

The Phenylpropanals—Floral Aromatic Aldehydes

Chemistry and application in fragrance

Michael Zviely, CIC; mzviely@cathay-israel-chemistry.com

The phenylpropanal family is one of the most important fragrance ingredients, both olfactorily and commercially. This family consists mostly of synthetic molecules having the phenylpropanal moiety.

From the structural point of view, this family's members start with the most simple structure—3-phenylpropanal (dihydrocinnamaldehyde; FEMA# 2887, CAS# 104-53-0) (**F-1**), which has a green, aldehydic, floral and melon odor¹—toward molecules having different substituents and in various positions on the aromatic ring and/or the side chain. 2-Phenylpropanal (hydratropaldehyde, FEMA# 2886, CAS# 93-53-8) (**F-2**) is a side-chain isomer of the basic phenylpropanal structure, and it has a fresh, green leafy-floral, tart, hyacinth odor^a.

An addition of three carbon atoms in the *para* position of 3-phenylpropanal gives 3-(4-isopropylphenyl)propanal (Cyclemax^b, CAS# 7775-00-0; **F-3**), which has a fresh, floral, muguet odor with a fruity melon nuance^c. The addition of four carbon atoms to the basic 3-phenylpropanal structure—one ethyl group to the aromatic ring and two methyl groups on the α position to the propanal side chain—gives 3-(4-ethylphenyl)-2,2-dimethylpropanal (Floralozone^d, Florone^e, CAS# 67634-15-5; **F-4**), which has a powerful, clean, green odor containing a fresh air note reminiscent of an ocean breeze. This material gives lift to fragrances without dominating due to its neutral nature. The watery facets of 3-(4-ethylphenyl)-2,2-dimethylpropanal form a typical aquatic accord that can be found in fragrances such as *Cool Water* (Davidoff), *L'Eau d'Eden* (Cacharel) and *Polo Sport Woman* (Ralph Lauren).

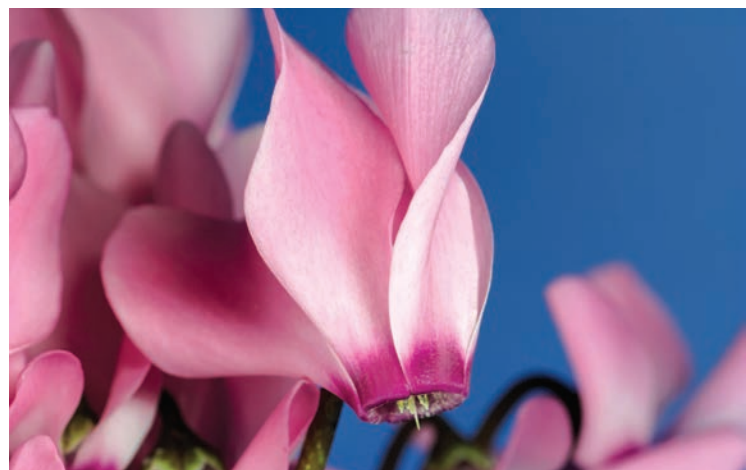
^a Information from Moellhausen S.p.A. datasheet.

^b Cyclemax is a trade name of IFF.

^c Information from IFF datasheet.

^d Floralozone is a trade name of IFF.

^e Florone is a trade name of Symrise.



One of the disadvantages of aldehydes is their relative low stability. A well-known method to overcome this problem is to use their nitrile derivative, in this case 3-(4-ethylphenyl)-2,2-dimethylpropanenitrile (Fleuranil^f, CAS# 134123-93-6) (**F-5**), which has a fresh, floral, ozone, salted odor with basillic herbal notes and good diffusion.

A different arrangement of the four added carbon atoms is demonstrated in the structure of 3-(4-*tert*-butylphenyl)propanal (Bourgeonal^g, Lilional^h, CAS# 18127-01-0; **F-6**), which has a floral, green, muguet, fresh, powerful odor and a diffusive fresh floral muguet with a watery green characterⁱ. This can be found in fragrances such as *Alien* (Thierry Mugler). Another isomer of the four added carbons is 2-methyl-3-(*p*-isopropylphenyl)propionaldehyde (cyclamen aldehyde, FEMA# 2743, CAS# 103-95-7; **F-7**), which has a floral-cyclamen, green, powerful odor.

