Diol-substituted boron complexes of dipyrrolyl diketones as anion receptors and covalently linked 'pivotal' dimers†

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Diol-substitution at a boron unit results in the formation of anion receptors consisting of dipyrrolyl diketones and covalently linked dimers, which exhibit selective binding for dianions with appropriate lengths.

Regularly arranged multiple binding sites in π-conjugated oligomeric systems[1] are fascinating as efficient receptors for polyionic species. One of the advantages of receptors based on π-conjugated oligomers is that they have amplifying properties that are sensitive to subtle perturbations caused by guest species. Among the various external stimuli, inorganic and organic anions such as halide, acetate and phosphate, which are involved in many biological processes, are essential for enzymatic activities, hormone transportation, protein synthesis and DNA regulation.[2,3] The simple acyclic geometries of oligopyrrole receptors make them suitable for use even with anionic species having various conformation changes and their binding behaviours can be modulated by the structural modifications.[4] We have reported the synthesis of pyrrole oligomers, such as BF_2 complexes of 1,3-dipyrrolyl-1,3-propanediones (*e.g.*, **1a,b**, Fig. 1(a)),[5,6] in which anions are efficiently bound by the *inversion* of pyrrole rings. According to the number of monomeric units, covalently linked oligomeric systems can exhibit not only efficient binding behaviours for biotic polyanions but also anion-controllable dynamic conformation changes. The replacement of fluorine substituents in a boron moiety by 1,2-diol units such as 'catechol' derivatives enables the attachment of acyclic anion receptors to the π-conjugated 'backbone'.[7] In this communication, we report the synthesis and anion binding properties of diol-substituted boron complexes of dipyrrolyl diketones and covalently linked dimers.

We synthesized catechol-substituted receptors **2a** and **2b** (Fig. 1(a)) in 22 and 68% yields, respectively, from the corresponding dipyrrolyl diketones[6,8] by treatment with BCl_3 and then with excess catechol in refluxing CH_2Cl_2. The B–O linkages were fairly stable and therefore the structures of the receptors were maintained during purification by silica gel column chromatography. We determined the chemical identities of **2a** and **2b** by ^{1}H NMR and FAB-MS. A singlet signal was observed at 8.45 ppm in the ^{11}B NMR spectrum of **2b** in $CDCl_3$. The signal exhibited a downfield shift in comparison with the singlet signal of **1b**, which appeared at 0.44 ppm.[9] The UV/Vis absorption spectra of **2a** and **2b** in CH_2Cl_2 exhibited the absorption maxima (λ_{max}) at 435 and 454 nm, respectively. These values were red shifted by 2–3 nm in comparison with the maxima of the corresponding BF_2 complexes: unsubstituted **1a** (432 nm) and β-ethyl **1b** (452 nm). Further, compared with the high-intensity fluorescence of **1b** at 471 nm (λ_{em} excited at 420 nm; emission quantum yield: Φ_F = 0.98), the weak

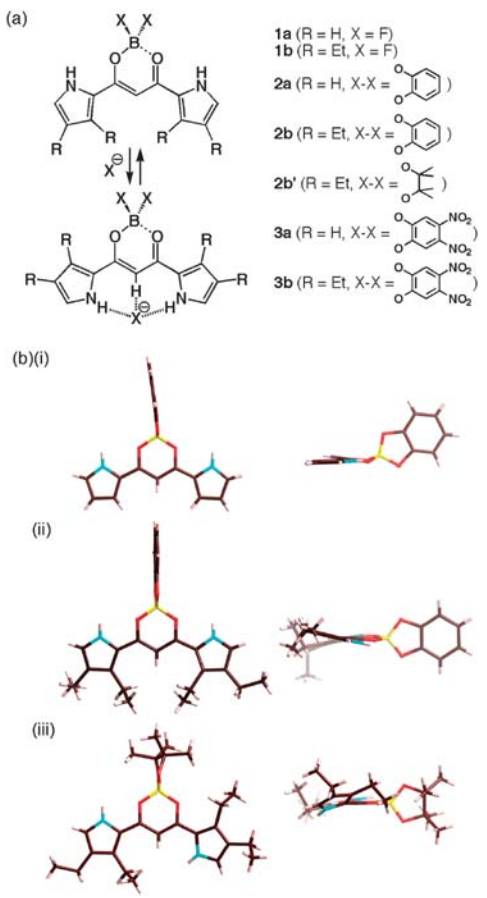

Fig. 1 (a) Dipyrrolyl diketone boron complexes (**1–3**) and their anion binding scheme and (b) single-crystal X-ray structures (top and side views) of (i) **2a**, (ii) **2b** and (iii) **2b′**. Atom colour code: brown, pink, yellow, blue and red represent C, H, B, N and O, respectively.

