

HYDROGENOLYSIS OF BICYCLIC MONOTERPENE EPOXIDES IN THE PRESENCE OF RANEY NICKEL AND DETERMINATION OF THE STRUCTURES OF α - AND β -3,4-EPOXY CARANES

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(Received 2 November 1966)

Abstract—Bicyclic monoterpene epoxides, α -pinene oxide, 2,3-epoxybornane, α - and β -3,4-epoxycaranes were hydrogenated under high hydrogen pressure in the presence of Raney nickel catalyst. The products obtained were analysed by VPC and were identified by comparison with authentic samples. The effect of anions, OH^- , Cl^- , Br^- and I^- for the hydrogenolysis was also examined. The results are summarized in the Tables. From the results, the structures of these bicyclic monoterpene epoxides, α -pinene oxide, 2,3-epoxybornane, α - and β -3,4-epoxycaranes were confirmed to be V, XII, XIX and XXI, respectively.

ALTHOUGH various workers¹ have dealt with the hydrogenolysis of epoxides, only a few attempts have been made to systematically discuss the stereochemistry of the reaction. Recently, Mitsui *et al.*²⁻⁴ have reported on the stereochemistry of epoxide hydrogenolysis and on the stereoselectivity of the metallic catalysts used. According to their conclusions, the hydrogenolysis of an epoxide produces different products when nickel and palladium are used as catalysts. For example, the catalytic hydrogenolysis³ of *cis*- α , α' -dimethylstilbene oxide (I) using Raney nickel predominantly gives *erythro*-2,3-diphenylbutan-2-ol (II), while in the case of palladium on charcoal *threo*-isomer III is mainly obtained. These experimental results were interpreted by the authors as follows: the epoxide I may be hydrogenated predominantly in a *SNi* type reaction, in which the oxygen atom of epoxide ring is located upon the surface of Raney nickel as shown in Fig. 1a. Consequently, the reaction gives II as the main product. On the other hand, it appears that hydrogenolysis with inversion

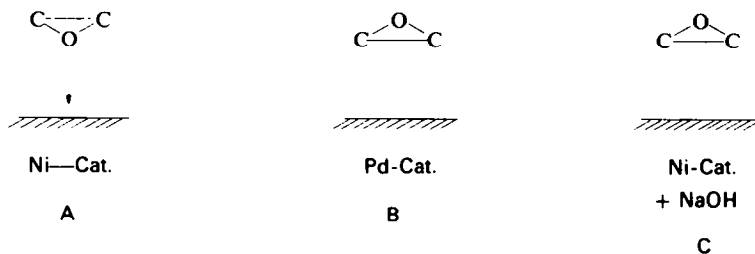


FIG. 1 Orientation of epoxides on the surface of catalysts.

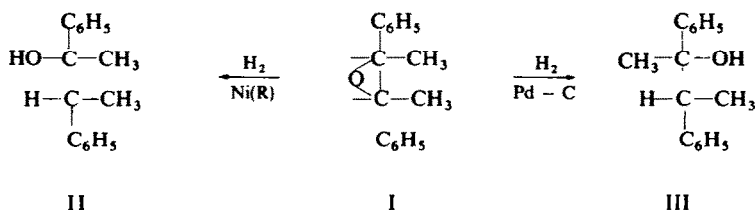
¹ For example, R. E. Parker and N. S. Isaacs, *Chem. Revs.* **59**, 737 (1959).

² S. Mitsui and S. Imaizumi, *J. Chem. Soc. Japan (Nippon Kagaku Zasshi)*, **86**, 219 (1965).

³ S. Mitsui and Y. Nagahisa, *Chem. & Ind.* 1975 (1965).

⁴ S. Mitsui and Y. Nagahisa, *19th Annual Meeting of Chem. Soc. Japan. Abstract Papers III*, p. 161 (1966).

mainly occurs in the case of palladium on charcoal, because the affinity of palladium catalyst for the oxygen atom is weaker than that of Raney nickel and also because epoxide I is orientated as indicated in Fig. 1b.



In addition, it was also shown that the hydrogenolysis with inversion increased on addition of sodium hydroxide with Raney nickel catalyst. The above-mentioned workers explained this to be the result of the epoxides having an orientation as shown in Fig. 1c.

