Hop bitterness in beer evaluated by computational analysis

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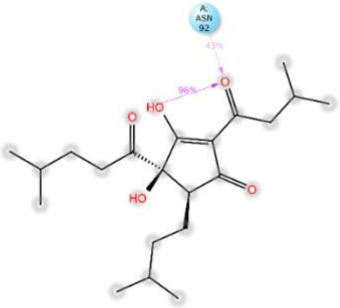
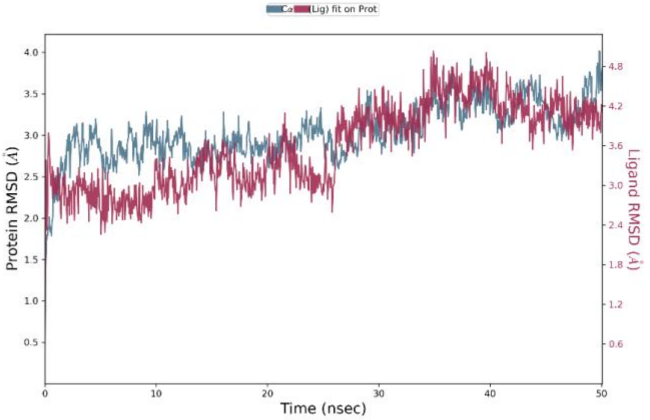
1. TAS2R10

1.1. Cis-tetrahydroisohumulone (25015707)





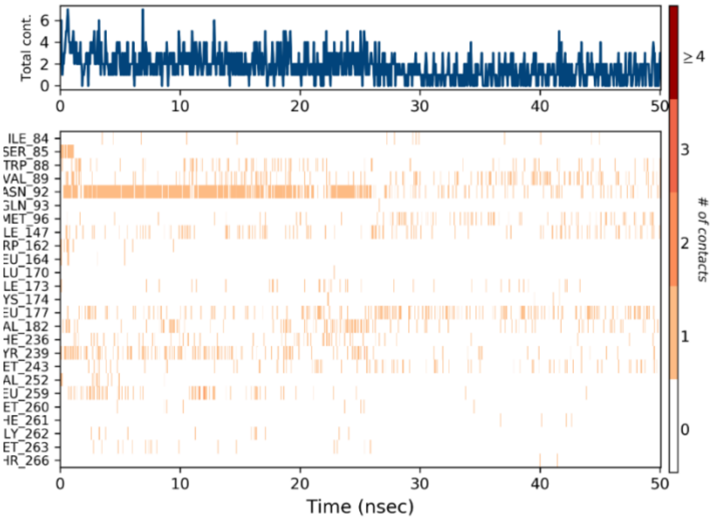
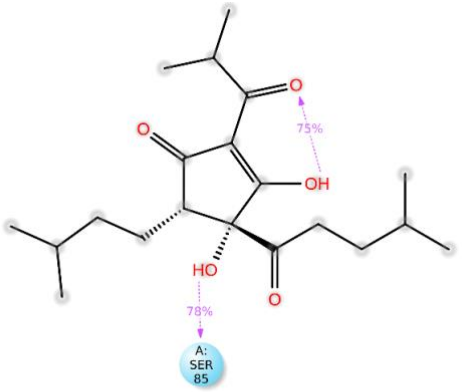


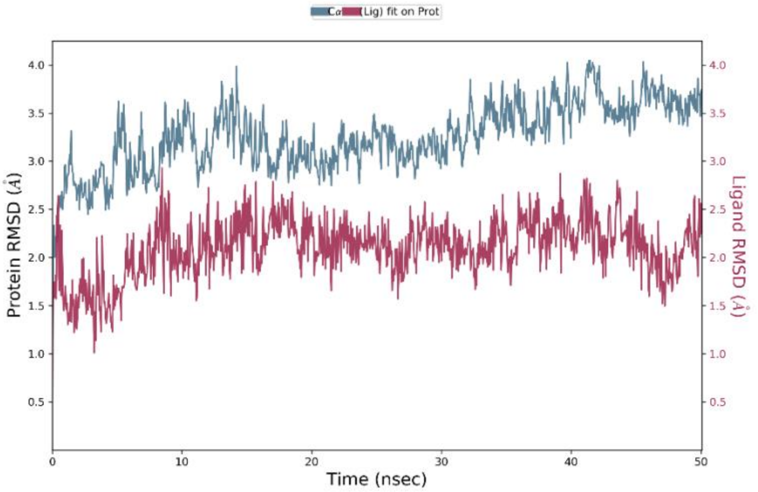
Figure s.i. 1. TAS2R10 molecular dynamics analysis for cis-tetrahydroisohumulone.

This ligand shows normal RMSD values, both for protein and ligand.

The only relevant contact is with the key residue Asn92, although it is intermittent. The other contacts with protein residues occur very intermittently and are therefore not relevant.

1.2. Cis-tetrahydroisocohumulone (21671995)





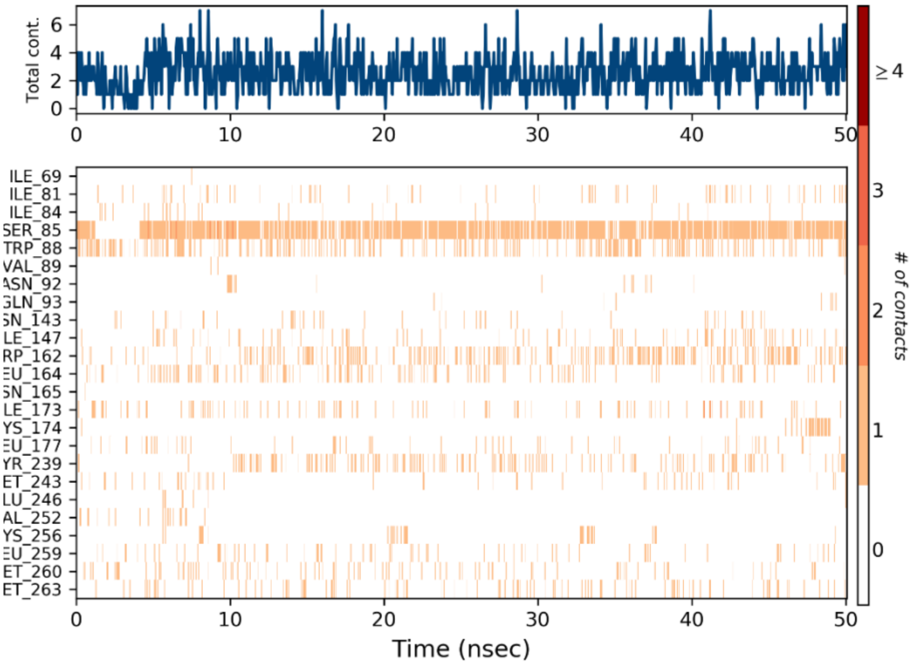


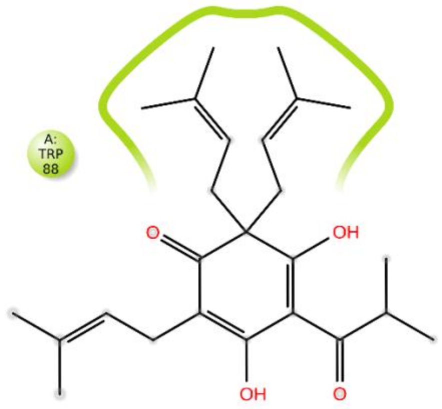
Figure s.i. 2. TAS2R10 molecular dynamics analysis for cis-tetrahydroisocohumulone.

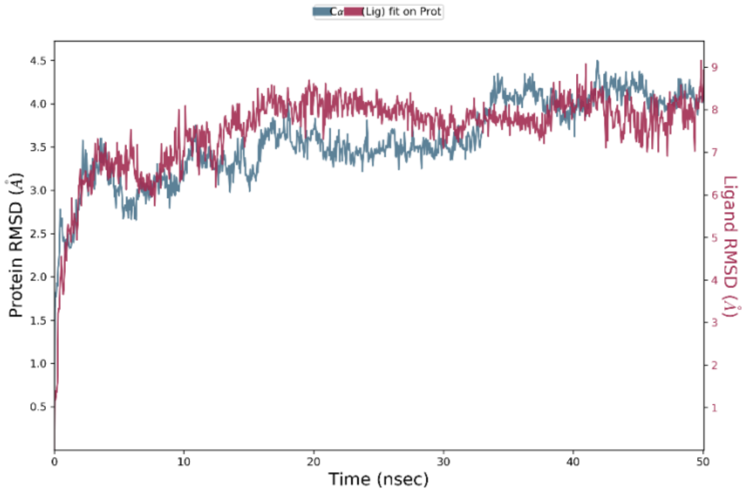
RMSD values are low for protein and ligand.

The most relevant contact occurs with the key residue Ser85, which is stable throughout the simulation. There is also interaction with Trp88, although much more intermittently.

The other contacts are very intermittent and therefore of little relevance.

1.3. Colupulone (20009040)





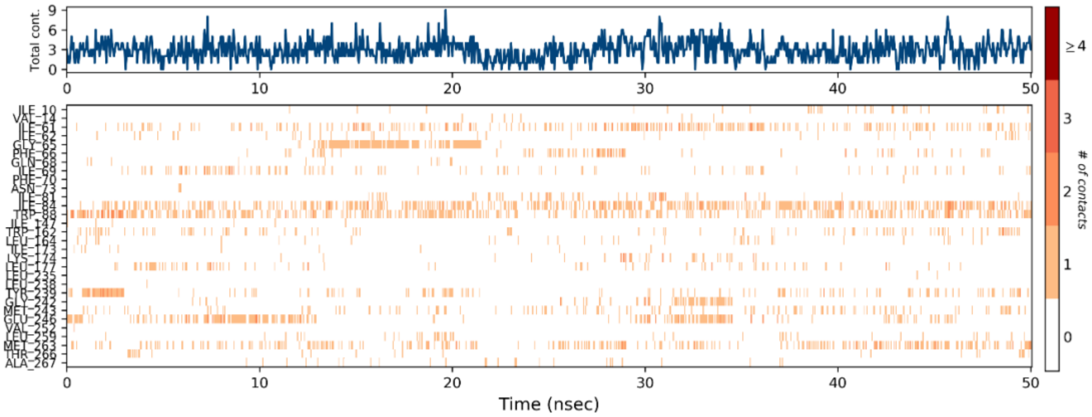
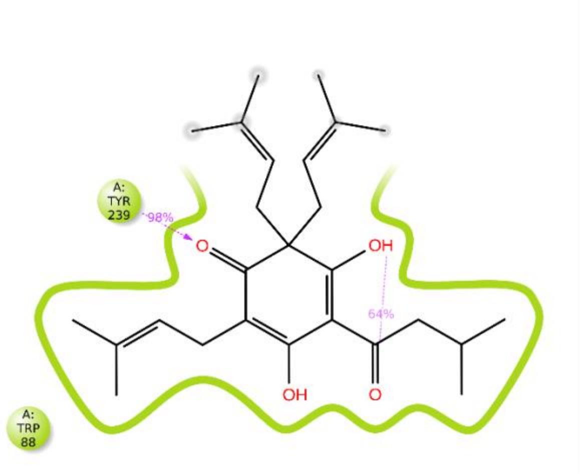


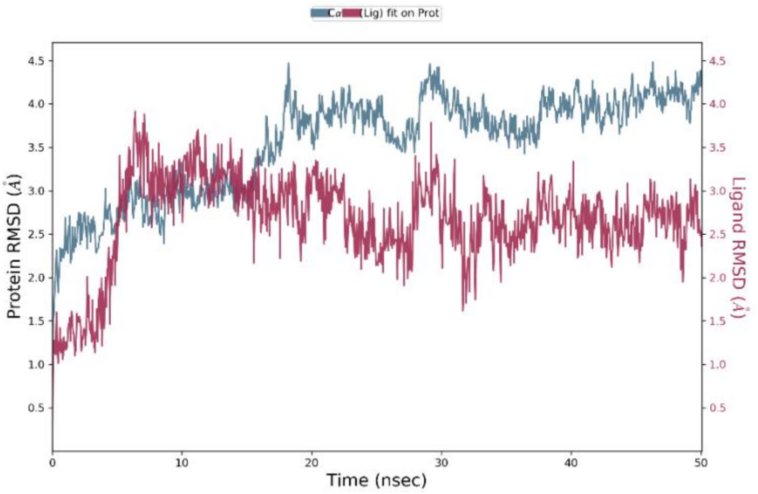
Figure s.i. 3. TAS2R10 molecular dynamics analysis for colupulone.

The RMSD value for the ligand is slightly elevated but remains constant throughout the simulation.

