ramidal with a Co–Cl axial bond length of 2.384 (5) Å and crystallographically equivalent N–Co–N angles of 163.3 (4)° spanning the base of the pyramid. The geometry of [CoCl(TC-3,4)] (**2**) is best described as intermediate between square pyramidal and trigonal bipyramidal with a Co–Cl bond distance of 2.343 (1) Å and analogous N–Co–N bond angles of 171.5° and 142.1°. Finally, [CoCl(TC-4,4)] (**3**) adopts nearly perfect trigonal bipyramidal stereochemistry with the chloride ion in the equatorial plane and a Co–Cl bond distance of 2.288 (1) Å. As was the case for the [M(TC-*n*,*m*)] complexes, geometric changes occur as $n + m$ varies from 6 to 7 to 8 in order to relieve steric crowding in the polymethylene linker chains. In particular, the α,ω linker chain carbon atoms move farther apart as the structure changes from square pyramidal toward trigonal bipyramidal (see discussion in ref 1). To our knowledge, the only other crystallographically characterized trigonal bipyramidal Co(III) complexes are the paramagnetic species $[Co(PMe_3)_2I_3]$[5] and $[Co(PEt_3)_2Cl_3]$.[6,7] A later report of an improved synthetic route to $[Co(PR_3)_2X_3]$, X = Br, Cl, compounds[8] indicated that they were difficult to purify, decomposing rapidly in anaerobic solution or as solids in the air at room temperature. By contrast, solutions of [CoCl(TC-4,4)] only slowly decompose in air and the solid is indefinitely stable.

The compounds [CoCl(TC-4,4)] and [CoCl(TC-3,4)] display no solution NMR spectra at room temperature, a property indicative of paramagnetism. Measurement of the magnetic susceptibility of a microcrystalline sample of [CoCl(TC-4,4)] by SQUID susceptometry revealed a magnetic moment of 3.0 μ_B from 300 to 50 K, corresponding to the presence of two unpaired electrons. Below 50 K, however, the moment drops sharply and reaches a value of 1.1 μ_B at 5 K, apparently approaching a nonmagnetic ground state. The temperature dependence of the magnetic moment is characteristic of zero field splitting from a spin triplet, and a nonlinear least-squares fitting of the susceptibility data to an expression accounting for this phenomenon gave $D = 55$ cm^{-1}.[9] This value is similar to that reported for $[Co(PEt_3)_2Cl_3]$, 49 cm^{-1}.[7] Observed and calculated χ vs T and μ_{eff} vs T plots are included as supplementary material (Figure S1).

Molecular orbital calculations were carried out with an SCF-multiple scattering-Xα program[10-12] on a simplified model system in which the tropocoronand ligand was replaced by four amido (NH_2^-) groups. Both the trigonal bipyramidal and square pyramidal cobalt(III) chloride complexes were found to have paramagnetic, $S = 1$, ground states. In the case of the trigonal bipyramidal complex, the calculations revealed the paramagnetism to arise from a set of nearly degenerate d_{xy}, $d_{x^2-y^2}$, and d_{yz} orbitals, corresponding to a ground-state configuration of $(d_{xz})^2(d_{yz})^2(d_{x^2-y^2})^1(d_{xy})^1$. An energy level diagram is provided as Figure S2 in the supplementary material. The paramagnetic ground state calculated for the square pyramidal complex is $(d_{xy})^2(d_{xz},d_{yz})^3(d_{z^2})^1$. The near degeneracy among the d_{xz}, d_{yz}, and d_{z^2} orbitals arises because the normally low-lying degenerate d_{xz},d_{yz} pair is raised substantially in energy, to within 0.19 eV of the d_{z^2} orbital, as a result of π-antibonding interactions with the nitrogen lone pairs (see Figure S3, supplementary material, for an energy level diagram). This orbital arrangement differs from the electronic configuration proposed for two other paramagnetic square pyramidal $[CoX(N)_4]$ complexes, $(d_{xz})^2(d_{yz})^2(d_{xy})^1(d_{z^2})^1$,[13,14] in which π-bonding effects were not considered.

