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The Oxidation of (+)-3-Carene and the Related Compounds with *t*-Butyl Chromate[1,2]

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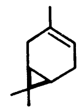
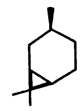
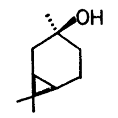
The oxidation of (+)-3-carene with *t*-butyl chromate was found to afford 3,α-dimethylstyrene (**2**), eucarvone (**3**), 1,1,4-trimethylcyclohepta-2,4-dien-6-one (**4**), 3-methylacetophenone (**5**), 8-hydroxy-*m*-cymene (**6**), car-3-en-2-one (**7**), (−)-car-3-en-5-one (**8**), and (−)-car-3-ene-2,5-dione (**9**). The aromatized compound (**6**) was a major product in the oxidation in an acidic medium, whereas the oxidation in the neutral and the basic media gave the enedione (**9**) and the enone (**8**) as major products. It was, furthermore, proved that methylenes adjacent to the cyclopropane ring of (−)-*cis*-carane (**10**) and (+)-caran-3*β*-ol (**11**) were scarcely attacked by *t*-butyl chromate.

Recently the oxidation of (+)-3-carene (**1**) with permanganate[3] or with chromium trioxide[4] has been reported. The *t*-butyl chromate oxidation of a compound with a cyclopropane ring has not yet been examined, although the endocyclic mono-[5] and diunsaturated[6,7] compounds have been subjected to this oxidation. We have now examined the oxidation of (+)-3-carene (**1**), (−)-*cis*-carane (**10**), and (+)-caran-3*β*-ol (**11**) in order to establish further details of the oxidative behavior of *t*-butyl chromate in relation to compounds with both a cyclopropane ring and an ethylenic bond. While we were preparing the manuscript of this report on our results, there appeared a brief paper[8] reporting the oxidation of **1** with *t*-butyl chromate. This prompted us to publish our paper involving the results of a more detailed examination of the reaction conditions which control the yield of products in the oxidation of (+)-3-carene (**1**) with *t*-butyl chromate.


(**1**)


(**10**)



(**11**)

Results and Discussion

(+)-3-Carene (**1**) was oxidized at 50°C for 48 hr under the reaction conditions shown in Table 1, with an equimolar or with three molar equivalents of the oxidant in various solvents, such as benzene, a mixture of benzene, glacial acetic acid and acetic anhydride, benzene admixed with pyridine. After the usual treatment[9] or the reaction mixture, the gas-liquid chromatographic analysis of a neutral product showed the presence of at least eight components, in a different ratio of the components in every oxidation. The neutral fraction was subjected to separation, purification, and identification as based on a combination of fractional distillation, column chromatography, analytical and preparative glc, spectroscopic analyses, comparisons of its physical data with those of known specimens, and the preparation of the crystalline derivatives. The procedure indicated neutral products to be composed of such compounds as 3,α-dimethylstyrene (**2**), eucarvone (**3**), 1,1,4-trimethylcyclohepta-2,4-dien-6-one (**4**), 3-methylacetophenone (**5**), 8-hydroxy-*m*-cymene (**6**), car-3-en-2-one (**7**), (−)-car-3-en-5-one (**8**), and (−)-car-3-ene-2,5-dione (**9**). The results are shown in Table 1. In addition to the formation of compounds **2**, **6**, **7**, **8**, and **9**, which have recently been reported by another group,[8] compounds **3**, **4**, and **5** were newly identified in this study.

8-Hydroxy-*m*-cymene (**6**) was the main reaction product in Experiments 1 and 2, in which the oxidation was carried out in an acidic medium. The yield

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[1] This paper has been read at the 23rd Annual Meeting of the Chemical Society of Japan, Tokyo, April 3, 1970. It forms Part X[2] in the Hiroshima University series on "Oxidation of Terpene Compounds with *t*-Butyl Chromate."

[2] Part IX, T. Suga, M. Sugimoto, K. Fujita, and T. Matsuura, This Bulletin, **39**, 2546 (1966).