We have previously reported a study⁵ on hydroboration of 3-carene and proposed new configurational assignments for the 4-caranols and 4-caranones. Since the structures of α - and β -3,4-epoxycaranes were not confirmed in the course of the study, we have attempted to determine their structures by applying Mitsui's rule to the hydrogenolysis of epoxides, 3,4-epoxycaranes as well as α -pinene oxide and 2,3-epoxybornane.

RESULTS AND DISCUSSION

Since Prileschaev⁶ first prepared α -pinene oxide by the action of perbenzoic acid on α -pinene, it is a well known compound. Kergomard *et al.*⁷ attempted to determine the structure of this epoxide from the structures of alcohols which are obtained by hydrogenation in the presence of Raney nickel. As for the structures of pinocampheols, Schmidt⁸ first gave assignments which were based mainly on the Auwers-Skita rule.

According to Schmidt's assignment, the structures of pinocampheol, neopinocampheol, isopinocampheol and neoisopinocampheol are VI, VII, VIII and IX, respectively. However, these structures were later challenged by Bose⁹ and by Hückel,¹⁰ who proposed the structures for these alcohols as VII, VI, IX and VIII, respectively, based on conformational analysis⁹ and on rate studies of the tosylates.¹⁰ Based on the above findings Kergomard⁷ adopted the latter structural assignment and considered that if the structure of α -pinene oxide is IV, the main product obtained by hydrogenolysis must be pinocampheol (VII), while it should be neoisopinocampheol (VIII) in the case where the structure is regarded as V. As the main product actually obtained in the presence of Raney nickel was isopinocampheol (IX), it was

⁵ H. C. Brown, A. Suzuki, *J. Am. Chem. Soc.* in press (1967).

⁶ A. Prileschaev, *Ber. Dtsch. Chem. Ges.* **42**, 4814 (1909).

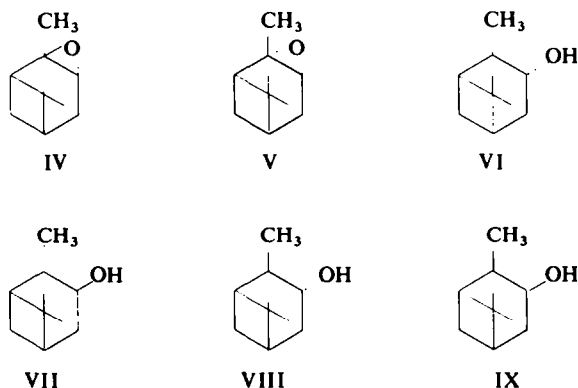
⁷ A. Kergomard and M. M. T. Geneix, *Bull. Soc. Chim. Fr.*, 394 (1958).

⁸ H. Schmidt, *Ber.* **77**, 544 (1944).

⁹ K. Bose, *J. Org. Chem.* **20**, 1003 (1955).

¹⁰ W. Hückel and D. S. Nag, *Liebigs Ann.* **645**, 101 (1961).

concluded that the first prepared product by hydrogenation may be neoisopinocampheol (VIII) which is then isomerized by the influences of heat and the catalyst into IX. However, that Schmidt's assignment for pinocampheols was right has been



recently verified by hydroboration¹¹ and the NMR studies.¹¹ Consequently, isopinocampheol (VIII) can be produced as the main product if α -pinene oxide has the structure of V.

In the present work, epoxides were hydrogenated in the presence of Raney nickel (W-4) and the influence of alkali on the catalyst was also examined. The results are summarized in Table 1. Judging from the experimental results, it is now accepted as correct that the structure of α -pinene oxide is V having a *trans*-relationship between the epoxy ring and the *gem*-dimethyl group.

TABLE 1. PERCENTAGE OF ISO-PINOCAMPHEOL (VIII) OBTAINED FROM HYDROGENOLYSIS OF α -PINENE OXIDE IN THE PRESENCE OF RANEY NICKEL CATALYST*

Exp. No	Catalyst	Additives (m.mole)	% of VIII
P-1	Raney Ni	none	77.7
P-2	Raney Ni	NaOH (1)	78.3
P-3	Raney Ni	NaOH (2)	76.6

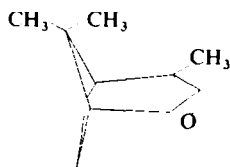
* Reaction condition: α -pinene oxide 0.1 g; solvent 99% ethanol 20 ml; amount of cat. 1 g; initial pressure of H₂ 95 atm.; reac. temp. 95 \pm 5°C; reac. time 3 hr.

