

Electronic Supplementary Information

Carbonic anhydrase activity of dinuclear Cu^{II} complexes with patellamide model ligands

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Table S1. Dependence of the catalyzed CO₂ hydration rate k_{Cat} for the H₄pat¹-based system as a function of the CO₂ association constant K_{Cat} (see Table 1 and equation 3); the $\log K_{\text{Cat}}$ value used in the general fitting procedures is 4, and it has been argued that this is only moderately dependent on the metal ion and ligand structure (values generally used are between 3.9 and 4),^{1,2} which is largely supported by our data (note that in contrast to the data in Table 1 in the main manuscript (average of 5 measurements) data in this table are based on one of the measurements).

H ₄ pat ¹ log K_{Cat}	k_{Cat}						
	3.00	3.50	3.90	4.00	4.08	4.50	5.00
pK _a 6.21	4.77·10 ⁻³	3.22·10 ⁻³	6.66·10 ⁻³	2.51·10 ⁻³	3.22·10 ⁻³	3.29·10 ⁻³	2.59·10 ⁻³
pK _a 7.14	9.36·10 ¹	7.02·10 ¹	7.00·10 ¹	6.96·10 ¹	6.96·10 ¹	6.86·10 ¹	6.84·10 ¹
pK _a 8.07	7.15·10 ⁴	2.22·10 ⁴	8.80·10 ³	7.13·10 ³	5.9·10 ³	2.84·10 ³	1.63·10 ³
pK _a 8.22	1.84·10 ³	5.36·10 ²	5.08·10 ²	5.06·10 ²	5.04·10 ²	5.01·10 ²	5.01·10 ²

Table S2. Dependence of the catalyzed CO₂ hydration rate k_{Cat} for the H₄pat¹-based system as a function of the protonation constant of the catalyst (K_{H}).

	$\log K_{\text{H}}$		
	6.50	7.00	7.74
pK _a 8.07	1.12·10 ³	2.84·10 ³	7.13·10 ³

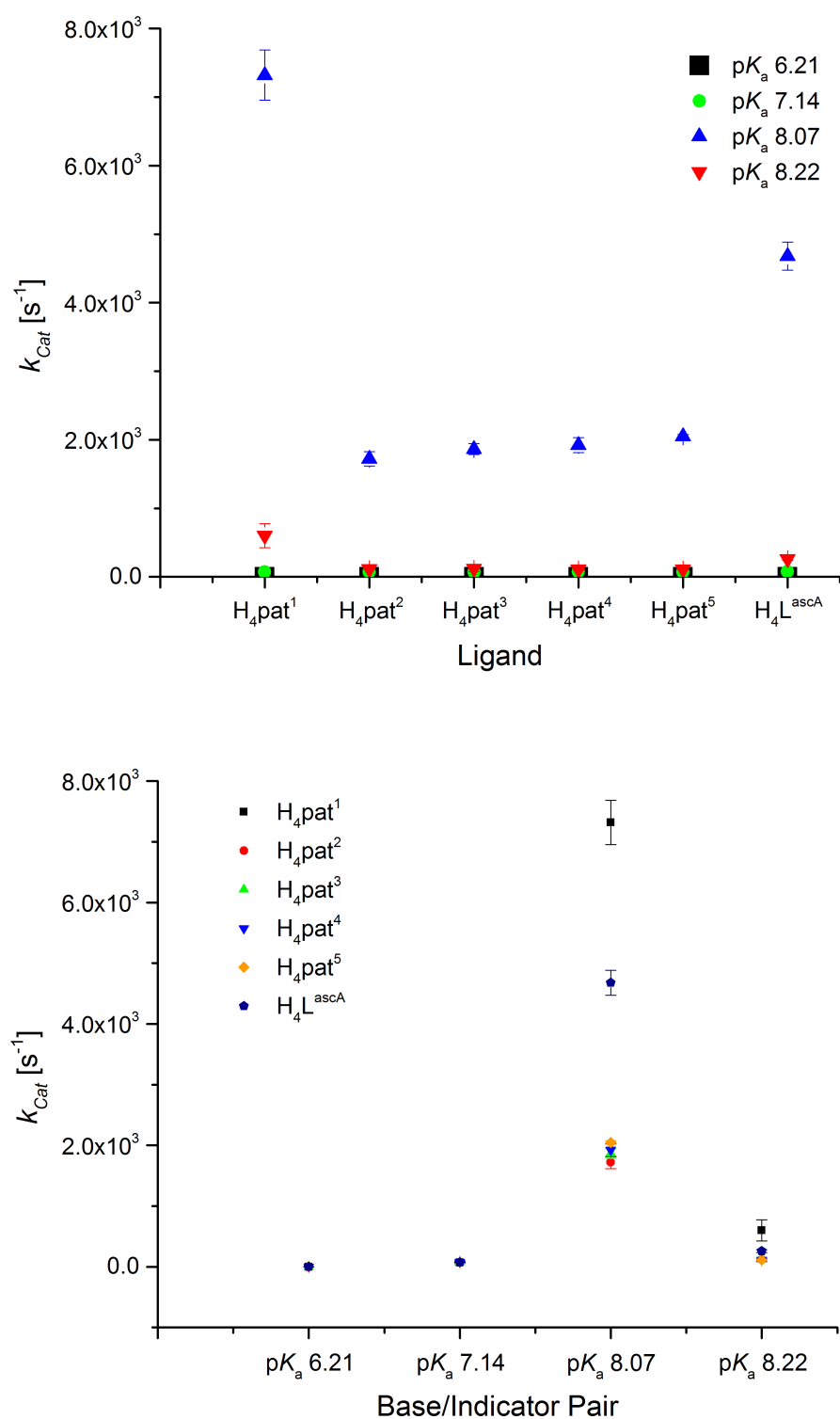


Figure S1. Distribution of the k_{cat} values as a function of the ligand (top) and the pK_a value of the added base (bottom).

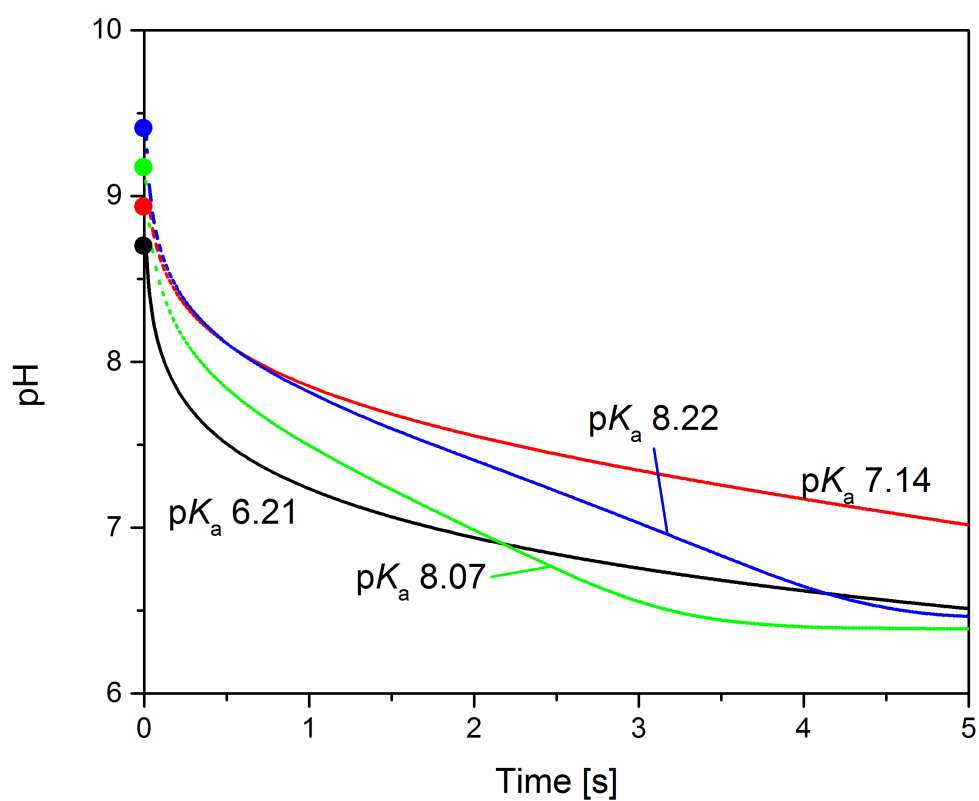


Figure S2. Comparison of pH progresses during the hydration of 17 mM CO₂ with 8.5 mM base by the [Cu₂^{II}(H₂pat¹)(OH)]⁺ complex. Used base: 3,5-lutidine (pK_a 6.21, black line), imidazole (pK_a 7.14, red line), Tris (pK_a 8.07, green line) and 1,2-dimethylimidazole (pK_a 8.22, blue line). Colored dots mark the beginning of each pH trace.

