(a)

	104 101-loop	164 Ω-loop	237 S3 strand	238 238-loop	240 238-loop	69 H2 helix	130 SDN loop	244 S4 β-strand	275 H11 helix	276 H11 helix
104 101-loop	6	11	–	15	–	–	–	–	–	–
164 Ω-loop	10	12	–	–	10	1	–	–	–	–
237 S3 strand	4	7	–	–	–	–	–	–	–	–
238 238-loop	6	3	1	6	9	–	–	–	–	–
240 238-loop	5	10	7	1	1	–	–	–	–	–
69 H2 helix	2	5	–	1	1	8	–	1	5	6
130 SDN loop	1	–	–	1	–	–	2	–	–	–
244 S4 β-strand	1	1	1	–	1	–	–	12	–	–
275 H11 helix	–	–	–	1	1	–	–	–	3	–
276 H11 helix	1	4	–	1	1	5	–	–	–	1

(b)

	104 101-loop	164 Ω-loop	237 S3 β-strand	238 238-loop	240 238-loop	69 H2 helix	130 SDN-loop	244 S4 β-strand	275 H11 helix	276 H11 helix
39 H1 helix	19	15	6	12	10	1	2	4	–	–
165 Ω-loop	–	1	–	–	–	7	–	–	2	3
182 H8 helix	17	9	2	10	5	2	1	–	1	–
265 S5 β-strand	4	8	1	9	8	–	–	2	1	–

Figure 6.4 Distribution of combinations of mutations in TEM-type β-lactamases isolated from clinical strains. For each residue, the location in the secondary structure of the protein is indicated. (a) Amount of the enzymes with combinations of the key mutations: single (diagonal cells), double (cells located above the diagonal), and multiple (cells located below the diagonal). (b) Amount of the enzymes with combinations of the key and secondary mutations.

6.3.1 Single Key Mutations in TEM-Type ESBLs (2be)

TEM-type ESBLs with a single key mutation account for about 30% ($n = 25$) of all β-lactamases of this phenotype (Figure 6.4). The residue R164 is the most frequently mutable ($n = 12$), it is located in the Ω-loop, and the salt bridge between R164 and D179 defines its configuration. Substitution of arginine leads to the disappearance of this bond, which increases the mobility of the loop and changes the position of the catalytically important residues E166 and N170 (Knox 1995). As a result, catalytic efficiency for the hydrolysis of ceftazidime enhances significantly (by 4 orders of magnitude) (Figure 6.6). In contrast, catalytic efficiency toward penicillins, which are substrates with small