Table III. Isomerization of I in Soft Glass at 278°

Time, hr	% volatile components I	X	IV	III	$C_{12}H_{26}$ (internal std)	V + VI[a]
0.0	96.7	0.0	0.0	0.0	3.3	0.0
0.25	83.8	2.5	1.7	7.7	3.6	0.6
0.50	79.2	5.3	3.5	8.1	3.2	0.7
1.0	76.7	6.9	4.7	8.0	3.0	0.6
2.0	61.6	14.7	10.4	9.8	3.0	0.5
3.0	59.7	15.2	11.5	10.3	3.1	0.5
4.0	54.7	16.1	15.1	10.4	3.1	0.4
6.0	40.3	19.4	22.4	14.0	3.5	0.4
12.0	19.9	6.8	37.5	32.0	3.6	0.2
24.0	1.4	3.0	45.0	45.1	5.4	0.1

[a] Identified by retention times only.

soft glass). Sodium hydroxide coated tubes were prepared by filling soft glass tubes with a 1% solution of base up to the constriction, withdrawing the excess solution with a syringe, and baking the wet tubes at 150° for 48 hr.

Isomerizations in the temperature range 140–200° were carried out on samples ranging in size from 30 to 50 μl. The isomerizations at 278° were conducted in soft glass tubes of about 1 ml volume and the sample size was reduced to 5–7 μl. Temperature control in the lower range was provided by a silicon oil bath equipped with an immersion heater and a temperature controller which maintained a desired temperature within ±0.1°. The higher temperature isomerizations were carried out in the air furnace of an Aerograph 90-P gas chromatograph equipped with a temperature controller.

Table IV. Isomerization of V in Soft Glass at 140 and 278°

Time, hr	% composition V	I	X	IV	III	VI	% material balance
			T = 140°				
0.0	100	0	0	0	0	0	100
1.0	87	0	8.3[a]	3.5[a]	1.2	0	98
17.6	49.7	0.7[a]	10.7[a]	5.4[a]	34.1	0	80
			T = 278°				
1.0	5.1	17.1	57.3	15.1	4.0	1.1[a]	b
7.5	Trace	Trace	2.5	61.0	36.5	0	b

[a] Identified by retention times only. [b] Not determined.

Analyses of isomerization mixtures were performed on column D at 150°; integrations were made with either a Perkin-Elmer D-2 integrator or a Nester/Faust summatic integrator. The analytical method was tested with synthetic mixtures of the reaction components and showed a much higher reproducibility than that observed in the isomerization experiments themselves. Representative data showing the isomerization results are reproduced in Tables II, III, and IV.

Acknowledgments. This investigation was supported in part by Grant No. 3140-A4 from the Petroleum Research Fund, administered by the American Chemical Society. Fellowship support and instrumentation facilities provided by the Laramie Petroleum Research Center of the U. S. Bureau of Mines are also gratefully acknowledged.

The Claisen Rearrangement of 2-Methyl-2-vinyl-5-methylenetetrahydrofuran[1]

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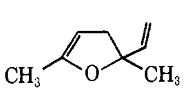
Abstract: 2-Methyl-2-vinyl-5-(bromomethyl)tetrahydrofuran, prepared by brominative cyclization of 3-methylhepta-1,6-dien-3-ol with *N*-bromosuccinimide, undergoes base-catalyzed dehydrohalogenation to form 2-methyl-2-vinyl-5-methylenetetrahydrofuran (III). The Claisen rearrangement of III to 4-methyl-4-cycloheptenone (II), studied over the temperature range 155–185°, is a first-order process with $k_{170°} = 4.13 \times 10^{-5}\ \text{sec}^{-1}$, $\Delta H^{\ddagger} = 32.7$ kcal/mol, and $\Delta S^{\ddagger} = -5.6$ eu. In the absence of basic inhibitors, III rapidly interconverts with 2,5-dimethyl-2-vinyl-2,3-dihydrofuran (I) to give an equilibrium mixture consisting of 6.6% III and 93.4% I at ambient temperatures.

