Tryptophan Anion Complexes of β-Cyclodextrin (Cyclomaltaheptaose), an Aminopropylamino-β-cyclodextrin and its Enantioselective Nickel(II) Complex

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6^{I}-(3-Aminopropylamino)-6^{I}-deoxy-cyclomaltaheptaose (βCDpn) exhibits enhanced complexation of tryptophan anion, by comparison with βCD, while the nickel(II) complex of βCDpn complexes tryptophan anion even more strongly and exhibits a tenfold enantioselectivity in favour of the (*S*)-tryptophan anion.

As part of a study of the complexation characteristics of modified cyclodextrins we have prepared 6^{I}-(3-aminopropylamino)-6^{I}-deoxy-cyclomaltaheptaose (βCDpn) and its nickel(II) complex {[Ni(βCDpn)]$^{2+}$} and investigated the complexation of tryptophan anion (trp^{-}) by these species. The complexation characteristics of unmodified cyclodextrins and their ability to discriminate between enantiomers are well documented.[1-5] Substituents on a cyclodextrin are known to affect the extent of complexation and chiral discrimination. Thus, by comparison with βCD, 6^{I}-amino-6^{I}-deoxy-cyclomaltaheptaose shows greater enantioselectivity in its complexation of sodium 2-phenylpropanoate, although the complexes with βCD are more stable.[4] The aminopropylamino substituent of βCDpn offers greater structural flexibility for interaction with guests, and provides an opportunity for chelation of metal ions. Such metal complexes, or metallocyclodextrins, have been studied as metalloprotein models[6] and recently their enantiomeric complexation characteristics have attracted attention.[7,8] We now report that βCDpn, by comparison with βCD, exhibits enhanced complexation of trp^{-}, while [Ni(βCDpn)]$^{2+}$ exhibits a further enhancement in complexation and also a tenfold enantioselectivity between (*R*)-trp^{-} and (*S*)-trp^{-}, which is much higher than reported previously for a metallocyclodextrin.[7,8]

βCDpn [^{13}C NMR (D_2O): 32.5 (C2′), 39.6 (C3′), 47.4 (C1′) and 50.4 (C6^{I})] was prepared by treatment of 6^{I}-*O*-(4-methylphenylsulfonyl)-cyclomaltaheptaose[9] with 1,3-diaminopropane (1.5 equiv.) in *N*,*N*-dimethylformamide at 313 K for 24 h, and isolated in 93% yield after recrystallization from water–acetone of the precipitate obtained by diluting the cooled reaction mixture with acetone.

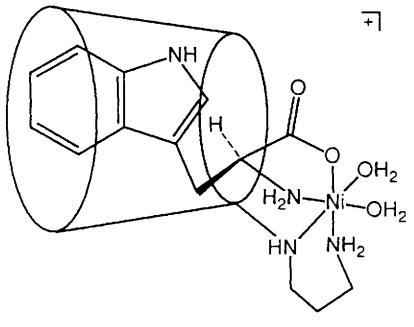

Fig. 1 A possible structure for [Ni(βCDpn)(*S*)-trp]$^{+}$, where the cyclodextrin annulus is shown as a truncated cone with the narrow and wide ends representing the circles delineated by the primary and secondary hydroxy groups, respectively

Table 1 Stability constants (*K*) for cyclodextrin and tryptophan anion complexes in aqueous solution at 298.2 K and I = 0.10 ($NaClO_4$)

Complexation	log (K/dm^3 mol^{-1})
βCD + (*R*)-trp^{-} ⇌ βCD(*R*)-trp^{-}	2.33 ± 0.06
βCD + (*S*)-trp^{-} ⇌ βCD(*S*)-trp^{-}	2.33 ± 0.08
βCDpn + (*R*)-trp^{-} ⇌ βCDpn(*R*)-trp^{-}	3.41 ± 0.05
βCDpn + (*S*)-trp^{-} ⇌ βCDpn(*S*)-trp^{-}	3.40 ± 0.07
βCDpn + Ni^{2+} ⇌ [Ni(βCDpn)]$^{2+}$	5.2 ± 0.1
[Ni(βCDpn)]$^{2+}$ + (*R*)-trp^{-} ⇌ [Ni(βCDpn)(*R*)-trp]$^{+}$	4.1 ± 0.2
[Ni(βCDpn)]$^{2+}$ + (*S*)-trp^{-} ⇌ [Ni(βCDpn)(*S*)-trp]$^{+}$	5.1 ± 0.2
Ni^{2+} + trp^{-} ⇌ [Ni(trp)]$^{+}$	5.42 ± 0.03

The stability constants for complexation of Ni^{2+} by βCDpn, and (*R*)-trp^{-} and (*S*)-trp^{-} by Ni^{2+}, βCD, βCDpn and [Ni(βCDpn)]$^{2+}$, determined using standard automated pH titration procedures,[4] are presented in Table 1. Neither βCDpn nor βCD discriminate between the enantiomers of trp^{-}, whereas the metallocyclodextrin [Ni(βCDpn)]$^{2+}$ complexes (*S*)-trp^{-} enantioselectively. It appears that the metal is important for chiral discrimination and, since the chirality of βCDpn is essential to the enantioselectivity displayed by [Ni(βCDpn)]$^{2+}$, it seems likely that [Ni(βCDpn)(*S*)-trp]$^{+}$ has both (*S*)-trp^{-} and βCDpn coordinated to Ni^{2+} as shown in Fig. 1. A similar structure is anticipated for [Ni(βCDpn)(*R*)-trp]$^{+}$. It has been suggested that discrimination between the enantiomers of trp^{-} by metallocyclodextrins requires the indole moiety of the more strongly bound enantiomer to be inside the cyclodextrin annulus while that of the other enantiomer is excluded from it.[7,8] We have no evidence for such a major structural difference in our system.

The stronger complexation of trp^{-} by the metallocyclodextrin [Ni(βCDpn)]$^{2+}$, relative to that by βCDpn and βCD, is consistent with bidentate coordination of trp^{-} stabilizing its complexation. However, this stronger complexation does not result from a simple combination of the effects of the cyclodextrin annulus and Ni^{2+}, as is apparent from the observation that the stability constant for [Ni(trp)]$^{+}$ is greater than that for either [Ni(βCDpn)(*R*)-trp]$^{+}$ or [Ni(βCDpn)(*S*)-trp]$^{+}$.

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