There are quite intermittent contacts, only those with the key residue Trp88, the key residue Met263 (more intermittent than the previous one) and the non-key residue Ile84 being relevant.

1.4. Lupulone (13433819)





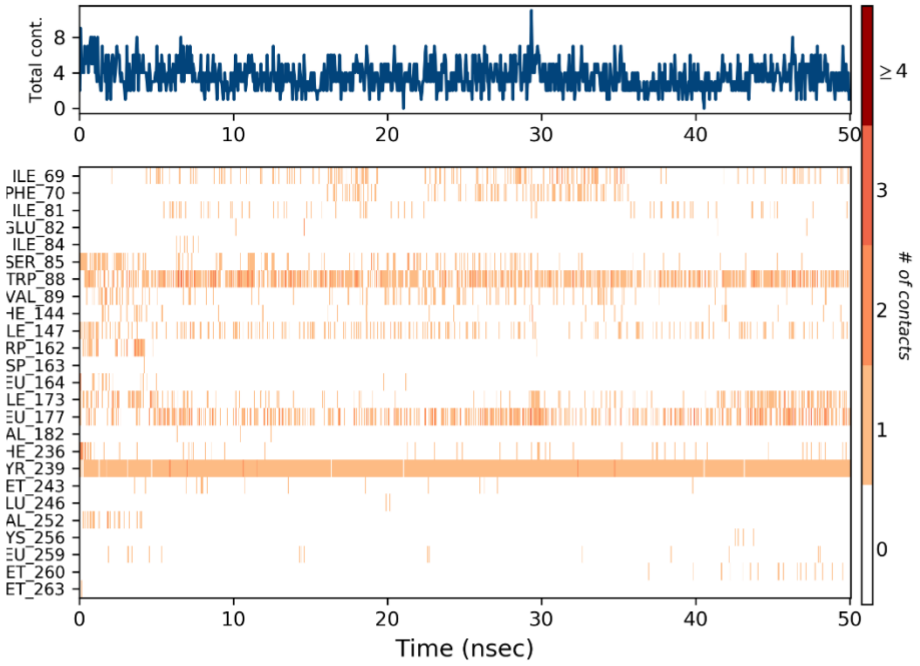


Figure s.i. 4. TAS2R10 molecular dynamics analysis for lupulone.

This simulation presents RMSD values for protein and ligand at normal and stable values.

There is interaction with the key residue Trp88, slightly intermittent but stable throughout the simulation.

Non-key residues include Leu177, with intermittent but stable contact, and Tyr239, which interacts with the ligand permanently throughout the simulation.

1.5. Isoxanthohumol (513197)

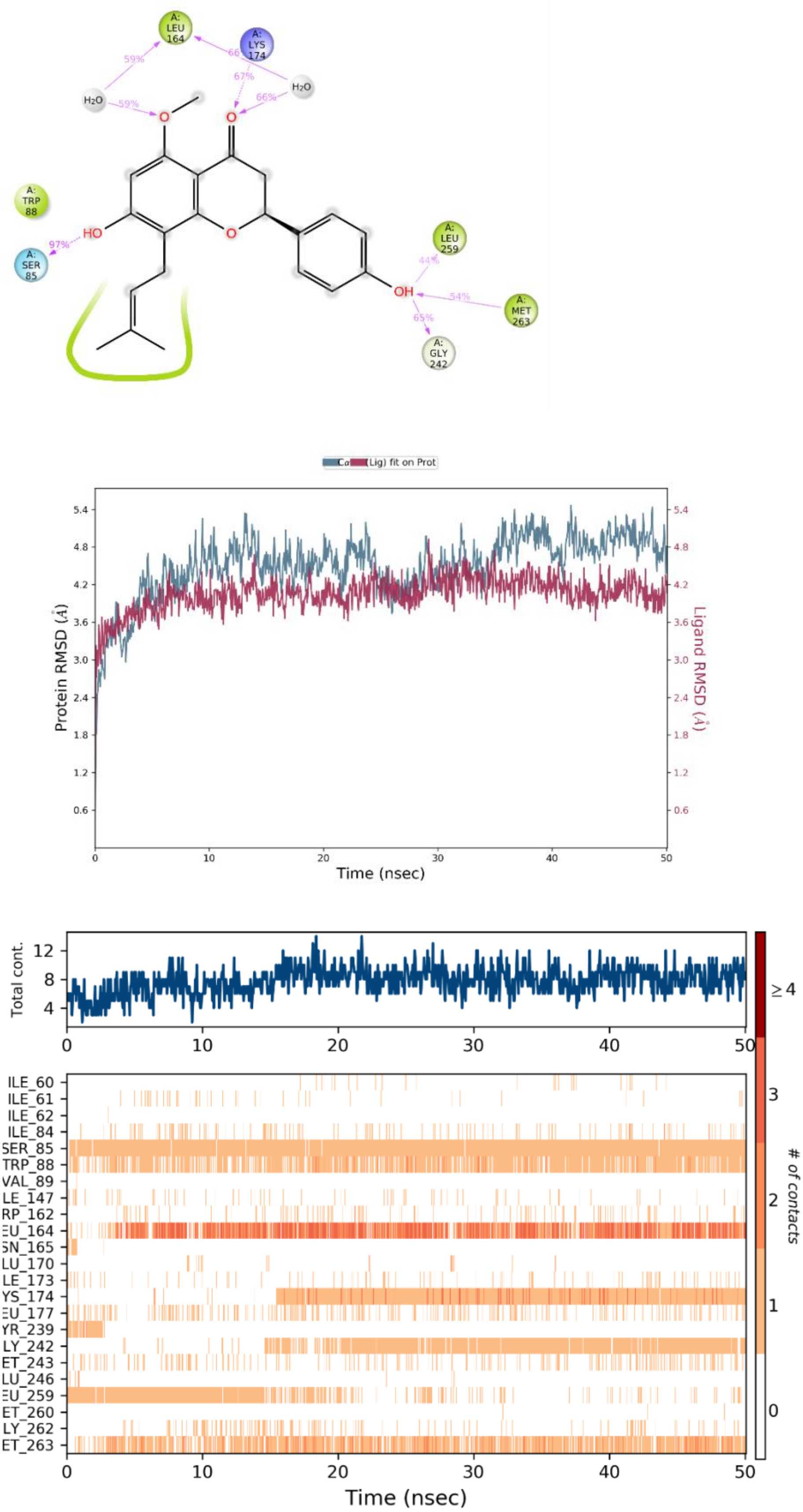


Figure s.i. 5. TAS2R10 molecular dynamics analysis for isoxanthohumol.

Shows normal and stable RMSD values throughout the simulation.

It interacts permanently with the key residue Ser85 and slightly more intermittently, but very constantly, with Trp88 and Met263.

In addition, it has very stable contacts with Leu164, Lys174 and Gly242, which are not key residues, but help stabilise the ligand within the binding site.

1.6. 8-prenylnaringenin (421848)

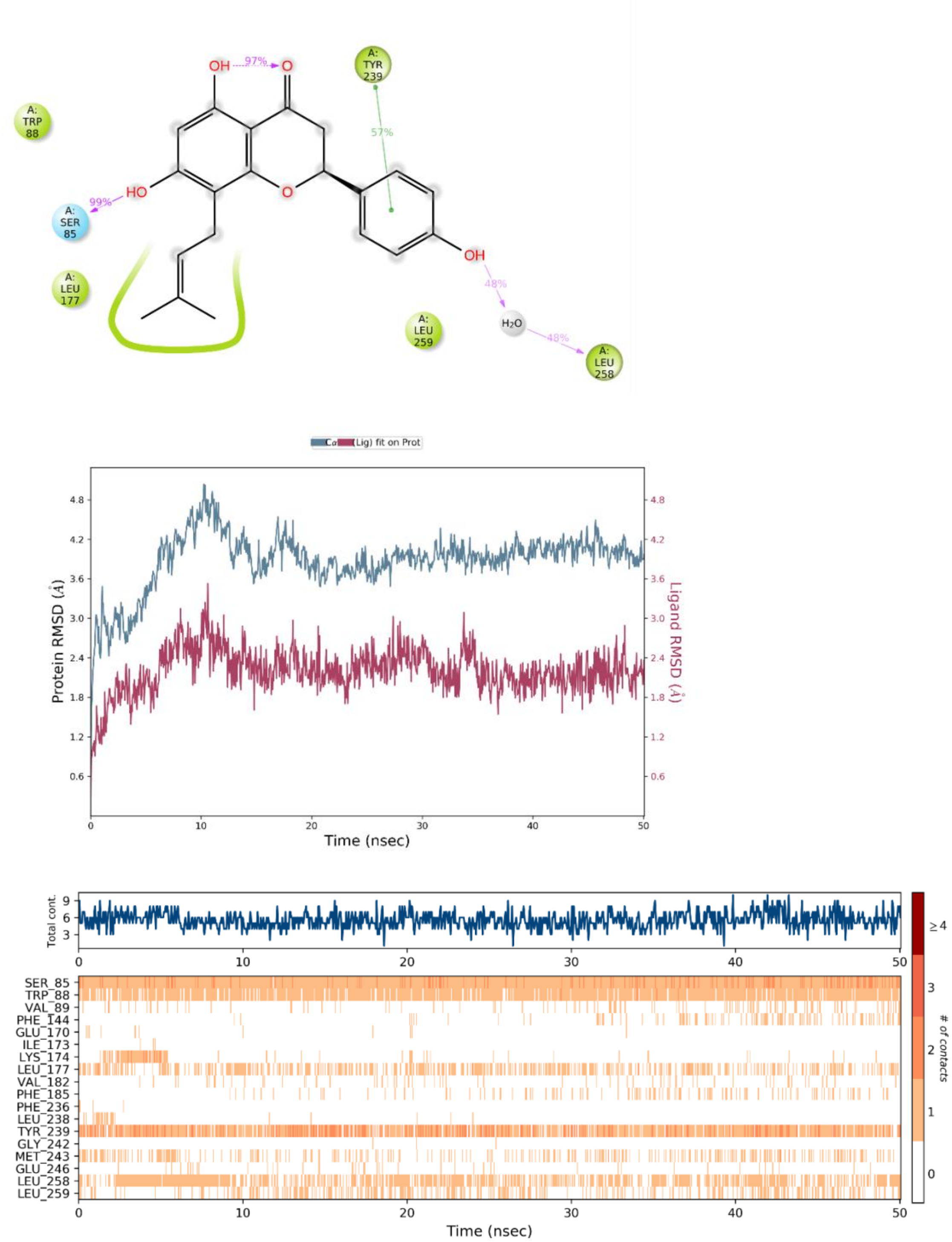


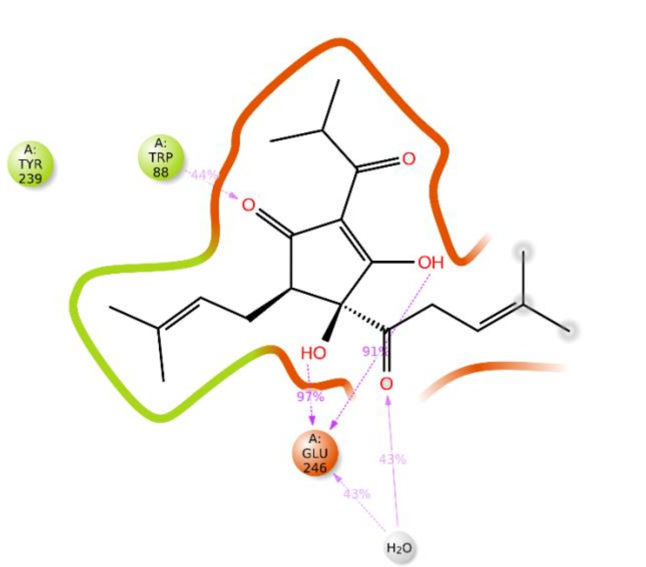
Figure s.i. 6. TAS2R10 molecular dynamics analysis for 8-prenylnaringenin.

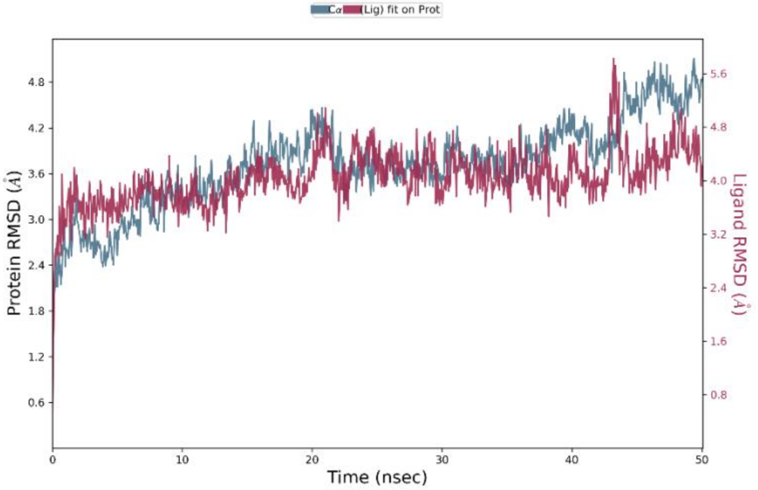
Very low RMSD values, especially for the ligand.

