The Synthesis of Carvone from α-Terpinyl Acetate

By Takayuki SUGA

(Received February 22, 1958)

Up to the present, the synthesis of *l*-carvone from *d*-limonene has been attained through the intermediates of *d*-limonene nitrosochloride and *l*-carvoxime[1,2]. In these cases the conversion of limonene into carvone resulted in relatively high yields (35% and 56~60%, respectively), but it was necessary to use toxic nitrosylchloride gas. Recently, two alterative methods[3] of the conversion of *d*-limonene into *l*-carvone have been reported. The first involves conversion of limonene monoxide into limonene glycol, oxidation of the glycol to a keto alcohol with *tert*-butyl chromate, and dehydration of the keto alcohol to *l*-carvone. In the second, the oxide is first converted into limonene glycol diacetate, which is in turn pyrolyzed to carveol acetate, saponified to carveol, and then oxidized to carvone. The overall yields of *l*-carvone from *d*-limonene in these cases do not exceed 9.2% and 7%, respectively.

Oppenauer and Oberrauch[4] previously found that *tert*-butyl chromate, described by Wienhaus and Treibs[5], is useful as an oxidant, and that *tert*-butyl chromate dissolved in a non-polar solvent with addition of a small amount of an organic acid oxidizes the methylene group adjacent to a double bond to the ketonic group without attacking the double bond.

The oxidation of terpene compounds with *tert*-butyl chromate has been investigated in this laboratory, and it has been reported that the oxidation of α-pinene[6] gives mainly verbenone and a little verbenyl acetate, and the oxidation of carvomenthene[7] produces carvotanacetone. It has been also described by Dupont et al.[8] that, on oxidation with *tert*-butyl chromate, carvomenthene yields carvotanacetone and piperitone, both α- and β-pinenes give verbenone only, and camphene remains unchanged. Thus it is evident that when a terpene hydrocarbon containing an isolated double bond is treated with *tert*-butyl chromate, the methylene group in the α-position to an ethylenic linkage in the ring is oxidized to a ketonic group.

Oxidation of α-terpineol with tert-butyl chromate[9]. The author considered that, if the methylene group adjacent to the ethylenic linkage of α-terpineol (I_a) was oxidized to a ketonic group with *tert*-butyl chromate as in the cases of terpene hydrocarbons and if 8-hydroxycarvotanacetone (II_a) was thus obtained in a high

---

[1] C. Bordenca, F. K. Allison and P. H. Dirstine, *Ind. Eng. Chem.*, **43**, 1196 (1951).

[2] E. E. Royals and S. E. Horne, Jr., *J. Am. Chem. Soc.*, **73**, 5856 (1951).

[3] S. M. Linder and F. P. Greenspan, *J. Org. Chem.*, **22**, 949 (1957).

[4] R. V. Oppenauer and H. Oberrauch, *Anales Asoc. Quim. Argentina*, **37**, 246 (1949).

[5] H. Wienhaus and W. Treibs, *Ber.*, **56**, 1648 (1923).

[6] T. Matsuura and K. Fujita, *J. Sci. Hiroshima Univ.*, **A16**, 173 (1952).

[7] K. Fujita and T. Matsuura, ibid., **A18**, 455 (1955).

[8] G. Dupont, R. Dulou and O. Mondou, *Bull. soc. chim. France*, **1953**, 60.

[9] T. Matsuura and T. Suga, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **78**, 1117 (1957).

TABLE I

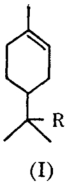
CONDITIONS AND RESULTS IN OXIDATION OF *dl*-α-TERPINEOL

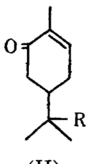
Expt.	Conditions			Reaction Products**		
	Sample/Chromic acid (mole ratio)	Temp. (°C)	Time*	8-Hydroxy-carvotan-acetone (%)	8-Hydroxy-piperitone (%)	Homoterpenyl methyl ketone (%)
1	1:5	50	36 hr., then 4 days at R.T.	8	5	22
2	1:2.5	35	36 hr., then 12 hr., at R.T.	15	7	20
3	1:2.5	20	10 days at R.T.	14	7	18

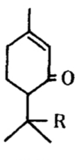
* R.T.: Room temperature.

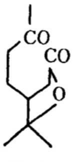
** Yields represent wt.% for α-terpineol used.

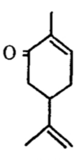
yield, it would be possible to convert the latter into carvone by dehydration to form an isopropenyl group from the hydroxy-isopropyl group. Then, an attempt was first made to study the action of *tert*-butyl chromate on *dl*-α-terpineol. A benzene solution of *tert*-butyl chromate containing glacial acetic acid and acetic anhydride was used as an oxidizing agent, and the oxidation was carried out in a current of carbon dioxide under three different conditions as shown in Table I. From the results (Table I) it was found that the reaction products consisted of 8-hydroxycarvotanacetone ($\mathrm{II_a}$), 8-hydroxypiperitone ($\mathrm{III_a}$), a new compound, and homoterpenyl methyl ketone (IV), but in all cases unchanged α-terpineol was recovered in amounts ranging from 32% to 44%.


(I)


(II)


(III)


(IV)


(V)

a, R=OH
b, R=OAc

Considerable amounts of homoterpenyl methyl ketone were produced from α-terpineol by oxidative fission of the double bond in the ring. Such cleavage occurred scarcely ever or only a little in the oxidation of α-pinene, carvomenthene and limonene (to be described later). It was difficult to suppress the cleavage of the ethylenic bond even by using milder conditions, viz., a small amount of the oxidant at a low temperature (e.g., Expt. 3).

