# Metallamacrocycle formation through dimerization of metal bioconjugates derived from amino acids and peptides.

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**Supporting Information**.

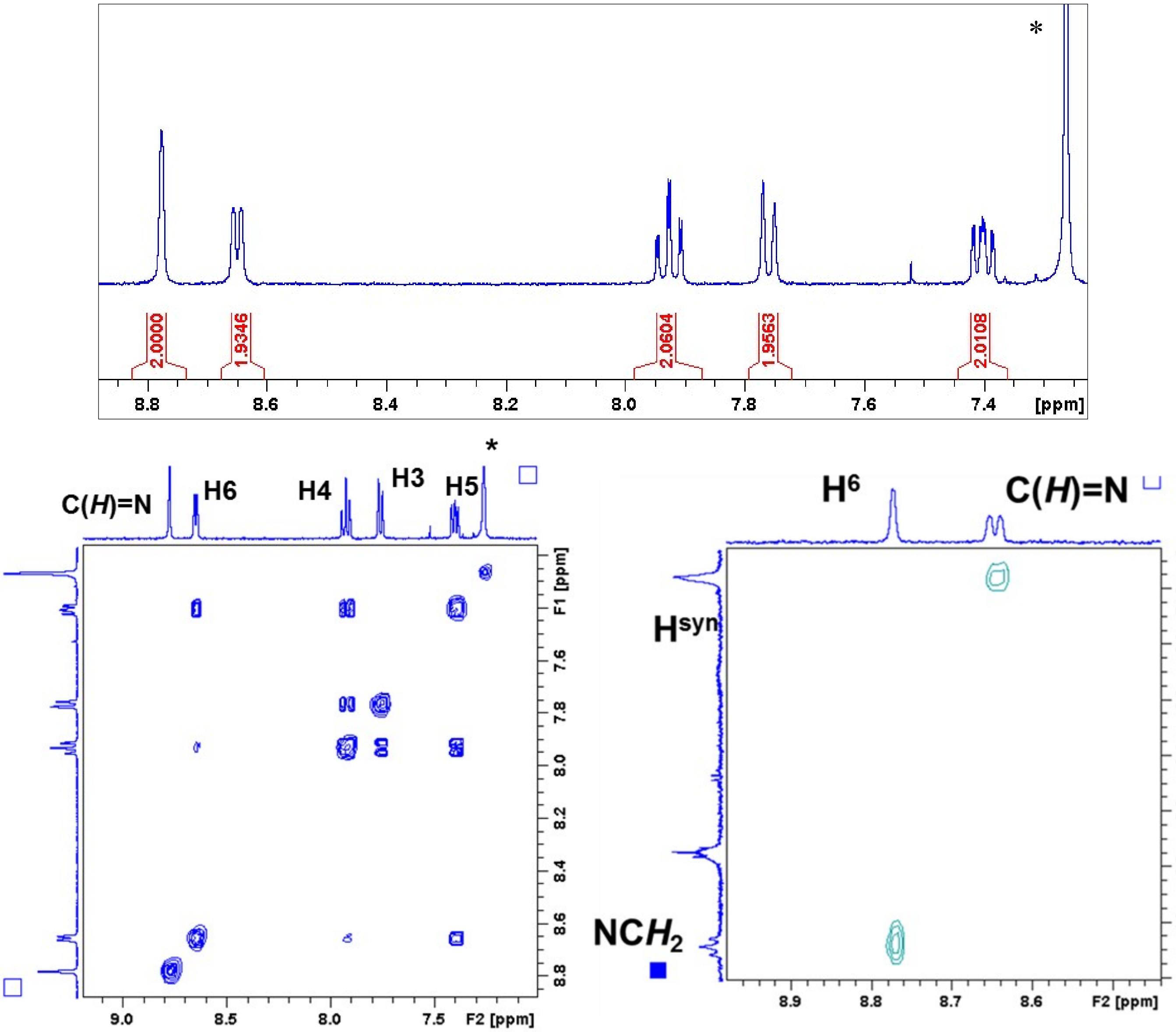


**Figure S1.** (above) $^{1}$H NMR in $CDCl_3$ (* represents residual solvent peak) of dimer **2c** (aromatic region) showing the equivalence of the iminopyridine signals, which suggest that an effective centrosymmetric structure is maintained in solution. The assignments of the signals were carried out with the help of 2D experiments, $^{1}$H-$^{1}$H COSY (below left) and $^{1}$H-$^{1}$H NOESY (below right). The $^{1}$H-$^{1}$H NOESY NMR of **2c** shows the spatial proximity of the H$^{6}$ proton of the pyridine with one of the syn protons of the methallyl system, which indicates a relative *trans* conformation of the methallyl group and the chlorine. A crosspeak is also observed between the imine proton C(*H*)=N and one of the protons of the $NCH_2$ group, confirming that this group is the one bonded to the imine nitrogen (see also figure S2)