1N-NaOH in ethanol was added in the desired amount.

On the other hand, a remarkable influence of sodium hydroxide cannot be found in the case of α -pinene oxide (Exp. No. P-2 and P-3), such as stated in Mitsui's data³ and seen in α - and β -epoxycaranes which will be described later in this report. The steric hindrance of the *gem*-dimethyl group which hangs in the upper space of the epoxide ring as shown in X seems to be one of the reasons why the effect of sodium

¹¹ G. Zweifel and H. C. Brown, *J. Am. Chem. Soc.* **86**, 393 (1964).

hydroxide addition is not remarkable in α -pinene oxide, because the hydrogenolysis in the adsorption state (c) in Fig. 1 does not readily take place.



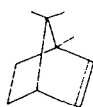
X

Although 2,3-epoxybornane is obtained by careful oxidation¹² of bornylene (XI) with organic peracid, and the structural assignment appears to be XII from the mechanistic speculation of epoxidation reaction¹³, no reports which discuss the stereochemistry are available. Applying Mitsui's rule to 2,3-epoxy bornane, it is possible to consider that borneol (XIV) and epiborneol (XV) may be produced by Raney nickel hydrogenation if the epoxide has a structure as seen in XII. In Table 2 the results obtained are summarized.

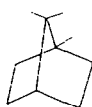
TABLE 2. PERCENTAGE OF ALCOHOLS OBTAINED FROM HYDROGENOLYSIS OF 2,3-EPOXYBORNANE IN THE PRESENCE OF RANEY NICKEL CATALYST*

Exp. No.	Catalyst	% of alcohols obtained		
		XIV	XV	XVI
B-1	Raney Ni	56.7	36.4	6.9

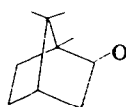
* Reaction condition: 2,3-epoxybornane 180 mg; solvent 99%-ethanol 20 ml; amount of catalyst 1 g; initial pressure of H₂ 95 atm; reac. temp. 95 ± 5°C; reac. time 4.5 hr.



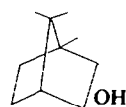
XI



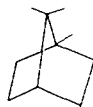
XII



XIII

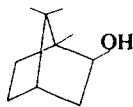


XIV

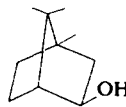


OH

XV



XVI



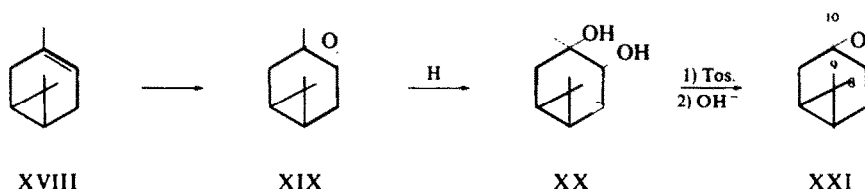
XVII

The data undoubtedly supports the conclusion that the structure of 2,3-epoxybornane may be regarded as XII with a *trans*-configuration between *gem*-dimethyl group and epoxide ring.

¹² M. Vilkas. *Bull. Soc. Chim., Fr.*, 1401 (1959).

¹³ i.e. D. Swern. *Organic Reaction* Vol. 7, p. 378 (1953).

The epoxide of 3-carene (XVIII) or α -3,4-epoxycarane is easily prepared by epoxidation^{5, 14-17} with organic peracids. Kuczynski *et al.*¹⁸ reported that the structure of α -epoxide may be XIX having a *trans*-configuration between the *gem*-dimethyl group and the epoxy ring from the structures of alcohols which were prepared by hydrogenation. On the other hand, β -3,4-epoxycarane is obtained by the following procedure:¹⁹ the α -epoxide is hydrolyzed by dilute sulfuric acid to glycol XX from which the monotosylate is obtained which then is detosylated with alcoholic potassium hydroxide to β -epoxide. The Polish workers proposed the structure XXI, based on a mechanistic speculation of these reactions and a hydrogenolysis study of β -epoxide in the manner of the former α -epoxide.