In the preceding paper,[2] the responsible intermediate species in the rearrangement of 2,5-dimethyl-2-vinyl-2,3-dihydrofuran (I) to 4-methyl-4-cycloheptenone (II) was identified as 2-methyl-2-vinyl-5-methylenetetrahydrofuran (III). With this finding, the synthesis and direct study of III became a major objective. In this paper, we report the successful synthesis of the tetrahydrofuran derivative and a kinetic study of its thermal rearrangement to II.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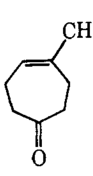
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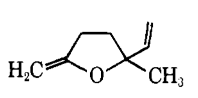
III

Results

After several unsuccessful synthetic approaches, III was prepared in an amazingly simple series of reactions (Scheme I). This method was brought to our attention by recent work of Demole and Enggist[3] who applied

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[1] The support of this investigation under a grant from the Petroleum Research Fund (3140-A4) administered by the American Chemical Society is gratefully acknowledged.

[2] S. J. Rhoads and C. F. Brandenburg, *J. Amer. Chem. Soc.*, 93, 5805 (1971).

[3] E. Demole and P. Enggist, *Chem. Commun.*, 264 (1969).

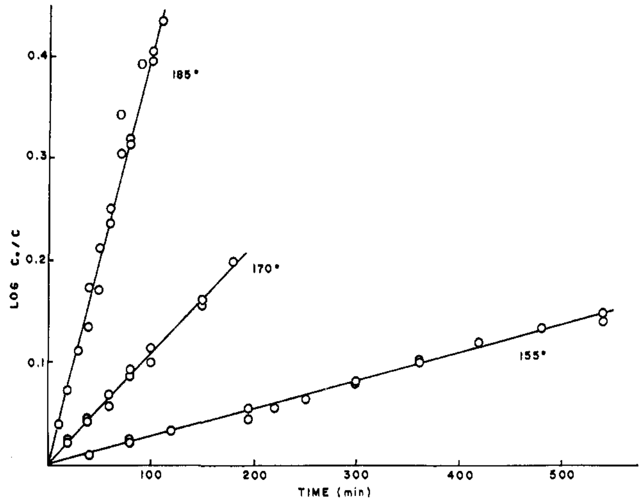
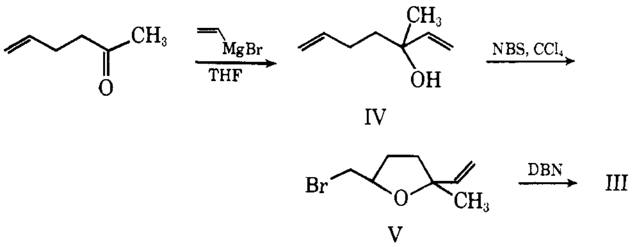


Figure 1. First-order plots for the rearrangement of III at three temperatures.

the reaction sequence (including the Claisen rearrangement of analogs of III) to the synthesis of cycloheptenones from terpene alcohols of the linalool type. In the present synthesis, allylacetone has been converted in good yield to the dienic alcohol IV with vinylmagnesium bromide. Bromination and cyclization of IV to yield the (bromomethyl)tetrahydrofuran derivative, V, occurs smoothly when IV is heated with *N*-bromosuccinimide in carbon tetrachloride.[4] Dehydrohalogenation of the bromomethyl derivative may be accomplished by a variety of bases, but we have found 1,5-diazobicyclo[4.3.0]non-5-ene (DBN) to be superior for the preparation of the extremely sensitive III. Isolation of III in pure form may be achieved by sweeping it out of the reaction mixture as it forms with a stream of inert gas and collecting it in a cold trap containing solid potassium hydroxide. Without these precautions, isomerization to I is extensive.

Scheme I



The spectral properties of III, detailed in the Experimental Section, fully substantiate its structure as the exo methylene isomer. In particular, the vinyl proton signals in the nmr spectrum correspond exactly to those deduced in the earlier work.[2] Chemically, III is a typical enol ether; it is extremely sensitive to traces of acid, undergoing equilibration with the more stable endocyclic isomer I on simple standing at room temperature in ordinary glassware. III also is quite sensitive to traces of water; in samples which are not suitably protected from atmospheric moisture, hydrolysis is soon evident by the appearance of alcoholic and carbonyl absorptions in the infared spectra.

