Reverse Engineering Fragrance and Flavors with MMP Flavor Plus

Molecular Modeling Pro Flavor Plus (**FFOS Software and Norgwyn Montgomery Software**) has been used by Food and Flavor, Fragrance, Health and Environmental companies to aid in calculating various physical and chemical properties of small volatile organic compounds. The program also uses an algorithm based on molecular structure and thermodynamic properties to calculate odor and taste thresholds of small molecules in various liquid media as well as in air.

Based on structure only, MMP Flavor Plus rapidly provides boiling point and density data and estimates melting point, vapor pressure, heat of formation, ionization potential, heat capacity, critical properties (Temperature, Pressure and Volume), dipole moments, moments of inertia, and diffusion coefficient. Structure and functionality are determined using a rotational/translation factor and G (acceleration) factors derived from the model used to determine odor thresholds.

Recently, olfactory information was also programmed into the model. A database of over 4000 compounds was used to compare much of the thermodynamic and other calculated parameters to the scent characteristics of the molecule. Three structural parameters were found which can be used to describe scent characteristics. These three parameters are called scent increments and are derived from the rotational/translational factor, and from thermodynamics such as boiling point, number of atoms and critical properties.

This simple model assumes that these three parameters can be used to estimate the odor properties of any molecule based on structure. The model is not based on neural networks nor A. I. but only on molecular properties that engineers and chemists have been able to calculate for decades.

In this short publication I will demonstrate how a new flavor molecule can be designed and engineered by MMP Flavor Plus. First, a molecule is chosen from our database with known scent properties and scent increments. I have chosen Limonene $C_{10}H_{16}$ in this example (see Figure 1).

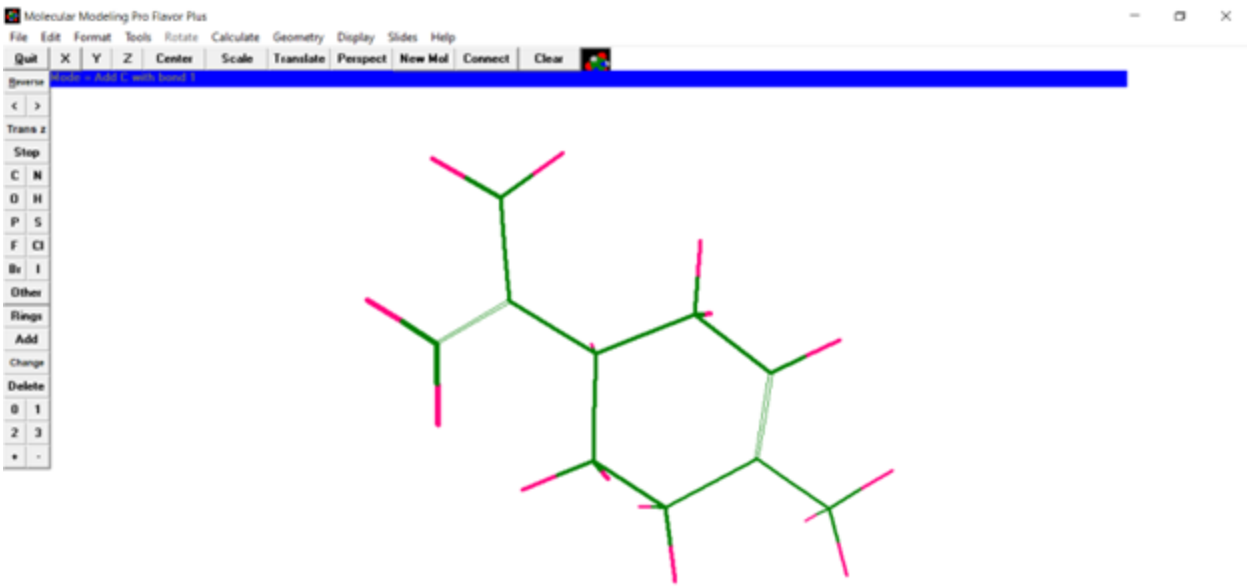

Figure 1. Structure of Limonene drawn on MMP Pro Flavor Plus. Either drawing tools shown on the left panel or MDL or SMILES structures can be used to draw the structure.

Using the calculation mode this structure can be energy minimized. Scent increments for the molecule are obtained by applying odor and flavor calculations and Thermodynamics, all found under the calculation mode. The data is found in Table 1.

Table 1. Scent increments and scent odor descriptors published for Limonene

Parameters Calculated	Values	Limonene Odor Descriptors
Boiling Point	172.13 C	Citrus , gasoline,
Scent increment 1	0.0692	fresh, orange, sweet,
Scent increment 2	0.2090	herbal
Scent increment 3	0.0057	

Second, the above limonene molecule is modified by changing its structure. The easiest change could be made to the propylene side group. This could be based on an organic chemist's decision to synthesize the new molecule. He may be experienced in regioselectivity using metal or enzyme catalysts. He may have access to new A.I. models used for efficient chemical synthesis.