[3] W. D. P. Burns, M. S. Carson, W. Cocker, and P. V. R. Shannon, *J. Chem. Soc., C*, **1968**, 3073.

[4] M. S. Carson, W. Cocker, D. H. Grayson, and P. V. R. Shannon, *ibid., C*, **1969**, 2220.

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[6] T. Matsuura and T. Suga, *J. Org. Chem.*, **30**, 518 (1965).

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[8] P. H. Boyle, W. Cocker, D. H. Grayson, and P. V. R. Shannon, *J. Chem. Soc., C*, **1971**, 1073.

[9] T. Suga, This Bulletin, **31**, 569 (1958).

TABLE 1. THE OXIDATION OF (+)-3-CARENE WITH *t*-BUTYL CHROMATE

Exp.	Type of oxidant[a]	Sample to oxidant (mol ratio)	Yield of a neutral product (%)[b]	Products (%)[c]								I/II[d]
				2	**3**	**4**	**5**	**6**	**7**	**8**	**9**	
1	B	1 : 1	11.8	24.8	2.5	8.6	10.9	34.2	3.2	9.5	6.3	0.36
2	B	1 : 3	68.8	11.8	1.2	3.3	8.8	43.6	1.2	4.1	26.0	0.54
3	A	1 : 1	29.2	16.8	3.4	6.3	9.2	27.1	1.0	6.5	29.7	0.88
4	A	1 : 3	21.0	18.7	0.8	10.1	7.1	14.3	0.4	14.6	34.0	1.49
5	C	1 : 1	28.4	2.4	1.1	5.3	9.5	9.3	0.6	28.9	42.9	3.72
6	C	1 : 3	71.1	1.9	0.6	2.1	7.1	6.7	0.3	27.1	54.2	5.37

a) A denotes *t*-butyl chromate dissolved in benzene, B does the chromate dissolved in a mixture of benzene, glacial acetic acid and acetic anhydride, and C does the chromate dissolved in benzene containing pyridine.

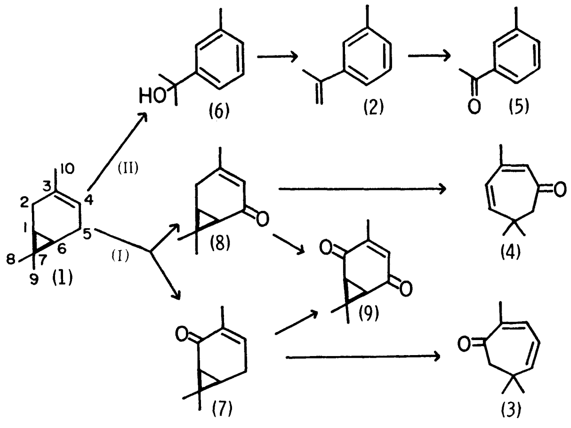
b) The yield is based on the sample, (+)-3-carene, taken.

c) The yield of products is based on the peak area on the glc of the neutral product.

d) 'I/II' denotes the ratio of the sum of percentages of **3**, **4**, **7**, **8**, and **9** to the sum of these of **2**, **5**, and **6**.

of **6** is, however, reduced to nearly a half in Experiments 3 and 4, and to nearly a quarter in Experiments 5 and 6, which employed a mixture of benzene and pyridine as the solvent. The same incident as above was also observed for the formation of 3,α-dimethylstyrene (**2**). This seems to suggest the initial opening of the cyclopropane ring, followed by the formation of the aromatized compounds. The formation of increased amounts of car-3-en-5-one (**8**) was observed upon oxidation in a rather basic medium. This indicates that the oxidation in the basic status is favorable for the allylic oxidation at the C-5 position of 3-carene (**1**). The same tendency was observed in the formation of car-3-ene-2,5-dione (**9**). The oxidation using three molar equivalents of the oxidant in the presence of pyridine afforded a neutral product in the highest yield, which was almost entirely composed of the dione (**9**). The seven-membered ring compounds, (**3**) and (**4**), might have resulted from the isomerization of the bicyclic ketones, (**7**) and (**8**), as in the case of the oxidation of **1** with permanganate[3)] or with chromium trioxide.[4)] In all the experiments, **7** and **3** were produced in lower yields than **8** and **4** respectively.