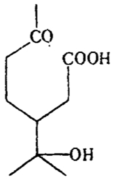
Oxidation of α-terpinyl acetate with tert-butyl chromate[10]. Accordingly it is of interest to attempt an oxidation of *dl*-α-terpinyl acetate ($\mathrm{I_b}$) to see whether, by acetylating the hydroxyl group of α-terpineol, it is possible to suppress the cleavage reaction of the ethylenic linkage in the ring*.

A benzene solution of *tert*-butyl chromate (three moles of chromic anhydride to one mole of α-terpinyl acetate) containing glacial acetic acid and acetic anhydride was used as in the case of α-terpineol. Treatment of α-terpinyl acetate with this oxidant at room temperature (the average temperature was 20°C) for fifteen days in a current of carbon dioxide led to the formation of 8-acetoxycarvotanacetone ($\mathrm{II_b}$) (the yield was 23% to α-terpinyl acetate), which had not yet been described, and homoterpenyl methyl ketone (15%), but in this case no product resulting from the oxidation of the methylene group in the $\mathrm{C_{(3)}}$ position of α-terpinyl acetate was detected. The oxidation of a large amount of α-terpinyl acetate, however, gave a small amount (ca. 3%) of a new compound, 8-acetoxypiperitone ($\mathrm{III_b}$), in which the methylene group in the $\mathrm{C_{(3)}}$ position was changed into a ketonic group, while the yields of 8-acetoxycarvotanacetone and homoterpenyl methyl ketone were

---

[10] T. Matsuura, T. Suga and K. Suga, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zassi)*, **78**, 1122 (1957).

* It is interpreted by J. L. Simonsen ("The Terpenes", University Press, Cambridge, 1947, Vol. 1, p. 259) that on oxidation of α-terpineol, homoterpenyl methyl ketone is formed by loss of water from a γ-hydroxyacid (VI).


(VI)

26% and 10%, respectively. A respectable amount of α-terpinyl acetate (26% and 43%, respectively) was recovered unchanged.

Thus it was made quite clear that, on action of *tert*-butyl chromate on α-terpinyl acetate, the oxidation of the methylene group in the $C_{(6)}$ position in the ring to a ketonic group (to give 8-acetoxycarvotanacetone) proceeds prominently, while both the oxidation of the $C_{(3)}$ position (to 8-acetoxypiperitone) and the cleavage of the double bond (to homoterpenyl methyl ketone) are restrained.

Dehydroacetoxylation of 8-acetoxycarvotanacetone[11]. There have been a great deal of works showing that the pyrolysis of esters is an excellent method for the introduction of the unsaturated linkage, and it has frequently been used for the syntheses of olefins. Bailley et al.[12] have recently shown that the vapor phase pyrolysis of acetates of secondary and tertiary alcohols proceeds selectively with the formation of the least alkylated olefin, and the direction of elimination is always such that the hydrogen is abstracted in the order: primary>secondary >tertiary. It has also been reported by Aratani and Matsuura[13] that the pyrolysis of terpin diacetate produced β-terpinyl acetate in 57% yield.

It is of interest, therefore, to study the pyrolysis of 8-acetoxycarvotanacetone (II_b) to produce carvone (V) by the elimination of acetic acid.

The pyrolysis was carried out by the distillation through a Vigreux column under an atmospheric pressure in an airbath, the temperature of which was raised gradually from the room temperature to 340°C during the operation. Acetic acid was liberated in an amount of 92% of the theoretical and the pyrolysate which distilled out was 91% of the starting material. The pyrolysate freed from acetic acid gave a neutral oil (66%), which contained 72% (or 59% of the theoretical amount to the starting material) of the desired ketone, *dl*-carvone, and the undesired substances, carvacrol (7%) and piperitenone (13%). It was sure that piperitenone was formed through the dehydroacetoxylation of 8-acetoxypiperitone which existed as a contaminate in 8-acetoxycarvotanacetone. A small amount (ca. 7%) of 8-acetoxycarvotanacetone was recovered.

Thus, it has been established that when 8-acetoxycarvotanacetone is pyrolyzed in the liquid phase, the dehydroacetoxylation takes place in the direction of a primary hydrogen atom to form an isopropenyl group and gives a relatively high yield of *dl*-carvone.

Selection of the conditions in the oxidation of α-terpinyl acetate. As mentioned above, the pyrolysis of 8-acetoxycarvotanacetone proceeds in a highly selective manner to give the prominent yield of carvone, but the conversion of α-terpinyl acetate into 8-acetoxycarvotanacetone is unsatisfactory in respect of the yield under the employed circumstances.

An extensive study was then made in order to develop a satisfactory procedure for the conversion of α-terpinyl acetate into 8-acetoxycarvotanacetone and to accumulate, in addition, fundamental data for the *tert*-butyl chromate oxidation. The effects of the solvent, (acetic acid), and the reaction temperature, and the catalytic action of benzoyl peroxide, on the yield of the reaction products from oxidation of α-terpinyl acetate, particularly the desired α,β-unsaturated ketone, were studied.

The relative yields of crude 8-acetoxycarvotanacetone in the reaction mixtures were determined by measuring the absorption at the maximum 235 mμ, specific to the α,β-unsaturated ketone, and the yields were estimated by weighing the desired ketone isolated by fractional distillation.

