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Supporting Information for

Placement of Hydrosulfide in the Hofmeister Series through Development of Bambus[6]uril-based ChemFET Sensor

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This PDF file includes:

N,N'-dibutyl glycoluril ¹H NMR Dodeca-n-butyl bambus[6]uril ¹H NMR Dodeca-n-butyl bambus[6]uril ¹H NMR Dodeca-n-butyl bambus[6]uril ¹³C NMR Dodeca-n-butyl bambus[6]uril Crystal Structure ChemFET and Reference Electrode Construction and Operation Counter-cation analysis

Other Supplementary Materials for the manuscript include the following:

cu_dwj334_0m_a_sq.cif cu_dwj334_0m_a_sq.res



Dodeca-n-butyl bambus[6]uril Mass Spectrometry



Dodeca-n-butyl bambus[6]uril ¹H NMR



Dodeca-n-butyl bambus[6]uril ¹³C NMR



dodecabutyl bambus[6]uril ¹³C NMR (126 MHz, Chloroform-*d*) δ: 159.3, 159.1, 69.1, 48.7, 44.0, 30.2, 20.1, 13.9



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Dodeca-n-butyl bambus[6]uril Crystal Structure (side view, C-H hydrogen bond donors depicted, all other hydrogens omitted for clarity)



Dodeca-n-butyl bambus[6]uril Crystal Structure (top view, C-H hydrogen bond donors depicted, all other hydrogens omitted for clarity)



X-ray Crystallography. Diffraction intensities for DWJ334 were collected at 173 K on a Bruker Apex2 CCD diffractometer using a Incoatec Cu IuS source, CuKa radiation, 1.54178 Å. Space group was determined based on systematic absences. Absorption correction was applied by SADABS[*]. Structure was solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms were refined in calculated positions in a rigid group model. X-ray diffraction at high angles was very weak due to the high disorder of solvent molecules and terminal -CH₂-CH₂-CH₂-CH₃ groups inside the structure. Even by using a strong *Incoatec* Cu *I*µS source it was possible to collect diffraction data only up to $2\theta_{max} = 99.83^{\circ}$. The data collected provide appropriate number of measured reflections per refined parameters, 9438 per 1028. Thermal parameters for some of the terminal -CH₂-CH₃ groups show significant elongations. Solvent molecules fill out cavities in the neutral main molecule and in the packing and are highly disordered. All these solvent molecules were treated by SQUEEZE[**] and not included into the formula of the compound given in the CIF file. Correction of the X-ray diffraction by SQUEEZE was 304 electron/cell. The RIGU option was used in the final refinement. The structure was determined inside space group $P2_1$, but absolute configuration was not determined. The structure of **DWJ334** has not been determined at high resolution, but it corroborates the chemical structure of the macrocycle and other results discussed in the paper. All calculations were performed by the Bruker SHELXL-2014/7 package [***].

Crystallographic Data for **DWJ334**: C₇₈H₁₃₂N₂₄O₁₂, M = 1598.07, 0.16 x 0.16 x 0.07 mm, T = 173(2) K, Monolinic, space group $P2_1$, a = 13.0608(10) Å, b = 24.6448(2) Å, c = 15.6448(13) Å, $\beta = 102.704(3)^\circ$, V = 4916.1(7) Å³, Z = 2, Dc = 1.080 Mg/m³, μ (Cu) = 0.606 mm⁻¹, F(000) = 1728, $2\theta_{max} = 99.83^\circ$, 20913 reflections, 9438 independent reflections [R_{int} = 0.0328], R1 = 0.0754, wR2 = 0.2085 and GOF = 1.009 for 9438 reflections (1028 parameters) with I>2 σ (I), R1 = 0.0860, wR2 = 0.2220 and GOF = 1.035 for all reflections, max/min residual electron density +0.541/-0.295 eÅ⁻³.

References:

[*] G. M. Sheldrick, *Bruker/Siemens Area Detector Absorption Correction Program*, Bruker AXS, Madison, WI, 1998.

[**] Van der Sluis, P. & Spek, A. L. (1990) Acta Cryst., Sect. A, A46, 194-201.

[***] Sheldrick, G. M. (2015). Acta Cryst. C71, 3-8.

ChemFET Sensor and Construction

Silicon nitride-gated field effect transistors (FETs) were purchased from Winsense (http://www.winsense.co.th, WIPS-C) and cleaned with ethanol and soaked in H_2O_2 for 10 minutes prior to functionalization. Polyvinyl chloride (PVC), 2-nitrophenyl octyl ether (NPOE), and Tetraoctylammonium Nitrate (TOAN) were obtained from Fisher Scientific and TCI Chemicals. All receptor-containing sensors contained 65 weight percent PVC, 32 weight percent NPOE, 2 weight percent TOAN, and 1 weight percent bambusuril receptor. Control sensors membrane composition were 66 weight percent PVC, 32 weight percent NPOE, and 2 weight percent TOAN. Chemically selective membranes were deposited onto the FET surface by manual drop-casting. Four aliquots of 1.6 μ L were applied at 30-minute increments before being placed in an oven at 60 °C for at least 4 hours, yielding an approximate film thickness of 50 μ m.

