Base-Catalyzed Isomerization of Vinylcyclohexene and Dipentene[1]

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The base-catalyzed isomerization of 4-vinylcyclohexene and dipentene have been examined in the system potassium *t*-butoxide–dimethyl sulfoxide. At 55° the rate constant for the isomerization of 4-vinylcyclohexene is 2.97×10^{-4} sec^{-1}. The principal products of the isomerization are *cis*- and *trans*-3-ethylidenecyclohexene. At 55° the first-order rate constant for the isomerization of dipentene is 4.5×10^{-6} sec^{-1}. The principal products of the isomerization are a mixture of α-terpinene, *p*-mentha-2,4(8)-diene, and γ-terpinene in the ratio of 5:3:1. Procedures are given for obtaining large quantities of pure *cis*- and *trans*-3-ethylidenecyclohexene and *p*-mentha-2,4(8)-diene.

For some time we have been interested in the base-catalyzed isomerization of olefins in homogeneous media.[4] To date considerable information about the role of olefin structure,[4a,c,d] base,[4b] and solvent[4c] has been reported. With regard to mechanistic considerations, in sum, structural effects[4d] isotopic effects,[4d] and studies with related reactions[4d] have led us to depict a tightly bound allylic ion pair as the reactive intermediate.

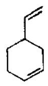
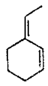
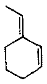
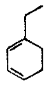
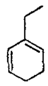
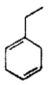
The study of the facile prototropic shift in simple olefins is made possible mostly by the application of dipolar, aprotic solvents, such as dimethyl sulfoxide, together with strong bases, such as potassium *t*-butoxide. In the main, previous studies have focused attention on the factors influencing the reaction profile. At the same time, the marked ease of double bond migration in these base solvent systems readily lend themselves to preparative reactions. This paper describes an investigation of the base-catalyzed isomerization of two readily available alicyclic olefins, namely 4-vinylcyclohexene and dipentene.

The compounds, 4-vinylcylohexene and dipentene, are readily available by Diels–Alder dimerization of butadiene[5] and isoprene,[6] respectively. They have a cyclic double bond as well as a side-chain double bond. Isomerization of these nonconjugated diolefins using acid catalysts or metals is characterized by low recovery, poor selectivity, skeletal rearrangements, and polymerization.[7] At elevated temperatures, dipentene is isomerized over a promoted sodium catalyst.[8] In contrast, homogeneous base-catalyaed isomerization is both mild and selective. We have found it possible to isomerize stepwise and obtain in good yield diolefins which could be interesting intermediates for other reactions.

Isomerization of 4-Vinylcyclohexene.—At 55° 4-vinylcyclohexene is rapidly isomerized in a 0.7 *M* solution of potassium *t*-butoxide in dimethyl sulfoxide. The first-order rate constant is 2.97×10^{-4} sec^{-1} with $\Delta H^* = 19.5$ kcal/mole and $\Delta S^* = -15.5$ eu. The principal products of the isomerization as determined by gas chromatography, nmr, and ultraviolet and infrared spectroscopy are *cis*- (**1**) and *trans*-3-ethylidenecyclohexenes (**2**). Table I records the product composition after 50 min. Inspection of Table I suggests that the procedure could be used to obtain the isomeric ethylidenecyclohexenes since they are considerably higher boiling than the other isomers. And indeed distillation of a large-scale isomerization reaction mixture afforded a 40% yield of 99% pure *cis*- and *trans*-3-ethylidenecyclohexene.

TABLE I

BASE-CATALYZED ISOMERIZATION OF VINYLCYCLOHEXENE[a]

Compd	Mole %
	40.0
 1  2	51.0
	4.7
	1.9
	2.4

[a] Using potassium *t*-butoxide in dimethyl sulfoxide (0.7 *M*) at 55°.

