Supplementary Information

A Highly Li^+-selective glass optode based on fluorescence ratiometry

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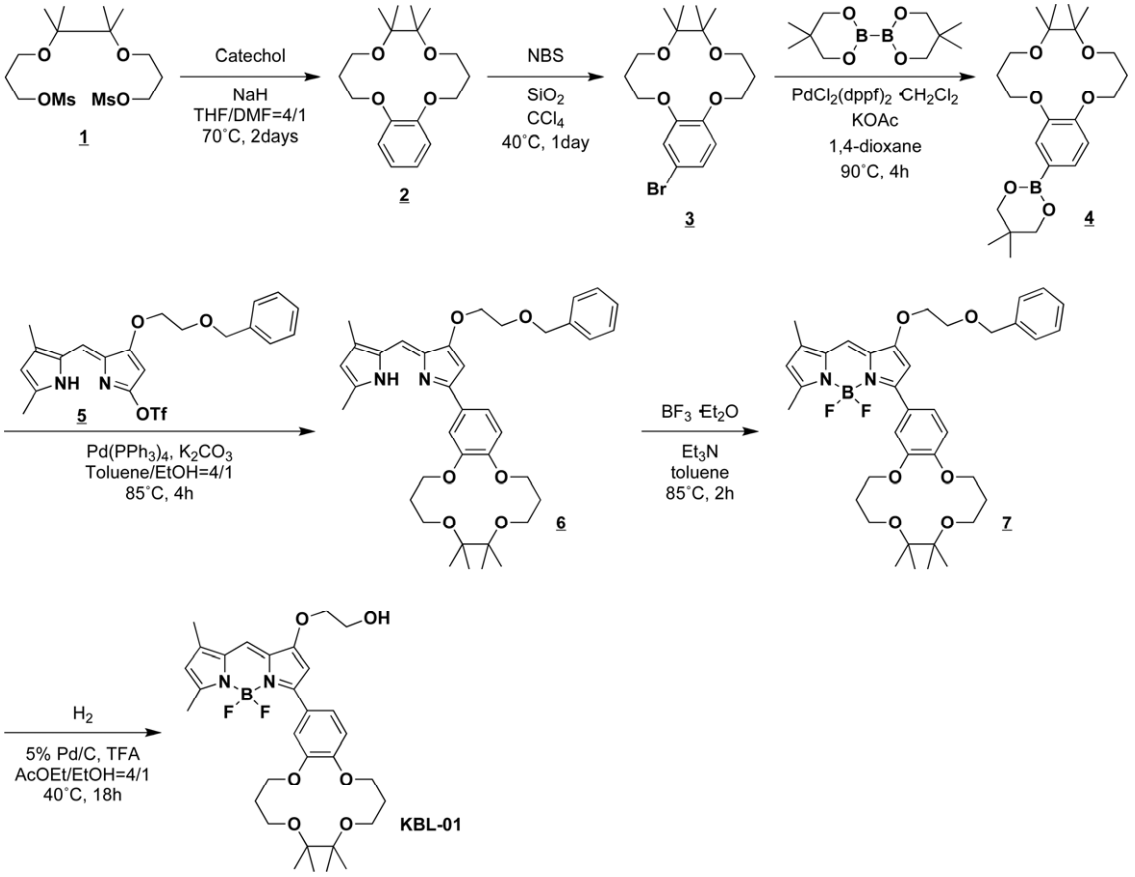
1. Materials and methods

General: All reagents and solvents were purchased from commercial suppliers (Sigma-Aldrich, TCI, Kanto Chemical, Wako Pure Chemical) and used without further purification. All moisture-sensitive reactions were carried out under an atmosphere of argon or nitrogen. A YFLC-Al-560 chromatograph and Hi-Flash columns (Yamazen) were used for purification by flash column chromatography. All NMR spectra were recorded on a JEOL JNM-LA 300 or VARIAN MERCURY spectrometer (300 MHz). Chemical shifts (δ, given in ppm) are relative to tetramethylsilane as an internal reference (δ = 0.0). Coupling constants (*J*) are given in Hz. High-resolution mass spectra (HRMS) were recorded on a Waters LCT premier XE (ESI-TOF).



Scheme S1 Reagents and conditions for the synthesis of KBL-01.