There are permanent interactions with key residues Ser85 and Trp88. Tyr239 and Leu258 are two other very stable contacts, which, despite not being key residues, allow stabilisation of the ligand into the binding site.

Leu177, Met243 and Leu259 are also residues that present intermittent interaction, not so relevant, but they are important for the stability of the ligand, hence the low RMSD values detected.

1.7. Isocohumulone (91370)





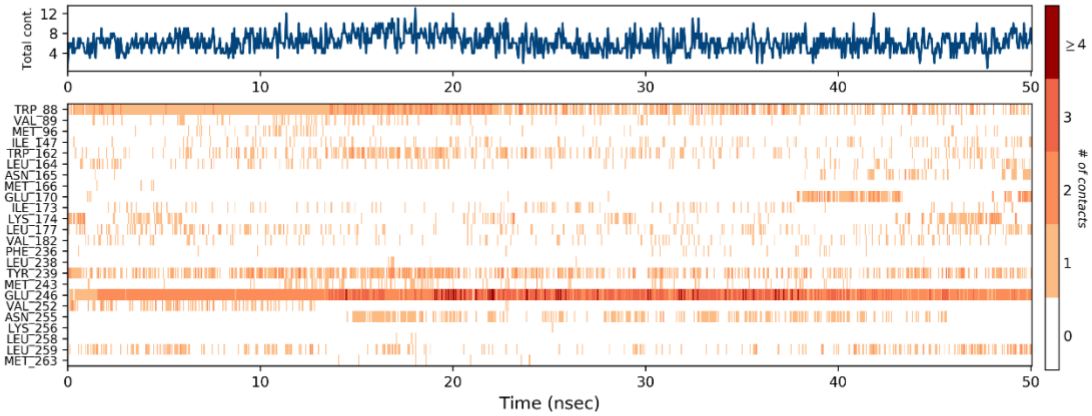


Figure s.i. 7. TAS2R10 molecular dynamics analysis for isocohumulone.

Presents normal and stable RMSD values.

It shows interaction with the key residue Trp88, permanently up to 25 ns of simulation and more intermittently in the second half.

It also has permanent binding with the non-key residue Glu246 and more intermittent binding with residues such as Tyr239 or Leu259. These contacts contribute to the stability of the ligand.

1.8. Xanthohumol (555077)

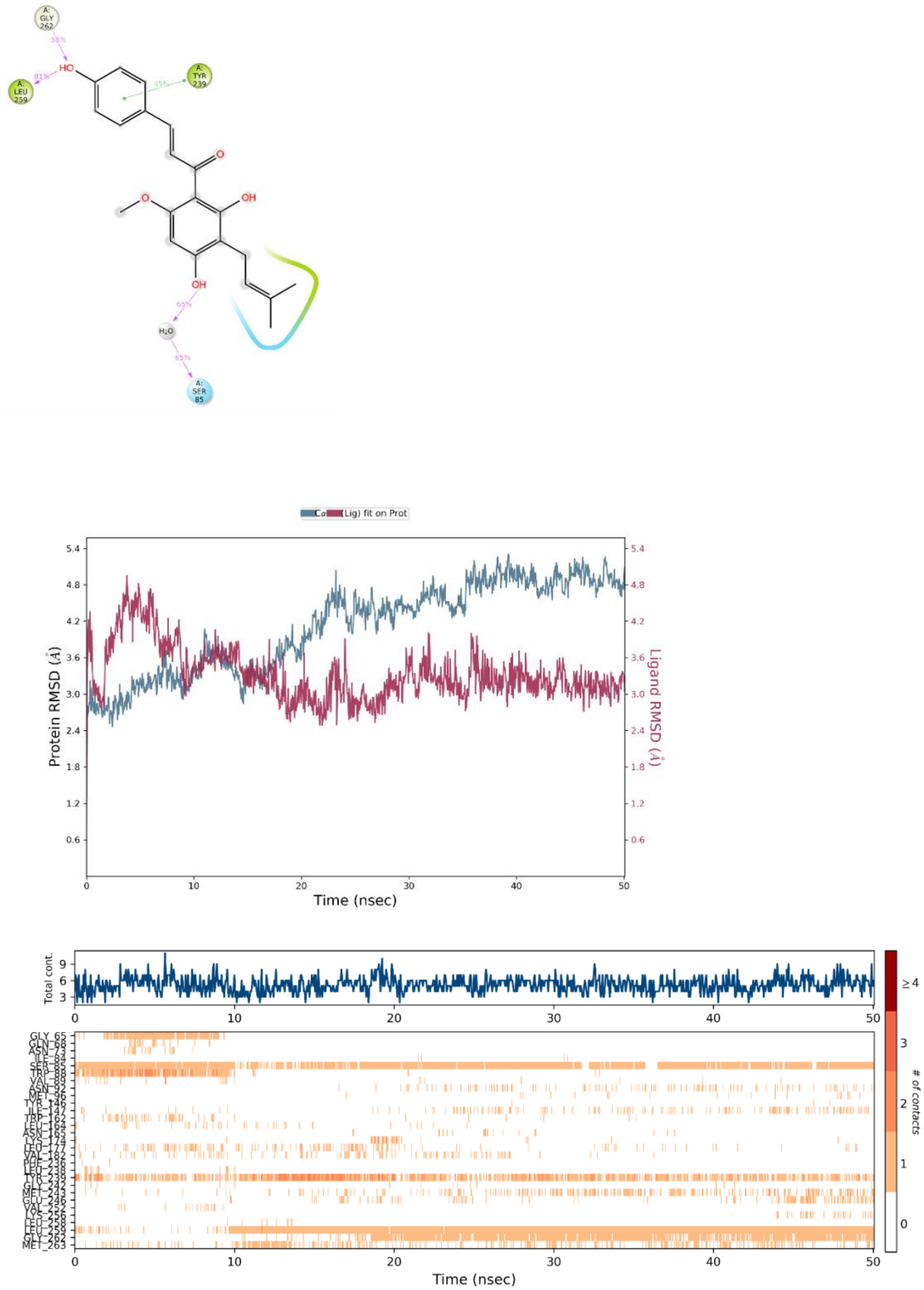


Figure s.i. 8. TAS2R10 molecular dynamics analysis for xanthohumol.

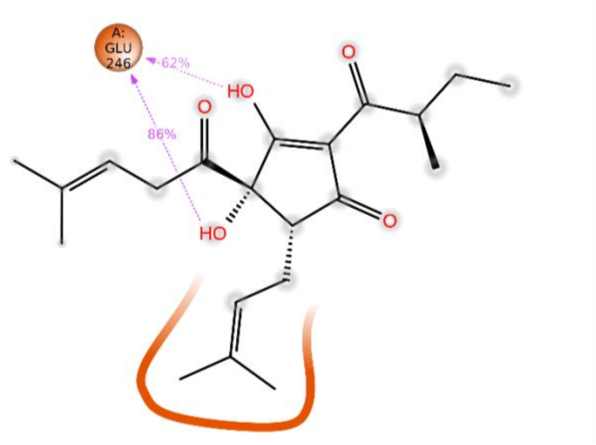
Normal RMSD value for protein and lower RMSD values for the ligand.

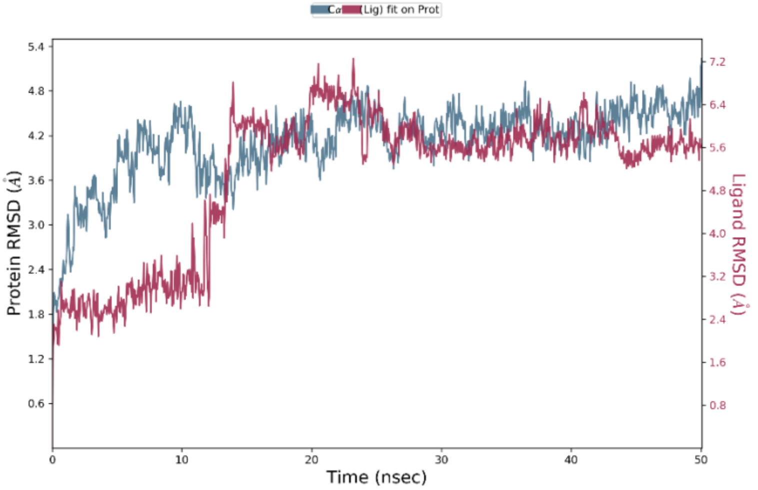
Interacts permanently with the key residue Ser85. In the first 10 ns of simulation, it also interacts very stably with Trp88, but then this interaction is lost.

It also has more intermittent contact with the key residue Met263 throughout the simulation.

In addition, the non-key residues Tyr239, Leu259 and Gly262 show relevant contacts, especially after 10-20 ns of simulation. These contacts help to anchor the ligand to the binding site.

1.9. Isoadhumulone (117231)





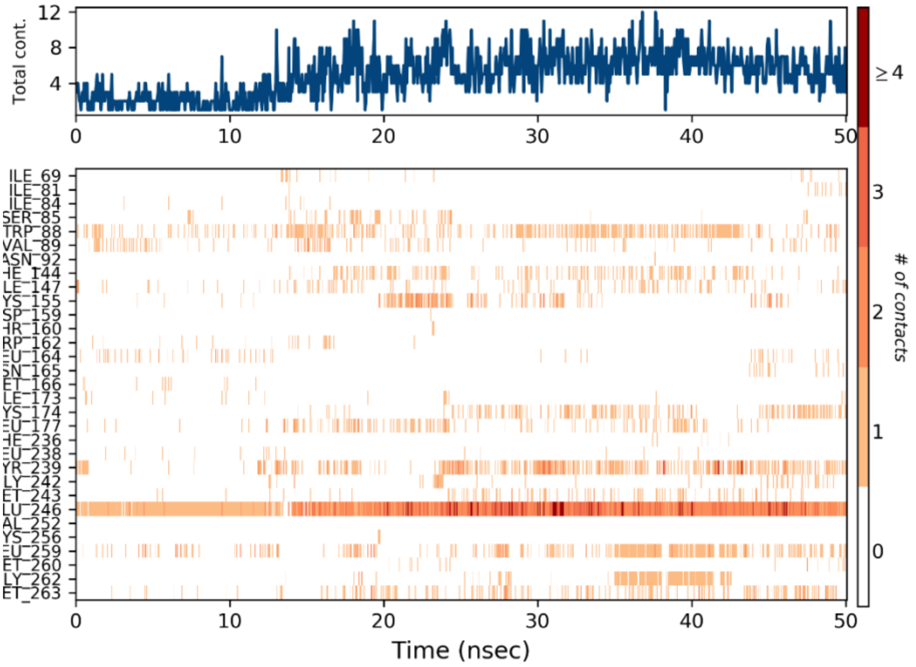


Figure s.i. 9. TAS2R10 molecular dynamics analysis for isoadhumulone.

Slightly elevated RMSD values for the ligand, normal for the protein. Both values are very stable after 20 ns of simulation.

Contacts with the key residues Trp88, Val89 and Met263 are very intermittent. Only one stable contact occurs with Glu246, a non-key residue.

2. TAS2R14

2.1. 8-prenylnaringenin (421848)

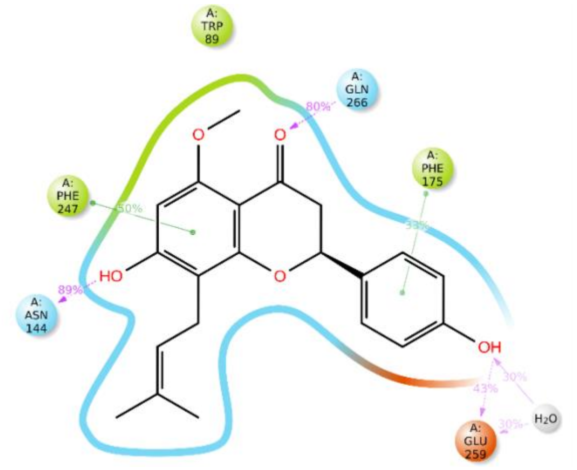
The RMSD values of the ligand are low, and slightly higher for the protein.

