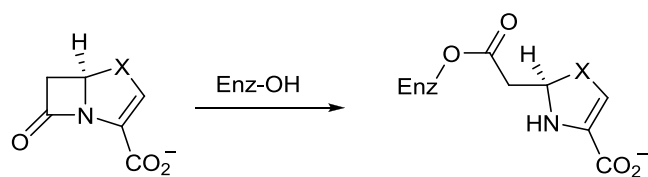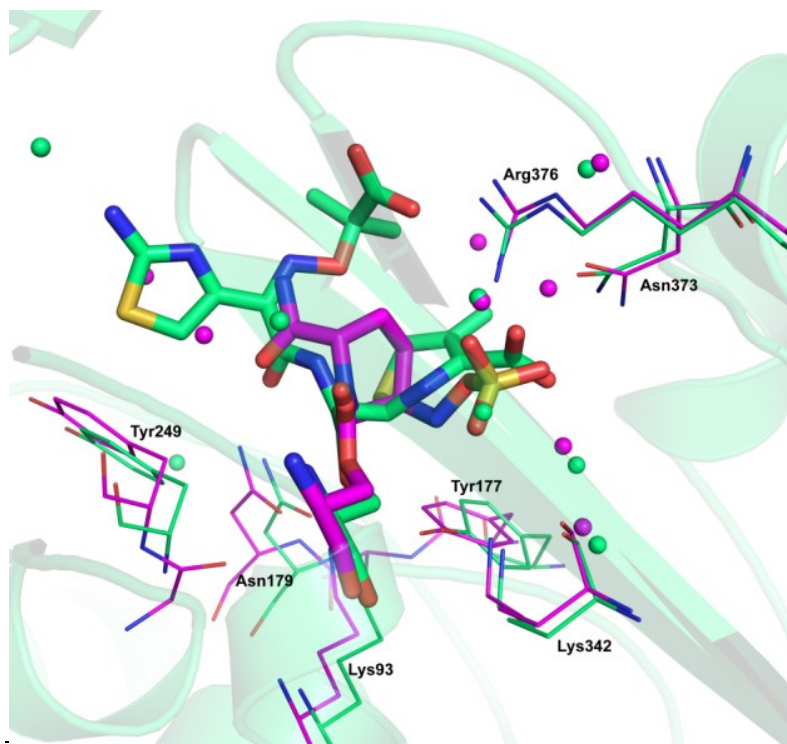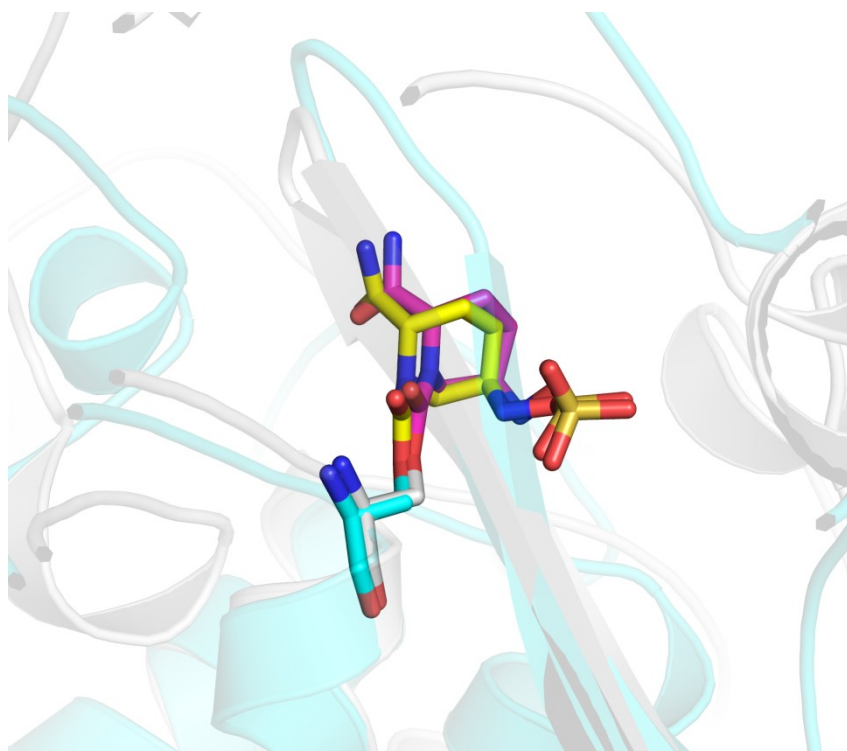b



Figure S1: Bond cleavage upon covalent inhibition by: a) avibactam and b) carbapenem.