ChemFET Reference Electrode (RE) Construction

Ag/Ag₂S reference electrodes (REs) were used for hydrosulfide testing, and Ag/AgCl Res were used in all other potentiometric experiments. All REs in this report were made in-house following previously-reported procedures. (T. J. Sherbow, G. M. Kuhl, G. A. Lindquist, J. D. Levine, M. D. Pluth, D. W. Johnson and S. A. Fontenot, *Sensing and Bio-Sensing Research*, 2021, **31**, 100394.)

ChemFET Sensor and Reference Electrode (RE) Operation

The ChemFETs were driven by a benchtop power source. In operation, the drain voltage (V_{ds}) is held at 617.5 mV and the drain current (I_{ds}) at 100 mA. The external RE is held at ground, and the voltage between ground and the source (Vgs) terminal changes to maintain the values of V_{ds} and I_{ds} . V_{gs} is recorded as the measurement signal. NI-DAQ 6009 at a rate of 1 kHz was used for data acquisition paired with a custom Labview program for collection. All potentiometric tests were recorded for 300 seconds, and comprised of four identically-constructed ChemFETs. The four ChemFET sensors were run through a series of 12 solutions of 0.1M, 0.05M, 0.01M, 0.0005M, 0.0001M, 0.00005M, 0.00001M, 0.000001M, and 0.0000005M analyte, each with constant 50 mM PIPES.

Each data point consisted of four identically-constructed ChemFET sensors run through 12 solutions, in triplicate, of alternating order (low to high concentration, then high to low concentration, then low to high concentration).

Counter-cation analysis

Initial ChemFET screening was accomplished via identical sensor membrane formulation as the rest of the analysis presented in this paper (dodeca-n-butyl bambus[6]uril, tetraoctyl ammonium nitrate, polyvinyl chloride, and nitrophenyl octyl ether). This screening evaluation was accomplished via 5 solutions of constant 50mM PIPES and varying analyte concentration. To study the effect of the counter cation, the anion was kept constant and a number of counter cations evaluated to study impact on two metrics: sensitivity and detection limit. The four counter cations were selected to evaluate impact of differing size (cesium vs lithium), shape (spherical cations vs ammonium), and charge (Ca²⁺ vs NH₄⁺, Cs⁺, and Li⁺).

	Sensitivity	Detection Limit (mM)
Salt	± 2 standard deviations	± Confidence interval at 2 standard deviations
C aCl₂	60 ± 12	6 ± 2
NH₄CI	50 ± 8	6 ± 1
CsCl	50 ± 6	5 ± 2
LiCl	40 ± 2	3±1

Table 1. Initial counter cation screening. This quick analysis indicated potential impact of counter cation on sensitivity and detection limit of chloride. The screening comprised of four sensors containing dodeca-n-butyl bambus[6]uril evaluated through five series of salt solutions in order of magnitude concentration intervals. Results of this quick analysis prompted a follow-on more robust, in-depth study on any statistically-significant impacts of counter cation on anion measurement by ChemFET.

Initial screening results suggested possible differences in detection limits between calcium, ammonium, cesium, and lithium. Calcium and lithium represented the extreme differences, so a more in-depth characterization was accomplished of the full 12 solutions of constant 50 mM PIPES and varying concentration of these two chloride salts.

The full run of 12 solutions comprised 0.1M, 0.05M, 0.01M, 0.005M, 0.001M, 0.0005M, 0.0001M, 0.00005M, 0.000001M, and 0.0000005M analyte, each with constant 50 mM PIPES.

Upon running four dodeca-n-butyl bambus[6]uril sensors through the full 12-series of LiCl and CaCl₂ solutions (in triplicate), any suspected differences in figures of merit caused by changing counter-cations disappeared. No statistically significant impacts to sensitivity or detection limit were observed by changing counter cation of the chloride salt.

	Sensitivity	Detection Limit (mM)
Salt	± 2 standard deviations)	± Confidence interval at 2 standard deviations
CaCl ₂	43 ± 3.2	3.2 ± 0.97
LiCl	40 ± 4.3	2.6 ± 0.59

Table 2. Comprehensive counter cation analysis. This robust analysis focused on the two counter cations observed during screening to have the most differing figures of merit (sensitivity and detection limit). As indicated by the results in the table, upon a more in-depth evaluation there were no statistically-significant observed differences to ChemFET figures of merit by changing counter-cations.