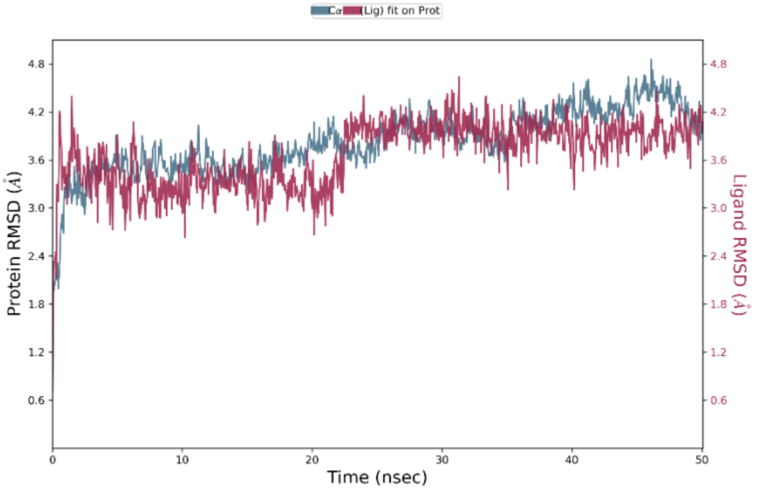
This ligand interacts stably with the key residues Trp89 and Phe247 and somewhat more intermittently with Asn93. It also interacts slightly with Ile262.

With non-key residues, it interacts stably with Trp66 and Asn144 throughout the simulation. From 10 to 50 ns it interacts with Asn157 and between 10 to 30 ns it also interacts with Ser167.

All these contacts, both with key and non-key residues, are responsible for a stable interaction of this ligand within the binding site.

2.2. Isoxanthohumol (513197)





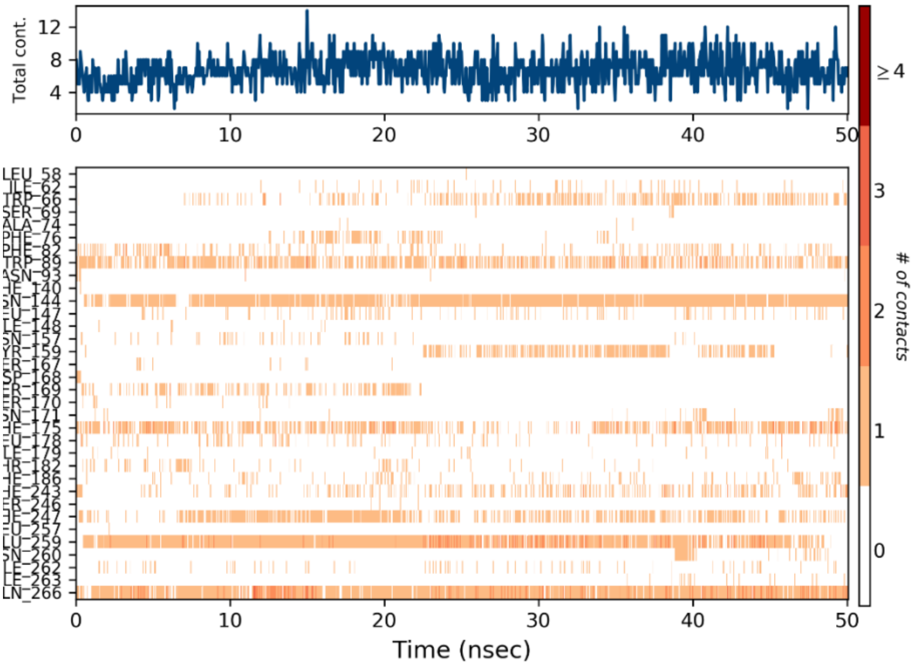


Figure s.i. 10. TAS2R14 molecular dynamics analysis for isoxanthohumol.

The RMSD presents normal and very stable values throughout the simulation, both for protein and ligand.

It stably interacts with the key residue Trp89 and intermittently with Phe186.

It also interacts with non-key residues such as Asn144, Glu259 and Gln266, which help to keep the ligand in a very stable position.

2.3. Xanthohumol (555077)

RMSD values are normal for the protein and slightly higher for the ligand.

Stable interaction occurs with the key residue Trp89, and somewhat more intermittently with residues Asn93 and Phe243. It also interacts with Phe186 and Ile262, but much more intermittently, so these last two contacts are not very relevant.

Regarding non-key residues, Thr86 and Gln266 contacts stand out, which, although they are not stable interactions throughout the simulation, they do help to fix the position of the ligand in the binding site.

2.4. Isocohumulone (91370)

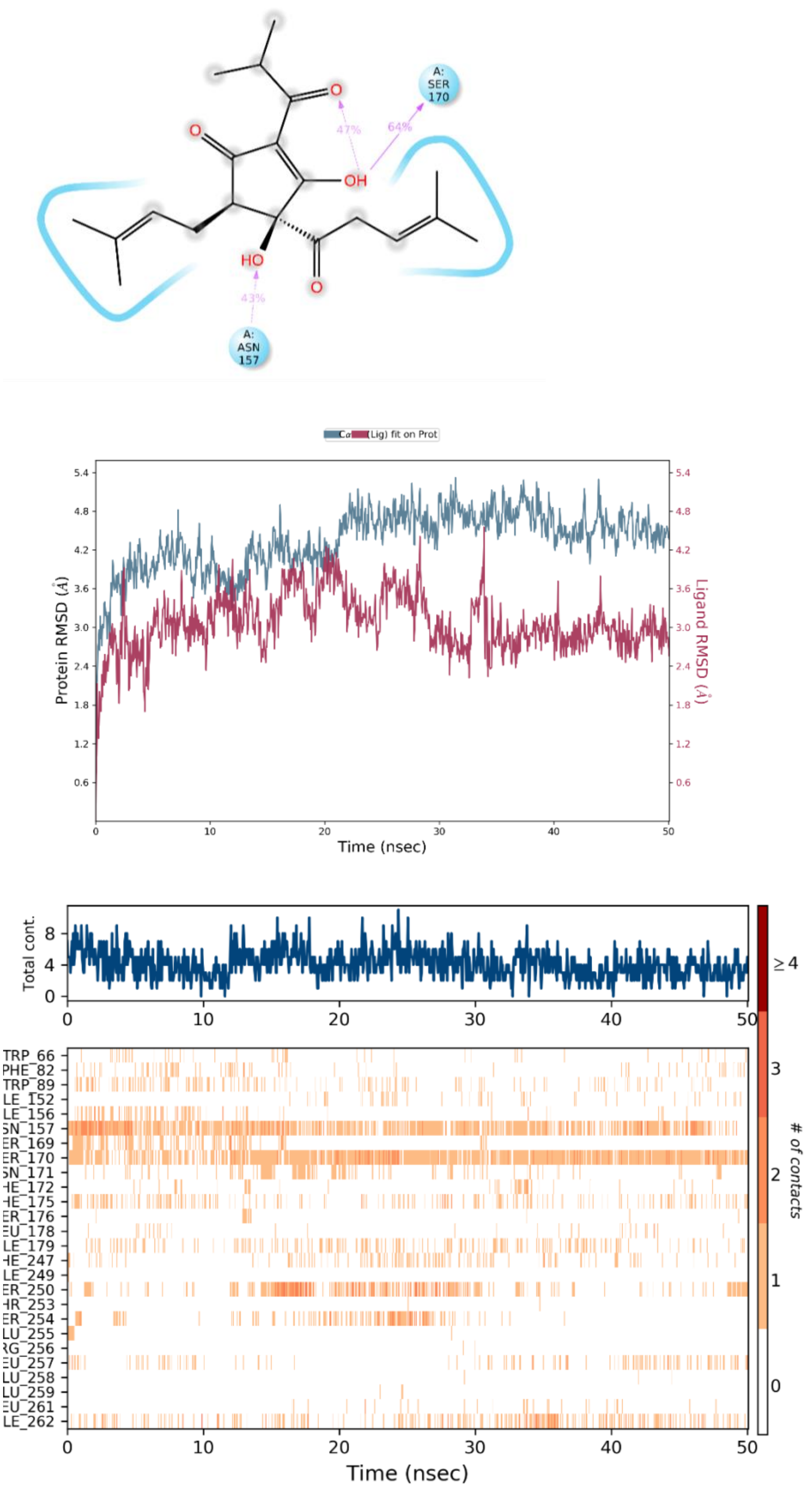


Figure s.i. 11. TAS2R14 molecular dynamics analysis for isocohumulone.

Normal RMSD value for the protein and lower for the ligand.

It has very intermittent interactions, except with the non-key residues Asn157 and Ser170. Regarding key residues, it interacts very intermittently with Trp89, Phe247 and Ile262, but these are not very relevant contacts.

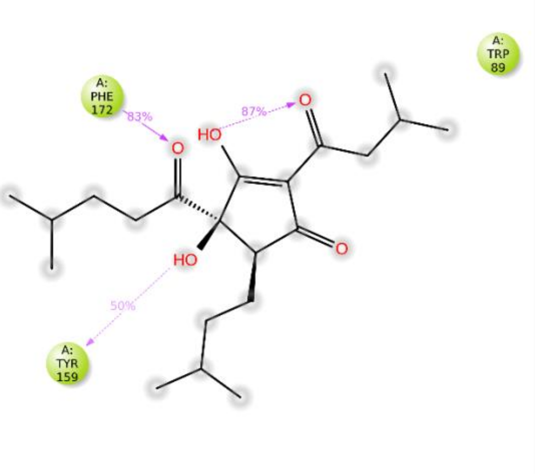
2.5. Isoadhumulone (117231)

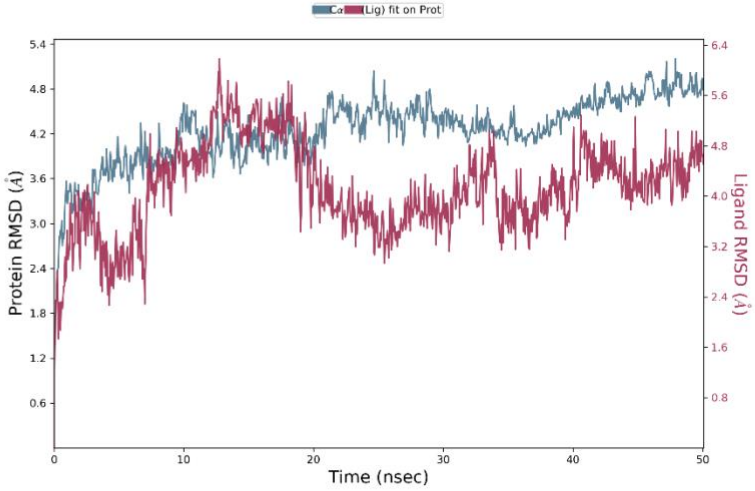
Normal RMSD values for protein and ligand.

It shows intermittent interactions with the key residues Trp89 and Phe247, maintaining both contacts throughout the simulation. It also interacts with the key residue Ile262, although more intermittently.

As a non-key residue, there are permanent interactions from 10 ns onwards with Thr86 and Asn157.

2.6. Cis-tetrahydroisohumulone (25015707)





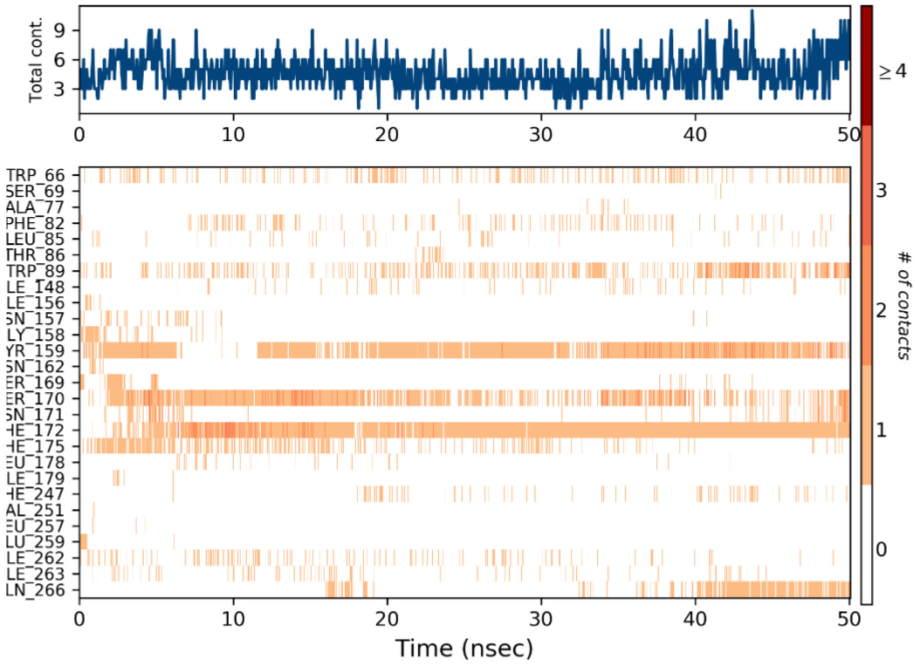


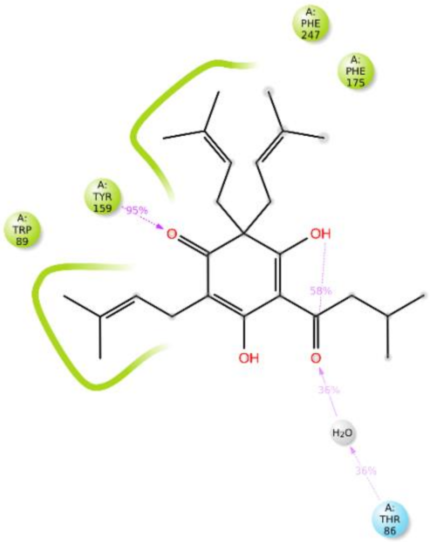
Figure s.i. 12. TAS2R14 molecular dynamics analysis for cis-tetrahydroisohumulone.

