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TRANS-CARVONE OXIDE, A MONOTERPENE EPOXIDE FROM THE FRAGRANCE OF *CATASETUM*

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Key Word Index—*Catasetum maculatum*; Orchidaceae; (−)-carvone; (−)-carveol; *cis*-carvone epoxide; (−)-*trans*-carvone epoxide.

Abstract—A new monoterpene epoxide *trans*-carvone oxide (**1**) has been isolated from the floral fragrance of *Catasetum maculatum*, characterized by spectral data and synthesized.

INTRODUCTION

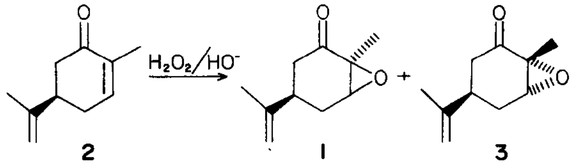
The floral fragrance of *Catasetum maculatum* L. C. Rich (sensu lato) consists of a variety of terpenes and simple aromatics, in addition to an unknown component comprising a major portion of the fragrance [1]. We now report the isolation characterization, and an efficient synthesis, of this major fragrance component identified as (2*S*,5*R*)-(−)-2,3-epoxy-5-isopropenyl-2-methyl-cyclohexanone and designated as *trans*-carvone oxide (**1**). Compound **1** has not previously been reported. The taxonomic distribution of compound **1** and its role in the pollination biology of orchids are discussed elsewhere [2].

RESULTS AND DISCUSSION

Prep. GC of the fragrance from *C. maculatum*, using a Carbowax column, provided *trans*-carvone oxide (**1**) as a colorless liquid, $[\alpha]_D^{23}$ −44° ± 5° (hexanes, *c* 0.002). The EI mass spectrum of this compound showed a low-intensity peak at the highest observed *m/z* 166.1019 (0.3%), analysed for $C_{10}H_{14}O_2^+$, and the base peak at *m/z* 43.0198 for CH_3CO^+. The former mass was substantiated as the $[M]^+$ by observation of a strong peak at *m/z* 165 and at *m/z* 167 in the negative and positive chemical ionization spectra, respectively. Analysis of the ^{13}C and ^{1}H NMR spectra (Tables 1 and 2) revealed the presence of an isopropenyl group and one Me group linked to a quaternary carbon atom in the molecule. The ^{13}C NMR spectrum was also indicative of a carbonyl group. In addition, these spectral data were closely similar to those of a series of 2,3-epoxycyclohexanones, which had been synthesized in this laboratory. Indeed a close, but not identical match was obtained for *cis*-carvone epoxide (**3**), available from alkaline epoxidation of carvone (**2**) [3–5]. We, therefore, reasoned that a likely structural candidate for the isolated fragrance component was **1**, the *trans*-isomer of **3**.

Careful product analysis of the alkaline hydrogen peroxide oxidation of carvone revealed that the *trans*-isomer **1** is also formed in this reaction, albeit in a very low yield (**1**:**3** = 6:94) (Scheme 1). This mixture was readily separated using standard silica gel flash chromatography, thus affording a sample of compound **1** which showed virtually identical ^{13}C NMR, ^{1}H NMR and mass spectra with those of the major component in the fragrance of *C. maculatum*.

We obtained further proof for the structure and stereochemistry of carvone oxide (**1**) by an independent stereocontrolled synthesis starting from (−)-carvone (Scheme 2). Our synthesis called for stereoselective reduction of the carvone carbonyl group, stereospecific hydroxyl-assisted epoxidation of the allylic alcohol [6] and oxidative regeneration of the carbonyl group. The required *cis*-carveol (**4**) was obtained by reduction of carvone with diisobutylaluminum hydride in Et_2O. This treatment gave a mixture of diastereomeric carveols **4** and **5** in the ratio of 4:1, in a virtually quantitative yield. Therefore, for our needs this reduction is superior to the Ponndorf reaction on carvone which gives a roughly equimolar mixture of the two alcohols [7] and to $LiAlH_4$ reduction [8] which may lead to saturation of the conjugated double bond [9]. After chromatographic separation, compound **4** was epoxidized with *m*-chloroperbenzoic acid in C_6H_6 to give epoxy alcohol **6** as a major product. Compound **6** was purified by flash chromatography on silica gel and oxidized with a CrO_3–pyridine complex to furnish *trans*-carvone oxide (**1**), identical in all respects with the material isolated from the epoxidation of carvone and from *C. maculatum*. On the basis of these chemical transformations and the



Scheme 1. Alkaline hydrogen peroxide oxidation of carvone.

