Aromatic Chemicals from Heptaldehyde

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The history of heptaldehyde (n-heptanal, enanthaldehyde) as a starting material for the production of odor compounds goes back to the beginning of the 20th century. Since then it has established itself as an important chemical in the synthesis of aroma compounds.

Heptanal belongs to the cheapest aldehydic starting materials suitable for synthesis of odoriferous compounds. This article is intended to survey its chemistry in this aspect.

The major use for heptanal is in the flavor and fragrance industry. This article will describe selected areas of groups of compounds where perfumery interest and organic chemical developments have impinged on each other.

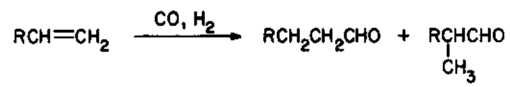
Nowadays any rich natural source of the aldehyde is not known, but fortunately it can be produced easily from olefine hydrocarbons or by pyrolysis of ricinoleic acid esters.

Manufacture

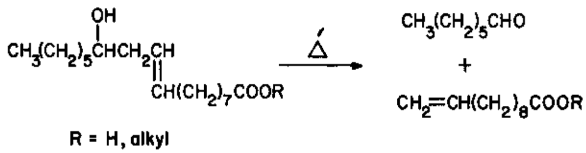
Heptaldehyde can be obtained in the oxidative processes of 1-heptene[1,2] or 1-octene.[3] But one of the more important methods for the synthesis of aliphatic aldehydes is hydroformylation of α-olefines (Scheme 1).

The VIIIth group metals (such as cobalt,[4,5] rhodium,[6-18] ruthenium,[19] iridium[20]) or their salts or complexes are catalysts of the process. The catalysts are selected so as to prefer n-aldehyde formation. As a rule, the hydroformylation is carried out at 100-200°C temperature range and under 20-300 atm. In some cases ultrasonics accelerate this reaction.[18] Heptaldehyde is also manufactured by pyrolysis of ricinoleic acid esters (Scheme 2) obtained from castor oil.[21-23]

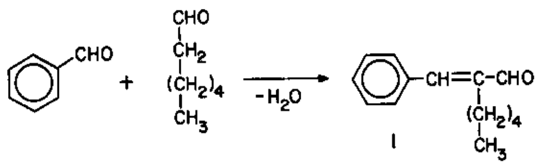
Ricinoleic acid or its esters decompose into n-heptanal and undecylenic acid or its esters, when heated to 220-700°C.



Scheme 1. Synthesis of aldehydes by hydroformylation of α-olefines



Scheme 2. Manufacture of heptaldehyde from ricinoleic acid or its esters



Scheme 3. Synthesis of α-amyl cinnamic aldehyde [1]

Compounds with Floral Odor

α-n-Amyl cinnamic aldehyde [1] (jasmine aldehyde, jasmal, jasminal, buxine, floxine, yaminal) belongs today to the most popular synthetics in perfumery. It smells something like jasmine, gardenia and tuberose.

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Aldol condensation of heptaldehyde with benzaldehyde is the classical method for the synthesis of α-amyl cinnamic aldehyde (Scheme 3).

The reaction is catalyzed by bases such as sodium hydroxide placed on silicagel,[24] potassium carbonate[25] or by NaOH in glycol solutions.[26] The unwanted product of the reaction is 2-pentyl-2-nonenal.

Jasmone and dihydrojasmone [**2**] are the compounds resembling jasmine in blossom and they have a wide application in perfumery. Heptaldehyde seems to be a good starting material for the manufacture of dihydrojasmone [**2**]. Moore reports a six-step synthesis of the ketone [2] from heptanal and vinyl magnesium bromide (Scheme 4).[27]

A shorter method for the synthesis of dihydrojasmone [**2**] is based on the condensation of heptaldehyde with methyl vinyl ketone, which directly does result in formation of 2,5-undecandione.[28-32] Thiazolinum salts such as 5-(2-hydroxyethyl)-4-methyl-3-benzylthiazolinum chloride or benzoyl peroxide are the catalysts of the reaction (yield amounts to 66-75%).

