

Syntheses, Characterization and Antibacterial Studies of Manganese (II) Complexes of Hexamethyl Tetraazacyclotetradecadiene Ligand and Isomers of its Reduced Form

Rahul Das¹, Pranta Sarker¹, Saswata Rabi^{1,2}, Tumpa Rani Majumder¹, AM Masudul Azad Chowdhury³, Debashis Palit¹ and Tapashi Ghosh Roy^{1*}

¹Department of Chemistry, University of Chittagong, Chattogram, Bangladesh

²Department of Chemistry, Chittagong University of Engineering and Technology, Chattogram, Bangladesh

³Department of Genetic Engineering and Biotechnology, University of Chittagong, Chattogram, Bangladesh

*Corresponding Author: Tapashi Ghosh Roy, Department of Chemistry, University of Chittagong, Chattogram, Bangladesh.

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Abstract

A 14-membered hexamethyl-tetraazamacrocyclic, Me₆[14]diene.2HClO₄ (L.2HClO₄) on reduction with NaBH₄ followed by extraction with CHCl₃ at pH above 12 resulted in a mixture of isomeric ligands, Me₆[14]anes which were separated by fractional crystallization from xylene and designated by 'tet-a' and 'tet-b'. Interaction of the ligands L.2HClO₄, 'tet-a' and 'tet-b' with manganese(II) chloride tetrahydrate produced brown products of [Mn(L)(ClO₄)₂], [Mn(tet-a)Cl₂] and [Mn(tet-b)Cl₂] respectively which are octahedral in geometry. Moreover substituted manganese(II) salts (Mn(SCN)₂, Mn(NO₃)₂, Mn(NO₂)₂ and MnBr₂) prepared by the reaction of manganese(II) chloride tetrahydrate with KSCN, KNO₃, NaNO₂ and KBr respectively on interactions with the ligand 'tet-b' afforded brown products, [Mn(tet-b)(NCS)₂], [Mn(tet-b)(NO₃)₂], [Mn(tet-b)(NO₂)₂] and [Mn(tet-b)Br₂] respectively. The complexes have been characterized by using different modern analytical and spectroscopic techniques. The antibacterial activities of the concerned ligands and their manganese(II) complexes have been investigated against four selected bacteria.

Keywords: N-pendant Tetraazamacrocyclic Ligand; Manganese(II) Complexes; Spectroscopic Techniques; Antibacterial Activities

Introduction

Due to the fascinating role of the macrocyclic compounds in different sectors [1-6] of modern science, scientists are driving their movement toward the development of the area of macrocyclic chemistry. Macrocyclic compounds are being remarkably used as antibacterial [5], antifungal [5], and antitumor agents [6]. So it is quite reasonable to perform some study on new macrocyclic compounds. In this context, different types of macrocyclic ligands and their various metal complexes were studied elaborately by the modern researchers [1-11]. Some reports [7-11] on the different

metal complexes of the concerned ligands are also available in the literature. However, no work on manganese(II) complexes of the concerned ligands has been carried out so far. So it was interesting to see whether five or six coordinated complexes of this ligand could be prepared using manganese(II) as metal template. It was our first approach to synthesize and characterize manganese(II) complexes. Thus an effort to do so was successful. So, this study deals with the synthesis, characterization and biological evaluation of the azamacrocyclic ligand Me₆[14]diene.2HClO₄, isomeric ligands 'tet-a' & 'tet-b' and their Mn(II) complexes.

Experimental

Materials and Methods

The chemicals were of analytical reagent grade (Sigma Aldrich, USA) which were used without further purification. Microanalysis of C, H, N and S of the compounds have been carried out on a CHNS analyzer at the Department of Chemistry, Friedrich Schiller University, Jena, Germany. Melting points of the complexes were obtained with an electrothermal melting point apparatus at the Inorganic Research Laboratory of Chittagong University. Conductance measurements of the metal complexes were done in DMSO solutions using HANNA instrument with HI 8820N conductivity cell at the University of Chittagong. The infrared spectra of the complexes were taken as KBr discs in the range 4000-400 cm^{-1} at the Department of Chemistry, University of Chittagong, Chattogram, Bangladesh. Electronic spectra of the samples were recorded on a Shimadzu UV-visible spectrophotometer. All the magnetic measurements have been carried out by SHERWOOD SCIENTIFIC magnetic susceptibility balance. All measurements on antibacterial activities against four bacteria have been carried out at the Department of Microbiology, University of Chittagong as described in experimental section.