When III is dissolved in spectral grade deuteriochloroform, it slowly interconverts with I—a process which conveniently can be followed by nmr spectroscopy. An equilibrium composition of 6.6% III and 93.4% I was measured in this way, in excellent agreement with the value derived in the rearrangement studies reported in the preceding paper.[2]

Kinetic studies of the rearrangement of III to II were carried out in base-coated soft glass reaction tubes[2] over the temperature range 155–185°. Under these conditions, III smoothly isomerizes to II in a first-order process with less than 2% diversion to I. Rate constants and activation quantities are summarized in Table I. First-order plots of the rearrangement at the three temperatures are shown in Figure 1.

Table I. Kinetic Data for the Rearrangement of 2-Methyl-2-vinyl-5-methylenetetrahydrofuran (III) to 4-Methyl-4-cycloheptenone (II)

T, °C	$k \times 10^5$ sec^{-1} [a]	E_a, kcal/mol[b]	$\Delta H^{\ddagger}$, kcal/mol[b]	$\Delta S^{\ddagger}$, eu[b]
155	1.06 ± 0.02			
170	4.13 ± 0.07	33.6 ± 0.6	32.7 ± 0.6	-5.6 ± 1.2
185	15.9 ± 0.4			

[a] Uncertainties are probable errors. [b] Uncertainties are statistical errors assessed by the method of E. L. Purlee, R. W. Taft, and C. A. Defazio, *J. Amer. Chem. Soc.*, **77**, 837 (1955).

Discussion

The rearrangement of III to II displays the characteristics of a one-step concerted process, *i.e.*, a relatively low activation energy of 33.6 kcal/mol and a negative entropy of activation, and thus conforms, energetically as well as structurally, to the general class of [3,3] sigmatropic transformations which includes the Claisen rearrangement.[5] It is of interest to compare the activation quantities for the rearrangement of III with those found for unconstrained vinyl allyl ethers in open-chain systems. The parent compound, vinyl allyl ether itself, rearranges with an activation energy of 30.6 kcal/mol and an entropy of activation of −7.7 eu,[6] whereas isopropenyl allyl ether, bearing a methyl substituent on the α carbon of the vinyl group, isomerizes with the same entropy of activation and an only slightly smaller activation energy of 29.3 kcal/mol.[7] Alkyl substitution on the α position of the allylic group of the ether has a more marked effect on lowering the activation energy for the isomerization; a value of 27.9 kcal/mol has been reported for vinyl α-methyallyl ether.[8] The vinyl allyl ether system in III, formally, is α,α,α'-trialkylated, but the bridging of the second and fourth atoms of the six-atom system by an ethyl-

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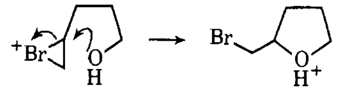
[4] This facile bromination and cyclization of γ,δ-unsaturated alcohols apparently was first observed by J. Levisalles and H. Rudler [*Bull. Soc. Chim. Fr.*, 2059 (1967)] and investigated in some detail by O. Tanaka and coworkers [*Tetrahedron Lett.*, 4235 (1968)] who encountered the reaction in dammarane-type triterpenes. The reaction does not appear to involve normal allylic bromination and may most simply be viewed as an ionic addition of bromine to the double bond followed by participation of the hydroxy function, *i.e.*



[5] G. B. Gill, *Quart. Rev., Chem. Soc.*, **22**, 338 (1968).

[6] F. W. Schuler and G. W. Murphy, *J. Amer. Chem. Soc.*, **72**, 3155 (1950).

[7] L. Stein and G. W. Murphy, *ibid.*, **74**, 1041 (1952).

[8] H. M. Frey and D. C. Montague, *Trans. Faraday Soc.*, **64**, 2369 (1968).

ene group undoubtedly provides a significant counterbalance to the activating effects of the alkyl substituents. The somewhat higher activation energy observed for III in comparison with the open-chair ethers seems compatible with the requirements imposed by the restraining ethylene bridge. Inspection of Petersen molecular models of III suggests that the vinyl allyl ether system can adopt the preferred "four-centered" arrangement for the transition state[5,9] with the expenditure of only a moderate amount of extra energy in the form of ring puckering (Figure 2).

