

Chemical and Sensory Data Supporting the Difference between the Odors of the Enantiomeric Carvones

(+)- and (-)-carvone of high chemical and optical purity were synthesized from (-)- and (+)-limonene. An odor panel of 21-26 persons characterized the odor of the (+)-carvone as caraway-like and the (-)-carvone as spearmint-like. Thresholds of the natural and synthetic optical isomers were de-

termined. No significant difference was found between natural and synthetic (+)-carvone or between natural and synthetic (-)-carvone. On the other hand, highly significant differences were observed between the (+)- and (-)-carvones from both sources.

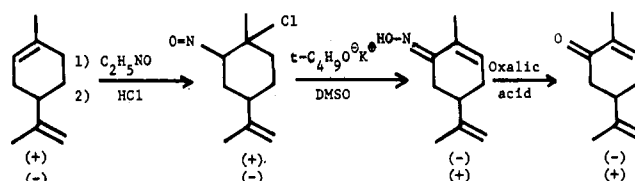
The difference between the odors of the two optical isomers of carvone has been recognized for some time; (+)-carvone was characterized as caraway-like while (-)-carvone was characterized as spearmint-like (Friedman, 1969; Langenau, 1968; Russell, 1969). However, the (+)-isomer was isolated from caraway oil and the (-)-isomer from spearmint oil, and certain impurities of very low threshold and low concentration might be responsible for the observed dissimilar odors. Samples purified by gas-liquid chromatography (glc) with very high chemical and optical purity still exhibited the two characteristic odors (Langenau, 1968). Moreover, (-)-carvone was synthesized from (+)-limonene and was found to have a spearmint odor (Langenau, 1968). A spearmint and a caraway aroma were detected in a racemic mixture of the two carvones (Langenau, 1968). However, since (+)-carvone was not synthesized from (-)-limonene and its odor was not evaluated, this evidence, although convincing, is not complete. In addition, detailed sensory data have not, as yet, been provided for the enantiomeric carvones.

The object of this investigation was to demonstrate that impurities from the natural sources are not responsible for the dissimilar odors and that the difference is, indeed, due to the difference in configuration of the two optical isomers. This was accomplished by synthesizing unequivocally both isomers with high chemical and optical purity, studying the sensory properties of each isomer, and comparing these synthetic samples to purified natural ones.

PREPARATION OF SYNTHETIC AND NATURAL (+)- AND (-)-CARVONE SAMPLES

The (+)- and (-)-limonenes (Fluka) were carefully distilled, bp 67° C (20 mm) for both [(Guenther, 1949) bp 64.4° C (15 mm)], to a purity >99.9% by glc and exhibited rotations of $[\alpha]^{27D} +116.4^\circ$ and -106.4° (*c* 0.77 and 0.84, 95% ethanol, respectively) [(Guenther, 1949) $[\alpha]^{20D} +126.8^\circ$ and -122.6° (neat), respectively].

The synthetic sequence involved the reaction of limonene with ethyl nitrite and hydrogen chloride to give limonene nitrosochloride (Royals and Horne, 1951). Subsequent elimination of hydrogen chloride with potassium *tert*-butoxide in dimethyl sulfoxide gave carvoxime, which was hydrolyzed with refluxing 5% oxalic acid to give the desired carvone.



Care was taken to avoid any cross-contamination of flasks and other equipment.

Thus, (+)-limonene was converted to (-)-carvone, which was isolated by distillation, bp 62-63° C (0.07 mm), followed by preparative glc, $[\alpha]^{27D} -59.2^\circ$ (*c* 0.22, 95% ethanol) [(Simonsen, 1947) bp 97-98° (9 mm), $[\alpha]^{25D} -62.46^\circ$ (neat)]. In a similar manner (-)-limonene gave (+)-carvone, bp 61-62° C (0.07 mm), $[\alpha]^{27D} +58.3^\circ$ (*c* 0.24, 95% ethanol) [(Simonsen, 1947) bp 96-97° C (9 mm), $[\alpha]_D +62.32^\circ$ (neat)]. Both samples were >99.9% pure by glc.

The commercial samples of the two optical isomers were prepared for sensory studies by distillation and preparative glc to a purity of >99.9%; (-)-carvone from Chemical Procurement Laboratories gave $[\alpha]^{27D} -54.2^\circ$ (*c* 0.45, 95% ethanol) and (+)-carvone from Fritzsche Borthers gave $[\alpha]^{27D} +59.6^\circ$ (*c* 0.26, 95% ethanol). The synthetic samples and these purified commercial samples had identical spectroscopic properties (ir, nmr, *m/e*, uv).