The variable geometries observed in the [CoCl(TC-*n*,*m*)] systems led us to investigate the corresponding Co–alkyl complexes. Reaction of the $[Co(TC\text{-}3,3)]^-$ or $[Co(TC\text{-}3,4)]^-$ anions, obtained from [Co(TC-*n*,*m*)] by reduction with 40% Na/Hg, with EtBr or *n*-PrBr cleanly yielded the corresponding Co(III) alkyls, whereas [CoMe(TC-4,4)] was prepared by addition of MeLi to a THF solution of [CoCl(TC-4,4)].[3] X-ray structural analyses[15] of [CoR(TC-3,3)] (R = Et, *n*-Pr) and [CoMe(TC-4,4)] revealed that *both* TC-3,3 and TC-4,4 complexes adopt square pyramidal geometries, and their sharp solution NMR spectra indicate that both are diamagnetic in solution. It is intriguing that the solid-state structures of the Co(III) alkyls are relatively insensitive to changes in the ligand steric constraints, whereas the geometry of the Co(III) chlorides has a marked dependence on the size of the macrocycle. The square pyramidal stereochemistry may be favored in both Co(III) alkyls because strong Co–C σ-interactions, preferred by the alkyl ligands, are better accommodated through bonding to the d_{z^2} orbital of the square pyramid than to the $d_{xy},d_{x^2-y^2}$ set in the equatorial plane of a trigonal bipyramid. We are currently investigating differences in reactivity among the various cobalt tropocoronand chloride and alkyl derivatives.

Acknowledgment. This work was supported by grants from the National Science Foundation and the National Institute of General Medical Sciences, for which we are grateful. We also thank K. L. Taft for help with the magnetic measurements.

Supplementary Material Available: Listings of analytical and spectroscopic data for **1**–**3** and the Co(III) alkyl complexes, Tables S1, S2, and S3 reporting atomic positional and equivalent isotropic thermal parameters for **1**, **2**, and **3**, respectively, Figure S1 depicting the observed and calculated χ vs T and μ vs T curves for **3**, and Figures S2 and S3 showing energy level diagrams for trigonal bipyramidal and square pyramidal $[CoX(N)_4]$ complexes, respectively (7 pages). Ordering information is given on any current masthead page.

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UO_2–Salenes: Neutral Receptors for Anions with a High Selectivity for Dihydrogen Phosphate

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Received July 9, 1992

The design and synthesis of neutral macrocyclic receptors that complex cations in apolar solvents with a high degree of selectivity are based on the ability to organize nucleophilic binding sites (Lewis bases) in a complementary array.[1] Although macrocycles with quaternary ammonium salts are known to complex anions,[2] selectivity is not simply introduced. Macrocyclic and acyclic ligands that contain Lewis acidic binding sites such as boron,[3]

[†] Laboratory of Organic Chemistry.

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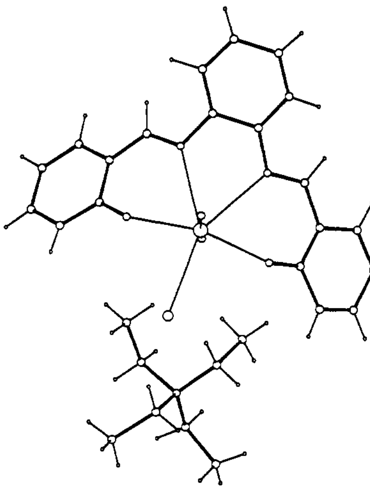


Figure 1. View of the X-ray structure of the complex of **1** with $Et_4N^+Cl^-$.