3,3'-(2,3-dimethylbutane-2,3-diyl)bis(oxy)bis(propane-3,1-diyl) dimethanesulfonate (**1**): Compound **1** was synthesized as we have reported previously.[1]

*6,6,7,7-tetramethyl-2,3,4,6,7,9,10,11-octahydrobenzo[*b*][1,4,8,11]tetraoxacyclotetradecine* (**2**): To a solution of catechol (1.09 g, 9.97 mmol) in a mixture of THF (530 ml) and DMF (150 ml) was added dropwise a suspension of NaH (1.9 g, 47 mmol, rinsed with hexane to remove the oil) in THF (40 ml). After stirring at 50 ˚C for 3 hours, a solution of compound **1** (3.90 g, 9.98 mmol) in THF (70 ml) was added dropwise over 3 hours. Then, the reaction mixture was stirred at 70 ˚C for 2 days. After cooling to room temperature, methanol was slowly added to the mixture to quench excess sodium hydride and the solvents were evaporated. The residue was taken up in ethyl acetate and the organic phase was washed with water followed by brine, before drying over Na_2SO_4 and evaporation of the solvent. The raw product was purified by flash column chromatography (silica gel, gradient elution: hexane / ethyl acetate 8:1 to 1:1) to yield

1.55 g (5.02 mmol, 51 %) of the target compound **2** as a colorless oil. δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.20 (s, 12H, -C*H*$_3$), 1.95-2.03 (m, 4H, -CH_2-C*H*$_2$-CH_2-), 3.82 (t, 4H, -$C(CH_3)_2$-O-C*H*$_2$-, *J* = 6.3 Hz), 4.08 (t, 4H, Ar-O-C*H*$_2$-, *J* = 5.7 Hz), 6.91-6.99 (m, 4H, Ar-*H*).

*14-bromo-6,6,7,7-tetramethyl-2,3,4,6,7,9,10,11-octahydrobenzo[*b*][1,4,8,11]tetraoxacyclotetradecine* (**3**): To a solution of the compound **2** (512 mg, 1.66 mmol) in CCl_4, silica gel (2.5 g) and N-bromosuccinimide (293 mg, 1.65 mmol) were added and the reaction mixture was stirred at 40 ˚C for 1 day. After cooling to room temperature, the resulting mixture was filtrated and the solvent was evaporated. The residue was taken up in ethyl acetate and the organic phase was washed with $Na_2S_2O_3$ solution, before drying over Na_2SO_4 and evaporation of the solvent. The raw product was purified by flash column chromatography (silica gel, gradient elution: hexane / chloroform 1:1 to chloroform) to yield 590 mg (1.52 mmol, 92 %) of the target compound **3** as a pale yellow oil. δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.19 (s, 12H, -C*H*$_3$), 1.92-2.02 (m, 4H, -CH_2-C*H*$_2$-CH_2-), 3.75-3.84 (m, 4H, -$C(CH_3)_2$-O-C*H*$_2$-), 4.03-4.09 (m, 4H, Ar-O-C*H*$_2$-), 6.84 (d, 2H, Ar-*H*, *J* = 8.5 Hz), 7.03 (dd, 1H, Ar-*H*, *J* = 8.4; 2.4 Hz), 7.07 (d, 1H, Ar-*H*, *J* = 2.4 Hz).

*5,5-dimethyl-2-(6,6,7,7-tetramethyl-2,3,4,6,7,9,10,11-octahydrobenzo[*b*][1,4,8,11]tetraoxacyclotetradecin-14-yl)-1,3,2-dioxaborinane* (**4**): To a solution of compound **3** (487 mg, 1.26 mmol) in 1,4-dioxane (7.5 ml), bis-(neopentylglycolato) diboron (345 mg, 1.53 mmol), $PdCl_2(dppf)_2 \cdot CH_2Cl_2$ (108 mg, 0.13 mmol) and potassium acetate (370 mg, 3.77 mmol) were added. The reaction mixture was deaerated with argon and then stirred at 85 °C for 4 hours. After cooling to room temperature and vacuum filtration through celite, the filtrate was concentrated under reduced pressure and the oily residue was purified by flash column chromatography (silica gel, gradient elution: hexane / ethyl acetate 8:1 to 1:1) to yield 295 mg (0.70 mmol, 56 %) of the target compound **4** as a colorless oil. δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.01 (s, 6H, -CH_2-$C(CH_3)_2$-CH_2-), 1.19 (s, 12H, -O-$C(CH_3)_2$-), 1.93-2.03 (m, 4H, -CH_2-C*H*$_2$-CH_2-), 3.74 (s, 4H, -B-O-C*H*$_2$-), 3.77-3.86 (m, 4H, -$C(CH_3)_2$-O-C*H*$_2$-), 4.07-4.13 (m, 4H, Ar-O-C*H*$_2$-), 6.93 (d, 1H, Ar-*H*, *J* = 8.3 Hz), 7.39-7.42 (m, 2H, Ar-*H*).

