

The Seven Primary Hexenols and Their Olfactory Characteristics

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All seven primary hexenols were purified by means of preparative gas chromatography and were submitted to teams of expert perfumers and flavorists for evaluation. In each instance, marked olfactory differences were found between the *cis* and *trans* isomers. It was also noted that the position of the double bond in the molecule caused appreciable

changes in the odor of the alcohol. Most of the experts preferred the *cis* isomer to the *trans* isomer. Of the seven primary alcohols, the sensory properties of *cis*-3-hexen-1-ol received the highest rating, followed by *trans*-3-hexenol and the 2-hexenols. The odor of 4-hexenol was judged to be decidedly less attractive, and that of 5-hexenol was unpleasant.

The purpose of this work was to prepare all the primary hexenols and their acetates in order to compare their olfactory characteristics. The hexenols were submitted to experienced perfumers and flavor chemists whose comments were then tabulated so that some general conclusions could be drawn.

The purified acetates were also examined by experts, but the generally fruity nature of the acetates made it impossible for the panel to be sufficiently discriminating in their evaluation.

It may be of interest to mention that the alcohols and their esters were submitted to the Entomological Division of the Department of Agriculture in the hope that their relative attractiveness, if any, to insects might be learned. To date, laboratory experiments with economically important insects such as the male gypsy moth, the pink bollworm moth, the male codling moth, and others, have yielded no evidence that the insects are lured or attracted by either the alcohols or their esters.

One apparently very significant finding, however, is now under investigation. *cis*-3-Hexen-1-ol, the most widely occurring "leaf alcohol," proved to be a feeding stimulant to the gypsy moth. Used in this way, it could change the life cycle of the insect, with consequences still to be determined.

OCCURRENCE OF HEXENOLS

Hexenols occur in nature in trace quantities and only recently has their widespread occurrence been recognized. The occurrence, preparation, and properties of *cis*-3-hexen-1-ol and its esters were reviewed by Bedoukian (1963), and since then many reports of the occurrence of both the 3- and 2-hexenols have appeared in the literature. For example, in the past 8 years, nearly 30 cases have been reported of the occurrence of *cis*-3-hexen-1-ol, 10 of *trans*-3-hexen-1-ol (along with 15 instances of mixed *cis-trans*-3-hexenols), 16 of *trans*-2-hexen-1-ol, and 5 of *cis*-2-hexen-1-ol (along with 10 of mixed *cis-trans*-2-hexenols), with more undoubtedly to come. The occurrence of 4-hexenol or 5-hexenol has not been reported.

The 2- and 3-hexenols occur mostly in fruits and vegetables. The odor of freshly cut grass is largely due to the presence of *cis*-3-hexen-1-ol.

PREPARATION OF HEXENOLS

The preparation of all seven hexenols and their 3,5-dinitrobenzoates has been reported in the literature (Hatanaka *et al.*, 1960).

Various approaches can be used. One convenient route is to make the corresponding hexynols and then hydrogenate them to the *cis*- or *trans*-hexenol. Hydrogenation with poisoned palladium catalyst gives the *cis* form and reduction with sodium in liquid ammonia gives the *trans* form. Any residual hexynol can be removed by treatment with mercury salts in an acid medium.

The hexynols were prepared according to the reaction equations shown in Figure 1. Although some of these represent new approaches to the preparation of particular hexenols, in themselves they do not constitute an original contribution, as they are applications of well-known reactions.

Commercial *cis*-3-hexenol and *trans*-2-hexenol were used, after proper purification. All the other hexenols were prepared in our laboratory.

PURIFICATION

It was recognized that olfactory examination of the seven hexenols would be of little value unless the materials were of a high degree of purity. The hexenols were first distilled through a 4-ft packed fractional distillation column and the heart fractions subjected to purification by preparative gas chromatography. The conditions used for gc analysis were as follows. Column: 12-ft $\frac{1}{8}$ -in. o.d. stainless steel; solid support and stationary phase: Carbowax 20M, 5% on Chromosorb (acid-washed) high performance, 80-100 mesh; Column temperature: start 100° C; program, + 2° C/min to 225° C; injection port temperature: 240° C; detector: T. C./Aux. 180 mA at 300° C; helium at 30 cm³/min; and sample size: 0.4.

