Electronic Supplementary Material (ESI) for RSC Advances.

Investigating the Structure-Activity Relationship of Marine Natural Polyketides as Promising SARS-CoV-2 Main Protease Inhibitors

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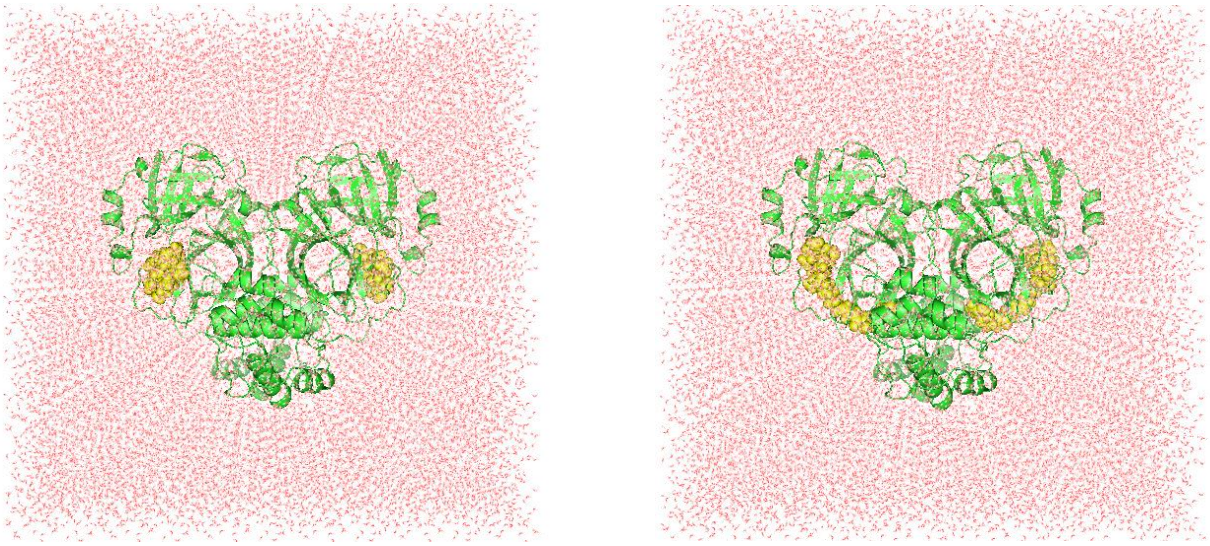
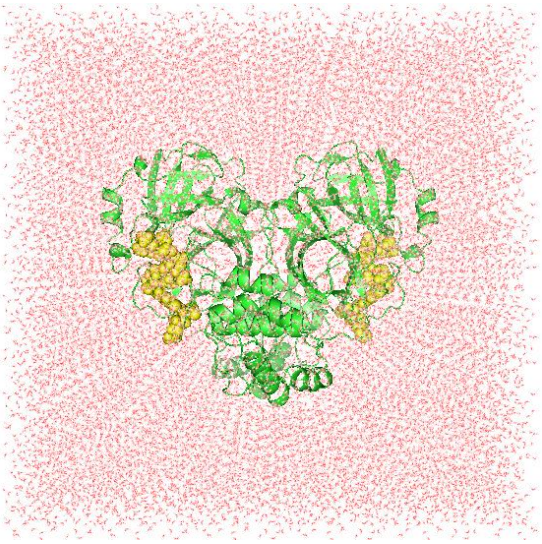
Figure S11. Side-view of the full ligand-Mpro complexes embedded within the TIP3P system. (**A**) D1; (**B**) D2; (**C**) D3; (**D**) D4; (**E**) D5; (**F**) O6K; (**G**) N3. Proteins are represented as cartoon coloured green, ligand atoms are displayed as yellow spheres, while as TIP3P water molecules as lines. The ions are hidden for clarity.

