

## Table of $\beta$ -Lactamase Inhibitors <sup>a</sup>

Jarrold W. Johnson and Gary I. Dmitrienko

*Department of Chemistry, University of Waterloo,  
200 University Avenue West, Waterloo, Ontario, Canada N2L 3G1*

jwjohnso@uwaterloo.ca; dmitrien@uwaterloo.ca

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**$\beta$ -Lactamases.** The most important mechanism for bacterial resistance to  $\beta$ -lactam antibiotics involves  $\beta$ -lactamases, enzymes that inactivate  $\beta$ -lactams through hydrolysis. Serine  $\beta$ -lactamases (classes A, C, and D) hydrolyze  $\beta$ -lactams through a covalent (acylenzyme) intermediate while the metallo- $\beta$ -lactamases (class B) use a zinc-bound hydroxide as the active-site nucleophile.

**$\beta$ -Lactamase Inhibitors.** The combination of  $\beta$ -lactamase inhibitors with  $\beta$ -lactam antibiotics has been a very successful strategy for overcoming resistance due to  $\beta$ -lactamases since the early 1980s. The inhibitors that are clinically available (clavulanate, sulbactam, and tazobactam), however, are inherently less effective against the class C  $\beta$ -lactamases of Gram-negative bacteria and not effective against strains producing inhibitor-resistant  $\beta$ -lactamases or metallo- $\beta$ -lactamases. There is an urgent need for the development of new inhibitors that can prolong the lifetime of  $\beta$ -lactam antibiotics against resistant bacteria.

**Purpose of this Table.** This table was initiated several years ago as a small list of metallo- $\beta$ -lactamase inhibitors for our in-house use and has slowly developed into a much larger list of serine- and metallo- $\beta$ -lactamase inhibitors. We hope that this table may serve as a useful resource to those interested in the design and development of new  $\beta$ -lactamase inhibitors, particularly for researchers who may be new to the field.

We apologize for any errors and we welcome any comments, corrections, and suggestions for improvements.

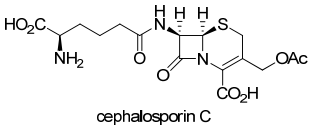
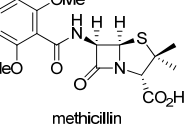
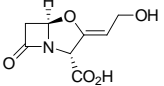
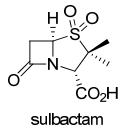
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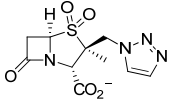
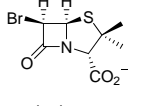
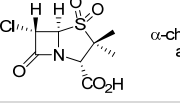
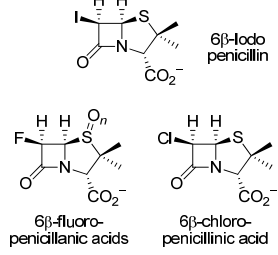
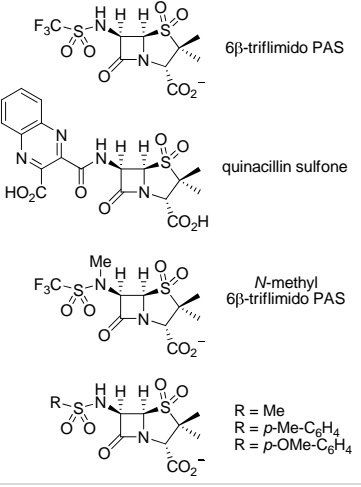
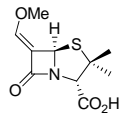
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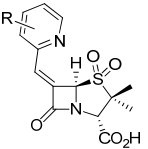
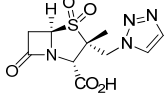
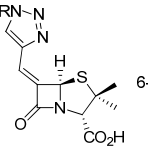
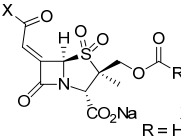
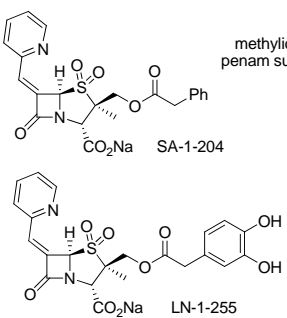
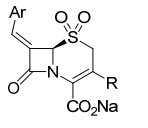
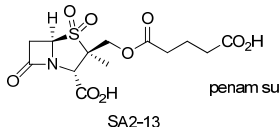
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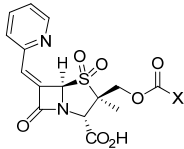
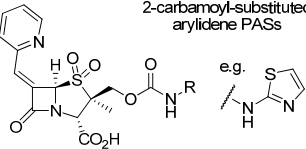
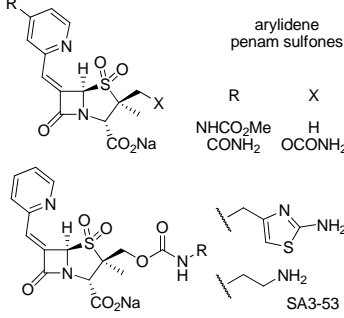
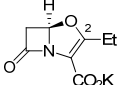
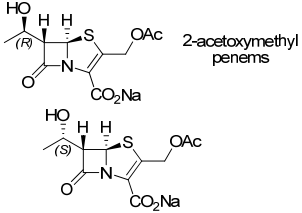
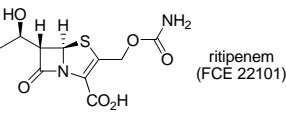
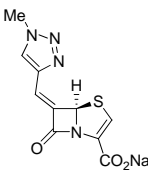
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<sup>a</sup> Adapted from: Johnson, J. W. Ph.D. Thesis, University of Waterloo, 2011.