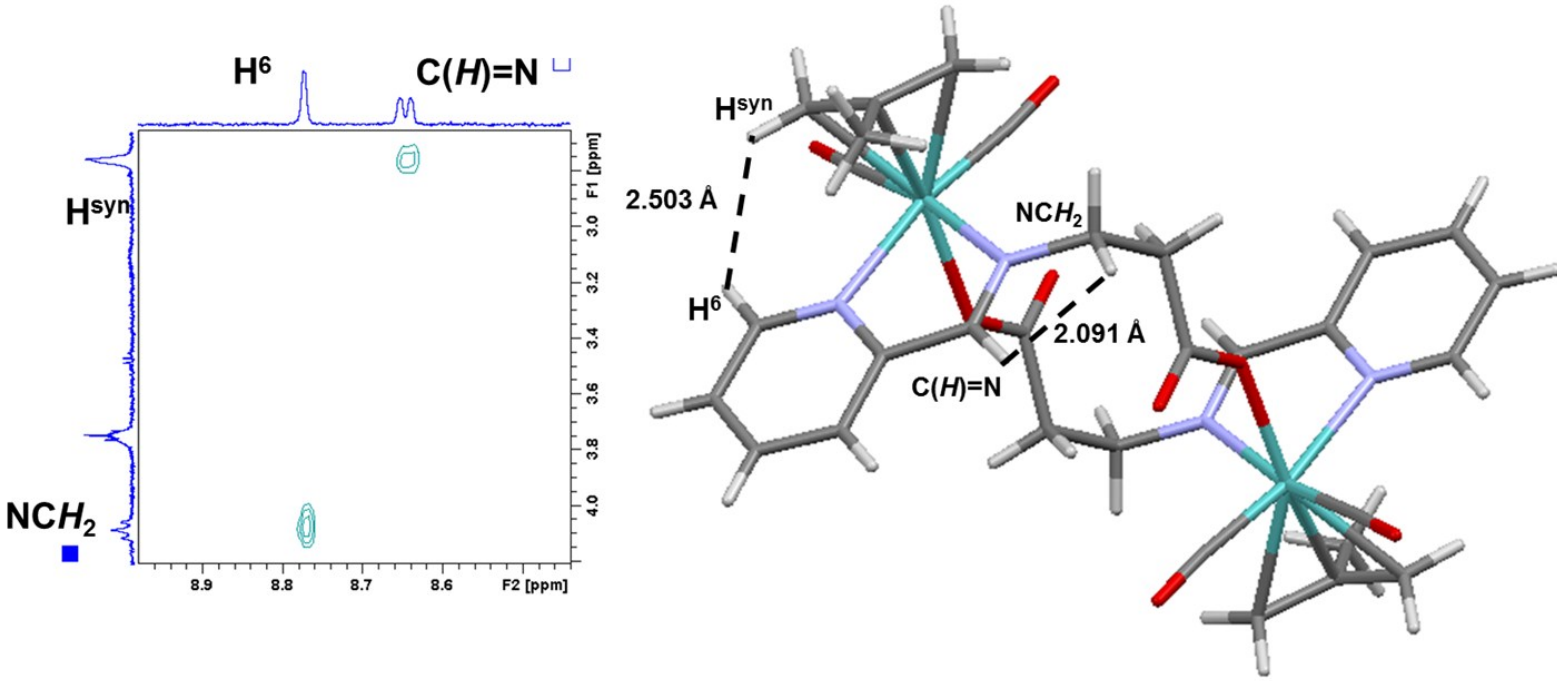


**Figure S2**: $^1$H-$^1$H NOESY experiment showing spatial proximity between the H$^6$ proton and one H$_{syn}$ proton and between one proton of the NCH$_2$ group and the iminic proton. The distance between both sets of protons in the structure obtained by X-ray diffraction is 2.503 and 2.091 Å respectively, which is in agreement with the spatial proximity observed in solution.

