Crystal Structures of Class A, B, and D β-Lactamases

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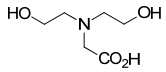
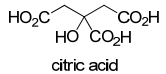
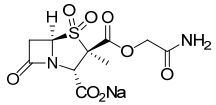
β-Lactamases. The most widely-used class of antibiotics are the β-lactams. Bacterial resistance to β-lactams has developed into a serious clinical problem and the most important mechanism for resistance involves β-lactamases, enzymes that inactivate β-lactams through hydrolysis. Serine β-lactamases (classes A, C, and D) hydrolyze β-lactams through a covalent (acylenzyme) intermediate while the metallo-β-lactamases (class B) use a zinc-bound hydroxide as the active-site nucleophile. The list of concerning β-lactamases is long and includes the class C (AmpC) β-lactamases of Gram-negative bacteria, inhibitor-resistant class A β-lactamases, and extended-spectrum β-lactamases (ESBLs) that can hydrolyze third-generation cephalosporins. The β-lactamases of greatest concern, in regard to the carbapenem class of β-lactam antibiotics, are the class A carbapenemases (e.g. KPCs), class D carbapenemases (OXAs), and metallo-β-lactamases (MBLs) that confer resistance to virtually all β-lactams.

Purpose of this File and the Tables Below. Our research in the development of β-lactamase inhibitors involves molecular modeling with enzyme–inhibitor complexes. Given the large number of β-lactamase crystal structures now available, we decided to assemble a list of PDB files with references, inhibitor structures, metal content, etc. We hope that this list could become a useful resource to others as well. We have started this as a list of carbapenemase structures, but it may be expanded later to include more β-lactamases. Comments, corrections, and suggestions for improvements are welcome.

TABLE of CONTENTS

Table 1. Class A carbapenemases.[a]

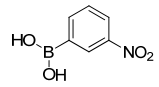
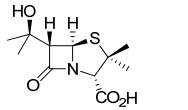
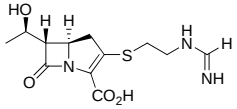
PDB Code	Enzyme, mutations	Source, Ambler[b] class, Bush–Jacoby[c,d] functional group	Year	Resolution	pH	Ligand	Comments and References
KPC-2 (class A carbapenemase, group 2f)							
2OV5	KPC-2	*K. pneumoniae*, class A, group 2f	2007	1.85 Å	pH 9	 bicine	- Ke, W.; Bethel, C. R.; Thomson, J. M.; Bonomo, R. A.; van den Akker, F. Crystal structure of KPC-2: Insights into carbapenemase activity in class A β-lactamases. *Biochemistry* **2007**, *46*, 5732–5740.
3DW0 (2ODS)	KPC-2	*E. coli*, class A, group 2f	2008	1.60 Å	pH 5.5	–	- Petrella, S.; Ziental-Gelus, N.; Mayer, C.; Renard, M.; Jarlier, V.; Sougakoff, W. Genetic and structural insights into the dissemination potential of the extremely broad-spectrum class A β-lactamase KPC-2 identified in an *Escherichia coli* strain and an *Enterobacter cloacae* strain isolated from the same patient in France. *Antimicrob. Agents Chemother.* **2008**, *52*, 3725–3736.
3C5A	KPC-2, C-term del.	*E. coli*, class A, group 2f	2008	1.23 Å	pH 4.0	 citric acid	- Structure of the C-terminal deleted mutant of KPC-2. - Petrella et al. *Antimicrob. Agents Chemother.* **2008**, *52*, 3725–3736.
3E2K 3E2L	KPC-2, G175S	*K. pneumoniae*, class A, group 2f	2009	2.10 Å 1.87 Å	pH 4.5 pH 5.0	BLIP	- Hanes, M. S.; Jude, K. M.; Berger, J. M.; Bonomo, R. A.; Handel, T. M. Structural and biochemical characterization of the interaction between KPC-2 β-lactamase and β-lactamase inhibitor protein. *Biochemistry* **2009**, *48*, 9185–9193.
3RXW	KPC-2	*K. pneumoniae*, class A, group 2f	2012	1.26 Å	pH 4.0	 PSR-3-226	- Ke, W.; Bethel, C. R.; Papp-Wallace, K. M.; Pagadala, S. R. R.; Nottingham, M.; Fernandez, D.; Buynak, J. D.; Bonomo, R. A.; van den Akker, F. Crystal structures of KPC-2 β-lactamase in complex with 3-nitrophenyl boronic acid and the penam sulfone PSR-3-226. *Antimicrob. Agents Chemother.* **2012**, *56*, 2713–2718.

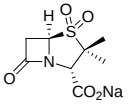
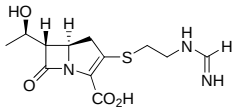
[a] PDB = Protein data bank (www.rcsb.org/pdb).

[b] Ambler classesification (classes A, B, C, or D). See: Ambler, R. P. The structure of β-lactamases. *Philos. Trans. R. Soc. London, Ser. B* **1980**, *289*, 321–331.

[c] For the 2010 Bush–Jacoby functional group classification, see: Bush, K.; Jacoby, G. A. Updated functional group classification of β-lactamases. *Antimicrob. Agents Chemother.* **2010**, *54*, 969–976.

[d] For previous functional group classifications, see: (a) Bush, K. Recent developments in β-lactamase research and their implications for the future. *Rev. Infect. Dis.* **1988**, *10*, 681–690. (b) Bush, K.; Classification of β-lactamases: Groups 1, 2a, 2b, and 2b′. *Antimicrob. Agents Chemother.* **1989**, *33*, 264–270. (c) Bush, K.; Classification of β-lactamases: Groups 2c, 2d, 2e, 3, and 4. *Antimicrob. Agents Chemother.* **1989**, *33*, 271–276. (d) Bush, K.; Jacoby, G. A.; Medeiros, A. A. A functional classification scheme for β-lactamases and its correlation with molecular structure. *Antimicrob. Agents Chemother.* **1995**, *39*, 1211–1233.

PDB Code	Enzyme, mutations	Source, Ambler[b] class, Bush–Jacoby[c,d] functional group	Year	Resolution	pH	Ligand	Comments and References
3RXX	KPC-2	*K. pneumoniae*, class A, group 2f	2012	1.62 Å	pH 4.0	 3-nitrophenylboronic acid	- Ke, W.; Bethel, C. R.; Papp-Wallace, K. M.; Pagadala, S. R. R.; Nottingham, M.; Fernandez, D.; Buynak, J. D.; Bonomo, R. A.; van den Akker, F. Crystal structures of KPC-2 β-lactamase in complex with 3-nitrophenyl boronic acid and the penam sulfone PSR-3-226. *Antimicrob. Agents Chemother.* **2012**, *56*, 2713–2718.
SME-1 (class A carbapenemase, group 2f)							
1DY6	SME-1	*S. marcescens*, class A, group 2f	2002	2.13 Å	pH 8.5	–	- Sougakoff, W.; L'Hermite, G.; Pernot, L.; Naas, T.; Guillet, V.; Nordmann, P.; Jarlier, V.; Delettré, J. Structure of the imipenem-hydrolyzing class A β-lactamase SME-1 from *Serratia marcescens*. *Acta Cryst.* **2002**, *D58*, 267–274.
NMC-A (class A carbapenemase, group 2f)							
1BUL	NMC-A	*E. cloacae*, class A, group 2f	1998	1.89 Å	pH 7.5	 6α-hydroxypropyl penicillinate	- Mourey, L.; Miyashita, K.; Swaren, P.; Bulychev, A.; Samama, J.-P.; Mobashery, S. Inhibition of the NMC-A β-lactamase by a penicillanic acid derivative and the structural bases for the increase in substrate profile of this antibiotic resistance enzyme. *J. Am. Chem. Soc.* **1998**, *120*, 9382–9383.
1BUE	NMC-A	*E. cloacae*, class A, group 2f	1998	1.64 Å	pH 5.25	–	- Swarén, P.; Maveyraud, L.; Raquet, X.; Cabantous, S.; Duez, C.; Pédelacq, J.-D.; Mariotte-Boyer, S.; Mourey, L.; Labia, R.; Nicolas-Chanoine, M.-H.; Nordmann, P.; Frère, J.-M.; Samama, J.-P. X-ray analysis of the NMC-A β-lactamase at 1.64-Å resolution, a class A carbapenemase with broad substrate specificity. *J. Biol. Chem.* **1998**, *273*, 26714–26721.
GES-1 (class A ESBL, group 2be)							
2QPN	GES-1	*K. pneumoniae*, class A, group 2be	2008	1.10 Å	na	–	- Smith, C. A.; Caccamo, M.; Kantardjieff, K. A.; Vakulenko, S. Structure of GES-1 at atomic resolution: Insights into the evolution of carbapenemase activity in the class A extended-spectrum β-lactamases. *Acta Cryst.* **2007**, *D63*, 982–992.
4GOG	GES-1	*K. pneumoniae*, class A, group 2be	2012	1.10 Å	na	 imipenem	- Smith, C. A.; Frase, H.; Toth, M.; Kumarasiri, M.; Wiafe, K.; Munoz, J.; Mobashery, S.; Vakulenko, S. B. Structural basis for progression toward the carbapenemase activity in the GES family of β-lactamases. *J. Am. Chem. Soc.* **2012**, *134*, 19512–19515.

PDB Code	Enzyme, mutations	Source, Ambler[b] class, Bush–Jacoby[c,d] functional group	Year	Resolution	pH	Ligand	Comments and References
GES-2 (class A carbapenemase, group 2f)							
3NI9	GES-2	*P. aeruginosa*, class A, group 2f	2011	2.00 Å	pH 8.8	–	- Frase, H.; Smith, C. A.; Toth, M.; Champion, M. M.; Mobashery, S.; Vakulenko, S. B. Identification of products of inhibition of GES-2 β-lactamase by tazobactam by X-ray crystallography and spectrometry. *J. Biol. Chem.* **2011**, *286*, 14396–14409.
3NIA	GES-2	*P. aeruginosa*, class A, group 2f	2011	1.65 Å	na	 tazobactam	- Frase, H.; Smith, C. A.; Toth, M.; Champion, M. M.; Mobashery, S.; Vakulenko, S. B. Identification of products of inhibition of GES-2 β-lactamase by tazobactam by X-ray crystallography and spectrometry. *J. Biol. Chem.* **2011**, *286*, 14396–14409.
GES-5 (class A carbapenemase, group 2f)							
4GNU	GES-5	*P. aeruginosa*, class A, group 2f	2013	1.09 Å	na	–	- Smith, C. A.; Frase, H.; Toth, M.; Kumarasiri, M.; Wiafe, K.; Munoz, J.; Mobashery, S.; Vakulenko, S. B. Structural basis for progression toward the carbapenemase activity in the GES family of β-lactamases. *J. Am. Chem. Soc.* **2012**, *134*, 19512–19515.
4H8R	GES-5	*P. aeruginosa*, class A, group 2f	2013	1.25 Å	pH 7	 imipenem	- Smith, C. A.; Frase, H.; Toth, M.; Kumarasiri, M.; Wiafe, K.; Munoz, J.; Mobashery, S.; Vakulenko, S. B. Structural basis for progression toward the carbapenemase activity in the GES family of β-lactamases. *J. Am. Chem. Soc.* **2012**, *134*, 19512–19515.
GES-11 (class A carbapenemase, group 2f)							
3V3R	GES-11	*A. baumannii*, class A, group 2f	2012	1.90 Å	na	–	- Delbrück, H.; Bogaerts, P.; Kupper, M. B.; de Castro, R. R.; Bennink, S.; Glupczynski, Y.; Galleni, M.; Hoffmann, K. M.; Bebrone, C. Kinetic and crystallographic studies of extended-spectrum GES-11, GES-12, and GES-14 β-lactamases. *Antimicrob. Agents Chemother.* **2012**, *56*, 5618–5625.
GES-14 (class A carbapenemase, group 2f)							
3TSG	GES-14	*A. baumannii*, class A, group 2f	2012	1.90 Å	na	–	- Delbrück, H.; Bogaerts, P.; Kupper, M. B.; de Castro, R. R.; Bennink, S.; Glupczynski, Y.; Galleni, M.; Hoffmann, K. M.; Bebrone, C. Kinetic and crystallographic studies of extended-spectrum GES-11, GES-12, and GES-14 β-lactamases. *Antimicrob. Agents Chemother.* **2012**, *56*, 5618–5625.