Figure 2 illustrates the purity of the seven hexenols which were subjected to olfactory examination.

Since trace impurities present would be related materials, it was felt that they caused little interference in olfactory examinations of the alcohols.

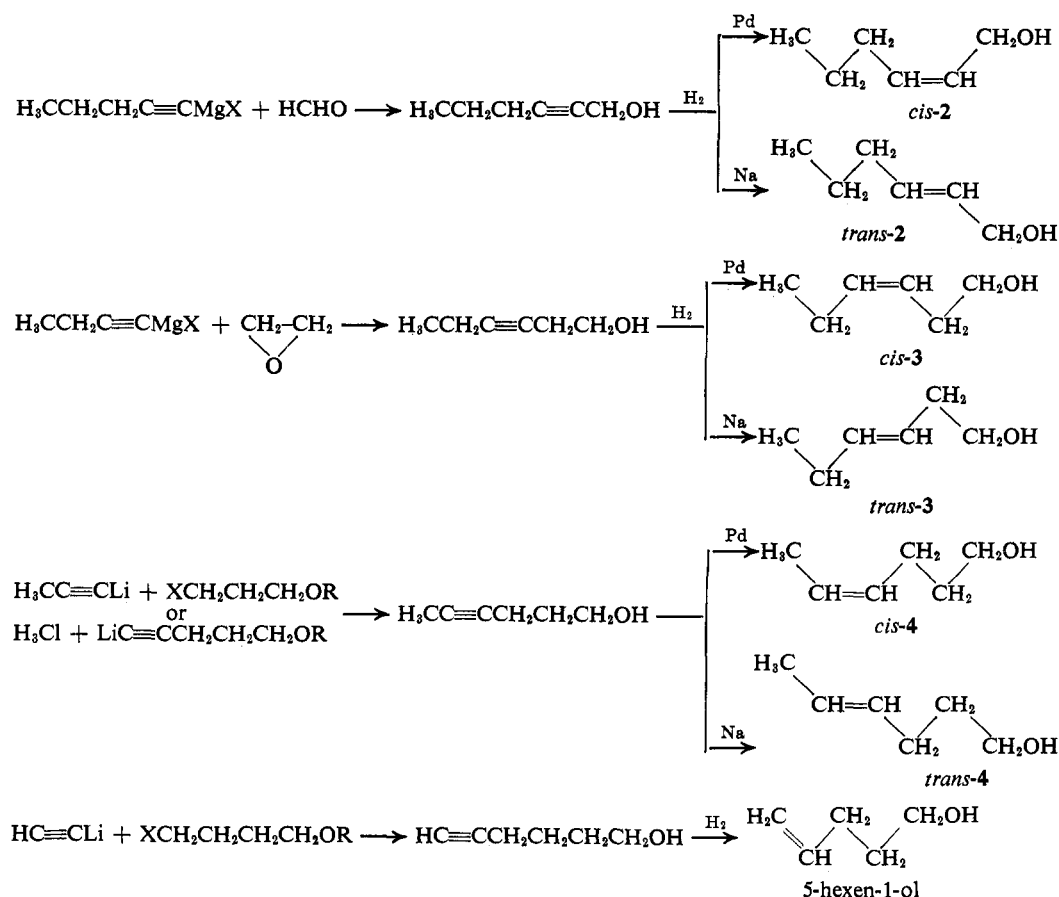


Figure 1. Preparation of hexynols and hexenols

OLFACTORY EXAMINATION

Four groups of experts (a total of 26 persons) participated in the examination of the hexenols. The procedure consisted of dipping perfumery blotters into the *cis* and *trans* forms of each alcohol, smelling them, and writing impressions. The same bottles of hexenols were used in all experiments.

