is mainly Coulombic charge-charge interaction, which is reflected in the association constants obtained for complexes formed between 1 and dianionic AMP \( (K_a = 2.5 \times 10^3 \text{ mol}^{-1}) \), trianionic ADP \( (K_a = 3.2 \times 10^6 \text{ mol}^{-1}) \), and tetraanionic ATP \( (K_a = 7.9 \times 10^8 \text{ mol}^{-1}) \), as determined by pH-metric titration \( (T = 293 \text{ K}) \).

In the case of macrocycle 5, the selectivity for the complexation of the doubly charged monophosphate derivatives AMP, GMP, CMP, and UMP should be noted. The binding constants increase slightly with the size of the flat base moiety of the guest, with derivatives of purine being more strongly complexed than those of pyrimidine. Thus, GMP \( (K_a = 7.9 \times 10^4 \text{ mol}^{-1}) \) and AMP \( (K_a = 2 \times 10^4 \text{ mol}^{-1}) \) form the most stable complexes. UMP is also bound quite strongly \( (K_a = 1.3 \times 10^4 \text{ mol}^{-1}) \), whereas the complex of CMP \( (K_a = 5 \times 10^3 \text{ mol}^{-1}) \) is least stable, as determined by \(^1\)H-NMR and fluorimetric titration in aqueous solution \( (T = 296 \text{ K}) \) [7].
The ditopic receptor 18, containing a macrocyclic polyamine as anion recognition subunit (in its multiply protonated form) and an acridine group for π-π stacking interactions, strongly binds nucleotides in aqueous solution by multiple site binding. It also catalyses ATP hydrolysis [18,19].

![Diagram of receptor 18](image)

*Schneider et al.* investigated the capability of the tetracationic cyclophane 8 to bind nucleotides in water [20]. As evidenced by ¹H-NMR studies, only in the case of purine nucleosides is the base moiety included inside the host cavity.

![Diagram of cyclophane 8](image)

Cryptand 8 binds tightly to mono- and oligonucleotides and moreover appears able to discriminate between homopyridine and homopurine sequences by its light-sensitive response [10].

The water-soluble receptor 20, used for the complexation of adenosine derivatives, was described by *Rebek* and co-workers [21]. The modular structure of the receptor allows exploitation of hydrophobic interactions, hydrogen bonding, and guanidinium-phosphate ion pairing to bind cyclic adenosine monophosphates (cAMP). The binding constants determined for 2',3'-cAMP are 6601 mol⁻¹ and 3301 mol⁻¹ at 51 and 501 mM ionic strength, respectively (H₂O/D₂O 9:1, pH = 6.0, T = 283 K).
The flexible dicationic guanidinium host 15 binds biologically relevant phosphates in aqueous solution with binding constants $K_a = 840 \text{ mol}^{-1}$ for ATP and $K_a = 970 \text{ mol}^{-1}$ for HPO$_4^{2-}$ as determined by $^1$H-NMR titration ($T = 300 \text{ K}$) [22].

Cationic carriers for the transport of nucleotide 5'-triphosphates across liquid organic membranes were described by Diederich and co-workers [23,24]. The tetracationic compound 21, with two diquaternary 1,4-diaza[2.2.2]bicyclooctane units, forms carrier-nucleotide complexes of 1:1 stoichiometry in dichloromethane and strongly accelerates nucleotide transport across this solvent.

Sapphyrin, a pentapyrrolic expanded porphyrin, was examined by Sessler and co-workers in further attempts to use large lipophilic cations as mediators for the carriage of anions through an organic membrane. The cytosine derivative of sapphyrin 22 selectively transports GMP through a model membrane at neutral pH [25]. This receptor basepairs with the guanine base of the guest, and the monophosphate moiety undergoes ion-pairing and H-bonding with the sapphyrin ring, which is monoprotonated and cationic at neutral pH.
1.1.3. Sulfate Recognition

Using potentiometric measurements it was found that sulfate anions bind strongly ($K_a = 3 \cdot 10^4 \text{ mol}^{-1}$, $T = 293 \text{ K}$) to the highly positively charged macrocycle 23 even in competitive media, such as an aqueous solution of Me₄N⁺Cl⁻ (0.1 mol l⁻¹) [5].

![Diagram of guanidinium receptor 24 in methanol]

Binding of sulfate anions by guanidinium receptor 24 in methanol was described by Berger and Schmidtchen [26]. Complexation was studied using ¹H-NMR titrations and isothermal titration calorimetry (ITC). Binding of sulfate ($K_a = 6.8 \cdot 10^6 \text{ mol}^{-1}$, $\Delta G_{303}^\circ = -39.6 \text{ kJ mol}^{-1}$) was found to be strongly endothermic ($\Delta H_{303}^\circ = +32.2 \text{ kJ mol}^{-1}$), and thus entropy driven ($T \Delta S_{303}^\circ = +71.8 \text{ kJ mol}^{-1}$).
1.2. Chorismate Mutase Mimics

The conversion of chorismate (25) (Scheme 1) to prephenate (26) is an important step in the biosynthetic pathway towards aromatic amino acids in bacteria, fungi, and higher plants [27]. This Claisen rearrangement, one of the rare biochemical pericyclic reactions, is catalyzed by chorismate mutases which are capable of accelerating the reaction about two million-fold. Although the exact origin of the catalysis is not fully understood, much experimental and theoretical data are consistent with selective binding of the pseudodiaxial conformer of chorismate by arginine side-chains of the enzyme as the first step towards the compact transition state. This transition state (TS) is not only stabilized by ionic hydrogen bonding between the carboxylates and arginine side-chains of the enzyme, but presumably also by hydrogen bonding to the "ether" oxygen and additional electrostatic interactions [28-32].

![Scheme 1. The Claisen rearrangement of chorismate to prephenate.](image)

Different organisms have different chorismate mutases (CMs). Some of their kinetic features are similar, but there are also differences (Table 1). One difference is, for example, the part of the activation free enthalpy $\Delta G^\ddagger$ that results from reducing entropic barriers of the reaction. Whereas in the conversions catalyzed by most of the studied chorismate mutases, these barriers are reduced to almost zero, the CM from *Bacillus subtilis* catalyzes the reaction mostly by reducing its activation enthalpy. Remarkably, a similar difference has been observed in the evaluation of two catalytic antibodies which catalyze this reaction by factors of $10^4$ and 250, respectively.
Table 1. Selected activation parameters for the conversion of 25 to 26 at 298 K.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>$\Delta G^{\ddagger}_{298}$ [kJ mol$^{-1}$]</th>
<th>$\Delta H^{\ddagger}_{298}$ [kJ mol$^{-1}$]</th>
<th>$\Delta S^{\ddagger}_{298}$ [J mol$^{-1}$ K$^{-1}$]</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacillus subtilis</em> CM</td>
<td>64.5</td>
<td>53.1</td>
<td>-38.1</td>
<td>[33]</td>
</tr>
<tr>
<td><em>Escherichia coli</em> CM</td>
<td>66.3</td>
<td>68.2</td>
<td>6.3</td>
<td>[34,35]</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> CM</td>
<td>67.9</td>
<td>66.5</td>
<td>-4.6</td>
<td>[36]</td>
</tr>
<tr>
<td><em>Methanococcus jannaschii</em> CM</td>
<td>69.9</td>
<td>67.8</td>
<td>-7.1</td>
<td>[37]</td>
</tr>
<tr>
<td><em>Streptomyces aureofaciens</em> CM</td>
<td>62.7</td>
<td>60.7</td>
<td>-6.7</td>
<td>[36]</td>
</tr>
<tr>
<td>Catalytic antibody 11F1-2E11</td>
<td>78.1</td>
<td>76.6</td>
<td>-5.0</td>
<td>[38]</td>
</tr>
<tr>
<td>Catalytic antibody 1F7</td>
<td>90.2</td>
<td>62.8</td>
<td>-92.0</td>
<td>[39]</td>
</tr>
<tr>
<td>Uncatalyzed reaction</td>
<td>102.7</td>
<td>86.6</td>
<td>-54.0</td>
<td>[40]</td>
</tr>
</tbody>
</table>

Figure 2. X-ray crystal structure of *Escherichia coli* (left) and *Bacillus subtilis* chorismate mutase (right), complexed to the Bartlett inhibitor 27.

*Figure 2* shows ribbon diagrams of the X-ray crystal structures formed by the chorismate mutases from *Escherichia coli* and *Bacillus subtilis* with an inhibitor prepared by Bartlett [41]. This transition state analog 27 (Figure 3) has played an important role in the identification of chorismate mutase active sites and as a hapten in the synthesis of monoclonal catalytic antibodies. Furthermore, the dicarboxylate 27, which broadly inhibits chorismate mutases from *E. coli*, *B. subtilis*, and *Saccharomyces cerevisiae* with low-micromolar $K_i$ values, is still the most potent competitive chorismate mutase inhibitor [42].

Figure 3. Transition state analog 27 (Bartlett inhibitor).
The X-ray crystal structures of the chorismate mutases from *B. subtilis* (Figure 4) [43], *E. coli* (Figure 5) [44], and the antibody 1F7 [45] show a rather similar arrangement of positively charged guanidinium residues from arginine side-chains in the active site - despite the completely different architectures of these species.

**Figure 4.** Bartlett inhibitor 27 bound in the active site of *Bacillus subtilis* chorismate mutase [43].

**Figure 5.** Bartlett inhibitor 27 bound in the active site of *Escherichia coli* chorismate mutase [44].

Site directed mutagenesis [46-48] has also helped to identify the residues important for catalysis. These studies showed the relative importance of specific active site residues in *B. subtilis* and *E. coli* chorismate mutases. The crucial residues are Arg90, Arg7, and Glu78 in *B. subtilis* CM and Lys39, Arg11', Glu52, Gln88, and Arg28 in *E. coli* CM.
Development of an artificial synthetic chorismate mutase remains a formidable intellectual challenge for supramolecular chemistry and chemical biology. A small, rationally designed non-proteinogenic receptor with CM activity would help to define the minimum requirements for catalysis of this pericyclic process, and thus provide a better understanding of the catalytic mechanisms involved.

1.3. Analysis of Complexation Data

A molecular complex can be defined as a noncovalently bound species of definite host-guest stoichiometry that is formed in a facile equilibrium process in solution [49]. An analysis of some consequences of molecular association under conditions of a fast equilibrium is presented below.

1.3.1. 1 : 1 Complexation Model

\[ 
H + G \rightleftharpoons HG 
\]

The association of host \( H \) and guest \( G \) leading to their complex \( HG \) is described using following equations (1-3).

\[
K_a = \frac{c(HG)}{c(H)c(G)} \quad [1 \text{ mol}^{-1}] \quad (1)
\]

\[
c_\delta(H) = c(H) + c(HG) \quad [\text{mol l}^{-1}] \quad (2)
\]

\[
c_\delta(G) = c(G) + c(HG) \quad [\text{mol l}^{-1}] \quad (3)
\]

The complex \( HG \) is characterized by its association constant \( K_a \) and by a physically detectable property, e.g. the NMR chemical shift of the \( HG \) proton signals \( \delta_{\text{sat}}(HG) \), which are generally different than those of uncomplexed \( H \) or \( G \). This difference \( \Delta\delta_{\text{sat}}(HG) \) is conveniently used in (4).

\[
\Delta\delta(H) = \Delta\delta_{\text{sat}}(HG) \frac{c(HG)}{c_\delta(H)} \quad [\text{ppm}] \quad (4)
\]

The observed change of the chemical shift of the host signals (\( \Delta\delta(H) \)), ranging from zero for pure \( H \) and reaching \( \Delta\delta_{\text{sat}}(HG) \) in its limit, is directly proportional to the concentration of the \( HG \) complex. Substituting for \( c_\delta(H) \) from (2) and for \( c(HG) \) from (1) in (4), gives \( \Delta\delta(H) \) as a function of \( c(G) \) (5).
\[
\Delta \delta(H) = \Delta \delta_{\text{ad}}(HG) \frac{K_a c(G)}{1 + K_a c(G)}
\] 

Concentration of the free guest \(c(G)\) is generally unknown. It can be calculated from the known total guest concentration \(c_0(G)\): Substituting for \(c(HG)\) and \(c(H)\) from (1) and (2) in (3) yields (6). Solving the equation (6) for the unknown \(c(G)\) gives (7).

\[
c_0(G) = c(G) + \frac{K_a c_0(H) c(G)}{1 + K_a c(G)}
\]

\[
c(G) = \frac{1}{2} \left[ c_0(G) - c_0(H) - \frac{1}{K_a} + \sqrt{\frac{4 c_0(G)}{K_a} + \left( c_0(G) - c_0(H) - \frac{1}{K_a} \right)^2} \right]
\]

Substituting for \(c(G)\) from (7) in (6) yields (8), which describes analytically the 1 : 1 host - guest system using only physically measurable parameters.

\[
\Delta \delta(H) = \frac{\Delta \delta_{\text{ad}}(HG)}{2 c_0(H)} \left( c_0(H) + c_0(G) + \frac{1}{K_a} \right) \left[ 1 - \sqrt{1 - \frac{4 c_0(H) c_0(G)}{\left( c_0(H) + c_0(G) + \frac{1}{K_a} \right)^2}} \right]
\]

![Figure 6](image)

**Figure 6.** Binding isotherms for 1 : 1 host - guest model generated using (8). Constant host concentration \(c_0(H) = 10^3 \text{ mol}^{-1}\), \(\Delta \delta_{\text{ad}}(HG) = 1 \text{ ppm}\), and \(K_a = 500 \text{ l mol}^{-1}\) (a), 2000 \text{ l mol}^{-1} (b), 8000 \text{ l mol}^{-1} (c), 32000 \text{ l mol}^{-1} (d), and \(10^8 \text{ l mol}^{-1}\) (e).

The association constant \(K_a\) can be determined by following \(\Delta \delta(H)\) in a titration experiment, in which the initial concentration of one component \(c_0(G)\) is varied, while the initial concentration of the other one \(c_0(H)\) is kept constant. A fit of the experimental data \([\Delta \delta(H); c_0(G)]\) to (8) gives the association constant \(K_a\) and \(\Delta \delta_{\text{ad}}(HG)\)
as independent parameters (e.g. using the program Associate 1.6 [50]). Binding curves for hypothetical systems are shown in Figure 6; they were generated using the program proFit 5.0 [51].

The curvature of binding isotherms for the 1:1 host-guest model increases with increasing magnitude of the binding constant $K_a$ (Figure 6). For accurate $K_a$ determination, titration experiments should be performed over concentration ranges at which the host is 20-80% complexed. As $K_a \to \infty$, the binding isotherm is composed of two linear regions. In the first region, $\Delta \delta(H)$ grows linearly with $c_0(G)$: $\Delta \delta(H) = \Delta \delta_{\text{sat}}(H)c_0(G)/c_0(H)$, reaching $\Delta \delta_{\text{sat}}(HG)$ at $c_0(G) = c_0(H)$. From this point on, $\Delta \delta(H)$ is constant and equal to $\Delta \delta_{\text{sat}}(HG)$. In this region, the concentration of the free guest $c(G)$ grows linearly with $c_0(G)$. Such a binding isotherm (e.g. (e) in Figure 6) does not allow calculation of the association constant $K_a$, since there is no curvature present which could be iteratively evaluated by a nonlinear least-squares curve-fitting procedure. The highest $K_a$ which can be determined using $^1$H-NMR titration technique is around $10^5$ (mol$^{-1}$) ($c_0(H) = 10^{-4}$ mol l$^{-1}$, $c_0(G) = 2 \times 10^{-5}$-2 $\times 10^{-4}$ mol l$^{-1}$).

1.3.2. 1:2 Complexation Model

\[
\begin{align*}
H + G & \rightleftharpoons HG \\
HG + G & \rightleftharpoons HG_2
\end{align*}
\]

It is chemically reasonable to assume that every complex is formed in a bimolecular process. Therefore, the formation of 1:2 host-guest complex $HG_2$ can be described by two equilibria and the corresponding stepwise binding constants (9-12).

\[
K_1 = \frac{c(HG)}{c(H)c(G)} \quad [\text{mol}^{-1}] \quad (9)
\]

\[
K_2 = \frac{c(HG_2)}{c(HG)c(G)} \quad [\text{mol}^{-1}] \quad (10)
\]

\[
c_0(H) = c(H) + c(HG) + c(HG_2) \quad [\text{mol l}^{-1}] \quad (11)
\]

\[
c_0(G) = c(G) + c(HG) + 2c(HG_2) \quad [\text{mol l}^{-1}] \quad (12)
\]

The formation of the complex $HG_2$ adds two parameters ($K_2$ and $\Delta \delta_{\text{sat}}(HG_2)$) to the model function (13).

\[
\Delta \delta(H) = \frac{\Delta \delta_{\text{sat}}(HG)c(HG) + \Delta \delta_{\text{sat}}(HG_2)c(HG_2)}{c_0(H)} \quad [\text{ppm}] \quad (13)
\]
Introduction

When the $\Delta \delta(H)$ of host signals is followed during analogous titration experiments as described in the previous section, the binding curve function cannot be easily expressed analytically. Numerical solution of (15) is necessary to overcome this problem. This approach was implemented using the program Matlab 5.3 [52] to plot binding curves for hypothetical 1 : 2 host - guest systems (Figure 7).

From (9-13): 

$$
\Delta \delta(H) = \frac{K_1 c(G) \left( \Delta \delta_{sat}(HG) + \Delta \delta_{sat}(HG_2) K_2 c(G) \right)}{1 + K_1 c(G) + K_1 K_2 c(G)^2}
$$

(14)

$$
c_0(G) = c(G) + \frac{c_0(H) \left( K_1 c(G) + 2 K_1 K_2 c(G)^2 \right)}{1 + K_1 c(G) + K_1 K_2 c(G)^2}
$$

(15)

In this case, the shape of the binding isotherm depends not only on the association constants, but also on the relative values of $\Delta \delta_{sat}(HG)$ and $\Delta \delta_{sat}(HG_2)$ characterizing the 1 : 1 and 1 : 2 host - guest complexes, respectively. The formation of the 1 : 2 host -
guest complex becomes dominant for \( c_0(G) \gg c_0(H) \), and thus if \( \Delta \delta_{\text{sat}}(HG) > \Delta \delta_{\text{sat}}(HG_2) \), the binding isotherm first increases due to formation of the \( HG \) complex, then after reaching a maximum, it decreases to reach its limit \( \Delta \delta_{\text{sat}}(HG_2) \) as \( c_0(G) \to \infty \).

If both \( \Delta \delta_{\text{sat}}(HG) \) and \( \Delta \delta_{\text{sat}}(HG_2) \) are equal, the value of \( K_2 \) does not significantly influence the binding isotherm. If \( \Delta \delta_{\text{sat}}(HG) < \Delta \delta_{\text{sat}}(HG_2) \), the binding isotherm is similar to that of the 1 : 1 host-guest model.

Similarly, when the \( \Delta \delta(G) \) of guest signals is followed during the titration experiment, the binding curve function cannot be analytically expressed, and numerical solution of the equation set is necessary. In this case only the graphical representation is presented (Figure 8). Note that in contrast to the previous case, the change in chemical shift \( \Delta \delta \) of the guest in the 1 : 2 host-guest complex is discussed. The formation of the \( HG_2 \) complex is dominant for \( c_0(H) < c_0(G) \). Therefore, if \( \Delta \delta_{\text{sat}}(HG_2) < \Delta \delta_{\text{sat}}(HG) \), a sigmoidal shape of the binding isotherm may be observed depending on the values of

![Figure 8. Binding isotherms for 1 : 2 host-guest complexation. Constant guest concentration \( c_0(G) = 10^3 \text{ mol} \cdot \text{L}^{-1} \), \( \Delta \delta_{\text{sat}}(HG) = 1 \text{ ppm} \), \( K_1 = 8000 \text{ mol} \cdot \text{L}^{-1} \), \( K_2 = 500 \text{ mol} \cdot \text{L}^{-1} \) (a), \( 2000 \text{ mol} \cdot \text{L}^{-1} \) (b), \( 8000 \text{ mol} \cdot \text{L}^{-1} \) (c), and \( 32000 \text{ mol} \cdot \text{L}^{-1} \) (d).](image-url)
$K_1$ and $K_2$. The curve approaches $\Delta \delta_{sat}(HG_2)$ at $c_0(H) = c_0(G)/2$ and then grows to the limit $\Delta \delta_{sat}(HG)$ as $c_0(H) \to \infty$. For $\Delta \delta_{sat}(HG) = \Delta \delta_{sat}(HG_2)$, the binding isotherm is similar to that of the 1 : 1 host-guest model. If $\Delta \delta_{sat}(HG_2) > \Delta \delta_{sat}(HG)$, the curve first increases due to formation of the $HG_2$ complex, then after reaching a maximum, it decreases to reach its limit $\Delta \delta_{sat}(HG)$ as $c_0(H) \to \infty$.

Fitting of experimental data to the described complexation models was performed using the program Specfit 2.11 [53-57].

1.3.3. Job's Method (1 : 1 Model)

Knowing the stoichiometry of complexation is crucial for choosing the right model for data evaluation. In some cases, deviations from 1 : 1 stoichiometry can be identified from the shape of the binding curve, as seen in the previous section. In general, the method of continuous variation (Job's method) is used to determine complexation stoichiometry [49]. In such an experiment, a measurable property of a component ($\Delta \delta$) is followed as function of its molar fraction $x$, while the total initial concentration of both components $c_0(H) + c_0(G)$ is kept constant. In a plot, $\Delta \delta$ is replaced by the normalized values $\Delta \delta x$, yielding a maximum at $c_0(H)/c_0(G)$, which is equal to the complex stoichiometry.

This method will be illustrated for two hypothetical systems. The 1 : 1 host-guest model will be analyzed first.

\[ H + G \rightleftharpoons HG \]

The association of host $H$ and guest $G$ leading to their complex $HG$ is described using equations (1-3). In addition, $c_T$ is defined as the total initial concentration of both components and $x(H)$ as the molar fraction of the host.

\[ c_T = c_0(H) + c_0(G) \quad [\text{mol} \; \text{l}^{-1}] \quad (20) \]

\[ x(H) = \frac{c_0(H)}{c_T} \quad (21) \]

Then using equation (4), $\Delta \delta(H) x(H)$ is expressed, yielding an analytical description of the Job's plot for 1 : 1 complexation (22). Selection of host and guest is arbitrary in this case, the same equation is valid for $\Delta \delta(G) x(G)$.

\[ \Delta \delta(H) x(H) = \frac{\Delta \delta_{sat}(HG)}{2 K_a c_T} \left( K_a c_T + 1 - \sqrt{(K_a c_T + 1)^2 - 4 K_a^2 c_T^2 x(H)(1 - x(H))} \right) \quad (22) \]
A graphical representation of (22) is shown in Figure 9, illustrating the effect of the magnitude of the binding constant on the sharpness of the obtained maximum at $x = 0.5$.

![Figure 9](image)

*Figure 9. Job's plot for a 1:1 host-guest model generated using (22). Total concentration $c_T = 2 \times 10^3 \text{ mol l}^{-1}$, $\Delta \delta_{\text{sat}}(\text{HG}) = 1 \text{ ppm}$, and $K_a = 400 \text{ mol}^{-1} (a)$, $4000 \text{ mol}^{-1} (b)$, and $10^8 \text{ mol}^{-1} (c)$."

### 1.3.4. Job's Method (1:2 Model)

Another hypothetical system is an equilibrium between a $\text{HG}_2$ complex and its components, which is described by the total association constant $K$ (equation 23).

$$
\text{H} + 2\text{G} \rightleftharpoons \text{HG}_2
$$

$$
K = K_1 K_2 = \frac{c(\text{HG}_2)}{c(\text{H}) c(\text{G})^2} \quad \text{[l}^2 \text{ mol}^{-2}] \quad (23)
$$

$$
c_0(\text{H}) = c(\text{H}) + c(\text{HG}_2) \quad \text{[mol l}^{-1}] \quad (24)
$$

$$
c_0(\text{G}) = c(\text{G}) + 2c(\text{HG}_2) \quad \text{[mol l}^{-1}] \quad (25)
$$

$$
\Delta \delta(\text{H}) = \frac{\Delta \delta_{\text{sat}}(\text{HG}_2)c(\text{HG}_2)}{c_0(\text{H})} \quad \text{[ppm]} \quad (26)
$$

Using (21), $\Delta \delta(\text{H}) x(\text{H})$ is expressed yielding the analytical description of the Job's plot for 1:2 complexation (27) (see Appendix). A similar solution was derived for $\Delta \delta(\text{G}) x(\text{G})$. The plots show maxima at $x = 0.33$ and 0.67, respectively (Figure 10) and feature a characteristic sigmoidal limb. Real systems display a sum of contributions of all existing complexes, however.
Figure 10. Job's plot for a 1:2 host-guest model generated using (27) (see Appendix). Total concentration $c_T = 2 \times 10^{-3}$ mol l$^{-1}$, $\Delta \delta_{\text{eq}}(\text{HG}_2) = 1$ ppm, and $K = 10^6$ l mol$^{-1}$.
2. 1,1'-Binaphthalene Receptor for Carboxylates

2.1. Introduction

The first approach to dicarboxylate recognition was inspired by a previously prepared 1,1'-binaphthalene-based receptor for α,ω-dicarboxylic acids [58,59]. The receptor 28 binds derivatives of aspartic and glutamic acid with an enantioselectivity that depends on the dihedral angle about the chirality axis of the binaphthalene cleft. In the new receptors, amidinium ions were introduced for binding to carboxylate residues of guests.

![Receptor 28](image)

2.2. Design

The first generation of amidinium receptors was designed to bind dicarboxylates of the size of chorismate. A 1,1'-binaphthalene derivative with two benzamidine moieties attached to the 6,6' positions was selected using computer modeling (Macromodel [60]). Such a receptor was found to readily adopt a complementary geometry to the pseudodiaxial chorismate conformer. We hoped that this receptor would also stabilize the transition state of the rearrangement of chorismate to prephenate. The major interactions in the modeled complex between receptor 29 and the Bartlett inhibitor 27 are bidentate H-bonding interactions between the two carboxylates of 27 and the two amidinium ions of the receptor, paired with the corresponding Coulombic ion-pairing interactions (Figure 11).
Figure 11. The energy-minimized structure of the complex formed between 1,1'-binaphthalene receptor 29 and the Bartlett inhibitor 27 (MacroModel V.6.0, AMBER® force field). Shown are the intermolecular amidinium-carboxylate H-bonding N–O distances in the complex: (a) 2.59 Å, (b) 2.58 Å, (c) 2.48 Å, (d) 3.25 Å. The dihedral angle about the chirality axis C(2)-C(1)-C(1')-C(2') amounts to 110°.

2.3. Synthesis

Naphthalene-2,7-diol (30) was brominated to give a mixture of 1,3- and 1,6-dibromo derivatives which, after hydrogenolysis of the more labile C(1)-Br bond [61], afforded 31. Selective methylation of C(2)-OH led to 32, which was oxidatively coupled to form 33. After methylation of the residual OH groups, 34 was metallated by Br → Li exchange, the dilithiated intermediate was reacted with BH₃·THF, and aqueous workup afforded the corresponding bisboronic acid. Suzuki cross-coupling [62,63] of
the bisboronic acid with 2-bromobenzonitrile yielded dinitrile 35. The final bisamidinium receptor 29 was successfully prepared by the Garigipati reaction [64] for the conversion of "obstinate" (sterically hindered) nitriles [65] to amidines. The reagent in this reaction, methylchloroaluminum amide (MeAlNH₂Cl), was prepared from trimethylaluminum and ammonium chloride in toluene.

2.4. ¹H-NMR Complexation Studies

The ability of 29 to bind dicarboxylates 36-39 (Figure 12) in (CD₃)₂SO, CD₃CN, and CD₃OD was proven by several 500 MHz ¹H-NMR complexation studies. Titration in aprotic solvents (CD₃)₂SO and CD₃CN were run at constant receptor concentration. Large, complexation-induced downfield shifts Δδ of receptor proton H-C(8) were observed upon complexation with the dicarboxylate guests. However, the association constants were too high to be accurately determined using ¹H-NMR titrations (Table 2).
**Figure 12.** Dicarboxylates selected as guests for $^1$H-NMR complexation studies in (CD$_3$)$_2$SO, CD$_3$CN, and CD$_3$OD. The carboxylates were used as tetrabutylammonium salts (see Experimental Section).

**Table 2.** Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced downfield shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titrations for the complexes formed between 29 and dicarboxylates at 300 K. Titrations were run at constant receptor concentration.

<table>
<thead>
<tr>
<th>Guest</th>
<th>Solvent</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$ in 29 $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>(CD$_3$)$_2$SO</td>
<td>higher order association</td>
<td>—</td>
<td>+0.262</td>
</tr>
<tr>
<td>39</td>
<td>(CD$_3$)$_2$SO</td>
<td>&gt; 1 000 000</td>
<td>&gt; 34.5</td>
<td>+0.282</td>
</tr>
<tr>
<td>37</td>
<td>CD$_3$CN</td>
<td>&gt; 1 000 000</td>
<td>&gt; 34.5</td>
<td>+0.444</td>
</tr>
</tbody>
</table>

$^a$) Monitored proton resonance: H-C(8).

Addition of a more competitive solvent, CD$_3$OD, decreased the binding constant for the complexes of 29 with the dicarboxylate guests and suppressed the higher order association. However, the association constants obtained using the program Associate 1.6 [50] are still at the upper limit of values for which the use of the $^1$H-NMR technique is reasonable and therefore not very accurate (Table 3).
Table 3. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and complexation-induced downfield shifts $\Delta \delta_{\text{max}}$ (maximum observed) and $\Delta \delta_{\text{sat}}$ (calculated for saturation binding), determined by $^1$H-NMR titrations for the complexes formed between 29 and dicarboxylates in CD$_3$CN/CD$_3$OD 4:1 at 300 K. Constant receptor concentration: 1·10$^4$ or 2·10$^4$ mol$^{-1}$.

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$ ($\Delta \delta_{\text{sat}}$) in 29$^a$ [ppm, + = downfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>140 000 ± 30 000</td>
<td>29.6 ± 0.5</td>
<td>+0.225 (0.240)</td>
</tr>
<tr>
<td>37</td>
<td>118 000 ± 59 000</td>
<td>29.1 ± 1.4</td>
<td>+0.218 (0.228)</td>
</tr>
</tbody>
</table>

$^a$ Monitored protons resonance: H-C(8).

In order to adjust the complexation strength to a level which allowed meaningful determination of thermodynamic quantities from $^1$H-NMR titrations, the pure protic solvent CD$_3$OD was used in subsequent complexation studies. In titrations at constant receptor concentration, however, the complexation-induced shifts of the receptor proton signals were too small (<0.03 ppm) in CD$_3$OD. Inverse titrations at constant guest concentration were therefore performed in which resonances of the dicarboxylates were monitored and evaluated. For H-C(2) of the guests, complexation-induced upfield shifts larger than 0.1 ppm were measured and a satisfactory fit of the titration data to the 1:1 host-guest complex model was obtained.

Association constants for the complexes formed between isophthalates 37-39 and receptor 29 in CD$_3$OD were found in the range of 5 000-10 000 l mol$^{-1}$ (Table 4). The rigidity of the guests does not affect complexation in CD$_3$OD; glutarate 36 is bound with similar affinity. More important is the effect of the isophthalate substituents. Electron-rich 5-alkoxyisophthalates (38, 39) form more stable complexes with the bisamidinium receptor 29 in CD$_3$OD than electron-deficient 5-nitroisophthalate 37.
Table 4. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced upfield shifts $\Delta \delta_{\text{max}}$ (in parenthesis: calculated shift $\Delta \delta_{\text{sat}}$ at saturation binding) determined by $^1$H-NMR titrations for the complexes formed between 29 and dicarboxylates in CD$_3$OD at 300 K. Constant guest concentration: 5-10$^{-4}$ mol l$^{-1}$.

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$ ($\Delta \delta_{\text{sat}}$) in guest$^a$ [ppm, $-$ = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>8 200 ± 2 000</td>
<td>22.5 ± 0.6</td>
<td>$-0.119$ ($-0.138$)</td>
</tr>
<tr>
<td>37</td>
<td>5 100 ± 400</td>
<td>21.3 ± 0.2</td>
<td>$-0.092$ ($-0.119$)</td>
</tr>
<tr>
<td>38</td>
<td>8 300 ± 600</td>
<td>22.5 ± 0.2</td>
<td>$-0.123$ ($-0.141$)</td>
</tr>
<tr>
<td>39</td>
<td>10 000 ± 1 000</td>
<td>23.0 ± 0.3</td>
<td>$-0.183$ ($-0.205$)</td>
</tr>
</tbody>
</table>

$^a$ Evaluated protons resonances: H-C(2) in isophthalates, H-C(3) in glutarate.

The complexation of dicarboxylates with binaphthalene receptor 29 in D$_2$O led to precipitation of a solid. The precipitate was dissolved in (CD$_3$)$_2$SO, and integration of its $^1$H-NMR signals confirmed the 1 : 1 host-guest stoichiometry. In D$_2$O/CD$_3$OD mixture, the binding of isophthalate 37 was found too weak to be determined by $^1$H-NMR titration (Table 5), since the limited solubility of receptor 29 in this mixture did not allow the use of appropriate concentration ranges.

Table 5. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced upfield shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titration for the complex between 29 and dicarboxylate 37 at 300 K in aqueous solvents. Constant guest concentration: 10$^{-2}$ mol l$^{-1}$.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$ in 37$^a$ [ppm, $-$ = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>D$_2$O</td>
<td>precipitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D$_2$O/CD$_3$OD 1 : 1</td>
<td>&lt; 50</td>
<td>&lt; 10</td>
<td>$-0.097$</td>
</tr>
</tbody>
</table>

$^a$ Monitored protons resonance: H-C(2).

2.5. Variable Temperature $^1$H-NMR Complexation Studies

To estimate the changes in enthalpy ($\Delta H^\circ$) and entropy ($\Delta S^\circ$) for the complexation of dicarboxylates by 29 in methanol, a van’t Hoff analysis (28) was applied to the binding
data obtained at different temperatures. The change in enthalpy $\Delta H^\circ$ is assumed to be constant in the temperature range used (275-306 K).

$$R\ln K_a = -\frac{\Delta H}{T} + \Delta S$$ (28)

The bis(tetrabutylammonium) salt of 5-nitroisophthalate 37 (Figure 12) was chosen as a guest since its sharp and well isolated signals in the $^1$H-NMR spectra in CD$_3$OD were easy to be followed during titrations. The concentration of isophthalate 37 was kept constant at $5 \times 10^{-4}$ mol l$^{-1}$ and the concentration of host 29 was varied ($1.25 \times 10^{-4}-1.25 \times 10^{-3}$ mol l$^{-1}$). The same titration samples were measured at five different temperatures between 275 K and 306 K. Surprisingly, the binding constant $K_a$ for the complexation of isophthalate 37 in CD$_3$OD was found to increase with increasing temperature (Table 6). This is a characteristic behavior for an endothermic processes, thus the $\Delta H^\circ$ for the complexation process is positive (Figure 13) and the association is purely entropy-driven.

The entropic driving force can be explained by considering the solvation of the free and complexed states. In the free state, the ionic groups in both receptor 29 and guest 37 are strongly solvated by CD$_3$OD molecules. Upon complexation, these CD$_3$OD molecules are largely released into the bulk, which provides the entropic driving force for the complexation process. On the other hand, the solvation of the free components presumably is more exothermic than the host-guest complexation event, which could explain the unfavorable enthalpic term. Thus, part of the entropic gain is compensated by a loss in enthalpy upon complexation.

Table 6. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, complexation-induced upfield shifts $\Delta\delta_{\text{max}}$ (maximum observed) and $\Delta\delta_{\text{sat}}$ (calculated for saturation binding), for the complexes formed between 29 and 37 in CD$_3$OD at different temperatures.

<table>
<thead>
<tr>
<th>$T$ [K]</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta\delta_{\text{max}}$ ($\Delta\delta_{\text{sat}}$) in 37$^{a)}$ [ppm, $\text{=} \text{upfield}$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>275</td>
<td>3750 ± 250</td>
<td>18.8 ± 0.2</td>
<td>−0.125 (−0.164)</td>
</tr>
<tr>
<td>283</td>
<td>4160 ± 150</td>
<td>19.6 ± 0.1</td>
<td>−0.131 (−0.168)</td>
</tr>
<tr>
<td>289</td>
<td>4450 ± 190</td>
<td>20.2 ± 0.1</td>
<td>−0.134 (−0.170)</td>
</tr>
<tr>
<td>299</td>
<td>4940 ± 250</td>
<td>21.1 ± 0.1</td>
<td>−0.140 (−0.174)</td>
</tr>
<tr>
<td>306</td>
<td>5330 ± 260</td>
<td>21.8 ± 0.1</td>
<td>−0.146 (−0.180)</td>
</tr>
</tbody>
</table>

$^{a)}$ Monitored protons resonance: H-C(2).
Chapter 2

\[ R \ln K_a = -\frac{7717}{T} + 96.6 \quad [\text{J mol}^{-1} \text{K}^{-1}] \]

Figure 13. The variable temperature titration data fitted to the von\’t Hoff equation.

Table 7. Thermodynamic parameters for the complex between 29 and 37 obtained by the variable temperature \(^1\)H-NMR study in CD\(_3\)OD.

<table>
<thead>
<tr>
<th>(-\Delta S°_{300}) [J mol(^{-1}) K(^{-1})]</th>
<th>(-T \Delta S°_{300}) [kJ mol(^{-1})]</th>
<th>(\Delta H°_{300}) [kJ mol(^{-1})]</th>
<th>(\Delta G°_{300}) (^a) [kJ mol(^{-1})]</th>
</tr>
</thead>
<tbody>
<tr>
<td>96.6 ± 5.1</td>
<td>-29.00 ± 1.5</td>
<td>7.7 ± 1.5</td>
<td>-21.3 ± 3.0</td>
</tr>
</tbody>
</table>

\(^a\) Calculated as \(\Delta H°_{300} - T \Delta S°_{300}\); \(\Delta G°_{298}\) was determined as \(-21.1 ± 0.1\) (Table 6)

2.6. Microcalorimetric Titrations

In order to confirm the thermodynamic data obtained from variable temperature \(^1\)H-NMR titrations, the binding of dicarboxylates to receptor 29 was studied using isothermal titration calorimetry (ITC). This method gives \(\Delta H°\) directly as a primary parameter of measurement, whereas \(\Delta G°\) and \(K_a\) are estimated from the titration curve fitting. The complexation entropy \(\Delta S°\) may then be readily calculated.