More severe reaction conditions lead to a disproportionation reaction. With increased time or temperature or the use of the more potent isomerizing system, lithium dimethylamide in hexamethylphosphoramide (HMPA), ethylbenzene and ethylcyclohexene are formed at the expense of the 3-ethylidenecyclohexenes. Evidently a base-catalyzed disproportionation similar to that observed for cyclohexadiene is operative.[9] Quite likely, the disproportionation proceeds from the more slowly formed conjugated cyclic diolefin since

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[4] (a) S. Bank, C. A. Rowe, Jr., A. Schriesheim, and L. A. Naslund, *J. Am. Chem. Soc.*, **89**, 6897 (1967); (b) S. Bank, C. A. Rowe, Jr., A. Schriesheim, and L. A. Naslund, Abstracts, 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966, p U38; (c) S. Bank, A. Schriesheim, and C. A. Rowe, Jr., *J. Am. Chem. Soc.*, **87**, 3244 (1965); (d) S. Bank, A. Schriesheim, and C. A. Rowe, Jr., *ibid.*, **85**, 2115 (1963), and other papers in the series.

[5] D. J. Cram and G. S. Hammond, "Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1964, p 413.

[6] L. F. Fieser and M. Fieser, "Organic Chemistry," 2nd ed, D. C. Heath and Co., Boston, Mass., 1950, p 1009.

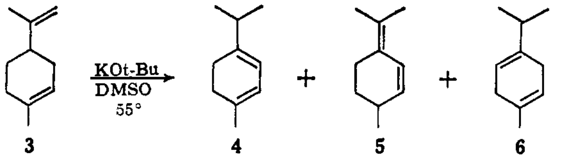
[7] (a) G. Egloff, G. Hulla, and V. I. Kamarewsky, "Isomerization of Pure Hydrocarbons," Reinhold Publishing Corp., New York, N. Y., 1942, p 128 ff; (b) Y. M. Slobodin, *J. Gen. Chem. USSR*, **6**, 129 (1936).

[8] H. Pines and H. E. Eschinazi, *J. Am. Chem. Soc.*, **77**, 6314 (1955).

[9] J. E. Hofmann, P. A. Argabright, and A. Schriesheim, *Tetrahedron Letters*, 1005 (1964).

these diolefins are found only in the initial periods of the reaction.

Isomerization of Dipentene.—Base-catalyzed isomerization of dipentene (**3**), using potassium *t*-butoxide in dimethyl sulfoxide, compared to 4-vinylcyclohexene, is considerably slower; the pseudo-first-order rate constant at 55° is 4.5×10^{-6} sec^{-1}. The initial products of the isomerization are a 5:3:1 mixture of α-terpinene (**4**) *p*-mentha-2,4(8)-diene (**5**), and γ-terpinene (**6**) (eq 1); these identifications are discussed in the Experimental Section. The product diolefins are readily interconverted; isomerization of α-terpinene or *p*-mentha-2,4(8)-diene under the same conditions as the isomerization of dipentene gives the same 5:3:1 mixture in 30 min. Evidently the slow step in the isomerization is conversion to an isopropylidene group.



(1)

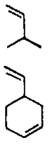
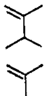
The mixture of isomers is a pseudoe-quilibrium since with increased time or temperature *p*-cymene and *p*-menthene are formed at the expense of these isomers. Interestingly, use of the more powerful isomerizing medium lithium dimethylamide in HMPA at room temperature affords only unreacted dipentene and an equimolar mixture of *p*-cymene and *p*-menthene.

Of synthetic interest, distillation of the reaction mixture afforded an 11% yield of pure *p*-mentha-2,4(8)-diene, the highest boiling isomer. Since the other diolefins could be isomerized easily to the 5:3:1 mixture and recycled, this method affords a convenient means of preparing large-scale quantities of this unusual diolefin in pure form.

Finally, some comment on the marked inertness of the dipentene isomerization is in order. For this purpose, Table II records the relative rates of cyclic and acyclic olefins with similar alkyl substitution. Inspection of Table II reveals that the isomerization of dipentene is comparable to that of 2,3-dimethylbutene and therefore is not unusually slow. Essentially the relative rates are governed by steric factors; the decrease in rate with increasing steric requirements has been both observed and discussed previously.[4d]

Table II

Base-Catalyzed Isomerization of Acyclic and Cyclic Olefins

Compd	Rel rate[a]
	1.0[b]
	0.24[c]
	0.45[d]
	0.007[c]
	0.005[d]

[a] At 55° using KO-*t*-Bu in DMSO. [b] $k = 8.4 \times 10^{-4}$ sec^{-1} per hydrogen.[4d] [c] Reference 4d. [d] This work.