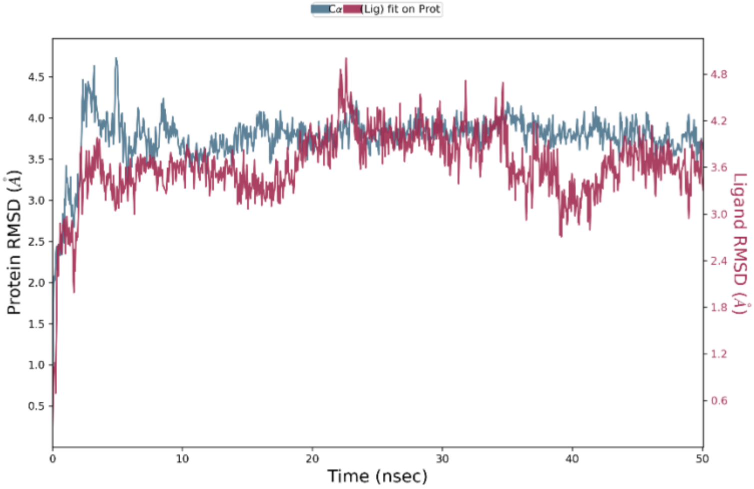
RMSD at normal values for both protein and ligand.

This ligand interacts intermittently with the key residue Trp89. Interactions with Phe247 and Ile262 are practically negligible.

With non-key residues, it interacts permanently with Phe172 and not permanently, but very stably, with Tyr159 and Ser170.

2.7. Lupulone (13433819)





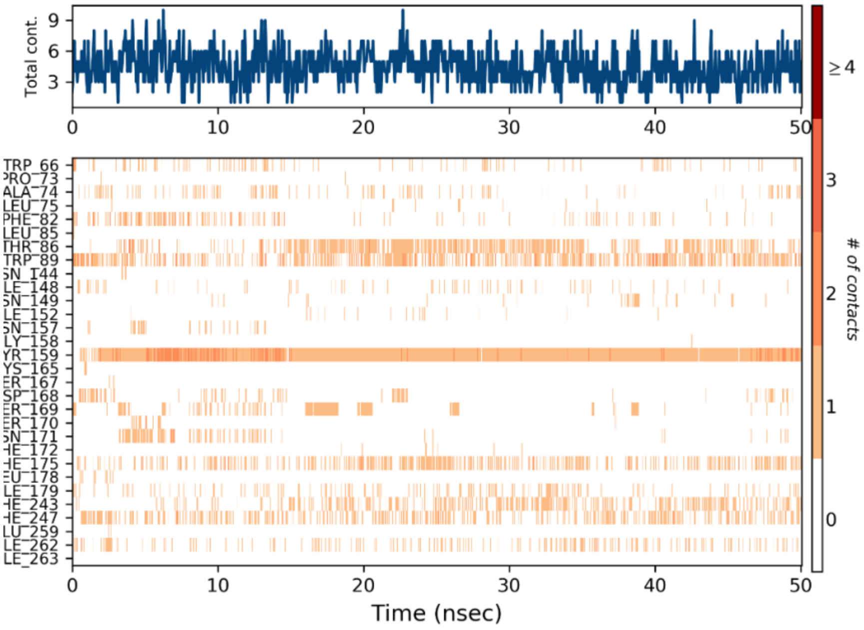


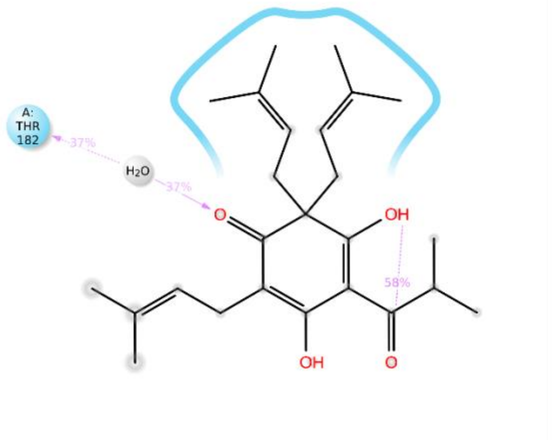
Figure s.i. 13. TAS2R14 molecular dynamics analysis for lupulone.

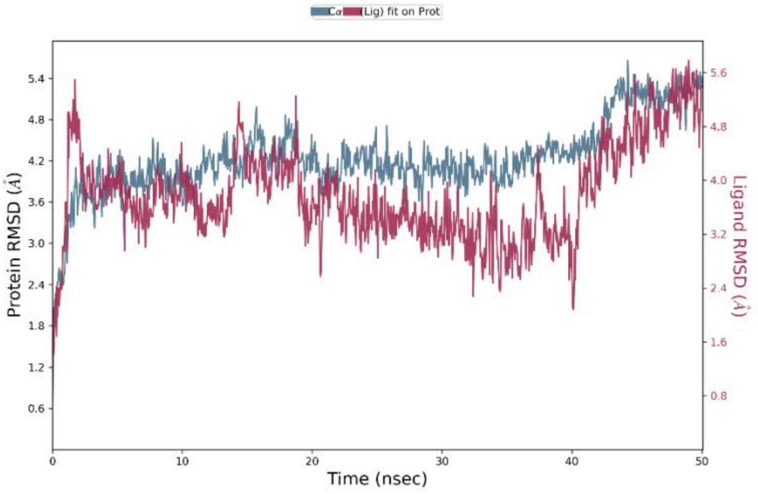
Low RMSD values for both protein and ligand.

Stable interaction with key residues Trp89 and more intermittent interaction with Phe246 and Ile262.

It also interacts with non-key residues, especially with Tyr159. It has other intermittent interactions with Thr86, Phe175 or Phe243, being the other interactions of little relevance due to their high instability.

2.8. Colupulone (20009040)





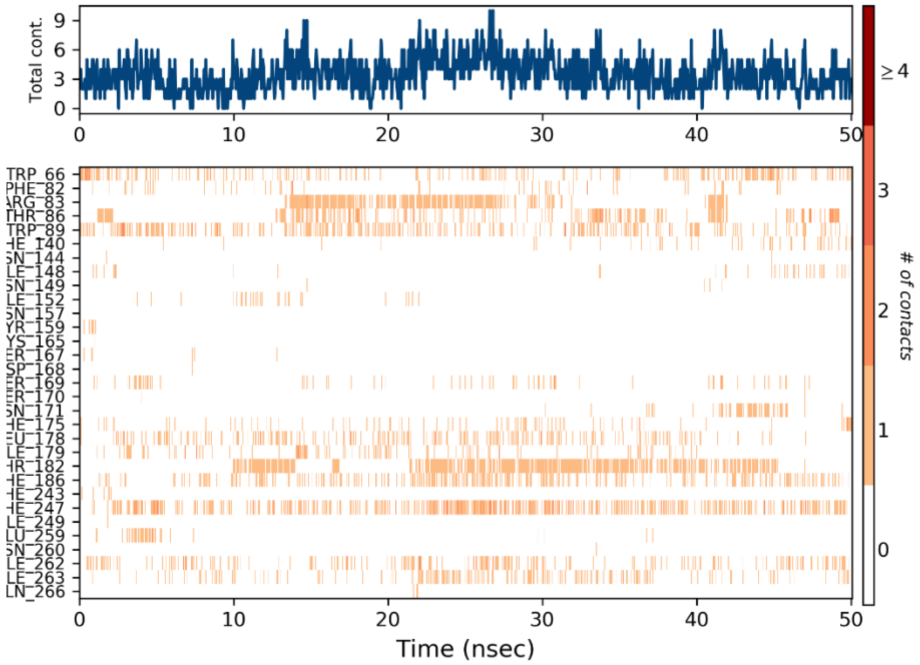


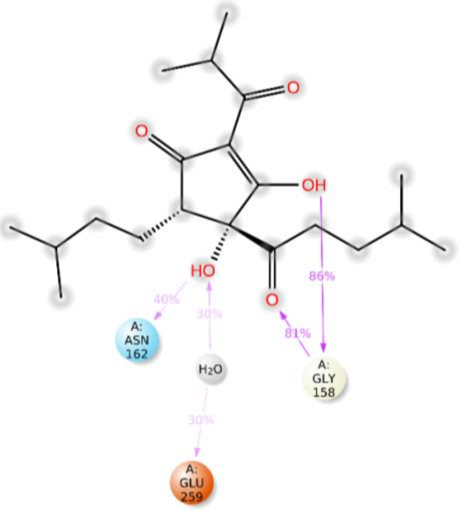
Figure s.i. 14. TAS2R14 molecular dynamics analysis for colupulone.

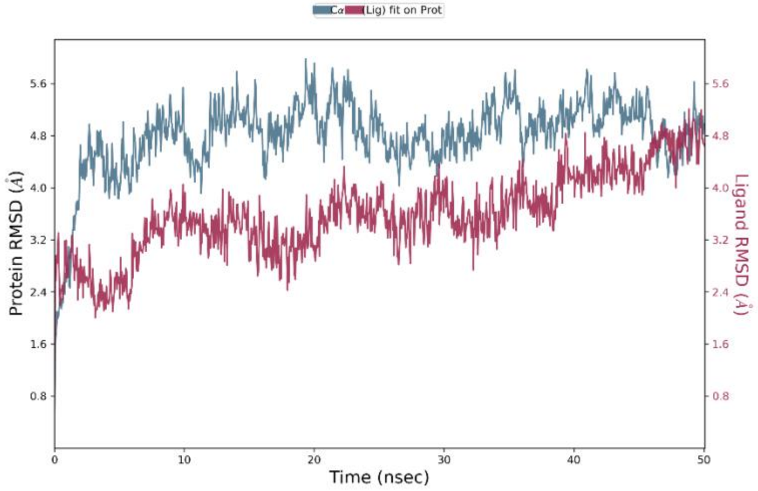
Normal RMSD values, both for protein and ligand, but shows a high fluctuation towards the last 10 ns of the simulation.

All ligand-receptor contacts are very intermittent. Among them, Trp89, Phe186 and Phe247 stand out. Ile262 also shows interaction, but in an even more unstable way.

There is also contact with non-key residues Trp66, Leu178 and Thr182, but they are not very relevant due to their instability.

2.9. Cis-tetrahydroisocohumulone (21671995)





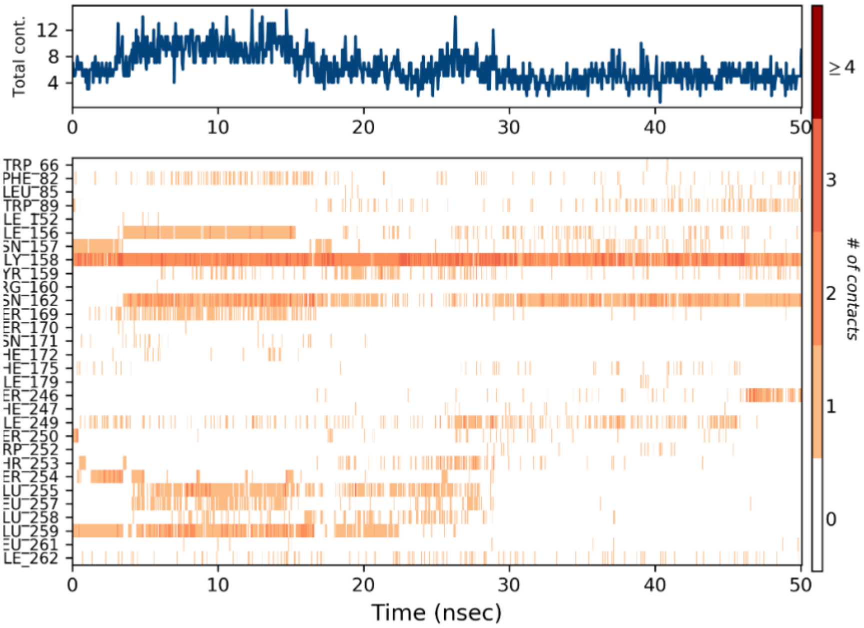


Figure s.i. 15. TAS2R14 molecular dynamics analysis for cis-tetrahydroisocohumulone.

