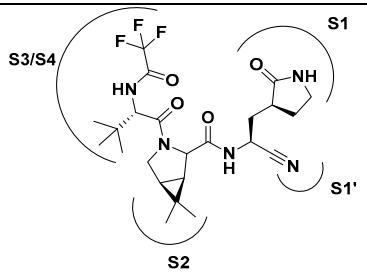
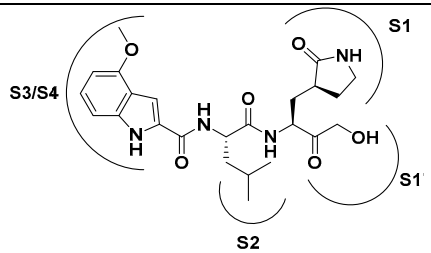
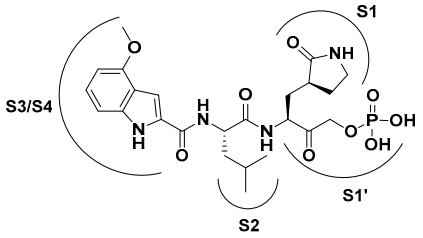
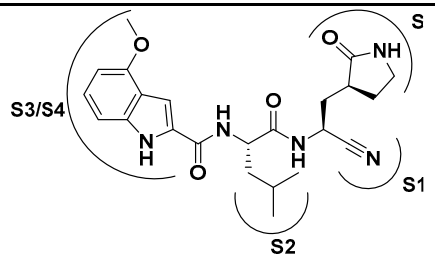
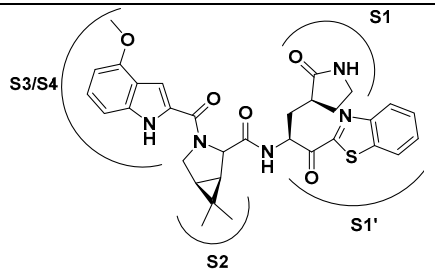
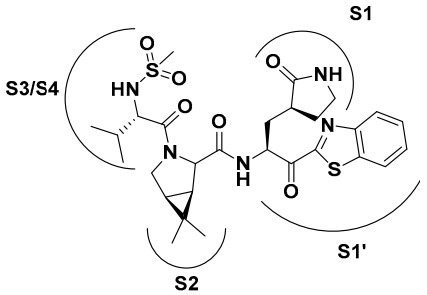
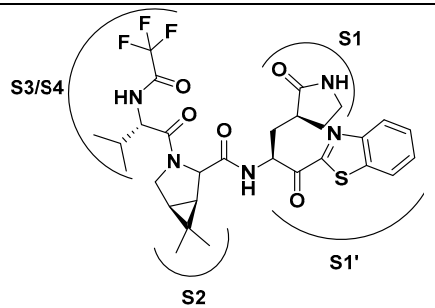
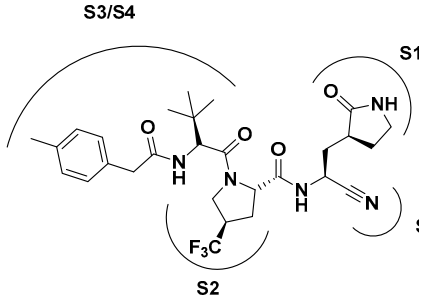
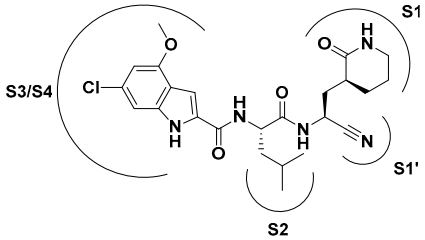
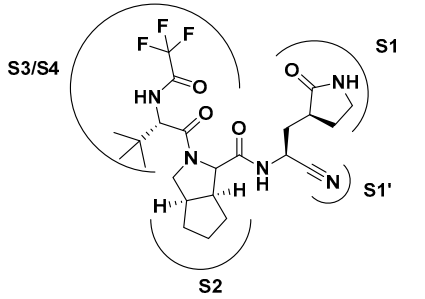
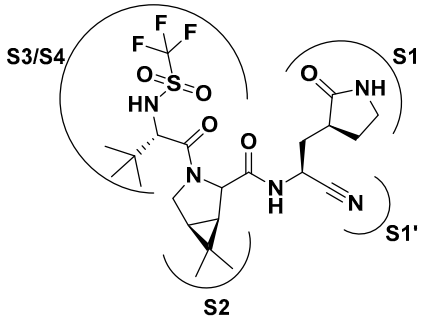
Supplementary Material for:

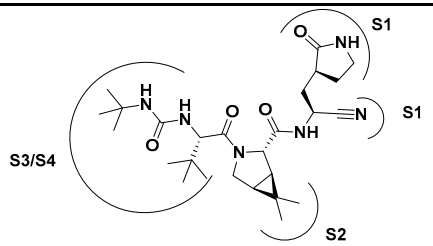
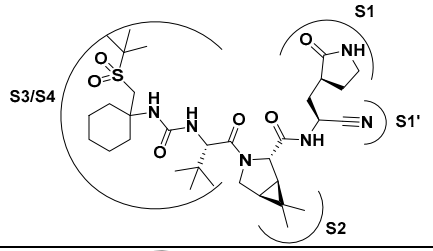
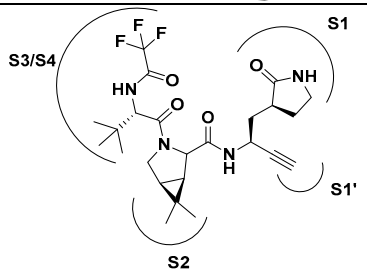
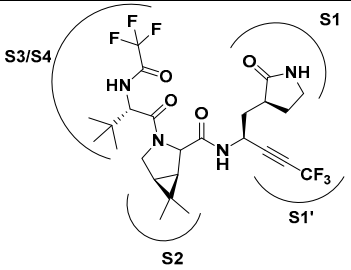
Recent Advances in SARS-CoV-2 Main Protease Inhibitors: From Nirmatrelvir to Future Perspectives

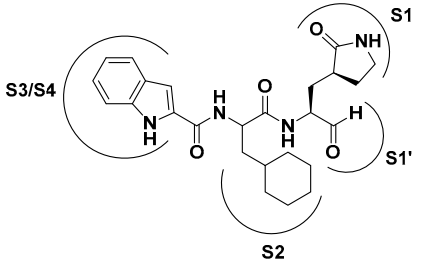
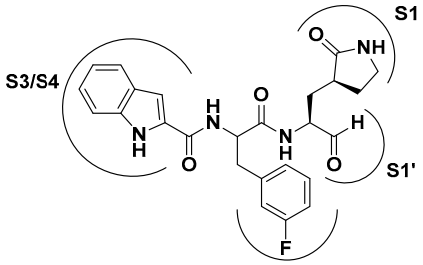
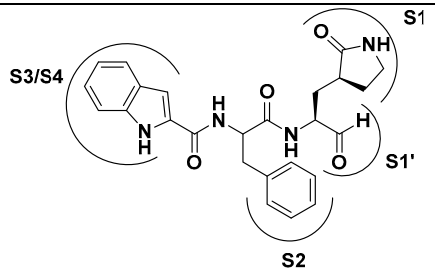
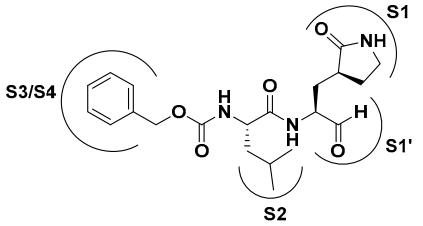
Table S1. Most relevant SARS-CoV-2 M^{pro} inhibitors discovered so far.

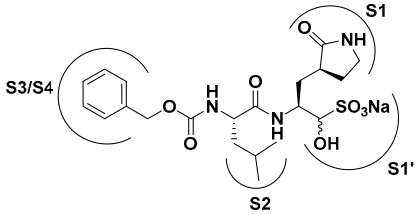
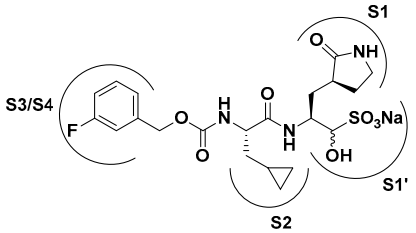
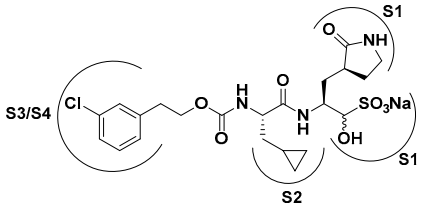
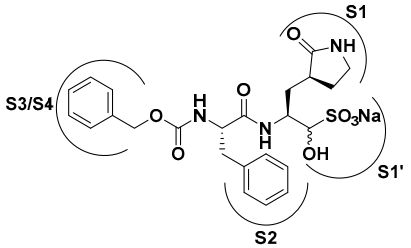
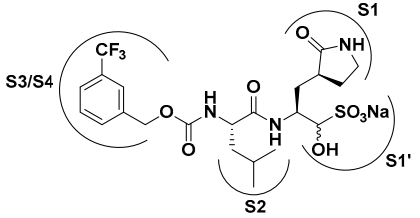
Compound	Chemical class	Structure	IC_{50} (nM)[a]	Mechanism	EC_{50} (μM)[c]	Discovery method	References
1 NIRMATRELVIR	Nitriles		3.11[b]	Covalent Reversible	0.075	Lead optimization	[1]
2 PF-00835231	Hydroxy ketones		4[b]	Covalent Reversible	0.23	Drug repurposing	[1]
3 PF-07304814	Hydroxy ketones (phosphate prodrug)		27.9[b]	Covalent Reversible	1.4	Drug repurposing	[1]

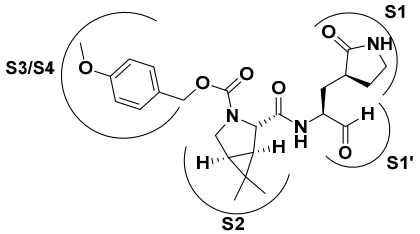
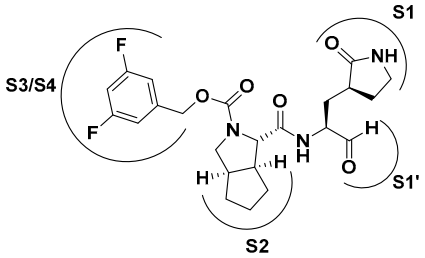
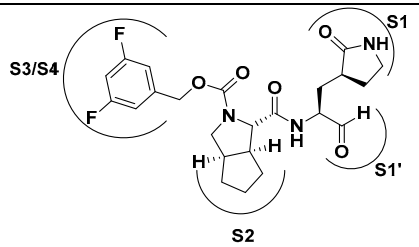
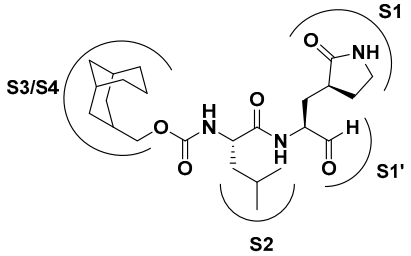
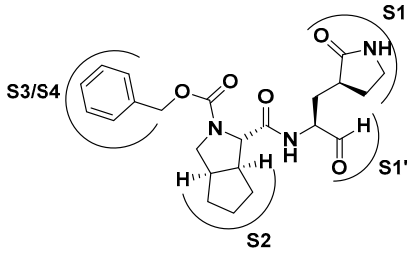
4	Nitriles		27.7[b]	Covalent Reversible	1.4	Lead optimization	[1]
5	Ketones		230[b]	Covalent Reversible	5.6	Lead optimization	[1]
6	Ketones		7.93[b]	Covalent Reversible	0.9	Lead optimization	[1]
7	Ketones		12.1[b]	Covalent Reversible	0.85	Lead optimization	[1]

