Design of a Musk Fragrance from a Violet Berry Fragrance

MMP Flavor Plus is a molecular modeling program developed by FFOS Software. As mentioned in the previous note, it functions as a predictor of molecular properties from structure. It also has a built-in thermodynamic algorithm to calculate odor and taste thresholds from structure.

Recently, scent characterization of a molecule was made possible through the thermodynamic algorithm. Based on three calculated structural and functional increments, odor character can be predicted from a variety of fragrances and flavors with one or more functional groups.

Scent increment 1 (S1) is based on the model's rotational/translational variable which is sensitive to functional groups, molecular conformations and hydrophobic/hydrophilic properties. Scent increment 2 (S2) is calculated from molecular structure and thermodynamic properties. Scent increment 3 (S3) is calculated from secondary thermodynamic properties and the number of atoms per molecule.

Although S1 characterizes the functional groups it alone does not distinguish odor character. S2 and S3 separate odor character from S1. The coordinates (S1,S2,S3) define the odor character of a given structure and can be used to determine the descriptive odor.

These coordinates are also useful in the *in-silico* design of flavor and fragrances. Compounds with similar coordinates are judged to have a similar odor character. Since S1 is also dependent on molecular conformation, if multiple S1 values are found to be similar for two compounds then there is a high probability that they have a similar odor profile.

In this example of design, a compound of known odor characteristic is converted to a desired odor characteristic by modification of its structure. The desired odor characteristic is compared to a molecule of known odor character.

Ionol (figure 1) is known to have violet and berry notes. It has a cyclohexene group with a side chain of 4 carbons and an OH group.

Ebanol (figure 2) has a characteristic of musk. It has a trimethyl cyclopentenyl group with a side chain of 6 carbons and an OH group.

The design goal is to create a new and previously unknown structure from ionol, with musk odor character. This is done by keeping the cyclohexene structure and modifying the side groups of ionol.

The coordinates (S1,S2, S3) are calculated for ionol and ebanol . S1 is equivalent for both but S2 and S3 differ. (see Table 1). There is also a secondary S1 calculation after rotation of the side groups for both ionol and ebanol which are equivalent.

The first attempt is to change the 4-carbon side group to a 6-carbon side chain on ionol. The new values of S1, S2, S3 suggest a compound with an intermediate odor to ionol and ebanol, but not a definite match of either.

Various changes to the methyl side groups of ionol were unsuccessful. However, removal of one of the methyl groups resulted in a compound with a predicted odor character of ebanol. (see Figure 3 and Table 1)

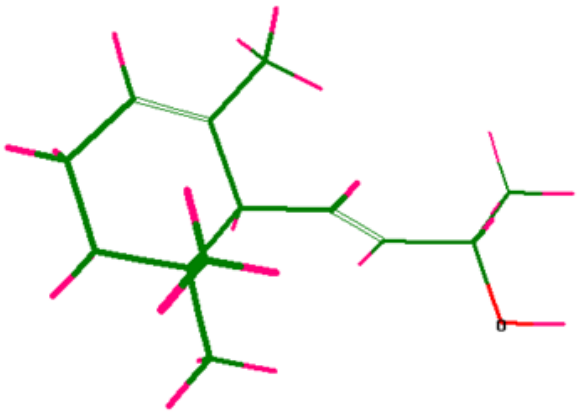

Figure 1 Structure of Ionol $C_{13}H_{22}O$

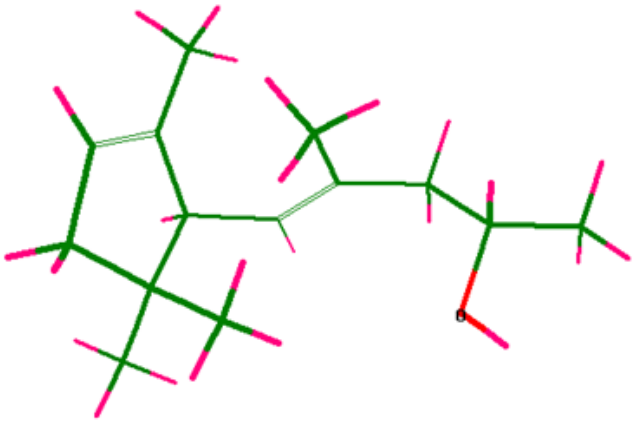

Figure 2 Structure of Ebanol $C_{14}H_{24}O$

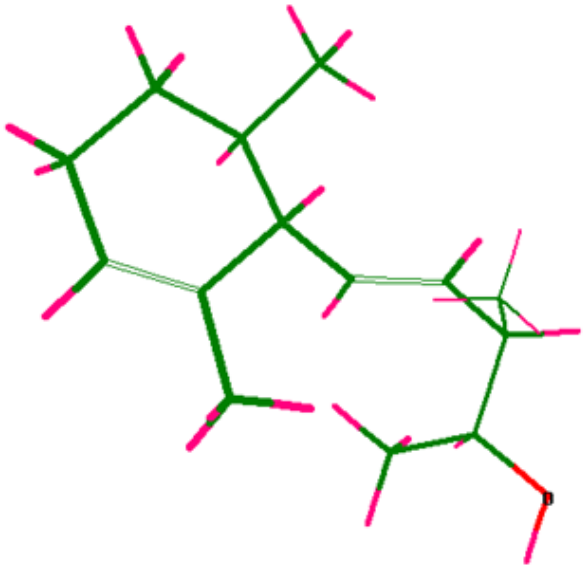

Figure 3 Structure of a modified Ionol $C_{14}H_{24}O$

Table 1 Coordinates and odor character of 3 compounds

Coordinates	Ionol	Ebanol	Modified Ionol
S1	0.07685	0.07685	0.07685
S1 rotation	0.06570	0.06570	0.06570
S2	0.2140	0.2116	0.2117
S3	0.0206	0.0189	0.0169
Odor Predicted	Violet/berry	Musk	Musk
Odor Threshold (ppb) in air	0.22-0.95	0.13-0.63	0.09-0.51

Note that a slight lowering of odor threshold in air occurs with a modified ionol producing a musk scent.

Should this note be of interest to your company's fragrance or flavor development please contact FFOS Software.

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