Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.
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Supporting Information for:

“Zn^{2+} and Cd^{2+} Cationized Serine Complexes: Infrared Multiple Photon Dissociation Spectroscopy and Density Functional Theory Investigations”

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Theoretical Results for $[Zn(Ser-H)ACN]^+$. Optimized structures of select and distinctive low-lying conformations of $[Zn(Ser-H)ACN]^+$ are shown in Figure S1. Energies at 0 and 298 K of the calculated conformations of these complexes relative to the ground structure (GS) calculated at four different levels of theory are given in Table 1. In all $[Zn(Ser-H)ACN]^+$ complexes, the acetonitrile ligand binds in a near linear configuration on the opposite side of the zinc cation away from the amino acid. All levels of theory predict that the lowest energy structure has deprotonated Ser binding in a tridentate fashion to Zn; however, the preferred site of deprotonation differs with the level of theory (Table 1). DFT levels of theory, including B3LYP with empirical dispersion corrections, find that the lowest energy structure at 0 and 298 K is $[N,CO,O^-]$tgg, Zn bound to the amino nitrogen and carbonyl of the Ser backbone with added complexation to the deprotonated side-chain hydroxyl. In contrast, the MP2(full) level of theory predicts that deprotonation occurs at the carboxylic acid terminus, $[N,CO^-,OH]$ggt, although this conformer is lower in free energy at 298 K by only 0.2 kJ/mol. Comparison of bond lengths in the manuscript’s Table 2 reveals the $[N,CO^-,OH]$ggt conformer has shorter $M^{2+} – OC$ and $M^{2+} – N$ bond distances than the $[N,CO,O^-]$tgg conformer by 0.29 and 0.07 Å, respectively. Conversely, the tridentate deprotonated side-chain hydroxyl, $[N,CO,O^-]$tgg, conformer binds more closely at the $M^{2+} – O_s$ site by 0.29 Å. This shift in coordination distances between the two conformers can be clearly seen in the optimized structures provided in Figure S1.

The next lowest energy conformer of $[Zn(Ser\text{-}H)ACN]^+$ is the deprotonated tridentate $[N,CO,O^-]$cgg conformer (Figure S1). In the tgg GS, the carboxylic hydrogen forms an intramolecular hydrogen bond (H-bond) with the carbonyl oxygen. The cgg conformer breaks this intramolecular bond, leading to a 19 – 20 kJ/mol increase in the free energy at 298 K relative to the tgg GS. The tridentate $[N,OH,O^-]$tgg conformer again coordinates the metal by the amino nitrogen and deprotonated side-chain hydroxyl, but the carboxylic acid reorients to bind the metal to the hydroxyl rather than the carbonyl, which costs 35 – 41 kJ/mol. Likewise, deprotonation can occur at the amine group, although this is much less favorable energetically. The lowest energy conformer with deprotonation at the amine is another tridentate conformer, $[N^-,CO,OH]$tggt, which lies 48 – 54 kJ/mol above the GS.

The lowest energy bidentate species for $[Zn(Ser\text{-}H)ACN]^+$ is the metal bound to the amine and deprotonated side-chain hydroxyl, $[N,O_s^-]$tgt, 29 – 37 kJ/mol above the GS. Alternatively, losing interaction with the side-chain but binding to the amine and deprotonated carboxylic acid forms $[N,CO^-]$tgt and requires another 3 – 4 kJ/mol. Several structures in which the metal binds to the carbonyl and deprotonated side-chain were found, $[CO,O^-]$. The lowest of these has a ctc conformation with a NH_3^+/CO_2^- salt bridge interaction, i.e., $[CO^-,O^-]$ctc (Figure S1). Conformations where the zinc binds to both oxygens of a deprotonated carboxylic acid group, $[CO_2^-]$, are relatively high in energy, >67 kJ/mol above the GS.