RESULTS OF OLFACTORY EXAMINATION

The 26 panel members wrote a total of 30 to 35 comments per product. In order to make the results reproducible and more meaningful, remarks of infrequent occurrence have been omitted here, and odor descriptions have been simplified (Table I).

EXPERIMENTAL

The seven hexenols used in the tests were obtained in the following manner:

***cis*-2-Hexen-1-ol.** Commercial 2-hexyn-1-ol (Farchan) weighing 48.5 g was hydrogenated in a Parr apparatus using poisoned palladium catalyst on calcium carbonate (Engelhardt). At 45 lb pressure and temperatures of 77 to 94° C, 1 mol of hydrogen was absorbed in 78 min. The product was then fractionally distilled and purified by preparative gas chromatography.

***trans*-2-Hexen-1-ol.** Commercial *trans*-2-hexen-1-ol (Compagnie Parento Inc.) was further purified by preparative gas chromatography.

***cis*-3-Hexen-1-ol.** Commercial product (Compagnie Parento Inc.) of high purity was further purified by preparative gas chromatography.

***trans*-3-Hexen-1-ol.** Commercial 3-hexyn-1-ol (Compag-

nie Parento Inc.) was reduced with sodium in liquid ammonia. To 2 l. of refluxing ammonia was added 97 g of sodium in 25 min. Hexynol (97 g) was added to this mixture with stirring over a period of 35 min. After the completion of the reaction, 225 g of ammonium chloride was added to the mixture and ammonia was allowed to evaporate. The residue was carefully diluted with water and extracted with ethylene chloride. The crude hexenol was then distilled and treated with a solution of 400 g of methanol, 100 g of water, 20 g of mercuric acetate, and 20 g of sulfuric acid. This effectively removed any unreacted hexynol and the solution was washed with saturated salt solution. The unreacted hexenol was extracted with ether; it was, as usual, fractionally distilled and purified by preparative gas chromatography.

***cis*-4-Hexen-1-ol.** 4-Pentyn-1-ol (200 g) was mixed with 300 g of dihydropyran and a trace of hydrochloric acid added. The pyran derivative formed (345 g) was neutralized with sodium methoxide and purified by distillation (bp 107° C at 20 mm, refractive index 1.456 at 20° C). It was mixed with 1 l. of tetrahydrofuran and 58 g of LiNH₂, refluxed for 5 hr, and the liberated ammonia allowed to escape. The mixture was cooled to room temperature and 375 g of methyl iodide added. It was then refluxed for 5 hr, washed with salt water, and distilled. The pure fraction (286 g) of the pyran derivative of 4-hexyn-1-ol boiled at 98° C at 3 mm. It was mixed with 240 g of acetic acid and 240 g of acetyl chloride and refluxed for 2 hr to give 4-hexyn-1-yl acetate (197 g) (bp 68° C at 5 mm). The hexynol was obtained by saponification with alcoholic potassium hydroxide.

***cis*-4-Hexen-1-ol** was obtained by hydrogenation with poisoned palladium catalyst (see procedure of *cis*-2-hexen-1-ol).