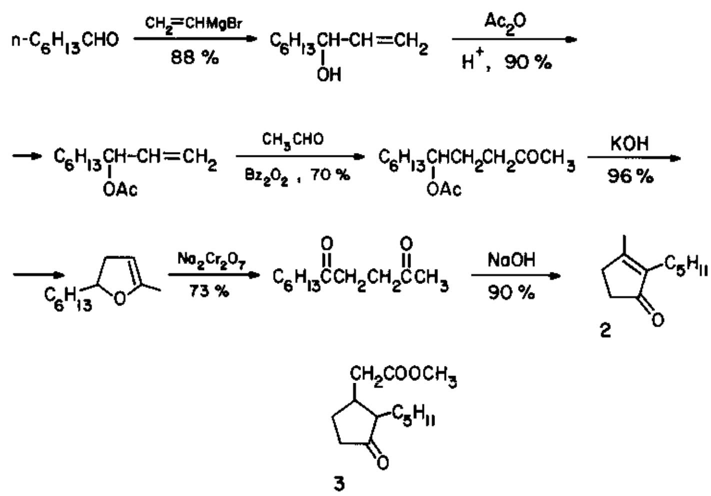
Methyl dihydrojasmonate [**3**] can also be obtained from heptanal and Z-EtOOCCH=CHCOOEt in a multi-step cycle of the reactions.[33] Interestingly, as far as the odor is concerned, compounds are synthesized from aliphatic aldehydes (Scheme 5), vinyl magnesium chloride, and allylic amines.[34]

From the heptanal ($R=C_5H_{11}$), 2-n-pentyl-4-isopropyl-2-cyclohexen-1-one [**4**] is obtained which is characterized by a fruity and herbal and floral odor.

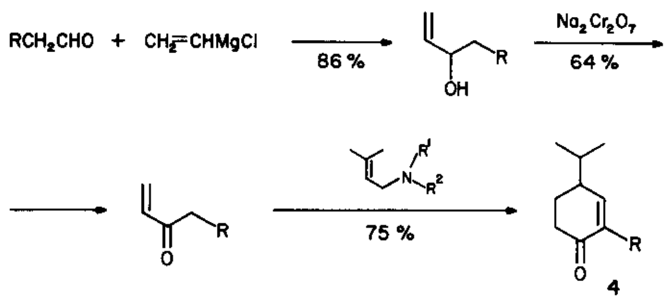
A number of the cyclic acetals of heptaldehyde synthesized by known methods show a floral smell. Table I gives the odor characteristics of a few [**5-14**] compounds of this type.[35-39]

Heptaldehyde can be subjected to a different kind of condensation with 3-buten-1-ol (Scheme 6).[35]

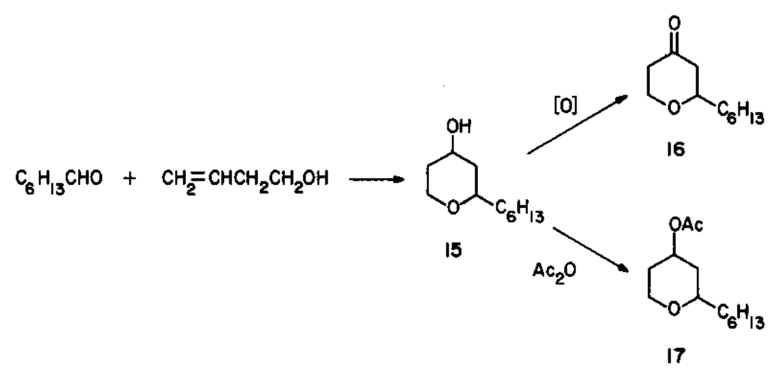
2-Hexyltetrahydropyran-4-ol [**15**] has a weak, floral scent but oxidation produces the ketone [**16**] which possesses an intense, floral odor with a fatty note. On the other hand, the acetylation of [**15**] leads to 4-acetoxy-2-hexyltetrahydropyran [**17**] of a jas-



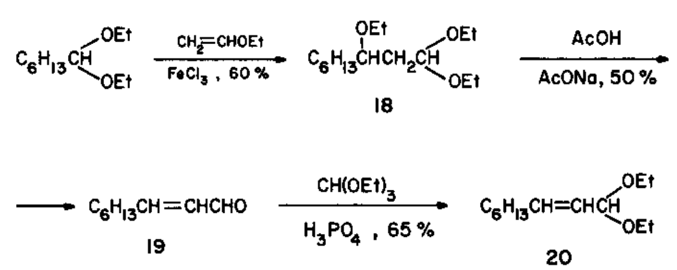
Scheme 4. Synthesis of dihydrojasmone [2] from heptanal according to Moore[27]



Scheme 5. Conversion of aliphatic aldehydes into cyclohexenone derivatives [4]