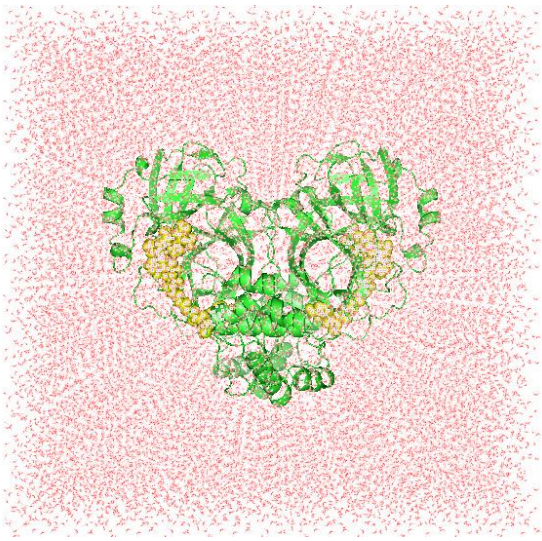
(A) **(B)**



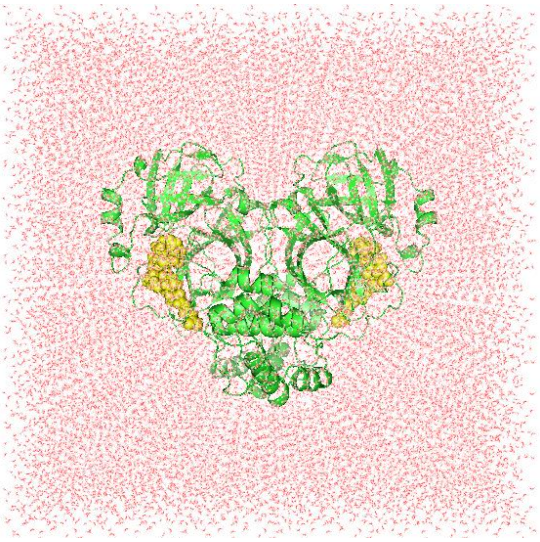
(C)



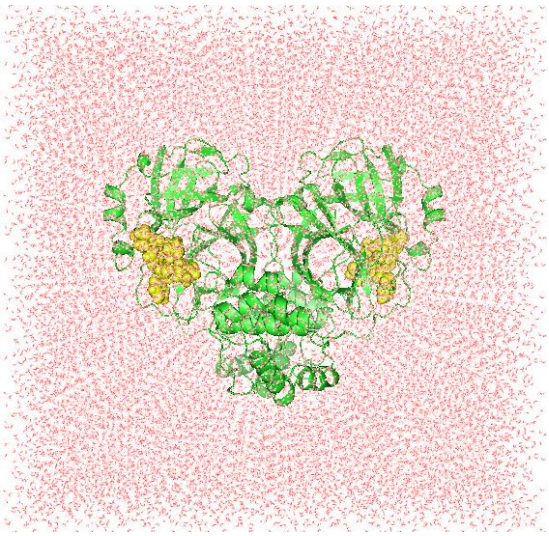
(D)



(E)



(F)



(G)