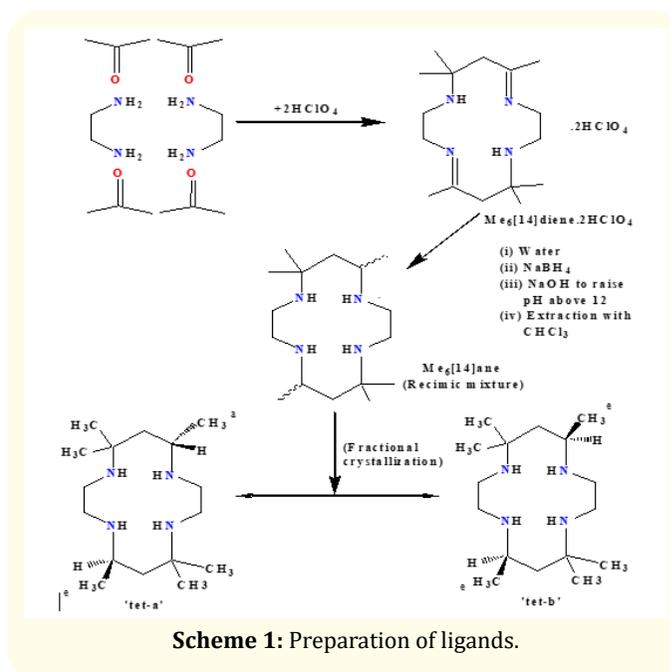
Ligands

Ligand salt, hexamethyl-tetraazacyclotetradecadiene dihydroperchlorate ($\text{L}\cdot 2\text{HClO}_4$), its reduced isomeric ligands, 'tet-a' and 'tet-b' (Scheme 1) have been prepared as per literature [12].

Manganese(II) complexes of ligands

$[\text{Mn}(\text{L})(\text{ClO}_4)_2]$

Ligand $\text{L}\cdot 2\text{HClO}_4$ (0.481g, 1.0 mmol) and manganese(II) chloride tetrahydrate (0.197g, 1.0 mmol) were dissolved separately in 100 mL hot methanol. The ligand solution was added drop wise to salt solution while hot. The mixture was heated under reflux for 6 hours. A brown product of $[\text{Mn}(\text{L})(\text{ClO}_4)_2]$ started to appear. Since the filtration was not possible due to the stickiness of the product, so the mixture was fully dried on water bath until the solid powder was formed. Thereafter the solid was washed with methanol for several times, followed by ethanol and diethyl ether. Then the product was dried under vacuum for 24 hours, finally stored in a desiccator over silica gel.



For $[\text{Mn}(\text{L})(\text{ClO}_4)_2]$ (534.30): Color: brown. M. p. above 250 °C. Anal. Calcd.(%): C, 35.97; H, 6.04; N, 10.49. Found (%): C, 35.96; H, 6.05; N, 10.51. IR (KBr disc, cm^{-1}): $\nu(\text{N-H})$, 3188vs; $\nu(\text{C-H})$, 2993; $\delta(\text{C-H})$, 1510; $\nu(\text{CH}_3)$, 1350s; $\nu(\text{C-C})$, 1445s; $\nu(\text{Mn-N})$, 426w; $\nu(\text{ClO}_4)$, 1111s, 624vs; $\nu(\text{C=N})$, 1589. UV-vis (in nm): 586, 495, 341. Magnetic moment μ_{eff} (BM): 5.705.

$[\text{Mn}(\text{L}')\text{Cl}_2]$ (L' = 'tet-a' or 'tet-b')

Ligand L'. (L' = 'tet-a' or 'tet-b') (0.320 g, 1.0 mmol) and of manganese(II) chloride tetrahydrate (0.197 g, 1.0 mmol) were dissolved separately in 100 mL hot methanol. The ligand solution was added drop wise to the salt solution while hot. The mixture was heated under reflux for 6 hours. A brown product of $[\text{Mn}(\text{L}')\text{Cl}_2]$ (L' = 'tet-a' or 'tet-b') started to appear. Since filtration was not possible as the product was sticking to the filter paper, so the solution was fully dried on water bath until the solid powder was formed. Later the product was washed with methanol for several times, followed by ethanol and diethyl ether. Then the product was dried under vacuum for 24 hours, finally stored in a desiccator over silica gel.