However, for scent character it is important to keep scent increment 1 nearly constant or equivalent to the original molecule. Changes in the value of scent increment 1 correlate to functionality and to hydrophobic and hydrophilic properties of the molecule.

In Figure 2 I have added a cyclopentenyl group to replace the propenyl group of limonene.

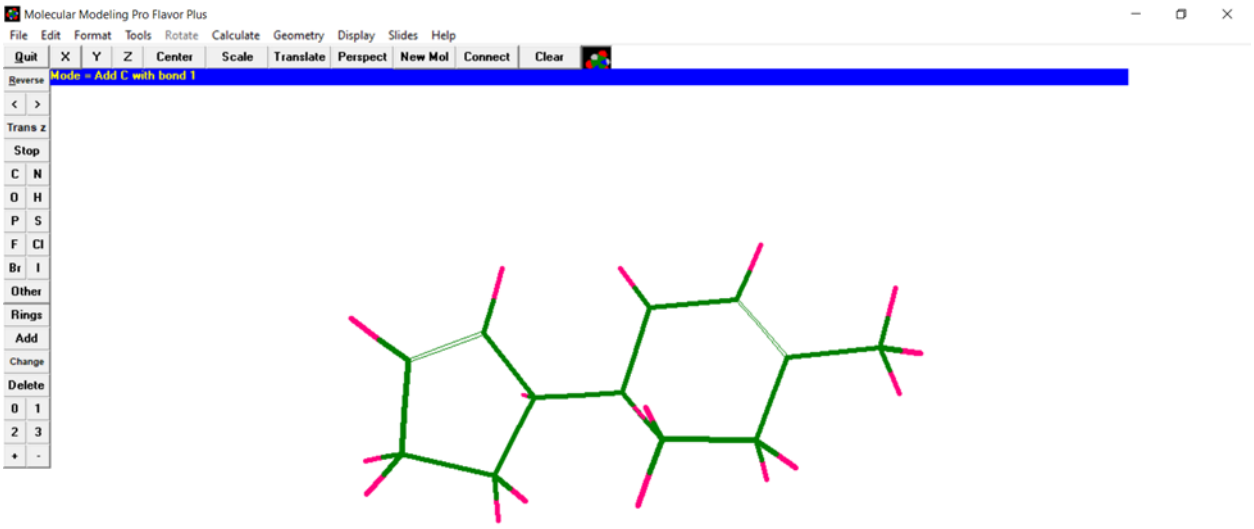

Figure 2. Using the left side drawing tools the structure of limonene is changed to 1-(2-cyclopentenyl) 4 methylbenzene $C_{12}H_{18}$.

The new SMILES for this molecule (C1=C(C)CCC(C2C=CCC2)C1) can be generated in MMP. As for limonene, Table 2 shows the MMP calculated parameters used to predict the odor characteristics of the new molecule. A total of 9 hits were found in the Scent Character prediction. However, only 3 results that matched scent increment 3 are shown below:

['fruity', 'herbal', 'woody']

CCCC(=O)O[C@H]1C[C@H]2CC[C@@]1(C)C2(C)C

Bornyl butyrate

C 14 H 24 O 2

['pine', 'fruity', 'tobacco', 'herbal', 'woody']

CCCCC(=O)O[C@@H]1CC2CCC1(C)C2(C)C

Bornyl valerate

C 15 H 26 O 2

['pine', 'fruity', 'warm', 'herbal', 'woody']

CCCC(=O)OC1CC2(C)CC[C@@H]1C2(C)C

Isobornyl butyrate

C 14 H 24 O 2

Table 2. Scent increments and scent odor descriptors predicted for a modified Limonene

Parameters Calculated	Values	1-(2-cyclopentenyl) 4 methylbenzene odors predicted by MMP
Boiling Point	207.59 C	Fruity, , herbal,
Scent increment 1	0.0692	woody, pine, tobacco,
Scent increment 2	0.2194	warm
Scent increment 3	0.0162	

These results show that the predicted odor character of 1-(2-cyclopentenyl) 4 methylbenzene, matches the odor profiles of bornyl and isobornyl esters. I find that both scent increments 1 and 2 also match these compounds.

MMP calculates the odor thresholds of these compounds in water and in air. The results show a lower threshold for 1-(2-cyclopentenyl) 4 methylbenzene (5.4 to 32 ppb) than Limonene (21 – 98 ppb) in water and (1.7 -13 $\mu g/M^3$) vs (5.5 – 31 $\mu g/M^3$) in air, respectively.

Please feel free to contact me at FFOS Software if you have any questions or wish to conduct your own experiments with MMP Flavor Plus on designing potential flavorings or fragrances.

Please thank FFOS Software if you have hired a chemist to synthesize this compound and find this molecule helpful to your product line.

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