A different isomer of the former phenylpropanal derivative is 3-(3-isopropylphenyl)-butanal (Florhydral^j, CAS# 125109-85-5; **F-8**). In this isomer, the isopropyl group is in the *meta* position to the propanal side chain versus the *para* position of the former structure. Also the side chain hanging methyl group is β to the aldehyde, versus the former α position. 3-(3-Isopropylphenyl)-butanal has a very floral, fresh, trendy, green, muguet, natural odor, such as lily of the valley, hyacinth and so on, and can be found in fragrances like *Good Life Woman* (Davidoff).

^f Fleuranil is a trade name of IFF.

^g Bourgeonal is a trade name of Givaudan.

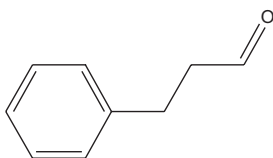
^h Lilional is a trade name of O'Laughlin.

ⁱ Information from Givaudan datasheet.

^j Florhydral is a trade name of Givaudan.

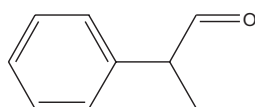
3-Phenylpropanal

F-1



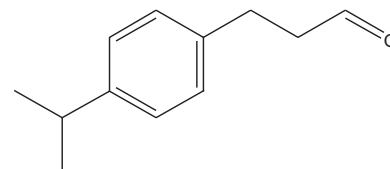
2-Phenylpropanal

F-2

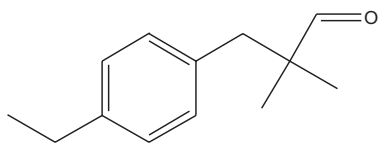


3-(4-Isopropylphenyl)propanal

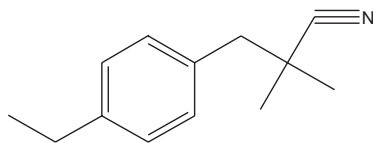
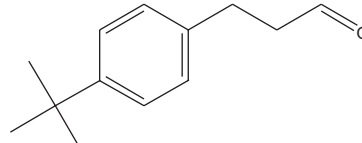
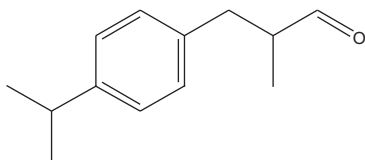
F-3



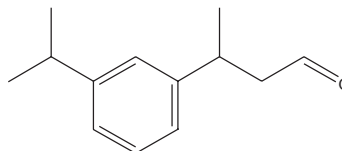
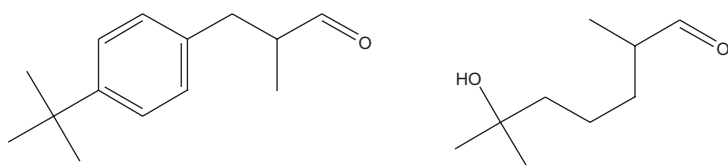
3-(4-Ethylphenyl)-2,2-dimethylpropanal

F-4

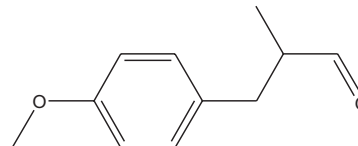
3-(4-Ethylphenyl)-2,2-dimethylpropanenitrile

F-53-(4-*tert*-Butylphenyl)propanal**F-6**2-Methyl-3-(*p*-isopropylphenyl)propionaldehyde**F-7**

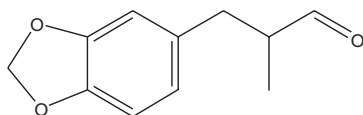
3-(3-Isopropylphenyl)-butanal

F-82-Methyl-3-(4-*tert*-butylphenyl)propanal and hydroxycitronal**F-9**

3-(4-Methoxyphenyl)-2-methylpropanal

F-10

3-(1,3-Benzodioxol-5-yl)-2-methylpropanal

F-11

The addition of a fifth carbon atom to this basic phenylpropanal structure presents 2-methyl-3-(4-*tert*-butylphenyl)butanal (Lilial^k, Lysmeral^l, Lilestralis^m, CAS# 80-54-6), which has a fresh, light, green floral, strongly diffusive odor reminiscent of lilyⁿ. The interesting structural resemblance of 2-methyl-3-(4-*tert*-butylphenyl)propanal to hydroxycitronellal (FEMA# 2583, CAS# 107-75-5)—which has a muguet, floral, sweet, green odor, reproducing the odor of lily of the valley quite closely—can be seen in **F-9**.

