*A - Synthesis of the macrocycle [15]aneN4S*

The macrocycle 1-thia-4,7,10,13-tetraazacyclopentadecane ([15]aneN4S) was prepared according to the reactions depicted in Figure 1. The first step involved the synthesis of the precursor diamide, 1-thia-4,7,10,13-tetraazacyclopentadecane-3,14-dione (dioxo-[15]aneN4S) by reaction of the dimethyl ester of thiodiglycolic acid, with triethylenetetramine in dry methanol. The compound was purified by chromatography. Yield = 74%.

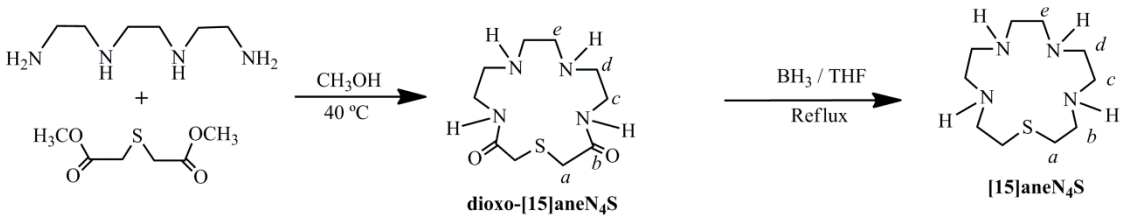


**Figure S1.** Schematic synthesis of [15]aneN4S.

The reduction of the cyclic diamide dioxo-[15]aneN4S with borane, in refluxing dry THF under nitrogen afforded the macrocycle [15]aneN4S. The compound was purified by chromatography. Yield = 68%.

*B - Characterization of the macrocycles dioxo-[15]aneN4S and [15]aneN4S*

*dioxo-[15]aneN4S:*
$^1$H NMR (400.13 MHz; $D_2O$; DSS; pD = 3.4): δ 3.26 (t, 4H, (triplet), $H_d$) 3.35 (s, 4H, (singlet), $H_a$), 3.53 (t, 4H, $H_c$), 3.57 (s, 4H, $H_e$) ppm.
$^{13}$C NMR (100.61 MHz; $D_2O$; dioxane; pD = 3.4): δ 35.3 ($C_c$), δ 37.5 ($C_a$), 42.8 ($C_e$), 48.2 ($C_d$), 175.0 ($C_2$) ppm.
FT-IR (KBr, cm$^{-1}$): ν 3427 (N–H), 1652 (C=O).

*[15]aneN4S:*
$^1$H NMR (400.13 MHz; $D_2O$; DSS; pD = 1.72): δ 3.17 (t, 4H, $^3J$ = 6, $H_a$), 3.34 (s, 4H, $^3J$ = 6, $H_e$), 3.44 (t, 4H, $H_d$), δ 3.50 (t, 4H, $^3J$ = 6, $H_b$), 3.57 (t, 4H, $^3J$ = 6, $H_c$) ppm.
$^{13}$C NMR (100.61 MHz; $D_2O$; dioxane; pD = 1.72): δ 29.55 ($C_a$), 43.64 ($C_d$), 45.00 ($C_c$), 45.37 ($C_e$), 46.94 ($C_b$).
FT-IR (KBr, cm$^{-1}$):ν 3426 (N–H).
*m*/*z* (ESI-MS; methanol; positive ion mode) 233.20 $[M + H]^+$.

Supplementary **Table S1.** Mean ± Standard Error for each experimental group in Figures 2, 3, 4 and 5.

| **Figure 2a** | |
|---|---|
| **Experimental group** | **Mean ± SE** |
| Control | 100 |
| MeHg | 24 ± 3.7 |
| MeHg + [15]aneN4S 40μM | 48 ± 7.9 |
| [15]aneN4S 40μM | 97 ±6.8 |
| MeHg + BAL 40μM | 36 ± 2.8 |
| BAL 40μM | 94 ± 2.6 |
| MeHg + DMSA 40μM | 53 ± 6.3 |
| DMSA 40μM | 95 ± 6.2 |
| **Figure 2b** | |
| **Experimental group** | **Mean ± SE** |
| Control | 100 |
| MeHg | 49 ± 6.0 |
| MeHg + [15]aneN4S 40μM | 70 ± 2.7 |
| [15]aneN4S 40μM | 102 ±6.2 |
| MeHg + BAL 40μM | 93 ± 3.2 |
| BAL 40μM | 102 ± 3.7 |
| MeHg + DMSA 40μM | 81 ± 6.4 |
| DMSA 40μM | 93 ± 7.2 |
| **Figure 3** | |
| **Experimental group** | **Mean ± SE** |
| Control | 100 |
| [15]aneN4S 10μM | 96 ± 2.0 |
| [15]aneN4S 20μM | 106 ± 11 |
| [15]aneN4S 40μM | 111 ± 4.1 |
| [15]aneN4S 80μM | 102 ± 8.1 |
| [15]aneN4S 120μM | 103 ± 14.6 |
| BAL 10μM | 91 ± 1 |
| BAL 20μM | 87 ± 4.8 |
| BAL 40μM | 87 ± 9.8 |
| BAL 80μM | 86 ± 9.1 |
| BAL 120μM | 74 ± 10.1 |
| DMSA 10μM | 100 ± 5.2 |
| DMSA 20μM | 106 ± 1.2 |
| DMSA 40μM | 108 ± 8.0 |
| DMSA 80μM | 115 ± 3.3 |
| DMSA 120μM | 115 ± 2.6 |
| **Figure 4a** | |
| **Experimental group** | **Mean ± SE** |
| Control | 100 |
| MeHg | 33 ± 8.8 |
| MeHg + [15]aneN4S 40μM | 36 ± 12 |
| [15]aneN4S 40μM | 111 ± 26 |
| MeHg + BAL 40μM | 35 ± 16 |
| BAL 40μM | 106 ± 16 |
| MeHg + DMSA 40μM | 28 ± 11 |
| DMSA 40μM | 82 ± 1.6 |
| **Figure 4b** | |
| **Experimental group** | **Mean ± SE** |
| Control | 100 |
| MeHg | 47 ± 3.7 |
| MeHg + [15]aneN4S 40μM | 105 ± 17 |
| [15]aneN4S 40μM | 102 ± 7.4 |
| MeHg + BAL 40μM | 112 ± 16 |
| BAL 40μM | 94 ± 9.4 |
| MeHg + DMSA 40μM | 48 ± 3.0 |
| DMSA 40μM | 111 ± 15 |
| **Figure 5b** | |
| **Experimental group** | **Mean ± SE** |
| C | 1.0 |
| M | 0.87 ± 0.015 |
| M+N | 0.99 ± 0.19 |

| | |
|---|---|
| N | 0.99 ± 0.16 |
| M+B | 0.99 ± 0.092 |
| B | 1.0 ± 0.039 |
| M+D | 1.0 ± 0.12 |
| D | 1.02 ± 0.043 |

**Figure 5c**

| **Experimental group** | **Mean ± SE** |
|---|---|
| C | 1.0 |
| M | 0.88 ± 0.12 |
| M+N | 1.1 ± 0.15 |
| N | 1.0 ± 0.17 |
| M+B | 0.89 ± 0.20 |
| B | 0.77 ± 0.19 |
| M+D | 0.71 ± 0.060 |
| D | 0.69 ± 0.16 |