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

Supporting Information

Molecular Crowding Effect in Hantzch Pyridine Synthesis in Polyethylene Glycol Aqueous Solution

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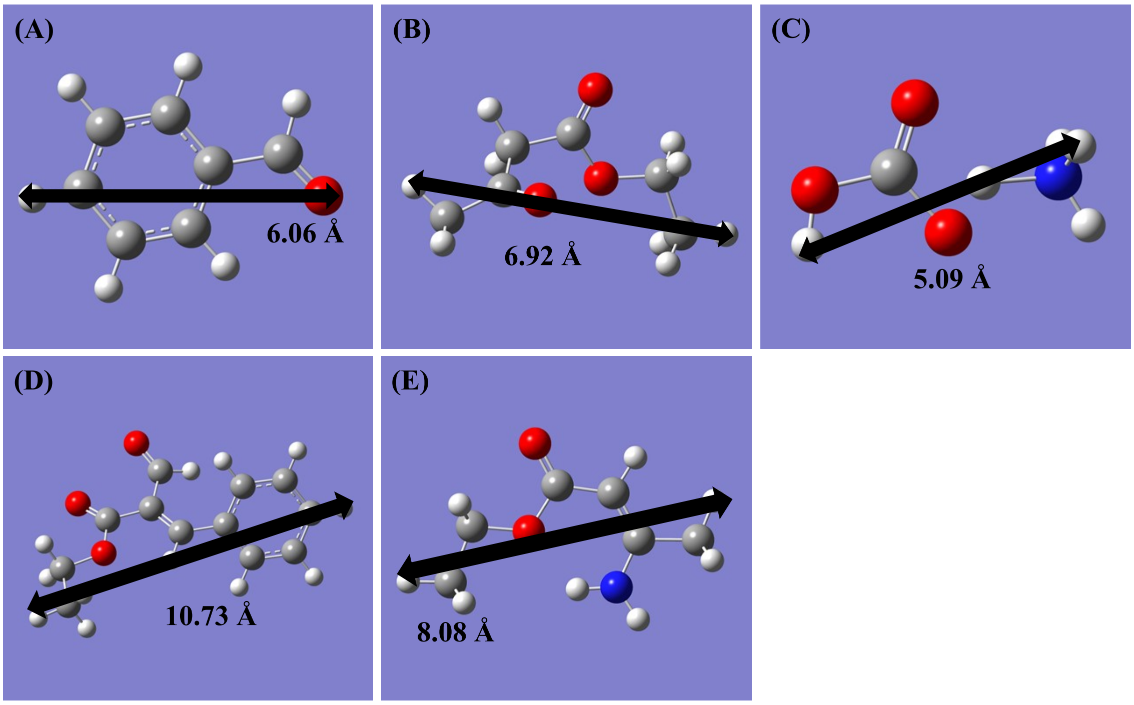

Figure S1. Optimized structures of chemical species for **A**, **B**, **C**, **D**, and **E** using density functional theory, implemented in Gaussian 16.