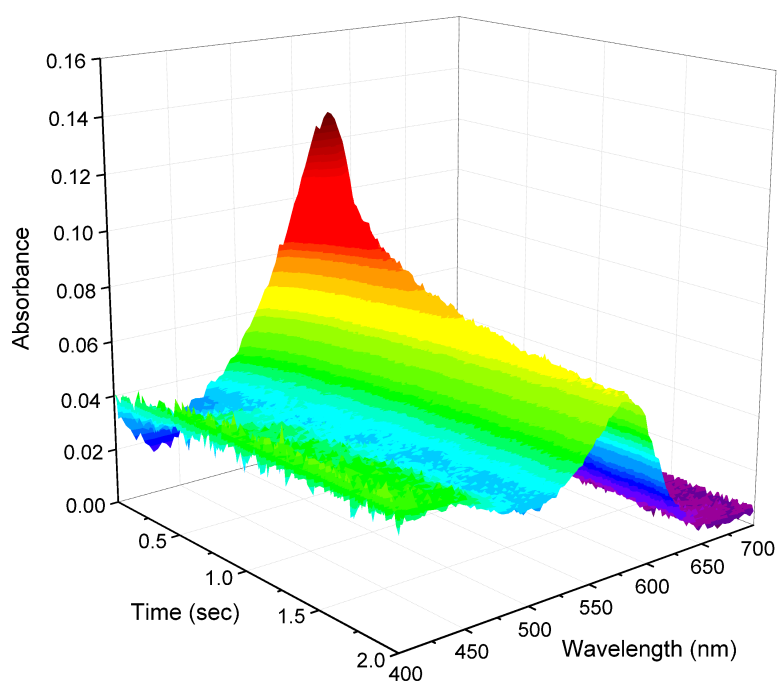
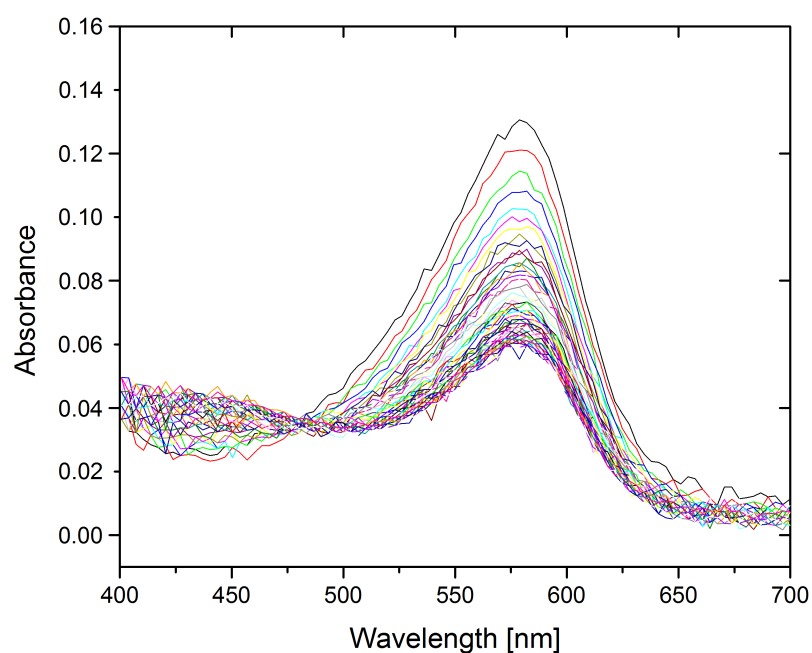


Figure S3. Two dimensional (absorbance vs. wavelength, top) and three dimensional (absorbance vs. wavelength vs. time, bottom) representation of absorbance data for the hydration of CO₂ by the [Cu₂^{II}(H₂pat²)(OH)]⁺ complex. Reaction with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] and 17 mM CO₂(aq) in a water/methanol 9:1 mixture at 25°C.

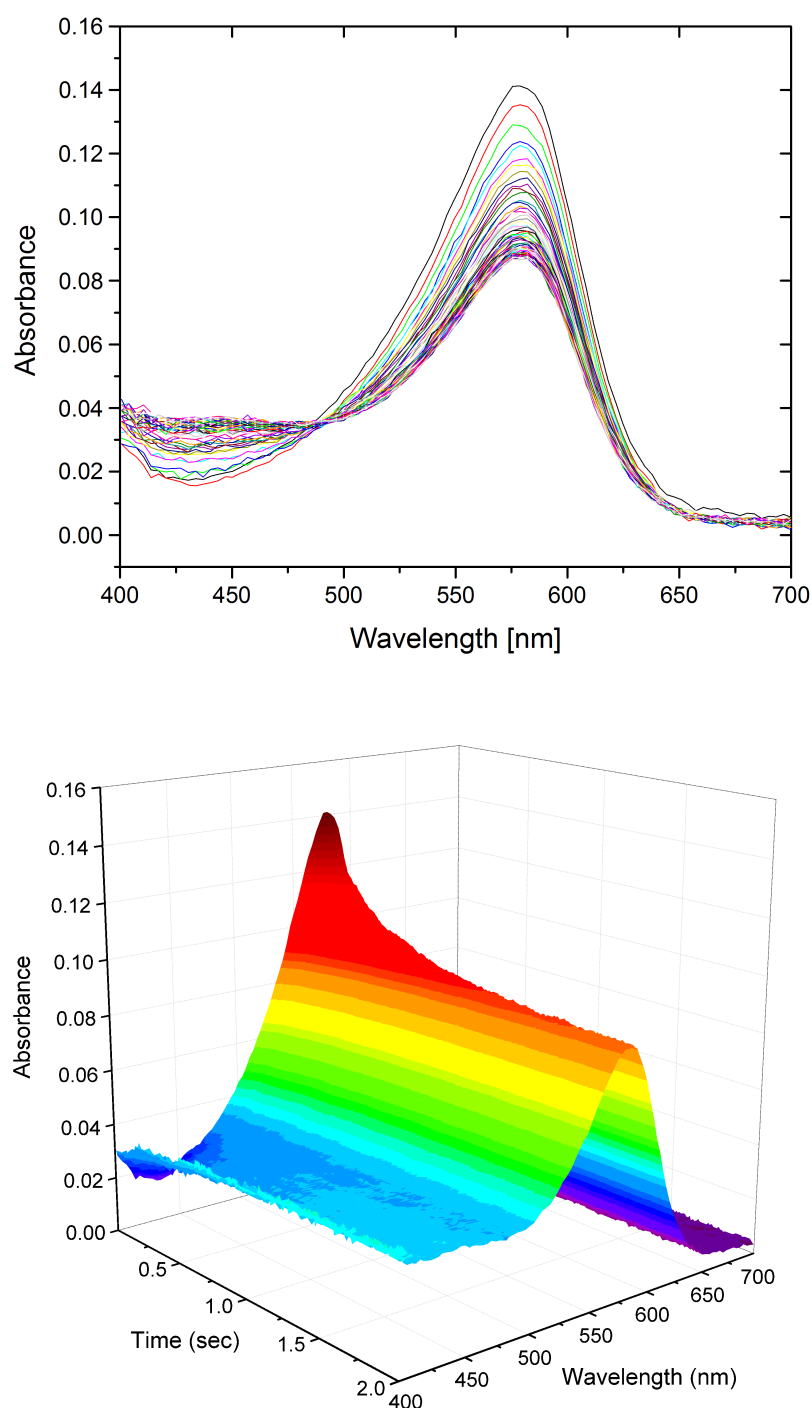


Figure S4. Two dimensional (absorbance vs. wavelength, top) and three dimensional (absorbance vs. wavelength vs. time, bottom) representation of absorbance data for the hydration of CO₂ by the [Cu₂^{II}(H₂pat³)(OH)]⁺ complex. Reaction with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] and 17 mM CO₂(aq) in a water/methanol 9:1 mixture at 25°C.