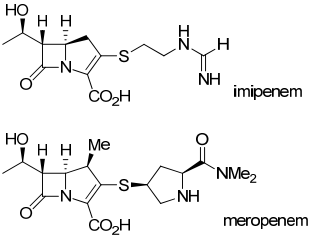
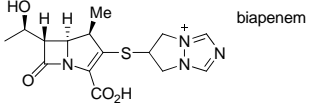
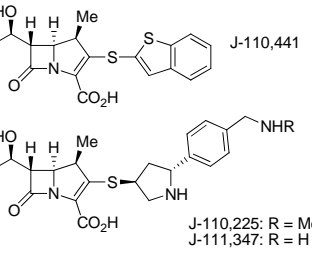
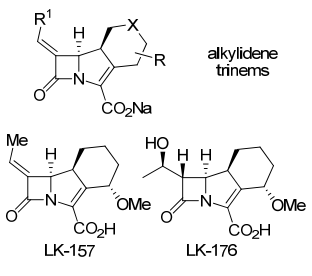
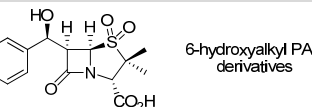
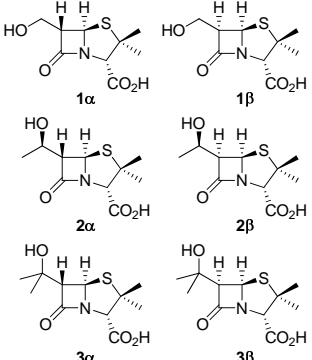
Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
<b>1. Early Cephalosporins and Penicillins</b>			
1.01	 cephalosporin C	A	- Abraham, E. P.; Newton, G. G. F. <i>Biochem. J.</i> <b>1956</b> , <i>63</i> , 628–634.
1.02	 methicillin penicillins with bulky sidechains	A	- Rolinson, G. N.; Stevens, S.; Batchelor, F. R.; Wood, J. C.; Chain, E. B. <i>Lancet</i> <b>1960</b> , 564–567. - Sutherland, R.; Batchelor, F. R. <i>Nature</i> <b>1964</b> , <i>201</i> , 868–869. - Cole, M. Inhibition of $\beta$ -Lactamases. In <i>Beta-Lactamases</i> ; Hamilton-Miller, J. M. T.; Smith, J. T. Eds.; Academic Press: London, 1979; pp 205–289. - Rolinson, G. N. <i>Rev. Infect. Dis.</i> <b>1991</b> , <i>13</i> (Suppl. 9), S727–S732. - Kiener, P. A.; Waley, S. G. <i>Biochem. J.</i> <b>1977</b> , <i>165</i> , 279–285. - Persaud, K. C.; Pain, R. H.; Virden, R. <i>Biochem. J.</i> <b>1986</b> , <i>237</i> , 723–730. - Fink, A. L.; Behner, K. M.; Tan, A. K. <i>Biochemistry</i> <b>1987</b> , <i>26</i> , 4248–4258.
<b>2. Clavulanic Acid, Sulbactam, and Tazobactam</b>			
2.01	 clavulanic acid	A, (C), (D)	- Brown, A. G.; Butterworth, D.; Cole, M.; Hanscomb, G.; Hood, J. D.; Reading, C. Naturally-occurring $\beta$ -lactamase inhibitors with antibacterial activity. <i>J. Antibiot.</i> <b>1976</b> , <i>29</i> , 668–669. - Howarth, T. T.; Brown, A. G.; King, T. J. <i>J. Chem. Soc., Chem. Commun.</i> <b>1976</b> , 266–267. - Cherry, P. C.; Newall, C. E. Clavulanic acid. In <i>Chemistry and Biology of <math>\beta</math>-Lactam Antibiotics</i> ; Morin, R. B., Gorman, M., Eds.; Academic Press: New York, 1982; Vol. 2, pp 361–402. - Reading, C.; Cole, M. <i>Antimicrob. Agents Chemother.</i> <b>1977</b> , <i>11</i> , 852–857. - Durkin, J. P.; Viswanatha, T. <i>J. Antibiot.</i> <b>1978</b> , <i>31</i> , 1162–1169. - Bush, K. <i>Clin. Microbiol. Rev.</i> <b>1988</b> , <i>1</i> , 109–123. - Bebrone, C.; Lassaux, P.; Vercheval, L.; Sohier, J.-S.; Jehaes, A.; Sauvage, E.; Galleni, M. <i>Drugs</i> <b>2010</b> , <i>70</i> , 651–679. - Chen, C. C. H.; Herzberg, O. <i>J. Mol. Biol.</i> <b>1992</b> , <i>224</i> , 1103–1113. (PDB: 1BLC). - Sulton, D.; Pagan-Rodriguez, D.; Zhou, X.; Liu, Y.; Hujer, A. M.; Bethel, C. R.; Helfand, M. S.; Thomson, J. M.; Anderson, V. E.; Buynak, J. D.; Ng, L. M.; Bonomo, R. A. <i>J. Biol. Chem.</i> <b>2006</b> , <i>280</i> , 35528–35536. - Tremblay, L. W.; Hugonnet, J. E.; Blanchard, J. S. <i>Biochemistry</i> <b>2008</b> , <i>47</i> , 5312–5316. (PDB: 3CG5). - Padayatti, P. S.; Helfand, M. S.; Totir, M. A.; Carey, M. P.; Carey, P. R.; Bonomo, R. A.; van den Akker, F. <i>J. Biol. Chem.</i> <b>2005</b> , <i>280</i> , 34900–34907. (PDB: 2A49) - Totir, M. A.; Padayatti, P. S.; Helfand, M. S.; Carey, M. P.; Bonomo, R. A.; Carey, P. R.; van den Akker, F. <i>Biochemistry</i> <b>2006</b> , <i>45</i> , 11895–11904. (PDB: 2H0T). - Livermore, D. M.; Hope, R.; Mushtaq, S.; Warner, M. <i>Clin. Microbiol. Infect.</i> <b>2006</b> , <i>14</i> (Suppl. 1), 189–193. - English, A. R.; Retsema, J. A.; Girard, A. E.; Lynch, J. E.; Barth, W. E. <i>Antimicrob. Agents Chemother.</i> <b>1978</b> , <i>14</i> , 414–419. - Bebrone, C.; Lassaux, P.; Vercheval, L.; Sohier, J.-S.; Jehaes, A.; Sauvage, E.; Galleni, M. <i>Drugs</i> <b>2010</b> , <i>70</i> , 651–679. - Labia, R.; Lelievre, V.; Peduzzi, J. <i>Biochim. Biophys. Acta</i> <b>1980</b> , <i>611</i> , 351–357. - Fisher, J.; Charnas, R. L.; Bradley, S. M.; Knowles, J. R. <i>Biochemistry</i> <b>1981</b> , <i>20</i> , 2726–2731. - Brenner, D. G.; Knowles, J. R.; Rihs, G. <i>Biochemistry</i> <b>1981</b> , <i>20</i> , 3680–3687. - Kemal, C.; Knowles, J. R. <i>Biochemistry</i> <b>1981</b> , <i>20</i> , 3688–3695. - Brenner, D. G.; Knowles, J. R. <i>Biochemistry</i> <b>1984</b> , <i>23</i> , 5833–5839. - Imtiaz, U.; Billings, E. M.; Knox, J. R.; Mobashery, S. <i>Biochemistry</i> <b>1994</b> , <i>33</i> , 5728–5738. - Totir, M. A.; Cha, J.; Ishiwata, A.; Wang, B.; Sheri, A.; Anderson, V. E.; Buynak, J.; Mobashery, S.; Carey, P. R. <i>Biochemistry</i> <b>2008</b> , <i>47</i> , 4094–4101. - Padayatti, P. S.; Helfand, M. S.; Totir, M. A.; Carey, M. P.; Carey, P. R.; Bonomo, R. A.; van den Akker, F. <i>J. Biol. Chem.</i> <b>2005</b> , <i>280</i> , 34900–34907. (PDB: 2A3U). - Totir, M. A.; Padayatti, P. S.; Helfand, M. S.; Carey, M. P.; Bonomo, R. A.; Carey, P. R.; van den Akker, F. <i>Biochemistry</i> <b>2006</b> , <i>45</i> , 11895–11904. (2H10). - Totir, M. A.; Helfand, M. S.; Carey, M. P.; Sheri, A.; Buynak, J. D.; Bonomo, R. A.; Carey, P. R. <i>Biochemistry</i> <b>2007</b> , <i>46</i> , 8980–8987. - Review: Akova, M. <i>Clin. Microbiol. Infect.</i> <b>2008</b> , <i>14</i> (Suppl. 1), 185–188.
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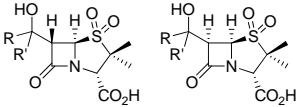
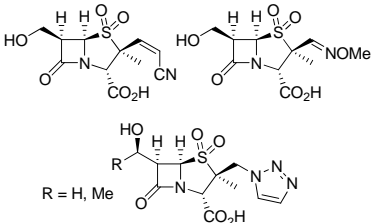
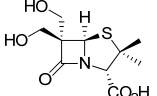
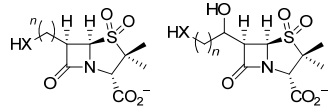
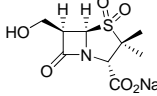
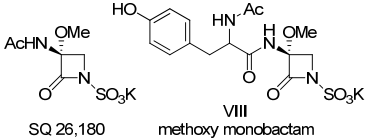
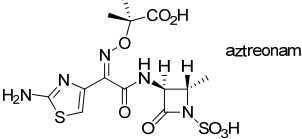
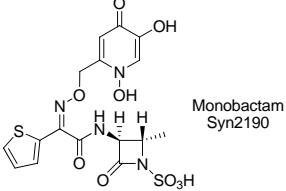
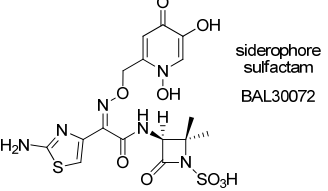
Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
2.03	 tazobactam	A	- Aronoff, S. C.; Jacobs, M. R.; Johanning, S.; Yamabe, S. <i>Antimicrob. Agents Chemother.</i> <b>1984</b> , <i>26</i> , 580–582. - Bush, K.; Macalintal, C.; Rasmussen, B. A.; Lee, V. J.; Yang, Y. <i>Antimicrob. Agents Chemother.</i> <b>1993</b> , <i>37</i> , 851–858. - Totir, M. A.; Cha, J.; Ishiwata, A.; Wang, B.; Sheri, A.; Anderson, V. E.; Buynak, J.; Mobashery, S.; Carey, P. R. <i>Biochemistry</i> <b>2008</b> , <i>47</i> , 4094–4101. - Kuzin, A. P.; Nukaga, M.; Nukaga, Y.; Hujer, A.; Bonomo, R. A.; Knox, J. R. <i>Biochemistry</i> <b>2001</b> , <i>40</i> , 1861–1866. (PDB: 1VMI), - Sun, T.; Bethel, C. R.; Bonomo, R. A.; Knox, J. R. <i>Biochemistry</i> <b>2004</b> , <i>43</i> , 14111–14117. (1TDG), - Padayatti, P. S.; Helfand, M. S.; Totir, M. A.; Carey, M. P.; Hujer, A. M.; Carey, P. R.; Bonomo, R. A.; van den Akker, F. <i>Biochemistry</i> <b>2004</b> , <i>43</i> , 843–848. (1RCJ), - Review: Zhanel, G. G.; Chung, P.; Adam, H.; Zelenitsky, S.; Denisuik, A.; Schweizer, F.; Lagace-Weins, P. R. S.; Rubinstein, E.; Gin, A. S.; Walkty, A.; Hoban, D. J.; Lynch, J. P.; Karlowsky, J. A. <i>Drugs</i> <b>2014</b> , <i>74</i> , 31–51.
<b>3. Penicillins and Penicillanic acid sulfones (PASs)</b>			
3.01	 brobactam	A	- Loosemore, M. J.; Pratt, R. F. <i>J. Org. Chem.</i> <b>1978</b> , <i>43</i> , 3611–3613. - Pratt, R. F.; Loosemore, M. J. <i>Proc. Natl. Acad. Sci. U.S.A.</i> <b>1978</b> , <i>75</i> , 4145–4149. - Knott-Hunziker, V.; Waley, S. G.; Orlek, B. S.; Sammes, P. G. <i>FEBS Lett.</i> <b>1979</b> , <i>99</i> , 59–61. - Loosemore, M. J.; Cohen, S. A.; Pratt, R. F. <i>Biochemistry</i> <b>1980</b> , <i>19</i> , 3990–3995. - Wise, R.; Andrews, J. M.; Patel, N. J. <i>Antimicrob. Chemother.</i> <b>1981</b> , <i>7</i> , 531–536.
3.02	 $\alpha$ -chloropenicillanic acid sulfone	A	- Cartwright, S. J.; Coulson, A. F. W. <i>Nature</i> <b>1979</b> , <i>278</i> , 360–361.
3.03	 6 $\beta$ -iodo penicillin 6 $\beta$ -fluoro-penicillanic acids 6 $\beta$ -chloro-penicillanic acid	A	- Kemp, J. E. G.; Closier, M. D.; Narayanaswami, S.; Stefaniak, M. H. <i>Tetrahedron Lett.</i> <b>1980</b> , <i>21</i> , 2991–2994. - Daehne, W. v. <i>J. Antibiot.</i> <b>1980</b> , <i>33</i> , 451–452. - Sauvage, E.; Zervosen, A.; Dive, G.; Herman, R.; Amoroso, A.; Joris, B.; Fonze, E.; Pratt, R. F.; Luxen, A.; Charlier, P.; Kerff, F. <i>J. Am. Chem. Soc.</i> <b>2009</b> , <i>131</i> , 15262–15269 (2WK0, 2WKE). - Danelon, G. O.; Laborde, M.; Mascaretti, O. A.; Boggio, S. B.; Roveri, O. A. <i>Bioorg. Med. Chem. Lett.</i> <b>1993</b> , <i>6</i> , 447–455.
3.04	 6 $\beta$ -triflimido PAS quinacillin sulfone N-methyl 6 $\beta$ -triflimido PAS R = Me R = <i>p</i> -Me-C <sub>6</sub> H <sub>4</sub> R = <i>p</i> -OMe-C <sub>6</sub> H <sub>4</sub>	A	- Mezes, P. S. F.; Clarke, A. J.; Dmitrienko, G. I.; Viswanatha, T. <i>J. Antibiotics</i> <b>1982</b> , <i>35</i> , 918–920. - Mezes, P. S. F.; Clarke, A. J.; Dmitrienko, G. I.; Viswanatha, T. <i>FEBS Lett.</i> <b>1982</b> , <i>143</i> , 265–267. - Mezes, P. S. F.; Friesen, R. W.; Viswanatha, T.; Dmitrienko, G. I. <i>Heterocycles</i> <b>1982</b> , <i>19</i> , 1207–1210. - Clarke, A. J.; Mezes, P. S.; Vice, S. F.; Dmitrienko, G. I.; Viswanatha, T. <i>Biochim. Biophys. Acta</i> <b>1983</b> , <i>748</i> , 389–397. - Hilhorst, I. M.; Dmitrienko, G. I.; Viswanatha, T.; Lampen, J. O. <i>J. Protein Chem.</i> <b>1984</b> , <i>3</i> , 275–286. - Dmitrienko, G. I.; Copeland, C. R.; Arnold, L.; Savard, M. E.; Clarke, A. J.; Viswanatha, T. <i>Bioorg. Chem.</i> <b>1985</b> , <i>13</i> , 34–46. - Guo, F.; Dmitrienko, G. I.; Clarke, A. J.; Viswanatha, T. <i>Microb. Drug Resist.</i> <b>1996</b> , <i>2</i> , 261–268. - Guo, F.; Huynh, J.; Dmitrienko, G. I.; Viswanatha, T.; Clarke, A. J. <i>Biochim. Biophys. Acta.</i> <b>1999</b> , <i>1431</i> , 132–147.
3.05	 6-(methoxymethylene) penicillinate	A	- Brenner, D. G.; Knowles, J. R. <i>Biochemistry</i> <b>1984</b> , <i>23</i> , 5839–5846.

Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
3.06	 6-(Heterocyclyl)-methylene penam sulfones	A, C, D	- Chen, Y. L.; Chang, C.-W.; Hedberg, K. <i>Tetrahedron Lett.</i> <b>1986</b> , 27, 3449–3452. - Chen, Y. L.; Chang, C.-W.; Hedberg, K.; Guarino, K.; Welch, W. M.; Kiessling, L.; Retsema, J. A.; Haskell, S. L.; Anderson, M.; Manousos, M.; Barrett, J. F. <i>J. Antibiot.</i> <b>1987</b> , 40, 803–822.
3.07	 2-epi-Tazobactam	A, C, D	- Maiti, S. N.; Spevak, P.; Reddy, A. V. N.; Micetich, R. G.; Ishida, N.; Miyake, Y.; Ogawa, K. <i>Eur. J. Med. Chem.</i> <b>1994</b> , 29, 795–798.
3.08	 6-(triazoly)methylene penam sulfones	A, C	- Eby, P.; Cummings, M. D.; Phillips, O. A.; Czajkowski, D. P.; Singh, M. P.; Spevak, P.; Micetich, R. G.; Maiti, S. N. <i>Heterocycles</i> <b>1996</b> , 42, 653–668.
3.09	 methylidene penam sulfones X = ONa, Me, NH <sub>2</sub> R = H, Me, CH <sub>2</sub> Cl, Bn, CH <sub>2</sub> Ar	A, C	- Buynak, J. D.; Rao, A. S.; Doppalapudi, V. R.; Adam, G.; Petersen, P. J.; Nidamarthy, S. D. <i>Bioorg. Med. Chem. Lett.</i> <b>1999</b> , 9, 1997–2002. - Buynak, J. D.; Rao, A. S. Preparation of 2 $\beta$ -Substituted-6-alkylidenepenicillanic Acid Derivatives as $\beta$ -Lactamase Inhibitors. PCT Int. Pat. Appl., WO 99/33838 A1, July 8, 1999.
3.10	 methylidene penam sulfones SA-1-204 LN-1-255	A, (C), D	- Buynak, J. D.; Rao, A. S.; Doppalapudi, V. R.; Adam, G.; Petersen, P. J.; Nidamarthy, S. D. <i>Bioorg. Med. Chem. Lett.</i> <b>1999</b> , 9, 1997–2002. - Buynak, J. D.; Rao, A. S. Preparation of 2 $\beta$ -Substituted-6-alkylidenepenicillanic Acid Derivatives as $\beta$ -Lactamase Inhibitors. PCT Int. Pat. Appl., WO 99/33838 A1, July 8, 1999. - Beharry, Z.; Chen, H.; Gadhachanda, V. R.; Buynak, J. D.; Palzkill, T. <i>Biochem. Biophys. Research Commun.</i> <b>2004</b> , 313, 541–545. - Kalp, M.; Sheri, A.; Buynak, J. D.; Bethel, C. R.; Bonomo, R. A.; Carey, P. R. <i>J. Biol. Chem.</i> <b>2007</b> , 282, 21588–21591. - Pattanaik, P.; Bethel, C. R.; Hujer, A. M.; Hujer, K. M.; Distler, A. M.; Taracila, M.; Anderson, V. E.; Fritsche, T. R.; Jones, R. N.; Pagadala, S. R. R.; van den Akker, F.; Buynak, J. D.; Bonomo, R. A. <i>J. Biol. Chem.</i> <b>2009</b> , 284, 945–953. (3D4F). - Drawz, S. M.; Bethel, C. R.; Doppalapudi, V. R.; Sheri, A.; Pagadala, S. R. R.; Hujer, A. M.; Skalweit, M. J.; Anderson, V. E.; Chen, S. G.; Buynak, J. D.; Bonomo, R. A. <i>Antimicrob. Agents Chemother.</i> <b>2010</b> , 54, 1414–1424. - Ke, W.; Pattanaik, P.; Bethel, C. R.; Sheri, A.; Buynak, J. D.; Bonomo, R. A.; van den Akker, F. <i>PLoS One</i> <b>2012</b> , 7, e49035. (4GD6).
3.11	 methylidene cephem sulfones	A, C	- Buynak, J. D.; Rao, A. S.; Adam, G. C.; Nidamarthy, S. D.; Doppalapudi, V. R. Synthesis, Antibacterial Activity and Formulations of $\beta$ -Lactamase Inhibiting Cephalosporins. PCT Int. Pat. Appl., WO 00/63213 A1, October 26, 2000. - Buynak, J. D.; Doppalapudi, V. R.; Adam, G. <i>Bioorg. Med. Chem. Lett.</i> <b>2000</b> , 10, 853–857. - Buynak, J. D.; Doppalapudi, V. R.; Frotan, M.; Kumar, R.; Chambers, A. <i>Tetrahedron</i> <b>2000</b> , 56, 5709–5718. - Crichlow, G. V.; Nukaga, M.; Doppalapudi, V. R.; Buynak, J. D.; Knox, J. R. <i>Biochemistry</i> <b>2001</b> , 40, 6233–6239. (1GA0). - Buynak, J. D.; Vogeti, L.; Chen, H. <i>Org. Lett.</i> <b>2001</b> , 3, 2953–2956. - Buynak, J. D.; Vogeti, L.; Doppalapudi, V. R.; Venkata, R.; Solomon, G. M.; Chen, H. <i>Bioorg. Med. Chem. Lett.</i> <b>2002</b> , 12, 1663–1666. - Buynak, J. D.; Vogeti, L. Preparation of 7-Alkylidene-3-Substituted-3-Cephem-4-Carboxylates as $\beta$ -Lactamase Inhibitors. PCT Int. Pat. Appl. WO 03/020732 A2, March 13, 2003.
3.12	 penam sulfone SA2-13	A	- Padayatti, P. S.; Sheri, A.; Totir, M. A.; Helfand, M. S.; Carey, M. P.; Anderson, V. E.; Carey, P. R.; Bethel, C. R.; Bonomo, R. A.; Buynak, J. D.; van den Akker, F. <i>J. Am. Chem. Soc.</i> <b>2006</b> , 128, 13235–13242.

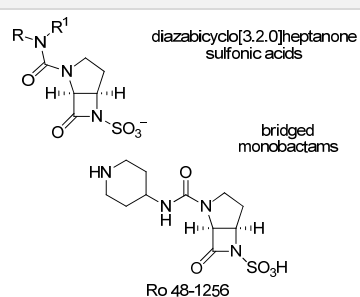
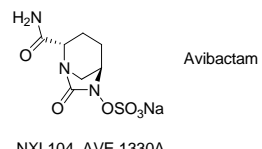
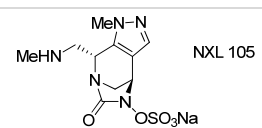
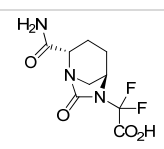
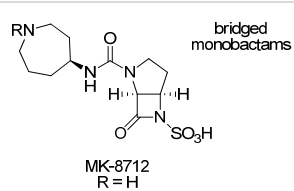
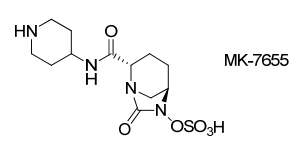
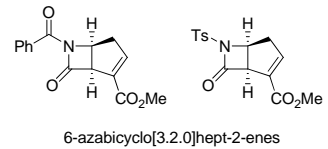
Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
3.13	 <p>2-substituted arylidene PASs</p> <p>ASR-II-292 X = Me                      LN-III-26 X = NHMe</p>	D	- Drawz, S. M.; Bethel, C. R.; Doppalapudi, V. R.; Sheri, A.; Pagadala, S. R. R.; Hujer, A. M.; Skalweit, M. J.; Anderson, V. E.; Chen, S. G.; Buynak, J. D.; Bonomo, R. A. <i>Antimicrob. Agents Chemother.</i> <b>2010</b> , <i>54</i> , 1414–1424.
3.14	 <p>2-carbamoyl-substituted arylidene PASs</p> <p>e.g.</p>	A, C, D	- Buynak, J. D.; Sheri, A.; Pagadala, S. R. R. Beta-lactamase inhibitory compounds. U.S. Patent Appl. US 2010/0009954 A1, January 14, 2010.
3.15	 <p>arylidene penam sulfones</p> <p>R X                      NHCO<sub>2</sub>Me H                      CONH<sub>2</sub> OCONH<sub>2</sub></p> <p>SA3-53</p>	A, D	- 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.; Romero, A.; Buynak, J. D. <i>J. Am. Chem. Soc.</i> <b>2010</b> , <i>132</i> , 13320–13331. - Ke, W.; Pattanaik, P.; Bethel, C. R.; Sheri, A.; Buynak, J. D.; Bonomo, R. A.; van den Akker, F. <i>PLoS One</i> <b>2012</b> , <i>7</i> , e49035. (PDB: 4GD8).
<b>4. Penems, Oxapenems, and Clavulanate Derivatives</b>			
4.01	 <p>oxapenems</p>	A, C	- Cherry, P. C.; Newall, C. E.; Watson, N. S. <i>J. Chem. Soc., Chem. Commun.</i> <b>1978</b> , 469–470.
4.02	 <p>2-acetoxymethyl penems</p>	A, C	- Sanfilippo, A.; Bruna, C. D.; Jabes, D.; Morvillo, E.; Schioppacassi, G.; Franceschi, G.; Arcamone, F.; Battistini, C.; Foglio, M.; Zarini, F. <i>J. Antibiot.</i> <b>1982</b> , <i>35</i> , 1248–1251.
4.03	 <p>ritipenem (FCE 22101)</p>	A, C, D	- Wise, R.; Andrews, J. M.; Danks, G. <i>Antimicrob. Agents Chemother.</i> <b>1983</b> , <i>24</i> , 909–914. - Neu, H. C.; Chin, N. X.; Labthavikul, P. <i>J. Antimicrob. Chemother.</i> <b>1985</b> , <i>16</i> , 305–313. - Yang, Y.; Livermore, D. M. <i>J. Antimicrob. Chemother.</i> <b>1989</b> , <i>23</i> (Suppl. C), 85–94. - For an issue dedicated to FCE 22101, see <i>J. Antimicrob. Chemother.</i> <b>1989</b> , <i>23</i> (Suppl. C).
4.04	 <p>BRL 42715</p>	A, C, D	- Coleman, K.; Griffin, D. R. J.; Page, J. W. J.; Upshon, P. A. <i>Antimicrob. Agents Chemother.</i> <b>1989</b> , <i>33</i> , 1580–1587. - Farmer, T. H.; Page, J. W. J.; Payne, D. J.; Knowles, D. J. C. <i>Biochem. J.</i> <b>1994</b> , <i>303</i> , 825–830. - Bulychhev, A.; Massova, I.; Lerner, S. A.; Mobashery, S. <i>J. Am. Chem. Soc.</i> <b>1995</b> , <i>117</i> , 4797–4801. - Matagne, A.; Ledent, P.; Monnaie, D.; Felici, A.; Jamin, M.; Raquet, X.; Galleni, M.; Klein, D.; François, I.; Frère, J.-M. <i>Antimicrob. Agents Chemother.</i> <b>1995</b> , <i>39</i> , 227–231. - Michaux, C.; Charlier, P.; Frère, J.-M.; Wouters, J. <i>J. Am. Chem. Soc.</i> <b>2005</b> , <i>127</i> , 3262–3263. (1Y54).