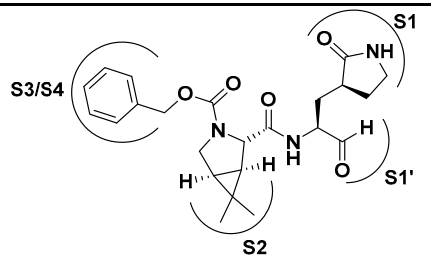
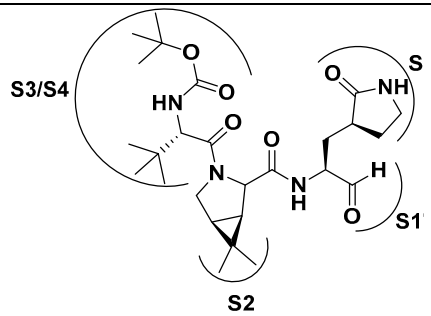
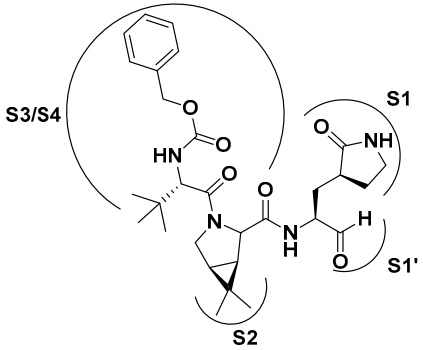
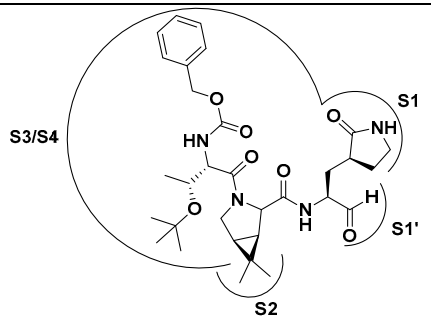
8	Nitriles		4[b]	Covalent Reversible	0.019	Lead optimization	[2]
9	Nitriles		9[b]	Covalent Reversible	2.2	Lead optimization	[3]
10	Nitriles		18	Covalent Reversible	0.31	Lead optimization	[4]
11	Nitriles		22	Covalent Reversible	0.17	Lead optimization	[4]

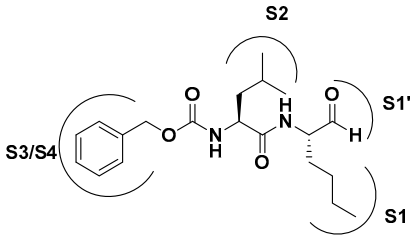
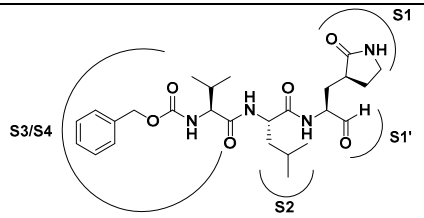
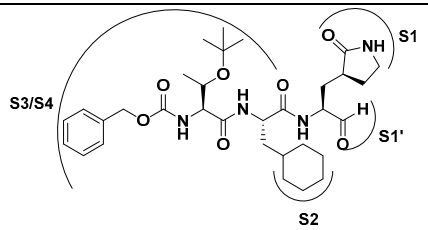
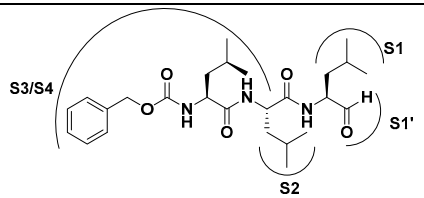
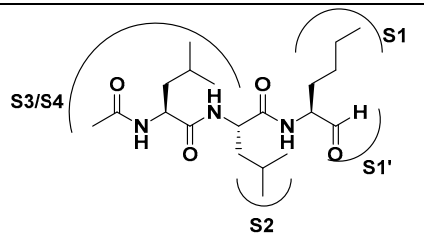
12 **BBH-2**	**Nitriles**		**26**[d]	**Covalent** **Reversible**	**0.88**	**Lead** **optimization**	[5]
13 **NBH-2**	**Nitriles**		**30**[d]	**Covalent** **Reversible**	**1.82**	**Lead** **optimization**	[5]
14	**Alkynes**		**140**	**Covalent** **Irreversible**	**25.7**	**Lead** **optimization**	[6]
15	**Alkynes**		**230**	**Covalent** **Irreversible**	**5.1**	**Lead** **optimization**	[6]

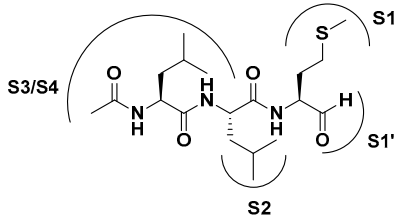
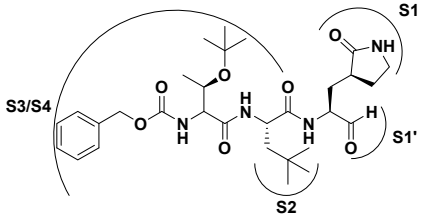
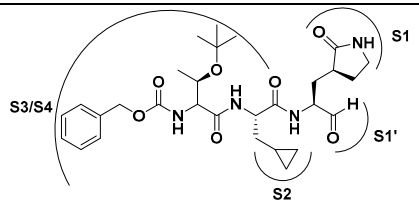
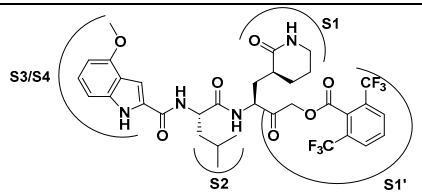
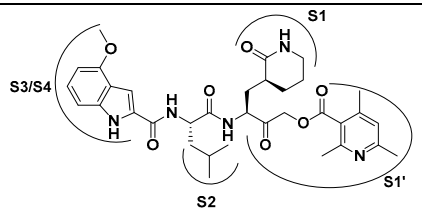
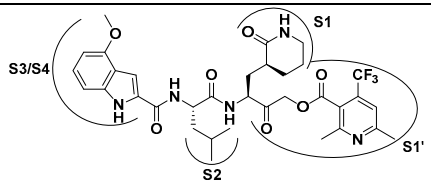
16	**Aldehydes**		**53**	**Covalent Reversible**	**0.53**	**Structure-based design**	[7]
17	**Aldehydes**		**40**	**Covalent Reversible**	**0.72**	**Structure-based design**	[7]
18	**Aldehydes**		**34**	**Covalent Reversible**	**0.29**	**Lead optimization**	[8]
19 GC-373	**Aldehydes**		**400**	**Covalent Reversible**	**1.5**	**Drug repurposing**	[9]

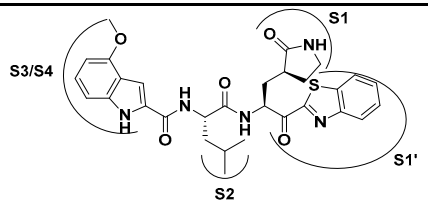
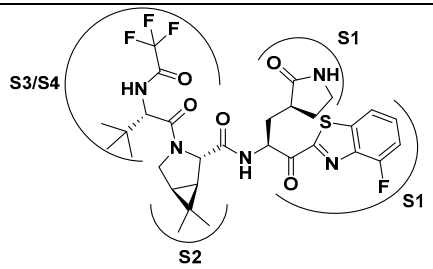
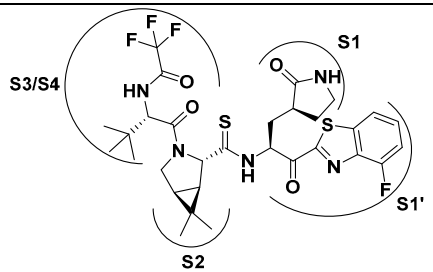
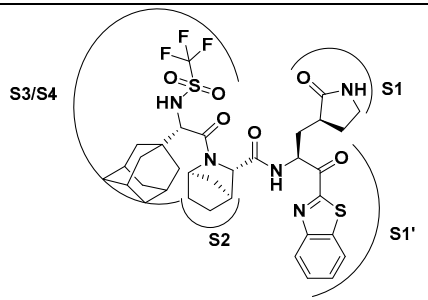
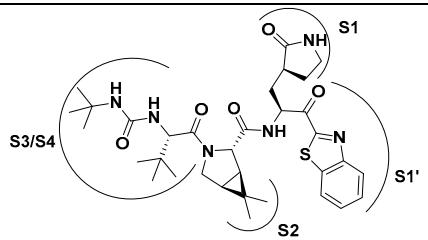
20 **GC-376**	**Aldehydes (phosphate prodrug)**		**190**	**Covalent Reversible**	**0.9**	**Drug repurposing**	[9]
21	**Aldehydes (phosphate prodrug)**		**70**	**Covalent Reversible**	**0.57**	**Lead optimization**	[10]
22	**Aldehydes (phosphate prodrug)**		**80**	**Covalent Reversible**	**0.7**	**Lead optimization**	[10]
23 **UAWJ247**	**Aldehydes (phosphate prodrug)**		**45**	**Covalent Reversible**	**6.8**	**Lead optimization**	[11]
24 **Coronastat**	**Aldehydes (phosphate prodrug)**		**16**	**Covalent Reversible**	**0.006**	**Lead optimization**	[12]

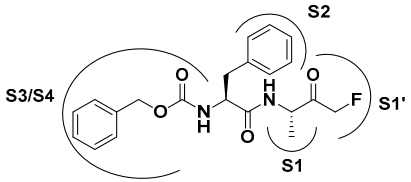
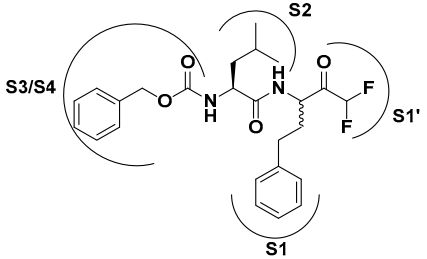
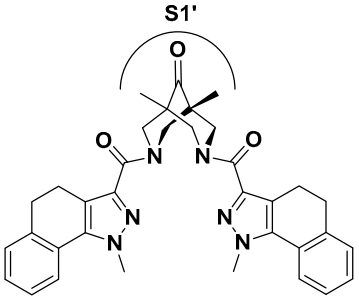
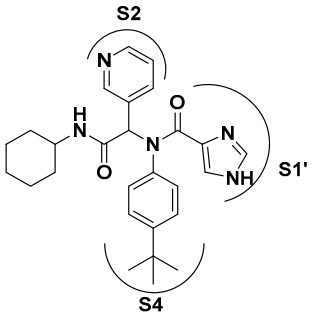
25 **MI-09**	**Aldehydes**		**15.2**	**Covalent Reversible**	**0.86**	**Structure-based design**	[13]
26 **Mi-23**	**Aldehydes**		**7.6**	**Covalent Reversible**	**n.d.**	**Structure-based design**	[13]
27 **MI-30**	**Aldehydes**		**17.2**	**Covalent Reversible**	**0.54**	**Structure-based design**	[13]
28	**Aldehydes**		**180**	**Covalent Reversible**	**0.035**	**Lead optimization**	[14]
29 **UAWJ9-36-1**	**Aldehydes**		**51**	**Covalent Reversible**	**2.6**	**Rational design**	[15]