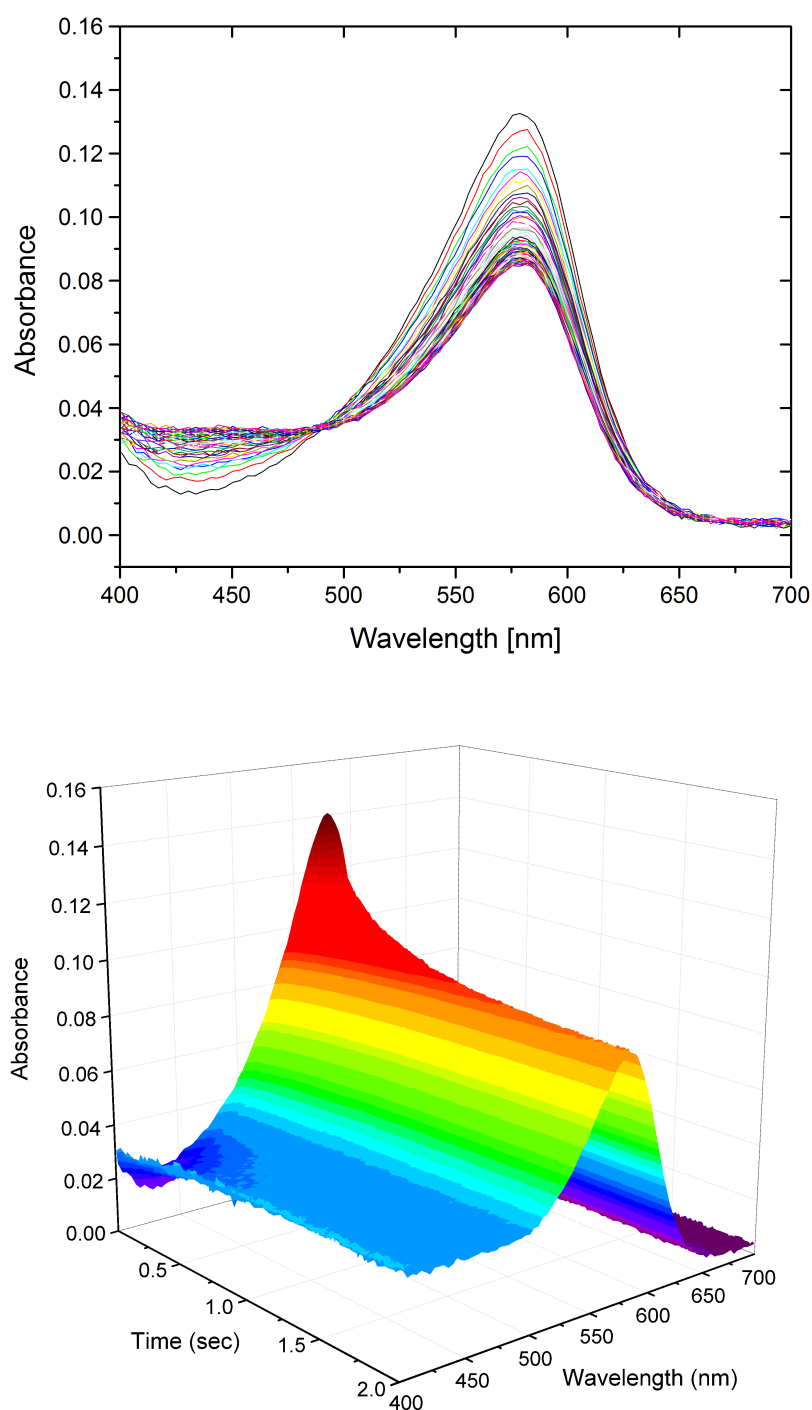


Figure S5. Two dimensional (absorbance vs. wavelength, top) and three dimensional (absorbance vs. wavelength vs. time, bottom) representation of absorbance data for the hydration of CO₂ by the [Cu₂^{II}(H₂pat⁴)(OH)]⁺ complex. Reaction with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] and 17 mM CO₂(aq) in a water/methanol 9:1 mixture at 25°C.

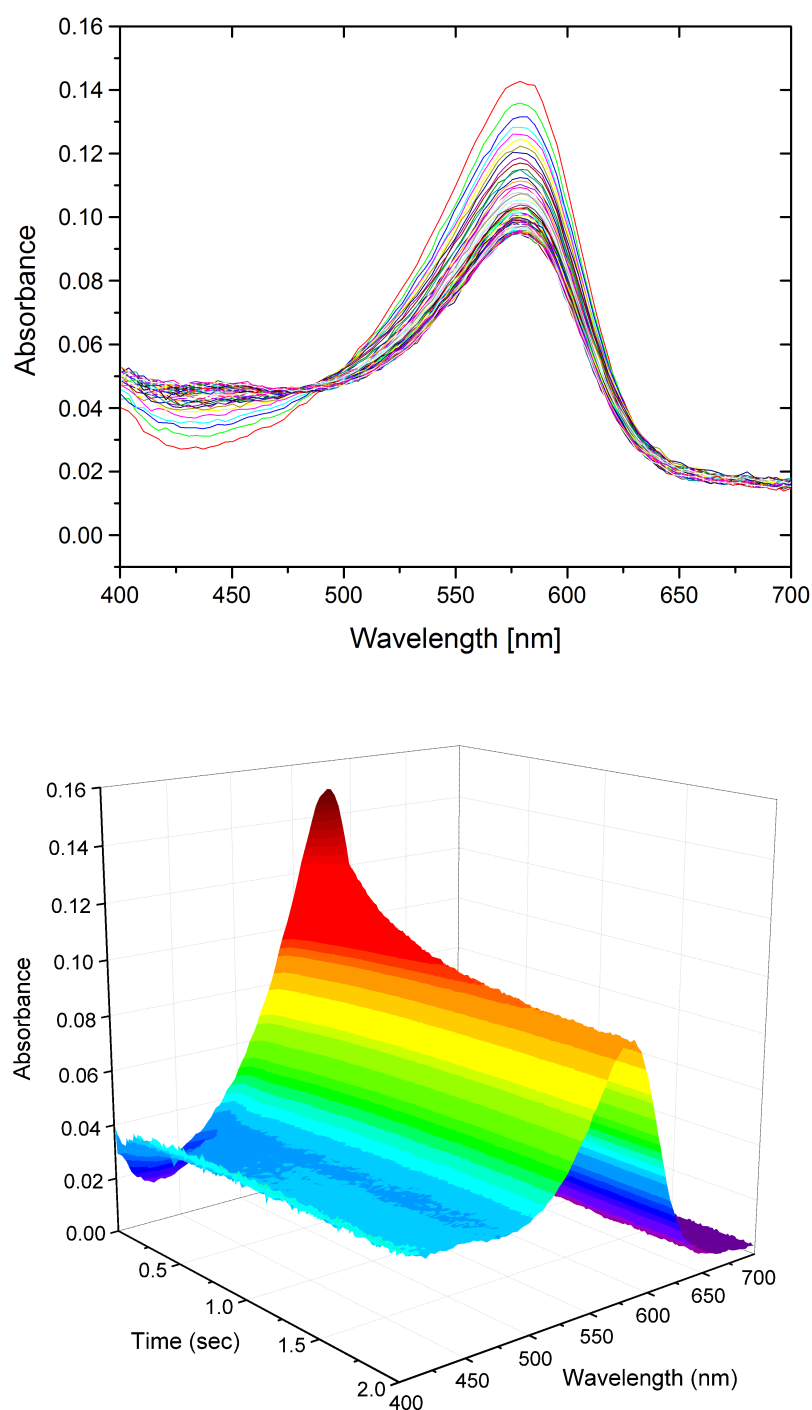


Figure S6. Two dimensional (absorbance vs. wavelength, top) and three dimensional (absorbance vs. wavelength vs. time, bottom) representation of absorbance data for the hydration of CO_2 by the $[\text{Cu}_2^{\text{II}}(\text{H}_2\text{pat}^5)(\text{OH})]^+$ complex. Reaction with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] and 17 mM $\text{CO}_2(\text{aq})$ in a water/methanol 9:1 mixture at 25°C .