Although the $[Zn(Ser\text{-}H)]^+$ species were not observed experimentally, it is valuable to compare the theoretical results for this complex with those for the species contaminated by ACN. Tables 2 and 3 provide direct comparison of the geometries and relative enthalpies, respectively, of low-lying ACN-free and ACN-contaminated deprotonated conformers. The $[Zn(Ser\text{-}H)]^+$ $[N,CO^-,OH]$ggt conformer is calculated to be 12 – 20 kJ/mol higher in free energy than the

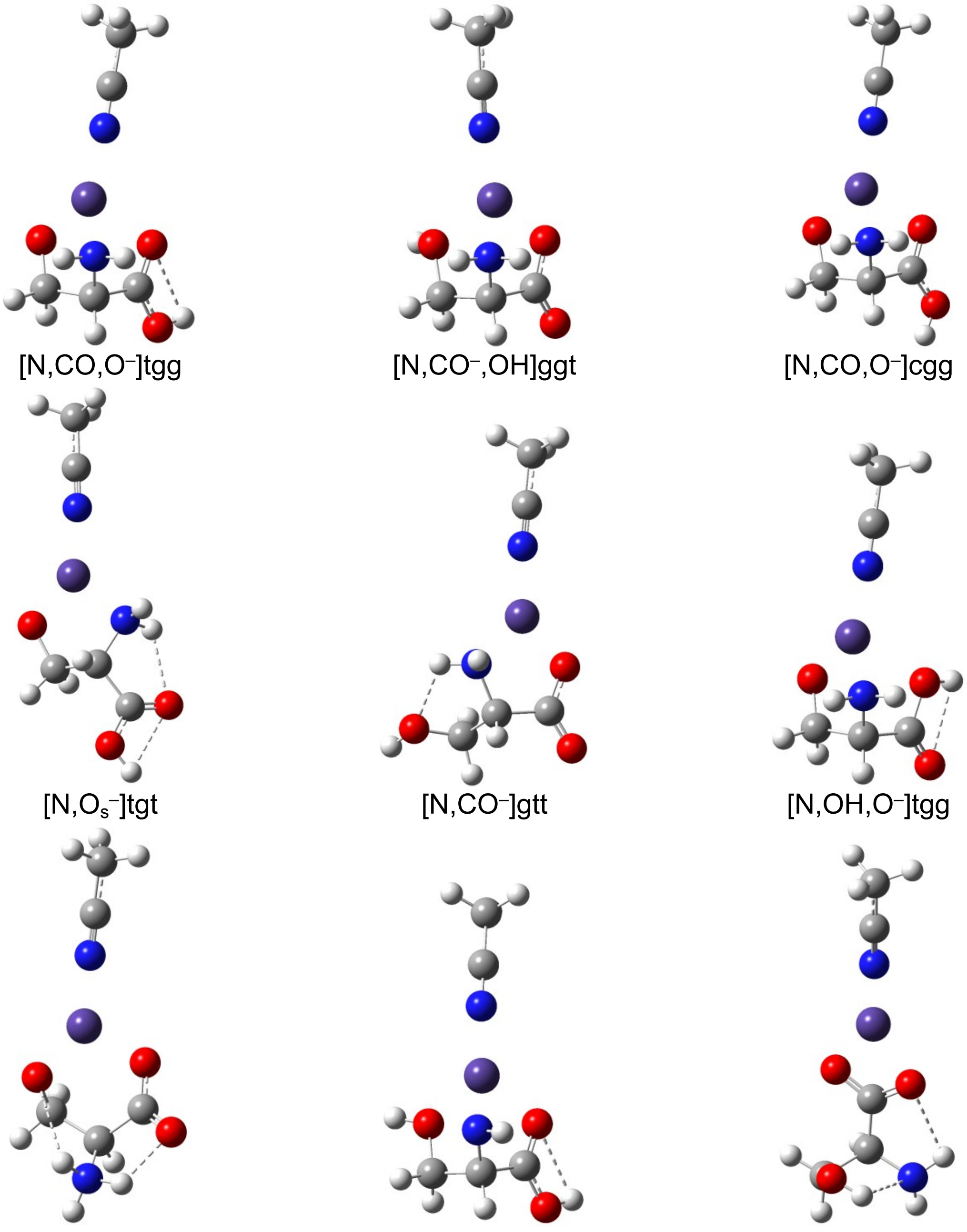
[N,CO,O$^-$] GS, meaning it could at most populate 0.8% of an ion population equilibrated at 298 K. In contrast, as seen in Table 1, the presence of the ACN ligand stabilizes the [N,CO$^-$,OH]ggt conformer such that it would populate between 8 – 52% of ions at 298 K. Zn^{2+} prefers to adopt a 4-coordinate geometry such that addition of the ACN ligand binding to the metal stabilizes the complexes (as demonstrated experimentally by the inability to remove the ACN ligand when irradiated with a high power CO_2 laser). Interestingly, comparison of [Zn(Ser-H)ACN]$^+$ and [Zn(Ser-H)]$^+$ relative free energies (Tables 1 and 3) shows that the ACN containing conformers all have a lower free energy relative to the ground conformer than the corresponding ACN-free structures, although [N,CO,O$^-$]cgg and [N$^-$,CO,OH]tggt are stabilized comparably to the GS. This phenomenon can be explained by examining the geometric effects of adding ACN to the [Zn(Ser-H)]$^+$ complexes, as seen in Table 2. For most complexes, addition of ACN increases the metal-ligand bond lengths, a natural consequence of electron donation from acetonitrile to the metal center. In contrast, the Zn – N bond of both [N,CO,O$^-$]tgg and [N$^-$,CO,OH]tggt decreases upon ACN addition as does the Zn – OC bonds of [CO_2^-]ggg, such that these structures benefit less from coordination of the fourth coordination site. With the exception of the [CO_2^-]ggg conformer, all of the complexes see a decrease in ligand binding site bond angles upon ACN attachment, again indicating that the metal generally moves away from the (Ser-H)$^-$ ligand. Overall, addition of the ACN ligand results in the [N,CO$^-$,OH]ggt conformer becoming comparable in energy to the [N,CO,O$^-$]tgg GS, with an inversion in the relative energies occurring at the MP2(full) level.