To examine the effect of the solvent on the yield, *n*-hexane, carbon tetrachloride, and benzene, were compared under the identical conditions (Expt. 1, 2 and 3 in Table II), and benzene was found the best. Therefore, benzene was henceforward used as the solvent for *tert*-butyl chromate.

Next, the influence of aeration was examined. The experiments showed that the yield of the α,β-unsaturated ketone in the acidic oxidation (Expt. 3 and 4) was greater in the current of air than in the current of carbon dioxide, but such was not the case in the neutral oxidation (Expt. 5 and 6). The results were similar irrespective of the amounts of the oxidant (Expt. 7 and 8) and of the acid (Expt. 9 and 10). The increase in the yield, however, seems not to be concerned with a simple autoxidation, because α-terpinyl acetate was fairly indifferent to air in

---

[11] T. Suga and T. Matsuura, ibid., **78**, 1089 (1957).

[12] W. J. Bailey, et al., *J. Am. Chem. Soc.*, **77**, 75, 357 (1955).

[13] T. Aratani and T. Matsuura, *J. Sci. Hiroshima Univ.*, **A20**, 191 (1957).

the same medium and under the same conditions as in the acidic oxidation (Expt. 11), infrared absorption (Fig. 1) showing that α-terpinyl acetate was not changed by air.

Further, in the acidic oxidation in the current of either carbon dioxide or air, the yield of α,β-unsaturated ketone increased with the addition of increasing quantities of acetic acid. However, the increase in the acid made difficult the separation of the benzene layer from the aqueous layer in the treatment of the reaction mixture with water.

The effect of the temperature on the yield of the products was studies with the results as follows. In the oxidation with the acidic oxidant in the air-stream, elevation of the temperature from 30°C to 50°C* brought a significant increase in the yield of the α,β-unsaturated ketone even when the amount of acetic acid was small (Expt. 12). The yield of the ketone was somewhat greater when more acid was used (Expt. 13), reaching 45% to α-terpinyl acetate used.

Thus it was established that the desired α,β-unsaturated ketone is produced in 45% yield to α-terpinyl acetate when the oxidation using the fixed quantity of the benzene solution of *tert*-butyl chromate (the mole ratio of α-terpinyl acetate to chromic anhydride is 1:2.7) is carried out with the addition of ca. 9% acetic acid at 50°C for one hundred hours in the current of air.

Then, in the acidic oxidation in the current of carbon dioxide, the effect of benzoyl peroxide, which has been frequently used as an initiator of radical reactions, was examined (Expt. 14 and 15). The acidic oxidation in the presence of benzoyl peroxide was carried out at 55°C, since it has been reported[14,15] that the catalytic ability of benzoyl peroxide increases with the elevation of the temperature, and results in an increase in the yield of the α,β-unsaturated ketone, compared with the oxidation in the absence of the peroxide.

Though not yet examined, a larger excess of the oxidant with benzoyl peroxide and air may increase more remarkably the yield of the desired ketone.

It was thus established that the conversion of *dl*-α-terpinyl acetate into *dl*-carvone through 8-acetoxycarvotanacetone is effected by means of the combined procedure of the *tert*-butyl chromate oxidation and the pyrolysis, giving an overall yield of 28 mole%.

In conclusion, it may be added that Fujita[16] of this laboratory treated *d*-limonene with a benzene solution of *tert*-butyl chromate containing acetic acid and acetic anhydride at 50°C for a period of thirty-six hours and obtained chiefly *dl*-carvone in a yield of 20% to limonene along with *d*-isopiperitenone (13%) and piperitenone (3%).

Experimental

Oxidation of *dl*-α-Terpineol—Expt. 2 (Table I) is described below in details. Expt. 1 and 3 followed in the wake of Expt. 2.

dl-α-Terpineol[17], b.p.$_2$ 79~80°C, n_D^{25} 1.4814, d_4^{25} 0.9310, was prepared by refluxing terpin hydrate with 0.5% aqueous solution of oxalic acid for 5 hr. and by rectifying the crude product.

tert-Butyl chromate[4] was prepared by adding 163 g. of chromic anhydride in small portions to 325 g. of *tert*-butyl alcohol with ice-cooling, diluting the resultant with 1000 g. of benzene, drying the resulted benzene solution over anhydrous sodium sulfate, and concentrating it to 75 vol.% in vacuo. To the solution were added 55 g. of glacial acetic acid and 75 g. of acetic anhydride just prior to the oxidation.

Oxidation and treatment of reaction products.—To 100 g. of α-terpineol in 150 g. of dry benzene was added dropwise the above oxidant in a period of 4 hr. with agitation at 35°C, and then the mixture was maintained at the same temperature for 32 hr. with stirring in an atmosphere of carbon dioxide, and left to stand at the room temperature for 12 hr. When the reaction was over, the whole reaction mixture was treated with 500 cc. of water and 290 g. of hydrated oxalic acid with vigorous stirring. The mixture was separated into two layers and the aqueous solution was repeatedly extracted with benzene. The combined benzene solution was treated with aqueous alkali and with water successively and dried. After removal of the solvent, 78.5 g. of a neutral oil was obtained (Product A). The alkaline solution was repeatedly extracted with ether and chloroform in succession. From the both extracts 4.5 g. of a brown viscous oil was obtained (Product B).