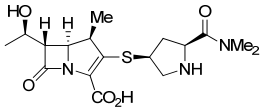
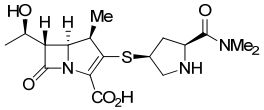
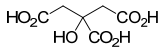
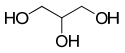
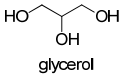
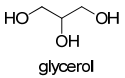
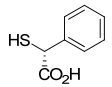
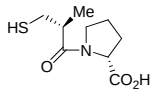
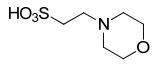
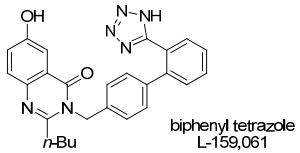
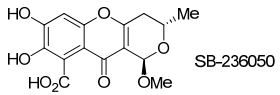
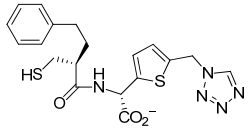
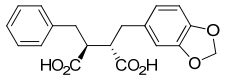
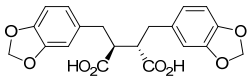
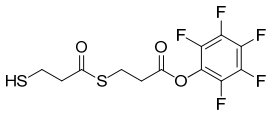
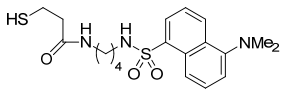
PDB Code	Enzyme, mutations	Source, Ambler[b] class, Bush–Jacoby[c,d] functional group	Year	Resolution	pH	Ligand	Comments and References
GES-18 (class A carbapenemase, group 2f)							
3V3S	GES-18	*P. aeruginosa*, class A, group 2f	2012	1.90 Å	pH 8.8	–	- Bebrone, C.; Bogaerts, P.; Delbrück, H.; Bennink, S.; Kupper, M. B.; de Castro, R. R.; Glupczynski, Y.; Hoffmann, K. M. GES-18, a new carbapenem-hydrolyzing GES-type β-lactamase from *Pseudomonas aeruginosa* that contains Ile80 and Ser170 residues. *Antimicrob. Agents Chemother.* **2013**, *57*, 396–401.
SFC-1 (class A carbapenemase, group 2f)							
4EQI	SFC-1	*S. fonticola*, class A, group 2f	2012	1.38 Å	pH 7	–	- Fonseca, F.; Chudyk, E. I.; van der Kamp, M. W.; Correia, A.; Mulholland, A. J.; Spencer, J. The basis for carbapenem hydrolysis by class A β-lactamases: A combined investigation using crystallography and simulations. *J. Am. Chem. Soc.* **2012**, *134*, 18275–18285.
4EUZ	SFC-1, S70A	*S. fonticola*, class A, group 2f	2012	1.08 Å	pH 7	 meropenem	- Fonseca, F.; Chudyk, E. I.; van der Kamp, M. W.; Correia, A.; Mulholland, A. J.; Spencer, J. The basis for carbapenem hydrolysis by class A β-lactamases: A combined investigation using crystallography and simulations. *J. Am. Chem. Soc.* **2012**, *134*, 18275–18285.
4EV4	SFC-1, E166A	*S. fonticola*, class A, group 2f	2012	1.30 Å	pH 7	 meropenem	- Fonseca, F.; Chudyk, E. I.; van der Kamp, M. W.; Correia, A.; Mulholland, A. J.; Spencer, J. The basis for carbapenem hydrolysis by class A β-lactamases: A combined investigation using crystallography and simulations. *J. Am. Chem. Soc.* **2012**, *134*, 18275–18285.

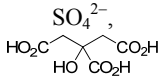
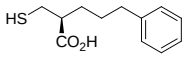
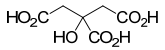
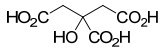
Table 2. Class B metallo-β-lactamases.

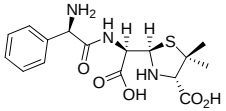
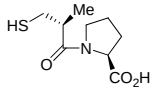
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
BcII (subclass B1, group 3a)								
1BMC	BcII	*B. cereus*, class B1, group 3a	1995	2.50 Å	Zn1	pH 5.6	–	- Carfi, A.; Pares, S.; Duée, E.; Galleni, M.; Duez, C.; Frère, J.-M.; Dideberg, O. The 3-D structure of a zinc metallo-β-lactamase from *Bacillus cereus* reveals a new type of protein fold. *EMBO J.* **1995**, *14*, 4914–4921.
1BME 1BVT	BcII	*B. cereus*, class B1, group 3a	1998	1.85 Å	Zn1, Zn2	pH 5.6	CO_3^{2-}	- Carfi, A.; Duée, E.; Galleni, M.; Frère, J.-M.; Dideberg, O. 1.85- Å resolution structure of the zinc^{II} β-lactamase from *Bacillus cereus*. *Acta Cryst.* **1998**, *D54*, 313–323.
1BC2	BcII	*B. cereus*, class B1, group 3a	1998	1.90 Å	Zn1, Zn2	pH 4.5	–	- Fabiane, S. M.; Sohi, M. K.; Wan, T.; Payne, D. J.; Bateson, J. H.; Mitchell, T.; Sutton, B. J. Crystal structure of the zinc-dependent β-lactamase from *Bacillus cereus* at 1.9 Å resolution: Binuclear active site with features of a mononuclear enzyme. *Biochemistry* **1998**, *37*, 12404–12411.
2BC2	BcII	*B. cereus*, class B1, group 3a	1999	1.70 Å	Zn1	pH 6.0	–	- BcII in trigonal crystal form - Cys168 oxidized to Cys-*S*-dioxide. - Fabiane, S. M.; Sutton, B. J., unpublished.
3BC2	BcII	*B. cereus*, class B1, group 3a	1999	1.70 Å	Zn1	pH 6.0	–	- BcII in monoclinic crystal form - Cys168 oxidized to Cys-*S*-dioxide. - Fabiane, S. M.; Sutton, B. J., unpublished.
1DXK	BcII, Cys168Ser	*B. cereus*, class B1, group 3a	2000	1.85 Å	Zn1	pH 5.6	–	- The mono-Zn form of this Cys168Ser mutant was inactive, but the di-Zn form active. - Chantalat, L.; Duée, E.; Galleni, M.; Frère, J.-M.; Dideberg, O. Structural effects of the active site mutation cysteine to serine in *Bacillus cereus* zinc-β-lactamase. *Protein Sci.* **2000**, *9*, 1402–1406.
1MQO	BcII	*B. cereus*, class B1, group 3a	2004	1.35 Å	Cd1, Cd2	pH 4.9	 citric acid	- High resolution structure of the Cd substituted BcII from *Bacillus cereus*. - Garcia-Saez, I.; Chantalat, L.; Dideberg, O., unpublished. - Structure is unusual in that Asp120 binds to Cd1 rather than Cd2.
2BFK 2BFL 2BFZ 2BG2 2BGA 2BG6 2BG7 2BG8	BcII, Arg121Cys	*B. cereus*, class B1, group 3a	2005	2.00 Å 1.80 Å 2.30 Å 2.40 Å 2.70 Å 2.30 Å 2.10 Å 2.50 Å	Zn1, Zn2 Zn1, Zn2 Zn1 Zn1, Zn2 Zn1, Zn2 Zn1 Zn1 Zn1	pH 7.0 pH 5.0 pH 4.5 pH 4.5 pH 7.0 pH 5.0 pH 4.5 pH 4.5	 glycerol Cl^-, N_3^-, SO_4^{2-}	- Used reducing agents, but Cys168 still gets oxidized when Zn not bound. - Davies, A. M.; Rasia, R. M.; Vila, A. J.; Sutton, B. J.; Fabiane, S. M. Effect of pH on the active site of an Arg121Cys mutant of the metallo-β-lactamase from *Bacillus cereus*: Implications for the enzyme mechanism. *Biochemistry* **2005**, *44*, 4841–4849.

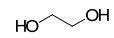
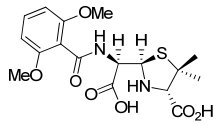
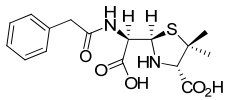
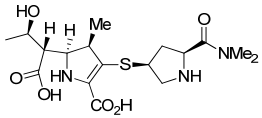
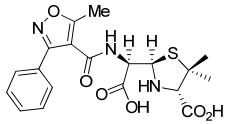
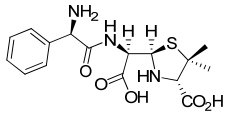
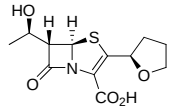
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
2UYX	BcII, D120S	*B. cereus*, class B1, group 3a	2007	1.95 Å	Zn1, Zn2	pH 5.5	 glycerol	- Llarrull, L. I.; Fabiane, S. M.; Kowalski, J. M.; Bennett, B.; Sutton, B. J.; Vila, A. J. Asp-120 locates Zn2 for optimal metallo-β-lactamase activity. *J. Biol. Chem.* **2007**, *282*, 18276–18285.
2NZE 2NZF	BcII, R121H, C221S	*B. cereus*, class B1, group 3a	2007	1.80 Å 2.28 Å	Zn1 Zn1	pH 4.9 pH 5.4	– –	- 2NZE space group is P3121; 2NZF space group is C2. - González, J. M.; Martín, F. J. M.; Costello, A. L.; Tierney, D. L.; Vila, A. J. The Zn2 position in metallo-β-lactamases is critical for activity: A study on chimeric metal sites on a conserved protein scaffold. *J. Mol. Biol.* **2007**, *373*, 1141–1156.
2NXA	BcII, R121H, C221D	*B. cereus*, class B1, group 3a	2007	2.29 Å	Zn1	pH 5.4	–	- González, J. M.; Martín, F. J. M.; Costello, A. L.; Tierney, D. L.; Vila, A. J. The Zn2 position in metallo-β-lactamases is critical for activity: A study on chimeric metal sites on a conserved protein scaffold. *J. Mol. Biol.* **2007**, *373*, 1141–1156.
2NYP	BcII, R121H, C221D	*B. cereus*, class B1, group 3a	2007	1.84 Å	Zn1, Zn2	pH 5.4	–	- González, J. M.; Martín, F. J. M.; Costello, A. L.; Tierney, D. L.; Vila, A. J. The Zn2 position in metallo-β-lactamases is critical for activity: A study on chimeric metal sites on a conserved protein scaffold. *J. Mol. Biol.* **2007**, *373*, 1141–1156.
3FCZ	BcII, N70S, V112A, L250S, G262S	*B. cereus*, class B1, group 3a	2008	2.80 Å	Zn1, Zn2	pH 5.5	–	- Tomatis, P. E.; Fabiane, S. M.; Simona, F.; Carloni, P.; Sutton, B. J.; Vila, A. J. Adaptive protein evolution grants organismal fitness by improving catalysis and flexibility. *Proc. Natl. Acad. Sci., U.S.A.* **2008**, *105*, 20605–20610.
3I0V 3I11 3I13 3I14 3I15	BcII	*B. cereus*, class B1, group 3a	2009	1.60 Å 1.45 Å 1.74 Å 1.55 Å 1.55 Å	apo Co1, Co2 Zn1, Zn2 Co1, Co2 Co1	pH 5.8 pH 5.8 pH 5.8 pH 5.8 pH 5.8	 glycerol	- González, J. M.; Bushiazzo, A.; Vila, A. J. Evidence of adaptability in metal coordination geometry and active-site loop conformation among B1 metallo-β-lactamases. *Biochemistry* **2010**, *49*, 7930–7938.
3KNR 3KNS	BcII, Cys221Asp	*B. cereus*, class B1, group 3a	2010	1.71 Å 1.58 Å	Zn1, Zn2	pH 4.9	–	- González, J. M.; Meini, M.-R.; Tomatis, P. E.; Martín, F. J. M.; Cricco, J. A.; Vila, A. J. Metallo-β-lactamases withstand low Zn(II) conditions by tuning metal-ligand interactions. *Nat. Chem. Biol.* **2012**, *8*, 698–700.
2M5C	BcII	*B. cereus*, class B1, group 3a	2013	NMR structure	Zn1, Zn2	pH 6.4	–	- Karsisiotis, A. I.; Damblon, C. F.; Roberts, G. C. K. Solution structures of the *Bacillus cereus* metallo-β-lactamase BcII and its complex with the broad spectrum inhibitor *R*-thiomandelic acid. *Biochem. J.* **2013**, *456*, 397–407.
2M5D	BcII	*B. cereus*, class B1, group 3a	2013	NMR structure	Zn1, Zn2	pH 6.4	 (*R*)-thiomandelic acid	- Karsisiotis, A. I.; Damblon, C. F.; Roberts, G. C. K. Solution structures of the *Bacillus cereus* metallo-β-lactamase BcII and its complex with the broad spectrum inhibitor *R*-thiomandelic acid. *Biochem. J.* **2013**, *456*, 397–407.