However, the Kuczynski's structural assignment to four 4-caranols has recently been revised and new structures have been proposed.^{5, 20, 21} Moreover, the NMR studies of the epoxides by Arbutov *et al.*²² have given opposite assignments, namely XXI to the α -epoxide and XIX to the β -isomer. In our previous work⁵, we assumed that although it was impossible to find direct proof, the epoxides may have structural

TABLE 3. PERCENTAGE OF ALCOHOLS OBTAINED BY HYDROGENOLYSIS OF α -3,4-EPOXYCARANE IN THE PRESENCE OF RANEY NICKEL CATALYST*

Exp. No.	Additives (m.mole)	% of alcohols obtained			
		XXII	XXIII	XXIV	XXV
C-A-1	none	11.0	trace	88.6	0.4
C-A-2	NaOH (1)	14.8	trace	82.6	2.5
C-A-3	NaOH (2)	19.8	trace	78.2	1.0
C-A-4	NaCl (2)	18.1	trace	81.0	0.9
C-A-5	NaBr (2)	18.3	trace	81.3	0.4
C-A-6	NaI (2)	18.8	trace	80.0	1.2

* Reaction condition: α -3,4-epoxycarane 0.1 g; solvent 99%-ethanol 20 ml (when NaCl, NaBr and NaI were added, 50%-ethanol was used as a solvent); amount of catalyst 1 g; initial pressure of H_2 100 atm.; reac. temp. $100 \pm 5^\circ C$; reac. time 3 hr.

¹⁴ B. A. Arbutov and B. Michajlow, *Z. Russ. Fiz. Chim. Obszcz.* **62**, 607 (1930).

¹⁵ B. A. Arbutov and B. Michajlow, *Z. Obszcz. Chim.* **9**, 255 (1939).

¹⁶ M. Bukala and H. Kuczynski, *Roczniki Chim.* **26**, 68 (1952).

¹⁷ H. Kuczynski and Z. Chabudzinski, *Roczniki Chim.* **29**, 437 (1955).

¹⁸ H. Kuczynski and K. Piatkowski, *Roczniki Chim.* **35**, 227 (1961).

¹⁹ H. Kuczynski and Z. Chabudzinski, *Roczniki Chim.* **34**, 177 (1960).

²⁰ K. Gollnick, *Tetrahedron Letter* No 13, 327 (1966).

²¹ W. Cocker, P. V. R. Shannon and P. A. Staniland, *Tetrahedron Letter* No 13, 1409 (1966).

²² B. A. Arbutov, Yu. Yu. Samitov and Z. G. Isaeva, *Dokl. Akad. Nauk. SSSR.* **150**, 1036 (1963).

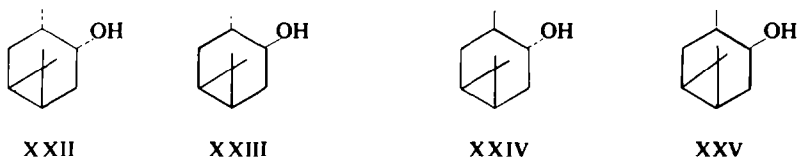
configurations such as shown by Kuczynski's and this was one of the important assumptions by which our new structural assignment to four 4-caranols was given. Consequently, the structures of the two epoxides had to be confirmed. This is the main reason why the present work was undertaken.

The results obtained in this work are summarized in Tables 3 and 4.

TABLE 4. PERCENTAGE OF ALCOHOLS OBTAINED FROM HYDROGENOLYSIS OF β -3,4-EPOXYCARANE IN THE PRÉSENCE OF RANEY NICKEL CATALYST*

Exp. No.	Additives (m.mole)	% of alcohols obtained			
		XXII	XXIII	XXIV	XXV
C-B-1	none	10.7	59.3	18.6	11.4
C-B-2	NaOH (1)	5.0	48.4	19.2	27.4
C-B-3	NaOH (2)	9.7	40.2	14.7	35.4
C-B-4	NaCl (2)	trace	55.8	0.6	43.6
C-B-5	NaBr (2)	trace	59.4	0.3	40.3
C-B-6	NaI (2)	trace	49.2	0.4	50.2

* Under the same reaction condition as in Table 3.