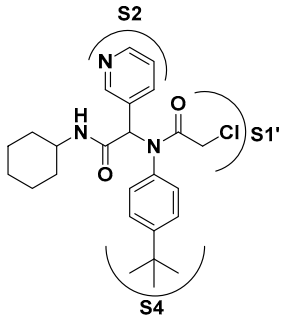
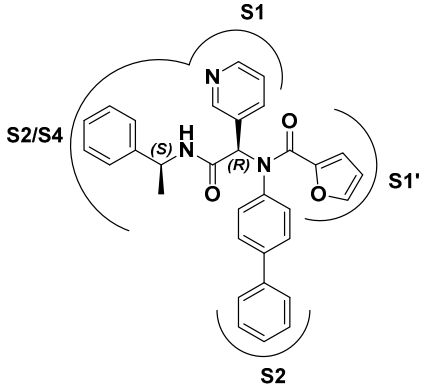
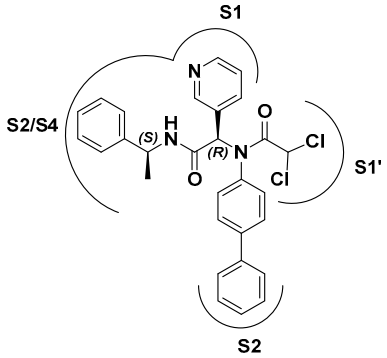
30 **UAWJ9-36-3**	**Aldehydes**		**54**	**Covalent Reversible**	**0.37**	**Rational design**	[15]
31 **MPI143**	**Aldehydes**		**45**	**Covalent Reversible**	**0.4 – 1.0[e]**	**Structure-based design**	[16]
32 **MPI144**	**Aldehydes**		**59**	**Covalent Reversible**	**0.9 – 2.9[e]**	**Structure-based design**	[16]
33 **MPI146**	**Aldehydes**		**120**	**Covalent Reversible**	**0.8 – 2.3[e]**	**Structure-based design**	[16]

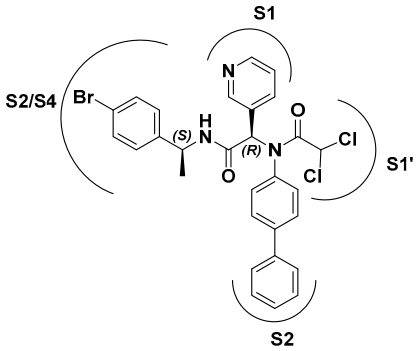
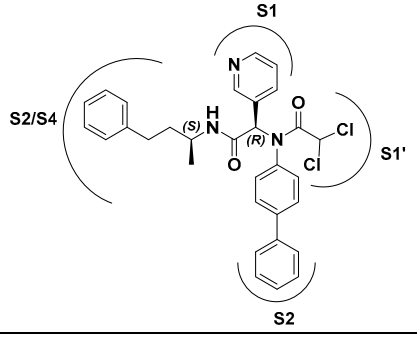
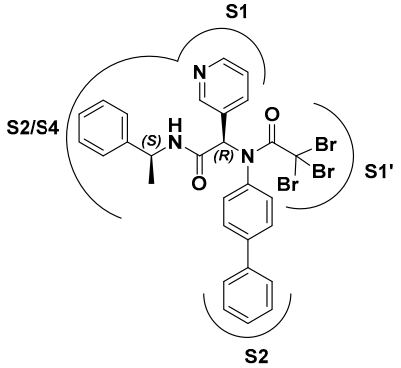
34 **Calpeptin**	**Aldehydes**		**10700**	**Covalent Reversible**	**0.072**	**X-ray screening**	[17]
35 **MPI3**	**Aldehydes**		**8.5**	**Covalent Reversible**	**n.d.**	**Structure-based design**	[18]
36 **MPI8**	**Aldehydes**		**108**	**Covalent Reversible**	**2.5**	**Structure-based design**	[18]
37 **MGI132**	**Aldehydes**		**7500**	**Covalent Reversible**	**n.d.**	**Drug repurposing**	[19]
38 **Calpain inhibitor I**	**Aldehydes**		**970**	**Covalent Reversible**	**n.d.**	**Drug repurposing**	[11]

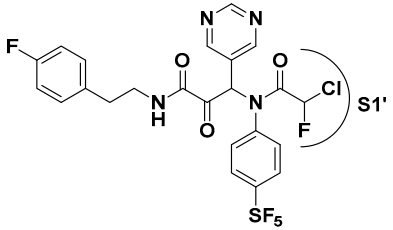
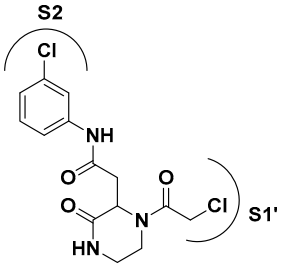
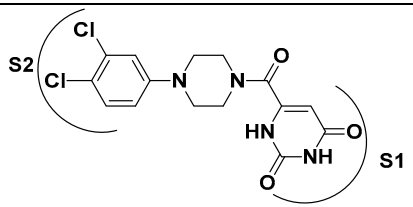
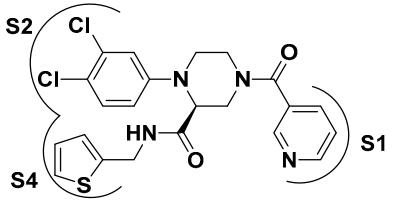
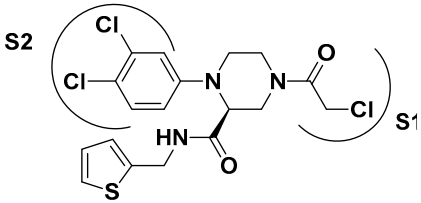
39 **Calpain inhibitor II**	**Aldehydes**		**8600**	**Covalent Reversible**	**2.07**	**Drug repurposing**	[11]
40 **MPI16**	**Aldehydes**		**105**	**Covalent Reversible**	**0.056**	**Lead optimization**	[20]
41 **MPI17**	**Aldehydes**		**60**	**Covalent Reversible**	**0.097**	**Lead optimization**	[20]
42	**Ketones**		**1.0**	**Covalent Reversible**	**0.16**	**Structure-based design**	[21]
43	**Ketones**		**19.0**	**Covalent Reversible**	**0.3**	**Structure-based design**	[21]
44	**Ketones**		**14.0**	**Covalent Reversible**	**0.47**	**Structure-based design**	[21]

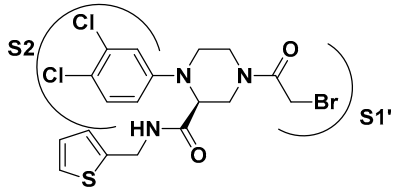
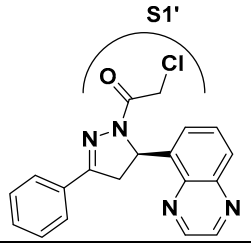
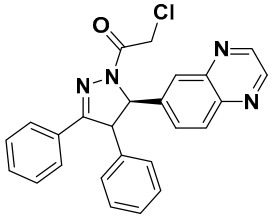
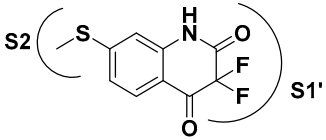
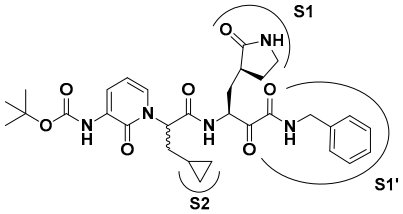
45 **YH-53**	**Ketones**		**130**	**Covalent Reversible**	**2.6**	**Drug repurposing**	[22]
46 **TKB245**	**Ketones**		**7**	**Covalent Reversible**	**0.03**	**Lead optimization**	[23]
47 **TKB248**	**Ketones**		**74**	**Covalent Reversible**	**0.22**	**Lead optimization**	[23]
48	**Ketones**		**1650**	**Covalent Reversible**	**0.18**	**Lead optimization**	[24]
49 **BBH1**	**Ketones**		**n.d.**	**Covalent Reversible**	**16.1**	**Lead optimization**	[5]

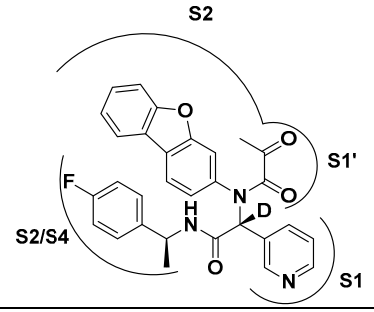
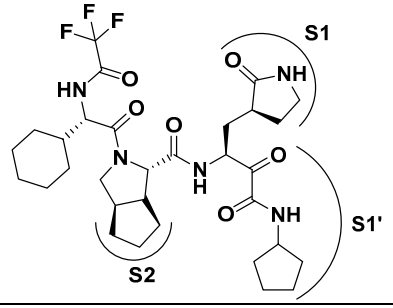
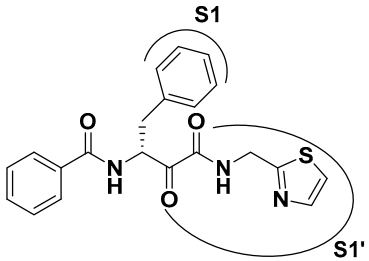
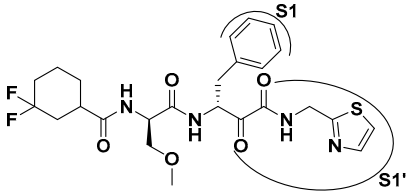
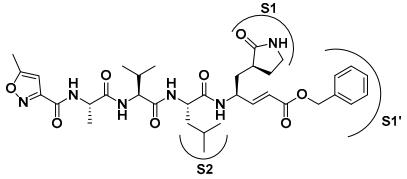
50 **Z-FA-FMK**	**Ketones**		**11400**	**Covalent Irreversible**	**0.13**	**High throughput screening**	[25]
52	**Ketones**		**n.d.**	**Covalent Reversible**	**12.9[f]**	**Warhead modification**	[26]
53	**Ketones**		**750**	**Covalent Reversible**	**n.d.**	**Structure-based design**	[27]
54 **X77**	**Miscellaneous**		**4100**	**Non Covalent**	**n.d.**	**n.d.**	[28]