For $[\text{Mn}(\text{'tet-a'})\text{Cl}_2]$ (410.33): Color: brown. M. p. above 250°C. Anal. Calcd.(%): C, 46.89; H, 8.84; N, 13.65. Found (%): C, 46.84;

H, 8.83; N, 13.63. IR (KBr disc, cm^{-1}): $\nu(\text{N-H})$, 3188s; $\nu(\text{C-H})$, 2972; $\delta(\text{C-H})$, 1431; $\nu(\text{CH}_3)$, 1365s; $\nu(\text{C-C})$, 1148m; $\nu(\text{Mn-N})$, 445w; UV-vis (in nm): 568, 489, 370. Magnetic moment μ_{eff} (BM): 5.821.

For $[\text{Mn}(\text{'tet-b'})\text{Cl}_2]$ (410.33): Color: brown. M. p. above 250 °C. Anal. Calcd.(%): C, 46.89; H, 8.84; N, 13.65. Found (%): C, 46.81; H, 8.86; N, 13.66. IR (KBr disc, cm^{-1}): $\nu(\text{N-H})$, 3213s; $\nu(\text{C-H})$, 2972; $\delta(\text{C-H})$, 1446; $\nu(\text{CH}_3)$, 1363s; $\nu(\text{C-C})$, 1168s; $\nu(\text{Mn-N})$, 437w. Molar conductivity ($\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$): in DMSO, 33. UV-vis (in nm): 576, 438, 387. Magnetic moment μ_{eff} (BM): 5.788.

Syntheses of manganese(II) complexes $[\text{Mn}(\text{'tet-b'})(\text{X})_2]$ ($\text{X}=\text{NCS}$, NO_3 , NO_2 or Br) of 'tet-b' produced from substituted manganese(II) salts of MnCl_2

Manganese(II) chloride tetrahydrate (0.197 g, 1.0 mmol) and 2.0 mmol of KSCN, KNO_3 , NaNO_2 or KBr were dissolved/suspended separately in 100 mL hot methanol. Both solutions/mixtures were heated separately on water bath. After 10 minutes, KSCN, KNO_3 , NaNO_2 or KBr solution/suspension was added drop-wise to $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ solution while hot. The resultant solution/mixture was heated for 45 minutes. Then it was allowed to stand for 1 hour at room temperature. The mixture was then filtered and the filtrate was again heated for 15 minutes. To this, a hot methanolic solution of 'tet-b' (0.302g, 1.0 mmol) was added slowly. The resulting mixture was heated for further 30 minutes. Brown precipitates were appeared in each case, except for diisothiocyanato complex where silvery grey precipitate appeared. Then the mixture was concentrated and brown solid products of $[\text{Mn}(\text{tet-b})(\text{NO}_3)_2]$, $[\text{Mn}(\text{tet-b})(\text{NO}_2)_2]$, $[\text{Mn}(\text{tet-b})\text{Br}_2]$ and shiny silver grey solid product of $[\text{Mn}(\text{tet-b})(\text{NCS})_2]$ were separated by filtration which were washed with methanol for several times, followed by water, ethanol and diethyl ether. Then the products were dried under vacuum for 24 hours, finally stored in a desiccator over silica gel.

For $[\text{Mn}(\text{'tet-b'})(\text{NCS})_2]$ (455.58): Color: shiny silvery grey. M. p. above 250 °C. Anal. Calcd.(%): C, 47.46; H, 7.96; N, 18.45. Found (%): C, 47.48; H, 7.94; N, 18.44. IR (KBr disc, cm^{-1}): $\nu(\text{N-H})$, 3199vs; $\nu(\text{C-H})$, 2962; $\delta(\text{C-H})$, 1460; $\nu(\text{CH}_3)$, 1363s; $\nu(\text{C-C})$, 1143s; $\nu(\text{Mn-N})$, 511; $\nu(\text{CN})$, 2069vs, 2044vs; $\nu(\text{CS})$, 804s; $\delta(\text{NCS})$, 480m. Molar conductivity ($\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$): in DMSO, 42. UV-vis (in nm): 580, 457, 345. Magnetic moment (μ_{eff} , BM): 5.906.