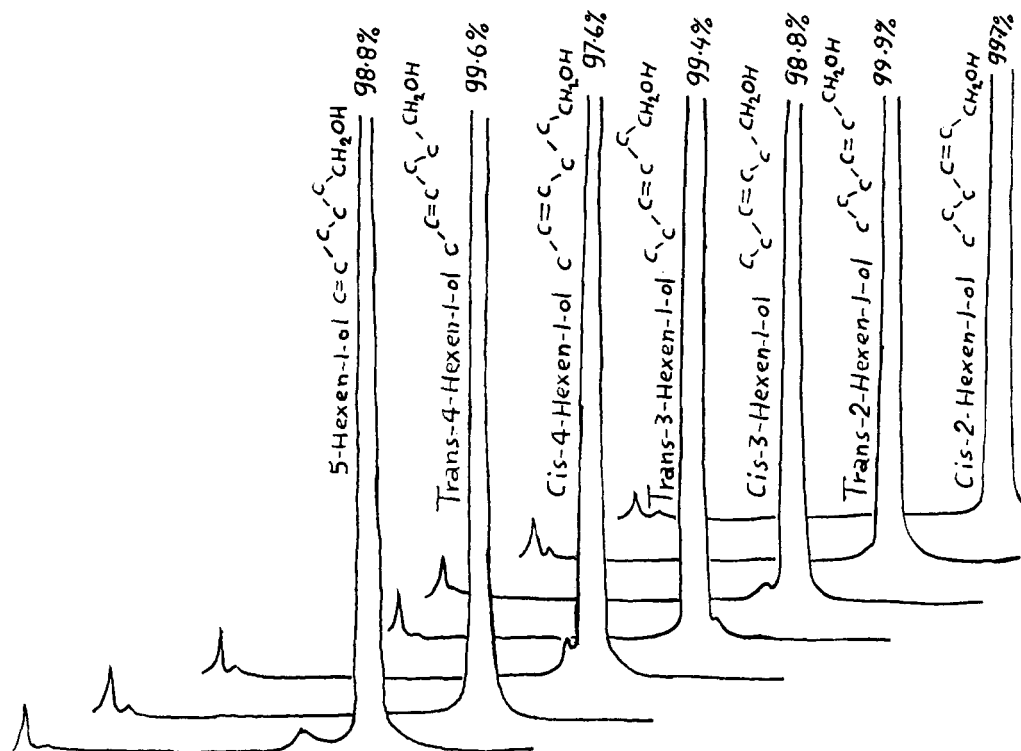


Figure 2. Glc curves of seven primary hexenols

trans-4-Hexen-1-ol. Reduction of 4-hexyn-1-ol with sodium in ammonia, as in the case of *trans*-3-hexen-1-ol, gave the *trans* isomer of this alcohol, which was subsequently purified in the usual manner.

5-Hexen-1-ol. Commercial 5-hexyn-1-ol (Farchan), on reduction with poisoned palladium catalyst, gave the required hexenol. It was purified in the usual manner by preparative gas chromatography.

CONCLUSIONS

An appreciable difference in odor exists between the *cis* and *trans* forms of each alcohol. The *cis* forms are consistently sharper and greener; the *trans* forms are more fatty. *cis*-3-Hexen-1-ol was judged the most pleasant, followed by *trans*-3-hexen-1-ol and the 2-hexenols. The 4-

hexenols were definitely less agreeable, and the 5-hexenol was unpleasant.

It was also noted that the difference was greatest between the *cis*- and *trans*-4-hexenols, and the least between the *cis*- and *trans*-2-hexenols. In general, the *cis* forms were judged to be more attractive than the *trans* forms, but one expert in five preferred the *trans* to the *cis* form.

COMMENTS

Much work has been done in the field of olfaction, and many attempts have been made to relate chemical structure to odor. A fruitful approach in this area might consist in preparing a set of related compounds in very pure form in order to study the significance of odor variations resulting from slight differences in structure. The present investiga-

Table I. Odor Characteristics of the Seven Primary Hexenols

Alcohol	Tally of odor descriptions cis isomer		Tally of odor descriptions trans isomer	
2-Hexen-1-ol	Pungent	18	Green	14
	Green	13	Fatty	13
	Fruity-vegetable	3	Fruity-vegetable	12
	Green	19	Fruity-vegetable	16
3-Hexen-1-ol	Fruity-vegetable	15	Fatty	11
	Pungent	8	Pungent	10
	Green	11	Fatty	0
4-Hexen-1-ol	Fruity-vegetable	11	Green	8
	Sharp	8	Fruity-floral	8
	Unpleasant	16	Unpleasant-fatty-green	
5-Hexen-1-ol	Fatty	10		
	Green	8		

tion was carried out with this objective in mind, and the results suggest the possibility that examination of pure samples of more complex molecules, such as dienols or even ionones, can lead to the discovery of some hitherto unknown or unobserved relationships between structure and odor, as well as the mechanism of olfaction.

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completion of the tests, the purity of the hexenols was checked by James Rogers, Fritzsche-D & O., who also supplied the individual glc curves which were used in the preparation of Figure 2.

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