A racemic mixture of the carvones was synthesized from (+)-limonene by allylic oxidation with chromium trioxide-pyridine complex (Dauben *et al.*, 1969). The racemization

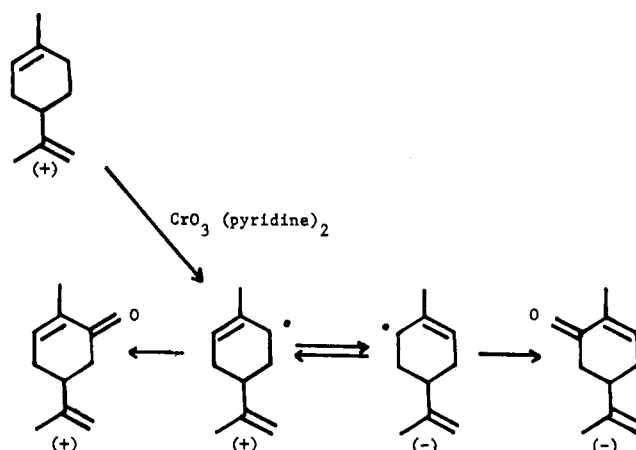


Table I. Thresholds of Natural and Synthetic Carvones Prepared from Different Sources

Sample	Source	Threshold in Water ^a
(+)-Carvone	Caraway oil (natural)	85
(+)-Carvone	Limonene (synthetic)	130
(-)-Carvone	Spearmint oil (natural)	2
(-)-Carvone	Limonene (synthetic)	2

^a Parts of compound per 10⁹ parts of water (v/v). Average threshold derived from total of 240-270 judgments for each compound.

probably results from the formation of the allylic radical which can equilibrate to give an equal mixture of the two enantiomers of carvone. Both the spearmint and caraway odors were indeed perceptible in the racemic mixture.

SENSORY EVALUATION

The odor characteristics of the natural and synthetic carvones were evaluated by an odor panel of 21-26 persons who had extensive experience and proven reliability in odor judgments. All judgments were conducted in a room equipped with individual booths and supplied with odor-free air at constant temperature and relative humidity (22° ± 1° C and 50% relative humidity). The samples were evaluated in the following manner.

Odor detection thresholds of the pure compounds were determined by previously described procedures (Guadagni *et al.*, 1963). The similarity of the purified (+)- and (-)-carvones to the odor of caraway or spearmint oil was determined by presenting the judges with a labeled standard of caraway or spearmint oils followed by two coded unknowns containing the (+)- and (-)-carvones in all possible combinations. The judges were required to select the sample in each pair which was more similar to the standard. As a further test of the odor character of the purified carvones, the judges were presented with single samples of (+)- or (-)-carvones, prepared from natural or synthetic sources, and were asked to identify the odor. Finally, odor differences among the various samples of purified carvones were determined by triangle tests. Position of each sample in

Table III. Association of Carvones with the Odor of Spearmint or Caraway Oil

Sample	N	No. who identified sample as	
		Caraway	Spearmint
(+)-Carvone (C) ^c	48	34 ^a	14
(+)-Carvone (L)	46	37 ^b	9
(-)-Carvone (L)	48	9	39 ^b
(-)-Carvone (S)	48	14	34 ^a

^a P ≥ 0.01. ^b P ≥ 0.001. ^c (C) Purified from caraway; (L) Synthesized from limonene; (S) Purified from spearmint.

pairs or triangles and order of sample presentation was randomized to avoid possible bias from these factors. Significance of the sensory results was determined from Tables of the Binomial Probability Distribution (1950).

Thresholds of the (+)- and (-)-carvones from natural (caraway and spearmint oil, respectively) and synthetic (limonene) sources are shown in Table I. The (-)-carvones had identical thresholds while the (+)-carvone from caraway had a somewhat lower threshold than the synthetic (+)-carvone. This may be due to a very slight impurity from the natural source, but in any event the (-)-carvones are substantially stronger odorants than the (+)-carvones on a threshold basis. This in itself indicates a fundamental difference in the odor properties of the (+)- and (-)-carvones. These threshold values and simple odor ranking tests were used to equalize odor intensity of the (+)- and (-)-carvones for the odor character tests. For these tests the concentration of (-)-carvone was 1 ppm v/v and for (+)-carvone was 5 ppm v/v. Table II shows that a highly significant proportion of the judgments (P < 0.01) identified the (-)-carvone as more like the spearmint oil standard and (+)-carvone as more like the caraway oil standard. Furthermore, the (+)- and (-)-carvones from natural and synthetic sources gave essentially the same results, indicating that the characteristic odor is indeed due to the difference between the configurations of the (+)- and (-)-carvone molecules rather than to impurities from natural sources. When synthetic and natural (+)-carvones were paired against a caraway oil standard, the judgments were almost equally divided as

