

Supporting Information for

**How does the mutation in the cap domain of methylcobalamin-  
dependent methionine synthase influence the photoactivation of the  
Co-C bond?**

Arghya Pratim Ghosh, Abdullah Al Mamun, Pawel M. Kozlowski\*

Department of Chemistry, University of Louisville, Louisville, Kentucky 40292,  
United States

\*Phone: (502) 852-6609. Fax: (502) 852-8149. E-mail: pawel@louisville.edu

## Contents

**Table S1:** Selected geometrical parameters for both the WT-MetH and F708A-MetH

**Figure S1:** Crystal structure of MetH obtained from the protein data bank (PDB ID:1BMT)

**Figure S2:** QM layer used for calculation of WT-MetH and F708A-MetH

**Figure S3:** Electron density differences between  $S_0$  and  $S_1$  states for the WT-MetH and F708A-MetH at  $S_{(1min)}$  MLCT point.

**Figure S4:** Corresponding ground state optimized geometries of WT-MetH and F708A-MetH with various axial bond lengths of selected points on the  $S_1$  PES (Figure 5a), **(a)** I ( $S_{1min}$ ) **(b)** IIB (MECP) **(c)** IIIB ( $S_{1min}$ ). QM region shown using the ball-and-stick model and MM region shown in ribbons

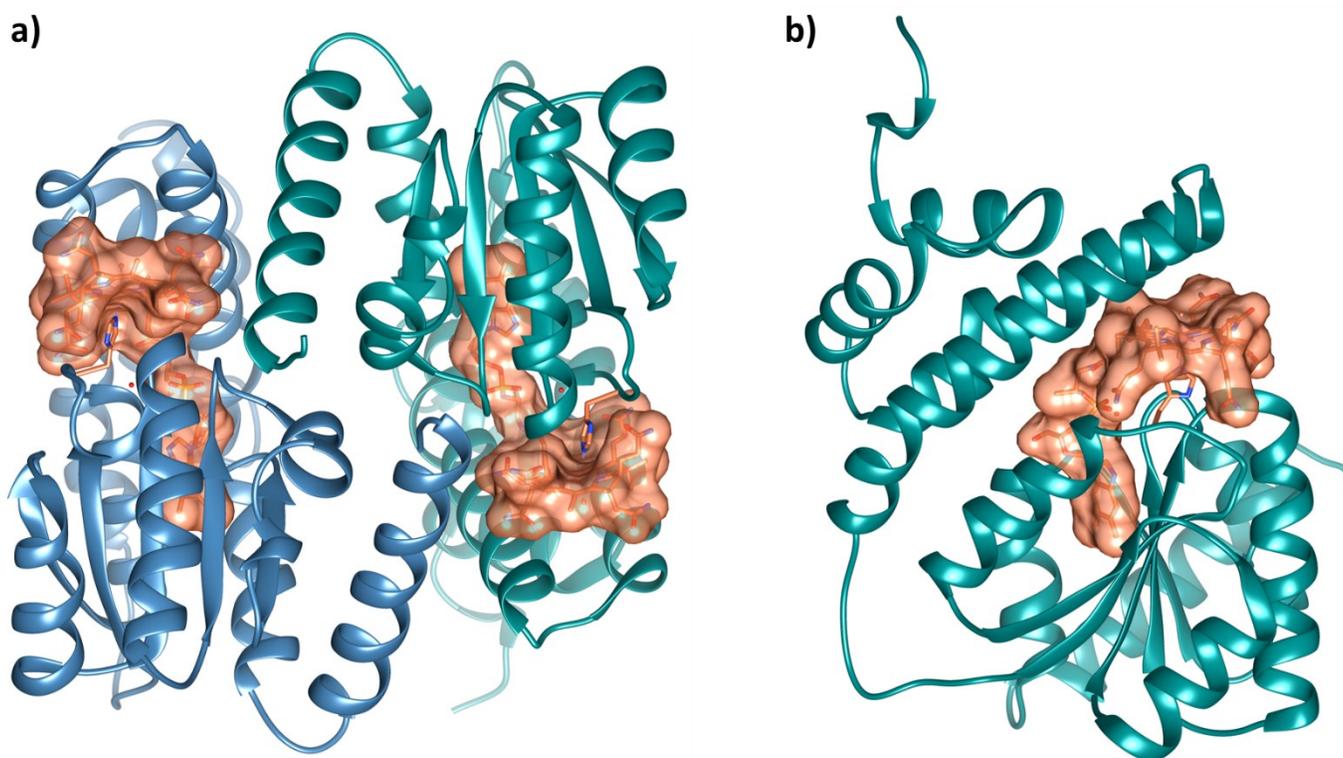
**Figure S5:** Relative energetics of the MLCT and LF state for (a) WT -Methionine Synthase (b) F708A -Methionine Synthase (c)  $Im-[Co^{III}(corrin)]-Me^+$