A dilution of 37 in methanol was found to be strongly exothermic (Figure 14, gray line) and thermally compensating the weakly endothermic association of 37 with 29 (Figure 14, bold line). Subtracted integrals of each pulse at each titration step were analyzed using the program DIGITAM 3.0 [66]. Complexation of 37 was found to be endothermic (\(\Delta H° = 11.6\) kJ mol\(^{-1}\)), but the fitting process revealed \(K_a = 12 600\) 1 mol\(^{-1}\). Therefore, the association is strongly entropy-driven with \(T\Delta S°\) outweighing the
unfavorable $\Delta H^\circ$ value. Similar results were obtained in the case of flexible glutarate 36 (Table 8).

Table 8. Results from calorimetric titrations of receptor 29 in methanol at 298 K.

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta H^\circ$ [kJ mol$^{-1}$]</th>
<th>$-T \Delta S^\circ$ [kJ mol$^{-1}$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>12 600 ± 2 000</td>
<td>23.4 ± 0.4</td>
<td>11.6 ± 0.4</td>
<td>35.0 ± 0.8</td>
</tr>
<tr>
<td>36</td>
<td>6 000 ± 2 000</td>
<td>21.4 ± 0.8</td>
<td>11.3 ± 1.0</td>
<td>32.7 ± 1.8</td>
</tr>
</tbody>
</table>

Figure 14. Thermogram of the calorimetric titration of receptor 29 (5 × 10$^{-4}$ mol l$^{-1}$, 3 ml) with 37 (1.9 × 10$^{-2}$ mol l$^{-1}$, 15 μl additions) in methanol at 298 K (bold line) compared with dilution of 37 in methanol (gray line). Negative $P$ values correspond to endothermic processes.

Different results were obtained from ITC in an aprotic solvent (Figure 15). A dilution of 37 in MeCN did not show any thermal response. Therefore, the ITC thermogram in MeCN corresponds directly to the enthalpy of association ($\Delta H^\circ$). Complexation of 37 with 29 was found to be strongly exothermic, but the exact $\Delta H^\circ$ and $K_a$ values could not be calculated due to the high binding constants and the complicated host-guest stoichiometry.
Figure 15. Thermogram of the calorimetric titration of receptor 29 (5 \times 10^{-4} \text{ mol} \cdot \text{l}^{-1}, 3 \text{ ml}) with 37 (1.9 \times 10^{-2} \text{ mol} \cdot \text{l}^{-1}, 15 \mu \text{l additions}) in MeCN.

2.7. Summary

The results presented here show the ability of 1,1'-binaphthalene receptor 29 to bind dicarboxylates even in competitive protic solvents. No selectivity was found for flexible or rigid guests. Binding is endothermic and entropy-driven in MeOH, but exothermic and presumably enthalpy driven in MeCN. Good agreement was found between variable temperature $^1$H NMR titration and isothermal titration calorimetry (ITC) in the qualitative description of carboxylate complexation in MeOH. The change in enthalpy $\Delta H^\circ$ for dicarboxylate complexation in methanol was found to be small and positive using both methods. However, the accuracy of the thermodynamic parameters obtained is quite low. Van't Hoff analysis applied to the variable temperature $^1$H NMR titration data requires ideal behavior of the system. The signal-to-noise ratio in the ITC method was not very high due to weak thermal changes associated with carboxylate complexation and a strong disturbing dilution effect.

The design of receptor 29 was based on expected favorable enthalpic interactions with carboxylates (charge-charge interaction, hydrogen bonds). This model may be correct for non-polar solvents, but it failed completely in the case of competitive protic solvents, where the desolvation entropy upon carboxylate binding is the main driving force for complexation. Therefore, solvation effects need always be considered and exploited in the molecular recognition of charged guests in protic solvents.
3. Small Bisamidinium Receptors

3.1. Towards Multi-Amidinium-Functionalized Acetylenic Macrocycles

Binding of the "ether" oxygen in the transition state for the chorismate to prephenate rearrangement by a positively charged hydrogen bond donor is important for catalysis. This was reflected in our attempts to bridge the ether oxygen and the adjacent carboxylate of the substrate by a suitable bisamidinium unit. Two such units could also be arranged around the transition state. With this idea in mind, the simple receptor 40 was proposed.

According to computer modeling, two molecules of 40 can bind to the presumed TS in two major orientations, one in which the receptor unit is bridging the secondary carboxylate and the "ether" oxygen, and the other one in which the receptor unit is bridging both carboxylates (Figure 16).

![Figure 16. The energy-minimized structure of the complex formed between two molecules of the receptor 40 and the Bartlett inhibitor 27 (MacroModel V.6.0, AMBER® force field). Shown are the intermolecular H-bonding N–O distances in the complex: (a) 2.76 Å, (b) 2.60 Å, (c) 2.62 Å, (d) 2.60 Å, (e) 2.63 Å, (f) 2.58 Å, (g) 2.56 Å, (h) 2.81 Å.](image-url)
Attempts to link both bisamidine units together yielded pentakisamidinium macrocycle 41. According to computer modeling, four of the five amidinium moieties in 41 adopt ideal positions to bind and stabilize the transition state of the chorismate to prephenate rearrangement, as modeled by the Bartlett inhibitor.

![Chemical structure of 41](image)

**Figure 17.** The energy-minimized structure of the complex formed between the receptor 41 and the Bartlett inhibitor 27 (MacroModel V.6.0, AMBER® force field). Shown are the intermolecular H-bonding N⋯O distances in the complex: (a) 2.76 Å, (b) 2.60 Å, (c) 2.62 Å, (d) 2.00 Å, (e) 2.63 Å, (f) 2.58 Å, (g) 2.56 Å, (h) 2.81 Å.
3.1.1. Synthesis

3,4,5-Trimethoxybenzonitrile 42 was iodinated [67] to yield 43, which was coupled with trimethylsilylacetylene (TMSA) under Sonogashira conditions [68]. The product 44 was deprotected, and the terminal alkyne was used without purification in an oxidative coupling [69] to yield 45.

The Garigipati method [64], used for the conversion of the dinitrile 45 to the bis(amidinium) salt 46, yielded a red insoluble solid. The bis(amidinium) salt 46 is unstable and undergoes an undesired subsequent intramolecular cyclization.
3.2. Diphenylnaphthalene Receptors

A naphthalene-2,7-diyl fragment was considered as an alternative to the buta-1,3-diynediyl linker in 46. The 2,7-diphenylnaphthalene receptor 47 was designed to contain one carboxylate binding site and another bridging site for the "ether" oxygen in the TS complex. In the computed TS complex, formed by the Bartlett inhibitor and two molecules of 47, one 47 derivative binds to one carboxylate and to the "ether" oxygen atom. The second molecule of 47 binds the tertiary carboxylate of the inhibitor in a bidentate fashion and also interacts via its second amidinium group with the secondary carboxylate (exo-lone pair) of the inhibitor (Figure 18).

Figure 18. The energy-minimized structure of the complex formed between two molecules of the receptor 47 and the Bartlett inhibitor 27 (MacroModel V.6.0, AMBER® force field). Shown are the intermolecular amidinium - carboxylate H-bonding N–O distances in the complex: (a) 2.66 Å, (b) 2.62 Å, (c) 2.62 Å, (d) 2.61 Å, (e) 2.57 Å, (f) 2.56 Å, (g) 2.62 Å, (h) 2.59 Å.
3.2.1. Synthesis

Naphthalene-2,7-diol 30 was dibrominated [61] and the product methylated to yield 48, which was dilithiated. This dilithiated intermediate was treated with borane/THF, and, after hydrolysis, the corresponding bisboronic acid was obtained. It was used without further purification in the Suzuki cross-coupling with 2-bromobenzonitrile to yield 49. The low yield of this step is due to the instability of the bisboronic acid. The dinitrile 49 was converted into amidinium chloride 47 in a good yield using the Garigipati method [64].

In an attempt to further rigidify the receptor and to enhance its preorganization for binding, the modified bisamidine precursor 50 was prepared, and its diastereotopic atropoisomers were separated and characterized. For the preparation of 50, 2-methyl-6-nitroaniline 51 was converted to 52 using diazotization and a Sandmeyer reaction with CuBr. The nitro group in 52 was reduced with Ni$_2$B in aqueous HCl [70] yielding 53, which was then converted without purification into 54.
3,6-Dimethoxy-2,7-bis(trimethyltin)naphthalene 55 was prepared by lithiation of 48 and quenching of the bislithium intermediate with trimethyltin chloride. *Stille* coupling of 54 with 55 in the presence of [Pd(PPh₃)₄] yielded a complicated mixture of products, from which both diastereoisomers of 50 could be isolated and characterized. The less polar isomer of 50 was crystallized and its structure was determined as *C₂*-symmetrical by X-ray crystallographic analysis. The crystal structure of *C₂*-50 was
solved and analyzed by Dr. B. Schweizer (for details of the X-ray crystal structure, see Appendix 10.1.).

Although both isomers of 50 could be easily separated, the atropoisomerization process was found to take place already at 50 °C, which makes the selective synthesis of the desired $C_8$-symmetrical bisamidinium receptor $C_8$-56 impossible. The bisamidinium salt would, presumably, also isomerize at this temperature, which would severely perturb kinetic investigations of the chorismate to prephenate rearrangement.

In order to circumvent the atropoisomerism problem of the 2,7-diphenynaphthalene receptors, their symmetry was increased, and the introduction of new binding site based on isophthalamidinium units was proposed. The precursor, 2-iodoisophthalonitrile 57, was easily prepared by directed ortho-lithiation of isophthalonitrile 58 with lithiumdiisopropylamide (LDA) and quenching of the aryllithium intermediate with iodine [71].

The $C_{2v}$-symmetric tetranitrile 59 was prepared by Suzuki cross-coupling of 60 with 57. Bisboronic acid 60 was prepared by dilithiation of 48, followed by addition of
BH$_3$-THF and esterification with pinacol. Because of the lower solubility of 59, 
$o$-dichlorobenzene was used as a co-solvent in the Garigipati conversion to the 
amidinium salt. However, instead of the tetraamidinium salt 61, a mixture of bis- and 
trisamidinium intermediates was isolated under all experimental conditions.
4. Cavitand Tetraamidinium Receptor

The resorcinarene cavitands (*Figures 19 and 20*) first prepared and studied by Cram [72] represent important building blocks in supramolecular chemistry. We became interested in utilizing this highly preorganized scaffold both as a cavity-containing recognition site and as a base to anchor four arylamidinium ions via Suzuki cross-coupling for carboxylate binding and possible catalysis of the chorismate to prephenate rearrangement. For this purpose a tetrabromoresorcinarene was required. In order to shape a suitably sized binding pocket, we selected, based on computer modeling, a resorcinarene cavitand with ethylene bridges. *Figure 19* shows the general synthetic strategy for preparing resorcinarennes and *Figure 20* shows the wider bowl shape adopted by resorcinarene cavitands with ethylene bridges rather than methylene bridges.

![Figure 19](image-url)

*Figure 19.* Synthesis of resorcinarene cavitands. Acid-catalyzed condensation of resorcinol with aldehydes leads to the tetrameric *cis, cis, cis* octols, which are converted to cavitands by four-fold ring closure to build methylene or polymethylene bridges.

![Figure 20](image-url)

*Figure 20.* Computer generated structure of methylene (left) and ethylene bridged (right) resorcinarene cavitands.
4.1. Synthesis

The octols 63 and 64 were prepared according to literature procedures [73] starting from resorcinol (62). It is known [74] that unsubstituted octols form cavitands by fourfold ring closures in considerably lower yields than their corresponding tetrabromo-
derivatives. Because we also needed bromine functionalities to anchor the arylamidinium groups on top of the bowl-type cavity, octols 63 and 64 were brominated with NBS in butanone [74]. The tetrabromooctols 65 and 66 were bridged using ethyleneglycol ditosylate and Cs₂CO₃ in Me₂SO to form 67 and 68, respectively. Triple bridged diphenol intermediates 67a and 68a were also isolated in this step. They were subsequently transformed to 67 and 68 by another bridging reaction in MeCN. Drying of 67 and 68 was crucial before the subsequent lithiation by Br/Li-exchange to introduce the arylamidinium groups. The residual solvent in the cavity (water, CH₂Cl₂) was removed by slow distillation of THF and benzene from solutions of the cavitands.

Crystals of 68 were grown from CH₂Cl₂ and the X-ray structure of the solvate with two CH₂Cl₂ molecules was solved by Prof. V. Gramlich (Figure 21). The solid state structure shows interesting enclathration phenomena similar to those previously described by Cram and co-workers [72-74]. One CH₂Cl₂ molecule is located inside the cavitand bowl with one Cl-atom pointing deeply into the cavity. The second CH₂Cl₂ molecule is embedded in a second cavity shaped by the four solubility providing phenylethyl feet (for details of the X-ray crystal structure, see Appendix 10.2.).
We found it very difficult to achieve a fourfold *Suzuki* cross-coupling with the tetrabromoresorcinarenes 67 and 68. Therefore, we exchanged the bromides via metallation and iodination to give tetraiodides 69 and 70. For this purpose, dry 67 and 68 were lithiated, and the resulting tetralithium intermediates were treated with iodine to afford the tetraiodocavitands 69 and 70, respectively, which have much higher reactivity in *Suzuki* cross-coupling reactions [62,63] than the starting tetrabromocavitands. The tetranitriles 71 and 72 were obtained by palladium-catalyzed coupling between 3-((4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)benzonitrile (73) and tetraiodocavitands 69, 70, respectively. Tetraamidinium salts 74 and 75 were prepared from 71 and 70, respectively, using the *Garigipati* method [64]. Isolation and purification of the tetraamidinium chlorides 74 and 75 was achieved using a new technique. The dried mixture of crude amidinium chlorides and NH₄Cl was stirred at r.t. for 8 h with a mixture of acetone (200 ml) and propan-2-ol (0.2 ml), and filtered. The solid was washed with acetone (500 ml), dried, and washed with water (500 ml). After drying again, the solid was recrystallized (MeOH/Et₂O 1:2) to afford the pure tetraamidinium chlorides 74 and 75.
The arylboronic esters were prepared as follows: Lithiation of 3-bromobenzonitrile 76 at -100 °C, quenching of the aryllithium intermediate with trimethylborate and transesterification with pinacol gave the arylboronate 73 in good yield. In a similar way, 77 was prepared starting from 4-bromobenzonitrile (78). A recently published method [75] - palladium catalyzed coupling of dialkoxyhydroborane with aryl halide - was used to prepare boronic ester 79 starting from 80.

4.2. Binding Studies

When we attempted binding studies with the tetraamidinium cavitands 74 and 75, we found as a major disadvantage that these systems only had low solubility in protic solvents. Therefore, no titration experiments could be successfully performed using these cavitands. For example, upon mixing equimolar solutions of 75 and AMP in methanol, a precipitate formed. The analysis of the solid using FAB-MS technique confirmed the formation of a 1 : 1 complex (Figure 22).

Figure 22. FAB-MS spectra (3-NOBA matrix) of receptor 75 (a), and of the 75-AMP complex (b).
5. Water-Soluble Cavitand Receptor

5.1. Introduction

In contrast to the calix[4]arenes, there are only a few examples of water-soluble, resorcin[4]arene-based cavitands. The synthesis of rim-functionalized methylene-bridged resorcin[4]arenes containing water-solubilizing propylphosphate groups was described by Mezo and Sherman [76]. The cavitands possess the synthetically useful benzylthiol or benzylbromide functionalities, which are suitable for further derivatization near the hydrophobic cavity of the cavitand. As an example of their synthetic utility in supramolecular studies, the phosphate-substituted cavitands 81 and 82 were reacted with cysteine-containing and chloroacetylated peptides, respectively, to afford the corresponding modified receptors 83 and 84.
Water-soluble resorcin[4]arene-based cavitands 85 were obtained in good yields by reaction of bromomethylcavitands with pyridine [77]. Their behavior in water depends on the alkyl chain length; the methylcavitand does not aggregate, whereas the pentyl- and undecylcavitands do, as shown by $^1$H-NMR spectroscopy and transmission electron microscopy.

A similar water-soluble resorcin[4]arene was synthesized by reaction of a bromomethylcavitand with hexamethylenetetramine [78]. The bowl-shaped host shows good binding affinity to anionic aromatic guests with 1 : 1 stoichiometry in D$_2$O. Guest inclusion within the host cavity was confirmed by $^1$H-NMR spectroscopy. Coulombic ion pairing as well as hydrophobic interactions turned out to act cooperatively as binding forces for a strong complex formation in water.

The synthesis of the first water-soluble hemicarcerand 86 and its spectral and binding properties with various guests in water were described by Yoon and Cram [79].
5.2. Design

In order to increase the solubility of the cavitand receptors in protic solvents, four triethyleneglycol monomethyl ether (TEG) chains were chosen to replace the hydrophobic "feet" of the cavitand. These groups should have enough favorable interactions with protic solvents to outweigh the hydrophobic effect of the rigid cavitand core. The pendant feet of the cavitand 87 represent new building blocks in these types of systems.

![Diagram of cavitand 87](image)

5.3. Synthesis

The synthesis of cavitand 87 proved to be more complicated than that of 74 or 75. Dodecol 88 was prepared by acid-catalyzed condensation of resorcinol and 2,3-dihydrofuran [80] in 90% yield. Compound 88 was then brominated using N-bromosuccinimide in butanone [74] to give tetrabromododecol 89 (77%).

![Synthesis reaction](image)
In the next step, ethylene bridges were incorporated into dodecol 89 to form the rigid cavitand 90 in 42% yield. This bridging is often the most difficult step in the formation of resorcinarene cavitands because of oligomerization. As successive bridges form, the molecules become more rigid, which slows down subsequent reaction substantially. Furthermore, in the case of 89 the bridging reaction is complicated by the pendant hydroxyl groups. The experiments showed that a long reaction time (7 days) and a large excess of reagents were necessary. Multiple side-products made the purification complicated and time-consuming.

The propanol-substituted cavitand 90 was mesylated at 0 °C to give 91 in 92% yield. A substitution of the mesylate groups with the sodium salt of triethylene glycol monomethyl ether 94 (prepared with NaH) yielded product 92, contaminated with a large amount of tribromocavitand 92a, resulting from partial reduction of 92 in the presence of the alkoxide base.
A new reagent for the substitution of mesylate 91 to polyether 92 was developed in this work. Triethyleneglycol monomethyl ether was heated with activated magnesium to form the very viscous dialkoxy magnesium derivative 93. This was found to react cleanly with 91 in dioxane to give 92 in a 78% yield.

\[
\text{O} \quad \text{O} \quad \text{O} \quad \text{O} \quad \text{OH} \quad \xrightarrow{\text{Mg, I2, 140 °C}} \quad \left(\text{O} \quad \text{O} \quad \text{O} \quad \text{O} \quad \text{Mg}\right)
\]

After removal of residual solvent complexed in the cavity, 92 was lithiated at -100 °C, and the tetralithiated cavitand was subsequently quenched with iodine to give 95 in 97% yield.

\[
\begin{align*}
\text{92} & \quad \xrightarrow{1.) \text{BuLi, THF, -100 °C}} \quad \text{95} \\
\text{87} & \quad \xrightarrow{\text{MeAlNH}2\text{Cl, o-DCB, 70-80 °C}} \quad \text{96}
\end{align*}
\]

Suzuki cross-coupling [62,63] of 95 with 3-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)benzonitrile (73) afforded tetranitrile 96. When [Pd(PhCN)2Cl2] was used as a catalyst, the product was contaminated with traces of Ph3PO, and all attempts to purify 96 failed. Replacing the catalyst with [Pd(PhCN)2Cl2] solved the problem without affecting the yield (84%) of the coupling. Tetranitrile 96 was finally converted to the tetraamidinium chloride 87 using the Garigipati reaction [64] in 91% yield.
The final product could be obtained in a gram scale. The product 87 proved to be quite soluble in MeOH and water, as expected.

5.4. Molecular Modeling of Cavitand Complexes

Molecular modeling (Monte Carlo method implemented in MacroModel V. 6.0, AMBER* force field, GB/SA solvation model for water, 4000 steps) supported our expectation that the new cavitand would form stable inclusion complexes with anionic guests. A variety of complexes were modeled and their low-energy conformations determined.

*Figure 23* shows the inclusion complexes of 87 with 5-nitroisophthalate and 5-methoxyisophthalate. The aromatic ring is embedded in the cavity while the carboxylate residues interact via H-bonding and ion-pairing with the surrounding benzamidinium residues.

Similarly, AMP and ADP were predicted to form stable inclusion complexes (*Figure 24*). Again, the purine base can be accommodated in the bowl-type cavity, while the phosphate groups have multiple H-bonding and ion-pairing interactions with the benzamidinium residues of the receptor. The models also predict stable complexation of cAMP and dinucleotide d(AA) (*Figure 25*). In the later complex, one adenine moiety would be included in the cavity and a second one would protrude out of the binding site, possibly also making apolar contacts with aryl rings of the receptor. Inclusion of the purine base deep in the cavity is also expected for GMP. In contrast, the smaller pyrimidine base UMP does not show a high propensity to bind to the bowl (*Figure 26*); and mainly forms phosphate - amidinium interactions.

Of particular interest was the modeling result showing that the Bartlett inhibitor would form a complex with 87, picking up several strong amidinium - carboxylate interactions. This is shown in *Figure 27*.

Finally, we also modeled the association of the cavitand 87 with a duplex of slightly distorted B-DNA made from two 14-mers d(3'-CGTATTTATTCTCG) and d(5'-GCATAAATAAGAGC). Expectedly, the receptor binds to the phosphate backbone where it makes several strong amidinium - phosphate contacts involving up to five phosphate residues (*Figure 28*).
Figure 23. The energy-minimized structure of the complex formed between the tetraamidinium cavitand 87 fragment and 5-nitroisophthalate (top) or 5-methoxyisophthalate (bottom) (Monte Carlo, MacroModel V.6.0, AMBER® force field, GB/SA solvation model for water, 4000 steps). Shown are the intermolecular H-bonding N····O distances in the complex. Top: (a) 2.63 Å, (b) 2.64 Å, (c) 2.70 Å, (d) 2.66 Å. Bottom: (a) 2.65 Å, (b) 2.74 Å, (c) 2.66 Å, (d) 2.66 Å, (e) 2.66 Å.
Figure 24. The energy-minimized structure of the complex formed between the tetraamidinium cavitand 87 fragment and AMP (top) and ADP (bottom) (Monte Carlo, MacroModel V.6.0, AMBER* force field, GB/SA solvation model for water, 4000 steps). Shown are the intermolecular H-bonding N···O distances in the complex. Top: (a) 2.69 Å, (b) 2.67 Å, (c) 2.66 Å, (d) 2.75 Å, (e) 2.91 Å, (f) 2.76 Å. Bottom: (a) 2.69 Å, (b) 2.67 Å, (c) 2.69 Å, (d) 2.90 Å, (e) 2.74 Å, (f) 2.77 Å, (g) 2.78 Å.
Figure 25. The energy-minimized structure of the complex formed between the tetraamidinium cavitand 87 fragment and cAMP (top) and dinucleotide d(AA) (bottom) (Monte Carlo, MacroModel V.6.0, AMBER® force field, GB/SA solvation model for water, 4000 steps). Shown are the intermolecular H-bonding N⋯O distances in the complex. Top: (a) 2.72 Å, (b) 2.83 Å, (c) 3.59 Å. Bottom: (a) 2.69 Å, (b) 2.86 Å.
Figure 26. The energy-minimized structure of the complex formed between the tetraamidinium cavitand 87 fragment and GMP (top) and UMP (bottom) (Monte Carlo, MacroModel 6.0, AMBER® force field, GB/SA solvation model for water, 4000 steps). Shown are the intermolecular H-bonding N-O distances in the complex. Top: (a) 2.70 Å, (b) 2.67 Å. Bottom: (a) 2.65 Å, (b) 2.69 Å, (c) 2.67 Å, (d) 2.83 Å, (e) 2.67 Å, (f) 2.99 Å.
Figure 27. The energy-minimized structure of the complex formed between the tetraamidinium cavitand 87 fragment and Bartlett inhibitor (Monte Carlo, MacroModel V.6.0, AMBER® force field, GB/SA solvation model for water, 4000 steps). Shown are the intermolecular H-bonding N····O distances in the complex: (a) 2.69 Å, (b) 2.67 Å, (c) 2.67 Å, (d) 3.07 Å, (e) 2.70 Å, (f) 2.66 Å, (g) 2.66 Å.
5.5. \(^1\)H-NMR Complexation Studies

With receptor 87 in hand, complexation studies with oxyanions were undertaken using \(^1\)H-NMR titration techniques. A variety of guests was employed in this investigation. Isophthalates 37, 97 and 98 (Figure 29) were chosen as carboxylate guests, nucleotides 99-109 (Figure 35) represented the phosphate family of substrates, and heparin analogs 110-111 (Figure 37) served as sulfate guests. The latter substrates were kindly provided by Dr. H.-P. Wessel (F. Hoffmann - La Roche, Basel). Sodium salts were prepared in aqueous solution, tetrabutylammonium salts in methanolic solution. Titrations were performed by adding a solution of both components (11 x 20-300 µl) to the solution of a component in a NMR tube. The signals of the component which was kept at constant concentration were followed. The experimental data were fitted using the program Specfit 2.11 [57].
5.5.1. Carboxylate Binding

![Chemical Structures](attachment:structures.png)

**Figure 29.** Dicarboxylates selected as guests for $^1$H-NMR complexation studies with receptor 87.

Complexation of isophthalate 37 with receptor 87 in CD$_3$OD could not be described using a simple 1 : 1 host - guest binding model. Instead, an analysis of the complexation data provided evidence for a significant contribution of 1 : 2 host - guest association (Figure 30).

![Graphs](attachment:graphs.png)

**Figure 30.** Complexation isotherms for binding of 5-nitroisophthalate (37) (5 · 10$^{-4}$ mol l$^{-1}$) to receptor 87 in CD$_3$OD at 300 K (solid curve). The dashed curve represents the calculated fit of the data to the 1 : 1 host - guest association model.

A good fit of the data to the 1 : 2 host - guest model was, however, obtained yielding high association constants for the complex of two isophthalate molecules 37 with receptor 87 in CD$_3$OD (Table 9).
Table 9. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between 87 and 37 in CD$_3$OD at 300 K. Constant concentration of 37: $5 \times 10^{-4}$ mol l$^{-1}$; receptor concentration: $3 \times 10^{-5}$-$5 \times 10^{-4}$ mol l$^{-1}$.

<table>
<thead>
<tr>
<th>$K_1$(HG) [l mol$^{-1}$]</th>
<th>$K_2$(HG$_2$) [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$(HG) [kJ mol$^{-1}$]</th>
<th>$-\Delta G^\circ$(HG$_2$) [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$(37) [ppm, $-$ = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>350 000</td>
<td>60 000</td>
<td>31.8 ± 2.7</td>
<td>27.3 ± 5.7</td>
<td>-0.145 H-C(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.092 H-C(4)</td>
</tr>
</tbody>
</table>

The $1:2$ stoichiometry was corroborated using Job’s method of continuous variations \[49\] (Figure 31), where the complexation-induced shifts of host or guest $^1$H-NMR signals were followed as a function of the host or guest mole fraction, respectively, keeping their total concentration constant.

![Figure 31](image_url)

The finding of strong binding of carboxylates in methanol encouraged us to investigate the binding properties of 87 in an even more competitive solvent like water. Due to the four triethyleneglycol monomethyl ether chains, 87 is soluble in water. In water, the rigid cavity of 87 should provide additional hydrophobic interactions with aromatic guests.

$^1$H-NMR titrations of isophthalates 97 and 98 with receptor 87 in D$_2$O confirmed the formation of the corresponding complexes. Surprisingly, a higher-order association was also found in D$_2$O. The relatively high association constants observed reflect good
electronic and geometric complementarity and favorable interactions between these anionic guests and receptor 87. Moderate selectivity for guest 98 can be seen. The estimated preference $\Delta (\Delta G^\circ)$ for a 1:1 complexation of 98 over 97 ($\approx 4$ $kJ$ $mol^{-1}$) is presumably due to the shape complementarity of the guest inside the cavity and the favourable C-H⋯π interactions between the methoxy group of 98 and the aromatic rings of the receptor cavity.

Table 10. Association constants $K_2$, binding free enthalpies $\Delta G^\circ$ and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between 87 and isophthalates 97 and 98 in D$_2$O at 300 K. Constant guest concentration: $5 \times 10^{-4}$ mol $l^{-1}$.

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_1(\text{HG})$ [l mol$^{-1}$]</th>
<th>$K_2(\text{HG}_2)$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ(\text{HG})$ [kJ mol$^{-1}$]</th>
<th>$-\Delta G^\circ(\text{HG}_2)$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}(\text{guest})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>97</td>
<td>14800</td>
<td>3800</td>
<td>24.0 ± 0.3</td>
<td>20.6 ± 1.0</td>
<td>$+0.076$ H-C(2) $-0.278$ H-C(4)</td>
</tr>
<tr>
<td>98</td>
<td>86000</td>
<td>7700</td>
<td>28.3 ± 0.4</td>
<td>22.3 ± 1.5</td>
<td>$+0.139$ H-C(2) $-0.548$ H-C(4)</td>
</tr>
</tbody>
</table>

Large complexation-induced upfield shifts of the isophthalate $^1$H-NMR signals (0.2-0.5 ppm) were observed for the complexes formed between 87 and 97 or 98 in D$_2$O. When compared with the induced shifts $\Delta \delta$ obtained in the case of the complexation in CD$_3$OD, two interesting aspects need to be highlighted. The largest $\Delta \delta$ in CD$_3$OD was found for the isophthalate H-C(2) signal, whereas in D$_2$O the H-C(4) signal was perturbed most. Furthermore, the isophthalate H-C(2) signal was shifted upfield in CD$_3$OD but downfield in D$_2$O upon complexation with 87.

Figure 32. Two models proposed for 1:2 isophthalate complexation with a cavitand receptor.
These observations indicate different binding geometries of the complexes formed in methanol and water. Due to only weak hydrophobic interactions in methanol, inclusion complexes do not dominate in this solvent. Rather, the proposed molecular complex A (Figure 32) features one or two isophthalates externally coordinated to the four benzamidinium moieties of 87, and the receptor cavity remains filled with methanol molecules. A different geometry is proposed for the complexes formed between 87 and isophthalates in water. Large upfield shifts of the isophthalate H-C(4) signal indicate an inclusion of the guest into the receptor cavity (Figure 32, model B). Water molecules are released upon isophthalate complexation from the cavity gaining more favorable interactions in the bulk solvent. This model also explains the observed downfield shift of the H-C(2) signal in water. In the proposed model, the proton H-C(2) is pointing out of the cavity, possibly lying in the plane of benzamidinium moieties, which would deshield the resonance.

Depending on pH or on ionic strength, association processes are influenced by changes of host or guest concentration. Therefore, buffering of aqueous solutions is an important factor in getting meaningful results from complexation studies. On the other hand, use of a buffer introduces several complications to the system, such as: (i) competitive interactions of the buffer with host or guest (or both), ranging from hydrogen bonds to covalent modifications, and (ii) a decrease of the signal-to-noise ratio for a given analytical method (e.g., overlap of the strong buffer resonances in the 1H-NMR spectrum with the weaker resonances of the binding partners), as the buffer concentration is at least one order of magnitude larger than that of the other components [81]. There is no "inert" buffer with sufficient buffering capacity over a wide pH range. Therefore, selection of a "good" buffer should be reconsidered in each case.

Table 11. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ determined by 1H-NMR titration for the complexes formed between 87 and isophthalates 97 and 98 in D$_2$O containing Na$_2$B$_4$O$_7$ (5·10$^{-3}$ mol l$^{-1}$) at 300 K, pD = 9.2. Constant guest concentration: 5·10$^{-4}$ mol l$^{-1}$ (97), 2·10$^{-4}$ mol l$^{-1}$ (98).

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$ (guest) [ppm, $-$ = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>97</td>
<td>4 000</td>
<td>20.7 ± 0.1</td>
<td>+0.082 H-C(2); -0.268 H-C(4)</td>
</tr>
<tr>
<td>98</td>
<td>96 500</td>
<td>28.6 ± 0.3</td>
<td>+0.148 H-C(2); -0.565 H-C(4)</td>
</tr>
</tbody>
</table>

A borate buffer was initially selected for carboxylate binding in aqueous solutions. The maximum buffering capacity is obtained at pH = 9.2, which keeps all carboxylic
functions in anionic form, but is not basic enough to deprotonate the benzamidinium chloride functions. A borate buffer solution with pH = 9.2 can be easily prepared by dissolving Na₂B₄O₇ or its hydrate in water. The buffer is readily deuterated, which is crucial for its successful application in ¹H-NMR studies.

Higher order association between isophthalate guests and receptor 87 observed in pure D₂O was suppressed in the presence of the borate buffer (Table 11). Complexation can be easily described using the 1 : 1 host - guest model. The association constant $K_a$ for the complex between 98 and 87 in borate buffer remains unchanged within experimental error when compared to the first association constant $K_a(\text{HG})$ of the complex in unbuffered D₂O. However, in the case of 97, the association constant $K_a$ in the borate buffer dropped by a factor of four. These observations support the inclusion model proposed for the isophthalate - cavitand complexes. Isophthalate 98 shows good complementarity for the receptor cavity, and therefore the inclusion complex is not significantly affected by the buffer. In contrast, in the case of 97, the fit to the receptor cavity is not optimal. Thus, the borate anion is competing with the isophthalate guest due to the large concentration difference, which in turn leads to the decrease in association strength. The 1 : 1 stoichiometry of the complexation of 97 with 87 in the borate buffer was confirmed using Job's method (Figure 33).

Figure 33. Job plots for the complex formed between 87 (H) and isophthalate 97 (G) in D₂O containing Na₂B₄O₇ (5·10⁻³ mol l⁻¹) at 300 K, pD = 9.2. Total concentration $c_0(\text{H}) + c_0(\text{G})$ was kept constant at 2·10⁻³ mol l⁻¹. Host 87 signal H-C(2') (left graph) and guest 97 signal H-C(4) (right graph) were followed. $x(\text{H})$ (host molar fraction) is defined as $c_0(\text{H})/(c_0(\text{H}) + c_0(\text{G}))$; $x(\text{G})$ (guest molar fraction) is defined similarly as $c_0(\text{G})/(c_0(\text{H}) + c_0(\text{G}))$.

The quality of the experimental titration data in borate buffer is shown in Figure 34. It is readily apparent that, with increasing receptor concentration, the H-C(2) signal of the
guests moves downfield, whereas the H-C(4) signal moves upfield. The fact that differential up- and downfield shifts are observed is generally an indicator for the formation of a geometrically highly-structured complex rather than unspecific aggregation or association.

![Diagram](image)

Figure 34. Two examples of $^1$H-NMR titrations with isophthalates in D$_2$O containing Na$_2$B$_4$O$_7$ (5·10$^{-3}$ mol l$^{-1}$) at 300 K, pD = 9.2. Left: Part of the $^1$H NMR spectrum of isophthalate 97 (5·10$^{-4}$ mol l$^{-1}$) alone (a), and in the presence of the receptor 87 at 1·10$^{-4}$ mol l$^{-1}$ (b), at 2·1·10$^{-4}$ mol l$^{-1}$ (c), at 5·0·10$^{-4}$ mol l$^{-1}$ (d), and at 1·0·10$^{-3}$ mol l$^{-1}$ (e). Right: Part of the $^1$H NMR spectrum of isophthalate 98 (2·0·10$^{-4}$ mol l$^{-1}$) alone (a) and in the presence of the receptor 87 at 4·9·10$^{-5}$ mol l$^{-1}$ (b), at 8·4·10$^{-5}$ mol l$^{-1}$ (c), at 2·0·10$^{-4}$ mol l$^{-1}$ (d), and at 4·1·10$^{-4}$ mol l$^{-1}$ (e).

Carboxylate binding by the cavitand receptor 87 in aqueous solution was further studied in the presence of Tris/HCl buffer at pD = 8.3 (Table 12). The results are in good agreement with the study using the borate buffer. Cationic Tris/HCl buffer (pD = 8.3) was found less competitive than anionic borate buffer (pD = 9.2), which was reflected in the increased value of the association constant especially in the case of 97. Furthermore, no higher order association was detected in the presence of Tris/HCl buffer.
Table 12. Association constants $K_a$, binding free enthalpies $\Delta G^*$, and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between 87 and isophthalates in D$_2$O containing Tris/HCl (2.5·10$^{-3}$ mol l$^{-1}$) at 300 K, pD = 8.3. Constant guest concentration: 5·10$^{-4}$ mol l$^{-1}$ (97), 3·10$^{-4}$ mol l$^{-1}$ (98).

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^*$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$(guest) [ppm, -- = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>97</td>
<td>12 200</td>
<td>23.5 ± 0.2</td>
<td>+0.094 H-C(2); -0.317 H-C(4)</td>
</tr>
<tr>
<td>98</td>
<td>118 900</td>
<td>29.2 ± 0.4</td>
<td>+0.159 H-C(2); -0.599 H-C(4)</td>
</tr>
</tbody>
</table>

5.5.2. Phosphate Binding

Various nucleotides (99-109; Figure 35) were chosen and their complexes with receptor 87 were studied in aqueous solutions.

(for continuation see next page)
Figure 35. Nucleotides selected as guests for 'H-NMR complexation studies with receptor 87. The phosphates were used as sodium salts except for dinucleotide d(AA) (102) which was used as an ammonium salt. The phosphate residues of ADP (104) and ATP (105) were fully deprotonated using borate (pD = 9.2) or Tris/HCl (pD = 8.3) buffers.

Adenosine 5'-monophosphate AMP (103) was selected as a reference phosphate guest among the nucleotides used in the binding studies. A preliminary study in unbuffered D$_2$O indicated 1 : 1 complex formation between adenosine 5'-phosphate derivatives (101, 103, 104, 105) and cavitand receptor 87 (Table 13). Although ADP (104) and ATP (105) were not fully deprotonated under the experimental conditions, good correlations between total guest charge and the association constants were found. Monoanionic cAMP (101) shows weak binding and small complexation-induced shifts of the receptor signals. Dianionic AMP (103) forms a moderately stable complex with 87. Large complexation-induced shifts of the receptor signal H-C(2') are observed.
In the case of adenosine 5'-diphosphate (104) and 5'-triphosphate (105), binding strength was further enhanced.

Table 13. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between $\text{87}$ and phosphates in $\text{D}_2\text{O}$ at $300\,\text{K}$. Constant concentration of $\text{87}$: $5 \times 10^{-4}\,\text{mol}\,\text{l}^{-1}$.