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† Electronic supplementary information (ESI) available: Synthetic procedures, spectroscopic data, anion binding behaviors (spectral changes and optimized structures) of the oligopyrrole derivatives, and CIF files for the X-ray structural analysis of **2a**, **2b**, **2a′** and **4b** (two types). CCDC 684820–684823 and 686903. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b806361c

fluorescent emission of **2b** observed at 474 nm (λ_{em} excited at 420 nm; Φ_F = 0.026) was attributed to the quenching path of the intramolecular electron transfer involved in the HOMO and HOMO−1, which were localized at catechol moiety.[10] This observation was consistent with the higher value of Φ_F = 0.82 (λ_{em} = 458 nm excited at 440 nm) of pinacol-substituted analog **2b′**, whose frontier orbitals were localized only at the π-conjugated receptor unit, possibly due to the sp^3 diol moiety.

X-Ray diffraction analyses of **2a**, **2b** and **2b′** revealed that their structures consisted of five-membered rings including two diol oxygens (Fig. 1b).‡ The two pyrrole NH sites of **2a** and **2b** were oriented in the same direction as the diketone oxygen sites and had intramolecular hydrogen bondings, as observed in the reported BF_2 derivative **1a**; in contrast, intriguingly, in **2b′**, one of the pyrrole rings was oriented in the opposite direction in the solid state. In a manner similar to **1a**, the 'BO_2' complexes **2a**, **2b** and **2b′** formed 1-D assembled chain structures by intermolecular interaction between pyrrole NH and catechol oxygens.

The anion binding property of **2b**, which was fairly soluble in ordinary organic solvents, was investigated by studying the changes in the UV/Vis absorption spectrum in CH_2Cl_2 upon the addition of anions in the form of tetrabutylammonium (TBA) salts. For example, when $H_2PO_4^-$ was added to CH_2Cl_2, it was observed that the absorbance at λ_{max} (454 nm) decreased and λ_{max} shifted to 459 nm. The binding constants K_a of **2b** (and the ratios to the K_a values of **1b**[6]) for several anions were 2300 (0.34) (Cl^-), 270 (0.23) (Br^-), 33 000 (0.10) ($CH_3CO_2^-$), 67 000 (0.74) ($H_2PO_4^-$) and 80 (0.07) (HSO_4^-) mol^{-1} dm^3. These values were obtained possibly because the electronegativity of catechol oxygens (**2b**) was lower than that of fluorines (**1b**). The K_a values of pinacol-substituted **2b′** for anions were comparable to those of **2b** in CH_2Cl_2: 1800 (Cl^-), 350 (Br^-), 23 000 ($CH_2CO_2^-$), 21 000 ($H_2PO_4^-$) and 280 (HSO_4^-) mol^{-1} dm^3. The binding stoichiometry (1 : 1) was determined by using a continuous titration method. The relatively low stability of the preorganized geometry of **2b** (5.32 kcal mol^{-1}), which had two inverted pyrrole rings, was comparable to that of **1b** (4.98 kcal mol^{-1}), as estimated by the DFT calculations.[10]

The substitution at a boron unit by the vicinal hydroxyl groups of various functional units enabled the formation of new derivatives. For example, nitro-substituted receptors **3a** and **3b** (Fig. 1(a)) were obtained in 24 and 23% yields, respectively, using procedures similar to those used for **2a** and **2b**. The absorption maxima (λ_{max}) and emission maxima (λ_{em} excited at λ_{max}) of **3b** in CH_2Cl_2 were 466 and 492 nm, respectively, and they were red shifted at 11 and 18 nm in comparison with the maxima (λ_{max} and λ_{em}) of **2b**. The Φ_F value of **3b** was determined to be 0.13. This value was higher than that of **2b** possibly because of the lower levels of MO in the catechol moiety of **3b** and, consequently, the smaller interactions with the frontier orbitals of the receptor moiety. The K_a values for anions of β-ethyl-substituted **3b** were higher, due to the effect of electron-withdrawing nitro groups, than those of **2b** in CH_2Cl_2. The K_a values of **3b** were 46 000 (Cl^-), 5400 (Br^-), 1 300 000 ($CH_3CO_2^-$), 150 000 ($H_2PO_4^-$) and 2300 (HSO_4^-) mol^{-1} dm^3.