**Figure S6:** The changes of  $N_{Im}-Co-C$  bond angles along the Co-C bond length elongation for WT-MetH.

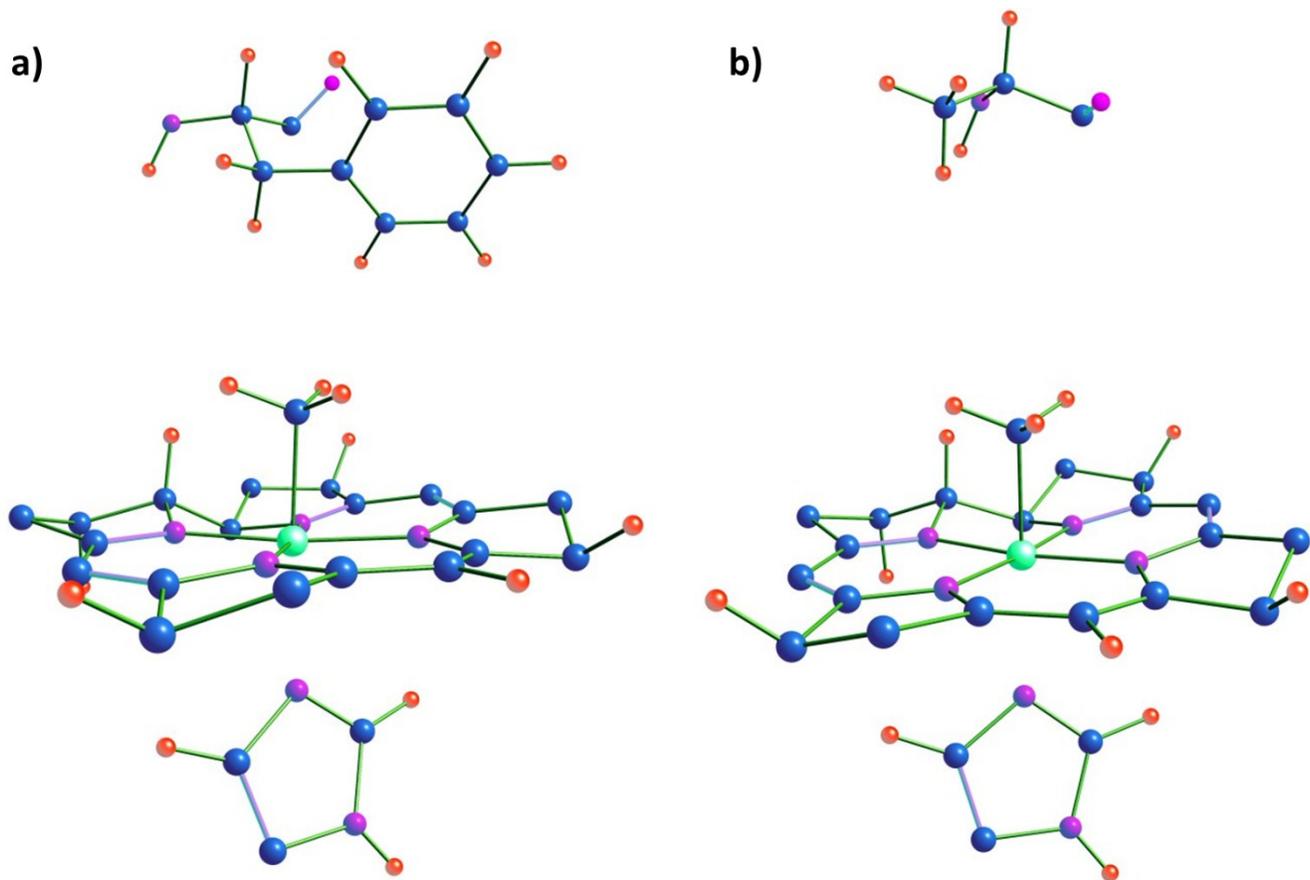
**Figure S7:** The changes of  $N_{Im}-Co-C$  bond angles along the Co-C bond length elongation for F708A-MetH.