Theoretical Results for CdCl$^+$(Ser). Optimized structures of select and distinctive low-lying conformations of CdCl$^+$(Ser) are shown in Figure S2 with relative energies in Table 4. Calculations at all four levels of theory find that the charge-solvated tridentate [N,CO,OH]tggt structure is the ground structure (GS) for CdCl$^+$(Ser). As seen in Figure S2, in this conformer, Cd is bound to the amino nitrogen, r(Cd-N) = 2.33 Å, carbonyl oxygen, r(Cd-O) = 2.39 Å, and side-chain hydroxyl oxygen, r(Cd-O) = 2.51 Å, and the carboxylic hydrogen forms an intramolecular H-bond with the carbonyl oxygen. Similar to the deprotonated species, when this intramolecular bond is broken, as in the [N,CO,OH]cggt conformer, the relative free energy at 298 K is found to be 28 – 30 kJ/mol higher than the tggt conformer. The C – N and C – OH bond distances for the higher energy [N,CO,OH]cggt structure are longer than the GS, whereas the loss of the intramolecular H-bond allows a stronger Cd – OC bond, as the coordination distance is shortened by 0.06 Å. In another tridentate conformer, [N,OH,OH]tggt, Cd binds to the hydroxyl oxygen rather than the carbonyl of the backbone carboxylic acid leading to a less favorable interaction with relative free energies 27 – 33 kJ/mol higher than the GS. This coordination change leads to a significantly longer Cd – OH bond distance than the Cd – OC bond of the [N,CO,OH] conformers by 0.26 – 0.32 Å, but shorter Cd – N and Cd – OH_s bond lengths by 0.07 – 0.10 Å and 0.08 – 0.09 Å, respectively.

