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Tricyclic pseudocryptand formed by reaction of Fe^{II} with tripodand bearing triazacrown ether

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Abstract—A novel protonated tricyclic pseudocryptand possessing a triazacrown moiety has been synthesized and characterized by X-ray crystallographic analysis. The protonated host exhibited a unique binding behavior toward alkaline earth metal ions.

Pseudomacrocyclic and pseudomacrobicyclic compounds possess a cavity as an effective binding site for guests.[1] The cyclic framework is formed by complexation of a suitable metal ion with the corresponding linear or branched compound bearing a ligating moiety at each terminal. The formation of the cyclic structure causes a dramatic change in the binding affinity to a guest. Thus, these compounds have often been utilized for artificial allosteric systems.[1,2] For example, we have recently achieved large positive and negative allosteric effects on ion recognition by using a pseudocryptand.[2] A series of pseudocryptands are of great interest and importance because a strong and versatile guest-binding mode is expected.[2,3] However, only a few examples of pseudocryptand as a bicyclic host bearing polyether chains have been reported so far.[4] In addition, a tricyclic pseudocryptand consisting of polyether chains has never been synthesized, although such would exhibit unique binding properties compared to those of bicyclic pseudocryptands. In this letter, we report the synthesis and X-ray crystal structure of a novel tricyclic pseudocryptand **1**$\cdot Fe^{II}\cdot H^+$ possessing a triazacrown moiety. The bipyridine moieties of the precursor **1** for **1**$\cdot Fe^{II}\cdot H^+$ were expected to react with an Fe^{II} ion very smoothly and quantitatively as seen in the nitrogen-pivot pseudocryptand.[2] Furthermore, the triazacrown ether may provide an additional binding affinity toward metal cations and proton (Fig. 1).

The synthetic route to **1** is shown in Scheme 1. Bromide **3**[5] was treated with diol **2**[6] in the presence of NaH to give **4** in 63% yield. Tosylate **5** was obtained from **4** in 41% yield. The reaction of **5** with triazacyclononane·3HCl (TACN·3HCl)[7] and Na_2CO_3 afforded **1** as a yellow oil in 40% yield. The host **1** was characterized by ^1H NMR, ^{13}C NMR, DEPT, H,H-COSY, HMQC, and HMBC. ESI-MS also confirmed the structure.

The host **1** readily reacted with an Fe^{II} ion to give the corresponding octahedral red complex. A new MLCT absorption (518 nm, $CHCl_3/MeOH = 1:1$) characteristic of a bipyridine–Fe^{II} octahedral complex appeared upon the addition of Fe^{II}. UV–vis spectroscopic titration suggested quantitative formation of the 1:1 complex (Fig. 2). The red complex **1**$\cdot Fe^{II}$ was isolable in 75% yield as a pure HBF_4 salt by the reaction of **1** and $Fe(BF_4)_2\cdot 6H_2O$ and subsequent treatment with HBF_4. ESI-MS and elemental analysis supported the protonated structure of **1**$\cdot Fe^{II}$ bearing BF_4^- as a counter anion. In addition, ^{19}F NMR spectroscopy strongly suggested that the host contains three BF_4^- anions by using 1,2,4,5-tetrafluorobenzene as an internal standard for determining the content of the fluorine nucleus. Free **1**$\cdot Fe^{II}$ was not obtained by neutralization with NaOH due to dissociation of the Fe^{II} ion from the complex. X-ray crystallographic analysis confirmed the formula of the protonated pseudocryptand (Fig. 3).[8] The asymmetric unit consists of one **1**$\cdot Fe^{II}\cdot H^+$ cation, three

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Keywords: Pseudocryptand; Fe complex; Bipyridine; Triazacrown ether; Supramolecule.