The main products from α - and β -3,4-epoxycaranes are respectively isocaranol (XXIV) and neo-caranol (XXIII) which definitely illustrates that the α - and β -epoxides have structures XIX and XXI respectively.

In the NMR spectrum of α -oxide (Fig. 2), there are three narrow peaks of equal

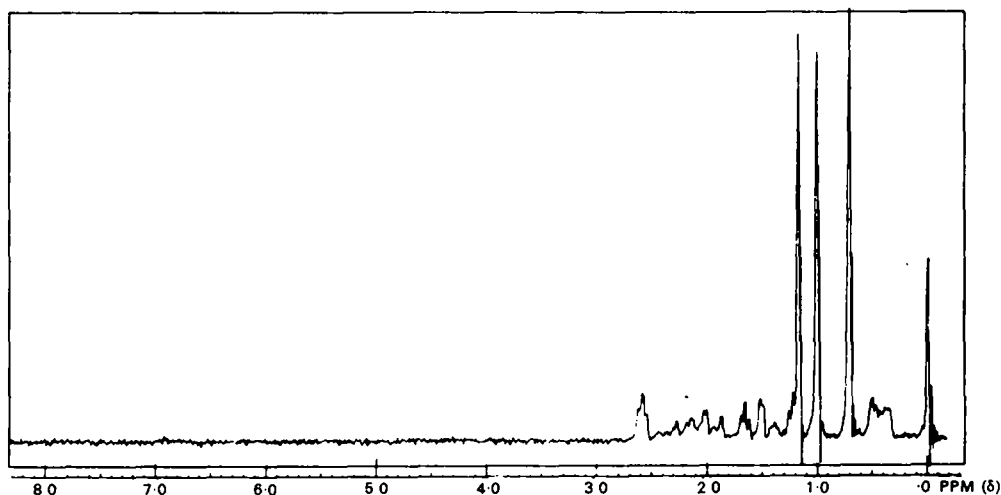


FIG. 2 NMR spectrum of α -3,4-epoxycarane in CCl_4 .

intensities in high magnetic fields (8.84, 9.00 and 9.28 in τ). The first of these peaks, with $\tau = 8.84$, arises from the resonance of the protons of the methyl group attached to the C_3 carbon of the oxide ring.²³ Regarding the hydrogens of the methyl radicals of the *gem*-dimethyl group, Arbuzov *et al.*²² gave the following explanation. One of the methyl groups comes under the diamagnetic effect of the oxide ring and therefore, the chemical shift of the protons is anomalously high and equal to $\tau = 9.28$. The hydrogens of the second methyl group are subjected to less of this influence, and their chemical shift is $\tau = 9.00$. On the other hand, a diamagnetic effect of the epoxide ring on the methyl radicals of the *gem*-dimethyl group is not apparent in the NMR spectrum of β -3,4-epoxycarane (Fig. 3). Therefore, the two methyls are

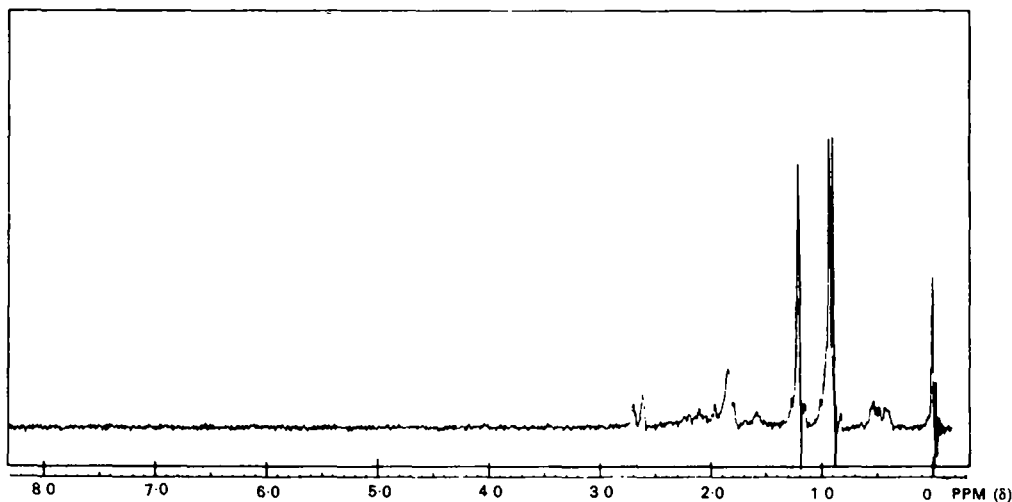


FIG. 3 NMR spectrum of β -3,4-epoxycarane in CCl_4 .

chemically equivalent, and their protons resonate at almost the same field strength (9.06 and 9.09 in τ). From these data, the Russian chemists concluded that the structure of α -oxide is XXI, whereas β -isomer should be XIX.