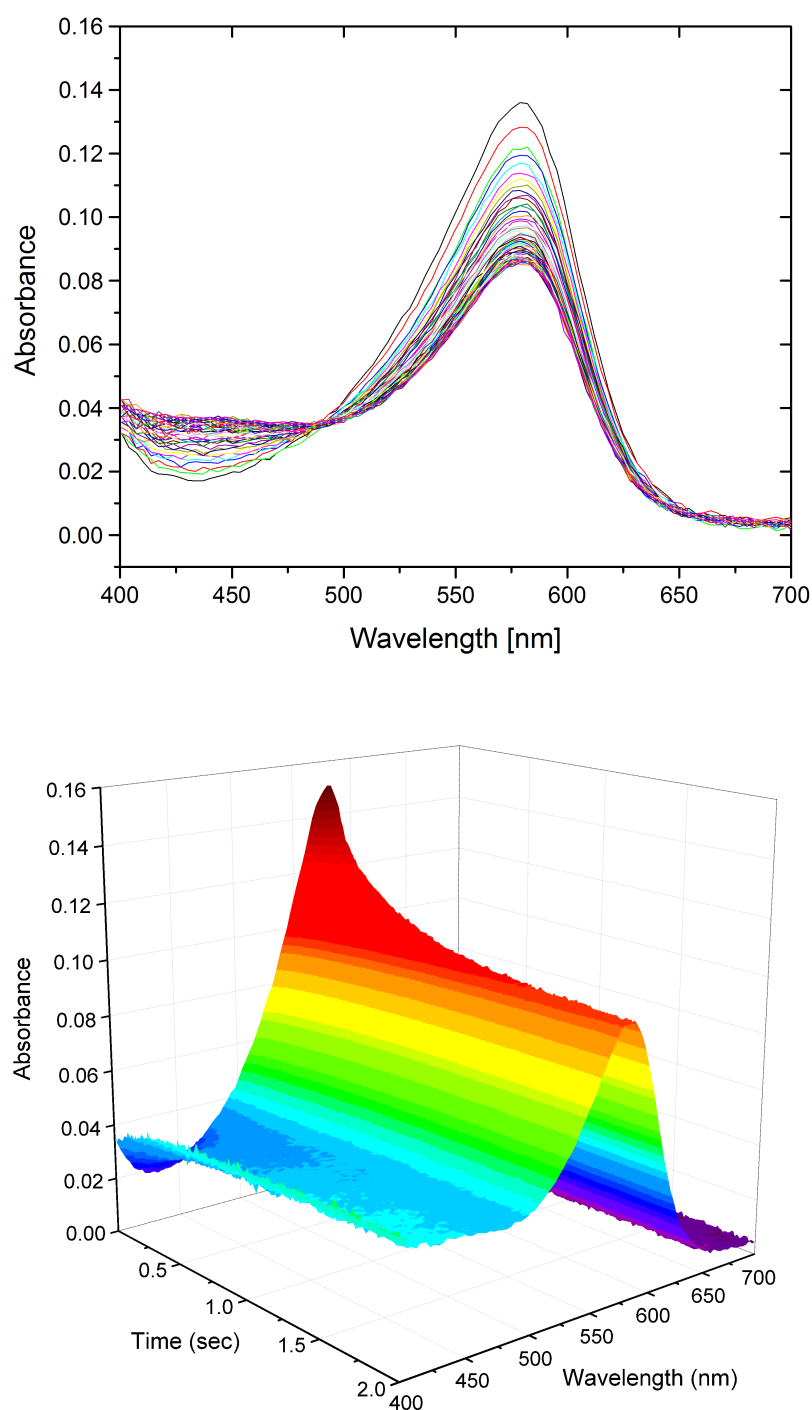


Figure S7. Two dimensional (absorbance vs. wavelength, top) and three dimensional (absorbance vs. wavelength vs. time, bottom) representation of absorbance data for the hydration of CO₂ by the [Cu₂^{II}(H₂L^{ascA})(OH)]⁺ complex. Reaction with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] and 17 mM CO₂(aq) in a water/methanol 9:1 mixture at 25°C.

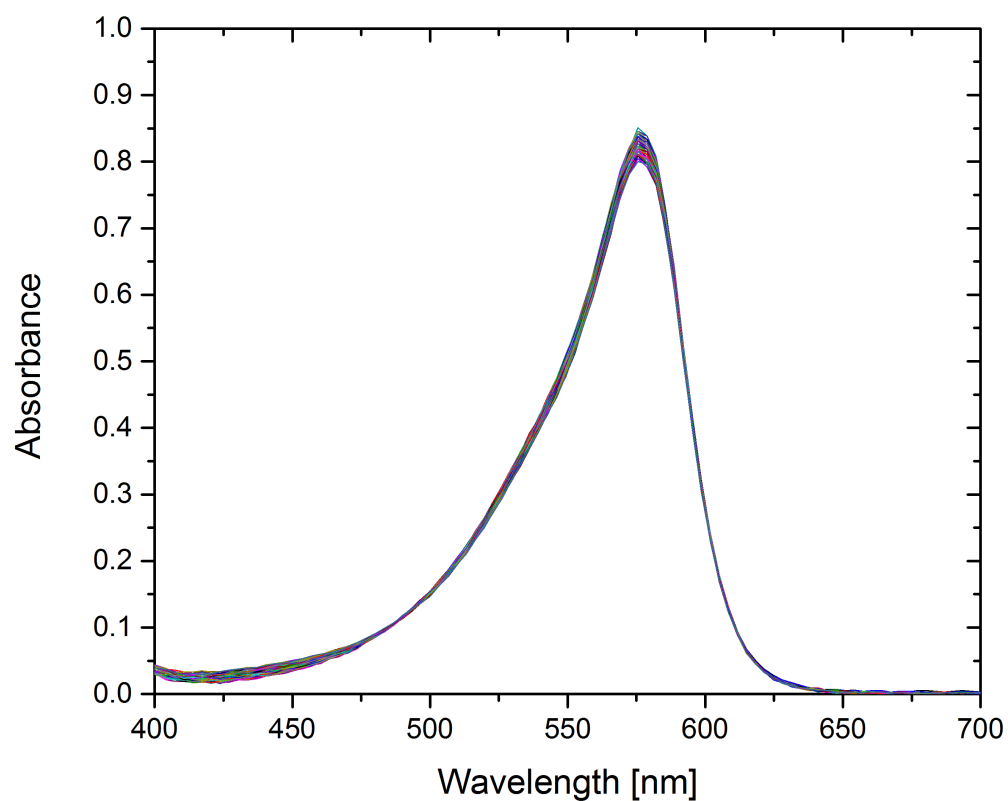


Figure S8. Two dimensional (absorbance vs. wavelength, top) representation of absorbance data for the hydration of CO₂ by the [Cu₂^{II}(H₂pat¹)(OH)]⁺ complex. Reaction with 8.5 mM 3,5-lutidine and 17 mM CO₂(aq) in a water/methanol 9:1 mixture at 25°C.

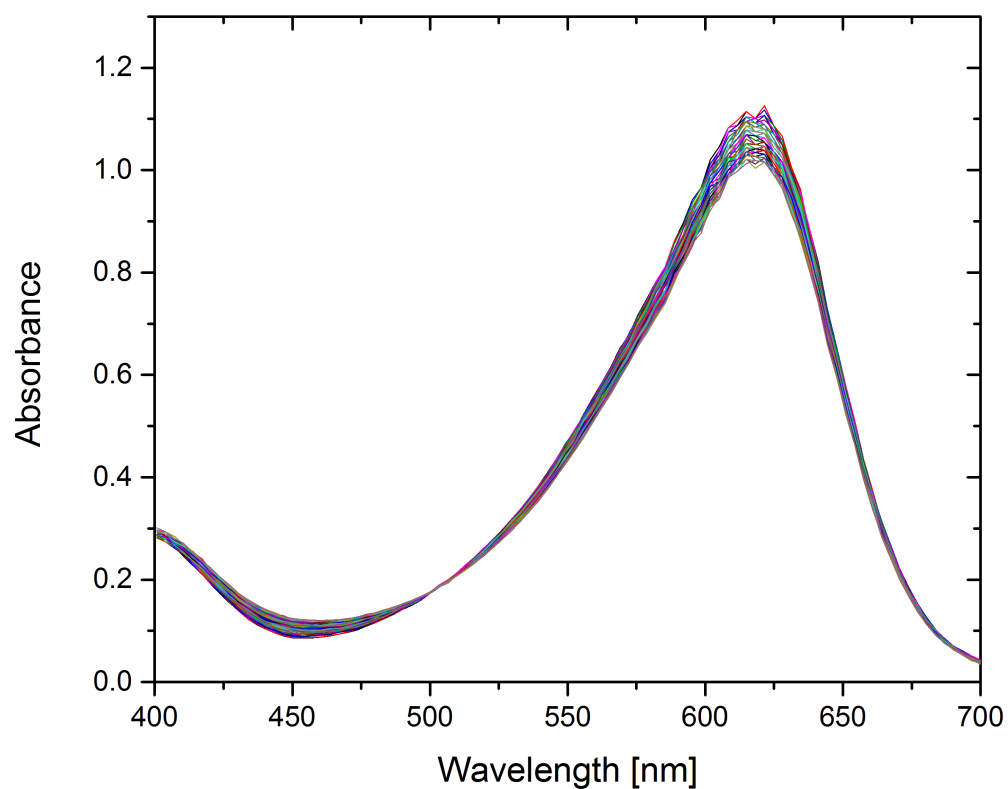


Figure S9. Two dimensional (absorbance vs. wavelength, top) representation of absorbance data for the hydration of CO₂ by the [Cu₂^{II}(H₂pat¹)(OH)]⁺ complex. Reaction with 8.5 mM imidazole and 17 mM CO₂(aq) in a water/methanol 9:1 mixture at 25°C.