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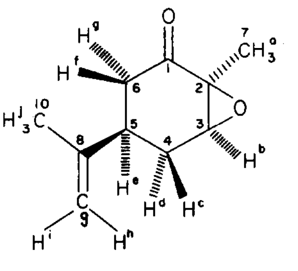
Table 1. ^{13}C NMR (75 MHz) spectral data of *trans*-carvone oxide (**1**) in $CDCl_3$ with δ-values relative to TMS as internal standard (data for isomer **3** are included for comparison)

	Carbon No.									
	1	2	3	4	5	6	7	8	9	10
1	208.2	59.3	64.8	28.9	44.9	40.5	14.8	146.0	110.7	19.6
3	204.9	58.4	61.0	28.4	34.7	41.5	15.0	146.0	110.2	20.3

Table 2. ^{1}H NMR (300 MHz) spectral data of *trans*-carvone oxide (**1**) in $CDCl_3$ (TMS as internal standard)

Proton	δ-values (ppm)	Multiplicity	J (Hz)
a	1.33	*s*	
b	3.38	*d*	$J_{bd} = 4.5$; $J_{bc} \sim 0$
c	1.95	*dd*	$J_{ce} = 11.6$; $J_{cd} = 15.2$
d*	2.04–2.17	*m*	
e	2.48–2.60	*m*	
f*	2.04–2.17	*m*	
g	2.74	*dd*	$J_{eg} = 14.0$; $J_{fg} = 11.7$
h and i	4.69 and 4.65	*m* and *br s*	
j	1.63	*br s*	

*A two-proton multiplet.



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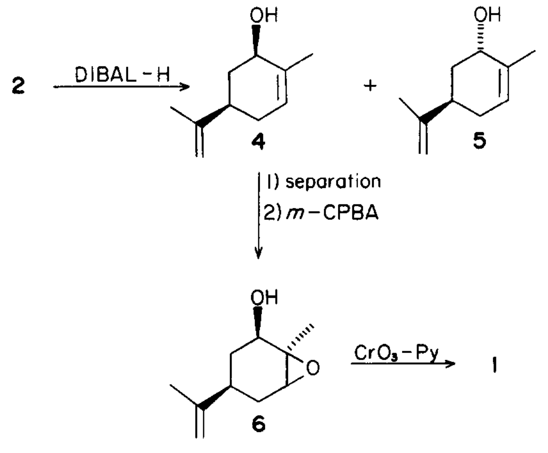
known absolute configuration of (−)-*cis*-carveol [10], the absolute structure of **1** was assigned as (2*S*,5*R*)-(−)-2,3-epoxy-5-isopropenyl-2-methylcyclohexanone. Bioassays of the synthetic **1** are reported elsewhere [2].

EXPERIMENTAL

Mps are uncorr. The CIMS (negative and positive) were obtained using CH_4 as an ionizing medium. Silica gel chromatography separations were monitored by GC using a fused silica OV-101 WCOT capillary column at 80° and FID.

Isolation and spectral characterization of trans-*carvone oxide* (**1**). The *C. maculatum* plants were cultivated at the University of Florida, Gainesville. The fragrance was collected by enclosing the intact flower stalks in a glass chamber, from which air was pulled through a glass tube containing Tenax GC. The adsorbed material was removed from Tenax by heating the glass tube to 200° while passing a stream of nitrogen through it and then through a capillary tube immersed in liquid N_2. The capillary tube was rinsed with pentane to remove the condensed volatiles. The carvone oxide was separated by prep. GC using a Carbowax column at 120°. High resolution EIMS 70 eV, *m/z* (rel. int.): 166:1019 $[M]^+$, $C_{10}H_{14}O_2$ (0.3%); 123.0879 $[C_8H_{11}O]^+$ (3); 109.0628 $[C_7H_9O]^+$ (42); 108.0547 $[C_7H_8O]^+$ (37); 95.0524 $[C_6H_7O]^+$ (15); 82.0349 $[C_5H_6O]^+$ (22); 67.0465 $[C_5H_7]^+$ (26); 55.0196 $[C_3H_3O]^+$ (26); 43.0198 $[C_2H_3O]^+$ (100). Negative CIMS: *m/z* 165 $[M-H]^-$. Positive CIMS: *m/z* 167 $[M+H]^+$. ^{13}C NMR (see Table 1). ^{1}H NMR (see Table 2).