We synthesized the ditopic receptors **4a** and **4b** (Fig. 2(a)) in 11 and 38% yields, respectively, by the treatment of intermediate BCl_2 complexes with *p*-phenylene-bridged dicatechol.[11] These receptors were extended systems bridged by 'spacer' moieties between the acyclic anion receptors. The structure of **4b** was determined by ^1H NMR ($CDCl_3$), wherein a signal attributed to the centre aryl moiety appeared as a single peak at 7.88 ppm at −60 °C. This suggested that the rotation around the terphenyl-bridge was rapid for the NMR time scale. The UV/Vis absorption spectrum of **4b** in CH_2Cl_2 at 453 nm was similar to that of monomer **2b**, thereby corroborating the observation that no significant interactions existed between the two receptor units. Further, single-crystal X-ray analysis of **4b** (**4b**(i)) suggested that both the receptor units were oriented in the same direction so that a Π-shaped *syn* conformation was generated with an intramolecular B–B distance of 8.68–9.17 Å (Fig. 2(b)).§[12] On the other hand, a single crystal from $CHCl_3$/octane (**4b**(ii)), which was not of high enough quality for detailed analysis, generated conformations where all four pyrrole rings were inverted and the NH groups were pointing away from the boron site (see ESI†).¶[12] In the solid data, any hydrogen bonding interactions of pyrrole NH were not observed.

The changes in the ^1H NMR spectra of the terphenyl-bridged dimer **4b** in $CDCl_3$ at −50 °C indicated stepwise but fairly complicated binding for ordinary monoanions. Due to the appropriate locations of the two receptor units, **4b** showed the [1 + 1] binding for linear dicarboxylates ($^-O_2C(CH_2)_nCO_2^-$, n = 2–6). Some of these carboxylates are essential factors in biotic process.[13] The K_a values for succinate (n = 2), glutarate (n = 3), adipate (n = 4), pimelate (n = 5) and suberate (n = 6) as their TBA salt forms in CH_2Cl_2 were 19 000, 72 000, 810 000, 2 600 000 and 440 000 mol^{-1} dm^3, respectively. The minimum and maximum distances between carboxylate oxygens estimated by the DFT calculation at B3LYP/6-31 + G(d,p) level[10] are 4.90 and 5.91 Å (n = 2), 5.78 and 7.28 Å (n = 3), 7.21 and 8.58 Å (n = 4), 8.05 and 9.90 Å (n = 5) and 9.65 and 11.22 Å (n = 6). This observation suggested that the distance between the receptor units (*ca.* 9 Å) was crucial in the determination of the selectivity of the dianions. The binding stoichiometry (1 : 1) of **4b** and the

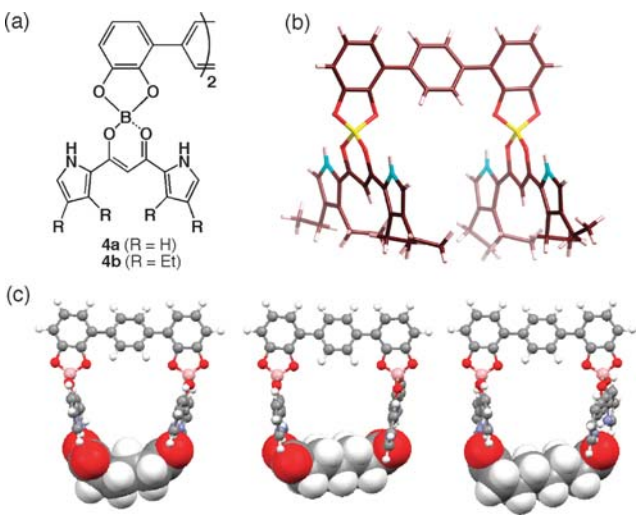

Fig. 2 (a) Schematic representation of dimers **4a,b**, (b) single-crystal X-ray structure (one of the four conformations) of **4b** (**4b**(i)) and (c) optimized structures of **4a**·($^-O_2C(CH_2)_nCO_2^-$) (n = 4–6) at AM1 level. Atom colour code: grey, white, pink, blue and red represent C, H, B, N and O, respectively, in (c).