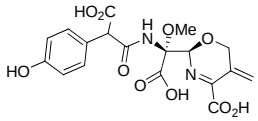
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
BlaB (subclass B1, group 3a)								
1M2X	BlaB	*C. meningo-speticum*, class B1, group 3a	2003	1.50	Zn1, Zn2	pH 8.4	 D-captopril	- Garcia-Sáez, I.; Hopkins, J.; Papamicael, C.; Franceschini, N.; Amicosante, G.; Rossolini, G. M.; Galleni, M.; Frère, J.-M.; Dideberg, O. The 1.5-Å structure of *Chryseobacterium meningosepticum* zinc β-lactamase in complex with the inhibitor, D-captopril. *J. Biol. Chem.* **2003**, *278*, 23868–23873.
CcrA (subclass B1, group 3a)								
1ZNB	CcrA	*B. fragilis*, class B1, group 3a	1996	1.85 Å	Zn1, Zn2	pH 7.0	–	- Concha, N. O.; Rasmussen, B. A.; Bush, K.; Herzberg, O. Crystal structure of the wide-spectrum binuclear zinc β-lactamase from *Bacteriodes fragilis*. *Structure* **1996**, *4*, 823–836.
2ZNB	CcrA	*B. fragilis*, class B1, group 3a	1997	2.15 Å	Cd1, Cd2	pH 7.0	–	- Concha, N. O.; Rasmussen, B. A.; Bush, K.; Herzberg, O. Crystal structures of the cadmium- and mercury-substituted metallo-β-lactamase from *Bacteriodes fragilis*. *Protein Sci.* **1997**, *6*, 2671–2676.
3ZNB	CcrA	*B. fragilis*, class B1, group 3a	1997	2.70 Å	Zn1, Hg2	pH 7.0	–	- Concha, N. O.; Rasmussen, B. A.; Bush, K.; Herzberg, O. Crystal structures of the cadmium- and mercury-substituted metallo-β-lactamase from *Bacteriodes fragilis*. *Protein Sci.* **1997**, *6*, 2671–2676.
1A7T	CcrA	*B. fragilis*, class B1, group 3a	1998	1.85 Å	Zn1, Zn2	pH 6.1	 MES	- Fitzgerald, P. M. D.; Wu, J. K.; Toney, J. H. Unanticipated inhibition of the metallo-β-lactamase from *Bacteriodes fragilis* by 4-morpholineethanesulfonic acid (MES): A crystallographic study at 1.85-Å resolution. *Biochemistry* **1998**, *37*, 6791–6800.
2BMI (1BMI)	CcrA	*B. fragilis*, class B1, group 3a	1998	2.00 Å	Zn1, Zn2	pH 9.0	–	- Carfi, A.; Duée, E.; Paul-Soto, R.; Galleni, M.; Frère, J.-M.; Dideberg, O. X-ray structure of the Zn^{II} β-lactamase from *Bacteriodes fragilis* in an orthorhombic crystal form. *Acta Cryst.* **1998**, *D54*, 47–57.
1A8T	CcrA	*B. fragilis*, class B1, group 3a	1998	2.55 Å	Zn1, Zn2	pH 6.6	 biphenyl tetrazole L-159,061	- Toney, J. H.; Fitzgerald, P. M. D.; Grover-Sharma, N.; Olson, S. H.; May, W. J.; Sundelof, J. G.; Vanderwall, D. E.; Cleary, K. A.; Grant, S. K.; Wu, J. K.; Kozarich, J. W.; Pompliano, D. L.; Hammond, G. G. Antibiotic sensitization using biphenyl tetrazoles as potent inhibitors of *Bacteriodes fragilis* metallo-β-lactamase. *Chem. Biol.* **1998**, *5*, 185–196.
1KR3	CfiA	*B. fragilis*, class B1, group 3a	2002	2.50	Zn1, Zn2	pH 6.0	 SB-236050	- Payne, D. J.; Hueso-Rodríguez, J. A.; Boyd, H.; Concha, N. O.; Janson, C. A.; Gilpin, M.; Bateson, J. H.; Cheever, C.; Niconovich, N. L.; Pearson, S.; Rittenhouse, S.; Tew, D.; Díez, E.; Pérez, P.; de la Fuente, J.; Rees, M.; Rivera-Sagredo, A. *Antimicrob. Agents Chemother.* **2002**, *46*, 1880–1886.

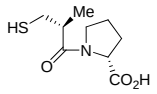
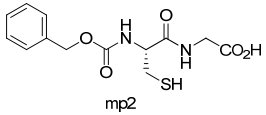
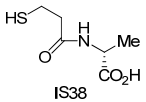
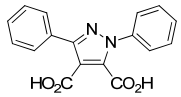
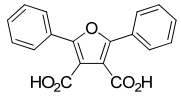
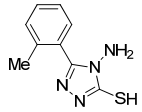
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
IMP-1 (subclass B1, group 3a)								
1DDK	IMP-1	*P. aeruginosa*, class B1, group 3a	2000	3.10 Å	Zn1, Zn2	pH 6.5	–	- Concha, N. O.; Janson, C. A.; Rowling, P.; Pearson, S.; Cheever, C. A.; Clarke, B. P.; Lewis, C.; Galleni, M.; Frère, J.-M.; Payne, D. J.; Bateson, J. H.; Abdel-Meguid, S. S. *Biochemistry* **2000**, *39*, 4288–4298.
1DD6	IMP-1	*P. aeruginosa*, class B1, group 3a	2000	2.00 Å	Zn1, Zn2	pH 6.5		- Concha, N. O.; Janson, C. A.; Rowling, P.; Pearson, S.; Cheever, C. A.; Clarke, B. P.; Lewis, C.; Galleni, M.; Frère, J.-M.; Payne, D. J.; Bateson, J. H.; Abdel-Meguid, S. S. *Biochemistry* **2000**, *39*, 4288–4298.
1JJE	IMP-1	*P. aeruginosa*, class B1, group 3a	2001	1.80 Å	Zn1, Zn2	pH 6.9	 succinic acid **11**	- Toney, J. H.; Hammond, G. G.; Fitzgerald, P. M. D.; Sharma, N.; Balkovec, J. M.; Rouen, G. P.; Olson, S. H.; Hammond, M. L.; Greenlee, M. L.; Gao, Y.-D. Succinic acids as potent inhibitors of plamid-borne IMP-1 metallo-β-lactamase. *J. Biol. Chem.* **2001**, *276*, 31913–31918.
1JJT	IMP-1	*P. aeruginosa*, class B1, group 3a	2001	1.80 Å	Zn1, Zn2	pH 6.9	 succinic acid **1**	- Toney, J. H.; Hammond, G. G.; Fitzgerald, P. M. D.; Sharma, N.; Balkovec, J. M.; Rouen, G. P.; Olson, S. H.; Hammond, M. L.; Greenlee, M. L.; Gao, Y.-D. Succinic acids as potent inhibitors of plamid-borne IMP-1 metallo-β-lactamase. *J. Biol. Chem.* **2001**, *276*, 31913–31918.
1VGN	IMP-1	*P. aeruginosa*, class B1, group 3a	2005	2.63 Å	Zn1, Zn2	pH 4.6		- Kurosaki, H.; Yamaguchi, Y.; Higashi, T.; Soga, K.; Matsueda, S.; Yumoto, H.; Misumi, S.; Yamagata, Y.; Arakawa, Y.; Goto, M. Irreversible inhibition of metallo-β-lactamase (IMP-1) by 3-(3-mercaptopropionylsulfanyl)propionic acid pentafluorophenyl ester. *Angew. Chem. Int. Ed.* **2005**, *44*, 3861–3864.
1WUO	IMP-1, D81A	*P. aeruginosa*, class B1, group 3a	2005	2.01 Å	Zn1	pH 6.5	AcO^-	- Yamaguchi, Y.; Kuroki, T.; Yasuzawa, Higashi, T.; Jin, W.; Kawanami, A.; Yamagata, Y.; Arakawa, Y.; Goto, M.; Kurosaki, H. Probing the role of Asp-120(81) of metallo-β-lactamase (IMP-1) by site-directed mutagenesis, kinetic studies, and X-ray crystallography. *J. Biol. Chem.* **2005**, *280*, 20824–20832.
1WUP	IMP-1, D81E	*P. aeruginosa*, class B1, group 3a	2005	3.00 Å	Zn1, Zn2	pH 6.5	AcO^-	- Yamaguchi, Y.; Kuroki, T.; Yasuzawa, Higashi, T.; Jin, W.; Kawanami, A.; Yamagata, Y.; Arakawa, Y.; Goto, M.; Kurosaki, H. Probing the role of Asp-120(81) of metallo-β-lactamase (IMP-1) by site-directed mutagenesis, kinetic studies, and X-ray crystallography. *J. Biol. Chem.* **2005**, *280*, 20824–20832.
2DOO	IMP-1	*P. aeruginosa*, class B1, group 3a	2006	2.43 Å	Zn1, Zn2	pH 6.5	 dansyl-derived thiol	- Kurosaki, H.; Yamaguchi, Y.; Yasuzawa, H.; Jin, W.; Yamagata, Y.; Arakawa, Y. Probing, inhibition, and crystallographic characterization of metallo-β-lactamase (IMP-1) with fluorescent agents containing dansyl and thiol groups. *ChemMedChem* **2006**, *1*, 969–972.

