Synthesis and Metal Binding Properties of the Novel Ligand N,N′,N″-tris(2-hydroxyethyl)-1,4,7-triazacyclononane

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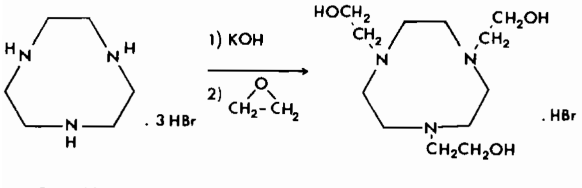
Tetraaza nitrogen-donor macrocycles with additional N-bonded coordinating groups such as acetate [1, 2] or hydroxyethyl groups [3] have recently been reported. The fit of such ligands onto metal ions is generally poor, as, for example, the tetraacetate derivatives of cyclam and its C-methyl substituted analogues appear to coordinate to metal ions through only two acetate and two nitrogen groups [4]. We have synthesized the title ligand, abbreviated THETAC, by the route outlined in Fig. 1. The ligand is obtained as the mono-hydrobromide, presumably because of the very high first pK_a value. The ligand is potentially hexa-dentate, and so should fit metal ions such as Ni(II) very much better than do potentially eight-coordinate ligands such as those reported above [1, 2].

We have measured the pK_a values for THETAC, and the formation constants with Cu(II) and Zn(II). The Cu(II) complex persists largely undecomposed by acid down to pH 2, so that to substantiate the results of the glass electrode study, a spectrophotometric study of the complex between pH 1 and 2 was undertaken. A broad peak at 720 nm belonging to the complex allowed us to determine the $\log K_1$ value for $[Cu(THETAC)]^{2+}$ as 15.50 ± 0.06. In Table I are shown the pK_a values for THETAC, compared with those for 9-aneN_3 (1,4,7-triazacyclononane) and dien (1,4,7-triazaheptane). It is seen that the first pK_a of THETAC is very much larger than that for 9-aneN_3 or dien. Since hydroxyethyl groups normally are electron-withdrawing, and lead to a lowering of the pK_a, it seems possible that the high pK_a value for THETAC is due to intramolecular hydrogen bonding involving the hydroxyethyl arms. The low second protonation constant suggests that this hydrogen bonded type of structure breaks down and the normal electron-withdrawing properties of the hydroxyethyl group become apparent.

The addition of hydroxyethyl groups to amines normally leads to a lowering of stability as compared to the analogues withtout hydroxyethyl substituents [5, 6]. This is probably due to the combined effects of steric strain caused by the formation of the chelate ring, and the electron-withdrawing properties of the hydroxyethyl group [5]. In contrast to this, Table II shows that the stability of the THETAC complexes is the same as, or larger than, that of the 9-aneN_3 complexes. This is quite remarkable, when one considers that recent structural studies [7] on the analogue of THETAC, 1,4,7-triazacyclononane-N,N′,N″-triacetate have shown that there is considerable



9-aneN_3 THETAC, M.Pt. 102°C

Fig. 1. Synthesis of N,N′,N″-tris(20hydroxyethyl)-1,4,7-triazacyclononane from 9-aneN_3, the latter prepared as described in reference 8 as the trihydrobromide. 9-aneN_3·3HBr is neutralised in H_2O/EtOH with KOH, and KBr filtered off. Ethylene oxide is added, and after standing overnight, the solvent is removed, and THETAC·HBr recrystallised from isopropanol.

TABLE I. pK_a Values for Some Triaza Ligands.

Ligand[a]	pK_1[b]	pK_2	Reference
dien	9.84	9.02	6
9-aneN_3	10.42	6.82	8
THETAC	11.52 ± 0.04	3.42 ± 0.02	this work[c]

[a] Abbreviations, see text. [b] pK_1 and pK_2 at 25 °C and ionic strength 0.1 [c] 25 °C, 0.1 *M* $NaNO_3$.

TABLE II. $\log K_1$ Values for Cu(II) and Zn(II) Complexes of 9-aneN_3 and THETAC.

Ligand	$\log K_1$ Cu(II)	$\log K_1$ Zn(II)	Reference
9-aneN_3	15.50	11.6	8
THETAC	15.50 ± 0.06	12.07 ± 0.06	this work[a]

[a] 25 °C, 0.1 *M* $NaNO_3$.

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steric strain in the metal to ligand bonds, with, for example, the three acetate oxygen donors being twisted around the C_3 axis by 35° relative to the positions expected for regular octahedral coordination. The same effect would be expected for the THETAC complexes, with considerable trigonal distortion produced by the fact that the hydroxyethyl arms are too short to permit regular octahedral coordination. The fact that the stability of the THETAC complexes is the same as, or even higher than, the mono-9-aneN_3 complexes suggests that all three hydroxyethyl groups are coordinated to the metal ion.

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