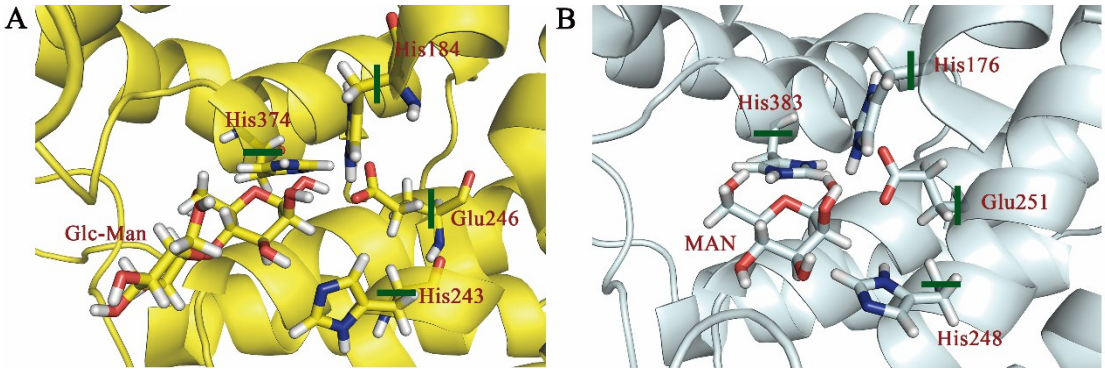


**Fig. S1** The QM regions for *Ra*CE and *Se*YihS. (A) The QM regions for *Ra*CE included the substrate (4-*O*-*β*-D-glucosyl-D-mannose), the side chain of residue His184, His243, Glu246 and His374. (B) The QM regions for *Se*YihS included the substrate (D-mannose), residue His176, His248, Glu251 and His383

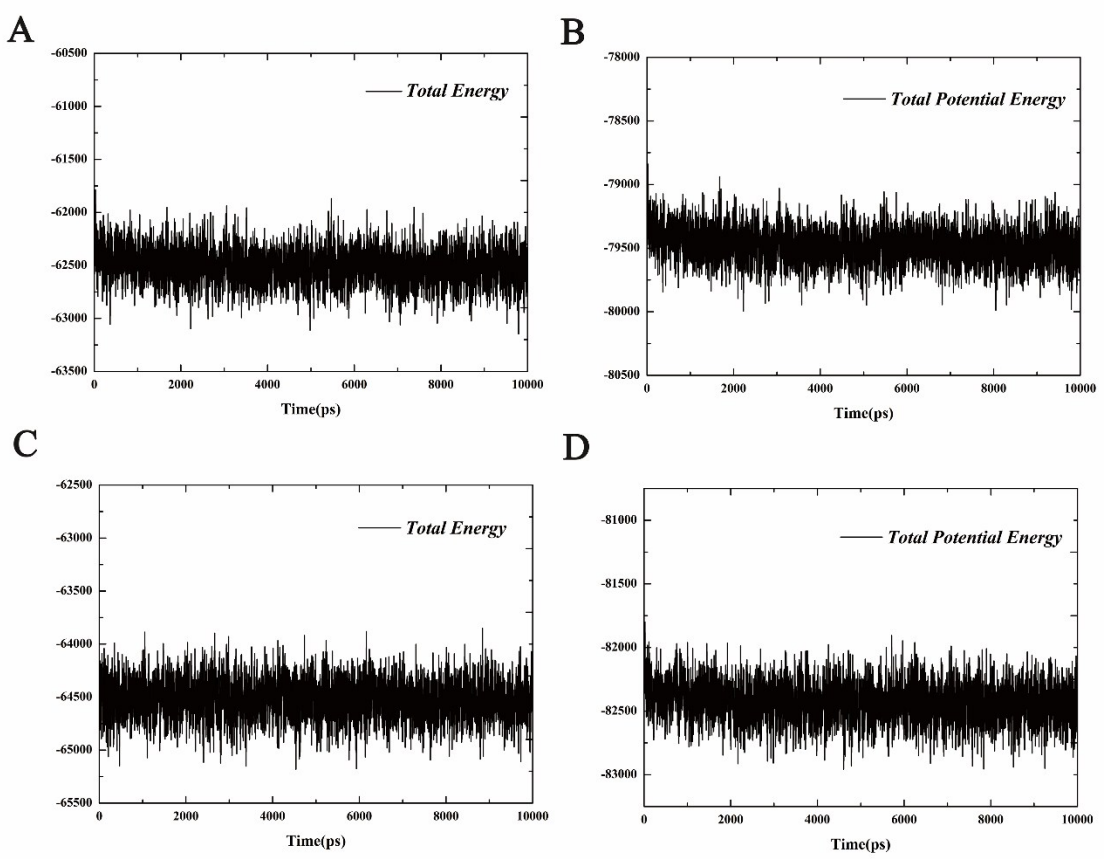


**Fig. S2** Total potential energy and total energy results of *Ra*CE and *Se*YihS. (A) The total energy curve of the *Ra*CE/Glc-Man complex. (B) The total potential energy curve of the *Ra*CE/Glc-Man complex. (C) The total energy curve of the *Se*YihS/MAN complex. (D) The total potential energy curve of the *Se*YihS/MAN complex.

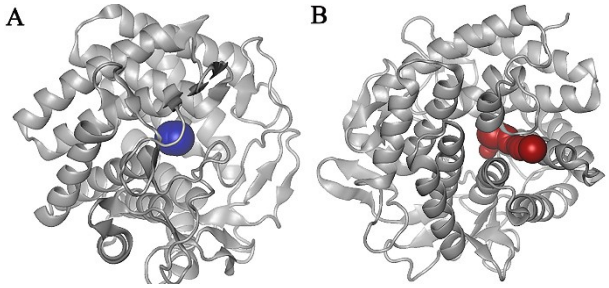


**Fig. S3** The substrate access channel analysis. (A) for the *Ra*CE/Glc-Man, and (B) for *Se*YihS/MAN complex.

**Table S1.** The average distances between catalytic residues and the substrate.

| **The average distances for *Ra*CE (Å)** | | **The average distances for *Se*YihS (Å)** | |
|---|---|---|---|
| HE2@His374 - O5@Glc-Man | 2.00 | 2.10 | HE2@His383 - O5@MAN |
| NE2@His374 - H@Glc-Man | 3.48 | 3.79 | NE2@His383 - H@MAN |
| OE1@Glu246 - H@Glc-Man | 1.76 | 1.77 | OE1@Glu251 - H@MAN |
| OE2@Glu246 - H@Glc-Man | 2.44 | 2.68 | OE2@Glu251 - H@MAN |
| NE2@His243 - H2@Glc-Man | 3.05 | 4.31 | NE2@His248 - H2@MAN |