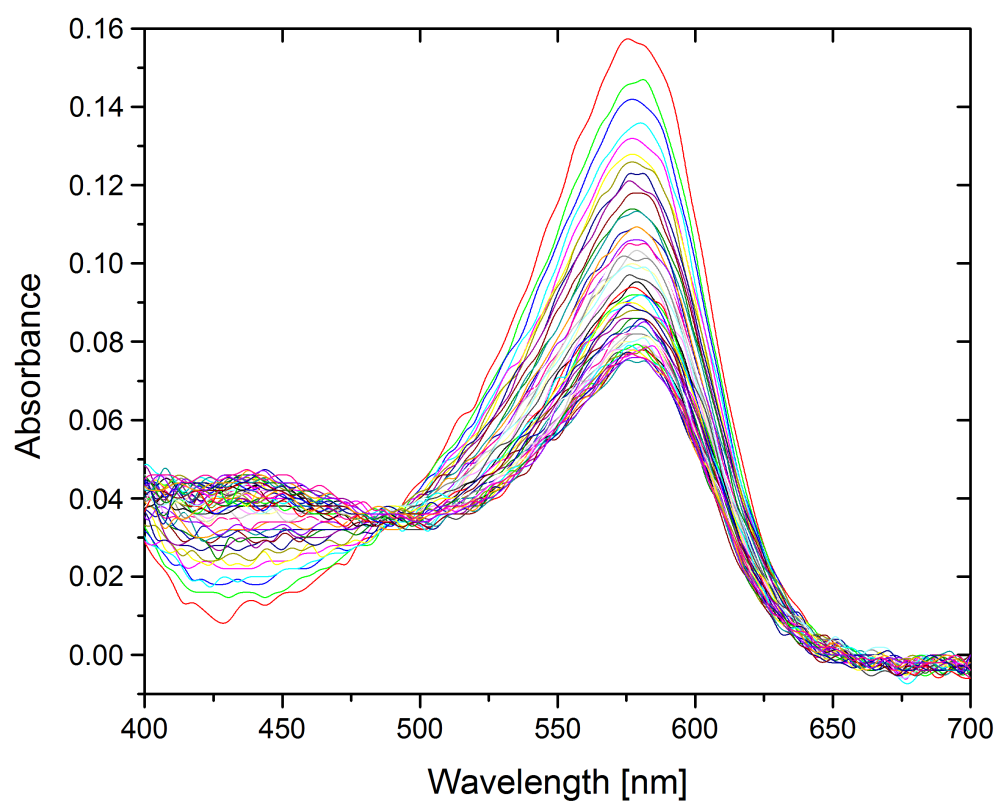


Figure S10. Two dimensional (absorbance vs. wavelength, top) representation of absorbance data for the hydration of CO₂ by the [Cu₂^{II}(H₂pat¹)(OH)]⁺ complex. Reaction with 8.5 mM 1,2-dimethylimidazole and 17 mM CO₂(aq) in a water/methanol 9:1 mixture at 25°C.

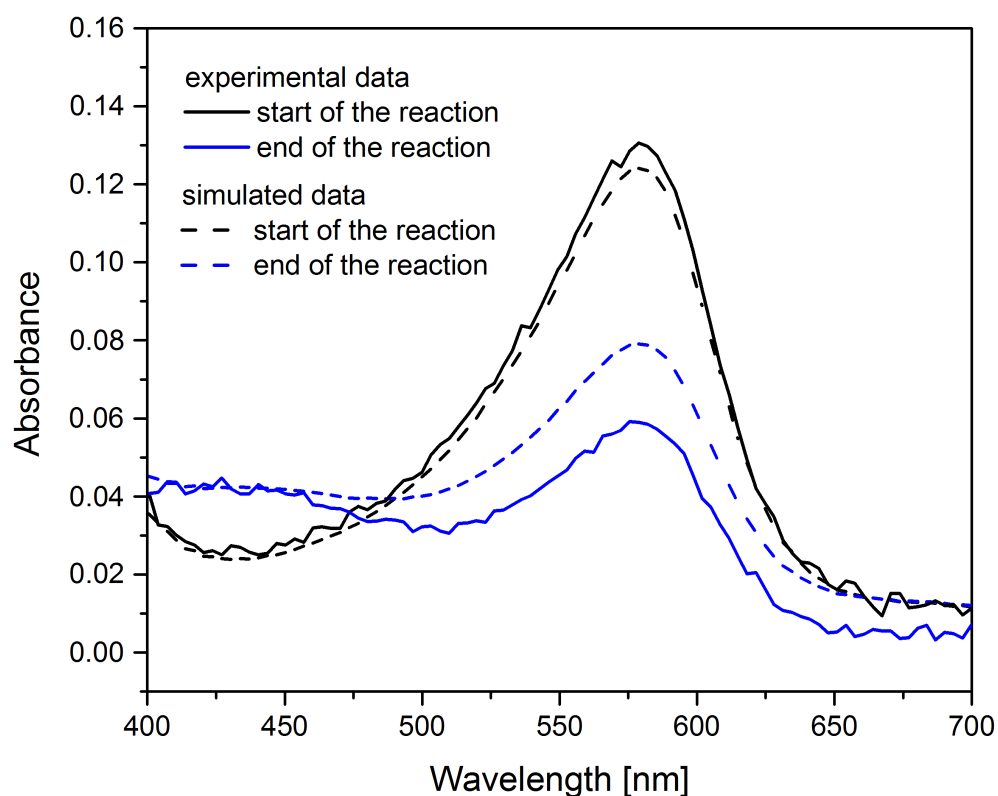


Figure S11. Comparison of experimental (solid lines) and simulated (dotted lines; parameters of Table 1 were used for simulation) absorbance data of the CO₂ hydration reaction of the [Cu₂^{II}(H₂pat²)(OH)]⁺ complex using the Tris/metacresol purple base/indicator system (pK_a 8.07/8.30; λ_{max} 578) at the beginning (black lines) and the end (blue lines) of the reaction.

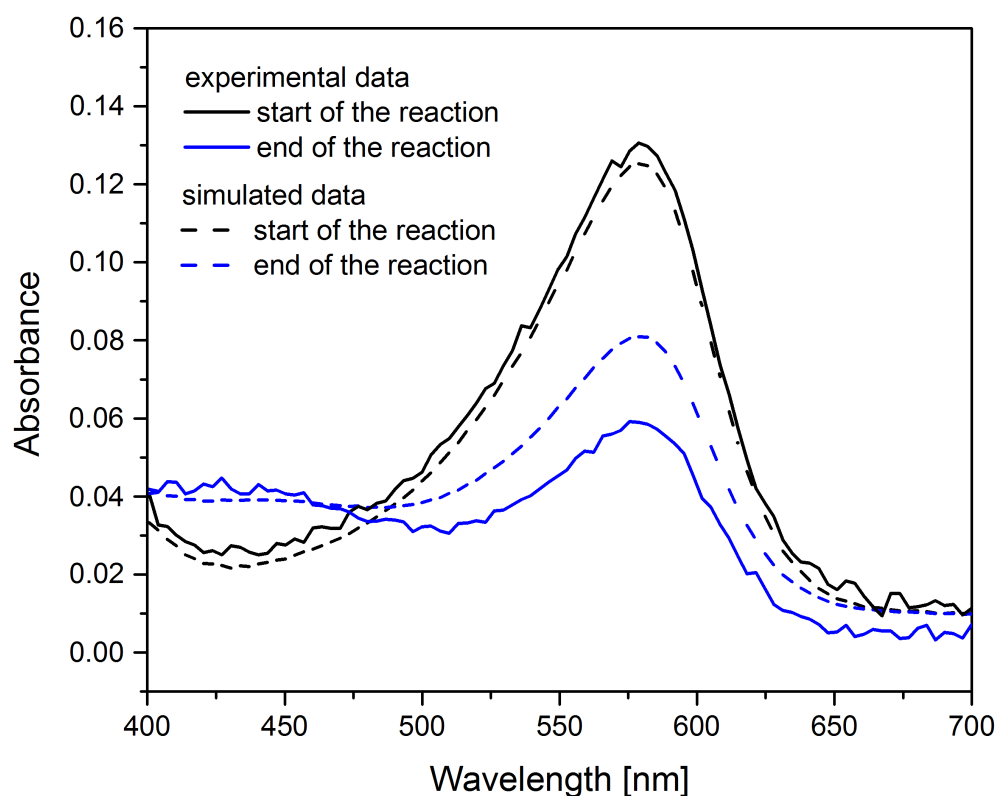


Figure S12. Comparison of experimental (solid lines) and simulated (dotted lines; parameters of Table 1 were used for simulation) absorbance data of the CO₂ hydration reaction of the [Cu₂^{II}(H₂pat³)(OH)]⁺ complex using the Tris/metacresol purple base/indicator system (p*K*_a 8.07/8.30; λ_{max} 578) at the beginning (black lines) and the end (blue lines) of the reaction.