(Z)-3-(2-(benzyloxy)ethoxy)-2-((3,5-dimethyl-1H-pyrrol-2-yl)methylene)-2H-pyrrol-5-yl trifluoromethanesulfonate (**5**): Compound **5** was synthesized as we have reported previously.[2]

*(Z)-2-((3-(2-(benzyloxy)ethoxy)-5-(6,6,7,7-tetramethyl-2,3,4,6,7,9,10,11-octahydrobenzo[*b*][1,4,8,11]tetraoxacyclotetradecin-14-yl)-2H-pyrrol-2-ylidene)methyl)-3,5-dimethyl-1H-pyrrole* (**6**): Compounds **4** (132 mg, 0.31 □mol) and **5** (162 mg, 0.34 □mol) were dissolved in a mixture of toluene (32 ml) and ethanol (8 ml) and deaerated with argon. To the solution were added $Pd(PPh_3)_4$ (39 mg, 0.034 mmol) and K_2CO_3 (353 mg, 2.55 mmol). The reaction mixture was deaerated once again and stirred at 85 °C for 4 hours. After cooling to room temperature and vacuum filtration through celite, the filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (alumina, hexane / chloroform 1:1) to yield 132 mg (0.21 mmol, 65 %) of the target compound **6** as a glossy black film. δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.20-1.21 (m, 12H, -O-C(C*H*$_3$)$_2$-), 2.00-2.05 (m, 4H, -CH_2-C*H*$_2$-CH_2-), 2.24 (s, 3H, Ar-C*H*$_3$), 2.37 (s, 3H, Ar-C*H*$_3$), 3.80 (t, 2H, Bn-O-C*H*$_2$-, *J* = 5.7 Hz), 3.85-3.90 (m, 4H, -C(CH_3)$_2$-O-C*H*$_2$-), 4.13-4.19 (m, 4H, Ar-O-C*H*$_2$-), 4.25 (t, 2H, Bn-O-CH_2-C*H*$_2$-, *J* = 4.8 Hz), 4.66 (s, 2H, Ph-C*H*$_2$-), 5.86 (s, 1H, Ar-*H*), 6.01 (s, 1H, Ar-*H*), 6.96 (s, 1H, Ar-*H*), 7.00 (d, 1H, Ar-*H*, *J* = 8.4 Hz), 7.29-7.41 (m, 5H, -O-CH_2-*Ph*), 7.56 (dd, 1H, Ar-*H*, *J* = 8.4; 2.1 Hz), 7.63 (d, 1H, Ar-*H*, *J* = 2.1 Hz).

*1-(2-Benzyloxy-ethoxy)-5,7-dimethyl-3-(6,6,7,7-tetramethyl-2,3,4,6,7,9,10,11-octahydrobenzo[*b*][1,4,8,11]tetraoxacyclotetradecin-14-yl)-4,4-difluoro-4-bora-3a,4a-diaza-(s)-indacene* (**7**): A solution of **6** (92 mg, 0.15 mmol) in 30 ml of toluene was heated to 80 °C with stirring under argon. Then, triethylamine (2.0 ml, 14.4 mmol) and $BF_3 \cdot Et_2O$ complex (2.0 ml, 15.8 mmol) were added and the resulting mixture was stirred at 80 °C for 2 hours. After cooling to room temperature, ethyl acetate was added and the organic phase was washed once with 0.1 M Cs_2CO_3 solution, before drying over $MgSO_4$ and evaporation of the solvent. The raw product was purified by column chromatography (silica gel, toluene / ethyl acetate 4:1), followed by preparative thin layer chromatography (silica gel, toluene / ethyl acetate 4:1) to yield 51.8 mg (0.077 mmol, 52 %) of the target compound **7** as a red film. δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.20-1.21 (m, 12H, -O-C(C*H*$_3$)$_2$-), 1.98-2.04 (m, 4H, -CH_2-C*H*$_2$-CH_2-), 2.24 (s, 3H, Ar-C*H*$_3$), 2.48

(s, 3H, Ar-C*H*$_3$), 3.78-3.86 (m, 6H, Bn-O-C*H*$_2$-; -C(CH$_3$)$_2$-O-C*H*$_2$-), 4.14 (t, 4H, Ar-O-C*H*$_2$, *J* = 5.4 Hz), 4.25-4.28 (m, 2H, Bn-O-CH$_2$-C*H*$_2$-), 4.66 (s, 2H, Ph-C*H*$_2$-), 5.93 (s, 1H, Ar-*H*), 6.03 (s, 1H, Ar-*H*), 6.99 (d, 1H, Ar-*H*, *J* = 8.5 Hz), 7.28-7.36 (m, 5H, -O-CH$_2$-*Ph*), 7.56 (dd, 1H, Ar-*H*, *J* = 8.3; 2.2 Hz), 7.60 (d, 1H, Ar-*H*, *J* = 2.2 Hz).