Table I. Conductometrically Determined Association Constants (K_{assoc}, M^{-1})[a–c]

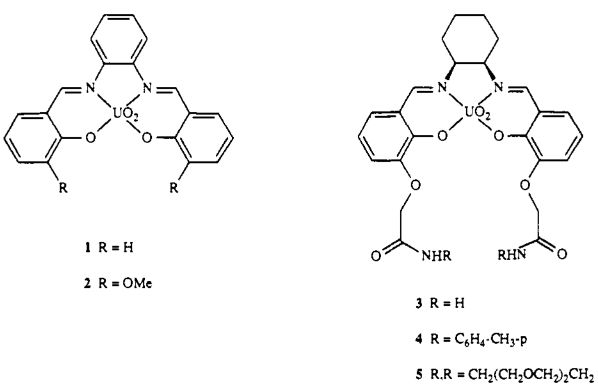
anion	**1**	**2**	**3**	**4**	**5**
Cl^-	4.0×10^2	6.8×10^1	4.0×10^3	1.7×10^3	1.2×10^4
$H_2PO_4^-$	1.4×10^4	2.0×10^4	1.9×10^4	2.5×10^6	$\geq 5.0 \times 10^6$
HSO_4^-	5.0×10^1	2.8×10^1	*d*	1.4×10^2	6.8×10^1
NO_2^-	3.1×10^2	6.7×10^1	8.3×10^2	4.5×10^2	1.5×10^3
SCN^-	5.0×10^1	1.4×10^1	*d*	7.1×10^1	*d*

[a] In acetonitrile containing 1% of DMSO. [b] The error is 5% for K values $>10^2$ M^{-1} and 10% for K values $<10^2$ M^{-1}. [c] The measurements were performed by dilution of the sample solution by the stock solution of the free salt. The sample solution was prepared by adding a small amount of free ligand to 10 mL of stock solution (starting concentrations: ligands 1–2 mM and salt 0.3–0.7 mM). The K_{assoc} values were determined with curve-fitting methods. [d] Not determined due to low solubility of free ligand.

silicon,[4] tin,[5] and mercury[6] bind anions, but these structures lack the possibility of subtle structural variation that is the basis for the selectivity in cation complexation. In this communication we report a novel class of neutral receptors for anions that contain an immobilized Lewis acidic binding site (UO_2^{2+}) and in which there are ample opportunities to introduce specific secondary binding sites. This concept leads to high thermodynamic stabilities combined with high selectivities. Neutral anion receptors are very important for application in sensors and membrane transport experiments.

Previously we reported that metallomacrocycles[7] and clefts[8] containing an immobilized Lewis acidic uranyl cation are excellent receptors for the complexation of neutral molecules due to coordination of a nucleophilic group (C=O, S=O, N) to the uranyl center in addition to H-bond formation and aromatic interactions, respectively. For the complexation of anions, we have studied first the simple uranyl-containing salophene **1**.[9] Red single crystals of the complex of **1** with tetraethylammonium chloride were grown from a dichloromethane solution. The crystal structure (Figure 1) was solved by Patterson methods.[10] The uranyl cation is coordinated to two oxygen atoms and two nitrogens of the salophene unit and to the chloride anion (U···Cl distance 2.76 Å), which clearly shows the anion complexation.

Chart I



1 R = H

2 R = OMe

3 R = H

4 R = C_6H_4-CH_3-p

5 R,R = $CH_2(CH_2OCH_2)_2CH_2$

From ^1H NMR dilution experiments[12] of **1** with tetrabutylammonium chloride in acetonitrile-d_3 (with 1% of DMSO-d_6) and by conductometry (see also Table I), high association constants (K_{assoc} values) of 4.2×10^2 and 4.0×10^2 M^{-1}, respectively, were determined.

In order to obtain more selective anion receptors, we introduced substituents which contain amido groups to the salene moiety. Compounds **3**–**5**[13] were prepared by reaction of the corresponding aldehydes and *cis*-1,2-cyclohexanediamine[14] in the presence of uranyl acetate [$UO_2(OAc)_2{\cdot}2H_2O$] in methanol in 50–75% yield. The influence of the amido moieties that are able to form H-bonds is demonstrated (except $H_2PO_4^-$) by comparing the K_{assoc} values of compounds **2** and **3** (Table I).