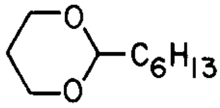
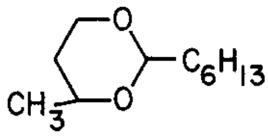
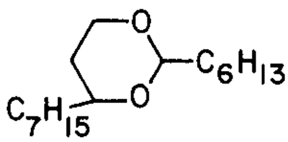
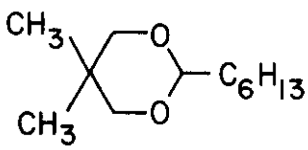
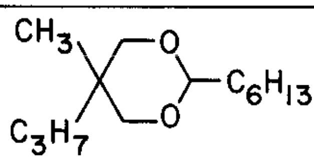
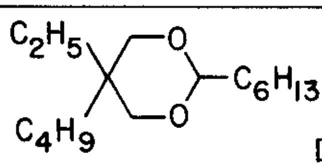
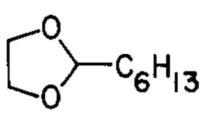
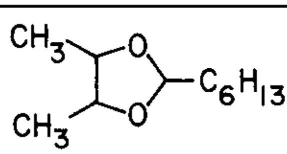
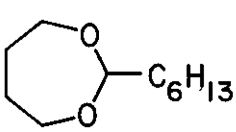
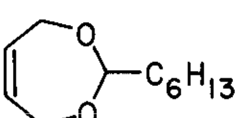


Scheme 6. Synthesis of tetrahydrofuran derivatives [15-17] from heptaldehyde



Scheme 7. Transformation of heptanal diethyl acetal into compounds enriching coffee flavor

Table I. Odor characteristics of some cyclic acetals of heptanal[35-39]

Substrate diol	Cyclic acetal	Odor
1,3-propanediol	 [5]	strong, green with a jasmine nuance
1,3-butanediol	 [6]	same as [5]
1,3-decanediol	 [7]	medium-intense, floral, a little jasmine and green
2,2-dimethyl-1,3-propanediol	 [8]	strong, floral, congenial with the jasmine blossom
2-methyl-2-propyl-1,3-propanediol	 [9]	pleasant with a mushroom note
2-butyl-2-ethyl-1,3-propanediol	 [10]	weak, floral
ethylene glycol	 [11]	floral, jasmine and green
2,3-butanediol	 [12]	weaker than [11] with a jasmine nuance
1,4-butanediol	 [13]	congenial with [11], a little fatty
2-butene-1,4-diol	 [14]	gentle, floral with a green note (more distinct floral tone than [11])

mine odor and a fatty note.

Compounds with Odor Other than Floral

A great number of other compounds, the odor of which is rather different from floral, have been published using heptaldehyde as a starting material. Some of them are also of commercial value. Examples of the ones that have been well known for a long time are γ-n-nonyllactone, dimethyl and diethyl acetals with penetrating fresh, green odor and glycerine acetals with mushroom aroma.

A study has been reported on the preparation of aroma compounds [**18-20**] that enrich the instant coffee flavor (Scheme 7).[40,41]

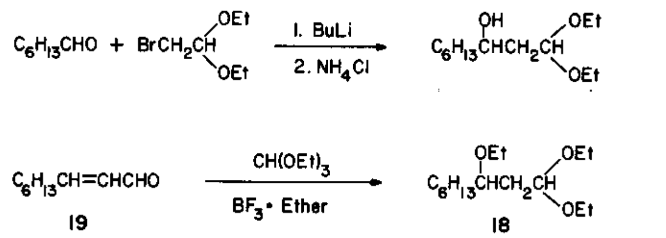
According to one patent,[41] both 2-nonenal [**19**] and its acetal [**20**] and 1,1,3-ethoxynonane [**18**] are used for enriching the coffee smell. A German patent[42] presents a different method of synthesizing the compound [**18**] (Scheme 8).

The flavoring 2-nonenal [**19**] can be obtained in the Wittig reaction as well.[43] It may be worth noting that from [**19**] one can synthesize 2-nonen-1-ol and its esters, which are applicable for the same purpose.[42]

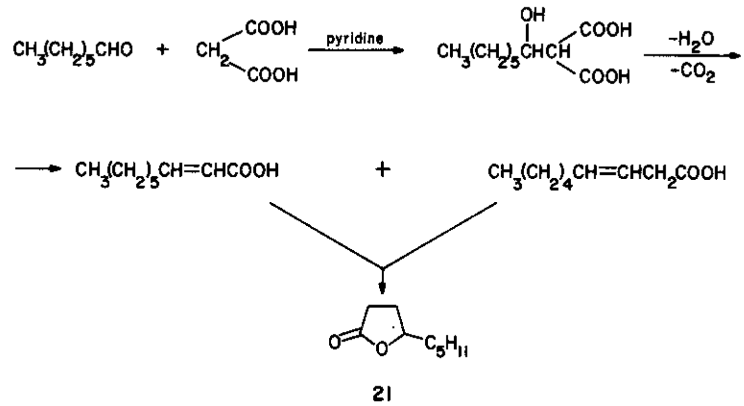
Heptanoic acid, which is formed in the heptanal autoxidation process, is used for the manufacture of esters possessing an interesting fruity odor.[44] On the other hand, the reduction of heptaldehyde gives alcohol that also has a fruity aroma. According to Pomazkow,[45] both the compounds—acid and alcohol—can be obtained from heptanal in the Cannizzaro reaction catalyzed by potassium hydroxide fixed on cation-exchange resin SG-1.