A different structural concept of the phenylpropanal structure is presented by oxygenated phenylpropanals, namely *para*-methoxy derivative. 3-(4-Methoxyphenyl)-2-methylpropanal (Canthoxal^o, anisyl propanal, CAS# 5462-06-6; **F-10**) has a licorice, basil, fennel odor, as well as anise notes with a slight fruity and a watery modification.

The addition of one more oxygen atom produces 3-(1,3-benzodioxol-5-yl)-2-methylpropanal (Helional^p, Heliogan^q, Tropional^r, CAS# 1205-17-0; **F-11**), which has a green, floral-cyclamen odor with top notes of ozone and freshly mown hay. 3-(1,3-Benzodioxol-5-yl)-2-methylpropanal can be found in relatively high concentration in *New West For Her* (Aramis, 7.5%), *L'Eau d'Issey* (Issey Miyake, 2%), *Escape* (Calvin Klein, 3.7%), *L'Eau d'Eden* (Cacharel, 1.5%), *Polo Sport Woman* (Ralph Lauren, 4.8%), *Cool Water* (Davidoff, 4.3%), and in many other fragrances, such as *Allure* (Chanel) and *Alien* (Thierry Mugler).²

^k Lilial is a trade name of Givaudan.

^l Lysmeral is a trade name of BASF.

^m Lilestralis is a trade name of Innospec.

ⁿ Information from Innospec datasheet.

^o Canthoxal is a trade name of IFF.

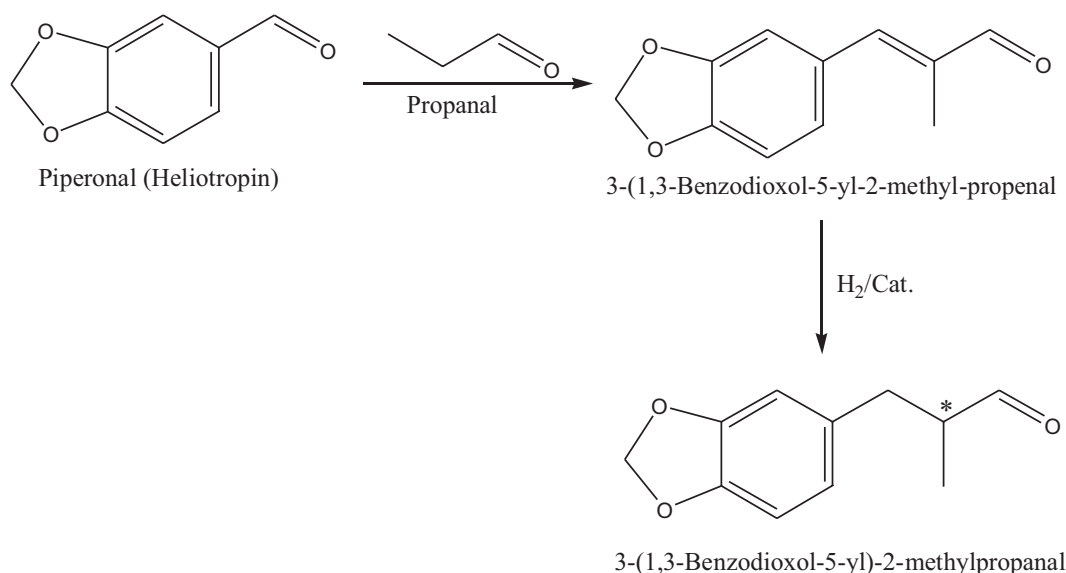
^p Helional is a trade name of IFF.

^q Heliogan is a trade name of Agan Aroma & Fine Chemicals.

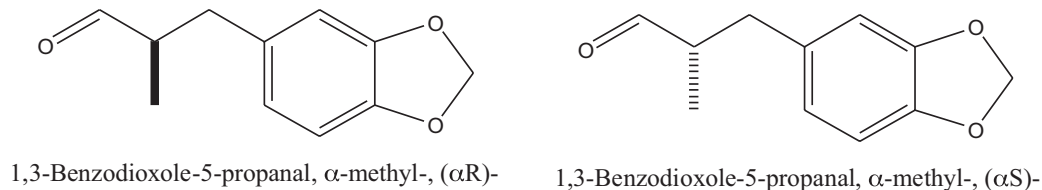
^r Tropional is a trade name of Vigon International.