Identification of products.—Distillation of Product A at 7 mmHg gave the following four fractions: (A) b.p.$_7$ 82~86°C, n_D^{25} 1.4775~1.4792, d_4^{25} 0.9445~0.9516, yield 43.9 g.; (B) b.p.$_7$ 111~121°C, n_D^{25} 1.4832~1.4850, d_4^{25} 1.0182~1.0202, yield 6.6 g.;

---

* It is described[4] that *tert*-butyl chromate explodes when heated above 60°C.

[14] S. Kamenskaya and S. Medvedev, *Acta Physicochim.*, **13**, 565 (1940); *Chem. Abst.*, **35**, 2400 (1941).

[15] M. F. R. Mulcahy and I. C. Watt, *J. Chem. Soc.*, **1954**, 2971.

[16] K. Fujita, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **78**, 1112 (1957).

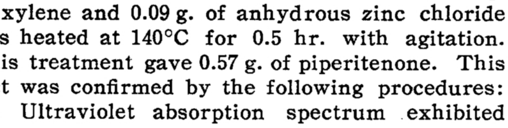
[17] K. Ono and Z. Taketa, *Reports of Saisei Shôno Co.*, **1**, 11 (1924).

(C) b.p.$_7$ 146~151°C, n_D^{25} 1.4914, d_4^{25} 1.0325, yield 14.9 g.; (D) b.p.$_7$ 166~170°C, yield 16.2 g.

(1) 8-Hydroxypiperitone (III_a). Ultraviolet absorption spectrum of fraction B gave λ_{max}^{alc}: 235mμ (strong), which corresponded to the *K*-band of the α,β-unsaturated ketone[18], and 276mμ (very weak). The chromatogram on Kirchner's chromatostrip[19], developed with 45 vol.% ethyl acetate in *n*-hexane and sprayed with 2,4-dinitrophenylhydrazine—hydrochloric acid, gave two spots. One, R_f value=0.20, was large and distinct, while the other, R_f value=0.73, was small and faint. Accordingly, the weak band at 276mμ seemed to be attributable to the impurity which gave the spot, R_f value=0.73. The heating of 3.3 g. of fraction B with 0.4 g. of palladium charcoal[20] (palladium: 30%) at 240~245°C for 9 hr. in the current of carbon dioxide gave 2.1 g. of thymol. This fact was established by the following procedures: (a) Ultraviolet absorption spectrum of the oil obtained exhibited the same λ_{max}^{alc} 277mμ (ε: 1870) as λ_{max}^{alc} 277mμ (ε: 2400) of thymol. (b) On heating with phthalic anhydride in presence of conc. sulfuric acid, thymolphthalein was obtained. (c) An alkaline solution of monochloroacetic acid[21] gave thymoxyacetic acid, m.p. and mixed m.p. 149~149.5°C.

Next, a mixture of 0.89 g. of fraction B, 0.90 g. of xylene and 0.09 g. of anhydrous zinc chloride was heated at 140°C for 0.5 hr. with agitation. This treatment gave 0.57 g. of piperitenone. This fact was confirmed by the following procedures: (a) Ultraviolet absorption spectrum exhibited λ_{max}^{alc} 242mμ (ε: 4760) and 276mμ (ε: 3180) identical with the *K*-band of the cross conjugated dienone chromophore in piperitenone[22]. (b) The chromatogram on chromatostrip did not give a spot of R_f value 0.20 corresponding to the original ketone but gave a spot of R_f value 0.73 corresponding to piperitenone. (c) A warm solution of 2,4-dinitrophenylhydrazine in alcoholic hydrochloric acid gave an isomeric mixture of piperitenone 2,4-dinitrophenylhydrazone. The separation by chromatography on silica—plaster of Paris (4:1) with benzene—petroleum ether (1:1) gave two isomers*, m.p. 152~153°C (67%) and m.p. 183.5~184°C (33%), of the 2,4-dinitrophenylhydrazone. Each showed no depression on admixture with the known specimens.

The results are schematically summarized as follows:



Thus, it was evident that fraction B consisted of 8-hydroxypiperitone.

(2) 8-Hydroxycarvotanacetone. (II_a) The chromatostrip—chromatogram of fraction C by the same method as above gave a single spot, R_f value=0.33. Ultraviolet absorption spectrum exhibited λ_{max}^{alc} 235mμ.

Treatment of a part of this fraction with palladium charcoal gave carvacrol, which was identified as the phenylurethane, m.p. and mixed m.p. 134.8~135°C.

Fraction C gave a semicarbazone, m.p. 175~176°C, and an oxime, m.p. 133~134°C. These were identified as the derivatives of 8-hydroxycarvotanacetone by mixing with known samples. By the treatment with a warm solution of 2,4-dinitrophenylhydrazine in alcoholic hydrochloric acid, 2,4-dinitrophenylhydrazone, m.p. 201~201.5°C (*Anal.* Found: N, 16.23. Calcd. for $C_{16}H_{20}O_5N_4$: N, 16.08%), was obtained.

Thus, it was established that fraction C consisted of 8-hydroxycarvotanacetone.

Ultraviolet absorption spectra of the derivatives: semicarbazone, λ_{max}^{alc} 264mμ (ε: 24000); oxime, λ_{max}^{alc} 234mμ (ε: 16300); 2,4-dinitrophenylhydrazone, λ_{max}^{alc} (the principal band) 378mμ (ε: 26650).