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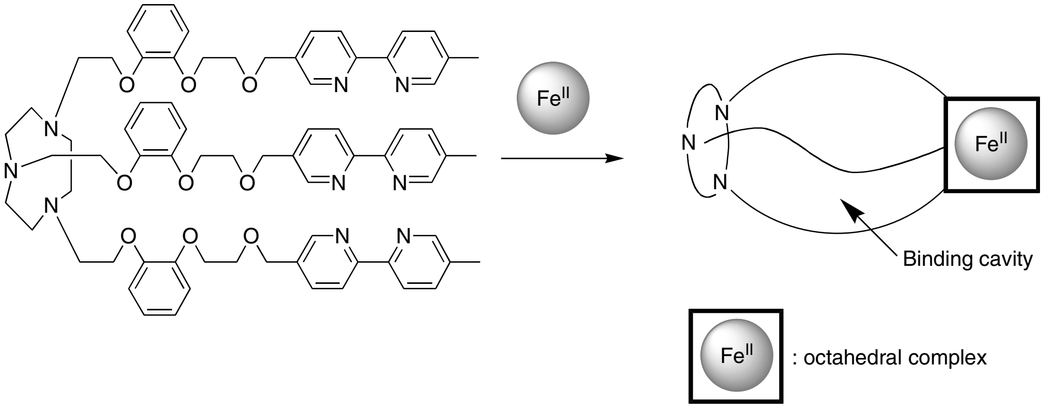
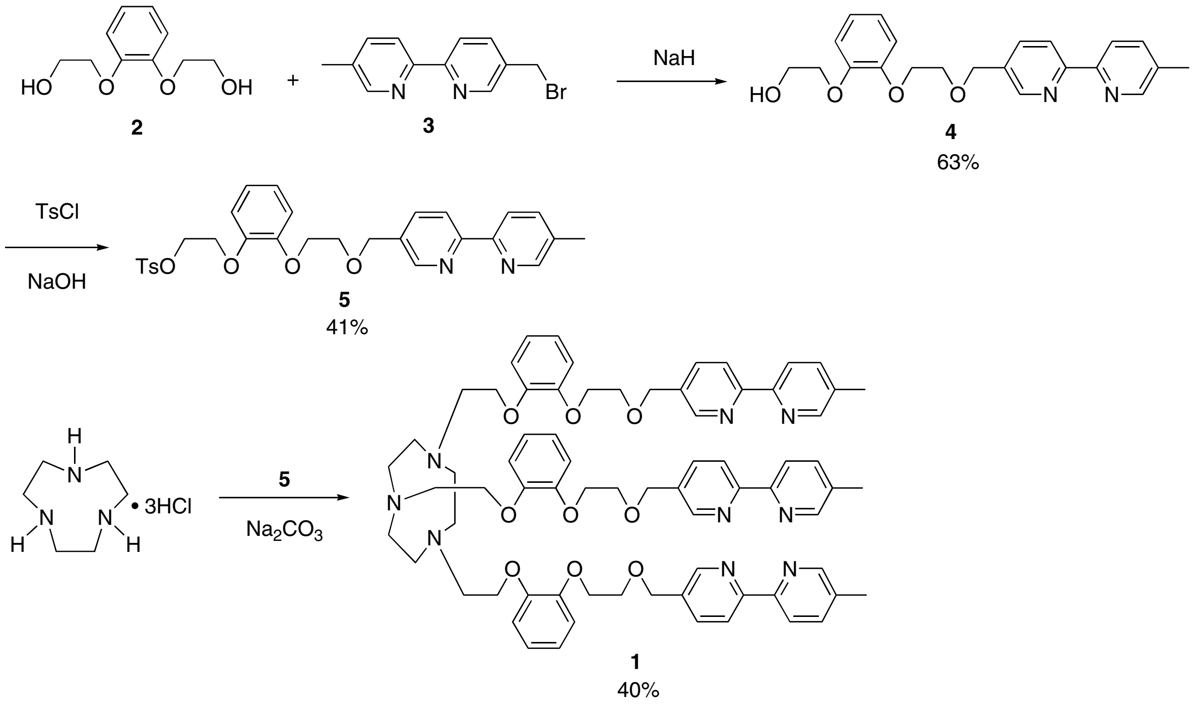


Figure 1. Formation of tricyclic pseudocryptand.



Scheme 1. Synthesis of tripodand **1**.

BF_4^-, and four chloroform molecules. The iron atom has a six-coordinate octahedral environment bonded to six nitrogen donors of the three bipyridine moieties (Fe–N distances: 1.956–1.978 Å). Three polyether chains assemble to form a triple helix ranging from the $Fe^{II}(bpy)_3$ moiety to N1 in the TACN moiety. Each chain winds around the Fe1–N1 axis of the molecule with a twist angle of 153–168°,[9] which is slightly smaller than that of the macrobicyclic analog.[2] The TACN ring (N1–N2–N3) sits at an angle of 60° with respect to the mean plane of the $Fe^{II}(bpy)_3$ cap (C37–C38–C39). Unlike the macrobicyclic analog, the cavity of **1**·Fe^{II}·H^+ shrinks and collapses in such a way that one of the polyether chains (O4–C31–C32–O7) fills up the concave part. This structural deformation can be attributed to intramolecular hydrogen bonds involving the NH proton of the TACN moiety. The hydrogen atom H1 was located in a difference Fourier map and its coordinates were refined with an isotropic displacement parameter. The N1–H1 distance 1.16(8) Å undoubtedly indicates that the proton is localized on N1 among the three nitrogen atoms of TACN as seen in the case of Me_3TACN[10] or bipyridine-substituted TACN.[3c] The NH proton forms hydrogen bonds to the two other nitrogen donors (N2 and N3) of the TACN moiety (1.8–2.0 Å) as well as ether oxygen O1 (2.4 Å), resulting in the pinched cavity.