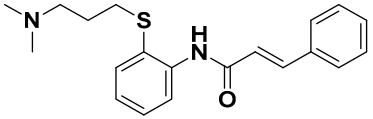
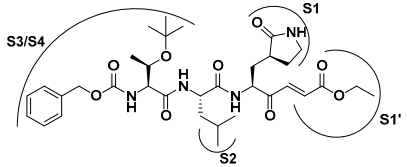
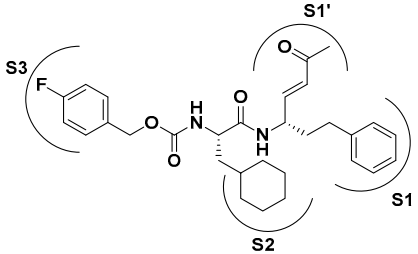
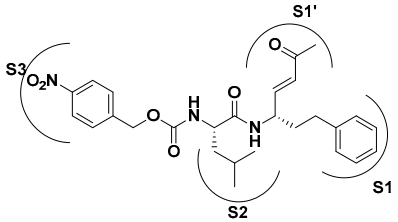
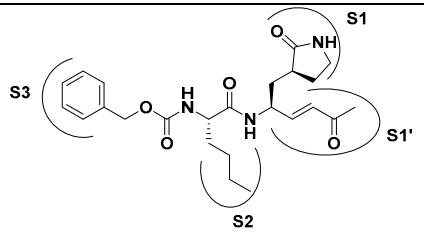
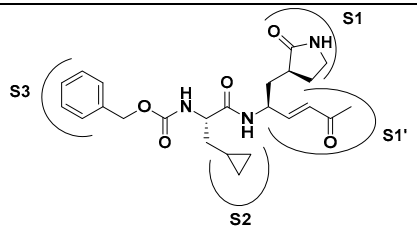
55	**α-haloacetamides**		**410**	**Covalent Irreversible**	**n.d.**	**Covalent docking**	[28]
56 23R	**Miscellaneous**		**200**	**Non Covalent**	**1.4**	**Structure-based design**	[29]
57 JUN9-62-2R	**α-haloacetamides**		**430**	**Covalent Irreversible**	**0.90**	**Warhead replacemnt**	[30]

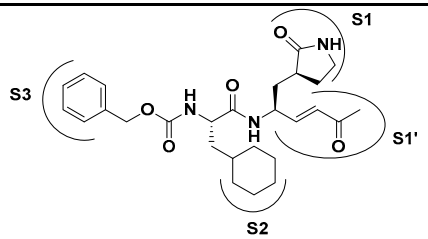
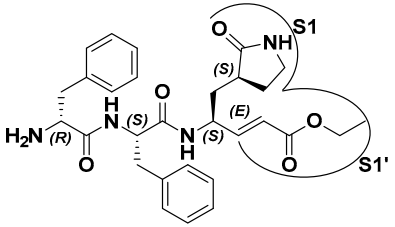
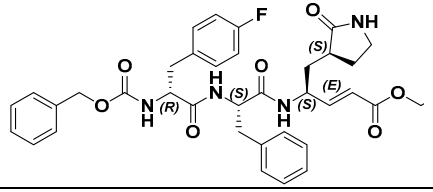
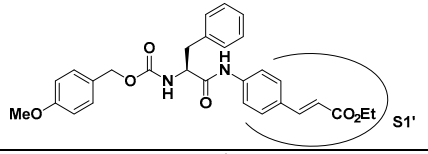
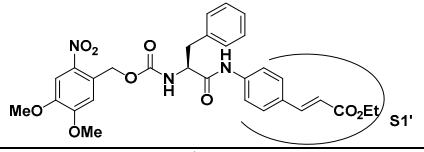
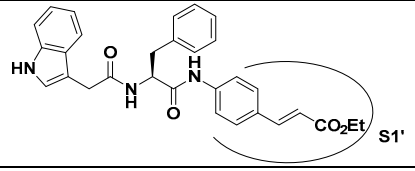
58 **JUN9-90-3R**	**α-haloacetamides**		**300**	**Covalent Irreversible**	**2.07**	**Warhead replacemnt**	[30]
59 **JUN9-90-4R**	**α-haloacetamides**		**460**	**Covalent Irreversible**	**1.10**	**Warhead replacemnt**	[30]
60 **JUN9-88-6R**	**α-haloacetamides**		**80**	**Covalent Irreversible**	**0.58**	**Warhead replacemnt**	[30]

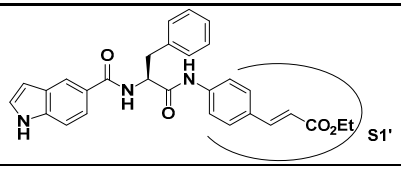
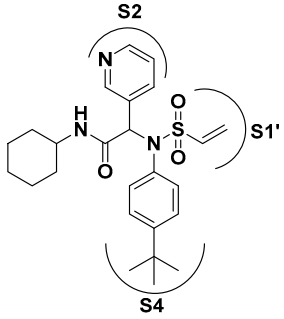
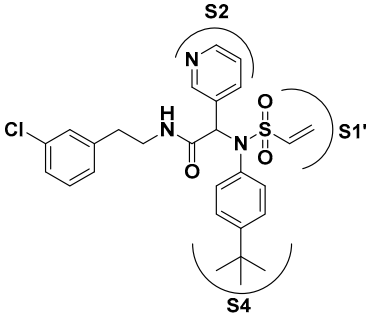
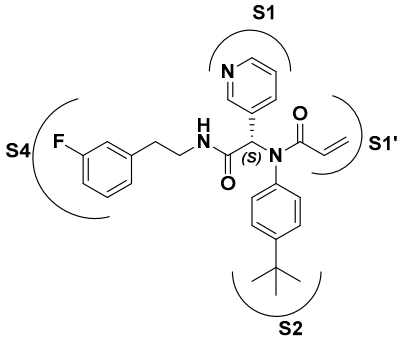
61	**α-haloacetamides**		**56**	**Covalent Reversible**	**n.d.**	**Lead optimization**	[31]
62 Y020-9948	**α-haloacetamides**		**8500**	**Covalent Irreversible**	**n.d.**	**In silico screening and covalent docking**	[32]
63 MCULE-5948770040	**Miscellaneous**		**4200**	**Non Covalent**	**n.d.**	**High throughput screening**	[33]
64 GC-14	**Miscellaneous**		**400**	**Non Covalent**	**1.1**	**Structure-based design**	[34]
65 GD9	**α-haloacetamides**		**180**	**Covalent Irreversible**	**2.6**	**Warhead replacement**	[35]

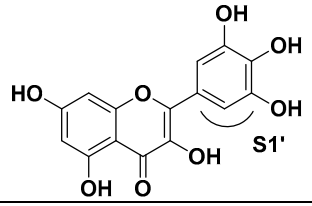
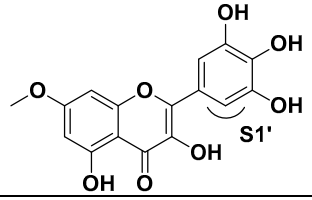
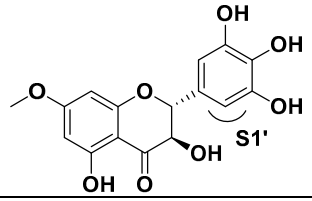
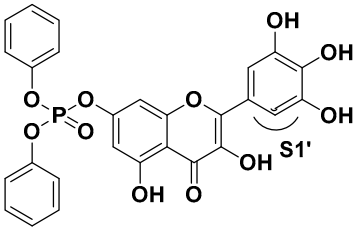
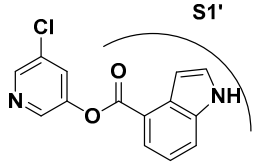
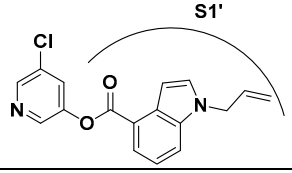
66 **GD13**	**α-haloacetamides**		**310**	**Covalent Irreversible**	**4.2**	**Warhead replacement**	[35]
67 **(R)-EN82**	**α-haloacetamides**		**530**	**Covalent Irreversible**	**n.d.**	**Covalent chemoproteomic strategies and structure-based design**	[36]
68 **HW-2-010b**	**α-haloacetamides**		**14**	**Covalent Irreversible**	**n.d.**	**Covalent chemoproteomic strategies and structure-based design**	[36]
69 **QUB-00006-Int-07**	**α-haloacetamides**		**830**	**Covalent**	**n.d.**	***In silico* strategies**	[37]
70	**α-ketoamides**		**670**	**Covalent Reversible**	**4-5**	**Lead optimization**	[38]

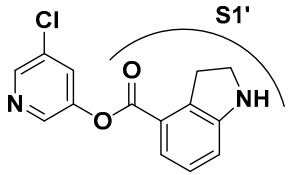
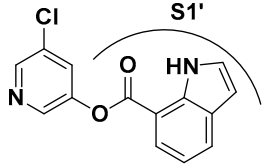
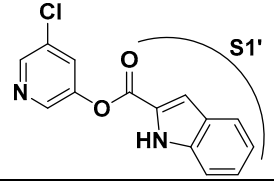
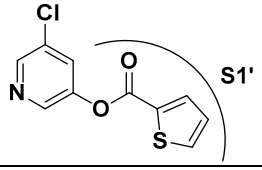
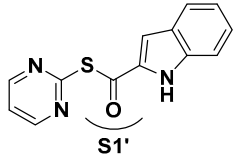
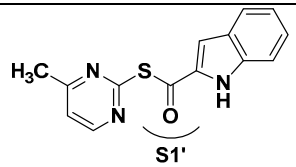
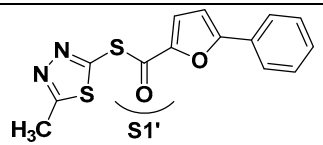
71 **Y180**	**α-ketoamides**		**8.1**	**Covalent Reversible**	**0.011**	**Structure-based design**	[39]
72 **RAY1216**	**α-ketoamides**		**8.4**[b]	**Covalent Reversible**	**0.13**	**Lead optimization**	[40]
73	**α-ketoamides**		**1300**	**Covalent Reversible**	**n.d.**	***In vitro* screening**	[41]
74 **SY110**	**α-ketoamides**		**14.4**	**Covalent Reversible**	**0.38 – 2.8**[e]	**Lead optimization**	[41]
75 **N3**	**Michael Acceptors**		**n.d.**	**Covalent Irreversible**	**16.8**	**Computer-aided drug design**	[42]

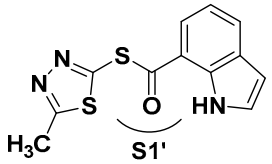
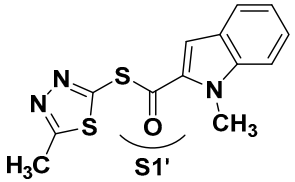
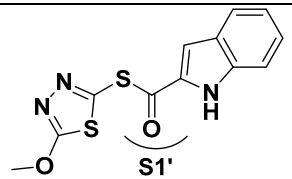
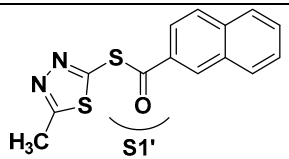
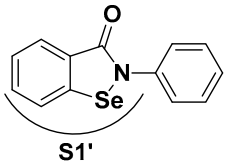
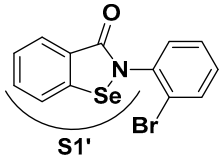
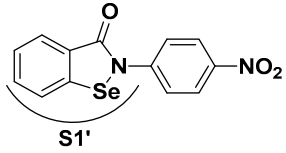
76 **CINANSERIN**	**Michael Acceptors**		**125000**	**Covalent Irreversible**	**20.6**	**Virtual screening**	[42]
77	**Michael Acceptors**		**151**	**Covalent Irreversible**	**2.9**	***In vitro* screening**	[43]
78	**Michael Acceptors**		**47200**	**Covalent Irreversible**	**n.d.**	**Virtual screening**	[44]
79	**Michael Acceptors**		**157000**	**Covalent Irreversible**	**n.d.**	**Virtual screening**	[44]
80 **SPR38**	**Michael Acceptors**		**260[b]**	**Covalent Irreversible**	**18.5**	**Lead optimization**	[45]
81 **SPR39**	**Michael Acceptors**		**250[b]**	**Covalent Irreversible**	**1.5**	**Lead optimization**	[45]

