An Aroma Chemical Profile

Para-Hydroxy Phenyl Butanone

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Para-hydroxy phenyl butanone is a material mainly used by the flavorist and only infrequently by the perfumer—and to most in the industry not recognized by its chemical name. The organoleptic impression of this chemical is so specific (somewhat like vanillin's relationship to vanilla), that most of us refer to this material by its functionally derived name—raspberry ketone. Thus shall it be referred to throughout this review.

Raspberry ketone falls into a group of mainly crystalline aroma chemicals which hide their potency when one smells them neat from the bottle. Only on dilution does the power and persistence of raspberry ketone become apparent. In aqueous media its low solubility results in the water giving the ketone a lift organoleptically. In organic media, mainly fragrances, raspberry ketone is somewhat subdued and becomes more a part of the dry-out effect.

As the name indicates, the organoleptic impression of raspberry ketone is that of the main body notes of raspberries, though it finds use in related fruit flavor compositions such as strawberries, kiwi, cherry and other berry flavors as a touch additive and in other berry fruit flavors.

Its use in perfumery tends to be limited to fine fragrances where a fruity dry-out is desired. It is also used in room fresheners having a fruity impact.

As all the commercially available material seems to be generated by the same chemical reactions, the off-notes

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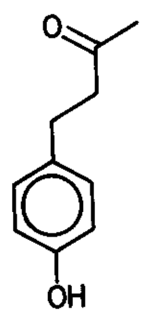

Mwt 164 $C_{10}H_{12}O_2$

CAS 5471-51-2 **FEMA** 2588

Classification:

Mono-cyclic aromatic phenol containing a para aliphatic ketone group.

Additional Names:[1,2]

4-(para-Hydroxyphenyl)-2-butanone
Raspberry ketone
Frambinone
Oxananone
Oxyphenylon
Rasketone
p-Hydroxybenzyl acetone

French: Framboise Ceton
German: Himbeer Keton

Physical Data:[3]

Appearance:	white crystalline powder
Melting Point:	82-83°C
Solubility:	1% in water at 20°C, soluble in ethanol, esters, DEP; insoluble in hydrocarbons and chlorinated solvents.

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occurring in this material from all sources are similar. Due to the reactants used, they are not very disruptive to raspberry ketone's organoleptic impression. The recrystallization steps used to purify the product usually completely remove any objectionable by-notes, resulting in a very reproducible odor profile.

As with most crystalline products with low neat impact, raspberry ketone will absorb impurities during storage and exhibit off-notes of more powerful aroma chemicals in a similar manner as vanillin will. Thus, prime grade material, if stored in indifferent surroundings, will pick up notes such as indol, musk, etc. which can render the product unusable.

Another facet of the nature of the raspberry ketone is the question of its organoleptic impact. Arctander stated that it is not very powerful, but others working with this material often disagree with this opinion and remain convinced that it is a high-impact material at low concentration.

Raspberry ketone is used at such low levels of formula concentration that both in flavors and fragrances, no instability problems (such as color or off-note generation due to reactions with other components) have been noted.

Natural Sources

To date, raspberry ketone has only been found in nature in raspberries, though its acetate has been identified as the pheramone (Cue-lure) of the Asian melon fly. Clearly, such chemical structures as raspberry ketone and zingerone arise metabolistically via the Shikimic pathway, but just what steps are involved is still unclear.

The occurrence of raspberry ketone in raspberries was for a long time elusive. Prior to 1962, raspberry flavors were formulated without this material. However, the flavors were never truly raspberry and the impression of raspberries was more than likely enforced by the red coloration of the food stuff as much as the flavor.

The argument of potency of this aroma chemical is answered for many in the work carried out by Firmenich[4] to isolate and identify the mysterious product that gave the critical notes that made raspberries—raspberries!

Firmenich extracted 500 kg of fresh raspberry fruit to isolate about 0.01 grams of raspberry ketone as well as about 25 other constituents.

The presence of raspberry ketone in raspberry juice at levels of 0.1-0.2 ppm and the importance of its organoleptic contribution to the flavor profile at this low level would seem to verify the opinion that the material is a high impact, potent aroma chemical. Moreover, this ketone makes its presence known through the vail of other more volatile, high impact materials such as leaf alcohol, leaf aldehyde ionone and β,β-dimethyl acrolein.

There are no commercially viable sources of natural raspberry ketone known at this time. Its trace concentration in raspberries would even make its isolation an impractical exercise for use as an aroma chemical. A great deal of work has been done on raspberry flavor as it is viewed as an odor-flavor of universal acceptance.[5]

Formula 1
Firmenich Imitation Raspberry Flavor

	Parts by weight
cis-3-Hexen-1-al (with trans isomer)	1
Iralia (mixture of isomeric ionones)	5
Raspberry ketone	50
γ-Undecalactone	5
Acetic acid	20
Ethyl acetate	50
Amyl propionate	5
Phenyl ethyl alcohol	5
Geraniol	5
Vanillin	10
Triacetin (as a solvent)	844
	1000

History

Raspberry ketone was first reported by Japanese chemists[6] who synthesized the material as part of a program to study the pungent properties of the ginger component zingerone. They failed to note the characteristic organoleptic profile of this material, but reported it as having a pungent taste.