A preparation of racemic 3-(1,3-benzodioxol-5-yl)-2-methylpropanal

F-12

1,3-Benzodioxole-5-propanal, α -methyl-, (αR)- and 1,3-benzodioxole-5-propanal, α -methyl-, (αS)-

F-13



The preparation of the racemic 3-(1,3-benzodioxol-5-yl)-2-methylpropanal (**F-12**) is accomplished in the following route, starting from piperonal, which undergoes aldol condensation with propanal to afford 3-(1,3-benzodioxol-5-yl)-2-methylpropenal intermediate, having a prochiral α to the aldehyde carbon atom. The second stage is a catalytic hydrogenation of the double bond, which affords the racemic product.

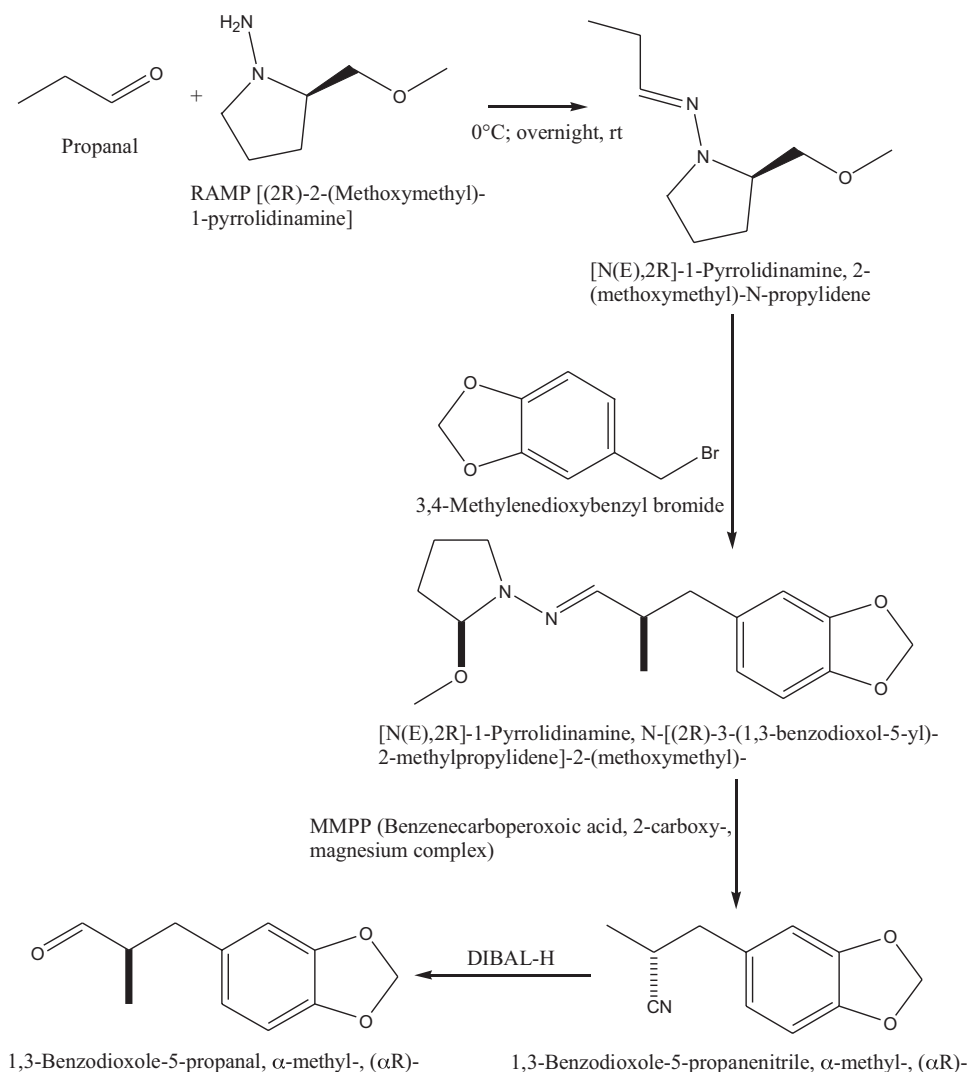
Some of the phenylpropanals do not possess a chiral center at the α position, such as 3-phenylpropanal, 3-(4-isopropylphenyl)propanal, 3-(4-ethylphenyl)-2,2-dimethylpropanal and 3-(4-*tert*-butyl)phenylpropanal. Similar to these phenylpropanals, 3-(1,3-benzodioxol-5-yl)-2-methylpropanal also has a chiral center at the α position to the aldehyde. In general, only in the case of 3-(3-isopropylphenyl)butanal is the chiral center on the β position.