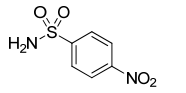
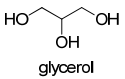
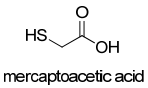
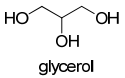
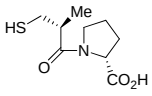
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
4F6H 4F6Z	IMP-1, C221G	*P. aeruginosa*, class B1, group 3a	2013	1.74 Å 2.00 Å	Zn1 Zn1	pH 7.5 pH 7.0	SO_4^{2-},  citric acid	- Horton, L. B.; Shanker, S.; Mikulski, R.; Brown, N. G.; Phillips, K. J.; Lykissa, E.; Prasad, B. V. V.; Palzkill, T. Mutagenesis of zince ligand residue Cys221 reveals plasticity in the IMP-1 metallo-β-lactamase active site. *Antimicrob. Agents Chemother.* **2012**, *56*, 5667–5677.
VIM-2 (subclass B1, group 3a)								
1KO2 1KO3	VIM-2	*P. aeruginosa*, class B1, group 3a	2003	2.20 Å 1.91 Å	Zn1 Zn1, Zn2	pH 6.5 pH 6.5	–	- Cys is oxidized in 1KO2 and in its reduced form in 1KO3. - Garcia-Saez, I.; Docquier, J.-D.; Rossolini, G. M.; Dideberg, O. The three-dimensional structure of VIM-2, a Zn-β-lactamase from *Pseudomonas aeruginosa* in its reduced and oxidised form. *J. Mol. Biol.* **2008**, *375*, 604–611.
2YZ3	VIM-2	*P. putida*, class B1, group 3a	2008	2.30 Å	Zn1, Zn2	pH 6.5	 mercaptocarboxylate inhibitor	- Yamaguchi, Y.; Jin, W.; Matsunaga, K.; Ikemizu, S.; Yamagata, Y.; Wachino, J.-i.; Shibata, N.; Arakawa, Y.; Kurosaki, H. Crystallographic investigation of the inhibition mode of a VIM-2 metallo-β-lactamase from *Pseudomonas aeruginosa* by a mercaptocarboxylate inhibitor. *J. Med. Chem.* **2007**, *50*, 6647–6653.
VIM-4 (subclass B1, group 3a)								
2WHG	VIM-4	*P. aeruginosa*, class B1, group 3a	2010	1.90 Å	Zn1, Zn2	pH 7.0	 citric acid	- Lassaux, P.; Traoré, D. A. K.; Loisel, E.; Favier, A.; Docquier, J.-D.; Sohier, J. S.; Laurent, C.; Bebrone, C.; Frere, J.-M.; Ferrer, J.-L.; Galleni, M. Biochemical and structural characterization of the subclass B1 metallo-β-lactamase VIM-4. *Antimicrob. Agents Chemother.* **2011**, *55*, 1248–1255.
2WRS	VIM-4	*P. aeruginosa*, class B1, group 3a	2010	2.79 Å	Zn1	pH 7.0	 citric acid	- Lassaux, P.; Hamel, M.; Gulea, M.; Dulbrück, H.; Mercuri, P. S.; Horsfall, L.; Dehareng, D.; Kupper, M.; Frère, J.-M.; Hoffmann, K.; Galleni, M.; Bebrone, C. Mercaptophosphonate compounds as broad-spectrum inhibitors of the metallo-β-lactamases. *J. Med. Chem.* **2010**, *53*, 4862–4876.
VIM-7 (subclass B1, group 3a)								
2Y87 2Y8A 2Y8B	VIM-7	*P. aeruginosa*, class B1, group 3a	2011	2.79 Å 2.33 Å 1.70 Å	Zn1, Zn2 Zn1, Zn2 Zn1, Zn2	pH 5.0 pH 5.0 pH 5.0	–	- Borra, P. S.; Leiros, H.-K. S.; Ahmad, R.; Spencer, J.; Leiros, I.; Walsh, T. R.; Sundsfjord, A..; Samuelsen, Ø. Structural and computational investigations of VIM-7: Insights into the substrate specificity of VIM metallo-β-lactamases. *J. Mol. Biol.* **2011**, *411*, 174–189. - Cysteine oxidized in 2Y8B, with S and O binding to Zn2.