Figure S2:



Overlay of avibactam on ceftazidime bound to AmpC. The carbon atoms of Avibactam are colored magenta, ceftazidime is colored green and the water molecules from each structure are shown in respective colors.

Figure S3:



Comparison of the binding modes. Overlay of avibactam bound to CTX-M-15 and AmpC. The backbone chain for each protein is shown in cartoon diagram where CTX-M-15 is colored grey, while AmpC is colored cyan. The avibactam is depicted as sticks and the carbon atoms are colored magenta for CTX-M-15 and yellow for AmpC forms.

Figure S4:

*E. coli* and *P. aeruginosa* sequence alignment:

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                        10         20         30         40         50         60
               ----|----| ----|----| ----|----| ----|----| ----|----| ----|----|
ADV18979.1_Eco   1 FKTT--LCAL LITASCSTFA APQQIN---- -----DIVHR TITPLIEQQK IPGMAVAVIY
BAE06837.1_Pae   1 MRDTRFPCLC GIAASTLLFA TTPAIAGEAP ADRLKALVDA AVQPVMKAND IPGLAVAISL

                        70         80         90        100        110        120
               ----|----| ----|----| ----|----| ----|----| ----|----| ----|----|
ADV18979.1_Eco  50 QGKPYYFTWG YADIAKKQPV TQQTLFELGS VSKTFTGVLG GDAIARGEIK LSDPATKYWP
BAE06837.1_Pae  61 KGEPHYFSYG LASKEDGRRV TPETLFEIGS VSKTFTATLA GYALAQDKMR LDDRASQHWP

                       130        140        150        160        170        180
               ----|----| ----|----| ----|----| ----|----| ----|----| ----|----|
ADV18979.1_Eco 110 ELTAKQWNGI TLLHLATYTA GGLPLQVPDE VKSSSDLLR- FYQNWQPAWA PGTQRLYANS
BAE06837.1_Pae 121 ALQGSRFDGI SLLDLATYTA GGLPLQFPDS VQKDQAQIRD YYRQWQPTYA PGSQRLYSNP

                       190        200        210        220        230        240
               ----|----| ----|----| ----|----| ----|----| ----|----| ----|----|
ADV18979.1_Eco 169 SIGLFGALAV KPSGLSFEQA MQTRVFQPLK LNHTWINVPP PEEKNYAWGY -REGKAVHVS
BAE06837.1_Pae 181 SIGLFGYLAA RSLGQPFERL MEQQVFPALG LEQTHLDVPE AALAQYAQGY GKDDRPLRVG

                       250        260        270        280        290        300
               ----|----| ----|----| ----|----| ----|----| ----|----| ----|----|
ADV18979.1_Eco 228 PGALDAEAYG VKSTIEDMAR WVRSNMNPRD INDKTLQQGI QLAQSRYWQT GDMYQGLGWE
BAE06837.1_Pae 241 PGPLDAEGYG VKTSAADLLR FVDANLHPER L-DRPWAQAL DATHRGYYKV GDMTQGLGWE

                       310        320        330        340        350        360
               ----|----| ----|----| ----|----| ----|----| ----|----| ----|----|
ADV18979.1_Eco 288 MLDWPVNPDS SIINGSGNKI ALAAHPVKAI TPPTPAVRAS WVHKTGATGG FGSYVAFIPE
BAE06837.1_Pae 300 AYDWPISLKR -LQAGNSTPM ALQPHRIARL PAPQALEGQR LLNKTGSTNG FGAYVAFVPG

                       370        380        390
               ----|----| ----|----| ----|----| ----|----
ADV18979.1_Eco 348 KELGIVMLAN KNYPNPARVA AAWQILNALQ ---------
BAE06837.1_Pae 359 RDLGLVILAN RNYPNAERVK IAYAILSGLE QQGKVPLKR
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