The oxidation of (−)-*cis*-carane (**10**) and (+)-caran-3β-ol (**11**) was carried out with three molar equivalents of the oxidant containing glacial acetic acid and acetic anhydride respectively over a 48-hr period. However, scarcely no oxidation products were produced, rather the starting material was recovered almost unchanged. It has been shown that *t*-butyl chromate does not attack methylenes adjacent to only the cyclopropane ring.



Scheme 1.

The following conclusions may be drawn from the results. The oxidation of 3-carene with *t*-butyl chromate involves two pathways, (I) and (II). Route I is mainly concerned with the oxidation of an allylic methylene to a carbonyl group, while Route II involves the aromatization of carene, followed by the subsequent oxidation of the benzillic position. As is shown in Scheme 1, the unsaturated ketones, (**7**), (**8**), and (**9**), may be given from **1** through Route I. The aromatized compounds, (**6**), (**2**), and (**5**), seem to be formed through Route II, such as has been observed previously in the oxidation of α-terpinene.[6)] The ratio (I/II) of the respective total sum of the yields of compounds produced by the two routes was larger in a basic medium than in an acidic one (Table 1). By considering the results of the oxidation of *cis*-carane (**10**) and caran-3β-ol (**11**), as well as endocyclic monounsaturated compounds,[5)] it seems that the double bond would contribute more than the cyclopropane ring to the formation of the α,β-unsaturated ketones, (**7**) and (**8**), and of the diketone, (**9**), by the preferential attack of the methylene situated between an ethylenic bond and a cyclopropane ring.

Experimental

Measurements. The melting points are uncorrected. The IR spectra were measured on a Hitachi, EPI-S, Infrared Spectrophotometer. The UV spectra were obtained on a JASCO, ORD/UV-5, Spectrophotometer. The NMR spectra were recorded on a Hitachi Perkin-Elmer, R-20, High-resolution Spectrometer at 60 MHz, using tetramethylsilane as the internal standard. Analytical glc was carried out on a Hitachi Perkin-Elmer, F6-D, Gas Chromatograph equipped with a flame-ionization detector at 160°, with a flow rate of nitrogen of 50 m*l*/min and using a 10% Carbowax column (3 mm × 2 m). Preparative glc was performed on a Shimadzu, GC-1A, Gas Chromatograph, using a 10% Carbowax column (10 mm × 2 m). The silica gel used was Kieselgel (Merck) (less than 0.08 mm).

Oxidation and Treatment of the Reaction Mixture.

Exp. 1: A *t*-butyl chromate solution was prepared from chromium trioxide (10.0 g, 0.1 mol), *t*-butyl alcohol (22.2 g, 0.3 mol), benzene (60 m*l*), acetic anhydride (10.2 g, 0.1 mol), and glacial acetic acid (6.0 g, 0.1 mol) in the same manner as in the previous report.[5,9] The oxidant solution was added, drop by drop, to (+)-3-carene (**1**) (13.6 g, 0.1 mol) (bp 168.0—168.5°C, d_4^{25} 0.8601, $[\alpha]_D^{25}$ +13.9°, neat) over a period of 4 hr, with agitation at 50°C, and then the mixture was maintained at the same temperature for 44 hr while being stirred in an atmosphere of dry nitrogen. The treatment of the mixture in the same manner as in our previous reports[9,10] afforded a neutral oily product (3.5 g); the reaction products were then identified.

Exp. 2: A solution of three molar equivalents of the oxidant with the same concentration as in Exp. 1 was added to **1** (50 g) in the same manner as in Exp. 1. The subsequent treatment of the reaction mixture in the same manner as above gave a neutral product (35.5 g).