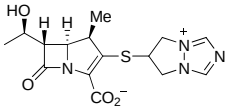
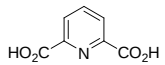
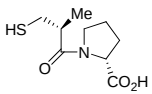
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
VIM-31 (subclass B1, group 3a)								
4FR7	VIM-31	*E. cloacae*, class B1, group 3a	2013	1.61 Å	Zn1, Zn2	pH 8.5	–	- Herzog, K.; Hoffmann, K. M., unpublished. - Cysteine oxidized in 2Y8B, with S and O binding to Zn2.
4FSB	VIM-31, oxidized	*E. cloacae*, class B1, group 3a	2013	1.88 Å	Zn1	pH 8.5	–	- Herzog, K.; Hoffmann, K. M., unpublished. - Cys221 oxidized to sulfonate.
NDM-1 (subclass B1, group 3a)								
3Q6X	NDM-1	*K. pneumoniae*, class B1, group 3a	2011	1.30 Å	Zn1, Zn2	pH 5.5	 hydrolyzed ampicillin	- Zhang, H.; Hao, Q. Crystal structure of NDM-1 reveals a common β-lactam hydrolysis mechanism. *FASEB J.* **2011**, *25*, 2574–2582.
3RKJ 3RKK 3SBL 3SFP	NDM-1	*K. pneumoniae*, class B1, group 3a	2011	2.00 Å 2.35 Å 2.31 Å 2.27 Å	apo apo apo Zn1	pH 7.5 pH 7.5 pH 4.6 pH 7.5	– AcO^- – –	- Kim, Y.; Tesar, C.; Mire, J.; Jedrzejczak, R.; Binkowski, A.; Babnigg, G.; Sacchettini, J.; Joachimiak, A. (Midwest genomics center). Structure of apo- and monometalated forms of NDM-1–A highly potent carbapenem-hydrolyzing metallo-β-lactamase. *PLoS One* **2011**, *6*, e24621.
3S0Z	NDM-1	*E. coli*, class B1, group 3a	2011	2.50 Å	Zn1, Zn2	pH 6.5	–	- Guo, Y.; Wang, J.; Niu, G.; Shui, W.; Sun, Y.; Zhou, H.; Zhang, Y.; Yang, C.; Lou, Z.; Rao, Z. A structural view of the antibiotic degradation enzyme NDM-1 from a superbug. *Protein Cell* **2011**, *2*, 384–394.
3ZR9	NDM-1	*K. pneumoniae*, class B1, group 3a	2011	1.91 Å	Zn1, Cd2	pH 7.5	–	- Green, V. L.; Verma, A.; Owens, R. J.; Phillips, S. E. V.; Carr, S. B. Structure of the New Delhi metallo-β-lactamase 1 (NDM-1). *Acta Cryst.* **2011**, *F67*, 1160–1164.
3SRX	NDM-1	*K. pneumoniae*, class B1, group 3a	2011	2.50 Å	Cd1, Cd2	pH 7.5	–	- Kim, Y.; Tesar, C.; Jedrzejczak, R.; Babnigg, G.; Binkowski, A.; Mire, J.; Sacchettini, J.; Joachimiak, A. (Midwest genomics center), unpublished.
3SPU	NDM-1	*K. pneumoniae*, class B1, group 3a	2011	2.10 Å	Zn1, Zn2	pH 8.5	–	- King, D.; Strynadka, N. Crystal structure of New Delhi metallo-β-lactamase reveals molecular basis for antibiotic resistance. *Protein Sci.* **2011**, *20*, 1484–1491.
3PG4	NDM-1	*K. pneumoniae*, class B1, group 3a	2011	2.00 Å	apo	na	–	- Kim, H. T.; Cho, Y. S.; Chang, H. J., unpublished.
4EXS	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	2.40 Å	Zn1, Zn2	pH 7.5	 L-captopril	- King, D. T.; Worrall, L. J.; Gruninger, R.; Strynadka, N. C. J. New Delhi metallo-β-lactamase: Structural insights into β-lactam recognition and inhibition. *J. Am. Chem. Soc.* **2012**, *134*, 11362–11365.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
4EXY	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	1.47 Å	Zn1, Zn2	pH 7.5	 ethylene glycol	- King, D. T.; Worrall, L. J.; Gruninger, R.; Strynadka, N. C. J. New Delhi metallo-β-lactamase: Structural insights into β-lactam recognition and inhibition. *J. Am. Chem. Soc.* **2012**, *134*, 11362–11365.
4EY2	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	1.17 Å	Zn1, Zn2	pH 5.5	 hydrolyzed methicillin	- King, D. T.; Worrall, L. J.; Gruninger, R.; Strynadka, N. C. J. New Delhi metallo-β-lactamase: Structural insights into β-lactam recognition and inhibition. *J. Am. Chem. Soc.* **2012**, *134*, 11362–11365.
4EYF	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	1.80 Å	Zn1, Zn2	pH 5.5	 hydrolyzed benzylpenicillin	- King, D. T.; Worrall, L. J.; Gruninger, R.; Strynadka, N. C. J. New Delhi metallo-β-lactamase: Structural insights into β-lactam recognition and inhibition. *J. Am. Chem. Soc.* **2012**, *134*, 11362–11365.
4EYL	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	1.90 Å	Zn1, Zn2	pH 6.5	 hydrolyzed meropenem	- King, D. T.; Worrall, L. J.; Gruninger, R.; Strynadka, N. C. J. New Delhi metallo-β-lactamase: Structural insights into β-lactam recognition and inhibition. *J. Am. Chem. Soc.* **2012**, *134*, 11362–11365.
4EYB	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	1.16 Å	Zn1, Zn2	pH 5.5	 hydrolyzed oxacillin	- King, D. T.; Worrall, L. J.; Gruninger, R.; Strynadka, N. C. J. New Delhi metallo-β-lactamase: Structural insights into β-lactam recognition and inhibition. *J. Am. Chem. Soc.* **2012**, *134*, 11362–11365.
4GYQ	NDM-1, D223A	*K. pneumoniae*, class B1, group 3a	2012	1.35 Å	apo	pH 6.5	–	- Kim, Y.; Tesar, C.; Jedrzejczak, R.; Babnigg, J.; Binkowski, T. A.; Mire, J.; Sacchettini, J.; Joachimiak, A. (Midwest center for structural genomics), unpublished.
4GYU	NDM-1, A121F	*K. pneumoniae*, class B1, group 3a	2012	1.80 Å	apo	pH 8.0	–	- Kim, Y.; Tesar, C.; Jedrzejczak, R.; Babnigg, J.; Binkowski, T. A.; Mire, J.; Sacchettini, J.; Joachimiak, A. (Midwest center for structural genomics), unpublished.
4H0D 4HL1 4HL2	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	1.50 Å 1.50 Å 1.05 Å	Mn1, Mn2 Cd1, Cd2 Zn1, Zn2	pH 7.5 pH 6.5 pH 5.5	 hydrolyzed ampicillin	- Kim, Y.; Tesar, C.; Jedrzejczak, R.; Babnigg, J.; Binkowski, T. A.; Mire, J.; Sacchettini, J.; Joachimiak, A. (Midwest center for structural genomics), unpublished.
4HKY	NDM-1	*K. pneumoniae*, class B1, group 3a	2012	2.00 Å	Cd1, Cd2	pH 5.5	 faropenem	- Kim, Y.; Tesar, C.; Jedrzejczak, R.; Babnigg, J.; Mire, J.; Sacchettini, J.; Joachimiak, A. (Midwest center for structural genomics), unpublished.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
GIM-1 (subclass B1, group 3a)								
2YNT 2YNU 2YNW 2YNV	GIM-1	*P. aeruginosa*, class B1, group 3a	2013	1.60 Å 2.06 Å 1.70 Å 2.05 Å	Zn1, Zn2 apo Zn1, Zn2 Zn1	pH 7.1 pH 7.1 pH 7.1 pH 7.1	–	- Cys221 oxidized to sulfinate in 2YNV. - Borra, P. S.; Samuelsen, O.; Spencer, J.; Walsh, T. R.; Lorentzen, M. S.; Leiros, H.-K. S. Crystal structures of *Pseudomonas aeruginosa* GIM-1: Active-site plasticity in metallo-β-lactamases. *Antimicrob. Agents Chemother.* **2013**, *57*, 848–854.
IND-7 (subclass B1, group 3a)								
3L6N	IND-7	*C. indologenes*, class B1, group 3a	2010	1.65 Å	Zn	pH 8.5	–	- Yamaguchi, Y.; Takashio, N.; Wachino, J.-i.; Yamagata, Y.; Arakawa, Y.; Matsuda, K.; Kurosaki, H. Structure of the metallo-β-lactamase IND-7 from a *Chryseobacterium indologenes* clinical isolate at 1.65-Å resolution. *J. Biochem.* **2010**, *147*, 905–915.
SPM-1 (monozinc, subclass B1, group 3a)								
2FHX	SPM-1	*P. aeruginosa*, class B1, group 3a	2006	1.90 Å	Zn1	pH 8.0	–	- Murphy, T. A.; Catto, L. E.; Halford, S. E.; Hadfield, A. T.; Minor, W.; Walsh, T. R.; Spencer, J. Crystal structure of *Pseudomonas aeruginosa* SPM-1 provides insights into variable zinc affinity of metallo-β-lactamases. *J. Mol. Biol.* **2006**, *357*, 890–897.
L1 (subclass B3, group 3a)								
1SML	L1	*S. maltophilia*, class B3, group 3a	1999	1.70 Å	Zn1, Zn2	pH 7.8	–	- Ullah, J. H.; Walsh, T. R.; Taylor, I. A.; Emery, D. C.; Verma, C. S.; Gamblin, S. J.; Spencer, J. The crystal structure of the L1 metallo-β-lactamase from *Stenotrophomonas maltophilia* at 1.7 Å resolution. *J. Mol. Biol.* **1998**, *284*, 125–136.
2AIO	L1	*S. maltophilia*, class B3, group 3a	2005	1.70 Å	Zn1, Zn2	pH 7.5	 hydrolyzed moxalactam	- Spencer, J.; Read, J.; Sessions, R. B.; Howell, S.; Blackburn, G. M.; Gamblin, S. J. Antibiotic recognition by binuclear metallo-β-lactamases revealed by X-ray crystallography. *J. Am. Chem. Soc.* **2005**, *127*, 14439–14444.
2FM6 2H6A 2FU6 2FU7	L1	*S. maltophilia*, class B3, group 3a	2007	1.75 Å 1.80 Å 2.06 Å 1.85 Å	Zn1, Zn2 Zn1 apo Cu	pH 7.5 pH 7.5 pH 7.5 pH 7.5	–	- Nauton, L.; Kahn, R.; Garau, G.; Hernandez, J. F.; Dideberg, O. Structural insights into the design of inhibitors for the L1 metallo-β-lactamase from *Stenotrophomonas maltophilia*. *J. Mol. Biol.* **2008**, *375*, 257–269.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
2FU8	L1	*S. maltophilia*, class B3, group 3a	2007	1.80 Å	Zn1, Zn2	pH 7.5	 D-captopril	- Nauton, L.; Kahn, R.; Garau, G.; Hernandez, J. F.; Dideberg, O. Structural insights into the design of inhibitors for the L1 metallo-β-lactamase from *Stenotrophomonas maltophilia*. *J. Mol. Biol.* **2008**, *375*, 257–269.
2FU9	L1	*S. maltophilia*, class B3, group 3a	2007	1.80 Å	Zn1, Zn2	pH 7.5	 mp2	- Nauton, L.; Kahn, R.; Garau, G.; Hernandez, J. F.; Dideberg, O. Structural insights into the design of inhibitors for the L1 metallo-β-lactamase from *Stenotrophomonas maltophilia*. *J. Mol. Biol.* **2008**, *375*, 257–269.
2QDT	L1	*S. maltophilia*, class B3, group 3a	2007	2.00 Å	Zn1, Zn2	pH 6.5	 IS38	- Liénard, B. M. R.; Garau, G.; Horsfall, L.; Karsisiotis, A. I.; Damblon, C.; Lassaux, P.; Papamicael, C.; Roberts, G. C. K.; Galleni, M.; Dideberg, O.; Frère, J.-M.; Schofield, C. J. Structural basis for the broad-spectrum inhibition of metallo-β-lactamases by thiols. *Org. Biomol. Chem.* **2008**, *6*, 2282–2294.
2GFJ	L1	*S. maltophilia*, class B3, group 3a	2007	1.80 Å	Zn1, Zn2	pH 7.8		- Nauton, L.; Kahn, R.; Garau, G.; Hernandez, J. F.; Dideberg, O. Structural insights into the design of inhibitors for the L1 metallo-β-lactamase from *Stenotrophomonas maltophilia*. *J. Mol. Biol.* **2008**, *375*, 257–269.
2GFK	L1	*S. maltophilia*, class B3, group 3a	2007	1.90 Å	Zn1, Zn2	pH 7.8		- Nauton, L.; Kahn, R.; Garau, G.; Hernandez, J. F.; Dideberg, O. Structural insights into the design of inhibitors for the L1 metallo-β-lactamase from *Stenotrophomonas maltophilia*. *J. Mol. Biol.* **2008**, *375*, 257–269.
2HB9	L1	*S. maltophilia*, class B3, group 3a	2007	1.75 Å	Zn1, Zn2	pH 7.8		- Nauton, L.; Kahn, R.; Garau, G.; Hernandez, J. F.; Dideberg, O. Structural insights into the design of inhibitors for the L1 metallo-β-lactamase from *Stenotrophomonas maltophilia*. *J. Mol. Biol.* **2008**, *375*, 257–269.
2QIN	L1, D120C	*S. maltophilia*, class B3, group 3a	2007	1.76 Å	Zn1, Zn2	pH 7.5	–	- Crisp, J.; Conners, R.; Garrity, J. D.; Carenbauer, A. L.; Crowder, M. W.; Spencer, J. Structural basis for the role of Asp-120 in metallo-β-lactamases. *Biochemistry* **2007**, *46*, 10664–10674.
2QJS	L1, D120N	*S. maltophilia*, class B3, group 3a	2007	2.25 Å	Zn1, Zn2	pH 8.0	–	- Crisp, J.; Conners, R.; Garrity, J. D.; Carenbauer, A. L.; Crowder, M. W.; Spencer, J. Structural basis for the role of Asp-120 in metallo-β-lactamases. *Biochemistry* **2007**, *46*, 10664–10674.
BJP-1 (subclass B3, group 3a)								
2GMN	BJP-1	*B. diazoefficiens*, class B3, group 3a	2006	1.40 Å	Zn1, Zn2	pH 8.5	–	- Stoczko, M.; Frere, J.-M.; Rossolini, G. M.; Docquier, J.-D. Postgenomic scan of metallo-β-lactamase homologues in Rhizobacteria: Identification and characterization of BJP-1, a subclass B3 ortholog from *Bradyrhizobium japonicum*. *Antimicrob. Agents Chemother.* **2006**, *50*, 1973–1981.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
3LVZ	BJP-1	*B. japonicum*, class B3, group 3a	2011	1.40 Å	Zn1, Zn2	pH 8.5	–	- Docquier, J.-D.; Benvenuti, M.; Calderone, V.; Stoczko, M.; Menciassi, N.; Rossolini, G. M.; Mangani, S. High-resolution crystal structure of the subclass B3 metallo-β-lactamase BJP-1: Rational basis for substrate specificity and interaction with sulfonamides. *Antimicrob. Agents Chemother.* **2010**, *54*, 4343–4351.
3M8T	BJP-1	*B. japonicum*, class B3, group 3a	2011	1.33 Å	Zn1, Zn2	pH 8.5	 4-nitrobenzenesulfonamide	- Docquier, J.-D.; Benvenuti, M.; Calderone, V.; Stoczko, M.; Menciassi, N.; Rossolini, G. M.; Mangani, S. High-resolution crystal structure of the subclass B3 metallo-β-lactamase BJP-1: Rational basis for substrate specificity and interaction with sulfonamides. *Antimicrob. Agents Chemother.* **2010**, *54*, 4343–4351.
SMB-1 (subclass B3, group 3a)								
3VPE	SMB-1	*S. marcescens*, class B3, group 3a	2013	1.60 Å	Zn1, Zn2	pH 5.8	 glycerol	- Wachino, J.-i.; Yamaguchi, Y.; Mori, S.; Kurosaki, H.; Arakawa, Y.; Shibayama, K. Structural insights into the subclass B3 metallo-β-lactamase SMB-1 and the mode of action by the common metallo-β-lactamase inhibitor mercaptoacetate. *Antimicrob. Agents Chemother.* **2013**, *57*, 101–109.
3VQZ	SMB-1	*S. marcescens*, class B3, group 3a	2013	2.20 Å	Zn1, Zn2	pH 6.0	 mercaptoacetic acid	- Wachino, J.-i.; Yamaguchi, Y.; Mori, S.; Kurosaki, H.; Arakawa, Y.; Shibayama, K. Structural insights into the subclass B3 metallo-β-lactamase SMB-1 and the mode of action by the common metallo-β-lactamase inhibitor mercaptoacetate. *Antimicrob. Agents Chemother.* **2013**, *57*, 101–109.
FEZ-1 (subclass B3, group 3a)								
1K07	FEZ-1	*F. gormanii*, class B3, group 3a	2003	1.65 Å	Zn1, Zn2	pH 5.0	 glycerol	- Garcia-Saez, I.; Mercuri, P. S.; Papamicael, C.; Kahn, R.; Frere, J.-M.; Galleni, M.; Rossolini, G. M.; Dideberg, O. Three-dimensional structure of FEZ-1, a monomeric subclass B3 metallo-β-lactamase from *Fluoribacter gormanii*, in native form and in complex with D-captopril. *J. Mol. Biol.* **2003**, *325*, 651–660.
1JT1	FEZ-1	*F. gormanii*, class B3, group 3a	2003	1.78 Å	Zn1, Zn2	pH 6.0	SO_4^{2-},  D-captopril	- The sulfur of D-captopril is not coordinated to the zinc in this structure. A sulfate molecule is. - Garcia-Saez, I.; Mercuri, P. S.; Papamicael, C.; Kahn, R.; Frere, J.-M.; Galleni, M.; Rossolini, G. M.; Dideberg, O. Three-dimensional structure of FEZ-1, a monomeric subclass B3 metallo-β-lactamase from *Fluoribacter gormanii*, in native form and in complex with D-captopril. *J. Mol. Biol.* **2003**, *325*, 651–660.
1L9Y	FEZ-1, Y228A	*F. gormanii*, class B3, group 3a	2003	2.01 Å	Zn1, Zn2	pH 6.0	SO_4^{2-}	- Garcia-Saez, I.; Mercuri, P. S.; Papamicael, C.; Kahn, R.; Frere, J.-M.; Galleni, M.; Rossolini, G. M.; Dideberg, O. Three-dimensional structure of FEZ-1, a monomeric subclass B3 metallo-β-lactamase from *Fluoribacter gormanii*, in native form and in complex with D-captopril. *J. Mol. Biol.* **2003**, *325*, 651–660.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
AIM-1 (subclass B3, group 3a)								
4AWZ 4AWY	AIM-1	*P. aeruginosa*, class B3, group 3a	2013	1.80 Å 1.60 Å	Zn1, Zn2 Zn1, Zn2	pH 5.0 pH 5.0	–	- Leiros, H.-K. S.; Borra, P. S.; Brandsdal, B. O.; Edvardsen, K. S. W.; Spencer, J.; Walsh, T. R.; Samuelsen, Ø. Crystal structure of the mobile metallo-β-lactamase AIM-1 from *Pseudomonas aeruginosa*: Insights into antibiotic binding and the role of Gln157. *Antimicrob. Agents Chemother.* **2012**, *56*, 4341–4353.
4AX0	AIM-1, Q157A	*P. aeruginosa*, class B3, group 3a	2013	1.74 Å	Zn1, Zn2	pH 5?	–	- Leiros, H.-K. S.; Borra, P. S.; Brandsdal, B. O.; Edvardsen, K. S. W.; Spencer, J.; Walsh, T. R.; Samuelsen, Ø. Crystal structure of the mobile metallo-β-lactamase AIM-1 from *Pseudomonas aeruginosa*: Insights into antibiotic binding and the role of Gln157. *Antimicrob. Agents Chemother.* **2012**, *56*, 4341–4353.
4AX1	AIM-1, Q157N	*P. aeruginosa*, class B3, group 3a	2013	1.40 Å	Zn1, Zn2	pH 5.0	–	- Leiros, H.-K. S.; Borra, P. S.; Brandsdal, B. O.; Edvardsen, K. S. W.; Spencer, J.; Walsh, T. R.; Samuelsen, Ø. Crystal structure of the mobile metallo-β-lactamase AIM-1 from *Pseudomonas aeruginosa*: Insights into antibiotic binding and the role of Gln157. *Antimicrob. Agents Chemother.* **2012**, *56*, 4341–4353.
CphA (monozinc, subclass B2, group 3b)								
1X8G	CphA	*A. hydrophyla*, class B2, group 3b	2004	1.70 Å	Zn2	pH 6.5	CO_3^{2-}	- Garau, G.; Bebrone, C.; Anne, C.; Galleni, M.; Frère, J.-M.; Dideberg, O. A metallo-β-lactamase enzyme in action: Crystal structures of the monozinc carbapenemase CphA and its complex with biapenem. *J. Mol. Biol.* **2005**, *345*, 785–795.
1X8H	CphA, N220G	*A. hydrophyla*, class B2, group 3b	2004	1.60 Å	Zn2	pH 6.5	CO_3^{2-}	- Garau, G.; Bebrone, C.; Anne, C.; Galleni, M.; Frère, J.-M.; Dideberg, O. A metallo-β-lactamase enzyme in action: Crystal structures of the monozinc carbapenemase CphA and its complex with biapenem. *J. Mol. Biol.* **2005**, *345*, 785–795.
1X8I	CphA, N220G	*A. hydrophyla*, class B2, group 3b	2004	1.90 Å	Zn2	pH 6.5	 biapenem	- Garau, G.; Bebrone, C.; Anne, C.; Galleni, M.; Frère, J.-M.; Dideberg, O. A metallo-β-lactamase enzyme in action: Crystal structures of the monozinc carbapenemase CphA and its complex with biapenem. *J. Mol. Biol.* **2005**, *345*, 785–795.
2GKL	CphA	*A. hydrophyla*, class B2, group 3b	2007	1.86 Å	Zn2	pH 6.5	 pyridine-2,4-dicarboxylate	- Horsfall, L. E.; Garau, G.; Liénard, B. M. R.; Dideberg, O.; Schofield, C. J.; Frère, J.-M.; Galleni, M. Competitive inhibitors of the CphA metallo-β-lactamase from *Aeromonas hydrophila*. *Antimicrob. Agents Chemother.* **2007**, *51*, 2136–2142.
2QDS	CphA	*A. hydrophyla*, class B2, group 3b	2007	1.66 Å	Zn2	pH 6.5	 D-captopril	- Liénard, B. M. R.; Garau, G.; Horsfall, L.; Karsisiotis, A. I.; Damblon, C.; Lassaux, P.; Papamicael, C.; Roberts, G. C. K.; Galleni, M.; Dideberg, O.; Frère, J.-M.; Schofield, C. J. Structural basis for the broad-spectrum inhibition of metallo-β-lactamases by thiols. *Org. Biomol. Chem.* **2008**, *6*, 2282–2294.