**Table S1:** Selected geometrical parameters for both the WT-MetH and F708A-MetH

Crystal structure	WT- MetH				F708A-MetH		
	Optimized Structure	I (S <sub>0min</sub> )	I (S <sub>1min</sub> )	Optimized Structure	I (S <sub>0min</sub> )	I (S <sub>1min</sub> )	
<b>Bond Distances (Å)</b>							
Co-C	1.957	1.999	2.000	2.000	1.976	2.000	2.000
Co-N <sub>1m</sub>	2.241	2.296	2.300	2.100	2.164	2.300	2.100
Co-N <sub>21</sub>	1.925	1.895	1.895	1.903	1.894	1.893	1.901
Co-N <sub>22</sub>	2.015	1.949	1.949	1.957	1.955	1.954	1.960
Co-N <sub>23</sub>	2.016	1.941	1.941	1.947	1.947	1.946	1.954
Co-N <sub>24</sub>	1.914	1.886	1.886	1.892	1.889	1.888	1.893
<b>Bond Angles (°)</b>							
C-Co-N <sub>1m</sub>	167.4	169.7	169.6	170.7	170.3	170.1	171.1
N <sub>21</sub> -Co-N <sub>23</sub>	172.9	173.8	173.8	173.6	173.9	174.0	173.5
N <sub>22</sub> -Co-N <sub>24</sub>	177.8	172.1	172.2	170.8	172.4	172.6	171.4
<b>Torsion Angles (°)</b>							
N <sub>21</sub> -N <sub>22</sub> -N <sub>23</sub> -N <sub>24</sub>	4.8	-3.4	-3.4	-3.4	-1.9	-1.8	-2.2
N <sub>21</sub> -N <sub>22</sub> -N <sub>23</sub> -Co	4.9	0.002	-0.1	1.3	0.7	0.5	1.6