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}(\text{87})$ a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cAMP (101)</td>
<td>590</td>
<td>15.9 ± 1.3</td>
<td>$-0.014,\text{H-C}(2')$, $-0.012,\text{H-C}(5')$, $-0.007,\text{H-C}(6')$</td>
</tr>
<tr>
<td>AMP (103)</td>
<td>3 500</td>
<td>20.4 ± 0.2</td>
<td>$-0.249,\text{H-C}(2')$, $-0.062,\text{H-C}(5')$, $-0.067,\text{H-C}(6')$</td>
</tr>
<tr>
<td>ADP (104)</td>
<td>15 900</td>
<td>24.1 ± 0.8</td>
<td>$-0.179,\text{H-C}(2')$, $-0.047,\text{H-C}(5')$, $-0.059,\text{H-C}(6')$</td>
</tr>
<tr>
<td>ATP (105)</td>
<td>167 000</td>
<td>30.0 ± 1.5</td>
<td>$-0.183,\text{H-C}(2')$, $-0.044,\text{H-C}(5')$, $-0.073,\text{H-C}(6')$</td>
</tr>
</tbody>
</table>

a) Receptor resonances of the arylamidinium moiety.

Borate buffer ($\text{pD} = 9.2$) was used to fully deprotonate all phosphate guests and control the pH during complexation studies. Due to increasing guest charge, larger differences in the association constants between AMP (103), ADP (104) and ATP (105) were expected in the presence of this buffer. The results of nucleotide complexation in borate buffer, however, did not confirm this expectation; the differences between association constants actually decreased. The seven-fold increase in $K_a$ for a complex between AMP (103) and 87 in borate buffer indicated that more complicated processes are taking place.
A possible reason for such behavior is formation of a cyclic boronate between the diol guest moiety and the borate anion. The products of this reaction presumably interact with the cavitand receptor 87 in a different way than the natural nucleotides.

Table 14. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between 87 and phosphates in D$_2$O containing Na$_2$B$_4$O$_7$ (5 mM) at 300 K, pH = 9.2. Constant guest concentration: 4 $\times$ 10$^{-4}$ mol l$^{-1}$ (103), 3 $\times$ 10$^{-4}$ mol l$^{-1}$ (104), 2 $\times$ 10$^{-4}$ mol l$^{-1}$ (105).

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$ (guest) [ppm, – = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMP (103)</td>
<td>24 500</td>
<td>25.2 ± 0.4</td>
<td>−0.224 H-C(2); −0.056 H-C(1')</td>
</tr>
<tr>
<td>ADP (104)</td>
<td>74 000</td>
<td>28.0 ± 0.5</td>
<td>−0.225 H-C(2); −0.047 H-C(1')</td>
</tr>
<tr>
<td>ATP (105)</td>
<td>82 600</td>
<td>28.2 ± 0.6</td>
<td>−0.188 H-C(2); −0.099 H-C(1')</td>
</tr>
</tbody>
</table>

On the other hand, the expected buffer effect on nucleotide complexation was observed in Tris/HCl buffer. The ratio between the association constants is significantly larger than in unbuffered D$_2$O, increasing from weak binding of cAMP to the very strong binding of ATP which exceeds the limits of the used $^1$H-NMR technique (Table 15).

Table 15. Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between 87 and phosphates in D$_2$O containing Tris/HCl (2.5 $\times$ 10$^{-3}$ mol l$^{-1}$) at 300 K, pH = 8.3. Constant guest concentration: 10$^{-3}$ mol l$^{-1}$ (101), 4 $\times$ 10$^{-4}$ mol l$^{-1}$ (103), 3 $\times$ 10$^{-4}$ mol l$^{-1}$ (104), 2 $\times$ 10$^{-4}$ mol l$^{-1}$ (105).

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta \delta_{\text{max}}$ (guest) [ppm, – = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>cAMP (101)</td>
<td>1 400</td>
<td>18.1 ± 0.2</td>
<td>−0.020 H-C(2); −0.091 H-C(8); −0.066 H-C(1')</td>
</tr>
<tr>
<td>AMP (103)</td>
<td>10 000</td>
<td>23.0 ± 0.3</td>
<td>−0.412 H-C(2); −0.091 H-C(8); −0.106 H-C(1')</td>
</tr>
<tr>
<td>ADP (104)</td>
<td>48 700</td>
<td>26.9 ± 0.4</td>
<td>−0.067 H-C(8); −0.186 H-C(1')</td>
</tr>
<tr>
<td>ATP (105)</td>
<td>660 000</td>
<td>33.4 ± 1.5</td>
<td>−0.100 H-C(8); −0.202 H-C(1')</td>
</tr>
</tbody>
</table>
The 1:1 stoichiometry of AMP complexation with receptor 87 in Tris/HCl buffer was confirmed using Job's method of continuous variation following both host and guest 1H-NMR signals.

Figure 36. Job plots for the complex formed between 87(H) and AMP 103(G) in D2O containing Tris/HCl (5·10^{-3} mol l^{-1}) at 300 K, pD = 8.3. Total concentration c_0(H) + c_0(G) was kept constant at 2·10^{-3} mol l^{-1}. Host (87) signal H-C(2) (left graph) and guest (103) signal H-C(2) (right graph) were followed. \( x(H) \) (host molar fraction) is defined as \( c_o(H)/(c_o(H) + c_o(G)) \); \( x(G) \) (guest molar fraction) is defined similarly as \( c_o(G)/(c_o(H) + c_o(G)) \).

Table 16. Association constants \( K_a \), binding free enthalpies \( \Delta G^\circ \), and maximum observed complexation-induced shifts \( \Delta \delta_{max} \) determined by 1H-NMR titration for the complexes formed between 87 and 103 in D2O containing Tris/HCl at 300 K, pD = 8.3. Constant guest concentration: 4·10^{-4} mol l^{-1} (103).

<table>
<thead>
<tr>
<th>( c(\text{Tris/HCl}) )</th>
<th>( c(\text{NaCl}) )</th>
<th>( K_a )</th>
<th>( -\Delta G^\circ )</th>
<th>( \Delta \delta_{max}(\text{guest}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>[10^{-3} mol l^{-1}]</td>
<td>[10^{-3} mol l^{-1}]</td>
<td>[l mol^{-1}]</td>
<td>[kJ mol^{-1}]</td>
<td>[ppm, ( - = ) upfield]</td>
</tr>
<tr>
<td>2.5</td>
<td>0.00</td>
<td>10 000</td>
<td>23.00 ± 0.3</td>
<td>-0.412 H-C(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.091 H-C(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.106 H-C(1')</td>
</tr>
<tr>
<td>10.0</td>
<td>0.00</td>
<td>9 600</td>
<td>22.9 ± 0.2</td>
<td>-0.358 H-C(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.077 H-C(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.093 H-C(1')</td>
</tr>
<tr>
<td>10.0</td>
<td>150.00</td>
<td>720</td>
<td>16.4 ± 0.3</td>
<td>-0.075 H-C(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.014 H-C(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.020 H-C(1')</td>
</tr>
</tbody>
</table>

The effect of buffer and salt (NaCl) concentration on AMP (103) complexation were the subject of further studies. It was found that a four fold increase of the Tris/HCl concentration did not significantly change the association constant (Table 16). On the other hand, introduction of high salt concentrations decreased the binding constant.
dramatically. This buffer/salt system (10 mM Tris/HCl + 150 mM NaCl), being the most competitive in the presented studies, is widely used as a standard medium in biochemistry for many DNA assays.

Complexation of adenosine 5'-monophosphate (103) with receptor 87 was further compared with that of AMP analogs: dAMP (99) missing the C(2')-OH and ε-AMP (100) with an extended aromatic system. Interestingly, dAMP and ε-AMP show similar binding to 87 as the reference AMP. The three association constants were found in the same range (Table 17). Thus, one can conclude that the interaction between the AMP C(2')-OH and the cavitand receptor does not contribute substantially to the total binding free enthalpy. As suggested by the strong upfield shifts of H-C(10) ($\Delta\delta_{\text{max}} = -0.619$ ppm) and H-C(11) ($\Delta\delta_{\text{max}} = -0.805$ ppm), ε-AMP is bound with its additional fused imidazole ring deeply in the cavity. However, despite these large $\Delta\delta$ values, which indicate a good fit of the extended tricyclic base to the hydrophobic receptor cavity, the association strength is not increased correspondingly. Presumably, due to the extension of the tricyclic base, the ion-pairing distance between the phosphate and benzamidinium moieties in the inclusion complex is unfavorably increased. This is supported by dramatically smaller $\Delta\delta$ value of H-C(2), H-C(8), and H-C(1') in complexed ε-AMP compared to complexed AMP.

Table 17. Association constants $K_a$, binding free enthalpies $\Delta G^o$, and maximum observed complexation-induced shifts $\Delta\delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between 87 and phosphates in D$_2$O containing Tris/HCl (2.5 $10^{-3}$ mol l$^{-1}$) at 300 K, pD = 8.3. Constant guest concentration 4 $10^{-4}$ mol l$^{-1}$.

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^o$ [kJ mol$^{-1}$]</th>
<th>$\Delta\delta_{\text{max}}$ (guest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMP (103)</td>
<td>10 000</td>
<td>23.0 ± 0.3</td>
<td>-0.412 H-C(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.091 H-C(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.106 H-C(1')</td>
</tr>
<tr>
<td>dAMP (99)</td>
<td>9 500</td>
<td>22.9 ± 0.2</td>
<td>-0.357 H-C(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.053 H-C(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.096 H-C(1')</td>
</tr>
<tr>
<td>ε-AMP (100)</td>
<td>9 200</td>
<td>22.8 ± 0.3</td>
<td>-0.201 H-C(2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.011 H-C(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.619 H-C(10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.805 H-C(11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.009 H-C(1')</td>
</tr>
</tbody>
</table>

The dinucleotide d(AA) 102 was used in further complexation studies. The monoanionic guest 102 binds weakly to receptor 87 in Tris/HCl buffer. It was concluded that only one adenine was selectively complexed within the receptor's cavity.
since no $\Delta\delta$ was observed for the $^1$H-NMR signals of the other one. Molecular modeling (Part 5.4) had suggested complexation of the adenine moiety attached to the phosphate with the 5'-OH group.

### Table 18.
Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta\delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between 87 and d(AA) 102 in D$_2$O containing Tris/HCl ($10^{-3}$ mol l$^{-1}$) at 300 K, pD = 8.3. Constant guest concentration.

<table>
<thead>
<tr>
<th>$c$(102) $[10^{-3}$ mol l$^{-1}$]</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta\delta_{\text{max}}$(102) [ppm, $-$ = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>330</td>
<td>14.5 ± 0.2</td>
<td>$-0.027$ H-C(2); $-0.052$ H-C(8)</td>
</tr>
<tr>
<td>0.5</td>
<td>280</td>
<td>14.0 ± 0.2</td>
<td>$-0.025$ H-C(2); $-0.050$ H-C(8)</td>
</tr>
</tbody>
</table>

### Table 19.
Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta\delta_{\text{max}}$ determined by $^1$H-NMR titration for the complexes formed between receptor 87 and phosphates in D$_2$O containing Tris/HCl ($2.5 \times 10^{-3}$ mol l$^{-1}$) at 300 K, pD = 8.3. Constant guest concentration $4 \times 10^{-4}$ mol l$^{-1}$.

<table>
<thead>
<tr>
<th>Guest</th>
<th>$K_a$ [l mol$^{-1}$]</th>
<th>$-\Delta G^\circ$ [kJ mol$^{-1}$]</th>
<th>$\Delta\delta_{\text{max}}$(guest) [ppm, $-$ = upfield]</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMP ($103$)</td>
<td>10 000</td>
<td>23.0 ± 0.3</td>
<td>$-0.412$ H-C(2); $-0.091$ H-C(8); $-0.106$ H-C(1')</td>
</tr>
<tr>
<td>GMP ($106$)</td>
<td>5 200</td>
<td>21.4 ± 0.2</td>
<td>$-0.023$ H-C(8); $-0.035$ H-C(1')</td>
</tr>
<tr>
<td>CMP ($107$)</td>
<td>3 500</td>
<td>20.4 ± 0.2</td>
<td>$-0.031$ H-C(5); $-0.021$ H-C(6); $-0.025$ H-C(1')</td>
</tr>
<tr>
<td>TMP ($109$)</td>
<td>5 900</td>
<td>21.6 ± 0.3</td>
<td>$-0.040$ CH$_3$; $-0.021$ H-C(6); $-0.026$ H-C(1')</td>
</tr>
<tr>
<td>UMP ($108$)</td>
<td>3 800</td>
<td>20.6 ± 0.3</td>
<td>$-0.033$ H-C(5); $-0.014$ H-C(6); $-0.018$ H-C(1')</td>
</tr>
</tbody>
</table>

The selectivity of natural nucleotide complexation was also studied. AMP ($103$) showed the largest $\Delta\delta$ values, presumably because a favorable inclusion complex was formed. The contribution of base inclusion to complex stability in the case of other nucleotides is much lower than in the case of AMP, which is reflected in the decrease of the $\Delta\delta$ values of the base protons, as compared to AMP. The major complexation driving force turns out to be the amidinium - phosphate interaction. Hydrophobic interactions play only a minor role, as seen from the small differences in binding free
energy between the nucleotide complexes with 87. From the data in Table 19, it can be concluded that only AMP seems to be incorporated with the purine base in the receptor cavity. However, the corresponding gain in free enthalpy from additional hydrophobic contacts between receptor and base is small and accounts for only 1-2 kJ mol\(^{-1}\).

5.5.3. Sulfate Binding

![Heparin analogs selected as guests for \(^1\)H-NMR complexations studies.](image)

Heparin analogs were used as sulfate guests in further complexation studies of 87 in D\(_2\)O. Due to their complicated \(^1\)H-NMR spectra, no guest signals could be followed. Therefore, the signals of receptor 87, whose concentration was kept constant, were monitored. Upon sulfate complexation, moderate \(\Delta \delta\)'s in 87 were observed.

![Complexation isotherms for binding of sulfates 110 (left) and 111 (right) with receptor 87 (5 \(\times\) 10\(^{-4}\) mol l\(^{-1}\)) in D\(_2\)O at 300 K (solid curve). The dashed curve represents the calculated fit of a data with the 1 : 1 association model.](image)

Tetraanion 110 (G) binds strongly to 87 (H), but the stoichiometry of this process is complicated. At low guest concentration, a weak \(\text{H}_2\text{G}\) complex is formed, at high guest
concentration a strong $\text{HG}_2$ complex dominates in the system. The complexity of the system introduces large inaccuracy in all fitted parameters (*Table 20*).

*Table 20.* Estimates of association constants $K_a$ and binding free enthalpies $\Delta G^\circ$ obtained from $^1$H-NMR titration for the complexes formed between $\text{87 (H)}$ and $\text{110 (G)}$ in D$_2$O at 300 K. Constant host concentration $5 \times 10^{-4}$ mol l$^{-1}$. Maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$ of host protons: $+0.045$ H-C(2'), $+0.057$ H-C(5')

<table>
<thead>
<tr>
<th>$K_1(\text{HG})$</th>
<th>$K_2(\text{HG}_2)$</th>
<th>$K_3(\text{H}_2\text{G})$</th>
<th>$-\Delta G^\circ(\text{HG})$</th>
<th>$-\Delta G^\circ(\text{HG}_2)$</th>
<th>$-\Delta G^\circ(\text{H}_2\text{G})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>[l mol$^{-1}$]</td>
<td>[l mol$^{-1}$]</td>
<td>[l mol$^{-1}$]</td>
<td>[kJ mol$^{-1}$]</td>
<td>[kJ mol$^{-1}$]</td>
<td>[kJ mol$^{-1}$]</td>
</tr>
<tr>
<td>471 000</td>
<td>158 000</td>
<td>700</td>
<td>32.6 ± 4.2</td>
<td>29.9 ± 9.7</td>
<td>16.5 ± 8.9</td>
</tr>
</tbody>
</table>

In the case of $\text{111}$, the $\text{H}_2\text{G}$ complex formation is more prominent. Association leading to the $\text{HG}_2$ complex was not observed in this case. The calculated association constants are more accurate than in the previous case, largely due to the simplified binding model. It is reasonable that the tetracationic amidinium host $\text{87}$ forms 2 : 1 complexes with the heptaanionic sulfate guest $\text{111}$, especially at high host/guest ratios at the beginning of the titration.

*Table 21.* Association constants $K_a$, binding free enthalpies $\Delta G^\circ$, and maximum observed complexation-induced shifts $\Delta \delta_{\text{max}}$, determined by $^1$H-NMR titration for the complexes formed between host $\text{87 (H)}$ and guest $\text{111 (G)}$ in D$_2$O at 300 K. Constant host concentration $5 \times 10^{-4}$ mol l$^{-1}$.

<table>
<thead>
<tr>
<th>$K_1(\text{HG})$</th>
<th>$K_3(\text{H}_2\text{G})$</th>
<th>$-\Delta G^\circ(\text{HG})$</th>
<th>$-\Delta G^\circ(\text{H}_2\text{G})$</th>
<th>$\Delta \delta_{\text{max}}(\text{87})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>[l mol$^{-1}$]</td>
<td>[l mol$^{-1}$]</td>
<td>[kJ mol$^{-1}$]</td>
<td>[kJ mol$^{-1}$]</td>
<td>[ppm, + = downfield]</td>
</tr>
<tr>
<td>176 000</td>
<td>4 000</td>
<td>30.1 ± 1.3</td>
<td>21.0 ± 4.0</td>
<td>$+0.045$ H-C(2')</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$+0.075$ H-C(5')</td>
</tr>
</tbody>
</table>
6. Kinetic Studies with Chorismate

6.1. Introduction

The uncatalyzed rearrangement of chorismate to prephenate is 100 times faster in water than in methanol, and the rate of the rearrangement in water is about 4200 times faster than that of allylvinylether in dibutylether [82]. This large solvent effect can be explained both by the conformational equilibrium of chorismate (in water, 12% of pseudodiaxial chorismate is present, whereas in methanol it is less than 2% [83]) and by a general solvent effect on the Claisen rearrangement (Table 22).

Table 22. Influence of the solvent on the rate constant of the Claisen rearrangement of allylvinylether [82].

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Rate enhancement relative to dibutylether</th>
</tr>
</thead>
<tbody>
<tr>
<td>dibutylether</td>
<td>1.0</td>
</tr>
<tr>
<td>acetone</td>
<td>1.4</td>
</tr>
<tr>
<td>ethanol</td>
<td>4.0</td>
</tr>
<tr>
<td>methanol - water (2 : 1)</td>
<td>58.0</td>
</tr>
</tbody>
</table>

In the case of chorismate, changing the solvent also leads to the appearance of products other than prephenate [83]. In water, chorismate rearranges smoothly to prephenate and only about 15% goes to \( p \)-hydroxybenzoate 112. Considerably more of this elimination product appears when the solvent is methanol. In aprotic solvents (acetonitrile, dimethylsulfoxide) the predominant product is \( O \)-(1-carboxyvinyl)-3-hydroxybenzoate 113 formed by elimination of water from chorismate (Scheme 2).
6.2. Kinetic Studies in Protic Solvents

Methanol was chosen for initial kinetic studies with chorismate because it is a less competitive solvent compared to water. The studies were done at 50 °C in a thermostated bath due to the slow conversion of chorismate in methanol. $^1$H-NMR spectra of the analyzed samples were repeatedly measured and the concentrations of components determined by integration using 115 as an internal standard ($10^{-3}$ mol l$^{-1}$). The bis(tetrabutylammonium) salt of chorismate was used (see Experimental Section for further details).

The initial rate of the disappearance of chorismate (25) $v_0$ is a sum of the initial rate of the formation of prephenate (26) $v_1$, the initial rate of the formation of $p$-hydroxybenzoate (112) $v_2$, and the initial rate of the formation of O-(1-carboxyvinyl)-3-hydroxybenzoate (113) $v_3$. The rates $v_0$, $v_2$, and $v_3$ were calculated directly from concentrations of corresponding components. As prephenate reacts further to phenylpyruvate (114), $v_1$ was calculated as $v_0 - v_2 - v_3$. The rate of reactions accelerated with amidinium receptors was corrected for the background chorismate decay which is described by equation (29), where $k = k_1 + k_2$.

$$c(\text{chorismate}) = c_0(\text{chorismate})e^{-kt} \quad (29)$$
**Table 23.** Initial rates of the reaction of chorismate (4·10⁻³ mol l⁻¹) to 26 (v₁), 112 (v₂), and 113 (v₃) in the presence of amidinium receptors in CD₃OD at 50 °C.

<table>
<thead>
<tr>
<th>receptor (R)</th>
<th>(R) mol l⁻¹</th>
<th>v₀ mol l⁻¹ h⁻¹</th>
<th>v₁ mol l⁻¹ h⁻¹</th>
<th>v₂ mol l⁻¹ h⁻¹</th>
<th>v₃ mol l⁻¹ h⁻¹</th>
<th>v₁/v₀</th>
<th>v₂/v₀</th>
<th>v₃/v₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 none</td>
<td>0</td>
<td>3.0·10⁻⁵</td>
<td>1.6·10⁻⁵</td>
<td>1.4·10⁻⁵</td>
<td>0</td>
<td>0.54</td>
<td>0.46</td>
<td>0</td>
</tr>
<tr>
<td>2 116</td>
<td>1·10⁻²</td>
<td>1.7·10⁻⁴</td>
<td>3.5·10⁻⁵</td>
<td>6.5·10⁻⁶</td>
<td>1.3·10⁻⁴</td>
<td>0.21</td>
<td>0.04</td>
<td>0.75</td>
</tr>
<tr>
<td>3 29</td>
<td>5·10⁻³</td>
<td>6.4·10⁻⁵</td>
<td>4.2·10⁻⁵</td>
<td>2.2·10⁻⁵</td>
<td>0</td>
<td>0.66</td>
<td>0.34</td>
<td>0</td>
</tr>
<tr>
<td>4 47</td>
<td>5·10⁻³</td>
<td>8.5·10⁻⁵</td>
<td>6.9·10⁻⁵</td>
<td>1.6·10⁻⁵</td>
<td>0</td>
<td>0.82</td>
<td>0.18</td>
<td>0</td>
</tr>
<tr>
<td>5 87</td>
<td>2·10⁻³</td>
<td>1.1·10⁻⁴</td>
<td>4.0·10⁻⁵</td>
<td>7.3·10⁻⁵</td>
<td>0</td>
<td>0.35</td>
<td>0.65</td>
<td>0</td>
</tr>
<tr>
<td>6 87</td>
<td>5·10⁻³</td>
<td>2.7·10⁻⁴</td>
<td>1.0·10⁻⁴</td>
<td>1.7·10⁻⁴</td>
<td>0</td>
<td>0.37</td>
<td>0.63</td>
<td>0</td>
</tr>
</tbody>
</table>

**Figure 39.** Kinetics of chorismate decay in CD₃OD at 50 °C (a) in the presence of 5·10⁻³ mol l⁻¹ 29 (b), 2·10⁻³ mol l⁻¹ 87 (c), and 5·10⁻³ mol l⁻¹ 87 (d). Initial chorismate concentration was 4·10⁻³ mol l⁻¹.

In the uncatalyzed reaction, only 54% of chorismate rearranged to prephenate 26, the rest being converted to 112 (Table 23). In the presence of benzamidinium chloride 116 (1·10⁻² mol l⁻¹) water-elimination product 113 dominates in CD₃OD, in contrast to the other studied receptors, where 113 was never detected. The smaller bis(amidinium) receptor 47 (5·10⁻³ mol l⁻¹) accelerates the rearrangement of chorismate (4·10⁻³ mol l⁻¹) to prephenate more efficiently (4.3 fold) than the larger molecular cleft 29 (5·10⁻³ mol l⁻¹) (2.6 fold), with prephenate formation being strongly preferred (82%) over the elimination leading to p-hydroxybenzoate. The largest acceleration of the
rearrangement of chorismate to prephenate (6.3 fold) as well as of formation of p-hydroxybenzoate (12.1 fold) was found in the presence of the tetrakis(amidinium) receptor 87 (5·10^3 mol l^1). Example of the kinetics of chorismate decay is shown on Figure 39.

Table 24. Initial rates of the reaction of chorismate (4·10^3 mol l^1) to 26 (v_1) and 112 (v_2) in the presence of 6·10^3 mol l^1 87 in CD_3OD at 50 °C corrected for the background chorismate decay.

<table>
<thead>
<tr>
<th>c_0 (mol l^1)</th>
<th>v_0 (mol l^1 h^1)</th>
<th>v_1 (mol l^1 h^1)</th>
<th>v_2 (mol l^1 h^1)</th>
<th>acceleration of</th>
<th>v_0</th>
<th>v_1</th>
<th>v_2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.8·10^{-3}</td>
<td>2.6·10^{-4}</td>
<td>1.1·10^{-4}</td>
<td>1.5·10^{-4}</td>
<td>10.4</td>
<td>7.5</td>
<td>14.1</td>
</tr>
<tr>
<td>2</td>
<td>9.4·10^{-3}</td>
<td>4.1·10^{-4}</td>
<td>2.3·10^{-4}</td>
<td>1.8·10^{-4}</td>
<td>6.5</td>
<td>6.4</td>
<td>6.6</td>
</tr>
<tr>
<td>3</td>
<td>2.2·10^{-2}</td>
<td>3.2·10^{-4}</td>
<td>1.7·10^{-4}</td>
<td>1.5·10^{-4}</td>
<td>2.2</td>
<td>2.0</td>
<td>2.4</td>
</tr>
<tr>
<td>4</td>
<td>4.7·10^{-2}</td>
<td>2.3·10^{-4}</td>
<td>1.2·10^{-4}</td>
<td>1.1·10^{-4}</td>
<td>0.7</td>
<td>0.7</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Figure 40. Initial rate of chorismate decay as a function of its concentration in CD_3OD at 50 °C in the presence 6·10^3 mol l^1 87.

The initial rate of chorismate decay was further studied as a function of its initial concentration in the presence of receptor 87 (6·10^3 mol l^1) in CD_3OD at 50 °C. The rate of reactions was corrected for the background chorismate decay. It was found that the initial rate of the disappearance of chorismate (25) v_0 and the initial rate of the formation of prephenate (26) v_1 reach a maximum at initial chorismate concentration 9.4·10^3 mol l^1 and then decrease with the increasing chorismate concentration.
This effect is less obvious at the initial rate of the formation of \( p \)-hydroxybenzoate (112) \( v_2 \). Thus the acceleration of the rearrangement of chorismate to prephenate is largest (7.5 fold) at low chorismate concentration (Table 24). Although modest, this acceleration to our knowledge represents the largest achieved today by a non-proteinogenic catalyst.

Similar kinetic studies were performed in a mixture CD\(_3\)OD/D\(_2\)O (1:1) at 50 °C. However, the rate of chorismate disappearance was not influenced much in the presence of receptor 87 (5 \( \times \) 10\(^{-3} \) mol l\(^{-1} \)). An acceleration of the rearrangement of chorismate to prephenate by receptor 87 was not observed in this solvent.

![Figure 41. Kinetics of chorismate decay in CD\(_3\)OD/D\(_2\)O (1:1) at 50 °C (a) in the presence of 5 \( \times \) 10\(^{-3} \) mol l\(^{-1} \)87 (b). Initial chorismate concentration was 2 \( \times \) 10\(^{-3} \) mol l\(^{-1} \).](image-url)
7. Towards Cavitand Capsules

7.1. Design

Stimulated by a sabbatical visit of Prof. F. Diederich with Prof. J. Rebek, Jr. at the Skaggs Institute of the Scripps Research Institute in La Jolla, we became interested in exploring the possibility of forming capsules by association of two resorcinarene cavitands, one containing four para-substituted benzamidinium and the other containing four para-substituted benzoate residues.

Computer modeling suggested that cavitands 117 and 118, which could both be prepared starting from tetranitrile 119, might associate via four amidinium - carboxylate hydrogen bonding pairs to yield a capsule with a perfect open space for accommodation of a guest as large as buckminsterfullerene, C\textsubscript{60}. Although the H-bonding amidinium - carboxylate arrays are not perfectly planar, a stable association of the two capsule moieties in a non competitive solvent such as CDCl\textsubscript{3} was expected in view of the possible formation of 8 H-bonds within the 4 ion pairs. Figure 42 shows the modeled capsule.
Towards Cavitand Capsules

Figure 42. Capsule formed by H-bonding association between the two cavitands 117 (bottom) and 118 (top), as suggested by computer modeling (Monte Carlo, MacroModel V. 5.0, AMBER* force field, 1000 steps). Shown are the intermolecular amidinium - carboxylate H-bonding N–O distances in the complex: (a) 2.64 Å, (b) 2.66 Å, (c) 2.70 Å.

7.2. Synthesis

The tetraiodocavitand 70 was coupled with boronic ester 77 under Suzuki-conditions to give tetrannitrile 119. A modified Garigipati method with o-dichlorobenzene as a solvent was used to convert 119 to the tetraamidinium chloride 117. The basic
hydrolysis of the tetranitrile 119 to the tetracarboxylic acid 118 required KOH at 140 °C to complete the reaction.

Experiments aimed at capsule formation are currently underway in collaboration with Prof. J. Rebek, Jr. at the Scripps Research Institute in La Jolla, California.
8. Outlook

The amidinium-containing receptors described in this work allow many structural modifications. They could lead to stronger and more selective complexations and improved catalytic properties of the modified receptors. Thus, tetraamidinium salt 120, the macrocyclic analog of 47 (Chapter 3), is proposed as a new receptor for anionic guests and especially for the Bartlett inhibitor. It contains two 2,7-diphenynaphthalene units linked by p-phenylene spacer. As the long-standing problem of diaryl ether synthesis has been recently solved [84], preparation of the rigid cyclophane core of the tetraamidinium receptor 120 is realistic using published catalytic methods.

![Figure 43](image_url)  
Figure 43. The energy-minimized structure of the complex formed between the receptor 120 and the Bartlett inhibitor 27 (MacroModel V.6.0, AMBER® force field). Short host - guest H-bonds are shown: (a) 2.82 Å, (b) 2.60 Å, (c) 2.62 Å, (d) 2.58 Å, (e) 2.58 Å, (f) 2.60 Å, (g) 2.71 Å, (h) 2.61 Å, (i) 2.84 Å.
Modular synthesis of receptor 87 (Chapter 5) allows easy modification of the aryl moiety attached at the top of the cavitand via a Suzuki cross-coupling reaction. As this aryl group bears the recognition sites of the receptor, systems with specific binding properties could be prepared by choosing the right reaction components. The four aryl groups could be identical (e.g. the possible chorismate receptor 121), or different, prepared, for example, by combinatorial synthesis with a library of components. In receptor 121, the meta-arylamidinium residues of 87 are replaced by para-benzylamidinium residues (Figure 44). Computer modeling predicts interactions in the complex of this cavitand with the inhibitor to be particularly strong, so it would be a worthwhile target for future work.

![Figure 44](image)

**Figure 44.** The energy-minimized structure of the complex formed between the novel tetraamidinium cavitand 121 featuring four para-benzylamidinium residues and Bartlett inhibitor (Monte Carlo, MacroModel V.6.0, AMBER® force field). Short intermolecular H-bonds are shown: (a) 2.54 Å, (b) 2.67 Å, (c) 2.62 Å, (d) 2.64 Å, (e) 2.56 Å, (f) 2.89 Å, (g) 2.64 Å, (h) 2.56 Å.
Capsule formation in aqueous solution is a big challenge in current supramolecular chemistry. Although the proposed cavitands 122 and 123 differ from cavitands 117 and 118 prepared in Chapter 7 only by the solubility-providing TEG groups, the aqueous medium could have a dramatic influence on capsule formation, especially in the presence of a suitable guest capable of filling the large hydrophobic cavity.
9. Experimental Section

9.1. Materials and Methods

Unless otherwise stated, commercially available reagents and solvents were used without further purification. Acetone was distilled from anhydrous K₂CO₃. THF and PhMe were freshly distilled from sodium benzophenone ketyl. N-Bromosuccinimide (NBS) was freshly recrystallized from boiling water and dried in vacuo over CaCl₂. Ni₂B was prepared from Ni(OAc)₂·4H₂O and NaBH₄ following the procedure in [70]. Compounds 31 [58] and 48 [61] were prepared according to literature procedures. Concentration in vacuo was done at water aspirator pressure; drying in vacuo at 0.05 Torr. Resorcinarene derivatives were dried in vacuo at 100-120°C for 12-24 h. Before lithiation of cavitands or conversion of nitriles to amidines, the residual solvents (CH₂Cl₂, water) were removed by distilling PhH and THF from their solutions through a Vigreux column and drying the resulting material in vacuo (100 °C, 0.05 Torr, 12 h).

**Melting points:** Büchi Smp-20, Büchi 510; uncorrected.

**Thin layer chromatography** (TLC): E. Merck plates precoated with silica gel 60 F₂₅₄, detection: UV-light at 254 or 366 nm.

**Column Chromatography** (CC): Silica gel 60 (40-63 μm) from Fluka, Merck, or Macherey-Nagel.

**Reverse Phase Chromatography:** Lichroprep RP-16 (40-63 μm) from Merck.

**UV/Vis spectra** (λₘₐₓ (nm), ε (M⁻¹ cm⁻¹)): Varian Cary 5 UV/Vis/NIR.

**IR Spectra** (cm⁻¹): Perkin Elmer FTIR1600.

**¹H- and ¹³C-NMR spectra** (δ (ppm), J (Hz)): Varian Gemini 200, 300; Bruker AMX 500.

**MS** (m/z, %): El-MS: VG-TRIBRID, 70 eV; FAB-MS: VG-ZAB2-SEQ, 3-NOBA as matrix.

**Elemental analyses:** Mikrolabor für organische Chemie at ETH Zürich.
\textbf{1H-NMR Titrations:} Starting from commercially available dicarboxylic acids, the bis(tetrabutylammonium) dicarboxylate guests 36-39 were prepared. Two equivalents of a 2M methanolic solution of tetrabutylammonium hydroxide were added to the methanolic solution of the acid. The resulting solution was concentrated \textit{in vacuo} and dried (0.01 Torr, 60 °C, 12 h). The disodium isophthalate salts 97 and 98 were prepared by neutralization of methanolic solutions of the corresponding isophthalic acids with two equivalents of an aq. IM NaOH solution. The resulting solution was concentrated \textit{in vacuo} and the residue was recrystallized from water/methanol mixture to give after drying (0.01 Torr, 80 °C, 12 h) pure disodium isophthalates 97 and 98. The nucleotides 99-109 were purchased from Sigma or Fluka and used without further purification. Heparin analogs 110-111 were kindly provided by Dr. H.-P. Wessel (F. Hoffmann-La Roche, Basel). Sodium salts were used in aqueous solution, tetrabutylammonium salts in methanolic solution. All 1H-NMR complexation studies were performed with a 500 MHz \textit{Bruker AMX 500} instrument. Borate buffer (pD = 9.2, 5-10^{-3} \text{ mol l}^{-1}) was prepared by dissolving anhydrous Na$_2$B$_4$O$_7$ (Aldrich) in D$_2$O. Tris/HCl buffer (pD = 8.3, 2.5-10^{-3} \text{ mol l}^{-1}) was prepared from solid Tris/HCl mixture (Fluka, pH = 8.3 when dissolved in H$_2$O at 20 °C) and D$_2$O.

\textit{Titration Method A} (used in studies described in Chapter 2): A set of 10-12 titration samples was prepared for each titration. In all samples concentration of one component was kept constant, whereas the concentration of the other component was varied to cover a 20-80% complexation range. The signals of the component, which was kept at constant concentration, were followed. The experimental data were fitted using the program \textit{Associate 1.6} [50].

\textit{Titration Method B} (used in studies described in Chapter 5): The titrations were performed by adding a solution of both components (11 x 20-300 \textmu l) to the solution of one component in a NMR tube. The signals of the component which was kept at constant concentration were followed. The experimental data were fitted using the program \textit{Specfit 2.11} [57].

\textit{Job Plots:} A set of 11 titration samples was prepared for each titration. In all samples the total concentration of both components was kept constant at 2 \times 10^{-3} \text{ mol l}^{-1}. The host-guest ratio was varied in such a way that the host molar fraction (c$_0$(H)/(c$_0$(H) + c$_0$(G))) increased (0, 0.10, 0.20, 0.30, 0.40, 0.50, 0.60, 0.70, 0.80, 0.90, 1.00) and the guest molar fraction (c$_0$(G)/(c$_0$(H) + c$_0$(G))) correspondingly decreased in the prepared samples. The signals of both components were followed. The plots were generated using the program \textit{profIt 5.0} [51]. All 1H-NMR spectra were measured with a 500 MHz \textit{Bruker AMX 500} instrument.
Isothermal Titration Calorimetry: The calorimetric titrations were performed on a TAM-Microcalorimeter (Thermometric). Using a computer-controlled syringe-pump (Lund), the guest solution ($1.9 \times 10^{-2} \text{ mol l}^{-1}$) was added in portions ($12 \times 15 \mu\text{l}$) to the host solution ($5 \times 10^{-4} \text{ mol l}^{-1}$, 3 ml) or to the pure solvent such as CH$_3$OH or CH$_3$CN (3 ml) (for dilution enthalpy determination) at 298 K. The thermal signal was integrated for each guest addition, corrected for the guest dilution, and evaluated as a function of guest concentration using the program DIGITAM 3.0 [66] to give $K_a$ and $\Delta H^\circ$.

Kinetic Assays: Bis(tetrabutylammonium) chorismate was prepared from the commercially available barium salt using ion-exchange chromatography. Dowex 50X8 ion-exchange resin (H$^+$ form, 20-50 mesh) from Fluka was washed with water, sat. aq. Bu$_4$NOH solution (Fluka) and again with water, until the eluted solution had a neutral pH. The chorismate solution was then added to the ion-exchange column. Using UV-detection, ($\lambda = 274$ nm) fractions containing chorismate salt were collected and the sample was freeze-lyophilized. The resulting bis(tetrabutylammonium) chorismate was dissolved in a solution of 115 ($10^{-3} \text{ mol l}^{-1}$, CD$_3$OD) and the chorismate concentration was determined by integration of its signals in the $^1\text{H}$-NMR spectrum. After addition of solid receptors 29 or 87, the NMR tubes were tightly closed and heated at 50 °C in a thermostated bath. $^1\text{H}$-NMR spectra of the samples were recorded at various time intervals and the concentration of the components determined by integration using 115 as internal standard. Chorismate protons H-C(2), H-C(5), H-C(6), H-C(9a) and H-C(9b) were monitored during the kinetics experiment.