If the metal ion interaction with the hydroxyl side-chain is lost and only the backbone amino acid interaction is maintained, bidentate [N,CO] conformers are formed with tcgt, tgtt, and tgtg orientations. The lowest of these bidentate conformers is [N,CO]tcgt, which lies 15 – 26 kJ/mol higher in energy than the tridentate GS (Table 4) and is stabilized by a NH•OH_s hydrogen bond. Although loss of the side-chain interaction is less favorable energetically, it allows stronger binding interactions between the metal and the amino nitrogen and carbonyl oxygen, as evidenced by shortening these bond distances by 0.09 and 0.03 Å, respectively. If the carboxylic acid is rotated 180°, bidentate [N,OH] conformers are formed as the C-terminus hydroxyl binds to the metal, further increasing the energy of the system (57 – 69 kJ/mol above the GS). If the metal ion interacts with the hydroxyl side-chain and amino group, bidentate [N,OH_s] conformers are formed with tgtt, tttt, and cgtt geometries. Notably, theory predicts [N,OH_s] conformers are 22 – 30 kJ/mol more favorable than their respective [N,OH] conformers relative to the GS, Table 4. This increase in relative energy for the [N,OH] conformers results from Cd – OH bonds that are consistently longer (by 0.08 – 0.27 Å) than those in than [N,OH$_s$], as well as having more constrained N – Cd – OH bond angles by 3 – 5°.

In another bidentate conformer, [CO,OH$_s$]cggt (Figure S2), the loss of the nitrogen interaction decreases the stability of the conformer by 44 – 63 kJ/mol (Table 4) from its corresponding tridentate [N,CO,OH]tggt GS. This bidentate structure is stabilized by an N•HO H-bond, whereas the [CO,OH]tggt variant is 17 – 21 kJ/mol higher in energy because it has a weaker CO•HO H-bond. The lowest energy salt-bridge (SB) structure for CdCl$^+$(Ser) is the [CO$_2^-$]cggt conformer, which is 18 – 31 kJ/mol higher than the tridentate GS. Interestingly, this SB conformer is lower by 32 – 39 kJ/mol than its corresponding nonzwitterionic [COOH]cggt conformer (Table 4), where the H remains on the carboxylic acid rather than transferring to the amino nitrogen. Both of these structures are also stabilized by NH•OH$_s$ H-bonds. Higher lying SB structures include cgtt and cggg variants, which lie 3 – 5 and 32 – 37 kJ/mol higher, respectively. In the latter case, the NH•OH$_s$ H-bond has been lost. In these two cases, the nonzwitterionic [COOH] variants collapse to the SB structures.

These results are analogous with our previous studies of the alkali metal cation interactions with Ser, where [N,CO,OH] ground conformers were found for M$^+$(Ser) where M$^+$ = Li$^+$, Na$^+$, and K$^+$.[8] The GS of CdCl$^+$(Ser) is also similar to the ground structure found for CdCl$^+$(CysOMe), [N,CO,S]tggg.[1]



