Isomerization of *d*-Limonene Oxide over Solid Acids and Bases[1]

K. ARATA, S. AKUTAGAWA,[2] AND K. TANABE[3]

Department of Chemistry, Hokkaido University of Education,
Hachiman-cho 1-2, Hakodate, Japan 040

The reaction of *d*-limonene oxide (a mixture of *cis* and *trans* forms) (I) over solid acids and bases was found to give the following products; cymene (II), 1-methyl-3-isopropenylcyclopentyl-1-carboxaldehyde (III), 1-methyl-3-isopropylidenecyclopentyl-1-carboxaldehyde (IV), carvenone (V), carvone (VI), *cis*- and *trans*-dihydrocarvone (VII), *cis*- and *trans*-exo-carveol (VIII) and *cis*- and *trans*-endo-carveol (IX). A large amount of II was formed over H_2SO_4/SiO_2, III and IV over SiO_2–Al_2O_3, V over H_2SO_4/SiO_2 and SiO_2-Al_2O_3, VII over SiO_2–Al_2O_3 and BF_3 and VIII and IX over Al_2O_3. Solid H_3PO_4 heat-treated at low temperature gave comparatively uniform yields of all the compounds. Solid $LiClO_4$ was surprisingly active for the formation of VII, but Li_3PO_4 was quite inactive. ZnO, MgO, and CaO were almost inactive. From the time variations of yields, IV and V were found to be formed by the rearrangments of III and the *cis* form of VII, respectively. The formations of carbonyl compounds (III and VII) and cymene (II) were explained by the isomerization over strong acid sites, while the allyl alcohol formation (VIII and IX) by an acid-base bifunctional mechanism over Al_2O_3.

INTRODUCTION

Occasional reports have appeared on the rearrangement of limonene oxide to the corresponding allylic alcohols or ketones *(1–4)*. Alumina at 310–325° and glacial acetic acid containing 1% of sulfuric acid were reported to isomerize the oxide to a mixture of dihydrocarvone and carvenone by Royals and Harrell *(1)*. Similar isomerizations accompanied by ring contraction were reported to occur in the presence of Lewis acid (ZnBr₂) by Settine *et al.* *(2)*. Along the same line, Nigam and Levi *(3)* reported that the oxide upon chromatography on active alumina yielded α,β-unsaturated alcohols together with some by-products, and the isomerization catalyzed by aluminum isopropoxide was found by Eschinasi *(4)* to provide a selective method of preparing allylic alcohols in high yields.

We have recently studied the isomerization of 1-methylcyclohexene oxide catalyzed by solid acids and bases and observed the strikingly different selectivities: Ketone was formed predominantly over SiO_2–Al_2O_3, solid H_3PO_4, and $LiClO_4$, while allyl alcohols were formed predominantly over Al_2O_3, TiO_2, and TiO_2–ZrO_2 *(5)*. Since only alumina among solid acids and bases has been investigated for the isomerization of *d*-limonene oxide, we examined the activity as well as the selectivity of several solid acids and bases for the isomerization reaction of *d*-limonene oxide.

EXPERIMENTAL

Materials

d-Limonene oxide (a mixture of *cis* and *trans* forms, 1:1) was more than 97% pure

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and toluene, a guaranteed reagent, used as a solvent was redistilled over sodium metal.

Aluminum oxide (KAT6 of Nishio Chemical Co.) and SiO–Al$_2$O$_3$ [N631(L) (Al$_2$O$_3$; 15 wt %) of Nikki Chemical Co.] were calcined at 500°C. The H$_2$SO$_4$/SiO$_2$ was prepared as follows. Ten grams of granular silica gel (White, Kanto Chemical Co.) was immersed in 12 ml of 1 N H$_2$SO$_4$, evaporated, dried, and then calcined at 150°C. Solid H$_3$PO$_4$, N501 of Nikki Chemical Co., was dried at 200°C for 1–2 hr, powdered below 100 mesh, and then calcined at various temperatures. Zinc oxide was prepared by the hydrolysis of zinc nitrate with 28% ammonia water, followed by the washing of the precipitate, drying at 110°C for 14 hr, and calcining at 400°C. Lithium perchlorate and Li$_3$PO$_4$ were prepared by drying LiClO$_4$·3H$_2$O and Li$_3$PO$_4$ at 120°C for 3 days. Magnesium oxide and CaO were prepared by calcining their hydroxides at 500°C. All the catalysts were calcined in pyrex glass tubes (quartz tubes for solid H$_3$PO$_4$ calcined at 900°C) in air for 3 hr and sealed to store until use.