n-Heptanal is the fundamental raw material for the production of γ-n-nonanoic acid lactone [**21**] (coconut aldehyde, aldehyde C_{18}), a compound of characteristic coconut flavor (Scheme 9). Lactone [**21**] is synthesized by condensation of heptaldehyde with malonic acid in the presence of amine followed by sulfuric acid lactonization.

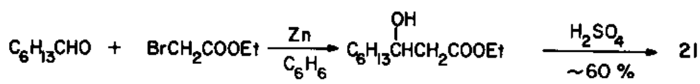
Amberlyst[46] and molecular sieves[47-49] can also catalyze the reaction. Other papers[50-52] mention coconut aldehyde [**21**] to be obtained in Reformatsky re-



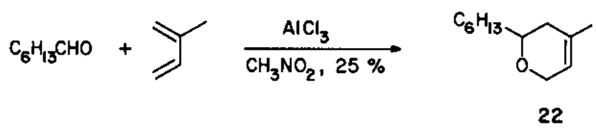
Scheme 8. Synthesis of coffee aroma components from heptanal



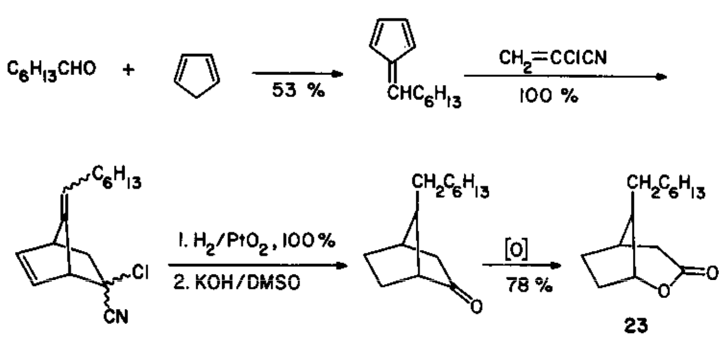
Scheme 9. Production of coconut aldehyde [21] from heptanal



Scheme 10. Condensation of heptaldehyde with ethyl bromoacetate (preparation of lactone [21])

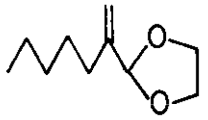
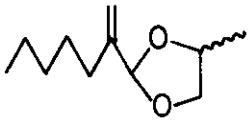
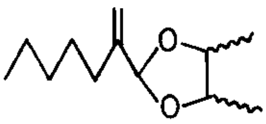
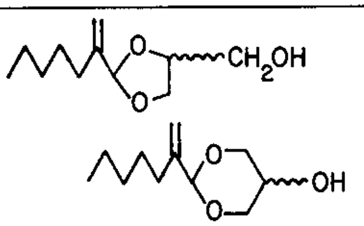
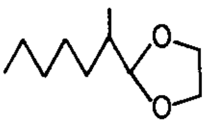


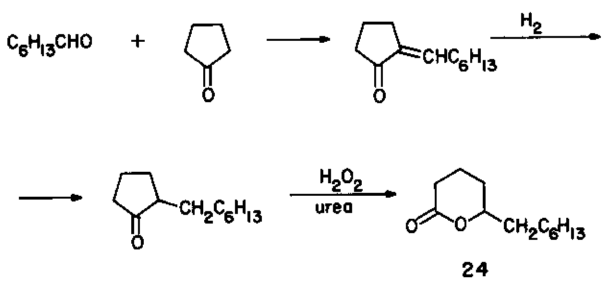
Scheme 11. Diels-Alder addition of heptanal and isoprene