Molecular Modeling: All calculations were carried on Silicon Graphics Indigo 2 or Octane workstations. Initial structures of molecular complexes were generated by a conjugate gradient minimization with the AMBER* force field and the BatchMin program implemented within Macromodel v. 4.0-6.0. In the case of resorcinarene cavitand complexes, the guest was placed outside the cavity in the initial structures. These structures were further refined by a 2000-4000 step Monte Carlo (MC) Multiple Minimum simulation. Molecular modeling of resorcinarene cavitand complexes was performed using the GB/SA solvation model for water. All conformations within 30 kJ mol$^{-1}$ of the computed global minima were stored and the representative lowest energy structure was analyzed for intermolecular close contacts and hydrogen bonds.
Nomenclature of resorcinarene derivatives:

![Diagram of resorcinarene derivatives](image)

Resorcinarene derivatives were named according to [74], e.g. \textbf{124} = penta-cyclo[19.3.1.1^{3,7,19}13.1^{5,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol (all cis stereoisomer); \textbf{125} = 5,6,10,11,15,16,20,21-octahydro-2,24:3,23-dimetheno-1\textit{H},25\textit{H},27\textit{H},29\textit{H}-bis[1,4]dioxonino[6,5-\textit{j};6',5'-\textit{j}']benzo[1,2-e:5,4-e']bis[1,4]benzodioxidonin (all cis stereoisomer). An alternative name for \textbf{125} is: 2,5,9,12,16,19,23,26-octaoxanonacyclo[25.15.1.1^{3,28,42,06,40,08,38,013,36,015,34,020,32,022,30}]tetratetraconta-1(43),6,8(38),13,15(34),20,22(30),27,31,35,39,42-dodecaene.

\section*{9.2. Experimental procedures for Chapter 2}

\textbf{6-Bromo-7-methoxy-2-naphthol (32).}

![Structure of 6-Bromo-7-methoxy-2-naphthol](image)

To a suspension of K$_2$CO$_3$ (1.16 g, 8.4 mmol) in DMF (25 ml) was added \textbf{31} (1.00 g, 4.2 mmol), and the mixture was stirred at r.t. under argon for 15 min. A solution of Mel (0.23 ml, 3.7 mmol) in DMF (2 ml) was added via syringe pump over 5 h. The mixture was stirred at r.t. for 30 min, filtered through a pad of Celite, and the solvent was removed in vacuo. Column chromatography (CC) (SiO$_2$, CH$_2$Cl$_2$) and recrystallization (PhMe/hexane) afforded \textbf{32} (572 mg, 54\%) as a white solid. M.p. 140-141 °C. UV/Vis (MeOH): 234 (ε=60500). IR (KBr): 3476s, 1635s, 1596m, 1573m, 1503s, 1462m, 1424m. $^1$H-NMR (CDCl$_3$, 200 MHz): 7.96 (s, 1 H, H-C(5)); 7.59 (d, J = 8.8, 1 H, H-C(4)); 7.04 (d, J = 2.5, 1 H, H-C(1)); 6.99 (s, 1 H, H-C(8)); 6.97 (dd, J = 8.8, 2.5, 1 H, H-C(3));
5.11 (s, 1 H, OH); 3.98 (s, 3 H, OCH3). \(^{13}\)C-NMR ((CD$_3$)$_2$CO, 75 MHz): 157.33; 154.98; 136.64; 132.82; 129.47; 125.46; 117.74; 110.19; 109.23; 106.60; 56.49. EI-MS: 254.0/252.0 (82/81, \(M^+\)); 211.0/209.0 (77/76); 102.1 (100). Anal. calc. for C$_{11}$H$_9$BrO$_2$ (253.09): C 52.20, H 3.58, Br 31.57; found: C 52.38, H 3.54, Br 31.28.

\((±)-6,6′\)-Dibromo-7,7′-dimethoxy-1,1′-binaphthalene-2,2′-diol (33).

To a solution of 32 (2.70 g, 10.7 mmol) in degassed MeOH (338 ml) was added CuCl$_2$ (2.95 g, 21.9 mmol), and the solution was stirred under argon at r.t. for 15 min. A solution of t-BuNH$_2$ (4.9 ml, 46.3 mmol) in degassed MeOH (34 ml) was added via syringe pump at r.t. over 30 min, and the mixture was refluxed for 4 h. The dark solution was cooled to 0 °C, and aq. HCl (6M, 60 ml) was added. The mixture was extracted with CH$_2$Cl$_2$ (5 × 200 ml), the combined organic layers were washed with water (2 × 300 ml), dried (MgSO$_4$), and concentrated in vacuo. CC (SiO$_2$, CH$_2$Cl$_2$) and recrystallization (PhMe/hexane, 1:1) yielded 33 (1.86 g, 69%) as white crystals. M.p. 228-229 °C. IR (KBr): 3450s, 2969w, 1611s, 1595m, 1497s, 1464s. UV/Vis (MeOH): 236 (91500). \(^1\)H-NMR (CDCl$_3$, 200 MHz): 8.1 (s, 2 H, H-C(5)); 7.83 (d, \(J = 9.0, 2\) H, H-C(4)); 7.26 (d, \(J = 9.0, 2\) H, H-C(3)); 6.44 (s, 2 H, H-C(8)); 5.05 (s, 2 H, OH); 3.59 (s, 6 H, OCH$_3$). \(^{13}\)C-NMR ((CD$_3$)$_2$CO, 50 MHz): 155.53; 155.12; 135.79; 133.31; 129.82; 126.10; 118.11; 114.30; 110.23; 105.09; 56.08. EI-MS: 504.1 (6, \(M^+\)); 100.0 (12); 28.0 (100). Anal. calc. for C$_{22}$H$_{16}$Br$_2$O$_4$ (504.17): C 52.41, H 3.20, Br 31.70; found: C 52.39, H 3.23, Br 31.42.

\((±)-6,6′\)-Dibromo-2,2′,7,7′-tetramethoxy-1,1′-binaphthalene (34).
Experimental Part

To a suspension of 33 (400 mg, 0.79 mmol) and K₂CO₃ (440 mg, 3.18 mmol) in dry acetone (5 ml) under argon was added Me₂S₀₄ (225 μl, 2.38 mmol). The mixture was refluxed for 4.5 h, cooled, and the solvent was removed in vacuo. The residue was suspended in water (7 ml), stirred at r.t. for 30 min, and extracted with CH₂Cl₂ (4 × 25 ml). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. CC (SiO₂, CH₂Cl₂) and recrystallization from PhMe/hexane yielded 34 (432 mg, 99%) as white crystals. M.p. 199-200 °C. IR (KBr): 2935w, 2835w, 1615s, 1586m, 1495s, 1461s, 1424m, 1406s. UV/Vis (MeOH): 238 (92000). ¹H-NMR (CDCl₃, 200 MHz): 8.06 (s, 2 H, H-C(5)); 7.82 (d, J = 9.0, 2 H, H-C(4)); 7.31 (d, J = 9.0, 2 H, H-C(3)); 6.41 (s, 2 H, H-C(8)); 3.76 (s, 6 H, CH₃OC(2)); 3.53 (s, 6 H, CH₃OC(7)). ¹³C-NMR (CDCl₃, 75 MHz): 155.71; 154.17; 154.17; 134.14; 132.36; 128.54; 125.40; 118.06; 112.22; 110.91; 104.08; 56.55; 55.79. El-MS: 531.9 (100, M⁺). Anal. calc. for C₂₄H₂₀Br₂O₄ (532.22): C 54.16, H 3.78, Br 30.02; found: C 54.03, H 3.95, Br 29.76.

(±)-2,2′-(2,2′,7,7′-Tetramethoxy-1,1′-binaphthalene-6,6′-diyl)bis(benzonitrile) (35).

Synthesis of the bisboronic acid. To dry THF (45 ml) at −78 °C under argon was added n-BuLi (1.6M in hexane, 10 ml, 15.95 mmol). A solution of 34 (1.70 g, 3.19 mmol) in dry THF (10 ml) was added dropwise, and the mixture was stirred at −78 °C for 50 min under argon. BH₃ (1M in THF, 48 ml, 47.85 mmol) was then added rapidly. The mixture was stirred at −78 °C for 2 h, warmed to r.t., stirred overnight, refluxed for 2 h, and concentrated in vacuo. Water (200 ml) was added, and the suspension was stirred for 3 h at r.t. After addition of aq. HCl (2M, 10 ml), the mixture was extracted with Et₂O (3 × 130 ml). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. The resulting crude arylboronic acid was used without further purification.

Suzuki coupling. A mixture of the crude arylboronic acid (3.19 mmol), 2-bromo-benzenitrile (1.16 g, 6.39 mmol), [PdCl₂(PPh₃)₂] (225 mg, 0.32 mmol), Na₂CO₃
(677 mg, 6.39 mmol), PhH (68 ml), EtOH (20 ml), and water (32 ml) was heated at reflux under argon for 21 h, cooled, and extracted with EtOAc (2 × 150 ml). The combined organic layers were washed with sat. aq. NaHCO₃ (2 × 100 ml) and sat. aq. NaCl soln. (2 × 100 ml), dried (MgSO₄), and concentrated in vacuo. The residue was purified by CC (SiO₂, hexane/AcOEt 4:1 → 3:2). Additional CC (SiO₂, CH₂Cl₂) and recrystallization (CH₂Cl₂) yielded 35 (982 mg, 53%) as a white solid. M.p. 245-246 °C. IR (KBr): 2934w, 2226m, 1626s, 1492s, 1461s, 1409m. UV/Vis (MeOH): 229 (158000). 

**1H-NMR (CDCl₃, 500 MHz):** 7.92 (d, J = 9, 2 H, H-C(4)); 7.75 (s, 2 H, H-C(5)); 7.72 (dd, J = 7.7, 1.3, 0.6, 2 H, H-C(6')); 7.62 (dt, J = 7.7, 1.3, 2 H, H-C(4')); 7.53 (ddd, J = 7.7, 1.3, 0.6, 2 H, H-C(3')); 7.41 (dt, J = 7.7, 1.3, 2 H, H-C(5')); 7.34 (d, J = 9.0, 2 H, H-C(3)); 6.61 (s, 2 H, H-C(8)); 3.82 (s, 3 H, CH₃OC(2)); 3.50 (s, 3 H, CH₃OC(7)). 

**13C-NMR (CDCl₃, 125 MHz):** 156.10; 155.31; 142.52; 135.30; 132.81; 132.22; 131.18; 130.79; 129.71; 127.31; 126.72; 124.33; 118.65; 118.12; 113.55; 111.86; 103.80; 56.70; 55.33. El-MS: 576.1 (100, M⁺). Anal. calc. for C₃₈H₂₈N₂O₄·0.5 H₂O (577.66 + 9.01): C 77.93, H 4.99, N 4.78; found: C 77.93, H 4.92, N 4.62.

**Preparation of MeAl(Cl)NH₂.** Me₃Al (2M in PhMe, 1.2 ml, 2.4 mmol) was slowly added to a stirred suspension of NH₄Cl (134 mg, 2.5 mmol) in dry PhMe (3 ml) at 0 °C under argon. The mixture was warmed to r.t. and stirred for 2.5 h.

**Amidinium salt synthesis.** To the solution of MeAl(Cl)NH₂ (2.4 mmol) in PhMe was added 35 (200 mg, 347 μmol). The solution was stirred at 90 °C under argon for 2 d, additional MeAl(Cl)NH₂ (2.4 mmol) in PhMe was added, the mixture was stirred at 90 °C for 2 d, cooled, slowly poured into a suspension of silica gel (20 g) in chloroform (50 ml), and stirred for 5 min. The silica gel was filtered off and washed with a MeOH/water mixture (1:1). The filtrate was concentrated in vacuo, the residue was...
Experimental Part

stirred with aq. NaOH soln. (5%, 100 ml) and extracted with CH₂Cl₂ (3 x 100 ml). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. The residue was dissolved in ethanolic HCl (10M, 10 ml), concentrated in vacuo, and the crude product was purified using MPLC (reverse phase RP16, MeOH/water 1:1) to give 29 (140 mg, 59%). M.p. 273-275 °C (dec.). IR (KBr): 3383s, 3100s, 1672s, 1626s, 1598w, 1490s, 1463m, 1409w. UV/Vis (MeOH): 232 (77200). ¹H-NMR (CD₃OD, 500 MHz): 7.97 (d, J = 8.8, 2 H, H-C(4)); 7.88 (s, 2 H, H-C(5)); 7.66-7.69 (m, 2 H, H-C(4')); 7.60 (d, J = 7.4, 2 H, H-C(6')); 7.49-7.54 (m, 4 H, H-C(3',5')); 7.39 (d, J = 8.8, 2 H, H-C(3)); 6.44 (s, 2 H, H-C(8)); 3.73 (s, 6 H, CH₃OC(2)); 3.34 (s, 6 H, CH₃OC(7)). ¹³C-NMR (CD₃OD, 50 MHz): 170.59; 157.98; 156.68; 139.22; 136.94; 134.24; 133.73; 132.94; 131.77; 131.38; 129.70; 129.42; 128.46; 126.56; 119.86; 113.48; 103.96; 57.30; 55.27. FAB-MS: 647.3 (41, M- Ck); 611.3 (100, M- HCl- Ck); 307.1 (25, M - 2Cl). FAB-HRMS: 611.2654 (M- HCl - Ck, C₃₈H₃₅N₄O₄+ calc. 611.2658).

9.3. Experimental procedures for Chapter 3

2-Iodo-3,4,5-trimethoxybenzonitrile (43).

A solution of 3,4,5-trimethoxybenzonitrile 42 (10.0 g, 51.76 mmol), iodine (14.45 g, 56.93 mmol), and HIO₄·H₂O (6.61 g, 29.00 mmol) in acetic acid (100 ml) was stirred at 33 °C for 24 h. The mixture was poured onto ice (500 g), the solid was filtered off and washed successively with aq. NaHSO₃ soln. (5%, 300 ml), aq. Na₂CO₃ soln. (10%, 100 ml), and water (2 l). The solid was dissolved in CH₂Cl₂, washed with aq. NaH.SO₃ soln. (5%, 100 ml), the organic layer was dried over MgSO₄ and concentrated in vacuo. The crude product was recrystallized from EtOH (100 ml) to give 43 (12.80 g, 78%) as white crystals. M.p. 119-120 °C. IR (KBr): 3079m, 2940m, 2841m, 2227s, 1577s, 1556s, 1478s, 1382s, 1335s. ¹H-NMR (CDCl₃, 500 MHz): 6.97 (s, 1 H, H-C(6)); 3.93 (s, 3 H, CH₃O); 3.878 (s, 3 H, CH₃O); 3.877 (s, 3 H, CH₃O). ¹³C-NMR (CDCl₃, 125 MHz): 154.42; 154.27; 146.45; 119.34; 114.95; 113.57; 87.85; 61.22; 61.02; 56.51.
EI-MS: 319.0 (100, M+), 304.0 (32), 260.9 (18). Anal. calc. for C_{10}H_{10}NO_{3}I (319.10): C 37.64, H 3.16, N 4.39, I 39.77; found: C 37.67, H 3.04, N 4.40, I 39.81.

3,4,5-Trimethoxy-2-[(trimethylsilyl)ethynyl]benzonitrile (44).

A mixture of 43 (3.0 g, 9.40 mmol), (trimethylsilyl)acetylene (6.6 ml, 47.0 mmol), [PdCl_{2}(PPh_{3})_{2}] (330 mg, 0.47 mmol), and Cul (150 mg, 0.76 mmol) in degassed diisopropylamine (30 ml) and THF (30 ml) was stirred under argon at 30 °C for 96 h, filtered, and concentrated in vacuo. The residue was dissolved in CH_{2}Cl_{2}, filtered through a plug of silicagel, and concentrated in vacuo. Recrystallization (diethylether/hexane 2:3, −20 °C) afforded 44 (1.98 g, 73%) as white needles. M.p. 86-87 °C. IR (KBr): 2948m, 2230m, 2154s, 1585s, 1554m, 1489s, 1465s, 1403s, 1338s. XH-NMR (CDCl_{3}, 200 MHz): 6.91 (s, 1 H, H-C(6)); 3.99 (s, 3 H, CH_{3}O); 3.93 (s, 3 H, CH_{3}O), 0.30 (s, 9 H, CH_{3}Si). 13C-NMR (CDCl_{3}, 125 MHz): 155.16; 153.97; 146.29; 117.15; 115.32; 111.12; 104.79; 96.83; 61.31; 61.25; 56.39; −0.30. EI-MS: 289.1 (46, M+), 274.1 (100, M+-Me). EI-HRMS: 289.1146 (M+, C_{15}H_{19}NO_{3}Si \text{calc.} 289.1134).

2,2'--(Butadiynediyl)bis(3,4,5-trimethoxybenzonitrile) (45).

\begin{center}
\includegraphics[width=0.2\textwidth]{image}
\end{center}

Deprotection. Sat. aq. Na_{2}CO_{3} (10 ml) was added to a solution of 44 (1.98 g, 6.84 mmol) in MeOH (400 ml). The mixture was stirred under argon for 2 h and concentrated in vacuo. The residue was extracted with diethylether (3 × 150 ml), the combined organic layers were dried (MgSO_{4}) and concentrated in vacuo. The crude product, silyl-deprotected 44, was used without further purification.

Oxidative coupling. To a stirred mixture of CuCl (203 mg, 2.05 mmol), TMEDA (0.4 ml, 2.74 mmol), and dimethoxyethane (20 ml) at 34 °C was added a solution of silyl-deprotected 44 (6.84 mmol) in dimethoxyethane (50 ml) over a period 10 min.
**Experimental Part**

The mixture was stirred at this temperature in an open flask for 1h. The solvents were removed *in vacuo*, and the residue was dissolved in CH$_2$Cl$_2$, filtered through a plug of Al$_2$O$_3$ (neutral, activity IV), concentrated *in vacuo*, and chromatographed (SiO$_2$, CH$_2$Cl$_2$) to afford 45 (1.28 g, 87%) as a pale yellow solid. M.p. 215-216 °C. IR (KBr): 2945m, 2227s, 1579s, 1489s, 1400s, 1329s. $^1$H-NMR (CDCl$_3$, 300 MHz): 6.90 (s, 2 H, H-C(6)); 3.99 (s, 6 H, CH$_3$O); 3.90 (s, 6 H, CH$_3$O); 3.89 (s, 6 H, CH$_3$O). $^{13}$C-NMR (CDCl$_3$, 75 MHz): 156.45; 154.98; 146.23; 116.91; 113.48; 111.65; 111.49; 81.64; 76.14; 61.78; 61.24; 56.44. EI-MS: 432.2 (100, $M^+$), 417.2 (16). Anal. calc. for C$_{24}$H$_{20}$N$_2$O$_6$ (432.44): C 66.66, H 4.66, N 6.48; found: C 66.64, H 4.79, N 6.41.

**2,2’-(3,6-Dimethoxynaphthalene-2,7-diyl)bis(benzonitrile) (49).**

*Synthesis of arylboronic acid.* To dry THF (100 ml) at -78 °C under argon was added n-BuLi (1.6M in hexane, 31.3 ml, 50.00 mmol). A solution of 48 (3.46 g, 10.00 mmol) in dry THF (30 ml) was added dropwise, and the mixture was stirred at -78 °C for 1 h. BH$_3$ (1M in THF, 100 ml, 100.0 mmol) was added rapidly, and the mixture was stirred at -78 °C for 2 h, then at r.t. for 24 h. The solvents were removed *in vacuo*, the residue was stirred with water (200 ml) for 1 h and extracted with Et$_2$O (3 x 330 ml). The combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo*. The crude arylboronic acid was used without further purification.

*Suzuki coupling.* A mixture of the crude arylboronic acid (5 mmol), 2-bromobenzonitrile (1.82 g, 10.00 mmol), [PdCl$_2$(PPh$_3$)$_2$] (350 mg, 0.50 mmol), Na$_2$CO$_3$ (1.06 g, 10.00 mmol), PhH (50 ml), EtOH (12 ml), and water (22 ml) was heated at reflux under argon for 24 h, cooled, and extracted with ethyl acetate (3 x 150 ml). The combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo*. CC (SiO$_2$, PhMe/AcOEt 95:5 → 90:10) and recrystallization (THF/Et$_2$O/hexane) afforded 49 (86 mg, 4.4%) as white crystals. M.p. 260-261 °C. IR (KBr): 2224m, 1629s, 1595w, 1466s, 1407m. $^1$H-NMR (CDCl$_3$, 500 MHz): 7.76 (ddd, $J = 7.7$, 1.3, 0.5, 2 H, H-C(6)); 7.69 (s, 2 H, H-C(1)); 7.65 (dt, $J = 7.7$, 1.3, 2 H, H-C(4)); 7.54 (ddd, $J = 7.7$, 1.3, 0.5, 2 H, H-C(3’)); 7.45 (dt, $J = 7.7$, 1.3, 2 H, H-C(5’)); 7.25 (s, 2 H, H-C(4’)); 3.96 (s, 6 H, CH$_3$O). $^{13}$C-NMR (CDCl$_3$, 125 MHz): 158.81; 142.26; 136.58; 132.69; 132.34; 131.03; 130.58; 127.45; 127.25; 123.45; 118.51; 113.69; 105.28; 55.56. FAB-MS:
390.3 (100, $M^+$). Anal. calc. for $C_{26}H_{18}N_2O_2.3$ Et$_2$O (390.45 + 22.24): C 79.17, H 5.13, N 6.79; found: C 79.18, H 5.07, N 6.88.

$2,2'$-(3,6-Dimethoxynaphthalene-2,7-diyl)bis(benzamidinium) dichloride (47).

$\text{NH}_2$ $\text{H}_2\text{N}$

\begin{center}
\begin{tikzpicture}
\node at (0,0) (A) {$\text{NH}_2$};
\node at (1,1) (B) {$\text{H}_2\text{N}$};
\node at (1,-1) (C) {$\text{H}_2\text{N}$};
\node at (2,0) (D) {$2 \text{Cl}^-$};
\node at (-1,1) (E) {$\text{O}$};
\node at (-1,-1) (F) {$\text{O}$};
\node at (0,2) (G) {$4'$};
\node at (0,1) (H) {$3'$};
\node at (0,0) (I) {$5'$};
\node at (0,-1) (J) {$6'$};
\node at (2,0) (K) {$\text{H}_2\text{N}$};
\node at (1,1) (L) {$\text{NH}_2$};
\node at (2,2) (M) {$\text{H}_2\text{N}$};
\node at (2,1) (N) {$\text{H}_2\text{N}$};
\node at (0,1) (O) {$\text{H}_2\text{N}$};
\node at (1,0) (P) {$\text{H}_2\text{N}$};
\node at (2,0) (Q) {$\text{H}_2\text{N}$};
\node at (2,-1) (R) {$\text{H}_2\text{N}$};
\node at (1,-1) (S) {$\text{H}_2\text{N}$};
\node at (0,-1) (T) {$\text{H}_2\text{N}$};
\node at (0,-2) (U) {$\text{H}_2\text{N}$};
\node at (1,-2) (V) {$\text{H}_2\text{N}$};
\node at (2,-2) (W) {$\text{H}_2\text{N}$};
\node at (2,-1) (X) {$\text{H}_2\text{N}$};
\node at (1,-2) (Y) {$\text{H}_2\text{N}$};
\node at (0,-2) (Z) {$\text{H}_2\text{N}$};
\end{tikzpicture}
\end{center}

**Preparation of MeAlNH$_2$Cl.** To a stirred suspension of NH$_4$Cl (600 mg, 11.2 mmol) in dry PhMe (3 ml) at 0 °C under argon was slowly added Me$_3$Al (2M in PhMe, 5 ml, 10.0 mmol). The mixture was stirred at r.t. for 1 h.

**Amidinium salt synthesis.** To the solution of MeAlNH$_2$Cl (3.7 mmol) in PhMe was added 49 (100 mg, 0.26 mmol), and the solution was stirred under argon at 80 °C for 1 d. Additional MeAlNH$_2$Cl (3.7 mmol) was added, and the mixture was stirred at the same temperature for 3 d, then slowly poured into a suspension of silica gel (20 g) in chloroform (50 ml), and stirred for 5 min. The silica gel was filtered off and washed with a MeOH/water mixture (1:1). The filtrate was concentrated in vacuo, the residue was washed with aq. NaOH (5%, 50 ml) and extracted with CH$_2$Cl$_2$ (4 × 100 ml). The combined organic layers were concentrated in vacuo, the residue was dissolved in ethanolic HCl (10M, 10 ml), concentrated in vacuo, and recrystallized (MeOH/Et$_2$O) to yield 47 (125 mg, 98%). M.p. 271-275 °C (dec.). IR (KBr): 3125br, 1670s, 1628s, 1480m, 1410m, 1226m, 1169m, 1031m, 780m. $^1$H-NMR (CDCl$_3$, 500 MHz): 7.93 (s, 2 H, H-C(1)); 7.79 (dt, $J = 7.5, 1.0$, 2 H, H-C(4')); 7.74 (dd, $J = 7.5, 1.0$, 2 H, H-C(6')); 7.64 (dt, $J = 7.5, 1.0$, 2 H, H-C(5')); 7.62 (d, $J = 7.5$, 2 H, H-C(3')); 7.41 (s, 2 H, H-C(4)); 3.95 (s, 6 H, CH$_3$O). $^{13}$C-NMR (CDCl$_3$, 125 MHz): 170.07; 156.87; 138.78; 137.94; 133.74; 123.24; 132.09; 131.42; 129.28; 129.06; 128.53; 125.30; 105.89; 55.67. FAB-MS: 425.1 (100, $M - $HCl - Cl$^-$. FAB-HRMS: 425.1977 ($M - $HCl - Cl$^-$, $C_{26}H_{25}N_4O_2^+$ calc. 425.1978).
2-Bromo-3-nitrotoluene (52).

\[
\begin{array}{c}
\text{H} \text{NO}_2 \\
\text{Br}
\end{array}
\]

2-Methyl-6-nitroaniline 51 (17.42 g, 114.49 mmol) was dissolved under heating in aq. HBr (30%, 130 ml), and the solution was cooled to -5 °C. A solution of NaNO₂ (7.90 g, 114.50 mmol) in water (45 ml) was slowly added at 0 °C. The resulting mixture was filtered and added at 0 °C to a cooled and stirred mixture of CuBr (24.70, 172.19 mmol), KBr (10.00, 84.03 mmol), and HBr (48%, 69 ml). The reaction mixture was warmed to r.t., refluxed for 2 h, cooled, and extracted with CH₂Cl₂ (3 x 100 ml). The combined organic layers were washed with aq. Na₂CO₃ (5%, 100 ml), dried (MgSO₄), and concentrated in vacuo. The residue was purified by CC (SiO₂, PhMe) to give 52 (23.70 g, 96%, lit. 97%). M.p. 39-40 °C (Lit. [85]: M.p. 39-40 °C). ¹H-NMR (CDCl₃, 500 MHz): 7.51-7.53 (m, 1 H, H-C(4)); 7.42-7.44 (m, 1 H, H-C(6)); 7.33 (t, J = 7.8, 1 H, H-C(5)); 2.52 (s, 3 H, CH₃).

2-Bromo-3-methylaniline (53).

\[
\begin{array}{c}
\text{NH}_2 \\
\text{Br}
\end{array}
\]

A mixture of 52 (6 g, 27.77 mmol), Ni₂B (24 g) [70], THF (60 ml), and aq. HCl (5M, 30 ml) was stirred at r.t. for 2 h. Aq. NH₃ (25%, 100 ml) was added, and the mixture was extracted with ether (3 x 150 ml). The combined organic layers were washed with sat. aq. NaCl soln. (100 ml), dried (Na₂SO₄), and concentrated in vacuo yielding crude 53 (6.18 g) as a brown oil which was used without further purification. ¹H-NMR (CDCl₃, 200 MHz): 7.03 (t, J = 7.7, 1 H, H-C(5)); 6.64-6.70 (m, 2 H, H-C(4,6)); 4.18 (bs, 2 H, NH₂); 2.40 (s, 3 H, CH₃). The ¹H-NMR spectrum matched the published data [85].
Chapter 9

2-Bromo-3-methylbenzonitrile (54).

Crude 53 (6.18 g, 27.77 mmol) was dissolved in aq. H2SO4 (50%, 10 ml), and the mixture was cooled to 0 °C. A solution of NaN02 (2.01 g, 29.16 mmol) in water (11.7 ml) was slowly added at 0 °C. The resulting viscous solution was added at 0 °C to a cooled and stirred mixture of CuCN (12.44 g, 138.85 mmol) and NaCN (10.00 g, 374.90 mmol) in water (83 ml). The reaction mixture was warmed to r.t. (formation of HCN!), refluxed for 20 min, cooled, and extracted with CH2Cl2 (4 x 100 ml). The combined organic layers were dried (MgSO4) and concentrated in vacuo. The residue was purified by CC (SiO2, CH2Cl2) to give 54 (4.50 g, 83%). M.p. 69-70 °C (hexane). IR (KBr): 2230m, 1571w, 1453m, 1385m, 1032m, 780s, 702m. 1H-NMR (CDCl3, 500 MHz): 7.43-7.48 (m, 2 H, H-C(4,6)); 7.30 (t, J = 7.7, 1 H, H-C(5)); 2.44 (s, 3 H, CH3). 13C-NMR (CDCl3, 125 MHz): 139.98; 134.72; 131.83; 127.46; 127.09; 117.56; 116.21; 23.27. EI-MS: 197.0/195.0 (14/15, M+); 116.1 (100); 115.1 (37); 89.1 (26). Anal. calc for C8H6NBr (196.05): C 49.01, H3.07, N7.14, Br 40.76; found: C 48.95, H3.05, N7.12, Br40.94.

2,7-Bis(trimethylstannyl)-3,6-Dimethoxynaphthalene (55).

To a solution of 48 (3.47 g, 10.0 mmol) in dry THF (100 ml) at -100 °C under argon was added n-BuLi (1.6M in hexane, 31.3 ml, 50.0 mmol), and the mixture was stirred at this temperature for 80 min. Me3SnCl (10.00 g, 50.0 mmol) was added at -100 °C, and the mixture was stirred at r.t. for 2.5 h. Sat. aq. NaHCO3 soln. (100 ml) was added, the organic layer was separated, and the aqueous layer was extracted with ether (2 x 100 ml). The combined organic layers were washed with water (3 x 100 ml), sat. aq. NaCl soln. (100 ml), dried (MgSO4), and concentrated in vacuo. CC (SiO2 washed with hexane/NEt3 95.5: hexane/NEt3 99.5:0.5 → hexane/Et2O/NEt3 94.5:5:0.5) yielded 55 (3.39 g, 66%) as a white solid. M.p. 164-165 °C (hexane). IR (KBr): 2933m, 1724v, 1611s, 1452m, 1420m, 1392s, 1220s, 1204m, 1168s, 1048m, 770s, 532s, 512m. 1H-NMR (CDCl3, 500 MHz): 7.76 (s, 2 H, H-C(1)); 7.00 (s, 2 H, H-C(4)); 3.91 (s, 6 H,
Experimental Part

OCH₃): 0.35 (s, 18 H, Sn(CH₃)₃). ¹³C-NMR (CDCl₃, 125 MHz): 162.28; 137.37; 136.31; 129.71; 125.51; 102.80; 55.22; -9.01. EI-MS: 514.0 (10, M⁺); 499.0 (100); 468.9 (26); 438.9 (19); 406.8 (15); 242.1 (38). Anal. calc for C₁₈H₂₈O₂Sn₂ (513.84): C 42.08, H 5.49; found: C 42.06, H 5.50.

2,2'-(3,6-Dimethoxynaphthalene-2,7-diyl)-3,3'-dimethylbis(benzonitrile) (50).

![Diagram]

A mixture of 54 (392 mg, 2.00 mmol), 55 (514 mg, 1.00 mmol), LiCl (254 mg, 6.00 mmol), [Pd(PPh₃)₄] (58 mg, 0.05 mmol), and BHT (11 mg, 0.05 mmol) in dry DMF (10 ml) was stirred under argon at 80 °C for 42 h. Water (100 ml) was added, and the suspension was extracted with ether (3 x 50 ml). The combined organic layers were washed with sat. aq. NaCl soln., dried (MgSO₄), and concentrated in vacuo. CC (SiO₂, CH₂Cl₂) gave two isomers of 50: 1) a C₂-symmetrical isomer (43 mg, 10%) and 2) a C₅-symmetrical isomer (65 mg, 16%). C₂-50: Rₜ (SiO₂, CH₂Cl₂): 0.11. ¹H-NMR (CDCl₃, 500 MHz): 7.59-7.61 (m, 2 H, H-C(6')); 7.55 (s, 2 H, H-C(1)); 7.50-7.52 (m, 2 H, H-C(4')); 7.36 (t, J = 7.7, 2 H, H-C(5')); 7.27 (s, 2 H, H-C(4)); 3.91 (s, 6 H, OCH₃); 2.19 (s, 6 H, CH₃). ¹³C-NMR (CDCl₃, 125 MHz): 155.91; 141.63; 138.55; 136.43; 134.00; 130.27; 127.63; 126.09; 123.50; 118.47; 114.27; 105.34; 55.70; 20.31. EI-MS: 418.1 (100, M⁺). C₅-50: M.p. 218-219°C. Rₜ (SiO₂, CH₂Cl₂): 0.47. IR (KBr): 2959w, 2224m, 1631s, 1467s, 1406s, 1227s, 1178s, 1035s, 788s. XH-NMR (CDCl₃, 500 MHz): 7.59-7.60 (m, 2 H, H-C(6')); 7.54 (s, 2 H, H-C(1)); 7.50-7.52 (m, 2 H, H-C(4')); 7.36 (t, J = 7.7, 2 H, H-C(5')); 7.25 (s, 2 H, H-C(4)); 3.90 (s, 6 H, OCH₃); 2.18 (s, 6 H, CH₃). ¹³C-NMR (CDCl₃, 125 MHz): 155.82; 141.90; 139.04; 136.52; 134.07; 130.15; 127.65; 126.13; 123.63; 118.71; 113.90; 105.22; 55.64; 20.25. EI-MS: 418.1 (100, M⁺). FAB-HRMS: 418.1684 (M⁺, C₂₈H₂₂N₂O₂⁺ calc. 418.1681). X-ray crystal structure analysis: see Section 10.1.

2-Iodoisophthalonitrile (57).
To a solution of LDA (2M in THF, 20.5 ml, 41.0 mmol) in dry THF (40 ml) at −100 °C under argon was slowly added a solution of isophthalonitrile 58 (5.0 g, 39.0 mmol) in dry THF (80 ml), and the mixture was stirred for 30 min at the same temperature. Iodine (10.9 g, 42.9 mmol) was added, the mixture was slowly warmed up to r.t. and concentrated in vacuo. The residue was extracted with CH₂Cl₂ (300 ml), washed with aq. NaHSO₃ soln. (100 ml), sat. aq. NaCl soln. (100 ml), dried (MgSO₄), and concentrated in vacuo. Plug filtration (SiO₂, CH₂Cl₂) and recrystallization (MeOH) afforded 57 (5.5 g, 55%) as pale yellow crystals. M.p. 207-208 °C (Lit. [71]: M.p. 208-209 °C). ¹H-NMR (CDCl₃, 200 MHz): 7.80 (A₂B, J = 8.0, 2 H, H-C(4)); 7.62 (A₂B, J = 8.0, 1 H, H-C(5)). ¹³C-NMR (CDCl₃, 50 MHz): 137.19; 129.13; 123.35; 118.14; 103.67.

2,2′-(3,6-Dimethoxynaphthalene-2,7-diyl)bis(isophthalonitrile) (59).

Preparation of the boronic ester (60). To a solution of n-BuLi (1.6M in hexane, 15.6 ml, 25.0 mmol) in dry THF (100 ml) at −100 °C under argon was added dropwise a solution of 48 (1.73 g, 5.0 mmol) in dry THF (30 ml). The mixture was stirred for 1 h at the same temperature, BH₃ (1M in THF, 50 ml, 50.0 mmol) was added rapidly, the mixture was stirred at −100 °C for 2 h and at r.t. for 24 h. The solvents were removed in vacuo, the residue was stirred with water (200 ml) and aq. HCl soln. (2M, 50 ml) for 1 h and extracted with AcOEt (4 × 50 ml). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Pinacol (5.91 g, 50 mmol), NH₄Cl (1 g, 18.7 mmol), and PhMe (20 ml) were added, and the mixture was heated at reflux for 2 h. The resulting yellow oil was extracted with CH₂Cl₂ (3 × 100 ml), and the combined organic layers were washed with water (200 ml), dried (MgSO₄), and concentrated in vacuo. Recrystallization (hexane/Et₂O, −20 °C) yielded crude arylboronic ester 60 (370 mg, 17%) which was used without further purification.

Suzuki coupling. A degassed mixture of 57 (115 mg, 0.45 mmol), 60 (100 mg, 0.23 mmol), Na₂CO₃ (50 mg, 0.45 mmol), [PdCl₂(dppf)] (3 mg, 3.7 μmol), PhH (13.2 ml), EtOH (3.6 ml), and water (6 ml) was heated at reflux under argon for 2 h and extracted with CH₂Cl₂ (3 × 70 ml). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. CC (SiO₂, CH₂Cl₂) afforded 59 (70 mg, 70%) as a white
solid. M.p. 378-379 °C (CHCl₃). IR (KBr): 3078w, 2956w, 2236m, 1631s, 1468s, 1230s, 1184s, 1031s. ¹H-NMR (CDCl₃, 500 MHz): 7.95 (d, J = 7.9, 4 H, H-C(4')); 7.81 (s, 2 H, H-C(1)); 7.57 (t, J = 7.9, 2 H, H-C(5')); 7.31 (s, 2 H, H-C(4)); 3.97 (s, 6 H, CH₃O). ¹³C-NMR (CDCl₃, 125 MHz): 155.71; 145.36; 138.13; 136.48; 131.48; 128.33; 123.42; 122.98; 116.61; 115.66; 105.94; 55.72. EI-MS: 440.1 (100, M⁺). FAB-HRMS: 440.1279 (M⁺, C₂₈H₁₆N₄O₂⁺ calc 440.1273). Anal. calc. for C₂₈H₁₆N₄O₂: 0.6 CHCl₃ (440.46 + 7.16): C 75.29, H 3.62, N 12.52; found: C 75.24, H 3.58, N 12.47.

9.4. Experimental procedures for Chapter 4

3-(4,4,5,5-Tetramethyl[1,3,2]dioxaborolan-2-yl)benzonitrile (73).