[N,CO,O^{-}]tgg

[N,CO^{-},OH]ggt

[N,CO,O^{-}]cgg

[N,O$_s^{-}$]tgt

[N,CO^{-}]gtt

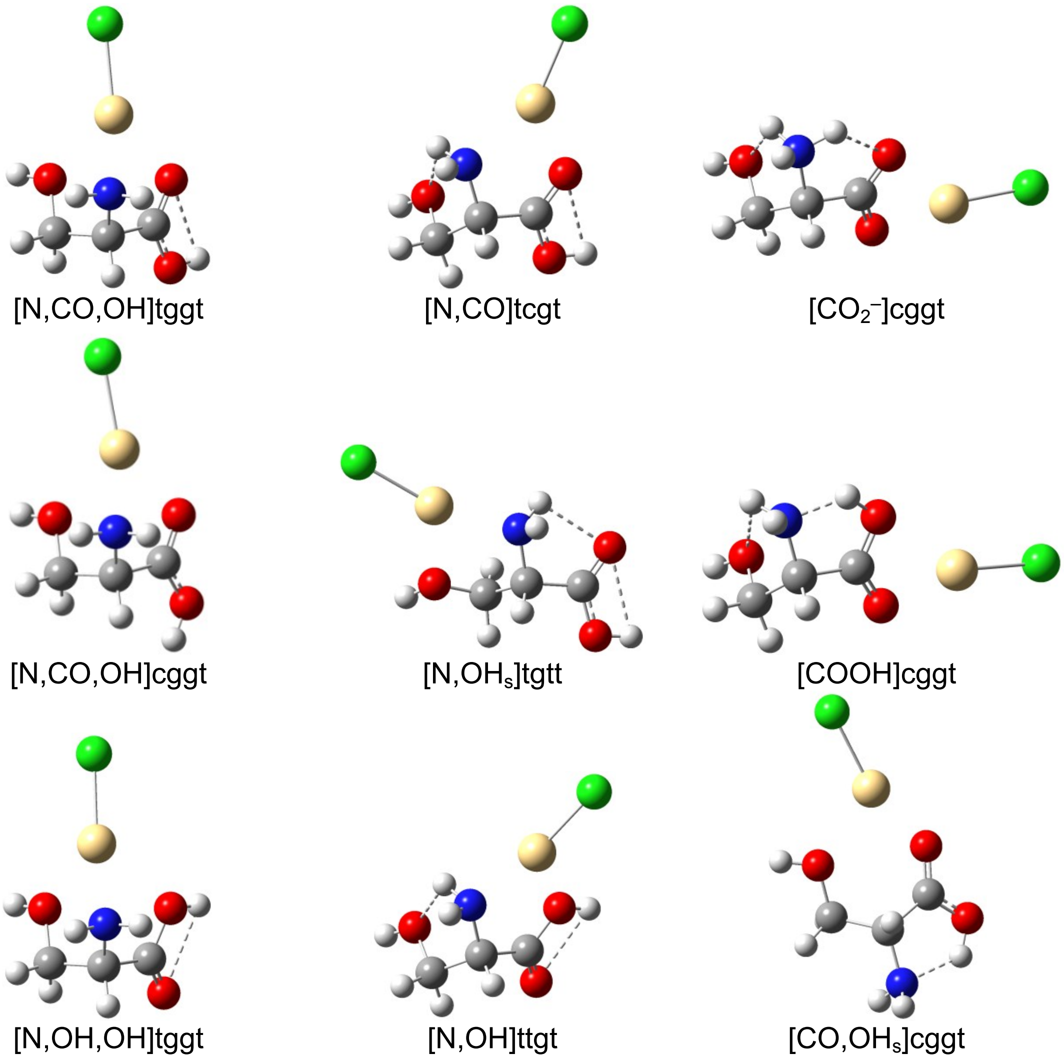
[N,OH,O^{-}]tgg

[CO^{-},O^{-}]ctc

[N^{-},CO,OH]tggt

[CO$_2^{-}$]ggg

Figure S1. Structures of select low-lying [Zn(Ser-H)ACN]$^{+}$ complexes calculated at the B3LYP/6-311+G(d,p) level of theory. Grey = C, red = O, blue = N, white = H, purple = Zn. Dashed lines indicate hydrogen bonds.



[N,CO,OH]tggt

[N,CO]tcgt

[CO_2^-]cggt

[N,CO,OH]cggt

[N,OH_s]tgtt

[COOH]cggt

[N,OH,OH]tggt

[N,OH]ttgt

[CO,OH_s]cggt

Figure S2. Structures of low-lying $CdCl^+$(Ser) complexes calculated at the B3LYP/def2-TZVP level of theory. Grey = C, red = O, blue = N, white = H, green = Cl, light yellow = Cd. Dashed lines indicate hydrogen bonds.