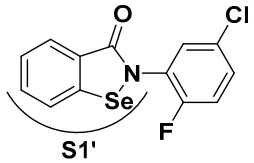
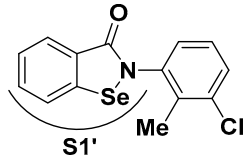
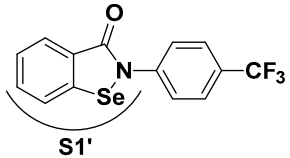
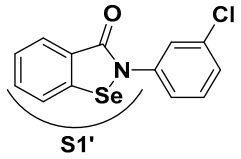
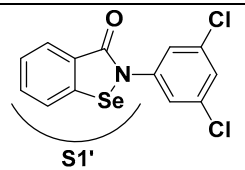
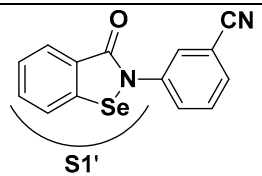
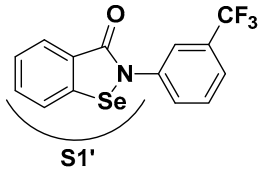
82 **SPR41**	**Michael Acceptors**		**180**[b]	**Covalent Irreversible**	**1.8**	**Lead optimization**	[45]
83 **SM141**	**Michael Acceptors**		**900**	**Covalent Irreversible**	**0.0082**	**Lead optimization**	[46]
84 **SM142**	**Michael Acceptors**		**1800**	**Covalent Irreversible**	**0.0147**	**Lead optimization**	[46]
85	**Michael Acceptors**		**1900**	**Covalent Irreversible**	**n.d.**	**Warhead replacement**	[47]
86	**Michael Acceptors**		**14000**	**Covalent Irreversible**	**5.3**[f]	**Warhead replacement**	[47]
87	**Michael Acceptors**		**12400**	**Covalent Irreversible**	**9.1**[g]	**Warhead replacement**	[47]

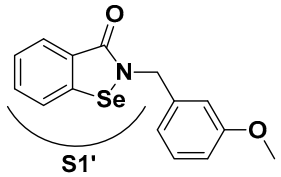
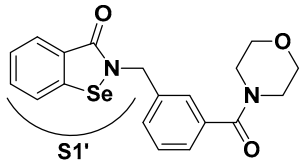
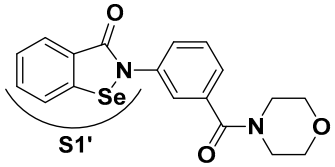
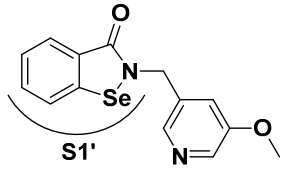
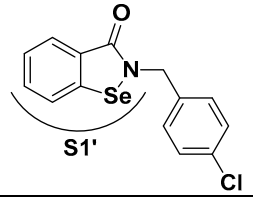
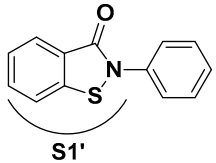
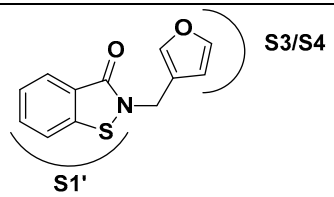
88	**Michael Acceptors**		**10100**	**Covalent Irreversible**	**10.1[g]**	**Warhead replacement**	[47]
89	**Michael Acceptors**		**420**	**Covalent Irreversible**	**n.d.**	**Covalent docking**	[28]
90	**Michael Acceptors**		**170**	**Covalent Irreversible**	**n.d.**	**Covalent docking**	[28]
92	**Michael Acceptors**		**2860**	**Covalent Irreversible**	**n.d.**	**Automatic pipeline**	[48]

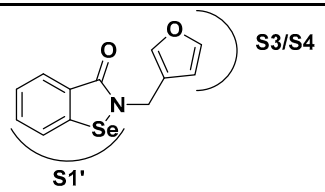
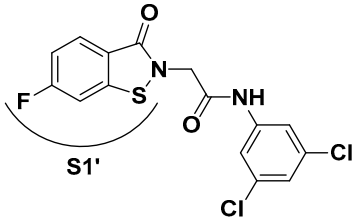
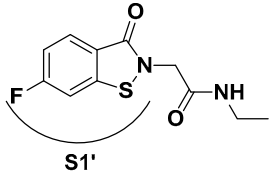
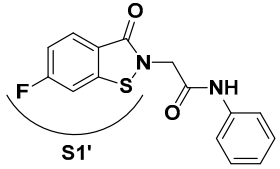
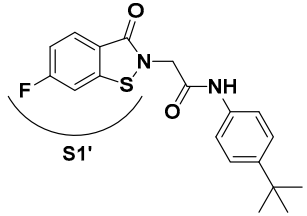
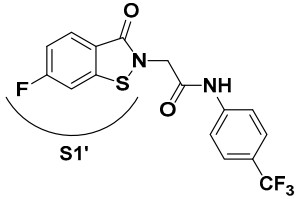
93 **MYRECITIN**	**Michael Acceptors**		**200 - 600**	**Covalent Irreversible**	**8**	**in Vitro Repurposing Screen**	[49]
94	**Michael Acceptors**		**300**	**Covalent Irreversible**	**12.6**	**Structure-based optimization**	[50]
95	**Michael Acceptors**		**260**	**Covalent Irreversible**	**11.5**	**Structure-based optimization**	[50]
96	**Michael Acceptors**		**3100**	**Covalent Irreversible**	**3.2**	**Structure-based optimization**	[50]
97 **GRL-0920**	**Esters**		**250**	**Covalent Irreversible**	**2.8**	**Drug repurposing**	[51]
98 **GRL-0820**	**Esters**		**73**	**Covalent Irreversible**	**15**	**Structure-based design**	[51]

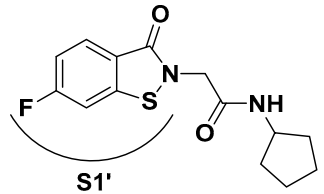
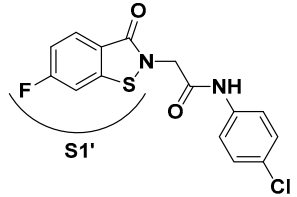
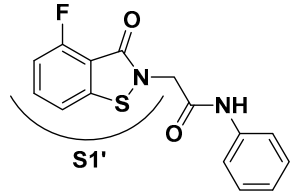
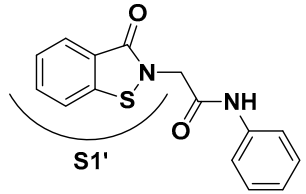
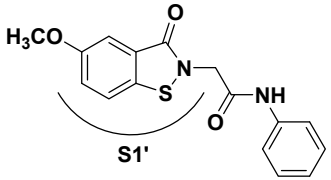
99 **GRL-1720**	**Esters**		**320**	**Covalent Irreversible**	**15**	**Lead optimization**	[52]
100	**Esters**		**55**	**Covalent Irreversible**	**n.d.**	**Lead optimization**	[53]
101	**Esters**		**34**	**Covalent Irreversible**	**n.d.**	**Lead optimization**	[53]
102	**Esters**		**81**	**Covalent Irreversible**	**n.d.**	***In vitro* screening**	[43]
103	**Thioesters**		**11**	**Covalent Irreversible**	**0.11**	**Virtual screening Structure-based design**	[54]
104	**Thioesters**		**88**	**Covalent Irreversible**	**0.73**	**Virtual screening Structure-based design**	[54]
105	**Thioesters**		**n.d.**	**n.d.**	**0.1**	**Virtual screening Structure-based design**	[54]

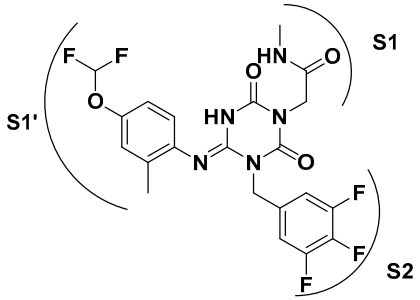
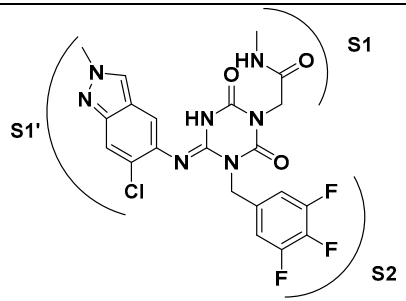
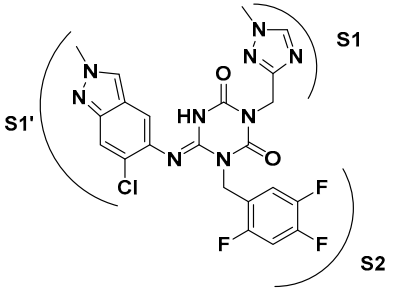
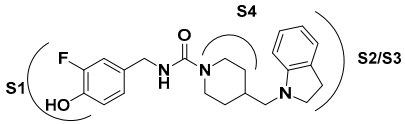
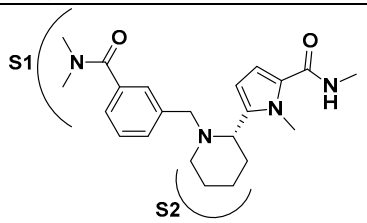
106	**Thioesters**		**n.d.**	**n.d.**	**0.44**	**Virtual screening Structure-based design**	[54]
107	**Thioesters**		**n.d.**	**n.d.**	**0.66**	**Virtual screening Structure-based design**	[54]
108	**Thioesters**		**n.d.**	**n.d.**	**0.038**	**Virtual screening Structure-based design**	[54]
109	**Thioesters**		**n.d.**	**n.d.**	**0.045**	**Virtual screening Structure-based design**	[54]
110 EBSELEN	**Selenium-based compounds**		**670**	**Covalent**	**4.67**	**Drug repurposing**	[42]
111	**Selenium-based compounds**		**25.7**	**Covalent**	**n.d.**	***In vitro* screening**	[55]
112	**Selenium-based compounds**		**27.9**	**Covalent**	**n.d.**	***In vitro* screening**	[55]

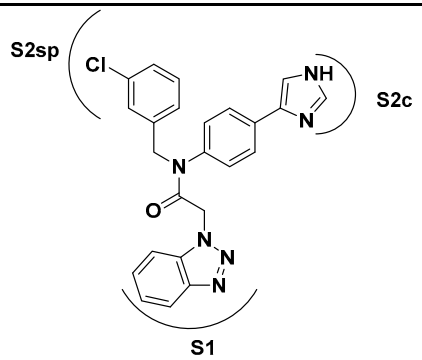
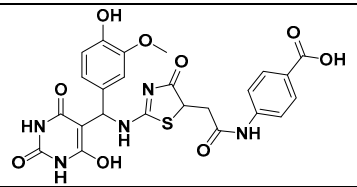
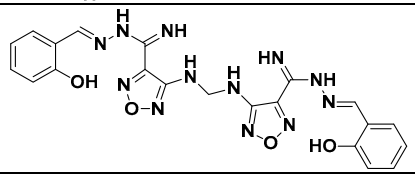
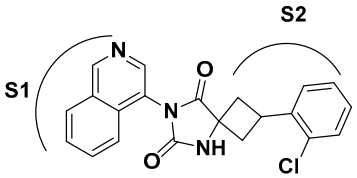
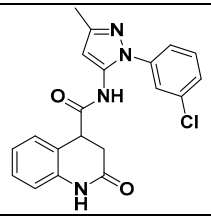
113	**Selenium-based compounds**		**15.2**	**Covalent**	**n.d.**	***In vitro* screening**	[55]
114	**Selenium-based compounds**		**27.4**	**Covalent**	**n.d.**	***In vitro* screening**	[55]
115	**Selenium-based compounds**		**900**	**Covalent**	**11.2**	**Structure-based design**	[56]
116	**Selenium-based compounds**		**680**	**Covalent**	**11.7**	**Structure-based design**	[56]
117	**Selenium-based compounds**		**640**	**Covalent**	**18.2**	**Structure-based design**	[56]
118	**Selenium-based compounds**		**380**	**Covalent**	**2.0**	**Structure-based design**	[56]
119	**Selenium-based compounds**		**2800**	**Covalent**	**0.8**	**Structure-based design**	[56]