The general synthetic utility of the reaction sequence of Scheme I bears reemphasis. As Demole and Enggist have pointed out,[3] the facile brominative cyclization of γ,δ-unsaturated alcohols to product (bromomethyl)-tetrahydrofurans coupled with a potential Clasien rearrangement in the dehydrohalogenation product opens the way to the synthesis of a variety of seven-membered ring derivatives.

Experimental Section

Infrared spectra were recorded as thin films on potassium bromide plates with a Perkin-Elmer Model 621 spectrophotometer. A Varian Mat CH-5 mass spectrometer was employed to obtain the mass spectra. Nmr spectra were run with a Varian HA-100 instrument; chemical shifts are reported in δ values relative to a TMS internal standard. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Glpc analyses were carried out in an Aerograph A-90P instrument with a variety of column materials detailed under individual experiments. Preparative glpc separations were accomplished with a Nester/Faust Model 850 Prepkromatic instrument.

3-Methylhepta-1,6-dien-3-ol (IV). To a stirring tetrahydrofuran solution of vinylmagnesium bromide[10] (500 ml of 1.2 *N* solution) was added dropwise 50.0 g (0.51 mol) of freshly distilled allylacetone (Aldrich) over a period of 20 min. The reaction mixture was heated under reflux for 2 hr, stirred at room temperature for an additional 60 hr, and finally hydrolyzed with 4 *N* sulfuric acid. Worked up in the usual way, the reaction afforded 41.7 g (65%) of IV: bp 53–57° (20 mm); purity by glpc 99%; ir 3410 (s) 3080, 1640, 990, 910 cm^{-1}; nmr (CCl_4) δ 5.95–5.5 (2, overlapping m's, $H{-}C{=}CH_2$), 5.25–4.7 (4, overlapping m's, $-\overset{|}{C}{=}CH_2$), 3.21 (1, br s, OH), 2.2–1.9 and 1.6–1.4 (4, m's, $-CH_2CH_2-$), 1.18 ppm (3, s, CH_3).

2-Methyl-2-vinyl-5-(bromomethyl)tetrahydrofuran (V). A solution of 23.1 g (0.18 mol) of IV and 35.6 g (0.20 mol) of *N*-bromosuccinimide in 100 ml of carbon tetrachloride was heated to reflux. After an induction period of about 1 hr, the reaction became quite vigorous and required external cooling. After the vigorous reaction had subsided, heating was continued for a total of 3 hr. The reaction mixture was filtered, concentrated, and rapidly distilled at reduced pressure from a polymeric residue. Redistillation gave 13.8 g (48%) of product, bp 75–78° (10 mm). Glpc analysis (10 ft × $^1/_4$ in. 15% diisodecyl phthalate on Gas-Chrom P, 150°) of the distillate showed it to consist of two components (geometric isomers) in a ratio of 1:1.7. Separated by preparative glpc (30 ft × $^3/_8$ in. 15% Reoplex 400 on Gas-Chrom P at 140°), the two components, A and B, revealed their isomeric nature by their almost identical spectral properties. Component A showed the following properties: nmr (CCl_4) δ 5.70, 5.10, and 4.90 (3, three d's of d's, ABX pattern with J_t = 18, J_c = 10, and J_{gem} = 2 Hz, vinyl group), 4.10 (1, m, H-5), 3.2 (2, m, $-CH_2Br$), 2.1–1.6 (4, complex envelope, $-CH_2CH_2-$), 1.22 ppm (3, s, CH_3). The proton signals of component B showed corresponding patterns and areas with δ values of 5.82, 5.10, 4.80, 4.12, 3.2, 2.2–1.6, and 1.17 ppm. The ir spectrum of the mixture of isomers showed characteristic absorptions at 3080, 1640, 1210, 1100, 1060, 990, and 915 cm^{-1}.