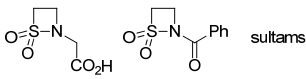
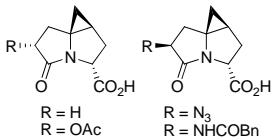
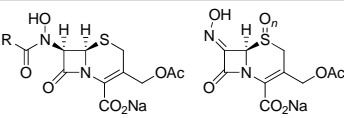
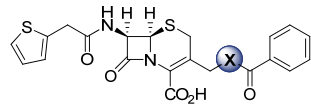
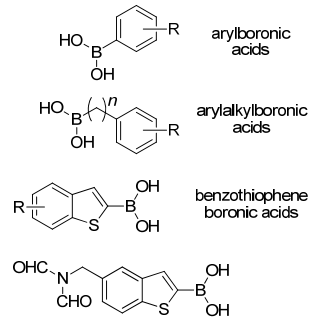
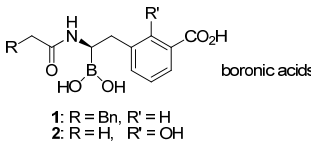
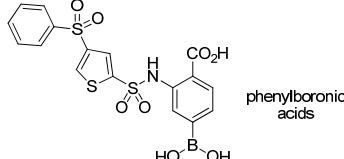
Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
4.05	<p>AM-113: R = Me                      AM-112: R = (CH<sub>2</sub>)<sub>3</sub>NH<sub>3</sub><sup>+</sup>                      AM-114: R = Me                      AM-115: R = (CH<sub>2</sub>)<sub>3</sub>NH<sub>3</sub><sup>+</sup></p>	A, C, D	- Wild, H.; Metzger, K.-G. <i>Bioorg. Med. Chem. Lett.</i> <b>1993</b> , 3, 2205–2210. - Pfandler, H. R.; Weisner, F.; Metzger, K. <i>Bioorg. Med. Chem. Lett.</i> <b>1993</b> , 3, 2211–2218. - Jamieson, C. E.; Lambert, P. A.; Simpson, I. N. <i>Antimicrob. Agents Chemother.</i> <b>2003</b> , 47, 2615–2618.
4.06	<p>SYN-1012</p>	A, C	- Phillips, O. A.; Czajkowski, D. P.; Spevak, P.; Singh, M. P.; Hanehara-Kunigita, C.; Hyodo, A.; Micetich, R. G.; Maiti, S. N. <i>J. Antibiot.</i> <b>1997</b> , 50, 350–356.
4.07	<p>BLI-489                      6-alkylidene penems</p>	A, B, C, D	- Nukaga, M.; Abe, T.; Venkatesan, A. M.; Mansour, T. S.; Bonomo, R. A.; Knox, J. R. <i>Biochemistry</i> <b>2003</b> , 42, 13152–13159. - Venkatesan, A. M.; Agarwal, A.; Abe, T.; Ushiroguchi, H.; Yamamura, I.; Kumagai, T.; Petersen, P. J.; Weiss, W. J.; Lenoy, E.; Yang, Y.; Shlaes, D. M.; Ryan, J. L.; Mansour, T. S. <i>Bioorg. Med. Chem.</i> <b>2004</b> , 12, 5807–5817. - Venkatesan, A. M.; Gu, Y.; Dos Santos, O.; Abe, T.; Agarwal, A.; Yang, Y.; Petersen, P. J.; Weiss, W. J.; Mansour, T. S.; Nukaga, M.; Hujer, A. M.; Bonomo, R. A.; Knox, J. R. <i>J. Med. Chem.</i> <b>2004</b> , 47, 6556–6568. - Weiss, W. J.; Petersen, P. J.; Murphy, T. M.; Tardio, L.; Yang, Y.; Bradford, P. A.; Venkatesan, A. M.; Abe, T.; Isoda, T.; Mihira, A.; Ushiroguchi, H.; Takasake, T.; Projan, S.; O'Connell, J.; Mansour, T. S. <i>Antimicrob. Agents Chemother.</i> <b>2004</b> , 48, 4589–4596. - Venkatesan, A. M.; Agarwal, A.; Abe, T.; Ushiroguchi, H.; Yamamura, I.; Ado, M.; Tsuyoshi, T.; Dos Santos, O.; Gu, Y.; Sum, F.-W.; Li, Z.; Francisco, G.; Lin, Y.-I.; Petersen, P. J.; Yang, Y.; Kumagai, T.; Weiss, W. J.; Shlaes, D. M.; Knox, J. R.; Mansour, T. S. <i>J. Med. Chem.</i> <b>2006</b> , 49, 4623–4637. - Mansour, T. S.; Venkatesan, A. M.; Bradford, P.; Petersen, P. J.; Projan, S. J. Bicyclic 6-Alkylidene-penem $\beta$ -Lactamase Inhibitors and $\beta$ -Lactam Antibiotic Combination: A Broad Spectrum Antibiotic. PCT Int. Appl. WO 2007/016134 A1, February 8, 2007. - Mansour, T. S.; Venkatesan, A. M. Bicyclic 6-Alkylidene-penems as Class D $\beta$ -Lactamase Inhibitors. PCT Int. Appl. WO 2006/130588 A1, December 7, 2006. - Venkatesan, A. M.; Agarwal, A.; Abe, T.; Ushiroguchi, H.; Ado, M.; Tsuyoshi, T.; Dos Santos, O.; Li, Z.; Francisco, G.; Lin, Y. I.; Petersen, P. J.; Yang, Y.; Weiss, W. J.; Shlaes, D. M.; Mansour, T. S. <i>Bioorg. Med. Chem.</i> <b>2008</b> , 16, 1890–1902. - Bethel, C. R.; Distler, A. M.; Rusczycky, M. W.; Carey, M. P.; Carey, P. R.; Hujer, A. M.; Taracila, M.; Helfand, M. S.; Thomson, J. M.; Kalp, M.; Anderson, V. E.; Leonard, D. A.; Hujer, K. M.; Abe, T.; Venkatesan, A. M.; Mansour, T. S.; Bonomo, R. A. <i>Antimicrob. Agents Chemother.</i> <b>2008</b> , 52, 3135–3143. - Endimiani, A.; Bethel, C.; Choudhary, Y.; Bonomo, R. A. <i>Antimicrob. Agents Chemother.</i> <b>2010</b> , 54, 1650–1651. - Ke, W.; Pattanaik, P.; Bethel, C. R.; Sheri, A.; Buynak, J. D.; Bonomo, R. A.; van den Akker, F. <i>PLoS One</i> <b>2012</b> , 7, e49035. (4GDB).
<b>5. Carbapenems and Trinems</b>			
5.01	<p>thienamycin: R<sup>1</sup> = Me, R<sup>2</sup> = H                      northienamycin: R<sup>1</sup> = H, R<sup>2</sup> = H                      N-acetylthienamycin: R<sup>1</sup> = Me, R<sup>2</sup> = Ac</p>	A, C	- Kahan, J. S.; Kahan, F. M.; Stapley, E. O.; Goegelman, R. T.; Hernandez, S. Antibiotics. U.S. Patent Appl. US 3,950,357 A. April 13, 1976. - Kahan, J. S.; Kahan, F. M.; Goegelman, R.; Currie, S. A.; Jackson, M.; Stapley, E. O.; Miller, T. W.; Miller, A. K.; Hendlin, D.; Mochales, S.; Hernandez, S.; Woodruff, H. B.; Birnbaum, J. <i>J. Antibiot.</i> <b>1979</b> , 32, 1–12. - Ratcliffe, R. W.; Albers-Schönberg, G. The Chemistry of Thienamycin and Other Carbapenem Antibiotics. In <i>Chemistry and Biology of <math>\beta</math>-Lactam Antibiotics</i> ; Morin, R. B., Gorman, M., Eds.; Academic Press: New York, 1982; Vol. 2, pp 227–313.

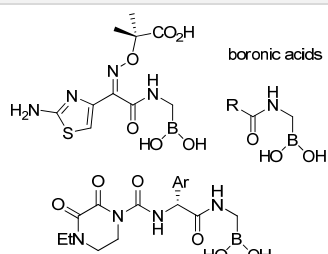
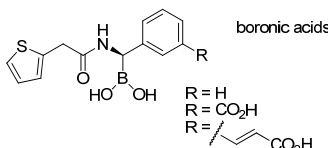
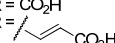
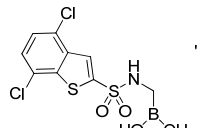
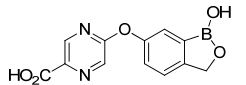
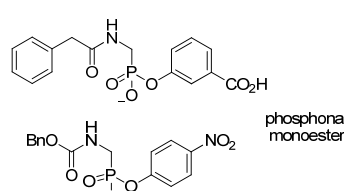
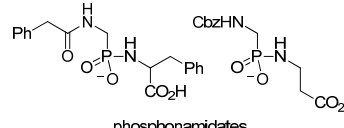
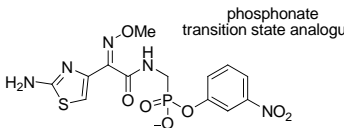
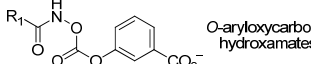
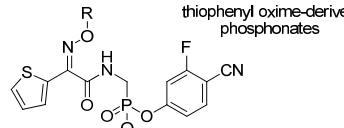
Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
5.02	 <p>imipenem meropenem</p>	A, C, (D)	- Taibi, P.; Mobashery, S. <i>J. Am. Chem. Soc.</i> <b>1995</b> , <i>117</i> , 7600–7605. - Maveyraud, L.; Mourey, L.; Kotra, L.; Pedelacq, J.-D.; Guillet, V.; Mobashery, S.; Samama, J.-P. <i>J. Am. Chem. Soc.</i> <b>1998</b> , <i>120</i> , 9748–9752. (1BT5). - Beadle, B. M.; Shoichet, B. K. <i>Antimicrob. Agents Chemother.</i> <b>2002</b> , <i>46</i> , 3978–3980. (1LL5). - Nukaga, M.; Bethel, C. R.; Thomson, J. M.; Hujer, A. M.; Distler, A.; Anderson, V. E.; Knox, J. R.; Bonomo, R. A. <i>J. Am. Chem. Soc.</i> <b>2008</b> , <i>130</i> , 12656–12662. (2ZD8). - Hugonnet, J. E.; Tremblay, L. W.; Boshoff, H. I.; Barry, C. E.; Blanchard, J. S. <i>Science</i> <b>2009</b> , <i>323</i> , 1215–1218. (3DWZ). - Queenan, A. M.; Shang, W.; Flamm, R.; Bush, K. <i>Antimicrob. Agents Chemother.</i> <b>2010</b> , <i>54</i> , 565–569.
5.03	 <p>biapenem</p>	A, B, C, D	- Felici, A.; Perilli, M.; Segatore, B.; Franceschini, N.; Setacci, D.; Oratore, A.; Steffani, S.; Galleni, M.; Amicosante, G. <i>Antimicrob. Agents Chemother.</i> <b>1995</b> , <i>39</i> , 1300–1305.
5.04	 <p>J-110,441 J-110,225: R = Me J-111,347: R = H</p>	B	- Nagano, R.; Adachi, Y.; Imamura, H.; Yamada, K.; Hashizume, T.; Morishima, H. <i>Antimicrob. Agents Chemother.</i> <b>1999</b> , <i>43</i> , 2497–2503. - Nagano, R.; Adachi, Y.; Hashizume, T.; Morishima, H. <i>J. Antimicrob. Chemother.</i> <b>2000</b> , <i>45</i> , 271–276. - Imamura, H.; Ohtake, N.; Sakuraba, S.; Shimizu, A.; Yamada, K.; Morishima, H. <i>Chem. Pharm. Bull.</i> <b>2000</b> , <i>48</i> , 310–311.
5.05	 <p>alkylidene trimems LK-157 LK-176</p>	A, C	- Vilar, M.; Galleni, M.; Solmajer, T.; Turk, B.; Frère, J.-M.; Matagne, A. <i>Antimicrob. Agents Chemother.</i> <b>2001</b> , <i>45</i> , 2215–2223. - Čopar, A.; Prevec, T.; Anžič, B.; Mesar, T.; Selič, L.; Vilar, M.; Solmajer, T. <i>Bioorg. Med. Chem. Lett.</i> <b>2002</b> , <i>12</i> , 971–975. - Plantan, I.; Selič, L.; Mesar, T.; Anderluh, P. Š.; Oblak, M.; Preželj, A.; Hesse, L.; Andrejašič, M.; Vilar, M.; Turk, D.; Kocijan, A.; Prevec, T.; Vilfan, G.; Kocijan, D.; Čopar, A.; Urleb, U.; Solmajer, T. <i>J. Med. Chem.</i> <b>2007</b> , <i>50</i> , 4113–4121. - Paukner, S.; Hesse, L.; Preželj, A.; Šolmajer, T.; Urleb, U. <i>Antimicrob. Agents Chemother.</i> <b>2009</b> , <i>53</i> , 505–511. (2Q9M, 2Q9N). - Preželj, A.; Urleb, U.; Vilfan, G. Use of Inhibitor of $\beta$ -Lactamases and its Combination with $\beta$ -Lactam Antibiotics for Treatment of Bacterial Infection. PCT Int. Pat. Appl., WO 2009/095387 A1. August 6, 2009.
<b>6. 6-Hydroxyalkyl Penams, Penam Sulfones, and Cephems</b>			
6.01	 <p>6-hydroxyalkyl PAS derivatives</p>	C	- Knight, G. C.; Waley, S. G. <i>Biochem. J.</i> <b>1985</b> , <i>225</i> , 435–439.
6.02	 <p>1<math>\alpha</math> 1<math>\beta</math> 2<math>\alpha</math> 2<math>\beta</math> 3<math>\alpha</math> 3<math>\beta</math></p>	A, D	- Miyashita, K.; Massova, I.; Taibi, P.; Mobashery, S. <i>J. Am. Chem. Soc.</i> <b>1995</b> , <i>117</i> , 11055–11059. - Maveyraud, L.; Massova, I.; Birck, C.; Miyashita, K.; Samama, J.-P.; Mobashery, S. <i>J. Am. Chem. Soc.</i> <b>1996</b> , <i>118</i> , 7435–7440. (1TEM). - Mourey, L.; Miyashita, K.; Swarén, P.; Bulychev, A.; Samama, J.-P.; Mobashery, S. <i>J. Am. Chem. Soc.</i> <b>1998</b> , <i>120</i> , 9382–9383. (1BUL). - Golemi, D.; Maveyraud, L.; Vakulenko, S.; Tranier, S.; Ishiwata, A.; Kotra, L. P.; Samama, J.-P.; Mobashery, S. <i>J. Am. Chem. Soc.</i> <b>2000</b> , <i>122</i> , 6132–6133. - Maveyraud, L.; Golemi-Kotra, D.; Ishiwata, A.; Meroueh, O.; Mobashery, S.; Samama, J.-P. <i>J. Am. Chem. Soc.</i> <b>2002</b> , <i>124</i> , 2461–2465. - Golemi, D.; Maveyraud, L.; Vakulenko, S.; Samama, J.-P.; Mobashery, S. <i>Proc. Natl. Acad. Sci., USA</i> <b>2001</b> , <i>98</i> , 14280–14285. (1K54).

Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
	 <p>hydroxyalkyl PASs</p>		
6.03	 <p>R = H, Me</p>	A, C	- Bitha, P.; Li, Z.; Francisco, G. D.; Rasmussen, B. A.; Lin, Y.-I. <i>Bioorg. Med. Chem. Lett.</i> <b>1999</b> , 9, 991–996. - Bitha, P.; Li, Z.; Francisco, G. D.; Yang, Y.; Petersen, P. J.; Lenoy, E.; Lin, Y.-I. <i>Bioorg. Med. Chem. Lett.</i> <b>1999</b> , 9, 997–1002.
6.04	 <p>6,6-Bis(hydroxymethyl) penicillinate</p>	A, C	- Nagase, T.; Golemi, D.; Ishiwata, A.; Mobashery, S. <i>Bioorg. Chem.</i> <b>2001</b> , 29, 140–145.
6.05		A, C	- Nottingham, M.; Bethel, C. R.; Pagadala, S. R. R.; Harry, E.; Pinto, A.; Lemons, Z. A.; Drawz, S. M.; van den Akker, F.; Carey, P. R.; Bonomo, R. A.; Buynak, J. D. <i>Bioorg. Med. Chem. Lett.</i> <b>2011</b> , 21, 387–393.
6.06	 <p>6<math>\beta</math>-hydroxymethyl PAS</p>	A, C	- Papp-Wallace, K.; Bethel, C. R.; Gootz, T. D.; Shang, W.; Stroh, J.; Lau, W.; McLeod, D.; Price, L.; Marfat, A.; Distler, A.; Drawz, S. M.; Chen, H.; Harry, E.; Nottingham, M.; Carey, P. R.; Buynak, J. D.; Bonomo, R. A. <i>Biochem. Pharmacol.</i> <b>2012</b> , 83, 462–471.
<b>7. Monobactams and Sulfactams</b>			
7.01	 <p>SQ 26,180 methoxy monobactam VIII</p>	C, PBPs	- Sakurai, Y.; Yoshida, Y.; Saitoh, K.; Nemoto, M.; Yamaguchi, A.; Sawai, T. <i>J. Antibiotics</i> <b>1990</b> , 43, 403–410.
7.02	 <p>aztreonam</p>	C	- Sykes, R. B.; Bonner, D. P.; Bush, K.; Georgopapadakou, N. H. <i>Antimicrob. Agents Chemother.</i> <b>1982</b> , 21, 85–92. - Bush, K.; Freudenberger, J. S.; Sykes, R. B. <i>Antimicrob. Agents Chemother.</i> <b>1982</b> , 22, 414–420. - Sakurai, Y.; Yoshida, Y.; Saitoh, K.; Nemoto, M.; Yamaguchi, A.; Sawai, T. <i>J. Antibiotics</i> <b>1990</b> , 43, 403–410.
7.03	 <p>Monobactam Syn2190</p>	(A), C	- Nishida, K.; Kunigita, C.; Uji, T.; Higashitani, F.; Hyodo, A.; Unemi, N.; Maiti, S. N.; Phillips, O. A.; Spevak, P.; Atchison, K. P.; Salama, S. M.; Atwal, H.; Micetich, R. G. <i>Antimicrob. Agents Chemother.</i> <b>1999</b> , 43, 1895–1900.
7.04	 <p>siderophore sulfactam BAL30072</p>	C	- Page, M. G. P.; Dantier, C.; Desarbre, E. <i>Antimicrob. Agents Chemother.</i> <b>2010</b> , 54, 2291–2302. - Russo, T. A.; Page, M. G. P.; Beanan, J. M.; Olson, R.; Hujer, A. M.; Hujer, K. M.; Jacobs, M.; Bajaksouzian, S.; Endimiani, A.; Bonomo, R. A. <i>J. Antimicrob. Chemother.</i> <b>2011</b> , 66, 867–873.

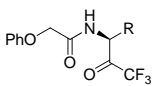
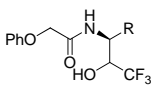
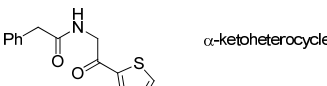
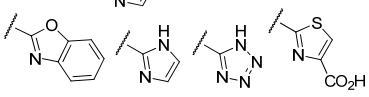
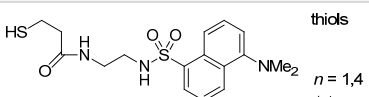
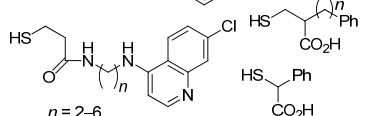
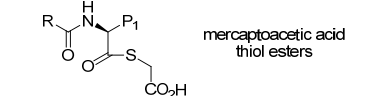
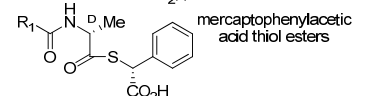
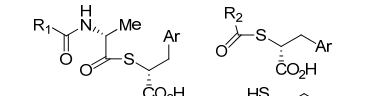
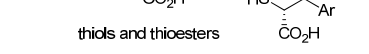
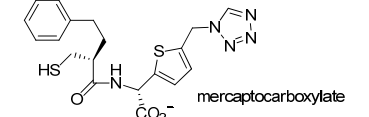
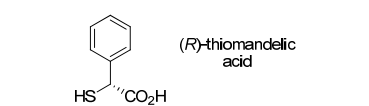
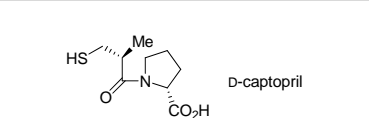


Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
<b>8. Bridged Monobactams and Avibactam Derivatives</b>			
8.01	 <p>diazabicyclo[3.2.0]heptanone sulfonic acids</p> <p>bridged monobactams</p> <p>Ro 48-1256</p>	C	<ul style="list-style-type: none"> <li>- Charnas, R.; Gubernator, K.; Heinze, I.; Hubschwerlen, C. Eur. Pat. Appl. 0508234 A2, 1992.</li> <li>- Heinze-Krauss, I.; Angehrn, P.; Charnas, R. L.; Gubernator, K.; Gutknecht, E.-M.; Hubschwerlen, C.; Kania, M.; Oefner, C.; Page, M. G. P.; Sogabe, S.; Specklin, J.-L.; Winkler, F. <i>J. Med. Chem.</i> <b>1998</b>, <i>41</i>, 3961–3971.</li> <li>- Bellettini, J. R.; Miller, M. J. <i>Tetrahedron Lett.</i> <b>1997</b>, <i>38</i>, 167–168.</li> <li>- Livermore, D. M.; Chen, H. Y. <i>J. Antimicrob. Chemother.</i> <b>1997</b>, <i>40</i>, 335–343.</li> </ul>
8.02	 <p>Avibactam</p> <p>NXL104, AVE 1330A</p>	A, C, (D)	<ul style="list-style-type: none"> <li>- Aszodi, J.; Fromentin, C.; Lampilas, M.; Rowlands, D. A. Heterocyclic compounds which are active as inhibitors of beta lactamases. PCT Int. Patent Appl. WO 2003/063864 A3, August 7, 2003.</li> <li>- Bonnefoy, A.; Dupuis-Hamelin, C.; Steier, V.; Delachaume, C.; Seys, C.; Stachyra, T.; Fairley, M.; Guitton, M.; Lampilas, M. <i>J. Antimicrob. Chemother.</i> <b>2004</b>, <i>54</i>, 410–417.</li> <li>- Livermore, D. M.; Mushtaq, S.; Warner, M.; Miossec, C.; Woodford, N. <i>J. Antimicrob. Chemother.</i> <b>2008</b>, <i>62</i>, 1053–1056.</li> <li>- Stachyra, T.; Levasseur, P.; Pêchereau, M.-C.; Girard, A.-M.; Claudon, M.; Miossec, C.; Black, M. T. <i>J. Antimicrob. Chemother.</i> <b>2009</b>, <i>64</i>, 326–329.</li> <li>- Endimiani, A.; Choudhary, Y.; Bonomo, R. A. <i>Antimicrob. Agents Chemother.</i> <b>2009</b>, <i>53</i>, 3599–3601.</li> <li>- Review: Coleman, K. <i>Curr. Opin. Microbiol.</i> <b>2011</b>, <i>14</i>, 550–555.</li> <li>- Xu, H.; Hazra, S.; Blanchard, J. S. <i>Biochemistry</i> <b>2012</b>, <i>51</i>, 4551–4557. (4df6).</li> <li>- Lahiri, S. D.; Mangani, S.; Durand-Reville, T.; Benvenuti, M.; De Luca, F.; Sanyal, G.; Docquier, J.-D. <i>Antimicrob. Agents Chemother.</i> <b>2013</b>, <i>57</i>, 2496–2506. (4HBU).</li> <li>- Ehmann, D. E.; Jahić, H.; Ross, P. L.; Gu, R.-F.; Hu, J.; Durand-Réville, T. F.; Lahiri, S.; Thresher, J.; Livchak, S.; Gao, N.; Palmer, T.; Walkup, G. K.; Fisher, S. L. <i>J. Biol. Chem.</i> <b>2013</b>, <i>288</i>, 27960–27971.</li> </ul>
8.03	 <p>NXL 105</p>	A, C	<ul style="list-style-type: none"> <li>- Lampilas, M.; Rowlands, D. A.; Keksi, A.; Ledoussal, B.; Pierres, C. Nitrogenous heterocyclic compounds, preparation thereof and use thereof as antibacterial medicaments. PCT Int. Patent Appl. WO 2008/142285 A1, November 27, 2008.</li> <li>- Review: Coleman, K. <i>Curr. Opin. Microbiol.</i> <b>2011</b>, <i>14</i>, 550–555.</li> </ul>
8.04		A, C	<ul style="list-style-type: none"> <li>- Ledoussal, B.; Gourdel, M.-E. Azabicyclic Compounds, Preparation Thereof and Use of Same as Drugs, Especially Beta-Lactamase Inhibitors. PCT Int. Pat. Appl., WO 2009/133442 A1. November 5, 2009.</li> </ul>
8.05	 <p>bridged monobactams</p> <p>MK-8712 R=H</p>	C	<ul style="list-style-type: none"> <li>- Blizzard, T. A.; Chen, H.; Kim, S.; Wu, J.; Young, K.; Park, Y.-W.; Ogawa, A.; Raghooobar, S.; Painter, R. E.; Hairston, N.; Lee, S. H.; Misura, A.; Felcetto, T.; Fitzgerald, P.; Sharma, N.; Lu, J.; Ha, S.; Hickey, E.; Hermes, J.; Hammond, M. L. <i>Bioorg. Med. Chem. Lett.</i> <b>2010</b>, <i>20</i>, 918–921.</li> <li>- Chen, H.; Blizzard, T. A.; Kim, S.; Wu, J.; Young, K.; Park, Y.-W.; Ogawa, A. M.; Raghooobar, S.; Painter, R. E.; Wisniewski, D.; Hairston, N.; Fitzgerald, P.; Sharma, N.; Scapin, G.; Lu, J.; Hermes, J.; Hammond, M. L. <i>Bioorg. Med. Chem. Lett.</i> <b>2011</b>, <i>21</i>, 4267–4270. (2WZX, 2WZZ).</li> </ul>
8.06	 <p>bridged monobactams</p> <p>MK-7655</p>	A, C	<ul style="list-style-type: none"> <li>- Miller, S. P.; Zhong, Y.-L.; Liu, Z.; Simeone, M.; Yasuda, N.; Limanto, J.; Chen, Z.; Lynch, J.; Capodanno, V. <i>Org. Lett.</i> <b>2013</b>, <i>16</i>, 174–177.</li> <li>- Blizzard, T. A.; Chen, H.; Kim, S.; Wu, J.; Bodner, R.; Gude, C.; Imbriglio, J.; Young, K.; Park, Y.-W.; Ogawa, A.; Raghooobar, S.; Hairston, N.; Painter, R. E.; Wisniewski, D.; Scapin, G.; Fitzgerald, P.; Sharma, N.; Lu, J.; Ha, S.; Hermes, J.; Hammond, M. L. <i>Bioorg. Med. Chem. Lett.</i> <b>2014</b>, <i>24</i>, 780–785.</li> </ul>
<b>9. Other <math>\beta</math>-Lactams and Analogues</b>			
9.01	 <p>6-azabicyclo[3.2.0]hept-2-enes</p>	C	<ul style="list-style-type: none"> <li>- Singh, R.; Cooper, R. D. G. <i>Tetrahedron</i> <b>1994</b>, <i>50</i>, 12049–12064.</li> </ul>

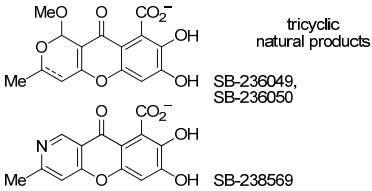
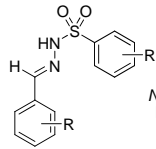
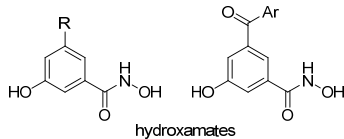
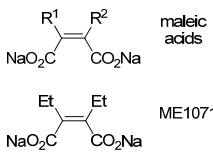
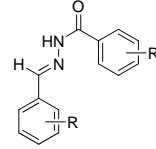
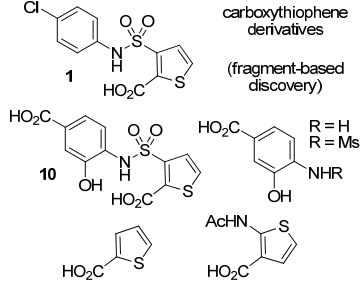
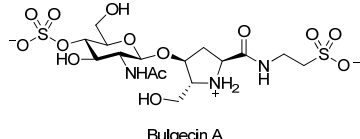
Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
9.02	 <p>sultams</p>	C	<p>- Baxter, N. J.; Laws, A. P.; Rigoreau, L.; Page, M. I. <i>J. Chem. Soc., Perkin Trans. 2</i> <b>1996</b>, 2245–2246.</p> <p>- Page, M. I.; Hinchliffe, P. S.; Wood, J. M.; Harding, L. P.; Laws, A. P. <i>Bioorg. Med. Chem. Lett.</i> <b>2003</b>, <i>13</i>, 4489–4492.</p>
9.03	 <p>R = H R = OAc</p> <p>R = N<sub>3</sub> R = NHCOBn</p>	C?	- Hanessian, S.; Buckle, R.; Bayraktarian, M. <i>J. Org. Chem.</i> <b>2002</b> , <i>67</i> , 3387–3397.
9.04	 <p>N-hydroxy cephalosporins    oximino cephalosporins</p>	B (A, C, D)	- Ganta, S. R.; Perumal, S.; Pagadala, S. R. R.; Samuelsen, Ø.; Spencer, J.; Pratt, R. F.; Buynak J. D. <i>Bioorg. Med. Chem. Lett.</i> <b>2009</b> , <i>19</i> , 1618–1622.
9.05	 <p>X = O: substrate X = S: inhibitor</p>	A, B, C, D	- Dmitrienko, G. I.; Ghavami, A.; Goodfellow, V. J.; Johnson, J. W.; Krismanich, A. P.; Marrone, L.; Viswanatha, T. Cephalosporin derivatives useful as $\beta$ -lactamase inhibitors and compositions and methods of use thereof. PCT Int. Patent Appl. WO 2011/103686 A1, September 1, 2011.
<b>10. Boronic Acids</b>			
10.01	 <p>arylboronic acids</p> <p>arylalkylboronic acids</p> <p>benzothiophene boronic acids</p>	A, C, D	<p>- Kiener, P. A.; Waley, S. G. <i>Biochem. J.</i> <b>1978</b>, <i>169</i>, 197–204.</p> <p>- Beesley, T.; Gascoyne, N.; Knott-Hunziker, V.; Perursson, S.; Waley, S. G.; Jaurin, B.; Grundström, T. <i>Biochem. J.</i> <b>1983</b>, <i>209</i>, 229–233.</p> <p>- Martin, R.; Gold, M.; Jones, J. B. <i>Bioorg. Med. Chem. Lett.</i> <b>1994</b>, <i>4</i>, 1229–1234.</p> <p>- Usher, K. C.; Blaszczak, L. C.; Weston, G. S.; Shoichet, B. K.; Remington, S. J. <i>Biochemistry</i> <b>1998</b>, <i>37</i>, 16082–16092.</p> <p>- Weston, G. S.; Blazquez, J.; Baquero, F.; Shoichet, B. K. <i>J. Med. Chem.</i> <b>1998</b>, <i>41</i>, 4577–4586.</p> <p>- Powers, R. A.; Blázquez, J.; Weston, G. S.; Morosini, M.-I.; Baquero, F.; Shoichet, B. K. <i>Protein Sci.</i> <b>1999</b>, <i>8</i>, 2330–2337. (1C3B).</p> <p>- Powers, R. A.; Shoichet, B. K. <i>J. Med. Chem.</i> <b>2002</b>, <i>45</i>, 3222–3234.</p> <p>- Venturelli, A.; Donatella, T.; Cancian, L.; Morandi, F.; Cannazza, G.; Segatore, B.; Prati, F.; Amicosante, G.; Shoichet, B. K.; Costi, M. P. <i>J. Med. Chem.</i> <b>2007</b>, <i>50</i>, 5644–5654. (2I72).</p> <p>- Chen, Y.; McReynolds, A.; Shoichet, B. K. <i>Protein Sci.</i> <b>2009</b>, <i>18</i>, 662–669. (3FKV).</p> <p>- 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. <i>Antimicrob. Agents Chemother.</i> <b>2012</b>, <i>56</i>, 2713–2718. (3RXX).</p>
10.02	 <p>boronic acids</p> <p>1: R = Bn, R' = H 2: R = H, R' = OH</p>	A	<p>- Martin, R.; Jones, J. B. <i>Tetrahedron Lett.</i> <b>1995</b>, <i>36</i>, 8399–8402.</p> <p>- Strynadka, N. C. J.; Martin, R.; Jensen, S. E.; Gold, M.; Jones, J. B. <i>Nat. Struct. Biol.</i> <b>1996</b>, <i>3</i>, 688–695. (1ERM, 1ERO, 1ERQ)</p> <p>- Ness, S.; Martin, R.; Kindler, A. M.; Paetzel, M.; Gold, M.; Jensen, S. E.; Jones, J. B.; Strynadka, N. C. J. <i>Biochemistry</i> <b>2000</b>, <i>39</i>, 5312–5321.</p>
10.03	 <p>phenylboronic acids</p>	C	- Tondi, D.; Calò, S.; Shoichet, B. K.; Costi, M. P. <i>Bioorg. Med. Chem. Lett.</i> <b>2010</b> , <i>20</i> , 3416–3419. (3BM6).