dicarboxylates were determined using methods similar to those used for **2b**, although the exact binding mode could not be determined due to complicated changes in the ^{1}H NMR spectrum. Instead, the binding mode of the dimer for dicarboxylates (n = 4–6) was estimated by the AM1 calculations[10] of the complexes using unsubstituted **4a** (Fig. 2(c)). In the optimized structures, the dihedral angles between two receptor planes that consisted of 16 core atoms were 24.37° (n = 4), 11.74° (n = 5) and 15.88° (n = 6); the conformation closer to being parallel in the pimelate binding complex was consistent with the selectivity. The guest dicarboxylates also underwent the conformation changes due to the interaction with the receptor dimer. The minimum and maximum distances between the carboxylate oxygens were changed from the values in anion-free states to 6.49 and 6.90 Å (n = 4), 8.45 and 9.06 Å (n = 5) and 8.40 and 9.25 Å (n = 6), respectively. The observation that pimelate exhibited the relatively smaller conformation change between the binding state and the free state also suggested that the preferred interaction of the receptor dimer with pimelate. Additionally, it was observed that the odd number of methylene units in pimelate was an essential factor for selective binding; this was confirmed by the changes in the structures of adipate and suberate due to their even number of methylene units. These observations suggest the [1 + 1]-type binding mode between the receptor dimer and dicarboxylates. Further, appropriate spacer units between multiple receptor units will enable selective binding and formation of various binding modes for a variety of existing polyanions including biotic ones.

In summary, we have synthesized monomer and dimer systems of π-conjugated acyclic anion receptors by diol-substitution in a boron unit. In contrast to α-linked oligomers,[14] systems based on the 'BO_2' complexes in this report behave as genuine multitopic receptors that can be incorporated in various macromolecules such as polymers. The utilization of these systems as receptors is currently under investigated.

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Notes and references

‡ *Crystal data* for **2a** (from EtOAc–hexane): $C_{17}H_{13}N_2O_4B$, M_r = 320.11, orthorhombic, $Pna2_1$ (no. 33), a = 9.035(3), b = 18.435(7), c = 8.794(3) Å, V = 1464.7(9) Å^3, T = 123(1) K, Z = 4, D_c = 1.451 g cm^{-3}, μ(Mo-Kα) = 0.103 mm^{-1}, R_1 = 0.0408, wR_2 = 0.0825, GOF = 1.037 ($I > 2\sigma(I)$). CCDC 684820. *Crystal data* for **2b** (from CH_2Cl_2–hexane): $C_{25}H_{29}N_2O_4B$, M_r = 432.33, tetragonal, $I4_1/a$ (no. 88), a = 23.638(8), c = 16.043(4) Å, V = 8964(5) Å^3, T = 123(1) K, Z = 16, D_c = 1.281 g cm^{-3}, μ(Mo-Kα) = 0.086 mm^{-1}, R_1 = 0.0627, wR_2 = 0.1423, GOF = 1.031 ($I > 2\sigma(I)$). CCDC 684821. *Crystal data* for **2b′** (from CH_2Cl_2–hexane): $C_{25}H_{37}N_2O_4B$, M_r = 440.38, monoclinic, $P2_1/n$ (no. 14), a = 12.663(3), b = 14.346(4), c = 27.938(6) Å, β = 95.864(9)°, V = 5049(2) Å^3, T = 123(1) K, Z = 8, D_c = 1.159 g cm^{-3}, μ(Mo-Kα) = 0.077 mm^{-1}, R_1 = 0.0530, wR_2 = 0.1232, GOF = 1.030 ($I > 2\sigma(I)$). CCDC 684822.

§ *Crystal data* for **4b**(i) (from CH_2Cl_2–octane): $C_{56}H_{60}N_4O_8B_2$, M_r = 938.70, triclinic, $P\bar{1}$ (no. 2), a = 15.6794(18), b = 19.643(2), c = 38.369(4) Å, α = 87.700(2), β = 83.602(2), γ = 80.897(2)°, V = 11593(2) Å^3, T = 90(2) K, Z = 8, D_c = 1.076 g cm^{-3}, μ(Mo-Kα) = 0.071 mm^{-1}, R_1 = 0.0993, wR_2 = 0.2622, GOF = 1.078 ($I > 2\sigma(I)$). CCDC 684823.