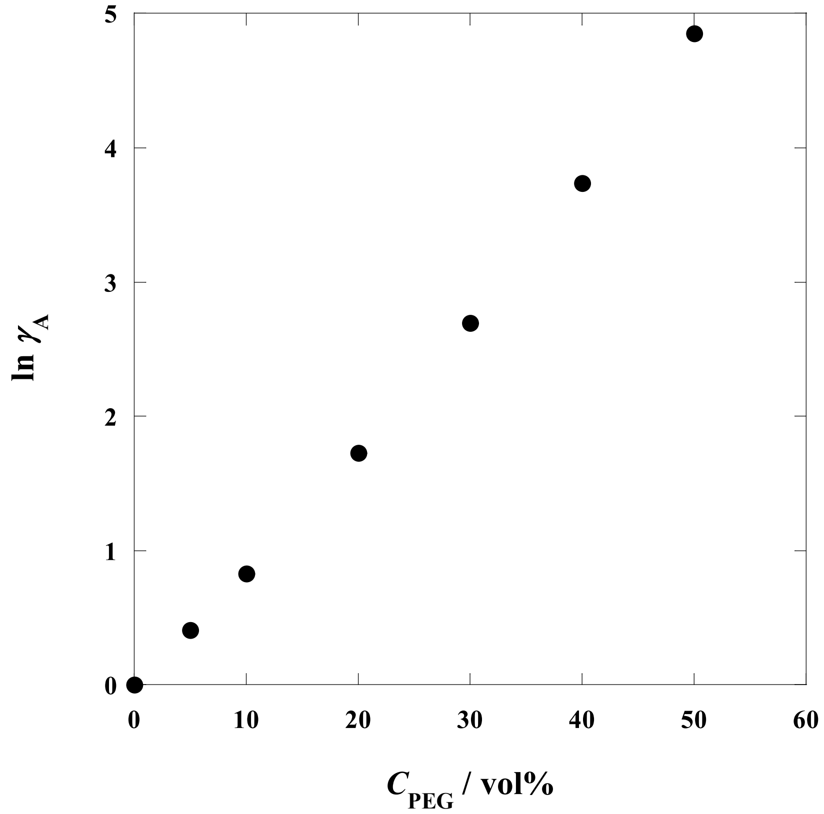

Figure S2. Relationship between C_{PEG} and ln γ_A.

Derivation of the Eq. (1).

The change in the absorption upon the titration was based on the Benesi-Hildebrand equation.[1] The reaction between the metal ion and HQ^- can be represented by the following reversible processes:

$$M^{2+} + HQ^- \underset{}{\overset{K_1'}{\rightleftarrows}} MQ + H^+$$

$$MQ + HQ^- \underset{}{\overset{K_2'}{\rightleftarrows}} MQ_2^{2-} + H^+$$

Thus, the equilibrium constants for the 1:1 and 1:2 complexes are given by

$$K_1' = \frac{[MQ][H^+]}{[M^{2+}][HQ^-]}, \tag{S1}$$

$$K_2' = \frac{[MQ_2^{2-}][H^+]}{[MQ][HQ^-]}. \tag{S2}$$

Moreover, the total absorbance of the 1:1 and 1:2 complexes is given by the following equation according to the Lambert-Beer law.

$$\Delta A = \frac{l\varepsilon_1 K_1'[M^{2+}][HQ^-]}{[H^+]} + \frac{l\varepsilon_2 K_1' K_2'[M^{2+}][HQ^-]^2}{[H^+]^2} \tag{S3}$$

where l is the optical path length. The mass balance of metal ion is represented by

$$[M^{2+}]_0 = [M^{2+}] + [MQ] + [(MQ_2)^{2-}] = [M^{2+}] + \frac{K_1'[M^{2+}][HQ^-]}{[H^+]} + \frac{K_1' K_2'[M^{2+}][HQ^-]^2}{[H^+]^2}. \tag{S4}$$

where $[M^{2+}]_0$ is the initial concentration of metal ion. By substituting Eq. (S4) into Eq. (S3), we obtain

$$\Delta A = \frac{l[M^{2+}]_0\left(K_1'\varepsilon_1[H^+][HQ^-] + K_1' K_2'\varepsilon_2[HQ^-]^2\right)}{[H^+]^2 + K_1'[H^+][HQ^-] + K_1' K_2'[HQ^-]^2}. \tag{S5}$$

Furthermore, when the acid dissociation constant of HQ^-, $K_{a2} = [Q^{2-}][H^+]/[HQ^-]$, is substituted into Eq. (S5), the following equation is obtained.

$$\Delta A = \frac{l[M^{2+}]_0\left(K_1 K_{a2}\varepsilon_1[H^+][HQ^-] + K_1 K_2 K_{a2}{}^2\varepsilon_2[HQ^-]^2\right)}{[H^+]^2 + K_1 K_{a2}[H^+][HQ^-] + K_1 K_2 K_{a2}{}^2[HQ^-]^2} \tag{S6}$$