2,4-Dinitrophenylhydrazone of 8-hydroxycarvotanacetone, and ultraviolet absorption spectra of the ketone and its derivatives, have not yet been described in the literatures.

(3) Homoterpenyl methyl ketone (IV). Fraction D solidified. The crystalline product had m.p. 62~63°C. Its semicarbazone had m.p. 205~206°C. Product B (described above), after being distilled (b.p.$_4$ 154~160°C), also gave a semicarbazone, m.p. 204.5~205°C. These were identified as homoterpenyl methyl ketone and its semicarbazone by mixing with the genuine specimens. From fraction D, 2,4-dinitrophenylhydrazone, m.p. 164~164.5°C (*Anal.* Found: N, 15.53. Calcd. for $C_{16}H_{20}O_6N_4$: N, 15.38%) was quantitatively prepared.

(4) Unchanged α-terpineol (I_a). Fraction A gave *dl*-α-terpinyl phenylurethane, m.p. and mixed m.p. 112~113°C, and nitrosochloride, m.p. and mixed m.p. 112~113°C.

Further, from the recovered benzene solution, a small amount of acetone was isolated as the semicarbazone, m.p. and mixed m.p. 187~188°C.

Oxidation of *dl*-α-Terpinyl Acetate—*dl-α-Terpinyl acetate*, b.p.$_{15}$ 112~113.5°C, n_D^{25} 1.4638, d_4^{25} 0.9563, ester value 286.4 (calcd. for $C_{12}H_{20}O_2$: 285.9), was prepared by refluxing *dl*-α-terpineol with acetic anhydride and anhydrous sodium acetate in xylene and by rectifying the product.

I. Identification of the Reaction Products.—To 90 g. of α-terpinyl acetate was added dropwise a benzene solution of *tert*-butyl chromate, which was prepared from 255 g. of *tert*-butyl alcohol, 138 g. of chromic anhydride, 560 g. of benzene,

---

[18] R. B. Woodward, *J. Am. Chem. Soc.*, **63**, 1123 (1941); L. K. Evans and A. E. Gillam, *J. Chem. Soc.*, **1941**, 815; ibid., **1943**, 565.

[19] J. G. Kirchner, J. M. Miller and G. J. Keller, *Anal. Chem.*, **23**, 420 (1951); J. M. Miller and J. G. Kirchner, ibid., **25**, 1107 (1953).

* Y. R. Naves[22] isolated the three isomers, m. p. 132~133°C, m. p. 152~153° and m. p. 183.5~184°C. We could also isolate these three isomers in another part of the experiments (described later).

[20] R. P. Linstead, K. O. A. Michaelis and S. L. S. Thomas, *J. Chem. Soc.*, **1940**, 1139.

[21] F. Koelsch, *J. Am. Chem. Soc.*, **53**, 304 (1931).

[22] Y. R. Naves, *Bull. soc. chim. France*, **1951**, 370.

100 g. of acetic acid and 100 g. of acetic anhyride, in a period of 6.5 hr. with stirring and cooling in ice, and then the mixture was maintained at the room temperature (20°C averaged) for 15 days with occasional agitation. Treated in the same way as in the case of α-terpineol, the benzene solution gave 59.5 g. of a neutral oily product and the alkaline aqueous solution gave 10.0 g. of a viscous oil (b.p.$_{12}$ 180～184°C).

Distillation of the neutral oily product at 7mmHg gave the following three fractions: (A) b.p.$_{7}$ 93～98°C, n_D^{25} 1.4592, d_4^{25} 0.9718, yield 23.1 g.; (B) b.p.$_{7}$ 139～142°C, n_D^{25} 1.4706, d_4^{25} 1.0498, yield 17.9 g.; (C) b.p.$_{7}$ 145～160°C, n_D^{25} 1.4737, d_4^{25} 1.0495, yield 6.2 g.

(1) 8-Acetoxycarvotanacetone (II_b). Ester value of fraction B was 263.6 (calcd. for $C_{12}H_{18}O_3$: 266.3). The λ_{max}^{alc} 235mμ in ultraviolet spectrum and the wave number of 1672 cm.$^{-1}$ (liquid film) in infrared spectrum indicated the presence of a ketonic group conjugated with a double bond. In the infrared spectrum, wave numbers 1729 cm.$^{-1}$ and 1246 cm.$^{-1}$, characteristic of acetate, were also observed. The saponified product gave 8-hydroxycarvotanacetone semicarbazone and oxime.

These results established that fraction B consisted of 8-acetoxycarvotanacetone.

The derivatives of 8-acetoxycarvotanacetone and their ultraviolet absorption spectra were as follows:

Semicarbazone, m.p. 191.5～192°C, λ_{max}^{alc} 264mμ (ε: 23710).

Anal. Found: C, 58.23; H, 7.91; N, 15.85. Calcd. for $C_{13}H_{21}O_3N_3$: C, 58.41; H, 7.92; N, 15.72%.

Oxime, m.p. 107.2～107.5°C, λ_{max}^{alc} 233mμ (ε: 15870).

Anal. Found: C, 64.16; H, 8.36; N, 6.51. Calcd. for $C_{12}H_{19}O_3N$: C, 63.98; H, 8.50; N, 6.22%.

2,4-Dinitrophenylhydrazone, m.p. 217.8～218°C, λ_{max}^{alc} (a principal band) 376mμ (ε: 27580).

Anal. Found: N, 14.64. Calcd. for $C_{18}H_{22}O_6N_4$: N, 14.35%.