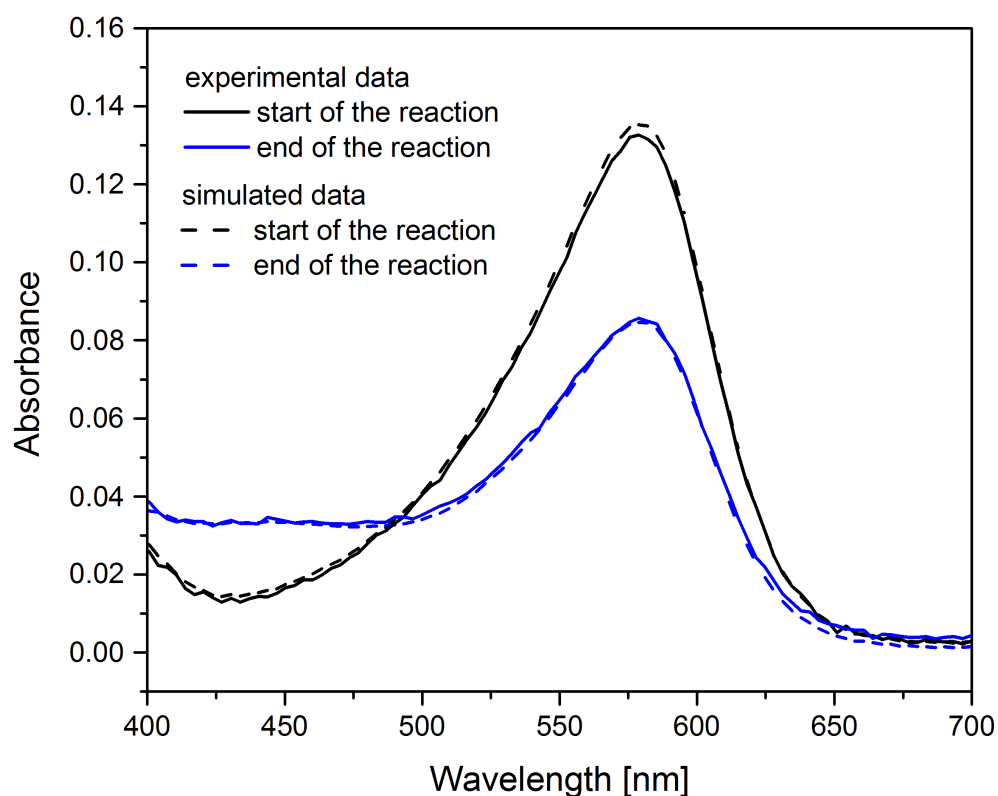


Figure S13. Comparison of experimental (solid lines) and simulated (dotted lines; parameters of Table 1 were used for simulation) absorbance data of the CO₂ hydration reaction of the [Cu₂^{II}(H₂pat⁴)(OH)]⁺ complex using the Tris/metacresol purple base/indicator system (pK_a 8.07/8.30; λ_{max} 578) at the beginning (black lines) and the end (blue lines) of the reaction.

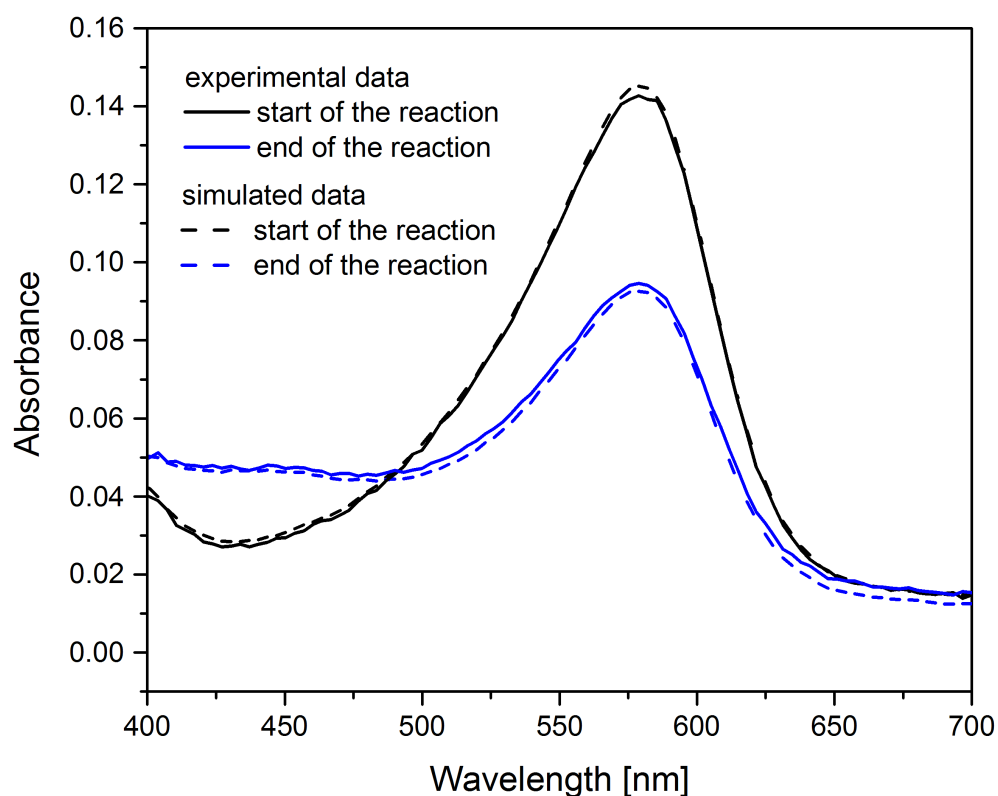


Figure S14. Comparison of experimental (solid lines) and simulated (dotted lines; parameters of Table 1 were used for simulation) absorbance data of the CO₂ hydration reaction of the [Cu₂^{II}(H₂pat⁵)(OH)]⁺ complex using the Tris/metacresol purple base/indicator system (pK_a 8.07/8.30; λ_{max} 578) at the beginning (black lines) and the end (blue lines) of the reaction.

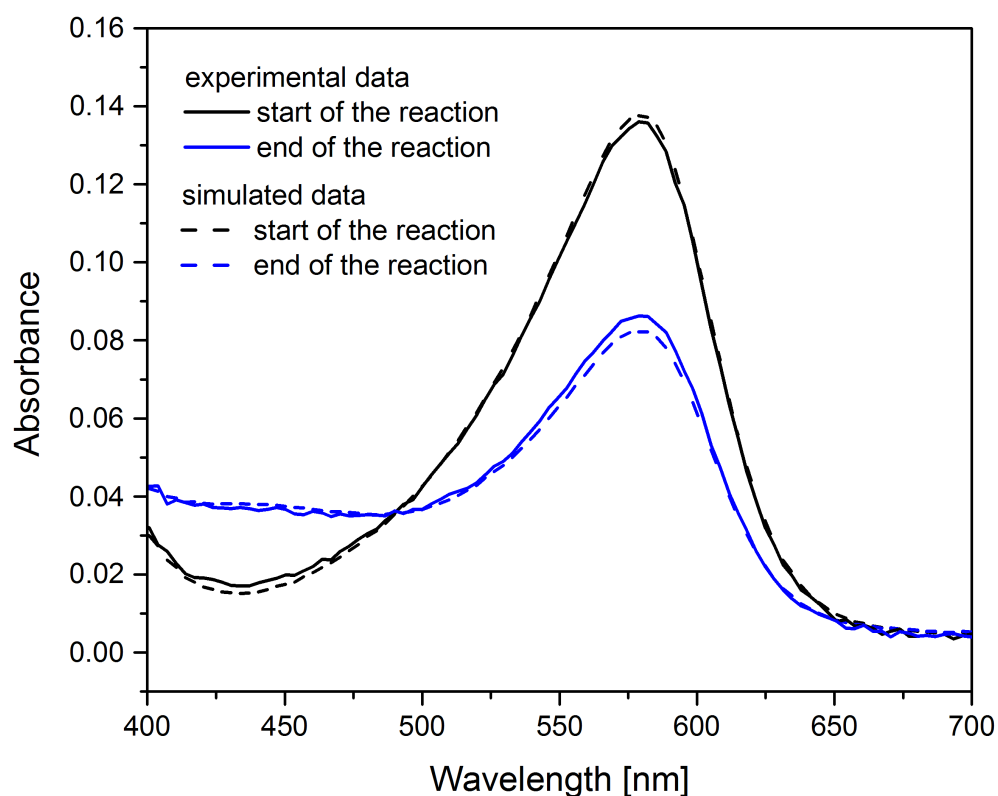


Figure S15. Comparison of experimental (solid lines) and simulated (dotted lines; parameters of Table 1 were used for simulation) absorbance data of the CO₂ hydration reaction of the [Cu₂^{II}(H₂L^{ascA})(OH)]⁺ complex using the Tris/metacresol purple base/indicator system (pK_a 8.07/8.30; λ_{max} 578) at the beginning (black lines) and the end (blue lines) of the reaction.