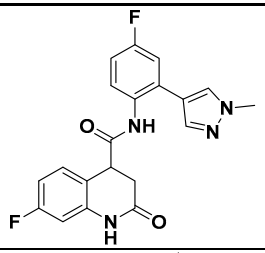
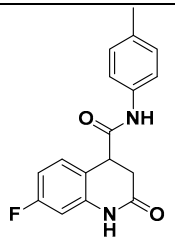
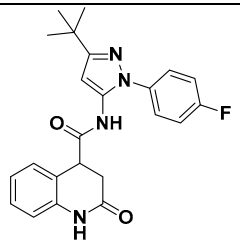
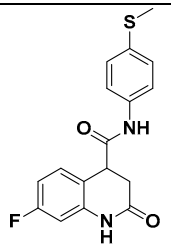
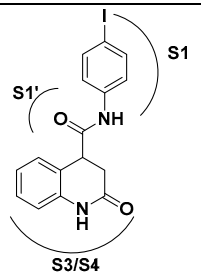
120 **MR6-7-2**	**Selenium-based compounds**		**360**	**Covalent**	**4.5**	**Drug repurposing**	[57]
121 **MR6-18-4**	**Selenium-based compounds**		**340**	**Covalent**	**3.7**	**Drug repurposing**	[57]
122 **MR6-17-1**	**Selenium-based compounds**		**700**	**Covalent**	**n.a.**	**Drug repurposing**	[57]
123 **MR6-26-2**	**Selenium-based compounds**		**470**	**Covalent**	**3.2**	**Drug repurposing**	[57]
124 **MR6-31-2**	**Selenium-based compounds**		**820**	**Covalent**	**1.8**	**Drug repurposing**	[57]
125 **EBSULFUR**	**Sulfur-based compounds**		**490**	**Covalent**	**n.d.**	***In vitro* screening**	[58]
126	**Sulfur-based compounds**		**110**	**Covalent**	**n.d.**	***In vitro* screening**	[58]

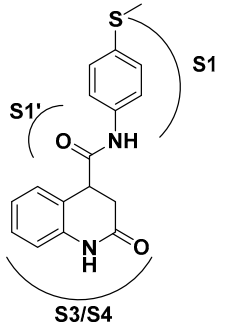
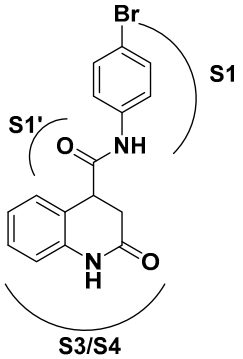
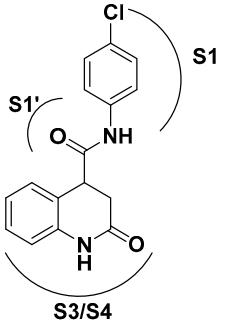
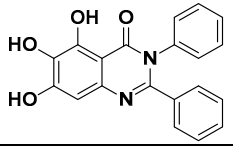
127	**Selenium-based compounds**		**74**	**Covalent**	**n.d.**	***In vitro* screening**	[58]
128	**Sulfur-based compounds**		**190**	**Covalent**	**n.d.**	**high-throughput screening**	[59]
129	**Sulfur-based compounds**		**160**	**Covalent**	**n.d.**	**Lead optimization**	[59]
130	**Sulfur-based compounds**		**180**	**Covalent**	**n.d.**	**Lead optimization**	[59]
131	**Sulfur-based compounds**		**140**	**Covalent**	**n.d.**	**Lead optimization**	[59]
132	**Sulfur-based compounds**		**150**	**Covalent**	**n.d.**	**Lead optimization**	[59]

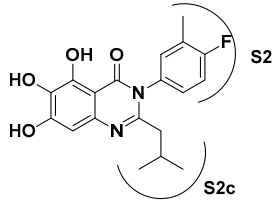
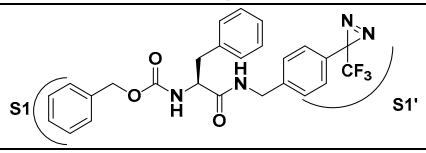
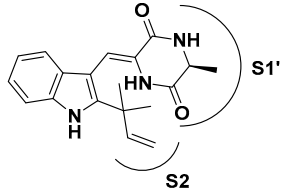
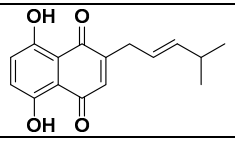
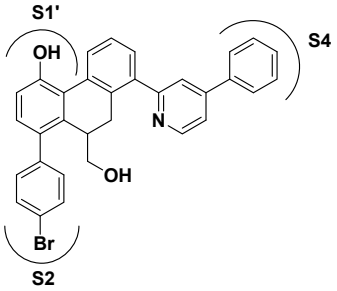
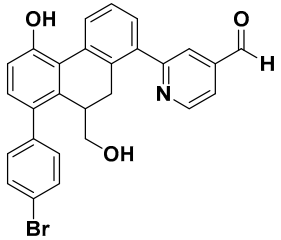
133	**Sulfur-based compounds**		**150**	**Covalent**	**n.d.**	**Lead optimization**	[59]
134	**Sulfur-based compounds**		**120**	**Covalent**	**n.d.**	**Lead optimization**	[59]
135	**Sulfur-based compounds**		**116**	**Covalent**	**n.d.**	**Lead optimization**	[59]
136	**Sulfur-based compounds**		**165**	**Covalent**	**n.d.**	**Lead optimization**	[59]
137	**Sulfur-based compounds**		**165**	**Covalent**	**n.d.**	**Lead optimization**	[59]

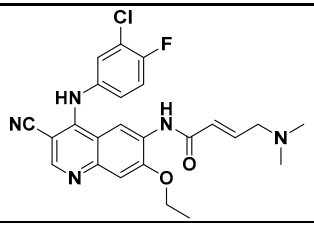
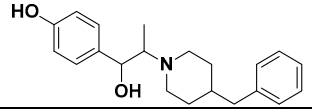
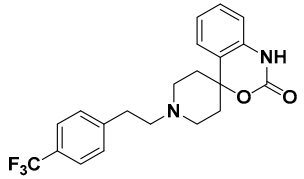
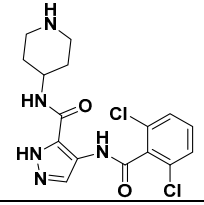
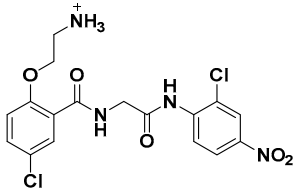
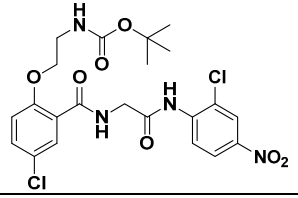
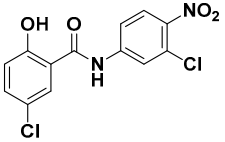
138	**Miscellaneous**		**8600**	**Non Covalent**	**n.d.**	**Virtual and *in vitro* screening**	[60]
139	**Miscellaneous**		**96**	**Non Covalent**	**12.5**	**Lead optimization**	[60]
140 S-217622	**Miscellaneous**		**13**	**Non Covalent**	**0.5 – 0.29[e]**	**Lead optimization**	[60]
141 Z1244904919	**Miscellaneous**		**730**	**Non Covalent**	**5**	**Virtual and *in vitro* screening**	[61]
142 Z1759961356	**Miscellaneous**		**690**	**Non Covalent**	**8.5**	**Virtual and *in vitro* screening**	[61]

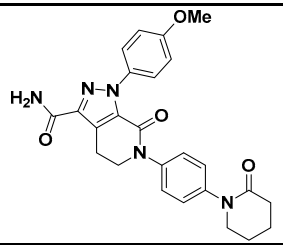
144 **CCF981**	**Miscellaneous**		**68**	**Non Covalent**	**0.5**	**Lead optimization**	[62]
145	**Miscellaneous**		**450**	**Non Covalent**	**0.77**	**Virtual and *in vitro* screening**	[63]
146	**Miscellaneous**		**110**	**Non Covalent**	**0.11**	**Virtual and *in vitro* screening**	[63]
149	**Miscellaneous**		**77**	**Non Covalent**	**0.11**	**Lead optimization**	[64]
150 **ZINC00037365906** **0**	**Miscellaneous**		**58000**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]

151 **ZINC000636416501**	**Miscellaneous**		**93000**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]
152 **Z228770960**	**Miscellaneous**		**4000**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]
153 **Z393665558**	**Miscellaneous**		**6000**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]
154 **Z225602086**	**Miscellaneous**		**7400**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]
155 **Z222979552**	**Miscellaneous**		**1000**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]

156 **Z228166018**	**Miscellaneous**		**1600**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]
157 **Z222977344**	**Miscellaneous**		**2000**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]
158 **Z222978028**	**Miscellaneous**		**5800**	**Non Covalent**	**n.d.**	**Virtual screening**	[65]
160	**Miscellaneous**		**83**	**Non Covalent**	**1.1**	**Structure-based design**	[66]

161	**Miscellaneous**		**100**	**Non Covalent**	**2.1**	**Structure-based design**	[66]
162	**Miscellaneous**		**4100**	**Non Covalent**	**n.d.**	**Warhead replacement**	[67]
163 Neoechinulin A	**Miscellaneous**		**470**	**Non Covalent**	**n.d.**	***in vitro* screening**	[68]
164 Shikonin	**Miscellaneous**		**1570**	**Non Covalent**	**n.d.**	**Virtual screening**	[69]
165 C1	**Miscellaneous**		**1500**	**Non Covalent**	**n.d.**	**Lead optimization**	[70]
166 C2	**Miscellaneous**		**1800**	**Non Covalent**	**n.d.**	**Lead optimization**	[70]

167 **Pelitinib**	**Miscellaneous**		**n.d.**	**Allosteric**	**1.25**	**X-ray screening** **Drug repurposing**	[17]
168 **Ifenprodil**	**Miscellaneous**		**n.d.**	**Allosteric**	**47**	**X-ray screening** **Drug repurposing**	[17]
169 **RS-102895**	**Miscellaneous**		**n.d.**	**Allosteric**	**19.8**	**X-ray screening** **Drug repurposing**	[17]
170 **AT7519**	**Miscellaneous**		**n.d.**	**Allosteric**	**25.2**	**X-ray screening** **Drug repurposing**	[17]
171 **JMX0286**	**Miscellaneous**		**4800**	**Allosteric**	**2.3**	***In vitro*** **screening**	[71]
172 **JMX0301**	**Miscellaneous**		**4500**	**Allosteric**	**2.4**	***In vitro*** **screening**	[71]
173 **JMX0941**	**Miscellaneous**		**3900**	**Allosteric**	**1.7**	***In vitro*** **screening**	[71]

174 **Apixaban**	**Miscellaneous**		**9.7**	**Allosteric**	**1.8**	**Drug repurposing**	[72]

References

[1] D. R. Owen *et al.*, 'An oral SARS-CoV-2 M ^{pro} inhibitor clinical candidate for the treatment of COVID-19', *Science (1979)*, vol. 374, no. 6575, pp. 1586–1593, Dec. 2021, doi: 10.1126/science.abl4784.