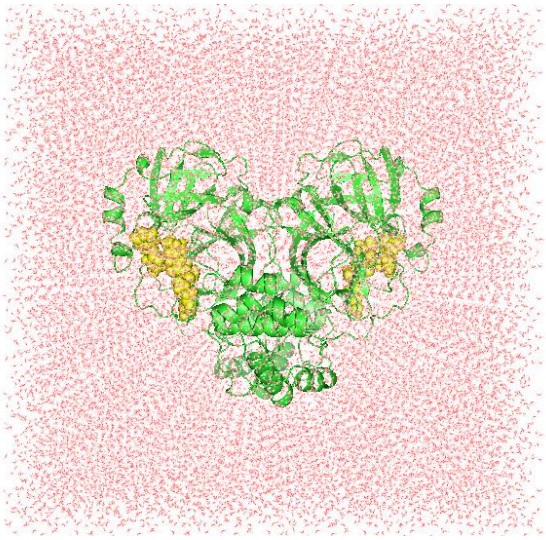
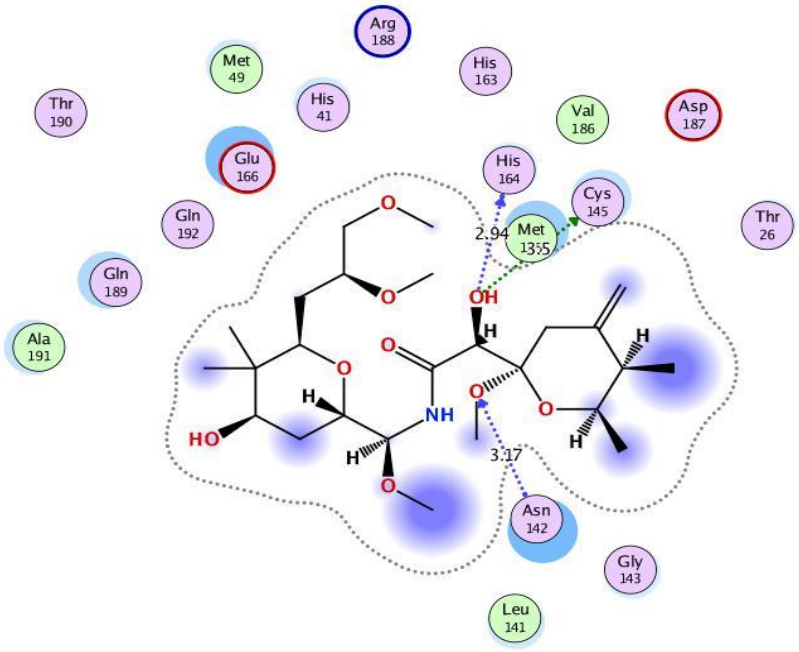
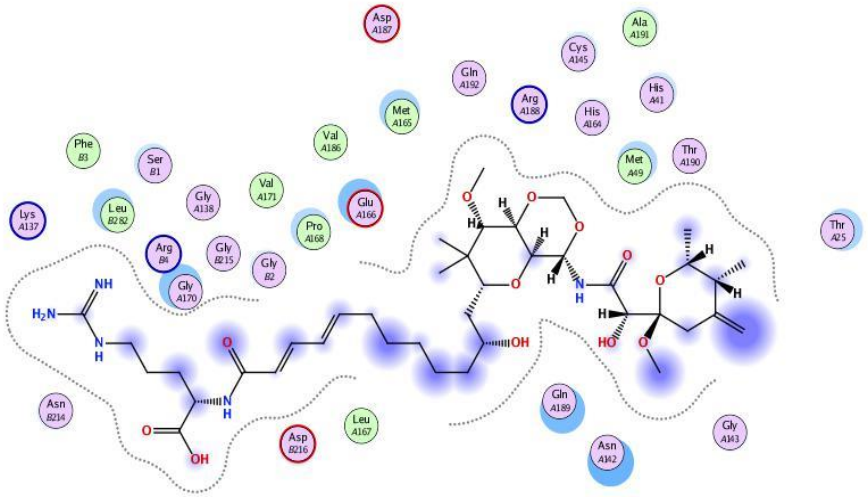
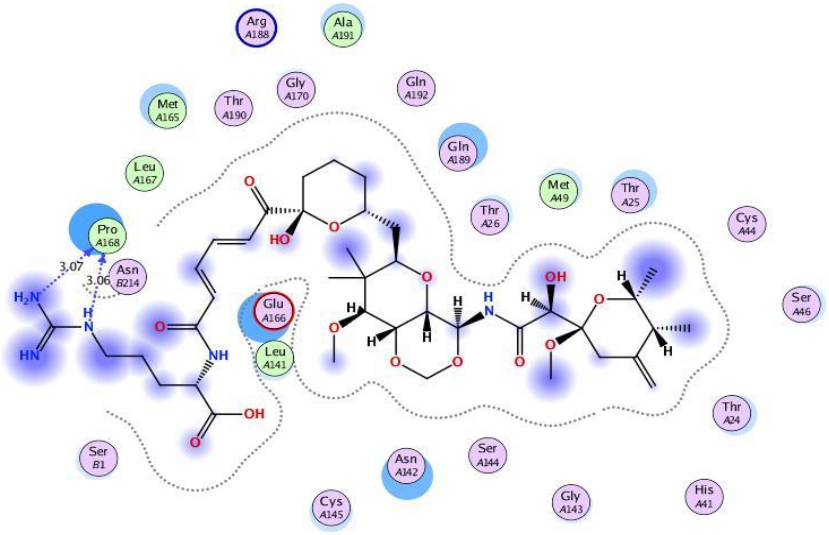
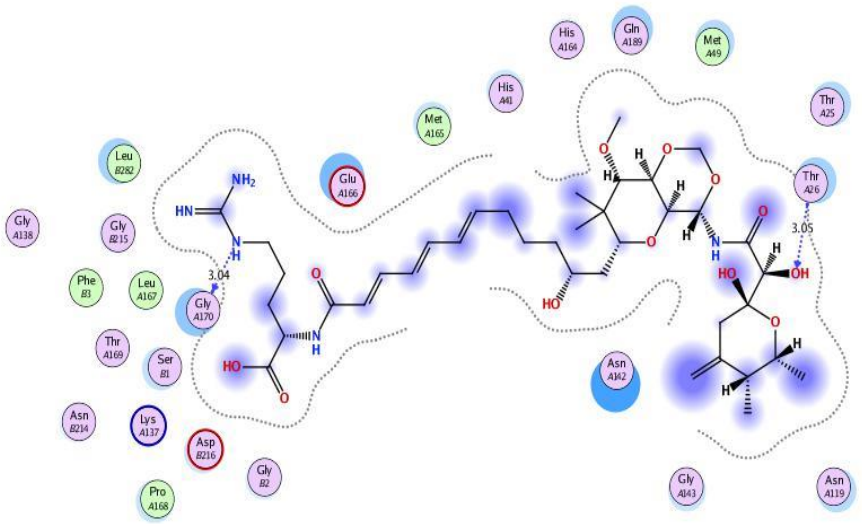
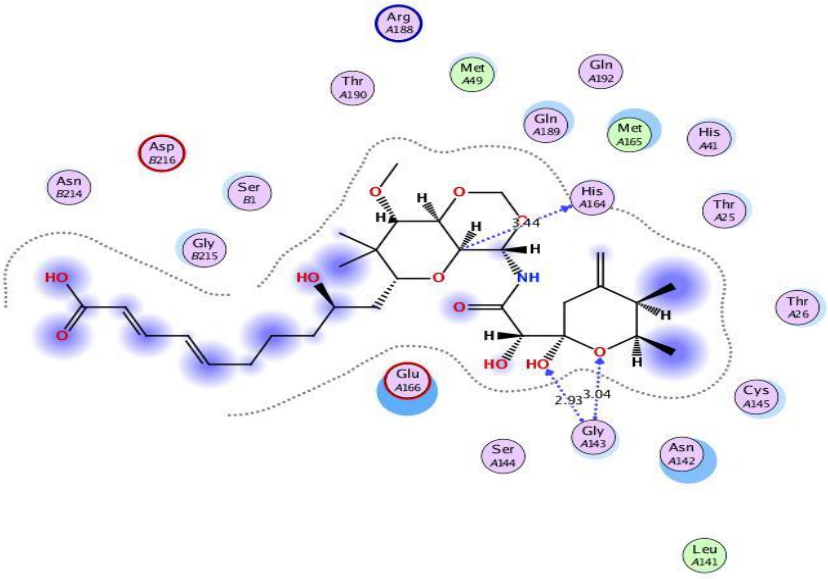
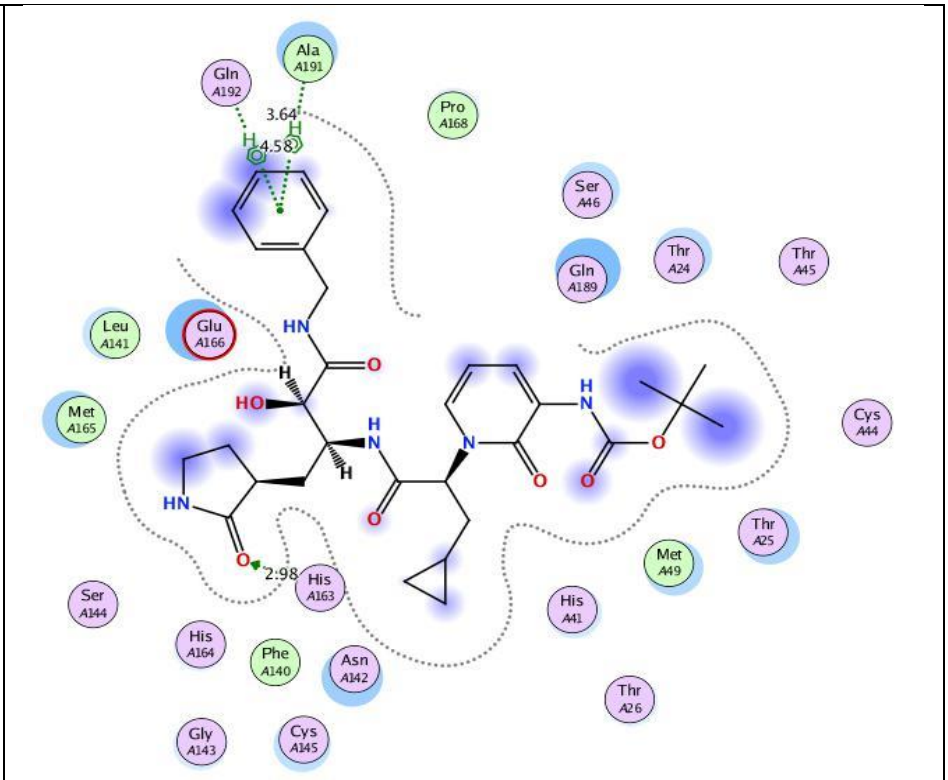