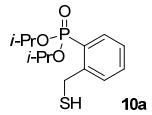
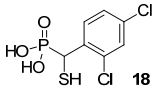
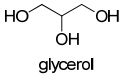
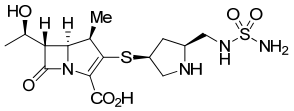
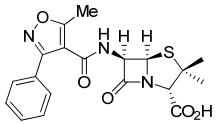
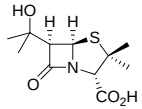
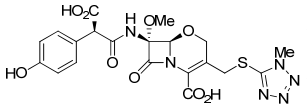
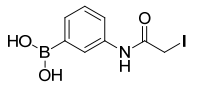
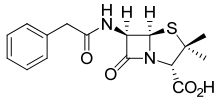
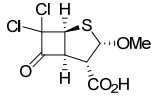
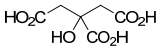
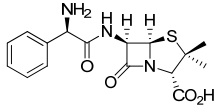
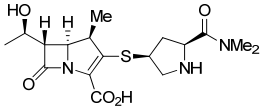
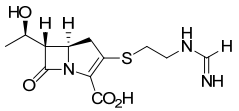
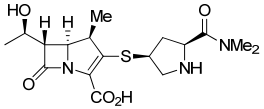
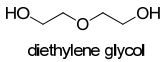
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Cofactors	pH	Ligand	Comments and References
3F9O	CphA	*A. hydrophyla*, class B2, group 3b	2009	2.03 Å	Zn1, Zn2	pH 6.0	SO_4^{2-}	- Bebrone, C.; Dellbruck, H.; Kupper, M.; B.; Schlömer, P.; Willmann, C.; Frère, J.-M.; Fischer, R.; Galleni, M.; Hoffman, K. M. V. The structure of the dizinc subclass B2 metallo-β-lactamase CphA reveals that the second inhibitory zinc ion binds in the histidine site. *Antimicrob. Agents Chemother.* **2009**, *53*, 4464–4471.
3FAI	CphA, N220G	*A. hydrophyla*, class B2, group 3b	2009	1.70 Å	Zn1, Zn2	pH 6.0	SO_4^{2-}	- Bebrone, C.; Dellbrück, H.; Kupper, M.; B.; Schlömer, P.; Willmann, C.; Frère, J.-M.; Fischer, R.; Galleni, M.; Hoffman, K. M. V. The structure of the dizinc subclass B2 metallo-β-lactamase CphA reveals that the second inhibitory zinc ion binds in the histidine site. *Antimicrob. Agents Chemother.* **2009**, *53*, 4464–4471.
3IOF	CphA, N220G	*A. hydrophyla*, class B2, group 3b	2010	1.44 Å	Zn2	pH 6.0	 **10a**	- Lassaux, P.; Hamel, M.; Gulea, M.; Dulbrück, H.; Mercuri, P. S.; Horsfall, L.; Dehareng, D.; Kupper, M.; Frère, J.-M.; Hoffmann, K.; Galleni, M.; Bebrone, C. Mercaptophosphonate compounds as broad-spectrum inhibitors of the metallo-β-lactamases. *J. Med. Chem.* **2010**, *53*, 4862–4876.
3IOG	CphA, N220G	*A. hydrophyla*, class B2, group 3b	2010	1.41 Å	Zn2	pH 6.0	 **18**	- Lassaux, P.; Hamel, M.; Gulea, M.; Dulbrück, H.; Mercuri, P. S.; Horsfall, L.; Dehareng, D.; Kupper, M.; Frère, J.-M.; Hoffmann, K.; Galleni, M.; Bebrone, C. Mercaptophosphonate compounds as broad-spectrum inhibitors of the metallo-β-lactamases. *J. Med. Chem.* **2010**, *53*, 4862–4876.
3SW3 3T9M	CphA, C221D	*A. hydrophyla*, class B2, group 3b	2012	2.35 Å 2.03 Å	apo apo	pH 4.6 pH 4.6	– AcO^-	- Crystal structures of mutant Cys221Asp of CphA (3T9M) and an EDTA-free structure (3SW3). - Dulbrück, H.; Hoffmann, K. M. V., unpublished.
Sfh-1 (monozinc, subclass B2, group 3b)								
3SD9	Sfh-1	*S. fonticola*, class B2, group 3b	2013	1.83 Å	Zn2	pH 7	–	- Fonseca, F.; Arthur, C. J.; Bromley, E. H. C.; Samyn, B.; Moerman, P.; Saavedra, M. J.; Correia, A.; Spencer, J. Biochemical characterization of Sfh-1, a subclass B2 metallo-β-lactamase from *Serratia fonticola* UTAD54. *Antimicrob. Agents Chemother.* **2011**, *55*, 5392–5395.
3Q6V	Sfh-1	*S. fonticola*, class B2, group 3b	2013	1.37 Å	Zn2	pH 7	 glycerol	- Fonseca, F.; Arthur, C. J.; Bromley, E. H. C.; Samyn, B.; Moerman, P.; Saavedra, M. J.; Correia, A.; Spencer, J. Biochemical characterization of Sfh-1, a subclass B2 metallo-β-lactamase from *Serratia fonticola* UTAD54. *Antimicrob. Agents Chemother.* **2011**, *55*, 5392–5395.

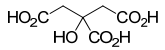
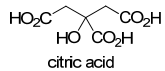
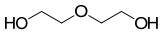
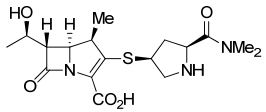
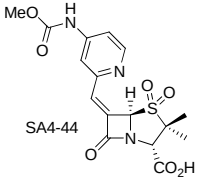
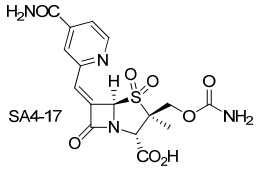
Table 3. Class D OXA β-lactamases.

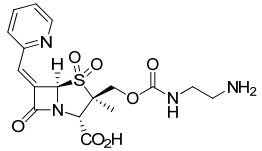
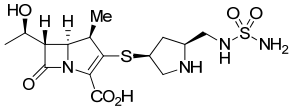
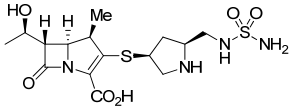
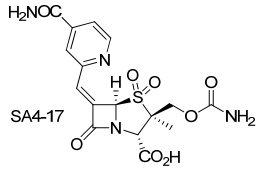
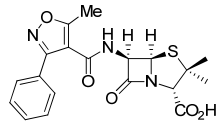
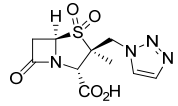
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Lys or Kcx	pH	Ligand	Comments and References
OXA-1 (class D, group 2d)								
1M6K	OXA-1	*E. coli*, class D, group 2d	2003	1.50 Å	Kcx70	pH 7.5	–	- Sun, T.; Nukaga, M.; Mayama, K.; Braswell, E. H.; Knox, J. R. Comparison of β-lactamases of classes A and D: 1.5-A crystallographic structure of the class D OXA-1 oxacillinase. *Protein Sci.* **2003**, *12*, 82–91.
3ISG	OXA-1	*E. coli*, class D, group 2d	2009	1.40 Å	Kcx70	pH 7.5	 doripenem	- Schneider, K. D.; Karpen, M. E.; Bonomo, R. A.; Leonard, D. A.; Powers, R. A. The 1.4 A Crystal structure of the class D β-lactamase OXA-1 complexed with doripenem. *Biochemistry* **2009**, *48*, 11840–11847.
4MLL (4F7Y)	OXA-1, K70D	*E. coli*, class D, group 2d	2013	1.37 Å	Asp70	pH 7.0	 oxacillin	- June, C. M.; Vallier, B. C.; Bonomo, R. A.; Leonard, D. A.; Powers, R. A. Structural origins of Oxacillinase specificitiy in class D β-lactamases. *Antimicrob. Agents Chemother.* **2014**, *58*, 333–341.
OXA-2 (class D, group 2d)								
1K38	OXA-2	*S. typhimurium*, class D, group 2d	2003	1.50 Å	Kcx70	pH 9	–	- Kerff, F.; Fonze, E.; Bouillenne, F.; Frère, J.-M.; Charlier, P., unpublished.
OXA-10 (= PSE-2, class D, group 2d)								
1FOF	OXA-10	*P. aeruginosa*, class D group 2d	2000	2.00 Å	Lys70	pH 6.5	SO_4^{2-}	- Paetzel, M.; Danel, F.; de Castro, L.; Mosimann, S. C.; Page, M. G. P.; Strynadka, N. C. J. Crystal structure of the class D β-lactamase OXA-10. *Nat. Struct. Biol.* **2000**, *7*, 918–925.
1EWZ	OXA-10	*P. aeruginosa*, class D group 2d	2000	2.40 Å	Lys70	pH 8.5	–	- Golemi, D.; Maveyraud, L.; Vakulenko, S.; Tranier, S.; Ishiwata, A; Kotra, L. P.; Samama, J.-P.; Mobashery, S. The first structural and mechanistic insights for class D β-lactamases: Evidence for a novel catalytic process for turnover of β-lactam antibiotics. *J. Am. Chem. Soc.* **2000**, *122*, 6132–6133.