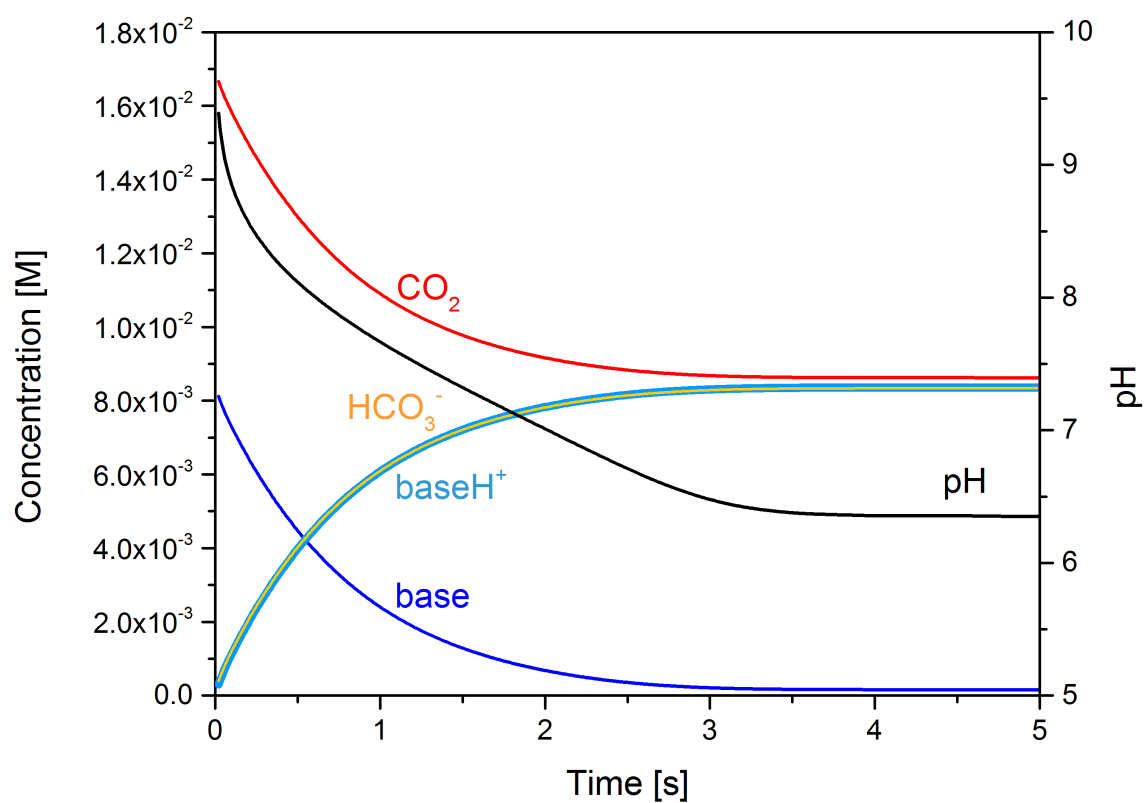


Figure S16. pH and concentration profile of the most important species (CO_2 , HCO_3^- , base , baseH^+) during the hydration of 17 mM CO_2 with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] by the $[\text{Cu}_2^{\text{II}}(\text{H}_2\text{pat}^2)(\text{OH})]^+$ complex at 25°C.

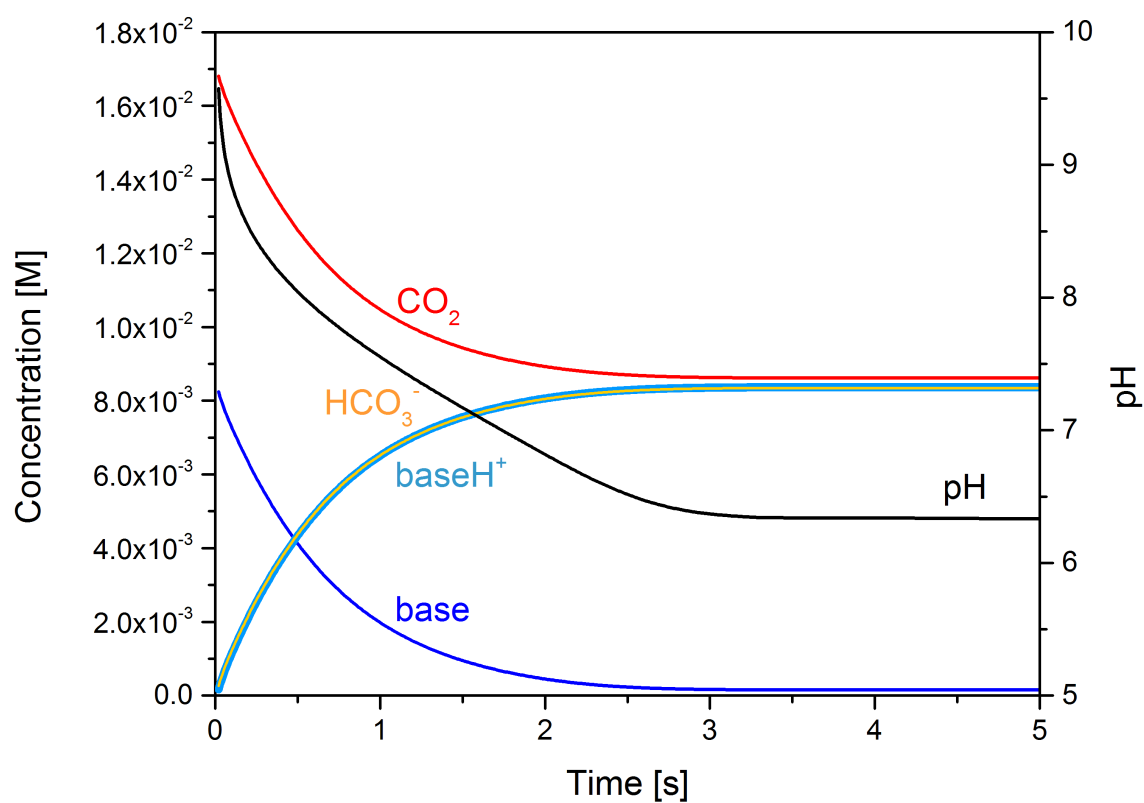


Figure S17. pH and concentration profile of the most important species (CO_2 , HCO_3^- , base , baseH^+) during the hydration of 17 mM CO_2 with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] by the $[\text{Cu}_2^{\text{II}}(\text{H}_2\text{pat}^3)(\text{OH})]^+$ complex at 25°C.