To a solution of 3-bromobenzonitrile 76 (3.50 g, 19.23 mmol) in dry THF (150 ml) at −100 °C under argon was added n-BuLi (1.6M in hexane, 30.1 ml, 48.16 mmol), and the solution was stirred for 15 min. B(OMe)₃ (22 ml, 193.7 mmol) was added at −100 °C, the mixture was slowly warmed up and stirred overnight at r.t. Solvents were removed in vacuo, and pinacol (2.80 g, 23.69 mmol), NH₄Cl (1 g), and PhMe (150 ml) were added. The mixture was heated at reflux for 3 h and concentrated in vacuo. The residue was suspended in water (300 ml), acidified with aq. HCl soln. (2M, 30 ml), and extracted with CH₂Cl₂ (3 x 100 ml). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. Kugelrohr distillation (100 °C, 0.1 Torr) yielded 73 (4.17 g, 95%) as white crystals. M.p. 80-81 °C (hexane). IR (KBr): 2976s, 2227s, 1604s, 1487m, 1421s, 1353s, 1272m, 1147s, 1091m, 966m, 879m, 847m, 804m, 700m, 560m. ¹H-NMR (CDCl₃, 200 MHz): 8.08 (bs, 1 H, H-C(2)); 8.00 (d, J = 7.6, 1 H, H-C(6)); 7.69-7.74 (m, 1 H, H-C(4)); 7.46 (t, J = 7.6, 1 H, H-C(5)); 1.34 (s, 12 H, CH₃). ¹³C-NMR (CDCl₃, 50 MHz): 138.71; 138.36; 134.36; 128.36; 118.78; 112.05; 84.46; 24.81. EI-MS: 229.2 (21, M⁺); 214.2 (66); 143.1 (100); 130.1 (65). Anal. calc. for C₁₃H₁₆BN₂O₂ (229.09): C 68.16, H 7.04, N 6.11; found: C 68.29, H 7.04, N 6.06.
Chapter 9

[4-(4,4,5,5-Tetramethyl[1,3,2]dioxaborolan-2-yl)phenyl]acetonitrile (79).

A solution of 4-bromophenylacetonitrile 80 (392 mg, 2.00 mmol), 4,4,5,5-tetramethyl[1,3,2]dioxaborole (512 mg, 4.00 mmol), and NEt₃ (1.1 ml, 8.00 mmol) in dry dioxane (8 ml) was degassed. [PdCl₂(PPh₃)₂] (70 mg, 0.1 mmol) was added, and the mixture was stirred under argon at 100 °C for 27 h. The solvents were removed in vacuo, the resulting dark oil was diluted with ether (40 ml), filtered through a pad of Celite, and concentrated in vacuo. Kugelrohr distillation (120 °C, 0.1 Torr) yielded 79 (165 mg, 34%) as a white crystalline solid. M.p. 79-80 °C (hexane). IR (KBr): 2985m, 2910w, 2247w, 1614m, 1400m, 1363s, 1143s, 1090s, 1022m, 963m, 858m, 815m, 658m. 1H-NMR (CDCl₃, 500 MHz): 7.81 (d, J = 8.2, 2 H, H-C(3)); 7.33 (d, J = 8.2, 2 H, H-C(2)); 3.77 (s, 2 H, CH₂); 1.35 (s, 12 H, CH₃). 13C-NMR (CDCl₃, 125 MHz): 135.54; 132.78; 127.22; 117.61; 84.00; 24.86; 23.78. EI-MS: 243.2 (20, M⁺); 228.2 (74); 157.1 (95); 144.1 (100). Anal. calc for C₁₄H₁₈BN₂O₂ (243.11): C 69.17, H 7.46, N 5.76; found: C 69.11, H 7.27, N 5.72.

2,8,14,20-Tetraundecylpentacyclo[19.3.1.1₃.₇.₁₉.₁₃.₁₅.₁₉]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol (all cis stereoisomer) (63).

A solution of resorcinol (62) (39.60 g, 0.36 mol) in a mixture of EtOH (150 ml) and aq. HCl (37%, 50 ml) was cooled to 2 °C. Dodecanal (66.40 g, 0.36 mmol) in EtOH (100 ml) was added dropwise under argon over a period of 2.5 h. The reaction mixture was allowed to warm to r.t. overnight and was then stirred at 75 °C for 21 h. The reaction mixture was cooled to 0 °C, the solid was filtered off, washed with cold MeOH (1 l), and dried in vacuo. Recrystallization (MeOH) afforded 63 (72.40 g, 72%, Lit. [73]: 68%) as a white solid. M.p. 300-303 °C (dec.) (Lit. [73]: M.p. 285 °C (dec.)). 1H-NMR ((CD₃)₂CO, 500 MHz): 8.41 (s, 8 H, OH); 7.53 (s, 4 H, H-C(5)); 6.23 (s, 4 H, H-C(2)); 4.30 (t, J = 6.5, 4 H, H-C(7)); 2.28-2.30 (m, 8 H, H-C(8)); 1.32-1.33 (m, 8 H,
98 Experimental Part

H-C(9)); 1.29 (bs, 64 H, H-C(10-17)); 0.88 (t, J = 6.9, 12 H, H-C(18)). $^{13}$C-NMR ((CD$_3$)$_2$CO, 125 MHz): 152.68; 125.37; 125.19; 103.68; 34.37; 34.32; 32.68; 30.60; 30.51; 30.49; 30.45; 30.13; 29.05; 23.35; 14.37.


![Chemical structure](image)

To a stirred solution of 63 (10.00 g, 9.00 mmol) in butanone (300 ml) at 35 °C was added portionwise NBS (18.50 g, 104.00 mmol). The mixture was stirred at r.t. under argon for 24 h in dark. The solid was filtered off, washed with cold butanone, and dried in vacuo to give 65 (6.69 g, 52%). M.p. 295-296 °C (dec). IR (KBr): 3396s, 2923s, 2852m, 1616w, 1471s, 1434m, 1313m, 1156m, 1090w. $^1$H-NMR ((CD$_3$)$_2$CO, 500 MHz): 8.28 (s, 8 H, OH); 7.61 (s, 4 H, H-C(5)); 4.44 (t, J = 6.5, 4 H, H-C(7)); 2.29-2.30 (m, 8 H, H-C(8)); 1.30-1.36 (m, 8 H, H-C(9)); 1.27 (bs, 64 H, H-C(10-17)); 0.88 (t, J = 6.9, 12 H, H-C(18)). $^{13}$C-NMR ((CD$_3$)$_2$CO, 125 MHz): 149.69; 126.03; 124.47; 100.90; 34.53; 32.67; 30.52; 30.43; 30.36; 30.20; 30.05; 29.90; 29.74; 28.82; 23.33; 14.35. FAB-MS: 1421.4 (MH$^+$, 48, C$_{72}$H$_{109}$Br$_{28}$O$_8$), 1342.5 (27, [M - C$_6$H$_6$]+), 1265.2 (100, MH$^+$ - 2C$_6$H$_6$), 1185.3 (35, MH$^+$ - 3C$_6$H$_6$ - H$_2$). Anal. calc. for C$_{72}$H$_{108}$O$_8$Br$_4$: C 60.85, H 7.66, Br 22.49; found: C 60.96, H 7.57, Br 22.56.


![Chemical structure](image)
A mixture of dry 65 (3.30 g, 2.32 mmol), TsO(CH₂)₂OTs (7.11 g, 19.20 mmol), anhydrous Cs₂CO₃ (12.12 g, 37.20 mmol), and dry Me₂SO (100 ml) was degassed and stirred under argon at 65 °C for 40 h. The mixture was cooled to 25 °C, filtered through a pad of Celite, and the filtrate was concentrated in vacuo. The residue was mixed with water (100 ml) and extracted with CH₂Cl₂ (3 x 100 ml). The combined organic layers were washed with water (2 x 100 ml), dried (MgSO₄), and concentrated in vacuo. CC (SiO₂, CH₂Cl₂) afforded 67 (1.20 g, 34%) as a colorless oil besides the triply bridged intermediate 67a (1.53 g, 43%) as a white solid. A mixture of 67a (1.45 g, 965 µmol), TsO(CH₂)₂OTs (715 mg, 1.93 mmol), anhydrous Cs₂CO₃ (1.80 g, 5.52 mmol), and dry MeCN (30 ml) was degassed and stirred under argon at 90 °C for 24 h. The solvent was removed in vacuo, and the residue was worked up as described before, yielding 67 (1.29 g, 88%) as a colorless oil. IR (KBr): 2918s, 2852s, 1464s, 1439s, 1302m, 1095s, 1061s, 1040m, 881m, 862m, 622m. ¹H-NMR (CDCl₃, 500 MHz): 7.24 (s, 4 H, H-C(5)); 5.26 (t, J = 8.2, 4 H, H-C(7)); 4.44-4.47 (m, 8 H, H-C(19), outer); 3.74-3.78 (m, 8 H, H-C(19), inner); 2.03-2.06 (m, 8 H, H-C(8)); 1.20-1.34 (m, 72 H, H-C(9-17)); 0.88 (t, J = 7.0, 12 H, H-C(18)). ¹³C NMR (CDCl₃, 75 MHz): 151.65; 137.10; 123.16; 113.29; 70.48; 34.89; 34.21; 31.85; 29.58; 29.55; 29.29; 27.63; 22.58; 13.99. FAB-MS: 1525.8 (100, MH⁺, C₈₀H₁₁₇O₂₈Br₂81Br₂O₈⁺). Anal. calc for C₈₀H₁₁₆O₈Br₄ (1525.41): C 62.99, H 7.66, Br 20.95; found: C 63.15, H 7.54, Br 20.74.


Dry 67 (4.78 g, 3.13 mmol) was dissolved in dry THF (150 ml) under argon, and the solution was cooled to -100 °C. n-BuLi (1.6M in hexane, 19.6 ml, 31.4 mmol) was slowly added, and the mixture was stirred for 35 min. Iodine (9.54 g, 37.6 mmol) was added, the mixture was warmed to r.t., concentrated in vacuo, washed with sat. aq. NaHSO₃ soln. (250 ml), and extracted with CH₂Cl₂ (3 x 100 ml). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. CC (SiO₂, CH₂Cl₂) yielded 69 (4.19 g, 78%) as a colorless oil, which solidified upon standing. M.p.
140 °C. IR (KBr): 2923s, 2852s, 1456m, 1094s, 1061s. 1H-NMR (CDCl₃, 500 MHz): 7.29 (s, 4 H, H-C(5)); 5.26 (t, J = 8.1, 4 H, H-C(7)); 4.44-4.47 (m, 8 H, H-C(19), outer); 3.74-3.77 (m, 8 H, H-C(19), inner); 2.01-2.06 (m, 8 H, H-C(8)); 1.17-1.35 (m, 72 H, H-C(9-17)); 0.88 (t, J = 7.0, 12 H, H-C(18)). 13C-NMR (CDCl₃, 125 MHz): 154.37; 136.44; 124.76; 89.86; 70.38; 35.49; 34.78; 31.92; 29.67; 29.66; 29.65; 29.62; 29.38; 27.70; 22.68; 14.10. FAB-MS: 1714.1 (100, MH⁺). Anal. calc for C₈₀H₁₁₆O₈I₄ (1713.41): C 56.08, H 6.82, I 29.63; found: C 56.00, H 6.70, I 29.71.


A degassed mixture of 69 (7.00 g, 4.09 mmol), 73 (9.36 g, 40.9 mmol), Cs₂CO₃ (19.97 g, 61.3 mmol), [PdCl₂(PPh₃)₂] (720 mg, 1.00 mmol), AsPh₃ (2.40 g, 7.80 mmol), dioxane (180 ml), and water (7.2 ml) was stirred under argon at 75 °C for 3 h, cooled to r.t., and water (200 ml) was added. The precipitated solid was filtered, washed with water, and dried in vacuo. CC (SiO₂, CH₂Cl₂ → CH₂Cl₂/AcOEt 98:2) yielded 71 (5.29 g, 80%) as a white solid. M.p. 237-238 °C. IR (KBr): 2922s, 2852s, 2230m, 1579w, 1458s, 1265m, 1095s, 1063s, 1043m, 796m. 1H NMR (CDCl₃, 500 MHz): 7.65 (td, J = 7.7, 1.3, 4 H, H-C(6')); 7.62 (s, 4 H, H-C(5)); 7.50 (t, J = 7.7, 4 H, H-C(5')); 7.47 (bs, 4 H, C(2')-H); 7.41 (d, J = 7.7, 4 H, H-C(4')); 5.23 (t, J = 8.1, 4 H, H-C(7)); 3.82-3.86 (m, 8 H, H-C(19), outer); 3.34-3.38 (m, 8 H, H-C(19), inner); 2.19-2.23 (m, 8 H, H-C(8)); 1.39-1.40 (m, 8 H, H-C(9)); 1.27 (bs, 64 H, H-C(10-17)); 0.88 (t, J = 7.0, 12 H, H-C(18)). 13C NMR (CDCl₃, 125 MHz): 151.53; 136.50; 136.37; 134.23; 133.24; 131.26; 129.00; 128.90; 124.85; 118.45; 112.38; 72.25; 34.74; 33.88; 31.94; 29.74; 29.72; 29.69; 29.41; 27.93; 22.69; 14.10. FAB-MS: 1615.2 (100, MH⁺, C₁₀₇H₁₃₃N₄O₈⁺). Anal. calc. for C₁₀₈H₁₃₂N₄O₈ (1614.25): C 80.36, H 8.24, N 3.47; found: C 80.25, H 8.14, N 3.41.
Chapter 9


Preparation of MeAlNH₂Cl: To a suspension of NH₄Cl (5.79 g, 108.2 mmol) in 1,2-dichlorobenzene (45 ml) at −10 °C under argon was slowly added Me₃Al (2M in PhMe, 50 ml, 100.0 mmol), and the mixture was stirred at r.t. for 2 h. PhMe was removed at r.t. in vacuo (0.1 Torr).

Amidinium salt synthesis: A suspension of 71 (5.29 g, 3.28 mmol) in a solution of MeAlNH₂Cl (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was stirred under argon at 70 °C for 24 h, additional MeAlNH₂Cl (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was added, and the mixture was stirred at 80 °C for 5 d. The mixture was cooled to 0 °C, ice (100 g) and MeOH (50 ml) were slowly added, and the suspension was filtered through a pad of Celite. The solid was washed with MeOH (500 ml), and the combined filtrates were concentrated in vacuo. The residue was dried in vacuo (0.01 Torr), stirred in a mixture of acetone (200 ml) and propan-2-ol (0.2 ml) at r.t. for 8 h, and filtered. The solid was washed with acetone (500 ml), dried, and washed with water (500 ml). The obtained solid was recrystallized (MeOH/Et₂O 2:3) to afford 74 (4.22 g, 70%) as a white solid. M.p. >300 °C (dec.). IR (KBr): 3406s, 2923s, 2853m, 1674s, 1458m, 1439m, 1093m. ¹H-NMR (CD₃OD, 500 MHz): 7.84 (td, J = 7.9, 1.5, 4 H, H-C(6')); 7.78 (bs, 8 H, H-C(2',4')); 7.74 (s, 4 H, H-C(5)); 7.66 (t, J = 7.9, 4 H, H-C(5')); 5.32 (t, J = 8.1, 4 H, H-C(7)); 3.72-3.76 (m, 8 H, H-C(19), outer); 3.56-3.60 (m, 8 H, H-C(19), inner); 2.29-2.33 (m, 8 H, H-C(8)); 1.47-1.49 (m, 8 H, H-C(9)); 1.38 (bs, 64 H, H-C(10-17)); 0.95 (t, J = 7.0, 12 H, H-C(18)). ¹³C-NMR (CD₃OD, 125 MHz): 167.98; 153.07; 1458m, 1439m, 1093m. ¹H-NMR (CD₃OD, 500 MHz): 7.84 (td, J = 7.9, 1.5, 4 H, H-C(6')); 7.78 (bs, 8 H, H-C(2',4')); 7.74 (s, 4 H, H-C(5)); 7.66 (t, J = 7.9, 4 H, H-C(5')); 5.32 (t, J = 8.1, 4 H, H-C(7)); 3.72-3.76 (m, 8 H, H-C(19), outer); 3.56-3.60 (m, 8 H, H-C(19), inner); 2.29-2.33 (m, 8 H, H-C(8)); 1.47-1.49 (m, 8 H, H-C(9)); 1.38 (bs, 64 H, H-C(10-17)); 0.95 (t, J = 7.0, 12 H, H-C(18)). ¹³C-NMR (CD₃OD, 125 MHz): 167.98; 153.07; 138.47; 137.41; 131.85; 130.57; 129.94; 129.07; 127.98; 125.94; 73.49; 35.52; 35.34; 33.16; 30.90; 30.87; 30.77; 30.59; 29.25; 23.80; 14.52. FAB-MS: 1682.0/1683.0 (91/100, M - 3 HCl - Cl⁻). FAB-HRMS: 1682.1199 (M -...
3 HCl - Cl-, C_{108}H_{145}N_{8}O_{8}^+ calc 1682.1185). Anal. calc. for C_{108}H_{148}N_{8}O_{8}Cl_{4} 1.5 CH_{3}OH (1828.22 + 24.03): C 70.10, H 8.27, N 5.97; found: C 70.11, H 8.19, N 5.99.

**2,8,14,20-Tetrakis(2-phenylethyl)pentacyclo[19.3.1.13'7.11913.11519]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol (all cis stereoisomer)** (64).

To a solution of resorcinol (62) (55.0 g, 0.50 mol) in EtOH (400 ml) was added aq. HCl (37%, 100 ml) under argon. The solution was cooled to 0 °C, and 3-phenylpropanal (66 ml, 0.50 mol) was added dropwise over a 30 min period. The mixture was stirred at r.t. for 24 h and heated at reflux for 3 d. Ice (200 g) was added, the solid was filtered off, washed with cold EtOH/water (1:1, 1 l), dried *in vacuo*, and recrystallized from MeOH (1 l) to give 64 (61.0 g, 54%, lit.: 69%) as white needles. M.p. 333-337 °C (dec.) (Lit. [73]: M.p. >280 °C (dec.)). $^{1}$H-NMR ((CD$_3$)$_2$SO, 300 MHz): 9.05 (s, 8 H, OH); 7.40 (s, 4 H, H-C(5)); 7.09-7.16 (m, 20 H, C$_6$H$_5$); 6.18 (s, 4 H, H-C(2)); 4.23 (t, J = 6.5, 4 H, H-C(7)); 2.44-2.47 (m, 16 H, H-C(8,9)). $^{13}$C-NMR ((CD$_3$)$_2$SO, 75 MHz): 151.86; 142.43; 128.59; 128.31; 125.72; 125.06; 123.62; 102.57; 35.87; 34.32; 33.18.

To a stirred solution of 64 (10.00 g, 11.0 mmol) in butanone (170 ml) was added portionwise NBS (15.73 g, 88.0 mmol), and the mixture was stirred under argon at r.t. for 1 d in the dark. The solid was filtered off, washed with cold butanone, and dried in vacuo to give 66 (11.80 g, 87%). M.p. 280 °C (dec.) (Lit. [86] M.p. 260 °C (dec.)). IR (KBr): 3404s, 3024m, 2937m, 2861w, 1613m, 1473s, 1305s, 1201s, 1157s, 1098s, 749m, 699s. *H-NMR ((CD3)2SO, 300 MHz): 9.24 (s, 8 H, OH); 7.49 (s, 4 H, H-C(5)); 7.10-7.20 (m, 20 H, C6H5); 4.39 (t, J = 6.5, 4 H, H-C(7)); 2.47 (bs, 16 H, H-C(8,9)). 13C-NMR ((CD3)2CO/CD3OD 1:1, 125 MHz): 150.10; 143.14; 129.41; 129.30; 126.67; 126.32; 124.40; 100.48; 37.35; 36.84; 35.49. FAB-MS: 1221.0 (67, MH+, C60H5379Br281Br2O8+), 1115.5 (100, MH+ - C8H10), 1037.4 (19, MH+ - C14H16). Anal. calc for C60H52O8Br4 (1220.68): C 59.04, H 4.29, Br 26.18; found: C 59.01, H 4.22, Br 25.97.


A mixture of dry 66 (18.95 g, 15.52 mmol), TsO(CH2)2OTs (46.0 g, 124.2 mmol), anhydrous Cs2CO3 (80.9 g, 248.4 mmol), and dry Me2SO (800 ml) was degassed, stirred under argon at 65 °C for 4 d, cooled to r.t., and filtered through a pad of Celite. The filtrate was concentrated in vacuo, and the residue mixed with water (400 ml) and extracted with CH2C12 (3 x 350 ml). The combined organic layers were washed with water (2 x 350 ml), dried (MgSO4), and concentrated in vacuo. CC (SiO2, CH2Cl2) gave 68 (6.65 g, 32%) and the triply bridged intermediate 68a (12.16 g, 60%) as white solids. A mixture of 68a (12.16 g, 9.36 mmol), TsO(CH2)2OTs (7.32 mg, 19.75 mmol), anhydrous Cs2CO3 (14.86 g, 45.6 mmol), and dry MeCN (300 ml) was degassed and stirred under argon at 120 °C for 3 d. The solvent was removed in vacuo, and the residue was worked up as described before, yielding 68 (9.38 g, 76%) as a white solid. M.p. 184-186 °C. IR (KBr): 2927m, 1774w, 1602w, 1496w, 1446s, 1301m, 1097s, 1060s, 881w, 751m, 700s. *H-NMR (CDCl3, 500 MHz): 7.31 (s, 4 H, H-C(5)); 7.17-
7.19 (m, 12 H, C₆H₅); 7.07-7.09 (m, 8 H, C₆H₅); 5.42 (t, J = 7.9, 4 H, H-C(7)); 4.49-4.52 (m, 8 H, H-C(10), outer); 3.81-3.85 (m, 8 H, H-C(10), inner); 2.51-2.55 (m, 8 H, H-C(9)); 2.37-2.40 (m, 8 H, H-C(8)). ¹³C-NMR (CDCl₃, 125 MHz): 151.75; 141.46; 136.85; 128.49; 128.35; 125.96; 122.87; 113.53; 70.52; 36.79; 35.33; 34.39. FAB-MS: 1325.1 (100, MH+, C₆₆H₆₁Br₂O₂⁺). Anal. calc. for C₆₈H₆₀O₈Br₄ (1324.83): C 61.65, H 4.56, Br 24.13; found: C 61.76, H 4.57, Br 24.38. X-ray crystal structure analysis: see Section 10.2.


Dry 68 (11.68 g, 8.82 mmol) was dissolved in dry THF (350 ml) under argon. The solution was cooled to −100 °C, n-BuLi (1.6M in hexane, 55.1 ml, 88.2 mmol) was slowly added, and the mixture was stirred for 30 min. Iodine (26.85 g, 105.8 mmol) was added, and the mixture was warmed to r.t. and stirred for 12 h. It was concentrated in vacuo, washed with sat. aq. NaHSO₃ soln. (300 ml), and extracted with CH₂Cl₂ (3 x 200 ml). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. CC (SiO₂, CH₂Cl₂) yielded 70 (11.92 g, 89%) as a white solid. M.p. 304-305 °C. IR (KBr): 3023m, 2923s, 1603m, 1496m, 1440s, 1297m, 1095s, 1060s, 862m, 749m, 699s. ¹H-NMR (CDCl₃, 500 MHz): 7.34 (s, 4 H, H-C(5)); 7.17-7.19 (m, 12 H, C₆H₅); 7.05-7.08 (m, 8 H, C₆H₅); 5.42 (t, J = 7.9, 4 H, H-C(7)); 4.49-4.52 (m, 8 H, H-C(10), outer); 3.79-3.83 (m, 8 H, H-C(10), inner); 2.50-2.53 (m, 8 H, H-C(9)); 2.34-2.39 (m, 8 H, H-C(8)). ¹³C-NMR (CDCl₃, 125 MHz): 154.65; 141.42; 136.30; 128.49; 128.35; 125.95; 124.51; 90.20; 70.42; 37.30; 35.84; 34.41. FAB-MS: 1512.5 (100, M⁺). Anal. calc. for C₆₈H₆₀O₈I₄ (1512.84): C 53.99, H 4.00, I 33.55; found: C 54.14, H 4.06, I 33.54.
3,3',3'',3'''-[5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetrakis(2-phenylethyl)-
2,24:3,23-dimetheno-1\(\text{H}\),25\(\text{H}\),27\(\text{H}\),29\(\text{H}\)-bis[1,4]dioxonino[6,5-\(\text{J}\):6',5'-\(\text{J}\)]benzo[1,2-
e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis(benzonitrile) (all cis
stereoisomer) (72).

A degassed mixture of 70 (6.54 g, 4.32 mmol), 73 (9.90 g, 43.2 mmol), Cs\(_2\)CO\(_3\)
(21.11 g, 64.8 mmol), [PdCl\(_2\)(PPh\(_3\))\(_2\)] (250 mg, 0.35 mmol), AsPh\(_3\) (1.00 g,
3.25 mmol), dioxane (170 ml), and water (6.8 ml) was stirred under argon at 75 °C for
3 h, cooled to r.t., and ice (180 g) was added. The solid was filtered off, washed with
water, and dissolved in CH\(_2\)Cl\(_2\) (250 ml). The solution was filtered, dried (MgSO\(_4\)),
and concentrated in vacuo. CC (SiO\(_2\), CH\(_2\)Cl\(_2\)/AcOEt 98:2) yielded 72 (5.17 g, 85%)
as a white solid. M.p. 355-357 °C. IR (KBr): 2926m, 2228m, 1652w, 1581w,
1455s, 1442s, 1268m, 1235w, 1096s, 1063s, 864w, 800m, 751m, 699s. \(^1\)H-NMR
(CDCl\(_3\)/CDCl\(_3\), 500 MHz): 7.66 (s, 4 H, H-C(5)); 7.57 (d, J = 7.7, 4 H, H-C(6'));
7.43 (t, J = 7.7, 4 H, H-C(5')); 7.37-7.38 (m, 8 H, C\(_6\)H\(_5\)); 5.28
(t, J = 7.9, 4 H, H-C(7)); 3.75-3.76 (m, 8 H, H-C(10), outer); 3.26-3.28 (m, 8 H,
H-C(11), inner); 2.50 (bs, 16 H, H-C(8,9)). \(^{13}\)C-NMR (CDCl\(_3\)/CDCl\(_3\), 125 MHz):
151.95; 142.02; 136.52; 136.48; 134.70; 133.54; 131.64; 129.42; 129.23; 128.83;
128.82; 126.32; 124.88; 119.15; 112.29; 72.59; 37.33; 34.86; 34.50. FAB-MS: 1413.2
(100, \(M^+\)). Anal. calc. for C\(_{96}\)H\(_{76}\)N\(_4\)O\(_8\)H\(_2\)O (1413.70 + 18.02): C 80.54, H 5.49,
N 3.91; found: C 80.64, H 5.64, N 3.89.
Experimental Part


**Preparation of MeAlNH₂Cl:** To a suspension of NH₄Cl (5.79 g, 108.2 mmol) in 1,2-dichlorobenzene (45 ml) at -10 °C under argon, Me₃Al (2M in PhMe, 50 ml, 100.0 mmol) was slowly added, and the mixture was stirred at r.t. for 2 h. PhMe was removed at r.t. in vacuo (0.1 Torr).

**Amidinium salt synthesis:** A suspension of 72 (5.29 g, 3.74 mmol) in a solution of MeAlNH₂Cl (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was stirred under argon at 80 °C for 24 h, then additional MeAlNH₂Cl (2.2M in 1,2-dichlorobenzene, 45 ml, 100.0 mmol) was added, and the mixture was stirred at the same temperature for 3 d. It was cooled to 0 °C, ice (100 g) and MeOH (50 ml) were slowly added, and the suspension was filtered through a pad of Celite. The solid was washed with MeOH (500 ml), and the combined filtrates were concentrated in vacuo. The residue was dried in vacuo (0.01 Torr), stirred at r.t. for 8 h with a mixture of acetone (200 ml) and propan-2-ol (0.2 ml), and filtered. The solid was washed with acetone (500 ml), dried, and washed with water (500 ml). The obtained solid was recrystallized (MeOH/El₂O 1:2) to afford 75 (4.81 g, 79%) as a white solid. M.p. 327-329 °C (dec.). IR (KBr): 3382 cm⁻¹, 3155 cm⁻¹, 1675 cm⁻¹, 1455 cm⁻¹, 1094 cm⁻¹, 700 cm⁻¹. ¹H-NMR (CD₃OD, 500 MHz): 7.82-7.87 (m, 16 H, H-C(5,2',4',6')); 7.68 (t, J = 8.0, 4 H, H-C(5')); 7.17-7.22 (m, 20 H, C₆H₅); 5.43 (t, J = 7.2, 4 H, H-C(7)); 3.73-3.77 (m, 8 H, H-C(10), outer); 3.59-3.64 (m, 8 H, H-C(10), inner); 2.62 (bs, 16 H, H-C(8,9)). ¹³C-NMR (CD₃OD, 125 MHz): 167.96; 153.29; 143.35; 138.43; 137.44; 137.34; 132.01; 130.58; 129.99; 129.54; 129.51; 129.05; 128.03; 126.91; 126.04; 73.53; 38.18; 35.68; 35.49. FAB-MS: 1482.6
9.5. Experimental procedures for Chapter 5


Resorcinol (62) (120 g, 1.09 mol) was dissolved in a cold mixture of MeOH (720 ml) and aq. 37% HCl (180 ml). 2,3-Dihydrofuran (82.8 ml, 1.09 mol) was added at r.t. under argon via a syringe pump over 6 h. The mixture was stirred at the same temperature for 12 h, then at 50 °C for 9 d. The solid was filtered off, washed with cold water (3 l), sonicated in water (1 l) for 1 h, filtered off, and dried in vacuo to afford 88 (176.7 g, 90%) as a white solid. M.p. 322-323 °C (Lit. [80]: M.p. >250 °C). \(^1\)H-NMR ((CD\(_3\))\(_2\)SO, 200 MHz): 8.96 (bs, 8 H, HO-C(1)); 7.24 (s, 4 H, H-C(5)); 6.17 (s, 4 H, H-C(2)); 4.39 (t, \(J = 4.6\), 4 H, HO-C(10)); 4.22 (t, \(J = 7.9\), 4 H, H-C(7)); 3.50-3.54 (m, 8 H, H-C(10)); 2.09-2.12 (m, 8 H, H-C(8)); 1.35-1.38 (m, 8 H, H-C(9)).

To a suspension of 88 (10.00 g, 13.9 mmol) in a mixture of butanone (133 ml) and MeOH (57 ml) at r.t. was added NBS (11.1 g, 62.4 mmol), and the resulting solution was stirred at r.t. in the dark for 3 h. Additional NBS (4.93 g, 27.7 mmol) was added, the mixture was stirred at r.t. in the dark for 12 h, the solid was filtered off, washed with cold butanone, and dried in vacuo to yield 89 (11.10 g, 77%) as a white powder. M.p. 282-283 °C (dec.) (Lit. [80]: M.p. 220 °C (dec.)). *H-NMR (CD3OD, 200 MHz): 7.15 (s, 4 H, H-C(5)); 4.50 (t, J = 7.7, 4 H, H-C(7)); 3.61 (t, J = 6.4, 8 H, H-C(10)); 2.13-2.24 (m, 8 H, H-C(8)); 1.47-1.54 (m, 8 H, H-C(9)).


To a mixture of TsO(CH2)2OTs (18.00 g, 48.6 mmol), anhydrous Cs2CO3 (45.74 g, 140.4 mmol), and BHT (1 mg) in dry DMA (400 ml) at r.t. under argon was added via syringe pump over 2 d a solution of 89 (11.19 g, 10.8 mmol) in DMA (50 ml). The suspension was stirred at r.t. for 1 d, additional TsO(CH2)2OTs (12.00 g, 32.4 mmol) and anhydrous Cs2CO3 (40.00 g, 122.8 mmol) were added, and the mixture was stirred at 45 °C for 1 d. Additional TsO(CH2)2OTs (12.00 g, 32.4 mmol) and anhydrous K2CO3 (43.70 g, 316.2 mmol) were added, and the mixture was stirred at 65 °C for 3 d. The solvent was removed in vacuo, and the residue was stirred with water (1 l) at r.t. for 2 d, filtered off, and dried. The solid was heated at reflux in dioxane (400 ml), the insoluble part was filtered off, and the filtrate was concentrated in vacuo. CC (SiO2, CH2Cl2/MeOH 95:5 → 90:10) and recrystallization (dioxane/PhMe/CH2Cl2 1:10:10) afforded 90 (5.14 g, 42%) as a white solid. M.p. 380-390 °C. IR (KBr): 3421s, 2932m, 2869m, 1447s, 1302m, 1100m, 1058s. *H-NMR ((CD3)2SO, 500 MHz): 7.82 (s, 4 H, H-C(5)); 5.11 (t, J = 8.3, 4 H, H-C(7)); 4.38 (t, J = 5.0, 4 H, OH); 4.29-4.33 (m, 8 H, H-C(11), outer); 3.69-3.73 (m, 8 H, H-C(11), inner); 3.40-3.43 (m, 8 H, H-C(10)); 2.48-2.50 (m, 8 H, H-C(8)); 1.24-1.30 (m, 8 H, H-C(9)). *C-NMR ((CD3)2SO, 125 MHz): 150.99; 136.60; 124.97; 112.57; 70.36; 60.27; 34.63; 30.83; 29.45. FAB-MS: 1140.0
Chapter 9

(53, $M^+$), 955.5 (100). FAB-HRMS: 1140.0150 ($M^+$, $C_{48}H_{52}^{79}Br_2^{81}BrO_{12}$ calc. 1140.0151).


To a solution of 90 (500 mg, 438 µmol) in dry dioxane (40 ml) and NEt$_3$ (20 ml) at 0 °C under argon was added via syringe pump over 40 min methanesulfonyl chloride (2.5 ml, 32.2 mmol), and the resulting suspension was stirred for 3 h at r.t. After addition of ice (100 g), the mixture was extracted with CH$_2$Cl$_2$ (3 x 100 ml). The organic layer was washed with sat. aq. NH$_4$Cl soln. (100 ml), sat. aq. NaHCO$_3$ soln. (100 ml), dried (Na$_2$SO$_4$), and concentrated in vacuo. CC (SiO$_2$, CH$_2$Cl$_2$/AcOEt 85:15 → 75:25) yielded 91 (589 mg, 92%) as a white solid. M.p. 160-165 °C. IR (KBr): 2936m, 1461s, 1446s, 1351s, 1173s, 1058s, 937s, 528s. H-NMR (CDCl$_3$, 500 MHz): 7.40 (s, 4 H, H-C(5)); 5.29 (t, J = 8.4, 4 H, H-C(7)); 4.45-4.48 (m, 8 H, H-C(11), outer); 4.31 (t, J = 6.1, 8 H, H-C(10)); 3.76-3.80 (m, 8 H, H-C(11), inner); 3.06 (s, 12 H, CH$_3$); 2.26-2.31 (m, 8 H, H-C(8)); 1.63-1.67 (m, 8 H, H-C(9)). C-NMR (CDCl$_3$, 125 MHz): 151.73; 136.42; 123.32; 113.45; 70.55; 70.33; 34.57; 29.80; 27.44. FAB-MS: 1451.7 (100, $M^+$). FAB-HRMS: 1449.9273 ($M^+$, $C_{52}H_{60}^{79}Br_2^{81}O_{20}$S$_4$ calc. 1449.9274); 1451.9249 ($M^+$, $C_{52}H_{60}^{79}Br_2^{81}O_{20}$S$_4$ calc. 1451.9253).
8,13,18,32-Tetrabromo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis[3-(2-{2-
[2-(methoxy)ethoxy]ethoxy}ethoxy)propyl]-2,24:3,23-dimetheno-1H,25H,27H,29H-
bis[1,4]dioxonio][6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin (all cis
stereoisomer) (92).

Preparation of Mg(O(CH₂CH₂O)₃Me)₂ (93): Mg (1.00 g, 41.1 mmol) was activated
with a crystal of iodine at 200 °C, triethylene glycol monomethyl ether (15 ml,
95.7 mmol) was added, and the suspension was stirred at 140 °C for 1.5 h. After
cooling to r.t., dioxane (10 ml) was added. To a solution of 91 (1.20 g, 826 µmol) in dioxane (20 ml) was added
Mg(O(CH₂CH₂O)₃Me)₂ (93) (41.1 mmol), and the mixture was stirred at 60 °C for
16 h. The solvent was removed in vacuo, the residue was dissolved in AcOEt (60 ml),
washed with sat. aq. NH₄Cl soln. (100 ml), and the aqueous layer was extracted with
AcOEt (4 x 100 ml). The combined organic layers were washed with sat. aq. NaHCO₃
soln. (150 ml) and water (150 ml). The aqueous layer was extracted with AcOEt
(3 x 80 ml). The combined organic layers were dried over MgSO₄, concentrated in
vacuo, and dried at 160 °C (Kugelrohr, 0.1 Torr). CC (SiO₂, CH₂Cl₂/MeOH 98:2 →
94:6) yielded 92 (1.11 g, 78%) as a colorless, viscous oil. IR (KBr): 2922s, 2868s,
1448s, 1349m, 1302m, 1246m, 1102s, 1056s, 934m, 862m, 623m. *H-NMR (CDCl₃,
500 MHz): 7.19 (s, 4 H, H-C(5)); 5.25 (t, J = 8.2, 4 H, H-C(7)); 4.38-4.42 (m, 8 H,
H-C(11)), outer); 3.70-3.74 (m, 8 H, H-C(11)), inner); 3.48-3.61 (m, 8 H, OCH₂-CH₂O);
3.44 (t, J = 6.5, 8 H, H-C(10)); 3.31 (s, 12 H, CH₃O); 2.08-2.10 (m, 8 H, H-C(8)); 1.43-
1.46 (m, 8 H, H-C(9)). ¹³C-NMR (CDCl₃, 125 MHz): 151.46; 136.57; 122.78; 113.17;
71.73; 70.41; 70.38; 70.35; 70.31; 70.28; 69.88; 58.82; 34.23; 30.29; 27.29. FAB-MS:
1725.4 (100, MH⁺).
8,13,18,32-Tetraiodo-5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis[3-(2-(2-
[ methoxy)ethoxy]ethoxy)ethoxy)propyl]-2,24:3,23-dimetheno-1H,25H,27H,29H-
bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin (all cis
stereoisomer) (95).