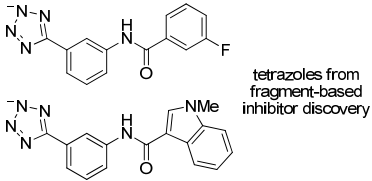
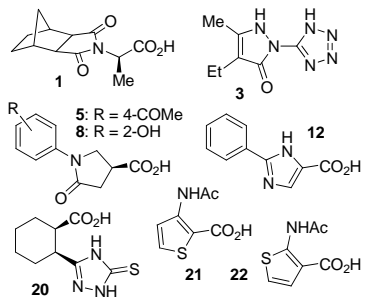
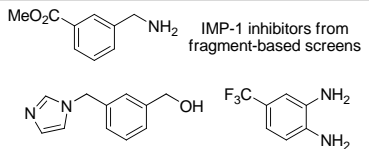
Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
10.04	 <p>boronic acids</p>	A, C	<ul style="list-style-type: none"> <li>- Caselli, E.; Powers, R. A.; Blaszczak, L. C.; Wu, C. Y. E.; Prati, F.; Shoichet, B. K. <i>Chem. Biol.</i> <b>2001</b>, <i>8</i>, 17–31.</li> <li>- Ke, W.; Sampson, J. M.; Ori, C.; Prati, F.; Drawz, S. M.; Bethel, C. R.; Bonomo, R. A.; van den Akker, F. <i>Antimicrob. Agents Chemother.</i> <b>2011</b>, <i>55</i>, 174–183.</li> </ul>
10.05	 <p>boronic acids</p> <p>R = H R = CO<sub>2</sub>H R = </p>	C	<ul style="list-style-type: none"> <li>- Roth, T. A.; Minasov, G.; Morandi, S.; Prati, F.; Shoichet, B. K. <i>Biochemistry</i> <b>2003</b>, <i>42</i>, 14483–14491.</li> <li>- Morandi, F.; Caselli, E.; Morandi, S.; Focia, P. J.; Blázquez, J.; Shoichet, B. K.; Prati, F. <i>J. Am. Chem. Soc.</i> <b>2003</b>, <i>125</i>, 685–695. (1MXO, 1MY8).</li> <li>- Chen, Y.; Minasov, G.; Roth, T. A.; Prati, F.; Shoichet, B. K. <i>J. Am. Chem. Soc.</i> <b>2006</b>, <i>128</i>, 2970–2976. (2FFY, 1PI4).</li> <li>- Shoichet, B. K.; Prati, F. Nanomolar <math>\beta</math>-Lactamase Inhibitors. U.S. Patent Appl., US 7,271,186 B1, September 18, 2007.</li> <li>- Morandi, S.; Morandi, F.; Caselli, E.; Shoichet, B. K.; Prati, F. <i>Bioorg. Med. Chem.</i> <b>2008</b>, <i>16</i>, 1195–1205. (2RCX).</li> </ul>
10.06	 <p>"DSABA"</p>	A, C, D	<ul style="list-style-type: none"> <li>- Tan, Q.; Ogawa, A. M.; Painter, R. E.; Park, Y.-W.; Young, K.; DiNinno, F. P. <i>Bioorg. Med. Chem. Lett.</i> <b>2010</b>, <i>20</i>, 2622–2624.</li> </ul>
10.07	 <p>benzoxaboroles</p>	A, C	<ul style="list-style-type: none"> <li>- Xia, Y.; Cao, K.; Zhou, Y.; Alley, M. R. K.; Rock, F.; Mohan, M.; Meewan, M.; Baker, S. J.; Lux, S.; Ding, C. Z.; Jia, G.; Kully, M.; Plattner, J. J. <i>Bioorg. Med. Chem. Lett.</i> <b>2011</b>, <i>21</i>, 2533–2536.</li> </ul>
<b>11. Phosphonates and Phosphoramidates</b>			
11.01	 <p>phosphonate monoesters</p>	A, C	<ul style="list-style-type: none"> <li>- Pratt, R. F. <i>Science</i> <b>1989</b>, <i>246</i>, 917–919.</li> <li>- Rahil, J.; Pratt, R. F. <i>Biochemistry</i> <b>1992</b>, <i>31</i>, 5869–5878.</li> <li>- Rahil, J.; Pratt, R. F. <i>Biochemistry</i> <b>1994</b>, <i>33</i>, 116–125.</li> <li>- Chen, C. C. H.; Rahil, J.; Pratt, R. F.; Herzberg, O. <i>J. Mol. Biol.</i> <b>1993</b>, <i>234</i>, 165–178. (1BLH).</li> <li>- Lobkovsky, E.; Billings, E. M.; Moews, P. C.; Rahil, J.; Pratt, R. F.; Knox, J. R. <i>Biochemistry</i> <b>1994</b>, <i>33</i>, 6762–6772.</li> <li>- Maveyraud, L.; Pratt, R. F.; Samama, J.-P. <i>Biochemistry</i> <b>1998</b>, <i>37</i>, 2622–2628. (1AXB).</li> </ul>
11.02	 <p>phosphoramidates</p>	C	<ul style="list-style-type: none"> <li>- Bateson, J. H.; Gasson, B. C.; Khushi, T.; Neale, J. E.; Payne, D. J.; Tolson, D. A.; Walker, G. <i>Bioorg. Med. Chem. Lett.</i> <b>1994</b>, <i>14</i>, 1667–1672.</li> </ul>
11.03	 <p>phosphonate transition state analogues</p>	C, PBPs	<ul style="list-style-type: none"> <li>- Nukaga, M.; Kumar, S.; Nukaga, K.; Pratt, R. F.; Knox, J. R. <i>J. Biol. Chem.</i> <b>2004</b>, <i>279</i>, 9344–9352. (1RGY, 1RGZ).</li> <li>- Silvaggi, N. R.; Anderson, J. W.; Brinsmade, S. R.; Pratt, R. F.; Kelly, J. A. <i>Biochemistry</i> <b>2003</b>, <i>42</i>, 1199–1208.</li> </ul>
11.04	 <p>O-aryloxycarbonyl hydroxamates</p>	C	<ul style="list-style-type: none"> <li>- Wyrembak, P. N.; Babaoglu, K.; Pelto, R. B.; Shoichet, B. K.; Pratt, R. F. <i>J. Am. Chem. Soc.</i> <b>2007</b>, <i>129</i>, 9548–9549. (2P9V).</li> <li>- Pelto, R. B.; Pratt, R. F. <i>Biochemistry</i> <b>2008</b>, <i>47</i>, 12037–12046.</li> </ul>
11.05	 <p>thiophenyl oxime-derived phosphonates</p>	C	<ul style="list-style-type: none"> <li>- Tan, Q.; Ogawa, A. M.; Raghoobar, S. L.; Wisniewski, D.; Colwell, L.; Park, Y.-W.; Young, K.; Hermes, J. D.; DiNinno, F. P.; Hammond, M. L. <i>Bioorg. Med. Chem. Lett.</i> <b>2011</b>, <i>21</i>, 4363–4365.</li> </ul>

Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
<b>12. Cyclobutanones</b>			
12.01	<p>2                      11: X = Cl                      13: X = H                      14: X = Cl                      4: X = H</p>		- Gordon, E. M.; Pluščec, J.; Ondetti, M. A. <i>Tetrahedron Lett.</i> <b>1981</b> , 20, 1871–1874.
12.02	<p>9b                      9d</p>		- Meth-Cohn, O.; Reason, A. J.; Roberts, S. M. <i>J. Chem. Soc., Chem. Commun.</i> <b>1982</b> , 90–92.
12.03	<p>1                      6                      12</p>	A	- Lowe, G.; Swain, S. <i>J. Chem. Soc., Chem. Commun.</i> <b>1983</b> , 1279–1281. - Lowe, G.; Swain, S. <i>J. Chem. Soc., Perkin Trans. 1</i> <b>1985</b> , 391–398.
12.04	<p>22                      10: Z = SOPh                      11: Z = SO<sub>2</sub>Ph</p>	A, PBP	- Cocuzza, A. J.; Boswell, G. A. <i>Tetrahedron Lett.</i> <b>1985</b> , 26, 5363–5366.
12.05	<p>R = H, CHPh<sub>2</sub></p>	A	- Boswell and Cocuzza (Du Pont), 1985. - Boswell, G. A.; Cocuzza, A. J. Cyclobutanone Antibacterials. U.S. Pat. Appl., US 4,505,905 A, March 19, 1985; Boswell, G. A.; Cocuzza, A. J. <i>Chem. Abstr.</i> <b>1985</b> , 103, 141731.
12.06	<p>7: R = H                      27: R = Et</p>	PBP	- Lange, G.; Savard, M. E.; Viswanatha, T.; Dmitrienko, G. I. <i>Tetrahedron Lett.</i> <b>1985</b> , 26, 1791–1794. - Kelly, J. A.; Knox, J. R.; Moews, P. C.; Hite, G. J.; Bartolone, J. B.; Zhao, H. J. <i>Biol. Chem.</i> <b>1985</b> , 260, 6449–6458. - Tomczuk, B. E. Ph.D. Thesis, University of Connecticut, 1980; <i>Diss. Abstr. Int. B</i> <b>1980</b> , 41, 576–577.
12.07			- Johnson, J. W.; Evanoff, D. P.; Savard, M. E.; Lange, G.; Ramadhar, T. R.; Assoud, A.; Taylor, N. J.; Dmitrienko, G. I. <i>J. Org. Chem.</i> <b>2008</b> , 73, 6970–6982.
12.08	<p>1: X = Cl                      2: X = H                      5: X = Cl                      6: X = H                      4<math>\alpha</math>                      4<math>\beta</math></p>	A, B, C, D	- Johnson, J. W.; Gretes, M.; Goodfellow, V. J.; Marrone, L.; Heynen, M. L.; Strynadka, N. C. J.; Dmitrienko, G. I. <i>J. Am. Chem. Soc.</i> <b>2010</b> , 132, 2558–2560. (3LCE).

Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
<b>13. Trifluoromethyl Ketones and <math>\alpha</math>-Ketoheterocycles</b>			
13.01	 trifluoromethyl ketones	B	- Walter, M. W.; Felici, A.; Galleni, M.; Soto, R. S.; Adlington, R. M.; Baldwin, J. E.; Frère, J.-M.; Gololobov, M.; Schofield, C. J. <i>Bioorg. Med. Chem. Lett.</i> <b>1996</b> , <i>6</i> , 2455–2458. - Walter, M. W.; Adlington, R. M.; Baldwin, J. E.; Schofield, C. J. <i>Tetrahedron</i> <b>1997</b> , <i>53</i> , 7275–7290. - Walter, M. W.; Adlington, R. M.; Baldwin, J. E.; Schofield, C. J. <i>J. Org. Chem.</i> <b>1998</b> , <i>63</i> , 5179–5192.
	 trifluoroethyl alcohols		
13.02	 $\alpha$ -ketoheterocycles	A, C	- Kumar, S.; Pearson, A. L.; Pratt, R. F. <i>Bioorg. Med. Chem.</i> <b>2001</b> , <i>9</i> , 2035–2044.
			