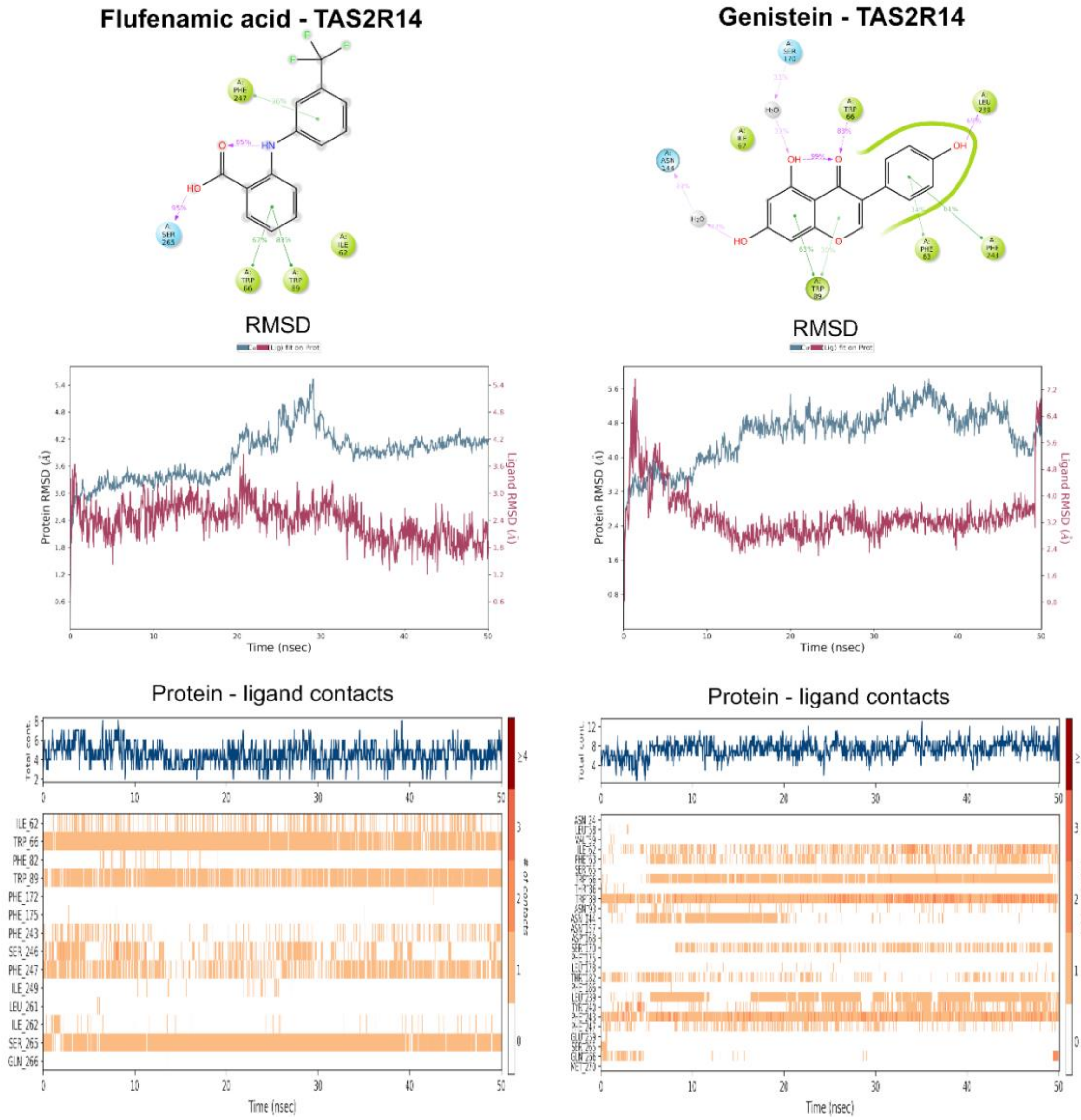
Normal RMSD values for both protein and ligand.

No relevant contact with key residues. Interacts with Trp89 and Ile262, but very intermittently.

Permanent interaction with the non-key residue Gly158, and very stable with Asn162. In addition, at the beginning of the simulation there are stable contacts with Ser169, Glu255 and Glu259, but these are lost after 25 - 30 ns of simulation.

It is a ligand that is well fixed at the binding site, but due to its interactions with non-key residues.

2.10. Fluflenamica acid and genistein



Flufenamic acid - TAS2R14

Genistein - TAS2R14

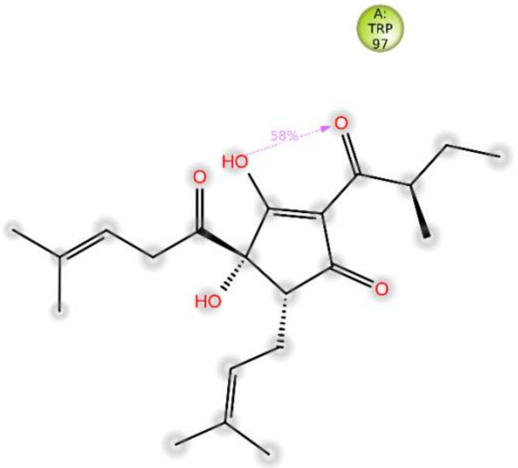
RMSD

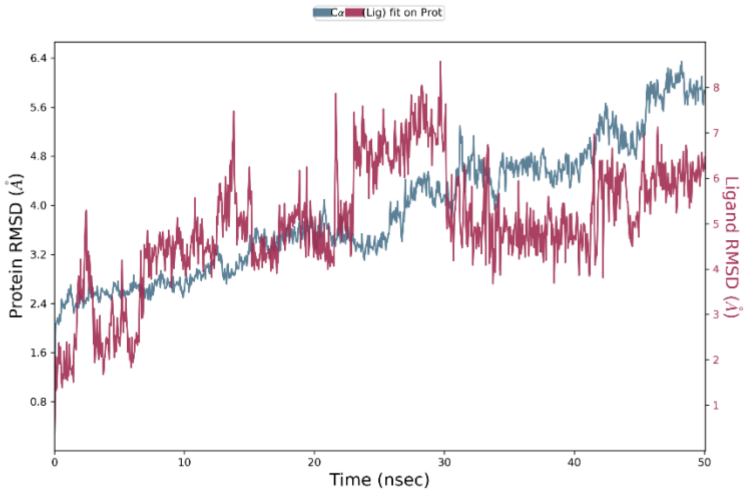
Protein - ligand contacts

Figure s.i. 16. TAS2R14 molecular dynamics analysis for flufenamic acid and genistein. Results obtained with Maestro software.

3. TAS2R46

3.1. Isoadhumulone (117231)





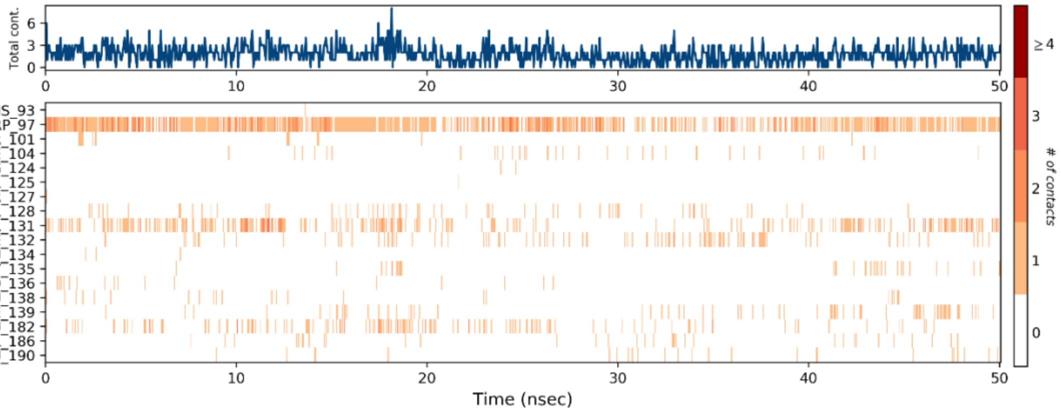
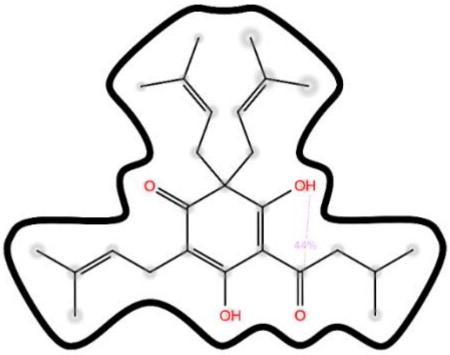


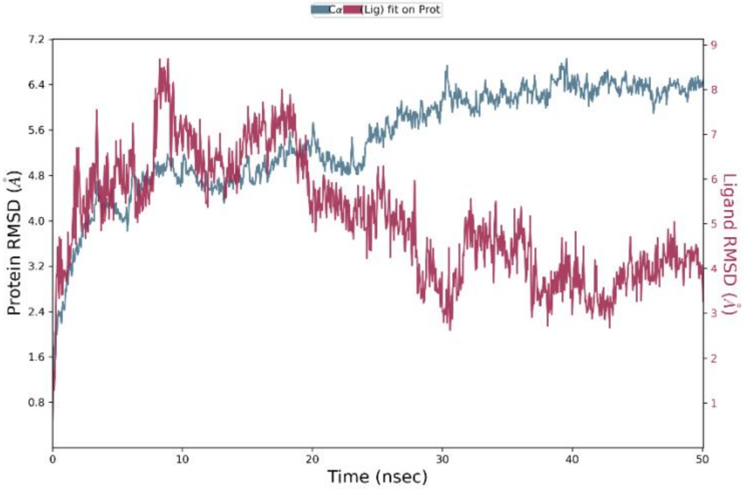
Figure s.i. 17. TAS2R46 molecular dynamics analysis for isoadhumulone.

The RMSD values are slightly higher than in the previous cases.

It shows very unstable contacts, except with Trp97 and does not interact with any key residues.

3.2. Lupulone (13433819)





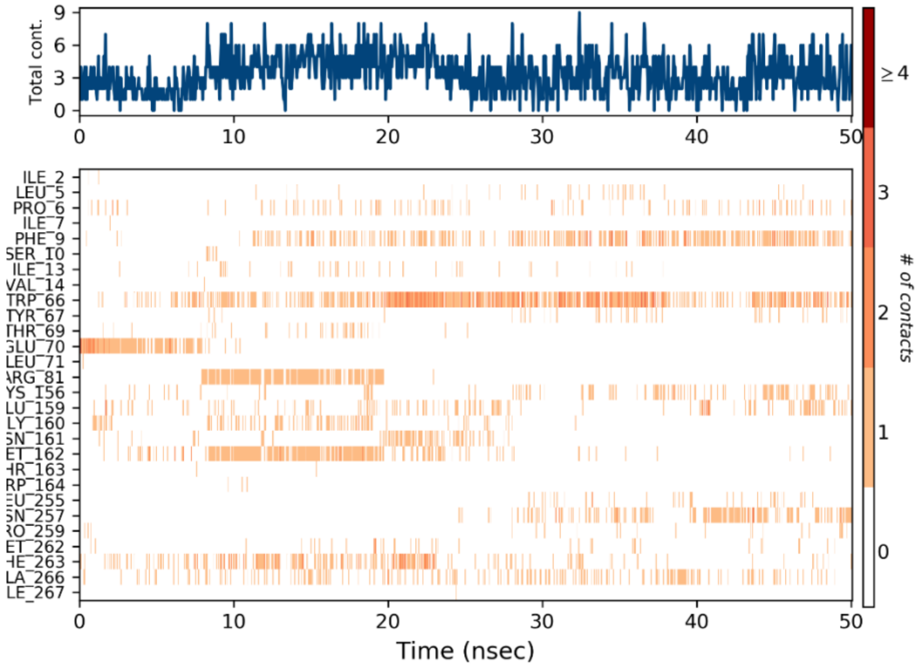
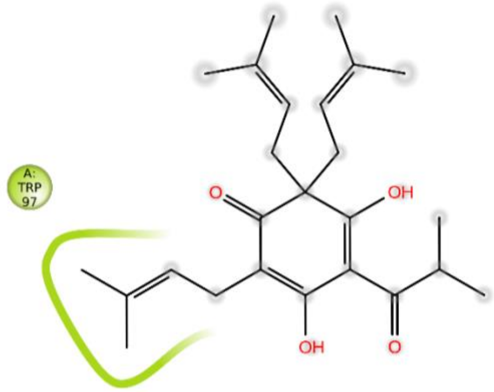


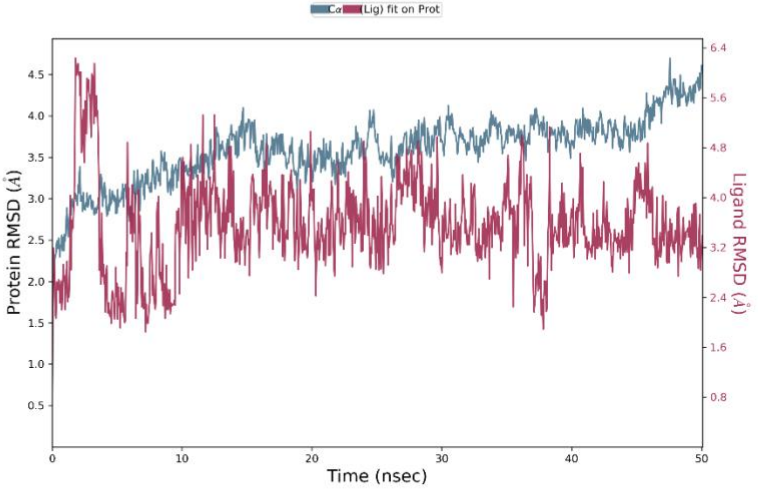
Figure s.i. 18. TAS2R46 molecular dynamics analysis for lupulone.