2-Methyl-2-vinyl-5-methylenetetrahydrofuran (III). Equivalent amounts of V (0.06 mol) and freshly distilled 1,5-diazobicyclo-[4.3.0]non-5-ene (DBN) were combined in a pear-shaped flask equipped with a capillary helium bubbler, a 6-in. distillation column, and a distillation head. The latter was fitted with a receiver containing several pellets of potassium hydroxide. The receiver was cooled to −75°, the system was evacuated to 10 mm, and the reaction vessel was held at a bath temperature of 70–90° for 2 hr. During this time, 2.3 g (31%) of product collected in the chilled receiver. Glpc analysis (3 ft × $^3/_8$ in. 10% Carbowax 400 on Gas-Chrom P, ambient temperature) of the distillate showed it to be a single substance: ir 3120, 3095, 1670 (s), 1590, 1270, 1235, 1195, 1165, 1120, 1090, 985–980 (s), 920, 790 (s) cm^{-1}; mass spectrum (7 eV) *m/e* 124 (M^+); nmr (neat) δ 5.76, 5.15, 4.92 (3, three d's of d's, ABX pattern, J_t = 17.5, J_c 10.3, J_{gem} = 2.0 Hz, vinyl side chain), 4.06 and 3.62 (1 H each, m's, exocyclic methylene group), 2.46 (2, complex m, allylic $-CH_2-$), 1.76 (2, complex m, $-CH_2-$), 1.25 (3, s, CH_3).

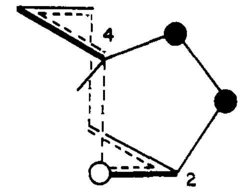


Figure 2. Four-centered transition state for the rearrangement of III.

Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.71; H, 10.18.

Samples of III are best stored over solid potassium hydroxide at low temperatures.

Equilibration of III and I. A sample of pure III was placed in an nmr tube, diluted with spectral grade deuteriochloroform (*ca.* 10% solution), and monitored at ambient temperature by following the intensity changes in the signals of the exocyclic methylene protons in III (δ 3.67 and 4.12 ppm) and the vinyl ring proton in I (δ 4.30 ppm). The presence of I was detectable within a few minutes after the addition of the solvent; after 3 hr the amounts of I and III were approximately equal. At the end of 9 days, the composition of the equilibrated mixture was 93.4% I and 6.6% III.

Rate Studies. Sample tubes of *ca.* 1 ml volume were fashioned with constricted necks and carefully rounded bottoms from 5 mm o.d. soft glass tubing. The tubes were carefully annealed and coated with potassium hydroxide in the manner described earlier[3] except that the final drying was carried out under vacuum at 140° in a drying pistol. Samples of III (1.5 μl) were vapor transferred to the sample tubes and thoroughly degassed before sealing. The rearrangements were carried out in a stirred silicon oil bath regulated to ±0.2° of the desired temperature.

The progress of the rearrangement was followed by glpc analysis with the following conditions: 3 ft × $^1/_8$ in. column of 10% Carbowax 400 on Gas-Chrom P, column and injector port at 30°, helium flow 100 ml/min. Independent experiments with pure samples and synthetic mixtures established that I and III were not interconverted under these analysis conditions and that they eluted with retention times of 5 and 12 min, respectively. The rearrangement product, II, was not eluted under these conditions, but manual programming of the column temperature to 85° immediately following the elution of III effected the elution of II within a reasonable length of time. Since the detector response was not linear for all the components, the analytical method was standardized with synthetic mixtures of I, II, and III. Integrations of the glpc traces were performed by the "cut-and-weigh" method. The material balance in the rearrangement was tested under experimental conditions against an internal octane standard and proved excellent ($\geq$91%). The rearrangements were followed through 35–65% completion and were run in duplicate. Although, generally, the use of the base-coated tubes successfully inhibited the isomerization of III to I so that the amount of material diverted in this manner was negligible (less than 2%), occasional samples showed appreciably larger amounts of I in the rearrangement mixture. Such results were discarded. Rate constants were evaluated by a least-squares treatment of the data and probable errors were assessed in the usual way.[11] Activation quantities were evaluated by the standard procedure.[12]

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[9] A. Jefferson and F. Scheinmann, *Quart. Rev., Chem. Soc.*, **22**, 391 (1968).

[10] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 213.

[11] L. P. Hammett, "Introduction to the Study of Physical Chemistry," McGraw-Hill, New York, N. Y., 1952, p 410.

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