



R = H (norepinephrine), CH₃ (epinephrine)

Supplementary information, Fig. S15| Epinephrine has weaker interaction with negatively charged oxygen of Asp^{3.32} than norepinephrine due to the charge difference.

Due to the addition of the methyl group, the molecular electrostatic potential (MEP) of epinephrine is 3.9 kcal/mol weaker compared to norepinephrine along the N-H axis at 1.8 Å, which is the distance observed for the interaction between the N-H hydrogen of the ligands and the negatively charged oxygen of Asp^{3.32} in crystal structures of β₁AR and β₂AR.