For $[\text{Mn}(\text{'tet-b'})(\text{NO}_3)_2]$ (463.44): Color: Brown. Anal. Calcd. (%): C, 41.47; H, 7.83; N, 18.13. Found (%): C, 41.45; H, 7.84; N,

18.14. IR (KBr disc, cm^{-1}): $\nu(\text{N-H})$, 3214s; $\nu(\text{C-H})$, 2970; $\delta(\text{C-H})$, 1459; $\nu(\text{CH}_3)$, 1362w, 1383s; $\nu(\text{C-C})$, 1143m; $\nu(\text{Mn-N})$, 559; $\nu(\text{NO}_3)$, 1339m, 1459m. UV-vis (in nm): 546, 440, 360. Magnetic moment μ_{eff} (BM): 5.657.

For $[\text{Mn}(\text{'tet-b'})(\text{NO}_2)_2]$ (431.44): Color: Brown. Anal. Calcd.(%): C, 44.54; H, 8.41; N, 19.48. Found (%): C, 44.55; H, 8.40; N, 19.47. IR (KBr disc, cm^{-1}): $\nu(\text{N-H})$, 3214s; $\nu(\text{C-H})$, 2970; $\delta(\text{C-H})$, 1458; $\nu(\text{CH}_3)$, 1362s, 1388s; $\nu(\text{C-C})$, 1143s; $\nu(\text{Mn-N})$, 512, 559; $\nu(\text{asym})(\text{NO}_2)$, 1458m; $\nu(\text{sym})(\text{NO}_2)$, 1362sh. UV-vis (in nm): 557, 456, 354. Magnetic moment μ_{eff} (BM): 5.803.

For $[\text{Mn}(\text{'tet-b'})\text{Br}_2]$ (499.23): Color: Brown. Anal. Calcd.(%): C, 38.49; H, 7.27; N, 11.22. Found (%): C, 38.50; H, 7.28; N, 11.20. IR (KBr disc, cm^{-1}): $\nu(\text{N-H})$, 3232m; $\nu(\text{C-H})$, 2973; $\delta(\text{C-H})$, 1443; $\nu(\text{CH}_3)$, 1371s, 1388s; $\nu(\text{C-C})$, 1144m; $\nu(\text{Mn-N})$, 527.

Antibacterial activities

Studies on antibacterial activity of concerned ligand 'tet-b' and its manganese(II) complexes were carried out for controlling the growth of pathogenic microorganisms by using disc diffusion method. Solutions of known concentration (mg/mL) of the test samples were made by dissolving measured amount of the samples in definite volume of solvents. Dried and sterilized filter paper disc (4 mm in diameter) were then impregnated with known amounts of test substances using micropipette and these were then allowed to dry. Discs containing the test material were placed on nutrient agar medium uniformly seeded with the test microorganism. Discs soaked in respective solvents without test material were used as negative control. These plates were then kept at low temperature (4°C) for 2-4 hours to allow maximum diffusion. During this time dried discs absorbed water from the surrounding media and then the test materials were dissolved and diffused out of the media. The diffusion occurred according to the physical law that controls the diffusion of molecules through agar gel. As a result, there was a gradual change of test materials concentration in the media surrounding the discs. The plates were then incubated at 35 °C for 24 hours to allow maximum growth of the organisms at inverted position. If the test materials had any antibacterial activity, it inhibited the growth of the microorganisms giving a clear distinct zone called "zone of inhibition". The antibacterial activity of the test agent was determined by measuring the zone of inhibition expressed in millimeter in diameter. The experiment was carried out more than once and mean of the readings was taken.

Results and Discussion

Ligand

The ligand hexamethyl-tetraazacyclotetradecadiene dihydroperchlorate (L·2HClO₄), its reduced isomeric ligands, 'tet-a' and 'tet-b' were prepared (Scheme 1) and characterized by the procedure adopted in our previous study [12].