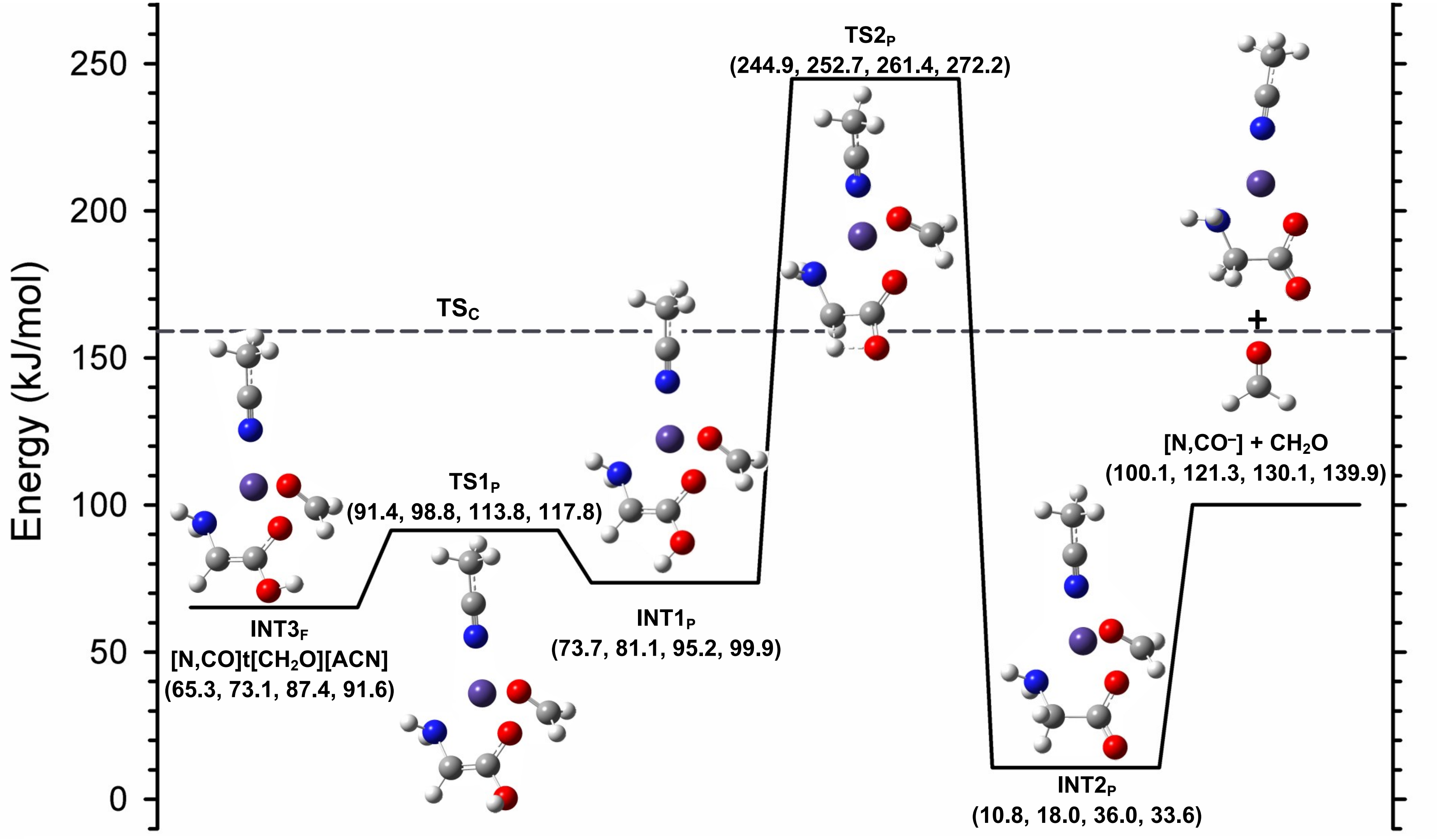


Figure S3. Proton transfer reaction coordinate from [Zn(Ser-H)ACN]$^+$ [N,CO]c[CH$_2$O] to form the lowest energy conformer product ion [N,CO$^-$] + CH$_2$O. The dark grey dashed line shows the relative energy of the rate limiting transition state to lose neutral CO$_2$ (TS$_C$). Energies are calculated at B3LYP/6-311+G(2d,2p)//B3LYP/6-311+G(d,p) level of theory including zero point energy corrections and are relative to [Zn(Ser-H)ACN]$^+$ [N,CO,O$^-$]tgg conformer. Values in parentheses are single point energies calculated at B3LYP, B3LYP-GD3BJ, B3P86, and MP2(full) levels, respectively, with 6-311+G(2d,2p) basis set.