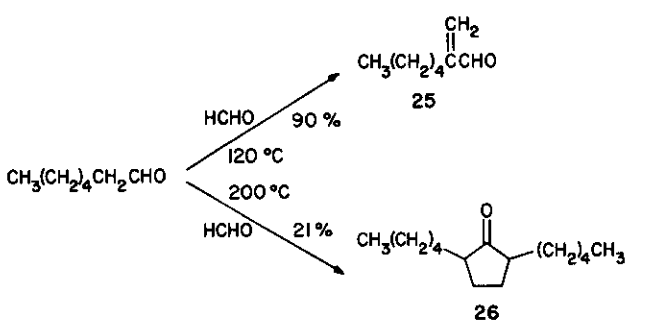
Scheme 12. Conversion of heptaldehyde and cyclopentadiene into bicyclic compounds

Table II. Odor characteristics of 2-pentylpropenal cyclic acetals[63]

Acetal	Odor
 [7]	intense, squashed greenery with a moss note
 [28]	anise with a mushroom note
 [29]	a fresh mushroom odor
 [30]	mushroom and forest-like, green
 [31]	fresh, green with an anise tone



Scheme 13. Synthesis of natural ingredient of butter aroma [24] from enanthaldehyde



Scheme 14. Condensation products of heptanal with formaldehyde

action in a moderate yield (Scheme 10).

The literature reports a few examples where interesting odoriferous compounds are formed in the reaction of heptanal with dienes; for example, Diels-Alder addition of heptaldehyde and isoprene gives a dihydropyran derivative [**22**] (Scheme 11).[53]

However, the reaction of this aldehyde with cyclopentadiene in the presence of a base leads to 6-hexylfulvene[54-57] which, after addition of chloro acrylonitrile and further transformations, furnish the aroma lactone [**23**] (Scheme 12).

A natural ingredient of butter aroma, 6-heptyl-δ-lactone [**24**], is synthesized from heptanal and cyclopentanone (Scheme 13).[58-60]

According to the reaction conditions, two types of condensations of heptaldehyde with formaldehyde catalyzed by dimethylamine hydrochloride can take place. At temperature 120°C using formaldehyde aqueous solution, 2-n-pentylpropenal [**25**] is originated,[61] however, at 200°C the two heptanal molecules with one molecule of formaldehyde condense to give a mixture of cis- and trans-cyclopentanones [**26**] (Scheme 14).[62]

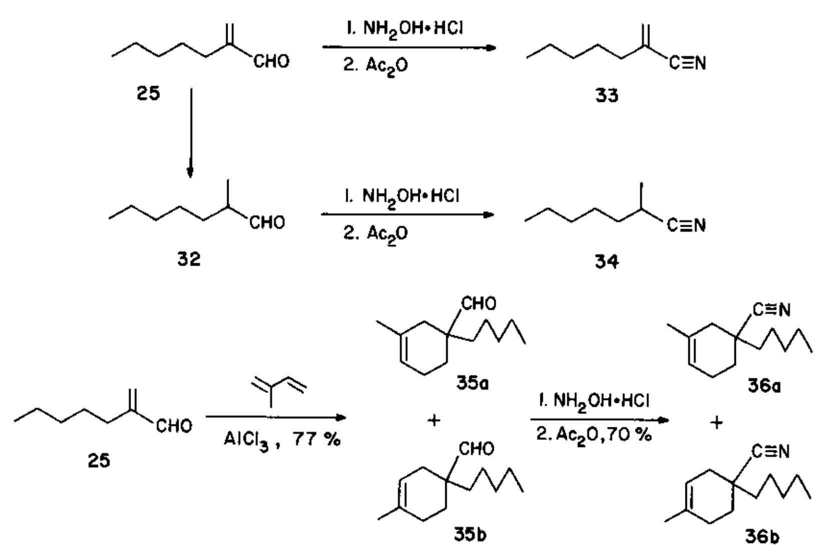
The unsaturated aldehyde [**25**] has a sharp, penetrative and green smell, but some cyclic acetals [**27-31**] have more interesting odor[63] (Table II).

Starting from [**25**], a few other compounds have been prepared (Scheme 15) where the nitriles [**33**], [**34**] and [**36**] smell more attractive than the parent aldehydes [**25**], [**32**] and [**35**].[63,64]

The nitriles [**33**] and [**34**] display a heavy, fatty scent while compound [**36**] (mixture of isomers) has an intense, elegant rather food-like aroma.

Conclusion

It should be mentioned that heptaldehyde is a starting material for the syntheses of many other compounds having a vague relationship with perfumery and cosmetics. For example, the more recent literature reports the following syntheses from n-heptanal: 27-arborol,[65] vinyl epoxides,66 dihydropyrons,[67] 2,6-substituted phenol derivatives,[68] secondary acetylene alcohols[69] and macrocyclic compounds.[70]



Scheme 15. Synthesis of nitriles from 2-n-pentylpropenal

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