Manganese(II) complexes

[Mn(L)(ClO₄)₂], [Mn('tet-a')Cl₂] and [Mn('tet-b')Cl₂]

Interaction of the ligands L·2HClO₄, 'tet-a' and 'tet-b' with manganese(II) chloride tetrahydrate produced [Mn(L)(ClO₄)₂], [Mn('tet-a')Cl₂] and [Mn('tet-b')Cl₂] respectively. Attempts to carry out axial substitution reactions on these complexes were unsuccessful. The IR spectra of these complexes exhibit intense C-H bands stretching at 2968-2993 cm⁻¹ and bending at 1431-1510 cm⁻¹, C-C at 1145-1168 cm⁻¹ and Mn-N at 426-445 cm⁻¹. The bands appearing at 3188-3213 cm⁻¹ and 1350-1365 cm⁻¹ are attributed to ν_{NH} and ν_{CH3} stretching frequencies respectively. In case of [Mn(L)(ClO₄)₂] the other bands appearing at 624 cm⁻¹ and 1112 cm⁻¹ are attributed to ν_{ClO4} stretching frequencies where the peak at 1112 cm⁻¹ was splitted into 1087 cm⁻¹ and 1145 cm⁻¹ which indicates that the ClO₄ is coordinated with manganese(II). A sharp band at 1589 cm⁻¹ due to the presence of C = N bond is observed. Since the IR spectra could not be run below 400 cm⁻¹, so, Mn-Cl stretch which is expected to be around 260 cm⁻¹ could not be detected for [Mn(L)Cl₂] (L= 'tet-b' or 'tet-b') complexes. The molar conductivity value of 33 ohm⁻¹cm²mole⁻¹ in DMSO of [Mn('tet-b')Cl₂] indicates that the complex is non electrolyte as expected for the formula assigned [13]. This means that the anions are in the coordination sphere as expected for the six coordinated octahedral geometry. Due to insolubility of other complexes in almost all common solvents, the conductivity of those complexes could not be measured. Since the conductivity value of the mentioned soluble Mn(II) complex corresponds to octahedral nonelectrolytic complexes and the Mn(II) complexes are generally expected to have octahedral geometries so analogously, all these complexes are assumed to have the octahedral geometries. The electronic spectra of these complexes display different d-d bands at 544-586, 438-495 and 341-387 nm for ⁶A_{1g} → ⁴T_{1g}, ⁶A_{1g} → ⁴T_{2g} and ⁶A_{1g} → ⁴A_{1g} respectively. The values obtained correspond to those reported earlier for the octahedral manganese(II) complexes [14]. The magnetic moment values of 5.705-5.906 BM corresponding to five unpaired

electrons indicate that, these complexes are paramagnetic as expected for manganese(II) complexes having d⁵ systems [14]. So, on the basis of the above discussion the following structures (Str. I, II and III) have been assigned for [Mn(L)(ClO₄)₂], [Mn('tet-a')Cl₂] and [Mn('tet-b')Cl₂] respectively.

Figure 1

[Mn('tet-b')(X)₂] (X=NCS, NO₃, NO₂ or Br)

Interaction of KSCN, KNO₃, NaNO₂ and KBr with manganese(II) chloride tetrahydrate at 2:1 ratio produced Mn(SCN)₂, Mn(NO₃)₂, Mn(NO₂)₂ and MnBr₂ respectively which on reactions with the ligand 'tet-b' furnished [Mn('tet-b')(NCS)₂], [Mn('tet-b')(NO₃)₂], [Mn('tet-b')(NO₂)₂] and [Mn('tet-b')Br₂] respectively. The IR spectra of these complexes exhibit intense C-H bands stretching at 2962-2973 cm⁻¹ and bending at 1443-1460 cm⁻¹, C-C bands at 1143-1144 cm⁻¹ and Mn-N bands at 511-559 cm⁻¹. The bands appearing at 3199-3232 cm⁻¹ and 1362-1388 cm⁻¹ are attributed to ν_{NH} and ν_{CH3} stretching frequencies respectively. Appearance of a ν_{CN} band at 2069 cm⁻¹, a single sharp δ_{NCS} band near 480 cm⁻¹ and ν_{CS} band at 804 cm⁻¹ in the complex, [Mn('tet-b')(NCS)₂] is a good indication of N-bonded isothiocyanate group. In [Mn('tet-b')(NO₃)₂], the spectrum displays additional bands at 1339 cm⁻¹ and 1459 cm⁻¹ attributed to coordinated NO₃⁻. The separation of these bands by 120 cm⁻¹ is accounted for unidentate mode of coordination [13]. Moreover the infrared spectrum of the complex [Mn('tet-b')(NO₂)₂] exhibits the ν_{asym}(NO₂) and ν_{sym}(NO₂) bands at 1458 cm⁻¹ and 1388 cm⁻¹ respectively. Appearance of band at 848 cm⁻¹ can be attributed to δ_{NO2} frequency. However, for [Mn('tet-b')Br₂] no additional peak corresponding to Mn-Br stretch which is expected to appear at around 260 cm⁻¹ could be detected as the spectra could not be run below 400 cm⁻¹. The molar conductivity value of 32 ohm⁻¹cm²mole⁻¹ in DMSO of [Mn('tet-b')(NCS)₂] indicates that the complex is non electrolyte as