This phenomenon enables the existence of two enantiomers. Frequently, such enantiomers differ in their odor characteristics, both qualitatively (olfactory characteristics) and quantitatively (ϕ value). A work was published on 2-methyl-3-(4-isopropylphenyl)propanal, of which the (-)

isomer was shown to possess a cyclamenlike odor and the (+) isomer has a lily bell-like odor.³ Work on 3-(4-*tert*-butylphenyl)propanal showed the (+) isomer has a lily of the valley odor and a slightly lower ϕ value than the (-) isomer, also described as aldehydic, chemical.⁴ In order to evaluate these distinctive olfactory characteristics in 3-(1,3-benzodioxol-5-yl)-2-methylpropanal, both enantiomers were synthesized and evaluated separately (**F-13**).⁵

The asymmetric synthesis of both enantiomers was accomplished via asymmetric alkylation by employing the SAMP/RAMP-hydrazone method, respectively. The alkylated hydrazones were oxidatively cleaved with magnesium monoperoxyphthalate (MMPP, CAS# 84665-66-7). Subsequent reduction of the resulting nitriles with diisobutyl aluminium hydride (DIBAL-H, CAS# 1191-15-7) led to the desired aldehydic enantiomers in good overall yields (52–53%) and enantiomeric excesses (ee = 90%).

The scheme in **F-14** describes the asymmetric synthesis of α -methyl-(αR)-1,3-benzodioxole-5-propanal (CAS# 737776-59-9) using RAMP ((2R)-2(methoxymethyl)-1-pyrrolidinamine). When SAMP ((2S)-2(methoxymethyl)-1-pyrrolidinamine) was used



as chiral auxiliary, α -methyl-(α S)-1,3-benzodioxole-5-propanal (CAS# 73776-68-0) was obtained.

The olfactory evaluation of the two enantiomers supplied considerable differences both in the intensity and in the characteristic smell notes. The intensity of the (α S)-enantiomer is stronger than the (α R)-enantiomer. Furthermore, the (α R)-enantiomer is nearly completely missing the marine and green notes typical for the racemic product. Altogether it could be said that the (α S)-enantiomer is responsible for the typical smell of the racemic product, even it has a lower ϕ value.

The α -methyl-(α R)-1,3-benzodioxole-5-propanal enantiomer has a floral (lily of the valley and cyclamen), aldehydic, sweet fruity (lemon) odor, with a ϕ value of 3.6×10^8 , while α -methyl-(α S)-1,3-benzodioxole-5-propanal enantiomer has a ϕ value of 6.8×10^7 , demonstrating a green floral, marine, ozonelike odor and a salty aspect, with fruity sweet and cuminlike undertone.⁶

References

1. G Mosciano, "Organoleptic Characteristics of Flavor Materials," *Perfum Flavor*, 19(3), 51 (1994)
2. P Kraft, JA Bajgrowicz, C Denis and G Frater, "Odds and trends: recent developments in the chemistry of odorants," *Angew Chem Int Ed*, 39, 2980 (2000)
3. H Kazuhiko, N Kanji, H Shiyuu and A. Tadatoshii, Pat JP JP55027166, assigned to Sumitomo Chemical Co. (1980)
4. T Yamamoto, *Current Topics in Flavours and Fragrances—Towards a New Millennium of Discovery*, KAD Swift, ed., Kluwer Academic Publishers (now Springer), New York (2000)
5. D Enders and M Backes, "First asymmetric synthesis of both enantiomers of Tropional and their olfactory evaluation," *Tetrahedron: Asymmetry*, 15(11), 1813–1817 (2004)
6. JCLeffingwell, Chirality&OdourPerception,2001,www.leffingwell.com/chirality/tropional.htm (Accessed Dec 12, 2011)