¶ *Crystal data* for **4b**(ii) (from $CHCl_3$–octane): $C_{56}H_{60}N_4O_8B_2$, M_r = 938.70, monoclinic, $P2_1/n$ (no. 14), a = 17.944(4), b = 23.283(5), c = 24.446(4) Å, β = 96.271(4)°, V = 10152(3) Å^3, T = 90(2) K, Z = 4, D_c = 0.614 g cm^{-3}, μ(Mo-Kα) = 0.041 mm^{-1}, R_1 = 0.1091, wR_2 = 0.2642, GOF = 0.817 ($I > 2\sigma(I)$). CCDC 686903.

1 T. M. Swager, in *Acetylene Chemistry*, ed. F. Diederich, P. J. Stang and R. R. Tykwinski, Wiley-VCH, New York, 2005, ch. 6; D. T. McQuade, A. E. Pullen and T. M. Swager, *Chem. Rev.*, 2000, **100**, 2537; A. Rose, Z. Shu, C. F. Madigan, T. M. Swager and V. Bulović, *Nature*, 2005, **434**, 876.

2 *Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James and E. García-España, Wiley-VCH, New York, 1997; *Fundamentals and Applications of Anion Separations*, ed. R. P. Singh and B. A. Moyer, Kluwer Academic/Plenum Publishers, New York, 2004; *Anion Sensing*, ed. I. Stibor, *Topics in Current Chemistry*, Springer-Verlag, Berlin, 2005, vol. 255, p. 238; J. L. Sessler, P. A. Gale and W.-S. Cho, *Anion Receptor Chemistry*, RSC, Cambridge, 2006.

3 F. P. Schmidtchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609; P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 487; R. Martínez-Mãnez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419; P. A. Gale and R. Quesada, *Coord. Chem. Rev.*, 2006, **250**, 3219.

4 C. B. Black, B. Andrioletti, A. C. Try, C. Ruiperez and J. L. Sessler, *J. Am. Chem. Soc.*, 1999, **121**, 10438; P. Anzenbacher, Jr, A. C. Try, H. Miyaji, K. Jursikova, V. M. Lynch, M. Marquez and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 10268.

5 H. Maeda, *Eur. J. Org. Chem.*, 2007, 5313.

6 H. Maeda and Y. Kusunose, *Chem. Eur. J.*, 2005, **11**, 5661; H. Maeda, Y. Kusunose, Y. Mihashi and T. Mizoguchi, *J. Org. Chem.*, 2007, **72**, 2612; H. Maeda, Y. Haketa and T. Nakanishi, *J. Am. Chem. Soc.*, 2007, **129**, 13661.

7 N. Kameta, K. Hiratani, H. Houjo and M. Kanesato, *Chem. Lett.*, 2004, **33**, 142; N. Kameta and K. Hiratani, *Chem. Commun.*, 2005, 725.

8 B. Oddo and C. Dainotti, *Gazz. Chim. Ital.*, 1912, **42**, 716; W. M. Stark, M. G. Baker, F. J. Leeper, P. R. Raithby and A. R. Battersby, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1187.

9 *Multinuclear NMR*, ed. J. Mason, Plenum Press, New York, 1987.

10 All calculations were carried out using the Gaussian 03 program; M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr, T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, *GAUSSIAN 03 (Revision C.01)*, Gaussian Inc., Wallingford, CT, 2004.

11 M. Albrecht and M. Schneider, *Synthesis*, 2000, 1557.

12 Some unassigned electron density due to severely disordered solvents was removed by using SQUEEZE in PLATON software package, SQUEEZE-PLATON: A. L. Spek, *PLATON, A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands, 2005; D. van der Sluis and A. L. Spek, *Acta Crystallogr., Sect. A*, 1990, **46**, 194.

13 For example, succinate (n = 2) is one of the intermediates in the citric acid cycle. D. Voet and J. G. Voet, *Biochemistry*, Wiley, New York, 2004.

14 H. Maeda and Y. Haketa, to be submitted.