expected for the formula assigned. This means that the anions are in the coordination sphere as expected for six coordinated octahedral geometry. However due to insolubility of the other three complexes, the molar conductivity for them could not be measured. The electronic spectra of these complexes display different d-d bands at 544-586, 438-495 and 341-387 nm for ${}^6A_{1g} \rightarrow {}^4T_{1g}$, ${}^6A_{1g} \rightarrow {}^4T_{2g}$ and ${}^6A_{1g} \rightarrow {}^4A_{1g}$ respectively [14]. The magnetic moment values of 5.705-5.906 BM corresponding to five unpaired electrons indicate that, these complexes are paramagnetic as expected for other manganese(II) complexes having d^5 system [14]. So, on the basis of the above discussion the following structures (Str. IV, V, VI and VII) have been assigned for $[Mn(tet-b)(NCS)_2]$, $[Mn(tet-b)(NO_3)_2]$, $[Mn(tet-b)(NO_2)_2]$ and $[Mn(tet-b)Br_2]$ respectively.

Antibacterial activities

Antibacterial activities of the concerned macrocycles and their soluble Mn(II) complexes have been studied against some specific bacteria. The results of this study explore that, while the ligands are ineffective in all cases but dichlorido and isothiocyanato Mn(II) complexes showed good activity against all bacteria except *Bacillus megaterium*. The concerned metal salts, experimental solvent (DMSO) as control were also tested and it was found that although experimental solvent had no activity, the concerned metal salt exhibit the activity to a little extent against the bacteria. Though the metal salt shows some activity, the activity showed by the complexes is not due to metal ions. Since the complexes are very much stable, so there is no possibility of dissociation of complexes to release metal ions [15]. Thus based on the positive results of this investigation it can be concluded that further studies are warranted in this area with analogous ligands and complexes. The overall findings of this investigation have been presented in table 1.

Conclusion

This study reveals that the ligands $L.2HClO_4$, 'tet-a' and 'tet-b' undergo facile complexation with $MnCl_2.4H_2O$ to produce octahedral complexes of formulae $[Mn(L)(ClO_4)_2]$, $[Mn(tet-a)Cl_2]$ and $[Mn(tet-b)Cl_2]$ respectively. But attempts to carry out axial substitution reactions on these complexes were unsuccessful. However attempts towards preparing more Mn(II) complexes of 'tet-b' with substituted Mn(II) salts were successful. Thus interaction of 'tet-b' with substituted Mn(II) salts like $Mn(SCN)_2$, $Mn(NO_3)_2$, $Mn(NO_2)_2$ and $MnBr_2$ (produced by the reactions of $MnCl_2.4H_2O$ with $KSCN$, KNO_3 , $NaNO_2$ and KBr respectively) resulted in corresponding octahedral Mn(II) complexes $[Mn(tet-b)(NCS)_2]$, $[Mn(tet-b)(NO_3)_2]$, $[Mn(tet-b)(NO_2)_2]$ and $[Mn(tet-b)Br_2]$ respectively. In antibacterial test, soluble investigated complexes are found to be potential as antibacterial agents, while the ligands are ineffective against almost all bacteria.

Figure 2

Table 1: Antibacterial data for the Ligand and their soluble Manganese(II) complexes

Sample no.	Ligands and their complexes	Zone of inhibition in diameter (mm)			
		Gram-positive bacteria		Gram-negative bacteria	
		<i>Bacillus megaterium</i>	<i>Shigella sonnei</i>	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>
R ₁	$[Mn(tetb)Cl_2]$	0	10	11	9
R ₂	$[Mn(tetb)(SCN)_2]$	0	8	11	9
M ₁	$MnCl_2$	7	6	6	8
Control	DMSO	0	0	0	0
L ₁	$L.2HClO_4$	0	0	0	0
L ₂	tet-b	0	0	0	0
Standard	Ampicillin	29	27	32	34

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Conflict of Interest

There is no conflict of interest.

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