[2] 'WO2021250648A1 - Nitrile-containing antiviral compounds - Google Patents'. https://patents.google.com/patent/WO2021250648A1/en (accessed Mar. 05, 2023).

[3] B. Bai *et al.*, 'Peptidomimetic nitrile warheads as SARS-CoV-2 3CL protease inhibitors', *RSC Med Chem*, vol. 12, no. 10, pp. 1722–1730, 2021, doi: 10.1039/D1MD00247C.

[4] M. Zhu *et al.*, 'Design, synthesis and biological evaluation of covalent peptidomimetic 3CL protease inhibitors containing nitrile moiety', *Bioorg Med Chem*, vol. 87, p. 117316, May 2023, doi: 10.1016/J.BMC.2023.117316.

[5] D. W. Kneller *et al.*, 'Covalent narlaprevir- and boceprevir-derived hybrid inhibitors of SARS-CoV-2 main protease', *Nat Commun*, vol. 13, no. 1, p. 2268, Apr. 2022, doi: 10.1038/s41467-022-29915-z.

[6] L. Brewitz *et al.*, 'Alkyne Derivatives of SARS-CoV-2 Main Protease Inhibitors Including Nirmatrelvir Inhibit by Reacting Covalently with the Nucleophilic Cysteine', *J Med Chem*, vol. 66, no. 4, pp. 2663–2680, Feb. 2023, doi: 10.1021/acs.jmedchem.2c01627.

[7] W. Dai *et al.*, 'Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease', *Science (1979)*, vol. 368, no. 6497, pp. 1331–1335, Jun. 2020, doi: 10.1126/science.abb4489.

[8] W. Dai *et al.*, 'Design, Synthesis, and Biological Evaluation of Peptidomimetic Aldehydes as Broad-Spectrum Inhibitors against Enterovirus and SARS-CoV-2', *J Med Chem*, vol. 65, no. 4, pp. 2794–2808, Feb. 2022, doi: 10.1021/acs.jmedchem.0c02258.

[9] W. Vuong *et al.*, 'Feline coronavirus drug inhibits the main protease of SARS-CoV-2 and blocks virus replication', *Nat Commun*, vol. 11, no. 1, p. 4282, Aug. 2020, doi: 10.1038/s41467-020-18096-2.

[10] W. Vuong *et al.*, 'Improved SARS-CoV-2 Mpro inhibitors based on feline antiviral drug GC376: Structural enhancements, increased solubility, and micellar studies', *Eur J Med Chem*, vol. 222, p. 113584, Oct. 2021, doi: 10.1016/j.ejmech.2021.113584.

[11] M. D. Sacco *et al.*, 'Structure and inhibition of the SARS-CoV-2 main protease reveal strategy for developing dual inhibitors against Mpro and cathepsin L', *Sci Adv*, vol. 6, no. 50, Dec. 2020, doi: 10.1126/SCIADV.ABE0751/SUPPL_FILE/ABE0751_SM.PDF.

[12] H. Liu *et al.*, 'Development of optimized drug-like small molecule inhibitors of the SARS-CoV-2 3CL protease for treatment of COVID-19', *Nat Commun*, vol. 13, no. 1, p. 1891, Apr. 2022, doi: 10.1038/s41467-022-29413-2.

[13] J. Qiao *et al.*, 'SARS-CoV-2 M ^{pro} inhibitors with antiviral activity in a transgenic mouse model', *Science (1979)*, vol. 371, no. 6536, pp. 1374–1378, Mar. 2021, doi: 10.1126/science.abf1611.

[14] C. S. Dampalla *et al.*, 'Structure-Guided Design of Conformationally Constrained Cyclohexane Inhibitors of Severe Acute Respiratory Syndrome Coronavirus-2 3CL Protease', *J Med Chem*, vol. 64, no. 14, pp. 10047–10058, Jul. 2021, doi: 10.1021/acs.jmedchem.1c00319.

[15] Z. Xia *et al.*, 'Rational Design of Hybrid SARS-CoV-2 Main Protease Inhibitors Guided by the Superimposed Cocrystal Structures with the Peptidomimetic Inhibitors GC-376, Telaprevir, and Boceprevir', *ACS Pharmacol Transl Sci*, vol. 4, no. 4, pp. 1408–1421, Aug. 2021, doi: 10.1021/acsptsci.1c00099.

[16] Y. R. Alugubelli *et al.*, 'A systematic exploration of boceprevir-based main protease inhibitors as SARS-CoV-2 antivirals', *Eur J Med Chem*, vol. 240, p. 114596, Oct. 2022, doi: 10.1016/j.ejmech.2022.114596.

[17] S. Günther *et al.*, 'X-ray screening identifies active site and allosteric inhibitors of SARS-CoV-2 main protease', *Science (1979)*, vol. 372, no. 6542, pp. 642–646, May 2021, doi: 10.1126/science.abf7945.

[18] K. S. Yang *et al.*, 'A Quick Route to Multiple Highly Potent SARS-CoV-2 Main Protease Inhibitors**', *ChemMedChem*, vol. 16, no. 6, pp. 942–948, Mar. 2021, doi: 10.1002/cmdc.202000924.

[19] E. Costanzi *et al.*, 'Structural and Biochemical Analysis of the Dual Inhibition of MG-132 against SARS-CoV-2 Main Protease (Mpro/3CLpro) and Human Cathepsin-L', *Int J Mol Sci*, vol. 22, no. 21, p. 11779, Oct. 2021, doi: 10.3390/ijms222111779.

[20] Y. Ma *et al.*, 'A multi-pronged evaluation of aldehyde-based tripeptidyl main protease inhibitors as SARS-CoV-2 antivirals', *Eur J Med Chem*, vol. 240, p. 114570, Oct. 2022, doi: 10.1016/j.ejmech.2022.114570.

[21] B. Bai *et al.*, 'Peptidomimetic α-Acyloxymethylketone Warheads with Six-Membered Lactam P1 Glutamine Mimic: SARS-CoV-2 3CL Protease Inhibition, Coronavirus Antiviral Activity, and *in Vitro* Biological Stability', *J Med Chem*, vol. 65, no. 4, pp. 2905–2925, Feb. 2022, doi: 10.1021/acs.jmedchem.1c00616.

[22] S. Hattori *et al.*, 'A small molecule compound with an indole moiety inhibits the main protease of SARS-CoV-2 and blocks virus replication', *Nat Commun*, vol. 12, no. 1, p. 668, Jan. 2021, doi: 10.1038/s41467-021-20900-6.

[23] N. Higashi-Kuwata *et al.*, 'Identification of SARS-CoV-2 Mpro inhibitors containing P1' 4-fluorobenzothiazole moiety highly active against SARS-CoV-2', *Nat Commun*, vol. 14, no. 1, p. 1076, Feb. 2023, doi: 10.1038/s41467-023-36729-0.

[24] H. Yang *et al.*, 'Design, synthesis and biological evaluation of peptidomimetic benzothiazolyl ketones as 3CLpro inhibitors against SARS-CoV-2', *Eur J Med Chem*, vol. 257, p. 115512, Sep. 2023, doi: 10.1016/J.EJMECH.2023.115512.

[25] W. Zhu *et al.*, 'Identification of SARS-CoV-2 3CL Protease Inhibitors by a Quantitative High-Throughput Screening', *ACS Pharmacol Transl Sci*, vol. 3, no. 5, pp. 1008–1016, Oct. 2020, doi: 10.1021/acsptsci.0c00108.

[26] A. Citarella *et al.*, 'Pseudo-Dipeptide Bearing α,α-Difluoromethyl Ketone Moiety as Electrophilic Warhead with Activity against Coronaviruses', *International Journal of Molecular Sciences 2021, Vol. 22, Page 1398*, vol. 22, no. 3, p. 1398, Jan. 2021, doi: 10.3390/IJMS22031398.

[27] D. Shcherbakov *et al.*, 'Design and Evaluation of Bispidine-Based SARS-CoV-2 Main Protease Inhibitors', *ACS Med Chem Lett*, vol. 13, no. 1, pp. 140–147, Jan. 2022, doi: 10.1021/acsmedchemlett.1c00299.

[28] J. K. Stille *et al.*, 'Design, synthesis and in vitro evaluation of novel SARS-CoV-2 3CLpro covalent inhibitors', *Eur J Med Chem*, vol. 229, p. 114046, Feb. 2022, doi: 10.1016/J.EJMECH.2021.114046.

[29] N. Kitamura *et al.*, 'Expedited Approach toward the Rational Design of Noncovalent SARS-CoV-2 Main Protease Inhibitors', *J Med Chem*, vol. 65, no. 4, pp. 2848–2865, Feb. 2022, doi: 10.1021/ACS.JMEDCHEM.1C00509/SUPPL_FILE/JM1C00509_SI_002.CSV.

[30] C. Ma *et al.*, 'Discovery of Di- and Trihaloacetamides as Covalent SARS-CoV-2 Main Protease Inhibitors with High Target Specificity', *J Am Chem Soc*, vol. 143, no. 49, pp. 20697–20709, Dec. 2021, doi: 10.1021/jacs.1c08060.