Normal RMSD value for the ligand, but higher for the protein.

It interacts quite stably with the key residue Trp66 and, for the first 10 ns also with Glu70, but later this contact is lost.

3.3. Colupulone (20009040)





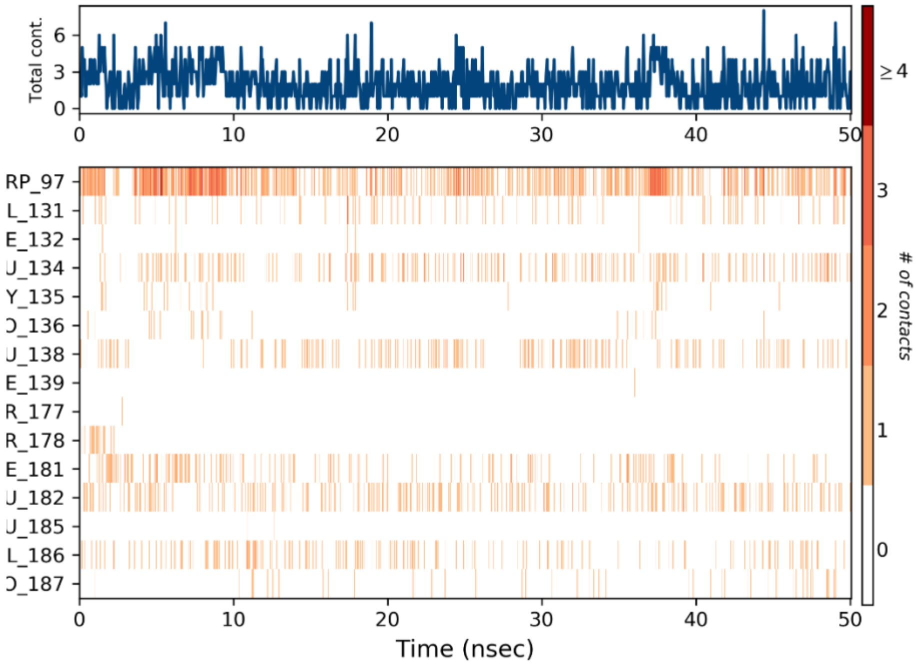


Figure s.i. 19. TAS2R46 molecular dynamics analysis for colupulone.

Normal RMSD value for the ligand, but slightly elevated for the protein.

No interaction with any key residue and very unstable contacts, except with residue Trp97.

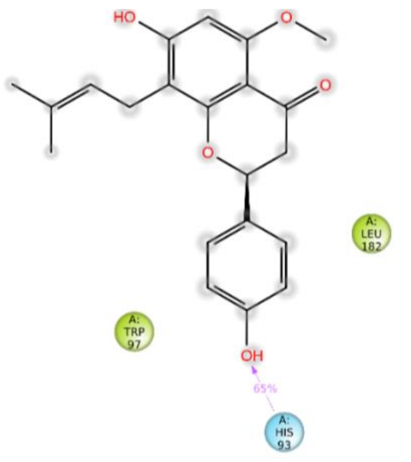
3.4. Xanthohumol (555077)

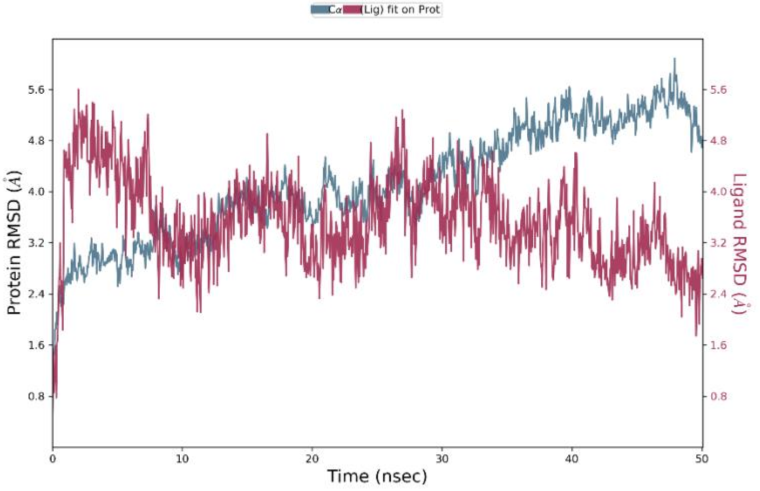
Normal RMSD values for both protein and ligand.

Forms stable contact with key residues Trp88 and Asn176. It also contacts more intermittently with key residue Asn92.

In addition, it has stable interactions with non-key residues Tyr85, Asn184 and Tyr241, which help to anchor the ligand at the binding site.

3.5. Isoxanthohumol (513197)





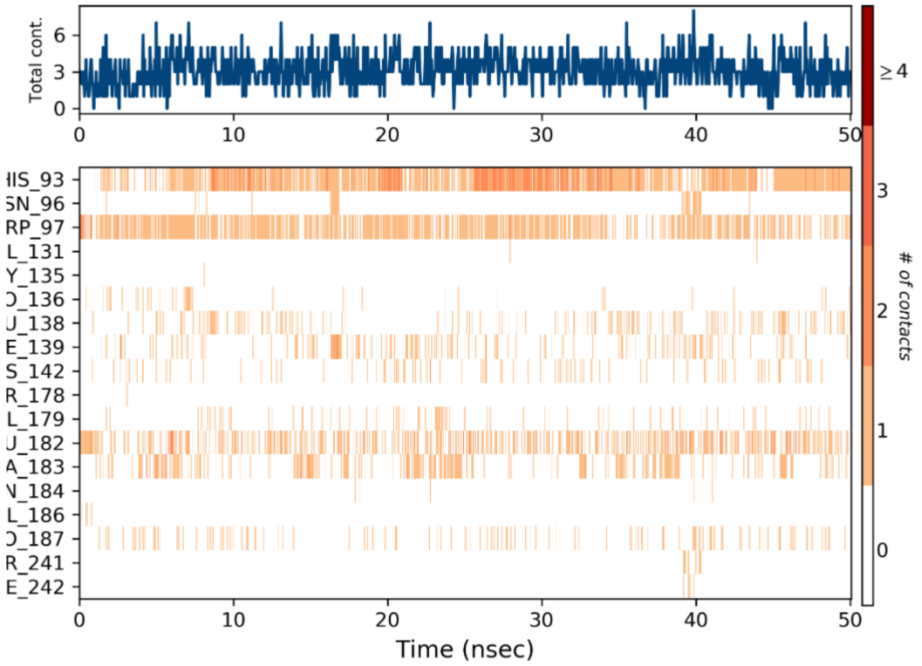
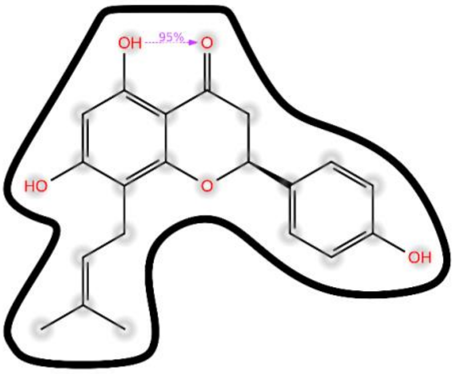


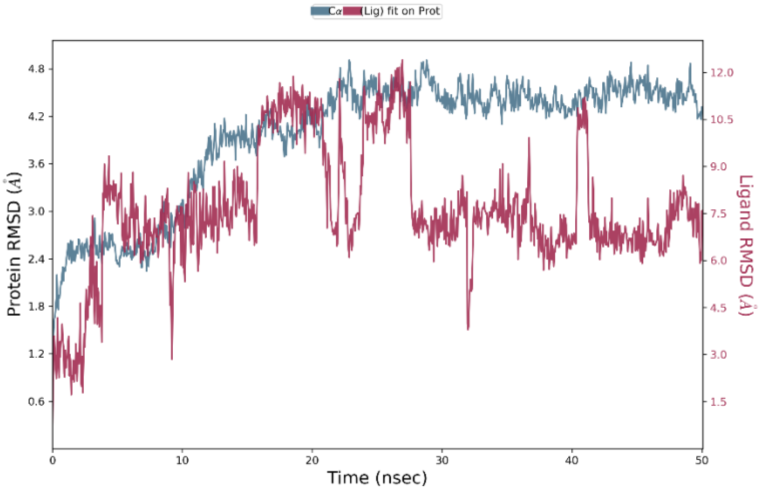
Figure s.i. 20. TAS2R46 molecular dynamics analysis for isoxanthohumol.

Normal RMSD values for both protein and ligand.

Stably interacts with His93 and Trp97, and more intermittently with Leu182, but does not interact with any key residues.

3.6. 8-prenylnaringenin (421848)





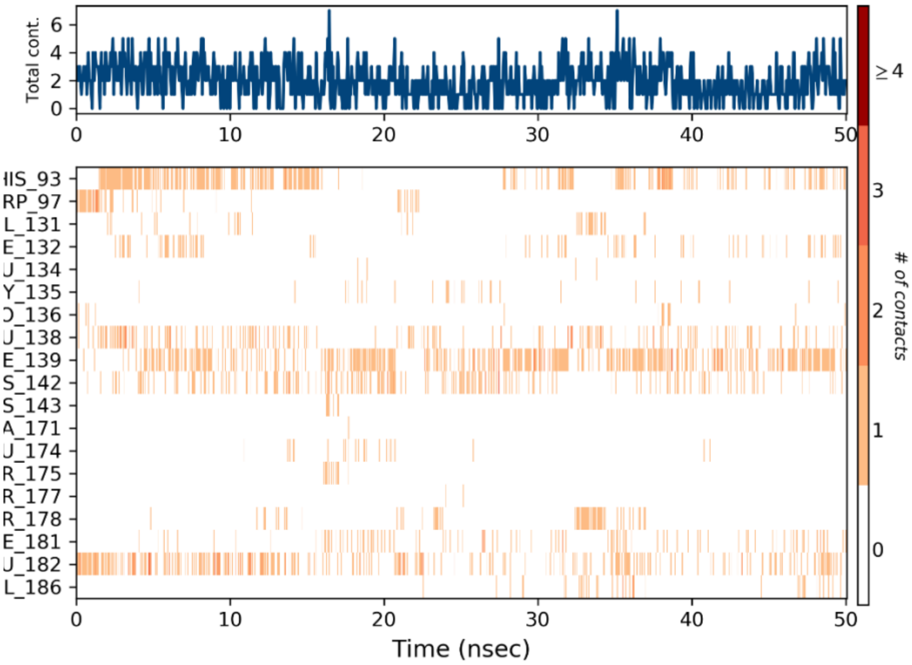


Figure s.i. 21. TAS2R46 molecular dynamics analysis for 8-prenylnaringenin.

Fluctuating and slightly elevated RMSD values, especially between 15 and 30 ns.