Standard Procedure for Reaction

In general, the reaction was carried out in the presence of toluene as a solvent at 108°C for 75 min. A mixture of 1 ml of the epoxide, 5 ml of toluene, and about 0.3 g of catalyst, ground to below 100 mesh, was stirred in a reaction vessel by a magnetic stirrer. At appropriate time intervals, a small amount of the sample was taken out by a 1 ml syringe, separated from catalyst, and analyzed by gas chromatograph with a hydrogen flame detector using a 3 m column of 20% polyethylene glycol 20 M on Celite 545 SK (150°C; N$_2$ 0.9 Kg/cm^2). The yields of products were calculated by measurement of GLC peak areas (uncorrected).

In the experiment where BF$_3$-etherate was used as a catalyst, 0.3 ml of the catalyst was added into a mixture containing 0.5 ml

of the epoxide and 2.5 ml of toluene at 0°C and the reaction was continued for 30 min. The reaction mixture was quenched with water, and the organic layer was separated, washed with saturated sodium bicarbonate solution and water, and dried.

Identification of Products

Most of the reaction products, which are cymene (II), carvone (VI), *cis*- and *trans*-dihydrocarvone (VI), *cis*- and *trans*-exo-carveol (VIII), and *cis*- and *trans*-endo-carveol (IX), were identified by GLC comparison with the authentic samples.

For the identification of carvenone (V), limonene epoxide (2 g) dissolved in 20 ml of 85% formic acid was stirred with conc. H$_2$SO$_4$ (20 mg) at room temperature for 5 hr. The reaction mixture was poured into a large amount of water, then extracted with ether to give compound V (1.1 g): bp 75–78/1.5 mm Hg [lit. (*6*) bp 77–79°/2 mm Hg]; ir (neat): 1740 cm^{-1} α,β-unsaturated ketone; NMR (δ): 5.1 (s, 1H, C=CH), 0.9 ppm (d, 9H, –CH$_3$). This sample showed the peak of compound V in GLC.

About 40 mg of compound III was obtained by using a preparative column (200 × 0.6 cm, packed with 20% PEG 20 M on Celite 545 SK of 60–80 mesh) and identified by its ir and NMR spectra: ir (neat): 1730 cm^{-1} carbonyl, 1650, 885 cm^{-1} C=CH$_2$; NMR (δ): 9.4 (s, 1H, CHO), 4.7 (s, 2H, C=CH$_2$),
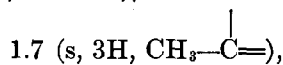
$$1.7 \ (s, \ 3H, \ CH_3{-}\overset{|}{C}\!\!=\!),$$

1,2 ppm (s, 3H, CH$_3$–).

Compound IV was obtained as the case of III and identified by its ir and NMR spectra: ir (neat): 1730 cm^{-1} carbonyl; NMR (δ): 9.4 (s, 1H, CHO),

$$1.6 \ (s, \ 6H, \ CH_3{-}\overset{\|}{C}{-}CH_3),$$
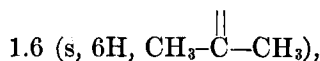
1.1 ppm (s, 3H, CH$_3$–).

RESULTS AND DISCUSSION

The reaction of *d*-limonene oxide (*cis* and *trans* in a 1:1 ratio) (I) catalyzed by solid acids and bases gave the following products: cymene (II), 1-methyl-3-isopropenylcyclopentyl-1-carboxaldehyde (III), 1-methyl-3-isopropylidenecyclopentyl-1-carboxaldehyde (IV), carvenone (V), carvone (VI), *cis*- and *trans*-dihydrocarvone (VII), *cis*- and *trans*-exocarveol (VIII) and *cis*- and *trans*-endocarveol (IX).
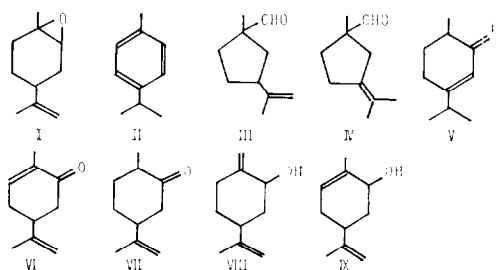
The catalytic activity and selectivity of several solid acids and bases in 75 min at 108°C are shown in Table 1. The products were divided into several categories, cymene (II), ring-contracted aldehydes (III and IV), ketone (V) formed by the isomerization of (VII), ketones (VII), and allyl alcohols (VIII and IX). A large amount of II was formed over H_2SO_4/SiO_2, III and IV over SiO_2–Al_2O_3, V over H_2SO_4/SiO_2, and SiO_2–Al_2O_3, VII over SiO_2–Al_2O_3, BF_3 and $LiClO_4$ and VIII and IX over Al_2O_3. Solid H_3PO_4 heat-treated at low temperature gave comparatively uniform yields of all the compounds, though ketone was relatively predominant. It is especially interesting that SiO_2–Al_2O_3, BF_3-etherate and $LiClO_4$ formed at least 80% of carbonyl compounds, whereas Al_2O_3 gave more than 80% of allyl alcohols when reacted at 80°.