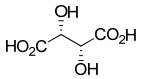
PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Lys or Kcx	pH	Ligand	Comments and References
1E3U	OXA-10	*P. aeruginosa*, class D group 2d	2001	1.66 Å	Lys70	pH 8.2	–	- MAD structure with $Au(CN)_2$. - Maveyraud, L.; Golemi, D.; Kotra, L. P.; Tranier, S.; Vakulenko, S.; Mobashery, S.; Samama, J.-P. Insights into class D β-lactamases are revealed by the crystal structure of the OXA10 enzyme from *Pseudomonas aeruginosa*. *Structure* **2000**, *8*, 1289–1298.
1E4D	OXA-10	*P. aeruginosa*, class D group 2d	2001	1.80 Å	Kcx70	pH 8.3	–	- Maveyraud, L.; Golemi, D.; Kotra, L. P.; Tranier, S.; Vakulenko, S.; Mobashery, S.; Samama, J.-P. Insights into class D β-lactamases are revealed by the crystal structure of the OXA10 enzyme from *Pseudomonas aeruginosa*. *Structure* **2000**, *8*, 1289–1298.
1K4E	OXA-10	*P. aeruginosa*, class D group 2d	2001	2.00 Å	Kcx70	pH 9	–	- MAD phasing with selenomethionine. - Kerff, F.; Fonze, E.; Bouillene, F.; Frère, J.-M.; Charlier, P., unpublished.
1K4F	OXA-10	*P. aeruginosa*, class D group 2d	2001	1.60 Å	Kcx70	pH 9	–	- Kerff, F.; Fonze, E.; Bouillene, F.; Frère, J.-M.; Charlier, P., unpublished.
1K55 1K56 1K57	OXA-10	*P. aeruginosa*, class D group 2d	2001	1.39 Å 1.90 Å 1.90 Å	Kcx70 3:1 1:1	pH 7.5 6.5 6.0	–	- Golemi, D.; Maveyraud, L.; Vakulenko, S.; Samama, J.-P.; Mobashery, S. Critical involvement of a carbamylated lysine in catalytic function of class D β-lactamases. *Proc. Natl. Acad. Sci., U.S.A.* **2001**, *98*, 14280–14285.
1K54	OXA-10	*P. aeruginosa*, class D group 2d	2001	1.70 Å	Kcx70	pH 7.5	 6β-hydroxypropyl penicillinate	- Golemi, D.; Maveyraud, L.; Vakulenko, S.; Samama, J.-P.; Mobashery, S. Critical involvement of a carbamylated lysine in catalytic function of class D β-lactamases. *Proc. Natl. Acad. Sci., U.S.A.* **2001**, *98*, 14280–14285.
1K6R	OXA-10	*P. aeruginosa*, class D group 2d	2003	2.30 Å	Lys70	pH 7	 moxalactam	- Kerff, F.; Fonze, E.; Sauvage, E.; Frere, J.-M.; Charlier, P., unpublished. - Compared with other structures in: Vercheval et al. *Biochem. J.* **2010**, *432*, 495–504.
1K6S	OXA-10	*P. aeruginosa*, class D group 2d	2003	2.03 Å	Kcx70	pH 7	 phenylboronic acid derivative	- The boronate end reacts with Ser67 and the iodoacetamide moiety reacts with Met99. - Kerff, F.; Fonze, E.; Sauvage, E.; Frere, J.-M.; Charlier, P., unpublished.
2HP5	OXA-10, W154G	*P. aeruginosa*, class D group 2d	2007	2.70 Å	Lys70	pH 7.0	–	- Baurin, S.; Vercheval, L.; Bouillenne, F.; Falzone, C.; Brans, A.; Jacquamet, L.; Ferrer, J.-L.; Sauvage, E.; Dehareng, D.; Frere, J.-M.; Charlier, P.; Galleni, M.; Kerff, F. Critical role tryptophan 154 for the activity and stability of class D β-lactamases. *Biochemistry* **2009**, *48*, 11252–11263.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Lys or Kcx	pH	Ligand	Comments and References
2RL3	OXA-10, W154H	*P. aeruginosa*, class D group 2d	2008	1.90 Å	1:1	pH 7.0	–	- Baurin, S.; Vercheval, L.; Bouillenne, F.; Falzone, C.; Brans, A.; Jacquamet, L.; Ferrer, J.-L.; Sauvage, E.; Dehareng, D.; Frere, J.-M.; Charlier, P.; Galleni, M.; Kerff, F. Critical role tryptophan 154 for the activity and stability of class D β-lactamases. *Biochemistry* **2009**, *48*, 11252–11263.
2HP9 2HP6 2HPB	OXA-10, W154A	*P. aeruginosa*, class D group 2d	2007	2.50 Å 2.20 Å 2.05 Å	Lys70 Lys70 Lys70	pH 6.0 pH 7.5 pH 9.0	– – –	- Baurin, S.; Vercheval, L.; Bouillenne, F.; Falzone, C.; Brans, A.; Jacquamet, L.; Ferrer, J.-L.; Sauvage, E.; Dehareng, D.; Frere, J.-M.; Charlier, P.; Galleni, M.; Kerff, F. Critical role tryptophan 154 for the activity and stability of class D β-lactamases. *Biochemistry* **2009**, *48*, 11252–11263.
2WGI	OXA-10, W154A	*P. aeruginosa*, class D group 2d	2009	2.85 Å	Lys70	pH 6.0	 penicillin G	- Baurin, S.; Vercheval, L.; Bouillenne, F.; Falzone, C.; Brans, A.; Jacquamet, L.; Ferrer, J.-L.; Sauvage, E.; Dehareng, D.; Frere, J.-M.; Charlier, P.; Galleni, M.; Kerff, F. Critical role tryptophan 154 for the activity and stability of class D β-lactamases. *Biochemistry* **2009**, *48*, 11252–11263.
3LCE	OXA-10	*P. aeruginosa*, class D, group 2d	2010	2.00 Å	Kcx70	pH 7.0	 3α-methoxy cyclobutanone	- Johnson, J. W.; Gretes, M.; Goodfellow, V. J.; Marrone, L.; Heynen, M. L.; Strynadka, N. C. J.; Dmitrienko, G. I. Cyclobutanone analogues of β-lactams revisited: Insights into conformational requirements for inhibition of serine- and metallo-β-lactamases. *J. Am. Chem. Soc.* **2010**, *132*, 2558–2560.
2WGV 2WGW	OXA-10, V117T	*P. aeruginosa*, class D, group 2d	2010	1.80 Å 1.80 Å	Lys70 1:1	pH 6.5 pH 8.0	 Cl^-, citric acid	- Vercheval, L.; Bauvois, C.; Di Paolo, A.; Borel, F.; Ferrer, J.-L.; Sauvage, E.; Matagne, A.; Frere, J.-M.; Charlier, P.; Galleni, M.; Kerff, F. Three factors that modulate the activity of class D β-lactamases and interfere with the post-translational carboxylation of Lys70. *Biochem. J.* **2010**, *432*, 495–504.
2WKI	OXA-10, K70C	*P. aeruginosa*, class D, group 2d	2010	2.10 Å	Cys70	pH 7.0	–	- Vercheval, L.; Bauvois, C.; Di Paolo, A.; Borel, F.; Ferrer, J.-L.; Sauvage, E.; Matagne, A.; Frere, J.-M.; Charlier, P.; Galleni, M.; Kerff, F. Three factors that modulate the activity of class D β-lactamases and interfere with the post-translational carboxylation of Lys70. *Biochem. J.* **2010**, *432*, 495–504.
2WKH	OXA-10, K70C	*P. aeruginosa*, class D, group 2d	2010	1.79 Å	Cys70	pH 7.0	 ampicillin	- Vercheval, L.; Bauvois, C.; Di Paolo, A.; Borel, F.; Ferrer, J.-L.; Sauvage, E.; Matagne, A.; Frere, J.-M.; Charlier, P.; Galleni, M.; Kerff, F. Three factors that modulate the activity of class D β-lactamases and interfere with the post-translational carboxylation of Lys70. *Biochem. J.* **2010**, *432*, 495–504.
2X01	OXA-10, S67A	*P. aeruginosa*, class D, group 2d	2010	1.90 Å	Kcx70	pH 7	–	- Vercheval, L.; Kerff, F.; Bauvois, C.; Sauvage, E.; Guiet, R.; Galleni, M.; Charlier, P., unpublished.
2X02	OXA-10	*P. aeruginosa*, class D, group 2d	2010	1.35 Å	Kcx70	pH 7	–	- Vercheval, L.; Kerff, F.; Sauvage, E.; Hermann, R.; Galleni, M.; Charlier, P., unpublished.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Lys or Kcx	pH	Ligand	Comments and References
3QNB	OXA-10 engineered variant	*E. coli*, class D, group 2d	2011	1.95 Å	Kcx70	pH 8.0	–	- De Luca, F.; Benvenuti, M.; Carboni, F.; Pozzi, C.; Rossolini, G. M.; Mangani, S.; Docquier, J.-D. Evolution to carbapenem-hydrolyzing activity in noncarbapenemase class D β-lactamase OXA-10 by rational protein design. *Proc. Natl. Acad. Sci., U.S.A.* **2011**, *108*, 18424–18429.
3QNC	OXA-10 engineered variant	*E. coli*, class D, group 2d	2011	1.60 Å	Kcx70	pH 9.0	–	- De Luca, F.; Benvenuti, M.; Carboni, F.; Pozzi, C.; Rossolini, G. M.; Mangani, S.; Docquier, J.-D. Evolution to carbapenem-hydrolyzing activity in noncarbapenemase class D β-lactamase OXA-10 by rational protein design. *Proc. Natl. Acad. Sci., U.S.A.* **2011**, *108*, 18424–18429.
OXA-13 (class D, group 2d)								
1H8Z	OXA-13	*P. aeruginosa*, class D, group 2d	2001	1.80 Å	Lys70	pH 5.5	–	- Pernot, L.; Frénois, F.; Rybkine, T.; L'Hermite, G.; Petrella, S.; Delettré, J.; Jarlier, V.; Collatz, E.; Sougakoff, W. Crystal structures of the class D β-lactamase OXA-13 in the native form and in complex with meropenem. *J. Mol. Biol.* **2001**, *310*, 859–874.
1H8Y	OXA-13	*P. aeruginosa*, class D, group 2d	2001	2.00 Å	Lys70	pH 5.5	 meropenem	- Pernot, L.; Frénois, F.; Rybkine, T.; L'Hermite, G.; Petrella, S.; Delettré, J.; Jarlier, V.; Collatz, E.; Sougakoff, W. Crystal structures of the class D β-lactamase OXA-13 in the native form and in complex with meropenem. *J. Mol. Biol.* **2001**, *310*, 859–874.
1H5X	OXA-13	*P. aeruginosa*, class D, group 2d	2002	1.90 Å	Lys70	pH 5.5	 imipenem	- Pernot, L.; Mayer, C.; Sougakoff, W., unpublished.
OXA-23 (class D carbapenemase, group 2df)								
4JF4	OXA-23	*A. baumannii*, class D, group 2df	2013	2.14 Å	Lys82	pH 4.1	 meropenem	- Smith, C. A.; Antunes, N. T.; Stewart, N. K.; Toth, M.; Kumarasiri, M.; Chang, M.; Mobashery, S.; Vakulenko, S. B. Structural basis for carbapenemase activity of the OXA-23 β-lactamase from *Acinetobacter baumannii*. *Chem. Biol.* **2013**, *20*, 1107–1115.
4JF5 4JF6	OXA-23	*A. baumannii*, class D, group 2df	2013	1.15 Å 2.50 Å	Lys82 Kcx82	pH 4.1 pH 7.0	 diethylene glycol	- Smith, C. A.; Antunes, N. T.; Stewart, N. K.; Toth, M.; Kumarasiri, M.; Chang, M.; Mobashery, S.; Vakulenko, S. B. Structural basis for carbapenemase activity of the OXA-23 β-lactamase from *Acinetobacter baumannii*. *Chem. Biol.* **2013**, *20*, 1107–1115.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Lys or Kcx	pH	Ligand	Comments and References
4K0X	OXA-23	*A. baumannii*, class D, group 2df	2013	1.61 Å	Kcx82	na	–	- Kaitany, K.-C. J.; Klinger, N. V.; June, C. M.; Ramey, M. E.; Bonomo, R. A.; Powers, R. A.; Leonard, D. A. Structures of the class D carbapenemases OXA-23 and OXA-146: Mechanistic basis of activity against carbapenems, extended-spectrum cephalosporins, and aztreonam. *Antimicrob. Agents Chemother.* **2013**, *57*, 4848–4855.
4K0W	OXA-23, A220dup	*A. baumannii*, class D, group 2df	2013	1.20 Å	Lys82	pH 4.2	 citric acid	- Kaitany, K.-C. J.; Klinger, N. V.; June, C. M.; Ramey, M. E.; Bonomo, R. A.; Powers, R. A.; Leonard, D. A. Structures of the class D carbapenemases OXA-23 and OXA-146: Mechanistic basis of activity against carbapenems, extended-spectrum cephalosporins, and aztreonam. *Antimicrob. Agents Chemother.* **2013**, *57*, 4848–4855.
4JF5 4JF6	OXA-23	*A. baumannii*, class D, group 2df	2013	1.15 Å 2.50 Å	Lys82 Kcx82	pH 4.1 pH 7.0	 citric acid  diethylene glycol	- Smith, C. A.; Antunes, N. T.; Stewart, N. K.; Toth, M.; Kumarasiri, M.; Chang, M.; Mobashery, S.; Vakulenko, S. B. Structural basis for carbapenemase activity of the OXA-23 β-lactamase from *Acinetobacter baumannii*. *Chem. Biol.* **2013**, *20*, 1107–1115.
4JF4	OXA-23	*A. baumannii*, class D, group 2df	2013	2.14 Å	Lys82	pH 4.1	 meropenem	- Smith, C. A.; Antunes, N. T.; Stewart, N. K.; Toth, M.; Kumarasiri, M.; Chang, M.; Mobashery, S.; Vakulenko, S. B. Structural basis for carbapenemase activity of the OXA-23 β-lactamase from *Acinetobacter baumannii*. *Chem. Biol.* **2013**, *20*, 1107–1115.
OXA-24/40 (class D carbapenemase, group 2df)								
2JC7	OXA-24	*A. baumannii*, class D, group 2df	2007	2.50 Å	Lys84	pH 6.5	–	- Santillana, E.; Beceiro, A.; Bou, G.; Romero, A. Crystal structure of the carbapenemase OXA-24 reveals insights into the mechanism of carbapenem hydrolysis. *Proc. Natl. Acad. Sci., U.S.A.* **2007**, *104*, 5354–5359.
3FV7	OXA-24	*A. baumannii*, class D, group 2df	2010	2.00 Å	Kcx84	pH 7.5	 SA4-44	- Bou, G.; Santillana, E.; Sheri, A.; Beceiro, A.; Sampson, J. M.; Kalp, M.; Bethel, C. R.; Distler, A. M.; Drawz, S. M.; Pagadala, S. R. R.; van den Akker, F.; Bonomo, R. A.; Buynak, J. D. Design, synthesis, and crystal structures of 6-alkylidene-2′-substituted penicillanic acid sulfones as potent inhibitors of *Acinetobacter baumannii* OXA-24 carbapenemase. *J. Am. Chem. Soc.* **2010**, *132*, 13320–13331.
3FYZ	OXA-24	*A. baumannii*, class D, group 2df	2010	2.10 Å	Kcx84	pH 7.5	 SA4-17	- Bou, G.; Santillana, E.; Sheri, A.; Beceiro, A.; Sampson, J. M.; Kalp, M.; Bethel, C. R.; Distler, A. M.; Drawz, S. M.; Pagadala, S. R. R.; van den Akker, F.; Bonomo, R. A.; Buynak, J. D. Design, synthesis, and crystal structures of 6-alkylidene-2′-substituted penicillanic acid sulfones as potent inhibitors of *Acinetobacter baumannii* OXA-24 carbapenemase. *J. Am. Chem. Soc.* **2010**, *132*, 13320–13331.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Lys or Kcx	pH	Ligand	Comments and References
3FZC	OXA-24	*A. baumannii*, class D, group 2df	2010	2.00 Å	Kcx84	pH 7.5	 SA3-53	- Bou, G.; Santillana, E.; Sheri, A.; Beceiro, A.; Sampson, J. M.; Kalp, M.; Bethel, C. R.; Distler, A. M.; Drawz, S. M.; Pagadala, S. R. R.; van den Akker, F.; Bonomo, R. A.; Buynak, J. D. Design, synthesis, and crystal structures of 6-alkylidene-2′-substituted penicillanic acid sulfones as potent inhibitors of *Acinetobacter baumannii* OXA-24 carbapenemase. *J. Am. Chem. Soc.* **2010**, *132*, 13320–13331.
3G4P	OXA-24	*A. baumannii*, class D, group 2df	2010	1.97 Å	Kcx84	pH 7.5	–	- Bou, G.; Santillana, E.; Sheri, A.; Beceiro, A.; Sampson, J. M.; Kalp, M.; Bethel, C. R.; Distler, A. M.; Drawz, S. M.; Pagadala, S. R. R.; van den Akker, F.; Bonomo, R. A.; Buynak, J. D. Design, synthesis, and crystal structures of 6-alkylidene-2′-substituted penicillanic acid sulfones as potent inhibitors of *Acinetobacter baumannii* OXA-24 carbapenemase. *J. Am. Chem. Soc.* **2010**, *132*, 13320–13331.
3PAE	OXA-24/40, K84D	*A. baumannii*, class D, group 2df	2011	2.10 Å	Asp84	pH 8.5	 doripenem	- Schneider, K. D.; Ortega, C. J.; Renck, N. A.; Bonomo, R. A.; Powers, R. A.; Leonard, D. A. Structures of the class D carbapenemase OXA-24 from *Acinetobacter baumannii* in complex with doripenem. *J. Mol. Biol.* **2011**, *406*, 583–594.
3PAG	OXA-24/40, V130D	*A. baumannii*, class D, group 2df	2011	2.25 Å	Lys84	pH 8.5	 doripenem	- Schneider, K. D.; Ortega, C. J.; Renck, N. A.; Bonomo, R. A.; Powers, R. A.; Leonard, D. A. Structures of the class D carbapenemase OXA-24 from *Acinetobacter baumannii* in complex with doripenem. *J. Mol. Biol.* **2011**, *406*, 583–594.
3MBZ	OXA-24	*A. baumannii*, class D, group 2df	2011	2.60 Å	Kcx84	pH 8.5	 SA4-17	- Bou, G.; Santillana, E.; Sheri, A.; Beceiro, A.; Sampson, J. M.; Kalp, M.; Bethel, C. R.; Distler, A. M.; Drawz, S. M.; Pagadala, S. R. R.; van den Akker, F.; Bonomo, R. A.; Buynak, J. D. Design, synthesis, and crystal structures of 6-alkylidene-2′-substituted penicillanic acid sulfones as potent inhibitors of *Acinetobacter baumannii* OXA-24 carbapenemase. *J. Am. Chem. Soc.* **2010**, *132*, 13320–13331.
4F94	OXA-24, K84D	*A. baumannii*, class D, group 2df	2013	2.40 Å	Asp84	pH 7.5	 oxacillin	- June, C. M.; Vallier, B. C.; Bonomo, R. A.; Leonard, D. A., unpublished.
3ZNT	OXA-24	*A. baumannii*, class D, group 2df	2014	1.95 Å	Kcx84	na	 tazobactam	- Power, P.; Sauvage, E.; Herman, R.; Kerff, F.; Charlier, P., unpublished.