Years passed and this material seemed to go unnoticed. In some areas of the world, the non-GRAS-FEMA material, ethyl-p-tolyl glycidate (raspberry aldehyde or aldehyde C-17) was used to impart a raspberry note in flavors and has been widely used in fragrances to obtain a similar effect.

The work of Schinz and Seidel of Firmenich rekindled interest in this material after it was discovered as a constituent in raspberry juice. Raspberry ketone then began life as an aroma chemical specialty, which was usually produced in-house in small lots by many of the world's flavor and fragrance houses.

Firmenich's original patents on the use of raspberry ketone give one greater insight into the critical position this aroma chemical holds for the creation of a "natural" raspberry flavor. Winter's patent of 1965[7] illustrates a rather simple formula (Formula 1) for a fresh raspberry flavor. This patent basically claimed three of the listed ingredients as being key to the raspberry effect; the ionones, cis-3-hexen-1-al and raspberry ketone. It is noteworthy that this formula is so simple, using only fairly pure aroma chemicals and no essential oils with their more complex chemical nature.

The late 1960s saw active research programs for the synthesis of the material; for usage not in flavor but as an intermediate for the production of p-acetoxy-phenyl butanone, which had been identified as the active sex attractant of the Asian melon fly.

The USDA had great interest in this pheramone, as the melon fly was a threat to the commercial pineapple crops in Hawaii and Guam. Their projections of usage, if an infestation of melon flies occurred in Guam, were annual pur-

Table I. Estimated consumption of synthetic raspberry ketone for 1992

	kg/year
Flavor Usage	
North America	6,000
Europe (includes East Block)	8,500
Japan	2,000
Others	1,500
Chemical Intermediate Usage	
for Cue-Lure	100,000
for other flavor derivatives	2,000
Total consumption	**120,000**

chases of 200,000-300,000 lbs, at prices in the $50/lb range. Thus, many specialty chemical firms worked on the synthesis of acetate ester of raspberry ketone and viewed the flavor market as an added, but minor, outlet for their planned production. Unfortunately (or fortunately) the pesty melon fly never reached Guam and the research efforts were terminated in the United States.

However, events in the homeland of the Asian melon fly took another course. The pest damaged melons, pineapples and other fruit crops. This resulted in the Japanese government's continued interest in controlling the pest, so pheramone and raspberry ketone research and production remained active in Japan and other Asian countries. Whereas once European firms (PFW, Dragoco, Firmenich, Givaudan, Birmingham Chemical) were the major suppliers of raspberry ketone, the agricultural needs for the pheramone in Asia have shifted production to that area. Today, Takasago is the major supplier of this critical, but low volume, aroma chemical.

World Consumption

The consumption of any low volume aroma chemical is difficult to assess exactly. Following is the best estimate that can be constructed.

Consumption of natural raspberry ketone via the fruit is estimated in the order of 400 kg/year worldwide, based on Stofberg's consumption ratios.[8] World consumption of synthetic raspberry ketone for all uses is estimated at 120,000 kg for 1992, and its breakdown is given in Table I.

Pricing

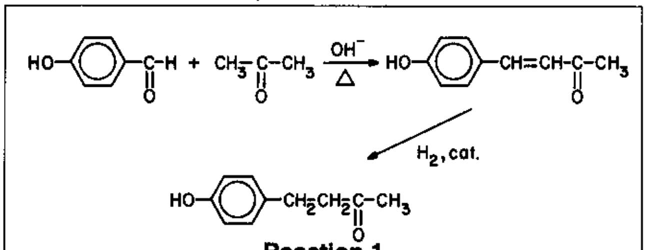
Raspberry ketone pricing is currently in the area of $20-25/lb and has been fairly stable over the last 20 years. The low volume of usage in the flavor and fragrance industry, coupled with its position as a secondary outlet for production of pheramone intermediate, have worked to keep prices fairly constant. Moreover, demand is inelastic versus pricing with little volume increase foreseen at appreciably lower prices.

However, this type of aroma chemical makes an inviting target for small third-world specialty chemical firms, as its current consumption rate of 120,000 lbs/year, and pricing are viewed as approaching desirable revenue levels. It is projected that new manufacturers will emerge in the next few years, which will result in eroding prices, but with very little increase in sales volume over the current 3-4% growth per annum. By 1995 prices could fall to the levels of $12-15/lb.

Raspberry ketone falls under the US Customs classification of an aromatic ketone-phenol or TSUS 2914.50.20.006 and bears a duty of 11% ad valerum—a rate normally found for aromatic organic products.

Supply/Suppliers

The world's supply of raspberry ketone is provided by a number of firms via one basic two-step reaction: The condensation of p-hydroxy benzaldehyde with acetone; followed by hydrogenation of the intermediate A to raspberry ketone (Reaction 1).