This ligand shows very unstable interactions. The only contacts that are maintained throughout the simulation, albeit intermittently, are Phe139, Cys142 and Leu182.

It does not interact with any key residues.

3.7. Isocohumulone (91370)

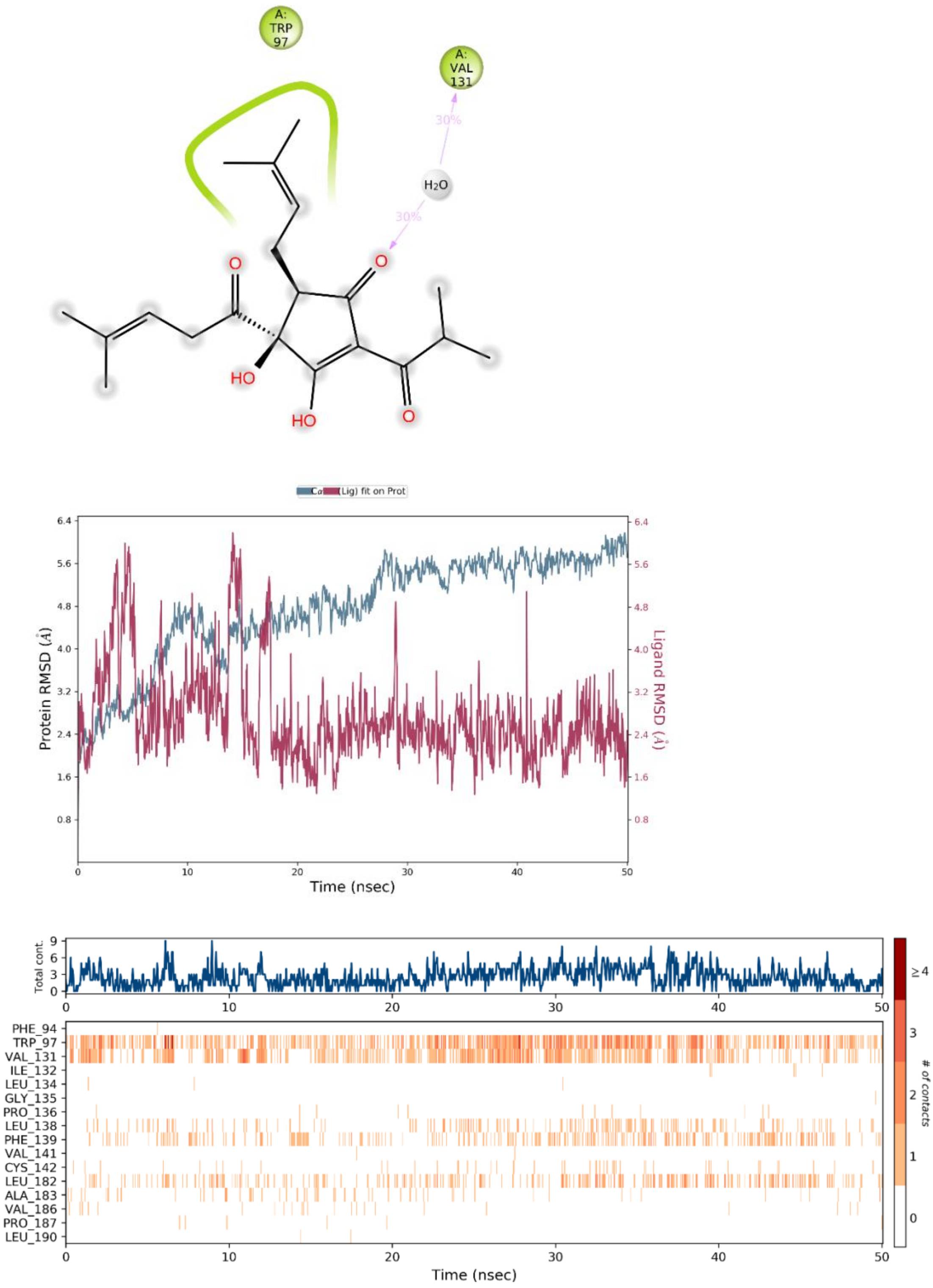


Figure s.i. 22. TAS2R46 molecular dynamics analysis for isocohumulone.

Low RMSD values, especially for the ligand.

It does not interact with any key residues but does form stable interactions with Trp97 and Val131. It also interacts more intermittently with Phe139 and Leu182.

3.8. Cis-tetrahydroisohumulone (25015707)

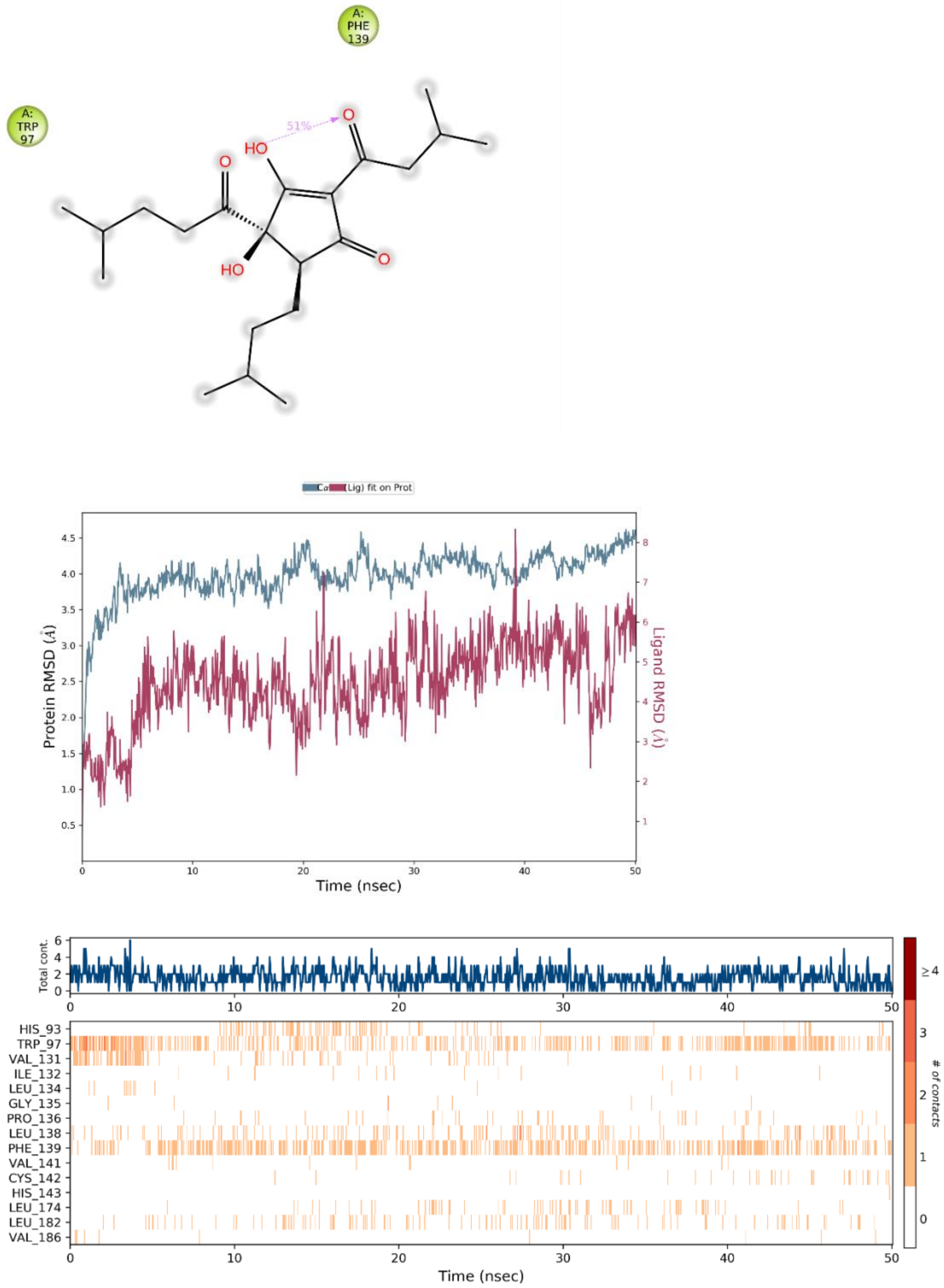


Figure s.i. 23. TAS2R46 molecular dynamics analysis for cis-tetrahydroisohumulone.

The RMSD value is normal for the protein, but very high for the ligand.

It does not interact with any key residues, although it does form intermittent interactions with Trp97 and Phe139.

3.9. Cis-tetrahydroisocohumulone (21671995)

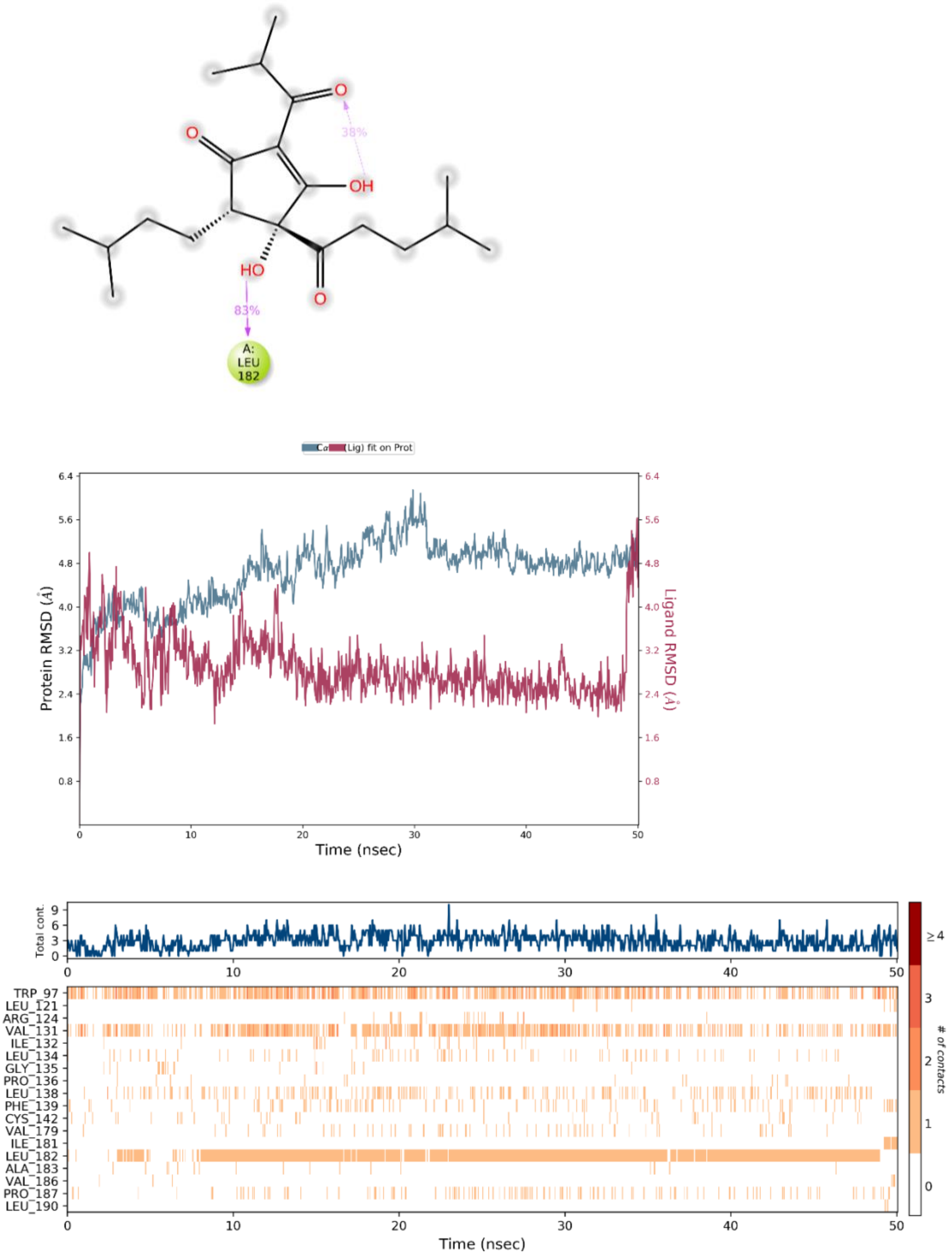


Figure s.i. 24. TAS2R46 molecular dynamics analysis for cis-tetrahydroisocohumulone.

The RMSD shows normal values for protein and ligand. Around ns 48, there is a significant fluctuation, which can be explained due to the change of Leu182 bond to a bond with Ile181.

It does not interact with any key residue, but it shows stable interactions with Trp97, Val131 and especially with Leu182.