To a solution of dry 92 (3.24 g, 1.88 mmol) in dry THF (100 ml) at -100 °C under
argon was added n-BuLi (1.6M in hexane, 13.5 ml, 21.6 mmol), and the resulting
solution was stirred for 30 min at that temperature. Iodine (6.67 g, 26.3 mmol) was
added at -100 °C, the reaction mixture was slowly warmed up and stirred for 2 h at r.t.
The solvents were removed in vacuo, and the residue was dissolved in CH₂Cl₂
(100 ml). The unreacted iodine was removed with sat. aq. NaHSO₃ soln. (100 ml), and
the aqueous layer was extracted with CH₂Cl₂ (4 x 100 ml). The combined organic
layers were dried (MgSO₄) and concentrated in vacuo. CC (SiO₂, CH₂Cl₂/MeOH
98:2 → 95:5) yielded 95 (3.50 g, 97%) as a colorless, viscous oil. IR (KBr): 2922s,
2868s, 1441s, 1349m, 1297m, 1104s, 1033s, 932m, 860m, 619m. ¹H-NMR (CDCl₃,
500 MHz): 7.23 (s, 4 H, H-C(5)); 5.24 (t, J = 8.2, 4 H, H-C(7)); 4.37-4.41 (m, 8 H,
H-C(11), outer); 3.69-3.71 (m, 8 H, H-C(11), inner); 3.47-3.61 (m, 48 H, OCH₂-CH₂O);
3.43 (t, J = 6.5, 8 H, H-C(10)); 3.31 (s, 12 H, CH₃O); 2.04-2.09 (m, 8 H, H-C(8)); 1.41-
1.44 (m, 8 H, H-C(9)). ¹³C-NMR (CDCl₃, 125 MHz): 154.30; 135.98; 124.40; 89.79;
71.68; 70.36; 70.33; 70.29; 70.26; 70.14; 69.82; 58.79; 34.71; 30.74; 27.25. FAB-MS:
A degassed mixture of 95 (760 mg, 397 µmol), Cs₂CO₃ (1.94 g, 5.96 mmol), [PdCl₂(PhCN)₂] (30 mg, 78 µmol), AsPh₃ (150 mg, 490 µmol), dioxane (9.6 ml), and water (0.4 ml) was stirred under argon at 70 °C for 2 h. The mixture was cooled to r.t. and filtered through a pad of Celite-MgSO₄ (1:1). The solid was washed with CH₂Cl₂ (200 ml) and AcOEt (100 ml), and the filtrate was concentrated in vacuo. CC (SiO₂, CH₂Cl₂/MeOH 98:2 → 95:5) yielded 96 (607 mg, 84%) as a colorless, viscous oil which solidified upon standing. M.p. 78-80 °C. IR (KBr): 2922s, 2868s, 2228m, 1457s, 1443s, 1266m, 1100s. ¹H-NMR (CDCl₃, 500 MHz): 7.62 (d, J = 7.8, 4 H, H-C(6')); 7.60 (s, 4 H, H-C(5)); 7.49 (t, J = 7.8, 4 H, H-C(5')); 7.45 (s, 4 H, H-C(2')); 7.42 (d, J = 7.8, 4 H, H-C(4')); 5.25 (t, J = 8.1, 4 H, H-C(7)); 3.80-3.83 (m, 8 H, H-C(10), outer); 3.51-3.65 (m, 64 H, OCH₂-CH₂O + H-C(10) + H-C(11), inner); 3.35 (s, 12 H, CH₃O); 2.24-2.28 (m, 8 H, H-C(8)); 1.54-1.59 (m, 8 H, H-C(9)). ¹³C-NMR (CDCl₃, 125 MHz): 151.61; 136.34; 136.00; 134.28; 133.13; 131.16; 129.05; 128.88; 124.57; 118.37; 112.16; 72.16; 71.84; 70.68; 70.51; 70.49; 70.42; 69.99; 58.92; 33.32; 30.78; 27.67. FAB-MS: 1815.0 (100, MH⁺). FAB-HRMS: 1813.8656 (MH⁺, C₁₀₄H₁₂₅N₄O₂₄⁺ calc. 1813.8684; M⁺, C₁₀₃¹³CH₁₂₄N₄O₂₄⁺ calc. 1813.8639).
To a solution of 96 (2.78 g, 1.53 mmol) in dry 1,2-dichlorobenzene (20 ml) was added a solution of MeAlNH2Cl (2M in 1,2-dichlorobenzene, 30 ml, 60.0 mmol). The mixture was stirred under argon at 70 °C for 24 h, and additional MeAlNH2Cl (2M in 1,2-dichlorobenzene, 30 ml, 60.0 mmol) was added. The mixture was stirred at 80 °C for 48 h, cooled to 0 °C, ice (50 g) and MeOH (20 ml) were slowly added, and the suspension was filtered through a pad of Celite. The solid was washed with MeOH (500 ml), and the combined filtrates were concentrated in vacuo. The residue was dried in vacuo (0.01 Torr), stirred with PhMe (300 ml) at r.t. for 4 h, and filtered off. The solid was washed with PhMe (200 ml), dried, washed with cold aq. NaOH soln. (20%, 100 ml) and water (800 ml). The residue was dissolved in MeOH (50 ml), ethanolic HCl (6M, 3 ml) was added, and the solvents were removed in vacuo. The obtained solid was dried in vacuo (0.05 Torr) and recrystallized (MeOH/Et2O 1:4) to afford 87 (2.83 g, 91%) as a white solid. M.p. 306-310 °C (dec.). IR (KBr): 3428 br, 2932 s, 2867 s, 1677 s, 1521 m, 1457 s, 1397 s. 1H-NMR (D2O, 500 MHz): 8.01 (s, 4 H, H-C(5)); 7.87 (d, J = 7.7, 4 H, H-C(6')); 7.70 (t, J = 7.7, 4 H, H-C(5')); 7.63 (d, J = 7.7, 4 H, H-C(4')); 7.62 (s, 4 H, C(2')-H); 5.25 (t, J = 8.2, 4 H, H-C(7)); 3.84-3.86 (m, 8 H, H-C(10); outer); 3.53-3.72 (m, 64 H, OCH2CH2O + H-C(10) + H-C(11), inner); 3.34 (s, 12 H, CH3O); 2.45-2.48 (m, 8 H, H-C(8)); 1.61-1.75 (m, 8 H, H-C(9)). 13C-NMR (CD3OD, 125 MHz): 167.93; 153.21; 138.45; 137.41; 137.30; 131.90; 130.62; 129.95; 129.05; 127.99; 126.08; 73.51; 72.96; 71.83; 71.63; 71.59; 71.56; 71.38; 71.30; 59.11; 34.90; 31.54; 29.16. FAB-MS: 1882.9 (100, M - 3 HCl - Cl-). FAB-HRMS: 1881.9748 (M - 3 HCl -
9.6. Experimental procedures for Chapter 7

4-(4,4,5,5-Tetramethyl[1,3,2]dioxaborolan-2-yl)-benzonitrile (77).

\[ \text{To a solution of 4-bromobenzonitrile (78) (10.0 g, 54.93 mmol) in dry THF (350 ml) at } -100 \degree \text{C under argon was added } n-\text{BuLi (1.6M in hexane, 85.8 ml, 137.28 mmol), and the resulting solution was stirred for 10 min. Trimethylborate (62.4 ml, 549.30 mmol) was added at } -100 \degree \text{C, the reaction mixture was slowly warmed to r.t. and stirred overnight. The solvents were removed } \text{in vacuo, and the residue was heated with pinacol (7.14 g, 23.69 mmol), NH}_4\text{Cl (1 g), and PhMe (150 ml) to reflux for 3 h. The solvent was distilled off, the residue was suspended in water and acidified with 2M HCl. The product was extracted with CH}_2\text{C}l_2 (3 \times 100 \text{ ml), the combined organic layers were dried (MgSO}_4\text{) and concentrated } \text{in vacuo. Kugelrohr distillation (150 } \degree \text{C, 0.2 Torr) gave pure 77 (8.81 g, 70%) as white crystals. M.p. 96-98 \degree \text{C.}} \]

IR (KBr): 2976\,m, 2227\,m (CN), 1400s, 1354s, 1143s, 1089m. \(^1\text{H-NMR (CDCl}_3\text{, 500 MHz): 7.88 (d, } J = 8.3, 2 \text{ H, H-C(2)); 7.63 (d, } J = 8.3, 2 \text{ H, H-C(3)); 1.35 (s, 12 H, CH}_3\text{).}} \)

\(^{13}\text{C-NMR (CDCl}_3\text{, 125 MHz): 135.08; 131.11; 118.84; 114.54; 84.48; 24.84; (C(4)-B not found).} \)

NMR spectra are in agreement with the published data [87].
4,4',4''',4'''-[5,6,10,11,15,16,20,21-Octahydro-1,25,27,29-tetrakis(2-phenylethyl)-
2,24:3,23-dimetheno-1H,25H,27H,29H-bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-
e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis(benzonitrile) (all cis
stereoisomer) (119).

A degassed mixture of 70 (1.00 g, 0.66 mmol), 77 (1.51 g, 6.61 mmol), Cs₂CO₃ (3.23 g,
9.91 mmol), [PdCl₂(PPh₃)₂] (100 mg, 0.14 mmol), AsPh₃ (329 mg, 1.07 mmol),
dioxane (25 ml), and water (1 ml) was stirred under argon at 75 °C for 3 h, cooled to r.t.,
and water (30 ml) was added. The solid was filtered off, washed with water, and dried.
CC (SiO₂, CH₂Cl₂ → CH₂Cl₂/AcOEt 98:2) yielded 119 (812 mg, 87%) as a white
solid. M.p. 398-400 °C. IR (KBr): 2926m, 2228m (CN), 1608m, 1441s, 1095s, 1062m,
699m. XH-NMR (CD₂Cl₂, 500 MHz): 7.69 (s, 4 H, H-C(5)); 7.69 (d, J = 8.3, 8 H,
H-C(2')); 7.30 (d, J = 8.3, 8 H, H-C(3')); 7.14-7.21 (m, 20 H, C₆H₅); 5.36 (t, J = 7.5,
4 H, H-C(7)); 3.79-3.82 (m, 8 H, H-C(10), outer); 3.40-3.42 (m, 8 H, H-C(10), inner);
2.55-2.59 (m, 16 H, H-C(8,9)). ¹³C-NMR (CD₂Cl₂, 125 MHz): 152.14; 142.29;
140.55; 136.76; 132.16; 131.04; 130.73; 128.85; 128.81; 126.29; 125.07; 118.91;
112.06; 72.74; 37.47; 34.79; 34.52. FAB-MS: 1413.2 (100, M⁺). Anal. calc. for
C₉₆H₇₆N₄O₈H₂O (1413.68 + 18.01): C 80.54, H 5.49, N 3.91; found: C 80.64, H 5.69,
N 3.95.
116 Experimental Part


Preparation of MeAlNH₂Cl: To a suspension of NH₄Cl (2.55 g, 47.6 mmol) in 1,2-dichlorobenzene (22 ml) at -10 °C under argon was slowly added Me₃Al (2M in PhMe, 22 ml, 44.0 mmol), and the mixture was stirred at r.t. for 1 h. PhMe was removed at r.t. in vacuo (0.1 Torr).

Amidinium salt synthesis: A suspension of 119 (1.50 g, 1.06 mmol) in a solution of MeAlNH₂Cl (2M in 1,2-dichlorobenzene, 22 ml, 44.0 mmol) was stirred under argon at 70 °C for 24 h. Additional MeAlNH₂Cl (2M in 1,2-dichlorobenzene, 44 ml, 88.0 mmol) was added, and the mixture was stirred at 80 °C for 48 h. The mixture was cooled to 0 °C, ice (50 g) and MeOH (20 ml) were slowly added, and the suspension was filtered through a pad of Celite. The solid was washed with MeOH (400 ml), and the combined filtrates were concentrated in vacuo. The obtained solid was recrystallized (MeOH/Et₂O 1:2) to afford 117 (1.30 g, 75%) as a white solid. M.p. 330-333 °C (dec). IR (KBr): 3458br, 1674s, 1613m, 1539m, 1489m, 1440m, 1267m, 1230v, 1093m, 1059m, 855m, 699m. ¹H-NMR (CD₃OD, 500 MHz): 7.87 (d, J = 8.5, 8 H, H-C(2′)); 7.87 (s, 4 H, H-C(5)); 7.63 (d, J = 8.5, 8 H, H-C(3′)); 7.18-7.21 (m, 20 H, C₆H₅); 5.41 (t, J = 7.5, 4 H, H-C(7)); 3.73-3.77 (m, 8 H, H-C(10), outer); 3.58-3.62 (m, 8 H, H-C(10), inner); 2.62 (bs, 16 H, H-C(8,9)). ¹³C-NMR (CD₃OD, 125 MHz): 168.34; 153.05; 143.40; 143.35; 137.35; 132.64;
FAB-MS: 1482.2 (100, \textit{M} - 3 \text{HCl} - \text{Cl}^{-}). FAB-HRMS: 1481.6804 (\textit{M} - 3 \text{HCl} - \text{Cl}^{-}, C_{96}H_{89}N_{8}O_{8} \text{calc.} 1481.6803).


![](image)

A mixture of 119 (1.45 g, 1.03 mmol), KOH (14.50 g, 258.4 mmol), \text{Et(OCH}_{2}CH_{2})_{2}OH (363 ml), and water (145 ml) was stirred under argon at 130-140 \degree C for 24 h, then cooled to r.t. Ice (500 g) was added, and the mixture was acidified with conc. HCl to pH = 2. The solid was filtered over Celite, washed with CH\textsubscript{2}Cl\textsubscript{2} (200 ml), AcOEt (200 ml), and MeOH (200 ml). The combined organic filtrates were concentrated in vacuo, and the residue was chromatographed (Si\textsubscript{2}, MeOH \rightarrow AcOH) to yield 118 (1.32 g, 87\%) as a white solid. M.p. >410 \degree C (dec.). IR (KBr): 3436br, 2927m, 1728s, 1700s, 1611m, 1440m, 1404m, 1267m, 1228m, 1175m, 1096s, 862m, 699m. \textsuperscript{1}H-NMR (CD\textsubscript{3}OD, 500 MHz): 8.04 (d, \textit{J} = 8.2, 8 H, H-C(2')); 7.83 (s, 4 H, H-C(5)); 7.38 (d, \textit{J} = 8.2, 8 H, H-C(3')); 7.19 (bs, 20 H, C\textsubscript{6}H\textsubscript{5}); 5.42 (t, \textit{J} = 7.5, 4 H, H-C(7)); 3.76-3.78 (m, 8 H, H-C(10), outer); 3.55-3.57 (m, 8 H, H-C(10), inner); 2.61-2.62 (m, 16 H, H-C(8,9)). \textsuperscript{13}C-NMR ((CD\textsubscript{3})\textsubscript{2}SO, 125 MHz): 167.13; 151.26; 141.80; 139.71; 135.58; 130.18; 130.05; 129.76; 128.64; 128.51; 128.18; 125.71; 125.56; 71.94; 36.01; 34.34; 34.05. FAB-MS: 1488.8 (100, \textit{M}^{+}). FAB-HRMS: 1488.5451 (\textit{M}^{+}, C_{96}H_{80}O_{16} \text{calc.} 1488.5446).
10. Appendix

10.1. X-Ray Crystal Structure Data of Dinitrile C$_2$-50

The less polar isomer of C$_2$-50 was crystallized (Et$_2$O/hexane) and its geometry and configuration was determined as C$_2$ by X-ray crystallographic analysis.

![ORTEP Plot of the X-ray crystal structure of C$_2$-50 solved and analyzed by Dr. B. Schweizer (ETH Zürich). The atom numbering is arbitrary.](image)

From a crystal (Et$_2$O/hexane) of size $0.35 \times 0.30 \times 0.15$ mm, 4747 reflexions were measured on an Enraf Nonius CAD-4 Diffractometer with CuK$_\alpha$ radiation (graphite monochromator, $\lambda = 1.54184$ Å). Part of the structure was solved by direct method map with SHELXS-96 (Sheldrick, 1993), the remaining non-H-atoms were found from a difference Fourier map. The non-H atoms (without the solvent molecule) were refined anisotropically with SHELXL-97 (Sheldrick, 1997). H-atoms were calculated at idealized positions and refined with constrained isotropic displacement parameters. The solvent (Et$_2$O) is disordered and is located near a centre of symmetry. Two positions of the molecule were refined isotropically with constrained bond length. The H-atoms were calculated and included in the structure factor calculation. Drawings of the molecule were done with PLUTO, ORTEP (Johnson, 1976). Final $R$ values and experimental data see Table 25.
Table 25. Crystal data and structure refinement for C_{25}H_{37}N_{2}O_{3}.

<table>
<thead>
<tr>
<th>Identification code</th>
<th>D25038</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{30}H_{27}N_{2}O_{3}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>463.54</td>
</tr>
<tr>
<td>Temperature</td>
<td>150(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>1.54184 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P21/c</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>( a = 11.982(2) ) Å, ( \alpha = 90) deg. ( b = 13.610(4) ) Å, ( \beta = 94.26(3)) deg. ( c = 15.342(8) ) Å, ( \gamma = 90) deg.</td>
</tr>
<tr>
<td>Volume</td>
<td>2495(2) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.234 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.637 mm⁻¹</td>
</tr>
<tr>
<td>( F(000) )</td>
<td>980</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.35 x 0.30 x 0.15 mm</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>3.70 to 67.03 deg.</td>
</tr>
<tr>
<td>Index ranges</td>
<td>( 0 \leq h \leq 14, 0 \leq k \leq 16, -18 \leq l \leq 18 )</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>4747</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>4452 ([R(int) = 0.0170])</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.9105 and 0.8078</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on ( F^2 )</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>3895 / 5 / 389</td>
</tr>
<tr>
<td>Goodness-of-fit on ( F^2 )</td>
<td>1.980</td>
</tr>
<tr>
<td>Final R indices ([I&gt;3\sigma(I)])</td>
<td>( R1 = 0.0562, wR2 = 0.2041 )</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>( R1 = 0.0629, wR2 = 0.2106 )</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.308 and -0.674 e Å⁻³</td>
</tr>
</tbody>
</table>
### Table 26

Atomic coordinates (× 10⁶) and equivalent isotropic displacement parameters (Å² × 10³) for C<sub>2</sub>-50. U(eq) is defined as one third of the trace of the orthogonalized U<sub>ij</sub> tensor.

<table>
<thead>
<tr>
<th>x</th>
<th>y</th>
<th>z</th>
<th>U(eq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(01)</td>
<td>6067(2)</td>
<td>2675(1)</td>
<td>518(1)</td>
</tr>
<tr>
<td>C(02)</td>
<td>6442(2)</td>
<td>3354(1)</td>
<td>1131(1)</td>
</tr>
<tr>
<td>C(03)</td>
<td>5731(2)</td>
<td>4165(1)</td>
<td>1306(1)</td>
</tr>
<tr>
<td>C(04)</td>
<td>4710(2)</td>
<td>4282(1)</td>
<td>850(1)</td>
</tr>
<tr>
<td>C(05)</td>
<td>3247(2)</td>
<td>3647(1)</td>
<td>-222(1)</td>
</tr>
<tr>
<td>C(06)</td>
<td>2844(2)</td>
<td>2913(1)</td>
<td>-772(1)</td>
</tr>
<tr>
<td>C(07)</td>
<td>3510(2)</td>
<td>2068(1)</td>
<td>-924(1)</td>
</tr>
<tr>
<td>C(08)</td>
<td>4563(2)</td>
<td>2004(1)</td>
<td>-515(1)</td>
</tr>
<tr>
<td>C(09)</td>
<td>4997(2)</td>
<td>2743(1)</td>
<td>68(1)</td>
</tr>
<tr>
<td>C(10)</td>
<td>4319(1)</td>
<td>3570(1)</td>
<td>224(1)</td>
</tr>
<tr>
<td>C(11)</td>
<td>7564(2)</td>
<td>3271(1)</td>
<td>1620(1)</td>
</tr>
<tr>
<td>C(12)</td>
<td>8533(2)</td>
<td>3469(1)</td>
<td>1194(1)</td>
</tr>
<tr>
<td>C(13)</td>
<td>9596(2)</td>
<td>3426(2)</td>
<td>1632(1)</td>
</tr>
<tr>
<td>C(14)</td>
<td>9705(2)</td>
<td>3184(2)</td>
<td>2506(1)</td>
</tr>
<tr>
<td>C(15)</td>
<td>8747(2)</td>
<td>2975(2)</td>
<td>2933(1)</td>
</tr>
<tr>
<td>C(16)</td>
<td>7683(2)</td>
<td>3015(1)</td>
<td>2508(1)</td>
</tr>
<tr>
<td>C(17)</td>
<td>8439(2)</td>
<td>3767(1)</td>
<td>287(1)</td>
</tr>
<tr>
<td>N(18)</td>
<td>8399(2)</td>
<td>4026(2)</td>
<td>-422(1)</td>
</tr>
<tr>
<td>C(19)</td>
<td>6676(2)</td>
<td>2793(2)</td>
<td>3008(1)</td>
</tr>
<tr>
<td>O(20)</td>
<td>6166(1)</td>
<td>4778(1)</td>
<td>1947(1)</td>
</tr>
<tr>
<td>C(21)</td>
<td>3043(1)</td>
<td>1250(1)</td>
<td>-1491(1)</td>
</tr>
<tr>
<td>C(22)</td>
<td>2840(2)</td>
<td>334(1)</td>
<td>-1115(1)</td>
</tr>
<tr>
<td>C(23)</td>
<td>2379(2)</td>
<td>-449(2)</td>
<td>-1614(1)</td>
</tr>
<tr>
<td>C(24)</td>
<td>2126(2)</td>
<td>-320(1)</td>
<td>-2500(1)</td>
</tr>
<tr>
<td>C(25)</td>
<td>2353(2)</td>
<td>573(1)</td>
<td>-2882(1)</td>
</tr>
<tr>
<td>C(26)</td>
<td>2808(1)</td>
<td>1363(1)</td>
<td>-2398(1)</td>
</tr>
<tr>
<td>C(27)</td>
<td>3124(2)</td>
<td>168(2)</td>
<td>-194(1)</td>
</tr>
<tr>
<td>N(28)</td>
<td>3360(2)</td>
<td>-6(2)</td>
<td>525(1)</td>
</tr>
<tr>
<td>C(29)</td>
<td>3079(2)</td>
<td>2304(2)</td>
<td>-2853(1)</td>
</tr>
<tr>
<td>O(30)</td>
<td>1799(1)</td>
<td>2908(1)</td>
<td>-1196(1)</td>
</tr>
<tr>
<td>C(31)</td>
<td>5413(2)</td>
<td>5485(2)</td>
<td>2271(1)</td>
</tr>
<tr>
<td>C(32)</td>
<td>1139(2)</td>
<td>3773(2)</td>
<td>-1117(2)</td>
</tr>
<tr>
<td>O(33)</td>
<td>295(7)</td>
<td>-48(5)</td>
<td>505(8)</td>
</tr>
<tr>
<td>C(34)</td>
<td>550(6)</td>
<td>919(5)</td>
<td>941(7)</td>
</tr>
<tr>
<td>C(35)</td>
<td>962(13)</td>
<td>727(10)</td>
<td>1878(9)</td>
</tr>
<tr>
<td>O(43)</td>
<td>121(6)</td>
<td>-69(5)</td>
<td>213(6)</td>
</tr>
<tr>
<td>C(44)</td>
<td>374(9)</td>
<td>883(6)</td>
<td>537(8)</td>
</tr>
<tr>
<td>C(45)</td>
<td>802(9)</td>
<td>757(8)</td>
<td>1475(8)</td>
</tr>
</tbody>
</table>
Table 27. Bond lengths [Å] and angles [°] for C$_2$-50.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length/Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(01)−C(02)</td>
<td>1.371(3)</td>
</tr>
<tr>
<td>C(01)−C(09)</td>
<td>1.413(2)</td>
</tr>
<tr>
<td>C(02)−C(03)</td>
<td>1.432(3)</td>
</tr>
<tr>
<td>C(02)−C(11)</td>
<td>1.494(2)</td>
</tr>
<tr>
<td>C(03)−O(20)</td>
<td>1.365(2)</td>
</tr>
<tr>
<td>C(03)−C(04)</td>
<td>1.368(2)</td>
</tr>
<tr>
<td>C(04)−C(10)</td>
<td>1.421(2)</td>
</tr>
<tr>
<td>C(05)−C(06)</td>
<td>1.372(3)</td>
</tr>
<tr>
<td>C(05)−C(10)</td>
<td>1.414(3)</td>
</tr>
<tr>
<td>C(06)−O(30)</td>
<td>1.367(2)</td>
</tr>
<tr>
<td>C(06)−C(07)</td>
<td>1.430(3)</td>
</tr>
<tr>
<td>C(07)−C(08)</td>
<td>1.369(2)</td>
</tr>
<tr>
<td>C(07)−C(21)</td>
<td>1.495(2)</td>
</tr>
<tr>
<td>C(08)−C(09)</td>
<td>1.419(2)</td>
</tr>
<tr>
<td>C(09)−C(10)</td>
<td>1.419(2)</td>
</tr>
<tr>
<td>C(11)−C(12)</td>
<td>1.400(3)</td>
</tr>
<tr>
<td>C(11)−C(16)</td>
<td>1.403(3)</td>
</tr>
<tr>
<td>C(12)−C(13)</td>
<td>1.396(3)</td>
</tr>
<tr>
<td>C(12)−C(17)</td>
<td>1.446(3)</td>
</tr>
<tr>
<td>C(13)−C(14)</td>
<td>1.378(3)</td>
</tr>
<tr>
<td>C(14)−C(15)</td>
<td>1.392(3)</td>
</tr>
<tr>
<td>C(15)−C(16)</td>
<td>1.389(3)</td>
</tr>
<tr>
<td>C(16)−C(19)</td>
<td>1.508(3)</td>
</tr>
<tr>
<td>C(17)−N(18)</td>
<td>1.142(3)</td>
</tr>
<tr>
<td>C(18)−C(31)</td>
<td>1.432(2)</td>
</tr>
<tr>
<td>C(21)−C(22)</td>
<td>1.403(3)</td>
</tr>
<tr>
<td>C(21)−C(26)</td>
<td>1.407(3)</td>
</tr>
<tr>
<td>C(22)−C(23)</td>
<td>1.401(3)</td>
</tr>
<tr>
<td>C(22)−C(27)</td>
<td>1.445(3)</td>
</tr>
<tr>
<td>C(23)−C(24)</td>
<td>1.383(3)</td>
</tr>
<tr>
<td>C(24)−C(25)</td>
<td>1.385(3)</td>
</tr>
<tr>
<td>C(25)−C(26)</td>
<td>1.395(2)</td>
</tr>
<tr>
<td>C(26)−C(29)</td>
<td>1.505(3)</td>
</tr>
<tr>
<td>C(27)−N(28)</td>
<td>1.144(3)</td>
</tr>
<tr>
<td>C(30)−C(32)</td>
<td>1.428(3)</td>
</tr>
<tr>
<td>C(33)−C(34)</td>
<td>1.450(7)</td>
</tr>
<tr>
<td>O(34)−C(35)</td>
<td>1.509(9)</td>
</tr>
<tr>
<td>O(43)−O(43)$^#1$</td>
<td>0.72(2)</td>
</tr>
<tr>
<td>O(43)−O(44)</td>
<td>1.412(8)</td>
</tr>
<tr>
<td>O(43)−C(44)$^#1$</td>
<td>1.67(2)</td>
</tr>
<tr>
<td>C(02)−C(01)−C(09)</td>
<td>122.0(2)</td>
</tr>
<tr>
<td>C(01)−C(02)−C(03)</td>
<td>118.7(2)</td>
</tr>
<tr>
<td>O(20)−C(03)−C(04)</td>
<td>125.2(2)</td>
</tr>
<tr>
<td>C(03)−C(04)−C(02)</td>
<td>120.8(2)</td>
</tr>
<tr>
<td>C(06)−C(05)−C(10)</td>
<td>120.7(2)</td>
</tr>
<tr>
<td>O(30)−C(06)−C(07)</td>
<td>114.9(2)</td>
</tr>
<tr>
<td>C(08)−C(07)−C(06)</td>
<td>118.9(2)</td>
</tr>
<tr>
<td>C(06)−C(07)−C(21)</td>
<td>120.2(2)</td>
</tr>
<tr>
<td>C(01)−C(09)−C(08)</td>
<td>122.6(2)</td>
</tr>
<tr>
<td>C(01)−C(09)−C(10)</td>
<td>118.7(2)</td>
</tr>
<tr>
<td>O(08)−C(09)−C(10)</td>
<td>118.7(2)</td>
</tr>
<tr>
<td>O(05)−C(10)−C(04)</td>
<td>121.6(2)</td>
</tr>
<tr>
<td>C(12)−C(11)−C(16)</td>
<td>118.2(2)</td>
</tr>
<tr>
<td>C(13)−C(12)−C(17)</td>
<td>118.6(2)</td>
</tr>
<tr>
<td>C(14)−C(13)−C(12)</td>
<td>119.7(2)</td>
</tr>
<tr>
<td>C(16)−C(15)−C(14)</td>
<td>122.0(2)</td>
</tr>
<tr>
<td>C(15)−C(16)−C(19)</td>
<td>119.6(2)</td>
</tr>
<tr>
<td>N(18)−C(17)−C(12)</td>
<td>177.3(2)</td>
</tr>
<tr>
<td>C(22)−C(21)−C(26)</td>
<td>118.4(2)</td>
</tr>
<tr>
<td>C(26)−C(21)−C(07)</td>
<td>121.6(2)</td>
</tr>
<tr>
<td>C(23)−C(22)−C(27)</td>
<td>118.0(2)</td>
</tr>
<tr>
<td>C(23)−C(24)−C(22)</td>
<td>119.3(2)</td>
</tr>
<tr>
<td>C(24)−C(25)−C(26)</td>
<td>122.2(2)</td>
</tr>
<tr>
<td>C(25)−C(26)−C(29)</td>
<td>119.9(2)</td>
</tr>
<tr>
<td>N(28)−C(27)−C(22)</td>
<td>176.9(2)</td>
</tr>
<tr>
<td>C(06)−O(30)−C(32)</td>
<td>116.7(2)</td>
</tr>
<tr>
<td>O(33)−C(34)−C(35)</td>
<td>104.2(6)</td>
</tr>
<tr>
<td>O(43)−O(43)−C(44)$^#1$</td>
<td>56.6(12)</td>
</tr>
<tr>
<td>O(43)−C(44)−O(43)$^#1$</td>
<td>154.8(5)</td>
</tr>
<tr>
<td>C(45)−C(44)−O(43)$^#1$</td>
<td>131.4(7)</td>
</tr>
<tr>
<td>Terminals</td>
<td>Equation</td>
</tr>
<tr>
<td>-----------</td>
<td>----------</td>
</tr>
<tr>
<td>C(09) - C(01) - C(02) - C(03)</td>
<td>-1.1(3)</td>
</tr>
<tr>
<td>C(01) - C(02) - C(03) - O(20)</td>
<td>177.9(2)</td>
</tr>
<tr>
<td>C(01) - C(02) - C(03) - C(04)</td>
<td>-2.4(3)</td>
</tr>
<tr>
<td>O(20) - C(03) - C(04) - C(10)</td>
<td>-176.8(2)</td>
</tr>
<tr>
<td>C(10) - O(05) - C(06) - O(30)</td>
<td>176.9(2)</td>
</tr>
<tr>
<td>O(30) - C(06) - C(07) - C(08)</td>
<td>-179.1(2)</td>
</tr>
<tr>
<td>O(30) - C(06) - C(07) - C(21)</td>
<td>-1.6(2)</td>
</tr>
<tr>
<td>C(06) - O(07) - C(08) - O(09)</td>
<td>1.4(3)</td>
</tr>
<tr>
<td>C(02) - C(01) - O(09) - C(08)</td>
<td>-174.7(2)</td>
</tr>
<tr>
<td>C(07) - C(08) - C(09) - C(01)</td>
<td>177.9(2)</td>
</tr>
<tr>
<td>O(06) - C(05) - C(10) - C(09)</td>
<td>2.7(3)</td>
</tr>
<tr>
<td>C(01) - C(09) - C(10) - O(05)</td>
<td>-179.9(2)</td>
</tr>
<tr>
<td>C(01) - C(09) - C(10) - C(04)</td>
<td>-2.3(2)</td>
</tr>
<tr>
<td>C(03) - C(04) - C(10) - C(05)</td>
<td>176.5(2)</td>
</tr>
<tr>
<td>C(01) - C(02) - C(11) - C(12)</td>
<td>73.1(2)</td>
</tr>
<tr>
<td>C(01) - C(02) - C(11) - C(16)</td>
<td>-108.1(2)</td>
</tr>
<tr>
<td>C(16) - C(11) - C(12) - C(13)</td>
<td>-0.6(3)</td>
</tr>
<tr>
<td>C(16) - C(11) - C(12) - C(17)</td>
<td>-177.9(2)</td>
</tr>
<tr>
<td>C(11) - C(12) - C(13) - C(14)</td>
<td>-0.1(3)</td>
</tr>
<tr>
<td>C(12) - C(13) - C(14) - C(15)</td>
<td>0.8(3)</td>
</tr>
<tr>
<td>C(14) - C(15) - C(16) - C(11)</td>
<td>0.2(3)</td>
</tr>
<tr>
<td>C(12) - C(11) - C(16) - C(15)</td>
<td>0.5(3)</td>
</tr>
<tr>
<td>C(12) - C(11) - C(16) - C(19)</td>
<td>180.0(2)</td>
</tr>
<tr>
<td>C(13) - C(12) - C(17) - N(19)</td>
<td>-35(5)</td>
</tr>
<tr>
<td>C(04) - C(03) - O(20) - C(31)</td>
<td>12.2(2)</td>
</tr>
<tr>
<td>C(08) - C(07) - C(21) - C(22)</td>
<td>65.1(2)</td>
</tr>
<tr>
<td>C(08) - O(07) - C(21) - C(26)</td>
<td>-114.1(2)</td>
</tr>
<tr>
<td>C(26) - C(21) - C(22) - C(23)</td>
<td>-2.2(3)</td>
</tr>
<tr>
<td>C(26) - C(21) - C(22) - C(27)</td>
<td>176.7(2)</td>
</tr>
<tr>
<td>C(21) - C(22) - C(23) - C(24)</td>
<td>0.6(3)</td>
</tr>
<tr>
<td>C(22) - C(23) - C(24) - C(25)</td>
<td>1.3(3)</td>
</tr>
<tr>
<td>C(24) - C(25) - C(26) - C(21)</td>
<td>0.0(3)</td>
</tr>
<tr>
<td>C(22) - C(21) - C(26) - C(25)</td>
<td>1.9(2)</td>
</tr>
<tr>
<td>C(22) - C(21) - C(26) - C(29)</td>
<td>-175.8(2)</td>
</tr>
<tr>
<td>C(23) - C(22) - C(27) - N(28)</td>
<td>33(4)</td>
</tr>
<tr>
<td>O(43) - O(43) - C(44) - C(45)</td>
<td>174.8(13)</td>
</tr>
</tbody>
</table>

Symmetry transformations used to generate equivalent atoms:

#1  -x, -y, -z

C(44) #1 - O(43) - C(44) - O(43) #1 -0.001(5)
### Table 28. Anisotropic displacement parameters ($A^2 \times 10^3$) for $C_2\cdot50$.

<table>
<thead>
<tr>
<th></th>
<th>U11</th>
<th>U22</th>
<th>U33</th>
<th>U23</th>
<th>U13</th>
<th>U12</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(01)</td>
<td>20(1)</td>
<td>26(1)</td>
<td>25(1)</td>
<td>-2(1)</td>
<td>3(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(02)</td>
<td>22(1)</td>
<td>26(1)</td>
<td>22(1)</td>
<td>1(1)</td>
<td>2(1)</td>
<td>-1(1)</td>
</tr>
<tr>
<td>C(03)</td>
<td>25(1)</td>
<td>23(1)</td>
<td>21(1)</td>
<td>-2(1)</td>
<td>3(1)</td>
<td>-5(1)</td>
</tr>
<tr>
<td>C(04)</td>
<td>24(1)</td>
<td>22(1)</td>
<td>24(1)</td>
<td>-1(1)</td>
<td>4(1)</td>
<td>0(1)</td>
</tr>
<tr>
<td>C(05)</td>
<td>23(1)</td>
<td>24(1)</td>
<td>25(1)</td>
<td>-2(1)</td>
<td>4(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(06)</td>
<td>20(1)</td>
<td>29(1)</td>
<td>24(1)</td>
<td>-2(1)</td>
<td>1(1)</td>
<td>1(1)</td>
</tr>
<tr>
<td>C(07)</td>
<td>23(1)</td>
<td>26(1)</td>
<td>22(1)</td>
<td>-3(1)</td>
<td>3(1)</td>
<td>0(1)</td>
</tr>
<tr>
<td>C(08)</td>
<td>24(1)</td>
<td>26(1)</td>
<td>24(1)</td>
<td>-2(1)</td>
<td>3(1)</td>
<td>3(1)</td>
</tr>
<tr>
<td>C(09)</td>
<td>23(1)</td>
<td>26(1)</td>
<td>21(1)</td>
<td>-1(1)</td>
<td>2(1)</td>
<td>0(1)</td>
</tr>
<tr>
<td>C(10)</td>
<td>22(1)</td>
<td>24(1)</td>
<td>21(1)</td>
<td>0(1)</td>
<td>5(1)</td>
<td>-1(1)</td>
</tr>
<tr>
<td>C(11)</td>
<td>24(1)</td>
<td>22(1)</td>
<td>25(1)</td>
<td>-2(1)</td>
<td>1(1)</td>
<td>-1(1)</td>
</tr>
<tr>
<td>C(12)</td>
<td>24(1)</td>
<td>26(1)</td>
<td>27(1)</td>
<td>2(1)</td>
<td>0(1)</td>
<td>1(1)</td>
</tr>
<tr>
<td>C(13)</td>
<td>21(1)</td>
<td>41(1)</td>
<td>39(1)</td>
<td>6(1)</td>
<td>2(1)</td>
<td>-2(1)</td>
</tr>
<tr>
<td>C(14)</td>
<td>24(1)</td>
<td>45(1)</td>
<td>40(1)</td>
<td>10(1)</td>
<td>-7(1)</td>
<td>-2(1)</td>
</tr>
<tr>
<td>C(15)</td>
<td>34(1)</td>
<td>35(1)</td>
<td>30(1)</td>
<td>7(1)</td>
<td>-5(1)</td>
<td>-3(1)</td>
</tr>
<tr>
<td>C(16)</td>
<td>28(1)</td>
<td>26(1)</td>
<td>27(1)</td>
<td>2(1)</td>
<td>1(1)</td>
<td>-2(1)</td>
</tr>
<tr>
<td>C(17)</td>
<td>24(1)</td>
<td>33(1)</td>
<td>30(1)</td>
<td>1(1)</td>
<td>5(1)</td>
<td>3(1)</td>
</tr>
<tr>
<td>C(18)</td>
<td>41(1)</td>
<td>55(1)</td>
<td>30(1)</td>
<td>7(1)</td>
<td>7(1)</td>
<td>6(1)</td>
</tr>
<tr>
<td>N(19)</td>
<td>34(1)</td>
<td>46(1)</td>
<td>30(1)</td>
<td>8(1)</td>
<td>7(1)</td>
<td>-2(1)</td>
</tr>
<tr>
<td>O(20)</td>
<td>27(1)</td>
<td>26(1)</td>
<td>29(1)</td>
<td>-8(1)</td>
<td>-3(1)</td>
<td>-1(1)</td>
</tr>
<tr>
<td>C(21)</td>
<td>17(1)</td>
<td>25(1)</td>
<td>27(1)</td>
<td>-5(1)</td>
<td>0(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(22)</td>
<td>24(1)</td>
<td>29(1)</td>
<td>28(1)</td>
<td>-3(1)</td>
<td>-1(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(23)</td>
<td>33(1)</td>
<td>25(1)</td>
<td>38(1)</td>
<td>-2(1)</td>
<td>0(1)</td>
<td>-2(1)</td>
</tr>
<tr>
<td>C(24)</td>
<td>26(1)</td>
<td>31(1)</td>
<td>36(1)</td>
<td>-10(1)</td>
<td>-4(1)</td>
<td>0(1)</td>
</tr>
<tr>
<td>C(25)</td>
<td>24(1)</td>
<td>32(1)</td>
<td>26(1)</td>
<td>-6(1)</td>
<td>-3(1)</td>
<td>4(1)</td>
</tr>
<tr>
<td>C(26)</td>
<td>21(1)</td>
<td>27(1)</td>
<td>28(1)</td>
<td>-5(1)</td>
<td>2(1)</td>
<td>3(1)</td>
</tr>
<tr>
<td>C(27)</td>
<td>35(1)</td>
<td>29(1)</td>
<td>33(1)</td>
<td>0(1)</td>
<td>-2(1)</td>
<td>0(1)</td>
</tr>
<tr>
<td>N(28)</td>
<td>54(1)</td>
<td>46(1)</td>
<td>36(1)</td>
<td>5(1)</td>
<td>-1(1)</td>
<td>0(1)</td>
</tr>
<tr>
<td>C(29)</td>
<td>36(1)</td>
<td>30(1)</td>
<td>28(1)</td>
<td>-3(1)</td>
<td>2(1)</td>
<td>0(1)</td>
</tr>
<tr>
<td>O(30)</td>
<td>20(1)</td>
<td>33(1)</td>
<td>38(1)</td>
<td>-12(1)</td>
<td>-5(1)</td>
<td>5(1)</td>
</tr>
<tr>
<td>C(31)</td>
<td>30(1)</td>
<td>31(1)</td>
<td>34(1)</td>
<td>-12(1)</td>
<td>2(1)</td>
<td>-1(1)</td>
</tr>
<tr>
<td>C(32)</td>
<td>30(1)</td>
<td>51(1)</td>
<td>77(2)</td>
<td>-33(1)</td>
<td>-19(1)</td>
<td>10(1)</td>
</tr>
</tbody>
</table>

The anisotropic displacement factor exponent takes the form:

\[-2 \pi^2 \{ h^2 a^2 + \ldots + 2 h k a^* b^* U12 \} \]
Table 29. Hydrogen coordinates (× 10^4) and isotropic displacement parameters (Å^2 × 10^3) for C_{2}-50.