Reaction 1

As more sources of the key raw material, p-hydroxy benzaldehyde, emerge and prices and availability become more favorable, more producers of raspberry ketone will enter the market.

The literature often mentions another route to raspberry ketone via the condensation of methyl vinyl ketone with phenol. This route produces low yields and other problems. Methyl vinyl ketone is difficult to obtain commercially, is unstable, and likes to climb out of the reaction vessel on its own, sometimes with great vigor. No current producer is known to employ the methyl vinyl ketone route.

The question of supply is one of blocking out reaction unit time as the required equipment and raw materials are available in amounts far greater than demand.

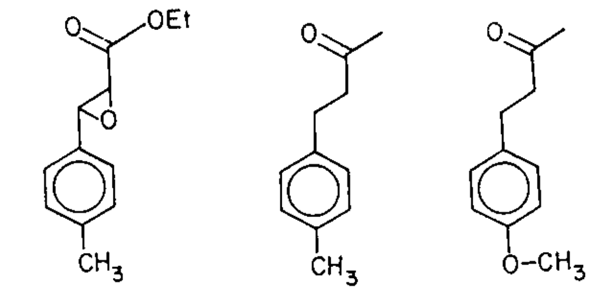
Producers

The low volume of consumption of this item has led to suppliers appearing and disappearing whenever market conditions changed. In the last three decades, this aroma chemical has been produced and offered by Birmingham Chemical (later Food Industries Ltd.), Givaudan, IFF, Dragoco and others.

Today, the US has no producer of raspberry ketone and all the commercially available material is manufactured in Asia with Takasago being the dominant supplier.

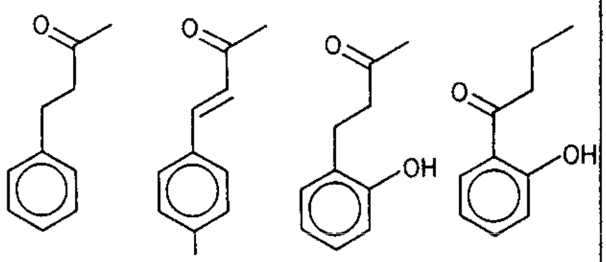
Substitutes

There are no real substitutes for this material, as one

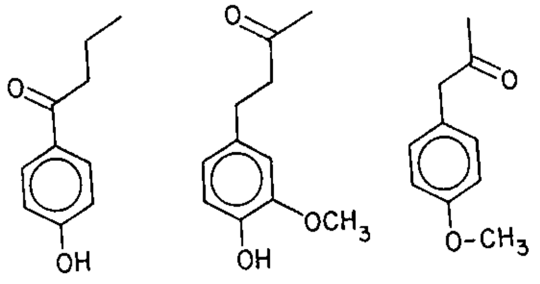


1307 Raspberry Aldehyde Non-FEMA | 2967 FEMA3074 | 248 FEMA2672

Figure 1. Three aroma chemicals that have raspberry impression (numbers refer to Arctander's work)



288 Floral green | 1725 Herbaceous Tea | weak phenolic | strong phenolic

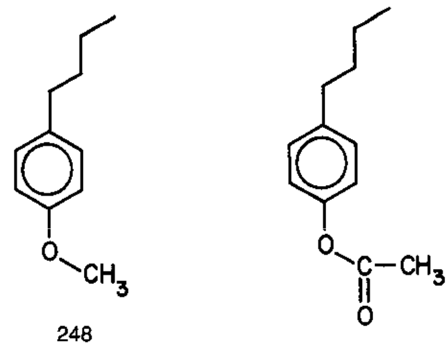


odorless | 3101 balsamic vanila | 1883 Anis Ketone

Figure 2. Materials with some structural relationship to raspberry ketone (numbers refer to Arctander's work)

might guess from the research expenditures by Firmenich to identify the key components of raspberry flavor. Three aroma chemicals that have some raspberry impression, but are not direct substitutes are shown in Figure 1.

These materials all have similar chemical structures and thus lead one to speculate as to the critical features necessary for the raspberry impression. Figure 2 shows the materials that have some structural relationship to raspberry ketone but do not display a raspberry impression.

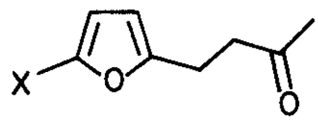


248
p-methoxy
phenyl butanone

Cue-Lure

Figure 3. Two known derivatives of raspberry ketone (numbers refer to Arctander's work)

What these structures indicate is that an unsaturated aromatic ring with para constituents is necessary, along with a two-carbon saturated group between the ring and a carbonyl function. Or, stated differently, the structure below (I) may show a raspberry impression,



(I)

where X could be OH, CH_3O or CH_3.

Derivatives

The only two known derivatives which are used in our industry are the methoxy derivative and the acetoxy ester, the pheramone "Cue-lure" (Figure 3).

References

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