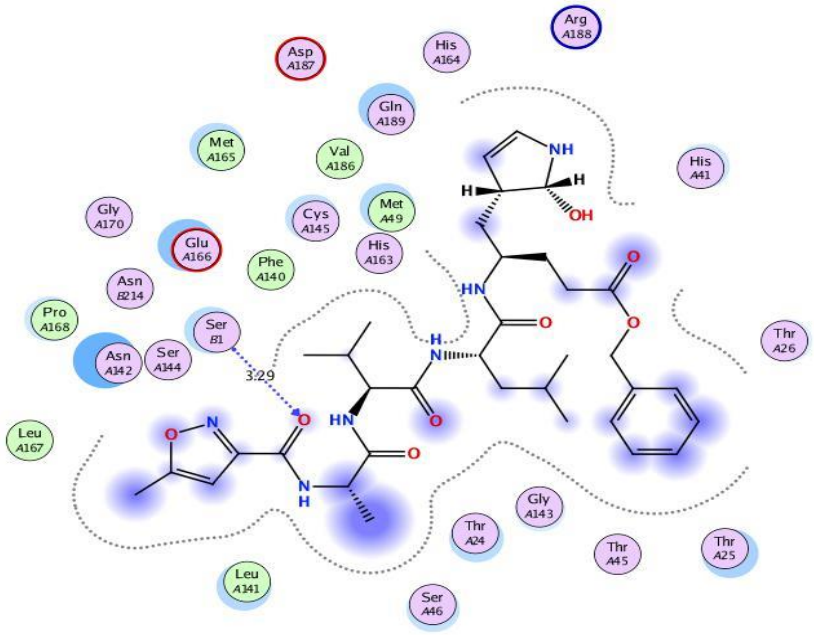


Figure SI2. 2D binding and positioning of the five examined marine products (**1**, **11**, **14**, **17**, and **29**) besides the docked co-crystallized inhibitors (**35** and **36**) towards the binding pocket of SARS-CoV-2 Mpro.

Compound	2D pocket binding (SARS-CoV-2 Mpro)
Pederin (**1**)	
Dihydro-onnamide A (**11**)	

Onnamide C (**14**)	
Pseudo-onnamide A (**17**)	
Theopederin G (**29**)	

6Y2G co-crystallized inhibitor **(O6K, 35)**	
6LU7 co-crystallized inhibitor **(N3, 36)**	

35