The total yields of *trans* and *cis* VII, VIII, and IX were estimated to be 54.5 and 37.9% for BF_3, 47.0 and 26.7 for Al_2O_3 at 108°, and 45.8 and 29.8 for $LiClO_4$, respectively. Since the reactant consists

of the same amount of *trans* and *cis* forms, it is considered that II–V have a tendency to be primarily formed from the *cis* form. However, with SiO_2–Al_2O_3 and solid H_3PO_4 the opposite tendency was observed. This is probably due to strong acid sites on the SiO_2–Al_2O_3 surface (7) or to a large number of Brönsted acid sites on solid H_3PO_4 (8).

The relation of the product distribution vs reaction time is shown in Fig. 1, where the reaction was carried out over SiO_2–Al_2O_3 at 108°. The yield of V remarkably increased with the large decrease of the *cis* form of VII, together with the slight decrease of *trans*-dihydrocarvone during the course of reaction. This suggests the preferential isomerization of the *cis* form to V over the catalyst. Group IV is supposed to be formed by the rearrangement of III in view of mechanistic considerations. The time variations of both products imply the above possibility, although those variations are not enough to verify this conclusion, probably owing to the very high reaction temperature.

Another time variation of the products over SiO–Al_2O_3 at a lower temperature, 80°, is shown in Fig. 2. The remarkable increase of IV and decrease of III were observed at the reaction temperature, though the rearrangement of ketone to V
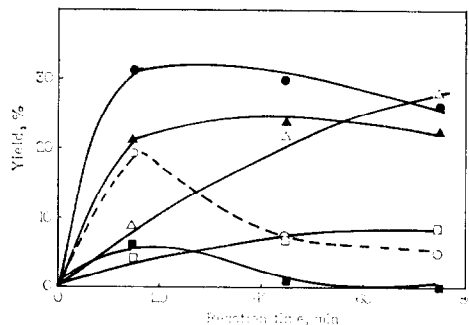

FIG. 1. Isomerization of *d*-limonene oxide over SiO_2–Al_2O_3 at 108°C. VII: *trans* (—●—); *cis* (−−○−−), V (—△—), IV (—▲—), III (—■—), II (—□—).

TABLE 1

CATALYTIC ACTIVITY AND SELECTIVITY FOR ISOMERIZATION OF d-LIMONENE OXIDE AT 108°C FOR 75 min

Catalysts	Catalyst amount (g)	Conversion (%)	Products (%)[a]										
			II	III	IV	V	VI	VII Trans	VII Cis	VIII Trans	VIII Cis	IX Trans	IX Cis
Solid H$_3$PO$_4$													
200°C	0.378	93.9	19.0	5.9	4.2	11.9		18.2	8.1	5.0	2.0	2.8	1.5
300°C	0.458	85.2	12.0	10.1	2.2	6.3		14.3	12.1	6.7	2.9	5.2	2.8
900°C	0.409	25.4						6.5	2.6	5.1	1.3	6.5	1.4
H$_2$SO$_4$/SiO$_2$[b]	0.481	100.0	35.4			61.8		0.3	5.3				
SiO$_2$-Al$_2$O$_3$	0.260	100.0	9.2		22.5	28.3		26.3	23.9				
SiO$_2$-Al$_2$O$_3$[c,d]	0.298	100.0	3.8	12.3	14.9	5.1		22.8	24.5	5.1	13.4		
BF$_3$·ether	0.3 (ml)	100.0		5.4	0.9			52.0	5.0	2.2	17.8		
Al$_2$O$_3$	0.479	96.8	1.8	14.3			2.7	9.0	0.7	32.2	10.4	6.8	3.9
Al$_2$O$_3$[d]	0.435	49.3						2.6	0.4	26.0		5.2	1.8
ZnO	0.284	4.4						0.9				0.8	
LiClO$_4$[e]	0.431	100.0	2.0	4.3	1.8	8.7		45.8	29.8	0.7			
Li$_3$PO$_4$	0.505	1.2											
MgO	0.237	1.3											
CaO	0.258	1.3											