Experimental Section

Potassium *t*-butoxide was obtained from the Mine Safety Appliance Company. Analysis showed it to be greater than 98.5% pure with K_2CO_3 as the major impurity. Dimethyl sulfoxide (Matheson Coleman and Bell Spectroquality) was distilled from 13 X Molecular Sieves. 4-Vinylcyclohexene was obtained from the Enjay Chemical Company. Dipentene and α-terpinene were obtained from the Hercules Powder Company.

Infrared spectra were taken on a Perkin-Elmer Model 521 spectrophotometer. A Cary 14 spectrometer was employed to record the ultraviolet absorption spectra and a Varian A-60 spectrometer was employed to record the nmr spectra.

Isomerization of 4-Vinylcyclohexene.—Solutions of potassium *t*-butoxide in dimethyl sulfoxide (DMSO) and in hexamethylphosphoramide (HMPA) were used as the isomerizing media. For the rate studies prethermostated quantities of 4-vinylcyclohexene were injected into rubber, serum, capped vials containing the base and solvent at the desired temperature. The concentrations of base and olefin were 0.7 and 0.4 *M*, respectively. Samples were withdrawn at intervals and quenched in 5.0 cc of ice water containing 0.5 cc of pentane. The pentane extract was analyzed by gas chromatography. Adequate separation of the isomers was obtained on a Model 609 F & M gas chromatograph equipped with a 6-ft column containing silver nitrate on glycol[10] at 30° and having helium flow rates of 40–50 cc/min.

First-order rate constants were obtained from the plot of the log of the concentration of 4-vinylcyclohexene remaining (internal standard) *vs.* time. The principal products of the isomerization were *cis*- and *trans*-3-ethylidenecyclohexene[7b] as established in the following manner. A large-scale isomerization mixture was quenched with water after eight half-lives. After extraction with ether, drying, and removal of solvent, the material was distilled. A fraction was obtained, 225 g, bp 148–148.5° (760 mm), which exhibited only two peaks on gas chromatographic analysis in the ratio of 59.5:39.5. Elution chromatography of this mixture on a silver nitrate on silica gel column separated these materials. Elution with 95:5 pentane–benzene afforded a sample of largely (>90%) one isomer. The compound exhibited a strong band at 952 cm^{-1} in the infrared and an ultraviolet absorption maximum at 237 mμ (ε 17,400) characteristic of a semicyclic conjugated diolefin.[11] The nmr spectrum had signals (measured in parts per million from TMS in carbon tetrachloride) at δ 6.4, d (1 H); 5.5–6.0, m (1 H); 5.2, q (*J* = 7 cps, 1 H); 1.75–2.45, m (6 H); 1.6, d (*J* = 7 cps, 3 H).

Elution with ether afforded largely the other isomer (>90%) which had an infrared band at 680 cm^{-1} and an ultraviolet absorption band envelope with peaks at 229 mμ (ε 15,600) and 235 mμ (ε 15,100) with a shoulder at 243 mμ. The nmr spectrum was similar to that of the previous compound. As expected the physical properties of the isomers are similar. Unfortunately, they are so similar that they do not permit an unequivocal identification. We suggest that the isomer that is eluted first is *trans*-3-ethylidenecyclohexene based on the extinction coefficients in the ultraviolet absorption. We expect the *cis* form to have a lower extinction coefficient due to greater steric hindrance. The infrared band at 952 cm^{-1} is consistent with the assignment but does not prove it since correlations for this type of olefin are largely unexplored.

The remaining minor products, 1-ethyl-1,3-cyclohexadiene, 2-ethyl-1,3-cyclohexadiene, and 1-ethyl-1,4-cyclohexadiene were isolated by preparative gas chromatography and identified by nmr spectroscopy. The nmr spectrum of 1-ethyl-1,3-cyclohexadiene had signals (measured in parts per million from external TMS) at δ 5.15–5.80, m (3 H); 1.5–2.0 m (6 H); 0.7, t (*J* = 7 cps, 3 H). The nmr spectrum of 2-ethyl-1,3-cyclohexadiene had signals (measured in parts per million from external TMS) at δ 5.4–5.6, m (2 H); 5.1–5.3, m (1 H); 1.45–2.0, m (6 H); 0.7, t (*J* = 7 cps, 3 H). The nmr spectrum of 1-ethyl-1,4-cyclohexadiene had signals (measured in parts per million from external TMS) at δ 5.6–5.75, m (2 H); 5.25–5.50, m (1 H); 2.5–2.8, broad s (4 H); 2.0, q (*J* = 7 cps, 2 H); 1.05, t (*J* = 7 cps, 3 H).