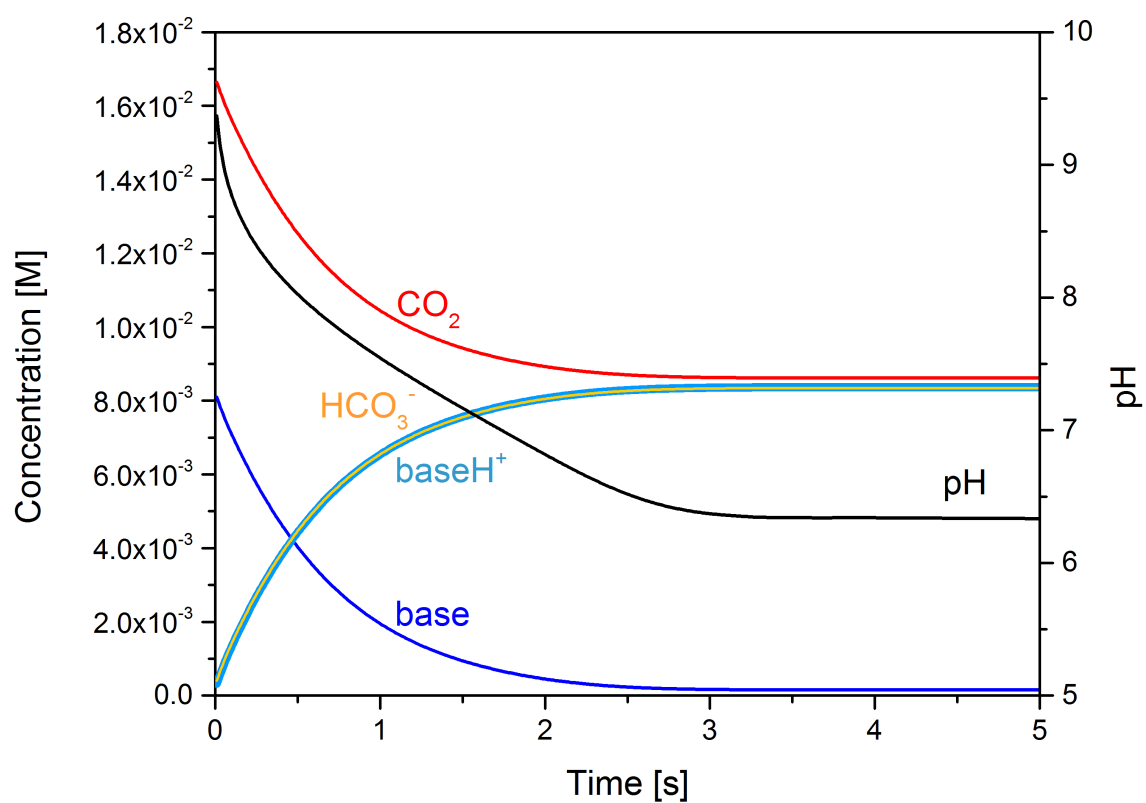


Figure S18. pH and concentration profile of the most important species (CO_2 , HCO_3^- , base , baseH^+) during the hydration of 17 mM CO_2 with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] by the $[\text{Cu}_2^{\text{II}}(\text{H}_2\text{pat}^4)(\text{OH})]^+$ complex at 25°C.

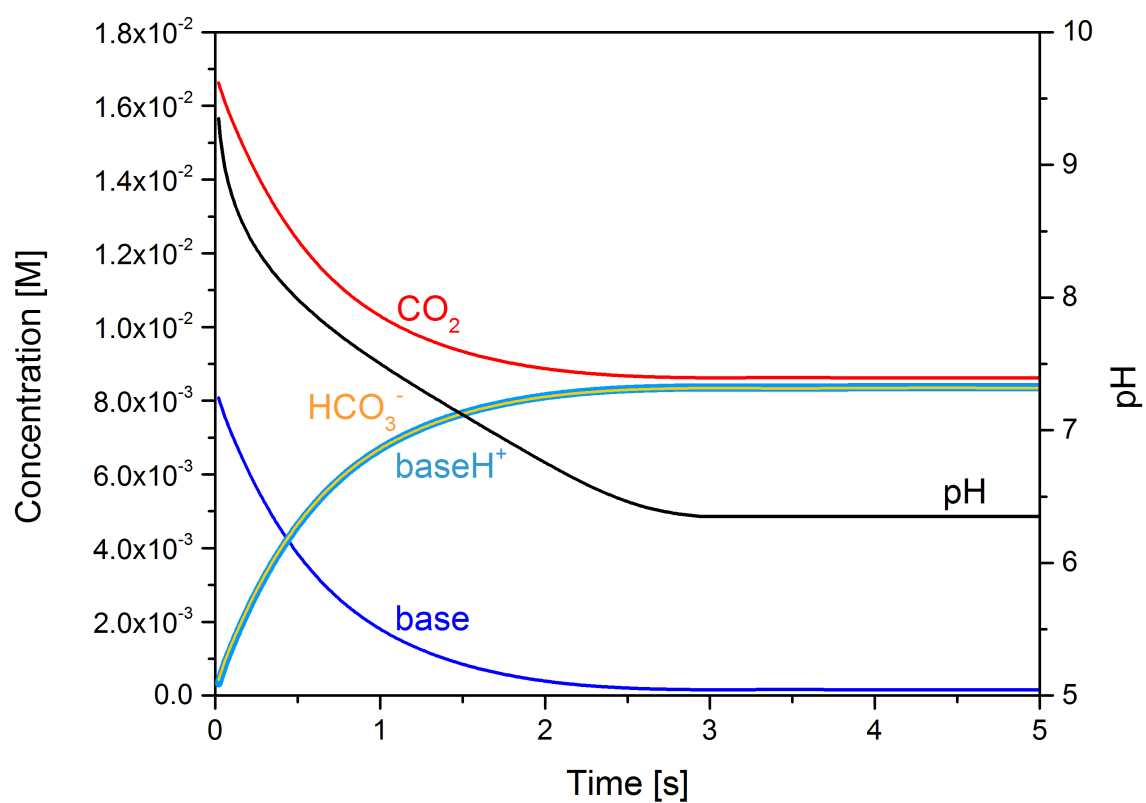


Figure S19. pH and concentration profile of the most important species (CO_2 , HCO_3^- , base, baseH^+) during the hydration of 17 mM CO_2 with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] by the $[\text{Cu}_2^{\text{II}}(\text{H}_2\text{pat}^5)(\text{OH})]^+$ complex at 25°C.

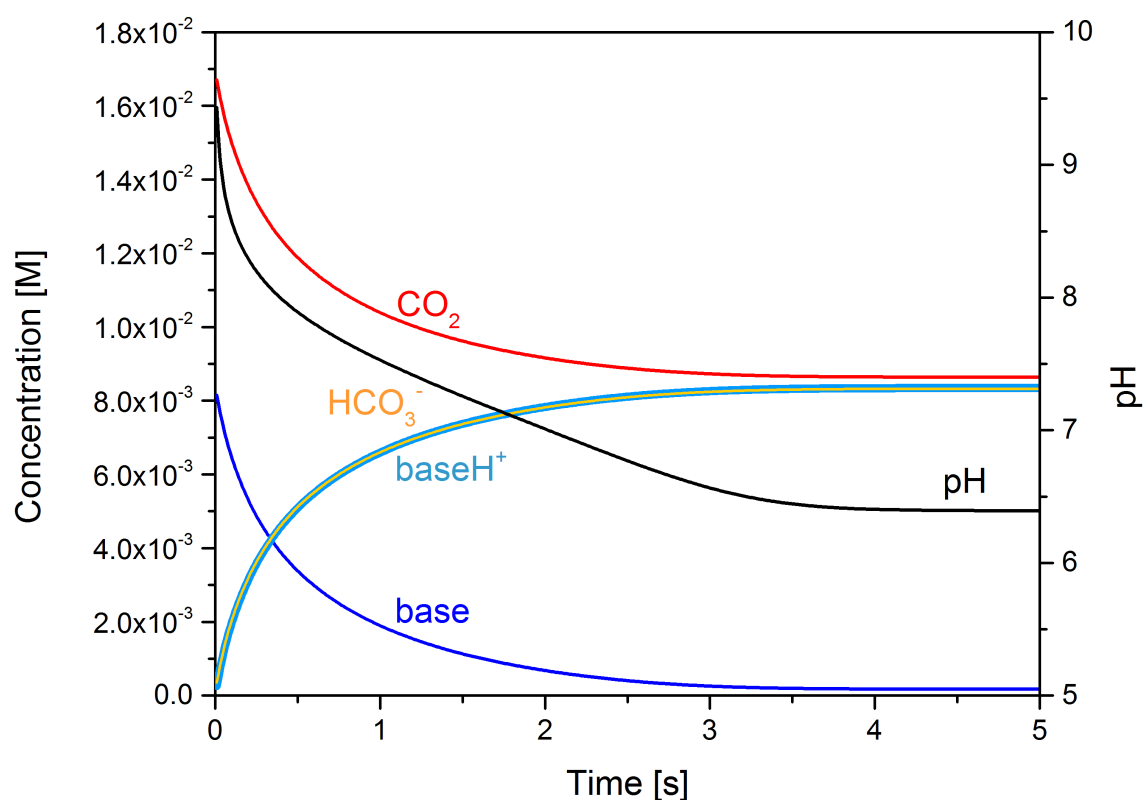


Figure S20. pH and concentration profile of the most important species (CO_2 , HCO_3^- , base, baseH $^+$) during the hydration of 17 mM CO_2 with 8.5 mM Tris [(tris-hydroxymethyl)-aminomethane] by the $[\text{Cu}_2^{\text{II}}(\text{H}_2\text{L}^{\text{ascA}})(\text{OH})]^+$ complex at 25°C.

References:

- 1 Palmer, D. A. & van Eldik, R. The chemistry of metal carbonato and carbon dioxide complexes. *Chem. Rev.* **83**, 651-731 (1983).
- 2 Bazzicalupi, C. *et al.* A new functionalized hexaazamacrocyclic. Effect of pyridine pendants on cation and anion binding. *J. Chem. Soc., Dalton Trans.*, 1101-1108 (1999).