In the interpretation of the NMR data, we have also made an examination from the points of ring current^{24, 25} and bond-anisotropy.²⁶ Although a detailed discussion will be published in the near future, it has been indicated that the Arbuzov's explanation to the NMR spectra is not correct.

An addition of sodium hydroxide to the reaction mixture of α -3,4-epoxycarane increases the amount of the inversion product or 4-caranol (XXII). In the case of β -oxide, the influence is much more remarkable and neoiso-4-caranol (XXV) is obtained in a 35.4% distribution when 2 m.moles of sodium hydroxide is added. This phenomenon may be explained on the supposition that the epoxide with the orientated state (c) of Fig. 1 increases in number, and the outstanding influence in β -oxide appears to be caused by steric hindrance of the *gem*-dimethyl group. It is also

²³ D. S. Tarbell, R. M. Carman and D. D. Chapman, *J. Am. Chem. Soc.* **83**, 3096 (1961).

²⁴ D. J. Patel, M. E. H. Howden and J. D. Roberts, *J. Am. Chem. Soc.* **85**, 3218 (1963).

²⁵ J. J. Burke and P. C. Lanterbur, *J. Am. Chem. Soc.* **86**, 1870 (1964).

²⁶ K. Tori and K. Kitahonoki, *J. Am. Chem. Soc.* **87**, 386 (1965).

found in Table 4 that a considerable amount of the β -epoxide is hydrogenated to 4-caranol (XXII) and 4-isocaranol (XXIV) which cannot be predicted to be formed by the above-mentioned mechanism. The oxide is surely more unstable than α -isomer, because a part of the former is isomerized to 4-caranones under the same condition without hydrogen gas. Although the unexpected alcohols, XXII and XXIV should be obtained in part by hydrogenation of the 4-caranones, it is impossible to imagine that all of XXII and XXIV are prepared by such a process. The details are not yet clear.

On the anion effect, Mitsui *et al.*²⁷ reported that in the addition of NaCl, NaBr and NaI, the amount of alcohol obtained by the inversion mechanism increases in the following order: $\text{Cl}^- < \text{Br}^- < \text{I}^- \approx \text{OH}^-$. However, such a remarkable effect was not noted in the two epoxides. These differences appear to be due to the interaction between the epoxide molecules and the absorbed anions, especially the steric interaction between them. It is especially noteworthy that 4-caranol (XXII) and 4-isocaranol (XXIV) are hardly obtainable in the case of β -oxide.

We have also carried out hydrogenolysis of the epoxides in the presence of palladium catalyst but have not obtained sufficient amount of the products.

EXPERIMENTAL

Perbenzoic acid and p-nitroperbenzoic acid were prepared by the methods of Braun²⁸ and Vilkas¹², respectively.

α -Pinene oxide. α -Pinene (Wako Pure Chemical Industries) was refluxed over sodium for 1 hr and then distilled, the fraction boiling at 154–157° was collected separately; n_D^{20} 1.4671 (lit.²⁹ 1.4689), $[\alpha]_D^{28} + 45.35$ (lit.²⁹ + 40.71°). The epoxide was prepared by Ritter's method.³⁰ In a 300 ml round-bottomed flask equipped with a thermometer, condenser, mechanical stirrer and a graduated dropping funnel was placed a solution of 13.8 g (0.10 mole) of perbenzoic acid in 90 ml of chloroform. α -Pinene (12.2 g, 0.09 mole) in 30 ml of chloroform was gradually added over a period of 1 hr while keeping the reaction temperature at 0°. Agitation was continued at 0 ~ 5°. After completion of the reaction (determined iodimetrically), the reaction mixture was extracted four times with 10% sodium hydroxide solution to free it of benzoic acid and then washed three times with cold water. After drying over anhydrous sodium sulphate, the mixture was distilled under reduced pressure: yield 9.0 g (66%); b.p. 43.2 ~ 44.8° (3 mm Hg); n_D^{20} 1.4707 (lit.³⁰ 1.4709); $[\alpha]_D^{28} + 80.4^\circ$ (lit.³⁰ + 65.3°). Vapor phase chromatographic analysis showed that the product was a completely pure α -pinene oxide.