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>U(eq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(01)</td>
<td>6510(2)</td>
<td>2162(17)</td>
<td>408(15)</td>
<td>28</td>
</tr>
<tr>
<td>H(04)</td>
<td>4222(19)</td>
<td>4810(17)</td>
<td>944(15)</td>
<td>28</td>
</tr>
<tr>
<td>H(05)</td>
<td>2806(19)</td>
<td>4216(18)</td>
<td>-153(15)</td>
<td>29</td>
</tr>
<tr>
<td>H(08)</td>
<td>4960(2)</td>
<td>1426(18)</td>
<td>-608(14)</td>
<td>29</td>
</tr>
<tr>
<td>H(13)</td>
<td>10220(2)</td>
<td>3620(19)</td>
<td>1305(17)</td>
<td>40</td>
</tr>
<tr>
<td>H(14)</td>
<td>10460(2)</td>
<td>3200(2)</td>
<td>2864(17)</td>
<td>44</td>
</tr>
<tr>
<td>H(15)</td>
<td>8810(2)</td>
<td>2836(19)</td>
<td>3589(17)</td>
<td>40</td>
</tr>
<tr>
<td>H(19A)</td>
<td>6890(3)</td>
<td>2400(2)</td>
<td>3520(2)</td>
<td>55</td>
</tr>
<tr>
<td>H(19B)</td>
<td>6130(3)</td>
<td>2340(2)</td>
<td>2642(19)</td>
<td>55</td>
</tr>
<tr>
<td>H(19C)</td>
<td>6450(2)</td>
<td>3430(2)</td>
<td>3240(2)</td>
<td>55</td>
</tr>
<tr>
<td>H(23)</td>
<td>2230(2)</td>
<td>-1020(2)</td>
<td>-1305(17)</td>
<td>39</td>
</tr>
<tr>
<td>H(24)</td>
<td>1820(2)</td>
<td>-918(18)</td>
<td>-2882(16)</td>
<td>38</td>
</tr>
<tr>
<td>H(25)</td>
<td>2160(2)</td>
<td>619(18)</td>
<td>-3525(16)</td>
<td>33</td>
</tr>
<tr>
<td>H(29A)</td>
<td>3880(2)</td>
<td>2330(2)</td>
<td>-2809(17)</td>
<td>47</td>
</tr>
<tr>
<td>H(29B)</td>
<td>2850(2)</td>
<td>2910(2)</td>
<td>-2556(18)</td>
<td>47</td>
</tr>
<tr>
<td>H(29C)</td>
<td>2800(2)</td>
<td>2330(2)</td>
<td>-3405(18)</td>
<td>47</td>
</tr>
<tr>
<td>H(31A)</td>
<td>5260(2)</td>
<td>6020(2)</td>
<td>1849(18)</td>
<td>47</td>
</tr>
<tr>
<td>H(31B)</td>
<td>5750(2)</td>
<td>5730(2)</td>
<td>2838(19)</td>
<td>47</td>
</tr>
<tr>
<td>H(31C)</td>
<td>4770(3)</td>
<td>5190(2)</td>
<td>2415(18)</td>
<td>47</td>
</tr>
<tr>
<td>H(32A)</td>
<td>980(3)</td>
<td>3870(3)</td>
<td>-470(3)</td>
<td>81</td>
</tr>
<tr>
<td>H(32B)</td>
<td>420(3)</td>
<td>3510(3)</td>
<td>-1390(2)</td>
<td>81</td>
</tr>
<tr>
<td>H(32C)</td>
<td>1560(3)</td>
<td>4450(3)</td>
<td>-1350(2)</td>
<td>81</td>
</tr>
<tr>
<td>H(34A)</td>
<td>-125</td>
<td>1340</td>
<td>908</td>
<td>88</td>
</tr>
<tr>
<td>H(34B)</td>
<td>1136</td>
<td>1244</td>
<td>621</td>
<td>88</td>
</tr>
<tr>
<td>H(35A)</td>
<td>319</td>
<td>423</td>
<td>1550</td>
<td>238</td>
</tr>
<tr>
<td>H(35B)</td>
<td>1028</td>
<td>466</td>
<td>2476</td>
<td>238</td>
</tr>
<tr>
<td>H(35C)</td>
<td>1646</td>
<td>577</td>
<td>1591</td>
<td>238</td>
</tr>
<tr>
<td>H(44A)</td>
<td>875</td>
<td>1445</td>
<td>440</td>
<td>91</td>
</tr>
<tr>
<td>H(44B)</td>
<td>-419</td>
<td>1037</td>
<td>365</td>
<td>91</td>
</tr>
<tr>
<td>H(45A)</td>
<td>332</td>
<td>399</td>
<td>1864</td>
<td>119</td>
</tr>
<tr>
<td>H(45B)</td>
<td>966</td>
<td>1413</td>
<td>1715</td>
<td>119</td>
</tr>
<tr>
<td>H(45C)</td>
<td>1504</td>
<td>399</td>
<td>1426</td>
<td>119</td>
</tr>
</tbody>
</table>
10.2. X-Ray Crystal Structure Data of Cavitand 68·2 CH$_2$Cl$_2$

The cavitand 68 was crystallized from CH$_2$Cl$_2$ and its geometry was determined by X-ray crystalographic analysis.

From a crystal (CH$_2$Cl$_2$) of size $0.60 \times 0.60 \times 0.15$ mm, 2913 reflexions were measured on Syntex P21 Diffractometer with MoK\textalpha radiation (graphite monochromator, $\lambda = 0.71073$ Å). The structure was solved by Patterson method with SHELXTL.
Figure 47. Top view ORTEP Plot of the X-ray crystal structure of $68 \cdot 2 \text{CH}_2\text{Cl}_2$ solved and analyzed by Prof. V. Gramlich (ETH Zürich). The atom numbering is arbitrary. Bottom part deleted.

H-atoms were calculated at idealized positions and refined with constrained isotropic displacement parameters. Final $R$ values and experimental data see Table 30.
Table 30. Crystal data and structure refinement for \(68 \cdot 2 \text{CH}_2\text{Cl}_2\).

<table>
<thead>
<tr>
<th>Identification code</th>
<th>L116</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C(71) H(66) Br(4) Cl(6) O(8)</td>
</tr>
<tr>
<td>Formula weight</td>
<td>1579.58</td>
</tr>
<tr>
<td>Temperature</td>
<td>293(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>(P2(1)/c)</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>(a = 16.853(9)) Å, (\alpha = 90) deg.</td>
</tr>
<tr>
<td></td>
<td>(b = 16.312(10)) Å, (\beta = 92.97(5)) deg.</td>
</tr>
<tr>
<td></td>
<td>(c = 24.37(2)) Å, (\gamma = 90) deg.</td>
</tr>
<tr>
<td>Volume</td>
<td>6691(7) Å(^3)</td>
</tr>
<tr>
<td>(Z)</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.568 Mg/m(^3)</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>2.701 mm(^{-1})</td>
</tr>
<tr>
<td>(F(000))</td>
<td>3192</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.6 x 0.6 x 0.15 mm</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>1.67 to 20.04 deg.</td>
</tr>
<tr>
<td>Index ranges</td>
<td>(-5 \leq h \leq 5, 0 \leq k \leq 15, 0 \leq l \leq 23)</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>2913</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>2913 [(R(\text{int}) = 0.0000)]</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Integration</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>.662 and .321</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on (F^2)</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>2913 / 1068 / 746</td>
</tr>
<tr>
<td>Goodness-of-fit on (F^2)</td>
<td>0.893</td>
</tr>
<tr>
<td>Final R indices [(I &gt; 2\sigma(I))]</td>
<td>(R_1 = 0.0361, \ wR_2 = 0.0764)</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>(R_1 = 0.0601, \ wR_2 = 0.0813)</td>
</tr>
<tr>
<td>Extinction coefficient</td>
<td>0.00093(10)</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.343 and -0.342 e.A(^{-3})</td>
</tr>
</tbody>
</table>
Table 31. Atomic coordinates ($\times 10^5$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for 68.2 CH$_2$Cl$_2$. $U_{eq}$ is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor.

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>$U_{eq}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(101)</td>
<td>2532 (8)</td>
<td>-116 (6)</td>
<td>-11 (4)</td>
<td>47 (6)</td>
</tr>
<tr>
<td>C(102)</td>
<td>1765 (9)</td>
<td>176 (6)</td>
<td>-326 (5)</td>
<td>69 (5)</td>
</tr>
<tr>
<td>C(103)</td>
<td>1193 (5)</td>
<td>-506 (4)</td>
<td>-454 (4)</td>
<td>51 (5)</td>
</tr>
<tr>
<td>C(104)</td>
<td>681 (7)</td>
<td>-766 (6)</td>
<td>-59 (3)</td>
<td>82 (6)</td>
</tr>
<tr>
<td>C(105)</td>
<td>158 (5)</td>
<td>-1409 (6)</td>
<td>-175 (4)</td>
<td>116 (6)</td>
</tr>
<tr>
<td>C(106)</td>
<td>146 (5)</td>
<td>-1792 (4)</td>
<td>-685 (5)</td>
<td>107 (7)</td>
</tr>
<tr>
<td>C(107)</td>
<td>657 (7)</td>
<td>-1531 (5)</td>
<td>-1079 (3)</td>
<td>87 (6)</td>
</tr>
<tr>
<td>C(108)</td>
<td>1181 (5)</td>
<td>-889 (6)</td>
<td>-963 (3)</td>
<td>76 (6)</td>
</tr>
<tr>
<td>C(251)</td>
<td>4462 (8)</td>
<td>-2191 (5)</td>
<td>812 (3)</td>
<td>40 (5)</td>
</tr>
<tr>
<td>C(252)</td>
<td>4768 (8)</td>
<td>-3017 (5)</td>
<td>971 (4)</td>
<td>61 (5)</td>
</tr>
<tr>
<td>C(253)</td>
<td>4230 (5)</td>
<td>-3701 (4)</td>
<td>774 (4)</td>
<td>53 (5)</td>
</tr>
<tr>
<td>C(254)</td>
<td>3579 (6)</td>
<td>-3927 (5)</td>
<td>1067 (2)</td>
<td>64 (6)</td>
</tr>
<tr>
<td>C(255)</td>
<td>3061 (4)</td>
<td>-4530 (6)</td>
<td>86 (6)</td>
<td>75 (6)</td>
</tr>
<tr>
<td>C(256)</td>
<td>3195 (5)</td>
<td>-4905 (4)</td>
<td>363 (4)</td>
<td>54 (6)</td>
</tr>
<tr>
<td>C(257)</td>
<td>3847 (6)</td>
<td>-4679 (5)</td>
<td>70 (2)</td>
<td>94 (6)</td>
</tr>
<tr>
<td>C(258)</td>
<td>4364 (4)</td>
<td>-4077 (5)</td>
<td>276 (3)</td>
<td>80 (5)</td>
</tr>
<tr>
<td>C(271)</td>
<td>2908 (9)</td>
<td>-2354 (6)</td>
<td>2464 (4)</td>
<td>57 (5)</td>
</tr>
<tr>
<td>C(272)</td>
<td>2242 (9)</td>
<td>-2667 (6)</td>
<td>2803 (4)</td>
<td>65 (6)</td>
</tr>
<tr>
<td>C(273)</td>
<td>1788 (8)</td>
<td>-3395 (5)</td>
<td>2534 (3)</td>
<td>59 (6)</td>
</tr>
<tr>
<td>C(274)</td>
<td>2202 (9)</td>
<td>-4090 (7)</td>
<td>2384 (3)</td>
<td>70 (6)</td>
</tr>
<tr>
<td>C(275)</td>
<td>1796 (7)</td>
<td>-4748 (4)</td>
<td>2139 (3)</td>
<td>75 (6)</td>
</tr>
<tr>
<td>C(276)</td>
<td>976 (7)</td>
<td>-4710 (5)</td>
<td>2045 (3)</td>
<td>73 (6)</td>
</tr>
<tr>
<td>C(277)</td>
<td>562 (5)</td>
<td>-4015 (8)</td>
<td>2195 (4)</td>
<td>88 (6)</td>
</tr>
<tr>
<td>C(278)</td>
<td>969 (8)</td>
<td>-3358 (5)</td>
<td>2440 (3)</td>
<td>77 (6)</td>
</tr>
<tr>
<td>C(291)</td>
<td>857 (8)</td>
<td>-299 (6)</td>
<td>1570 (4)</td>
<td>45 (5)</td>
</tr>
<tr>
<td>C(292)</td>
<td>347 (9)</td>
<td>-827 (6)</td>
<td>1915 (4)</td>
<td>64 (5)</td>
</tr>
<tr>
<td>C(293)</td>
<td>-110 (8)</td>
<td>-1463 (5)</td>
<td>1572 (3)</td>
<td>50 (5)</td>
</tr>
<tr>
<td>C(294)</td>
<td>328 (5)</td>
<td>-2128 (7)</td>
<td>1398 (4)</td>
<td>85 (6)</td>
</tr>
<tr>
<td>C(295)</td>
<td>-40 (7)</td>
<td>-2736 (5)</td>
<td>1076 (4)</td>
<td>114 (7)</td>
</tr>
<tr>
<td>C(296)</td>
<td>-846 (8)</td>
<td>-2677 (5)</td>
<td>927 (3)</td>
<td>88 (6)</td>
</tr>
<tr>
<td>C(297)</td>
<td>-1283 (5)</td>
<td>-2012 (8)</td>
<td>1101 (4)</td>
<td>85 (6)</td>
</tr>
<tr>
<td>C(298)</td>
<td>-915 (8)</td>
<td>-1405 (5)</td>
<td>1423 (4)</td>
<td>74 (6)</td>
</tr>
<tr>
<td>Br(4)</td>
<td>5966 (1)</td>
<td>1548 (1)</td>
<td>725 (1)</td>
<td>62 (1)</td>
</tr>
<tr>
<td>Br(1)</td>
<td>1645 (1)</td>
<td>3357 (1)</td>
<td>966 (1)</td>
<td>72 (1)</td>
</tr>
<tr>
<td>Br(3)</td>
<td>6508 (1)</td>
<td>-1584 (1)</td>
<td>3055 (1)</td>
<td>66 (1)</td>
</tr>
<tr>
<td>Br(2)</td>
<td>2788 (1)</td>
<td>1158 (1)</td>
<td>3788 (1)</td>
<td>85 (1)</td>
</tr>
<tr>
<td>C(17A)</td>
<td>2391 (10)</td>
<td>1879 (6)</td>
<td>649 (5)</td>
<td>49 (5)</td>
</tr>
<tr>
<td>C(32)</td>
<td>5157 (12)</td>
<td>723 (8)</td>
<td>674 (4)</td>
<td>27 (6)</td>
</tr>
<tr>
<td>O(17)</td>
<td>4807 (6)</td>
<td>-1612 (4)</td>
<td>3392 (2)</td>
<td>51 (4)</td>
</tr>
<tr>
<td>C(26A)</td>
<td>4103 (14)</td>
<td>-1520 (7)</td>
<td>2505 (5)</td>
<td>32 (6)</td>
</tr>
<tr>
<td>O(7)</td>
<td>2668 (7)</td>
<td>2342 (4)</td>
<td>224 (3)</td>
<td>47 (4)</td>
</tr>
<tr>
<td>C(31)</td>
<td>3979 (11)</td>
<td>-423 (7)</td>
<td>666 (4)</td>
<td>28 (6)</td>
</tr>
<tr>
<td>O(12)</td>
<td>1602 (6)</td>
<td>1361 (4)</td>
<td>2803 (2)</td>
<td>54 (4)</td>
</tr>
<tr>
<td>O(4)</td>
<td>4288 (6)</td>
<td>1696 (4)</td>
<td>254 (2)</td>
<td>50 (4)</td>
</tr>
<tr>
<td>O(19)</td>
<td>6371 (9)</td>
<td>-1582 (6)</td>
<td>1797 (4)</td>
<td>51 (6)</td>
</tr>
<tr>
<td>C(1)</td>
<td>3018 (11)</td>
<td>611 (6)</td>
<td>245 (4)</td>
<td>33 (5)</td>
</tr>
<tr>
<td>C(23)</td>
<td>5325 (14)</td>
<td>-72 (9)</td>
<td>845 (5)</td>
<td>34 (6)</td>
</tr>
<tr>
<td>C(16)</td>
<td>4906 (10)</td>
<td>-874 (7)</td>
<td>3702 (4)</td>
<td>64 (6)</td>
</tr>
<tr>
<td>C(1A)</td>
<td>2552 (9)</td>
<td>1037 (6)</td>
<td>669 (4)</td>
<td>44 (5)</td>
</tr>
<tr>
<td>O(9)</td>
<td>1033 (6)</td>
<td>2115 (4)</td>
<td>1792 (3)</td>
<td>52 (4)</td>
</tr>
<tr>
<td>O(14)</td>
<td>3542 (9)</td>
<td>-511 (5)</td>
<td>3606 (3)</td>
<td>47 (5)</td>
</tr>
<tr>
<td>C(27A)</td>
<td>2871 (9)</td>
<td>-837 (6)</td>
<td>2741 (4)</td>
<td>37 (5)</td>
</tr>
<tr>
<td>C(3)</td>
<td>4445 (14)</td>
<td>941 (8)</td>
<td>468 (5)</td>
<td>37 (6)</td>
</tr>
<tr>
<td>C(29)</td>
<td>1300 (8)</td>
<td>391 (6)</td>
<td>1877 (4)</td>
<td>39 (5)</td>
</tr>
<tr>
<td>C(21)</td>
<td>6379 (8)</td>
<td>-125 (6)</td>
<td>1549 (4)</td>
<td>59 (5)</td>
</tr>
<tr>
<td>C(10)</td>
<td>1392 (9)</td>
<td>2550 (6)</td>
<td>2260 (4)</td>
<td>61 (5)</td>
</tr>
</tbody>
</table>
Chapter 10

C(11) 1993 (9) 2068 (6) 2598 (4) 62 (5)
C(29A) 1718 (9) 930 (6) 1477 (4) 46 (5)
C(13A) 2991 (10) -291 (7) 3179 (4) 45 (5)
C(28A) 1892 (9) 119 (6) 2333 (4) 40 (4)
C(13) 2564 (10) 440 (6) 3186 (4) 46 (5)
C(18) 5573 (13) -1510 (8) 2605 (6) 39 (7)
C(30) 2210 (8) 604 (6) 1089 (4) 43 (5)
C(8A) 1567 (10) 1782 (7) 1442 (5) 52 (5)
C(28) 2316 (9) -606 (6) 2328 (4) 45 (5)
C(5) 4029 (9) 2299 (7) 625 (4) 58 (6)
C(20) 6820 (9) -865 (7) 1771 (4) 60 (5)
C(25A) 4954 (16) -1495 (8) 1695 (5) 37 (6)
C(25) 4983 (8) -1491 (5) 1074 (3) 35 (5)
C(6) 3358 (11) 2798 (7) 367 (5) 52 (6)
C(18A) 5634 (17) -1504 (9) 2018 (6) 40 (7)
C(8) 1913 (9) 2232 (6) 1030 (5) 50 (5)
C(26) 4213 (12) -1488 (7) 1932 (5) 34 (7)
O(22) 6127 (8) -273 (5) 987 (3) 51 (5)
C(15) 4314 (12) -220 (7) 3536 (5) 50 (7)
C(17A) 4851 (16) -1531 (9) 2821 (5) 40 (6)
C(12A) 2042 (10) 656 (7) 2775 (5) 54 (5)
C(5) 3926 (3) 788 (2) 1961 (1) 129 (3)
C(14) 4760 (14) -644 (7) 945 (4) 29 (6)
C(27) 3341 (12) -1633 (8) 2747 (5) 40 (7)
C(2) 3827 (13) 363 (8) 464 (4) 37 (6)
C(6) 5397 (4) 1052 (2) 2587 (1) 129 (3)
C(3C) 4613 (10) 1429 (7) 2176 (6) 155 (9)
C(21) 2195 (5) -2276 (5) 683 (4) 332 (5)
C(3) -759 (6) -6034 (5) 1400 (3) 370 (6)
C(4) -604 (8) -5124 (7) 484 (6) 586 (9)
C(2C) -1258 (21) -5535 (27) 816 (15) 583 (28)
C(1) 2483 (6) -2885 (5) -373 (4) 394 (6)
C(1C) 1768 (20) -3001 (19) 217 (11) 482 (29)

* crystal decomposed; data set incomplete; refinement restrained
  anisotropic (SHELX93 ISOR and SIMU restraints)
### Table 32.
Bond lengths [Å] and angles [°] for 68 2 CH₂Cl₂.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length [Å]</th>
<th>Angle [°]</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(101)−C(102)</td>
<td>1.544(14)</td>
<td></td>
</tr>
<tr>
<td>C(101)−C(1)</td>
<td>1.554(13)</td>
<td></td>
</tr>
<tr>
<td>C(102)−C(103)</td>
<td>1.494(12)</td>
<td></td>
</tr>
<tr>
<td>C(103)−C(108)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(103)−C(104)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(104)−C(105)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(105)−C(106)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(106)−C(107)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(107)−C(108)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(251)−C(252)</td>
<td>1.486(11)</td>
<td></td>
</tr>
<tr>
<td>C(251)−C(25)</td>
<td>1.556(12)</td>
<td></td>
</tr>
<tr>
<td>C(252)−C(253)</td>
<td>1.500(11)</td>
<td></td>
</tr>
<tr>
<td>C(253)−C(254)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(253)−C(258)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(254)−C(255)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(255)−C(256)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(256)−C(257)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(257)−C(258)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(271)−C(272)</td>
<td>1.52(2)</td>
<td></td>
</tr>
<tr>
<td>C(271)−C(27)</td>
<td>1.53(2)</td>
<td></td>
</tr>
<tr>
<td>C(272)−C(273)</td>
<td>1.540(12)</td>
<td></td>
</tr>
<tr>
<td>C(273)−C(278)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(273)−C(274)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(274)−C(275)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(275)−C(276)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(276)−C(277)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(277)−C(278)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(291)−C(292)</td>
<td>1.504(13)</td>
<td></td>
</tr>
<tr>
<td>C(291)−C(29)</td>
<td>1.525(12)</td>
<td></td>
</tr>
<tr>
<td>C(292)−C(293)</td>
<td>1.518(11)</td>
<td></td>
</tr>
<tr>
<td>C(293)−C(294)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(293)−C(298)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(294)−C(295)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(295)−C(296)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(296)−C(297)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>C(297)−C(298)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>Br(4)−C(32)</td>
<td>1.91(2)</td>
<td></td>
</tr>
<tr>
<td>Br(1)−C(8)</td>
<td>1.893(10)</td>
<td></td>
</tr>
<tr>
<td>Br(3)−C(18)</td>
<td>1.88(2)</td>
<td></td>
</tr>
<tr>
<td>Br(2)−C(13)</td>
<td>1.901(9)</td>
<td></td>
</tr>
<tr>
<td>C(7A)−C(8)</td>
<td>1.38(2)</td>
<td></td>
</tr>
<tr>
<td>C(7A)−O(7)</td>
<td>1.382(13)</td>
<td></td>
</tr>
<tr>
<td>C(7A)−C(1A)</td>
<td>1.401(12)</td>
<td></td>
</tr>
<tr>
<td>C(32)−C(3)</td>
<td>1.33(2)</td>
<td></td>
</tr>
<tr>
<td>C(32)−C(23)</td>
<td>1.39(2)</td>
<td></td>
</tr>
<tr>
<td>O(17)−C(17A)</td>
<td>1.404(13)</td>
<td></td>
</tr>
<tr>
<td>O(16)−C(16)</td>
<td>1.427(10)</td>
<td></td>
</tr>
<tr>
<td>C(26A)−C(26)</td>
<td>1.42(2)</td>
<td></td>
</tr>
<tr>
<td>C(26A)−C(17A)</td>
<td>1.44(3)</td>
<td></td>
</tr>
<tr>
<td>C(26A)−C(27)</td>
<td>1.45(2)</td>
<td></td>
</tr>
<tr>
<td>O(7)−C(6)</td>
<td>1.41(2)</td>
<td></td>
</tr>
<tr>
<td>C(31)−C(2)</td>
<td>1.392(14)</td>
<td></td>
</tr>
<tr>
<td>C(31)−C(24)</td>
<td>1.41(2)</td>
<td></td>
</tr>
<tr>
<td>O(12)−C(12A)</td>
<td>1.372(14)</td>
<td></td>
</tr>
<tr>
<td>O(12)−C(11)</td>
<td>1.431(12)</td>
<td></td>
</tr>
<tr>
<td>O(4)−C(3)</td>
<td>1.358(13)</td>
<td></td>
</tr>
<tr>
<td>O(4)−C(5)</td>
<td>1.420(11)</td>
<td></td>
</tr>
<tr>
<td>O(19)−C(18A)</td>
<td>1.38(3)</td>
<td></td>
</tr>
<tr>
<td>O(19)−C(20)</td>
<td>1.39(2)</td>
<td></td>
</tr>
<tr>
<td>C(1)−C(1A)</td>
<td>1.50(2)</td>
<td></td>
</tr>
<tr>
<td>C(1)−C(2)</td>
<td>1.49(2)</td>
<td></td>
</tr>
<tr>
<td>C(23)−C(24)</td>
<td>1.33(3)</td>
<td></td>
</tr>
</tbody>
</table>
C (23) – O (22)  1.42 (2)
C (16) – C (15)  1.50 (2)
C (1A) – C (30)  1.394 (13)
O (9) – C (8A)  1.383 (14)
O (9) – C (10)  1.448 (11)
O (14) – C (15)  1.40 (2)
O (14) – C (13A)  1.41 (2)
C (27A) – C (28)  1.391 (14)
C (27A) – C (13A)  1.395 (12)
C (27A) – C (27)  1.52 (2)
C (3) – C (2)  1.40 (2)
C (29) – C (29A)  1.515 (14)
C (29) – C (29A)  1.520 (14)
C (21) – O (22)  1.434 (11)
C (21) – C (20)  1.502 (13)
C (10) – C (11)  1.496 (13)
C (29A) – C (30)  1.39 (2)
C (29A) – C (8A)  1.414 (13)
C (13A) – C (13)  1.39 (2)
C (28A) – C (28)  1.382 (14)
C (28A) – C (12A)  1.401 (13)
C (13) – C (12A)  1.34 (2)
C (18) – C (17A)  1.35 (3)
C (18) – C (18A)  1.44 (2)
C (8A) – C (8)  1.40 (2)
C (5) – C (6)  1.50 (2)
C (25A) – C (18A)  1.36 (3)
C (25A) – C (26)  1.40 (3)
C (25A) – C (25)  1.517 (13)
C (25) – C (24)  1.528 (14)
Cl (5) – C (3C)  1.613 (13)
Cl (6) – C (3C)  1.729 (13)
Cl (1) – C (1C)  1.77 (2)
Cl (3) – C (2C)  1.81 (3)
Cl (4) – C (2C)  1.55 (3)
Cl (2) – C (1C)  1.93 (3)

C (102) – C (101) – C (1)  112.0 (10)
C (103) – C (102) – C (101)  112.8 (9)
C (108) – C (103) – C (104)  120.0
C (108) – C (103) – C (102)  120.0 (9)
C (104) – C (103) – C (102)  120.0 (9)
C (105) – C (104) – C (103)  120.0
C (104) – C (105) – C (106)  120.0
C (107) – C (106) – C (105)  120.0
C (106) – C (107) – C (108)  120.0
C (103) – C (108) – C (107)  120.0
C (252) – C (251) – C (25)  112.2 (9)
C (251) – C (252) – C (253)  113.3 (10)
C (254) – C (253) – C (258)  120.0
C (254) – C (253) – C (252)  121.0 (9)
C (258) – C (253) – C (252)  119.0 (9)
C (253) – C (254) – C (255)  120.0
C (256) – C (255) – C (254)  120.0
C (255) – C (256) – C (257)  120.0
C (258) – C (257) – C (256)  120.0
C (257) – C (258) – C (253)  120.0
C (272) – C (271) – C (27)  111.3 (11)
C (271) – C (272) – C (273)  113.2 (9)
C (278) – C (273) – C (274)  120.0
C (278) – C (272) – C (272)  120.2 (10)
C (274) – C (273) – C (272)  119.8 (11)
C (275) – C (274) – C (273)  120.0
C (276) – C (275) – C (274)  120.0
C (277) – C (276) – C (275)  120.0
C (278) – C (277) – C (276)  120.0
C (277) – C (278) – C (273)  120.0
C (292) – C (291) – C (29)  115.3 (9)
<table>
<thead>
<tr>
<th>Bond</th>
<th>Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(291) - C(292) - C(293)</td>
<td>111.8</td>
</tr>
<tr>
<td>C(294) - C(293) - C(298)</td>
<td>120.0</td>
</tr>
<tr>
<td>C(294) - C(293) - C(292)</td>
<td>116.1</td>
</tr>
<tr>
<td>C(298) - C(293) - C(292)</td>
<td>123.9</td>
</tr>
<tr>
<td>C(293) - C(294) - C(295)</td>
<td>120.0</td>
</tr>
<tr>
<td>C(296) - C(295) - C(294)</td>
<td>120.0</td>
</tr>
<tr>
<td>C(295) - C(296) - C(297)</td>
<td>120.0</td>
</tr>
<tr>
<td>C(298) - C(297) - C(296)</td>
<td>120.0</td>
</tr>
<tr>
<td>C(297) - C(298) - C(293)</td>
<td>120.0</td>
</tr>
<tr>
<td>C(8) - C(7A) - O(7)</td>
<td>120.4</td>
</tr>
<tr>
<td>C(8) - C(7A) - C(1A)</td>
<td>120.2</td>
</tr>
<tr>
<td>O(7) - C(7A) - C(1A)</td>
<td>119.2</td>
</tr>
<tr>
<td>C(3) - C(32) - C(23)</td>
<td>122.2</td>
</tr>
<tr>
<td>C(3) - C(32) - Br(4)</td>
<td>117.6</td>
</tr>
<tr>
<td>C(23) - C(32) - Br(4)</td>
<td>120.2</td>
</tr>
<tr>
<td>C(17A) - O(17) - C(16)</td>
<td>115.8</td>
</tr>
<tr>
<td>C(26) - C(26A) - C(17A)</td>
<td>112.2</td>
</tr>
<tr>
<td>C(26) - C(26A) - C(27)</td>
<td>125.2</td>
</tr>
<tr>
<td>C(17A) - C(26A) - C(27)</td>
<td>123.1</td>
</tr>
<tr>
<td>C(7A) - O(7) - C(6)</td>
<td>114.2</td>
</tr>
<tr>
<td>C(2) - C(31) - C(24)</td>
<td>120.2</td>
</tr>
<tr>
<td>C(12A) - O(12) - C(11)</td>
<td>113.4</td>
</tr>
<tr>
<td>C(3) - O(4) - C(5)</td>
<td>116.3</td>
</tr>
<tr>
<td>C(18A) - O(19) - C(20)</td>
<td>116.1</td>
</tr>
<tr>
<td>C(1A) - C(1) - C(2)</td>
<td>112.3</td>
</tr>
<tr>
<td>C(1A) - C(1) - C(101)</td>
<td>110.3</td>
</tr>
<tr>
<td>C(2) - C(1) - C(101)</td>
<td>112.9</td>
</tr>
<tr>
<td>C(24) - C(23) - C(32)</td>
<td>121.2</td>
</tr>
<tr>
<td>C(24) - C(23) - O(22)</td>
<td>121.2</td>
</tr>
<tr>
<td>C(32) - C(23) - O(22)</td>
<td>118.2</td>
</tr>
<tr>
<td>O(17) - C(16) - C(15)</td>
<td>113.5</td>
</tr>
<tr>
<td>C(30) - C(1A) - C(7A)</td>
<td>115.8</td>
</tr>
<tr>
<td>C(30) - C(1A) - C(1)</td>
<td>121.5</td>
</tr>
<tr>
<td>C(7A) - C(1A) - C(1)</td>
<td>122.6</td>
</tr>
<tr>
<td>C(8A) - O(9) - C(10)</td>
<td>114.7</td>
</tr>
<tr>
<td>C(15) - O(14) - C(13A)</td>
<td>113.9</td>
</tr>
<tr>
<td>C(28) - C(27A) - C(13A)</td>
<td>116.5</td>
</tr>
<tr>
<td>C(28) - C(27A) - C(27)</td>
<td>124.7</td>
</tr>
<tr>
<td>C(13A) - C(27A) - C(27)</td>
<td>118.9</td>
</tr>
<tr>
<td>C(32) - C(3) - O(4)</td>
<td>123.2</td>
</tr>
<tr>
<td>(32) - C(3) - C(2)</td>
<td>118.6</td>
</tr>
<tr>
<td>O(4) - C(3) - C(2)</td>
<td>119.2</td>
</tr>
<tr>
<td>C(29A) - C(29) - C(28A)</td>
<td>109.3</td>
</tr>
<tr>
<td>C(29A) - C(29) - C(291)</td>
<td>110.2</td>
</tr>
<tr>
<td>C(28A) - C(29) - C(291)</td>
<td>115.4</td>
</tr>
<tr>
<td>O(22) - C(21) - C(20)</td>
<td>108.9</td>
</tr>
<tr>
<td>O(9) - C(10) - C(11)</td>
<td>114.9</td>
</tr>
<tr>
<td>O(12) - C(11) - C(10)</td>
<td>107.7</td>
</tr>
<tr>
<td>C(30) - C(29A) - C(8A)</td>
<td>116.5</td>
</tr>
<tr>
<td>C(30) - C(29A) - C(29)</td>
<td>121.8</td>
</tr>
<tr>
<td>C(8A) - C(29A) - C(29)</td>
<td>121.5</td>
</tr>
<tr>
<td>C(13) - C(13A) - C(27A)</td>
<td>120.0</td>
</tr>
<tr>
<td>C(13) - C(13A) - O(14)</td>
<td>122.1</td>
</tr>
<tr>
<td>C(27A) - C(13A) - O(14)</td>
<td>117.8</td>
</tr>
<tr>
<td>C(28) - C(28A) - C(12A)</td>
<td>118.0</td>
</tr>
<tr>
<td>C(28) - C(28A) - C(29)</td>
<td>124.3</td>
</tr>
<tr>
<td>C(12A) - C(28A) - C(29)</td>
<td>117.7</td>
</tr>
<tr>
<td>C(12A) - C(13) - C(13A)</td>
<td>122.3</td>
</tr>
<tr>
<td>C(12A) - C(13) - Br(2)</td>
<td>120.6</td>
</tr>
<tr>
<td>C(13A) - C(13) - Br(2)</td>
<td>117.0</td>
</tr>
<tr>
<td>C(17A) - C(18) - C(18A)</td>
<td>120.2</td>
</tr>
<tr>
<td>C(17A) - C(18) - Br(3)</td>
<td>121.1</td>
</tr>
<tr>
<td>C(18A) - C(18) - Br(3)</td>
<td>119.2</td>
</tr>
<tr>
<td>C(29A) - C(30) - C(1A)</td>
<td>126.0</td>
</tr>
<tr>
<td>O(9) - C(8A) - C(8)</td>
<td>123.1</td>
</tr>
<tr>
<td>O(9) - C(8A) - C(29A)</td>
<td>118.0</td>
</tr>
<tr>
<td>C(8) - C(8A) - C(29A)</td>
<td>118.7</td>
</tr>
<tr>
<td>C(28A) - C(28) - C(27A)</td>
<td>123.6</td>
</tr>
<tr>
<td>Bond</td>
<td>Angle (°)</td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
</tr>
<tr>
<td>C(4) - C(5) - C(6)</td>
<td>110.9 (9)</td>
</tr>
<tr>
<td>O(19) - C(20) - C(21)</td>
<td>115.5 (13)</td>
</tr>
<tr>
<td>C(18A) - C(25A) - C(26)</td>
<td>120.2 (13)</td>
</tr>
<tr>
<td>C(18A) - C(25A) - C(25)</td>
<td>121 (2)</td>
</tr>
<tr>
<td>C(26) - C(25A) - C(25)</td>
<td>119 (2)</td>
</tr>
<tr>
<td>C(25A) - C(25) - C(24)</td>
<td>110.3 (9)</td>
</tr>
<tr>
<td>C(25A) - C(25) - C(251)</td>
<td>111.0 (10)</td>
</tr>
<tr>
<td>C(24) - C(25) - C(251)</td>
<td>113.1 (10)</td>
</tr>
<tr>
<td>O(7) - C(6) - C(5)</td>
<td>114.3 (10)</td>
</tr>
<tr>
<td>C(25A) - C(18A) - O(19)</td>
<td>121.6 (14)</td>
</tr>
<tr>
<td>C(25A) - C(18A) - C(18)</td>
<td>118 (2)</td>
</tr>
<tr>
<td>O(15) - C(18A) - C(18)</td>
<td>120 (2)</td>
</tr>
<tr>
<td>C(7A) - C(8) - C(8A)</td>
<td>122.8 (10)</td>
</tr>
<tr>
<td>C(7A) - C(8) - Br(1)</td>
<td>119.5 (9)</td>
</tr>
<tr>
<td>C(8A) - C(8) - Br(1)</td>
<td>117.5 (11)</td>
</tr>
<tr>
<td>C(25A) - C(26) - C(26A)</td>
<td>125 (2)</td>
</tr>
<tr>
<td>C(23) - O(22) - C(21)</td>
<td>115.2 (13)</td>
</tr>
<tr>
<td>O(14) - C(15) - C(16)</td>
<td>109.6 (11)</td>
</tr>
<tr>
<td>C(10) - C(17A) - O(17)</td>
<td>119 (2)</td>
</tr>
<tr>
<td>C(18) - C(17A) - C(26A)</td>
<td>124.8 (14)</td>
</tr>
<tr>
<td>O(17) - C(17A) - C(26A)</td>
<td>116 (2)</td>
</tr>
<tr>
<td>C(13) - C(12A) - O(12)</td>
<td>121.2 (11)</td>
</tr>
<tr>
<td>C(13) - C(12A) - C(28A)</td>
<td>119.5 (12)</td>
</tr>
<tr>
<td>O(12) - C(12A) - C(28A)</td>
<td>119.1 (13)</td>
</tr>
<tr>
<td>C(23) - C(24) - C(31)</td>
<td>118.4 (14)</td>
</tr>
<tr>
<td>C(23) - C(24) - C(25)</td>
<td>118 (2)</td>
</tr>
<tr>
<td>C(31) - C(24) - C(25)</td>
<td>123 (2)</td>
</tr>
<tr>
<td>C(26A) - C(27) - C(27A)</td>
<td>111.0 (12)</td>
</tr>
<tr>
<td>C(26A) - C(27) - C(271)</td>
<td>109.0 (12)</td>
</tr>
<tr>
<td>C(27A) - C(27) - C(271)</td>
<td>114.6 (14)</td>
</tr>
<tr>
<td>C(31) - C(2) - C(3)</td>
<td>120 (2)</td>
</tr>
<tr>
<td>C(31) - C(2) - C(1)</td>
<td>122 (2)</td>
</tr>
<tr>
<td>C(3) - C(2) - C(1)</td>
<td>118.9 (13)</td>
</tr>
<tr>
<td>Cl(5) - C(3C) - Cl(6)</td>
<td>117.2 (7)</td>
</tr>
<tr>
<td>Cl(4) - C(2C) - Cl(3)</td>
<td>107 (2)</td>
</tr>
<tr>
<td>Cl(1) - C(1C) - Cl(2)</td>
<td>100 (2)</td>
</tr>
</tbody>
</table>
### Table 33.
Anisotropic displacement parameters ($A^2 \times 10^3$) for 682 CH₂Cl₂.