PDB Code	Enzyme, mutations	Source, Ambler class, Bush–Jacoby functional group	Year	Resolution	Lys or Kcx	pH	Ligand	Comments and References
OXA-45 (class D ESBL, group 2de)								
4GN2	OXA-45	*P. aeruginosa*, class D, group 2de	2013	2.01 Å	Kcx66	pH 7.5	–	- Martin, J. D.; Xiong, X. L.; Catto, L. E.; Toleman, M. A.; Walsh, T. R.; Clarke, A. R.; Spencer, J., unpublished.
OXA-46 (class D, group 2d)								
3IF6	OXA-46	*P. aeruginosa*, class D, group 2d	2010	2.40 Å	Lys75:Kcx 2:1	pH 7.5	 tartrate	- Docquier, J.-D.; Benvenuti, M.; Calderone, V.; Giuliani, F.; Kapetis, D.; De Luca, F.; Rossolini, G. M.; Mangani, S. Crystal structure of the narrow-spectrum OXA-46 class D β-lactamase: Relationship between active-site lysine carbamylation and inhibition by polycarboxylates. *Antimicrob. Agents Chemother.* **2010**, *54*, 2167–2174.
OXA-48 (class D carbapenemase, group 2df)								
3HBR	OXA-48	*K. pneumoniae*, class D, group 2df	2009	1.90 Å	Kcx73	pH 7.5	–	- Docquier, J.-D.; Calderone, V.; De Luca, F.; Benvenuti, M.; Giuliani, F.; Bellucci, L.; Tafi, A.; Nordmann, P.; Botta, M.; Rossolini, G. M.; Mangani, S. Crystal structure of the OXA-48 β-lactamase reveals mechanistic diversity among class D β-lactamases. *Chem. Biol.* **2009**, *16*, 540–547.
OXA-58 (class D carbapenemase, group 2df)								
4OH0	OXA-58	*A. baumannii*, class D, group 2df	2014	1.30 Å	Kcx86	pH 8.5	Cl^-	- Smith, C. A.; Antunes, N. T.; Toth, M.; Vakulenko, S. B. Crystal structure of carbapenemase OXA-58 from *Acinetobacter baumannii*. *Antimicrob. Agents Chemother.* **2014**, *58*, 2135–2143.
OXA-85 (= FUS-1, class D, group 2d)								
4IED	OXA-85	*F. nucleatum*, class D, group 2d	2014	1.50 Å	Kcx60	pH 8.0	–	- Mangani, S.; Benvenuti, M.; Docquier, J.-D., unpublished.