Table II. Comparison of Natural and Synthetic Carvones to Standard Samples of Spearmint and Caraway Oil

Comparison	Standard	N	No. who identified each sample as most like the standard	
			Synthetic	Natural
(+)-Carvone (L) ^c vs. (+)-carvone (C)	Caraway	48	23	25
(+)-Carvone (L) vs. (+)-carvone (C)	Caraway	50	27	23
(-)-Carvone (S) vs. (-)-carvone (L)	Spearmint	52	26	26
(-)-Carvone (S) vs. (-)-carvone (L)	Spearmint	52	25	27
			(-)-Carvone	(+)-Carvone
(-)-Carvone (L) vs. (+)-carvone (L)	Spearmint	25	21 ^b	4
(-)-Carvone (S) vs. (+)-carvone (C)	Spearmint	22	17 ^a	5
(-)-Carvone (S) vs. (+)-carvone (C)	Caraway	25	5	20 ^a
(-)-Carvone (S) vs. (+)-carvone (L)	Caraway	22	5	17 ^a

^a P ≥ 0.01. ^b P ≥ 0.001. ^c (L) Synthesized from limonene; (C) Purified from caraway oil; (S) Purified from spearmint oil.

Table IV. Triangular Odor Comparisons Between Natural and Synthetic Carvones Prepared From Different Sources

Comparison ^a	Rep.	N	No. Correct	No. who said difference was due to ^c	
				Character	Intensity
(-)-Carvone (S) vs. (-)-carvone (L)	1	44	20	4	16
(-)-Carvone (S) vs. (-)-carvone (L)	2	48	16	4	12
(+)-Carvone (C) vs. (+)-carvone (L)	1	46	16	3	13
(+)-Carvone (C) vs. (+)-carvone (L)	2	44	18	7	11
(-)-Carvone (L) vs. (+)-carvone (L)	1	46	31 ^b	20	11
(-)-Carvone (S) vs. (+)-carvone (C)	1	42	25 ^b	13	12

^a S = Carvone purified from spearmint oil; L = Carvone synthesized from limonene; C = Carvone purified from caraway oil. ^b $P \geq 0.001$.
^c Of those who correctly identified duplicates.

to which sample was more like caraway, indicating no significant difference with respect to the odor of the two (+)-carvones. The same experiment conducted with (-)-carvones and spearmint oil as the standard gave essentially the same nonsignificant results for odor differences between the (-)-carvones from natural and synthetic sources. When the judges were presented with single samples containing (+)- or (-)-carvone from natural or synthetic sources, they were able to identify the (+)-carvone and (-)-carvone as having characteristic caraway and spearmint oil odors, respectively (Table III). These identifications were highly significant even without the benefit of caraway or spearmint oil standards, giving further evidence that (+)-carvone has a characteristic caraway odor and (-)-carvone a characteristic spearmint odor.

Table IV shows the results of direct triangular comparisons between the odors of (-)- and (+)-carvones from natural and synthetic sources. These results unequivocally show no significant differences as a result of the source (natural or synthetic) of either (+)- or (-)-carvone but very highly significant differences ($P < 0.001$) between (+)- and (-)-carvones from both sources.

Thus, the experimental evidence is entirely in favor of the claim that the optical isomers of carvone do indeed have characteristically different odors, the (-)-carvone resembling spearmint oil and the (+)-carvone resembling caraway oil. The possibility that the impurities in the synthetic (+)- and (-)-carvones are the same as the natural impurities is extremely small.

ACKNOWLEDGMENT

The authors wish to thank William Gaffield of this laboratory for the optical rotation studies.

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Received for review November 10, 1970. Accepted February 25, 1971. T. J. Leitereg expresses his gratitude for support from the National Research Council in the form of a Postdoctoral Research Associateship (1969-1971). Reference to a company or product name does not imply approval or recommendation of the product by the U.S. Department of Agriculture to the exclusion of others that may be suitable.