[31] D. Yamane *et al.*, 'Selective covalent targeting of SARS-CoV-2 main protease by enantiopure chlorofluoroacetamide', *Chem Sci*, vol. 13, no. 10, pp. 3027–3034, 2022, doi: 10.1039/D1SC06596C.
[32] M. Xiong, T. Nie, Q. Shao, M. Li, H. Su, and Y. Xu, 'In silico screening-based discovery of novel covalent inhibitors of the SARS-CoV-2 3CL protease', *Eur J Med Chem*, vol. 231, p. 114130, Mar. 2022, doi: 10.1016/j.ejmech.2022.114130.
[33] A. Clyde *et al.*, 'High-Throughput Virtual Screening and Validation of a SARS-CoV-2 Main Protease Noncovalent Inhibitor', *J Chem Inf Model*, vol. 62, no. 1, pp. 116–128, Jan. 2022, doi: 10.1021/ACS.JCIM.1C00851/ASSET/IMAGES/LARGE/CI1C00851_0005.JPEG.
[34] S. Gao *et al.*, 'Discovery and Crystallographic Studies of Trisubstituted Piperazine Derivatives as Non-Covalent SARS-CoV-2 Main Protease Inhibitors with High Target Specificity and Low Toxicity', *J Med Chem*, vol. 65, no. 19, pp. 13343–13364, Oct. 2022, doi: 10.1021/ACS.JMEDCHEM.2C01146/SUPPL_FILE/JM2C01146_SI_002.CSV.
[35] S. Gao *et al.*, 'Discovery and Crystallographic Studies of Nonpeptidic Piperazine Derivatives as Covalent SARS-CoV-2 Main Protease Inhibitors', *J Med Chem*, vol. 65, no. 24, pp. 16902–16917, Dec. 2022, doi: 10.1021/ACS.JMEDCHEM.2C01716/SUPPL_FILE/JM2C01716_SI_001.CSV.
[36] P. Moon *et al.*, 'Discovery of Potent Pyrazoline-Based Covalent SARS-CoV-2 Main Protease Inhibitors', *bioRxiv*, p. 2022.03.05.483025, Mar. 2022, doi: 10.1101/2022.03.05.483025.
[37] L. El Khoury *et al.*, 'Computationally driven discovery of SARS-CoV-2 Mpro inhibitors: from design to experimental validation', *Chem Sci*, vol. 13, no. 13, pp. 3674–3687, Mar. 2022, doi: 10.1039/D1SC05892D.
[38] L. Zhang *et al.*, 'Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α-ketoamide inhibitors', *Science (1979)*, vol. 368, no. 6489, pp. 409–412, Apr. 2020, doi: 10.1126/science.abb3405.
[39] B. X. Quan *et al.*, 'An orally available Mpro inhibitor is effective against wild-type SARS-CoV-2 and variants including Omicron', *Nature Microbiology 2022 7:5*, vol. 7, no. 5, pp. 716–725, Apr. 2022, doi: 10.1038/s41564-022-01119-7.
[40] X. Chen *et al.*, 'Inhibition mechanism and antiviral activity of an α-ketoamide based SARS-CoV-2 main protease inhibitor', *bioRxiv*, p. 2023.03.09.531862, Mar. 2023, doi: 10.1101/2023.03.09.531862.
[41] C. Huang *et al.*, 'A new generation Mpro inhibitor with potent activity against SARS-CoV-2 Omicron variants', *Signal Transduction and Targeted Therapy 2023 8:1*, vol. 8, no. 1, pp. 1–13, Mar. 2023, doi: 10.1038/s41392-023-01392-w.
[42] Z. Jin *et al.*, 'Structure of Mpro from SARS-CoV-2 and discovery of its inhibitors', *Nature 2020 582:7811*, vol. 582, no. 7811, pp. 289–293, Apr. 2020, doi: 10.1038/s41586-020-2223-y.
[43] S. Iketani *et al.*, 'Lead compounds for the development of SARS-CoV-2 3CL protease inhibitors', *Nature Communications 2021 12:1*, vol. 12, no. 1, pp. 1–7, Apr. 2021, doi: 10.1038/s41467-021-22362-2.
[44] G. Amendola *et al.*, 'Lead Discovery of SARS-CoV-2 Main Protease Inhibitors through Covalent Docking-Based Virtual Screening', *J Chem Inf Model*, vol. 61, no. 4, pp. 2062–2073, Apr. 2021, doi: 10.1021/acs.jcim.1c00184.
[45] S. Previti *et al.*, 'Structure-based lead optimization of peptide-based vinyl methyl ketones as SARS-CoV-2 main protease inhibitors', *Eur J Med Chem*, vol. 247, p. 115021, Feb. 2023, doi: 10.1016/j.ejmech.2022.115021.
[46] S. Mondal *et al.*, 'Dual Inhibitors of Main Protease (M ^{Pro}) and Cathepsin L as Potent Antivirals against SARS-CoV2', *J Am Chem Soc*, vol. 144, no. 46, pp. 21035–21045, Nov. 2022, doi: 10.1021/jacs.2c04626.
[47] A. Citarella *et al.*, 'Synthesis of SARS-CoV-2 Mpro inhibitors bearing a cinnamic ester warhead with in vitro activity against human coronaviruses', *Org Biomol Chem*, 2023, doi: 10.1039/D3OB00381G.

[48] D. Zaidman, P. Gehrtz, M. Filep, M. A. Walsh, F. Von Delft, and N. London Correspondence, 'An automatic pipeline for the design of irreversible derivatives identifies a potent SARS-CoV-2 M pro inhibitor', *Cell Chem Biol*, vol. 28, pp. 1795-1806.e5, 2021, doi: 10.1016/j.chembiol.2021.05.018.

[49] M. Kuzikov *et al.*, 'Identification of Inhibitors of SARS-CoV-2 3CL-Pro Enzymatic Activity Using a Small Molecule in Vitro Repurposing Screen', *ACS Pharmacol Transl Sci*, vol. 4, no. 3, pp. 1096–1110, Jun. 2021, doi: 10.1021/ACSPTSCI.0C00216/ASSET/IMAGES/LARGE/PT0C00216_0007.JPEG.

[50] H. Su *et al.*, 'Identification of pyrogallol as a warhead in design of covalent inhibitors for the SARS-CoV-2 3CL protease', *Nature Communications 2021 12:1*, vol. 12, no. 1, pp. 1–12, Jun. 2021, doi: 10.1038/s41467-021-23751-3.

[51] S. I. Hattori *et al.*, 'GRL-0920, an indole chloropyridinyl ester, completely blocks SARS-CoV-2 infection', *mBio*, vol. 11, no. 4, pp. 1–16, Jul. 2020, doi: 10.1128/MBIO.01833-20/ASSET/11D12B15-E56A-4381-A5F9-AD6A79F97BE2/ASSETS/GRAPHIC/MBIO.01833-20-F0005.JPEG.

[52] A. K. Ghosh *et al.*, 'Indole Chloropyridinyl Ester-Derived SARS-CoV-2 3CLpro Inhibitors: Enzyme Inhibition, Antiviral Efficacy, Structure-Activity Relationship, and X-ray Structural Studies', *J Med Chem*, vol. 64, no. 19, pp. 14702–14714, Oct. 2021, doi: 10.1021/ACS.JMEDCHEM.1C01214/SUPPL_FILE/JM1C01214_SI_002.CSV.

[53] J. Breidenbach *et al.*, 'Targeting the Main Protease of SARS-CoV-2: From the Establishment of High Throughput Screening to the Design of Tailored Inhibitors', *Angewandte Chemie International Edition*, vol. 60, no. 18, pp. 10423–10429, Apr. 2021, doi: 10.1002/ANIE.202016961.

[54] T. Pillaiyar *et al.*, 'Small-Molecule Thioesters as SARS-CoV-2 Main Protease Inhibitors: Enzyme Inhibition, Structure–Activity Relationships, Antiviral Activity, and X-ray Structure Determination', *J Med Chem*, vol. 65, no. 13, pp. 9376–9395, Jul. 2022, doi: 10.1021/acs.jmedchem.2c00636.

[55] M. Zmudzinski *et al.*, 'Ebselen derivatives are very potent dual inhibitors of SARS-CoV-2 proteases - PLpro and Mpro in in vitro studies', *bioRxiv*, p. 2020.08.30.273979, Aug. 2020, doi: 10.1101/2020.08.30.273979.

[56] S. Huff *et al.*, 'Discovery and Mechanism of SARS-CoV-2 Main Protease Inhibitors', *J Med Chem*, vol. 65, no. 4, pp. 2866–2879, Feb. 2022, doi: 10.1021/ACS.JMEDCHEM.1C00566/SUPPL_FILE/JM1C00566_SI_001.CSV.

[57] K. Amporndanai *et al.*, 'Inhibition mechanism of SARS-CoV-2 main protease by ebselen and its derivatives', *Nature Communications 2021 12:1*, vol. 12, no. 1, pp. 1–7, May 2021, doi: 10.1038/s41467-021-23313-7.

[58] L. Y. Sun *et al.*, 'Ebsulfur and Ebselen as highly potent scaffolds for the development of potential SARS-CoV-2 antivirals', *Bioorg Chem*, vol. 112, p. 104889, Jul. 2021, doi: 10.1016/J.BIOORG.2021.104889.

[59] W. Chen *et al.*, 'Discovery of highly potent SARS-CoV-2 Mpro inhibitors based on benzoisothiazolone scaffold', *Bioorg Med Chem Lett*, vol. 58, p. 128526, Feb. 2022, doi: 10.1016/j.bmcl.2022.128526.

[60] Y. Unoh *et al.*, 'Discovery of S-217622, a Noncovalent Oral SARS-CoV-2 3CL Protease Inhibitor Clinical Candidate for Treating COVID-19', *J Med Chem*, vol. 65, no. 9, pp. 6499–6512, May 2022, doi: 10.1021/acs.jmedchem.2c00117.

[61] J. Yang *et al.*, 'Structure-Based Discovery of Novel Nonpeptide Inhibitors Targeting SARS-CoV-2 M ^{pro}', *J Chem Inf Model*, vol. 61, no. 8, pp. 3917–3926, Aug. 2021, doi: 10.1021/acs.jcim.1c00355.

[62] S. H. Han *et al.*, 'Structure-Based Optimization of ML300-Derived, Noncovalent Inhibitors Targeting the Severe Acute Respiratory Syndrome Coronavirus 3CL Protease (SARS-CoV-2 3CLpro)', *J Med Chem*, vol. 65, no. 4, pp. 2880–2904, Feb. 2022, doi: 10.1021/ACS.JMEDCHEM.1C00598/SUPPL_FILE/JM1C00598_SI_002.CSV.

[63] S. A. Elseginy *et al.*, 'Promising anti-SARS-CoV-2 drugs by effective dual targeting against the viral and host proteases', *Bioorg Med Chem Lett*, vol. 43, p. 128099, Jul. 2021, doi: 10.1016/J.BMCL.2021.128099.

[64] A. Luttens *et al.*, 'Ultralarge Virtual Screening Identifies SARS-CoV-2 Main Protease Inhibitors with Broad-Spectrum Activity against Coronaviruses', *J Am Chem Soc*, vol. 144, no. 7, pp. 2905–2920, Feb. 2022, doi: 10.1021/JACS.1C08402/ASSET/IMAGES/LARGE/JA1C08402_0004.JPEG.

[65] G. G. Rossetti *et al.*, 'Non-covalent SARS-CoV-2 Mpro inhibitors developed from in silico screen hits', *Scientific Reports 2022 12:1*, vol. 12, no. 1, pp. 1–9, Feb. 2022, doi: 10.1038/s41598-022-06306-4.

[66] K. Zhang *et al.*, 'Discovery of quinazolin-4-one-based non-covalent inhibitors targeting the severe acute respiratory syndrome coronavirus 2 main protease (SARS-CoV-2 Mpro)', *Eur J Med Chem*, vol. 257, p. 115487, Sep. 2023, doi: 10.1016/j.ejmech.2023.115487.

[67] A. Citarella *et al.*, 'Discovery of a Novel Trifluoromethyl Diazirine Inhibitor of SARS-CoV-2 Mpro', *Molecules*, vol. 28, no. 2, Jan. 2023, doi: 10.3390/MOLECULES28020514.

[68] H. A. Alhadrami *et al.*, 'Neoechinulin A as a Promising SARS-CoV-2 Mpro Inhibitor: In Vitro and In Silico Study Showing the Ability of Simulations in Discerning Active from Inactive Enzyme Inhibitors', *Mar Drugs*, vol. 20, no. 3, p. 163, Mar. 2022, doi: 10.3390/MD20030163/S1.

[69] Y. Zhang *et al.*, 'Structure-Based Discovery and Structural Basis of a Novel Broad-Spectrum Natural Product against the Main Protease of Coronavirus', *J Virol*, vol. 96, no. 1, pp. 1253–1274, Jan. 2022, doi: 10.1128/JVI.01253-21/SUPPL_FILE/JVI.01253-21-S0001.PDF.

[70] J. W. Zhang *et al.*, 'Discovery of 9,10-dihydrophenanthrene derivatives as SARS-CoV-2 3CLpro inhibitors for treating COVID-19', *Eur J Med Chem*, vol. 228, p. 114030, Jan. 2022, doi: 10.1016/J.EJMECH.2021.114030.

[71] S. K. Samrat *et al.*, 'Allosteric inhibitors of the main protease of SARS-CoV-2', *Antiviral Res*, vol. 205, p. 105381, Sep. 2022, doi: 10.1016/j.antiviral.2022.105381.

[72] O. A. Chaves *et al.*, 'Apixaban, an orally available anticoagulant, inhibits SARS-CoV-2 replication and its major protease in a non-competitive way', *J Mol Cell Biol*, vol. 14, no. 6, Aug. 2022, doi: 10.1093/jmcb/mjac039.