[a] See text.
[b] The reaction was complete 98% in 25 min.
[c] The reaction was carried out at 80°C.
[d] The reaction was complete 100% in 15 min.
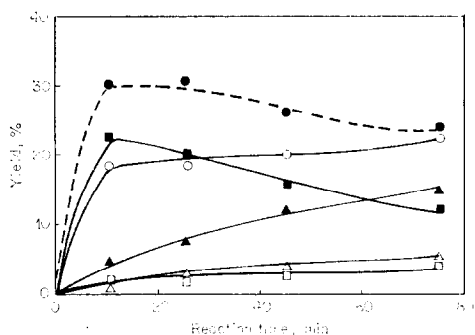[e] The reaction was complete 100% in 10 min.

FIG. 2. Isomerization of d-limonene oxide over $SiO_2-Al_2O_3$ at 80°. VII: trans (—O—); cis (--●--), V (--△--), IV (—▲—), III (—■—), II (—□—).

was quite slow. The figure suggests the slow isomeric conversion of cis to trans in ketones.

It is of interest that the isomerization occurs to form a compound containing an exo-double bond in a 5-membered ring and one with an endo-double bond in a 6-membered ring. This is considered to be due to their stabilities. Brown et al. (9, 10) have reported that exo-double bonds stabilize a 5-ring and destabilize a 6-ring and made the generalization that reactions proceed in such a manner as to favor the formation or retention of an exo double bond in a 5-ring and to avoid the formation or retention of an exo double bond in a 6-ring. The above rule is also supported by the result that the reactivity for enolization of cycloalkanones in hydrochloric acid–90% acetic acid as a function of ring size is 6 > 8 > 5 > 7 > 4, and the reactivity order being interpreted in terms of the differences in steric requirements for conversion of the ketones to transition states having endocyclic unsaturated character that is highly developed (11).

From the product distribution over solid H_3PO_4, H_2SO_4/SiO_2, and $SiO_2-Al_2O_3$, it is supposed that the double-bond migration was catalyzed by Brönsted acids. The formation of a very large amount of carvenone over H_2SO_4/SiO_2 suggests this

conclusion. There is also a report of the limonene oxide rearrangement into 35% carvenone, 16% dihydrocarvone and 10% cymene with $CH_3COOH–1\%$ H_2SO_4 at 16° for 8 hr (1). Thus, the reaction mechanisms for the preferential formation of carbonyl compounds and the isomerization are illustrated as follows.
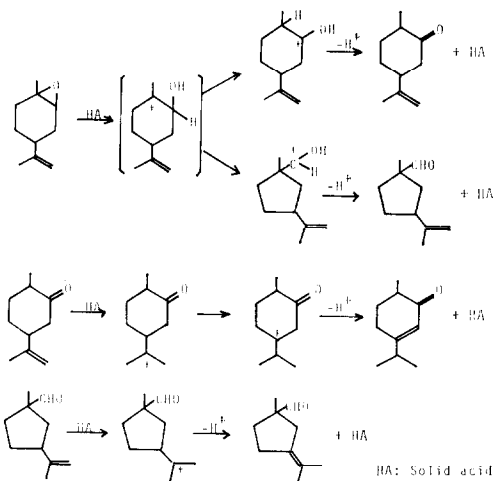
By analogy of the above mechanism, the cymene formation is also interpreted as a Brönsted acid-catalyzed dehydration of the reactant with a subsequent shift of double bond of the isopropenyl group to the 6-ring.
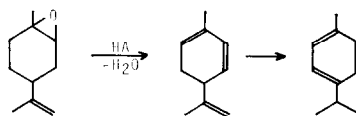
The catalytic activities of solid H_3PO_4 calcined at various temperatures correlate well with their acidities, determined by the titration method with n-butylamine using Hammett indicators, which are 4.5 mmol/g for 250°C, 1.6 for 400, and 0.4 for 980, between pKa = 1.5 and −5.6 (8). Since the acid strength of ZnO has been observed to be weaker than pKa = 1.5; that is, 1.81 mmol/g at pKa = 4.8, 0.52 at 3.3, 0.22 at 1.5, and 0.0 at −3.0 (12), and a quite low activity was shown over the

ZnO catalyst in the present work, this isomerization is concluded to proceed on the acidic sites stronger than pKa = 1.5.