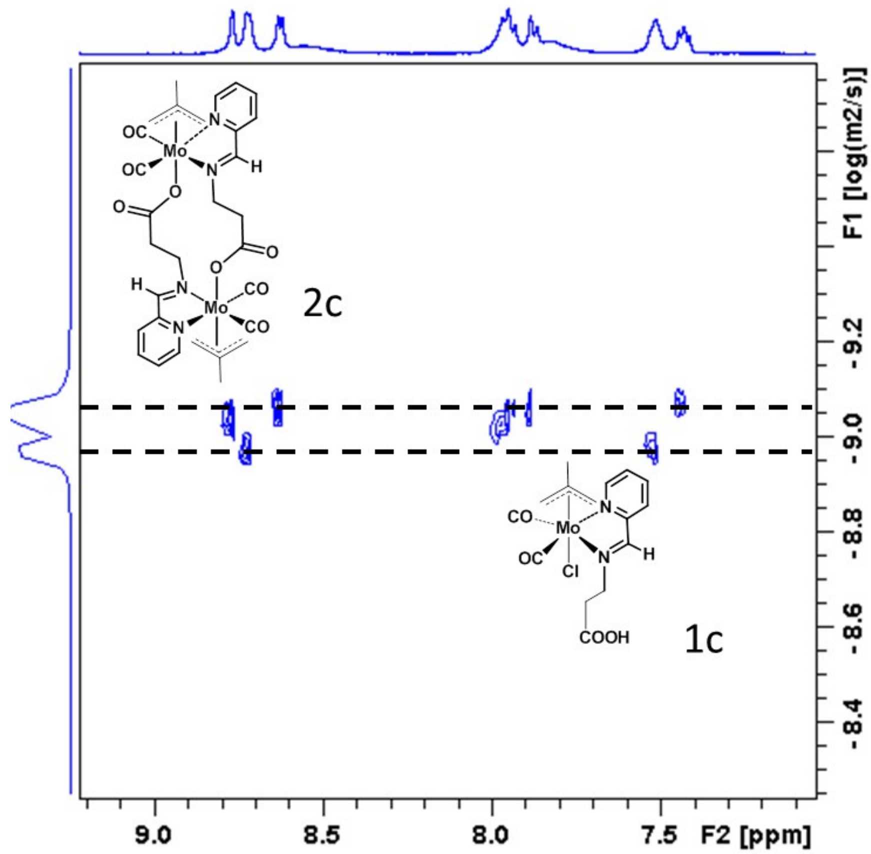


**Figure S3**: $^1$H NMR DOSY of an approximately equimolar mixture of dimer **2c** (upper line) and its monomeric precursor **1c** (lower line) in $CD_2Cl_2$

**Monitoring of formation of dimer 2c by $^1$H NMR.**

An NMR tube was charged with 10 mg of **1c** and $CDCl_3$ was added (0.6mL). To the resultant suspension 1.5 equivalents of $NEt_3$ were added (3 uL) to yield a purple solution. $^1$H NMR spectra showed broad signals suggesting some dynamic process. After 5 min at room temperature no changes were observed by $^1$H NMR and AgOTf was added (5 mg, 1.5 equivalents). The reaction was followed by $^1$H NMR. Several unidentified signals appeared and were evolving at room temperature in the $^1$H NMR spectra until after 3h at room temperature, the $^1$H NMR spectrum showed the formation of dimer **2c** as the only iminopyridine compound of the reaction.. Note: The same results were obtained by adding first AgOTf and subsequently $NEt_3$.

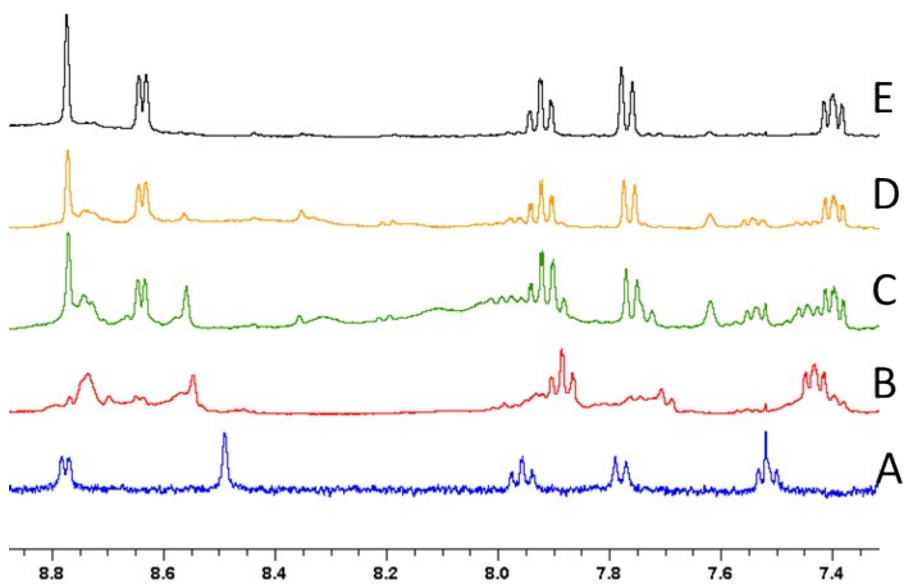


**Figure S4.** $^1$H NMR (room temperature) spectra in $CDCl_3$ showing the reaction of **1c** (spectrum A**)** in the presence of AgOTf and $NEt_3$ to produce dimer **2c** (spectrum E). From bottom to top: A) Compound **1c** before the addition of any reagent, B) After the addition of 1.5 eqv of $NEt_3$, C) After the addition of 1.5 eqv of $NEt_3$ and AgOTf and 15min at room temperature, D) After 40min at room temperature, E) after 3h at room temperature