In contrast to the solid state, the structure of **1**·Fe^{II}·H^+ in solution is much more complicated. While ^{19}F NMR indicated a mono-protonated structure (vide supra), ^1H NMR showed that **1**·Fe^{II}·H^+ consists of

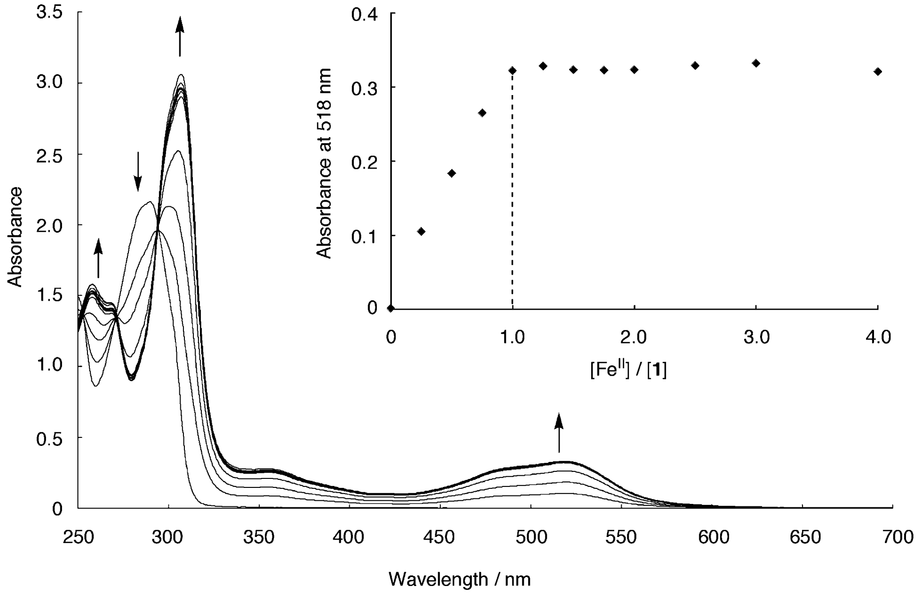


Figure 2. Absorption spectral changes of **1** upon addition of $Fe(BF_4)_2{\cdot}6H_2O$ in $CHCl_3/MeOH = 1:1$. $[\mathbf{1}] = 5.0 \times 10^{-5}$ M, $0 \leqslant ([Fe^{II}]/[\mathbf{1}]) \leqslant 4$.

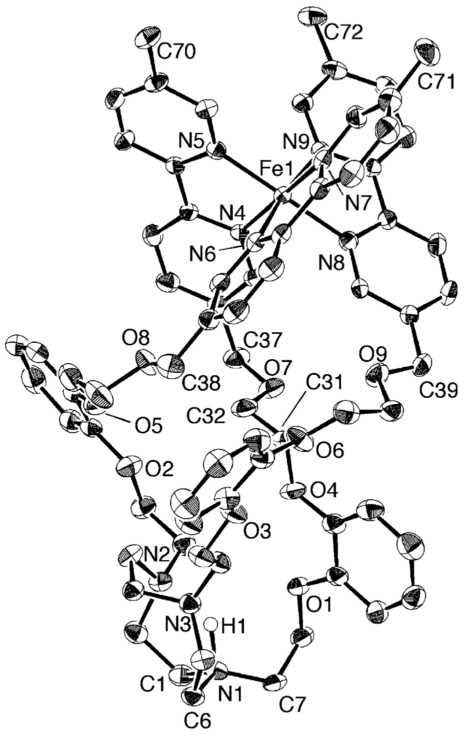


Figure 3. X-ray crystal structure of $\mathbf{1}{\cdot}Fe^{II}{\cdot}H^{+}$. Hydrogen atoms are omitted for clarity except for that of the NH group. Selected interatomic distances, Fe1–N4 1.956(4), Fe1–N5 1.969(4), Fe1–N6 1.965(4), Fe1–N7 1.978(4), Fe1–N8 1.976(4), Fe1–N9 1.969(4), N1–H1 1.16(8), N2–H1 1.80(8), N3–H1 2.00(8), O1–H1 2.39(8) Å.

two isomers with C_3 symmetry. Ratios of the isomers significantly depend on the solvent system used in the NMR measurement. In CD_3CN, the ratio is >4:1 but the content of $CDCl_3$ changed the ratio dramatically (1:1 in $CDCl_3/CD_3CN = 90:10$; 2:3 in $CDCl_3/CD_3CN = 95:5$). The ^1H NMR and H,H-COSY spectra supported the formation of pseudocryptand with an octahedral bipyridine–Fe^{II} complex. ^1H NMR titration in CD_3CN suggested the quantative 1:1 complexation, as seen in the UV–vis experiment. Definite structural determination could not be carried out due to complexity of the spectra. However, these are presumably isomers in which the conformations of the protonated TACN moiety are different. While the structures are unclear, this interesting solvent effect on the distribution of the isomers has never been observed in other pseudocryptands. The structural change would be utilized for controlling recognition ability toward guests.