Boron trifluoride, which is a typical Lewis acid catalyst, showed a similar selectivity for the formation of ketones to those of AlCl$_3$ and BBr$_3$ for the formation of ketones from 1-methylcyclohexene oxide (5a). Several authors have reported the ketone formation from epoxides with various Lewis acid catalysts. For example, from p-menthene and d-limonene oxides with ZnBr$_2$ (2), 3-carene oxide with ZnBr$_2$ (13–15), 2,3-butene oxide with BF$_3$-etherate (16), and 2,10-oxido-10β-pinane with BF$_3$-etherate (17). Our observations are in agreement with these results.

The remarkable activity of Al$_2$O$_3$ for the allyl alcohol formation was quite similar to Nigam and Levi's results (3), where limonene and α-pinene oxides upon chromatography on active alumina isomerized to the corresponding α,β-unsaturated alcohols, the yields being increased in order of acidic < neutral < basic alumina. The time variation of the products at 80° reaction temperature is shown in Fig. 3. The overall reaction followed first-order reaction kinetics with respect to the oxide concentration. The yields of all the alcohols increased almost parallel to each other during the course of reaction, indicating no isomerization between the products as observed in the case of SiO$_2$–Al$_2$O$_3$. It can also be seen that trans exceeded cis at all times. Alumina is known to have intrinsic basic sites as well as acid sites of Lewis type, and to act as an acid-base bifunctional catalyst (18). The reaction described above can be rationalized in terms of this character of Al$_2$O$_3$. Thus, epoxide opening to an allylic alcohol can be visualized as follows.
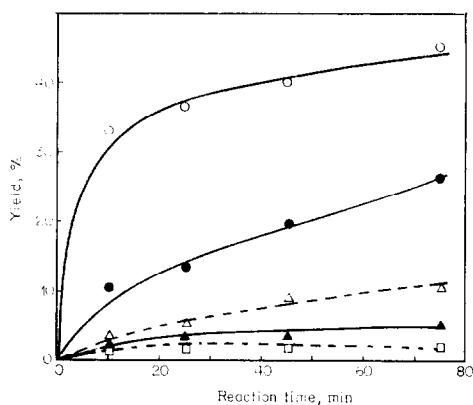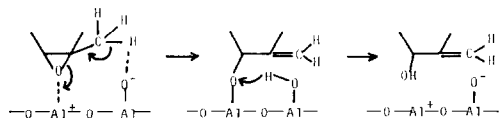

FIG. 3. Isomerization of d-limonene oxide over Al$_2$O$_3$ at 80°. Total conversion (—O—), VIII: trans (—●—); cis (--△--), IX: trans (—▲—); cis (--□--).

In allyl alcohol formation, VIII surpassed IX. This seems to be caused by the competition between primary and secondary proton abstraction. The preference for primary proton abstraction is due to the more enhanced acidity of primary hydrogen by electronic effects. Similar observations for limonene oxide were reported by Eschinasi, in which the reaction catalyzed by aluminum isopropoxide gave 76% of VIII and 24% of IX (4).

Solid lithium perchlorate was surprisingly active for the formation of ketone, but lithium phosphate was quite inactive. These results are very similar to those in the case of 1-methylcyclohexene oxide, in which other metal perchlorates and lithium salts in addition to lithium phosphate were almost inactive (5a). Since the partial dissolution of the catalyst or its complex with the epoxide was observed, the ketone formation can be interpreted by a process that allows the development of a planar carbonium ion at the cleaved tertiary center, as already shown in the case of 1-methylcyclohexene oxide (5a).
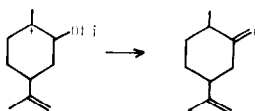
Magnesium and calcium oxides calcined in air, which have basic character (*19*, *20*), were almost inactive for this reaction. Since lithium dialkyl amide, a basic catalyst, have been used for the rearrangement of various epoxides (*21*, *22*), the basic strength of these oxides might not be enough to cause reaction. However, MgO was active for the isomerization of propylene oxide at 260–270°C in the gas phase (*23*). Experiments at more severe conditions are being planned.

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