Preparation of *cis*- and *trans*-3-Ethylidenecyclohexene.—In a 2-l. autoclave, 1 l. of 0.7 *M* potassium *t*-butoxide in DMSO was allowed to react with 166 g (1.53 moles) of 4-vinylcyclo-

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[10] J. Shabtai, J. Herling, and E. Gil-Av, *J. Chromatog.*, **1**, 406 (1959).

[11] J. P. Phillips, "Spectra-Structure Correlation," Academic Press Inc., New York, N. Y., 1964, p 42.

hexene at 100° for 75 hr. Analysis by gas chromatography revealed 1% 4-vinylcyclohexene and 83% *cis*- and *trans*-3-ethylidenecyclohexene. The reaction mixture was quenched in water and extracted with ether. After drying of the combined ether extracts with magnesium sulfate and filtration, the ether was removed. Fractional distillation of the remaining material on a 40-plate Podbielniak column under nitrogen at 760 mm afforded 66 g (0.3 mole, 40% yield) of *cis*- and *trans*-3-ethylidenecyclohexene (bp 146–148°). Analysis by gas chromatography revealed that the purity was 99.0%.

Isomerization of Dipentene.—Analogous procedures were used for the rate studies of the base-catalyzed isomerization of dipentene. Analyses were performed by gas chromatography on a 10-ft Carbowax 20 M column at 125° and a 6-ft silver nitrate column at 50°. The three main products of the isomerization were identified in the following manner. Large samples of the reaction mixture were injected on a 12-ft Carbowax 20 M on Chromosorb P column at 125° and under these conditions good separation of the three main peaks was obtained. The three fractions (A, B, and C in increasing retention time) were collected in Dry Ice–acetone cooled traps and were checked for purity *via* analytical glpc on a 6-ft silver nitrate column at 50°.

Fraction A with the shortest retention time, *p*-mentha-2,4(8)-diene, had an infrared spectrum identical withth at reported for this compound.[12] The molecular weight as determined by mass spectrometry was 136. The ultraviolet absorption spectrum had a maximum at 246 mμ (ϵ 17,800). The nmr spectrum exhibited peaks (measured in parts per million from TMS in carbon tetrachloride) at δ 6.20–6.48, m (1 H); 5.3–5.6, m (1 H); 1.6–2.8, m (4 H); 1.70, s (6 H); 1.1–1.6, m (1 H); 1.0, d (3 H).

Fraction B with the next longest retention time, α-terpinene, had an infrared spectrum in agreement with that reported for this compound.[13] The molecular weight determined by mass spectrometry was 136. The compound exhibited an ultraviolet absorption maximum at 265 mμ (ϵ 9100). The nmr spectrum exhibited peaks (measured in parts per million from TMS in carbon tetrachloride) at δ 5.2–5.8, m (2 H); 1.8–2.5, m (1 H); 2.02, s (4 H); 1.72, s (3 H); 1.0, d (6 H).

Fraction C with the longest retention time, γ-terpinene, had an infrared spectrum that agreed with the reported spectrum for this compound.[13] The molecular weight determined by mass spectrometry was 136. The ultraviolet absorption spectrum had a maximum at 235 mμ (ϵ 3950). The nmr spectrum exhibited peaks (measured in parts per million from TMS in carbon tetrachloride) at δ 5.2–5.5, m (2 H); 2.55, s (4 H); 1.62, s (3 H); 1.6–2.2, m (1 H); 1.0, d (6 H). Some *p*-cymene and a conjugated diene was present in this fraction. The ultraviolet absorption is probably due to this latter contaminant.