Hydrogen peroxide epoxidation of (−)-*carvone*. The reaction was performed and worked-up as previously described [5]. The GC analysis indicated two products in the ratio of 6:94. The



Scheme 2. Stereocontrolled synthesis of *trans*-carvone oxide.

mixture of epoxides **1** and **3** (1 g) was separated on a column packed with silica gel (50 g) in pentane, using Et_2O–pentane (1 : 19) as eluent. Epoxide **1** was eluted first (0.059 g), followed by **3** (0.92 g).

Reduction of (−)-*carvone.* A soln of (−)-carvone (12.7 g, 85 mmol, $[\alpha]_D^{20}$ − 58° ± 2°, neat) in Et_2O (20 ml) was cooled to − 78° under Ar and treated dropwise within 30 min with a soln of di*iso*butylaluminum hydride in Et_2O (1 M, 100 ml, 100 mmol). After the addition was completed, the reaction mixture was stirred for 15 min at − 78°, carefully quenched with MeOH (50 ml) and stirred at room temp for 10 min. Filtration was followed by removal of Et_2O on a rotary evaporator to give 12.8 g of a mixture of alcohols **4** and **5** in the ratio of 4 : 1 (GC analysis). The *cis*-carveol (**4**) was obtained by crystallization from pentane (10 ml) at a dry-ice temp; mp 22–23°, $[\alpha]_D^{23}$ − 29.4° (hexanes, *c* 0.03); reported [5] mp 24–25°, $[\alpha]_D^{25}$ − 23.9° (neat).

Epoxidation of cis-*carveol* (**4**). A soln of compound **4** (4.11 g, 27 mmol) in C_6H_6 (10 ml) was added at + 5° to a soln of *m*-chloroperbenzoic acid (6.52 g, 80 %, 30 mmol) in C_6H_6 (100 ml) and the resultant mixture was left at + 5° for 6 hr. A filtered soln was washed with 10 % aq $NaHSO_3$ (2 × 10 ml), with 10 % aq $NaHCO_3$ (2 × 10 ml) and concd on a rotary evaporator. Flash chromatography on a column packed with silica gel (150 g) in Et_2O–pentane (1 : 19), using Et_2O–pentane (1 : 3) as eluent, furnished 2.2 g (48 %) of epoxy alcohol **6**; mp 35–36°, $[\alpha]_D^{23}$ − 15.4° (hexanes, *c* 0.06). ^1H NMR (300 MHz, $CDCl_3$/TMS): δ 1.45 (*s*, CH_3); 1.68 (*br s*, CH_3); 3.16 (*d*, $J = 4.9$ Hz, oxirane-H); 3.86 (*m*, HO–C–H); 4.69 (*m*, C=CH_2). (Found: C, 71.45; H, 9.60. $C_{10}H_{16}O_2$ requires: C, 71.39; H, 9.59 %)

Oxidation of epoxy alcohol **6**. A CrO_3–pyridine complex (7.5 g, 42 mmol) was added to a soln of compound **6** (1.465 g, 8.7 mmol) in pyridine (125 ml) and the resultant mixture was stirred for 30 hr. A filtered soln was concd to 6 ml on a rotary evaporator and applied to a chromatography column packed with silica gel (90 g) in Et_2O–pentane (3 : 97). Elution with Et_2O–pentane (1 : 19) afforded 1.3 g (90 %) of *trans*-carvone oxide (**1**); $[\alpha]_D^{23}$ − 40.8° (hexanes, *c* 0.01). (Found: C, 72.12; H, 8.52. $C_{10}H_{14}O_2$ requires: C, 72.26; H, 8.48 %).

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