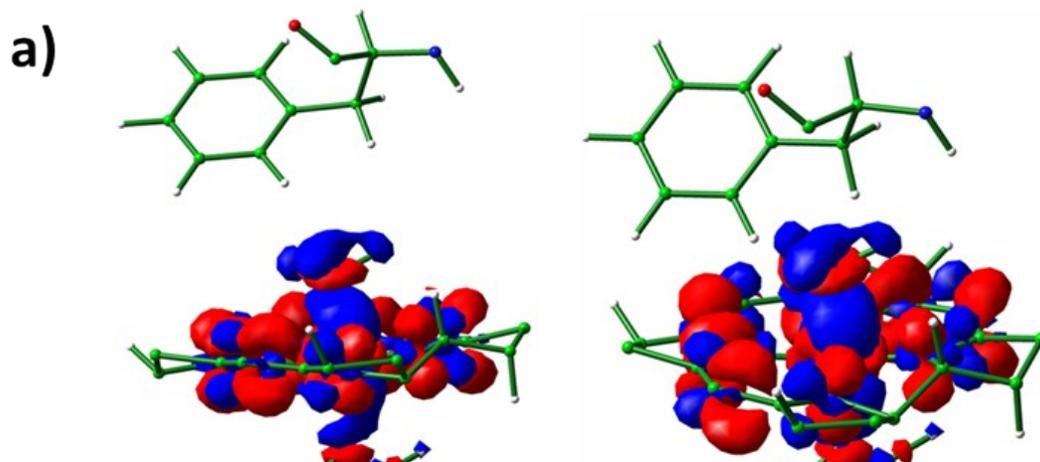


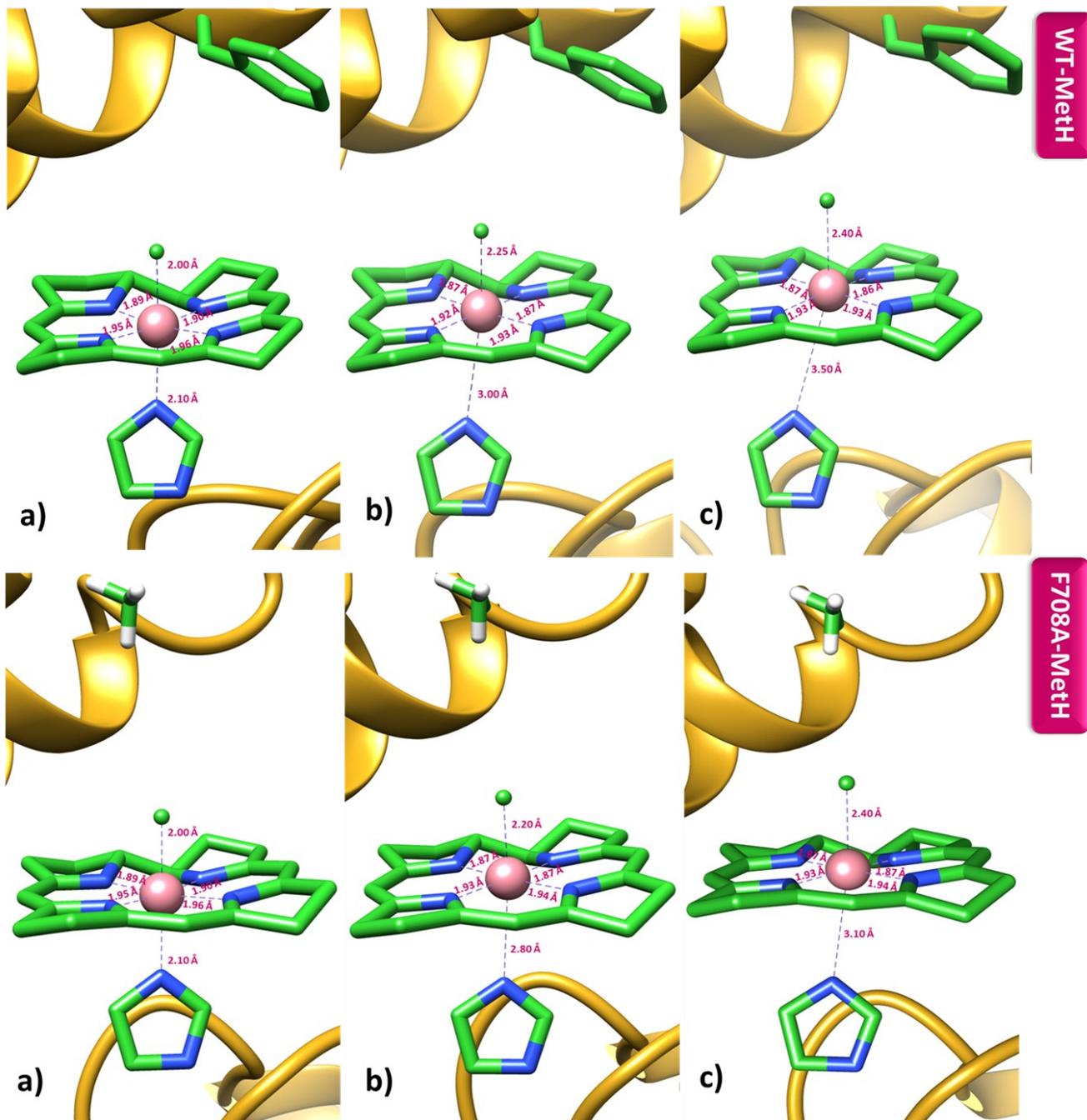
**Figure S1:** **a)** Crystal structure of MethH obtained from the protein data bank (PDB ID:1BMT). The structure contains two independent chains in one asymmetric unit. The cofactor is depicted by the surface and the orange color. **b)** Structure of one chain unit which is used for the calculations.