Exp. 3: A benzene solution, not containing acetic anhydride and glacial acetic acid, of the equimolar oxidant was added to **1** (13.6 g) in the same manner as in Exp. 1. A neutral oily product (11.5 g) was then obtained from the reaction mixture by the same treatment as above.

Exp. 4: The oxidation was carried out using a benzene solution of three molar equivalents of the oxidant and 8.0 g of **1** in the same manner as above. Thus, 2.83 g of a neutral product was obtained.

Exp. 5: A benzene solution of *t*-butyl chromate was prepared by adding chromium trioxide (2.21 g) to *t*-butyl alcohol (4.90 g), after which the solution was diluted with benzene (24 m*l*) as above. The solution, after having been dried over anhydrous sodium sulfate, was concentrated to 20 m*l*, and then pyridine (0.5 g) was added. To the oxidant solution, 3.0 g of **1** dissolved in 25 m*l* of benzene was added, drop by drop, over a 4-hr period at 50°C. The mixture was maintained at the same temperature for a further 44 hr with stirring. The subsequent treatment of the reaction mixture in a manner similar to that used in Exp. 1 gave 2.75 g of a neutral product.

Exp. 6: To an oxidant solution prepared in the same manner as in Exp. 5, 1.0 g of **1** dissolved in 25 m*l* of benzene was added. After 48 hr, the similar treatment of the reaction mixture gave a neutral product (0.87 g).

In each experiment, the glc of the neutral product showed the presence of at least eight components, **2** (retention time, 2.5 min), **3** (4.4), **4** (6.8), **5** (7.8), **6** (9.0), **7** (11.0), **8** (13.9), and **9** (16.9). The retention times of the peaks on the glc were the same in every experiment.

Identification of Reaction Products. The identification of the products is exemplified by Exp. 2, shown below. The distillation of a neutral product (25 g) gave 14.6 g of a distillate with a boiling point of 50—115°C/10 mmHg and 3.5 g of a residue which was almost entirely composed of yellow crystals (mp 100—102°C). The distillate was chromatographed on a silica-gel column with mixtures of *n*-hexane and increasing amounts of ethyl acetate; we thus separated it into eight eluates.

*3,α-Dimethylstyrene (**2**)*: This hydrocarbon was obtained as the first eluate of the column chromatography. Its IR spectrum was identical with that of 3,α-dimethylstyrene reported[11] and derived from 8-hydroxy-*m*-cymene (see below) by dehydration with phosphorous oxychloride. Ozonization of **2** afforded 3-methylacetophenone (the 2,4-dinitrophenylhydrazone, mp and mixed mp 207—208°C) and formaldehyde (the same phenylhydrazone derivative, mp and mixed mp 165—166°C).

*Eucarvone (**3**)*: The second eluate was identical in respects of the retention time on the glc and the IR spectrum with a specimen of eucarvone.[12] The 2,4-dinitrophenylhydrazone (mp 151—152°C) showed no depression of the melting point on admixed with the known specimen.

*1,1,4-Trimethylcyclohepta-2,4-dien-6-one (**4**)*: This compound was isolated as the third eluate. This eluate, after purified further by the preparative glc, gave a pale yellow oil: λ_{max}^{EtOH} 294 nm (log ε 3.31). The IR (1631 and 1575 cm^{-1}) and the NMR (1.10, 2.02, 2.51, 5.63, 5.91, and 6.03 ppm) spectra were identical with those of **4** reported.[3] The 2,4-dinitrophenylhydrazone melted at 176.5—177.5°C (lit,[3] mp 175—176°C).

*3-Methylacetophenone (**5**)*: The fourth eluate afforded an oil: ν_{max}^{liq} 1682 cm^{-1} (C=O); δ ($CDCl_3$) 2.36 (s, 3H, Ar–CH_3), 2.54 (s, 3H, $COCH_3$), and 7.0—7.8 ppm (m, 4H, Ar–H). The oil gave a 2,4-dinitrophenylhydrazone derivative (mp 207—208°C), which was identified as that[13] of 3-methylacetophenone by a mixed-melting-point determination.