2,3-Epoxybornane. Bornylene was prepared from d- α -bromocamphor³¹ (Tokyo Kasei Kogyo Co.) and the physical properties are shown to be as follows: m.p. 111.8 ~ 113° (lit.³¹ 112 ~ 113°); $[\alpha]_D^{20} - 22.43^\circ$ (C = 3.1 in benzene) (lit.³¹ -24°). The epoxidation of bornylene was carried out by reaction with p-nitroperbenzoic acid by a slightly modified method of Vilkas.¹²

A solution of 485 mg (3.57 m.moles) of bornylene in 10 ml of chloroform was placed into a 100 ml four necked flask equipped with a stirrer, thermometer, condenser and a graduated dropping funnel. p-Nitroperbenzoic acid (883 mg; 4.28 m.moles, purity 88.8%) in 10 ml of chloroform was added over a period of 1 hr at 0°. Stirring was continued at 0° for 12 hr to complete the reaction and then was determined by iodometric titration. The excess peracid was destroyed by a slow addition of 10% sodium sulphite until a test with starch-iodide paper was negative. The mixture was then washed with a 5% cold sodium hydroxide solution and finally was washed with saturated sodium chloride. The organic layer was dried over anhydrous sodium sulphate and stripped of solvent. The residue was recrystallized from a mixed solution of

²⁷ S. Mitsui and Y. Nagahisa, *Shokubai*, **7**, 292 (1965).

²⁸ G. Braun, *Organic Syntheses Col. Vol.* 1, p. 431 (1956).

²⁹ T. Kuwata, *J. Chem. Soc. Japan (Industrial Chemistry section)*, **39**, 814 (1936).

³⁰ J. J. Ritter and K. L. Russell, *J. Am. Chem. Soc.* **58**, 291 (1936).

³¹ G. Clement, M. Vilkas, G. Dupont and R. Dulou, *C. R. Acad. Sci., Paris* **242**, 1184 (1956)

methanol and water (3:1) to give 210 mg of 2,3-epoxy bornane: m.p. $170 \sim 172^\circ$ (lit.^{1,2} $170 \sim 171^\circ$); $[\alpha]_D^{18} + 13.4^\circ$ (lit.^{1,2} $+ 10.5^\circ$).

α - and β -3,4-Epoxy-carane. Authentic samples of the epoxides which were prepared in our previous work⁵ were used. These compounds have the following physical properties: α -epoxide, b.p. $92 \sim 93^\circ$ (23 mm Hg), $n_D^{20} 1.4664$, $[\alpha]_D^{26} + 13.35^\circ$; β -epoxide, b.p. $101 \sim 103^\circ$ (36 mm Hg), $n_D^{20} 1.4690$, $[\alpha]_D^{28} - 2.36^\circ$.

Raney nickel catalyst. The catalyst was prepared from Raney nickel alloy (Koso Chemical Co.) in such a manner as to produce W4 Raney nickel.^{3,2}

General procedure of hydrogenolysis. Each of the epoxides in ethanol only, or in aqueous ethanol was hydrogenated in an autoclave under the reaction condition presented in Tables 1-4. After separation from the catalyst, the product was analysed by vapour phase chromatographic analysis using 50 m capillary Carbowax 20 M column on Hitachi KGL - 2A at 120° .

Note added in proof—Recently, Kropp^{3,3} has independently come to the same conclusion regarding the structures of α - and β -3,4-epoxycaranes

Acknowledgement—We are indebted to Professor Herbert C. Brown of Purdue University and Dr. Tsuneichi Takeshita of Hokkaido University for supplies of the authentic samples.

^{3,2} A. A. Pavlic and H. Adkins, *J. Am. Chem. Soc.* **68**, 1471 (1946).

^{3,3} P. J. Kropp, *J. Am. Chem. Soc.* **88**, 4926 (1966).