(2) Homoterpenyl methyl ketone (IV). Fraction C (6.2 g.) was saponified with alkali and extracted with ether. From the ethereal solution 3.0 g. of 8-hydroxycarvotanacetone was isolated as the semicarbazone. The residual alkaline solution, after being acidified with dilute sulfuric acid and extracted with chloroform, gave 3.2 g. of homoterpenyl methyl ketone. The viscous oil (10.0 g.), b.p.$_{12}$ 180～184°C, from alkaline aqueous solution (vide ante) was also homoterpenyl methyl ketone.

(3) Unchanged α-terpinyl acetate (I_b). Ester value of fraction A was 283.2 (calcd. for $C_{12}H_{20}O_2$: 285.9). The saponified product gave *dl*-α-terpinyl phenylurethane and nitrosochloride.

(4) 8-Acetoxypiperitone (III_b). When 280 g. of α-terpinyl acetate was oxidized with *tert*-butyl chromate, prepared from 852 g. of *tert*-butyl alcohol, 426 g. of chromic anhydride, 3360 g. of benzene, 420 g. of acetic acid and 320 g. of acetic anhydride, at 50°C for 36 hr. and then at the room temperature for 3 days, 249 g. of the neutral oxidation product was obtained.

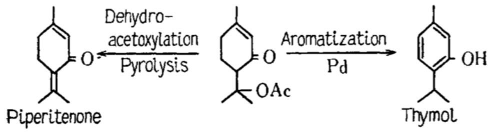
The product gave unchanged α-terpinyl acetate (43% to α-terpinyl acetate used), 8-acetoxycarvotanacetone (26%), homoterpenyl methyl ketone (10%) and a fraction of b.p.$_{3.5}$ 100～120°C, n_D^{25} 1.4670, d_4^{25} 1.0100, yield 7.3 g. (ca. 3%), which was the intermediate fraction between α-terpinyl acetate and 8-acetoxycarvotanacetone.

Ultraviolet absorption spectrum of this fraction exhibited λ_{max}^{alc} 235mμ (very strong) and 277mμ (very weak). In the chromatogram on chromatostrip, developed with 30 vol. % ethyl acetate in *n*-hexane and sprayed with 2,4-dinitrophenylhydrazine—hydrochloric acid, the major portion (λ_{mcx}^{alc} 235mμ) gave a large spot, R_f value=0.38 and the weak 277mμ band seemed to be attributable to an impurity which gave a faint spot, R_f value=0.62.

2,4-Dinitrophenylhydrazone, after being chromatographed on silica—plaster of Paris (4:1) with benzene—petroleum ether (1:1) and recrystallized from ethyl acetate, had m.p. 166～166.5°C and λ_{max}^{alc} 378mμ (ε: 30650) in the ultraviolet absorption spectrum. This absorption band and the λ_{mx}^{alc} 235mμ of the original ketone support that the ketonic group is conjugated with a double bond. The analysis of the hydrazone, C, 55.36; H, 5.74; N, 14.42%, agreed with the calculated values for $C_{18}H_{22}O_6N_4$ (8-acetoxypiperitone 2,4-dinitrophenylhydrazone): C, 55.38; H, 5.68; N, 14.35%.

Treatment of the fraction with palladium charcoal in the same manner as in the case of 8-hydroxypiperitone gave thymol and acetic acid (identified by paper-chromatography of the hydroxamic acid prepared[23]). The fraction (3.5 g.) was gently heated from 200°C to 300°C in an air-bath for 1.5 hr., and a distillate, b.p. 110～231°C, was collected. The distillate gave 0.91 g. (91% of the theoretical) of acetic acid and 1.2 g. of piperitenone. The identity of the piperitenone was established by the same way as in the case of 8-hydroxypiperitone.

The establishment of 8-acetoxypiperitone was schematically summarized as follows:



Acetone was also isolated as the semicarbazone from the recovered benzene solution in a very small amount.

II. Selection of the Conditions of the Oxidation. —Oxidation was carried out in a flask equipped with a reflux condenser, a mechanical stirrer, a thermometer and a gas inlet tube opening directly beneath the stirrer. The flask was held in a constant-temperature bath which could be regulated to ±1°C. Air, dried with conc. sulfuric

---

[23] Y. Inoue and M. Noda, *J. Agr. Chem. Soc. Japan*, (*Nippon Nôgei-Kagaku Kaishi*) **23**, 294 (1950); **24**, 291 (1951).

TABLE II

THE CONDITIONS OF OXIDATION AND THE YIELDS OF CRUDE 8-ACETOXYCARVOTANACETONE

Expt.	Sample	Conditions of oxidation							Product
	α-Terpinyl acetate (g.)	Terpinyl acetate/Chromic acid (mole ratio)	Sol-* vent	Acetic acid (g.)	Acetic anhydride (g.)	Gas** passed	Temp. (°C)	Time (hr.)	Crude*** 8-acetoxy-carvotan-acetone (%)
1	50	1:2.7	H	20	50	C	30	100	10.9
2	50	1:2.7	C	20	50	C	30	100	11.7
3	50	1:2.7	B	20	50	C	30	100	15.6
4	50	1:2.7	B	20	50	A	30	100	23.0
5	50	1:2.7	B	—	—	C	30	100	7.4
6	50	1:2.7	B	—	—	A	30	100	7.5
7	50	1:0.4	B	2.4	4.0	C	30	60	8.0
8	50	1:0.4	B	2.4	4.0	A	30	60	12.0
9	50	1:2.7	B	200	100	C	30	100	26.3
10	50	1:2.7	B	200	100	A	30	100	40.0
11	50	—	B	20	50	A	30	100	—
12	50	1:2.7	B	20	50	A	50	100	41.2
13	50	1:2.7	B	100	50	A	50	100	44.8
14	50	1:2.7	B	100	50	C	55	100	43.0
15****	50	1:2.7	B	100	50	C	55	100	53.2

* H: *n*-Hexane. C: Carbon tetrachloride. B: Benzene.