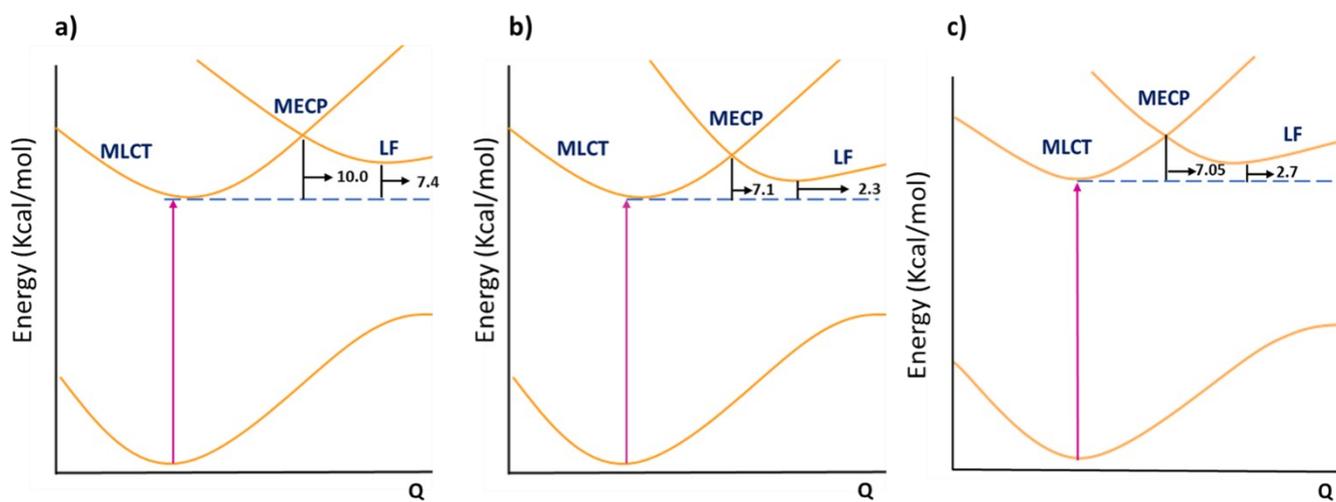
**Figure S2:** Active site figures treated with QM level of theory in the QM/MM calculations (a) WT-MetH and (b) F708A-MetH

**Figure S3:** Plot of electron density differences between  $S_0$  and  $S_1$  states for **(a)** WT-MetH **(b)** F708A-MetH at  $S_{(1min)}$  MLCT point. Results obtained from TD-DFT calculations. Isosurface plot value 0.002 was used.