*5,7-Dimethyl-1-(2-hydroxy-ethoxy)-3-(6,6,7,7-tetramethyl-2,3,4,6,7,9,10,11-octahydrob enzo[*b*][1,4,8,11]tetraoxacyclotetradecin-14-yl)-4,4-difluoro-4-bora-3a,4a-diaza-(s)-in dacene* (**KBL-01**): 5% Pd on activated carbon (8 mg) was added to a solution of **7** (18.5 mg, 0.027 mol) in a mixture of ethyl acetate (10 ml) and ethanol (2.5 ml), before trifluoroacetic acid (3 μl) was added. The reaction mixture was stirred vigorously under hydrogen at 40 °C for a day. After vacuum filtration through celite, the filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, chloroform) to yield 8.1 mg (0.014 mmol, 51 %) of the target compound **8** (KBL-01) as a red film. δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.20-1.21 (m, 12H, -O-C(C*H*$_3$)$_2$-), 1.99-2.04 (m, 4H, -CH$_2$-C*H*$_2$-CH$_2$-), 2.26 (s, 3H, Ar-C*H*$_3$), 2.49 (s, 3H, Ar-C*H*$_3$), 3.78-3.87 (m, 4H, -C(CH$_3$)$_2$-O-C*H*$_2$-), 4.03-4.05 (m, 2H, -C*H*$_2$-OH), 4.15 (t, 4H, Ar-O-C*H*$_2$, *J* = 5.6 Hz), 4.21-4.24 (m, 2H, -C*H*$_2$-CH$_2$-OH), 5.95 (s, 1H, Ar-*H*), 6.04 (s, 1H, Ar-*H*), 7.00 (d, 1H, Ar-*H*, *J* = 8.5 Hz), 7.57 (dd, 1H, Ar-*H*, *J* = 8.5; 2.2 Hz), 7.61 (d, 1H, Ar-*H*, *J* = 2.2 Hz). HRMS (ESI-TOF): m/z calcd. 587.3103; found 587.3104 for $C_{31}H_{42}BF_2N_2O_6$ [M+H$^+$].

2. Supplementary figures

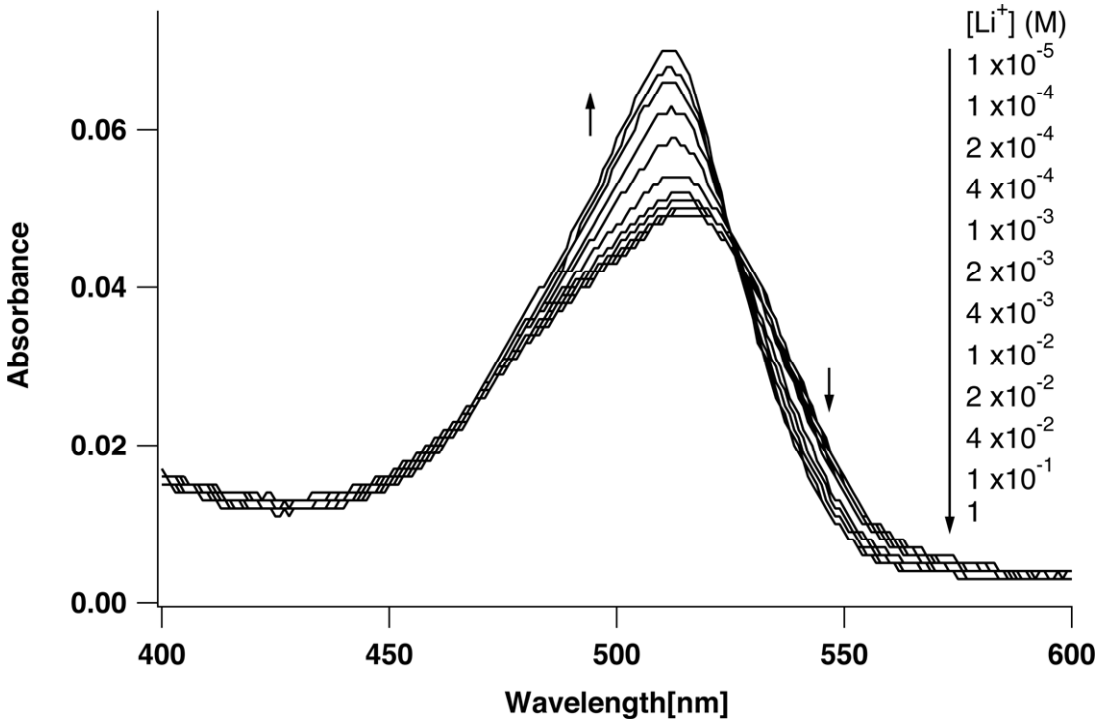


Fig. S1 Changes in the absorption spectra of the glass optode to aqueous solution of varying Li^+ concentrations.