The more preorganized[7,8] ligands **4** and **5** exhibit a very strong (K_{assoc} 2.5×10^6 and 5.0×10^6 M^{-1}, respectively) and selective complexation of $H_2PO_4^-$.[15] Addition of tetrabutylammonium dihydrogen phosphate to a solution of **4** and **5** in DMSO-d_6 gives, in the ^{31}P NMR spectra, significant downfield shifts from δ −1.62 (free salt) to δ 0.59 and 0.30 (complexed salt), respectively. The negative FAB mass spectrum (*m*-nitrobenzyl alcohol as a matrix) of the solid complex of **5** with tetrabutylammonium dihydrogen phosphate exhibits, in addition to a small peak of the free ligand, a very large $[L + H_2PO_4^-]^-$ signal, while a small $[L + Bu_4N^+H_2PO_4^-]^-$ peak is also present. Compound **4** shows for $H_2PO_4^-$ selectivities of $>10^3$ and $>10^4$ over Cl^- and HSO_4^-, NO_2^-, and SCN^-, respectively. The contribution of the C(O)NH···$H_2PO_4^-$ hydrogen-bond interaction to the overall anion complexation can clearly be seen in the ^1H NMR spectrum even in pure DMSO-d_6 as a solvent. In a ^1H NMR dilution experiment of **4** with tetrabutylammonium dihydrogen phosphate in DMSO-d_6, the NH signals of both the free and complexed ligand could be separately observed at δ 10.55 and 11.20, respectively. From this experiment a K_{assoc} value of 8.0×10^3 M^{-1} was calculated, which is in very good agreement with a K_{assoc} of 9.0×10^3 M^{-1} determined with conductometry.

The hydrogen bond induced selective complexation of anions has a precedent in nature; the selective biological recognition of phosphate by a transport receptor protein has recently been described.[16–18] In this communication we have demonstrated that

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(12) K_{assoc} values were determined by integration of the separated signals of the imine protons of both free ligand and complex upon dilution of a solution containing a fixed ratio of ligand and guest.

(13) Details of the synthesis and spectral data will be published in a full article.

(14) For solubility reasons *cis*-1,2-cyclohexanediamine instead of 1,2-benzenediamine was used.

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simple neutral uranyl-containing receptors show high association constants for anion complexation.[19] Moreover, the unique combination of a Lewis acidic uranyl center and the presence of amide NH groups which can form a favorable H-bond with a coordinated anion guest, in a preorganized receptor, can lead to highly specific anion recognition.

Acknowledgment. This investigation was supported by the Netherlands Technology Foundation [STW, Future Technology Science Branch of the Netherlands Organization for the Advancement of Pure Research (NWO)].

Supplementary Material Available: Tables of positional and thermal parameters, bond lengths, and bond angles for 1 (5 pages). Ordering information is given on any current masthead page.

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Total Synthesis of (±)-Byssochlamic Acid

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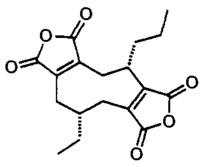
Received August 17, 1992

Byssochlamic acid (**1**), a metabolite first isolated from the ascomycete *Byssochlamys fulva*,[1] is a member of the small but structurally unique class of natural products known as nonadrides.[2] This family is characterized by the presence of a nine-membered carbocycle fused to two five-membered anhydride residues and includes the potent hepatotoxin rubratoxin B (**2**).[3] The constitution of **1** and its absolute configuration were established through an elegant series of degradative studies by Barton et al.,[4,5] and the relative configuration was confirmed by X-ray crystallographic analysis of its (*p*-bromophenyl)hydrazide.[6] We report here a synthesis of **1** which hinges on a photoaddition–cycloreversion metathesis to construct the core cyclononadiene system.[7] This route is significantly different from that described by Stork[8] in the only published synthesis of a nonadride.