*8-Hydroxy-*m*-cymene (**6**)*: The fifth eluate was the main component of the neutral part and gave an oil: mass *m/e* 150 (M$^+$); ν_{max}^{liq} 3381 (OH), 3027, 1618, and 1598 (benzene ring), 824, 789, and 710 cm^{-1} (1,3-disubst. benzene); δ ($CDCl_3$) 1.53 (s, 6H, $(CH_3)_2C$), 1.75 (s, 1H, OH exchanged with D_2O), 2.31 (s, 3H, Ar–CH_3), and *ca.* 7.1 ppm (m, 4H, Ar–H). These spectral data coincided with those[3,13] reported for **6**. The 3,5-dinitrobenzoate derivative showed a mp of 93—94°C (lit,[3] mp 93—94°C): (Found: C, 59.31; H, 4.59; N, 8.23%. Calcd for $C_{17}H_{16}N_2O_6$: C, 59.30; H, 4.68; N, 8.14%).

*Car-3-en-2-one (**7**)*: The sixth eluate showed a certainly different retention time from that of eucarvone upon glc. However, in the course of performing the preparative glc, the compound changed to eucarvone (**3**). It was, therefore, judged that the compound obtained from the sixth eluate was probably car-3-en-2-one (**7**).

*(−)-Car-3-en-5-one (**8**)*: The seventh eluate gave an oil showing $[\alpha]_D^{25}$ −265° (*c* 0.5, EtOH) and λ_{max}^{EtOH} 227 nm (log ε 3.55). Its IR and NMR spectral data were identical with those of car-3-en-5-one (**8**) previously reported.[3]

*(−)-Car-3-ene-2,5-dione (**9**)*: This was isolated, both from the residue in the distillation of the neutral product and from the last eluate in the column chromatography, as yellow crystals: mp 102—102.5°C, $[\alpha]_D^{25}$ −15.1° (*c* 0.3, EtOH); mass 164 (M$^+$); λ_{max}^{EtOH} 241 nm (log ε 4.11), 226 (sh. 4.03). The melting point and the IR and NMR spectra were identical with those reported for **9**.[3]

Found: C, 72.88; H, 7.56%. Calcd for $C_{10}H_{12}O_2$; C, 73.17; H, 7.32%.

*Oxidation of (−)-*cis*-Carane (**10**).* (−)-*cis*-Carane (bp 99—101°C/130 mmHg, n_D^{25} 1.4558, $[\alpha]_D^{25}$ −35.1° (*c* 1.1, *n*-hexane)) was prepared from (+)-3-carene (**1**) following the literature method.[14] The oxidation of **10** (1.0 g) was performed in the same manner as in Exp. 2. The molar ratio of **10** to the oxidant was 1 to 3. The same treatment of the reaction mixture as in Exp. 1 gave an oil (0.61 g). Glc and tlc analyses showed the presence of only a little oxygenated compound, but the sample was recovered.

*Oxidation of (+)-Caran-3β-ol (**11**).* (+)-3-Carene (**1**) was hydrated by the oxymercuration-demercuration.[15]

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[15] H. C. Brown and P. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967).

After the chromatographic purification, 0.8 g of **11** was obtained: mp 70.5—71.5°C (lit,[16] mp 71.5—72.5°C), $[\alpha]_D^{25}$ +10.2° (*c* 1.5, EtOH). The caranol (**11**) (0.8 g) was oxidized with three molar equivalents of the oxidant in the same manner as in Exp. 2. The product (0.6 g) was composed of unchanged **11** (over 95% by glc) and traces of other materials. The latter were impossible to subject to further investigations because of the very small quantities.

We wish to thank Miss S. Fujita, who assisted us in a part of this research.

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