** C: Carbon dioxide. A: Air.

*** Yields represent wt.% for α-terpinyl acetate used.

**** The oxidant contains benzoyl peroxide.

acid and calcium chloride, was passed in at 350 cc. per min.

In all experiments listed in Table II except Expt. 7 and 8, *tert*-butyl chromate was prepared from 138 g. of *tert*-butyl alcohol, 69 g. of chromic anhydride and 1060 cc. of the solvent in the same way as above. In Expt. 7 and 8, 20.4 g. of *tert*-butyl alcohol, 10.2 g. of chromic anhydride and 114 cc. of benzene were used. Acetic acid and acetic anhyride were added as shown in Table II. In Expt. 15 benzoyl peroxide, which corresponded to 2 mole % for α-terpinyl acetate, was further added to the acidic oxidant just prior to the oxidation.

In all cases, the oxidant was added at a time to 50 g. of α-terpinyl acetate dissolved in 57 cc. of the solvent. When oxidation was over, the same treatment of the oxidation mixture as above gave a neutral reaction mixture. The relative yield of α,β-unsaturated ketone in each reaction mixture was determined by measuring ultraviolet absorption spectrum at 235mμ (in ethyl alcohol). Then, the reaction mixture was fractionally distilled under the reduced pressure of carbon dioxide. The fractions were separated into the unchanged and the changed parts by the chromatostrip color test and the yield of crude 8-acetoxycarvotanacetone was determined. The conditions employed and the results obtained are summarized in Table II.

In Fig. 1 the infrared spectra (liquid film) of the reaction mixture in Expt. 11 and of *dl*-α-terpinyl acetate used were compared in the 2000~750 cm.$^{-1}$ range. Agreement between these spectra showed that in Expt. 11, *dl*-α-terpinyl acetate was not at all attacked by air.

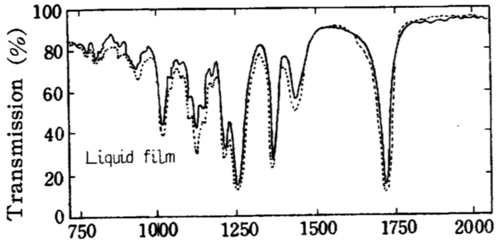


Fig. 1. Infrared spectra of the reaction mixture in Expt. 11 and of *dl*-α-terpinyl acetate used.
——: the reaction mixture in Expt. 11.
……: *dl*-α-terpinyl acetate used.

In Expt. 15 (the oxidation catalyzed by benzoyl peroxide) the same reaction products were also obtained as in Expts. 1~14.

Dehydroacetoxylation of 8-Acetoxycarvotanacetone—*8-Acetoxycarvotanacetone*, b.p.$_2$ 129~131°C, n_D^{25} 1.4820, d_4^{25} 1.0434, ester value 269.5 (calcd. for $C_{12}H_{18}O_3$: 266.8), was prepared by oxidation of *dl*-α-terpinyl acetate with *tert*-butyl chromate. The chromatogram on chromatostrip indicated that this ketone was contaminated by a small amount of 8-acetoxypiperitone.

Dehydroacetoxylation. — 8-Acetoxycarvotanacetone (35.7 g.) was distilled under an atmospheric pressure in a distilling flask equipped with a Vigreux column, the temperature of the air-bath being raised slowly to 340°C in a period of 4 hr. Dehydroacetoxylation took place actively at bath temperature 220~280°C (the reaction mixture 200~240°C). A pyrolysate (32.3 g., 91% to 8-acetoxycarvotanacetone), b.p. 114~245.5°C, distilled out leaving 2.8 g. (8%) of a polymer. Acid value of the pyrolysate was 271.0, corresponding to 9.4 g. (92% of the theoretical) of acetic acid.

Treatment and identification of the pyrolysate.—The pyrolysate was shaken with a dilute sodium bicarbonate solution to remove acetic acid, which was identified as *p*-acetotoluide. The solution of the neutral oil in petroleum ether was quickly shaken with a 5% sodium hydroxide solution. The alkaline solution was repeatedly extracted with ether. The ethereal solution gave 1.1 g. of carvacrol, which was characterized as the phenylurethane, m.p. and mixed m.p. 134.5~135.5°C. The petroleum ether solution gave 21.2 g. of a neutral oil.

Distillation of the oil at 5 mmHg gave the following three fractions: (A) b.p.$_5$ 85~90°C, n_D^{25} 1.4978~1.4985, d_4^{25} 0.9569~0.9571, yield 14.9 g.; (B) b.p.$_5$ 90~122°C, n_D^{25} 1.5200~1.5232, d_4^{25} 0.9746~0.9829, yield 5.6 g.; (C) b.p.$_5$ 122~126°C, yield 0.6 g.