<b>14. Thiols and Thioesters</b>			
14.01	 thiols	B	- Goto, M.; Takahashi, T.; Yamashita, F.; Koreeda, A.; Mori, H.; Ohta, M.; Arakawa, Y. <i>Biol. Pharm. Bull.</i> <b>1997</b> , <i>20</i> , 1136–1140. - Jin, W.; Arakawa, Y.; Yasuzawa, H.; Taki, T.; Hashiguchi, R.; Mitsutani, K.; Shoga, A.; Yamaguchi, Y.; Kurosaki, H.; Shibata, N.; Ohta, M.; Goto, M. <i>Biol. Pharm. Bull.</i> <b>2004</b> , <i>27</i> , 851–856.
	 thioesters		
14.02	 mercaptoacetic acid thiol esters	B	- Payne, D. J.; Bateson, J. H.; Gasson, B. C.; Proctor, D.; Khushi, T.; Farmer, T. H.; Tolson, D. A.; Bell, D.; Skett, P. W.; Marshall, A. C.; Reid, R.; Ghosez, L.; Combret, Y.; Marchand-Brynaert, J. <i>Antimicrob. Agents Chemother.</i> <b>1997</b> , <i>41</i> , 135–140. - Payne, D. J.; Bateson, J. H.; Gasson, B. C.; Khushi, T.; Proctor, D.; Pearson, S. C.; Reid, R. <i>FEMS Microbiol. Lett.</i> <b>1997</b> , <i>157</i> , 171–175.
	 mercaptothiophenylacetic acid thiol esters		
14.03	 thiols	B	- Greenlee, M. L.; Laub, J. B.; Balkovec, J. M.; Hammond, M. L.; Hammond, G. G.; Pompliano, D. L.; Epstein-Toney, J. H. <i>Bioorg. Med. Chem. Lett.</i> <b>1999</b> , <i>9</i> , 2549–2554. - Hammond, G. G.; Huber, J. L.; Greenlee, M. L.; Laub, J. B.; Young, K.; Silver, L. L.; Balkovec, J. M.; Pryor, K. D.; Wu, J. K.; Leiting, B.; Pompliano, D. L.; Toney, J. H. <i>FEMS Microbiol. Lett.</i> <b>1999</b> , <i>459</i> , 289–296.
	 thioesters		
14.04	 mercaptocarboxylate	B	- 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. <i>Biochemistry</i> <b>2000</b> , <i>39</i> , 4288–4298. (1DD6).
14.05	 (R)-thi mandelic acid	B	- Mollard, C.; Moali, C.; Papamicael, C.; Damblon, C.; Vessilier, S.; Amicosante, G.; Schofield, C. J.; Galleni, M.; Frère, J.-M.; Roberts, G. C. K. <i>J. Biol. Chem.</i> <b>2001</b> , <i>276</i> , 45015–45023. - Damblon, C.; Jensen, M.; Ababou, A.; Barsukov, I.; Papamicael, C.; Schofield, C. J.; Olsen, L.; Bauer, R.; Roberts, G. C. K. <i>J. Biol. Chem.</i> <b>2003</b> , <i>278</i> , 29240–29251.
14.06	 D-captopril	B	- García-Sáez, I.; Hopkins, J.; Papamicael, C.; Franceschini, N.; Amicosante, G.; Rossolini, G. M.; Galleni, M.; Frère, J.-M.; Dideberg, O. <i>J. Biol. Chem.</i> <b>2003</b> , <i>278</i> , 23868–23873. (1M2X). - 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. <i>Org. Biomol. Chem.</i> <b>2008</b> , <i>6</i> , 2282–2294. (2QDS).

Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
14.07	<p>various charged and neutral thiols</p>	B	- Siemann, S.; Clarke, A. J.; Viswanatha, T.; Dmitrienko, G. I. <i>Biochemistry</i> <b>2003</b> , <i>42</i> , 1673–1683.
14.08	<p>penicillin-derived thiols</p>	A, B, C	- Buynak, J. D.; Chen, H. Preparation of Penicillin Derivatives as Inhibitors of Serine and Metallo- $\beta$ -Lactamases. PCT Int. Pat. Appl. WO 03/087105 A1, October 23, 2003. - Buynak, J. D.; Chen, H.; Vogeti, L.; Gadhachanda, V. R.; Buchanan, C. A.; Palzkill, T.; Shaw, R. W.; Spencer, J.; Walsh, T. R. <i>Bioorg. Med. Chem. Lett.</i> <b>2004</b> , <i>14</i> , 1299–1304. - Beharry, Z.; Chen, H.; Gadhachanda, V. R.; Buynak, J. D.; Palzkill, T. <i>Biochem. Biophys. Research Commun.</i> <b>2004</b> , <i>313</i> , 541–545.
14.09	<p>thiols</p>	B	- Kurosaki, H.; Yamaguchi, Y.; Higashi, T.; Soga, K.; Matsueda, S.; Yumoto, H.; Misumi, S.; Yamagata, Y.; Arakawa, Y.; Goto, M. <i>Angew. Chem. Int. Ed.</i> <b>2005</b> , <i>44</i> , 3861–3864. (1VGN).
14.10	<p><math>n = 2-6</math>                      dansyl-derived thiols</p>	B	- Kurosaki, H.; Yamaguchi, Y.; Yasuzawa, H.; Jin, W.; Yamagata, Y.; Arakawa, Y. <i>ChemMedChem</i> <b>2006</b> , <i>1</i> , 969–972. (2DOO).
14.11	<p>(<math>\pm</math>)                      mercaptocarboxylate</p>	B	- Yamaguchi, Y.; Jin, W.; Matsunaga, K.; Ikemizu, S.; Yamagata, Y.; Wachino, J.-i. Shibata, N.; Arakawa, Y.; Kurosaki, H. <i>J. Med. Chem.</i> <b>2007</b> , <i>50</i> , 6647–6653. (2YZ3).
14.12	<p>RSH library</p> <p>Bchl</p> <p><math>K_i = 6 \mu\text{M}</math></p> <p><math>K_i = 0.74 \mu\text{M}</math></p>	B	- Liénard, B. M. R.; Selevsek, N.; Oldham, N. J.; Schofield, C. J. <i>ChemMedChem</i> <b>2007</b> , <i>2</i> , 175–179. - Liénard, B. M. R.; Hüting, R.; Lassaux, P.; Galleni, M.; Frère, J.-M.; Schofield, C. J. <i>J. Med. Chem.</i> <b>2008</b> , <i>51</i> , 684–688.
<b>15. Carboxylates, Tetrazoles, and Hydroxamates</b>			
15.01	<p>biphenyl tetrazoles</p> <p>L-159,061</p> <p><i>n</i>-Bu</p>	B	- 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. <i>Chem. Biol.</i> <b>1998</b> , <i>5</i> , 185–196. (1A8T). - Toney, J. H.; Cleary, K. A.; Hammond, G. G.; Yuan, X.; May, W. J.; Hutchins, S. M.; Ashton, W. T.; Vanderwall, D. E. <i>Bioorg. Med. Chem. Lett.</i> <b>1999</b> , <i>9</i> , 2741–2746.
15.02	<p>succinic acids</p>	B	- 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. <i>J. Biol. Chem.</i> <b>2001</b> , <i>276</i> , 31913–31918. (1JJE, 1JJT). - Moloughney, J. G.; Thomas, J. D.; Toney, J. H. <i>FEMS Microbiol. Lett.</i> <b>2005</b> , <i>243</i> , 65–71.

Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
15.03	 <p>tricyclic natural products            SB-236049, SB-236050            SB-238569</p>	B	- 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. <i>Antimicrob. Agents Chemother.</i> <b>2002</b> , <i>46</i> , 1880–1886. (1HLK, 1KR3).
15.04	 <p>N-arylsulfonyl hydrazones</p>	B	- Siemann, S.; Evanoff, D. P.; Marrone, L.; Clarke, A. J.; Viswanatha, T.; Dmitrienko, G. I. <i>Antimicrob. Agents Chemother.</i> <b>2002</b> , <i>46</i> , 2450–2457.
15.05	 <p>hydroxamates</p>	B	- Liénard, B. M. R.; Horsfall, L. E.; Galleni, M.; Frère, J.-M.; Schofield, C. J. <i>Bioorg. Med. Chem. Lett.</i> <b>2007</b> , <i>17</i> , 964–968.
15.06	 <p>maleic acids            ME1071</p>	B	- Chikauchi, K.; Kurazono, M.; Abe, T.; Hiraiwa, Y.; Morinaka, A.; Kudo, T. Metallo- $\beta$ -Lactamase Inhibitors Containing Maleic Acid Derivatives, and Use Thereof with $\beta$ -Lactam Antibiotics. PCT Int. Pat. Appl. WO 2007/034924 A1, March 29, 2007. - Chikauchi, K.; Ida, M.; Abe, T.; Hiraiwa, Y.; Morinaka, A.; Kudo, T. Preparation of Maleic Acid Derivatives as Metallo- $\beta$ -Lactamase Inhibitors. U.S. Pat. Appl. US 2008/090825 A1, April 17, 2008. - Morinaka, A.; Konnai, T.; Ida, M.; Abe, T.; Hiraiwa, Y.; Kudo, T. Pharmaceutical Compositions Containing Maleic Acid Derivatives and Cephem Antibiotics. JP 2009/040743, February 26, 2009. - Ishii, Y.; Eto, M.; Mano, Y.; Tateda, K.; Yamaguchi, K. <i>Antimicrob. Agents Chemother.</i> <b>2010</b> , <i>54</i> , 3625–3629.
15.07	 <p>N-acyl hydrazones</p>	B, D	- Dmitrienko, G. I.; Johnson, J. W.; Ramadhar, T. R.; Viswanatha, T.; Viswanatha, S. $\beta$ -Lactamase Inhibitors. U.S. Pat. Appl., US 2011/0046101 A1, February 24, 2011.
<b>16. Other Noncovalent Inhibitors</b>			
16.01	 <p>carboxythiophene derivatives            (fragment-based discovery)</p>	C	- Powers, R. A.; Morandi, F.; Shoichet, B. K. <i>Structure</i> <b>2002</b> , <i>10</i> , 1013–1023. - Tondi, D.; Morandi, F.; Bonnet, R.; Costi, M. P.; Shoichet, B. K. <i>J. Am. Chem. Soc.</i> <b>2005</b> , <i>127</i> , 4632–4639. (1XGJ, 1XGI). - Babaoglu, K.; Shoichet, B. K. <i>Nat. Chem. Biol.</i> <b>2006</b> , <i>12</i> , 720–723. (2HDQ, 2HDR, 2HDS, 2HDU).
16.02	 <p>Bulgecin A</p>	B	- Simm, A. M.; Loveridge, E. J.; Crosby, J.; Avison, M. B.; Walsh, T. R.; Bennett, P. M. <i>Biochem. J.</i> <b>2005</b> , <i>387</i> , 585–590.

Entry	$\beta$ -Lactamase Inhibitor Structural Type	Target Classes	References
16.03	 <p>tetrazoles from fragment-based inhibitor discovery</p>	A,(C)	- Chen, Y.; Shoichet, B. K. <i>Nat. Chem. Biol.</i> <b>2009</b> , <i>5</i> , 358–364.
16.04	 <p>1 2 3 4 5: R = 4-COMe 8: R = 2-OH 12 20 21 22</p>	C	- Teotico, D. G.; Babaoglu, K.; Rocklin, G. J.; Ferreira, R. S.; Giannetti, A. M.; Shoichet, B. K. <i>Proc. Natl. Acad. Sci., U.S.A.</i> <b>2009</b> , <i>106</i> , 7455–7460. (PDB: 3GSG, 3GR2, 3GQZ, 3GVB, 3GRJ, 3GTC, 3GV9, 2HDU).
16.05	 <p>IMP-1 inhibitors from fragment-based screens</p>	B	- Vella, P.; Hussein, W. M.; Leung, E. W. W.; Clayton, D.; Ollis, D. L.; Mitić, N.; Schenk, G.; McGearry, R. P. <i>Bioorg. Med. Chem. Lett.</i> <b>2011</b> , <i>21</i> , 3282–3285.