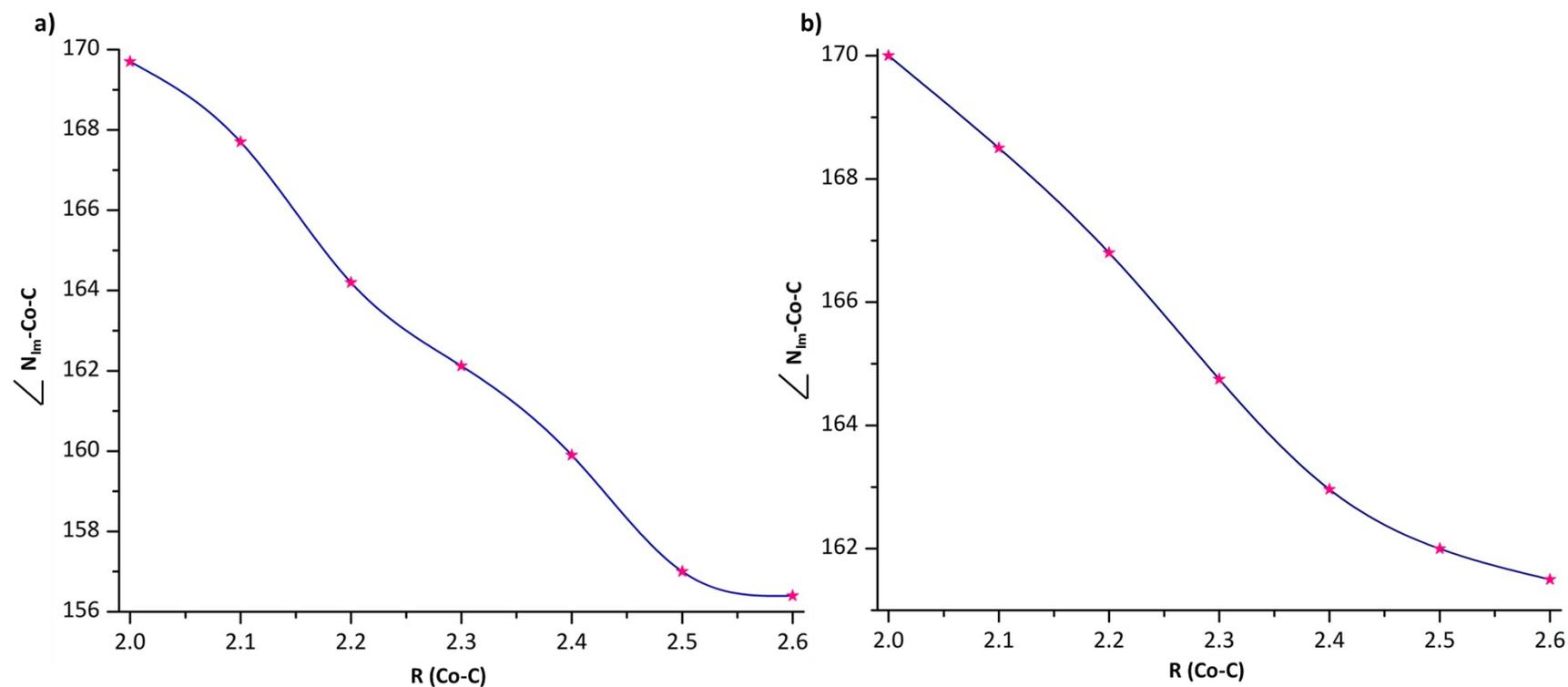




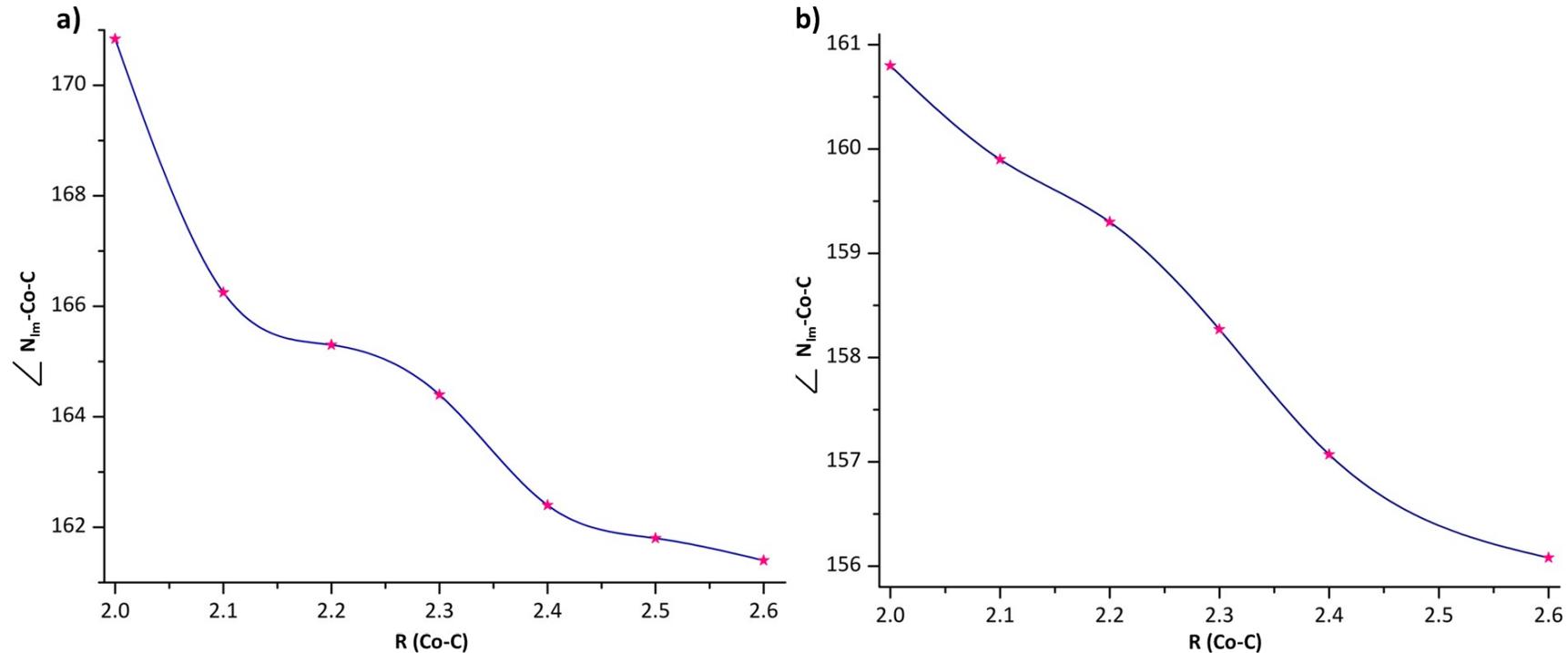
**Figure S4:** Corresponding ground state optimized geometries of WT-MetH and F708A-MetH with various axial bond lengths of selected points on the  $S_1$  PESs (Figure 5a), (a) I ( $S_{1min}$ ) (b) IIB (MECP) (c) IIIB ( $S_{1min}$ ). QM region shown using the ball and stick model and MM region shown in ribbons.



**Figure S5:** Relative energetics of the MLCT and LF state for (a) WT-MetH (b) WT-MetH (c) Im-[Co<sup>III</sup>(corrin)]-Me<sup>+</sup> of isolated MeCbl cofactor in solution



**Figure S6:** The changes of N<sub>Im</sub>-Co-C bond angles along the Co-C bond length elongation for WT-MetH. **(a)** QM/MM calculations were performed to elongate the Co-C bond length from 2.00 Å to 2.60 Å with a step size of 0.1 Å. At each point the bond angle of N<sub>Im</sub>-Co-C were determined and plotted as a function of Co-C bond length to show the escape of the CH<sub>3</sub> radical pair along the designated line. **(b)** Molecular dynamics (MD) simulation were performed to construct the one-dimensional plot of N<sub>Im</sub>-Co-C vs Co-C bond length. The equilibrium structure from QM/MM optimization was used to prepare the model for the MD simulation. Harmonic restraints were employed during MD simulation. The Co-C bond length were constraint from 2.0 Å to 2.6 Å with a step size of 0.1 Å. Each constrained distance was minimized, equilibrated and sampled for 10 ps. The corresponding structures were then scrutinized, and the N<sub>Im</sub>-Co-C bond lengths were determined and plotted as a function of the Co-C bond length. This has been done to compare the results and the structure with the QM/MM optimization. In both cases similar pattern was observed.



**Figure S7:** The changes of  $N_{Im}-Co-C$  bond angles along the  $Co-C$  bond length elongation for F708A-MetH. **(a)** QM/MM calculations were performed to elongate the  $Co-C$  bond length from 2.00 Å to 2.60 Å with a step size of 0.1 Å. **(b)** MD simulation were performed to construct the one-dimensional plot of  $N_{Im}-Co-C$  vs  $Co-C$  bond length.

#### References:

- 1) C. L. Drennan, S. Huang, J. T. Drummond, R. G. Matthews and M. L. Lidwig, *Science*, 1994, **266**, 1669-1674