(1) *dl*-Carvone (V). Ultraviolet absorption spectrum of fraction A exhibited $\lambda_{\max}^{\text{alc}}$ 235mμ identical with that of carvone[24]. The chromatogram on chromatostrip, developed with 30 vol. % ethyl acetate in *n*-hexane and sprayed with 2,4-dinitrophenylhydrazine — hydrochloric acid, gave a single spot. This fraction yielded *dl*-carvone semicarbazone, m.p. and mixed m.p. 155~156°C, *dl*-carvoxime, m.p. and mixed m.p. 92~92.5°C, and 2,4-dinitrophenylhydrazone, m.p. 187~187.2°C[25] (*Anal.* Found: N, 17.03. Calcd. for $C_{16}H_{18}O_4N_4$: N, 16.96%). These showed that this fraction consisted of *dl*-carvone only.

(2) Piperitenone. Ultraviolet absorption spectrum of fraction B showed $\lambda_{\max}^{\text{alc}}$ 243mμ and 277mμ, and the chromatogram on the chromatostrip developed as above gave three spots which possessed R_f value 0.75, 0.62 and 0.51, respectively. Then, 1.0 g. of fraction B was separated into these fractions by the elution-chromatography on silica (20 g.) with *n*-hexane—ether (3:2).

The fraction, yield 36%, which gave a spot of R_f value 0.75, consisted of *dl*-carvone (77%) and carvacrol (23%).

The fraction, yield 59%, which gave a spot of R_f value 0.62, consisted of piperitenone. This was established as follows: (a) Ultraviolet absorption spectrum exhibited $\lambda_{\max}^{\text{alc}}$ 243mμ (ε: 9930) and 277mμ (ε: 7250) characteristic of piperitenone[22]. (b) Treatment of 0.20 g. of this fraction with palladium charcoal gave 0.18 g. of thymol. (c) Ozonolysis of the fraction in ethyl acetate—acetic acid gave levulinic acid (semicarbazone, m.p. and mixed m.p. 183.2~184°C) and acetone (2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 123~125°C). (d) The separation of 2,4-dinitrophenylhydrazone by chromatography on silica—plaster of Paris with benzene—petroleum ether and recrystallization gave three isomers, (i) m.p. 151~152°C, $\lambda_{\max}^{\text{alc}}$ 387mμ (ε: 29780), (*Anal.* Found: C, 58.30; H, 5.96; N, 16.94%). (ii) m.p. 132~133°C, $\lambda_{\max}^{\text{alc}}$ 388mμ (ε: 29700). (iii) m. p. 183.8~184.5°C, $\lambda_{\max}^{\text{alc}}$ 389mμ (ε: 27520). (*Anal.* Found: C, 58.23; H, 5.66; N, 17.39. Calcd. for $C_{16}H_{18}O_4N_4$: C, 58.17; H, 5.49; N, 16.96%). These were identical with the three isomers of piperitenone 2,4-dinitrophenylhydrazone reported by Naves[22], respectively.

The fraction, yield 5%, which gave a spot of R_f value 0.51, yielded 2,4-dinitrophenylhydrazone in reddish violet needles, m.p. 171~171.5°C, $\lambda_{\max}^{\text{alc}}$ 392mμ. The fraction was so small that it was not investigated further.

(3) Unchanged 8-acetoxycarvotanacetone. 2,4-Dinitrophenylhydrazone of fraction C, chromatographed on alumina with benzene, melted at 215~216°C. It was identified as 8-acetoxycarvotanacetone 2,4-dinitrophenylhydrazone.

Summary

(1) Oxidation of *dl*-α-terpineol with *tert*-butyl chromate yielded 8-hydroxypiperitone, which has not previously been described, 8-hydroxycarvotanacetone and homoterpenyl methyl ketone. In this case the oxidative fission of the double bond in the ring took place to a remarkable extent.

(2) Oxidation of *dl*-α-terpinyl acetate with *tert*-butyl chromate gave 8-acetoxypiperitone, 8-acetoxycarvotanacetone (neither have previously been described) and homoterpenyl methyl ketone. In this oxidation the cleavage of the ethylenic linkage was suppressed, and the yield of 8-acetoxycarvotanacetone was relatively good.

Moreover, the effects of the solvent, acetic acid, benzoyl peroxide, air, and the reaction temperature, on the yield of 8-acetoxycarvotanacetone were investigated.

(3) 8-Acetoxycarvotanacetone was converted into *dl*-carvone when acetic acid was eliminated by pyrolysis.

(4) The synthesis of carvone from α-terpinyl acetate was attained through the intermediate of 8-acetoxycarvotanacetone. The overall yield of carvone from α-terpinyl acetate was 28 mole%.

The author wishes to express his hearty gratitude to Professor Tamon Matsuura for his guidance and encouragement, to

---

[24] R. G. Cooke and A. K. Macbeth, *J. Chem. Soc.*, **1938**, 1408.

[25] A. Kergomard [*Ann. chim.* (*Paris*), **8**, 193 (1953)] has reported m.p. of *dl*-carvone 2,4-dinitrophenylhydrazone to be 185~186°C.

Assistant Professor Syûichi Hayashi for his advice, and to Mr. Tadami Sakoda, Miss Miyoko Sakai and Mrs. Kiyoko Suga who assisted in a part of the experiment. This research was aided by a grant from the Ministry of Education.

Department of Chemistry
Faculty of Science
Hiroshima University
Hiroshima