<table>
<thead>
<tr>
<th></th>
<th>u11</th>
<th>u22</th>
<th>u33</th>
<th>u23</th>
<th>u13</th>
<th>u12</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(101)</td>
<td>68.17</td>
<td>40.7</td>
<td>33.6</td>
<td>3.5</td>
<td>-16.9</td>
<td>-1.9</td>
</tr>
<tr>
<td>C(102)</td>
<td>72.17</td>
<td>53.8</td>
<td>79.8</td>
<td>-10.6</td>
<td>-37.10</td>
<td>6.10</td>
</tr>
<tr>
<td>C(103)</td>
<td>49.15</td>
<td>55.7</td>
<td>48.7</td>
<td>-11.6</td>
<td>-11.9</td>
<td>1.9</td>
</tr>
<tr>
<td>C(104)</td>
<td>90.17</td>
<td>80.9</td>
<td>76.8</td>
<td>-5.7</td>
<td>-2.10</td>
<td>-11.10</td>
</tr>
<tr>
<td>C(105)</td>
<td>126.17</td>
<td>114.11</td>
<td>106.10</td>
<td>10.8</td>
<td>-1.11</td>
<td>-11.12</td>
</tr>
<tr>
<td>C(106)</td>
<td>103.17</td>
<td>92.9</td>
<td>123.11</td>
<td>13.9</td>
<td>-24.12</td>
<td>-27.11</td>
</tr>
<tr>
<td>C(107)</td>
<td>91.17</td>
<td>92.9</td>
<td>77.8</td>
<td>-9.8</td>
<td>-6.10</td>
<td>-40.11</td>
</tr>
<tr>
<td>C(108)</td>
<td>95.16</td>
<td>67.8</td>
<td>66.8</td>
<td>-10.6</td>
<td>-7.10</td>
<td>-36.10</td>
</tr>
<tr>
<td>C(251)</td>
<td>60.16</td>
<td>40.6</td>
<td>19.5</td>
<td>7.5</td>
<td>-4.7</td>
<td>4.8</td>
</tr>
<tr>
<td>C(252)</td>
<td>110.16</td>
<td>27.6</td>
<td>47.6</td>
<td>4.5</td>
<td>-11.8</td>
<td>5.9</td>
</tr>
<tr>
<td>C(253)</td>
<td>91.15</td>
<td>35.7</td>
<td>32.6</td>
<td>-1.5</td>
<td>-3.9</td>
<td>6.9</td>
</tr>
<tr>
<td>C(254)</td>
<td>58.17</td>
<td>60.8</td>
<td>73.8</td>
<td>7.7</td>
<td>0.10</td>
<td>-29.10</td>
</tr>
<tr>
<td>C(255)</td>
<td>63.16</td>
<td>84.9</td>
<td>78.9</td>
<td>11.7</td>
<td>7.10</td>
<td>-24.10</td>
</tr>
<tr>
<td>C(256)</td>
<td>64.16</td>
<td>26.8</td>
<td>91.9</td>
<td>-9.6</td>
<td>6.10</td>
<td>-9.6</td>
</tr>
<tr>
<td>C(277)</td>
<td>112.17</td>
<td>93.10</td>
<td>80.9</td>
<td>-13.8</td>
<td>17.10</td>
<td>-54.11</td>
</tr>
<tr>
<td>C(258)</td>
<td>121.16</td>
<td>82.9</td>
<td>62.8</td>
<td>-10.7</td>
<td>7.10</td>
<td>-7.10</td>
</tr>
<tr>
<td>C(271)</td>
<td>71.17</td>
<td>55.7</td>
<td>45.7</td>
<td>1.6</td>
<td>8.9</td>
<td>-32.9</td>
</tr>
<tr>
<td>C(272)</td>
<td>67.17</td>
<td>55.7</td>
<td>72.8</td>
<td>-5.6</td>
<td>2.10</td>
<td>-11.10</td>
</tr>
<tr>
<td>C(273)</td>
<td>60.16</td>
<td>56.8</td>
<td>63.7</td>
<td>11.7</td>
<td>12.10</td>
<td>20.10</td>
</tr>
<tr>
<td>C(274)</td>
<td>76.17</td>
<td>54.8</td>
<td>79.8</td>
<td>16.7</td>
<td>-20.10</td>
<td>4.11</td>
</tr>
<tr>
<td>C(275)</td>
<td>66.18</td>
<td>58.8</td>
<td>98.9</td>
<td>6.7</td>
<td>-32.11</td>
<td>-14.10</td>
</tr>
<tr>
<td>C(276)</td>
<td>48.17</td>
<td>71.9</td>
<td>95.9</td>
<td>-13.7</td>
<td>-5.11</td>
<td>-10.10</td>
</tr>
<tr>
<td>C(277)</td>
<td>222.18</td>
<td>105.10</td>
<td>109.10</td>
<td>0.9</td>
<td>16.11</td>
<td>-13.11</td>
</tr>
<tr>
<td>C(278)</td>
<td>57.18</td>
<td>77.9</td>
<td>99.9</td>
<td>6.8</td>
<td>28.11</td>
<td>-3.11</td>
</tr>
<tr>
<td>C(291)</td>
<td>41.15</td>
<td>45.7</td>
<td>50.7</td>
<td>6.6</td>
<td>3.8</td>
<td>-21.9</td>
</tr>
<tr>
<td>C(292)</td>
<td>66.16</td>
<td>64.8</td>
<td>60.7</td>
<td>-1.6</td>
<td>-8.9</td>
<td>-19.9</td>
</tr>
<tr>
<td>C(293)</td>
<td>50.16</td>
<td>43.7</td>
<td>57.7</td>
<td>5.6</td>
<td>-1.10</td>
<td>-15.9</td>
</tr>
<tr>
<td>C(294)</td>
<td>62.17</td>
<td>70.8</td>
<td>122.10</td>
<td>-15.8</td>
<td>-10.11</td>
<td>-21.11</td>
</tr>
<tr>
<td>C(295)</td>
<td>113.18</td>
<td>85.9</td>
<td>142.11</td>
<td>-11.8</td>
<td>-9.13</td>
<td>-50.11</td>
</tr>
<tr>
<td>C(296)</td>
<td>90.18</td>
<td>83.9</td>
<td>88.9</td>
<td>2.8</td>
<td>-15.12</td>
<td>-26.11</td>
</tr>
<tr>
<td>C(297)</td>
<td>77.17</td>
<td>82.9</td>
<td>94.10</td>
<td>20.8</td>
<td>-8.10</td>
<td>-15.11</td>
</tr>
<tr>
<td>C(298)</td>
<td>59.18</td>
<td>80.9</td>
<td>80.9</td>
<td>17.7</td>
<td>-15.11</td>
<td>-3.11</td>
</tr>
<tr>
<td>Br(4)</td>
<td>80.3</td>
<td>49.1</td>
<td>56.1</td>
<td>3.1</td>
<td>-1.1</td>
<td>-10.1</td>
</tr>
<tr>
<td>Br(1)</td>
<td>103.3</td>
<td>35.1</td>
<td>77.1</td>
<td>2.1</td>
<td>0.1</td>
<td>9.1</td>
</tr>
<tr>
<td>Br(3)</td>
<td>77.4</td>
<td>74.1</td>
<td>45.1</td>
<td>6.1</td>
<td>-14.1</td>
<td>9.1</td>
</tr>
<tr>
<td>Br(2)</td>
<td>123.3</td>
<td>70.1</td>
<td>59.1</td>
<td>-27.1</td>
<td>-22.1</td>
<td>25.1</td>
</tr>
<tr>
<td>C(7A)</td>
<td>77.15</td>
<td>28.7</td>
<td>42.7</td>
<td>-9.6</td>
<td>-3.9</td>
<td>-4.9</td>
</tr>
<tr>
<td>C(32)</td>
<td>29.19</td>
<td>27.8</td>
<td>24.7</td>
<td>-4.5</td>
<td>-2.9</td>
<td>-14.11</td>
</tr>
<tr>
<td>O(17)</td>
<td>72.13</td>
<td>49.4</td>
<td>31.4</td>
<td>1.4</td>
<td>2.5</td>
<td>11.6</td>
</tr>
<tr>
<td>C(26A)</td>
<td>41.17</td>
<td>21.7</td>
<td>33.7</td>
<td>-1.6</td>
<td>-11.10</td>
<td>-4.10</td>
</tr>
<tr>
<td>O(7)</td>
<td>57.15</td>
<td>39.5</td>
<td>45.5</td>
<td>9.4</td>
<td>0.6</td>
<td>-3.6</td>
</tr>
<tr>
<td>C(31)</td>
<td>23.19</td>
<td>33.8</td>
<td>28.7</td>
<td>-8.5</td>
<td>0.9</td>
<td>-7.11</td>
</tr>
<tr>
<td>O(12)</td>
<td>66.13</td>
<td>41.5</td>
<td>54.5</td>
<td>-6.4</td>
<td>8.6</td>
<td>7.7</td>
</tr>
<tr>
<td>O(4)</td>
<td>82.13</td>
<td>33.4</td>
<td>35.4</td>
<td>-4.4</td>
<td>6.5</td>
<td>0.6</td>
</tr>
<tr>
<td>O(19)</td>
<td>50.18</td>
<td>50.5</td>
<td>52.5</td>
<td>0.5</td>
<td>0.8</td>
<td>3.9</td>
</tr>
<tr>
<td>C(1)</td>
<td>46.16</td>
<td>30.6</td>
<td>22.6</td>
<td>-3.5</td>
<td>5.9</td>
<td>2.10</td>
</tr>
<tr>
<td>C(23)</td>
<td>33.18</td>
<td>46.8</td>
<td>25.7</td>
<td>0.7</td>
<td>13.10</td>
<td>3.12</td>
</tr>
<tr>
<td>C(16)</td>
<td>72.17</td>
<td>70.8</td>
<td>45.7</td>
<td>-9.7</td>
<td>-5.9</td>
<td>15.10</td>
</tr>
<tr>
<td>C(1A)</td>
<td>67.15</td>
<td>30.6</td>
<td>35.6</td>
<td>5.6</td>
<td>7.8</td>
<td>-14.9</td>
</tr>
<tr>
<td>O(9)</td>
<td>63.12</td>
<td>47.5</td>
<td>45.5</td>
<td>-10.4</td>
<td>-8.6</td>
<td>9.6</td>
</tr>
<tr>
<td>O(14)</td>
<td>49.17</td>
<td>55.6</td>
<td>37.5</td>
<td>3.4</td>
<td>5.8</td>
<td>-3.8</td>
</tr>
<tr>
<td>C(27A)</td>
<td>49.14</td>
<td>26.6</td>
<td>35.6</td>
<td>4.6</td>
<td>0.8</td>
<td>14.8</td>
</tr>
<tr>
<td>C(3)</td>
<td>54.17</td>
<td>36.8</td>
<td>22.7</td>
<td>1.6</td>
<td>1.9</td>
<td>-5.11</td>
</tr>
<tr>
<td>C(29)</td>
<td>35.14</td>
<td>40.6</td>
<td>42.6</td>
<td>-3.6</td>
<td>-6.8</td>
<td>-17.8</td>
</tr>
<tr>
<td>C(21)</td>
<td>70.15</td>
<td>64.7</td>
<td>43.7</td>
<td>0.6</td>
<td>-10.9</td>
<td>12.9</td>
</tr>
<tr>
<td>C(10)</td>
<td>70.16</td>
<td>57.7</td>
<td>55.7</td>
<td>-8.6</td>
<td>-19.9</td>
<td>15.9</td>
</tr>
<tr>
<td>C(11)</td>
<td>83.16</td>
<td>47.7</td>
<td>53.7</td>
<td>-10.6</td>
<td>-21.9</td>
<td>-16.10</td>
</tr>
<tr>
<td>C(29A)</td>
<td>61.14</td>
<td>38.7</td>
<td>36.7</td>
<td>1.6</td>
<td>-15.8</td>
<td>-4.8</td>
</tr>
<tr>
<td>C(13A)</td>
<td>55.15</td>
<td>48.7</td>
<td>31.6</td>
<td>0.7</td>
<td>9.8</td>
<td>-10.9</td>
</tr>
</tbody>
</table>
### Chapter 10

| C(28A) | 48 (14) | 31 (6) | 39 (7) | 2 (6) | -7 (8) | -5 (9) |
| C(13)  | 72 (16) | 31 (7) | 36 (7) | -13 (6) | -2 (9) | 1 (9) |
| C(18)  | 38 (20) | 32 (6) | 47 (9) | 6 (7) | -4 (12) | 7 (12) |
| C(30)  | 61 (15) | 24 (6) | 43 (7) | -9 (6) | -3 (9) | -2 (8) |
| C(8A)  | 74 (14) | 49 (8) | 32 (7) | -14 (6) | 0 (8) | 4 (9) |
| C(28)  | 59 (15) | 39 (7) | 37 (7) | 4 (6) | -7 (8) | 7 (9) |
| C(5)   | 76 (17) | 42 (7) | 55 (7) | 1 (6) | 3 (10) | 7 (10) |
| C(29)  | 57 (16) | 72 (8) | 48 (7) | 18 (7) | -7 (9) | 18 (11) |
| C(25A) | 43 (18) | 25 (6) | 42 (8) | -2 (7) | -5 (10) | 9 (11) |
| C(25)  | 49 (14) | 37 (6) | 19 (5) | -2 (5) | -4 (7) | -2 (8) |
| C(6)   | 51 (18) | 43 (8) | 62 (8) | 10 (6) | 5 (10) | -12 (10) |
| C(18A) | 44 (18) | 26 (6) | 50 (9) | 5 (8) | -5 (11) | 11 (11) |
| C(8)   | 77 (16) | 36 (6) | 37 (7) | 1 (6) | -7 (9) | 1 (9) |
| C(26)  | 43 (20) | 21 (6) | 37 (7) | 4 (6) | -5 (10) | 4 (11) |
| C(22)  | 60 (16) | 59 (5) | 32 (5) | 2 (4) | -7 (8) | 5 (8) |
| C(15)  | 52 (20) | 49 (8) | 48 (7) | -8 (6) | 1 (12) | -4 (11) |
| C(17A) | 51 (18) | 31 (6) | 37 (8) | 1 (7) | -16 (11) | 10 (12) |
| C(12A) | 76 (15) | 48 (7) | 37 (7) | 2 (7) | -7 (9) | 4 (9) |
| Cl(5)  | 162 (9) | 128 (3) | 94 (3) | 9 (2) | -22 (4) | -44 (4) |
| C(24)  | 35 (17) | 29 (7) | 25 (6) | -10 (6) | 2 (9) | 1 (11) |
| C(27)  | 50 (17) | 39 (7) | 32 (7) | 4 (6) | 15 (10) | 4 (11) |
| C(2)   | 46 (17) | 45 (8) | 19 (6) | 5 (6) | -8 (9) | 3 (11) |
| Cl(6)  | 159 (10) | 140 (3) | 87 (3) | -20 (2) | -1 (4) | -26 (4) |
| C(3C)  | 209 (24) | 61 (9) | 184 (14) | 15 (9) | -102 (16) | -34 (13) |
| Cl(1)  | 198 (14) | 259 (8) | 539 (14) | 188 (9) | 29 (10) | 70 (8) |
| Cl(3)  | 391 (17) | 391 (11) | 361 (10) | -106 (9) | 96 (10) | -134 (11) |
| Cl(4)  | 652 (24) | 402 (13) | 716 (20) | 81 (14) | 158 (16) | -78 (14) |
| Cl(2)  | 293 (16) | 378 (10) | 500 (14) | 244 (10) | -84 (11) | -120 (10) |

The anisotropic displacement factor exponent takes the form:

\[ -2 \pi^2 [ h^2 a^2 \sigma^2 U_{11} + \ldots + 2 h k a^* b^* U_{12} ] \]
Table 34. Hydrogen coordinates ($\times 10^3$) and isotropic displacement parameters ($\AA^2 \times 10^3$) for 68-2 CH$_2$Cl$_2$.

<p>| H(10A) | 2848 (8) | -432 (6) | -250 (4) | 71 |
| H(10B) | 2371 (8) | -466 (6) | 280 (4) | 71 |
| H(10C) | 1918 (9) | 430 (6) | -660 (5) | 104 |
| H(10D) | 1505 (9) | 578 (6) | -111 (5) | 104 |
| H(10E) | 690 (10) | -502 (8) | 293 (3) | 123 |
| H(10F) | -195 (7) | -1589 (9) | 97 (6) | 173 |
| H(10G) | -216 (7) | -2235 (6) | -766 (7) | 160 |
| H(10H) | 649 (10) | -1795 (8) | -1432 (3) | 131 |
| H(10I) | 1534 (7) | -709 (9) | -1236 (5) | 114 |
| H(25A) | 3953 (8) | -2120 (5) | 965 (3) | 60 |
| H(25B) | 4401 (8) | -2136 (5) | 420 (3) | 60 |
| H(25C) | 4875 (8) | -3040 (5) | 1361 (4) | 92 |
| H(25D) | 5261 (8) | -3090 (5) | 796 (4) | 92 |
| H(25E) | 3486 (9) | -3667 (7) | 1411 (3) | 96 |
| H(25F) | 2611 (6) | -4686 (8) | 1064 (5) | 112 |
| H(25G) | 2838 (7) | -5322 (5) | 221 (6) | 81 |
| H(25H) | 3939 (9) | -4939 (7) | -275 (3) | 142 |
| H(25I) | 4814 (6) | -3920 (8) | 73 (5) | 132 |
| H(27A) | 2735 (9) | -2239 (6) | 2091 (4) | 85 |
| H(27B) | 3292 (9) | -2788 (6) | 2460 (4) | 85 |
| H(27C) | 1867 (9) | -2227 (6) | 2829 (4) | 97 |
| H(27D) | 2416 (9) | -2827 (6) | 3169 (4) | 97 |
| H(27E) | 2768 (5) | -4117 (11) | 2449 (5) | 105 |
| H(27F) | 2081 (11) | -5228 (6) | 2035 (5) | 113 |
| H(27G) | 695 (11) | -5164 (7) | 1876 (4) | 107 |
| H(27H) | -4 (5) | -3989 (12) | 2130 (6) | 133 |
| H(27I) | 683 (11) | -2878 (7) | 2544 (5) | 115 |
| H(29A) | 529 (8) | -77 (6) | 1273 (4) | 68 |
| H(29B) | 1235 (8) | -664 (6) | 1419 (4) | 68 |
| H(29C) | -50 (9) | -479 (6) | 2061 (4) | 96 |
| H(29D) | 664 (9) | -1060 (6) | 2215 (4) | 96 |
| H(29E) | 884 (5) | -2169 (11) | 1501 (6) | 128 |
| H(29F) | 262 (11) | -3195 (6) | 956 (5) | 171 |
| H(29G) | -1100 (11) | -3096 (8) | 704 (4) | 131 |
| H(29H) | -1839 (5) | -1972 (12) | 998 (6) | 127 |
| H(29J) | -1217 (11) | -946 (7) | 1543 (5) | 110 |
| H(31A) | 3627 (11) | -882 (7) | 613 (4) | 42 |
| H(31A) | 3098 (11) | 1001 (6) | -41 (4) | 49 |
| H(31A) | 5404 (10) | -642 (7) | 3606 (4) | 96 |
| H(31A) | 4927 (10) | -987 (7) | 4089 (4) | 96 |
| H(31A) | 925 (8) | 752 (6) | 2036 (4) | 59 |
| H(31A) | 6730 (8) | 337 (6) | 1539 (4) | 89 |
| H(31A) | 5958 (8) | 210 (6) | 1784 (4) | 89 |
| H(31A) | 960 (9) | 2671 (6) | 2488 (4) | 92 |
| H(31A) | 1624 (9) | 3057 (6) | 2150 (4) | 92 |
| H(31A) | 2309 (9) | 1910 (6) | 2357 (4) | 93 |
| H(31B) | 2237 (9) | 2386 (6) | 2892 (4) | 93 |
| H(31A) | 2302 (8) | 27 (6) | 1105 (4) | 64 |
| H(31A) | 2259 (9) | -957 (6) | 2014 (4) | 68 |
| H(31A) | 5487 (9) | 2644 (7) | 686 (4) | 87 |
| H(31A) | 3894 (9) | 2065 (7) | 970 (4) | 87 |
| H(20A) | 7255 (9) | -962 (7) | 1543 (4) | 89 |
| H(20B) | 7039 (9) | -718 (7) | 2128 (4) | 89 |
| H(25J) | 5492 (8) | -1565 (5) | 922 (3) | 53 |
| H(6A) | 3227 (11) | 3232 (7) | 613 (5) | 78 |
| H(6B) | 3525 (11) | 3047 (7) | 36 (5) | 78 |
| H(26A) | 3743 (12) | -1463 (7) | 1692 (5) | 51 |
| H(15A) | 4353 (12) | -68 (7) | 3158 (5) | 74 |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>H(15B)</td>
<td>4363(12)</td>
<td>271(7)</td>
<td>3752(5)</td>
<td>74</td>
</tr>
<tr>
<td>H(27J)</td>
<td>3397(12)</td>
<td>-1772(8)</td>
<td>3130(5)</td>
<td>60</td>
</tr>
<tr>
<td>H(3CA)</td>
<td>4363(10)</td>
<td>1860(7)</td>
<td>2372(6)</td>
<td>233</td>
</tr>
<tr>
<td>H(3CB)</td>
<td>4827(10)</td>
<td>1663(7)</td>
<td>1854(6)</td>
<td>233</td>
</tr>
<tr>
<td>H(2CA)</td>
<td>-1816(21)</td>
<td>-5412(27)</td>
<td>790(15)</td>
<td>875</td>
</tr>
<tr>
<td>H(2CB)</td>
<td>-1148(21)</td>
<td>-6010(27)</td>
<td>661(15)</td>
<td>875</td>
</tr>
<tr>
<td>H(1CA)</td>
<td>1226(20)</td>
<td>-2893(19)</td>
<td>99(11)</td>
<td>722</td>
</tr>
<tr>
<td>H(1CB)</td>
<td>1812(20)</td>
<td>-3543(19)</td>
<td>369(11)</td>
<td>722</td>
</tr>
</tbody>
</table>
1 : 1 Host - Guest Association Model
Host: **29**, Guest: **36**
Solvent: CD$_3$CN/CD$_3$OD 4:1
$c_0(H) = 1 \times 10^{-4}$ mol 1$^{-1}$, $T = 300$ K
$K_a = 140000 \pm 30000$ 1 mol$^{-1}$
$\Delta G^\circ = -29.6 \pm 0.5$ kJ mol$^{-1}$
$\Delta \delta_{sat} = +0.240$ ppm

1 : 1 Host - Guest Association Model
Host: **29**, Guest: **37**
Solvent: CD$_3$CN/CD$_3$OD 4:1
$c_0(H) = 2 \times 10^{-4}$ mol 1$^{-1}$, $T = 300$ K
$K_a = 118000 \pm 59000$ 1 mol$^{-1}$
$\Delta G^\circ = -29.1 \pm 1.4$ kJ mol$^{-1}$
$\Delta \delta_{sat} = +0.228$ ppm

1 : 1 Host - Guest Association Model
Host: **29**, Guest: **36**
Solvent: CD$_3$OD
$c_0(G) = 5 \times 10^{-4}$ mol 1$^{-1}$, $T = 300$ K
$K_a = 8200 \pm 2000$ 1 mol$^{-1}$
$\Delta G^\circ = -22.5 \pm 0.6$ kJ mol$^{-1}$
$\Delta \delta_{sat} = -0.138$ ppm

1 : 1 Host - Guest Association Model
Host: **29**, Guest: **38**
Solvent: CD$_3$OD
$c_0(G) = 5 \times 10^{-4}$ mol 1$^{-1}$, $T = 300$ K
$K_a = 8300 \pm 600$ 1 mol$^{-1}$
$\Delta G^\circ = -22.5 \pm 0.2$ kJ mol$^{-1}$
$\Delta \delta_{sat} = -0.141$ ppm
1 : 1 Host - Guest Association Model
Host: 29, Guest: 37
Solvent: CD$_3$OD
$c_0(G) = 5 \times 10^{-4}$ mol l$^{-1}$, $T = 275$ K
$K_a = 3750 \pm 2501$ mol$^{-1}$
$\Delta G^o = -18.8 \pm 0.2 \text{ kJ mol}^{-1}$
$\Delta \delta_{sat} = -0.164 \text{ ppm}$

1 : 1 Host - Guest Association Model
Host: 29, Guest: 37
Solvent: CD$_3$OD
$c_0(G) = 5 \times 10^{-4}$ mol l$^{-1}$, $T = 283$ K
$K_a = 4160 \pm 1501$ mol$^{-1}$
$\Delta G^o = -19.6 \pm 0.1 \text{ kJ mol}^{-1}$
$\Delta \delta_{sat} = -0.168 \text{ ppm}$

1 : 1 Host - Guest Association Model
Host: 29, Guest: 37
Solvent: CD$_3$OD
$c_0(G) = 5 \times 10^{-4}$ mol l$^{-1}$, $T = 299$ K
$K_a = 4940 \pm 2501$ mol$^{-1}$
$\Delta G^o = -21.1 \pm 0.1 \text{ kJ mol}^{-1}$
$\Delta \delta_{sat} = -0.174 \text{ ppm}$

1 : 1 Host - Guest Association Model
Host: 29, Guest: 37
Solvent: CD$_3$OD
$c_0(G) = 5 \times 10^{-4}$ mol l$^{-1}$, $T = 306$ K
$K_a = 5330 \pm 2601$ mol$^{-1}$
$\Delta G^o = -21.8 \pm 0.1 \text{ kJ mol}^{-1}$
$\Delta \delta_{sat} = -0.180 \text{ ppm}$
1 : 1 Host - Guest Association Model
Host: 87, Guest: 97
D$_2$O, Na$_2$B$_4$O$_7$ (5·10$^{-3}$ mol l$^{-1}$), pD = 9.2
c$_0$(G) = 5·10$^{-4}$ mol l$^{-1}$, $T$ = 300 K
$K_a$ = 4000 ± 200 l mol$^{-1}$
$\Delta G^\circ$ = $-20.7 \pm 0.1$ kJ mol$^{-1}$
$\Delta \delta_{sat}$ = $-0.364$ ppm

1 : 1 Host - Guest Association Model
Host: 87, Guest: 98
D$_2$O, Na$_2$B$_4$O$_7$ (5·10$^{-3}$ mol l$^{-1}$), pD = 9.2
c$_0$(G) = 2·10$^{-4}$ mol l$^{-1}$, $T$ = 300 K
$K_a$ = 96 500 ± 9500 l mol$^{-1}$
$\Delta G^\circ$ = $-28.6 \pm 0.3$ kJ mol$^{-1}$
$\Delta \delta_{sat}$ = $-0.589$ ppm

1 : 1 Host - Guest Association Model
Host: 87, Guest: 97
D$_2$O, Tris/HCl (2.5·10$^{-3}$ mol l$^{-1}$), pD = 8.3
c$_0$(G) = 5·10$^{-4}$ mol l$^{-1}$, $T$ = 300 K
$K_a$ = 12 200 ± 1100 l mol$^{-1}$
$\Delta G^\circ$ = $-23.5 \pm 0.2$ kJ mol$^{-1}$
$\Delta \delta_{sat}$ = $-0.355$ ppm

1 : 1 Host - Guest Association Model
Host: 87, Guest: 98
D$_2$O, Tris/HCl (2.5·10$^{-3}$ mol l$^{-1}$), pD = 8.3
c$_0$(G) = 3·10$^{-4}$ mol l$^{-1}$, $T$ = 300 K
$K_a$ = 118 900 ± 15 700 l mol$^{-1}$
$\Delta G^\circ$ = $-29.2 \pm 0.4$ kJ mol$^{-1}$
$\Delta \delta_{sat}$ = $-0.616$ ppm
Chapter 10

1 : 1 Host - Guest Association Model
Host: 87, Guest: 101 (cAMP)
D$_2$O, Tris/HCl (2.5·10$^{-3}$ mol l$^{-1}$), pD = 8.3
c$_0$(G) = 1·10$^{-3}$ mol l$^{-1}$, T = 300 K
K_a = 1400 ± 80 l mol$^{-1}$
$\Delta G^o = -18.1 ± 0.2$ kJ mol$^{-1}$
$\Delta \delta_{sat} = -0.130$ ppm

1 : 1 Host - Guest Association Model
Host: 87, Guest: 103 (AMP)
D$_2$O, Tris/HCl (2.5·10$^{-3}$ mol l$^{-1}$), pD = 8.3
c$_0$(G) = 4·10$^{-4}$ mol l$^{-1}$, T = 300 K
K_a = 10000 ± 1000 l mol$^{-1}$
$\Delta G^o = -23.0 ± 0.3$ kJ mol$^{-1}$
$\Delta \delta_{sat} = -0.494$ ppm

1 : 1 Host - Guest Association Model
Host: 87, Guest: 104 (ADP)
D$_2$O, Tris/HCl (2.5·10$^{-3}$ mol l$^{-1}$), pD = 8.3
c$_0$(G) = 2·10$^{-4}$ mol l$^{-1}$, T = 300 K
K_a = 48700 ± 6900 l mol$^{-1}$
$\Delta G^o = -26.9 ± 0.4$ kJ mol$^{-1}$
$\Delta \delta_{sat} = -0.198$ ppm

1 : 1 Host - Guest Association Model
Host: 87, Guest: 105 (ATP)
D$_2$O, Tris/HCl (2.5·10$^{-3}$ mol l$^{-1}$), pD = 8.3
c$_0$(G) = 2·10$^{-4}$ mol l$^{-1}$, T = 300 K
K_a = 660000 ± 300000 l mol$^{-1}$
$\Delta G^o = -33.4 ± 1.5$ kJ mol$^{-1}$
$\Delta \delta_{sat} = -0.100$ ppm
1:1 Host - Guest Association Model
Host: 87, Guest: 99 (dAMP)
D$_2$O, Tris/HCl (2.5-10$^{-3}$ mol l$^{-1}$), pD = 8.3
$c_0$(G) = 4·10$^{-4}$ mol l$^{-1}$, $T = 300$ K
$K_a = 9500 \pm 570$ l mol$^{-1}$
$\Delta G° = -22.9 \pm 0.2$ kJ mol$^{-1}$
$\Delta \delta_{in} = -0.432$ ppm

1:1 Host - Guest Association Model
Host: 87, Guest: 100 (e-AMP)
D$_2$O, Tris/HCl (2.5-10$^{-3}$ mol l$^{-1}$), pD = 8.3
$c_0$(G) = 4·10$^{-4}$ mol l$^{-1}$, $T = 300$ K
$K_a = 9200 \pm 930$ l mol$^{-1}$
$\Delta G° = -22.8 \pm 0.3$ kJ mol$^{-1}$
$\Delta \delta_{in} = -0.947$ ppm

1:1 Host - Guest Association Model
Host: 87, Guest: 105 (d(AA))
D$_2$O, Tris/HCl (1·10$^{-2}$ mol l$^{-1}$), pD = 8.3
$c_0$(G) = 1·10$^{-3}$ mol l$^{-1}$, $T = 300$ K
$K_a = 330 \pm 20$ l mol$^{-1}$
$\Delta G° = -14.5 \pm 0.2$ kJ mol$^{-1}$
$\Delta \delta_{in} = -0.079$ ppm

1:1 Host - Guest Association Model
Host: 87, Guest: 105 (d(AA))
D$_2$O, Tris/HCl (1·10$^{-2}$ mol l$^{-1}$), pD = 8.3
$c_0$(G) = 5·10$^{-4}$ mol l$^{-1}$, $T = 300$ K
$K_a = 280 \pm 20$ l mol$^{-1}$
$\Delta G° = -14.0 \pm 0.2$ kJ mol$^{-1}$
$\Delta \delta_{in} = -0.081$ ppm
Figure 48. Selected parts of $^1$H-NMR spectra for kinetic study with chorismate at 323 K. Uncatalyzed sample containing chorismate (25) (initial concentration $4 \times 10^{-3}$ mol l$^{-1}$), internal standard 115 (1 $\times 10^{-3}$ mol l$^{-1}$) in CD$_3$OD. Signals assignment: chorismate 25 H-C(2) (a), H-C(6) (b), H-C(5) (c), H-C(9b) (d), H-C(3,4) (e), H-C(9a) (f); 4-hydroxybenzoate 112 H-C(2) (g), H-C(3) (h); standard 115 H-C(ar) (i), H$_2$C-O (j); solvent HO (k).
Selected parts of $^1$H-NMR spectra for kinetic study with chorismate 25 (initial concentration $4\times10^{-3}$ mol l$^{-1}$) at 323 K in the presence of the 1,1'-binaphthalene receptor 29 ($5\times10^{-3}$ mol l$^{-1}$) and internal standard 115 ($1\times10^{-3}$ mol l$^{-1}$) in CD$_3$OD. Signals assignment: chorismate 25 H-C(2) (a), H-C(6) (b), H-C(5) (c), H-C(9b) (d), H-C(3,4) (e), H-C(9a) (f); 4-hydroxybenzoate 112 H-C(2) (g), H-C(3) (h); standard 115 H-C(ar) (i), H$_2$C-O (j); solvent HO (k); prephenate 26 H-C(2) (l), H-C(3) (m).
Figure 50. Selected parts of $^1$H-NMR spectra for kinetic study with chorismate 25 (initial concentration $4 \times 10^{-3}$ mol l$^{-1}$) at 323 K in the presence of the cavitand receptor 87 ($5 \times 10^{-3}$ mol l$^{-1}$) and internal standard 115 ($1 \times 10^{-3}$ mol l$^{-1}$) in CD$_3$OD. Signals assignment: chorismate 25 H-C(2) (a), H-C(6) (b), H-C(5) (c), H-C(9b) (d), H-C(4) (e), H-C(3) (f), H-C(9a) (g); 4-hydroxybenzoate 112 H-C(3) (h); standard 115 H-C(ar) (i), H$_2$C-O (j); solvent HO (k); prephenate 26 H-C(2) (l), H-C(3) (m).
\[
\Delta \delta(H) \times (H) = \Delta \delta(HG_1)^{(2-x(H))} \frac{\sqrt{4\Delta \delta(HG_1)} K c_f (\frac{x}{H} - 2)^2 + 3(x(H) - 1)}{2/2K c_f \sqrt{\Delta \delta(HG_1)^{xK c_f c_f (x(H) - 2) + 2/2K c_f c_f (2x(H) - 1)^2 + 3(16 + K^2 c_f c_f (x(H) - 1)(2x(H) - 1)^2 + K c_f c_f (8 + 4x(H) - 13x(H)^2))}}
\]

*Equation 27* describing Job's plot curve for 1:2 host-guest model.
11. References


Chapter 11


Chapter 11

151


CURRICULUM VITAE

1971  Born on November 10, in Čadca, Slovakia

1978-1986  Elementary school, Žilina, Slovakia

1986-1990  Secondary grammar school, Žilina, Slovakia

1990-1995  Undergraduate chemistry studies at Comenius University, Faculty of Science, Department of Organic Chemistry, Bratislava, Slovakia

1995  Diploma thesis with Prof. Štefan Toma: Study of the stereoselectivity of Michael addition using dimethyl malonate as a chiral nucleophile.


1996-1997  Teaching assistant in the organic chemistry practica

Zürich, September 1999  Ľubomír Šebo