Preparation of *p*-Mentha-2,4(8)-diene.—In a 3-l. flask under nitrogen, 2000 cc of dimethyl sulfoxide, 156.8 g (1.4 moles) of potassium *t*-butoxide, and 463 g (3.47 moles) of dipentene were stirred at 100° for 96 hr. The reaction mixture was quenched with water and extracted three times with *n*-pentane. The combined *n*-pentane extracts were dried (magnesium sulfate) and filtered. After evaporation of the pentane, analysis by gas chromatography showed 23.4% dipentene remaining. The material was distilled and 50.5 g (0.37 mole, 11%) of *p*-mentha-2,4(8)-diene, bp 188–193° (760 mm) (lit.[8] bp 188–189° (760 mm)), was collected. Analysis by gas chromatography on a 6-ft silver nitrate column established the purity of this material as greater than 99%.

Registry No.—Vinylcyclohexene, 100-40-3; **1**, 15094-05-0; **2**, 15094-06-1; **3**, 138-86-3; **4**, 99-86-5; **5**, 586-63-0; **6**, 99-85-4.

Acknowledgment.—The authors wish to thank Dr. Boyd M. Hudson for his nmr measurements and interpretations.

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(12) "The Sadtler Standard Spectra Catalog," Vol. XII, Midget ed, Sadtler Research Laboratories, Philadelphia, Pa., 1965, compound no. 12962.

(13) H. Westaway and J. F. Williams, *J. Appl. Chem.* (London), **9**, 443 (1959).

The Reaction of Hindered Phenols with Diazomethane

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The reaction of 2,6-di-*t*-butyl-4-nitrophenol with diazomethane yields the nitronic ester exclusively, whereas 2,6-diisopropyl-4-nitrophenol reacts with diazomethane to give a mixture of the nitronic ester and the corresponding anisole. The reaction of 10-nitro-9-anthrone with diazomethane gives the monoxime of anthraquinone and formaldehyde. Silation of 2,6-di-*t*-butyl-4-nitrophenol with bis(trimethylsilyl)acetamide gives an unstable nitronic ester which rearranges to the trimethylsilyl ether.

The methylation of hindered acids to give methyl esters is well known, but the methylation of hindered phenols does not seem to have been widely investigated. Examination of the literature failed to reveal that the methylation of picric acid, 2,4,6-tribromophenol, pentabromophenol, mesitol, or 2,4,6-triiodophenol with diazomethane had ever been attempted. In this reaction of a phenol, the oxygen atom which is methylated is attached to the aromatic ring, whereas in a hindered acid such as mesitoic acid the alkylated oxygen atom is separated from the ring by a carbon atom. Thus the hindered phenols should show greater sensitivity toward alkylation.

2,4,6-Tribromophenol, pentabromophenol, and 2,4,6-triiodophenol liberated nitrogen vigorously with diazomethane and each gave the corresponding anisole.

The next hindered phenol to be considered was 2,6-di-*t*-butylphenol, which has been shown to be so hindered that in excess it can react with only two of the hydrogen atoms in lithium aluminum hydride.[2] In addition, this phenol, unlike triiodophenol, is insoluble in sodium hydroxide. This presumably is due to the fact that the removal of a proton gives an anion which is too hindered for solvation to be an aid to solution.

Treatment of 2,6-di-*t*-butylphenol with diazomethane in ether failed to give the immediate nitrogen evolution shown by the more acidic phenols, so 2,6-di-*t*-butyl-4-nitrophenol, I, was prepared. This compound is soluble in sodium hydroxide. This may be explained by the fact that the di-*t*-butyl-nitrophenoxide ion, being a resonance hybrid (II) has the negative charge delocalized in the nitro group which is solvated. This anion, II, formed from the phenol by either triethylamine or sodium hydroxide, has the typical yellow color of a quinoid system. 2,6-Di-*t*-butyl-4-nitrophenol has been reported to be slightly more acidic than *p*-nitrophenol.[3]

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(1) (a) National Institutes of Health Predoctoral Fellow, 1966–1967; (b) National Science Foundation Summer Research Participant.

(2) J. S. Meek and C. Bouboulis, *J. Org. Chem.*, **26**, 1302 (1960).

(3) W. R. Vaughn and G. K. Finch, *ibid.*, **21**, 1201 (1956).