Binding ability of the protonated host to cations in CD_3CN was preliminarily examined by ^1H NMR spectroscopy (Fig. 4). The host was considered not to interact with Na^+, K^+, Rb^+, and Cs^+ at all because these metal ions did not result in any spectral change of the host. In contrast, Mg^{2+} and Ca^{2+} caused considerable spectral changes, which are indicative of 1:1 complexation because excess metal ions did not affect the NMR spectra meaningfully.[12] Interestingly, the spectrum of the host was not influenced by Ba^{2+} and tetrabutylammonium ions. These results suggest that the cavity of the protonated host acts as a selective binding site for cationic guests. The binding mode is not clear but the proton in the positively charged TACN ring may contribute to the selectivity.[12]

We have here synthesized and clarified the crystal structure of tricyclic pseudocryptand $\mathbf{1}{\cdot}Fe^{II}{\cdot}H^{+}$ as a novel protonated host, which exhibited a significantly unique binding behavior to cations. This new framework might be applied not only to a new ion recognition system responding to the solvent but also to sensing of solvent polarity. We are currently studying the detailed structure of the protonated host in solution and the binding mode on the complexation with alkaline earth metal ions.

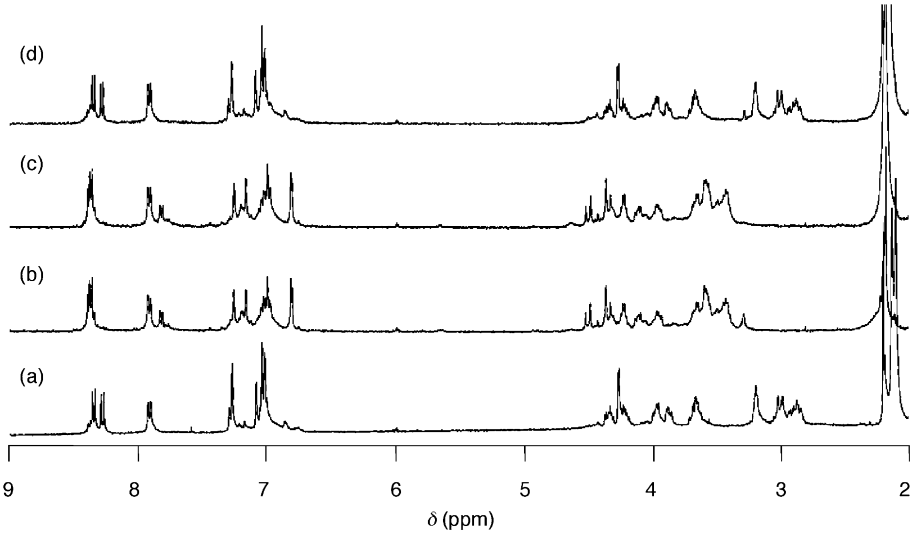


Figure 4. 400 MHz ^{1}H NMR spectra of (a) **1**·Fe^{II}·H$^+$ (2.0×10^{-3} M) in CD_3CN in the presence of 1.0 equiv of (b) $Mg(ClO_4)_2$, (c) $Ca(ClO_4)_2$, and (d) $Ba(ClO_4)_2$.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.03.084.

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8. Crystallographic data for **1**·Fe^{II}·H$^+$·$(BF_4^-)_3$·$4CHCl_3$: $C_{76}H_{86}B_3Cl_{12}F_{12}FeN_9O_9$ (2011.22), red prism ($0.4 \times 0.3 \times 0.25$ mm^3), triclinic, $P\bar{1}$, $a = 13.912(6)$, $b = 16.804(7)$, $c = 20.084(9)$ Å, $\alpha = 84.609(15)°$, $\beta = 82.051(15)°$, $\gamma = 71.580(13)°$, $V = 4405(3)$ Å^3, $Z = 2$, $D_{calc} = 1.516$ g cm^{-3}, $T = 120$ K, Mo-Kα ($\lambda = 0.71069$ Å), collected reflections 27,733, unique reflections 14,901 ($R_{int} = 0.0305$), $2\theta_{max} = 50.2°$, $R1 = 0.0757$ ($I > 2\sigma(I)$), $wR2 = 0.1921$ (all data), GOF (F^2) = 1.030.[11] CCDC-295398 contains the supplementary crystallographic data for this letter. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
9. Twist angles are defined as the torsion angles of C1–N1–Fe1–C71, C6–N1–Fe1–C72, and C7–N1–Fe1–C72.
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