Subject: Pentavalent carbonyl issue (urea formation?)
Posted by padster on Thu, 22 Jun 2023 19:14:13 GMT
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Hi, I am trying to create a combinatorial library (macrocyclic peptide) in DataWarrior. The issue I run into however is that every amide bond forms correctly with the next amino acid, but for some reason it also forms a bond (red bond in image) between the N and C=O of the same amino acid, creating a urea-like motif (refer to image attached). If the red bond is deleted, it forms the correct structure. Curiously, this issue does not happen when running DW on Mac. Is there a way to fix this on Windows so that it runs correctly as well, or is there some sort of setting that changes this? I reinstalled DW, but still run into the same issue.

Macrocycle:
Reaction:

```
File Attachments
1) Screenshot_1.png, downloaded 285 times
2) Screenshot_2.png, downloaded 272 times
```

Subject: Re: Pentavalent carbonyl issue (urea formation?)
Posted by thomas on Fri, 23 Jun 2023 07:26:41 GMT
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Can you post the reaction as .rxn file, please? Or better a small macro containing the complete combinatorial library task with reaction and one real reactant for each generic reactant? This way I could directly reproduce the issue. Thanks in advance...

Subject: Re: Pentavalent carbonyl issue (urea formation?)
Posted by padster on Fri, 23 Jun 2023 18:02:09 GMT
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Sure thing, attached are four .dwar files with one structure each for one cycle and the .rxn file:

I'm not sure how to provide a macro to be honest

```
File Attachments
1) Cycle1.dwar, downloaded 90 times
2) Cycle2.dwar, downloaded 81 times
3) Cycle3.dwar, downloaded 80 times
4) Cycle4.dwar, downloaded 69 times
5) 4 macrocycle disulphide.rxn, downloaded 74 times
```

Subject: Re: Pentavalent carbonyl issue (urea formation?)
Posted by padster on Fri, 23 Jun 2023 18:27:57 GMT
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Perhaps this macro works?

Subject: Re: Pentavalent carbonyl issue (urea formation?)
Posted by thomas on Sat, 24 Jun 2023 14:53:12 GMT
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Thank you for the files. To me it seems that your atom mapping is incorrect. The reactants fragments consisting out of a carbonyl group with attached bridge bond to nitrogen should not break bonding in the reaction, thus they should appear in the product the same way with the same mapping numbers. I have attached the updated macro file, which seems to work fine now.

The upper reaction shows your original mapping, the lower one shows the updated mapping:

Subject: Re: Pentavalent carbonyl issue (urea formation?)
Posted by padster on Sat, 24 Jun 2023 21:45:29 GMT
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Hi Thomas, thanks for getting back to me. However, I still get the incorrect product when I run your macro. When I try to make it myself, it rearranges the mapping so that each nitrogen is 1, 6, 9 or 12 and the first carbonyl is 2-3, but the second one is 4-5 (see attached image). It is also strange how my old mapping does not work on Windows, but it worked perfectly fine on Mac. I'm getting the idea that the Windows version is reading the mapping different or automatically changes it somehow (if that's even possible).

Image:
Structure:

Subject: Re: Pentavalent carbonyl issue (urea formation?)
Posted by thomas on Sun, 25 Jun 2023 11:31:38 GMT

If I import and run the macro from my last message, then I get the following product (with both versions 5.5.0 and with the current dev update):

If you use the same version on MacOS, Linux, or Windows, then it should behave exactly the same. Which version do you use anyway? The official 5.5.0, that mean the most recent (but 2 years old) official installer? Then I would recommend to update to the newest dev build (on the download page click on the 'read and understood checkbox, then click the link in the small print for you platform and download the respective archive with patch files for your installation)

Did you manually map as many atoms as it needs for auto-mapper to correctly map all remaining atoms of the reaction? If not, I suggest to remove all manual mapping and start from scratch to map at least all four O=C...N fragments manually.

Another tip: Typically, one does not use atom or bond query features on the product side of the generic reaction. Bridge bonds are an exception, because whatever matches on the reactant side needs to be reconstructed on the product side. If all your real reactants have the same bridge length, then I would remove the bridge bond from the reaction and replace it with real bonds and atoms.

One more tip: A part of the new medium sized ring comes from unknown components. For the sake of complete and perfect mapping and a stoichiometrically complete reaction you might introduce a fifth reactant with the missing atoms, that is always the same.

File Attachments
1) correctProduct.png, downloaded 240 times

Subject: Re: Pentavalent carbonyl issue (urea formation?)
Posted by padster on Sun, 25 Jun 2023 18:56:21 GMT

Installing the dev build seems to have done the trick! Thanks a ton!