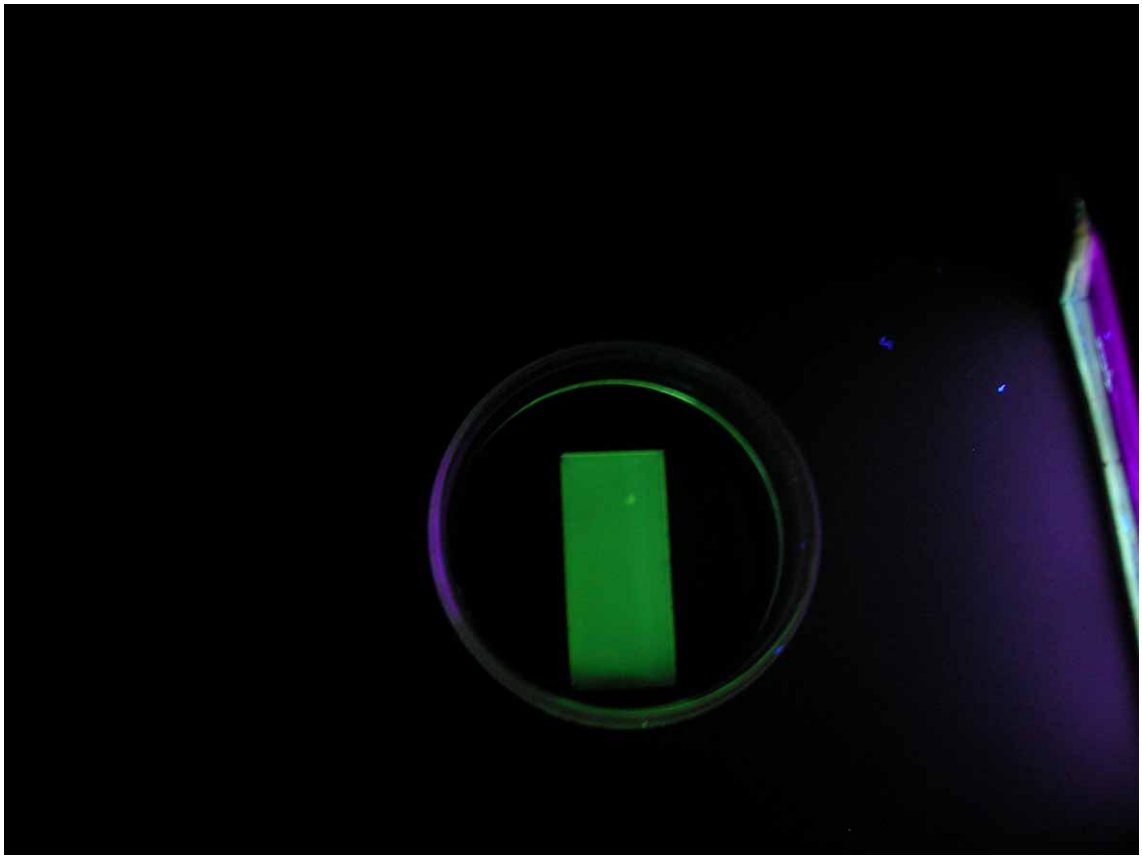


Fig. S2 Photograph of a freshly prepared glass optode soaked in deionized water (as seen under a black light excited at 365 nm)

3. The mathematical equation of the sigmoidal fitting curve (the dashed line shown in Fig.6)

$$y = base + \frac{max}{1 + exp\frac{xhalf - x}{rate}}$$

base=0.62909, *max*=-0.083289, *xhalf*=-2.3384, *rate*=0.00988

References

1 D. Citterio, J. Takeda, M. Kosugi, H. Hisamoto, S. Sasaki, H. Komatsu and K. Suzuki, *Anal. Chem.*, 2007, **79**, 1237-1242.

2 Y. Ando, S. Iino, K. Yamada, K. Umezawa, N. Iwasawa, D. Citterio and K. Suzuki, *Sens. Actuators B*, 2007, **121**, 74-82.