Before embarking on our approach to **1**, we confirmed by experiment the prediction made from theory that the natural, cis configuration of alkyl chains is more stable than the trans orientation.[9] This removed the potential difficulty of controlling relative stereochemistry across a medium-sized ring en route to **1**.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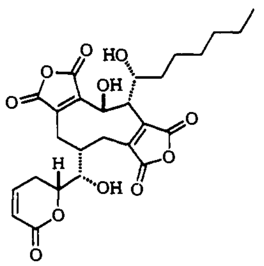

2

Sensitized irradiation through Pyrex of bromomaleic anhydride in the presence of 1-pentene afforded a mixture of three photoadducts in the ratio 4:1:1 (Scheme I). These were conveniently isolated as the corresponding diacids **3** after basic hydrolysis and characterized as dimethyl esters **4**.[10] Dehydrobromination of **4** cleanly afforded the cyclobutene **5**, which was saponified to give dicarboxylic acid **6**. The second component required for the synthesis, diol **11**, was prepared by the sequence shown in Scheme II. Thus, 4-ethylcyclohexanone (**7**), obtained by Jones' oxidation of the corresponding alcohol, was carboxylated and the resulting β-keto ester **8** was brominated to give **9**. Favorskii rearrangement of the latter yielded diester **10**,[11] which was reduced with the ate complex of diisobutylaluminum hydride[12] to **11**.

The dipotassium alkoxide from **11** was reacted with **5** but gave the desired cyclobutene half-ester in only low yield. Although this hydroxy acid lactonized readily to **12**, an improved procedure for preparation of the latter was found by treatment of a mixture of **6** and **11** under Steglich–Keck conditions.[13] This resulted in diolide **12** directly as a mixture of cis and trans stereoisomers (Scheme III). Irradiation of this mixture in dilute solution afforded the intramolecular photoadducts **13**, **14**, and **15** in the ratio 2:1.6:1. Careful 2D NMR analysis[14] of these adducts indicated that they were exo-exo, exo-endo, and endo-endo stereoisomers with respect to the propyl and ethyl side chains. Conformational analysis using MM2 calculations suggests that the apparent, severe steric congestion of the side chains in **15** can be relieved by folding of the cyclopentane into a pronounced envelope conformation. No evidence for formation of the fourth, endo-exo isomer was found, implying that the trans isomer of **12** gives only **14**.

Exposure of the mixture of **13**, **14**, and **15** to refluxing toluene led to quantitative cycloreversion by opening of the central cyclobutane ring in the direction opposite to that by which it was formed. This produced a 2:1 mixture of cis and trans cyclononadienes, **16** and **17**, the former presumably originating from **13** and **15**, and the latter from **14**.[15] Direct oxidation of the bis(butenolide) moieties to **1** and its trans isomer was unsuccessful, but basic hydrolysis of the mixture of **16** and **17**, followed by oxidation of the carboxylates **18** with permanganate and acidification, afforded **1** exclusively. Evidently, in the process of oxidizing **17**, epimerization of the propyl side chain had occurred

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(9) MM2 calculations predict that **1** is more stable than its trans isomer by ca. 3.8 kcal/mol. Treatment of **1** with base (NaH, THF) under conditions which led to formation of a sodium enolate resulted in *no* isomerization to the trans compound.

(10) Thus far, it has not been possible to assign regio- and stereochemistry to these photoadducts.

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(14) After identification of protons associated with each stereoisomer using ^{1}H–^{1}H COSY, analysis of one-dimensional sections of the phase-sensitive ^{1}H–^{1}H COSY gave the coupling constants of protons on the cyclobutane ring for **13**, **14**, and **15**. Confirmation of stereochemistry was obtained by ^{1}H–^{1}H NOESY, which showed a large NOE for the lactone methylene protons and a smaller NOE for the protons on the carbocyclic rings.

(15) Small amounts of the cycloreversion products **16** and **17** invariably accompanied the photoadducts in the irradiation of **12**.

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